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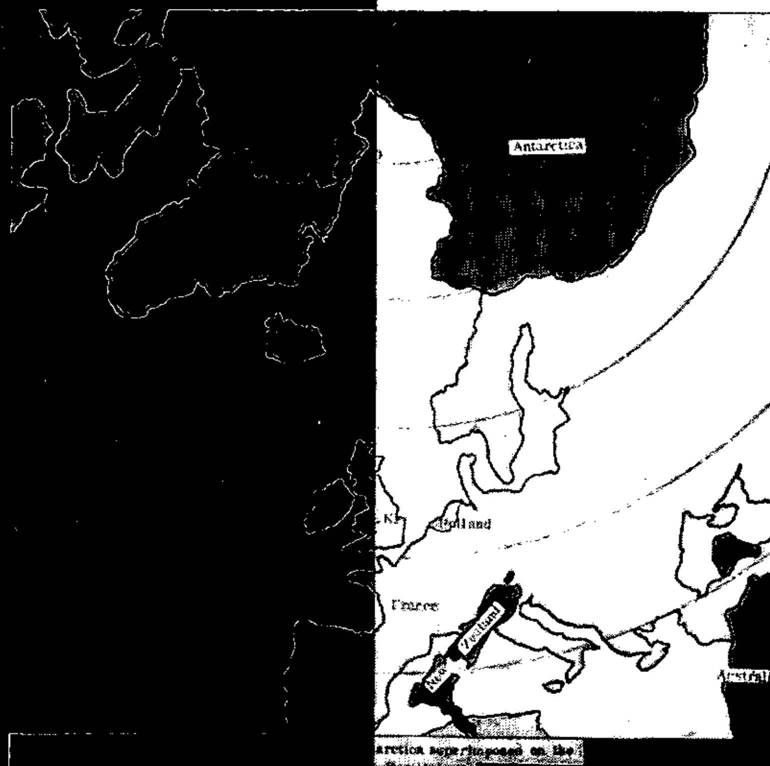

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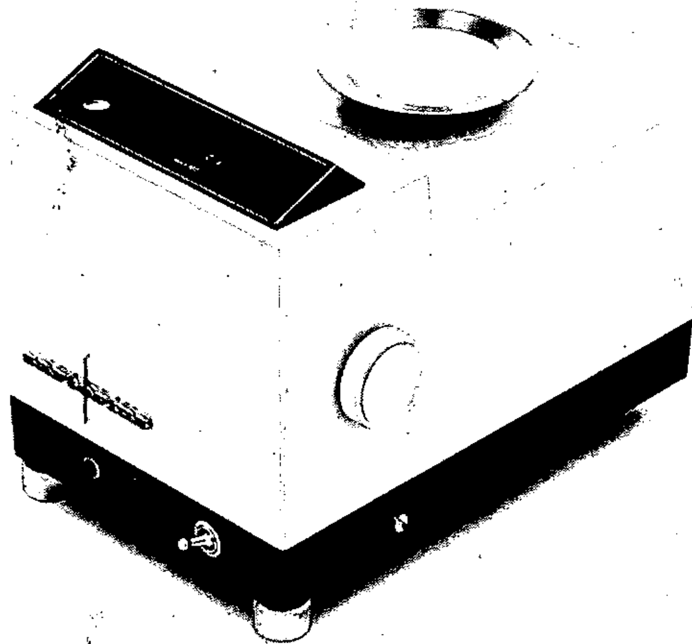

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EDITORIAL

The use of animals for estimation of biological molecules is now historical, the methods are classical and in some cases have become a habit. This may have been justified while physiology was still in its infancy, biochemistry still a foetus and modern analytical chemistry just getting onto its feet. Now biochemistry is grown up and physiology leans heavily on it like a man past his prime leans on his vigorous young offspring. Biochemistry now uses the sophisticated physico-chemical tools of analytical chemistry; many 'pure' chemists use their elaborate equipment to elucidate the structure of complex inorganic and organic molecules. If only a few of these 'pure' chemists could bring their highfalutin' machinery and specialised intellects to bear on some of the problems of the physiological chemists!

Sadistic scientists are few, despite science fiction (or so we would like to believe), and probably most of us who are forced by circumstance to estimate biological molecules using living animals question at times our own morality, indeed our humanity. How valid really is it to say that in order to measure one person's pituitary hormone output it is justifiable to sacrifice six mice? Is it valid to acquire knowledge to relieve human suffering by making animals suffer? Is not our attitude to animals in the same category as the attitudes of our predecessors to slaves or to the poor—there for us better creatures to use for our own ends?

And what of the effect on those humans who do think it valid? Does it help to make them appear less human in the eyes of others? The animals are bred for this use they say. Does this make it any better? Does it excuse the use, or the breeding?

In the U.S.A. big business has moved into the field of producing animals already prepared for biological estimations. You can buy them (according to the advertisements) sans anything you like—sans pituitary, adrenals, etc., etc. The accompanying picture is of frisky healthy animals, eager to join your work! How can any animal without its controlling mechanisms for salt balance, hormones and feedback control be feeling frisky? We know how a human feels in such a state of chemical imbalance—very sick. Because we don't know how the animal feels, we find it easy to believe that they don't feel at all. If the money fed into big business production of such animals were instead fed into chemical research directed to isolation, purification and development of methods of analysis for such biological molecules, we would soon not need to use animals. A disturbing moral dilemma would be resolved. And if even one chemist on reading Dr. Whittlestone's article has the urge to apply his techniques to even one of the molecules and succeeds, he will earn the grateful thanks of a number of physiological chemists.

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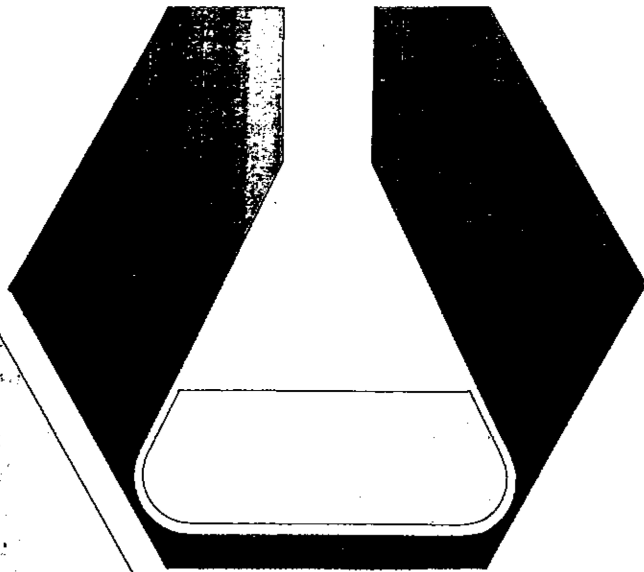

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THE ASSAY OF THE POSTERIOR PITUITARY HORMONES

W. G. Whittlestone, D.Sc., F.N.Z.I.C.
Ruakura Agricultural Research Centre, Hamilton

Introduction

The hormones of the posterior pituitary are of great interest to the physiologist. They are ancient phylogenetically in that their "ancestors" are to be found even in the most primitive fishes. They are all octapeptides of extreme physiological activity. All vertebrates examined so far have been found to have two peptides of this type with the exception of the cyclostome fishes which are probably direct descendants of an archaic ancestor. These animals have only one peptide, vasotocin. It is possible that this is the parent moleclue from which, by mutation involving an amino acid at a time, all of the other pituitary peptides have evolved. Seven such peptides have been isolated so far, but only three are of interest to us in our study of the mammal. The parent molecule, vasotocin, has a five-amino acid ring consisting of cystine, tyrosine, isoleucine, glutamic acid and asparagine. The ring is closed by the disulphide linkage of the cystine, and a side chain branches at this point. This consists of proline, arginine, and glycine. The three hormones in which we are interested are oxytocin, arginine-vasopressin and lysine-vasopressin. Oxytocin has the same ring structure as vasotocin but the arginine is replaced by leucine. Arginine vasopressin differs from vasotocin in the ring structure, the isoleucine being replaced by phenylalanine; the side chain is identical with that in vasotocin. Lysine vasopressin has the side chain arginine of arginine-vasopressin replaced by lysine.*

Whole pituitary extracts under the name Pituitrin were used long before the physiology of these hormones was understood, because of the pharmacological properties of this preparation. Thus assays were developed which did not necessarily bear a relation to the physiological role of the hormone concerned. Vasopressin was so named because of its effect on blood pressure, though it seems unlikely that this is its rôle in the organism. However, assays based on blood pressure changes are still used. The primary role of vasopressin, or antidiuretic hormone (ADH) as it is also called, would appear to be in regulating the osmotic pressure of the blood, the regulation taking place at the loop of Henle in the kidney. Oxytocin is so named because of its effect on the uterus and this would appear to be a true physiological role. It also ejects milk and is sometimes called the milk ejecting hormone. In this case the assays using strips of uterine muscle were based on the physiological role of the hormone concerned.

In this review of the assay of the posterior pituitary hormones I thought it most convenient first to examine the history of oxytocin assays, then the more complex history of assays for vasopressin. However, because of the special role of the rat in the assay of antidiuretic and vasopressor substances, in the third section of the review I discuss the use of this animal. Finally I wish to examine the methods which have been developed at Ruakura.

Oxytocin Assay

The earliest assay of oxytocin using the guinea pig uterus was described in 1913 by Dale and Laidlaw. They used a strip of guinea pig uterine muscle in an organ bath at 37°c. Ringer-Locke solution was used and

Based on a paper presented at the Symposium on Quantitative Biology, University of Waikato, Hamilton. 1969.

* See The Vertebrate Pituitary Neuro-hormones, Chemistry in New Zealand. Vol. 33, No. 3, p. 69.

the strip attached to an isotonic lever. This was a relatively successful method which was followed by the chicken blood pressure method developed by Coon (1939). Oxytocin has the effect of producing a transient fall in blood pressure in the chicken. Using an adult cockerel between 1.1 and 2.3 kg in weight the arterial pressure of the popliteal artery was measured while the standard and unknown solutions were injected into either the crural or the brachial vein in a volume between 0.14 and 0.4 ml. Depending on the preparation, regular intervals between 3 and 10 minutes were observed between injections. This is still an official method (BP 1968). In 1948 Holton, and in 1949 Gaddum *et al* introduced the use of the rat uterus. This involved further modification in using only a quarter the concentration of calcium in the Ringer solution and a bath temperature of 33°c to reduce spontaneous contractions. The threshhold of sensitivity of this method was about 0.01 international units (i.u.) per ml. An interesting *in vivo* method was introduced by Fuchs & Fuchs in 1960. These workers used estrogen-treated virginal rabbits in which a portion of the uterine horn was exposed and clamped off in such a way that tension changes in it could be measured by means of a thread passing round the tissue and connecting to an isometric lever. The threshold for this assay was between 0.005 and 0.05 i.u. A further step in sensitivity was developed by Siddiqi and Walker in 1960. In this case a superfused rat uterus soaked in dibenamine was used as the measuring tissue. The Ringer solution was allowed to "superfuse" over the surface of the tissue in the organ bath. This assay had a workable range between 0.16 and 0.32 m.u.* per ml. of blood. The superfusion technique was carried a step further by Wiqvist *et al* in 1962 when they used a superfused rat uterus with the pacemaker area exercised. A Krebs solution with only one-fifth of its normal calcium content was used as the superfusion liquid, and electrical stimulation was applied to the strip in the form of 15 second pulses at 50 Hz up to 6 volts. Electrical stimulation decreased the threshold at which the uterine strip responded to oxytocin. This assay was quantitative in the range 5 to 20 microunits per ml. Knifton in 1967 introduced the pig myometrium as an assay tissue. He examined both changes in isometric tension and in isotonic shortening under the influence of oxytocin, and found that isotonic shortening exaggerated the response of the tissue to oxytocin. The two official methods for the assay of oxytocin in the British Pharmacopaea 1968 are: The depression of blood pressure (Coon 1939) and the rat uterine method (Holton 1948, Gaddum *et al* 1949).

The measurement of milk ejection as a means of assaying oxytocin has almost as venerable a history as the use of a uterine strip. Gaines (1915) developed a qualitative method of estimating the activity of pituitrin by observing its effect on the cut surface of a piece of lactating guinea-pig gland under the binocular magnifier. He also measured the intramammary pressure effect of pituitary extract after injection. However, he did not attempt to make these reactions quantitative. The first effective aplication of milk ejection for the assay of oxytocin was described by Turner and Cooper in 1941. This was based on the observation of the mammary area of a rabbit which had been trained for use in the assay. Fur was clipped away from around the mammary glands and intravenous injections given of the substance to be measured. The dose required to produce a just visible dilation of the duct system was discovered and compared with a known solution. This is a tedious assay which tends to be somewhat subjective. The lactating sow was introduced as an assay animal in 1951 at Ruakura, two criteria being used initially, namely milk volume and duration of flow from one or more glands following the intravenous injection of the unknown solution which was compared with a standard. Relatively low levels of hormone were used so that several assays could be carried out on any one gland. Later the method was based on changes in intramammary pressure. Van Dyke *et al* (1955)

* micro-units.

developed an assay based on intramammary pressure changes in the rabbit. This proved to be very satisfactory. The use of the change in weight of a suckled litter of rats was described by Grosvenor and Turner in 1957 as a means of assaying oxytocin. This is a somewhat cumbersome technique.

An interesting change in the trends in oxytocin assay occurred in 1961 when Smith applied strips of rat mammary tissue set up in the standard organ bath in Ringer solution at 37°c. The tension changes under isometric conditions were measured and recorded and found to provide an adequate basis for an assay. Shortly after this development Tindal and Yokoyama (1962) introduced the use of intramammary pressure changes in the guinea pig as the basis for an assay. Under good conditions this assay is both sensitive and quantitative; the range for intra-arterial injections was 16 to 60 micro-units and occasionally the threshold could be as low as 1 micro-unit. Recent assay work at Ruakura has been based on this preparation with some modifications. Another sensitive assay was developed in the same year by Ryden and Sjöholm (1962). This was based on strips of rat mammary tissue in an organ bath at 38°c using oxygenated Tyrode solution and coupled to an isometric lever. The sensitivity of this assay was shown to be 2 micro-units of oxytocin. The dose response was linear and the index of precision given as 0.109. This assay seems to have gained fair acceptance among reesarch workers interested in milk ejection. Van Dongen and Hays (1966) reverted to the original method of Gaines but using rat mammary tissue cut up into small cubes. These cubes were stored in Tyrode solution at 15°c and the assay carried out by placing a cube in a small vessel containing the unknown solution and observing it under a 15 x dissecting microscope. The time for the appearance of milk on the surface of the cube was measured. The log time-dose response of this assay was linear and the threshold given at 1×10^{-12} i.u. with a range starting at 1×10^{-10}. This is the most sensitive assay described in the literature. A number of workers have attempted to use it but so far difficulty has been found in repeating the original Van Dongen results. An attempt was made at Ruakura to apply this assay without success, and several laboratories which I visited in Europe last year had had the same negative results.

Vasopressin Assay

The first pharmacological property of whole pituitary extract which excited attention was its vasopressor activity. The earliest assays were therefore based on this, although there is reason to doubt the vasopressor role of vasopressin in the normal animal. Hamilton in 1912 described an assay of pituitrin using dog arterial blood pressure as the parameter. The spinal cat as a preparation was used by Hogben *et al* (1924); carotid blood pressure was measured and the preparation injected intravenously at intervals of 30 minutes. This was rather a slow assay due to the time taken for the preparation to recover from an active dose. Water-loaded mice were introduced as an assay animal by Gibb in 1930. The urine output of mice sitting in glass funnels was measured after the subcutaneous injection of the solutions to be assayed. Nelson & Woods (1934) extended Gibb's method using intraperitoneal water loading to 5 percent of the body weight. Urine output was measured for three hours after each injection. The assay operated at a dose level of the order of 20 m.u.

Dogs were re-introduced into the assay of vasopressin by Samaan (1935) who used trained animals which were water-loaded with 20-25 ml. of warm water by stomach tube, this operation being repeated to give constant diuresis. Urine was collected at five-minute intervals by gentle pressure. Change in urine secretion following intravenous injection of the preparation was the basis of the assay. A more sophisticated version of the dog assay was described by Melville (1937) who used bladder fistulae, hydration being carried out by means of a stomach tube. The dogs were trained to lie prone on a table so

that the urine flow through the fistula could be recorded continuously. Intravenous injection of the preparation was used.

The rabbit made its debut as a vasopressin assay subject in 1939 when Walker published a description of an assay based on rabbits kept on a standard diet and hydrated by means of a stomach tube. 100 ml of water containing paraldehyde at tranquiliser dose levels was used and urine collected by means of a catheter. A steady rate of diuresis was maintained by running in appropriate volumes of the paraldehyde solution. The method proved to be rather variable. Perhaps the most entertaining assay for vasopressin in the record so far is that of Boyd & Mack (1940). This was based on changing water losses through the skin of a frog under the influence of vasopressor substances. In a typical assay 50 frogs were each placed in a 400 ml beaker containing about 150 ml of water. The frogs were kept at 4°c for 12 hr prior to the assay. They were then lifted from the beaker, the skin dried, the bladder emptied by expression and the animal weighed. An injection of the extract to be assayed was then made into the dorsal lymph sac and 18 hr later the frog dried and weighed again. This has not become a popular assay.

The elimination of endogenous vasopressin was effected by hypophysectomy in dogs used as assay subjects by O'Connor & Verney (1942). Hydration was carried out by the use of a stomach tube and the bladders were catheterised. An initial hydration of 300 ml of water was used and the urine flow measured continuously. The subjects to be assayed were injected intravenously. Stalk section as an alternative to hypophysectomy was used by Hare *et al* (1945); again the dog was used as the experimental animal. Twenty-four hours before the assay, food was removed and 3 hr before, water was removed. Urine output was measured via catheters placed in the bladder and the animals kept on padded boards without restraint. The assay was based on the creatinine clearance determined from the difference between blood and urine creatinine levels. Two clearance periods were run each hour, 20 min. for the control and 40 min. for the assay injection which was intravenous. The range of the assay was 0.3-3.0 m.u.

A water-loaded rabbit assay was described by Fugo & Aragon (1947). These workers water-loaded the rabbit to 5 percent of its body weight 3 hr before the commencement of the assay. An important development was that of the intravenous water-loading of the animal after the initial load had been introduced. This was done with a saline drip at 60-70 drops per minute. Diuresis was started by the injection of 20-40 ml of 20 percent glucose and the effect of the substance assayed on the urine flow measured. The sensitivity of the method was given as 0.1 m.u. The normal trained dog was used by O'Connor (1950) as an assay animal, the bladder being cannulated and prior to the assay the animal dosed with 200 ml of 0.9 percent saline and deprived of water. Three hours after this treatment a catheter was inserted and urine flow measured. Standard and unknown injections were given intravenously. The dose range for this assay was 0.1-0.6 m.u.

Heller & Blackmore (1952) used mice, a polythene cannula being used to water load to 5 percent of the body weight. On the day before the experiment the mice were trained to accept the stomach pump and food was removed the night before. Throughout the assay, water loading was carried out at hourly intervals and the solutions measured injected intravenously. Urine volume was measured every 10 minutes. The sensitivity of this assay was 12.5 m.u. per 10 g of body weight. The main objection to it is the fact that the amount of material which can be injected is very small. Ginsburg & Heller (1953) reintroduced the rabbit vasopressin assay. They used adult females which were deprived of food for 18 hr and then given a 5 percent water loading orally—two doses 1 hr apart. Injections were given via the ear vein starting with normal saline. The urine output was measured after manual compression. This

method had a sensitivity of 32.5-125 micro-units per kg of body weight.

Vasopressin Assay Using Rats

Because we ended up using the rat ourselves as an assay animal for vasopressin, I thought it would be interesting to trace the history of the application of this animal by itself. The very multiplicity of the methods which have been described indicates that at least as far as other animals are concerned, no satisfactory assay has been developed. It would appear that the rat has so far become the most satisfactory animal on which to base the assay of antidiuretic substances.

The first pituitary assay based on the rat was described by Burn (1931). He used male and female animals 140-240 g in weight, but found that the males gave more reliable results, particularly if deprived of food, though given access to water, some time before the experiment. The animal is water-loaded to 5 percent of the body weight by means of a stomach tube and placed in a metabolism cage so that urine output can be measured. Doses of the order of 6 m.u. per 100 g of body weight were found suitable and these were given intravenously. The time of water-loading and injection and the interval to the point of maximum urine excretion were recorded. In a typical assay 16 rats were used in four groups of four. Two groups were given standard injections, and two groups the unknown solution. The next day the procedure was repeated with the treatments reversed. Gilman & Goodman (1937) improved the Burn assay by giving a preliminary dose of water to the rats three or four hours before the commencement of the test. Landgrebe *et al* (1946) used rat blood pressure changes as an assay.

Another modification of the Burn method suggested by Teel & Reid (1949) involved the use of two water loads of 5 and 3 percent respectively, 1 hour apart before the injection of solutions, 20 minutes after the second water load. A further modification of the original Burn assay was described by Ham & Landis (1942) who grouped their rats in threes, such that the total weight within the group did not differ by more than 10 percent. Six groups were used, two as controls and four for duplicate assays of two unknown solutions. A priming dose of 0.2 percent sodium chloride at 2.5 percent of the body weight was given by stomach tube. Two hours after this the bladder was emptied and each rat given a hydrating dose of 0.2 percent sodium chloride equivalent to 5 percent of the body weight. The solution to be assayed was injected peritoneally in a volume totalling 1 ml per 100 g of body weight. The control groups were given a similar injection of 0.9 percent sodium chloride. The volume of urine excreted was recorded at 15 minute intervals for 3 hours. The rats were used for not more than three assays at intervals of 10 days or more. The method was claimed to be accurate within the range of 0.5-m.u. of vasopressin.

Another version of the Burn assay was that of Birnie *et al* (1950). In this case the rats were water-loaded at a rate of 3 ml per 100 sq. cm of body surface. Two doses of water were administered 1 hour apart, the animals being kept in metabolism cages. One hour after administration of the second water dose the urine output was measured and rats which deviated by more than 50 percent from the mean of the group of six were rejected. The test material was injected intraperitoneally and a third water load given. Urine output was then measured at 30 minute intervals for a period of 3 hours. The results were expressed as the percentage of urine excreted in any one period based on the total water given minus the percentage excreted prior to injection of the test material. The definitive figure was the percentage of water excreted at 90 minutes after injecting the test material. Ginsburg (1951) improved the precision of the rat assay method by using 18 adult male rats of 200 g weight. These were water-loaded before the test as a training method to eliminate nervousness. The animals were deprived of food for 18 hours before the experiment and water removed

1 hour before. The rats were then placed in individual metabolism cages and urine collected. Each animal was given two doses of tepid water at a rate of 5 percent of the body weight at 1 hour intervals. A similar dose of water was then given, the rats injected subcutaneously with test material, and the urine output thereafter measured at intervals of 30 minutes for 120-150 minutes. The volume of urine V_2 was expressed as the percentage of urine administered in the first two water loads. Rats deviating by more than 33 percent from the mean for the group were discarded. Thirty minutes were allowed for absorption of the injected material following subcutaneous injection. The assay results were cvalculated as follows:

$$\% \text{ of water excretion} = \frac{V_E - V_{30}}{3V_1 - (V_2 + V_{30})} \times \frac{100}{1}$$

Where V_1 = Volume of water administered in each dose.

V_2 = Volume of urine in two hours before injection.

V_{30} = Volume of urine in first thirty minutes after injection.

V_E = Volume of urine excreted during the period.

Thus the percentage of water excretion at a given time was the volume of urine passed from 30 minutes after injection expressed as a percentage of water administered, minus that excreted, at 30 minutes after injection. Two dose levels of both standard and unknown were used in the assay and the ratio of these was 2.0 or 3.0. On a 4 point assay the mean standard error in 12 assays was 8.9 percent and it was possible to assay down to 10 m.u. of vasopressin. This assay was adopted in 1953 by the British Pharmacopaea.

Hypophysectomised rats were used by Leaf & Mamby (1952). A similar weight of animal was used (about 200 g), hydration being at the rate of 8 ml per 100 sq. cm of surface following 12 hours of fasting. Two-fifths of this water was administered initially and one-fifth at subsequent hourly intervals. Normal saline was injected intraperitoneally at the start of the third hour of hydration. The unknown solution was injected intraperitoneally at the beginning of the fourth hour, and urine samples collected from the rats in metabolism cages during the third and fourth hours. The anti-diuretic index was calculated by determining the solute concentration of each urine sample and comparing the mean increase in concentration of the samples following the injection with that of the preceding control hour samples. Stein et al (1952) described a technique in which the rats were given two water loads consisting of 0.2 percent sodium chloride at a rate of 5 percent of the body weight. The anti-diuretic response was expressed as the reciprocal of the ratio of the volume of urine excreted after 60 minutes to that excreted at 20 minutes followed the second water load. The response had a linear relationship to the dose. Applying the Bliss (1944) design with 10 rats on standard and 10 on unknown, this assay gave a mean standard error of ± 30.27 percent and the index of precision was 0.33.

An interesting concept was applied to the problem of ADH assay by Crawford & Pinkham (1954). These authors reasoned that as the role of ADH is to promote the resorption of water from the intraluminal renal tubular fluid as a final step in the elaboration of urine, the assay should aim at measuring precisely this phenomenon. ADH activity should thus be directly reflected by the ratio of water to total osmotically effective solute in the urine. Male rats averaging 250 g in weight were used as the test animal and trained to accept a stomach tube. A synthetic fibre-free diet was used to simplify the problem of faecal contamination of urine, and urine measured in metabolism cages. Food was withdrawn 16 to 18 hours before the assay and the rats hydrated at the beginning of the procedure with 350 ml. of water per sq. metre of body surface at 37°c. Diuresis commenced in about 45 minutes. After 75 minutes another dose of 250 ml. of water per sq. metre was given, and urine collection started. If 4 ml. of urine were voided during the next 45 minutes period the animal was

deemed suitable for assay purposes. 250 ml. of warm water per square metre of body surface was given at the commencement of each of three consecutive 45 minute periods, the material to be assayed being injected intraperitoneally at the commencement of the third period. The water concentration of the urine samples was estimated by determination of the freezing point. Data from animals showing evidence of endogenous ADH release were rejected and the responses calculated from the following formula:

$$\text{Response} = \frac{\frac{\text{ml. } H_2O}{\text{mos. M}} U_3 - \frac{\text{ml. } H_2O}{\text{mos. M}} U_2}{\frac{\text{ml. } H_2O}{\text{mos M}} U_2} \times 100$$

U_1, U_2, U_3 = Urine collected during three consecutive 45 min. periods.

$\frac{\text{ml. } H_2O}{\text{mos. M}}$ = ratio of water to total osmotically effective solute.

The log-dose response curve for this assay was linear and the index of precision 0.13. The assay was effective over a range of 0.1 to 0.4 m.u. The female rat was once more given status as an assay animal by McCreary *et al* (1957). These workers found female animals to be eminently suitable for this work when they were housed under controlled temperature conditions with free access to food and water. In their assay four rats were used for each determination, hydration being by stomach tube to a level of 5 percent of the body weight. Urine output was recorded at 15 minute intervals over a 3-hour period in a metabolism cage. After an hour's rest the animals were re-hydrated and again the urinary output measured. The output curves were plotted and the area below the curves measured with a planimeter. The procedure was then repeated but at the first hydration 2.5 ml. of water was injected subcutaneously along the dorsal spine and at the time of the second hydration a similar volume of test solution injected. The area beneath the two time-urine volume curves was compared and used as the basis for estimation.

An interesting assay was described by Ginsburg & Heller (1953) using a technique for giving intravenous injections without disturbing unaneasthetised rats. A polythene cannula was fitted into the right external jugular vein and brought out through the skin between the ears. This cannula was capped. The assay was commenced by giving each rat tepid tap water to 5 percent of the body weight followed after 50 minutes by a second dose. Fifteen minutes after the second administration of water the bladders were emptied and measurements of urine output made at intervals of 10 minutes thereafter. Before injections the water load was kept between 6 and 9 percent of the body weight and the urine flow at least 1.5 ml. in 10 minutes. The first injection was always an appropriate volume of heparin and if no inhibition of urine flow resulted, injections of standard and unknown were made via the indwelling cannula. A great variation in sensitivity to vasopressin was discovered, some animals showing no response to 200 micro-units while others showed a marked response to 50 micro-units.

All of the rat assays described so far depend on the statistical treatment of responses of a number of animals. A new approach to the problem was suggested by Jeffers *et al* (1942). These workers made the rat diuretic by the administration of water and ethanol. Van Dyke and Ames (1951) showed that ethanol suppressed the secretion of endogenous ADH, thus increasing the sensitivity of the rat as an assay animal. Jeffers *et al* had shown that their alcohol-anaesthetised rat could detect ADH in doses as little as 20 micro-units. Male rats between 180 and 220 g were starved for 80 hours prior to the assay during which they were maintained at a temperature between 29 and 30°c. All solutions administered by stomach tube were at 40°c. Water loading was at the rate of 5 percent of the body weight and consisted of 12 percent of 90 percent ethanol in water. This was followed 30 minutes later by a 3 percent water load of plain water. A needle was placed in the femoral vein and a glass-

tipped connection of a rubber cystostomy tube of $\frac{1}{16}$" bore was tied into the urinary bladder through a suprapubic incision. The bladder was then replaced and the wound closed by a single suture. The urethra was occluded by means of a ligature. Urine output was measured in a cylinder at 10 minute intervals until a steady flow of 3.1 to 8.1 ml. per hour was obtained. This usually occurred about 90 to 120 minutes after the first water load. The first injection of vasopressin was then given and readings made at 4 minute intervals during the period of antidiuresis. The degree of antidiuresis was calculated by subtracting the volume of urine excreted 20 minutes after injection from that for the same period prior to injection. A maximum of four injections was given to each animal.

This assay was refined by Dicker (1953). He used female rats deprived of food for 18 hours before the trial, but with access to water. The first water load was given by stomach tube at the rate of 5 percent of the body weight of tepid water, followed 45 minutes later by a similar loading of 12 percent ethanol solution. The bladder and one external jugular vein were cannulated and the bulk of the bladder tied off to decrease dead space. When urine flow reached 3-4 ml. per hour the second oral dose of 2 percent ethanol at 3-4 percent of the body weight was given, and the stomach tube left in position. When water loading reached about 8 percent the animal was placed in a holder on a balance, the jugular vein being connected to a set of three syringes; one a tuberculin syringe containing 0.9 percent sodium chloride and two micrometer syringes. The bladder catheter and stomach tube were connected respectively to the outflow and inflow mechanisms of the apparatus which ensured a continuous recording of urine flow and the maintenance of constant water loading. The stomach tube inflow rate of 2 percent ethanol was adjusted to 0.103 ml. for each 0.1 ml. of urine excreted. The test was carried out in a thermoregulated room at 23°c. There was a lag of 2 minutes between the time of injection and onset of the antidiuretic effect, and uniform responses could be obtained if similar amounts of vasopressin were injected at intervals of 50-60 minutes. Shorter intervals resulted in tachyphylaxis. The lowest dose producing a significant effect was 3.5 micro-units per 100 g of body weight. The upper limit for assay purposes was 50 micro-units per 100 g of body weight. This method was adopted by the British Pharmacopaea in 1958 with very small modification. Male rats were used in the BP method, the first water loading being 3 percent of water, the second 5 percent of a 12 percent ethanol solution, 1 hour after the first. The preparation was virtually as described by Dicker. Another modification of the Jeffers' Livezey & Austin assay was described by Ames and van Dyke (1952). The urethra in the ethanol and water-treated rats was ligated and a shortened urethral catheter inserted through a cystostomy and anchored by a ligature. Injections were made intravenously into the saphenous vein a distance of about 20 mm. 0.20 m.u. of vasopressin could be detected with this assay.

A great improvement in the instrumentation applied to the rat antidiuretic assay was described by Boura & Dicker (1953). The alcohol anaesthetised rat was used as described by Dicker (1953). The urine output flowed into a Woulfe bottle connected to a similar bottle containing boiled water which has a constant surface tension. The urine inflow into the first bottle displaced a similar volume of boiled water from the second bottle which passed through a drop counter on its way to a small reservoir. The latter was connected to a small pipette fitted with electrodes at the top and the bottom. At appropriate times an electro-magnetic valve opened between the reservoir and pipette thus allowing the latter to fill. Immediately it filled the inlet valve closed and an outlet valve opened allowing the liquid to drain away until its level reached the bottom electrode of the pipette. This operation was recorded on a chart and continued until the reservoir was empty. A similar type of measuring arrangement was used to maintain hydration; for

every 0.1 ml. of urine excreted, 0.103 ml. of water was run in through the metering system to the stomach tube. The rat was located in a holder suspended from one arm of a balance, the other arm of which worked a frontal lever on the recording drum, thus producing a graph indicating any imbalance in the water loading system. The whole apparatus was controlled by an automatic electronic timer and relay system. Some improvements were made to this system by Dettelbach (1958). He also introduced a considerable amount of pre-treatment in order to standardise the animal's response.

Female rats between 200 and 250 g weight were obtained one month in advance of their use. All were spayed to eliminate the effect of the oestrous cycle on water load sensitivity. Seven to ten days after spaying each animal was given a 5 ml. load of tepid tap water by stomach tube, and this was repeated with the load increased by 1 ml. increments until a 10 ml. level had been reached. This 10 ml. gavage was repeated every 4-5 days until the animals were ready for use. The day before the assay two or three animals were selected and given a 10 ml. load of 2 percent ethanol, fasted overnight but allowed access to water. On the day of the test each received 5 percent of its body weight of 12-15 percent ethanol by stomach tube, followed 45 minutes later by the same volume of 2 percent ethanol. One hour later the bladder was emptied and the total urine output measured. The animal with the largest volume was selected and the load of this animal brought up to between 6 and 8 percent of its body weight with warm 2 percent ethanol. The urinary bladder was catheterised and a polythene stomach tube inserted. A 25 gauge needle was also inserted into the femoral vein for injection purposes. The assays were started when the steady flow of urine reached 50 micro-litres per min. Injection volumes were maintained between 0.05 and 0.2 ml. The urine flow and water loading during assay were carried out as in the method of Boura & Dicker (1953). The water loading solution was 5 percent glucose in 2 percent ethanol. The log dose-response characteristic of the assay was linear within the range 2 to 64 micro-units per 0.1 ml. The index of precision was ± 0.232 in log dosage units and the lowest dose of vasopressin accurately detectable was 4 micro-units per rat. No tachyphylaxis was detected with repeated doses of 8 or 16 micro-units.

The assay method on which we based the technique used at Ruakura was described by Hunter *et al* (1959). Male rats were used in the weight range 150-250 g. On the day preceding the assay they were anaesthetised with 12 percent ethanol by gavage supplemented if necessary with ether. Cannulae were inserted into the stomach and the urinary bladder. These were fitted with caps. On the day of the assay the caps were removed and polythene tubing attached. A cannula was also inserted into the external jugular vein after the animals had been given 1 mg. of perphenazine per 100 g of body weight. Initial hydration to a level of 7 to 8 percent of body weight was carried out by means of a gastric cannula, a 0.05 percent solution of sodium chloride being used in the final form of the assay. The rat was placed in a small wooden box so that it was draught free and the urinary output measured by visual drop counting. The solution to be assayed was injected by means of a micro-meter syringe in a constant volume not exceeding 0.1 ml. and flushed in with 0.2 ml. of saline. Up to nine injections were given to the same rat within a day without any sign of tachyphylaxis. The index of precision for the assay was 0.143 with a standard error of 0.03. The minimum dose capable of giving a measurable response was about 25 micro-units in a 200-250 g. rat, and the studies were carried out over a dose range from 25 to 140 micro-units. The equipment used in this assay was relatively unsophisticated and there are many possible sources of unwanted variations. Wolfman *et al* (1964) described apparatus which maintained a constant water load and provided a very satisfactory system for recording urine flow rate. This was a development of the method described by Dettelbach (1958). The same principle was maintained but it was

improved in precision. Female rats were used anaesthetised by the use of 10 percent ethanol solution dosed at the rate of 5 percent of the body weight. 45 minutes later a 2 percent ethanol solution was given in equal volume and the urinary bladder catheterised. Finally, a fine catheter was fitted into the femoral vein for injection purposes. The urine flowed down a spinal needle to the bottom of a Woulfe bottle containing 20 percent ethanol with 1 percent sodium chloride. This solution is a good electrical conductor and has a satisfactory surface tension for drop formation. The urine being denser than the ethanol-salt solution remained as a layer at the bottom of the bottle displacing an equal volume of the solution from the top where it flowed through a drop counter and thence into the drop collector. As in the Boura & Dicker apparatus, magnetic valves controlled the measuring of the urine flow in accordance with the regulation of a timer circuit. The volume of urine lost was replaced as liquid via the gastric tube, the solution being 5 percent glucose with 0.05 percent sodium chloride in 2 percent ethanol. This solution replaced the volume of urine in equal amount. Over a large number of determinations this apparatus was found to be very satisfactory and permitted estimations from as little as 10 micro-units. The optimum range for assay was found to be from 20-60 micro-units per 0.25 ml.

An important advance was made by Pliska & Richlik (1967) when they introduced the continuous measurement of electrical conductivity into the rat antidiuretic assay. The preparation was very similar to those described previously using female rats in the 160-230 g range, initially anaesthetised with 12 percent ethanol in tap water administered by stomach tube to 7 percent of the total body weight. Either a stomach tube or a catheter inserted through the abdominal wall was used during the assay for hydration with 1-2 percent ethonol in tap water mixed with saline. Hydration was maintained by the use of a micro-pump controlled through a relay system. A cannula was placed in the urinary bladder through the urethra. The preparation rested on one pan of a balance which was heavily damped by the use of oil and the movement of the balance was used to compensate by hydration for the loss in weight due to urine flow. The latter was measured by the use of a vacuum drop-divider which gave between 500 and 3,500 drops per ml. Near the proximal end of the catheter the urine passed through a conductivity cell consisting of two stainless steel tubes held in an acrylic block. Conductivity was recorded continuously and found to be a very satisfactory parameter for assay purposes.

Assay Methods Applied at Ruakura

(Fell, 1968)

The assay procedure for oxytocin adopted at Ruakura is based on the Tindal & Yokoyama method. The preparation of the solution for assay is briefly as follows:

Twenty ml. of whole blood is collected in cold polythene bottles containing anticoagulant, stored in melting ice, and spun down in a refrigerated centrifuge at about 4°c. Ten ml. of plasma is then immediately placed on a column of Sephadex G.25 and eluted with distilled water. The fraction containing the peptides is collected, freeze dried, and stored at —12°. When redissolved in normal saline the freeze dried extract is ready for injection. The anaesthetised lactating guinea pig is used as an assay animal, the preferred weight range being 600-800 g. Intramammary pressure is continuously recorded and hormone injected intra-arterially. The use of close arterial retrograde injection improves the sensitivity of the preparation. The animal is prepared by first anaesthetising with intraperitoneal Nembutal. The trachea is cannulated and artificial respiration applied. The jugular vein is cannulated for intravenous administration of anaesthetic and the internal saphenous artery in the leg is exposed and cannulated using a No. 25 needle, connected to a 3-way tap for the administration of saline or hormone doses. The four main side branches of the artery

are ligated to provide an efficient retrograde route to the mammary gland. The ipsilateral mammary gland is cannulated using a blunted No. 20 needle and connected to a pressure transducer in a liquid filled system. A linear dose response curve is normally obtained within the range 100-400 micro-units of oxytocin. The threshhold is commonly of the order of 50 micro-units. The mean index of precision of ten 2 x 2 assays is 0.044 and mean fiducial limits 10.2 percent.

The assay of vasopressin is based on the technique described by Hunter *et al* (1959) but incorporating Pliska & Richlik's method of using electrical conductivity as the measuring parameter and introducing a simplified constant hydration technique. 24 hours before the assay the rat is anaesthetised with ether and a small brass cannula fitted into the urinary bladder. On the day of the assay the rat receives 12 percent ethanol to 8 percent of its body weight by stomach tube. It is then placed in a temperature controlled perspex cage. The caudal vein is cannulated using a No. 24 needle connected to a constant infusion pump. Hormone injections are given via the caudal vein also. The bladder cannula is connected to a small conductivity cell which is based on the use of a capillary glass tube fitted with two fine platinized electrodes. Conductivity is recorded directly on a potentiometric recorder. Water loading and anaesthesia throughout the assay are maintained by intravenous infusion of hypotonic saline (0.25 percent NaCl with 2 percent Dextrose) plus 2 percent ethanol. This maintains very light anaesthesia and a high rate of urine flow, (about 5 ml. per hour). The introduction of intravenous water loading achieves a constant high urine flow rate within 30-40 minutes. A simple feedback mechanism maintains the degree of hydration reasonably constant. After passing through the conductivity cell the urine flows into a small cup on one arm of a balance. A similar cup is placed on the other arm and fed from a tube coupled to the second piston of the infusion pump. When the vessel containing the urine exceeds the weight of the balance vessel, a contact closes and the infusion pump operates delivering an additional dose of saline and an equal volume to the balancing vessel, thus opening the contacts and stopping the pump. Maximum conductivity has been found to be a very useful parameter and a linear log dose-response curve is usually obtained in the range 25-500 micro-units of vasopressin. About one-third of the rats respond to 1 micro-unit, but higher levels are preferable for normal assay. Doses can be given every half hour and the sensitivity maintained for up to 8 hours if necessary. In a normal assay 2 rats are used simultaneously and a four point assay used with 24-48 responses. The mean index of precision of 10 assays, each using four rats, is 0.125 with mean fiducial limits at 18 percent. Precision could be increased by the use of more animals, but as it is it compares favourably with other assays for the purpose, and it is relatively easy to operate.

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Reminder . . . Conference—August

FARMERS, FERTILISERS AND FUNDS *

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This talk is a kind of song. It is not a song of sixpence, or a pocketful of rye, or of four and twenty blackbirds baked in a pie. This song deserves to be sung loudly—triple forte, *fff*. The three *f*'s are for farmers, fertilisers and funds (chiefly overseas). Other people would sing this song differently and better, but I hope to convey some of the interest I have found in three years of association with the fertiliser industry. Its management and well-qualified staff have been the key to quickly getting busy together. There is a sense of urgency about these folk and their problems which I find exciting and perhaps it can be best expressed in the lines from Alice in Wonderland, "Will you walk a little faster" said a whiting to a snail, "there's a porpoise right behind us and he's treading on my tail". Then again this industry literally is, and has been for 88 years, at the grass (and clover) roots of New Zealand's economic development.

Farmers

Let's begin with a few words about farmers —they are this industry's customers, they are the people who order cobalt potassic super, "moly super" etc. In New Zealand we are fortunate in the high level of education of our farmers and community generally. Good education aids rapid transfer of research findings to practice. If you are one of the million New Zealanders who are in the habit of watching "Country Calendar" on Sunday evening, you will be aware also of successful research and development by farmers themselves. The neighbours of a good farmer can see the rewards of advanced practices in the production of the protein and fibres discussed also at this conference. The operation of a topdressing plane is an example of an advanced practice. This ability to see what the other fellow does and his results is, I think, a real advantage which agriculture has over other industry.

I began by talking about farmers for two reasons. The first I have already mentioned. Farmers are the industry's customers; they are the people for whom fertilisers are made. Fertiliser is the biggest single item in a farmer's budget—twenty-five percent of it usually. Secondly, farmers are the human element which, in my experience, is primary in science as well as other affairs.

Historical Development of Fertiliser Industry

Dunedin is a most appropriate place to talk about making fertilisers to the New Zealand Institute of Chemistry Conference, particularly when we are celebrating the centennial of the University of Otago. The industry started here 88 years ago. Thomas Kempthorne of Kempthorne Prosser and Co's N.Z. Drug Co. in 1881, won the Government's prize of £1500 for building New Zealand's first superphosphate works. Dunedin also chalked up another first when, during the 1939-45 war, a small contact acid plant using platinum supported on magnesium sulphate as catalyst made several hundred tons of oleum for chlorsulphonic acid production. Professor Soper, Mr. McLean and Mr. Higgins were three Institute members associated with that job.

You will recall that in 1840 Liebig discovered that treating bones with sulphuric

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* An address to N.Z.I.C. Conference, August 1969, "The Future in New Zealand for Science-Based Industries".

acid made the phosphate more soluble and available to plants. You will also recall that Lawes had made superphosphate, a mixture of monocalcium dihydrogen phosphate and calcium sulphate, in England in 1843. The initial capacity of the Dunedin works was 3,000 tons per annum and it was 25 years before the company built New Zealand's second fertiliser plant at Westfield, Auckland, with an initial capacity of 8,000 tons. Fifteen years passed before another company, New Zealand Farmers' Fertilizer, built a works in Auckland, this time (1921) with an initial capacity of 16,000 tons per annum. By 1931 there were four private companies manufacturing superphosphate in two works in Dunedin, three works in Auckland and one each in Christchurch, Wanganui and New Plymouth. Growth of fertiliser use was steady until 1940 when there was a fall because raw materials were restricted by war. All sulphuric acid was made by the chamber process.

1954 was the next landmark with the establishment of the first farmer co-operative fertiliser company at Napier. It built a contact plant to make 110 tons per day of sulphuric acid. Two more co-operatives built works at Mt. Maunganui in 1958 and Invercargill in 1959. Currently 89% of the total sulphuric acid is made in contact plants which are run by engineers—not chemists. The largest has a capacity of 300 tons of acid per day compared to recently built units in the United States of 1500 tons per day. The first Lurgi plant in this country is at Ravensbourne. It has a capacity of 205 tons per day and was commissioned 2 years ago.

Sulphuric acid capacity installed is 811,000 tons per annum. To make the current production of about 600,000 tons, New Zealand imports about 200,000 tons of sulphur—one percent of the world's annual production at a cost of about $8 million. The 500 lb. of sulphuric acid used per head of population in New Zealand is 50 percent more than in any other country. Australia is next on the list. Almost all of this acid is used to make superphosphate to keep New Zealand's pastures green. Remember however, the fact that our *total production is small by world standards.* Dr. McGillivray made a similar point* when he mentioned that although New Zealand rightly takes pride in being the world's largest exporter of agricultural products, these are a very small part of total world production of protein and fibre.

Currently then this country's fertiliser industry has the capacity to make 2.7 million tons of fertiliser per annum in the 12 works of six companies. In this season, ending 30 June 1970, sales are likely to break through the 2 million tons "barrier". The first million was achieved in 1955-56, 75 years after the industry began. There are forecasts that production may reach 4 million tons by 1980.

Why Superphosphate?

Why is superphosphate the dominant fertiliser in New Zealand? This question can best be discussed in terms of the cover photo showing New Zealand's corresponding latitude in the Northern Hemisphere Mediterranean. Notice how much nearer the equator we are than the United Kingdom and Holland. In our climate clovers will grow longer and fix more nitrogen each year than in the U.K. and Holland, even allowing for the Gulf Stream. New Zealand's grassland scientists—Sir Bruce Levy, James Melville and Peter Sears were some of the pioneers—who have developed our clover-ryegrass pasture system of farming with the animals cycling plant nutrients and building a "shower of fertility", were well aware of our special climatic advantages. The phosphorus and often the sulphur in superphosphate are the key to the clover's ability in New Zealand to fix nitrogen in the North Island equivalent to about a ton of ammonium sulphate per acre. This is worth about $50 on the land. The amount fixed is less in the South Island where the growing season is shorter. Professor Walker of Lincoln College has recently estimated that clovers in New Zealand pasture fix the equivalent of five million tons of ammonium sulphate annually. At current world prices

* Previous speaker at this meeting.

this would cost $250 million. A good return for the $60 million it costs us to get superphosphate on New Zealand farms each year. Professor Walker's estimate is conservative and I think he would concede that the bill could be twice as much ($500 million) to replace clover nitrogen with manufactured nitrogen. New Zealand's current use of nitrogen fertilisers is about 30,000 tons, or only part of one month's production of the large ammonia plants going up in the United States, Japan, Middle East and elsewhere.

Nitrogen

Recently, publicity has been given to a paper by Dr. Mitchell, Director of D.S.I.R.'s Plant Physiology Division at the Conference of the New Zealand Institute of Agricultural Science in Palmerston North (August 1969). Dr. Mitchell has been examining the replacement of our pastoral system of farming based on clover-ryegrass pastures by production technology based on nitrogen fertiliser and storage. He suggests that this farming system would deliver feed to the animal at about two-thirds the cost of the present one of clover-ryegrass-grazing, and that there would be big increases in production per acre, better quality feed and higher net returns for a well organised enterprise. Dr. Mitchell points out that it has taken almost 30 years for most of our research effect to bring the present system to its high standard, and although change may be fast it certainly will not be overnight. The capital expenditure involved in such a farming revolution is just one of the many factors to be evaluated. Naturally the fertiliser industry is giving careful thought to the effect of such possible development on its future.

The recent discoveries of inorganic compounds which will fix nitrogen at atmospheric pressure are potentially of great interest. One of the discoverers told me that so far it had not been possible to convert nitrogen to ammonia and he thought this work would be most useful in helping to unravel the mysteries of the biological fixation of nitrogen. However, perhaps by the time the tonnage of nitrogen fertilisers used in this country justifies building a manufacturing unit, there will be an economic alternative to the Haber process—simpler and requiring less capital investment.

Christmas Island Phosphates

To summarise some recent achievements and current developments: This year the British Phosphate Commissioners will bring into New Zealand about a million tons of phosphate rock containing 160,000 tons of phosphorus at a landed cost of $15 to $16 million. Phosphate rock, the mineral apatite, is a cheap international raw material. There are large reserves in various parts of the world. The other major raw materials presently imported are 200,000 tons of sulphur and about the same amount of potassium chloride. The cost is $8 million and $7 million in overseas funds in round figures.

About 30 percent of the phosphate rock will come from Christmas Island in the Indian Ocean and the rest from Nauru and Ocean Islands in the Pacific. Five years ago the first shipment of only a few thousand tons of rock came from Christmas Island. This rapid change in source of supply has been important in keeping fertiliser costs down in New Zealand. Christmas Island belongs to Australia and New Zealand. The Governments bought it in 1948 from the Christmas Island Phosphate Company. There is no indigenous population so the question of royalty payments does not arise.

The phosphate mineral resources of Christmas Island are not only calcium phosphate. Overlying the apatite are much greater tonnages, perhaps as much as 200 million, of phosphates containing about 12 percent phosphorus and 20 to 25 percent iron and aluminium. Crandallite and millisite are the chief phosphate minerals in this overburden which is known as "C" ore. Between the "C" and "A" ore horizons is a mixture called "B" ore. Superphosphate can be made from the "A" ore, but not from "C".

Christmas Island phosphates are a challenge to the industry, to its Research Association and to others of Australasia's scientific community. The "A" ore contains 5 percent of iron and aluminium oxides as it has 10 percent of "C" ore mixed with the apatite. It is not economically possible to separate them. The iron and aluminium form phosphates during the manufacture of superphosphate. These are gel-like compounds and affect the physical properties of the calcium sulphate deleteriously. The industry blends Christmas with Nauru rock (40:60) to minimise these problems and has installed granulation plants to further improve the handling and flow properties of the product.

For a number of years now at Otara, our Chief Chemist, Mr. P. J. Gallaher, has been studying the effects of variables such as acid strength, temperature, rock fineness, and acid/rock ratio on the rate of reaction of sulphuric acid with phosphate rocks and the quality of the product. With the establishment of chemical engineering and physical chemistry sections at F.M.R.A., a major effort has got underway this year to use and extend this background of experience to find ways of overcoming the difficulties of making superphosphate from Christmas Island rock. We use the "convergent" approach, each staff member tackling parts of the job for which training and experience have fitted him best. Needless to say, we work more and more closely with our colleagues in industry.

The Christmas Island Phosphate Commissioners, and in particular the New Zealand Commissioner Mr. R. B. Tennent, have since 1964 backed studies at F.M.R.A. of ways of using the "C" ore, bearing in mind of course, the point made by Mr. J. W. Rowe* about the "have got, must use syndrome". This work has involved international co-operation. The Commissioners have contracted with Amdel for the processing studies while F.M.R.A. has contributed pot and field trial studies of the response of pasture plants to the products. Most of this work has been based on the discovery at Otara, and elsewhere, in 1964 that heating the "C" ore to 500°c broke up the lattice of the phosphate minerals (analogous to clays) which became amorphous. The phosphate in the calcined material, known as "Calciphos", was then soluble in citrate solutions and available to plants. Unfortunately "Calciphos" has to be pelletised to be handled. This reduces the plant response so we are looking for a formulation which will disintegrate the pellets when they are spread on pasture. The problem is similar to that of drug formulation but the cost must be much less.

Dr. H. P. Rothbaum of Chemistry Division, who was a foundation member of one of F.M.R.A.'s Technical Committees, has interested himself in Christmas "C" ore and Calciphos. He worked on pelletising and more recently, having noticed that the silica in "C" ore is low, has published a paper on the extraction of phosphate and alumina by leaching with caustic soda. All the aluminium is dissolved and two-thirds of the phosphate as sodium phosphate, with the other third being precipitated as a reactive calcium phosphate. The sodium hydroxide can be recovered by treating the sodium phosphate with lime and recycled. This process, in effect, produces calcium phosphate with the 25 percent of alumina in the ore as a bonus. At present it does not appear economically attractive. An ion exchange process studied at Amdel works too, but it would also appear to be a costly way of obtaining phosphoric acid. The search continues.

Sulphur

A brief note on the 6 million tons of sulphur which American Cyanamid announced they have proved near Lake Taupo—this is 30 years supply for New Zealand. It is adjacent to geothermal steam so we may have liquid sulphur being shipped from Taupo to the fertiliser works. As the technology of extraction and other feasibility studies are still under consideration, I do not intend to say any more other than to emphasise that this, like oil, is one of the most important

* Previous speaker at this meeting.

discoveries which could have been made. We will use it in this country and multiply its value many times by passing it through our pastures into our agricultural products. Ironically the price of sulphur now is beginning to fall quite dramatically after a period at high levels.

These brief remarks about fertiliser raw materials are all there is room for. Such matters as additives like trace elements, pesticides, and weedicides, the growth of bulk fertiliser sales, the trend to more mixtures, manufacture of copper and aluminium sulphate, recovery of fluoride, will have to be left unexplored.

Financing of the Industry

Consider the record of the Southland Co-op. Phosphate Company which began manufacturing at Invercargill in 1959. The tonnage sold that year was 26,000 and the turnover $0.5 million. In 1969 the tonnage sold was 185,000 and turnover $4.5 million. This seven-fold increase in sales in 11 years resulted in net earnings of $5 million on an initial capital of $2.6 million. Over half of this, largely borrowed from the Meat Board has been repaid. Much of the earnings have been ploughed back into new buildings and plant. The Company's sales did not fall in 1967 and 1968 as elsewhere. The national declines were 12 and 9 percent in those years, largely as a result of the recession caused by the fall in wool prices. In 1969 much of this has been regained by a 15 percent increase in sales. There is every prospect of a record in the current year. The implications of this for farmers and the economy are good, as last year New Zealand's overseas earnings exceeded $1000 million for the first time, and 87 percent of this total came from agricultural products (83 percent pastoral in origin) —an increase of 4 percent—although manufacturing had its most successful year. I think it is likely that the National Development Conference targets for pastoral exports of $910 million by 1972-73 will have a stimulating effect on production similar to that of the Agricultural Production Conference in 1962. The industry's spending on research doubled in 1967 and was trebled last year and this, on the 1966 expenditure, despite the drop in sales. Estimated expenditure by the fertiliser industry in 1967-72 is $11 million on land, buildings and plant ($15 million was spent on these items in 1962-67).

This is a lot of money by anyone's standards, and it must come largely from retained profits, with smaller contributions from increased share capital and loan finance. The economics are not simple as this industry is not a high profit one and is in fact strictly profit controlled. This probably explains the lack of interest shown to date by large overseas organisations in entering the production field here. Low costs must be maintained if the farmer is to use the maximum amount of fertiliser for pasture improvement. Despite fluctuations in raw material costs and wage increases, improvement in manufacturing efficiency has enabled the price of fertiliser to be kept remarkably constant over the last 20 years.

The Future

Finally, what of the future? Mr. R. .A. Warburton, Chairman of F.M.R.A., had this to say in 1967. (Mr. Warburton who has been General Manager of the East Coast Farmers' Fertiliser Co. since it began in Napier in 1954, is a graduate in chemistry from Birmingham University. He came to New Zealand about 15 years ago from Scotland where he worked with Scottish Agricultural Industries (a branch of I.C.I.).)

> "The industry will continue to grow, because New Zealand primary production must grow, and fertiliser will always be an essential input in agricultural production. There will be changes—many changes—but for a number of years to come, I foresee that superphosphate and mixtures of superphosphate with other essential elements, will continue to be the backbone of the industry. We are often told that by sticking to single super we are behind the times. 'We should be making

triple super and complex concentrated fertiliser. We should be replacing the clover in our pastures with nitrogen from the bag.' Our critics unfortunately, don't appreciate all the factors; when comparing triple with ordinary single super, no account seems to be taken of the sulphur content, now known to be an essential plant nutrient. When our research scientists show conclusively that it will be more economical to apply nitrogen which has been produced synthetically than to grow clovers, we, as an industry will be prepared to move into this field.

"The industry keeps a close watch on these developments which have taken place, and which are taking place overseas. The basis of our assessment will be, what is in the best interests of the consumer—what is the cheapest unit of plant food on the paddock. We do not intend to play the game of 'follow the leader', neither do we intend to make changes just to 'keep up with the Jones's'."

It is good to be associated with men like Mr. Warburton and the agricultural scientists who are behind so much of our country's development. Let me end with another line from the song in Alice in Wonderland. It is an invitation.

"Will you, won't you, will you join the dance?"

There is a lot to learn. The steps are intricate, but I find the dancing partners are magnificent.

IUPAC NEWS

N.Z. National Committee for Chemistry

Information has been received from IUPAC on forthcoming international chemistry meetings as follows:

1. International Symposium on Macromolecules—Leiden, Netherlands—31 August-4 September 1970.
2. International Symposium on Chemistry of Pesticides under Metabolic and Environmental Conditions — Bonn/Birlinghoven, Germany—8-11 September 1970.
3. IInd International Symposium on Organic Solid-State Chemistry—Rehovot, Israel—14-18 September 1970.
4. Ist Discussion Conference on Macromolecules: Models of Bipolymer Structures and Functions — Mariaske Lazne, Czechoslovakia—14-19 September 1970.
5. International Conference on Chemical Pollution and Human Ecology — Prague, Czechoslovakia — 12-17 October 1970.
6. IInd International Congress of Pesticide Chemistry—Tel Aviv, Israel—21-26 February 1971.

C. J. Wilkins, Hon. Sec.

FROM INFORMATION BULLETIN NUMBER 36, NOVEMBER 1969

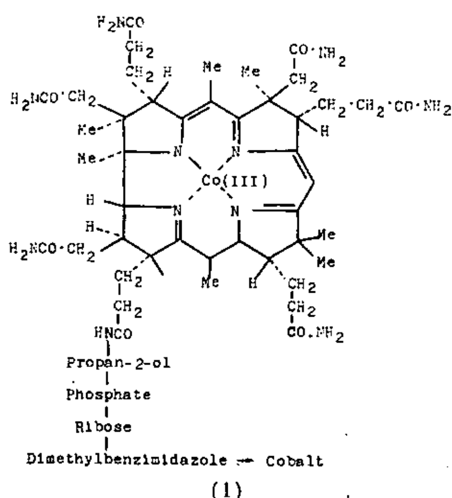
"The problems of environmental pollution have . . . become of major concern to the general population . . . An appeal is hereby made for the services of the most talented analytical chemists in the scientific community . . . to provide the expertise required to introduce unique and advanced methods for determination of pollutants. Many of the analytical methods now being used in air pollution studies are shockingly obsolete and crude . . . Most authorities feel that the quality of the air is deteriorating rapidly and that the situation is critical. A number of areas are known where air pollution is already intolerable and the situation may be world wide within 25 to 30 years. Without question the problem is challenging and urgently requires the combined efforts of scientists throughout the world."

Philip P. West. Analytical Methods for the Study of Air Pollution (Introductory Remarks). Plenary Lecture at the International Symposium on Analytical Chemistry. Birmingham 1969.

THE CONSERVATION OF ORBITAL SYMMETRY

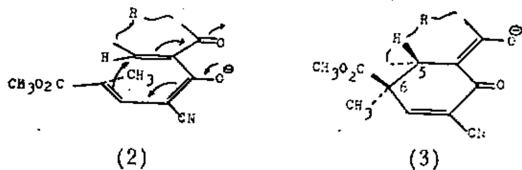
J. M. Coxon, M.Sc., Ph.D.
Chemistry Department, University of Canterbury

Professor R. B. Woodward has been aptly described as a kind of academic Godfather to organic chemists.[1] At the age of twelve years he was devising plausible syntheses for a host of different compounds. This interest has recently come to involve him in the synthesis of the vitamin B_{12} molecule[2] (1).



(1)

His synthetic reaction scheme involved a base catalysed stereospecific internal addition process from the open structure compound (2) to the cyclic structure (3). On the then current understanding of reaction mechanisms, confidence could be placed in the stereochemistry at carbon atoms 5 and 6 being as shown for compound (3). The



(2) (3)

reaction was not successful. However, on simply heating compound (2) (fig. I) cyclisation did occur but gave the isomeric compound (4) having different stereochemistry at carbon atom 6. In addition to the formation of this product some of the required compound (3) was formed but was subsequently shown to have resulted from cyclisation of compound (5), a product of thermal isomerisation of compound (2). Irradiation of the cyclic compounds (3) and (4) caused their smooth conversion into the open chain compounds (2) and (5) respectively, the reaction course being in the

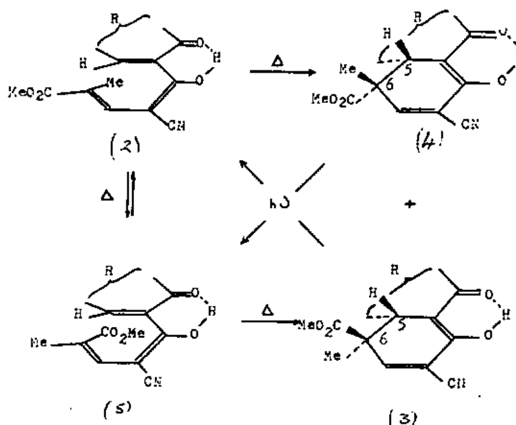


Fig. 1

opposite stereochemical sense for the photochemical and thermal reactions. Thus, the required compound (3) could be made, and the synthesis could continue.

The observation of the difference in the stereochemical course for the thermal and the photochemical reactions led Woodward and Hoffman to an imaginative rationale,[3] perhaps the most significant in organic chemistry in recent years. The problem when reduced to essentials involves the cyclisation of a triene to a cyclohexadiene system taking place in the direction of the arrows, namely in a disrotatory sense (Fig. 2). This is in contrast to the earlier observation of Vogel[4]

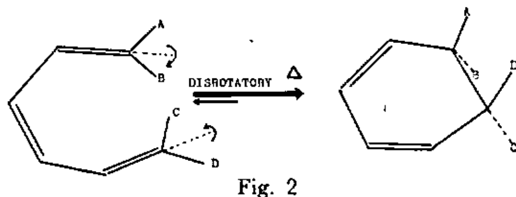


Fig. 2

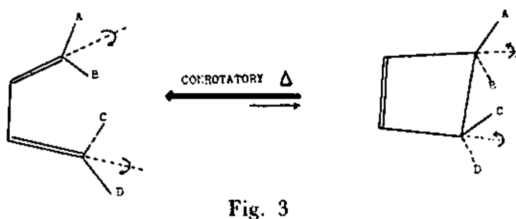


Fig. 3

on the stereospecific thermal opening of a substituted cyclobutene, opening of the ring taking place in the opposite or conrotatory sense (Fig. 3). These two closely related reactions differ in that the stereospecificity of the reactions are the opposite.

Woodward and Hoffman have correlated these observation with the symmetry of the highest occupied π molecular orbital involved in the reaction, noting that as the highest occupied orbitals for the diene and triene have different symmetry (Fig. 4) cyclisation will occur with conservation of orbital symmetry in the direction as shown by the arrows. The difference in stereochemical course for the photochemical reactions can also be understood by a similar consideration of the highest occupied molecular orbital. The molecular orbital to be considered will be the next highest in energy, an electron having been excited to this orbital by the light. The orbital now to be considered for

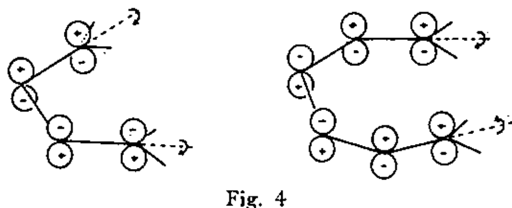


Fig. 4

butadiene (Fig. 5) has the symmetry such that conservation of orbital symmetry rationalises the photochemical disrotatory mode of ring closure.

The consideration of conservation of orbital symmetry was shown to be applicable to cyclo-addition (e.g., Diels-Alder), sigma-

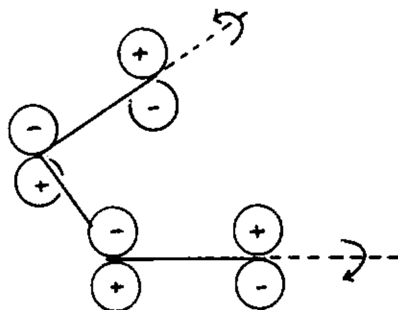


Fig. 5

tropic (e.g., Cope and Claisen) and electrocyclic reactions, and predictions could be made regarding the feasibility and stereochemical consequences of these concerted reactions. The literature over the past four years is now filled with examples substantiating the usefulness of this theory.[5]

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ORGANIC CHEMISTRY RESEARCH IN NEW ZEALAND

(Report from the Organic Chemistry Section, N.Z.I.C.)

One of the major objects in the formation of the Organic Chemistry Section of the N.Z.I.C. was to inform members of the research interests of their colleagues in other centres. The following summary is based on information provided in response to a circular posted to all members of the Organic Chemistry Section, supplemented by material from a much wider survey published in "Science Record", 1969. Material obtained from the latter source is asterisked*. In order to conserve space the names of research students have been omitted. Names are listed in alphabetical order for each institution.

AUCKLAND

University

Professor R. C. Cambie. Utilisation of New Zealand natural products; oxidation of aromatic steroids, fungal triterpenes; utilisation of dehydrobietic acid, podocarpic acid and phyllocladene for synthesis; perfumes related to ambergris.

Associate Professor B. R. Davis. Synthetic and mechanistic studies; dissolving metal reductions, dienone-phenol rearrangement, aspects of photochemistry and physical methods in these fields; the Clemmensen reduction of diketones; photochemistry of hydroxycylohexadienones.

Professor P. B. D. de la Mare. Studies of mechanisms of organic reactions; halogenation of triphenylene; intermediates in the halogenation of phenols; dehydrochlorination of polychlorides derived from naphthalene and its derivatives; electrophilic substitution and rearrangement in phenolic esters; kinetics and products of addition of halogenation of diacetoxybenzenes and related compounds.

Professor P. B. D. de la Mare and Dr. C. J. O'Connor. Stereochemistry of addition of chlorine acetate to olefinic compounds; kinetics and products of addition of halogen esters to olefinic compounds.

Professor P. B. D. de la Mare, Professor T. N. M. Waters and Dr. J. Waters. Structures of selected products obtained by addition of chlorine to unsaturated compounds.

Dr. D. J. McLennan. Kinetics and mechanism of substitution and elimination reactions; Nucleophilicity, dipolar aprotic solvents, hydrogen and heavy atom isotope effects; positive halogen transfer; hydrogen nucleophilicity of bases; thermodynamic and kinetic acidity of fluorene-type hydrocarbons; a Hammett study of the dehydrochlorination of DDT with chloride and acetate ions in dimethylformamide.

Dr. J. E. Packer. A study of the factors which control the chain length of the reactions between benzenediazonium ions and two-electron reducing agents; reactions of p-tolyl-diazonium ion with methanol, ethanol, isopropanol, and hypochlorous acid; a study of the radiation chemistry of the protecting agents, cysteine, cysteamine and homocysteine thiolactone.

***Dr P. S. Rutledge.** Organic synthesis.

Dr. B. E. Swedlund. Halogen addition and substitution reactions, particularly of α, β-unsaturated systems; acid-catalysed bromination of cinnamaldehyde; rearrangement reactions, Hoffman rearrangements.

Auckland Farmers' Freezing Co-operative Ltd. Laboratory

Mr. D. E. Cooper. Research interests centre on the field of meat waste treatment with particular reference to anaerobic digestion and the chemical and physical natures of solid and liquid wastes with emphasis on their utilisation and conservation. Current investi-

gations include: (i) the composition of fresh meat waste solids obtained after primary settlement, (ii) examination of rumen contents from freshly slaughtered animals; nutrient value of such materials as stock foods or fertiliser; (iii) use of digester gas as a heat or power source.

D.S.I.R. Plant Diseases Division

Dr. H. Young. Isolation, characterisation and structural elucidation of biologically active compounds from plants; synthesis of biologically active compounds.

HAMILTON

University

Dr. M. D. Carr. Isomerisations of acetylenes and allenes using homogeneous catalysts; the hexyne-hexadiene system-isomerisations using acid and base catalysts.

Professor A. T. Wilson. Determination and identification of intermediates important in the early germination of seeds, pollen and spores.

Ruakura Agricultural Research Centre

Mr. J. W. Ronaldson. Isolation, characterisation and structural elucidation of the phytoecdysones of ferns, and of the constituent compounds which quench the fluorescence of silica gel GF_{254}.

Dr. E. P. White. Isolation, characterisation and structural elucidation of alkaloids and other toxic principles of plants (mainly introduced species), higher fungi, and of cultures of lower fungi.

PALMERSTON NORTH

University

Dr. L. F. Blackwell. Variable kinetic isotope effects in base-catalysed elimination from the β-phenethyl bromide system.

Drs. L. F. Blackwell, K. W. Jolley and P. D. Buckley. NMR studies of hydrogen bonding in model systems containing amide functions.

***Professor R. Hodges.** Organic mass spectrometry; the mechanism of electron-impact induced fragmentation of molecules; structural studies on biological molecules.

Dr. E. L. Richards. Carbohydrate chemistry; the interaction of amino compounds with sugars; isolation and structural studies on pasture polysaccharides; a study of the complexing of divalent cations with plant constituents.

Dairy Research Institute

*Studies of aspects of organic and biochemistry connected with milk, cheese and butter, and derived products; the triglyceride structure of milk lipids; free fatty acids in New Zealand Cheddar cheese; casein studies.

Mr. C. R. Southward. Chemical and physical properties of casein and other milk proteins.

D.S.I.R. Applied Biochemistry Division

Dr. R. W. Bailey. Composition of extracellular polysaccharides of Rhizobium bacteria; monosaccharide composition and identity; mannose polysaccharides in fern cell wall polysaccharides; polymer mannose occurrence and correlation with fern classification; lignin-carbohydrate links in plant cell walls; development of methods of extraction and fractionation of plant polysaccharides.

Drs. R. W. Bailey and G. Roughan. Polysaccharide mucilage of *Entellia aborescens* leaves; structure and monosaccharide composition.

Mr. R. P. Hansen. Isolation and identification of trace fatty acid constituents (including branched-chain fatty acids) from meat fats, milk fats and other fats of animal, plant and marine origin; periodical investigation of the lipids of human and animal tissues to determine if any particular disease is associated with a specific fatty acid, as is the case with Refsum's syndrome; isolation and identification of fatty acid constituents of pine wood and tall oil.

Dr. G. B. Russell. Isolation, characterisation and structural elucidation of insect hormones from plant and animal sources.

Dr. G. B. Russell and Mr. P. Fenemore. Physiological studies of insect hormones.

Dr. E. Wong. Plant phenolic compounds of biological interest; biosynthesis of the flavonoid and isoflavonoid groups of natural products; flavour studies on lamb and mutton.

WELLINGTON

University

Dr. J. T. Craig. Synthesis of new carbocyclic and heterocyclic aromatic systems, particularly condensed polycylic compounds containing a seven-membered ring.

Dr. B. Halton. The synthesis and properties of strained and fused ring systems; small ring compounds, non-benzenoid aromatics, photochemistry.

Associate Professor W. E. Harvey. Synthesis of substituted cyclohexanes and carane derivatives.

Dr. R. W. Hay. Mechanisms of organic reactions in solution with particular reference to the hydrolysis of carboxylic phosphate and sulphate esters; the hydrolysis of glycosides and peptides; decarboxylation of β-ketoacids; metal ion catalysis of organic reactions, particularly those of biological importance; model enzyme systems and enzyme chemistry, e.g. model systems for metalloenzymes with esterase and peptidase activity.

I.C.I. N.Z. Ltd., Lower Hutt

Mr. D. V. Madle. Chemistry of formaldehyde based resins; terpene chemistry relating to products from turpentine.

CHRISTCHURCH

University

Professor J. Vaughan, Drs. J. W. Blunt, J. M. Coxon, D. A. R. Happer, M. P. Hartshorn, M. G. H. Munro, K. E. Richards and G. J. Wright. The major fields of investigation include:

(i) Structure-reactivity relationships and reaction mechanisms in selected aromatic substitution reactions; reactions of quinonemethides; reactions of hydrazide derivatives with electrophiles; organic mass spectrometry.

(ii) Molecular rearrangements of alicyclic and related model systems.

(iii) Biosynthesis and reactions of diterpenes, calciferol and related compounds.

Specific topics under study by research students comprise the following: Reactions of acyclic epoxides, steroid epoxides, 1, 1 disubstituted ethylene oxides, epoxides with neighbouring nucleophiles; rearrangements of bicyclicmonoterpenes, steroids of unnatural configuration, steroid epoxides, α- and β-amyrin derivatives, diterpenes, and 5-α-oxygenated steroids; BF_3 catalysed rearrangements of 12-phenyl-11, 12-epoxy steroids; biosynthetic studies of tetracyclic diterpenes; pinane monoterpenes and derivatives; reactions of exocyclic methylene compounds, organic sulphur-sulpher bonds, α-halogenoesters with trialkyl phosphites, and phenylhydrazine with isothiocyanates; aromatic nitration; displacement reactions of carbon-silicon bonds; carbonium ion chemistry; substituent effects in the mass spectra of aromatic compounds, polyolefin hydrogenations; base-catalysed cleavage of phosphonium compounds; hydrogen exchange in aromatic ethers; synthesis of monosubstituted benzils; alkylation of phenylhydrazine.

LINCOLN

Wool Research Organisation

Dr. I. L. Weatherall. Isolation and analysis of ϵ-N-methyllysine from sheep plasma; isolation and characterisation of proteins from wool roots and wool root cells; studies on the synthesis and reactivity of optically active 1,3,2,-dioxaphosphorinanes and phospholanes; development of gas-chromatographic methods for amino acid analysis.

DUNEDIN

University Pharmacy Department

Dr. G. F. Laws. Preparation of model compounds, especially new amino acids, which may elucidate membrane transfer mechanisms.

Mr. R. H. McKeown. Structure-reactivity relationships in heterocyclic compounds containing the imide group; analytical studies on drugs; investigation of some barbituric acids; detection and analysis of ouabain (one of the toxic principles of an arrow poison); periodate oxidation applied to the estimation of drugs containing vicinal amino-hydroxy functions; phenyl-group detection in drug molecules; pharmacologically active substances in *Urtica ferox.*

Chemistry Department

Dr. D. Brasch. Chemistry of the main polysaccharide systems present in N.Z. woods, especially *Pinus radiata;* the reactions of the hemicelluloses in technical pulping processes; structural analysis of the glucuronoxylan from *Pinus radiata;* reactions of this polymer during pulping.

Dr. A. D. Campbell. Analysis of organic compounds containing metals and other interfering elements; synthesis and characterisation of substituted hippuric acids and sulphate esters; synthesis of high molecular weight derivatives of ethylenediaminetetraacetic acid.

Professor R. E. Corbett. Structural elucidation and synthesis of extractives from New Zealand plants with particular emphasis on triterpenoids from *Sticta* lichen and di- and sesquiterpenoids from essential oils.

Dr. P. K. Grant. Synthesis and transformations of diterpenes; microbial oxidations of diterpenes; utilisation of New Zealand natural products; stereochemical and conformational studies in fused cyclopentane systems.

Dr. M. R. Grimmett. Thermally-induced rearrangements of 1-substituted imidazoles; separation and estimation of mixtures of N-substituted and C-substituted imidazoles; application of Bredereck's formamide synthesis to the preparation of alkyl-substituted imidazoles and oxazoles; synthesis of isomeric 2- and 4-substitued imidazoles for NMR and mass spectrometric (with Professor R. Hodges) studies; the reaction of ammonia with simple α-dicarbonyl compounds.

CAMBRIDGE, U.K.

University Chemical Laboratory

Dr. K. M. Baker. Synthesis of sex attractants of *Pectinophora gossypiella;* structure elucidation of peptides and antibiotics using computer-aided interpretation of mass spectra; mass spectrometry of nucleotides and nucleosides..

COUNCIL NOTES

Council approved the establishment of specialist groups for Organic Chemistry (Chairman, Professor R. E. Corbett and Secretary, Dr. M. R. Grimmett), for Analytical Chemistry (Chairman, Dr. R. R. Brooks) and for Biochemistry.

One hundred reprints of the Salary Survey (1969) will be printed for distribution outside the Institute.

Further discussions with Officers of the Chemical Society has resulted in the following: That the N.Z.I.C. will offer every possible assistance to the Chemical Society in distributing notices, advertising material, etc., and by mentioning, when requested, Chemical Society matters in the N.Z.I.C. Journal. The Chemical Society will accord to N.Z.I.C. members visiting the U.K., on production of a letter of introduction from the Registrar of the N.Z.I.C., the right to use the Society's Library and to register for all Chemical Society meetings at the Chemical Society's Fellows rate.

BRANCH NEWS

Auckland

Branch Meeting

The Chairman's Address was delivered by Dr. J. Rogers on 24 March to a gathering of 38 Fellows and Associates, and 8 members of the Australasian Institute of Mining and Metallurgy. Dr. Rogers spoke on *Minerals and Agriculture* and covered the broad historical and economic factors leading to the present close relationship between agricultural production and artificial fertilisers based on phosphorus and sulphur minerals. The significance of recent mineral discoveries (Maui oil and Taupo sulphur) and the development of mineral industries (steel smelting, aluminium extraction, and the exploitation of Christmas Island phosphate ones) was discussed.

A record number of 17 applications for membership of the Institute was dealt with at the April meeting of the Branch committee.

Chemists on Safari

The Waikato and Auckland Branches jointly organised a coach tour of the Rotorua-Taupo region on the weekend of 11-12 April. The party of 29 members and wives included 2 guests from the Australasian Institute of Mining and Metallurgy: Miss B. E. Jacka and Mr. G. B. O'Malley. Dr. W. M. H. Saunders, Chairman of the Waikato Branch, conducted a brief tour of the Ruakura Agricultural Research Centre and then proceeded to comment on the topography, soil types, fertiliser problems and agricultural methods of the farming country through which the party travelled. At Kinleith members were entertained at lunch by N.Z. Forest Products Ltd.; this was followed by a tour of the timber and paper mills led by Dr. A. F. Wilson, Technical Superintendent, and members of his staff. Particular interest was shown in the manufacture of chemicals such as chlorine, chlorine dioxide, lime, sodium sulphide liquors and turpentine.

The party spent Saturday night in Rotorua where an evening launch excursion to Mokoia Island was enjoyed by all. The following morning Dr. G. M. Will showed the party through the Forest Research Institute. The tour continued south with visits to the Waiotapu, Broadlands and Wairakei thermal areas. Mr. W. A. J. Mahon and Dr. Finlayson of Chemistry Division, D.S.I.R., accompanied the party through the region and described the exploration, geochemistry and development of geothermal power resources.

The members of the party are grateful to all those who made available their time and expert knowledge to describe the points of scientific interest in this part of the North Island. Particular thanks are due to the Auckland Chairman, Dr. J. Rogers, who did so much to make the tour interesting and enjoyable.

University of Auckland

At the Graduation Ceremony held on 8 May Ph.D. degrees in Chemistry were conferred on J. P. Bartley, Valerie F. Carlisle, D. R .Crump and D. Shooter. There were 14 M.Sc. graduates in Chemistry. Mr. J. C. Hawthorn, M.Sc., was among the first group to be awarded the new Diploma in Business and Industrial Administration.

Dr. D. J. Spedding has returned from 2 years research at A.E.R.E., Harwell, to resume his lectureship.

Major research instruments recently acquired by the Department of Chemistry include a Varian T60 Nuclear Magnetic Resonance Spectrometer, a Hilger-Watts Automatic X-ray Diffractometer with a PDP/8 Computer, a Tricarb Scintillation Counter, and a Chemical Electronics TR70/2A Potentiostat. A Varian CH7 Mass Spectrometer is on order.

Nelson

Dr. J. R. L. Walker has resigned from the staff of the Cawthron Institute, Nelson, in order to take up a Senior Lectureship in the Department of Botany, University of Canterbury; there he hopes to specialise in plant and microbial biochemistry.

Canterbury

Dr. J. R. L. Walker has been appointed Senior Lecturer in the Botany Department, University of Canterbury. He was formerly Senior Biochemist at the Cawthron Institute, Nelson.

Mr. M. S. Carrie has been appointed Research and Development Manager for Canterbury Frozen Meat Co. Ltd., Christchurch. Mr. G. M. Keeley succeeds Mr. Carrie as Chief Chemist.

The 1970 "Chemistry in Action" lecture was delivered in Christchurch in April by Dr. D. E. Wright of Ruakura Agricultural Research Centre. His lecture was entitled "The Tale of a Toxin".

CORRECTION

Auckland Branch Chairman 1969/70

Dr. John Rogers is Chairman of the Auckland Branch. In the April issue of the *Journal* (p. 53) his name was incorrectly spelt.

COMMERCIAL NEWS

VARIAN NOW MARKETING HIGH PRECISION ROTARY MOTION SAMPLE MANIPULATORS

Three models of High Precision Rotary Motion Manipulators are now offered by the Vacuum Division of Varian Associates. Although designed primarily for positioning crystal samples in Varian Surface Research Systems like LEED and Auger Spectrometers, these manipulators can be used as precise locating devices in other vacuum systems.

The manipulators have full 360° precision rotation readable and resettable ±0.1°. Micrometer translations on X and Y motion are repeatable to better than 0.1 mm, readable to 0.01 mm and have less than 0.005" run out at shaft tip. The Z motion is single-screw driven and has a scale with 0.5 mm divisions. The manipulators are bakeable to 250°c and feature high quality bellows-sealed construction. Permanent dry lubricant throughout the device assures compatibility with ultrahigh vacuum.

The basic model manipulator features Rotary Motion and 2-¾" O.D. ConFlat® Flange mounting. Two other models, the Rotary Motion and X, Y, Z Manipulator with Flip Mechanism, Sample Holder and Heater Assembly are compatible with systems that will adapt to 6" O.D. ConFlat Flange mounting. On the latter two models it is possible to have the simultaneous use of four electrical feedthrough ports which are located around the 6" mounting flange. The ports have convenient Mini-ConFlat Flanges.

The Flip Mechanism is integral with the rotary motion and has a tilt motion regardless of shaft position. Its rotation (axis perpendicular to shaft) is 100° total. Position repeatability is ±0.5°.

The Indirect Sample Holder and Heater Assembly is designed to allow measurements of LEED and Auger intensities at elevated temperatures. A toroidally-wound coil radiantly heats the sample to 1200°c. The Sample Holder is insulated from its supports and accommodates samples up to 6 mm diameter.

To obtain data sheets describing High Precision Manipulators, write Varian, Vacuum Division, 611 Hansen Way, Palo Alto, Calif. 94303.

Further information is available from Geo. W. Wilton and Co. Ltd., P.O. Box 367, Wellington.

"THE LABORATORY ELECTROMAGNET AND ITS APPLICATIONS"

Free booklet from Varian

"The Laboratory Electromagnet and Its Applications", a 37-page booklet prepared and published by the Varian Analytical Instrument Division, is now available free of charge to physicists, chemists, biologists and engineers.

Through simple qualitative discussions the booklet acquaints the reader with the basic features of the laboratory electromagnet, its principle applications and the terms which describe the electromagnet's performance. References are furnished throughout for readers who wish to study an application in depth.

A complimentary copy of the booklet can be obtained by writing to Geo. W. Wilton and Co. Ltd., P.O. Box 367, Wellington.

A NEW HIGH PERFORMANCE, LOW COST INFRARED INSTRUMENT FROM PYE UNICAM

A breakthrough in performance and cost has been achieved by Pye Unicam Ltd. of Cambridge with their new infrared spectrophotometer.

The new instrument, known as the Unicam SP1000, is a double beam recording spectrophotometer offering exceptional standards of performance coupled with first class presentation of spectra for a wide range of infrared techniques and sample types.

Dual scanning speeds are provided to cover the wide spectral range of the instrument; 625—3800cm^{-1}. Using the fast scan speed, high quality, full range spectra are obtained in only two minutes. For work of the highest precision, or for accurate recording of high resolution spectra, a second, slow scanning speed, taking five minutes twenty seconds, may be selected at the push of a button.

Accurate recording of the true profile of absorption bands is achieved using a high resolution monochromator. The SP1000 employs an Ebert grating monochromator, chosen for its excellent dispersion and low aberrations. The resolution obtained by the instrument approaches that found on more expensive models and ensures that a true spectrum is obtained for reliable qualitative analysis. The high resolution also enables quantitative measurements to be made on sharp absorption bands. Accurate quantitative work is also facilitated by the good stray light characteristics of the monochromator. Spectra are recorded on the new integral, precision strip-chart recorder. A very fine trace is obtained by the use of a cartridge loading type wet-ink pen which writes clearly even at high pen speeds during fast scanning. Location of the charts is simple, and once the first chart is correctly positioned, the subsequent charts on the role are automatically aligned.

The ruled area of each chart is 15 x 39 cm, pre-calibrated linearly in transmittance and wavenumber. Space is provided for the insertion of data relating to the sample and recording conditions. The large chart permits the resolution capability of the instrument to be fully utilised over the whole range, particularly below 2000cm^{-1} at which point there is a 3X wavenumber scale change. A manual advance control permits the scan to be started at any chosen wavenumber and provides rapid manual scan facilities.

A wide range reference beam attenuator is built into the SP1000 permitting the recording of excellent spectra of samples where the energy loss is high, e.g. in ART work, microsampling, etc. Operation of the attenuator automatically regulates the amplifier again to maintain constant recorder pen

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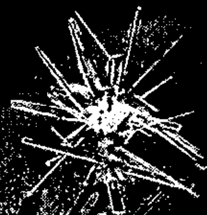

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response. This feature overcomes the need to purchase a separate beam attenuator in most cases.

The high performance offered by the SP1000 is substantially due to the quality of the detector employed. This new detector, the Unicam IR50 Infrared Detector, is of the pneumatic type and incorporates full solid state circuitry. The high sensitivity of this type of detector means that little amplification of its output is required resulting in an excellent signal to noise ratio. The detector is effectively a black body and is uniformly sensitive over the full infrared region, its range of response being limited only by the window material employed. The excellent sensitivity has also allowed the monochromator slitwidth to be reduced resulting in improved resolution. A high degree of ruggedness is achieved due to the large sensitive area of the detector eliminating the need for critical alignment.

A very important factor, which users of this instrument will appreciate, is that no operator skill is required. The design incorporates only four controls and inexperienced staff can effectively use the SP1000 after only a few minutes of instruction. The chart paper roll is located and, after switching on, it is only necessary to select the required scan speed, adjust the 100 percent T level, and select 'scan' to record a full range infrared spectrum. After the completion of each scan the instrument automatically resets to synchronise the monochromator with the beginning of the next chart grid and a new scan may be started immediately.

For further information contact Philips Professional and Industrial Division. Head Office: P.O. Box 2097, Wellington. Branches: P.O. Box 5124, Auckland; P.O. Box 1488, Christchurch.

BOOK REVIEW

Introduction to Organic and Biological Chemistry. By John R. Holum (John Wiley and Sons Inc., New York, London, Sydney, Toronto, 1969). Pp. 610. NZ$10.45.

This book is the author's suggestion for a changed organic chemistry course oriented towards the life sciences. It was written for those going in for medical technology, nursing, nutrition, physical therapy and other paramedical occupations, or for agricultural science and high school teaching. It is, as it claims, an introduction; it is a general purpose book and not intended for the professional organic chemist. It gives very good coverage of the syllabus for the N.Z. Certificate of Science Biochemistry I course.

The early parts of the book follow the usual pattern of organic texts starting with aliphatic and aromatic compounds and working through alcohols, amines, aldehydes, carboxylic acids and other related compounds. Reaction mechanisms are well discussed as 'tools for illuminating biochemical reactions at the molecular level of life'. Then follow chapters on the carbohydrates, lipids and proteins, the latter including discussion of primary, secondary and tertiary structures and also a well illustrated account of Davies' theory of muscle contraction chemistry. The last half of the book is concerned with the 'molecular basis of human uniqueness'. Chapters on biochemical regulation and defence and the important fluids of the body involve discussion of enzyme action, hormones, vitamins and chemotherapy. 'Energy for Living' brings in chapters on the metabolism of carbohydrates, lipids and proteins; finally a chapter on the chemistry of heredity rounds off the book with an account of the work which aims to provide a molecular basis for the way in which the uniqueness of species is maintained.

The book is well set out and a pleasure to read. Molecular structures are clearly drawn; separate tables provide convenient summaries of, for instance, the conditions causing denaturation of proteins; the historical background is kept apart in clearly defined inserts. An understanding of what chemistry is occurring and whereabouts in the body is greatly helped by good sketches of things such as fluid exchange processes in capillaries, the structure of mitochondria, the step by step growth of a polypeptide chain and, of course, the DNA double helix. There are accounts of topics of general interest such as diabetes, sickle cell anaemia and phenylketonuria. Each chapter contains exercises and problems, and references to relevant books and recent review articles—often in *Scientific American*—are given.

G. S. McNaughton.

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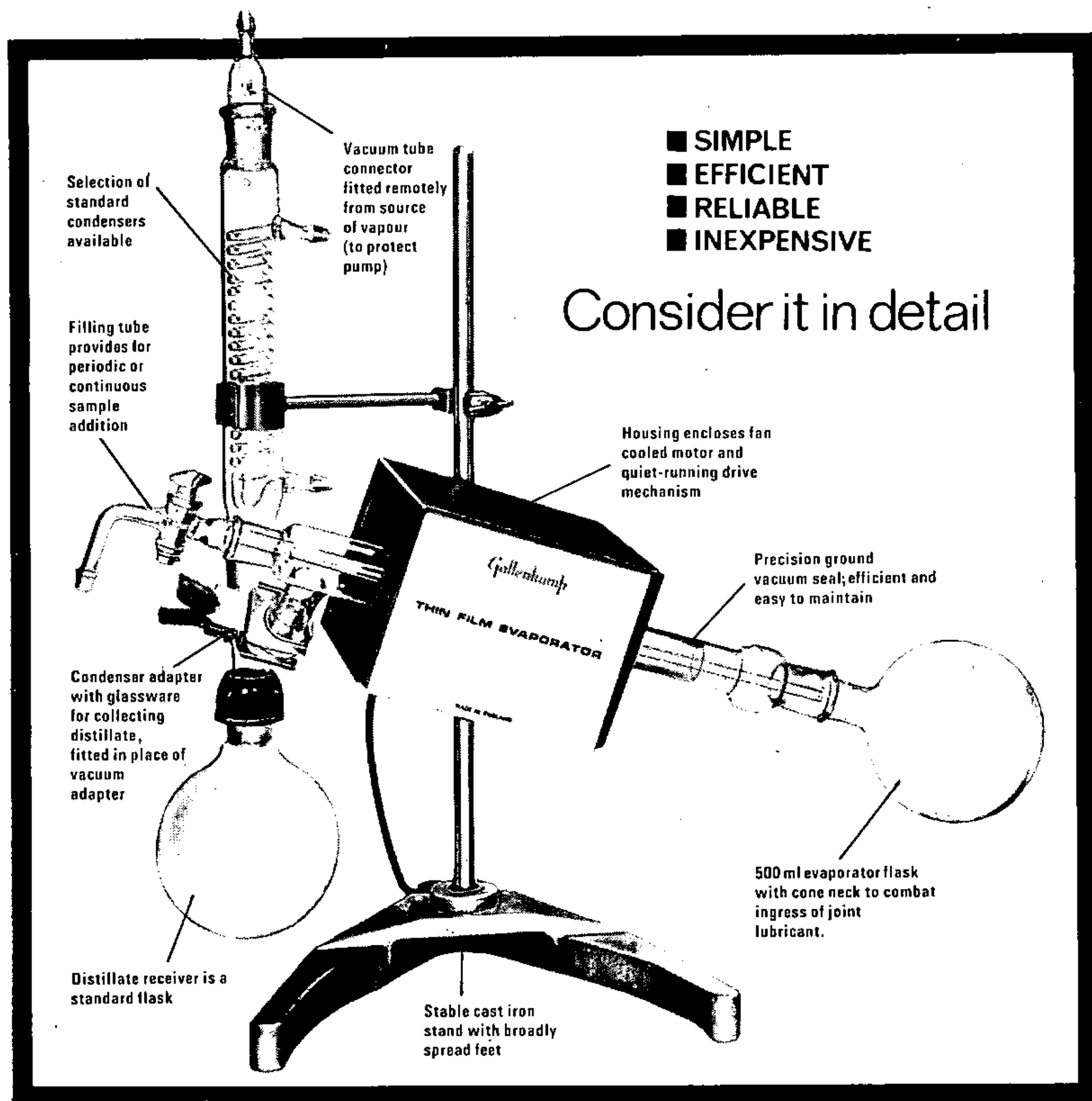

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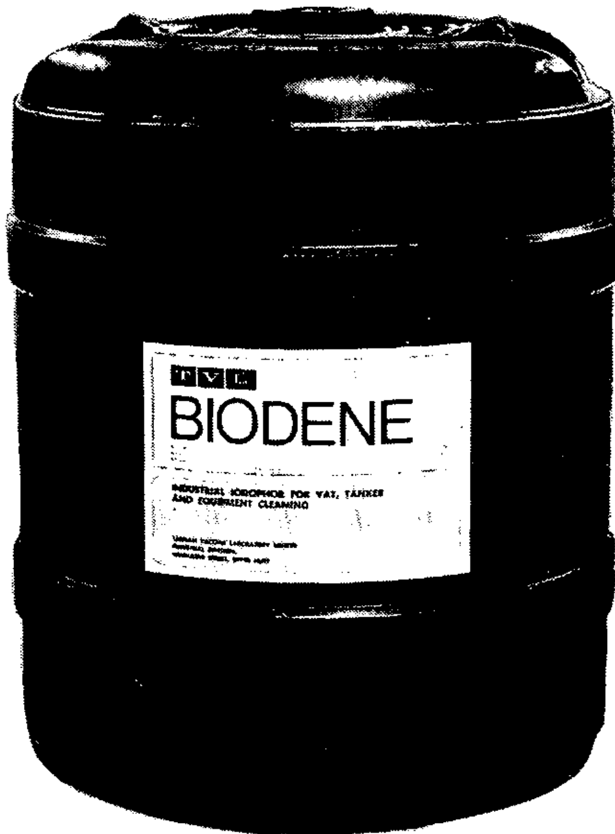

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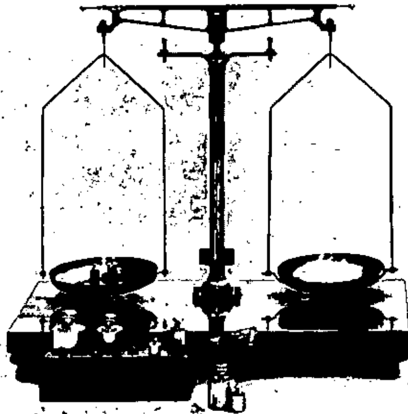
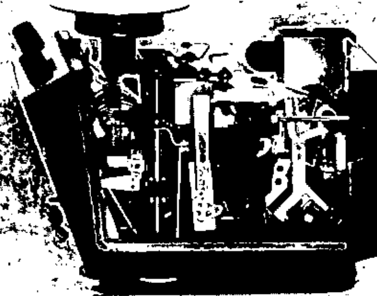

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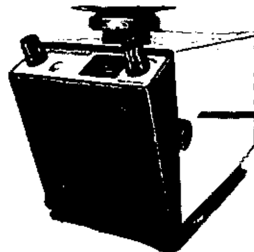

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