cultivation originated in those areas. The presence of a large number of varieties was explained by the view that the plants have had a longer time in their original home in which to vary. Whether this is true or not, it seems clear from the information published that the areas in which the greatest specific and varietal diversity are found, are the mountain regions of the tropics and warm temperate regions, while the varieties in the lowlands are much less numerous even though extensive cultivation has been carried on, as in Egypt, for a very long period. Thus Vavilov found sixty varieties of *Triticum vulgare* in Afghanistan, fifty-two in Persia, forty-six in Baluchistan, while India has thirty-two, Mongolia thirty-one, and Italy twelve. In Afghanistan, fifty varieties of *Triticum compactum* were also found, and many of these wheat varieties were endemic. The *durum* group of wheats showed its greatest diversity in Abyssinia, where there are many more forms than in Egypt or North Africa.

By similar work, Vavilov distinguished seven or eight centres in which crop plants show such variety as to suggest that they may be considered as the foci of world agriculture; almost all these are on high mountains or plateaux, not more than 40° from the equator. In addition to Afghanistan and Abyssinia, the mountains of Central America from Chile to Mexico are very rich in varieties of maize, potatoes, beans, all of which are grown up to 12,000 ft. in Peru[19], cotton and fruit trees, as well as forms like the agaves and many of the ornamental plants of our gardens. Other centres are the southern ranges of Caucasus, the south-eastern Himalayas, Asia Minor and Portugal, together with a tract in western China not yet localised. In most of these areas cultivation has not, so far as we know, been very extensive compared with that in many lowland regions of the world, and if there was no external cause of variability at high altitudes one would expect the greatest number of variations to appear in the areas where crop production had been most extensive and the chances of mutation consequently greatest.

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(*To be continued.*)

Progress in Enzyme Chemistry*

THERE is once more definite progress in enzyme chemistry to report, largely due to the resumption of the study of enzymes from the purely chemical point of view. The appreciation on the Continent of the concept adumbrated by Willstätter that enzymes are composed of a colloid carrier, and of one or more specific active groups through which they are associated with or bound to the substrate on which they act, has opened the way for practical work which, inspired by the successful isolation by Sumner and by Northrop of highly active enzyme preparations in crystalline form, is affording some clues to their inner structure. Willstätter postulates the colloidal carrier as responsible for the catalytic activity and for the stability of the active group, which latter controls the specificity. Kraut has recently suggested the names *Agon* for the active group and *Pheron* for the carrier, which have been adopted by Oppenheimer in his books.

Willstätter's conception differs very little from that advanced by the Armstrongs so long ago as 1913, when the dual function of an enzyme in holding the hydrolyte and determining its hydrolysis was enunciated. According to them, the enzyme, which was a large colloid molecule with a particular, active centre, consisted of an acceptor together with an agent. The acceptor was

* This article is based upon (but much expanded) a paper read on September 6 by Prof. E. Waldschmidt-Leitz before Section B (Chemistry) at the Norwich meeting of the British Association.

compatible with the substance to be hydrolysed in such manner that a temporary attachment took place, whilst the agent was considered possibly to be a carboxyl or some other acid group of the colloid protein molecule. As this conclusion was based in the main on experimental work done with the enzymes which act as hydrolytic agents on carbohydrates, where the very highly specific nature of the enzyme in relation to the slightest change in structure of a glucoside is manifested, due consideration had to be given to the necessity for the structure of the acceptor corresponding in every detail with that of the hydrolyte, that is, it had to be something more than a combination of a single grouping in the enzyme with the substrate, such as suffices for the attachment of a peptide. Accordingly a glucose unit was pictured as an integral part of the enzyme.

Urease, pepsin, trypsin and chymotrypsin, an enzyme which coagulates milk, have been obtained as active crystalline preparations which are proteins having the greatest similarity to one another, so that Northrop is inclined to believe the enzymes to be only proteins.

Waldschmidt-Leitz, who is to-day the active worker of the Willstätter school, only admits the protein to be the carrier of the real prosthetic group, and points out that invertase preparations of equal activity, but of different composition, can be obtained by altering the manner of purification.

The crystalline active urease withstands tryptic digestion but loses activity when its protein is more profoundly hydrolysed by the combined action of pepsin and trypsin. Experimental work has made it possible to divide the peptidases which hydrolyse synthetic polypeptides, though they do not attach natural proteins, into carboxy- and amino-poly-peptidases, dipeptidases and imino-peptidase according to the structural characteristics of the peptides on which they act. The dipeptidase and the amino-poly-peptidase attach themselves to the free amino group of the peptide, so that the presence of such group in the substrate is an essential before hydrolysis takes place. If it is acylated the enzymes are inactive. The removal or alteration of the carboxyl group has no effect. The action of the enzyme in such instances is to split off that amino acid which originally carried the free amino group.

The carboxypolypeptidase unites with the carboxyl group and splits off that amino acid which carries this group in the free state. It is suggested by Euler in particular that the haptophore group of the aminopeptidase is an aldehyde or keto group which definitely anchors the peptide through the formation of a Schiff's base.

Following union of enzyme and substrate, there is decomposition into free enzyme and the hydrolysed products. This is also attributed to a definite atomic grouping, namely, the imino group as a second point of attachment. In this connexion Bergmann has produced evidence that the substitution of the imino-hydrogen even by a methyl group makes the peptide resist the enzyme: whereas glycyl-glycine is split, glycyl-sarcosine is unattacked.

It is suggested that all peptidases have in common the power of uniting with the imino group of a peptide, but they differ in regard to the other group with which they first combine.

This theory, termed the Two Affinities theory, allows enzyme action to be explained as an ordinary chemical reaction between definite chemical groups and gives precision to the original additive compound theory advanced by the Armstrongs.

A further example is afforded by protaminase; that from the pancreatic gland requires a free carboxyl group in the substrate and its action splits off free arginine from the carboxyl end of the molecule, whereas trypsin acts on the protamines by dissolving the linkages between two arginine residues in the middle of the peptide chain of a protamine, this enzyme requiring neither a free amino nor a carboxyl group at the end of the chain.

The view that certain, if not all, enzymes are proteins is strongly represented by the American school, especially Sumner and Northrop. The former claims that urease is a crystalline globulin, whilst the latter associates peptic activity completely with crystalline pepsin: both refute work of Waldschmidt-Leitz and others to the contrary. Crystalline trypsin may be inactivated reversibly, or irreversibly, the former being accompanied by the formation of reversibly denatured protein. Crystalline chymotrypsinogen and chymotrypsin have been isolated from the pancreas: the latter crystallises in plates which, after three recrystallisations, showed no change in proteolytic activity. Warburg's yellow oxidation enzyme has been purified to a stage when it can be split into pigment and protein: the two components are inactive but when they are brought together, the activity of the enzyme is restored. On the basis of these facts, Sumner (*Science*, **78**, 335; 1933) considers that it is very unlikely there is any such thing as an enzyme carrier.

A recent discovery is the importance of the sulph-hydryl compounds such as reduced glutathione as activators in intracellular enzyme action. This is true both of proteolysis, for example, of papain and cathepsin, and also of arginase which brings about the hydrolysis of arginine into ornithine and urea. The co-operation of heavy metals like iron in the system appears to be helpful,

if not essential. It is believed from the work so far done with different sulph-hydryl heavy metal complexes that a dissociable compound of enzyme and activator is formed which has an increased affinity to the substrate. The alternative possibility that an active group in the enzyme itself is reduced is not favoured.

Strong evidence for the above theory is afforded by the specific co-glyoxalase action of glutathione, which has been recently followed quantitatively (NATURE, p. 645, October 19, 1935) by comparing lactic acid production with the amount of free —SH group as measured by iodine consumption. It is established that the glutathione first combines by means of this group with the substrate methyl glyoxal and then, as the reaction catalysed by the enzyme develops, enters into further changes which again involve its —SH group. In other words, the amount of free —SH group remains at a minimum during the reaction, but it all reappears when this is finished.

A second and quite different type of enzyme activation is produced by purely physical means. Certain substances which favour the splitting of fats and esters by animal lipase act through the production of colloidal particles which absorb both the enzyme and the substrate and facilitate the reaction between them.

It is established that the purified and recrystallised hæmoglobins of different animals, whilst containing identically the same hæmin, are made up of different globins. There is a quantitative difference between the peroxydase activity of such hæmoglobins of as much as 50 per cent under like conditions, which inasmuch as the active iron-porphyrin group is the same must be due to differences in the structure of the colloidal protein carrier.

It is clear that, for the moment, judgment between the rival carrier and protein theories must be suspended. The assumption of an active group or series of groups at the surface of the enzyme molecule, which definitely combines with the substrate in a normal chemical way, seems well founded. The subsequent hydrolysis of such addition compounds by other recognised groups in the enzyme molecule appears also to be highly probable: it is to be expected that experimental work, for which the way is indicated, will enable such groups to be identified. It remains to establish the structure of the groups in the enzyme which bring about its highly specific activity. This is especially desirable for the carbohydrases where the specificity is so fine; it is to be expected that the progress now being made with the inquiry into the protein splitting enzymes will be continued among the carbohydrases. To-day, however, there is the added complication to face, namely, that the enzyme so often seems to require additional help from some other substance.

Earthquake-proof Buildings

By Dr. Charles Davison

ONCE more, the recent Quetta earthquake has emphasised the importance of erecting none but earthquake-proof buildings in a district subject to destructive shocks. The few houses in Quetta that could lay claim to such a title seem to have survived the earthquake unharmed, not even their chimneys having been thrown down.

How needless the loss of life may be was strikingly shown by Prof. Omori[1]. During the Mino-Owari earthquake of 1891, only 190 persons were killed in Nagoya, a city with a population of 165,000. In the earthquake of 1908, Omori estimated the number of lives lost in Messina as 75,000, the intensity of the shock being nearly the same in both cities. Taking the population of the Messina district as about equal to that of Nagoya, he thus concluded that, out of every thousand persons killed in Messina, 998 lost their lives needlessly, owing to the faulty construction of the houses. Omori's estimate of the number of deaths has been much reduced in later reports on the earthquake. But, even if we take the lowest figure of 25,450, given by Baratta, and the previous population as 90,000, the number 998 is only reduced by 2*.

The influence of site on intensity is shown in every earthquake. In the California earthquake of 1906, the distribution of damage was studied with unusual care in several districts, and especially by Mr. H. O. Wood in San Francisco[2]. The whole of the city lies between about one and nine miles on the north-east side of the San Andreas rift, and thus, if there were no variation in the site, the intensity should have decreased gradually from south-west to north-east. The areas of lowest intensity, in which a few chimneys fell, lay

* It should be remembered, however, that the Messina earthquake occurred at 5.20 a.m., and the Mino-Owari earthquake at 6.37 a.m., both local times.