later, the animals were killed and complete serial sections prepared through the whole of the olfactory cavity in order to determine the regional distribution of retrograde degeneration in the olfactory epithelium. A preliminary study of these sections now makes it clear that there is certainly some degree of regional projection of the olfactory epithelium on to the bulb in the rabbit, and that the inference made on the basis of the earlier material of Clark and Warwick was premature.

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## Stability of some Metal Complexes of Histidine

IN the course of measuring the stability constants of internal complexes formed by the combination of a number of different bivalent metal ions with a series of α-amino-acids, including histidine, it was noticed that the last-named substance formed complexes that were much more stable than those of any other amino-acid studied.

The overall stability constant $(K)$ for some of the different metal α-amino-acid complexes in water at $25°$ C. was determined by measuring the individual step reaction equilibrium constants :

$$Me^{++} + A^- \xrightarrow{k_1} Me^+A$$
$$Me^+A + A^- \xrightarrow{k_2} MeA_2,$$
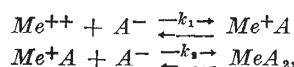
where $Me^{++}$ is the bivalent metal ion and $A^-$ is the ligand (α-amino-acid). The overall stability constant of the complex $MeA_2$ is given by the relation $K = k_1.k_2$. Some values obtained for log $K$ are shown in the accompanying table.

| | Histidine | Glycine | α-Alanine | Valine | Leucine |
|---|---|---|---|---|---|
| Cu | 18·33 | 15·42 | 14·83 | 14·45 | 14·34 |
| Co | 13·86 | 8·94 | 8·78 | 8·24 | 8·26 |
| Zn | 12·88 | 9·72 | 9·50 | 9·10 | 8·93 |
| Mn | 7·74 | 6·63 | 6·05 | 5·56 | 5·45 |

In the table, the order of the metals as regards the stability of their complexes is similar to that already noted with other ligands[1-4]. The interchange of the positions of the metals zinc and cobalt with some ligands has been noted previously[5].

If the complexes of any one metal are considered, it will be seen that the stability constants of the complexes formed with the α-amino-acids glycine, alanine, valine and leucine are of much the same order ; the stability of the histidine complex, however, is much greater than any of these. This suggests that histidine is attached to a metal atom by groups different from those involved in the co-ordination of the other amino-acids. The latter are attached through carboxyl and amino-groups[6], the former probably through amino- and imino-groups[7].

In a study of the inhibiting effect of cobalt on various aerobic and anaerobic organisms and tumours, Burk and his collaborators[8] observed that, of a number of amino-acids tested, histidine and two of its derivatives were able to nullify the inhibiting effect

of the metal. The data reported in the table provide, to some extent, a quantitative basis for the explanation offered by these authors[8] for the mechanism of the nullifying action of histidine. The two series of amino-acids studied were not identical, and further information on the stability constants of metal-amino-acid and other complexes is required before inhibiting actions like the above can be understood in detail. It is evident, however, that similar compounds which are capable of forming complexes of the same order of stability as those of histidine should be equally effective in overcoming the inhibiting effect of metal ions.

A fuller account of this work will shortly be published in the *Australian Journal of Scientific Research*.

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## Additive Effects of Substituents

THE present practice of analysing data relating to reaction-rates in solution in terms of the parameters of the modified Arrhenius equation,

$$k = PZ \exp - E/RT,$$

has led to a more complete understanding of the way in which polar substituents affect chemical reactivity by focusing attention on the fact that the differences in rate may arise through changes in the energy of activation or in the entropy of activation (non-exponential term) or in both. Among the several reactions investigated, a number have been found in which the differences in rate can be accounted for almost entirely by changes in the energy of activation, variations in $PZ$ in comparison being almost negligible.

Three such reactions are (I) the nuclear chlorination of phenolic ethers[1], (II) the benzoylation of anilines[2], and (III) the alkaline hydrolysis of ethyl benzoates[3]. Hitherto, in both the benzoylation of anilines and the hydrolysis of ethyl benzoates, investigations have been confined to the study of the influence of a single substituent in the benzene nucleus. Only in the first reaction, the chlorination of phenolic ethers, were the influences of two or more substituents determined. The rates of reaction of some two hundred ethers have been examined, and the important conclusion was reached that in ethers of the types $p-RO.C_6H_4.X$ and $RO.C_6H_3.X_2$ the effects of the groups $R$ and $X$ are additive.

The recent publication[4] of the results of a study of the rates of benzoylation of twenty-one disubstituted anilines in which it was found that "the resultant effect on the activation energy of two substituents in the same benzene nucleus is very closely the sum of their individual effects" is important, since it provides new and valuable evidence for the additive effect of substituents.