

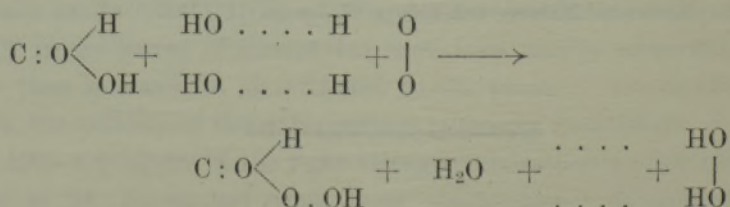
Studies on Enzyme Action. XXIV.—The Oxidase Effect and the Phenomena of Oxidation in General: Carbonic Oxide.

By HENRY E. ARMSTRONG, F.R.S.

(Received March 2, 1925.)

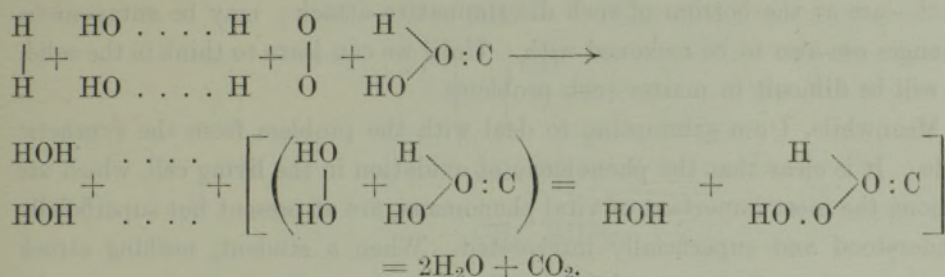
In 1904 I presented a brief communication to the Society on "The Retardation of Combustion by Oxygen" ('Proceedings,' vol. 74, p. 86). Friends smiled at the title and no notice has been taken of my argument. Of late years, however, Moureu and his fellow-workers have brought before the French Academy a series of masterly studies of the inhibition of the oxidation of highly oxidisable materials, such as acrolein and linseed oil, by substances which are themselves oxidisable, including phenol and potassium iodide. The explanation they have put forward, involving the recognition of an active antagonism between peroxides, which constitute a reversing mechanism, is essentially that I have long held, the difference being mainly that I have gone more fully into the details of the process. In a recent fascinating brief communication to the Chemical Society ('Chem. Soc. Journ.,' 1925, p. 1), Moureu and Dufraisse discuss the stoppage, by carbonic oxide, of the interaction of hydrogen and oxygen, at a platinum surface, contending that this also is an instance of inhibition owing to the antagonism of incompatible "peroxides," formed in the initial stages of change. I fully share their views and regard this communication as the settlement of a problem of prime importance which has been open to solution since early in last century (1833).

I have discussed the peculiar "indifferent" behaviour of carbonic oxide on many occasions before the Society and elsewhere. I would now take one further and perhaps final step, and proclaim it to be *per se* an incombustible gas. If the process of combustion be, as I have frequently argued, one in which an electrolytic determinant is concerned (comp. First Messel Memorial Lecture, 'Soc. Chem. Ind.,' 1922, pp. 253-270r), primarily as represented by the schematic equation



it is one involving the electrolysis of water, and the "energy" developed in the interaction must be at least equal to that involved in the combustion of hydrogen. Actually, the heat of combustion of carbonic oxide is below that of hydrogen (67960 : 68360).

Therefore, the change should not take place. An explanation may be found in the assumption that when a moist carbonic oxide mixture is sparked or fired, some hydrone is decomposed and sufficient hydrogen set free to act in a "depolarising" circuit together with the oxide, as thus:—



The observations on carbonic oxide made by Bone and his colleagues seem to me all to meet with a natural interpretation when considered from the point of view now advocated.

The Oxidase Effect.—Having dealt with hydrolytic enzymes, in a long series of communications to the Society, of late years, with its aid I have turned my attention to the even more mysterious class of intermediary agents, the *Oxidases*—using this term in its widest sense but excluding soluble "peroxides." The *Oxidases* are commonly regarded and usually spoken of as *Enzymes*.

The question to consider is, What is an Enzyme? I would say, first, a catalyst, a solid particulate agent, which has the faculty of attracting to and assembling upon its surface the substances whose interaction it promotes.

Second, a *strictly selective* catalyst—one that, in some way, corresponds in structure with the affected substance; in other words, one that fits upon it through absolute likeness, not merely as lock and key, as Emil Fischer suggested. Enzymes are so selective that, apparently, they act only upon like, never upon analogous, compounds. Thus *invertase* will hydrolyse both cane-sugar and raffinose—but raffinose is but cane-sugar with a galactose-glucose tail. The glucosides (a large class) all contain one glucose.

An Enzyme being thus defined, the *Oxidases* do not fall under the definition; they are but catalysts, which promote the oxidation of allied substances but not of like substances alone. *Tyrosinase*, for example, will determine not only the oxidation of Tyrosin (to Melanin) but also of a number of phenols.

The only instances of apparently selective oxidation, presumably by Oxidases, are those afforded by *Bacterium aceti* and *B. xylinum* and by *Xanthin oxydase*, which last affects both Xanthin and Hypoxanthin but none of the allied compounds.

Bacterium aceti is entirely peculiar in that it promotes the oxidation of ethylic and propylic alcohols but not of methylic and isopropylic. In absence of all precise knowledge of the process, it can only be supposed that either peculiarities in configuration of the molecules or energy differences—perhaps both—are at the bottom of such discriminative attack; may be antagonistic changes are also to be reckoned with. Until we can learn to think in the solid, it will be difficult to master such problems.

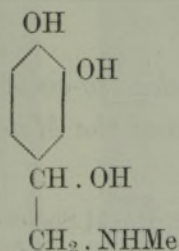
Meanwhile, I am attempting to deal with the problem from the synthetic side. It is clear that the phenomena of oxidation in the living cell, which are among the most important of vital phenomena, are at present but superficially understood and superficially interpreted. When a student, nothing struck me so much as the production of molecular oxygen from atomic oxygen by the interaction of oxides—*e.g.*, hydrogen peroxide and silver oxide, hydrogen peroxide and permanganate. The intense affinity of oxygen for oxygen, thus made obvious, has always been before my eyes. To-day, no one thinks in terms of oxygen—only the hydrogen ion is considered: we fail to see that the Giver-of-Life is also the Giver-of-Acidity and, through water, the connecting link in the vast majority of chemical changes.

Addendum.—March 12, 1925.

Vital Oxidation Phenomena.—The extent to which the inhibition of oxidation is of vital significance is yet to be appreciated. Moureu and Dufraisse have, indeed, pointed out the possible bearings of their work and have dealt very generally with the problem; Moureu has even suggested that thyroxin may act by controlling oxidation. I have long believed and taught that hydrogen cyanide kills because it stays oxidation at nerve centres. At present, we have no explanation of the manner in which the functions of the various secretions of endocrine organs are exercised, and even more mysterious are the aditants in food, which now figure so largely in all discussions on nutrition. It has long seemed to me important to attempt, in the first place, to explain the function of a substance of known origin and localised activity, and of established chemical structure, such as Adrenaline; if we cannot account for the special behaviour of so simple a substance, we are not likely to be able to deal with agents of more complex character.

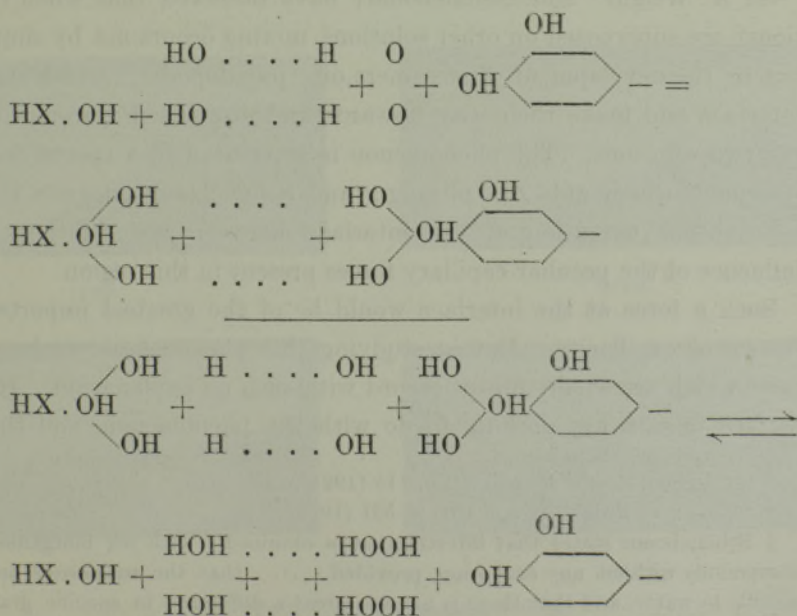
Adrenaline is remarkable in that it causes constriction of the blood vessels, even when used in very high dilutions, its efficiency being far above that of any other substance producing a like effect, including its optical opposite, δ -adrenaline. It is a product of the sympathetic system and it acts especially upon the sympathetic system. We may well suppose that it is specially attracted to sympathetic centres in virtue of the structure of its asymmetric centre, if not of the molecule as a whole.

Adrenaline is a derivative of Pyrocatechol of the formula



Pyrocatechol is one of the substances that Moureu and Dufraisse have found to be most active in antagonising oxidation.

The possible action of Adrenaline may be pictured as follows:—



The superior activity it exhibits may be referred to the fact that, by fitting

the sympathetic centre, enzyme-like, it specially controls oxidation at the centres. This explanation may at least serve to direct further inquiry, not only with adrenaline. I would venture to suggest that it may be worth while to consider whether phloridzin-diabetes, always a matter of wonder to me since I became aware of the peculiar action of the glucoside, may not be the consequence of inhibited oxidation.

An Explanation of the so-called Intertraction Phenomenon between Solutions, and the Molecular Significance of Negative Surface Tension.

By N. K. ADAM, M.A., Royal Society Sorby Research Fellow, and
G. JESSOP, Ph.D.

(Communicated by Sir William Hardy, Sec.R.S.—Received March 7, 1925.)

(PLATES 19–21.)

Sir A. Wright* and Schoneboom† have observed that when certain solutions‡ are superposed on other solutions, mixing occurs not by simple diffusion but by the development of streamers or “pseudopodia,” which start from the interface and make their way upwards and downwards through the body of the two solutions. The phenomenon is attributed to a special force, “intertraction,” which aids the mixing; and Schoneboom suggests that this is a spontaneous extension of the interface between the solutions, under the influence of the peculiar capillary forces present in this region.

Such a force at the interface would be of the greatest importance for the theory of capillarity. But in studying this phenomenon we have observed facts which are wholly out of accord with such an explanation. It seems that surface tension has nothing to do with the phenomenon, and that the two

* ‘Roy. Soc. Proc.’ B, vol. 92, p. 118 (1921).

† ‘Roy. Soc. Proc.’ A, vol. 101, p. 531 (1922).

‡ Schoneboom states that intertraction is obtained “with *all* inorganic and organic compounds without any exception, provided . . . that the substances are sufficiently soluble in water, and that there is not too great a difference in specific gravity between the upper and lower solutions.” The sequel shows that this is not the case, a definite difference in diffusivity between the dissolved substances in the upper and lower solutions being necessary for the phenomenon; it is also essential that the slower diffusing solution should be on top.