Comments and Communications

The Search for Truth Versus Bigotry

SELDOM have I read what is ostensibly so fine a statement of natural science in its ideal purity, and never one so misapplied, as that of Clarence W. Metcalf (SCIENCE, **113**, 696 [1951]). The title given his communication, "The Search for Truth," was taken in vain, for it was written to condone the withholding of truth from some school children. By generalities he sought to justify the New York state law—sponsored by a religious sect alleged to disbelieve in all disease—which exempts the children of this sect from school instruction in the science of health and hygiene.

"Who is to say what constitutes the 'truth' claimed for 'scientific laws . . . established beyond a doubt?' " So runs the query and academic discussion of this man who appears as the scientist-philosopher. "There is today no avenue of scientific investigation in which the intellectually honest scientist will assert that the theories on which current investigations are conducted have been 'established beyond doubt.' "

The writer of the above has confused established scientific facts and generalizations with the current investigations of new theories that are constantly proceeding on all borders of natural science, where there are always unknowns, and always questions and new problems. Indeed, the continuing quest for more truth is the most commendable characteristic of science.

In health science, school children hear about the gradual collapse of the medieval concept of disease, of the work of Pasteur and others establishing the germ theory of disease. They may learn a thousand and one facts—that tuberculosis is caused by a certain bacterium, diphtheria by another; that antitoxin saves life from diphtherial death; that certain mosquitoes transmit malaria; that countless people in history died of malaria; and so on *ad finitum*. And pupils learn of many things vital to health and life. They also learn about the developing science so that they may have the critical, cautious attitude about all things in this field, to the end that they may become wiser than their fathers.

It is an absurdity to call health science instruction "a tendency to statism, with its enslavement of body and mind to the whims of the relatively few men whose aim is to force conformity. . . ." It is rather the effort to enlighten with the facts discovered by the relatively few, for the benefit of the life and health of all, including Christian Scientists.

It is sheer rhetoric to proclaim: "Any attempt to abrogate the right of the individual citizen to refuse acceptance of a scientific theory . . . is an expression of bigotry. And bigotry of any nature—scientific or religious—is intolerable to free men."

No one is forced to accept a scientific theory. On the other hand, in some unscientific sects and groups, the leaders do all they can to make their followers disbelieve certain scientific theories and facts. They would prevent their children from knowing about them. They would keep them blind to what their American birthright would guarantee them, freedom to learn all things. They fear, apparently, that if their children learn of the findings of science, they may prefer these findings to the dogma of their fathers. Therein lies the bigotry of the elders—and bigotry is intolerable to free men.

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Hemolytic and Antihemolytic Substances in Guinea Pig Liver

IN 1949 we reported that simple 0.9% saline extracts of fetal guinea pig liver possess high hemolytic activity, whereas similar extracts of the adult are inactive (*1*). This was followed by a paper (*2*) demonstrating that it is not the absence of a lysin that accounts for the inactivity of the adult extracts, but the presence of inhibitors in the mitochondria and microsome fractions of the liver cells. It was shown that, when these inhibitors are separated out of inactive adult extracts by ultracentrifugal fractionation, very active preparations are obtained. Recombining the centrifugally separated fractions restores the inactive state. That is principally what the paper was about (*2*).

In between the time these two reports appeared in print, Laser published a paper (*3*) reporting the isolation of a hemolytic substance of high activity from the serum, spleen, liver, red blood cell, and the brain of the horse, the brain and blood of humans, and the spermatozoa of hogs. He prepared this substance from such organs by a procedure involving some 14 steps, including hot ethanol and ether extraction, transference of alkali-soluble material from ether extract into 1.5% KOH solution, formation of a lead precipitate, and, finally, molecular distillation in high vacuum at a temperature of about 60° C. The end product, he reports, was a substance identified as cis-vaccenic acid ($CH_3 \cdot (CH_2)_5 \cdot CH=CH \cdot (CH_2)_9 \cdot COOH$). These experiments of Laser's have convinced him (*4*) that the ether-soluble "hemolytic acid" thus isolated—for example, from the horse serum—is the same as the *heat-labile* lysin we described in saline extracts of guinea pig liver. Since the agent in guinea pig liver appears to be inactivated by many of the procedures used by Laser in the preparation of his "hemolytic acid," we believe it wise to leave for future investigation to determine whether there are any resemblances structurally, chemically, or otherwise between the two substances.

It was also implied (*4*) that we are completely unaware of the identity of some of the inhibitors in the plasma or the serum. This is contrary to the facts presented in our paper (*2*). What we are uncertain about is the nature of the inhibitors associated with the *mitochondria or microsome fractions of the liver cell.* We have no evidence, as yet, that those inhibitors are the same as the inhibitors present in the plasma or serum (i.e., albumin globulin, calcium, cholesterol, and lecithin).

There are many other discrepancies between what we actually wrote in the paper (*2*) and what Laser interpreted as having been written (*4*). Those interested are referred to the two papers in question.

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References

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The Decarboxylation Reaction

SEVERAL specific objections have been raised to the author's proposal (*1, 2*) that transitory carbanions are hypothetical intermediates in the base-catalyzed decarboxylation of alpha amino acids. Three of these objections (the first three discussed) involve emphasis on negative findings as limitations to the generality of the reaction. As such they should be considered with some skepticism. The failure of ethyl isobutyrate to undergo the Claisen condensation was long thought to impose restrictions on the mechanism which experience indicated were nonexistent. Others (the last two) are comments involving interpretations of the transitory existence, method of formation, and structure of the carbanion, and the generalized scope of the carbanion explanation.

1) *The role of the carbonyl function as an acceptor.* The fact (*3, 4*) that aldehydes fail to act as acceptors in the decarboxylation of various acids has been stated as a serious objection to the proposal that addition of a *transitory* carbanion to the carbonyl group of the anhydride plays a role in the decarboxylation. There are, however, decarboxylation reactions in which the aldehyde functions do act as acceptors. These are the spontaneous formation of 1-indanone on decarboxylation of *o*-formylcinnamic acid (*5*) and the base-catalyzed formation of carbinols on decarboxylation of quinaldinic acid in the presence of aldehydes (*6*). Both of these can be visualized as proceeding through a transitory carbanion. These reactions are much stronger evidence than negative findings, particularly in light of our finding that decarboxylation of acetylglycine, although long thought not to take place, does in fact react as other acylamido acids (*2*).

2) *Failure of the reaction in the absence of an alpha hydrogen.* The formation of a carbanion by decarboxylation does not require an alpha hydrogen. It has been reported (*6*), however, that α-phenyl-α-aminopropionic acid does not undergo the reaction, and this has prompted the suggestion that the formation of the carbanion by decarboxylation is unlikely. The decarboxylation of quinaldinic acid in its condensations to form carbinols from aldehydes is an example of a decarboxylation reaction that requires no hydrogen alpha to the carboxylic acid function. Again, this fact indicates that negative evidence to the contrary is likely to be untrustworthy.

3) *The fact that acylamido acids do not lose carbon dioxide in the absence of an anhydride.* This can be interpreted as meaning that the anhydride acts as an acceptor and in doing so provides the driving force for the reaction. One should not lose sight of the fact that the decarboxylation of acylamido acids in the presence of acetic anhydride may be a limited aspect of a general reaction. Many acids lose carbon dioxide in the presence of a base, and possibly it will be demonstrated that additions to carbonyl functions can take place in these reactions also. Hammett (*7*) discusses the relative roles of acceptor and reactant in providing the driving force for acid- and base-catalyzed Claisen condensations.

4) *The transitory role of the carbanion.* The carbanion has a transitory existence in decarboxylation (*1, 2*). This concept may vary from the usually accepted *transitory* carbanion of the aldol type of condensation to the bare possibility of existence even in the absence of resonance stabilization, which is the basis for an explanation of β-elimination reactions (*8*). The usually accepted statement on the transitory nature of ionic intermediates in organic reactions has been given by Hammett (*9*). The extent to which resonance stabilizes the carbanion raises interesting questions, because the only apparent factor involved is the inductive effect of the acyl- or sulfonyl- (12) group. This structure, $RCONHCH_2CO_2H$, is not to be compared, however, to that in which the inductive effect is transmitted through a methylene group. The amino group with its unshared electrons can aid in transmitting the inductive effect of the acyl- or sulfonyl- group to the alpha carbon. Electron-withdrawing effects of the acetamido group are not unknown. The formation of 4′-bromo-4-acetamido diphenyl ether on bromination of 4-acetamido diphenyl ether is an example of the inductive effect produced by the acylamido group (*10*). This group also acts as an electron donor in substitution reactions of acetanilide. It is also recognized that carbanions can be formed as transitory intermediates from compounds where apparently no resonance is involved, such as the bicyclic sulfone of Doering and Levy (*11*) and 3-alkylpyridines (*12*). It would appear from these observations that resonance stabilization of an intermediate carbanion, although of significance in terms of its possible independent existence, is not a reliable criterion for postulating its participation as the sole intermediate in a reaction mechanism. Presumably, increased stabilization would decrease the energy barrier for the formation of an intermediate by an amount equal to the increased energy barrier for the following reaction, with a net result of no obvious gain in lowering the net energy barrier.