it seems that in the particular phenomenon observed the energy came just short of leaving the sun and therefore was incapable of creating a magnetic disturbance on the earth.

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On the Use of the Capital Letter Prefixes L and D

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Under the current rules of nomenclature for the α-amino acids (*1*) and for carbohydrates (*2*), D and L are used to signify that the configuration of the asymmetric center in the substance named *has been correlated strictly with the configuration of* D- *or* L-*glyceraldehyde*. The standard substance for the amino acids is, in effect, serine, but D- and L-serine have now been correlated respectively with D- and L-glyceraldehyde (*3*).

In carbohydrate nomenclature, D or L refers to the configuration of the *highest numbered* asymmetric center. In amino acid nomenclature, D or L refers to the configuration of the α-carbon atom—i.e., the *lowest numbered* asymmetric center. In the few cases where confusion can arise as to which nomenclature is being employed, subscript g (glyceraldehyde) is written to denote the use of carbohydrate nomenclature, subscript s (serine) to denote the use of amino acid nomenclature.

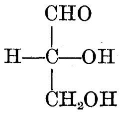
Recently, the use of the capital letter nomenclature has been extended in practice to a few substances other than carbohydrates or amino acids, the configuration of which has been correlated to the standard substances D-glyceraldehyde or L-glyceraldehyde. Thus, it is proper to write L-lactic acid and L-malic acid for the enantiomorphs of these two α-hydroxy acids, which are commonly found in nature. However, there is a regrettable tendency to extend the use of the capital letter nomenclature to other substances, the correlation of which has not yet been established. In some cases that have come to the attention of the writer, this has been done apparently under the impression that the prefix L is the present-day method of designating the enantiomorph of the substance which occurs in nature, without consideration of the true significance of this symbol. In other cases, capital letter prefixes appear to have been used with the mistaken view that uniformity is for some reason to be desired, even at the sacrifice of clarity.

At the present time, chemical nomenclature is undergoing change in order to keep step with advances in knowledge. The capital letter prefixes have been introduced to provide an unequivocal method of conveying certain specific information regarding the configuration of the asymmetric center or centers in the substances to the names of which these prefixes can properly be attached. An error in their use may be compared, for example, with an error in the number or Greek letter employed to denote position of substitution or point of attachment in the structure, and inevitably leads to confusion.

A case where confusion in the nomenclature has already occurred may be used as an illustration. The dextrorotatory enantiomorph of isocitric acid is present in relatively large amounts in certain succulent plants and is also one of the intermediate substances concerned in the well-known tricarboxylic acid cycle. It is doubtless widely, if not universally, distributed in living cells. In the literature of the past few years, this substance has been variously designated *d*-isocitric acid, *l*-isocitric acid, D-isocitric acid, (+)-isocitric acid, and (−)-isocitric acid. Which of these names is correct? Let us consider the use of the capital letter prefix first.

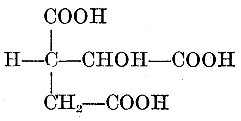
When one sees the name D-isocitric acid, there is no way to tell, in the absence of a subscript s or g, which of the two asymmetric centers present in this substance is referred to; that is to say, one is in doubt whether carbohydrate or amino acid nomenclature is being used. On the assumption that the D is intended to refer to the configuration of the α-carbon atom—i.e., that amino acid nomenclature is employed—the name carries the implication that the configuration of the asymmetric α-carbon atom of isocitric acid has been correlated with that of the asymmetric center of D-glyceraldehyde. No record has yet appeared in the literature to indicate that this has been accomplished, and, on the contrary, because of the general relationship of naturally occurring isocitric acid to L-malic acid in metabolism, and from analogy with the configuration of other related substances, it is far more likely that the α-carbon atom of the enantiomorph of the isocitric acid found in plants has the configuration of L-glyceraldehyde. That is to say, the chances are that investigation will ultimately show that this substance is L_s-isocitric acid.

On the assumption that the D is intended to refer to the configuration of the β-carbon atom of isocitric acid—that is to say, that carbohydrate nomenclature is employed—the name implies that the configuration of this asymmetric center has been correlated with that of D-glyceraldehyde. This in turn suggests that chemists have agreed on a correlation rule with respect to certain of the groups surrounding the asymmetric centers in formulae A and B.



$$\begin{array}{l} \quad\;\text{CHO} \\ \quad\;\;| \\ \text{H—C—OH} \\ \quad\;\;| \\ \quad\;\text{CH}_2\text{OH} \end{array}$$

FORMULA A
D-Glyceraldehyde



$$\begin{array}{l} \quad\;\text{COOH} \\ \quad\;\;| \\ \text{H—C—CHOH—COOH} \\ \quad\;\;| \\ \quad\;\text{CH}_2\text{—COOH} \end{array}$$

FORMULA B
Isocitric Acid

There would be little doubt that —COOH in B is to be correlated with —CHO in A, and —H is common to both. However, it is doubtful that all would agree that the group —CHOH—COOH in B should be correlated with the group —OH in A and, further, that the group —CH$_2$—COOH in B should be correlated with the group —CH$_2$OH in A. In the absence of a widely accepted rule that permits such correlations to be made, to say nothing of the absence of any direct chemical evidence upon the actual configuration of the β-carbon atom of this substance, it is impossible to use a capital letter nomenclature for isocitric acid which signifies the configuration of the asymmetric center at the β-carbon atom; that is, neither of the names D$_\text{g}$-isocitric acid nor L$_\text{g}$-isocitric acid is currently admissible.

In view of the fact that the isomer of isocitric acid found in plant leaves is dextrorotatory in water solution (*4, 5*), the substance may be designated *d*-isocitric acid where the italic *d* has its original significance *dextrorotatory*.[1] Nevertheless, *d* and *l* have been ambiguous ever since they were first used by Fischer to denote configuration rather than direction of rotation in the carbohydrate field, and this practice was extended to amino acids by Wohl and Freudenberg. Accordingly, where one wishes to avoid all possibility of being misunderstood, the name should be written *dextro*-isocitric acid or (+)-isocitric acid, the latter method of expression being admissible under present amino acid rules and in common use, especially in papers of British origin.

The lactone that is readily formed when a water solution of *dextro*-isocitric acid is evaporated to a sirup is strongly levorotatory (*4*) and should be named *levo*-isocitric lactone, or (−)-isocitric lactone or even *l*-isocitric lactone, provided it is made clear that the prefix is being used in its original sense. However, the greatest possibility of confusion in naming isocitric acid arises from the fact that the ammonium molybdate complex compound of *dextro*-isocitric acid has an extraordinarily high *levorotation* (*6–9*), and it is customary to employ the molybdate complex in examining the rotation of solutions of isocitric acid. There is thus a tendency to designate the naturally occurring substance *l*-isocitric acid (or (−)-isocitric acid) or its salt as *l*-isocitrate. A number of papers have appeared in which this error occurs, and care must therefore be taken in reading the literature of this substance.

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[1] Although the use of the prefixes *d*- and *l*- is not recognized, under the rules approved by the American Chemical Society for carbohydrate nomenclature or for amino-acid nomenclature, to indicate the direction of rotation of a solution of the substance, they are widely and entirely properly employed for this purpose in other fields; e.g., for optically active amines, alcohols, hydrocarbons, vitamins, alkaloids, etc. The α-hydroxy acids are chemically and metabolically closely allied with both amino acids and carbohydrates, and their nomenclature at the present time is in a state of flux. Divergent opinions have, for example, been expressed as to whether *dextro*-tartaric acid should be named as a D compound or as an L compound. Unusual care should therefore be taken in naming this group of substances.

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The Reported Adrenergic Blocking Action of β-Haloethylammonium Compounds

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Recently Nyman and co-workers (*1–3*) have reported the preparation of two quaternary derivatives of N,N-dibenzyl-β-chloroethylamine (Dibenamine[3]). One of these, dibenzyl-β-chloroethyl ethylammonium bromide, was claimed (*3*) to be an effective adrenergic blocking agent and, furthermore, to exert its full effect within 5 min after intravenous injection. In a few other instances quaternization of β-haloethylamines has been reported to produce active salts (*4*). The materials tested were noncrystalline, however, and therefore of questionable purity, and, in each case, the potency was less than that of the corresponding tertiary amine.

In our experience, the ability of β-haloethylamines of the Dibenamine type to undergo intramolecular alkylation with the formation of ethylenimonium ions appears to be of prime importance for adrenergic blocking action. Also, the rate of onset of the blocking effect seems to be dependent upon the reactivity of the halogen. Further alkylation of the amino group would be expected to produce inactive compounds, since the nitrogen is unable to participate in the initial cyclization reaction unless dissociation to a tertiary amine were to occur under physiological conditions. As further evidence for our hypothesis that imonium ions are the active intermediate, we prepared a num-

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[3] Smith, Kline & French trade-mark.