The Validity of the Emil Fischer Concept

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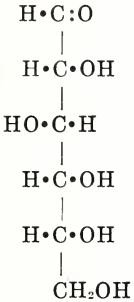
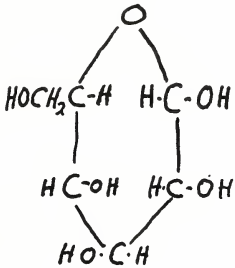
The author has previously shown that (1) it is possible to make a straightforward transition from the aldehyde formula of a sugar to the pyranose or furanose formula and thus present a spatial concept of the molecule, and that (2) the configurational concept proposed by Emil Fischer visualizes the hydrogen atom and the hydroxyl group of an asymmetric grouping as *lying above the plane of the paper*, with the two other groups below the plane of the paper.

These two concepts enable one to make the transition from an aldehyde formula to a pyranose formula with ease, as indicated by:

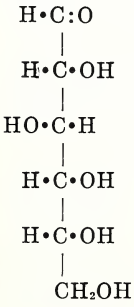


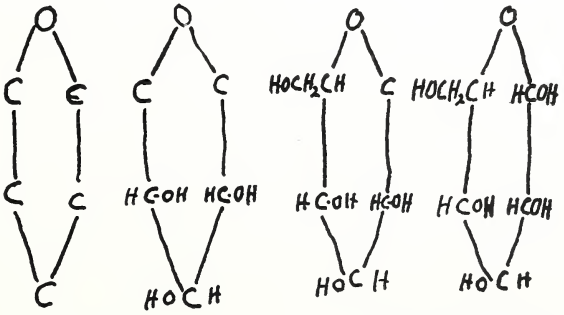


The open chain formula on the left, by ring formation and orientation so that the hetero atom is placed at the top and *the corresponding groups read left to right*, the same as in the aldehyde formula, becomes the pyranose formula shown at right.

D+-glucose, aldehyde formula — α-D+-glucopyranose

The transition from an open chain aldose sugar formula to a pyranose formula, consists of (1) writing the open chain aldose formula, (2) writing a pyranose ring, with the oxygen atom oriented at the top and the carbon atoms numbered clockwise, (3) filling in the corresponding asymmetric groups so that they read *left to right in both formulas*, (4) placing the terminal HO•CH_2-group to the left with the H-atom to the right in the *D*-series or *vise versa* in the *L*-series, and (5) filling in the H- and OH-groups on carbon atom grouping No. 1 so as to give the *alpha*- or *beta*-form as desired. Diagramatically, the steps are:





α-*D*-glucopyranose, by Degering

Step No. 1 — Step No. 2 — Step No. 3 — Step No. 4 — Step No. 5

Even the beginning student in organic chemistry makes the transition with ease, whereas graduate students encounter extreme difficulty in making the transition from the open chain formula of α-D+-glucose, for example, to the Haworth formula which is indicated below. The transition to the Haworth formula would be comparatively simple if the conventional method of writing the formula of D-glucose, for example, was as follows:

```
      H   H   H  OH  H   O
      |   |   |   |   |   ||
HO—C—C—C—C—C—C—H
      |   |   |   |   |
      H  OH  OH  H  OH
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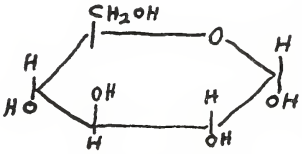

α-*D*-glucopyranose, by Haworth

In view of the fact, however, that the formulas of the open chain sugars are written vertically with the aldehyde group at the top, the transition to the Haworth formula becomes difficult. One should not discount the significant contribution which was made to the chemistry of the carbohydrates by the introduction of the ring or closed chain formulas by Haworth and Peat[3], nor should one be a slave to a concept that does not follow the accepted orientation of heterocyclic systems[5] nor permit of ready transition from the open chain system with which the student is most familiar to the closed chain, ring, or pyranose system.

At the same time, moreover, one is able to visualize the spatial arrangement of the atoms in the pyranose formula in that all of the groups lying to the *right* of a carbon atom are *below* the plane of the paper, whereas those lying to the *left* of the same carbon atom are *above* the plane of the paper. This may be indicated by making the proper lines heavy so as to give a perspective as well as a projection representation. This relative position of the H- and OH-groups with respect to the plane of the molecule may be confirmed readily by the construction of a tinker-toy model of the sugar concerned.

This concept seems the more significant now that Werner Kuhn has produced mathematical proof to vindicate the correctness of the Emil Fischer guess and thus increase the probability that the representation of α-D+-glucopyranose as shown above is correct.

Actually, Kuhn established the absolute configuration of D—-lactic acid, but by so doing he likewise established the absolute configuration of the simple sugars and all closely related compounds.

This contribution is so significant to the organic chemist that a few paragraphs, as translated by the author, are taken from theoretical dessertation by Werner Kuhn as it appeared in the Zeitschrift fur physikalische chemie in 1935, where it has since remained buried[4].

"A start for the theoretical calculation of the absolute configuration of lactic acid is made by determining by means of a simplified

model, the sign of rotation of methyl ethyl carbinol, the steric relation of which to lactic acid is chemically defined.

"In the simplified model the methyl group, the active carbon atom, and the ethyl group are each represented by an isotropic resonator, whereby the charge of the ethyl group is assumed to be larger than either charge in the centers of gravity of the methyl group or of the active carbon atom. The reciprocal action of resonance occurring in these parts of the molecule is accurately calculated. For the alcoholic hydroxyl group we take respectively an isotropic and an anisotropic resonator of different directions of vibration as a starting point.

"For the calculation of the reciprocal action, the peripheral one caused by Van der Waal forces is neglected and consideration given to the reciprocal action due to direct chemical linkage.

"If at first the optical vibration localized at the OH-absorption band of highest wave length is assumed to be anisotropic, one arrives at an optical activity of the second order. If the hydroxyl group is, however assumed to be isotropic, the rotation disappears in this order.

"By virtue of the Kerr-effect and the dispersion of light as observed on hydroxyl compounds, it is probable that in the carbonhydroxyl group the hydroxyl absorption band of highest wave length vibrates in the plane defined by the carbon, oxygen, and hydrogen. The result in this case is that the D—-lactic acid, which according to Emil Fischer is wherein the substituents connected by the *dotted line should be pictured behind the plane o fthe drawing.*

```
      COOH
        :
    H - C - OH
        :
      CH3
```

Formula I

```
      COOH
        :
    H———C———OH
        :
      CH3
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Formula II

"It will be shown that vibrations which correspond to optical absorption bands of molecules should be considered anisotropic for theoretical as well as experimental reasons. Experimentally this is particularly evidenced by the Weigert-effect as observed on dye stuff molecules.

"Generally the optical vibrations of the absorption band of highest wave length of any given molecule takes place in that direction in which the polarizability (which is measured by the Kerr-effect and light dispersion) is at a maximum. From the Kerr-effect one can therefore conclude with good probability the direction of vibration which is characteristic for the absorption bands of highest wave length of the molecule."

Kuhn then proceeds to convince his reader by a thirty three page discussion, which is loaded with seven pages of mathematics. When one has traversed this long and weary way with Kuhn, he is convinced

that Emil Fischer guessed right and the absolute configuration of D—-lactic acid is that shown at the right, in which the carbon atom at the asymmetric center lies in the plane of the paper, whereas the H- and OH-groups lie in front of the plane and the CO_2H- and CH_3-groups lie behind the plane of the page.

$$\begin{array}{c} CO_2H \\ : \\ H - C - OH \\ : \\ CH_3 \end{array}$$

D—-Lactic Acid

Having accepted the absolute configuration of lactic acid as that postulated by Emil Fischer, one is at once in a position to accept the absolute configuration of D^+-glucose as represented by the α-D^+-glucopyranose formulation at the outset of this article.

Literature Cited

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4. Kuhn, Werner, Absolute Configuration of Lactic Acid, Zeitschrift fur physik. chem., (B) **31,** 33 (1935-36).

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