A SUGGESTION LOOKING TO THE EXTENSION INTO SPACE OF THE STRUCTURAL FORMULAS AT PRESENT USED IN CHEMISTRY. AND A NOTE UPON THE RELATION BETWEEN THE OPTICAL ACTIVITY AND THE CHEMICAL CONSTITUTION OF ORGANIC COMPOUNDS.

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[Reader's Note; All figures are in one 44K file at the end of the text.]

I desire to introduce some remarks which may lead to discussion and hope to avail myself of the discussion to give my ideas more definiteness and breadth. Since the starting point for the following communication is found in the chemistry of the carbon compounds, I shall for the present do nothing more than state the points having reference to it.

It appears more and more that the present constitutional formulas are incapable of explaining certain cases of isomerism; the reason for this is perhaps the fact that we need a more definite statement about the actual positions of the atoms.

If we suppose that the atoms lie in a plane, as for example with isobutyl alcohol (Figure I) where the four affinities are represented by four lines in this plane occupying two directions perpendicular to one another, then methane (CH_4) (to start with the simplest case) will give the following isomeric modifications (the different hydrogen atoms being replaced one after the other by univalent groups R' R" etc.):

<div style="text-align:center">

One for $CH_3(R')$ and for $CH(R')_3$

Two for CH_2R_2' (Figures II and III), for

$CH_2R'R''$ and for $CHR_2'R''$

Three for CHR'R"R'''   and for   CR'R"R'''R""

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(Figures IV, V, and VI); numbers that are clearly greater than the numbers actually known thus far.

The theory is brought into accord with the facts if we consider the affinities of the carbon atom directed toward the corners of a tetrahedron of which the carbon atom itself occupies the center.

The number of isomers is then reduced and will be as follows:

<div style="text-align:center">

One for CH_3R', CH_2R_2', $CH_2R'R''$, CHR_3',

and $CHR_2'R''$ but

Two for CHR'R"R''' or more general, for

CR'R"R'''R"".

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If one imagines himself in the line R'R''' in Figures VII and VIII with head toward R' and looking toward the line R"R''' then R" may be on the right (Figure VII) or on the left (Figure VIII) of the observer; in other words:

When the four affinities of the carbon atom are satisfied by four univalent groups differing among themselves, two and not more than two different tetrahedrons are obtained, one of which is the reflected image of the other, they cannot be superposed; that is, we have here to deal with two structural formulas isomeric in space. According to this hypothesis the combination CR'R''R'''R'''' presents a condition not presented by the combinations CR_2'R''R''', CR_3'R'' or CR_4', a condition not expressed by the ordinary mode of representation. According to the present mode there would be between CR'R''R'''R'''' and CR_2'R''R''' a difference quite as great as between CR_2'R''R''' and CR_3'R'', or between CR_3'R'' and CR_4'.

Submitting the first result of this hypothesis to the control of facts, I believe that it has been thoroughly established that some combinations which contain a carbon atom combined with four different univalent groups (such carbon atoms will henceforth be called asymmetric carbon atoms) present some anomalies in relation to isomerism and other characteristics which are not indicated by the constitutional formulas thus far used.

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FIRST PART
I. Relation Between The Asymmetric Carbon And The Property of Optical Activity:

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(a) *All of the compounds of carbon which in solution rotate the plane of polarized light possess an asymmetric carbon atom.*

In order to convince oneself of the justice of these remarks it is necessary to run through the following list of optically active compounds in the formula of which the asymmetric carbon is indicated by **C** :

Ethylidene lactic acid,	CH_3**C**.H.OH.COOH.
Aspartic acid,	COOH **C**.H.NH_2.(CH_2COOH).
Asparagine,	COOH **C**.H.NH_2.($CH_2$$COOH_2$).
Malic acid,	COOH **C**.OH.H.(CH_2COOH).
Glutaric acid [Itamalic acid]	CH_2OH **C**.H.COOH.(CH_2COOH).
Tartaric acid,	COOH **C**.H.OH**C**.H.OH.COOH.
Dextrose, Laevelose, Galactose, Maltose. Sorbin, Eucalyn, etc.	CH_2OH.**C**.H.OH.($C_4$$HO_4$).**C**.H.OH.$CH_2$OH.
Mannite, Quercite, Pinite:	($C_4$$H_9$$O_4$).**C**.H.OH.$CH_2$OH.

Cane sugar, milk sugar, Melezitose, Melitose, Parasaccharose, and Trehalose; Starch, Inuline, Glycogen, Dextrine, and Arabin all contain the asymmetric carbon atom that was present in the previous compounds inasmuch as they are compound ethers of the previous compounds.

Camphor, according to Kekule (Figure XII)
Borneol, according to the same (Figure XIII)
Camphoric acid, according to the same.
COOH **C**H($C_8$$H_{14}$O.).
Terpinolene which apparently has the structure shown in Figure XIV
and Menthol which perhaps has the structure shown in Figure XV.

Concerning the active alkaloids, albumens, etc., too little is as yet known of their structure to permit of any conclusion being reached in regard to the relation between their structures and the rotatory power.

The sole definite exception to this rule that I have been able to find is the active propyl alcohol of Chancell, but, according to a private communication of Henniger, this relatively small rotatory power is due to the presence of an impurity.

(b) *The derivatives of optically active compounds lose their rotatory power when the asymmetry of all the carbon atoms disappears; in the contrary case they do not usually lose this power.*

A few examples will be sufficient here:

Inactive malonic, fumaric, and maleic acids from the active malic acid; inactive succinic and tartronic acids form the active tartaric acid; inactive cymene from active camphor, etc.

In the contrary case there are,

Active malic acid from active tartaric acid;
Active tartaric acid from active lactose;
Active glucose from active glucosides;
Active nitro mannite from active mannite;
Active camphoric acid and Borneol from active camphor;
Active salts and esters from active acids, etc.

(c) *If one makes a list of compounds which contain an asymmetric carbon atom it is then seen that in many cases the converse of (a) is not true, that is, not every compound with such an atom has an influence upon polarized light.*

This may be ascribed to three causes:

1. The compounds consist of an inactive mixture of two isomers with equal but opposite optical power, which owing to their close agreement in all other properties can be separated with great difficulty, and which have not up to the present been separated.
2. The study of the rotatory power has been imperfect, either on account of the slight solubility of the compounds or on account of the slight specific rotatory power of many compounds, as for example, in the case of mannite.
3. The asymmetric carbon atom may not in itself be sufficient to cause optical activity, the latter may not depend solely upon the mutual diversity of the groups which are in combination with the carbon atom, but may also be dependent upon their character.

However the case may be the facts noted indicate a probable relation between constitution and active power which may be made use of in the following cases when more convincing arguments fail:
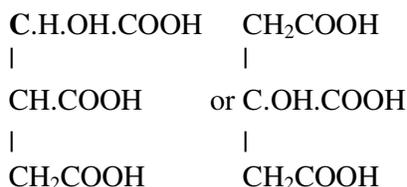
1. A compound which rotates the plane of polarized light probably possesses an asymmetric carbon atom; which gives a means of choosing between possible structures in the case of compounds where the structure is not completely determined.

For example, active amyl alcohol with an asymmetric carbon atom can have only the formula

$$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} CHCH_2OH.$$

a formula which has also been suggested by Erlenmeyer but upon altogether different grounds.

2. A compound which up to the present has shown no physical isomers acting upon polarized light in all probability contains no asymmetric carbon atom; this fact also may be of service in choosing between possible structural formulas; as for example, citric acid, which on account of its transformation into aconitic acid and tricarballylic acids must have one of the two formulas:

$$\begin{matrix} \mathbf{C}.H.OH.COOH & & CH_2COOH \\ | & & | \\ CH.COOH & or & C.OH.COOH \\ | & & | \\ CH_2COOH & & CH_2COOH \end{matrix}$$

its inactivity gives preference to the second formula; the first, however, contains an asymmetric carbon atom for which reason I hope to be able to produce the acid named by following the method of Frankland and Duppa from oxalic acid and iodo acetic acid esters by the aid of zinc.

3. Finally the limits of the rotatory power can be stated with some measure of probability, that is to say, the simplest combinations which will show active power can be indicated; for exampe, the simplest active monatomic alcohol will be:
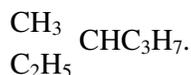
$$CH_3C.H.OH.CH_2CH_3.$$

The simplest active monobasic acid:

$$CH_3C.H.COOH.CH_2CH_3.$$

The simplest active diatomic alcohol:

$$CH_3CHOH\ CH_2OH.$$

The simplest active saturated hydrocarbon:

$$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} CHC_3H_7.$$

The simplest active aromatic hydrocarbon:

$$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} CHC_6H_5 \text{ etc.}$$

At the same time it is probable that some series will be excluded from active power, as for example:

The normal hydrocarbons $CH_3(CH_2)_nCH_3$
The normal alcohols $CH_3(CH_2)_nCH_2OH$
The normal acids $CH_3(CH_2)_nCOOH$ etc.

It is more noteworthy that in consequence of the assumptions made, the compound CHBrClI can probably be split up into two isomers which will act upon polarized light. . . .

SECOND PART

Thus far we have considered the influence of the hypothesis upon compounds in which the carbon atoms are united by a single affinity only, (leaving out some aromatic bodies); there remains now to be considered:

The influence of the new hypothesis upon compounds containing doubly linked carbon atoms.
Double linking is represented by two tetrahedrons with one edge in common (Figure IX) in which A and B represent the union of the two carbon atoms, and R'R"R'''R"" represent the univalent groups which saturate the remaining free affinities of the carbon atoms.

If R'R"R'''R"" all represent the same group, then but one form is conceivable, and the same is true if R' and R" or R''' and R"" are identical, *but if R' differs from R" and at the same time R''' differs from R"", which does not preclude R' and R''', R" and R"" from being equal, then two figures become possible shown in Figures IX and X, which differ from one another in regard to the positions of R' and R" with respect to R''' and R"". The dissimilarity of these figures, which are limited to two, indicates a case of isomerism not shown by the ordinary formulas.*

Turning to the facts, I believe that I have met with such cases among organic compounds.
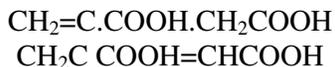
1. Maleic and fumaric acids, all explanations of the isomerism between these have made shipwreck, (I count here also the assumption of a bivalent carbon atom since this can exist alone in the case of carbon monoxide and the carbylamines, for evident reasons, without doubling of the molecule); as a matter of fact these acids realize the conditions outlined above: *Two doubly linked carbon atoms each carrying two unlike univalent groups, H and COOH.*

2. Brom and isobrom maleic acid, the explanation of the isomerism here is entirely the same as before, one has only to replace an H in the fumaric and maleic acid by a Br.

3. Citra-, ita- and mesaconic acids. With the adoption of

$$CH_3CHCOOHCH_2COOH$$

for pyrotartaric acids there remain for the acids mentioned only the formulas

$$CH_2=C.COOH.CH_2COOH$$
$$CH_2C\ COOH=CHCOOH$$

and if the latter does not contain two isomers (probably ita- and citra-conic acids) in accordance with my hypothesis, no plausible explanation can be given.

4. Solid and liquid crotonic acids. The constitution of the solid crotonic acid according to Kekule is without doubt

$$CH_3CH=CH_2COOH$$

for the liquid crotonic acid there remains therefore (thus it is held) only the formula

$$CH_2=CHCH_2COOH$$

to explain their lack of identity.

But if we take into consideration the following facts with regard to this acid:

(a) Fused with KOH it gives, according to M. Hemilian, acetic acid only:
(b) Oxidizing agents, according to the same authority, convert it into acetic and oxalic acids, and indirectly from oxalic acid into carbonic acid.
(c) At 170-180 degrees, also according to Hemilian, it goes over into the solid crotonic acid. Thus there is nothing in favor of the formula $CH_2=CHCH_2\ COOH$ and everything in favor of the isomer $CH_3CH=CHCOOH$, exactly like fumaric and maleic acids. The formula $CH_3CH=CHCOOH$ really satisfies the conditions exacted by my hypothesis for the possibility of two isomers: two doubly linked carbon atoms, the free affinities of each of which are saturated by two unlike univalent groups, in this case H and CH_3, H and COOH.

Geuther's chlorcrotonic acid and chlorisocrotonic acid, the isomerism of which has hitherto been expressed by the formulas

$$CH_2=CClCH_2COOH$$

and

$$CH_3CCl=CHCOOH$$

according to Froelich give with nascent hydrogen the acids treated under

(4) whence the constitution of both becomes

$$CH_3CCl=CHCOOH$$

and this case of isomerism strengtens my hypothesis.

Third Part

There remain now to be treated carbon atoms which are united by a triple union as in acetylene; this combination is represented by two tetrahedrons with three summits in common or with one of their faces in common (Figure XI). ACB is the triple union, R' and R" are the univaalent groups which saturate the two remaining affinities of the carbon atoms. The new hypothesis does not in this case lead to any discordance with the views previously held.

In closing, I wish to remark that

1. The new hypothesis leaves nothing unexplained that is clearly set forth by the previous conceptions.
2. Certain properties and isomers not explained by the unusual theories receive some light from this point of view.
3. Finally my remarks about active compounds in solution, that is active molecules, are related to the views of Rammelsberg upon active crystals.

Extending the observations of Herschell and Pasteur, Rammelsberg maintains that the property of acting upon the plane of polarization in the solid state (that is the active condition of crystals with inactive molecules as well as the inactive condition of crystals with active molecules) coincides with the appearance of two crystal forms, one of which is the reflected image of the other.

If is evident that we have here to deal with an arrangement of the groups of atoms in the active molecule according to my hypothesis; an arrangement in which neither the crystal mention by Rammelsberg not the active molecules, represented in a general way by Figures VII and VIII have a plane of symmetry.

Fig. I.   *Fig. II.*   *Fig. III.*

Fig. IV.   *Fig. V.*   *Fig. VI.*

Fig. VII.   *Fig. VIII.*   *Fig. IX.*   *Fig. X.*   *Fig. XI.*

Fig. XII.   *Fig. XIII.*   *Fig. XIV.*   *Fig. XV.*