

Citation:

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organism used by us has been another form than that employed by PASTEUR in his classic experiment and the continued investigations of one of us ¹⁾ (H. J. WATERMAN) have exactly demonstrated that the phenomena of growth are dependent in a high degree on the variation.

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Chemistry. — “*On a method for a more exact determination of the position of the hydroxyl groups in the polyoxycompounds*”.

(4th Communication on the configuration of the ring systems).²⁾

By Prof. J. BÖESEKEN. (Communicated by Prof. A. F. HOLLEMAN).

The investigations as to the action of the polycompounds on the conductivity of boric acid were started to furnish a contribution to our knowledge as to the situation of the carbon atoms, and the groups attached thereto, in benzene.

This object has been attained to a certain extent, but, in addition, the measurements have also taught us something about the position of the hydroxyl groups in the saturated polyvalent alcohols.

The influence of polyoxycompounds and boric acid on each other has been known for a long time.

So, for instance, the increase of the acidic properties of boric acid by means of glycerol was made use of in the titration of that acid and, reversely, the large increase in rotation exerted by boric acid on mannitol went to demonstrate that this polyatomic alcohol was indeed optically-active³⁾. These few empirical data were very considerably added to by G. MAGNANINI⁴⁾; at the same time an experimental foundation was given to the surmise that these phenomena might be due to the formation of compounds.

He demonstrated that mannitol strongly increased the electric conductivity power of boric acid and that, although to a less extent, this was also the case with oxy-acids such as tartaric acid, salicylic acid, lactic acid, glycerine acid, gallic acid, mandelic acid and glycollic acid. He thus proved the formation of complex ions, consequently of a chemical combination between the two components.

VAN 'T HOFF⁵⁾, on account of these investigations, was of opinion

¹⁾ H. J. WATERMAN. These Proc. 29 June 1912, p. 124.

²⁾ Recueil 30, 392; 31, 80 and 86.

³⁾ VIGNON. Ann. Chim. Phys. 5e S. II 433. (1874).

⁴⁾ Gazz. chim. 20, 428; 21, II, 134, 215. Zeitschr. phys. Chem. 6. 58.

⁵⁾ Lagerung der Atome im Raume. 3e Ed. p. 90.

that a compound can only then be formed when the conditions are favourable for the formation of a 5-ring (and eventually of a 6-ring). A substance like mannitol might then unite readily with one or more mols. of boric acid, because the position of the hydroxyl groups would favour the formation of 5- or 6-rings.

In the case of a hexatomic alcohol like mannitol, the conditions for the ring formation are, however, probably favourable, because to each carbon group is attached a hydroxyl group and because of the very great probability that two of these with the two carbon atoms attached thereto, are situated at the same side and in the same plane; and this especially because it is a saturated non-cyclic substance.

It occurred to me that a further study of the influence of these compounds on boric acid might become of more importance still, if the more simple alcohols were chosen for that purpose.

Now, with the polyoxyderivatives of benzene the conditions are exceedingly simple.

When in the benzene derivatives the six carbon atoms with the groups attached thereto, are situated in one plane, the *orthodioxy*-compounds only (eventually also the *orthoxyacids* have a configuration that offers the best chances for the formation of the said cyclic systems.

In fact, the measurements carried out by myself and A. VAN ROSSEM (l. c.) have shown that of the polyoxyderivatives of benzene only the *orthocompounds* exert a very great positive influence on the conductivity of boric acid.

The specific conductivity of $\frac{1}{2}$ mol. solution of this acid at 25° is increased:

by $\frac{1}{2}$ mol. pyrocatechol	from 25.7×10^{-6}	to 553.2×10^{-6}
„ $\frac{1}{2}$ „ pyrogallol		608.9×10^{-6}
„ $\frac{1}{32}$ „ pyrocatechol		116×10^{-6}
„ $\frac{1}{32}$ „ pyrogallol		131×10^{-6}
„ $\frac{1}{32}$ „ 1.2-dioxynaphtalene		112×10^{-6}

(measured by Mr. J. D. Rurs)

on the other hand, the *meta*- and *para*derivatives exerted an insignificant negative influence. The spec. conductivity was lowered:

by $\frac{1}{2}$ mol. resorcinol	from 25.7×10^{-6}	to 25.0×10^{-6}
„ $\frac{1}{2}$ „ hydroquinone		24.3×10^{-6}
„ $\frac{1}{8}$ „ phloroglucinol		24.8×10^{-6}

Gallic acid and protocatechuic acid also suffer a considerably larger increase in conductivity by addition of boric acid than would agree with this acid's own conductivity.

$\frac{1}{8}$ mol. protocatechuic acid had at 25° a specific conductivity	= 703.1×10^{-6}
$\frac{1}{2}$ mol. boric acid	= 25.7×10^{-6}
Found a conductivity of the mixture	= 847.7×10^{-6}
Increase	= <u>118.9×10^{-6}</u>
$\frac{1}{8}$ mol. of gallic acid had at 25° a spec. conductivity	= 750.7×10^{-6}
$\frac{1}{2}$ „ of boric acid	= 25.7×10^{-6}
Found for the mixture	= 917.6×10^{-6}
Increase	= <u>141.2×10^{-6}</u>

From this influence on the conductivity we may conclude that with the polyoxybenzene derivatives an important reaction only then takes place when the hydroxyl groups are situated in the *ortho*-positions in regard to each other,

Of a specific aromatic influence there can be no question because it would then be difficult to understand why resorcinol, hydroquinone and phloroglucinol do not exert an increasing action whereas mannitol, pentaerythrol and glycerol do increase the conductivity (MAGNANINI, BÖESEKEN and VAN ROSSEM l. c.).

We are constrained, as stated above, to look for the cause in the favourable situation of the hydroxyl groups in regard to the boric acid molecule.

Now, the peculiar property of pyrocatechol and other orthodioxo- (and also of amido-oxy and diamido-) compounds of benzene and other ring systems to readily absorb another atom and to form with this, as a rule, very stable compounds has been known for a long time.

This is attributed to the exceedingly ready 5-ring formation, therefore to the favourable position of the *ortho*-placed groups.

Without troubling, provisionally, about the configuration of the compounds formed between boric acid and the polyoxyderivatives, we may take it as very probable that an analogous cause determines their origin.

The importance of demonstrating the influence of the polyoxy-compounds on the conductivity of boric acid is not related to the fact itself but lies in the sensitiveness of the method and its simple application.

It enables us to announce the formation of compounds without having to isolate the same and even more: *from the degree of influence we can draw important conclusions as to the position of the hydroxyl groups in the original polyoxycompound.*

If, for instance, we find that the increase of the specific conductivity at 25° caused by:

$\frac{1}{2}$ n. glycol	on $\frac{1}{2}$ n. boric acid =	4.9×10^{-6}
$\frac{1}{2}$ n. glycerol	„ =	8.7×10^{-6}
$\frac{1}{2}$ n. pentaerythrol	„ =	231.2×10^{-6}
$\frac{1}{2}$ n. pyrocatechol	„ =	514.1×10^{-6}
$\frac{1}{2}$ n. dulcitol	„ =	717×10^{-6}

we may conclude therefrom that in pentaerythrol, at least two of the hydroxyl groups are situated rather favourably, but not by a long way so as in the case of pyrocatechol; that in dulcitol more than *one* pair of hydroxyl groups exert an influence on the boric acid; that in glycol, they are very unfavourably situated and that they are also unfavourably situated in glycerol although three of them are present. This is shown in a still more striking manner when we compare the trivalent pyrogallol with glycerol at a somewhat greater concentration of the alcohol:

1 n. pyrogallol on $\frac{1}{2}$ n. boric acid =	911.3×10^{-6}
1 n. glycerol =	12.9×10^{-6}

In the determination of the influence exerted on the conductivity we possess a very simple and sensitive method to get some information as to the situation of the hydroxyl groups in regard to each other without strongly attacking the molecule and so disturbing the existing equilibrium.

In consequence of the preceding we submit the following suppositions:

1. If the hydroxyl groups, as in pyrogallol or in pyrocatechol, are situated in the same plane and at the same side of the carbon atoms to which they are attached and if there is no entering atom as in the case of resorcinol, hydrochinone or phloroglucinol, the influence is very great.

2. This influence becomes less when the OH-groups are leaving this favourable position.

The simple glycols as yet investigated by us: aethylene glycol, pinacone, propanediol 1,3, butanediol 1,4¹⁾, do not increase the conductivity of boric acid.

We surmise that the hydroxyl groups in these molecules repel each other and then, in consequence of the mobility of the saturated molecule, get situated as far as possible from each other, still in the same plane but at the opposite side of the carbon atoms to which they are attached.

We will see whether a more extensive experimental material confirms these suppositions.

¹⁾ Butanediol (1.4) can be prepared very readily by reduction of succiniediethyl ester according to the directions given by HARRIES for the preparation of methyl (2) butanediol (1.4) from pyrotartariediethyl ester.

The influence of glycerol is certainly in harmony with these views. As we have stated this influence is very slight; two of the OH-groups are therefore, most likely, not situated so favourably as in pyrocatechol. But still they are not situated so unfavourably as in the simple glycols and this cannot be otherwise, for even when the three OH-groups repel each other as far as possible the situation of these groups viewed two by two must still be more favourable than in the said bivalent alcohols.

The fact that on the other hand the position of the hydroxyl groups in pyrocatechol and in dioxynaphtalene is so particularly favourable must be attributed to the ring-system of the benzene, which forces them to remain in the plane of the ring and at the same, or outer, side.

The fact that, according to MAGNANINI'S measurements, the α -oxy-acids and salicylic acid affect the conductivity of boric acid positively, points to a position of the hydroxyl groups, in regard to each other, which is more favourable than in the glycols. This is very comprehensible when we consider that the OH-group of the α -carbon atom finds at the other side of the acid OH-group of the carboxyl group an oxygen atom, and not the hydrogen atoms of the glycols.

If the number of hydroxyl groups in saturated compounds is greater than two, it is obvious that the chances of a favourable position increase and in harmony therewith we find that erythrol exerts a stronger influence on the conductivity of boric acid than glycerol and that the action of mannitol and dulcitol is more important still.

For $\frac{1}{2}$ mol. of the alcohols on $\frac{1}{2}$ mol. of boric acid was found:
 $K \times 10^{-6} =$

Glycerol	Erythrol	Mannitol	Dulcitol
8.7	64.1	685	717

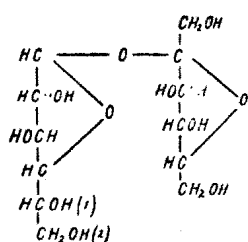
In the case of these saturated polyalcohols it is, at the present, still somewhat difficult to point out the most probable position of the hydroxyl groups by means of a determination of the influence exerted on the conductivity.

This is much more easy in the case of cyclic systems where the mobility of the molecule has been lessened to a considerable extent by the closing of the ring thus causing the position of the groups to become much more defined. We have already made use of this property in criticising the action of the polyoxycompounds of benzene; but the action of *sucrose* is also that which may be expected from this molecule.

The influence of sucrose on the conductivity of boric acid is very trifling, and reversely, also that of boric acid on the rotatory power of sucrose.

The change of $\frac{1}{34.2} N$ sucrose to $\frac{1}{2} N$ boric acid = ± 0
 " " " $\frac{1}{8.42} N$ " " = -1×10^{-6}
 " " " $\frac{1}{1.71} N$ " " = -3×10^{-6}

The change in the rotation for these concentrations kept below 0.13° and like that of the conductivity was exceedingly small indeed.



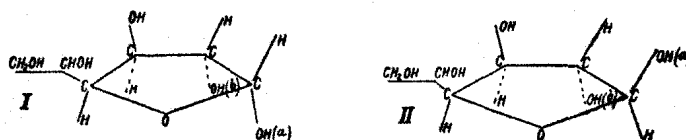
If now we observe the subjoined symbol of sucrose in space, which is considered by TOLLENS and E. FISCHER¹⁾ as the most probable one, we notice that of the eight hydroxyl groups only those indicated by (1) and (2) can have a favourable position, that is to say, in the same plane and at the same side of the carbon

atoms to which they are attached and undisturbed by other atoms.

It was, however, to be expected that these two OH-groups will *not* be situated favourably, for they possess a freedom of motion analogous to that in the simple glycol and if in the latter the OH-groups repel each other it would be difficult to understand why they should not do so in the sucrose molecule.

The almost complete indifference of sucrose towards boric acid (and probably towards many other compounds) now finds in its configuration a very simple explanation.

These observations thus confirm the configuration of the sucrose as well as the value of the process for the more exact determination of the hydroxyl groups of organic compounds. I have been able to employ the method for determining the configuration of α - and β -dextrose.



It is known that the above configurations are now imputed to both these isomers. If this be correct they must behave differently in regard to boric acid.

¹⁾ E. FISCHER, B 45, 461 (1912).

According to the researches of H. J. WATERMAN and myself described in these Proc. (30 Dec. 1911 and 30 March 1912) retardation is usually associated with a strong solubility in fat or with a too large concentration of hydrogen ions.

Now, boric acid is much more readily soluble in water than in olive oil and is moreover an exceedingly feeble acid so that these two properties cannot, therefore, explain to us why boric acid so very much retards the growth of *penicillium glaucum* as we have indeed observed.

The formation of compounds with the polyalcohols which play such an important rôle in the living beings, compounds which can, moreover, be much more strongly acid than boric acid itself, offers a very simple explanation of the powerful action of this apparently so innocuous substance.

Under the influence of the development of the chemistry of the colloids, the origin of physiological processes has been perhaps searched for a little too much in purely physical phenomena: diffusion, change in surface tension, discharge of negative-charged colloids by positive ions and reversely, etc. Undoubtedly, all these actions play an exceedingly important rôle, but in many cases a chemical phenomenon is involved; it is like this with boric acid and so it will be, presumably, with the toxic action of many metals (I further refer to a communication from H. J. WATERMAN and myself in the "Folia microbiologica").

The question whether the strong action of some of the hydroxyl compounds is associated with an easy ring formation, as surmised by VAN 'T HOFF, has, as yet, been discussed by me only casually.

Last year, FOX and GAUGE (Trans. Chem. Soc. 1911, 1075) have succeeded in isolating mannitoboric acid and in preparing some of its salts, but as it appears from the analytical figures that there is present one molecule of water in excess of that required for the 5-ring closure, the configuration still remains uncertain.

As pyrocatechol causes a very strong increase of the conductivity I have endeavoured to obtain pyrocatecho-boric acid. Although we have not succeeded in doing so, we have yet managed to prepare a series of readily crystallizable complex salts some of which are characterised by a very slight solubility, so that they may, presumably, serve for the quantitative separation of boric acid.

A full description of these salts, also of the experiments mentioned above, which have been carried out mainly by Mrs. N. H. SIEWERTS VAN REESEMA, C. E. KLAMER and J. D. RUYS, will be given later.

Delft, May 1912.

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