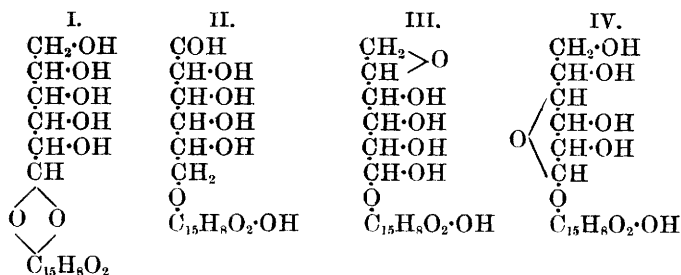


LXXXV.—*The Constitution of Rubiadinglucoside and Rubiadin.*

By L. MARCHLEWSKI.

IN the case of glucosides, derived from a single molecule of glucose containing a bivalent radicle, the constituents may be associated in various ways; thus, in the case of rubiadinglucoside, the following formulæ are possible.



The first three of these formulæ are based on the Baeyer-Fittig formula of glucose, the fourth being based on the formula proposed by Tollens (*Ber.*, 16, 921). The first expresses the idea that methyl-purpuroxanthin associates with glucose, forming a compound of the nature of an acetal, and that all the hydroxyls of the glucoside are carbinolic. The second presupposes the existence of an aldehyde group in the glucoside, four of the five hydroxyl groups being represented as carbinolic, the fifth as phenolic. The third formula represents the glucoside as a compound of an aldol type. The fourth formula both precludes the existence of aldehydic groups, and exhibits differences between the five hydroxyl groups.

In deciding which of these four formulæ represents the actual con-

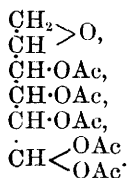
stitution of the compound under discussion, the following questions are of importance.

1. Does the glucoside contain an active aldehydic group?
2. Does the glucoside contain a concealed aldehydic group?
3. Are the five hydroxyls of the glucoside of carbinolic nature, or is one of them phenolic?

In discussing these points, the question necessarily arises—a closer examination of which might lead us too far, but which, nevertheless, may be shortly alluded to—What is the constitution of glucose?

Notwithstanding numerous researches on this subject, no final conclusion has been arrived at. The formula generally employed is that suggested by Baeyer and Fittig, although it is scarcely in accordance with all the known facts: thus, glucose fails to give the magenta test for aldehydes, but, on the other hand, it has been maintained that this test does not apply unconditionally to aldehydes containing a large number of hydroxyl groups.

Even at the time when Fischer (*Ber.*, **23**, 2114) discussed the constitution of glucose, important facts had been observed, which did not agree with the aldehydic formula; the non-occurrence of action when pentacetyl-dextrose and phenylhydrazine are brought together is one of these facts. Erwig and Koenigs (*Ber.*, **22**, 1464, 2207), who made this observation, therefore concluded that either Baeyer and Fittig's formula was incorrect, or that complications occurred within the dextrose molecule at the moment of acetylation, resulting in the formation of a substance unattackable by phenylhydrazine; they therefore represent pentacetyl dextrose by the formula



In other words, they suggest that an acetyl-group is formed by the combination of the elements of acetic anhydride with the aldehyde group, dehydration of the glucose molecule also taking place. There is, however, as these authors point out, nothing to support such an assumption, as dehydration does not attend acetylation in the case of similar compounds such as mannitol.

To this observation must be added another lately made by Skraup (*Ber.*, **22**, 669c), that the pentabenzoyl derivative prepared by Baum and Baumann's method (*Ber.*, **19**, 3218, 307c; **21**, 2744) is also unaffected by phenylhydrazine. Skraup therefore maintains that

glucose may exist in two forms, one of which possesses the character of an aldehyde, as represented by the Baeyer-Fittig formula; the other being the anhydride of a heptad alcohol. Skraup's view is materially confirmed by the fact that glucose yields two isomeric hydrazones.

On considering the facts in connection with the four formulæ by which rubiadinglucoside might be represented, it is at once necessary to dismiss the first formula, as the hydroxyls of the glucoside are clearly not identical in function.

As previously mentioned (this vol., p. 969), the glucoside is formed by boiling the madder extract with dilute acid; it is probably formed by the partial hydrolysis of some complex soluble glucoside containing two glucose residues to one of methylpurpuroxanthin. Such an interaction would involve the setting free of one of the hydroxyl groups of methylpurpuroxanthin; and on this assumption the glucoside contains one phenolic and four carbinolic hydroxyls. This conclusion is supported by the fact that rubiadinglucoside affords potassium and barium derivatives, which are dark red in colour.

Liebermann and Bergami (*Ber.*, 20, 2241) have assumed that ruberythric acid contains an alizarin hydroxyl, on account of the deep colour shown by the salts of this acid, which contains two glucose residues to one molecule of alizarin; and it is equally legitimate in the present case to assume that a phenolic hydroxyl is present in rubiadinglucoside. The composition of the barium derivative of the glucoside favours this assumption, although, on the other hand, some doubt may arise from the fact that the compound cannot be obtained in a crystalline form.

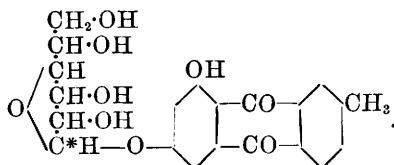
The view here taken derives support from analogy. An acetal-like combination, such as is represented by the first of the formula on p. 1137, can only take place easily when the two phenolic hydroxyls occupy adjacent positions. In the case of glucosides yielding products in which the hydroxyls take up a para-position, no acetal-like coupling takes place. This point is well illustrated in the case of arbutin, which on treatment with acids splits up into *d*-glucose and hydroquinone. The fact that arbutin is capable of forming methylarbutin, which on hydrolysis yields glucose and methylhydroquinone, conclusively proves the accuracy of the above assertion.

In the case of salicin again, which is derived from glucose and ortho-hydroxybenzylalcohol, only one hydroxyl takes part in the combination, salicin on oxidation yielding helicin, the formation of which involves the oxidation of one of the hydroxyls of saligenin.

The second formula is precluded by the fact that rubiadinglucoside is not acted on by phenylhydrazine. This was ascertained in the following manner.

A concentrated alcoholic solution of molecular quantities of the glucoside and of phenylhydrazine was heated in the water-bath during three hours, and finally steam was passed into the liquid. The product which separated out on cooling was washed with acetic acid, and proved to be unaltered rubiadinglucoside. A qualitative examination by means of Lassaigne's test, proved that no nitrogen compound had been formed, consequently formulæ 3 and 4 alone remain for discussion.

The third formula is analogous to that given to euxanthic acid by Graebe (*Annalen*, **254**, 278). This formula presupposes the association of methylpurpuroxanthin and glucose to be affected in such manner that an aldol is formed, and agrees generally with the observations made on the glucoside. The formula does not contain any active aldehydic group; and of the five hydroxyl groups, one is phenolic. Nevertheless the formula would appear very improbable, as in order to account for the empirical composition of the glucoside, it would be necessary to assume that dehydration of the glucose takes place, which is as improbable as that dehydration of glucose should occur during its acetylation. Therefore, as long as two different formulæ equally well express the constitution of glucose, the fourth of the formulæ given on p. 1137 is to be preferred, and this, moreover, appears to be in every respect in accordance with facts. In its fully developed form, and taking into consideration the formula for rubiadin to be referred to later on, the constitutional formula of rubiadinglucoside is as follows:—



The position of the ethylene-oxide-like oxygen in the glucose residue, as well as that of the hydroxyl of the methylpurpuroxanthin which is united with this residue, have, of course, been arbitrarily selected. The combination of the methylpurpuroxanthin with the glucose residue will necessarily take place at the point marked with an asterisk, *i.e.*, at the carbon-atom, which can, under certain conditions, according to Tollens (*Handbuch der Kohlenhydrate*, p. 11) be the origin of the aldehyde groups of dextrose, a transformation which cannot take place in the case of the glucoside on account of the presence of the methylpurpuroxanthin residue.

*d*-Glucose is apparently always present in natural glucosides in the form of a residue derived from an anhydride of a heptad alcohol,

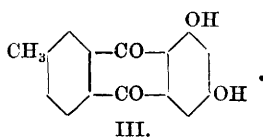
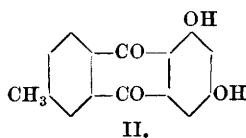
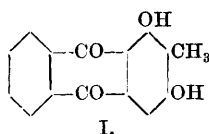
my observations showing that neither arbutin nor salicin are capable of interacting with phenylhydrazine, consequently they must be represented by formulæ similar to that assigned to rubiadinglucoside.

*Constitution of Rubiadin.*

All the properties of rubiadin afford proof that it is a methylated purpuroxanthin (compare Schunck and Marchlewski, this vol., 969). To determine its constitution, I have endeavoured to effect its synthesis.

The synthesis is, however, attended by considerable difficulties, as no fewer than six isomeric methylpurpuroxanthins may exist. By assuming, however, that it is derived from methylantracene, from which other natural methylantracene derivatives (emodine, chrysophanic acid, &c.) are formed, the task is considerably simplified.

On this assumption, one of the following formulæ must represent the constitution of rubiadin :—

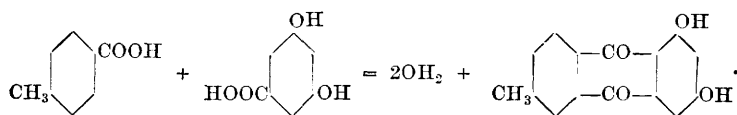


At first sight the first of these formulæ would appear improbable, as the presence of the methyl group between the two hydroxyls might conceivably so modify the properties of the substance that it would differ very much from a homologue of purpuroxanthin; but as methylquinizarin—in which the methyl and hydroxyl groups occur in the same nucleus—differs very little from quinizarin, this conclusion is not justified.

The second formula is certainly not that of rubiadin; it having been already assigned, on sufficient grounds, to another substance.

Noah (*Annalen*, **241**, 266), by condensing benzoic acid and symmetrical metadihydroxybenzoic acid obtained purpuroxanthin; thereby determining the constitution of that compound, and in like manner we might, *a priori*, expect to obtain methylpurpuroxanthin from paratoluic or paramethylbenzoic acid and metadihydroxybenzoic acid, thus :—

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I have accomplished this synthesis in the following manner: a mixture consisting of 4 grams of metadihydroxybenzoic acid, 15 grams of paramethylbenzoic acid, and 200 grams of concentrated sulphuric acid was heated at 110° during eight hours. The product was poured while still warm into a large quantity of water. A green flocculent precipitate was produced, containing, besides the expected methylpurpuroxanthin, anthrachryson and unaltered metadihydroxybenzoic acid and paratoluic acid; by directly extracting with ether all these substances excepting anthrachryson were dissolved out. The ethereal extract was now evaporated, the residue was suspended in water and steam was passed in during some time in order to expel the methylbenzoic acid. The remaining pale yellow residue was then twice extracted with benzene, in which neither anthrachryson nor dihydroxybenzoic acid are soluble. The methylpurpuroxanthin remaining after evaporating off the benzene was twice recrystallised from benzene.

The analysis of the product dried at 130° showed that the substance sought for had, indeed, been obtained.

0.1520 gave 0.3934 CO<sub>2</sub> and 0.0552 H<sub>2</sub>O. C = 70.58; H = 4.03.

C<sub>15</sub>H<sub>10</sub>O<sub>4</sub> requires C = 70.86; H = 3.93.

This artificial methylpurpuroxanthin strongly resembles rubiadin; the solubility of the two substances in ether, alcohol, and benzene, the form of the crystals, the absorption spectra of the alcoholic, alkaline, and sulphuric acid solutions being indistinguishable. Still the artificial product differs from the natural compound, in that the former melts at 267° and the latter at 290°. At first it appeared probable that this difference was due to slight impurities obstinately adhering to the substance, but this did not prove to be the case, as on preparing the acetyl derivative (which crystallises from benzene in pale yellow needles) and hydrolysing it with potash, a product was obtained also melting at 267°. Rubiadin, therefore, is probably represented either by the first or by the last of the three formulæ given on p. 1141, and between these only synthetic experiments can decide.