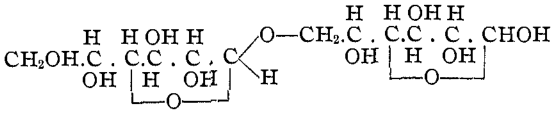


1,6- β-glucosido glucose (gentiobiose)

Maltose and gentiobiose thus constitute the first known α, β pair of compound sugars to be definitely allocated. Some deductions from this allocation will be discussed in a subsequent article.

Finally, mention may be made that the present proof of the identity of the biose of amygdalin with gentiobiose points the way to the synthesis of amygdalin and also to the preparation of gentiobiose from amygdalin. One should expect the synthesis to start with β-gentiobiose octa-acetate and proceed through the conversion of this to a halogen-acetyl gentiobiose,[17] which can doubtless be united with ethyl mandelate and the synthesis continued to amygdalin by the same reactions through which Fischer and Bergmann[18] have synthesized Fischer's glucoside, prulaurasin and sambunigrin from bromo-acetyl glucose and ethyl mandelate. To produce gentiobiose from amygdalin, one must seek to obtain an enzyme preparation, either from emulsin or from some other source, which hydrolyzes β-glucosides (or in particular Fischer's glucoside) but does not hydrolyze gentiobiose. There is little doubt that the hydrolyses are caused by separate enzymes, since Fischer has shown that amygdalin can be hydrolyzed to a mixture of Fischer's glucoside and glucose by the enzymes of yeast without the occurrence of any hydrolysis of the former substance.

WASHINGTON, D. C.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF CORNELL UNIVERSITY]

ORTHO-CRESOL-TETRACHLOROPHTHALEIN AND SOME OF ITS DERIVATIVES

E. L. ARNOLD[1]

RECEIVED NOVEMBER 17, 1923

o-Cresol-tetrachlorophthalein was made for the purpose of comparing its absorption spectrum with that of phenolphthalein and phenol-tetrachlorophthalein. It was prepared by the method of Fraude[2] for making *o*-cresolphthalein using anhydrous stannic chloride as the condensing agent.

A mixture of 60 g. of *pure* *o*-cresol (2 molecular equivalents), 84 g. of *pure* crystallized

---

[17] Bromo-acetyl gentiobiose has been prepared in amorphous form by Hudson and Johnson, THIS JOURNAL, **39**, 1275 (1917).

[18] Table I, Footnote *a*.

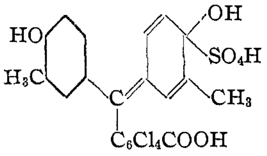
[1] Work done in partial fulfilment of the requirement for the degree of Bachelor of Chemistry by E. L. Arnold, holder of the Grasselli Undergraduate Scholarship in Chemistry at Cornell University, 1922–1923.

[2] Fraude, *Am.*, **202**, 154 (1880).

tetrachlorophthalic acid[3] (1 equivalent) and 60 g. of fuming stannic chloride was heated for 15 hours at 120–125° in a flask connected with a reflux condenser. At the end of this time the mass was practically solid. It was treated with water and distilled in steam until all of the unchanged *o*-cresol was removed. The liquid in the flask was then decanted and the solid was boiled with water and a small amount of hydrochloric acid to remove unchanged tetrachlorophthalic acid and stannic chloride. The solid was then filtered off and dissolved in 10% sodium hydroxide solution, forming a deep purple solution, which was filtered to remove dimethyltetrachlorofluoran, and the phthalein precipitated from the alkaline solution by pouring it into an excess of dil. hydrochloric acid. An amorphous buff-colored precipitate resulted. This was again dissolved in the alkaline solution, the solution diluted and filtered to remove traces of dimethyltetrachlorofluoran and again precipitated with an excess of hydrochloric acid. It was then thoroughly washed with hot water until free from chlorides and dried in the water-oven; 69 g. of the crude *o*-cresol-tetrachlorophthalein was obtained, a yield of about 53% of that calculated from the tetrachlorophthalic acid taken. The phthalein was crystallized from methyl alcohol, using boneblack to decolorize the solution. After three crystallizations the phthalein was obtained in colorless crystals which melted at 292–293° with decomposition. It lost no weight when heated at 110° and therefore contained no water or alcohol of crystallization.

Analyses. Subs., 0.3384, 0.2546: AgCl, 0.4010, 0.3006. Calc. for $C_{22}H_{14}O_4Cl_4$: Cl, 29.30. Found: 29.31, 29.21.

o-Cresol-tetrachlorophthalein resembles *o*-cresolphthalein, phenolphthalein and phenol-tetrachlorophthalein very closely in its properties. It is readily soluble in hot methyl and ethyl alcohols and in acetone. It is slightly soluble in glacial acetic acid, ether and benzene. The amorphous phthalein obtained by precipitation from a cold alkaline solution with an acid seems to be more readily soluble than the crystalline product. The phthalein is only slightly soluble in water even at the boiling point. When the alcoholic solution of the phthalein is poured into a large volume of water a milky suspension results. As the mixture stands the phthalein precipitates as a fine white powder, having the same melting point as the substance crystallized from alcohol. In conc. sulfuric acid the phthalein dissolved readily in the cold with a reddish color probably due to the formation of a sulfate.



Water precipitates the unchanged phthalein from this solution. *o*-Cresol-tetrachlorophthalein, like phenolphthalein, is a very weak acid and does not give well-characterized salts. In solutions of the caustic alkalies or alkaline carbonates it dissolves readily, forming colored solutions of the alkaline salts. In concentrated solutions the color is deep purple and in dilute solutions it is a lighter reddish purple. The addition of a large

[3] See Delbridge, *Am. Chem. J.*, **41**, 393 (1909).

excess of the caustic alkalies to the dilute alkaline solution of the phthalein decolorizes it on standing due to the formation of the tripotassium or sodium salt of the carbinolcarboxylic acid, $KOOCC_6Cl_4C(OH)(C_6H_3(OK)(CH_3))_2$. The dilute alkaline solution is also decolorized by the addition of a considerable quantity of alcohol due to the formation of the monopotassium or sodium salt of the carbinolcarboxylic acid. Solutions of calcium hydroxide and of barium hydroxide also dissolve the phthalein with the development of a purple color. The solution in ammonium hydroxide also is purple. The addition of acids to the purple solution in alkalies decolorizes it at once and precipitates the phthalein, as it is insoluble in water. For this reason *o*-cresol-tetrachlorophthalein may be used as an indicator in acidimetry and alkalimetry in the same way that phenolphthalein is used. The hydrogen-ion concentration at the end-point was determined by adding two drops of a saturated methyl alcoholic solution of the *o*-cresol-tetrachlorophthalein to 10 cc. of solutions of $P_H = 8$, $P_H = 8.5$ and $P_H = 9$. A slight white precipitate was obtained with $P_H = 8$, no precipitate or color with $P_H = 8.5$ and a purple color with $P_H = 9$. Therefore the end-point is between $P_H = 8.5$ and $P_H = 9$. This is practically the same concentration of hydrogen ions at which *o*-cresolphthalein gives an end-point.

o-Cresol-tetrachlorophthalein must have the lactone structure since it is a colorless compound and gives a colorless diacetate and a colorless dimethyl ether. The slightest trace of even the weakest base is sufficient to break up the lactone ring and give a salt of the phthalein having the quinoid structure.

o-Cresol-tetrachlorophthalein Diacetate was made by heating 5 g. of the pure *o*-cresol-tetrachlorophthalein, 5 g. of freshly fused sodium acetate and 25 g. of pure acetic anhydride to boiling for one hour in a flask connected with a return condenser. The mixture was poured into water and the whole allowed to stand, The diacetate was filtered off, washed with water until free from acetic acid and sodium acetate and dried. The yield of the diacetate was practically quantitative. It was crystallized from benzene until it was colorless and melted constantly at 207–208° and then analyzed. The product dried at 110° lost no weight.

Analyses. Subs., 0.3382, 0.3440: AgCl, 0.3420, 0.3466.
Calc. for $C_{22}H_{12}O_2Cl_4(OCOCH_3)_2$: Cl, 24.97. Found: 25.02, 24.93.

The diacetate is readily soluble in benzene and slightly soluble in acetone, ether, glacial acetic acid and in methyl alcohol. It is saponified slowly by aqueous alkalies or dil. sulfuric acid. Alcoholic solutions of the caustic alkalies saponify it readily especially when heated and the pure phthalein results when the alkaline solution is neutralized with acid. Conc. sulfuric acid saponifies it at once in the cold and the pure phthalein is precipitated on the addition of water. As the diacetate is colorless it has the lactoid structure.

Dimethyl Ether of o-Cresol-tetrachlorophthalein.—This ether was made by shaking a sodium hydroxide solution of the phthalein with an excess of dimethyl sulfate. The ether separated in yellowish-brown lumps. These were filtered off, washed with water until free from sulfates and boiled repeatedly with 10% sodium hydroxide solution for the purpose of removing any unchanged phthalein or monomethyl ether. When the alkaline extract had becomes colorless, the dimethyl ether, which is insoluble in solutions of the alkalies, was filtered off, washed with water and dried. It was then dissolved in benzene and a large amount of methyl alcohol added. The dimethyl ether crystallized slowly from the mixture. It was recrystallized thrice in this way from the mixture of benzene and methyl alcohol, until the melting point became constant and the substance was colorless. It was then analyzed for chlorine by the Parr bomb method. The substance lost no weight when heated to 100°.

Analyses. Subs., 0.2701, 0.3370: AgCl, 0.2998, 0.3747. Calc. for $C_{22}H_{12}O_2Cl_4(OCH_3)_2$: Cl, 27.70. Found: 27.46, 27.51.

The dimethyl ether of *o*-cresol-tetrachlorophthalein melts at 212–213°. It dissolves readily in benzene and slightly in acetone and in methyl and ethyl alcohols. It is insoluble in aqueous alkalies, but dissolves in a concentrated solution of alcoholic potassium hydroxide without color, probably forming the potassium salt of the carbinol-carboxylic acid, $KOOCC_6Cl_4C(OH)(C_6H_3(CH_3)(OCH_3))_2$. The dimethyl ether dissolves in conc. sulfuric acid forming a red solution, and water precipitates the unchanged product from this solution. The color is probably due to the formation of a quinoid sulfate similar to that formed by the phthalein in conc. sulfuric acid.

Absorption Spectrum of *o*-Cresol-tetrachlorophthalein

Miss S. Alice McNulty has studied the absorption spectra of solutions of *o*-cresol-tetrachlorophthalein, phenol-tetrachlorophthalein and of phenolphthalein in absolute ethyl alcohol. She found that the spectrum of *o*-cresol-tetrachlorophthalein is very similar to that of phenol-tetrachlorophthalein, but differs from that of phenolphthalein. *o*-Cresol-tetrachlorophthalein shows *four* bands in the ultraviolet, all of them weak. Phenol-tetrachlorophthalein in alcoholic solution also gives *four* absorption bands situated in about the same positions as those of *o*-cresol-tetrachlorophthalein. Phenolphthalein in alcoholic solution gives only *two* bands in the ultraviolet and these correspond closely to two of the more prominent bands in the spectra of *o*-cresol-tetrachlorophthalein and of phenol-tetrachlorophthalein. These bands are located at frequency numbers 3523 and 3613.

Summary

1. *o*-Cresol-tetrachlorophthalein, its diacetate and dimethyl ether have been prepared and analyzed. All are colorless compounds and therefore have the lactoid formula.

2. *o*-Cresol-tetrachlorophthalein like the other phthaleins investigated acts as a tautomeric compound for it dissolves in solutions of the alkalies with color, due to the formation of salts having a quinoid structure.

3. *o*-Cresol-tetrachlorophthalein can be used as an indicator in the same way as *o*-cresolphthalein. The end-point is between $P_H = 8.5$ and $P_H = 9$.

4. The ultraviolet absorption spectrum of *o*-cresol-tetrachlorophthalein in alcohol is very similar to that of phenol-tetrachlorophthalein. Both

give *four* bands, all of them weak. Phenolphthalein in alcohol gives only *two* bands corresponding closely to two of the more prominent bands found in phenol-tetrachlorophthalein and in *o*-cresol-tetrachlorophthalein.

ITHACA, NEW YORK

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

THE MECHANISM OF THE REACTION OF ISOCYANATES AND ISOTHIOCYANATES WITH THE GRIGNARD REAGENT

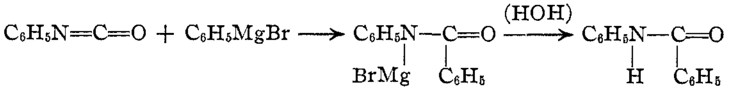
BY HENRY GILMAN AND CORLISS R. KINNEY

RECEIVED NOVEMBER 19, 1923

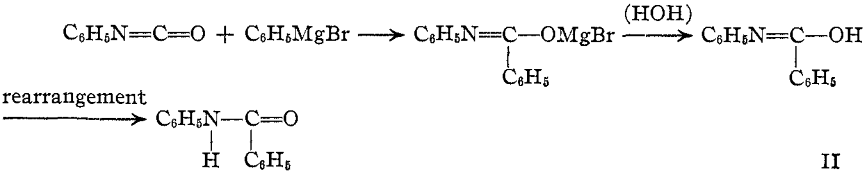
In connection with a series of studies concerned with the mechanism of reaction between the Grignard reagent and compounds having more than one reactive group, it has been shown[1] that with ketenes addition takes place at the carbonyl group and not at the ethylenic linkage. Because of the marked similarity in chemical behavior between ketenes and isocyanates, attention was directed at that time to the desirability of determining the mode of addition of the Grignard reagent to isocyanates, particularly because this class of compounds has two reactive groups ($—N{=}C{=}$ and ${=}C{=}O$) which can add the Grignard reagent.

The reactions of ketenes, isocyanates and isothiocyanates with the Grignard reagent have several points in common. First, a liberal excess of the Grignard reagent gives, with each of the types mentioned, one compound. Second, this compound (obviously different in each case) involves the addition of but one molecule of the Grignard reagent. Third, the product formed by hydrolysis in each case throws no light on the mechanism of reaction.

For example, in the formation of benzanilide from phenyl isocyanate and phenylmagnesium bromide the Grignard reagent may have added to the $—N{=}C{=}$ linkage (I) or to the carbonyl group (II).



$$C_6H_5N{=}C{=}O + C_6H_5MgBr \longrightarrow \underset{BrMg}{C_6H_5N}{-}\underset{C_6H_5}{C}{=}O \xrightarrow{(HOH)} \underset{H}{C_6H_5N}{-}\underset{C_6H_5}{C}{=}O \qquad I$$



$$C_6H_5N{=}C{=}O + C_6H_5MgBr \longrightarrow C_6H_5N{=}\underset{C_6H_5}{C}{-}OMgBr \xrightarrow{(HOH)} C_6H_5N{=}\underset{C_6H_5}{C}{-}OH$$

$$\xrightarrow{\text{rearrangement}} \underset{H}{C_6H_5N}{-}\underset{C_6H_5}{C}{=}O \qquad II$$

Blaise[2] has shown that when isocyanates react with RMgX compounds

---

[1] Gilman and Heckert, THIS JOURNAL, **42**, 1010 (1920). Later it was shown that ethylmagnesium iodide does not add to several typical ethylenic hydrocarbons under varying conditions [Gilman and Crawford, THIS JOURNAL, **45**, 554 (1923)].

[2] Blaise, *Compt. rend.*, **132**, 40 (1901).