THE STRUCTURE OF DISALICYL ALDEHYDE

By Roger Adams, M. F. Fogler and C. W. Kreger

Every chemist who has had occasion to use salicyl aldehyde to any extent has obtained at one time or another one of its very common derivatives designated in the literature as disalicyl aldehyde. As early as 1845[1] this substance was found along with salicyl aldehyde when the copper salt of salicyl aldehyde was distilled. In 1851 Cahours[2] obtained this same product by the action of benzoyl chloride upon salicyl aldehyde while attempting to prepare the benzoyl derivative; Perkin,[3] a little later, showed that acetyl chloride or succinyl chloride on acting upon salicyl aldehyde yielded the same product. Since that time it has been shown that practically all types of acid chlorides cause this same reaction to take place; thus phosphorus trichloride,[4] urea chloride,[5] phosgene in pyridine,[6] and oxalyl chloride in pyridine.[7] Investigations have indicated that the product is readily prepared by the action of acetyl chloride upon salicyl aldehyde in glacial acetic acid as a solvent; moreover, many of the substituted salicyl aldehydes yield substituted disalicyl aldehydes by the same treatment.[8]

The empirical formula and properties of disalicyl aldehyde have been determined in part by many of the investigators who obtained this product.[9] It has the formula $C_{14}H_{10}O_3$, corresponding to two molecules of salicyl aldehyde with a molecule of water eliminated; it gives no reaction for an aldehyde or ketone group with such reagents as phenyl hydrazine, hydroxylamine or sodium hydrogen sulfite; it gives no reaction for an hydroxyl group with such reagents as ferric chloride, acetyl chloride, acetic anhydride and is insoluble in sodium hydroxide solution. Disalicyl aldehyde is extraordinarily stable toward alkali, being undecomposed after long boiling with a concentrated potassium hydroxide solution or even fusion with potassium hydroxide; on the other hand, warm conc. sulfuric acid dissolves it to give a red solution which, upon careful dilution, yields salicyl aldehyde. Bromine gives a mixture of bromosalicyl

[1] Ettling, *ibid.*, **53**, 77 (1845).

[2] Cahours, *ibid.*, **78**, 228 (1851).

[3] Perkin, *ibid.*, **145**, 299 (1868).

[4] Zwenger, *Ann. Spl.*, **8**, 42 (1870).

[5] Gatterman, *Ann.*, **244**, 46 (1888).

[6] Einhorn, *Ber.*, **38**, 3630 (1905).

[7] Adams, THIS JOURNAL, **37**, 2719 (1915).

[8] Bradley, *Ber.*, **22**, 1134 (1889); *Am. Chem. J.*, **14**, 293 (1892); Dains, *ibid.*, **16**, 634 (1894).

[9] See previous references, and also Rivals, *Compt. rend.*, **124**, 368 (1897).

aldehyde and dibromo-disalicyl aldehyde. Strong nitric acid decomposes it and yields a certain amount of dinitro-salicylic acid.

In spite of the ease with which this substance is formed, and the number of times it has appeared in the literature, no satisfactory formula has as yet been suggested for it. An attempt was made to write structural formulas which would account for the properties of the substance, with the result that two have been found.
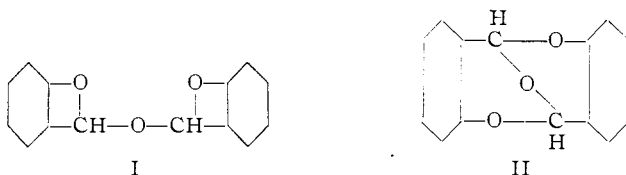
These structures contain no hydroxyl or carbonyl groups; moreover, being acetals, they would be expected to be stable to alkalies and unstable to acids. Formula I would seem unlikely on account of the 4-membered rings which are ordinarily difficult to form and rare. It was, therefore, eliminated and the investigation started to determine whether Formula II was the correct structure for disalicyl aldehyde.[10]

A possible mechanism by which such a substance could be produced from salicyl aldehyde is as follows.
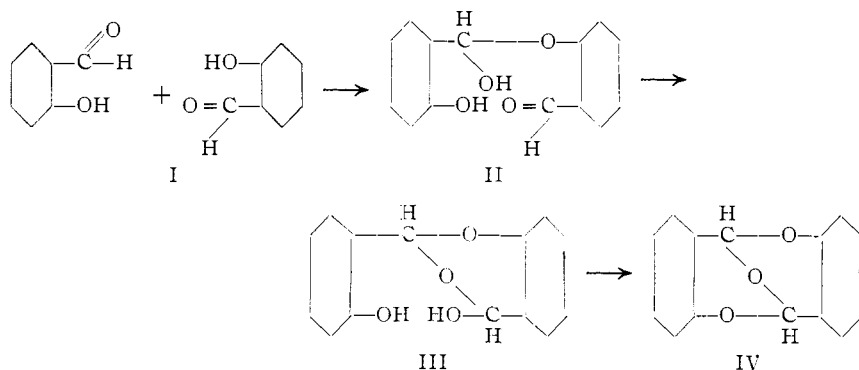
It may be seen that the first step involves the formation of an acetal between the hydroxyl of one molecule of salicyl aldehyde and the aldehyde

[10] An outline of this work was presented at the New York meeting of the American Chemical Society, 1921. At that time, Professor F. B. Dains who many years ago had been interested in disalicyl aldehyde, kindly pointed out to the authors of this communication that in the inaugural dissertation of Walter P. Bradley for the degree of Doctor of Philosophy at Goettingen in 1890, Formula II given above was mentioned as a possibility for the structure of disalicyl aldehyde. A copy of this dissertation was loaned to us by Dr. Dains. No proof was given by Bradley, however, that this structure was correct, and in publishing an abstract of his thesis in the *Ber.*, **22**, 1134 (1889), he did not even mention this formula.

group of the second molecule. This reaction corresponds to that which takes place when phenols or naphthols react with benzaldehyde. Phenols or naphthols do not react with benzaldehyde unless a mineral acid is used and then the reaction proceeds readily, with or without a solvent such as glacial acetic acid.[11] Ordinarily, triphenylmethane derivatives are obtained, but Claisen[12] has shown that, by working at low temperatures, the acetals from certain of the phenols and naphthols could be isolated as intermediate products. Whereas ordinary phenol-benzaldehyde acetals tend chiefly to rearrange to triphenylmethane compounds, this salicyl aldehyde hemi-acetal of salicyl aldehyde has a tendency to condense as shown in Steps III and IV, which involve, respectively, acetal formation and dehydration to form disalicyl aldehyde.

If this explanation is correct, it may be understood why various acid chlorides cause the reaction to take place. A small amount of acid chloride reacts first with the hydroxyl of the salicyl aldehyde, giving hydrochloric acid. This mineral acid being the catalyst usually used for the formation of an acetal causes Steps II and III to occur. The remaining portion of the acid chloride now acts as a dehydrating agent to remove water and thus gives Step IV. This deduction leads to the conclusion that any very small amount of mineral acid in the presence of a dehydrating agent should cause this reaction to take place. Experiments fully substantiated this. Salicyl aldehyde is unaffected by cold acetic anhydride even after long standing. If to this mixture, however, a small drop of conc. sulfuric acid is added, an immediate reaction takes place. The mixture turns red and heat is evolved sufficient to boil the acetic anhydride, if it is not cooled. Inside of 3 minutes after the sudden reaction is over, disalicyl aldehyde separates from the cooled reaction mixture in yields which amount to more than 85% of those calculated. In place of sulfuric acid, phosphoric acid or hydrochloric acid may be used.

Acids are catalyzers for the decomposition as well as for the formation of acetals. Treatment of disalicyl aldehyde with conc. sulfuric acid to yield salicyl aldehyde has already been mentioned. Warming with strong acid is rather drastic treatment, however. A very simple experiment showing the decomposition of disalicyl aldehyde with acids consists in treating pure disalicyl aldehyde with an excess of acetic anhydride. No reaction takes place, even on long boiling. When, however, a drop of sulfuric acid is added to the cold solution and the mixture allowed to remain at room temperature, large, heavy transparent crystals separate from the solution within 24 hours. These crystals are salicyl aldehyde triacetate.

If Steps III and IV described abovea re correct, it should be possible to form with ease a compound of properties similar to disalicyl aldehyde by

[11] Russanow, *Ber.*, **22**, 1944 (1889). Michael, *Am. Chem. J.*, **9**, 130 (1886).
[12] Claisen, *Ann.*, **237**, 269 (1887).

$$+ \; 3(CH_3CO)_2O \; \xrightarrow{(H_2SO_4)} \; CH(OCOCH_3)_2 + 3CH_3CO_2H \; \; OCOCH_3$$
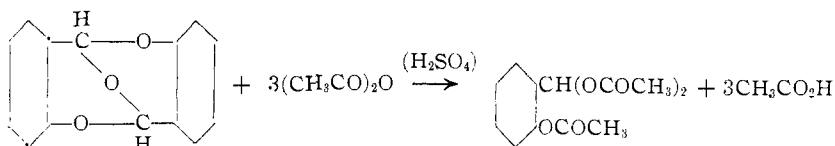
the condensation of saligenin with benzaldehyde. The analogy is best shown by the following two equations.
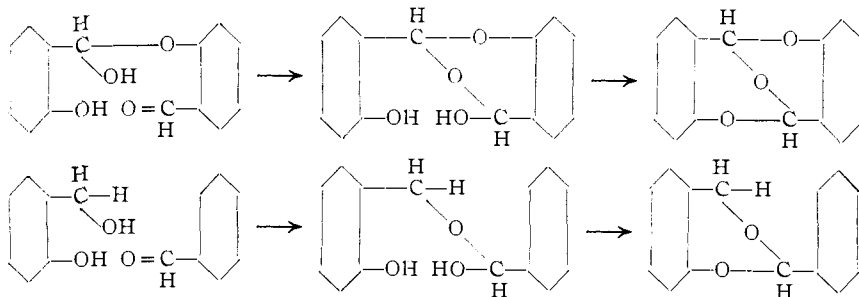
It is true that the hydroxyl group in the saligenin is an alcohol group, while that in the intermediate step of the formation of disalicyl aldehyde is a hemi-acetal hydroxyl; nevertheless the reactions should proceed in a somewhat similar manner. The experiments came up to expectations. The reaction between saligenin and benzaldehyde does take place with the greatest ease and does give a compound which is exactly analogous to disalicyl aldehyde in properties. In fact, the reaction takes place so readily that it is merely necessary to warm these two substances together in the presence of a very small amount of acid without the use of a solvent or dehydrating agent. To get the best results in forming disalicyl aldehyde, a high temperature must be avoided; likewise a high temperature must be avoided in the formation of this new product. The compound forms with such ease that even benzoic acid acts as a catalyst and in fact it is preferable to use this, rather than hydrochloric acid, since the latter tends to cause saligenin to condense with itself to a certain extent, thus lowering the yield of desired product.

This new condensation product of saligenin and benzaldehyde is 2-phenyl-1,3-benzodioxan or phenyl-methylene saligenin. It is a well crystallized compound, unreacted upon by hydroxyl or carbonyl group reagents, insoluble in and extremely stable to alkalies. It dissolves in warm conc. sulfuric acid to give a red solution which, on dilution, yields benzaldehyde and a resinous substance, presumably a saligenin condensation product. The compound decomposes in a manner similar to that of disalicyl aldehyde when dissolved in acetic anhydride and treated with a drop of sulfuric acid. Benzylidene di-acetate is readily obtained, together with a saligenin resin.

The reaction represented by the condensation of saligenin and benz-aldehyde to give a benzo-dioxan is not a limited one. It has already been shown that other aldehydes react in the same way with saligenin and an investigation as to the scope of this reaction is now under way.

The structure represented by disalicyl aldehyde involves a new type of nucleus and consequently it is necessary to outline a convenient system of nomenclature. The following formula represents the nucleus and numbered as in the figure should be called a 2,6,9 bis-dioxan.
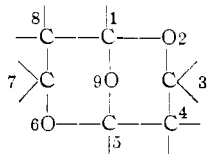
By using this system of nomenclature, disalicyl aldehyde is then dibenzo-2,6,9-bis-dioxan.

A compound which is probably of analogous structure to disalicyl aldehyde is formed when o-amino arsine oxide is diazotized in dilute aqueous solution and the diazo compound treated with sulfurous acid. Two molecules of the intermediate o-hydroxy-arsine oxide, which is very similar in constitution to salicyl aldehyde, lose a molecule of water spontaneously and form the anhydride, a substance which the writer designates as o-hydroxy-phenyl-arsinoxide anhydride.[13]
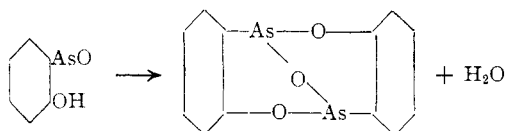
The formation of such a compound as disalicyl aldehyde from salicyl aldehyde is of more than ordinary interest because of the fact that aliphatic β-hydroxy aldehydes should resemble salicyl aldehyde in their reactions. The former substances should, therefore, be expected to form bis-dioxans, and preliminary experimental evidence leads to the conclusion that such is the case. Since the monosaccharides are β-hydroxy aldehydes, it is possible that some of the complex condensation products of the monosaccharides contain this bis-dioxan grouping.

Experimental Part

Preparation of Disalicyl Aldehyde (dibenzo-2,6,9-bis-dioxan).—Thirty g. (1 mole) of salicyl aldehyde and 25 g. (1 mole) of acetic anhydride are mixed and cooled to 0° in an ice-and-salt mixture. One drop of conc. sulfuric acid is added and the mixture immediately stirred to make it homogeneous. Within 10 seconds a deep cherry-red color has developed and a vigorous reaction takes place which is complete within 2 or 3 minutes, after which time the mixture practically solidifies. The mass is stirred thoroughly in

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[13] Kalb, $Ann.$, **423**, 70 (1921).

order to be sure that all of the salicyl aldehyde has reacted, and it is best to allow the mixture to stand in the ice for 5 or 10 minutes longer. By filtration with suction and washing with water, then drying, 24 g. of disalicyl aldehyde is obtained which corresponds to over 85% of the calculated amount. There is a small additional amount of product formed by allowing the filtrate from the crystals to stand in ice for 10 to 15 minutes longer.

The product is best purified by recrystallization from alcohol, from which it forms white, prismatic needles melting at 130° (corr.). The melting points previously reported in the literature vary from 127° to 130°.

If a larger amount of acetic anhydride is used, the reaction takes place in essentially the same way but not so good a yield results. It is also necessary to take certain precautions in using larger amounts of acetic anhydride; the mixture should not be allowed to stand too long before filtering the disalicyl aldehyde since the latter reacts with acetic anhydride in the presence of acid to form salicyl aldehyde tri-acetate. With the smaller amount of acetic anhydride, the product precipitates so quickly that there is no need for longer standing.

If the reaction mixture is not very carefully controlled in an ice and salt bath, the heat evolved is so great that the mixture will boil, and on cooling it, a poorer yield of disalicyl aldehyde is obtained.

In place of conc. sulfuric acid, a drop of glacial phosphoric acid may be used. Hydrochloric acid is also a catalyst but it is necessary to alter the procedure slightly. One-half of the acetic anhydride is saturated with dry hydrogen chloride. This saturated solution is then added to the mixture of salicyl aldehyde and the other half of the acetic anhydride at room temperature. The reaction develops heat, but not so much as in the case of the other acids. A somewhat longer time is required for the precipitation of the disalicyl aldehyde and the yields are not quite so high.

Trichloro-acetic acid may also be used as a catalyst but the results are still poorer than in the cases already mentioned.

Conversion of Disalicyl Aldehyde to Salicyl Aldehyde Tri-acetate.—Five g. (1 mole) of disalicyl aldehyde is dissolved in 14 g. (6 moles) of acetic anhydride, and one drop of conc. sulfuric acid is added. This mixture is allowed to stand at room temperature for a day or two. The tri-acetate of salicyl aldehyde separates in large, heavy crystals of rhombic form, some of which are 6 to 12 mm. on a side. They melt at 100-101° and do not lower the melting point of salicyl aldehyde tri-acetate (m. p. 100-101°) prepared according to the method of Barbier.[14]

Preparation of 2-Phenyl-1,3-Benzo-dioxan (Phenylmethylene Saligenin).— Ten g. (1.1 mole) of saligenin and 10 g. (1 mole) of benzaldehyde which has previously been saturated with benzoic acid, are heated for 2 hours on a steam cone. A light yellow resinous looking product results. The reaction mixture, after standing at room temperature for 2 hours, is treated with 300 cc. of a 5% sodium hydroxide solution and cooled in ice so that the product will solidify. The white solid is filtered and washed with water. It is crude 2-phenyl-1,3-benzo-dioxan and corresponds to practically a quantitative yield of product. It is best purified by dissolving 3 g. in 70 cc. of 95% alcohol, adding 30 cc. of water, warming this solution until it is clear and then allowing it to stand in an open beaker at room temperature. Within half an hour a white crystalline precipitate forms. After two crystallizations, pure material is produced, melting at 54°.

A drop of conc. hydrochloric acid may be used as a catalyst in place of the benzoic acid. It is then necessary merely to heat the reaction mixture of saligenin, benzaldehyde and a drop of hydrochloric acid until solution takes place. The mixture is allowed to stand for several hours at room temperature. The product is isolated in the same man-

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[14] Barbier, *Bull. soc. chim.*, [2] **33**, 53 (1880).

ner as described above, but the yields are not so good as with the benzoic acid method. If the reaction mixture, when hydrochloric acid is used, is heated longer, the yields are in general still poorer, due probably to a partial resinification of the saligenin.

Analyses. Subs. 0.1342: CO_2, 0.3885; H_2O, 0.0715. Subs. 0.5957, 0.4810: C_6H_6, 43.9, 43.9; ΔTF, 0.319°, 0.257°. Calc. for $C_{14}H_{12}O_2$: C, 79.24; H, 5.66; mol. wt., 212. Found: C, 78.97; H, 5.92; mol. wt., 212, 213.

2-Phenyl-1,3-benzo-dioxan is soluble in all the common organic solvents. It does not dissolve in solutions of alkali and is unchanged even after long boiling with 20% sodium hydroxide solution. When treated with conc. sulfuric acid, an immediate decomposition takes place with the formation of benzaldehyde and red lumps of resinified saligenin. The product gives no aldehyde or ketone test with sodium hydrogen sulfite, phenylhydrazine or hydroxylamine; it gives no test with hydroxyl group reagents such as ferric chloride or acetic anhydride even after long boiling.

Conversion of 2-Phenyl-1,3-benzo-dioxan to Benzylidene Diacetate and Saligenin Resin.—Ten g. (1 mole) of 2-phenyl-1,3-benzo-dioxan is mixed with 30 g. (6 moles) of acetic anhydride and one drop of conc. sulfuric acid at room temperature. The mixture is then allowed to stand for several days. At the end of this time the acetic anhydride is distilled *in vacuo*, the residue taken up in ether, washed with water and then with a dilute solution of sodium carbonate. The ether solution is then dried over anhydrous sodium sulfate, the ether distilled, then the residue distilled *in vacuo*. A constant boiling, colorless fraction comes over at 125° at 4 mm. pressure which on cooling and inoculating with a crystal of benzylidene diacetate almost completely solidifies. The melting point is 45°, which agrees with that found in the literature for benzylidene diacetate. The residue in the distilling flask consists of a pale yellow, heavy oil which does not distil at 250° at 4 mm. pressure and at ordinary temperatures forms a resin-like mass which is without question a saligenin resin.

Summary

1. Disalicyl aldehyde has been shown to have the following formula
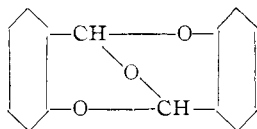
and may be called dibenzo-2,6,9-bis-dioxan. The formula accounts for all of the known properties of this substance.

2. A possible mechanism for the formation of such a structure from salicyl aldehyde is given and from this mechanism conclusions have been drawn as to new methods by which it should be possible to prepare disalicyl from salicyl aldehyde.

3. Disalicyl aldehyde may be formed almost quantitatively by the action of a drop of mineral acid upon a solution of salicyl aldehyde in acetic anhydride.

4. It was concluded from the mechanism of the formation of disalicyl aldehyde that a compound should form from saligenin and benzaldehyde which should possess similar properties to disalicyl aldehyde. This substance does form and may be looked upon as 2-phenyl-1,3-benzo-dioxan,

or phenylmethylene saligenin, forming white plates with a melting point of 54° and having the structure
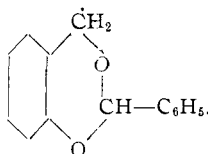
URBANA, ILLINOIS

RACEMIC ACID IN SOLUTION

BY STUART WORTLEY PENNYCUICK

Several physical methods have been used to show the existence (or nonexistence) of the racemic molecule in solution. Some have given positive results, while others point to its complete breakdown into the two active forms.

Bruni and Padoa[1] from molecular-weight determinations conclude that racemic acid exists in solution in the presence of excess of one of the active forms. Kuster[2] by solubility determinations, and Dunstan and Thole[3] by a viscosity method find positive results. Stewart[4] by absorption spectra observations, and Rankin and Taylor[5] also find evidence of its existence. On the other hand specific gravity and heat of neutralization determinations,[6] as well as a rotatory dispersion method,[7] show no evidence of its independent existence.

An interfacial tension method as described in this paper leaves little doubt that the racemic molecule does exist in solution.

The interfacial tensions between aqueous solutions of (a) *dextro* tartaric, (b) *levo* tartaric, (c) racemic acid, and an inert liquid have been measured and the results compared. As a comparison of the interfacial tensions was aimed at, the drop method as developed by Tate,[8] Morgan[9] and co-workers, and Lohnstein[10] was adopted. The apparatus used was as

[1] Bruni and Padoa, *Atti accad. Lincei.*, **11**, 212 (1902).

[2] Kuster, *Ber.*, **31**, 1847 (1898).

[3] Dunstan and Thole, *J. Chem. Soc.*, **93**, 1815 (1908).

[4] Stewart, *ibid.*, **91**, 1537 (1907).

[5] Rankin and Taylor, *Proc. Roy. Soc. Edinburgh*, **27**, 172 (1907).

[6] Jahn, *Wied. Ann.*, **43**, 306 (1891).

[7] Darmois, *Trans. Faraday Soc.*, **10**, 80 (1914).

[8] Tate, *Phil. Mag.*, [iv] **27**, 176 (1864).

[9] Morgan, THIS JOURNAL, **30**, 360 (1908).

[10] Lohnstein, *Z. physik. Chem.*, **64**, 686 (1908).