5-Brom-2-acetanthranil was warmed with freshly distilled aniline. The condensation took place smoothly and rapidly. The crude product was treated with bone-black and crystallized from 95 per cent. alcohol, giving colorless six-sided prisms, melting at 185–186° (corr.) when rapidly heated.

Bromine found, 25.9; calculated for $C_{15}H_{11}ON_2Br$, 25.4.

6-*Brom-2-methyl-3-orthotolyl-4-ketodihydroquinazoline.*—This was prepared in similar fashion, from 5-brom-2-acetanthranil and *o*-toluidine. The crude product was dissolved in alcohol, precipitated by the addition of water, the precipitate washed with acetic acid to remove any excess of *o*-toluidine, and recrystallized from dilute alcohol. Colorless crystals were thus obtained, melting at 137–138° (corr.) when rapidly heated.

Bromine found, 24.32; calculated for $C_{16}H_{13}ON_2Br$, 24.30.

In both this case and in the foregoing, the anthranil was carefully washed with carbon tetrachloride before use, to remove any excess of acetic anhydride which might contaminate the product with anilide or toluide.

It will be observed that, with the exception of the methyl derivative, the melting-points of these quinazolines steadily sink with rising molecular weight, and that the iso compounds melt higher than the normal. We have elsewhere called attention to the same condition of affairs in other series of quinazolines.

COLUMBIA UNIVERSITY AND
MISSISSIPPI AGRICULTURAL AND MECHANICAL COLLEGE,
November, 1905.

CONTRIBUTION FROM THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY.]

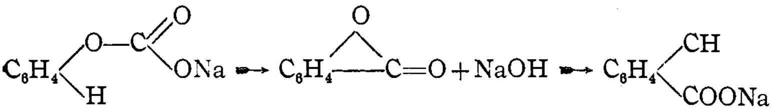
THE ACTION OF PYRIMIDINE ON SALICYL CHLORIDES.

BY RICHARD B. EARLE AND H. LOUIS JACKSON.

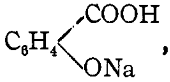
Received November 25, 1905.

(PRELIMINARY PAPER.)

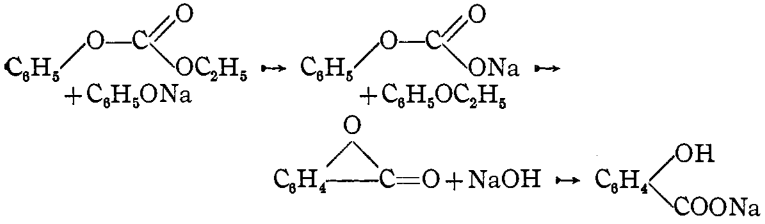
THE explanation generally given of the reaction involved in the preparation of salicylic acid from sodium phenolate and carbon dioxide is that the sodium phenol carbonate, first formed, rearranges to sodium salicylate. An obvious way of explaining this rearrangement is to assume the formation of an intermediate product, an inner anhydride or lactone of salicylic acid;



$$C_6H_4\left\langle\begin{matrix}O-C\begin{matrix}\diagup\!\!\diagup O\\ \diagdown ONa\end{matrix}\\ H\end{matrix}\right. \rightarrow C_6H_4\overset{O}{\triangle}C=O+NaOH \rightarrow C_6H_4\left\langle\begin{matrix}OH\\ COONa\end{matrix}\right.$$

Recently Lobry de Bruyn and S. Tijmstra[1] have brought forward evidence that this view of the formation of salicylic acid is not supported by the facts, and consider that the acid is formed by the direct addition of carbon dioxide to give  $C_6H_4\left\langle\begin{matrix}COOH\\ ONa\end{matrix}\right.$, no rearrangement taking place. The arguments, however, do not seem conclusive.

Phenyl ethyl carbonate,[2] if heated with sodium phenolate, reacts readily to form sodium salicylate and phenetol. This also may be considered as a case of the formation of an intermediate body, salicylid,

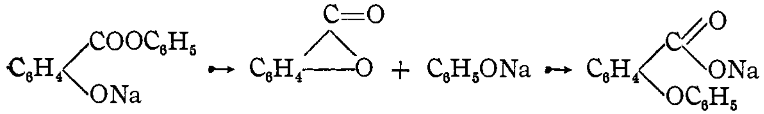


$$C_6H_5\diagup O-C\begin{matrix}\diagup\!\!\diagup O\\ \diagdown OC_2H_5\end{matrix} + C_6H_5ONa \rightarrow C_6H_5\diagup O-C\begin{matrix}\diagup\!\!\diagup O\\ \diagdown ONa\end{matrix} + C_6H_5OC_2H_5 \rightarrow$$

$$C_6H_4\overset{O}{\triangle}C=O+NaOH \rightarrow C_6H_4\left\langle\begin{matrix}OH\\ COONa\end{matrix}\right.$$

Attempts have been made by one of us to obtain support for this view by studying the action of sodium and sodium phenolate upon other phenol esters as phenol acetate[3] and benzoate. The results, although interesting, throw no light upon this problem.

A similar rearrangement, which might be explained on the same basis, is that of the sodium salt of salol to the sodium salt of the phenyl ether of salicylic acid,



$$C_6H_4\left\langle\begin{matrix}COOC_6H_5\\ ONa\end{matrix}\right. \rightarrow C_6H_4\overset{C=O}{\triangle}O + C_6H_5ONa \rightarrow C_6H_4\left\langle\begin{matrix}C\begin{matrix}\diagup\!\!\diagup O\\ \diagdown ONa\end{matrix}\\ OC_6H_5\end{matrix}\right.$$

On account of the possibility that this lactone of salicylic acid may be an intermediate stage in reactions of the sort and also because it would be a β-lactone, the writers were led to attempt

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[1] Rec. trav. chim. Pays-Bas. 23, 385 (1904); Ber. 38, 1375 (1905).

[2] J. pr. Chem. [2] 27, 39 (1883).

[3] Perkin and Hodgkinson: Chem. News, 41, 222 (1880); J. Chem. Soc. 37, 487 (1880).

its isolation in the case of two substituted acids. A large amount of work has already been done in this field, a very brief mention of which follows.

Kraut[1] obtained by heating salicylic acid with acetyl chloride a light yellow resinous mass which he named salicylo-salicylic acid.

Schiff[2] prepared two anhydrides by heating salicylic acid with phosphorus oxychloride, which he called salicylid and tetrasalicylid, and showed that the anhydride gives no color with ferric chloride. He doubted the homogeneity of Kraut's compound.

The action of acetic anhydride on salicylic acid was tried by Perkin.[3] His product was a resinous mass, the physical properties of which were similar to those of the salicylo-salicylic acid of Kraut.

The best work on the subject is that of Anschütz,[4] who obtained two anhydrides which are presumably individuals. These were obtained by heating the acid with phosphorus oxychloride in an indifferent solvent such as toluene or xylene. One of them, which melted at 260–261°, was named by him salicylid, and the other which melted at 322–325°, polysalicylid. Salicylid was found, by its lowering of the freezing-point of phenol to have four times the molecular weight of the true salicylid. A comparison of these anhydrides of Anschütz with those of the earlier investigators establishes the fact that none of the older preparations were at all homogeneous.

F. Hofmann-La Roche and Co.[5] have patented a process for the preparation of salicylid by heating acetylsalicylic acid. Their product possesses a melting-point ranging from 110° C to 210° C. It is probably a mixture. The lack of uniformity of so many of these anhydrides leads to the conclusion that they polymerize on heating.

In all these attempts to prepare salicyl anhydrides the acid is subjected to the action of dehydrating agents with the aid of heat. If, as is probable, they polymerize on heating, such methods do not seem promising. The reaction used in this

[1] Ann. 150, 13 (1869).

[2] Ibid. 163, 218 (1872).

[3] Ber. 16, 339 (1883).

[4] Friedl. Pt., III, 1890–'94, 822.

[5] Friedl. Pt., VI, 1900–'02, 1106.

work seemed hopeful inasmuch as it can be carried out below zero.

The reaction made use of was that of splitting off hydrochloric acid from a substituted salicyl chloride by means of a tertiary base, pyridine being found most convenient. The chloride of salicylic acid itself is not readily made, phosphorus pentachloride acting on the hydroxyl group also, giving compounds containing phosphorus. Anschütz[1] has shown that when salicylic acid contains a substituent ortho to the hydroxyl, it is protected, and phosphorus pentachloride gives the normal acid chloride. The chloride of salicylic acid itself can be made by the action of *p*-toluene sulphone chloride on the acid.[2] However, the easy accessibility of the dichlor and dibrom acid chlorides led us to begin the study of the reaction with them. These chlorides were dissolved in suitable solvents and the calculated amount of pyridine, diluted by the solvent, gradually added.

The results with the dichlor acid chloride were as follows: Benzene was first used as a solvent but its use was given up, as the chief product was a gum from which only a small amount of a substance of a definite melting-point could be obtained. Chloroform gave better results, if used at its boiling-point, the experiments at —10° giving the same sticky gum that was obtained with benzene. This gave about 50 per cent. of the theory of a white amorphous powder, which after recrystallization from nitrobenzene melted with decomposition at about 330° C. It gave no color with ferric chloride. A molecular weight determination was made, using boiling anisol as solvent. As we were unable to find the experimental constant for anisol in the literature, it was determined. The molecular weight found was 734, while that calculated for $(C_6H_2Cl_2OCO)_4$ is 755.6. It is, therefore, a polymer of the substance desired.

The rest of the material dissolved in the chloroform was left on evaporation as a sticky gum which solidified on standing and could be pulverized. Attempts to work with this were unsatisfactory as the substance contained pyridine which we were unable to wash out, it being set free only on decomposition of the substance by boiling alkali solutions, cold solutions of alkali having no effect.

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[1] Ber. 30, 221 (1897).

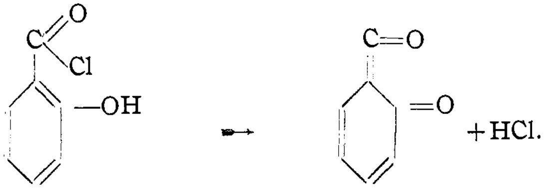
[2] Friedl. Pt., VI, 1900–'02, 35.

The results with the dibrom acid chloride were as follows: As a solvent, petroleum ether at about —10° was first used but it was found that the product contained pyridine from which we were unable to free it. Carbon tetrachloride gave a like result.

The best results were obtained with acetone, cooled to about —10°. The anhydride obtained in this way was found to be free from pyridine, and gave no color with ferric chloride. The melting-point is indeterminate, the substance passing slowly from the solid condition to that of a liquid, over a range of about 100°. Molecular weight determinations indicated it to be heptasalicylid. The behavior on heating indicates, apparently, a lack of homogeneity, but this is not certain.

A very interesting color change was noticed during the action of the pyridine on both of the chlorides. When the pyridine solution is added to that of the chloride, the solution takes on a bright yellow tinge, the color fading quickly, leaving the solution colorless as before. This was the case with all the solvents used, the duration of the color being longest in xylene, in which it lasted for about a minute.

The appearance of this color is so striking and unexpected, that it has led to some speculations as to its cause. It is obviously closely connected with the first stage in the reaction, as its appearance is simultaneous with the addition of the first drops of pyridine solution. One explanation for it consists in the assumption that the first step in the reaction is the breaking off of hydrochloric acid to form an ortho-quinoid body;



Willstätter's[1] recent isolation of quinone diimine has shown that a quinoid grouping of the affinities in the benzene ring does not necessarily imply the presence of color. But the near relationship of this substance to *o*-benzoquinone,[2] a highly colored substance, makes it probable that such a body, if capable of independent existence, would be highly colored.

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[1] Ber. 37, 4605 (1904).

[2] Jackson and Koch: Am. Ch. J. **26**, 10 (1901).

This explanation of the course of the reaction leads to a clearer understanding of the results obtained. A body of the constitution given would tend to form aggregates containing two or more salicylic acid molecules rather than to form the simpler monosalicylid. The tendency of *o*-benzoquinone to form complex compounds with substances containing hydroxyl groups is well known.[1]

Several attempts to isolate derivatives of this hypothetical substance were made without success. Not enough work has been done yet in this direction to even indicate a suitable method of attack.

EXPERIMENTAL PART.

Preparation of 3,5-*Dichlorsalicylic Acid.*—Tarugi's[2] method was used at first, but was found to give poor yields of impure substance. The method of Smith[3] gave better results. Fifty grams of salicylic acid were suspended in 250 cc. of glacial acetic acid and a slight excess over the theory of chlorine was passed in, the solution being kept at room temperature by cooling. After an hour's standing the reaction product was filtered off and recrystallized from 90 per cent. acetic acid. About 75 per cent. of the theory was obtained of pure acid, melting at 219.5° C.

Preparation of 3,5-*Dichlorsalicyl Chloride.*[4]—Ten grams of finely powdered dichlorsalicylic acid were heated on the steam-bath in a small flask with 10.2 grams of phosphorus pentachloride. The action is smooth, although it is often necessary to add a slight excess of the chloride to complete the reaction. After an hour's heating on the steam-bath it was diluted with ligroin, cooled to —10° C. and filtered. The white needles thus obtained were found to be practically pure after one crystallization from ligroin. The yield is about 50 per cent. of the theory. Nothing could be gotten from the ligroin mother-liquors but uncrystallizable gums.

Both this and the dibrom acid chlorides are rather unstable; they give off hydrochloric acid slowly on boiling with 60–80° ligroin. Even long standing in a vacuum desiccator causes them to lose hydrochloric acid with the formation of anhydrides.

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[1] Am. Ch. J. 26, 10 (1901).

[2] Gazz. Chim. [2] 30, 487 (1900).

[3] Ber. 11, 1225 (1878).

[4] Anschütz: Ber. 30, 222 (1897).

The Action of Pyridine on Dichlorsalicyl Chloride.—Twelve grams of the chloride were dissolved in chloroform, in which it is very easily soluble. Four and three-tenths grams (one molecule) of pyridine, mixed with chloroform, were gradually added. Much heat was developed and the solution turned yellow with each addition of pyridine, the color vanishing almost instantly. The clear reaction mixture was evaporated to a small volume and the gummy mass so obtained washed with benzene. The insoluble matter was washed with water and dried. We obtained thus about 6 grams of a white amorphous powder. It was practically insoluble in all the ordinary solvents, but soluble in boiling nitrobenzene and anisol. It was recrystallized from nitrobenzene, from which it crystallizes in short prismatic crystals, until it melted constant, with decomposition, at about 330° C. It gave no color in alcoholic solution with ferric chloride. It is remarkably stable; boiling with 1 : 1 potassium hydroxide solution dissolves it only slowly, although alcoholic potassium hydroxide hydrolyzes it to the acid in a few seconds. This is obviously due to its extreme insolubility in water.

Analyses by the Dennstedt[1] combustion method gave the following results:

	Calculated for $C_7H_2O_2Cl_2$.	Found.	
		I.	II.
Carbon	44.44	44.44	45.02
Hydrogen	1.06	....	1.52
Chlorine	37.57	37.34	37.67

The molecular weight was determined in boiling anisol. The experimental constant of anisol was determined, as it seems not to have been published.

Boiling-Point Constant of Anisol.—The anisol used was prepared from phenol and dimethyl sulphate[2] and purified by repeated fractional distillation until the portion taken for the experiment varied only 0.3° C. in boiling-point. The usual Beckmann apparatus was used.

(1) 0.2395 gram of *s*-trinitrobenzene dissolved in 16.16 grams of anisol raised the boiling-point 0.315° C.

(2) 0.5116 gram of *s*-trinitrobenzene dissolved in 16.16 grams of anisol raised the boiling-point 0.663° C.

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[1] Ber. 30, 1590, 2861 (1897).

[2] Werner: Ibid. 37, 3658 (1904).

(3) 0.8092 gram of *s*-trinitrobenzene dissolved in 16.16 grams of anisol raised the boiling-point 1.061° C.

	Calculated for K.[1]	Found.
1	4595	4529
2	....	4463
3	....	4515
	Average =	4502

Molecular Weight of the Anhydride.—0.6250 gram of substance dissolved in 17 grams of anisol raised the boiling-point 0.225° C.

Calculated for $(C_6H_2Cl_2OCO)_4$.	Found.
755.6	733.6

The substance has, therefore, a molecular weight four times that of dichlorsalicylid. It will be noticed that the melting-point is about 70° higher than that of the analogous salicylid of Anschütz, while the difference between the melting-points of the two acids is about 65°.

The remainder of the product of the preceding reaction, obtained by evaporation of the benzene washings, was a colorless gum which gradually solidified to a hard friable mass. It contains, as has so often been the case in this work, pyridine, from which it cannot be freed without decomposition. It is odorless, but develops a strong odor of pyridine on boiling with strong alkalies, although it is scarcely attacked by them in the cold. Work on this substance has proved very puzzling and unsatisfactory, and has been abandoned for the present.

Preparation of 3,5-*Dibromsalicylic Acid.*[2]—Seventy-five grams of salicylic acid were suspended in 375 cc. of glacial acetic acid, and five molecules of bromine added from a burette. The solution was warmed on the steam-bath for several hours, and, after cooling, was filtered from the dibrom acid which separated. This was recrystallized from glacial acetic acid until pure. If, instead of pure acetic acid, the mother-liquors from a previous preparation are used for the bromination, the yield approximates the theory.

Preparation of Dibromsalicyl Chloride.—An intimate mixture of dibrom acid and phosphorus pentachloride was warmed in a flask on the steam-bath until the contents were entirely liquid. In most cases it has been found necessary to add an excess of

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[1] Longuinine: Ann. chim. phys. [7] 27, 105-144 (1902).

[2] Ber. 17, 2728 (1884).

pentachloride to complete the reaction. The phosphorus oxychloride was distilled off under reduced pressure and the dibrom chloride purified by recrystallization from ligroin until it melted at 83–85° C. The yield was a little over 50 per cent. of the theory.

Action of Pyridine on the Dibromsalicyl Chloride in Ligroin Solution.—Twenty-five grams of the chloride were dissolved in a liter of ligroin,[1] and cooled by a freezing-mixture. Six grams of pyridine dissolved in 30 cc. of ligroin were added, drop by drop, the temperature being kept below —6° C. The first drop of pyridine caused the appearance of a yellow precipitate, the color fading immediately. After the precipitate had been filtered off and dried on an unglazed tile it was found to melt at about 77° C.–125° C. The melting-points of the several preparations varied considerably. It gives no color with ferric chloride, but contains pyridine which cannot be removed by treatment with cold alkalies. All attempts to purify it by crystallization or precipitation were failures. The work, however, indicated it to be a mixture.

The Action of Pyridine on Dibromsalicyl Chloride in Acetone Solution.—Ten grams of the chloride were dissolved in 140 cc. of acetone, the solution cooled to —16° C. and the calculated amount (2.5 grams) of pyridine diluted with acetone added slowly with constant stirring. The temperature was allowed to rise to —9° C. After standing in the freezing-mixture a short time, the acetone solution was filtered. The precipitate averaged about 50 per cent. of the theory. Dilution of the acetone filtrate with water gave, in some experiments a precipitate, in others a pinkish oil which afterwards solidified. This substance gave a deep purple color with ferric chloride and was, therefore, not further investigated.

The substance which precipitated during the reaction gave no color with ferric chloride and all traces of pyridine were easily washed out with water. We were unable to find any means of purifying it further. On attempting to determine the melting-point it was found that the body passed very slowly from the

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[1] It was found in every case that some of the chloride failed to dissolve in the ligroin. This insoluble matter melted at about 170° C. and was evidently an anhydride of some sort. Experiments showed that on boiling the chloride with ligroin, hydrochloric acid was given off, as was easily shown by hanging strips of litmus paper in the condenser. Fifteen minutes' boiling suffices to decompose the chloride to an appreciable extent.

solid to the liquid phase, through a range of about 100°, finally becoming a thick brown liquid at about 223° C.

It is easily soluble in chloroform and benzene, slightly soluble in ether and ethyl acetate, and almost insoluble in ligroin. The act of solution seems to alter the substance, as upon spontaneous evaporation of a benzene or chloroform solution none of the original anhydride could be obtained. One gets instead gummy substances or solids of varying melting-points. It is almost insoluble in ligroin, but ligroin fails to precipitate it from its solutions.

A cryoscopic molecular weight determination in benzene indicated seven molecules in the aggregate, but entire confidence cannot be placed in this because of the possibility that the composition of the substance changes on solution.

As it seemed probable to us that the lack of a definite melting-point might indicate changes in the molecular weight of the substance, a brief study of its behavior on warming was undertaken, with the help of a dilatometer. Two dilatometers containing cotton-seed oil were immersed side by side in an oil-bath provided with a mechanical stirrer. In one of the bulbs the substance was inserted and the bulb sealed. The curve of the oil alone is a straight line from 75–200°. The curve of the substance +oil is a straight line from 75–110° and parallel to that of the oil alone. From 110–170° the substance contracts slowly at a constant rate, while from 170–200° it expands at a rapidly increasing rate. No breaks in the curve were observed.

Duration of the Color Change.—A brief comparison of the duration of the yellow color in various solvents is given in the following table:

	Solvent.	Boiling-point.	Time in seconds.
1	Ether	35.4°	Only a flash of color.
2	Ethyl acetate	77°	0.5
3	Acetone	56.3°	1
4	Ligroin	50°–60°	1–2
5	Chloroform	61°	4
6	Mesitylene	165°	5
7	Carbon tetrachloride	76°	30
8	Cymene	175°	30
9	Benzene	80.4°	35–40
10	Toluene	110°	40
11	Carbon disulphide	46°	45
12	Xylene	142°	70

In this experiment approximately equal amounts of chloride and pyridine were used, without precautions in regard to cooling. As the time of existence of color seemed to increase from benzene to xylene, mesitylene and cymene were used to ascertain whether the progression would continue. This is seen not to be the case.

The addition of various organic bases to the colored solution gave colorless precipitates, some possessing sharp melting-points. Lack of time alone has prevented the investigation of these compounds, which, it is hoped, will be continued this year.

[CONTRIBUTIONS FROM THE HAVEMEYER CHEMICAL LABORATORY, NEW YORK UNIVERSITY.]

ON FISCHER'S CLASSIFICATION OF STEREO-ISOMERS.[1]

BY M. A. ROSANOFF.

Received November 22, 1905.

FISCHER divides optically active substances into two enantiomorphous families. For example, ordinary glucose and levulose (fructose) are classed as members of one family because of their intimate genetic relationship; the two antipodal substances are classed together as members of the opposite family because of a similar relationship. The chemical relationships are indicated by the letters *d* and *l* prefixed to the names of compounds. Thus, ordinary glucose and its corresponding fructose (levulose) are designated, respectively, *d*-glucose and *d*-fructose, notwithstanding the levo-rotation of the latter.

The substances so correlated include, as yet, only the monosaccharides and their derivatives. In other cases the symbols *d* and *l* denote dextro- and levo-rotation. The reform proposed in the following pages, and the importance of avoiding possible confusion, will justify my employing in this paper the Greek δ and λ as family-symbols in place of the customary but misleading *d* and *l*.[2]

The great value of Fischer's classification to systematic stereochemistry is self-evident. The subdivision, however, as established by him in the celebrated memoirs[3] on the configuration of the

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[1] Presented before the New York Section of the American Chemical Society on November 10, 1905.

[2] In cases in which misunderstanding is possible, it would be well to prefix the rotation-symbols + or — to the family-symbols, designating ordinary levulose, for instance,—δ-fructose. [On the symbols *d* or *l* might be used, these *l*-δ- fructose. *Editor.*)

[3] Ber. **24**, 1836 and 2683 (1891); Ibid. **27**, 382 and 3208 (1894); etc.