

This will not affect materially the carbon-chlorine distance of 1.72 Å. we obtained assuming 1.54 Å.

Of the compounds discussed in this paper only ethyl chloride and ethyl bromide have been studied previously by the electron diffraction method.¹⁸ The results were: 1.81 ± 0.1 Å. for the carbon-chlorine distance in ethyl chloride and 2.07 ± 0.07 Å. for the carbon-bromine distance in ethyl bromide. Both of these values are somewhat higher than the values reported by us. We believe our values to be more reliable because of the advances which have been made in electron diffraction technique since the other work was done.

Summary

Electron diffraction has been used to determine

(18) L. Bru, *Añal. soc. españ. fis. quim.*, **31**, 115 (1933).

the molecular structures of ethyl chloride, ethyl bromide, isopropyl chloride, isopropyl bromide, methyl chloroform and isocrotyl chloride. The results are given in Table VII.

TABLE VII

| Compound | C-Cl distance, Å. | |
|--------------------|-------------------|-----------------------------|
| | C-Cl distance, Å. | C-C-Cl angle |
| Ethyl chloride | 1.76 ± 0.02 | $111^\circ 30' \pm 2^\circ$ |
| Isopropyl chloride | 1.75 ± 0.03 | $109 \pm 3^\circ$ |
| | C-Br | |
| Ethyl bromide | 1.91 ± 0.02 | $109 \pm 2^\circ$ |
| Isopropyl bromide | 1.91 ± 0.03 | $109^\circ 28' \pm 3^\circ$ |
| | C-Cl | |
| Methylchloroform | 1.76 ± 0.02 | $109 \pm 2^\circ$ |
| Isocrotyl chloride | 1.72 ± 0.02 | $123 \pm 2^\circ$ |

PRINCETON, NEW JERSEY

RECEIVED JULY 28, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF NORTH CAROLINA]

The Constitution of Natural Tannins. VI.¹ Coloring Matters Derived from 2,5-Dihydroxyacetophenone

BY ALFRED RUSSELL AND SAMUEL FRIEND CLARK²

The material already reported includes a description of polyhydroxychalcones derived from various 2-hydroxy ketones (notably resacetophenone, phloracetophenone, and gallacetophenone) and hydroxyaldehydes (notably protocatechualdehyde, vanillin, *m*-hydroxybenzaldehyde, and *p*-hydroxybenzaldehyde). By reduction of these 2'-hydroxychalcones with zinc dust and dilute alcoholic acids are obtained light colored amorphous products; when these amorphous products are water-soluble (those derived from protocatechualdehyde only), they are qualitatively indistinguishable from natural phlobatanins. On various grounds it is probable that the amorphous products are flavopinacols hydroxylated on the patterns of the parent chalcones; for the sake of simplicity they are formulated as of the *bis* type, although their structure may be more complicated.

To continue the series so far described, polyhydroxychalcones derived from the various hydroxyaldehydes with three other hydroxy ketones should

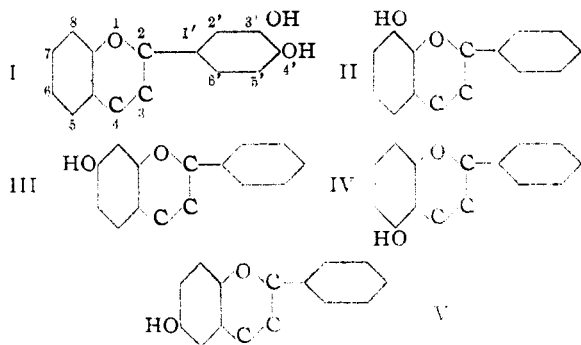
(1) The present paper forms a continuation of a series of five articles published in the *Journal of the Chemical Society*; Russell and co-workers, *J. Chem. Soc.*, 218, 1066, 1506, 1940 (1934); 421 (1937); cf. also Russell, *Chem. Rev.*, **17**, 155 (1935).

(2) From a dissertation submitted to the Faculty of the University of North Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1939.

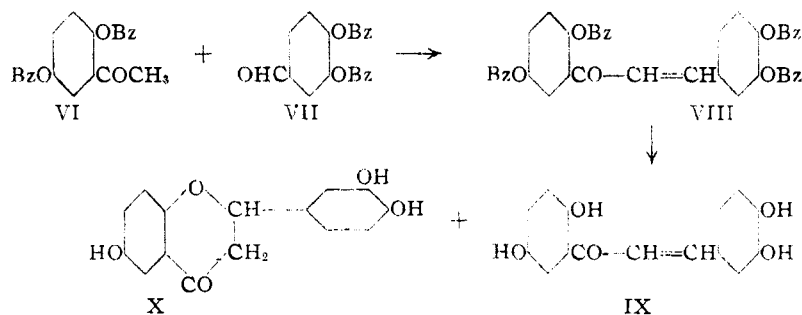
be examined; these ketones are the dihydroxyacetophenones, 2,3-, 2,6- and 2,5-. The reason for selecting 2,3-dihydroxyacetophenone is the frequent occurrence of catechol as a fission product of natural materials, it not being at all certain that this always comes from a benzopyran compound hydroxylated in the 3',4'-positions (I)—an hydroxyl group may in some cases be located in the 8-position (II) (the second one ortho to the first appearing after fission). 2,6-Dihydroxyacetophenone must be included because of the frequent occurrence of resorcinol, not necessarily resulting from a compound hydroxylated in the 7-position (III) but possibly from a compound hydroxylated in the 5-position (IV). 2,5-Dihydroxyacetophenone is selected because of the occasional occurrence of quinol as a decomposition product of natural materials, suggesting a benzopyran compound hydroxylated in the 6-position (V). In particular, the monomethyl ether of quinacetophenone has been isolated as a decomposition product of a yellow coloring matter from a European variety of stemless primrose.³ Moreover, Nierenstein⁴ has reported finding quinol amongst the decomposition products of quebracho tannin.

(3) Goris and Canal, *Compt. rend.*, **200**, 1990 (1935).

(4) Nierenstein, *Collegium*, **65** (1905).



There are now described syntheses of polyhydroxychalcones,⁵ flavanones, and anthocyanidins derived from 2,5-dihydroxyacetophenone (quinacetophenone) and various hydroxyaldehydes. The anthocyanidins are of the luteolinidin type.



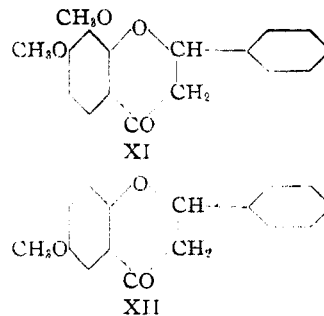
containing no hydroxyl group in the 3-position. There is also included a qualitative comparison of the amorphous reduction product of 3,4,2',5'-tetrahydroxychalcone—*bis*-(6,3',4'-trihydroxy)-flavopinacol—with natural hemlock and mimosa tannins in aqueous solution.

The synthesis of a typical stable polyhydroxychalcone may be outlined first. Quinacetophenone dibenzoate (VI) was condensed with protocatechualdehyde dibenzoate (VII) in solution of dry ethyl acetate using anhydrous hydrogen chloride to give 3,4,2',5'-tetrabenzoyloxychalcone (VIII). This, by debenzoylation with alcoholic potassium hydroxide, gave 3,4,2',5'-tetrahydroxychalcone (IX) and 6,3',4'-trihydroxyflavanone (X). The chalcone is stable in the sense of remaining unchanged by ordinary laboratory treatment of the dry solid. However, an easy equilibrium exists between the flavanone and chalcone in dilute alcoholic solution, the formation of the flavanone being favored at higher temperatures.

(5) The numbering system used for the hydroxychalcones is that of *Chemical Abstracts*, following the original system of v. Kostanecki. The benzene ring nearer the carbonyl group bears the prime numbers. It is to be noted that this is contrary to the English system of the *British Chemical Abstracts* and the *Journal of the Chemical Society*.

This made the task of isolating a pure sample of the chalcone extremely difficult.

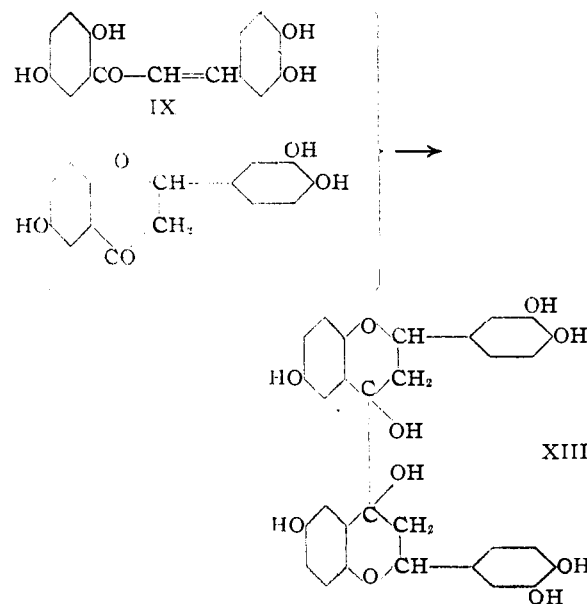
The ready formation of flavanone has been noted by v. Kostanecki,⁶ who has isolated flavanone to the exclusion of chalcone in two cases (XI and XII). Further, it is in concordance with



the suggestion of Wheeler⁷ that this process of making polyhydroxychalcones might, in some instances, give rise to some quantity of flavanone.

Reduction of pure 6,3',4'-trihydroxyflavanone (X), or of a mixture of flavanone and 3,4,2',5'-tetrahydroxychalcone (IX) consisting mostly of the latter, with zinc dust and alco-

holic hydrochloric acid, gave an amorphous light red material—*bis*-(6,3',4'-trihydroxy)-flavopinacol (XIII).



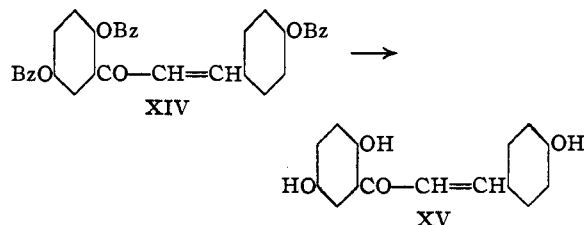
(6) Woker, v. Kostanecki and Tambor, *Ber.*, **36**, 4235 (1903); v. Kostanecki and Lampe, *ibid.*, **37**, 773 (1904).

(7) Nadkarni and Wheeler, *J. Chem. Soc.*, 1320 (1938).

Similarly to the above-described synthesis of a polybenzoyloxychalcone, the preparation of seven other polybenzoyloxychalcones was accomplished. These were 4,2',5'-tribenzoyloxychalcone (XIV) from *p*-hydroxybenzaldehyde, 3,2',5'-tribenzoyloxychalcone (XVI) from *m*-hydroxybenzaldehyde, 4,2',5'-tribenzoyl-oxy-3-methoxychalcone (XIX), vanillin, 2,2',5'-tribenzoyloxychalcone (XXI) from salicylaldehyde, 2,4,2',5' - tetrabenzoyloxychalcone (XXV) from resorcyaldehyde, 2,4,2',5'-tetrabenzoyloxy-6-methylchalcone (XXVIII) from orcyaldehyde, and 2,4,6,2',5'-pentabenzoyloxychalcone (XXXI) from phloroglucinaldehyde. With the exception of the last one, which is an oil, the polybenzoyloxychalcones are pale yellow, difficultly crystalline and without sharp melting points.

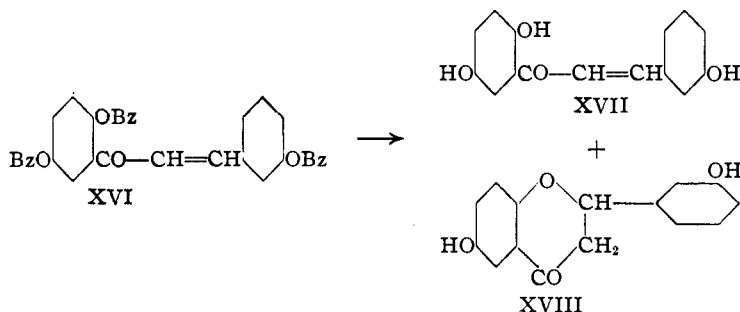
Considerable difficulty was experienced in effecting debenzoylation of the polybenzoyloxychalcones without causing fission of the products to initial materials. Even under the mild conditions of saponification finally adopted, the product required was always accompanied by some quantity of quinacetophenone (the hydroxyaldehydes are more soluble and do not appear). This is evidenced by the fact that, although the yield of polybenzoyloxychalcone was upward of 70% of the theoretical, the actual yield of polyhydroxychalcone and other products by hydrolysis in many cases was below 40% of the theoretical. It is clear that the polyhydroxychalcones hydroxylated on the 2',5'-pattern are particularly sensitive to alkaline fission. Thus, the results were so varied as to necessitate separate description.

The synthesis of 4,2',5'-trihydroxychalcone (XV) proceeded comparatively smoothly with some accompanying quinacetophenone, but no flavanone.

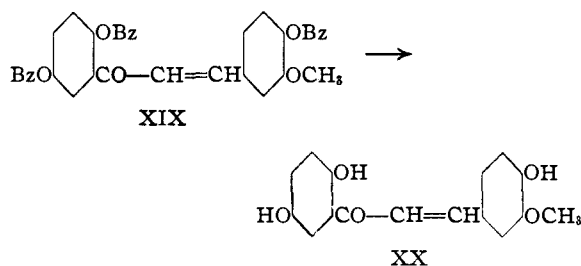


The synthesis of 3,2',5'-trihydroxychalcone (XVII) furnished some difficulty, because the chalcone was accompanied by quinacetophenone

and almost an equal quantity of 6,3'-dihydroxyflavanone (XVIII). The equilibrium between chalcone and flavanone was more evenly balanced in this instance than in that first described (IX and X); consequently, the separation of the two substances by fractional crystallization from dilute alcohol was comparatively easy.

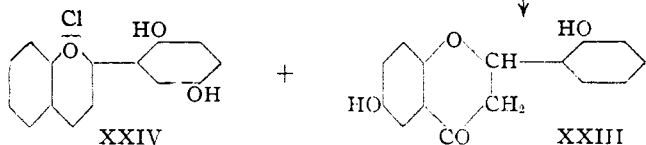
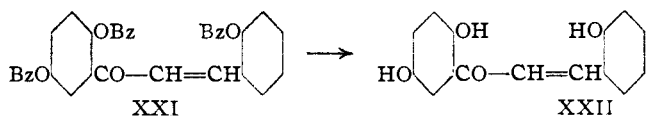


4,2',5'-Trihydroxy-3-methoxychalcone (XX) was prepared with some accompanying decomposition. In this case the benzoyloxychalcone more stubbornly resisted the action of alkali and was recovered in part. No flavanone could be found, although it appears probable that repetition of the synthesis here or in the case of 4,2',5'-trihydroxychalcone might yield some quantity of flavanone.

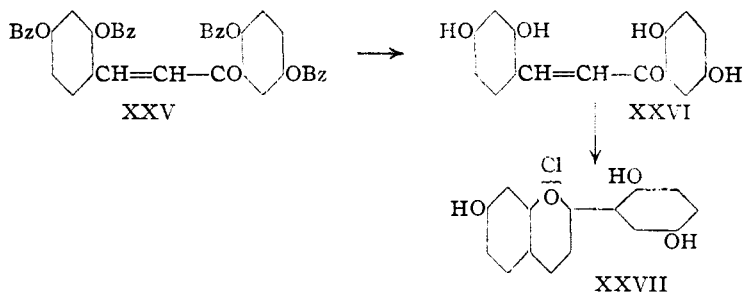


In those cases where the liberated hydroxychalcone had an hydroxyl group in the 2-position, acidification of the alkaline solution after debenzoylation caused cyclization to the anthocyanidin. Thus, 2,2',5'-trihydroxychalcone (XXII) gave 2',5'-dihydroxy-2-phenylbenzopyrylium chloride (XXIV) on boiling with 10% hydrochloric acid. The accompanying production of 6,2'-dihydroxyflavanone (XXIII) in considerable quantity was noted. It is believed to be a rare occurrence for a flavanone to be formed in competition with an anthocyanidin.

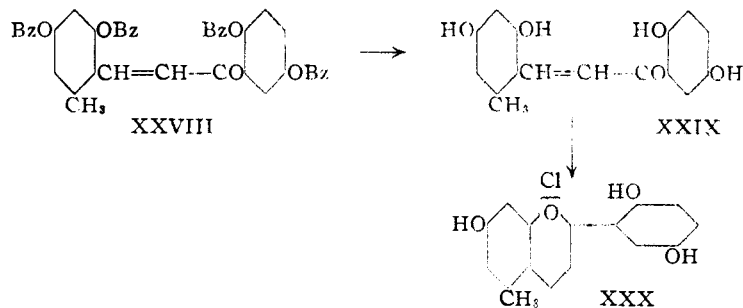
The benzoyloxychalcone (XXV) from resorcyaldehyde was converted to the anthocyanidin—7,2',5'-trihydroxy-2-phenylbenzopyrylium chlo-



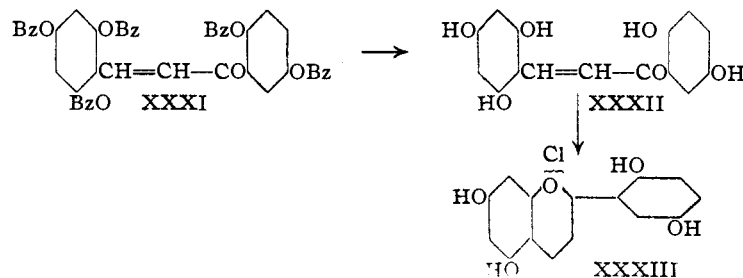
ride (XXVII)—through the intermediate hydroxychalcone (XXVI).



Similarly, the benzoyloxychalcone (XXVIII) from orcyaldehyde was converted to 7,2',5'-trihydroxy-5-methyl-2-phenylbenzopyrylium chloride (XXX).



Finally, the synthesis of 5,7,2',5'-tetrahydroxy-2-phenylbenzopyrylium chloride (XXXIII) was accomplished from the benzoyloxychalcone (XXXI). Some difficulty was experienced in isolating this substance due to the usual decomposition and its appreciable water solubility.



The polyhydroxychalcones are various shades of orange, the color deepening as the number of hydroxyl groups increases, and are definitely crystalline with sharp melting points. The anthocyanidins are red in color and are associated with water of crystallization, as R. Robinson⁸ previously has noted in other instances. The flavanones are white crystalline substances with a faint yellowish tinge. The flavopinacol is a light red amorphous powder that is difficult to dry and retains traces of solvents with great obstinacy—its analysis was not attempted.

In view of the relationship between chalcone and flavanone exhibited in the present work, it may be that such a relationship exists in other series. For example, Kurth⁹ has reported the synthesis of yellow 3,4,2',3',4' - pentahydroxychalcone, m. p. 249°, by the action of cold alkali on gallacetophenone and protocatechualdehyde, followed by acidification and crystallization from dilute alcohol. This substance was previously reported by Russell² as a deep orange material, m. p. 233°.

Since the color of polyhydroxychalcones deepens (yellow-deep orange) as the number of hydroxyl groups increases, it is possible that Kurth's product is the corresponding flavanone. Moreover, the fact that it gave a pentabenzoate is not relevant evidence that it is a pentahydroxychalcone, as many instances are on record¹⁰ where acylation of hydroxyflavones produced the fully acylated chalcones corresponding.

The table below gives a qualitative comparison, by means of various reagents, of *bis*-(6,3',4'-trihydroxy)-flavopinacol with natural hemlock and mimosa tannins, using approximately 1% aqueous solutions. It will be seen that the resemblance is very close.

Experimental

Quinacetophenone.—This ketone was prepared more than twenty times. A typical

(8) Cf. Irvine and Robinson, *J. Chem. Soc.*, 2091 (1927).

(9) Kurth, *THIS JOURNAL*, 61, 861 (1939).

(10) Cf. Asahina, Shinoda and Inubuse, *J. Pharm. Soc. Japan*, 48, 207 (1928); *C. A.*, 22, 2946 (1928), for discussion.

TABLE I

| Reagent | bis-(6,3',4'-Trihydroxy-flavopinacol) | Hemlock tannin | Mimosa tannin |
|---|---|---|---|
| Alcoholic FeCl ₃ | Dark green color | Dark green color | Dark blue-violet color |
| Aqueous FeCl ₃ | Dark green color; dark ppt. | Dark green color; dark ppt. | Dark blue-violet color; dark ppt. |
| Gelatin | Dirty white ppt. | Dirty white ppt. | Dirty white ppt. |
| Lead acetate | Light colored ppt. soluble in acetic acid | Light colored ppt. soluble in acetic acid | Light colored ppt. soluble in acetic acid |
| Boiling dil. HCl (phlobaphene reaction) | Solution reddens slowly and red-brown ppt. separates | Solution reddens slowly and red ppt. separates | Solution reddens slowly and red ppt. separates |
| Bromine water | Immediate heavy yellow ppt. | Immediate heavy yellow ppt. | Immediate heavy orange ppt. |
| Calcium hydroxide | Faint green ppt. with blue-violet fluorescence | Pink color; faint pink ppt. | Violet color; faint violet ppt. |
| Sodium sulfite | Yellow color | Pink color | Pink color |
| HCHO + HCl | Ppt. on warming | Ppt. on warming | Ppt. on warming |
| Nitrous acid | Immediate brown ppt. | Immediate brown ppt. | Immediate brown ppt. |
| Copper sulfate | No change in color; addition of NH ₃ gives dark ppt. | Faint green color; addn. of NH ₃ gives heavy dark ppt. | Faint green color; addn. of NH ₃ gives heavy dark ppt. |
| Aqueous NH ₃ | Solution darkens slowly | Solution darkens slowly | Solution darkens slowly |
| Potassium dichromate | Brown precipitate | Brown precipitate | Brown precipitate |
| Potassium ferricyanide | Yellow-orange color, turning orange-brown on NH ₃ addition | Orange-red on NH ₃ addition | Orange-red on NH ₃ addition |
| Hide powder | Absorbed quantitatively | Absorbed quantitatively | Absorbed quantitatively |

cal run is cited. Quinol (100 g.) was dissolved in boiling glacial acetic acid (200 cc.). Freshly fused zinc chloride (400 g.) was added, and the mixture refluxed for an hour. The temperature rose to 150–165°, and the solution became dark red. At the end of the reflux period the solution was poured into ice water. The precipitated crude quinacetophenone was recrystallized from dilute alcohol with several charcoal treatments. Quinacetophenone crystallized in greenish-yellow plates, m. p. 200–201°. The yield averaged 20–25%, being rather low due to the necessity of heavy charcoaling to free the ketone from colored material.

Preparation of Aldehydes.—Protocatechualdehyde was prepared by the method of Pauly¹¹ from piperonal. Resorcyraldehyde, orcyraldehyde, and phloroglucinaldehyde were prepared by the Adams modification¹² of the Gattermann reaction, using the corresponding phenol, zinc cyanide, and dry hydrogen chloride in ice-cold ether solution. Vanillin, salicylaldehyde, *p*-hydroxybenzaldehyde, and *m*-hydroxybenzaldehyde were the best Eastman Kodak Co. grade.

Preparation of Benzoates.—The same method was employed for all benzoates. The ketone or aldehyde (0.3 mole) was dissolved in pyridine (150 cc.) and benzoyl chloride in 10–15% excess of that required to benzoylate all hydroxy groups was added with shaking over a period of ten minutes. The mixture was warmed on the steam-bath for twenty to thirty minutes and then set aside overnight at room temperature. The mixture was poured into cold water (1500 cc.) and stirred until the benzoate solidified. It was usually tan to light brown in color. The crude material was washed thoroughly with water and finally with dilute hydrochloric acid. It was then recrystallized from alcohol (charcoal) and dried in the air. The yields were in the range 65–90%, depending on the purity of the initial material. The benzoates were all

colorless, although quinacetophenone dibenzoate was difficult to obtain free from yellow coloration.

TABLE II

| Benzoate | M. p., °C. | % yield |
|-------------------------------|--------------------|---------|
| Quinacetophenone | 113 | 88 |
| <i>p</i> -Hydroxybenzaldehyde | 89 | 81 |
| <i>m</i> -Hydroxybenzaldehyde | 37–38 | 65 |
| <i>o</i> -Hydroxybenzaldehyde | B. p. 208 (15 mm.) | 60 |
| Vanillin | 97 | 73 |
| Protocatechualdehyde | 75 | 78 |
| Resorcyraldehyde | 98 | 85 |
| Orcylaldehyde | 134–135 | 82 |
| Phloroglucinaldehyde | 130 | 46 |

***m*-Benzoyloxybenzaldehyde.**—This benzoate apparently has not been reported before. It melted at a rather low temperature, which necessitated dissolving it in alcohol at room temperature and immersing the solution in a freezing mixture of salt and ice to induce crystallization. It crystallized in colorless prismatic needles, m. p. 37–38°.

Anal. Calcd. for C₁₄H₁₀O₃: C, 74.3; H, 4.5. Found: C, 74.2; H, 4.5.

Resorcyraldehyde Dibenzoate.—This benzoate has not been reported previously. It crystallized from alcohol in clusters of colorless prismatic needles, m. p. 98°. *Anal.* Calcd. for C₂₁H₁₄O₅: C, 72.8; H, 4.1. Found: C, 72.5; H, 4.1.

Orcylaldehyde Dibenzoate.—This benzoate has not been reported previously. It crystallized from alcohol as a mass of white felted needles, m. p. 134–135°. *Anal.* Calcd. for C₂₂H₁₆O₅: C, 73.3; H, 4.5. Found: C, 73.1; H, 4.5.

General Method for Benzoyloxychalcones.—Quinacetophenone dibenzoate (0.07 mole) and the aldehyde benzoate (0.07 mole) were dissolved in anhydrous ethyl acetate (350–400 cc.) (dried over calcium chloride, distilled, and stored over sodium sulfate). Dry hydrogen chloride was passed in for two to five days at ice temperatures. The

(11) Pauly, *Ber.*, **40**, 3098 (1907).

(12) Adams and Levine, *This Journal*, **45**, 2373 (1923).

solution turned in color from a pale yellow to a clear dark red. When the solution had been thoroughly saturated for at least a day, it was evaporated on the steam-bath to a thick red sirup. On triturating with cold alcohol, the material usually hardened after ten minutes. It was boiled with alcohol (100 cc.) to remove initial materials, cooled to room temperature, and the alcohol decanted. The material was considered sufficiently pure for conversion to the free hydroxychalcone. For analysis a sample of the benzoyloxychalcone was recrystallized from alcohol, in which it was difficultly soluble.

It had been found previously¹ that benzoyloxychalcones retained alcohol rather tenaciously, which tended to disturb the analytical results. The benzoyloxychalcones were dried in a vacuum desiccator over sodium hydroxide for several days at room temperature. The analytical results were in rather good agreement with the calculated values, considering the nature of the substances.

General Method for Hydroxychalcones.—The preparation of the free hydroxychalcones from the benzoyloxychalcones constituted an unexpected and stubborn problem. The debenzoylation of benzoyloxychalcones derived from resacetophenone and phloracetophenone proceeded smoothly under the conditions previously described.¹ Repetition of this work in the case of 4,2',4'-trihydroxychalcone and 4,2',4'-trihydroxy-3-methoxychalcone gave the expected results without difficulty. The method of debenzoylation involved solution of the benzoyloxychalcone in acetone, replacement of acetone by alcohol, slow addition under nitrogen of an aqueous solution of twice the theoretical quantity of potassium hydroxide, distillation of the alcohol over a period of three to four hours, cooling, and finally acidification of the solution to precipitate the hydroxychalcone.

When this method was applied to representative benzoyloxychalcones in the quinacetophenone series, hydrolytic fission of the molecule occurred at the double bond, and quinacetophenone appeared on acidification. The aldehydes were soluble and did not appear. Numerous modifications of the procedure were tried with the view to decreasing the extent of fission at the double bond. It was thought that the excess of potassium hydroxide together with the extended heating period were responsible for the decomposition. (The heating period was quite long due to the large amount of alcohol required to dissolve the benzoyloxychalcones, which seem more insoluble than those of other series.) Accordingly, the following scheme finally was worked out.

The benzoyloxychalcone from the above preparation was introduced into a 3-necked, 1-liter flask, so placed in a steam-bath that most of the surface could be heated directly by the live steam. The small necks of the flask were fitted with a dropping funnel and a tube bent downward for distillation. The large neck bore a mercury-seal stirrer and a gas inlet tube. Alcohol (500–600 cc.) was added and brought to boiling with mechanical stirring under an atmosphere of nitrogen. No attempt was made to dissolve the benzoyloxychalcone completely. An aqueous solution of potassium hydroxide (1 g. excess over requisite theoretical quantity in 200 cc. of water) was added over a period of forty to sixty minutes to the boiling solution. The color turned from a pale yellow to a dark

red, and all suspended matter disappeared. Distillation of the alcohol was continued for an hour longer until the original volume was collected.

The solution was then chilled in an ice-bath and acidified with dilute sulfuric acid (20 cc. of concd. acid in 50 cc. of water). The precipitated chalcone and benzoic acid were filtered off and washed with cold water. Separation of the benzoic acid was effected either with cold sodium bicarbonate solution or with hot benzene in a Soxhlet. The specific method employed is described in each case below. The resulting hydroxychalcone contained quinacetophenone and in certain instances flavanone. These were separated by fractional crystallization from dilute alcoholic solutions, the quinacetophenone being more soluble than the hydroxychalcone and the flavanone less soluble. Due to the apparently unavoidable decomposition and to the tedious separation required, the yields (calculated on the basis of quinacetophenone dibenzoate) were much lower than those previously reported.²

4,2',5'-Tribenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and *p*-benzoyloxybenzaldehyde (0.07 mole) were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 134–136°. The yield was 31 g. (78%). *Anal.* Calcd. for $C_{36}H_{24}O_7$: C, 76.0; H, 4.3. Found: C, 75.3; H, 4.5.

4,2',5'-Trihydroxychalcone.—The benzoyloxychalcone (31 g.) was debenzoylated as described above. The hydroxychalcone was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 200 cc. of water saturated with carbon dioxide). The chalcone was filtered, washed with cold water, and recrystallized from 35% alcohol (600 cc.). The yield was 10 g. (56%). The crystals were orange-yellow prismatic needles, m. p. 222–224°. *Anal.* Calcd. for $C_{18}H_{12}O_4$: C, 70.3; H, 4.7. Found: C, 70.3; H, 4.8. No trace of flavanone could be found.

3,2',5'-Tribenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and *m*-benzoyloxybenzaldehyde (0.07 mole) were converted to the benzoyloxychalcone, a light yellow semi-crystalline solid, m. p. 174–175°. The yield was 27 g. (67%). *Anal.* Calcd. for $C_{36}H_{24}O_7$: C, 76.0; H, 4.3. Found: C, 75.6; H, 4.4.

3,2',5'-Trihydroxychalcone.—The benzoyloxychalcone (27 g.) was debenzoylated as described above. The hydroxychalcone was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 250 cc. of water saturated with carbon dioxide). The chalcone was filtered and washed with cold water. The product proved to be a mixture, containing quinacetophenone, chalcone, and flavanone. The chalcone was finally separated by fractional crystallization from 20% alcohol as orange needles, m. p. 204–206°. The yield was 3.5 g. (20%). *Anal.* Calcd. for $C_{18}H_{12}O_4$: C, 70.3; H, 4.7. Found: C, 70.2; H, 4.8.

6,3'-Dihydroxyflavanone.—The flavanone was separated from the corresponding chalcone by fractional crystallization. It was finally crystallized in colorless needles, having faint yellow coloration, m. p. 234–236°, from 70% alcohol (charcoal). The yield was 2.0 g. (12%). *Anal.* Calcd. for $C_{18}H_{12}O_4$: C, 70.3; H, 4.7. Found: C, 70.4; H, 4.9.

4,2',5' - Tribenzoyloxy - 3 - methoxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and vanillin benzoate (0.07 mole) were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 145–147°. The yield was 37 g. (88%).

Anal. Calcd. for $C_{35}H_{26}O_8$: C, 74.2; H, 4.4. Found: C, 74.1; H, 4.5.

4,2',5'-Trihydroxy-3-methoxychalcone.—The benzoyloxychalcone was debenzoylated as described above. The hydroxychalcone was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 250 cc. of water saturated with carbon dioxide). The chalcone was dissolved in dilute alcohol and filtered. The residue was unconverted benzoyloxychalcone (10 g.). The hydroxychalcone crystallized in dark orange needles, m. p. 172–173°. The yield was 5 g. (46%). *Anal.* Calcd. for $C_{15}H_{14}O_6$: C, 67.1; H, 4.9. Found: C, 67.1; H, 5.0. No trace of flavanone could be found.

3,4,2',5' - Tetrabenzoyloxychalcone.—Quinacetophenone dibenzoate (0.14 mole) and protocatechualdehyde dibenzoate (0.14 mole) were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 182–184°. The yield was 75 g. (78%). *Anal.* Calcd. for $C_{43}H_{26}O_8$: C, 75.0; H, 4.1. Found: C, 74.7; H, 4.2.

3,4,2',5'-Tetrahydroxychalcone.—The benzoyloxychalcone was debenzoylated as described above. The chalcone was separated from benzoic acid by extraction of the latter with hot benzene in a Soxhlet. (The 3,4-dihydroxy grouping increases the water solubility of the chalcone to the point where the sodium bicarbonate solution would dissolve an appreciable amount. Since the benzene solubility is at the same time decreased, this method of separation was used successfully.) The crude material was recrystallized from dilute alcohol (1 liter). The recrystallized product obtained weighed 25 g. (66%). However, it was found to be a mixture of chalcone and flavanone. Attempted fractional crystallization from dilute alcohol seemed to establish the equilibrium between chalcone and flavanone in favor of the latter. Consequently, only a small amount of pure chalcone (less than a gram) was obtained. It crystallized in dark orange micro-crystals, m. p. 225–227°. *Anal.* Calcd. for $C_{15}H_{12}O_6$: C, 66.1; H, 4.5. Found: C, 65.8; H, 4.6.

6,3',4'-Trihydroxyflavanone.—The flavanone was separated from the chalcone by fractional crystallization and finally by the action of charcoal. It crystallized in a mass of white felted needles with a slight yellowish tinge, m. p. 218–220° (dec.). *Anal.* Calcd. for $C_{15}H_{12}O_6$: C, 66.1; H, 4.5. Found: C, 66.1; H, 4.5.

2,2',5'-Tribenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and salicylaldehyde benzoate (0.07 mole) were converted to the benzoyloxychalcone, a bright yellow semi-crystalline solid, m. p. 137–139°. The yield was 32.5 g. (82%). *Anal.* Calcd. for $C_{30}H_{24}O_7$: C, 76.0; H, 4.3. Found: C, 75.6; H, 4.3.

2',5'-Dihydroxy-2-phenylbenzopyrylium Chloride.—The benzoyloxychalcone (27.5 g.) was debenzoylated as described above. The free hydroxychalcone was precipitated with hydrochloric acid and separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (11 g. of sodium carbonate in 150 cc.

water saturated with carbon dioxide). The resulting material was recrystallized from 10% alcoholic hydrochloric acid, separation from a considerable quantity of quinacetophenone being effected. The recrystallized product (3.5 g.) proved to consist of chalcone, flavanone, and a very small quantity of anthocyanidin. The anthocyanidin was separated from the chalcone and flavanone by extraction of the latter two substances with ether in which the salt was not soluble. The anthocyanidin (less than 1 g.) formed a reddish micro-crystalline powder, m. p. 175° (dec.). *Anal.* Calcd. for $C_{15}H_{11}O_6Cl \cdot 1/2 H_2O$: Cl, 12.5. Found: Cl, 12.6. It gave a red solution in acid and a blue solution in sodium carbonate.

6,2'-Dihydroxyflavanone.—This substance, separated from the colored material as described above, was recrystallized from dilute alcohol. It apparently is formed in preference to the anthocyanidin. It crystallized in very pale yellow prismatic needles, m. p. 178–180° (dec.). *Anal.* Calcd. for $C_{15}H_{12}O_4 \cdot H_2O$: C, 65.8; H, 5.1. Found: C, 66.2; H, 5.1. No attempt was made to isolate the chalcone of which only a trace was present.

2,4,2',5' - Tetrabenzoyloxychalcone.—Quinacetophenone dibenzoate (0.07 mole) and resorcyaldehyde dibenzoate (0.07 mole) were converted to the benzoyloxychalcone, a yellow crystalline solid, m. p. 137–139°. The yield was 39 g. (81%). *Anal.* Calcd. for $C_{43}H_{26}O_8$: C, 75.0; H, 4.1. Found: C, 74.7; H, 4.2.

7,2',5'-Trihydroxy-2-phenylbenzopyrylium Chloride.—The benzoyloxychalcone (34 g.) was debenzoylated as described above. The hydroxychalcone was precipitated by the addition of hydrochloric acid and was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution (12 g. sodium carbonate in 200 cc. of water saturated with carbon dioxide). The product was crystallized from dilute alcoholic 10% hydrochloric acid. The yield of anthocyanidin was 7 g. (39%). A portion was recrystallized for analysis. It separated as a dark red microcrystalline powder, m. p. 190° (dec.). Its solution in acid was red and in sodium carbonate blue. *Anal.* Calcd. for $C_{15}H_{11}O_6Cl \cdot 5/2 H_2O$: Cl, 9.1. Found: Cl, 9.1.

2,4,2',5' - Tetrabenzoyloxy - 6 - methylchalcone.—Quinacetophenone dibenzoate (0.07 mole) and orcyaldehyde dibenzoate were converted to the benzoyloxychalcone, a pale yellow semi-crystalline solid, m. p. 125–127°. The yield was 42 g. (86%).

Anal. Calcd. for $C_{44}H_{30}O_8$: C, 75.2; H, 4.3. Found: C, 74.7; H, 4.5.

7,2',5' - Trihydroxy - 5 - methyl - 2 - phenylbenzopyrylium Chloride.—The benzoyloxychalcone (37 g.) was debenzoylated as described above. The hydroxychalcone was precipitated with hydrochloric acid and separated from the benzoic acid by extraction of the latter with hot benzene in a Soxhlet. The brown residue was crystallized from dilute alcoholic 10% hydrochloric acid as dark, red, iridescent plates, m. p. 285–287° (dec.). Its solution in acid was red and in sodium carbonate blue. *Anal.* Calcd. for $C_{16}H_{13}O_6Cl \cdot H_2O$: Cl, 11.0. Found: Cl, 11.1.

2,4,6,2',5' - Pentabenzoyloxychalcone.—Quinacetophenone dibenzoate (7 g.) and phloroglucinaldehyde tribenzoate (9 g.) were converted to the benzoyloxychalcone, a

yellow oil, which was not analyzed but transformed into the anthocyanidin.

5,7,2',5'-Tetrahydroxy-2-phenylbenzopyrylium Chloride.—The benzoylchalcone was debenzoylated as described above. The hydroxychalcone was precipitated with hydrochloric acid and was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution. The residue was crystallized from 10% hydrochloric acid in which it was very soluble. The dark red crystal mass was extracted with ether, leaving less than a gram of anthocyanidin. It was a brownish-red crystalline powder, m. p. above 300°. *Anal.* Calcd. for $C_{16}H_{11}O_5Cl \cdot 2H_2O$; Cl, 10.4. Found: Cl, 10.3. It gave a red solution in acid and blue in sodium carbonate.

bis-(6,3,4'-Trihydroxy)-flavopinacol.—This flavopinacol, possessing the possible phlobatannin structure, was prepared by reduction of pure 6,3',4'-trihydroxyflavanone (1 g.) and also by reduction of a mixture (1 g.) of flavanone and 3,4,2',5'-tetrahydroxychalcone, consisting mostly of the latter. The flavanone (or mixture of chalcone and flavanone) was dissolved in alcohol (40 cc.) and zinc dust (5 g.) and concd. hydrochloric acid (12 cc.) were added. The solution was boiled for five minutes, during which time the color changed from dark orange (in the case of the mixture) to a pale yellow. The solution was filtered from unreacted zinc and nearly neutralized with sodium bicarbonate, a tan precipitate separating. The solution

was saturated with sodium chloride and extracted without filtering with two portions (75 cc. each) of ethyl acetate. The ethyl acetate was dried over sodium sulfate overnight and evaporated on the steam-bath. Most of the remaining solvent was removed in a vacuum desiccator over sodium hydroxide. The final product was a light red friable solid, retaining traces of solvent with great tenacity. It was readily soluble in acetone, alcohol, and ethyl acetate and partially soluble in water. The water-soluble portion was qualitatively indistinguishable from natural phlobatannins such as mimosa and hemlock tannins, as indicated in the table above. No analysis was attempted.

Summary

1. The production of a new flavopinacol from quinacetophenone and protocatechualdehyde is reported. This substance is qualitatively indistinguishable from such natural phlobatannins as hemlock and mimosa tannins.

2. New benzoyloxychalcones, hydroxychalcones, flavanones, and anthocyanidins derived from quinacetophenone are reported.

3. The peculiar sensitivity of 2',5'-hydroxychalcones to alkali is noted.

CHAPEL HILL, N. C.

RECEIVED JULY 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, THE COLLEGE OF THE CITY OF NEW YORK]

Alkanolamines. VII. Condensation Products of Monoethanolamine and the Isomeric Dichloronitrobenzenes

BY CHESTER B. KREMER AND AARON BENDICH

The activation of a halogeno or nitro group on the benzene nucleus by the presence of other substituted groups is well known. The reactions among such molecules and the amino alcohols were originally investigated in these laboratories. This present paper records our findings with the isomeric dichloronitrobenzenes.

Quite recently, Waldkötter¹ has extended our findings dealing with the condensing ability of monoethanolamine. In general, however, he has dealt with benzene molecules which are quite heavily substituted in the nucleus and contain, usually, at least two nitro groups on the ring. Under such conditions, it is frequently an active nitro group that is split out on condensing with the amino alcohol rather than a halogeno group. Work carried out in our laboratories checks exactly with these results. Our investigations, however, have not been limited to reactions with the ethanolamines and we ex-

pect to publish these data in our next article.

The preparation of all six dichloronitrobenzenes is not an easy task. The 2,5- and 3,4-isomers are readily available, but the others are usually prepared through a number of intermediate syntheses. The fundamental researches dealing with the preparation of most of the isomers were carried out by Beilstein and Kurbatow² and improved and extended by Holleman and Reiding³ and Holleman and De Mooy.⁴ In preparing the 3,5- and the 2,6-dichloronitrobenzenes we followed their procedures with slight modifications. 2,4-Dichloronitrobenzene usually is prepared by the nitration of *m*-dichlorobenzene. We synthesized this material from a by-product formed in the synthesis of 2,6-dichloronitrobenzene. An outline of the complete synthesis of these three dichloronitrobenzenes is given in Chart I.

Theoretically, it should be possible to obtain

(2) Beilstein and Kurbatow, *Ann.*, **196**, 228 (1879).

(3) Holleman and Reiding, *Rec. trav. chim.*, **33**, 357-379 (1904).

(4) Holleman and De Mooy, *ibid.*, **35**, 1-66 (1916).

(1) Waldkötter, *Rec. trav. chim.*, **57**, 1294 (1938).