[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

# Benzopyrylium Salts. II. Ozonization

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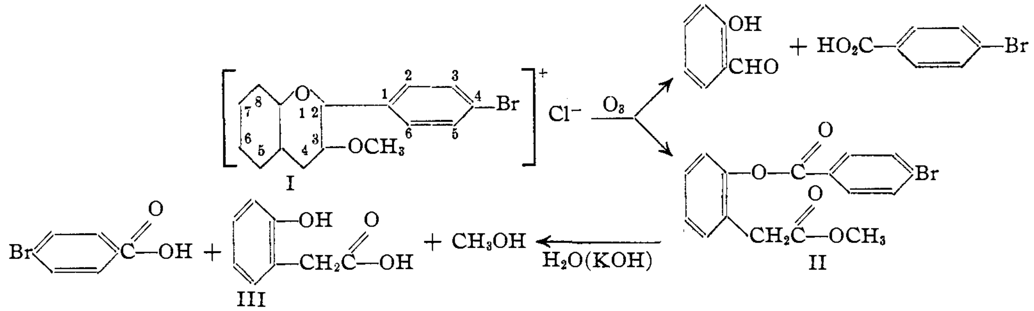
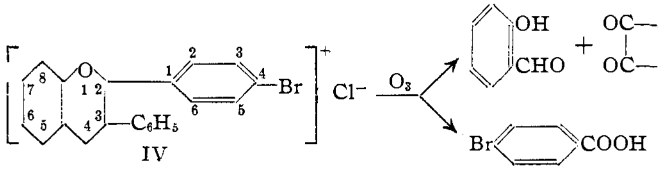
Degradation procedures used previously for determining the structure of benzopyrylium salts have always been carried out in the presence of water. Since water hydrolyzes the salts to the pyranol bases it is possible that the degradation products may not have been derived from the original pyrylium salt. In the present work the ozonization of two benzopyrylium salts has been carried out in glacial acetic acid, in which solvent the salt structure is retained. Flavylium salts, having substituents on both carbon atoms 2 and 3, were chosen for the present work in order that the fate of the atoms constituting the heterocyclic nucleus could be determined. By characterizing the degradation products the point of attack by the ozone could be deduced and thus information concerning the location of the double bonds obtained.

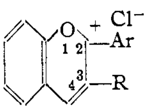
Ozonization of 3-methoxy-4′-bromoflavylium chloride (I) in glacial acetic acid followed by decomposition of the ozonide with water and zinc dust yielded salicylaldehyde, *p*-bromobenzoic acid and methyl *o*-(*p*-bromobenzoxy)-α-toluate (II). The latter was characterized by hydrolysis to *p*-bromobenzoic acid, *o*-hydroxy-α-toluic acid (III) and methanol.

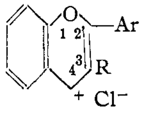


The degradation of 3-phenyl-4′-bromoflavylium chloride (IV) by ozonolysis yielded salicylaldehyde, *p*-bromobenzoic acid and 4-bromobenzil (V).

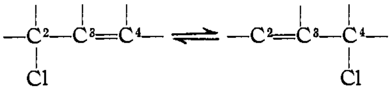


The formation of salicylaldehyde from both of these salts (I and IV) indicates that the molecules were split between carbon atoms 3 and 4 in each case; and hence a double union was present between these carbon atoms. On the other hand, the isolation of the ester (II) and *p*-bromobenzoic acid shows that ozone also cleaved these same molecules between carbon atoms 2 and 3. These results suggest that the flavylium salts resonate between the two structures VI and VII.


VI

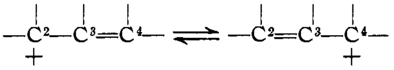

VII

Inspection of these structures shows that the carbon atoms numbered 2, 3 and 4 in the heterocyclic ring represent a special case of the allylic three-carbon-atom system in which the α,γ-shift of a group takes place very readily.



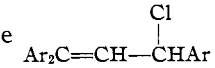
$$-\underset{\underset{\displaystyle Cl}{|}}{\overset{|}{C^2}}-\overset{|}{C^3}=\overset{|}{C^4}- \rightleftharpoons -C^2=\overset{|}{C^3}-\underset{\underset{\displaystyle Cl}{|}}{\overset{|}{C^4}}-$$

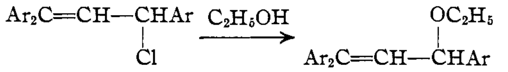
It has been suggested that the intermediates in this shift may be the mesomeric ions. In the



$$-\underset{+}{\overset{|}{C^2}}-\overset{|}{C^3}=\overset{|}{C^4}- \rightleftharpoons -\overset{|}{C^2}=\overset{|}{C^3}-\underset{+}{\overset{|}{C^4}}-$$

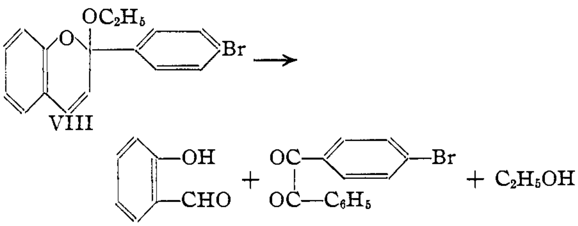
flavylium salts the ions are stabilized by the substituents and the possibility of resonance. The nature of the substituents would determine which of the two ions would predominate. In an ionizing solvent both forms would probably be in equilibrium. This viewpoint not only explains the present experimental data but also is in agreement with the work of Dilthey and his collaborators who suggested that the flavylium salts were "carbenium" salts with carbon atom number 2 as the heteropolar atom[1] (Formula VI). On the other hand Hill and Melhuish[2] obtained flavones from certain flavylium salts and hence concluded that carbon atom number 4 carried the positive charge (formula VII).

The three-carbon allylic system in these compounds parallels in its properties and chemical reactions the open chain systems studied by Meyer and Schuster[3] and by Straus and his co-workers.[4] The latter demonstrated that the compounds of the general type  $Ar_2C{=}CH{-}\underset{}{\overset{Cl}{\overset{|}{C}}}HAr$ formed colored complex salts with ferric chloride and perchloric acid, possessed an appreciable conductivity in liquid sulfur dioxide and reacted with alcohols to produce alkoxy derivatives. All of these reactions are given by the flavylium salts.

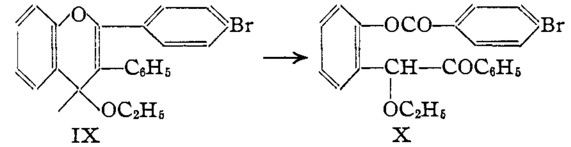


$$Ar_2C{=}CH{-}\underset{Cl}{\underset{|}{C}}HAr \xrightarrow{C_2H_5OH} Ar_2C{=}CH{-}\overset{OC_2H_5}{\overset{|}{C}}HAr$$

For example, in the present work the flavylium salt IV was treated with ethanol and the ethoxy derivative isolated. It consisted of colorless crystals which melted sharply and behaved in all respects like a pure compound. Ozonolysis of this ethoxy derivative produced salicylaldehyde, 4-bromobenzil, ethanol and a trace of *p*-bromobenzoic acid. These degradation products indicate that the ethoxy derivative possessed the structure VIII rather than IX. The latter would be expected to produce X (or its hydrolysis products) by ozonolysis.

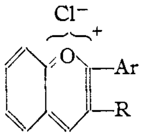


VIII

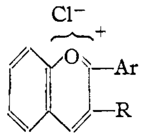


IX X

The present work provides some evidence against the quinoid oxonium salt structure XI which frequently has been ascribed to benzopyrylium salts.[5]



XI

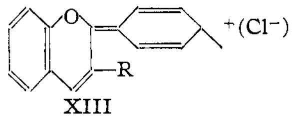


XII

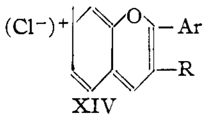
During the ozonization of both of the salts (I and IV) the deep red color gradually faded and the solution became pale yellow. The ozonide of the flavylium salt (IV) was decomposed by water alone and a careful search made for the red *o*-benzoquinone which is a possible degradation product of XI. No *o*-benzoquinone was detected and also no evidence for the presence of any of its degradation products (such as glyoxal) could be found.

A second oxonium structure shown in formula XII has been rendered unlikely by the observation of Le Fèvre[6] that nitration of flavylium salts produced only the 3′-nitro derivative; this indicates that the heterocyclic oxygen atom cannot carry a positive charge. Löwenbein[7] has also shown that the oxonium structures XI and XII cannot furnish a satisfactory basis to account for the products obtained by the action of phenylmagnesium bromide on flavylium salts.

Two other quinoid structures as shown in formulas XIII and XIV have been disproved by the observation that the bromine atoms in 3-methoxy-4′-bromoflavylium chloride and 3-methoxy-7-bromoflavylium chloride are non-reactive.[8]



XIII



XIV

In conclusion it may be said that all the chemical properties and degradation products indicate that benzopyrylium salts may best be represented by the two structures shown in formulas VI and VII. Further experiments are now under way to test this concept.

## Experimental

**Ozonization of 3-Methoxy-4′-bromoflavylium Choride.**—Ozonized oxygen was passed for six hours into a solution of 5 g. of 3-methoxy-4′-bromoflavylium chloride[8] dissolved

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[1] Dilthey, *J. prakt. Chem.*, **94**, 53 (1916); *ibid.*, **95**, 107 (1917); *Ber.*, **53**, 261 (1920); *J. prakt. Chem.*, **131**, 1 (1931); *ibid.*, **138**, 42 (1933); *Ber.*, **64**, 2082 (1931).

[2] Hill and Melhuish, *J. Chem. Soc.*, 1161 (1935).

[3] Meyer and Schuster, *Ber.*, **55**, 815 (1922).

[4] Straus, Krier and Lutz, *Ann.*, **374**, 121 (1910); Straus, *ibid.*, **393**, 235 (1912); Straus and Dützmann, *J. prakt. Chem.*, **103**, 1 (1921); Straus and Ehrenstein, *Ann.*, **442**, 93 (1925).

[5] See Hill (*Chem. Rev.*, **19**, 27 (1936)) for a summary of the evidence bearing on the structure of benzopyrylium salts.

[6] Le Fèvre, *J. Chem. Soc.*, 2771 (1929).

[7] Löwenbein, *Ber.*, **57**, 1517 (1924); Löwenbein and Katz, *ibid.*, **59**, 1377 (1926); Löwenbein and Rosenbaum, *Ann.*, **448**, 223 (1926).

[8] Shriner and Moffett, THIS JOURNAL, **61**, 1474 (1939).

in 75 cc. of glacial acetic acid. After the ozone had been passed in for about one and one-fourth hours, the dark red color of the solution had disappeared and it had become light yellow. At the end of the six hours 75 cc. of ice water was added to the mixture, which caused a white precipitate to separate. About a gram of zinc dust was added, the mixture thoroughly stirred, and placed in the refrigerator. The next day the mixture was diluted until no more precipitate formed, and filtered. The precipitate was extracted with ether, the ether solution evaporated, and the residue crystallized from alcohol. The crude product was recrystallized from a 50% mixture of benzene and petroleum ether by dissolving it in this solvent while hot, filtering, and allowing the filtrate to stand overnight in the refrigerator. A yield of 0.38 g. of nearly colorless crystals of methyl *o*-(*p*-bromobenzoxy)-$\alpha$-toluate was obtained which melted at 87–88°. An additional yield of 0.3 g. was obtained from the various other fractions of the ozonized mixture.

*Anal.* Calcd. for $C_{16}H_{13}O_4Br$: C, 55.01; H, 3.75; Br, 22.90. Found: C, 55.24; H, 3.85; Br. 22.90.

The filtrate from the original ozonization mixture was distilled at about 20 mm. pressure and 30–40°. About 0.05 g. of *p*-bromobenzoic acid was obtained from the residue. The distillate was treated with 0.5 g. of *p*-nitrophenylhydrazine and shaken for one hour. About 0.5 g. of an orange colored precipitate of salicylaldehyde *p*-nitrophenylhydrazone formed, a portion of which when recrystallized from methyl alcohol melted at 218–222° in a capillary tube. On the hot stage microscope it began to sublime at about 175° and new crystals formed on the cover glass. These new crystals melted at 226–229°.[9] This compound dissolved in potassium hydroxide to give a dark red color.[10] A known sample of salicylaldehyde-*p*-nitrophenylhydrazone behaved in the same way and a mixed melting point showed no depression.

**Hydrolysis of Methyl *o*-(*p*-Bromobenzoxy)-$\alpha$-toluate.**—Three-tenths of a gram of methyl *o*-(*p*-bromobenzoxy)-$\alpha$-toluate was hydrolyzed by refluxing with 15 cc. of 25% potassium hydroxide solution for four hours. By acidification and a system of fractional crystallizations from water, *p*-bromobenzoic acid and *o*-hydroxy-$\alpha$-toluic acid were obtained. The *p*-bromobenzoic acid, after recrystallization from alcohol, was characterized by its melting point and a mixed melting point with known material. The *o*-hydroxy-$\alpha$-toluic acid, after recrystallization from chloroform, was characterized by its melting point of 144.5–146.5°[11,12] and the violet color it gave with ferric chloride solution.[12]

**3-Phenyl-4′-bromoflavylium Chloride and 3-Phenyl-4′-bromo-flavylium Ferrichloride.**—Dry hydrogen chloride was passed for forty-five minutes into a mixture of 20 g. of *p*-bromo-$\alpha$-phenylacetophenone, prepared by the method of Kohler and Peterson,[13] and 8 cc. of salicylaldehyde dissolved in 60 cc. of dioxane. When the solution became saturated with hydrogen chloride, it turned a yellow color, and a small amount of solid separated. The large test-tube containing this mixture was stoppered and placed in the refrigerator. After twenty-four hours the solid had redissolved and the solution had become red in color. After two more days clean yellow crystals of 3-phenyl-4′-bromoflavylium chloride had separated. The dioxane solution was decanted from the crystals in a dry box and the product was washed with absolute ether, which was removed by filtration in the dry box; yield, 24.74 g. (78.5% of theoretical).

Absolute ether was added to the dioxane solution and an oily layer separated. This was dissolved in concentrated hydrochloric acid and ferric chloride (also in concentrated hydrochloric acid) was added. A yellow precipitate of crude 3-phenyl-4′-bromoflavylium ferrichloride formed. This was removed by filtration through glass wool and recrystallized from glacial acetic acid. The yield was 7.80 g. (19.4% of theoretical) of brown crystals which melted at 162–163.5°.

*Anal.* Calcd. for $C_{21}H_{14}OBrFeCl_4$: Cl, 25.33; Fe, 10.01. Found: Cl, 25.17; Fe, 10.20.

**Ozonization of 3-Phenyl-4′-bromoflavylium Chloride.**—Ozonized oxygen was passed for two hours into a solution of 3.85 g. of 3-phenyl-4′-bromoflavylium chloride dissolved in 25 cc. of glacial acetic acid. At the end of this time the dark red color of the solution had changed to a light yellow. The mixture was decomposed by adding 50 cc. of water, but no zinc dust. A yellow gummy precipitate formed leaving a colorless solution. The solution was decanted, the precipitate dissolved in ether and a 5% solution of sodium hydroxide was added. After shaking the layers were separated.

An excess of carbon dioxide (dry-ice) was added to the water layer and then it was extracted with ether, which on evaporation yielded a small residue which gave a violet color with ferric chloride.

The aqueous solution was then acidified with dilute hydrochloric acid giving a precipitate of 0.6 g. of *p*-bromobenzoic acid. After recrystallization from alcohol it melted at 251–252° and a mixed melting point with a known sample gave no depression. The melting point of *p*-bromobenzoic acid is best observed in a sealed capillary tube since it was found to sublime noticeably at 175°.

The ether solution was evaporated by a stream of air leaving an oily residue which was dissolved in hot alcohol and cooled in the refrigerator overnight. The next day a precipitate of 4-bromobenzil had separated, partly as an oil and partly crystalline. The crystals were collected and found to weigh 0.12 g. and melted at 85–86°.

A sample of 4-bromobenzil prepared by selenium dioxide oxidation of *p*-bromo-$\alpha$-phenylacetophenone[14] melted at 86–87°. A mixed melting point showed no depression.

The aqueous solution from the ozonization mixture was steam distilled and phenylhydrazine was added to the distillate. A precipitate of about 0.85 g. of salicylaldehyde phenylhydrazone was obtained which after two recrystallizations from alcohol melted at 140–142°. A mixed melting point with a known sample showed no depression.

In another experiment the ozonization mixture from 3-phenyl-4′-bromoflavylium chloride was decomposed with water and zinc dust. *p*-Bromobenzoic acid, 4-bromobenzil and salicylaldehyde were isolated.

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(9) Biltz and Sieden, *Ann.*, **324**, 310 (1902).

(10) Bamberger, Büsdorf and Sand, *Ber.*, **31**, 1513 (1898).

(11) Czaplicki, v. Kostanecki and Lampe, *ibid.*, **42**, 827 (1909).

(12) Stoermer, *Ann.*, **313**, 79 (1900).

(13) Kohler and Peterson, THIS JOURNAL, **55**, 1073 (1933).

(14) Hatt, Pilgrim and Hurran, *J. Chem. Soc.*, 93 (1936).

**Preparation of 2-Ethoxy-2-(*p*-bromophenyl)-3-phenyl-1,2-benzopyran.**—Five and eight-tenths grams of 3-phenyl-4′-bromoflavylium ferrichloride was dissolved in 200 cc. of ethyl alcohol and 2.5 g. of potassium hydroxide in 50 cc. of ethyl alcohol was added. The mixture was heated to boiling and filtered. The ferric hydroxide remaining on the filter paper was extracted with ethyl alcohol. The combined filtrate was evaporated to a small volume and cooled in the refrigerator. The crystals were removed by filtration and another yield was obtained from the filtrate by further evaporation and cooling. The crude product was recrystallized from ethyl alcohol yielding 3.48 g. (82.7% of the theoretical) of white needles which melted at 101–102.5°.

*Anal.* Calcd. for $C_{23}H_{19}O_2Br$: C, 67.80; H, 4.70; Br, 19.63. Found: C, 67.68; H, 4.92; Br, 20.06.

2-Ethoxy-2-(*p*-bromophenyl)-3-phenyl-1,2-benzopyran was also prepared from 3-phenyl-4′-bromoflavylium chloride by dissolving 4.3 g. of it in ethyl alcohol and cooling in the refrigerator. The resulting crude product was removed by filtration and a further yield was obtained from the filtrate by evaporation and cooling. This second crop was recrystallized from alcohol and then combined with the first yield and recrystallized from alcohol with the aid of Norit. The yield was 2.91 g. (72.1% of theoretical).

**Ozonization of 2-Ethoxy-2-(*p*-bromophenyl)-3-phenyl-1,2-benzopyran.**—Ozonized oxygen was passed for three hours into a cold solution of 10 g. of 2-ethoxy-2-(*p*-bromophenyl)-3-phenyl-1,2-benzopyran dissolved in 50 cc. of carbon tetrachloride. About 3 g. of zinc dust and 50 cc. of water containing 5 cc. of glacial acetic acid was then added, and the mixture thoroughly shaken.

The mixture was filtered from the slight residue of zinc and the water layer was separated and extracted with a little carbon tetrachloride. This extract was added to the carbon tetrachloride layer and the mixture was distilled at room temperature under reduced pressure. The distillate was condensed in a trap cooled by a dry-ice and acetone mixture.

The oily residue was placed in the refrigerator and the next day crystals of 4-bromobenzil had formed. After recrystallizing twice from alcohol 1.3 g. of long silky light yellow needles were obtained which melted at 86–86.5°. A mixed melting point with a known sample prepared as above[14] showed no depression.

*Anal.* Calcd. for $C_{14}H_9O_2Br$: C, 58.13; H, 3.14. Found: C, 58.15; H, 3.29.

Water and a trace of hydrochloric acid were added to the filtrate and the mixture was distilled. Salicylaldehyde distilled over with the water. It was separated by extraction with benzene and the benzene was evaporated on a water-bath. The residue weighed 1.5 g. This was characterized by conversion to the phenylhydrazone which melted at 141.5–142°. A mixed melting point with a known sample of salicylaldehyde phenylhydrazone gave no depression.

The residue from the distillation was separated from the water, dissolved in hot alcohol and placed in the refrigerator. After two days an additional crop of crystals of 4-bromobenzil was obtained which weighed 1.5 g.

The alcoholic filtrate was evaporated on a water-bath and the residue dissolved in benzene. A 10% aqueous solution of sodium hydroxide was added and the mixture was thoroughly shaken. The layers were separated and the aqueous layer acidified with dilute hydrochloric acid. The resulting precipitate was removed by filtration and recrystallized from alcohol. About 0.03 g. of *p*-bromobenzoic acid was obtained which melted at 250–251° and gave no depression in a mixed melting point.

The aqueous layer from the original ozonization mixture was made alkaline with sodium hydroxide and the resulting zinc hydroxide removed by filtration. The filtrate was distilled using a fractionating column. The first 3 cc. of distillate collected gave a positive test for ethyl alcohol by the iodoform test.

## Summary

Ozonolysis of two flavylium salts, 3-methoxy-4′-bromoflavylium chloride and 3-phenyl-4′-bromoflavylium chloride, yielded degradation products whose formation indicated that these salts may be cleaved between either carbon atoms 2 and 3 or carbon atoms 3 and 4. It is pointed out that these degradation products and the chemical properties of flavylium salts can best be expressed by two resonating structures of an allylic system.

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