[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

STUDIES IN THE CYCLOPROPANE SERIES. V.

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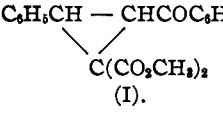
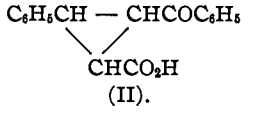
All the cyclopropane derivatives described in the earlier papers had two carboxyl groups in combination with one of the carbon atoms of the ring. In order to determine to what extent the peculiar properties of those substances are due to this fact we have studied derivatives which differ from them only in having hydrogen in place of one of the carboxyl groups. The relation between the two types is shown by the formulas

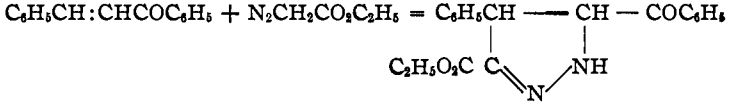


(I).

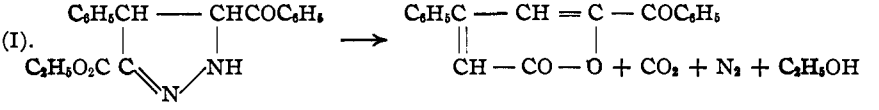


(II).

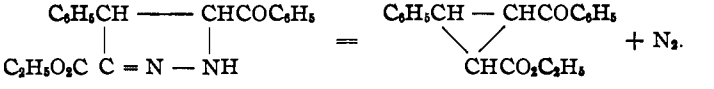
The preparation of cyclopropane derivatives of the general type represented by Formula II proved exceedingly difficult; but was finally accomplished by an adaptation of the pyrazoline method used by Buchner for preparing cyclopropane acids. Under suitable conditions, α,β-unsaturated ketones combine with ethyl diazo-acetate to form pyrazoline derivatives:



These ketonic pyrazolines decompose when heated but unlike the corresponding esters give, almost exclusively, pyrone derivatives:

(I). 

A small quantity of cyclopropane derivative is, however, formed in accordance with the equation



The yield of cyclopropane ester is less than 1% but we found that by heating the pyrazoline in contact with polished platinum it was possible to speed up the second reaction at the expense of the first and thus increase the yield to more than 40%. The pyrone derivatives, which always constitute the main product, are not due to a decomposition of the cyclopropane compounds at high temperatures because these are far more stable than the corresponding substances of Type I, and can be heated without change to temperatures more than 100° above those used for decomposing the pyrazolines.

We have studied the behavior of our substances with all the reagents that give characteristic results with the cyclopropane derivatives of Type I: oxidizing agents, reducing agents, halogen acids, halogens, phosphorus pentachloride and alcoholates. Toward oxidizing agents they present the same contrast with ethylenic compounds that was noted in the earlier work, being quite unaffected by permanganate but readily reduced by zinc and acetic acid. Reduction results in addition of hydrogen to the ring carbon atoms, (1) and (3), and the product is a saturated δ-ketonic ester.

$$C_6H_5CH\text{—}CHCOC_6H_5 \quad (\text{ring: } CHCO_2CH_3) + H_2 = C_6H_5COCH_2CH(C_6H_5)CH_2CO_2C_2H_5.$$

Both the acids and their esters combine with halogen acids at least as readily as do α,β-unsaturated ketones, the ring opening between carbon atoms (2) and (3).

$$C_6H_5CH\text{—}CHCOC_6H_5 \quad (\text{ring: } CHCO_2CH_3) + HCl = C_6H_5CHClCH(CO_2CH_3)CH_2COC_6H_5.$$

The resulting chloro ester loses hydrogen chloride to potassium acetate with the greatest ease, and it is noteworthy that while it is a β-chloro ester as well as a γ-chloro ketone, not a trace of unsaturated ester is formed in the process, the sole product being the cyclopropane derivative. The corresponding chloro acid, however, behaves toward sodium carbonate like a typical β-halogen acid, giving β-benzal-propiophenone.[1]

$$C_6H_5CHClCH(CO_2Na)CH_2COC_6H_5 = C_6H_5CH = CHCH_2COC_6H_5 + HCl.$$

The reactions with halogen acids and reducing agents in which the ring is opened in different positions constitute the real proof that these substances are cyclopropane derivatives and not isomeric unsaturated δ-ketonic acids.

Dehydrating agents like acetic acid and acetic anhydride by themselves do not have any effect on the cyclopropane derivatives but in their presence hydrogen bromide rapidly transforms the cyclopropane acids into unsaturated lactones.

$$C_6H_5CH\text{—}CHCOC_6H_5 \quad (\text{ring: } CHCO_2H) + HBr \longrightarrow C_6H_5CHBrCH\text{—}CH_2COC_6H_5 \quad (CO_2H)$$

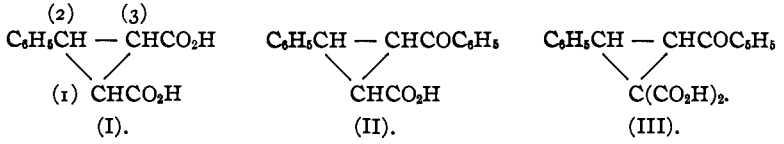
$$\longrightarrow C_6H_5CH = C\text{—}CH = C\text{—}C_6H_5 \quad (\text{ring: } CO\text{—}O) + HBr + H_2O.$$

Thionyl chloride and phosphorus pentachloride convert the cyclopropane acid into its chloride without attacking the ring. The acid chloride cannot, however, be used for the preparation of ketones by the Friedel

[1] Wieland, *Ber.*, 40, 4830 (1907).

and Crafts reaction because when it is treated with benzene and aluminum chloride it immediately passes into the unsaturated lactone. This is probably merely another illustration of the action of the halogen acids in the presence of dehydrating agents.

A comparison of 3 closely related types of cyclopropane derivatives shows some significant differences.



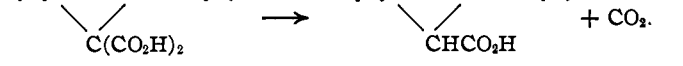
Buchner found that the acids of Type I as well as their esters are perfectly stable at high temperatures, and also that the cyclopropane ring in these substances can not be opened with reagents. We have verified this; both the acids and their esters behave in every respect like saturated compounds. In contrast with this, the other two types of substances give many of the addition reactions of unsaturated compounds.

The most conspicuous difference between the substances represented by II and III is in their behavior towards basic reagents. The esters of the dibasic acids combine with the greatest ease with alcoholates, sodium amide, and similar substances, the ring opening between carbon atoms (1) and (3). In contrast with this the esters of the monobasic acid are indifferent to dry alcoholates, and no reagents were found which would open the ring at this point. Both types combine with hydrogen, the halogen acids, and probably the halogens.

The *mode* of addition to substances of Types II and III is the same in all cases in which they combine with the same reagents. The *ease* of addition, however, is quite different. The acids of Type III pass into lactones, essentially an addition reaction, at temperatures at which those of Type II are perfectly stable. With halogen acids, on the other hand, the substances of Type II combine far more readily than those of Type III.

Experimental Part.

Preparation of the Cyclopropane Derivatives.—When benzoylphenylcyclopropane dicarboxylic acid is heated, one of the products is the corresponding monobasic acid.[1]



The amount of cyclopropane derivative obtained in this way is insignificant but it seemed probable that by using ester acids, acid salts, or suitable catalytic agents, it would be possible to lower the temperature

[1] THIS JOURNAL, 39, 1418 (1917).

to the point where the cyclopropane derivative would be the principal product. All of our efforts in this direction proved fruitless.

The second method of preparation that we tried depended on the elimination of hydrobromic acid from an α-bromo ketonic ester. For the work in this direction we selected methyl β-phenyl-γ-(4-bromobenzoyl)-butyrate, because it was more likely to give solid products than the unsubstituted ester.

β-Phenyl-γ(4-bromobenzoyl)-butyric Acid, $BrC_6H_4COCH_2CH(C_6H_5)CH_2CO_2H$.—The acid was obtained in calculated quantity by heating the corresponding malonic acid[1] to 135–140° until effervescence ceased. It was purified by recrystallization from aqueous alcohol. It separated in needles and melted at 152–153°.

Calc. for $C_{17}H_{15}O_3Br$: C, 58.8; H, 4.3. Found: C, 58.5; H, 4.5.

The methyl ester was obtained by saturating a concentrated solution of the acid in methyl alcohol with hydrochloric acid. It separated in solid form as the solution cooled. The solid was washed with water and recrystallized from methyl alcohol. The ester crystallizes in stout needles, is moderately soluble in methyl alcohol and ether, and melts at 93°.

Calc. for $C_{18}H_{17}O_3Br$: C, 49.1; H, 3.6. Found: C, 48.9; H, 3.6.

Methyl β-Phenyl-γ-bromo-γ-(4-bromobenzoyl)-butyrate, $BrC_6H_4COCHBrCH(C_6H_5)CH_2CO_2CH_3$.—The ester was brominated in carbon tetrachloride. The product was left as an oil when the solvent was removed under diminished pressure, but it solidified on addition of a little ether. By recrystallization from methyl alcohol the solid was separated into two monobromo derivatives. The one that is formed in largest quantity crystallized in fine needles and melted at 81–82°. The other separated in small quantity from the mother liquors, in long, feathery crystals that melted at 92°.

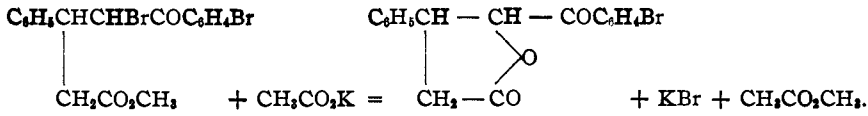
Calc. for $C_{18}H_{16}O_3Br_2$: C, 49.1; H, 3.6. Found: C, 49.0, 49.1; H, 3.6, 3.9.

Elimination of Hydrogen Bromide.—Methyl alcoholic solutions of the γ-bromo esters were boiled with magnesium methylate, potassium acetate, and sodium methylate. The substance was not affected at all by magnesium methylate. The solutions containing potassium acetate deposited nearly the calculated amount of potassium bromide in the course of 5 hours. Most of the alcohol was then removed. It left a pale yellow oil. This was dissolved in ether, the ethereal solution washed, dried and allowed to evaporate. The pale yellow oil that was left eventually solidified. The solid was purified by recrystallization from alcohol and thus obtained in fine, colorless needles that melted at 158°.

Calc. for $C_{17}H_{13}O_3Br$: C, 59.1; H, 3.8. Found: C, 58.8; H, 3.4.

The analysis indicated a lactone, formed in accordance with the equation

[1] THIS JOURNAL, 39, 2408 (1917).

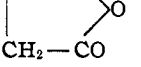


In order to verify this the γ-lactone was made by way of the bromo acid.

β-Phenyl-γ-bromo-γ-(4-bromobenzoyl)-butyric Acid, $BrC_6H_4COCHBrCH(C_6H_5)CH_2CO_2H$.—Bromine was added to finely powdered phenyl-*p*-bromobenzoyl-butyric acid, suspended in hot carbon tetrachloride, until a permanent red color appeared. The acid dissolved in the process and the solution on cooling deposited the bromo ester in calculated quantity. The fine, white powder was recrystallized from ethyl acetate, as it was found to be excessively soluble in alcohol and ether. It crystallized in needles and melted at 146–147°.

Calc. for $C_{17}H_{14}O_3Br_2$: C, 47.9; H, 3.3. Found: C, 47.8; H, 3.1.

β-Phenyl-γ-(4-bromobenzoyl)-butyrolactone, $C_6H_5CH(CH_2)CHOCOC_6H_4Br$.—



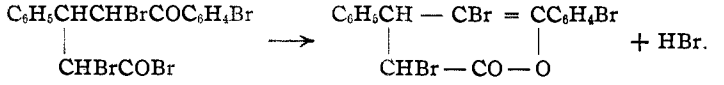
The γ-bromo acid was dissolved in a cold solution of sodium carbonate. After 3 or 4 minutes the clear solution became turbid and soon a precipitate formed. This was recrystallized from alcohol and a mixed melting point showed that it was identical with the product obtained from the reaction between the bromo ester and potassium acetate.

The product of the reaction between the bromo ester and sodium methylate likewise was an oil that solidified after long standing. The solid proved to be a mixture of the same lactone and the bromine-free saturated ester in approximately equal amounts. These results showed that it was hopeless to attempt to get the cyclopropane derivative from the γ-bromo ester.

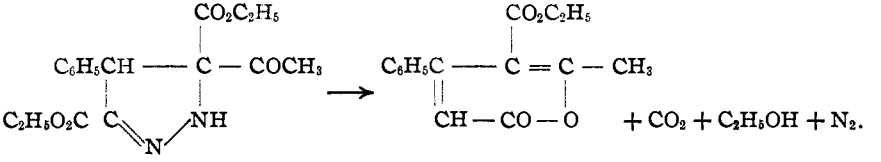
3,5-Dibromo-4-phenyl-6-(4-bromo-phenyl)-dehydropyrone-1,2, $C_6H_5CH(CHBrCO)CBr=C(O)C_6H_4Br$.—A third attempt to make the cyclopropane derivative was based on the elimination of bromine from an α,γ-dibromo ketonic ester. As the γ-bromo ester does not react with bromine we undertook the bromination of the γ-bromo acid by the Hell-Volhard-Zelinsky method. For this purpose 5 g. of the acid was dissolved in 12 g. of phosphorus tribromide with gentle warming. An excess of bromine was added and the mixture boiled until the evolution of hydrogen bromide ceased. The solution was then allowed to cool and poured into ice water. This precipitated a brick-red solid which was insoluble in alcohol and ether. It was recrystallized from ethyl acetate from which it separated in large, rhombic crystals of the color of smoky quartz. These melted at 170°.

Calc. for $C_{17}H_{11}O_2Br_3$: Br, 49.3. Found: 49.4.

The substance was insoluble in alkaline carbonates. No attempt was made to determine its structure, but it seems altogether probable that it is a pyrone derivative formed from the acid bromide.



Ketonic Pyrazolines.—Since all of the more direct methods for getting the desired cyclopropane derivatives failed it became necessary to resort to the pyrazoline reaction which Buchner used for making cyclopropane acids. The outlook was far from promising. Ketonic pyrazolines are not nearly so easy to make as the pyrazoline esters; and only few are known.[1] Most of these were made by Buchner for the purpose of getting cyclopropane derivatives, but when he heated them he invariably obtained only pyrone derivatives.[2]



The diazo ester used in the earlier experiments was a very pure preparation obtained by the method of Curtius.[3] It was found later that a product obtained by the more convenient method given by Weyl[4] served equally well. After removing the last of the ether under diminished pressure the pale yellow liquid could be kept in brown bottles for many weeks without change. In a colorless bottle one specimen polymerized to the triethyl ester of pyrazoline triacid-1,2,3, melting at 98–99°.

Phenyl-(4-bromobenzoyl)-pyrazole Carboxylic Acid, $C_6H_5C(=C(COC_6H_4Br)-N=NH)-HO_2C$.—A mixture of equivalent amounts of ethyl diazo-acetate and benzal-*p*-bromo-acetophenone was warmed gently on a steam-bath. At 90° a slight effervescence was noted and at 95° a vigorous reaction took place. After this was over the temperature of the mixture was gradually raised to 175° in the course of 4 hours. The product on cooling turned to a glue-like mass which did not solidify in contact with alcohol. It was, therefore, treated with alcoholic potassium hydroxide. The solid potassium salt which separated was washed with alcohol until colorless. It gave a colorless acid which crystallized from alcohol in feathery needles. The acid melted, with decomposition, at 216–217°.

[1] *Ber.*, **28**, 221 (1895); **35**, 34, 785 (1902).

[2] *Ber.*, **35**, 789 (1902).

[3] *J. prakt. Chem.*, [2] **38**, 401 (1888).

[4] *Meth. d. org. Chem.*, p. 848.

Calc. for $C_{17}H_{12}O_2N_2Br$: Br, 21.6. Found: Br, 21.2.

Phenyl-(4-bromobenzoyl)-pyrazol, $C_6H_5-C=CCOC_6H_4Br$ (CH=N—NH). — The pyrazol carboxylic acid began to effervesce freely at 245°. The gas evolved was carbon dioxide. The light brown residue was recrystallized from alcohol, which deposited it in colorless needles melting at 159°.

An analysis of this substance showed that it was a pyrazol derivative; the condensation product from which it was obtained therefore was not the desired ketonic pyrazoline.

Calc. for $C_{16}H_{11}ON_2Br$: C, 58.7; H, 3.4. Found: C, 58.7; H, 3.7.

Ethyl 4-Phenyl-5-(4-bromobenzoyl)-pyrazoline Carboxylate, $C_6H_5CH=CHCOC_6H_4Br$ ($C_2H_5O_2C$ C = N — NH).—A solution of 15 g. of ethyl-diazo-acetate and 37 g. benzal-*p*-bromo-acetophenone in high boiling ligroin was heated on a steam-bath. After a time a fine, white precipitate began to separate. The reaction appeared to be complete after 2.5 hours when 26.5 g. of product was filtered from the hot solution. Recrystallization of this product from alcohol gave colorless, rhombic plates which melted at 150–154° with effervescence.

Calc. for $C_{19}H_{17}O_3N_2Br$: C, 56.8; H, 4.2. Found: C, 56.9; H, 4.5.

4-Phenyl-6-(4-bromophenyl)-pyrone-1,2, $C_6H_5C=CH-C-C_6H_4Br$ (CH — CO — O).— The pyrazoline derivative began to give off nitrogen at 160°. A quantity of it was therefore heated in an oil-bath at 170–200° for two hours. The resulting oil on cooling deposited a mixture of two kinds of crystals. These were separated by systematic fractional crystallization from alcohol. The principal product was sparingly soluble in alcohol from which it separated in fine, feathery crystals. When pure it melted sharply at 183° and contained no nitrogen. This was evidently a pyrone derivative formed in the same way as those obtained by Buchner in a similar reaction.

Calc. for $C_{17}H_{11}O_2Br$: C, 62.4; H, 3.4. Found: C, 62.2; H, 3.6.

Ethyl 2-Phenyl-3-(4-bromophenyl)-cyclopropane Carboxylate, $C_6H_5CH-CHC_6H_4Br$ ($CHCO_2C_2H_5$).—The mother liquors from the pyrone derivative deposited a small quantity of another substance. By recrystallization from alcohol this was obtained in colorless needles which melted at 118–119°.

Calc. for $C_{19}H_{17}O_2Br$: C, 61.1; H, 4.6. Found: C, 61.0; H, 4.4.

This substance was undoubtedly the cyclopropane derivative, but the

amount obtained was extremely small—less than 0.1 g. from 10 g. of pyrazoline derivative. Its relatively high melting point and its sparing solubility in alcohol indicated that a corresponding compound obtained by starting with benzal-acetophenone would likewise be a crystalline solid. We therefore used the more convenient unsaturated ketone in all subsequent experiments.

Ethyl 4-Phenyl-5-benzoyl-pyrazoline Carboxylate-3,

$$\begin{array}{l} \quad\quad\; C_6H_5CH \text{ --- } CHCOC_6H_5 \\ \quad\quad\quad\;\; | \quad\quad\quad\;\; | \\ C_2H_5O_2C - C = N - NH \end{array}$$

.—A solution of 43.8 g. of benzal-acetophenone and 24 g. of ethyl diazo-acetate in the minimum quantity of ligroin (90–120°) was heated on a steam-bath for 3 hours. A red oil accumulated on the bottom and sides of the flask. The ligroin was decanted and a small quantity of ether poured on top of the oil, which soon solidified under this treatment. The solid, purified by recrystallization from alcohol, was obtained in hexagonal plates melting at 156–158°.

Calc. for $C_{19}H_{18}O_4N_2$: C, 70.8; H, 5.6. Found: C, 70.5; H, 5.9.

In later experiments it was found that a much purer product could be obtained by inoculating the hot ligroin solution of benzal-acetophenone and ethyl diazo-acetate with some of the crystalline pyrazoline derivative and then by frequent shaking induce the product to separate as a fine crystal powder. After this was washed with ether it was pure enough for use. It was found also that on a small scale, at any rate, the reaction can be carried out without using a solvent. Thus 2 g. of unsaturated ketone and 1.2 g. of the diazo compound were heated at 60–65° for 5 hours. The pyrazoline derivative began to separate spontaneously after about an hour. After washing with ether the product weighed 2. g. The average yield when ligroin was used as a solvent was 64%.

The pyrazoline derivative is moderately soluble in boiling alcohol, sparingly in cold alcohol and ether, insoluble in ligroin. Its solutions in alcohols turn to a brilliant red color when a little hydrogen chloride is passed into them. On protracted heating below the temperature at which it decomposes it passes into an isomer that crystallizes in needles which are readily soluble in alcohol and ether and which melt at 102.5–103°. This substance is also formed in small quantities during the condensation of the unsaturated ketone and diazo ester, and accumulates in the mother liquors. It is probably a stereoisomer because its alcoholic solutions with hydrochloric acid give the same color as the higher melting product.

Calc. for $C_{19}H_{18}O_4N_2$: C, 70.8; H, 5.6. Found: C, 70.5; H, 5.6.

4,6-Diphenyl-pyrone-1,2,

$$\begin{array}{l} C_6H_5C \text{ --- } CH = C - C_6H_5 \\ \quad\;\; \| \quad\quad\quad\quad\;\; | \\ \quad CH - CO - O \end{array}$$

.—This is always the principal product that is formed when the pyrazoline compounds are

decomposed at high temperatures. It is most easily purified by first distilling the oily melt under diminished pressure and then recrystallizing the solid distillate from alcohol. It is very sparingly soluble in cold alcohol, readily soluble in ether and boiling alcohol, and crystallizes in yellow plates which melt at 138–139°.

Calc. for $C_{17}H_{12}O_2$: C, 82.3; H, 4.8. Found: C, 82.2; H, 5.0.

Ethyl 2-Phenyl-3-benzoyl-cyclopropane Carboxylate, $C_6H_5CH(CHCOC_6H_5)CHCO_2C_2H_5$.—The cyclopropane derivative is probably formed whenever the pyrazoline is decomposed at high temperature but the yield is always small, for we never got over 2% when the pyrazoline was heated by itself. In an effort to improve the yield we decomposed the substance under a variety of different conditions: in solution in high boiling liquids, under increased and reduced pressures, and in contact with charcoal, a variety of porous materials that promote gas reaction, platinized asbestos, and all the common metals. Of these only platinum and gold proved useful.

The method of preparation finally adopted was therefore as follows: The pyrazoline was heated in a metal bath in 10 g. lots with 3 g. of platinum scrap to each lot. At 220–225° nitrogen was given off very rapidly and the decomposition was usually complete in 2–3 minutes. The resulting oil was dissolved in alcohol and the cyclopropane derivative allowed to crystallize slowly. The crystals were always yellow owing to contamination with a trace of the pyrone and several recrystallizations were necessary to get a colorless product. The average yield was 37%.

Calc. for $C_{19}H_{18}O_3$: C, 77.6; H, 6.1. Found: C, 77.6; H, 6.1.

The cyclopropane ester crystallizes in thin plates and melts at 103°. It is readily soluble in boiling alcohol and in acetone. moderately soluble in cold alcohol, ether, benzene, and acetic acid. It does not reduce a solution of permanganate in acetone. In a good vacuum it can be distilled without loss and it was recovered unchanged after it had been heated above 300° for several hours.

2-Phenyl-3-benzoyl-cyclopropane Carboxylic Acid, $C_6H_5CH(CHCOC_6H_5)CHCO_2H$.—For the purpose of hydrolysis an excess of 2:3 aqueous potassium hydroxide solution was added to an alcoholic solution of the ester. After 10 minutes the solution could be diluted with water without becoming turbid—indicating complete hydrolysis. The solution was acidified, the curdy precipitate thoroughly washed with water, dried and dissolved in benzene. The solution first deposited a small quantity of fine needles, then the main product in long, thin filaments, like thistledown. These are two stereoisomeric acids.

The acid which crystallizes in needles is easily purified. It melts at 176°, and is very readily soluble in alcohol and ether, moderately in benzene, almost insoluble in ligroin.

Calc. for $C_{16}H_{14}O_3$: C, 76.7; H, 5.3. Found: C, 76.4; H, 5.4.

It is difficult to get the other acid in a form in which it will give a sharp melting point because it is always contaminated with a small quantity of its isomer. After a number of recrystallizations from benzene it melted at 147–150°.

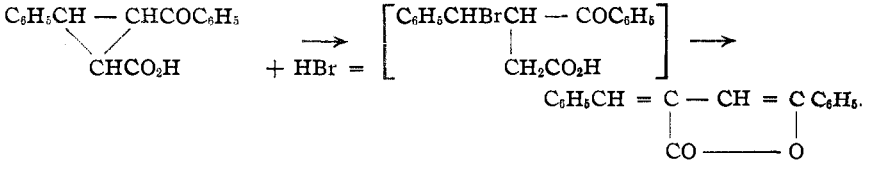
Calc. for $C_{16}H_{14}O_3$: C, 76.7; H, 5.3. Found: C, 76.5; H, 5.2.

Each of the cyclopropane acids was re-esterified by way of the silver salt and ethyl iodide. The higher melting acid gave the ester from which the acids had been obtained by hydrolysis. The lower melting acid gave an isomeric ester which melted at 93–94°. This crystallized from alcohol in stout needles and from ether in 6-sided plates.

Calc. for $C_{19}H_{18}O_3$: C, 77.6; H, 6.0. Found: C, 77.4; H, 6.0.

Action of Hydrobromic Acid on the Cyclopropane Acid.—In order to compare the behavior of this acid with that of the corresponding dibasic acid studied by Buchner, it was sealed up in a tube with excess of conc. aqueous hydrobromic acid. No reaction took place in the cold. The tube was therefore heated in a steam-jacketed furnace. It was extensively decomposed and gave only tarry products, while Buchner's acid under the same conditions remained unchanged.

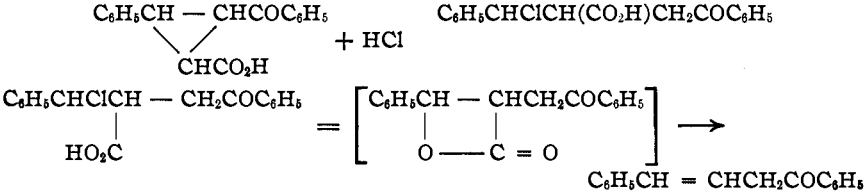
For the purpose of comparing the behavior of the acid with those described in earlier papers, its solution in glacial acetic acid was saturated with hydrogen bromide. The solution turned yellow at once and in a few hours deposited a yellow crystalline solid, melting at 149–150°. This was identified as α-benzal-γ-phenyl-crotonic lactone by comparison with a specimen on hand. The acid, therefore in this respect, behaves exactly like the ketonic cyclopropane acids which contain two carboxyl groups, the ring opening between carbon atoms (2) and (3).



Action of Hydrogen Chloride.—A solution of the lower melting acid in glacial acetic acid was saturated with hydrogen chloride. It remained colorless and after a time deposited a colorless acid which melted with decomposition at about 131–132°, and contained chlorine. This acid was extremely unstable, losing both hydrochloric acid and carbon dioxide with the greatest ease. When dissolved in alcohol, however, it formed the corresponding ester which was perfectly stable. An analysis of the ester

showed that the acid must have the composition $C_{17}H_{14}O_3Cl$, and, therefore, that it is formed by addition of a molecule of hydrogen chloride to the cyclopropane acid.

When this chloro acid was heated above its melting point for a few minutes it lost carbon dioxide and hydrochloric acid and gave a neutral, halogen-free product which melted at 92–93°. This was identical with the β-benzal-propiophenone which Wieland obtained by hydrolysis of α,δ-diphenyl-α-nitro-butadiene. Wieland's compound melted at 93° and gave an oxime that at 104° melted to a turbid liquid which became clear at 106°. Our product melted at 92–93° and gave an oxime which behaved exactly like Wieland's. Hydrochloric acid therefore adds in the manner assumed for hydrobromic acid, the proof being based on the following equations:



Ethyl α-Phenacyl-β,β-chloro-phenyl Propionate, $C_6H_5CHClCH(CO_2C_2H_5)CH_2COC_6H_5$.—The ester was obtained not only by dissolving the corresponding acid in alcohol but also, and much more easily, by saturating an alcoholic solution of either the cyclopropane acid or its ester with hydrogen chloride. This is the first case that we have met in which a cyclopropane derivative combines with a halogen acid in alcoholic solution.

Calc. for $C_{19}H_{19}O_3Cl$: C, 69.0; H, 5.8. Found: C, 68.6; H, 6.1.

The ester crystallizes from alcohol in hexagonal plates which melt at 68–69°. Its most characteristic property is the ease with which it loses hydrogen chloride to potassium acetate and forms a cyclopropane derivative. Although it is a β-chloro ester, not a trace of ethylenic compound is formed in the process.

Reduction.—A solution of the cyclopropane ester in acetic acid was boiled with excess of zinc dust for half an hour. On cooling it deposited a flocculent ester which melted at 59–61°. For the purpose of identification this was hydrolyzed to the corresponding acid. It gave an acid melting at 152–154° which was identified as β-phenyl-γ-benzoyl-propionic acid by comparison with a specimen of this acid prepared in another way.[1]

Reaction with Acid Chlorides.—Both the cyclopropane acid and its ethyl ester were treated with thionyl chloride and with phosphorus pentachloride. The ester was not attacked by either reagent. The acid was

[1] *Ann.*, **46**, 235 (1843).

transformed into the acid chloride but aside from a trace of yellow color there was no evidence that the ring was affected. Thus a solution of the acid in carbon tetrachloride was boiled with excess of phosphorus pentachloride until evolution of hydrogen chloride ceased. The pentachloride was then filtered off and the solvent evaporated under diminished pressure. It left a pale yellow oil. This, when dissolved in alcohol gave almost the calculated quantity of the ethyl ester. An attempt to use the acid chloride in a Friedel and Crafts reaction proved unsuccessful, the sole product being the same benzal-phenyl-crotonic lactone that had been previously obtained by the action of hydrogen bromide.

Experiments with 3-Phenylcyclopropane Diacid-2,2, $C_6H_5CH\text{—}CHCO_2H$ / $CHCO_2H$ —The acid and its ester were prepared by the method of Buchner. A solution of the ester in absolute alcohol was saturated with hydrogen chloride and allowed to stand at the ordinary temperature for several days. The ester was recovered unchanged. Solutions of the acid in glacial acetic acid were saturated with hydrochloric and hydrobromic acid and likewise allowed to stand for several days, but here also the original substance was recovered. It is evident, therefore, that the diacid is not affected by hydrochloric or hydrobromic acids, under conditions under which the acids produce ring cleavage in the corresponding ketonic acid.

Ethyl 4-Phenyl-pyrazol-carboxylate-3, $C_6H_5 - C = CH.$ / $C_2H_5O_2C - C = N$ \ NH —In order to determine whether nitro-cyclopropane derivatives could be obtained from the corresponding pyrazolines, a mixture of diazo-acetic ester and β-nitro-styrene in molecular proportions was gently warmed on a steam-bath. The reaction which started soon became so vigorous that it had to be moderated by cooling. The resulting brown oil crystallized spontaneously in thin plates. Recrystallization from alcohol gave colorless plates melting at 164-165°.

Calc. for $C_{12}H_{12}O_2N_2$: C, 66.7; H, 5.6. Found: C, 66.7; H, 5.9.

Its composition indicated a pyrazol derivative. The ester was therefore hydrolyzed and the resulting acid, which melted at 252-253°, heated above its melting point until effervescence ceased. The product, after crystallization from alcohol, appeared in leaflets melting at 228°—the properties of 4-phenyl-pyrazol. The reaction between nitro-styrene and ethyl diazo-acetate is, therefore, represented by the equation

$$C_6H_5CH = CHNO_2 + N_2CH_2CO_2C_2H_5 = \left[\begin{array}{l} C_6H_5CH \text{——} CHNO_2 \\ C_2H_5O_2C\ C = N - NH \end{array}\right] \longrightarrow$$

$$\begin{array}{l} C_6H_5C \equiv\equiv CH \\ \quad\quad | \quad\quad\quad | \\ C_2H_5O_2C\ C = N - NH \end{array} + HNO_2.$$

The reaction was also tried in ligroin and in ether at the lowest temperature at which it would take place. In each oxides of nitrogen appeared soon after the reaction started and the only product was the pyrazol derivative.

Summary.

1. Four methods were tried for making cyclopropane derivatives having one ketonic and one carboxyl group in combination with the ring: decomposition of a ketonic cyclopropane diacid, eliminating hydrogen bromide from a γ-bromo-ketonic acid, removing bromine from an α,γ-dibromo ketonic acid, and decomposing a pyrazoline-ketonic ester. All these methods gave cyclic compounds, but only the last could be used for preparing a cyclopropane derivative.

2. Reagents that combine readily with α,β-unsaturated ketones also combine with this type of cyclopropane derivatives. The addition products are open chained saturated compounds.

3. Diazo-acetic ester readily combines with nitro-styrene; but the product loses nitrous acid so easily that a pyrazol derivative is obtained instead of the nitro-pyrazoline which is first formed.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY.]

COLORED CONDENSATION PRODUCTS FROM KETONIC PYRAZOLINE DERIVATIVES.

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The ketonic pyrazolines described in the previous paper give highly colored, fluorescent solutions in alcohol containing a trace of hydrochloric acid. We have isolated several of the products; they are high melting, sparingly soluble solids resembling the most brilliantly colored rhodamine dyes.

The pyrazoline derivative obtained by adding diazo-acetic ester to benzal-acetophenone gave a crimson product which was free from halogen. Its composition and molecular weight are represented by the formula $C_{38}H_{32}O_4N_4$. It is, therefore, formed in accordance with the equation

$$\begin{array}{l} C_6H_5CH \text{———} CHCOC_6H_5 \\ \quad\quad | \quad\quad\quad | \\ 2C_4H_5O_2C.C = N - NH \end{array} = C_{38}H_{32}O_4N_4 + 2H_2O.$$

When the substance is allowed to remain in contact with a saturated solution of hydrochloric acid in alcohol, it takes up one molecule of the acid and one of water. The result is a yellow compound which readily