detoxication is built within 6 hours, while for the detoxication of a corresponding dose of phenylacetic acid a somewhat longer period of time is required for the synthesis of glutamine.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

THE REACTION BETWEEN ALKALIES AND CERTAIN NITROCYCLOPROPANE DERIVATIVES

BY E. P. KOHLER AND L. I. SMITH

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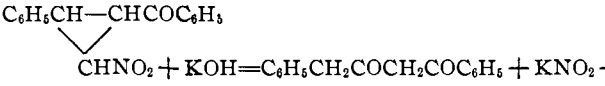
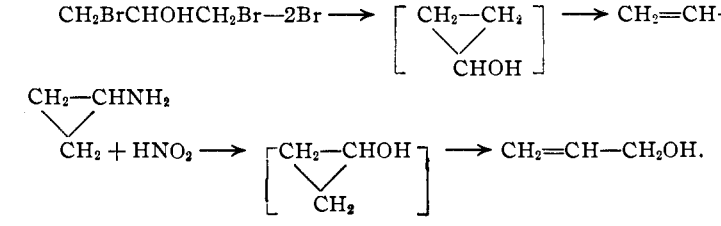
The action of alkalies on all known cyclopropane derivatives is peculiar. A typical reaction is that between phenyl-benzoyl-nitrocyclopropane and potassium hydroxide which gives potassium nitrite and an open chained β-diketone.[1]



$$C_6H_5CH{-}CHCOC_6H_5 \quad (\text{bridge: } CHNO_2) + KOH = C_6H_5CH_2COCH_2COC_6H_5 + KNO_2 + H_2O.$$

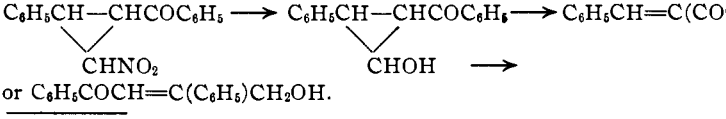
Since the reaction involves the elimination of the nitro group, it is conceivable that the first step in the process might be the replacement of this group by hydroxyl. This would give as the primary product a cyclopropanol derivative; but it is probable that cyclopropanols are unstable and like the corresponding ethylenic compounds immediately undergo rearrangement, for when zinc removes bromine from dibromo-*iso*propyl alcohol the product is not the cyclopropanol which would be expected but allyl alcohol,[2] and when cyclopropyl amine is treated with nitrous acid the product is likewise the unsaturated and not the cyclic alcohol.[3]



$$CH_2BrCHOHCH_2Br - 2Br \longrightarrow [\,CH_2{-}CH_2 \;(\text{bridge: } CHOH)\,] \longrightarrow CH_2{=}CH{-}CH_2OH$$

$$CH_2{-}CHNH_2 \;(\text{bridge: } CH_2) + HNO_2 \longrightarrow [\,CH_2{-}CHOH \;(\text{bridge: } CH_2)\,] \longrightarrow CH_2{=}CH{-}CH_2OH.$$

A cyclopropanol obtained by replacing the nitro group with hydroxyl would therefore probably be unstable, but it would not be expected to rearrange into anything related to the diketone that is obtained:



$$C_6H_5CH{-}CHCOC_6H_5 \;(\text{bridge: } CHNO_2) \longrightarrow C_6H_5CH{-}CHCOC_6H_5 \;(\text{bridge: } CHOH) \longrightarrow C_6H_5CH{=}C(COC_6H_5)CH_2OH,$$

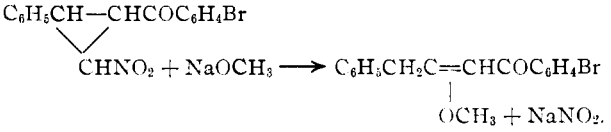
or $C_6H_5COCH{=}C(C_6H_5)CH_2OH$

[1] THIS JOURNAL, **41**, 1383 (1919).

[2] *J. prakt. Chem.*, **46**, 158 (1892).

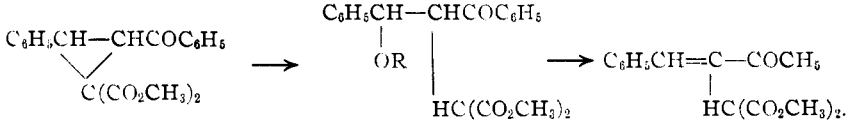
[3] *Zentr.*, **76**, [1] 1709 (1905).

Even if it were assumed that the benzoyl group in some way alters the mode of rearrangement it would still be impossible to account for the action of alcoholates upon the nitro compound. Cyclopropyl ethers ought to be at least as stable as cyclopropyl amines, but when these nitro compounds are treated with alcoholates they likewise yield only open chained compounds.[4]

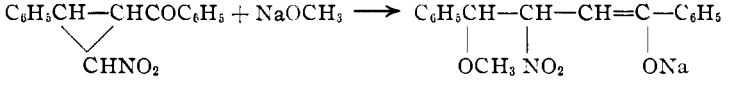


It seems certain, therefore, that the replacement of the nitro group is not the first step in the process.

Cyclopropane derivatives that are constituted like these nitro compounds but which have carboxyl in place of the nitro group are also exceedingly sensitive to alkalies. They behave like unsaturated compounds and it is always possible to account for the products obtained by assuming addition and subsequent elimination of water or alcohol:[5]



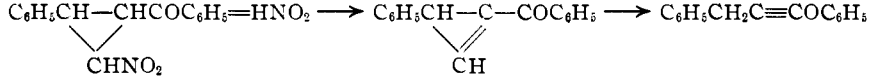
Meisenheimer[6] and Wieland[7] have shown that unsaturated as well as certain cyclic nitro compounds undergo remarkable transformations under the influence of alkalies. Like the reactions of the cyclopropane esters these generally start with the addition of alcoholates. It would not have been surprising, therefore, to find that these nitrocyclopropanes combine with alcoholates and thus form open chained compounds. It is quite certain, however, that if a compound which has both benzoyl and nitro groups were to combine with an alcoholate the metal would go to oxygen. In order to form the straight chain in both the diketone and the unsaturated methoxyl compound the ring must be opened between the phenyl and benzoyl groups. The addition of alcoholate would therefore have to take place as follows.



No plausible series of rearrangements of such an addition product could give the substances actually formed. The first step in the reaction is, therefore, not addition of the base.

[4] THIS JOURNAL, **41**, 1651 (1919).
[5] *Ibid.*, **39**, 1408 (1917).
[6] Meisenheimer, *Ann.*, **330**, 145 (1904).
[7] Wieland, *ibid.*, **424**, 102 (1921).

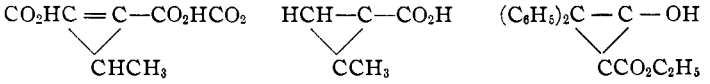
There remains the possibility that the first step in the process consists in the elimination of nitrous acid and that the resulting cyclopropene derivative immediately undergoes rearrangement to an acetylenic compound.



This mechanism would account admirably for the products that are obtained, because in the presence of alkalies acetylenic ketones readily combine with water to form β-diketones[8] and with alcohols to form unsaturated alkyloxy compounds.[9]

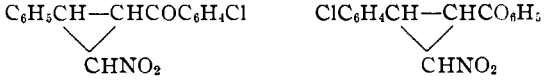
Nitrous acid is not one of the things that we commonly think of as being removed to form unsaturated compounds; but this may be due largely to our inadequate knowledge of aliphatic nitro compounds. In earlier papers[10] it was shown that some of these nitro compounds lose nitrous acid with great ease. The first assumption is, therefore, consistent with known facts.

There are few facts on which to base conclusions on the stability of cyclopropene derivatives. Only three such compounds have been described. By the action of alkalies on bromo-*iso*dehydro-acetic ester Feist[11] obtained a dibasic acid which in all probability is the cyclopropene di-acid (I). Addition of bromine to this acid and subsequent reduction gave a new acid which Feist regards as an isomer of the first and to which he ascribes Formula II. Quite recently Staudlinger[12] made a substance which he is inclined to represent by Formula III.



An examination of these formulas shows that none of these substances has the requisite number of hydrogen atoms to permit of rearrangement to an acetylenic compound. They therefore supply no useful evidence on the problem under consideration.

The following investigation was undertaken with a view to securing such evidence. Most of the experiments were performed with the two isomeric nitro cyclopropanes,



[8] Nef, *Ann.*, **308**, 276 (1899).

[9] Moureu and Brachin, *Ann. chim.*, **33**, 131 (1905).

[10] This Journal, **41**, 1383, 1651, 1703 (1919).

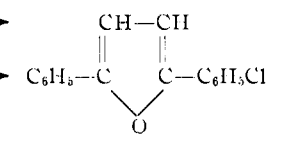
[11] Feist, *Ber.*, **26**, 750 (1893); **34**, 136 (1911).

[12] Staudinger, *Helvetica Chim. Acta*, **4**, 5 (1921).

These substances were easily made in accordance with the general scheme of adding nitromethane to unsaturated ketones, brominating the product, and eliminating hydrogen bromide from the resulting α-bromo-γ-nitro ketones. That they are isomeric cyclopropane derivatives is shown by the fact that they combine with hydrogen bromide to form isomeric addition products which lose nitrous and hydrobromic acids and yield the same furane derivative.

I. $C_6H_5CH(CHNO_2)CHCOC_6H_4Cl + HBr = C_6H_5CHBr\ CHNO_2CH_2COC_6H_4Cl$

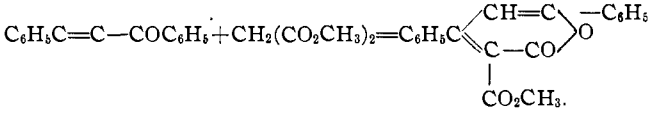
II. $ClC_6H_4CH(CHNO_2)CHCOC_6H_5 + HBr = ClC_6H_4CHBrCHNO_2CH_2COC_6H_5$

III. $C_6H_5CHBrCHNO_2CH_2COC_6H_4Cl \longrightarrow$  $+ HBr + HNO_2$

$ClC_6H_4ClHBrCHNO_2CH_2COC_6H_5 \longrightarrow$

By loading the phenyl groups with chlorine atoms we hoped to diminish the solubility sufficiently to enable us to isolate intermediate cyclopropene derivatives. This was not realized; these compounds react less readily with alkalies than those described in earlier papers and the reactions are correspondingly more confused. We therefore turned our attention to the next stage, the acetylenic ketones. These likewise could not be isolated, but we secured very definite evidences of their presence in the alkaline liquids.

In a recent paper [13] it was shown that in the presence of alkalies malonic esters rapidly combine with acetylenic ketones and form sparingly soluble α-pyrone derivatives which have very characteristic properties.



We have found, now, that similar pyrone esters are formed when nitrocyclopropane derivatives are treated with alkali in the presence of malonic ester. In order to get these pyrone esters it is necessary to add the malonic ester before the alkali; not a trace of the substances is obtained if the reagents are applied in the reverse order. This shows that they are formed from an intermediate compound which rapidly disappears in the alkaline medium. We regard this as a proof that acetylenic ketones play a part in the reaction and it seems almost equally certain that cyclopropene derivatives which have the requisite number of hydrogen atoms readily undergo rearrangement to isomeric acetylenic compounds.

[13] THIS JOURNAL, **44**, 379 (1921).

The study of the action of alkalies on the nitro cyclopropanes has led to the discovery that alcoholic ammonia rapidly transforms these substances into isomeric compounds. These are stereo-isomers, for boiling alcoholic potassium acetate converts either isomer into a mixture of the two, and whenever both substances enter into the same reaction they give the same products. The isomers, however are remarkably different in activity. The lower-melting derivatives that are obtained by eliminating hydrogen bromide from bromo ketones are unsaturated compounds. They combine with hydrogen and with hydrogen bromide as readily and in the same manner as would the corresponding ethylenic ketones. The higher-melting isomers show none of this unsaturation. The activity of cyclopropane derivatives, therefore, depends to an extraordinary degree upon the space relations of the substituting groups.

Experimental Part

β-Phenyl-γ-nitro-*p*-chloro-butyrophenone, $C_6H_5CHCH_2COC_6H_4Cl$ (with CH_2NO_2).—Sodium nitromethane combines readily with benzal-*p*-chloro-acetophenone when a thin paste of the sodium compound in dry methyl alcohol is added to a suspension of the ketone in the same solvent and the mixture is heated to the boiling point. The nitro ketone itself is obtained by acidifying the cold, clear, amber colored solution. This must be done with great caution, for, if the acid is added too rapidly, the precipitate is an oil from which it is almost impossible to obtain any solid ketone. The yield, about 70%, is better with small than with large quantities.

The ketone crystallizes from methyl alcohol in white needles that melt at 80°.

Analysis. Calc. for $C_{16}H_{14}O_3NCl$: C, 63.2; H, 4.6. Found: C, 63.8; H, 4.6.

β-Phenyl-γ-nitro-α-bromo-*p*-chloro-butyrophenone, $C_6H_5CHCHBrCOC_6H_4Cl$ (with CH_2NO_2).—The bromination of the ketone was carried out in chloroform. The reaction is sluggish and unless the ketone is very pure it is best to start it with a drop of acetone. It results in a mixture of isomeric bromine compounds, only one of which was isolated in pure form. This crystallized in thin white needles and melted at 88–89°. An analysis of the washed and dried mixture showed that it was composed mainly of isomeric compounds.

Analysis. Calc. for $C_{16}H_{13}O_3NClBr$: C, 50.2; H, 3.4. Found: C, 49.4; H 3.8.

1-[*p*-chloro-benzoyl]-2-phenyl-3-nitro cyclopropane, $C_6H_5CHCHCOC_6H_4Cl$ (with $CHNO_2$).—The cyclopropane ring was closed by eliminating hydrogen bromide from the bromo compound with potassium acetate in the usual manner. The yield from pure bromine compound is about 65%. It is not necessary, however, to use pure bromo ketone for making the cyclopropane derivative. Indeed, we seldom isolated any of the intermediates between the unsaturated ketone and the cyclopropane derivative. Generally our procedure was as follows. The crude nitro ketone that was precipitated on acidifying the condensation product was thoroughly washed with water and a little methyl alcohol, then immediately dissolved in chloroform. The chloroform solution was dried

with calcium chloride, warmed and treated with bromine in slight excess. Solvent and excess of bromine were then evaporated. The residue, a thick, orange colored oil, was dissolved in methyl alcohol and treated with potassium acetate in the usual manner.

The cyclopropane derivative was purified by crystallization from methyl alcohol; it separates in needles and melts at 121°.

Analysis. Calc. for $C_{16}H_{12}O_3NCl$: C, 63.7; H, 4.0. Found: C, 63.7: H, 4.5.

ISOMERIC CYCLOPROPANE DERIVATIVE.—The product obtained by the action of potassium acetate on the bromo ketone always melts at 120°, but it can be converted into an isomer by treatment with ammonia, weak bases, or even a boiling solution of potassium acetate. The most effective of these agents is ammonia. Ten g. of the finely powdered substance was suspended in 20 cc. of dry methyl alcohol which had been saturated with ammonia at 0°. The mixture was allowed to warm and stand in a stoppered flask overnight, when the solid was filtered and recrystallized from methyl alcohol. This gave 7.5 g. of a product that crystallized in flat needles and melted at 144°.

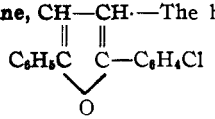
Analysis. Calc. for $C_{16}H_{12}O_3NCl$: C, 63.7; H, 4.0. Found: C, 63.9; H, 4.1.

When the transformation is incomplete, either because less concentrated ammonia is employed or because the process is stopped too soon the product melts not quite sharply at 103–106°. The same product is obtained when the lower-melting cyclopropane derivative is digested with dilute alkalies or when either of the cyclopropane derivatives is boiled with a solution of potassium acetate. It ultimately proved to be a mixture which, owing to the solubility relations, it is extremely difficult to separate. It can, however, be separated by dissolving it in a large volume of boiling ethyl alcohol, carefully avoiding contamination while this solution is cooling and then inoculating it, first with the high-melting, and then with the low-melting component.

β-Nitro-γ-bromo-γ-phenyl-*p*-chloro-butyrophenone, $C_6H_5CHBrCHNO_2CH_2COC_6H_4Cl$.—The low-melting cyclopropane derivative combines with hydrogen bromide very readily, while the high-melting one combines with it only with great difficulty, if at all. A solution of 2 g. of the lower-melting isomer in 25 cc. of glacial acetic was cooled to 0° and saturated with hydrogen bromide. The solution was cooled in a freezing mixture and allowed to stand for an hour during which a colorless solid separated in granular form. This was purified by dissolving it in a little cold-chloroform and filtering the solution into twice its volume of methyl alcohol. It crystallizes in plates which turn green and begin to soften at about 105°, and melt with effervescence at about 128°.

Analysis. Calc. for $C_{16}H_{13}O_3NClBr$: C, 50.2; H, 3.4. Found: C, 49.8; H, 3.4.

When the higher-melting isomer was treated in the same way it was recovered unchanged even after the solution had stood overnight. After more protracted action at the ordinary temperature some of it had disappeared but the product was oily and it was impossible to determine the nature of the process that had taken place.

1-Phenyl-4-(*p*-chlorophenyl)-furane,  —The hydrogen bromide addition product to the cyclopropane derivative loses both hydrobromic and nitric acids with the greatest ease, and passes into a furane derivative. This may be made by maintaining the bromo compound above the melting point until effervescence ceases; but it is easier to obtain it by boiling an alcoholic solution of the same compound for

several hours. The furane derivative separates from this solution in pale yellow flakes which melt at 123°.

Analysis. Calc. for $C_{16}H_{11}OCl$: C, 75.4; H, 4.4. Found: C, 75.6; H, 4.5.

ACTION OF ALKALIES ON THE CYCLOPROPANE DERIVATIVE.—The nitrocyclopropane derivative seems to be incapable of forming a metallic derivative. Cold conc. aqueous potassium hydroxide has no effect on it whatsoever. Dil. alcoholic potassium hydroxide and conc. alcoholic ammonia merely turn the lower into the higher melting isomer. This may take place through a metallic derivative but there is no evidence that such is the case. Cold conc. alcoholic potassium hydroxide and cold alcoholic sodium methylate attack both isomers, and the solutions turn slightly yellow in color; but nitrites begin to separate at once and it is impossible to secure any evidence that metallic derivatives are formed.

Phenacetyl-*p*-chloro-acetophenone, $C_6H_5CH_2COCH_2COC_6H_4Cl$.—This is the sole organic compound that could be isolated from the product of the action of conc. alkalies upon either of the isomeric nitrocyclopropanes. It is most easily obtained by treating the lower-melting isomer with sodium methylate. Ten g. of this substance was added to a solution of 10 g. of sodium in dry methyl alcohol, the mixture heated until the solution was clear, allowed to stand for an hour during which sodium nitrite separated, and then cooled in a freezing mixture and poured into iced hydrochloric acid. The resulting mixture was extracted with ether and the ethereal solution repeatedly shaken with small quantities of copper acetate solution. It gave about 4 g. of a light gray copper compound, which melted with decomposition at 218–220°.

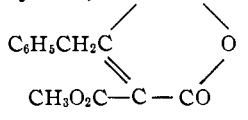
The copper compound was decomposed with dil. acid, and the resulting diketone recrystallized from methyl alcohol. It crystallized in plates and melted at 78°.

Analysis. Calc. for $C_{16}H_{15}O_2Cl$: C, 70.4; H, 4.8. Found: C, 70.5; H, 5.1.

The structure of the diketone was established by synthesis from ethyl phenylacetate and *p*-chloro-acetophenone, in accordance with the general procedure recommended by Bulow Grotowski.[14] This gave the same substance with a yield of about 40%.

With a view to stopping the reaction at an earlier stage the two nitrocyclopropanes were boiled with potassium acetate in methyl alcohol. This had no effect whatsoever on the higher melting substance and merely transformed the lower into the higher melting isomer.

Methyl-3-benzyl-5-[*p*-chlorophenyl]-pyrone carboxylate-2,



—The pyrone ester was formed when either of the isomeric nitrocyclo propanes was warmed with a methyl alcoholic solution of the sodium derivative of dimethyl malonate. Thus 11 g. of the finely powdered cyclopropane derivative was added to a solution obtained by dissolving 1.6 g. of sodium and 9 g. of dimethyl malonate in 70 cc. of dry methyl alcohol. There was no evidence of action in the cold, but when the solution was warmed for a few minutes it suddenly turned blood-red in color, the temperature rose to the boiling point, and the solid cyclopropane derivative rapidly disappeared. A part of the product crystallized when the blood-red solution was cooled in a freezing mixture; the rest was precipitated by acidifying the solution with glacial acetic acid. The solid was purified by dissolving it in boiling chloroform and pouring this solution into twice its volume of boiling methyl alcohol.

[14] Grotowski, *Ber.*, **34**, 1483 (1901).

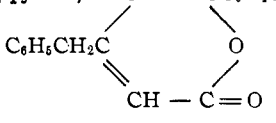
Analysis. Calc. for $C_{20}H_{15}O_4Cl$: C, 67.7; H, 4.3. Found: C, 68.0; H, 4.4.

The pyrone derivative crystallizes in long colorless needles which have a beautiful sky-blue fluorescence and melt at 171°. It is very sparingly soluble in alcohol and in ether, moderately soluble in acetone, readily soluble in boiling chloroform and in benzene. The yield was small, about 20%. It was not increased either by varying the relative amounts of ester and alcoholate, or by changing the concentration of the alcoholic solution.

THE PYRONE ACID.—It was shown in a recent paper that α-pyrone esters that have an ester group in the 3-position can be distinguished from their isomers by their behavior towards alkalies; they can be hydrolyzed to the corresponding acid. The pyrone in question is hydrolyzed with difficulty, but a fair yield of the acid was obtained by proceeding as follows. A solution of sodium methylate was prepared by dissolving 0.7 g. of sodium in 20 cc. of methyl alcohol to which 0.5 cc. of water had been added. This was dropped into a boiling solution of 3.5 g. of the ester in benzene. As long as any ester remained in the benzene layer each addition of alkali produced a blood-red color which rapidly faded to yellow. The mixture was poured into water and the stronger alkaline aqueous layer acidified with hydrochloric acid. This precipitated a mixture of solid and oily acids which was dissolved in ether, and ultimately separated into a yellow acid which melted with decomposition at 155–157°, and a colorless acid which melts with effervescence at about 147°.

The yellow pyrone acid crystallizes from alcohol in thick prisms. It is sparingly soluble in ether, but readily soluble in alcohol.

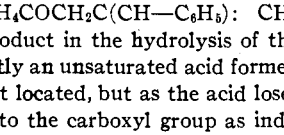
Analysis. Calc. for $C_{19}H_{13}O_4Cl$: C, 67.0; H, 3.8. Found: C, 66.5; H, 3.8.

4-Benzyl-6-[*p*-chlorophenyl]-pyrone,  —The pyrone acid was heated in a metal bath to 165–170° until evolution of gas ceased. The residue, which solidified on cooling, was recrystallized from methyl alcohol. It separated in pale yellow plates which melted at 167–168°; it did not reduce permanganate, and was insoluble in concentrated aqueous alkali.

Analysis. Calc. for $C_{18}H_{13}O_2Cl$: C, 72.8; H, 4.4. Found: C, 72.5; H, 4.6.

β-Benzyl-γ-(*p*-chlorobenzoyl)-crotonic acid, $ClC_6H_4COCH_2C(CH{-}C_6H_5){:}CH\text{-}CO_2H$.—The colorless acid which is obtained as a by-product in the hydrolysis of the pyrone ester readily reduces permanganate. It is evidently an unsaturated acid formed by opening the pyrone ring. The double linkage was not located, but as the acid loses carbon dioxide at the melting point it is probably next to the carboxyl group as indicated.

Analysis. Calc. for $C_{18}H_{15}O_3Cl$: C, 68.7; H, 4.8. Found: C, 68.8; H, 4.8.

1-Hydroxy-2-carboxyethyl-3-benzyl-5-(*p*-chlorophenyl)-pyridine, 

A suspension of 5.6 g. of the pyrone ester in 50 cc. of a saturated solution of ammonia in dry methyl alcohol was shaken overnight. The liquid was then pale yellow in color and it held a small quantity of a fine powder in suspension. This was removed by filtration and the filtrate allowed to evaporate slowly in the air. It deposited a mass of fluffy needles which were recrystallized from a mixture of chloro-

form and methyl alcohol. The substance melted fairly sharply but on analysis it gave results that were persistently high, for both carbon and hydrogen. An examination of the alcohol obtained by hydrolyzing it showed that at some stage one of the substances had come in contact with ethyl alcohol and that the methoxyl group had been replaced by ethoxyl. The ester melts at 210°.

Analysis. Calc. for $C_{21}H_{18}O_3NCl$: C, 68.6; H, 4.91. Found: C, 68.4; H, 9.4.

β-[*p*-Chlorophenyl]-γ-nitrobutyrophenone, $ClC_6H_4CHCH_2COC_6H_5$ (with CH_2NO_2).—An excellent yield of this nitro ketone was obtained by condensing nitromethane with *p*-chlorobenzal-acetophenone in the usual way. It crystallizes from methyl alcohol in needles and melts at 96°.

Analysis. Calc. for $C_{16}H_{14}O_3NCl$: C, 63.2; H, 4.6. Found: C, 62.8; H, 4.2.

α-Bromo-β-[*p*-chlorophenyl]-γ-nitro-butyrophenone, $Cl_6C_6H_4CH\ CHBrCOC_6H_5$ (with CH_2NO_2).—Bromination of the nitro ketone gave a mixture of two stereo-isomeric bromine derivatives. One of these, the principal product, was isolated in pure condition. It crystallized in white needles melting at 116°.

Analysis. Calc. for $C_{16}H_{13}O_3NClBr$: C, 50.2; H, 3.4. Found: C, 50.1; H, 3.4.

1-Benzoyl-2-[*p*-chlorophenyl]-3-nitrocyclopropane, $ClC_6H_5CH—CHCOC_6H_5$ (with $CHNO_2$).—The yield of cyclopropane derivative obtained by eliminating hydrogen bromide from the bromo compound with potassium acetate was extremely poor, about 20%, but all efforts to improve it failed. The substance crystallizes with alcohol of crystallization. Immediately after removal from the solution it melts sharply at 59°, but on exposure to the air it soon becomes sticky. In this form it loses alcohol very slowly, but in the course of 2 or 3 weeks, during which it resolidifies, its weight becomes constant, and it then melts at 66–67°.

Analysis. Calc. for $C_{16}H_{12}O_3NCl$: C, 63.7. H, 4.0. Found: C, 63.1; H, 4.3.

ISOMERIZATION.—Like all the other nitrocyclopropane derivatives of this series, this one is very readily changed into a higher-melting less active steroisomer. This is most conveniently accomplished by allowing the finely powdered solid to remain in contact with a saturated solution in alcohol. Under the most favorable conditions this gives a product which melts at 157–159°.

Analyses. Calc. for $C_{16}H_{12}O_3NCl$: C, 63.7; H, 4.0; N, 4.6. Found: C, 63.6; H, 4.1; N, 4.9.

Under less favorable conditions the action of ammonia gives a product that melts at 110–112°. This has the same composition as the former and is in all probability composed of mixed crystals similar to those described in an earlier part of this paper.

Analyses. Calc. for $C_{16}H_{12}O_3NCl$: C, 63.7; H, 4.0; Cl, 11.4. Found: C, 63.8; H, 4.1; Cl, 11.2.

β-Nitro-γ-bromo-γ-(*p*-chlorophenyl)-butyrophenone, $ClC_6H_4CHBrCHNO_2CH_2COC_6H_5$.—Twenty g. of the cyclopropane derivatives melting at 67° was dissolved in 50 cc. of glacial acetic acid, and the solution was cooled, saturated with hydrogen bromide and allowed to stand. As no solid separated in the course of an hour, the mixture was poured into cracked ice and the oily precipitate extracted with ether. The dried ethereal solution on evaporation deposited 10 g. of a crystalline solid which, after recrystallization from ether-alcohol, melted with effervescence at 112–114°.

Analysis. Calc. for $C_{16}H_{12}O_3NClBr$: C, 50.2; H, 3.4. Found: C, 49.8; H, 3.6.

The high-melting cyclopropane derivative does not combine with hydrogen bromide; it was recovered unchanged even after the solution in glacial acetic acid was saturated with hydrogen bromide at zero and allowed to stand at the ordinary temperature overnight.

β-Nitro-γ-hydroxy-γ-(*p*-chlorophenyl)-butyrophenone, $ClC_6H_4CHOHCHNO_2CH_2COC_6H_5$.—The hydrogen bromide addition product very easily loses both nitrous and hydrobromic acids and passes into the same furane that was described earlier in the paper. By very cautious treatment with silver acetate, however, it is possible to replace the bromine with hydroxyl. For this purpose an alcoholic solution of 5 g. of the addition product and 2.1 g. of silver acetate was gently warmed and persistently shaken for an hour. The silver bromide was then removed and the filtrate cooled in ice water. It deposited a crystalline solid which was purified from alcohol from which it separated in needles melting at 142°.

Analysis. Calc. for $C_{16}H_{14}O_4NCl$: C, 60.4; H, 4.4. Found: C, 60.5; H, 4.4.

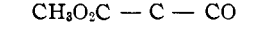
The hydroxyl compound reduces permanganate. When treated with alkalies it loses water and nitrous acid and forms the same furane that is obtained by heating the bromine compound.

α,γ-Dibromo-β-nitro-γ-(*p*-chlorophenyl)-butyrophenone, $ClC_6H_4CHBrCHNO_2CHBrCOC_6H_5$.—The hydrobromic acid addition product is very easily brominated. The product crystallizes in plates and melts at 143°. The substance was made for the purpose of determining which of the two stereo-isomeric bromine compounds would be obtained when bromine was eliminated, but all attempts to remove the bromine and leave the rest of the molecule intact were unsuccessful.

Analysis. Calc. for $C_{16}H_{12}O_3NClBr_2$: C, 41.6; H, 2.6. Found: C, 41.2; H, 2.7.

***p*-Chloro-phenacetyl-acetophenone,** $ClC_6H_4CH_2COCH_2COC_6H_5$.—The behavior of the nitrocyclopropane towards alkalies is exactly like that of the isomer described earlier in the paper. The product of the action of sodium methylate is a diketone which melts at 52–54° and forms a gray-green copper derivative that melts with decomposition at 229–230°.

Analysis. Calc. for $C_{16}H_{13}O_2Cl$: C, 70.4; H, 4.8. Found: C, 70.0; H, 4.8.

Methyl-4-(*p*-chlorophenyl)-pyrone-carboxylate-3,  .—Nine g. of the

finely powdered cyclopropane derivative was added in small portions to a solution of 1.4 g. of sodium and 9 g. of dimethyl malonate in 50 cc. of dry methyl alcohol. The nitro compound dissolved rapidly in the cold and the solution assumed the characteristic blood-red color. It was cooled in a freezing mixture and acidified with 4 g. of glacial acetic acid. The solid that separated was recrystallized from methyl alcohol which deposited it in long silky needles that showed the blue fluorescence characteristic of these pyrone esters.

Analysis. Calc. for $C_{20}H_{15}O_4Cl$: C, 67.7; H, 4.3. Found: C, 67.2; H, 4.6.

Summary

1. The elimination of hydrogen bromide from α-bromo-γ-nitro ketones results in the formation of nitrocyclopropane derivatives which com-

bine with hydrogen bromide as readily as do ethylenic ketones, and the mode of addition is the same in both cases.

2. Ammonia transforms these substances into stereo-isomers which do not combine with hydrogen bromide

3. Although these cyclopropane derivatives are constituted like secondary nitro compounds they do not form metallic derivatives.

4. Concentrated alkalies remove nitrous acid from the nitrocyclopropanes and transform them into diketones. The probable steps in this process are: first, elimination of nitrous acid; second, rearrangement of the resulting cyclopropane to an acetylenic ketone; third, addition of water to the ketone.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

SESQUI-MUSTARD GAS OR BIS-β-CHLORO-ETHYL ETHER OF ETHYLENE DITHIO-GLYCOL

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In view of the remarkable properties shown by ββ′-dichloro-ethyl sulfide, it seemed of interest to prepare a compound of the same type but having 2 sulfur atoms separated by an ethylene group, $ClCH_2CH_2SCH_2$-$CH_2SCH_2CH_2Cl$, with a view to comparing the chemical and physiological properties with those of the monosulfur compound.

Two ways of preparing the corresponding dihydroxy compound were studied; (1) the reaction of the sodium salt of monothio-glycol on ethylene bromide and (2) of ethylene chlorohydrin on the sodium salt of ethylene dithio-glycol.

Preparation of Monothio-ethylene Glycol, $HSCH_2CH_2OH$.—Our work with this compound was done before the paper of Bennett[1] came to hand, but our conclusions agree well with his, though our yields were not so good. We, too, had great difficulty in repeating the work of Carius.[2] In a number of experiments, in which his directions were followed as closely as possible, we obtained only insignificant yields.

The best method we found to be as follows.

Two hundred and forty g. of crystallized sodium sulfide is melted on the water-bath and saturated with hydrogen sulfide; 150 g. of alcohol is added and the mixture resaturated. To this solution, which is kept below 20°, 120 g. ethylene chlorohydrin is added slowly. This material is allowed to stand for 36 hours at room temperature. Then hydrogen chloride is passed in until the mixture is acid, and the sodium chloride filtered off. The filtrate is fractionated under reduced pressure. The yield was 26 to

[1] Bennett, *J. Chem. Soc.*, **120**, 422 (1921).

[2] Carius, *Ann.*, **124**, 257 (1862).