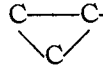
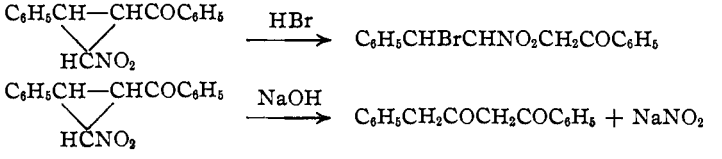
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

STUDIES IN THE CYCLOPROPANE SERIES. XI. CYCLOPROPANE DERIVATIVES WITH A TERTIARY NITRO GROUP ATTACHED TO THE RING

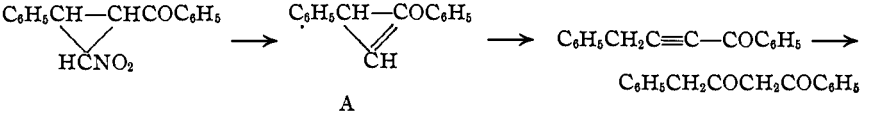
BY E. P. KOHLER AND PAUL ALLEN, JR.

RECEIVED DECEMBER 1, 1927 PUBLISHED MARCH 7, 1928

In earlier papers dealing with the characteristics of the unsaturated system  , it was shown that most of the compounds containing this complex behave essentially like those containing the conjugated system C=C—C=O. The only notable exception to this rule occurs in the case of those nitrocyclopropane derivatives in which a nitro group is attached to the ring. Even these combine with acids in a normal manner, but the products formed by bases do not appear to be the result of a process that starts with addition.[1]



The evidence accumulated by a study of a number of such nitrocyclopropane derivatives[2] led to the conclusion that the first step in the reaction with bases is elimination of nitrous acid, and that the final product of the reaction is due to the instability of the resulting cyclopropene derivative. The probable mechanism of the reaction was, therefore, represented as follows



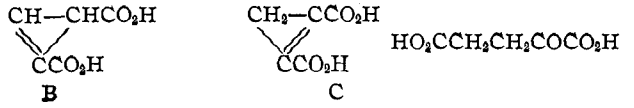
A

This mechanism is in complete accord with the general experience that bases tend to transform unsaturated compounds into more acidic forms. At the time it was proposed it was also consistent with all that was known about the behavior of cyclopropene derivatives, because the few that had been studied are so constituted that they are incapable of rearrangement into acetylenic compounds. Since then, however, Farmer and Ingold[3] have made cyclopropene dicarbonic acid—B or C—and have found that boiling alkalies transform it into α-ketoglutaric acid.

[1] Kohler and Engelbrecht, THIS JOURNAL, 41, 1379 (1919).

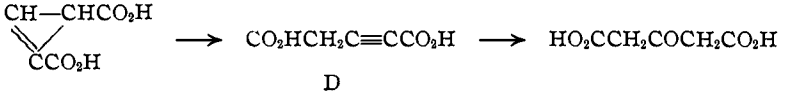
[2] (a) Kohler and Williams, *ibid.*, 41, 1644 (1919); (b) Kohler and Srinivasa Rao, *ibid.*, 41, 1697 (1919); (c) Kohler and Smith, *ibid.*, 44, 624 (1922).

[3] Farmer and Ingold, *J. Chem. Soc.*, 119, 2015 (1921).



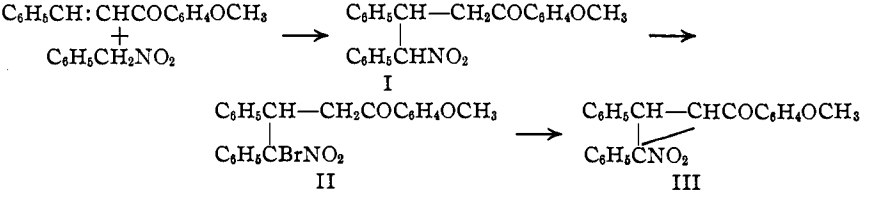
B C

In accordance with the mechanism proposed for the nitro compounds, this cyclopropene acid could undergo rearrangement to an acetylenic derivative, but this would of necessity be the acid D which he expected to give acetone dicarbonic acid in place of the ketoglutaric acid that was actually obtained.



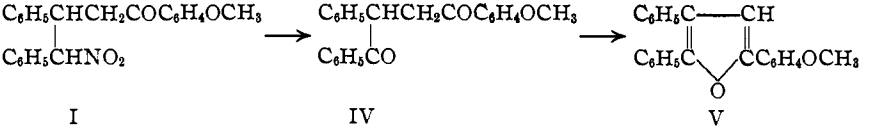
D

Even though these new facts are not necessarily inconsistent with the proposed mechanism—because the cyclopropene acid has possibilities of conjugation that are lacking in A—it nevertheless seemed advisable to test this mechanism further by studying the action of bases on a nitro-cyclopropane derivative so constituted that it might lose nitrous acid but could not form an acetylenic compound. To this end we undertook the preparation of 1-nitro-1,2-diphenyl-3-anisoyl cylopropane by the following steps



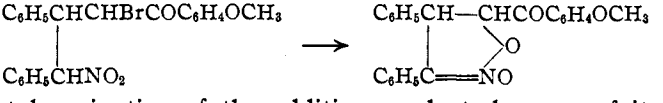
I II III

The addition of phenylnitromethane to the unsaturated ketone was accomplished with comparative ease, and the structure of the addition product was established by hydrolysis to a diketone which was readily condensed to a furane derivative—a characteristic property of γ-diketones.



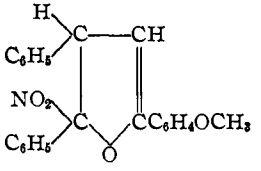
I IV V

Direct bromination of the addition product yielded two isomeric α-bromo derivatives which proved to be useless for our purpose because, unlike the corresponding derivatives of the nitromethane addition product, they formed only isoxazoline oxides when treated with reagents capable of eliminating hydrogen bromide.



Indirect bromination of the addition product, by way of its sodium salt, gave the γ-bromo derivative II. This served our purpose, but the

elimination of hydrogen bromide was troublesome. Even under the most favorable conditions—prolonged digestion with methyl alcoholic potassium acetate—it resulted in a mixture containing the addition product I, the diketone IV, variable quantities of uncrystallizable oils and two substances formed by elimination of hydrogen bromide. By derivation these two substances might be dihydrofurane derivatives, ethylenic compounds or the desired cyclopropane derivatives; but since neither of them forms an ozonide, they must be two of the four possible stereoisomeric cyclopropane derivatives represented by III.



$C_6H_5CCH_2COC_6H_4OCH_3$
$C_6H_5CNO_2$

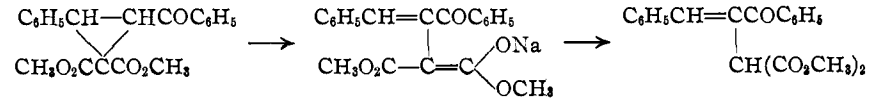
$C_6H_5C{=}CHCOC_6H_4OCH_3$
$C_6H_5CHNO_2$

$C_6H_5CH{-}CHCOC_6H_4OCH_3$
$C_6H_5CNO_2$
III

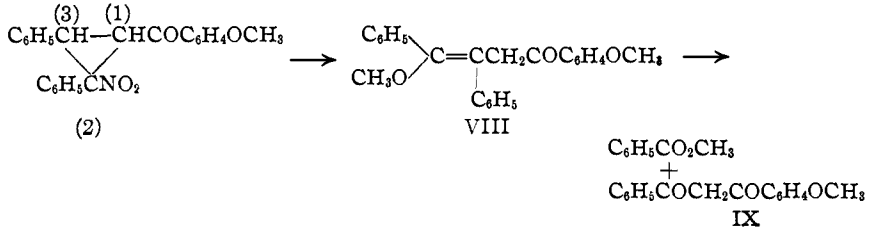
These cyclopropane derivatives react very readily with strong bases, and, fortunately, in view of the difficulty of securing the materials, the reactions are quite definite. Cold concentrated sodium methylate converts the higher-melting isomer quantitatively into a sodium compound that crystallizes in thick, yellow needles. This sodium compound, when acidified with due caution, yields two colorless products, of which one regenerates the same sodium compound when it is treated with sodium methylate, while the other forms a sodium compound that crystallizes in yellow prisms. The two colorless products are isomeric with each other as well as with the cyclopropane derivative from which they are formed. Each of them reduces permanganate and each also forms an ozonide which, when decomposed with water, yields benzaldehyde as one of the products. These substances are, therefore, stereoisomeric ethylenic compounds formed by opening the cyclopropane ring without eliminating the nitro group

$C_6H_5CH{-}CHCOC_6H_4OCH_3 \longrightarrow C_6H_5CH{=}CCOC_6H_4OCH_3 \longrightarrow C_6H_5CH{=}CCOC_6H_4OCH_3$
$C_6H_5CNO_2$ $C_6H_5C{=}NO.ONa$ $C_6H_5CHNO_2$
III VI VII

Evidently the mechanism of the reaction between bases and this tertiary nitro compound is totally different from that of the corresponding reaction with cyclopropane derivatives containing a secondary nitro group; the ring is opened at a different point and the product is a nitro compound which is stable toward bases. Indeed the behavior of this cyclopropane derivative is precisely the same as that of the dicarboxylic esters described and discussed in the first paper of this series.



The lower-melting cyclopropane derivative dissolves rapidly in sodium methylate without producing more than a trace of color and the solution promptly begins to deposit a colorless solid which contains neither nitrogen nor sodium. This product does not reduce permanganate but it combines with ozone, and when the resulting ozonide is decomposed with water it yields methyl benzoate and benzoyl-anisoyl-methane



As not infrequently happens in studies of the mechanism of reactions, these results start more problems than they solve. Inasmuch as they show that β-diketones are not formed from those cyclopropane derivatives which are incapable of yielding acetylenic ketones, they bring a measure of support to the mechanism under investigation; but since we failed to secure any indication of the intermediate formation of cyclopropene derivatives, the evidence in favor of that mechanism is still far from conclusive.

A comparison of the products obtained from the two stereoisomers shows that the action of alkalies on nitrocyclopropane derivatives depends to a surprising degree upon their configuration. In order to obtain the ethylenic compound VII from the higher-melting isomer it is necessary to open the ring between carbon atoms (2) and (3); the ethylenic compound VIII from the lower-melting isomer cannot be formed by opening the ring at this point. From the behavior of unsaturated compounds containing conjugated systems it might be anticipated that these stereoisomers would neither add bases nor lose nitrous acid with the same ease, and that consequently the three-membered ring would be opened more readily in one of the isomers than in the other. But nothing in the chemistry of either cyclic or unsaturated compounds would lead to the expectation that in these stereoisomers the ring would be opened at different points by the same reagent.

Experimental Part

I. The Saturated Compounds

Phenylnitromethane cannot be added quite as easily or as completely to benzal acetyl anisole as to benzalacetophenone, mainly because the for-

mer is only moderately soluble in boiling methyl alcohol. For this reason it is best to prepare a small sample of the addition product by boiling a solution of equivalent quantities of ketone, nitro compound and sodium methylate in the requisite quantity of methyl alcohol. Once a sample is available for inoculation, it is possible to add in the presence of a much smaller proportion of the methylate and thereby increase the yield as well as simplify the isolation of the addition product. The procedure then is as follows.

To a solution of the unsaturated ketone in six times its weight of boiling, anhydrous, methyl alcohol are added in succession an equivalent quantity of the nitro compound and enough concentrated sodium methylate solution to produce decided alkalinity. The resulting mixture is boiled for half an hour, then inoculated with a sample of the addition product. This usually starts crystallization throughout the liquid but it is sometimes necessary to heat for a longer period before the mixture can be successfully inoculated. Even after crystallization has begun the mixture is kept boiling vigorously until it becomes so nearly solid as to render this impossible. It is then cooled and filtered. The solid is washed with boiling methyl alcohol until colorless. Filtrate and washings are combined, made decidedly alkaline with sodium methylate and slowly concentrated by distillation. In one operation 120 g. of ketonic and 70 g. of the nitro compound in 750 cc. of methyl alcohol gave, after two hours, 153 g. of almost pure addition product, and an additional 18 g. of somewhat less pure substance was obtained from the filtrate, making a total yield of 171 g. or 90%. Recrystallization from chloroform reduced this to 86%.

α-Anisoyl-β,γ-diphenyl-γ-nitro Propane, I.—The addition product is sparingly soluble in all common solvents except boiling glacial acetic acid. Relatively pure material is purified further by crystallization from chloroform, less pure material by crystallizing first from glacial acetic acid. The substance crystallizes in thin, feathery, white needles and melts at 164–165°.

Anal. Calcd. for $C_{23}H_{21}O_4N$: C, 73.6; H, 5.6. Found: C, 73.2; H, 5.6.

α-Anisoyl-β-phenyl-β-benzoyl Ethane, IV.—The addition product can be recrystallized from methyl alcoholic hydrochloric acid without loss, and it can also be dissolved in sodium methylate solution and, without loss, recovered by addition of acetic acid, but if the methylate is acidified with hydrochloric acid most of the substance is hydrolyzed to the diketone. This separates in well-formed, colorless prisms. It is readily soluble in chloroform, hot benzene and boiling methyl alcohol, sparingly soluble in ether, and it melts at 155–156°.

Anal. Calcd. for $C_{23}H_{20}O_3$: C, 80.2; H, 5.8. Found: C, 80.9; H, 5.9.

The **dioxime** was obtained by boiling the ketone for two and one-half hours with excess of hydroxylamine and potassium hydroxide in methyl alcohol. It crystallizes from aqueous methyl alcohol in colorless prisms melting at 180–181°.

Anal. Calcd. for $C_{23}H_{22}O_3N_2$: C, 73.8; H, 5.9. Found: C, 73.6; H, 6.1.

2,3-Diphenyl-5-(*p*-methoxyphenyl) Furane, V.—A solution of 1.4 g. of the finely powdered diketone in 25 cc. of cold concentrated sulfuric acid was left to itself for several hours, then poured onto cracked ice. In the course of an hour the deep red solution changed into a pasty solid which was purified by recrystallization from methyl alcohol. It separated in bunches of fine, white needles melting at 94–95°; yield, 75.5%.

Anal. Calcd. for $C_{23}H_{18}O_2$: C, 84.7; H, 5.5. Found: C, 84.6; H, 5.6.

α-Anisoyl-β,γ-diphenyl-γ-nitro-γ-bromo Propane, II.—A solution of 190 g. of the crude washed and dried addition product in the minimum quantity of 30% sodium

methylate solution was cleared by filtration, then cooled in ice water. The cooled solution was shaken vigorously while bromine was added drop by drop until the color was no longer discharged—about 90 g. The mixture was then stirred into water containing a little bisulfite. This dissolved the sodium bromide which separated during the reaction and precipitated the bromo compound as a pale yellow solid. After thorough washing and drying the bromo compound was recrystallized from chloroform and methyl alcohol. This gave 212 g. of pure product—a yield of 92%. The bromo compound is always contaminated with a small quantity of the dibromide of benzal acetyl anisole, which can be removed only by repeated recrystallization from methyl alcohol. It, therefore, generally melts at 135–139° while the perfectly pure substance melts at 140°. It crystallizes in colorless plates or tables.

Anal. Calcd. for $C_{28}H_{20}O_4NBr$: C, 60.8; H, 4.4. Found: C, 60.2; H, 4.5.

II. The Cyclopropane Derivatives

The preparation of the cyclopropane derivatives from the bromo compound is troublesome for various reasons. One is that the γ-bromo compound is easily reduced to the saturated nitro compound and this is gradually hydrolyzed to the diketone by potassium acetate and acetic acid. This difficulty can be avoided in part by using dilute solutions of strong bases but these more or less rapidly destroy the cyclopropane derivatives. We tried alcoholic sodium hydroxide, alcoholates, organic bases and solutions of potassium acetate in various alcohols. In the end we decided that methyl alcoholic potassium acetate was the most serviceable, hence only the results obtained with this reagent will be described. Our procedure was as follows.

A suspension of equal weights of powdered bromo compound and potassium acetate in 5 times their combined weight of methyl alcohol is boiled for twenty-four hours, then set aside for six to eight hours. The liquid soon turns yellow and all of the bromo compound usually is in solution after six to seven hours. The solution generally still contains some bromo compound after twenty-four hours but the yield of cyclopropane derivatives is less if the heating is more prolonged. On cooling, the clear solution gradually deposits a solid which is composed almost entirely of the higher-melting cyclopropane derivative and the reduction product, and which is separated without great difficulty by means of methyl alcohol. If the solution is set aside for a longer period it deposits also unchanged bromo compound, diketone, and at times, also, the lower-melting cyclopropane derivative—a mixture extremely difficult to separate.

The filtrate from the less soluble products is distilled until most of the methyl alcohol is gone, then poured into a large quantity of water, which precipitates a yellow oil or a pasty solid. Ether is added, the mixture is shaken vigorously for some time, then set aside for several hours. The resulting solid, when washed with ether until it is free from color, is composed almost entirely of the lower-melting cyclopropane derivative and the reduction product; it is separated without any great difficulty by recrystallization from methyl alcohol. When the ether-water mixture is allowed to stand for longer periods, the solid contains also unchanged bromo compound and diketone, and then is extremely difficult to separate. The ethereal layer contains unchanged bromo compound and all of the products, including a large quantity of yellow oil; its separation is unremunerative. In one experiment 90 g. of the bromo compound yielded 22 g. of the cyclopropane melting at 137°, 9 g. of the cyclopropane melting at 187°, 3.4 g. of the reduction product, 2.7 g. of diketone and 1.1 g. of unchanged bromo compound.

1-Anisoyl-2,3-diphenyl-2-nitro Cyclopropane, III.—The higher-melting isomer is sparingly soluble in ether, alcohol and acetone, readily soluble in chloroform and in ethyl bromide. It crystallizes in flattened needles and melts at 187°.

Anal. Calcd. for $C_{23}H_{19}O_4N$: C, 74.0; H, 5.1. Found: C, 73.5; H, 5.2.

Ozonization.—A rapid current of ozonized oxygen containing about 6% of ozone was passed for two hours through a solution of one gram of the substance in ethyl bromide. The solution assumed a pale yellow color but remained clear. It was poured into water, the mixture was boiled for a short time, then distilled with steam; the distillate contained only ethyl bromide. The residue in the flask—a solid contaminated with a little yellow oil—was filtered. After washing with ether, the solid proved to be 0.86 g. of unchanged substance. The ether contained a little oil which was doubtless due to some general oxidation because a similar oil was obtained whenever any of these anisyl derivatives was subjected to prolonged action of ozone.

Behavior toward Bases.—The cyclopropane derivative is not attacked by organic bases; it was recovered after it had been boiled for twenty minutes with pyridine, piperidine and methyl alcoholic piperidine. A solution in methyl alcoholic ammonia slowly assumed a pale yellow tint, but the solid that was recovered by evaporating both ammonia and solvent still melted at 185–187°. Methyl alcoholic sodium hydroxide and sodium methylate act readily in the cold but in order to ensure complete conversion it is safest to warm the substance with a solution of the methylate.

A suspension of 2 g. of the finely ground material in 15 cc. of 5% sodium methylate was warmed for a few minutes on a steam-bath until solution was complete, then allowed to cool. It deposited a sodium compound in fine, yellow needles. These were collected on a glass filter and thoroughly washed with anhydrous ether; yield, 2.05 g.

The sodium compound, suspended in 5 cc. of ether, was shaken with iced dilute hydrochloric acid until completely colorless. After washing with ether and drying the solid suspended in the ethereal layer, it melted at 140°; yield, 1.1 g. When entirely free from acid this solid can be recrystallized without serious loss by dissolving it rapidly in boiling methyl alcohol and cooling the solution at once. The melting point steadily falls if the crystallization is slow, and when the solutions contain a trace of acid they deposit an isomeric product.

Anal. Calcd. for $C_{23}H_{19}O_4N$: C, 74.0; H, 5.1. Found: C, 73.8; H, 5.2.

α-Benzal-α-anisoyl-β-phenyl-β-nitro Ethane, VII.—The rearrangement product crystallizes in small, thin needles. It is sparingly soluble in ether and in cold methyl alcohol, readily soluble in boiling alcohols. Its solution in cold concentrated sodium methylate deposits the yellow sodium compound in needles. Solutions in alcoholic sodium hydroxide gradually turn red and then smell of benzaldehyde.

Ozonization.—Ozonized oxygen containing about 6% of ozone was passed for half an hour through a solution of one gram of the substance in ethyl bromide. The ozonized solution was poured into water, the mixture warmed to remove the ethyl bromide, boiled for a few minutes, then distilled with steam. Drops of liquid which had the odor of benzaldehyde collected in the distillate. The presence of benzaldehyde was confirmed by adding semicarbazide and comparing the resulting semicarbazone with an authentic specimen.

The Isomeric Ethylene Derivative.—The ethereal solution from which the product melting at 140° had been removed gradually deposited another colorless product which had a lower melting point. After several recrystallizations from methyl alcohol this was obtained in the form of lustrous prisms which melted at 118°. The same substance was obtained also by repeated recrystallization of the higher-melting compound and by one crystallization from methyl alcohol containing a trace of acetic acid.

Anal. Calcd. for $C_{23}H_{19}O_4N$: C, 74.0; H, 5.1. Found: C, 74.2; H, 5.1.

The isomer is readily soluble in ether and methyl alcohol. Its solution in cold concentrated sodium methylate deposits a yellow sodium compound which crystallizes in stout prisms and which on acidification regenerates the lower-melting compound. This substance, when ozonized in the same manner as the preceding one, likewise gave benzaldehyde as one of the products. Since neither of these substances gives the reactions of isonitro compounds, they must be the geometrical isomers represented by formula VII.

The Lower-Melting Cyclopropane Derivative, III.—The lower-melting isomer is readily soluble in chloroform and in acetone, moderately soluble in boiling methyl alcohol, sparingly soluble in cold alcohol and ether. It crystallizes in thick needles or prisms and melts at 137°. Its behavior when ozonized in ethyl bromide was exactly the same as that of the higher melting isomer.

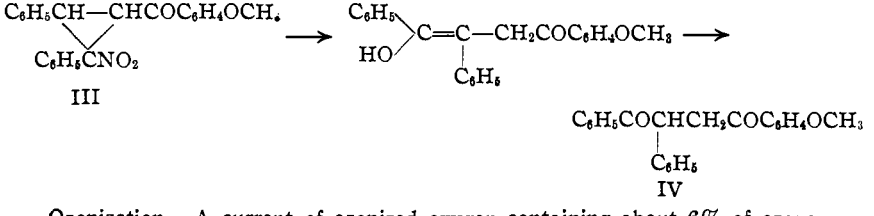
Anal. Calcd. for $C_{23}H_{19}O_4N$: C, 74.0; H, 5.1. Found: C, 73.8; H, 5.2.

Action of Bases.—The substance is altered by alcoholic ammonia, primary and secondary amines, alcoholic sodium hydroxide and alcoholates. All of these remove nitrous acid and open the cyclopropane ring but the nature of the organic product varies with the reagent and the solvent. In the presence of methyl alcohol one of the products is always a methoxyl compound. This can be obtained quantitatively by using a solution of sodium methylate in perfectly dry methyl alcohol.

A slightly warm 5% solution of sodium methylate was added, in 3 times the calculated quantity, to 3 g. of the finely powdered substance. This dissolved immediately and the very pale yellow solution soon deposited a crystalline solid. It was set aside for several hours, then filtered. The yield of washed and dried solid was 2.4 g. The diluted filtrate deposited 0.2 g. more of somewhat less pure material. The solid was recrystallized from methyl alcohol, from which it separated in long, thin needles melting at 144–145°.

Anal. Calcd. for $C_{24}H_{22}O_5$: C, 80.4; H, 6.0. Found: C, 80.1; H, 6.2.

β,γ-Diphenyl-γ-Methoxy Allyl Anisyl Ketone, VIII.—The unsaturated ketone is readily soluble in methyl alcohol, less soluble in ether. It is not altered by dilute solutions of bases but it is extremely sensitive to acids. None of it can be recovered from a solution in methyl alcohol containing a drop of acetic acid; the solution deposits only the diketone IV, and when dry hydrogen chloride is substituted for the acetic acid, the principal product is the furane V. The diketone IV also generally appears as one of the products of the reaction even when contact with acid is carefully avoided, but its origin then is different. Its formation is due to the presence of sodium hydroxide in the alcoholate, and hence it becomes the principal product when methyl alcoholic sodium hydroxide is substituted for the methylate.



III

IV

Ozonization.—A current of ozonized oxygen containing about 6% of ozone was passed for an hour through a solution of 2 g. of the methoxyl compound in ethyl bromide. The solution was poured into water, the mixture freed from ethyl bromide and distilled with steam. The distillate, which contained drops of an oil that had the odor of methyl benzoate, was extracted with ether, the extract freed from acid by extraction with sodium carbonate, then evaporated. Half of the residue when hydrolyzed gave pure benzoic acid; the remainder gave benzamide when warmed with alcoholic ammonia.

The residue left after the methyl benzoate had been distilled with steam was extracted with ether. The ethereal solution was freed from acid by extraction with bicarbonate, then shaken with saturated aqueous copper acetate. It deposited a greenish-yellow copper compound which on acidification turned into a pale yellow solid crystallizing in plates melting at 129°. As the yield of this product was only 0.11 g. it seemed wise to synthesize benzoyl anisoyl methane for comparison. This was readily accomplished by adding bromine to benzal acetyl anisole, boiling the dibromide with sodium alcoholate and digesting the resulting ethoxyl compound with acetic acid $C_6H_5CHBrCHBrCOC_6H_4OCH_3 \longrightarrow C_6H_5C(OC_2H_5)=CHCOC_6H_4OCH_3 \longrightarrow C_6H_5COCH_2COC_6H_4OCH_3$

Both the diketone obtained in this manner and a mixture of the synthetic and the ozonization product melted at 129°.

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.6; H, 5.5. Found: C, 75.5; H, 5.6.

The ethoxyl compound corresponding to the methoxyl compound VIII.—For the sake of comparison, the low-melting cyclopropane derivative was treated also with sodium ethylate. It dissolved just as readily but the product separated much more slowly. It was recrystallized from absolute ethyl alcohol from which it separated in colorless cubical prisms melting at 89–90°.

Anal. Calcd. for $C_{25}H_{24}O_3$: C, 80.6; H, 6.4. Found: C, 80.6; H, 6.5.

Summary

The paper contains:

1. A method for the preparation of cyclopropane derivatives in which a tertiary nitro group is attached to one of the carbon atoms of the ring.
2. An account of the behavior of cyclopropane derivatives of this type toward bases.

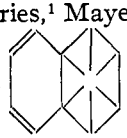
CAMBRIDGE 38, MASSACHUSETTS

[CONTRIBUTION FROM THE SPECTROGRAPHIC LABORATORY OF THE DEPARTMENT OF PHYSICS, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

THE RELATIONS BETWEEN SOME PHYSICAL PROPERTIES AND THE CONSTITUTION OF CERTAIN NAPHTHALENE DERIVATIVES

BY HENRY DE LASZLO

RECEIVED DECEMBER 1, 1927 PUBLISHED MARCH 7, 1928

The structural formula of naphthalene is a vexing problem that has called forth a number of suggestions, more especially in recent years. Harries,[1] Mayer and Bansa,[2] and others suggest an aromatic olefinic structure  . Willstätter[3] was inclined to support this view, but admitted later[4] that it is not necessarily right. On the other hand, v. Wein-

[1] Harries, *Ann.*, **343**, 337 (1905).
[2] Mayer and Bansa, *Ber.*, **54**, 19 (1921).
[3] Willstätter, *Ber.*, **44**, 3430 (1911).
[4] Willstätter, *Ber.*, **56**, 1407 (1923).