each case; while this vibration for 2,2,4,4-tetramethylaldol, where the neopentyl group is not part of a ring system, drops to 770 cm.$^{-1}$. These two neopentyl lines were extremely useful in following the formation of H in the mixtures of isobutyraldehyde and 2,2,4,4-tetramethylaldol.[3]

The Raman lines in the 1750 cm.$^{-1}$ region for the acetates are due, of course, to the vibrations of the ester carbonyl group. It is interesting to note the similarity of the spectra of these acetates to the spectra of the parent 6-hydroxy-1,3-dioxanes.

Experimental

Preparation of the 6-Acetoxy-1,3-dioxanes.—The parent aldehyde was aldolized as described previously,[3] and the ether separated from the dried reaction product at the water pump. Equal volumes of this crude 1,3-dioxane, anhydrous pyridine, and acetic anhydride were mixed, and the reaction mixture allowed to stand overnight at room temperature. The acetic acid, pyridine, and excess acetic anhydride were then distilled off and the product fractionated under reduced pressure.

Preparation of G.—To 300 g. of 1% anhydrous methyl alcoholic hydrochloric acid was added 60 g. of H. This reaction mixture was sealed up in a 500-cc. flask for eighteen days. At the end of this time the reaction mixture was neutralized, diluted with water, and the organic layer fractionated under reduced pressure. Nineteen grams of the methyl ether was obtained; for physical properties see Table I.

The Aldolization of 2,2,4,4-Tetramethylaldol.—The aldolization of 14.4 g. of 2,2,4,4-tetramethylaldol was performed by the method previously described.[3] The crude product was washed well with water, dried, and freed of ether at the water pump. Distillation of this material produced 8.7 g. of H, and 3.5 g. of a white solid remained in the distilling flask. This white solid after two recrystallizations from petroleum ether melted at 105–107° which is the melting point found for the paraldol of 2,2,4,4-tetramethylaldol after recrystallization from the same solvent. This paraldol does not melt sharply and has a different melting point (within a range of 15°) when recrystallized from different solvents. This is probably due to the presence of several isomeric forms.

The apparatus and experimental technique for obtaining the Raman spectra are the same as were used in previous work.[3] The compounds studied gave very weak spectra so that long exposures were necessary.

Summary

1. The acetates of 2,4-diethyl-5-methyl-6-hydroxy-1,3-dioxane and 2,4-dipropyl-5-ethyl-6-hydroxy-1,3-dioxane, and the acetate and methyl ether of 2,4-diisopropyl-5,5-dimethyl-6-hydroxy-1,3-dioxane have been prepared and characterized.

2. The Raman spectra of the above compounds, of 2,4-dipropyl-5-ethyl-6-hydroxy-1,3-dioxane, and of 2,4-dimethyl-6-acetoxy-1,3-dioxane are reported.

3. It has been shown that the main product from the aldolization of 2,2,4,4-tetramethylaldol is 2,4-diisopropyl-5,5-dimethyl-6-hydroxy-1,3-dioxane.

CHICAGO, ILL. RECEIVED OCTOBER 8, 1943

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

A Study of the Haloform Reaction

BY RICHARD T. ARNOLD, ROBERT BUCKLES[1] AND JANET STOLTENBERG

Except for halogen-containing intermediates,[2,3] no neutral compounds have been isolated as products from the haloform reaction. In order to establish the structure of the methyl ketone (I) obtained from 5-methoxytetralin by means of the Friedel–Crafts reaction, the substance was treated with an aqueous methanol hypochlorite solution. To our surprise there was obtained, in addition to the small amount of expected carboxylic acid (II), a considerable quantity of a neutral, halogen-free solid whose analysis and molecular weight indicated the formula $C_{13}H_{16}O_3$. An 83% yield of this same compound was obtained if hypobromite solutions were employed. The method of preparation and the constitution of the starting materials permit only two reaonable structures for this formula, namely, III and IV.

It was at first supposed that the neutral substance was the ketol (IV) formed by hydrolysis of the phenacyl chloride which is presumably the first intermediate in the haloform reaction.[2] That this supposition was incorrect was indicated by the stability of the substance toward potassium permanganate, lead tetraacetate and periodic acid. Furthermore, no methane was liberated in the Zerewitinoff test.

Proof of the ester structure III was established by saponification to the acid II and the reconversion of II into III by treatment with diazomethane.

It seems surprising that methyl esters have not been reported previously as products of the haloform reaction since the procedure employed above is a typical one. We now believe that in aqueous methanol solution methyl esters are always formed but are so readily hydrolyzed that their isolation is difficult. In the experiment reported here, the temperature of the reaction mixture was not permitted to rise and the insoluble methyl ester crystallized from the solution as it was formed.

When the haloform reaction was carried out in aqueous dioxane solution (to prevent ester formation), a chlorine-containing acid (V) was formed as the sole product. That this substance was not formed during the haloform reaction but in-

(1) du Pont Postdoctorate Fellow, 1942–1943.

(2) Fuson and Bull, *Chem. Rev.*, **15**, 275 (1934).

(3) Aston, Newkirk, Dorsky and Jenkins, THIS JOURNAL, **64**, 1413 (1942).

stead resulted from a rapid chlorination of the expected acid II (by excess hypochlorite) during the isolation process was shown in two ways. First, only compound II resulted if the excess hypochlorite were destroyed with acetone before acidification of the reaction mixture, and, second, an independent experiment proved that II was chlorinated (to give V) at an exceedingly rapid rate in acidic hypochlorite solutions.

Molecules having the $-\overset{O}{\overset{\|}{C}}-CCl_3$ group often react in a manner analogous to that of acid chlorides. The work of Houben and Fischer[4] indicates that trichloromethyl ketones react more rapidly with alcohols than with water in the presence of an alkaline catalyst. This difference in reaction

$$R-\overset{O}{\overset{\|}{C}}-CCl_3 + R'OH \longrightarrow R-\overset{O}{\overset{\|}{C}}-OR' + CHCl_3$$

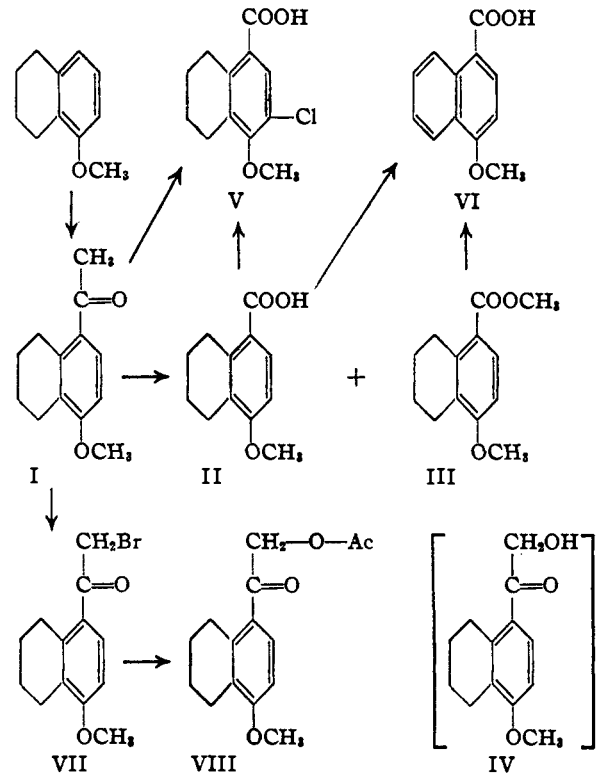
rate is remarkably similar to that observed in the Schotten–Baumann reaction of acid chlorides.[5]

The pseudo-halogen nature of the $-C-Cl_3$ group is also shown by the transformation of trichloroacetic acid esters into carbonates by reaction with alcohols.[6]

$$Cl_3-C\overset{O}{\overset{\|}{C}}-OR + R'OH \longrightarrow R'-O-\overset{O}{\overset{\|}{C}}-O-R + CHCl_3$$

An attempt to prepare IV was unsuccessful because of our inability to isolate a pure product from the hydrolysis of the acetate VIII.

The structure of the starting ketone employed in the haloform reaction was established by the dehydrogenation of III to 4-methoxy-1-naphthoic acid (VI). A reaction diagram is given below.



Experimental

5-Acetyl-8-methoxytetralin (I).—Into a 500-cc. three necked flask fitted with stirrer and reflux condenser there was placed a mixture of 200 cc. of redistilled nitrobenzene and 90 g. of aluminum chloride. While the temperature of this mixture was held at 0–5° by means of an ice-bath, 26 g. of acetic anhydride and 39 g. of 5-methoxytetralin were added at such a rate that the temperature did not exceed 5°. After four hours the reaction mixture was decomposed with ice and hydrochloric acid. The nitrobenzene was removed by steam distillation, and from the residue there was obtained 33.3 g. of ketone; b. p. 164–166° (8 mm.). The oxime prepared in the usual manner melted at 136–139° with decomposition.

Anal. Calcd. for $C_{13}H_{17}O_2N$: C, 71.2; H, 8.7. Found: C, 71.5; H, 7.8.

Preparation of 5-Carbomethoxy-8-methoxytetralin (III).—To a solution of 15 g. of calcium hypochlorate in 60 cc. of hot water was added a warm solution of 10.5 g. of potassium carbonate and 2 g. of potassium hydroxide in 30 cc. of water. After stirring thoroughly the mixture was filtered and the precipitate was washed with 12 cc. of water. One gram of the above-mentioned ketone was dissolved in 30 cc. of methanol and transferred to a separatory funnel. The hypochlorite solution was added slowly in small portions and following each addition the mixture was thoroughly shaken and cooled from time to time in an ice-bath. As soon as the hypochlorite addition was complete an oily solid formed. The solution was extracted with ether and the ether layer was evaporated. Crystallization of the residue first from aqueous methanol and finally from dilute acetic acid gave the methyl ester; m. p. 63–64°; yield 0.87 g. (80%).

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.90; H, 7.26. Found: C, 70.96; H, 7.09.

From the basic solution there was obtained 0.1 g. of 8-methoxy-5-tetralincarboxylic acid; m. p. 215.5–216° after recrystallization from methanol.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8. Found: C, 70.5; H, 7.2.

This acid was also formed quantitatively by the saponification of the methyl ester.

4-Methoxy-1-naphthoic Acid.—Eight-tenths of a gram of 8-methoxy-5-tetralin-carboxylic acid was treated with excess diazomethane in ether and when the evolution of nitrogen ceased the ether was evaporated. The residue was heated with 0.25 g. of sulfur for two hours at 250°. Extraction of the residue with ether, filtration and evaporation of the ether produced a residue which was readily saponified with aqueous-alcoholic sodium hydroxide. Acidification of the basic solution gave 4-methoxy-1-naphthoic acid; m. p. 243.5–244° (after recrystallization from ethanol). This sample was identical with an authentic specimen.[7]

7-Chloro-8-methoxy-5-tetralincarboxylic Acid (V).—The hypochlorite solution was prepared as described above except that 6 g. of potassium hydroxide was used. The hypochlorite was added to a solution of 1 g. of the ketone (I) dissolved in 30 cc. of dioxane. The mixture was shaken continuously for ten minutes and extracted with ether. Acidification of the aqueous layer resulted in the precipitation of an acid which melted at 154–156° after recrystallization from aqueous ethanol. A qualitative test for chlorine was positive.

Anal. Calcd. $C_{12}H_{13}O_3Cl$: C, 59.9; H, 5.4. Found: C, 60.08; H, 5.44.

If in the above experiment the excess hypochlorite were

(4) Houben and Fischer, *Ber.*, **64**, 240 (1931).
(5) Menalda, *Rec. trav. chim.*, **49**, 967 (1930).
(6) Meerwein and Sönke, *Ber.*, **64**, 2379 (1931).
(7) Danilov and Venus-Danilova, *ibid.*, **67**, 24 (1934).

destroyed before acidification, a quantitative yield of 8-methoxy-5-tetralincarboxylic acid II was obtained.

Preparation of 8-Methoxy-5-bromoacetyltetralin (VII).—To a solution of 6.5 g. of ketone (I) dissolved in 100 cc. of glacial acetic acid there was added 5.1 g. of bromine dissolved in 25 cc. of acetic acid. After standing for twelve hours the solution was poured into ice-water and the precipitate was collected on a filter; weight 4.5 g.; m. p. 73–74° after recrystallization from aqueous acetic acid.

Anal. Calcd. for $C_{13}H_{15}O_2Br$: C, 55.1; H, 5.3. Found: C, 55.15; H, 5.51.

8-Methoxy-5-acetoxyacetyltetralin (VIII).—Two grams of the aforementioned bromoketone (VII), 2 g. of fused potassium acetate and 15 cc. of ethanol were refluxed for five hours. After cooling the solution, the potassium bromide was collected on a filter and the filtrate was poured into ice-water. The precipitate was dried and recrystallized first from petroleum ether (90–100°) and finally from dilute alcohol; m. p. 91–92°; yield 90%.

Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.7; H, 6.87. Found: C, 68.88; H, 6.79.

This compound reduced Fehling solution but could not be hydrolyzed to give a pure compound.

Summary

1. It has been shown that methyl esters may be obtained directly as products of the haloform reaction.

2. These esters probably result from the action of methanol on the trihalomethyl ketones which are intermediates in this reaction.

MINNEAPOLIS, MINNESOTA RECEIVED SEPTEMBER 25, 1943

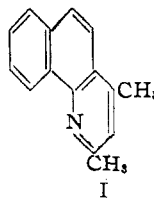
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Cyclization Studies in the Benzoquinoline Series

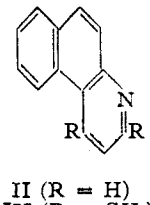
BY WILLIAM S. JOHNSON AND FREDERICK J. MATHEWS[1]

The Doebner–Miller type of quinoline synthesis[2a] with paraldehyde, acetone and β-naphthylamine gives a benzoquinoline derivative, $C_{15}H_{13}N$, m. p. 126–127°.[3] In contrast the quinoline synthesis of Combes[4] is reported to give with β-naphthylamine and acetylacetone a benzoquinoline of the same molecular formula, but m. p. 66–67°.[5] Both syntheses are known to be quite general for the production of quinoline derivatives. Thus from α-naphthylamine the Doebner–Miller and Combes' methods give bases[3,5] which are shown in the present work to be identical (formula I). The discrepancy regarding the benzoquinolines derived from β-naphthylamine presents a problem in proof of structures which is considered in this communication.

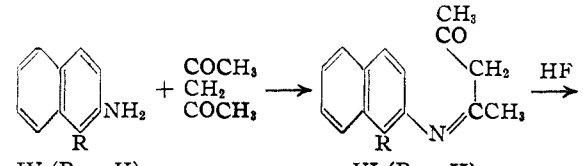
Previous studies suggest a similarity in mechanism—particularly at the cyclization step—between the Doebner–Miller and Skraup syntheses.[2] Since the latter is known[6] to give the angular base, benzo[f]quinoline (II) from β-naphthylamine, it would seem reasonable for Reed's 127° base to be 1,3-dimethylbenzo[f]quinoline (III). If the 127° base is III, the base reported by Combes could be 2,4-dimethylbenzo[g]quinoline (VIII) arising from the alternate—and indeed unexpected[7]—linear cyclization into the 3-position of the naphthalene nucleus. That these postulates are correct is shown below.



I

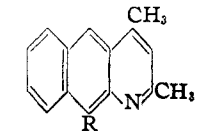


II (R = H)
III (R = CH_3)



IV (R = H)
V (R = CH_3)

VI (R = H)
VII (R = CH_3)



VIII (R = H)
IX (R = CH_3)

When the anil VI, which could be obtained in excellent yield from β-naphthylamine and acetylacetone, was treated with warm concentrated sulfuric acid according to the procedure of Combes,[5] only a small yield (4%) of basic material, m. p. 128.5–129° cor. (pure), was obtained. This substance proved to be identical with material which was prepared by the procedure of Reed.[3] The main product of the reaction was the monosulfonic acid (91% yield) of the expected base of Combes. The sulfonic acid (position of acid group unknown) could be hydrolyzed with dilute sulfuric acid at 220° to give the desired benzoquinoline. It was found, however, that under

(1) Present address: Röhm and Haas, Philadelphia, Pa.

(2) (a) Sidgwick, "Organic Chemistry of Nitrogen," Oxford University Press, 2nd ed., 1937, pp. 546–547; (b) *idem.*, pp. 544–546.

(3) Reed, *J. prakt. Chem.*, [2] **35**, 298 (1887).

(4) Hollins, "Synthesis of Nitrogen Ring Compounds," D. Van Nostrand Company, New York, N. Y., 1924, pp. 266–270.

(5) Combes, *Compt. rend.*, **106**, 1536 (1888).

(6) Skraup and Cobenzl, *Monatsh.*, **4**, 436 (1883).

(7) There is a general tendency for 2,1-cyclization to occur in the naphthalene nucleus. In the case of the Skraup reaction, for example, this tendency is so strong that a methyl group at position-1 prevents the reaction while a bromine atom or a nitro group is displaced to give 2,1 instead of 2,3 cyclization [Lellmann and Schmidt, *Ber.*, **20**, 3154 (1887); Marckwald, *Ann.*, **274**, 331 (1893); **279**, 1 (1894)].