

2. A new method of preparation for mono-*m*-nitrobenzoic anhydride and for mono-*p*-nitrobenzoic anhydride has been described.
3. The stability of some of these anhydrides has been discussed.
4. The behavior of eleven of the anhydrides with benzene and aluminum chloride has been investigated and the products of the reaction identified.

TORONTO, CANADA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

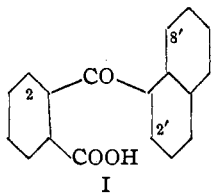
## REARRANGEMENTS IN THE CONDENSATION OF METHYLATED DERIVATIVES OF $\alpha$ -NAPHTHOYL-2-BENZOIC ACID

BY LOUIS F. FIESER AND MARY A. PETERS

RECEIVED MAY 24, 1932

PUBLISHED SEPTEMBER 5, 1932

While 1,2-benzanthraquinone is the sole condensation product formed by the action of sulfuric acid on  $\alpha$ -naphthoyl-2-benzoic acid (I), the quinone is accompanied by about 10% of an isomeric substance when molten sodium aluminum chloride is used as the condensing agent.<sup>1</sup> The isomer, which has the properties of a lactone, is probably formed either by a Scholl benzanthrone condensation between positions 2 and 8' or by intramolecular addition of position 8' to the carbonyl group to give a substance of the type formed by 2'-hydroxy-1-naphthoyl-2-benzoic acid.<sup>1b</sup> In order to study this matter further and to determine if possible which type of *peri* condensation actually takes place, we have investigated the behavior of a few substituted acids with which it seemed reasonable to expect a higher proportion of the abnormal reaction product.

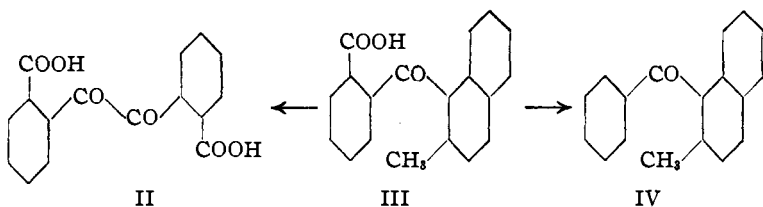


By blocking position 2' with a methyl group we hoped to prevent entirely the formation of an anthraquinone, but this expectation was not realized. On heating 2'-methyl-1-naphthoyl-2-benzoic acid (III) in sodium aluminum chloride at 150°, there was produced a yellow substance having the composition and the properties of a methyl-1,2-benzanthraquinone. Such a compound could be formed from an acid of the structure indicated only as the result of a rearrangement. In view of the unexpected results, it seemed advisable to establish beyond question the structure of the starting material. There can be little doubt on this point, for Scholl and Tritsch, who prepared the acid by condensing phthalic anhydride with  $\beta$ -methyl-naphthalene, noted that the substance is not converted into an anthraquinone by concentrated sulfuric acid.<sup>2</sup> More positive evidence was

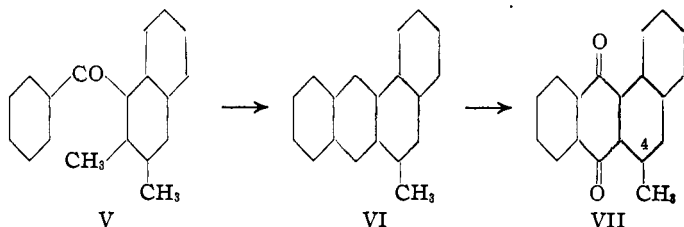
<sup>1</sup> (a) I. G. Farbenind., English Patent 303,375 (1930); (b) Fieser, *THIS JOURNAL*, **53**, 3546 (1931).

<sup>2</sup> Scholl and Tritsch, *Monatsh.*, **32**, 997 (1911).

found on the one hand in the oxidation of the acid to diphthalic acid, II, and on the other hand by decarboxylation to the known ketone IV.



Though the yellow condensation product obtained from III gave well-formed crystals, it did not melt sharply and after repeated fractionation it was separated into two isomeric quinones melting at 185 and 167°. Since all of the known methyl-1,2-benzanthraquinones melt in this same range, the melting temperature in itself is hardly characteristic and it was necessary to secure samples for comparison. The simplest course for the reaction to take would involve a displacement of the methyl group of III from the 2' to the 3' position, giving 4-methyl-1,2-benzanthraquinone, VII. We therefore synthesized the latter compound by carrying out an Elbs condensation on 1-benzoyl-2,3-dimethylnaphthalene, V, and oxidizing the product. The quinone, VII, melted at 167° but it was not identical with the lower melting isomer described above. It is a matter of interest that



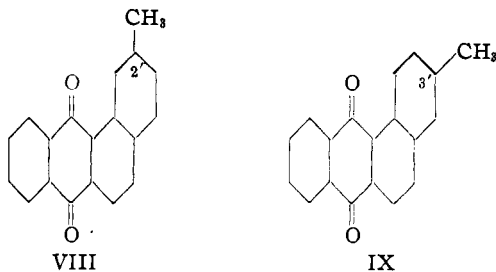
the product obtained by heating the ketone was found to contain both the hydrocarbon VI and the corresponding anthrone. The formation of an anthrone in the Elbs reaction has been observed only in rare instances.<sup>3</sup> The present synthesis is of further interest in connection with the recent observations of Cook.<sup>4</sup> It might be inferred from his statements that the cyclization of the ketone V could not be accomplished without the loss of a methyl group. Our results show that there is no such elimination of the alkyl group from this particular  $\alpha$ -position (4) of the resulting benzanthracene. The generalization of Cook thus should be modified as follows: elimination of an alkyl group in the course of the Elbs reaction is to be expected when the group occupies an  $\alpha$ -position in the naphthalene nucleus of the ketone.

<sup>3</sup> Morgan and Coulson, *J. Chem. Soc.*, 2551 (1929).

<sup>4</sup> Cook, *ibid.*, 456 (1932).

A second possible course of the rearrangement of the acid III would involve a displacement of the methyl group to the 4' position. This would give 3-methyl-1,2-benzanthraquinone, a compound described by Scholl and Tritsch<sup>3</sup> as melting at 175°. This compound was likewise prepared for comparison but it was not identical with either of the two condensation products.

It thus seems evident that the methyl group of the benzanthraquinones in question is not attached to the anthraquinone nucleus but to the fused-on ring. Cook<sup>4</sup> recently has described 2'-methyl and 3'-methyl-1,2-benzanthraquinone (formulas VIII and IX) and their melting points are close to those of the compounds obtained in the present work. A comparison of our compounds with those prepared by Cook's method indeed proved the two pairs of compounds to be identical. The quinone melting at 185° has the structure of VIII, the isomer melting at 167° is IX.

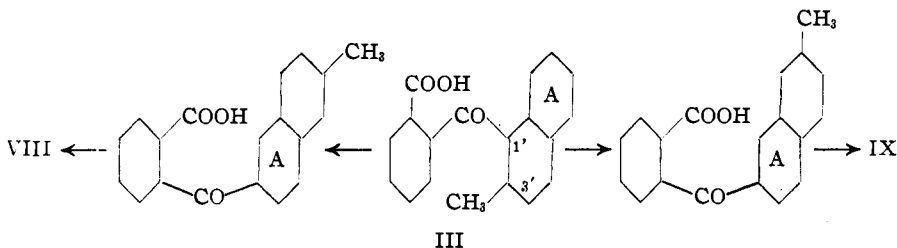


The formation of the quinones VIII and IX could of course be the result of a migration of the methyl group in the starting material (III) to the unsubstituted ring of the naphthalene nucleus. Methyl migrations, though not of such an extensive kind, have been observed by Mayer, Fleckenstein and Günther in studying the Scholl condensation of aroyl-methylnaphthalenes.<sup>5</sup> There is, however, a much more plausible way of accounting for the reaction, namely, that the rearrangement involves a migration of the aroyl rather than the methyl group. The mobility of an acyl or aroyl group in the  $\alpha$ -position of naphthalene has been adequately demonstrated by Cook, both by direct<sup>6</sup> and by indirect<sup>7</sup> evidence. The migration is always from an  $\alpha$ - to a  $\beta$ -position. In the present case the migration of the phthalic acid residue cannot be to a  $\beta$ -position of the ring which it originally occupied (position 1'  $\rightarrow$  position 3' in III, below) for this would give 4-methyl-1,2-benzanthraquinone instead of the 2' and 3' derivatives, VIII and IX. The formation of these quinones must be the result of a migration to both of the  $\beta$ -positions in the unsubstituted ring (A), in the following manner

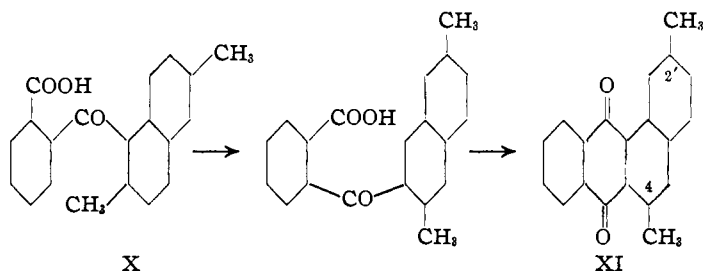
<sup>5</sup> Mayer, Fleckenstein and Günther, *Ber.*, **63**, 1464 (1930).

<sup>6</sup> Cook and Galley, *J. Chem. Soc.*, 2012 (1931).

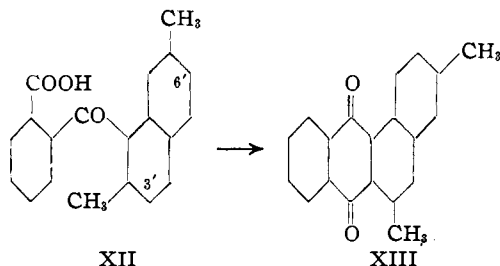
<sup>7</sup> Cook, *ibid.*, 487, 489 (1931).



In order to test further this conception of the reaction, the condensation of three dimethylnaphthoylbenzoic acids was investigated. With the acid X, obtained from phthalic anhydride and 2,6-dimethylnaphthalene,



there are only two free  $\beta$ -positions to which the phthalic acid residue could migrate and these are identical. It is thus evident that if the reaction follows the course indicated it should yield only one product. This was found to be the case; dehydration with sodium aluminum chloride yielded a single, pure substance. We regard the product as 2',4-dimethyl-1,2-benzanthraquinone (XI), and consider it to be formed by the rearrangement indicated. Starting with 2,7-dimethylnaphthalene, which is likewise symmetrical in structure, we next prepared the acid XII and carried out a dehydration. Here again the acroyl group can migrate in only one way, to

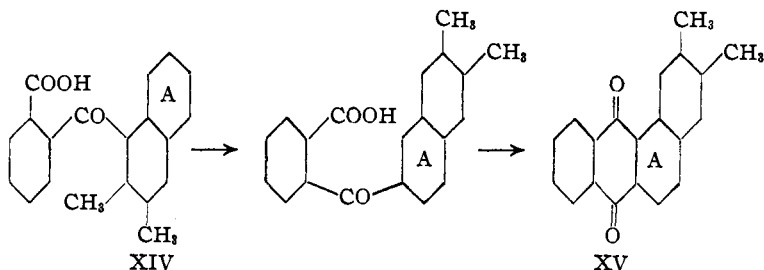


the identical  $\beta$ -positions 3' and 6'. The condensation thus should give a single substance, XIII, and this should be an isomer of the dimethylbenzanthraquinone, XI, from 2,6-dimethylnaphthalene. The results were found to be in accord with both of these predictions.

It should be pointed out that it is quite impossible to predict the struc-

tures of these condensation products on the basis of the alternate hypothesis that the formation of the benzanthraquinones is the result of the migration of a methyl group. It does not appear likely, however, that the acids X and XII would each give a single quinone and that these quinones would be different, if a methyl migration were involved.

A further interesting application of the mechanism suggested for the reaction is found in the condensation of the 2',3'-dimethyl derivative, XIV.



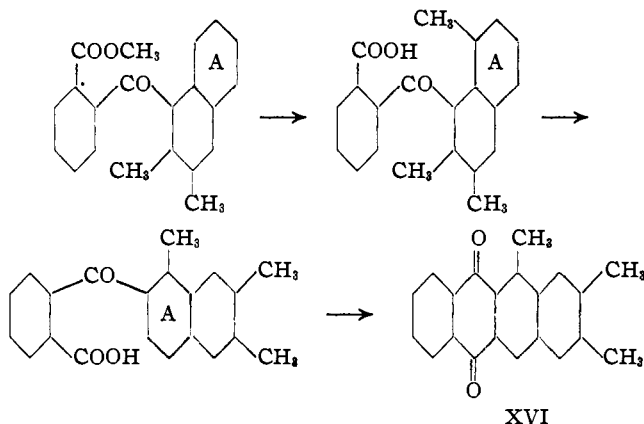
Here a rearrangement to a  $\beta$ -position in the ring originally carrying the aroyl group is not possible without the displacement of a methyl group. Any such displacement would probably lead to a mixture of substances. On the other hand, the migration to the unsubstituted ring, A, could give rise to only one compound, the dimethyl quinone, XV. In the reaction product actually obtained we found only one substance and it corresponded in properties to a substance having the structure of XV.

From the observations which have been made it seems clear that the reaction may be described in the following general terms. Under the influence of sodium aluminum chloride an  $\alpha$ -naphthoylbenzoic acid carrying an alkyl group in such a position as to prevent direct quinone formation rearranges in such a way that the phthalic acid group migrates to any free  $\beta$ -position of the ring which does not contain the blocking alkyl group.

One other interesting observation was made in the course of this work. The intramolecular condensation of the aroyl benzoic acids was usually brought about by using the free acid in question, but in one or two cases an attempt was made to improve the yield by using the methyl ester. When the ester of 2',3'-dimethyl-1'-naphthoyl-2-benzoic acid (XIV) was so employed the reaction mixture was found to contain in addition to the dimethyl-1,2-benzanthraquinone, XV, a substance having the composition and properties of a trimethylbenzanthraquinone. It differed, however, in a striking manner from the other methylated quinones which have been described or discussed in this paper, for it did not form the characteristic hyposulfite vat. Such a behavior is a highly characteristic property of the linear tetracyclic quinones and it is an indication that the compound in question is a derivative of naphthacenequinone rather than of the angular

1,2-benzanthraquinone. As for the source of the third methyl group it is significant that the trimethyl compound was obtained from the ester but not from the free acid. This suggests that the alkylation is brought about by the action of methyl chloride formed by the hydrolysis of the ester group. The ethyl ester was investigated but it yielded only the dimethyl quinone, XV. In view of the decreased reactivity of ethyl as compared with methyl chloride the result is not surprising.

The yield of the trimethyl derivative is so low that it seemed impractical to attempt to establish its structure. In view of this difficulty we may record here what we regard as the probable course of the reaction even though this is based upon very meager evidence (see formulas). The rearrange-



ment here postulated is in accord with the transformations observed above. The assumption that  $\alpha$ -alkylation in Ring A precedes the migration is the only way of accounting for the formation of a linear, rather than an angular, quinone.

## Experimental Part

### 1. Preparation of the Naphthoic Acids

The methyl and dimethyl naphthalenes used for the condensation with phthalic anhydride were the highly purified products supplied by the Gesellschaft für Teerverwertung. As the solvent, both nitrobenzene and carbon disulfide proved less satisfactory than tetrachloroethane, and the best results were obtained by working at a low temperature. The general procedure adopted was as follows. A solution of 0.1 mole of the hydrocarbon and 0.11 mole of phthalic anhydride in 100 cc. of tetrachloroethane (warmed) was stirred mechanically in an ice-bath and 0.22 mole of aluminum chloride was added in the course of one hour. Stirring was continued for about five hours and the mixture was allowed to stand overnight. The product was worked up in the usual manner and precipitated from a cold soda solution. The crude acid in most cases separated in the form of an unstable hydrate and the product was best dried by heating it on the steam-bath, cooling and pouring off the water. The yield usually was quantitative and the crude product pure enough for most reactions. The acids do not form particularly good crystals and they are most conveniently purified through the esters,

where this is possible. The properties and analyses<sup>8</sup> of the acids are recorded in Table I, the corresponding esters are described in Table II. The methyl ester of 2'-methyl-1'-naphthoyl-2-benzoic acid was obtained only as an oil.

TABLE I  
ALKYL DERIVATIVES OF 1'-NAPHTHOYL-2-BENZOIC ACID

Positions of substituents	Carbon, %		Hydrogen, %		Melting point, °C.
	Calcd.	Found	Calcd.	Found	
2'-Methyl <sup>2</sup>	78.60	78.40	4.86	4.91	193
2',6'-Dimethyl	78.92	78.12	5.30	5.42	238
2',7'-Dimethyl	78.92	79.09	5.30	5.45	210
2',3'-Dimethyl	78.92	79.06	5.30	5.40	205

TABLE II  
ESTERS OF THE DIMETHYL-1'-NAPHTHOYL-2-BENZOIC ACIDS

Positions of substituents	Ester group	Carbon, %		Hydrogen, %		Melting point, °C.
		Calcd.	Found	Calcd.	Found	
2',6'	Methyl	79.23	79.02	5.70	5.80	162
2',7'	Methyl	79.23	78.88	5.70	5.82	131
2',3'	Methyl	79.23	79.18	5.70	5.85	170
2',3'	Ethyl	79.49	79.58	6.07	6.11	165

## 2. Proof of Structure

2'-Methyl-1'-naphthoyl-2-benzoic acid (2.9 g.) was oxidized in alkaline solution with potassium permanganate (13 g.) in essentially the manner described by Graebe for the unmethylated acid.<sup>9</sup> In working up the product, however, it was found convenient to take advantage of the sparing solubility of the manganese salt of the oxidation product. At the end of the reaction the mixture was treated with sulfur dioxide until the manganese dioxide was dissolved and the manganese salt referred to had separated as a white precipitate. This was boiled with alkali, the solution was filtered and acidified and the diphtalyllic acid (1 g.) precipitated at this point in nearly pure condition. Crystallized from nitrobenzene it melted at 277°.

*Anal.* Calcd. for C<sub>16</sub>H<sub>10</sub>O<sub>6</sub>: C, 64.42; H, 3.38. Found: C, 63.98; H, 3.64.

The acid was definitely identified by the preparation of the colorless and the yellow methyl derivatives described by Graebe and Juillard,<sup>10</sup> which were found to melt at 276 and 192°, respectively. The yellow ester was prepared with diazomethane instead of through the silver salt.

The decarboxylation of 2'-methyl-1'-naphthoyl-2-benzoic acid was accomplished by heating it with a trace of copper powder at 300°, and quickly distilling the product in vacuum in order to avoid an Elbs condensation. The resulting ketone had to be seeded but it then crystallized well, melted at 71°, and showed no depression on admixture with an authentic sample of 1-benzoyl-2-methylnaphthalene (m. p. 71°).<sup>11</sup>

A further derivative of the keto acid may be described. 2'-Methyl-1'-naphthylmethyl-2-benzoic acid, prepared by reducing the keto acid with zinc dust in alkaline solution, melted at 187° after crystallization from benzene-ligroin.

*Anal.* Calcd. for C<sub>19</sub>H<sub>16</sub>O<sub>2</sub>: C, 82.58; H, 5.84. Found: C, 82.44; H, 5.93.

<sup>8</sup> The analyses (semi-micro) reported in this paper were all carried out by Mr. C. L. Bickel.

<sup>9</sup> Graebe, *Ann.*, **340**, 249 (1905).

<sup>10</sup> Graebe and Juillard, *ibid.*, **242**, 214 (1887).

<sup>11</sup> Mayer and Sieglitz, *Ber.*, **55**, 1851 (1922).

The structure of 2',3'-dimethyl-1'-naphthoyl-2-benzoic acid was established by oxidation in the manner described above to a product which was identified as diphthalic acid.

### 3. Condensation to the 1,2-Benzanthraquinones

The condensations were all carried out in much the same manner. Thus for the reaction of 10 g. of 2'-methyl-1'-naphthoyl-2-benzoic acid a melt was made by heating a mixture of 12.5 g. of sodium chloride and 62.5 g. of aluminum chloride over a free flame until fusion was complete. The melt was allowed to cool until it began to crystallize (about 100°), and the acid was slowly added with good stirring. The mixture was then heated for one-half hour with continued stirring in an oil-bath at 150°. The mixture changed from a bright red color at the beginning to brown. On pouring the hot melt onto ice the quinone separated as a greenish-yellow solid. The material did not filter well and became somewhat oily on being heated and it was found expedient to extract the quinone by shaking the suspension with ether. The material left on evaporation of the ether did not crystallize well until after it had been distilled *in vacuo*. Crystallization from glacial acetic acid then gave a very good product; yield, 6.6 g. (71%).

No separation of the isomers present was accomplished by repeated crystallization from glacial acetic acid or from alcohol, the melting point remaining at 168–170°. The composition was that of a methylbenzanthraquinone.

*Anal.* Calcd. for  $C_{19}H_{12}O_2$ : C, 83.80; H, 4.45. Found: C, 83.39; H, 4.62.

After further purification by vating, the product gave extremely well-formed crystals but the melting point remained unsharp and variable. A separation was finally accomplished by fractional crystallization from methyl ethyl ketone, the higher melting isomer crystallizing first. There is very little difference in the solubilities, and the amounts of the two pure components isolated were small. One isomer after further repeated crystallization from glacial acetic acid melted at 185° and showed no melting-point depression with 2'-methyl-1,2-benzanthraquinone, which we prepared according to Cook<sup>4</sup> and for which we found a melting point of 186°. The other isomer, crystallized from benzene-ligroin, melted at 167° and was identical with an authentic sample of 3'-methyl-1,2-benzanthraquinone which melted at 168°.

The condensation of the dimethylbenzoic acids was carried out in exactly the manner described above. The yields of material which had been extracted, distilled and crystallized were all about 70% of the theoretical amount, and we found no sign of the presence of isomers. The quinones all crystallized from glacial acetic acid in the form of good yellow needles, and the melting points were sharp. The properties are recorded in Table III.

TABLE III  
DIMETHYL-1,2-BENZANTHRAQUINONES,  $C_{20}H_{14}O_2$

Positions of substituents	Formula	Color in $H_2SO_4$	Melting point, °C.	Analyses, %	
				Calcd.: C	Calcd.: H
2',4	XI	Blue	190	83.68	5.12
3',4	XIII	Dull red	195	83.74	5.08
2',3'	XV	Purple	236	83.70	4.96

The condensation product obtained from the methyl ester of 2',3'-dimethyl-1'-naphthoyl-2-benzoic acid was worked up in a somewhat different manner. The suspension obtained on pouring the melt onto ice gave a good solid product on being digested at the boiling point. This was extracted with successive portions of boiling glacial acetic acid from a small amount of residue and the quinone was precipitated with water, dried and distilled. This was crystallized repeatedly from glacial acetic acid until the crystals no longer gave a red vat with alkaline hyposulfite solution. The crystals were those of



the trimethyl quinone described below, yield 4%. The dimethyl quinone present in the mother liquors was easily isolated in pure form by taking advantage of the fact that, unlike the trimethyl derivative, it forms a characteristic red hyposulfite vat. After crystallization of the vatted material, 2',3'-dimethyl-1,2-benzanthraquinone melting at 236° was obtained in 60% yield.

**1,2',3'-Trimethyl-2,3-benzanthraquinone, XVI.**—The first product obtained from the condensation formed long, orange-yellow needles, melting at 275°. The solution in concentrated sulfuric acid is bluish-green in color.

*Anal.* Calcd. for  $C_{21}H_{16}O_2$ : C, 83.97; H, 5.37. Found: C, 83.83; H, 5.62.

The compound is distinctly less soluble and higher melting than the dimethyl-1,2-benzanthraquinones. In these properties and in the appearance of the crystals it strongly resembles naphthacenequinone. A further striking resemblance is in the behavior toward reducing agents. The new substance is not affected by boiling with alkaline hyposulfite solution, it forms a green vat on adding this reducing agent to an alcoholic suspension of the quinone, and a red color, which is rapidly discharged by shaking with air, is produced by the action of zinc dust in glacial acetic acid solution.

#### 4. Synthesis of 4-Methyl-1,2-benzanthraquinone

**1-Benzoyl-2,3-dimethylnaphthalene (V).**—The ketone was prepared both by the usual synthesis and by the Perrier method of carrying out the Friedel and Crafts reaction. The latter method was found to be much more rapid and to give a better yield of the pure product. To a suspension in carbon disulfide of the addition compound from 14.1 g. of benzoyl chloride and 14.0 g. of aluminum chloride, 15.6 g. of 2,3-dimethylnaphthalene was added in the course of a few minutes. After heating on the steam-bath for ten minutes to complete the reaction, the mixture was cooled and the crystalline addition product was collected and washed with carbon disulfide. It was decomposed by stirring it into ice and the ketone formed in this operation was obtained as a good solid by crushing the lumps and washing with a little ether; yield, 18 g., 79%. One crystallization from alcohol gave a pure product melting at 126°. It crystallizes well from alcohol as stout colorless needles.

*Anal.* Calcd. for  $C_{19}H_{16}O$ : C, 87.65; H, 6.15. Found: C, 87.46; H, 6.26.

The Elbs condensation was carried out by heating the ketone at the temperature necessary to maintain gentle boiling for three to four hours. On distillation in vacuum a considerable residue was left and the distillate was an oil which did not solidify. The hydrocarbon and the anthrone were isolated from this oil only in small amounts and in separate experiments. The corresponding quinone is easily obtained by oxidizing the crude distillate, but the yield from the ketone was only 16%. The anthrone was isolated by dissolving the oil in ligroin; the solution slowly deposited a small crop of yellow crystals. The hydrocarbon was separated from an alcoholic solution as the picrate. This was purified to a constant melting point and converted into the hydrocarbon.

**4-Methyl-1,2-benz-9-anthrone** forms yellow leaflets melting at 150° from ligroin. The solution in alcoholic alkali is yellow with a green fluorescence.

*Anal.* Calcd. for  $C_{19}H_{14}O$ : C, 88.34; H, 5.46. Found: C, 88.09; H, 5.45.

**4-Methyl-1,2-benzanthracene (VI)** forms colorless microscopic clusters of needles from alcohol, m. p. 107°. The picrate crystallizes from alcohol as fine dark red needles, melting at 119–120°.

*Anal.* Calcd. for  $C_{19}H_{14}$ : C, 94.18; H, 5.83. Found: C, 94.05; H, 5.88.

**4-Methyl-1,2-benzanthraquinone (VII)** crystallizes from glacial acetic acid as well-formed yellow needles, melting at 167°. It is dull green in concentrated sulfuric acid. It forms a hydroquinone diacetate melting at 220°.

*Anal.* Calcd. for  $C_{19}H_{12}O_2$ : C, 83.80; H, 4.45. Found: C, 83.42; H, 4.53.

### Summary

It was expected that the substitution of a methyl group in the 2'-position of 1'-naphthoyl-2-benzoic acid would prevent the formation of an anthraquinone on subjecting this substance to condensation in the sodium aluminum chloride melt. It was found, however, that two isomeric methyl-1,2-benzanthraquinones are produced and a study has been made of the rearrangement obviously involved in the course of the reaction. Through the identification of the methylbenzanthraquinones and a study of the condensation of various dimethyl-1'-naphthoyl-2-benzoic acids it has been found that the rearrangement involves the migration of the phthalic acid residue to a  $\beta$ -position of the originally unsubstituted ring.

CONVERSE MEMORIAL LABORATORY  
CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

## RESEARCHES ON PYRIMIDINES. CXXX. SYNTHESIS OF 2-KETO-1,2,3,4-TETRAHYDROPYRIMIDINES

BY KARL FOLKERS,<sup>1</sup> H. J. HARWOOD<sup>1</sup> AND TREAT B. JOHNSON

RECEIVED MAY 25, 1932

PUBLISHED SEPTEMBER 5, 1932

This paper is presented as a preliminary contribution dealing with methods of synthesis and the chemistry of 2-keto-1,2,3,4-tetrahydropyrimidine compounds. The structural relationship between uracil and the mother substance of such a series (acroleinarnstoff) is expressed by formulas I and II, respectively. Theoretically the pyrimidine II should



be formed by the action of acrolein on urea, but, thus far, all attempts to prepare this compound by interaction of these reagents have been unsuccessful.<sup>2,3,4</sup>

A practical procedure for preparing derivatives of this pyrimidine II was first described by Biginelli<sup>5</sup> in 1893. This is based on that investigator's discovery that an aldehyde will combine with a  $\beta$ -keto ester and urea in alcohol solution with smooth formation of a tetrahydropyrimidine. With benzaldehyde and ethyl acetoacetate, for example, he was able to

<sup>1</sup> Squibb and Sons Research Fellows in Organic Chemistry, 1931-1932.

<sup>2</sup> Schiff, *Ann.*, 151, 203 (1869); *Ber.*, 15, 1393 (1882).

<sup>3</sup> Leeds, *Ber.*, 15, 1159 (1882).

<sup>4</sup> Lüdy, *Monatsh.*, 10, 300 (1889).

<sup>5</sup> Biginelli, *Gazz. chim. ital.*, 23, 360 (1893); *Atti. accad. Lincei*, [5] 3, 195 (1894); *Chem. Zentr.*, 65, 823 (1894); *Ber.*, 24, 1317 (1891).