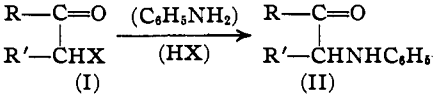
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE GLIDDEN COMPANY, SOYA PRODUCTS DIV.]

Studies in the Indole Series. IX. The Reactions of α-Halogenated and α-Hydroxy Ketones with Arylamines. Part I

BY PERCY L. JULIAN, EDWIN W. MEYER, ARTHUR MAGNANI AND WAYNE COLE

The reaction in which indoles are formed when α-halogenated or α-hydroxy ketones—the latter in the presence of a hydrohalogen acid—are heated with arylamines has been the subject of numerous investigations but the mechanism is still not clarified. The Bischler mechanism[1] which until recently went unchallenged[2] suggests that the reaction proceeds in three stages as follows:

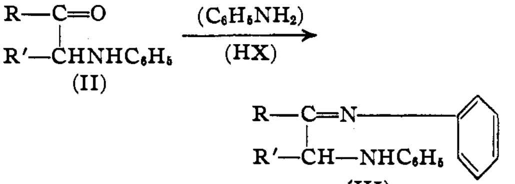
1. Direct replacement of the α-halogen or α-hydroxy group by the arylamino group.
2. Reaction of a second mole of arylamine with the arylamino ketone (II) to yield the "aniline-anil" (III).
3. Elimination of a molecule of arylamine and indeed the *first* molecule which entered the reaction to form presumably the indolenine (IV) which rearranges into the stable indole modification (V).



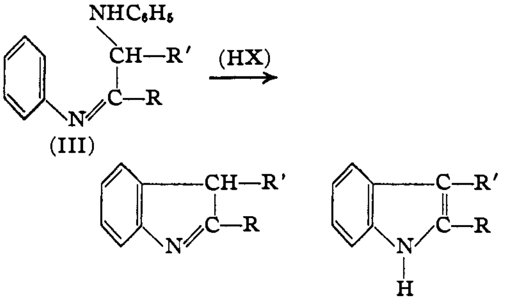
$$\begin{array}{l} \mathrm{R—C{=}O} \\ \quad | \\ \mathrm{R'—CHX} \end{array} \xrightarrow[\mathrm{(HX)}]{\mathrm{(C_6H_5NH_2)}} \begin{array}{l} \mathrm{R—C{=}O} \\ \quad | \\ \mathrm{R'—CHNHC_6H_5} \end{array} \qquad (1)$$

(I) (II)

(R, R' = H, alkyl or aryl)

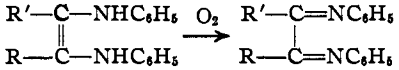


(II) (III) (2)



(III) (IV) (V) (3)

Our first interest in this reaction resided in its possible usefulness for preparing indoles of specific structures, since it is suggested in Step 3 that the positions of R and R' in the indole nucleus are fixed by the fact that the "first" molecule of arylamine entering the reaction is the one eliminated on ring closure to the indole. On the face of it this portion of the mechanism appeared weak, since in an ene-diol-like structure for III, such as III-a, the designation of "first" to any mole of aniline entering the reaction loses its significance.



$$\begin{array}{l} \mathrm{R'—C—NHC_6H_5} \\ \quad \| \\ \mathrm{R—C—NHC_6H_5} \end{array} \xrightarrow{\mathrm{O_2}} \begin{array}{l} \mathrm{R'—C{=}NC_6H_5} \\ \quad | \\ \mathrm{R—C{=}NC_6H_5} \end{array}$$

(III-a) (VI)

Indeed Strain[3] prepared an "aniline-anil" (III) by a benzoin-like condensation of benzalaniline in the presence of potassium cyanide in liquid ammonia, and showed that it behaved like a nitrogen analog of a typical ene-diol, (III-a), greedily taking up atmospheric oxygen to form the nitrogen analog of an α,ά-diketone (VI). What is also of significance for the Bischler hypothesis is Strain's conversion of III into 2,3-diphenylindole (V, R, R' = phenyl) in good yield by heating it in the presence of a small quantity of hydrochloric acid.

Conceivably then, one would expect in certain cases to secure a mixture of isomeric indoles where the positions of R' and R are reversed in the indole nucleus. This is actually the case and was first pointed out clearly by Julian and Pikl[2a] several years ago, at which time these authors promised a later report on the Bischler mechanism. For more than a decade this report has been in progress and it is perhaps fortunate that circumstances have delayed its publication[4] for constant repetition and review of the many reactions involved have given us some advantage over investigators who have recently entered this field.

Thus Crowther, Mann and Purdie[2b] and likewise Verkade and Janetzky[2d,5] have recently published rather sweeping generalizations and speculations based upon a few special cases and have not had sufficient facts to report an over-all picture of the steps of the reaction in question. This will, we believe, be evident in the discussion of each step of the mechanism which follows.

Step 1. The Formation of α-Arylamino Ketones from α-Bromo and α-Hydroxy Ketones.—In the interest of clarity of presentation we

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(1) Bischler and Fireman, *Ber.*, **25**, 2860 (1892); **26**, 1336 (1893).

(2) (a) Julian and Pikl, THIS JOURNAL, **55**, 2106 (1933): (b) Crowther, Mann and Purdie, *J. Chem. Soc.*, 58 (1943); (c) Verkade and Janetzky, *Rec. trav. chim.*, **62**, 763 (1943); (d) *ibid.*, **62**, 775 (1943).

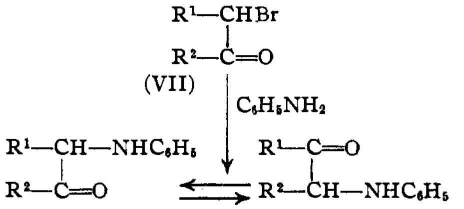
(3) Strain, THIS JOURNAL, **50**, 2218 (1928); **51**, 269 (1929).

(4) This work was actually begun in 1931 with Dr. Walter Passler of Vienna in the laboratory of the senior author at Howard University. Following his two years of work, it was continued at intervals by various collaborators over a period of nearly ten years. An unfortunate theft of valuable papers a few years ago lost to us all records of this work. All of the investigations had to be reconstituted. Some of the experimental data recorded in this paper had been accumulated by Dr. Passler, with whom unfortunately we have been unable to communicate because of the war, but to whom we are greatly indebted.

(5) The first paper of these authors contains an excellent historical summary of certain of the investigations of this useful reaction.

shall confine ourselves in this first paper to only one arylamine, aniline, and we shall later deal with other arylamines.

The reaction between an α-bromo ketone and aniline is not always a simple substitution reaction as Bischler and many others have assumed. Thus in 1933, Julian[6] reported that α-bromopropiophenone on treatment with aniline gave not only the expected yellow anilino ketone (VIII, $R^1 = CH_3$, $R^2 = C_6H_5$)



(VIII) *Yellow* (IX) *Colorless*

($R^1 = CH_3$ or $C_6H_5CH_2$; $R^2 = C_6H_5$)

but also a *colorless* anilino ketone (IX, $R^1 = CH_3$, $R^2 = C_6H_5$). The constitution of IX was proved by the fact that it is the main product of the reaction between α-bromobenzyl methyl ketone and aniline, and further that on standing, it rapidly undergoes oxidative decomposition whereupon benzanilide can be separated from the decomposition products. Also on treatment with phenylmagnesium bromide IX ($R' = CH_3$, $R^2 = C_6H_5$) gave an addition product which on oxidation yielded acetophenone.[7] In this same paper it was also reported that α-bromo-β-phenylpropiophenone (VII, $R^1 = C_6H_5—CH_2—$; $R^2 = C_6H_5$) behaved similarly and yielded two anilino ketones, the one yellow (VIII, $R^1 = C_6H_5—CH_2—$; $R^2 = C_6H_5$) and the other colorless (IX, $R^2 = C_6H_5$; $R^1 = C_6H_5—CH_2—$). Thus the extended conjugated unsaturation represented by VIII serves to characterize this derivative by its pronounced color in contradistinction to IX where this continued conjugated unsaturation is absent.

Two years later McGeoch and Stevens[8] unaware of the work of Julian, rediscovered this behavior of α-bromo-β-phenylpropiophenone.

The importance of these findings for the Bischler mechanism is deep-seated. Certainly, no mechanism, based on the structure of the end-product, the indole, can be postulated for the reaction between an α-halogenated ketone and aniline until the structure of the intermediate α-anilino-ketone is definitely proved. If, moreover, this structure demonstrates, as shown above, that the reaction is not one of mere replacement, then one faces two possibilities of fundamental significance, (a) that the reaction between an α-halogenated ketone and aniline may involve addition of the arylamine to the carbonyl group and subsequent elimination of hydrogen halide and (b) that the initially formed anilino ketone may itself rearrange into its isomer. These two possibilities are schematically indicated without showing intermediates in the formulas above showing the formation of both colorless and yellow anilino ketones from α-bromopropiophenones.

The first of these possibilities has been clearly forecasted by Kohler and Brown[9] who express the belief that very few, if any, reactions of α-halogenated ketones are simple replacement reactions. Certainly it is difficult to explain the reactions of the α-bromopropiophenones recorded above by replacement reactions unless we assume further that the rearrangement indicated as possibility (b) follows immediately under the conditions of the experiment. Thus Step 1 of the Bischler mechanism is either incorrect in that the reaction is not a replacement reaction, or if it be correct it must be supplemented by a second step involving a rearrangement of the originally formed α-anilino ketone.

We have at present no direct evidence that Step 1 involves an addition rather than a replacement reaction. We have, however, secured definite evidence that an anilino ketone like VIII can rearrange into IX and *vice versa*. When, for example, α-bromopropiophenone is treated with aniline in the usual way (one mole of bromo ketone to two of aniline) the mixture of yellow and colorless anilino ketones is obtained. Collet[10] reported only the yellow anilino ketone as product of the reaction. In our first experiment attempting to duplicate his results we secured only the colorless isomer and could not find any of Collet's compound. Thereafter, however, for some time we could not duplicate our first experiment, securing invariably a mixture of both anilides. When, however, we treated one mole of bromo ketone with one mole of aniline and an excess of sodium bicarbonate[11] we secured only Collet's yellow anilino ketone in excellent yield. It therefore appeared certain that hydrogen bromide (or aniline hydrobromide) was responsible for the production of the colorless isomer. We then warmed the *pure* yellow α-anilinopropiophenone in the presence of aniline hydrobromide. A mixture of the yellow and colorless anilinoketones was isolated and this mixture was separated by careful fractional recrystallization into the two components (VIII) and (IX). Likewise the pure, colorless, α-anilinobenzyl methyl ketone on warming in alcoholic solution in the presence of aniline hydrobromide was partially converted into its yellow isomer, and this mixture was separated by fractional recrystallization into the two pure components.

These rearrangement or interconversion experiments with the α-anilino ketones were repeated

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[6] Read at Fall meeting of the American Chemical Society in Chicago, 1933.

[7] These experiments on proof of the structure of the colorless anilino derivative were carried out by Dr. R. P. Barnes with the senior author at Howard University in 1932.

[8] McGeoch and Stevens, *J. Chem. Soc.*, 1032 (1935).

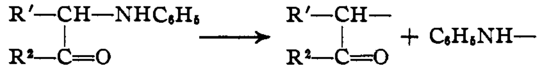
[9] Kohler and Brown, This Journal, **55**, 4299 (1933).

[10] M. A. Collet, *Bull. soc. chim.*, [3] **15**, 716 (1895); **17**, 72 (1897).

[11] *Cf.* Verkade and Janetzky, ref. 2c.

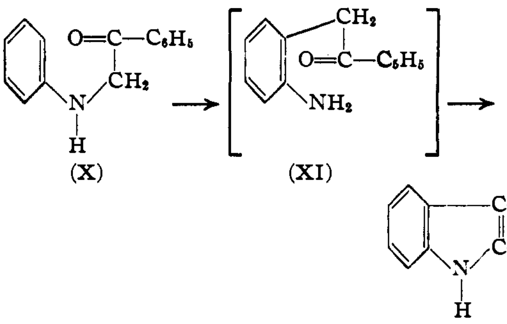
with the yellow anilino ketone (VIII, $R^1 = C_6H_5—CH_2$; $R^2 = C_6H_5$) derived from α-bromo-β-phenylpropiophenone and with IX, the colorless isomer. Here the anilino ketones were heated with aniline in the presence of hydrochloric acid. In each case, beginning with the pure anilino ketone, a mixture resulted which could be separated into the two pure isomers. In order to remove the possibility that condensation of the anilino ketone with aniline took place, we carried out the interconversions in the absence of aniline with hydrochloric acid present. The results were the same and the yields were about the same. Thus definite proof is presented for an interconversion of α-anilino ketones in the presence of a hydrohalogen acid.

Step 1 of the Bischler mechanism, if correct, must therefore be modified by the additional possibility of rearrangement of the originally formed anilino ketone. Such a rearrangement, without the additional data presented in this paper, could readily be employed to support the hypothesis of direct ring closure of the anilino ketone, proposed by Crowther, Mann and Purdie and by Verkade and Janetzky.[2c] These authors reject the Bischler assumption of intermediate "aniline-anil" formation and suggest instead, without experimental proof, a dissociation of the anilino-ketone in the sense represented below.



$$\begin{matrix} R'—CH—NHC_6H_5 \\ | \\ R^2—C{=}O \end{matrix} \longrightarrow \begin{matrix} R'—CH— \\ | \\ R^2—C{=}O \end{matrix} + C_6H_5NH—$$

Crowther, Mann and Purdie further postulate an "ortho" shift after dissociation, and in this way explain the formation of 2-phenylindole (XII) instead of 3-phenylindole from phenacylaniline (X) making use of the already known fact that



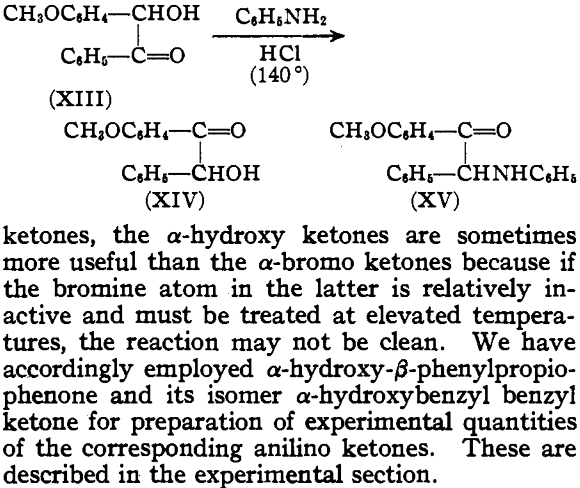
(X) (XI)

(XII)

o-aminodesoxybenzoin (XI) does undergo ring closure immediately to 2-phenylindole.[12] These authors do not explain, however, why an ortho shift takes place, let us say, in the case of α-anilinopropiophenone to give 2-phenyl-3-methylindole, but does not appear to take place in the case of α-anilinobenzyl methyl ketone, which likewise gives 2-phenyl-3-methylindole in the same, nearly quantitative yield! Had they been aware of this rearrangement of α-anilinopropiophenone into its isomer, they could readily have proposed this rearrangement as the preliminary step, followed by the "ortho" shift. The formation of the same indole from both anilino ketones would then become plausible without recourse to Bischler's proposed second step, especially since under ordinary conditions, α-bromobenzyl methyl ketone because of the great reactivity of the bromine atom gives the expected substitution product with aniline without contamination by noticeable quantities of the isomeric α-anilinopropiophenone. This demonstrates the grave danger of a hasty interpretation of this reaction based upon a few isolated cases.

We have also examined over a period of several years a number of α-hydroxy ketones in their behavior toward aniline. Here the situation is even more complicated than in the case of the α-bromo ketones, for it is well known that the ketols or benzoins may rearrange into one another quite readily, either under the influence of acids and bases[13] or on subjection to heat.[14]

Generally speaking the benzoins readily may be converted into the anilino ketones by heating with an equimolecular quantity of aniline in the presence of a few drops of hydrochloric acid at 140° for a short time. If one subjects benzoylanisylcarbinol (XIII) to this treatment, one secures α-anilinobenzyl anisyl ketone (XV) which undoubtedly arises by virtue of conversion of (XIII) into its isomer (XIV) at the temperature in question.[14] For securing the desired α-anilino



$$\begin{matrix} CH_3OC_6H_4—CHOH \\ | \\ C_6H_5—C{=}O \end{matrix} \xrightarrow[\text{HCl}\ (140°)]{C_6H_5NH_2}$$

(XIII)

$$\begin{matrix} CH_3OC_6H_4—C{=}O \\ | \\ C_6H_5—CHOH \end{matrix} \qquad \begin{matrix} CH_3OC_6H_4—C{=}O \\ | \\ C_6H_5—CHNHC_6H_5 \end{matrix}$$

(XIV) (XV)

ketones, the α-hydroxy ketones are sometimes more useful than the α-bromo ketones because if the bromine atom in the latter is relatively inactive and must be treated at elevated temperatures, the reaction may not be clean. We have accordingly employed α-hydroxy-β-phenylpropiophenone and its isomer α-hydroxybenzyl benzyl ketone for preparation of experimental quantities of the corresponding anilino ketones. These are described in the experimental section.

Step 2. The Intermediate "Aniline-Anils" or Unsaturated Diamines.—The reaction of α-bromopropiomesitylene with aniline supports the Bischler claim that a "second" molecule of aniline participates in the over-all reaction system to form the indole. In this bromo ketone where definite hindrance to addition reactions involving the carbonyl group is afforded, we might expect that, if any reaction takes place, the end-product

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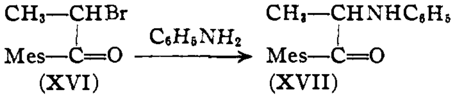
(12) Pictet, *Ber.*, **19**, 1064 (1886).

(13) *Cf.* von Auwers, Ludewig and Müller, *Ann.*, **526**, 143 (1936); von Auwers, Pötz and Noll, *ibid.*, **535**, 219 (1938).

(14) *Cf.* Julian and Passler, THIS JOURNAL, **54**, 4756 (1932).

would be the α-anilino ketone (XVII) and no trace of an isomer would be formed. We should further expect to secure no indole from (XVII) because of hindrance to addition of the "second" mole of aniline to the carbonyl group. This is actually the case.

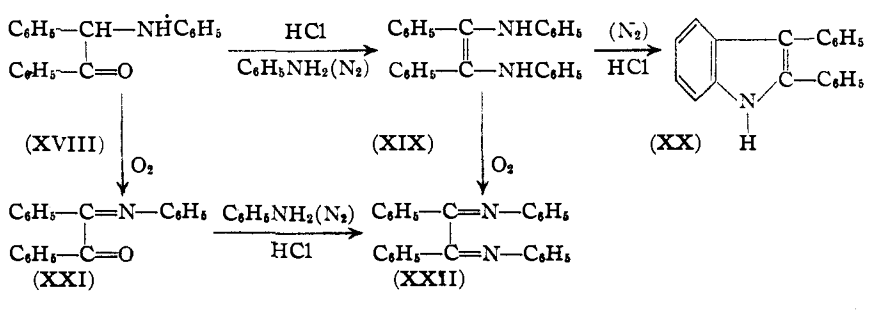


$$\begin{array}{c}CH_3—CHBr\\ |\\ Mes—C{=}O\\ (XVI)\end{array} \xrightarrow{C_6H_5NH_2} \begin{array}{c}CH_3—CHNHC_6H_5\\ |\\ Mes—C{=}O\\ (XVII)\end{array}$$

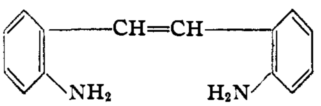
α-Bromopropiomesitylene does not react with aniline at ordinary temperature as does α-bromopropiophenone. Only when the two have been heated to at least 100° does perceptible reaction take place. The colorless end-product (XVII) was puzzling for a long time because we had confidently expected it to be yellow in view of long experience with α-anilino-alkyl aryl ketones. We are satisfied, however, that it has the structure represented by (XVII) and it remains for subsequent investigations to explain this peculiar deviation due to the mesityl group.[15]

Desylaniline (XVIII) has served as an excellent model for a study which affords additional evidence in support of the intermediate "aniline-anil" or diamine hypothesis. When desylaniline is heated for several hours with one molecule of aniline in the presence of a few drops of hydrochloric acid and in an atmosphere of nitrogen, 2,3-diphenylindole (XX) is obtained in excellent yield. When the same experiment is repeated, except that dimethylaniline is substituted for aniline, no indole is obtained and 98% of unchanged desylaniline is recovered. This failure of "direct ring closure" in the presence of a substance so closely related to aniline offers strong support for the participation of a "second" mole of aniline in the reaction. It now remains to attempt an actual isolation of such an intermediate diamine under conditions which leave no doubt that it is the intermediate in the reaction.

When the experiment with desylaniline, aniline and hydrochloric acid described in the foregoing paragraph is repeated in the same manner except that oxygen is bubbled through the reaction mixture during the entire course of the reaction, benzil dianil (XXII) is obtained. Whether this can be considered evidence for the formation of the intermediate unsaturated diamine (XIX) depends in part on whether desylaniline alone, without aniline, is transformed on heating in the presence of oxygen into benzil monoanil (XXI), and whether the latter in turn is transformed with aniline and hydrochloric acid into the dianil. Both of these reactions take place with ease, and indeed these reactions we find constitute the best methods of obtaining the mono- and dianil pure and in good yield.



Thus the formation of benzil dianil in this reaction with oxygen constitutes no explicit proof of the intermediate formation of the "aniline-anil" (XIX). Likewise the fact that Strain secured 2,3-diphenylindole (XX) from (XIX) also does not constitute unequivocal proof that (XIX) is the intermediate in the reaction by which desylaniline (XVIII) is converted into the indole (XX). A compound such as (XIX) might be expected to undergo ring closure to indole with loss of aniline, just as Thiele and Dimroth[16] found that *o,o'*-diaminostilbene (XXIII) was readily converted into indole on heating in the presence of hydrochloric acid. The two reactions may be related and may involve an ortho shift. This still does not complete the proof, however, against the contention of Crowther, Mann and Purdie,[2b] that desylaniline (XVIII) may undergo the "ortho" shift and ring closure to 2,3-diphenylindole, without interaction with a second mole of aniline.



(XXIII)

Final proof that the second mole of aniline participates in the reaction, with (XIX) as the intermediate, came from the isolation of desylaniline anil (XIX) from the reaction mixture resulting on heating desylaniline (XVIII) with aniline in the presence of hydrochloric acid. From our experience with the dianil formation discussed above we found that although both aniline-anil formation and ring closure to indole are catalyzed by hydrochloric acid, the rate of the latter reaction is definitely slower than that of the former. Thus, by stopping the reaction at definite intervals we were finally able to arrive at conditions whereby reasonably pure desylaniline anil was isolated, identical with the compound prepared by Strain. We furthermore divided our product into two parts, one of which was converted in excellent yield into the dianil with oxygen, and the other in equally as excellent yield into the indole with hydrochloric acid.

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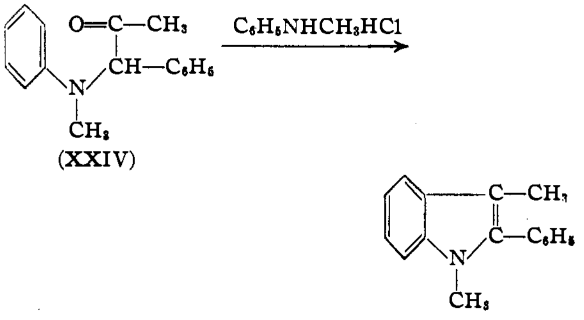
(15) *Cf.* Kohler and Barnes, THIS JOURNAL, **56**, 211 (1934); Barnes, *ibid.*, **57**, 937 (1935).

(16) Thiele and Dimroth, *Ber.*, **28**, 1412 (1895).

These experiments together with those on α-bromopropiomesitylene show definitely that Step 2 of the Bischler hypothesis does occupy a place in the mechanism of this complex system of reactions. Whether every case of indole formation by this reaction takes place through the intermediate diamine is yet to be determined, in view of the many reactions that already have been found to take place simultaneously in such a reaction system.

Step 3. The Elimination of Arylamine from the Intermediate Diamine.—The isolation of the intermediate diamine (XIX), recorded above, casts serious doubt upon the correctness of the sweeping generalizations postulated by Verkade and Janetzky,[17] since every single experimental finding of theirs can be explained by the formation of an intermediate diamine and preferential elimination of arylamine equally as readily as or more readily than by their postulated cleavage of the arylamino ketone and reaction of the cleaved "ketone component" with the added amine. These authors base their conclusions upon the following experiments.

1. They heat 1-phenyl-1-phenylmethylamino-propanone (XXIV) with methylaniline hydrochloride and secure 1,3-dimethyl-2-phenylindole (XXV).

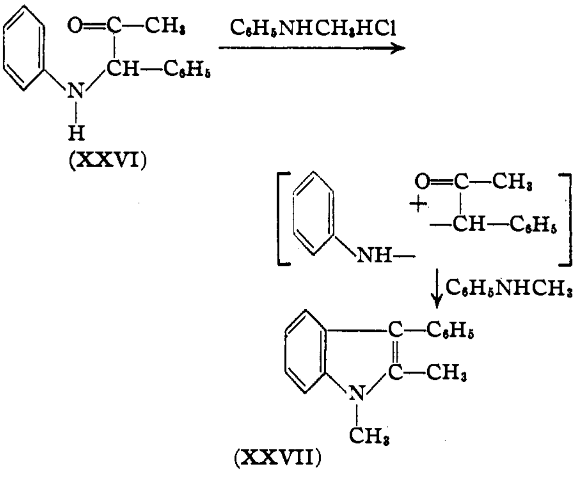


(XXIV)

(XXV)

They reject the Bischler idea of intermediate diamine formation and call this "indole formation under true ring closure," yet they use equal weights of amino ketone (XXIV) and methylaniline hydrochloride.

2. They heat 1-phenyl-1-phenylamino-propanone (XXVI) with six times its weight of methylaniline hydrochloride and secure 1,2-dimethyl-3-phenylindole (XXVII).



(XXVI)

(XXVII)

This latter case they call "indole formation under apparent ring closure" and postulate a cleavage of (XXVI) as indicated above but reject a diamine such as could be formed from (XXVI). In their first paper where they were dealing with phenyl indoles without the complication of the methyl group they attributed this purely to rearrangement of the phenyl group. In this latter case they naturally recoil from the idea of both phenyl and methyl groups rearranging and have, therefore—in the absence of isolated intermediates—no adequate explanation.

The following comments can be made with reference to this work:

1. It is obvious that the formation of (XXV) from (XXIV) could be as readily explained with the aid of the diamine hypothesis as by direct ring closure, especially since it was necessary to use methylaniline hydrochloride to induce ring closure. Had they effected ring closure in good yield in the presence of dimethylaniline hydrochloride instead, their case would have appeared to have merit.

2. The conversion of (XXVI) into (XXVII) is equally as readily accounted for by assuming diamine formation from (XXVI), followed by loss of aniline, rather than methylaniline, from the diamine.

3. There is ample precedent in the indole series for preferential ring closure to (XXVII) rather than to 1-phenyl-2-methylindole. Chloracetanilide, for example, undergoes ring closure to oxindole with much greater difficulty and in much poorer yield than does N-methylchloracetanilide to 1-methyloxindole. Indeed the temperatures necessary for ring closure to oxindoles not substituted onto nitrogen are as much as 100° higher than for the N-methyl analogs. Similarly oxanilic acid chloride ($C_6H_5NH—CO—CO—Cl$) does not give isatin under attempted ring closure with aluminum chloride while N-methyloxanilic acid chloride gives 1-methyl-isatin readily under such conditions. Likewise dimethyloxanilide ($C_6H_5—NCH_3—CO—CO—NCH_3—C_6H_5$) gives 1-methyl-isatin on ring closure, while the monomethylated derivative, N-methyloxanilic acid anilide ($C_6H_5—N(CH_3)—CO—CO—NHC_6H_5$) likewise yields 1-methyl-isatin and no trace of isatin.[18] These facts clearly indicate that one would expect the intermediate diamine, resulting from the reaction of (XXVI) with methylaniline to yield (XXVII), and such evidence lends more support to the

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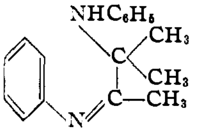
[17] See ref. 2c, pp. 775–779.

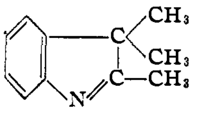
[18] Unpublished results from this Laboratory; private communication from R. Stollé to senior author, 1935; *cf.* Stollé, *J. prakt. Chem.*, [2] **128**, 1 (1930).

Bischler hypothesis than to the claims of Verkade and Janetzky.

Finally, to complete our entire survey of the proposals in the Bischler mechanism, we must consider the last portion of Step 3, namely, that indole formation may proceed through the indolenine form of the indole, which means that in certain cases the "diamine" is actually stabilized under the conditions of the experiment as an "aniline-anil." There is some justification for this point of view. Garry[19] has shown clearly that true "aniline-anils" like (XXVIII) actually give indolenines like (XXIX) when heated in the presence of hydrochloric acid.



(XXVIII)



(XXIX)

It should be noted that in certain of the experiments by Verkade and Janetzky employing methylaniline discussed above no true "aniline-anils" can exist and this assumption of Bischler is not necessary for ring closure.

The experiments recorded in this paper justify on the whole the Bischler hypothesis, with modifications. They do not rule out of consideration "direct" ring closure with loss of water, and until more evidence is obtained we prefer to take the point of view that both reactions may take place, the evidence at present being still predominantly in favor of the Bischler hypothesis of intermediate diamine formation.

Experimental

Anilino Ketones from α-Bromopropiophenone and Aniline.—A solution of 13.4 g. of α-bromo-propiophenone and 12.0 g. of aniline in 20 ml. of ethanol was allowed to stand for two hours. Heat developed slowly and the color changed from yellow to red. Some aniline hydrobromide had separated. The mixture was diluted with water and extracted with ether. The ether layer was washed well with water and dried. After removal of solvent, the residue was crystallized from ethanol yielding 7.0 g. of a mixture melting over the range 60–65°. The mixture could not be separated by crystallization from methanol.

In one instance, a more dilute methanolic solution of the reactants was seeded with the pure compound and a small quantity of the yellow anilino compound was isolated. The yield amounted to 0.5 g., m. p. 100–103°, from 3.0 g. of α-bromopropiophenone.

α-Anilinopropiophenone.—A solution of 13.8 g. (0.064 mole) of α-bromopropiophenone and 7.4 g. (0.08 mole) of aniline in 50 ml. of ethanol containing 8.4 g. (0.1 mole) of sodium bicarbonate was stirred rapidly for seven hours at room temperature and one hour at reflux temperature. The yellow solid which separated upon dilution with water was filtered, washed with water, partially dried and crystallized from ethanol. There resulted 12.1 g. (83%) of pale yellow prisms melting at 100–102°.

α-Anilinobenzyl Methyl Ketone.—A mixture of 3.5 g. of α-bromobenzyl methyl ketone and 3.5 g. of aniline in 10 ml. of ethanol was allowed to stand for several hours. Shortly after mixing, heat was developed and the color progressively changed from yellow to deep red. At this point, the solution was poured into water and extracted with ether. The ether solution was washed with 2% hydrochloric acid, water, dilute sodium carbonate solution and water. The solid residue remaining after removal of solvent from the dried solution was crystallized from methanol yielding 2.1 g. (57%) of slightly yellow needles melting at 87–90°. Recrystallization of a 1.1-g. sample from methanol gave 0.8 g. of white needles melting at 89–92°.

The same anilino compound was obtained in a better yield by the method described by Verkade and Janetzky.[2c]

α-Anilinopropiomesitylene.—A solution of 10 g. of α-bromopropiomesitylene in 25 ml. of aniline was refluxed for one hour. During this period, the color changed to deep red and some solid separated. The mass was taken up in ether and water. The ether layer was washed with water. Titration of the combined aqueous liquors indicated that 96% of the theoretical amount of halogen had been liberated. The ether solution was further washed with 2% hydrochloric acid (900 ml. portion-wise), water, dilute sodium hydroxide, water several times and dried. The residue, after removal of solvent, yielded 7.2 g. of sirup boiling over the range 100–230° at 4 mm. This was separated into two fractions by distillation at 5 mm.; one an oily fraction of 2.3 g. which distilled up to 150° and another of 4.7 g. distilling at 150–250°. The first fraction which proved to be free of nitrogen was reserved for later study.

The second fraction which solidified upon standing was triturated with cold petroleum ether (b. p. 36–60°) to give 2.1 g. of a white solid melting at 71–73.5°. Several recrystallizations from petroleum ether gave white needles melting at 72.5–74.5°.

Anal. Calcd. for $C_{18}H_{21}ON$: C, 80.85; H, 7.92; N, 5.23. Found: C, 80.67; H, 7.21; N, 5.31.

This material formed a sulfate melting at 180–182° and a hydrochloride melting at 190–193°. In an attempt to form an indole, this aniline compound was recovered.

Reduction of α-Anilinopropiomesitylene.—A suspension of 0.9 g. of the anilino compound in 40 ml. of 15% sulfuric acid was treated with 5 g. of zinc dust and warmed on a steam-bath for two and one-half hours. The solid slowly went into solution. The mixture was extracted with ether and the ether solution washed with water, dilute sodium bicarbonate, water and dried. Upon removal of solvent, 0.5 g. of a colorless oil remained. This material was dissolved in 25 ml. of absolute ethanol and treated portionwise with 3 g. of sodium metal. To speed the reaction to completion, the volume was increased to 65 ml. An ether extract of the diluted reaction solution was washed, dried and distilled in a bulb tube. The colorless, oily distillate, when treated with 2 ml. of phenyl isocyanate for ten minutes at steam-bath temperature, yielded 0.5 g. of a white solid melting at 135–141°. One recrystallization from ligroin (b. p. 88–98°) produced needles melting at 142–144°. This material gave no depression in melting point when mixed with the phenylurethan of mesitylethylcarbinol.[20]

Anilino Ketones from α-Bromo-β-phenylpropiophenone and Aniline.—A mixture of 23.0 g. of α-bromo-β-phenylpropiophenone, 22 ml. of aniline and 50 ml. of ethanol was refluxed for two hours. The red solution was chilled, diluted with water and extracted with ether. The extract was washed successively with water, dilute hydrochloric acid (1:10), 5% sodium hydroxide solution and water. The dried solution was then concentrated to the point of crystallization and cooled. The colorless needles of α-anilinodibenzyl ketone were separated, washed with ether and dried. This ketone, 5.2 g., melted at 126°.

Anal. Calcd. for $C_{21}H_{19}ON$: C, 83.68; H, 6.37. Found: C, 83.47; H, 6.46.

The residue from the ethereal filtrate was crystallized from methanol yielding 8.7 g. of the yellow α-anilino-β-phenylpropiophenone melting at 102–104°

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(19) Garry, *Compt. rend.*, **211**, 399 (1940); **212**, 401 (1941); *Ann. chim.*, **17**, 5 (1942).

(20) A. Klages, *Ber.*, **35**, 2245 (1902).

Anal. Calcd. for $C_{21}H_{19}ON$: C, 83.68; H, 6.37. Found: C, 82.82; H, 6.39.

By fractional crystallization of the remaining material from ether and methanol, there was obtained 1.0 g. of the colorless ketone and 2.0 g. of the yellow isomer.

α-Hydroxy-β-phenylpropiophenone and α-Hydroxydibenzyl Ketone.—Five grams of potassium formate was added to 10 g. of α-bromo-β-phenyl-propiophenone in 30 ml. of methanol and the mixture refluxed for five hours. It was then diluted with water and extracted with ether. The ethereal solution after washing with water and drying was concentrated *in vacuo* and the residue crystallized from ether–petroleum ether (b. p. 35–60°). The product, 5.7 g. of α-hydroxy-β-phenylpropiophenone, melted at 66°.

Hydrolysis of α-bromo-β-phenylpropiophenone with water alone, or with sodium bicarbonate in aqueous ethanol, gave poor yields of this hydroxy ketone. With sodium bicarbonate, the isomeric α-hydroxydibenzyl ketone was also formed. In one experiment, 9.0 g. of the α-bromo ketone gave 1.2 g. of α-hydroxy-β-phenylpropiophenone and 1.1 g. of α-hydroxydibenzyl ketone melting at 116°.

The lower melting isomer was partially transformed into the higher melting one by heating with sodium bicarbonate in aqueous alcohol. Thus by refluxing for one hour a mixture of 5.0 g. of α-hydroxy-β-phenylpropiophenone, 75 ml. of methanol and 15 ml. of water containing 0.5 g. of sodium bicarbonate, there was obtained 1.8 g. of the isomeric α-hydroxydibenzyl ketone melting at 116° and 2.8 g. of the original ketone.[21]

α-Anilino-β-phenylpropiophenone.—A mixture of 5.8 g. of α-bromo-β-phenylpropiophenone, 3.0 g. of aniline, 3.4 g. of sodium bicarbonate in 20 ml. of ethanol was refluxed with vigorous agitation for four hours. Upon adding 50 ml. of water to the mixture, a yellow oil separated which solidified on standing overnight. The solid was dissolved in ether and the ethereal solution washed with dilute hydrochloric acid and water. Crystallization from methanol of the residue from the dried ether solution gave 4.2 g. of the yellow α-anilino-β-phenylpropiophenone melting at 103–105°. An additional 0.4 g. (m. p. 102–104°) was obtained from the mother liquor. None of the colorless isomer was obtained.

Reaction of α-Hydroxy-β-phenylpropiophenone and Aniline.—A solution of 2.0 g. of α-hydroxy-β-phenylpropiophenone in 6 ml. of aniline was heated on a steam-bath for two hours. The solution was then diluted with water and extracted with ether. The extract was washed successively with dilute hydrochloric acid, dilute sodium hydroxide and water. Concentration of the dried solution gave 1.5 g. of the colorless, crystalline α-anilinodibenzyl ketone melting at 127°. None of the yellow isomer was obtained.

A similar reaction mixture to which two drops of concd. hydrochloric acid was added appeared to react with greater ease. After one-half hour on a steam-bath, the mixture was worked up as described above. The product was the colorless α-anilinodibenzyl ketone (1.6 g.). There was no evidence of the presence of the yellow isomer.

Reaction of α-Hydroxydibenzyl Ketone and Aniline.—Two grams of α-hydroxydibenzyl ketone and 6 ml. of aniline were heated on a steam-bath for two hours. The yellow solution after dilution with water was extracted with ether and the ethereal solution washed successively with water, dilute hydrochloric acid, dilute sodium hydroxide and water. The dried solution was concentrated and the residue crystallized from methanol. There resulted 1.4 g. of yellow α-anilino-β-phenylpropiophenone which melted at 97–100°. One recrystallization from methanol raised the melting point to 105°. None of the colorless isomer was evident.

A similar solution to which two drops of concd. hydrochloric acid was added reacted more rapidly. After one-half hour on the steam-bath, the reaction mixture was worked up as previously described. Crystallization from methanol gave 1.7 g. of a mixture of colorless needles and yellow prisms. The mixture was separated into the isomers by fractional crystallization from ether and methanol and also mechanically. This afforded 1.23 g. of the yellow α-anilino-β-phenylpropiophenone and 0.27 g. of colorless α-anilinodibenzyl ketone.

Rearrangement of α-Anilinopropiophenone.—A solution of 2.25 g. (0.01 mole) of the yellow anilino compound and 1.74 g. (0.01 mole) of aniline hydrobromide in 25 ml. of ethanol was refluxed for two hours. The chilled solution was diluted with water and the solid collected, washed with water and dried. The solid, 2.2 g., melted over a range of 72–90°. By fractional crystallization from ethanol, it was separated into 0.99 g. of yellow prisms (m. p. 95–103°) and 0.42 g. of white needles (m. p. 87–90°). Recrystallization of each fraction from methanol gave materials melting at 100–103° and 89.5–91°. These showed no depression in melting point when mixed with samples of α-anilinopropiophenone and α-anilinobenzyl methyl ketone, respectively.

Rearrangement of α-Anilinobenzyl Methyl Ketone.—A solution of 2.25 g. of the white anilino compound and 1.74 g. of aniline hydrobromide in 25 ml. of ethanol was refluxed for two hours. After dilution with water, the separated gum was extracted with ether and washed with water. The sirup remaining after removal of solvent from the dried ethereal solution was crystallized from methanol. The product, 0.96 g. of a mixture, melted at 70–77°. The mother liquor was dark and possessed a strong isonitrile-like odor. By fractional crystallization from methanol, the mixture was separated into 0.21 g. of yellow prisms (m. p. 94–103°) and 0.25 g. of white needles (m. p. 88–91°). Recrystallization of each fraction from methanol gave materials melting at 100–102.5° and 89–92°. These showed no depression in melting point when mixed with samples of α-anilinopropiophenone and α-anilinobenzyl methyl ketone, respectively.

Rearrangement of α-Anilino-β-phenylpropiophenone.—To 2.0 g. of pure α-anilino-β-phenylpropiophenone in 5.0 ml. of aniline, there was added one drop of concd. hydrochloric acid and the mixture was heated on a steam-bath for one-half hour. The solution was taken up in ether and washed successively with water, dilute hydrochloric acid, dilute sodium hydroxide and water. The residue from the dried ethereal solution upon crystallization from methanol gave a mixture of colorless needles, yellow prisms and a brown gum. Several crystallizations from methanol were required to remove the brown gum thus enabling a separation of the crystalline products from a concentrated solution. The mixture of colorless and yellow crystals (0.6 g.) was separated manually and by fractional crystallization. There resulted 0.4 g. of unchanged α-anilino-β-phenylpropiophenone and 0.04 g. of colorless needles which proved to be the isomeric α-anilinodibenzyl ketone. The combined mother liquors yielded an additional 0.7 g. of the crystalline mixture.

Rearrangement of α-Anilinodibenzyl Ketone.—Two grams of the colorless anilino ketone was treated in the fashion described above. Concentration of the dried ethereal solution gave 1.0 g. of unchanged ketone, m. p. 126°. The ether was removed from the mother liquor and the residue crystallized from methanol. The resulting mixture of colorless needles and yellow prisms was separated mechanically. The colorless needles (0.02 g.) proved to be additional unchanged ketone. The yellow prisms (0.03 g.) upon recrystallization from methanol melted at 103–104° and showed no depression in melting point when mixed with a sample of α-anilino-β-phenylpropiophenone.

In another experiment α-anilinodibenzyl ketone was treated with hydrochloric acid in the absence of aniline. Two grams of the colorless ketone was melted at 130–135° in a metal bath. Upon addition of two drops of concd. hydrochloric acid, the melt became semi-solid. This was heated at 130–135° with agitation for one hour. It was then dissolved in ether with the aid of dilute alkali. The ethereal solution was washed with water, dried and concentrated to the point of crystallization. In this manner, 1.8 g. of the unchanged colorless ketone was recovered. The residue from the mother liquor was crystallized from

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[21] *Cf.* Kohler and Kimball, This Journal, **56**, 729 (1934).

methanol. The yellow prisms were separated from solution and deposited oil and recrystallized from methanol yielding 0.1 g. of material melting at 105–106°. This gave no depression in melting point when mixed with a sample of α-anilino-β-phenylpropiophenone.

2-Phenyl-3-methylindole

(a) **From α-Bromopropiophenone.**—A solution of 10.5 g. of bromopropiophenone in 30 ml. of aniline was refluxed for one hour under a nitrogen atmosphere. The cooled solution was taken up in methanol and ether, and washed with water. Excess aniline was separated from the ethereal solution by repeated washing with 2% aqueous hydrochloric acid. After washing with dilute sodium bicarbonate solution and water, the dried solution was concentrated and the residue crystallized from methanol–petroleum ether (35–60°). Three crops of crude 2-phenyl-3-methylindole were obtained, 8.6 g., m. p. 90–94°. The residue contained in the mother liquor of crystallization was distilled at 5 mm. over a range of 150–200°. The yellow distillate gave an additional 0.5 g. of the crude indole, m. p. 85–93°, upon crystallization from methanol–petroleum ether (35–60°). Recrystallization of the crude indole from methanol–petroleum ether yielded 7.5 g. of material melting at 93–95°.

The oily residue from the crystallization of the distillate yielded 1.0 g. of a brick-red picrate melting at 150–152°.

(b) **From α-Bromobenzyl Methyl Ketone.**—A solution of 15.3 g. of the bromoketone in 30 ml. of aniline was allowed to stand at room temperature under a nitrogen atmosphere until the initial reaction had subsided. During this period, the solution became quite dark and warm. Considerable anilinium bromide separated. The mixture was then refluxed under nitrogen for one hour, allowed to cool and dissolved in ether and water. The ethereal solution was washed with water several times, 2% aqueous hydrochloric acid repeatedly (900 ml. total volume), then dilute sodium bicarbonate solution and finally water. The dark, sirupy residue remaining after removal of solvent from the dried solution was distilled at 4 mm. over a range of 180–200°. Considerable tarry residue having an isonitrile-like odor remained. The yellow distillate which crystallized upon standing was triturated with petroleum ether (35–60°) and filtered. The resulting indole, 7.8 g., melted at 90–92.5°. One recrystallization from ligroin (89–99°) gave 6.9 g. of prisms which melted at 92.5–94°. This showed no depression in melting point when mixed with the indole from α-bromopropiophenone. The residue from the petroleum ether wash of the crystalline indole was converted to a picrate melting at 151–152°.

(c) **From α-Anilinopropiophenone.**—A solution of 10.0 g. of the anilino ketone and 5.0 g. of aniline hydrochloride in 40 ml. of aniline was refluxed for one hour under nitrogen. The solution was then taken up in ether and water and extracted with ether. The ether layer was washed with water, portion-wise with 900 ml. of 2% hydrochloric acid, dilute sodium bicarbonate solution and water. The residue remaining after removal of solvent from the dried solution was distilled at 1 mm. and a bath temperature of 150–160°. A very small residue of tarry material remained. The distillate which solidified on standing weighed 8.9 g. (96.5%) and melted at 88–95°. One recrystallization from ligroin (b. p. 88–98°) yielded 8.1 g. of colorless prisms melting at 93–94.5°. This material gave no depression in melting point when mixed with an authentic sample of 2-phenyl-3-methylindole.

(d) **From α-Anilinobenzyl Methyl Ketone.**—This anilino ketone was treated in the same manner as described above for its isomer. Seven grams of the ketone yielded 6.1 g. (94.5%) of the crude distillate melting at 85–93°. A recrystallization from ligroin (b. p. 88–98°) gave 5.6 g. of colorless prisms melting at 94–95°. This also proved to be 2-phenyl-3-methylindole.

2-Phenyl-3-benzylindole and 2-Benzyl-3-phenylindole

(a) **From α-Bromo-β-phenylpropiophenone.**—A mixture of 4.0 g. of the bromo ketone and 12.0 ml. of aniline was refluxed in an atmosphere of nitrogen for one hour. The dark solution was taken up in ether and washed with water, dilute hydrochloric acid, dilute alkali and water. After removal of solvent from the dried solution, the residue was distilled at 3 mm. The fraction distilling at 185–193°, 2.9 g., was crystallized from ether–petroleum ether (b. p. 35–60°). The product, 1.2 g. of crystalline material, was a mixture of 2-phenyl-3-benzylindole and 2-benzyl-3-phenylindole melting at 80–97°.

The separation of the isomeric indoles proved tedious. It was accomplished by repeated crystallization from ether–petroleum ether of varying concentrations. During these crystallizations, the two indoles both crystallized but in different forms. As a rule the indole present in greater quantity deposited as fine crystals and the indole present in lesser quantity formed clusters of crystals. After mechanical separation the isomers were purified by crystallization. When relatively pure each isomer could be nicely crystallized from ligroin (b. p. 88–98°).

There was obtained 0.6 g. of the known 2-benzyl-3-phenylindole[22] melting at 101°. It is readily soluble in ether, methanol and benzene, but less soluble in petroleum ether (b. p. 35–60°). The other isomer, 2-phenyl-3-benzylindole (0.1 g.), melted at 119°.

Anal. Calcd. for $C_{21}H_{17}N$: C, 89.05; H, 6.01. Found: C, 89.17; H, 6.43.

(b) **From α-Anilinodibenzyl Ketone.**—A mixture of 10.0 g. of α-anilino-dibenzyl ketone, 40 ml. of aniline and 5.0 g. of aniline hydrochloride was gently refluxed under nitrogen for one hour. After chilling and making alkaline, the mixture was extracted with ether and the ethereal solution washed successively with dilute hydrochloric acid, dilute alkali and water. The residue oil from the dried solution was distilled at 3 mm. The fraction, 7.0 g., distilling at 185–195° bath temperature was crystallized from petroleum ether (b. p. 35–60°) yielding 6.4 g. (68%) of a mixture of indoles melting at 82–98°. The isomeric indoles were separated as described above. There resulted 3.0 g. of 2-benzyl-3-phenylindole melting at 100–101° and 1.7 g. of 2-phenyl-3-benzylindole melting at 118–119°.

(c) **From α-Anilino-β-phenylpropiophenone.**—Ten grams of the yellow anilino ketone was treated with aniline and aniline hydrochloride as described above. The distillation fraction gave 7.7 g. (80%) of an indole mixture melting at 82–97°. When separated in the manner previously described, the mixture gave 4.1 g. of 2-benzyl-3-phenylindole melting at 100–101° and 1.8 g. of 2-phenyl-3-benzylindole melting at 118–119°.

Desylaniline.—Desylaniline was prepared by heating a mixture of equivalent quantities of benzoin and aniline containing two drops of concd. hydrochloric acid in a metal bath at 140–150° for two hours. The generated water vapor was allowed to escape during the last half hour. The reaction mixture was dissolved in the least quantity of boiling ethanol and allowed to crystallize. For further work, the crude product was recrystallized from ethanol giving an 80% yield of desylaniline melting at 98–100°.

2,3-Diphenylindole from Desylaniline.—Ten grams of desylaniline in 8 ml. of aniline containing two drops of 10% hydrochloric acid was heated under nitrogen in a metal bath at 150–160° for six hours. Crystallization of the chilled solution from ethanol gave 1.6 g. of the indole melting at 123–126°. The mother liquor was dissolved in ether and washed repeatedly with 2% hydrochloric acid and water. The oil remaining after removal of solvent from the dried solution crystallized from methanol yielding 6.3 g. of the diphenylindole melting at 123–126°. The total yield, 7.9 g., was 84% of theoretical.

Benzil Dianil (a) Condensation of Benzil Monoanil with Aniline.—Five grams of the monoanil in 4 ml. of aniline containing three drops of 10% hydrochloric acid at 150–160° under nitrogen for one hour. The solution turned dark and possessed some green fluorescence. Its chilled methanol solution deposited 4.6 g. (71%) of the dianil melting at 138–145°. Recrystallization from methanol gave a product melting at 140–145°.

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(22) Beilstein, Vol. 20, p. 523.

(b) **From Desylaniline.**—Ten grams of desylaniline in 8 ml. of aniline containing 2 drops of 10% hydrochloric acid was heated at 150–160° for 1.75 hours while passing oxygen through the solution. The dark solution was chilled, diluted with ethanol and seeded with dianil. There separated 3.0 g. of yellow dianil melting at 138–143°. Upon recrystallization from methanol the product melted at 143–145°. This gave no depression with material from the previously described preparations.

Preparation of Benzil Monoanil from Desylaniline. (a) **Oxygen.**—A solution of 10 g. of desylaniline in 8 ml. of dimethylaniline was heated at 150–160° in a metal bath for six hours while bubbling oxygen through the solution. The dark solution was taken up in ether and washed repeatedly with 2% hydrochloric acid to remove the dimethylaniline. Some resinous material was present. The ethereal layer was further washed with water, dilute sodium hydroxide and water. The dark sirup remaining after removal of solvent from the dried solution crystallized from a small volume of methanol yielding 5.8 g. (58%) of yellow monoanil melting at 103–106°.

The dark mother liquor upon further concentration gave 0.2 g. of a tan solid melting at 155–160°. The residue possessed a strong isonitrile-like odor. Recrystallization of the solid from methanol raised the melting point to 162–164°. This gave no depression in melting point when mixed with a sample of benzanilide.

(b) **Potassium Ferricyanide.**—A solution of 5.0 g. of desylaniline in 50 ml. of benzene and 100 ml. of ethanol was mixed with 100 ml. of water containing 2.0 g. of potassium hydroxide and 12.0 g. of potassium ferricyanide. The mixture was warmed to 60–70° and stirred for a period of three and one-half hours. It was then diluted with water and extracted with ether. The ethereal solution, after washing free of alkali and drying, was concentrated to an orange residue which crystallized from ethanol. The product, 3.4 g. (68%) of a yellow benzil monoanil, melted at 103–106°. The second crop proved to be a mixture (m. p. 75–83°) which could not be separated readily by crystallization.

Desylaniline Anil.—A mixture of 10 g. of desylaniline and 6 ml. of aniline containing four drops of concd. hydrochloric acid was heated under nitrogen (bubbled nitrogen through the solution) in a metal bath at 150–160° for fifteen minutes. The contents of the flask were allowed to cool to a viscous sirup, diluted with 50 ml. of absolute ethanol and then induced to crystallize by scratching. During the preceding stages and through the chilling period, the nitrogen atmosphere was maintained. The yellow-green solid was filtered on an assembly surrounded by carbon dioxide atmosphere. The solid was washed with 175 ml. of absolute ethanol. The last trace of solvent was removed *in vacuo*. The material weighed 7.0 g. and melted at 160–185°, after softening slightly at 155°.

Anal. Calcd. for $C_{26}H_{22}N_2$: C, 86.15; H, 6.12. Found: C, 85.87, 86.07; H, 6.22, 6.16.

The ethanol solution separated from the desylaniline anil was diluted with water and extracted with ether. The ether layer was washed with 900 ml. (portion-wise) of 2% aqueous hydrochloric acid, water, dilute sodium bicarbonate solution, water, dried and concentrated. The yellow solid which resulted from crystallization of the residue from methanol, weighed 1.1 g. and melted at 139–142°. This gave no melting point depression with an authentic specimen of benzil dianil. The methanolic mother liquor yielded a second crop of 1.3 g. which proved to be a mixture of desylaniline and the dianil.

2,3-Diphenylindole from Desylaniline Anil.—A 6.5-g. sample of desylaniline anil was dissolved in 10 ml. of aniline containing six drops of concd. hydrochloric acid and the solution refluxed for one and one-half hours under nitrogen. The solution was diluted with ether and washed with water, portion-wise with 900 ml. of 2% aqueous hydrochloric acid, then water, followed by dilute sodium bicarbonate solution and water. The orange sirup remaining after removal of solvent from the dried ethereal solution was distilled at 4 mm. over a range of 150–200°. The distillate upon crystallization from ligroin (89–99°) yielded 3.4 g. (70%) in two crops, of 2,3-diphenylindole melting at 124–125.5°.

Anal. Calcd. for $C_{20}H_{15}N$: N, 5.19. Found: N, 5.05.

The mother liquor of crystallization was treated with picric acid and 0.5 g. of brick-red picrate isolated. The needle-like crystals melted at 152–155° when crystallized from methanol.

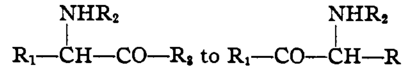
Benzil Dianil from Desylaniline Anil.—Dry air was passed through a solution of 2.2 g. of desylaniline anil in 50 ml. of benzene for one hour. After removal of benzene *in vacuo*, the residue when crystallized from methanol yielded 1.9 g. of a yellow solid melting at 139–142° (frothed at 128–130° and solidified). Recrystallization from methanol gave 1.7 g. of plates melting at 145–147°. A further recrystallization from ethanol did not change the melting point.

Anal. Calcd. for $C_{26}H_{20}N_2$: C, 86.62; H, 5.66. Found: C, 86.44; H, 5.95.

Acidic hydrolysis of the dianil gave benzil which formed a quinoxaline derivative melting at 123–126°.

Summary

1. The formation of substituted indoles in the reactions of α-hydroxy and α-halogenated ketones with arylamines has been reinvestigated. The mechanism which seems most probable is: (a) direct replacement of the α-halogen or α-hydroxy group by an arylamino group; (b) rearrangement of an arylaminoketone like



$$R_1-\overset{\overset{\displaystyle NHR_2}{|}}{CH}-CO-R_3 \text{ to } R_1-CO-\overset{\overset{\displaystyle NHR_2}{|}}{CH}-R_3,$$

this rearrangement usually resulting in an equilibrium mixture but conceivably at times consisting of mainly one isomer; (c) reaction of the arylamino ketone with a second mole of arylamine to form a diamine or aniline-anil; (d) ring closure with elimination of arylamine to form the indole.

2. The Bischler mechanism is probably sound for (a) and (c) above, but does not take account of (b) and is unsound in the hypothesis that at stage (d) the "first" molecule of arylamine taking part is the one eliminated.

3. The reaction between an α-bromo ketone and an arylamine is a complicated system and may involve simultaneously in the presence of atmospheric oxygen: (a) replacement reactions, (b) addition reactions, (c) rearrangement of anilino ketones, (d) monoanil formation, (e) dianil formation, (f) aniline-anil or diamine formation, (g) cleavage of arylamine from the diamine to form the indole.

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