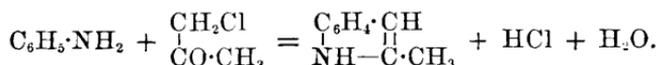


LXXII.—*Preparation of 2' : 3'-Diphenylindoles from Benzoïn and Primary Benzenoid Amines.*

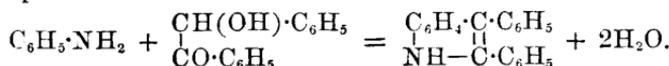
By FRANCIS R. JAPP, F.R.S., and T. S. MURRAY, D.Sc.

NENCKI and Berlinerblau were the first to show (*Ber.*, **20**, R. 753) that indoles could be obtained by the interaction of  $\alpha$ -halogen-aldehydes, or  $\alpha$ -halogen-ketones, with primary benzenoid amines. Thus, from chloraldehyde and aniline, they prepared indole itself, and from chloroacetone and aniline, 2'-methylindole ("methylketole"), the latter interaction occurring according to the equation



Numerous other substituted indoles have since been prepared in an analogous manner.

It occurred to us that it might be possible to replace the  $\alpha$ -halogen-ketones in the foregoing class of interactions by  $\alpha$ -hydroxy-ketones. We therefore heated a mixture of benzoïn, aniline, and zinc chloride, and found that E. Fischer's 2' : 3'-diphenylindole was formed according to the equation



In like manner, by employing orthotoluidine, paratoluidine,  $\alpha$ -naphthylamine, and  $\beta$ -naphthylamine, in place of aniline, we obtained respectively the corresponding diphenylorthotoluidindole, diphenyl-

paratoluindole, diphenyl- $\alpha$ -naphthindole, and diphenyl- $\beta$ -naphthindole.

The investigation had proceeded thus far when a paper appeared by Bischler and Fireman (*Ber.*, **26**, 1336), in which the preparation of these indoles (with the exception of diphenyl- $\alpha$ -naphthindole) by a different method was described. This method consisted in first acting on desylbromide with a primary benzenoid amine in the cold, so as to obtain a desylanilide, thus  $C_6H_5 \cdot CO \cdot CH(NH \cdot C_6H_5) \cdot C_6H_5$ , and then boiling this compound with an excess of amine, when, according to Bischler and Fireman, it is converted into an indole.

We were at once struck by the close agreement of the melting points of Bischler and Fireman's supposed new series of desylanilides with those of an already known and obviously very similar series, which had been prepared by Voigt (*J. pr. Chem.*, [2], **31**, 544; **34**, 2), by the action of primary benzenoid amines on benzoïn. Thus, by heating benzoïn with aniline, Voigt obtained a compound which he at first described as "benzoïn anidil" (desylanilide), but which he afterwards, and in our opinion on insufficient evidence, formulated as anilbenzoïn,  $C_6H_5 \cdot CH(OH) \cdot C(N \cdot C_6H_5) \cdot C_6H_5$ . By substituting paratoluidine and  $\beta$ -naphthylamine for aniline, he obtained analogous compounds. We subjoin the two series with the melting points assigned to them:—

<i>Voigt.</i>		<i>Bischler and Fireman.</i>
	M. p.	M. p.
Anilbenzoïn .....	99°	Desylanilide.....
Acetylanilbenzoïn .....	153	97—98°
Paratolilbenzoïn .....	144	Acetyl desylanilide..
$\beta$ -Naphthilbenzoïn .....	130	155
		Desylparatoluide ...
		145
		Desyl- $\beta$ -naphthalide
		131—132

We, therefore, prepared anilbenzoïn by Voigt's method and desylanilide by that of Bischler and Fireman, and found that the two preparations were absolutely indistinguishable. Simultaneous determinations of the melting points in the same bath gave 98—99° for both. The two series are therefore identical.

Judging, however, from the mode of formation from desylbromide and amines, the compounds are in all probability desylanilides, as assumed by Bischler and Fireman.

As Voigt's method of preparation is by far the simpler of the two, we resorted to it to obtain the substance required for our subsequent experiments.

Pure desylanilide, thus prepared, was boiled for two hours with four times its weight of aniline, as prescribed by Bischler and Fireman, in order to convert it into diphenylindole. To our surprise, not only was the greater part of the desylanilide unchanged, but not

a trace of the indole had been formed, as was shown by the fact that the product gave no coloration when a trace of solid sodium nitrite was added to its solution in concentrated sulphuric acid, whereas we have found that diphenylindole, when thus treated, gives an intense bluish-green coloration.

As, however, in another experiment, we were able to confirm Bischler and Fireman's statement that desylbromide when boiled with excess of orthotoluidine yields diphenylorthotoluidole, it occurred to us that in the latter case the liberated hydrobromic acid might have effected the condensation of the desylorthotoluide, which would be formed in the first instance, to the corresponding indole. We therefore repeated our experiment with desylanilide and aniline, but, before heating the mixture, added a little aniline hydrochloride, the hydrochloric acid of which might be expected to act like the hydrobromic acid in the preceding case. Under these altered conditions the condensation readily took place with elimination of water, and an excellent yield of diphenylindole was obtained.

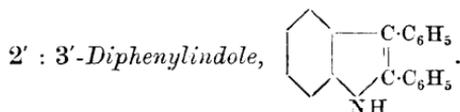
We are, therefore, forced to the conclusion that Bischler and Fireman must have employed in their experiments a desylanilide which had not been entirely freed from the amine hydrobromide that is formed along with it in their method of preparation, and that the hydrobromic acid was responsible for the condensation which they attributed to the amine alone.

Guided by these considerations, we next tried the effect of heating benzoïn with a mixture of aniline and aniline hydrochloride. Here Voigt's desylanilide would be first formed, and would then undergo condensation to diphenylindole. As a fact, we found that an excellent yield of diphenylindole could be thus obtained. The yield is better than by the zinc chloride method, as there is far less resinification. Substituting other benzenoid amines for aniline, we prepared by this new method the various other diphenylindoles already referred to. The yield of diphenyl- $\beta$ -naphthindole, however, is very poor, since, as Bischler and Fireman also found,  $\beta$ -dinaphthylamine is formed in large quantity. But a good yield of this indole may be obtained by the zinc chloride method.

We further found that all these diphenylindoles are deposited from an acetone solution with 1 mol. of "acetone of crystallisation." Most of these double compounds part very readily with their acetone; that of diphenyl- $\alpha$ -naphthindole, however, is permanent in air at the ordinary temperature, and this indole also yields stable crystalline compounds with 1 mol. each of methylethylketone and diethylketone. The unstable acetone compounds cannot always be obtained with certainty; sometimes the indole separates from the solution unchanged.

In the following account of our experimental results, we describe, under the heading of each indole, only that method of preparation which gave the best yield, except in the case of the first member of the series, diphenylindole, for the preparation of which both the zinc chloride method and the amine hydrochloride method are given.

## EXPERIMENTAL PART.



*Preparation from Benzoin, Aniline, and Zinc Chloride.*—The proportions employed were: benzoin, 21 grams; aniline, 15 grams; zinc chloride, 30 grams. The benzoin and zinc chloride were powdered together, mixed with the aniline, and the whole was heated in a retort over a free flame. The mass fused, water was given off, and as the temperature rose, the mixture became dark-coloured, whilst aniline distilled over along with the water. As soon as the evolution of water had ceased, the fused mass was poured into water, boiled, first with dilute hydrochloric acid and then with water, and extracted with boiling benzene. The tarry mass which remained on distilling off the benzene was distilled under reduced pressure. The distillate, which was solid when cold and of a clear brown colour, was redistilled; it came over about 272—275° under 17 mm. pressure, and was now of a clear yellow colour. It was recrystallised twice from benzene, from which it was deposited in rosettes of oblique prisms, and afterwards from light petroleum, from which it separated in large, snowball-like masses consisting of slender, colourless needles melting at 123—124°. The solutions displayed a blue fluorescence, as described by E. Fischer and by Bischler and Fireman.

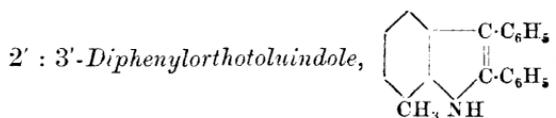
	Calculated for C <sub>20</sub> H <sub>15</sub> N.	Found.
N .....	5.20	5.16 per cent.

*Preparation from Benzoin, Aniline, and Aniline Hydrochloride.*—A mixture of 10.6 grams of benzoin, 16 grams of aniline, and 6.5 grams of aniline hydrochloride was heated to its boiling point in a small flask fitted with a short upright air condenser. By regulating the heating, the operation could be so conducted that the water which was formed during the reaction was driven off from the top of the condenser whilst the aniline flowed back into the flask. After heating for two hours no more water was given off. The fused mass was poured into water, and then shaken in a separating globe with ether and excess of dilute hydrochloric acid simultaneously, until every-

thing dissolved. The ethereal layer, which contained the diphenylindole, was separated; the ether was expelled by warming, and the substance which remained was purified, first by distillation under reduced pressure, and subsequently by recrystallisation from benzene and light petroleum, as in the previous experiment. The diphenylindole thus obtained, agreed in all its properties with that already described. The yield was about 75 per cent. of the theory. Dark-coloured bye-products are not formed in this process, so that the substance is easily purified.

*Acetone Compound.*—A solution of diphenylindole in acetone yielded, by spontaneous evaporation, crystals melting, when rapidly heated, between 80° and 90°. They effloresced on exposure to air.

0.3373 gram lost, on heating at 100°, 0.0592 gram = 17.55 per cent.  
Calculated for  $C_{20}H_{15}N, C_3H_6O$ : acetone = 17.74 per cent.



10.6 grams of benzoïn, 16.5 grams of orthotoluidine, and 7.5 grams of orthotoluidine hydrochloride were heated to the boiling point of the mixture for 2—3 hours. The crude product was extracted with boiling fairly strong hydrochloric acid to remove basic substances, and the residue distilled under reduced pressure. It was then further purified by recrystallisation.

The different crystalline forms and different melting points which we have observed with this substance lead to the conclusion that it is trimorphous. Owing to the complexity of the problem we venture to give the experimental details somewhat fully.

Thus, when the crude redistilled substance was dissolved in benzene and light petroleum then added, it was deposited in rosettes of flat prisms with bevelled ends, melting at 100—101°. When recrystallised from light petroleum, it melted at 101°; again recrystallised from a mixture of absolute alcohol and light petroleum, at 102°; again recrystallised from the same solvent at 102°. A little substance from the previous crop was used to start each crystallisation.

This specimen, melting at 102°, was analysed and gave figures agreeing with the expected formula  $C_{21}H_{17}N$ .

Calculated . . . .	C, 89.05	H, 6.01	N, 4.94 per cent.
Found . . . . .	C, 89.10	H, 6.22	N, 5.03 „

After standing in a stoppered bottle for two months the same specimen had become opaque, and was found to melt at 136°, previously softening at 128°. It had thus spontaneously changed into a

mixture of the two modifications melting respectively at 128° and 136°, which we describe later on.

Three specimens of diphenylorthotoluindole, which we prepared by three different methods—by the zinc chloride method, by the hydrochloride method, and by Bischler and Fireman's method of boiling desylbromide with orthotoluidine—all exhibited this behaviour; when the freshly distilled product was recrystallised, no matter from which of the foregoing solvents, crystals melting at temperatures between 99° and 102° were obtained; and these, on keeping, changed their melting point to 128—136°, as already described.

This modification of low melting point was obtained only from the freshly-distilled crude substance.\*

When the substance which had undergone the change of melting point was dissolved in a little boiling absolute alcohol, taking care that nothing was left undissolved, and then light petroleum added, the solution on standing deposited thick plates melting sharply at 128°.† Solutions in light petroleum, or in a mixture of benzene and light petroleum, yield the same forms, frequently, however, grouped together into rosettes. Recrystallisation does not change the form or the melting point. This is the modification described by Bischler and Fireman.

A third form, melting at 136°, may be obtained as follows:—

A small quantity of pure substance melting at 128° is introduced into a widish melting-point tube, which is then sealed up to prevent oxidation. The upper part of the tube is gently warmed, so as to melt all adhering particles. These solidify when cold, but in an amorphous form, which does not complicate the subsequent result. The tube is then heated in a sulphuric acid bath to 128°, so as to melt nearly the whole of the crystalline substance, after which the temperature is allowed to fall to about 126—127°, and kept there from 10 to 15 minutes. (If, through inadvertence, the whole of the substance has been melted, a fresh tube of substance must be taken and the experiment started anew.) At this slightly lower temperature

\* Since writing the above, we have made two further attempts to obtain this unstable modification, but without success. Two fresh specimens of orthotoluindole were prepared, one by the hydrochloride method, the other by the zinc chloride method; but in both cases the solutions of the crude distillate deposited only the stable form melting at 128°. We are not sure that in all three preparations above described the low-melting modification was obtained independently, *i.e.*, without starting the crystallisation. It was first obtained from a preparation made by the zinc chloride method.

† Very likely the unchanged pure substance melting at 102° would yield by recrystallisation this modification melting at 128°, if it were allowed to crystallise spontaneously, instead of starting it with its own crystals. Unfortunately we had no more of it to try the experiment.

the substance begins to resolidify. Needle-shaped crystals are seen to form in the melted substance, which is thus ultimately converted into a mass of needles. Finally the temperature may be raised to  $130^{\circ}$ , to make sure that none of the modification melting at  $128^{\circ}$  is left.

If now some pure substance melting at  $128^{\circ}$  be dissolved in boiling light petroleum, and the crystallisation be started with a few fragments of the foregoing resolidified substance, the solution will deposit large tufts of slender, colourless, silky needles, melting at  $136^{\circ}$ , and these are in like manner capable of inducing their own form of crystallisation in other solutions. When a little absolute alcohol is mixed with the light petroleum in this experiment, well-developed, concentrically-grouped, thin prisms are obtained, also melting at  $136^{\circ}$ . In order to obtain the modification melting at  $136^{\circ}$ , pure substance must be employed, for when the needles are introduced into a yellowish solution of impure substance in light petroleum, they do not grow, and the liquid deposits the tabular form melting at  $128^{\circ}$ . A solution of the pure acicular substance (m. p.  $136^{\circ}$ ) in light petroleum, when care is taken to leave nothing undissolved, and the crystallisation is allowed to start spontaneously, deposits the tabular form melting at  $128^{\circ}$ .\*

The following crystalline modifications of diphenylorthotoluindole are therefore to be distinguished:—

$\alpha$ . Flat prisms with bevelled ends, melting at  $102^{\circ}$ . Gradually changes at ordinary temperatures into a mixture of  $\beta$  and  $\gamma$ .

$\beta$ . Thick tabular crystals, melting at  $128^{\circ}$ . Stable at ordinary temperatures, but changed just below its melting point into  $\gamma$ .

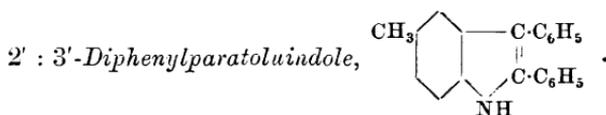
$\gamma$ . Acicular form, melting at  $136^{\circ}$ . Stable at all temperatures up to its melting point. Transformed by recrystallisation into  $\beta$ .

*Acetone Compound.*—A solution of diphenylorthotoluindole in acetone yielded, by spontaneous evaporation, efflorescent, flat prisms, containing acetone of crystallisation. When rapidly heated, they softened at about  $50^{\circ}$ , and melted at  $90^{\circ}$ .

0.1602 gram, heated at  $100^{\circ}$ , lost 0.0267 gram = 16.66 per cent.

Calculated for  $C_{21}H_{17}N, C_3H_6O$ : acetone = 17.01 per cent.

\* The acicular form melting at  $136^{\circ}$  was first accidentally obtained by us under conditions which we unfortunately did not note at the time. It was used to start subsequent crystallisations, and consequently, so long as we adhered to this practice, our specimens, when pure, always had this melting point. Indeed, we assumed that this was the true melting point of the substance, and in a preliminary note (*Ber.*, 26, 2641) called attention to the fact that Bischler and Fireman had not obtained a melting point higher than  $128^{\circ}$ . We were not at that time aware that this was the melting point of a distinct form. Afterwards, when we had recognised that all the supposed discrepancies were due to the existence of different modifications, it was some time before we succeeded in discovering the conditions under which the acicular form melting at  $136^{\circ}$  could be independently obtained.



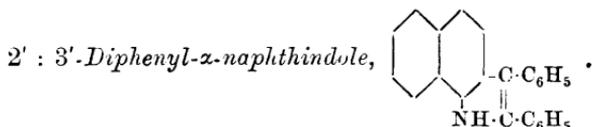
10.6 grams of benzoïn, 16.5 grams of paratoluidine, and 7.5 grams of paratoluidine hydrochloride were heated together as in the previous experiment. The product was shaken with ether and hydrochloric acid; the ethereal solution was dried with calcium chloride and allowed to evaporate spontaneously, when it deposited needle-shaped crystals melting constantly at 152—153°. The substance remaining after expulsion of the ether from the mother liquor was distilled under reduced pressure, and further purified by recrystallisation from a mixture of acetone and light petroleum. This product was identical with the foregoing. The total yield of pure substance was close upon 10 grams.

Analysis gave results agreeing with the formula  $C_{21}H_{17}N$ .

Calculated . . . .	C, 89.05	H, 6.01	N, 4.94	per cent.
Found . . . . .	C, 88.81	H, 6.20	N, 4.91	„

*Acetone Compound.*—This substance was obtained by the spontaneous evaporation of a solution of diphenylparatoluindole in acetone. The melting point of the crystals was very indefinite, and they rapidly effloresced on exposure to air.

0.2788 gram, heated at 100°, lost 0.0484 gram = 17.36 per cent.  
Calculated for  $C_{21}H_{17}N, C_3H_6O$ : acetone = 17.01 per cent.



This compound was not prepared by Bischler and Fireman.

10.6 grams of benzoïn, 21 grams of  $\alpha$ -naphthylamine, and 4.5 grams of  $\alpha$ -naphthylamine hydrochloride were heated to the boiling point of the mixture for 2½ hours. The proportion of hydrochloride is only half of that employed in the previous experiments, as it was found that the addition of a larger quantity prevented the fusion of the mixture. The product was treated exactly as in the preparation of diphenylindole by the hydrochloride method. The substance distilled under a pressure of 10 mm. at 315—330°. The crude distillate, which weighed 12.5 grams, was purified by recrystallisation from a mixture of acetone and light petroleum; this furnishes a practically pure product. For analysis, it was subsequently recrystallised from a mixture of ether and light petroleum, and from a

mixture of benzene and light petroleum. It formed tufts of slender needles, melting constantly at 140—141°. It is readily soluble in benzene, ether, and acetone, but only sparingly so in light petroleum.

Analysis gave figures agreeing with the formula  $C_{24}H_{17}N$ .

0.1566 gave 0.5162  $CO_2$  and 0.0772  $H_2O$ . C = 89.89; H = 5.48.

0.2021 „ 7.6 c.c. moist nitrogen at 17° and 762 mm. N = 4.37.

$C_{24}H_{17}N$  requires C = 90.28; H = 5.33; N = 4.39 per cent.

We have not overlooked the possibility of formulating the foregoing compound as a peri-derivative of naphthalene. In this case, however, the nitrogen ring would consist of six atoms, and the compound would not be an indole, a class to which, bearing in mind its close resemblance to the other indubitable diphenylindoles here described, we have preferred to assign it.

*Acetone Compound.*—This is very easily obtained. It crystallises from a solution of diphenyl- $\alpha$ -naphthindole in acetone, or even from the solution in a mixture of acetone and light petroleum, unless the petroleum greatly predominates. It forms oblique plates, generally grouped together in large rosettes, melting between 90° and 100°. The crystals do not effloresce when exposed to air.

0.6199 gram heated at 110° lost 0.0950 gram = 15.32 per cent.

Calculated for  $C_{24}H_{17}N, C_3H_6O$ : acetone = 15.38 per cent.

*Compound with Methyl Ethyl Ketone.*—Obtained, like the foregoing, using methyl ethyl ketone as a solvent. Large rosettes of flat prisms. Non-efflorescent.

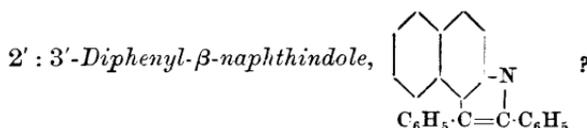
0.3305 gram lost, on heating, 0.0610 gram = 18.46 per cent.

Calculated for  $C_{24}H_{17}N, C_4H_8O$ : methyl ethyl ketone = 18.39 per cent.

*Compound with Diethyl Ketone.*—Obtained like the acetone compound, using diethyl ketone. Short, flat prisms or plates. Non-efflorescent.

0.1450 gram lost, on heating, 0.0309 gram = 21.31 per cent.

Calculated for  $C_{24}H_{17}N, C_5H_{10}O$ : diethyl ketone = 21.21 per cent.



As already mentioned, the hydrochloride method is not, any more than Bischler and Fireman's method, suited for the preparation of this compound. On performing the experiment in the manner described in the case of the other indoles, hardly any water is elimi-

nated, and the product consists mainly of  $\beta$ -dinaphthylamine. The zinc chloride method, however, gives a satisfactory yield of the indole.

21 grams of benzoïn, 21 grams of  $\beta$ -naphthylamine, and 50 grams of zinc chloride were heated together in a retort, the operation being conducted, and the product treated, as in the preparation of diphenylindole by the zinc chloride method. It was twice distilled under reduced pressure. On the second occasion it passed over at 330—340° under a pressure of 15 mm. It was recrystallised first from benzene, from which it separated in minute, granular crystals; then from a mixture of acetone and light petroleum, which deposited it in small rosettes of prisms of a greenish colour. The colour was removed by further recrystallisation from a mixture of alcohol and light petroleum and finally from alcohol alone. It melted constantly at 166—167°. (Bischer and Fireman give the melting point 153—158°, but state that, owing to the difficulty of getting rid of the  $\beta$ -dinaphthylamine which is formed in their process, their product was only approximately pure.)

Analysis gave figures agreeing with the formula  $C_{24}H_{17}N$ .

Calculated . . . .	C, 90.28	H, 5.33	N, 4.39	per cent.
Found . . . . .	C, 89.90	H, 5.46	N, 4.35	„

Of course this compound might be a  $\beta\beta$ -naphthalene derivative [2 : 3], instead of as here represented, an  $\alpha\beta$ -derivative [1 : 2]. Analogy, however, is strongly in favour of the assumption which we have made.

*Acetone Compound.*—By spontaneous evaporation of a solution of diphenyl- $\beta$ -naphthindole in acetone, large prismatic crystals containing acetone of crystallisation were obtained. They parted with their acetone so rapidly, especially on heating, that they gave only the melting point of the indole itself. For analysis they were dried between folds of filter paper.

0.7660 gram, heated at 100°, lost 0.1170 gram = 15.27 per cent.  
Calculated for  $C_{24}H_{17}N, C_3H_6O$  : acetone = 15.38 per cent.

#### *Colour Reactions of the 2' : 3'-Diphenylindoles.*

*With Nitrous acid.*—When any of these indoles is dissolved in concentrated sulphuric acid and a few small crystals of sodium nitrite are added, an intense bluish-green coloration is produced.

*With Benzotrichloride and Zinc Chloride.*—When the diphenylindoles are heated at 100° with benzotrichloride and a little zinc chloride, the following colour reactions are observed.

Diphenylindole. Violet.

## OXIDATION OF TARTARIC ACID IN PRESENCE OF IRON. 899

Diphenylorthotoluindole } Violet, changing to intense red.  
Diphenylparatoluindole }

Diphenyl- $\alpha$ -naphthindole. Red, changing to dark brown.

Diphenyl- $\beta$ -naphthindole. Reddish-violet.

These colouring matters dye silk without a mordant, but the shades have no brilliancy.

*Chemical Department,  
University of Aberdeen.*

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