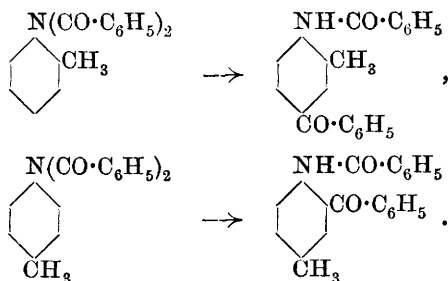


LVII.—*Isomeric Change of Diacylanilides into Acylaminoketones. Transformation of the Dibenzoyltoluidines into the Isomeric Benzoylaminomethylbenzophenones.*

By FREDERICK DANIEL CHATTAWAY and WILLIAM HENRY LEWIS.

It has been shown recently (this vol., p. 386) that acyl groups must be included among those which, under suitable conditions, can pass from the nitrogen of an aromatic amine into the nucleus, thereby displacing a hydrogen atom in a para- or an ortho-position relatively to the nitrogen.

An excellent illustration of this intramolecular rearrangement in the diacylanilides is furnished by the behaviour of the dibenzoyl-toluidines, which, at a high temperature under the influence of hydrogen chloride, are converted into the isomeric benzoylamino-methylbenzophenones, thus :

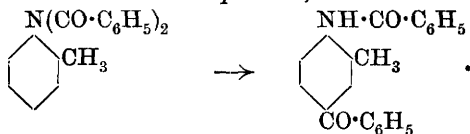


In the transformation of dibenzoyl-*o*-toluidine, where a para- and an ortho-position are unoccupied, the benzoyl group apparently takes up exclusively a para-position with respect to the nitrogen, whilst in the transformation of dibenzoyl-*p*-toluidine an ortho-position is assumed, this being the only vacant position into which the migrating group can enter.

As in the analogous intramolecular rearrangement of the acylchloroamines, interchange between a para-hydrogen atom and the acyl group takes place more readily than that in which an ortho-hydrogen is concerned.

The properties of the aminomethylbenzophenones produced are exactly those which might have been predicted from our knowledge of the properties of the *o*- and *p*-aminobenzophenones obtained by the intramolecular rearrangement of dibenzoylaniline. For example, the compound in which the benzoyl group occupies the ortho-position relatively to the nitrogen has a bright yellow colour, is volatile in steam, and has a low melting point, whilst the isomeride in which the benzoyl group is in the para-position is almost colourless, is not volatile in steam, and melts at a much higher temperature.

*Transformation of Dibenzoyl-o-toluidine into Benzoyl-4-amino-5-methylbenzophenone,*

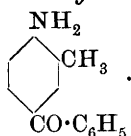


The authors have proved that when the benzoyl derivative of either *o*- or *p*-toluidine is heated with benzoyl chloride, the hydrogen chloride

formed being removed, the dibenzoyl derivative of the base is produced. It is unnecessary, however, to isolate these derivatives in order to study their transformation, as the hydrogen chloride acts as a catalyst and brings about the intramolecular rearrangement. The following procedure gave a good result.

*o*-Toluidine (1 mol.) was added gradually to the equivalent quantity of benzoyl chloride (2 mols.) and the whole gradually heated in an oil-bath up to 220—230°, this temperature being maintained for about 15 hours. A brown, viscid liquid was produced, which solidified on cooling to a hard, resinous mass. The benzoyl-4-amino-3-methylbenzophenone can be isolated from this product with some difficulty, but it is best to hydrolyse it, as the corresponding base can be much more readily separated. The whole mass was therefore dissolved in excess of alcohol containing about half its bulk of concentrated hydrochloric acid, and heated to boiling for 14 hours. A rapid current of steam was then blown through the liquid, when alcohol and ethyl benzoate distilled over successively. The strongly acid residue was then boiled for some time with a quantity of water, and the hot solution containing the hydrochlorides of the bases present filtered from the brown, tarry matter which is always formed in considerable amount in the transformation. The filtrate was next made slightly alkaline with caustic soda and again distilled in steam. A little *o*-toluidine (about 10 per cent. of that used), derived from untransformed dibenzoyl-*o*-toluidine, first passed over. On continuing the distillation, a perfectly colourless\* distillate was obtained, showing that no appreciable transference of the benzoyl group into the vacant ortho-position had taken place. After cooling, the solid separating from the alkaline liquid in the distillation flask was filtered off and extracted with alcohol. This alcoholic solution was evaporated to a small bulk, and a few drops of strong sulphuric acid added; on diluting with a little ether, the almost pure base crystallised in colourless needles. It can be obtained perfectly pure by one recrystallisation from water slightly acidified with sulphuric acid. The yield, which is about 50 per cent. of the weight of *o*-toluidine used, can be slightly increased by adding a small quantity of dry powdered zinc chloride to the mixture of benzoyl chloride and *o*-toluidine before heating.

\* A brilliant yellow colour and volatility in steam are among the most characteristic properties of *o*-aminobenzophenone and its homologues, and a very small quantity of these ketones can be recognised by the yellow colour of the distillate.

*4-Amino-3-methylbenzophenone,*

This compound is very sparingly soluble in hot water, but readily so in alcohol; it crystallises from boiling water in glistening, transparent, flattened prisms, almost colourless, but showing a faint yellow tint. The hot aqueous solution shows a distinct pale yellow colour. From its solution in alcohol, which has a deep yellow colour, the base separates in very pale yellow, flattened prisms with domed ends; it melts at  $112^\circ$ .

0.2224 gave 0.6502  $\text{CO}_2$  and 0.1244  $\text{H}_2\text{O}$ .  $\text{C} = 79.73$ ;  $\text{H} = 6.26$ .

0.3016 „ 17.6 c.c. nitrogen at  $15^\circ$  and 732 mm.  $\text{N} = 6.69$ .

$\text{C}_{14}\text{H}_{13}\text{ON}$  requires  $\text{C} = 79.57$ ;  $\text{H} = 6.21$ ;  $\text{N} = 6.65$  per cent.

The base readily dissolves in hot dilute sulphuric acid, forming a sparingly soluble sulphate,  $2\text{C}_6\text{H}_5 \cdot \text{CO} \cdot \text{C}_6\text{H}_3(\text{CH}_3) \cdot \text{NH}_2, \text{H}_2\text{SO}_4$ , which crystallises out on cooling the solution in glistening, transparent, colourless plates. When heated rapidly, the sulphate softens and begins to decompose at about  $105$ — $110^\circ$ .

0.2663 yielded 0.1192  $\text{BaSO}_4$ .  $\text{SO}_4 = 18.42$ .

$2\text{C}_{14}\text{H}_{13}\text{ON}, \text{H}_2\text{SO}_4$  requires  $\text{SO}_4 = 18.46$  per cent.

It also dissolves readily in warm concentrated hydrochloric acid, forming a sparingly soluble chloride,  $\text{C}_6\text{H}_5 \cdot \text{CO} \cdot \text{C}_6\text{H}_3(\text{CH}_3) \cdot \text{NH}_2, \text{HCl}$ , which crystallises from the cooled solution in thin, colourless, transparent, four-sided plates. On heating rapidly, the chloride reddens strongly, and melts with decomposition at about  $215$ — $220^\circ$ .

0.2624 yielded 0.1520  $\text{AgCl}$ .  $\text{Cl} = 14.32$ .

$\text{C}_{14}\text{H}_{13}\text{ON}, \text{HCl}$  requires  $\text{Cl} = 14.32$  per cent.

A number of derivatives of this base and of its isomeride have been prepared, either by the action of the corresponding acyl chloride or anhydride, or by condensing the base with methyl or ethyl chloro-carbonate. As a rule, equivalent quantities were heated together for a short time on the water-bath, the acid liberated being then removed by warming with a dilute solution of potassium hydrogen carbonate. The solid product was repeatedly crystallised from alcohol. In preparing the acetylchloro-amino-derivatives, the acetyl compound was dissolved in alcohol and the solution shaken with a well-cooled slightly acid solution of bleaching powder. To complete the conversion, the

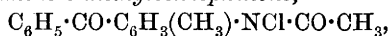
product was extracted with chloroform, and the solution repeatedly shaken with cold, freshly prepared bleaching powder solution slightly acidified with acetic acid. Finally, the chloroform solution was separated, dried over calcium chloride, and the solvent driven off in a current of dry air.

*Acetyl-4-amino-3-methylbenzophenone,*



crystallises from alcohol, in which it is readily soluble in glistening, transparent, flattened rhombs or rhombic plates melting at  $175^\circ$ .

*Acetyl-4-chloroamino-3-methylbenzophenone,*

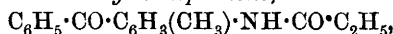


is very soluble in chloroform, but dissolves only sparingly in light petroleum; it crystallises from the latter solvent in small, colourless, slender prisms melting at  $110^\circ$ .

0.2080 liberated  $\text{I} = 14.3$  c.c.  $\text{N}/10$  I.  $\text{Cl}$  (as  $\text{NCl}$ ) = 12.18.

$\text{C}_{16}\text{H}_{14}\text{O}_2\text{NCl}$  requires  $\text{Cl}$  (as  $\text{NCl}$ ) = 12.32 per cent.

*Propionyl-4-amino-3-methylbenzophenone,*

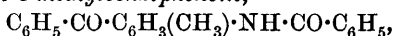


is readily soluble in alcohol, from which it crystallises in colourless, silky, needle-shaped crystals (m. p.  $128^\circ$ ).

0.4120 gave 19.2 c.c. nitrogen at  $17^\circ$  and 758 mm.  $\text{N} = 5.50$ .

$\text{C}_{17}\text{H}_{17}\text{O}_2\text{N}$  requires  $\text{N} = 5.25$  per cent.

*Benzoyl-4-amino-3-methylbenzophenone,*

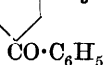
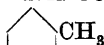
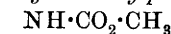


crystallises from alcohol in glistening, colourless, transparent prisms with domed ends which melt at  $158^\circ$ .

0.3632 gave 13.6 c.c. nitrogen at  $16^\circ$  and 752 mm.  $\text{N} = 4.40$ .

$\text{C}_{21}\text{H}_{17}\text{O}_2\text{N}$  requires  $\text{N} = 4.45$  per cent.

*Methyl 4-Benzoyl-2-methylphenylcarbamate,*



This substance crystallises from alcohol, in which it is very readily soluble, in clusters of transparent, colourless, glistening plates (m. p.  $107^\circ$ ).

0.3051 gave 13.2 c.c. nitrogen at  $14^\circ$  and 756 mm.  $\text{N} = 5.14$ .

$\text{C}_{18}\text{H}_{18}\text{O}_3\text{N}$  requires  $\text{N} = 5.22$  per cent.

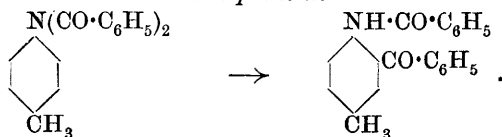
*Ethyl 4-Benzoyl-2-methylphenylcarbamate,*  
 $\text{C}_6\text{H}_5 \cdot \text{CO} \cdot \text{C}_6\text{H}_3(\text{CH}_3) \cdot \text{NH} \cdot \text{CO}_2 \cdot \text{C}_2\text{H}_5,$

This compound is very soluble in chloroform and alcohol, sparingly so in light petroleum; it crystallises from the latter in small, slender, glistening, transparent, colourless prisms (m. p.  $88^\circ$ ).

0.2480 gave 10.2 c.c. nitrogen at  $15^\circ$  and 758 mm.  $\text{N} = 4.88$ .

$\text{C}_{17}\text{H}_{17}\text{O}_3\text{N}$  requires  $\text{N} = 4.96$  per cent.

*Transformation of Dibenzoyl-p-toluidine into Benzoyl-2-amino-3-methyl benzophenone.*

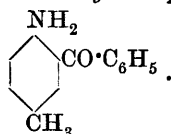


*p*-Toluidine (1 mol.) was added gradually to the equivalent quantity of benzoyl chloride (2 mols.) and the whole gradually heated in an oil-bath to  $220$ — $230^\circ$ , this temperature being maintained for about 15 hours. A brown, viscid liquid was produced which solidified on cooling to a yellowish-brown, semi-crystalline mass; this was hydrolysed by heating for 14 hours with excess of a mixture of alcohol and strong hydrochloric acid, and the alcohol and ethyl benzoate expelled in a rapid current of steam. The acid liquid in the distilling flask was then filtered while hot from the considerable amount of viscid, tarry matter produced, and the latter was several times extracted with boiling dilute hydrochloric acid. The mixed filtrates containing the hydrochlorides of the bases were then made slightly alkaline with caustic soda and again distilled in steam. At first, *p*-toluidine, derived from the untransformed dibenzoyl derivative, passed over; a clear, bright yellow distillate was then obtained from which 2-amino-3-methylbenzophenone separated in deep yellow, oily drops which soon solidified.

The *o*-aminoketone only comes over very slowly in steam, and the distillation must be continued for many hours until the distillate is no longer yellow. The compound is obtained perfectly pure by one crystallisation from alcohol, in which it is very easily soluble. The yield amounts to about 20 per cent. of the weight of *p*-toluidine used. The transference of the benzoyl group from the nitrogen to the ortho-position in the ring does not appear to take place so readily as the corresponding migration into the para-position when the latter is vacant, and resembles in this respect the analogous transference of a

halogen atom. Corresponding with this greater difficulty of transformation, a larger percentage of the toluidine used is recovered, and a larger amount of tarry matter, which appears to be the only other product obtained in the transformation, is also formed. As before, a little zinc chloride may be added with advantage, as this appears to facilitate the transformation.

*2-Amino-3-methylbenzophenone,*



This compound crystallises from alcohol in long, transparent, brilliant yellow, four-sided, rhombic prisms terminated by basal faces. It is very easily soluble in alcohol, chloroform, or acetone, sparingly so in petroleum or water. It is intensely coloured, and a very small quantity gives a distinct pure yellow colour to a large bulk of any solvent. It melts at 66°.

0.2364 gave 0.6884 CO<sub>2</sub> and 0.1320 H<sub>2</sub>O. C = 79.42; H = 6.25.

0.3192 „ 17.8 c.c. nitrogen at 13° and 749 mm. N = 6.59.

C<sub>14</sub>H<sub>13</sub>ON requires C = 79.57; H = 6.21; N = 6.65 per cent.

The base dissolves readily in dilute sulphuric acid, forming a colourless, very soluble sulphate. It also dissolves easily in warm dilute hydrochloric acid, forming a colourless solution from which the hydrochloride C<sub>6</sub>H<sub>5</sub>·CO·C<sub>6</sub>H<sub>3</sub>(CH<sub>3</sub>)·NH<sub>2</sub>·HCl separates on cooling in colourless, transparent, flattened prisms which partially decompose and become yellow on washing with water or alcohol, owing to the liberation of the base, but are permanent in dry air. The hydrochloride, when heated rapidly, reddens and melts with decomposition at about 195—197°.

0.3400 gave 0.1988 AgCl. Cl = 14.46.

C<sub>14</sub>H<sub>13</sub>ON, HCl requires Cl = 14.32 per cent.

*Acetyl-2-amino-3-methylbenzophenone,*

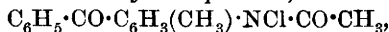


crystallises from alcohol in large, colourless, four-sided, rhombic plates (m. p. 159°).

0.2259 gave 10.7 c.c. nitrogen at 13° and 752 mm. N = 5.62.

C<sub>16</sub>H<sub>15</sub>O<sub>2</sub>N requires N = 5.55 per cent.

*Acetyl-2-chloroamino-5-methylbenzophenone,*



is very soluble in chloroform, moderately so in warm light petroleum,

from which it crystallises in colourless, transparent, four-sided plates (m. p. 116°).

0.2668 liberated I = 18.7 c.c.  $N/10$  I. Cl (as NCl) = 12.42.

$C_{16}H_{14}O_2NCl$  requires Cl (as NCl) = 12.32 per cent.

*Propionyl-2-amino-5-methylbenzophenone,*



is very readily soluble in alcohol, and crystallises from it in transparent, colourless, rhombic plates (m. p. 99°).

0.3535 gave 16.1 c.c. nitrogen at 16° and 762 mm.  $N = 5.42$ .

$C_{17}H_{17}O_2N$  requires  $N = 5.25$  per cent.

*Benzoyl-2-amino-5-methylbenzophenone,*



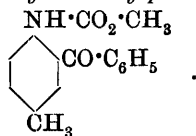
is moderately soluble in alcohol, from which it crystallises in long, slender, very pale yellow prisms (m. p. 118°).

0.2706 gave 10.5 c.c. nitrogen at 17° and 755 mm.  $N = 4.56$ .

$C_{21}H_{17}O_2N$  requires  $N = 4.45$  per cent.

All the acyl derivatives of 2-amino-5-methylbenzophenone give yellow solutions, but only the benzoyl derivative shows any yellow tint in the crystalline form.

*Methyl 2-Benzoyl-4-methylphenylcarbamate,*



This ester crystallises from alcohol, in which it is readily soluble, in colourless, transparent, rhombic plates (m. p. 110°).

0.3132 gave 13.6 c.c. nitrogen at 14° and 752 mm.  $N = 5.13$ .

$C_{16}H_{15}O_3N$  requires  $N = 5.22$  per cent.

*Ethyl 2-Benzoyl-4-methylphenylcarbamate,*



This compound is very soluble in chloroform, alcohol or light petroleum; from the last of these solvents it crystallises in transparent, very pale yellow, four-sided prisms (m. p. 58°).

0.2576 gave 10.4 c.c. nitrogen at 18° and 758 mm.  $N = 4.74$ .

$C_{17}H_{17}O_3N$  requires  $N = 4.96$  per cent.