XLVIII.—*Studies in the Diphenyl Series. Part I.* *Acetylation of Benzidine Derivatives.*

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IN a previous communication (Trans., 1909, **95**, 714) it was shown by one of us that when aqueous-alcoholic solutions of benzidine or tolidine are treated with a molecular proportion of acetic anhydride in the cold (compare Pinnow, *Ber.*, 1900, **33**, 417), a large proportion of the base is converted into the monoacetyl derivative, the proportion of monoacetyl to diacetyl compound being roughly two to one in the case of benzidine and three to one in the case of tolidine. It was also mentioned that dianisidine, under the same conditions, furnishes no diacetyl compound.

It was thought, therefore, that it would be of interest to study this reaction further, with the view of throwing some light on the influence of substituents in the acetylation of benzidine derivatives, and this has been done by acetylating various bases of the diphenyl series in the above manner, and determining the relative amounts of mono- and di-acetyl derivatives formed. The results of these experiments are given in the following table:

Base.	Proportion in product of:	
	Monoacetyl.	Diacetyl.
Benzidine	65 per cent.	35 per cent.
3 : 3'-Dimethylbenzidine (tolidine)	75 ,,	25 ,,
3 : 3'-Dimethoxybenzidine (dianisidine).	only product	—
3 : 3'-Dichlorobenzidine	chief ,,	small amount
2 : 2'-Dichlorobenzidine	75 per cent.	25 per cent.
2 : 2'-Dinitrobenzidine	trace	none
2-Nitrobenzidine	only product	—
3-Ethoxybenzidine	75 per cent.	25 per cent.

In those cases where no diacetyl compound was formed by this method, it was prepared for purposes of comparison by boiling the dry substance with acetic anhydride.

From the above table it will be seen that the reactivity of the amino-groups in the benzidine molecule is considerably diminished by the introduction of substituents. Considering first those di-substituted derivatives in which each substituent is in the ortho-position with respect to the amino-group, it will be noticed that the introduction of the methyl group (tolidine) produces the least effect; the diminution in the amount of diacetyl derivative can only, we think, be attributed to steric hindrance. When, however, the substituent groups are negative, the effect is very much greater, a very small amount of diacetyl compound being produced in the case of the dichloro-derivative, none in the case of the dimethoxy-derivative, and in the case of the dinitro-derivative the inhibition is so great that only a very small amount of the monoacetyl compound is obtained. Moreover, the fact that 2:2'-dichlorobenzidine (where the chlorine atoms are in the meta-position with respect to the amino-groups) furnishes about 25 per cent. of the diacetyl compound points to the conclusion that in the case of negative substituents in the ortho-position with respect to the amino-groups, steric hindrance also plays a part in inhibiting the acetylation.

What, however, is the cause of the increased effect of the negative groups in this reaction? That negative groups have the same effect in the acetylation of amines of the benzene series has also been shown by Ulfers and von Janson (*Ber.*, 1894, 27, 93), who performed their experiments under widely different conditions at high temperatures.

The question raises the much greater one of the general effect of the introduction of negative substituents on groups or atoms already in the molecule. We have no intention of enlarging on this point, but attention may be directed to the fact that in modern chemical constitutional formulæ there is nothing to indicate any relationship between groups which undoubtedly influence each other, a relationship which undoubtedly exists.

We are inclined to suggest that when a negative atom or group is introduced into a base, thus, for example, in the case of *o*-chloroaniline (and, in a less degree, perhaps the *m*- and *p*-derivatives), it is possible that the constitution is not truly represented by the formula (I), but that the residual affinities of the nitrogen and chlorine atoms come into play, with the result

(I.)

(II.)

that the compound is more correctly represented by the formula

(II). A similar configuration would be assigned to those bases containing an oxygenated substituent, the oxygen thereby becoming quadrivalent. The effect of this in acetylation would be that the amino-group, being thus bound or influenced by the negative substituent, would be more difficult of attack than when free, as in aniline. We put this suggestion forward tentatively, but it is significant that Ulffers and von Janson (*loc. cit.*) found that when the acetyl group had been introduced into a negatively ortho-substituted monoamine, the same substituent facilitated (no longer retarded?) the introduction of a second acetyl group to form a diacetyl compound. The explanation may be that after the breaking of the double linking between chlorine and nitrogen, the basicity of the acetylated amino-group is so weak that a union with chlorine can no longer take place.

The effect of introducing one substituent in the benzidine molecule is what was to be expected from what has been shown to take place in the case of the disubstituted derivatives. The 2-nitro-derivative furnishes no diacetyl, but a quantitative yield of the monoacetyl compound, whilst the 3-ethoxy-derivative gives rise to both compounds, but the amount of diacetyl derivative is less than that produced in the case of benzidine itself.

For the purpose of comparison, aniline and *m*-nitroaniline were acetylated in the same way. In the former case a nearly quantitative yield of acetanilide was obtained, but in the latter most of the base was recovered unchanged, only about 10 per cent. of *m*-nitroacetanilide being produced.

EXPERIMENTAL.

The preparation of monoacetyl-benzidine and -tolidine has already been described (Cain, *loc. cit.*). It has since been found that Biehringer and Borsum (*Ber.*, 1906, **39**, 3348) described a monoacetyl-*o*-tolidine as being produced by heating the base with the diacetyl derivative. This compound is stated to form pale yellow crystals, melting at 133–135°, becoming green when exposed to the atmosphere, and decomposing when moist at 100°. The product obtained by one of us crystallises in white, shining plates, containing one molecule of water of crystallisation, and melting at 103°. Its constitution was fully proved, and it can only be concluded that Biehringer and Borsum's compound had not the constitution assigned to it, especially as it was stated to crystallise from water, apparently in the anhydrous state.

Acetylation of Dianisidine.

The acetylation of this and the other bases described in this paper was carried out as previously mentioned (*loc. cit.*, p. 717).

Monoacetyldianisidine,* $\text{NHAc} \cdot \text{C}_{14}\text{H}_{12}\text{O}_2 \cdot \text{NH}_2 \cdot \text{H}_2\text{O}$, is readily soluble in alcohol, and crystallises from water in white nodules, melting at 67° . The water of crystallisation is lost at 100° , and the anhydrous substance melts at 116° :

0.1448 gave 11.8 c.c. N_2 at 20° and 758 mm. $\text{N}=9.5$.

$\text{C}_{16}\text{H}_{18}\text{O}_3\text{N}_2 \cdot \text{H}_2\text{O}$ requires $\text{N}=9.2$ per cent.

Acetylation of 3: 3'-Dichlorobenzidine.

3: 3'-*Dichloroacetylbenzidine*,* $\text{NHAc} \cdot \text{C}_{12}\text{H}_6\text{Cl}_2 \cdot \text{NH}_2$, dissolves readily in alcohol, but sparingly in water, and forms white, feathery needles, melting at $104-105^\circ$:

0.0837 gave 6.8 c.c. N_2 at 19° and 756 mm. $\text{N}=9.5$.

$\text{C}_{14}\text{H}_{12}\text{ON}_2\text{Cl}_2$ requires $\text{N}=9.5$ per cent.

3: 3'-*Dichlorodiacetylbenzidine* has been mentioned incidentally in Eng. Pat. 25725 of 1896 (I. Levinstein and Levinstein, Ltd.). It crystallises from glacial acetic acid in slender, white needles, melting at 302° .

Acetylation of 2: 2'-Dichlorobenzidine.

This base was first obtained by Laubenheimer (*Ber.*, 1875, **8**, 1625) from *m*-chloronitrobenzene by conversion first into dichloro-azoxybenzene and then into the hydrazo-compound. We have prepared the latter direct by reducing *m*-chloronitrobenzene in the modern manner with zinc and sodium hydroxide, and subsequently effecting the "benzidine change" by means of hydrochloric acid. The base crystallises from water in white needles, melting at 165° (Laubenheimer obtained small, flat prisms from alcohol, m. p. 163°).

In the acetylation no insoluble diacetyl compound separated from the hot solution, but, on dilution and cooling, the crystals which were obtained were found to consist of a mixture of the mono- with the di-acetyl compound, and were separated by means of dilute hydrochloric acid. The diacetyl compound is soluble in 50 per cent. aqueous alcohol, and thus differs from most of the other diacetyl compounds of this class.

2: 2'-*Dichloroacetylbenzidine*, $\text{NHAc} \cdot \text{C}_{12}\text{H}_6\text{Cl}_2 \cdot \text{NH}_2$, separates

* This compound was described at the International Congress of Applied Chemistry, London, 1909. The diacetyl compound (m. p. 231°) was prepared by Starke (*J. pr. Chem.*, 1899, [ii], **59**, 214).

from hot water in white, feathery crystals, melting at 195° . It is readily soluble in glacial acetic acid or alcohol, sparingly so in ether, chloroform, or ethyl acetate, and insoluble in benzene:

0.1765 gave 15.0 c.c. N_2 at 18° and 759 mm. $N=10.0$.

$C_{14}H_{12}ON_2Cl_2$ requires $N=9.5$ per cent.

2: 2'-Dichlorodiacylbenzidine, $NHAc \cdot C_{12}H_6Cl_2 \cdot NHAc$, crystallises from glacial acetic acid, in which it is very soluble, in short, white needles, melting above 310° . It is moderately soluble in alcohol, and insoluble in hot water, ether, acetone, ethyl acetate, or chloroform:

0.1098 gave 8.0 c.c. N_2 at 17° and 761 mm. $N=8.6$.

$C_{16}H_{14}O_2N_2Cl_2$ requires $N=8.3$ per cent.

Acetylation of 2: 2'-Dinitrobenzidine.

The base was prepared by nitrating benzidine as described by Täuber (*Ber.*, 1890, **23**, 795), and was found to possess all the characteristics attributed to it by him. From the mother liquors, however, after crystallising the product of nitration, beautiful yellow needles were obtained, which melted at 198° (Täuber's dinitrobenzidine, like ours, crystallised in leaflets, melting at 214°). These proved, on analysis, to be an isomeric dinitrobenzidine:

0.0917 gave 15.8 c.c. N_2 at 18° and 752 mm. $N=20.1$.

$C_{12}H_{10}O_4N_4$ requires $N=20.4$ per cent.

This compound seems to be identical with the dinitrobenzidine described by Bandrowski (*Monatsh.*, 1887, **8**, 472), which he obtained by the hydrolysis of dinitrodiphtalylbenzidine. Its melting point is given as $196-197^{\circ}$, and its constitution was not determined.

On acetylating 2: 2'-dinitrobenzidine under the stated conditions, only a minute trace of a monoacetyl derivative was formed, almost the whole of the base being recovered unchanged.

2: 2'-Dinitrodiacylbenzidine was, however, prepared by heating the base with acetic anhydride. It is insoluble in acetone, ether, or cold alcohol, sparingly soluble in hot alcohol or chloroform, and fairly so in glacial acetic acid, from which it separates in small, almost colourless needles, melting and decomposing above 290° :

0.1222 gave 15.5 c.c. N_2 at 15° and 770 mm. $N=15.3$.

$C_{16}H_{14}O_6N_4$ requires $N=15.6$ per cent.

Acetylation of 2-Nitrobenzidine.

The base was obtained from the technical product (sulphate), after recrystallisation from water, by neutralising with ammonia; it crystallised from water in dark red needles, melting at 143° .

2-Nitro-4'-acetylbenzidine, $\text{NHAc} \cdot \text{C}_6\text{H}_4 \cdot \text{C}_6\text{H}_3(\text{NO}_2) \cdot \text{NH}_2$, was obtained in a quantitative yield by the acetylation of the base. The fact that 2: 2'-dinitrobenzidine does not yield any (or only a trace of) monoacetyl derivative under the same conditions would appear to be conclusive evidence in favour of the above constitution. The compound is soluble in alcohol, hot water, ethyl acetate, or glacial acetic acid, very sparingly so in ether, chloroform, or benzene, and insoluble in cold water. It crystallises from alcohol or hot water in yellow plates, melting at $186-187^\circ$:

0.1515 gave 20.3 c.c. N_2 at 21° and 764 mm. $\text{N}=15.7$.

$\text{C}_{14}\text{H}_{13}\text{O}_3\text{N}_3$ requires $\text{N}=15.5$ per cent.

2-Nitrodiacetylbenzidine, prepared by boiling the monoacetyl compound with acetic anhydride, is insoluble in water, alcohol, ethyl acetate, chloroform, ether, or benzene, but sparingly soluble in glacial acetic acid, from which it separates in small, white crystals, melting above 310° :

0.3212 gave 36.4 c.c. N_2 at 15° and 773 mm. $\text{N}=13.7$.

$\text{C}_{16}\text{H}_{15}\text{O}_4\text{N}_3$ requires $\text{N}=13.4$ per cent.

Acetylation of 3-Ethoxybenzidine.

The base was obtained by recrystallising the technical product from hot water. On acetylation it was found that, as in the case of 2: 2'-dichlorobenzidine, the diacetyl derivative was soluble in 50 per cent. aqueous alcohol, so that, on cooling the solution, a mixture of mono- and di-acetyl derivatives was obtained. This was separated by means of cold dilute hydrochloric acid.

4'-Acetyl-3-ethoxybenzidine, $\text{NHAc} \cdot \text{C}_{12}\text{H}_7(\text{OEt}) \cdot \text{NH}_2$ (the inhibitive effect of the ethoxy-group, as shown in the table on p. 720, renders it certain that the acetyl and ethoxy-groups are in different rings) dissolves in alcohol or hot water, but is insoluble in ether, benzene, or light petroleum. It crystallises from hot water in small, white leaflets, melting at $137-138^\circ$:

0.1029 gave 9.1 c.c. N_2 at 15° and 765 mm. $\text{N}=10.6$.

$\text{C}_{16}\text{H}_{18}\text{O}_2\text{N}_2$ requires $\text{N}=10.4$ per cent.

Diacetyl-3-ethoxybenzidine is readily soluble in glacial acetic acid or alcohol, sparingly so in ethyl acetate or chloroform, and insoluble in benzene or water. It crystallises from acetic acid or alcohol in small, white needles, melting at 240° :

0.1227 gave 9.25 c.c. N_2 at 15° and 755 mm. $\text{N}=9.2$.

$\text{C}_{18}\text{H}_{20}\text{O}_3\text{N}_2$ requires $\text{N}=9.0$ per cent.

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