Synthesis and Proton Magnetic Resonance Spectra of Substituted Biphenyls

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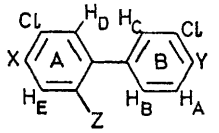
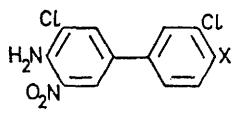
A series of new acylamino-, amino-, chloro-, and nitro-derivatives of 3,3′-dichlorobiphenyl have been prepared from 3,3′-dichlorobenzidine, and their structures have been confirmed by ^{1}H n.m.r. spectroscopy. The electronic and steric effects of a nitro-group *ortho* to the internuclear linkage are discussed.

NITRATION of 4,4′-diaminobiphenyl (benzidine) gives the 2-nitro-derivative,[1] which can readily be diacylated with acryloyl chloride at low temperatures to give 4,4′-bis(acryloylamino)-2-nitrobiphenyl.[2] Reduction gives the 2-amino-derivative, which has been used as a diazo component in the preparation of fibre-reactive azo dyes for wool.[2] In an attempt to extend the range of dyes obtainable by this method, we have investigated the nitration and subsequent acylation of 3,3′-dichlorobenzidine.† A mononitro-derivative was obtained which, under the mild conditions used to convert 2-nitrobenzidine into the *NN*′-diacyl derivative, gave only a monoacetyl derivative. This could have been compound (Ia) or compound (Ib) depending on whether



(I)



(II)

a; X = NH_2, Y = NHAc, Z = NO_2
b; X = NHAc, Y = NH_2, Z = NO_2

or not the 4-amino-group was deactivated by the inductive effect of the 6-nitro-substituent to a greater extent than the 4′-amino-group was deactivated by the mesomeric effect of the 6-nitro-substituent transmitted through conjugative interaction between the two benzene rings. Structure (II; X = NHAc), in which the 4-amino group is deactivated by the steric and electronic effects of the 5-nitro-substituent, was also a possibility. The following results show conclusively that structure (Ia) is the correct one.

The ^{1}H n.m.r. spectrum of the mononitro-derivative of 3,3′-dichlorobenzidine (Table, no. 2) shows the signals for aromatic protons (H_D and H_E) of the nitrated ring (A) as singlets, as required for the 6-nitro-derivative (I; X = Y = NH_2, Z = NO_2), rather than as *meta*-split doublets as required for the 5-nitro-derivative (II; X = NH_2). The fact that protons H_D and H_E have similar chemical shifts (τ 2·70 and 2·72) is also only explicable in terms of structure (I), the shielding and deshielding effects, respectively, of the amino- and nitro-groups (both *ortho* or both *meta*) thus cancelling out. This assignment has been confirmed by conversion of the nitrodichlorobenzidine into the tetrachloronitrobiphenyl (I; X = Y = Cl, Z = NO_2), in the spectrum of which these protons now give singlets at τ 2·18 and 1·74 (Table, no. 3), and into the dichloronitrobiphenyl (I; X = Y = H, Z = NO_2), in the spectrum of which only the proton *ortho* to the nitro-group is clearly resolved, as an *ortho*-split doublet (Table, no. 4). Structure (II) is therefore ruled out.

The ^{1}H n.m.r. spectrum of the monoacetyl derivative of 3,3′-dichloro-6-nitrobenzidine (Table, no. 7) again shows that the aromatic protons of the nitrated ring (A) have similar chemical shifts (τ 2·48 and 2·52) and indicates that the amino- and nitro-substituents are in the same ring, as in structure (Ia). This has been confirmed by conversion into the acetylaminotrichlorobiphenyl (Sandmeyer reaction). The ^{1}H n.m.r. spectrum (Table, no. 8) of this substance shows considerable differences in the chemical shifts of H_D and H_E, the signals of which are also at considerably lower field.

† For convenience, all derivatives of this compound are numbered in the same way; *i.e.* compound (I; X = Y = NH_2, Z = NO_2) we refer to as a 6- rather than a 2-nitro-derivative, although the latter is more correct.

[1] A. W. von Hofmann, *Ber.*, 1890, **23**, 794.
[2] F. Bowman and P. W. Hickmott, B.P. 984,802.

The chemical shifts of the aromatic protons of ring B are virtually the same as those of the corresponding protons in the parent amino-compound (Table, no. 7). This proves that the monoacetyl derivative has structure (Ia).

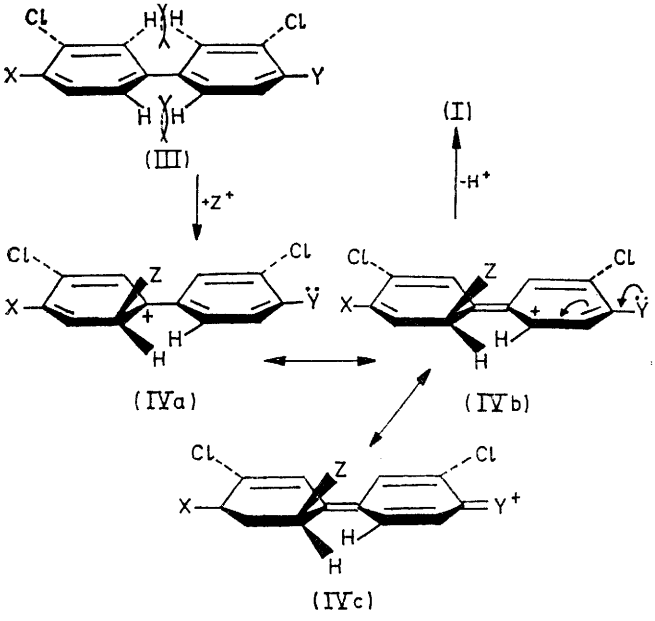
Although under mild conditions only the monoacetyl derivative of 3,3′-dichloro-6-nitrobenzidine was obtained, more forcing conditions gave the diacetyl derivative. This was identical with the product derived by nitration of *NN*′-diacetyl-3,3′-dichlorobenzidine. This fact supports the suggestion [3] that the van der Waals forces acting between the *ortho*- and *ortho*′-hydrogen atoms of the biphenyl system (III), and causing the rings to be inclined to each other at *ca.* 45°, are reduced by the act of electrophilic substitution at the 6- (or 2-) position, and thus additional stabilisation of the corresponding transition state, as depicted in (IVa ⟷ b), is allowed. However, once the act of electrophilic substitution has been completed, and the aromatic system has been re-formed [(IV ⟶ (I)], the increased steric interactions between the *ortho*- and *ortho*′-substituents must be relieved by an increase in the dihedral angle between the rings, or by twisting the nitro-group out of the plane of ring A,[4] or by both. These effects operate against effective conjugative interaction between the 6-nitro- and 4′-amino-groups, and the deactivating effect of the nitro-substituent will therefore be felt mainly by the 4-amino-group. Monoacylation therefore gives the 4′-acetylamino-derivative (Ia).

The lack of conjugative interaction between the nitro-group and ring B is also reflected in the ^{1}H n.m.r. spectra. Thus, although the proton *ortho* to the nitro-group is deshielded [*cf.* H_A in nos. 1 and 5 with H_E in nos. 2 and 6, respectively (Table)], the signal due to H_A in ring B is unchanged [*cf.* H_A in nos 1 and 2, and 5 and 6 (Table)], indicating that the electron density in ring B has been unaffected by introduction of a nitro-group into ring A. Furthermore the signals due to H_B and H_C of ring B are moved to higher field by introduction of a nitro-group into ring A [*cf.* H_B and H_C of 1 and 2, and 5 and 6 (Table)]. This can be attributed partly to shielding by the nitro-group [4] in a non-planar biphenyl system, and partly to decreased deshielding by ring A, as a result of the increased dihedral angle between the two rings; this moves H_B and H_C further from the centre of the deshielding region of ring A. The proton *meta* to the nitro-group in ring A is not deshielded [*cf.* H_C in nos 1 and 5 with H_D in nos. 2 and 6, respectively (Table)], despite the fact that it must experience a deshielding effect due to the nitro-group. This must reflect the decreased deshielding by ring B in the nitro-derivative, as compared to the parent compound, owing to the increased dihedral angle between the rings. The 6-acetylamino-group shows a similar effect on the dihedral angle [*cf.* nos 5 and 9 (Table)].

^{1}H N.m.r. assignments (τ) of substituted 3,3′-dichlorobiphenyls (I)

No.	Conditions *	X	Y	Z	H_A	H_B	H_C	H_D	H_E	NH_2	NH·CO	Ac
1	A	NH_2	NH_2	H	3·16	2·80	2·65			5·28		
2	A	NH_2	NH_2	NO_2	3·18	3·10	2·87	2·70	2·72	4·56 and 5·04		
3	A	Cl	Cl	NO_2	2·36	2·66	2·36	2·18	1·74			
4	A	H	H	NO_2		2·5—3·0(m)			2·18			
5	B	AcNH	AcNH	H	2·07	2·33	2·15				0·4	7·86
6	B	AcNH	AcNH	NO_2	2·07	2·65	2·37	2·17	1·31		0·35 and 0·03	7·86 and 7·78
7	C	NH_2	AcNH	NO_2	1·68	2·69	2·54	2·48	2·52	7·15	4·3	7·76
8	A	Cl	AcNH	NO_2	1·67	2·68	2·49	2·19	1·78		1·32	7·85
9	B	Cl	AcNH	AcNH	2·05	2·60	2·42	2·32	2·07		0·38 and 0·43	7·85 and 8·03

* A, [$^2H_6$]acetone at 100 MHz; B, [$^2H_6$]dimethyl sulphoxide at 60 MHz; C, [$^2H_6$]acetone at 60 MHz.



EXPERIMENTAL

3,3′-Dichloro-6-nitrobenzidine.—Dichlorobenzidine (13·84 g.) was added gradually to concentrated sulphuric acid (158 g.) below 50° with stirring; the solution was then cooled to 10° and potassium nitrate (5·4 g.) was added during 2 hr. below 20°. After a further 3 hr. at 20° the

[3] P. B. D. de la Mare and M. Hassan, *J. Chem. Soc.*, 1957, 3004.

[4] R. W. Franck and M. A. Williamson, *J. Org. Chem.*, 1966, **31**, 2420, and references therein.

solution was poured into water (350 ml.), and the precipitated salt was collected, resuspended in boiling water (6 l.), and basified with ammonia to give the free *base* (11·1 g.), m.p. 165—168° [from benzene–light petroleum (b.p. 40—60°)–ether] (Found: C, 48·4; H, 3·0; Cl, 23·0; N, 13·7. $C_{12}H_7Cl_2N_3O_2$ requires C, 48·3; H, 3·2; Cl, 23·8; N, 14·1%).

3,3′,4,4′-*Tetrachloro*-6-*nitrobiphenyl*.—A solution of 3,3′-dichloro-6-nitrobenzidine (15·0 g.) in glacial acetic acid (450 ml.) was added, at 20—25° with cooling, to nitrosylsulphuric acid prepared by adding sodium nitrite (9·0 g.) to concentrated sulphuric acid (90 ml.) and heating the mixture to 70°. The ' tetrazo '-solution was added during 5 min. to copper(I) chloride (11·1 g.) in concentrated hydrochloric acid (110 ml.); the mixture was stirred for 1 hr. and the precipitated solid was collected and washed thoroughly with water to give 3,3′,4,4′-*tetrachloro*-6-*nitrobiphenyl* (12·8 g.), m.p. 86—89° (from aqueous ethanol) (Found: C, 43·0; H, 1·8; Cl, 40·25; N, 3·9. $C_{12}H_5Cl_4NO_2$ requires C, 42·7; H, 1·5; Cl, 42·1; N, 4·15%).

6-*Amino*-3,3′,4,4′-*tetrachlorobiphenyl*.— 3,3′,4,4′-Tetrachloro-6-nitrobiphenyl (10·0 g.) was dissolved in glacial acetic acid (450 ml.) at 100°; tin(II) chloride dihydrate (34·5 g.) in concentrated hydrochloric acid (150 ml.) was added and the mixture was stirred for 2 hr. The solution was then basified with sodium hydroxide (300 g.) and extracted with ether to give 6-*amino*-3,3′,4,4′-*tetrachlorobiphenyl* (4·29 g.) as an oil which slowly solidified, m.p. 79—82° (from aqueous ethanol) (Found: C, 47·9; H, 2·6; N, 4·7. $C_{12}H_7Cl_4N$ requires C, 46·9; H, 2·3; N, 4·6%).

3,3′,4,4′,6-*Pentachlorobiphenyl*.— 6-Amino-3,3′,4,4′-tetrachlorobiphenyl (3·0 g.) in glacial acetic acid (100 ml.) was diazotised with nitrosylsulphuric acid [sodium nitrite (2·0 g.) in concentrated sulphuric acid (20 ml.)] and the solution was added to copper(I) chloride (2·0 g.) in concentrated hydrochloric acid (20 ml.). The resulting solution was basified and extracted with ether to give the *pentachlorobiphenyl* (1·89 g.), m.p. 105—107° (from aqueous dimethylformamide) (Found: C, 44·3; H, 2·0. $C_{12}H_5Cl_5$ requires C, 44·1; H, 1·5%).

3,3′-*Dichloro*-6-*nitrobiphenyl*.— 3,3′-Dichloro-6-nitrobenzidine (2·5 g.) in glacial acetic acid (55 ml.) was ' tetrazotised ' with ice-cooled nitrosylsulphuric acid [sodium nitrite (1·5 g.) in concentrated sulphuric acid (20 ml.)] and added, after 20 min., to a suspension of copper(I) oxide monohydrate (5·0 g.) in ethanol (275 ml.). The mixture stirred for 15 hr., then diluted with water and extracted with ether to give 3,3′-*dichloro*-6-*nitrobiphenyl* (1·58 g.) as an oil which slowly solidified, m.p. 87—88° (from aqueous dimethylformamide) (Found: C, 54·1; H, 3·2; Cl, 25·9; N, 5·15. $C_{12}H_7Cl_2NO_2$ requires C, 53·7; H, 2·6; Cl, 26·5; N, 5·2%).

4′-*Acetylamino*-4-*amino*-3,3′-*dichloro*-6-*nitrobiphenyl*.— Acetyl chloride (14·4 g.) was added dropwise to 3,3′-dichloro-6-nitrobenzidine (10·0 g.) in acetone (400 ml.) and water (100 ml.) at 0—5° during 2 hr. The solution was neutralised (Congo Red) with sodium acetate solution, stirred for a further 2 hr. at 0—5° in a stoppered flask, and poured into water. The resulting precipitate was collected and washed with aqueous acetone (1 : 1) to give the *monoacetyl derivative* (10·4 g.) m.p. 147—149° (from aqueous ethanol) (Found: C, 49·1; H, 3·5; Cl, 20·3; N, 12·15. $C_{14}H_{11}Cl_2N_3O_3$ requires: C, 49·4; H, 3·2; Cl, 20·9; N, 12·35%).

4′-*Acetylamino*-3,3′4-*trichloro*-6-*nitrobiphenyl*.— 4′-Acetylamino-4-amino-3,3′-dichloro-6-nitrobiphenyl (5·66 g.) in glacial acetic acid (100 ml.) was diazotised with nitrosylsulphuric acid [sodium nitrite (3·0 g.) in concentrated sulphuric acid (30 ml.)] and added to copper(I) chloride (3·7 g.) in concentrated hydrochloric acid (37 ml.). The solution was stirred for 1 hr., then diluted with water, and the precipitate (6·05 g.) gave 4′-*acetylamino*-3,3′,4-*trichloro*-6-*nitrobiphenyl*, m.p. 202—203° (from aqueous dimethylformamide) (Found: N, 7·95. $C_{14}H_9Cl_3N_2O_3$ requires N, 7·8%).

4′,6-*Bisacetylamino*-3,3′,4-*trichlorobiphenyl*.—4′-Acetylamino-3,3′,4-trichloro-6-nitrobiphenyl (11·0 g.) was dissolved in glacial acetic acid (300 ml.) and tin(II) chloride dihydrate (51·75 g.) in concentrated hydrochloric acid (220 ml.) was added. After 2 hr. at room temperature the solution was basified with sodium hydroxide and extracted with ether to give impure 4′-acetylamino-6-amino-3,3′,4-trichlorobiphenyl (8·3 g.) as an oil. The crude amine was refluxed with glacial acetic acid (50 ml.) and acetic anhydride (14 ml.) for 2 hr., diluted with water, and filtered to give the *bisacetylamino-derivative* (8·3 g.), m.p. 213—214° (from benzene) (Found: N, 7·2. $C_{16}H_{13}Cl_3N_2O_2$ requires N, 7·5%).

4,4′-*Bisacetylamino*-3,3′-*dichloro*-6-*nitrobiphenyl*.— (*a*) A solution of 3,3′-dichloro-6-nitrobenzidine (10·0 g.) in glacial acetic acid (15 ml.) was refluxed with acetic anhydride (15 ml.) and concentrated sulphuric acid (1 ml.) for 2 hr., and diluted with water to give the *bisacetyl derivative* (11·6 g.), m.p. 256—258° (from aqueous ethanol) (Found: C, 49·95; H, 3·55; Cl, 18·5; N, 11·2. $C_{16}H_{13}Cl_2N_3O_4$ requires C, 50·25; H, 3·4; Cl, 18·6; N, 11·0%).

(*b*) A solution of dichlorobenzidine (8·4 g.) in glacial acetic acid (110 ml.) was refluxed with acetic anhydride (15 ml.) and concentrated sulphuric acid (5 drops) for 3 hr. and poured into water to give the bisacetyl derivative, m.p. 314—315° (from dimethylformamide) (lit.[5] >340°) (Found: C, 56·8; H, 4·3; Cl, 21·05; N, 8·3. Calc. for $C_{16}H_{14}Cl_2N_2O_2$: C, 57·0; H, 4·15; Cl, 21·1; N, 8·3%). The bisacetyl derivative (9·15 g.) was dissolved in concentrated sulphuric acid (79·0 g.) and potassium nitrate (2·7 g.) was added gradually below 20° during 2 hr. The solution was stirred for 3 hr., then poured into water, and the precipitate was washed thoroughly to give 4,4′-bisacetylamino-3,3′-dichloro-6-nitrobiphenyl (9·65 g.), m.p. and mixed m.p. 254—256° (from aqueous dimethylformamide).

The structure was confirmed by hydrolysis of a portion (1·0 g.) with 80% sulphuric acid to give 3,3′-dichloro-6-nitrobenzidine (0·5 g.), which was identical with an authentic sample obtained by nitration of 3,3′-dichlorobenzidine.

[0/1213 *Received, July 15th*, 1970]

[5] F. L. W. van Roosmalen, *Rec. Trav. chim.*, 1934, **53**, 359.