Oxidations with Phenyl Iodosoacetate. Part V. The Oxidation of* p-*Anisidine and* p-*Phenetidine.*

By JOAN MITCHELL and K. H. PAUSACKER.

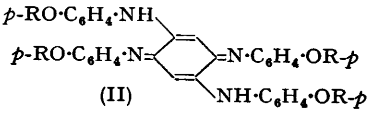
[Reprint Order No. 5499.]

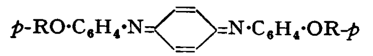
The oxidations named in the title yield the 4 : 4′-dialkoxyazobenzene (in one case), the *NN*′-di-(4-alkoxyphenyl)-*p*-phenylenediamine, the benzoquinone di-*p*-alkoxyphenylimine, the tetra-*p*-alkoxyazophenine, and a compound which is believed to be an azo-substituted diphenylamine. The course of the reaction is discussed.

p-ANISIDINE has been oxidised by a number of reagents with the formation of different products: with bromine water, *p*-benzoquinone is obtained (Wieland, *Ber.*, 1910, **43**, 714); and with peroxymonosulphuric acid (Baeyer and Knorr, *Ber.*, 1902, **35**, 3034) a mixture of *p*-nitrosoanisole and *p*-nitroanisole. Hydrogen peroxide, in the presence of peroxidase, gives 4 : 4′-dimethoxyazobenzene, 2-amino-5-*p*-anisidinobenzoquinone di-*p*-methoxyphenylimine, and tetra-*p*-methoxyazophenine (Daniels and Saunders, *J.*, 1951, 2112). When hydrogen peroxide is used in an acid medium, "*p*-anisidine brown" ($C_{21}H_{16}O_5N_2$) is formed (Pavolini, Gambarin, and Mazini, *Chem. Abs.*, 1952, **46**, 4550). A possible structure is proposed for this compound. Mehta and Vakilwala (*J. Amer. Chem. Soc.*, 1952, **74**, 563) found that the use of sodium perborate gives 4 : 4′-azoxyanisole. Malaviya and Dutt (*Chem. Abs.*, 1936, **30**, 1066) claim that 3 : 7-dimethoxyphenazine is formed on storage in strong sunlight in acid solution.

The oxidation of *p*-phenetidine has not been examined in such detail, but Kinzel (*Arch. Pharm.*, 1891, **229**, 330) has found that hydrogen peroxide in acid medium gives 4 : 4′-diethoxyazobenzene, *p*-benzoquinone, a compound, m. p. 178°, and a compound $C_{24}H_{22}O_5N_2$ (cf. Pavolini, Gambarin, and Mazini, *loc. cit.*). Neu (*Ber.*, 1939, **72**, 1507) stated that phenyl iodosoacetate in acetic acid gave 3 : 7-diethoxyphenazine as the sole isolatable product: it is shown below that this is not correct. Malaviya and Dutt (*loc. cit.*) also claim that 3 : 7-diethoxyphenazine is formed on storage in strong sunlight in acid solution.


(I)


(II)


(III)

(*a*, R = Me; *b*, R = Et)

---

* Part IV, preceding paper.

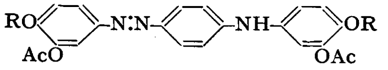
When *p*-anisidine and *p*-phenetidine were treated with phenyl iodosoacetate in benzene, subsequent chromatography yielded the following crystalline products: the 4 : 4′-dialkoxybenzenes (5% and 6% respectively); the tetra-*p*-alkoxyazophenines (II*a* and *b*) (1%); the *p*-benzoquinone di-*p*-alkoxyphenylimines (III*a* and *b*) (16% and 12% respectively); substances (*A* and *B*), $C_{18}H_{11}N_3(OAc)_3(OR)_2$ (R = Me or Et) (11% and 5% respectively); and, from *p*-phenetidine, *NN*′-di-*p*-ethoxyphenylphenylenediamine (I*b*) (5%).

The structure of the diamine (I*b*) followed from its analysis and from its identity with the product prepared by heating quinol, *p*-phenetidine, calcium chloride, and zinc chloride (cf. Calm, *Ber.*, 1883, **16**, 2805). [The dimethoxy-analogue (I*a*) was similarly prepared.]

The structures of the imines (III*a* and *b*), suspected because these products contained two fewer hydrogen atoms than the diamines (I*a* and *b*), were proved when the former pair were obtained from the latter by oxidation with chromic acid in aqueous acetic acid (cf. Piccard, *Ber.*, 1913, **46**, 1853). The diamines (I*a* and *b*) were also immediately oxidised to the di-imines (III*a* and *b*) by phenyl iodosoacetate in benzene; so the diamines are not precursors of the di-imines, but rather they are produced by reduction of the di-imines by some other substance present in the reaction mixture after all the phenyl iodosoacetate has been consumed.

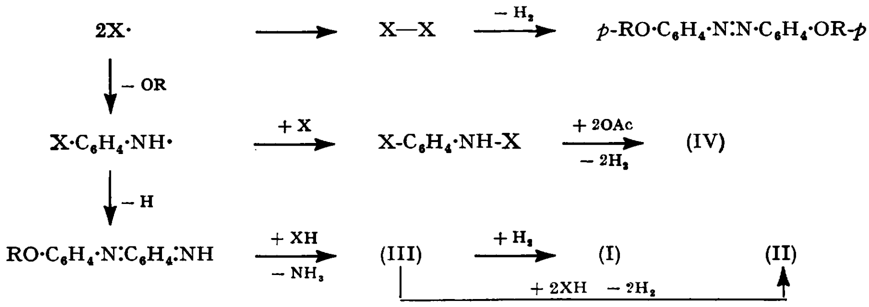
Identity of the compounds, shown to be tetra-*p*-alkoxyazophenines (II*a* and *b*), was proved by their comparison with the products obtained by heating the *pp*′-dialkoxydiazoaminobenzenes with the appropriate *p*-alkoxyaniline (cf. Daniels and Saunders, *loc. cit.*).

Compounds (*A* and *B*) are the first acetoxylated products isolated on oxidation of primary aromatic amines with phenyl iodosoacetate, although Barlin and Riggs (*J.*, 1954, 3125) noted that certain acetylated primary aromatic amines are acetoxylated with phenyl iodosoacetate in acetic acid. It appears that compounds (*A* and *B*) are produced by condensation of three molecules of the amine with the loss of one molecule of alkanol and two molecules of hydrogen, and replacement of two hydrogen atoms by acetoxyl groups. In the presence of Adams's catalyst, compound (*B*) absorbed one mol. of hydrogen, forming a colourless solution, which regenerated the deep-red compound (IV*b*) in air. These two compounds are probably the azo-substituted diphenylamine (IV*a* and *b*). These structures (suggested to us by a Referee) are in accord with the hydrogenation and subsequent re-oxidation of compound (*B*); the acetoxyl groups are assumed to be *ortho* to the alkoxyl groups in view of Barlin and Riggs's work (*loc. cit.*).



(IV; *a*, R = Me; *b*, R = Et)

(X = *p*-RO·C_6H_4·NH·)



The sparingly soluble, supposed 3 : 7-diethoxyphenazine which Neu (*loc. cit.*) obtained from *p*-phenetidine and phenyl iodosoacetate in acetic acid—he gives neither a melting point nor solvent of crystallisation—is probably "*p*-phenetidine black" (cf. "aniline black;" Cain and Thorpe, "The Synthetic Dyestuffs and Intermediate

Products," Griffin, London, 1946, p. 301), which would give the same analytical figures. When Neu's work was repeated the same sparingly soluble product was obtained, but extraction of this with benzene and chromatography on alumina afforded the true 4 : 4′-diethoxyazobenzene in 6% yield and, in amount too small for analysis, a product that gave the colour tests for compound (IV*b*); these tests agree with those reported by Neu for his " 3 : 7-diethoxyphenazine " but they are not given by the residue which remains after the benzene extraction. Earlier (Part III, *J.*, 1954, 3122) it was reported that 4 : 4′-dimethoxyazobenzene (4% yield) is the only product isolated from the similar oxidation of *p*-anisidine.

The dual function of phenyl iodosoacetate as an oxidising and acetoxylating agent, and the importance of the solvent, are again noted (cf. Parts III and IV, *locc. cit.*).

With the exception of the 4 : 4′-dialkoxyazobenzenes, the above products result from the condensation of a number of molecules of *p*-alkoxyaniline with the elimination of one, or more, molecules of alkanol, ammonia, and hydrogen : elimination of methanol has been observed by Daniels and Saunders (*loc. cit.*), and replacement of methoxyl groups by free aryl radicals by Pauson and Smith (*J. Org. Chem.*, 1953, **18**, 1403).

On the assumption that *p*-RO·C_6H_4·NH· radicals are first produced (*J.*, 1953, 1989; cf. Daniels and Saunders, *loc. cit.*, and Goldschmidt, *Ber.*, 1920, **53**, 35) as intermediates in the oxidation of primary aromatic amines, the annexed reaction mechanism is suggested. The formation of compounds (I) by reduction of compounds (III) (see above) is substantiated by the isolation of compounds (I*b*) and (IV*b*) in practically equivalent amounts. Attempts to isolate compound (I*a*) have been unsuccessful.

EXPERIMENTAL

Oxidation of p-*Anisidine.*—Freshly distilled *p*-anisidine (12·7 g.) was added to a solution of phenyl iodosoacetate (50 g.) in dry thiophen-free benzene (1200 ml.). After 28 hr., the filtered solution was chromatographed on alumina, giving (*a*) yellow, (*b*) mustard, (*c*) bright-red, and (*d*) dull-red bands. Each band was eluted with benzene; the materials recovered were heated at 80°/0·2 mm. to remove iodobenzene.

Band (*a*) gave 4 : 4′-dimethoxyazobenzene (0·60 g.) which, crystallised from methanol, had m. p. 164° (Found : N, 11·6. Calc. for $C_{14}H_{14}O_2N_2$: N, 12·0%). It gave a red colour with concentrated sulphuric acid.

The solution of band (*b*) deposited tetra-*p*-methoxyazophenine (0·08 g.), which crystallised from toluene as bright-red needles, m. p. 234° (Found : C, 73·1; H, 5·5; N, 10·3. Calc. for $C_{34}H_{32}O_4N_4$: C, 72·9; H, 5·7; N, 10·0%). It gave a royal-blue colour, changing to purple on dilution with water, with concentrated sulphuric acid. Its mixed m. p. with tetra-*p*-methoxyazophenine was 234°.

Band (*c*) gave a solid (1·98 g.) which crystallised from benzene–light petroleum (b. p. 40—60°) as red needles, m. p. 199° (Found : C, 75·5; H, 5·6; N, 8·6; OMe, 19·1. Calc. for $C_{20}H_{18}O_2N_2$: C, 75·5; H, 5·7; N, 8·8; 2OMe, 19·5%). It gave a Prussian-blue colour, unchanged on dilution with water, with concentrated sulphuric acid. Its mixed m. p. with benzoquinone di-*p*-methoxyphenylimine (see below) was 199°.

Band (*d*) gave (?) *3-acetoxy-4′-(3-acetoxy-4-methoxyanilino)-4-methoxyazobenzene* (1·37 g.) which crystallised from benzene–light petroleum (b. p. 40—60°) as dark-mauve needles, m. p. 175—176° [Found : C, 64·6; H, 5·4; N, 9·2; OMe, 14·4; Ac, 15·6; *M* (by isothermal distillation in benzene), 500. $C_{24}H_{23}O_6N_3$ requires C, 64·1; H, 5·1; N, 9·4; 2OMe, 13·8; 2Ac, 19·2%; *M*, 449]. It gave a blue colour, changing to red on dilution with water, with concentrated sulphuric acid. No identifiable products were obtained on reductive acetylation or oxidation with alkaline potassium permanganate. It could not be acetylated with acetic anhydride and did not form a methiodide when refluxed with methyl iodide.

*Benzoquinone Di-*p-*methoxyphenylimine.*—Quinol (5·0 g.), freshly distilled *p*-anisidine (24·6 g.), calcium chloride (19·5 g.), and zinc chloride (3·4 g.) were heated at 190—195° for 13 hr. in a sealed tube. The resultant solid was extracted alternately with boiling benzene and water. Chromatography (alumina) of the benzene layer gave, in the first band *NN′-di-(4-methoxyphenyl)-*p-*phenylenediamine* (1·6 g.) which crystallised from *cyclo*hexane as off-white plates, m. p. 199·5° (Found : C, 75·0; H, 6·4; N, 8·8. $C_{20}H_{20}O_2N_2$ requires C, 75·0; H, 6·3; N, 8·8%). Oxidation with chromic acid in aqueous acetic acid or phenyl iodosoacetate in benzene gave benzoquinone di-*p*-methoxyphenylimine which crystallised from benzene–light petroleum (b. p. 40—60°) as red needles, m. p. 196°.

Oxidation of p-*Phenetidine.*—*p*-Phenetidine was oxidised in the same manner as *p*-anisidine. Chromatography of the product gave the following principal bands: (*a*) yellow, (*b*) orange, (*c*) bright-red, (*d*) dull-red.

Band (*a*) gave 4 : 4′-diethoxyazobenzene (0·84 g.) which, crystallised from *cyclo*hexane, had m. p. 160° (Found: C, 71·4; H, 7·0; N, 10·4. Calc. for $C_{16}H_{18}O_2N_2$: C, 71·1; H, 6·7; N, 10·4%). It gave a red colour, unchanged on dilution with water, with concentrated sulphuric acid.

Band (*b*) deposited a solid (0·14 g.) which crystallised from toluene as bright-red needles, m. p. 260° (Found: C, 74·3; H, 6·7; N, 8·9; OEt, 28·6. $C_{38}H_{40}O_4N_4$ requires C, 74·0; H, 6·5; N, 9·1; 4OEt, 29·2%). With concentrated sulphuric acid, it gave a violet colour rapidly changing to ultramarine-blue, which remained on dilution with water. Its mixed m. p. with *tetra*-p-*ethoxyazophenine* (II*b*) (prepared by the method described above for tetra-*p*-methoxyazophenine) was 258°. The filtrate after removal of (II*b*) afforded a solid (0·74 g.) which crystallised from *cyclo*hexane as light-tan plates, m. p. 160° (Found: C, 75·7; H, 6·8; N, 8·1; OEt, 25·5. $C_{22}H_{24}O_2N_2$ requires C, 75·9; H, 6·9; N, 8·05; 2OEt, 25·8%). It gave a very pale blue colour with concentrated sulphuric acid. Its mixed m. p. with NN′-*di*-(4-*ethoxyphenyl*)-p-*phenylenediamine* (prepared as described for the methoxy-analogue) was 160°. When the latter preparation was done in an open tube, tetra-*p*-ethoxyazophenine (m. p. and mixed m. p. 258°) was the only product isolated.

Band (*c*) gave a solid (1·65 g.) which crystallised from *cyclo*hexane as deep-red plates, m. p. 177° (Found: C, 76·5; H, 6·5; N, 8·4; OEt, 26·4. $C_{22}H_{22}O_2N_2$ requires C, 76·3; H, 6·3; N, 8·4; 2OEt, 26·0%). It gave an intense Prussian-blue colour, unchanged on dilution with water, with concentrated sulphuric acid. Its mixed m. p. with *benzoquinone di*-p-*ethoxyphenylimine* (prepared as described above for the di-*p*-methoxyphenylimine) was 178°.

Band (*d*) gave (?)3-*acetoxy*-4′-(3-*acetoxy*-4-*ethoxyanilino*)-4-*ethoxyazobenzene* (0·76 g.), which crystallised from *cyclo*hexane as red-brown needles, m. p. 169° (Found: C, 65·6; H, 5·9; N, 8·9; OEt, 18·6; Ac, 15·5. $C_{26}H_{27}O_6N_3$ requires C, 65·4; H, 5·7; N, 8·8; 2OEt, 18·9; 2Ac, 18·0%). It gave an ultramarine-blue colour, changing to red on dilution with water, with concentrated sulphuric acid. No identifiable products were obtained from reductive acetylation. It could not be acetylated with acetic anhydride and did not form an ethiodide. When it (0·084 g.) was hydrogenated in ethanol in the presence of Adams's catalyst, hydrogen (4·2 ml., 0·93 mol.) was absorbed and a colourless solution resulted, which in air became deep-red, and the original compound (m. p. and mixed m. p. 169°) was obtained on evaporation.

Oxidation of p-*Phenetidine in Acetic Acid.*—Freshly distilled *p*-phenetidine (6·5 g.) was added to phenyl iodosoacetate (16·1 g.) in acetic acid (450 ml.). After 5 hr., the acid was removed under reduced pressure (20 mm.) and the residue extracted with boiling benzene (4 × 200 ml.). The residue (2·9 g.) gave a blue-grey colour in concentrated sulphuric acid. Chromatography of the benzene extract on alumina gave 4 : 4′-diethoxyazobenzene (0·37 g.; m. p. 160°) in the first (yellow) band. A later (dull-red) band furnished a material which in concentrated sulphuric acid gave an ultramarine-blue colour, changing to red on dilution with water. Although it could not be obtained pure, it is probably identical with compound (IV*b*).

Microanalyses are by Dr. W. Zimmermann.

UNIVERSITY OF MELBOURNE, N.3, VICTORIA, AUSTRALIA. [*Received, June* 28*th*, 1954.]