OXIDATION OF PRIMARY AROMATIC AMINES WITH MANGANESE DIOXIDE

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Abstract—Active manganese dioxide in benzene oxidizes substituted anilines to symmetrically substituted azobenzenes, with the exception of nitranilines and aminobenzoic acids which are not attacked and polycyclic aromatic amines which polymerize.

SUBSTITUTED anilines can be oxidized to symmetrycally substituted azobenzenes with a variety of reagents including peracids,[2a] phenyliodoacetate,[2b] lead tetraacetate[2c] and sodium borate.[2d] Manganese dioxide[3] has also been shown to oxidize aniline to azobenzene and this would seem to offer a simple and general method for preparing substituted azobenzenes from primary aromatic amines. The manganese dioxide oxidation of N-alkyl- and -dialkyl-anilines resulting in dealkylation, formation of formanilide and other products,[4a] and the oxidation of benzylamine to benzalimine[4b] have also been reported.

In the present work it was found that the following simple anilines were smoothly oxidized to azobenzenes with active manganese dioxide[5] in benzene solution in over 90% yield (see Table 1): aniline, p-fluoro-, p-chloro-, p-bormo- and p-iodo-aniline, p-anisidine, p-biphenylamine, m-chloro-, o-fluoro, o-iodo- and o-ethyl-aniline and o-anisidine (the oxidation of o- and p-chloraniline and p-toluidine has been previously reported[3]). The ease of oxidation, as judged by the rate of separation of water in a Dean-Stark separator,[5b] showed only small differences. However, p-substituted anilines generally reacted more rapidly and the order F > Cl > Br > I was obeyed. o-Iodoaniline showed no great steric retardation to oxidation.

3,5-Dichloraniline and 2,6-dimethoxy-aniline reacted normally as did 3-chloro-4,6-dimethoxy- and 4-chloro-2,5-dimethoxy-aniline. The structure of their products was confirmed by elemental analysis (see Table 1) and UV and visible spectra (see below).

The three isomeric nitranilines, however, were recovered unchanged in benzene[3] and pyridine solution with periods of reflux of up to 24 hours. A small yield (ca. 5%)

[1] The Puerto Rico Nuclear Center is operated by the University of Puerto Rico under contract with the Atomic Energy Commission.

[2] [a] O. Fischer and J. Frost, *Ber Dtsch. Chem. Ges* **26**, 3083 (1893); N. Prileschajew, *Ibid.*, **42**, 4815 (1909); [b] R. Neu, *Ibid.*, **72**, 1505 (1939); [c] K. H. Pausacher and J. G. Scroggie, *J. Chem. Soc.* 4003 (1954); [d] S. M. Mehta and M. V. Vakilwala, *J. Amer. Chem. Soc.* **74**, 563 (1952).

[3] M. Z. Barakat, M. F. Abdel-Wahab and M. M. El-Sadr, *J. Chem. Soc.* 4685 (1956).

[4] [a] H. B. Henbest and A. Thomas, *J. Chem. Soc.* 3032 (1957); [b] R. J. Highet and W. C. Wildman, *J. Amer. Chem. Soc.* **77**, 4399 (1955).

[5] [a] J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen and T. Walker, *J. Chem. Soc.* 1094 (1952); [b] E. F. Pratt and J. F. Van de Castle, *J. Org. Chem.* **26**, 2973 (1961); [c] F. Pratt and S. P. Suskind, *Ibid.* **28**, 638 (1963).

of azo-compound was obtained from *o*- and *p*-nitraniline by prolonged (24 hr) heating in toluene solution. A number of substituted nitranilines (2-iodo-4-nitraniline, 2,6-diiodonitraniline and 2-methyl-5-nitroaniline) were similarly unreactive. While part of the reason for the low reactivity of some of these compounds may be steric hindrance of the amino group, the general lack of reactivity of nitranilines must be due to some other factor. The effect cannot be electronic since in other cases[5b,c] nitro groups facilitate oxidation with manganese dioxide.

It seems reasonable that a nitraniline will be preferentially adsorbed by the nitro group on the active oxidation centers in the manganese dioxide, thus preventing oxidation of the amino-group, which can only take place on the surface of the manganese dioxide. In support of this 3,5-dichloro-4-nitraniline, in which adsorption of the nitro group is hindered by the neighboring chlorine atoms gave a small yield of azo-compound. The isomeric 3,5-dichloro-2-nitraniline (in which electronic effects of the chlorine atoms on the amino group are the same) gave no azobenzene.

p-Aminobenzoic acid and anthranilic acid also gave no azo-compound. (The latter has been recently reported[6] to give a small yield (ca. 5%) of phenazine-1,6-dicarboxylic acid.) Here again adsorption will preferably occur through the carboxyl group. The reduction of the polarity of this group in ethyl *p*-aminobenzoate resulted in the formation of the azobenzene, albeit in low (10%) yield.

While 2-aminopyridine readily reacted, *α*- and *β*-naphthylamine gave only poor yields (4 and 5%, respectively) of azo-derivatives, accompanied by a tarry polymer. These two compounds have been reported not to react.[3] 1-Aminoanthracene gave only tars, together with a small amount of unidentified high-melting material. Polynuclear aromatics may well be oxidized to quinones and polymerize.

The oxidation of anilines to azobenzenes with manganese dioxide is one of the few examples of bimolecular oxidation with this reagent.[5c,7]

Oxidation must take place on the surface of the oxide, and the reaction can either occur by successive adsorption of two molecules of aniline, or by simultaneous adsorption of both of them on two adjacent "active sites". (The exact nature of the oxidizing species; chemi-adsorbed oxygen, manganese dioxide itself or a higher oxide; is in doubt,[5b,7] but is immaterial to the present discussion.) In the oxidation of a mixture of two anilines, the more basic aniline will be preferentially adsorbed. If the oxidation involves the attack of a second aniline molecule on an adsorbed molecule of aniline, then a mixture of anilines would afford three azobenzenes (the two simple products and the product of "cross-oxidation").[8] A mechanism involving dual adsorption would result in the oxidation of the more basic aniline to a disubstituted azobenzene, followed by its deadsorption and subsequent oxidation of the less basic aniline on the active sites so vacated. This would result in the formation of two symmetrical azobenzenes. The oxidation of a mixture of aniline and *p*-chloraniline gave only azobenzene and 4,4'-dichloroazobenzene and no 4-chloroazobenzene, and the oxidation of a mixture of aniline and *p*-anisidine afforded azobenzene and 4,4'-dimethoxyazobenzene (see Experimental). The reaction must thus proceed by a

[6] L. R. Morgan and C. C. Aubert, *Proc. Chem. Soc.* 73 (1962); cf. T. A. Davidson and A. I. Scott, *J. Chem. Soc.* 4075 (1961).

[7] R. M. Evans, *Quart. Rev. Chem. Soc.* 13, 61 (1959).

[8] Since electronic effects of substituents are small it is unlikely that one aniline will react completely before the other.

bimolecular adsorption process. The relative unimportance of substituents in the oxidation of benzyl alcohols[3b] (cf. above) has been interpreted as evidence for a free-radical oxidation. However, the importance of the step of adsorption of the aniline (a weekly basic aniline will be less easily adsorbed, but more readily oxidized in an ionic mechanism) may well obscure any electronic effects in the actual oxidation step.

The UV spectra of the azobenzenes showed the characteristic visible absorption (R-band)[9a] of such compounds, which is not shown by azoxybenzenes.[9b] The main band (near 320 mμ) in 4,4'-dicarbethoxyazobenzene gave the expected bathochromic shifts and increase in intensity as compared to azobenzene (λ_{max} 320 mμ; ε 17,300).[9a] 2,2'-Diethyl- and 2,2'-difluoro-azobenzene both had a decreased intensity, without a hypsochromic shift characteristic of low order steric hindrance. 2,2',6,6'-Tetramethoxyazobenzene had a large hypsochromic shift (cf. 4,4'-dimethoxyazobenzene, λ_{max} 354 mμ[9a]) while 3,3',5,5'-tetrachloroazobenzene absorbed at much the same wavelength as 3,3'-dichloroazobenzene (λ_{max} 320 mμ[9a]), since the *meta*-chlorine atoms cannot exert a resonance effect. The two isomeric dichlorotetramethoxyazobenzenes showed two maxima in this same region and this probably results from the superimposition of a number of chromophores, due to *ortho*, *meta*, and *para* substitution. The absorption spectra of the other azobenzenes prepared were in agreement with the previously reported data.[9a]

TABLE 1. M.P. OF SUBSTITUTED AZOBENZENES

	m.p.	lit. m.p.
Azobenzene	68°	68° [a]
4,4'-Difluoro-	100°	101° [b]
4,4'-Dichloro-	185°	188° [c]
4,4'-Dibromo-	204°	205° [a]
4,4'-Diiodo-	235°	237° [a]
4,4'-Dimethoxy-	160°	160·5–162·5° [a]
4,4'-Diphenyl-	248°	249–250° [a]
4,4'-Dicarbethoxy-	143°	145° [a]
3,3'-Dichloro-	99°	101° [a]
2,2'-Difluoro-	98°	71° [d]
2,2'-Diiodo-	151°	149·8–150·5° [a]
2,2'-Diethyl-	44°	46·5° [a]
2,2'-Dimethoxy-	143°	141° [a]
3,3',5,5'-Tetrachloro-	189°	—[f]
2,2',6,6'-Tetramethoxy-	110°	—[g]
3,3'-Dichloro-4,4',6,6'-tetramethoxy-	243°	—[h]
4,4'-Dichloro-2,2',5,5'-tetramethoxy-	184°	—[i]

[a] Ref. 12. [b] J. Lichtenberger and R. Thermet, *Bull. soc. chim. Fr.*, 318 (1951). [c] G. M. K. Hughes and B. C. Saunders, *J. Chem. Soc.* 4630 (1954). [d] G. Olah, A. Pavlath and I. Kuhn, *Acta Chim. Acad. Sci. Hung.* 7, 71 (1955). (Found: C, 65·94; H, 3·74. Calc. for $C_{12}H_8F_2N_2$: C, 66·01; H, 3·69%). [e] J. E. Leffler and A. F. Wilson, *J. Org. Chem.* 25, 424 (1960). [f] (Found: 45·08; H, 2·09. Calc. for $C_{12}H_6Cl_4N_2$: C, 44·99; H, 1·89%). [g] (Found: C, 63·38; H, 5·95. Calc. for $C_{16}H_{18}N_2O_4$: C, 63·56; H, 5·00%). [h] (Found: C, 52·23; H, 4·18. Calc. for $C_{16}H_{16}Cl_2N_2O_4$: C, 51·75; H, 4·34%). [i] (Found: C, 52·13; H, 4·33; Calc. for $C_{16}H_{16}Cl_2N_2O_4$: C, 51·75; H, 4·34%).

[a] P. H. Gore and O. H. Wheeler, *J. Org. Chem.* 26, 3295 (1961); [b] P. H. Gore and O. H. Wheeler, *J. Amer. Chem. Soc.* 78, 2160 (1956).

TABLE 2. SPECTRA OF AZOBENZENES[a]

4,4'-Dicarbethoxy-	223[b](16,800)[18]	327(29,000)	465(800)
2,2'-Diethyl-	240(11,400)	336(14,100)	446(830)
2,2'-Difluoro-	227(16,500)	325(12,400)	465(690)
2,2',6,6'-Tetramethoxy-	208(35,200)	345(21,300)	444(1,020)
	236(18,350)		
3,3',5,5'-Tetrachloro-	216(32,100)	317(19,300)	430(680)
3,3'-Dichloro-4,4',6,6'-tetramethoxy-	215(29,500)	274(24,800)	415(1,050)
		314(4,600)	
4,4'-Dichloro-2,2',5,5'-tetramethoxy-	215(14,000)	278(13,300)	434(750)
		318(6,950)	

[a] Spectra measured in 95% ethanol; wavelength in mμ; molar extinction coefficients in parenthesis. [b] Inflection.

EXPERIMENTAL

Active manganese dioxide was prepared according to the method of Attenburrow *et al.*,[5a] as modified by Pratt and Van de Castle,[5b] dried at 100–120° for 24 hr and stored in a desiccator.

Anilines. Most of the substituted anilines were commercial samples of high purity and were used without further purification. Ethyl *p*-aminobenzoate was prepared by esterification of *p*-aminobenzoic acid.[10]

2-Nitro- and 4-nitro-3,5-dichloraniline. 3,5-Dichloraniline (Aldrich Chemical Co.) (2 g) in acetic acid (4 ml) was stirred with acetic anhydride (6 ml), for 1/2 hr. The precipitate was dissolved by adding more acetic acid (4 ml), and nitrated by dropwise addition with stirring and cooling to below 30° of conc. HNO$_3$ (3 ml) and conc. H$_2$SO$_4$ (6 ml). The mixture was left overnight at room temp, the precipitate filtered off, washed with water and dried. The mixed nitro-acetanilides were hydrolysed by refluxing with 10% KOH in ethanol for 2 hr. The mixed nitranilines were precipitated with water and washed and dried. 2-Nitro-3,5-dichloraniline (0·5 g), m.p. 78–79°, from ethanol (lit. m.p. 79°[11]) was extracted with hot carbon disulfide, leaving 4-nitro-3,5-dichloraniline (1·3 g), m.p. 169–170°. from ethanol (lit. m.p. 171°[11]). Nitration could not be effected with conc. HNO$_3$ acid in acetic acid, and 3,5-dichloracetanilide, m.p. 186°, was recovered.

Oxidations. The amine (0·01 mole) and dried active manganese dioxide (0·05–0·06 mole) in benzene (50–60 ml) were refluxed for 6 hr, and the water formed was removed with a Dean-Stark water separator. The hot solution was filtered and the manganese dioxide washed with hot benzene until the filtrate was colorless. The filtrate was evaporated to a small volume, and hexane added to crystallize the product, which was recrystallized from benzene-hexane or ethanol. The m.p.s of the azobenzenes formed are given in Table 1. 2-Aminopyridine gave 2-azopyridine, m.p. 85° (lit. m.p. 87°[12]).

The yields were all above 90%, except in the cases of ethyl *p*-aminobenzoate (10%), α-naphthylamine (4%; 1-azonaphthalene, m.p. 185-90°, lit m.p. 190°[12]) and β-naphthylamine (5%; 2-azonaphthalene, m.p. 204–206°, lit. m.p. 208°[12]). 3,5-Dichloro-4-nitraniline gave 4,4'-dinitro-3,3',5,5'-tetrachloroazobenzene (10% yield), m.p. 271°. (Found: C, 35·04; H, 1·42. Calc. for C$_{12}$H$_4$Cl$_4$N$_4$O$_4$: C, 35·13; H, 0·98%).

1-Aminoanthracene gave a tarry product from which a small amount of material, m.p. 350°, could be extracted with chloroform.

The following amines were recovered unchanged on refluxing with active manganese dioxide in benzene for up to 24 hr; *o*-, *m*- and *p*-nitraniline, anthranilic acid, *p*-aminobenzoic acid, 2-iodo-4-nitraniline, 2,6-diiodo-4-nitraniline, 2-methyl-5-nitraniline and 3,5-dichloro-2-nitraniline. *p*- and *o*-Nitraniline gave small yields (<5%) of 4,4'-dinitroazobenzene (m.p. 220°, lit. m.p. 222–223°[12]) and 2,2'-dinitrazobenzene (m.p. 217°; lit. m.p. 217·8°[12]) on refluxing for 24 hr in toluene. No azobenzene was formed in pyridine solution.

[10] A. I. Vogel, *Textbook of Practical Organic Chemistry* p. 866. Longmans Green, London (1948).
[11] A. Beilstein and V. Kurbatov, *Liebigs Ann.* 196, 227 (1879).
[12] *Dictionary of Organic Compounds* (Edited by I. Heilbron and H. M. Bunbuxy), Oxford University Press, New York, N.Y. (1953).

4-Aminoazobenzene was oxidized in the normal manner to 4,4'-bis-(phenylazo)-azobenzene m.p. 234° (lit. m.p. 236–236·5° [13]).

Oxidation of a mixture of aniline (5 mmole) and p-chloraniline (5 mmole) with manganese dioxide (50 mmole) in benzene for 4 hr gave a product m.p. 160–165°. This was chromatographed on alumina from hexane and eluted with hexane–benzene giving fractions of azobenzene (m.p. 65–66°) and 4,4'-dichlorazobenzene (m.p. 184–185°). No intermediate fractions of 4-chlorazobenzene were found. The IR spectrum of 4-chlorazobenzene showed peaks (in CS_2) also found in the spectra of either azobenzene or 4,4'-dichlorazobenzene and could not be used for analysis.

Similarly the oxidation of equimolar amounts of aniline and p-anisidine gave azobenzene (m.p. 66°) and 4,4'-dimethoxyazobenzene (m.p. 160–161°), with no intermediate fractions of 4-methoxyazoben-zene. It is estimated that 5% of mono-substituted azobenzene could have been detected in these separations.

Ultraviolet spectra. The UV and visible spectra (Table 2) were determined in purified 95% ethanol in 1 cm cells at concentrations to give optical densities of 0·4–0·8, using a Bausch-Lamb Spectronic 505 spectrophotometer.

[13] K. Ueno, *J. Amer. Chem. Soc.* **74**, 4508 (1952).