369. The Effect of Substituents on the Reduction of Azo-compounds.

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The course of reduction of a number of azo-compounds is correlated with the electron density on the azo-group.

FOR the synthesis of 3,5-dioxopyrazolidines[1] some 4-substituted hydrazo-compounds were required. When preparing these from the azo-derivatives, $4\text{-R}\cdot C_6H_4\cdot N\!:\!N\cdot C_6H_4R'$, it was found that the product (hydrazo-compound or amine) depended on the nature of R and R′.

The azo-compounds were prepared by recorded methods. An attempt to prepare 4′-hydroxyazobenzene-4-carboxylic acid[2] from azobenzene-4-carboxylic acid by oxidation with peracetic acid followed by Wallach rearrangement of the azoxy-compound gave unsatisfactory results. However, this azo-compound was obtained in 17% yield by a

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[1] Linnell and Khalifa, *J.*, 1959, 1315.

[2] Angeli and Valori, *Atti R. Accad. Lincei*, 1913, **22**, 132.

procedure[3] reported for preparation of the 4-hydroxy-4′-nitroazobenzene (which was obtained in 90% yield). Potassium azobenzene-4,4′-disulphonate was prepared from potassium sulphanilate by oxidation with potassium permanganate.[4] The ready solubility of the starting material and its oxidation product in water is largely responsible for the good yield (60%) in this oxidation, since from *p*-nitroaniline the yield was only 15%, and about 35% of unchanged *p*-nitroaniline was recovered.[1]

Reduction of the azo-compounds was by (1) zinc dust and acetic acid according to Khalifa and Linnell's modification[5] of Jacobson and Steinbrenk's method,[6] or (2) alcoholic ammonium sulphide according to Werner and Stiasny's method.[7]

By method (1), monosubstituted azo-compounds containing electron-attracting substituents, *e.g.*, CO_2H, CO_2Me, which produce a $-M$ effect, lowering the electron-density on the azo-group, were reduced to hydrazo-compounds. On the other hand, azo-compounds containing one or two electron-repelling *para*-substituents, *e.g.*, OH, OEt, inducing a $+M$ effect and thus increasing the electron-density on the azo-group, gave the amines. Jacobson[8] found that 3-hydroxyazobenzene was reduced to the hydrazo-compound while the 2- and the 4-isomer yielded aniline and the aminophenol. In these compounds, mesomeric electron-release occurs only when the unshared electrons on the hydroxyl group are conjugated with the azo-group. Such conjugation is absent in 3-hydroxyazobenzene, where only the $-I_s$ effect is operative, lowering the electron-density on the azo-group. In the 2- and the 4-isomers, conjugation is present and the $+M$ effect operates, rendering the azo-group a centre of high electron-density. 4,4′-Diacetoxy- and 4,4′-dibenzoyloxy-azobenzene are reduced to the hydrazo-derivatives because, although conjugation is present, yet electron-release to the *para*-position (*i.e.*, to the azo-group) is largely diminished by the acyl residues attached to the oxygen atoms.[9] For the same reason acetylguaiacol is nitrated exclusively *para* to the methoxy-group.[10]

When $R = H$ or R' a single effect—either electron-attraction or electron-repulsion—is exerted. With unsymmetrical 4,4′-substituted compounds the situation is different. 4′-Hydroxyazobenzene-4-carboxylic acid contains an electron-attracting carboxyl group and a powerful electron-repelling hydroxyl group, the effect of the latter predominating. The result is an increase in the electron-density of the azo-group and accordingly on reduction the compound is cleaved. Moderating the effect by alkylating or acylating the hydroxyl group leads to the hydrazo-derivatives.

With the second method of reduction the work was extended to include nitro- and sulphonate groups. On the whole, the results were consistent with those obtained with method (1). When $R' = H$ and R and is electron-attracting, the products were the hydrazo-derivatives. Azo-compounds containing two electron-repelling substituents behaved in a heterogeneous manner. While 4,4′-dihydroxyazobenzene yielded *p*-aminophenol, its diethyl ether was unaffected.[11] Both were cleaved by method (1). Now, alkylation of the hydroxyl group diminishes its electron-repellency, and it may be that fission by method (2) requires a very high electron-density on the azo-group, so that the free hydroxy-compound was cleaved while the other was not. Similarly, 4,4′-diacetoxyazobenzene yielded the hydrazo-compound by method (1) but did not respond to method (2). A plausible explanation is that for reduction to the hydrazo-stage by method (2) a low electron-density on the azo-group is necessary, and this is not the case with 4,4′-diacetoxyazobenzene. 4′-Ethoxy- and 4′-acetoxy-azobenzene-4-carboxylic acid

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[3] Bamberger, *Ber.*, 1892, **25**, 846.
[4] Laar, *Ber.*, 1881, **14**, 1928.
[5] Khalifa and Linnell, *J. Org. Chem.*, 1959, **24**, 853.
[6] Jacobson and Steinbrenk, *Annalen*, 1898, **303**, 384.
[7] Werner and Stiasny, *Ber.*, 1899, **32**, 3272.
[8] Jacobson and Hönigsberger, *Ber.*, 1903, **36**, 4093.
[9] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 240.
[10] Reverdin and Crépieux, *Ber.*, 1903, **36**, 2257.
[11] Khalifa and Abo-Ouf, *J.*, 1958, 3740.

responded equally to the two methods of reduction. Compounds where $R \neq H$ and $R' = NO_2$ behaved in a unique manner. 4′-Hydroxy-, 4′-ethoxy-, and 4′-acetoxy-4-nitroazobenzene all afforded the corresponding amino-azo-compounds. That the nitro- rather than the azo-group is attacked is due to the fact that the electron-donor substituents are in conjugation with the electron-sink nitro-group and it is the latter whose electron-density is increased and hence it is this group which is reduced (in agreement with Meldola's findings [12,13]).

EXPERIMENTAL

Microanalyses are by Messrs. Ciba, Switzerland, and Alfred Bernhardt, Germany.

4′-Hydroxyazobenzene-4-carboxylic Acid.—*p*-Aminobenzoic acid (14 g.) was heated with 70% nitric acid (27 ml.) and water (175 ml.) until a clear solution was obtained, which was then cooled to 0—5° with stirring. 10% Aqueous sodium nitrite (80 ml.) was added and stirring continued for a further ¼ hr. The excess of nitrite was decomposed with urea, and the diazonium salt solution was diluted with ice-cold water to 1¼ l. and coupled with phenol (9 g.) in alcohol (50 ml.). Stirring and cooling were maintained for several hours, then the mixture was kept at 15—20° for 48 hr. The crude product (4·5 g.) formed red crystals (from aqueous ethanol), m. p. 270° (decomp.) [lit.,[2] 266° (decomp.)].

4′-Ethoxyazobenzene-4-carboxylic acid, prepared in 80% yield from the sodio-derivative of the hydroxy-compound and ethyl iodide, formed orange crystals, m. p. 254° (from ethanol) (Found: C, 66·8; H, 5·35; N, 10·6. $C_{15}H_{14}O_3N_2$ requires C, 66·65; H, 5·2; N, 10·4%).

Acetyl chloride in presence of acetic acid gave the *4′-acetoxy-acid,* orange needles (from ethanol), m. p. 258—260° (Found: C, 63·4; H, 4·3; N, 9·9. $C_{15}H_{12}O_4N_2$ requires C, 63·4; H, 4·3; N, 9·8%).

4-Hydroxy-4′-nitroazobenzene.—Prepared by Bamberger's method,[3] this had m. p. 212—213° as reported by Bamberger (Meldola [12] gives m. p. 183—184°). As above, it gave the red *4-ethoxy-*, m. p. 160—161° (from ethanol) (Found: C, 62·0; H, 4·9; N, 15·6. $C_{14}H_{13}O_3N_3$ requires C, 62·0; H, 4·8; N, 15·5%), and *4-acetoxy-compound,* red needles (from ethanol), m. p. 150—151° (Found: C, 59·1; H, 4·0; N, 14·7. $C_{14}H_{11}O_4N_3$ requires C, 58·9; H, 3·9; N, 14·7%).

4,4′-Dihydroxyazobenzene.—This was obtained in 46% yield by fusing *p*-nitrophenol with potassium hydroxide according to Willstätter and Benz's method.[14] Attempts to raise the yield to 60—70% as claimed by Bigiavi and Carrara [15] were abortive. The diethyl ether, diacetate, and dibenzoate were prepared by recorded methods.[14,16]

Potassium Azobenzene-4,4′-disulphonate.—This was prepared by oxidation of potassium sulphanilate according to Laar's procedure; [4] also by electrolytic reduction [17] of potassium *p*-nitrobenzenesulphonate [18] which was obtained from *p*-chloronitrobenzene by treatment with sodium disulphide, and the di-*p*-nitrophenyl disulphide being oxidised by fuming nitric acid and the sulphonic acid thus obtained converted into the potassium salt.

4,4′-Dinitroazobenzene.—This was obtained in 60% yield by Cook and Jones's procedure.[19]

Azobenzene-4-carboxylic Acid.—The acid was prepared by Anspon's method [20] which is essentially that described by Angeli.[2] Fischer's method of esterification afforded the ester in only 15% yield: the silver salt and an excess of methyl iodide gave a 40% yield.

Reduction of the Azo-compounds.—(1) To the azo-compound in boiling alcohol, zinc dust (30—35 times the theoretical amount for reduction to the hydrazo-stage) was added, then acetic acid with stirring, dropwise, until the solution became colourless. The filtrate was concentrated under diminished pressure and diluted with cold water.

(2) The azo-compound, suspended in alcohol, was treated at the b. p. with a saturated solution of ammonium sulphide (12 times the theoretical amount for reduction to the hydrazo-stage) prepared just before use by saturating a mixture of equal parts of concentrated aqueous

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[12] Meldola, *J.*, 1885, **47**, 659.
[13] Meldola, *J.*, 1884, **45**, 106.
[14] Willstätter and Benz, *Ber.*, 1906, **39**, 3495.
[15] Bigiavi and Carrara, *Gazzetta*, 1923, **53**, 285.
[16] Willstätter and Benz, *Ber.*, 1907, **40**, 1582.
[17] Elbs and Wohlfahrt, *Z. Elektrochem.*, 1902, **8**, 790.
[18] Bell, *J.*, 1928, 2776.
[19] Cook and Jones, *J.*, 1939, 1310.
[20] Anspon, *Org. Synth.*, 1945, **20**, 86.

ammonia and water with hydrogen sulphide. The mixture was boiled for 2—7 min. then diluted with an equal volume of water.

The principal results are recorded in the Tables.

Azo-compound (I)		Method of redn.	M. p.	Solvent crystn.	Hydrazo-compound *						
					Found (%)				Required (%)		
R′	R				C	H	N	Formula	C	H	N
H	CO_2H §	1, 2	194—195° ‡	Aq. EtOH	—	—	—		—	—	—
H	CO_2Me ¶	1, 2	114—115	EtOH	—	—	—		—	—	—
NO_2	NO_2 ¶	2	248—250	$COMe_2$	—	—	—		—	—	—
SO_3K	SO_3K ¶	2		H_2O	—	—	—		—	—	—
OAc	OAc	1	138—140	C_6H_6–Pet †	63·8	5·2	9·3	$C_{16}H_{16}O_4N_2$	64·0	5·3	9·3
OBz	OBz	1	188—190	EtOH	74·1	4·65	6·6	$C_{26}H_{20}O_4N_2$	73·6	4·7	6·6
OEt	CO_2H §	1, 2	256—258	Aq. EtOH	66·3	5·3	10·9	$C_{15}H_{16}O_3N_2$	66·2	5·9	10·3
OAc	CO_2H §	1, 2	202—204	Aq. MeOH	63·0	4·9	9·6	$C_{15}H_{14}O_4N_2$	62·9	4·9	9·8

* Yields between 75 and 85%. † Pet = light petroleum (b. p. 80—100°). ‡ Ref. 6, m. p. 192—193°. § In method (2), the mixture is acidified with acetic acid for liberating the hydrazo-compound. ¶ Reported in the literature.

Method 2 gave 4-amino-4′-hydroxy-, m. p. 187° (from water) (lit.,[12] 181°), and -4′-*ethoxyazobenzene*, m. p. 135—136° (from aqueous ethanol) (negative Meldola test [13]) (Found: C, 69·1; H, 6·1; N, 17·1. $C_{14}H_{15}ON_3$ requires C, 69·7; H, 6·2; N, 17·4%), also 4-*acetoxy*-4′-*aminoazobenzene*, m. p. 198—200° (from chloroform) (positive Meldola test) (Found: N, 17·0. $C_{14}H_{13}O_2N_3$ require N, 16·5%).

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