Dyes and Pigments 2 (1981) 215–217

A NOVEL SYNTHESIS OF 6-AMINOQUINOXALINES

MILOS BIL and JOHN F CORBETT

Clairol Research Laboratories, 2 Blachley Road, Stamford, Connecticut 06902, USA

SUMMARY

In the course of a study of amine exchange reactions with some diaminonitrobenzenes, we observed that a remarkable conversion of some of these compounds into 6-aminoquinoxalines resulted from heating the nitro compound with monoethanolamine

1 DISCUSSION

During a study of the stability of the diaminonitrobenzene hair dyes in various media, we observed that 5-amino-2-(β-hydroxyethyl)aminonitrobenzene (**1**)[1] in ammoniacal systems was slowly converted into 2,5-diaminonitrobenzene (**2**) The reaction presumably involved nucleophilic displacement of the hydroxyethylamino group by ammonia This was of interest since the lability of an amino group under the influence of a single nitro group had not previously been reported.

In trying to establish the generality of the reaction we stored 2,5-diaminonitrobenzene (**2**) or 5-amino-2-methylaminonitrobenzene (**4**) in an aqueous solution of monoethanolamine (MEA) In time, chromatography revealed the formation of some compound (**1**) and the presence of ammonia or methylamine could be demonstrated Longer storage resulted in the formation of a fluorescent yellow dye which was shown to be 6-aminoquinoxaline (**3**) by mass spectroscopy, elemental analysis and comparison with an authentic sample [2] 6-Aminoquinoxaline has previously been obtained by condensation of 1,2,4-triaminobenzene with glyoxal[2] or by the reduction of 6-nitroquinoxaline.[3] We have now obtained the quinoxaline (**3**) in 63 % yield by heating 2,5-diaminonitrobenzene (**2**) in 45 % w/w monoethanolamine/water at 105–107 °C for 60 hours

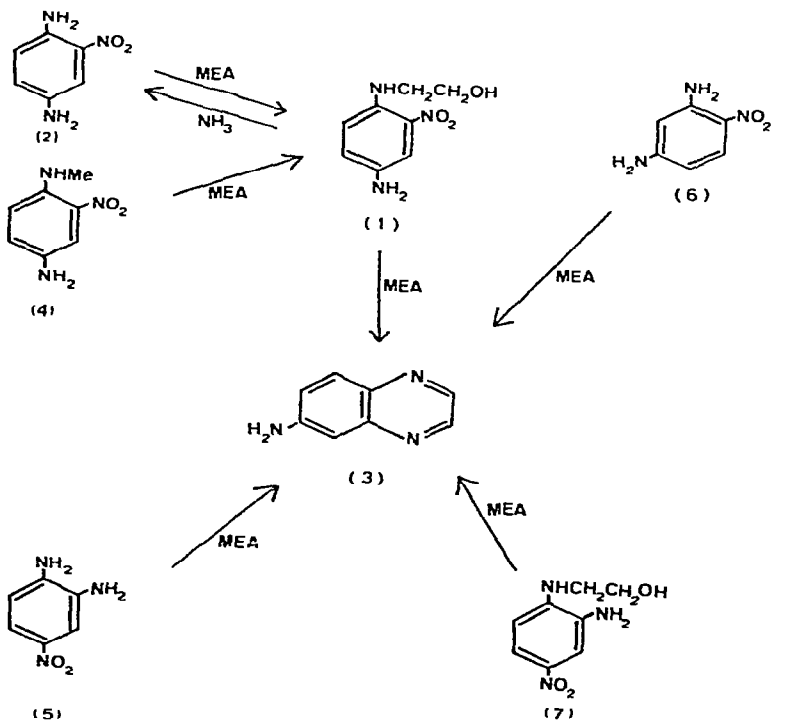
Dyes and Pigments 0143-7208/81/0002-0215/$02 50

From the initial experiment, it was evident that 5-amino-2-(β-hydroxyethyl)-aminonitrobenzene (**1**) is an intermediate in the reaction. This was confirmed by conversion of (**1**) into the quinoxaline (**3**) in 62% yield. The conversion of (**2**) into (**3**) requires reduction of the nitro-group followed by ring closure and, presumably, oxidation of the resulting dihydroquinoxaline. The ability of monoethanolamine to act as a reducing agent for aromatic nitro-groups was observed by Meltzner *et al* and by Kremer[4] who reported the conversion of 2- and 4-chloronitrobenzenes to mixtures of the chloroaniline and dichloroazobenzenes.

In investigating the scope of this reaction, we obtained 6-aminoquinoxaline from 2,4-dinitroaniline, 3,4-diaminonitrobenzene (**5**); 2,4-diaminonitrobenzene (**6**); and 3-amino-4-(β-hydroxyethyl)aminonitrobenzene (**7**)[5] by refluxing with monoethanolamine However, (**7**) was not detectable as an intermediate in the conversion of (**5**) to (**3**) even though the conversion of (**7**) to (**3**) is relatively slow

It is thus evident that the cyclization step must be intramolecular in the conversion of (**2**) and (**4**) via (**1**) to (**3**) but intermolecular in the conversion of (**5**) to (**3**).

We have also found that 6-(*N*-substituted amino)-quinoxalines can be prepared by this route Thus both 2-methylamino-5-(bis-β-hydroxyethyl)aminonitrobenzene[1] and 2-(β-hydroxyethyl)amino-5-bis(β-hydroxyethyl)aminonitrobenzene[1]



give good yields of 6-(bishydroxyethyl)aminoquinoxaline and 2-(β-hydroxyethyl)-amino-5-dimethylaminonitrobenzene[6] gives 6-dimethylaminoquinoxaline on heating with aqueous monoethanolamine

2 EXPERIMENTAL

2.1 *6-Aminoquinoxaline*

49.3 g of compound (**1**) in 18.8 g of MEA and 100 g of water was refluxed at 100–103 °C for 36 h. After cooling, 22.7 g of crude 6-aminoquinoxaline (**3**) was obtained by extraction with $CHCl_3$ and evaporation of the solvent. Recrystallization from propanol/chloroform (1·1) gave pale yellow needles m.p. 156.5–158.5 °C (Lit.[2] 158–9 °C): λ_{max} (95% ethanol) 218, 262, 396 nm. Using similar procedures the yields of compound (**3**) were 63% from (**2**), 55% from (**5**) and 47% from 2,4-dinitroaniline.

2.2 *6-Bis-(β-hydroxyethyl)aminoquinoxaline*

7.1 g of 2-(β-hydroxyethyl)amino-5-bis(β-hydroxyethyl)aminonitrobenzene, 10.8 g of MEA and 12.5 g of water were refluxed for 30 h to give 3.6 g (66%) of the quinoxaline which on recrystallization had m.p. 131–2 °C, λ_{max} 220, 272, 421 nm. Found: C, 62.0, H, 6.4; N, 18.1%. Calc. for $C_{12}H_{15}O_2N_3$: C, 61·8, H, 6·5, N, 18.0%. The sulphate forms red crystals, m.p. 133–5 °C. The same product was obtained in 38% yield from the 2-methylamino analogue.

2.3 *6-Dimethylaminoquinoxaline*

28.1 g of 2-(β-hydroxyethyl)amino-5-dimethylaminonitrobenzene refluxed in 49 g of MEA and 50 g of water for 30 h gave 21·5 g (63%) of the quinoxaline sulphate, m.p. 223–5 °C. Found: C, 42·6; H, 5·0; N, 14·7; S, 11.9%. $C_{10}H_{11}N_3.H_2SO_4$ requires C, 44.3, H, 4.3, N, 15.5, S, 11·8%. The free base had m.p. 32–4 °C, λ_{max} (95% ethanol) 207, 260, 415 nm.

REFERENCES

1 CLAIROL, US Pat. 3,632,582 (1972)
2 O. HINSBERG, *Chem. Ber.*, **17**, 319 (1884)
3 K. A. JENSEN, *Acta Chem. Scand.*, **2**, 91 (1948)
4 M. MELTZNER, C. WOHLBERG and M. KLEINER, *J. Amer. Chem. Soc.*, **57**, 2554 (1935), C. B. KREMER, *J. Amer. Chem. Soc.*, **59**, 1681 (1937)
5 CLAIROL, US Pat. 3,088,978 (1963)
6 SANDOZ, Swiss Pat. 479,302 (1969)