819. *Polycyclic Cinnoline Derivatives. Part I. Reduction of 2 : 2′-Dinitrodiaryls and Related Compounds.*

By R. S. W. Braithwaite, P. F. Holt, and A. N. Hughes.

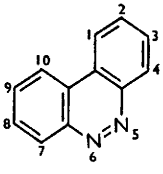
Methods for the reduction of 2 : 2′-dinitrodiaryls, 5 : 6-dinitroacenaphthene, and 1 : 8-dinitronaphthalene have been studied, to facilitate the preparation of polycyclic cinnoline derivatives. Direct reduction may give a polycyclic cinnoline derivative, its *N*-oxide, an amine, a nitroamine, or a polymer.

Certain polycylic cinnoline derivatives would be interesting as analogues of carcinogens, but few complex cinnoline derivatives are known, and there has been little study of the general preparative methods. The formation of a ring-homologous cinnoline system usually involves synthesis and reduction of a 2 : 2′-dinitrodiaryl but the yields are sometimes poor. The reduction of 6 : 6′-dinitrobenzidine, 6 : 6′-dinitro-*o*-tolidine, 4 : 4′-dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls (halogen = Cl, Br, and I) and 2 : 6 : 2′ : 6′-tetranitrodiphenyl has now been examined, and also that of 5 : 6-dinitroacenaphthene (Ring Index numbering, No. 1779) and 1 : 8-dinitronaphthalene where an internal azo-link can be formed. The reducing agents used were lithium aluminium hydride, zinc in aqueous-alcoholic potassium hydroxide, sodium amalgam in methanol or ethanol, aqueous-alcoholic sodium sulphide, and aqueous-alcoholic sodium polysulphide. From published results[1] it would seem that from simple 2 : 2′-dinitrodiaryls aqueous-ethanolic sodium

---

[1] Simpson, "Condensed Pyridazine and Pyrazine Rings," Interscience Publ., New York, 1953, p. 53.

sulphide normally forms an *N*-oxide, electrolytic reduction a cinnoline, sodium amalgam in methanol a cinnoline, and zinc dust in potassium hydroxide the mono- and the di-*N*-oxide. We find that the reduction products may also include amines and polymers, and that nuclear halogen may be eliminated.


(I)

Lithium Aluminium Hydride.—Benzo[*c*]cinnoline (I) has been prepared[2,3] (90% yield) by reducing 2 : 2′-dinitrodiphenyl with lithium aluminium hydride. This reducing agent normally gave satisfactory yields (70—90%) of cinnoline when applied to the sterically unhindered dinitro-compounds listed above, but the nitroamines were not reduced unless a large excess of the reagent was used because an initial reaction involving the amino-groups utilises 0·5 mol. of the reagent.

Mićović and Mihailović[4] quote a number of authors as stating that nuclear halogen is not eliminated under normal conditions during reductions with lithium aluminium hydride. In the production of cinnolines we find that chlorine and bromine are unaffected, but that iodine is eliminated, from 4 : 4′-dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls. (Hill[2] found that the reduction of *o*-chloronitrobenzene gives azobenzene.) 2 : 6 : 2′ : 6′-Tetranitrodiphenyl gives a polymer and not a cinnoline.

Zinc and Potassium Hydroxide.—Täuber,[5] using a slight excess of zinc dust and potassium hydroxide in aqueous ethanol to reduce 2 : 2′-dinitrodiphenyl, obtained a mixture of benzo[*c*]cinnoline mono- and (mostly) di-*N*-oxide. 4 : 4′-Dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls (halogen = Cl, Br, or I) all gave cinnolines, but bromine and iodine were removed.

Sodium Sulphide.—Sodium sulphide and aqueous ethanol, first used to form cinnoline derivatives by Ullmann and Dieterle,[6] have usually given *N*-oxides. We confirmed this. The retention or elimination of nuclear-substituted iodine can depend on the alkalinity of the reducing agent. When sodium sulphide and sodium hydroxide are used 4 : 4′-di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gives the cinnoline oxide containing only one atom of iodine, but sodium sulphide alone gives the di-iodocinnoline oxide.

Certain dinitro-compounds do not give the expected cyclic azo-compounds. 1 : 8-Dinitronaphthalene gives a polymer with aqueous-ethanolic sodium sulphide although under some other reducing conditions it gives an intramolecular hydrazo-compound.[7] Likewise, 2 : 6 : 2′ : 6′-tetranitrodiphenyl and 5 : 6-dinitroacenaphthene give polymers. In the latter case even aqueous-ethanolic sodium hydroxide produces a polymer, though this reagent does not reduce the dinitronaphthalene. When polymers are formed, the yield is approximately constant over a wide range of experimental conditions, indicating that the polymer is not an intermediate in the production of other soluble end-products, such as amines.

Sodium Polysulphide.—This reagent reduced 2 : 6 : 2′ : 6′-tetranitrodiphenyl to 2-amino-6 : 2′ : 6′-trinitrodiphenyl and a diaminodinitrodiphenyl. The latter could be 2 : 6-diamino-2′ : 6′-dinitrodiphenyl but is most probably 2 : 2′-diamino-6 : 6′-dinitrodiphenyl since, by analogy with the reduction of 1 : 3-dinitrobenzene with sodium polysulphide (when one nitro-group only is reduced), it is improbable that both nitro-groups in one ring of the diphenyl molecule would be reduced.

Sodium Amalgam and Alcohol.—Sodium amalgam and methanol has been reported generally to give a cinnoline (Täuber[5] and, later, others). Our results confirm that cinnolines are normally formed although 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gives a mixture of the cinnoline and its oxide. Nuclear chlorine and bromine are

---

[2] Hill, Ph.D. thesis, University of Reading, 1952.

[3] Badger, Seidler, and Thomson, *J.*, 1951, 3207.

[4] Mićović and Mihailović, " Lithium Aluminium Hydride in Organic Chemistry," Serbian Academy of Sciences, Belgrade, 1955, p. 104.

[5] Täuber, *Ber.*, 1891, **5**, 3081.

[6] Ullmann and Dieterle, *Ber.*, 1904, **37**, 23.

[7] Vorozhtsov and Kozlov, *J. Gen. Chem. U.S.S.R.*, 1937, **7**, 793.

unaffected but iodine is eliminated when 4 : 4′-dihalogeno-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyls are reduced. 2 : 6 : 2′ : 6′-Tetranitrodiphenyl and the diaminodinitrodiphenyl obtained above are reduced to 2 : 6 : 2′ : 6′-tetra-aminodiphenyl. Different products may be obtained if ethanol rather than methanol is used in the reduction. Thus 2 : 6 : 2′ : 6′-tetranitrodiphenyl yields a polymer with sodium amalgam and ethanol, but the tetramine with sodium amalgam and methanol.

The results fit the generalisation that 2 : 2′-dinitrodiphenyls give cinnolines with lithium aluminium hydride and with sodium amalgam, but *N*-oxides with sodium sulphide. 2 : 6 : 2′ : 6′-Tetranitro- and 2 : 2′-diamino-6 : 6′-dinitro-diphenyl are exceptions; cinnolines are not formed, possibly because of steric hindrance. Similarly, an internal azo-link is not formed from 1 : 8-dinitronaphthalene and 5 : 6-dinitroacenaphthene. In all these cases amines, nitroamines, or polymeric azo-compounds are produced. Under some conditions, methyl groups in the 6- and the 6′-position of 2 : 2′-dinitrodiphenyl permit cinnoline formation,[8, 9] although nitroamines may also be formed.[9]

Bismark Brown and the reduction products of *m*-dinitrobenzene derivatives appear to be the only known polymers similar to the azo- and azoxy-polymers here described. The latter, however, appear to be of high molecular weight. Hill[2] found that *m*-dinitrobenzene is reduced by lithium aluminium hydride to a product similar to Bismark Brown, and others[10] produced substances which were probably not simple reduction products from substituted *m*-dinitrobenzenes.

The polymeric azo- and azoxy-compounds reported here are black, hygroscopic, infusible, and insoluble in all the common solvents. Some are slightly soluble in dimethylformamide to give intensely coloured solutions. Probably owing to their refractory nature and to their avidity for moisture, widely varying values were obtained in replicate analyses. The values, always very low, were somewhat increased if a higher temperature of combustion was used. Evidently the Liebig and the Dumas methods are inadequate.

EXPERIMENTAL

Preparation of oo′-*Dinitro-compounds.*—4 : 4′-*Dichloro-*, 4 : 4′-*dibromo-*, *and* 4 : 4′-*di-iodo-*3 : 3′-*dimethyl-*6 : 6′-*dinitrodiphenyl.* 6 : 6′-Dinitro-*o*-tolidine[11] (10 g.) was tetrazotised with sodium nitrite (20 g.) in concentrated sulphuric acid (140 ml.) at 0°, diluted with acetic acid (120 ml.), and poured into cuprous chloride (10 g.) in concentrated hydrochloric acid (300 ml.), cuprous bromide (10 g.) in 60% hydrobromic acid (300 ml.), or potassium iodide (50 g.) in water (100 ml.). (Iodine was removed with sodium hydroxide and thiosulphate.) The precipitate in acetone solution was boiled with charcoal. The filtered solution gave yellow needles of the dichloro- (9·3 g.), dibromo- (9·9 g.), or di-iodo-compound (9·3 g.).

Recrystallisation gave 4 : 4′-dichloro- (from aqueous acetone), m. p. 217° (lit.,[12] m. p. 211—212°), 4 : 4′-dibromo- (from aqueous acetone), m. p. 240° (lit.,[12] m. p. 230—233°), and 4 : 4′-*di-iodo-*3 : 3′-*dimethyl-*6 : 6′-*dinitrodiphenyl* (from benzene), yellow needles, m. p. 230—233° (Found: C, 32·5; H, 2·2; N, 5·3; I, 48·7. $C_{14}H_{10}O_4N_2I_2$ requires C, 32·2; H, 1·9; N, 5·3; I, 48·5%). These compounds slowly decompose under the influence of light.

Reduction of Dinitro-compounds.—(a) *With lithium aluminium hydride.* The dinitro-compound (1 g.) in benzene–ether was refluxed with an excess of lithium aluminium hydride in ether. The excess of hydride was decomposed by the addition of water, the resulting mixture filtered, and the filtrate concentrated. A solid product was separated by filtration and was recrystallised from benzene. By this method 6 : 6′-dinitro-*o*-tolidine gave 3 : 8-diamino-2 : 9-dimethylbenzo[*c*]cinnoline (0·15 g.), m. p. 272—274° (decomp.); 6 : 6′-dinitrobenzidine gave 3 : 8-diaminobenzo[*c*]cinnoline (0·13 g.), m. p. 265°; 4 : 4′-dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-*dichloro-*2 : 9-*dimethylbenzo*[c]*cinnoline* (0·6 g.), yellow bars, m. p. 279° (Found: C, 60·0;

---

[8] Wittig and Stichnoth, *Ber.*, 1935, **68**, 928.

[9] Sako, *Bull. Chem. Soc. Japan*, 1934, **9**, 393.

[10] Meyer and Michler, *Ber.*, 1873, **6**, 746; Michler, *Ber.*, 1874, **7**, 421; *Ann. Chem. Pharm.*, 1875, **175**, 152; Meier and Böhler, *Chem. Ber.*, 1956, **89**, 2301.

[11] Beilstein's " Handbuch der organischen Chemie," 4th edn., Vol. 13, p. 261.

[12] Le Fèvre and Turner, *J.*, 1928, 963.

H, 3·8; N, 10·0; Cl, 26·0. $C_{14}H_{10}N_2Cl_2$ requires C, 60·6; H, 3·6; N, 10·1; Cl, 25·7%); 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-*dibromo*-2 : 9-*dimethylbenzo*[c]*cinnoline* (0·69 g.) as yellow needles, m. p. 280° (Found: C, 45·7; H, 2·8; N, 7·7; Br, 43·9. $C_{14}H_{10}N_2Br_2$ requires C, 45·9; H, 2·7; N, 7·7; Br, 43·7%); and 4 : 4′-di-iodo-5 : 5′-dimethyl-2 : 2′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·18 g.), m. p. 185°. 2 : 6 : 2′ : 6′-Tetranitrodiphenyl gave a polymeric azo-compound, dissolving in sulphuric acid (*d* 1·84) to a dark brown solution from which the polymer was reprecipitated by water, and in strong aqueous sodium hydroxide to give a purple solution from which the polymer was reprecipitated by acid. No sample was completely free from ash.

(b) *With zinc and potassium hydroxide.* Aqueous 40% potassium hydroxide was added to the dinitro-compound (1 g.) in hot ethanol. An excess of zinc dust was added to the boiling solution. After 10 min. the liquid was filtered, concentrated, and diluted with water. The solid which separated was dissolved in acetone or benzene, and the solution was boiled with charcoal. After concentration, a crystalline product separated. By this method, 4 : 4′-dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dichloro-2 : 9-dimethylbenzo[*c*]cinnoline (0·6 g.), m. p. 279°; 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·16 g.), m. p. 185°; 4 : 4′-di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·26 g.), m. p. 186°.

(c) *With sodium amalgam and alcohol.* An excess of sodium amalgam was added to the di- or tetra-nitro-compound (1 g.) in dry methanol. After several hours' stirring the mixture was boiled and filtered. The filtrate was evaporated and water added.

4 : 4′-Dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dichloro-2 : 9-dimethylbenzo-[*c*]cinnoline (0·23 g.), m. p. 277°. 4 : 4′-Dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dibromo-2 : 9-dimethylbenzo[*c*]cinnoline (0·1 g.), m. p. 280°, soluble in benzene, and its 5-*oxide* (0·04 g.), m. p. 284° (decomp.) (Found: C, 44·3; H, 2·7; N, 7·2; Br, 42·0. $C_{14}H_{10}ON_2Br_2$ requires C, 44·0; H, 2·6; N, 7·3; Br, 42·0%), insoluble in benzene and recrystallised from dimethylformamide. 4 : 4′-Di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 2 : 9-dimethylbenzo[*c*]cinnoline (0·23 g.), needles (from acetone), m. p. 184°. 2 : 6 : 2′ : 6′-Tetranitrodiphenyl gave 2 : 6 : 2′ : 6′-*tetra-aminodiphenyl* (0·26 g.), needles (from ether) or prisms (from benzene), m. p. 200° (Found: C, 67·8; H, 6·9. $C_{12}H_{14}N_4$ requires C, 67·3; H, 6·6%). 2 : 2′(?)-Diamino-6 : 6′(?)-dinitrodiphenyl (24 mg.) gave 2 : 6 : 2′ : 6′-tetra-aminodiphenyl (12 mg.), m. p. 197—198°.

2 : 6 : 2′ : 6′-Tetranitrodiphenyl was reduced by this procedure, but with ethanol replacing methanol. A black polymeric azo-compound (0·4 g.) was precipitated similar to that produced with lithium aluminium hydride.

(d) *With sodium sulphide.* Aqueous sodium sulphide was added to the polynitro-compound (1 g.), dissolved in boiling 90% ethanol, and the mixture was refluxed for ½—2 hr. Water was added and the product was filtered off and recrystallised or purified by chromatography on alumina.

By this method 4 : 4′-dichloro-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-*dichloro*-2 : 9-*dimethylbenzo*[c]*cinnoline* 5-*oxide* (0·3 g.), a light yellow powder (from dimethylformamide), m. p. 275° (decomp.) (Found: C, 56·6; H, 3·5; N, 9·8; Cl, 24·4. $C_{14}H_{10}ON_2Cl_2$ requires C, 57·3; H, 3·4; N, 9·6; Cl, 24·2%); 4 : 4′-dibromo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-dibromo-2 : 9-dimethylbenzo[*c*]cinnoline 5-oxide (0·27 g.), pale yellow needles (from dimethylformamide), m. p. 286° (decomp.); 4 : 4′-di-iodo-3 : 3′-dimethyl-6 : 6′-dinitrodiphenyl gave 3 : 8-di-iodo-2 : 9-dimethylbenzo[*c*]cinnoline 5-oxide with acetone of crystallisation (31 mg.), as yellow crystals from acetone. The material could not be freed from acetone because of its thermal instability (Found: C, 38·4; H, 2·4; I, 48·8. Calc. for $C_{14}H_{10}ON_2I_2,C_3H_6O$: C 38·2; H, 3·0; I, 47·6%). The material was unstable in light, the m. p. 242—246° (decomp.) falling to *ca.* 225° in a few hours. If the reduction was carried out with added sodium hydroxide, the product was 2 : 9-*dimethyl*-3-*iodobenzo*[c]*cinnoline* 5-*oxide* (37 mg.), m. p. 212—215° (decomp.) (Found: C, 48·0; H, 3·4; I, 36·2. $C_{14}H_{11}ON_2I$ requires C, 48·0; H, 3·1; I, 36·3%). Repetition of this reduction did not always give an identical product, but, probably, a mixture of mono- (mainly) and di-iodo-compounds (*e.g.*, Found: C, 42·8; I, 46·6; C, 43·2; I, 44·0; C, 41·7; I, 44·0%).

1 : 8-Dinitronaphthalene and 2 : 6 : 2′ : 6′-tetranitrodiphenyl gave impure polymeric azo-compounds.

2 : 6 : 2′ : 6′-Tetranitrodiphenyl (1 g.), boiled with sodium sulphide (1·5 g.) and sulphur

(1·5 g.) in hot ethanol, gave an amine which was extracted with ether, transferred to water as the hydrochloride, then again extracted with ether after basification. The ethereal solution yielded 2-*amino*-6 : 2′ : 6′-*trinitrodiphenyl* (0·14 g.), m. p. 159—160°, orange prisms from ethanol (Found: C, 47·7; H, 2·9; N, 18·8. $C_{12}H_8O_6N_4$ requires C, 47·4; H, 2·6; N, 18·5%). An excess of sulphide (sodium sulphide, 10 g.; sulphur, 3 g.) gave 2 : 2′(?)-*diamino*-6 : 6′(?)-*dinitrodiphenyl* (87 mg.), as orange blades (from ethanol), m. p. 241° (Found: C, 53·0; H, 3·6. $C_{12}H_{10}O_4N_4$ requires C, 52·6; H, 3·7%).

(e) *With sodium hydroxide in ethanol.* 5 : 6-Dinitroacenaphthene (0·65 g.) in ethanol (300 ml.) and acetone (20 ml.) was refluxed with sodium hydroxide (0·9 g.) in water (10 ml.), then acidified. A black infusible polymeric azo-compound (0·5 g.) was formed.

One of the authors (R. S. W. B.) is indebted to the Department of Scientific and Industrial Research, and another (A. N. H.) to Imperial Chemical Industries Limited, Paints Division, for grants.

UNIVERSITY OF READING. [*Received, June* 17*th*, 1958.]