369. *Proximity Effects in Diaryl Derivatives. Part II.*[1] *The Formation of Phenazines by Reduction of 2,2′-Dinitrodiphenyl Ethers.*

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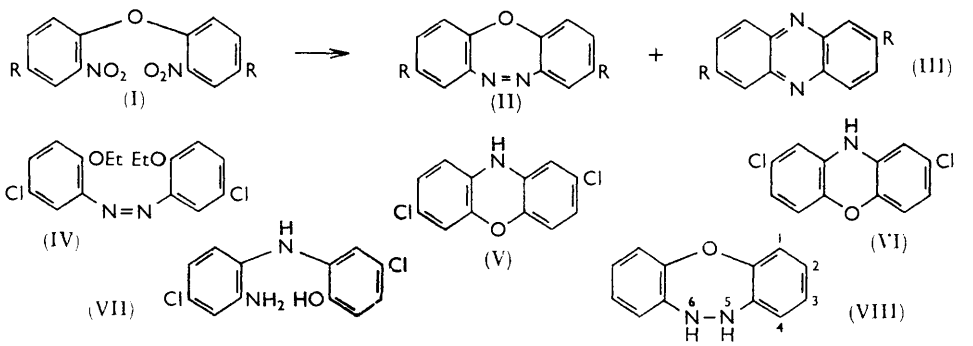
Reaction of 2,2′-dinitrodiphenyl ethers with lithium aluminium hydride or with zinc and sodium hydroxide results in reductive rearrangements to phenazines and, in one case, to a phenoxazine. Dibenz[1,4,5]oxadiazepine is similarly converted into phenazine.

Reduction of 2,2′-dinitrodiphenyl ether (I; R = H) with lithium aluminium hydride at 20° gave dibenz[1,4,5]oxadiazepine (II; R = H) as the major isolated product (25%), but phenazine (III; R = H) was also obtained in small yield (2%).[1] When the reaction conditions were varied, the yield of phenazine increased considerably, but less oxadiazepine was obtained. Thus, reduction of the dinitro-compound (I; R = H) with lithium aluminium hydride at 66° afforded phenazine (18%) and the oxadiazepine (4%). The two products were isolated in almost equal yield (15% and 13%) when the reaction was carried out with zinc and alkali at 20°, but in boiling ethanol phenazine (50%) was the only non-acidic product obtained.

The formation of phenazine appears to involve a reductive rearrangement, and the nature of the process was further explored by studying the reduction of 2,2′-dinitrodiphenyl ethers containing additional ring substituents. This extension of the enquiry was hampered by the inaccessibility of many 2,2′-dinitrodiphenyl ethers. 4,4′-Dimethyl-2,2′-dinitrodiphenyl ether (I; R = Me), for example, has been prepared by nitration of 4,4′-dimethyldiphenyl ether or by heating potassium 4-methyl-2-nitrophenoxide with 4-bromo-3-nitrotoluene,[2] but we were unable to obtain more than a 2% yield by these methods.



Similarly, sodium 2-methyl-6-nitrophenoxide and 2-chloro-3-nitrotoluene furnished only a 7% yield of 6,6′-dimethyl-2,2′-dinitrodiphenyl ether. However, 4,4′-dichloro-2,2′-dinitrodiphenyl ether (I; R = Cl) was readily available,[3] and for this reason most of our experiments were conducted with this compound. 4,4′-Dimethoxycarbonyl-2,2′-dinitrodiphenyl ether (I; R = CO_2Me) was prepared by the reaction of methyl 4-hydroxy-3-nitrobenzoate with its toluene-*p*-sulphonate in pyridine, but proved to be unsuitable for our studies (see below).

4,4′-Dimethyl-2,2′-dinitrodiphenyl ether (I; R = Me) with zinc and sodium hydroxide in boiling ethanol gave 2,7-dimethylphenazine (III; R = Me) (7%), and in the same way 4,4′-dichloro-2,2′-dinitrodiphenyl ether (I; R = Cl) was converted into 2,7-dichlorophenazine (III; R = Cl) (13%). The phenazines were identified by comparisons with

[1] Part I, Grundon, Johnston, and Wasfi, *J.*, 1963, 1436.
[2] Reilly, Drum, and Barrett, *J.*, 1927, 67.
[3] Le Fèvre, Saunders, and Turner, *J.*, 1927, 1168.

authentic samples prepared by standard procedures. In the reaction of the dichloro-derivative, the major product was an orange compound, $C_{16}H_{16}Cl_2N_2O_2$, insoluble in dilute acid or alkali; it is probably 5,5′-dichloro-2,2′-diethoxyazobenzene (IV), and is formed apparently by displacement of an aryloxy-group and subsequent reduction of the resultant 5-chloro-2-ethoxynitrobenzene. In order to avoid the formation of the azo-derivative, reduction of the dichloro-compound (I; R = Cl) was conducted in aqueous dioxan at 20°; in these conditions the phenazine (III; R = Cl) was obtained in 40% yield. Other products were isolated from this reaction (see Experimental section) but have not yet been identified. A phenazine was not obtained by the action of zinc and alkali on 4,4′-dimethoxycarbonyl-2,2′-dinitrodiphenyl ether (I; R = CO_2Me). It appears that the diester is hydrolysed to 4-hydroxy-3-nitrobenzoic acid, since methylation of the product with diazomethane afforded methyl 4-methoxy-3-nitrobenzoate.

In contrast to 2,2′-dinitrodiphenyl ether,[1] the dichloro-compound (I; R = Cl) was not converted by lithium aluminium hydride into an oxadiazepine (II). Chromatography of the products showed that the major component, 2,7-dichlorophenazine (III; R = Cl) (35%), was accompanied by two colourless compounds, m. p. 206—207° (9%) and m. p. 161—162° (1%). The former is considered to be a dichlorophenoxazine, since it has a molecular formula $C_{12}H_7Cl_2NO$ and infrared absorption at 3430 cm.$^{-1}$ (NH). Like phenoxazine, the compound is insoluble in aqueous acid and in aqueous alkali but dissolves in concentrated sulphuric acid to give a violet solution and in benzene to give a fluorescent solution. The phenoxazine is probably the 2,7-dichloro-derivative (V) or its 2,8-isomer (VI), but a choice between these alternatives cannot be made at present and must await an independent synthesis. The reduction product, m. p. 161—162°, $C_{12}H_{10}Cl_2N_2O$, has amphoteric properties, and is regarded as the aminophenol (VII).

Phenazines might conceivably be formed by reductive condensation of 2 mol. of an *o*-nitrophenol produced by hydrolysis of the 2,2′-dinitrophenyl ethers. This route is unlikely to apply to reactions 1, 2, 6, and 7 (Table) since 2,2′-dinitrodiphenyl ether is unaffected by sodium hydroxide at 20°. In the reactions conducted at elevated temperatures (Nos. 4, 5, and 8, Table) hydrolysis certainly occurs and phenols as well as phen-

Reduction of 2,2′-dinitrodiphenyl ethers (I).

Reaction no.	Reactants and conditions	Yield (%) of oxadiazepine (II)	Yield (%) of phenazine (III)
1	(I; R = H) with $LiAlH_4$ at 20° [1]	25	2
2	(I; R = H) with Zn–OH^- at 20°	13	15
3	(I; R = H) with $LiAlH_4$ at 66°	4	18
4	(I; R = H) with Zn–OH^- at 78°	0	50
5	(I; R = Me) with Zn–OH^- at 78°	0	7
6	(I; R = Cl) with $LiAlH_4$ at 20°	0	35 *
7	(I; R = Cl) with Zn–OH^- at 20°	0	40
8	(I; R = Cl) with Zn–OH^- at 78°	0	13 †

* A dichlorophenoxazine (9%) was also isolated. † The azo-derivative (IV) (30%) was also obtained.

azines are invariably formed, but in these cases also the nitrophenol route is improbable because *o*-nitrophenol does not afford phenazine when heated with zinc and alkali.

A consideration of reactions 1—3 (Table) shows that an increase in the yield of phenazine is accompanied by a decrease in the yield of dibenz[1,4,5]oxadiazepine (II; R = H). Further, phenazines are formed most readily in those reactions (4, 6, and 7) in which oxadiazepines are not obtained. One explanation of this behaviour is that oxadiazepines are intermediates in the formation of phenazines, and, in support of this theory, heating dibenz[1,4,5]oxadiazepine with zinc and sodium hydroxide afforded phenazine in 27% yield. The formation of phenazine from 2,2′-dinitrodiphenyl ether also occurs at 20° (reaction 2, Table), and in this case dibenz[1,4,5]oxadiazepine cannot be an intermediate since it is not converted into phenazine under these conditions; the sole product of the

latter reaction is 5,6-dihydrodibenz[1,4,5]oxadiazepine (VIII).[1] It appears therefore that there are two routes to phenazines from 2,2'-dinitrodiphenyl ethers; the route predominating at room temperature apparently involves non-cyclic intermediates. A Smiles rearrangement is probably a key step in each pathway, but we intend to study the properties of some possible intermediates before discussing further the mechanisms of the reactions.

Experimental

6,6'-Dimethyl-2,2'-dinitrodiphenyl Ether.—Sodium 2-methyl-6-nitrophenoxide (1·8 g.) (obtained by heating an equimolecular mixture of sodium hydroxide and 2-methyl-6-nitrophenol at 180° for 2 hr.) was heated with 2-chloro-3-nitrotoluene (2·2 g.) at 220—240° for 3 hr. The mixture was then treated with aqueous sodium hydroxide and extracted with ether. Evaporation of the ether solution and crystallisation of the residue from light petroleum (b. p. 60—80°) gave *6,6'-dimethyl-2,2'-dinitrodiphenyl ether* in yellow needles (0·15 g., 7%), m. p. 96—97° (Found: C, 58·4; H, 3·9; N, 9·8. $C_{14}H_{12}N_2O_5$ requires C, 58·2; H, 4·1; N, 9·6%).

4,4'-Dimethoxycarbonyl-2,2'-dinitrodiphenyl Ether.—A mixture of methyl 4-hydroxy-3-nitrobenzoate (19·7 g.), its toluene-*p*-sulphonate [4] (35 g.), and pyridine (100 c.c.) was refluxed for 6 hr. Most of the pyridine was removed under reduced pressure, water was added, and the mixture was extracted with chloroform. The chloroform solution was shaken with dilute hydrochloric acid and then with aqueous sodium hydroxide. Evaporation of the chloroform solution, and crystallisation of the residue from ethanol, furnished *4,4'-dimethoxycarbonyl-2,2'-dinitrodiphenyl ether* in yellow needles (2·0 g., 15%), m. p. 144—145° (Found: C, 51·1; H, 3·3; N, 7·3. $C_{16}H_{12}N_2O_9$ requires C, 51·1; H, 3·2; N, 7·4%).

Reduction of 2,2'-Dinitrodiphenyl Ether.—(*a*) A mixture of 2,2'-dinitrodiphenyl ether [1] (1 g.), ethanol (20 c.c.), 40% aqueous sodium hydroxide (10 c.c.), and zinc powder (3 g.) was stirred and refluxed for 6 hr. After filtration, the solution was concentrated to remove ethanol, and the resultant mixture was extracted with ether. Evaporation of the ether and crystallisation of the residue from light petroleum (b. p. 80—100°) gave phenazine as yellow needles (0·35 g., 50%), m. p. 171—172° (Found: C, 80·0; H, 4·5; N, 16·0. Calc. for $C_{12}H_8N_2$: C, 80·0; H, 4·5; N, 15·5%). Identity with an authentic sample of phenazine was established by a mixed m. p. determination and by a comparison of infrared spectra.

(*b*) Zinc powder (2 g.) was added to a solution of 2,2'-dinitrodiphenyl ether (1 g.) in dioxan (30 c.c.) containing 40% aqueous sodium hydroxide (5 c.c.), and the mixture was stirred at 20° for 6 hr. and then filtered. The filtrate was concentrated under reduced pressure and then shaken with benzene. The benzene solution was concentrated to 10 c.c. and added to a column of alumina (30 g.). Elution with benzene (100 c.c.) and evaporation of the eluate gave dibenz[1,4,5]oxadiazepine, separating from light petroleum (b. p. 40—60°) in orange needles (0·10 g., 13%), m. p. 48—50°, undepressed by mixing with an authentic sample.[1] Further elution of the column with benzene, evaporation of the eluate, and crystallisation of the residue from light petroleum (b. p. 80—100°) gave phenazine in yellow needles (0·10 g., 15%), m. p. 171—172°.

(*c*) A solution of 2,2'-dinitrodiphenyl ether (2 g.) in tetrahydrofuran (50 c.c.) was added slowly to lithium aluminium hydride (2 g.) in tetrahydrofuran (30 c.c.), and the solution was refluxed for 3 hr. After decomposition of excess of the reagent with water, the mixture was filtered and tetrahydrofuran was removed by evaporation. Extraction with ether and evaporation of the ether solution gave a red gum. The product in benzene was chromatographed on alumina as described in (*b*), and afforded dibenz[1,4,5]oxadiazepine (0·05 g., 4%), m. p. 47—50°, and phenazine (0·25 g., 18%), m. p. 171—172°.

Reduction of 4,4'-Dimethyl-2,2'-dinitrodiphenyl Ether.—4,4'-Dimethyl-2,2'-dinitrodiphenyl ether (1 g.) was reduced as described for 2,2'-dinitrodiphenyl ether, method (*a*), except that heating was discontinued after 2 hr. Crystallisation of the crude product from benzene gave 2,7-dimethylphenazine in yellow needles (0·05 g., 7%), m. p. 163—165°, identical (mixed m. p. and infrared) with an authentic sample.

2,7-Dimethylphenazine.—A mixture of 3-bromo-4-nitrotoluene (15 g.), *p*-toluidine (10 g.), and fused sodium acetate (10 g.) was heated at 220—230° for 24 hr., and then steam-distilled. The product, presumably 4',5-dimethyl-2-nitrodiphenylamine, was not volatile in steam, and was obtained as a red solid (6 g.), m. p. 80°, by filtration and crystallisation from ethanol.

[4] McRae, Moir, Ursprung, and Gibbs, *J. Org. Chem.*, 1954, **19**, 1500.

A mixture of the diphenylamine (4 g.) and iron powder (30 g.) was heated at 300° for 30 min., allowed to cool, and extracted with ether. Evaporation of the ether solution gave 2,7-dimethylphenazine, separating from light petroleum (b. p. 60—80°) in yellow needles (1 g., 30%), m. p. 163—165° (Found: C, 80·8; H, 5·4; N, 13·2. Calc. for $C_{14}H_{12}N_2$: C, 80·8; H, 5·8; N, 13·4%).

2,7-Dimethylphenazine, m. p. 162—165°, has been obtained previously [5] in small yield by the action of concentrated sulphuric acid on *p*-nitrosotoluene.

Reduction of 4,4′-Dichloro-2,2′-dinitrodiphenyl Ether.—(*a*) A solution of 4,4′-dichloro-2,2′-dinitrodiphenyl ether (20 g.) in tetrahydrofuran (100 c.c.) was added slowly to lithium aluminium hydride (15 g.) in tetrahydrofuran (150 c.c.). After 12 hr., the excess of the reagent was decomposed with water, and the mixture was filtered. Tetrahydrofuran was removed under reduced pressure, and the aqueous mixture was extracted with ether. After being shaken with 5% aqueous sodium carbonate, the ether solution was evaporated, and the residue (7·3 g.) in benzene (50 c.c.) was chromatographed on alumina (70 g.). Elution with benzene (200 c.c.) gave a *dichlorophenoxazine*, separating from benzene–light petroleum (b. p. 60—80°) in plates (1·05 g., 9%), m. p. 206—207° (Found: C, 57·0; H, 2·8; N, 5·5. $C_{12}H_7Cl_2NO$ requires C, 57·1; H, 2·8; N, 5·5%). The phenoxazine was insoluble in 2N-sodium hydroxide and in 2N-hydrochloric acid.

Further elution of the alumina column with benzene (200 c.c.) gave a colourless *compound*, separating from light petroleum (b. p. 60—80°) in needles (0·1 g.), m. p. 161—162° (Found: C, 53·7; H, 3·5; N, 10·8. $C_{12}H_{10}Cl_2N_2O$ requires C, 53·5; H, 3·7; N, 10·5%). The compound was sparingly soluble in water, but dissolved in 2N-hydrochloric acid and in 2N-sodium hydroxide.

A third fraction, obtained by further elution with benzene (500 c.c.), crystallised from benzene in yellow needles (5·3 g., 35%), m. p. 266—267° (Found: C, 58·0; H, 2·6; N, 11·1; Cl, 28·3. Calc. for $C_{12}H_6Cl_2N_2$: C, 57·8; H, 2·4; N, 11·2; Cl, 28·5%). The compound was identical (mixed m. p. and infrared) with a sample of 2,7-dichlorophenazine, m. p. 267—268°, obtained by a known procedure.[6]

(*b*) A mixture of 4,4′-dichloro-2,2′-dinitrodiphenyl ether (5 g.), zinc powder (15 g.), 40% aqueous potassium hydroxide (20 c.c.), and ethanol (50 c.c.) was stirred and refluxed for 2 hr. After filtration, ethanol was removed by evaporation. The product, obtained by chloroform-extraction, was chromatographed in benzene on alumina (50 g.). Elution with benzene (200 c.c.) and evaporation of the solution gave *5,5′-dichloro-2,2′-diethoxyazobenzene*, separating from light petroleum (b. p. 80—100°) in orange needles (1·5 g., 30%), m. p. 168—169° (Found: C, 56·6; H, 4·7; N, 8·3. $C_{16}H_{16}Cl_2N_2O_2$ requires C, 56·6; H, 4·6; N, 8·2%).

Further elution of the column with benzene (200 c.c.) and evaporation of the eluate gave 2,7-dichlorophenazine, crystallising from benzene in yellow needles (0·5 g., 13%), m. p. 264—265°.

(*c*) 4,4′-Dichloro-2,2′-dinitrodiphenyl ether (1 g.) was reduced with zinc and sodium hydroxide at 20° as described for 2,2′-dinitrodiphenyl ether, method (*b*). The product was treated with acetone to give an insoluble compound crystallising from light petroleum (b. p. 80—100°) in yellow plates, m. p. 205—206°. The acetone solution was evaporated and the residue in benzene was chromatographed on alumina (40 g.). Elution with benzene, evaporation of the eluate, and crystallisation of the residue from benzene gave 2,7-dichlorophenazine in yellow needles (0·3 g., 40%), m. p. 266—267°.

The compound, m. p. 205—206°, was not always obtained in this reaction; in one case, the product was completely soluble in acetone, and chromatography afforded 2,7-dichlorophenazine and a compound separating from light petroleum (b. p. 80—100°) in yellow needles, m. p. 175—178°.

Reaction of 4,4′-Dimethoxycarbonyl-2,2′-dinitrodiphenyl Ether, with Zinc and Alkali.—A mixture of 4,4′-dimethoxycarbonyl-2,2′-dinitrodiphenyl ether (2 g.), zinc powder (2 g.), ethanol (30 c.c.), and 40% aqueous sodium hydroxide (20 c.c.) was refluxed for 4 hr., and then filtered. Ethanol was removed by evaporation, and the solution was acidified with hydrochloric acid. Ether-extraction gave an oil which did not crystallise but with excess of an ethereal solution of diazomethane afforded methyl 4-methoxy-3-nitrobenzoate, separating from light petroleum (b. p. 60—80°) in yellow needles (0·3 g.), m. p. 109—110° (lit.,[7] m. p. 109—110°) (Found: C, 51·5; H, 4·3; N, 6·5. Calc. for $C_9H_9NO_5$: C, 51·2; H, 4·3; N, 6·6%).

[5] Bamberger and Ham, *Annalen*, 1911, **382**, 82.
[6] Vivian, *J. Amer. Chem. Soc.*, 1951, **73**, 457.
[7] Auwers, *Ber.*, 1897, **30**, 1473.

Reduction of Dibenz[1,4,5]*oxadiazepine*.—Dibenz[1,4,5]oxadiazepine (0·2 g.), when reduced as described for 2,2′-dinitrodiphenyl ether, method (*a*), gave phenazine, separating from light petroleum (b. p. 80—100°) in yellow needles (0·05 g., 27%), m. p. 171—172° alone or mixed with an authentic sample.

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