45. *A Rearrangement of* o-*Aminodiphenyl Ethers. Part II.*

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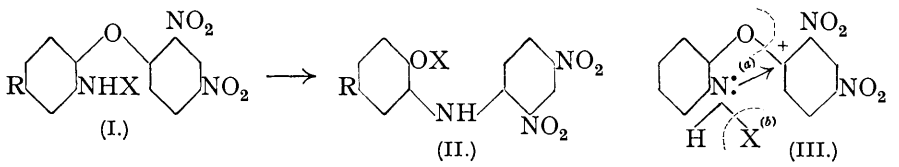
In extension of the observations recorded in Part I (Roberts and de Worms, J., 1934, 727) an investigation has now been made of the influence of a number of nuclear substituents in the 4-position [I; R = NH_2, OMe, Me, H, I, Br, Cl, $CO{\cdot}O{\cdot}C_6H_3(NO_2)_2$, CO_2H] on the behaviour of *o*-aminodiphenyl ethers of type (I, X = H).

The seven ethers in the sequence from the 4-amino-derivative to the 4-chloro-derivative all undergo rearrangement to the isomeric 5-substituted *o*-hydroxydiphenylamines of



(I.) (II.) (III.)

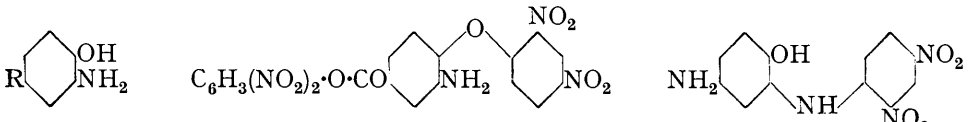
type (II, X = H). The condition most favourable to the rearrangement was in all cases the same as that recorded in the earlier work, *viz.*, the presence of very slightly ionisable basic or hydroxylic solvents such as alcohol and pyridine, particularly in presence of water. The 4-carboxy-ether and its dinitrophenyl ester, however, proved stable under all the conditions investigated.

It is suggested that two factors determine the proneness of the ethers to rearrange: (*a*) the ability of an unshared electron pair of the *o*-amino-nitrogen to form a co-ordinate link with the positive α-carbon atom of the second nucleus (cf. III and also Kent and Smiles, J., 1934, 422); and (*b*) the ability of a group X attached to the *o*-amino-nitrogen to become a free positively charged radical, in the present examples, proton. In presence of these factors the molecules of a hydroxylic or weakly basic solvent may operate to effect the change (I ⟶ II). When the rearrangement is brought about by the action of heat alone, it appears that the substance itself may be regarded as a basic solvent for the rearranging molecules. The inductive effect of a particular substituent R could clearly facilitate the operation of one of these factors only while retarding the operation of the other, and it therefore appears that an optimum condition for the change might occur when R is a group having an intermediate value of the inductive effect. The rates of rearrangement of the active ethers have been compared by a comparative method depending on the marked difference in colour between equimolecular solutions of a given ether

R	OH	OBz	NH_2	OMe	Me	H	I	Br	Cl	CO_2Ar	CO_2H	NO_2
Time (mins.) for complete change	Ethers not obtd.		50	13	7	5	15	30	60	No change		Ether not obtd.
			Increasing $-I$ ←					→ Decreasing $-I$		$+I$		

and of its isomeric diphenylamine. The results (see table) show a distinct maximum for the rate of change when R = H. On the above view the retardation in the direction of increasing $-I$ will be due to inhibition of the operation of factor (*b*), while that in the direction of decreasing $-I$ will be due to the reduced availability of the lone electrons of nitrogen (factor *a*). The extreme cases of complete inhibition of the rearrangement are met with when R (= CO_2Ar and CO_2H) has a positive inductive effect. It has not been possible to extend the series in the direction either of increasing $-I$ or of increasing $+I$, owing to difficulties attending the synthesis of the 4-hydroxy- and the 4-nitro-ethers (I, R = OH and NO_2). It is hoped to throw further light on the mechanism of the rearrangement by a study both of a variety of *N*-substituted derivatives (I and II, X = acyl and alphyl) and also of a series of 5-substituted *o*-aminodiphenyl ethers.

The new diphenyl ethers described have been obtained by condensing 1-chloro-2 : 4-dinitrobenzene with the sodium or potassium derivative of the appropriate *o*-aminophenol (IV) under very mild conditions. Condensation of the disodio-derivative of 3-amino-*p*-hydroxybenzoic acid was, however, carried out with two mols. of chlorodinitrobenzene to yield the dinitrophenyl ester (V), which was hydrolysed to the free acid.



(IV.) (V.) (VI.)

In general, condensation of the phenol (IV) with chlorodinitrobenzene in presence of sodium acetate under usual conditions gave the corresponding dinitrodiphenylamine, but 2′ : 4′-*dinitro*-5-*amino*-2-*hydroxydiphenylamine* (VI) could not be obtained by use either of 2 : 4-diaminophenol, which gives the isomeric 3-amino-4-hydroxydiphenylamine (D.R.-P. 107,971), or of its 4-acetyl derivative, which proved too liable to oxidation for the purpose. But when sodium 2 : 4-diacetamidophenoxide was condensed with excess of chlorodinitrobenzene, hydrolysis of the 2-acetamido-group occurred and was accompanied by rearrangement of the resulting ether, with formation of 2′ : 4′-*dinitro*-5-*acetodinitrophenylamido*-2-*hydroxydiphenylamine*, which on hydrolysis yielded the required substance (VI). The *o*-aminophenols (IV) were in general prepared by hydrosulphite reduction of the corresponding nitro-compound, but 2 : 4-diaminophenol was obtained by acid reduction (iron) of 2 : 4-dinitrophenol (D.R.-P. 269,542). 2-Nitro-*p*-iodophenol was most conveniently obtained by direct nitration of *p*-iodophenol.

Experimental.

Comparison of the Rates of Rearrangement of Diphenyl Ethers.—The figures recorded in the table (above) were arrived at by adding 0·0005 g.-mol. of the ether to 12·5 c.c. of an acetic acid–pyridine mixture (4 : 1) at 50° and observing the time occupied by this solution in reaching the same tint as that of an identical solution of the isomeric diphenylamine, also at 50°.

2-*Aminoquinol* 4-*Benzoate* (IV, R = OBz).—2-Nitroquinol 4-benzoate (*Ber.*, 1893, **26**, 1909; 1916, **49**, 1401), dissolved in aqueous alcohol, was treated at the boiling point with sodium hydrosulphite (*q.s.*). The cooled filtered solution on addition of much water yielded 2-*aminoquinol* 4-*benzoate* as colourless needles; recrystallised from aqueous alcohol, this formed colourless plates, m. p. 161—164° (darkening) (Found: C, 67·9; H, 4·6. $C_{13}H_{11}O_3N$ requires C, 68·1; H, 4·8%).

2′ : 4′-*Dinitro*-2 : 4-*diaminodiphenyl Ether* (I; R = NH_2, X = H).—2 : 4-Diaminophenol dihydrochloride (1 mol.), from 2 : 4-dinitrophenol (D.R.-P. 269,542), in contact with alcohol was treated with an alcoholic solution of 1-chloro-2 : 4-dinitrobenzene (1 mol.), and to the mixture was added at room temperature sodium ethoxide (3 mols.) in alcohol. The reacting mixture was cooled in running water and then kept for 1 hour. The crystalline product, recrystallised from alcohol (charcoal), gave the *ether* as a dark orange substance, soluble in hydrochloric acid, insoluble in aqueous caustic soda. It sintered at 166—170°, then darkened, and finally decomposed at 181° (Found: C, 49·5; H, 4·8. $C_{12}H_{10}O_5N_4$ requires C, 49·6; H, 3·4%).

2′ : 4′-*Dinitro*-5-*amino*-2-*hydroxydiphenylamine* (VI).—(a) When a solution of the isomeric ether (above) in aqueous pyridine was warmed, it rapidly darkened, and on treatment with water yielded a brown flocculent material, which formed a sparingly soluble, black sodium derivative with aqueous caustic soda. Crystallised from alcohol (charcoal), the *diphenylamine* formed small red plates, which turned dark purple at 225—230° and decomposed at 237—240° (Found: C, 49·2; H, 3·8%). The diphenylamine was also obtained by rearrangement of the ether either in aqueous-alcoholic solution or on heating it alone at about 150°.

(b) 2 : 4-Diacetamidophenol (*Bull. Soc. chim.*, 1905, **33**, 785) (1 mol.) in alcohol was treated with sodium ethoxide (1 mol.), and the mixture with chlorodinitrobenzene (1 mol.). The liquid rapidly darkened and deposited sodium chloride but no organic matter. After 1 hour the liquid, freed from sodium chloride, was treated with much water; a deep red, flocculent solid, insoluble in hydrochloric acid and forming a sparingly soluble sodium derivative with aqueous caustic soda, then resulted. It separated from alcohol in dark red crystals of 2′ : 4′-*dinitro*-5-*acetodinitrophenylamido*-2-*hydroxydiphenylamine*, which turned yellow at 135° and decomposed above 250° (Found: C, 47·8; N, 16·9. $C_{20}H_{14}O_{10}N_6$ requires C, 48·1; N, 16·8%). Treatment of this substance at 100° for 1½ hours with concentrated hydrochloric acid yielded a red solution, which on treatment with water and sodium bicarbonate deposited a reddish flocculent solid; this after purification from alcohol was identical with the product described under (a) (Found: N, 19·3. $C_{12}H_{10}O_5N_4$ requires N, 19·3%).

2′ : 4′-*Dinitro*-2-*amino*-4-*methoxydiphenyl Ether* (I; R = OMe, X = H).—2-Nitro-4-methoxyphenol (Robinson and Smith, J., 1926, 392) in aqueous alcohol was treated on the water-bath with sodium hydrosulphite (*q.s.*). The product was filtered hot, the filtrate depositing white plates, m. p. 124°, in 70% yield. The aminomethoxyphenol, being unstable, was analysed as the *hydrochloride*, white needles, m. p. 171° (Found: Cl, 20·5. $C_7H_9O_2N$,HCl requires Cl, 20·2%).

The above hydrochloride (1 mol.), treated for 2—3 hours at room temperature with alcoholic potassium ethoxide (2 mols.) and chlorodinitrobenzene (1 mol.), deposited crystals of 2′ : 4′-*dinitro*-2-*amino*-4-*methoxydiphenyl ether*, which, washed with water and recrystallised from benzene, formed yellow needles, m. p. 178° (yield, 40%) (Found : C, 51·1; H, 3·5. $C_{13}H_{11}O_6N_3$ requires C, 51·1; H, 3·6%). An unidentified substance, m. p. 78°, was isolated from the alcoholic filtrate, but none of the isomeric diphenylamine was observed.

2′ : 4′-*Dinitro*-2-*hydroxy*-5-*methoxydiphenylamine* (II; R = OMe, X = H).—(a) A pyridine solution of the above diphenyl ether slowly darkened at room temperature, and the isomeric diphenylamine was isolated. The rearrangement took place very rapidly in hot aqueous pyridine, hot aqueous alcohol, or hot aqueous acetic acid, slowly in absolute alcohol or hot aqueous caustic soda, but not at all in glacial acetic acid, benzene, or acetone.

(b) 2-Amino-4-methoxyphenol hydrochloride (1 mol.) in alcohol was treated with chlorodinitrobenzene (1 mol.) in presence of anhydrous sodium acetate under usual conditions. Treatment of the resulting solution with water yielded a red flocculent solid, which crystallised from acetic acid in needles, m. p. 157° (Found : C, 51·2; H, 3·4. $C_{13}H_{11}O_6N_3$ requires C, 51·1; H, 3·6%). The *diphenylamine* was chromoisomeric, becoming violet-black at 100°.

2′ : 4′-*Dinitro*-2-*aminodiphenyl Ether*.—*o*-Aminophenol (5·5 g.) in absolute alcohol (50 c.c.) containing sodium ethoxide (1 mol.) was treated below 20° with chlorodinitrobenzene (1 mol.). The shaken mixture after some minutes deposited the crystalline *ether*, which was collected after 3 hours, washed (yield, 45%), and recrystallised from benzene, forming bright yellow plates, m. p. 123° (Found : C, 52·2; N, 15·5. $C_{12}H_9O_5N_3$ requires C, 52·3; N, 15·2%). From the red alcoholic filtrate, the isomeric 2′ : 4′-dinitro-2-hydroxydiphenylamine was isolated. This was also prepared by usual methods, and from the above ether in contact with water or aqueous alkali or in warm pure or aqueous alcohols or pyridine; acetic acid, except in hot aqueous solution, acted only very slowly.

2′ : 4′-*Dinitro*-4-*aminodiphenyl Ether*.—*p*-Aminophenol (5·5 g.) in alcohol (100 c.c.) containing sodium ethoxide (1 mol.) was poured slowly into alcohol (50 c.c.) containing chlorodinitrobenzene (1 mol.), the temperature being kept below 20°. After 3 hours the *ether* was collected and crystallised from benzene, forming small orange prisms, m. p. 223° (decomp.) (Found : N, 15·4. $C_{12}H_9O_5N_3$ requires N, 15·2%). This ether gave no indication of rearrangement in the usual solvents.

4-*Iodo*-2′ : 4′-*dinitro*-2-*aminodiphenyl Ether*.—Difficulty being encountered in the preparation of 4-iodo-2-nitrophenol by Hodgson's method (J., 1927, 1141), *p*-iodophenol (11 g.) in glacial acetic acid (80 c.c.) was added slowly to glacial acetic acid (50 c.c.) containing fuming nitric acid (6·3 g.). The product, poured on ice, gave the iodonitrophenol in 75% yield. This was purified by distillation in steam, and reduced in alkaline solution with sodium hydrosulphite.

4-Iodo-2-aminophenol (2·3 g. in well-cooled alcohol, 20 c.c., containing potassium ethoxide, 1 mol.) was poured slowly into alcohol (20 c.c.) containing chlorodinitrobenzene (2 g.) below 20°. After 3 hours, the crystals were washed with alcohol and with water and recrystallised from benzene or acetic acid, bright yellow needles, m. p. 125°, of 4-*iodo*-2′ : 4′-*dinitro*-2-*aminodiphenyl ether* being obtained (Found : C, 36·1; N, 10·4. $C_{12}H_8O_5N_3I$ requires C, 35·9; N, 10·4%).

5-*Iodo*-2′ : 4′-*dinitro*-2-*hydroxydiphenylamine*.—(a) Treatment of the above ether with hot aqueous alkali or water effected the usual rearrangement to the isomeric diphenylamine, which proceeded more rapidly in alcohol or pyridine. Glacial acetic acid was without effect on the ether.

(b) Equimolecular quantities of 4-iodo-2-aminophenol (5 g.), chlorodinitrobenzene, and anhydrous sodium acetate in alcohol (100 c.c.) were heated on the water-bath (2 hours). The product, isolated by usual methods, crystallised from alcohol in long red-brown needles or from glacial acetic acid in small prisms, m. p. 145° (Found : C, 35·6; H, 2·6. $C_{12}H_8O_5N_3I$ requires C, 35·9; H, 2·0%).

4-*Bromo*-2′ : 4′-*dinitro*-2-*hydroxydiphenyl Ether*.—4-Bromo-2-nitrophenol (5 g.) in aqueous caustic soda (large excess) was treated at 80° with sodium hydrosulphite (*q.s.*). Acidification of the resulting colourless solution with acetic acid gave the corresponding aminophenol in 90% yield.

The usual reaction (4-bromo-2-aminophenol, 4·5 g., alcohol, 40 c.c., sodium ethoxide, 1 mol.; alcohol, 20 c.c., chlorodinitrobenzene, 5 g.; below 20°) gave the *ether* (55% yield), which, recrystallised from benzene or glacial acetic acid, formed yellow plates, m. p. 140° (Found : C, 40·7; N, 12·0. $C_{12}H_8O_5N_3Br$ requires C, 40·6; N, 11·8%).

5-*Bromo*-2′ : 4′-*dinitro*-2-*hydroxydiphenylamine*.—(a) The usual rearrangement of the cor-

responding ether was effected by pyridine or alcohol, pure or aqueous; also by aqueous alkali or water, but very slowly.

(b) Condensation of 4-bromo-2-aminophenol, chlorodinitrobenzene, and sodium acetate by the usual method gave the *diphenylamine* in 75% yield. It crystallised from alcohol in deep red needles and from glacial acetic acid in crimson plates, m. p. 190° (Found : C, 40·7; N, 12·2. $C_{12}H_8O_5N_3Br$ requires C, 40·6; N, 11·8%), readily soluble in aqueous alkali.

4-Chloro-2′ : 4′-dinitro-2-aminodiphenyl ether, obtained in 60% yield (4-chloro-2-aminophenol, 3·7 g., alcohol, 100 c.c., sodium ethoxide, 1 mol.; alcohol, 40 c.c., chlorodinitrobenzene, 5 g.), formed yellow needles from benzene or glacial acetic acid, m. p. 152° (Found : C, 46·3; N, 13·6. $C_{12}H_8O_5N_3Cl$ requires C, 46·5; N, 13·5%).

5-Chloro-2′ : 4′-dinitro-2-hydroxydiphenylamine.—(a) Rearrangement of the ether took place slowly in pyridine, alcohol, aqueous acetic acid, and water.

(b) Condensation of 4-chloro-2-aminophenol and chlorodinitrobenzene gave the *diphenylamine* (long, deep red needles from alcohol, crimson plates from acetic acid; m. p. 215°) in 80% yield (Found : C, 46·3; N, 13·6. $C_{12}H_8O_5N_3Cl$ requires C, 46·5; N, 13·5%).

2′ : 4′-Dinitro-2-amino-4-carboxydiphenyl Ether.—3-Nitro-4-hydroxybenzoic acid was obtained in 75% yield by treating *p*-hydroxybenzoic acid (0·1 mol.) in glacial acetic acid (100 c.c.) with fuming nitric acid (0·1 mol.) in glacial acetic acid (20 c.c.) at 30—40°, the mixture being poured on ice after 15 minutes.

3-Amino-4-hydroxybenzoic acid resulted in 70% yield when an alkaline solution of the nitro-acid on the steam-bath was treated with sodium hydrosulphite (*q.s.*), cooled, and carefully acidified with acetic acid.

When a solution of 3-amino-4-hydroxybenzoic acid (1 mol.) in alcohol containing potassium ethoxide (2 mols.) was treated at room temperature for 30 minutes with chlorodinitrobenzene (2 mols.) in alcohol, the 2 : 4-*dinitrophenyl* ester (V) of 2′ : 4′-dinitro-2-amino-4-carboxydiphenyl ether separated in excellent yield; it crystallised from alcohol in white spear-like needles, m. p. 89° (Found : C, 46·8; H, 2·8. $C_{19}H_{11}O_{11}N_5$ requires C, 47·0; H, 2·2%). The substance was not affected by prolonged contact with aqueous pyridine, even at 170° in a sealed tube. On treatment of the ester with hot aqueous caustic soda, yellow needles separated which appeared to be the sodium salt of the corresponding *carboxylic acid*. Treatment of the alkaline mixture with concentrated hydrochloric acid yielded a pale cream solid, which was purified from alcohol as cream-coloured needles, m. p. 115° (Found : C, 48·7; H, 2·9. $C_{13}H_9O_7N_3$ requires C, 48·9; H, 2·8%). Aqueous pyridine, alcohol, acetic acid and alkali were all without action on the substance.

The 2 : 4-*dinitrophenyl* ester of 2′ : 4′-dinitro-2-hydroxy-5-carboxydiphenylamine [II; R = CO·O·$C_6H_3(NO_2)_2$, X = H] resulted when 3-amino-4-hydroxybenzoic acid (1 mol.) in alcohol was treated with chlorodinitrobenzene (2 mols.) in presence of anhydrous sodium acetate under reflux for 2—3 hours. The product which resulted when the mixture was poured into water was taken up in aqueous alkali, and the dinitrophenyl ester was isolated from the filtered alkaline solution by addition of hydrochloric acid (60% yield). It formed reddish-orange needles from glacial acetic acid, m. p. 155° (Found : C, 46·9; H, 2·5. $C_{19}H_{11}O_{11}N_5$ requires C, 47·0; H, 2·2%). Hot aqueous alkali (30 mins.) converted the ester into the corresponding *carboxylic acid*, which was isolated from the red alkaline solution as a yellow solid and was obtained as deep yellow, microcrystalline needles, m. p. 185°, by precipitation with acid from its solution in alcoholic ammonia (Found : C, 48·7; H, 3·2. $C_{13}H_9O_7N_3$ requires C, 48·9; H, 2·8%). The substance was stable towards aqueous pyridine.

4 : 2′ : 4′-*Trinitro-2-aminodiphenylamine* (II; R = NO_2, X = H) resulted when equimolecular quantities of 4-nitro-2-aminophenol (Amer. Pat. 1,689,014), anhydrous sodium acetate, and chlorodinitrobenzene in alcohol were heated under reflux. It was purified from alcohol as a bright yellow substance, m. p. 225° (decomp.), which formed a dark-coloured sodium derivative with aqueous caustic soda (Found : C, 45·2; H, 3·4. $C_{12}H_8O_7N_4$ requires C, 45·0; H, 2·5%). Treatment of the nitroaminophenol with chlorodinitrobenzene in alcohol in presence of sodium ethoxide or potassium ethoxide yielded the same substance. Under no conditions tried was the isomeric trinitroaminodiphenyl ether obtained.

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