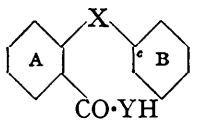
391. *A Rearrangement of* o-*Carbamyl Derivatives of Diphenyl Ether.*

By Bernard T. Tozer and Samuel Smiles.

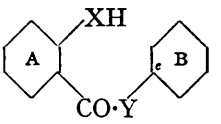
Further investigation of the interconversion of systems such as (I) and (II) (J., 1936, 329; this vol., p. 1897) has shown that amides of type (I; X = O, YH = NH_2) which contain a sufficiently positive carbon atom at *c* may be converted into substituted salicylarylamides derived from (II); for example, when o-2′ : 4′-*dinitrophenoxybenzamide* is heated, *salicylo*-2′ : 4′-*dinitroanilide* is readily formed. A study of the influence of substitution in the nucleus B and of the character of the amide nitrogen in (I) has been made and in the course of this it is shown that the *o*-sulphonamides of diphenyl ether may be converted into phenol-*o*-sulphonarylamides. Attempts to isolate aniline-*o*-sulphonacetamide were unsuccessful; acetylation of the sodium salt of aniline-*o*-sulphonamide gave the isomeric acetanilide-*o*-sulphonamide and reduction of *o*-nitrobenzenesulphonacetamide gave the *thiadiazine dioxide* (XII).

During a study of the interconversion of the types (I) and (II) it was shown (this vol., p. 1897) that aryl salicylates (II, X = Y = O) containing suitable substituents in A and B may be converted into 2-carboxydiphenyl ethers (I, X = Y = O). Roberts and his colleagues (J., 1934, 727; 1935, 196, 1309) have demonstrated the smooth conversion of 2-aminodiphenyl ethers into 2-hydroxydiphenylamines; their experiments together with those of Ransom (*Ber.*, 1900, **33**, 199) and of Raiford (*J. Amer. Chem. Soc.*, 1924, **46**, 2305) concerning the rearrangement of *o*-acyl derivatives of 2-aminophenols furnish con-

vincing evidence of the intramolecular displacement of positive groups from phenolic oxygen by the aromatic amino-group. The results obtained by these and other investigators of analogous systems indicate that a reversal of the salicylic ester–diphenyl ether type of rearrangement might be attained with the amides of 2-carboxydiphenyl ethers (I; X = O, YH = NH_2). In fact, 2-p-*nitrophenoxybenzamide* (III, H instead of Ph) is converted at 50° in alkaline media into salicylo-4′-nitroanilide; the more rapid conversion of 2-op-*dinitrophenoxybenzamide* into *salicylo-2′ : 4′-dinitroanilide*, which may be effected by heat alone, serves to illustrate the influence of increasing the positive character of *c* from which oxygen is displaced.



(I.)



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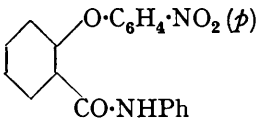
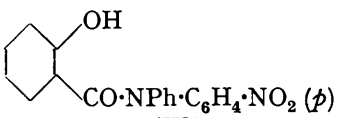
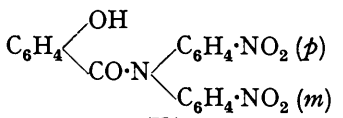


(III.)

Previous experiments dealing with the conversion of *o*-amino-sulphones into diphenylamine-*o*-sulphinic acids (J., 1935, 183) showed that, although this intramolecular displacement of the sulphonyl by the amino-group is favoured by acylating the latter group with an acid of moderate strength, acylation with strong acids such as picric or benzenesulphonic retards the process. In explanation of this circumstance it was pointed out that acylation, by promoting the necessary release of a proton from the amino-group, must be expected generally to favour the change unless the formation of a stable ion at the acylamino-group suppresses the essential donor capacity of the nitrogen; the latter condition was evidently present in the picryl and benzenesulphonyl derivatives. The behaviour of substituted derivatives of type (I) accords with this view. For example, the conversion of (III) into (IV) and of the corresponding *m*-nitroanilide into (V) takes place more readily than the rearrangement of the parent amide (III, H instead of Ph). In these cases (III), phenylation of carbamyl evidently promotes liberation of the proton without excessive depression of the donor function of the nitrogen. Similar relations were observed with the derivatives of glycollamide; the amide (VI) was merely hydrolysed and no



(IV.)



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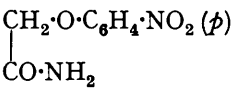
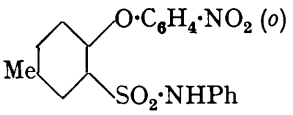
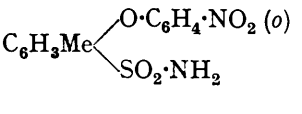


(VI.)

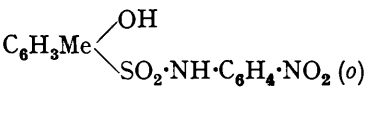
rearrangement was effected, but the corresponding anilide yielded glycollo-4-nitrodiphenylamide or the products of its hydrolysis. Rearrangement of the *sulphonamide* (VIII) and its N-*methyl* derivative, effected under usual conditions, yielded (IX) and the corresponding *methylamide* respectively; the identity of these products was established by complete methylation, which gave products identical with that obtained by synthesis from 4-methoxytoluene-3-sulphonyl chloride. The effect of converting the amide nitrogen of (VIII) into a more stable ion is illustrated by the inertness of (VII), which was unaltered by hot aqueous alkali hydroxide. This adverse influence of phenylating the sulphonamide (VIII) is particularly interesting when contrasted with the favourable effect of this substitution in the carbamyl derivative. The relations observed are evidently due to the known difference in the characters of the carbamyl and the sulphonamide-group and may be adequately explained by the views already mentioned. Quantitative comparison of the behaviour of the amides examined was not possible owing to the hydrolysis which usually accompanied their rearrangement.



(VII.)

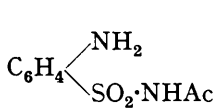


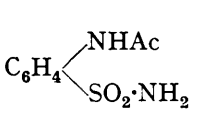
(VIII.)

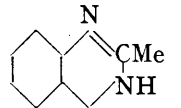


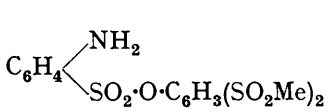
(IX.)

Rearrangements of the type now recorded are regarded as displacements of a positive group from oxygen by nitrogen of an *o*-carbamyl group. From this point of view they appear as essentially similar to the conversion of *O*-acylsalicylamides into the *N*-acyl derivatives and there seems no adequate reason for assuming that the fundamental type of mechanism of rearrangement is different in either case. Titherley and his colleagues (J., 1905, **87**, 1207; 1906, **89**, 1318) have maintained that the interconversion of acylsalicylamides involves the intermediate formation of a metoxazine structure, but this view has been disputed by Auwers (*Ber.*, 1907, **40**, 3507) and by Anschutz (*Annalen*, 1924, **442**, 19). In order to obtain further information on this question attempts were made to isolate the isomeric acetyl derivatives (X) and (XI) with a view to studying their interconversion. Acetyl chloride and the sodium salt of 2-aminobenzenesulphonamide gave a product which according to its properties was (XI). It was expected that the isomeride (X) would be obtained by reduction of 2-*nitrobenzenesulphonacetamide*, but this yielded instead the *thiadiazine dioxide* (XII). The latter was also formed by heating the *amide* (XI), but it was not converted by any simple means into either (X) or (XI).


(X.)


(XI.)


(XII.)


(XIII.)

In conclusion it is worth notice that neither the *sulphonate* (XIII) nor the corresponding anthranilate could be rearranged under the conditions effective with (III) or (VIII). This result was unexpected, since the mobility of halogen in 1-chloro-2 : 4-bismethylsulphonylbenzene has been established (this vol., p. 901), and Ullmann and Nadal (*Ber.*, 1908, **41**, 1870) have shown the intermolecular displacement of 2-nitrophenyl from 2-nitrophenyl *p*-toluenesulphonate by aniline. Further investigation of this question is desirable.

Experimental.

(1) 2-p-*Nitrophenoxybenzamide*.—2-*p*-Nitrophenoxybenzoic acid (this vol., p. 1899) was converted into the chloride by excess of thionyl chloride (45°), which was then removed. Ammonia was led through a benzene solution of the chloride until reaction was complete. After the solvent had been removed, the residue was washed with water before purification from aqueous acetone. The *amide* formed plates, m. p. 167° (Found: C, 60·5; H, 4·3; N, 10·9. $C_{13}H_{10}O_4N_2$ requires C, 60·5; H, 3·9; N, 10·9%).

(2) 2-p-*Nitrophenoxybenzanilide* (III), obtained by reaction of aniline with the chloride in boiling benzene, separated from benzene in needles, m. p. 127° (Found: C, 68·3; H, 4·5; N, 8·6. $C_{19}H_{14}O_4N_2$ requires C, 68·3; H, 4·2; N, 8·4%).

(3) 2-p-*Nitrophenoxybenzo*-m-*nitroanilide*, prepared in a similar manner, formed prisms from alcohol, m. p. 141° (Found: C, 60·3; H, 4·0; N, 11·2. $C_{19}H_{13}O_6N_3$ requires C, 60·2; H, 3·4; N, 11·1%).

(4) 2-op-*Dinitrophenoxybenzamide*.—When 2 : 4-dinitrochlorobenzene (1 mol.) was added to a solution of methyl salicylate (1 mol.) in methyl alcohol containing sodium methoxide (1 mol.), reaction began at once and was complete in 6 hours (18°). The insoluble product, after being washed with water, was purified from methyl alcohol. *Methyl* 2-op-*dinitrophenoxybenzoate* (70% of the theoretical yield) formed prisms, m. p. 88° (Found: N, 8·8. $C_{14}H_{10}O_7N_2$ requires N, 8·8%). When this methyl ester (10 g.) was warmed with sulphuric acid (20 c.c., 100°, 15 mins.), it was hydrolysed; 2-op-*dinitrophenoxybenzoic acid*, which separated when the resulting solution was diluted, formed pale yellow prisms from aqueous acetic acid, m. p. 164° (Found: N, 9·4. $C_{13}H_8O_7N_2$ requires N, 9·2%). With thionyl chloride (8 c.c., 50°) in presence of a little aluminium chloride this acid (5 g.) yielded the chloride, which remained as a colourless solid after the excess of thionyl chloride had been removed under diminished pressure. The required *amide* separated (5 g.) in the crystalline state when ammonia was led into a benzene solution (50 c.c.) of the crude acid chloride; it formed pale yellow needles, m. p. 121°, from benzene–light petroleum (Found: C, 51·6; H, 3·1. $C_{13}H_9O_6N_3$ requires C, 51·5; H, 3·0%).

(5) 4-*Nitrophenoxyacetanilide*, from aniline and 4-nitrophenoxyacetyl chloride (Jacobs and Heidelberger, *J. Amer. Chem. Soc.*, 1917, **39**, 1437, 2424), formed prisms from alcohol, m. p. 172° (Found: N, 10·3. $C_{14}H_{12}O_4N_2$ requires N, 10·3%).

(6) 4-o-*Nitrophenoxy*-m-*toluenesulphonamide* (VIII), obtained from the corresponding sulphonyl chloride (this vol., p. 1899) in the usual manner, formed prisms from alcohol, m. p. 159° (Found : N, 9·2. $C_{13}H_{12}O_5N_2S$ requires N, 9·1%).

(7) 4-o-*Nitrophenoxy*-m-*toluenesulphonmethylamide*, obtained from the chloride used for the preparation of the amide (6), formed prisms, m. p. 145° (Found : C, 52·3; H, 4·5; N, 8·8. $C_{14}H_{14}O_5N_2S$ requires C, 52·2; H, 4·4; N, 8·7%).

Rearrangement of the Amides.—This, unless otherwise stated, was effected by an aqueous acetone (1 : 4) solution of sodium hydroxide (1·25 mols., 1/5N) at suitable temperatures, its progress being indicated by the change in colour of the solution from yellow to red. The mixture was then diluted, and the products liberated by dilute sulphuric acid.

Salicylo-4′-nitroanilide, from the amide (1) at 50° (1 hr.), had m. p. 231° (Bell, J., 1875, **28**, 747) and was identical with the product obtained from 4-nitroaniline and salicyl chloride.

Salicylo-4′-nitrodiphenylamide (IV), from the amide (2) at 18° (30 mins.), formed yellow prisms from acetone, m. p. 134° (Found : C, 68·1; H, 4·5; N, 8·6. $C_{19}H_{14}O_4N_2$ requires C, 68·3; H, 4·2; N, 8·4%), and on alkaline hydrolysis yielded 4-nitrodiphenylamine and salicylic acid.

Salicylo-3′ : *4″-dinitrodiphenylamide* (V), from the amide (3) at 18° (5 mins.), formed plates from acetone, m. p. 168° (Found : C, 60·0; H, 4·0; N, 11·1. $C_{19}H_{13}O_6N_3$ requires C, 60·2; H, 4·4; N, 11·1%). It was also obtained from the amide (3) at 18° in piperidine (3 hrs.) or pyridine (24 hrs.). Alkaline hydrolysis of the substance gave salicylic acid and 3 : 4′-*dinitrodiphenylamine*, orange needles, m. p. 217°, which were identical with the product synthesised from 3-nitroaniline and 4-bromonitrobenzene by the method of Eckert and Steiner (*Monatsh.*, 1914, **35**, 1153) (Found : N, 16·3. $C_{12}H_9O_4N_3$ requires N, 16·2%).

Salicylo-2′ : *4′-dinitroanilide*, from the amide (4) at 18° (2 mins.), formed yellow needles from benzene, m. p. 213° (Found : N, 13·9. $C_{13}H_9O_6N_3$ requires N, 13·9%). When the molten amide (4) was heated at 200°, it became yellow and solidified a few degrees higher, giving a product identical (m. p. 213°) with the dinitroanilide obtained by interaction with alkali. The substance was synthesised by shaking 2 : 4-dinitrochlorobenzene (1 mol.) with an alcoholic solution of salicylamide (1 mol.) and sodium ethoxide (1 mol.); separation of the sodium salt of the dinitroanilide was complete in 3 hours (18°).

When a solution of the amide (5) in N-sodium hydroxide (1·25 mols.) was heated (100°, 30 mins.), 4-nitrodiphenylamine separated in an impure condition. This was evidently formed by hydrolysis of the primary product of rearrangement, glycollo-4-nitrodiphenylamide, but attempts to isolate the latter by varying the conditions were unsuccessful.

4-*Hydroxytoluene*-3-*sulphon*-o-*nitroanilide* (IX).—When a solution of the sulphonamide (6) (VIII) in N-sodium hydroxide (2·5 mols.) was heated (100°), the red sodium salt of (IX) was gradually formed, the change being complete in 1 hour. The product, isolated as usual, formed yellow prisms from alcohol, m. p. 160° (Found : N, 9·1. $C_{13}H_{12}O_5N_2S$ requires N, 9·1%). It was identified by complete methylation as described below.

4-*Hydroxytoluene*-3-*sulphon*-o-*nitromethylanilide* was obtained (3·9 g.) from the sulphonamide (7) (4 g.) under similar conditions and formed yellow plates from alcohol, m. p. 135° (Found : C, 52·6; H, 4·6; N, 8·8. $C_{14}H_{14}O_5N_2S$ requires C, 52·2; H, 4·4; N, 8·7%). It was identified by complete methylation. 4-*o*-Nitrophenoxy-*m*-toluenesulphonanilide (this vol., p. 1899) was recovered after treatment which effected complete rearrangement of the sulphonamides (6) and (7).

4-*Methoxytoluene*-3-*sulphon*-o-*nitroanilide*, from 4-methoxytoluene-3-sulphonyl chloride, *o*-nitroaniline, and sodium acetate at 120°, formed yellow needles from acetic acid, m. p. 116° (Found : N, 9·0. $C_{14}H_{14}O_5N_2S$ requires N, 8·7%). Methylation of this anilide in warm alkaline solution (methyl sulphate) yielded 4-*methoxytoluene*-3-*sulphon*-o-*nitromethylanilide*, which formed pale yellow plates from alcohol, m. p. 140° (Found : C, 53·9; H, 5·1. $C_{15}H_{16}O_5N_2S$ requires C, 53·6; H, 4·8%). The same substance was obtained by alkaline methylation of the anilides, m. p. 160° and m. p. 135°, obtained by rearrangement of the amides (6) and (7) respectively.

2 : 4-*Bismethylsulphonylphenyl* o-*nitrobenzoate* was formed when an acetone solution of *o*-nitrobenzoyl chloride and the phenol was boiled in presence of potassium carbonate (1 hr.); it formed prisms, m. p. 186°, from toluene (Found : S, 15·7. $C_{15}H_{13}O_8NS_2$ requires S, 16·0%), and was converted into 2 : 4-*bismethylsulphonylphenyl anthranilate* by a solution of stannous chloride in acetic acid which had been saturated with hydrogen chloride. After 1 hour (16°) the solution was diluted, and the insoluble product purified from aqueous acetone; the ester had m. p. 204° (Found : C, 49·1; H, 4·3. $C_{15}H_{15}O_6NS_2$ requires C, 48·8; H, 4·1%).

2 : 4 : 6-*Trichlorophenyl* o-*nitrobenzenesulphonate*, obtained from the phenol, *o*-nitrobenzenesulphonyl chloride, and potassium carbonate in boiling acetone, had m. p. 142° (Found: N, 3·6. $C_{12}H_6O_5NCl_3S$ requires N, 3·7%) and was reduced by stannous chloride in acetic acid. 2 : 4 : 6-*Trichlorophenyl* o-*aminobenzenesulphonate* was then obtained; it formed prisms from alcohol, m. p. 153° (Found: N, 4·0. $C_{12}H_8O_3NCl_3S$ requires N, 4·0%), and was recovered or partly hydrolysed after treatment with boiling alkali hydroxide (N).

2 : 4-*Bismethylsulphonylphenyl* o-*Aminobenzenesulphonate* (XIII).—The product obtained from the interaction of 2 : 4-bismethylsulphonylphenol and *o*-nitrobenzenesulphonyl chloride in presence of potassium carbonate was reduced with stannous chloride in acetic acid (18°). Dilution of the mixture yielded the *base*, which formed needles, m. p. 169° (Found: C, 41·7; H, 4·0. $C_{14}H_{15}O_7NS_3$ requires C, 41·5; H, 3·7%). The substance was recovered after treatment (80°) with aqueous sodium hydroxide (N).

2-*Nitrobenzenesulphonacetamide*, from 2-nitrobenzenesulphonamide and acetic anhydride in pyridine (18°), formed prisms from dilute acetic acid, m. p. 190° (Found: N, 11·3. $C_8H_8O_5N_2S$ requires N, 11·5%).

2-*Amidosulphonylacetanilide* (XI).—A suspension of the sodium salt of 2-aminobenzenesulphonamide in benzene was shaken (6 hrs.) with acetyl chloride (1 mol.). The *product*, obtained from the benzene solution, crystallised from water in needles, m. p. 164° (Found: N, 13·3. $C_8H_{10}O_3N_2S$ requires N, 13·1%), which were soluble in aqueous alkali hydroxide, insoluble in hydrochloric acid, and could not be diazotised.

3-*Methylbenz*-1 : 2 : 4-*thiadiazine* 1 : 1-*Dioxide* (XII).—2-Nitrobenzenesulphonacetamide was reduced with stannous chloride in acetic acid under usual conditions (1 hr., 18°). The *product*, isolated by dilution of the mixture, crystallised from alcohol in plates, m. p. 268° (Found: C, 49·0; H, 4·4; N, 14·3. $C_8H_8O_2N_2S$ requires C, 49·0; H, 4·1; N, 14·3%). The substance was not attacked by boiling hydrochloric acid and was soluble in cold aqueous sodium hydroxide; it was recovered after the latter solution had been boiled. Reduction of the nitro-sulphonamide by alkaline hyposulphite also yielded the substance. The thiadiazine was also obtained by heating (200°) the sulphonamide (XI) and by the reaction of acetic anhydride with 2-aminobenzenesulphonamide in pyridine (1 hr., 18°).

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