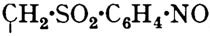
74. A Rearrangement of Carbamyl-sulphones and -sulphides.

By Wilfrid J. Evans and Samuel Smiles.

The conversion of 2′-nitro-2-acetamidodiphenylsulphone into nitroacetyldiphenylamine-2-sulphinic acid by alkaline media (J., 1935, 181) suggests that the *anilide* (I) should behave in a similar manner, since it provides the intramolecular conditions which promote this type of rearrangement (*loc. cit.*). The formation of 2-nitro-*N*-acetyldiphenylamine from (I) by reaction with alkali hydroxide shows that the expected rearrangement may be effected; evidently the sulphinic acid (II) at first formed suffers hydrolysis during the latter stages of the process. Similarly the m-*nitroanilide* of 2-nitrophenylsulphonylacetic acid (I, $C_6H_4{\cdot}NO_2$ instead of Ph) yielded 2 : 3′-dinitrodiphenylamine. With the homologous *sulphone* (III), evidence of rearrangement could not be obtained, 2-nitrobenzenesulphinic acid being the only product containing the nitrophenyl nucleus isolated after reaction with alkali. A similar result was obtained with the corresponding *sulphide*. In these cases the suppression of the intramolecular displacement observed with the sulphide corresponding to (I) may be attributed to the less favourable steric relations between the positive carbon of the nitrophenyl nucleus and the amido-nitrogen; the products arising from the tendency (Nicolet, *J. Amer. Chem. Soc.*, 1931, **53**, 3066) of β-thio-derivatives of propionic acid to suffer cleavage at the sulphur group thus predominate. The sulphonyl group of the *anilide* (IV) is less easily removed by hydrolysis than that of (III); in this case rearrangement proceeded readily, yielding the sulphinic acid (V), which after methylation was identified by hydrolysis, the products being 2-methylsulphonylbenzoic acid and 2-nitrodiphenylamine. Also the *sulphide* corresponding to (IV) gave with warm alkali hydroxide a thiol (V, SH instead of SO_2H), which after methylation and oxidation yielded the methylsulphone derived from (V). The *o*-nitroanilide of 2-thiolbenzoic acid was obtained from the amide (VI) by rearrangement and was characterised by the *methyl* ether, which was also synthesised. This behaviour of the amide (VI) contrasts with the inactivity of 2′-nitro-2-aminodiphenyl sulphide (VI, NH_2 instead of $CO{\cdot}NH_2$) under similar conditions and accords with the results of previous experiments (J., 1935, 183) which showed that acylation of the amino-group with an acid of moderate strength favours the rearrangement.



$$\begin{array}{l}\mathrm{CH_2{\cdot}SO_2{\cdot}C_6H_4{\cdot}NO_2}\\ \mathrm{CO{\cdot}NHPh}\end{array}$$

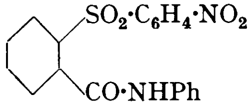
(I.)

$$\begin{array}{l}\mathrm{CH_2{\cdot}SO_2H}\\ \mathrm{CO{\cdot}NPh{\cdot}C_6H_4{\cdot}NO_2}\end{array}$$

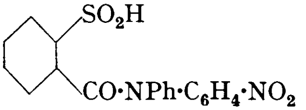
(II.)

$$\mathrm{H_2C}\begin{cases}\mathrm{CH_2{\cdot}SO_2{\cdot}C_6H_4{\cdot}NO_2}\\ \mathrm{CO{\cdot}NHPh}\end{cases}$$

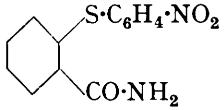
(III.)



(IV.)



(V.)

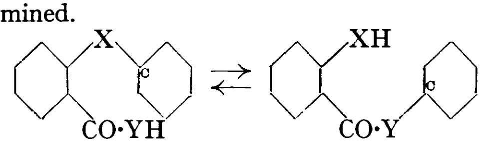


(VI.)

Further consideration of the intramolecular conditions (*loc. cit.*) governing the process shows that the influence of acylation on less active groups than amino which serve as YH (VIII, *loc. cit.*, p. 182) may have an adverse influence. This may occur when YH is hydroxyl; *e.g.*, whereas derivatives of 2′-nitro-2-hydroxydiphenylsulphone (IV, OH instead of CO·NHPh) are converted (J., 1934, 422) into sulphinic acids by cold alkali hydroxide, the 2′-nitrodiphenylsulphone-2-carboxylic acid (IV, CO_2H instead of CO·NHPh) is unattacked under these conditions.

The rearrangement of the sulphone (IV), that of the sulphide (VI) and of their derivatives now described forecasts the interconversion of systems such as (VII) and (VIII), which contain suitable intramolecular conditions (compare J., 1935, 184). Some of these systems are being examined.

(VII.)



(VIII.)

EXPERIMENTAL.

2-*Nitrophenylthioacetanilide.*—The acid (21 g.) (Claasz, *Ber.*, 1912, **45**, 747) was dissolved in excess of warm thionyl chloride (55 c.c.), the latter removed by evaporation under diminished pressure, the oily chloride dissolved in acetone (65 c.c.), and the solution treated with excess of aniline in presence of sodium bicarbonate. The *anilide* was isolated by admixture with dilute hydrochloric acid and crystallised from alcohol; m. p. 159—160° (Found : C, 58·2; H, 4·6; N, 9·6. $C_{14}H_{12}O_3N_2S$ requires C, 58·3; H, 4·2; N, 9·7%).

2-*Nitrophenylsulphonylacetanilide* (I) was obtained from the sulphide (3·1 g.) by oxidation (1·5 hours) with "hyperol" (5·2 g.) in acetic acid (30 c.c.; 100°). The product, isolated in the usual manner and purified from alcohol, had m. p. 151—152° (Found: C, 58·2; N, 8·8; S, 9·8. $C_{14}H_{12}O_5N_2S$ requires C, 52·5; N, 8·8; S, 10·0%). Rearrangement of this sulphone (1·0 g.) in boiling alcohol (10 c.c.) was rapidly (5 mins.) effected by the addition of *N*-sodium hydroxide (1 mol.). The solution then contained a mixture of 2-nitro-*N*-acetyldiphenylamine and the sulphinic acid (II); hydrolysis of the latter was completed by addition of more *N*-sodium hydroxide (1 mol.) and further heating (10 mins.). 2-Nitro-*N*-acetyldiphenylamine (0·5 g.) separated when the solution was cooled; after purification it had m. p. 133—134° (Found : N, 11·1. Calc. : N, 10·9%) and was converted into 2-nitrodiphenylamine by hydrolysis with 60% sulphuric acid.

2-*Nitrophenylthioaceto*-m-*nitroanilide* was obtained by boiling (20 mins. a solution of the chloride of the acid (10 g.) and *m*-nitroaniline (14 g.) in benzene. It was purified from acetic acid and had m. p. 216—217° (Found : N, 12·6. $C_{14}H_{11}O_5N_3S$ requires N, 12·6%).

2-*Nitrophenylsulphonylaceto*-m-*nitroanilide.*—Acetic acid (100 c.c.) containing the sulphide (6·6 g.) and hydrogen peroxide (10 c.c., 30%) was heated (100°), after 30 minutes more hydrogen peroxide (5 c.c.) was added, then (15 mins.) the solution was cooled and the product, which separated, was purified from acetic acid; it had m. p. 207° (Found : C, 46·2; N, 11·4; S, 8·9. $C_{14}H_{11}O_7N_3S$ requires C, 46·0; N, 11·5; S, 8·8%). After a suspension of this sulphone (1·0 g.) in *N*-sodium hydroxide (10 c.c.) had been boiled for a few minutes, 2 : 3′-dinitrodiphenylamine (0·6 g.) separated; this had m. p. 159° and was identified by comparison with a synthetic specimen (Evans and Smiles, J., 1935, 187).

2-*Nitrophenylthioacetamide* was obtained (82%) by interaction of ammonia and the chloride in benzene solution; it had m. p. 178—179° (Found: N, 13·1. $C_8H_8O_3N_2S$ requires N, 13·2%).

2-*Nitrophenylsulphonylacetamide*, obtained from the sulphide by oxidation with hydrogen peroxide in the usual manner, was purified from alcohol and had m. p. 155—156° (Found : C, 39·4; N, 11·7; S, 13·1. $C_8H_8O_5N_2S$ requires C, 39·3; N, 11·5; S, 13·1%). For comparison with the behaviour of the corresponding anilide which has been recorded it is worth notice that after a solution of this sulphone (1·0 g.) in *N*-sodium hydroxide (1·25 mols.) had been boiled (1 hour), a part (0·25 g.) was recovered, the only products observed being those arising from hydrolysis.

β-2-*Nitrophenylthiopropionic Acid* (compare III).—An aqueous solution of the sodium salts of β-chloropropionic acid and 2-nitrophenylthiol was boiled (1·5 hour), then cooled, and acidified with dilute sulphuric acid. The product contained 2-nitrophenylthiol, which was removed by conversion into the disulphide; the *acid* was then purified from alcohol, it had m. p. 147° (Found : C, 47·4; H, 4·1. $C_9H_9O_4NS$ requires C, 47·6; H, 4·0%). The *anilide* obtained from this acid as in the case of the acetic acid derivative had m. p. 166° after purification from acetic acid (Found : C, 59·8; H, 4·9; N, 9·1. $C_{15}H_{14}O_3N_2S$ requires C, 59·6; H, 4·6; N, 9·2%).

β-2-*Nitrophenylsulphonylpropionanilide* (III) separated (7·2 g.) from the cooled reaction mixture which had been obtained by oxidising (30 mins.) the corresponding sulphide (10 g.) with hydrogen peroxide (16·4 c.c., 30%) in hot acetic acid (100 c.c.). After purification from alcohol it had m. p. 186—187° (Found : N, 8·2; S, 9·5. $C_{15}H_{14}O_5N_4S$ requires N, 8·4; S, 9·6%). Treatment of this sulphone and of the sulphide in hot alcohol with aqueous sodium hydroxide yielded 2-nitrobenzenesulphinic acid and 2-nitrophenylthiol respectively, which were each identified by methylation and by conversion into the disulphide.

Derivatives of o-*Thiolbenzoic Acid.*—(1) 2-o-*Nitrophenylthiobenzamide* (VI). A mixture of *o*-nitrophenylthiobenzoic acid (20 g.) and thionyl chloride (40 c.c.) was warmed (below 60°) until solution of the former was complete. The crystalline acid chloride which remained after the excess of thionyl chloride had been removed was converted into the *amide* by reaction with ammonia in benzene (15—20°). The product was purified (80%) from alcohol and then had

m. p. 164° (Found: C, 56·7; H, 4·0; S, 11·4. $C_{13}H_{10}O_3N_2S$ requires C, 56·9; H, 3·7; S, 11·7%).

(2) 2-o-*Nitrophenylthiobenzanilide*, obtained from the acid chloride by reaction with excess of warm aniline, had m. p. 127—128° (Found: C, 64·8; H, 4·3; N, 7·9. $C_{19}H_{14}O_3N_2S$ requires C, 65·1; H, 4·0; N, 8·0%).

The sulphones were obtained from the sulphides (1) and (2) by oxidation (100°) with excess of hydrogen peroxide (4 mols.; 30%) in acetic acid. Purified from alcohol, 2-o-*nitrobenzenesulphonylbenzamide* (3) had m. p. 193—194° (Found: C, 51·2; S, 10·4. $C_{13}H_{10}O_5N_2S$ requires C, 51·0; S, 10·5%), and 2-o-*nitrobenzenesulphonylbenzanilide* (IV) (4) had m. p. 184° (Found: C, 59·8; N, 7·2; S, 8·4. $C_{19}H_{14}O_5N_2S$ requires C, 59·7; N, 7·3; S, 8·4%).

Rearrangements.—A solution of the sulphide (1) (1·0 g.) in alcohol (10 c.c.) containing sodium hydroxide (*N*/2, 1·25 mols.) was boiled (40 mins.). When it was cooled, a small quantity of the sulphide (1) separated; this was removed and methyl iodide was added to the solution, which was again boiled (10 mins.). The 2-*methylthiobenzo*-o-*nitroanilide* crystallised (0·22 g.) from the reacting mixture; after purification from alcohol it had m. p. 111° and was identified by comparison with the product synthesised from the interaction of *o*-nitroaniline and 2-methylthiobenzoyl chloride in benzene (Found: C, 58·0; H, 4·4. $C_{14}H_{12}O_3N_2S$ requires C, 58·3; H, 4·1%).

When the sulphone (3) (2 g.) was suspended in boiling *N*-sodium hydroxide (1·25 mols.), it soon (10 mins.) dissolved. 2-*Methylsulphonylbenzo*-o-*nitroanilide* separated when the product of this rearrangement was methylated; it had m. p. 221° and was identical with the material obtained by oxidising the above methylthiol with hydrogen peroxide in acetic acid (Found: C, 52·6; N, 8·6; S, 10·2. $C_{14}H_{12}O_5N_2S$ requires C, 52·5; N, 8·7; S, 10·0%).

Rearrangement of the sulphone (4) (2 g.) was easily (5 mins.) effected by boiling *N*-sodium hydroxide (1·25 mols.). The product present in the deep red solution was isolated after methylation (1·9 g.). Thus obtained, 2-*methylsulphonylbenzo*-2′-*nitrodiphenylamide* (compare V) was purified from acetic acid and had m. p. 206° (Found: C, 60·4; N, 7·1; S, 8·0. $C_{20}H_{16}O_5N_2S$ requires C, 60·6; N, 7·1; S, 8·1%). It was identified by hydrolysis (2 hours) with hot alcoholic sodium hydroxide. When the solution then obtained had been cooled and diluted, 2-nitrodiphenylamine separated; acidification of the filtrate yielded 2-methylsulphonylbenzoic acid. These products were identified in the usual manner.

Rearrangement of the sulphide (2) took place when it (4 g.) was kept (15 mins.) in boiling alcohol (35 c.c.) containing 0·5*N*-sodium hydroxide (1·25 mols.). Methyl iodide was then added and methylation was assisted by further boiling (15 mins.). After the excess of methyl iodide had been removed, the product separated from the cooled mixture (2·7 g.); after being purified from alcohol, it had m. p. 145—146° and was identified as 2-*methylthiobenzo*-2′-*nitrodiphenylamide* (Found: C, 66·3; H, 4·6; N, 7·7. $C_{20}H_{16}O_3N_2S$ requires C, 65·9; H, 4·4; N, 7·7%) by oxidation, which yielded the above sulphone obtained by rearrangement of sulphone (4).

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