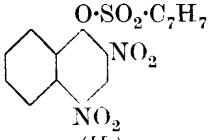
LXXXII.—*The Interaction of Sulphonates and Sulphonamides with Piperidine.*

By FRANK BELL.

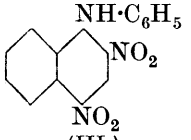
TURNER and his co-workers (J., 1929, 512; 1930, 932, 1853) have shown that aryl sulphonates can be very neatly severed by piperidine according to the general equation (I), the oxygen–sulphonoxy-bond being broken in every case. It is now found that, although

$$R{\cdot}O{\cdot}SO_2R' + H{\cdot}NC_5H_{10} = R{\cdot}OH + C_5H_{10}N{\cdot}SO_2R' \quad (I.)$$

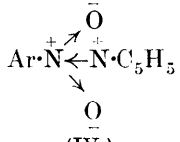
this type of reaction occurs with the mononitrophenyl sulphonates, *e.g.*, 2-nitrophenyl *p*-toluenesulphonate, with 2 : 4-dinitrophenyl *p*-toluenesulphonate the reaction may follow a second course. In this case the nuclear link is severed and 2′ : 4′-dinitro-1-phenylpiperidine results. The possibility that 2 : 4-dinitrophenol is an intermediate product is ruled out by the fact that this phenol forms a stable piperidine salt which shows no tendency to undergo change under the conditions of the experiment. Ullmann (*Ber.*, 1908, **41**, 1870, 3932; D.R.-P. 194951) has described other reactions in which dinitrophenyl *p*-toluenesulphonates undergo severance at the nuclear bond. To give only one example, 2 : 4-dinitro-α-naphthyl *p*-toluenesulphonate (II) is easily converted into 2 : 4-dinitro-α-naphthylphenylamine (III) when heated with aniline. The sulphonate



(II.)



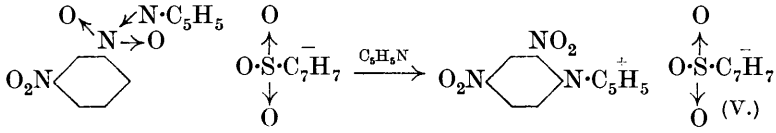
(III.)



(IV.)

group can hardly separate as other than a negative ion, leaving the nucleus with a positive charge, and yet this type of reaction occurs only when the nucleus is already overburdened with positively charged groups. A line of escape would be provided if it could be shown that the nitro-group is so combined with the base that its normal electrical character is lost, as is that of the amino-group on solution in sulphuric acid. Bennett and Willis (J., 1929, 256) have

suggested that bases can add on to the nitro-group by the conversion of the nitrogen–oxygen double bond into a semipolar double bond : the additive compounds involving pyridine might therefore be written as (IV). Although it is difficult to conceive of such a complex acting as an electron source, the electron-absorbing character of the nitro-group is clearly destroyed. It would therefore be of interest to isolate such additive compounds, but it has been found that isolable pyridine compounds can be obtained only when the mode of linkage is clearly not through the nitro-group. Thus 4′-nitro-4-*p*-toluenesulphonoxydiphenyl and 3 : 4′-dinitro-4-*p*-toluenesulphonoxydiphenyl can be crystallised unchanged from pyridine, and the compound formed by 2 : 4-dinitrophenyl *p*-toluenesulphonate is a pyridinium salt (V) (Freudenberg and Hess, *Annalen*, 1926, **448**, 121), in the formation of which again the sulphonate group has been separated from the nucleus. It is possible that additive compounds are formed only when the nitro-group tends to be specially positive owing to the presence of many other electron-absorbing groups in the same molecule, and that when formed lead to immediate reaction. With tertiary bases the primary result may be slight ionisation of the sulphonate group, followed by immediate introduction of a further molecule of the tertiary base to give the salt, and with secondary bases the mechanism may be the same or may involve a migration of the secondary radical as suggested by Brewin and Turner (J., 1928, 335).



(V.)

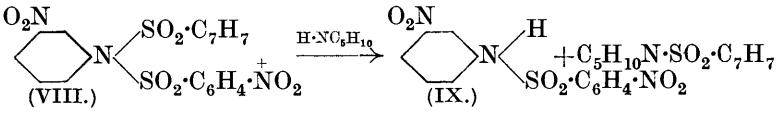
In previous papers it has been shown that, whereas the sulphonamido-group is comparable with the hydroxyl group (J., 1928, 2772), the disulphonamido-group, $-N(SO_2)_2$, is comparable with the sulphonoxy-group (J., 1929, 2788). It was therefore anticipated that most disulphonamides would react with piperidine according to equation (VI), and dinitrodisulphonamides might react as in (VII). Actually, all the disulphonamides investigated passed smoothly into monosulphonamides. This reaction is of interest when the two sulphonamide residues are not identical. Thus

$$R{\cdot}N(SO_2R')_2 + H{\cdot}NC_5H_{10} = R{\cdot}NH{\cdot}SO_2R' + C_5H_{10}N{\cdot}SO_2R' \quad \text{(VI.)}$$

$$R{\cdot}N(SO_2R')_2 + H{\cdot}NC_5H_{10} = R{\cdot}NC_5H_{10} + H{\cdot}N(SO_2R')_2 \quad \text{(VII.)}$$

m-nitrobenzenesulphon-*p*-toluenesulphon-*m*′-nitroanilide (VIII) gave rather unexpectedly *m*-nitrobenzenesulphon-*m*′-nitroanilide. This result suggests that the change is initiated by the hydrogen atom of

the piperidine becoming attached to the nitrogen lone pair of electrons. The nitrogen atom tends to regain neutrality by displacing

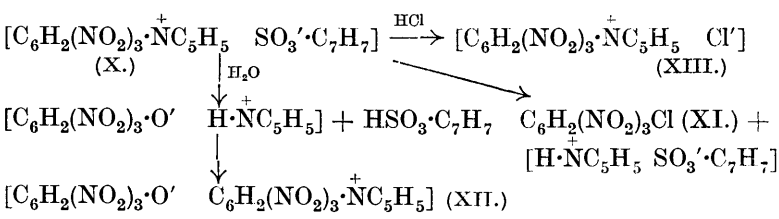


(VIII.) (IX.)

bonding electrons towards it, those most readily available being in the *p*-toluenesulphonoxy-group. Consequently, when rearrangement takes place with separation of the piperidine residue in a negatively charged state, it is the *p*-toluenesulphonyl residue which can most readily be severed as a positive ion and give rise to *p*-toluenesulphonylpiperidine.

In conclusion, attention is again directed to the curious fact that, although nitroamines may react sluggishly, if at all, with *p*-toluenesulphonyl chloride, the corresponding nitrosulphonamides (obtained indirectly) are easily converted into disulphonamides. Thus 5 : 4′-dinitro- and 3 : 5-dinitro-2-aminodiphenyls and 3 : 4′-dinitro- and 3 : 5 : 4′-trinitro-4-aminodiphenyls and 2 : 4-dinitroaniline do not react with *p*-toluenesulphonyl chloride under the usual conditions, whereas 3 : 5-dinitro-2-*p*-toluenesulphonamidodiphenyl, 3 : 5-dinitro-4-*p*-toluenesulphonamidodiphenyl, and *p*-toluenesulphon-2 : 4-dinitroanilide are converted into disulphonamides with the utmost ease. Since phenols are more allied to sulphonamides than amines, nitrophenols would be expected to react easily with *p*-toluenesulphonyl chloride. Polynitrophenols are usually converted into the corresponding chloro-compounds by the action of *p*-toluenesulphonyl chloride (Ullmann, *loc. cit.*; Sané and Joshi, J., 1924, **125**, 2481), but it can scarcely be doubted that sulphonates are intermediate products. Thus Ullmann has shown that many nitrophenols may be made to give their sulphonyl derivatives by working at a low temperature, whereas from the hot reactants the chloro-compounds are obtained, and Borsche and Feske (*Ber.*, 1926, **59**, 685) have obtained from dinitro-*o*-cresol a mixture of the sulphonate and dinitro-*o*-chlorotoluene. The only compound which had been obtained by the interaction of picric acid and *p*-toluenesulphonyl chloride was picryl chloride. This reaction has been re-examined to see if the nitro-groups do inhibit sulphonate formation in the cold. No difficulty was experienced in isolating picrylpyridinium *p*-toluenesulphonate (X) in almost quantitative yield, and therefore it appears that all nitrophenols do react easily with *p*-toluenesulphonyl chloride. Picrylpyridinium *p*-toluenesulphonate was a rather unstable compound which readily gave rise to the already known picrylpyridinium picrate (XII) (Busch and Kogel,

J. pr. Chem., 1911, **84**, 507; Hodges, J., 1926, 2417) either by repeated crystallisation or by solution in cold acetic acid. With alcoholic hydrogen chloride it gave an easily separable mixture of



picryl chloride (XI) and picrylpyridinium chloride (XIII), and the latter was easily decomposed by warm water to give picrylpyridinium picrate.

EXPERIMENTAL.

2 : 4-Dinitrophenyl *p*-toluenesulphonate (6 g.) (Ullmann and Nadai, *Ber.*, 1908, **41**, 1870) reacted vigorously with piperidine (6 c.c.). The portion of the gummy product insoluble in water crystallised from alcohol, containing hydrogen chloride, in yellow needles (2·2 g.), m. p. 95° (alone or mixed with 2 : 4-dinitrophenylpiperidine); the mother-liquor from these deposited distinguishable crystals of 2 : 4-dinitrophenol and *p*-toluenesulphonylpiperidine. The aqueous filtrate, neutralised with hydrochloric acid, deposited 2 : 4-dinitrophenol (0·4 g.).

2 : 4-Dinitrophenol and piperidine were heated together for ½ hour. After cooling, the liquid was diluted with water; the pure *piperidine* salt thus precipitated formed bright yellow needles, m. p. 171° (Found: N, 15·2. $C_{11}H_{15}O_5N_3$ requires N, 15·6%). It was alternatively prepared by addition of piperidine to a boiling benzene solution of 2 : 4-dinitrophenol.

On crystallisation of 2 : 4-dinitrophenol from pyridine or by addition of pyridine to a solution of the phenol in benzene there was obtained the *pyridine* salt in long golden-yellow needles, m. p. *ca.* 85° (Found: loss on drying at 90°, 30·6. $C_6H_4O_5N_2,C_5H_5N$ requires loss, 30·0%). This salt very readily regenerated the phenol on standing in the atmosphere.

2′ : 4′-Dinitro-1-phenylpyridinium *p*-toluenesulphonate was recovered unchanged after solution in acetic acid, but reacted vigorously with piperidine. The dark plum-coloured solution obtained was treated with water; the precipitate formed, after crystallisation from alcohol, gave 2 : 4-dinitroaniline in stout needles, m. p. 178° (Found: C, 39·6; H, 2·8; N, 22·5. Calc.: C, 39·3; H, 2·7; N, 23·0%). 2-Nitrophenyl *p*-toluenesulphonate has no tendency to

yield 2-nitrophenylpyridinium *p*-toluenesulphonate even when boiled with pyridine for several hours.

It was not found possible to prepare 2 : 4 : 6-trinitrophenyl *p*-toluenesulphonate by the application of the above method to picric acid.

A solution of picric acid in piperidine was boiled under reflux for 1 hour. On cooling, there separated orange needles, m. p. *ca.* 135°, of a *piperidine* compound of piperidine picrate (Found : loss on drying at 90°, 23·0. $C_{11}H_{14}O_7N_4,C_5H_{11}N$ requires loss, 21·3%), which readily decomposed when warmed to give *piperidine picrate*, m. p. 150° (Found : N, 17·8. $C_{11}H_{14}O_7N_4$ requires N, 17·8%). Piperidine picrate could be prepared alternatively by addition of piperidine to a solution of picric acid in benzene or acetic acid and formed pale yellow needles. It was recovered unchanged after being boiled with *p*-toluenesulphonyl chloride (1 mol.) in benzene solution for 2 hours.

A solution of molecular amounts of picric acid and *p*-toluenesulphonyl chloride was after 12 hours poured into water. The yellow precipitate, m. p. *ca.* 190°, was dried and boiled with acetone, and the solution filtered hot. The pale yellow residue after one crystallisation from alcohol gave pure *picrylpyridinium* p-*toluenesulphonate* as lustrous plates, m. p. 197° (decomp.) (Found : C, 46·6; H, 3·0; N, 11·9; S, 6·8. $C_{18}H_{14}O_9N_4S$ requires C, 46·7; H, 3·0; N, 12·1; S, 6·9%); the acetone deposited golden-yellow prisms, m. p. 218°, of picrylpyridinium picrate. Picrylpyridinium *p*-toluenesulphonate dissolved easily in cold acetic acid, but on addition of water there was precipitated picrylpyridinium picrate; it dissolved also in water, but when the solution was warmed picrylpyridinium picrate, m. p. 222°, crystallised. When it was added to an alcoholic solution of hydrogen chloride, a clear solution was obtained which soon deposited crystals of picrylpyridinium chloride, m. p. 128° after crystallisation from absolute alcohol. The mother-liquor on dilution with water gave crystals of picryl chloride, m. p. 85°.

Picrylpyridinium *p*-toluenesulphonate underwent vigorous reaction with piperidine, but no definite product was isolated. The conditions of formation and the reactions of pyridinium arylsulphonates will be made the subject of further study.

Picrylpyridinium picrate evolved pyridine on treatment with warm sodium hydroxide, and, when boiled with acetic acid, gave pyridine picrate in needles, m. p. 167°. Amorphous pyridine picrate prepared by addition of pyridine to a benzene solution of picric acid undergoes transformation to the needle variety in contact with acetic acid.

The following substances were recovered in a pure condition after

solution in boiling pyridine: 4′-nitro-4-*p*-toluenesulphonoxydiphenyl, 3 : 4′-dinitro-4-*p*-toluenesulphonoxydiphenyl, di-*p*-toluenesulphon-*p*′-nitroanilide, *p*-toluenesulphon-*p*′-nitroanilide, and di-*p*-toluenesulphon-*o*′-nitroanilide. 3-Bromo-5 : 4′-dinitro-4-hydroxydiphenyl gave only an unstable red pyridine salt, which soon decomposed in the air and immediately in contact with acetic acid. 3 : 5 : 4′-Trinitro-4-hydroxydiphenyl gave a *pyridine* salt, red needles, m. p. 198° (Found: N, 14·2. $C_{17}H_{12}O_7N_4$ requires N, 14·6%), which could be recrystallised from acetic acid with only slight decomposition.

With piperidine, *p*-toluenesulphon-*p*′-nitroanilide gave a bright yellow *piperidine* salt, m. p. 138° (Found: N, 10·8. $C_{18}H_{23}O_4N_3S$ requires N, 11·1%), and di-*p*-toluenesulphon-*p*′-nitroanilide underwent vigorous reaction to give a thick liquid. This liquid was poured into water and filtered after solidification of the precipitated oil. On neutralisation of the filtrate with hydrochloric acid *p*-toluenesulphon-*p*′-nitroanilide was precipitated; the residue after crystallisation from alcohol gave *p*-toluenesulphonylpiperidine, m. p. 103°.

m-Nitrobenzenesulphon-*p*-toluenesulphon-*m*′-nitroanilide (VIII) was dissolved in piperidine by slight warming, and the solution diluted with water. The precipitate after crystallisation from alcohol had m. p. 98—102° (mixed with *p*-toluenesulphonylpiperidine, m. p. 101—103°). The filtrate was treated with excess of hydrochloric acid, and the resulting precipitate crystallised from acetic acid. It gave a 70% yield of *m*-nitrobenzenesulphon-*m*′-nitroanilide, m. p. 144—147° alone or 145—149° when mixed with an authentic specimen.

Although 2 : 4-dinitroaniline did not react with *p*-toluenesulphonyl chloride under the ordinary conditions, *di*-p-*toluenesulphon*-2 : 4-*dinitroanilide* was readily obtained by interaction of *p*-toluenesulphon-2 : 4-dinitroanilide (J., 1929, 2789) with *p*-toluenesulphonyl chloride in pyridine solution. It crystallised from acetic acid in lustrous prisms, m. p. 217° (Found: C, 49·4, 49·1; H, 3·6, 3·5. $C_{20}H_{17}O_8N_3S_2$ requires C, 48·9; H, 3·5%). This compound was dissolved in piperidine by gentle warming, and the solution diluted with water. The precipitated solid proved to be *p*-toluenesulphonylpiperidine, and the filtrate after neutralisation with hydrochloric acid furnished *p*-toluenesulphon-2 : 4-dinitroanilide.

3:5-*Dinitro*-4-*di*-p-*toluenesulphonamidodiphenyl*, prepared by interaction of 3 : 5-dinitro-4-*p*-toluenesulphonamidodiphenyl (J., 1928, 2775) with *p*-toluenesulphonyl chloride in pyridine solution, crystallised from acetic acid in needles, m. p. 249° (Found: C, 55·1; H,

3·8. $C_{26}H_{21}O_8N_3S_2$ requires C, 55·0; H, 3·7%). This compound was dissolved in warm piperidine, and the solution poured into dilute hydrochloric acid. The precipitate on fractional crystallisation from acetic acid readily gave 3 : 5-dinitro-4-*p*-toluenesulphonamidodiphenyl (less soluble) and *p*-toluenesulphonylpiperidine (more soluble).

3 : 4′-Dibromo-4-di-*p*-toluenesulphonamidodiphenyl (J., 1930, 1076) was dissolved in piperidine by warming on a steam-bath (about 1 hour). The solution was poured into dilute hydrochloric acid; the resulting precipitate after crystallisation from acetic acid gave pure 3 : 4′-dibromo-4-*p*-toluenesulphonamidodiphenyl.

The above experiment was repeated with 3 : 5-dibromo-4-di-*p*-toluenesulphonamidodiphenyl, and 3 : 5-*dibromo*-4-p-*toluenesulphonamidodiphenyl* was obtained. It formed needles, m. p. 196°, after recrystallisation from acetic acid (Found: C, 46·8; H, 3·2. $C_{19}H_{13}O_2NBr_2S$ requires C, 47·4; H, 3·1%).

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