12. *Some Products formed in the Reaction of* p-*Acetamidobenzenesulphonyl Azide with Pyridine.*

By J. N. Ashley, Geo. L. Buchanan, and (in part) A. P. T. Easson.

The reaction of *p*-acetamidobenzenesulphonyl azide with pyridine has been investigated, and four reaction products isolated. Three of these have been identified as N-(p-*acetamidobenzenesulphonimido*)*pyridine* (I; R = Ac), 4 : 4′-diacetamidobenzenesulphonanilide (II; R = Ac), and N^4-acetylsulphanilamide.

Curtius and Rissom (*Z. angew. Chem.*, 1913, **26**, 134) investigated the reaction of aromatic sulphonyl azides with aromatic hydrocarbons, and showed that sulphonamides were produced

according to the equation (1). Curtius and his co-workers continued their researches on the scope of the reaction where R = phenyl, substituted phenyl, and naphthyl, and R′ = phenyl,

$$R{\cdot}SO_2{\cdot}N_3 + R'H \longrightarrow R{\cdot}SO_2{\cdot}NHR' + N_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

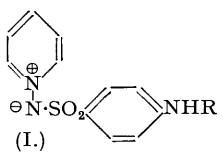
substituted phenyl, pyridyl, and quinolyl. Their results (*J. pr. Chem.*, 1921, **102**, 85; 1922, **106**, 66; 1925, **112**, 65, 88, 117; 1928, **120**, 89; 1930, **125**, 303) showed that the reaction was not always as simple as suggested in equation (1), but in most of the cases the reaction products were identified. In the case where R′ = pyridyl, compounds were isolated which were claimed to be substituted sulphonamidopyridines. Hydrolysis of these with hydrochloric acid yielded basic products which had the composition of aminopyridines but these were not identified; they were, however, characterised as mercuric chloride complexes or picrates. In one case only, where R = β-naphthyl, the evidence indicated, but not conclusively, formation of a substituted α-sulphonamidopyridine (*ibid.*, 1930, **125**, 303).

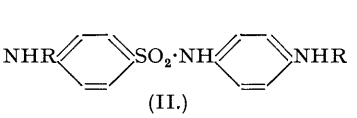
Curtius did not investigate the reaction between *p*-acetamidobenzenesulphonyl azide and pyridine, so it was decided to investigate this, as it appeared probable that it might afford an alternative method of preparation of 2-*p*-acetamidobenzenesulphonamidopyridine (N^4-acetylsulphapyridine). While the work now described was in progress, Alamela and Ganapathi (*Current Sci.*, 1943, **12**, 119) reported that they had studied this reaction and obtained a product, m. p. 280°. They concluded that this was 3-*p*-acetamidobenzenesulphonamidopyridine since this m. p. was closer to that of the 3-isomeride (272—275°) than to those of the 2- and the 4-isomeride, m. p. 224—227° and 252°, respectively. No analytical or other data were given in support of this conclusion.

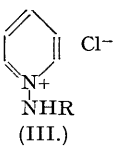
We found that when a solution of *p*-acetamidobenzenesulphonyl azide in a large excess of pyridine was boiled for 50—70 hours (in some cases Curtius employed several days; in others, 35 or 36 hours) a complex mixture of products was formed. Four products were readily isolated; the first (A) separated during the course of the reaction or on removal of some of the pyridine, the second (B) was obtained by addition of water to the concentrated pyridine solution, while the third (C) and fourth (D) crystallised out when the aqueous pyridine liquors were concentrated to a syrup. Although these four products account for only *ca.* 50% of the *p*-acetamidobenzenesulphonyl azide employed, the fate of the remainder has not yet been ascertained. It is hoped to report later on the examination of the dark red syrupy residue.

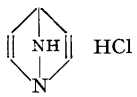
(A) is a colourless crystalline solid, m. p. 300°, insoluble in alkali but soluble in boiling water and in dilute mineral acids. The analytical data indicated the composition $C_{13}H_{13}O_3N_3S$, but the above properties eliminated the possibility that it was 2-, 3-, or 4-*p*-acetamidobenzenesulphonamidopyridine. Hydrolysis with boiling dilute alkali removed an acetyl group with formation of another crystalline compound, $C_{11}H_{11}O_2N_3S$, which was also insoluble in alkali, but very soluble in dilute acid. It contained a diazotisable amino-group, and was reconverted into (A) by acetylation.

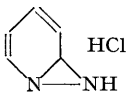
Hydrolysis of (A), with dilute hydrochloric acid yielded sulphanilic acid and the hydrochloride of a base, $C_5H_6N_2$,HCl, m. p. 160°, not identical with any of the three known aminopyridine hydrochlorides, and which could be reconverted into (A) by treatment with *p*-acetamidobenzenesulphonyl chloride. Attempts to liberate the free base with sodium hydroxide, bicarbonate, or acetate resulted in formation of very dark resinous products with a distinct odour of pyridine.

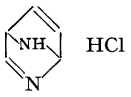

(I.)


(II.)

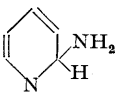

(III.)


(IV.)


(V.)


(VI.)


(VII.)

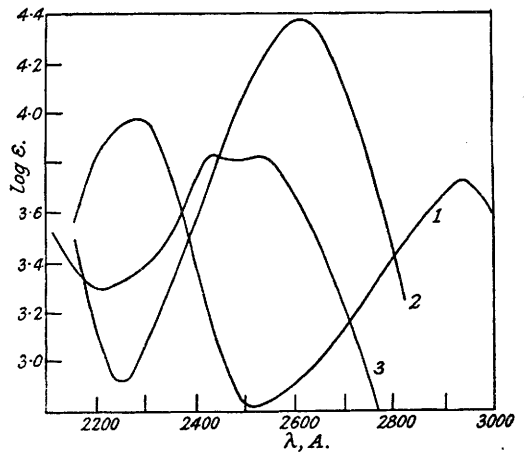

(VIII.)

When treated with nitrous acid the hydrochloride gave no diazo-reaction, but pyridine (identified as picrate) was liberated. Distillation with zinc dust and soda-lime gave ammonia and pyridine, and acetylation yielded a product which analysed for the hydrochloride of the monoacetylated base. A *picrate* was also obtained, and although all these compounds gave analytical data in agreement with derivatives of an aminopyridine they were not identical with the corresponding

derivatives of the three known aminopyridines. As the base hydrochloride apparently contained a pyridine or closely related ring, and an amino- or imino-group, two possibilities remained: (*a*) linkage through the pyridine nitrogen atom (III, R = H) and (*b*) bicyclic structures of the types (IV), (V), (VI). Although structure (V) is somewhat strained, it merits consideration, since it was shown by Curtius and Schmidt (*Ber.*, 1922, **55**, 1571, 1581) that sulphuryl azide $N_3 \cdot SO_2 \cdot N_3$ reacted with benzene and *p*-xylene to form bicyclic structures such as (VII).

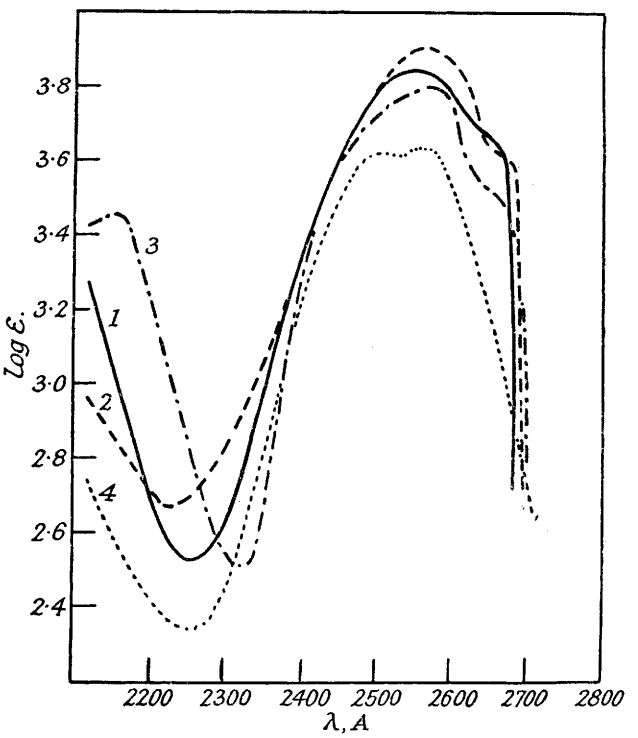
In an attempt to establish the type of linkage, the base hydrochloride was hydrogenated in aqueous solution by using Adams's catalyst. The reaction was stopped after a slow uptake of 6 atoms of hydrogen although hydrogenation was still proceeding extremely slowly. The reaction mixture contained ammonium chloride, pyridine (identified as picrate), and piperidine (identified as hydrochloride and picrate). This result can only be interpreted on formulæ (IV) and (VI) if it is assumed that the mild conditions of the hydrogenation were sufficient to break the C–N linkages.

FIG. 1.



1. 2-*Aminopyridine hydrochloride in water* (0·04% *w./v.*).
2. 4- ,, ,, ,, ,, ,,
3. N- ,, ,, ,, ,, ,,

FIG. 2.



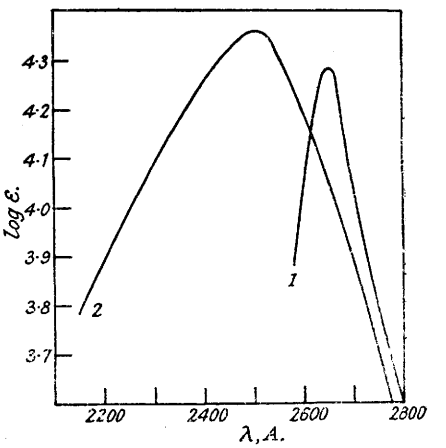
1—3. *As in Fig.* 1, *in* H_2SO_4 (0·02% *w./v.*).
4. *Pyridine in* H_2SO_4 (0·02% *w./v.*).

On the other hand, the result can readily be interpreted on formula (III) and even on (V). The latter might reasonably be expected to be reduced to 2-amino-1 : 2-dihydropyridine (VIII),

which could then either decompose into ammonia and pyridine or be hydrogenated to 2-aminopiperidine. The latter was shown by Kirsanov and Ivastchenko (*Bull. Soc. chim.*, **1936**, **3**, 2279) to lose ammonia spontaneously with formation of Δ^2-tetrahydropyridine, which is then hydrogenated to piperidine.

By analogy with the work of Kirsanov and Ivastchenko (*loc. cit.*), who found that when the above hydrogenation was carried out in presence of excess of acetic anhydride the product was 2-acetamido-*N*-acetylpiperidine, an attempt was made to anchor the extra-nuclear nitrogen atom by carrying out the hydrogenation of the acetylated base hydrochloride (III; R = Ac) in acetic acid solution in presence of acetic anhydride. Hydrogenation ceased after rapid absorption of 6 atoms of hydrogen, and the product was proved by analysis to be a *mono-acetamidopiperidine hydrochloride*. This fact that no new acetylatable group has been formed by hydrogenation is strongly in favour of structure (III) as against (V). Hydrolysis of this hydrogenation product with acid yielded the known *N*-aminopiperidine hydrochloride, and a direct comparison was made with an authentic sample, prepared as described by Knorr (*Annalen*, **1883**, **221**, 299). Similarly, a synthetic sample of *N*-acetamidopiperidine hydrochloride was shown to be identical with the hydrogenation product. It therefore follows that the acetylated base hydrochloride which was hydrogenated should be N-*acetamidopyridinium chloride* (III; R = Ac), and the base hydrochloride is N-*aminopyridinium chloride* (III; R = H).

FIG. 3.

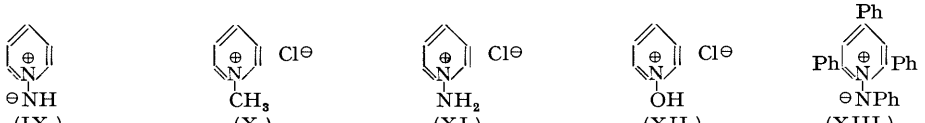


1. *In* n-*amyl alcohol.* 2. *In* H_2SO_4.

During the course of this work Dr. E. A. Braude, of the Imperial College of Science and Technology, kindly examined for us the ultra-violet light absorption of the base hydrochloride together with that of 2- and 4-aminopyridine for comparison, and independently suggested formula (III) from the results obtained in aqueous and concentrated sulphuric acid solutions. Dr. Braude reported: "In aqueous solution, the hydrochlorides are largely hydrolysed and the absorption is characteristic of the bases; it varies markedly with the position of the amino-substituent but the absorption of the isomeric base is similar to that of pyridine itself (Fig. 1). In concentrated sulphuric acid, the bases exist largely in the form of their salts and all exhibit light absorption closely resembling that of pyridine (Fig. 2), the auxochromic properties of the amino-group being almost completely lost by fixation of the free electron pair. The persistence of a low wave-length absorption in the case of the isomeric base also indicates the presence of the $N{\cdot}NR_2$ grouping."

All the evidence so far obtained supports the view that the base hydrochloride is represented by (III; R = H), and hence the free base, which was never isolated, must be (IX), while compound (A), which separated from the original reaction mixture, must be N-(p-*acetamido-benzenesulphonimido*)*pyridine* (I; R = Ac). Support for this formula is provided by the fact that the compound is insoluble in alkali since it contains no replaceable hydrogen atom, and by the ultra-violet absorption, also determined by Dr. Braude, which still shows typical pyridine-like absorption (Fig. 3).

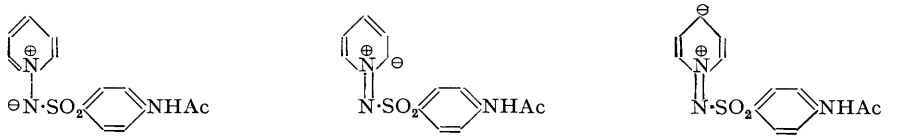
The formation of compounds of the type (III; R = H) and (I; R = Ac) is of theoretical interest since the former represents the hitherto undescribed member of the series (X, XI, and XII), while (I; R = Ac) is closely related to the type $R_3\overset{\oplus}{N}\text{–}\overset{\ominus}{N}{\cdot}SO_2R'$ which Mann and Pope (*J.*,



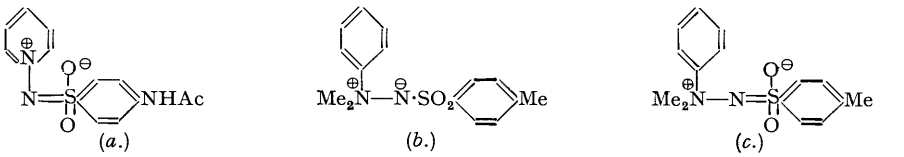
(IX.) (X.) (XI.) (XII.) (XIII.)

1922, **121**, 1052) attempted to prepare by the action of chloramine-T on dimethylaniline, and to the 2 : 4 : 6-triphenylpyridine-*N*-phenylimine (XIII) described by Schneider (*Annalen*, **1924**, **438**, 115). Similarly to the related azoxysulphones described by Farrar and Gulland (*J.*, **1944**, 368),

(I; R = Ac) conforms to the resonance requirements postulated by these authors. The resonance involving the N–N linkage is between structures such as the following :

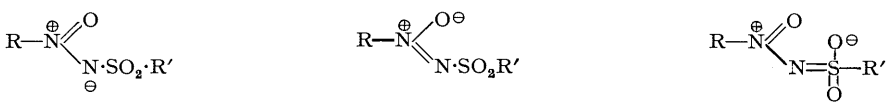


The stability of the compound can probably be attributed to this resonance. However, recent bond-length and dipole-moment determinations, *e.g.*, by Phillips, Hunter, and Sutton (*J.*, 1945, **146**), show that the dative bond $\overset{+}{S}\text{–}\overset{-}{O}$ of sulphones, etc., should almost certainly be amended to S=O. Accordingly, it has been suggested by Mr. R. P. Bell, M.A., F.R.S. (private communication), that the main contributory resonance form of (I; R = Ac) should be represented by structure (*a*). This is a very attractive idea since it provides a much more



(*a*.) (*b*.) (*c*.)

plausible seat for the negative charge, but it should be pointed out that structure (*b*), which is incapable of ring resonance, is also capable of resonance of this type [*i.e.*, with structure (*c*)], though Mann and Pope (*loc. cit.*) failed to prepare this compound from the interaction of chloramine-T and dimethylaniline. This is, of course, negative evidence, but it suggests that resonance involving the N–S bond [*i.e.*, type (*a*)] is not *per se* responsible for the stability of (I; R = Ac). In this connection, it is noticeable that the pyridine-phenylimine (XIII) can only show ring resonance although, owing to the phenyl groups, a greater number of structures contribute, while the azoxysulphones, which are closely related to the general type $R_3\overset{+}{N}\text{–}\overset{-}{N}\cdot SO_2R'$ show two types of resonance, *viz.*,



Compound (B), which was precipitated by water from the concentrated pyridine liquors, was readily soluble in alkali and insoluble in dilute acids. Hydrolysis with dilute alkali gave a product $C_{12}H_{13}O_2N_3S$ which was soluble in dilute acid and alkali, and contained one or more diazotisable amino-groups; on acetylation it yielded (B).

Hydrolysis of (B) with acid under pressure yielded sulphanilic acid and *p*-phenylenediamine. In accordance with this evidence, one would expect the product of alkaline hydrolysis to be (II, R = H) and compound (B) to be its diacetyl derivative, 4 : 4′-diacetamidobenzenesulphonanilide. The latter compound was synthesised by condensation of *p*-acetamidobenzenesulphonyl chloride with *p*-aminoacetanilide, and shown to be identical with (B). On hydrolysis with dilute mineral acid it yielded 4 : 4′-diaminobenzenesulphonanilide (II; R = H) identical with the product of alkaline hydrolysis of (B).

The formation of (II; R = Ac) in the reaction between pyridine and *p*-acetamidobenzenesulphonyl azide is of interest. It could readily arise from reaction of the azide with acetanilide, but the possibility of the latter's being present as an impurity in the crude sulphonyl chloride from which the azide was prepared was eliminated by the preparation and use of specially purified azide, the same yield of (II; R = Ac) then being obtained. It must therefore arise from 2 mols. of the azide. Although at present there is no evidence for the mechanism of this reaction, it is possible that the group $\cdot SO_2N_3$ is replaced by the radical $R\cdot SO_2\cdot NH^-$ in the same way as the $\cdot SO_3H$ group of sulphanilic acid is replaced by $\cdot NO_2$ during nitration (Zincke and Kuchenbecker, *Annalen*, 1905, **339**, 226) and by Br during bromination (Schmitt, *ibid.*, 1861, **120**, 136). This suggestion does not account for the presence of the hydrogen atom in the $\cdot SO_2\cdot NH\cdot$ grouping, but analogous reductions ($R\cdot SO_2\cdot N_3 \longrightarrow R\cdot SO_2\cdot NH_2$) are well known in this field [see compound (C), below]. It is noteworthy that the formation of compounds of type (II) was not recorded by Curtius and his co-workers.

Compound (C) was identified as N^4-acetylsulphanilamide. The formation of this product is not unexpected since Curtius (*J. pr. Chem.*, 1930, **125**, 303) found that, besides the reaction represented by equation (1), an important side reaction was the conversion of the azide, $R{\cdot}SO_2{\cdot}N_3$, into the corresponding amide $R{\cdot}SO_2{\cdot}NH_2$. At present we are unable to state the source of this hydrogen; Curtius assumed that the azide first decomposed into the radical $R{\cdot}SO_2{\cdot}N<$ which then " abstracted " two atoms of hydrogen from the " solvent ". In some cases he was able to isolate the resulting oxidation product. Thus, after boiling benzenesulphonyl azide with aniline small amounts of benzidine in addition to the normal products were isolated from the reaction mixture (Bertho, *ibid.*, 1929, **120**, 94).

Compound (D) was obtained in small amount only and has not yet been identified. Its empirical formula appears to be $C_{13}H_{15}O_3N_3S$.

N-(p-*Aminobenzenesulphonimido*)*pyridine* (I; R = H) exhibited no antibacterial activity when tested against *Staph. aureus* by the slide cell technique.

Further investigations of this reaction and in the sulphonyl azide field are in progress.

Experimental.

p-*Acetamidobenzenesulphonyl Azide*.—This was prepared from the corresponding sulphonyl chloride and sodium azide, as described by Curtius (*J. pr. Chem.*, 1926, **112**, 117), *i.e.*, using aqueous alcohol as solvent, but although he claimed 93% yields, our yields varied between 62 and 79% of very crude product (m. p. *ca.* 100°). This could be recrystallised to give pure material agreeing with Curtius's m. p. of 107°, but as it was considered that the low yields were probably due to ester formation (and, indeed, in one instance we isolated ethyl *p*-acetamidobenzenesulphonate, m. p. 115°; no depression with a synthetic sample), the alcohol was replaced by acetone, giving consistent yields (77—81%) of the required product. *p*-Acetamidobenzenesulphonyl chloride (118 g.), dissolved in acetone (1500 c.c.), was treated with sodium azide (33 g.) in water (150 c.c.). The resulting mixture formed two layers and further amounts of water (350 c.c.) and acetone (150 c.c.) were required to give a homogeneous solution, which was kept for 3 hours at room temperature, and then poured into *ca.* 10 l. of water. The product had m. p. 109° (yield 95 g., 79%). Recrystallisation from benzene raised the m. p. to 113—114° (Found: N, 23·5. Calc. for $C_8H_8O_3N_4S$: N, 23·3%).

Condensation of p-*Acetamidobenzenesulphonyl Azide with Pyridine*.—The best results were obtained as follows: the azide (82 g.) was dissolved in pyridine (1·6 l.; dried over solid potassium hydroxide) and the solution refluxed gently for 65 hours. During this time the solution became dark brown and a solid (A) separated. The mixture was allowed to cool and this solid was filtered off. A little more was obtained by concentration. The total yield was 29 g. When the highly concentrated mother-liquor was poured into water a second product (B) (12·25 g.) separated. A mixed m. p. of purified samples of (A) and (B) (see later) gave a depression. Concentration of the aqueous pyridine liquor gave 8·85 g. of product (C), and further concentration to a thick syrup yielded 3·3 g. of crude product (D).

N-(p-*Acetamidobenzenesulphonimido*)*pyridine*, Compound (A) (I; R = Ac).—The crude product had m. p. *ca.* 270°, but repeated recrystallisation (charcoal) from hot water or aqueous alcohol gave pure crystals, colourless plates, m. p. 295—300° (decomp.) depending on rate of heating (Found: C, 53·6; H, 4·4; N, 14·3; S, 11·1. $C_{13}H_{13}O_3N_3S$ requires C, 53·6; H, 4·5; N, 14·45; S, 11·0%).

Alkaline hydrolysis of compound (A). The product (2·6 g.) was refluxed for 3 hours with aqueous sodium hydroxide (50 c.c., 20%) and a few c.c. of alcohol. The resulting solution was cooled, and long needles (1·8 g.), m. p. 230°, separated. Repeated recrystallisation (charcoal) from hot water gave N-(p-*aminobenzenesulphonimido*)*pyridine* (I; R = H), pale yellow needles, m. p. 235—236° (Found: C, 53·45; H, 4·65; N, 16·9; S, 13·1; *M*, 235. $C_{11}H_{11}O_2N_3S$ requires C, 53·0; H, 4·4; N, 16·9; S, 12·85%; *M*, 249). A small amount when acetylated with acetic anhydride and a few drops of sulphuric acid (*d* 1·84) gave a product, which after recrystallisation from water formed colourless plates, m. p. 290°, not depressed on admixture with compound (A).

Acid hydrolysis of compound (A). The product (3 g.) was refluxed for 2 hours with hydrochloric acid (30 c.c.; 1 : 1). On cooling, needles (1·2 g.) separated. This substance did not melt below 300°; it contained S and N, was soluble in acids and alkali, was a primary amine, and was identified as sulphanilic acid by conversion into monoethyl-orange by the method of Bernthsen and Goske (*Ber.*, 1887, **20**, 924). The mother-liquors from which the sulphanilic acid had separated were made strongly alkaline with potassium hydroxide, and extracted with ether and chloroform. During this operation both layers became deep red, and concentration of the extracts gave a dark red intractable gum (and a distinct odour of pyridine). Accordingly, an attempt was made to isolate the hydrochloride of the basic component and compound (A) (20·6 g.) was refluxed for 3 hours with hydrochloric acid (206 c.c.; 1 : 1). After removal of sulphanilic acid the filtrate was repeatedly concentrated and each batch of crystals separated. In this way two products were obtained: (i) 11·4 g. of sulphanilic acid, and (ii) 8·1 g. of colourless N-*aminopyridinium chloride*, m. p. 156°, which recrystallised from alcohol in stout colourless needles, m. p. 160° (Found: C, 45·7; H, 5·3; N, 21·6; Cl, 27·3. $C_5H_6N_2$,HCl requires C, 46·0; H, 5·4; N, 21·4; Cl, 27·2%). The *picrate* recrystallised from aqueous alcohol in fine yellow needles, and from alcohol in rhombs, m. p. 154—155° (Found: C, 41·1; H, 2·9; N, 21·5. $C_5H_6N_2,C_6H_3O_7N_3$ requires C, 40·9; H, 2·8; N, 21·7%). The chloride was very soluble in water and gave no reaction for a primary amine. Attempts to liberate the free base from the chloride with potassium carbonate or potassium acetate gave the dark red gum and the odour of pyridine encountered before.

Treatment of the chloride with acetic anhydride, and warming until solution occurred gave, on cooling, crystals of the *monoacetyl* derivative, m. p. 216°. These recrystallised from alcohol in stout

colourless needles, m. p. 222° (Found : C, 48·5; H, 5·4; N, 16·1; Cl, 20·1. $C_7H_8ON_2$,HCl requires C, 48·75; H, 5·2; N, 16·25; Cl, 20·6%).

A small amount of the chloride was intimately mixed with zinc dust and gently distilled. Ammonia was identified by smell, and a colourless liquid distilled over. This gave a picrate, m. p. 165°, undepressed on admixture with authentic pyridine picrate (m. p. 165—166°). Distillation with soda-lime gave an identical result.

The chloride (0·28 g.), dissolved in a small amount of water, was treated with 3 drops of hydrochloric acid (*d* 1·16) and sodium nitrite (0·15 g.). The solution was gently refluxed for a few minutes, diluted with water, and aqueous picric acid added. The resulting picrate, m. p. 166°, gave no depression with pyridine picrate.

Catalytic reductions. (*a*) *N*-Aminopyridinium chloride (2 g.), dissolved in distilled water (30 c.c.), was hydrogenated in presence of Adams's (PtO_2) catalyst (0·1 g.). After 8½ hours, almost 1100 c.c. of hydrogen (at 22°; 756 mm.) had been absorbed, and the reaction was stopped. The catalyst was filtered off, and a small sample of the clear, colourless filtrate treated with aqueous picric acid. The resulting picrate recrystallised from water in yellow needles, m. p. 149°, undepressed when mixed with authentic piperidine picrate, m. p. 149—150°.

The rest of the filtrate was made acid to litmus with hydrochloric acid and concentrated. Crystals appeared which were identified as ammonium chloride.

The mother-liquors, on further concentration, gave an oily solid, which was separated by treatment with alcohol into a very soluble portion and a less soluble solid. The soluble portion gave a picrate, m. p. 166°, which gave no depression in mixed m. p. with pyridine picrate. The less soluble solid had m. p. 222° and was probably piperidine hydrochloride (m. p. 232°), since it gave a picrate m. p. 149—150° which showed no depression in mixed m. p. with an authentic sample of piperidine picrate.

(*b*) *N*-Acetamidopyridinium chloride (1·5 g.), dissolved in acetic anhydride (10 c.c.) and glacial acetic acid (20 c.c.), was hydrogenated in presence of Adams's catalyst (0·2 g.). After 25 minutes, 680 c.c. of hydrogen had been absorbed at 22° and 765 mm., and uptake then ceased (Calc. for 6H : 670 c.c.). The solution was filtered from catalyst, and the solvent removed under reduced pressure. The residual pale green oil solidified when kept for 24 hours over potassium hydroxide in a vacuum. The pasty solid recrystallised from dioxan and gave yellow-green needles of *N-acetamidopiperidine hydrochloride*, m. p. 172—173° (0·9 g.; 58%) (Found : C, 47·1; H, 8·7; N, 15·2; Cl, 19·7. $C_7H_{14}ON_2$,HCl requires C, 47·1; H, 8·4; N, 15·7; Cl, 19·9%). This product (110 mg.) in hydrochloric acid (*d* 1·16; 3 c.c.) was heated on the steam-bath for 1 hour, concentrated, and the solid product recrystallised from alcohol, forming stout needles of *N*-aminopiperidine hydrochloride, m. p. and mixed m. p. 162—163°. The authentic sample was prepared by Knorr's method (*Annalen*, 1883, **221**, 299) and characterised as its benzoyl derivative (m. p. 198° from alcohol) and acetyl derivative (m. p., and mixed m. p. with hydrogenation product, 172—173°).

Re-synthesis of *N*-(*p*-acetamidobenzenesulphonimido)pyridine was effected as follows : *N*-Aminopyridinium chloride (1·35 g.) in water (2·5 c.c.) was treated with solid potassium carbonate until the solution was strongly alkaline, and some was left undissolved. This solution was then added to *p*-acetamidobenzenesulphonyl chloride (2·4 g.) in acetone (15 c.c.). Two layers were formed, and small amounts of water and acetone were added till a homogeneous solution was obtained. The solution was shaken for some time, and after standing overnight, the insoluble product was filtered off; 1·40 g., m. p. 270° (decomp.). Repeated recrystallisation from dilute ethanol gave colourless plates, m. p. 292—298° (depending on rate of heating) which gave no depression in mixed m. p. with authentic *N*-(*p*-acetamidobenzenesulphonimido)pyridine.

4 : 4′-*Diacetamidobenzenesulphonanilide* (Compound B), (II; R = Ac).—The crude compound had m. p. *ca.* 300°, and repeated recrystallisation from glacial acetic acid (charcoal) gave irregular buff-coloured micro-prisms, m. p. 308°. It was not analysed as it was difficult to purify completely. A mixed m. p. with compound (A) was markedly depressed.

The anilide (3 g.) was refluxed for 2 hours with aqueous sodium hydroxide (50 c.c.; 20%). This yielded the diamine (II; R = H), which crystallised from aqueous alcohol (charcoal) in colourless, light-sensitive needles, m. p. 138° (Found : C, 53·0, 53·1; H, 4·9, 5·0; N, 15·2; S, 12·4. Calc. for $C_{12}H_{13}O_2N_3S,\frac{1}{2}H_2O$: C, 53·0; H, 5·1; N, 15·45; S, 11·8%).

Hydrolysis of compound (B) with aqueous hydrochloric acid (1 : 1) gave sulphanilic acid and the diamine, m. p. 138°, and *p*-phenylenediamine was isolated after hydrolysis with hydrochloric acid (*d* 1·16) in a sealed tube at 120° for 6 hours.

There was no depression in mixed m. p. of compound (B) with authentic 4 : 4′-diacetamidobenzenesulphonanilide, m. p. 310° (micro-prisms from glacial acetic acid), prepared by condensation of 4-acetamidobenzenesulphonyl chloride with 4-aminoacetanilide (cf. E.P. 486,449; Webster and Powers, *J. Amer. Chem. Soc.*, 1939, **60**, 1553; Rubzow, *J. Gen. Chem. Russ.*, 1940, **10**, 831). The first two references give no m. p. for this compound, but Rubzow quotes m. p. 245—246°. Hydrolysis of this compound with dilute alkali gave 4 : 4′-diaminobenzenesulphonanilide (colourless needles, m. p. 138° from dilute alcohol), which was shown by mixed m. p. to be identical with the product of alkaline hydrolysis of compound (B). Webster and Powers (*loc. cit.*), Kolloff and Hunter (*J. Amer. Chem. Soc.*, 1940, **62**, 3355), and Ganapathi (*J. Indian Chem. Soc.*, 1938, **15**, 525) give 155—156° as the m. p. of 4 : 4′-diaminobenzenesulphonanilide, but Rubzow (*loc. cit.*), a number of patents (Swiss, 191,673; 199,682—4; Swedish, 90,259), and unpublished work from these laboratories give 136—138°. Recrystallisation of the product, m. p. 138°, from absolute alcohol gave the anhydrous compound, colourless plates, m. p. 155° (Found : C, 54·8; H, 5·1; N, 15·8; S, 12·3. Calc. for $C_{12}H_{13}O_2N_3S$: C, 54·75; H, 4·95; N, 16·0; S, 12·15%).

N^4-*Acetylsulphanilamide* (Compound C).—The crude material had m. p. *ca.* 200°. Recrystallisation from glacial acetic acid (charcoal) gave colourless needles, m. p. 219—220° (undepressed after admixture with N^4-acetylsulphanilamide), soluble in 2N-sodium hydroxide, and insoluble in 2N-hydrochloric acid and in aqueous sodium bicarbonate.

Compound (D).—The crude *compound* had m. p. 265—268°, and was insoluble in 2N-sodium hydroxide, but soluble in hydrochloric acid (*d* 1·16); it appeared to be partly soluble in 2N-hydrochloric acid. It was practically insoluble in boiling water, pyridine, glacial acetic acid, and the usual organic solvents but crystallised from aqueous pyridine or aqueous acetic acid in colourless prisms, m. p. 269° (decomp.) (Found: C, 53·15; H, 4·95; N, 14·45; S, 10·6, 11·3. $C_{13}H_{15}O_3N_3S$ requires C, 53·25; H, 5·1; N, 14·35; S, 10·95%).

The authors acknowledge their indebtedness to Dr. E. A. Braude for the ultra-violet absorption spectra determinations, to Mr. R. P. Bell, M.A., F.R.S., and Mr. G. Newbery, B.Sc., F.R.I.C., for much valuable discussion and criticism, to Mr. S. Bance, B.Sc., A.R.I.C., for the semimicro-analyses, and to the Directors of Messrs. May and Baker Ltd. for permission to publish these results.

THE RESEARCH LABORATORIES,
MAY & BAKER LTD., DAGENHAM.

[*Received, May 2nd,* 1946.