54. *The Condensation of* 6-*Amino*-2-*hydroxypyridine with* p-*Acetamidobenzenesulphonyl Chloride.*

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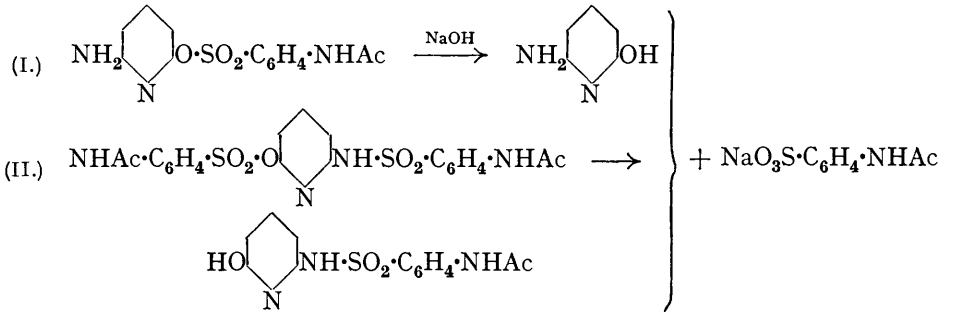
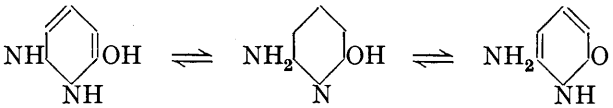
When 6-amino-2-hydroxypyridine sulphate in suspension in pyridine is condensed with *p*-acetamidobenzenesulphonyl chloride, 6-*amino*-2-*pyridyl* p-*acetamidobenzenesulphonate* and not 6-hydroxy-2-(*p*-acetamidobenzenesulphonamido)pyridine, is formed. The amino-compound corresponding to the latter compound is obtained by alkaline hydrolysis of 6-p-*acetamidobenzenesulphonamido*-2-*pyridyl* p-*acetamido*-

benzenesulphonate, which is itself formed from the above aminopyridyl ester by further condensation with the sulphonyl chloride.

WHEN 6-amino-2-hydroxypyridine sulphate in suspension in pyridine is treated with one equivalent of *p*-acetamidobenzenesulphonyl chloride, condensation proceeds mainly on the hydroxy- and not on the amino-group, 6-*amino*-2-*pyridyl* p-*acetamidobenzenesulphonate* (I) being obtained in good yield together with a small amount of 6-p-*acetamidobenzenesulphonamido*-2-*pyridyl* p-*acetamidobenzenesulphonate* (II). This compound is more readily obtained from the ester (I) by further condensation in pyridine with one equivalent of the acid chloride. These esters are readily hydrolysed by warm dilute sodium hydroxide solution :



That condensation proceeds in the first instance on the hydroxy-group may be related to the peculiar tautomeric structure of the aminohydroxypyridine, which, like all other 2-amino-pyridines and -quinolines examined in this laboratory, does not give dyes when treated with nitrous acid and subsequently with the usual coupling reagents and hence presumably does not contain a true amino-group.



The amino-ester (I), when treated with anhydrous hydrogen chloride in alcohol, gives 6-*amino*-2-*pyridyl* p-*aminobenzenesulphonate*. 6-*Hydroxy*-2-(p-*aminobenzenesulphonamido*)-*pyridine*, like the parent 2-(*p*-aminobenzenesulphonamido)pyridine (Phillips, this vol., p. 9), is exceedingly stable to boiling sodium hydroxide solution and readily hydrolysed by hot mineral acids.

EXPERIMENTAL.

6-*Amino*-2-*pyridyl* p-*Acetamidobenzenesulphonate* (I).—To a suspension of 6-amino-2-hydroxypyridine sulphate (10·0 g.) in pyridine (60 c.c.) was added, with cooling, *p*-acetamidobenzenesulphonyl chloride (14·0 g.) at 60°. The resulting solution was heated on the steam-bath for 10 minutes; addition of water (500 c.c.) gave an oil which slowly solidified. The solid, after being washed with water, was crystallised from alcohol (charcoal), giving the above *ester* (10·1 g.; 67·5%) (Found : N, 13·5. $C_{13}H_{13}O_4N_3S$ requires N, 13·7%). Extraction of the charcoal with acetone (Soxhlet) gave 0·3 g. of 6-p-*acetamidobenzenesulphonamido*-2-*pyridyl* p-*acetamidobenzenesulphonate* (II), m. p. 222° after crystallisation from 50% acetic acid, which was better obtained as follows. To a solution of the ester (I) (25·2 g.) in pyridine (68 c.c.) was added *p*-acetamidobenzenesulphonyl chloride (20·4 g.). The solution became warm; after 30 minutes, water (800 c.c.) was added, followed by sufficient acetic acid to render the mixture acid to litmus. The gum which formed slowly hardened. The bulk (A) was used in the alkaline hydrolysis described below; a small amount crystallised from 70% alcohol in colourless needles, m. p. 222°, not depressed by admixture with the product from the first experiment. It was sparingly soluble in the ordinary organic solvents (Found : N, 11·0. $C_{21}H_{20}O_6N_4S_2$ requires N, 11·1%).

6-*Amino*-2-*pyridyl* p-*Aminobenzenesulphonate*.—Through a suspension of the corresponding acetyl compound (I) (2·0 g.) in dry alcohol (20 c.c.), dry hydrogen chloride was passed without

cooling. The mixture became hot and solution ensued, followed within a few minutes by precipitation of a crystalline solid. After 30 minutes, dry ether was added, and the presumed hydrochloride filtered off, washed with dry ether, and dissolved in water (30 c.c.). Ammonia precipitated the *ester*; it consisted of colourless needles, m. p. 148°, and was insoluble in cold dilute sodium hydroxide solution. It gave positive diazo-coupling reactions (Found: N, 15·9. $C_{11}H_{11}O_3N_3S$ requires N, 15·8%).

Action of Warm Dilute Sodium Hydroxide Solution on the Acetamidobenzenesulphonate (I).—The compound (4·5 g.) was dissolved in 2N-sodium hydroxide (45 c.c.) at 50°. After 30 minutes the mixture was neutralised with acetic acid and concentrated to low bulk in a vacuum. On cooling, 2·3 g. of sodium sulphanilate were obtained. The filtrate from this, on extraction with chloroform, gave 6-amino-2-hydroxypyridine as an oil (1·1 g.), which was identified as its dihydrochloride (Found: Cl, 38·9. Calc.: Cl, 38·8%).

Action of Sodium Hydroxide Solution on the Ester (II).—The ester obtained above (A) weighed 38 g. in the moist condition. The estimated dry weight was 32·8 g. (79·5% of the theoretical amount). The wet solid was refluxed for 1 hour with 2N-sodium hydroxide; acidification with acetic acid gave a precipitate of 6-*hydroxy*-2-(p-*aminobenzenesulphonamido*)-*pyridine* (rectangular plates, m. p. 239—240°, not raised by recrystallisation from 50% acetic acid). The yield was 19 g. (94%) (Found: N, 15·7. $C_{11}H_{11}O_3N_3S$ requires N, 15·8%). The pyridylamide was readily soluble in cold dilute sodium hydroxide solution; it was unchanged by boiling with 25% sodium hydroxide solution for several hours, but after 10 minutes' boiling with 2N-hydrochloric acid, sodium sulphanilate was precipitated in 70% yield. Diazo-coupling tests were positive.

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