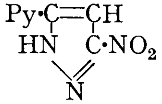
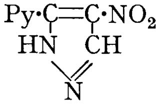
90. *Pyridylnitropyrazole. Part II. Derivatives of 4-Nitro-5-pyridylpyrazole.*

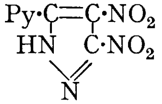
By Hakon Lund

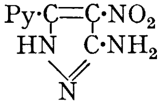
In Part I (J., 1933, 686) it was shown that the by-product formed when nicotine is oxidised with nitric acid (Gough and King, J., 1931, 2968; 1933, 350; King, J., 1932, 2768) is 3-nitro-5-(3′-pyridyl)pyrazole (I), and this structure has been confirmed by Clemo and Holmes (J., 1934, 1739). The isomeric 4-nitro-5-pyridylpyrazole (II) is obtained by nitration of 5-pyridylpyrazole; a number of its derivatives are now described.

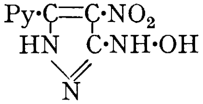
(I), on nitration, yields a *dinitro*-derivative (III), but (II) cannot be nitrated under similar conditions. Reducing agents attack the nitro-group in the 3-position before attacking the other one. 4-*Nitro*-3-*amino*-5-*pyridylpyrazole* (IV) on deamination yields (II), a proof of the 3-position of the amino-group.


(I.)


(II.)


(III.)


(IV.)


(V.)

The series of reactions (I) ⟶ (III) ⟶ (IV) ⟶ (II) is the most advantageous way of preparing (II).

Reduction of (III) with stannous chloride without heating leads, not to the amine (IV), but to 4-*nitro*-3-*hydroxylamino*-5-*pyridylpyrazole* (V), which is remarkably stable in acid solution and is oxidised in alkaline solution to the corresponding *azoxy*-compound by air or potassium ferricyanide.

In acid solution bromic acid oxidises (V) to the corresponding nitroso-compound, which is green in acid solution and light yellow in the solid state. It has been isolated as the *perchlorate* because the free substance seems to be amorphous. In acid solution it oxidises the iodide ion to free iodine and is thereby reduced to (V). On reduction of (V) in hot sodium hydroxide solution with hydrogen sulphide, (IV) is formed, indicating the 3-position of the hydroxylamino-group. (V) is also formed when (III) is reduced by zinc dust in ammoniacal solution. For the preparation of (V) this procedure has the disadvantage that in order to avoid oxidation to the azoxy-compound the process should be carried out in an oxygen-free atmosphere.

(IV) can be diazotised. The diazonium salts in aqueous solution can be heated to 70—80° without marked decomposition. The dry salts explode, the *perchlorate* violently, when heated. Some of the diazo-reactions proceed normally, but others take an unexpected course; *e.g.*, when a diazo-salt is added to aqueous ammonia, nitrogen is evolved and the 3-amine is formed in good yield (normally, bisdiazoimides are produced). These reactions are being studied in greater detail and the results will be published later.

Sodium hydrosulphite reduces the dinitro-compound (III) in alkaline solution to 3 : 4-diamino-5-pyridylpyrazole, isolated as a colourless *dihydrochloride.* The free base is very soluble in water and is oxidised by air.

EXPERIMENTAL.

3 : 4-*Dinitro*-5-*pyridylpyrazole* (III).—3-Nitro-5-pyridylpyrazole (25 g.), dissolved in concentrated sulphuric acid (60 c.c.) by gentle heating, is treated with nitric acid (*d* 1·50, 25 c.c.), the mixture heated on the steam-bath for 30 minutes, cooled and poured into cold water (500 c.c.), concentrated aqueous ammonia added until the precipitate formed is redissolved, and the solution acidified with acetic acid. The yellow product is filtered off with suction and washed with water. 3 : 4-*Dinitro*-5-*pyridylpyrazole,* obtained pure and in quantitative yield, decomposes at 230° (Found: C, 40·9; H, 2·05; N, 29·6. $C_8H_5O_4N_5$ requires C, 40·85; H, 2·1; N, 29·8%).

The substance is soluble in aqueous ammonia even in presence of ammonium salts, in contrast with the initial material. It dissolves in hot dilute hydrochloric acid and, on cooling, a *hydrochloride* crystallises (Found : Cl, 13·2. $C_8H_5O_4N_5$,HCl requires Cl, 13·1%).

4-*Nitro*-3-*amino*-5-*pyridylpyrazole* (IV).—The moist preparation of (III) is dissolved in water (500 c.c.) containing sodium hydroxide (15 g.) and reduced at about 90° with hydrogen sulphide. The solution instantly becomes dark red and when it is saturated with the gas 4-*nitro*-3-*amino*-5-*pyridylpyrazole* has separated quantitatively in fine needles. After being washed with water the amine is pure enough for use, but it may be recrystallised from alcohol or dissolved in very dilute sodium hydroxide solution and reprecipitated by carbon dioxide. Yield, 26 g. or 97% (Found : C, 46·8; H, 3·5; N, 34·1. $C_8H_7O_2N_5$ requires C, 46·8; H, 3·4; N, 34·1. Found for the *hydrochloride* : Cl, 14·7. $C_8H_7O_2N_5$, HCl requires Cl, 14·7%). The amine is insoluble in aqueous ammonia, but dissolves in aqueous sodium hydroxide and in dilute hydrochloric acid, giving an orange and a yellow solution respectively. The acetyl derivative melts at 175°.

The diazonium nitrate. When (IV) is diazotised in 4*N*-nitric acid (4 mols.) without cooling, a clear solution is obtained which deposits crystals of the *diazonium nitrate* when cooled in ice-water (yield, 80%). The salt is recrystallised from water below 70° [Found : N (micro-Dumas), 35·0. $C_8H_5O_5N_7$ requires N, 35·1%].

The *diazonium perchlorate,* which is rather slightly soluble in water, is prepared by diazotising (IV) in 4*N*-hydrochloric acid, filtering the luke-warm solution, and adding 70% perchloric acid; the perchlorate soon crystallises. The dry salt can be ground in a mortar without exploding, but when knocked with a hammer or when heated to 160° it explodes with great violence (Found: N, 26·3. $C_8H_5O_6N_6Cl$ requires N, 26·55%).

4-*Nitro*-5-*pyridylpyrazole.*—The amine (IV) (41 g.) is diazotised in hydrochloric acid (90 c.c + 50 c.c. of water) by addition of sodium nitrite (19 g.). The paste of the diazonium chloride formed is poured into boiling alcohol (500 c.c.); a moderate evolution of nitrogen takes place; after 20 minutes' boiling the alcohol is evaporated, water added until the hydrochloride redissolves, and the filtered solution made ammoniacal and then slightly acid with acetic acid. The 4-nitro-5-pyridylpyrazole obtained has m. p. 220° after recrystallisation from water (yield, 28 g.) (Found : N, 29·5. Calc. for $C_8H_6O_2N_4$: N, 29·6%).

4-*Nitro*-3-*hydroxylamino*-5-*pyridylpyrazole* (V).—3 : 4-Dinitro-5-pyridylpyrazole (III) (12 g.) is dissolved in hydrochloric acid (20 c.c. + 25 c.c. of water), a solution of stannous chloride (25 g.) in concentrated hydrochloric acid (25 c.c.) rapidly added, and the mixture cooled in running water. When the reaction is over, the solution is cooled in ice-water, and concentrated hydrochloric acid (10 c.c.) added. The yellow crystalline product is washed with ice-cold 20% hydrochloric acid, dissolved in hot water, and, after addition of concentrated hydrochloric acid, cooled in ice (yield of the hydrochloride, 10 g.). The *hydroxylamino*-compound, obtained in quantitative yield from an aqueous solution of the hydrochloride and excess of sodium acetate, decomposes at 177—178° (Found: C, 43·45; H, 3·4; N, 31·5. $C_8H_7O_3N_5$ requires C, 43·4; H, 3·2; N, 31·6%). It is a yellow substance which forms yellow solutions in acids, orange solutions in weak bases, and intensely red-violet (cherry) solutions in strong bases. It is reduced in hot alkaline solution to (IV) by hydrogen sulphide.

4-*Nitro*-3-*azoxy*-5-*pyridylpyrazole*.—Air or oxygen is passed through a solution of (V) in dilute aqueous sodium hydroxide until the violet-red colour has disappeared; a yellow compound (the sodium salt of the azoxy-compound) crystallises if the solution is not very dilute. Acetic acid is added, and the *azoxy*-compound is obtained in quantitative yield. It is purified by dissolving it in hot dilute hydrochloric acid and cooling. The hydrochloride is soluble in water, but when it is boiled with about 50 parts of water it is completely hydrolysed and the free base separates as an orange-yellow, very finely divided substance (Found: C, 45·4; H, 2·5; N, 28·0. $C_{16}H_{10}O_5N_{10}$ requires C, 45·5; H, 2·4; N, 33·2%).

4-*Nitro*-3-*nitroso*-5-*pyridylpyrazole Perchlorate*.—A solution of the hydrochloride of (V) (5·1 g.) in dilute hydrochloric acid becomes green on addition of potassium bromate (1·1 g.). After 10 minutes, sodium acetate in excess is added, the nitroso-compound filtered off and dissolved in dilute lukewarm hydrochloric acid, and 70% perchloric acid added; the *perchlorate* crystallises. Neither the free nitroso-compound nor the hydrochloride could be obtained crystalline. In an attempt to recrystallise the perchlorate from alcohol the smell of aldehyde was noticed. The perchlorate explodes on heating and therefore no combustion was made (Found: N, 21·9. $C_8H_6O_7N_5Cl$ requires N, 21·9%).

The nitroso-perchlorate liberates iodine from an acid solution of potassium iodide; 0·0858 g. gave an amount corresponding to 5·30 c.c. 0·1*N*-sodium thiosulphate (calc. for 2 equivs. of iodine per mol., 5·35 c.c.). After the titration an excess of sodium hydroxide was added, whereby the solution became intensely red-violet, indicating the presence of (V).

3 : 4-*Diamino*-5-*pyridylpyrazole*.—To a solution of the dinitro-compound (III) (23·5 g.) in aqueous sodium hydroxide (8 g. in 300 c.c. of water) at 90°, sodium hydrosulphite (about 75 g.) is added in small portions, a little sodium hydroxide being added to keep (III) in solution. The hot, almost colourless solution is treated with an excess of concentrated hydrochloric acid, filtered from sulphur, and evaporated to dryness under reduced pressure. Alcohol (200 c.c.) and potassium carbonate (50 g.) are added to the residue and the mixture is boiled under reflux for 2 hours. After filtration the solid mass is washed with alcohol (100 c.c.), and to the combined filtrate and washings is added an excess of alcoholic hydrogen chloride (concentrated hydrochloric acid may be used without greatly diminishing the yield). The *diamine dihydrochloride* (24·8 g.) is immediately precipitated. It can be recrystallised from hot 25% hydrochloric acid by addition of alcohol; the colourless crystals, however, soon again acquire a brownish colour in contact with air (Found: N, 28·5; Cl, 28·6. $C_8H_7N_5,2HCl$ requires N, 28·2; Cl, 28·6%).

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