174. *Pyridylnitropyrazole, an Oxidation Product of Nicotine. The Position of the Nitro-group.*

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GOUGH and KING (this vol., p. 350) have shown that the compound $C_8H_6O_2N_4$ (I) obtained as a by-product in the oxidation of nicotine with nitric acid is a nitro-5-(3-pyridyl)pyrazole by converting it, by elimination of the nitro-group, into a substance identical with synthetic 5-(3-pyridyl)pyrazole. They assumed that the nitro-group is in position 4 in the by-product.

Before their work was published I had obtained the same compound : the identity has since been proved by direct comparison through the courtesy of Dr. King.

Gough and King state that the compound (I) is stable to boiling potassium permanganate solution, whereas I have found that it is oxidised by that agent in acid, alkaline, or neutral solution. In alkaline solution the reaction takes place almost quantitatively according to the equation $C_8H_6O_2N_4 + 7O \longrightarrow C_5H_4N{\cdot}CO_2H + N_2 + HNO_3 + 2CO_2$, nicotinic acid being formed. This oxidation is interesting because usually the pyrazole ring is stable to alkaline permanganate.

The substance (I) and the compound formed from it when the nitro-group is replaced by iodine react with bromine with formation of monobromo-substituted derivatives. Since pyrazole itself reacts with bromine with formation of 4-bromopyrazole (and no dibromo-derivatives), there is reason to believe that the nitro-group of (I) does not—as assumed by Gough and King—occupy the 4-position. I, therefore, ascribe to (I) the structure of 3-*nitro*-5-(3-*pyridyl*)*pyrazole.*

In support of this structure is the fact that pyridylpyrazole on nitration yields a compound, isomeric with (I), which is probably 4-*nitro*-5-(3-*pyridyl*)*pyrazole* (since pyrazole itself on nitration gives 4-nitropyrazole) : it has the usual properties of the pyrazoles and is not attacked by permanganate and bromine.

The work on (I) and the new nitro-compound is being continued.

EXPERIMENTAL.

3-*Nitro*-5-(3-*pyridyl*)*pyrazole* (I).—The crude by-product can be purified by addition of NH_4Cl to, or by passing CO_2 through, its solution in NaOH aq. My analytical data agree exactly with those of Gough and King. A Kjeldahl analysis gave a nitrogen content exactly half of the correct value : probably two of the four nitrogen atoms escaped as gaseous N_2.

Oxidation.—(*a*) To $KMnO_4$ (20 g.) in H_2O (450 c.c.) at 65°, (I) (3·00 g.) in NaOH (1 g. in 30 c.c. H_2O) was added. In 3 hr., 338 c.c. of N were collected (calc. for 1 mol., 354 c.c.).

(*b*) (I) (20 g.), dissolved in dil. NaOH aq., was added to $KMnO_4$ (80 g.) in 2500 c.c. of H_2O and kept at 65° for 16 hr. The filtered solution was acidified with HCl aq. and evaporated to dryness on the steam-bath. The residue was ground and boiled with EtOH (2 × 100 c.c.), from which, on cooling, a cryst. mass (14 g.) separated, consisting of nicotinic acid hydrochloride and nitrate, the latter forming the main part. The HNO_3 could have originated only by the oxidation of (I).

(*c*) 1·00 G. was oxidised as above, the mixture acidified with H_2SO_4, and CO_2-free air passed through it. The CO_2 formed was absorbed in soda-lime (Found : 0·523 g. Calc., 0·463 g.).

These results show that the oxidation follows the equation given on p. 686.

Bromination.—A quant. bromination in aq. solution proved that 1 mol. of Br reacted with 1 mol. of (I). The bromo-compound was prepared in AcOH solution, the HBr being neutralised with NaOAc. After recrystn. from AcOH or EtOH, 4-*bromo*-3-*nitro*-5-(3-*pyridyl*)*pyrazole* had m. p. 240—242° (Found : Br, 29·8, 29·5. $C_8H_5O_2N_4Br$ requires Br, 29·7%).

Benzoylation.—When (I) was benzoylated in the usual way, 3-*nitro*-1-*benzoyl*-5-(3-*pyridyl*)-*pyrazole* was obtained in about 45% yield, m. p. 169° (Found : C, 61·3; H, 3·2. $C_{15}H_{10}O_3N_4$ requires C, 61·2; H, 3·4%). Hydrolysis with boiling EtOH and HCl aq. gave ethyl benzoate and (I).

Reduction.—The compound (I) (30 g.), dissolved in hot H_2O (500 c.c.) containing 10 g. of NaOH, was treated gradually at about 90° with $Na_2S_2O_4$ (about 75 g.), NaOH being added when necessary to prevent the separation of (I). The solution was boiled, conc. HCl (125 c.c.) cautiously added, and the filtered solution evaporated under reduced press. The dry residue was mixed with K_2CO_3 (40 g.) and extracted with boiling EtOH (300 c.c.) for ½ hr., conc. HCl (40 c.c.) added to the alc. solution, and the 3-amino-5-(3-pyridyl)pyrazole dihydrochloride filtered off and washed with EtOH (yield, 32—34 g.). The *acetyl* derivative, prepared in dil. AcOH by means of Ac_2O, had m. p. 308° after recrystn. from EtOH (Found : C, 59·4; H, 4·7; N, 27·7. $C_{10}H_{10}ON_4$ requires C, 59·4; H, 5·0; N, 27·7%).

Diazo-reactions of the Amine.—(1) The amine (5 g.) and dimethylaniline (2·5 g.) in H_2O (30 c.c.) gave with *N*-$NaNO_2$ (22 c.c.) at 0° a brick-red *azo-dye* (Found by reduction with $TiCl_3$: *M*, 296. $C_{16}H_{16}N_6$ requires *M*, 292).

(2) The amine (5 g.) in 4*N*-H_2SO_4 (25 c.c.) was diazotised at 0°, KI (15 g.) in H_2O (25 c.c.) added, and after 10 min. the solution slowly heated to about 50° and cleared with H_2SO_3. After being boiled, the solution, on cooling, deposited a hydriodide, from a boiling aq. solution of which Na_2CO_3 liberated 3-*iodo*-5-(3-*pyridyl*)*pyrazole*; colourless crystals, m. p. 180°, after recrystn. from H_2O (charcoal); sol. in acids and strong bases (Found : I, 46·9. $C_8H_6N_3I$ requires I, 46·9%).

(3) The amine was converted by the usual $NaNO_2$–EtOH process (cf. Gough and King, *loc. cit.*) into 5(-3-pyridyl)pyrazole, isolated as the nitrate (yield, 6·5 g. from 14 g. of the amine hydrochloride).

Nitration of Pyridylpyrazole. Formation of 4-*Nitro*-5-(3-*pyridyl*)*pyrazole.*—Pyridylpyrazole nitrate (2 g.) was dissolved in 15 c.c. of conc. H_2SO_4 and heated on the steam-bath for 1 hr., and the cooled solution poured into H_2O, made alkaline, and acidified with AcOH. The *nitro*-compound was recrystallised from H_2O. Yield, 1·2 g.; m. p. 220° (Found: C, 50·7; H, 3·4. $C_8H_6O_2N_4$ requires C, 50·5; H, 3·2%). The *hydrochloride* is sol. in H_2O and slightly sol. in EtOH (Found : Cl, 16·0. $C_8H_6O_2N_4$,HCl requires Cl, 16·1%).

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