The Preparation of a Nitropyrido[3,4-c]furoxan : 7-Nitro[1,2,5]oxadiazolo-[3,4-c]pyridine 3-Oxide

By A. S. Bailey,* M. W. Heaton, and Miss J. I. Murphy, Dyson Perrins Laboratory, South Parks Road, Oxford

7-Nitro[1,2,5]oxadiazolo[3,4-c]pyridine 3-oxide has been obtained by decomposition of 4-azido-3,5-dinitropyridine. The compound formed charge-transfer complexes with aromatic hydrocarbons and added the elements of water to yield a crystalline hydrate.

INTEREST has recently been shown in the structure of benzofuroxans,1-3 their complex-forming ability,4 and the reactions of 4,6-dinitrobenzofuroxan with alkali.5,6 It was of interest to extend this work by preparation of pyridofuroxans. Boyer 7 described the preparation of pyrido[2,3-c]furoxan (I) but was unable to prepare pyrido[3,4-c]furoxan (II; R = H) by heating solid 4-azido-3-nitropyridine (III; R = H), high-melting amorphous material being obtained. We have examined the decomposition of compound (III; R = H) in a variety of solvents and have failed to isolate the furoxan (II; R = H). The volume of nitrogen evolved was 0.98-1.0 moles in either ethyl benzoate or in 2-azidonaphthalene solution at $60-70^{\circ}$. The activation energy for this decomposition $(30.1 + 1.3 \text{ kcal.})^8$ was higher that that of 1-azido-2,4-dinitrobenzene $(25.5 \pm 0.8 \text{ kcal.})^8$ and lower than that of phenylazide



(39.0 kcal.).⁹ Failure to isolate the furoxan could be due to attack by the azene formed by loss of nitrogen from (III; R = H) on the pyridine nitrogen atom

 D. Britton and W. E. Noland, J. Org. Chem., 1962, 27, 3218.
 P. Diehl, H. A. Christ, and F. B. Mallory, Helv. Chim. Acta, 1962, 45, 504.

- ³ A. J. Boulton and P. B. Ghosh, Adv. Heterocyclic Chem. 1969, **10**, 1.
- ⁴ A. S. Bailey and J. R. Case, Tetrahedron, 1958, 3, 113; A. S. Bailey, J. Chem. Soc., 1960, 4710; A. S. Bailey, R. J. P. Williams,

Balley, J. Chem. Soc., 1960, 4710, A. S. Balley, K. J. F. Williams, and J. D. Wright, *ibid.*, 1965, 2579.
⁵ W. P. Norris and J. Osmundsen, J. Org. Chem., 1965, 30, 2407; N. E. Brown and R. T. Keyes, *ibid.*, p. 2452.
⁶ A. J. Boulton and D. P. Clifford, J. Chem. Soc., 1965, 5414.
⁷ J. H. Boyer, D. J. McCane, W. J. McCarville, and A. T. Tweedie, J. Amer. Chem. Soc., 1953, 75, 5298.
⁸ J. E. White, D.Phil. Thesis, Oxford, 1965.

rather than the oxygen atom of the nitro-group in the ortho position. Repetition of this process would give a polymer. It is known that the nitrogen atom of pyridine is attacked by azenes.¹⁰ However, the value of the energy of activation for the decomposition of compound (III; R = H) suggests that the loss of nitrogen is assisted by the ortho-nitro group; 11 if an azene was produced from compound (III; R = H) it could react with the 2-azidonaphthalene used as solvent to give an unstable tetrazene, which would decompose with evolution of a second molecule of nitrogen.¹² We failed to quaternise compound (III; R = H) with methyl iodide to prevent attack on the nitrogen atom. 3-Azido-4-nitropyridine 1-oxide and 4-azido-3-nitropyridine 1-oxide were also prepared but only yielded amorphous high-melting solids on heating in solution. Compound (II; R = H) and its simple derivatives appear to be unstable at room temperature. Smalley and his coworkers have recently reported on their failure to obtain compound (II; R = H).¹³

The nitropyrido [3,4-c] furoxan (II; $R = NO_2$) was then prepared from the corresponding azide (III; R = NO₂), which is readily prepared from 4-chloro-3,5-dinitropyridine. This chloro-compound was prepared via 3,5-dinitro-4-hydroxypyridine,¹⁴ and from 3,5-dinitro-4-hydroxypyridine 1-oxide.¹⁵ The last-named compound was observed to form highly crystalline salts with bases (including hydrazine) and transition metals (such as copper, cobalt, manganese, and nickel). It was also observed to form charge-transfer compounds with three hydrocarbons (naphthalene, 2,6-dimethylnaphthalene, and pyrene). These complexes contained two molecules of the reagent per molecule of hydrocarbon, in contrast to the picric acid complexes of these hydrocarbons. Decomposition of the azide (III; $R = NO_2$) under various conditions was examined. In dry benzene it decomposed smoothly giving the pyridofuroxan (II; $R = NO_2$), a bright yellow solid whose identification was supported by a molecular weight determination (benzene solution). The n.m.r. spectrum (CDCl₃) showed two

⁹ P. Walker and W. A. Waters, J. Chem. Soc., 1962, 1632. ¹⁰ R. A. Abramovich and K. A. H. Adams, Canad. J. Chem.,

1961, 39, 2516; J. I. G. Cadogan, *Quart. Rev.*, 1968, 22, 224.
 ¹¹ G. L'Abbé, *Chem. Rev.*, 1969, 69, 345.

12 L. Horner, A. Christmann, and A. Gross, Chem. Ber., 1963,

96, 399. ¹³ J. J. Eatough, L. S. Fuller, R. H. Good, and R. K. Smalley, J. Chem. Soc. (C), 1970, 1874.

¹⁴ W. H. Crowe, J. Chem. Soc., 1925, 2029; V. A. Petrow and
 E. L. Rewald, *ibid.*, 1945, 313.
 ¹⁵ E. Hayashi, J. Pharm. Soc. Japan, 1950, 70, 142; E. Ochiai

and K. Futaki, ibid., 1952, 72, 274.

sharp bands at τ 0.54 (6-H) and 0.69 (4-H); the i.r. spectrum contained bands at 1610, 1532, 1465, and 1336 cm.⁻¹ due to nitro- and furoxan groups.^{4,16} We failed to quaternise compound (II; $R = NO_2$) but obtained crystalline derivatives with three hydrocarbons; analysis of these derivatives confirmed the formula $C_5H_2N_4O_4$ for (II; $R = NO_2$). When the azide (III; $R = NO_2$) was decomposed in acetic acid and the solution diluted with water, pale brown needles of a dihydrate of (II; $R = NO_2$) were obtained. Drying at 100° for 1 hr. *in vacuo* gave the monohydrate, which was stable to drying for 10 hr.; however, sublimation at 140° gave the anhydrous furoxan (much of the material was decomposed at this temperature). Crystallisation of the anhydrous material from aqueous acetic acid gave the dihydrate; hence the two forms are easily interconvertible.

The i.r. spectrum of the dihydrate (KBr disc) contained very broad bands at 3500 and 3240 cm⁻¹; the spectrum of the hydrate contained a broad band at 3240 cm.⁻¹. 2,4-Dinitrophenylhydroxylamine shows bands at 3440 and 3300 cm.⁻¹; thus the monohydrate was not the hydroxylamine (IV). 4,6-Dinitrobenzofuroxan reacts with alkali to form the anion (V) 5,6 and the hydration of nitrogen-containing heterocycles is well known;¹⁷ for example 6,7-dichloropteridine forms the hydrate (VI)¹⁸ and tetrazolo[1,5-a]pyrimidine forms the hydrate (VII).19

The n.m.r. spectrum of the hydrate (VIII) in $[{}^{2}H_{e}]$ dimethyl sulphoxide contained four bands of equal intensity; a broad singlet $\tau - 0.30$ (NH), a sharp singlet at τ 1.32 (H_a), a broad doublet at τ 2.40 (J ca. 9 Hz, OH), and a broad doublet at τ 3.68 (J ca. 9 Hz, H_b). In the spectrum of a concentrated solution the broad doublets were replaced by broad singlets and on addition of deuterium oxide the signals at -0.30 and 2.4disappeared, leaving two sharp singlets at τ 1.32 and 3.68. The spectrum 6 of the ion (V) shows signals at τ 1.27 (H_a), 4.06 (H_b), and 3.74 (OH).

Since all attempts to prepare pyrido[3,4-c] furoxan by decomposition of compound (III; R = H) failed, we examined the reactions of this azide with an olefin, 3a,4,7,7-tetrahydro-4,7-methanoindene,²⁰ and with triphenylphosphine,²¹ to discover if the azide group in (III; R = H) showed other anomalous reactions. With both reagents the azide reacted smoothly and the expected products were obtained.

EXPERIMENTAL

I.r. spectra were measured for Nujol mulls unless otherwise stated, and n.m.r. spectra were measured with a Perkin-Elmer R10 spectrometer (60 MHz). 4-Chloro-

¹⁶ R. J. Gaughran, J. P. Picard, and J. V. R. Kaufman, J. Amer. Chem. Soc., 1954, 76, 2233. ¹⁷ A. Albert and W. L. F. Armarego, Adv. Heterocyclic Chem.,

1965, **4**, 1.

¹⁶ A. Albert and J. Clark, J. Chem. Soc., 1964, 1666.
 ¹⁹ C. Temple, jun., R. L. McKee, and J. A. Montgomery, J. Org. Chem., 1965, 30, 829.

J. Chem. Soc. (C), 1971

3-nitropyridine²² was converted into 4-azido-3-nitropyridine, pale yellow rods, m.p. 86-88° (from methanol) (lit.,⁷ 89°). 4-Azido-3-nitropyridine (1 g.) was dissolved in dimethyl sulphoxide (7 ml.) and added to a solution of 3a,4,7,7a-tetrahydro-4,7-methanoindene (0.9 ml.) in ethanol (2 ml.). The resulting solution was left in the dark for 7 days. Gas was steadily evolved. The aziridine which separated was recrystallised from light petroleum (b.p. 60-80°) and then from methanol, to give yellow rods, m.p. 191-193° (Found: C, 66.7; H, 5.9; N, 15.1; O, 12.3. $C_{15}H_{15}N_{3}O_{2}$ requires $C_{15}6.9$; H, 5.6; N, 15.6; O, 11.9%). Equimolar quantities of the azide and triphenylphosphine were mixed in dioxan. Nitrogen was evolved immediately. Next day the solid which had separated was collected and recrystallised from ethanol. 3-Nitro-4-triphenylphosphoranylideneaminopyridine formed yellow plates, m.p. 200-201° (Found: C, 69·1; H, 4·3; N, 10·5. C₂₃H₁₈N₃O₂P requires C, 69.1; H, 4.5; N, 10.5%).

4-Azido-3-nitropyridine was heated separately in twelve different solvents; in each case a dark black solid was obtained which could not be crystallised. A sample of the azide was heated in a test-tube to just above its m.p. Immediate decomposition was observed and the tube was cooled rapidly. The residue was extracted with ether and the ethereal solution was evaporated at room temperature. A pale yellow solid was obtained which melted on warming to 25° and rapidly darkened.

3-Azido-4-nitropyridine 1-Oxide.-3-Bromo-4-nitropyridine 1-oxide²³ was converted into 3-hydrazino-4-nitropyridine 1-oxide.²⁴ This hydrazine (0.3 g.) was dissolved in hydrochloric acid (2N; 5 ml.) and sodium nitrite (10%)solution; 1.2 ml.) was added dropwise. After 30 min. the solution was neutralised (sodium carbonate) and extracted with chloroform, and the dried (MgSO₄) extract was evaporated. The azide was recrystallised from water (m.p. 95°) (Found: C, 33·1; H, 1·7. $C_5H_3N_5O_3$ requires C, 33·1; H, 1.7%), v_{max} . 2130 cm.⁻¹ (azide). Decomposition of this azide gave amorphous high-melting material.

4-Azido-3-nitropyridine 1-Oxide.-4-Hydroxy-3-nitropyridine 1-oxide was prepared by the method of den Hertog.²⁵ We were unable to repeat (twelve attempts) the preparation described by Hayashi.15 4-Chloro-3-nitropyridine 1-oxide ¹⁵ (m.p. 145-147°; 1.8 g.) was dissolved in acetone (15.0 ml.) and a solution of sodium azide (1.5 g.) in water (18 ml.) was added with stirring. After 15 min. the solid was collected (1.5 g.). Crystallisation from benzene gave orange-yellow plates, m.p. 137° (exploded) (Found: C, 33.2; H, 1.8. C₅H₃N₅O₃ requires C, 33.2; H, 1.7%), ν_{max} 2110 cm.⁻¹ (azide). All attempts to decompose this azide gave amorphous material.

4-Azido-3,5-dinitropyridine. --- 3,5-Dinitro-4-hydroxypyridine 1-oxide was prepared by Hayashi's method.¹⁵ Equal weights of the compound and copper acetate were dissolved in boiling water and the two solutions were mixed; the copper salt separated as dark red prisms (Found: C, 22.1; H, 2.5; N, 15.4. C₁₀H₄CuN₆O₁₂,4H₂O requires C, 22.4; H,

²⁰ A. S. Bailey and J. J. Wedgwood, J. Chem. Soc. (C), 1968, 682.

²¹ P. A. S. Smith, 'Open-chain Nitrogen Compounds,' vol. II, Benjamin, New York, 1966, p. 248.
 ²² S. Kruger and F. G. Mann, *J. Chem. Soc.*, 1955, 2755.
 ²³ H. J. den Hertog and J. Overhoff, *Rec. Trav. chim.*, 1950, 60 (460)

- **69**, 468. T. Talik, Roczniki Chem., 1962, 36, 1465.
 - ²⁵ H. J. den Hertog, Rec. Trav. chim., 1955, 74, 59.

2.2; N, 15.7%). The nickel salt formed purple-brown prisms (Found: C, 22.7; H, 2.5; N, 15.8. C10H4N6NiO12,-4H₂O requires C, 22.6; H, 2.3; N, 15.8%); the manganese salt formed green-black prisms (Found: C, 23.1; H, 2.2; N, 16.0. C₁₀H₄MnN₆O₁₂,4H₂O requires C, 22.8; H, 2.3; N, 15.9%; the *cobalt salt* formed dark red prisms (Found: C, 23.1; H, 2.5. C₁₀H₄CoN₆O₁₂,4H₂O requires C, 22.6; H, $2\cdot3\%$). Addition of hydrazine hydrate (1 equiv.) to an alcoholic solution of the hydroxypyridine gave red needles of the hydrazine salt, m.p. 79-80° (Found: C, 25.7; H, 3.3; N, 30.5. C₅H₇N₅O₆ requires C, 25.7; H, 3.0; N, 30.0%). Pyrene was added to a boiling solution of 3,5-dinitro-4-hydroxypyridine 1-oxide in acetic acid; the complex separated as purple-brown needles, m.p. 192-200° (decomp.) (Found: C, 51.4; 51.6; H, 2.7, 2.9. C₁₆H₁₀,-2C₅H₃N₃O₆ requires C, 51.6; H, 2.7); naphthalene complex, yellow needles, m.p. 186-190° (decomp.) (Found: N, 16.5. C₁₀H₈, 2C₅H₃N₃O₆ requires N, 15.9%); the 2,6-dimethylnaphthalene complex formed yellow needles, m.p. 168-170° (decomp.) (Found: N, 14.8. C₁₂H₁₂, 2C₅H₃N₃O₆ requires N, 15.1%).

Dry 3,5-dinitro-4-hydroxypyridine 1-oxide (4 g.), phosphoryl chloride (20 ml.), phosphorus trichloride (10 ml.), and dimethylaniline (1.5 ml.) were boiled together (oil-bath at 120-130°) for 1.5 hr., and volatile material was removed in vacuo on a water-bath. The residue was treated with ether (150 ml.) and ice-water (150 ml.), and the mixture was made alkaline with sodium hydrogen carbonate and then filtered. After separation of the organic layer, the aqueous layer was extracted with ether $(2 \times 100 \text{ ml.})$; the extracts were dried (MgSO₄) and evaporated. Recrystallisation of the residue from light petroleum (b.p. 40-60°) gave 4-chloro-3,5-dinitropyridine, m.p. 68-70° (lit.,¹⁵ 68°) (yields were erratic: 35-60%). The chloro-compound was also prepared via 3,5-dinitro-4-hydroxypyridine.¹⁵ 4-Chloro-3,5-dinitropyridine (9.7 g.) was dissolved in acetone (12 ml.) and a solution of sodium azide (7.5 g.) in water (40 ml.) and ethanol (40 ml.) was added during 5 min. with stirring. After a further 5 min. the mixture was poured into water. The solid was collected and recrystallised from water-methanol (1:9) to give pale brown needles, m.p. 37-39° (7.1 g.) (Found: C, 28.9; H, 1.0; N, 40.0. C₅H₂N₆O₄ requires C, 28.6; H, 1.0; N, 40.0%), 2140 cm.⁻¹ (azide). The azide (0.5 g.) was dissolved ν_{max.} in ethyl acetate (2 ml.) and a solution of 3a,4,7,7a-tetrahydro-4,7-methanoindene (0.35 ml.) in ethyl acetate (2 ml.) was added. The temperature of the solution rose to 40°,

gas was evolved, and a solid separated. The *aziridine* formed fine yellow needles from ethanol, m.p. 170–172° (Found: C, 57·4; H, 4·5; N, 17·7. $C_{15}H_{14}N_4O_4$ requires C, 57·3; H, 4·5; N, 17·8%).

7-Nitro[1,2,5]oxadiazolo[3,4-c]pyridine 3-Oxide (II; R =NO₂).—After dissolving of azido-3,5-dinitropyridine (3 g.) in benzene (45 ml.; sodium-dry), the solution was boiled for 1 hr. It was then poured into light petroleum (b.p. 40-60°) (100 ml.; sodium-dry). The resultant solid was collected and dissolved in benzene; the solution was filtered from insoluble material, and dry light petroleum (b.p. 40-60°) was added until the furoxan separated, pale yellow plates, m.p. 134° (decomp.; softening at 120°) (Found: C, 33.2; H, 1.3; N, 30.6. C₅H₂N₄O₄ requires C, 33.0; H, 1.1; N, 30.8%), M (Mechrolab Vapour Pressure Osmometer; benzene) 184 (required 182). Yields varied between 45 and 70%. The compound decomposed slowly and was stored at -40° . Charge-transfer complexes of the furoxan were prepared by dissolving it in the minimum of dry benzene and adding a slight excess of the hydrocarbon. The mixture was then warmed to dissolve the hydrocarbon and allowed to cool slowly. The naphthalene complex formed orange-brown needles, m.p. 108-110° (Found: C, 58-1; H, 3.6; N, 18.1. $C_{10}H_8, C_5H_2N_4O_4$ requires C, 58.1; H, 3.3; N, 18.1%; the *pyrene complex* formed brown-purple needles, m.p. 179-180° (Found: C, 65.5; H, 3.3; N, 14.2. C₁₆H₁₀,- $C_5H_2N_4O_4$ requires C, 65.6; H, 3.1; N, 14.6%); the hexamethylbenzene complex formed bright red needles, m.p. 168° (softening at 150°) (Found: N, 16.3. C12H18,C5H2N4O4 requires N, 16.3%).

A solution of the azide (3 g.) in acetic acid (45 ml.) was heated (water-bath) for 0.5 hr. and then poured into water. The solid was collected and crystallised from water containing 5% acetic acid (charcoal). The *dihydrate* formed pale brown needles, m.p. 175° (decomp.) (1.8 g.) [Found: C, 27.5, 27.5; H, 2.8, 3.0; N, 25.7, 25.8. $C_5H_2N_4O_4, 2H_2O$ requires C, 27.5; H, 2.8; N, 25.7. Found (after drying at 100° for 1 hr.): C, 30.1; H, 2.0; N, 27.8. $C_5H_2N_4O_4, H_2O$ requires C, 30.0; H, 2.0; N, 27.8% [Found (10 hr. drying): C, 30.2; H, 2.2; N, 28.2%], *M* (in methyl ethyl ketone) 204 (calc. 200).

A sample of the anhydrous compound (II; $R = NO_2$) was recrystallised from 5% acetic acid, yielding the dihydrate. When a sample of the dihydrate was sublimed at 140°/ 0·1 mm. a bright yellow sublimate (20%) of compound (III; $R = NO_2$) formed.

[0/1953 Received, November 16th, 1970]