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73. *The Action of Hydrazine on Benzoxazolones.*

By J. D. Bower and F. F. Stephens.

Reaction of 6-nitrobenzoxazolone with alcoholic hydrazine hydrate gives a hydrazine salt which easily breaks down into 4-(2-hydroxy-4-nitrophenyl)-semicarbazide. In this reaction benzoxazolone gives 4-*o*-hydroxyphenyl-semicarbazide, and 2-mercaptobenzoxazoles give *o*-aminophenols.

2-Amino-5-nitrophenol is best obtained by the action of ammonia on 6-nitrobenzoxazolone in an autoclave (F.I.A.T. Final Report No. 1313, p. 203). It seemed possible that ring opening could be achieved more simply by treatment with hydrazine (cf. Boggust and Cocker, *J.*, 1949, 355) although it is reported (D.R.-P. 614,327; *Chem. Centr.*, 1935, II, 2583) that this reaction yields 2-hydrazinobenzazoles.

6-Nitrobenzoxazolone in hot alcoholic hydrazine hydrate gave an unstable, bright red, crystalline solid, $C_7H_{12}O_4N_6$, changed by dilute acetic acid into a stable, bright yellow compound, $C_7H_8O_4N_4$, the latter being obtained directly from 6-nitrobenzoxazolone and hydrazine in aqueous solution. When either compound was heated with 25% sulphuric acid 6-nitrobenzoxazolone together with hydrazine sulphate was obtained. Clearly the red compound was a hydrazine salt of the yellow one and reactions of the latter led us to the opinion that it was 4-(*o*-hydroxy-*p*-nitrophenyl)semicarbazide (III) (see Experimental). It is probable that the reactions described above accord with the annexed scheme: the mesomeric *aci*-nitro-form

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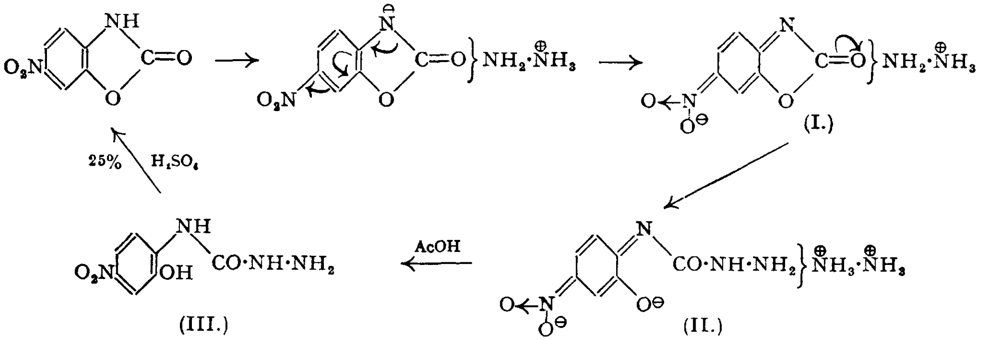
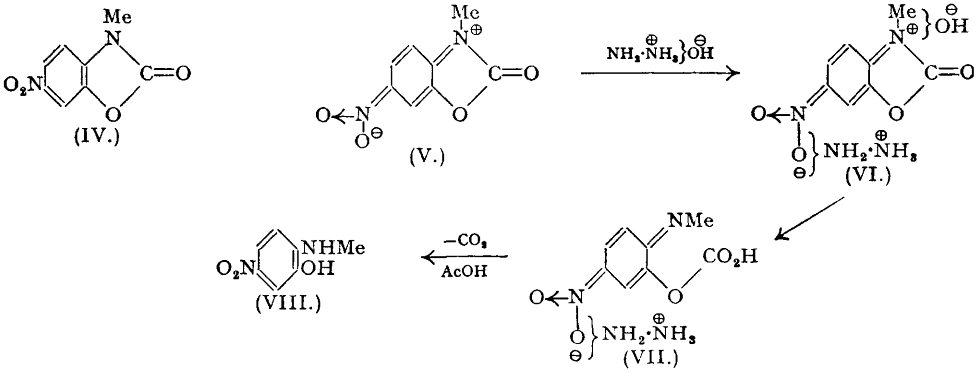
(I) of the initial hydrazine salt reacts further with hydrazine to give the unstable red salt (II) and thence the yellow compound (III). The final cyclisation of the semicarbazide to the benzoxazolone is supported by the statement (Beilstein, " Handbuch der organischen Chemie," 4th Edn., XIII, p. 391) that 2-hydroxy-4-nitrophenylurea is converted into 6-nitrobenzoxazolone by hot mineral acids [see also Darapsky (*J. pr. Chem.*, 1936, **147**, 145) on the opening of lactone rings with hydrazine]. Finally, the semicarbazide (III) was prepared by reaction of 2-hydroxy-4-nitrophenylurethane (Desai, Hunter, and Khalidi, *J.*, 1938, 327) with hydrazine hydrate and was identical with the above-mentioned yellow compound.



Application of this reaction to benzoxazolone itself produced 4-*o*-hydroxyphenylsemicarbazide, also synthesised from *o*-hydroxyphenylurethane (Groenvik, *Bull. Soc. chim.*, 1876, **25**, 177; see also Raiford *et al.*, *J. Org. Chem.*, 1939, **4**, 207; 1941, **6**, 858) and hydrazine.

In order to prevent the initial formation of a negative charge on the ring-nitrogen atom the reaction was repeated with 3-methyl-6-nitrobenzoxazolone. Attempts to prepare this compound by methylation of 6-nitrobenzoxazolone with methyl sulphate and alkali were unsuccessful. Benzoxazolone was easily methylated under these conditions (cf. Desai, Hunter, *et al.*, *J.*, 1934, 1186) and nitration of the resulting 3-methyl compound gave the desired substance. When this was heated with alcoholic hydrazine hydrate 2-methylamino-5-nitrophenol (VIII) was obtained. The failure to form a semicarbazide in this reaction is readily intelligible if reaction proceeded as shown :



(IV) reacts with hydrazine hydrate as if it possesses the zwitterion resonance form (V) to produce the *aci*-nitro-quaternary hydroxide (VI) and this undergoes a transformation, analogous to ψ-base formation or the ring opening of pyridinium compounds with alkali, leading to the unstable carbonate (VII) and thence (VIII).

The mechanisms suggested above require as an essential preliminary the formation of either a negative or a positive charge on the ring-nitrogen atom. In the case of 3-methylbenzoxazolone this would not be possible and it was deduced that this substance should remain unchanged on refluxing with hydrazine hydrate. This was found to be the case.

Reaction of 2-mercapto-6-nitrobenzoxazole (Desai, Hunter, and Khalidi, *J.*, 1938, 327) with hydrazine hydrate gave hydrogen sulphide, ammonia (see Boggust and Cocker, *loc. cit.*),

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and 2-amino-5-nitrophenol. Under these conditions 2-mercaptobenzoxazole gave hydrogen sulphide and *o*-aminophenol, together with an unidentified solid. Methylation of 2-mercapto-6-nitrobenzoxazole by methyl sulphate and alkali proceeded very easily (contrast the behaviour of 6-nitrobenzoxazolone), and the product (2-methylthio-6-nitrobenzoxazole) reacted with hydrazine to give methanethiol and 2-amino-5-nitrophenol. It is clear that in these mercapto-compounds hydrogenolysis of the heterocyclic carbon–sulphur bond is followed by the oxidation-reduction reaction described by Boggust and Cocker (*loc. cit.*).

EXPERIMENTAL.

Hydrazine salt of 4-(2-*hydroxy*-4-*nitrophenyl*)*semicarbazide.*—6-Nitrobenzoxazolone (1 g.), hydrazine hydrate (2 ml.; 100%), and ethanol (7 ml.) were boiled together under reflux for a few minutes, the mixture becoming nearly solid with bright red crystals (1·25 g.), m. p. 235° (decomp.). The solid was filtered off, washed with anhydrous ether, and dried in a vacuum-desiccator over phosphoric oxide [Found: C, 34·6; H, 5·25; N, 34·4; N_2H_4 (determined, after warming the compound with 4N-HCl) (Kolthoff, *J. Amer. Chem. Soc.*, 1924, **46**, 2009), 25·4. $C_7H_{12}O_4N_6$ requires C, 34·4; H, 4·9; N, 34·4; N_2H_4, 26·2%].

4-(2-*Hydroxy*-4-*nitrophenyl*)*semicarbazide.*—(*a*) To the above hydrazine salt (1·25 g.) were added acetic acid (5 ml.), then water (10 ml.), and the bright yellow semicarbazide (1·06 g.), m. p. 226—228°, was removed and dried. Recrystallisation from benzonitrile did not change the m. p. The *semicarbazide* was soluble in dilute alkali and dilute mineral acids, in alcoholic solution gave an olive-green colour with ferric chloride (cf. Semper and Lichtenstadt, *Annalen*, 1913, **400**, 326, for the case of 2-hydroxy-4-nitrophenylurea), and reduced both Fehling's and ammoniacal silver nitrate solutions (Found: C, 40·0; H, 3·9; N, 26·5. $C_7H_8O_4N_4$ requires C, 39·6; H, 3·8; N, 26·4%). The 1-p-*nitrobenzylidene* derivative, m. p. 267°, was recrystallised from aqueous pyridine (Found: C, 49·4; H, 3·7; N, 20·7. $C_{14}H_{11}O_6N_5$ requires C, 48·7; H, 3·2; N, 20·3%).

(*b*) 2-Hydroxy-4-nitrophenylurethane (1 g.), hydrazine hydrate (5 ml.; 100%), and ethanol (10 ml.) were refluxed for 7 hours. The mixture formed a bright red solution which was diluted and neutralised with 50% acetic acid to give yellow needles (0·5 g.), m. p. 226—228° alone or when mixed with the product from (*a*).

(*c*) 6-Nitrobenzoxazolone (1 g.) was boiled for 3 minutes with hydrazine hydrate (1·75 ml.; 90%) in water (6·5 ml.). The solution was cooled and filtered and the precipitate washed with water. The yield of yellow crystals, m. p. 228°, was 1·05 g.

6-*Nitrobenzoxazolone.*—The above semicarbazide (1 g.) was boiled under reflux with sulphuric acid (50 ml.; 25%) for 30 minutes. At first the semicarbazide dissolved but after 15 minutes a white precipitate appeared. Dilution with water gave 6-nitrobenzoxazolone (0·8 g.), m. p. 248—249°, alone or mixed with 6-nitrobenzoxazolone.

3-*Methylbenzoxazolone.*—Benzoxazolone (6·7 g.) was dissolved in 2N-sodium hydroxide solution (60 ml.) and methylated by the addition of two successive portions of methyl sulphate (each 5 ml.), the mixture being kept alkaline to phenolphthalein. The precipitated methyl compound (5 g.) was recrystallised from ligroin, giving white crystals, m. p. 85—85·5° (Found: N, 9·3. Calc. for $C_8H_7O_2N$: N, 9·4%).

3-*Methyl*-6-*nitrobenzoxazolone.*—3-Methylbenzoxazolone (4·5 g.) was added to concentrated nitric acid (35 ml.; *d* 1·42) at 90° and the mixture kept at this temperature for 15 minutes. The *product* was isolated by dilution and recrystallised from ethanol as white needles (4·7 g.), m. p. 186—187° (Found: N, 14·2. $C_8H_6O_4N_2$ requires N, 14·4%).

2-*Methylamino*-5-*nitrophenol.*—3-Methyl-6-nitrobenzoxazolone (1 g.) was refluxed with ethanol (7 ml.) and hydrazine hydrate (2 ml.; 100%) for 4 hours. The mixture was poured into water (50 ml.) and acidified with acetic acid, and the bright orange *phenol* (0·65 g.) collected. Recrystallisation from water gave orange needles (0·5 g.), m. p. 188° (Found: N, 16·8. $C_7H_8O_3N_2$ requires N, 16·7%).

4-o-*Hydroxyphenylsemicarbazide.*—(*a*) Benzoxazolone (2 g.), ethanol (16 ml.), and hydrazine hydrate (4 ml.; 100%) were boiled under reflux for 2·5 hours. The mixture was poured into water (50 ml.) and acidified with acetic acid, giving the *semicarbazide* (2 g.), m. p. 156°. Recrystallisation from water (charcoal) gave blunt white needles (becoming pale yellow) (1·3 g.), m. p. 156° (Found: C, 51·0; H, 5·9; N, 25·3. $C_7H_9O_2N_3$ requires C, 50·3; H, 5·39; N, 25·1%). The compound gave a cherry-red colour in Smith's test (*Analyst*, 1935, **60**, 171) (2-hydrazinobenzoxazole gave a yellow colour), was soluble in cold dilute sodium hydroxide solution, and gave a red-brown colour with ferric chloride.

(*b*) *o*-Hydroxyphenylurethane (1 g.), ethanol (3·5 ml.), and hydrazine hydrate (2·5 ml.; 100%) were refluxed for 7 hours, and the product was isolated as described under (*a*), giving white needles (0·5 g.), m. p. 156° not depressed on admixture with the above product. When the compound was heated with 25% sulphuric acid, benzoxazolone (m. p. 140—141° alone or mixed with pure benzoxazolone) was obtained.

2-*Methylthio*-6-*nitrobenzoxazolone.*—2-Mercapto-6-nitrobenzoxazole (1 g.), suspended in sodium hydroxide solution (16 ml.; 2N.), was treated with two (1·5-ml.) portions of methyl sulphate, the mixture being kept alkaline to phenolphthalein. After 15 minutes, 2-*methylthio*-6-*nitrobenzoxazole* (0·83 g.) was removed, washed with water, and recrystallised from ethanol as pale yellow needles, m. p. 124° (Found: N, 13·6. $C_8H_6O_3N_2S$ requires N, 13·3%).

2-*Amino*-5-*nitrophenol.*—2-Mercapto-6-nitrobenzoxazole (1 g.) was refluxed with ethanol (8 ml.) and hydrazine hydrate (2 ml.; 100%) for 2·5 hours (by this time the evolution of hydrogen sulphide had

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stopped and ammonia was being evolved). The mixture was cooled, diluted, neutralised with acetic acid, and extracted with ether, to give 2-amino-5-nitrophenol (0·55 g.). Recrystallisation from water gave orange needles, m. p. 207—208° alone or mixed with a pure specimen (Found: N, 18·9. Calc. for $C_6H_6O_3N_2$: N, 18·2%).

2-Methylthio-6-nitrobenzoxazole (1 g.) reacted under the conditions described above, to give methanethiol and 2-amino-5-nitrophenol (0·5 g.), m. p. 207—208°. 2-Mercaptobenzoxazole (1 g.) gave *o*-aminophenol (0·6 g.) and an unidentified solid (0·16 g.), m. p. 248°.

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