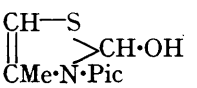
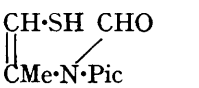
355. *The Condensation of Picryl Chloride with 4-Methylthiazole and Benzthiazole.*

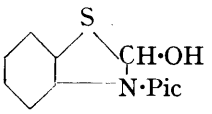
By (Miss) M. L. Tomlinson.

When Williams and his co-workers (*J. Amer. Chem. Soc.*, 1935, **57**, 229, 536) expressed the opinion that vitamin B_1 was a quaternary thiazolium salt in which the thiazole was directly linked to the nucleus of an aminopyrimidine, it seemed of interest to discover whether such salts could be prepared by the condensation of a chloronitropyrimidine with a thiazole (see Zincke, *Annalen*, 1903, **330**, 361, for the condensation of chloro-2 : 4-dinitrobenzene with pyridine). It was therefore decided to investigate the reaction between thiazoles and chloronitrobenzenes in order to determine how readily this reaction occurred. Since this work was started, Todd, Bergel, and Karimullah (*Ber.*, 1936, **69**, 217) have stated that negative results were obtained when attempts were made to condense halogenated benzenes or 5-halogenated pyrimidines with thiazoles.

There was no indication of a reaction taking place between 4-methylthiazole and chloro-, bromo-, or iodo-2 : 4-dinitrobenzene under any of the conditions investigated and so attention was turned to picryl chloride where the halogen atom is further activated by the additional nitro-group. Here, in the absence of moisture, a yellow uncrystallisable mass was obtained, but when the reaction mixture had access to moisture from the air a product $C_{10}H_8O_7N_4S$ was slowly formed. This compound appears to be *2-hydroxy-3-picryl-4-methyl-2 : 3-dihydrothiazole* (I). It is considered that the quaternary salt, which is probably the first product of the reaction, is unstable and that the chlorine passes into the 2-position, from which it is easily hydrolysed. The facile nature of this hydrolysis and the failure to isolate the chloro-compound itself are reminiscent of the behaviour of some dihydroindole derivatives (Plant and Tomlinson, J., 1931, 3324, and later papers). The substance (I) dissolves slowly in alkali to give a salt of (II). Acidification of the

(I.)   (II.)

solution yields a transient red precipitate; this, which may be (II) itself, rapidly loses its colour and reverts to (I).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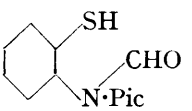
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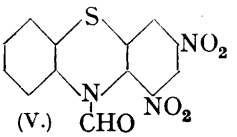
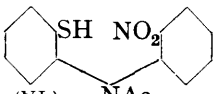

(V.)

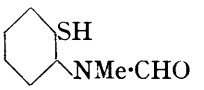
Benzthiazole condenses with picryl chloride under similar conditions to give *1-hydroxy-2-picryl-1 : 2-dihydrobenzthiazole* (III), which undergoes similar changes with alkali, dissolving to give a salt of (IV). The red compound (IV) changes spontaneously into a

mixture of (III) and 2 : 4-*dinitro*-5-*formylphenthiazine* (V). Treatment of (III) with hot alkali also yields (V). 2 : 4-Dinitrophenthiazine was obtained in an analogous way by Kehrmann and Steinberg (*Ber.*, 1912, **44**, 3011) by the action of alkali on picrylaminothiophenol. It has not been found possible to convert their compound into its formyl derivative nor yet to remove the formyl group from (V), but the two compounds are similar in appearance and properties.

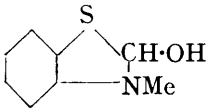
Aniline reacts with (I) and (III) with the formation of 2 : 4 : 6-trinitrodiphenylamine and the corresponding thiazole. There is no indication of the conversion of (I) or (III) into a thiazolium salt with anhydrous hydrogen chloride, a fact which must be due to the very large effect of the three nitro-groups in preventing the use of the unshared electrons of the nitrogen for salt formation. Evans and Smiles (J., 1935, 183) state that *N*-acetylthiols such as (VI) readily form salts with acids. The fact that neither (I) nor



(VI.)



(VII.)



(VIII.)

(III) forms an ether with alcohol is evidence for the non-existence of these compounds in the ammonium base form. Mills, Clark, and Aeschlimann (J., 1923, **123**, 2353) have shown that the product formed by the action of alkali on benzthiazole methiodide is (VII) rather than (VIII), but here the evidence seems to point to (I) and (III) rather than (II) and (IV). The molecular weight of (III), determined by the elevation of the boiling point of ethylene dibromide, is 365 ± 10, so there can be no possibility that oxidation to a disulphide has occurred; it is surprising, however, that (III) could not be oxidised to a disulphide in alkaline solution.

Picryl chloride could not be condensed with 2 : 2′-*bisformamidodiphenyl disulphide* to give the *NN*′-dipicryl derivative, which should yield (III) or (IV) on reduction. This derivative also could not be prepared by the action of formic acid on 2 : 2′-bispicramidodiphenyl disulphide. When, however, picryl chloride and 2 : 2′-bisformamidodiphenyl disulphide were heated in the presence of copper powder, reduction occurred at the same time as condensation and a 50% yield of (III) was obtained.

Experimental.

2-*Hydroxy*-3-*picryl*-4-*methyl*-2 : 3-*dihydrothiazole* (I).—A mixture of 4-methylthiazole (1·9 g.) and picryl chloride (4·9 g.) was kept at 40° for several hours; the solid *product* crystallised when rubbed with glacial acetic acid. After being freed from 4-methylthiazole picrate by washing with hot alcohol, it crystallised from xylene in fine yellow needles (1·5 g.), m. p. 181° (decomp.) (Found: C, 36·6; H, 2·3; N, 16·7; S, 9·6. $C_{10}H_8O_7N_4S$ requires C, 36·6; H, 2·4; N, 17·1; S, 9·8%). Dilution of the acetic acid mother-liquor with methyl alcohol caused the precipitation of a large quantity of 4-methylthiazole picrate together with a little of an orange *substance* (prisms from glacial acetic acid), m. p. 194° (decomp.), which gave the analytical figures required for a picrate of (I) (Found: C, 35·8; H, 2·0; N, 18·1; S, 6·0. $C_{10}H_8O_7N_4S,C_6H_3O_7N_3$ requires C, 35·8; H, 2·0; N, 18·2; S, 6·0%). On trituration with sodium hydroxide (3%) or sodium carbonate (10%) solution, (I) dissolved very slowly to give a deep reddish-brown solution, which became an intense crimson on acidification. A red precipitate then formed, but the colour disappeared fairly quickly and a colourless solution containing a precipitate of the initial material was obtained. When (I) (1 g.) was boiled with aniline (1 g.) in alcohol (20 c.c.) for ½ hour, 2 : 4 : 6-trinitrodiphenylamine was formed. This separated almost quantitatively on cooling, and 4-methylthiazole was isolated (as its picrate) when the mother-liquor was acidified with hydrochloric acid and evaporated and the residue treated with picric acid. After the compound (I) had been kept in dry ethereal hydrogen chloride for some days, almost the whole of it was recovered unchanged; no crystalline product was obtained.

1-*Hydroxy*-2-*picryl*-1 : 2-*dihydrobenzthiazole* (III).—Benzthiazole (1·4 g.) and picryl chloride (2·3 g.) were condensed in a manner similar to that described above. The *product* was triturated with glacial acetic acid, washed with hot alcohol and crystallised from xylene, forming

fine yellow needles (1·0 g.), m. p. 180° (decomp.) (Found: C, 43·1; H, 2·5; N, 15·2; S, 9·0. $C_{13}H_8O_7N_4S$ requires C, 42·9; H, 2·2; N, 15·4; S, 8·8%). A large quantity of benzthiazole picrate was also formed. When (III) was heated with 20% sodium carbonate solution at 100° for 1 hour, a quantitative yield of 2 : 4-*dinitro*-5-*formylphenthiazine* (V) was obtained. This crystallised from xylene or glacial acetic acid in orange-brown prisms, m. p. 243° (decomp.) (Found: C, 49·3; H, 2·5; N, 13·2. $C_{13}H_7O_5N_3S$ requires C, 49·2; H, 2·2; N, 13·3%). It gave an intense violet colour with alkali in alcohol or acetone; the colour was destroyed by acids and restored by alkali. (V) was unchanged by boiling with concentrated hydrochloric acid for several hours. Nitrite ions could easily be detected in the solution when (V) was formed from (III). The substance (III) dissolved very slowly on trituration with dilute aqueous caustic soda or sodium carbonate to give a deep red solution. Careful acidification of this solution caused intensification of the colour and finally the formation of a scarlet precipitate, the colour of which faded in ½ hr; the precipitate was then found to be a mixture of (III) and (V). The solution gave a positive test for nitrite. When potassium ions were added to the red soda solution, a brownish-red crystalline precipitate of what appeared to be a potassium salt separated. It was only very sparingly soluble in water, when treated with acid it yielded the original substance (III), and when boiled in almost any solvent it readily formed (V) and a nitrite. The compound (III) was converted into benzthiazole and 2 : 4 : 6-trinitrodiphenylamine when treated with aniline as described above, and it was unaffected by ethereal hydrogen chloride.

2 : 2′-*Bisformamidodiphenyl Disulphide.*—2 : 2′-Diaminodiphenyl disulphide was warmed with an excess of formic acid (90%) on a water-bath for a few minutes. The *diformyl* compound, precipitated by water, crystallised from alcohol in colourless needles, m. p. 161° (Found: C, 55·4; H, 4·2. $C_{14}H_{12}O_2N_2S_2$ requires C, 55·3; H, 3·9%).

2 : 2′-Bisformamidodiphenyl disulphide (1·5 g.), picryl chloride (2 g.), and copper powder (0·5 g.) were heated together at 100° for 1 hour. Extraction of the mass with hot xylene gave a 50% yield of (III), leaving a bluish powder containing copper.

Benzthiazole from 2 : 2′-*Bisformamidodiphenyl Disulphide.*—The disulphide (1·0 g.) was dissolved in alcohol and treated with crystalline sodium sulphide (1·0 g.), dissolved in a little water. The mixture was warmed, acidified, and treated with picric acid and benzthiazole picrate (2·5 g.) was obtained.

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