The Reaction of Phenylacetonitrile with Carbon Disulphide and the Preparation of 4-Aryl Isothiazoles

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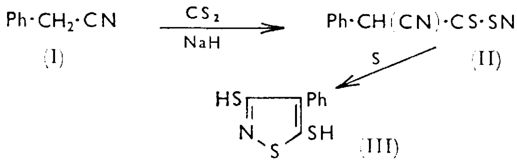
Dithioacid salts have been prepared in good yield from phenylacetonitrile and related compounds by reaction with carbon disulphide in benzene solution using sodium hydride as the base; substituted isothiazoles are formed on heating these salts, in ethanol solution, with sulphur.

SALTS of dithioacetic acids may be readily prepared[1-5] by the action of carbon disulphide and base on a compound possessing an active methylene group. However, we could find only one report, in the patent literature,[6] of phenylacetonitrile or related compounds (I) being used in this reaction. We were unable to obtain a satisfactory reaction using the method of this patent[6] and we have now found that, although phenylacetonitrile does not react readily with carbon disulphide in the presence of sodium hydroxide or sodium ethoxide, good yields of the required dithio-acid salts are obtained if sodium hydride is used as the base.

The reaction, which is best carried out in benzene solution, is promoted by the addition of a small quantity of dimethylformamide. The sodium salts of the cyanophenyldithioacetic acids (II) prepared in this way are, in general, very hygroscopic yellow solids which slowly decompose on standing.

Treatment of the sodium salts (II) with sulphur in refluxing ethanol, and acidification of the resulting solution, gave the corresponding isothiazoles (III) in moderate yield.



EXPERIMENTAL

Sodium Cyanophenyldithioacetate (II).—Dimethylformamide (20 ml.) was added dropwise to a stirred mixture of sodium hydride (10 g. of 50% dispersion in oil), benzene (200 ml.), phenylacetonitrile (23·4 g.,), and carbon disulphide (15·2 g.). The mixture was heated under reflux for 1 hr., cooled, and the yellow product separated, washed with benzene and light petroleum (b. p. 60—80°), and dried in a vacuum desiccator. Recrystallisation from isopropanol containing *ca.* 3% water afforded the *sodium salt* as yellow needles of the trihydrate, m. p. 120° (decomp.) (40 g., 74%) (Found: C, 39·8; H, 4·7; N, 5·15; S, 23·7. $C_9H_6NNaS_2,3H_2O$ requires C, 40·15; H, 4·5; N, 5·2; S, 23·8%).

Analogous products were obtained from *o*-chlorophenylacetonitrile and from *p*-methoxyphenylacetonitrile, but these could not be satisfactorily recrystallised.

3,5-*Dimercapto*-4-*phenylisothiazole* (III).—The above sodium salt trihydrate (54 g.), sulphur (6·4 g.), and ethanol (200 ml.) were heated together under reflux for 3 hr. The dark red solution, on acidification and extraction with chloroform, afforded orange-red needles of the *isothiazole* (13·2 g., 37%), which after recrystallisation from chloroform had m. p. 181—183° (Found: C, 48·4; H, 3·1; N, 6·3; S, 42·8. $C_9H_7NS_3$ requires C, 48·0; H, 3·1; N, 6·2; S, 42·6%).

In the same way, from the corresponding sodium salts (II) were prepared 4-o-*chlorophenyl*-3,5-*dimercaptoisothiazole*, m. p. 232° (Found: C, 41·8; H, 2·3; N, 5·6. $C_9H_6ClNS_3$ requires C, 41·6; H, 2·3; N, 5·4%), and 3,5-*dimercapto*-p-*methoxyphenylisothiazole*, m. p. 191° (Found: C, 47·4; H, 3·6; N, 5·25; S, 37·6. $C_{10}H_9NOS_3$ requires C, 47·1; H, 3·55; N, 5·5; S, 37·6%).

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