CXIII. SYNTHESIS OF *l*- α -NAPHTHYL-MERCAPTURIC ACID.

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IN the preceding paper the isolation of an acid $C_{15}H_{15}O_3NS$ from the urine of rabbits fed with naphthalene was described and evidence presented which identified it with reasonable certainty as *l*- α -naphthylmercapturic acid, $C_{10}H_7S.CH_2.CH(NHAc).CO_2H$. In order to put this identification beyond doubt, the synthesis of this acid was attempted and has now been achieved.

The best method of synthesising mercapturic acids appeared to be the condensation of the appropriate aryldiazonium salt with acetylcysteine. Diazonium salts, ArN_2X , condense with thiol compounds to form $ArN_2S.R$, which decompose when heated in a suitable solvent, evolving nitrogen and forming thio-ethers, $Ar.S.R$ [Kalle and Co., 1907]. Friedmann [1904] prepared *p*-bromophenylmercapturic acid in this way by condensing *p*-bromophenyldiazonium chloride with cysteine and acetylating the *p*-bromophenylcysteine so obtained. In our experiments α -naphthyldiazonium acetate was condensed with *d*-acetylcysteine and the condensation product decomposed in hot water. *l*- α -Naphthylmercapturic acid was obtained in poor yield and found to be identical with the mercapturic acid isolated from rabbits' urine.

EXPERIMENTAL.

d-Acetylcysteine was prepared by the method of Pirie and Hele [1933]. It melted at 108° (uncorr.) and a solution in water had $[\alpha]_D^{21} 5.5^\circ$ ($c = 2.7\%$).

α -Naphthylamine (3.2 g.), recrystallised from light petroleum, was dissolved by warming in water (60 ml.) containing concentrated hydrochloric acid (2.5 ml.). The solution was cooled in ice with stirring and a further 2.5 ml. of concentrated hydrochloric acid and 30 g. of ice added. This suspension of α -naphthylamine hydrochloride was diazotised at 0° with a solution of sodium nitrite (1.6 g.) in water (15 ml.), which had been rendered acid to Congo paper by the addition of very dilute ice-cold hydrochloric acid [Bulow and Sprosser, 1908]. Sodium acetate (4 g.) in the least amount of water was then added to neutralise the hydrochloric acid and the solution filtered to remove a small amount of diazoaminonaphthalene. The filtrate was added slowly to a 10% solution of *d*-acetylcysteine (3.2 g.) in water. An orange-coloured amorphous precipitate was formed, which was collected, suspended in water containing a few per cent. of alcohol and heated with the addition of copper-bronze powder on the water-bath until the evolution of nitrogen ceased. The hot solution was filtered, the

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copper powder and insoluble material washed with boiling water and the united filtrates evaporated to small bulk. The semi-crystalline solid material which separated was collected and dissolved in potassium carbonate solution, and the solution was filtered from resinous material and acidified. The crude mercapturic acid, which was precipitated, was extracted with chloroform, and the solid residue from the evaporation of the chloroform was crystallised by dissolution in a little alcohol and, after treatment with charcoal, addition of water. Yellowish crystals were obtained melting at 169–170°.

The crude acid (0.25 g. from 5 g. of acetylcysteine) was purified by conversion into its sodium salt which, like the sodium salt of the natural mercapturic acid, crystallises from excess of 2*N* sodium hydroxide. The free acid was recovered by acidifying an aqueous solution of the sodium salt and was crystallised from aqueous alcohol. This process was repeated once more and the acid finally crystallised from ethyl malonate, from which it separated in well-formed but still faintly coloured needles; yield 0.13 g. (Found: C, 62.30; H, 5.24; N, 4.60; S, 10.95 %. $C_{15}H_{15}O_3NS$ requires C, 62.28; H, 5.23; N, 4.84; S, 11.09 %.)

The synthetic α -naphthylmercapturic acid melted at 170–171°, the natural *l*- α -naphthylmercapturic acid at 170.5–171° and a mixture of the two at 170–171°.

The natural mercapturic acid in 1 % solution in alcohol had $[\alpha]_D^{25} - 25^\circ$ and the synthetic acid in 1.005 % solution in alcohol had $[\alpha]_D^{25} - 23.9^\circ$.

The synthetic *l*- α -naphthylmercapturic acid, like the natural product, was soluble in conc. H_2SO_4 and gave a green colour on warming.

SUMMARY.

l- α -Naphthylmercapturic acid has been synthesised and proved to be identical with the mercapturic acid isolated from the urine of rabbits fed with naphthalene.

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