LETTERS TO THE EDITORS

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Nidulin and 'Ustin': Two Chlorine-containing Metabolic Products of *Aspergillus nidulans*

A MOULD, isolated by Kurung[1] in 1944 and considered to be a strain of *Aspergillus ustus* (Bain.) Thom and Church, was shown to produce a metabolic liquor which possessed a marked antibiotic activity towards *Mycobacterium tuberculosis* and *M. rancæ*. Afterwards, Hogeboom and Craig[2], by application of a counter-current technique, were able to isolate, from an ethereal extract of this mould and its substrate, two crystalline products, called compound I and compound II, which showed a very high activity against *M. rancæ*. Doering, Dubos, Noyce and Dreyfus[3], using the same strain of mould, isolated a number of chlorine-containing metabolic products, one of which was proved to be identical with Hogeboom and Craig's compound I. Doering *et al.* proposed the name 'ustin' for this compound, established its empirical formula ($C_{19}H_{15}O_5Cl_3$) and published a superficial account of some of its chemical properties.

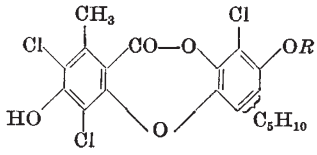
Kurung's original strain has now been examined more exhaustively, and we conclude that it is, in fact, a non-ascosporic strain of *Aspergillus nidulans*.

When this mould is grown at 30° C. on a medium containing Czapek–Dox salts, 4 per cent glucose and 0·1 per cent 'Marmite', some 'ustin' is produced in the substrate and much fatty material is to be found in the mycelium. However, when the mould is grown on the same substrate but at a much lower temperature, the amount of fat is considerably reduced and, from the dried mycelium, a crystalline compound for which we propose the name 'nidulin', can be isolated as the main product. The yield of this compound is very variable, but on one occasion it formed as much as 5 per cent of the dried mycelium.

Crude nidulin is deposited as a brownish crystalline mass when a light petroleum (boiling point 40–60° C.) extract of the dried and powdered mycelium is allowed to stand for six days. (A further quantity is obtainable by extracting the petroleum-extracted mycelium with ether and evaporating the solvent.) The crude product may be purified by successive crystallizations from ethanol (95 per cent) and from light petroleum (boiling point 60–70° C.). Pure nidulin, $C_{20}H_{17}O_5Cl_3$, crystallizes from ethanol in colourless rhombs and from light petroleum in slender, shining rods, melting point 180° C. (Found: C, 54·3; H, 4·0; Cl, 23·7; OMe, 6·9 per cent; equiv., by titration, 435; *M* (Micro-Rast), 463. $C_{19}H_{14}O_4Cl_3(OMe)$ requires C, 54·1; H, 3·9; Cl, 24·0; OMe, 7·0 per cent; *M*, 443·7.) Nidulin is insoluble in water, but soluble in aqueous solutions of sodium hydroxide and of sodium bicarbonate, easily soluble in chloroform, sparingly soluble in ethanol (95 per cent) and benzene and very sparingly soluble in hot light petroleum (boiling point 60–70° C.). A 4 per cent solution in chloroform shows no optical activity.

Nidulin has been shown to be the mono-methyl ether of 'ustin', and the chemistry of these compounds has been investigated in some detail. Since nidulin is, at least under certain specified conditions, the main metabolic product, and since also the mould is now considered to be a strain of *A. nidulans*, we suggest that the name 'ustin' be dropped and that Hogeboom and Craig's compound I or 'ustin' be now called '*nor*-nidulin'.

We suggest the following partial structures for nidulin and for *nor*-nidulin ('ustin'):



Nidulin ($R=CH_3$). *Nor*-nidulin or 'ustin' ($R=H$)

The antibiotic activity of nidulin has been investigated, through the courtesy of Dr. W. F. Short, by Messrs. Boots Pure Drug Co., Nottingham, to whom we are indebted for the following information. Nidulin completely inhibits the growth of *M. tuberculosis* for four weeks at a dilution of between 1 in 5,000 and 1 in 10,000; the test was carried out in presence of serum, by modified Long's medium and the floating-pellicle method. A 0·1 per cent solution also inhibits the growth of the human parasitic fungi *Trichophyton tonsurans* and *Microsporum audouini*, but shows little or no activity towards quite a wide range of other micro-organisms. It is inactive against bacteriophage. (For microbiological testing a solution of nidulin is made by dissolving a known quantity in a little warm ethanol, adding one equivalent of aqueous 0·1 *N* sodium hydroxide solution and diluting with water.)

Full details of the chemistry of nidulin will shortly be published elsewhere.

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[2] Hogeboom, G. H., and Craig, L. C., *J. Biol. Chem.*, **162**, 363 (1946).
[3] Doering, W. E., Dubos, R. J., Noyce, D. S., and Dreyfus, R., *J. Amer. Chem. Soc.*, **68**, 725 (1946).

Biogenesis of Alkaloids of Solanaceæ

THIRTY-SIX years ago[1] I directed attention to the structural relations between hygrine, cuskhygrine, tropine and other similar bases, and drew the conclusion that the units concerned in the biogenesis were ornithine or proline on one hand, and an acetone equivalent on the other. P. I. Mortimer[2] now advances a different hypothesis on the sole new ground that hyoscine and nicotine have been found to be congeneric in one instance at least[3].

This latter fact is of great interest; but it is in full accord with my early paper[1]. The matter will be developed from my own point of view in another place.