The Functional Groupings of α-Elaterin (Cucurbitacin E)

SIR,—At the British Pharmaceutical Conference, Llandudno, 1958, Gilbert and Mathieson described[1] the functional groupings of α-elaterin (Cucurbitacin E) and omitted to refer to information already published[2,3]. Meanwhile we have obtained valuable degradation products which shed light on the position of some of the groupings referred[4,5].

The presence of the diosphenol system (enolised 1:2-diketone) has been [2,3] indicated by the bathochromic shift with alkali observed in the ultra-violet light; this shift of the maximum at 267 mμ to 318 mμ is accompanied by a characteristic decrease in the relative intensity of absorption. Specific bands in the infra-red at 1660 and 1413 cm.$^{-1}$ confirmed this grouping. Further, this system has been shown to be attached to a six membered ring and to react with *o*-phenylenediamine to form a quinoxaline derivative. Elaterin formed a red tris-2:4-dinitrophenylhydrazone indicating the three keto groupings present in the molecule (αβ-unsaturated ketone in addition to the diosphenol system).

The side chain of α-elaterin has now been elucidated. This side chain $Me_2C(OH)\cdot CH:CH\cdot CO\cdot C(OH)RR'$ excluded any possibility of a pentacyclic molecule. Further, during the alkaline degradation of α-elaterin three rearrangements occur thereby clarifying the different degradation products obtained. Hot alkali induces a benzilic acid type rearrangement of the diosphenol system leading to a ring contraction and the formation of an α-hydroxy acid; the αβ-unsaturated ketone in the side chain undergoes at the same time a reversed aldol condensation, with the subsequent formation of a methyl ketone (iodoform test of ecballic acid)[6], thereby 2-hydroxy*iso*butyraldehyde is liberated. In the presence of alkali 2-hydroxy*iso*butyraldehyde undergoes an acyloin rearrangement thus forming ultimately acetoin[4–6]. This aldehyde has also been obtained during the ozonolysis of α-elaterin. Elaterin as well as other compounds of this series have been found[2,7] to have strong antitumour activity on hard tumours, Sarcoma 37 and Black Sarcoma, in mice and are now under investigation. They have also been found to have a definite action on a transplanted tumour in the cheekpouch of the golden hamster. (Schwenk, private communication.)

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