336. *Buckley's Substance, m. p.* 183°, *from* Derris *Extract.*

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Evidence is adduced in favour of the structure (II) for the substance isolated from *Derris* by Buckley (*J. Soc. Chem. Ind.*, 1936, **55**, 285T). The substance is held not to occur naturally as such and is probably derived by degradation of deguelin (I) by the alkali used in its isolation.

Buckley (*loc. cit.*) isolated from *Derris* extract a substance, m. p. 183°, the individuality of which was, however, considered by Cahn, Phipers, and Boam (this vol., p. 513) to be insufficiently established. Mr. Buckley has very kindly given us a sample, from examination of which we are now satisfied that the substance is substantially homogeneous and differs from other substances obtained from *Derris*.

The substance appears to contain at least rings *A*, *B*, and *C* of rotenone, deguelin (I), and other substances obtained from *Derris*. Thus, Buckley reports that it gives the

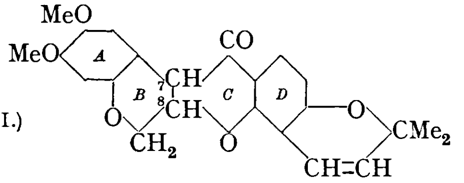
Durham (Jones and Smith, *Ind. Eng. Chem., Anal.*, 1933, **5**, 75) and Rogers and Calamari (*ibid.*, 1936, **8**, 135) colour tests and forms an oxime. Further, it gives the Goodhue (*J. Assoc. Off. Agric. Chem.*, 1936, **16**, 118) and Meijer (*Rec. Trav. chim.*, 1936, **55**, 954) colour tests, contains two methoxyl groups, and with iodine yields an iodo-derivative, reduced by zinc dust in acetic acid to a dehydro-compound (Buckley mistook the former for the latter).

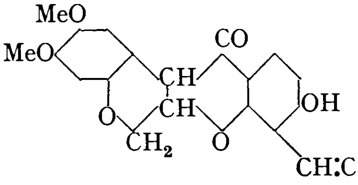
Solely from a nitrogen analysis of the oxime, Buckley apparently assigned to the substance the formula, $C_{23}H_{22}O_6$, common to rotenone and deguelin. Our analyses of the solvent-free crystals and of the *solvate* obtained from benzene exclude this formula and agree best with $C_{20}H_{16}O_6$, or less well with $C_{20}H_{18}O_6$.

The substance gives no colour with alcoholic ferric chloride, but is very slowly removed from ether by aqueous alkali. It is recovered unchanged from the alkaline solution by rapid acidification, but more prolonged contact leads to degradation; this unfortunately caused loss of most of our material. The phenolic nature of the substance is supported by the formation of the iodo-derivative, which is typical of rotenone derivatives containing a hydroxyl group in ring *D*, those without this substituent giving only the unsubstituted dehydro-compound.

The chemical findings reported above and the known structure of other *Derris* derivatives fall best into line with the constitution (II) for Buckley's substance. Its great instability in alkali is accounted for by the presence of the vinyl group, and its cryptophenolic nature may be due to co-ordination between the vinyl and the hydroxyl group.

(I.)





(II.)

This demands the formula $C_{20}H_{18}O_6$; we have been unable to devise a structure which will account satisfactorily for the reactions of the substance on the basis of $C_{20}H_{16}O_6$, which, as stated, is the formula preferentially indicated by analysis. Our specimen had a slight optical rotation, whereas Buckley reports the substance to be optically inactive; it seems probable that our specimen was slightly impure and that the small discrepancy in the analytical figures for hydrogen originates in the impurity. The material available did not suffice for further experiments.

It is almost certain that the substance does not occur as such in *Derris*; for all the substances occurring naturally therein have 23 carbon atoms and are optically active at C7 and C8, whereas Buckley's substance has 20 carbon atoms and is unchanged by sodium acetate in hot alcohol, which invariably racemises C7 and C8 (Cahn, Phipers, and Boam, *loc. cit.*). It is noteworthy that it is isolated alongside *dl*-deguelin, which occurs naturally as the *l*-form, so that racemising conditions existed during its isolation. Buckley's substance may occur naturally in an optically active form, but we consider it more probably derived by destruction of deguelin. Heyes and Robertson (J., 1935, 681) showed that acetone is formed from deguelin by hot 33% alcoholic potassium hydroxide, the $CH{:}CH{\cdot}CMe_2$ chain being assumed, by analogy with toxicarol, to be entirely detached from ring *D* under these conditions. With hot 20% alcoholic alkali, Heyes and Robertson obtained no acetone. However, prolonged contact with the very dilute alkali used in Buckley's experiments might lead to the first stage of the decomposition, *i.e.*, formation of (II) from (I). The natural assumption that the conditions necessary for formation and survival of such an unstable substance are critical then explains the failure of ourselves and other investigators to isolate it from *Derris* extract.

EXPERIMENTAL.

The material provided was in well-formed crystals, which, however, melted unsharply at 184—187°. As is general in the rotenone series, the m. p. seems to be variable and not a criterion of purity: Buckley reported m. p. from 180° to 185° for different specimens and we found

m. p. as low as 179°. In view of past experience with *l*-toxicarol (Cahn, Phipers, and Boam, *loc. cit.*) and deguelin and tephrosin (Boam, Cahn, and Stuart, *J. Soc. Chem. Ind.*, 1937, **56**, 91T) and of the small amount available, a search for impurities by crystallisation alone was impracticable. The substance is sparingly soluble in ether; however, when added in acetone to a water–ether mixture, it passes into the ethereal layer, whence it is gradually removed by shaking with successive amounts of dilute aqueous sodium hydroxide. When this operation was not carried to completion, the materials recovered from the alkaline and ethereal solutions were identical (mixed m. p.). This is strong evidence that the material is homogeneous and is supported by the facts that no change (m. p. and mixed m. p.) was caused by heating 0·25 g. under reflux with sodium acetate (0·5 g.) in alcohol (10 c.c.) or by adding 0·05 g. to a mixture of concentrated sulphuric acid (0·175 c.c.) and acetic acid (0·6 c.c.) at about 50°. The acid treatment was used by Buckley (*loc. cit.*) in an attempt to prepare an *iso*-derivative, and by us with the hope also of effecting ring-closure between the hydroxyl and the vinyl group (cf. Haller, *J. Amer. Chem. Soc.*, 1931, **53**, 733).

The substance crystallises from alcohol in solvent-free needles [Found: C, 68·1, 68·2, 68·3; H, 4·6, 4·6, 4·5; OMe, 18·4, 18·3; loss at 80°/vac., nil. $C_{18}H_{10}O_4(OMe)_2$ requires C, 68·1; H, 4·6; OMe, 17·6%. $C_{20}H_{18}O_6$ requires C, 67·8; H, 5·1%], and from benzene in needles, which, although solvated, have the same m. p. (181—182°) [Found (air-dried): C, 70·05; H, 4·8; loss at 80°/vac., 8·7, 8·6. $C_{20}H_{16}O_6,0{\cdot}5C_6H_6$ requires C, 70·6; H, 4·9; loss, 10·0%. $C_{20}H_{18}O_6,0{\cdot}5C_6H_6$ requires C, 70·1; H, 5·1; loss, 9·9%. Found for material dried at 80°/vac.: C, 68·0; H, 4·6%]. As received, the substance had $[\alpha]_D$ about + 10° in chloroform; it was too sparingly soluble for measurement in benzene, the solvent used by Buckley. In the Meijer test it gives the same shade of colour as does rotenone, but with greater intensity: 1 g. is equivalent to 1·25 g. of rotenone. On the basis of molecular weights the ratio might be expected to be 1·12; however, the ratio found for apotoxicarol is 1·42, whereas that calculated from the molecular weights is 1·3, so that this mode of calculation is invalid. By contrast, Buckley's substance gives in the Goodhue test a colour substantially equal in both shade and intensity to that given by rotenone.

Dehydrogenation. Iodine (0·25 g.) in a little alcohol was added to the substance (0·25 g.) and sodium acetate (0·5 g.) in boiling alcohol (10 c.c.). Boiling was continued for 1 hour. The material, recovered by pouring into water and extraction with ether, crystallised from alcohol. It melted at about 270° with evolution of iodine. Reduction with zinc dust in the way usual for toxicarol derivatives gave the halogen-free dehydro-compound as yellow needles (from alcohol–acetic acid), m. p. 260° without decomposition. This establishes the difference of Buckley's substance from other *Derris* derivatives.

Attempts to acetylate the substance or its dehydro-derivative failed.

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