

## ALKALOIDS OF THE GRAMINEAE: *THELEPOGON ELEGANS*\*

By W. D. CROW†

The immense economic importance of the grasses has led to a large number of investigations, but these are primarily concerned with the use of such plants as pasture materials. The possibility that alkaloids might be present in grasses has nevertheless not been entirely overlooked. The occurrence of the indole bases, gramine in barley (von Euler and Hellstrom 1932) and 5-methoxy-*N*-methyltryptamine in *Phalaris arundinacea* L. (Wilkinson 1958), are recorded in the literature, as also is the occurrence of perloline,  $C_{20}H_{18}O_4N_2$  (Melville and Grimmett 1941) in *Lolium perenne*. The same compound was later shown to occur in two other species of *Lolium*, as well as in *Festuca arundinacea* and *Setaria lutescens* by Reifer and White (1945), who examined a number of grasses specifically for alkaloids. More recently, Yunusov and Akramov (1960) have isolated the pyrrolizidine derivatives loline, lolinine, and lolinidine from *Lolium cuneatum*.

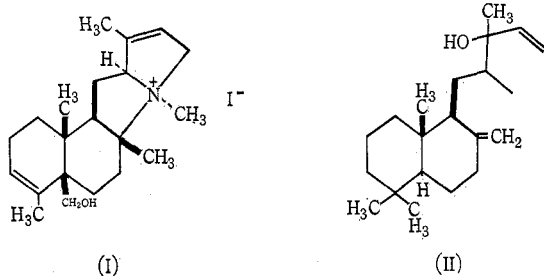
The observation that *Thelepogon elegans*, a sample of which was available from the Plant Introduction Section, C.S.I.R.O., contained alkaloids, was therefore followed up by extraction and isolation of the constituents. Paper chromatography showed the presence of at least five bases, two of which were isolated in sufficient amount for purification. Thelepogine ( $C_{20}H_{31}ON$ ) showed the presence of an hydroxyl group ( $3300\text{ cm}^{-1}$ ) in the infrared, but was transparent at  $m/20000$  in the ultraviolet. The associated base thelepogidine ( $C_{18}H_{29}O_2N$ ) showed no evidence of hydroxyl or carbonyl absorption in the infrared, so that both oxygen atoms must be in the form of ether linkages.

In view of the shortage of material a heavy atom derivative of thelepogine was prepared for X-ray diffraction studies. The methiodide was examined by Fridrichsons and Mathieson (1960) of these Laboratories who have reported the structure (I) as a result of their investigations, and have indicated a possible

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relationship to manool (II) and the pyrrolizidine alkaloids. One point which seems worthy of comment concerns the C-methyl analysis (1·2C-methyl group) for thelepogine. That the angular methyl groups should not be revealed in the determination is understandable, but the situation regarding the other two methyl groups is not clear. Possibly the fact that both are activated by double bonds leads to a certain amount of oxidation at the allylic H-atoms in competition with the normal production of acetic acid.



### Experimental

All melting points are corrected. Microanalyses were carried out by the C.S.I.R.O. and University of Melbourne Microanalytical Laboratory.

(a) *Isolation of the Alkaloids*.—The dried, milled grass (3·2 kg) was exhaustively extracted with methanol, the extract concentrated to small volume at 40 °C, and diluted with water to 1·5 l. The pH was adjusted to 2–3 (HCl) and the extract washed several times with light petroleum (b.p. 100–120 °C) at 45 °C to remove chlorophyll and waxy materials. The residual aqueous liquid was basified with  $\text{NH}_3$  and extracted six times with ether (A). After making strongly alkaline with NaOH, the aqueous layer was then extracted eight times with chloroform (B), and discarded. The ether extracts (A), after removal of nonbasic material by the usual acid/base treatment, afforded a brown syrup (5·1 g, 0·16%).

The chloroform extract B was evaporated to dryness and the residue, dissolved in 20 c.c. methanol, was poured into 10% acetic acid (250 c.c.). Filtration, basification (NaOH) and repeated extraction with chloroform afforded 4·0 g base (0·13%).  $R_F$  values (Whatman No. 1 paper developed in n-butanol/acetic acid/water in the ratio 80/3/17 by volume) were as follows:

A: ..... 0·47, [0·57], [0·63].

B: [0·16], 0·37, 0·52, 0·63, [0·75].

(Values in square brackets indicate minor spots only.)

The basic gum isolated from B was refluxed in dry acetone, cooled, and filtered. Recrystallization of the solid from ethanol gave *thelepogidine* as colourless needles, m.p. 254–255 °C (Found: C, 74·1; H, 10·0; O, 11·4; N, 4·6%. Calc. for  $\text{C}_{18}\text{H}_{28}\text{O}_2\text{N}$ : C, 74·2; H, 10·0; O, 11·0; N, 4·8%). The mother liquors were combined with the basic fraction from A, and chromatographed over alumina (neutral, activity I) in benzene. Continued elution with benzene (1·5 l.) afforded *thelepogine*, crystallizing from methanol/acetone in colourless needles, m.p. 184–185 °C (Found: C, 79·5; H, 10·8; N, 4·8; Me(C), 5·9%. Calc. for  $\text{C}_{20}\text{H}_{31}\text{ON}$ : C, 79·7; H, 10·4; N, 4·7; 1×Me(C), 5·0%). *Thelepogine methiodide*, formed by the action of methyl iodide on the base in acetone solution, crystallized from acetone/methanol in colourless prisms, m.p. 254–255 °C (Found: C, 57·0; H, 8·1; N, 3·0; I, 28·2;  $\text{CH}_3(\text{N})$ , 3·9%. Calc. for  $\text{C}_{20}\text{H}_{31}\text{ON} \cdot \text{CH}_3\text{I}$ : C, 56·9; H, 7·7; N, 3·2; I, 28·6;  $(\text{CH}_3)\text{N}$ , 3·4%).

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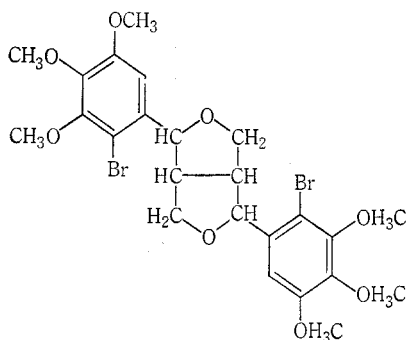
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## THE STEREOCHEMISTRY OF LIRIORESINOL-B\*

By E. N. MASLEN,† C. NOCKOLDS,† and M. PATON†

The gross structure of Lirioresinol-B dimethyl ether has been established by Dickey (1958) and independently by Jefferies, Knox, and White (1961). In addition evidence for the *cis*-fusion of the tetrahydrofuran rings was presented. Dickey, by consideration of the molecular rotation differences concluded that the stereochemical arrangement was probably identical with that in (+)-pinioresinol (Erdtman and Gripenberg 1947).



(1)

It was thought worth while investigating the molecular conformation by an independent means to confirm the probable structure. Accordingly an X-ray diffraction structure investigation was made of the 2,2'-dibromodimethyl ether derivative (I), kindly provided by Knox for this purpose. Assuming the *cis*-fusion of the tetrahydrofuran rings only three distinct stereochemical arrangements of the molecule are possible (II, III, IV).

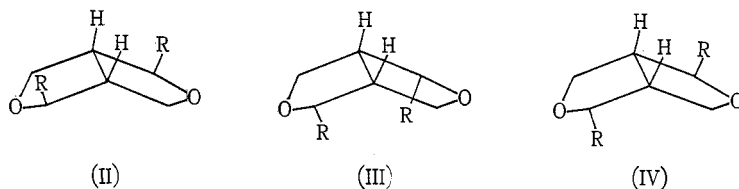
Crystals of the material prepared by slow recrystallization from ethanol were acicular in shape, and conformed to the orthorhombic system. A series

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of oscillation and zero and higher level Weissenberg photographs were taken. These showed that the unit cell belonged to space group  $P_{2,2,2}$  and from them the cell dimensions were found to be:  $a=16.7 \text{ \AA}$ ;  $b=15.8 \text{ \AA}$ ;  $c=4.70 \text{ \AA}$ .

An approximate density determination showed that there were two molecules in the unit cell, and hence half a molecule in the asymmetric unit. This is possible only if the molecule contains a twofold rotation axis of symmetry,



which enables structure (IV) to be eliminated. Moreover the cell dimension in the direction of the rotation axis, which sets a limit to the thickness of the molecule in that direction, is  $4.70 \text{ \AA}$ . This, as may readily be shown from a model, is incompatible with structure (III). Structure (II) must therefore be the correct molecular configuration.

As this is in full agreement with the stereochemical arrangement postulated by Dickey from the molecular rotation differences, no further work on the structure is contemplated.

#### References

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