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SHORT COMMUNICATION

The relationship between thin-layer chromatographic behaviour and the stereochemistry of some heteroyohimbine alkaloids

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A NUMBER of thin-layer chromatography systems have been used to distinguish and identify some indole and oxindole alkaloids isolated from various species of the genus *Mitragyna* (Shellard & Phillipson, 1964). It has been suggested moreover that a relationship exists between the stereochemistry of these alkaloids and their behaviour on thin-layer chromatograms (Phillipson & Shellard, 1966). Two new heteroyohimbine alkaloids, mitrajavine and hirsutine, have recently been isolated from *Mitragyna* species (Shellard, Beckett, Tantivatana, Phillipson & Lee, 1966) and their behaviour on thin-layers has been compared with some related alkaloids of known stereochemistry. Based on this, certain suggestions have been made about the stereochemistry of these two new alkaloids.

EXPERIMENTAL

Details of plate preparation, development of the chromatograms and detection of the alkaloids have already been published (Phillipson & Shellard, 1966). The following systems were used: 1, silica gel, benzene–ethyl acetate (7:2); 2, alumina, chloroform–benzene (1:1); 3, alumina, chloroform–benzene–diethylamine (1:1:0·001); 4, alumina, benzene–ethyl acetate (7:2); 5, alumina, ether; 6, silica gel, ether; 7, silica gel, chloroform–acetone (5:4); 8, alumina, cyclohexane–chloroform (3:7); 9, alumina, cyclohexane–chloroform–diethylamine (3:7:0·005); 10, silica gel, benzene–ethyl acetate–diethylamine (7:2:1).

RESULTS

The results of the separations obtained are illustrated in Fig. 1A and B. The Rf values were determined by averaging the results from six separate determinations.

DISCUSSION

It has been proposed that all naturally occurring heteroyohimbine alkaloids of the corynantheidine type (I) and of the ajmalicine type (II) have C(15)-Hα as a common stereochemical factor (Wenkert & Bringi, 1959). Individual alkaloids of each type may differ in the following particulars:

(*a*) Substituents in positions 9, 10, 11, 12 (I, II).

(*b*) Different configurations at C(3) and C(20) giving four possible isomers classified thus: allo, C(3)-Hα; C(20)-Hα: epiallo, C(3)-Hβ;

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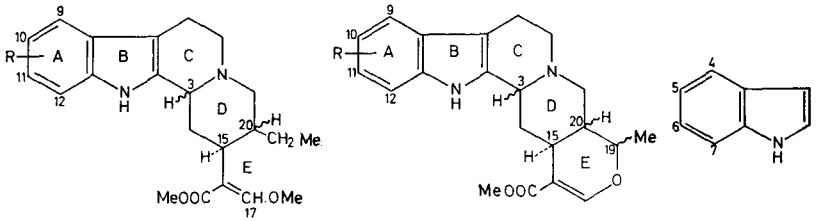

I II III

C(20)-Hα: normal, C(3)-Hα; C(20)-Hβ: pseudo, C(3)-Hβ; C(20)-Hβ (Saxton, 1956, 1960).

(*c*) C(17)-H *cis* or *trans* to the carbomethoxy group in E seco alkaloids (I).

(*d*) C(19) - Me α or β in closed E ring alkaloids (II).

Six heteroyohimbine alkaloids (I) of known stereochemistry have been examined by the ten thin-layer systems given above. It has been proposed

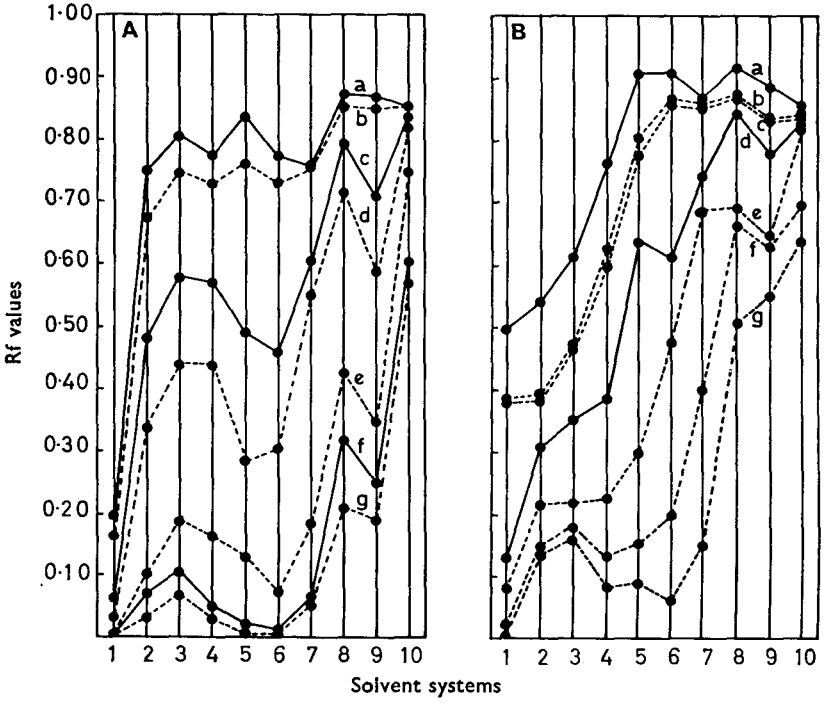

FIG. 1A. Rf values of (*a*) corynantheidine (I, R = H, allo), (*b*) mitragynine (I, R = 9 — OMe, allo), (*c*) dihydrocorynantheine (I, R = H, normal), (*d*) speciogynine (I R = 9 — OMe, normal), (*e*) speciociliatine (I, R = 9 — OMe, epiallo), (*f*) hirsutine (I, R = H), (*g*) mitraciliatine (I, R = 9 — OMe, pseudo).

FIG. 1B. Rf values of (*a*) tetrahydroalstonine (II, R = H, allo), (*b*) aricine (II, R = 10 — OMe, allo), (*c*) reserpinine (II, R = 11 — OMe, allo), (*d*) ajmalicine (II, R = H, normal), (*e*) tetraphylline (II, R = 11 — OMe, normal), (*f*) isoreserpinine (II, R = 11 — OMe, epiallo), (*g*) mitrajavine (II, R = 9 — OMe).

that these alkaloids have the C(17)-H *cis* to the carbomethoxy group as a common stereochemical factor (Weisbach, Kirkpatrick, Williams, Anderson, Yim & Douglas, 1965; Phillipson, 1965; Lee, Trager & Beckett, personal communication). The alkaloids differ from each other as follows: corynantheidine (I, R = H), allo (van Tamelen, Aldrich & Katz, 1956); mitragynine (I, R = 9-OMe), allo (Joshi, Raymond-Hamet & Taylor, 1963; Zacharias, Rosenstein & Jeffrey, 1965); dihydrocorynantheine (I, R = H), normal (Wenkert & Bringi, 1959); speciogynine (I, R = 9-OMe), normal; speciociliatine (I, R = 9-OMe), epiallo; mitraciliatine (I, R = 9-OMe), pseudo (Lee, Trager & Beckett, personal communication).

Fig. 1 shows that when the 9-methoxy substituted alkaloids are arranged in order of decreasing Rf values, the sequence is allo, normal, epiallo and pseudo. The allo and normal alkaloids (I, R = H) have higher Rf values than the two 9-methoxy alkaloids with the corresponding stereochemistry. Hirsutine has been shown to be an isomer of the corynantheidine type (I, R = H) (Shellard & others, 1966). If it is assumed that hirsutine has the same stereochemistry across the double bond as the other six alkaloids, i.e. C(17)-H *cis* to the carbomethoxy group, then hirsutine can differ from corynantheidine (allo) or dihydrocorynantheine (normal) by being an epiallo or pseudo compound. Fig. 1 shows that in the ten thin-layer systems used, hirsutine has slightly higher Rf values than mitraciliatine but lower Rf values than speciociliatine. These observations suggest that hirsutine is stereochemically similar to mitraciliatine in having the pseudo configuration.

Six heteroyohimbine alkaloids of the ajmalicine type (II) and of known stereochemistry have been examined by the same ten thin-layer systems. The alkaloids differ from each other as follows: tetrahydroalstonine (II, R = H), allo; aricine (II, R = 10-OMe), allo; reserpinine (II, R = 11-OMe), allo; ajmalicine (II, R = H), normal; tetraphylline (II, R = 11-OMe), normal; isoreserpinine (II, R = 11-OMe), epiallo (Wenkert, Wickberg & Leicht, 1961; Shamma & Moss 1961, 1962). C(19)-Meα is a common stereochemical factor in these alkaloids.

Fig. 1B shows that when the 11-methoxy substituted alkaloids are arranged in order of decreasing Rf values then the sequence of allo, normal and epiallo is the same as with the E seco alkaloids. It is probable therefore, that the behaviour of the pseudo alkaloid in this series would be similar in having the lowest Rf values. The allo and normal alkaloids (II, R = H) have higher Rf values than the two 11-methoxy alkaloids (II, R = 11-OMe) with the corresponding stereochemistry. When indole (III) and some methoxy indoles were examined by thin-layer systems 1–6, the sequence in order of decreasing Rf value was indole, 4-, 5- and 6-methoxyindole. If the thin-layer behaviour of these simple indoles can be related to the heteroyohimbine alkaloids then the expected sequence in order of decreasing Rf value would be 9-, 10- and 11-methoxy The case of aricine (II, R = 10-OMe, allo) which has Rf values slightly higher than those of reserpinine (H, R = 11-OMe, allo), agrees with this suggestion.

Mitrajavine has been shown to be of the ajmalicine type (II, R = 9-OMe) (Shellard & others, 1966). It would be expected that on these ten thin-layer systems, the Rf values of mitrajavine would be higher than those of the 11-methoxy substituted alkaloid with an identical stereochemistry. Fig. 1B shows that mitrajavine has lower Rf values than the 11-methoxy substituted alkaloids of the allo, normal and epiallo configurations, thus *if it be assumed that mitrajavine has a C*(19)*-Me α-configuration*, then its behaviour on these ten thin-layer systems suggests that it is a pseudo compound.

These results tentatively suggest that in heteroyohimbine alkaloids there appears to be a relationship between alkaloidal structure and thin-layer chromatographic behaviour, as follows:

1. Methoxy substituents lower Rf values.
2. Rf values of 10-substituted alkaloids of allo configuration and with a closed E ring (II), are slightly higher than the corresponding 11-substituted alkaloid.
3. The E seco alkaloids (I) can be arranged in order of decreasing Rf values as allo, normal, epiallo and pseudo.
4. The closed E ring alkaloids (II) can be arranged in order of decreasing Rf values as allo, normal and epiallo.

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