CHAPTER II

HISTORICAL

1. Alkaloids isolated from species of *Uncaria*

The alkaloids reported to be present in the leaves of *Uncaria attenuata* Korth. by Phillipson and Hemingway (1975b) and Phillipson *et al.* (1978) are :-

3-isoajmalicine

19-epi-3-isoajmalicine

akuammigine

dihydrocorynantheine

hirsutine

hirsuteine

epiallo-corynantheine

isomitraphylline and its N-oxide

mitraphylline and its N-oxide

uncarine A (isoformosanine)

uncarine B (formosanine)

speciophylline

isorhynchophylline and its N-oxide

rhynchophylline and its N-oxide

isocorynoxeine

corynoxeine

rotundifoline

isorotundifoline

corynoxine B

speciofoline

harmane

pseudoyohimbine

yohimbine isomer

yohimbine oxindole (M^+ 370)

dihydrocorynantheine pseudoindoxyl

and unidentified indole alkaloid (M^+ 347).

Phillipson and Hemingway (1975b) and Phillipson *et al.* (1978) have reported that the alkaloids found in the stem bark and stem wood of *Uncaria attenuata* Korth. are :-

dihydrocorynantheine

hirsutine

hirsuteine

isorhynchophylline and its N-oxide

rhynchophylline and its N-oxide

isocorynoxeine

corynoxeine

pseudoyohimbine

yohimbine isomer

yohimbine oxindole

and unidentified oxindole alkaloid.

The alkaloids which have been reported as being found in other species of *Uncaria* are summarised as follows (abbreviation of plant parts shown on p. 62) :-

U. acida (Hunt.) Roxb.

[*U. acida* (Hunt.) Roxb. var. *acida* Roxb.*]

Plant Part	Alkaloid	Reference
l	isorhynchophylline rhynchophylline and its N-oxide harmane	Phillipson *et al.*, 1978

U. acida (Hunt.) Roxb. var. *papuana* Val.*

Plant Part	Alkaloid	Reference
l	3-isoajmalicine isorhynchophylline and its N-oxide rhynchophylline and its N-oxide corynoxeine	Phillipson *et al.*, 1978.
l/st	isomitraphylline mitraphylline speciophylline	

Uncaria acida (Hunt.) Roxb. var. *papuana* Val.* (continued)

Plant Part	Alkaloid	Reference
l/st	isorhynchophylline rhynchophylline	Phillipson *et al.*, 1978.

U. africana (G. Don) Baill.

[*U. africana* G. Don ssp. *africana* G. Don*]

Plant Part	Alkaloid	Reference
l	ajmaliciñe 3-isoajmalicine 19-epi-ajmalicine tetrahydroalstonine dihydrocorynantheine isomitraphylline mitraphylline and its N-oxide isorhynchophylline rhynchophylline dihydrocorynantheine pseudoindoxyl	Phillipson *et al.*, 1978.
l/st	africanine	Saxton, 1968; Phillipson *et al.*, 1978.

Uncaria africana (G. Don) Baill. var. *domatifera* Petit

[*U. africana* G. Don ssp. *africana* G. Don*]

Plant Part	Alkaloid	Reference
l	ajmalicine 3-isoajmalicine 19-epi-3-isoajmalicine isomitraphylline mitraphylline	Phillipson *et al.*, 1978.

U. africana (G. Don) Baill. var. *xerophila* Petit

[*U. africana* G. Don ssp. *africana* G. Don*]

Plant Part	Alkaloid	Reference
l	isomitraphylline mitraphylline	Phillipson *et al.*, 1978.

Uncaria angolensis Welw.

[*U. africana* G. Don ssp. *angolensis* (Havil.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isorhynchophylline and its N-oxide rhynchophylline and its N-oxide	Phillipson *et al.*, 1978.

U. appendiculata Benth.

[*U. lanosa* Wall. var. *appendiculata* (Benth.) Ridsd. f. *appendiculata* (Benth.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide mitraphylline isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.
st	isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	

Uncaria avenia Val.

[*U. callophylla* Bl. ex Korth.*]

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine isorhynchophylline rhynchophylline	Phillipson *et al.*, 1978.
st	isorhynchophylline	

U. barbata Merr.*

Plant Part	Alkaloid	Reference
l	harmane	Phillipson *et al.*, 1978.
fr	same as in the leaves	

U. bernaysii F. v. Muell.*

Plant Part	Alkaloid	Reference
l	tetrahydroalstonine akuammigine	Phillipson and Hemingway, 1973a, b; Phillipson *et al.*, 1978.

Uncaria bernaysii F. v. Muell.* (continued)

Plant Part	Alkaloid	Reference
l	isopteropodine	Johns and Lamberton, 1966; Beecham *et al.*, 1968; Phillipson and Hemingway, 1973b; Phillipson *et al.*, 1978.
	pteropodine	
	speciophylline	
	uncarine F	
	isopteropodine N-oxide	Phillipson and Hemingway, 1973a, b; Phillipson *et al.*, 1978.
	pteropodine N-oxide	
	speciophylline N-oxide	
	uncarine F N-oxide	
st	tetrahydroalstonine	Phillipson and Hemingway, 1973a, b; Phillipson *et al.*, 1978.
	akuammigine	
	isopteropodine N-oxide	
	pteropodine N-oxide	
	speciophylline N-oxide	
	uncarine F N-oxide	
fl	ajmalicine	Phillipson *et al.*, 1978.
	3-isoajmalicine	
	tetrahydroalstonine	Phillipson and Hemingway, 1973a, b; Phillipson *et al.*, 1978.
	akuammigine	
	isomitraphylline	Phillipson *et al.*, 1978.
	mitraphylline	

Uncaria bernaysii F. v. Muell.* (continued)

Plant Part	Alkaloid	Reference
fl	isopteropodine	Johns and Lamberton, 1966; Beecham *et al.*, 1968; Phillipson and Hemingway, 1973b; Phillipson *et al.*, 1978.
	pteropodine	
	speciophylline	
	uncarine F	
	isopteropodine N-oxide	Phillipson and Hemingway, 1973a, b; Phillipson *et al.*, 1978.
	pteropodine N-oxide	
	speciophylline N-oxide	
	uncarine F N-oxide	
	angustine	Phillipson *et al.*, 1974, 1978.
h	isopteropodine and its N-oxide	Phillipson and Hemingway, 1973a.
	pteropodine and its N-oxide	
	speciophylline and its N-oxide	
	uncarine F and its N-oxide	

Uncaria bernaysii F. v. Muell. f. *inermis* K. Schum.

[*U. bernaysii* F. v. Muell.*]

Plant Part	Alkaloid	Reference
1	isorhynchophylline and its N-oxide rhynchophylline and its N-oxide	Phillipson *et al.*, 1978.

U. bernaysioides Merr. et Perry

[*U. bernaysii* F. v, Muell.*]

Plant Part	Alkaloid	Reference
1	isorhynchophylline and its N-oxide rhynchophylline and its N-oxide	Phillipson *et al.*, 1978.

U. borneensis Havil.*

Plant Part	Alkaloid	Reference
1	harmane	Phillipson *et al.*, 1978.

Uncaria brevicarpa Elm.

[*U. roxburghiana* Korth.*]

Plant Part	Alkaloid	Reference
l	isopteropodine and its N-oxide	Phillipson *et al.*, 1978.
	pteropodine and its N-oxide	
	speciophylline and its N-oxide	
	uncarine F and its N-oxide	
fr/se	speciophylline	

U. bulusanensis Elm.

[*U. attenuata* Korth.*]

Plant Part	Alkaloid	Reference
l	19-epi-3-isoajmalicine	Phillipson and Hemingway, 1975b.
	dihydrocorynantheine	Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.
	epiallo-corynantheine	
	rhynchophylline	Phillipson and Hemingway, 1975b;
	rotundifoline	Phillipson and Hemingway, 1975b.
	isorotundifoline	Phillipson *et al.*, 1978.

Uncaria bulusanensis Elm. (continued)

Plant Part	Alkaloid	Reference
l	corynoxine B speciofoline	Phillipson and Hemingway, 1975b.

U. callophylla Bl. ex Korth.*

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine	Phillipson *et al.*, 1978.
	gambirine	Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.
	isomitraphylline mitraphylline isorhynchophylline rhynchophylline harmane	Phillipson *et al.*, 1978.

Uncaria canescens Korth.*

Plant Part	Alkaloid	Reference
l	harmane	Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.
st	same as in the leaves	Phillipson *et al.*, 1978.

U. cordata (Lour.) Merr.

[*U. cordata* (Lour.) Merr. var. *cordata* Merr. f, *cordata* Merr.*]

Plant Part	Alkaloid	Reference
l	isorhynchophylline	Phillipson *et al.*, 1978.
	rhynchophylline	
st	same as in the leaves	
fl	same as in the leaves	

Uncaria dasyoneura Korth.

[*U. elliptica* R. Br. ex G. Don*]

Plant Part	Alkaloid	Reference
1	roxburghine D roxburghine E	Phillipson *et al.*, 1978.

U. donisii Petit*

Plant Part	Alkaloid	Reference
1	isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.

U. elliptica R. Br. ex G. Don*

Plant Part	Alkaloid	Reference
1	roxburghines	Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.

Uncaria ferrea (Bl.) DC.

[*U. lanosa* Wall. var. *ferrea* (Bl.) Ridsd. f. *ferrea* (Bl.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline	Johns and Lamberton, 1966; Phillipson *et al.*, 1978.
	mitraphylline	
	isopteropodine	Beecham *et al.*, 1966; Johns and Lamberton, 1966; Phillipson *et al.*, 1978.
	pteropodine	
	speciophylline	
	uncarine F	
	mitraphylline N-oxide	
	isopteropodine N-oxide	
	pteropodine N-oxide	
	speciophylline N-oxide	
	uncarine F N-oxide	
	harmane	
st	isopteropodine and its N-oxide	Phillipson *et al.*, 1978.
	pteropodine and its N-oxide	
	speciophylline and its N-oxide	
	uncarine F	
	harmane	
fl	isomitraphylline	
	mitraphylline and its N-oxide	
	isopteropodine	

Uncaria ferrea (Bl.) DC. (continued)

Plant Part	Alkaloid	Reference
fl	pteropodine	Phillipson *et al.*, 1978.
	speciophylline and its N-oxide	
	uncarine F	
fr/se	isopteropodine	
	pteropodine	
	speciophylline	
	uncarine F	

U. ferruginea (Bl.) DC.

[*U. cordata* (Lour.) Merr. var. *ferruginea* (Bl.) Ridsd.
f. *ferruginea* (Bl.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine	Phillipson *et al.*, 1978.
st	same as in the leaves	
fl	same as in the leaves	

Uncaria florida Vidal

[*U. lanosa* Wall. var. *appendiculata* (Benth.) Ridsd.
f. *setiloba* (Benth.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isopteropodine	Aimi *et al.*, 1972;
	pteropodine	Phillipson *et al.*, 1978.
	speciophylline	Phillipson *et al.*, 1978.

U. formosana (Matsum.) Hayata

[*U. hirsuta* Havil.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide	Phillipson *et al.*, 1978.
	mitraphylline and its N-oxide	
	uncarine A	
	uncarine B	
st	gambirine	Willaman and Schubert, 1961.
	mitragynine	
	mitraphylline	
	uncarine B	Saxton, 1960; Willaman and Schubert, 1961.

Uncaria formosana (Matsum.) Hayata (continued)

Plant Part	Alkaloid	Reference
st	rhynchophylline	Willaman and Schubert, 1961.
	rotundifoline	
	isorotundifoline	
	mitraversine	
fl	3-isoajmalicine	Phillipson *et al.*, 1978.
	isomitraphylline	
	mitraphylline	
	uncarine A	
	uncarine B	

U. gambir (Hunt.) Roxb.*

Plant Part	Alkaloid	Reference
l	tetrahydroalstonine	Phillipson *et al.*, 1978.
	dihydrocorynantheine	Merlini *et al.*, 1970, 1972b; Phillipson *et al.*, 1978.
	gambirine	Merlini *et al.*, 1967a, 1970, 1972a; Phillipson *et al.*, 1978.

Uncaria gambir (Hunt.) Roxb.* (continued)

Plant Part	Alkaloid	Reference
l	isorhynchophylline	Merlini *et al.*, 1970, 1972a; Phillipson *et al.*, 1978.
	rhynchophylline	
	rotundifoline	
	roxburghine A	Merlini *et al.*, 1970; Phillipson *et al.*, 1978.
	roxburghine B	
	roxburghine C	
	roxburghine D	
	roxburghine E	
st	tetrahydroalstonine	Merlini *et al.*, 1970, 1972b; Phillipson *et al.*, 1978.
	4-R-tetrahydroalstonine N-oxide	Merlini *et al.*, 1972b.
	akuammigine	
	4-R-akuammigine N-oxide	Merlini *et al.*, 1972b; Phillipson *et al.*, 1978.
	4-S-akuammigine N-oxide	
	dihydrocorynantheine	Merlini *et al.*, 1970.
	gambirine	Phillipson *et al.*, 1978.
	mitraphylline	Chan, 1968; Phillipson *et al.*, 1978.
	roxburghine B	Merlini *et al.*, 1972b.
	roxburghine D	Merlini *et al.*, 1970, 1972b.
	roxburghine E	Merlini *et al.*, 1970.

Uncaria gambir (Hunt.) Roxb.* (continued)

Plant Part	Alkaloid	Reference
st	isogambirdine	Chan, 1968; Merlini *et al.*, 1970, 1972a; Bindra, 1973; Phillipson *et al.*, 1978.
	gambirdine	
gambir	gambirine	Merlini *et al.*, 1967a; Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.
	gambirtannine	Merlini *et al.*, 1967b; Phillipson and Hemingway, 1973d; Phillipson *et al.*, 1978.
	oxogambirtannine	
	dihydrogambirtannine	
	neo-oxygambirtannine	Saxton, 1968.
	ourouparine	Saxton, 1968; Phillipson and Hemingway, 1973d.

Uncaria gambir Thw.

[*U. elliptica* R. Br. ex G. Don*]

Plant Part	Alkaloid	Reference
l	3-isoajmalicine	Phillipson *et al.*, 1978.
	dihydrocorynantheine	
	gambirine	
	isorhynchophylline	
	rhynchophylline	
	rotundifoline	
	isorotundifoline	
	roxburghine C	
	roxburghine D	
	roxburghine E	
	harmane	
st	dihydrocorynantheine	

Uncaria glabrata (Bl.) DC.

[*U. lanosa* Wall. var. *glabrata* (Bl.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.
st	speciophylline	

U. glabrescens Merr. et Perry

[*U. lanosa* Wall. var. *appendiculata* (Benth.) Ridsd.
f. *glabrescens* (Merr. et Perry) Ridsd.*]

Plant Part	Alkaloid	Reference
l	akuammigine isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978

Uncaria guianensis (Aubl.) Gmel.*

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine	Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978
	hirsutine	
	hirsuteine	
	isomitraphylline and its N-oxide	Phillipson *et al.*, 1978.
	mitraphylline and its N-oxide	Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.
	isorhynchophylline and its N-oxide	
	rhynchophylline	Saxton, 1960; Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.
	rhynchophylline N-oxide	Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.
	angustine	Phillipson *et al.*, 1974, 1978.
	angustoline	Phillipson *et al.*, 1978.
st	dihydrocorynantheine	Phillipson *et al.*, 1978
	hirsutine	
	hirsuteine	
	mitraphylline	
	isorhynchophylline	

Uncaria guianensis (Aubl.) Gmel.* (continued)

Plant Part	Alkaloid	Reference
st	rhynchophylline and its N-oxide	Phillipson *et al.*, 1978.
	angustine	
	angustoline	Phillipson *et al.*, 1974, 1978.
fl	same as in the stem	

U. hallii Korth.

[*U. cordata* (Lour.) Merr. var. *ferruginea* (Bl.) Ridsd. f. *insignis* (Bart. in DC.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isorhynchophylline	Phillipson *et al.*, 1978.
	rhynchophylline	

U. homomalla Miq.*

Plant Part	Alkaloid	Reference
l	tetrahydroalstonine	Vitayanatpaisan, 1979.
	3-isoajmalicine	Phillipson *et al.*, 1978.

Uncaria homomalla Miq.* (continued)

Plant Part	Alkaloid	Reference
l	isomitraphylline	Phillipson *et al.*, 1978.
	mitraphylline	
	isopteropodine	Ponglux *et al.*, 1977; Phillipson *et al.*, 1978 Vitayanatpaisan, 1979.
	pteropodine	
	speciophylline	
	uncarine F	
	isopteropodine N-oxide	Phillipson *et al.*, 1978
	pteropodine N-oxide	
	speciophylline N-oxide	
	uncarine F N-oxide	
	angustine	Phillipson *et al.*, 1974, 1978.
	angustoline	
	angustidine	
st	isomitraphylline	Phillipson *et al.*, 1978.
	isopteropodine and its N-oxide	
	pteropodine and its N-oxide	
	speciophylline and its N-oxide	
	uncarine F and its N-oxide	
	angustine	
	angustoline	
	angustidine	

Uncaria hookeri Val.

[*U. perrottetii* (A. Rich.) Merr.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline mitraphylline and its N-oxide isopteropodine pteropodine speciophylline uncarine F	Phillipson *et al.*, 1978.

U. jasminiflora Hook. f.

[*U. callophylla* Bl. ex Korth.*]

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine gambirine isomitraphylline mitraphylline isorhynchophylline rhynchophylline	Phillipson *et al.*, 1978.

Uncaria kawakamii Hayata

[*U. lanosa* Wall. var. *appendiculata* (Benth.) Ridsd, f. *philippinensis* (Elm.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isopteropodine and its N-oxide	Phillipson *et al.*, 1978.
	pteropodine and its N-oxide	
	speciophylline and its N-oxide	
	uncarine F and its N-oxide	
st	mitraphylline	Kariyone, 1958; Nozoye, 1958b; Chan *et al.*, 1966.
	uncarine A	Kariyone, 1958; Saxton, 1960; Yeoh *et al.*, 1966; Chan *et al.*, 1966.
	uncarine B	Nozoye, 1958a; Saxton, 1960; Yeoh *et al.*, 1966; Chan *et al.*, 1966.
	hanadamine	Saxton, 1960; Willaman and Schubert, 1961.

Uncaria kawakamii Hayata (continued)

Plant Part	Alkaloid	Reference
r	same as in the stem	Kariyone, 1958; Nozoye, 1958a, b; Saxton, 1960; Willaman and Schubert, 1961; Yeoh *et al.*, 1966; Chan *et al.*, 1966.
sb	same as in the stem	
fr/se	uncarine F	Nozoye, 1958a.

U. korrensis Kanehira

[*U. lanosa* Wall. var. *korrensis* (Kanehira) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide mitraphylline and its N-oxide isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.

Uncaria kunstleri King*

Plant Part	Alkaloid	Reference
l	hirsutine isorhynchophylline and its N-oxide rhynchophylline and its N-oxide corynoxine corynoxine B	Phillipson *et al.*, 1978.
l/tw	isorhynchophylline rhynchophylline	

U. laevifolia Elm.

[*U. longiflora* (Poir.) Merr. var. *pteropoda* (Miq.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline mitraphylline isopteropodine pteropodine speciophylline uncarine F	Phillipson *et al.*, 1978.

Uncaria laevigata Wall. ex G. Don*

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide mitraphylline and its N-oxide uncarine A uncarine B isopteropodine speciophylline	Phillipson *et al.*, 1978.

U. lancifolia Hutch.*

Plant Part	Alkaloid	Reference
l	isomitraphylline mitraphylline and its N-oxide	Phillipson *et al.*, 1978.

Uncaria lanosa Wall.

[*U. lanosa* Wall. var. *lanosa* Wall.*]

Plant Part	Alkaloid	Reference
l	isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.

U. lobbii Hook. f.

[*U. lanosa* Wall. var. *glabrata* (Bl.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isopteropodine pteropodine speciophylline and its N-oxide uncarine F	Phillipson *et al.*, 1978.

Uncaria longiflora (Poir.) Merr.

[*U. longiflora* (Poir.) Merr. var. *longiflora* Merr.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide mitraphylline and its N-oxide isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F	Phillipson and Hemingway, 1973b; Phillipson *et al.*, 1978.
	uncarine F N-oxide isorhynchophylline and its N-oxide rhynchophylline isocorynoxeine or corynoxine corynoxeine or corynoxine B	Phillipson *et al.*, 1978.
st	isorhynchophylline and its N-oxide rhynchophylline and its N-oxide	

Uncaria macrophylla Wall.*

Plant Part	Alkaloid	Reference
l	isorhynchophylline	Phillipson and Hemingway, 1973c; Phillipson *et al.*, 1978
	rhynchophylline	
	isorhynchophylline N-oxide	Phillipson *et al.*, 1978.
	rhynchophylline N-oxide	
	corynoxine	Phillipson and Hemingway, 1973c; Phillipson *et al.*, 1978
	corynoxine B	
st	same as in the leaves	Shellard *et al.*, 1978a.

U. orientalis Guill.*

Plant Part	Alkaloid	Reference
l	ajmalicine	Phillipson *et al.*, 1978.
	3-isoajmalicine	Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.
	19-epi-3-isoajmalicine	Phillipson *et al.*, 1978.
	akuammigine	

Uncaria orientalis Guill.* (continued)

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide mitraphylline and its N-oxide isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide harmane	Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978.
st fl	harmane isopteropodine pteropodine speciophylline	Phillipson *et al.*, 1978.

U. ovata Hook. f.

[*U. canescens* Korth.*]

Plant Part	Alkaloid	Reference
l	harmane	Phillipson *et al.*, 1978.

Uncaria parviflora Ridl

[*U. homomalla* Miq.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide	Phillipson *et al.*, 1978.
	mitraphylline and its N-oxide	
	isopteropodine	
	pteropodine	
	speciophylline	
	uncarine F	
	angustine	
	angustoline	
	angustidine	
st	isomitraphylline	
	mitraphylline	
	angustine	
	angustoline	
	angustidine	

Uncaria pedicellata Roxb.

[*U. cordata* (Lour.) Merr. var. *cordata* Merr. f. *cordata* Merr.*]

Plant Part	Alkaloid	Reference
l	isorhynchophylline rhynchophylline corynoxine corynoxine B	Phillipson *et al.*, 1978.

U. perrottetii (A. Rich.) Merr.*

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide mitraphylline and its N-oxide isopteropodine pteropodine speciophylline uncarine F	Phillipson *et al.*, 1978.

Uncaria philippinensis Elm.

[*U. lanosa* Wall. var. *appendiculata* (Benth.) Ridsd. f. *philippinensis* (Elm.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isopteropodine pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.

U. pilosa Roxb,

[*U. scandens* (Smith) Hutch.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide mitraphylline and its N-oxide isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide unoarine F	Phillipson *et al.*, 1978.

Uncaria pteropoda Miq.

[*U. longiflora* (Poir.) Merr. var. *pteropoda* (Miq.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide	Phillipson *et al.*, 1978.
	mitraphylline and its N-oxide	
	isopteropodine and its N-oxide	
	pteropodine and its N-oxide	
	speciophylline and its N-oxide	
	uncarine F	
	isorhynchophylline	
	rhynchophylline	
	isocorynoxeine	
	corynoxeine	
st	isopteropodine	Yeoh *et al.*, 1966; Chan *et al.*, 1966.
	pteropodine	
sb	same as in the stem	
r	same as in the stem	

Uncaria quadrangularis Geddes

[*U. homomalla* Miq.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline	Tantivatana *et al.*, 1979.
	mitraphylline	
sb	isopteropodine	
	pteropodine	

U. rhynchophylla (Miq.) Miq. ex Havil.*

Plant Part	Alkaloid	Reference
l	isorhynchophylline	Nozoye, 1958c; Saxton, 1960; Aimi *et al.*, 1972, 1977; Phillipson *et al.*, 1978.
	rhynchophylline	
	rhynchophylline N-oxide	Phillipson *et al.*, 1978.
	isocorynoxeine	
	corynoxeine	
	angustine	Phillipson *et al.*, 1974, 1978.
	angustoline	
	angustidine	

Uncaria rhynchophylla (Miq.) Miq. ex Havil.* (continued)

Plant Part	Alkaloid	Reference
st	mitragynine	Willaman and Schubert, 1961.
	rotundifoline	
	isorotundifoline	
	mitraversine	
st/r	dihydrocorynantheine	Phillipson *et al.*, 1978.
	corynantheine	
	hirsutine	
	hirsuteine	
	isorhynchophylline	
	rhynchophylline	
	isocorynoxeine	
	corynoxeine	
h	isorhynchophylline	Nozoye, 1958c; Saxton, 1965a.
	rhynchophylline	
wh	akuammigine	Aimi *et al.*, 1977.
	dihydrocorynantheine	Aimi *et al.*, 1972, 1977.
	corynantheine	
	hirsutine	
	hirsuteine	
	isocorynoxeine	
	corynoxeine	

Uncaria rhynchophylla (Miq.) Miq. ex Havil.* (continued)

Plant Part	Alkaloid	Reference
wh	geissoschizine methyl ether	Aimi *et al.*, 1977.
-	uncarine A	Willaman and Schubert, 1961.

U. rhynchophylla (Miq.) Miq. ex Havil. var. *kouteng* Yamazaki

[*U. rhynchophylla* (Miq.) Miq. ex Havil.*]

Plant Part	Alkaloid	Reference
l	Isorhynchophylline and its N-oxide rhynchophylline isocorynoxeine corynoxeine angustine angustoline angustidine	Phillipson *et al.*, 1978.

Uncaria rostrata Pierre ex Pitard

[*U. elliptica* R. Br. ex G. Don*]

Plant Part	Alkaloid	Reference
l	3-isoajmalicine akuammigine roxburghine D	Phillipson *et al.*, 1978.

U. roxburghiana Korth.*

Plant Part	Alkaloid	Reference
l	isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F	Phillipson *et al.*, 1978.
st	isopteropodine and its N-oxide pteropodine speciophylline and its N-oxlde uncarine F	

Uncaria salaccensis Bakh. f. nom provis

[*U. attenuata* Korth.*]

Plant Part	Alkaloid	Reference
l	3-isoajmalicine 19-epi-3-isoajmalicine mitraphylline uncarine B	Wongseripipatana, 1979.

U. sclerophylla Havil.

[*U. cordata* (Lour.) Merr. var. *ferruginea* (Bl.) Ridsd. f. *leiantha* Risds.*]

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine isorhynchophylline rhynchophylline	Phillipson *et al.*, 1978.

Uncaria sessilifructus Roxb.*

Plant Part	Alkaloid	Reference
1	3-isoajmalicine 19-epi-3-isoajmalicine akuammigine hirsutine isomitraphylline and its N-oxide mitraphylline and its N-oxide uncarine A uncarine B uncarine F isorhynchophylline rhynchophylline corynoxine corynoxine B	Phillipson *et al.*, 1978.

Uncaria setiloba Benth.

[*U. lanosa* Wall. var. *appendiculata* (Benth.) Ridsd. f. *setiloba* (Benth.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.
st	same as in the leaves	

U. sinensis (Oliv.) Havil.*

Plant Part	Alkaloid	Reference
l	akuammigine isopteropodine and its N-oxide pteropodine and its N-oxide speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.
fr/se	same as in the leaves	

Uncaria sterrophylla Merr. et Perry*

Plant Part	Alkaloid	Reference
l	3-isoajmalicine	Phillipson *et al.*, 1978.
	isomitraphylline	
	mitraphylline	
	isopteropodine	
	pteropodine	
	speciophylline and its N-oxide	
	uncarine F	
	isorhynchophylline	
	rhynchophylline	
st	isopteropodine	
	pteropodine	
	speciophylline	
	isorhynchophylline	
	rhynchophylline	
sb	isopteropodine	
	pteropodine	
	speciophylline	
	uncarine F	
	isorhynchophylline	
	rhynchophylline	
sw	isorhynchophylline	
	rhynchophylline	

Uncaria talbotii Wernh.*

Plant Part	Alkaloid	Reference
l	isorhynchophylline	Phillipson *et al.*, 1978.
	rhynchophylline	
fl	same as in the leaves	

U. tomentosa (Willd.) DC.*

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine and its N-oxide	Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.
	hirsutine and its N-oxide	
	hirsuteine	
	isomitraphylline	Phillipson *et al.*, 1978.
	isomitraphylline N-oxide	Hemingway and Phillipson, 1974.
	mitraphylline	Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.
	isorhynchophylline and its N-oxide	
	rhynchophylline and its N-oxide	
	rotundifoline	
	isorotundifoline	

Uncaria tomentosa (Willd.) DC.* (continued)

Plant Part	Alkaloid	Reference
st	dihydrocorynantheine and its N-oxide	Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.
	hirsutine and its N-oxide	
	hirsuteine	
	isomitraphylline	
	isomitraphylline N-oxide	Hemingway and Phillipson, 1974.
	mitraphylline	Hemingway and Phillipson, 1974; Phillipson *et al.*, 1978.
	isorhynchophylline and its N-oxide	
	rhynchophylline and its N-oxide	
	rotundifoline	
	isorotundifoline	
fl	dihydrocorynantheine	Phillipson *et al.*, 1978.
	hirsutine	
	hirsuteine	
	isomitraphylline	
	mitraphylline	
	isorhynchophylline and its N-oxide	
	rhynchophylline and its N-oxide	

Uncaria tomentosa (Willd.) DC.* (continued)

Plant Part	Alkaloid	Reference
fl	rotundifoline isorotundifoline	Phillipson *et al.*, 1978.

U. tonkinensis Havil.

[*U. homomalla* Miq.*]

Plant Part	Alkaloid	Reference
l	angustine angustoline angustidine	Phillipson *et al.*, 1978.

Uncaria toppingii Merr.

[*U. lanosa* Wall. var. *toppingii* (Merr.) Ridsd.
f. *toppingii* (Merr.) Ridsd.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline and its N-oxide	Phillipson *et al.*, 1978.
	mitraphylline and its N-oxide	
	isopteropodine and its N-oxide	
	pteropodine	
	speciophylline and its N-oxide	
	uncarine F	
st	isomitraphylline	
	mitraphylline	
	isopteropodine	
	speciophylline	
fl	isomitraphylline	
	mitraphylline	
	isopteropodine	
	pteropodine	
	speciophylline	
	uncarine F	

Uncaria valetoniana Merr. et Perry

[*U. nervosa* Elm.*]

Plant Part	Alkaloid	Reference
l	dihydrocorynantheine hirsutine hirsuteine	Phillipson *et al.*, 1978.

U. velutina Havil.

[*U. canescens* Korth.*]

Plant Part	Alkaloid	Reference
l	isomitraphylline mitraphylline	Phillipson *et al.*, 1978.
	isopteropodine and its N-oxide pteropodine and its N-oxide	Phillipson and Hemingway, 1975b;
	speciophylline and its N-oxide uncarine F and its N-oxide	Phillipson *et al.*, 1978.

* Indicates Ridsdale's accepted name

Plant part abbreviations :-

fl	=	flowers	sw	=	stem wood
fr	=	fruits	tw	=	twigs
h	=	hooks	wh	=	whole plant
l	=	leaves	fr/se	=	fruits and seeds
r	=	roots	l/st	=	leaves and stems
sb	=	stem bark	l/tw	=	leaves and twigs
se	=	seeds	st/r	=	stems and roots
st	=	stems	-	=	not mentioned.

2. *Uncaria* alkaloids isolated from other botanical sources

2.1 Heteroyohimbine alkaloids

2.1.1 Closed E ring heteroyohimbine alkaloids

Ajmalicine (δ-yohimbine, raubasine, py-tetrahydroserpentine)

- *Catharanthus lanceus* (Boj. ex A. DC.) Pich.
  (Saxton, 1960; Farnsworth, 1972; Taylor and Farnsworth, 1975).
- *C. longifolius* (Pich.) Pich.
  C. pusillus (Murray) G. Don
  (Taylor and Farnsworth, 1975).
- *C. roseus* (Linn.) G. Don
  (Saxton, 1960; Taylor and Farnsworth, 1975; Sarin *et al.*, 1975; Aren *et al.*, 1978).
- *C. trichophyllus* (Baker) Pich.
  (Rungsiyakul, 1973; Taylor and Farnsworth, 1975).

- *Corynanthe yohimbe* K. Schum.

  (Robinson and Thomas, 1954; Saxton, 1960;

  Taylor and Farnsworth, 1975).

- *Mitragyna javanica* Koord et Val.

  (Shellard, 1971).

- *M. javanica* Koord et Val. var. *microphylla* Koord et Val.

  (Shellard *et al.*, 1967a; Taylor and Farnsworth, 1975).

- *M. parvifolia* (Roxb.) Korth.

  (Shellard, 1971; Shellard and Houghton, 1972c).

- *M. speciosa* Korth.

  (Beckett *et al.*, 1966b; Trager *et al.*, 1968a; Shellard, 1971;

  Shellard *et al.*, 1978b, c).

- *Picralima nitida* (Stapf.) Th. et H. Durand

  (Robinson and Thomas, 1954).

- *Rauvolfia affinis* Muell. - Arg.

  (Schlittler, 1965).

- *R. amsoniaefolia* A. DC.

  (Rungsiyakul, 1973).

- *R. beddomei* Hook. f.

  (Saxton, 1960; Schlittler, 1965).

- *R. caffra* Sond.

  (Schlittler, 1965; Taylor and Farnsworth, 1975;

  Madati *et al.*, 1977).

- *R. canescens* Linn.

  (Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975).

- *Rauvolfia chinensis* (Hance) Hemsl.

  (Rungsiyakul, 1973; Taylor and Farnsworth, 1975).

- *R. cumminsii* Stapf.

  (Iwu and Court, 1978b).

- *R. fruticosa* Burck.

  (Schlittler, 1965).

- *R. heterophylla* Roem. et Schult.

  (Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975).

- *R. javanica* Koord et Val.

  (Schlittler, 1965).

- *R. ligustrina* Roem. et Schult.

  (Müller, 1957; Schlittler, 1965).

- *R. micrantha* Hook. f.

  (Saxton, 1960; Willaman and Schubert, 1961; Schlittler, 1965;
  Taylor and Farnsworth, 1975).

- *R. mombasiana* Stapf.

  (Iwu and Court, 1978a).

- *R. nitida* Jacq.

  R. pentaphylla Ducke

  R. rosea K. Schum.

  (Willaman and Schubert, 1961; Schlittler, 1965).

- *R. sellowii* Muell. - Arg.

  (Hochstein, 1955; Saxton, 1960; Schlittler, 1965).

- *R. serpentina* Benth. ex Kurz.

  (Marion, 1952; Saxton, 1960; Schlittler, 1965;
  Taylor and Farnsworth, 1975; Sarin *et al.*, 1977).

- *Rauvolfia sumatrana* (Miq.) Jack.

  (Schlittler, 1965).

- *R. tetraphylla* Linn.

  (Taylor and Farnsworth, 1975).

- *R. verticillata* (Lour.) Baill.

  (Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975).

- *R. vomitoria* Afzel.

  (Marion, 1952; Schlittler, 1965; Taylor and Farnsworth, 1975).

- *R. yunnanensis* Tsaing

  Stemmadenia obovata K. Schum.

  (Taylor and Farnsworth, 1975).

- *Tonduzia longiflora* (A. DC.) Mgf.

  Vinca erecta Rgl. et Schmalh.

  (Rungsiyakul, 1973).

3-Isoajmalicine

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Shellard *et al.*, 1968b, 1969b; Shellard, 1971, 1974;
  Shellard and Houghton, 1972c).

- *M. rotundifolia* (Roxb.) O. Kuntze

  (Houghton and Shellard, 1974).

- *M. speciosa* Korth.

  (Shellard *et al.*, 1978c).

Tetrahydroalstonine

- *Alstonia constricta* F. v. Muell.

  (Saxton, 1965b; Beecham *et al.*, 1968;

  Taylor and Farnsworth, 1975).

- *A. scholaris* R. Br.

  (Dutta *et al.*, 1976).

- *Catharanthus lanceus* (Boj. ex A. DC.) Pich.

  (Saxton, 1965b; Farnsworth, 1972; Taylor and Farnsworth, 1975).

- *C. roseus* (Linn.) G. Don

  (Saxton, 1965b; Taylor and Farnsworth, 1975).

- *C. trichophyllus* (Baker) Pich.

  (Taylor and Farnsworth, 1975).

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Shellard, 1971; Shellard and Houghton, 1971, 1972c, 1974b).

- *Rauvolfia ligustrina* Roem. et Schult.

  (Müller, 1957; Taylor and Farnsworth, 1975).

- *R. obscura* K. Schum.

  (Timmins and Court, 1976a).

- *R. sellowii* Muell. - Arg.

  (Hochstein, 1955; Saxton, 1960, 1965b;

  Taylor and Farnsworth, 1975).

- *R. vomitoria* Afzel.

  (Taylor and Farnsworth, 1975; Sabri and Court, 1978).

- *Vinca major* Linn.

  (Rungsiyakul, 1973).

Rauniticine

- *Rauvolfia nitida* Jacq.

  (Salkin *et al.*, 1961).

Akuammigine (3-Isotetrahydroalstonine)

- *Alstonia scholaris* R. Br.

  (Boonchuay and Court, 1976).

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Shellard *et al.*, 1968a, b, 1969a, b; Shellard, 1971;

  Shellard and Houghton, 1972c, 1974b; Shellard and Lala, 1977).

- *M. speciosa* Korth.

  (Shellard *et al.*, 1978c).

- *Picralima nitida* (Stapf.) Th. et H. Durand

  (Henry, 1932; Robinson and Thomas, 1954; Saxton, 1960;

  Sarin *et al.*, 1977).

Akuammigine N-oxide

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Rungsiyakul, 1973; Shellard and Houghton, 1974b).

2.1.2 Open E ring heteroyohimbine alkaloids

Dihydrocorynantheine

- *Cephalanthus occidentalis* Linn.

  (Phillipson and Hemingway, 1974).

- *Corynanthe yohimbe* K. Schum.

  (Karrer *et al.*, 1952; Rungsiyakul, 1973).

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Shellard *et al.*, 1969a, b; Shellard, 1971;

  Shellard and Houghton, 1972c).

- *Pseudocinchona africana* Aug. Chev.

  (Cu *et al.*, 1957; Rungsiyakul, 1973).

Corynantheine

- *Catharanthus roseus* (Linn.) G. Don

  (Taylor and Farnsworth, 1975).

- *Corynanthe yohimbe* K. Schum.

  (Karrer and Salomon, 1926; Marion, 1952).

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Shellard and Houghton, 1972c).

- *Pseudocinchona africana* Aug. Chev.

  (Marion, 1952; Cu *et al.*, 1957).

Hirsutine

- *Cephalanthus occidentalis* Linn.

  (Phillipson and Hemingway, 1974a).

- *Mitragyna hirsuta* Havil.

  (Shellard *et al.*, 1967b; Shellard, 1971;

  Phillipson *et al.*, 1973b; Houghton and Shellard, 1974).

- *M. parvifolia* (Roxb.) Korth.

  (Shellard *et al.*, 1969a, b; Shellard, 1971;

  Shellard and Houghton, 1972c; Shellard and Lala, 1977).

- *Mitragyna rubrostipulata* (K. Schum.) Havil.

  (Shellard and Lala, 1978).

- *M. stipulosa* (DC.) O. Kuntze

  (Houghton *et al.*, 1976).

- *M. tubulosa* Havil.

  (Rungsiyakul, 1973).

Hirsuteine

- *Mitragyna hirsuta* Havil.

  (Phillipson *et al.*, 1973b).

- *M. parvifolia* (Roxb.) Korth.

  (Shellard and Houghton, 1972b, c; Phillipson *et al.*, 1973b).

- *M. rubrostipulata* (K. Schum.) Havil.

  (Shellard and Lala, 1978).

- *Pseudocinchona africana* Aug. Chev.

  (Shellard and Houghton, 1972b).

Mitragynine

- *Mitragyna inermis* (Willd.) O. Kuntze

  M. parvifolia (Roxb.) Korth.

  M. rotundifolia (Roxb.) O. Kuntze

  (Willaman and Schubert, 1961).

- *M. speciosa* Korth.

  (Field, 1921; Ing and Raison, 1939; Saxton, 1960;

  Willaman and Schubert, 1961; Beckett *et al.*, 1963a, 1965b;

  Shellard and Phillipson, 1964a; Trager *et al.*, 1968a;

Shellard, 1971; Iwu and Court, 1978a; Shellard *et al.*, 1978b,c).

- *Mitragyna stipulosa* (DC.) O. Kuntze

(Willaman and Schubert, 1961).

2.2 Oxindole alkaloids

2.2.1 Closed E ring oxindole alkaloids

Isomitraphylline

- *Mitragyna hirsuta* Havil.

(Shellard *et al.*, 1967b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Phillipson *et al.*, 1973b).

- *M. javanica* Koord et Val.

(Shellard and Alam, 1968; Shellard, 1971).

- *M. javanica* Koord et Val. var. *microphylla* Koord et Val.

(Shellard *et al.*, 1967a; Bindra, 1973).

- *M. parvifolia* (Roxb.) Korth.

(Shellard and Alam, 1968; Shellard *et al.*, 1968b, 1969b; Shellard, 1971; Shellard and Houghton, 1972c; Bindra, 1973).

- *M. rotundifolia* (Roxb.) O. Kuntze

(Houghton and Shellard, 1974).

- *M. rubrostipulata* (K. Schum.) Havil.

(Shellard and Lala, 1978).

- *M. speciosa* Korth.

(Beckett *et al.*, 1966a; Shellard and Alam, 1968; Trager *et al.*, 1968a; Shellard, 1971; Bindra, 1973; Shellard *et al.*, 1978b, c).

- *Mitragyna tubulosa* Havil.

  (Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973).

Mitraphylline

- *Catharanthus roseus* (Linn.) G. Don

  (Bindra, 1973; Taylor and Farnsworth, 1975).

- *Mitragyna hirsuta* Havil.

  (Shellard *et al.*, 1967b; Shellard and Alam, 1968;

  Shellard, 1971; Bindra, 1973; Phillipson *et al.*, 1973b).

- *M. javanica* Koord et Val.

  (Shellard and Alam, 1968; Shellard, 1971).

- *M. javanica* Koord et Val. var. *microphylla* Koord et Val.

  (Shellard *et al.*, 1967a; Bindra, 1973).

- *M. parvifolia* (Roxb.) Korth.

  (Shellard and Alam, 1968; Shellard *et al.*, 1968b, 1969b;

  Shellard, 1971; Shellard and Houghton, 1972c; Bindra, 1973).

- *M. rotundifolia* (Roxb.) O. Kuntze

  (Shellard and Phillipson, 1964a; Houghton and Shellard, 1974).

- *M. rubrostipulata* (K. Schum.) Havil.

  (Badger *et al.*, 1950; Willaman and Schubert, 1961;

  Shellard and Lala, 1978).

- *M. speciosa* Korth.

  (Shellard and Phillipson, 1964a; Beckett *et al.*, 1966a;

  Shellard and Alam, 1968; Trager *et al.*, 1968a; Shellard, 1971;

  Bindra, 1973; Shellard *et al.*, 1978b, c).

- *Mitragyna stipulosa* (DC.) O. Kuntze

  (Barger *et al.*, 1939; Saxton, 1960; Beckett *et al.*, 1963a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*, 1976).

- *M. tubulosa* Havil.

  (Rungsiyakul, 1973, Shellard and Rungsiyakul, 1973).

Isopteropodine (Uncarine E)

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Shellard and Alam, 1968; Shellard *et al.*, 1968a, b, 1969a, b; Shellard, 1971; Shellard and Houghton, 1972c, 1974b; Bindra, 1973; Shellard and Lala, 1977).

Pteropodine (Uncarine C)

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Shellard and Alam, 1968; Shellard *et al.*, 1968a, b, 1969a, b; Shellard, 1971; Shellard and Houghton, 1972c, 1974b; Bindra, 1973; Shellard and Lala, 1977).

Speciophylline (Uncarine D)

- *Mitragyna inermis* (Willd.) O. Kuntze

  (Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973),

- *M. parvifolia* (Roxb.) Korth.

  (Shellard and Alam, 1968; Shellard *et al.*, 1968a, b, 1969b; Shellard, 1971; Shellard and Houghton, 1972c, 1974b; Bindra, 1973; Shellard and Lala, 1977).

- *Mitragyna speciosa* Korth.

  (Beckett *et al.*, 1966a; Johns and Lamberton, 1966; Shellard and Alam, 1968; Shellard *et al.*, 1968a, 1978b; Shellard, 1971; Bindra, 1973).

Speciophylline N-oxide

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Rungsiyakul, 1973; Shellard and Houghton, 1974b).

Uncarine F

- *Mitragyna inermis* (Willd.) O. Kuntze

  (Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973).

- *M. parvifolia* (Roxb.) Korth.

  (Shellard and Alam, 1968; Shellard *et al.*, 1968a, b, 1969b; Shellard, 1971; Shellard and Houghton, 1972c, 1974b; Bindra, 1973; Shellard and Lala, 1977).

Uncarine F N-oxide

- *Mitragyna parvifolia* (Roxb.) Korth.

  (Rungsiyakul, 1973; Shellard and Houghton, 1974b).

2.2.2 Open E ring oxindole alkaloids

Isorhynchophylline

- *Cephalanthus occidentalis* Linn.
  (Phillipson and Hemingway, 1974).
- *Mitragyna ciliata* Aubrev. et Pellegr.
  (Beckett *et al.*, 1963b; Shellard and Phillipson, 1964a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971).
- *M. hirsuta* Havil.
  (Shellard *et al.*, 1967b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Phillipson *et al.*, 1973b).
- *M. inermis* (Willd.) O. Kuntze
  (Shellard and Alam, 1968; Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973; Shellard *et al.*, 1978b).
- *M. parvifolia* (Roxb.) Korth.
  (Shellard and Phillipson, 1964b; Shellard *et al.*, 1968b, 1969a, b; Shellard and Alam, 1968; Shellard, 1971; Shellard and Houghton, 1972c; Shellard and Lala, 1977).
- *M. rotundifolia* (Roxb.) O. Kuntze
  (Shellard and Phillipson, 1964a; Shellard and Alam, 1968; Shellard, 1971; Houghton and Shellard, 1974).
- *M. rubrostipulata* (K. Schum.) Havil.
  (Beckett *et al.*, 1963a; Shellard and Phillipson, 1964a; Shellard and Lala, 1978).

- *Mitragyna speciosa* Korth.

  (Shellard and Alam, 1968; Shellard *et al.*, 1978b, c).

- *M. stipulosa* (DC.) O. Kuntze

  (Beckett *et al.*, 1963a; Shellard and Phillipson, 1964a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*, 1976).

- *M. tubulosa* Havil.

  (Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973).

Isorhynchophylline N-oxide

- *Cephalanthus occidentalis* Linn.

  (Phillipson and Hemingway, 1974).

- *Mitragyna inermis* (Willd.) O. Kuntze

  (Shellard, 1971; Shellard *et al.*, 1971).

- *M. rotundifolia* (Roxb.) O. Kuntze

  (Shellard *et al.*, 1971; Houghton and Shellard, 1974).

Rhynchophylline (Mitrinermine)

- *Cephalanthus occidentalis* Linn.

  (Phillipson and Hemingway, 1974).

- *Crossopteryx kotschyana* Fenzl.

  (Saxton, 1965a).

- *Mitragyna ciliata* Aubrev. et Pellgr.

  (Badger *et al.*, 1950; Saxton, 1960, 1965a; Willaman and Schubert, 1961; Beckett *et al.*, 1963a, b; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971).

- *Mitragyna hirsuta* Havil.

  (Shellard *et al.*, 1967b; Shellard and Alam, 1968; Shellard, 1971; Bindra, 1973; Phillipson *et al.*, 1973b; Houghton and Shellard, 1974).

- *M. inermis* (Willd.) O. Kuntze

  (Barger *et al.*, 1939; Saxton, 1960, 1965a; Willaman and Schubert, 1961; Beckett *et al.*, 1963a; Shellard and Alam, 1968; Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973; Shellard *et al.*, 1978b).

- *M. parvifolia* (Roxb.) Korth.

  (Willaman and Schubert, 1961; Shellard and Phillipson, 1964b; Shellard *et al.*, 1968b, 1969a, b; Shellard and Alam, 1968; Shellard, 1971; Shellard and Houghton, 1972c; Shellard and Lala, 1977).

- *M. rotundifolia* (Roxb.) O. Kuntze

  (Barger *et al.*, 1939; Saxton, 1960, 1965a; Willaman and Schubert, 1961; Shellard and Phillipson, 1964a; Shellard and Alam, 1968; Shellard, 1971; Houghton and Shellard, 1974).

- *M. rubrostipulata* (K. Schum.) Havil.

  (Hendrickson and Sims, 1963; Shellard and Lala, 1978).

- *M. speciosa* Korth.

  (Willaman and Schubert, 1961; Hendrickson and Sims, 1963; Shellard and Phillipson, 1964a; Beckett *et al.*, 1965b; Shellard and Alam, 1968; Trager *et al.*, 1968a; Bindra, 1973; Shellard *et al.*, 1978b, c).

- *Mitragyna stipulosa* (DC.) O. Kuntze

  (Barger *et al.*, 1939; Saxton, 1960, 1965a; Willaman and Schubert, 1961; Beckett *et al.*, 1963a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*, 1976).

- *M. tubulosa* Havil.

  (Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973).

Rhynchophylline N-oxide

- *Cephalanthus occidentalis* Linn.

  (Phillipson and Hemingway, 1974).

- *Mitragyna inermis* (Willd.) O. Kuntze

  (Shellard, 1971; Shellard *et al.*, 1971).

- *M. rotundifolia* (Roxb.) O. Kuntze

  (Shellard *et al.*, 1971; Houghton and Shellard, 1974).

- *M. rubrostipulata* (K. Schum.) Havil.

  (Shellard and Lala, 1978).

Isocorynoxeine

- *Mitragyna rotundifolia* (Roxb.) O. Kuntze

  (Houghton and Shellard, 1974).

Corynoxeine

- *Corynanthe yohimbe* K. Schum.

  (Cu *et al.*, 1957).

- *Mitragyna hirsuta* Havil.

  (Houghton and Shellard, 1974).

- *M. parvifolia* (Roxb.) Korth.

  (Shellard and Houghton, 1972b, c; Shellard *et al.*, 1978b).

- *M. rotundifolia* (Roxb.) O. Kuntze

  (Shellard *et al.*, 1967b; Houghton and Shellard, 1974).

- *M. speciosa* Korth.

  (Shellard *et al.*, 1978b).

- *M. stipulosa* (DC.) O. Kuntze

  (Houghton *et al.*, 1976).

- *Pseudocinchona africana* Aug. Chev.

  (Cu *et al.*, 1957; Shellard and Houghton, 1972b).

Rotundifoline (Stipulatine)

- *Mitragyna ciliata* Aubrev. et Pellegr.

  (Badger *et al.*, 1950; Saxton, 1960; Willaman and Schubert, 1961; Beckett *et al.*, 1963b; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971).

- *M. inermis* (Willd.) O. Kuntze

  (Willaman and Schubert, 1961; Shellard and Alam, 1968; Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973).

- *M. parvifolia* (Roxb.) Korth.

  (Shellard and Phillipson, 1964b; Shellard *et al.*, 1968b; Shellard and Alam, 1968; Shellard, 1971; Hemingway *et al.*, 1975).

- *Mitragyna rotundifolia* (Roxb.) O. Kuntze

  (Barger *et al.*, 1939; Saxton, 1960; Willaman and Schubert, 1961; Shellard and Phillipson, 1964a, b).

- *M. rubrostipulata* (K. Schum.) Havil.

  (Hendrickson and Sims, 1963; Shellard and Lala, 1978).

- *M. speciosa* Korth.

  (Willaman and Schubert, 1961; Hendrickson and Sims, 1963; Shellard and Phillipson, 1964a; Beckett *et al.*, 1965b; Shellard and Alam, 1968; Bindra, 1973).

- *M. stipulosa* (DC.) O. Kuntze

  (Willaman and Schubert, 1961; Beckett *et al.*, 1963a; Shellard and Alam, 1968; Shellard and Sarpong, 1970; Shellard, 1971; Houghton *et al.*, 1976).

- *M. tubulosa* Havil.

  (Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973).

anti-Rotundifoline N-oxide

- *Mitragyna rubrostipulata* (K. Schum.) Havil.

  (Shellard *et al.*, 1977; Shellard and Lala, 1978).

Isorotundifoline (Mitragynol, Dihydrorotundifoline)

- *Mitragyna ciliata* Aubrév. et Pellegr.

  (Beckett *et al.*, 1963b; Shellard and Alam, 1968; Shellard and Sarpone, 1970; Shellard, 1971).

- *Mitragyna inermis* (Willd.) O. Kuntze

  (Willaman and Schubert, 1961; Shellard and Alam, 1968; Shellard and Sarpong, 1969, 1970; Shellard, 1971; Bindra, 1973).

- *M. parvifolia* (Roxb.) Korth.

  (Willaman and Schubert, 1961; Shellard and Phillipson, 1964b; Shellard *et al.*, 1968b; Shellard and Alam, 1968; Shellard, 1971; Hemingway *et al.*, 1975).

- *M. rotundifolia* (Roxb.) O. Kuntze

  (Badger *et al.*, 1950; Willaman and Schubert, 1961; Beckett *et al.*, 1963a; Shellard and Phillipson, 1964a, b).

- *M. rubrostipulata* (K. Schum.) Havil.

  (Shellard and Lala, 1978).

- *M. speciosa* Korth.

  (Willaman and Schubert, 1961; Shellard and Alam, 1968).

- *M. stipulosa* (DC.) O. Kuntze

  (Badger *et al.*, 1950; Willaman and Schubert, 1961; Beckett *et al.*, 1963a; Shellard and Alam, 1968; Shellard, 1971; Houghton *et al.*, 1976).

- *M. tubulosa* Havil.

  (Rungsiyakul, 1973; Shellard and Rungsiyakul, 1973).

Corynoxine

- *Corynanthe yohimbe* K. Schum.

  (Cu *et al.*, 1957).

- *Mitragyna speciosa* Korth.

  (Shellard *et al.*, 1978b).

- *Pseudocinchona africana* Aug. Chev.

  (Cu *et al.*, 1957; Phillipson and Hemingway, 1973c).

Corynoxine B

- *Mitragyna speciosa* Korth.

  (Shellard *et al.*, 1978b).

Speciofoline

- *Mitragyna speciosa* Korth.

  (Beckett *et al.*, 1965b; Shellard and Alam, 1968;

  Shellard, 1971; Bindra, 1973; Hemingway *et al.*, 1975;

  Shellard *et al.*, 1978b).

2.3 Pyridino-indolo-quinolizidinone alkaloids

Angustine

- *Mitragyna javanica* Koord et Val.

  M. parvifolia (Roxb.) Korth.

  Nauclea coadunata Roxb. ex J.E. Smith

  Strychnos angolensis Gilg.

  (Phillipson *et al.*, 1974).

- *S. angustiflora* Benth.

  (Au *et al.*, 1973; Phillipson *et al.*, 1974).

- *Strychnos borneensis* Leenh.

  (Phillipson *et al.*, 1974).

- *S. camptoneura* Gilg. et Busse

  (Verpoorte *et al.*, 1975; Phillipson *et al.*, 1974).

- *S. floribunda* Gilg.

  S. ledermannii Gilg. et Bened

  S. minor Dennst.

  S. odorata A. Chev.

  S. ovata A. W. Hill

  S. potatorum Linn. f.

  S. samba Duvign

  S. scheffleri Gilg.

  S. trichoneura Leeuwenberg

  S. umbellata (Lour.) Merr.

  S. usambarensis Gilg.

  S. vanprukii Craib

  S. xantha Leeuwenberg

  (Phillipson *et al.*, 1974).

Angustoline

- *Strychnos angustiflora* Benth.

  (Au *et al.*, 1973; Phillipson *et al*, 1974).

- *S. borneensis* Leenh.

  S. minor Dennst.

  S. odorata A, Chev.

  (Phillipson *et al.*, 1974).

- *Strychnos ovata* A. W. Hill

  S. samba Duvign

  S. scheffleri Gilg.

  S. trichoneura Leeuwenberg

  S. umbellata (Lour.) Merr.

  S. vanprukii Craib

  S. xantha Leeuwenberg

  (Phillipson *et al.*, 1974).

Angustidine

- *Strychnos angolensis* Gilg.

  (Phillipson *et al.*, 1974).

- *S. angustiflora* Benth.

  (Au *et al.*, 1973; Phillipson *et al.*, 1974).

- *S. borneensis* Leenh.

  S. floribunda Gilg.

  S. minor Dennst.

  S. odorata A. Chev.

  S. ovata A. W. Hill

  S. potatorum Linn. f.

  S. samba Duvign

  S. scheffleri Gilg.

  S. trichoneura Leeuwenberg

  S. umbellata (Lour.) Merr.

  S. usambarensis Gilg.

  (Phillipson *et al.*, 1974).

- *Strychnos vanprukii* Craib

  S. xantha Leeuwenberg

  (Phillipson *et al.*, 1974).

2.4 β-Carboline alkaloid

Harmane (Aribine, Loturine, Passiflorine)

- *Arariba rubra* Mart.

  Calligonum minimum Lipski

  Passiflora actinea Hook.

  P. alata W. Ait.

  P. bryonioides H.B.K.

  P. capsularis Linn.

  (Hesse, 1964).

- *P. coerulea* Linn.

  P. decrisneana Hort.

  (Lohdefink and Kating, 1974).

- *P. edulis* Sims.

  (Hesse, 1964; Lohdefink and Kating, 1974).

- *P. eichleriana* Mast.

  (Hesse, 1964).

- *P. foetida* Linn.

  (Lohdefink and Kating, 1974).

- *P. incarnata* Linn.

  (Hesse, 1964; Lohdefink and Kating, 1974).

- *Passiflora quadrangularis* Linn.

  P. suberosa Linn.

  (Hesse, 1964).

- *P. subpeltata* Orteg.

  P. warmingii Mart.

  (Lohdefink and Kating, 1974).

- *Symplocos racemosa* Roxb.

  (Hesse, 1964).

2.5 Yohimbine alkaloids

Yohimbine (Quebrachamine, Quebrachine)

- *Alchornea floribunda* Meull. - Arg.

  (Hesse, 1964; Manske, 1965).

- *Aspidosperma excelsum* Benth.

  A. oblongum A. DC.

  (Taylor and Farnsworth, 1975).

- *A. peroba* Saldanha da Gama

  (Hesse, 1964).

- *A. pyricollum* Muell. - Arg.

  (Taylor and Farnsworth, 1975).

- *A. quebrachoblanco* Schlecht.

  (Hesse, 1964; Manske, 1965; Taylor and Farnsworth, 1975).

- *Catharanthus lanceus* (Boj. ex A. DC.) Pich.

  (Manske, 1965; Farnsworth, 1972; Taylor and Farnsworth, 1975).

- *Corynanthe yohimbe* K. Schum.

  C. macroceras K. Schum.

  C. paniculata Welw.

  Diplorrhynchus condylocarpon Pich.

  (Hesse, 1964; Manske, 1965; Taylor and Farnsworth, 1975).

- *Hunteria eburnea* Pich.

  (Manske, 1965).

- *Pausinystalia trillesii* Beille

  Pouteria sp.

  (Manske, 1965; Taylor and Farnsworth, 1975).

- *Rauvolfia amsoniaefolia* A. DC.

  R. canescens Linn.

  (Hesse, 1964; Taylor and Farnsworth, 1975).

- *R. cumminsii* Stapf.

  (Iwu and Court, 1978b).

- *R. fruticosa* Burck.

  R. heterophylla Roem. et Schult.

  (Hesse, 1964; Taylor and Farnsworth, 1975).

- *R. ligustrina* Roem. et Schult.

  (Hesse, 1964).

- *R. mombasiana* Stapf.

  (Iwu and Court, 1978a).

- *R. serpentina* (Linn.) Benth. ex Kurz.

  R. sumatrana (Miq.) Jack.

  (Hesse, 1964; Taylor and Farnsworth, 1975).

- *Rauvolfia verticillata* (Lour.) Baill.

  (Taylor and Farnsworth, 1975).

- *R. vomitoria* Afzel.

  (Hesse, 1964).

Corynanthine (Rauhimbine)

- *Corynanthe yohimbe* K. Schum.

  (Hesse, 1964).

- *Pseudocinchona africana* A. Chev.

  (Hesse, 1964; Manske, 1965).

- *P. mayumbensis* (Good) Hamet

  Rauvolfia canescens Linn.

  R. serpentina (Linn.) Benth. ex Kurz.

  (Hesse, 1964).

β-Yohimbine

- *Amsonia elliptica* Roem. et Schult.

  Aspidosperma oblongum A. DC.

  Corynanthe yohimbe K. Schum.

  (Hesse, 1964; Manske, 1965).

- *C. paniculata* Welw.

  (Manske, 1965).

- *Diplorrhynchus condylocarpon* Pich.

  (Hesse, 1964; Manske, 1965).

- *Rauvolfia canescens* Linn.

  (Hesse, 1964).

11-Methoxy Yohimbine

- *Aspidosperma oblongum* A. DC.

  (Hesse, 1964).

Pseudoyohimbine

- *Catharanthus trichophyllus* (Baker) Pich.

  (Cordell and Farnsworth, 1976).

- *Corynanthe yohimbe* K, Schum.

  (Hesse, 1964; Manske, 1965).

- *Rauvolfia canescens* Linn.

  R. tetraphylla Linn.

  (Hesse, 1964).

Alloyohimbine (Dihydroyohimbine)

- *Corynanthe yohimbe* K. Schum.

  (Hesse, 1964; Manske, 1965).

α-Yohimbine (Rauwolscine)

- *Alstonia constricta* F. v. Muell.

  (Hesse, 1964; Saxton, 1965b; Manske, 1965).

- *Corynanthe yohimbe* K. Schum.

  Pseudocinchona africana A. Chev.

  (Hesse, 1964; Manske, 1965).

- *Rauvolfia canescens*

  (Salkin *et al.*, 1961; Hesse, 1964).

- *Rauvolfia cumminsii* Stapf.

  (Iwu and Court, 1978b).

- *R. heterophylla* Roem. et Schult.

  R. ligustrina Roem. et Schult.

  (Hesse, 1964).

- *R. obscura* K. Schum.

  (Timmins and Court, 1976b).

- *R. serpentina* (Linn.) Benth. ex Kurz.

  R. sumatrana (Miq.) Jack.

  R. vomitoria Afzel.

  (Hesse, 1964).

Epi-3-α-yohimbine (Isorauhimbine, Epi-3-rauwolscine)

- *Rauvolfia serpentina* (Linn.) Benth. ex Kurz.

  (Hesse, 1964; Manske, 1965).

3. Chemistry of the alkaloids

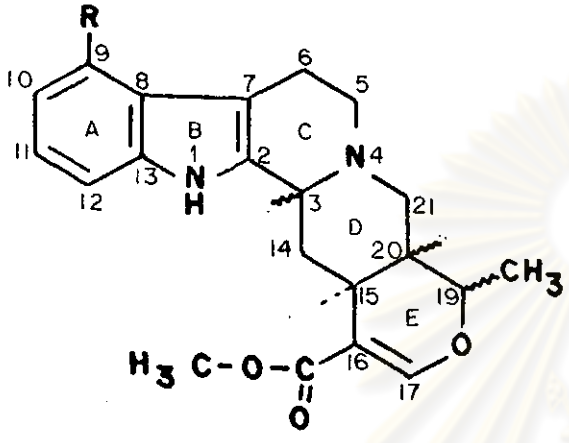
3.1 Heteroyohimbine and oxindole alkaloids

3.1.1 Basic structures

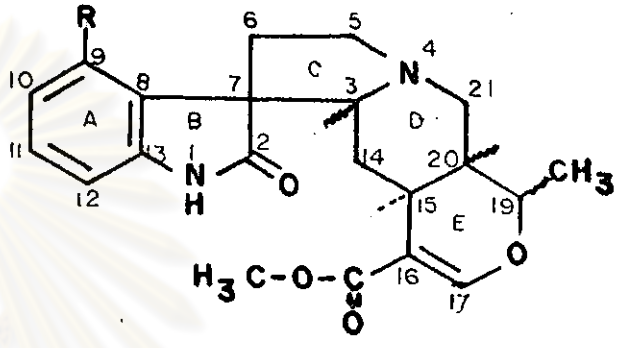
Most of the alkaloids reported to be present in *Mitragyna* and *Uncaria* species are of heteroyohimbine-types and the corresponding oxindoles. It will be seen that both types of alkaloids may have a closed E ring (1, 2) or an open E ring (E *seco*) (3, 4) as shown in Fig. 11.

Fig. II

Basic structure of heteroyohimbine and oxindole alkaloids

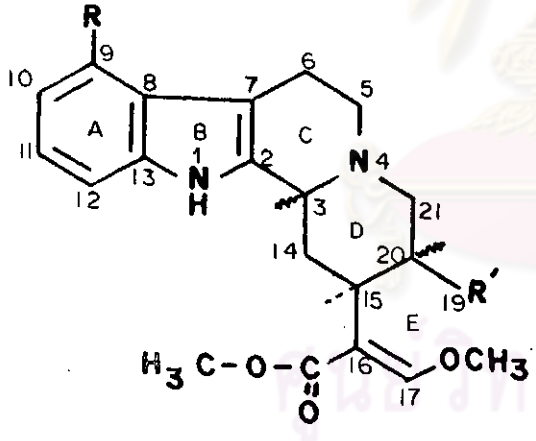


1

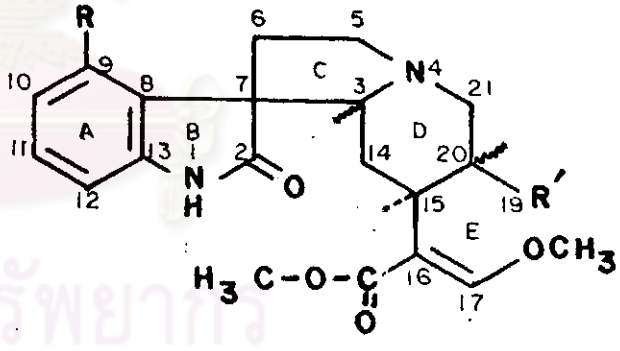


2

Closed E ring



3



4

Open E ring

1, 3 heteroyohimbines; 2, 4 oxindoles.

3.1.2 Configuration of heteroyohimbine and oxindole alkaloids

All alkaloids have asymmetric centres at C(3), C(15) and C(20), though all those isolated so far have C(15) - H α, since these alkaloids are all derived from the monoterpene *seco*-loganin (Phillipson *et al.*, 1978). Four diastereoisomers can thus exist, designated as *normal*, *pseudo*, *allo* and *epiallo*. The closed E ring alkaloids also have an asymmetric centre at C(19). In all known *Mitragyna* alkaloids the C(19) - CH_3 is α, but isomers with C(19) - CH_3 α and β configurations are known to occur in members of the genus *Uncaria*. The E *seco* alkaloids may show geometric isomerisation because of the double bond between C(16) and C(17). In all known alkaloids the C(17) - H is *cis* to the C(16) carbomethoxy group.

Substitutions in the aromatic ring have been found, but only at C(9), the group being either an hydroxy or a methoxy group for those found in *Mitragyna* species. Only 9-hydroxy substituted alkaloids are reported to be present in *Uncaria* species (Phillipson *et al.*, 1978). However Willaman and Schubert (1961) stated that in 1955 Orekhov reported the presence of mitragynine, a 9-methoxy substituted open E ring heteroyohimbine, in some species of *Uncaria*. In the open E ring alkaloids R' may be either an ethyl or a vinyl groups.

In addition, the oxindole alkaloids have an asymmetric centre at C(7), i.e. ring C attached to ring B at the spiro C-atom, C(7), in two different ways. One of which the lactam carbonyl lies below the plane of C/D ring resulting in the alkaloids termed the A series and those of which the lactam carbonyl lies above the plane of C/D ring

giving rise to the alkaloids termed the B series (Fig. III). Thus eight isomers of oxindoles are possible.

Fig. III

A series B series

The four isomers of heteroyohimbines and eight of oxindole alkaloids are summarised with their configurations in Table I.

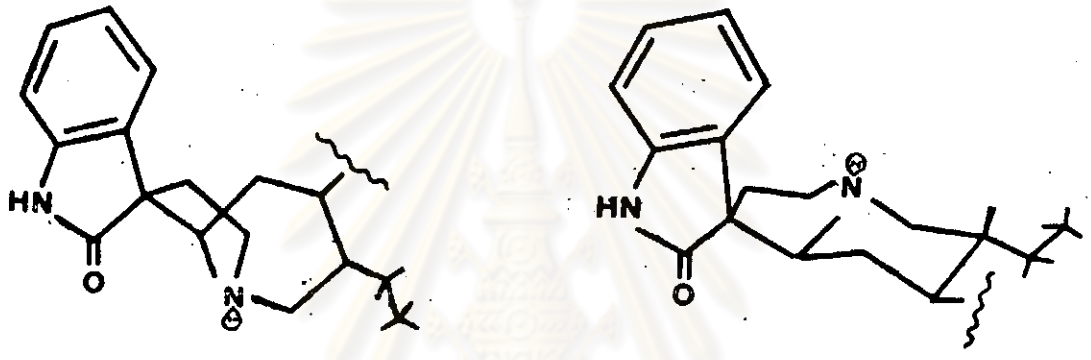
Table I

Configuration terminology for heteroyohimbine and oxindole alkaloids

Configuration	C(3) - H	C(15) - H	C(20) - H	C(7) series of oxindole
Normal	α	α	β	A or B
Pseudo	β	α	β	A or B
Allo	α	α	α	A or B
Epiallo	β	α	α	A or B

Further, in both types of oxindole alkaloids, the lone pair of electrons on N(4) may either be on the same side of the C(7) as the lactam carbonyl group or on the opposite side, the former are known as *syn* and the latter as *anti* alkaloids (Fig. IV).

Fig. IV



syn *anti*

Names of the heteroyohimbine and oxindole alkaloids together with their configurations and substitutions are summarised in Tables II - V.

Table II

Closed E ring heteroyohimbine alkaloids

Alkaloid	C(9) - R	Configuration	C(19) - CH_3
Ajmalicine	H	*normal*	α
19-Epi-ajmalicine	H	*normal*	β
Isomitrajavine#	OCH_3	*normal*	α

Table II (continued)

Alkaloid	C(9) - R	Configuration	C(19) - CH_3
3-Isoajmalicine	H	*pseudo*	α
19-Epi-3-isoajmalicine	H	*pseudo*	β
(Mitrajavine)	OCH_3	*pseudo*	α
Tetrahydroalstonine*	H	*allo*	α
Rauniticine	H	*allo*	β
Akuammigine*	H	*epiallo*	α
(3-Isorauniticine)	H	*epiallo*	β

Table III

Open E ring heteroyohimbine alkaloids

Alkaloid	C(9) - R	R'	Configuration
Dihydrocorynantheine*	H	CH_2CH_3	*normal*
Corynantheine	H	$CH{=}CH_2$	*normal*
Gambirine	OH	CH_2CH_3	*normal*
(Speciogynine)	OCH_3	CH_2CH_3	*normal*
(Paynantheine)	OCH_3	$CH{=}CH_2$	*normal*
Hirsutine*	H	CH_2CH_3	*pseudo*
Hirsuteine	H	$CH{=}CH_2$	*pseudo*
(Isogambirine)	OH	CH_2CH_3	*pseudo*

Table III (continued)

Alkaloid	C(9) - R	R'	Configuration
(Mitraciliatine)	OCH_3	CH_2CH_3	*pseudo*
(Isopaynantheine)	OCH_3	$CH{=}CH_2$	*pseudo*
(Corynantheidine)	H	CH_2CH_3	*allo*
Mitragynine	OCH_3	CH_2CH_3	*allo*
(Isocorynantheidine)	H	CH_2CH_3	*epiallo*
Epiallo-corynantheine	H	$CH{=}CH_2$	*epiallo*
(Speciociliatine)	OCH_3	CH_2CH_3	*epiallo*

Table IV

Closed E ring oxindole alkaloids

Alkaloid	C(9) - R	Configuration	Series	C(19) - CH_3
Isomitraphylline*	H	*normal*	A	α
Mitraphylline*	H	*normal*	B	α
Uncarine A	H	*normal*	A	β
Uncarine B	H	*normal*	B	β
(Javaphylline)	OCH_3	*normal*	A	α
Isojavaphylline#	OCH_3	*normal*	B	α
Isopteropodine*	H	*allo*	A	α

Table IV (continued)

Alkaloid	C(9) - R	Configuration	Series	C(19) - CH_3
Pteropodine*	H	*allo*	B	α
(Rauniticine oxindole A)	H	*allo*	A	β
(Rauniticine oxindole B)	H	*allo*	B	β
Speciophylline*	H	*epiallo*	A	α
Uncarine F*	H	*epiallo*	B	α
(Rauniticine epi-oxindole A)	H	*epiallo*	A	β
(Rauniticine epi-oxindole B)	H	*epiallo*	B	β
Gambirdine+	H	-	-	-
Isogambirdine+	H	-	-	-

+Gambirdine and isogambirdine are two interconvertible stereoisomers of mitraphylline. There is no definitive information concerning their stereochemistry (Saxton, 1973).

Table V

Open E ring oxindole alkaloids

Alkaloid	C(9) - R	R'	Configuration	Series
Isorhynchophylline*	H	CH_2CH_3	*normal*	A
Rhynchophylline*	H	CH_2CH_3	*normal*	B

Table V (continued)

Alkaloid	C(9) - R	R'	Configuration	Series
Isocorynoxeine	H	$CH{=}CH_2$	*normal*	A
Corynoxeine	H	$CH{=}CH_2$	*normal*	B
Rotundifoline (*)	OH	CH_2CH_3	*normal*	A
Isorotundifoline (*)	OH	CH_2CH_3	*normal*	B
(Rotundifoleine)	OH	$CH{=}CH_2$	*normal*	A
(Isorotundifoleine)	OH	$CH{=}CH_2$	*normal*	B
(Rhynchociline)	OCH_3	CH_2CH_3	*normal*	A
(Cillaphylline*)	OCH_3	CH_2CH_3	*normal*	B
(Isospecionoxeine)	OCH_3	$CH{=}CH_2$	*normal*	A
(Specionoxeine)	OCH_3	$CH{=}CH_2$	*normal*	B
Corynoxine	H	CH_2CH_3	*allo*	A
Corynoxine B	H	CH_2CH_3	*allo*	B
(Mitrafoline)	OH	CH_2CH_3	*allo*	A
(Isomitrafoline)	OH	CH_2CH_3	*allo*	B
(Mitragynine oxindole A)	OCH_3	CH_2CH_3	*allo*	A
(Mitragynine oxindole B)	OCH_3	CH_2CH_3	*allo*	B
(Isospeciofoline)	OH	CH_2CH_3	*epiallo*	A
Speciofoline	OH	CH_2CH_3	*epiallo*	B
Speciociliatine oxindole A#	OCH_3	CH_2CH_3	*epiallo*	A
Speciociliatine oxindole B#	OCH_3	CH_2CH_3	*epiallo*	B

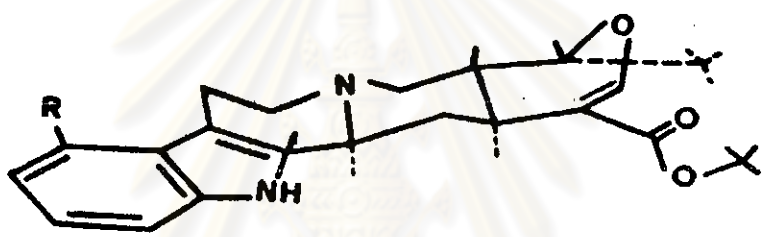
3.1.3 Preferred conformations

The preferred conformations of the heteroyohimbine and oxindole alkaloids are established as follows (Trager *et al.*, 1967; Phillipson and Shellard, 1967) :-

Heteroyohimbine alkaloids

Closed E ring

Normal

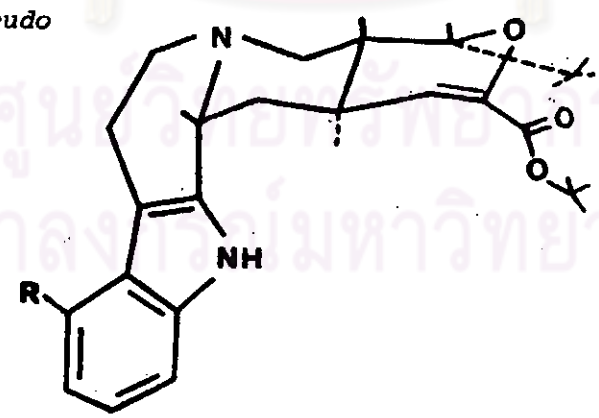


R = H : Ajmalicine

R = H, C(19) - CH_3 β : 19-Epi-ajmalicine

R = OCH_3 : Isomitrajavine#

Pseudo

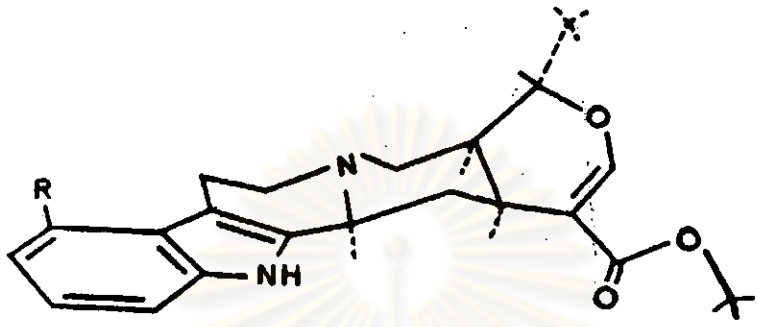


R = H : 3-Isoajmalicine

R = H, C(19) - CH_3 β : 19-Epi-3-isoajmalicine

R = OCH_3 : (Mitrajavine)

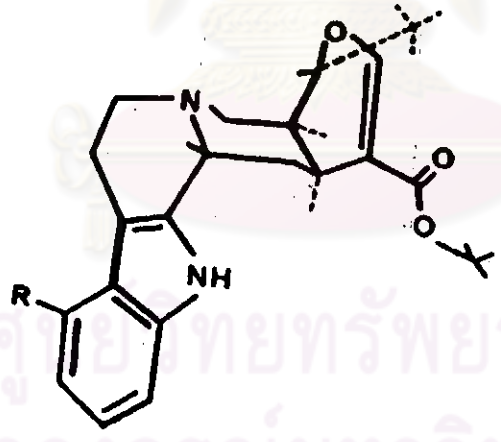
Allo



R = H : Tetrahydroalstonine

R = H, C(19) - CH_3 β : Raunlticine

Epiallo

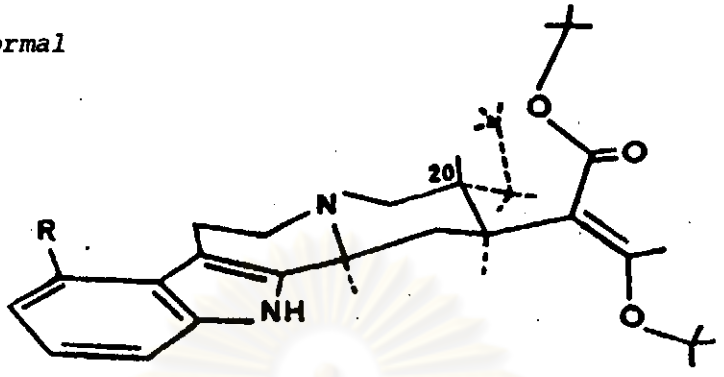


R = H : Akuammigine

R = H, C(19) - CH_3 β : (3-Isorauniticine)

Open E ring

Normal



R = H : Dihydrocorynantheine

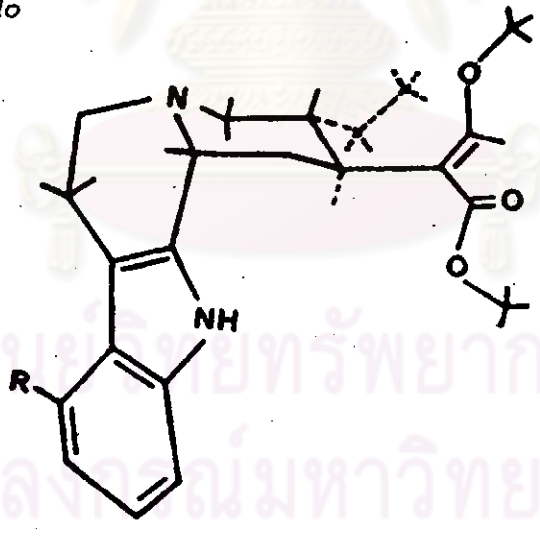
R = H, C(20) Et = vinyl : Corynantheine

R = OH : Gambirine

R = OCH_3 : (Speciogynine)

R = OCH_3, C(20) Et = vinyl : (Paynantheine)

Pseudo



R = H : Hirsutine

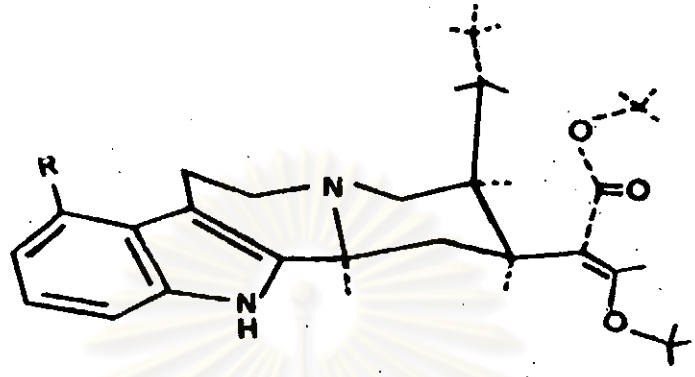
R = H, C(20) Et = vinyl : Hirsuteine

R = OH : (Isogambirine)

R = OCH_3 : (Mitraciliatine)

R = OCH_3, C(20) Et = vinyl : (Isopaynantheine)

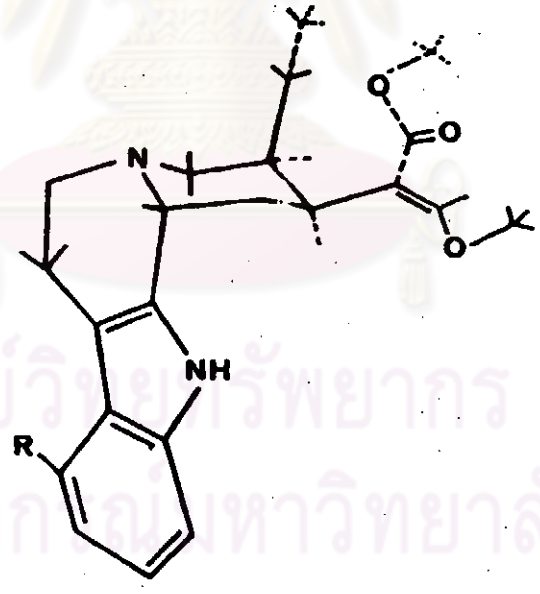
Allo



R = H : (Corynantheidine)

R = OCH_3 : Mitragynine

Epiallo



R = H : (Isocorynantheidine)

R = H, C(20) Et = vinyl : *Epiallo*-corynantheine

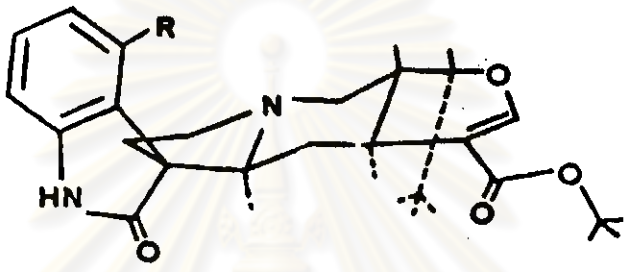
R = OCH_3 : (Speciociliatine)

Oxindole alkaloids

Closed E ring

Normal

A

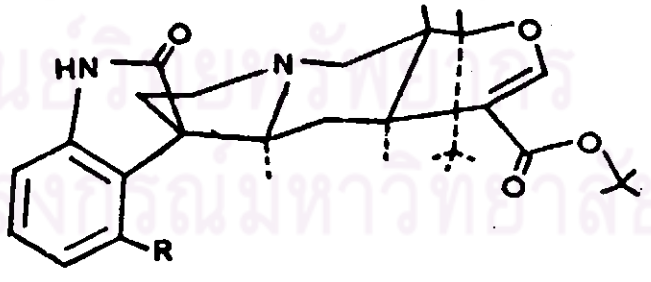


R = H : Isomitraphylline

R = H, C(19) - CH_3 β : Uncarine A (Isoformosanine)

R = OCH_3 : (Javaphylline)

B



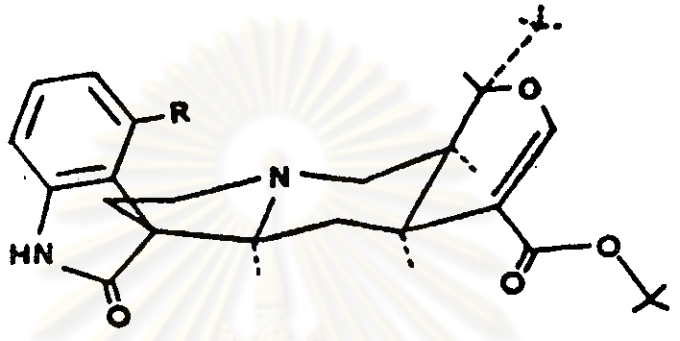
R = H : Mitraphylline

R = H, C(19) - CH_3 β : Uncarine B (Formosanine)

R = OCH_3 : IsoJavaphylline#

Allo

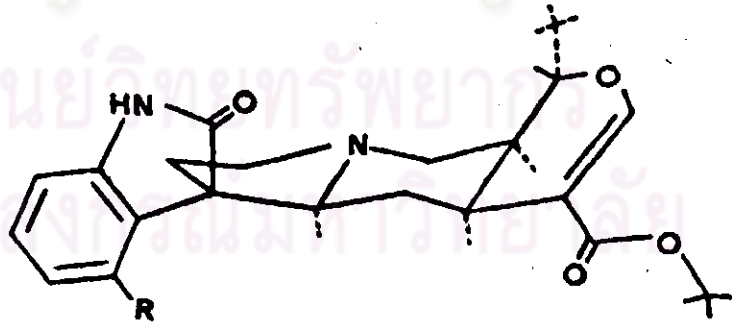
A



R = H : Isopteropodine (Uncarine E)

R = H, C(19) - CH_3 β : (Raunlticine oxindole A)

B

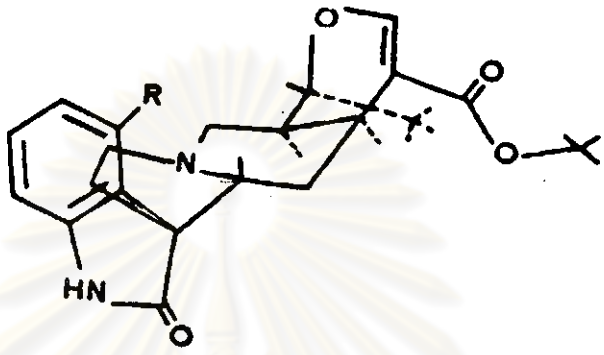


R = H : Pteropodine (Uncarine C)

R = H, C(19) - CH_3 β : (Raunltlcine oxindole B)

Epiallo

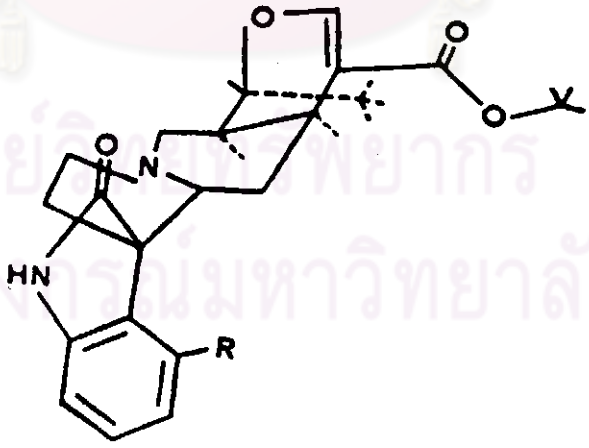
A



R = H : Speciophylline (Uncarine D)

R = H, C(19) - CH_3 β : (Raunitlcine epi-oxindole A)

B



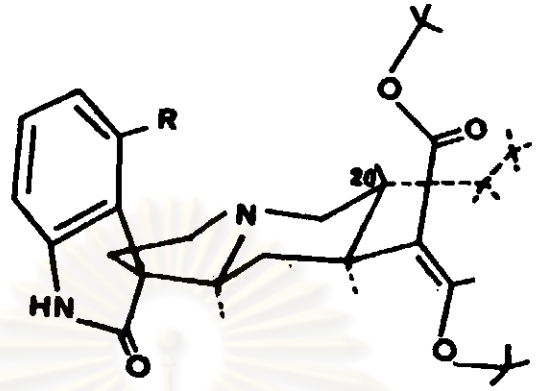
R = H : Uncarine F

R = H, C(19) - CH_3 β : (Raunitlcine epi-oxindole B)

Open E ring

Normal

A



R = H : Isorhynchophylline

R = H, C(20) Et = vinyl : Isocorynoxeine

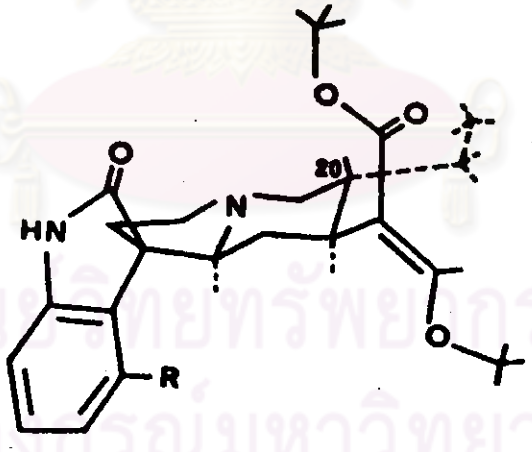
R = OH : Rotundifoline

R = OH, C(20) Et = vinyl : (Rotundifoleine)

R = OCH_3 : (Rhynchociline)

R = OCH_3, C(20) Et = vinyl : (Isospecionoxeine)

B



R = H : Rhynchophylline

R = H, C(20) Et = vinyl : Corynoxeine

R = OH : Isorotundifoline

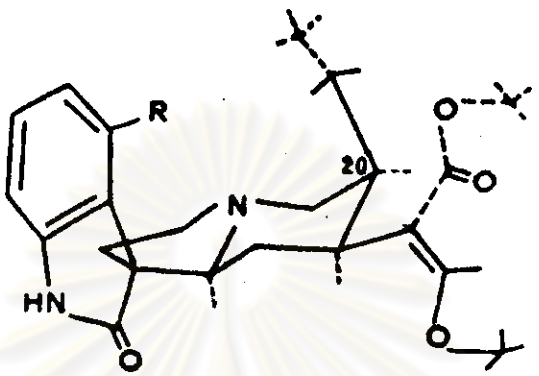
R = OH, C(20) Et = vinyl : (Isorotundifoleine)

R = OCH_3 : (Ciliaphylline)

R = OCH_3, C(20) Et = vinyl : (Specionoxeine)

Allo

A

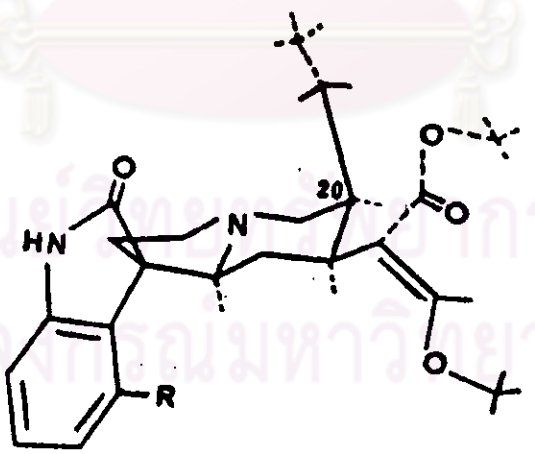


R = H : Corynoxine

R = OH : (Mitrafoline)

R = OCH_3 (Mitragynine oxindole A)

B



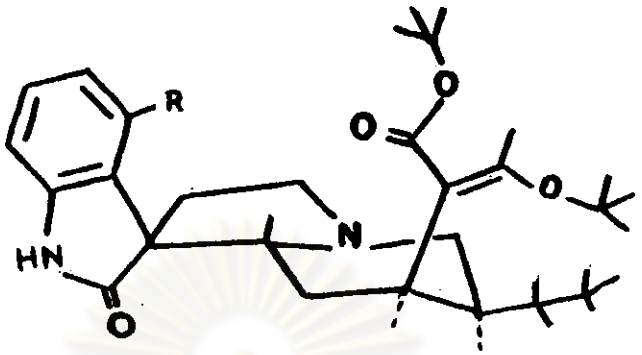
R = H : Corynoxine B

R = OH : (Isomitrafoline)

R = OCH_3 : (Mitragynine oxindole B)

Epiallo

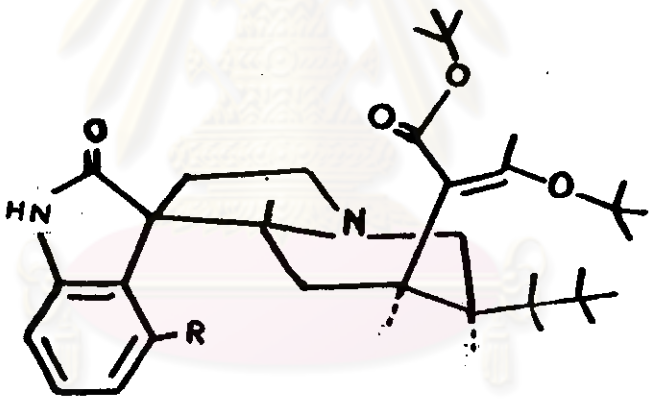
A



R = OH : (Isospeciofoline)

$R = OCH_3$: Speciociliatine oxindole A#

B



R = OH : Speciofoline

$R = OCH_3$ Speciociliatine oxindole B#

(____) Not found in *Uncaria* species.

\# Synthetic alkaloids not yet isolated from plant material.

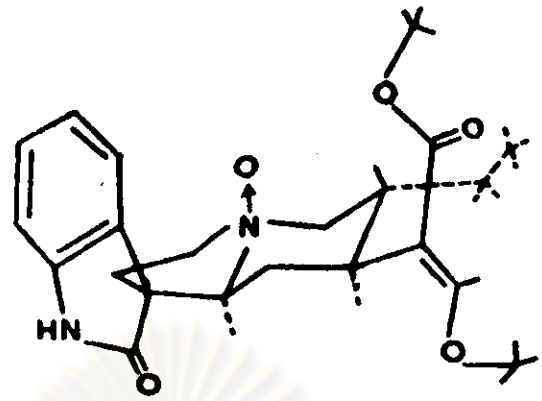
* With its N-oxide.

(*) N-oxide not found in *Uncaria* species.

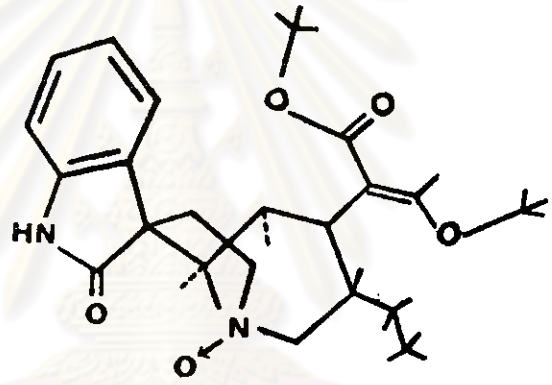
Pseudo oxindole alkaloids cannot exist because of steric interference between the oxindole unit and the underside of ring D and consequently are expected to be too unstable to exist (Trager *et al.*, 1968a).

3.1.4 Alkaloid N-oxides

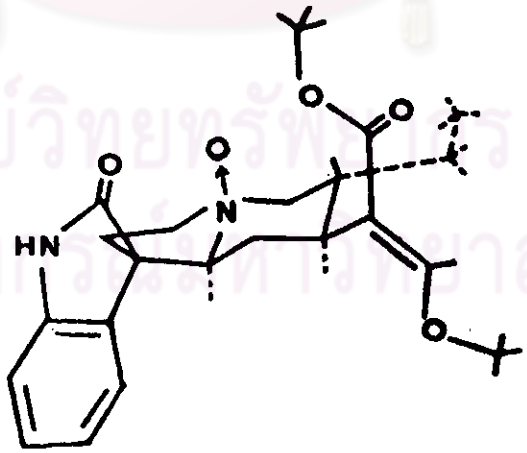
Shellard and Phillipson (1964a) investigated the leaves of *Mitragyna rotundifolia* (Roxb.) O. Kuntze and reported the presence of 'base-line' alkaloid which remained on the base line of thin layer chromatograms with various solvent systems. Similar 'base-line' alkaloids were obtained from *M. inermis* (Willd.) O. Kuntze (Shellard and Sarpong, 1969), one of which was identified to be identical with the 'base-line' alkaloid previously reported and characterised as isorhynchophylline N-oxide (Shellard *et al.*, 1971). Further detailed study by Phillipson *et al.* (1973a) shown it to be *anti*-isorhynchophylline N-oxide. Another polar isomer reported by Shellard and Sarpong (1969) was identified as rhynchophylline N-oxide (Shellard *et al.*, 1971). Phillipson *et al.* (1973a) had also established the absolute conformation for *syn*-isorhynchophylline N-oxide. This detailed study was undertaken in order to establish the absolute conformation of another new polar alkaloid isolated from *M. tubulosa* Havil. by Rungsiyakul (1973) which was subsequently characterised as ciliaphylline N-oxide.



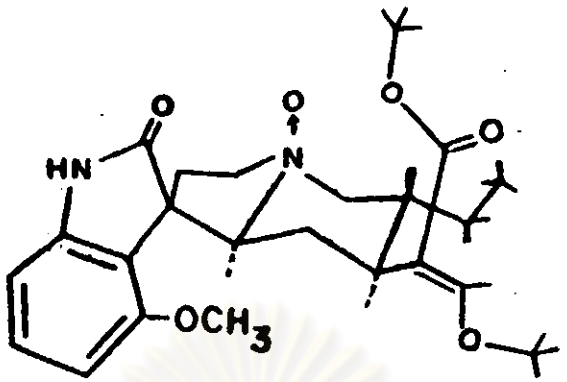
anti-Isorhynchophylline N-oxide



syn-Isorhynchophylline N-oxide

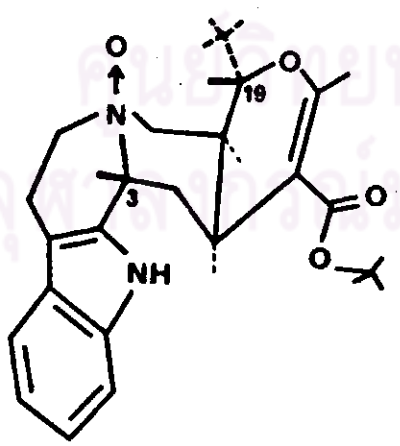


Rhynchophylline N-oxide

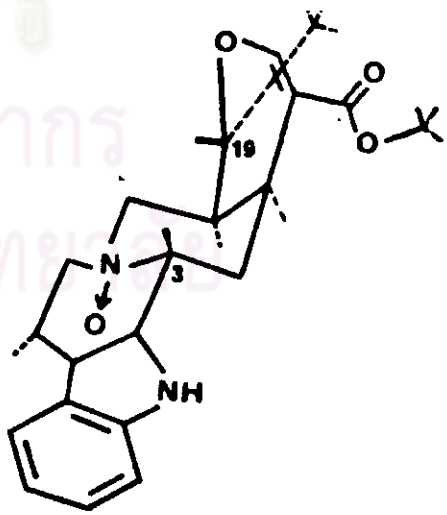


Ciliaphylline N-oxide

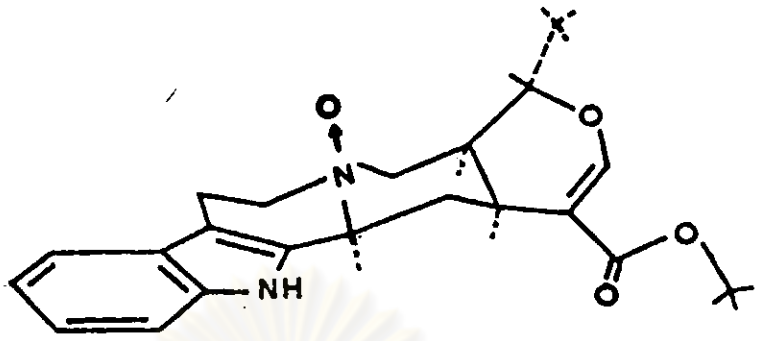
Merlini *et al.* (1972b) have isolated a group of substances, that appear to be the first examples of N-oxides of heteroyohimbine alkaloids, from a species of *Uncaria*. They reported two diastereoisomeric akuammigine N-oxides having different C/D ring junction, one *cis* and the other *trans* because of the conformational mobility of akuammigine, an *epiallo* alkaloid which could exist in either or both preferred conformations (Trager *et al.*, 1968a). They also isolated tetrahydroalstonine N-oxide from the same plant.



4-R-Akuammigine N-oxide

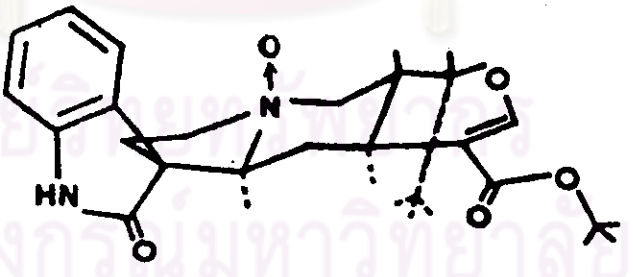


4-S-Akuammigine N-oxide

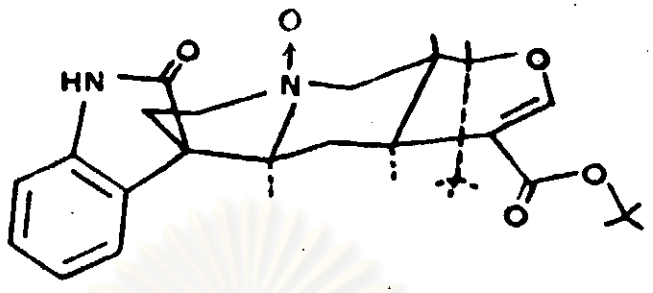


Tetrahydroalstonine N-oxide

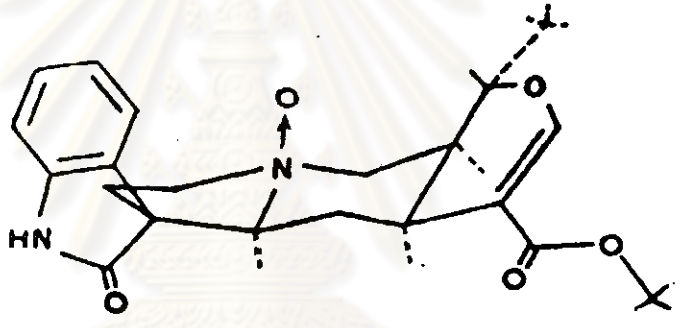
Most of the N-oxides found in several species of *Uncaria* are of oxindoles, both of closed E ring and open E ring. They are of isomitraphylline, mitraphylline, isopteropodine, pteropodine, speciophylline and uncarine F; and of Isorhynchophylline and rhynchophylline respectively.



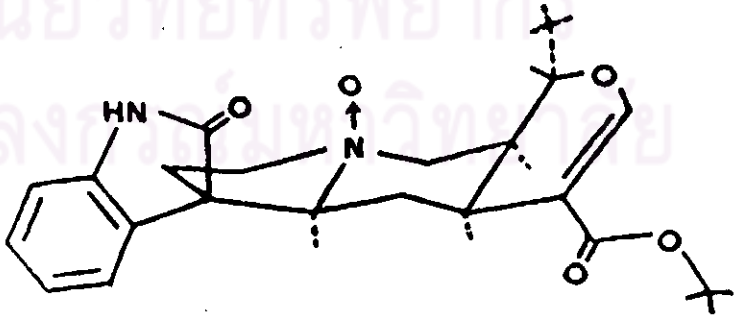
4-R-Isomitraphylline N-oxide



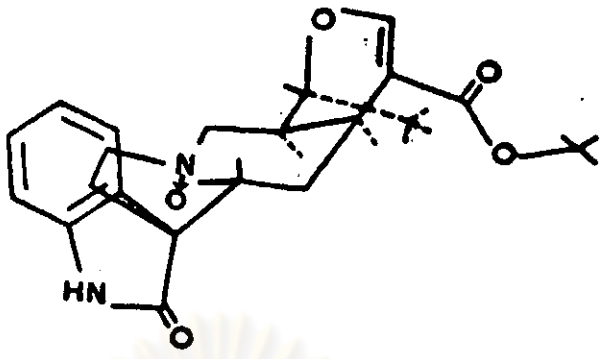
4-R-Mitraphylline N-oxide



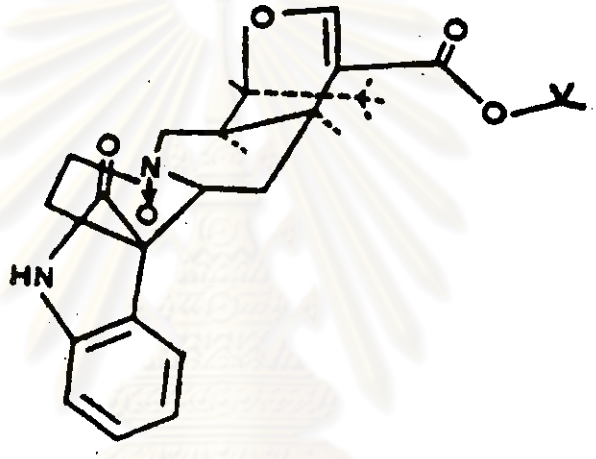
4-R-Isopteropodine N-oxide



4-R-Pteropodine N-oxide



4-S-Speciophylline N-oxide



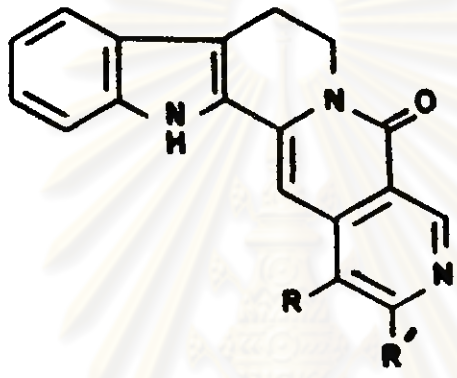
4-S-Uncarine F N-oxide

Only two species of *Uncaria* were reported as having the N-oxides of heteroyohimbines, i.e. *U. gambir* (Hunt.) Roxb. and *U. tomentosa* (Willd.) DC. The N-oxides isolated from the former species were of closed E ring tetrahydroalstonine and two isomeric forms, as previously mentioned, of akuammigine (Merlini *et al.*, 1972b; Phillipson *et al.*, 1978). Those isolated from the latter species were the N-oxides of open E ring isomers, dihydrocorynantheine and hirsutine. This is the first report of these N-oxides as being occurred naturally (Hemingway and Phillipson, 1974).

3.2 Other indole alkaloids isolated from species of *Uncaria*

3.2.1 Pyridino-indolo-quinolizidinone alkaloids

These alkaloids have the following basic structure :



R = $CH{=}CH_2$, R' = H : Angustine

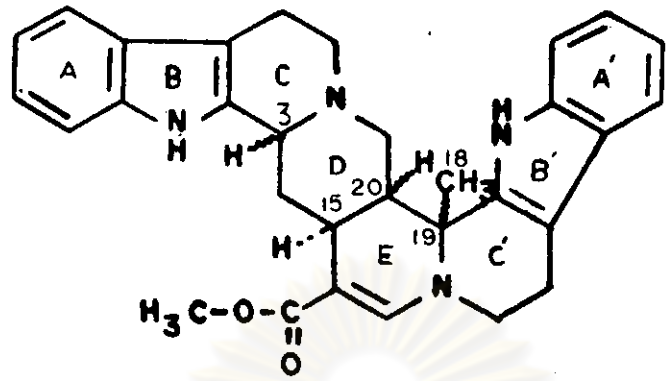
R = $CH(OH)CH_3$, R' = H : Angustoline

R = H, R' = CH_3 : Angustidine

3.2.2 Roxburghines A, B, C, D and E

The roxburghines A, B, C, D and E are new diastereoisomeric indole alkaloidal bases found in a methanolic extract of *Uncaria gambir* (Hunt.) Roxb. leaves and the roxburghines B, D and E are from its stem (Merlini *et al.*, 1970, 1972b).

These alkaloids have the following basic structure :



Epiallo, C(18) - β : Roxburghine B

Normal, C(18) - α : Roxburghine C

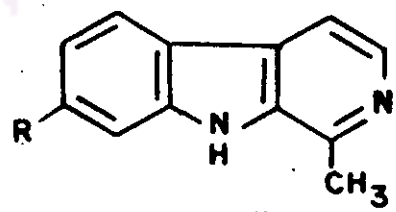
Pseudo, C(18) - α : Roxburghine D

Pseudo, C(18) - β : Roxburghine E

The skeleton of ABCDE rings in the roxburghines is the same as that of heteroyohimbines. The four asymmetric centres in both types of alkaloids are equivalent, i.e. C(3), C(15), C(19) and C(20) (Merlini *et al.*, 1970).

3.2.3 β-Carboline alkaloids

A β-carboline alkaloid, harmane, has been reportedly isolated from several species of *Uncaria*. This group of alkaloids have the following basic structure :

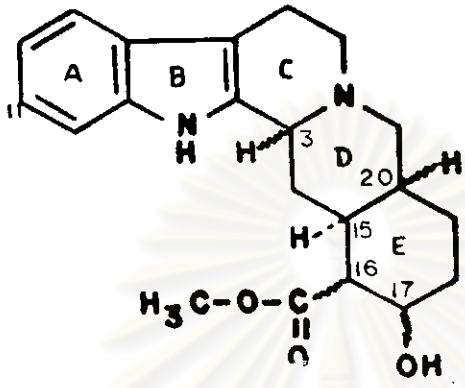


R = H : Harmane

R = OCH_3 : (Harmine)

3.2.4 Yohimbine and its isomers

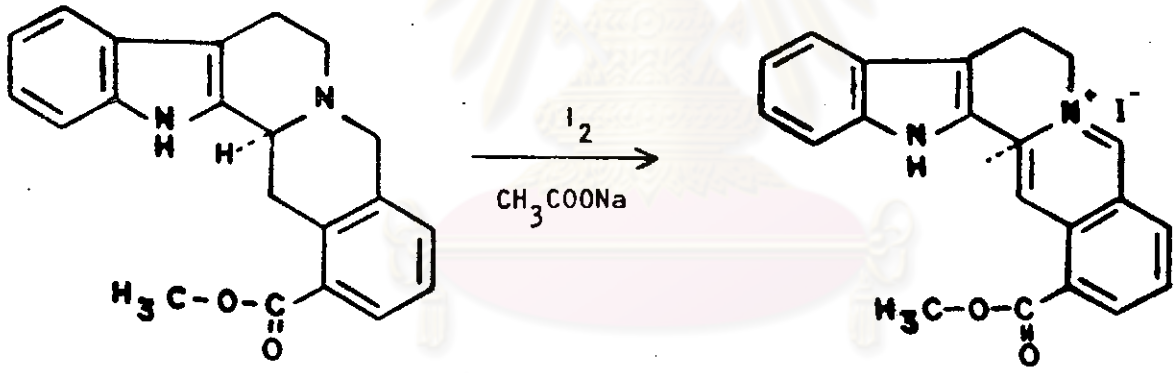
These alkaloids have the following basic structure :



Alkaloid	Configuration	C(11)	C(15) -H	C(16) $-COOCH_3$	C(17) -OH
Yohimbine	*normal*	H	α	α	α
Corynanthine	*normal*	H	α	β	α
β-Yohimbine	*normal*	H	α	α	β
11-Methoxy yohimbine	*normal*	OCH_3	α	α	β
Pseudoyohimbine	*pseudo*	H	α	α	α
Epi-3-corynanthine	*pseudo*	H	α	β	α
Epi-3-β-yohimbine	*pseudo*	H	α	α	β
Alloyohimbine	*allo*	H	α	β	β
α-Yohimbine	*allo*	H	α	β	α
Epi-3-alloyohimbine	*epiallo*	H	α	β	β
Epi-3-α-yohimbine	*epiallo*	H	α	β	α

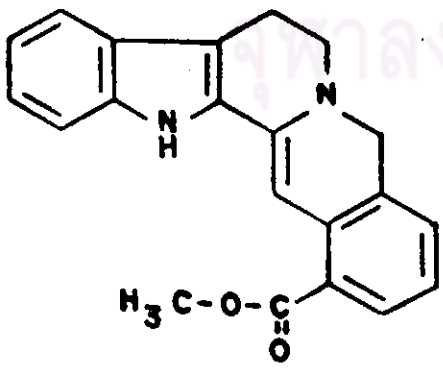
3.2.5 Ourouparine, gambirtannines and related alkaloids

The structures assigned to ourouparine and the other alkaloids of this group have been confirmed by transformations within the series and by total synthesis. Ourouparine was identified as the quaternary alkaloid 11-demethoxy-alstoniline. It is closely related to the gambirtannines. Reaction of dihydrogambirtannine with iodine and sodium acetate results in dehydrogenation and formation of ourouparine iodide which with alkali is readily transformed into a mixture of gambirtannine, oxogambirtannine and neo-oxygambirtannine (Saxton, 1973).

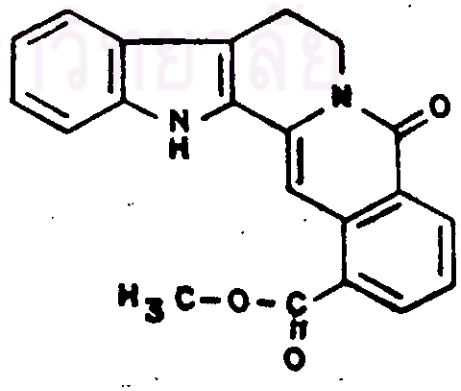


Dihydrogambirtannine

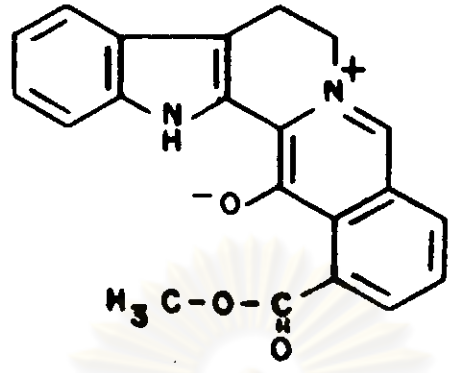
Ourouparine iodide



Gambirtannine



Oxogambirtannine

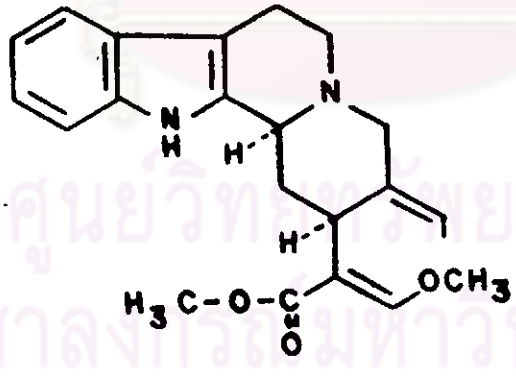


Neo-oxygambirtannine

Gambirtannine, oxogambirtannine and dihydrogambirtannine were extracted from gambir and neo-oxygambirtannine were obtained during the workup of the extract (Merlini *et al.*, 1967b).

3.2.6 Geissoschizine methyl ether

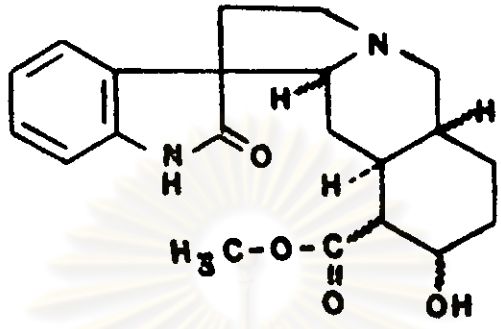
The structure of geissoschizine methyl ether is shown below :



3.2.7 Yohimbine oxindole alkaloids

In *Uncaria attenuata* Korth., the yohimbine oxindole found was not yet identified (Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978).

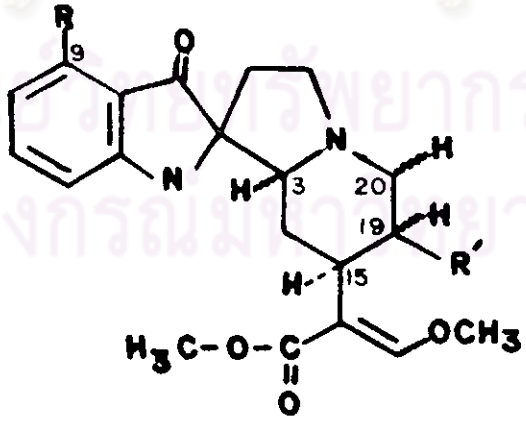
These alkaloids have the following basic structure :



3.2.8 Tetracyclic pseudoindoxyl alkaloids

Dihydrocorynantheine pseudoindoxyl has been reported from only two species of *Uncaria*, i.e. *U. africana* (G. Don) Baill. (Phillipson *et al.*, 1978) and *U. attenuata* Korth. (Phillipson and Hemingway, 1975b; Phillipson *et al.*, 1978).

These alkaloids have the following basic structure :



R = H, R' = CH_2CH_3, *normal* : Dihydrocorynantheine pseudoindoxyl

Dihydrocorynantheine pseudoindoxyl may be prepared by dissolved dihydrocorynantheine in dimethylsulphoxide and sodium methoxide. Oxygen was bubbled through the mixture for 45 minutes at 50° C and extracted into ethyl acetate resulting dihydrocorynantheine pseudoindoxyl, which was major alkaloid and separated by preparative T.L.C. (Phillipson and Hemingway, 1975b).

3.2.9 Africanine and hanadamine

Africanine and hanadamine are of doubtful structure. Africanine, reportedly from *Uncaria africana* (G. Don) Baill. and hanadamine from *U. kawakamii* Hayata have been only partly characterised (Phillipson *et al.*, 1978).

3.2.10 Mitraversine

Mitraversine was found by T.L.C. to be a mixture of four alkaloids (Shellard and Phillipson, 1964a; Shellard *et al.*, 1978b). It has never been possible to relate this alkaloid to any isolated alkaloids.

4. Chemical Transformations

There are interesting biogenetic problems in living plants, e.g. whether inter-relationships within the heteroyohimbines, the oxindoles, and between heteroyohimbines and oxindoles take place. It is of value, therefore, to study the chemical transformations of the alkaloids performed both *in vitro* and *in vivo*.

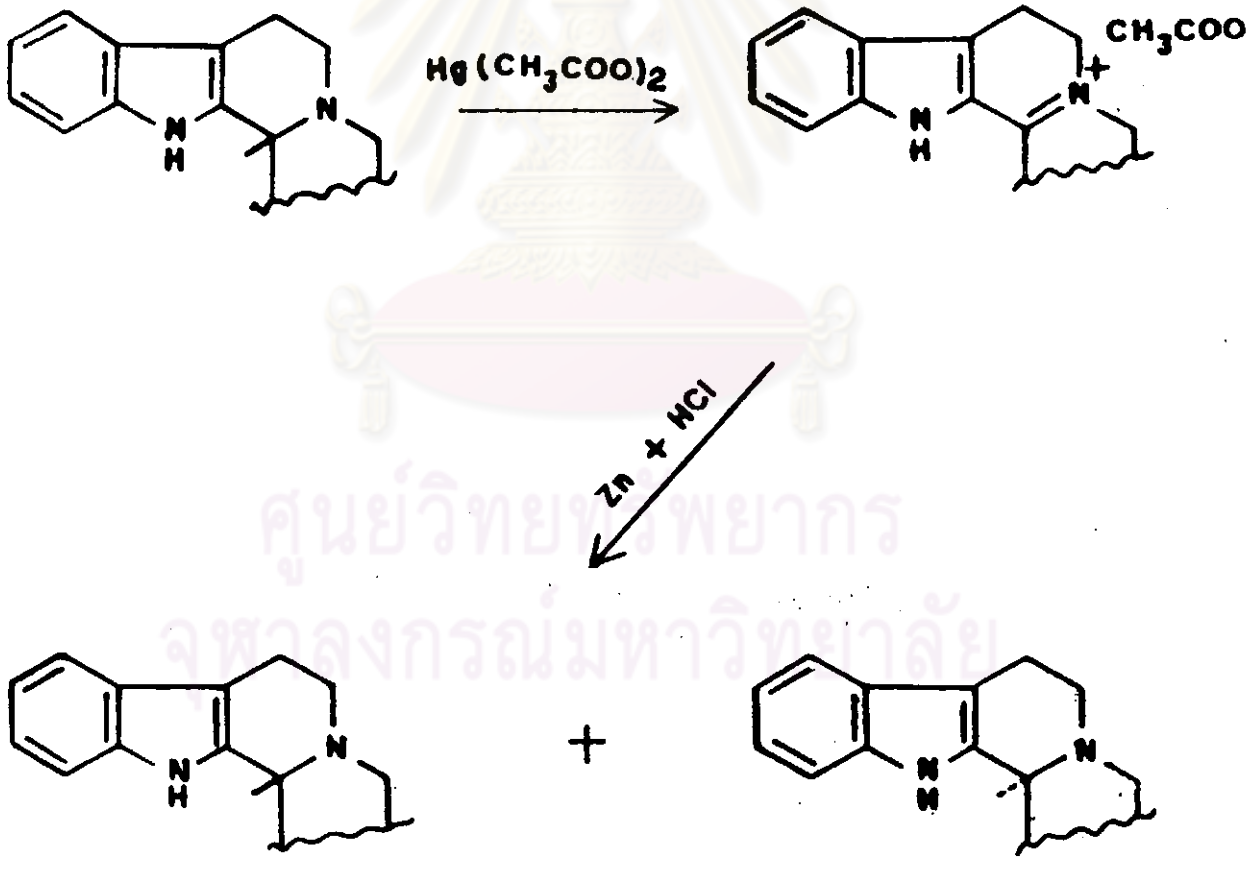
4.1 *In vitro*

4.1.1 Isomerisation of heteroyohimbine alkaloids

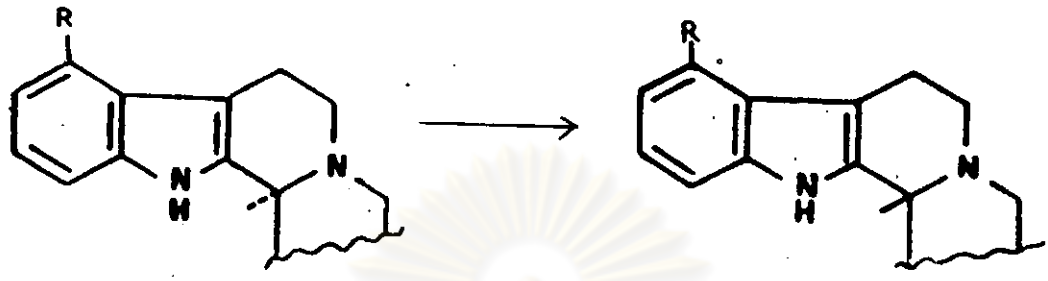
The heteroyohimbine alkaloids may be isomerised at C(3) by using mercuric acetate as an oxidising agent and zinc and hydrochloric acid as a reducing agent (Wenkert and Roychaudhuri, 1956; Weisenborn and Diassi, 1956). The reaction is shown in Fig. V.

Fig. V

Oxidation-reduction reaction of heteroyohimbine alkaloids



In terms of configuration, the isomerisation of heteroyohimbine alkaloids involves the conversion of C(3) - H α to C(3) - H β.



normal, allo *pseudo, epiallo*

Examples of the isomerisation of heteroyohimbine alkaloids using this method are given in Table VI.

Table VI

Isomerisation of heteroyohimbine alkaloids

Conversion	Reference
ajmalicine (*normal*) ⟶ 3-isoajmalicine (*pseudo*)	Wenkert and Roychaudhuri, 1956.
19-epi-ajmalicine (*normal*) ⟶ 19-epi-3-iso-ajmalicine (*pseudo*)	Phillipson and Hemingway, 1975b.
mitrajavine (*pseudo*) ⟶ isomitrajavine (*normal*)	Shellard and Sarpong, 1971a, b.
hirsutine (*pseudo*) ⇌ dihydrocorynantheine (*normal*)	Trager *et al.*, 1968b.

Table VI (continued)

Conversion	Reference
speciogynine (*normal*) ⟶ mitraciliatine (*pseudo*)	Trager *et al.*, 1968b; Shellard *et al.*, 1978c.
paynantheine (*normal*) ⟶ isopaynantheine (*pseudo*)	Beckett *et al.*, 1969; Shellard *et al.*, 1978c.
corynantheidine (*allo*) ⟶ isocorynantheidine (*epiallo*)	Trager *et al.*, 1968b; Beckett *et al.*, 1969; Shellard *et al.*, 1978c.
mitragynine (*allo*) ⟶ speciociliatine (*epiallo*)	Trager *et al.*, 1968b; Shellard *et al.*, 1978c.

4.1.2 Isomerisation of oxindole alkaloids

Oxindole alkaloids may be isomerised about the C(3) and/or spiro C(7) centres by treatment with either pyridine (basic isomerisation) or acetic acid (acidic isomerisation) or simply by heating. The isomerisation involves scission and reformation at the C(3) - C(7) bond and hence possible inversion of one or both of the centres (Trager *et al.*, 1968a).

Four isomeric compounds should result upon isomerisation of an isomer, i.e. two (A and B) with C(3) - H α and two (A and B) with C(3) - H β. Isomerisation of *normal* A or B oxindoles results in only two products, which are the two *normal* isomers supporting the conformational analysis by Trager *et al.* (1968a) that *pseudo* oxindole alkaloids are too unstable to exist.

Trager *et al.* (1968a) suggested that in the acidic isomerisation, the B series oxindoles predominate due to stabilisation of the conjugated base by formation of intramolecular hydrogen bond between the protonated lone pair of N(4) and the lactam carbonyl group. This stabilisation is not possible with the A series oxindoles as the lactam carbonyl is below the plane of C/D ring.

In basic pyridine isomerisation the A isomers predominate and this is thought to be destabilisation due to the electrostatic repulsion between the lone pair of electrons of N(4) and the lactam carbonyl group in the free base form of the B isomers.

Examples of the isomerisation of oxindole alkaloids are given in Table VII.

Table VII

Isomerisation of oxindole alkaloids

Conversion	Reference
isomitraphylline ⟶ isomitraphylline + mitraphylline	Seaton *et al.*, 1960.
mitraphylline ⟶ isomitraphylline + mitraphylline	Beckett *et al.*, 1965a.
uncarine B ⟶ uncarine A + uncarine B	Seaton *et al.*, 1960.
isorhynchophylline ⟶ isorhynchophylline + rhynchophylline	Nozoye, 1958c; Seaton *et al.*, 1960; Trager *et al.*, 1968a.
rhynchophylline ⟶ isorhynchophylline + rhynchophylline	Seaton *et al.*, 1960; Trager *et al.*, 1968a.
rotundifoline ⟶ rotundifoline + isorotundifoline	Trager *et al.*, 1968a; Hemingway *et al.*, 1975.
isorotundifoline ⟶ rotundifoline + isorotundifoline	Hemingway *et al.*, 1975.
rhynchociline ⟶ rhynchociline + ciliaphylline	Trager *et al.*, 1968a.
specionoxeine ⟶ isospecionoxeine + specionoxeine	Trager *et al.*, 1968a.
corynoxine B ⟶ corynoxine + corynoxine B	Beckett *et al.*, 1969.

Table VII (continued)

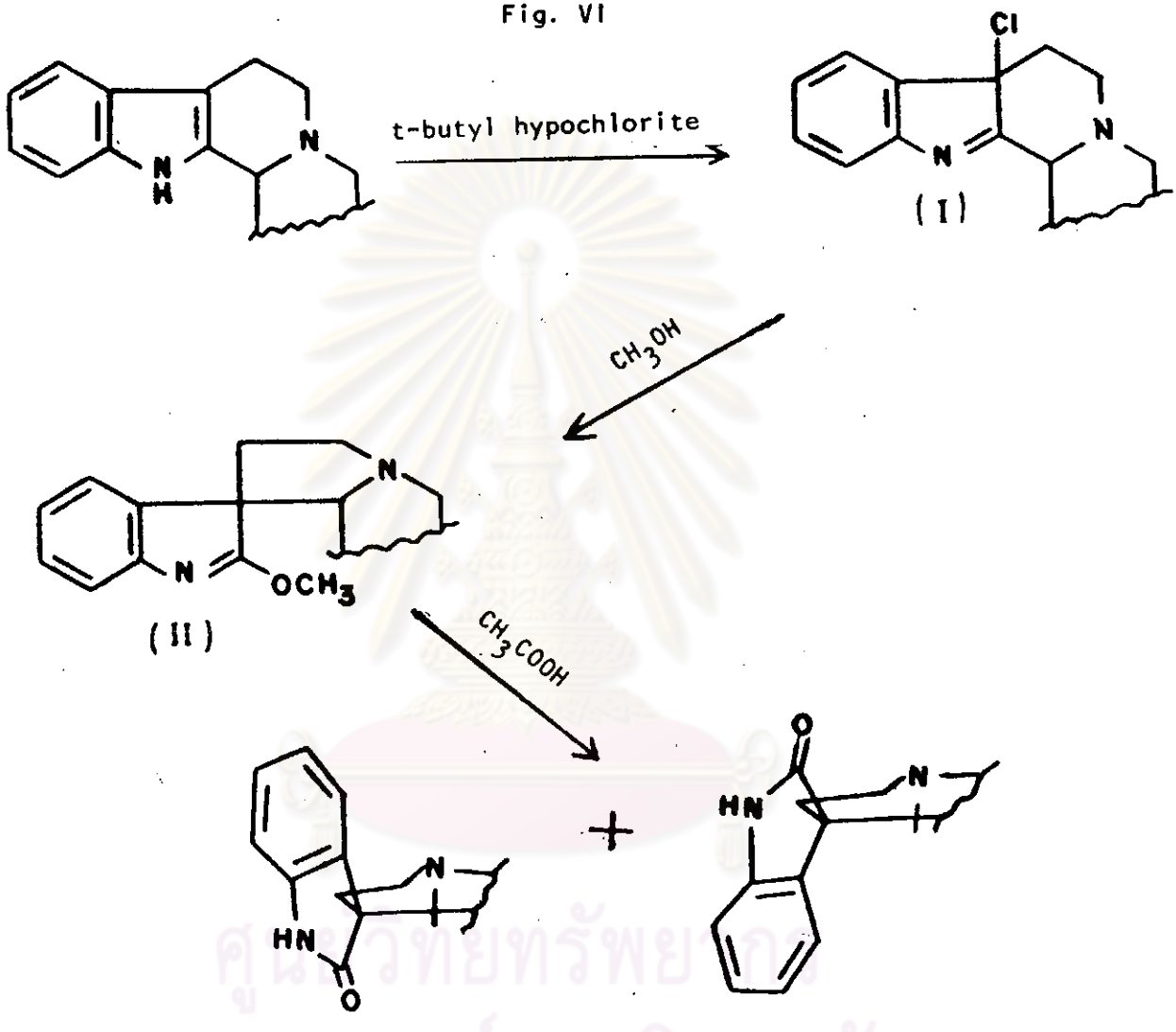
Conversion	Reference
mitrafoline ⟶ mitrafoline + isomitrafoline + isospeciofoline + speciofoline	Hemingway *et al.*, 1975.
speciofoline ⟶ mitrafoline + isomitrafoline + isospeciofoline + speciofoline	Hemingway *et al.*, 1975.
isomitrafoline ⟶ mitrafoline + speciofoline	Hemingway *et al.*, 1975.
isospeciofoline ⟶ mitrafoline + speciofoline	Hemingway *et al.*, 1975.
mitragynine oxindole B ⟶ mitragynine oxindole A + mitragynine oxindole B	Beckett *et al.*, 1969.

4.1.3 Conversion of heteroyohimbine alkaloids to oxindole alkaloids

Finch and Taylor (1962a, b) and Shavel Jr. and Zinnes (1962) have shown that yohimbine and heteroyohimbine alkaloids are transformed into a mixture of epimeric C(7) chloroindolenines (I) by the action of tertiary-butyl hypochlorite. Methanolysis of chloroindolenines

yield the imido ether (II) which hydrolyse in aqueous acetic acid to give the two isomers of oxindole, A and B (Fig. VI).

Fig. VI



Oxindole A Oxindole B

The examples of the conversion of some heteroyohimbine alkaloids to their corresponding oxindoles using this method is summarised in Table VIII.

Table VIII

Conversion of heteroyohimbine alkaloids

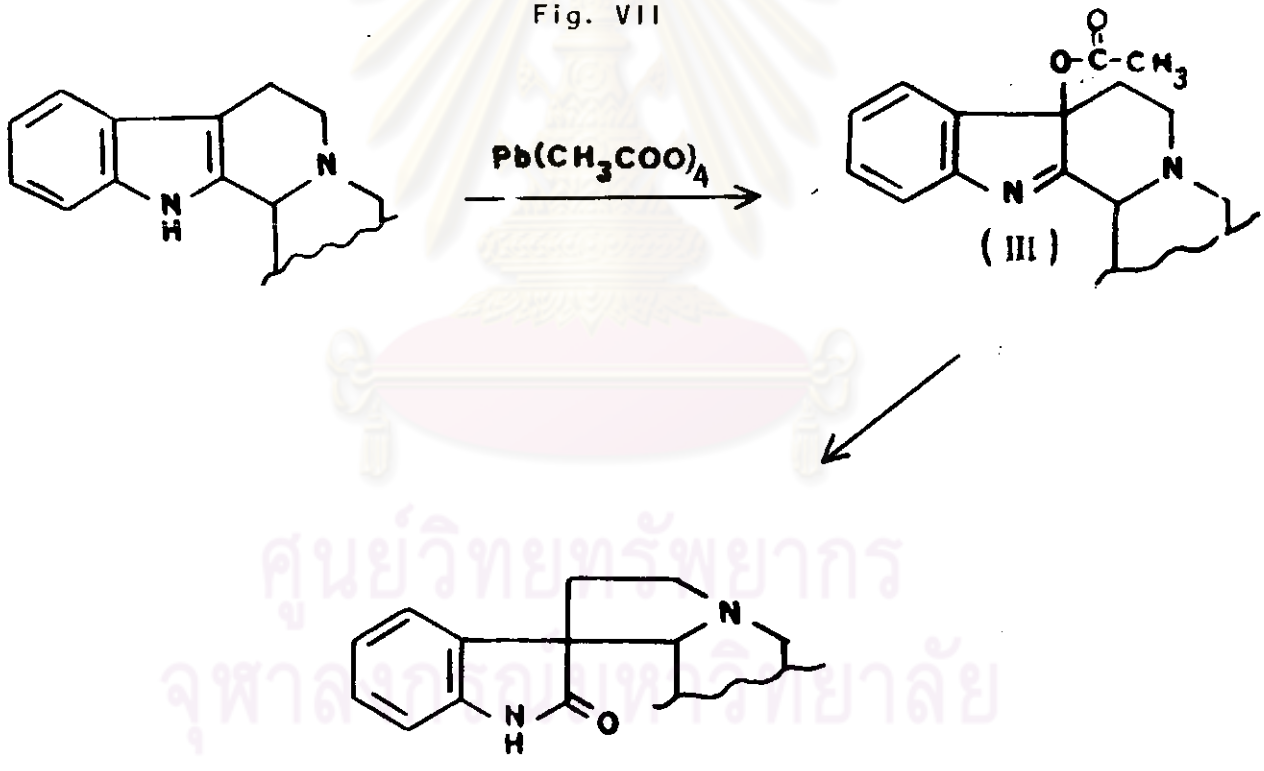
Heteroyohimbine	Oxindole	Reference
ajmalicine	isomitraphylline + mitraphylline	Finch and Taylor, 1962a; Shavel Jr. and Zinnes, 1962; Shellard and Houghton, 1973.
mitrajavine	isojavaphylline + javaphylline	Shellard and Sarpong, 1971a.
dihydrocorynantheine	isorhynchophylline + rhynchophylline	Finch and Taylor, 1962a.
corynantheine	corynoxeine	Finch and Taylor, 1962b.
mitraciliatine	rhynchociline + cillaphylline	Shellard and Sarpong, 1971a
corynantheidine	corynoxines A, B	Beckett *et al.*, 1969.
mitragynine	mitragynine oxindoles A, B	Beckett *et al.*, 1969;
speciociliatine	speciociliatine oxindoles A, B	Shellard *et al.*, 1978a.

In 1966 Zinnes and Shavel converted the carboxylic E ring indole alkaloid, *pseudo*-yohimbine into *normal* oxindoles (Shellard and Sarpong, 1971b). Therefore there is the possibility that the *pseudo*

heteroyohimbine alkaloids could al·o be transformed to the *normal* oxindoles which certainly occ rred in some *Mitragyna* species where *pseudo* heteroyohimbine alkaloids were found (Shellard and Sarpong, 1971b).

Another method of converting heteroyohimbines to oxindoles is the use of lead tetra-acetate to give an acetoxy indolenine (III) which on refluxing with methyl alcohol containing acetic acid gives the oxindoles (Hart *et al.*, 1967) (Fig. VII).

Fig. VII



Hart *et al.* (1967) used this method to prepare isopteropodine, pteropodine, specipphylline and uncarine F from the heteroyohimbine tetrahydroalstonine.

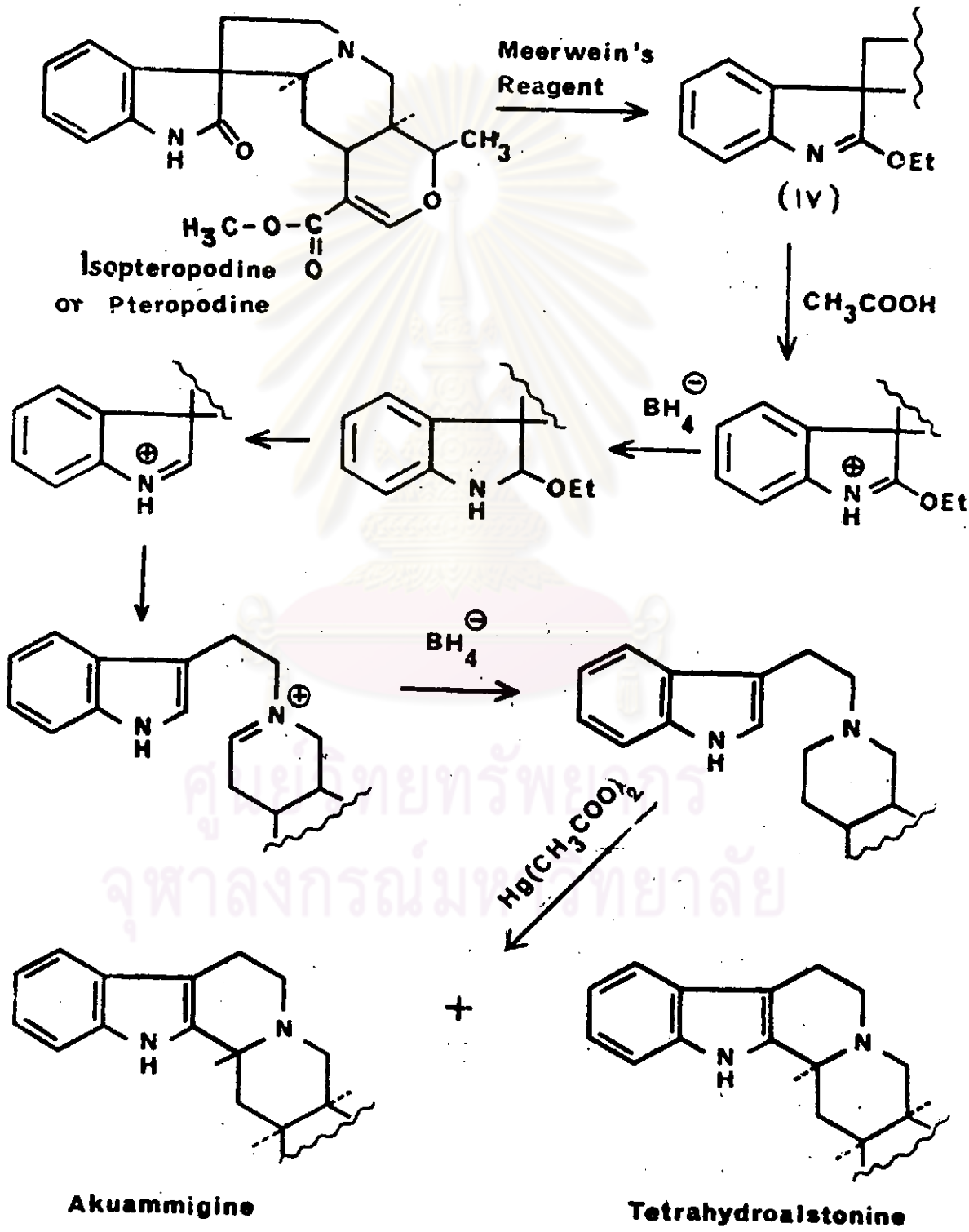
4.1.4 Conversion of oxindoles to heteroyohimbine alkaloids

Aimi *et al.* (1972) treated the oxindoles with Meerwein's reagent in acetic acid to form the ethyliminoethers (IV). They found that sodium borohydride in acetic acid is a suitable reduction reagent for the iminoether system, which is a potential oxindole. This was then oxidatively cyclised in diluted acetic acid with mercuric acetate and the two heteroyohimbines were isolated with benzene.

They used this method in the treatment of isopteropodine and pteropodine and in each case the corresponding heteroyohimbines tetrahydroalstonine and its isomer, akuammigine were obtained (Fig. VIII). They have also similarly converted isorhynchophylline into dihydrocorynantheine and hirsutine.

Fig. VIII .

Conversion of oxindoles to heteroyohimbines



4.2 *In vivo*

By using feeding experiments with unlabelled alkaloids, Shellard and Houghton (1972a) observed the presence of isomitraphylline and mitraphylline both after feeding young plant of *Mitragyna parvifolia* (Roxb.) Korth., grown from seed obtained from Sri Lanka, with ajmalicine and 3-isoajmalicine into the stem xylem. Thus showing that conversions of *normal* and *pseudo* heteroyohimbine alkaloids to *normal* oxindoles occur *in vivo*. The interconversion of the heteroyohimbines did not seem to take place since no 3-isoajmalicine were detected after feeding the plant with ajmalicine and vice versa.

Their work also revealed that the specificity of the enzyme systems in this plant might be for the C(9) unsubstituted alkaloids because no oxindoles were detected after feeding with C(9) - methoxy substituted *normal* and *pseudo* heteroyohimbine alkaloids, isomitrajavine and mitrajavine. The enzyme systems appeared to be also specific for the closed E ring alkaloids since there was no evidence of any oxindole corresponding to the open E ring heteroyohimbine alkaloids after they were fed to the plant.

The first part of these observations was confirmed by work with labelled alkaloids by Shellard and Houghton (1973). They fed ^{14}C-tetrahydroalstonine and ^{14}C-akuammigine separately to *M. parvifolia* (Roxb.) Korth. plant, labelled isopteropodine, pteropodine, speciophylline and uncarine F were detected in both cases.

Shellard and Houghton (1974a) further examined the distribution of alkaloids in young plants of this species. They fed ^{14}C-alkaloids into the stem bark, stem xylem and root bark just below the hypocotylar region. The evidence pointed to the possibility of this plant possessing two biogenetic sites - the leaves and the roots - with mitraphylline being the alkaloid which links the two sites. They fed pteropodine and mitraphylline separately through the stem bark and pteropodine was shown to be converted to mitraphylline, and mitraphylline into corynoxeine and rhynchophylline.

By feeding rhynchophylline into the root phloem rhynchophylline, a *normal* oxindole, was converted to the *pseudo* heteroyohimbine hirsutine and vice versa. This clearly showed that neither *normal* oxindole nor *pseudo* heteroyohimbine could be converted to the corresponding *normal* heteroyohimbine since no dihydrocorynantheine the *normal* heteroyohimbine corresponding to rhynchophylline could be detected. There was no evidence to indicate whether the dominant alkaloid in the root, rhynchophylline, was derived from mitraphylline (from pteropodine) or from hirsutine which was found in the root.

Shellard and Houghton (1972a), using unlabelled alkaloids, found that when mitraphylline was fed into the stem xylem, rhynchophylline was found in the leaves. Their result (1974a) with labelled mitraphylline revealed that rhynchophylline in the leaves was not necessarily from the main stem xylem but that the mitraphylline itself is converted via corynoxeine to rhynchophylline. When large amount of ^{14}C-rhynchophylline was fed, both mitraphylline

and rhynchophylline were detected in the leaf together with ^{14}C-labelled *allo* and *epiallo* closed E ring oxindoles. It would appear that the interconversion involving rhynchophylline $\rightleftharpoons$ mitraphylline $\rightleftharpoons$ pteropodine occurs normally in the leaf base but since only small quantities are present in the transportation stream, only the final products - the *allo* and *epiallo* oxindoles are found.

5. N-oxidation of heteroyohimbine and oxindole alkaloids

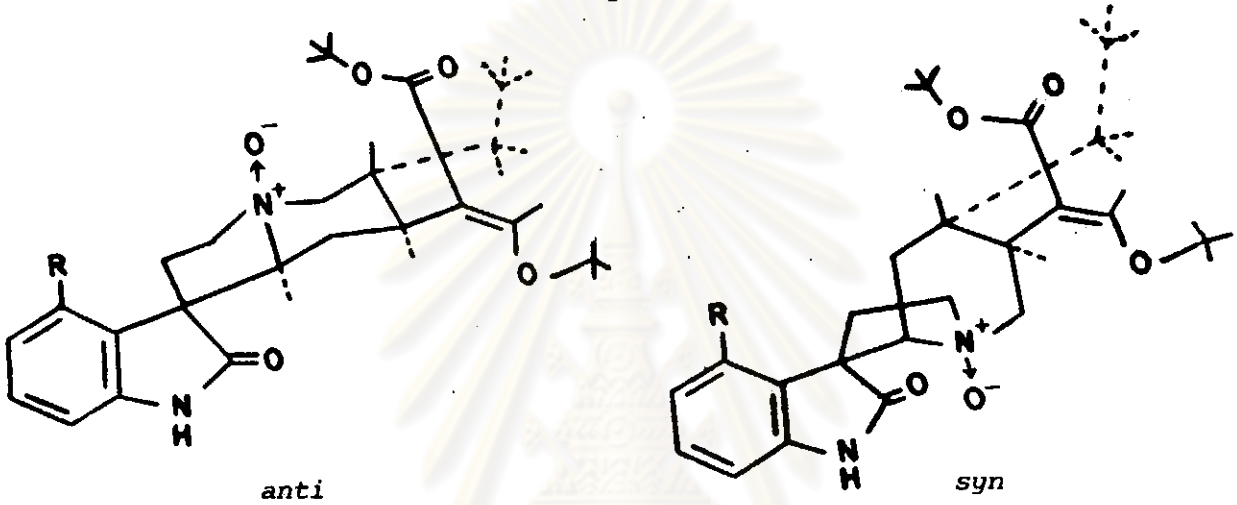
Shellard *et al.* (1971) prepared the N-oxides of isorhynchophylline and rhynchophylline by treating an ethanolic solution of the alkaloid with hydrogen peroxide solution overnight at room temperature, followed by heating on a boiling water bath for 30 minutes.

Merlini *et al.* (1972b) synthesised N-oxides of closed E ring unsubstituted heteroyohimbine alkaloids by treatment with m-chloroperbenzoic acid. Those synthesised were 4-R-ajmalicine, 4-R-3-isoajmalicine, 4-R-tetrahydroalstonine, 4-R-akuammigine and 4-S-akuammigine N-oxides.

Phillipson *et al.* (1973a) have used both methods in preparing N-oxides of isorhynchophylline (A series), rhynchophylline (B series), rhynchociline (A series) and ciliaphylline (B series) in order to characterise naturally occurring ciliaphylline N-oxide isolated from *Mitragyna tubulosa* Havil. and found that whereas the B series oxindoles give only one N-oxide, the A series give two - an *anti* and a *syn* N-oxides. Thus isorhynchophylline and rhynchociline appear to form two N-oxides while rhynchophylline and ciliaphylline form only one.

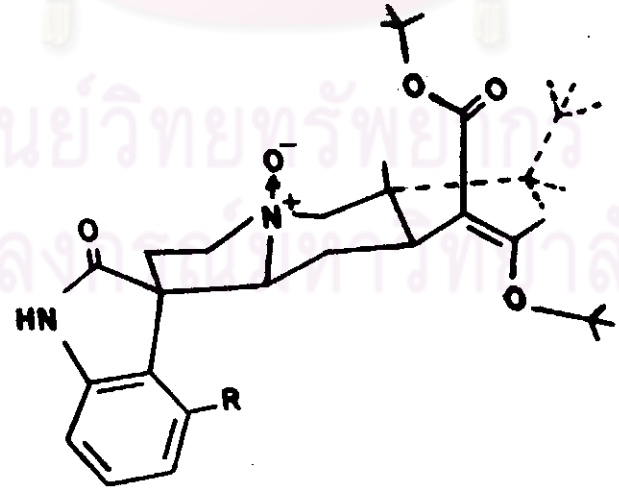
Shellard *et al.* (1977) used the latter method to prepare N-oxides of rotundifoline (A series) and isorotundifoline (B series) and obtained two rotundifoline N-oxides (*anti* and *syn*) and one isorotundifoline N-oxide.

Fig. IX



anti *syn*

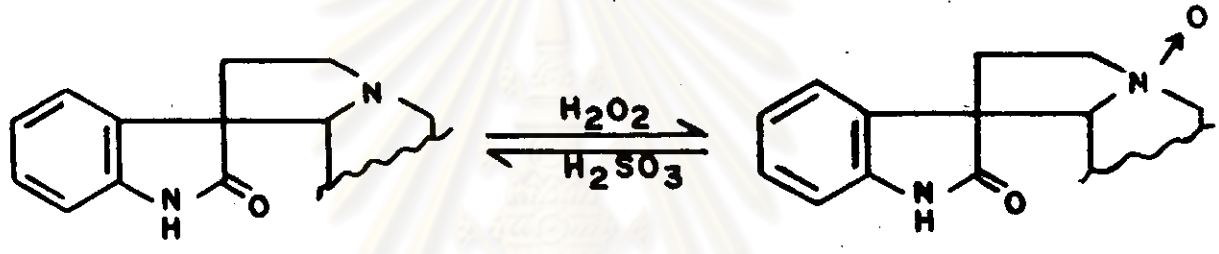
N-oxides of oxindole A



N-oxide of oxindole B

The N-oxides are readily reconverted to the parent alkaloids by reduction with sulphurous acid (Shellard *et al.*, 1971) or treated with excess ferrous sulphate and heated on a steam bath for 30 minutes (Merlini *et al.*, 1972b) (Fig. X). There is no isomerisation of N-oxides.

Fig. X



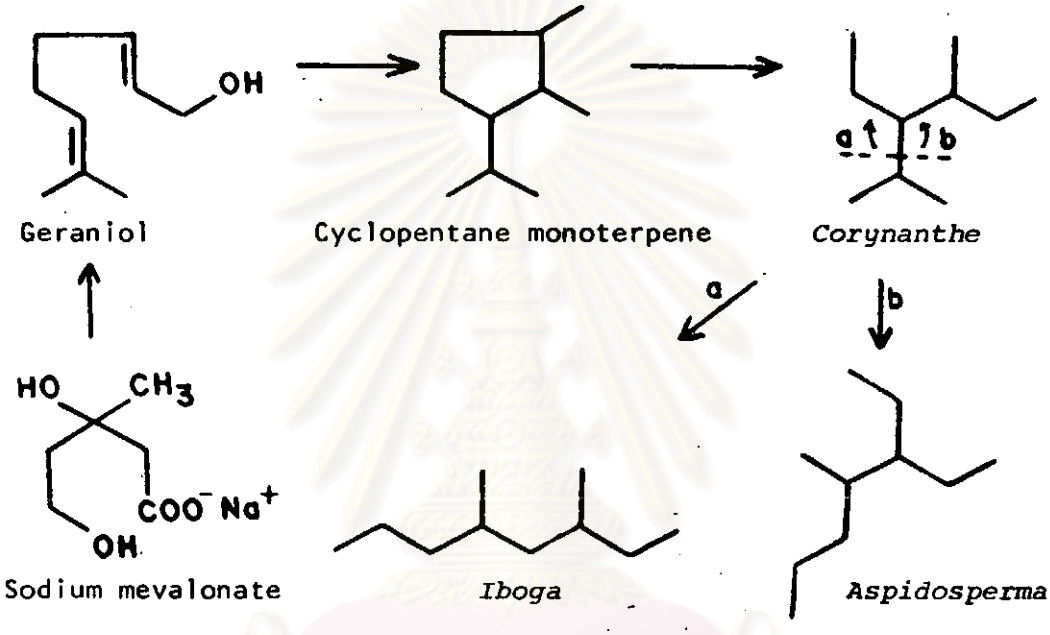
6. Biogenesis

6.1 Heteroyohimbine alkaloids

The suggestion that indole alkaloids are biosynthesised from a cyclopentane monoterpene skeleton has been strongly supported by feeding experiments with sodium mevalonate and geraniol labelled at various positions to *Catharanthus roseus* plant (Battersby *et al.*, 1966b). Degradation of the labelled catharanthine and dehydroaspidospermidine gave results in agreement with head-to-tail combination of the two C_5 units and the logical deduction that geraniol is a precursor of the indole alkaloids was proved to be correct for the *Iboga*, *Corynanthe*, and *Aspidosperma* groups of bases (Battersby *et al.*, 1966a, c). Fig. XI

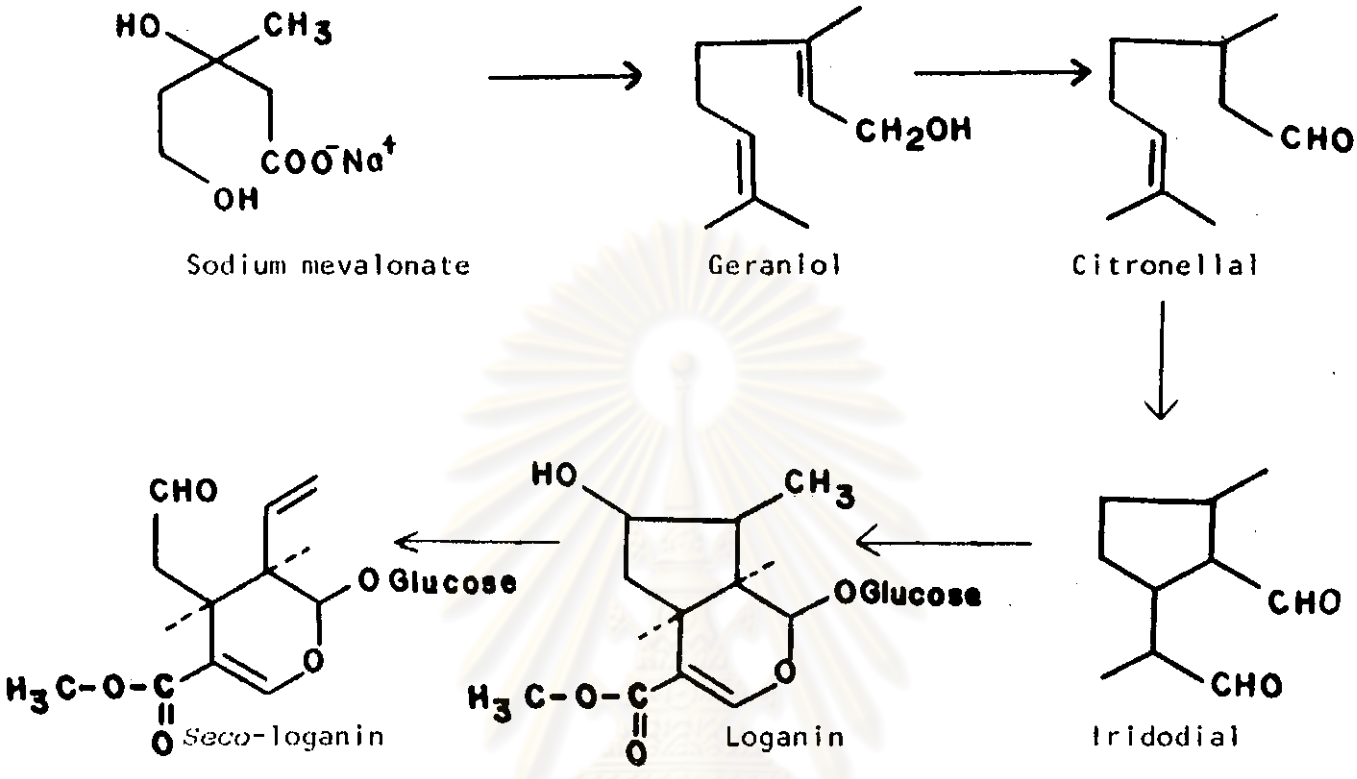
shows how such a cyclopentanoid monoterpene could form the C_{9-10} unit of the three major groups of indole alkaloids.

Fig. XI



Battersby *et al.* (1966b) found the evidence to be strongly in support that loganin was the most probable cyclopentanoid monoterpene precursor of the indole alkaloids. Battersby *et al.* (1968) stated that the biogenesis of indole alkaloids is through the pathway from mevalonate through geraniol and loganin to *seco*-loganin which then serves as precursor of the non-tryptamine units present in the three large groups of indole alkaloids (Fig. XII).

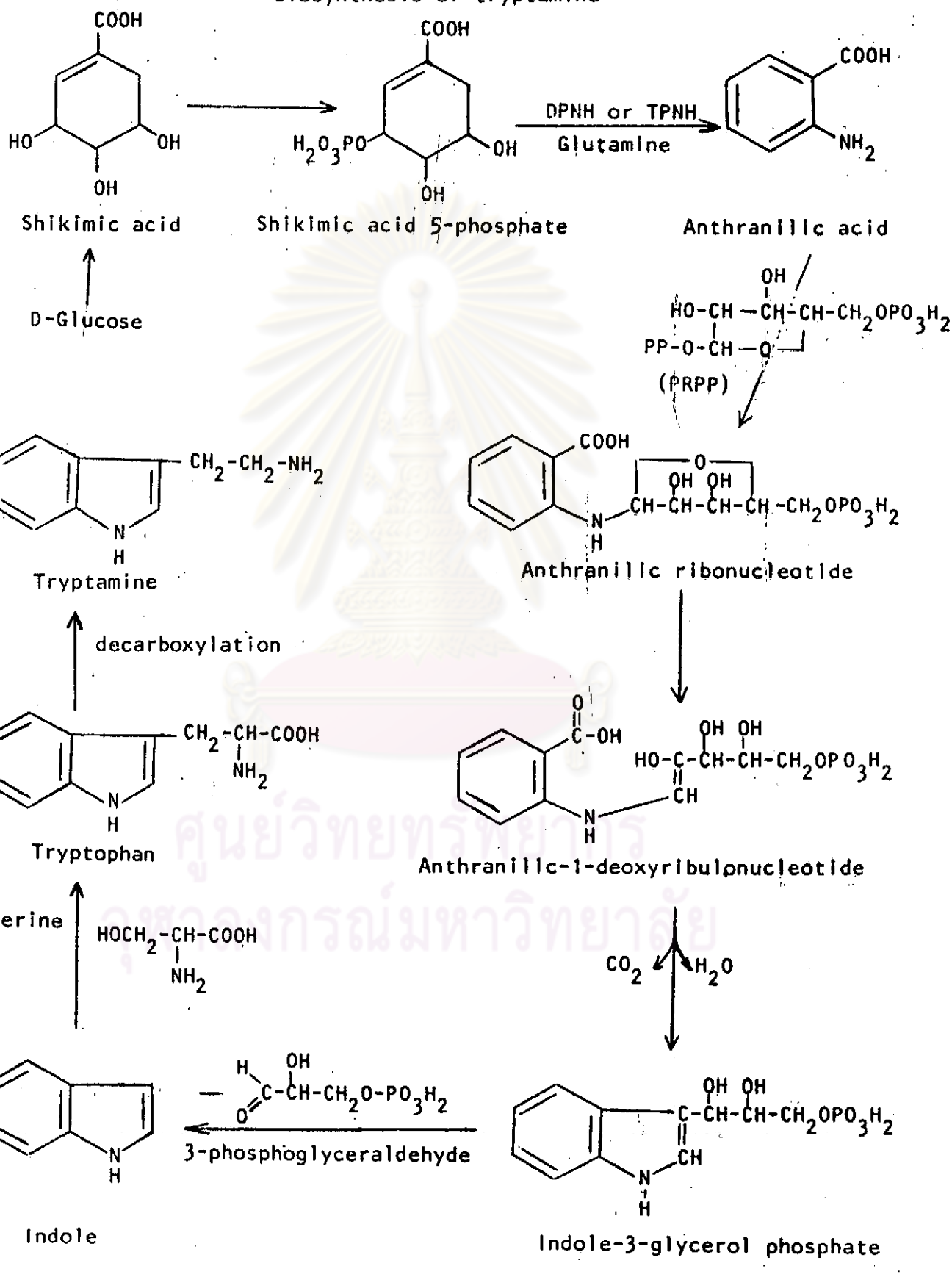
Fig. XII



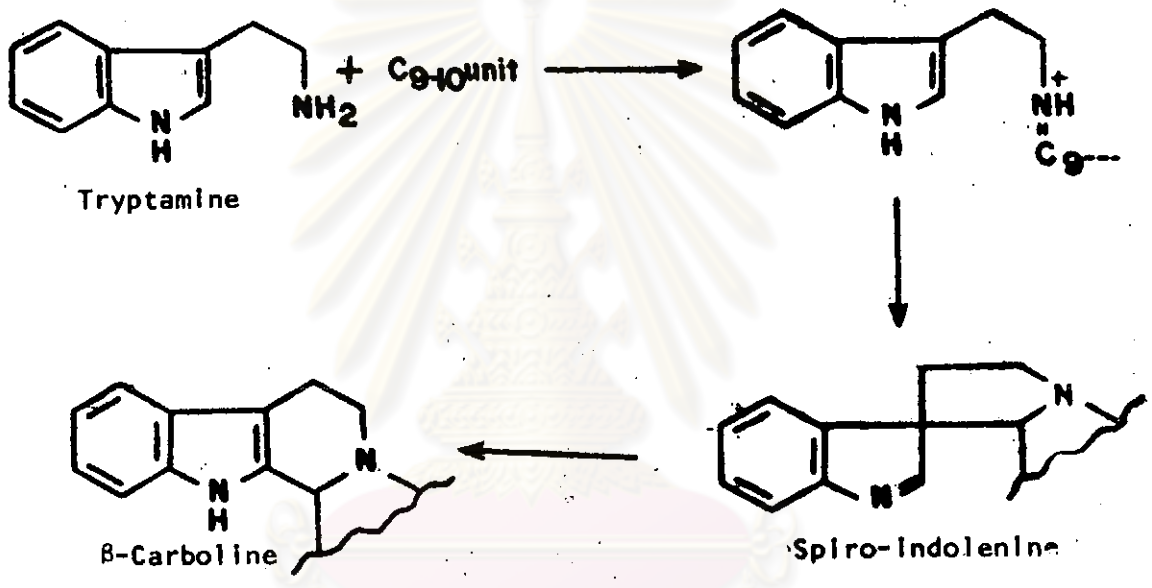
It was accepted that tryptamine provided the β-carboline portion of the indole alkaloids. Tryptophan, from which tryptamine is derived, is biosynthesised from shikimic acid, having anthranilic acid as an intermediate (Mattoon, 1963; Mahler and Cordes, 1966), and that decarboxylation occurs to yield tryptamine which is then utilised (Battersby *et al.*, 1968) (Fig. XIII).

Fig. XIII

Biosynthesis of tryptamine

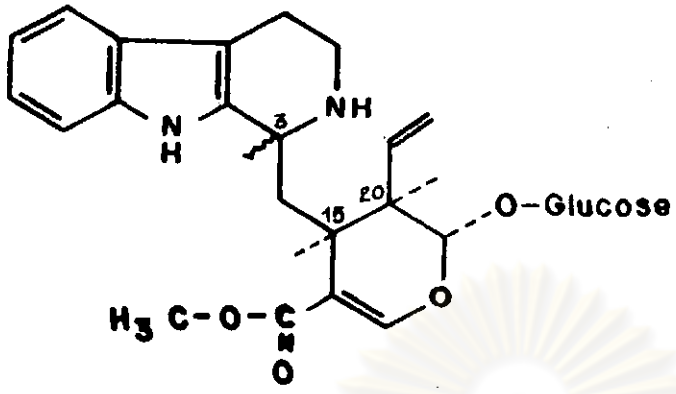


Tryptamine or tryptophan condense with various aldehydes, generally a C_{9-10} unit to give the corresponding indole alkaloids. Jackson and Smith (1968a, b) have shown that a β-carboline is formed, the condensation initially yields a spiro-indolenine which immediately rearranges to give the β-carboline as shown below :



It was shown that *seco*-loganin reacted with tryptamine to generate the β-carbolines, vincoside and strictosidine (isovincoside) (Battersby *et al.*, 1968), so seemed to support the Jackson and Smith hypothesis.

From a comparison of molecular rotation differences in vincoside and ipecoside derivatives, it was deduced that vincoside had the 3 α and strictosidine the 3 β orientation (Battersby *et al.*, 1968), but later Blackstock *et al.* (1971) obtained the absolute configuration at C(3) in vincoside as β.



C(3) - H β : Vincoside

C(3) - H α : Strictosidine

This was also reported by De Silva *et al.* (1971). Thus the real reason for the dominance of *epiallo* and *pseudo* indole alkaloids becomes apparent. This seems to be the major route of biogenesis and since both can be converted to the *allo* and *normal* oxindoles, the absence of the *allo* and *normal* indole alkaloids for long period of time are not surprising so far as the conversion to oxindoles is concerned.

The schemes represent the biogenetic pathway to the heteroyohimbine alkaloids can therefore be worked out following these pattern.

Fig. XIV shows the combination of tryptamine with *seco*-loganin to give an intermediate (V) which goes directly by α condensation to give the β indolene vincoside (VI) or goes via the β condensation to the spiro-indolenine (VII) and then to vincoside (VI). The loss of the glucoside link, the formation of the aldehyde group and the opening of ring E to give (VIII) lead to the formation of an intermediate (IX) (Shellard and Houghton, 1973).

Fig. XIV

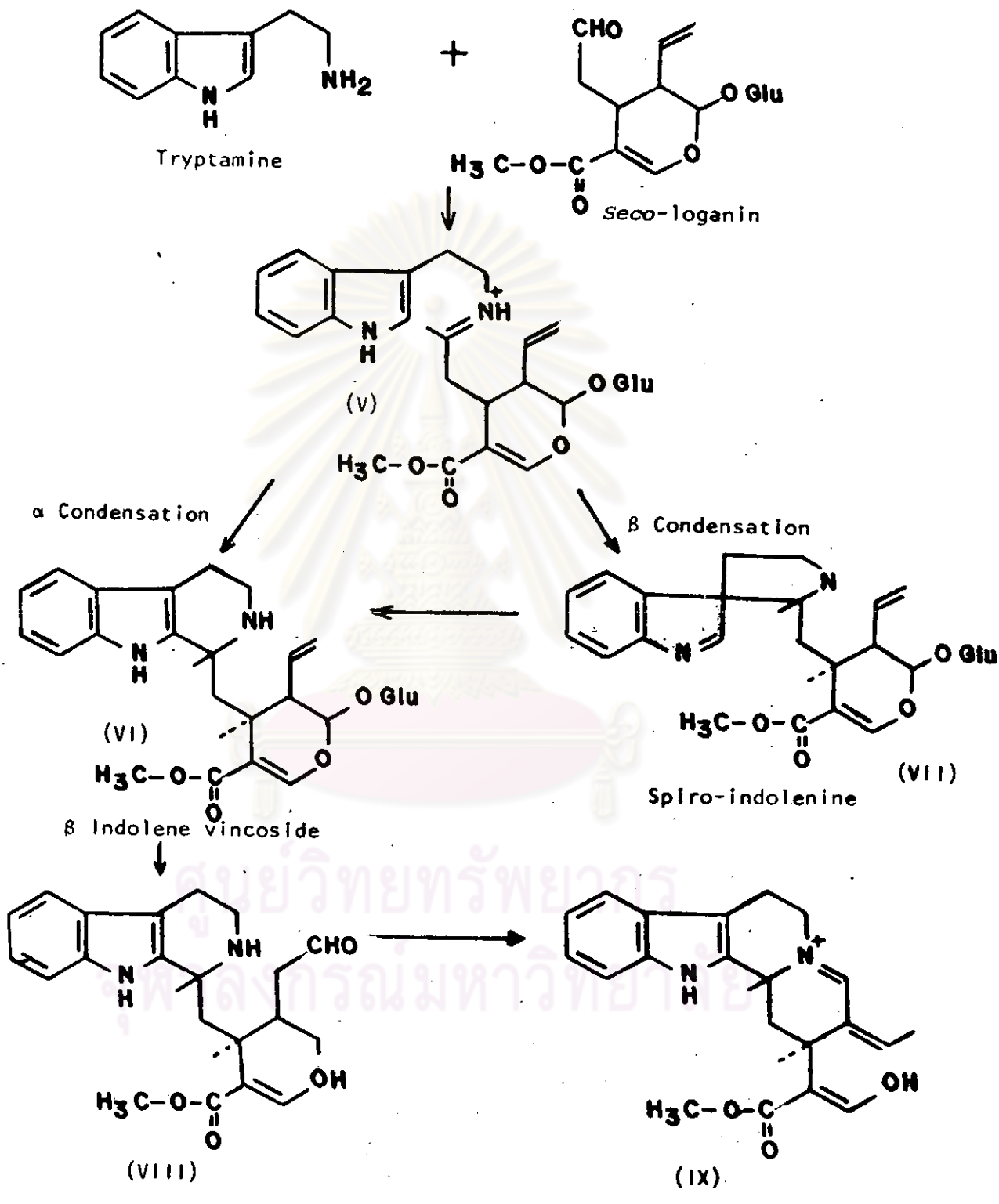


Fig. XV and XVI show the relationships between intermediate (IX) and the heteroyohimbine-oxindole alkaloids (Shellard and Houghton, 1973).

Fig. XV

Biogenesis of closed E ring alkaloids

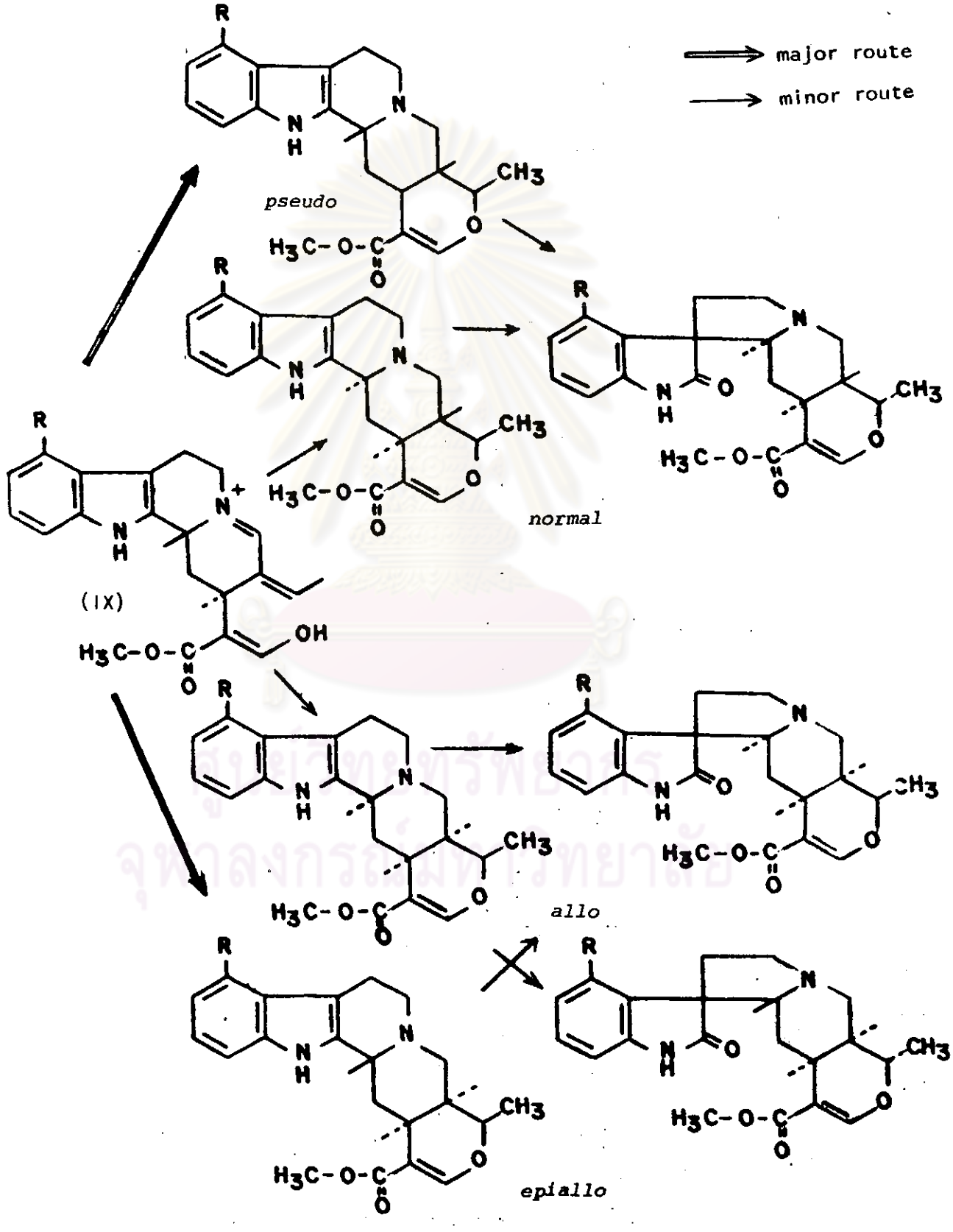
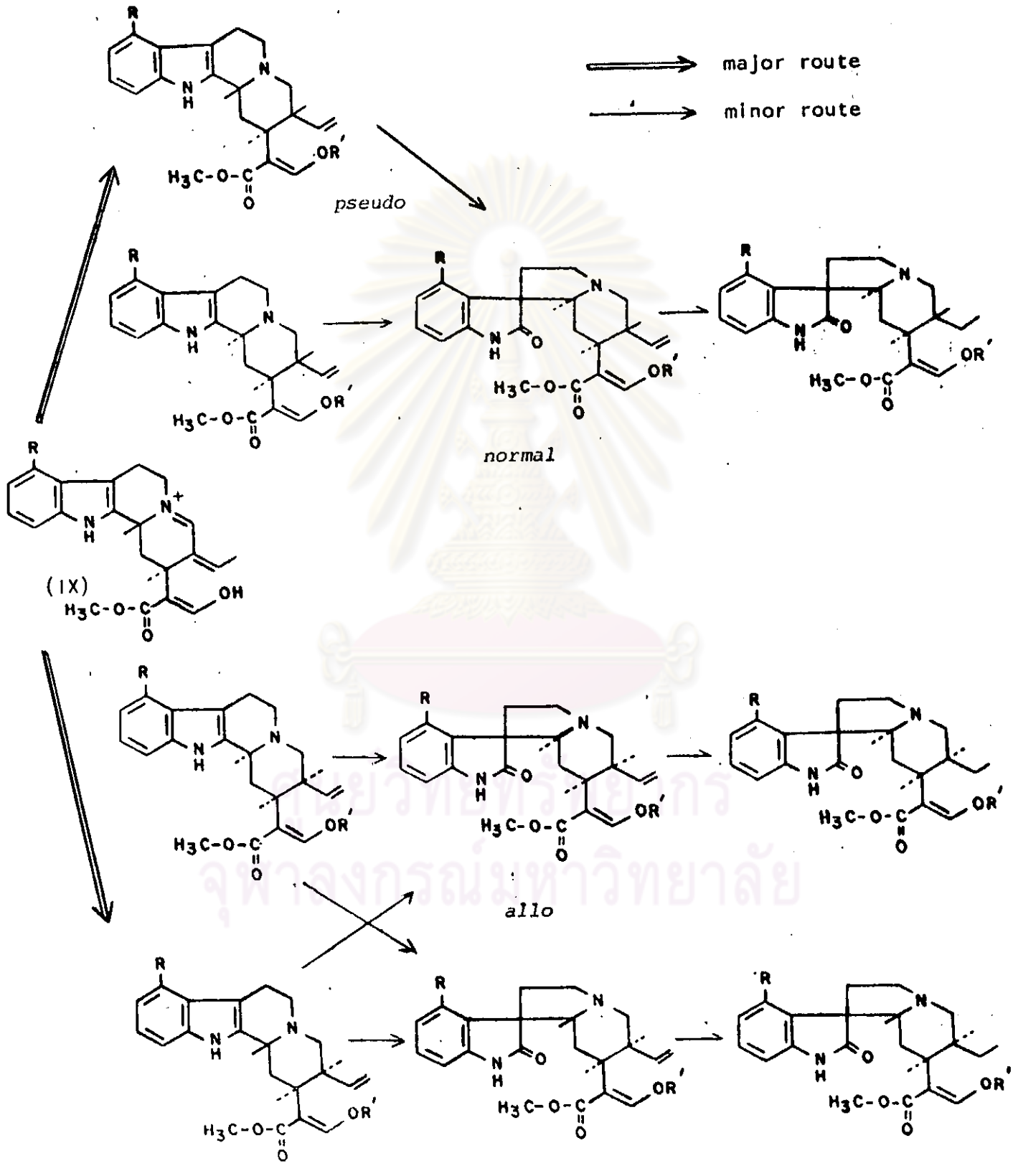


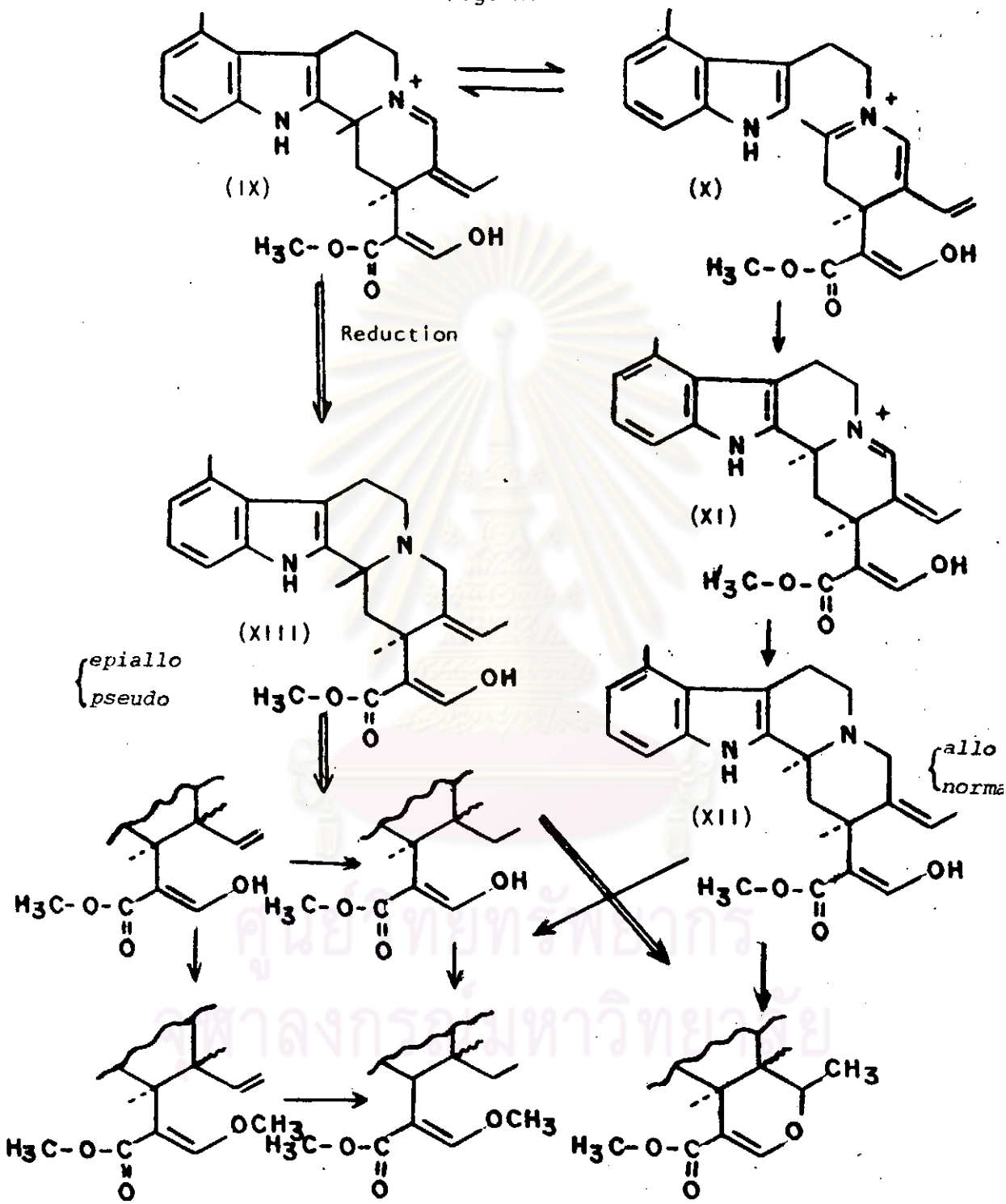
Fig. XVI

Biogenesis of open E ring alkaloids



Details of the pathway in Fig. XV and XVI are shown in Fig. XVII. Reduction of (IX) gives an isomer of geissoschizine. The minor pathway involves an opening of ring C in (IX) to give an intermediate with a conjugated double bond system (X). The closure or ring C gives two isomers, C(3) - H α (XI) and C(3) - H β (IX), the former then being reduced to give geissoschizine (XII). The conversion of (IX) to geissoschizine involves three enzymatic stages whereas the conversion to the geissoschizine isomer involves a single stage. This may be a factor relative to the amount of C(3) - H β and C(3) - H α alkaloids present in plants. Both geissoschizine and its isomer can be converted by closure of ring E to the closed E ring alkaloids. By reduction and methylation the vinyl and ethyl derivatives can be formed (usually through the aldehyde intermediates) to give open E ring alkaloids (Shellard and Houghton, 1973). Geissoschizine has also been shown to be an intermediate in indole alkaloid synthesis (Battersby, 1971) and found to be one of the first formed alkaloids in *Catharanthus roseus* being derived from the glycosidic alkaloids vincoside and isovincoside (Timmins and Court, 1976a).

Fig. XVII


(IX)
(X)
Reduction
(XI)
(XIII)
epiallo
pseudo
(XII)
allo
norma
Open E ring alkaloids
Closed E ring alkaloids
major route
minor route

However, recently Rueffer *et al.* (1978) reported that the key intermediate in the biogenesis of the majority of monoterpenoid alkaloids is strictosidine (isovincoside) with 3 α (S) configuration rather than vincoside with 3 β (R) configuration as had previously been assumed.

Their feeding experiments of labelled strictosidine and vincoside separately to two plant species belonging to different plant families, *Rauvolfia canescens* Linn. and *Mitragyna speciosa* Korth., both known to contain 3 α as well as 3 β alkaloids revealed that strictosidine with 3 α (S) stereochemistry is the universal precursor for monoterpenoid indole alkaloids.

Concurrently Stöckigt *et al.* (1978) also detected strictosidine and cathenamine as pivotal intermediates in the enzymatic formation of monoterpenoid indole alkaloids of the heteroyohimbine type in cell-free extracts from *Catharanthus roseus* cell suspension cultures.

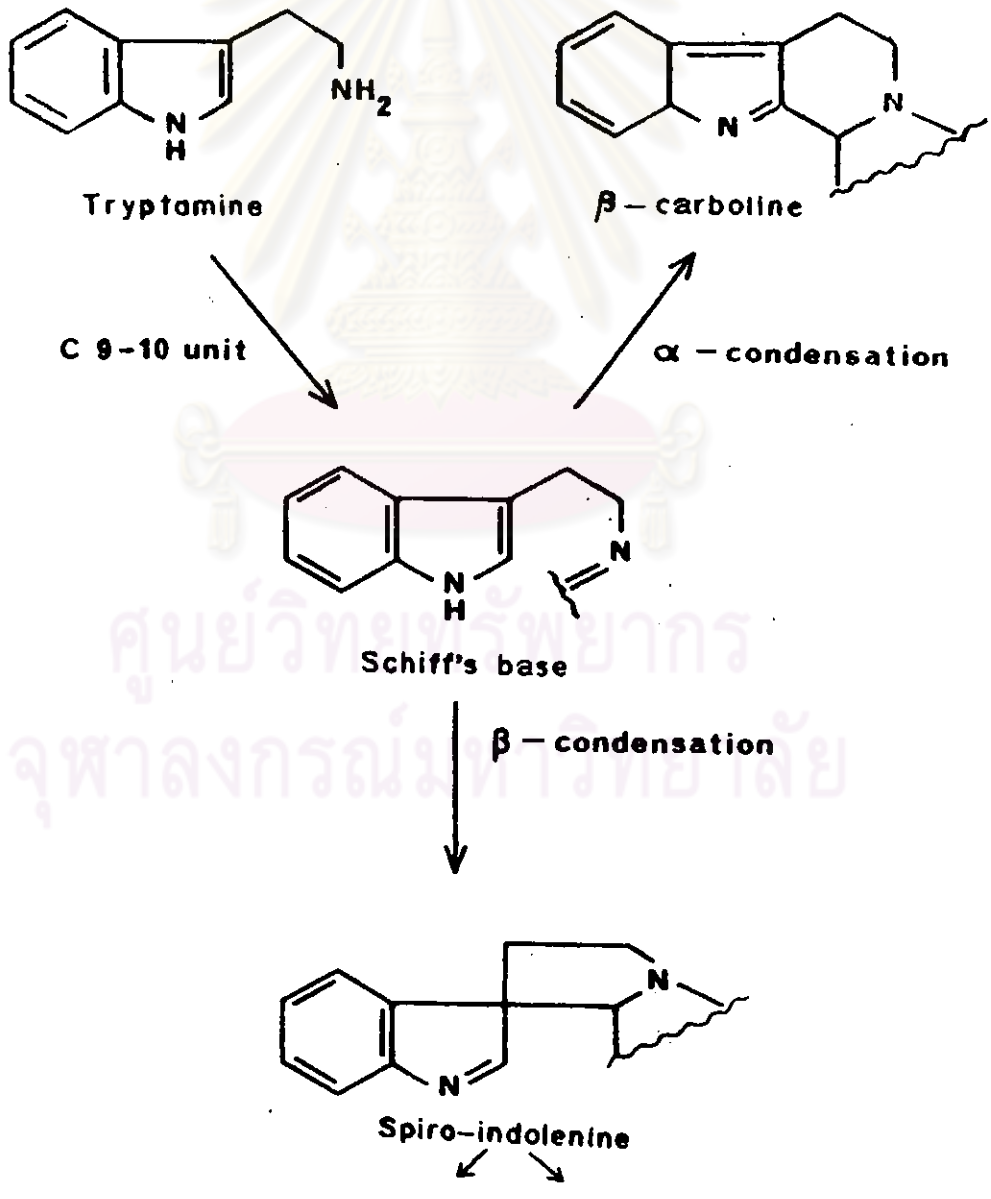
6.2 Oxindole alkaloids

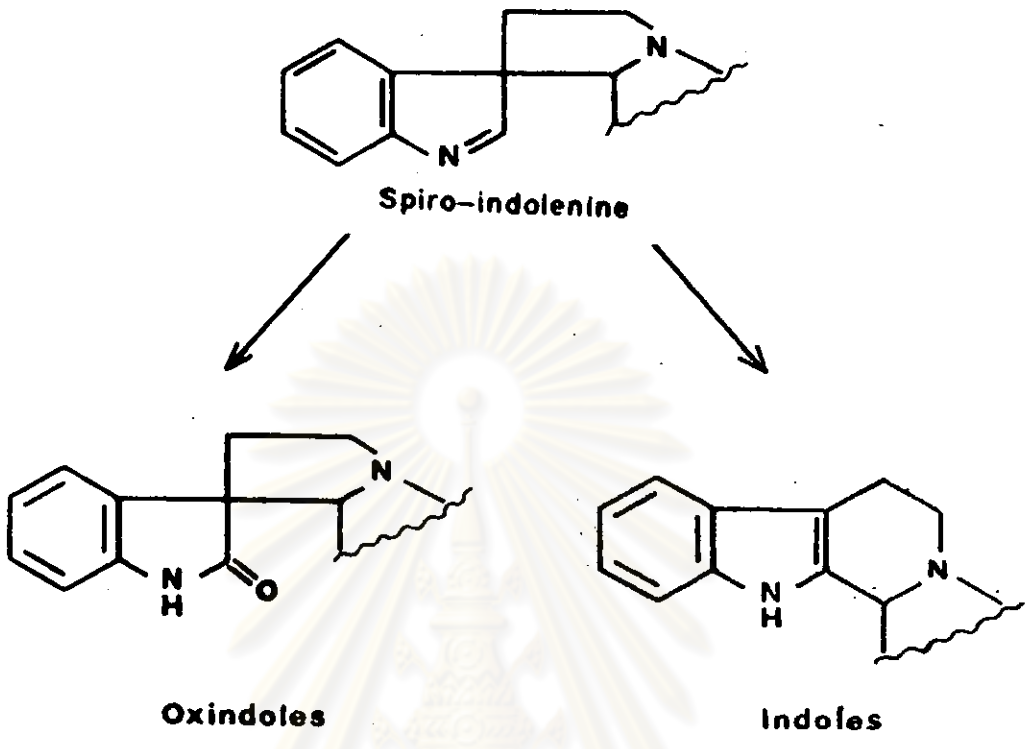
The Woodward proposals regarding the condensation of tryptamine and the C_{10} unit suggest that this may be either an α condensation to give indoles or β condensation to give oxindoles (Shellard *et al.*, 1969b).

Jackson and Smith (1968a, b) have suggested that tryptamine reacts with C_{10} unit (*seco*-loganin) to give a Schiff's base which undergoes cyclisation at either the α or β position of the indole nucleus forming the β-carboline or the spiro-indolenine intermediate. They argued that the β condensation is more favoured because the

intermediate product indolenine does not necessitate a rearrangement of the π electron system of the benzene ring which would be the case with the α condensation. The indolenine can readily isomerise to the β-carboline in mild acid conditions and can be oxidised to give oxindole alkaloids. This is illustrated in Fig. XVIII.

Fig. XVIII

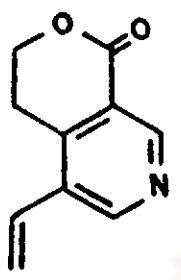




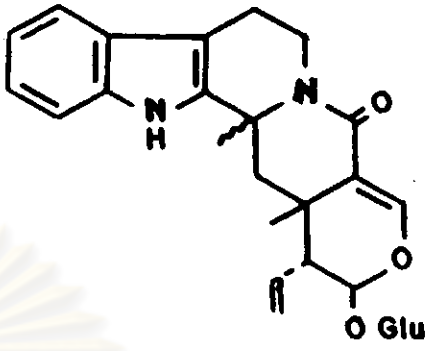
6.3 Biogenesis of other indole alkaloids

6.3.1 Pyridino-indolo-quinolizidinone alkaloids

Angustine and angustoline are possibly derived from a tryptamine unit combined with a *seco*-loganin unit closely related to gentianine. Alternatively angustine might arise possibly by reaction of vincoside or isovincoside-lactam with ammonia. The biogenesis of angustidine might involve the loss of carbon atom (C-21) from the *seco*-loganin portion of a corynanthe precursor (Au *et al.*, 1973).



Gentianine



C(3) - H β : Vincoside lactam

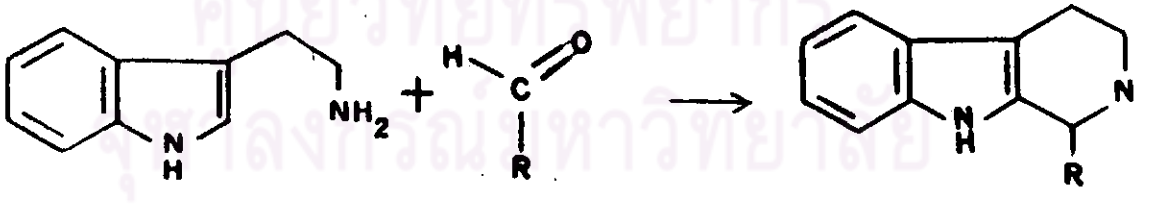
C(3) - H α : Isovincoside lactam

6.3.2 Roxburghines A, B, C, D and E

They are examples of alkaloid derived from two tryptamine moieties and C_{10} monoterpene unit (Merlini *et al.*, 1970).

6.3.3 β-Carboline alkaloids

Simple derivatives of β-carboline are readily synthesised *in vitro* by the reaction of tryptamine and aldehydes :



Tryptamine Aldehyde β-Carboline derivative

Such reactions are believed to account for the biosynthesis of such alkaloids as harmane, harmaline, etc. Simple acid hydrolysis of tryptophan-containing proteins gives rise to harmane and its derivatives. No *in vivo* experiments are available to clarify their

biosynthesis (Robinson, 1968).

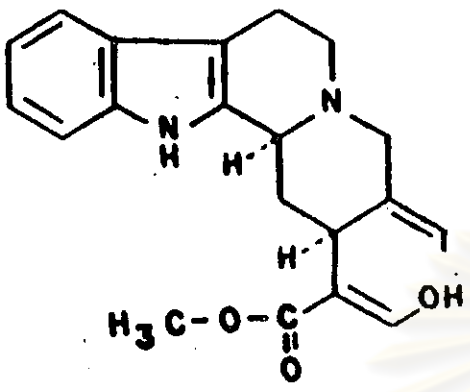
6.3.4 Yohimbine alkaloids

Robinson (1968) assumed that yohimbine alkaloids themselves are formed starting with corynantheine-type skeleton. According to traditional ideas of indole alkaloid biosynthesis, it was thought to have a similar origin from tryptophan and a monoterpenoid unit (an aldehyde).

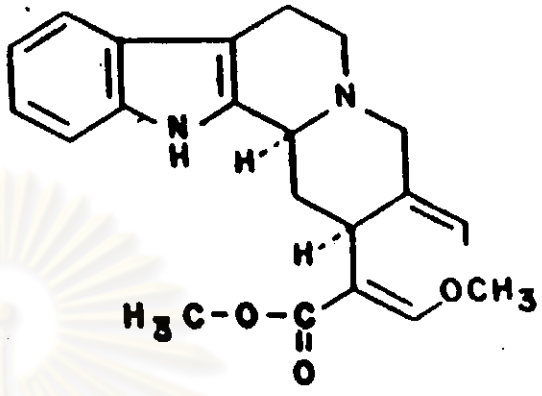
It has not yet been established if the yohimbine alkaloids are biosynthesised from a *seco*-loganin precursor, but if this is so, and only C(3) - H β epimer vincoside has been incorporated into indole alkaloids, thus an isomerisation process is necessary to yield the *allo* and *normal*, C(3) - H α, alkaloids. The nature of such a process has not been elucidated and it may be that vincoside does not have this unique status in all indole-alkaloid yielding species (Timmins and Court, 1976a).

6.3.5 Geissoschizine methyl ether

Geissoschizine is considered to be one of the first formed alkaloids in *Catharanthus roseus*(Linn.) G. Don, being derived from the glycosidic alkaloids vincoside and isovincoside (Timmins and Court, 1976a). Geissoschizine methyl ether is resulted probably from simple methylation.



Geissoschizine



Geissoschizine methyl ether

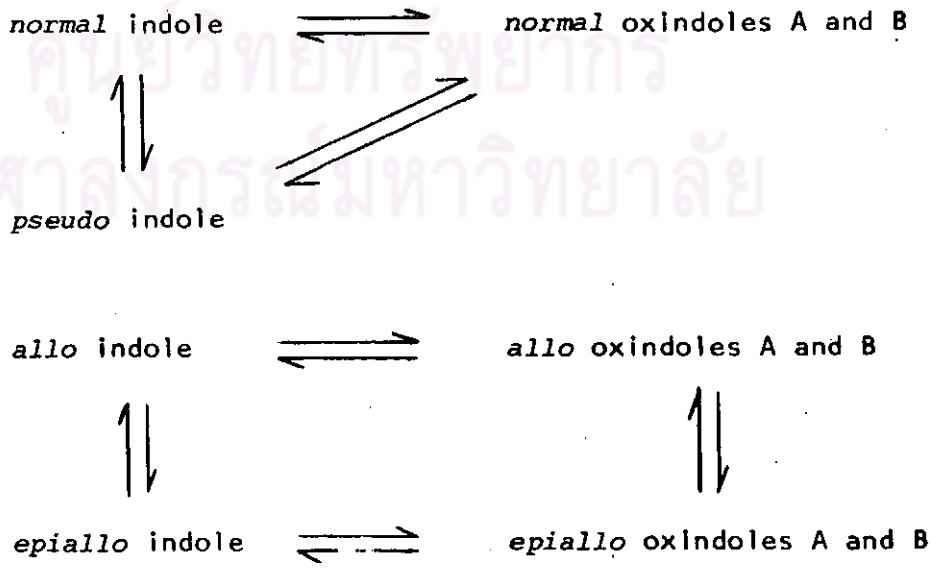
6.4 Biogenesis of the *Uncaria* alkaloids

Phillipson and Hemingway (1973a) studied the relationships between heteroyohimbine and oxindole alkaloids found in *U. bernaysii* F. v. Muell. and reported that the major alkaloids in both leaves and stems are the same. They are four interconvertible stereoisomeric closed E ring oxindole alkaloids, isopteropodine, pteropodine, speciophylline and uncarine F. They also reported six minor alkaloids which are four N-oxides of the major alkaloids and two closed E ring heteroyohimbines, i.e. tetrahydroalstonine (*allo*) and akuammigine (*epiallo*). The latter two alkaloids possess D and E ring systems identical to the major oxindole alkaloids isolated.

Similar situations exist for *U. avenia* Val., *U. rhynchophylla* Miq. and *U. sclerophylla* Havil. where the open E ring heteroyohimbine and oxindole alkaloids isolated also have identical D/E ring systems (Aimi *et al.*, 1972; Phillipson *et al.*, 1978). In *U. bernaysii* flowers there are additional alkaloids which are ajmalicine, isoajmalicine,

isomitraphylline and mitraphylline.

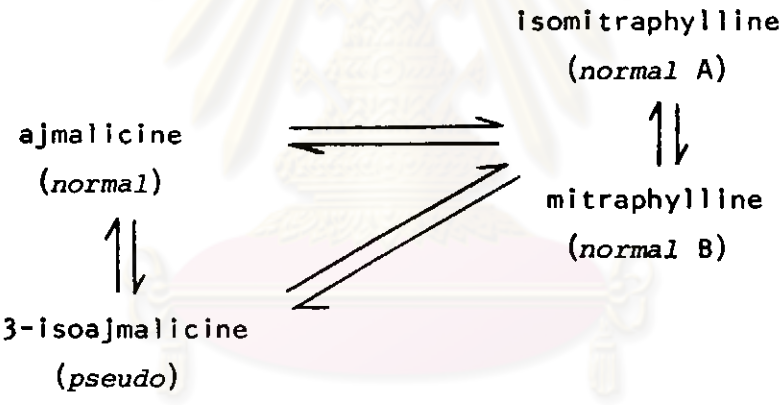
Closed E ring heteroyohimbine and oxindole alkaloids with common D/E ring systemd are also found to occur together in several species of the closely related genus *Mitragyna*. Since heteroyohimbine alkaloids are readily converted chemically into the corresponding oxindole alkaloids it has been postulated that heteroyohimbines are first synthesised in the plant and converted into oxindole alkaloids (Shellard and Phillipson, 1964b). Recently isopteropodine and pteropodine have been converted into tetrahydroalstonine and akuammigine (Aimi *et al.*, 1972) and it is possible that oxindole alkaloids may be converted to heteroyohimbine alkaloids within the plant. Furthermore, tetrahydroalstonine and akuammigine are readily interconvertible chemically as are isopteropodine, pteropodine, speciophylline and uncarine F. Hence the following relationships may be possible within species of *Uncaria* (Phillipson and Hemingway, 1973a) :-



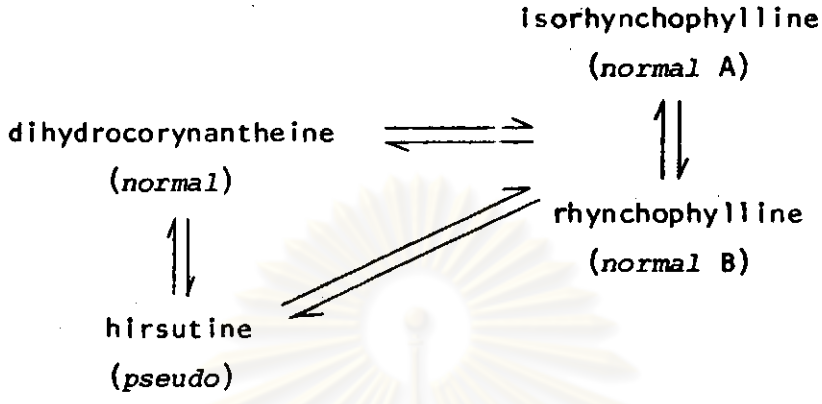
The alkaloidal sequences in some species of *Uncaria* would seem to be as shown below :-

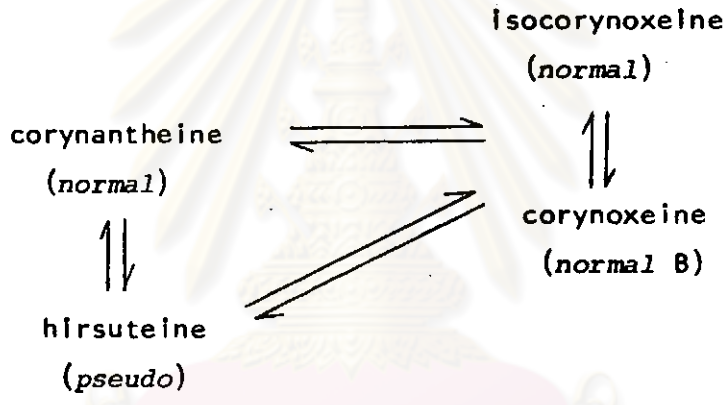
a) in *U. avenia* Val.

b) in *U. bernaysii* F. v. Muell.



c) In *Uncaria rhynchophylla* Miq.





d) In *U. sclerophylla* Havil.