CHAPTER II

HISTORICAL

1. Alkaloids isolated from species of *Mitragyna*

Mitragyna diversifolia (Wall. ex G. Don) Havil.

(*M. javanica* Koord et Val. var. *microphylla* Koord et Val.)

leaf :- ajmalicine, mitrajavine, angustine, isomitraphylline, mitraphylline, javaphylline
(Shellard, Beckett, Tantivatana, Phillipson and Lee, 1966, 1967; Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974).

M. hirsuta Havil.

leaf :- mitrajavine, hirsutine, hirsuteine, mitraciliatine, isomitraphylline, mitraphylline, isorhynchophylline, rhynchophylline, corynoxeine
(Shellard, Tantivatana and Beckett, 1967; Phillipson, Tantivatana, Tarpo and Shellard, 1973).

M. inermis (Willd.) O. Kuntze

leaf :- speciogynine, mitraciliatine, speciophylline, uncarine F, isorhynchophylline and its N-oxide, rhynchophylline and its N-oxide, rotundifoline, isorotundifoline, rhynchociline, ciliaphylline.

(Badger, Cook and Ongley, 1950; Beckett and Tackie, 1963a; Shellard and Sarpong, 1969, 1970, 1971a; Shellard, Phillipson and Sarpong, 1971).

root bark and stem bark :- speciophylline, uncarine F, isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline, rhynchociline, ciliaphylline (Shellard and Sarpong, 1970).

Mitragyna ledermannii (K. Krause) Ridsd.
(*M. ciliata* Aubr. et Pellegr.)

leaf :- mitraciliatine, isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline, rhynchociline, ciliaphylline (Badger, Cook and Ongley, 1950; Beckett and Tackie, 1963a; Beckett, Shellard and Tackie, 1963b; Shellard and Sarpong, 1970).

stem bark :- oxindole alkaloids as in the leaves (Badger, Cook and Ongley, 1950; Shellard and Sarpong, 1970).

root bark :- oxindole alkaloids as in the leaves (Shellard and Sarpong, 1970).

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

leaf :- ajmalicine, 3-isoajmalicine, tetrahydroalstonine, akuammigine and its N-oxide, dihydrocorynantheine, dihydrocorynantheol and its N-oxide, hirsutine, corynantheidol, angustine, isomitraphylline, mitraphylline, isopteropodine, pteropodine, speciophylline and its N-oxide, uncarine F and its N-oxide, isorhynchophylline, rhynchophylline, rotundifoline, rotundifoleine, isorotundifoline, isorotundifoleine, corynoxeine, rhynchociline, ciliaphylline (Shellard and Phillipson, 1964b; Phillipson, 1965; Shellard, Phillipson and Gupta, 1968a, b, 1969a, b; Shellard and Houghton, 1971, 1972a, b, c, d, 1973a, c, 1974b; Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974; Hemingway, Houghton, Phillipson and Shellard, 1975; Shellard and Lala, 1977).

stipule :- isomitraphylline, mitraphylline, isopteropodine, pteropodine, speciophylline, uncarine F (Shellard and Houghton, 1972c, d).

growing point :- isomitraphylline, mitraphylline, isopteropodine, pteropodine, speciophylline, uncarine F, corynoxeine (Shellard and Houghton, 1972c, d).

stem bark :- ajmalicine, tetrahydroalstonine, akuammigine, hirsutine, isomitraphylline, mitraphylline, isopteropodine, pteropodine, speciophylline, uncarine F, isorhynchophylline, rhynchophylline, rhynchociline, ciliaphylline (Shellard, Phillipson and Gupta, 1969b; Shellard and Houghton, 1971, 1972b, c, d).

stem xylem :- isomitraphylline, mitraphylline, isorhynchophylline, rhynchophylline, corynoxeine (Shellard and Houghton, 1972c, d).

root bark :- dihydrocorynantheine, hirsutine, hirsuteine, corynantheine, isomitraphylline, mitraphylline, isopteropodine, pteropodine, speciophylline, uncarine F, isorhynchophylline, rhynchophylline, corynoxeine (Shellard and Houghton, 1971, 1972b, c, d).

root xylem :- dihydrocorynantheine, hirsutine, hirsuteine, isomitraphylline, mitraphylline, isorhynchophylline, rhynchophylline, corynoxeine
(Shellard and Houghton, 1972c, d).

Mitragyna rotundifolia (Roxb.) O. Kuntze

leaf :- 3-isoajmalicine, isomitraphylline, mitraphylline, isorhynchophylline and its N-oxide, rhynchophylline and its N-oxide, isocorynoxeine, corynoxeine, rotundifoline, isorotundifoline
(Barger, Dyer and Sargent, 1939; Badger, Cook and Ongley, 1950; Shellard and Phillipson, 1964a; Phillipson, 1965; Shellard, Phillipson and Sarpong, 1971; Houghton and Shellard, 1974).

stem bark :- isomitraphylline, mitraphylline, isorhynchophylline, rhynchophylline, isocorynoxeine, corynoxeine, ciliaphylline (Houghton and Shellard, 1974).

root :- isomitraphylline, mitraphylline, isorhynchophylline, rhynchophylline, isocorynoxeine, corynoxeine, rhynchociline, ciliaphylline

(Houghton and Shellard, 1974).

Mitragyna rubrostipulata (K. Schum.) Havil.

leaf :- mitraphylline

(Badger, Cook and Ongley, 1950).

root bark :- hirsutine, hirsuteine, isomitraphylline, mitraphylline, isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline

(Shellard and Lala, 1978).

stem bark :- mitraphylline, isorhynchophylline, rhynchophylline, rotundifoline

(Seaton, Tondeur and Marion, 1958; Seaton, Nair, Edwards and Marion, 1960; Hendrickson and Sims, 1963).

M. speciosa (Korth.) Havil.

(*M. speciosa* Korth.)

leaf :- ajmalicine, 3-isoajmalicine, akuammigine, mitrajavine, corynantheidine, isocorynantheidine, speciogynine, paynantheine, mitraciliatine, isopaynantheine, mitragynine, speciociliatine, isomitraphylline, mitraphylline, speciophylline, javaphylline, isorhynchophylline, rhynchophylline, rotundifoline, mitrafoline, isomitrafoline, isospeciofoline, speciofoline, isospecionoxeine, specionoxeine

(Field, 1921; Ing and Raison, 1939; Beckett, Lee and Tackie, 1963; Hendrickson and Sims, 1963; Beckett, Shellard and

Tackie, 1965; Beckett, Shellard, Phillipson and Lee, 1965, 1966a, b; Phillipson, 1965; Beckett, Shellard and Phillipson, 1966c; Hemingway, Houghton, Phillipson and Shellard, 1975; Shellard, Houghton and Resha, 1978a, b).

stem bark :- speciogynine, mitraciliatine, speciociliatine, isomitraphylline, mitraphylline, javaphylline, isorhynchophylline, rhynchophylline, rotundifoline, rhynchociline, ciliaphylline, isospecionoxeine, specionoxeine, mitragynine oxindole A, mitragynine oxindole B (Hendrickson and Sim, 1963; Shellard, Houghton and Resha, 1978b).

root bark :- mitrajavine, speciogynine, mitraciliatine, speciociliatine, isorhynchophylline, rhynchophylline, rhynchociline, ciliaphylline, isospecionoxeine, specionoxeine (Shellard, Houghton and Resha, 1978b).

Mitragyna stipulosa (DC.) O. Kuntze

leaf :- hirsutine, mitraphylline, isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline, corynoxeine (Beckett, Shellard and Tackie, 1963a; Beckett and Tackie, 1963b; Shellard and Sarpong, 1970; Houghton, Lala, Shellard and Sarpong, 1976).

stipule :- isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline (Beckett, Shellard and Tackie, 1963a).

stem bark :- mitraphylline, isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline, (Beckett, Shellard and Tackie, 1963a; Shellard and Sarpong, 1970).

root bark :- isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline (Shellard and Sarpong, 1970).

Mitragyna tubulosa (Arn.) Havil.
(*M. tubulosa* Havil.)

leaf :- hirsutine, mitraciliatine, isomitraphylline, mitraphylline, isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline, rhynchociline, ciliaphylline and its N-oxide

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

stem bark, stem xylem and root bark :-

hirsutine, mitraciliatine, isorhynchophylline, rhynchophylline, rhynchociline, ciliaphylline (Rungsiyakul, 1973).

root xylem :- isorhynchophylline (Rungsiyakul, 1973)

2. *Mitragyna* alkaloids isolated from other botanical sources

2.1 Indole alkaloids

2.1.1 Closed E ring heteroyohimbine alkaloids

Ajmalicine (δ-Yohimbine, Raubasine, py-Tetrahydroserpentine)

- *Catharanthus lanceus* (Boj. ex A. DC.) Pich.
  (*Vinca lancea* Boj. ex A. DC., *Lochnera lancea* (Boj. ex A. DC.) K. Schum.)
  (Saxton, 1960; Willaman and Schubert, 1961; Farnsworth, 1972; Taylor and Farnsworth, 1975).
- *C. longifolius* (Pich.) Pich.
- *C. pusillus* (Myrray) G. Don
  (Taylor and Farnsworth, 1975).
- *C. roseus* (Linn.) G. Don
  (*Vinca rosea* Linn., *Lochnera rosea* (Linn.) Reichb.)
  (Saxton, 1960; Taylor and Farnsworth, 1975; Sarin, Nandi, Kapil and Khanna, 1977; Arens, Stöckigt, Weiler and Zenk, 1978).
- *C. trichophyllus* (Baker) Pich.
  (Rungsiyakul, 1973; Taylor and Farnsworth, 1975).
- *Corynanthe yohimbe* K. Schum.
  (*Pausinystalia yohimbe* Pierre.)
  (Robinson and Thomas, 1954; Saxton, 1960; Taylor and Farnsworth, 1975).
- *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; Hesse, 1964; Schlittler, 1965).

- *R. caffra* Sond.

  (Schlittler, 1965; Habib and Court, 1974b: Taylor and Farnsworth, 1975; Madati, Kayani, Pazi and Nyamgenda, 1977).

- *R. canescens* Linn.

  (Saxton, 1960; Willaman and Schubert, 1961; Hesse, 1964; Schlittler, 1965; Taylor and Farnsworth, 1975).

- *R. chinensis* (Hance) Hemsl.

  (Hesse, 1964; Rungsiyakul, 1973; Taylor and Farnsworth, 1975).

- *R. cumminsii* Stapf.

  (Iwu and Court, 1977b).

- *R. fruticosa* Burck.

  (Schlittler, 1965).

- *R. heterophylla* Roem. et Schult.

  (Hochstein, Murai and Boegemann, 1955; Saxton, 1960; Willaman and Schubert, 1961; Hesse, 1964; Schlittler, 1965; Taylor and Farnsworth, 1975).

- *R. inebrians* K. Schum.

- *R. javanica* Koord et Val.

  (Hesse, 1964; Schlittler, 1965).

- *Rauvolfia ligustrina* Roem. et Schult.

  (Müller, 1957; Willaman and Schubert, 1961; Hesse, 1964; Schlittler, 1965).

- *R. macrophylla* Stapf.

  (Timmins and Court, 1974a).

- *R. micrantha* Hook. f.

  (Saxton, 1960; Willaman and Schubert, 1961; Hesse, 1964; Schlittler, 1965; Taylor and Farnsworth, 1975).

- *R. mombasiana* Stapf.

  (Iwu and Court, 1978).

- *R. nitida* Jacq.

  (Hesse, 1964; Schlittler, 1965).

- *R. oreogiton* Mgf.

  (Timmins and Court, 1974b).

- *R. pentaphylla* Ducke

  (Hesse, 1964; Schlittler, 1965).

- *R. rosea* K. Schum.

  (Willaman and Schubert, 1961; Hesse, 1964; Schlittler, 1965).

- *R. sandwicensis* A. DC.

  (Willaman and Schubert, 1961; Hesse, 1964).

- *R. sellowii* Muell. Arg.

  (Pakrashi, Djerassi, Wasicky and Neuss, 1955; Willaman and Schubert, 1961; Hesse, 1964; Schlittler, 1965).

- *R. serpentina* Benth. ex Kurz.

  (Siddiqui and Siddiqui, 1931; Klohs, Draper, Keller, Malesh and Petracek, 1954; Saxton, 1960; Hesse, 1964; Schlittler, 1965; Taylor and Farnsworth, 1975; Sarin, Nandi, Kapil and Khanna, 1977).

- *R. sumatrana* (Miq.) Jack.
  (Hesse, 1964; Schlittler, 1965).
- *R. tetraphylla* Linn.
  (Taylor and Farnsworth, 1975).
- *R. verticillata* (Lour.) Baill.
  (Saxton, 1960; Schlittler, 1965; Taylor and Farnsworth, 1975).
- *R. viridis* (Muell. Arg.) Guill.
  (Schlittler, 1965).
- *R. vomitoria* Afzel.
  (Willaman and Schubert, 1961; Hesse, 1964; Schlittler, 1965; Taylor and Farnsworth, 1975).
- *R. yunnanensis* Tsaing
  (Taylor and Farnsworth, 1975).
- *Tonduzia longiflora* (A. DC.) Mgf.
  (Rungsiyakul, 1973).

- *Uncaria africana* (G. Don) Baill.
- *U. africana* (G. Don) Baill. var. *domatifera* Petit
- *U. bernaysii* F. v. Muell
- *U. orientalis* Guill.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *Vinca erecta* Rgl. et Schmalh.
  (Rungsiyakul, 1973).

3-Isoajmalicine

- *Uncaria acida* (Hunt.) Roxb. var. *papuana* Val.
- *U. africana* (G. Don) Baill.
- *U. africana* (G. Don) Baill. var. *domatifera* Petit
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. attenuata* Korth.
  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. bernaysii* F. v. Muell.
- *U. formosana* (Matsum.) Hayata
- *U. gambir* Thw.
- *U. homomalla* Miq.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. orientalis* Guill.
  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. rostrata* Pierre ex Pitard
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. salaccensis* Bakh. f. nom provis
  (Wongseripipatana, 1979).
- *U. sessilifructus* Roxb.
- *U. sterrophylla* Merr. et Perry
  (Phillipson, Hemingway and Ridsdale, 1978).

Tetrahydroalstonine

- *Alstonia constricta* F. v. Muell.

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

- *A. scholaris* R. Br.

  (Dutta, Bhattacharya and Ray, 1967).

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

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

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

  (Willaman and Schubert, 1961; Moza and Troján̈ek, 1962; Hesse, 1964, Saxton, 1965b; Taylor and Farnsworth, 1975).

- *C. trichophyllus* (Baker) Pich.

  (Taylor and Farnsworth, 1975).

- *Rauvolfia caffra* Sond.

  (Habib and Court, 1974a).

- *R. ligustrina* Roem. et Schult.

  (Müller, 1957; Hesse, 1964; Taylor and Farnsworth, 1975).

- *R. obscura* K. Schum.

  (Timmins and Court, 1976a, b; Madati, Kayami, Pazi and Nyamgenda, 1977).

- *R. sellowii* Muell. Arg.

  (Hochstein, 1955; Hesse, 1964; Saxton, 1960, 1965b; Taylor and Farnsworth, 1975).

- *R. serpentina* Benth. ex Kurz.

  (Neuss, Boaz and Forbes, 1954).

Akuammigine

- *Picralima nitida* (Stapf.) Th. et H. Durand
  (*P. klaineana* Pierre)
  (Henry, 1932; Robinson and Thomas, 1954; Willaman and Schubert, 1961; Hesse, 1964).
- *Uncaria attenuata* Korth.
  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. bernaysii* F. v. Muell.
  (Phillipson and Hemingway, 1973a; Phillipson, Hemingway and Ridsdale, 1978).
- *U. gambir* (Hunt.) Roxb.
  (Merlini, Nasini and Haddock, 1972).
- *U. glabrescens* Merr. et Perry
- *U. orientalis* Guill.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. rhynchophylla* (Miq.) Miq. ex Havil.
  (Aimi, Yamanaka, Shinma, Fujiu, Kurita, Sakai and Haginiwa, 1977; Phillipson, Hemingway and Ridsdale, 1978).
- *U. rostrata* Pierre ex Pitard
- *U. sessilifructus* Roxb.
- *U. sinensis* (Oliv.) Havil.
  (Phillipson, Hemingway and Ridsdale, 1978).

Akuammigine N-oxide

- *Uncaria gambir* (Hunt.) Roxb.

  (Merlini, Nasini and Haddock, 1972; Phillipson, Hemingway and Ridsdale, 1978).

2.1.2 Open E ring heteroyohimbine alkaloids

Dihydrocorynantheine

- *Corynanthe yohimbe* K. Schum.

  (Blumental, Eugster and Karrer, 1954; Hesse, 1964).

- *Pseudocinchona africana* Aug. Chev.

  (Cu, Goutarel and Janot, 1957; Willaman and Schubert, 1961; Hesse, 1964).

- *Uncaria africana* (G. Don) Baill.
- *U. attenuata* Korth.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. avenia* Val.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. bulusanensis* Elm.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. callophylla* Bl. ex Korth.
- *U. ferruginea* (Bl.) DC.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria gambir* (Hunt.) Roxb.

  (Merlini, Mondell, Nasini and Hesse, 1970; Merlini, Nasini and Haddock, 1972; Phillipson, Hemingway and Ridsdale, 1978).

- *U. gambir* Thw.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. guianensis* (Aubl.) Gmel.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

- *U. jasminiflora* Hook. f.

  (Phillipson, Hemingway and Ridsdale, 1978).

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

  (Aimi, Yamanaka, Shinma, Fujiu, Kurita, Sakai and Haginiwa, 1977; Phillipson, Hemingway and Ridsdale, 1978).

- *U. sclerophylla* Havil.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. tomentosa* (Willd.) DC.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

- *U. valetoniana* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).

Corynantheine

- *Corynanthe yohimbe* K. Schum.
- *Pseudocinchona africana* Aug. Chev.

  (Willaman and Schubert, 1961; Hesse, 1964).

- *Pseudocinchona pachyceras* Aug. Chev.
  (Willaman and Schubert, 1961).
- *Uncaria rhynchophylla* (Miq.) Miq. ex Havil.
  (Nozoye, 1958c; Saxton, 1965a; Phillipson, Hemingway and Ridsdale, 1978).

Corynantheidine

- *Pseudocinchona africana* Aug. Chev.
  (Willaman and Schubert, 1961).

Hirsutine

- *Uncaria attenuata* Korth.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. guianensis* (Aubl.) Gmel.
  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. kunstleri* King
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. rhynchophylla* (Miq.) Miq. ex Havil.
  (Aimi, Yamanaka, Shinma, Fujiu, Kurita, Sakai and Haginiwa, 1977; Phillipson, Hemingway and Ridsdale, 1978).
- *U. sessilifructus* Roxb.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. tomentosa* (Willd.) DC.
  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria valetoniana* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).

Hirsuteine

- *Uncaria attenuata* Korth.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. guianensis* (Aubl.) Gmel.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. rhynchophylla* (Miq.) Miq. ex Havil.

  (Aimi, Yamanaka, Shinma, Fujiu, Kurita, Sakai and Haginiwa, 1977; Phillipson, Hemingway and Ridsdale, 1978).
- *U. tomentosa* (Willd.) DC.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. valetoniana* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).

Dihydrocorynantheol

- *Aspidosperma auriculatum* Mgf.

  (Hesse, 1964).
- *A. marcgravianum* Woods.

  (Gilbert, Antonaccio and Djerassi, 1962; Hesse, 1964).

2.1.3 Other indole alkaloid

Angustine

- *Nauclea coadunata* Roxb. ex J.E. Smith
- *Strychnos angolensis* Gilg.

  (Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974).
- *S. angustiflora* Benth.

  (Au, Cheung and Sternhell, 1973).
- *S. borneensis* Leenh.
- *S. camptoneura* Gilg. et Busse
- *S. floribunda* Gilg.
- *S. ledermannii* Gilg. et Bended
- *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, Hemingway, Bisset, Houghton and Shellard, 1974).
- *Uncaria bernaysii* F. v. Muell.

  (Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria guianensis* (Aubl.) Gmel.
- *U. homomalla* Miq.

  (Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. parviflora* Ridl.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. rhynchophylla* (Miq.) Miq. ex Havil.

  (Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. rhynchophylla* (Miq.) Miq. ex Havil. var. *kouteng* Yamazaki
- *U. tonkinensis* Havil.

  (Phillipson, Hemingway and Ridsdale, 1978).

2.2 Oxindole alkaloids

2.2.1 Closed E ring oxindole alkaloids

Isomitraphylline

- *Uncaria acida* (Hunt.) Roxb. var. *papuana* Val.
- *U. africana* (G. Don) Baill.
- *U. africana* (G. Don) Baill. var. *domatifera* Petit
- *U. africana* (G. Don) Baill. var. *xerophila* Petit
- *U. appendiculata* Benth.
- *U. attenuata* Korth.
- *U. bernaysii* F. v. Muell.
- *U. callophylla* Bl. ex Korth.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria ferrea* (Bl.) DC.
- *U. formosana* (Matsum.) Hayata
- *U. guianensis* (Aubl.) Gmel.
- *U. homomalla* Miq.
- *U. hookeri* Val.
- *U. jasminiflora* Hook. f.
- *U. korrensis* Kanehira
- *U. laevifolia* Elm.
- *U. laevigata* Wall. ex G. Don
- *U. lancifolia* Hutch.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. longiflora* (Poir.) Merr.
- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. parviflora* Ridl.
- *U. perrottetii* (A. Rich.) Merr.
- *U. pilosa* Roxb.
- *U. pteropoda* Miq.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. quadrangularis* Geddes

  (Silpavisavanont, 1976; Tantivatana, Ponglux, Jirawongse and Silpavisavanont, 1979).
- *U. sessilifructus* Roxb.
- *U. sterrophylla* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria tomentosa* (Willd.) DC.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

- *U. toppingii* Merr.
- *U. valetoniana* Havil.

  (Phillipson, Hemingway and Ridsdale, 1978).

Isomitraphylline N-oxide

- *Uncaria appendiculata* Benth.
- *U. attenuata* Korth.
- *U. ferrea* (Bl.) DC.
- *U. formosana* (Matsum.) Hayata
- *U. guianensis* (Aubl.) Gmel.
- *U. korrensis* Kanehira
- *U. laevigata* Wall.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. parviflora* Ridl.
- *U. perrottetii* (A. Rich.) Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria pilosa* Roxb.
- *U. pteropoda* Miq.
- *U. sessilifructus* Roxb.

(Phillipson, Hemingway and Ridsdale, 1978).

- *U. tomentosa* (Willd.) DC.

(Hemingway and Phillipson, 1974).

- *U. toppingii* Merr.

(Phillipson, Hemingway and Ridsdale, 1978).

Mitraphylline

- *Uncaria acida* (Hunt.) Roxb. var. *papuana* Val.
- *U. africana* (G. Don) Baill.
- *U. africana* (G. Don) Baill. var. *domatifera* Petit
- *U. africana* (G. Don) Baill. var. *xerophila* Petit
- *U. appendiculata* Benth.
- *U. bernaysii* F. v. Muell.
- *U. callophylla* Bl. ex Korth.

(Phillipson, Hemingway and Ridsdale, 1978).

- *U. ferrea* (Bl.) DC.

(Johns and Lamberton, 1966; Phillipson, Hemingway and Ridsdale, 1978).

- *U. formosana* (Matsum.) Hayata

(Willaman and Schubert, 1961; Phillipson, Hemingway and Ridsdale, 1978).

- *U. gambir* (Hunt.) Roxb.

(Chan, 1968; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria guianensis* (Aubl.) Gmel.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. homomalla* Miq.
- *U. hookeri* Val.
- *U. jasminiflora* Hook. f.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. kawakamii* Hayata

  (Nozoye, 1958b; Saxton, 1960; Willaman and Schubert, 1961; Chan, Morsingh and Yeoh, 1966).
- *U. korrensis* Kanehira
- *U. laevifolia* Elm.
- *U. laevigata* Wall.
- *U. lancifolia* Hutch.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. perrottetii* (A. Rich.) Merr.
- *U. pilosa* Roxb.
- *U. pteropoda* Miq.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria quadrangularis* Geddes

  (Silpavisavanont, 1976; Tantivatana, Ponglux, Jirawongse and Silpavisavanont, 1979).

- *U. salaccensis* Bakh. f. nom provis

  (Wongseripipatana, 1979).

- *U. sessilifructus* Roxb.

- *U. sterrophylla* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. tomentosa* (Willd.) DC.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

- *U. toppingii* Merr.

- *U. velutina* Havil.

  (Phillipson, Hemingway and Ridsdale, 1978).

Mitraphylline N-oxide

- *Uncaria africana* (G. Don) Baill.

- *U. attenuata* Korth.

- *U. ferrea* (Bl.) DC.

- *U. formosana* (Matsum.) Hayata

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. guianensis* (Aubl.) Gmel.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

- *U. hookeri* Val.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria korrensis* Kanehira
- *U. laevigata* Wall.
- *U. lancifolia* Hutch.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. parviflora* Ridl.
- *U. perrottetii* (A. Rich.) Merr.
- *U. pilosa* Roxb.
- *U. pteropoda* Miq.
- *U. sessilifructus* Roxb.
- *U. toppingii* Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).

Isopteropodine (Uncarine E)

- *Uncaria appendiculata* Benth.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. bernaysii* F. v. Muell.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton, 1968; Phillipson and Hemingway, 1973a, b; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria brevicarpa* Elm.
- *U. donisii* Petit

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. ferrea* (Bl.) DC.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton, 1968; Phillipson, Hemingway and Ridsdale, 1978).
- *U. florida* Vidal

  (Aimi, Yamanaka, Endo, Sakai and Haginiwa, 1972; Phillipson, Hemingway and Ridsdale, 1978).
- *U. glabrata* (Bl.) DC.
- *U. glabrescens* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. homomalla* Miq.

  (Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974; Ponglux, Tantivatana and Pummangura, 1977; Phillipson, Hemingway and Ridsdale, 1978; Vitayanatpaisan, 1979).
- *U. hookeri* Val.
- *U. kawakamii* Hayata
- *U. korrensis* Kanehira
- *U. laevifolia* Elm.
- *U. laevigata* Wall. ex G. Don
- *U. lancifolia* Hutch.
- *U. lanosa* Wall.
- *U. lobbii* Hook. f.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. parviflora* Ridl.
- *U. perrottetii* (A. Rich.) Merr.
- *U. philippinensis* Elm.
- *U. pilosa* Roxb.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. pteropoda* Miq.

  (Chan, Morsingh and Yeoh, 1966; Yeoh, Chan and Morsingh, 1966; Phillipson, Hemingway and Ridsdale, 1978).

- *U. quadrangularis* Geddes

  (Silpavisavanont, 1976; Tantivatana, Ponglux, Jirawongse and Silpavisavanont, 1979).

- *U. roxburghiana* Korth.
- *U. setiloba* Benth.
- *U. sinensis* (Oliv.) Havil.
- *U. sterrophylla* Merr. et Perry
- *U. toppingii* Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. velutina* Havil.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

Pteropodine (Uncarine C)

- *Uncaria appendiculata* Benth.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. bernaysii* F. v. Muell.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton, 1968; Phillipson and Hemingway, 1973a; Phillipson, Hemingway and Ridsdale, 1978).

- *U. brevicarpa* Elm.

- *U. donisii* Petit

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. ferrea* (Bl.) DC.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton, 1966; Phillipson, Hemingway and Ridsdale, 1978).

- *U. ferrea* (Bl.) DC. var. *appendiculata* Val.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. florida* Vidal

  (Aimi, Yamanaka, Endo, Sakai and Haginiwa, 1972; Phillipson, Hemingway and Ridsdale, 1978).

- *U. glabrata* (Bl.) DC.

- *U. glabrescens* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. homomalla* Miq.

  (Phillipson, Hemingway, Bisset, Houghton and Shellard, 1974; Ponglux, Tantivatana and Pummangura, 1977; Phillipson, Hemingway and Ridsdale, 1978; Vitayanatpaisan, 1979).

- *Uncaria hookeri* Val.
- *U. kawakamii* Hayata
- *U. korrensis* Kanehira
- *U. laevifolia* Elm.
- *U. lanosa* Wall.
- *U. lobbii* Hook. f.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. parviflora* Ridl.
- *U. perrottetii* (A. Rich.) Merr.
- *U. philippinensis* Elm.
- *U. pilosa* Roxb.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. pteropoda* Miq.

  (Chan, Morsingh and Yeoh, 1966; Yeoh, Chan and Morsingh, 1966; Phillipson, Hemingway and Ridsdale, 1978).
- *U. quadrangularis* Geddes

  (Silpavisavanont, 1976; Tantivatana, Ponglux, Jirawongse and Silpavisavanont, 1979).
- *U. roxburghiana* Korth.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria setiloba* Benth.
- *U. sinensis* (Oliv.) Havil.
- *U. sterrophylla* Merr. et Perry
- *U. toppingii* Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. velutina* Havil.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

Speciophylline (Uncarine D)

- *Uncaria appendiculata* Benth.
- *U. attenuata* Korth.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. bernaysii* F. v. Muell.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton; 1968; Phillipson and Hemingway, 1973a; Phillipson, Hemingway and Ridsdale, 1978).
- *U. brevicarpa* Elm.
- *U. donisii* Petit

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. ferrea* (Bl.) DC.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton; 1968; Phillipson, Hemingway and Ridsdale, 1978).
- *U. ferrea* (Bl.) DC. var. *appendiculata* Val.
- *U. florida* Vidal

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria glabrata* (Bl.) DC.
- *U. glabrescens* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. homomalla* Miq.

  (Ponglux, Tantivatana and Pummangura, 1977; Phillipson, Hemingway and Ridsdale, 1978; Vitayanatpaisan, 1979).
- *U. hookeri* Val.
- *U. kawakamii* Hayata
- *U. korrensis* Kanehira
- *U. laevifolia* Elm.
- *U. laevigata* Wall. ex G. Don
- *U. lanosa* Wall.
- *U. lobbii* Hook. f.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. parviflora* Ridl.
- *U. perrottetii* (A. Rich.) Merr.
- *U. philippinensis* Elm.
- *U. pilosa* Roxb.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria pteropoda* Miq.
- *U. roxburghiana* Korth.
- *U. setiloba* Benth.
- *U. sinensis* (Oliv.) Havil.
- *U. sterrophylla* Merr. et Perry
- *U. toppingii* Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. velutina* Havil.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

Speciophylline N-oxide

- *Uncaria appendiculata* Benth.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. bernaysii* F. v. Muell.

  (Phillipson and Hemingway, 1973a; Phillipson, Hemingway and Ridsdale, 1978).
- *U. brevicarpa* Elm.
- *U. donisii* Petit
- *U. ferrea* (Bl.) DC.
- *U. glabrata* (Bl.) DC.
- *U. glabrescens* Merr. et Perry
- *U. homomalla* Miq.
- *U. kawakamii* Hayata
- *U. korrensis* Kanehira

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria lanosa* Wall.
- *U. lobbii* Hook. f.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1973b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. philippinensis* Elm.
- *U. pilosa* Roxb.
- *U. pteropoda* Miq.
- *U. roxburghiana* Korth.
- *U. setiloba* Benth.
- *U. sinensis* (Oliv.) Havil.
- *U. sterrophylla* Merr. et Perry
- *U. toppingii* Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. velutina* Havil.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

Uncarine F

- *Uncaria appendiculata* Benth.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria bernaysii* F. v. Muell.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton, 1968; Phillipson and Hemingway, 1973a; Phillipson, Hemingway and Ridsdale, 1978).

- *U. brevicarpa* Elm.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. ferrea* (Bl.) DC.

  (Johns and Lamberton, 1966; Beecham, Hart, Johns and Lamberton, 1968; Phillipson, Hemingway and Ridsdale, 1978).

- *U. glabrata* (Bl.) DC.

- *U. glabrescens* Merr. et Perry

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. homomalla* Miq.

  (Ponglux, Tantivatana, Pummangura, 1977; Phillipson, Hemingway and Ridsdale, 1978; Vitayanatpaisan, 1979).

- *U. hookeri* Val.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. kawakamii* Hayata

  (Nozoye, 1958a; Phillipson, Hemingway and Ridsdale, 1978).

- *U. korrensis* Kanehira

- *U. laevifolia* Elm.

- *U. lanosa* Wall.

- *U. lobbii* Hook. f.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. longiflora* (Poir.) Merr.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. parviflora* Ridl.
- *U. perrottetii* (A. Rich.) Merr.
- *U. philippinensis* Elm.
- *U. pilosa* Roxb.
- *U. pteropoda* Miq.
- *U. roxburghiana* Korth.
- *U. sessilifructus* Roxb.
- *U. setiloba* Benth.
- *U. sinensis* (Oliv.) Havil.
- *U. sterrophylla* Merr. et Perry
- *U. toppingii* Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. velutina* Havil.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

Uncarine F N-oxide

- *Uncaria appendiculata* Benth.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. bernaysii* F. v. Muell.

  (Phillipson and Hemingway, 1973a; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria brevicarpa* Elm.
- *U. ferrea* (Bl.) DC.
- *U. glabrata* (Bl.) DC.
- *U. glabrescens* Merr. et Perry
- *U. homomalla* Miq.
- *U. kawakamii* Hayata
- *U. korrensis* Kanehira
- *U. lanosa* Wall.
- *U. longiflora* (Poir.) Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. orientalis* Guill.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. philippinensis* Elm.
- *U. setiloba* Benth.
- *U. sinensis* (Oliv.) Havil.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. velutina* Havil.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

2.2.2 Open E ring oxindole alkaloids

Isorhynchophylline

- *Uncaria acida* (Hunt.) Roxb.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria africana* (G. Don) Baill.
- *U. angolensis* Welw.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. attenuata* Korth.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. avenia* Val.
- *U. bernaysii* F. v. Muell. f. *inermis* K. Schum.
- *U. bernaysioides* Merr. et Perry
- *U. callophylla* Bl. ex Korth.
- *U. cordata* (Lour.) Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. gambir* (Hunt.) Roxb.

  (Merlini, Mondell, Nasini and Hesse, 1970; Merlini, Nasini and Haddock, 1972a; Phillipson, Hemingway and Ridsdale, 1978).
- *U. gambir* Thw.

  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. guianensis* (Aubl.) Gmel.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. hallii* Korth.
- *U. jasminiflora* Hook. f.
- *U. kunstleri* King
- *U. longiflora* (Poir.) Merr.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria macrophylla* Wall.
  (Phillipson and Hemingway, 1973c; Phillipson, Hemingway and Ridsdale, 1978).
- *U. pedicellata* Roxb.
- *U. pteropoda* Miq.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. rhynchophylla* (Miq.) Miq. ex Havil.
  (Nozoye, 1958c; Saxton, 1960; Hesse, 1964; Phillipson, Hemingway and Ridsdale, 1978).
- *U. sclerophylla* Havil.
- *U. sessilifructus* Roxb.
- *U. sterrophylla* Merr. et Perry
- *U. talbotii* Wernh.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. tomentosa* Wernh.
  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

Isorhynchophylline N-oxide

- *Uncaria acida* (Hunt.) Roxb. var. *papuana* Val.
- *U. angolensis* Welw.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. attenuata* Korth.
  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria bernaysii* F. v. Muell. f. *inermis* K. Schum.
- *U. bernaysioides* Merr. et Perry
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. guianensis* (Aubl.) Gmel.
  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. homomalla* Miq.
- *U. kunstleri* King
- *U. longiflora* (Poir.) Merr.
- *U. macrophylla* Wall.
- *U. rhynchophylla* (Miq.) Miq. ex Havil. var. *kouteng* Yamazaki
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. tomentosa* (Willd.) DC.
  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

Rhynchophylline (Mitrinermine)

- *Uncaria acida* (Hunt.) Roxb.
- *U. acida* (Hunt.) Roxb. var. *papuana* Val.
- *U. angolensis* Welw.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. attenuata* Korth.
  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. avenia* Val.
  (Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria bernaysii* F. v. Muell. f. *inermis* K. Schum.
- *U. bernaysioides* Merr. et Perry
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. bulusanensis* Elm.
  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. callophylla* Bl. ex Korth.
- *U. cordata* (Lour.) Merr.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. formosana* (Matsum.) Hayata
  (Willaman and Schubert, 1961).
- *U. gambir* (Hunt.) Roxb.
  (Merlini, Mondell, Nasini and Hesse, 1970; Merlini, Nasini and Haddock, 1972a; Phillipson, Hemingway and Ridsdale, 1978).
- *U. gambir* Thw.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. guianensis* (Aubl.) Gmel.
  (Saxton, 1960; Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).
- *U. hallii* Korth.
- *U. jasminiflora* Hook. f.
- *U. kunstleri* King
- *U. longiflora* (Poir.) Merr.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. macrophylla* Wall.
  (Phillipson and Hemingway, 1973c; Phillipson, Hemingway

and Ridsdale, 1978).

- *Uncaria perrottetii* (A. Rich.) Merr.
- *U. pteropoda* Miq.

(Phillipson, Hemingway and Ridsdale, 1978).

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

(Nozoye, 1958c; Saxton, 1960; Aimi, Yamanaka, Shinma, Fujiu, Kurita, Sakai and Haginiwa, 1977; Phillipson, Hemingway and Ridsdale, 1978).

Corynoxine

- *Pseudocinchona africana* Aug. Chev.

(Cu, Goutarel and Janot, 1957; Hesse, 1964).

- *U. kunstleri* King

(Phillipson, Hemingway and Ridsdale, 1978).

- *U. macrophylla* Wall.

(Phillipson and Hemingway, 1973c; Phillipson, Hemingway and Ridsdale, 1978).

- *U. pedicellata* Roxb.
- *U. sessilifructus* Roxb.

(Phillipson, Hemingway and Ridsdale, 1978).

Corynoxine B

- *Uncaria kunstleri* King

(Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria macrophylla* Wall.

  (Phillipson and Hemingway, 1973c; Phillipson, Hemingway and Ridsdale, 1978).

- *U. pedicellata* Roxb.
- *U. sessilifructus* Roxb.

  (Phillipson, Hemingway and Ridsdale, 1978).

Isocorynoxeine

- *Uncaria attenuata* Korth.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. pteropoda* Miq.

  (Phillipson, Hemingway and Ridsdale, 1978).

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

  (Aimi, Yamanaka, Shinma, Fujiu, Kurita, Sakai and Haginiwa, 1977; Phillipson, Hemingway and Ridsdale, 1978).

Corynoxeine

- *Pseudocinchona africana* Aug. Chev.

  (Hesse, 1964).

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

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. attenuata* Korth.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *Uncaria pteropoda* Miq.
- *U. rhynchophylla* (Miq.) Miq. ex Havil.
- *U. rhynchophylla* (Miq.) Miq. ex Havil. var. *kouteng* Yamazaki
  (Phillipson, Hemingway and Ridsdale, 1978).

Rotundifoline (Stipulatine)

- *Uncaria attenuata* Korth.
- *U. bulusanensis* Elm.
  (Phillipson and Hemingway , 1975b; Phillipson, Hemingway and Ridsdale, 1978).
- *U. formosana* (Matsum.) Hayata
  (Willaman and Schubert, 1961).
- *U. gambir* (Hunt.) Roxb.
  (Merlini, Mondell, Nasini and Hesse, 1970; Merlini, Nasini and Haddock, 1972a).
- *U. gambir* Thw.
  (Phillipson, Hemingway and Ridsdale, 1978).
- *U. rhynchophylla* (Miq.) Miq. ex Havil.
  (Willaman and Schubert, 1961).
- *U. tomentosa* (Willd.) DC.
  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

Isorotundifoline (Mitragynol, Dihydrorotundifoline)

- *Uncaria bulusanensis* Elm.

  (Phillipson and Hemingway, 1975b; Phillipson, Hemingway and Ridsdale, 1978).

- *U. formosana* (Matsum.) Hayata

  (Willaman and Schubert, 1961).

- *U. gambir* Thw.

  (Phillipson, Hemingway and Ridsdale, 1978).

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

  (Willaman and Schubert, 1961).

- *U. tomentosa* (Willd.) DC.

  (Hemingway and Phillipson, 1974; Phillipson, Hemingway and Ridsdale, 1978).

Speciofoline

- *Uncaria attenuata* Korth.

  (Phillipson, Hemingway and Ridsdale, 1978).

- *U. bulusanensis* Elm.

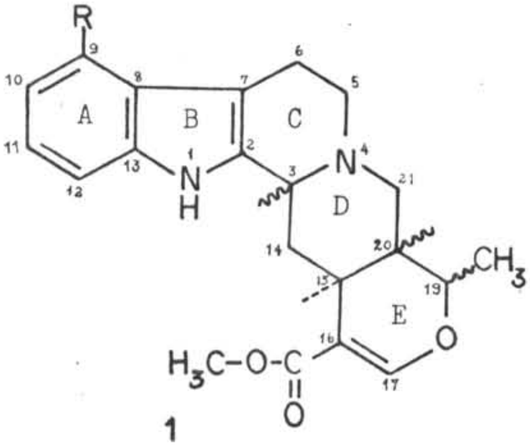
  (Phillipson and Hemingway, 1975b).

3. Chemistry of alkaloids from *Mitragyna*

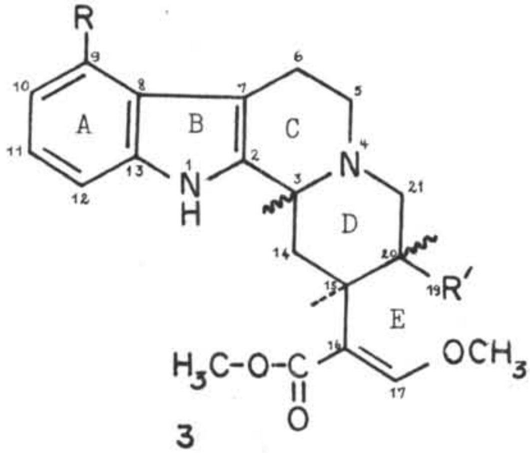
3.1 Heteroyohimbine and oxindole alkaloids

3.1.1 Basic structures

Most of the alkaloids reported to be present in *Mitragyna* are of heteroyohimbine - type and the corresponding oxindole. The alkaloids represent variants of these structures, differing in their stereochemistry and/or aromatic substitution. There are two types of heteroyohimbine and oxindole alkaloids depending upon the nature of ring E, they are closed E ring (1, 2) and open E ring (E *seco*) (3, 4) as shown in Fig. I.

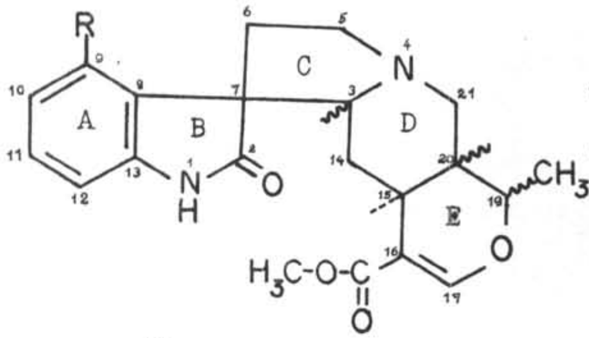


1

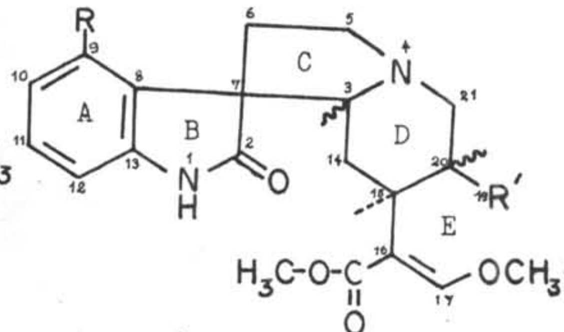


3

Heteroyohimbines



2



4

Oxindoles

Fig. I Basic structures of heteroyohimbine and oxindole alkaloids.

1 and 2 : closed E ring

3 and 4 : open E ring

3.1.2 Configurations

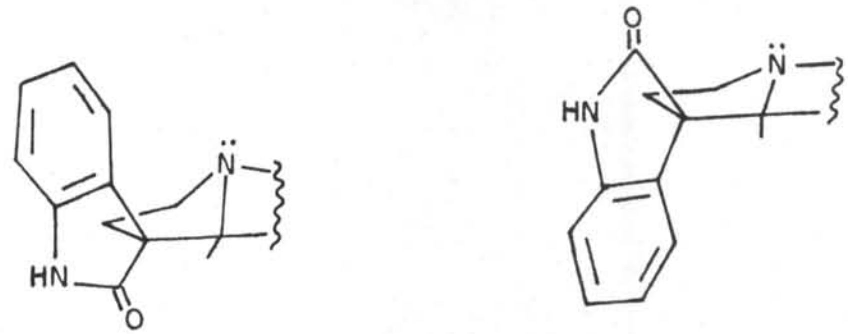
Heteroyohimbine and the corresponding oxindole alkaloids have asymmetric centres at C(3), C(15) and C(20), although all those isolated so far have C(15) - H α. Isomerism at C(3) and C(20) allows four possible configurations for heteroyohimbine alkaloids (Table I).

Table I

Configuration terminology for heteroyohimbine alkaloids

Configuration	C(3) - H	C(20) - H
normal	α	β
pseudo	β	β
allo	α	α
epiallo	β	α

In addition, the oxindole alkaloids have another asymmetric centre at C(7), those alkaloids in which the lactam carbonyl lies below the plane of the C/D rings being termed the A series and those in which the lactam carbonyl lies above the plane of the C/D rings being termed the B series (Finch and Taylor, 1962a, b). The configurations of which are shown in Fig. II.



A series B series

Fig. II A and B series of oxindole alkaloids.

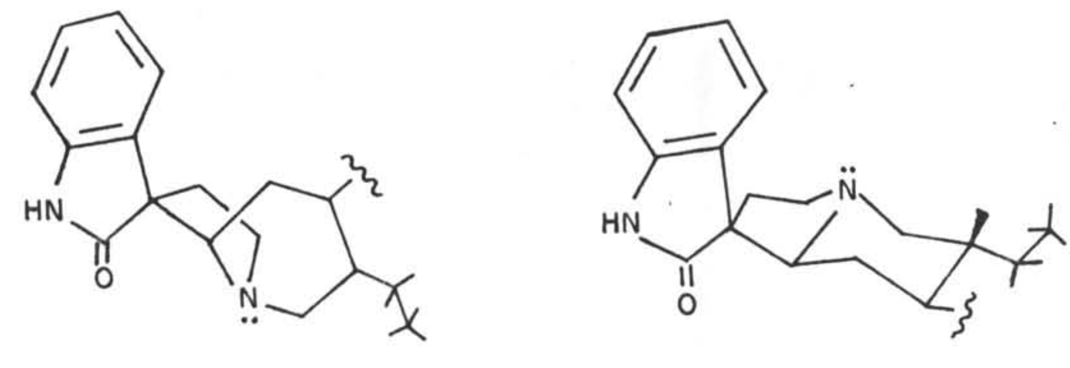
Thus eight isomers of oxindole alkaloids are possible (Table II).

Table II

Configuration terminology for oxindole alkaloids

Configuration	C(3) - H	C(20) - H	C(7) series of oxindoles
normal	α	β	A or B
pseudo	β	β	A or B
allo	α	α	A or B
epiallo	β	α	A or B

Furthermore, in both types of oxindole alkaloids the lone pair of electrons on N(4) may either be on the same side of 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. III) (Shamma, Shine, Kompis, Sticzay, Morsingh, Poisson and Pousset, 1967).



syn- *anti-*

Fig. III *syn-* and *anti-* oxindole alkaloids.

The open E ring alkaloids may show geometric isomerisation because of the double bond between C(16) and C(17), though in all known alkaloids the C(17) - H is *cis* to the C(16) carbomethoxy group. The closed E ring alkaloids have another asymmetric centre at C(19), and isomers with C(19) - CH_3 α and β configurations, though the isomers with β configuration have not yet been reported from any *Mitragyna* species, are known to occur in members of the closely related genus *Uncaria* (Phillipson, Hemingway and Ridsdale, 1978; Supavita, 1979; Wongseripipatana, 1979).

In *Mitragyna* alkaloids, substitutions (R) may occur in the aromatic ring at C(9) and is either a hydroxy or methoxy group. In contrast, only 9-hydroxy substituted alkaloids are reported to be present in *Uncaria* species (Phillipson, Hemingway and Ridsdale, 1978). Recently, a totally new heteroyohimbine alkaloid with C(14) - hydroxy substitution has been isolated and characterised as 14-hydroxy-3-iso-rauniticine which is the first alkaloid being reported as having the substitution at the position other than in the aromatic ring (Supavita, 1979).

In the open E ring alkaloids R' may be either an ethyl or a vinyl group.

Names of known heteroyohimbine and oxindole alkaloids together with their configurations are summarised in Tables III - VI.

Table III

Closed E ring heteroyohimbine alkaloids

Alkaloid	C(9) - R	Configuration	C(19) - CH_3
Ajmalicine	H	*normal*	α
(19-Epiajmalicine)	H	*normal*	β
3-Isoajmalicine	H	*pseudo*	α
(19-Epi-3-isoajmalicine)	H	*pseudo*	β
Tetrahydroalstonine(*)	H	*allo*	α
(Rauniticine)	H	*allo*	β
Akuammigine*	H	*epiallo*	α
(3-Isorauniticine)	H	*epiallo*	β
(14-hydroxy-3-isorauniticine)	H	*epiallo*	β
Isomitrajavine#	OCH_3	*normal*	α
Mitrajavine	OCH_3	*pseudo*	α

* = with its N-oxide

\# = semi-synthetic

( ) = not yet isolated from *Mitragyna* species

Table IV

Open E ring heteroyohimbine alkaloids

Alkaloid	C(9) - R	R'	Configuration
Dihydrocorynantheine*	H	CH_2-CH_3	*normal*
Dihydrocorynantheol*	H	CH_2-CH_3	*normal*
Corynantheine	H	CH=CH_2	*normal*
Hirsutine*	H	CH_2-CH_3	*pseudo*
Hirsuteine	H	CH=CH_2	*pseudo*
Corynantheidine	H	CH_2-CH_3	*allo*
Corynantheidol	H	CH_2-CH_3	*allo*
Isocorynantheidine	H	CH_2-CH_3	*epiallo*
(*epiallo*-Corynantheine)	H	CH=CH_2	*epiallo*
(Gambirine)	OH	CH_2-CH_3	*normal*
(Isogambirine)	OH	CH_2-CH_3	*pseudo*
Speciogynine	OCH_3	CH_2-CH_3	*normal*
Paynantheine	OCH_3	CH=CH_2	*normal*
Mitraciliatine	OCH_3	CH_2-CH_3	*pseudo*
Isopaynantheine	OCH_3	CH=CH_2	*pseudo*
Mitragynine	OCH_3	CH_2-CH_3	*allo*
Speciociliatine	OCH_3	CH_2-CH_3	*epiallo*

Table V

Closed E ring oxindole alkaloids

Alkaloid	C(9) - R	Configuration	C(7) 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
Isopteropodine(*)	H	*allo*	A	α
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	-	-	-
Javaphylline	OCH_3	*normal*	A	α
Isojavaphylline#	OCH_3	*normal*	B	α

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

Table VI

Open E ring oxindole alkaloids

Alkaloid	C(9) - R	R'	Configuration	C(7) series
Isorhynchophylline*	H	CH_2-CH_3	*normal*	A
Rhynchophylline*	H	CH_2-CH_3	*normal*	B
Isocorynoxeine	H	CH=CH_2	*normal*	A
Corynoxeine	H	CH=CH_2	*normal*	B
Corynoxine	H	CH_2-CH_3	*allo*	A
Corynoxine B	H	CH_2-CH_3	*allo*	B
Rotundifoline*	OH	CH_2-CH_3	*normal*	A
Isorotundifoline*	OH	CH_2-CH_3	*normal*	B
Rotundifoleine	OH	CH=CH_2	*normal*	A
Isorotundifoleine	OH	CH=CH_2	*normal*	B
Mitrafoline	OH	CH_2-CH_3	*allo*	A
Isomitrafoline	OH	CH_2-CH_3	*allo*	B
Isospeciofoline	OH	CH_2-CH_3	*epiallo*	A
Speciofoline	OH	CH_2-CH_3	*epiallo*	B
Rhynchociline	OCH_3	CH_2-CH_3	*normal*	A
Ciliaphylline*	OCH_3	CH_2-CH_3	*normal*	B
Isospecionoxeine	OCH_3	CH=CH_2	*normal*	A
Specionoxeine	OCH_3	CH=CH_2	*normal*	B
Mitragynine oxindole A	OCH_3	CH_2-CH_3	*allo*	A
Mitragynine oxindole B	OCH_3	CH_2-CH_3	*allo*	B

Table VI (continued)

Alkaloid	C(9) - R	R'	Configuration	C(7) series
Speciociliatine oxindole A#	OCH_3	CH_2-CH_3	*epiallo*	A
Speciociliatine oxindole B#	OCH_3	CH_2-CH_3	*epiallo*	B

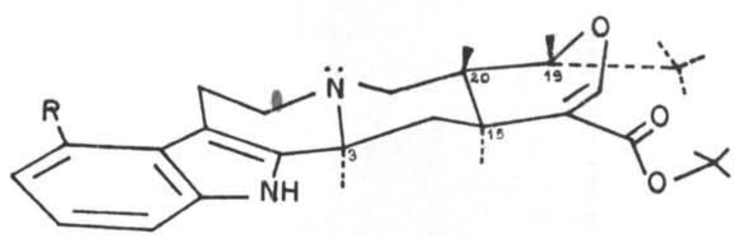
3.1.3 Preferred conformations

The preferred conformations of the heteroyohimbine and oxindole alkaloids are established as follows (Phillipson and Shellard, 1967; Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1967) :-

Heteroyohimbine alkaloids

Closed E ring

Normal (C(3) - H α, C(20) - H β)

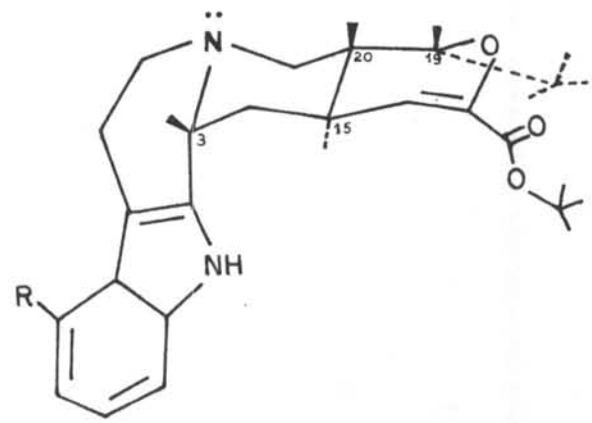


R = H : Ajmalicine

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

R = OCH_3 : Isomitrajavine#

Pseudo (C(3) - H β, C(20) - H β)

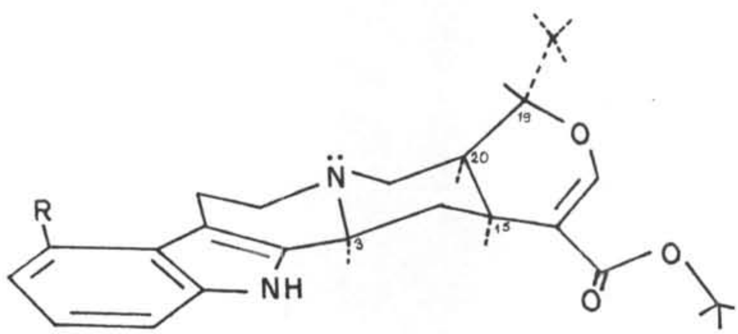


R = H : 3-Isoajmalicine

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

R = OCH_3 : Mitrajavine

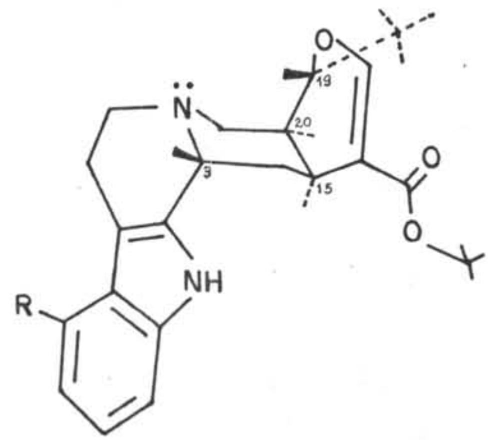
Allo (C(3) - H α, C(20) - H α)



R = H : Tetrahydroalstonine

R = H, C(19) - CH_3 β : (Rauniticine)

Epiallo (C(3) - H β, C(20) - H α)

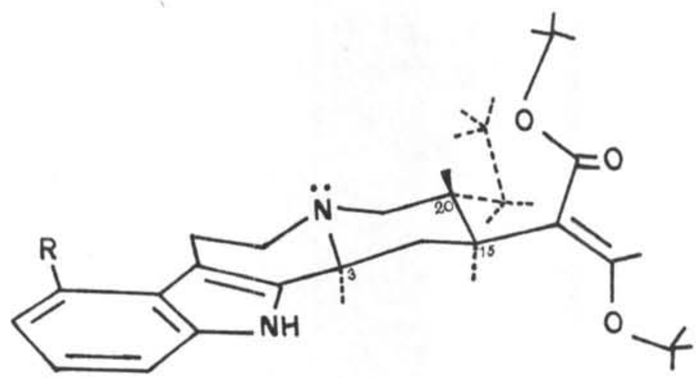


R = H : Akuammigine

. R = H, C(19) - CH_3 β : (3-Isoraunitic ine)

Open E ring

Normal (C(3) - H α, C(20) - H β)



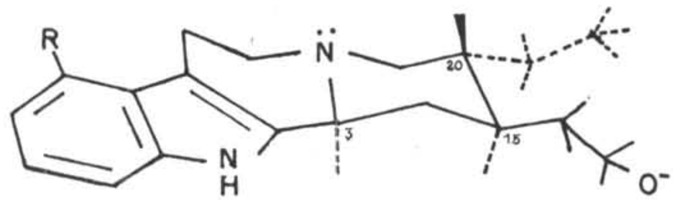
R = H : Dihydrocorynantheine

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

R = OH : (Gambirine)

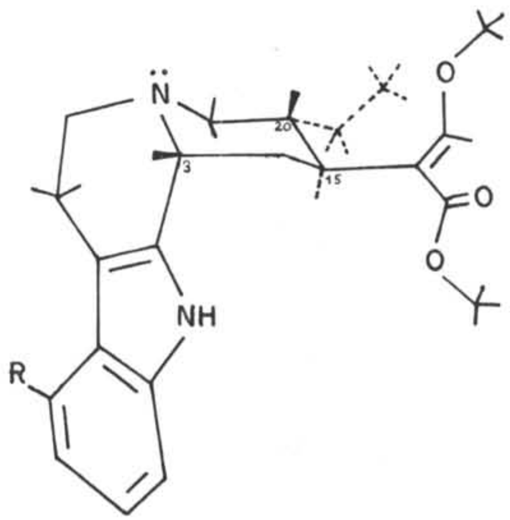
R = OCH_3 : Speciogynine

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



Dihydrocorynantheol

Pseudo (C(3) - H β, C(20) - H β)



R = H : Hirsutine

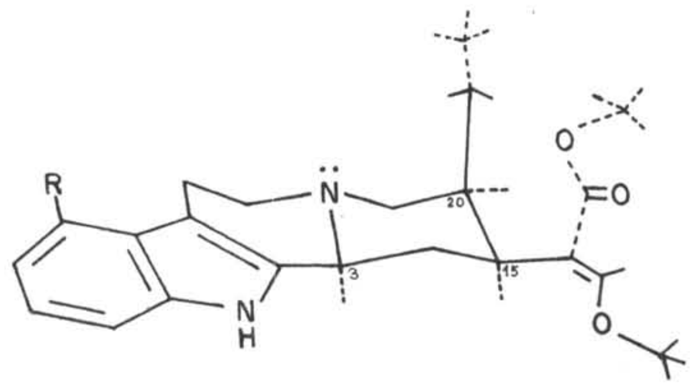
R = H, C(20) - Et = vinyl : Hirsuteine

R = OH : (Isogambirine)

R = OCH_3 : Mitraciliatine

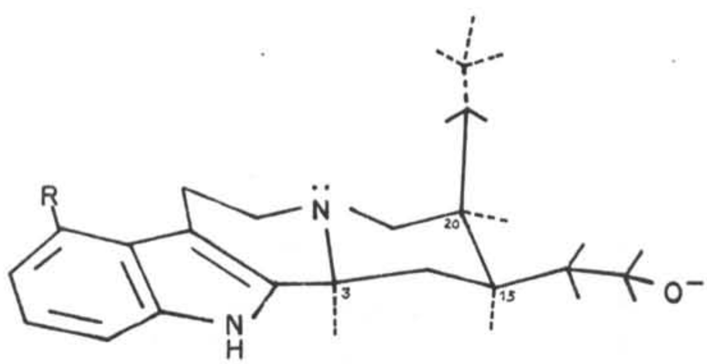
R = OCH_3, C(20) - Et = vinyl : Isopaynantheine

Allo (C(3) - H *a*, C(20) - H *a*)



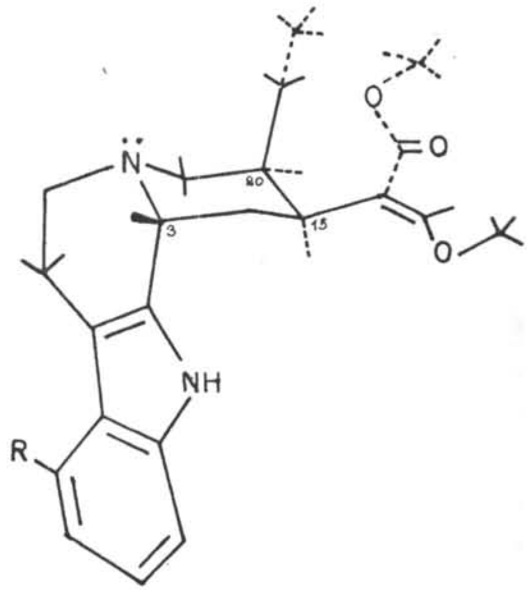
R = H : Corynantheidine

R = OCH_3 : Mitragynine



Corynantheidol

Epiallo (C(3) - H β, C(20) - H α)



R = H : Isocorynantheidine

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

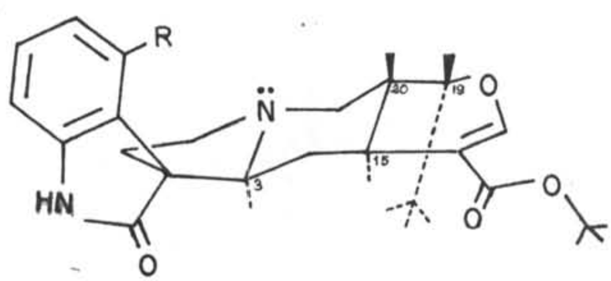
R = OCH_3 : Speciociliatine

Oxindole alkaloids

Closed E ring

Normal (C(3) - H α, C(20) - H β)

A

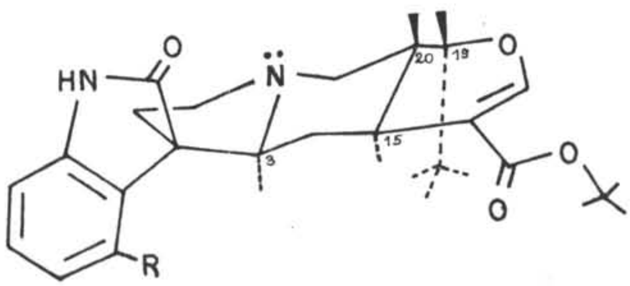


R = H : Isomitraphylline

R = H, C(19) - CH_3 β : (Uncarine A)

R = OCH_3 : Javaphylline

B



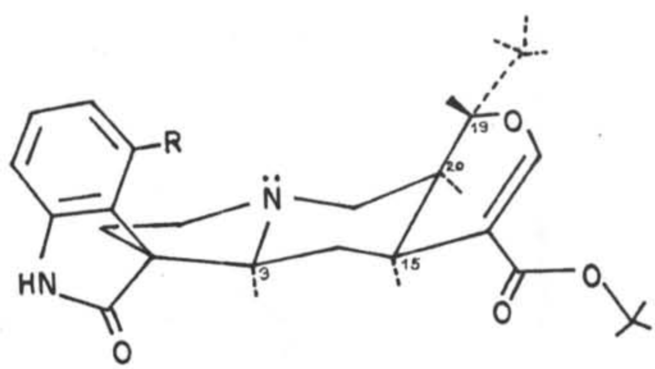
R = H : Mitraphylline

R = H, C(19) - CH_3 β : (Uncarine B)

R = OCH_3 : Isojavaphylline#

Allo (C(3) - H α, C(20) - H α)

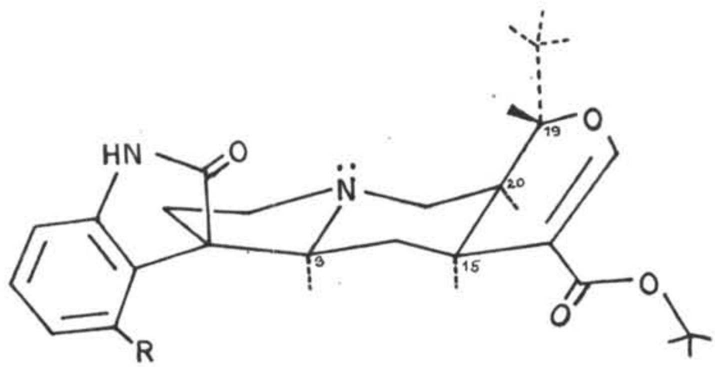
A



R = H : Isopteropodine

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

B

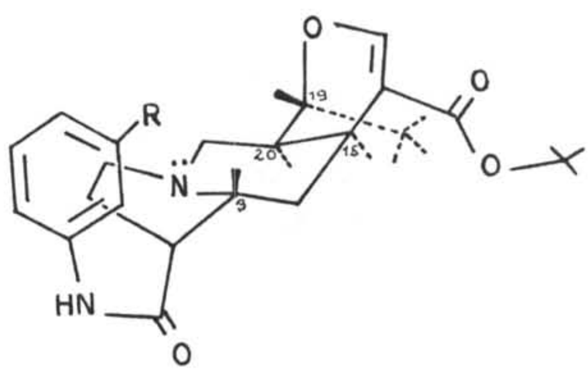


R = H : Pteropodine

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

Epiallo (C(3) - H β, C(20) - H α)

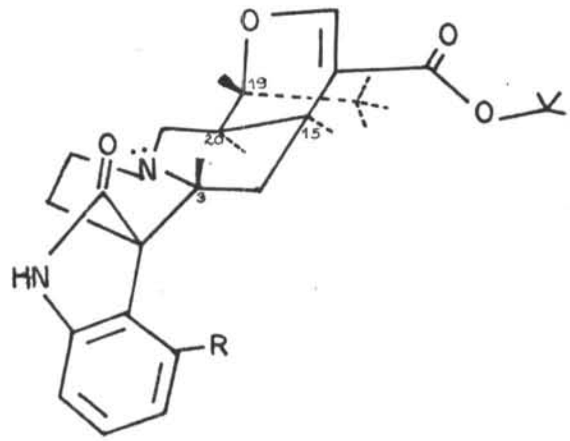
A



R = H : Speciophylline

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

B



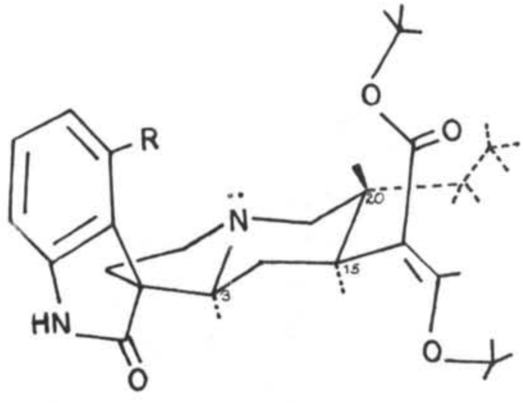
R = H : Uncarine F

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

Open E ring

Normal (C(3) - H α, C(20) - H β)

A



R = H : Isorhynchophylline

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

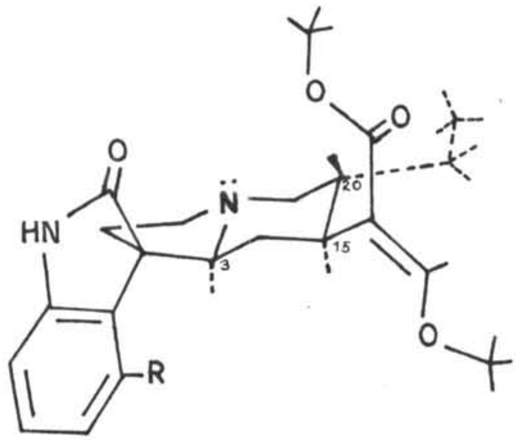
R = OH : Rotundifoline

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

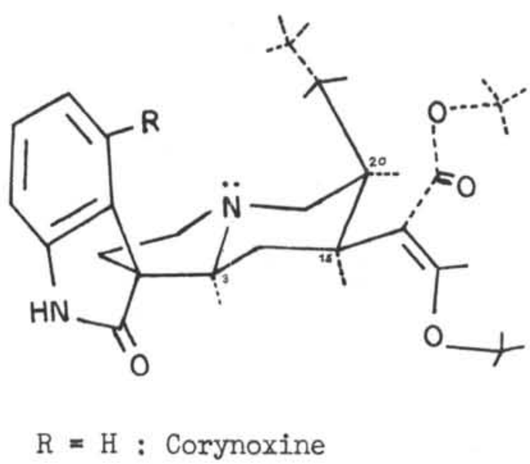
R = OH, C(20) - Et = vinyl : Isorotundifoleine

R = OCH_3 : Ciliaphylline

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

Allo (C(3) - H α, C(20) - H α)

A

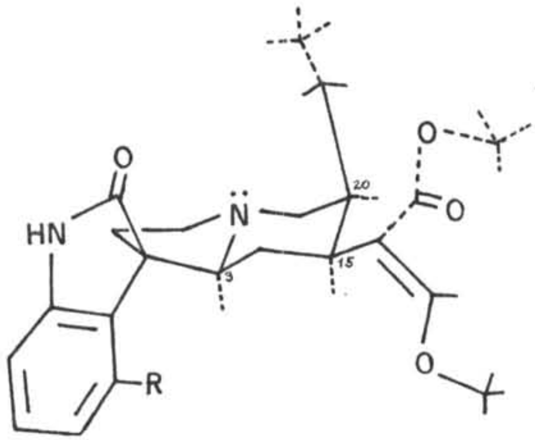


R = H : Corynoxine

R = OH : Mitrafoline

R = OCH_3 : Mitragynine oxindole A

B



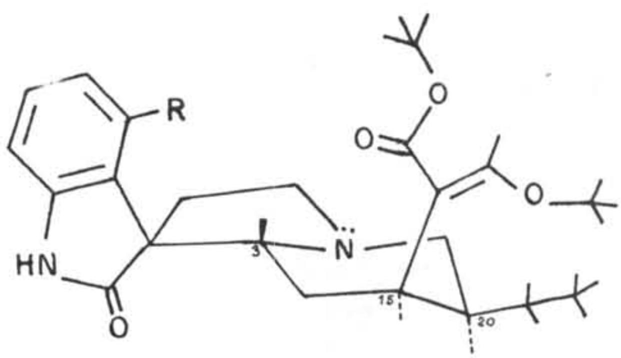
R = H : Corynoxine B

R = OH : Isomitrafoline

R = OCH_3 : Mitragynine oxindole B

Epiallo (C(3) - H β, C(20) - H α)

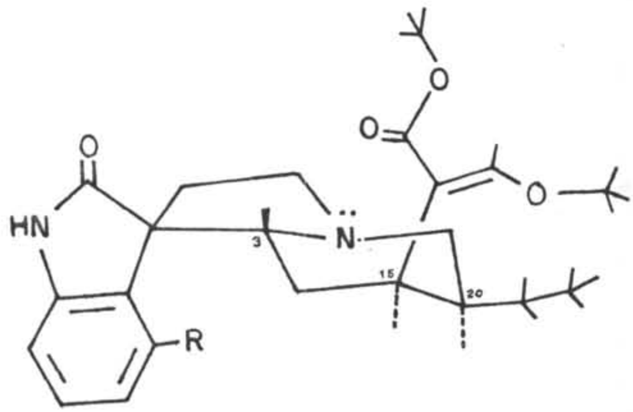
A



R = OH : Isospeciofoline

R = OCH_3 : Speciociliatine oxindole A#

B



R = OH : Speciofoline

R = OCH_3 : Speciociliatine oxindole B#

Pseudo (C(3) - H β, C(20) - H β)

The *pseudo* oxindole alkaloids were formerly concluded to be unstable to exist because of the steric interference between the oxindole unit and the underside of ring D (Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968a). Not until 1976 that Brown and Platt has clearly shown by synthesis from dihydrosecologanin aglycone that alkaloids of this conformation can exist and are reasonably stable. However, no *pseudo* oxindole alkaloid has yet been reported from natural sources.

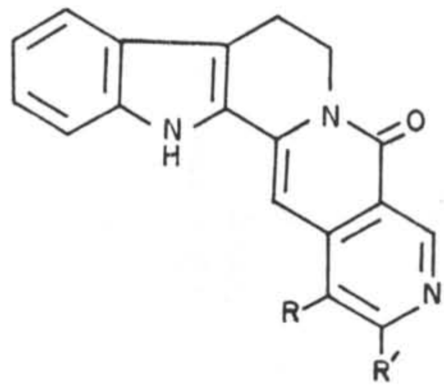
3.1.4 Alkaloid N-oxides from *Mitragyna* species

In 1964 Shellard and Phillipson reported the presence of a 'base-line' alkaloid isolated from the leaves of *Mitragyna rotundifolia* (Roxb.) O. Kuntze but were unable to determine its structure. The isolation of a similar substance from the leaves of *M. inermis* (Willd.) O. Kuntze enabled Shellard, Phillipson and Sarpong (1971) to characterise it as isorhynchophylline N-oxide. Further study shown it to be *anti*-isorhynchophylline N oxide (Phillipson, Rungsiyakul and Shellard, 1973). They are also isolated and characterised rhynchophylline N-oxide from the same plant. Shellard and Rungsiyakul (1973) isolated and characterised ciliaphylline N-oxide from the leaves of *M. tubulosa* (Arn.) Havil. The presence of N-oxides of four other alkaloids, viz. akuammigine, speciophylline, uncarine F and dihydrocorynantheol were reported from *M. parvifolia* (Roxb.) Korth. by Shellard and Houghton in 1974. In 1978, Shellard and Lala reported the presence of rhynchophylline N-oxide and *anti*-rotundifoline N-oxide from the root bark, stem bark and leaves of *M. rubrostipulata* (K. Schum.) Havil.

Most of the isolated N-oxides from several species of *Mitragyna* are of open E ring oxindole alkaloids. They are of isorhynchophylline, rhynchophylline, rotundifoline, isorotundifoline and ciliaphylline respectively. The other N-oxides isolated are of akuammigine, dihydrocorynantheol, speciophylline and uncarine F.

3.2 Other indole alkaloid from *Mitragyna* species

The only other indole alkaloid reported to be present in species of *Mitragyna* is angustine which belongs to the pyridino-indolo-quinolizidinone group. Other alkaloids in this group, having the following basic structure, were reported to be present in *Strychnos* and *Uncaria* species.



R = CH=CH_2, R' = H : Angustine

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

R = H, R' = CH_3 : (Angustidine)

4. Chemical transformations

4.1 *In vitro*

4.1.1 Isomerisation of heteroyohimbine alkaloids

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

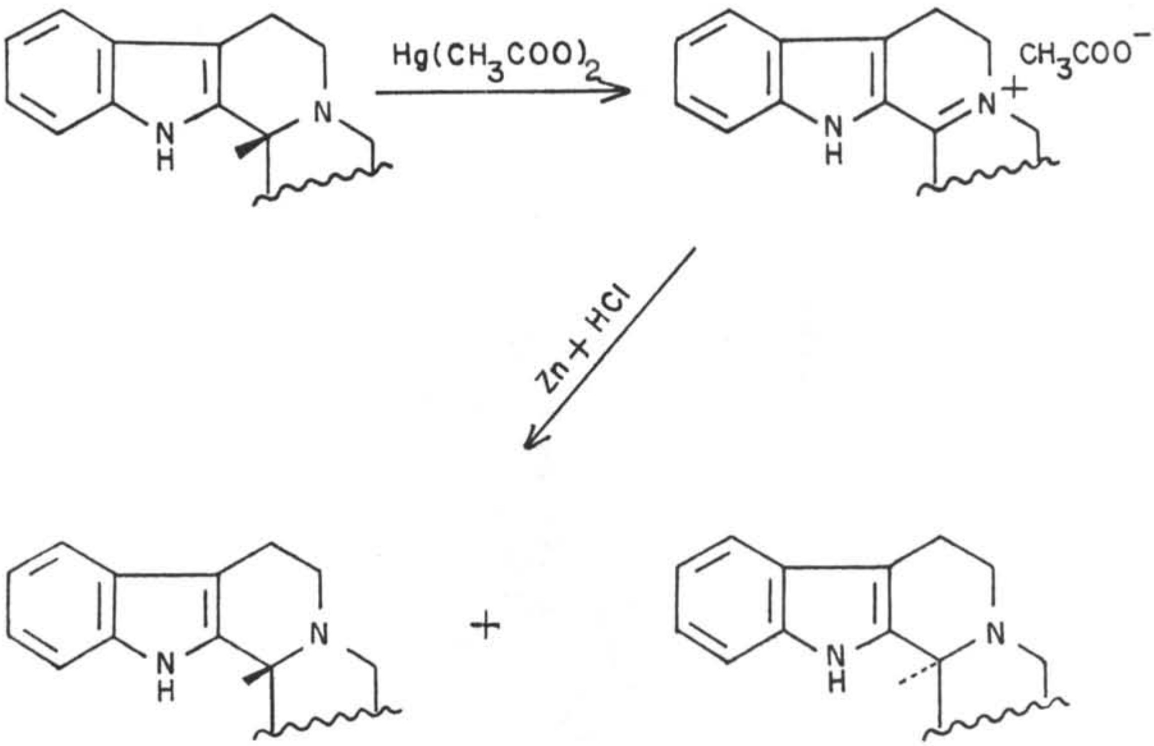
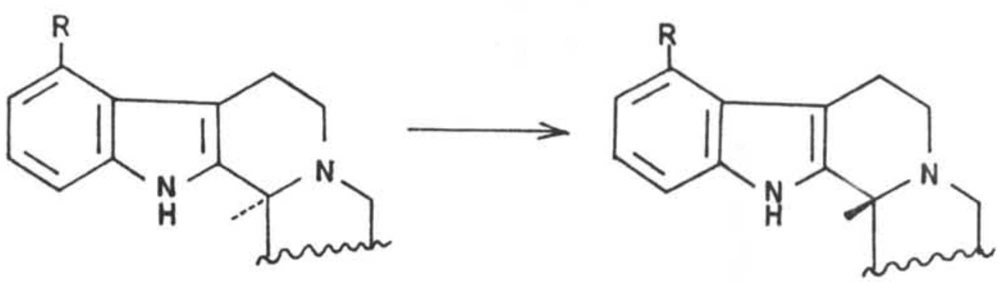


Fig. IV Oxidation-reduction reaction of heteroyohimbine alkaloids

In term 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 VII.

Table VII

Isomerisation of heteroyohimbine alkaloids

Conversion	Reference
ajmalicine ⟶ 3-isoajmalicine (*normal*) (*pseudo*)	Wenkert and Roychaudhuri, 1956.
19-epi-ajmalicine ⟶ 19-epi-3-iso-ajmalicine (*normal*) (*pseudo*)	Phillipson and Hemingway, 1975b.
mitrajavine ⟶ isomitrajavine (*pseudo*) (*normal*)	Shellard and Sarpong, 1971a, b.
tetrahydroalstonine ⟶ akuammigine (*allo*) (*epiallo*)	Supavita, 1979.
rauniticine ⟶ 3-isorauniticine (*allo*) (*epiallo*)	Supavita, 1979.
hirsutine ⟶ dihydrocorynantheine (*pseudo*) (*normal*)	Trager, Phillipson and Beckett, 1968.
speciogynine ⟶ mitraciliatine (*normal*) (*pseudo*)	Trager, Phillipson and Beckett, 1968; Shellard, Houghton and Resha, 1978c.

Table VII (continued)

Conversion	Reference
paynantheine ⟶ isopaynantheine (*normal*) (*pseudo*)	Beckett, Dwuma-Badu and Haddock, 1969; Shellard, Houghton and Resha, 1978c.
Corynantheidine ⟶ Isocorynantheidine (*allo*) (*epiallo*)	Trager, Phillipson and Beckett, 1968; Beckett, Dwuma-Badu and Haddock, 1969; Shellard, Houghton and Resha, 1978c.
mitragynine ⟶ speciociliatine (*allo*) (*epiallo*)	Trager, Phillipson and Beckett, 1968; Shellard, Houghton and Resha, 1978c.

4.1.2 Isomerisation of oxindole alkaloids

Oxindole alkaloids may be isomerised at C(3) and/or spiro C(7) centres by heating in pyridine (basic isomerisation) or acetic acid (acidic isomerisation). The isomerisation involves scission and reformation at the C(3) - C(7) bond and hence possible inversion of one or both of the centres (Seaton, Nair, Edwards and Marion, 1960; Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968). Starting with a given oxindole isomer, four isomeric compounds should result upon isomerisation, i.e. two (A and B) with C(3) - H α and two (A and B) with C(3) - H β. The isomerisation of a *normal* oxindole results in only two products, which are the *normal* A and B isomers, hence supported the former conclusion by Trager *et al.* (1968) that *pseudo* oxindole alkaloids are too unstable to exist.

The isomerisation medium determines the predominant isomer in the final mixture. In acidic isomerisation, the B 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 oxindoles as the lactam carbonyl is below the plane of the C/D rings.

In basic isomerisation, the A oxindoles predominate and this is thought to be destabilisation due to the electrostatic repulsion between the lone pair of electron of N(4) end lactam carbonyl group in the free base form of the B isomers (Finch and Taylor, 1962a, b; Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968).

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

Table VIII

Isomerisation of oxindole alkaloids

Conversion	Reference
isomitraphylline or mitraphylline $\xrightarrow{Py}$ 80 % isomitraphylline + 20 % mitraphylline	Seaton, Nair, Edwards and Marion, 1960.

Table VIII (continued)

Conversion	Reference
isomitraphylline or mitraphylline $\xrightarrow{Ac}$ 20 % isomitraphylline + 80 % mitraphylline	Seaton, Nair, Edwards and Marion, 1960; Beckett, Shellard, Phillipson, and Lee, 1966a.
uncarine A or uncarine B $\xrightarrow{Py}$ 80 % uncarine A + 20 % uncarine B	Seaton, Nair, Edwards and Marion, 1960.
Isopteropodine $\xrightarrow{Py}$ 100 % isopteropodine + traces of pteropodine	Beecham, Hart, Johns and Lamberton, 1968.
pteropodine $\xrightarrow{Py}$ 10 % isopteropodine + 90 % pteropodine	Beecham, Hart, Johns and Lamberton, 1968.
speciophylline $\xrightarrow{Py}$ 20 % isopteropodine + 20 % pteropodine + 30 % speciophylline + 30 % uncarine F	Beecham, Hart, Johns and Lamberton, 1968.
Isorhynchophylline or rhynchophylline $\xrightarrow{Py}$ 70 % isorhynchophylline + 30 % rhynchophylline	Seaton, Nair, Edwards and Marion, 1960.

Table VIII (continued)

Conversion	Reference
isorhynchophylline or rhynchophylline $\xrightarrow{Py}$ 80 % isorhynchophylline + 20 % rhynchophylline	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.
isorhynchophylline or rhynchophylline $\xrightarrow{Ac}$ 20 % isorhynchophylline + 80 % rhynchophylline	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.
isorhynchophylline $\xrightarrow{Ac}$ 40 % isorhynchophylline + 60 % rhynchophylline	Nozoye, 1958c.
corynoxine or corynoxine B $\xrightarrow{Py}$ 80 % corynoxine + 20 % corynoxine B	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968
corynoxine or corynoxine B $\xrightarrow{Ac}$ 20 % corynoxine + 80 % corynoxine B	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.
rotundifoline or isorotundifoline $\xrightarrow{Py}$ 90 % rotundifoline + 10 % isorotundifoline	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.

Table VIII (continued)

Conversion	Reference
rotundifoline or isorotundifoline $\xrightarrow{Ac}$ 60 % rotundifoline + 40 % isorotundifoline	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.
isorotundifoline $\xrightarrow{Py}$ (135°C, 23 hr) 10 % rotundifoline + 80 % isorotundifoline + 3-epi-isorotundifoline $\downarrow$ (135°C, 17 hr, Py) 10 % rotundifoline + 90 % isorotundifoline	Hemingway, Houghton, Phillipson and Shellard, 1975.
3-epi-isorotundifoline $\xrightarrow{Ac}$ 60 % rotundifoline + 40 % isorotundifoline	Hemingway, Houghton, Phillipson and Shellard, 1975.
isorotundifoleine $\xrightarrow{Py}$ 60 % rotundifoleine + 40 % isorotundifoleine	Hemingway, Houghton, Phillipson and Shellard, 1975.
mitrafoline or speciofoline $\xrightarrow{Py}$ 40 % mitrafoline + 40 % speciofoline + 10 % isomitrafoline + 10% isospeciofoline	Hemingway, Houghton, Phillipson and Shellard, 1975.

Table VIII (continued)

Conversion	Reference
mitrafoline or speciofoline —Ac→ 50 % mitrafoline + 25 % speciofoline + 15 % isomitrafoline + 10 % isospeciofoline	Hemingway, Houghton, Phillipson and Shellard, 1975.
isomitrafoline or isospeciofoline —Py→ (major) mitrafoline + speciofoline + (minor) isomitrafoline + isospeciofoline	Hemingway, Houghton, Phillipson and Shellard, 1975.
rhynchociline or ciliaphylline —Py→ 35 % rhynchociline + 65 % ciliaphylline	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.
rhynchociline or ciliaphylline —Ac→ 50 % rhynchociline + 50 % ciliaphylline	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.
speciononoxeine or isospecionoxeine —Py→ 65 % specionoxeine + 35 % isospecionoxeine	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.
specionoxeine or isospecionoxeine —Ac→ 50 % specionoxeine + 50 % isospecionoxeine	Trager, Lee, Phillipson, Haddock, Dwuma-Badu and Beckett, 1968.

Py = basic isomerisation using pyridine

Ac = acidic isomerisation using acetic acid and mercuric acetate

4.1.3 Conversion of heteroyohimbine to oxindole alkaloids

Finch and Taylor (1962a, b) and Shavel Jr. and Zinnes (1962) show that the yohimbine and heteroyohimbine alkaloids are transformed into an epimeric mixture of C(7) chloroindolenines (I) by action of tertiary butyl hypochlorite. The chloroindolenines are then methanolysed to give the imido ester (II) which hydrolyses in aqueous acetic acid to give the A and B oxindoles (Fig. V)

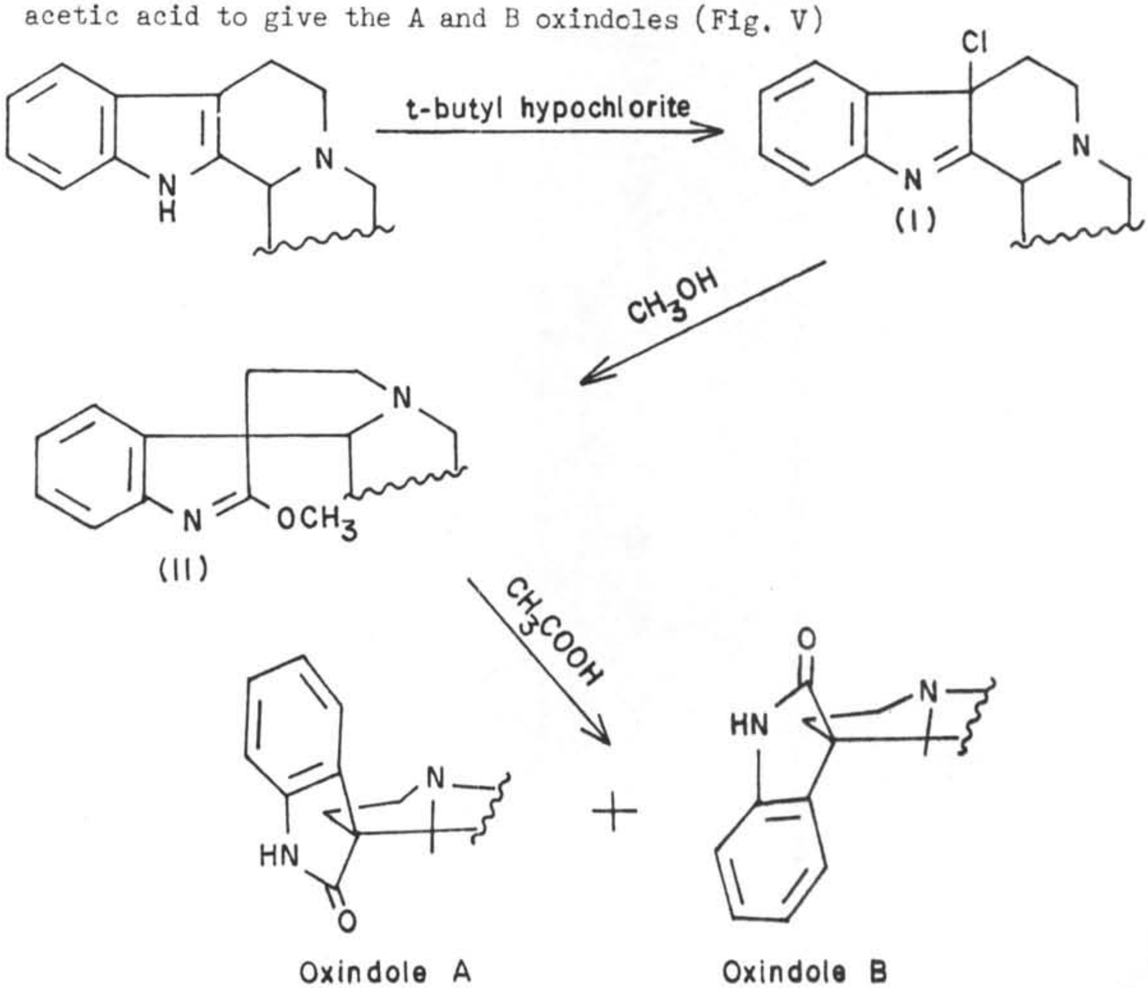


Fig. V

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

Table IX

Conversion of heteroyohimbine alkaloids

Conversion	Reference
ajmalicine → isomitraphylline (*normal*) (*normal* A) + mitraphylline (*normal* B)	Finch and Taylor, 1962a; Shavel Jr. and Zinnes, 1962; Shellard and Houghton, 1973a.
mitrajavine → isojavaphylline (*pseudo*) (*normal* A) + javaphylline (*normal* B)	Shellard and Sarpong, 1971b.
dihydrocorynantheine → isorhynchophylline (*normal*) (*normal* A) + rhynchophylline (*normal* B)	Finch and Taylor, 1962a.
corynantheine → corynoxeine (*normal*) (*normal* B)	Finch and Taylor, 1962a.

Table IX (continued)

Conversion	Reference
mitraciliatine (*pseudo*) → rhynchociline (*normal* A) + ciliaphylline (*normal* B)	Shellard and Sarpong, 1971b.
corynantheidine (*allo*) → corynoxine A (*allo* A) + corynoxine B (*allo* B)	Beckett, Dwuma-Badu and Haddock, 1969.
mitragynine (*allo*) → mitragynine oxindole A (*allo* A) + mitragynine oxindole B (*allo* B)	Beckett, Dwuma-Badu and Haddock, 1969; Shellard, Houghton and Resha, 1978a.
speciociliatine (*epiallo*) → speciociliatine oxindole A (*epiallo* A) + speciociliatine oxindole B (*epiallo* B)	Beckett, Dwuma-Badu and Haddock, 1969; Shellard, Houghton and Resha, 1978a.

Zinnes and Shavel Jr. (1966) converted the carboxylic E ring indole alkaloid, *pseudo*-yohimbine into *normal* oxindoles. Therefore there is possibility that the *pseudo* heteroyohimbine alkaloids in some *Mitragyna* species could also be transformed to the *normal* oxindoles (Shellard and Sarpong, 1971a).

Another method of converting heteroyohimbine 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 (Fig. VI).

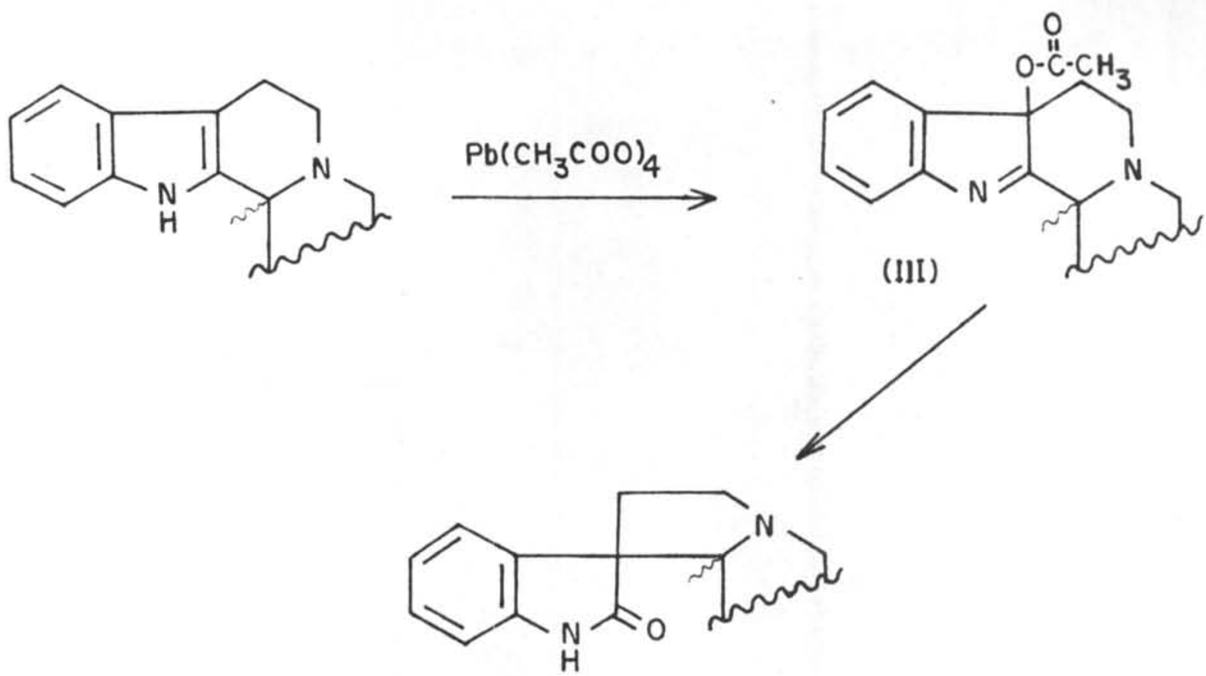


Fig. VI

Hart, Johns and Lamberton (1967) used this method to prepare isopteropodine, pteropodine, speciophylline and uncarine F from the corresponding heteroyohimbine tetrahydroalstonine.

4.1.4 Conversion of oxindole to heteroyohimbine alkaloids

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

They used this method, converted isopteropodine and pteropodine to their corresponding heteroyohimbine alkaloids tetrahydroalstonine and its isomer,akuammigine (Fig. VII). They have also similarly converted isorhynchophylline into dihydrocorynantheine and hirsutine.

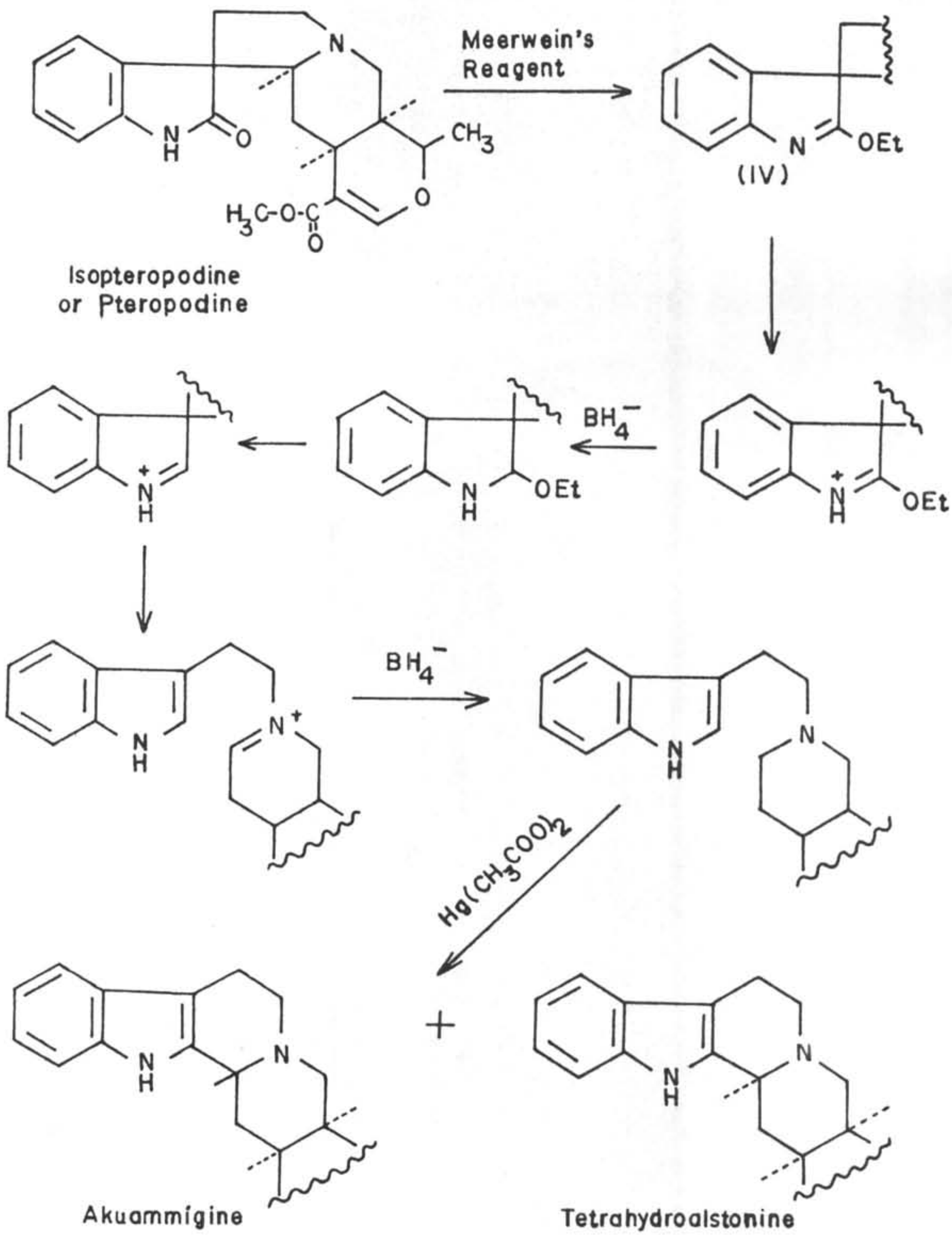


Fig. VII Conversion of oxindole to heteroyohimbines.

4.2 *In vivo*

By feeding the young plant of *Mitragyna parvifolia* (Roxb.) Korth. with unlabelled alkaloids, Shellard and Houghton (1972a) observed the presence of isomitraphylline in the leaves both after feeding ajmalicine and 3-isoajmalicine into the stem xylem. Showing that conversion of *normal* and *pseudo* heteroyohimbine to *normal* oxindole alkaloids occur *in vivo*. The interconversion of the heteroyohimbines did not seem to take place since no 3-isoajmalicine was detected after ajmalicine was fed into the plant and vice versa.

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

Shellard and Houghton (1973b) confirmed their work in 1972 by using the ^{14}C-alkaloids in the young plant of *M. parvifolia* (Roxb.) Korth. They fed ^{14}C-tetrahydroalstonine and ^{14}C-akuammigine separately into the stem xylem of young plant and 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 xylem and pteropodine was shown to be converted to mitraphylline and mitraphylline was converted via corynoxeine to rhynchophylline.

Evidence obtained by feeding rhynchophylline into the root phloem showed that rhynchophylline, a *normal* oxindole alkaloid, is converted to the *pseudo* indole hirsutine as well as conversion of hirsutine to rhynchophylline. This clearly showed that neither *normal* oxindole alkaloid nor *pseudo* heteroyohimbine alkaloid could be converted to corresponding *normal* heteroyohimbine alkaloid since no dihydrocorynantheine, the *normal* heteroyohimbine alkaloid corresponding to rhynchophylline could be detected.

Shellard and Houghton (1972a) found that when mitraphylline was fed into the stem xylem, rhynchophylline was found in the leaves. The use of ^{14}C-mitraphylline (1974a) showed that it was not necessarily the rhynchophylline from the main stem xylem but that the mitraphylline itself was converted via corynoxeine to rhynchophylline. When ^{14}C-rhynchophylline was used - incorporated in large amounts of rhynchophylline - both mitraphylline and rhynchophylline were detected in the leaf together with ^{14}C-labelled *allo* and *epiallo* closed E ring oxindole alkaloids. It would appear that the interconversion involving rhynchophylline $\rightleftharpoons$ mitraphylline $\rightleftharpoons$ pteropodine occurs normally in the leaf but since only small quantities are present in the transportation stream, only the final product - the *allo* and *epiallo* oxindole alkaloids are found.

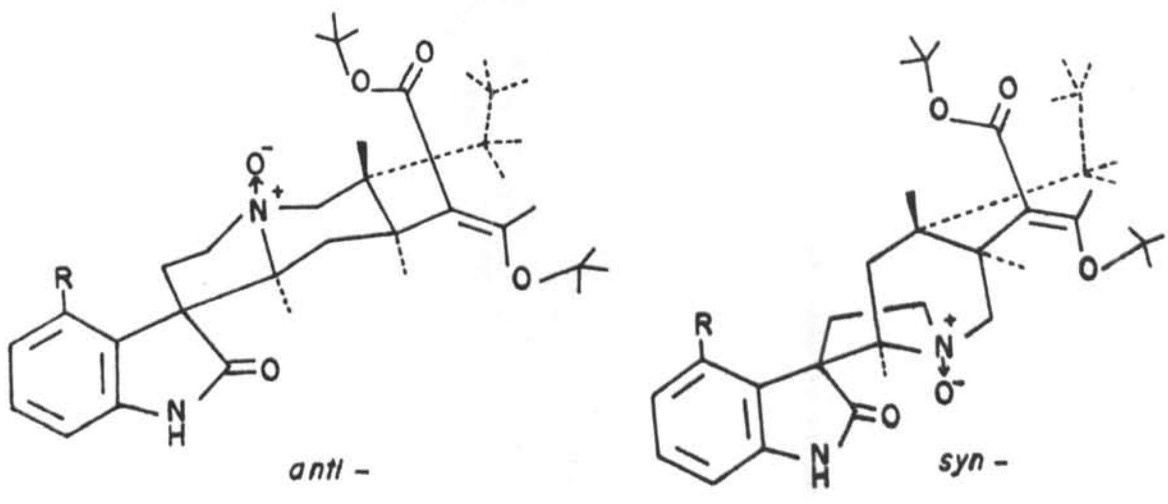
5. N-oxidation of heteroyohimbine and oxindole alkaloids

Shellard, Phillipson and Sarpong (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.

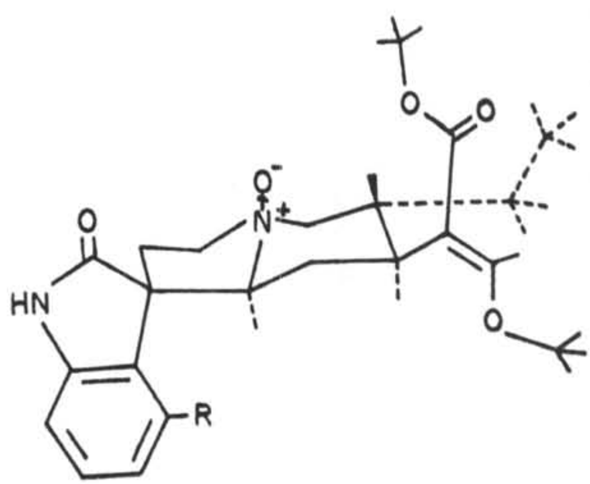
Merlini, Nasini and Phillipson (1972) synthesis N-oxides of closed E ring unsubstituted heteroyohimbine alkaloids by treatment with m-chloroperbenzoic acid. Those synthesised were 4-R-ajmalicine, 4-R-3-isoajmalicine, 4-R-tetrahydroalstonine, 4-R-akuammigine and 4-S-akuammigine N-oxides.

Phillipson, Rungsiyakul and Shellard (1973) 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* (Arn.) Havil. and found that whereas the B series oxindole alkaloids 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 one N-oxide.

Shellard, Houghton and Lala (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.



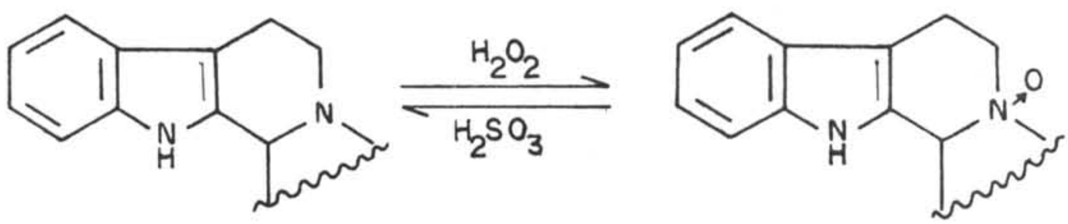
N-oxides of oxindole A



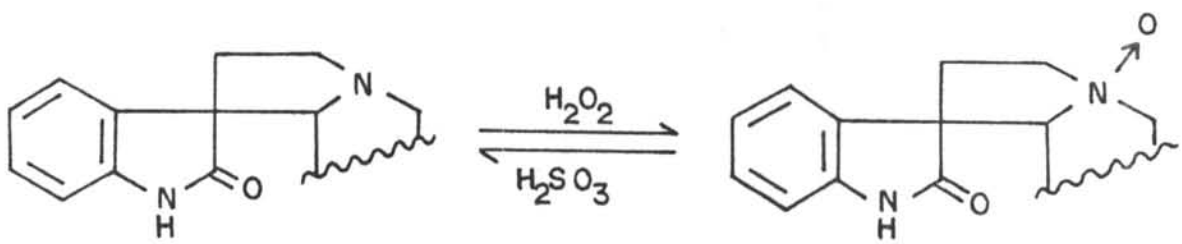
N-oxide of oxindole B

Fig. VIII

The alkaloidal N-oxides are readily reduced to their parent alkaloids without isomerisation at C(7) by treated with sulphurous acid and allowed to stand overnight (Shellard, Phillipson and Sarpong, 1971) or treated with concentrated ammonium hydroxide solution and excess ferrous sulphate and heated on a steam bath for 30 minutes (Merlini, Nasini and Phillipson, 1972) (Fig. IX).



Heteroyohimbine alkaloid



Oxindole alkaloid

Fig. IX Formation and reduction of alkaloid N-oxides.

6. Biogenesis

6.1 Indole alkaloids

It has now been well established, by the use of radioactive tracer studies that the biosynthesis of indole alkaloids involves the formations and condensation of the following :

a) Formation of tryptophan or its decarboxylation product, tryptamine, which is the precursor of the indole portion,

b) formation of non-tryptophan unit, i.e. C_{9-10} residue, and

c) appropriate condensation of the products from a) and b) to build up the indole alkaloids.

6.1.1 Formation of tryptamine

Tryptophan is known to originate in plant cells from shikimic acid, having anthranilic acid as an intermediate. In the next step of the sequence, the formation of the pyrrole ring, phosphoribosyl pyrophosphate (PRPP) provided the two necessary carbon atoms while the carbonyl carbon atom of anthranilic acid is lost. The immediate product of the interaction of PRPP and anthranilate is anthranilic ribonucleotide, which appears to form anthranilic-1-deoxy-ribulonucleotide. Ring closure, with accompanying production of carbon dioxide and water gives rise to indole-3-glycerol phosphate. Many enzymes catalyse the reversible formation of free indole and triose phosphate or condensation of serine and indole to form tryptophan which undergoes decarboxylation reaction and tryptamine is formed (Mattoon, 1963; Mahler and Cordes, 1966).

The reaction is illustrated in Fig. X.

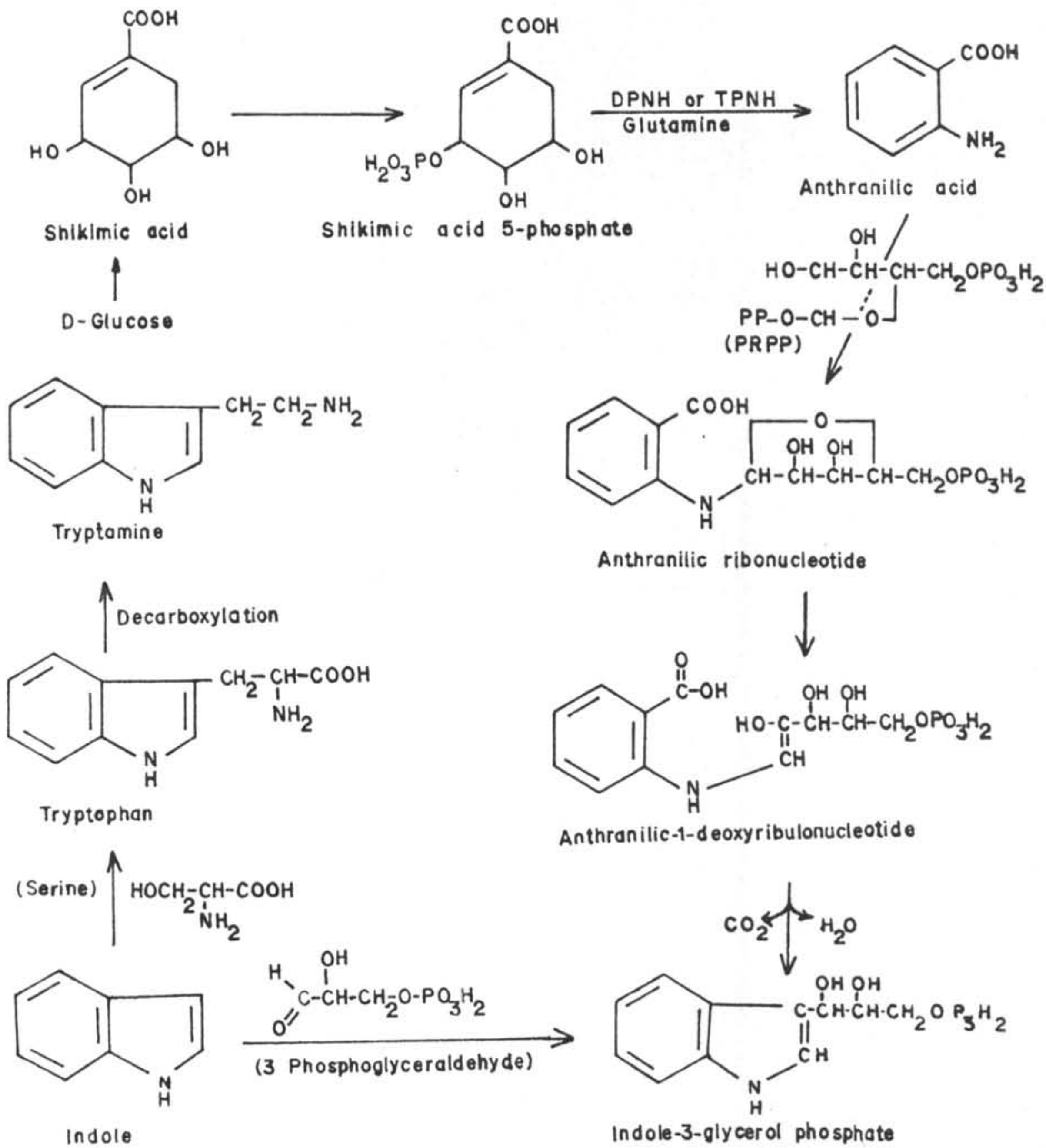


Fig. X Formation of tryptamine.

6.1.2 Formation of non-tryptamine unit

Battersby, Brown, Kapil, Martin and Plunkett (1966) proposed a pathway of non-tryptamine unit, *seco*-loganin, from mevalonic acid, having geraniol, citronellal, iridodial and loganin as intermediates (Battersby, Burnett and Parsons, 1968; Shellard, Phillipson and Gupta, 1969b). The outline of formation is shown in Fig. XI.

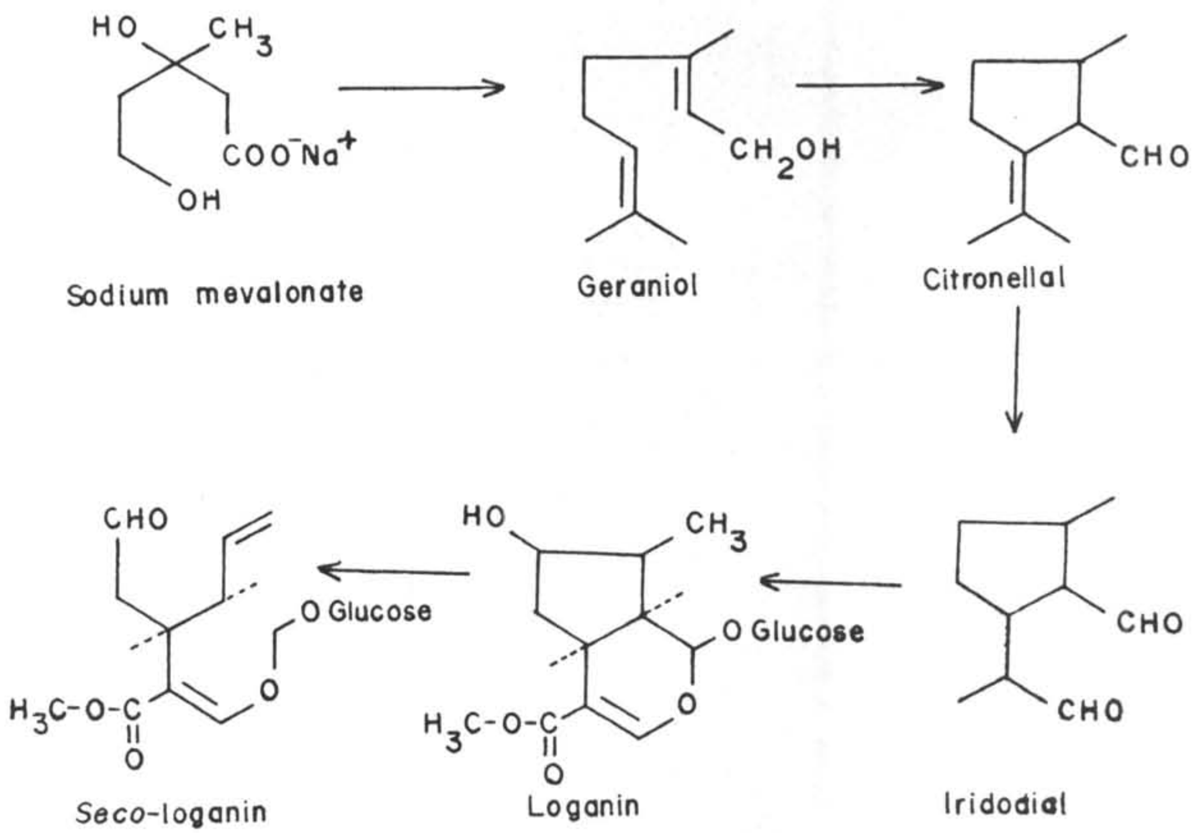


Fig. XI Formation of loganin and *seco*-loganin.

Geraniol was also proved to be a precursor of the three types of indole alkaloids, i.e. *Iboga*, *Corynanthe* and *Aspidosperma* types (Battersby, Brown, Kapil, Plunkett and Taylor, 1966;

Battersby, Brown, Knight, Martin and Plunkett, 1966; Loew, Goeggel and Arigoni, 1966; Shellard, Phillipson and Gupta, 1969b) (Fig. XII).

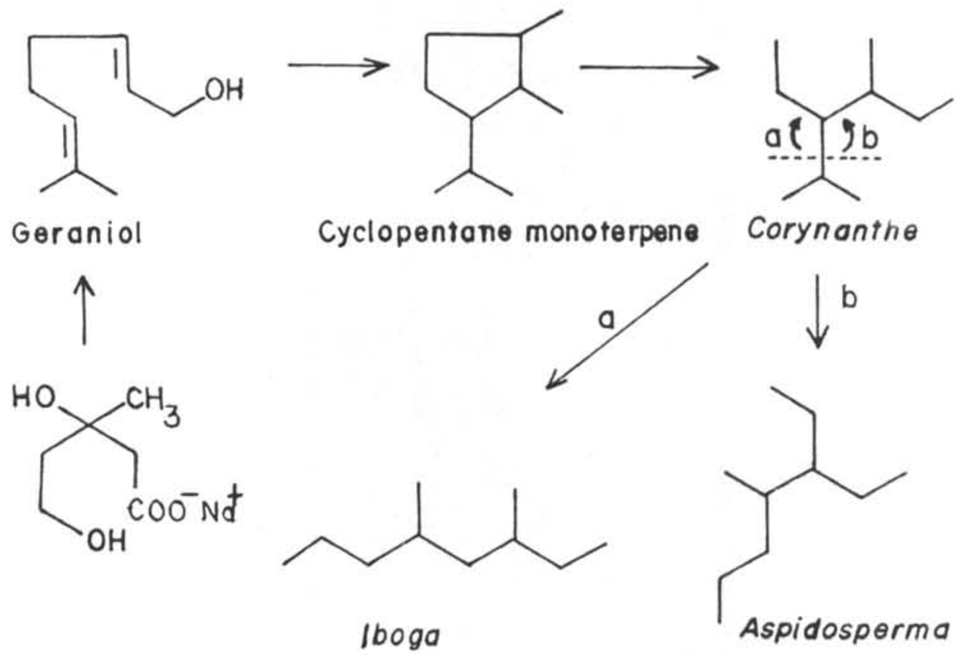


Fig. XII

6.1.3 Formation of closed E ring and open E ring heteroyohimbine alkaloids

When tryptamine reacts with *seco*-loganin two diastereoisomers, vincoside (C(3) - H β) and strictosidine (isovincoside, C(3) - H α) are formed (Blackstock, Brown and Lee, 1971). It has been concluded that vincoside is the precursor of the heteroyohimbine alkaloids and the pathways have been proposed and discussed in details (Fig. XIII).

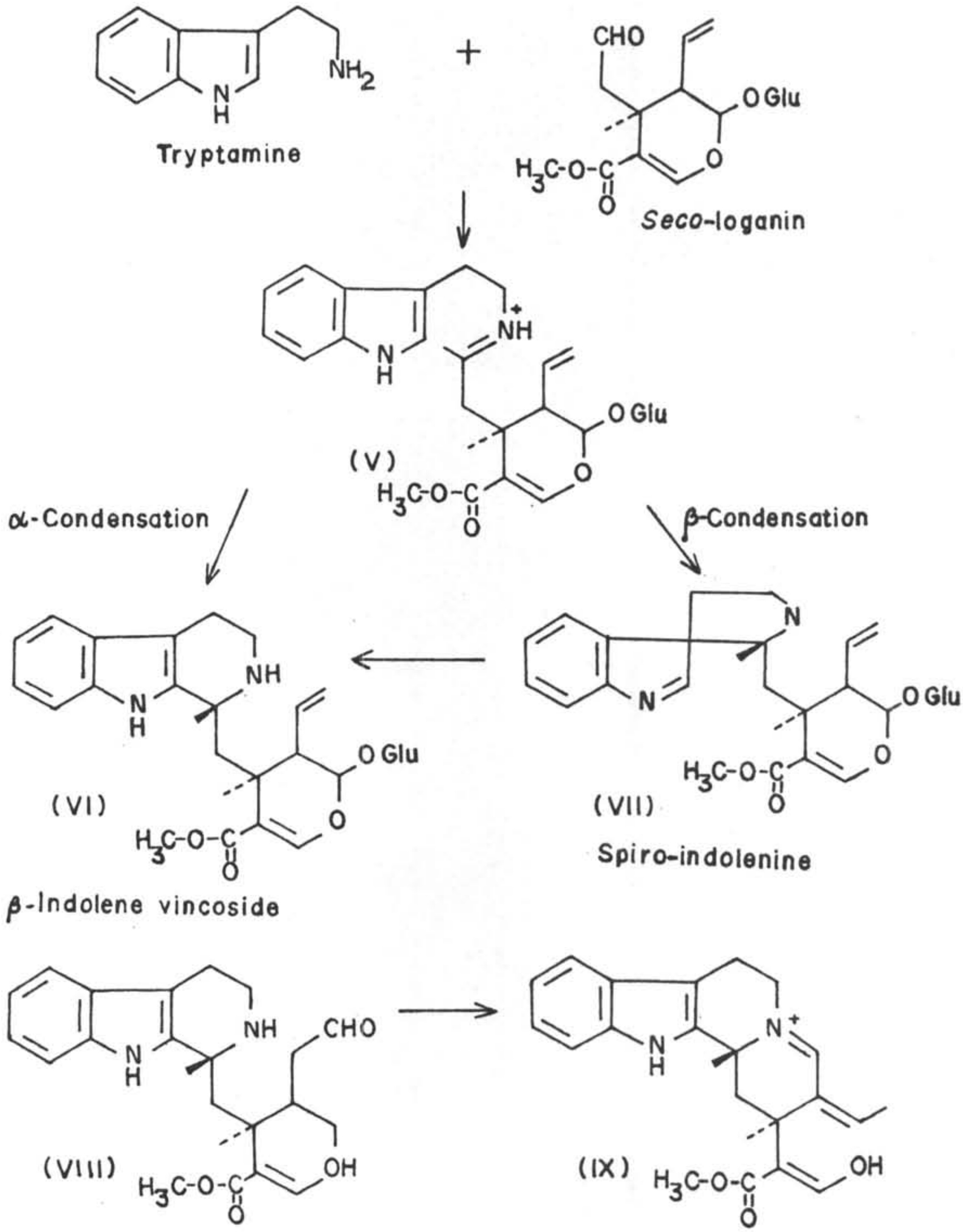

Tryptamine
NH2
CHO
O Glu
H3C-O-C
Seco-loganin
NH
(V)
α-Condensation
β-Condensation
(VI)
β-Indolene vincoside
(VII)
Spiro-indolenine
CHO
OH
(VIII)
(IX)

Fig. XIII

Fig. XIII 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, 1973b).

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

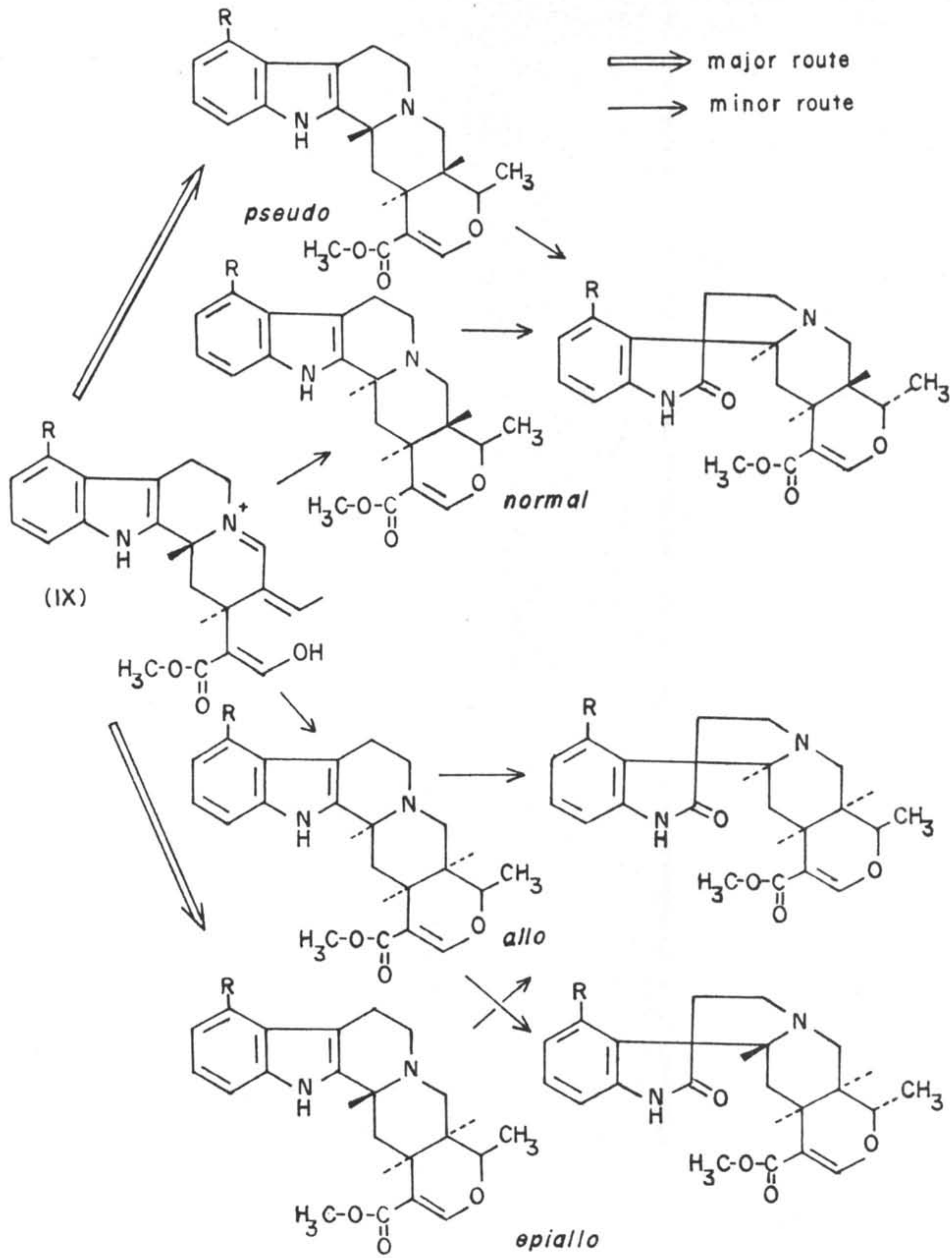


Fig. XIV Biogenesis of closed E ring alkaloids.

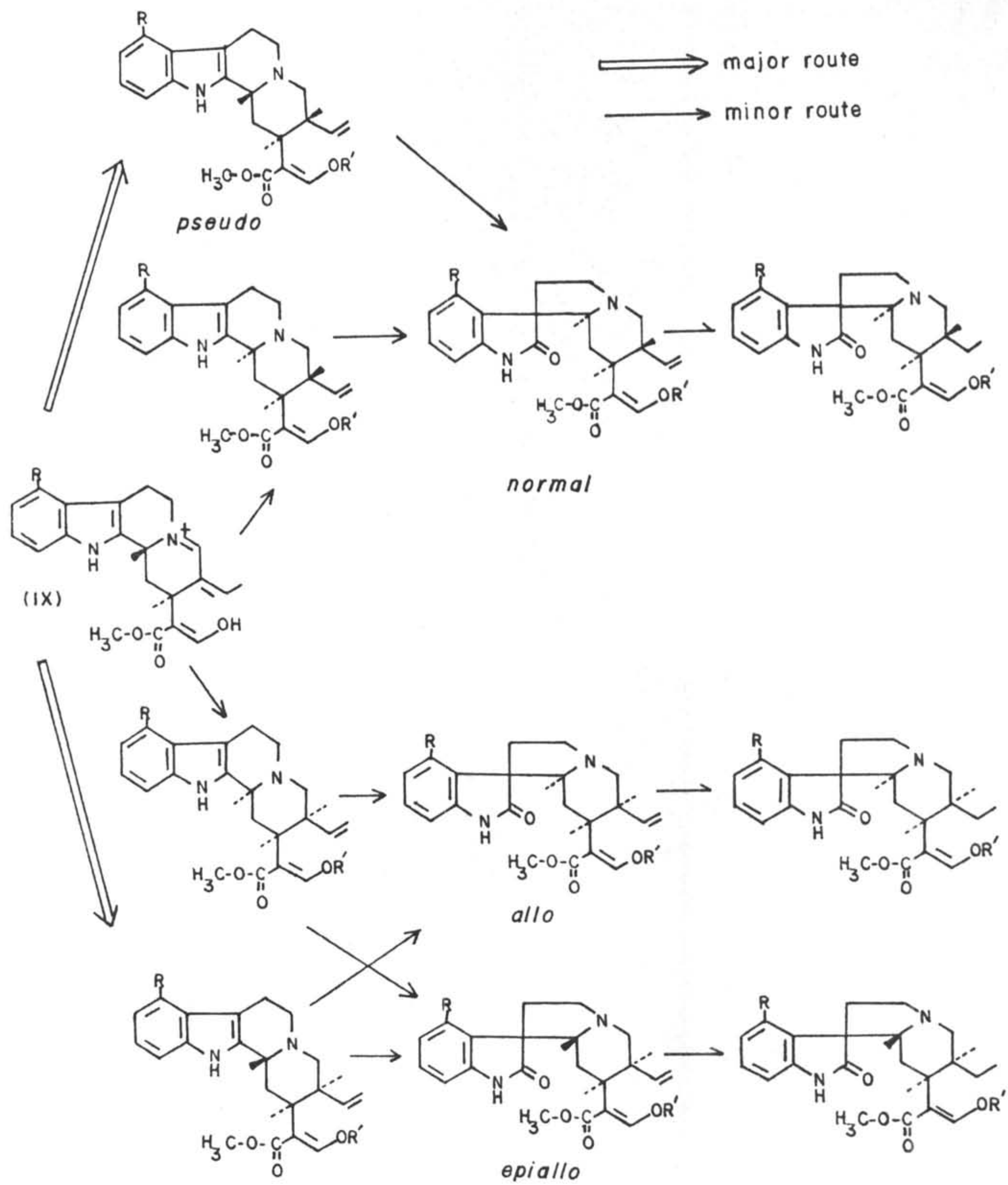


Fig. XV Biogenesis of open E ring alkaloids.

Fig. XVI shows details of the pathway in Fig. XIV and Fig. XV. Reduction of (IX) gives an isomer of geissoschizine (XII). The minor pathway involves an opening of ring C in (IX) to give an intermediate with a conjugated double bond system (X). The closure of 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, 1973b). 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* (Linn.) G. Don being derived from the glycosidic alkaloids vincoside and isovincoside (Timmins and Court, 1976a).

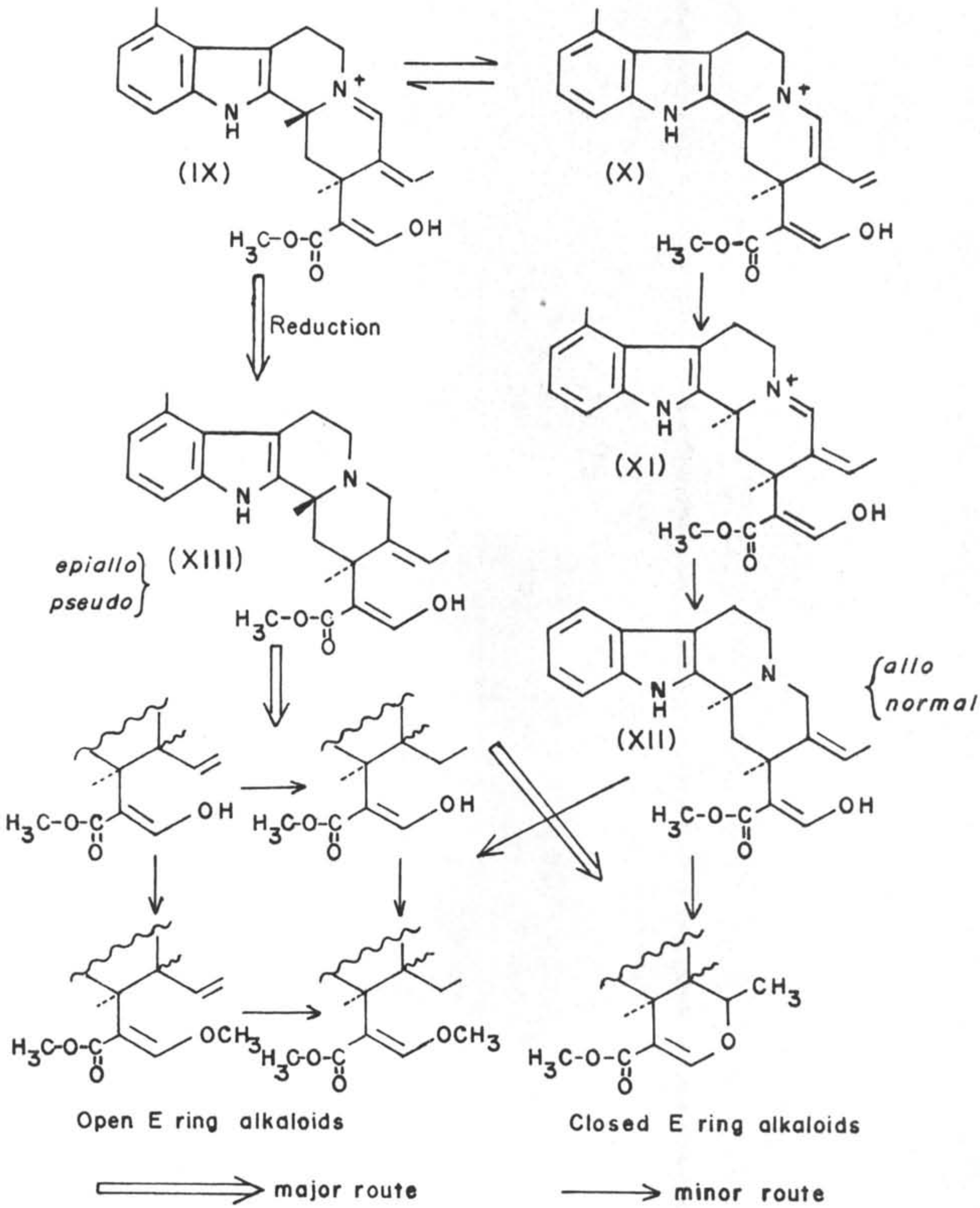

(IX)
(X)
Reduction
(XI)
epiallo
pseudo
(XIII)
allo
normal
(XII)
OH
OCH3
CH3
Open E ring alkaloids
Closed E ring alkaloids
major route
minor route

Fig. XVI

However, recently Rueffer, Nagakura and Zenk (1978) reported that the key intermediate in the biosynthesis 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 and proved that strictosidine with *3* α (*S*) stereochemistry is the universal precursor for monoterpenoid indole alkaloids.

Concurrently Stöckigt and Zenk (1977) and Stöckigt, Rueffer, Zenk and Hoyer (1978) also detected strictosidine and cathenamine as a pivotal intermediates in enzymatic formation of monoterpenoid indole alkaloids of the heteroyohimbine type in cell-free extracts from *Catharanthus roseus* (Linn.) G. Don cell suspension cultures.

6.2 Oxindole alkaloids

The Woodward proposals regarding the condensation of tryptamine and C_{10} unit suggested that this may be either an α condensation to give indoles or a β condensation to give oxindoles (Shellard, Phillipson and Gupta, 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 cyclisationat either α- or β- position of the indole nucleus to yield the β-carboline or the spiro-indolenine intermediate. They argued that β-condensation is more favoured because the intermediate product, spiro-indolenine, does not necessitate a rearrangement of the π electron system of the benzene ring which would be the case with an α-condensation. The indolenine can readily isomerise to the indoles in acid conditions and can be oxidised to give oxindole alkaloids (Fig. XVII).

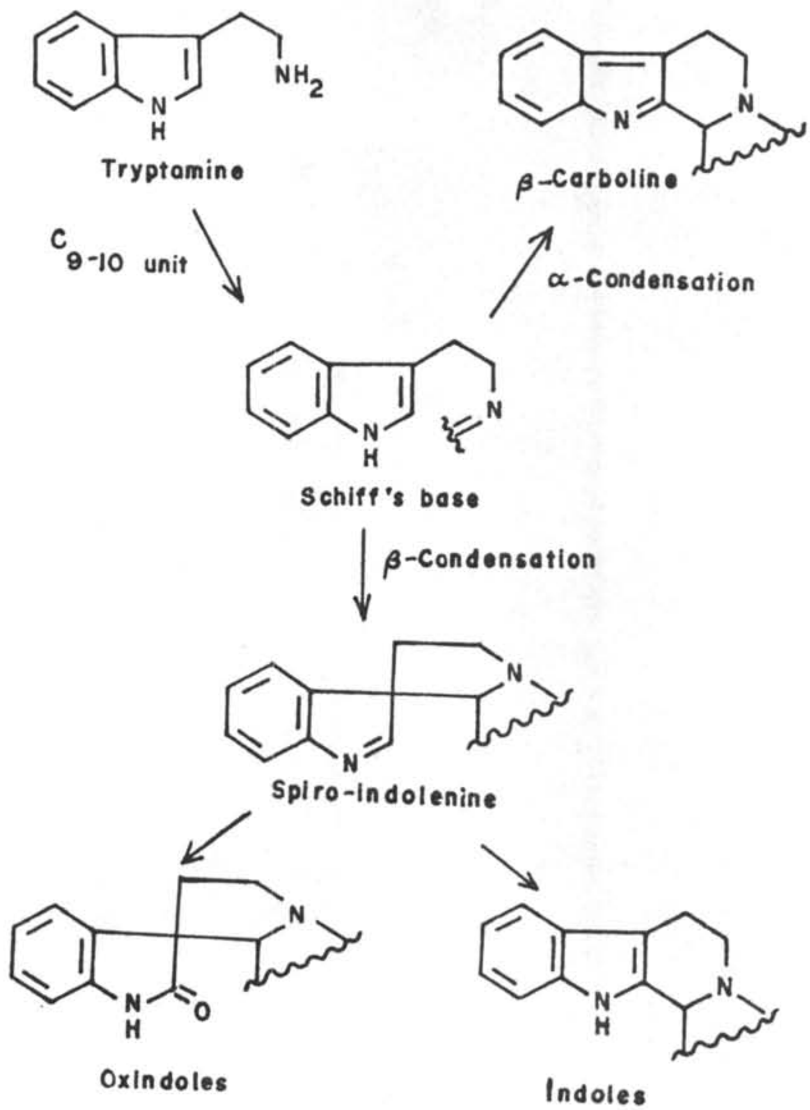
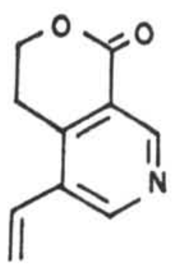


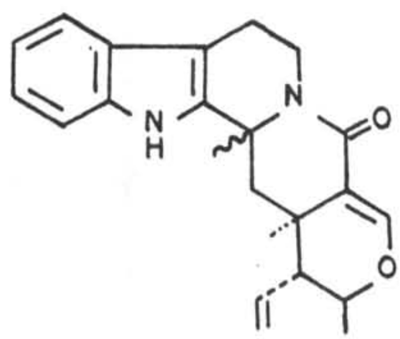
Fig. XVII

6.3 Pyridino-indolo-quinolizidinone alkaloids

Au, Cheung and Sternhell (1973) proposed that angustine and angustoline might possibly be derived from a combination of tryptamine unit and a *seco*-loganin unit closely related to gentianine. Alternatively angustine might possibly be formed by reaction of vincoside or isovincoside - lactam with ammonium hydroxide solution. Angustidine might be formed by the loss of C(21) from the *seco*-loganin portion of a corynanthe precursor.



Gentianine



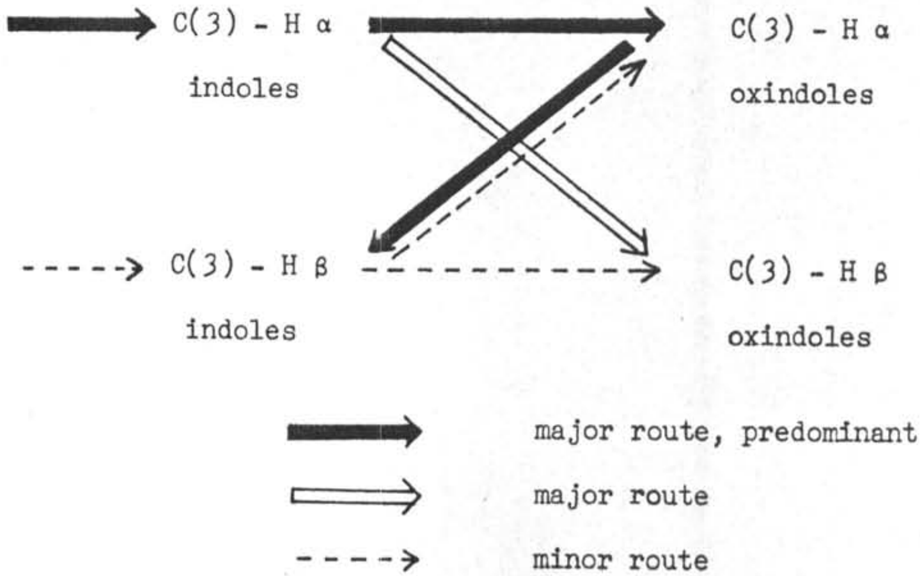
C(3) - H β : Vincoside lactam

C(3) - H α : Isovincoside lactam

6.4 *Mitragyna* alkaloids

Since the last ten years, basing on the progressive knowledge of chemistry of alkaloids reported to be present in several *Mitragyna* species, their chemical transformations and the biogenesis of indole and oxindole alkaloids, Shellard and his co-workers have subsequently been postulating hypotheses, and also their modifications, regarding the biogenesis of *Mitragyna* alkaloids (Shellard, Phillipson and Gupta, 1969b; Shellard and Houghton, 1973b, 1974a). Those hypotheses and their modifications have now been considered inapplicable in the light of the newly discovered evidence. Shellard, Houghton and Resha (1978a) has then recently proposed a modified hypothesis following the evidence reported by Stöckigt and Zenk (1977) that the precursor of indole alkaloids is in fact strictosidine (isovincoside), the C(3) - H α isomer of vincoside, rather than the vincoside itself as previously been considered. Subsequently, Rueffer, Nagakura and Zenk (1978) have also shown that strictosidine is the precursor for the *allo* and *epiallo* alkaloids mitragynine and speciociliatine in *M. speciosa* Korth.

The evidence now available suggests that the major route of biogenesis is via the C(3) - H α indole alkaloids which are then converted primarily to the corresponding C(3) - H α oxindole alkaloids and that these oxindole alkaloids are then converted to the C(3) - H β indole alkaloids. There is probably, in addition, a minor route via the C(3) - H β indole alkaloids which are converted to the corresponding oxindoles since this has been shown to occur by *'in vivo'* studies (Shellard and Houghton, 1974a; Shellard and Lala, 1978). The scheme proposed by Shellard, Houghton and Resha (1978c) may be shown diagrammatically as follows :-



They also proposed a probable biogenetic route of alkaloids in *Mitragyna speciosa* Korth. as shown below (Fig. XVIII) :-

Closed E ring alkaloids (C(9) - H)

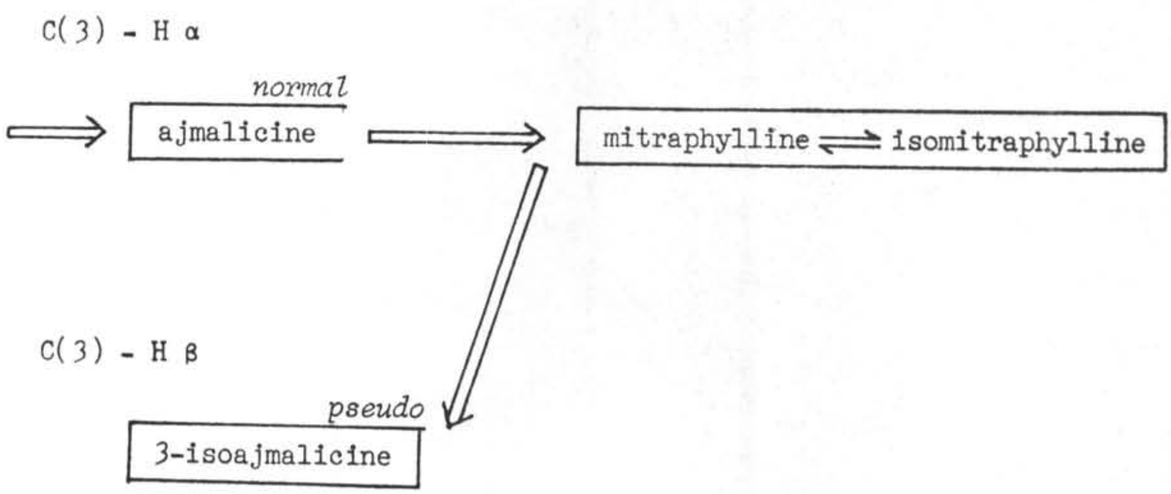


Fig. XVIII Probable biogenetic route of alkaloids in *M. speciosa* Korth. (C(3) - H α precursor).

Fig. XVIII (continued)

Open E ring alkaloids ($C(9) - OCH_3$)