

Biosynthesis and synthesis of biologically active alkaloids of Indian medicinal plants[†]

Dewan S. Bhakuni

Central Drug Research Institute, Lucknow-226 001, India

E-mail : Root@cdriik.Sirnetd.ernet.in Fax : 91-0522-223405/223938

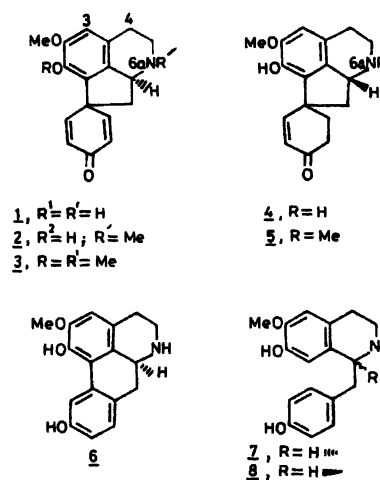
The structure and stereochemistry of biologically active alkaloids isolated from *Croton sparsiflorus*, *Cocculus laurifolius*, *C. pendulus*, *Corydalis meifolia* and *Stephania glabra* were established. Biosynthetic studies were carried out on proaporphine and dihydroproaporphine alkaloids, crotsparine and crotsparinine, and abnormal aporphine alkaloid sparsiflorine; abnormal *Erythrina* alkaloid isococculidine; morphinan-dienone alkaloid sebiferine; quaternary aporphine bases magnoflorine and laurifoline; bisbenzylisoquinoline alkaloids, pendulin, cocsulinin, (±)-hayatin, (*S,R*)-hayatidin, (*R,R*)-isochondrodendrine and (*R,R*)-bebeerine; biphenylbisbenzylisoquinoline alkaloids tiliacrine, tiliacrinine and tiliagine; aporphine-1-benzylisoquinoline alkaloid thalicarpine; aporphine alkaloid glaucine; and lpecac-β-carboline alkaloid tubulosine. Synthesis of (+)-ophicarpinone, crotsparine, sparsiflorine, tetrahydroprotuberberine alkaloids, (±) scoulerine, (±)-tetrahydropalmatine and their bromo derivatives and biogenetic type synthesis of phenanthroindolizidine alkaloid, tylophorine, *seco*-phenanthroindolizidine alkaloid, septicin, antofine and alkaloid C, are presented.

The chemical investigation of plants has been a favourite area of research in India for several decades. Several distinguished chemists in India have worked on plants. Their contributions to the chemistry of natural products have been recognized nationally and internationally. However, most of the work on plants has been of an academic nature with little attempt at biological evaluation of compounds isolated.

At Central Drug Research Institute, Lucknow, we had excellent facilities for biological evaluation. Some years ago, my group at the Institute initiated a programme to study the alkaloidal constituents of the plants which either had a reputation in folklore medicine or the extract of which showed consistent biological activity when evaluated. Detailed chemical investigation of only those plants were undertaken in which the biological activity was concentrated in the alkaloidal fraction of the alcoholic extract in the follow-up studies.

A search for hypotensive agent(s) in the active alkaloidal fraction of the alcoholic extract of the leaves and stems of *Croton sparsiflorus*, a weed that grows in the plains of India, led to the isolation of proaporphine alkaloids crotsparine (1), *N*-methylcrotsparine (2), *N,O*-dimethylcrotsparine (3), dihydroproaporphine alkaloids crotsparinine (4) and *N*-methylcrotsparinine (5) and the known aporphine alkaloid sparsiflorine (6). The structure and stereochemistry of these alkaloids were assigned¹ (Scheme 1).

Crotsparine, *N*-methylcrotsparine and *N*-methylcrotsparinine are hypotensive agents. *N*-Methylcrotsparinine pro-



Scheme 1. Alkaloids of *Croton sparsiflorus*

duces a sharp but short lived fall in blood pressure which could be antagonized by atropine to a large extent suggesting, thus, a cholinergic mechanism of action. *N*-Methylsparsiflorine methiodide is a potent neuromuscular blocking agent. At 5–10 mg/kg (i.v.) dose in cats it produces 100% blockage of neuromuscular transmission for 30–60 min. Glaziovine, an enantiomer of (*S*)-*N*-methylcrotsparine, is a potent tranquilizer devoid of depressant effects.

Crotsparine (1) and crotsparinine (4) had opposite configuration at C-6a while sparsiflorine (6) and crotsparine (1) had the same configuration at the corresponding asymmetric centre. If crotsparine is the biological precursor of crotsparinine, a change in configuration should occur at

[†]Acharya P C Ray Memorial Lecture (2000) delivered under the auspices of Indian Chemical Society on December 26, 2001 at Jodhpur

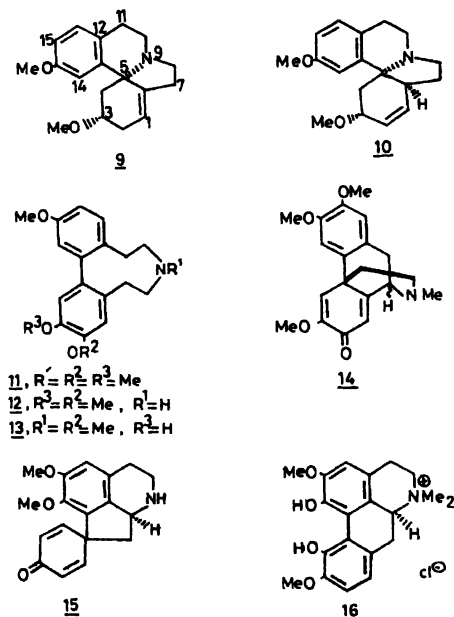
position C-6a of the proaporphine during the course of biotransformation. Alternately crotsparine (1) and crotsparinine (4) could be biosynthesized in plants by independent routes. Tracer experiments conducted by us in *Croton sparsiflorus* confirmed that the latter route is followed in the biosynthesis of these enantiomeric alkaloids².

It is interesting to mention that proaporphine alkaloids such as crotsparine (1) were hypothetical intermediates in the biogenetic scheme proposed by Barton³. It is gratifying that after several years, crotonosine, the first member of this hypothetical group, was isolated from *Croton linearis*⁴ and a number of other bases by us from *C. sparsiflorus*¹. Today there are more than 40 members in this group and most of them exhibit biological activities.

Cocculus laurifolius DC (Menispermaceae), an ever-green shrub, grows in tropical and subtropical regions of the world. A 50% ethanolic extract of the leaves of the plant when subjected to a broad biological screening by us at C.D.R.I., Lucknow, hypotensive and neuromuscular blocking activities were observed. In the follow-up studies, these activities were concentrated in the alkaloidal mixture of the alcoholic extract. A thorough investigation of the active alkaloidal fraction by us led to the isolation of ten new abnormal *Erythrina* alkaloids. Prominent of these are cocculidine (9) and isococculidine (10), and three new dibenz[*d,f*]azonines laurifoline (11), laurifine (12) and laurifinine (13). In addition to these new bases, known morphinan-dienone alkaloid sebiferine (14); two proaporphines stephanine (15) and *N*-methylstephanine; five quaternary aporphines magnoflorine (16), laurifoline chlorides, isocorydine, *O*-methylisocorydine and boldine, methochlorides and 1-benzylisoquinolines, coclaurine, *N*-methylcoclaurine, reticuline and laudanidine and aporphine base, boldine. The structures of the new bases were determined and stereochemistry assigned^{5,6} (Scheme 2).

Isococculidine (9), the major alkaloid of the leaves of *C. laurifolius*, displayed neuromuscular blocking and hypotensive activities. Cocculidine (10) and cocculine exhibited hypotensive activity. This activity was found due to ganglionic blocking action. The quaternary aporphines, *O*-methylisocorydine, isocorydine, boldine methochlorides, exhibited d-tubocurarine-like curarising action on sciatic skeletal muscles. These quaternary bases also induced hypotensive effects in dogs, cats and rabbits. This activity was found due to ganglionic blocking action on various sympathetic and parasympathetic ganglia.

We then turned our attention towards the biosynthetic studies of these biologically active alkaloids. Tracer experiments with plausible precursors showed that (±)-



Scheme 2. Alkaloids of *Cocculus laurifolius*

norprotosinomenine is an efficient precursor of the abnormal *Erythrina* alkaloid isococculidine (9). Parallel experiments with (+)- and (–)-norprotosinomenines showed that bioconversion of 1-benzylisoquinoline precursor is stereospecific, and isococculidine (9) in *C. laurifolius* is biosynthesized from (+)-norprotosinomenine⁷. Tracer experiments were then conducted on dibenz[*d,f*]azonine alkaloid laurifinine (13) and the following sequence was established: tyrosine → norlaudanoline → (*S*)-*N*-norprotosinomenine → laurifinine (13)⁸.

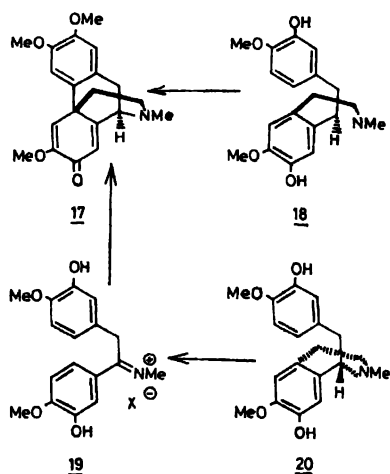
A synthesis of laurifoline (11) from 4,4'-5-trimethoxy-2,2'-bisphenylaldehyde was achieved⁹.

The absolute configuration of morphinan-dienone alkaloid sebiferine (17) isolated by us from *C. laurifolius* was not known. It was then determined as follows. Tritium labeled (±)-, (+)-, and (–)-reticuline were synthesized and then separately oxidized with potassium ferricyanide in a two-phase system. The product, so obtained, in each case was treated with diazomethane to give *O*-Me derivatives. Sebiferine (17) from the mixture was isolated by dilution technique. Sebiferine (17) was obtained only from (±)- and (–)-(*R*)-reticulines. The absolute configuration of sebiferine (17) is therefore, that of (–)-(*R*)-reticuline (18)¹⁰.

Sebiferine (17) could be biosynthesized in *C. laurifolius* from suitably substituted 1-benzyltetrahydroisoquinoline precursors through alternative biosynthetic routes. Feeding experiments demonstrated that (±)-reticuline is an efficient precursor of sebiferine (17). The precursor used, however,

was racemic. The enzyme system which carries out the oxidative coupling step would be expected to be stereospecific, and only one of the enantiomers of reticuline should normally act as a direct substrate. Parallel feeding of (–)-reticuline (**18**) and (+)-reticuline (**20**) demonstrated that (+)-reticuline (**20**) was incorporated almost as efficiently as the (–)-enantiomer (**18**). The evidence established the presence of a highly active oxidation-reduction system in *C. laurifolius*, as had been observed in poppy¹¹. Sobiferine (**17**) was isolated in (–)-form from the bark of *Nemuaron virillardii*¹² and in (±)-form and (–)-form from the roots of *Rhigiocarya racemosa*^{13,14}. The occurrence of the racemic form in the plant was most probably due to the presence of an active oxidation-reduction system.

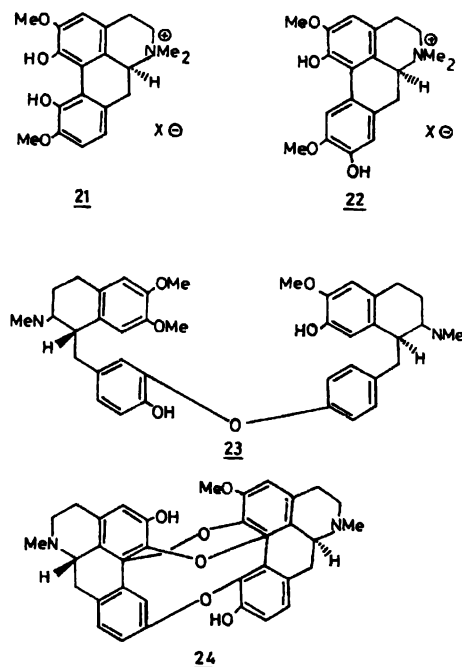
The foregoing results strongly support the following sequence for the biosynthesis of sebiferine (**17**) in *C. laurifolius*¹⁵: nor-reticuline → (+)-reticuline (**20**) ↔ dihydroreticuline (**19**) ↔ (–)-reticuline (**18**) → sebiferine (**17**) (Scheme 3).



Scheme 3. Absolute configuration and biosynthesis of sebiferine (**17**).

Tracer experiments conducted by us in *C. laurifolius* supported the following sequence for the biosynthesis of magnoflorine (**21**) and laurifoline (**22**): tyrosine → norlaudanosoline → (*S*)-reticuline (**18**) → magnoflorine (**21**) and laurifoline¹⁶ (**22**) (Scheme 4).

Search for hypotensive and anticancer principles in the alkaloidal fraction of the 50% alcoholic extracts of the leaves and stems of *Cocculus pendulus* Diels, a shrub which grows in the dry parts of North and Western India, resulted in the isolation of five bisbenzylisoquinoline alkaloids, namely, pendulin, cocsulin, cocsolin, pendulinin and pendin. The structure and stereochemistry of these new bases were assigned¹⁷. Of the isolated bases pendulin (**23**) showed



Scheme 4. Magnoflorine (**21**), laurifoline (**22**), pendulin (**23**) and cocsulinin (**24**).

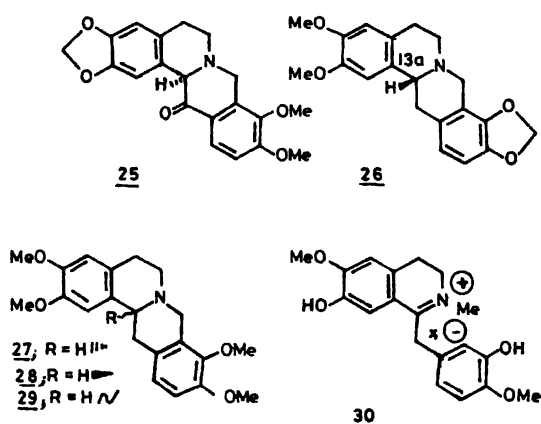
hypotensive activity and cocsulinin (**24**) was found active against cells derived from human carcinoma of the nasopharynx (9 KB).

Tracer experiments conducted by us strongly supported the following sequence for the biosynthesis of cocsulinin (**24**) in *C. laurifolius*¹⁸: norcoclaurine → coclaurine → (+)-(*S*)-*N*-methylcoclaurine → dimerization → (+)-(*S,S*)-*O*-methylcocsulinin → (+)-(*S,S*)-cocsulinin.

(+)-Ophiocarpinone (**25**), a minor alkaloid isolated from the stems and leaves of *C. pendulus*, was assigned by us the structure and stereochemistry as shown in **25**. A synthesis of (±)-ophiocarpinone from berberine was also achieved¹⁹.

(–)-Sinactine and (±)-sinactine had been isolated from several plant species. (+)-Sinactine (**26**), however, was isolated by us for the first time from *Corydalis meifolia* Wall. We determined its absolute configuration by biosynthetic approach. Feeding of (±)-[1-³H, 3-¹⁴C]nor-reticuline and degradation of biosynthetic sinactine established that the regiospecificity is maintained in the bioconversion of 1-benzyltetrahydroisoquinoline precursor into the tetrahydropprotoberberine alkaloid. Further, feeding of doubly labeled precursor demonstrated that the H-atom at the asymmetric center in reticuline is retained in the bioconversion into sinactine. Parallel feedings of (*R*)- (**18**) and (*S*)-reticulines and chemical conversion of (+)-sinactine (**26**) into (*R*)-tetrahydropalmatine established that (+)-sinactine (**26**)

had *R*-configuration at the asymmetric center C-13a²⁰ (Scheme 5).



Scheme 5. Ophiocarpinone (25), (+)-sinactine (26), (-)-tetrahydropalmatine (27), (+)-tetrahydropalmatine (28), didehydroreticuline (30).

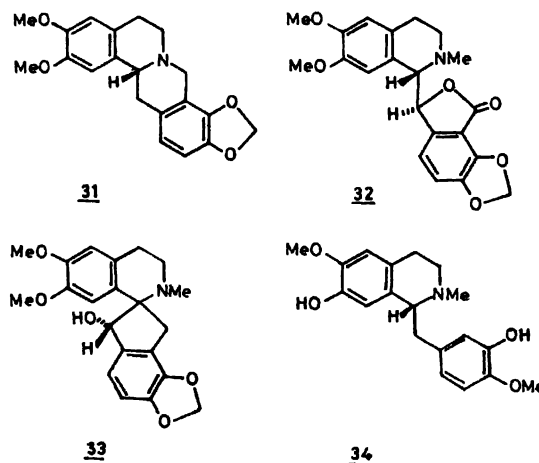
Tetrahydropalmatine is a representative of tetrahydropprotoberberine alkaloids which are important biosynthetic intermediates in the formation of a large number of 1-benzyltetrahydroisoquinoline derived alkaloids. The occurrence of the base in Nature in both the enantiomeric and racemic forms was of interest. We had studied this aspect and demonstrated that (-)-(*S*)-tetrahydropalmatine (27) is stereospecifically biosynthesized from (+)-(*S*)-reticuline²¹. Further, it was shown that (+)-(*R*)-tetrahydropalmatine (28) was stereospecifically biosynthesized from (-)-(*R*)-reticuline. Feeding of [1-³H, 4'-methoxy-¹⁴C]reticuline suggested that reticuline was not converted in the plant into didehydroreticuline (30) and racemisation of optically active forms of tetrahydropalmatine does not take place via dehydrotetrahydropalmatine²².

Corydalis meifolia Wall. (Papaveraceae), a perennial herb, grows at an altitude of 12000–15000 in the Himalayan region¹. The extract of the plant is used by the natives in the treatment of various ailments. Thorough investigation of the alkaloidal fraction of the alcoholic extract of the plant by us resulted in the isolation of known tetrahydropprotoberberines, (+)-sinactine, stylophine, cheilanthifoline, (+)-cavidine, apocavidine, and dehydrocavidine; spirobenzylisoquinolines, yenusomine and yenusomidine; phthalideisoquinoline, corlumine; benzophenanthridine, dihydrosanguinarine and protopine.

(+)-Cavidine (31), protopine, corlumine (32), yenusomine (33) and dehydrocavidine exhibited spasmolytic activity. Tracer experiments conducted by us showed that (+)-cavidine (31), corlumine (32) and yenusomine (33) are stereospecifically biosynthesized from (*R*)-(-)-reticuline

(34)²³ (Scheme 6).

Stephania glabra (Roxb.) Miers, a glabrous climber indigenous to the Lower Himalayas of India, has long been used by the natives in the treatment of various ailments. The plant has been extensively investigated for its alkaloidal constituents. The alkaloids isolated from the rhizome,

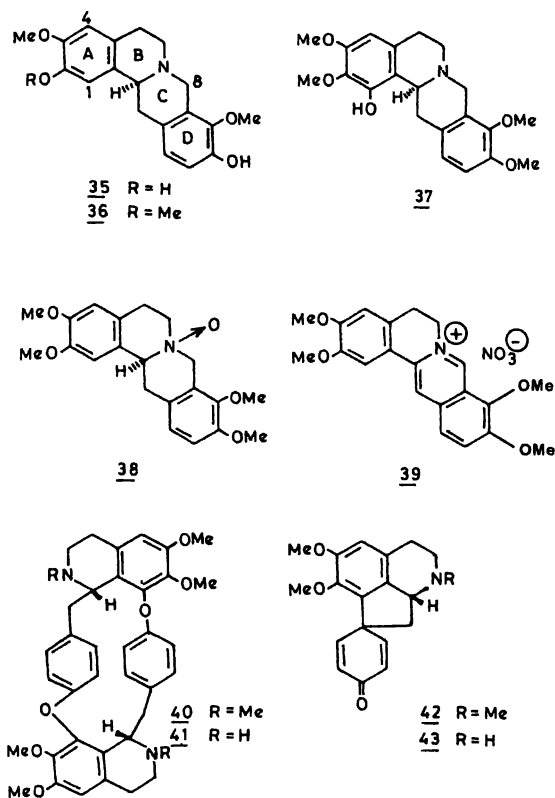


Scheme 6. Alkaloids of *Corydalis meifolia* Wall.

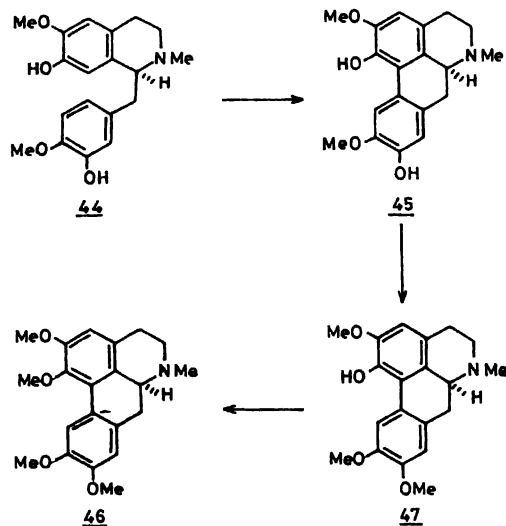
leaves and stems of the plant are tetrahydropprotoberberines, stepholidine (35), corydalmine (36), capaurine (37) and corynoxidine (38); the quaternary protoberberines palmatine (39), dehydrocorydalmine; jatrorrhizine and stepharanine; bisbenzylisoquinolines, cycleanine (40), *N*-desmethyl-cycleanine (41) and the proaporphine alkaloids pronuciferine (42) and stepharine (43) (Scheme 7).

Tracer experiments conducted by us showed that 35, 36, 38 and 39 are stereospecifically biosynthesized from (*S*)-reticuline, whereas 40, 41, 42 and 43 were derived from *N*-methylcocclaurine in young *S. glabra* plants. The quaternary protoberberine alkaloids such as 39 were formed in the plants by dehydrogenation of the corresponding tetrahydropprotoberberine alkaloids²⁴.

Glaucine (46), the antithrombotic, anti-inflammatory and analgesic principle of several plant species, had been isolated both in (+)- and (-)-forms. (-)-Glaucine (46) has been isolated from *Corydalis* tubers. Glaucine could be formed in Nature from 1-benzyltetrahydroisoquinoline precursors, such as reticuline, protosinomenine and orientaline by alternative biosynthetic routes. We conducted tracer experiments using labeled reticuline, protosinomenine, orientaline, laudanosine, isoboldine, boldine, thaliporphine and dicentrine in young *Litsea glutinosa* var. *glabraria* plants. The results provided evidence that (*S*)-reticuline (44) is converted by oxidative coupling into (*S*)-isoboldine (45). Selective *O*-methylation of 45 gives (*S*)-thaliporphine (47) and



Scheme 7. Alkaloids of *Stephania glabra*



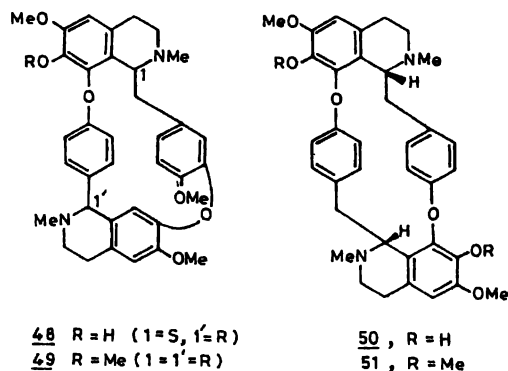
Scheme 8. Biosynthesis of glaucine (46)

finally *O*-methylation of 47 furnishes (*S*)-glaucine (46)²⁵ (Scheme 8).

Cissampelos pariera Linn., a perennial shrub found in the plains of India, was one of the earliest plants investigated at C.D.R.I., Lucknow²⁶. Its roots are used in heart ailments, asthma, dysentery and intestinal tuberculosis. Wa-

ter-soluble fraction of the total alkaloidal mixture possessed neuromuscular blocking activity²⁶. (±)-Hayatin was isolated from this active fraction. Its methiodide showed neuromuscular blocking activity comparable to that of d-tubocurarine chloride²⁸. However, it could not be developed as drug because it produced a transient but at times steep fall in blood pressure in clinical trials.

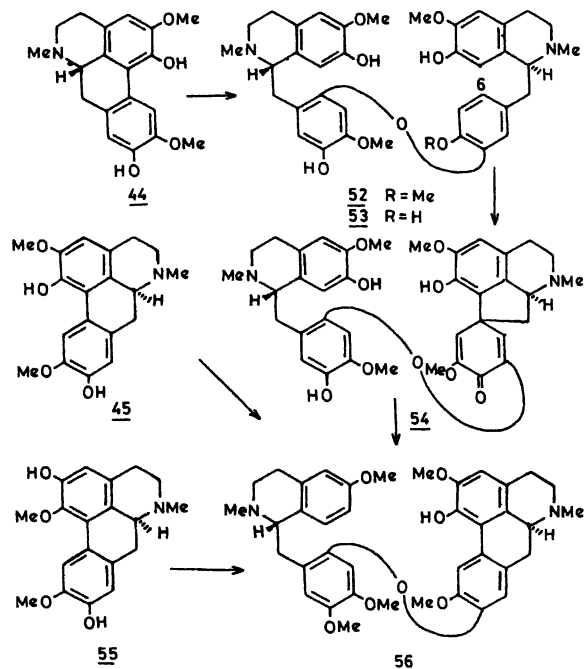
Several other biologically active alkaloids, such as (*S,S*)-4''-*O*-methylbebeerine, (*S,R*)-hayatidin, (*R,R*)-bebeerine, (*R,R*)-isochondrodendrine, (*R,R*)-cycleanine, (*dl*)-hayatin, (*dl*)-hayatinin, cissamparein, insularine and sepeerine had been isolated from the plant. We studied the biosynthesis of some of these alkaloids. Trace experiments showed that (*S,R*)-hayatidin (48) is stereospecifically biosynthesized in young *C. pariera* Linn. plants by intermolecular oxidative coupling of (*S*)- and (*R*)-*N*-methylcoclaurines, whereas (*R,R*)-isochondrodendrine (50) and (*R,R*)-bebeerine (51) are formed in the plants by oxidative dimerization of (*R*)-*N*-methylcoclaurine²⁹ (Scheme 9).



Scheme 9. Alkaloids of *Cissampelos pariera*

Tumor inhibitory base, thalicarpine (56) which also exhibited hypotensive activity, is a representative of aporphine-1-benzylisoquinoline alkaloids. Biogenetically thalicarpine is unique. It is one of the rare dimeric alkaloids which can derive in Nature from two reticuline units. We studied the biosynthesis of thalicarpine and demonstrated specific incorporation of (±)-reticuline into thalicarpine (56) in *Cocculus laurifolius*. The precursor used, however, was racemic. The enzyme system involved in the relevant biotransformation would be expected to be stereospecific. Parallel feeding with (*R*)- and (*S*)-reticuline (44) showed that the configuration at C-1 is maintained in the oxidative dimerization of reticuline into 52 and in subsequent transformation into thalicarpine (56). (*S*)-Reticuline (44) was incorporated about 100 times more efficiently than (*R*)-reticuline into thalicarpine (56). A double-labeling experiment with (±)-[1-³H, 4'-¹⁴CH₃]norreticuline showed that the me-

thyl function of 4'-OMe of a norreticuline unit is lost in the biotransformation into thalicarpine. Feeding experiments also revealed that the plants can take up (*S*)-boldine (**55**) and (*S*)-isoboldine (**45**) to form thalicarpine (**56**). The results thus strongly support the following sequence for the biosynthesis of thalicarpine in *C. laurifolius*³⁰: norreticuline → (*S*)-reticuline (**44**) → (dimerization) → (selective *O*-demethylation) → thalicarpine (**56**) (Scheme 10).

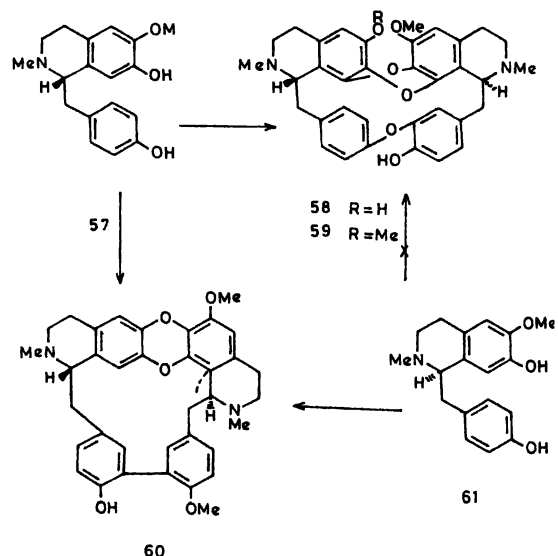


Scheme 10. Biosynthesis of thalicarpine (**56**)

Cocsulinin, the anticancer agent isolated by us from the leaves and stems of *Cocculus pendulus*¹⁷ was assigned the structure and stereochemistry as shown in **58**. We then studied its biosynthesis. Intermolecular oxidative coupling of two *N*-methylcoclaurine (**57**) units could generate first the ether 'bridge' between benzylic portion of the base. Further intermolecular oxidative coupling could then form the two ether 'bridges' in the benzylic half of the base

Tracer experiments demonstrated specific utilization of the ($\pm$)-*N*-methylcoclaurine to form cocsulinin (**58**). Experiments with ($\pm$)-*N*-[¹⁴C]methyl[1-³H]coclaurine showed that the hydrogen atom at asymmetric centre in the precursor was retained in the bioconversion into **58**. Parallel feedings of labeled (+)-(*S*)- and (-)-(*R*)-*N*-methylcoclaurines revealed that the configuration at C-1 is maintained in the biosynthesis of cocsulinin (**58**) from the 1-benzylisoquinoline precursor. A double labeling experiment with ($\pm$)-*N*-methyl[1-³H, 6-*O*-methyl-¹⁴C]coclaurine showed that the methyl function of 6-*O*-Me of an *N*-methylcoclaurine unit was lost in

the biotransformation into **58**. Incorporation of (+)-(*S,S*)-*O*-methylcocsulinin (**59**) into **58** established that de-*O*-methylation is the terminal step in the biosynthesis of cocsulinin (**58**)³¹ (Scheme 11).

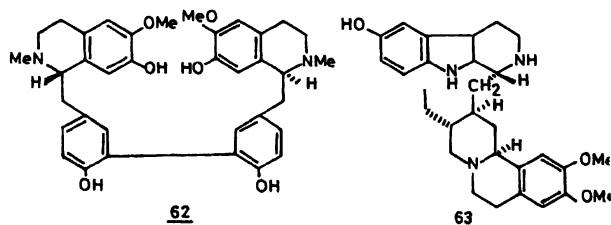


Scheme 11. Biosynthesis of tiliacrine + tiliacrinine and cocsulinin

Govindachari *et al*³² isolated two biphenylbis-benzylisoquinoline alkaloids, namely, tiliacrine and tiliacrinine from *Tiliacora racemosa* and assigned their structures. However, the absolute configuration of both the bases at the asymmetric centre remained undefined because the benzylic halves of these bases were linked through a direct carbon-to-carbon bond, rather than through the common diaryl ether bridge and due to this, sodium ammonia cleavage method was not applicable. Using (*R*)- and (*S*)-*N*-methylcoclaurines in tracer experiments we established that tiliacrine (**60**) had the (*S*)- and (*R*)-configurations at the asymmetric centres C-1 and C-1', respectively, and tiliacrinine had the (*S,S*)-configuration at both the asymmetric centres³³. Tiliacrine (**60**) and tiliacrinine had a 1,4-dioxin bridge in the isoquinoline portions. Double-labeling experiments conducted by us with ($\pm$)-*N*-methyl[1-³H, 6-*O*-methyl-¹⁴C]coclaurine showed that the *O*-methyl function from one of the *N*-methylcoclaurine units was lost in the formation of 1,4-dioxin bridge probably as formaldehyde or its equivalent³⁴.

Isomeric bases nortiliacrinine A and B had been isolated from *Tiliacora* species. The position of *N*-Me function and absolute configuration at the asymmetric centres in these bases remained undefined. Using tracer experiments we established the structure and absolute configuration of these bases.

Tracer experiments conducted by us established that tiliageine (**62**) from *Tiliacora dinklagei* had *S*- and *R*-configurations at the asymmetric centers C and C₁, respectively. Further the experiments demonstrated that **62** is biosynthesized in the plants from (*R*)-*N*-methylcoclaurine (**57**) and (*S*)-*N*-methylcoclaurine (**61**)³⁶ (Scheme 12).



Scheme 12. Tiliageine (**62**) and tubulosine (**63**).

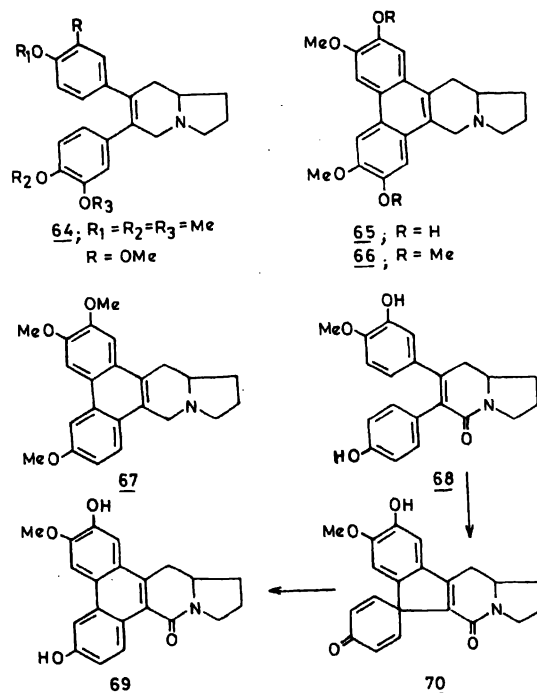
Tubulosine (**63**), an amoebicidal agent, was first isolated from the Argentinian plant *Pogonopus tubulosus*. Subsequently, the base was isolated from the South African plant *Cassinopsis ilicifolia* and by Pakrashi *et al.*³⁷ from *Alangium lamarckii*.

We studied the biosynthesis of tubulosine (**63**) in young *Alangium lamarckii*. Tracer experiments demonstrated specific utilization of desacetylisoepicoside into **63**. Parallel experiment with didemethyldeoxytubulosine and deoxytubulosine provided evidence for the late stages of biosynthesis of **63**. Biosynthetic status of tubulosine (**63**) in *A. lamackii* is : tyrosine → dopamine + secologanin → desacetylisoepicoside → deoxytubulosine → tubulosine (**63**)³⁸.

Phenanthroindolizidine alkaloids tylophorine (**66**), tylophorinine, tylophorinidine and tylocrebrine, and closely related base cryptopleurine from *Tylophora* and *Cryptocarpa* species were known for their wide range of biological activities. 6,7-Diphenylhexahydroindolizidines such as **64** were *seco*-analogs of *Tylophora* alkaloids (Scheme 13). We achieved the synthesis of some of these alkaloids.

6,7-Diphenyl-1,2,3,5,8, 8*a*-hexahydroindolizidines were synthesized by two methods. In one, condensation of substituted 2-phenacylpyrrolidines with substituted phenylacetyl chlorides afforded substituted 2-phenacyl-*N*-phenylacetylpyrrolidines (yields 90–93%) which underwent cyclization with alkali to the corresponding lactams in 70–80% yields. Reduction with LAH-AlCl₃ gave the protected 6,7-diphenylhexahydroindolizidines in 65–72% yields. Acid-catalyzed hydrogenolysis finally afforded the desired phenolic bases³⁹.

We developed a convenient synthesis of septicine (**64**) by which ¹⁴C-label can be introduced at position-5 in the indolizidine system⁴⁰. A biogenetic type synthesis of



Scheme 13. Synthesis of *Tylophora* alkaloids.

tylophorine (**66**) from 6,7-di(3-hydroxy-4-methoxyphenyl)-6,7-dehydroindolizidine (**64**, R₁ = R₂ = Me, R₃ = H and R = OH) was achieved⁴¹. We also synthesized⁴² the phenanthroindolizidine alkaloid-C and tetrahydropyprotoberberines, (±)-scoularine, (±)-coreximine and (±)-tetrahydropalmatine⁴³.

The studies carried out by us showed that the Indian medicinal plants which either have a reputation in folklore medicine or the extracts of plants which exhibit biological activities are good source of biologically active alkaloids. The biosynthetic studies of biologically active alkaloids are fascinating and rewarding.

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