CHAPTER II

HISTORICAL

1. The Chemistry of Genus *Artocarpus*

Chemical constituents isolated from the genus *Artocarpus* were reported as flavonoids, stilbenes and triterpenoids. List of the compounds found in various parts of *Artocarpus* spp. is shown in Table 1.

Table 1 Chemical constituents of *Artocarpus* spp.

Plant and chemical compound	Category	Plant part	Reference
Artocarpus altilis Fosberg			
Amyrin, Alpha :	Triterpene	Fruit	Altman and Zito, 1976
Artocarpin	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpus chalcone I	Flavonoid	Flower	Fujimoto, Agusutein and Made, 1987
Artocarpus flavone KB-1	Flavonoid	Bark	Fujimoto et al, 1990
Artocarpus flavone KB-2	Flavonoid	Bark	Fujimoto et al, 1990
Artomunoxanthentrione	Flavonoid	Root bark	Shieh and Lin, 1992
Artomunoxanthone	Flavonoid	Root bark	Shieh and Lin, 1992
Artomunoxanthotrione epoxide	Flavonoid	Root bark	Lin, Shieh and Jong, 1992
Artonin E	Flavonoid	Bark	Hano et al, 1990
Artonin F	Flavonoid	Bark	Hano et al, 1990
Butyric acid, Gamma-amino	Proteid	Leaf	Durand et al, 1962
Chalcone, 2-Geranyl-2'-3-4-4'-tetrahydroxy :	Flavonoid	Flower	Fujimoto et al, 1988
Chalcone, Dihydro : 2'-3-4-4'-tetrahydroxy-2-geranyl :	Flavonoid	Flower	Koshihara, Fujimoto and Inoue, 1988
Chalcone, Dihydro : 2'-4-4'-trihydroxy-5'-geranyl :	Flavonoid	Flower	Koshihara, Fujimoto and Inoue, 1988
Cudraflavone A	Flavonoid	Root bark	Shieh and Lin, 1992

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Cycloaltilisin	Flavonoid	Stem	Chen, Huang and Ou, 1993
Cycloart-23-ene-3-beta-25-diol	Triterpene	Fruit	Altman and Zito,1976
Cycloart-24-ene-3-beta-ol	Triterpene	Fruit	Altman and Zito,1976
Cycloart-25-ene-3-beta-24-diol	Triterpene	Fruit	Altman and Zito,1976
Cycloartenyl acetate	Triterpene	Bark	Panasasivam and Sultanbawa, 1973
Cycloartenol	Triterpene	Bark	Panasasivam and Sultanbawa, 1973
Cycloartenone	Triterpene	Bark	Panasasivam and Sultanbawa, 1973
Cycloartobiloxanthone	Flavonoid	Bark	Hano et al, 1990
Cycloartocarpin	Flavonoid	Heartwood	Venkataraman, 1972
Cycloartomunin	Flavonoid	Root bark	Lin and Shieh, 1991
Cycloartomunin, Dihydro :	Flavonoid	Root bark	Lin and Shieh, 1991
Cycloartomunoxanthone	Flavonoid	Root bark	Lin and Shieh, 1991
Cycloartomunin, Iso : Dihydro :	Flavonoid	Root bark	Lin and Shieh, 1992
Cyclocommunin	Flavonoid	Root bark	Lin and Shieh, 1992
Cyclocommunol	Flavonoid	Root bark	Lin and Shieh, 1992
Cyclomorusin	Flavonoid	Root bark Stem	Lin and Shieh, 1991 Chen, Huang and Ou, 1993
Cyclomulberrin	Flavonoid	Rootbark Stem	Lin and Shieh, 1992 Chen, Huang and Ou, 1993
Engeletin	Flavonoid	Stem	Chen, Huang and Ou, 1993
Flavanone, 3'-4'-7-trihydroxy-2'-geranyl :	Flavonoid	Flower	Koshihara, Fujimoto and Inoue, 1988
Flavanone, 4'-5-7-trihydroxy-8-geranyl :	Flavonoid	Flower	Koshihara, Fujimoto and Inoue, 1988

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Isocyclomorusin	Flavonoid	Stem	Chen, Huang and Ou, 1993
Isocyclomulberrin	Flavonoid	Stem	Chen, Huang and Ou, 1993
Lupeol acetate	Triterpene	Root bark	Shieh and Lin, 1992
Morin	Flavonoid	Heartwood	Venkataraman, 1972
Morusin	Flavonoid	Bark	Fujimoto *et al*, 1990
Norartocarpetin	Flavonoid	Heartwood	Venkataraman, 1972
Propan-3-one, 1-[8-hydroxy-2-methyl-2-(4-methyl-pent-3-enyl)-chromene]-3-[2-4-dihydroxy-phenyl] :	Oxygen Heterocycle	Flower	Koshihara,Fujimoto and Inoue, 1988
Sitosterol, Beta :	Steroid	Root bark	Shieh and Lin, 1992
Artocarpus chaplasha Roxb.			
Artocarpesin	Flavonoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Artocarpin	Flavonoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Chaplashin	Flavonoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Cycloartenol acetate	Triterpene	Stem bark	Chakravarti, Mahato and Banerjee, 1971
Cycloartenol, Iso : acetate	Triterpene	Stem bark	Chakravarti, Mahato and Banerjee, 1971
Cycloartocarpesin	Flavonoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Cycloartocarpin	Flavonoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Lupeol acetate	Triterpene	Stem bark	Chakravarti, Mahato and Banerjee, 1971
Resorcinol	Benzenoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Resorcylaldehyde, Beta :	Benzenoid	Heartwood	Rao, Rathi and Venkataraman, 1972

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Resveratrol	Benzenoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Resveratrol, Oxy :	Benzenoid	Heartwood	Rao, Rathi and Venkataraman, 1972
Sitosterol, Beta :	Steroid	Stembark	Chakravarti, Mahato and Banerjee, 1971
Artocarpus elasticus Reinw. ex Bl.			
Artocarpin	Flavonoid	Heartwood	Pendse *et al*, 1976
Artocarpin, Nor :	Flavonoid	Heartwood	Pendse *et al*, 1976
Cycloartocarpesin	Flavonoid	Heartwood	Pendse *et al*, 1976
Cycloartocarpin	Flavonoid	Heartwood	Pendse *et al*, 1976
Integrin	Flavonoid	Heartwood	Pendse *et al*, 1976
Sitosterol, Beta :	Steroid	Heartwood	Pendse *et al*, 1976
Artocarpus gomezianus Wall. ex Trec.			
Artocarpesin	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpetin, Nor :	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpin	Flavonoid	Heartwood	Venkataraman, 1972
Cycloartocarpin	Flavonoid	Heartwood	Venkataraman, 1972
Mesoerythritol	Phenolic compound	Heartwood	Venkataraman, 1972
Morin	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpus hirsuta Lamk.			
Agglutinin, Lympho :	Protein	Seed	Arora *et al*, 1987
Artocarpanone	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpesin	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpesin, Dihydro : Oxy :	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpetin	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpetin, Nor :	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpin	Flavonoid	Heartwood	Venkataraman, 1972
Cyanomaclurin	Flavonoid	Heartwood	Venkataraman, 1972
Cycloartocarpesin	Flavonoid	Heartwood	Venkataraman, 1972
Cycloartocarpin	Flavonoid	Heartwood	Venkataraman, 1972

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Morin	Flavonoid	Heartwood	Venkataraman, 1972
Morin, Dihydro	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpus integer (Thunb.) Merr.			
Artocarpanone	Flavonoid	Heartwood	Pendse *et al*, 1976
Artocarpesin	Flavonoid	Heartwood	Pendse *et al*, 1976
Artocarpesin, Dihydro : Oxy :	Flavonoid	Heartwood	Pendse *et al*, 1976
Artocarpetin	Flavonoid	Heartwood	Pendse *et al*, 1976
Artocarpetin, Nor :	Flavonoid	Heartwood	Pendse *et al*, 1976
Artocarpin	Flavonoid	Heartwood	Pendse *et al*, 1976
Artocarpus integra alpha-D-galactose specific lectin	Protein	Seed	Suresh, Appukuttan and Basu, 1982
Artocarpus lectin C	Protein	Seed	Hashim, Gendeh and Jaafar, 1992
Catechin, (DL) :	Flavonoid	Leaf	Yamazaki *et al*, 1987
Chaplashin	Flavonoid	Heartwood	Pendse *et al*, 1976
Cyanomaclurin	Flavonoid	Heartwood	Pendse *et al*, 1976
Cycloartocarpesin	Flavonoid	Heartwood	Pendse *et al*, 1976
Cycloartocarpin	Flavonoid	Heartwood	Pendse *et al*, 1976
Cyclointegrin	Flavonoid	Heartwood	Pendse *et al*, 1976
Cyclointegrin, Iso : Oxy :	Flavonoid	Heartwood	Pendse *et al*, 1976
Integrin	Flavonoid	Heartwood	Pendse *et al*, 1976
Morin	Flavonoid	Heartwood	Pendse *et al*, 1976
Morin, Dihydro :	Flavonoid	Heartwood	Pendse *et al*, 1976
Sitosterol, Beta :	Steroid	Heartwood	Pendse *et al*, 1976
Artocarpus heterophyllus Lamk.			
Agglutinin, Lympho :	Protein	Seed	Arora *et al*, 1987
Artocarpanone	Flavonoid	Heartwood	Parthasarathy *et al*, 1969
Artocarpesin	Flavonoid	Heartwood	Parthasarathy *et al*, 1969
Artocarpesin, Dihydro : Oxy :	Flavonoid	Heartwood	Parthasarathy *et al*, 1969

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Artocarpetin	Flavonoid	Heartwood	Parthasarathy *et al*, 1969
Artocarpetin, Nor :	Flavonoid	Heartwood	Parthasarathy *et al*, 1969
Artocarpin	Flavonoid	Heartwood	Parthasarathy *et al*, 1969
Artocarpus integrifolia lectin	Protein	Seed	1. Namjuntra and Chulavatnatol, 1985 2. Chatterjee, Sarkar and Rao, 1982
Artocarpus lectin CE-A-I	Protein	Seed	Ferreira *et al*, 1992
Artoflavone	Flavonoid	Root	Dayal and Seshadri, 1974
Artonin A	Flavonoid	Root bark	Hano *et al*, 1989
Artonin B	Flavonoid	Root bark	Hano *et al*, 1989
Artonin C	Flavonoid	Root bark	Hano, Aida and Nomura, 1990
Artonin D	Flavonoid	Root bark	Hano, Aida and Nomura, 1990
Artonin I	Flavonoid	Root bark	Hano *et al*, 1992
Artonin J	Flavonoid	Root bark	Aida *et al*, 1993
Artonin K	Flavonoid	Root bark	Aida *et al*, 1993
Artonin L	Flavonoid	Root bark	Aida *et al*, 1993
Aurantiamide acetate	Protein	Seed	Chakraborty and Mandal, 1981
Betulin	Triterpene	Root bark	Lu and Lin, 1994
Betulinic acid	Triterpene	Heartwood	Rao, Varadan and Venkataraman, 1973
		Root	Dayal and Seshadri, 1974
Choline, Acetyl :	Alkaloid-Miscellaneous	Seed	Pereira, Medina and Bustos, 1962

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Cyanomaclurin	Flavonoid	Heartwood	Parthasarathy *et al*, 1969
Cycloartenyl acetate	Triterpene	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenol	Triterpene	Bark	Pavanasasivam and Sultanbawa, 1973
		Latex	Pant and Chaturvedi, 1989
Cycloartenone	Triterpene	Bark	Pavanasasivam and Sultanbawa, 19731
		Root	Dayal and Seshadri, 1974
		Latex	Pant and Chaturvedi, 1989
Cycloartocarpesin	Flavonoid	Heartwood	Parthasarathy *et al*, 1969
Cycloartocarpin	Flavonoid	Heartwood	1. Parthasarathy *et al*, 1969 2. Rao, Varadan and Venkataraman, 1973
Cycloartocarpin A	Flavonoid	Root bark	Lu and Lin,1994
Cycloheterophyllin	Flavonoid	Heartwood	Rao, Varadan and Venkataraman, 1973
		Root bark	Hano *et al*, 1989
Cycloheterophyllin, Iso :	Flavonoid	Bark	Rao, Varadan and Venkataraman, 1973
9,19-Cyclolanost-3-one-24, 25-diol, (24 R) :	Triterpene	Latex	Barik *et al*, 1994
9,19-Cyclolanost-3-one-24, 25-diol, (24 S) :	Triterpene	Latex	Barik *et al*, 1994
Heteroflavanone A	Flavonoid	Root bark	Lu and Lin, 1993
Heteroflavanone B	Flavonoid	Root bark	Lu and Lin, 1993
Heteroflavanone C	Flavonoid	Root bark	Lu and Lin, 1994

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Heterophyllin	Flavonoid	Root bark	Hano *et al*, 1989
Heterophylol	Phenolic compound	Root bark	Lin and Lu, 1993
Jacalin	Protein	Seed	1. Hagiwara *et al*, 1988 2. Ferreira *et al*, 1992
Morin	Flavonoid	Heartwood	1. Mu and Li, 1982 2. Parthasarathy *et al*, 1969
Morin-calcium-chelate	Flavonoid	Heartwood	Mu and Li, 1982
Ricinoleic acid	Lipid	Seed oil	Daulatabad and Mirajkar, 1989
Sitosterol, Beta :	Steroid	Heartwood	Parthasarathy *et al*, 1969
		Root	Dayal and Seshadri, 1974
Tridecyl-docosanoate, 9-Hydroxy :	Lipid	Root bark	Lu and Lin, 1994
Undecyl-docosanoate, 4-Hydroxy :	Lipid	Latex	Pant and Chaturvedi, 1989
Ursolic acid	Triterpene	Root	Dayal and Seshadri, 1974
Artocarpus lakoocha Roxb.			
Amylin acetate	Triterpene	Bark	Kapil and Joshi, 1960
Agglutinin, Lympho :	Protein	Seed	Arora *et al*, 1987
Artocarpin	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpin, Nor :	Flavonoid	Heartwood	Venkataraman, 1972
Artocarpus Lakoocha lectin	Protein	Seed	Chatterjee, Sarker and Rao, 1982
Cycloartenol	Triterpene	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenone	Triterpene	Bark	Pavanasasivam and Sultanbawa, 1973

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Cycloartocarpin	Flavonoid	Heartwood	Venkataraman, 1972
Cycloartocarpin, Nor :	Flavonoid	Heartwood	Venkataraman, 1972
Flavone,5-7-Dihydroxy : 3-O-alpha-L-rhamnoside	Flavonoid (glycoside)	Root bark	Chauhan and Kumari, 1979
Flavone,5-Hydroxy-7-2'-4'-trimethoxy	Flavonoid	Wood	Pavaro and Reutrakul, 1976
Galangin-3-O-beta-d-galactosyl-(1-4)-alpha-l-rhamnoside	Flavonoid (glycoside)	Root bark	Chaunhan, Kumari and Saraswat, 1979
Kaempferol-3-O-beta-d-xylopyranoside	Flavonoid (glycoside)	Root bark	Chaunhan *et al*, 1982
Lupeol	Triterpene	Root bark	Chauhan and Kumari, 1979
Lupeol acetate	Triterpene	Bark	Mahato, Banerjee and Chakravarti, 1966
Quercetin-3-O-alpha-l-rhamnopyranoside	Flavonoid (glycoside)	Rootbark	Chaunhan *et al*, 1982
Resorcinol	Benzenoid	Heartwood	Venkataraman, 1972
Resveratrol	Benzenoid	Heartwood	Venkataraman, 1972
Sitosterol, Beta :	Steroid	Root bark	Chauhan and Kumari, 1979
Stilbene,2-4-3'-5'-tetrahydroxy	Benzenoid	Wood	1. Mongolsuk, Robertson and Towers, 1957 2. Sambhandharaksa and Ratanachai, 1962 3. Ratanachai, 1962
		Heartwood	Ratanachai, 1962
		Root	1. Sambhandharaksa and Ratanachai, 1962 2. Ratanachai, 1962
		Branches	Sambhandharaksa and Ratanachai, 1962

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Artocarpus nobilis Thw.			
Artobilochromene	Flavonoid	Bark	1. Pavanasasivam, Sultanbawa and Mageswaran, 1974 2. Sultanbawa and Surendrakumar, 1989
Artobiloxanthone	Flavonoid	Bark	Sultanbawa and Surendrakumar, 1989
(-)-Artobiloxanthone	Flavonoid	Trunk bark	1. Kuma *et al*, 1977 2. Fukai and Nomura,1993
Artonin E	Flavonoid	Trunk bark	1. Kuma *et al*, 1977 2. Fukai and Nomura,1993
Chromanoartobilochromene A	Flavonoid	Trunk bark	Kuma *et al*, 1977
Chromanoartobilochromene B	Flavonoid	Bark	Pavanasasivam, Sultanbawa and Mageswaran, 1974
Cycloartenyl acetate	Triterpene	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenol	Triterpene	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartenone	Triterpene	Bark	Pavanasasivam and Sultanbawa, 1973
Cycloartobiloxanthone	Flavonoid	Bark	Sultanbawa and Surendrakumar, 1989
Furanoartobilochromene A	Flavonoid	Bark	Pavanasasivam, Sultanbawa and Mageswaran, 1974

Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Furanoartobilochromene B-1	Flavonoid	Bark	Pavanasasivam, Sultanbawa and Mageswaran, 1974
Furanoartobilochromene B-2	Flavonoid	Bark	Pavanasasivam, Sultanbawa and Mageswaran, 1974
Furanoartobilochromene B-1 Dihydro : (-) :	Flavonoid	Trunkbark	Kuma *et al*, 1977
Furanoartobilochromene B-2 Dihydro :	Flavonoid	Trunkbark	Kuma *et al*, 1977
Morusin, Dihydro : Oxy :	Flavonoid	Trunkbark	1. Kuma *et al*, 1977 2. Fukai and Nomura, 1993
Artocarpus pithecogalla C.Y. Wu.			
Morin	Flavonoid	Heartwood	Mu and Li, 1982
Morin-calcium-chelate	Flavonoid	Heartwood	Mu and Li, 1982
Artocarpus rigida Blume.			
Artobiloxanthone	Flavonoid	Bark	Hano, Inami and Nomura, 1990
Artonin E	Flavonoid	Bark	Hano, Inami and Nomura, 1990
Artonin G	Flavonoid	Bark	Hano, Inami and Nomura, 1990
Artonin H	Flavonoid	Bark	Hano, Inami and Nomura, 1990
Artonin M	Flavonoid	Bark	Hano, Inami and Nomura, 1993
Artonin N	Flavonoid	Bark	Hano, Inami and Nomura, 1993
Artonin O	Flavonoid	Bark	Hano, Inami and Nomura, 1993
Artonin P	Flavonoid	Bark	Hano, Inami and Nomura, 1993

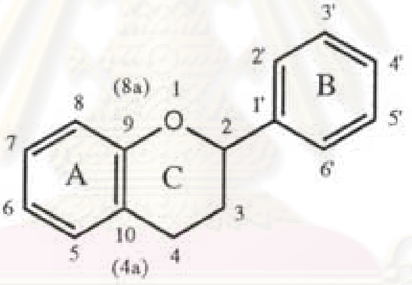
Table 1 (Continued)

Plant and chemical compound	Category	Plant part	Reference
Cycloartobiloxanthone	Flavonoid	Bark	Hano, Inami and Nomura, 1990

2. Flavonoids of *Artocarpus* species

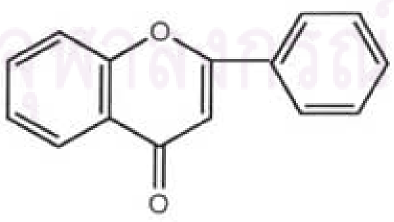
2.1 Introduction to flavonoids

Flavonoids constitute one of the largest groups of naturally occuring phenols. In plants, flavonoid aglycones (i.e. flavonoids without attached sugars) occur in a variety of structural forms. All contain fifteen carbon atoms in their basic nucleus and these are arranged in a C_6-C_3-C_6 configuration, that is two aromatic rings linked by a three carbon unit which may or may not form a third ring. For convenience the rings are labelled A, B and C and individual carbon atoms are referred to by a numbering system which utilized ordinary numerals for the A- and C-rings and "primed" numevals for the B-ring (Markham, 1982).



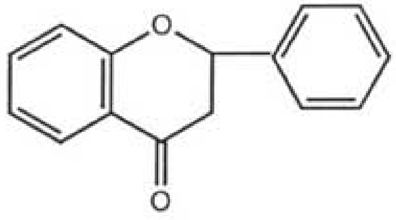
Flavonoid Nucleus

The variation in the state of oxidation of the connecting C_3 moiety determines the properties and class of each such compound. The classes are shown below (Ikan, 1991).

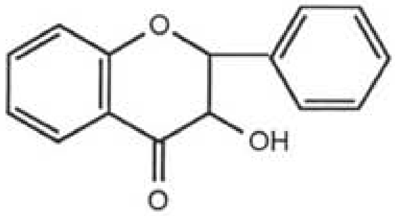


Flavone

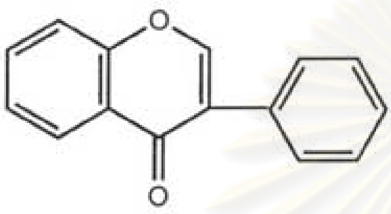
Flavonol



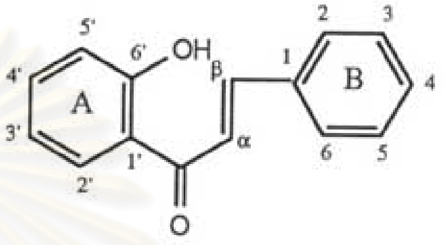
Flavanone



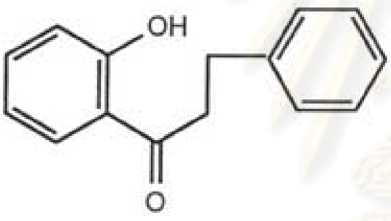
Flavanonol



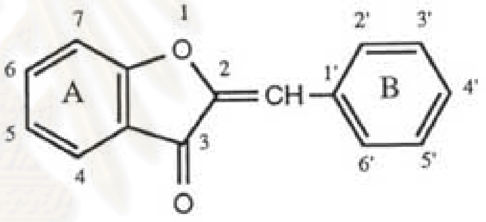
Isoflavone



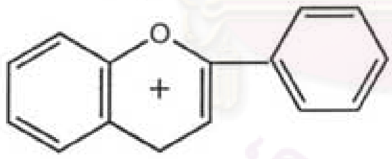
Chalcone



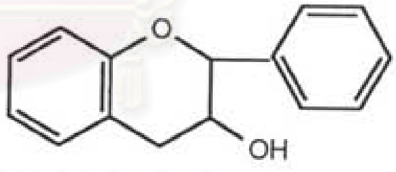
Dihydrochalcone



Aurone



Anthocyanidin



Flavan-3-ol
(Catechin)

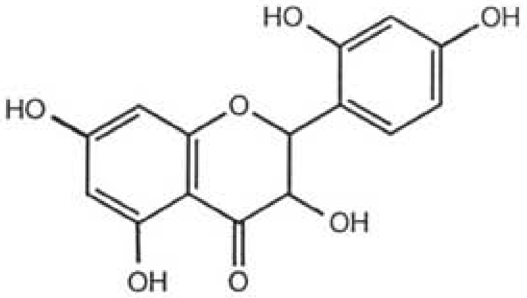
Flavan-3,4-diol
(Leucoanthocyanidin)

Chalcones, dihydrochalcones and aurones are not strictly flavonoids but their close relationship, both chemically and biosynthetically, makes it sensible to include them in the flavonoid grouping. However, care must be taken over the numbering of these molecules which is different from that of the flavonoids. The chalcone numbering is particularly confusing whereas the aurone change in merely a consequence of the contraction of the heterocyclic ring (Goodwin and Mercer, 1983).

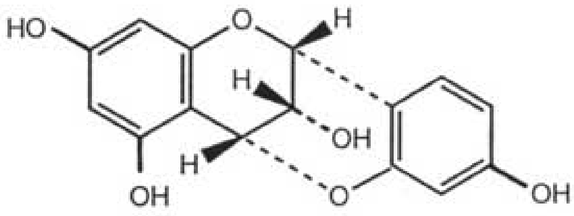
Flavonoid compounds and the related coumarins usually occur in plants as glycosides in which one or more of the phenolic hydroxyl groups are combined with sugar residues. The hydroxyl groups are nearly always found in positions 5 and 7 in ring A, while ring B commonly carries hydroxyl or alkoxyl groups at the 4' position, or at both 3'- and 4'-positions. Glycoside of flavonoid compounds may bear the sugar on any of the available hydroxyl groups (Ikan, 1991).

2.2 Hydroxyl Derivative Flavonoids

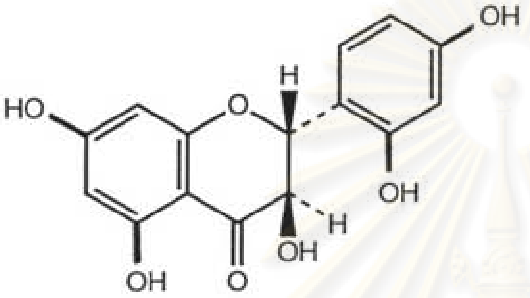
They are flavonoids with the common features of hydroxyls in the 5,7,2',4'-positions. From the heartwood of *Artocarpus heterophyllus*, Perkin and Cope (1895) isolated morin (5,7,2',4'-tetrahydroxyflavonol) and cyanomaclurin. Perkin gave cyanomaclurin its name because of the intense blue color it gave with aqueous alkali. Morin is well known as a reagent for aluminium, based on the brillient bluish green fluorescence produced by the addition of an aluminium salt to a solution of morin in ethanol or water. Dihydromorin, which occurs in the some heartwood of some *Artocarpus* and *Morus* species, can be converted both to morin and to cyanomaclurin, although the formation of the latter is indicated only by the characteristic color reaction. Artocarpanone, norartocarpetin and artocarpetin have been isolated from this wood. The norartocarpetin structure was once assigned erroneously to 'lotoflavin' occuring as a cyanogenetic glycoside in *Lotus arabicus* Linn.; 5,7,2',4'-tetrahydroxyflavone was synthesised in 1926 by Robinson and Venkataraman. 'Lotoflavin' was later shown to be quercetin contaminated with kaempferol (Venkataraman, 1972).



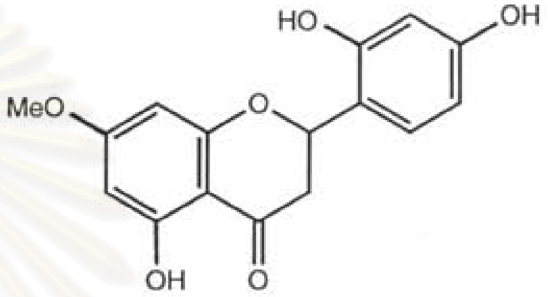
Morin



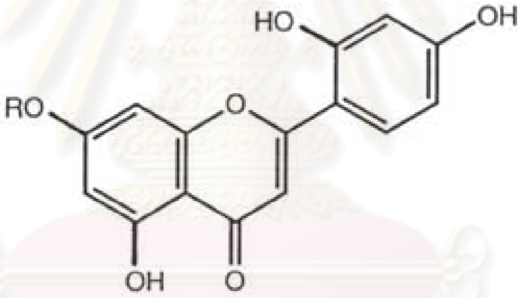
Cyanomaclurin



Dihydromorin



Artocarpanone



Norartocarpetin; R=H
Artocarpetin; R=Me

2.3 Isoprene Substituted Flavones and Flavanones

The occurrence of flavones with C_5, OH-C_5 and C_{10} side chains is still almost completely restricted to the Moraceae. However, in addition to the one solitary earlier example of 8-prenyl-luteolin from *Xanthium* (Asteraceae), two more 8-prenylated flavones have now been found in *Tephrosia* (Leguminosae) (Wollenweber, 1982).

Artocarpus flavones and flavanones carry isoprenoid substitutents as C-prenyl or modified groups in the 6-, 3,6- or 3,6,8 positions (Venkataraman, 1972). Simple C_5 and C_{10} side chains occur as well as additional pyran and furan (or dihydrofuran) rings. The terms pyranoflavonoid and furanoflavonoid have come into use in recent year. If the pyran or furan ring jointly with the aromatic ring to which they are linked form a benzochromene or a furanochromene system, these flavonoids can also be called chromenoflavonoids. This term cannot be used for those in which annulation takes place from C-6' to C-3 (Wollenweber, 1982).

2.3.1 Flavones and Flavanone with C_5, OH-C_5 and C_{10} side chains

Examples of flavones and flavanone with simple C_5 and C_{10} side chains are shown in Table 2.

Table 2 Flavones and flavanone with simple C_5 and C_{10} side chains

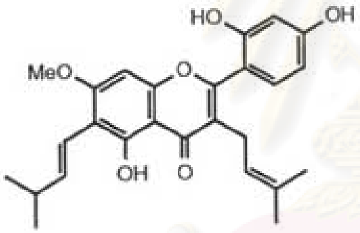
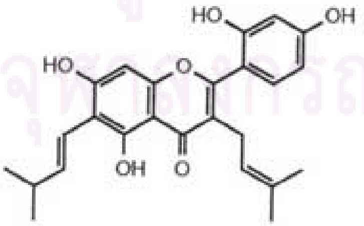
Compound	Source	Reference
Artocarpin  	*A. altilis* *A. chaplasha* *A. elasticus* *A. gomezianus* *A. hirsuta* *A. integer* *A. heterophyllus* *A. lakoocha*	Venkataraman, 1972 Rao, Rathi and Venkataraman, 1972 Pendse *et al*, 1976 Venkataraman, 1972 Venkataraman, 1972 Pendse *et al*, 1976 Parthasarathy *et al*, 1976 Venkataraman, 1972
Norartocarpin  	*A. elasticus* *A. gomezianus* *A. lakoocha*	Pendse *et al*, 1976 Venkataraman, 1972 Venkataraman, 1972

Table 2 (Continued)

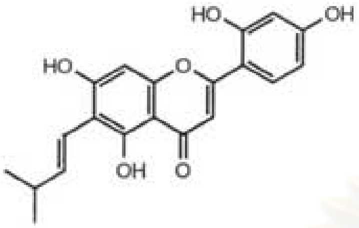
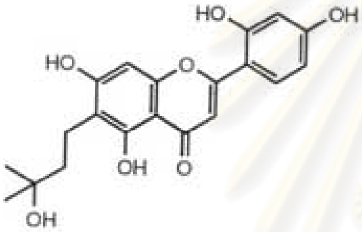
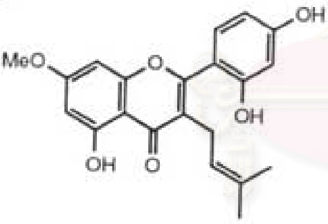
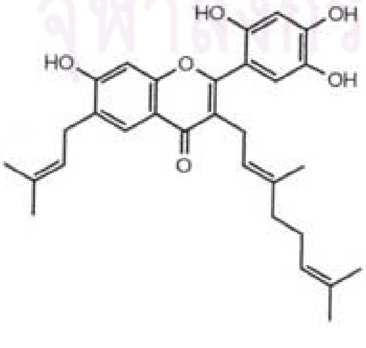
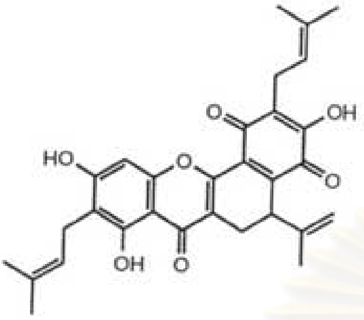
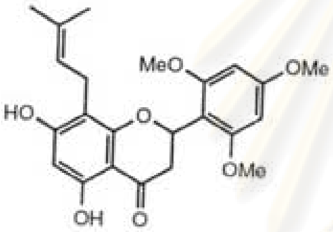
Compound	Source	Reference
Artocarpesin 	*A. chaplasha* *A. gomezianus* *A. hirsuta* *A. integer* *A. heterophyllus*	Rao, Rathi and Venkataraman, 1972 Venkataraman, 1972 Venkataraman, 1972 Pendse *et al*, 1976 Parthasarathy *et al*, 1969
Oxydihydroartocarpesin 	*A. integer* *A. heterophyllus*	Pendse *et al*, 1976 Parthasarathy *et al*, 1969
Integrin 	*A. elasticus* *A. integer*	Pendse *et al*, 1976 Pendse *et al*, 1976
Artonin H 	*A. rigida*	Hano, Inami and Nomura, 1990

Table 2 (Continued)

Compound	Source	Reference
Artonin O 	*A. rigida*	Hano, Inami and Nomura, 1993
Heteroflavanone C 	*A. heterophyllus*	Lu and Lin, 1994

2.3.2 Pyranoflavones and Pyranoflavanones

The first flavone with an additional pyran ring D is cycloartocarpin. Flavandiol derivatives with an isomeric ring system are peltogynol in the heartwood of *Peltogyne porphyrocardia* and mopanol in *Colophospermum mopane*. It has been suggested that peltogynol could arise biogenetically by condensation of formaldehyde (or its equivalent) with the corresponding flavan-3,4-diol (Venkataraman, 1972).

Examples of Pyranoflavones and Pyranoflavanones are shown in Table 3.

Table 3 Pyranoflavones and Pyranoflavanones

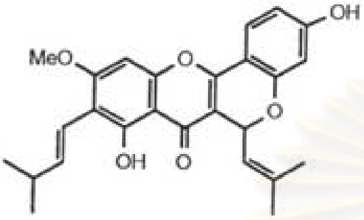
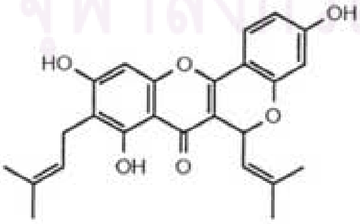
Compound	Source	Reference
Cycloartocarpin  	*A. altilis* *A. chaplasha* *A. elasticus* *A. gomezianus* *A. hirsuta* *A. integer* *A. heterophyllus* *A. lakoocha*	Venkataraman, 1972 Rao, Rathi and Venkataraman, 1972 Pendse *et al*, 1976 Venkataraman, 1972 Venkataraman, 1972 Pendse *et al*, 1976 Parthasarathy *et al*, 1969 Venkataraman, 1972
Cyclocommunol  	*A. altilis*	Lin and Shieh, 1992
Cyclocommunin  	*A. altilis*	Lin and Shieh, 1992

Table 3 (Continued)

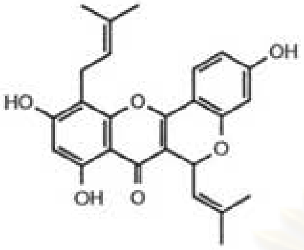
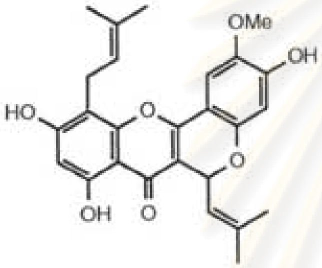
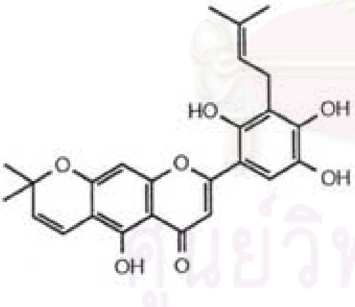
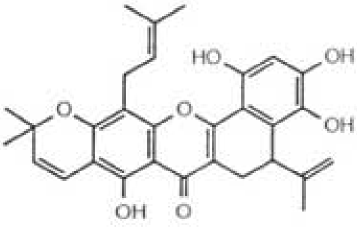
Compound	Source	Reference
Cyclomulberrin 	*A. altilis*	1. Lin and Shieh, 1992 2. Chen, Huang and Ou, 1993
Dihydroisocycloartomunin 	*A. altilis*	Lin and Shieh, 1992
Artobilochromene 	*A. nobilis* *A. rigida*	Sultanbawa and Surendrakumar, 1989 Hano, Inami and Nomura, 1990
Artonin B 	*A. heterophyllus*	Hano *et al*, 1989

Table 3 (Continued)

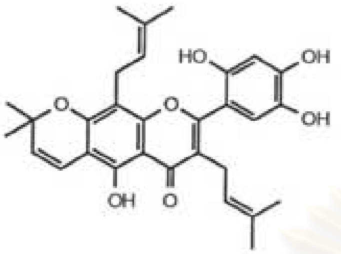
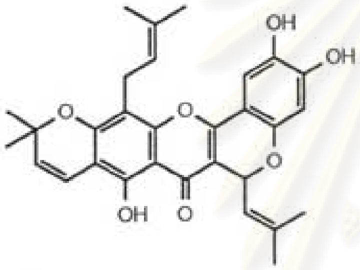
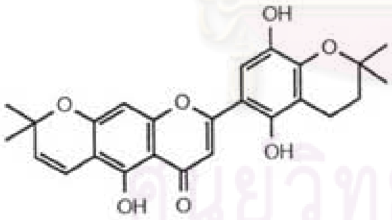
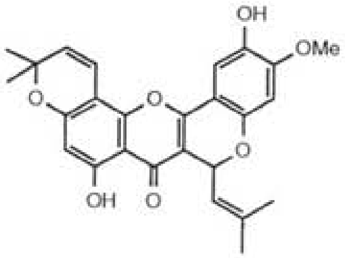
Compound	Source	Reference
Heterophyllin 	*A. heterophyllus*	Hano *et al*, 1989
Cycloheterophyllin 	*A. heterophyllus*	1. Rao, Varadan and Venkataraman, 1973 2. Hano *et al*, 1989
Chromanoartobilochromene-b 	*A. nobilis*	Pavanasasivam, Sultanbawa and Mageswaran, 1974
Cycloartomunin 	*A. altilis*	Lin and Shieh, 1991

Table 3 (Continued)

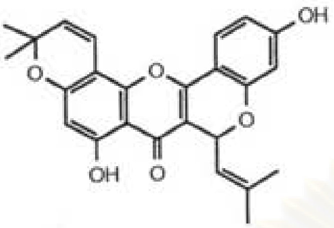
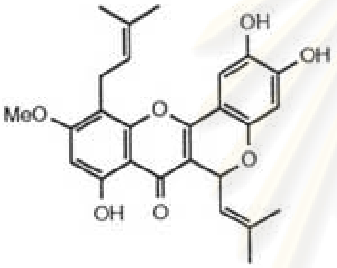
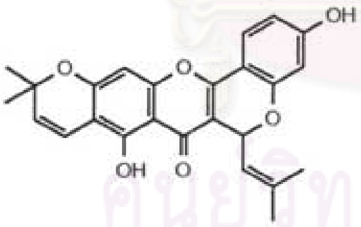
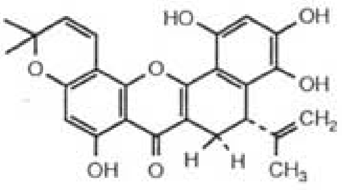
Compound	Source	Reference
Cyclomorusin 	*A. altilis*	1. Lin and Shieh, 1991 2. Chen, Huang and Ou, 1993
Dihydrocycloartomunin 	*A. altilis*	Lin and Shieh, 1991
Isocyclomorusin 	*A. altilis*	Chen, Huang and Ou, 1993
Artocarpus flavone KB-1 	*A. altilis*	Fujimoto *et al*, 1990

Table 3 (Continued)

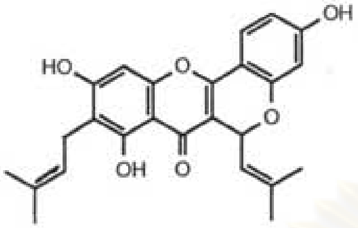
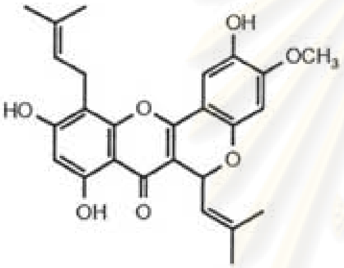
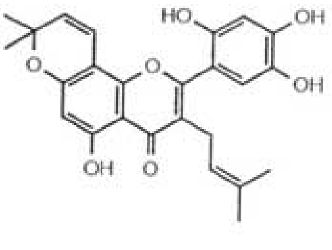
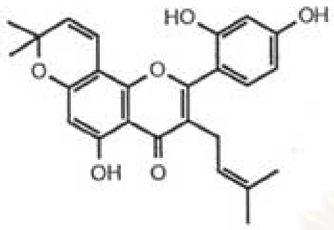
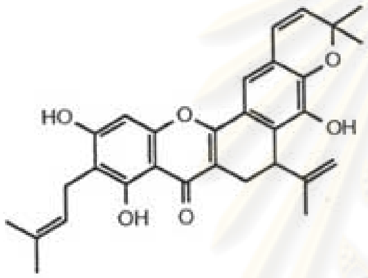
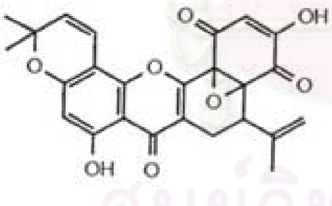
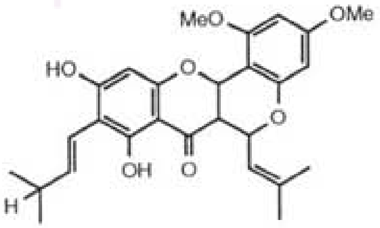
Compound	Source	Reference
Isocyclomulberrin 	*A. altilis*	Chen, Huang and Ou, 1993
Cycloaltilicin 	*A. altilis*	Chen, Huang and Ou, 1993
Artocarpus flavone KB-2 	*A. altilis*	Fujimoto *et al*, 1990
Artonin E 	*A. altilis* *A. nobilis* *A. rigida*	Hano *et al*, 1990 1. Kuma *et al*, 1977 2. Fukai and Nomara, 1993 Hano, Inami and Nomura, 1990

Table 3 (Continued)

Compound	Source	Reference
Morusin 	*A. altilis*	Fujimoto *et al*, 1990
Artonin N 	*A. rigida*	Hano, Inami and Nomura, 1990
Artonin P 	*A. rigida*	Hano, Inami and Nomura, 1993
Cycloartocarpin A 	*A. heterophyllus*	Lu and Lin, 1994

2.3.3 Furanoflavones

Examples of furanoflavones are shown in Table 4

Table 4 Furanoflavones

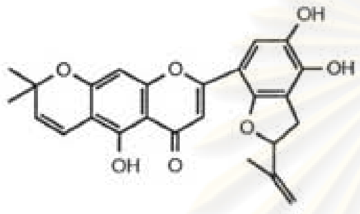
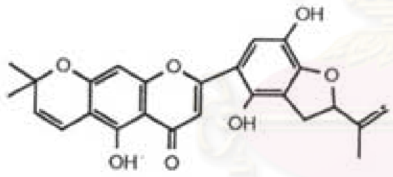
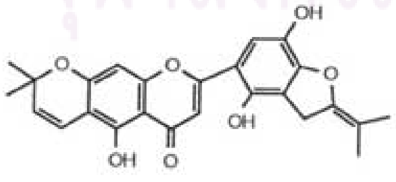
Compound	Source	Reference
Furanoartobilochromene-a 	*A. nobilis*	Panasasivam, Sultanbawa and Mageswaran, 1974
Furanoartobilochromene-b$_1$ 	*A. nobilis*	Panasasivam, Sultanbawa and Mageswaran, 1974
Furanoartobilochromene-b$_2$ 	*A. nobilis*	Panasasivam, Sultanbawa and Mageswaran, 1974

Table 4 (Continued)

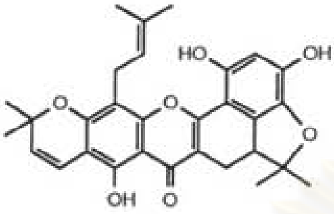
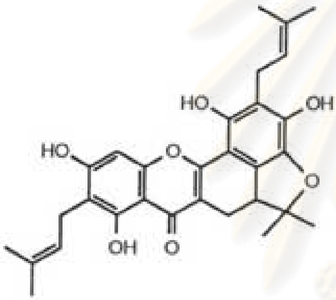
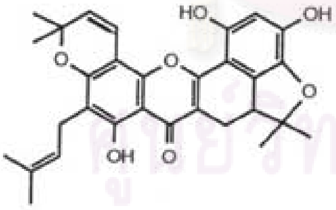
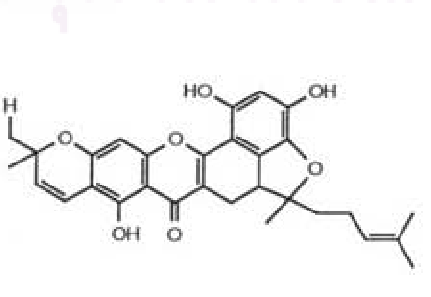
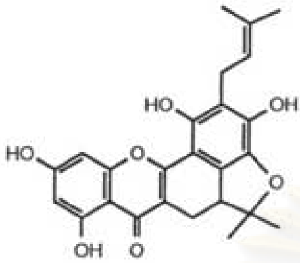
Compound	Source	Reference
Artonin A 	*A. heterophyllus*	Hano *et al*, 1989
Artonin G 	*A. rigida*	Hano, Inami and Nomura, 1990
Artonin F 	*A. altilis*	Hano *et al*, 1990
Artonin M 	*A. rigida*	Hano, Inami and Nomura, 1993

Table 4 (Continued)

Compound	Source	Reference
Artonin J 	*A. heterophyllus*	Aida *et al*, 1993
Artonin K 	*A. heterophyllus*	Aida *et al*, 1993
Artonin L 	*A. heterophyllus*	Aida *et al*, 1993

2.3.4 Flavones with oxepine and oxocin ring

Cyclointegrin is the first natural flavone with an oxocin ring system and is also the first natural product of this type. A 2H-3,4-dihydrooxocin ring system is formed by cyclization of a prenyl group in the 3-position with the 2'-hydroxyl (Pendse et al, 1976).

Chaplashin , the first flavone with oxepine ring was isolated form *A. chaplasha* (Rao, Rathi and Venkataraman, 1972). Flavones with oxepine and oxocin ring of *Artocarpus* species are shown in Table 5.

Table 5 Flavones with oxepine and oxocin ring.

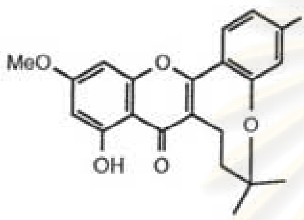
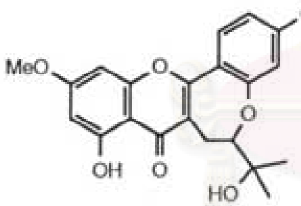
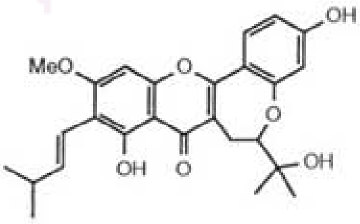
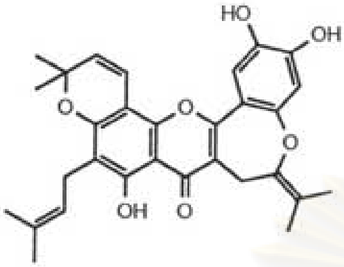
Compound	Source	Reference
Cyclointegrin  	*A. integer*	Pendse *et al*, 1976
Oxyisocyclointegrin  	*A. integer*	Pendse *et al*, 1976
Chaplashin  	*A. chaplasha*	Rao, Rathi and Venkataraman, 1972

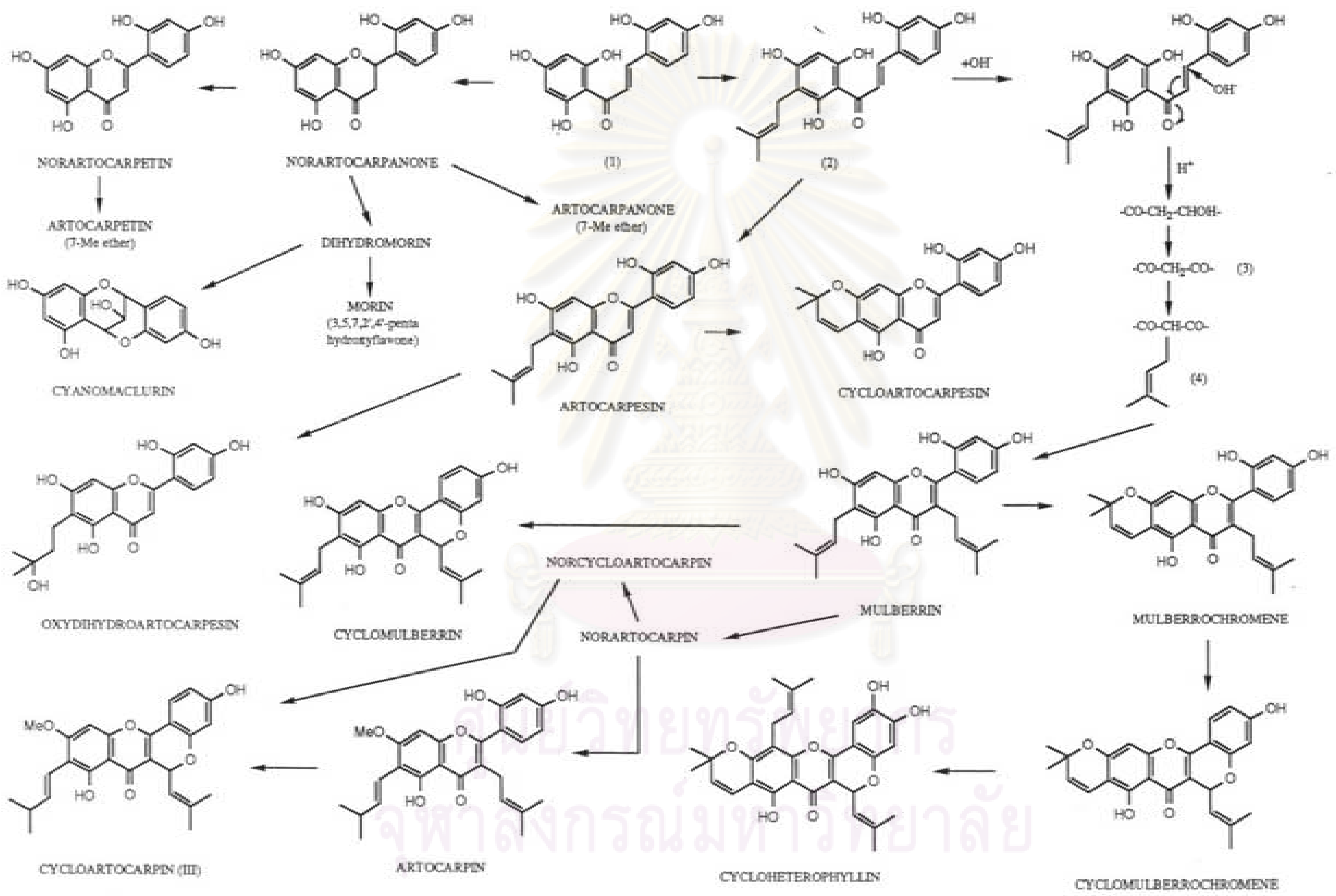
Table 5 (Continued)

Compound	Source	Reference
Isocycloheterophyllin 	*A. heterophyllus*	Rao, Varadan and Venkataraman, 1973

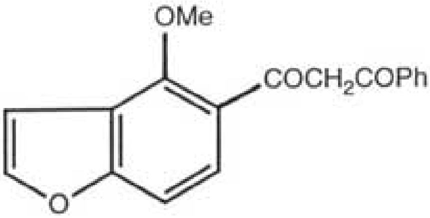
2.4 Biogenetic Aspects of *Artocarpus* Pigments

The biogenesis of *Artocarpus* pigments is of special interest because of their unique structural features : the β-resorcylic acid orientation of hydroxyl groups in the B-ring in all the compounds and the C_5 substituent in the 3-position in artocarpin, cycloartocarpin and cycloheterophyllin. All the flavonoids isolated so far from *A. heterophyllus* fit into a biosynthetic scheme (Scheme 1) in which the hydroxylation pattern of both the A and B rings is fixed at the chalcone stage : an exception is cycloheterophyllin (Rao *et al*, 1971).

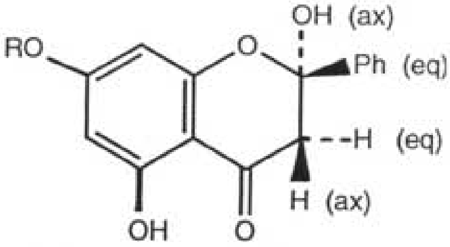
Ring-A in the chalcone (1) may react with, γ,γ-dimethylallyl pyrophosphate at this or a later stage, but the introduction of the second γ,γ-dimethylallyl group must be effected before the cyclization of (1) to a flavone. (Rao et al., 1971) In the biogenesis of artocarpin, the highly nucleophilic phloroglucinol nucleus in (1) is probably first attacked by dimethylallyl pyrophosphate to form (2) as shown by the presence in the heartwood of artocarpesin and its derivative, cycloartocarpesin and oxydihydroartocarpesin. The chalcone (2) then undergoes the indicated reactions (or others which are equally plausible) to form the 1,3-diketone (3); the olefinic bond shift at some stage to conjugate with the A-ring of the flavone. The reactive methylene group now provides a suitable site for attack by a second dimethylallyl pyrophosphate group, leading to (4) and ultimately to a flavone with a 3-prenyl group-a type unknown when the structure of artocarpin was determined. At least one dibenzoylmethane is known as a plant product : pongamol in seeds of *Pongamia glabra* Vent.; two others (5), occuring in *Malus* leaf and *Populus nigra* buds, are intramolecular hemiketals of dibenzoylmethane (Venkataraman, 1975).



Scheme 1 Biosynthesis of the flavonoids isolated from *A. heterophyllus*



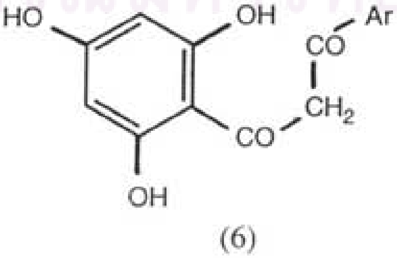
Pongamol



(5) R=Glucosyl or Me

In the biosynthesis of cycloheterophyllin the attack of the third γ,γ-dimethylallyl group may occur at any stage (Rao et al, 1971). But the additional hydroxylation in the B-ring probably represents the final step. Although a number of isoflavones having 2',4',5'-pattern of oxygenation are known, few such flavones are reported (e.g. oxyayanin-A, cycloheterophyllin and isocycloheterophyllin, of which the latter two were isolated from the bark of *Artocarpus heterophyllus* Lam.). The other flavonoids isolated thus far from *Artocarpus* have the 2',4'-pattern of oxygenation; it is likely that the additional hydroxylation on ring B occurs during the final step of the biosynthesis (Kumar *et al*, 1977).

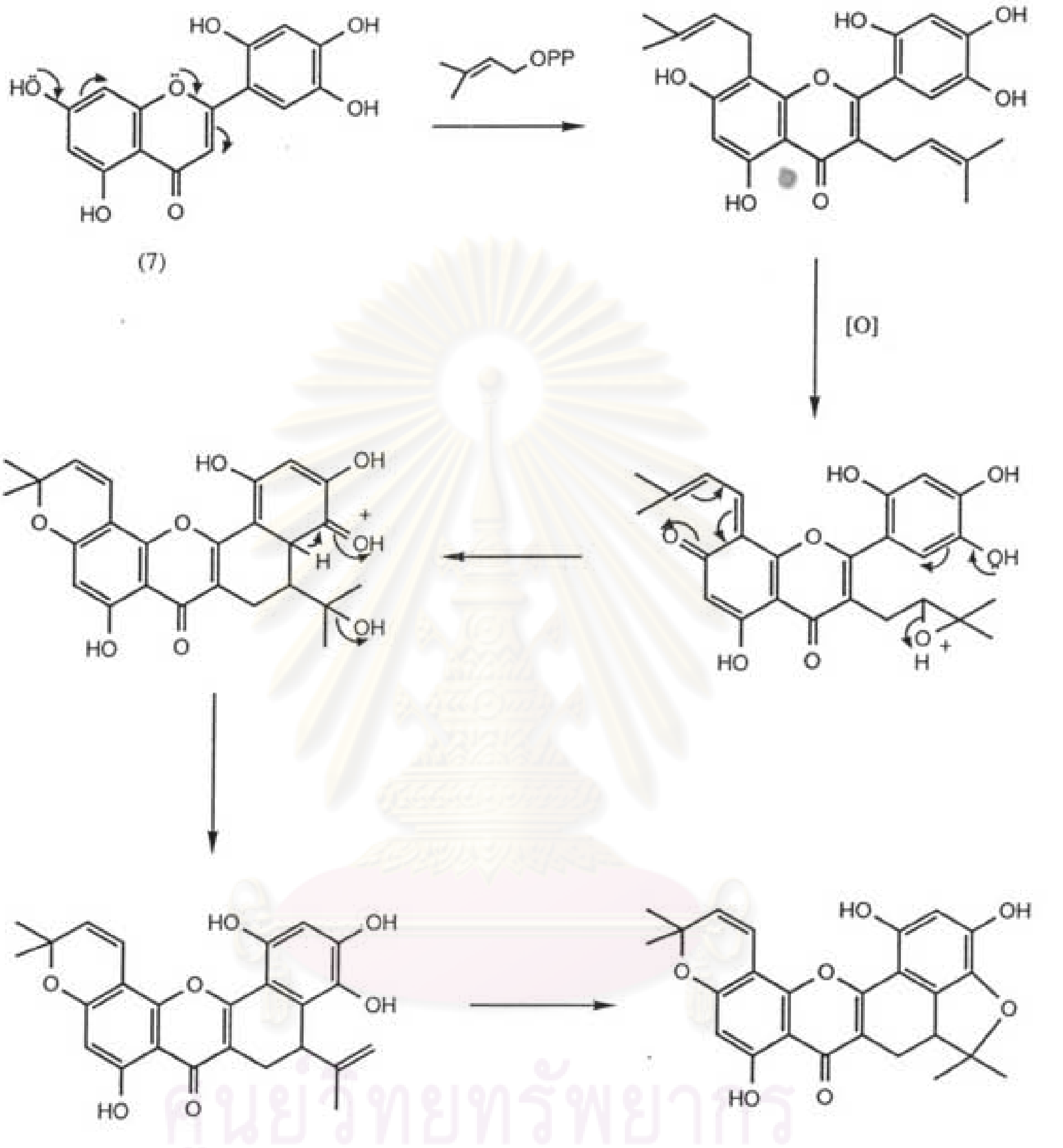
The biogenesis of integrin and the two related flavones, cyclointegrin and oxyisocyclointegrin, is of interest because they are the first natural flavones in which the A-ring is derived from phloroglucinol and C-prenylation occurs in the 3-position, and not on one of the strongly nucleophilic carbon atoms of the phloroglucinol moiety. If a dibenzoylmethane (6) is the intermediate in the biosynthesis of the *Artocarpus* pigments, the presence of a specific enzyme in *A. integer* and *A. elasticus*, which preferentially prenylates the -COCH$_2$CO- group and not the phloroglucinol nucleus, must be assumed. Other possibilities are the attack of the prenyl cation on (a) the 3-position of a flavone in which the electron density at this position is increased by 2'- and 4'-hydroxyl groups; or (b) the α-carbon of the chalcone intermediate (Pendse *et al*, 1976).



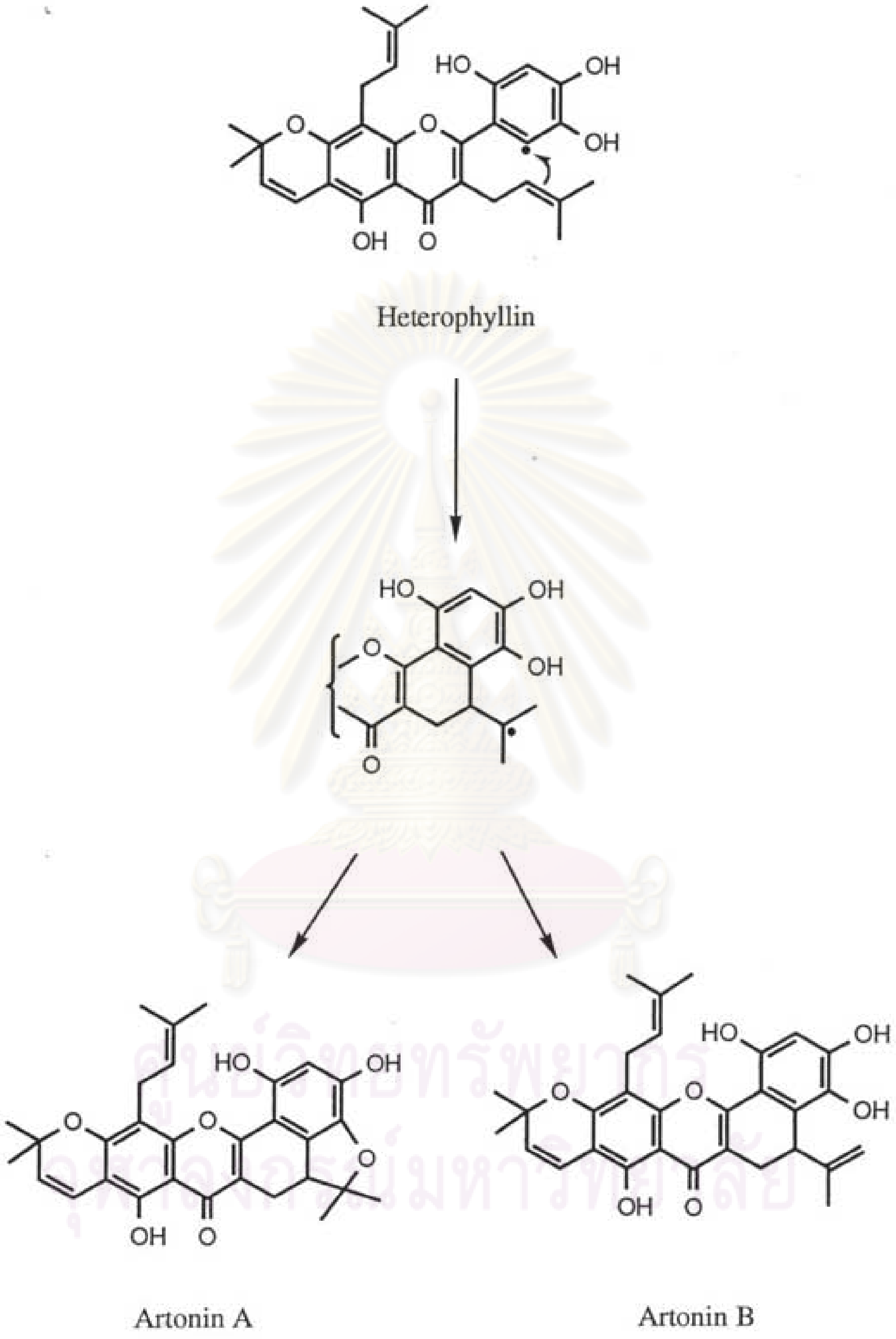
(6)

Artobiloxanthone and cycloartobiloxanthone are pyranodihydrobenzoxanthone which were isolated from *Artocarpus nobilis*. They are the first dihydrobenzoxanthone in plants. A feasible biosynthetic route for the formation of artobiloxanthone and cycloartobiloxanthone from a simple flavone (7) is suggested in Scheme 2. The epoxidation-dehydration mechanism is similar to that proposed for the biosynthesis of the rotenoid, amorphigenin. As artobiloxanthone and artobilochromen have the same oxygenation pattern as the simple flavone (7), a biogenetic relationship between dihydrobenzoxanthones and flavones seems likely (Sultanbawa and Surendrakumar, 1989).

Artonin A and B have unique structure in which the C-C linkage takes place between the C-6' position of the B ring and the C-10 position of isoprenoid moiety located at the C-3 position. Taking no optical activities into account, artonin A and B are biogenetically assumed to be derivatives from heterophyllin through the oxidative coupling reaction as shown in Scheme 3 (Hano *et al*, 1989).



Scheme 2 A feasible biosythetic route for formation of artobiloxanthone and cycloartobiloxanthone

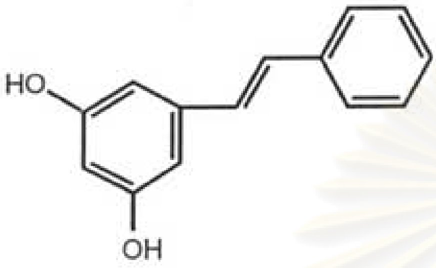


Scheme 3 Biosynthesis of artonin A and artonin B from heterophyllin

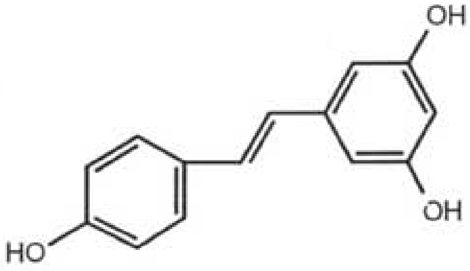
3. Stilbenes of *Artocarpus* species

3.1 Introduction to Stilbenes

Stilbenes themselves exist as compounds such as pinosylvin in *Pinus* and resveratrol in *Eucalyptus* spp. (Goodwin and Mercer, 1983).



Pinosylvin



Resveratrol

Stilbene are rare plant constituents. These compounds appear to be generally species specific except in *Pinus* genus where pinosylvin occurs in the heartwood of at least 50 species (Vickery M.L. and Vickery B, 1981). Table 6 gives the hydroxylation patterns of natural stilbenes and dihydrostilbene (Venkataraman, 1972).

Table 6 Hydroxylation patterns in natural stilbenes (includes Me ethers and glucosides)

Stilbenes	
4-OH	Pinaceae
3,5-$(OH)_2$	Pinaceae ; Fagaceae
3,5,4'-$(OH)_3$	Pinaceae ; Leguminosae ; Myrtaceae ; Moraceae ; Fagaceae ; Liliaceae
3,5,2',4'-$(OH)_4$	Moraceae (also 4-geranyl) ; Liliaceae
3,5,3'-4'-$(OH)_4$	Pinaceae ; Leguminosae ; Myrtaceae; Polygonaceae ; Moraceae
3,5,3',4',5'-$(OH)_5$	Leguminosae ; Myrtaceae
3,4'-$(OH)_2$-2-COOH	Saxifragaceae

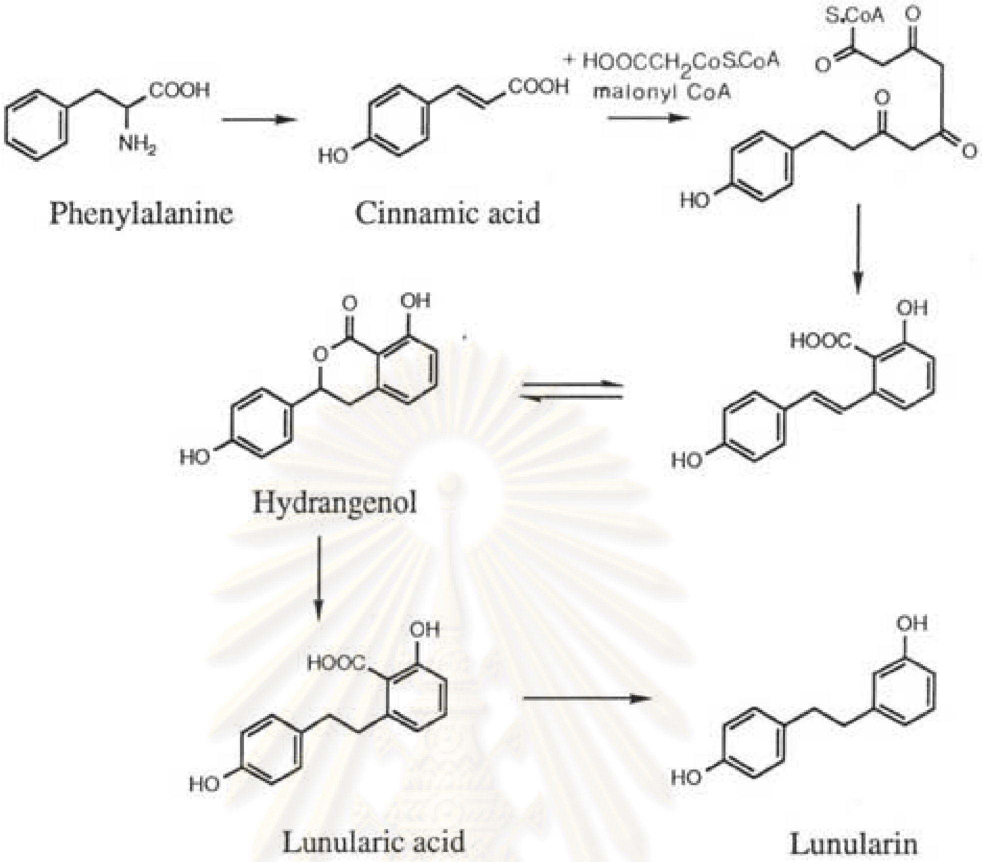
Table 6 (Continued)

Dihydrostilbenes	
3,5-$(OH)_2$	Detected in 7 *Pinus* species
	Me isolated from one
3,5,3',4'-$(OH)_4$	*Picea excelsa* Link. bark
3,4'-$(OH)_2$	
3,2',4'-$(OH)_3$	4 *Morus* species
3,5,2',4'-$(OH)_4$	

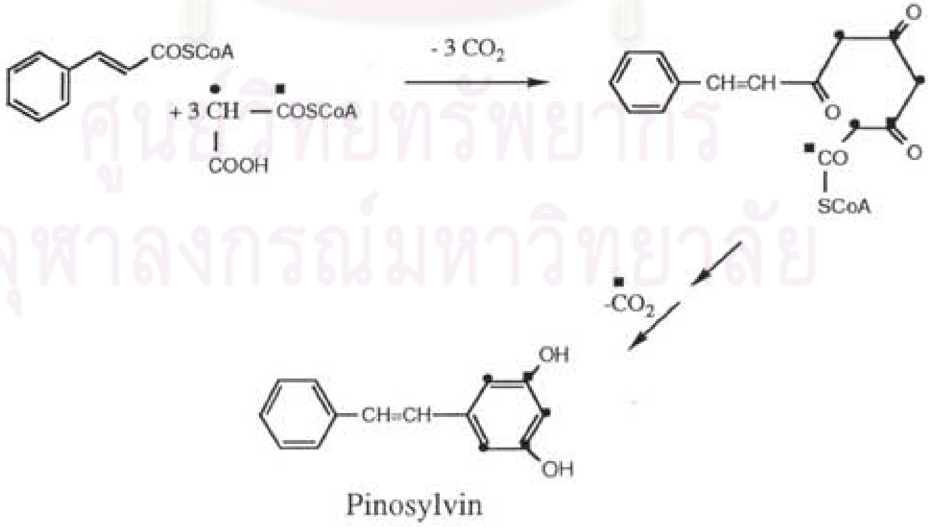
3.2 Biosynthesis of Stilbenes

Stilbenes are biosynthesised from cinnamate and malonate, probably by the pathway shown in Scheme 4. Both phenylalanine and acetate were incorporated into lunularic acid in *Lunularia cruciata*, while the incorporation of hydrangenol suggest that this compound is an intermediate. Lunularic acid was found to be metabolized to lunularin in *L. cruciata*. (Vickery M.L. and Vickery B, 1981).

Scheme 5 has been demonstrated experimentally for pinosylvin through feeding *Pinus resinosa* boughs with appropriately labelled precursors.



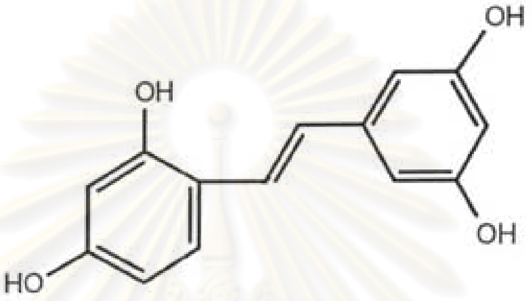
Scheme 4 The biosynthesis and degradation of lunularic acid



Scheme 5 Experimental biosynthesis of pinosylvin

3.3 Oxyresveratrol and Resveratrol

In *Artocarpus* species, stilbenes were isolated from only *A. lakoocha* and *A. chaplasha*. They are oxyresveratrol (2,4,3',5'-tetrahydroxystilbene) and resveratrol (4,3',5'-trihydroxystilbene). Erdtman (1963) found oxyresveratrol in the heartwood of one out of about 60 species of *Artocarpus*, but Rathi (1970) encountered of this stilbene in two of the six species examined by him (Venkataraman, 1972).



Oxyresveratrol

According to Barns and Gerber (1955) the identification of oxyresveratrol was complicated by the fact that it is usually obtained as an amorphous partially hydrated material, which can be crystallized in an anhydrous form only with difficult. They believed that the presence of oxyresveratrol was the main reason for the remarkable resistance of the wood decay. Mongolsuk *et al* (1957) isolated this stilbene as the crystalline dihydrate, m.p. 201°C, from water by merely concentrating an aqueous extract of the wood of *Artocarpus lakoocha* and ether-extracting the crude product (Venkataraman, 1972).

Oxyresveratrol is an active ingredient in Puag Hadd which has been widely used as a taeniacide for a long time in Thailand. The anthelmintic activity of this compound was checked against hog ascaris and earthworms. It was found to be active especially against earthworms (ชุมพิศ, ธงชัย, และไฉน, 2508; ชุมพิศ และคณะ , 2508). This stilbene was tested for antimicrobial activity against several kinds of bacteria, yeasts and fungi. Result indicated that it was effective, invarying degree, in inhibiting growth of most microorganisms tested (Atthasampunna, 1975).

4. Triterpenes of *Artocarpus* species.

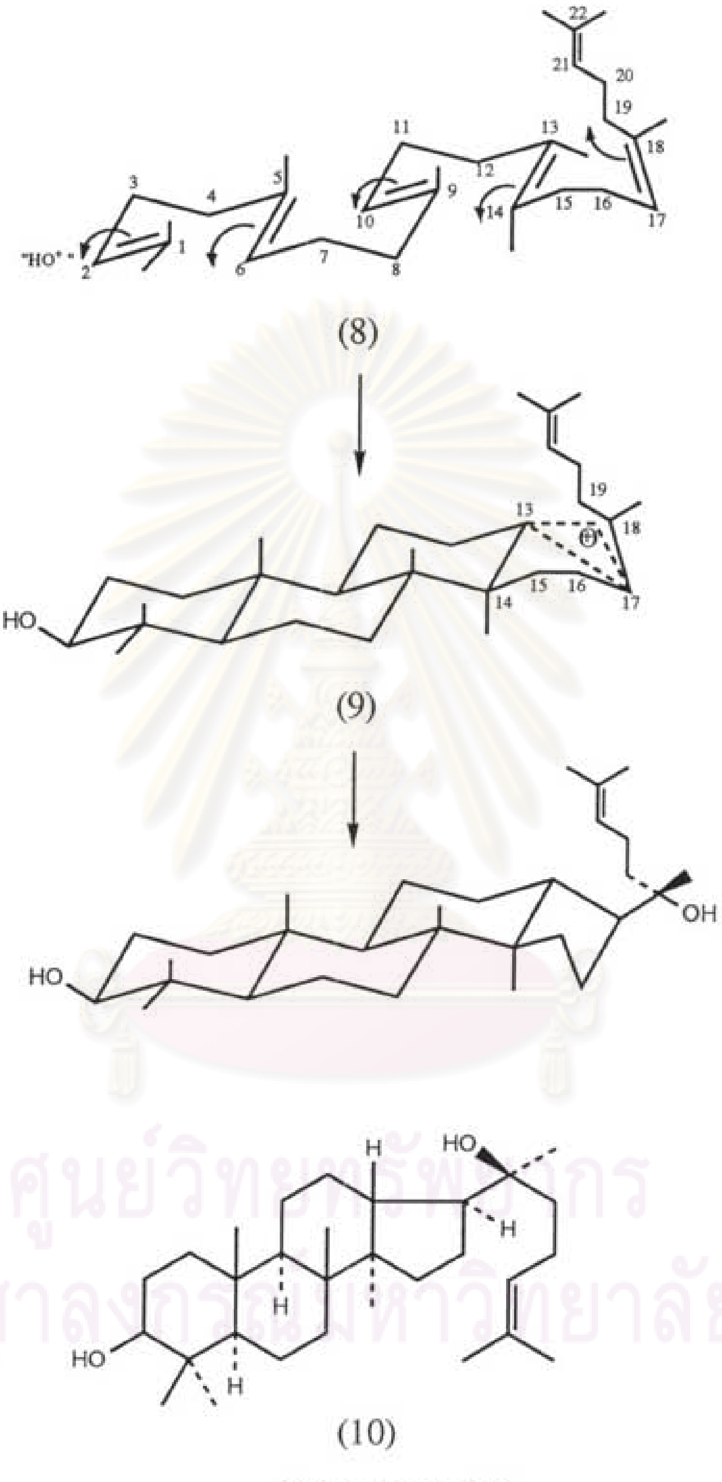
4.1 Introduction to triterpenes

The triterpenes are a group of natural products containing about thirty carbon atoms. Their structures can be considered as being derived from that of squalene by various cyclization or other changes. (Ourisson,Crabbe and Rodig, 1964) These substances are widely distributed in the plant and animal kingdoms, where they occur either in the free state, as ester, or as glycosides (Ikan, 1991). They may be classified into three groups : (1) tetracyclic ; (2) pentacyclic ; (3) miscellaneous groups. The naturally occuring triterpenes can be suitably placed into 29 main skeleta. (Devon and Scott, 1972)

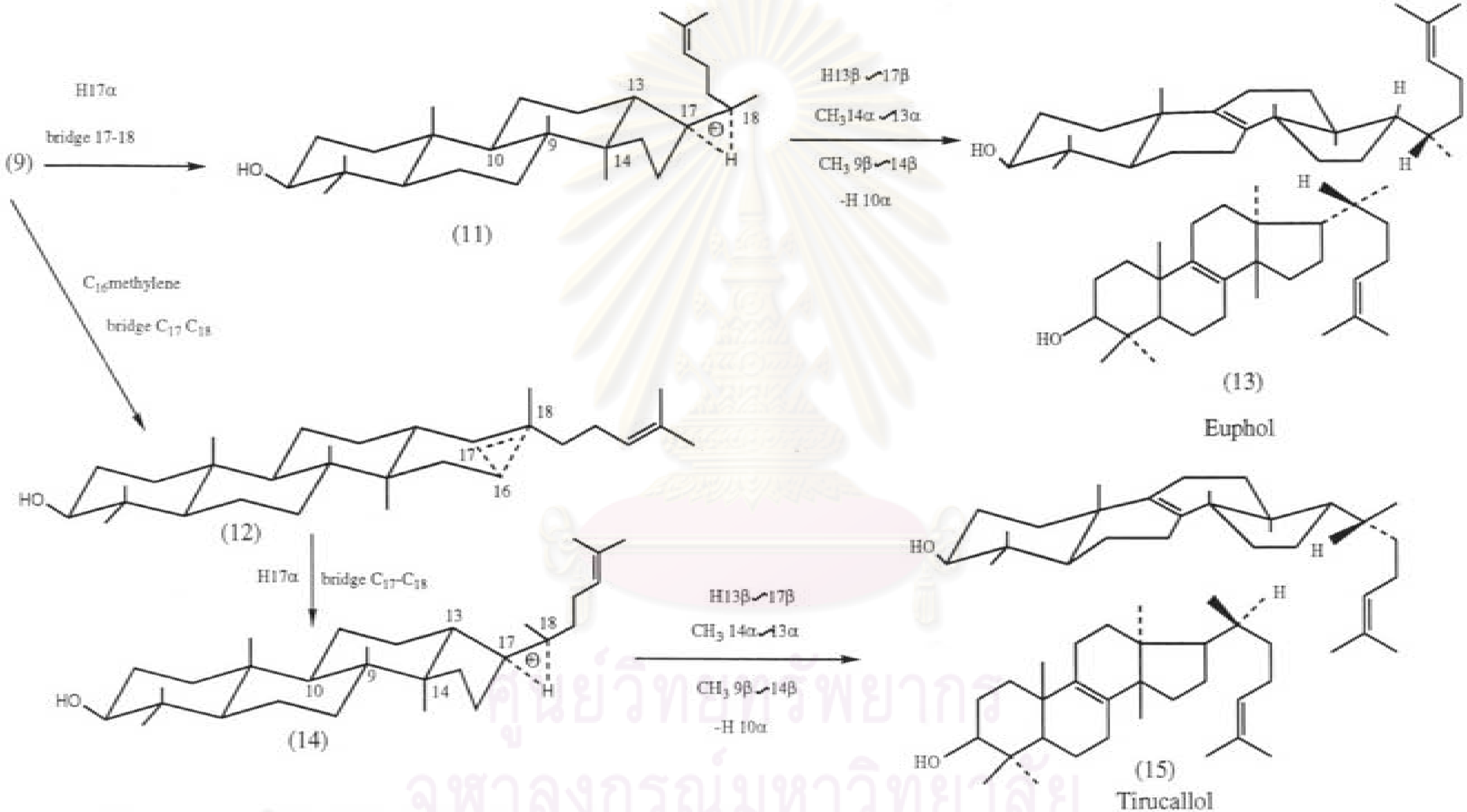
4.2 Biosynthesis of tetracyclic triterpenes

(Richarts and Hendrickson, 1964)

Cyclization of a squalene chain oriented chair-chair-chair-boat-unfolded (8) will lead to an intermediate (9) that can directly acquire a nucleophile and produce a dammarenediol (10) as shown in Scheme 6. On the other hand, the intermediate (9) can rearrange by hydrid migration to another intermediate (11) or by migration of the C-16 methylene carbon to still another intermediate (12). The path from (11) can lead by an appropriate series of Wagner-Meerwein rearrangements, followed by proton loss, to euphol (13). If the other intermediate (12) undergoes a hydride migration to (14), followed by a series of rearrangements, tirucallol (15) results as shown in Scheme 7. It is readily seen that all these rearrangements involve groups moving sequentially *trans* to one another. A point of particular interest is that the sequence (8)-->(12)-->(14) has as its objective the production of a stereochemistry at C-21 in tirucallol, which is epimeric to that at C-21 in euphol. Loss of the nucleophile from dammarenediol concerted with the appropriate subsequent rearrangements would also serve as an acceptable biogenetic mechanism for tirucallol except for the simplifying (but not necessarily true) assumption that all transformations from squalene to the final products shall occur in a nonstop fashion.



Scheme 6 Biosynthesis of Dammarenediol

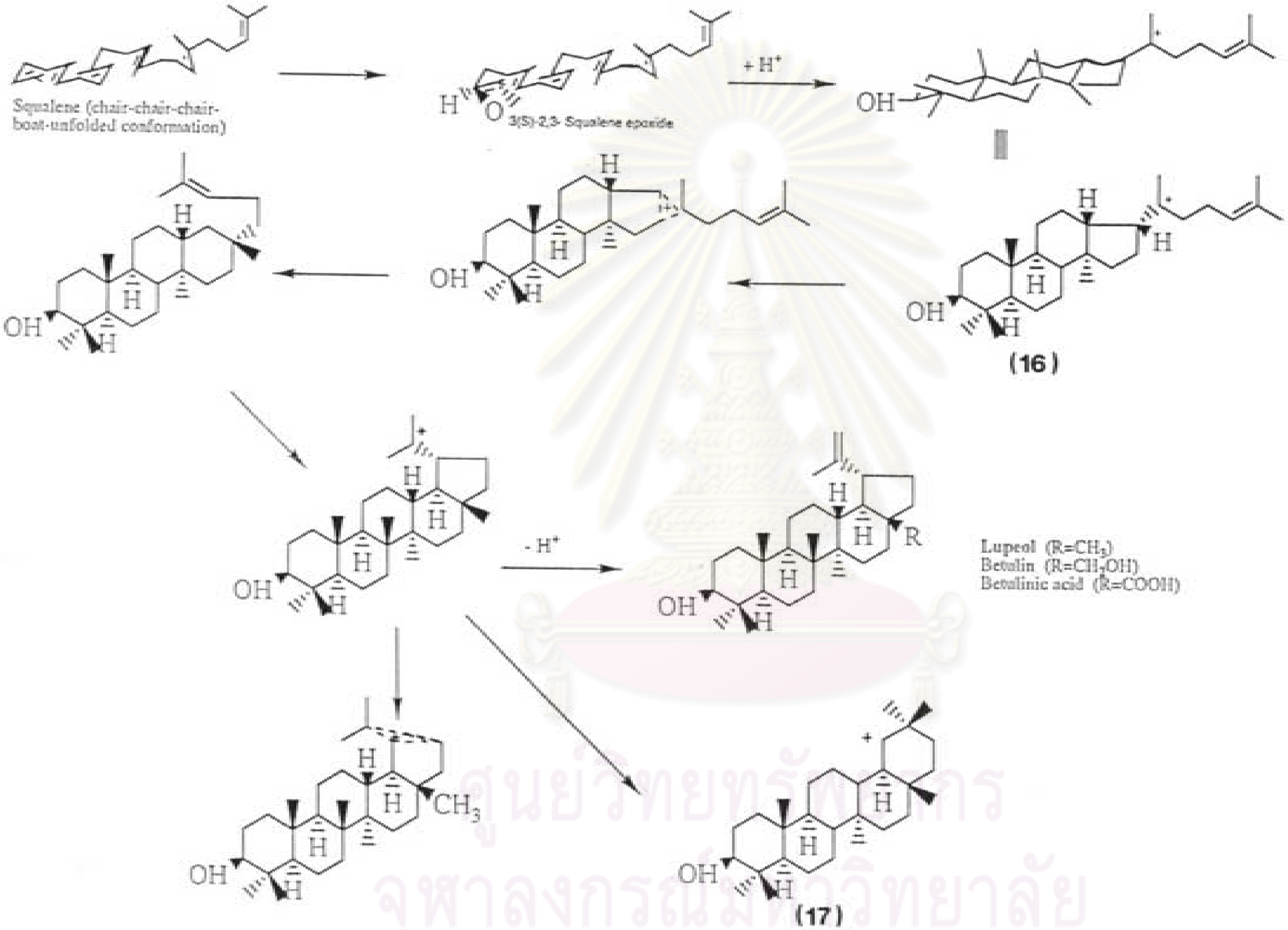


Scheme 7 Biosynthesis of tetracyclic triterpenes

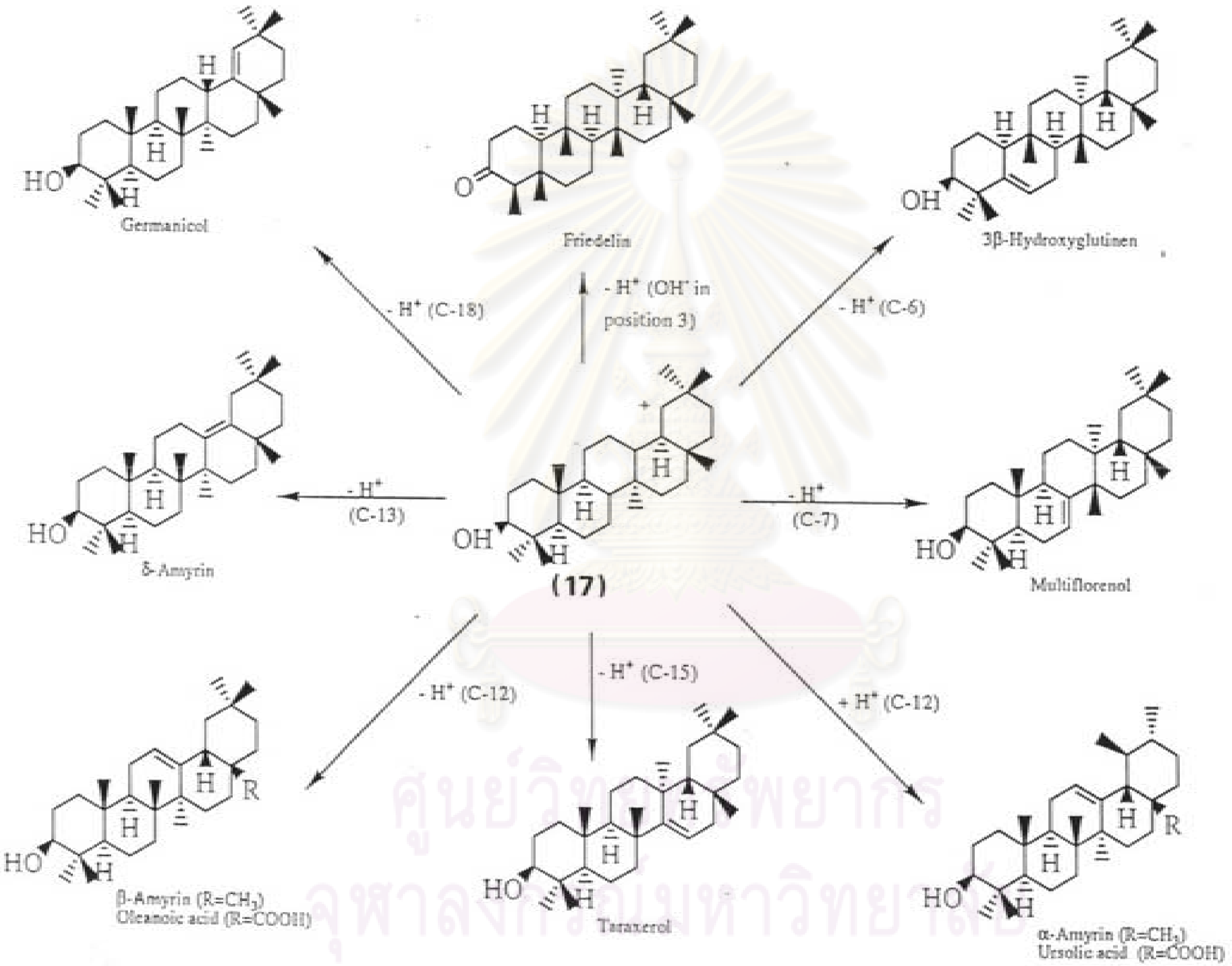
4.3 Biosynthesis of pentacyclic triterpenes

(Luckner, 1990; Porter and Spurgeon, 1981)

The pentacyclic triterpenes are derived from 3(S)-2,3-squalene epoxide in chair-chair-chair-boat-unfolded conformation. In pentacyclic triterpenes, ring D of the steroid cation (16) (Scheme 8) formed as an intermediate, may be enlarged by a Wagner-Meerwein rearrangement, and an additional five-membered ring may be formed as shown in Scheme 8 (biosynthesis of lupeol-type compounds). Enlargement of ring E by a further Wagner-Meerwin rearrangement lead to the cation (17), from which a large number of different amyrin-type compounds are derived by Z-anionotropy and elimination of a proton as shown in Scheme 9.



Scheme 8 Biosynthesis of pentacyclic triterpenoids, part I



Scheme 9 Biosynthesis of pentacyclic triterpenoids, part II

4.4 Triterpenes of *Artocarpus* species

Triterpenes isolated from *Artocarpus* species are tetracyclic triterpenes and pentacyclic triterpenes as shown in table 7.

Table 7 Triterpenes isolated from *Artocarpus* spp.

Triterpene	Source	Reference
Tetracyclic triterpene		
Cycloart-23-ene-3-beta-25-diol	*A. altilis*	Altman and Zito, 1976
Cycloart-24-ene-3-beta-ol	*A. altilis*	Altman and Zito, 1976
Cycloart-25-ene-3-beta-24-diol	*A. altilis*	Altman and Zito, 1976
Cycloartenol	*A. altilis*	Panasasivam and Sultanbawa, 1973
	A. lakoocha	Panasasivam and Sultanbawa, 1973
	A. heterophyllus	Panasasivam and Sultanbawa, 1973
	A. nobilis	Panasasivam and Sultanbawa, 1973
Cycloartenol acetate	*A. chaplasha*	Chakravarti, Mahato and Banerjee, 1971
Cycloartenone	*A. altilis*	Panasasivam and Sultanbawa, 1973
	A. heterophyllus	Panasasivam and Sultanbawa, 1973
	A. lakoocha	Panasasivam and Sultanbawa, 1973
	A. nobilis	Panasasivam and Sultanbawa, 1973
Cycloartenyl acetate	*A. altilis*	Panasasivam and Sultanbawa, 1973
	A. heterophyllus	Panasasivam and Sultanbawa, 1973
(24R) 9,19-Cyclolanost-3-one-24,25-diol	*A. heterophyllus*	Barix *et al*, 1994

Table 7 (Continued)

Triterpene	Source	Reference
(24S) 9,19-Cyclolanost-3-one-24,25-diol	*A. heterophyllus*	Barix *et al*, 1994
Isocycloartenol acetate	*A. chaplasha*	Chakravarti, Mahato and Banerjee, 1971
Pentacyclic triterpene		
α-Amyrin	*A. altilis*	Altman and Zito, 1976
Amyrin acetate	*A. lakoocha*	Kapil and Joshi, 1960
Betulin	*A. heterophyllus*	Lu and Lin, 1994
Betulinic acid	*A. heterophyllus*	1. Rao, Varadan and Venkataraman, 1973 2. Dayal and Seshadri, 1974
Lupeol	*A. lakoocha*	Chauhan and Kumari, 1979
Lupeol acetate	*A. altilis*	Shieh and Lin, 1992
	A. chaplasha	Chakravarti, Mahato and Benerjee, 1971
	A. lakoocha	Mahato, Banerjee and Chakravarti, 1966
Ursolic acid	*A. heterophyllus*	Dayal and Seshadri, 1974