Recent Advances in Annonaceous Acetogenins

By: Lu Zeng, Qing Ye, Nicholas H. Oberlies, Guoen Shi, Zhe-Ming Gu, Kan He and Jerry L. McLaughlin

Zeng, L.; Ye, Q.; Oberlies, N.H.; Shi, G.; Gu, Z.-M.; He, K. and McLaughlin, J.L. (1996) Recent advances in Annonaceous acetogenins. *Natural Product Reports*, 13, 275-306.

Made available courtesy of Royal Society of Chemistry: http://www.rsc.org/Publishing/Journals/np/

*****Note: Figures may be missing from this format of the document**

1 Introduction

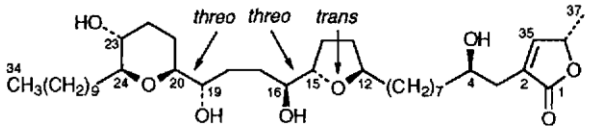
Annonaceous acetogenins are waxy substances consisting of C_{32} or C_{34} long chain fatty acids which have been combined with a propan-2-ol unit at C-2 to form a gama-lactone. They are only found in several genera of the plant family, Annonaceae. Their diverse bioactivities as antitumour, immunosuppressive, pesticidal, antiprotozoal, antifeedant, anthelmintic and antimicrobial agents have attracted more and more interest worldwide. Recently, we reported that the Annonaceous acetogenins can selectively inhibit the growth of cancerous cells and also inhibit the growth of adriamycin resistant tumour cells.[1] As more acetogenins have been isolated and additional cytotoxicity assays have been conducted, we have noticed that, al(hough most acetogenins have high potencies among several solid human tumour cells lines, some of the derivatives within the different structural types and some positional isomers show remarkable selectivities among certain cell lines, *e.g.* against prostate cancer (PC-3).[2]

We now understand the primary modes of action for the acetogenins. They are potent inhibitors of NADH : ubiquinone oxidoreductase, which is an essential enzyme in complex I of the electron transport system (ETS) which eventually leads to oxidative phosphorylation in mitochondria.[3-5] A recent report showed that they act directly at the ubiquinone catalytic site(s) within complex 1 and in microbial glucose dehydrogenase.[6] They also inhibit the ubiquinone-linked NADH oxidase that is peculiar to the plasma membranes of cancerous cells and functions to permit cytosolic phosphorylation (substrate level phosphorylation) by restoration of NAD levels. Thus, the end result of both of these mechanisms is ATP deprivation.[7]

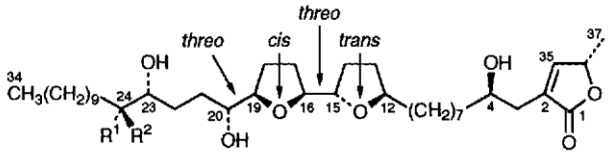
Using advanced Mosher ester methodology,[8] more and more acetogenins are being reported with defined stereochemistries. Recently, the stereostructures of gigantecin, an acetogenin containing non-adjacent bis-tetrahydrofuran (THF) rings, was proven by X-ray analysis and Mosher ester determination.[9] Several other acetogenins, such as those with adjacent bis-THF rings — *e.g.* asimicin,[10.11] parviflorin,[12] bullatacin10,11[.13] and rolliniastatin-l[14] and those with mono-THF rings — *e.g.* solamin,[15-17] reticulatacin,[15,17] corossolone,[18] corossolin[18] and gigantetrocin A (13,14-threo-densicomacin)[19] — have now been synthesized. As additional information regarding the stereo- chemistries of acetogenins has accumulated, we consider that it is now most logical to classify the Annonaceous acetogenins according to their stereostructures across their THF rings.

Since publishing our last three reviews, which summarized research on Annonaceous acetogenins up to June 1994,[20] six new species of Annonaceae have been reported to contain acetogenins: they are *Annona atemoya,*[21-23] *A. coriacea,*[9,24] *A. crassiflora,*[23] *A. glauca,*[26] *Asimina longifolia*[27-29] and *Uvaria tonkinesis.*[30]

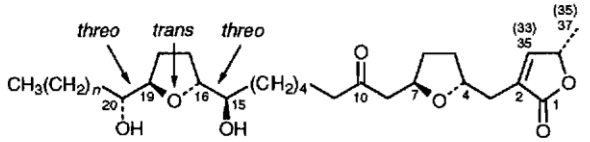
A new structural type of acetogenin, mucocin 207,[31] is the first acetogenin containing both a THF ring and a tetrahydropyran (THP) ring. Rollidecins A 176 and B 177[32] are the first acetogenins bearing adjacent bis-THF rings and one



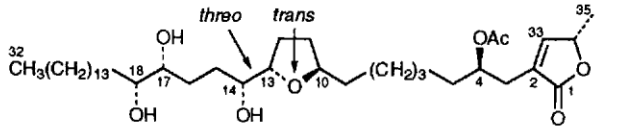
207 mucocin



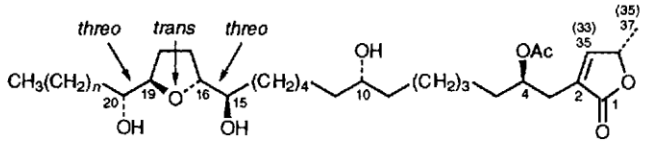
176 rollidecin A R^1 = OH; R^2 = H
177 rollidecin B R^1 = H; R^2 = OH



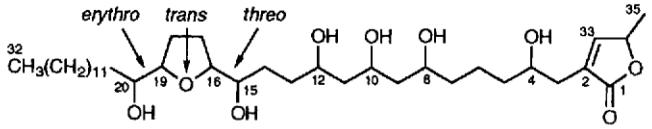
205 aromin n = 11
206 aromicin n =13



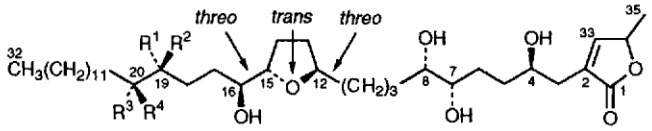
79 4-acetyl gigantetrocin A



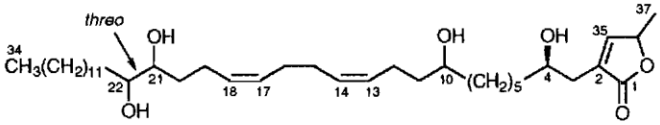
20 4-acetyl annonacin $n = 11$
38 4-acetyl xylomaticin $n = 13$



64 annohexocin



82 murihexocin A $R^1 = R^3 = OH$; $R^2 = R^4 = H$
83 murihexocin B $R^1 = R^3 = H$; $R^2 = R^4 = OH$



223 coriadienin

flanking hydroxyl with relative stereoconfigurations of *transthreo-cis-threo* (we always designate relative stereochemistries from lower to higher positions down the hydrocarbon chain). Aromin 205 and aromicin 206[33] are the first acetogenins having two non-adjacent THF rings at C-4 and C-15.

Three mono-acetyl acetogenins, 4-acetyl gigantetrocin A 79,[34] 4-acetyl annonacin 20,[28] and 4-acetyl xylomaticin 38,[28] have recently been isolated; no naturally acetylated acetogenins have been reported since the first acetogenin, uvaricin,[35] with a mono-acetyl group at C-24, was published. Three six hydroxyl mono-THF acetogenins, annohexocin 64u and murihexocins A 82 and B 83,[37] have been reported. Annohexocin has a 1,3,5- triol moiety between the THF and gama-lactone rings, and murihexocins A and B have two threo-1,2-diols in their molecules. The isolation of coriadienin 223,[24] the first acetogenin bearing two double bonds, has provided further evidence for the hypothesized biogenetic pathway.

In our first review in 1990, we described 28 Annonaceous acetogenins isolated from 11 species ;[38] in our second review in 1993, we summarized 61 acetogenins isolated from 16 species;[39] in our third review in 1995, another 80 acetogenins from 20 species of Annonaceae were added to this class of compounds.[20] Some recent reviews

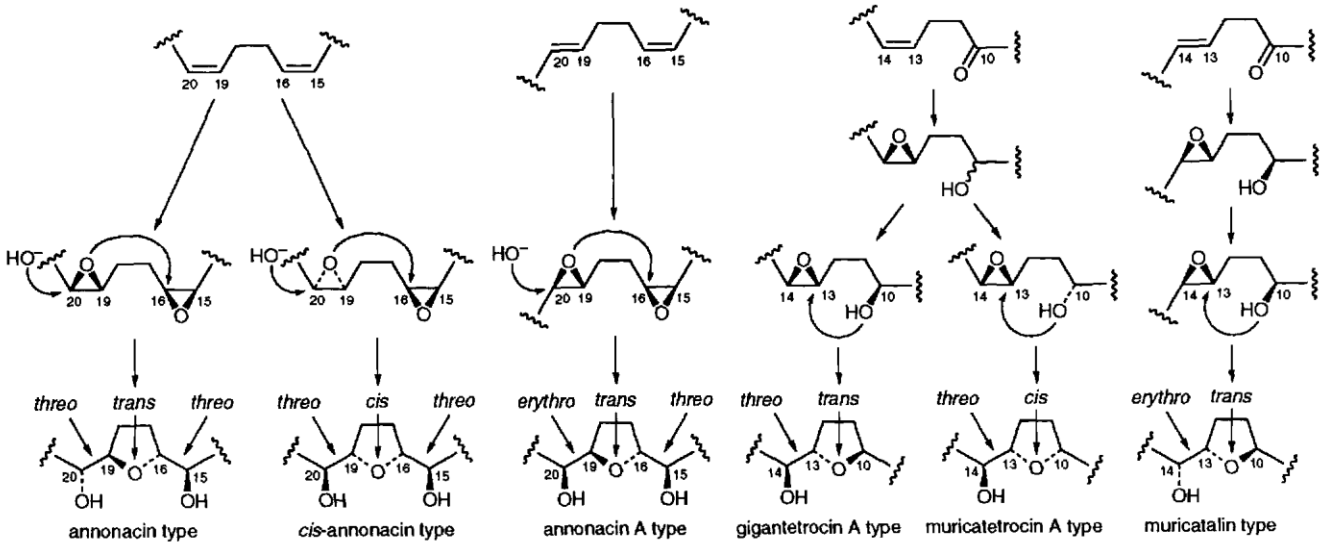
of more limited scope have been published by other groups.[40-42] At the time of preparation (January 1996) of this, our fourth review, over 220 Annonaceous acetogenins have been reported from 26 species.

2. Biosynthesis and Classification

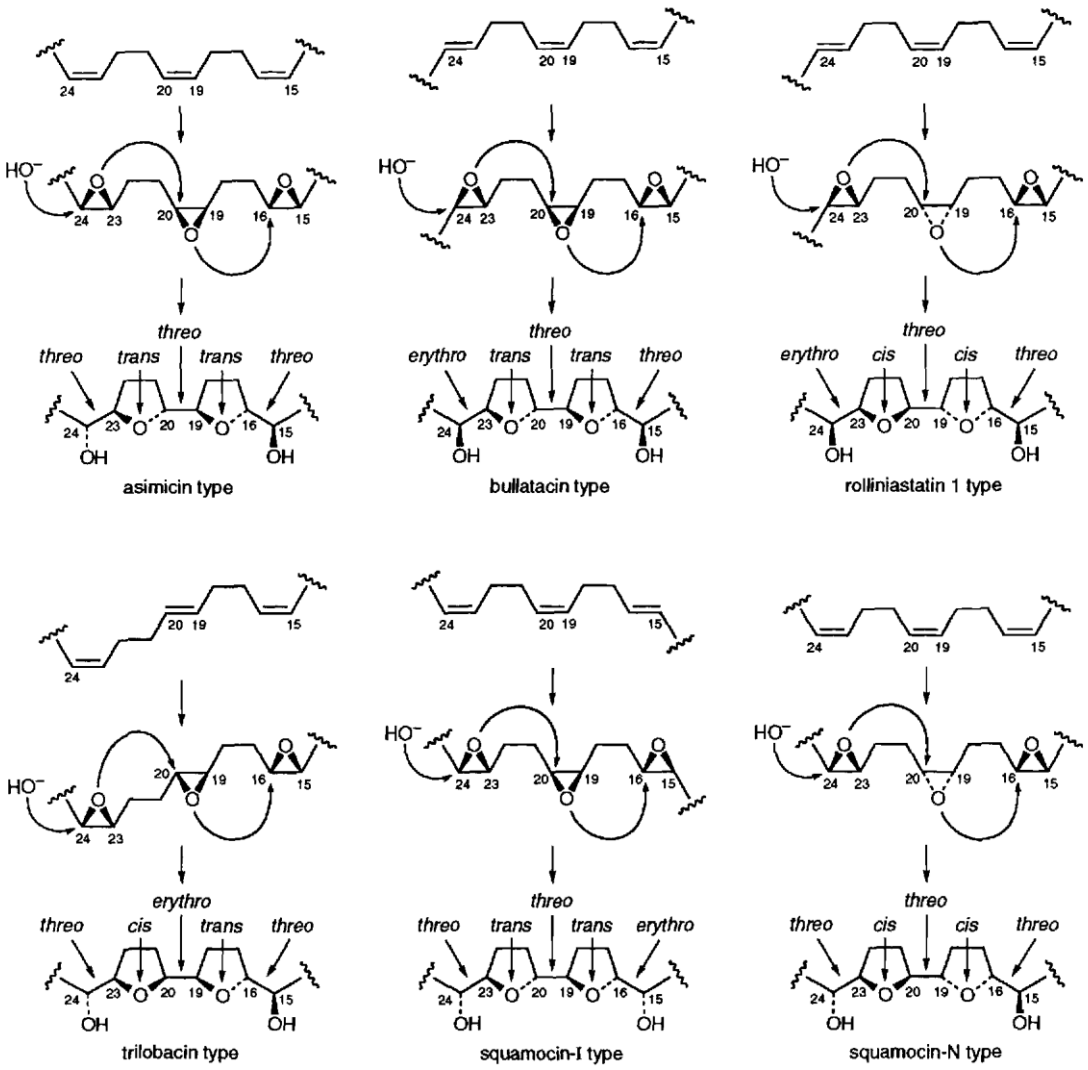
In our previous reviews, [20, 38, 39] the Annonaceous acetogenins were classified as mono-THF, adjacent bis-THF, non-adjacent bis-THF, and non-THF ring compounds, followed by subclassification of the gama-lactone, substituted gama-lactone or ketolactone variations. As more Annonaceous acetogenins have been found and, especially, as the absolute stereochemistries of the acetogenins have been proven, either by total synthesis or by the Mosher ester method, we have realized that the type of stereostructures across the THF rings offer a more convenient method for classifying these compounds.

Previously, we have proposed biogenetic pathways likely to lead to the acetogenins.[20] Most of the acetogenins, including those with mono-THF rings with one flanking hydroxyl, mono- THF rings with two flanking hydroxyls, adjacent bis-THF rings with one flanking hydroxyl, adjacent bis-THF rings with two flanking hydroxyls, and non-adjacent bis-THF rings, can be hypothetically related in a similar way (see Schemes 1-4). Three types of acetogenins bearing a mono-THF ring with two flanking hydroxyls (the annonacin, cis-annonacin and annonacin A types) are considered to be formed from *cis-cis* or *trans-cis* dienes, through epoxidation followed by cyclization starting from the left hand side of the molecule. Three types of acetogenins bearing a mono-THF ring with one flanking hydroxyl (gigantetrocin A, muricatetrocin A and muricatalin types) can be formed from a keto cis-alkene or keto *trans*- alkene through reduction of the keto group followed by cyclization starting from the right side (see Scheme 1).

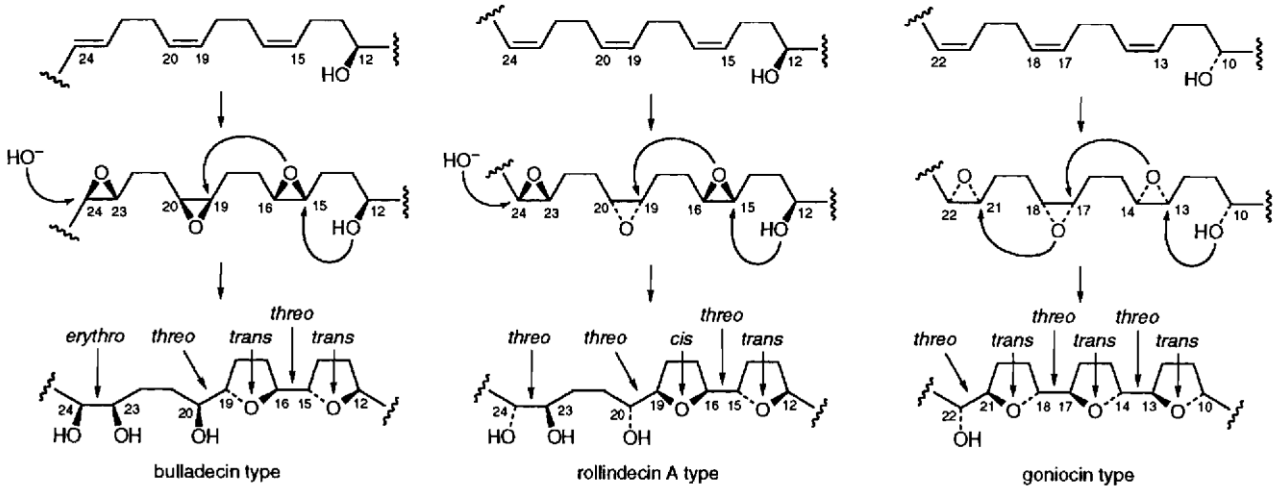
Six types of adjacent bis-THF ring acetogenins having two flanking hydroxyls (asimicin, bullatacin, rolliniastatin 1, trilobacin, squamocin-I and squamocin-N types) can be classified in a similar way. After epoxidation, these six types all start from the left side to pursue further cyclizations (Scheme 2).



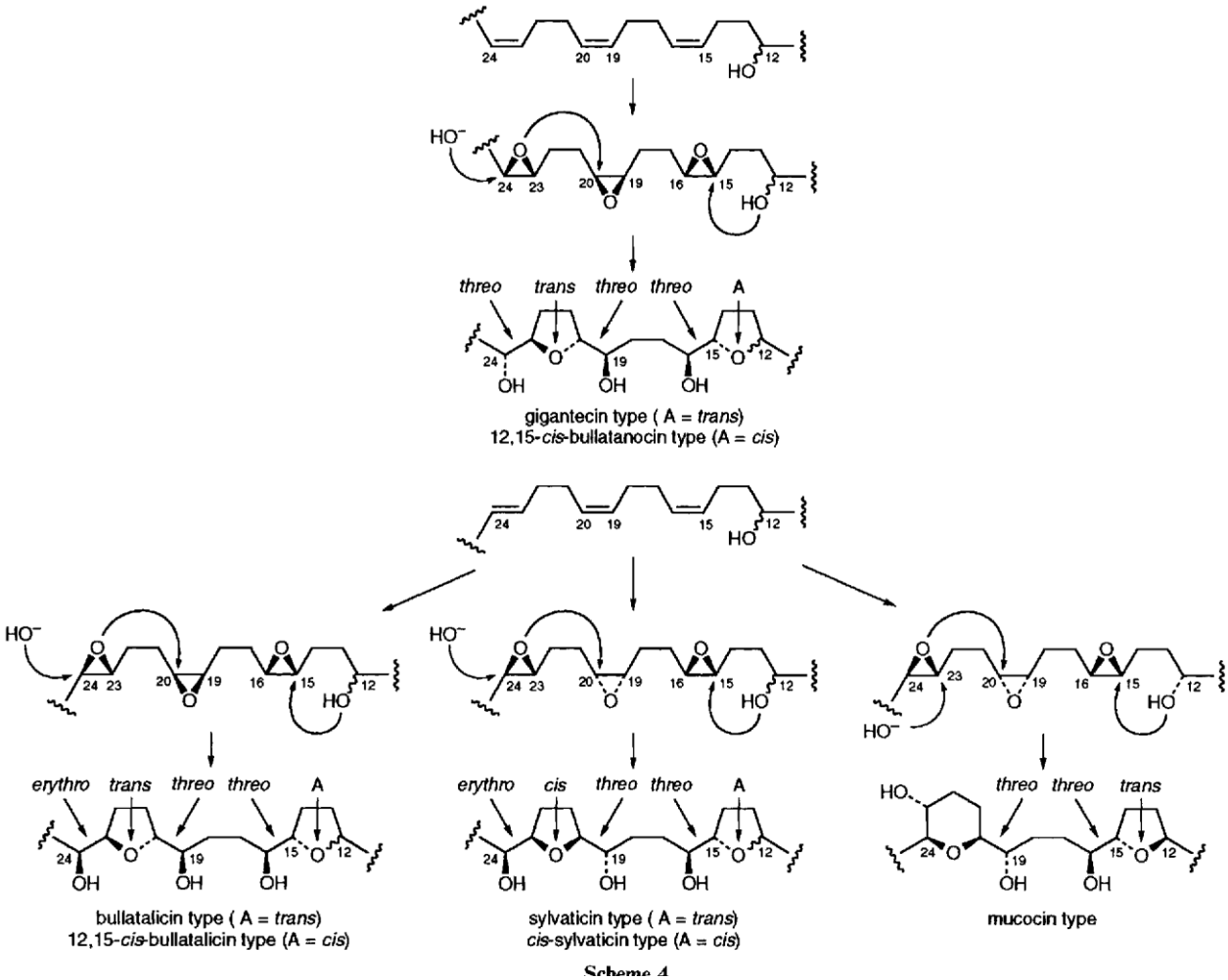
Scheme 1


asimicin type
bullatacin type
rolliniastatin 1 type
trilobacin type
squamocin-I type
squamocin-N type

Scheme 2



Scheme 3



Scheme 4

Two other types of acetogenins, bearing adjacent bis-THF rings with one flanking hydroxyl (bulladecin and rollindecin A types), can be formed from hydroxylated *cis—cis—trans* or hydroxylated *cis—cis—cis* trienes, through epoxidation and cyclization starting from the right side (Scheme 3).

The formation of acetogenins bearing adjacent tri-THF rings (goniocin type) which was found recently in *Goniothalamus giganteus*,[43] can also be explained in the same way; this is a new type of Annonaceous acetogenin of which only one example has been found, so far. Two semisynthetic products, cyclogoniodenins T (with a *trans—threo—trans—threo—trans—threo* tri- THF ring moiety) and C (with a *trans—threo—trans—*

threo cis—threo tris-THF ring moiety) derived from goniodenin, are other examples of adjacent tri-THF ring compounds." Goniocin and cyclogoniodenin T have the same relative stereo- chemistries around the adjacent tri-THF ring moiety, *Le. trans—threo—trans—threo—trans—threo,* but the absolute configurations are different. Goniocin has C-24R, and cyclogoniodenin T has C-24S.

Six types of acetogenins having non-adjacent bis-THF rings (gigantecin, 12, 15-cis-bullatanocin, bullatalicin, *12,15-cis*bullatalicin, sylvaticin, and cis-sylvaticin types) have been found. These compounds consist of one mono-THF ring bearing one flanking hydroxyl and one mono-THF ring bearing

Table 1 Separations of certain Annonaceous acetogenins (pairs of epimers or isomers) by HPLC

Compounds	Retention time (min)	Column[a]	Solvents	UV detector (nm)
Asimicin **105** Bullatacin **126**	51 56	Si gel, 8μ	9% MeOH/THF in hexane	230
Bullatalicin **191** 12,15-*cis*-Bullatacin **199**	60 62	C-18, 8μ	70% CH_3CN in water	230
Rollinecin A **72** Rollinecin B **73**	150 155	C-18, 8μ	70% CH_3CN in water	230
Squamotacin **123** Bullatacin **126**	95 99	Si gel, 8μ	7% MeOH/THF in hexane	230
Murihexocin A **82** Murihexocin B **83**	89 91	Si gel, 8μ	gradient, 0–3% MeOH in CH_3Cl	not used
2,4-*cis*-Asimicinone **114** 2,4-*trans*-Asimicinone **115**	19 22	C-18, 8μ	gradient, 70–80% CH_3CN in water	205

[a] Column size: 21.4 × 250 mm, flow rate: 10 ml min^{-1} usually 20–50 mg samples can be separated

two flanking hydroxyls, separated by two methylenes. The formation of these acetogenins can be considered to result from cyclization starting from both sides (Scheme 4). The new type of acetogenin, mucocin 207, which has non-adjacent THF and tetrahydropyran (THP) rings,[31] likely has quite a similar biogenetic pathway; the cyclization would start from the left side, the same as with other non-adjacent bis-THF acetogenins, but it would start at C-23 instead of C-24; the stereochemistries of mucocin are consistent with this hypothesis (Scheme 4).

Aromin 205 and aromicin 206 from *Xylopia aromatica* belong to another new type of non-adjacent bis-THF acetogenin.[33] Two THF rings are located beginning at C-4 and C-16. The THF ring at C-16 is likely formed as with all the other mono-THF ring compounds, and the THF ring at C-4 may be formed by the loss of one molecule of water (dehydration) between hydroxyls at C-4 and C-7. Two acetogenins bearing 4,7-hydroxyl groups, murihexocins A 82 and B[37] 83, recently isolated from *A. muricata,* provide evidence for such a mechanism of formation of the aromin type compounds.

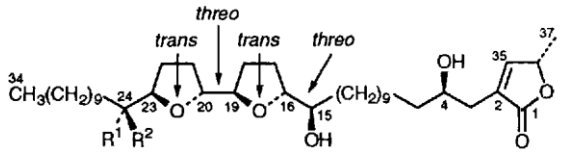
3 Extraction, Isolation and Purification

Ethanol extraction of plant biomass to yield the acetogenins is used in our laboratory as a general method. Although most of the acetogenins are easily soluble in chloroform or dichloromethane, recently we found that some six hydroxyl acetogenins, such as annohexocin 64 and murihexocins A 82 and B 83, are not as soluble as other acetogenins in these chlorinated solvents and might be lost if ethanol were not used. Several partitioning operations, starting from the residue of the ethanol extract, can concentrate the acetogenins. The concentration can be easily demonstrated by using the brine shrimp lethality test (BST) to guide their activity directed fractionation.[20,45,46]

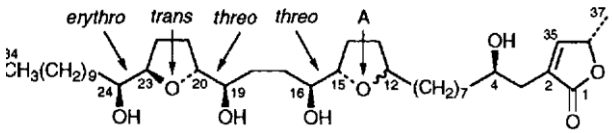
Separation of acetogenins by repeated open column chromatography and HPLC can be achieved, depending on their polarities. Polarities are controlled by THF rings and other functional groups, such as hydroxyls, ketones,

epoxides and double bonds, and sometimes depend on the positions of the THF rings and functional groups along the hydrocarbon chain.

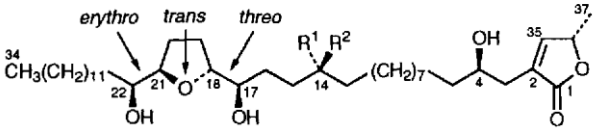
Some successful separations of epimers using HPLC in different systems are given in Table 1. Asimicin 105 and bullatacin 126, adjacent bis-THF acetogenins, are epimers and are different only at C-24. Asimicin has C-24R and bullatacin has C-24S. Bullatalicin 191 and 12,15-cis-bullatalicin 199, nonadjacent bis-THF acetogenins, are epimeric at C-12. Bullatalicin has C-12R and 12,15-cis-bullatalicin has C-12S. Rollinecins A 72 and B 73 are epimeric mono-THF acetogenins which are different at C-14. Rollinecin A has C-14R and rollinecin B has C-14S. Squamotacin 123 and bullatacin 126 are different only in the placement of their adjacent bis-THF ring systems and the flanking hydroxyls. The adjacent bis-THF ring starts at C-14 in squamotacin, while it starts at C-16 in bullatacin. 2,4-cisAsimicinone 114 and 2,4-trans-asimicinone 115 are epimers at C-2 of the ketolactone ring; the former has C-2R and the later has C-2S.



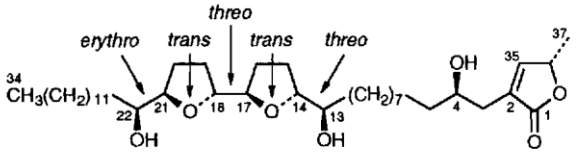
105 asimicin R^1 = OH; R^2 = H
126 bullatacin R^1 = H; R^2 = OH



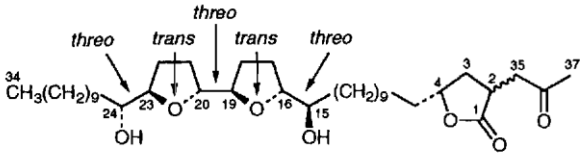
191 bullatalicin A = *trans*
199 12,15-*cis*-bullatalicin A = *cis*



72 rollinecin A R^1 = OH; R^2 = H
73 rollinecin B R^1 = H; R^2 = OH



123 squamotacin



114 2,4-*cis*-asimicinone
115 2,4-*trans*-asimicinone

Separation of murihexocins A 82 and B 83, two six-hydroxyl mono-THF acetogenins which differ at their C-19, 20 vicinal diols (the former has C-19S, 20S , and the latter has C-19R, 20R), was conducted using chloroform and methanol. Since the UV detector cannot be used as a monitor in this system, careful control of the blind collection of small fractions and monitoring their retention times separated the pure compounds.

Using program control systems, HPLC separations of these isomeric acetogenins are usually reproducible.

4 Structural Elucidation Strategies

Several strategies for the structural elucidation of Annonaceous acetogenins have been summarized in our previous reviews.[20, 33, 39] From the first acetogenin, uvaricin, found in 1982, until 1992, most acetogenins were reported as planar structures.[33,39] During this time several adjacent bis-THF acetogenins have been reported with their relative stereochemical relationships among the stereogenic centres around the THF rings based on the 'H NMR data from synthetic adjacent bis- THF ring model compounds (twelve acetylated isomers of adjacent bis-THF ring systems bearing two flanking hydroxyls have been reported).[47].[48] Synthetic efforts on the relative stereochemistries of single THF rings provide data for determinations of the relative stereochemistries of mono-THF ring acetogenins with one flanking hydroxyl (four isomers of this type of compound have been synthesized)[49] and mono- THF ring acetogenins with two flanking hydroxyls (four isomers of this type of compound have been synthesized).[49]

Using these models the relative stereochemistries of nonadjacent bis-THF acetogenins can also be solved by ^{1}H NMR. However, no model compounds of adjacent bis-THF rings bearing one flanking hydroxyl and adjacent tris-THF rings bearing one flanking hydroxyl have been synthesized. Thus, systematic studies synthesizing models for these types of compounds, such as a bulladecin, rollindecin A and goniocin types of acetogenins, are still needed.

Diols are common structural features found in the acetogenins and include 1,2-, 1,3-, 1,4- or 1,5-diols. ^{1}H NMR analyses of acetonide or formaldehyde acetal derivatives can usually solve the relative stereochemistries of these diols.50, 51

Advanced Mosher ester methodology was introduced to determine the absolute configurations of stereogenic carbinol centres in Annonaceous acetogenins in late 1992. Since then, most of the acetogenins reported by our group[20] and by Fujimoto's group[52] have been defined with absolute stereo- chemistries. Basically, the Mosher ester method can be directly used to determine the absolute stereochemistries of carbinol centres (the flanking hydroxyls of THF ring moieties) in the acetogenins which have mono-THF rings bearing one flanking hydroxyl, mono-THF rings bearing two flanking hydroxyls, adjacent bis-THF rings bearing one flanking hydroxyl and adjacent bis-THF rings bearing two flanking hydroxyls. Combined with the formation of formaldehyde acetals of the 1,4-diols between the two THF rings, the absolute stereo- chemistries of (he non-adjacent bis-THF ring acetogenins (except for the aromicin type) can also be solved.[51] The stereochemistries of isolated mono-hydroxyl groups near the terminal methyl group (including C-28, 29, 30, 31 or 32- hydroxyl compounds)" and mono-hydroxyl groups near the gama-lactone ring (including C-4, 5 or 6-hydroxyls) can be also directly solved by the Mosher ester method.

The positions of the THF ring and other functional groups along the hydrocarbon chain are important for controlling their bioactivities, and, thus, the placements of such groups are essential in the structural determination of acetogenins. Usually, a combination of chemical methods, 'H and ^{13}C NMR analysis, and mass spectrometry with high resolution mass analyses of certain fragments can give satisfactory results. The placements of hydroxyls can be achieved by EI-MS of the trimethylsilyl (TMS) or perdeutero-TMS derivatives, most of the time; the cleavages between hydroxylated carbons and adjacent carbons provide relatively prominent peaks. Amine derivatives *(N,N*dimethylethylenediamine) of precursor-ion scanning FABMS/MS[52] and lithium cationization B/E linked scan FABMS[54] are also useful for this purpose.

4.1 Structural Elucidation of THF or THP Ring(s) and Flanking Hydroxyls

1H and ^{13}C NMR are useful in recognizing the different structural types of acetogenins. By identifying the ^{1}H NMR signals, which appear around 8 3.0-4.0, one can usually distinguish the specific THF or THP types. Table 2 summarizes ^{1}H NMR data of different acetogenins. Sometimes, the signals of 1,2- or 1,3-diols in the molecule may interfere with these characterizations. The signals of 1,2-threo-diols appear at about *8* 3.4, and both *l,3-threo-* or *erythro-diols* appear at about *d 3.8 3.95.*[55,56]

The structural elucidations of adjacent bis-THF ring acetogenins with two flanking hydroxyls sometimes pose a question as to which side is which. These situations happen in the cases of asymmetric structures, such as with

the bullatacin, squamocin I**,** trilobacin and rolliniastatin 1 types. Indeed, we initially placed the *erythro* arrangement of bullatacin on the wrong side,[8], [57] and we initially picked the wrong model for the relative stereochemistries of trilobacin.[58,59, 59]

In the structural elucidation of trilobacin, which has a

Table 2 The characteristic ^{1}H NMR patterns (in $CDCl_3$) for identification of THF (or THP) Annonaceous acetogenins

	Annonacin Type	*cis*-Annonacin Type	Annonacin A Type	Gigantetrocin A Type	*cis*-Gigantetrocin Type	Muricatalin Type
δ 3.35–3.47	2H	2H	1H	1H	1H	–
δ 3.7	—	—	—	—	1H	—
δ 3.75–3.95	2H	2H	3H	2H	1H	3H
	Asimicin Type	Bullatacin Type	Rolliniastatin 1 Type	Trilobacin Type	Squamocin-I Type	Squamocin-N Type
δ 3.35–3.47	2H	1H	1H	2H	1H	2H
δ 3.75–3.95	4H	5H	5H	2H	5H	5H
δ 3.95–4.05	–	–	–	2H	–	–
	Gigantacin Type	Bullatalicin Type	Sylvaticin Type	12,15-*cis*-Bullatanocin Type	12,15-*cis*-Bullatalicin Type	*cis*-Sylvaticin Type
δ 3.35–3.47	3H	2H	2H	3H	2H	2H
δ 3.7	—	—	—	1H	1H	1H
δ 3.75–3.95	4H	5H	5H	3H	4H	4H
	Bulladecin Type	Rollindecin A Type	Goniocin Type	Mucocin Type	Aromicin Type	
δ 3.0–3.3	—	—	—	3H	—	
δ 3.35–3.47	1H	1H	1H	2H	2H	
δ 3.6	—	—	—	—	1H	
δ3.75–3.95	4H	4H	6H	2H	3H	

relative stereochemical relationship across the adjacent THF rings and flanking hydroxyls of *threo-trans-erythro-cis-threo,* with the two flanking hydroxyls both *R,* the questions that needed to be answered were which side is *cis* and which side is *trans.* By selective acetylation of one hydroxyl adjacent to the THF-ring system, followed by ^{1}H NMR and MS analyses, the correct stereostructure of trilobacin was finally determined.[59] Similarly, bullatacin has a relative stereochemical relationship for the adjacent THF rings and two flanking hydroxyls of *threo-trans-threo-trans-erythro* and is *R,S* for the two flanking hydroxyls. By formation of the mono-MTPA ester, followed by MS analysis of the TMS derivative, the S-configuration was assigned at C-25 placing the *erythro* on this side of the ring system.[60]

For mono-THF ring acetogenins bearing two flanking hydroxyls, such as in the annonacin A type of compound with a relative stereochemical relationship of *threo-trans-erythro* and in the cis-annonacin type of compound which are *threo-cis-threo,* it is necessary to decide on which side the *threo* configuration is located in the annonacin A type of compound or which flanking hydroxyl is *R* or *S* in the cis-annonacin type of compound. The different ^{1}H NMR patterns for mono-THF ring acetogenins bearing two flanking hydroxyls (the annonacin type) are quite distinguishable when another hydroxyl is located two, four or six carbons away. These were called the goniothalamicin, annonacin and annomontacin patterns.[20] In the goniothalamicin pattern, the signals of the methine protons of two flanking hydroxyls become two separated peaks; one appears at *delta* 3.43.[61] Characteristic chemical shift values are found among several other types of acetogenins, *e.g.* the hydroxymethine protons adjacent to the THF ring with a *threo* relationship appear at *ca. delta* 3.36-3.41. When there is another hydroxyl located two carbons away, the above protons will shift downfield to S 3.43-3.46.[36] In this way, the *threo* configurations are unambiguously assigned to several annonacin A type of acetogenins (muricatocins B[56] and C," longicin,2[7] annohexocin[36] and rollinecins A and B[62]**).** For structural determination of cis-annonacin, the C-15 and C-20 mono-MTPA esters were prepared, and the absolute configurations were assigned as C-1 *5R* and C-20S, respectively; also, the successful formation of the formaldehyde acetal across the two ring flanking hydroxyls served to prove the cis-THF structure.[63]

4.2 Absolute Configuration of Stereogenic Centres bearing Hydroxyl Groups Distant from the THF Rings

The absolute configurations of a chiral alcohol which is located close to the gama-lactone ring or the terminal methyl group can be easily determined by analysis of 'H NMR spectra of perMTPA esters, because the signals of the gama-lactone ring and terminal methyl are easily differentiated from signals of other protons. It is more

difficult to recognize the nearby proton signals when a hydroxyl is close to the THF ring system or in the case of 1,2- or I,3-diols.

By controlling the experimental esterification conditions, the mono-MTPA esters have been made to prove the configurations of C-10R in cis-annonacin63 and of C-18S in gigantetrocin B (another hydroxyl is at C-17).[69].[65] By the obsevation of the differences in the 'H NMR signals at H-4 between per *R*- and S-MTPA esters, the C-10 hydroxyl in trilobin was determined to be of the R-configuration.[59].[66] By transformation of longicin to its ketolactone derivative and then observing the differences of the signals at H-4 between the *S*- and *R*- per-MTPA esters, the C-10 hydroxyl in longicin was also proven to be of the *Rconfiguration.*[27] By formation of formaldehyde acetal derivatives between the C-10 and C-13 hydroxyls in goniothalamicin51 and longifolicin,[67] and between the C-14 and C-17 hydroxyls in gigantetrocin A,[51] and then tracing their relative stereo-chemistries, the absolute configurations of these compounds have been assigned to be C-10 *R* in the first two and C-1SR in the last.

A new approach for using the Mosher ester method to determine the absolute stereochemistries of epimers or enantiomers has been recently explored.[68] The AS values of ^{1}H NMR signals of the same S(or R)-MTPA esters in two epimers (instead of using the two different *S*- and R-MTPA esters of one epimer as is performed in the conventional method8) can predict the absolute configuration of the two epimers. Two models given in Figure 1 demonstrate how the new approach works. When there are multichiral centres in the same molecule, the method still can assign the epimeric centres, but each of the epimers must be separated and in hand. Several such examples of epimeric pairs of acetogenins, bullatacin 126 and asimicin 105, bullatalicin 191 and bullatanocin 182, rollinecins A 72 and B 73, and rollidecins A 176 and B 177, shown in Figure 2, have illustrated the application of the method.[68]

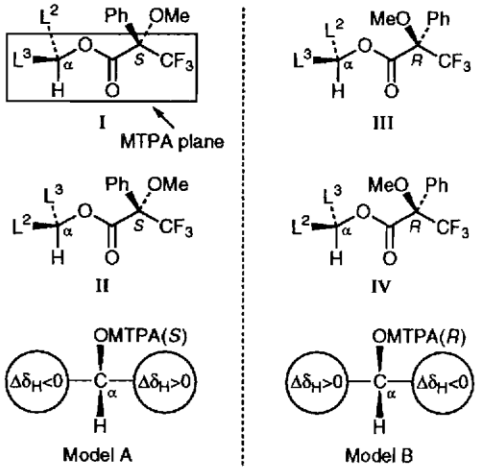
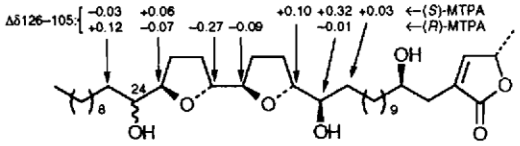
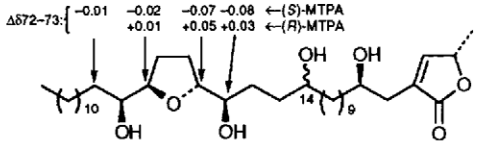


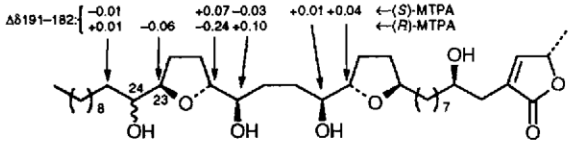
Figure 1 New Mosher ester approach for determination of the absolute stereochemistries of epimers or enantiomers



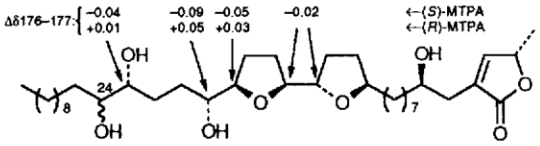
126 bullatacin (C-14*S*) and **105** asimicin (C-24*R*)



72 rollinecin A (C-14*R*) and **73** rollinecin B (C-14*S*)



191 bullatalicin (C-24*S*) and **182** bullatanocin (C-24*R*)



176 rollidecin A (C-24*R*) and **177** rollidecin B (C-24*S*)

Figure 2 Epimeric pairs of acetogenins assigned using the method shown in Figure 1

The 1,2,5-triol group is a fairly common structural feature among the Annonaceous acetogenins; thirteen examples are found among mono-THF ring compounds with one flanking hydroxyl group. Twelve of these 1,2,5-triol groups have a *threo* configuration for their vicinal 1,2-diol, and the absolute stereochemistries may either be *R,R* or *S,S.* By formation of the formaldehyde acetal to connect the two hydroxyl groups of the 2,5-diols and subsequent Mosher esterification of the 1-alcohol, the stereochemistries of the 1,2-diol at C-17,18 of gigantetrocin A were determined as *R,R.*[51] By using mono-Mosher esterifications at C-18 in both gigantetrocins A and B, the stereochemistries of their 1,2-diols were proven to be *R,R* and *S,S,* respectively64 [6a] The 'H NMR spectra of the acetonides of the hydroxy methine protons in the 1,2,5-triol moiety gave a different pattern, *i.e.* a doublet of double doublets for an *R,R* 1,2-diol; and a quartet for an *S,S* 1,2-diol. Analyses of the tri- Mosher

ester data of the 1,2,5-triol moieties in all of these acetogenins provide characteristic chemical shift values of the esterified methine proton signals, *e.g.* at *ca. S* 4.91-4.94 and *8* 5.01-5.03 *(8* 4.91-4.94 and *8* 5.05 in cases where another double bond is located two carbons away) for the S-Mosher esters in the *R,R* 1,2-diols, and at *ca. 8* 5.10-5.15 and *8* 5.16-5.19 *(8* 5.16 and *8* 5.18-5.20 in cases where another double bond is located two carbons away) for the R-Mosher esters in *R,R* 1,2-diols. In contrast, these signals are located at *ca. 8* 5.03-5.06 and *8* 5.10-5.16 for the S-Mosher esters in the *S,S* 1,2-diols and at *ca. 8* 5.03-5.04 and *8* 5.17 for the R-Mosher esters in the *S,S,* 1,2-diols.

5 Biological Activities

5.1 Studies of Mitochondrial Complex I

In our last review,[20] we predicted that the Annonaceous acetogenins would become valuable tools for the examination of complex **I** in the mitochondria. Indeed, Friedrich *et al.*[6] have now studied the binding sites of complex 1 inhibitors including annonacin (annonin VI). In this work, they found that, with respect to ubiquinone 2, annonacin inhibits mammalian NADH: ubiquinone oxidoreductase in a partially competitive manner while inhibiting the bacterial equivalent, ubiquinone- linked glucose dehydrogenase, in a competitive manner. Other molecules, such as piericidin A, fenpyroximate, phenalamid A2, thiangazole and the aurachins responded similarly, and the authors collectively grouped these as class 1 inhibitors'. Alternatively, compounds such as rotenone, phenoxan, aureothin and benzimidazole, which inhibit complex I in a noncompetitive manner with respect to ubiquinone 2 and have no effect on the bacterial glucose dehydrogenase, were termed class II inhibitors'. Thus, the acetogenins may act at a different site than rotenone as proposed by Espositi *et al.*[96]

Complex I is a complicated protein system in the mitochondria; its biochemistry will, undoubtedly, be deciphered more thoroughly in the future, and the acetogenins will become instrumental in those future experiments.

5.2 Inhibition of Tumour Cell Growth

An *in vitro* disk diffusion assay,[1] which measures zones of inhibition of cell growth around a filter paper disk, was used to test the anticancer potential of ten different Annonaceous acetogenins. All the compounds were extremely potent to both normal' cancer cells, as well as to adriamycin (multidrug) resistant cancer cells, while the effects on the growth of noncancerous rat GI epithelial cells (I18) were minimal. This study also showed how important careful dosing is when dealing with this class of compounds. For example, in Figure 3, note how bullatacin (126) at a concentration of 2.5 µg/disk is cytotoxic to all of the cell lines. At a one-tenth dilution to 0.25 µg/disk, bullatacin remained still more effective than adriamycin (at a dose of 2.5 g/disk) in all cell lines, including the multidrug resistant mouse mammary cell line, M17/Adr. Furthermore, the acetogenins are only equipotent or less potent than adriamycin to the non-cancerous I18 cells.

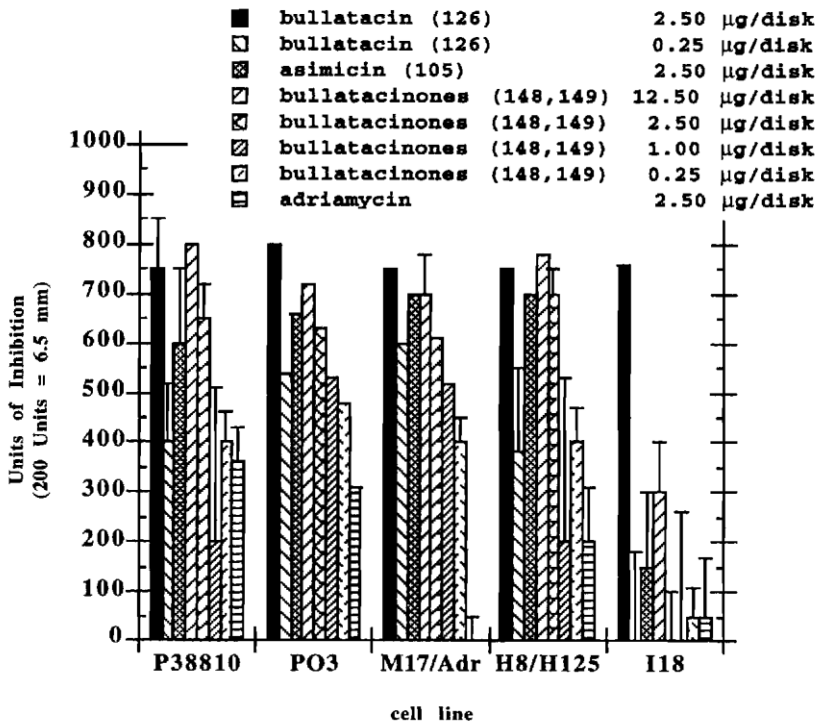


Figure 3 Inhibition of cell growth in an *in vitro* disk diffusion assay.[1] A clear zone, indicating no tumour cell growth up to a definite point, is given a number representing distance from the disk (200 units = 6.5 mm) and is illustrated by the height of the bars in the graph; beyond such a distance, 'normal' tumour cell growth exists. Further, if there is cell growth beyond the clear zone which is sporadic and fewer in number, an 'error' bar is drawn to illustrate how far such a region exists before 'normal' tumour cell growth commences. Note; not all determinations displayed sporadic growth, and therefore, they do not all receive error bars. Murine tumour cells: P388 – B cell lymphoma; PO3 – pancreatic ductile adenocarcinoma; M17/Adr – adriamycin resistant mammary carcinoma. Human cells; H8/H125 – either human colon carcinoma 8 or human lung carcinoma 125; results with either are considered comparable.[1] 'Normal' cells: I18 – immortalized rat GI epithelial cells

Table 3 Mitochondrial data compared as a Bullatacin Index. Mitochondrial data have been normalized by the daily determination of bullatacin, such that a value < 1.00 signifies an activity more potent than that of bullatacin **126**.[78]

Compound	Normalized value
Bullatacin **126**	1.00
Trilobin **164**	0.85
Trilobacin **163**	3.72
Asiminacin **109**	0.58
Motrilin **132**	1.70
Aromin **205**	28.7
Mucocin **207**	1.94
Asiminenin A **56**	33.0
Asiminenin B **40**	8.01
Longicoricin **41**	17.9
Longifolicin **1**	3.22
Gigantetroneninones **90** and **91**	4.89
Annomuricin A **60**	41.2
Annomuricin C **14**	45.9

It cannot be overemphasized how essential it is to examine carefully a wide range of concentrations when studying this class of compounds. The selectivity for cancerous cells *vs* noncancerous cells is reminiscent of the inhibition of the ubiquinone linked NADH oxidase, which is peculiar to the plasma membranes of cancerous cells, as proposed by Morré *et al.*[7] An *in vivo* study[70] with a murine teratoma model failed to test bullatacin 126 at its proven effective dose, *i.e.* 50 *fig* $kg^{-1.4}$ this teratoma study also failed to include a positive control to demonstrate that any drug is effective against this highly differentiated tumour.

5.3 Potential as Pesticides

Ratnayake *et al. 71* tested several different plant parts of *Asimina triloba,* the North American pawpaw, to determine which parts yielded both the greatest quantity of F005 (a partitioned 90 % aqueous methanol extract containing a complex mixture of acetogenins) and which parts had the most potent bioactivity in the brine shrimp lethality test, BST.[45,46] It was found that although the unripe fruit and seeds produced the highest yield, their harvest is not always reliable. Therefore, it was concluded that the harvesting of small twigs and stems may be the optimum source of biomass to supply a pesticidal mixture of the Annonaceous acetogenins.

Johnson *et al.* [72] have now improved the extraction screen for the pes(icidal preparation, by reducing it to one step, and have studied the variation in bioactivity of twigs from single trees, grown in New York state, over the course of one year. A single extraction with dichloromethane yielded an extract of equal potency to the partitioned F005 in the Ratnayake *et al.* study.[71] The potency of this extract decreased significantly in the plant material collected in the late fall and winter months. Their conclusion was that the prime collection time is from May to July which likely coincides with the time when the plant tissue is in the greatest need of protection against insects.

Thus, biomasses consisting of twigs and small branches of pawpaw and the seeds of guanabana *(Annona muricata)* could well serve as sustainable sources of acetogenin mixtures. The guanabana juice industry produces tons of guanabana seeds as a by-product,[73] and these are, currently, quite likely the most abundant readily available source of natural acetogenins. Unfortunately, these seeds only contain the less potent mono-THF ring compounds,[73] yet their extracts are still quite effective against several insect pest species. The use of the Annonaceous acetogenins in pest control is protected by our US patents.[74,75]

In the late 1800s, Eli Lilly and Company offered a fluid extract of the seeds of pawpaw *(Asimina triloba)* for sale to physicians and pharmacists to be used as an emetic.[76] In unpublished results at Asta Laboratories, bullatacin was emetic to pigs at 185 ,ug kg¯'. Such emetic effects are encouraging and serve as a safeguard against poisoning from accidental ingestion of the pesticidal acetogenin mixture.

5.4 SARs and Tumour Selectivities

The structure—activity relationships (SARs) of twenty diverse Annonaceous acetogenins in the inhibition of oxygen uptake in the rat liver mitochondrial assay[77] were explained in our last review.[20] This SAR work has now been extended to include thirteen additional compounds.[78] The latter study examined new structurally diverse compounds that have been recently isolated. A positive control of bullatacin 126 was examined during every separate determination so that the data could be both normalized to this value and compared in a bullatacin index' (Table 3) thereby limiting day to day, rat to rat, and other variabilities that are inherent in an assay of this nature.

The results (Table 3) show that two compounds, trilobin 164 and asiminacin 109, are both more active than bullatacin 126. Also, the new structural type having a hydroxylated tetrahydropyrane ring (THP), mucocin 207, was nearly as active as bullatacin 126. With non-adjacent bis-THF ring compounds, such as aromin 205, separation by more than 4 carbons between the rings caused a decrease in potency to that of a mono-THF ring acetogenin. With two virtually identical mono- THF ring acetogenins, asiminenin A 56 *vs* asiminenin B 40, the latter, with a *trans* THF ring, was approximately four times more potent than the former, with a *cis* THF ring. The mitochondrial assay measures activity at the sub-cellular level which, of course, does not address absorption, protein binding, metabolism, excretion and transport across cellular membranes.

In several recent papers, some acetogenins appear to be selectively cytotoxic for certain cancer types; altered biological transport or slight variations in receptor geometry in the membranes of such cell lines might explain these selectivities, and we hope to be able to have these compounds tested in the larger panel of human tumour cell lines at the National Cancer Institute. Longicin 57, a mono-THF ring compound, shows a potent ED_{50} value of 1.25×10^{-9} ppm in PaCa-2 cells (human pancreatic carcinoma) ;[27] longicoricin, another mono-THF ring acetogenin, showed a selective ED_{50} of $< 1 \times 10^{-}$' ppm in PC-3 cells (human prostate adenocarcinoma)." Usually, the mono- THF ring acetogenins show much reduced levels of cyto- toxicities in cell cultures.

Trilobacin 163, while not being very active against A-549 or MCF-7 cells (human lung and human breast carcinomas, respectively) had an ED_{50} of < 1 x 10^{-}'' in HT-29 cells (human colon carcinoma); trilobin, a trilobacin analogue with the 4-OH shifted to the 10 position, was more generally cytotoxic but extremely potent in all cell lines.59 *cis*Annonacin 54 also showed a surprising selectivity (ED_{50} of 1.0 x 10^{-8} ppm) against HT-29 cells (colon carcinoma).[73]

Squamotacin 123, with the hydroxylated bis-THF ring system of bullatacin 126 shifted from C-15 to C-13, and its 35 carbon counterpart, molvizarin 117, both exhibited significant selective cytotoxicities against PC-3 (prostate) cells (on the order of ED_{50} 1 x 10^{-8} ppm) with only moderate toxicity to the five other cell lines.[2] Similarly, longimicin D 103, with the bis-THF ring system of asimin 107 shifted from C-15 to C-13, showed an ED_{50} value of 1.69 x 10^{-7} ppm against PaCa-2 (pancreatic) cells.[29] The new structural type, mucocin 207, with its hydroxylated THP ring, had significant cytotoxicity to both the PaCa-2 and A-549 cell lines (pancreatic and lung carcinomas, respectively), while its formaldehyde acetal derivative was only toxic to the A-549 cells.[31] In all of the above studies, which are from our laboratories, adriamycin, a standard anticancer agent, was always run as a positive control and consistently showed nonselective cytotoxicities at ED_{50} values ranging from 10^{-1} to 10^{-3} ppm with variation between runs of not greater than two orders of magnitude (10 to 100 times).

A notable point in these comparisons is that slight variations in structure may lead to significant variability in bioactivities.[39,20] Additional *in vivo* studies[4] are sorely needed to verify such *in vitro* selectivities. These observations serve to demonstrate the necessity and merit of a search for new structural themes in this rapidly growing class of compound. Less than thirty Annonaceous species have yielded more than 220 acetogenins; there are undoubtedly many more diverse compounds to be found among the > 2000 various species in this family.[79] Some of these compounds will be optimum in structure for specific tumour types and various other uses.

6 Annonaceous acetogenins containing a Mono-THF Ring

Mono-THF compounds are the largest group of Annonaceous acetogenins. A total of ninety-four of these compounds has been reported. They can be further divided into six types according to the stereochemistries of the THF ring and flanking hydroxyl(s). These are the annonacin, cis-annonacin, annonacin A, gigantetrocin A, muricatetrocin A and muricatalin types of acetogenins (see Scheme 1, before). The first three are mono- THF ring acetogenins with two flanking hydroxyls, and the latter three are mono-THF acetogenins with one flanking hydroxyl. Usually, the potencies of mono-THF acetogenins to the different human solid tumour cell lines are around 10^{-}I to 10^{-}s ,ug $m1^{-1}$; they are usually not so active when compared to the adjacent bis-THF acetogenins. Recently, a mono-THF acetogenin, longicin, isolated from *Asimina longifolia* showed surprisingly potent selectivity to the human pancreatic carcinoma (PaCa-2) cell line at ED_{50} 10^{-9} μg $m1^{-1.27}$

6.1 Annonacin Type

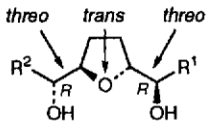
The annonacin type of acetogenin contains a mono-THF ring bearing two flanking hydroxyls. The flanking hydroxyls have R,R-stereochemistry, and the relative relationship of the THF ring and flanking hydroxyls is *threo-trans-threo;* thus, the 2,5- positions of the substituted THF ring also have an absolute configuration of *R,R.* There are fifty-one compounds now included in this type, 1-51; thirty-three are C-35 compounds and eighteen are C-37 compounds. Nearly half (twenty-four) of this compound class have been published with defined stereostructures. Four compounds, solamin 5, reticulatacin 47, corossolin 7 and corossolone 8 have been synthesized. Besides the THF ring, this type of compound usually has two to five hydroxyls, with *1,2-threo-* or *erythro-diols*, ketones and acetoxy groups sometimes present. cis-Double bonds have only been found, so far, among the C-37 compounds. The THF ring is usually positioned at C-14, 16, 18 or 20.

In the following tabulations, under the core structure, the compound name is followed by the functional groups and their positions in the carbon chain; the plant resource is given in the parentheses. R^2 represents the terminal hydrocarbon chain; R^I represents the hydrocarbon chain ending with the gama-lactone or ketolactone. An asterisk (*) indicates those compounds which are new in this review and are not included in our previous

reviews. Full structures, spectroscopic data, biological activities and sources for these (*) new compounds are given in the Appendix (Section 15). The plant names, in alphabetical order are as follows: (a) *Annona atemoya;* (b) *An. bullata;* (c) *An. cherimolia;* (d) *An. coriacea;* (e) *An. crassiflora;* (f) *An. densicoma;* (g) *An. glauca;* (h) *An. montana; (i) An. muricata;* (j) *An. purpurea;* (k) *An. reticulata; (1) An. senegalensis;* (m) *An. squamosa;* (n) *Asimina parvii fora;* (o) *As. longifolia;* (p) *As triloba;* (q) *Goniothalamus giganteus;* (r) *Rollinia membranacea;* (s) *R. mucosa; (t) R. papilionella; (u) R. sylvatica; (y) R. ulei; (w) Uvaria acuminata;* (x) *U. narum; (y) U. tonkinesis* and (z) *Xylopia aromatica.*

6.2. cis-Annonacin Type

The cis-annonacin type of acetogenins has a mono-THF ring bearing two flanking hydroxyls. The flanking hydroxyls have



C-35 compounds

1	*longifolicin[27]	14-THF, 10*R*,13*R*,18*R*-OH (o)
2	goniothalamicin[51,61]	14-THF, 4*R*,10*R*,13*R*,18*R*-OH (i, n, q)
3	*arianacin[73]	16-THF, 4*R*,12*S*,15*R*,20*R*-OH (i)
4	*javoricin[73]	16-THF, 4*R*,12*R*,15*R*,20*R*-OH (i)
5	solamin[80]	16-THF, 15,20-OH (k)
6	murisolin[81]	16-THF, 4,15,20-OH (i)
7	corossolin[82]	16-THF, 10,15,20-OH (i)
8	corossolone[82]	16-THF, 15,20-OH, 10-oxo (i)
9	annoreticuin-9-one[80]	16-THF, 4,15,20-OH, 9-oxo (k)
10	*reticulacinone[83]	16-THF, 4,15,20-OH, 11-oxo (k)
11	xylopianin[84]	16-THF, 4,8,15,20-OH (z)
12	annoreticuin[85]	16-THF, 4,9,15,20-OH (k)
13	*muricatocin A[56]	16-THF, 4*R*,10,12(*th*),15*R*,20*R*-OH (i)
14	*annomuricin C[55]	16-THF, 4*R*,10,11(*th*),15*R*,20*R*-OH (i)
15	annonacin[61,84,86,87]	16-THF, 4*R*,10*R*,15*R*,20*R*-OH (f, h, i, m, n, q, z)
16	annonacin-10-one[88,89]	16-THF, 4*R*,15*R*,20*R*-OH, 10-oxo (f, h, i)
17	8-hydroxyannonacin[90]	16-THF, 4,8,10,15,20-OH (f)
18	annomonicin[80,91]	16-THF, 4,8,13,15,20-OH (h, k)
19	*muricatalin C[92]	16-THF, 4,15,20,25-OH, 10-oxo (i)
20	*4-acetyl annonacin[28]	16-THF, 4*R*-OAc, 10*R*,15*R*,20*R*-OH (o)
21	*annotemoyin-1[93]	18-THF, 17,22-OH
22	*(2,4-*cis*)-goniothalamicinone[27]	14-THF, 10*R*,13*R*,18*R*-OH, ketolactone (2,4-*cis*) (o)
23	*(2,4-*trans*)-goniothalamicinone[27]	14-THF, 10,13,18-OH, ketolactone (2,4-*trans*) (o)
24	(2,4-*cis*)-isoannoreticuin[85]	16-THF, 9,15,20-OH, ketolactone (2,4-*cis*) (k)
25	(2,4-*trans*)-isoannoreticuin[85]	16-THF, 9,15,20-OH, ketolactone (2,4-*trans*) (k)
26	*(2,4-*cis*)-murisolinone[94]	16-THF, 15*R*,20*R*-OH, ketolactone (2,4-*cis*) (p)
27	*(2,4-*trans*)-murisolinone[94]	16-THF, 15*R*,20*R*-OH, ketolactone (2,4-*trans*) (p)
28	(2,4-*cis*)-squamone[80,95]	16-THF, 15,20-OH, 9-oxo, ketolactone (2,4-*cis*) (k, m)
29	(2,4-*trans*)-squamone[80,95]	16-THF, 15,20-OH, 9-oxo, ketolactone (2,4-*trans*) (k, m)
30	(2,4-*cis*)-isoannonacin[96]	16-THF, 10*R*,15*R*,20*R*-OH, ketolactone (2,4-*cis*) (i, p)
31	(2,4-*trans*)-isoannonacin[96]	16-THF, 10*R*,15*R*,20*R*-OH, ketolactone (2,4-*trans*) (f, p)
32	(2,4-*cis*)-isoannonacin-10-one[88,96]	16-THF, 15*R*,20*R*-OH, 10-oxo, ketolactone (2,4-*cis*) (f, i)
33	(2,4-*trans*)-isoannonacin-10-one[88,96]	16-THF, 15*R*,20*R*-OH, 10-oxo, ketolactone (2,4-*trans*) (f, i)

C-37 compounds

34	uvariamicin IV[97,98]	14-THF, 13,18-OH (b, x)
35	giganenin[34,99]	14-THF, 10*R*,13*R*,18*R*-OH, 21-ene (q)
36	gonionenin[100]	14-THF, 4,10,13,18-OH, 21-ene (q)
37	uvariamicin I[97,98]	16-THF, 15,20-OH (b, x)
38	*4-acetyl xylomaticin[28]	16-THF, 4*R*-OAc, 10*R*,15*R*,20*R*-OH (o)
39	bullatenin[98]	16-THF, 15,20-OH, 23-ene (b)
40	*asiminenin B[101]	16-THF, 4*R*,15*R*,20*R*-OH, 23-ene (p)
41	*longicoricin[67]	16-THF, 10*R*,15*R*,20*R*-OH (o)
42	xylopiacin[84]	16-THF, 4,8,15,20-OH (z)
43	xylopien[102]	16-THF, 4*R*,8,15*R*,20*R*-OH, 23-ene (z)
44	xylomaticin[84]	16-THF, 4,10,15,20-OH (z)
45	xylomatenin[102] (annogalene[103])	16-THF, 4*R*,10,15*R*,20*R*-OH, 23-ene (z)
46	squamosten-A[104]	16-THF, 4*R*,12,15*R*,20*R*-OH, 23-ene (m)
47	reticulatacin[98,105] (uvariamicin I[97])	18-THF, 17,22-OH (b, k, x)
48	*tonkinecin[30]	18-THF, 5*S*,17*R*,22*R*-OH (y)
49	annomontacin[84]	18-THF, 4,10,17,22-OH (h, q, z)
50	uvariamicin III[97,98]	20-THF, 19,24-OH (b, x)
51	montanacin[91]	20-THF, 4,8,10,19,24-OH (h)

R,S-stereochemistry and the relative stereochemical relationship of the THF ring and flanking hydroxyls is *threo—cis—threo;* thus the 2,5-positions of the substituted THF ring also have an absolute configuration of *R,S.* Five acetogenins 52-56 have been reported, so far, with the cis-annonacin type of structure. There are four C-35 compounds and one C-37 compound in this type. The stereostructure of cis-annonacin 54 has been directly assigned by the mono-MTPA ester method,[63,73] which proves the *R* and *S* configurations at C-15 and C-20; thus the *R* and *S* configurations were assigned for C-16 and C-19. The absolute stereochemistries of cis-goniothalamicin can be indirectly solved by observation of the chemical shift of one oxymethine proton (H-13), which appears downfield at fi 3.47 because there is another hydroxyl at the C-10 position. To distinguish between the cis-annonacin and annonacin types of acetogenin,[1]H NMR signals around *8* 1.5-2.0 are examined: with the cis-THF ring, two groups of signals (the protons on the THF ring) appear at *ca. 8* 1.74 and 1.93; in contrast, with the *trans-THF* ring, these are at *ca. 8* 1.66 and 1.98, respectively.

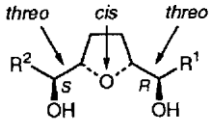
There are seventeen acetogenins reported so far with the annonacin A type of structure, 57-73; twelve of them are C-35, and five are C-37. These types of acetogenin are mono-THF ring compounds bearing two flanking

hydroxyls with a *threo—trans—erythro* relative relationship. The flanking hydroxyls have R,S-stereochemistry and thus the 2,5-positions of the substituted THF ring also have an absolute configuration of *R,R.* The stereochemistries of several compounds of this type (muricatocins B 62[56] and C 63,[55] longicin 57[2'] and rollinecins A 72 and B 73[62]) have been proven to have the R-configuration for the flanking hydroxylated carbon on the gama-lactone or ketolactone side of the THF ring and the S-configuration forthe flanking hydroxylated carbon on the hydrocarbon chain side. The hexahydroxylated compound, annohexocin [64,36] which has a 1,3,5-triol group at the C-8, 10 and 12 positions, and the 33-0H compound, jetein 65,[107] which has a saturated gama-lactone ring, are unique structural features for the annonacin A type of acetogenins.

6.4 Gigantetrocin A Type

The gigantetrocin A type of acetogenin has a mono-THF ring bearing one flanking hydroxyl. There are eighteen compounds included in this type, 74-91; twelve are C-35 compounds and six are C-37 compounds. All compounds of this type have the ring flanking hydroxyl on the hydrocarbon chain side of the THF ring; all have a 1,2-diol two carbons away from the flanking hydroxyl of the ring, with either the *threo* or *erythro* configurations. The flanking hydroxyls have S-stereochemistry, and the relative relationship of the THF ring and flanking hydroxyls is *trans—threo;* thus, the 2,5-positions of the substituted THF ring also have an absolute configuration of *R,R.* Two hexahydroxylated compounds of this type, murihexocins A 82 and B 83,[37] have been reported to bear two 1,2threo-diol s. Two pentahydroxylated acetogenins of this type, muricatatins A 77 and B 78[92] have been isolated. Muricatatin B has a 1,2,3-triol at C-17, 18 and 19 with a relative stereochemical relationship as *threo—erythro.* A mono-acetyl derivative, 4-acetyl gigantetrocin A 79,[31] has recently been found, and its absolute structure has been determined by correlation to gigantetrocin A 75 whose absolute stereochemistry is known.

Generally, the Mosher ester method can be used directly to determine the absolute configurations of the flanking hydroxyl. The absolute configurations of the 1,2-diol in the 1,2,5-triol moiety, with *R,R* or S,S-stereochemis(ry, among the gigantetrocin A type of acetogenin, can be solved either by use of per- Mosher esters or by acetonide derivatives. An effort to solve the absolute configurations of the 1,2-erythro-diols of muricatetrocin C 81, using the per-Mosher ester method, has been made,[32] but careful assignments of the ^{1}H NMR signals are necessary, since it is difficult to distinguish the signals of 1,2diols in the per-Mosher esters.



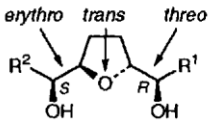
C-35 compounds

52	**cis*-goniothalamicin[73]	14-THF, 4*R*,10*R*,13*R*,18*S*-OH (i)
53	*16,19-*cis*-murisolin[106]	16-THF, 4*R*,15*R*,20*S*-OH (p)
54	**cis*-annonacin[73]	16-THF, 4*R*,10*R*,15*R*,20*S*-OH (i)
55	**cis*-annonacin-10-one[73]	16-THF, 4*R*,15*R*,20*S*-OH, 10-oxo (i)

C-37 compound

56	*asiminenin A[101]	16-THF, 4*R*,15*R*,20*S*-OH, 23-ene (p)

6.3 Annonacin A Type

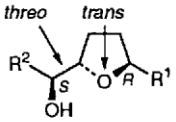


C-35 compounds

57	*longicin[27]	14-THF, 4*R*,10*R*,13*R*,18*S*-OH (o)
58	*murisolin A[106]	16-THF, 4*R*,15*R*,20*S*-OH (p)
59	annonacin A[86]	16-THF, 4,10,15,20-OH (m)
60	annomuricin A[89]	16-THF, 4*R*,10,11(*th*),15*R*,20*S*-OH (i)
61	annomuricin B[89]	16-THF, 4*R*,10,11(*ery*),15*R*,20*S*-OH (i)
62	*muricatocin B[56]	16-THF, 4*R*,10,12(*ery*),15*R*,20*S*-OH (i)
63	*muricatocin C[55]	16-THF, 4*R*,10,12(*th*),15*R*,20*S*-OH (i)
64	*annohexocin[36]	16-THF, 4,8,10,12,15,20-OH (i)
65	jetein[97,107]	16-THF, 10,15,20,33-OH, 2,33-saturated (c)
66	*annotemoyin-2[93]	18-THF, 17,22-OH (a)
67	(2,4-*cis*)-annonacin-A-one[108]	16-THF, 10*R*,15*R*,20*S*-OH, ketolactone (2,4-*cis*) (p)
68	(2,4-*trans*)-annonacin-A-one[108]	16-THF, 10*R*,15*R*,20*S*-OH, ketolactone (2,4-*trans*) (p)

C-37 compounds

69	*annosenegalin[103]	16-THF, 4,10,15,20-OH (c, l)
70	*reticulatain-1[109]	18-THF, 17,22-OH (k)
71	*reticulatain-2[109]	20-THF, 19,24-OH (k)
72	*rollinecin A[62]	18-THF, 4,14*R*,17*R*,22*S*-OH (s)
73	*rollinecin B[62]	18-THF, 4,14*S*,17*R*,22*S*-OH (s)



C-35 compounds

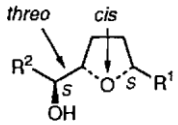
74	gigantriocin[34,110]	10-THF, 14*S*,17*R*,18*R*-OH (q)
75	gigantetrocin A[110,51,64,65,84] (10-13-*trans*-13,14-*threo*-densicomacin[111])	10-THF, 4*R*,14*S*,17*R*,18*R*-OH (f, i, q, z)
76	gigantetrocin B[64,65] (10-13-*trans*-13,14-*erythro*-densicomacin[111])	10-THF, 4*R*,14*S*,17*S*,18*S*-OH (f, i)
77	*muricatatin A[92]	10-THF, 4,14,17,18(*th*),23-OH (*i*)
78	*muricatatin B[92]	10-THF, 4,14,17,18(*th*),19(*ery*)-OH (i)
79	*4-acetyl gigantetrocin A[34]	10-THF, 4*R*-OAc, 14*S*,17*R*,18*R*-OH (q)
80	muricatetrocin B[64,65]	12-THF, 4*R*,16*S*,19*R*,20*R*-OH (i)
81	*muricatetrocin C[32]	12-THF, 4*R*,16*S*,19*R*,20*S*(*ery*)-OH (s)
82	*murihexocin A[34,37]	12-THF, 4*R*,7*S*,8*S*,16*S*,19*R*,20*R*-OH (i)
83	*murihexocin B[34,37]	12-THF, 4*R*,7*S*,8*S*,16*S*,19*S*,20*S*-OH (i)
84	(2,4-*cis*)-gigantetrocin-A-one[108]	10-THF, 14*S*,17*R*,18*R*-OH, ketolactone (2,4-*cis*) (p)
85	(2,4-*trans*)-gigantetrocin-A-one[108]	10-THF, 14*S*,17*R*,18*R*-OH, ketolactone (2,4-*trans*) (p)

C-37 compounds

86	gigantrionenin[34,112]	10-THF, 14*S*,17*R*,18*R*-OH, 21-ene (q)
87	gigantetronenin[112] (senegalene[113])	10-THF, 4,14,17,18(*th*)-OH, 21-ene (l, q, z)
88	*coriacin[114]	10-THF, 4,14,21,22-OH, 17-ene (d)
89	*4-deoxycoriacin[114]	10-THF, 14,21,22-OH, 17-ene (d)
90	*(2,4-*cis*)-gigantetroneninone[67]	10-THF, 14*S*,17*R*,18*R*(*th*)-OH, 21,22-ene, ketolactone (2,4-*cis*) (o)
91	*(2,4-*trans*)-gigantetroneninone[108]	10-THF, 14*S*,17*R*,18*R*(*th*)-OH, 21-ene, ketolactone (2,4-*trans*) (o)

6.5 Muricatetrocin A Type

Two examples 92 and 93 of the muricatetrocin A type of acetogenins have been published, and both are C-35. This type of acetogenin has a mono-THF ring and one flanking hydroxyl. The relative stereochemistries are *cis—threo.* The flanking hydroxyl is on the terminal hydrocarbon chain side of the THF ring and is proven to have an S-configuration; thus, the 2,5- positions of the substituted THF ring have an absolute stereochemistry of *S,S.*



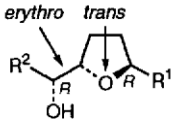
C-35 compounds

92 **cis*-gigantrionenin[34] 10-THF, 14*S*,17*R*,18*R*-OH (q)

93 muricatetrocin A[64,65] 12-THF, 4*R*,16*S*,19*R*,20*R*-OH (i)

6.6 Muricatalin Type

One acetogenin, muricatalin 94,[15] was recently reported from *Annona muricata* to have a mono-THF ring and one flanking hydroxyl with a relative stereochemical relationship of *transerythro.* From the hypothetical biogenetic pathway for the formation of mono-THF acetogenins, this type of compound can be assumed to have an R,S,R-configuration; however, further experiments are still needed to prove its absolute stereochemistry. 10,13-trans-13,14-erythro-Densicomacin[111] was initially reported to be of the muricatalin type; however, comparisons of published data have led us to conclude that it is identical to gigantetrocin B.[64,65]



C-35 compound

94 **muricatalin*[115] 10-THF, 4,14,15(*ery*),17,18(*th*)-OH (i)

7 Annonaceous Acetogenins containing Adjacent Bis-THF Rings

Adjacent bis-THF ring compounds are the second largest group among the Annonaceous acetogenins. Eighty adjacent bis-THF acetogenins have been reported. They can be divided into eight types considering the stereochemistries of the THF rings and flanking hydroxyl(s). They are the most potent group biologically among all the acetogenins; some of them, *e.g.* bullatacin 126, asimicin 105, trilobacin 163 and trilobin 164, are active at ED_{50} values of $< 10^{-12}$ μg ml^{-1} to certain human tumour cell lines.

7.1 Asimicin Type

The asimicin type of acetogenin has adjacent bis-THF rings bearing two flanking hydroxyls with relative stereochemistries of *threo—trans—threo—trans—threo.* Twenty-one compounds of this type 95-115 have been reported. The THF ring is usually placed at C-10, C-12 or C-14 in the C-35 compounds and at C-12, C-14 or C-16 in the C-37 compounds. The system of the bis-THF rings and the two flanking hydroxyls is pseudo-symmetrical, and the two flanking hydroxyls have *R,R*stereochemistry; thus, the 2,5-positions of the substituted THF rings all have an absolute stereochemistry of *R.* Usually, the terminal methyl group of adjacent bis-THF ring acetogenins shows a characteristic ^1H NMR signal at *8* 0.878 as a triplet (in 500 MHz, $CDC1_3$) (there are nine carbons between the terminal methyl group and the nearest flanking hydroxyl carbon). Recently, we found that longimicins A 102 and C 95 exhibit their terminal methyl signals at *delta* 0.880 under the same conditions (these have 13 carbons between the terminal methyl group and the flanking hydroxyl carbon), which is the same value as those of most mono-THF ring acetogenins (usually, these also have 13 carbons between the terminal methyl group and the flanking hydroxyl carbon).[29]

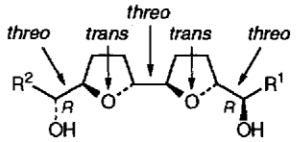
7.2 Bullatacin Type

The bullatacin type acetogenins are epimers of the asimicin type of compound. Bullatacin and asimicin differ only at C-24; the former has C-24S and the latter has C-24R. Thus, the bullatacin type acetogenins have a *threo—trans—threo—transerythro* relative relationship across their bis-THF rings and two flanking hydroxyls. Forty-six compounds of the bullatacin type 116-161 have so far been reported; seven of them are C-35 and thirty-nine are C-37 compounds. The THF ring system is usually placed at C-14 or C-16, and they have two to four hydroxyl groups; a *1,2-erythro-diol* has been found in annonin XIV 144.[127] To place the *R* or *S*

configurations on the proper side of the bis-THF ring system, the mono-MTPA ester method was applied to bullatacin 126 which proved its C-25S configuration,[60] and the formaldehyde acetyl method, combined with the MTPA ester method was applied to squamocin 129 which proved its C-15R configuration.[51]

7.3 Squamocin-I Type

The squamocin-I type of acetogenin has exactly the same relative and absolute stereochemistries of the bis-THF ring and flanking hydroxyls as the bullatacin type; however, the *R* and *S* flanking hydroxyl carbons are on the opposite side, making them *erythro—trans—threo—trans—threo* (from right to left). The

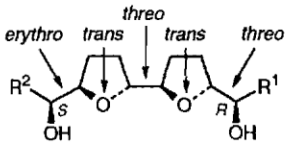


C-35 compounds

95	*longimicin C[29]	10,14-bis-THF, 4*R*,9*R*,18*R*-OH (o)
96	*longimicin B[29]	12,16-bis-THF, 4*R*,11*R*,20*R*-OH (p)
97	squamocin-K[116] (atemoyin[23])	14,18-bis-THF, 13*R*,22*R*-OH (a, m)
98	parviflorin[117–118] (squamocin-E,[116] atemoyacin A[21])	14,18-bis-THF, 4*R*,13*R*,22*R*-OH (a, b, m, n)
99	bullacin[118]	14,18-bis-THF, 6*S*,13*R*,22*R*-OH (b)
100	*cis*-isomolvizarin-2[23]	14,18-bis-THF, 13,22-OH, ketolactone (2,4-*cis*) (k)
101	*trans*-isomolvizarin-2[23]	14,18-bis-THF, 13,22-OH, ketolactone (2,4-*trans*) (k)

C-37 compounds

102	*longimicin A[29]	12,16-bis-THF, 4*R*,11*R*,20*R*-OH (o)
103	*longimicin D[29]	14,18-bis-THF, 10*R*,13*R*,22*R*-OH (o)
104	isodesacetyluvaricin[119] (4-deoxyasimicin,[98] squamocin-M[116])	16,20-bis-THF, 15,24-OH (b, m, x)
105	asimicin[120–122,8] (squamocin-H[116])	16,20-bis-THF, 4*R*,15*R*,24*R*-OH (c, l, m, p)
106	narumicin I[119]	16,20-bis-THF, 5,15,24-OH (x)
107	asimin[123]	16,20-bis-THF, 10*R*,15*R*,24*R*-OH (p)
108	squamocin-F[116]	16,20-bis-THF, 12,15*R*,24*R*-OH (m)
109	asiminacin[123] (squamocin-D[116,124])	16,20-bis-THF, 15*R*,24*R*,28*S*-OH (m, p)
110	asiminecin[123]	16,20-bis-THF, 15*R*,24*R*,29*S*-OH (p)
111	*asiminocin[125]	16,20-bis-THF, 15*R*,24*R*,30*S*-OH (p)
112	*compound-2[52]	16,20-bis-THF, 4*R*,10,15*R*,20*R*-OH (m)
113	*compound-1[52]	16,20-bis-THF, 12,15*R*,20*R*,28*S*-OH (k)
114	(2,4-*cis*)-asimicinone[126]	16,20-bis-THF, 15*R*,24*R*-OH, ketolactone (2,4-*cis*) (p)
115	(2,4-*trans*)-asimicinone[126]	16,20-bis-THF, 15*R*,24*R*-OH, ketolactone (2,4-*trans*) (p)



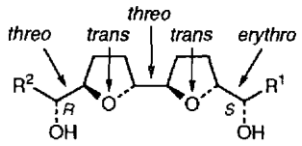
C-35 compounds

116	neoannonin[116] (squamocin-J[128])	14,18-bis-THF,	13*R*,22*S*-OH (m)
117	molvizarin[120,90,113]	14,18-bis-THF,	4,13,20-OH (c, l, n)
118	squamocin-B[116,124]	14,18-bis-THF,	26*S*,13*R*,22*S*-OH (m)
119	itrabin[90,130]	14,18-bis-THF,	13,22,23-OH, 2,33-saturated (c)
120	*atemoyacin B[22]	14,18-bis-THF,	13,22,27-OH
121	*cis*-isomolvizarin-1[23]	14,18-bis-THF,	13,22-OH, ketolactone (2,4-*cis*) (k)
122	*trans*-isomolvizarin-1[23]	14,18-bis-THF,	13,22-OH, ketolactone (2,4-*trans*) (k)

C-37 compounds

123	*squamotacin[2] (glaucanisin[131])	14,18-bis-THF,	4,13,22-OH (g, m)
124	uvaricin[35,8,132]	16,20-bis-THF,	15*R*-OH, 24*S*-OAc (j, w)
125	desacetyluvaricin[130,133] (squamocin-L[116])	16,20-bis-THF,	15*R*,24*S*-OH (b, m, w)
126	bullatacin[57,8,58,95,105] (squamocin-G,[116] 14-hydroxy-25-desoxyrollinicin,[134,135] rolliniastatin 2,[135,90] annonin VI[122])	16,20-bis-THF,	4*R*,15*R*,24*S*-OH (b, c, l, k, m, n, p, s)
127	narumicin II[119]	16,20-bis-THF,	5,15,24-OH (x)
128	bullatin[136]	16,20-bis-THF,	10*S*,15*R*,24*S*-OH (r)
129	squamocin[90,99,113,124, 128,137,138,51] (annonin I[122])	16,20-bis-THF,	15*R*,24*S*,28*S*-OH (b, c, m, l, r, k)
130	rollinicin[139]	16,20-bis-THF,	15,24,28-OH (t)
131	squamocin-28-one[140]	16,20-bis-THF,	15,24-OH, 28-oxo (x)
132	motrilin (squamocin-C)	16,20-bis-THF,	15*R*,24*S*,29*S*-OH (c, m)
133	bullanin[136]	16,20-bis-THF,	15,24,30-OH (p)
134	*(30*S*)-bullanin[141]	16,20-bis-THF,	15*R*,24*S*,30*S*-OH (p)
135	*(30*R*)-bullanin[141]	16,20-bis-THF,	15*R*,24*S*,30*R*-OH (p)
136	purpureacin[132]	16,20-bis-THF,	4,12,15,24-OH (j)
137	*annoglaucin[26]	16,20-bis-THF,	4,10,15,24-OH (g)
138	rioclarin[138]	16,20-bis-THF,	4,15,24,28-OH (r)
139	*(30*S*)-hydroxybullatacin[142]	16,20-bis-THF,	4*R*,15*R*,24*S*,30*S*-OH (b)
140	*(30*R*)-hydroxybullatacin[142]	16,20-bis-THF,	4*R*,15*R*,24*S*,30*R*-OH (b)
141	*31-hydroxybullatacin[142]	16,20-bis-THF,	4*R*,15*R*,24*S*,31*R*-OH (b)
142	*32-hydroxybullatacin[142]	16,20-bis-THF,	4*R*,15*R*,24*S*,32*R*-OH (b)
143	panalicin[140]	16,20-bis-THF,	5,15,24,28-OH (x)
144	annonin XIV[127]	16,20-bis-THF,	11,12(*ery*),15-24-OH (m)
145	laherradurin[90,121]	16,20-bis-THF,	15,24,35-OH, 2,35-saturated (c)
146	(2,4-*cis*)-bullatacinone[8,57,95,23,58]	16,20-bis-THF,	15,24-OH, ketolactone (2,4-*cis*) (b, k, m, p)
147	(2,4-*trans*)-bullatacinone[8,57,95,23,58]	16,20-bis-THF,	15,24-OH, ketolactone (2,4-*trans*) (b, k, m, p)
148	(2,4-*cis*)-10-hydroxybullatacinone[143,142]	16,20-bis-THF,	10,15,24-OH, ketolactone (2,4-*cis*) (b)
149	(2,4-*trans*)-10-hydroxybullatacinone[143,142]	16,20-bis-THF,	10,15,24-OH, ketolactone (2,4-*trans*) (b)
150	(2,4-*cis*)-12-hydroxybullatacinone[143,142]	16,20-bis-THF,	12,15,24-OH, ketolactone (2,4-*cis*) (b)
151	(2,4-*trans*)-12-hydroxybullatacinone[143,142]	16,20-bis-THF,	12,15,24-OH, ketolactone (2,4-*trans*) (b)
152	*(2,4-*cis*)-28-hydroxybullatacinone[142]	16,20-bis-THF,	15*R*,24*S*,28*S*-OH, ketolactone (2,4-*cis*) (b)
153	*(2,4-*trans*)-28-hydroxybullatacinone[142]	16,20-bis-THF,	15*R*,24*S*,28*R*-OH, ketolactone (2,4-*trans*) (b)
154	(2,4-*cis*)-29-hydroxybullatacinone[143,142]	16,20-bis-THF,	15*R*,24*S*,29*S*-OH, ketolactone (2,4-*cis*) (b)
155	(2,4-*trans*)-29-hydroxybullatacinone[143,142]	16,20-bis-THF,	15*R*,24*S*,29*R*-OH, ketolactone (2,4-*trans*) (b)
156	(2,4-*cis*)-30-hydroxybullatacinone[53,142]	16,20-bis-THF,	15*R*,24*S*,30-OH, ketolactone (2,4-*cis*) (b)
157	(2,4-*trans*)-30-hydroxybullatacinone[53,142]	16,20-bis-THF,	15*R*,24*S*,30-OH, ketolactone (2,4-*trans*) (b)
158	(2,4-*cis*)-31-hydroxybullatacinone[53,142]	16,20-bis-THF,	15*R*,24*S*,31-OH, ketolactone (2,4-*cis*) (b)
159	(2,4-*trans*)-31-hydroxybullatacinone[53,142]	16,20-bis-THF,	15*R*,24*S*,31-OH, ketolactone (2,4-*trans*) (b)
160	(2,4-*cis*)-32-hydroxybullatacinone[53,142]	16,20-bis-THF,	15*R*,24*S*,32-OH, ketolactone (2,4-*cis*) (b)
161	(2,4-*trans*)-32-hydroxybullatacinone[53,142]	16,20-bis-THF,	15*R*,24*S*,32-OH, ketolactone (2,4-*trans*) (b)

assignments of the stereochemistries of this compound were made by direct comparison of squamocin-J (neoannonin) and squamocin-I;116 the two compounds have different retention times on reversed phase HPLC, and also there are tiny differences of some signals in the 13C NMR spectra. Since squamocin-I 162 represents a new type of structure, further evidence would be helpful to confirm its absolute stereochemistry.

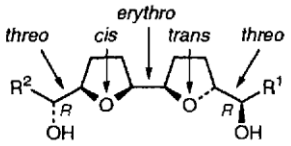


C-35 compound

162	squamocin-I[116]	14,18-bis-THF,	13*S*,22*R*-OH (m)

7.4 Trilobacin Type

The trilobacin type of acetogenin has a *threo—trans—erythrocis—threo* relative stereochemistry and *R*, R-configurations for their adjacent bis-THF rings and two flanking hydroxyls. Three C-37 compounds of this type 163-165 have been isolated so far from *Asimina triloba.* They are probably the most potent acetogenins discovered so far; in several solid human tumour cell lines they are active at ED,$_{50}$ values of < 10^{-1}Z µg m1-1 56.59 Since they have the *erythro* configuration between the two THF rings, these *erythro* protons show characteristic signals in their 'H NMR spectra at d 3.95-4.05 as two separated multiplets.

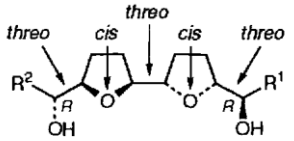


C-37 compounds

163	trilobacin[58,59]	16,20-bis-THF, 4*R*,15*R*,24*R*-OH (p)
164	trilobin[59]	16,20-bis-THF, 10*R*,15*R*,24*R*-OH (p)
165	*asitribin[94]	16,20-bis-THF, 15*R*,24*R*,28*S*-OH (p)

7.5. Squamocin-N Type

The squamocin-N type of acetogenin has a *threo—cis—threocis—threo* relative stereochemical relationship and *R,R* configurations for the adjacent bis-THF rings and their flanking hydroxyls. This type of structure is pseudo-symmetrical, and using the MTPA ester method can give definite results. Only one C-37 compound of this type 166 has been reported.[116]

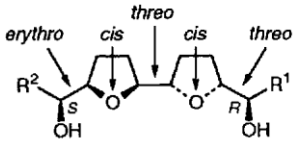


C-37 compound

166	squamocin-N[116]	16,20-bis-THF, 15*R*,24*R*-OH (m)

7.6 Rolliniastatin 1 Type

Five acetogenins 167-171 have been published, so far, having the rolliniastatin 1 type of adjacent bis-THF structure with two flanking hydroxyls. They have a *threo—cis—threo—cis—erythro* relative stereochemical relationship and *R,S* configurations around the adjacent bis-THF rings and flanking hydroxyls. The absolute stereochemistry of rolliniastatin 1 168 was proven by Mosher ester analysis and has now been confirmed by total synthesis.[14]



C-37 compounds

167	membranacin[138]	16,20-bis-THF, 15,24-OH (r)
168	rolliniastatin 1[144,8,138,132]	16,20-bis-THF, 4*R*,15*R*,24*R*-OH (j, r, s)
169	4-hydroxy-25-deoxyneorollinicin[145]	16,20-bis-THF, 4,15,24-OH (t)
170	(2,4-*cis*)-rollinone[133,146]	16,20-bis-THF, 15,24-OH, ketolactone (2,4-*cis*) (s)
171	(2,4-*trans*)-rollinone[133,146]	16,20-bis-THF, 15,24-OH, ketolactone (2,4-*trans*) (s)

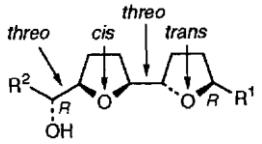
7.7 Bulladecin Type

The bulladecin type acetogenins have adjacent bis-THF rings and one flanking hydroxyl. The MTPA ester method was applied to asimilobin 172 and goniodenin 173; in this way, the absolute stereochemistry of the flanking hydroxyl carbon was determined to be *S.* By tracing the *trans—threo—trans—threo* relative relationship, the 2,5-substituted THF rings have an absolute stereochemistry of *R,S,S,S,* respectively. This unique structural feature prompts us to speculate that their biogenesis starts with cyclization from the left hand side of the molecule (see Scheme 3).

7.8 Rollidecin A Type

Two rollidecin A types of C-37 acetogenin, 176 and 177, have been isolated recently from *Rollina mucosa.* The flanking hydroxyl carbon was determined to have an absolute configuration of *R* by the Mosher ester method,

and the two THF rings were deduced to be *trans* and *cis*, respectively. Since no model compounds are available for comparison, further evidence is needed to confirm the absolute stereochemistry of this type of acetogenin.



C-37 compounds

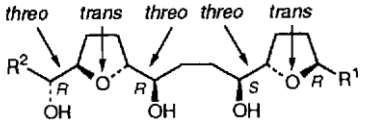
176	*rollidecin A[32]	12,16-bis-THF, 4*R*,20*R*,23*R*,24*R*-OH (s)
177	*rollidecin B[32]	12,16-bis-THF, 4*R*,20*R*,23*R*,24*S*-OH (s)

8 Annonaceous Acetogenins containing Nonadjacent Bis-THF Rings

Twenty-eight non-adjacent bis-THF acetogenins have been reported, so far, and they can be divided into seven types. They are the gigantecin, 12, 15-cis-bullatanocin, bullatalicin, 12,15cis-bullatalicin, sylvaticin, cis-sylvaticin and aromin types. The first six types consist of two separated mono-THF rings, one bearing one flanking hydroxyl and the other bearing two flanking hydroxyls, and the two THF rings are separated by four carbons. The last type, the aromin type, has two THF rings at C-4 and C-14. Because the spectral features are quite similar to some of the adjacent bis-THF ring acetogenins, some incorrect structures and/or assignments of relative stereochemistries exist in the literature.[127,147] The formaldehyde acetal method was introduced to determine the absolute stereochemistries of the non-adjacent bis-THF ring acetogenins and provided unambiguous solutions of the absolute structures for bullatanocin 182, bullatalicin 191, *cis*- and trans-bullatanocinones, and *cis*- and trans-bullatalicinones.[51] Later, the same method was used with sylvaticin 203 and cis-sylvaticin 204.[148] Using per-Mosher ester derivatives compared with model compounds, the absolute stereostructures of squamostatins-C 184, and –E 181, and squamostatins-A194, -B 192 and -D 190, have been determined.[149] Recently, the absolute structure of gigantecin 180 has also been determined by X-ray crystallography and the Mosher ester method.[9]

8.1 Gigantecin Type

The gigantecin type acetogenins have two non-adjacent THF rings separated by four carbons. One THF ring has one flanking hydroxyl, and the other has two flanking hydroxyls. By comparisons with model compounds of mono-THF rings bearing one or two flanking hydroxyls, it is not difficult to determine their relative configurations. They are *trans—threo*, *threo—trans—threo* (from right to left). Several compounds of this type have had their absolute stereostruc(ures defined by using the formaldehyde acetal and Mosher ester methods.[51] The stereochemistry of the mono-THF ring with *one* flanking hydroxyl is the same as that of the gigantetrocin A type of mono-THF acetogenin, and the stereochemistry of the other mono-THF ring with *two* flanking hydroxyls is the same as that of the annonacin type of acetogenin. Nine compounds 178-186 belong to the gigantecin type: one is C-35, and eight are C-37.



C-35 compound

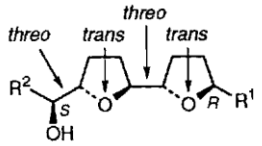
178	parvifloracin[117]	10,18-bis-THF, 4,14,17,22-OH (n)

C-37 compounds

179	4-deoxygigantecin[99]	10,18-bis-THF, 14,17,22-OH (q)
180	gigantecin[150,9]	10,18-bis-THF, 4,14,17,22-OH (d, q)
181	squamostatin-E[149]	12,20-bis-THF, 16*S*,19*R*,24*R*-OH (m)
182	bullatanocin[51,151,152] (annonin IV,[127] crassiflorin[25])	12,20-bis-THF, 4*R*,16*S*,19*R*,24*R*-OH (b, e, m)
183	cherimolin-2[90]	12,20-bis-THF, 4,16,19,24-OH (c)
184	squamostatin-C[149]	12,20-bis-THF, 4*R*,16*S*,19*R*,24*R*-OH (m)
185	(2,4-*cis*)-bullatanocinone[51,152]	12,20-bis-THF, 16*S*,19*R*,24*R*-OH, ketolactone (2,4-*cis*) (b)
186	(2,4-*trans*)-bullatanocinone[51,152]	12,20-bis-THF, 16*S*,19*R*,24*R*-OH, ketolactone (2,4-*trans*) (b)

8.2. 12,15-cis-Bullatanocin Type

The 12,15-cis-bullatanocin type of acetogenin is different from the gigantecin type at only one chiral centre; it has an S- configuration at the first THF ring on the non-flanking hydroxyl side, whereas the gigantecin type has an R-configuration at this



C-35 compound

172	*asimilobin[94,44]	10,14-bis-THF, 4*R*,18*S*-OH (p, q)

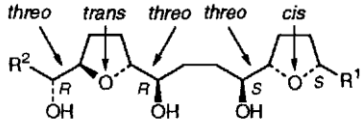
C-37 compounds

173	*goniodenin[44]	10,14-bis-THF, 4*R*,18*S*-OH, 21,22-ene (q)
174	(2,4-*cis*)-bulladecinone[142,50]	12,16-bis-THF, 20,23,24(*ery*)-OH, ketolactone (2,4-*cis*) (b)
175	(2,4-*trans*)-bulladecinone[142,50]	12,16-bis-THF, 20,23,24(*ery*)-OH, ketolactone (2,4-*trans*) (b)

chiral centre. These acetogenins have *cis—threo, threo—transthreo* relative stereochemical relationships with their respective THF rings and flanking hydroxyls. Three C-37 acetogenins of this type 187-189 have been found and all have C-12S configurations.

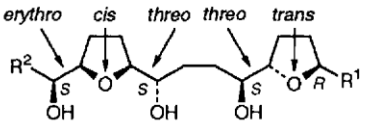
8.5 Sylvaticin Type

The sylvaticin type of acetogenin, so far, has only one example. This type of compound has a *trans—threo, threo—cis—erythro* relationship for the THF rings and flanking hydroxyls. Sylvaticin 203 was the third example reported of the nonadjacent bis-THF ring acetogenins; incorrect assignments were made for the *erythro* configuration at C-19/20, and both THF rings were assigned as *trans.*[158] The revision of the structure was first made in our third review based on the reanalysis of published spectral data ;[2o] later the formaldehyde acetal and Mosher ester methods provided experimental evidence of the absolute structure.[148] In sylvaticin 203, the second THF ring and flanking hydroxyls have a *threo—cis—erythro* relationship. No other natural mono-THF ring acetogenins, so far, have been found to have this relationship.



C-37 compounds

187	12,15-*cis*-bullatanocin[153]	12,20-bis-THF, 4*R*,16*S*,19*R*,24*R*-OH (b)
188	(2,4-*cis*)-12,15-*cis*-bullatanocinone[153]	12,24-bis-THF, 16*S*,19*R*,24*R*-OH, ketolactone (2,4-*cis*) (b)
189	(2,4-*trans*)-12,15-*cis*-bullatanocinone[153]	12,24-bis-THF, 16*S*,19*R*,24*R*-OH, ketolactone (2,4-*trans*) (b)

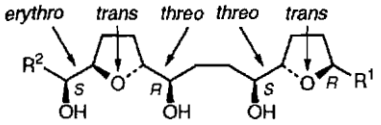


C-37 compound

203	sylvaticin[158,132,148] (uleicin A[159])	12,20-bis-THF, 4*R*,16*S*,19*R*,24*S*-OH (j, u, s, v)

8.3 Bullatalicin Type

The bullatalicin type of acetogenin is also epimeric with the gigantecin type of compounds. The difference between the bullatalicin type and the gigantecin type is at the flanking hydroxyl carbon of the second THF ring on the side of the terminal hydrocarbon chain. The bullatalicin type have *trans—threo, threo—trans—erythro* relative stereochemical relationships at the two THF rings and flanking hydroxyls. Nine C-37 compounds 190-198 belong to this type of acetogenin, andall are C-24S.

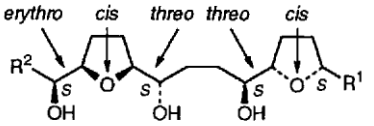


C-37 compounds

190	squamostatin-D[149,119]	12,20-bis-THF, 16*S*,19*R*,24*S*-OH (m, x)
191	bullatalicin[154,102,51,149,151] (annonin VIII[127])	12,20-bis-THF, 4*R*,16*S*,19*R*,24*R*-OH (b, m)
192	squamostatin-B[102,149]	12,20-bis-THF, 4*R*,16*S*,19*R*,24*R*-OH (m)
193	cherimolin-1[155,90,132]	12,20-bis-THF, 4,16,17,24-OH (c, j)
194	squamostatin-A[124,51,149,156] (annonin XVI,[127] squamostatin-B[157])	12,20-bis-THF, 16*S*,19*R*,24*R*,28*S*-OH (m)
195	almunequin[90,23,121]	12,20-bis-THF, 16*S*,19*R*,24*R*,28*S*-OH (c, k)
196	otivarin[90] (dihydrocherimolin)[155]	12,20-bis-THF, 16,19,24,35-OH, 2,35-saturated (c)
197	(2,4-*cis*)-bullatalicinone (*cis*-iso-cherimolin[23,51,147,151])	12,20-bis-THF, 16*S*,19*R*,24*R*-OH, ketolactone (2,4-*cis*) (b, k)
198	(2,4-*trans*)-bullatalicinone (*trans*-isocherimolin[23,51,147,151])	12,20-bis-THF, 16*S*,19*R*,24*R*-OH, ketolactone (2,4-*trans*) (b, k)

8.6 cis-Sylvaticin Type

The cis-sylvaticin type of acetogenin also has only one example. cis-Sylvaticin 204 and sylvaticin 203 are epimeric. They are different at C-12, as cis-sylvaticin is C-12S and sylvaticin is C- 12R. The absolute stereostructure of cis-sylvaticin 204 has been recently determined also by the formaldehyde acetal and Mosher ester methods. It has S,S,S-stereochemistry for the first THF ring and its one flanking hydroxyl and *S,S,R,S,-stereochemistry* for the second THF and its two flanking hydroxyls.



C-37 compound

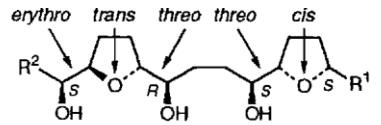
204	**cis*-sylvaticin[148]	12,20-bis-THF, 4*R*,16*S*,19*S*,24*S*-OH (s)

8.4 12,15-cis-Bullatalicin Type

The 12,15-cis-bullatalicin type acetogenins are epimeric to the bullatalicin type just as the 12,15-cis-bullatanocin type is epimeric with the gigantecin (bullatanocin) type. They are different at the first THF ring on the non-flanking hydroxyl side. They have *cis—threo, threo—trans—erythro* relative relationships at the THF rings and flanking hydroxyls. Four C-37 acetogenins 199-202 belong to this type, and all are C-12S and C-24S.

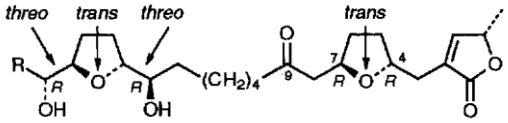
8.7 Aromin Type

Aromin 205 and aromicin 206 represent a new type of acetogenin recently isolated from *Xylopia aromatica.* This type of compound has two-non-adjacent THF rings at C-4 and C15, the first THF ring without any flanking hydroxyls and the second THF ring bearing two flanking hydroxyls. They differ in that aromin 205, is C-35 and aromicin 206 is C-37 with two additional methylenes on the hydrocarbon end of the chain.



C-37 compounds

199	12,15-*cis*-bullatalicin[153]	12,20-bis-THF, 4*R*,16*S*,19*R*,24*S*-OH (b)
200	12,15-*cis*-squamostatin-A[156,149]	12,20-bis-THF, 16*S*,19*R*,24*S*,28*S*-OH (m)
201	(2,4-*cis*)-12,15-*cis*-bullatalicinone[153]	12,24-bis-THF, 16*S*,19*R*,24*S*-OH, ketolactone (2,4-*cis*) (b)
202	(2,4-*trans*)-12,15-*cis*-bullatalicinone[153]	12,24-bis-THF, 16*S*,19*R*,24*S*-OH, ketolactone (2,4-*trans*) (b)



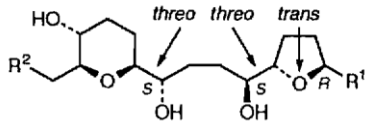
C-35 compound
205 *aromin[33] 4,16-bis-THF, 15*R*,20*R*-OH, 9-oxo (z)

C-37 compound
206 *aromicin[33] 4,16-bis-THF, 15*R*,20*R*-OH, 9-oxo (z)

9 Annonaceous Acetogenins containing Nonadjacent THF and THP Rings

9.1 Mucocin Type

A unique acetogenin containing a tetrahydropyran (THP) ring, mucocin 207, has been recently isolated from *Rolling mucosa."* Mucocin has a mono-THF ring bearing one flanking hydroxyl and a 2,6-substituted, 5-hydroxy pyran ring. The hypothetical biogenetic pathway for mucocin (Scheme 4) is quite similar to those of several other non-adjacent bis-THF ring acetogenins, such as sylvaticin 203, and bullatalicin 191; it seems that the cyclization simply started from C-23 instead of from C-24. Mucocin 207 showed very good potencies against several human solid tumour cell lines (lung carcinoma, ED, 1.0 x 10^{-6} pg ml^{-1}; pancreas carcinoma, ED_{50} 4.7 x 10^{-7} *pg* ml^{-1}) and was active in inhibiting oxygen uptake by rat liver mitochondria; the latter observation demonstrated that some new cytotoxic mechanism was not created by the THP ring.[31]

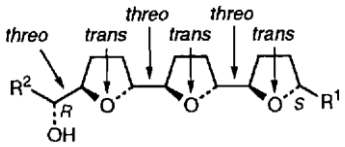


C-37 compound
207 *mucocin[31] 12-THF, 20-THP, 4*R*,16*S*,19*S*,23*R*-OH (s)

10 Annonaceous Acetogenins containing Adjacent Tris-THF Rings

10.1 Goniocin Type

The goniocin type of acetogenin has only one example, 208. The relative stereochemical relationship seems to be *transthreo—trans—threo—trans—threo* based on the analysis of ^{1}H NMR data. Using the Mosher ester method, the flanking hydroxyl carbon was determined to have the R-configuration. The other chiral centres, thus, were deduced from the relative stereochemistries.



C-37 compound
208 goniocin[43] 10,14,18-tri-THF, 4*R*,22*R*-OH (q)

11 Annonaceous Acetogenins containing no THF or THP Rings

These refer to the growing list of Annonaceous compounds with C-35 or C-37 long hydrocarbon chains and a methylated alpha,beta-unsaturated gama-lactone at one end, but no THF or THP rings. They often bear hydroxyls, ketones, epoxides and/or double bonds. Due to the locations of their dienes, expoxides or hydroxyls, they are considered to be precursors in the formation of the THF or THP acetogenins. So far, fifteen non-ring acetogenins 209-223 have been isolated.

C-35 compounds		
209	reticulatamol[160]	15-OH (k)
210	*reticulatamone[109]	15-oxo (k)
211	giganin[161]	4,10,17,18(*th*)-OH, 13-ene (q)
212	epomuricenin-B[162]	13-epoxy, 17-ene (i)
	epomuricenin-A[162] (epoxymurin-A[163])	15-epoxy, 19-ene (i)
213	epoxymurin-B[163]	19-epoxy, 15-ene (i)
214	diepomuricanin[164,165]	15,19-epoxy (i, k)
215	corepoxylone[166]	15,19-epoxy, 10-oxo (i)
216	*venezenin[167]	4,17,18(*th*)-OH, 21-ene, 10-oxo (z)
C-37 compounds		
217	*tonkinelin[168]	17,18(*th*)-OH (y)
218	dieporeticanin-1[165]	17,21-epoxy (k)
219	dieporeticanin-2[165]	19,23-epoxy (k)
220	dieporeticenin[165]	15,19-epoxy, 23-ene (k)
221	tripoxyrollin[169]	15,19,23-epoxy (r)
222	trieporeticanin[165]	15,19,23-epoxy (k)
223	*coriadenin[114]	4,10,21,22(*th*)-OH, 13,17-diene (d)

12 Semi- and Totally-synthesized Annonaceous Acetogenins

The potent and diverse bioactivities of Annonaceous acetogenins are attracting the attention of many synthetic chemists who are striving to achieve their total syntheses. Earlier results have been summarized in our previous three reviews.[38,39].[20] More recent successes include the total syntheses of bullatacin 126,[10,11,13] asimicin 105,[10]. [11](+)-15,24-bisepi-bullatacin227," corossolone 8 and corossolin 7,[10] gigantetrocin A 75 [13,14threo-densicomacin],[19] and parviflorin 98.[12] It is interesting to observe that the unnatural (+)-15,24-bisepi-bullatacin 227 has decreased *in vitro* antitumour activity against P388 compared with bullatacin 126, its natural stereoisomer.[13]

To date, most synthesized acetogenins belong to the mono- THF ring and adjacent bis-THF ring compounds. It is generally difficult to synthesize acetogenins of the latter type due to the increased complexities of their stereochemical structures, although their superior bioactivities are attractive. Almost without exception, convergent strategies based on the coupling of a bis-THF ring core and a terminal gama-lactone synthon are employed.

Although the tactical details are very individualistic with each synthetic team, it seems that, for most cases, the construction of the bis-THF ring moiety involves the opening of epoxide(s) by neighbouring hydroxyl(s), which are often masked in the earlier stages of the synthesis. This idea, which was termed as directional 'epoxide cascading' by Hoye *et al.,* [170] is very reminiscent of the hypothesized biogenesis of the acetogenins (Schemes 1-4).[20].[38].[38] To achieve the specific stereochemistry, either chiral starting materials or some efficient asymmetric reactions, such as Sharpless asymmetric epoxidation and Sharpless asymmetric dihydroxylation, are employed. The enantiomeric excesses of the intermediates are usually monitored by applying Mosher's method. It is amazing that several teams have already achieved two-digit total yield returns after executing fifteen or more synthetic steps.

No successful syntheses of the other major type acetogenins, *i.e.* those having adjacent bis-THF rings bearing one flanking hydroxyl, non-adjacent bis-THF rings, non-adjacent THF and THP rings, and adjacent tris-THF rings, have been reported to date. This could be related to the challenge of modifying the existing protocols for synthesizing other types of acetogenin.

For more details about the syntheses, interested readers are asked to refer to the original papers as listed above and some reviews which are devoted to this specific area.[42,171.172]

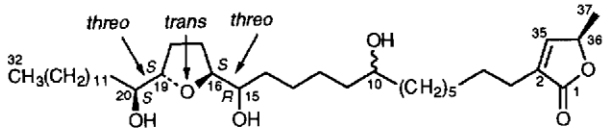
During the structural determinations and total syntheses of acetogenins, some unnatural acetogenins have been produced. Because these compounds are unnatural, they could not be conveniently classified in the same way as the natural acetogenins. These are:

(i) the mono-THF ring acetogenin, 10,15*R*,16*S*,19*S*,20*S*,34*R*-corossolin **224**[173]

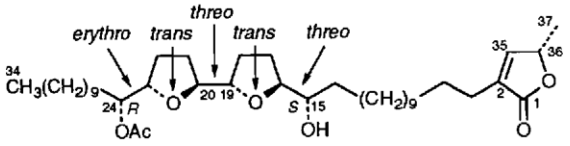
(ii) the adjacent bis-THF acetogenins, (+)-15,16,19,20,23,24-*hexepi*-uvaricin **225**,[174] (−)-bullatacin **226**,[175] (+)-15,24-*bisepi*-bullatacin **227**[13] and cyclogonionenins C **228** and T **229**[100]

(iii) the non-adjacent bis-THF acetogenin, C-18,21-*cis*-gigantecin **230**[100]

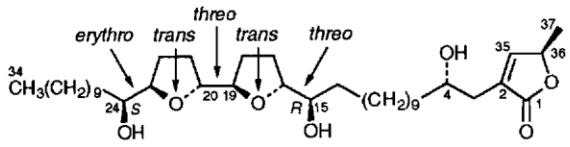
(iv) the adjacent tris-THF acetogenins, cyclogoniodenins C **231** and T **232**[44]



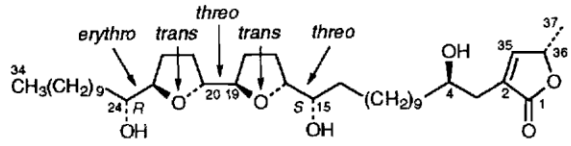
224 10ξ,15*R*,16*S*,19*S*,20*S*,34*R*-corossolin



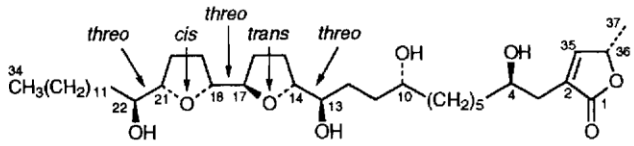
225 (+)-15,16,19,20,23,24-*hexepi*-uvaricin



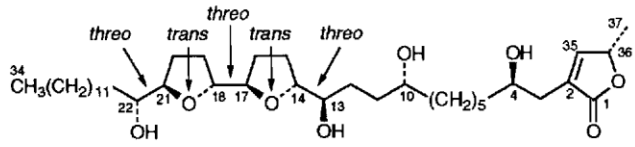
226 (–)-bullatacin



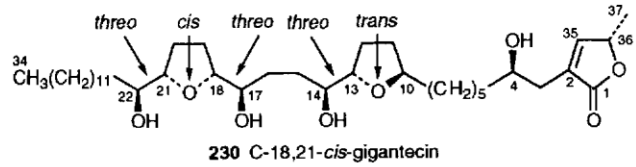
227 (+)-15,24-*bisepi*-bullatacin



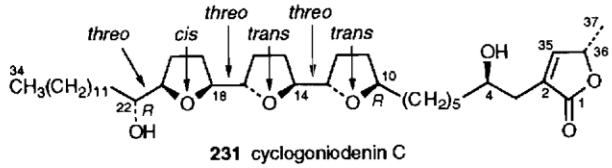
228 cyclogonionenin C



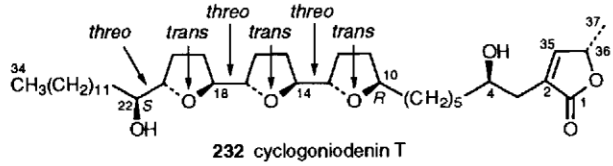
229 cyclogonionenin T



230 C-18,21-*cis*-gigantecin



231 cyclogoniodenin C



232 cyclogoniodenin T

13 Uncertain Structures of Acetogenins

In our previous reviews we revised several incorrect structures of acetogenins. However, there are still some published structures of acetogenins which remain uncertain. These structures will be presented here. Isorollinicin was reported as a non-ring acetogenin with one hydroxyl, but the placement of the hydroxyl was unknown.[139] Uleicins-B, D and E have been described as adjacent bis-THF ring acetogenins bearing two flanking hydroxyls, a 4-hydroxyl, and one more hydroxyl which could not be defined; uleicin-C was a non-adjacent bis- THF acetogenin.[159] The authors mentioned in a more recent publication that their published structures were incorrect." Purpureacin-1 was published as a non-adjacent bis-THF acetogenin without the assignment of relative stereochemistries. From the published data it seems to be a mixture of C-12/15- *cis* and -*trans* isomers.[132] Annonastatin and epoxyrollins A and B were reported to be C-38 or C-36 compounds.86,[176].[159] No high resolution MS data supported the proposed molecular formulae; these structures could be highly unusual, and it is unlikely that they will be confirmed. A diepoxide acetogenin, diepoxymotin, has been reported to have an adjacent epoxide moiety at C-11 and C-13;[147] since no high resolution MS data supported the fragmentations, further evidence is needed for the placement of these epoxides.

Acknowledgements. Support from ROI grant no. CA30909 from the National Cancer Institute, National Institutes of Health, and fellowship support from the Purdue Research Foundation and the Indiana Elks Cancer Research Fund are gratefully acknowledged. This review is dedicated to the memory of Janean A. (McLaughlin) Kistel whose courageous battle with breast cancer serves as a continual inspiration.

14 References

1 N. H. Oberlies, J. L. Jones, T. H. Corbett, S. S. Fotopoulos and J. L. McLaughlin, *Cancer Lett.,* 1995, 96, 55.
2 D. C. Hopp, L. Zeng, Z.-M. Gu and J. L. McLaughlin, *J. Nat. Prod.,* 1996, 59, 96.
3 M. Londershausen, W. Leicht, F. Lieb, H. Moeschler and H. Weiss, *Pectic. Sci.,* 1991, 33, 427.
4 K. I. Ahammadsahib, R. M. Hollingworth, J. P. McGovren, Y.-H. Hui and J. L. McLaughlin, *Life Sci.,* 1993, 53, 1113.
5 M. A. Lewis, J. T. Arnason, N. J. R. Philogene, J. K. Rupprecht and J. L. McLaughlin, *Pectic. Biochem. Physiol.,* 1993, 45, 1523.
6 T. Friedrich, P. Van Heek, H. Leif, T. Ohmishi, E. Forsche, B. Kunze, R. Jansen, W. Trowitzsch-Kienast, G. Hofle, H. Reichenbach and H. Weiss, *Eur. J Biochem.,* 1994, 219, 691.
7 J. D. Morre, R. Decabo, C. Farley, N. H. Oberlies and J. L. McLaughlin, *Life Sci.,* 1995, 56, 343.
8 M. J. Rieser, Y.-H. Hui, J. K. Rupprecht, J. F. Kozlowski, K. V. Wood, J. L. McLaughlin, P. R. Hanson, A. Zhuang and T. R. Hoye, *J. Am. Chem. Soc.,* 1992, 144, 10203.
9 J. G. Yu, X.-F. Hu, D. K. Ho, M. F. Bean, R. E. Stephens and J. M. Cassady, *J. Org. Chem.,* 1994, 59, 1598.
10 T. R. Hoye and L.-S. Tan, *Tetrahedron Lett.,* 1995, 36, 1981.
11 S. C. Sinha, A. Sinha-Bagchi, A. Yazbak and E. Keinan, *Tetrahedron Lett.,* 1995, 36, 9257.
12 T. R. Hoye and Z.-X. Ye, *J. Am. Chem. Soc.,* 1996, 118, 1801.
13 H. Naito, E. Kawahara, K. Maruta, M. Maeda and S. Sasaki, *J. Org. Chem.,* 1995, 60, 4419.
14 U. Koert, *Tetrahedron Lett.,* 1994, 35, 2517.
15 S. C. Sinha and E. Keinan, *J. Am. Chem. Soc.,* 1993, 115, 4891.
16 B. M. Trost and Z.-P. Shi, *J. Am. Chem. Soc.,* 1994, 116, 7459.
17 H. Makabe, A. Tanaka and T. Oritani, *J. Chem. Soc., Perkin Trans,* I, 1994, 1975.
18 Z.-J, Yao and Y.-L. Wu, *J. Org, Chem.,* 1995, 60, 1170.
19 T.-L. Wang, X. E. Hu and J. M. Cassady, *Tetrahedron Lett.,* 1995, 36, 9031.
20 Z.-M. Gu, G. X. Zhao. N. H. Oberlies, L. Zeng and J. L. McLaughlin, in *Recent Advances in Phytochemistry,* ed. J. T. Arnason, R. Mata and J. T. Romeo, Plenum Press, New York, 1995, vol. 29, pp. 249-310.
21 W.-S. Chen, Z.-J. Yao, Y.-B. Zhang, Y.-Z. Xu and Y.-L. Wu, *Chin. J. Chem.,* 1995, 13, 263.
22 W.-S. Chen, Z.-J. Yao and Y.-L. Wu, *Acta Pharm. Sinica,* 1995, 53, 516.
23 P. Duret, R. Hocquemiller, A. Laurens and A. Cave, *Nat. Prod. Lett.,* 1995, 5, 295.
24 E. L. M. Silva, F. Roblot, J. Mahuteau and A. Cave, *J. Nat. Prod.,* 1996, in the press.
25 L. P. Santos and M. A. D. Boaventura, *Quim. Nova,* 1994, 17, 387.

26 S. Etcheverry, S. Sahpaz, D. Fall, A. Laurens and A. Cave, *Phytochemistry,* 1995, 38, 1423.
27 Q. Ye, L. Zeng, Y. Zhang, G.-X. Zhao, J. L. McLaughlin, M. H. Woo and D. R. Evert, *J. Nat. Prod.,* 1995, 58, 1398.
28 Q. Ye, L. Zeng, G.-E. Shi, D. Evert and J. L. McLaughlin, *Nat. Prod. Lett.,* 1996, in the press.
29 Q. Ye, K. He, N. H. Oberlies, L. Zeng, G.-E. Shi, D. Evert and J. L. McLaughlin, *J. Med. Chem.,* 1996, in the press.
30 Y. Chen and D.-Q. Yu, *J. Nat. Prod.,* 1996, in the press.
31 G.-E. Shi, D. Alfonso, M. O. Fatope, L. Zeng, Z.-M. Gu, G.-X. Zhao, K. He, J. M. MacDougal and J. L. McLaughlin, *J. Am. Chem. Soc.,* 1995, 117, 10409.
32 G.-E. Shi, L. Zeng, K. He, Q. Ye, Z.-M. Gu, J. M. MacDougal and J. L. McLaughlin, *Bioorg. Med. Chem.,* 1996, in the press.
33 D. Alfonso, T. Colman-Saizarbitoria, G.-X. Zhao, G.-E. Shi, Q. Ye. J. T. Schwedler and J. L. McLaughlin, *Tetrahedron,* 1996, in the press.
34 L. Zeng, Y. Zhang, Q. Ye, G.-E. Shi, K. He and J. L. McLaughlin, *Bioorg. Med. Chem.,* 1996, in the press.
35 S. D. Jolad, J. J. Hoffmann, K. H. Schram and J. R. Cole, *J. Org. Chem.,* 1982, 47, 3151.
36 L. Zeng, F.-E. Wu and J. L. McLaughlin, *Bioorg. Med. Chem. Lett.,* 1995, 5, 1865.
37 L. Zeng, F.-E. Wu, Z.-M. Gu and J. L. McLaughlin, *Tetrahedron Lett.,* 1995, 36, 5291.
38 J. K. Rupprecht, J.-H. Hui and J. L. McLaughlin, *J. Nat. Prod.,* 1990, 53, 237.
39 X.-P. Fang, M. J. Rieser, Z.-M. Gu, G.-X. Zhao and J. L. McLaughlin, *Phytochem. Anal.,* 1993, 4, 27.
40 A. Cave, D. Cortes, B. Figadere, L. O. Hocquemiller, O. Laprevote and M. Leboeuf, in *Recent Advances in Phytochemistry,* ed. K. R. Downum, J. T. Romeo and *H.* A. Stafford, Plenum Press, New York, 1993, vol. 27, pp. 167-202.
41 A. Cave, in *Phytochemistry of Plants Used in Traditional Medicine,* ed. K. Hostettmann, A. Marston, M. Maillard and M. Hamburger, Clarendon Press, Oxford, 1995, pp. 227-248.
42 Z.-J. Yao and Y.-L. Wu, *Org. Chem. (Shanghai),* 1995, 15, 120.
43 Z.-M. Gu, X.-P. Fang, L. Zeng, and J. L. McLaughlin, *Tetrahedron Lett.,* 1994, 35, 5367.
44 Y. Zhang, L. Zeng, M.-H. Woo, Z.-M. Gu, Q. Ye, F.-E. Wu and J. L. McLaughlin, *Heterocycles,* 1995, 41, 1743.
45 B. N. Meyer, N. R. Ferrigni, J. E. Putnam, L. B. Jacobson, D. E. Nichols and J. L. McLaughlin, *Planta Med.,* 1982, 45, 31.
46 J. L. McLaughlin, in *Methods in Plant Biochemistry,* ed. K. Hostettmann, Academic Press, London, 1991, vol. 6, pp. 1-33.
47 T. R. Hoye and J. C. Suhadolnik, *J. Am. Chem. Soc.,* 1987, 109, 4402.
48 T. R. Hoye and Z. Zhuang, *J. Org. Chem.,* 1988, 53, 5578.
49 Y. Fujimoto, C. Murasaki, H. Shimada, S. Nishioka, K. Kakinuma, S. Singh, M. Singh, Y. K. Gupta and M. Sahai, *Chem. Pharm. Bull.,* 1994, 42, 1175.
50 Z.-M. Gu, X.-P. Fang, L. Zeng, J. F. Kozlowski and J. L. McLaughlin, *Bioorg. Med. Chem. Lett.,* 1994, 4, 473.
51 Z.-M. Gu, L. Zeng, X.-P. Fang, T. Colman-Saizarbitoria, M. Huo and J. L. McLaughlin, *J. Org. Chem.,* 1994, 59, 5162.
52 H. Araya, Y. Fujimoto and K. Hirayama, *J. Synth. Org. Chem.,* 1994, 52, 765.
53 Z.-M. Gu, X.-P. Fang, L. R. Miesbauer, D. L. Smith and J. L. McLaughlin, *J. Nat. Prod.,* 1993, 56, 870.
54 O. Laprevote and B. C. Das, *Tetrahedron Lett.,* 1994, 50, 8479.
55 F.-E. Wu, L. Zeng, G.-X. Zhao, Y. Zhang, J. T. Schwedler and J. L. McLaughlin, *J. Nat. Prod.,* 1995, 58, 909.
56 F.-E. Wu, L. Zeng, G.-X. Zhao, Y. Zhang, J. T. Schwedler and J. L. McLaughlin, *J. Nat. Prod.,* 1995, 58, 830.
57 Y. H. Hui, J. K. Rupprecht, J. E. Anderson, Y. M. Liu, D. L. Smith, *C.* J. Chang and *J.* L. McLaughlin, *J. Nat. Prod.,* 1989, 52, 463.
58 G. X. Zhao, Y. H. Hui, J. K. Rupprecht and J. L. McLaughlin,
J. Nat. Prod., 1992, 347.
59 G.-X. Zhao, Z.-M. Gu, L. Zeng, J.-F. Chao, J. F. Kozlowski,

K. V. Wood and J. L. McLaughlin, *Tetrahedron*, 1995, 26, 7149.
60 Y.-H. Hui, *The Search for Bioactive Constituents from* Annona bullata *Rich. (Annonaceae)*, PhD Thesis, Purdue University, 1991.
61 A. Alkofahi, J. K. Rupprecht, D. L. Smith, C.-J. Chang and J. L. McLaughlin, *Experientia*, 1988, 44, 83.
62 G.-E. Shi, Q. Ye, K. He and J. L. McLaughlin, *J. Nat. Prod.*, 1996, in the press.
63 M. J. Rieser, *Annonaceous Acetogenins from the Seeds of* Annona muricata PhD Thesis, Purdue University, 1993.
64 M. J. Rieser, Z.-P. Fang, J. E. Anderson, L. R. Miesbauer, D. L. Smith and J. L. McLaughlin, *Helv. Chim. Acta*, 1994, 76, 2433.
65 M. J. Rieser, Z. P. Fang, J. E. Anderson, L. R. Miesbauer, D. L. Smith and J. L. McLaughlin, *Helv. Chim. Acta*, 1994, 77, 882.
66 S. Nishioka, H. Araya, C. Murasaki, M. Sahai and Y. Fujimoto, *Nat. Prod. Lett.*, 1994, 5, 117.
67 Q. Ye, D. Alfonso, D. Evert and K. L. McLaughlin, *Bioorg. Med. Chem.*, 1996, in the press.
68 G.-E. Shi, L. Zeng, K. He, Q. Ye and J. L. McLaughlin, *Bioorg. Med. Chem.*, 1996, in the press.
69 M. D. Espositi, A. Ghelli, M. Batta, D. Cortes and E. Estornell, *Biochem. J.*, 1995, 301, 161.
70 C. H. Holschneider, M. T. Johnson, R. M. Knox, A. Rezai, W. J. Ryan and F. J. Montz, *Cancer Chemother. Pharmacol.*, 1994, 34, 166.
71 S. Ratnayake, J. K. Rupprecht, W. M. Potter and J. L. McLaughlin, *J. Econ. Entomol.*, 1992, 85, 2353.
72 H. A. Johnson, J. Gorden and J. L. McLaughlin, in *New Crops, ed.* T. Janick and J. E. Simon, John Wiley and Sons, New York, 3rd edn, 1996.
73 M. J. Rieser, Z.-M. Gu, X.-P. Fang, L. Zeng, K. V. Wood and J. L. McLaughlin, *J. Nat. Prod.*, 1996, 59, 100.
74 K. J. Mikolajczak, J. L. McLaughlin and J. K. Rupprecht, *US Pat.*, US 4721727, 1988.
75 K. J. Mikolajczak, J. L. McLaughlin and J. K. Rupprecht, *US Pat.*, US 4855319, 1989.
76 Anonymous, *Lilly,s Hand Book of Pharmacy and Therapeutics*, Eli Lilly & Company, Indianapolis, 13th edn, 1898.
77 J. L. Landolt, K. I. Ahammadsahib, R. M. Hollingworth, R. Barr, F. L. Crane, N. L. Buerck, G. P. McCabe and J. L. McLaughlin, *Chem.-Biol. Interact.*, 1995, 98, 1.
78 D. A. Alfonso, H. A. Johnson, T. Colman-Saizarbitoria, P. P. Presley, G. P. McCabe and J. L. McLaughlin, *Natural Toxins*, 1996, in the press.
79 M. Leboeuf, A. Cave, P. K. Bhaumik, N. Mukherjee and R. Mukherjee, *Phytochemistry*, 1982, 21, 2783.
80 F. R. Chang, Y.C., Wu, C. Y. Duh and S. K. Wang, *J. Nat. Prod.*, 1993, 56, 1688.
81 S. H. Myint, A. Laurens, R. Hocquemiller and A. Cave, *Heterocycles*, 1990, 31.
82 D. Cortes, S. H. Myint, A. Laurens, R. Hocquemiller, M. Leboeuf and A. Cave, *Can. J. Chem.*, 1991, 69, 8.
83 A. Hisham, C. Sunitha, U. Sreekala, L. Pieters, T. D. Bruyne,
H. V. Heuvel and M. Claeys, *Phytochemistry*, 1994, 35, 1325.
84 T. Colman-Saizarbitoria, J. Zambrano, N. R. Ferrigni, Z.-M. Gu, J. H. Ng, D. L. Smith and J. L. McLaughlin, *J. Nat. Prod.*, 1994, 57, 486.
85 Y. C. Wu, F. R. Chang, C. Y. Duh and S. K. Wang, *Heterocycles*, 1992, 34, 667.
86 F. Lieb, M. Nonfon, U. Wachendorff-Neumann and D. Wendisch, *Planta Med.*, 1990, 56, 317.
87 T. G. McCloud, D. L. Smith, C. J. Chang and J. M. Cassady, *Experientia*, 1987, 43, 947.
88 L.-Z. Xu, C.-J. Chang, J.-G. Yu and J. M. Cassady, *J. Org. Chem.*, 1989, 54, 5418.
89 F.-E. Wu, Z.-M. Gu, L. Zeng, G.-X. Zhao, Y. Zhang and J. L. McLaughlin, *J. Nat. Prod.*, 1995, 58, 830.
90 D. Cortes, S. H. Myint, B. Dupont and D. Davoust, *Phytochemistry*, 1993, 32, 1475.
91 A. Jossang, B. Dubaele and A. Cave, *Tetrahedron Lett.*, 1990, 31, 1861.
92 C.-M. Li, Q. Mu, X.-J. Hau, H.-D. Sun, H.-L. Zheng and Y.-C. Wu, *Chin. Chem. Lett.* 1994, 5, 747.
93 P. Duret, A.-I. Waechter, R. Hocquemiller and A. Cave, *Nat. Prod. Lett.*, 1996, in the press.
94 M.-H. Woo, K.-Y. Cho, Y. Zhang, L. Zeng, Z.-M. Gu and J. L. McLaughlin, *J. Nat. Prod.*, 1995, 58, 1533.
95 X.-H. Li, Y.-H. Hui, J. K. Rupprecht, Y.-M. Liu, K. V. Wood, D. L. Smith, C.-J. Chang and J. L. McLauglin, *J. Nat Prod.*, 1990, 53, 81.
96 M. J. Rieser, X.-P. Fang, J. K. Rupprecht, Y. H. Hui, D. L. Smith and J. L. McLaughlin, *Planta Med.*, 1993, 59, 91.

97 A. Hisham, L. A. C. Pieters, M. Claeys, E. Esmans, R. Dommisse and A. J. Vlietinck, *Tetrahedron Lett.,* 1990, 31, 4649.
98 Y.-H. Hui, K. V. Wood and J. L. McLaughlin, *Natural Toxins,* 1992, 1, 4.
99 X.-P. Fang, J. E. Anderson, D. L. Smith, K. V. Wood and J. L. McLaughlin, *Heterocycles,* 1991, 34, 1075.
100 Z.-M. Gu, X.-P. Fang, L. Zeng, R. Song, J. H. Ng, K. V. Wood,
D. L. Smith and J. L. McLaughlin, *J. Org. Chem.,* 1994, 59, 3472.
101 M.-H. Woo, L. Zeng and J. L. McLaughlin, *Heterocycles,* 1995, 41, 1731.
102 T. Colman-Saizarbitoria, Z.-M. Gu and J. L. McLaughlin, *J. Nat. Prod.,* 1994, 57, 1661.
103 S. Sahpaz, M. C. Gonzalez, R. Hocquemiller, M. C. Zafra-polo and D. Cortes, *Phytochemistry,* 1996, in the press.
104 H. Araya. N. Hara, Y. Fujimoto and A. S. M. Srivastava, *Chem. Pharm. Bull.,* 1994, 42, 388.
105 J. M. Saad, Y.-H. Hui, J. K. Rupprecht, J. E. Anderson, J. F. Kozlowski, G. X. Zhao, K. V. Wood and J. L. McLaughlin, *Tetrahedron,* 1991, 47, 2751.
106 M.-H. Woo, L. Zeng, Q. Ye, Z.-M. Gu, G.-X. Zhao and J. L. McLaughlin, *Bioorg. Med. Chem. Lett.,* 1995, 5, 1135.
107 D. Cortes, S. H. Myint, M. Leboeuf and A. Cave, *Tetrahedron Lett.,* 1991, 32, 6133.
108 G. X. Zhao, M. J. Rieser, Y. H. Hui, L. R. Miesbauer, D. L. Smith and J. L. McLaughlin, *Phytochemistry,* 1993, 33, 1065.
109 V. T. Tam, P. Q. C. Hieu, B. Chappe, F. Roblot, B. Figadere and A. Cave, *Bull. Soc. Chim. Fr.,* 1995, 132, 324.
110 X.-P. Fang, J. K. Rupprecht, A. Alkofahi, Y.-H. Hui, Y.-M. Liu,
D. L. Smith, K. V. Wood and J. L. McLaughlin, *Heterocycles,* 1991, 32, 11.
111 J. G. Yu, D. K. Ho, J. M. Cassady, L. Z. Xu and C. J. Chang,
J. Org. Chem., 1992, 57, 6198.
112 X.-P. Fang, J. E. Anderson, D. L. Smith, J. L. McLaughlin and
K. V. Wood, *J. Nat. Prod.,* 1992, 55, 1655.
113 S. Sahpaz, A. Laurens, R. Hocquemiller and A. Cave, *Can. J. Chem.,* 1994, 72, 1.
114 E. L. M. Silva, F. Roblot, O. Laprevote, P. Varenne and A. Cave, *Nat. Prod. Lett..* 1995, 7, 235.
115 H.-Q. Gui, J.-G. Yu and Z.-L. Yu, *Chin. Chem. Lett.,* 1995, 6, 45.
116 M. Sahai, S. Singh, M. Singh, Y. K. Gupta, S. Akashi, R. Yuji, K. Hirayama, H. Asaki, H. Araya, N. Hara, T. Eguchi, K. Kakinuma and Y. Fujimoto. *Chem. Pharm. Bull.,* 1994, 42, 1163.
117 S. Ratnayake. Z.-M. Gu, L. R. Miesbauer, D. L. Smith, K. V. Wood, D. R. Evert and J. L. McLaughlin, *Can. J. Chem.,* 1994, 72, 287.
118 Z.-M. Gu, X.-P. Fang, L. Zeng, K. V. Wood and J. L. McLaughlin, *Heterocycles,* 1993, 36, 2221.
119 A. Hisham, L. A. C. Pieters, M. Claeys, E. Esmans, R. Dommisse and A. J. Vlietinck, *Phytochemistry,* 1991, 30, 2373.
120 J. K. Rupprecht, C.-J. Chang, J. M. Cassady and J. L. McLaughlin, *Heterocycles,* 1986, 24, 1197.
121 J. L. Rios, D. Cortes and S. Valerde, *Planta Med.,* 1989, 55, 321.
122 L. Born, F. Lieb, J. P. Lorentzen, H. Moescher, M. Nonfon, R. Sollner and D. Wendisch, *Planta Med.,* 1990, 56, 312.
123 G.-X. Zhao, L. R. Miesbauer, D. L. Smith and J. L. McLaughlin, *J. Med. Chem.,* 1994, 37, 1971.
124 S. Hishioka, H. Araya, C. Murasaki, M. Sahai and Y. Fujimoto, *Nat. Prod. Lett.,* 1994, 5, 117.
125 G.-X. Zhao, J.-F,. Chao, L. Zeng, M. J. Rieser and J. L. McLaughlin, *Bioorg. Med. Chem.,* 1996, 4, 25.
126 G.-X. Zhao, J.-F. Chao, L. Zeng, and J. L. McLaughlin, *Natural Toxins,* 1996, 4, 128.
127 M. Nonfon, F. Lieb, H. Moeschler and D. Wendisch, *Phytochemistry,* 1990. 29, 1951.
128 K. Kawazu, J. P. Alcatara and A. Kobayashi, *Agric. Biol. Chem.,* 1989, 53, 2719.
129 D. Cortes, S. H. Myint and R. Hocquemiller, *Tetrahedron,* 1991, 47, 8195.
130 S. D. Jolad, J. J. Hoffmann and J. R. Cole, *J. Nat. Prod.,* 1985, 48, 644.
131 A.-I. Waechter, R. Hocquemiller, A. Laurens and A. Cave, *Nat. Prod. Lett.,* 1995, 6, 133.
132 F. Cepleanu, K. Ohtani, M. Hamburger, M. P. Gupta, P. Solis and K. Hostettmann, *Helv. Chim. Acta,* 1993, 76, 1379.
133 M. J. Abreo and A. T. Sneden, *J. Nat. Prod.,* 1989, 53, 983.

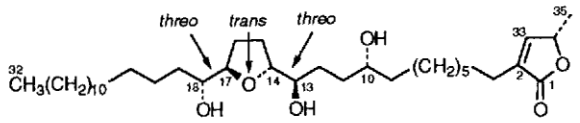
134 J. T. Etse and P. G. Waterman, *J. Nat. Prod.,* 1986, 49, 684.
135 G. R. Pettit, R. Riesen, J. E. Leet, J. Polonsky, C. R. Smith, J. M. Schmidt, C. Dufresne, D. Schaufelberger and C. Moretti, *Heterocycles,* 1989, 28, 213.
136 G.-X. Zhao, J. H. Ng, J. F. Kozlowzki, D. L. Smith and J. L. McLaughlin, *Heterocycles,* 1994, 38, 1897.
137 Y. Fujimoto, T. Eguchi, K. Kakinuma, N, Ikekawa, M. Sahia and Y. K. Gupta, *Chem. Pharm. Bull.,* 1988, 36, 4802.
138 J. Saez, S. Sahpaz, L. Villaescusa, R. Hocquemiller, A. Cave and D. Cortes, *J. Nat. Prod.,* 1993, 56, 351.
139 T. T. Dabrah and A. Sneden, *J. Nat. Prod.,* 1984, 23, 2013.
140 A. Hisham, L. A. C. Pieters, M. Claeys, E. Esmans, R. Dommisse and A. J. Vlietinck, *Phytochemistry,* 1991, 30, 545.
141 G.-X. Zhao, *Bioactive Components from the Stem Bark of the Paw Paw Tree.* Asiminia triloba, PhD Thesis, Purdue University, 1995.
142 Z.-M. Gu, L. Zeng, J. T. Schwedler, K. V. Wood and J. L. McLaughlin, *Phytochemistry,* 1995, 40, 467.
143 Z.-M. Gu, X.-P. Fang, Y.-H. Hui and J. L. McLaughlin, *Natural Toxins,* 1994, 2, 49.
144 G. R. Pettit, G. M. Cragg, J. Polonsky, D. L. Herald, A. Goswami,
C. R. Smith, C. Moretti, J. M. Schmidt and D. Weisleder, *Can J. Chem.,* 1987, 65, 1433.
145 M. J. Abreo and A. T. Sneden, *J. Nat. Prod.,* 1989, 52, 822.
146 T. T. Dabrah and A. Sneden, *J. Nat. Prod.,* 1984, 47, 652.
147 Y.-H. Hui, J. K. Rupprecht, J. E. Anderson, K. V. Wood and J.
L. McLaughlin, *Phytother. Res.,* 1991, 5, 124.
148 G.-E. Shi, L. Zeng, Z.-M. Gu, J. M. MacDougal and J. L. McLaughlin, *Heterocycles,* 1995, 41, 229.
149 H. Shimada, S. Nishioka, S. Singh, M. Sahai and Y. Fujimoto, *Tetrahedron Lett.,* 1994, 35, 3961.
150 A. Alkofahi, J. K. Rupprecht, Y.-M. Liu, C.-J. Chang, D. L. Smith and J. L. McLaughlin, *Experientia,* 1990, 46, 539.
151 X.-P. Fang, Z.-M. Gu, M. J. Rieser, Y.-H. Hui and J. L. McLaughlin, *J. Nat. Prod.,* 1993, 56, 1095.
152 Z.-M. Gu, X.-P. Fang, M. J. Rieser, Y.-H. Hui, L. R. Miesbauer,
D. L. Smith, K. V. Wood and J. L. McLaughlin, *Tetrahedron,* 1993, 49, 747.
153 Z.-M. Gu, L. Zeng and J. L. McLaughlin, *Heterocycles,* 1995, 41, 229.
154 Y.-H. Hui, J. K. Rupprecht, Y. M. Liu, J. E. Anderson, D. L. Smith, C.-J. Chang and J. L. McLaughlin, *Tetrahedron,* 1989, 45, 6941.
155 D. Cortes, J. L. Rios, A. Villar and S. Valverde, *Tetrahedron Lett.,* 1984, 25, 3199.
156 Y. Fujimoto, C. Murasaki, K. Kakinuma, T. Eguchi, N. Ikekawa,
M. Furuya, K. Hirayama, T. Ikekawa, M. Sahai, Y. K. Gupta and A. Ray, *Tetrahedron Lett.,* 1990, 31, 535.
157 J.-G. Yu, X.-Z. Luo, L. Sun, C.-Y. Liu, S.-L. Hong and L. B. Ma, *Chin. Chem. Lett.,* 1993, 4, 423.
158 K. J. Mikolajczak, R. V. Madrigal, J. K. Rupprecht, Y. H. Hui,
Y. M. Liu, D. L. Smith and J. L. McLaughlin, *Experientia,* 1990, 46, 324.
159 O. Laprevote, F. Roblot, R. Hocquemiller, A. Cave, B. Charles and J. C. Tabet, *Phytochemistry,* 1991, 30, 2721.
160 V. T. Tam, C. Chaboche, B. Figadere, B Chappe, B. C. Hieu and A. Cave, *Tetrahedron Lett.,* 1994, 35, 883.
161 X.-P. Fang, S. Rong, Z.-M. Gu, M. J. Rieser, L. R. Miesbauer, D. L. Smith and J. L. McLaughlin, *Bioorg. Med. Chem. Lett.,* 1993, 3, 1153.
162 F. Roblot, T. Laugel, M. Leboeuf, A. Cave and O. Laprevote, *Phytochemistry,* 1993, 34, 281.
163 A. Hisham, U. Sreekala, L. Pieters, T. D. Bruyne, H. V. D. Heuvel and M. Claeys, *Tetrahedron,* 1993, 31, 6913.
164 O. Laprevote, C. Girard and B. C. Das, *Rapid Commun. Mass Spectrum.,* 1992, 6, 352.
165 V. T. Tam, P. Q. C. Hieu, B. Chappe, F. Roblot, O. Laprevote, B. Figadere and A. Cave, *Nat. Prod. Lett.,* 1994, 4, 255.
166 D. Gromek, B. Figadere, R. Hocquemiller and A. Cave, *Tetrahedron,* 1993, 49, 5247.
167 T. Colman-Saizarbitoria, Z.-M. Gu, G.-X. Zhao, L. Zeng and J. L. McLaughlin, *J. Nat. Prod.,* 1995, 58, 532.
168 Y. Chen and D.-Q. Yu, *Planta Med.,* 1996, in the press.

169 S. Sahpaz, B. Figadere, J. Saez, R. Hocquemiller, A. Cave and D. Cortes, *Nat. Prod. Lett.*, 1994, 2, 301.
170 T. R. Hoye and J. C. Suhadolnik, *J. Am. Chem. Soc.*, 1985, 107, 5312.
171 B. Figadere, *Acc. Chem. Res.*, 1995, 28, 359.
172 U. Koert, *Synthesis*, 1995, 115.
173 Z. J. Yao and Y. L. Wu, *Tetrahedron Lett.*, 1994, 35, 157.
174 T. R. Hoye, P. R. Hanson, A. C. Kovelesky, T. D. Ocain and Z. P. Zhuang, *J. Am. Chem. Soc.*, 1991, 113, 9369.
175 T. R. Hoye and P. R. Hanson, *Tetrahedron Lett.*, 1993, 34, 5043.
176 O. Laprevote, F. Roblot, R. Hocquemiller and A. Cave, *Tetrahedron Lett.*, 1990, 31, 2283.
177 Y.-C. Wu, F.-R. Chang, K.-S. Chen, S.-C. Liang and M.-R. Lee, *Heterocycles*, 1994, 38, 1475.

15 Appendix: New Structures of Annonaceous Acetogenins (July 1994–January 1996)

Note: Compound numbers corresponding to those in the main text article are placed *after* the compound name.

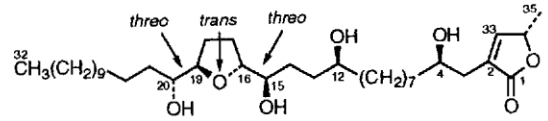
1. Longifolicin 1,[27] $C_{35}H_{64}O_6$, MW 580



Carbon No.	10	13	14	17	18
$^1H(\delta)$	3.63 m	3.45 m	3.83 m	3.82 m	3.41 m
$^{13}C(\delta)$	71.61	74.32	82.71	82.59	74.03

White waxy solid; **MP**: 83 °C; $[\alpha]_D$ +13.0° (*c* 0.001, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 228, (log ε = 2.43); **IR** (ν_{max}, film, cm^{-1}): 3400, 2900, 2820, 1750, 1440, 1300, 1073, 667; **MS**: CI-MS (isobutane, *m/z*) 581, 563, 545, 527; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: tri-acetate (^1H NMR); formal acetal (^1H NMR); TMS (EI-MS); per-Mosher ester (^1H NMR); **Biological activities**: BST LC_{50} = 3.52 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 1.13 \times 10^{-6}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.23 \times 10^{-5}\ \mu g\ ml^{-1}$, HT-29 ED_{50} = 1.23 $\mu g\ ml^{-1}$, A-498 $ED_{50} = 4.55 \times 10^{-1}\ \mu g\ ml^{-1}$, PA-3 $ED_{50} < 10^{-7}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 4.22 \times 10^{-3}\ \mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

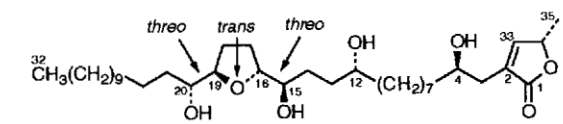
2. Arianacin 3,[73] $C_{35}H_{64}O_7$, MW 596



Carbon No.	12	15	16	19	20
$^1H(\delta)$	3.60 m	3.46ddd	3.80 m	3.80 m	3.41dt
$^{13}C(\delta)$	71.8	74.4	82.6	82.7	74.1

White amorphous powder; **MP**: 64 °C; $[\alpha]_D$ +12.5° (*c* 0.14, $CHCl_3$); **UV** ±(λ_{max}, MeOH, nm): 215 (ε = 12500); **IR** (ν_{max}, film, cm^{-1}): 3629, 2925, 2847, 1734, 1469; **MS**: CI-MS (isobutane, *m/z*) 597, 561, 543, 526; EI-MS (*m/z*) 327, 309, 291, 269, 199; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: formal acetal (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 7.1 $\mu g\ ml^{-1}$, PD% inhibition = 26%, A-549 $ED_{50} = 4.7 \times 10^{-3}\ \mu g\ ml^{-1}$, MCF-7 ED_{50} = 0.4 $\mu g\ ml^{-1}$, HT-29 ED_{50} = 4.4 $\mu g\ ml^{-1}$, **Source**: *Annona muricata*, seeds.

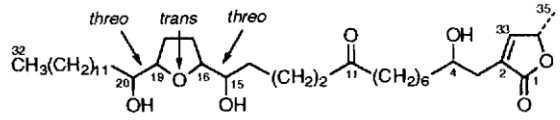
3. Javoricin 4,[73] $C_{35}H_{64}O_7$, MW 596



Carbon No.	12	15	16	19	20
$^1H(\delta)$	3.63 m	3.46ddd	3.77–3.85 m	3.77–3.85 m	3.41dt
$^{13}C(\delta)$	71.6	74.3	82.5	82.7	74.1

White amorphous powder; **MP**: 70 °C; $[\alpha]_D$ +13.6° (*c* 0.1, $CHCl_3$); **UV** (λ_{max}, MeOH, nm): 217 (ε = 11800); **IR** (ν_{max}, film, cm^{-1}): 3450, 2924, 2853, 1750, 1457; **MS**: CI-MS (isobutane, *m/z*) 597, 561, 543, 526; EI-MS (*m/z*) 327, 309, 291; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 4.9 $\mu g\ ml^{-1}$, PD% inhibition = 47%, A-549 $ED_{50} = 1.7 \times 10^{-2}\ \mu g\ ml^{-1}$, MCF-7 ED_{50} = 0.23 $\mu g\ ml^{-1}$, HT-29 ED_{50} = 1.8 $\mu g\ ml^{-1}$, **Source**: *Annona muricata*, seeds.

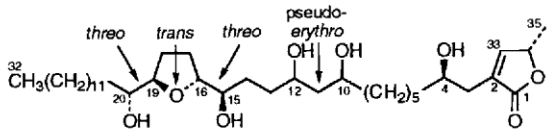
4. Reticulacinone 10,[83] $C_{35}H_{62}O_7$, MW 594



Carbon No.	11	15	16	19	20
$^1H(\delta)$	—	3.4 m	3.8–3.95 m	3.8–3.95 m	3.40 m
$^{13}C(\delta)$	211.5	74.1	82.6	82.6	73.9

Waxy solid: **MS**: EI-MS (*m/z*) 583, 581, 571, 557, 555, 529, 489, 487, 471, 459, 431, 429, 401, 375, 361, 359, 357, 331, 301, 259; **NMR**: ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona reticulata*, stem bark.

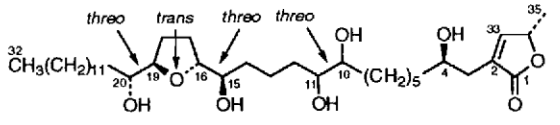
5. Muricatocin A 13,[56] $C_{35}H_{64}O_8$, MW 612



Carbon No.	10	12	15	16	19	20
$^1H(\delta)$	3.94 m	3.86 m	3.45 m	3.85 m	3.87 m	3.46 m
$^{13}C(\delta)$	72.82	72.60	74.39	82.69	82.45	74.03

White powder; $[\alpha]_D$ +21.8° (*c* 0.001, EtOH); **UV** (λ_{max}, MeOH, nm): 216 (ε = 8500); **IR** (ν_{max}, film, cm^{-1}): 3433, 2920, 2851, 1747, 1466, 1321, 1076; **MS**: CI-MS (BuOH, *m/z*) 613, 595, 577, 559, 541, 523, 413, 395, 377, 359, 353, 343, 325, 285, 271, 269, 241, 223, 205, 199, 141; EI-MS (*m/z*) 325, 307, 269, 241, 223, 213, 199, 141; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: acetonide (^1H NMR), per-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 6.99 \times 10^{-1}\ \mu g\ ml^{-1}$, A-549 $ED_{50} = 7.55 \times 10^{-2}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.23 \times 10^{-1}\ \mu g\ ml^{-1}$, HT-29 ED_{50} = 1.56 $\mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

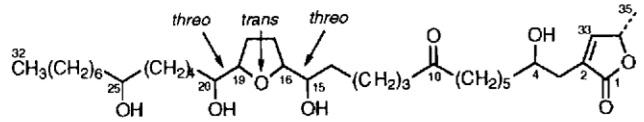
6. Annomuricin C 14,[55] $C_{35}H_{64}O_8$, MW 612



Carbon No.	10	11	15	16	19	20
$^1H(\delta)$	3.43 m	3.43 m	3.41 m	3.83 m	3.85 m	3.40 m
$^{13}C(\delta)$	74.14	74.16	74.39	82.72	82.56	74.39

White powder; $[\alpha]_D$ +57.7° (*c*. 0.0005, EtOH); **UV** (λ_{max}, MeOH, nm): 220 ($\epsilon = 3800$); **IR** (ν_{max}, film, cm^{-1}): 3411, 2920, 2851, 1743, 1467, 1321, 1073; **MS**: CI-MS (BuOH, *m/z*) 613, 595, 577, 559, 541, 395, 377, 353, 325, 271, 269, 253, 241, 223, 205, 199, 141; EI-MS (*m/z*) 341, 325, 307, 269, 241, 223, 213, 205, 199, 141; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: acetonide (^1H NMR), per-acetate (^1H NMR), per-MTPA esters (^1H NMR), (EI-MS); **Biological activities**: BST $LC_{50} = 6.13 \times 10^{-1}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 3.08 \times 10^{-1}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 2.28 \times 10^{-1}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.54$ $\mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

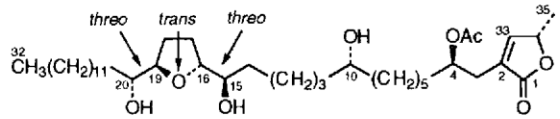
7. Muricatatin C 19,[92] $C_{35}H_{66}O_8$, MW 614



Carbon No.	10	15	16	19	20	25
$^1H(\delta)$	—	3.37 m	3.80 m	3.80 m	3.37 m	3.80 m
$^{13}C(\delta)$	211.04	73.77	82.58	82.72	74.06	74.34

Amorphous solid; **MP**: 61 °C; $[\alpha]_D$ +15.40° (*c* 0.49, MeOH); **IR** (ν_{max}, film, cm^{-1}): 3400, 1740; **MS**: EI-MS (*m/z*) 511, 481, 463, 445, 427, 425, 407, 389, 395, 377, 359, 325, 307, 289, 239, 211, 141; **NMR**: ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$); **Source**: *Annona muricata*, seeds and stem bark.

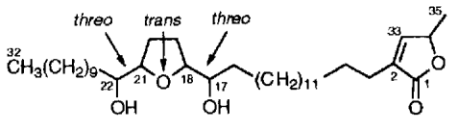
8. 4-Acetyl annonacin 20,[28] $C_{37}H_{66}O_8$, MW 638



Carbon No.	4	10	15	16	19	20
$^1H(\delta)$	5.10 m	3.59 m	3.41 m	3.80 dt	3.80 dt	3.41 m
$^{13}C(\delta)$	71.9	71.7	74.0	82.6	82.6	74.0

Colourless wax; **MP**: 67–68 °C $[\alpha]_D$ +13° (*c* 0.10, MeOH); **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 21.86$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 3.38 \times 10^{-5}$ $\mu g\ ml^{-1}$, MCD-7 $ED_{50} = 2.65 \times 10^{-1}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.85 \times 10^{-5}$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 3.59 \times 10^{-4}$ $\mu g\ ml^{-1}$, PA-3 $ED_{50} = 3.56 \times 10^{-1}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.46 \times 10^{-3}$ $\mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

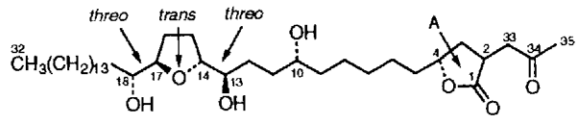
9. Annotemoyin-1 21,[93] $C_{35}H_{65}O_5$, MW 564



Carbon No.	17	18	21	22
$^1H(\delta)$	3.40 m	3.80 m	3.80 m	3.40 m
$^{13}C(\delta)$	74.17	82.71	82.71	74.17

White waxy solid; $[\alpha]_D$ +21° (*c* 0.13, MeOH); **UV** (λ_{max}, EtOH, nm): 216.9 (log $\epsilon = 3.63$); **IR** (ν_{max}, film, cm^{-1}): 3448, 2927, 2857, 1756, 1652, 1452, 1376, 1321, 1116, 1064, 1028, 952, 872, 754, 724; **MS**: CI-MS (methane) 565, 547, 529, 511, 393, 375, 323, 305, 295, 267, 241, 223, 171, 167, 153, 139, 125, 111, 97; EI-MS: 528, 375, 357, 347, 323, 295, 267, 241, 223, 205, 153, 139, 135, 125, 111, 97; **NMR**: ^1H NMR (200 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona atemoya*, seeds.

Goniothalamicinone 22/23,[27] $C_{35}H_{64}O_7$, MW 596 (reported as a *cis* and *trans* mixture)



10. (2,4-*cis*)-Goniothalamicinone 22 (A = *cis*)

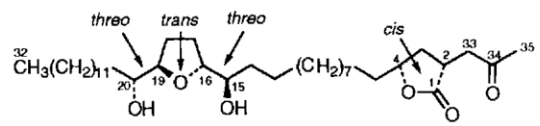
Carbon No.	10	13	14	17	18
$^1H(\delta)$	3.65 m	3.45 m	3.83 m	3.83 m	3.41 m
$^{13}C(\delta)$	71.6	74.4	82.6	82.6	74.0

11. (2,4-*trans*)-Goniothalamicinone 23 (A = *trans*)

Carbon No.	10	13	14	17	18
$^1H(\delta)$	3.65 m	3.45 m	3.83 m	3.83 m	3.41 m
$^{13}C(\delta)$	71.6	74.4	82.6	82.6	74.0

Whitish wax; **MP**: 98 °C; $[\alpha]_D$ +22.9° (*c* 1.0, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 210 ($\epsilon = 10000$); **IR** (ν_{max}, film, cm^{-1}): 3450, 2900, 2820, 1782, 1726, 1457, 1388, 1218, 1072; **MS**: CI-MS (isobutane, *m/z*) 597, 561, 543, 525, 351, 333, 309, 297, 281, 263, 245, 241, 141; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: tri-acetate (^1H NMR), per-MTPA esters (^1H NMR), tri-TMS (EI-MS); **Biological activities**: BST $LC_{50} = 0.14$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 2.06 \times 10^{-5}$) $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 9.67 \times 10^{-1}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 4.05 \times 10^{-4}$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 2.91 \times 10^{-1}$ $\mu g\ ml^{-1}$, PA-3 $ED_{50} = 1.37 \times 10^{-1}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.33 \times 10^{-3}$ $\mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

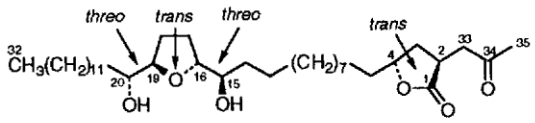
12. (2,4-*cis*)-Murisolinone 26,[94] $C_{35}H_{64}O_6$, MW 580



Carbon No.	15	16	19	20
$^1H(\delta)$	3.40 m	3.80 m	3.80 m	3.40 m
$^{13}C(\delta)$	74.04	82.61	82.61	74.03

Amorphous powder; **MP**: 92–93 °C; $[\alpha]_D$ +13.3° (*c* 0.1, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm); 220 (log $\epsilon = 3.8$); **IR** (ν_{max}, film, cm^{-1}): 3494, 2916, 2848, 1764, 1723, 1587, 1531, 1467, 1188, 1069; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: tri-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 12.3$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 1.48 \times 10^{-1}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 7.93 \times 10^{-2}$ $\mu g\ ml^{-1}$, HT-29 ED_{50} 7.54×10^{-1} $\mu g\ ml^{-1}$, A-498 $ED_{50} = 3.44$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.48$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.07 \times 10^{-1}$ $\mu g\ ml^{-1}$; **Source**: *Asimina triloba*, seeds.

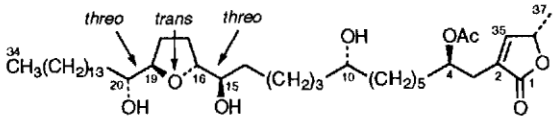
13. (2,4-*trans*)-Murisolinone 27,[94] $C_{35}H_{64}O_6$, MW 580



Carbon No.	15	16	19	20
$^1H(\delta)$	3.40 m	3.80 m	3.80 m	3.40 m
$^{13}C(\delta)$	74.04	82.61	82.61	74.03

Amorphous powder; **MP**: 101–102 °C; $[\alpha]_D$ +20.0° (*c* 0.1, CH_2Cl_2); **UV** (λ_{max}, EtOH, nm): 218 (log ϵ = 3.43); **IR** (ν_{max}, film, cm^{-1}): 3490, 2916, 2848, 1744, 1713, 1589, 1183, 1070; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMSi (EI-MS), **Biological activities**, BST LC_{50} = 18.2 μg ml^{-1}, A-549 $ED_{50} = 2.76 \times 10^{-2}$ μg ml^{-1}, MCF-7 $ED_{50} = 2.96 \times 10^{-2}$ μg ml^{-1}, HT-29 $ED_{50} = 1.16$ μg ml^{-1}, A-498 $ED_{50} = 1.23$ μg ml^{-1}, PC-3 $ED_{50} = 2.14 \times 10^{-1}$ μg ml^{-1}, PaCa-2 $ED_{50} = 5.90 \times 10^{-3}$ μg ml^{-1}; **Source**: *Asimina triloba*, seeds.

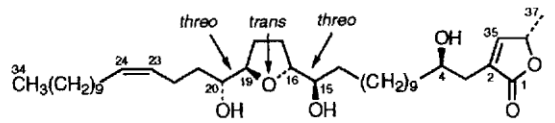
14. 4-Acetyl xylomaticin 38,[28] $C_{39}H_{68}O_8$, MW 666



Carbon No.	4	10	15	16	19	20
$^1H(\delta)$	5.10 m	3.59 m	3.41 m	3.80 dt	3.80 dt	3.41 m
$^{13}C(\delta)$	71.9	71.7	74.0	82.6	82.6	74.0

Colourless wax; **MP**: 67–68 °C; $[\alpha]_D$ +13° (*c* 0.10, MeOH); **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); Biological activities: BST LC_{50} = 34.12 μg ml^{-1}, A-549 $ED_{50} = 1.25 \times 10^{-6}$ μg ml^{-1}, MCF-7 $ED_{50} = 3.04 \times 10^{-1}$ μg ml^{-1}, HT-29 $ED_{50} = 1.12 \times 10^{-6}$ μg ml^{-1}, A-498 $ED_{50} = 2.66 \times 10^{-4}$ μg ml^{-1}, PA-3 $ED_{50} = 3.51 \times 10^{-1}$ μg ml^{-1}, PaCa-2 $ED_{50} = 6.22 \times 10^{-4}$ μg ml^{-1}; **Source**: *Asimina longifolia*, leaves and twigs.

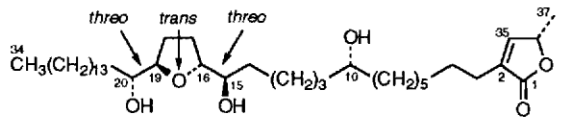
15. Asiminenin B 40,[101] $C_{37}H_{66}O_6$, MW 606



Carbon No.	15	16	19	20	23	24
$^1H(\delta)$	3.42 m	3.81 m	3.81 m	3.42 m	5.36 m	5.39
$^{13}C(\delta)$	74.03	82.55	82.65	73.50	128.92	130.83

Amorphous powder; **MP**: 54–55 °C; $[\alpha]_D$ +17.0° (*c* 0.1, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 230 (log ϵ = 2.93); **IR** (ν_{max}, film, cm^{-1}): 3458, 2918, 2850, 1764, 1731, 1590, 1316, 1081, 669; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 5.82 \times 10^{-1}$ μg ml^{-1}, A-549 $ED_{50} = 3.22 \times 10^{-6}$ μg ml^{-1}, MCF-7 $ED_{50} = 3.61 \times 10^{-6}$ μg ml^{-1}, HT-29 $ED_{50} = 6.94 \times 10^{-5}$ μg ml^{-1}, A-498 $ED_{50} = 5.72 \times 10^{-3}$ μg ml^{-1}, PC-3 $ED_{50} = 3.66 \times 10^{-5}$ μg ml^{-1}, PaCa-2 $ED_{50} = 6.34 \times 10^{-7}$ μg ml^{-1}; **Source**: *Asimina triloba*, seeds.

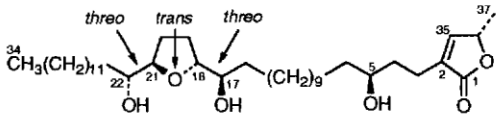
16. Longicoricin 14,[67] $C_{37}H_{68}O_6$, MW 608



Carbon No.	10	15	16	19	20
$^1H(\delta)$	3.59 m	3.41 m	3.80 dt	3.80 dt	3.41 m
$^{13}C(\delta)$	71.85	74.03	82.65	82.59	73.97

Whitish wax; **MP**: 74–75°C; $[\alpha]_D$ +12.0° (*c* 0.001, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 222 (log ϵ = 2.93); **IR** (ν_{max}, film, cm^{-1}): 3422, 2923, 2855, 1734, 1650, 1456, 1076; **MS**: CI-MS (isobutane) 609, 591, 573, 555; EI-MS 381, 363, 345, 311, 293, 275, 225, 207; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 1.56 μg ml^{-1}, A-549 ED_{50} = 1.04 μg ml^{-1}, MCF-7 ED_{50} = 2.31 μg ml^{-1}, HT-29 $ED_{50} = 1.36 \times 10^{-3}$ μg ml^{-1}, A-498 ED_{50} = 1.71 μg ml^{-1}, PC-3 $ED_{50} = 3.04 \times 10^{-6}$ μg ml^{-1}, PaCa-2 ED_{50} = 1.36 μg ml^{-1}; **Source**: *Asimina longifolia*, leaves and twigs.

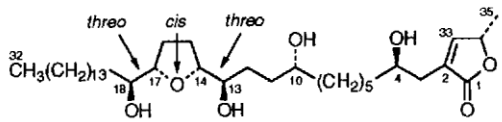
17. Tonkinecin 48,[30] $C_{37}H_{68}O_6$, MW 608



Carbon No.	3	4	5	17	18	21	22
$^1H(\delta)$	2.40 m	1.65 m	3.58 m	3.39 m	3.79 m	3.79 m	3.39 m
$^{13}C(\delta)$	21.49	35.34	70.87	74.13	82.66	82.66	74.13

White crystals; **MP**: 70–72 °C; $[\alpha]_D$ +26.54° (*c*. 0.09, $CHCl_3$); **IR** (ν_{max}, film, cm^{-1}): 3441, 2920, 2851, 1743, 1709, 1469, 1074; **MS**: CI-MS (isobutane) 591, 573, 555, 537; EI-MS 483, 465, 447, 409, 391, 373, 339, 321, 303, 271, 269; 155; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: HCT-8 $IC_{50} = 3.8 \times 10^{-1}$ μm, Bel7402 IC_{50} = 1.5 μM, BGC IC_{50} = 5.1 μM, HL-60 $IC_{50} = 5.2 \times 10^{-1}$ μM; **Source**: *Uvaria tonkinesis*, roots.

18. *cis*-Goniothalamicin 52,[73] $C_{35}H_{64}O_7$, MW 596

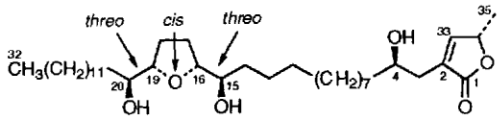


Carbon No.	10	13	14	17	18
$^1H(\delta)$	3.65 m	3.47 m	3.83 m	3.83 m	3.41dt
$^{13}C(\delta)$	71.5	74.3	82.6	82.7	74.4

White amorphous powder; **MP**: 80 °C $[\alpha]_D$ +7.2° (*c* 0.03, $CHCl_3$); **UV** (λ_{max}, MeOH, nm): 213 (ϵ = 10500); **IR** (ν_{max}, film, cm^{-1}): 3628, 2923, 1750, 1469; **MS**: CI-MS (isobutane) 597, 579, 561, 543, 525; EI-MS 281, 263, 241, 223; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} =

5.2 μg ml^{-1}, PD% inhibition = 47%, A-549 $ED_{50} = 1.3 \times 10^{-1}$ μg ml^{-1}, MCF-7 $ED_{50} = 1.05$ μg ml^{-1}, HT-29 $ED_{50} = 5.3 \times 10^{-3}$ μg ml^{-1}; **Source:** *Annona muricata*, seeds.

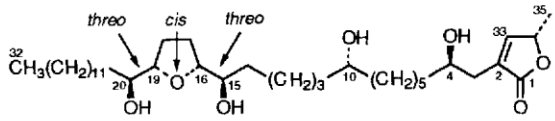
19. 16,19-*cis*-Murisolin 53,[106] $C_{35}H_{64}O_6$, MW 580



Carbon No.	15	16	19	20
^{1}H(δ)	3.42 m	3.82 m	3.82 m	3.42 m
^{13}C(δ)	74.36	82.65	82.65	74.36

White amorphous powder; **MP**: 67–68 °C; $[\alpha]_D$ +11.0° (*c* 0.1, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 213 (log ϵ = 3.57); **IR** (ν_{max}, film, cm^{-1}): 3433, 1740; **MS**: CI-MS (isobutane) 581, 563, 545, 527, 311, 293, 275, 269, 251, 381, 363, 345; **NMR**: ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^{1}H NMR), per-MTPA esters (^{1}H NMR), TMS (EI-MS): **Biological activities:** BST $LC_{50} = 3.46 \times 10^{-1}$ μg ml^{-1}, A-549 $ED_{50} = 3.41 \times 10^{-3}$ μg ml^{-1}, MCF-7 $ED_{50} = 1.58 \times 10^{-2}$ μg ml^{-1}, HT-29 $ED_{50} = 1.27$ μg ml^{-1}, A-498 $ED_{50} = 4.16$ μg ml^{-1}, PC-3 $ED_{50} = 1.42$ μg ml^{-1}, PaCa-2 $ED_{50} = 1.53 \times 10^{-2}$ μg ml^{-1}; **Source**: *Asimina triloba*, seeds.

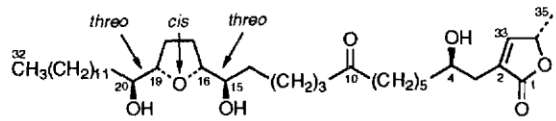
20. *cis*-Annonacin 54,[73] $C_{35}H_{64}O_7$, MW 596



Carbon No.	10	15	16	19	20
^{1}H(δ)	3.59 m	3.42 m	3.82 m	3.82 m	3.42 m
^{13}C(δ)	71.6	74.3	82.7	82.7	74.3

White amorphous powder; **MP**: 77 °C; $[\alpha]_D$ +10° (*c* 0.17, $CHCl_3$); **UV** (λ_{max}, MeOH, nm): 215 (ϵ = 9700); **IR** (ν_{max}, film, cm^{-1}): 3395, 2920, 2851, 1734, 1469; **MS**: CI-MS (isobutane) 597, 579, 561, 543, 525; EI-MS 327, 309, 291, 273; **NMR**: ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^{1}H NMR), per-MTPA esters (^{1}H NMR), mono-MTPA esters at each individual OH position (^{1}H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 2.3$ μg ml^{-1}, PD% inhibition = 28%, A-549 $ED_{50} = 2.3 \times 10^{-1}$ μg ml^{-1}, MCF-7 $ED_{50} = 1.18$ μg ml^{-1}, HT-29 $ED_{50} = 1.0 \times 10^{-8}$ μg ml^{-1}; **Source**: *Annona muricata*, seeds.

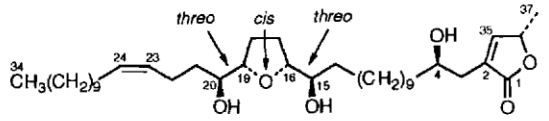
21. *cis*-Annonacin-10-one 55,[73] $C_{35}H_{62}O_7$, MW 594



Carbon No.	10	15	16	19	20
^{1}H(δ)	—	3.42 m	3.82 m	3.82 m	3.42 m
^{13}C(δ)	211.3	74.3	82.7	82.7	74.3

White amorphous powder; **MP**: 70 °C; $[\alpha]_D$ +6.2° (*c* 0.07, $CHCl_3$); **UV** (λ_{max}, MeOH, nm): 209 (ϵ = 8400); **IR** (ν_{max}, film, cm^{-1}): 3444, 2918, 2850, 1750, 1705, 1467; **MS**: CI-MS (isobutane) 595, 577, 559, 541, 325, 307; **NMR**: ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^{1}H NMR), per-MTPA esters (^{1}H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 1.8$ μg ml^{-1}, PD% inhibition = 32%, A-549 $ED_{50} = 3.5 \times 10^{-1}$ μg ml^{-1}, MCF-7 $ED_{50} = 2.9 \times 10^{-1}$ μg ml^{-1}, HT-29 $ED_{50} = 9.0 \times 10^{-4}$ μg ml^{-1}; **Source**: *Annona muricata*, seeds.

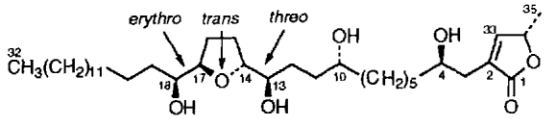
22. Asiminenin A 56,[101] $C_{37}H_{66}O_6$, MW 606



Carbon No.	15	16	19	20	23	24
^{1}H(δ)	3.43 m	3.83 m	3.83 m	3.43 m	5.36 m	5.39
^{13}C(δ)	74.31	82.61	82.68	73.82	128.96	130.77

Amorphous powder; **MP**: 58–59 °C; $[\alpha]_D$ +10.0° (*c* 0.1, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 228 (log ϵ = 3.55); **IR** (ν_{max}, film, cm^{-1}): 3411, 2921, 2852, 1756, 1588, 1078, 669; **NMR**: ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^{1}H NMR), per-MTPA esters (^{1}H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 4.73 \times 10^{-1}$ μg ml^{-1}, A-549 $ED_{50} = 2.85 \times 10^{-4}$ μg ml^{-1}, MCF-7 $ED_{50} = 2.39 \times 10^{-3}$ μg ml^{-1}, HT-29 $ED_{50} = 8.12 \times 10^{-2}$ μg ml^{-1}, A-498 $ED_{50} = 6.26 \times 10^{-2}$ μg ml^{-1}, PC-3 $ED_{50} = 1.66$ μg ml^{-1}, PaCa-2 $ED_{50} = 8.58 \times 10^{-4}$ μg ml^{-1}; **Source**: *Asimina triloba*, seeds.

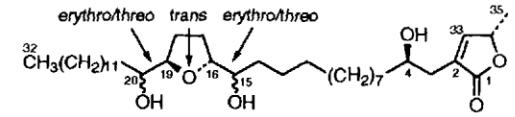
23. Longicin 57,[27] $C_{35}H_{64}O_7$, MW 596



Carbon No.	10	13	14	17	18
^{1}H(δ)	3.64 m	3.45 m	3.84 m	3.81 m	3.88 m
^{13}C(δ)	71.5	74.6	83.1	82.2	71.6

Whitish wax; **MP**: 83 °C $[\alpha]_D$ +13.0° (*c* 1.0, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 228 (log ϵ = 3.70); **IR** (ν_{max}, film, cm^{-1}): 3400, 2900, 2820, 1750, 1440, 1300, 1073; **MS**: CI-MS (isobutane, *m/z*) 597, 579, 561, 543, 525, 351, 333, 281; **NMR**: ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: peracetate (^{1}H NMR); TMS (EI-MS); per-Mosher ester (^{1}H NMR), longicinone (^{1}H NMR); **Biological activities**: BST $LC_{50} = 0.11$ μg ml^{-1}, A-549 $ED_{50} = 1.77 \times 10^{-6}$ μg ml^{-1}, MCF-7 $ED_{50} > 1$ μg ml^{-1}, HT-29 $= 2.4 \times 10^{-5}$ μg ml^{-1}, A-498 $ED_{50} = 1.99 \times 10^{-4}$ μg ml^{-1}, PA-3 $ED_{50} = 4.26 \times 10^{-3}$ μg ml^{-1}, PaCa-2 $ED_{50} = 1.25 \times 10^{-9}$ μg ml^{-1}; **Source**: *Asimina longifolia*, leaves and twigs.

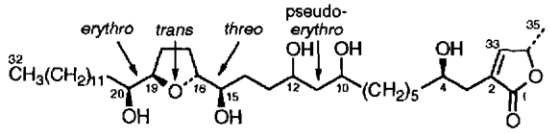
24. Murisolin A 58,[106] $C_{35}H_{64}O_6$, MW 580



Carbon No.	15	16	19	20
^{1}H(δ)	3.40 m	3.82 m	3.88 m	3.82 m
^{13}C(δ)	74.33	83.21	82.12	71.51

Colourless powder; **MP**: 83–84 °C; $[\alpha]_D$ +17.0° (*c* 0.1, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 226 (log ϵ = 3.02); **IR** (ν_{max}, film, cm^{-1}): 3433, 1740; **MS**: CI-MS (isobutane) 581, 563, 545, 527, 311, 293, 275, 269, 251, 381, 363, 345; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = -1.83 \times 10^{-1}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 3.16 \times 10^{-6}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 5.40$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.06 \times 10^{-8}$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 6.67 \times 10^{-2}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 8.41$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 5.18 \times 10^{-2}$ $\mu g\ ml^{-1}$; **Source**: *Asimina triloba*, seeds.

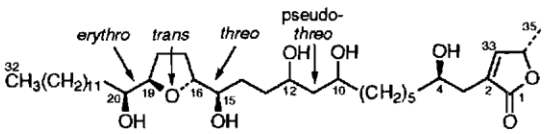
25. Muricatocin B 62,[56] $C_{35}H_{64}O_8$, MW 612



Carbon No.	10	12	15	16	19	20
$^1H(\delta)$	3.94 m	3.86	3.45 m	3.85 m	3.80 m	3.89 m
$^{13}C(\delta)$	72.87	72.63	74.61	82.96	82.21	71.52

White powder; $[\alpha]_D$ +62.5° (*c* 0.001, EtOH); **UV** (λ_{max}, MeOH, nm): 214 (ϵ = 9500); **IR** (ν_{max}, film, cm^{-1}): 3416, 2920, 2850, 1744, 1467, 1322, 1075; **MS**: CI-MS (BuOH, *m/z*) 613, 595, 577, 559, 541, 523, 413, 395, 377, 359, 343, 325, 285, 271, 269, 267, 253, 241, 223, 205, 199; EI-MS (*m/z*) 413, 377, 359, 343, 325, 307, 285, 269, 253, 241, 223, 213, 199, 141; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: acetonide (^1H NMR), per-acetate (^1H NMR), per-MTPA esters (^1H NMR), penta-TMS (EI-MS); **Biological activities**: BST $LC_{50} = 5.57 \times 10^{-1}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 3.34 \times 10^{-2}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.03 \times 10^{-1}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.66$ $\mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

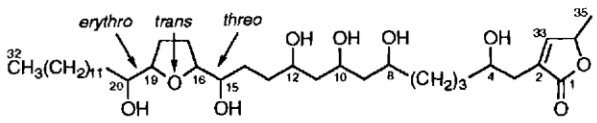
26. Muricatocin C 63,[55] $C_{35}H_{64}O_8$, MW 612



Carbon No.	10	12	15	16	19	20
$^1H(\delta)$	3.94 m	3.86 m	3.45 m	3.85 m	3.80 m	3.89 m
$^{13}C(\delta)$	69.62	69.23	74.28	83.04	82.22	71.48

White powder; $[\alpha]_D$ +32.5° (*c* 0.001, EtOH); **UV** (λ_{max}, MeOH, nm): 225 (ϵ = 9100); **IR** (ν_{max}, film, cm^{-1}): 3410, 2920, 2850, 1745, 1466, 1322, 1074; **MS**: CI-MS (BuOH, *m/z*), 613, 595, 577, 559, 541, 523, 413, 395, 377, 359, 343, 325, 285, 271, 269, 267, 253, 241, 223, 205, 199; EI-MS (*m/z*) 413, 377, 359, 343, 325, 307, 285, 269, 253, 241, 223, 213, 199, 141; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: acetonide (^1H NMR), per-acetate (^1H NMR), per-MTPA esters (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 6.04 \times 10^{-1}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 9.09 \times 10^{-2}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 6.45 \times 10^{-2}$ $\mu g\ ml^{-1}$, HT-29 ED_{50} = 1.48 $\mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

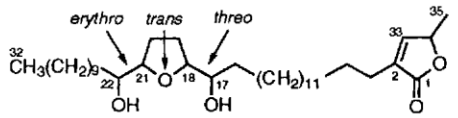
27. Annohexocin 64,[36] $C_{35}H_{64}O_9$, MW 628



Carbon No.	8	10	12	15	16	19	20
$^1H(\delta)$	3.95 m	4.13 dt	3.89 m	3.45 dt	3.88 m	3.86 m	3.81 m
$^{13}C(\delta)$	72.3	73.7	72.3	74.6	86.2	82.8	71.5

White powder; $[\alpha]_D$ +18.5° (*c* 0.33, $CHCl_3$); **UV** (λ_{max}, MeOH, nm): 208 (log ϵ = 3.24); **IR** (ν_{max}, film, cm^{-1}): 3410, 2920, 2850, 1745, 1466, 1322, 1074; **MS**: FAB-MS 629; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 34.4$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 0.34$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 2.26$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 0.78$ $\mu g\ ml^{-1}$, A-498 ED_{50} = 2.36 $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 0.0195$ $\mu g\ ml^{-1}$, PaCa-2 ED_{50} = 0.77 μg ml; **Source**: *Annona muricata*, leaves.

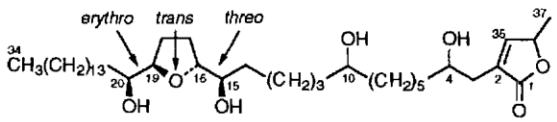
28. Annotemoyin-2 66,[93] $C_{35}H_{64}O_5$, MW 564



Carbon No.	17	18	21	22
$^1H(\delta)$	3.39 m	3.81 m	3.87 m	3.81 m
$^{13}C(\delta)$	74.30	83.30	82.05	71.63

White waxy solid; $[\alpha]_D$ +20° (*c* 0.11, MeOH); **UV** (λ_{max}, EtOH, nm): 217.1 (log ϵ = 3.66); **IR** (ν_{max}, film, cm^{-1}): 3448, 2927, 2858, 1756, 1661, 1459, 1376, 1319, 1200, 1066, 1028, 954, 875, 756, 723; **MS**: CI-MS (methane) 565, 547, 529, 511, 393, 375, 323, 295, 267, 241, 223, 171, 111, 97; EI-MS: 528, 393, 375, 357, 323, 295, 267, 241, 235, 223, 209, 195, 181, 167, 153, 139, 125, 111, 97; **NMR**: ^1H NMR (200 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona atemoya*, seeds.

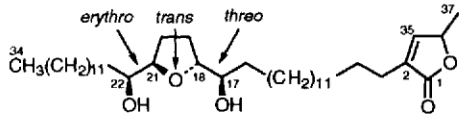
29. Annosenegalin 69,[103] $C_{37}H_{68}O_7$, MW 624



Carbon No.	10	15	16	19	20
$^1H(\delta)$	3.57 m	3.40 m	3.82 m	3.82 m	3.82 m
$^{13}C(\delta)$	71.70	74.31	83.24	82.26	71.70

Amorphous form: $[\alpha]_D$ +15° (*c* 0.27, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 207; **IR** (ν_{max}, film, cm^{-1}): 3400, 2910, 2845, 1745; **MS**: FAB-MS (NBa+LiCl) 631, 625, 613, 595, 577, 559; EI-MS: 397, 379, 361, 343, 327, 309, 297, 291, 273, 241, 227, 223, 141, 111; **NMR**: ^1H NMR (200 MHz, $CdCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona senegalensis*, seeds.

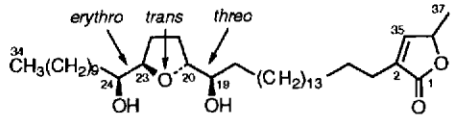
30. Reticulatain-1 70,[109] $C_{37}H_{68}O_5$, MW 592



Carbon No.	17	18	21	22
$^1H(\delta)$	3.40 m	3.84 m	3.84 m	3.84 m
$^{13}C(\delta)$	71.45	82.08	83.16	74.24

Whitish amorphous solid; **[α]$_D$** +22° (*c* 1, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 207; **IR** (ν_{max}, film, cm^{-1}): 3500, 3930, 2850, 1750; **MS**: CI-MS (isobutane) 593; EI-MS: 592, 574, 556, 403, 375, 351, 323, 295, 241; **NMR**: ^1H NMR (200 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona reticulata*, seeds.

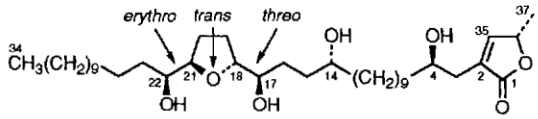
31. Reticulatain-2 71,[109] $C_{37}H_{68}O_5$, MW 592



Carbon No.	19	20	23	24
$^1H(\delta)$	3.40 m	3.84 m	3.84 m	3.84 m
$^{13}C(\delta)$	71.74	82.25	83.25	74.32

Whitish amorphous solid; **[α]$_D$** +28° (*c* 1, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 207; **IR** (ν_{max}, film, cm^{-1}): 3500, 2930, 2850, 1750; **MS**: CI-MS (isobutane) 593; EI-MS: 592, 574, 556, 403, 385, 351, 323, 241; **NMR**: ^1H NMR (200 MHZ, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona reticulata*, seeds.

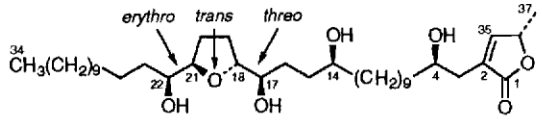
32. Rollinecin A 72,[62] $C_{37}H_{68}O_7$, MW 624



Carbon No.	14	17	18	21	22
$^1H(\delta)$	3.63 m	3.44 m	3.85 m	3.86–3.90 m	3.86–3.90 m
$^{13}C(\delta)$	71.72	74.59	83.10	82.18	71.55

Whitish waxy solid; **MP**: 61–62 °C **[α]$_D$** +10.0° (CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 227 (log ϵ = 3.80); **IR** (ν_{max}, film, cm^{-1}): 3400, 2910, 2800, 1745, 1665, 1075; **MS**: EI-MS (*m/z*) 407, 389, 371, 337, 319, 301, 297, 279, 141; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 3.1 \times 10^{-1}$ μg ml^{-1}, A-549 $ED_{50} = 1.14 \times 10^{-4}$ μg ml^{-1}, MCF-7 $ED_{50} = 1.44$ μg ml^{-1}, HT-29 $ED_{50} = 1.60$ μg ml^{-1}, A-498 $ED_{50} = 7.25 \times 10^{-4}$ μg ml^{-1}, PC-3 $ED_{50} = 2.62 \times 10^{-4}$ μg ml^{-1}, PaCa-2 $ED_{50} = 3.47 \times 10^{-5}$ μg ml^{-1}, **Source**: *Rollinia mucosa*, leaves.

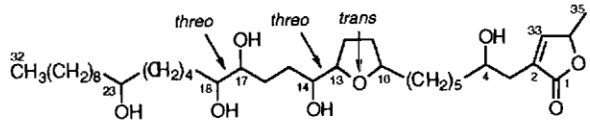
33. Rollinecin B 73,[62] $C_{37}H_{68}O_7$, MW 624



Carbon No.	14	17	18	21	22
$^1H(\delta)$	3.62 m	3.44 m	3.85 m	3.86–3.90 m	3.86–3.90 m
$^{13}C(\delta)$	71.90	74.67	83.11	82.19	71.54

Whitish waxy solid; **MP**: 61–62 °C; **[α]$_D$** +12.7° (CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 227 (log ϵ = 3.80); **IR** (ν_{max}, film, cm^{-1}): 3400, 2910, 2800, 1745, 1665, 1075; **MS**: EI-MS (*m/z*) 407, 389, 371, 337, 319, 301, 297, 279, 141; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities:** BST $LC_{50} = 1.3 \times 10^{-1}$ μg ml^{-1}, A-549 $ED_{50} = 4.23 \times 10^{-4}$ μg ml^{-1}, MCF-7 $ED_{50} = 2.72$ μg ml^{-1}, HT-29 $ED_{50} = 1.44$ μg ml^{-1}, A-498 $ED_{50} = 2.29 \times 10^{-4}$ μg ml^{-1}, PC-3 $ED_{50} = 3.62 \times 10^{-4}$ μg ml^{-1}, PaCa-2 $ED_{50} = 2.53 \times 10^{-4}$ μg ml^{-1}, **Source**: *Rollinia mucosa*, leaves.

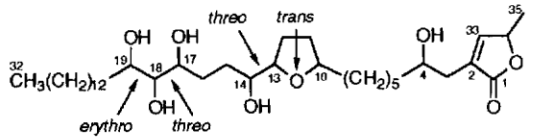
34. Muricatatin A 77,[92] $C_{35}H_{64}O_8$, MW 612



Carbon No.	10	13	14	17	18	23
$^1H(\delta)$	3.83 m	3.78 m	3.37 m	3.37 m	3.37 m	3.78 m
$^{13}C(\delta)$	79.30	81.81	74.70	74.36	74.26	74.51

Amorphous solid; **MP**: 83 °C; **[α]$_D$** +7.10° (*c* 0.63, MeOH); **UV** (λ_{max}, MeOH, nm): 227 (log ϵ = 3.80); **IR** (ν_{max}, film, cm^{-1}): 3400, 1740; **MS**: EI-MS (*m/z*) 485, 467, 449, 431, 399, 381, 363, 369, 351, 333, 315, 281, 263, 239, 221, 141; **NMR**: ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$); **Source**: *Annona muricata*, seeds and stem bark.

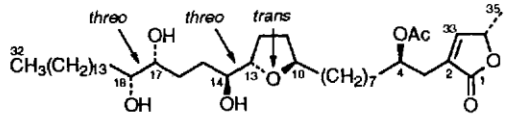
35. Muricatatin B 78,[92] $C_{35}H_{64}O_8$, MW 612



Carbon No.	10	13	14	17	18	19
$^1H(\delta)$	3.82 m	3.78 m	3.37 m	3.37 m	3.78 m	3.78 m
$^{13}C(\delta)$	80.36	80.57	74.56	74.67	70.38	71.36

Amorphous solid; **MP**: 128 °C **[α]$_D$** −11.43° (*c* 0.18, MeOH); **UV** (λ_{max}, MeOH, nm): 227 (log ϵ = 3.80); **IR** (ν_{max}, film, cm^{-1}): 3400, 1740; **MS**: EI-MS (*m/z*) 429, 401, 383, 355, 369, 351, 333, 315, 297, 281, 263, 239, 221, 141; **NMR**: ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (100 MHz, $CDCl_3$); **Source**: *Annona muricata*, seed and stem bark.

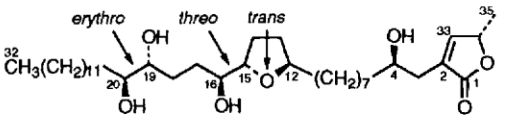
36. 4-Acetyl Gigantetrocin A 79,[34] $C_{37}H_{66}O_8$, MW 638



Carbon No.	4	10	13	14	17	18
$^1H(\delta)$	5.10 ddt	3.88 m	3.81q	3.42 m	3.44 m	3.44 m
$^{13}C(\delta)$	71.9	79.2	81.8	74.6	74.3	74.4

Colourless oil; $[\alpha]_D$ +13.5° (*c* 0.11, MeOH); **UV** (λ_{max}, EtOH, nm): 208 (log ϵ = 3.2); **IR** (ν_{max}, film, cm^{-1}): 3445, 2930, 2867, 1750, 1745, 1430, 1347; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **CD**: negative Cotton effect at 243 nm; **Derivatives**: per-acetate (^1H NMR), acetonide (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 6.78\ \mu g\ ml^{-1}$, A-549 $ED_{50} < 10^{-2}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 8.50 \times 10^{-1}\ \mu g\ ml^{-1}$, HT-29 $ED_{50} < 10^{-2}\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 1.55 \times 10^{-1}\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.02\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} < 10^{-2}\ \mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

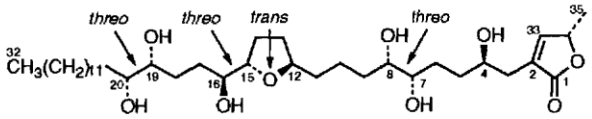
37. Muricatetrocin C 81,[32] $C_{35}H_{64}O_7$, MW 596



Carbon No.	12	15	16	19	20
$^1H(\delta)$	3.89 m	3.82 m	3.45 m	3.62 m	3.62 m
$^{13}C(\delta)$	79.3	81.7	74.3	74.4	7.47

White amorphous powder; **MP**: 65–66 °C; $[\alpha]_D$ +6.3° (CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 224 (log ϵ = 3.80); **IR** (ν_{max}, film, cm^{-1}): 3400, 2910, 2800, 1745, 1665, 1075; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), tetra-TMS (EI-MS); **Biological activities**: BST $LC_{50} = 7.6 \times 10^{-1}\ \mu g\ ml^{-1}$, A-549 $ED_{50} = 5.55 \times 10^{-6}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 3.19\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.98\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 3.39 \times 10^{-2}\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.35 \times 10^{-7}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 5.69 \times 10^{-7}\ \mu g\ ml^{-1}$; **Source**: *Rollinia mucosa*, leaves.

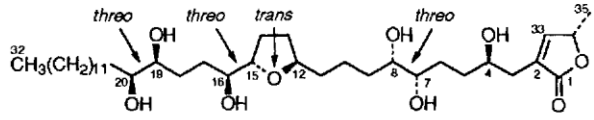
38. Murihexocin A 82,[34,37] $C_{35}H_{64}O_9$, MW 628



Carbon No.	7	8	12	15	16	19	20
$^1H(\delta)$	3.43 m	3.43 m	3.90 m	3.84 q	3.45 m	3.43 m	3.43 m
$^{13}C(\delta)$	74.4	74.5	79.4	81.7	74.1	74.3	74.5

White wax; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$): **Derivatives**: per-acetate (^1H NMR), acetonide (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 28.6\ \mu g\ ml^{-1}$, A-549 $ED_{50} = 1.32\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 12.54\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 3.0\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 2.51\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.71 \times 10^{-2}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 9.73 \times 10^{-2}\ \mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

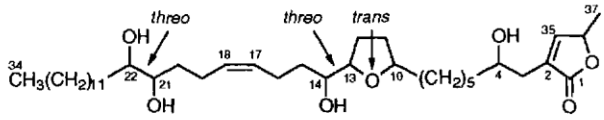
39. Murihexocin B 83,[34,37] $C_{35}H_{64}O_9$, MW 628



Carbon No.	7	8	12	15	16	19	20
$^1H(\delta)$	3.43 m	3.43 m	3.90 m	3.84 q	3.45 m	3.43 m	3.43 m
$^{13}C(\delta)$	74.4	74.5	79.4	81.9	74.7	74.4	74.5

White wax; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), acetonide (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 33.7\ \mu g\ ml^{-1}$, A-549 $ED_{50} = 1.08\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 6.95\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 2.30\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 4.92\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.26 \times 10^{-1}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 4.13 \times 10^{-1}\ \mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

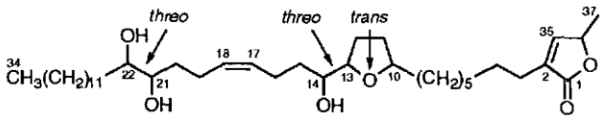
40. Coriacin 88,[114] $C_{37}H_{66}O_7$, MW 622



Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.90 m	3.80 dt	3.37 m	5.37 m	5.37 m	3.38 m	3.39 m
$^{13}C(\delta)$	79.4	81.6	74.3	129.8	129.9	73.0	72.7

Amorphous waxy solid; **MP**: 49–50 °C $[\alpha]_D$ +14.0° (*c* 1.0, EtOH); **UV** (λ_{max}, EtOH, nm): 204 (log ϵ = 3.98); **IR** (ν_{max}, film, cm^{-1}): 3473, 2931, 2858, 1762, 1542, 1075; **NMR**: ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **MS**: EI-MS, CID-B/E-MS, **Derivatives**: per-acetate (^1H NMR), acetonide (^1H NMR); oxidized and cyclized to gigantecin (^1H NMR); **Source**: *Annona coreacea*, roots.

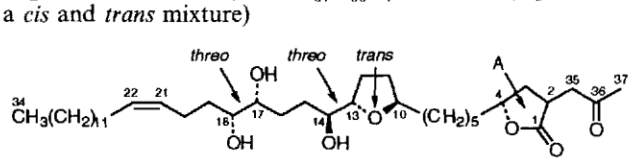
41. 4-Deoxycoriacin 89,[114] $C_{37}H_{66}O_6$, MW 606



Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.88 m	3.78 m	3.38 m	5.29 m	5.39 m	3.38 m	3.38 m
$^{13}C(\delta)$	79.5	74.3	74.3	129.9	130.1	72.9	72.7

White waxy solid; $[\alpha]_D$ +10.0° (*c* 1.0, EtOH); **UV** (λ_{max}, EtOH, nm): 207 (log ϵ = 3.93); **IR** (ν_{max}, film, cm^{-1}): 3591, 3007, 2934, 2858, 1752, 1459, 1076; **NMR**: ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **MS**: EI-MS, CID-B/E-MS, **Derivatives**: per-acetate (^1H NMR), acetonide (^1H NMR); oxidized and cyclized to 4-deoxygigantecin (^1H NMR); **Source**: *Annona coreacea*, roots.

Gigantetroneninone 90/91,[67] $C_{37}H_{66}O_7$, MW 622 (reported as a *cis* and *trans* mixture)



42. (2,4-*cis*)-Gigantetroneninone 90 (A = *cis*)

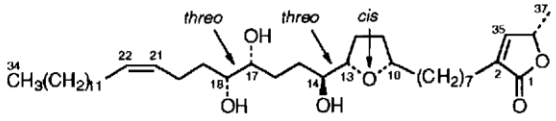
Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.88 m	3.81ddd	3.44 m	3.44 m	3.44 m	5.37 dt	5.39 dt
$^{13}C(\delta)$	79.20	81.73	74.40	74.16	74.21	128.96	130.77

43. (2,4-*trans*)-Gigantetroneninone 91 (A = *trans*)

Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.88 m	3.81ddd	3.44 m	3.44 m	3.44 m	5.37 dt	5.39 dt
$^{13}C(\delta)$	79.20	81.73	74.40	74.16	74.21	128.96	130.77

Whitish wax; **MP**: 98 °C; $[\alpha]_D$ +22.9° (*c* 0.01, CH_2Cl_2); **UV** (λ_{max}, MeOH, nm): 210 (ϵ = 10000); **IR** (ν_{max}, film, cm^{-1}): 3450, 2900, 2853, 1782, 1726, 1457, 1388, 1218, 1072; **MS**: CI-MS (isobutane, *m/z*) 623, 605, 587, 569; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: tri-acetate (^1H NMR), acetonide (^1H NMR), per-MTPA esters (^1H NMR), tri-TMS (E-MS); **Biological activities**: BST LC_{50} = 0.11 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 1.0 \times 10^{-6}\ \mu g\ ml^{-1}$, MCF-7 ED_{50} = 1.98 $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 4.81 \times 10^{-7}\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 1.12 \times 10^{-7}\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 8.35 \times 10^{-3}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.79 \times 10^{-7}\ \mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

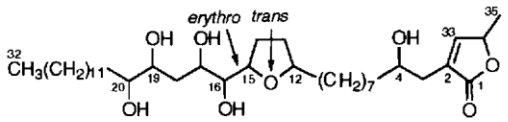
44. *cis*-Gigantrionenin 92,[34] $C_{37}H_{66}O_6$, MW 606



Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.87 m	3.73q	3.41 m	3.45 m	3.45 m	5.40 dt	5.36 dt
$^{13}C(\delta)$	80.0	82.0	74.9	74.2	74.2	129.0	130.8

Colourless oil; $[\alpha]_D$ +8.5° (*c* 0.18, MeOH); **UV** (λ_{max}, EtOH, nm): 207 (log ϵ = 3.1); **IR** (ν_{max}, film, cm^{-1}): 3440, 2928, 2860, 1750, 1455, 1325; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **CD**: 243 nm; **Derivatives**: acetonide (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 2.52 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 5.99 \times 10^{-2}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 2.68 \times 10^{-1}\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 6.94 \times 10^{-6}\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 1.39 \times 10^{-2}\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.11 \times 10^{-1}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.15 \times 10^{-1}\ \mu g\ ml^{-1}$; **Source**: *Annona muricata*, leaves.

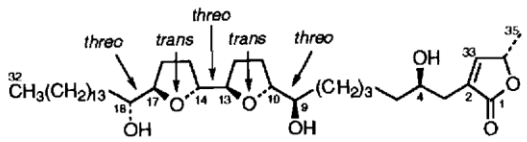
45. Muricatalin 94,[115] $C_{35}H_{64}O_8$, MW 612



Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.88 m	3.78 m	3.38 m	5.39 m	5.39 m	3.38 m	3.38 m
$^{13}C(\delta)$	79.5	74.3	74.3	129.9	130.1	72.9	72.7

White waxy solid; **MP**: 143–144 °C; $[\alpha]_D$ +8.8° (*c* 0.06, MeOH); **UV** (λ_{max}, EtOH, nm): 220 (log ϵ = 3.75); **IR** (ν_{max}, film, cm^{-1}): 3410, 1740; **NMR**: ^1H NMR (400 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **MS**: EI-MS, CID-B/E-MS, **Derivatives**: TMS (EI-MS): **Source**: *Annona muricata*, seeds.

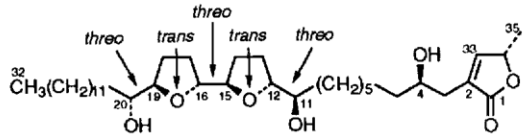
46. Longimicin C 95,[29] $C_{37}H_{66}O_7$, MW 622



Carbon No.	9	10	13	14	17	18
$^1H(\delta)$	3.39 m	3.83 m	3.83 m	3.83 m	3.83 m	3.39 m
$^{13}C(\delta)$	73.82	83.16	81.76	81.76	83.00	74.09

Colourless wax; $[\alpha]_D$ +14° (*c* 1, EtOH); **UV** (λ_{max}, EtOH, nm): 208 (log ϵ = 3.2); **IR** (ν_{max}, film, cm^{-1}): 3400, 2925, 2855, 1750, 1457, 1318, 1200, 1069, 954, 870; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 9.42 $\mu g\ ml^{-1}$, YFM LC_{50} = 75.7 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 4.55 \times 10^{-1}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 8.80 \times 10^{-2}\ \mu g\ ml^{-1}$, HT-29 ED_{50} = 1.00 $\mu g\ ml^{-1}$, A-498 $ED_{50} = 1.27 \times 10^{-1}\ \mu g\ ml^{-1}$, PC-3 ED_{50} = 2.96 $\mu g\ ml^{-1}$, PaCa-2 ED_{50} = 1.09 $\mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

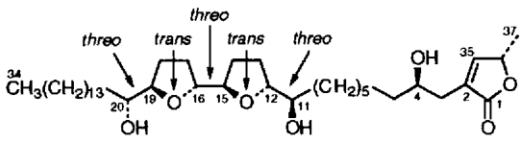
47. Longimicin B 96,[29] $C_{35}H_{62}O_7$ MW 594



Carbon No.	11	12	15	16	19	20
$^1H(\delta)$	3.39 m	3.83 m	3.83 m	3.83 m	3.83 m	3.39 m
$^{13}C(\delta)$	74.00	83.14	81.74	81.74	83.14	74.09

Colourless wax; $[\alpha]_D$ +14° (*c* 1, EtOH); **UV** (λ_{max}, EtOH, nm): 208 (log ϵ = 3.2); **IR** (ν_{max}, film, cm^{-1}): 3400, 2925, 2855, 1750, 1457, 1318, 1200, 1069, 954, 870; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 7.34 $\mu g\ ml^{-1}$, YFM LC_{50} = 30.4 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 1.43 \times 10^{-1}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.54 \times 10^{-2}\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 3.32 \times 10^{-3}\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 6.40 \times 10^{-2}\ \mu g\ ml^{-1}$, PC-3 ED_{50} = 2.20 $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 7.92 \times 10^{-2}\ \mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

48. Longimicin A 102,[29] $C_{37}H_{66}O_7$ MW 622

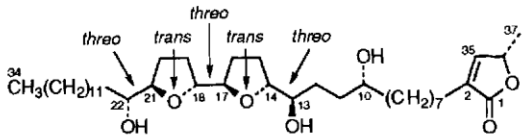


Carbon No.	11	12	15	16	19	20
$^1H(\delta)$	3.39 m	3.83 m	3.83 m	3.83 m	3.83 m	3.39 m
$^{13}C(\delta)$	74.09	83.23	81.82	81.82	83.15	74.17

Colourless wax; $[\alpha]_D$ +14° (*c* 1, EtOH); **UV** (λ_{max}, EtOH, nm): 208 (log ϵ = 3.2); **IR** (ν_{max}, film, cm^{-1}): 3400, 2925, 2855, 1750, 1457, 1318, 1200, 1069, 954, 870; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate

(^{1}H NMR), per-MTPA ester (^{1}H NMR), TMS (EI-MS); **Biological activities** : BST $LC_{50} = 18.7\ \mu g\ ml^{-1}$, YFM $LC_{50} = 141\ \mu g\ ml^{-1}$, A-549 $ED_{50} = 2.95 \times 10^{-1}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 8.89 \times 10^{-1}\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 5.25 \times 10^{-1}\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 5.54 \times 10^{-1}\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 7.01 \times 10^{2}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.73 \times 10^{-2}\ \mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

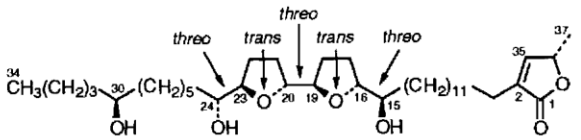
49. Longimicin D 103,[29] $C_{37}H_{66}O_7$, MW 622



Carbon No.	11	12	15	16	19	20
^{1}H(δ)	3.39 m	3.83 m	3.83 m	3.83 m	3.83 m	3.39 m
^{13}C(δ)	74.09	83.23	81.82	81.82	83.15	74.17

Colourless wax; $[\alpha]_D$ +14° (*c* 1, EtOH); **UV** (λ_{max}, EtOH, nm): 208 (log ϵ = 3.2); **IR** (ν_{max}, film, cm^{-1}): 3400, 2925, 2855, 1750, 1457, 1318, 1200, 1069, 954, 870; **NMR**: ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^{1}H NMR), per-MTPA ester (^{1}H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 4.58\ \mu g\ ml^{-1}$, YFM $LC_{50} = 8.29\ \mu g\ ml^{-1}$, A-549 $ED_{50} = 4.93 \times 10^{-4}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 2.15 \times 10^{-1}\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.16 \times 10^{-2}\ \mu g\ ml^{-1}$, A-498 $ED_{50} = 3.53 \times 10^{-2}\ \mu g\ ml^{-1}$, PC-3 $ED_{50} = 2.42 \times 10^{-4}\ \mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.69 \times 10^{-7}\ \mu g\ ml^{-1}$; **Source**: *Asimina longifolia*, leaves and twigs.

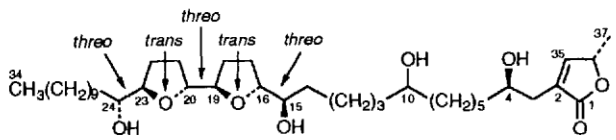
50. Asiminocin 111,[125] $C_{37}H_{66}O_7$, MW 622



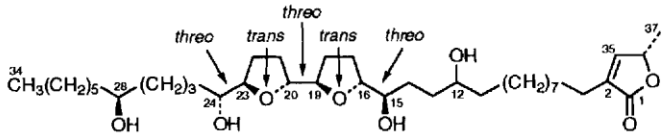
Carbon No.	15	16	19	20	23	24	30
^{1}H(δ)	3.40 m	3.86 m	3.86 m	3.86 m	3.86 m	3.40 m	3.59 m
^{13}C(δ)	74.07	83.15	81.80	81.78	83.07	73.99	71.92

Colourless wax; $[\alpha]_D$ +26° (*c* 1, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 215 (log ϵ = 3.1); **CD**: 237 nm; **IR** (ν_{max}, film, cm^{-1}): 3445, 2927, 2854, 1753, 1457, 1414, 1266, 1180, 1021, 926, 729; **NMR**: ^{1}H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^{1}H NMR), per-MTPA ester (^{1}H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 4.9 \times 10^{-3}\ \mu g\ ml^{-1}$, A-549 $ED_{50} = 3.1 \times 10^{-12}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} = 2.9 \times 10^{-12}\ \mu g\ ml^{-1}$, HT-29 $ED_{50} < 10^{-2}\ \mu g\ ml^{-1}$; **Source**: *Annona triloba*, stem bark.

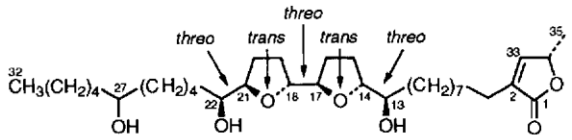
51. Compound-2 112,[52]



52. Compound-1 113,[52]



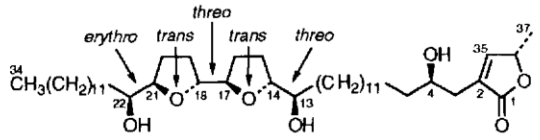
53. Atemoyacin B 120,[22] $C_{35}H_{62}O_7$, MW 594



Carbon No.	13	14	17	18	21	22	27
^{1}H(δ)	3.41 m	3.88 m	3.94 m	3.94 m	3.88 m	3.88 m	3.61 m
^{13}C(δ)	74.17	83.33	82.55	82.66	82.27	71.48	71.63

Colourless wax; $[\alpha]_D$ +12.9° (*c* 0.021, MeOH); **UV** (λ_{max}, MeOH, nm): 210 (ϵ = 7147); **IR** (ν_{max}, film, cm^{-1}): 3445, 3079, 2927, 2855, 1756, 1652, 1461, 1374, 1319, 1198, 1117, 1069, 1027, 953, 875, 722; **MS**: EI-MS; **NMR**: ^{1}H NMR (600 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Source**: *Annona atemoya*, seeds.

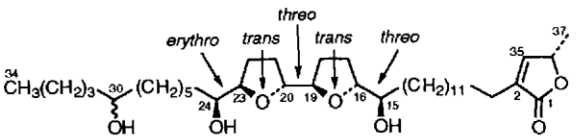
54. Squamotacin 123,[2] $C_{37}H_{66}O_7$, MW 622



Carbon No.	13	14	17	18	21	22
^{1}H(δ)	3.39 m	3.85 m	3.93 m	3.85 m	3.93 m	3.85 m
^{13}C(δ)	74.08	83.20	82.52	82.28	82.81	71.36

MS: CI-MS 623, EI-MS 283, 335; **NMR**: ^{1}H NMR (500 MHz $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: TMS (EI-MS); **Biological activities**: BST $LC_{50} = 6.80 \times 10^{-3}\ \mu g\ ml^{-1}$, A-549 $D_{50} = 2.77 \times 10^{-2}\ \mu g\ ml^{-1}$, MCF-7 $ED_{50} > 1\ \mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.00 \times 10^{-3}\ \mu g\ ml^{-1}$, A-498 $ED_{50} > 1\ \mu g\ ml^{-1}$; PC-3 $ED_{50} = 1.72 \times 10^{-9}\ \mu g\ ml^{-1}$; PaCa-2 $ED_{50} = 1.33 \times 10^{-4}$; **Source**: *Annona squamosa*, bark.

Bullanin 134/135,[141] $C_{37}H_{66}O_7$, MW 622 (isolated as 30*S*/*R* mixture)



55. (30*S*)-Bullanin 134,[141]

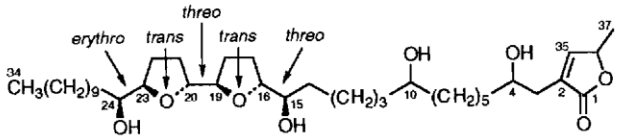
Carbon No.	15	16	19	20	23	24	30
^{1}H(δ)	3.40 m	3.85 m	3.83 m	3.93 m	3.93 m	3.88 m	3.58 m
^{13}C(δ)	74.1	83.3	82.5	82.3	82.7	71.3	71.87

56. (30*R*)-Bullanin 135,[141]

Carbon No.	15	16	19	20	23	24	30
$^1H(\delta)$	3.40 m	3.85 m	3.83 m	3.93 m	3.93 m	3.88 m	3.58 m
$^{13}C(\delta)$	74.1	83.3	82.5	82.3	82.7	71.3	71.93

Colourless wax; $[\alpha]_D$ +28° (*c* 0.5, EtOH); **UV** (λ_{max}, EtOH, nm): 220 (log ϵ = 2.42); **IR** (ν_{max}, film, cm^{-1}): 3442, 2927, 2852, 1747, 1459, 1320, 1193, 1070; **MS**: EI-MS 565, 511, 417, 295, 277, 291, 239, 221, 187, 169, 151; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS),tris-Si $(CD_3)_3$ (EI-MS); **Biological activities**: BST $LC_{50} = 6.0 \times 10^{-3}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} < 10^{-12}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} < 10^{-12}$ μg ml ^{1}, HT-29 $ED_{50} = 4.8 \times 10^{-12}$ $\mu g\ ml^{-1}$; **Source**: *Asimina triloba*, stem bark.

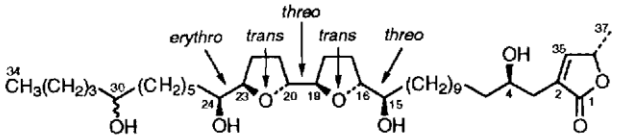
57. Annoglaucin 137,[26] $C_{37}H_{66}O_8$, MW 638



Carbon No.	10	15	16	19	20	23	24
$^1H(\delta)$	3.59 m	3.39 m	3.80 m	3.90 m	3.90 m	3.80 m	3.85 m
$^{13}C(\delta)$	71.6	74.0	83.1	82.4	82.1	82.6	71.3

Waxy solid; $[\alpha]_D$ +15.4° (*c* 0.6, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 210 (ϵ = 10000); **IR** (ν_{max}, film, cm^{-1}): 3430, 2930, 2855, 1740, 1460, 1320, 1070; **MS**: CI-MS (CH_4) 639, 621, 603, 585; EI-MS: 590, 570, 520, 471, 467, 379, 361, 341, 323, 309, 305, 297, 291, 279, 261, 241, 223, 205, 141, 123; **NMR**: ^1H NMR (200 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona glauca*, roots.

30-Hydroxybullatacin 139/140,[142] $C_{37}H_{66}O_8$, MW 638
(reported as 30*S*/*R* mixture)



58. (30*S*)-Hydroxybullatacin 139

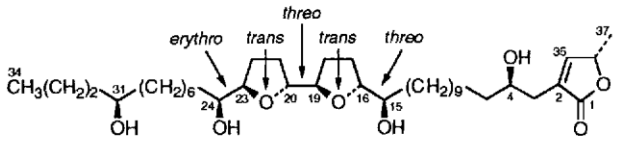
Carbon No.	15	16	19	20	23	24	30
$^1H(\delta)$	3.40 m	3.85 m	3.93 m	3.85 m	3.93 m	3.87 m	3.58 m
$^{13}C(\delta)$	74.1	83.2	82.3	82.5	82.8	71.3	71.77

59. (30*R*)-Hydroxybullatacin 140

Carbon No.	15	16	19	20	23	24	30
$^1H(\delta)$	3.40 m	3.85 m	3.93 m	3.85 m	3.93 m	3.87 m	3.58 m
$^{13}C(\delta)$	74.1	83.2	82.3	82.5	82.8	71.3	71.84

White powder; $[\alpha]_D$ +14° (*c* 0.5, $CHCl_3$); **IR** (ν_{max}, film, cm^{-1}): 3629, 2928, 1753; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), tri-TMS (EI-MS); **Biological activities**: BST $LC_{50} = 6.55 \times 10^{-2}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.17$ $\mu g\ ml^{-1}$, A-498 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 4.33 \times 10^{-3}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$; **Source**: *Annona bullata*, bark.

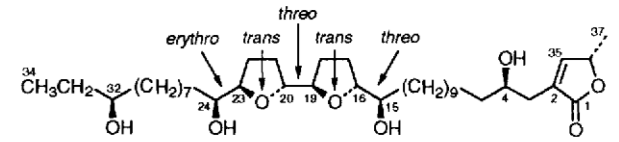
60. 31-Hydroxybullatacin 141,[142] $C_{37}H_{66}O_8$, MW 638



Carbon No.	15	16	19	20	23	24	31
$^1H(\delta)$	3.40 m	3.85 m	3.93 m	3.85 m	3.93 m	3.87 m	3.60 m
$^{13}C(\delta)$	74.1	83.2	82.3	82.5	82.8	71.3	71.7

White powder; $[\alpha]_D$ +19° (*c* 0.08, $CHCl_3$); **IR** (ν_{max}, film, cm^{-1}): 3630, 2926, 2854, 1752; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), tri-TMS (EI-MS); **Biological activities**; BST $LC_{50} = 5.72 \times 10^{-2}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.21$ $\mu g\ ml^{-1}$, A-498 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 3.16 \times 10^{-1}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$; **Source**: *Annona bullata*, bark.

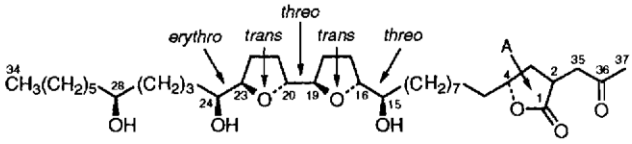
61. 32-Hydroxybullatacin 142,[142] $C_{37}H_{66}O_8$, MW 638



Carbon No.	15	16	19	20	23	24	32
$^1H(\delta)$	3.40 m	3.85 m	3.93 m	3.85 m	3.93 m	3.87 m	3.52 m
$^{13}C(\delta)$	74.1	83.2	82.3	82.5	82.8	71.3	73.3

White powder; $[\alpha]_D$ +19° (*c* 0.08, $CHCl_3$); **IR** (ν_{max}, film, cm^{-1}): 3630, 2926, 2854, 1752; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), tri-TMS (EI-MS); **Biological activities**: BST $LC_{50} = 8.00 \times 10^{-2}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.48$ $\mu g\ ml^{-1}$, A-498 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.62 \times 10^{-2}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$; **Source**: *Annona bullata*, bark.

28-Hydroxybullatacinone 152/153,[142] $C_3H_{66}O_8$, MW 638
(reported as a *cis* and *trans* mixture)



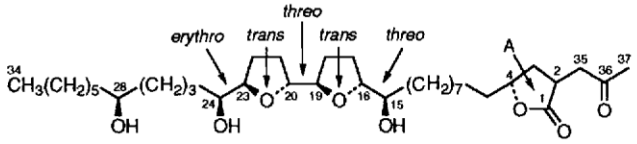
62. (2,4-*cis*)-28-Hydroxybullatacinone 152 (A = *cis*)

Carbon No.	15	16	19	20	23	24	28
$^1H(\delta)$	3.40 m	3.86 m	3.93 m	3.86 m	3.93 m	3.87 m	3.62 m
$^{13}C(\delta)$	74.1	83.3	82.3	82.5	82.8	71.8	71.4

Whitish wax; $[\alpha]_D$ +19° (*c* 0.08, $CHCl_3$); **IR** (ν_{max}, film, cm^{-1}): 3621, 1760, 1716; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C

NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR) TMS (EI-MS); **Biological activities**: BST $LC_{50} = 7.98 \times 10^{-2}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 4.38 \times 10^{-4}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 4.46 \times 10^{-4}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 6.9 \times 10^{-4}$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 4.35$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 2.33$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.02 \times 10^{-8}$ $\mu g\ ml^{-1}$; **Source**: *Annona bullata*, bark.

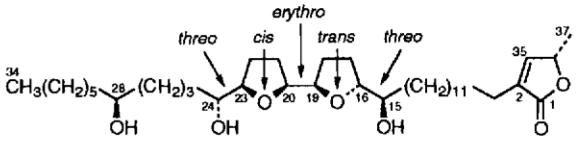
63. (2,4-*trans*)-28-Hydroxybullatacinone 153 (A = *trans*)



Carbon No.	15	16	19	20	23	24	28
$^1H(\delta)$	3.40 m	3.86 m	3.93 m	3.86 m	3.93 m	3.87 m	3.62 m
$^{13}C(\delta)$	74.1	83.3	82.2	82.5	82.8	71.8	71.4

Whitish wax; $[\alpha]_D$ 19° (*c* 0.08, $CHCl_3$); **IR** (ν_{max}, film, cm^{-1}): 3621, 1760, 1716; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 7.98 \times 10^{-3}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 3.18 \times 10^{-2}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.71$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.45$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 1.00 \times 10^{-3}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 9.04$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.19 \times 10^{-5}$ $\mu g\ ml^{-1}$; **Source**: *Annona bullata*, bark.

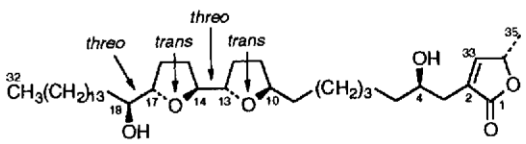
64. Asitribin 165,[94] $C_{37}H_{66}O_7$, MW 622



Carbon No.	15	16	19	20	23	24	28
$^1H(\delta)$	3.36 m	3.85 m	3.97 m	4.08 m	3.84 m	3.42 m	3.59 m
$^{13}C(\delta)$	74.58	83.01	81.69	80.97	82.48	73.56	71.77

Colourless powder; $[\alpha]_D$ +19° (*c*. 0.08, $CHCl_3$); **IR** (ν_{max}, film cm^{-1}): 3448, 2925, 2827, 1757, 1589, 1073; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: tri-acetate (^1H NMR, EIMS), per-MTPA ester (^1H NMR), tri-TMS (EI-MS); **Biological activities**: BST $LC_{50} = 2.35 \times 10^{-2}$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 2.25 \times 10^{-10}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.24 \times 10^{-4}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 7.04 \times 10^{-5}$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 1.69$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.30$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.25 \times 10^{-4}$ $\mu g\ ml^{-1}$; **Source**: *Asimina triloba*, seeds.

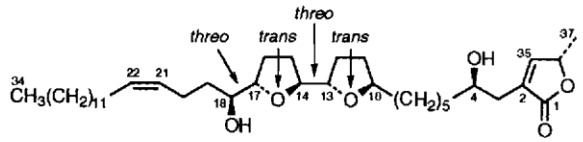
65. Asimilobin 172,[44,94] $C_{35}H_{62}O_6$, MW 578



Carbon No.	10	13	14	17	18
$^1H(\delta)$	3.85 m	3.94 m	3.85 m	3.85 m	3.38 m
$^{13}C(\delta)$	79.88	81.25	82.03	83.09	74.13

White needles; **MP** 56–57 °C; $[\alpha]_D$ +6.0° (*c* 0.05, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 228 (log $\epsilon = 2.98$); **IR** (ν_{max}, film, cm^{-1}): 3440, 2924, 2853, 1755, 1597, 1448, 1319, 1065, 845; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 1.06$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 3.01 \times 10^{-2}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 2.14$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 6.30 \times 10^{-2}$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 2.26 \times 10^{-2}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.47$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.04 \times 10^{-1}$ $\mu g\ ml^{-1}$; **Source**: *Asimina triloba*, seeds.

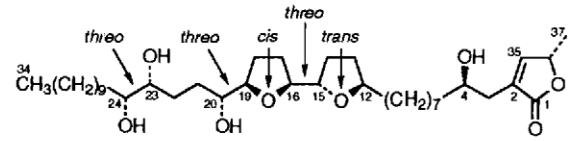
66. Goniodenin 173,[44] $C_{37}H_{64}O_6$, MW 604



Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.93 m	3.92–3.83 m	3.92–3.83 m	3.83 m	3.41 m	5.36 m	5.39 m
$^{13}C(\delta)$	79.90	81.24	82.09	83.02	73.57	129.09	130.62

Colourless oil; **MP** 56–57 °C; $[\alpha]_D$ +5.0° (*c* 1.10, CH_2Cl_2); **UV** (λ_{max}, EtOH, nm): 209 ($\epsilon = 1000$); **IR** (ν_{max}, film, cm^{-1}): 3435, 2926, 2856, 1755, 1454, 1320; **MS**: CI-MS 621; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), cyclogoniodenins T and C (^1H NMR), MTPA ester of cyclogoniodenins T and C (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 0.85$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 1.86 \times 10^{-2}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 8.40$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 4.45 \times 10^{-3}$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 8.98 \times 10^{-2}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.21$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.88 \times 10^{-1}$ $\mu g\ ml^{-1}$; **Source**: *Goniothalamus giganteus*, bark.

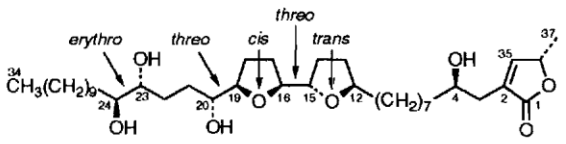
67. Rollidecin A 176,[32] $C_{37}H_{66}O_8$, MW 638



Carbon No.	12	15	16	19	20	23	24
$^1H(\delta)$	3.92–3.98 m	3.92–3.98 m	3.92–3.98 m	3.92–3.98 m	3.41 m	3.54 m	3.60 m
$^{13}C(\delta)$	80.3	80.7	81.4	82.6	74.6	74.8	75.4

Colourless waxy solid; **MP** 60–61 °C; $[\alpha]_D$ +13.0° (CH_2Cl_2); **UV** (λ_{max}, EtOH, nm): 222 ($\epsilon = 3300$); **IR** (ν_{max}, film, cm^{-1}): 3441, 2930, 2855, 1739, 1671, 1072; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST $LC_{50} = 0.42$ $\mu g\ ml^{-1}$, A-549 $ED_{50} = 1.04 \times 10^{-2}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.78$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 1.42$ $\mu g\ ml^{-1}$, A-498 $ED_{50} = 5.4 \times 10^{-1}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.65 \times 10^{-4}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 1.41 \times 10^{-6}$ $\mu g\ ml^{-1}$; **Source**: *Rollinia mucosa*, leaves.

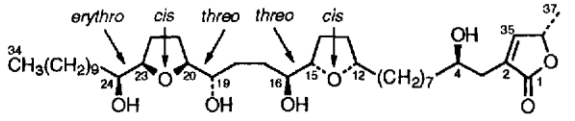
68. Rollidecin B 177,[32] $C_{37}H_{66}O_8$, MW 638



Carbon No.	12	15	16	19	20	23	24
$^1H(\delta)$	3.92–3.98 m	3.92–3.98 m	3.92–3.98 m	3.92–3.98 m	3.41 m	3.39–3.42 m	3.39–3.42 m
$^{13}C(\delta)$	80.2	80.8	81.4	82.7	74.6	74.9	75.6

Colourless waxy solid: **MP** 57–58°C $[\alpha]_D$ +8.8° (CH_2Cl_2); **UV** (λ_{max}, EtOH, nm): 224 (ϵ = 2800); **IR** (ν_{max}, film, cm^{-1}): 3445, 2935, 2854, 1739, 1670, 1074; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 0.28 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 3.73 \times 10^{-5}$ $\mu g\ ml^{-1}$, MCF-7 ED_{50} = 1.32 $\mu g\ ml^{-1}$, HT-29 ED_{50} = 1.69 $\mu g\ ml^{-1}$, A-498 $ED_{50} = 2.28 \times 10^{-5}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.73 \times 10^{-5}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 3.44 \times 10^{-6}$ $\mu g\ ml^{-1}$, **Source**: *Rollinia mucosa*, leaves.

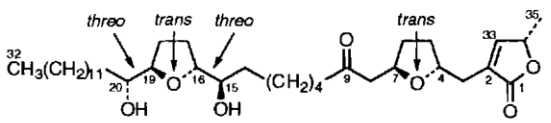
69. *cis*-Sylvaticin 204,[148] $C_{37}H_{66}O_8$, MW 638



Carbon No.	12	15	16	19	20	23	24
$^1H(\delta)$	3.88 m	3.71 q	3.41 m	3.51 m	3.86 m	3.93 m	3.86 m
$^{13}C(\delta)$	80.05	82.08	74.89	74.23	82.45	82.99	72.51

Colourless waxy solid: **MP**: 63–64 °C $[\alpha]_D$ +5.2° (CH_2Cl_2); **UV** (λ_{max}, EtOH, nm): 224; **IR** (ν_{max}, film, cm^{-1}): 1752; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: formal acetal (^1H NMR), per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 1.1 $\mu g\ ml^{-1}$, A-549 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 1.50 \times 10^{-1}$ $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 5.23 \times 10^{-1}$ 5.23×10^{-1} $\mu g\ ml^{-1}$, A-498 ED_{50} = 1.41 $\mu g\ ml^{-1}$, PC-3 ED_{50} = 1.80 $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} < 10^{-8}$ $\mu g\ ml^{-1}$; **Source**: *Rollinia mucosa*, leaves.

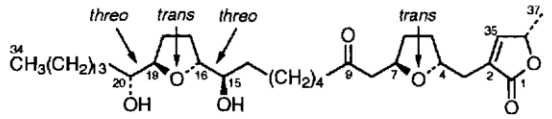
70. Aromin 205,[33] $C_{35}H_{60}O_7$, MW 592



Carbon No.	4	7	9	15	16	19	20
$^1H(\delta)$	3.59 m	3.84 m	—	3.40 m	3.79 m	3.79 m	3.40 m
$^{13}C(\delta)$	75.6	74.1	209.3	74.1	82.7	82.5	73.7

White waxy solid; **MP**: 48–49 °C; $[\alpha]_D$ +10.3° (c 0.25, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 230 (ϵ = 965); **CD** (MeOH): $[\theta]_{235.8}$ 1514.57, $[\theta]_{277.0}$ −810.15; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA ester (^1H NMR), 9-hydroxyl aromin (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 31.86 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 2.89 \times 10^{-1}$ $\mu g\ ml^{-1}$, MCF-7 ED_{50} = 1.22 $\mu g\ ml^{-1}$, HT-29 ED_{50} = 1.18 $\mu g\ ml^{-1}$, A-498 $ED_{50} = 7.50 \times 10^{-1}$ $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 5.98 \times 10^{-1}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 8.99 \times 10^{-1}$ $\mu g\ ml^{-1}$; **Source**: *Xylopia aromatica*, stem bark.

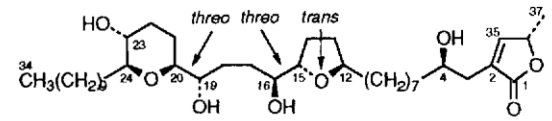
71. Aromicin 206,[33] $C_{37}H_{64}O_7$, MW 620



Carbon No.	4	7	9	15	16	19	20
$^1H(\delta)$	3.59 m	3.85 m	—	3.40 m	3.79 m	3.79 m	3.40 m
$^{13}C(\delta)$	75.6	74.0	209.3	73.7	82.7	82.5	73.7

White waxy solid; **MP**: 61–63 °C; $[\alpha]_D$ +9.9° (c 0.43, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 230 (ϵ = 965); **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-acetate (^1H NMR), per-MTPA ester (^1H NMR), 9-hydroxyl aromicin (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 10.28 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 2.17 \times 10^{-1}$ $\mu g\ ml^{-1}$, MCF-7 $ED_{50} = 4.24 \times 10^{-1}$ $\mu g\ ml^{-1}$, HT-29 ED_{50} = 1.09 $\mu g\ ml^{-1}$, A-498 $ED_{50} = 2.61 \times 10^{-1}$ $\mu g\ ml^{-1}$, PC-3 ED_{50} = 3.01×10^{-1} $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 2.25 \times 10^{-1}$ $\mu g\ ml^{-1}$, **Source**: *Xylopia aromatica*, stem bark.

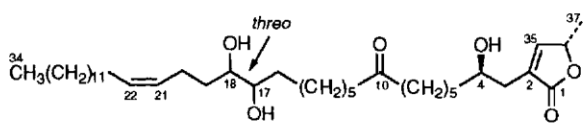
72. Mucocin 207,[31] $C_{37}H_{66}O_8$, MW 638



Carbon No.	12	15	16	19	20	23	24
$^1H(\delta)$	3.88	3.80	3.43	3.48	3.15	3.28	3.05
$^{13}C(\delta)$	79.3	81.9	73.8	73.5	80.1	70.5	82.0

Colourless waxy solid; **MP**: 57–58 °C; $[\alpha]_D$ −10.8° (CH_2Cl_2); **UV** (λ_{max}, EtOH, nm): 207 (log ϵ = 3.84); **IR** (ν_{max}, film, cm^{-1}): 3419, 2925, 2853, 1748, 1716, 1456, 1066; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: formal acetal (^1H NMR), per-MTPA ester (^1H NMR), tri-TMS (EI-MS); **Biological activities**: BST LC_{50} = 1.3 $\mu g\ ml^{-1}$, A-549 $ED_{50} = 1.0 \times 10^{-6}$ $\mu g\ ml^{-1}$, MCF-7 ED_{50} = 1.8 $\mu g\ ml^{-1}$, HT-29 $ED_{50} = 9.4 \times 10^{-1}$ $\mu g\ ml^{-1}$, A-498 ED_{50} = 2.6 $\mu g\ ml^{-1}$, PC-3 $ED_{50} = 1.6 \times 10^{-1}$ $\mu g\ ml^{-1}$, PaCa-2 $ED_{50} = 4.7 \times 10^{-7}$ $\mu g\ ml^{-1}$; **Source**: *Rollinia mucosa*, leaves.

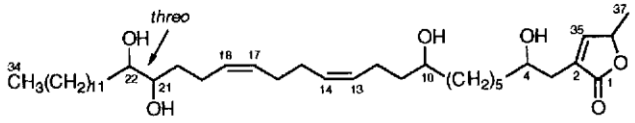
73. Venezenin 216,[167] $C_{37}H_{66}O_6$, MW 606



Carbon No.	10	17	18	21	22
$^1H(\delta)$	—	3.42 m	3.42 m	5.36 dd	5.40 dd
$^{13}C(\delta)$	211.5	74.4	74.2	128.8	131.0

White waxy solid; **MP**: 72–73 °C; $[\alpha]_D$ +16.8° (*c* 0.001, MeOH); **UV** (λ_{max}, EtOH, nm): 225 (log ϵ = 3.28); **IR** (ν_{max}, film, cm^{-1}): 3375, 2924, 2854, 1732, 1700, 1642, 1490, 1282, 1074, 669; **MS**: FAB-MS (606, 588, 570, 552; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: per-MTPA ester (^1H NMR), TMS (EI-MS); **Biological activities**: BST LC_{50} = 9.33 $\mu g\ ml^{-1}$, A-549 ED_{50} = 1.08×10^{-2} $\mu g\ ml^{-1}$, HT-29 ED_{50} = 1.58 $\mu g\ ml^{-1}$; **Source**: *Xylopia aromatica*, bark.

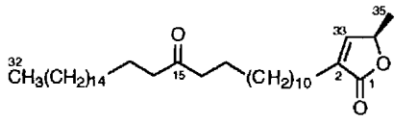
74. Coriadienin 223, [114] $C_{37}H_{66}O_6$, MW 606



Carbon No.	10	13	14	17	18	21	22
$^1H(\delta)$	3.58 m	5.43–5.35	5.43–5.35	5.43–5.35	5.43–5.35	3.41 m	3.39 m
$^{13}C(\delta)$	71.5	129.7	129.9	129.8	129.6	74.0	74.5

White waxy solid; **MP**: 58–60 °C $[\alpha]_D$ +6.2° (*c* 0.30, EtOH); **UV** (λ_{max}, EtOH, nm): 203 (log ϵ = 4.08); **IR** (ν_{max}, solution in CCl_4, cm^{-1}): 3468, 3009, 2934, 2857, 1732, 1750, 1600, 1457; **MS**: FABMS 606, 588, 570, 552; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: acetonide (^1H NMR), 13, 14, 17, 18-bisepoxycoriadienin (^1H NMR); **Biological activities**: 9KB ED_{50} = 1.9×10^{-6} $\mu g\ ml^{-1}$, VERO ED_{50} = 1.5×10^{-1} $\mu g\ ml^{-1}$; **Source**: *Annona coriacea*, roots.

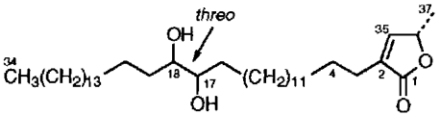
75. Reticulatamone 210, [109] $C_{37}H_{64}O_3$, MW 638



Carbon No.	15
$^1H(\delta)$	—
$^{13}C(\delta)$	211.51

White solid; **MP**: 83–85 °C; $[\alpha]_D$ +12° (*c* 1.0, $CHCl_3$); **IR** (ν_{max}, film, cm^{-1}), 2914, 2848, 1750, 1710, 1470; **MS**: CI-MS (isobutane) 533, 505; **NMR**: ^1H NMR (200 MHz, $CDCl_3$), ^{13}C NMR (50 MHz, $CDCl_3$); **Source**: *Annona reticulata*, seeds.

76. Tonkinelin 217, [168] $C_{37}H_{70}O_4$, MW 578



Carbon No.	17	18
$^1H(\delta)$	3.42	3.42
$^{13}C(\delta)$	74.53	74.53

White amorphous powder; **MP**: 64–66 °C; $[\alpha]_D$ +14.49° (*c* 0.07, $CHCl_3$); **UV** (λ_{max}, EtOH, nm): 203 (log ϵ = 4.08); **IR** (ν_{max}, solution in CCl_4, cm^{-1}): 3341, 2915, 2848, 1742; **MS**: CI-MS (isobutane); EI-MS; **NMR**: ^1H NMR (500 MHz, $CDCl_3$), ^{13}C NMR (125 MHz, $CDCl_3$); **Derivatives**: acetonide (^1H NMR), **Biological activities**: HL-60 IC_{50} = 1 μM, HCT-8 IC_{50} = 6.7 μM, KB IC_{50} > 10 μM, A 2780 IC_{50} > 10 μM; **Source:** *Uvaria tonkinesis*, bark roots.