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THE MARINE BROMOTYROSINE DERIVATIVES

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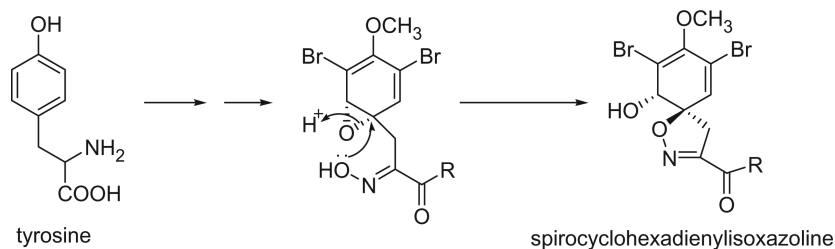
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I. Introduction

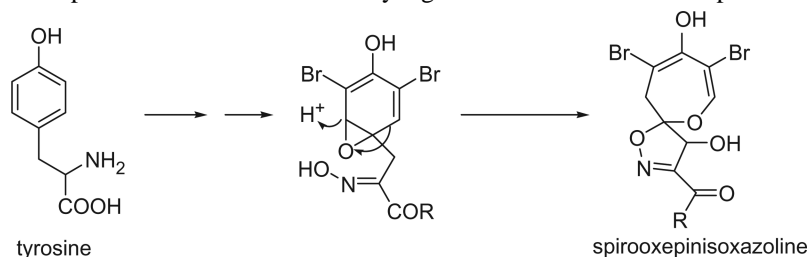
The isolation of bromotyrosine secondary metabolites from marine organisms can be traced back to 1913, when Morner reported the isolation of dibromotyrosine from two coral species (1). There were no reports provided for these secondary metabolites again until 1967, when Sharma and Burkholder isolated 2,6-dibromo-4-acetamide-4-hydroxycyclohexadienone (**1**) and the dimethoxyketal **2** from two marine sponges *Verongia fistularis* and *V. cauliformis* (2–4). Since then, driven by the diverse bioactivities, more and more bromotyrosine-derived marine natural products have been reported. To date, there are over 280 bromotyrosine-derived alkaloids reported from marine invertebrates with a variety of biological activities including: antimicrobial, anticancer, antifouling, antiviral, ATPase regulator, calcium channel modulator, etc.

In this review, we discuss the isolation, structure, physicochemical and spectral data of all bromotyrosine derivatives isolated from marine organisms. The biosynthesis, total synthesis, and bioactivity of the bromotyrosine derivatives are also reviewed. Neither tyrosine derivatives without halogenation, nor indole alkaloids (with or without halogenation), are included in this review. Proteins or peptides containing bromotyrosine units are not included in this review since they are considered as primary metabolites. Cyclopeptides containing halogenated tyrosine units are, however, discussed in this review.

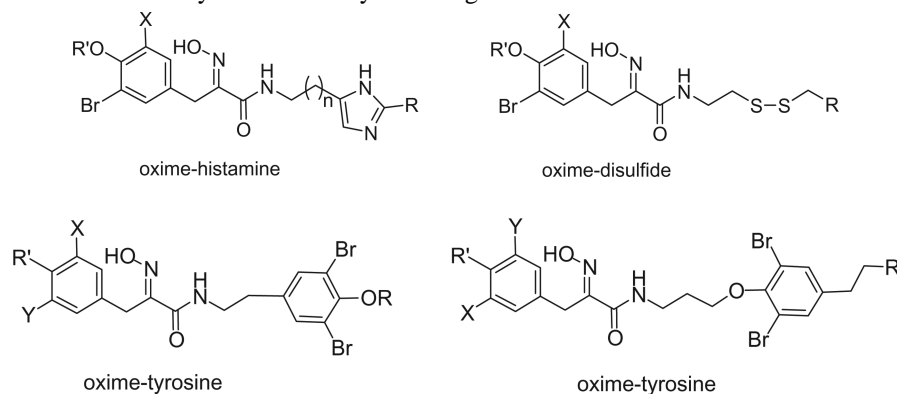
For convenience, the bromotyrosine derivatives are divided into six categories: simple bromotyrosine derivatives, spirocyclohexadienylisoxazolines, spirooxepinisoloxazolines, oximes, bastadins, and other structural classes. The simple bromotyrosine derivatives are products of one bromotyrosine undergoing degradation, reduction, hydroxylation, alkylation, or esterification with simple functional groups. In spirocyclohexadienylisoxazoline bromotyrosine derivatives, one or two bromotyrosine units are transformed into a spirocyclohexadienylisoxazoline undergoing an arene oxide biosynthetic pathway. This class of alkaloids generally consists of one to three bromotyrosine-derived units, as well as other functional groups, such as histamine.



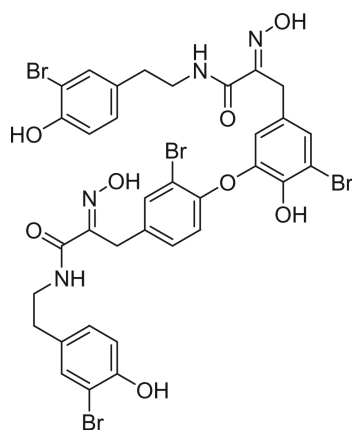
In the spirooxepinisoxazoline bromotyrosine derivatives, one bromotyrosine is transferred into a spirooxepinisoxazoline. There are only eight alkaloids in this class reported to date.



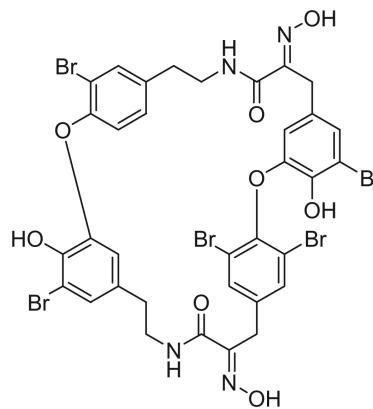
The amine functionality is transferred into an oxime in the oxime class of bromotyrosine derivatives. The geometries of the oxime functionalities were determined to be *E* in almost every case of this class of compounds. Although the geometries of some alkaloids in this class were not reported, it is easy to assign the *E* geometries for most of them from the ^{13}C NMR data. There are basically three structural groups in this class of bromotyrosine derivatives. The first group of alkaloids consists of a bromotyrosine oxime and a histamine moiety. The second group of alkaloids has one or two bromotyrosine oximes connected with a disulfide chain, cysteine. The third group of alkaloids has a bromotyrosine oxime connected to a bromotyramine directly or through a three carbon chain.



The bastadins are a series of predominantly macrocyclic bromotyrosine derivatives, which are biogenetically derivable from four bromotyrosines by the oxidative phenolic coupling of two tyramine–tyrosine units connected through an amide bond. Until now, there are four acyclic, twenty cyclic bastadins, and sixteen hemibastadins isolated from marine sponges and ascidians. Examples of this class of alkaloids are bastadins-1 (**204**) and -5 (**209**).



bastadin-1 (204)



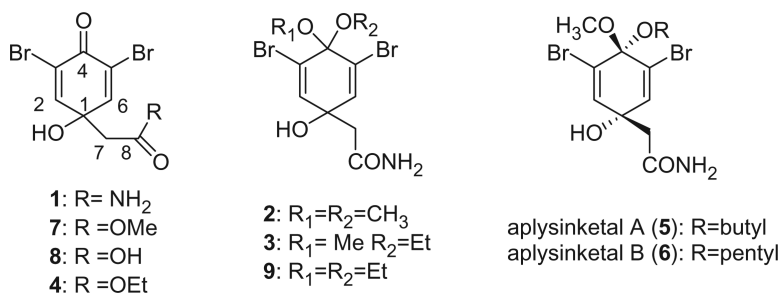
bastadin-5 (209)

There are a number bromotyrosine derived compounds not belonging to any of the above structure classes. Geodiamolides, a series of cyclic depsipeptides, are included in this review since they contain halogenated tyrosine. Polycitones and polycitrins are condensation products of substituted bromotyrosine molecules, isolated from ascidians, and are also included in this review. Similar structures including lamellarins are not included due to the absence of halogenation. For the same reason, polyandrocarpamides A-C (**253–255**), chelonin B (**256**), and 5-bromochelonin B (**257**) are included.

II. Isolation and Structure Elucidation

A. SIMPLE BROMOTYROSINE DERIVATIVES

The first two members of this series, 2,6-dibromo-4-acetamide-4-hydroxycyclohexadienone (**1**) and the dimethoxyketal **2**, were isolated from the methanolic extracts of *Verongia fistularis* and *V. cauliformis* by Sharma and Burkholder in 1967 (2–4). Anderson and Faulkner isolated a mixed methoxy–ethoxy ketal **3** from *Verongia* sp. in 1973. Since the ^1H NMR spectrum of **3** showed two methoxy signals, indicating that **3** is a mixture of two diastereoisomers, **2** and **3** were considered as artifacts generated during the extraction process (5). Faulkner *et al.* also reported the dienone **4** from *Tylodina fungina* (6). Two additional mixed ketals, aplysinketal A (**5**) and aplysinketal B (**6**), along with **7** and **8**, were obtained from the Mexican sponge *Aplysina (Verongia) thiona* (7). Unlike **2** and **3**, the structure of aplysinketal A (**5**) was shown to be only one of the two diastereoisomers by X-ray and NMR data. Furthermore, the mixed ketals **5** and **6** would not be expected to be formed without simultaneous formation of the dimethoxy ketal **2**, which was never detected. According to these results, aplysinketal A (**5**) and aplysinketal B (**6**) are very likely to be natural products. The diethyl ketal **9** was obtained from a Turkish sponge *V. aerophoba* (8).



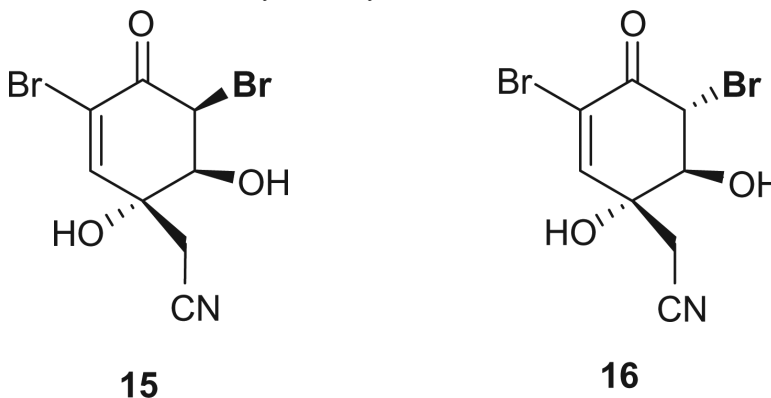
Monobromo- (**10**), bromochloro- (**11**), and dichloro- (**12**) dienones were isolated from *Aplysina cavernicola* (9,10). Both **10** and **11** were isolated as racemic mixtures. The dienone **13** was first obtained as a synthetic product after treatment of aeroplysinin-1 (**14**) with trifluoroacetic acid (11). Our group isolated **13** from the Jamaican sponge *Verongula gigantea* as a natural product (12).



3-bromoverongiaquinol (**10**): X = Br Y = H
 3-bromo-5-chloroverongiaquinol (**11**): X = Br Y = Cl
 dichloroverongiaquinol (**12**): X = Y = Cl

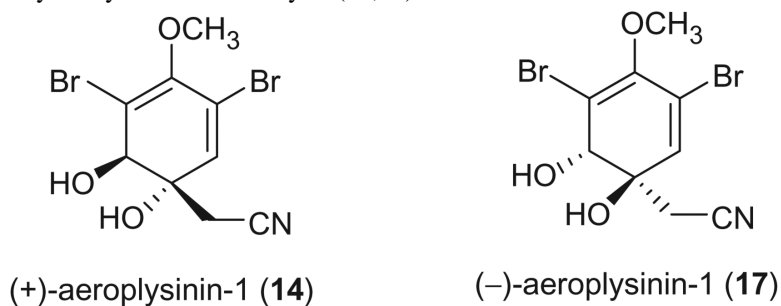
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A 3:1 mixture of the two epimeric dibromonitriles, **15** and **16**, was isolated from an Australian sponge *Aplysina laevis* (11). Attempts to resolve the mixture by either normal or reverse-phase HPLC, as well as GC, proved unsuccessful. Treatment of (+)-aeroplysinin-1 (**14**) with neat trifluoroacetic acid resulted in a good yield of **15** and **16** (3:1 mixture) with a small optical rotation value, which permitted the assignment of the absolute stereochemistries of **15** and **16** as shown. Molecular modeling calculations suggested that the *cis* isomer **15** was the thermodynamically more stable isomer.

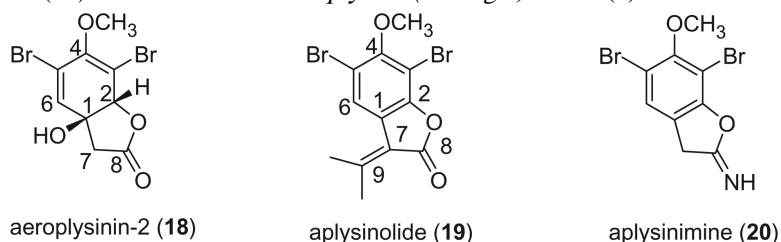


Aeroplysinin-1 (**14**), the first naturally occurring 1,2-dihydroarene-1,2-diol (13), was initially isolated as a dextrorotatory isomer from *V. aerophoba* [the species name was later revised to *V. cavernicola* (72)] (14,15). Fulmor *et al.* isolated the laevorotatory antipode of aeroplysinin-1 from a closely related sponge *Ianthella ardis*, for which the absolute configuration was proposed as shown in **17** on the basis of chemical, CD and NMR data

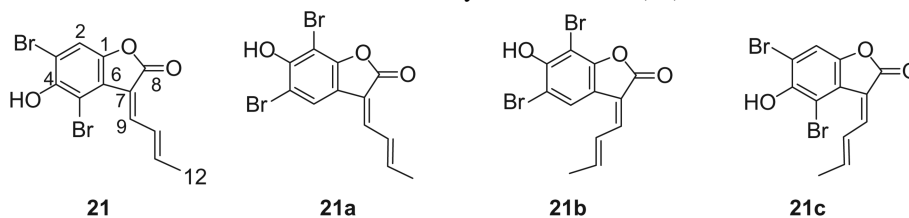
(16). The absolute stereochemistries of both antipodes, as shown in **14** and **17**, were firmly established by X-ray diffraction analysis (17,18).



Aerophysinin-2 (**18**), the first bromotyrosine derivative with a lactone functionality, was isolated from *V. aerophoba* in 1972 [the species name was later revised to *V. cavernicola* (69)] (19), and its structure was established on the basis of proton NMR and chemical methods. The small coupling (0.7 Hz) between the olefinic and methine protons suggested a W relationship for these two protons, indicating a quasi-equatorial orientation for the methine proton and accordingly, a quasi-diaxial orientation for the hydroxyl- and acyloxy-groups. The circular dichroism curve indicated a right-handed helicity for the diene, and therefore confirmed the absolute configuration as depicted in **18**. Aplysinolide (**19**) and aplysinimine (**20**) were obtained from *Aplysina (Verongia) thiona* (7).

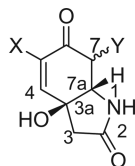


The isolation of aplysinimine (**20**) is remarkable because this alkaloid could be considered as a possible precursor of other bromo compounds obtained from *Aplysina* sponges. Aplysinolide (**19**) has an unusual α,β -unsaturated side chain. Another bromotyrosine derivative containing an α,β -unsaturated side chain is aplysinadiene (**21**), isolated from *Aplysina aerophoba* (20). The structure was determined by comparison of the NMR data with the synthesized isomers **21a** and **21b**. Structure **21c** was precluded due to the interaction of the bromine atom with the butenylide side chain (21).

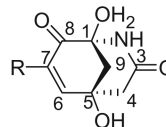


Eight lactams, including cavernicolin-1 (**22**), cavernicolin-2 (**23**), 5-bromocavernicolin (**24**), 5-chlorocavernicolin (**25**), 7 β -bromo-5-chlorocavernicolin (**26**), 7 α -bromo-5-chlorocavernicolin (**27**), 5-bromo-7 β -chlorocavernicolin (**28**), and 5-bromo-7 α -chlorocavernicolin (**29**), were identified from *V. cavernicola* (9,22,23). 5-Bromocavernicolin

(**24**) and 5-chlorocavernicolin (**25**) were the first examples of marine products with low enantiomeric purity. Cavernicolin-1 (**22**) and cavernicolin-2 (**23**), 7 β -bromo-5-chlorocavernicolin (**26**) and 7 α -bromo-5-chlorocavernicolin (**27**), 5-bromo-7 β -chlorocavernicolin (**28**) and 5-bromo-7 α -chlorocavernicolin (**29**), could be separated by HPLC, but they quickly equilibrate as a 3:1 mixture (9).



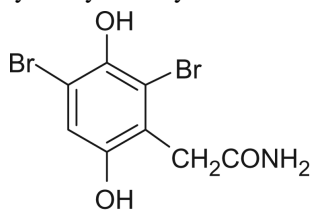
cavernicolin-1 (**22**): X = Br Y = β -Br
 cavernicolin-2 (**23**): X = Br Y = α -Br
 5-bromocavernicolin (**24**): X = Br Y = H
 5-chlorocavernicolin (**25**): X = Cl Y = H
 7 β -Bromo-5-chlorocavernicolin (**26**): X = Cl Y = β -Br
 7 α -Bromo-5-chlorocavernicolin (**27**): X = Cl Y = α -Br
 5-Bromo-7 β -chlorocavernicolin (**28**): X = Br Y = β -Cl
 5-Bromo-7 α -chlorocavernicolin (**29**): X = Br Y = α -Cl



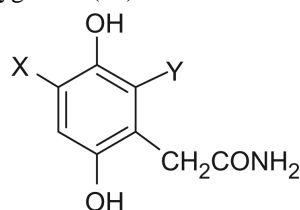
7-bromocarvernicolenone (**30**): R = Br
 7-chlorocarvernicolenone (**31**): R = Cl

Two δ -lactams, 7-bromocarvernicolenone (**30**) and 7-chlorocarvernicolenone (**31**), were also isolated from *V. cavernicola* (24, 25) and exhibited mild antibacterial activities. The structure and relative stereochemistry of 7-bromocarvernicolenone (**30**) was confirmed by X-ray diffraction analysis. 7-Bromocarvernicolenone (**30**) and 7-chlorocarvernicolenone (**31**) are additional examples of marine natural products having low enantiomeric purity.

The first, skeletally rearranged dibromotyrosine metabolite, and also the first hydroquinone in this family of marine natural products, **32**, whose structure was determined by X-ray crystallography, was isolated from *Verongia aurea*, along with **33** or **34**, as detected by gas chromatography–mass spectrometry of the ether extract (26). It represented a major departure from the normal dibromotyrosine metabolites, in which the aliphatic side chain remained in the *para* position relative to the hydroxyl group flanked by bromine atoms. An analogy for such a rearrangement of the tyrosine skeleton is available, however, in the conversion of 4-hydroxyphenylpyruvic acid into 2,5-dihydroxyphenylacetic (homogentisic acid), catalyzed by an enzyme classified as a mono-oxygenase (27).



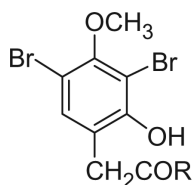
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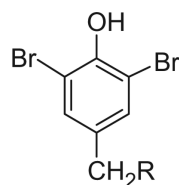
33: X=H Y=Br

34: X=Br Y=H

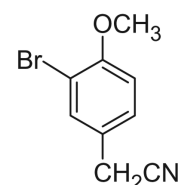
Additional aromatic bromotyrosine derivatives, **35–41**, were isolated from *Psammaphysilla purpurea*, *Verongia aerophoba*, *V. archeri*, and *Pseudoceratina crassa*, respectively (28–33).



- 35: R=NH₂
 36: R=OMe
 37: R=OH

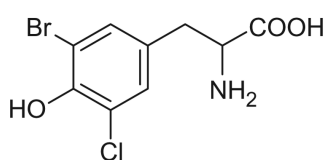


- 38: R=CONH₂
 39: R=CN
 40: R=COOH

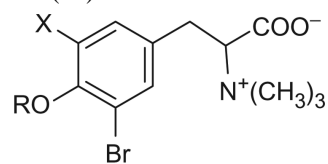


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3'-Chloro-5'-bromotyrosine (**42**) was identified from hydrolysates of a sclero-protein constituting the operculum of the gastropod mollusk *Baccinum undatum* in 1971 (34). *N,N,N*-Trimethyl halogenated tyrosines, **43**, **44**, **45**, and **46** were isolated from the Caribbean sponge *Pseudoceratina crassa* by Fattorusso's group (35). The absolute stereochemistries of **43** and **44** were determined to be *L* by Gao and Hamann (36).

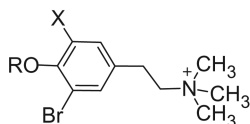


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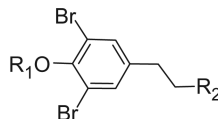


- 43: R = Me X = H
 44: R = H X = H
 45: R = Me X = Br
 46: R = H X = Br

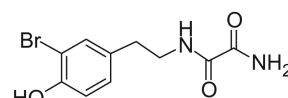
The first tyramine derivative, *N,N,N*-trimethyl-dibromotyramine (**47**), was identified from the sponge *Verongia fistularis* as a dual adrenergic compound in 1978 (37). Compound **48** was obtained as a natural and major bromo compound (1.7% dry weight) from a Caribbean sponge *Verongula* sp. (38). *N,N,N*-Trimethyl-3'-bromotyramine (**49**) and *N,N*-dimethyl-3', 5'-dibromotyramine (**50**) were isolated from the marine sponge *Verongula gigantea* (39). An undescribed ascidian *Eudistoma* sp. was found to contain 3',5'-dibromo-4'-methoxyphenethylamine (**51**), tryptamine and 4-hydroxyphenylacetamide (40). The 3'-bromotyramine amide of oxalic acid amide (**207**) was obtained from the Papua New Guinea sponge *Ianthella basta* (41).



- 47: R=H X=Br
 48: R= Me X=Br
 49: R=X=H



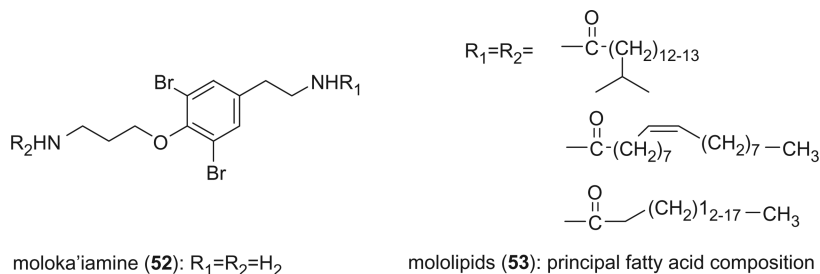
- 50: R₁=H R₂=NMe₂
 51: R₁=Me R₂=NH₂



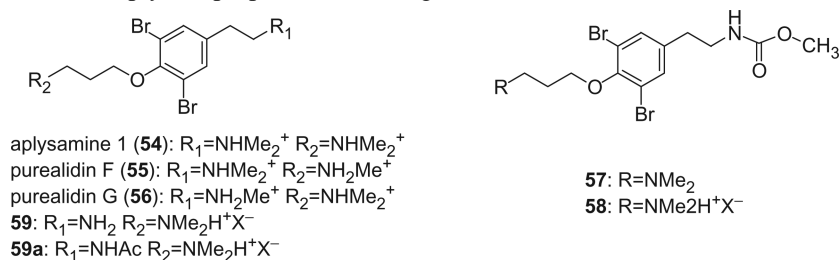
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Moloka'iamine (**52**), which is often represented as a substructure of many bromotyrosine derivatives, was reported as an independent entity from an undescribed Hawaiian *Verongia* sponge by Hamann and Scheuer (42). Mololipids (**53**) are a mixture of bisamides of moloka'iamine with long chain fatty acids and were isolated as an anti-HIV agent from this sponge more recently (43). The fatty acids of the mololipid mixture (**53**) are a homologous series of saturated linear and methyl branched fatty acids ranging from C₁₄ to C₂₀. Included

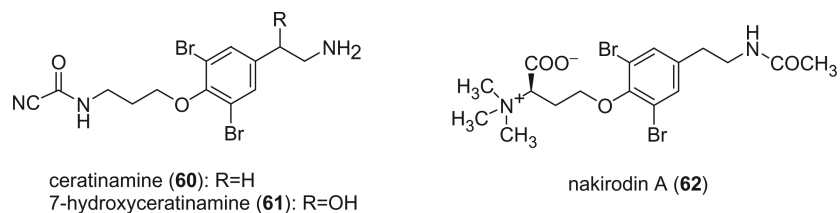
is at least one monounsaturated fatty acid of 18 carbon atoms, with a double bond at C-9. There were no fatty acids with more than one double bond detected. There are also mono-, di-, and trimethyl, internally branched, fatty acids containing 15, 17, and 19 carbons. The positions of the methyl substituents vary in the carbon chain. The ^{13}C NMR data clearly showed that the internal branching of the most abundant fatty acids did not occur at positions α , β , or γ from the carbonyl carbon or the terminal methyl group. There were no data to support or dismiss the possibility that the individual acids may occur randomly on either nitrogen of the core moloka'iamine nucleus.



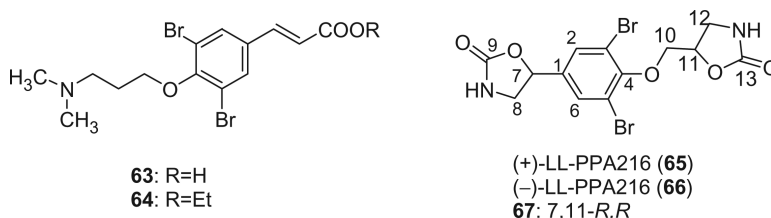
Different *N*-methylation derivatives of moloka'iamine, aplysamine 1 (**54**) (44), purealidin F (**55**), and G (**56**) (45), were obtained from an Australian sponge *Aplysina* sp. and the Okinawan sponge *Psammaphysilla pura*, respectively. 3,5-Dibromo-4-(3-dimethylaminopropoxy)phenethyl carbamic acid methyl ester (**57**) and its salt **58** were obtained as the first bromotyrosine derivatives containing a carbamate group from an Indian sample of *Psammaphysilla purpurea* (46), along with 59 (47,48).



An unprecedented cyanofornyl derivative, ceratinamine (**60**), was reported from the marine sponge *Pseudoceratina purpurea* by Fusetani's group in 1996 (49). Ceratinamine (**60**) was the first report of a cyanofornamide metabolite in natural products. It exhibited antifouling activity against *Balanus amphitrite* cyprides and cytotoxicity against P388 murine leukemia cells. The second example of a naturally occurring cyanofornamide metabolite, 7-hydroxyceratinamine (**61**), was isolated from a Micronesian sponge *Aplysinella* sp. by Fu and Schmitz (50). Nakirodin A (**62**) was isolated from an Okinawan marine Verongid sponge (51). The absolute configuration was determined to be *R* by the CD spectrum, of which *N,N,N*-trimethylhomoserine hydrolyzed from nakirodin A (**62**) showed a positive Cotton effect at 203.5 nm ($\epsilon +2.0$) that was identical to that of the authentic sample of *N,N,N*-trimethyl-*D*-homoserine. Although many bromotyrosine alkaloids possess one or more aminopropanol units (52), bromotyrosine alkaloids having an *N,N,N*-trimethylhomoserine residue, such as nakirodin A (**62**), are very rare (35,36). The structure of **62** indicated that the aminopropanol units found in many bromotyrosine alkaloids may be biogenetically derived from a homoserine through decarboxylation.



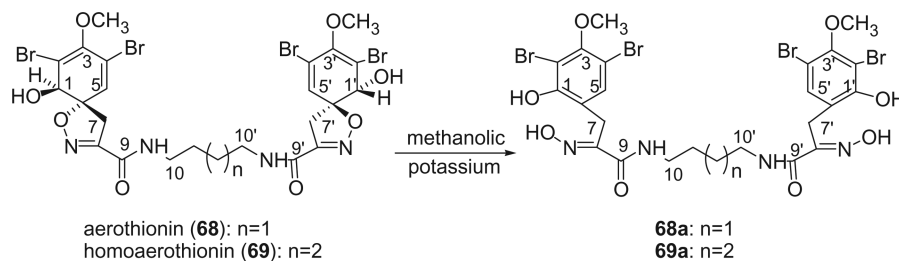
3,5-Dibromo-4-(3'-N,N-dimethylaminopropoxy)cinnamic acid (**63**) and its ethyl ester (**64**) were identified from the Caribbean sponge *Pseudoceratina crassa* by spectroscopic methods and total synthesis (53). LL-PPA216 (**65**) was first isolated as dextrorotatory ($[\alpha]_D + 8.9^\circ$) from the sponge *Verongia lacunosa* collected off the coast of Puerto Rico by Borders *et al.* in 1977 (54), and appeared to be the first bromine compound containing 2-oxazolidone rings isolated from a sponge. Makarieva *et al.* later reported the isolation of the (–)-enantiomer of LL-PPA216 (**66**, $[\alpha]_D = -6.5^\circ$) from *Aplisina* sp. collected in Cuba (55). Another isomer **67** was identified from the marine sponge *Aplysina aerophoba* by Norte *et al.* in 1988 and its absolute configuration was determined as *R, R* by X-ray analysis (21). The optical rotation of **67** ($[\alpha]_D = -33^\circ$) is significantly different from that of **65** and **66**, indicating that it is a new diastereomer of **65** and **66**.



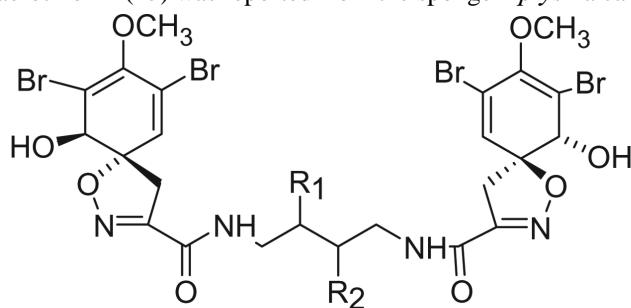
B. SPIROCYCLOHEXADIENYLISOXAZOLINE BROMOTYROSINE DERIVATIVES

1. Bis-Spirocyclohexadienylisoxazolines—The first

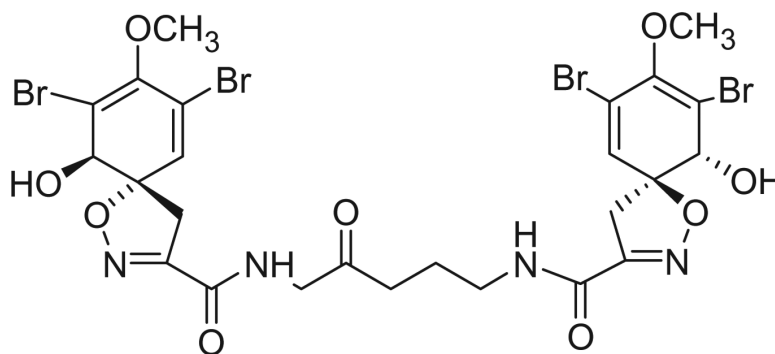
spirocyclohexadienylisoxazoline type bromotyrosine derivatives were aerothionin (**68**) and homoaerothionin (**69**), which were initially isolated from the marine sponge *Verongia aerophoba* [the species name was later revised to *V. cavernicola* (69)] and *V. thiona* by Fattorusso *et al.* in 1970 (56–58). The structure of aerothionin, the major component of both sponges (*ca.* 10% in *V. aerophoba*), was a result of a collaborative effort between Minale's laboratory and Thomson's laboratory based on proton NMR and chemical methods (59). Treatment of aerothionin with aqueous methanolic potassium converted it quantitatively into the oxime **68a**. This reaction was used to identify the spirocyclohexadienylisoxazoline structure. It must be noted that since aerothionin is optically active ($[\alpha]_D + 252^\circ$), the asymmetric end units must be identical and not in a mirror-image relationship. The structures of aerothionin and related bispirocyclohexadienylisoxazoline derivatives were mistakenly drawn as mirror-image relationships in many later publications. 3',5'-Dibromotyrosine is the probable precursor of the spirocyclohexadienylisoxazoline, and the C₄N₂ and C₅N₂ chains are derived from ornithine and lysine, respectively. The absolute stereochemistry was determined by X-ray crystallographic analysis and circular dichroism (60). The ¹³C NMR chemical shift assignments of C-2 and C-4 were inverted based on the correlation peaks between H-1/H-1' with C-2/C-2' and between H-5/H-5' and C-4/C-4' in the COLOC NMR experiment (61).



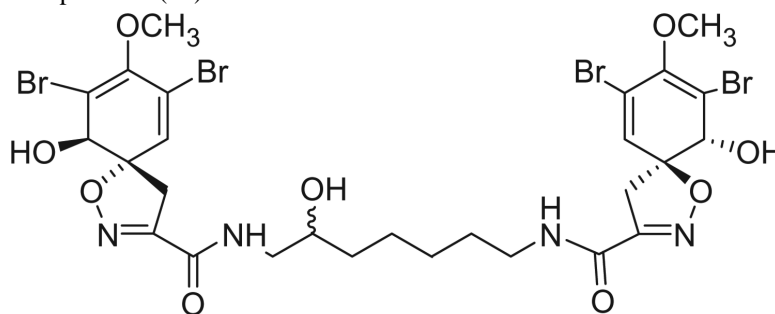
Dihydroxaerothionin (**70**) was isolated from the sponge *Verongula rigida* collected from Sweetings Cay, Bahamas at a depth of 228 feet using an untethered manned submersible. Its structure was determined based on the NMR data and the stereochemistry of the hydroxy group in the central chain was not determined (62). 11-Hydroxaerothionin (**71**) was identified from the sponge *Pseudoceratina durissima*, collected from the Great Barrier Reef, Australia, as an antimicrobial component against *Staphylococcus aureus* at 100 µg/disk, *Bacillus subtilis* at 50 µg/disk, and *Candida albicans* at 50 µg/disk. The relative stereochemistry of the 11-hydroxyl group was not determined (63). 11-Oxaerothionin (**72**) was isolated from a Caribbean sponge *Aplysina lacunosa* (64). It showed pronounced selective cytotoxicity toward the human colon HCT-116 cell line within a limited concentration range (0.01–0.1 µg/mL), in addition to moderate antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Two epimeric 11-oxo-12-hydroxaerothionins, **73** and **74**, were isolated from the Caribbean sponge *Aplysina fistularis* forma *fulva* (Pallas) by Fattorusso's group (61). Their ¹³C NMR, UV, and IR spectra are identical. However, their ¹H NMR spectra have minor differences, suggesting that they differ only in some stereochemical details. Because their CD spectra, which are sensitive to the configuration of the spirocyclohexadiene chromophore, are superimposable, **73** and **74** were concluded to be epimers at C-12. The configurations of 12-hydroxyl groups were determined as 12*S* for **73** and 12*R* for **74** using the modified Mosher's method. Oxohomoaerothionin (**75**) was reported from the sponge *Aplysina cavernicola* (65).



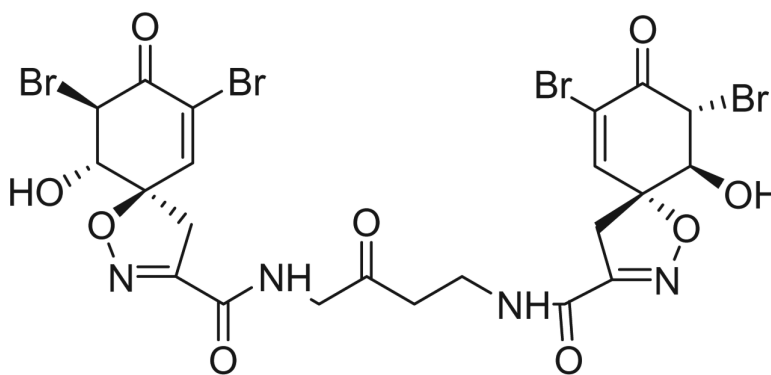
- dihydroxaerothionin (**70**): R₁=R₂=OH
 11-hydroxaerothionin (**71**): R₁=OH R₂=H
 11-oxaerothionin (**72**): R₁=oxo R₂=H
 12(*S*)-hydroxy-11-oxaerothionin (**73**): R₁=oxo R₂=S-OH
 12(*R*)-hydroxy-11-oxaerothionin (**74**): R₁=oxo R₂=R-OH

oxohomoaerothionin (**75**)

Structurally related to aerothionin and homoaerothionin, caissarine B (**76**), recently isolated from the Brazilian sponge *Aplysina caissara*, is the only bromotyrosine-derived alkaloid bearing a 1,7-diamino-3-hydroxyheptane chain, a diamine moiety that has no precedent among natural products (66).

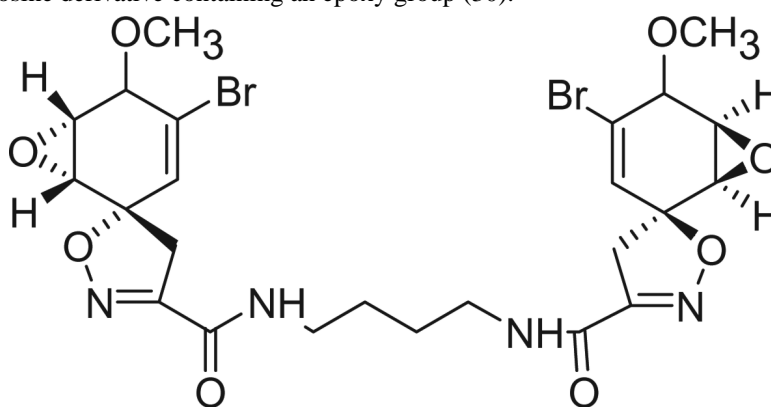
caissarine B (**76**)

Modification of the spirocyclohexadienylisoxazoline is very rare, which includes compound **77** and calafianin (**78**). Alkaloid **77**, isolated from the sponge *Aplysina archeri*, was the second example of a bromotyrosine derivative with a spirocyclohexenonylisoxazole ring. Its structure was assigned on the basis of spectroscopic evidence, including 2D-NMR experiments, and the absolute configuration shown in the structure has been suggested using the helicity rule (67).



77

Calafianin (78), isolated from the Mexican sponge *Aplysina gerardogreeni*, is the only bromotyrosine derivative containing an epoxy group (30).

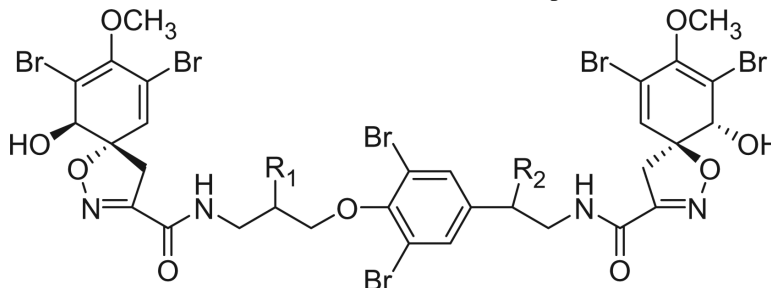


calafianin (78)

Fistularin-3 (79) was isolated from *Aplysina fistularis* forma *fulva* as a cytotoxic component by Gopichand and Schmitz in 1979 (68). Its planar structure was determined as two spirocyclohexadienylisoxazolines connected by a bromotyramine central chain based on proton NMR and alkaline hydrolysis. The relative stereochemistry of the spirocyclohexadienylisoxazoline was the same as aroethionin, based on the proton chemical shifts and coupling constants of H-1/1' and H-7/7'. The absolute stereochemistry was also determined to be the same as aroethionin based on comparable CD spectrum (36). The configuration of the two chiral centers at C-11 and C-17 remain to be determined. Three stereoisomers of fistularin-3 were reported later. Cimino *et al.* argued that isofistularin-3 (80), which was isolated from *Verongia aerophoba* with practically identical UV, IR and optical rotation, was different from fistularin-3 in the stereo-chemistry at one (or more) of the chiral centers based on minor differences when the proton NMR spectra of the acetates of both isofistularin-3 and fistularin-3 were directly compared (69).

König and Wright reported a C-11 stereoisomer of fistularin-3, 11-*epi*-fistularin-3 (81), from the tropical sponge *Agelas oroides* (70). Comparison of the ^{13}C and ^1H NMR of 81 with

those for fistularin-3 revealed small, but significant, differences, notably at C-11 (70.7 ppm in **81** and 69.5 ppm in fistularin-3). All other differences between the two sets of ^{13}C NMR data were in the range of 0.1 to 0.2 ppm. The optical rotation of **81** is $+66^\circ$ compared to $+104^\circ$ (68) and $+102^\circ$ (71) for fistularin-3. The stereochemistry of the spiroisoxazole moiety was deduced as $1R, 1'R, 6S,$ and $6'S$ by CD analysis, leaving the configuration of the hydroxyl groups at C-11 and C-17 undetermined. 11-*epi*-Fistularin-3 was not cytotoxic towards KB-cells ($\text{IC}_{50} > 20 \mu\text{g/mL}$) in contrast to fistularin-3 ($\text{IC}_{50} > 4.1 \mu\text{g/mL}$) (68) and isofistularin-3 ($\text{IC}_{50} > 4 \mu\text{g/mL}$) (69). Aydogmus et al. claimed another stereoisomer of fistularin-3, 1-*epi*-fistularin-3, based on the minor differences (less than 0.03 ppm) of the proton chemical shifts of H-1,1' and H-7,7' for 1-*epi*-fistularin-3 tetraacetate compared to isofistularin-3 tetraacetate (69) and fistularin-3 (68), and an optical rotation of $+51.6^\circ$ (8).



fistularin-3 (**79**): $R_1=R_2=\text{OH}$

11-*epi*-fistularin-3 (**81**): $R_1=\textit{epi}\text{-OH}$ $R_2=\text{OH}$

11-ketofistularin-3 (**82**): $R_1=\text{oxo}$ $R_2=\text{OH}$

11,19-dideoxyfistularin-3 (**83**): $R_1=R_2=\text{H}$

19-deoxyfistularin-3 (**84**): $R_1=\text{OH}$ $R_2=\text{H}$

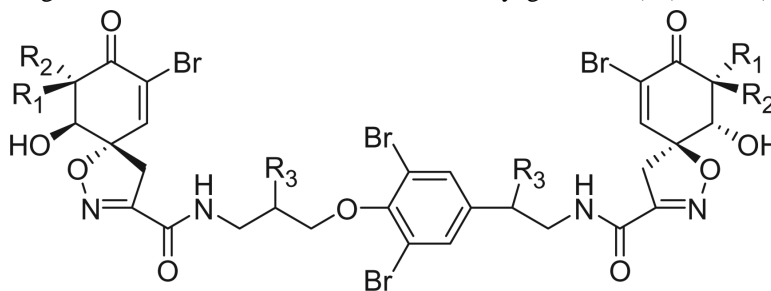
19-deoxy-11-oxofistularin-3 (**85**): $R_1=\text{oxo}$ $R_2=\text{H}$

11-dehydroxyfistularin-3 (**86**): $R_1=\text{H}$ $R_2=\text{S-OH}$

11-Ketofistularin-3 (**82**) and fistularin-3 were obtained from the sponge *Aplysina archeri* (71). Both compounds exhibited antiviral activity against feline leukemia virus with ED_{50} values of $42 \mu\text{M}$ and $22 \mu\text{M}$, respectively. 11,19-Dideoxyfistularin-3 (**83**) was reported as an antibiotic from the sponge *Pseudoceratina durissima*, which is more active than aethionin (**68**) and homoaethionin (**69**) (63). 19-Deoxyfistularin 3 (**84**) and 19-deoxy-11-oxofistularin 3 (**85**) were isolated from an undescribed Italian sponge *Verongia* sp. by Mancini *et al.* in 1993 (72). 19-Dehydroxyaethionin (**86**) was isolated from the sponges *Aplysina cavernicola* (65) and *Aplysina fistularis* (73). The absolute stereochemistry of the spirocyclohexadienylisoxazole moieties were determined to be the same as aethionin by the CD spectrum, and the configuration of C-19 was deduced as S by the modified Mosher's method (65).

Agelorins A and B (**87** and **88**) were isolated from the marine sponge *Agelas oroides* (Agelasidae, Axinellida) (70). The structures contain two units quite similar to the usual spirocyclohexadienylisoxazole fragments differing only by the presence of a cyclohexenone instead of a cyclohexadienyl ring. This structural feature is unique among the bromotyrosine derivatives. The relative stereochemistry of the spirocyclohexenonylisoxazole was

determined from the proton NMR and NOESY spectra. A collection of the marine sponge *Suberea* aff. *praetensa* from the Gulf of Thailand furnished the bromotyrosine derivatives fistularin-3, agelorin A and B, and the new 11,17-dideoxyagelorin A (**89**) and B (**90**) (74).



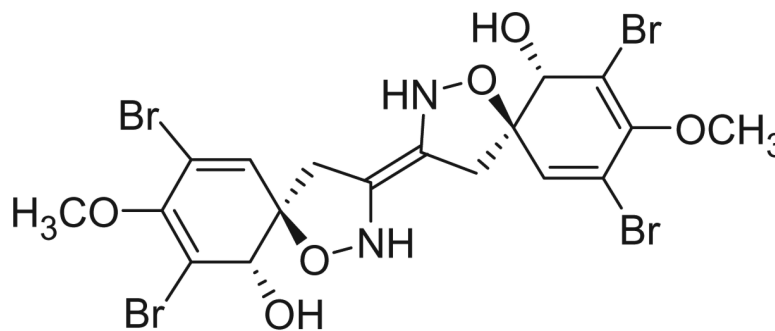
agelorin A (**87**): $R_1 = H$ $R_2 = Br$ $R_3 = OH$

agelorin B (**88**): $R_1 = Br$ $R_2 = H$ $R_3 = OH$

11,17-dideoxyagelorin A (**89**): $R_1 = H$ $R_2 = Br$ $R_3 = H$

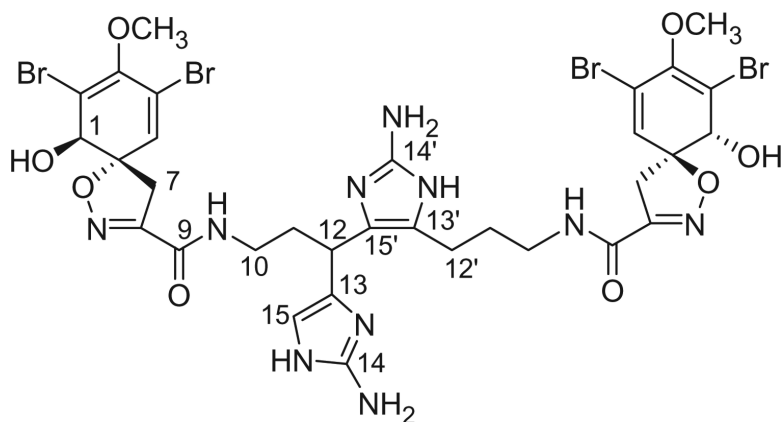
11,17-dideoxyagelorin B (**90**): $R_1 = Br$ $R_2 = H$ $R_3 = H$

Zamamistatin (**91**) was isolated from the sponge *Pseudoceratina purpurea* with significant antibacterial activity against *Rhodospirillum salexigens*, which has adhering properties, and may be a valuable candidate for novel antifouling agents (75,76). It was determined to be an optically active dimer of spirocyclohexadienylisoxazoline by the careful analysis of the 1D and 2D NMR spectra and its absolute stereochemistry was determined by the modified Mosher's method.

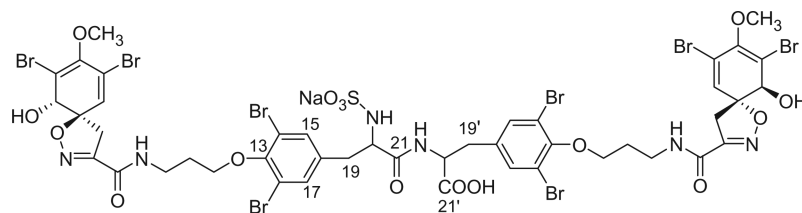


zamamistatin (**91**)

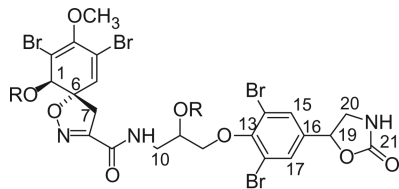
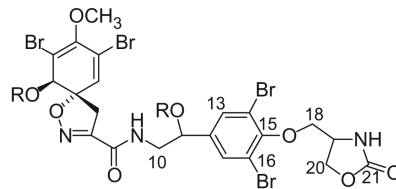
Archerine (**92**), a novel anti-histaminic bromotyrosine derivative, was identified from the Caribbean marine sponge *Aplysina archeri* by Fattorusso's group in 2001 (77). Its structure is novel in having the central chain formed by two 2-amino-homohistamine residues through a carbon-carbon bond. The configuration of C-12 remains to be assigned. Histamine or homohistamine are not unusual in bromotyrosine derivatives. However, archerine (**92**) is the only example having two homohistamine residues. The structure of archerine (**92**) suggests a biogenetic origin from a [1+1] intermolecular oxidative coupling of two molecules of aerophobin-2 (**114**), which also exists in this sponge.

archerine (**92**)

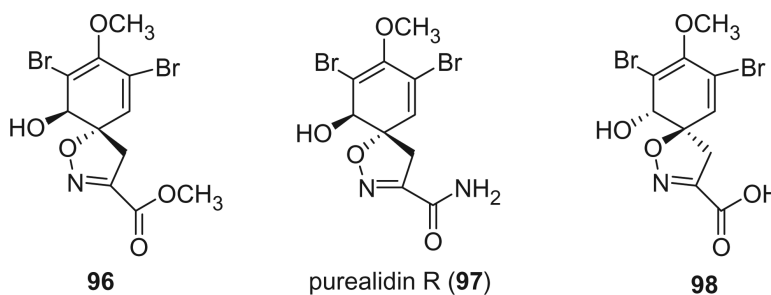
Ianthesine C (**93**) was isolated as a 3:2 mixture of diastereomers from an Australian marine sponge of the genus *Ianthella* sp. by Okamoto *et al.* in 2000 (78). It is a tetrameric bromotyrosine derivative having two spirocyclohexadienylisoxazoline ring systems linked by two bromotyrosines and two C3 units. The configurations of C-20 and C-20' of these diastereomers are unclear.

ianthesine C (**93**)

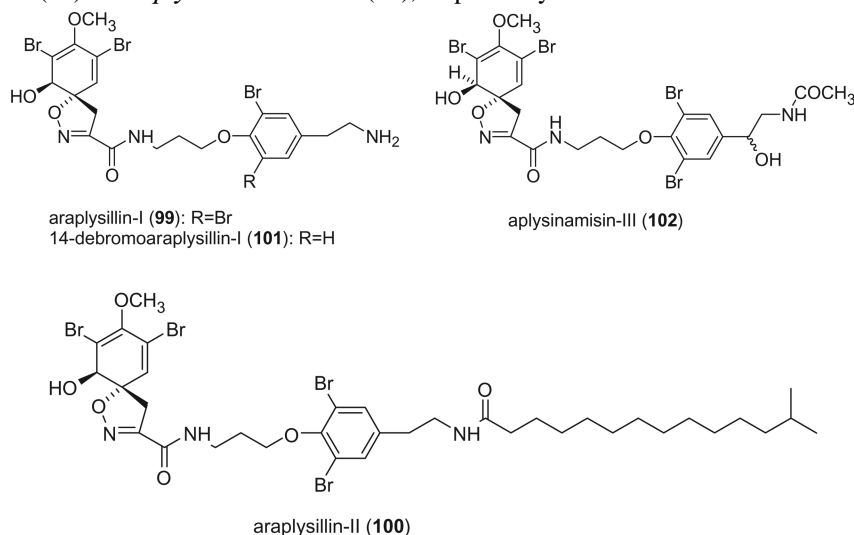
2. Mono-spirocyclohexadienylisoxazolines—This class of bromotyrosine derivatives contains one spirocyclohexadienylisoxazoline ring system. The first two alkaloids in this class are fistularin-1 (**94**) and fistularin-2 (**95**) isolated from the marine sponge *Aplysina fistularis* forma *fulva* by Gopichand and Schmitz in 1979 (68). Both compounds contain a spirocyclohexadienylisoxazoline, a bromotyramine, and a C3 unit.

fistularin-1 (**94**): R=H
fistularin-1 acetate (**94a**): R= COCH₃fistularin-2 (**95**): R=H
fistularin-2 acetate (**95a**): R= COCH₃

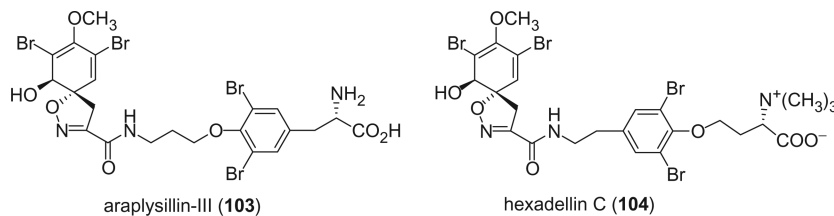
a. Simple Mono-spirocyclohexadienylisoxazolines: There are only three alkaloids in this group. Alkaloids **96** and **97** were reported by Ciminiello *et al.* from the Caribbean sponge *Verongula* sp. (38). Alkaloid **97** was also isolated from the Okinawan sponge *Psammaplysilla porea* and was named as purealidin R (79). Alkaloid **98** was isolated from a Caribbean sponge *Pseudoceratina* sp. as a major brominated metabolite (80).



b. Bromotyrosine Mono-spirocyclohexadienylisoxazoline: Araplysillins-I (**99**) and -II (**100**) were isolated from the sponge *Psammaphysilla arabica* and were established to be inhibitors of Na,K-ATPase and have antimicrobial activity (81). Two closely related alkaloids, 14-debromoaraplysillin-I (**101**) and aplysinamisin III (**102**) were isolated from *P. purpurea* (82) and *Aplysina cauliformis* (83), respectively.

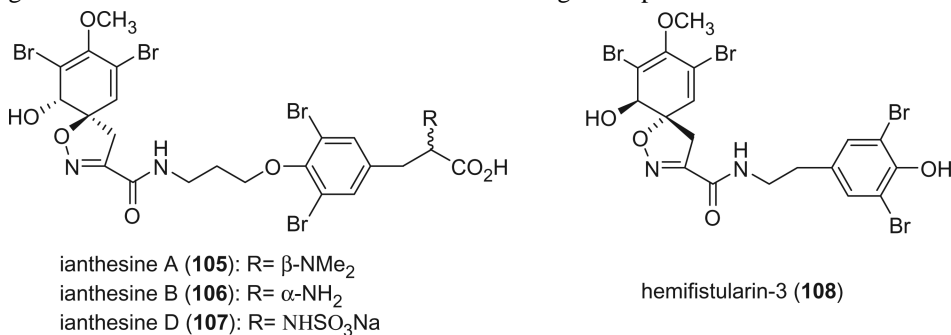


Gao *et al.* reported araplysillin-III (**103**) and hexadellin C (**104**) from the sponge *Aiolochoxia crassa* (36). The absolute configuration of the spiroisoxazoline of both alkaloids was determined by CD spectra. The absolute configuration at C-18 of araplysillin-III (**103**) was shown to be L by HPLC analysis according to Marfey's procedure. The configuration of the *N,N,N*-trimethylhomoserine moiety was deduced as L by comparison of the optical rotation with the D- and L- standards.

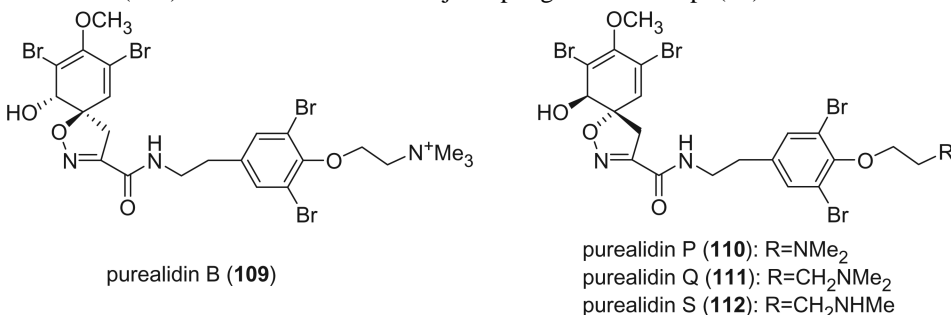


Ianthesines A (**105**), B (**106**), and D (**107**) were isolated from the Australian marine sponge *Ianthella* sp. as Na,K-ATPase inhibitors with an active range of 50–440 μ M (78). The 1*S*, 6*R* configuration of the ianthesines was deduced by the negative optical rotation and Cotton

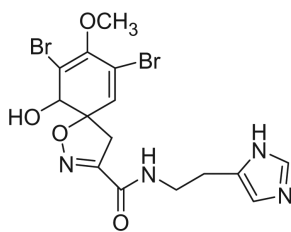
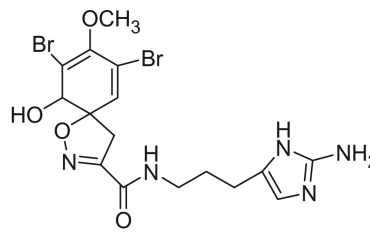
effects at 248 and 285 nm. The dibromo-*N,N*-dimethyltyrosine moiety of ianthesine A (**105**) was determined as D by chiral HPLC analysis of the hydrobromic acid hydrolysis product of **105**. The configuration of the dibromotyrosine moiety of ianthesine B (**106**) was found to be a mixture of L- and D-forms in the ratio of 7:3, using the same method. Chiral HPLC analysis revealed that ianthesine B (**106**) is a 7:3 mixture of two diastereomers, 1*S*, 6*R*, 20*S* and 1*S*, 6*R*, 20*R*. The minor diastereomer is an enantiomer of araplysillin-III (**103**). Hemifistularin-3 (**108**), which is the right-side portion of 11-oxofistularin-3 (**82**), was isolated from a new species of sponge in the family Aplysiniellidae Bergquist, order Verongida, collected in the Coral Sea (72). Hemifistularin-3 (**108**) can be obtained by treatment of 11-oxofistularin-3 with methanolic KOH. Since both hemifistularin-3 (**108**) and 11-oxofistularin-3 (**82**) were found to exist in the same sponge, it is possible that hemifistularin-3 is a product of the degradation of 11-oxofistularin-3 or an elaborated biogenetic precursor.



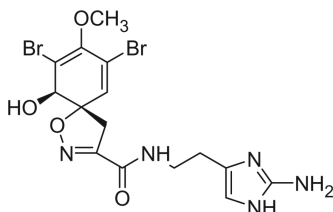
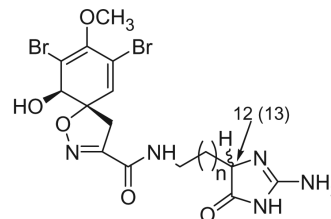
Purealidins B (**109**), P (**110**), and Q (**111**) were isolated from two different collections of an Okinawan sponge *Psammaplysilla purea* by Kobayashi *et al.* (79,84,85). The absolute stereochemistry of the spirocyclohexadienylisoxazoline in purealidin B (**109**) (84), as determined by the CD spectrum, was opposite of that in purealidin P (**110**) and Q (**111**) (79). Purealidin S (**112**) was isolated from the Fijian sponge *Druinella* sp. (86).



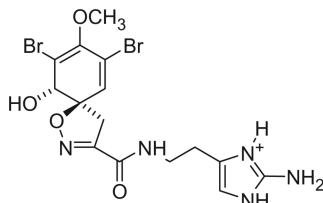
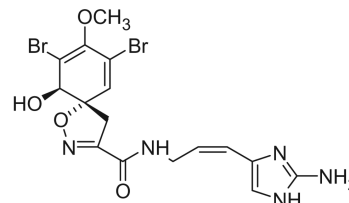
c. Histamine Mono-spirocyclohexadienylisoxazolines: Aerophobin-1 (**113**) and aerophobin-2 (**114**) were isolated from the sponge *Verongia aerophoba* by Cimino *et al.* in 1983 (69). Their structures consisted of a spirocyclohexadienylisoxazoline and a histamine or 2-amino-homohistamine and were determined by NMR spectroscopy and hydrolysis. A methylation derivative of aerophobin-2, *N*-methyl-aerophobin-2 (**115**), was isolated from a Caribbean sponge specimen of *Aiolochoira crassa* (87).

aerophobin-1 (**113**)aerophobin-2 (**114**): R=H
N-methyl-aerophobin-2 (**115**): R=Me

Purealidins J (**116**) and K (**117**) were isolated from the Okinawan sponge *Psammaplysilla purea* by Kobayashi *et al.* (79). The absolute stereochemistry of the spirocyclohexadienylisoxazoline was determined by the positive Cotton effects at 248 and 184 nm in the CD spectra. Purealidin K was subjected to ozonolysis, followed by oxidation with H₂O₂, and subsequently acid hydrolysis. Chiral HPLC analysis of the hydrolysate revealed D- and L-2,4-diaminobutyric acids in the ratio of 1:1, suggesting that C-12 of purealidin K is racemic. A similar alkaloid, 14-oxo-aerophobin-2 (**118**), was identified from the Caribbean sponge *Aplysina insularis* (88). The stereochemistry of C-13 was not determined.

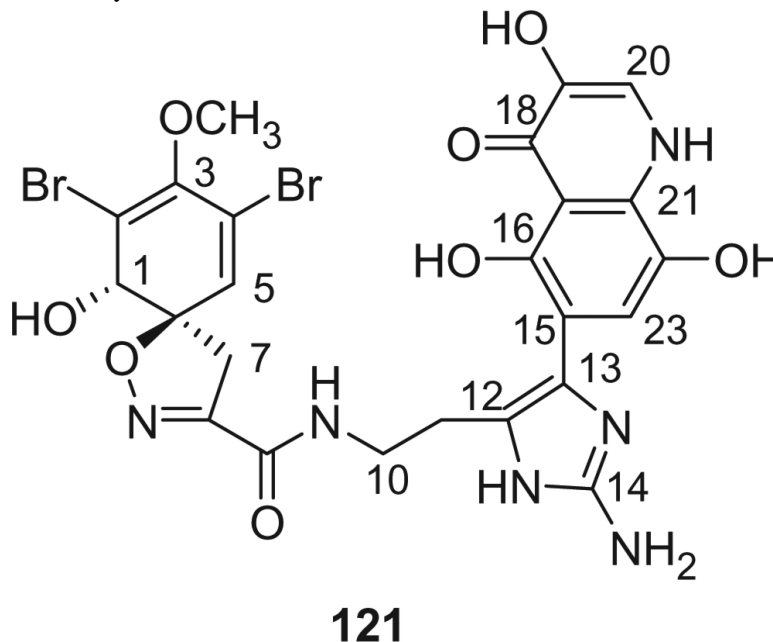
purealidin J (**116**)purealidin K (**117**): n=1
14-oxo-aerophobin-2 (**118**): n=2

The enantiomer of purealidin J, pseudoceratinine A (**119**), was reported one year later from *Pseudoceratina verrucosa* (89). Pseudoceratinine A showed a negative optical rotation and Cotton effects near 250 and 290 nm, which is opposite to that of aerothionin (**68**), whose absolute stereochemistry was determined by X-ray and CD spectra (60). Aplysinamisine I (**120**), which can be considered as a 11,12-dehydro product of aerophobin-2 (**114**), was isolated from the Caribbean sponge *Aplysina cauliformis* (83).

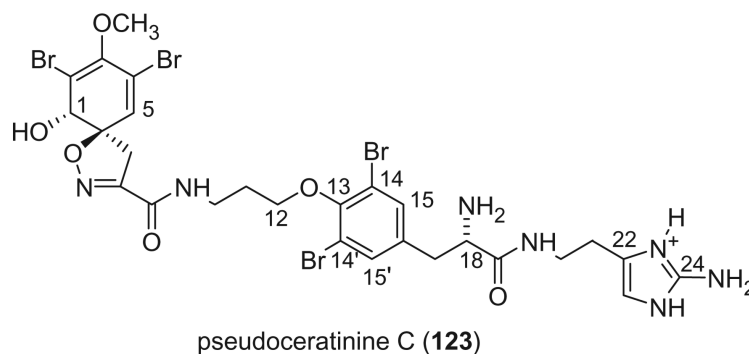
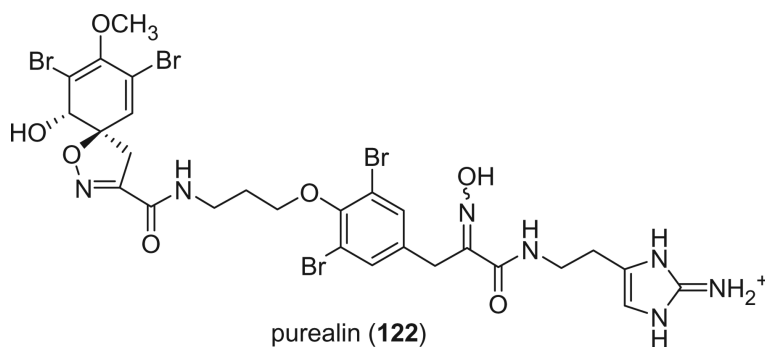
pseudoceratinine A (**119**)aplysinamisine I (**120**)

Alkaloid **121** was isolated from an Australian, non-verongid sponge *Oceanapia sp.* by Bewley's group in 2001 (90). Its structure was elucidated as an unprecedented imidazolyl-quinolinone substructure attached to a spirocyclohexadienylisoxazoline by 1D and 2D NMR, and its absolute configuration was determined to be 1-(S), 6-(R) by comparison of its specific rotation and CD spectrum with those of pseudoceratinine A (**119**) and purealidin J

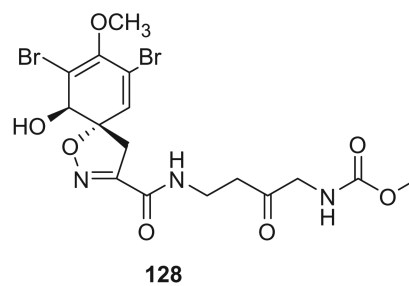
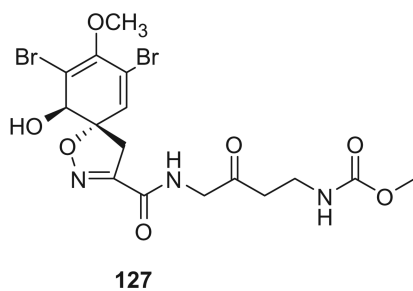
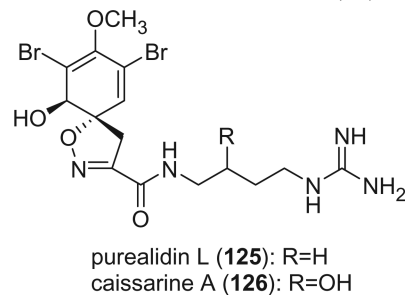
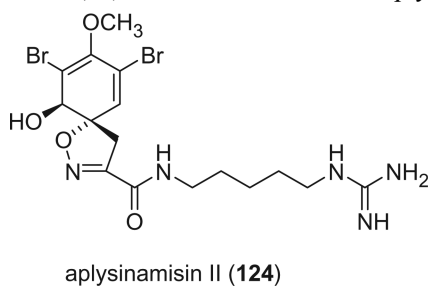
(116). Bromotyrosine-derived metabolites were initially limited exclusively to sponges of the order Verongida. While a voucher specimen corresponding to the sponge from which **121** was obtained was re-identified as *Oceanapia sp.*, it remains possible that a sample of a verongid sponge was present in the actual collection. Alkaloid **121** was the first example of a natural product that inhibits an enzyme central to a mycothiol-dependent detoxification pathway found in mycobacteria.



Purealin (**122**) and pseudoceratinine C (**123**) are two spirocyclohexadienylisoxazoline derivatives containing both bromotyrosine and 2-amino-histamine in the side chain. Purealin (**122**) was first isolated from *Psammoplysilla purea* by Nakamura *et al.* in 1985 (91). Both alkaloids were reported from *Pseudoceratina verrucosa* by Benharref and Pais in 1996 (89). The absolute configurations of 1-(*S*) and 6-(*R*) of both compounds were deduced by the negative specific rotation and the Cotton effects near 250 and 290 nm. The 18-(*S*) configuration of pseudoceratinine C (**123**) was also determined by a positive Cotton effect at 215 nm, corresponding to the *S*-configuration of the tyrosine residue (89).

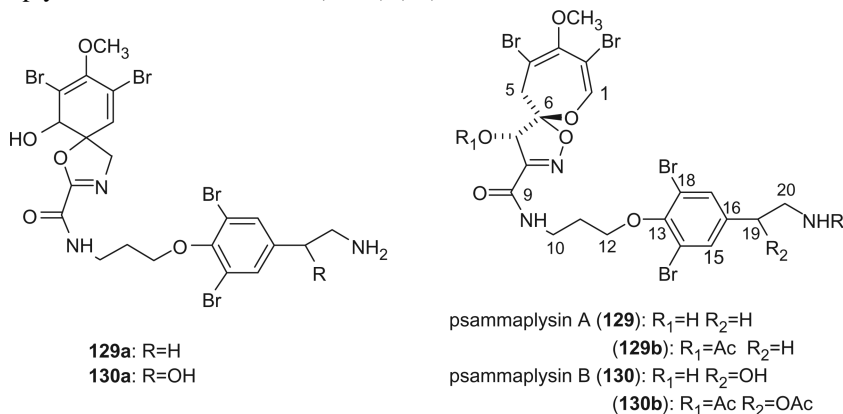


d. Linear Side Chain Mono-spirocyclohexadienylisoxazolines: Alkaloids in this class include aplysinamisin II (**124**) from the Caribbean sponge *Aplysina cauliformis* (83), purealidin L (**125**) from *Psammaphysilla pura* (79), caissarine A (**126**) from *Aplysina caissara* (66), and **127** and **128** from *Aplysina cauliformis* collected in the Bahamas (92).

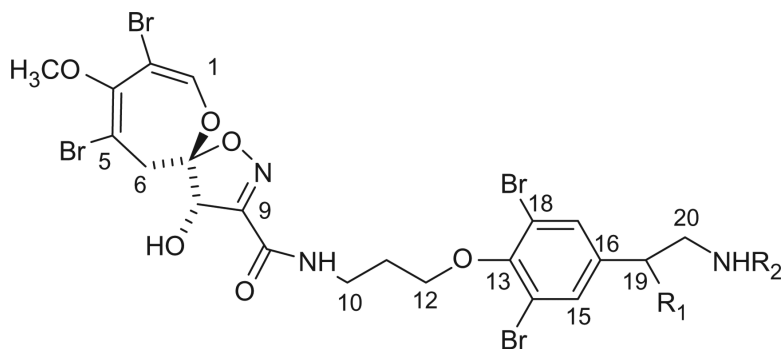


C. SPIROOXEPINISOXAZOLINE (OXEPIN) BROMOTYROSINE DERIVATIVES

Prompted by the antibiotic activity of the MeOH extract of *Psammaplysilla purpurea* collected from the southern part of the Gulf of Eilat (off the Red Sea), two spirooxepinisoxazoline type dibromotyrosine derivatives, psammaplysins A and B were first isolated by Kashman's group from *P. purpurea* in 1982 (93). The freeze-dried sponge was extracted with methanol and the extract was chromatographed on a Sephadex LH-20 column eluted with CHCl₃-MeOH 1:1 to yield psammaplysins A and a mixture of psammaplysins A and B. After acetylation, psammaplysins A and B were separated by silica gel column chromatography and eluted with 2% and 6% EtOH in CHCl₃. The structures were proposed as having a spiro[4.5]oxadecane skeleton (**129a** and **130a**) based mainly on the ¹H and ¹³C NMR spectra data and the alkaline degradation of psammaplysins A, which is different from that of aerothionin (58). In 1985, Scheuer's group isolated psammaplysins A and B from the sponge *P. purpurea* collected in Palau and revised the structures of spiro[4.5]oxadecane skeleton to a spiro[4.6]dioxazundecane (**129**) on the basis of two-dimensional ¹³C-¹³C connectivity and single-crystal X-ray diffraction studies on psammaplysins A acetamide acetate (**129b**) (94).

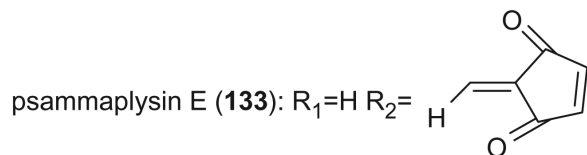


Psammaplysins C (**131**) was isolated from *P. purpurea* collected off Makaluva Island in Fiji in 1992, it exhibited *in vitro* cytotoxicity towards the human colon tumor cell-line HCT 116 with an IC₅₀ of 3 μg/mL (95). Psammaplysins D (**132**) and E (**133**) were identified from a new species of *Aplysinella* (order Verongida) collected from Pingelap Atoll, Micronesia in 1993 (96). Psammaplysins D is the isopentadecanoyl of psammaplysins B, while psammaplysins E has an unprecedented cyclopentenedione, which was not previously encountered in compounds from natural sources. Psammaplysins D displays anti-HIV activity against the Haitian RF strain of HIV-I with a 51% inhibition at 0.1 μg/mL. Psammaplysins E exhibits cytotoxicity against KB and LOVO cells at 5 μg/mL. Psammaplysins F (**134**) was isolated from an undescribed species of *Aplysinella* sponge, collected from Chuuk, Micronesia (97). Ceratinamides A (**135**) and B (**136**) were isolated from *P. purpurea* collected from Hachijo-jima in 1996 and were found to exhibit antifouling activity with EC₅₀ values of 0.10 and 2.4 μg/mL (98).



psammaplysin C (**131**): $R_1=OH$ $R_2=Me$

psammaplysin D (**132**): $R_1=OH$ $R_2=CO(CH_2)_{11}CHMe_2$



psammaplysin E (**133**): $R_1=H$ $R_2=$

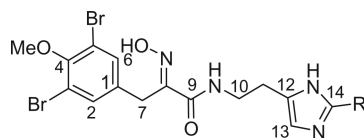
psammaplysin F (**134**): $R_1=H$ $R_2=Me$

ceratinamide A (**135**): $R_1=H$ $R_2=CHO$

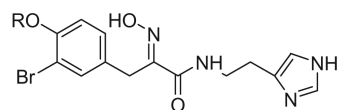
ceratinamide B (**136**): $R_1=H$ $R_2=CO(CH_2)_{11}CHMe_2$

D. OXIMES

1. Oxime-histamines—Ianthellin (**137**) was isolated from the sponge *Ianthella ardis*, collected in the Bahamas, and was determined to be the major antibiotic and antifungal component (99). 5-Bromoverongamine (**138**), a novel antifouling tyrosine alkaloid has been isolated from the Caribbean sponge *Pseudoceratina* sp. (100). Verongamine (**139**), a specific histamine-H3 antagonist at concentrations as low as 1.0 $\mu\text{g/mL}$, was isolated from *Verongula gigantea* (101). Alkaloid **140** was isolated from the Caribbean sponge *Pseudoceratina crassa* (33).

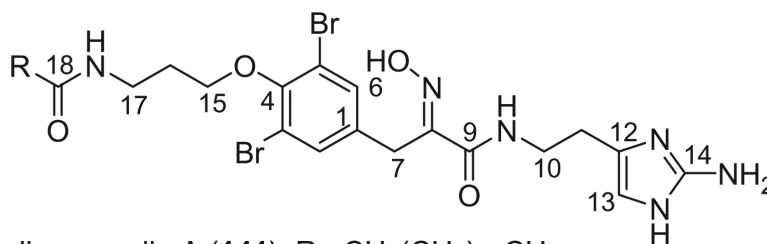


ianthellin (**137**): $R=NH_2$
5-bromoverongamine (**138**): $R=H$



verongamine (**139**): $R=CH_3$
140: $R=H$

Lipopurealins A (**141**), B (**142**), and C (**143**) are unique metabolites with a long alkyl chain, isolated from the marine sponge *Psammaplysilla purea* by Kobayashi's group in 1986 (102). Lipopurealins are inhibitors of Na,K-ATPase, and lipopurealin B is most active. Two additional lipopurealins, lipopurealins D (**144**) and E (**145**) were isolated from the same sponge in 1995 (103).



lipopurealin A (**141**): R= CH₃(CH₂)₁₁CH₂

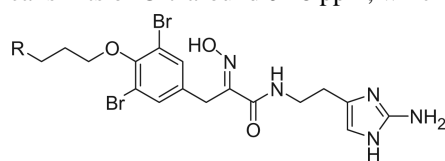
lipopurealin B (**142**): R= Me₂CH(CH₂)₁₀CH₂

lipopurealin C (**143**): R= CH₃(CH₂)₁₃CH₂

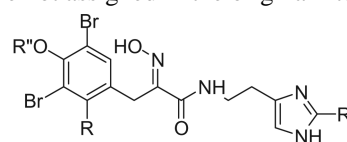
lipopurealin E (**145**): R= CH₃(CH₂)₁₆CH₂

lipopurealin D (**144**): R=

Additional oxime bromotyrosine derivatives containing a histamine group were reported by Kobayashi's group from *Psammophysilla purea*, including purealidins A (**146**), D (**147**), H (**148**), M (**149**), and N (**150**) (79,103-105). The *E*-geometries of the oxime in lipopurealins A (**141**), B (**142**), C (**143**), purealidins A (**146**), and D (**147**) were assigned based on the chemical shifts of C-7 around δ 28 ppm, which were not assigned in the original literature.

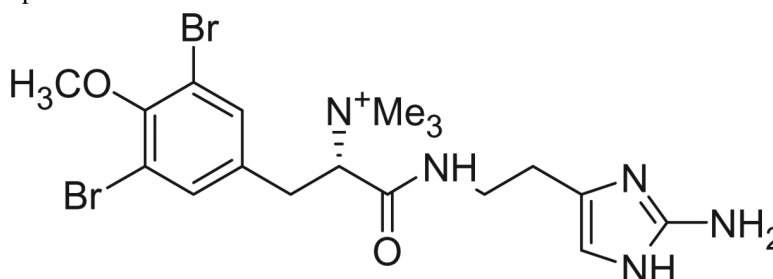


purealidin A (**146**): R= NH₂
purealidin D (**147**): R= 1-pyridine



purealidin H (**148**): R=H R'=NH₂ R''=H
purealidin M (**149**): R=OH R'=NH₂ R''=CH₃
purealidin N (**150**): R=OH R'=H R''=CH₃

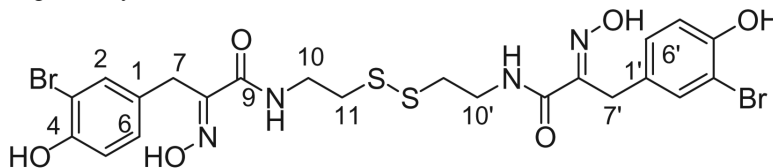
Pseudoceratinine B (**151**), in which the oxime is reduced and tri-methylated, was isolated from *Pseudoceratina verrucosa* (89). The absolute configuration of tyrosine was deduced from the positive Cotton effect at 212 nm, corresponding to an *S*-configuration (106). Pseudoceratinine B (**151**) is the second bromotyrosine alkaloid containing a non-oxidized amino group.



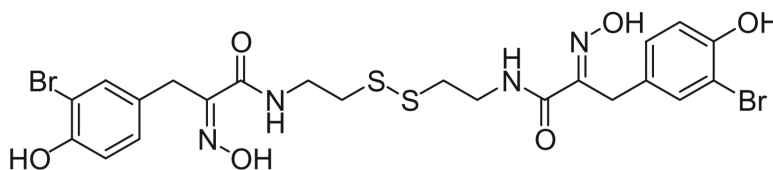
pseudoceratinine B (**151**)

2. Oxime-Disulfides—Alkaloids **152** and **153** were the first bromotyrosine derivatives characterized containing a disulfide moiety, and were isolated from an unidentified Verongida sponge by Arabshahi and Schmitz in 1987 (107). Almost at the same time, Quinoa and Crews reported the isolation of **152** from a marine sponge *Psammophysilla* sp.

collected from Tonga and gave the compound a trivial name of psammaplin A (108). The geometry of the oxime was determined by the carbon chemical shift of the methylene group (C-7) *a* to the oxime. The chemical shift of C-7 is about 28 ppm for an *E*-geometry and 35 ppm for a *Z*-geometry (107).

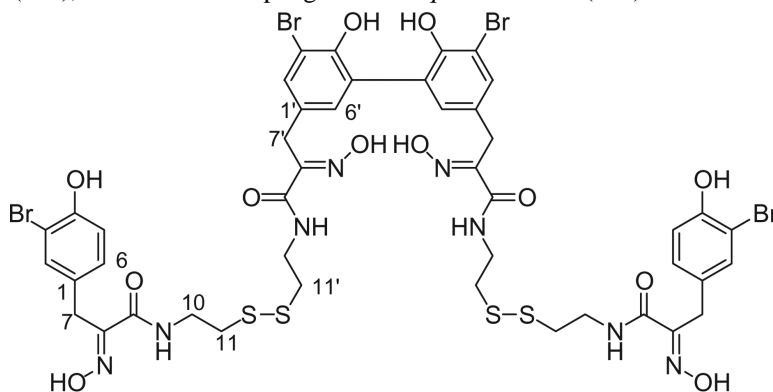


(*E,E*)-psammaplin A (**152**)



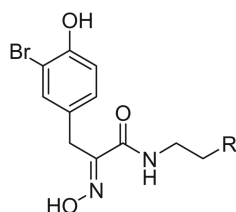
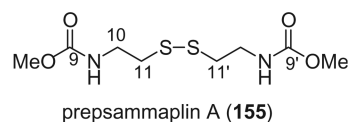
(*E,Z*)-psammaplin A (**153**)

Scheuer *et al.* later reported the psammaplin A (**152**) and the psammaplin A dimer, bisaprasin (**154**), from the Guam sponge *Thorectopsamma xana* (109).

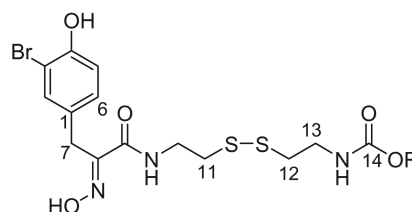


bisaprasin (**154**)

Prepsammaplin A (**155**) and psammaplins B (**156**), C (**157**), and D (**158**) were isolated from the marine sponge *Psammaplysilla purpurea* by Jimenez and Crews (110). The isolation of prepsammaplin A (**155**), a cysteine dimer, indicated that cysteine might be the precursor of the central part of psammaplin A. Interestingly, the R functional groups of psammaplin B (**156**) and C (**157**) are unique and do not appear to have counterparts among any known marine sponge amino acid derivatives (110). Additionally, the only precedent of the thiocyanate group, as found in psammaplin B (**156**), is the sesquiterpene thiocyanate isolated from the sponge *Trachyopsis aplysinoides* (111).

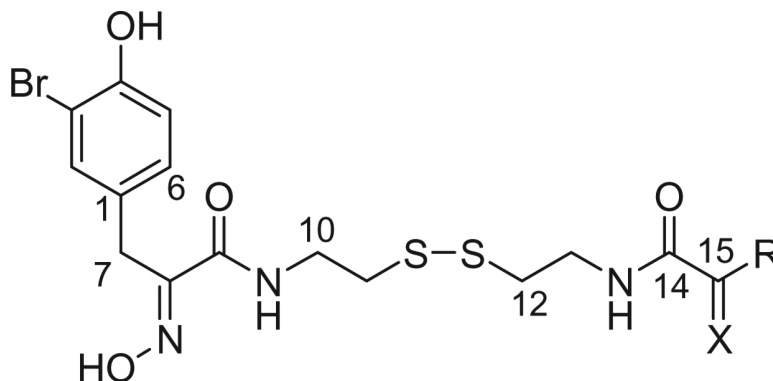


psammaplin B (156): R=-SCN
 psammaplin C (157): R=-SO₂NH₂
 psammaplin I (163): R=-SO₂CH₃

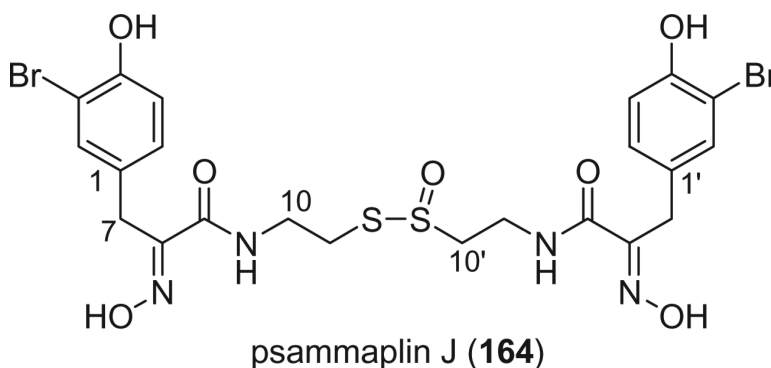


psammaplin D (158): R=CH₃
 psammaplin H (162): R=CH₂CH₃

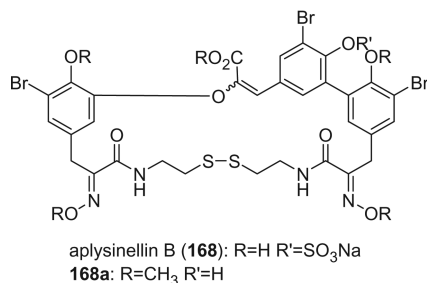
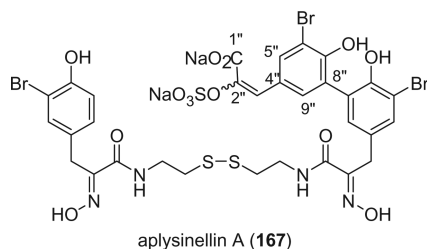
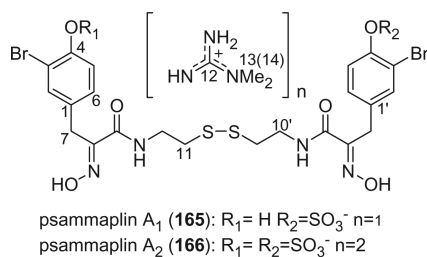
Additional disulfide bromotyrosine derivatives, psammaplin E (159), F (160), G (161), H (162), I (163), and J (164) were isolated from the sponge *Psammaplysilla purpurea* collected from Papua New Guinea by Crews' group in 2003 (112). Psammaplin D (158) and H (162) possess a methyl or ethyl carbamate moiety, respectively. The unprecedented functional groups in psammaplin E (159), F (160), G (161), and J (164) were identified by detailed spectroscopic analysis. The N-substituted oxalamide functionality of psammaplin E (159) is rare among marine natural products. The only known marine natural products that possess an oxalamide functional group are igzamide, isolated from the marine sponge *Plocamissa igzo* (113), and 3-bromotyramine amide, isolated from *Ianthella basta* (41). Psammaplin F (160) is the first marine natural product containing an oxalamic functionality. The functionality in psammaplin G (161) has no precedent in the natural products literature. Psammaplin A (152), F (160), and bisaprasin (154) are potent histone deacetylase inhibitors with mild cytotoxicity. Psammaplin A (152), G (161), and bisaprasin (154) are potent DNA methyltransferase inhibitors.



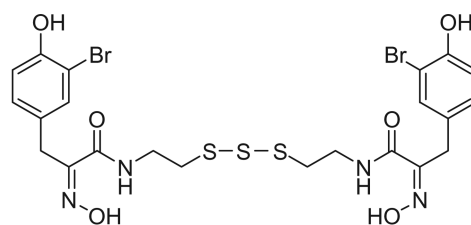
psammaplin E (159): R=NH₂ X=O
 psammaplin F (160): R=OH X=O
 psammaplin G (161): R=OH X=N-NH₂



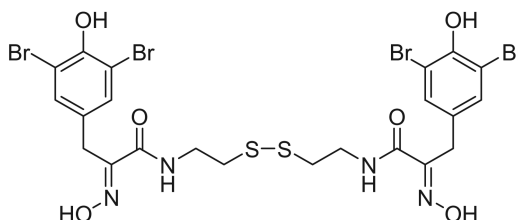
Shin and Paul reported four new psammaplin A analogs, psammaplins A₁ (**165**), A₂ (**166**), aplysinellin A (**167**), and B (**168**), from the marine sponge *Aplysinella rhax* collected from Guam, Palau, and Pohnpei Micronesia (114). Psammaplins A₁ (**165**) and A₂ (**166**) are mono- or bis-*N,N*-dimethylguanidinium salts of psammaplin A (**152**) monoor dualsulfate. Organic sulfates with *N,N*-dimethylguanidinium as counter ions are very rare among sponge metabolites. Suvanine and sulfircin, both sesterterpenoid sulfates from the sponge *Ircinia* sp., are two examples (115,116). Aplysinellin A (**167**) possesses a bromotyrosine-derived C₉-unit of the cinnamic acid type attached to psammaplin A by a biphenyl linkage, while aplysinellin B (**168**) is the corresponding cyclic enol ether. Treatment of aplysinellin B (**168**) afforded compound **168a**. Alkaloids **165–168** exhibited inhibitory activity against the growth of the K562 cell-line and against farnesyl protein transferase.



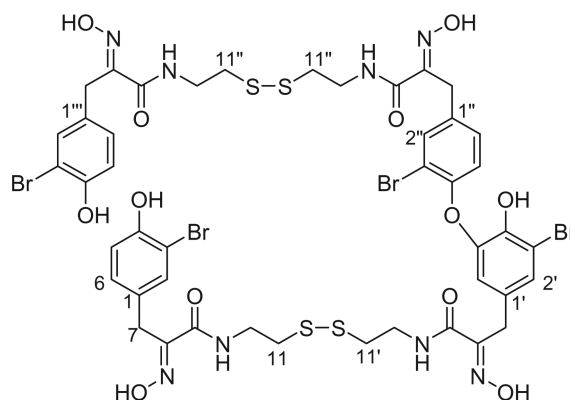
Jung's group reported the isolation of three new psammaplins, **169**, (*E,E*)-bromopsammaplins A (**170**), and bispsammaplins A (**171**), along with the known alkaloids (*E,E*)-psammaplins A (**152**), (*E,Z*)-psammaplins A (**153**), psammaplins D (**158**), and bisaprasins (**154**), from an association of two sponges, *Jaspis wondoensis* and *Poecillastra wondoensis* collected from Korea (117). Alkaloid **169** is the only bromotyrosine derivative containing a trisulfide moiety. This is the second report of bromotyrosine derivatives isolated from sponges not belonging to the order Verongida. The first example described the isolation of three bromotyrosine derivatives from a non-verongid sponge *Oceanapia* sp., but it remains possible that a sample of verongid sponge was present in the actual sample analyzed (90).



169

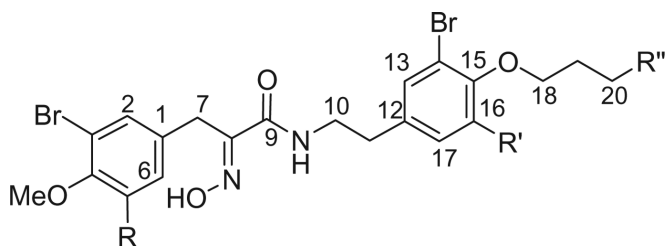


bromopsammaplins A (170)



bispsammaplins A (171)

3. Oxime-Bromotyramines—Xynas and Capon reported aplysamine 2 (**172**) from an Australian marine sponge *Aplysina* sp. in 1989 (44). Aplysamines 3 (**173**), 4 (**174**), and 5 (**175**) were isolated from the Hawaiian sponge *Psammaplysilla purpurea* by Scheuer's group (118). All of these alkaloids exhibited cytotoxic activity, while aplysamine 3 and 4 showed mild antibacterial activity against *Staphylococcus aureus*. Alkaloids **176** and **177** were isolated from the sponge *P. purpurea* collected in Okinawa by an Indian group (119,120).



aplysamine 2 (**172**): R=H R'=Br R''=NHMe₂⁺

aplysamine 3 (**173**): R=H R'=Br R''=NH₃⁺

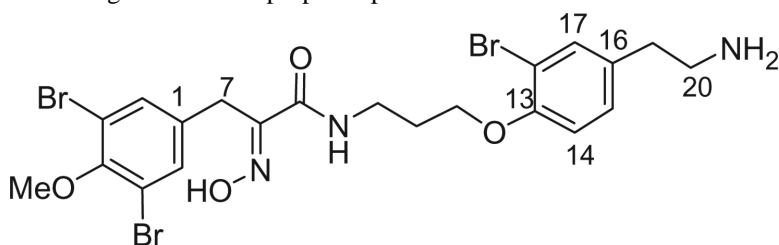
aplysamine 4 (**174**): R=Br R'=Br R''=NH₃⁺

aplysamine 5 (**175**): R=H R'=Br R''=NHCO(CH₂)₁₁CH(CH₃)₂

176: R=R'=H R''=NH₂

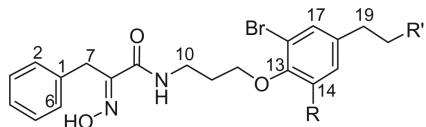
177: R=Br R'=H R''=NH₂

Alkaloid **178** was isolated from *P. purpurea* collected in the Seychelles by Faulkner's group (82). Since it is the presumed biogenetic precursor of 14-debromoaplysillin-I (**101**), the name 14-debromoprearaplysillin I was given. The isolation of spiroisoxazoline **101** and the oxime **178** from the same sponge was the first reported instance in which a spiroisoxazoline has been isolated together with its proposed precursor.



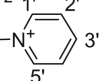
14-debromoprearaplysillin I (**178**)

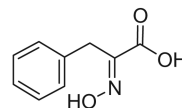
Fusetani *et al.* reported nine new bromotyrosine-derived metabolites, purpuramines A-I (**179–187**), from *P. purpurea* (121). The carboxylic acid oxime units present in the bromotyrosine-derived metabolites were exclusively derived from bromotyrosines, while the oxime function in purpuramines A-I (**179–183**) is part of a phenylalanine moiety, which is a new variant among verongid metabolites. Phenylpyruvic acid oxime (**188**), which is a building block for **179–183**, was also isolated from the sponge.



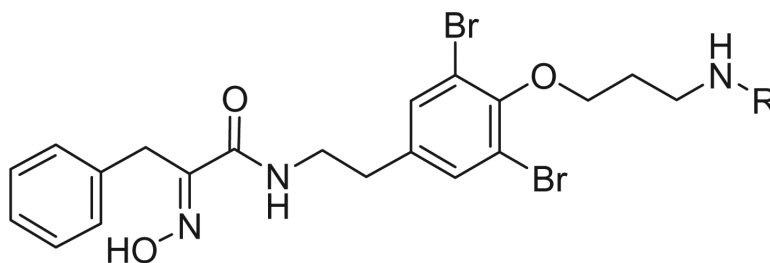
purpuramine A (**179**): R=Br R'=NH₂

purpuramine B (**180**): R=H R'=NH₂

purpuramine C (**181**): R=Br R' = 



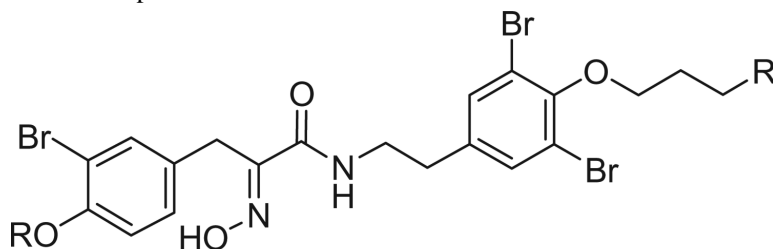
phenylpyruvic acid oxime (**188**)



purpuramine D (**182**): R=H

purpuramine E (**183**): R=CH₃

Purpuramines A-I (**179–187**) exhibited antibacterial activity against *Staphylococcus aureus*, but phenylpyruvic acid oxime (**188**) was not active. Purpuramine J (**189**) was isolated from the Fijian sponge *Psammaphysilla (Druinella)* sp., along with purpuramine I (**187**), aplysamine 2 (**172**), and eight other bromotyrosine derivatives (86). Purpuramine J (**189**) is the first bromotyrosine derivative containing an *N*-oxide functionality, which is considered rare in marine natural products.



purpuramine F (**184**): R=H R'=NH₂

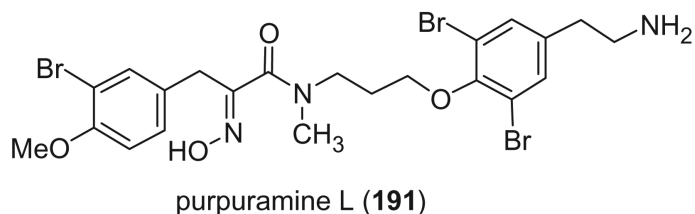
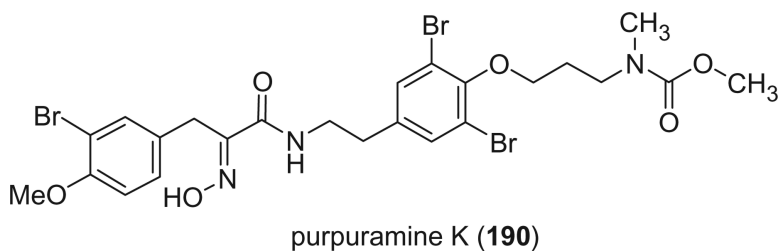
purpuramine G (**185**): R=H R'=NHCH₃

purpuramine H (**186**): R=CH₃ R'=NH₂

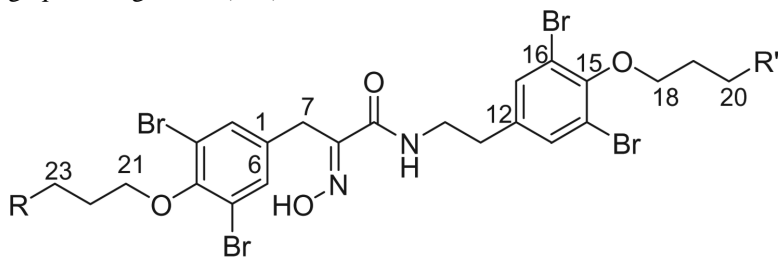
purpuramine I (**187**): R=CH₃ R'=NHCH₃

purpuramine J (**189**): R=CH₃ R'=N⁺Me₂O⁻

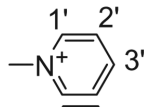
Purpuramines K (**190**) and L (**191**), isolated from the Indian sponge *Psammaphysilla purpurea*, exhibited antimicrobial activity against both Gram positive and Gram negative bacteria (122).

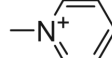


Purealidin C (**192**) was isolated from the Okinawan sponge *P. purea*, which exhibited cytotoxic, antifungal, and antimicrobial activities (84). Tokaradines A (**193**) and B (**194**), isolated from *Pseudoceratina purpurea*, are rare examples of marine bromotyrosine-derived metabolites containing an *N*-substituted pyridinium group. Another example is purpureamine C (**181**) (123). Tokaradines A (**193**) and B (**194**) were seen to be lethal to the crab *Hemigrapsus sanguineus* (123).

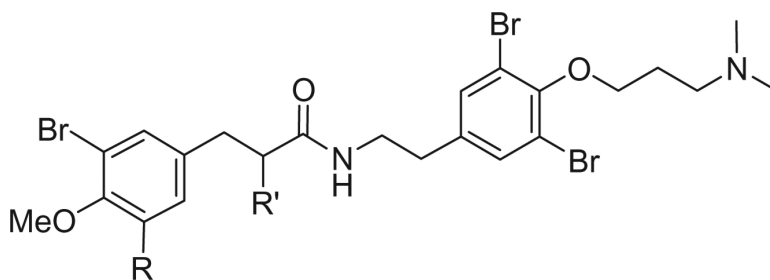


purealidin C (**192**): R=R'=NH₂

tokaradine A (**193**): R=NH₂ R'= 

tokaradine B (**194**): R'=NH₂ R= 

Anomoian A (**195**) was isolated from an Australian sponge *Anomoianthella popeae*, belonging to a new genus of the family Ianthellidae (124). Anomoian A is the first bromotyrosine-derived metabolite with a non-oxidized amino group and exhibited strong antimicrobial activity. Aplyzanzine A (**196**) was isolated from the sponge *Aplysina* sp. collected from Zanzibar (125). The stereochemistry at C-8 was not determined. Suberedamines A (**197**) and B (**198**) were isolated from an undescribed sponge of the genus *Suberea* (126). The absolute configurations at C-8 of both alkaloids were assigned as *S* by chiral HPLC analysis of the hydrobromic acid hydrolysate of each compound. Both suberedamines A (**197**) and B (**198**) exhibited moderate cytotoxic and antibacterial activity.



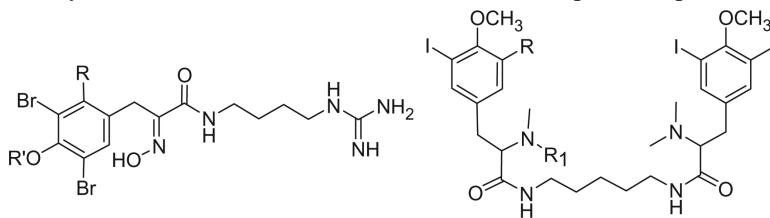
anomoian A (**195**): R=Br R'=NHMe

aplyzanzine A (**196**): R=Br R'=NMe₂

suberedamine A (**197**): R=H R'=α-NH₂

suberedamine B (**198**): R=H R'=α-NHMe

4. Other Oxime Structures—Compound **199** and purealidin O (**200**) are two oxime-type bromotyrosine-derived metabolites containing an agmatine moiety, isolated from *Psammaphysilla purea* and *Oceanapia* sp., respectively (79,90). Alkaloids **201**, **202**, and **203** were iodinated tyrosine derivatives isolated from the ascidian *Aplidium* sp. (127).

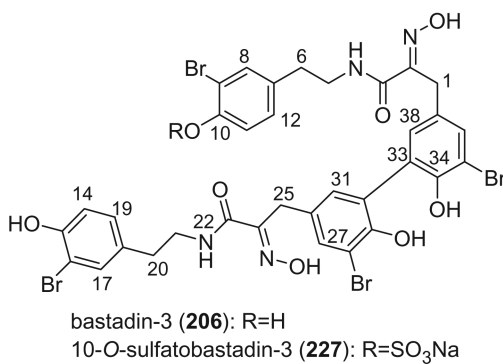
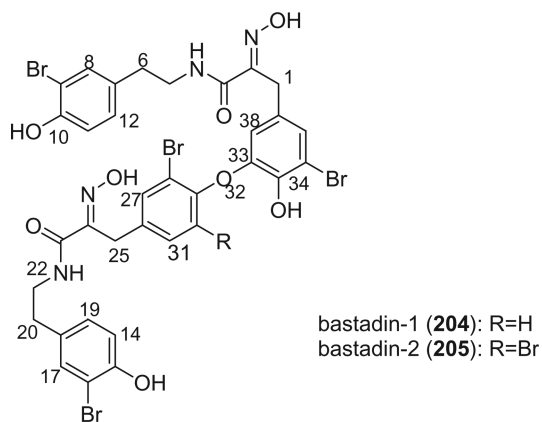


199: R=H R'=CH₂CH₂CH₂NH₂
 purealidin O (**200**): R=OH R'=CH₃

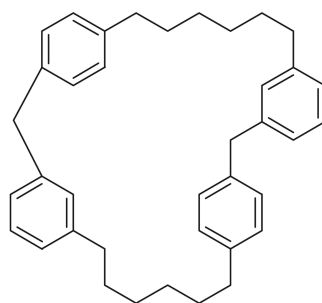
201: R=H R₁=Me
202: R=I R₁=Me
203: R=H R₁=H

E. BASTADINS

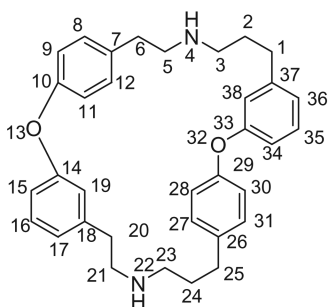
1. Bastadins—The bastadins are a series of predominantly macrocyclic sponge metabolites, which are biogenetically derivable from four bromotyrosines by oxidative phenolic coupling of two tyramine–tyrosine units connected through an amide bond. To date, there are 24 bastadins isolated from marine sponges. The pioneering studies of Wells and colleagues in the late 1970s led to the isolation and identification of bastadins 1–7 from *Ianthella basta* collected from Queensland, Australia (128,129). Bastadins-1 (**204**), 2 (**205**), and 3 (**206**), and 10-*O*-sulfatobastadin-3 (**227**) (130), are the only known acyclic bastadins. Bastadin-3 (**206**) and its sulfate (**227**) (130) both have a biaryl bond connecting two tyramine–tyrosine units, other than the ether bridge present in the remaining bastadins (129).



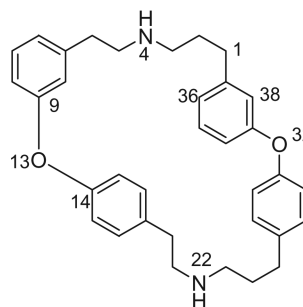
The remaining 20 bastadins possess a macrocyclic system, which was given a name *bastarane* and numbered as shown (129). According to the oxidative cyclization, there are two structural classes, i.e. 13,23-dioxa-4,22-diazabastarane and 13,32-dioxa-4,22-diazaisobastarane (131).



bastarane

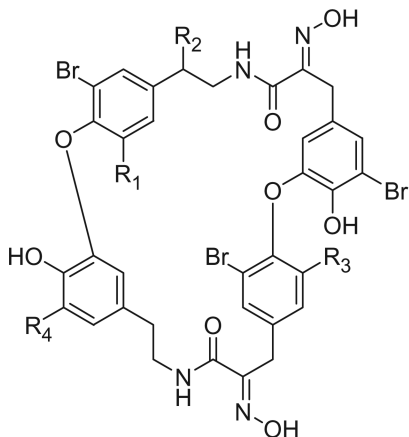


13,32-dioxa-4,22-diazabastarane

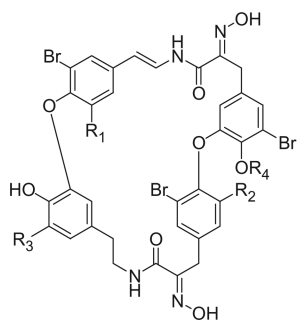


13,32-dioxa-4,22-diazaisobastarane

Most of the bastadins are of the 13,23-dioxa-4,22-diazabastarane type, including bastadins-4 (**208**), -5 (**209**), -6 (**210**), -7 (**211**) (129), -8 (**212**), -9 (**213**), -10 (**214**), -11 (**215**) (132), -12 (**216**), -14 (**218**) (133), -15 (**219**) (134), -16 (**220**), -17 (**221**) (135–137), -18 (**222**) (138), and 15,34-*O*-disulfatobstadin-7 (**228**) (130).

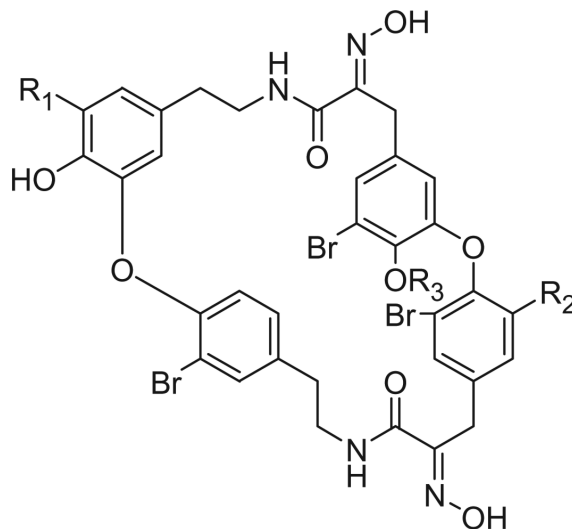


- bastadin-5 (**209**): $R_1=H$ $R_2=H$ $R_3=Br$ $R_4=Br$
 bastadin-6 (**210**): $R_1=Br$ $R_2=H$ $R_3=Br$ $R_4=Br$
 bastadin-8 (**212**): $R_1=H$ $R_2=OH$ $R_3=Br$ $R_4=Br$
 bastadin-9 (**213**): $R_1=H$ $R_2=H$ $R_3=Br$ $R_4=H$
 bastadin-10 (**214**): $R_1=H$ $R_2=OH$ $R_3=H$ $R_4=Br$
 bastadin-12 (**216**): $R_1=H$ $R_2=OH$ $R_3=Br$ $R_4=Br$
 bastadin-15 (**219**): $R_1=Br$ $R_2=H$ $R_3=H$ $R_4=Br$
 bastadin-16 (**220**): $R_1=Br$ $R_2=H$ $R_3=Br$ $R_4=H$
 bastadin-17 (**221**): $R_1=H$ $R_2=OH$ $R_3=Br$ $R_4=H$
 bastadin-18 (**222**): $R_1=H$ $R_2=H$ $R_3=H$ $R_4=Br$



bastadin-4 (**208**): R₁=H R₂=R₃=Br R₄=H
 bastadin-7 (**211**): R₁=H R₂=H R₃=Br R₄=H
 bastadin-11 (**215**): R₁=R₂=R₃=R₄=H
 bastadin-14 (**218**): R₁=Br R₂=H R₃=Br R₄=H
 15,34-O-disulfatobastadin-7 (**228**): R₁=R₂=H R₃=Br R₄=SO₃Na

Five bastadins contain the 13,32-dioxa-4,22-diazaisobastarane ring pattern, including bastadins-13 (**217**) (131), -19 (**223**) (139), -21 (**225**) (140), and 34-O-sulfatobastadin-13 (**226**) (141).



bastadin-13 (**217**): R₁=H R₂=Br R₃=H
 bastadin-19 (**223**): R₁=Br R₂=Br R₃=H
 bastadin-20 (**224**): R₁=Br R₂=R₃=H
 bastadin-21 (**225**): R₁=R₂=R₃=H
 34-O-sulfatobastadin-13 (**226**): R₁=H R₂=Br R₃=SO₃Na

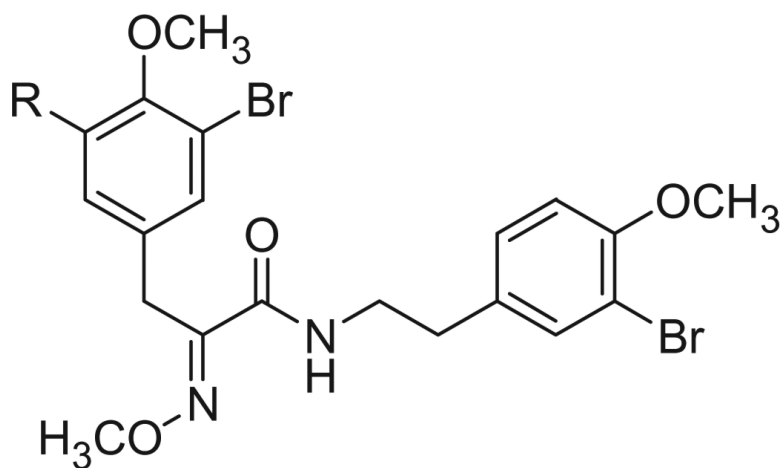
The majority of the bastadins were isolated from the marine sponge *Ianthella basta* (class Demospongiae, order Verongida, family Inthellidae) with several obtained from *I. flabelliformis*, *I. quadrangulata*, *Ianthella* sp., and *Psammaplysilla purpurea*. Bastadins 1–7 (**204–211**) were isolated from the Australian sponge *I. basta*, as antimicrobial agents against Gram positive organisms in 1980 (128,129). Their structures were determined by spectroscopic methods and alcoholic KOH hydrolysis. X-ray diffraction analyses were performed on a single crystal of bastadin-4 (**208**) and bastadin-5 permethylate. The X-ray structure showed that the conformations of bastadin-4 and bastadin-5 permethylate are considerably different. The macrocyclic ring of bastadin-5 permethylate appears to be open, whereas the ring of bastadin-4 is more elongated.

The studies of bastadins 8–13 were published simultaneously, unfortunately leading to the assignment of the same number to different bastadins. Scheuer *et al.* suggested that these alkaloids be renamed in the order of when they were received for publication. Thus, bastadins-8 to –11 of Pordesimo and Schmitz (132) retained their original numbering, bastadin-9 of Miao *et al.* (142) was renumbered as bastadin-12 (bastadin-8 from Miao *et al.* coincidentally has the same structure as bastadin-8 of Pordesimo and Schmitz), and bastadin-12 of Butler *et al.* (131) became bastadin-13. Bastadins-8 to –11 (**212–215**) were isolated from the sponge *I. basta* collected in Guam by Pordesimo and Schmitz in 1990 (132). Bastadin-4 (**208**), –8 (**212**), and –9 (**213**) exhibited cytotoxic and anti-inflammatory activities. Bastadins-8 and –12 were isolated from the Papua New Guinean sponge *I. basta* by Miao *et al.* (142).

The structure of bastadin-13 (**217**) was elucidated as a novel alternative oxidative cyclization of bastarane, which was proposed for nomenclature purposes as 13,32-dioxa-4,22-diazaisobastarane, based on detailed spectroscopic analyses and derivatization (131). The co-occurrence of bastadin-13 and bastadin-9 (**213**) in a single specimen of *I. basta* collected from Australia introduced another dimension to the structure elucidation of the bastadins, therefore it can no longer be assumed on biosynthetic grounds that all cyclic bastadins possess the same 13,32-dioxa-4,22-diazabastarane ring system (131). Bastadin-14 (**218**), isolated from *Psammaplysilla purpurea* collected in Pohnpei, Micronesia, is the only bastadin isolated from a sponge that does not belong to the genus *Ianthella*. Bastadin-15 was identified from an undescribed marine sponge of the genus *Ianthella* collected from Australia (134). Bastadin-16 (**220**) and –17 (**221**) were isolated from an Indonesian collection of *I. basta* (135–137). Bastadin-18, along with bastadins-1, –2, –5, –6, –8, and –10, were isolated from the marine sponge *I. basta* collected in Papua New Guinea (138). In addition, a mixture of bastadins-2 and –5 were also isolated from *I. flabelliformis*.

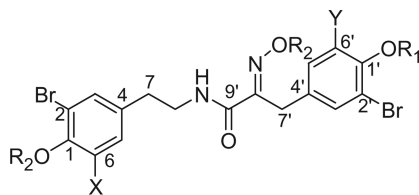
Bastadins-8 and –10 were found to be moderate inhibitors of inosine 5'-phosphate dehydrogenase (138). Molinski *et al.* reported bastadins-19 (**223**), –20 (**224**), 15,34-*O*-disulfatobastadin-7 (**228**), and 10-*O*-sulfatobastadin-3 (**227**) from *I. basta*, as novel modulators of the skeletal isoform of the ryanodine-sensitive sarcoplasmic reticulum calcium channel by a novel mechanism involving the FKBP12/RyR-1 complex (130,139). Bastadin-21 (**225**) was isolated from an Australian marine sponge *I. quadrangulata* (140). Bastadins-6 and –16 were also reported from the Indian sponge *Psammaplysilla purpurea*, along with other bromotyrosine derivatives (46). The absolute stereochemistry of the C-6 hydroxyl group in bastadins-8 (**212**), –10 (**214**), and –12 (**216**) were determined as *S* by Pettit *et al.* using the Mosher–Trost method (143).

2. Hemibastadins—Two dimers of bromotyrosine, trimethylhemibastadin-1 (**229**) and trimethylhemibastadin-2 (**230**), were isolated as their methyl ethers, along with bastadin-9 and bastadin-12 from the sponge *I. basta* (131). Although trimethylhemibastadin-1 (**229**) and trimethylhemibastadin-2 (**230**) were obtained from a methylated fraction, it is not clear whether the natural products themselves were methylated to any extent.

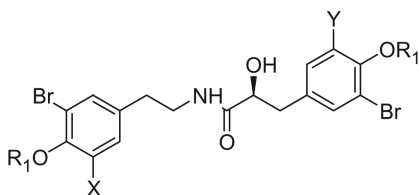


trimethylhemibastadin-1 (**229**): R=H
trimethylhemibastadin-2 (**230**): R=Br

Eight hemibastadins were identified from a scale-up (160 kg wet weight) collection of the sponge *I. basta*, including hemibastadins 1 (**231**), 2 (**232**), and 3 (**233**), hemibastadinols 1 (**234**), 2 (**235**) and 3 (**236**), and 1'-methoxyhemibastadin 1 (**237**) and 2 (**238**) (41). Hemibastadin 2 (**232**) and 3 (**233**) were obtained as a mixture (3:1), while hemibastadinol 2 (**235**) and 3 (**236**) were an optically active oily mixture (19:1) that effectively resisted separation. The absolute stereochemistry of hemibastadinols 1 (**234**), 2 (**235**), and 3 (**236**) was determined as S using Trost's modification of the Mosher's method (144).

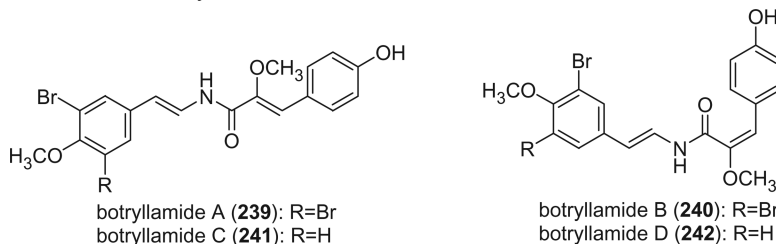


hemibastadin 1 (**231**): X=Y=R₁=R₂=H
 hemibastadin 2 (**232**): X=R₁=R₂=H Y=Br
 hemibastadin 3 (**233**): X=Br Y=R₁=R₂=H
 trimethoxyhemibastadin 3 (**233b**): X=Br Y=H R₁=R₂=Me
 1'-methoxyhemibastadin 1 (**237**): X=Y=R₂=H R₁=Me
 1'-methoxyhemibastadin 2 (**238**): X=R₁=R₂=H Y=Br



hemibastadinol 1 (**234**): X=Y=R₁=H
 1,1'-dimethoxyhemibastadinol 1 (**234a**): X=Y=H R₁=Me
 hemibastadinol 2 (**235**): X=R₁=H Y=Br
 hemibastadinol 3 (**236**): X=Br Y=R₁=H
 1,1'-dimethoxyhemibastadinol 2 (**235a**): X=H Y=Br R₁=Me
 1,1'-dimethoxyhemibastadinol 3 (**236a**): X=Br Y=H R₁=Me

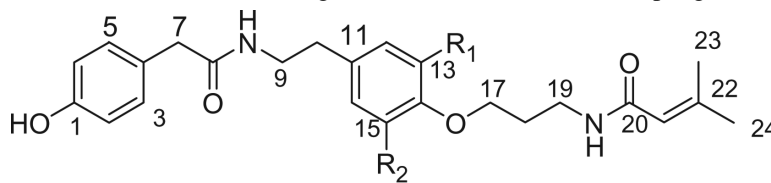
Botryllamides A–D (**239–242**), which have similar structures as the hemibastadins, but with two additional double bonds, were isolated from the Philippine ascidian *Botryllus* sp. and the Australian ascidian *Botryllus schlosseri* (145).



F. OTHER STRUCTURAL CLASSES

Three novel halogenated metabolites (**243–245**) were isolated from the Caribbean sponge *Iotrochota birotulata*, which is taxonomically far removed from the order Verongida (146). Bromotyrosine-derived metabolites have been considered to be characteristic of the sponges in the order of Verongida (147). *I. birotulata* is the first sponge that elaborates such metabolites which does not belong to the order Verongida. The presence of iodine atoms in alkaloids **244** and **245** is interesting. Iodo-compounds are relatively rare in marine chemistry, and particularly in sponges, even if all known haloperoxidases are effective in oxidizing iodide (148). The biosynthesis of iodinated metabolites seems to be related to the ability of the organism to concentrate iodide from sea water, rather than the presence of a specific peroxidase. Most iodo-metabolites have been isolated from red algae, which are known to contain as high as 0.5% of iodine by wet weight. Significant amounts of iodine (0.12–

1.21%), together with comparable quantities of bromine (0.16–2.66%), were reported to exist in the spicule tracts of *I. birotulata* (149), further supporting the relationship between the presence of iodo-metabolites and high concentrations of iodine in sponge tissues.

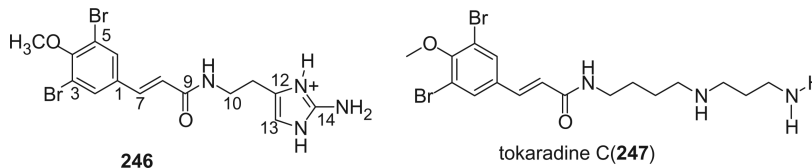


243: R₁=Br R₂=Br

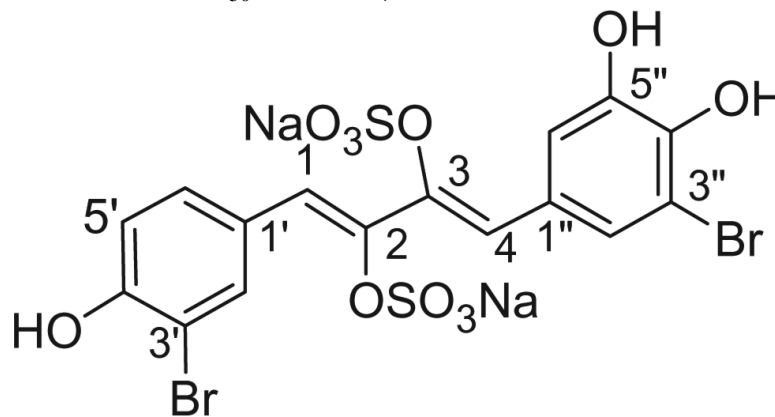
244: R₁=I R₂=Br

245: R₁=I R₂=I

Alkaloid **246** was isolated from the Caribbean sponge *Verongula* sp. (38). Tokaradine C (**247**) was isolated from the marine sponge *Pseudoceratina purpurea* as a toxic constituent against the crab *Hemigrapsus sanguineus* (123).



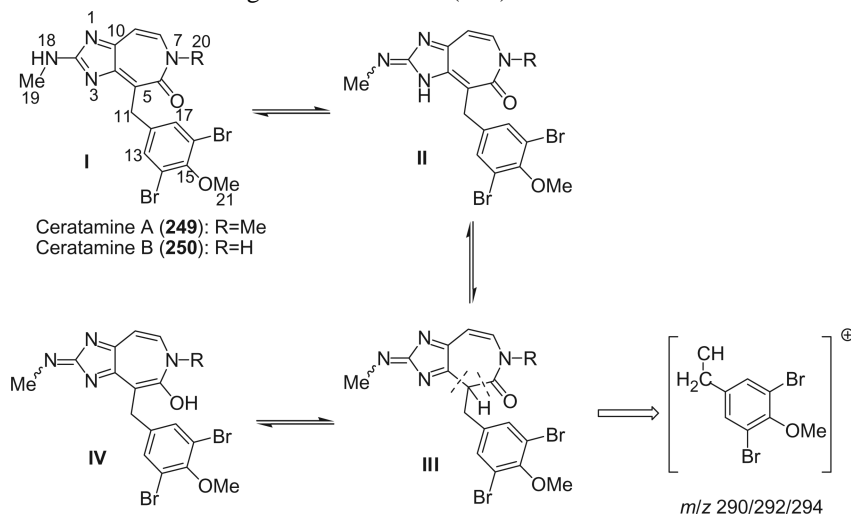
An unusual disulfate ester of a 1,4-diphenyl-1,3-butadiene, aplysillin A (**248**), was isolated from the sponge *Aplysina fistularis fulva*, collected at a depth of 369 feet off Sweetings Cay, Grand Bahama Island (150). Aplysillin A weakly inhibited the binding of thrombin to platelet membranes with an IC₅₀ value of 20 μM.



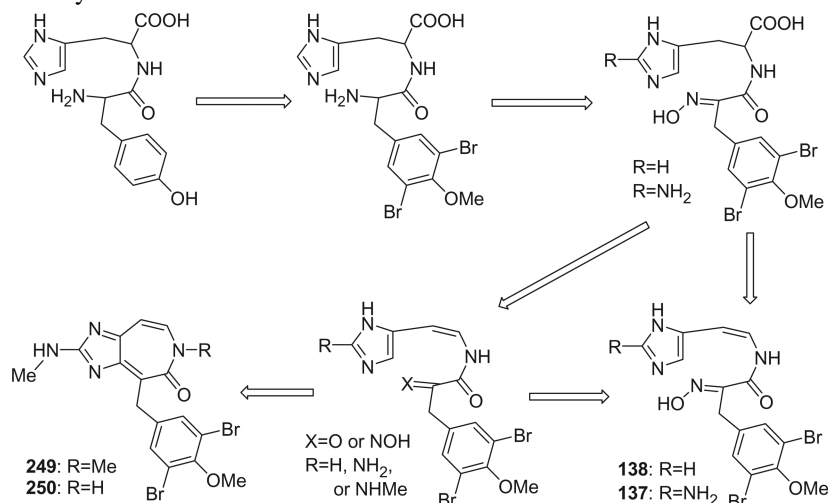
aplysillin A (248)

Two novel antimitotic heterocyclic alkaloids, ceratamines A (**249**) and B (**250**), were isolated from the marine sponge *Pseudoceratina* sp. collected in Papua New Guinea (151). Their structures were elucidated by analysis of the spectroscopic data. A number of possible tautomers exist for ceratamine A as shown below. Each of the constitutional isomers **II**, **III**, and **IV** can exist as the *E* and *Z* stereoisomers about the C-2/N-18 imine bond. Both ¹H and ¹³C NMR spectra showed evidence for two forms. Scalar coupling observed between

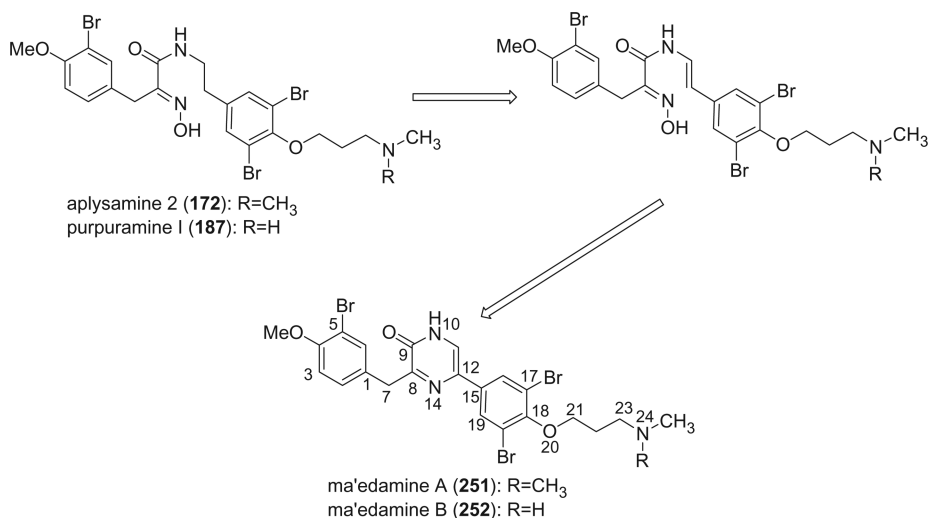
the Me-19 and NH-18 resonances provided evidence that the major tautomer observed in the ^1H NMR spectrum was **I**. A significant fragment peak cluster at m/z 290/292/294 (1:2:1) in the EIMS of ceratamine A could formally arise from tautomer(s) **III** via an α cleavage next to the carbonyl accompanied by cleavage of the bond linking the substituted phenethyl fragment to the imidazole ring carbon as shown (151).



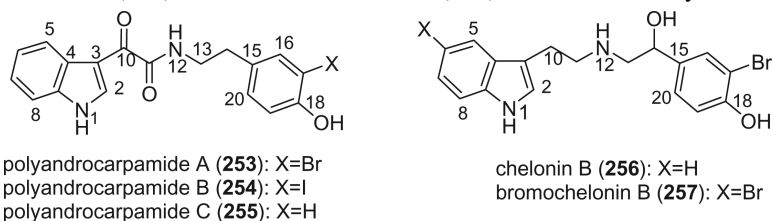
The obvious biogenetic relationship of ceratamines A and B to 5-bromoverogamine (**138**) (100), also isolated from a *Pseudoceratina* sp., and ianthelline (**137**) (99) supports the proposed structures **249** and **250**. The putative biogenetic precursors to these alkaloids are histidine and tyrosine as shown.



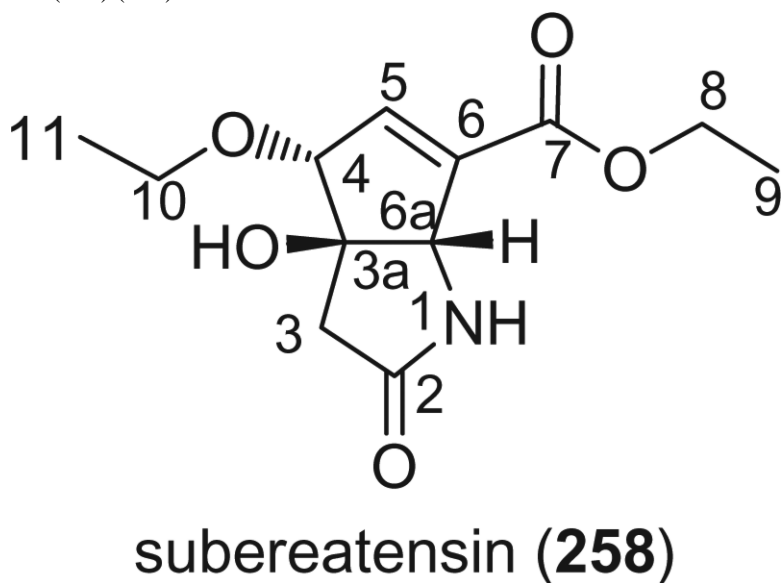
Two new cytotoxic bromotyrosine alkaloids, ma'edamines A (**251**) and B (**252**), with a unique 2(1*H*)pyrazinone ring were isolated from the Okinawan marine sponge *Suberea* sp., along with aplysamine 2 (**172**), purpuramine H (**186**), and purpuramine I (**187**) (152). Biogenetically, ma'edamines A (**251**) and B (**252**) may be generated from the 11,12-dehydro form of aplysamine-2 (**172**) and purpuramine I (**187**) through the formation of a six-membered ring and dehydroxylation.



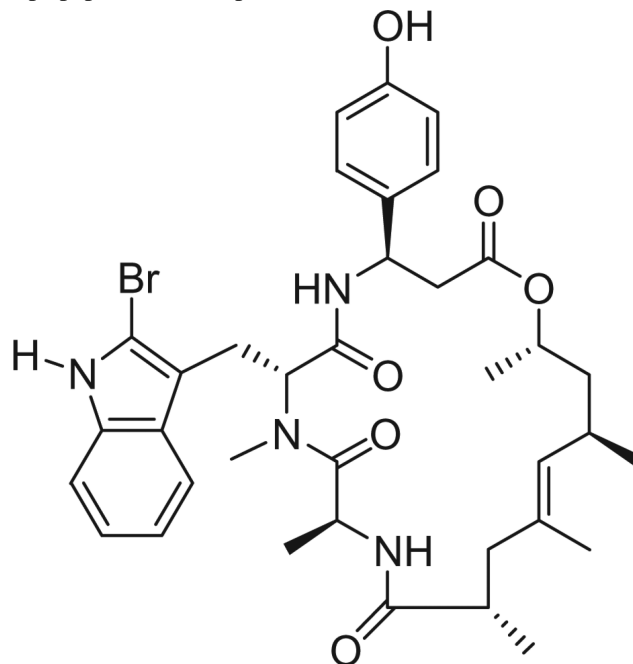
Polyandrocarpamides A–C (**253–255**), which are derived from tryptophan and tyrosine subunits, were isolated from the marine ascidian *Polyandrocarpa* sp. (153). Structurally related alkaloids, the chelonins, were reported from the marine sponge *Chelonaplysilla* sp., of which chelonin B (**256**) and 5-bromochelonin B (**257**) contain a bromotyrosine (154).



Examination of the marine sponge *Suberea* aff. *praetensa* (Row) from the Gulf of Thailand furnished, in addition to the known cavernicolins, an unusual rearranged tyrosine metabolite subereatensin (**258**) (155).



Geodiamolides and jaspamides are closely related cyclic depsipeptides isolated from a variety of tropical marine sponges. Jaspamide (**259**), also named jasplakinolide, obtained independently from *Jaspis* sp. collected in Palau (156) and Fiji (157), was the first member of this group of depsipeptides to be reported.

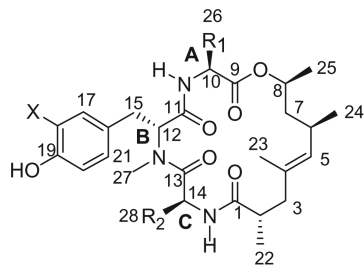


jaspamide (**259**)

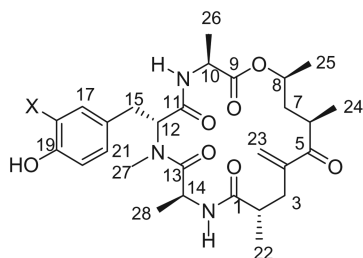
Shortly thereafter, geodiamolides A (**260**) and B (**261**) were isolated from the Caribbean sponge *Geodia* sp. (158). Subsequently, geodiamolides C–G (**262–265**, **266**) were reported from the sponge *Cymbastela (Pseudaxinyssa)* sp. collected in Papua New Guinea (159,160); geodiamolides H (**267**) and I (**268**) were reported from a *Geodia* sp. (161); geodiamolide TA (**269**) was reported from the South African sponge *Hemiastrella minor* (162); neosiphoniamolide A (**270**) was reported from the New Caledonian sponge *Neosiphonia superstes* (163); and geodiamolides J–P (**271–277**) and R (**279**) were isolated from a recollection of the sponge *Cymbastela* sp. from Papua New Guinea (164). Although no chloro analogue of geodiamolide O (**276**) was isolated, it is likely to exist as a natural product, and therefore Andersen *et al.* reserved the name geodiamolide Q (**278**) for the hypothetical structure in anticipation of its future discovery (164).

The structures of the geodiamolides were determined by 1D and 2D NMR spectroscopy, and the absolute stereochemistries of geodiamolides A (**260**) and H (**267**) were determined by X-ray crystallography (158,161). There are now 19 known members of the geodiamolide family of cyclic depsipeptides. Variations have been observed in all three amino acid positions, as well as the polyketide portion of the molecule. Amino acid A variants include alanine (**260**, **261**, **262–265**, **276**, **277**), serine (**273–275**, **267**), β -tyrosine (**267**, **268**), and valine (**269**, **270**); amino acid B variants include only the C-18 halogen atom, with iodine

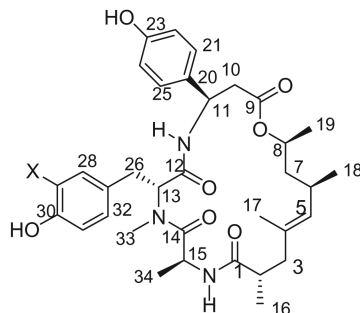
(260, 263, 266, 267, 273, 276, 278, 270), bromine (261, 264, 268, 271, 274, 277), and chlorine (262, 264, 272, 275, 269) all being observed; amino acid C variants include alanine (260, 261, 262, 267, 268, 273–275, 269), glycine (263–265), and serine (276, 277). The jaspamide/geodiamolide family of metabolites occurs across a taxonomically distant group of sponge species (156,158–160,162,163). To account for this observation, it has been suggested that microorganisms associated with the sponges produce these metabolites (162). The chondramides, which are jaspamide analogues from cultures of various strains of *Chondromyces myxobacteria* (165,166), strongly support the hypothesis of a microbial origin for the jaspamide/geodiamolides.



geodiamolide A (260): $R_1=Me$ $R_2=Me$ $X=I$
 geodiamolide B (261): $R_1=Me$ $R_2=Me$ $X=Br$
 geodiamolide C (262): $R_1=Me$ $R_2=Me$ $X=Cl$
 geodiamolide D (263): $R_1=Me$ $R_2=H$ $X=I$
 geodiamolide E (264): $R_1=Me$ $R_2=H$ $X=Br$
 geodiamolide F (265): $R_1=Me$ $R_2=H$ $X=Cl$
 geodiamolide L (273): $R_1=CH_2OH$ $R_2=Me$ $X=I$
 geodiamolide M (274): $R_1=CH_2OH$ $R_2=Me$ $X=Br$
 geodiamolide N (275): $R_1=CH_2OH$ $R_2=Me$ $X=Cl$
 geodiamolide O (276): $R_1=Me$ $R_2=CH_2OH$ $X=I$
 geodiamolide P (277): $R_1=Me$ $R_2=CH_2OH$ $X=Br$
 geodiamolide Q (278): $R_1=Me$ $R_2=CH_2OH$ $X=Cl$
 geodiamolide R (279): $R_1=CH_2OH$ $R_2=H$ $X=I$
 geodiamolide TA (269): $R_1=i-pr$ $R_2=Me$ $X=Cl$
 neosiphoniamolide (270): $R_1=i-pr$ $R_2=H$ $X=I$



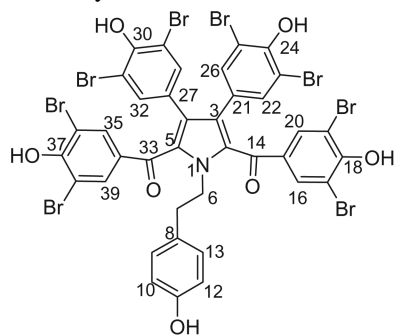
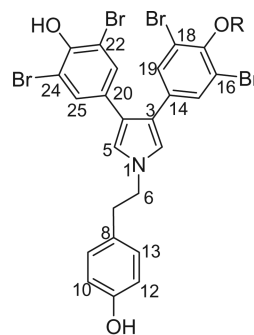
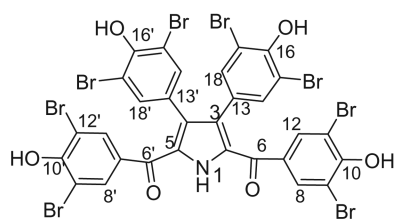
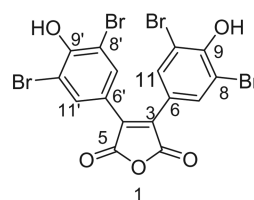
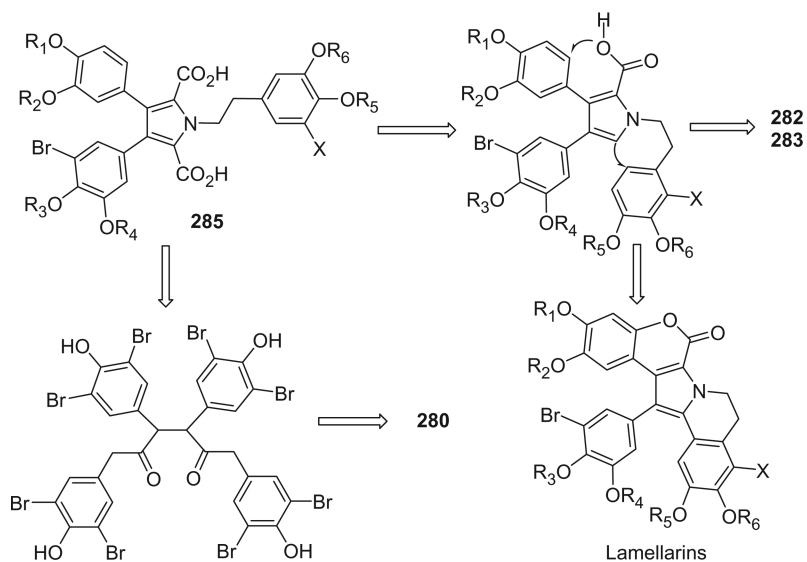
geodiamolide G (266): $X=I$
 geodiamolide J (271): $X=Br$
 geodiamolide K (272): $X=Cl$



geodiamolide H (267): $X=I$
 geodiamolide I (268): $X=Br$

Polycitone A (280) and B (281), polycitrin A (282) and B (283), and prepolycitrin A (284) were reported from the Indo-Pacific ascidians *Polycitor* sp. and *P. africanus* by Kashman's group (167,168). Their structures were established by spectroscopic and chemical methods. The structure of polycitone A (280) was confirmed by X-ray crystallography (167).

The structures of polycitone A (**280**) and B (**281**) and polycitrin A (**282**) and B (**283**) were close to the lamellarins isolated from the mollusk *Lamellaria* sp. (169) and an ascidian of the genus *Didemnum* (170,171). Lamellarins are not included in this review because of the absence of a halogen in their structures. A possible biogenetic relationship between the lamellarins, polycitone A (**280**), and polycitrin A (**282**) and B (**283**) is shown below. The lamellarins may be derived from a precursor **285**, which is a condensation product of three, suitably substituted tyrosine molecules.

polycitone A (**280**)polycitrin A (**282**): R=H
polycitrin B (**283**): R=Mepolycitone B (**281**)prepolycitrin A (**284**)

III. Spectroscopic Data

As seen from the previous section, bromotyrosine derivatives exhibit a variety of chemical structures. The structure elucidation of bromotyrosine derivatives was based on chemical methods and the contemporary spectroscopic methods, which include 1D proton and carbon NMR, 2D homo- and heteronuclear correlations, as well as different mass spectroscopic methods. Some of the structures were verified by X-ray diffraction analysis. The physicochemical properties are listed in Table I, including appearance, molecular formula, MS, MP, $[\alpha]_D$, UV, IR, and CD. The proton and carbon NMR data are collected in Table II. All of the ^{13}C -NMR resonance assignments for C-2 and C-4 of the spirocyclohexadienylisoxazoline type of compounds were revised based on Fattorusso's (61) COLOC NMR experiment, and our HMQC and HMBC experiment on a number of mono- and bis-spirocyclohexadienylisoxazoline bromotyrosine derivatives (12). The chemical shift of C-2 is at around 114 ppm and that of C-4 is around 122 ppm. The relative stereochemistry of the hydroxyl group at C-1 and the oxygen atom in the spirocyclohexadienylisoxazoline ring can be determined by comparison of the chemical shifts of H-1 and H-7 with synthesized *cis* and *trans* isomers (217). For the *trans* configuration, H-1 resonances at 4.2 ppm, H-7 resonances at 3.1 (d, $J = 18$ Hz) and 3.8 (d, $J = 18$ Hz) while in *cis* configuration δ 4.5 (H-1) and 3.42 (2H, H-7) were observed. The absolute configuration of aerothionin (**68**) was determined by X-ray crystallographic analysis and the CD spectrum (60). The stereochemistry of the spirocyclohexadienylisoxazoline ring in other alkaloids can be conventionally deduced by comparison of the CD spectrum with that of aerothionin.

The ^1H and ^{13}C NMR spectra of the spirooxepinisoxazoline type of alkaloids are significantly different from those of the spirocyclohexadieneisoxazoline type of alkaloids. The chemical shift of H-1 of the spirooxepinisoxazoline type at 7.3 ppm is 1.0 ppm lower than that of the corresponding proton (H-5) in the spirocyclohexadieneisoxazolines. The carbon-13 chemical shifts of C-1 and C-6 (the spiro-carbon) for the spirooxepinisoxazoline type are at 145 and 102 ppm, which are 15 and 12 ppm lower than those of the corresponding carbons (C-5, C-6) in the spirocyclohexadieneisoxazoline type of bromotyrosine derivatives.

The geometry of the oxime can be determined by the chemical shift of C-7, where 25.3–27.0 ppm indicated an *E*-geometry, while 35 ppm indicated a *Z*-geometry (107).

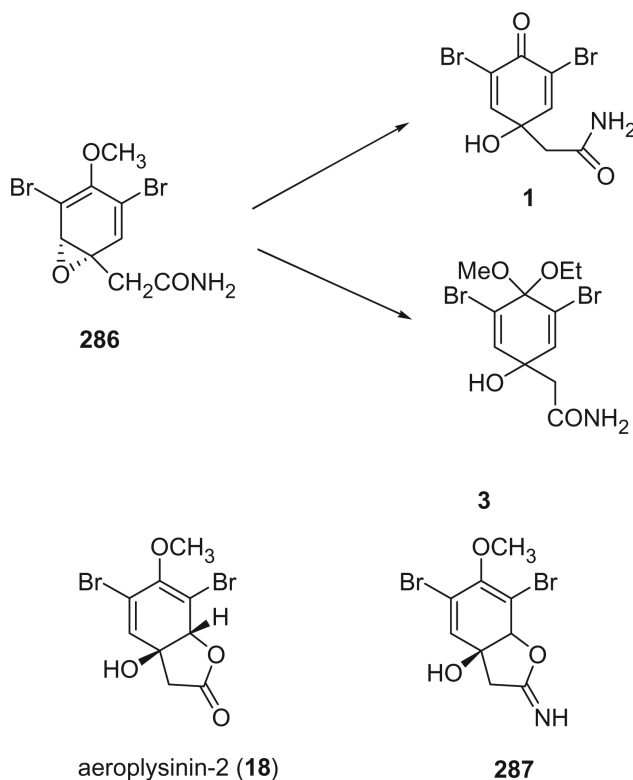
Bastadins are often spectroscopically similar to one another. ^1H and ^{13}C NMR alone are insufficient to discriminate bastarane and isobastarane isomers (130). For example, the structure of bastadin 5 (**209**) is almost impossible to distinguish from bastadin 19 (**223**) by 1D NMR, without recourse to 2D heteronuclear experiments. Molinski *et al.* reported that using “fingerprinting” of the MeO ^1H NMR signals of the permethyl derivatives of bastadins provided a partial solution to the problem (130). The chemical shift pattern of the MeO signals measured in CDCl_3 can be matched reliably against those of previously reported bastadins tetra-*O*-methyl ethers (see Table III). For example, the ^1H NMR of the three isomers, bastadin 5, bastadin 15, and bastadin 19, are very similar in CD_3OD or $\text{DMSO}-d_6$. However, the ^1H NMR signals of the MeO of the corresponding tetramethyl ethers are readily distinguishable in CDCl_3 .

IV. Biosynthesis of Bromotyrosine Derivatives

When the first bromotyrosine derivative, the dienone **1**, was isolated (3), the biogenetic precursor of this antibiotic was easily envisioned from tyrosine, which, after bromination, may be transformed into 3,5-dibromo-4-hydroxy-phenylacetaldehyde through a pathway already suggested in the literature (172). From the inspection of the structures, Minale *et al.* (19) and Moddy *et al.* (58) suggested that the Verongia bromo-metabolites are most likely biogenetically derived from 3,5-dibromo-tyrosine and, presumably, the central C₄N₂ and C₅N₂ chains of aerothionin (**68**) and homoaerothionin (**69**) are derived from ornithine and lysine, respectively.

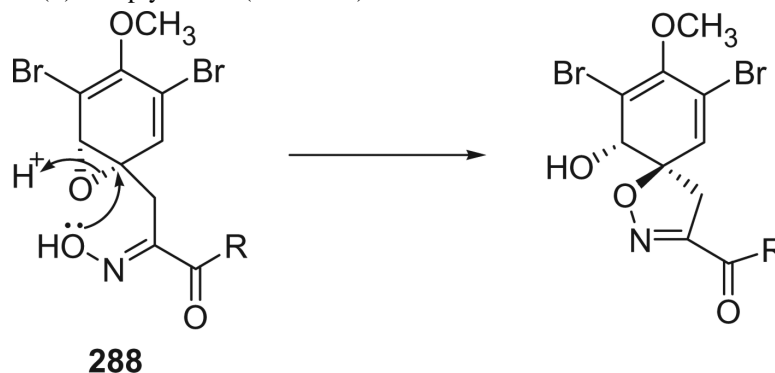
A. BIOGENESIS OF ISOSPIROXAZOLINE

Based on the acid-catalyzed addition of methanol to 1,4-dimethylbenzene oxide which gave 4-methoxy-1,4-dimethyl-2,5-cyclohexadienol (173), Anderson and Faulkner (5) proposed that an analogous 1,4-addition of solvent to an arene oxide **286** could result in the formation of dienone **1** or the corresponding ketal **3** (5). Although arene oxides have been proposed as intermediates in the biosynthetic oxidation of aromatic compounds, there is no evidence of their existence as natural products. The coexistence of the lactone aeroplysinin-2 (**18**) with dienone **1** and the ketal **3** suggested that the imino-ether **287** should also be considered as a possible precursor of these alkaloids.



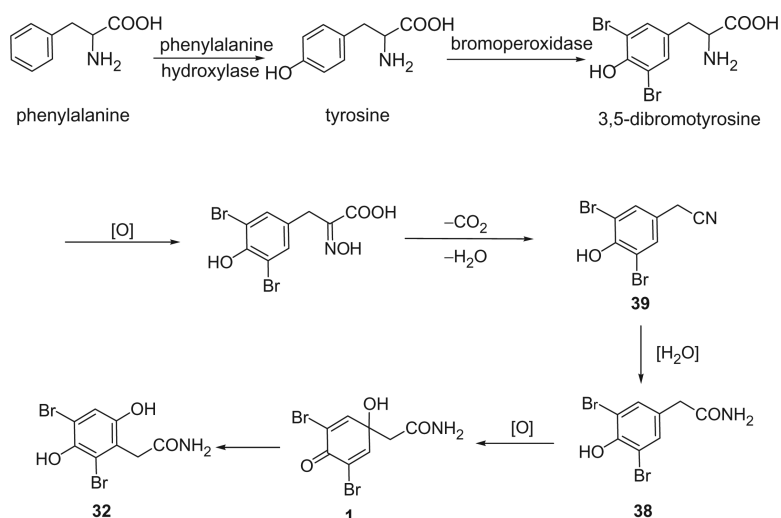
The spiro systems could arise in various ways, including nucleophilic attack by an oxime function on an arene oxide as shown in **288** (59). Following suggestions that nitriles may be

derived *in vivo* from α -amino acids (174), the oxime **288** could be speculated as a precursor of the nitrile (\pm)-aeropylsinin-1 (**14** and **17**).



Quite surprisingly, the first attempt to demonstrate the conversion of tyrosine into bromotyrosine derivatives was unsuccessful (175). In that experiment, *Verongia aerophoba* failed to incorporate radioactivity from {U-¹⁴C}-L-tyrosine into aerothionin (**68**), aeropylsinin-1 (**14**) and the dienone **1**. Inactive aerothionin (**68**) was also isolated when the sponge was fed with {U-¹⁴C}-L-ornithine and {CH₃-¹⁴C}methionine. However, the sponge utilized these amino acids for the synthesis of fatty acids. A very slow rate of biosynthesis might account for these results.

By using liposome-enclosed precursors and modified culture conditions, which allowed the sponge to survive in the laboratory for as long as 2 weeks, Rinehart's group demonstrated the conversion of phenylalanine and tyrosine to the dienone **1**, as well as the rearranged product dibromohomogetisamide (**32**), by the sponge *Aplysina fistularis* in 1981 (176). In addition to implying that the sponge can convert phenylalanine to tyrosine (177), the comparable radioactivity found in **1** and **32** supports the hypothesis (26) that **32** is formed from **1** via a skeletal rearrangement analogous to the mammalian catabolism of tyrosine to homogentisic acid. Although the enzymatic mechanism of the side chain migration is still unclear (178), the conversion of 4-hydroxy-2,5-cyclohexadienone-4-acetic acid to homogentisic acid in aqueous alkali has been demonstrated (179). Double labeling studies also revealed that the sponge can convert the side chain in phenylalanine to the acetamide side chain in **32** without deamination. In addition to corroborating the known occurrence of bromophenol nitriles and oximes in Verongid sponges, this work supported the following biosynthetic pathway:

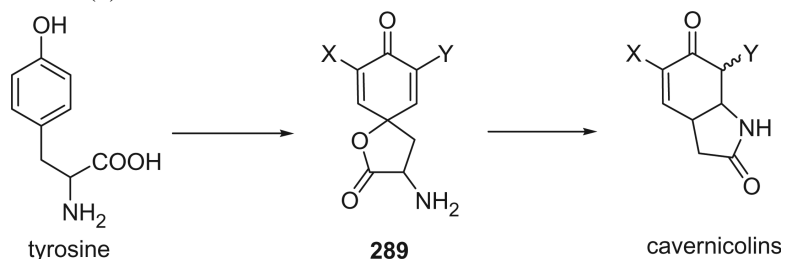


Moreover, it has been demonstrated that α -oximino acids undergo facile dehydration/ decarboxylation to give nitriles *in vitro* (180) and *in vivo* (181), that **1** was converted to **32** (182), and that (4-hydroxyphenyl)pyruvic acid oxime was isolated from *Hymeniacidon sanguinea* (183), further supporting the proposed mechanism.

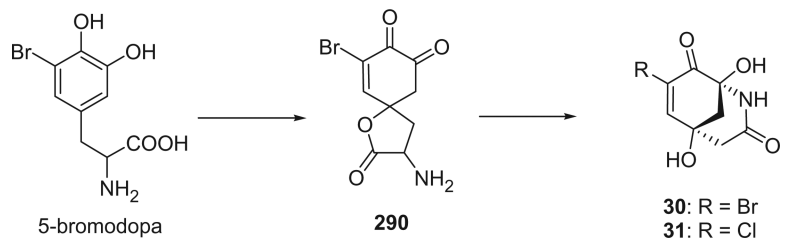
Carney and Rinehart reported the results of additional feeding experiments in the marine sponge *Aplysina fistularis* in 1995 (184). {U- ^{14}C }-L-tyrosine, {U- ^{14}C }-L-3-bromotyrosine, and {U- ^{14}C }-L-3,5-dibromotyrosine were incorporated into both the dienone **1** and aeroplysinin-1 (**14**), and {methyl- ^{14}C }-methionine was specifically incorporated into the *O*-methyl group of aeroplysinin-1. In contrast to expectations, tyrosine was incorporated more efficiently than 3-bromotyrosine, which is in turn incorporated more efficiently than 3,5-dibromotyrosine. This may result from the bulky bromines interfering with the permeability of the precursors across cell membranes. It was surprising that {methyl- ^{14}C }-L-methyltyrosine, {methyl- ^{14}C }-L-3,5-dibromo-*O*-methyltyrosine, 3-bromo-4-hydroxybenzyl cyanide, and 3,5-dibromo-4-hydroxybenzyl cyanide were not incorporated into the dienone **1** and aeroplysinin-1 (**14**). Both 3-bromo-4-hydroxybenzyl cyanide and 3,5-dibromo-4-hydroxybenzyl cyanide have been identified as metabolites of *A. fistularis* (185), and their involvement as a potential precursor to the dienone **1** seems reasonable. The possible reasons for the lack of incorporation into **1** and **14**, aside from the possibility of their not being part at the biosynthetic path, are poor transport of the halogenated nitriles across cell membranes, or poor solubility of the nitriles in sea water (184).

Although, from the above feeding experiments, it is clear that the Verongida bromotyrosine derivatives are biogenetically derived from tyrosine, it is still a matter of debate whether these alkaloids are produced via an arene oxide, or through phenol oxidative coupling (186). Based on the isolation of the racemic verongiaquinols, (\pm)-3-bromoverongiaquinol (**10**) and (\pm)-3-bromo-5-chloroverongiaquinol (**11**), and the low enantiomeric pure cavernicolins, 5-bromocavernicolin (**24**) (23) and 5-chlorocavernicolin (**25**), D'Ambrosio *et al.* (9) proposed a phenol oxidative (187) route based upon tyrosine precursors for their formation, since the proposal of an arene epoxide as a biogenetic precursor demands enantiomerically pure **11** and **10**. In fact, natural products derived from phenol oxidations occur in nature in both

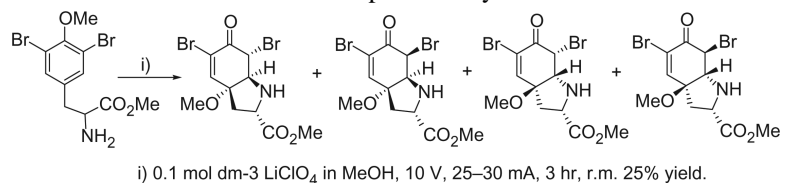
optically active forms or as racemates, or even in nearly racemic forms (188). One way to rationalize the formation of the cavernicolins in full respect of the classical *ortho-para* orientation rules for the oxidative coupling of phenolic compounds (188) is to postulate a racemic or nearly racemic spiro lactone **289** as the intermediate derived from the halotyrosine precursor (9). There is, in fact, ample precedent for cyclohexadienone spiro lactone in oxidative couplings of phenols (188). Hydrolysis of the lactone, followed by conjugate attack of the amino acid *N*-atom and decarboxylative oxidation may then be seen to lead to the cavernicolins (9).



7-Bromocavernicolenone (**30**) and 7-chlorocavernicolenone (**31**) may be biogenetically derived from 5-bromodopa undergoing a similar pathway (24,25).

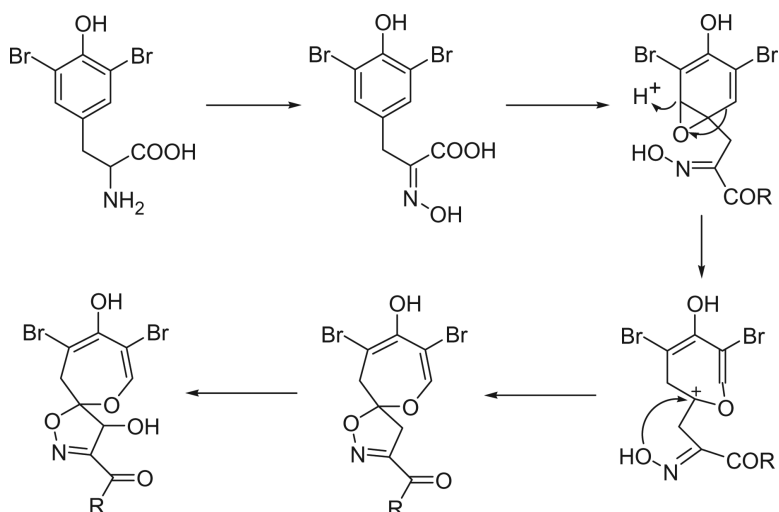


Anodic oxidation of 3',5'-dibromo-4'-methoxyphenylalanine methyl ester led to the cavernicolin model compounds as four possible stereoisomers (189,190). This may constitute a new model for the biogenesis of the cavernicolins as an alternative to a spiro lactone route from oxidation of amino-protected tyrosines



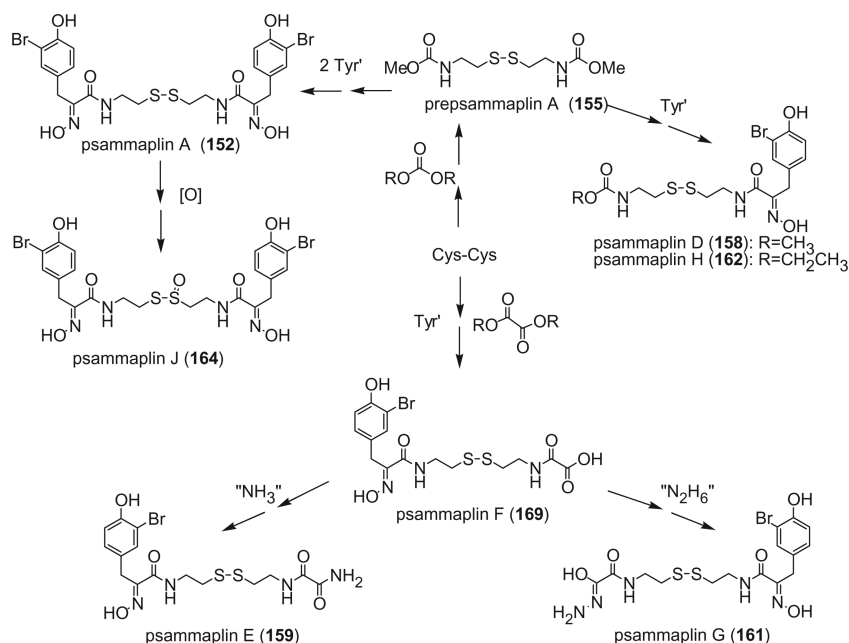
B. BIOGENESIS OF THE PSAMMAPLYSINS

Biogenesis of the psammaplysins may proceed through an oximino epoxide as shown in the scheme below (94). The epoxide ring opening leads to ring enlargement and results in the spiro[4.6]dioxazundecane. The benzene oxide-oxepin pathway, first adumbrated on theoretical grounds by Vogel and Günther, (191) was experimentally demonstrated through the biosynthesis of aranotin by Neuss *et al.* (192,193).

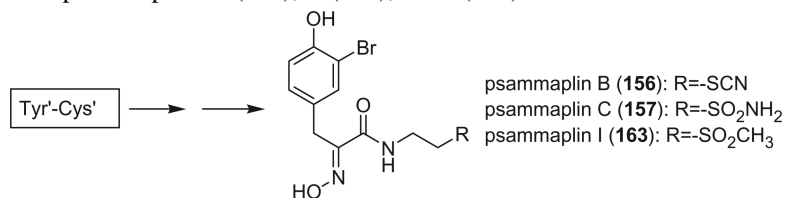


C. BIOSYNTHESIS OF PSAMMAPLIN TYPE OF COMPOUNDS

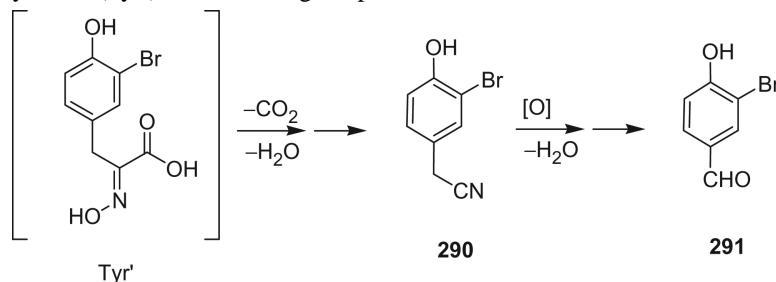
Crews *et al.* proposed a biogenetic pathway, based on the isolation of prep-sammaplins A (**155**), to rationalize the formation of psammaplins A (**152**) and other bromotyrosine derivatives isolated from *Pseudoceratina pura* by his group (110, 112). A straightforward dimerization of a rearranged cysteine ($\text{Cys}'=\text{HS}-\text{CH}_2-\text{CH}_2-\text{NHCOOMe}$) could generate prepsammaplins A (**155**). Condensation of the dimer **155** with either one or two functionalized tyrosine groups ($\text{Tyr}'=\text{the bromo oxime derivative}$) could rationalize the formation of psammaplins A (**152**), D (**158**), and H (**162**), respectively. Likewise, cysteine can lead to psammaplins F (**160**), which is envisioned to be the precursor of psammaplins E (**159**) and psammaplins G (**161**). Oxidation of psammaplins A (**152**) (possibly by a cytochrome P450 reaction) provides a connection to psammaplins J (**164**). The two esterified psammaplins D (**158**) and H (**162**) may be artifacts of the isolation derived from the acid formed via condensation of cysteine and tyrosine.



Similarly, condensation of the functional tyrosine (Tyr') and the rearranged cysteine (Cys') could generate psammaplins B (156), C (157), and I (163).



Modified tyrosine (Tyr') is also the logical precursor of alkaloids 290 and 291.

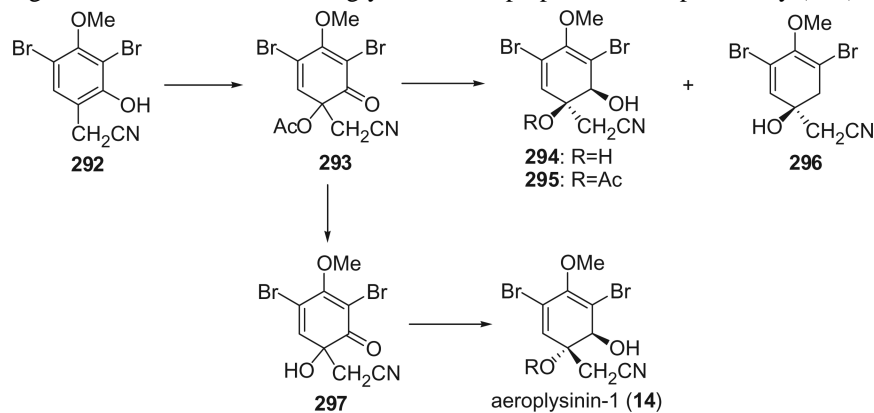


V. Synthesis

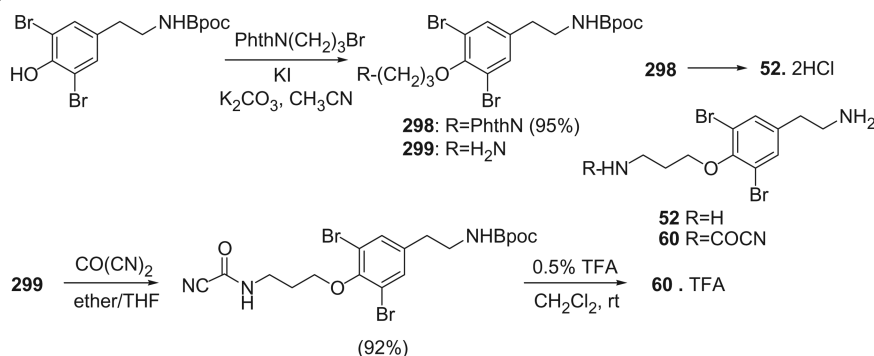
The diverse and unique chemical structures, and the variety of biological activities of bromotyrosine derivatives, make them ideal synthetic targets for synthetic and natural products chemists. Studies on the synthesis of bromotyrosine can be traced back to 1912 (194). In former studies, degradation, chemical transformation to known compounds, or even total synthesis were conducted for the purpose of verifying the structures. Later studies were focused on the total synthesis of more complex structures, such as the spirocyclohexadienylisoxazoline and bastadin ring systems.

A. SYNTHESIS OF SMALL BROMOTYROSINE DERIVATIVES

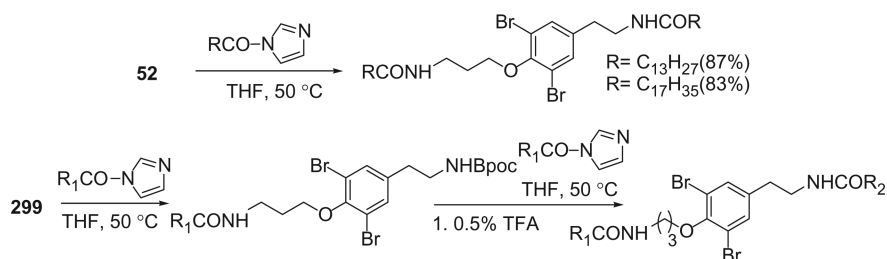
Synthesis of functionalized cyclohexadienones, dienols, and dienediols was studied, which may be useful for the synthesis of some bromotyrosine derived dienones or ketals (195). Andersen and Faulkner reported the synthesis of aeroplysinin-1 (**14**). 3,5-Dibromo-2-hydroxy-4-methoxyphenylacetonitrile (**292**) was oxidized with excess lead tetraacetate in acetic acid at 25°C for 18 h to obtain the dienone **293** in 35% yield. Reduction of **293** with sodium borohydride in absolute ethanol at 0°C gave three products: iso-aeroplysinin-1 (**294**) (40%), the corresponding monoacetate **295** (18%), and 2-deoxyaeroplysinin-1 (**296**) (22%). The failure to obtain a *trans*-diol was attributed to the influence of the acetoxy function. The dienone **293** was therefore transformed to the corresponding keto alcohol **297** by transesterification in methanol containing *p*-toluenesulfonic acid. Reduction of the keto alcohol **297** with sodium borohydride in absolute ethanol at 0°C for 10 min gave aeroplysinin-1 in 60% yield (**14**). This synthesis of aeroplysinin-1 (**14**) and iso-aeroplysinin-1 (**294**) constitutes a novel approach to the synthesis of arene glycols and has the added advantage in that both *cis*- and *trans*- glycols can be prepared stereospecifically (196).



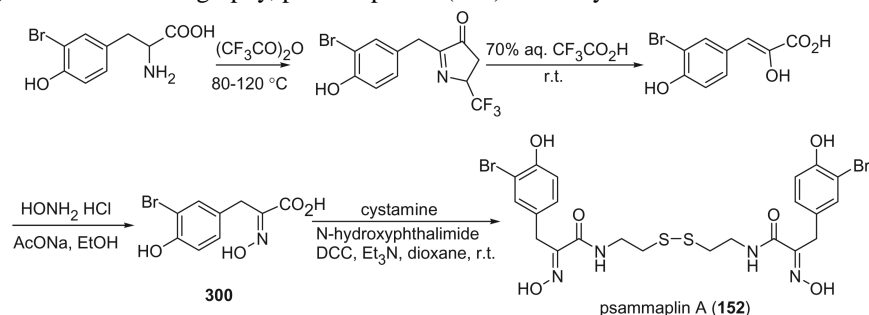
Ganem *et al.* synthesized ceratinamine (**60**), moloka'iamine (**52**), and mololipids (**53**), together with several analogues, for antifouling, anti-HIV and cytotoxicity studies (197–199).



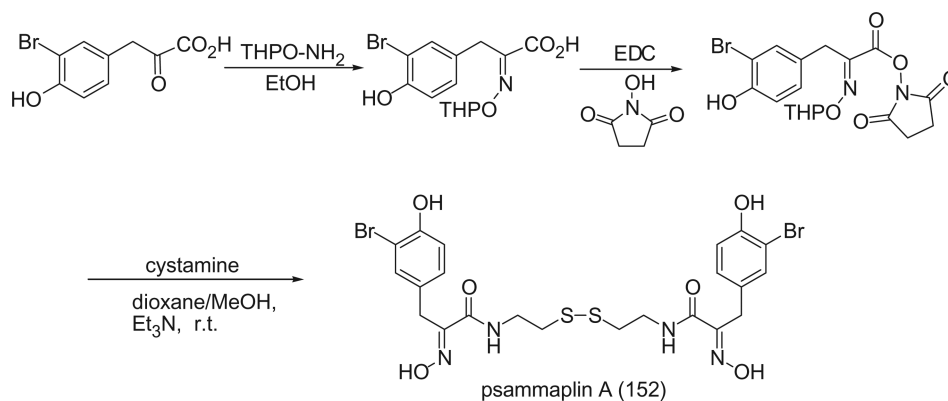
Mololipids can be produced smoothly by the direct dualacylation of moloka'iamine (**52**) with myristoyl, stearoyl, and oleoyl imidazoles or the step-wise acylation of a protected precursor with different fatty acyl groups (198).



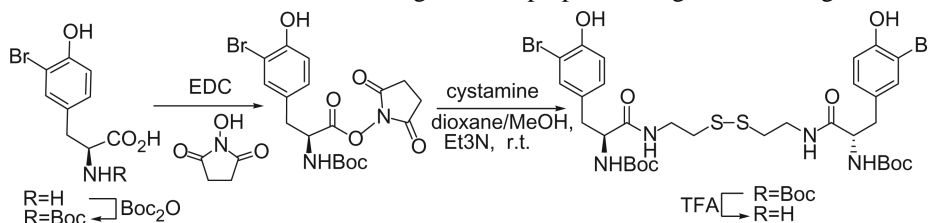
Hoshino *et al.* reported a convenient method to synthesize psammaplin A (**152**) (200). As for a synthetic strategy, direct coupling of the phenolic oxime-acid **300** with cystamine was considered, because **300** could be readily prepared from 3'-bromotyrosine. After several attempts to couple **300** directly with cystamine, a mixture of **300** (1.0 eq.) and free cystamine (0.5 eq.) in dioxane containing one equivalent of Et₃N, DCC and *N*-hydroxyphthalimide was stirred at room temperature for 12 h to afford, after purification using column chromatography, psammaplin A (**152**) in 67% yield.



Inspired by the structure of psammaplin A (**152**), a combinatorial scrambling strategy for the construction of heterodimeric disulfide analogues was developed and applied to the construction of a 3828-membered library starting from 88 homodimeric disulfides (201). The disulfide motif was utilized as a readily exchangeable linkage (202), which would allow rapid construction of a heterodimeric analogue library suitable for defining structure–activity relationships (203). It is well-precedented that disulfide bonds will readily undergo facile exchange reactions with other disulfides in high yield under mild conditions (204). For example, if two homodimeric disulfides, A-SS-A and B-SS-B, are mixed under basic conditions in the presence of a suitable catalyst they will undergo rapid exchange reactions to afford a statistical mixture of three disulfides: A-SS-A, A-SSB, and B-SS-B in a ratio of 1:2:1, respectively. Hoshino's synthesis of psammaplin A (200) was modified as shown in the following scheme to synthesize 44 homodimeric psammaplin A analogues.



Amino acid homodimeric disulfide analogues were prepared using the following scheme.

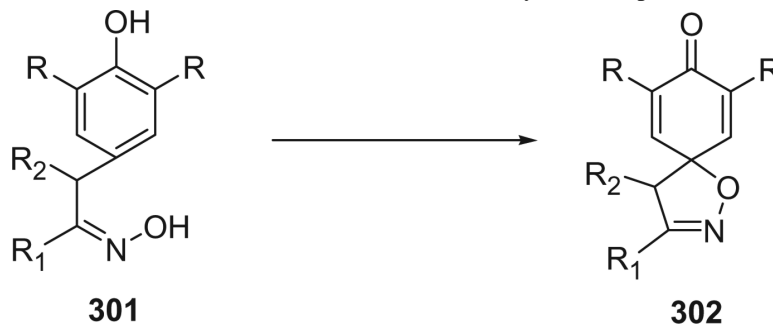


Additional sulfonamide analogues and amide analogues were synthesized by standard techniques. Finally, 43 homodimeric disulfide building blocks were obtained from commercial sources in order to enhance the library's structural diversity. The disulfide exchange reaction in DMSO/H₂O (3:1) by adding catalytic amounts of dithiothreitol was reproducible and led to a statistical mixture. Solution phase combinatorial synthesis of the psammaplin A (**152**) analogue library was conducted in 88 96-well plates. The disulfide products could be screened directly from the reaction mixture since the catalyst, dithiothreitol, and the byproduct *trans*-1,2-dithiane-4,5-diol did not show any detectable antibacterial activity at a concentration which was 50-fold greater than the concentration at which either of these compounds would be in the screen mixture. After screening, six structurally distinct psammaplin analogues from this library demonstrated higher antibacterial activity than psammaplin A (**201**).

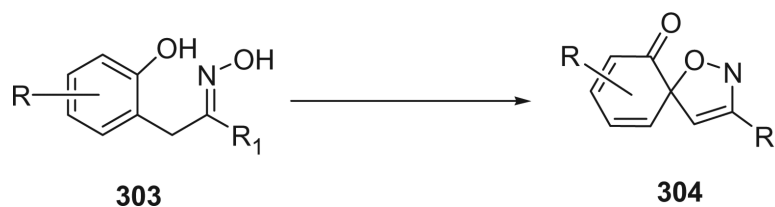
B. SYNTHESIS OF SPIROCYCLOHEXADIENYLISOXAZOLINE

The unique spirocyclohexadienylisoxazoline ring system of the bromotyrosine derivatives, such as aerothionin (**68**), aerophobin-1 (**69**), and fistularin 3 (**79**), and their wide range of bioactivities make them attractive targets for synthesis. A number of studies on the formation of the spiroisoxazoline through intramolecular oxidative cyclization of a phenolic oxime have been reported (205). Forrester *et al.* examined the reactions of oxime **301** with different oxidizing reagents including lead tetra-acetate, potassium ferricyanide, silver oxide, sodium periodate, Fremy's salt, and manganese tris(acetylacetonate) (206, 207). Of these, the manganese reagent was found to be the most effective oxidant, and gave the spiroisoxazoline **302** in fair yields of 19–62%. Oxidation with lead tetra-acetate did give the corresponding spiroisoxazolines, but in a much lower yield of 10%, while potassium ferricyanide, silver oxide, sodium periodate, and Fremy's salt failed to effect cyclization of

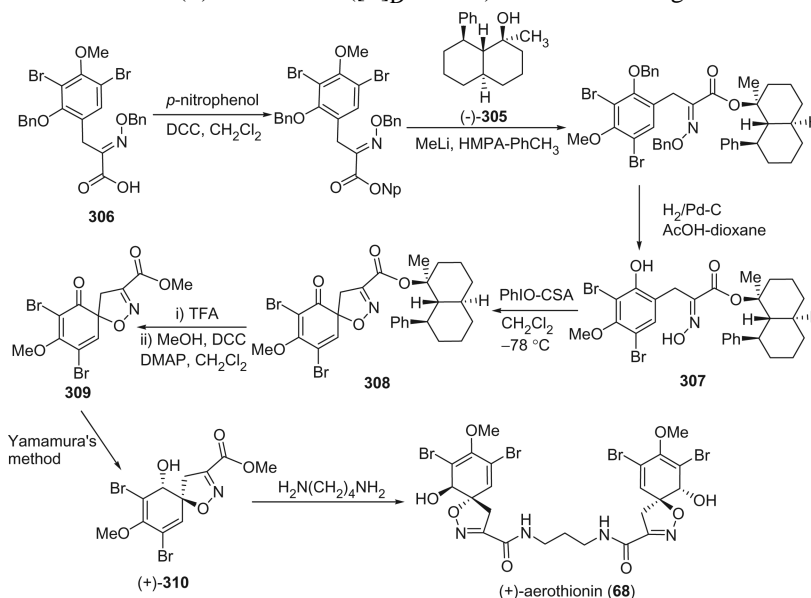
the phenolic oximes. In a subsequent study, the same researchers showed that oxidation of **301** (R=H, R₁=CO₂Me) with bromine water resulted in both electrophilic bromination and spirocyclization to give **302** (R=Br, R₁=CO₂Me) in 65% yield, while use of NBS with **301** (R = *t*-Bu, R₁ = Me) gave **302** (R = *t*-Bu, R₁ = Me) in 72% yield (208). Similarly, Boehlow *et al.* reported that addition of one equivalent of NBA to the oxime **301** (R = H, R₁ = CO₂Et) in THF at -60°C gave the monobromide **301** (R = 3-mono-Br, R₁ = CO₂Et, 60%). Addition of two equivalents of NBA to the oxime **301** (R = H, R₁ = CO₂Et) in THF or DMF at 0°C gave the dibromide **301** (R = 3,5-di-Br, R₁ = CO₂Et, 69%), and three equivalents at 0°C cleanly produced the spiroisoxazoline **302** (R = 3,5-di-Br, R₁ = CO₂Et, 74%) (209). Treatment of the oxime **301** (R = H, R₁ = CO₂Et) with Furia's bromoperoxidase enzyme mimic (210) of NH₄VO₃, H₂O₂, and KBr in water/chloroform resulted in the formation of both the monobromide **301** (R = 3-mono-Br, R₁ = CO₂Et) and dibromide **301** (R = 3,5-di-Br, R₁ = CO₂Et) without forming the spiroisoxazoline (209). Yamamura reported that oxidation of **301** (R = Br, R₁ = CO₂Me) with thallium (III) nitrate in methanol gave a mixture of products, which included 7–11% of **302** (R = Br, R₁ = CO₂Me) (211). Intriguingly, the same transformation could be carried out in quantitative yield by anodic oxidation (211). Kacan *et al.* reported phenyliodine (III) bis(trifluoroacetate) as an efficient reagent for the intramolecular oxidative cyclization. A series of oximes **301** (R = H, Br, R₁ = Me, Et, CMe₃, C₆H₅, CO₂Et, 4-BrC₆H₄) reacted with phenyliodine (III) bis(trifluoroacetate) in acetonitrile at 0 °C smoothly and rapidly to give the corresponding isoxazolines **302** in good to excellent yield (212). Application of this procedure to an *ortho*-phenolic oxime resulted in the formation of the [4 + 2] dimer of the initially formed spiroisoxazoline.



Cyclization of the *ortho*-phenolic oxime has also been studied. Forrester *et al.* found that of all the oxidants they examined, only tetrabromocyclohexa-2,5-dienone would convert **303** (R = 2,4-di-*t*Bu, R₁ = Me) into **304** (R = 2,4-di-*t*Bu, R₁ = Me) in 20% yield (208). An equally low yield of 27% was obtained by Yamamura, on oxidation of **303** (R = 2,4-di-Br, 3-OMe, R₁ = COOMe) to **304** (R = 2,4-di-Br, 3-OMe, R₁ = COOMe) with thallium trifluoroacetate in trifluoroacetic acid (213). Application of the above phenyliodine (III) bis(trifluoroacetate) to the *ortho*-phenolic oxime resulted in the direct formation of the [4 + 2] dimer of the initially formed spiroisoxazoline (212). Independently, Murakata *et al.* found that the hypervalent iodine compound phenyliodine diacetate (PIDA) was an efficient cyclization reagent of *o*-phenolic oxime-esters and oxime-amides (214). The cyclization of various oximes **303** (R = mono-, di-bromo, H, OMe, R₁ = OMe, O^tBu, NH(CH₂)₃OMe) in acetonitrile at 0°C proceeded smoothly to afford the spiroisoxazoline in good yield.

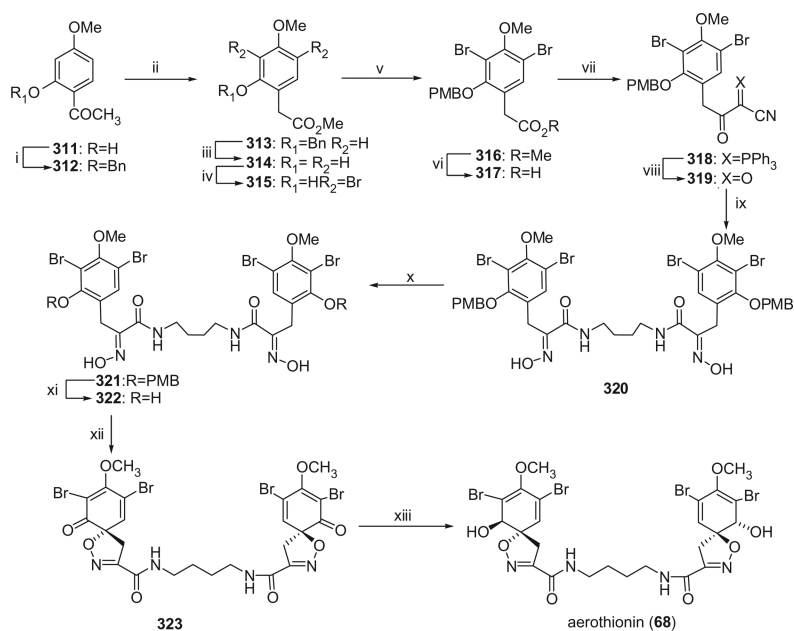


Asymmetric oxidative cyclization of *o*-phenolic oxime-esters was also studied by Murakata *et al.* (215). A novel, optically active tertiary alcohol (–)-**305** was synthesized as a chiral auxiliary. The *ortho*-phenolic oxime **306** was first transformed to the oxime ester **307** in three steps (see the following scheme). The reaction of **307** with PhIO in the presence of camphor sulfonic acid (CSA) in CH₂Cl₂ at –78 °C proceeded smoothly to afford the spiroisoxazoline **308** in 83% yield with 70–80% estimated diastereomeric excess by the ¹H NMR spectrum. The chiral auxiliary in **308** was removed by treatment with TFA at room temperature. Methylation using DCC and MeOH gave methyl ester (–)-**309** ([α]_D –56.4°) in 74% *ee* with the *S*-configuration. Optically active spiroisoxazoline **309** was reduced with Zn(BH₄)₂ to give cyclohexadienylisoxazoline (+)-**310**, amidation of which with butanediamine afforded (+)-aerotherionin ([α]_D + 166°) with the *S*-configuration.



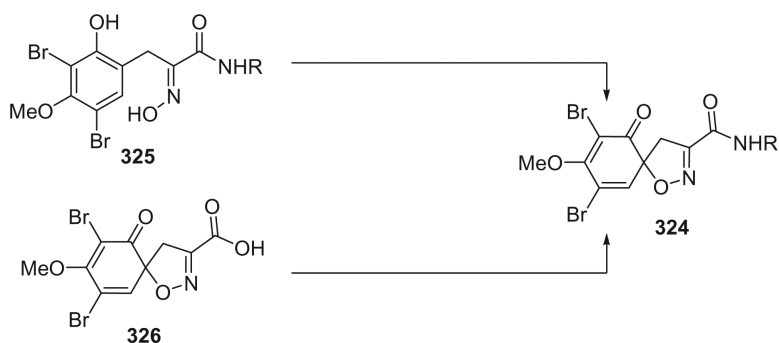
With the key spiroisoxazoline synthon in hand, total synthesis of some spirocyclohexadienylisoxazoline bromotyrosine derivatives was achieved. Forrester *et al.* reported that reducing tetrahydroaerotherionin using NaBH₄ did not yield the natural *trans*, *trans*-aerotherionin, but *cis*, *cis*-aerotherionin (216). Yamamura *et al.* reduced the spiroisoxazoline **309** using excess Zn(BH₄)₂ in CH₂Cl₂–Et₂O (3:2) to give the corresponding *cis*- and *trans*-isomers **310** in 29% and 40% yields, which were easily separated on preparative TLC (217, 213). Mixing *trans*-**310** with 1,4-butanediamine, 1,5-pentanediamine, or histamine, at room temperature overnight afforded aerotherionin (**68**), homoaerotherionin (**69**), and aerophobin-1 (**113**) in 18, 4.4, and 82% yields, respectively.

Wasserman *et al.* developed an efficient methodology for the formation of key α -keto amido residues common to many members of this family of natural products (218–221). Using this method, the α,β -diketo nitrile **319** was synthesized from the oxidation of the ylide **318** (222). The generation of **318** from 2-hydroxy-4-methoxyacetophenone (**311**) was accomplished according to the sequence outlined in the following scheme by protecting the phenolic hydroxyl as the benzyl ether **312**, rearrangement with $\text{Ti}(\text{NO}_3)_3$ to **313**, deprotection to **314**, and bromination to form dibromide **315**. Following reprotection to **316** and hydrolysis of the ester to the acid **317**, coupling with $\text{Ph}_3\text{P}=\text{CHCN}$ in the presence of EDCI yielded **318**. After the ylide **318** was oxidized by O_3 to the labile diketone nitrile **319**, generation of the bis- α -ketoamide **320** took place on treatment of **319** with 1,4-diaminobutane in CH_2Cl_2 . Conversion of **320** to the oxime **321** and deprotection provided the substrate **322**, which underwent the oxidative cyclization with tetrabromocyclohexadienone to afford **323** in 71% yield. Reduction of **323** with NaCNBH_3 in TFA gave the desired *trans,trans*-aerothionin (**68**) (222).

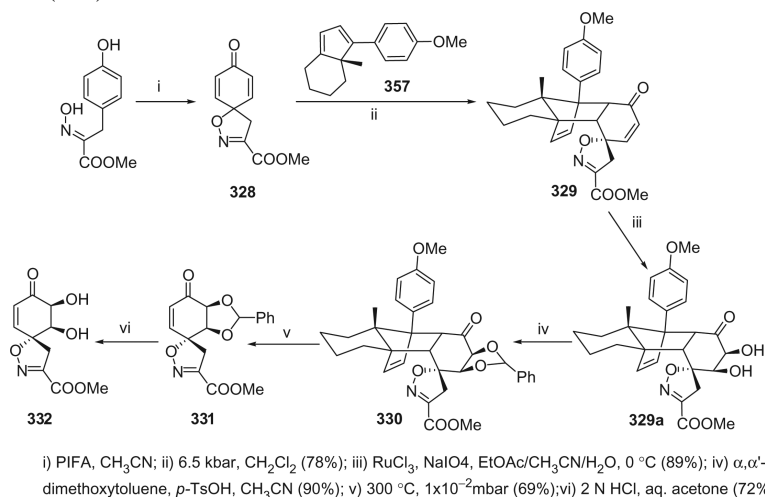


(i) BnBr , K_2CO_3 , acetone; (ii) $\text{Ti}(\text{NO}_3)_3$, MeOH , 76%; (iii) H_2 , Pd/C , MeOH , 96%; (iv) Br_2 , pyr , 90%; (v) PMBCl , K_2CO_3 , acetone, 93%; (vi) 2N NaOH , MeOH , 94%; (vii) $\text{Ph}_3\text{P}=\text{CHCN}$, EDCI, CH_2Cl_2 , 88%; (viii) O_3 , CH_2Cl_2 ; (ix) 1,4-diaminobutane, CH_2Cl_2 , 64% (two steps); (x) $\text{NH}_2\text{OH}\cdot\text{HCl}$, NaOAc , EtOH , 95%; (xi) TFA , CH_2Cl_2 , 92%; (xii) tetrabromocyclohexadienone, CH_3CN , 70%; (xiii) NaCNBH_3 , TFA , 25%.

Murakata *et al.* synthesized the cyclohexadienonespiroisoxazoline amides **324**, which could be useful as intermediates for the synthesis of araplysillin I (**99**) and II (**100**) (223). The synthesis of these metabolites was efficiently achieved using two routes. The first route is direct cyclization of *o*-phenolic oxime-amide **325** with phenyliodonium diacetate (PIDA) to produce **324**. The second is the amidation of the cyclohexadienonespiroisoxazoline-acid **326** to afford **324**.



Based on the enantioselective cycloaddition of the optically pure cyclopentadiene (**4**) with spiroactone (224,225), Winterfeldt *et al.* synthesized enantiomerically pure spirooxazoline **332**, which is the crucial intermediate en route to the agelorins (**87**, **88**) and their analogues (226). Face selectivity was successfully achieved in the cycloaddition of cyclopentadiene **327** and spirooxazoline **328** to form the enantiopure **329**. This may be due to the lower spatial demand of an oxygen atom than a methylene group. Flash-hydroxylation of **329** with ruthenium tetroxide afforded *cis*-diol **329a**, which underwent pyrolysis after it was transformed into the acetal **330** to generate the spirocyclohexenone **331**. Subsequently, hydrolysis afforded the enantiopure intermediate **332**, representing the agelorins (**87**, **88**) chromophore (226).

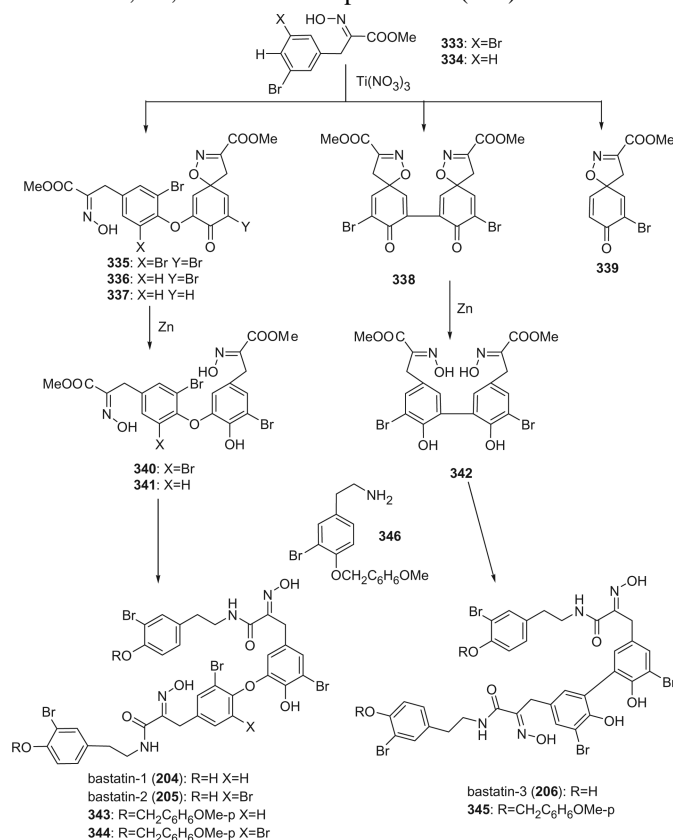


In a continuing report, several enantiopure spiroisoxazoline amides were prepared using the above method and tested on an isoxazoline-splitting enzyme, which is involved in an injury-induced defense reaction of the sponge *Aplysina cauliformis* (227). The results indicated that the bromoatoms in the cyclohexenone moiety are important for enzyme binding, while the presence of the N–H bond of a monoalkylamide turned out to be mandatory for ring fission.

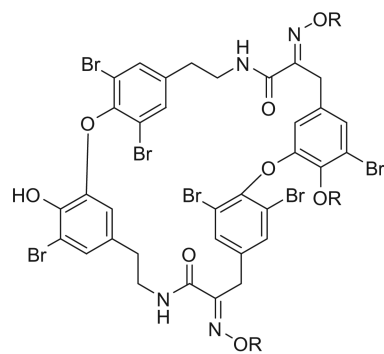
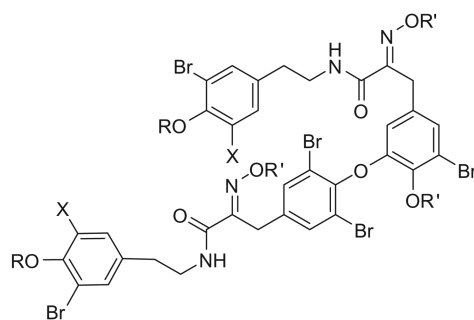
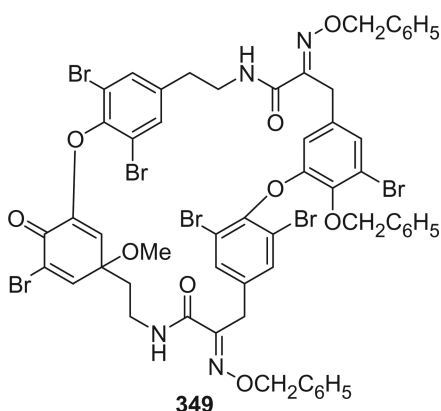
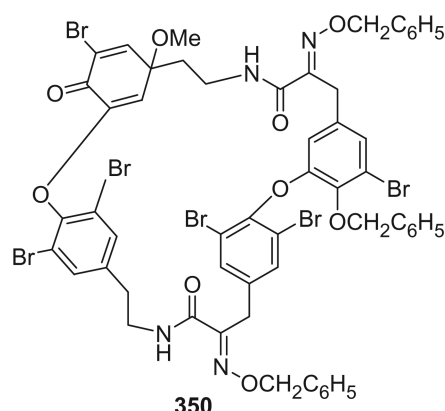
Boehlow *et al.* summarized the approach to the synthesis of some spirocyclohexadienylisoxazoline and oxime bromotyrosine derivatives and synthesized two oxime bromotyrosine derivatives verongamine (**139**) and purealidin N (**150**) (205).

C. SYNTHESIS OF BASTADINS

Yamamura's group reported the total synthesis of bastadins 1, 2, 3, and 6 (228,229,230). Biomimetic oxidation of methyl 3,5-dibromo-4-hydroxyphenylpyruvate oxime (**333**) was carried out using $\text{Ti}(\text{NO}_3)_3$ to afford 7–11% of spiroisoxazole **339** and 37–44% of the dimeric spiroisoxazole **335**. Reduction of **335** gave the biphenyl ether **340**, as a key intermediate for bastadins-2 synthesis, in almost quantitative yield (228). Similarly, on oxidation with thallium trifluoroacetate in trifluoroacetic acid containing a small amount of CH_2Cl_2 , methyl 3-bromo-4-hydroxyphenylpyruvate oxime (**334**) was converted into three spiroisoxazoles [**339** (7%), **336** (6%), and **337** (5%)] and a plausible compound **338**, which was directly reduced with Zn powder to the biphenyl compound **342** in 8% overall yield. Zn reduction of **336** afforded the biphenyl ether **341** in 48% yield. The biphenyl ether (**341**, **340**, and **342**) was reacted with excess amounts of 3-bromotyramine *p*-methoxybenzyl ether **346** (60°, 3–4 days) to give the desirable diamide (**343**, **344**, and **345**), which gave the corresponding bastadins-1, -2, and -3 after deprotection (230).

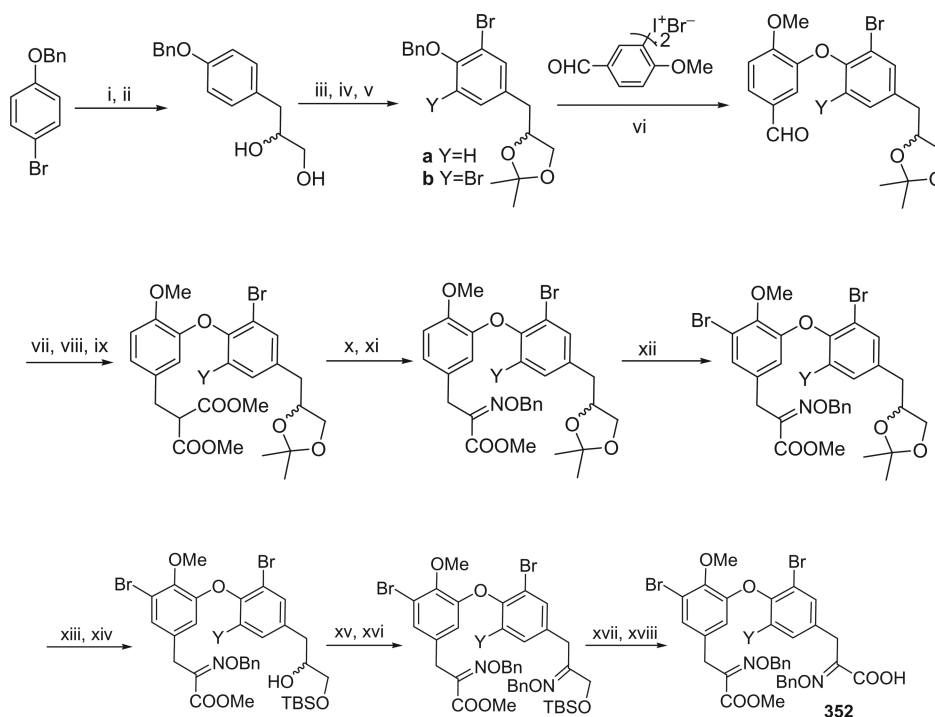


Bastadin-6 can be produced by phenolic oxidation of the corresponding acyclic precursor, bastadin-2 (229). Bis-*p*-methoxybenzyl bastadin-2 (**344**) was converted to tribenzyl bastadin-2 (**347**), which was further treated with Br_2 to afford dibromobastadin-2 tribenzyl ether (**348**). Under the same procedure, **348** was oxidized with $\text{Ti}(\text{NO}_3)_3$ to afford two macrocyclic dienones (**349** and **350**). Compound **349** was reduced with Zn to give the tribenzyl ether **351**. Finally, **351** was subjected to hydrogenolysis, using Pd black to afford bastadin-6 (229). Bastadin-6 trimethyl ether was produced in a similar procedure (231).

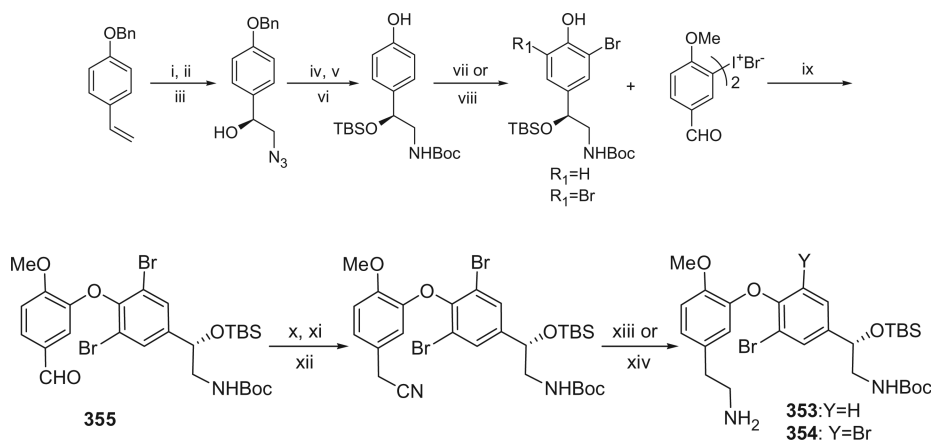
bastadin-6 (**210**): R=H**351**: R=CH₂C₆H₅**344**: R=CH₂C₆H₄OMe-p R'=H X=H**347**: R=H R'=CH₂C₆H₄OMe-p X=H**348**: R=H R'=CH₂C₆H₄OMe-p X=Br**349****350**

Guo *et al.* developed a chemoenzymatic strategy for the synthesis of bastadins-2, -3, and -6 (232). The requisite dimeric dityrosine and isodityrosine were successfully prepared by C–C and C–O oxidative phenolic coupling of mono- and dihalogenated derivatives of tyrosine and tyramine using horseradish (233) and soybean peroxidases. By carefully controlling the experimental conditions, the required synthons were prepared in synthetically useful yields without the exhaustive protection and deprotection of the sensitive functional groups. This mode of oxidative coupling may represent the biogenetic synthetic route for bastadins, which is, the isodityrosine and isodityromine are formed via the coupling of dihalogenated tyrosine and tyramine derivatives.

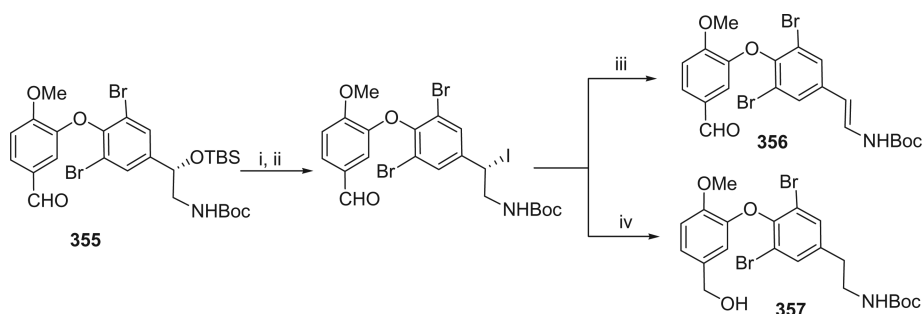
Couladouros and Moutsos reported a general synthetic route for the synthesis of the eastern and western parts of bastadins, which can be used for construction of bastadins 4–16 (234–236). The brominated biaryl ethers are synthesized using the iodonium salt method. The eastern segment **352** was synthesized within 18 steps in 15.5% overall yield. The western segment **353** and **354**, which can be used to construct bastadins-8 (**212**), -10 (**214**), -12 (**216**), and -17 (**221**), was synthesized in 13 steps (see the following scheme).



(i) Mg, THF, reflux, allyl bromide 93%; (ii) $K_2OsO_2(OH)_2$, *tert*-BuOH/H₂O, $K_3Fe(CN)_6$, K_2CO_3 , rt, 99%; (iii) 2,2-dimethoxypropane, acetone, PPTS, rt, 95%; (iv) H₂, AcOEt, 10% Pd/C, rt, 99%; (v) NBS, DMF, rt, 87% for **a**, 92% for **b**; (vi) NaH, DMF, 90 °C, 76% from **a**, 78% from **b**; (vii) NaBH₄, MeOH/THF, rt, 95%; (viii) I₂, Ph₃P, imidazole, rt, 90%; (ix) NaCH(CO₂Me)₂, Et₂O, rt, 85%; (x) BuONa, MeONa, MeOH, 0 °C, 85%; (xi) BnBr, NaH, DMF, rt, 87%; (xii) NBS, CH₃CN, 50 °C, 85%; (xiii) HCl 1N, THF, rt, 100%; (xiv) TBSCl, imidazole, DMF, rt, 97%; (xv) TEMPO, NaOCl, acetone, KBr, NaHCO₃, 0 °C, 85%; (xvi) BnONH₂HCl, pyridine/EtOH, 100 °C, 92%; (xvii) TBAF, THF, rt, 100%; (xviii) TEMPO, NaOCl, acetone, KBr, NaHCO₃, 0 °C, 78%.

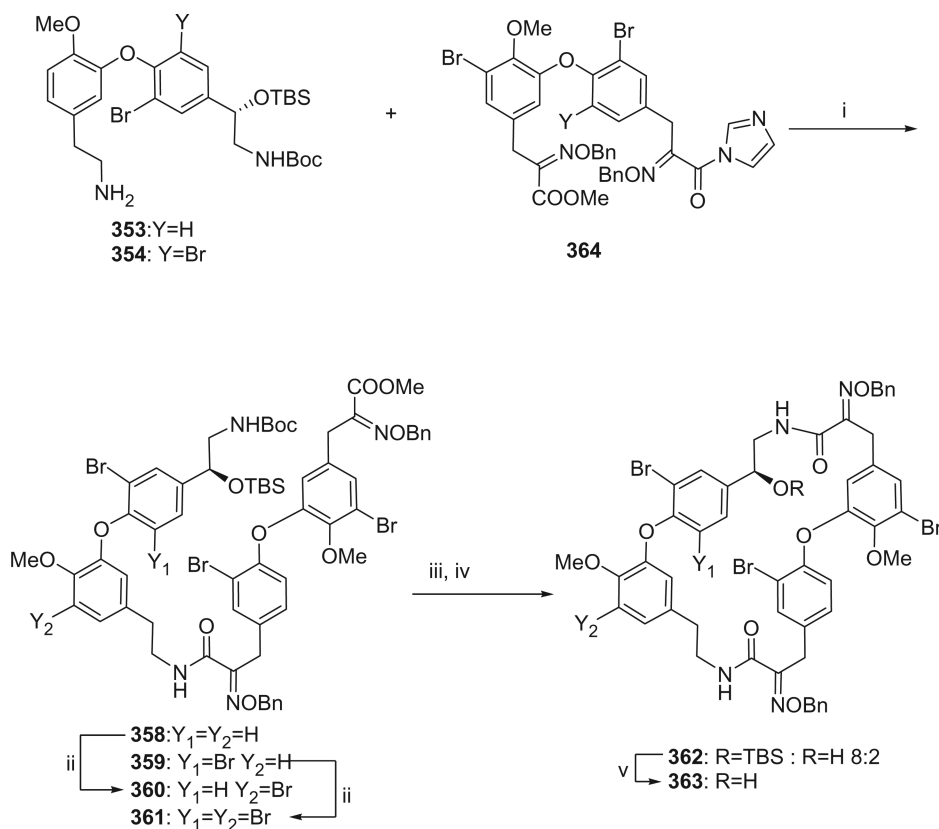


In order to utilize the hydroxyl group as a general precursor for all functionalities present at C-5 and C-6 of the bastadins, **355** was transformed after desilylation either to alkene **356** or alkane **357** using DBU or NaBH₄, respectively, providing the necessary intermediates for the construction of bastadins-4 to -7 (**208–211**), -9 (**213**), -11 (**215**), and -14 to -16 (**218–220**).



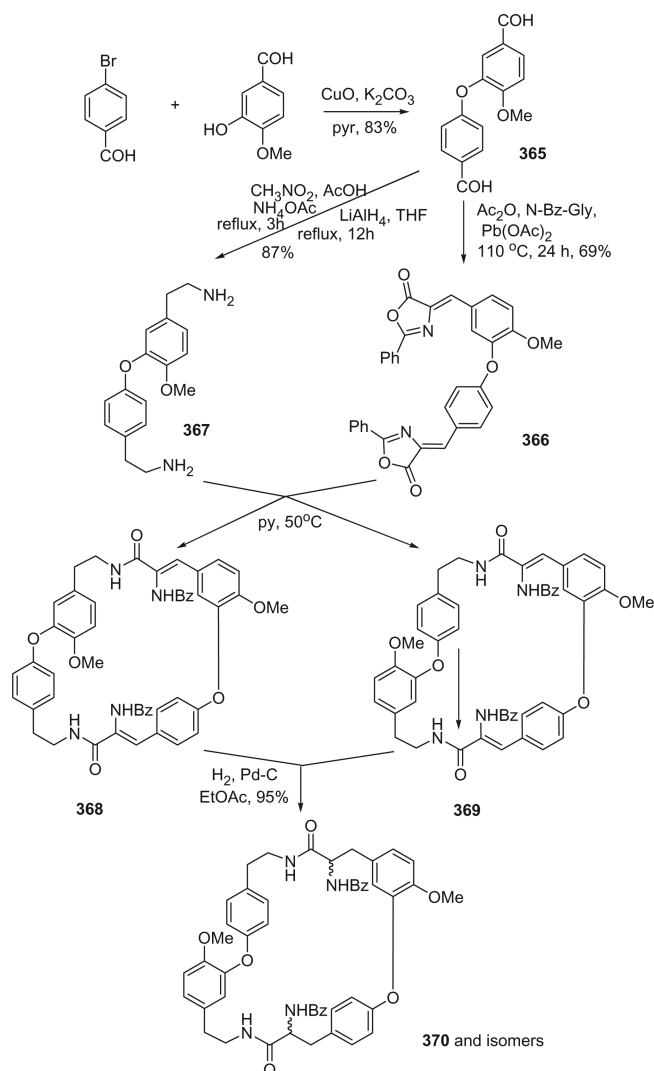
(i) TBAF, THF, rt, 98%; (ii) I₂, Ph₃P, imidazole, THF, rt, 90%; (iii) DBU, THF, rt, 85%; (iv) NaBH₄, THF/MeOH, rt, 62%.

Having the western and eastern parts of the molecule, the synthesis of the cyclic skeleton of bastadins was attempted. In order to study the efficiency of macrolactamization, four protected amino acids (**358**, **359**, **360**, and **361**) were used as advanced intermediates. Several experiments revealed that these amino acids could be synthesized in good yields through the coupling of imidazolide **364** with primary amines **353** or **354**. Subsequently, these open bastadin precursors could be selectively brominated at Y₂ position with TBS (237). The terminal amino and carboxylic acid were unmasked followed by *in situ* cyclization using EDC and *N*-hydroxybenzotriazole to afford a mixture of bastadin precursor **362** and its desilylated analog **363**. The mixture was treated with TBAF providing compound **393** in 67% yield from the precursor **361**. Compound **363** is protected bastadin-12, which possesses the unsymmetrical bromination pattern and asymmetric hydroxyl group.

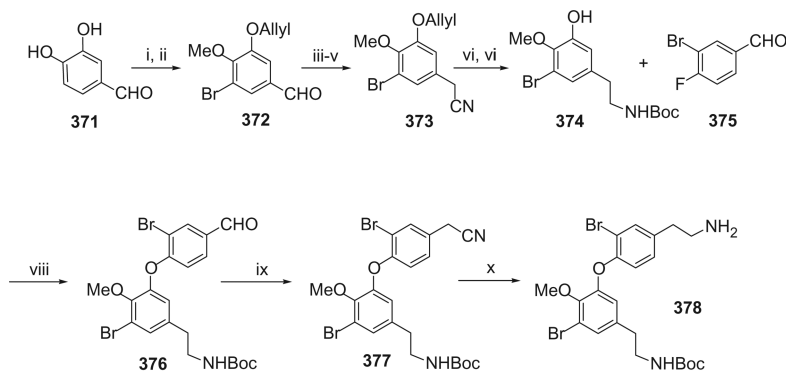


Scheme Synthesis of fully protected bastadin-12. (i) THF, 65% (**358**), 67% (**359**); (ii) NBS, CH₃CN, 80 °C, 75% (**360**), 78% (**361**); (iii) LiOH, 3N/MeOH/THF, rt, 95%; (iv) TFA/CH₂Cl₂, rt, 30 min then EDC, HOBT, DMF, 67%; (v) TBAF, THF, rt, 98%.

Bailey and Molinski presented a convergent strategy that allows the rapid assembly of isodityrosine-isodityrosine cyclic analogues of bastadin-5 in four steps from a common precursor, dialdehyde **365**, by exploiting a tandem Erlenmeyer condensation – macrolactamization (238). Dialdehyde **365**, prepared by Ullmann coupling of commercially available 3-hydroxy-4-methoxybenzaldehyde with 4-bromobenzaldehyde, was treated with *N*-benzoylglycine to obtain **366**. Diamine **367** was readily prepared from **365** by double Henry condensation-elimination followed by reduction of the resultant bis- β -nitrostyrene. Heating **366** and **367** in pyridine (50°C) resulted in the regioisomeric 28-membered macrocycles bastarane **368** and isobastarane **369** as a 1:1 mixture with a 30% combined yield. Hydrogenation of the mixture of **368** and **369** provides the isodityrosine cyclic peptide **370** as a mixture of isomers in 20–26% overall yield.

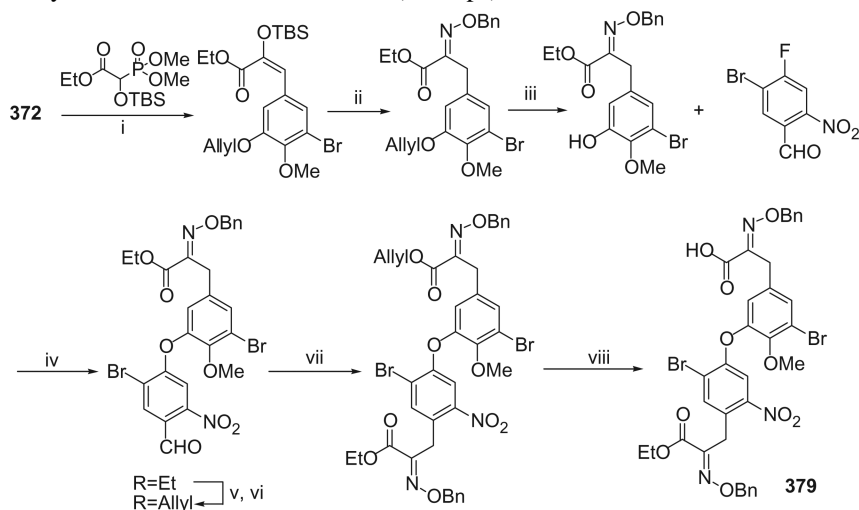


In order to gain control of the regiochemistry of the ring closure, Bailey and Molinski proposed an intermolecular S_NAr strategy to synthesize the unsymmetrical bastadin-5 analog **382** (239). Bromination of catechol **371** followed by two sequential directed alkylations gave the differentially protected benzaldehyde **372**, which was converted into phenylacetonitrile **373** in three steps. Reduction of **373** and simultaneous removal of the *O*-allyl protecting group was achieved in one step to give the expected phenethylamine, which was immediately protected as the *N*-Boc compound **374**. Intermolecular S_NAr substitution of **374** with 3-bromo-4-fluorobenzaldehyde (**375**) afforded aldehyde **376** in high yield (88%). Repetition of the homologation sequence on **376** (reduction-halide displacement-cyanide displacement) afforded **377** followed by nitrile reduction to give the monoprotected western diamine **378** (55% from **375**).

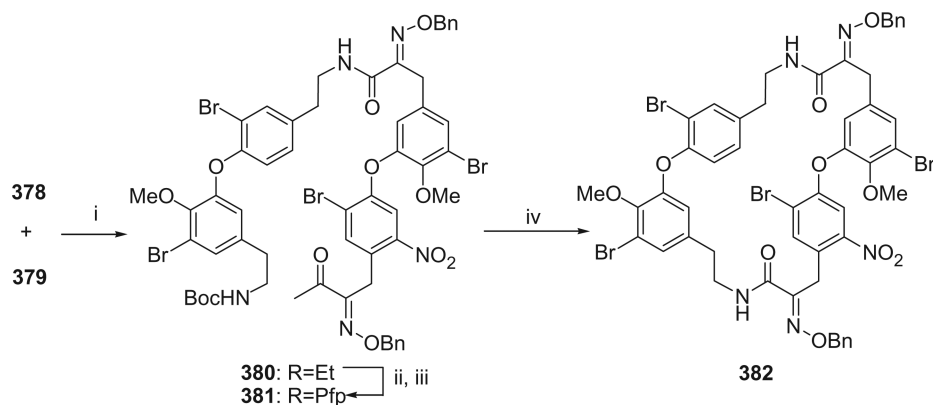


i) Br₂, HOAc, 92%; ii) MeI, Li₂CO₃, DMF, 4h, then allyl Br, K₂CO₃, 2h, 82%; iii) NaBH₄, MeOH, 0 °C, 30 min; iv) *n*-Bu₃P, CCl₄, 0 °C; v) Bu₄NCl, NaCN, CH₂Cl₂:H₂O (10:1 v/v), 89%; vi) BH₃:THF, THF, reflux, 6h then HCl/MeOH, reflux, 2h; vii) Et₃N, pH 8, (BOC)₂O, MeCN, 4h, 78%; viii) K₂CO₃, DMF, 5h, 88%; ix) repeat iii), iv), v) 91%; x) BH₃:THF, THF, 0 °C, 10h, 98%.

The eastern hemisphere intermediate **379** was also prepared from **372**, using a Horner–Emmons strategy for step-wise extension of each carboxyaldehyde group to the corresponding α -ketoxime (see the following scheme). The western diamine **378** and the eastern acid **379** were coupled to give the protected teracycle **380** in 78% yield. Compound **380** was transformed to the activated pentafluorophenol (Pfp) ester **381**, which underwent the macrolactamization upon removal of the *N*-Boc group to give the product **382**. The overall yield of **382** from **371** was 16% (16 steps).



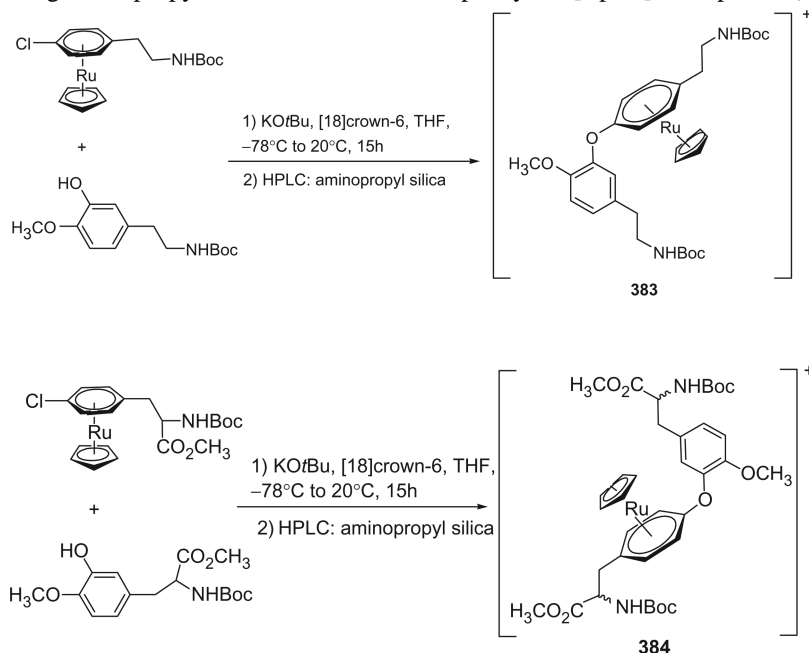
i) -78 °C to rt, 30 min, 82% (1:1 *E/Z*); ii) HF-pyr, HCl-H₂NOBn, rt, 10h, 89%; iii) RhCl₃:H₂O 4% w/v, EtOH, reflux, 12 h, 76%; iv) K₂CO₃, DMF, 4 h, 91%; v) LiOH, THF:MeOH:H₂O (4:1:1 v/v/v); vi) AllylBr, K₂CO₃, 83%; vii) repeat i) and ii), 73%; viii) Pd(OAc)₂, PPH₃, Et₃N, HCO₂H, THF, 3 h, 90%



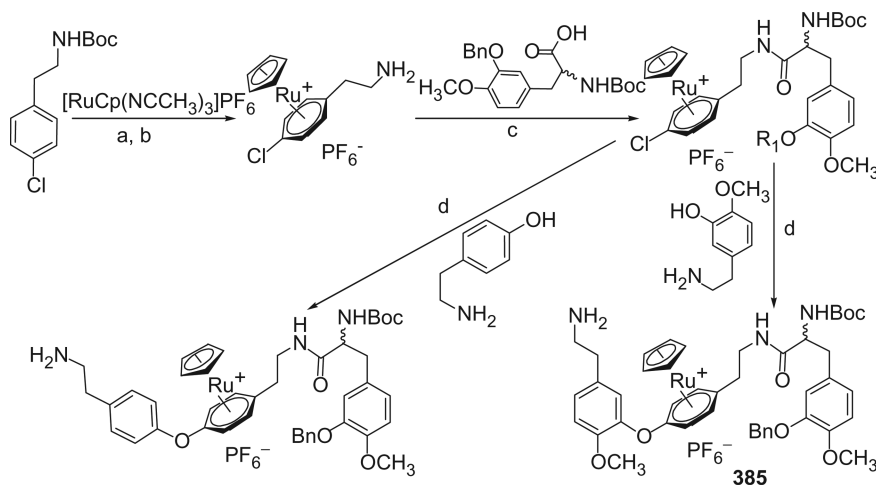
i) DCC, HOBT, CH₂Cl₂, 10 h, 78%; ii) LiOH, THF:MeOH:H₂O (4:1:1); iii) C₆F₅OH, DCC, CH₂Cl₂, 10 h, 81%; iv) HCl, CH₂Cl₂, pH 2, 4 h, dilute to 0.005 M in CH₂Cl₂, Et₃N, pH 8, rt 3 days, 60%.

Molinski *et al.* also reported the reduction of bastadin-4 (**208**) to bastadin-5 (**209**) using cationic hydrogenation (Et₃SiH, TFA, 60%) (240). Specific deuteration at H-5 of bastadin-5 was conducted following this method.

Leone-Stumpf and Lindel synthesized the ruthenium labeled western (**383**) and eastern (**384**) diaryl ether and tripeptide (**385**) of bastadin-5, and for the first time established an HPLC method using aminopropyl-functionalized silica to purify the [CpRu]⁺ complexes (241,242).



The free amino group of 4-*O*-methyltyramine and 4-*O*-methyltyramine react as nucleophiles in a chemoselective manner with [RuCp]⁺-complexed *p*-substituted chloroarenes. As a consequence, it is not necessary to use protecting groups for the synthesis of peptides with alternating amide and diaryl ether bonds.



a: 1,2-dichloroethane, 4H, reflux; b: 4N HCl/MeOH, 3h, room temp.; c: THF/MeOH (1:1), EDCI, HOBT, DIEA, room temp., 34h; d: KOtBu, [18]crown-6, THF/MeCN (1:1), -78°C to 0°C .

The total synthesis of polycytone A (**280**) and B (**281**) (**243**), and the cyclodepsipeptides, jaspamide (**259**) (**244**), geodiamolide A (**260**) (**245**), and geodiamolide B (**261**) (**246**) were also reported. Since these are not typical bromotyrosine derivatives, the details of the syntheses are not included here.

VI. Bioactivity

Bromotyrosine alkaloids provide a unique diversity in chemical structure and in bioactivity. Since the first bromotyrosine derivative, the dienone **1**, was isolated as an antibiotic, a large number of bromotyrosine derivatives have been found to have diverse activities, which include antibacterial, antifungal, anticancer, antiviral, antifouling, Na,KATPase inhibitor, etc. The majority of the dibromotyrosine-derived natural products from Verongida have been reported to possess significant antimicrobial and cytotoxic activity (**247**). The presence of antibacterial compounds in marine sponges has been reported as a general phenomenon (**248**), and has been suggested to reflect a defensive strategy of these sedentary, filter-feeding animals (**249**).

A. ANTIMICROBIAL ACTIVITY

Bromotyrosine derivatives were first isolated in the process of searching for antibiotics from marine sources. The dienone **1**, aeroplysinin-1 (**14**), and arothionin (**68**) are the earliest antimicrobial bromotyrosine derivatives (**2,14,58**). The antibacterial and antifungal activities of the bromotyrosine alkaloids are summarized in Table IV and Table V. Bromotyrosine derivatives exhibited a broad antimicrobial spectrum, which include Gram-positive bacteria such as *Streptococcus faecalis*, *Streptococcus pyogenes*, *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus luteus*, *Sarcina lutea*, Gram-negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa*, *Neisseria gonorrhoeae*, and *Alcaligena faecalis*, and fungi such as *Candida albicans*.

The active compounds distribute in all of the structural subclasses. The simple bromotyrosine derivatives that were reported to possess antibacterial activity include the

dienone **1**, aeroplysinin-1 (**14**), aeroplysinin-2 (**18**), 3-bromoverongiaquinol (**10**), 3-bromo-5-chloroverongiaquinol (**11**), aplysamine 1 (**54**), moloka'iamine (**52**), ceratina-mine (**60**), 7-bromocavernicolone (**30**), **38**, and **51**. The first bromotyrosine derivative, the dienone **1**, was reported as a broad-spectrum antibiotic (2). Both dextrorotatory and levorotary aeroplysinin-1 are active against Gram-positive and Gram-negative bacteria (14,16). The MICs (MBCs) of the dienone **1** and aeroplysinin-1 (**14**) ranged from 12.5–25 µg/mL against *Bacillus subtilis*, *Staphylococcus aureus*, and *Escherichia coli* (250). (+)-Aeroplysinin-1 showed greater than 65% inhibition of the growth of phytopathogenic fungus *Phytophthora infestans* (potatoes late blight) (251).

Although the bis-spirocyclohexadienylisoxazoline bromotyrosine derivatives, arothionin (**68**), homoarothionin (**69**), 11-hydroxyarothionin (**71**), and 11,19-dideoxyfistularin 3 (**83**), all had *in vitro* antimicrobial activity, 11,19-dideoxyfistularin 3 is the most active. Arothionin (**68**), homoarothionin (**69**), and 11-hydroxyarothionin (**71**) all inhibited the growth of *Staphylococcus aureus* at 100 µg/disk, *Bacillus subtilis* at 50 µg/disk, and *Candida albicans* at 50 µg/disk, whereas 11,19-dideoxyfistularin 3 (**83**) inhibited the growth of *S. aureus* at 25 µg/disk, *B. subtilis* at 10 µg/disk, and *C. albicans* at 25 µg/disk (63). Arothionin (**68**) was reported to be active against a group of monoresistant variants of *Mycobacterium tuberculosis* H37Rv at 12.5 µg/mL (252). It was also active against a group of multidrug resistant TB clinical isolates with MIC values between 6.5 and 25 µg/mL and active against three of nine nontuberculosis mycobacteria (252).

Both 11-oxo-12-hydroxyarothionin (**73**) and 11-hydroxyarothionin (**71**) induced 60 and 70% inhibition, respectively, of *Mycobacterium tuberculosis* growth at 12.5 µg/mL, while 11-oxoarothionin (**72**) induced no inhibition at all (253). Single spirocyclohexadienylisoxazoline bromotyrosine derivatives, aplysinamisine I (**120**), aplysinamisine II (**124**), aplysinamisine III (**102**), purealidin B (**109**), araplysinin-I (**99**), and araplysinin-II (**100**), showed moderate antimicrobial activity (81,83,84). Some of the oxime type bromotyrosine derivatives showed potent antimicrobial activity. Anomoian A (**195**), a reduced oxime, exhibited strong antimicrobial activity against *Staphylococcus aureus* at 10 µg/disk, *Bacillus subtilis* at 5 µg/disk, and *Candida albicans* at 25 µg/disk.

Purpuramine L (**191**) is highly active against *Staphylococcus aureus*, *Bacillus subtilis*, and *Chromobacterium violaceum*, moderately against *Bacillus sphaericus*, *K. aerogenes*, and *P. aeruginosa* (122). Purpuramine K (**190**) is moderately active against all the organisms. Interestingly, Gram-positive bacteria are highly susceptible to purpuramine L when compared to the positive control kanamycin (122). Psammaplin A (**152**) was found to possess antimicrobial activity (109,254,255). It also selectively inhibited the growth of methicillin-resistant *Staphylococcus aureus* (MRSA) (256). The minimal inhibitory concentration of psammaplin A against twenty-one MRSAs ranged from 0.78 to 6.25 µg/mL while that of ciprofloxacin was 0.39–3.13 µg/mL. Psammaplin A (**152**) could not bind to the penicillin binding protein, but inhibited the DNA synthesis and the DNA gyrase activity with the respective 50% (DNA synthesis) and 100% (DNA gyrase) inhibitory concentrations of 2.83 and 100 µg/mL. These results indicated that psammaplin A inhibited the growth of bacteria probably by inhibiting DNA gyrase (256). Since the significant antimicrobial activity of psammaplin A (**152**) was disclosed, the antibacterial activities against 40 drug-

resistant *Staphylococcus aureus* strains were determined for psammaphin D (**158**), **169**, bromopsammaphin A (**170**), bispsammaphin A (**171**), and bisaprasin (**154**) (117). Alkaloid **169** showed the highest potency, which is higher than that of meropenem against several strains (see Table VI.) (117). Bromopsammaphin A (**170**) and bisaprasin (**154**) exhibited strong to moderate activity against all these strains, while psammaphin D (**158**) and bispsammaphin A (**171**) did not show significant activity against all strains.

Bastadins-1 to- 7 (**204–211**) were isolated because of the potent activity against Gram-positive and Gram-negative bacteria, but data were not provided (129). Bastadin-13 showed a minimum inhibitory concentration of 6 µg/mL against *Bacillus subtilis*, while 34-sulfatobastadin-13 showed no activity at 50 µg/mL, suggesting the free phenolic group at C-34 is required for the antimicrobial activity (141). Pettit *et al.* evaluated the ability of bastadins-1 to 6 (**204–210**), hemibastadins (**231–233**, **237**), hemibastadinols (**234**, **235**, **236**), and amide **51** to inhibit growth of Gram-positive bacteria, Gram-negative bacteria, and two fungi (Table IV) (**41**). Except for bastadin-6, all of these alkaloids inhibited the growth of the Gram-negative pathogen *Neisseria gonorrhoeae*. Most of the compounds also inhibited the growth of the Gram-positive opportunists *Enterococcus faecalis* and *Staphylococcus aureus*. At up to 100 µg/disk, these alkaloids exhibited no antimicrobial activity against *Escherichia coli* or the fungi *Candida albicans* and *Cryptococcus neoformans* (**41**).

Antibiotic activity of sponge metabolites has frequently been demonstrated in the past (257–259). However, most of these studies were conducted with terrestrial rather than marine bacteria. For example, antibiotic activity of aeroplysinin-1 (**14**) and dienone **1** was proven using terrestrial Gram-positive and Gram-negative bacteria (250). Proksch *et al.* confirmed this activity using several marine bacteria such as *Alteromonas*, *Moraxella*, or *Vibrio* sp. (see Table VII) (260). The EC₅₀ values of aeroplysinin-1 (**14**) and the dienone **1** towards *Photobacterium phophoreum*, which is a well-established model for the analysis of water-borne toxins (261,262), are comparable to those of pentachlorophenol (EC₅₀: 1.3 µM), lead (EC₅₀: 1.9 mM) or cadmium ions (EC₅₀: 71 µM) which are known for their pronounced toxicity. At the same time, aeroplysinin-1 and the dienone **1** are also active against microalgae (260).

B. ANTICANCER ACTIVITY

Anticancer active bromotyrosine derivatives are summarized in Table VIII. Many of the bromotyrosine derivatives exhibited cytotoxicity, emphasizing the ecological relevance of this type of compounds in the sponge's chemical defense. The small molecules, aeroplysinin-1 (**14**) and the dienone **1**, which are from the enzymatic degradation of larger bromotyrosine derivatives such as isofistularin-3 (**80**), aerophobin-2 (**114**), fistularin-1 (**94**), and other alkaloids, are more toxic than the parent compounds, suggesting a wound defense reaction (250,263,264).

The anticancer activity of aeroplysinin-1 (**14**) was the most studied among all bromotyrosine derivatives. Kreuter *et al.* evaluated the *in vitro* and *in vivo* anticancer activity of (+)-aeroplysinin-1 (**14**) (265,266). Aeroplysinin-1 displayed pronounced cytostatic activity against L5178y mouse lymphoma cells (ED₅₀: 0.5 µM), Friend erythroleukemia cells (ED₅₀:

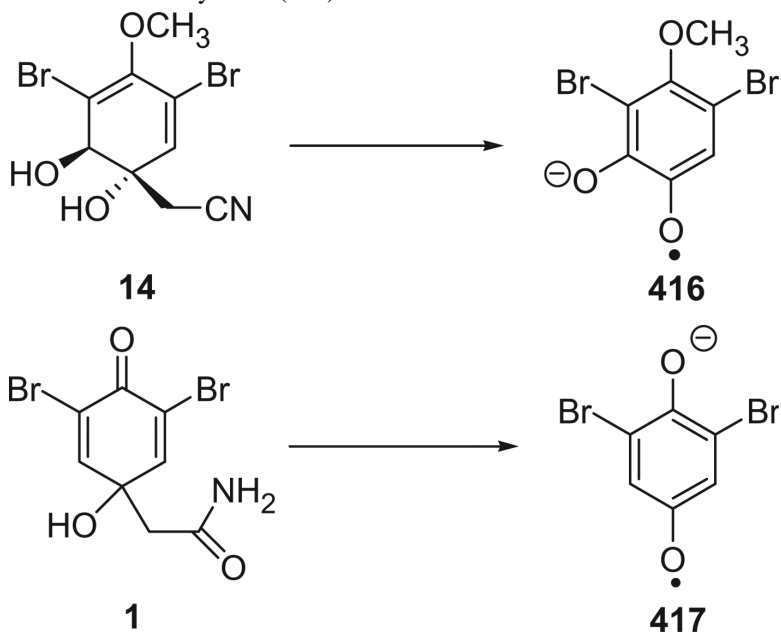
0.7 μM), human breast carcinoma cells (ED_{50} : 0.3 mM), and human colon carcinoma cells (ED_{50} : 5.0 mM), but not against the related normal cells *in vitro*. The ED_{50} values of aeroplysinin-1 for these cell lines are significantly lower than those obtained in cultures with non-transformed lymphocytes. The inhibitory activity of aeroplysinin-1 in the L5178y cell system is higher than other cytostatic agents including 9- β -D-arabinofuranosyladenine, ED_{50} 29 μM (267), 1- β -D-arabinofuranosylthymine, ED_{50} 9.8 μM (268), bleomycin, ED_{50} 0.9 μM (269), and distamycin, ED_{50} 13.1 μM (270). Aerothionin caused a preferential inhibition of [^3H]thymidine incorporation rates in L5178y mouse lymphoma cells when compared with murine spleen lymphocytes *in vitro*. These results showed that a higher concentration of the alkaloid is required to influence the incorporation rates in lymphocytes than in L5178y cells; e.g., at a concentration of 2.9 mM the incorporation rates in lymphocytes are reduced only by 40–50%, while those in L5178y cells are diminished by almost 100%. The same differential effect *in vitro* was found with the following epithelial cells: 14.7 μM of the compound was required to inhibit normal human fibroblasts to 50%, but only 2.9 μM in the assays with human malignant keratinocytes or malignant melanoma cells was needed to observe the same inhibitory effect.

Aeroplysinin-1 (**14**) also displayed antileukemic activity *in vivo* using the L5178y cell/NMRI mouse system. Administration of a dose of 50 mg/kg for five consecutive days, the life span T/C (%) value was determined to be 338. Preliminary toxicology studies revealed an acute LD_{50} of 202 mg/kg, a subacute LD_{50} of 150 mg/kg, and a subacute LD_{10} 133.3 mg/kg. A daily dose of 30 mg/kg for 30 consecutive days neither caused any toxicity nor a change of body weight compared to the controls. The animals were sacrificed for autopsy 40 days after the last injection. In no case were any morphological abnormalities detected in the peritoneal cavity. Using the *umu*-test system, which has been demonstrated to detect many types of DNA-damaging agents, such as base change mutagens, frameshift mutagens or oxidative mutagens (271), aeroplysinin-1 turned out to be neither a direct nor an indirect mutagen. The excellent T/C value of aeroplysinin-1 is the combined result of the antitumor effect and low toxicity. Following the arbitrary activity rating proposed (272), aeroplysinin-1 was classified to the markedly active (+ + \rightarrow + + +) to highly active anticancer agents (+ + +).

In the continuing paper, Kreuter *et al.* reported the inhibition of intrinsic protein tyrosine kinase activity of the EGF-receptor kinase complex from human breast cancer cells by (+)-aeroplysinin-1 (**14**) (273). Aeroplysinin-1, which possesses a close structure-relationship to tyrosine, blocks the epidermal growth factor (EGF) dependent proliferation of both MCF-7 and ZR-75-1 human breast cancer cells, and inhibited the ligand-induced endocytosis of the EGF receptor *in vitro*. Aeroplysinin-1 was found to inhibit the tyrosine-specific phosphorylation of lipocortin-like proteins, which have been established as major substrates of the EGF receptor-associated protein-tyrosine kinase (274), by a highly purified preparation of the EGF receptor protein-tyrosine kinase complex, isolated from MCF-7 cells. Treatment of aeroplysinin-1 in the concentration range of 0.25–0.5 μM resulted in MCF-7 cells losing their ability for EGF-mediated cell response and cell death occurred within 36–72 h. At a 10-fold higher concentration, aeroplysinin-1 did not reveal cytostatic activity in normal human fibroblasts. From these data, aeroplysinin-1 was concluded to be a

promising compound in a rational chemotherapy (273). Based on the potent anticancer activity, production of aeroplysinin-1 by the *in vitro* culturing of the sponge *Verongia aerophoba* was also studied (275).

In other studies, aeroplysinin-1 (**14**) and the related dienone **1** exhibited cytotoxicity against Ehrlich ascites tumor (EAT) cells and HeLa tumor cells in the microculture tetrazolium (MTT) and clonogenic assays (276). Both alkaloids were able to cause growth inhibition, as well as cell death, in these cell lines. When the cells were depleted of glutathione by pretreatment with buthionine sulfoximine, they were significantly more sensitive toward aeroplysinin-1 (**14**) and the dienone **1** in the MTT assay. A dose-enhancement factor as high as 11.8 was found in EAT cells after a 2-h incubation with the dienone **1**. These results suggested that in both tumor cell lines, glutathione may play an important role in the defense against the cytotoxic action of aeroplysinin-1 (**14**) and the dienone **1**, and a free-radical mechanism might be involved in the cytotoxicity of both compounds (277,278). Using electron paramagnetic resonance, the formation of free radicals from aeroplysinin-1 (**14**) and the dienone **1** were measured in a culture medium with tumor cells. When dissolved in pure H₂O, **1** yielded an EPR spectrum, but **14** failed to do so. Thus, metabolic activation by living cells may be required to obtain free radicals from aeroplysinin-1 (**14**). Structures **416** and **417** are possibilities for the semiquinone radicals that originate from **14** and **1**. Semiquinone radicals are known to be very toxic (279).



From the above results it may be concluded that free radicals are, at least in part, responsible for the cytotoxic effects of aeroplysinin-1 (**14**) and the dienone **1** *in vitro*. Although aeroplysinin-1 (**14**) and the dienone **1** were less effective than the clinically used anticancer drug cisplatin, their chemical structures may be of interest as leads for future drug development. The different reactivity of aeroplysinin-1 (**14**) and the dienone **1** fits very well in the defensive role of these alkaloids for *Aplysina aerophoba*, when the following hypothesis is used. As soon as a predator attacks this sponge, aeroplysinin-1 (**14**) is formed

due to enzymatic degradation of the larger precursors. Aeroplysinin-1 will generate free radicals after metabolic activation by the predator's cell, which results in an antifeedant effect. Simultaneously, the dienone **1** is released, which immediately yields free radicals in the water surrounding the sponge, thereby shielding the sponge from further predation or attack (276).

Recent studies revealed that (+)-aeroplysinin-1 (**14**) has a strong inhibitory antiangiogenic activity (280,281). Since the earliest hypothesis that tumor growth was dependent on angiogenesis (282), it has become clear that interfering with and/or preventing angiogenesis is an attractive therapeutic approach to the treatment of angiogenesis-dependent diseases (283,284). In a variety of experimental systems, representing the sequential events of the angiogenic process, aeroplysinin-1 treatment of endothelial cells resulted in strong inhibitory effects. Aeroplysinin-1 inhibited the growth of endothelial cells in culture with an IC_{50} of 2.1 μ M and induced endothelial cell apoptosis. Capillary tube formation on Matrigel was completely abrogated by addition of aeroplysinin-1 at the low micromolar range. Aeroplysinin-1 also exhibited a clear inhibitory effect on the migration capabilities of endothelial cells. Zymographic assays showed that aeroplysinin-1 treatment produced a decrease in the concentration of matrix metalloproteinase-2 and urokinase in conditioned medium from endothelial cells. Finally, aeroplysinin-1 exhibited a dose-dependent inhibitory effect on the *in vivo* chorioallantoic membrane assay, showing potent apoptosis-inducing activity in the developing endothelium. The *in vivo* inhibition of angiogenesis by aeroplysinin-1 was confirmed by the Matrigel plug assay. Together, all of these data indicate that aeroplysinin-1 is a compound that interferes with key events in angiogenesis, making it a promising drug for further evaluation in the treatment of angiogenesis-related pathologies (280).

Most of the bis-spirocyclohexadienylisoxazoline type of bromotyrosine derivatives tested exhibited moderate cytotoxicity against different cancer cell lines. These include fistularin-3 (**79**) (68), 11-oxoaerotherionin (**72**) (64), 11-*epi*-fistularin-3 (**81**) (70), 11-oxofistularin (**82**) (72), isofistularin-3 (**80**) (72), and 11-deoxyfistularin-3 (**86**) (73). 11-Oxoerotherionin (**72**) is the most potent agent and showed pronounced selective cytotoxic activity toward the human colon HCT cell line at a limited concentration range of 0.01–0.1 μ g/mL (64).

Purealidins, which are single spirocyclohexadienylisoxazoline or oxime type of bromotyrosine derivatives, exhibited moderate to strong cytotoxicity, among which purealidin N (**150**) is very potent against K1210 and KB cells with IC_{50} values of 0.07 and 0.074 μ g/mL, respectively (79,84,104).

The oxime disulfides, psammaplin A (**152**), psammaplin D (**158**), bromopsammaplin A (**170**), bispsammaplin A (**171**), and bisaprasin (**154**), were reported to have significant cytotoxicity against human lung A549, ovarian SK-OV-3, skin SK-MEL-2, CNS XF498, and colon HCT15 solid tumor cell lines (Table VIII). Psammaplin A (**152**) exhibited the highest potency among the five compounds (117). Inspired by its HDAC and DNMT enzyme inhibitory actions and unique structural features, the antiproliferative properties of psammaplin A (**152**) were thoroughly explored (112). Encouraging *in vitro* results were found as **152** inhibited cells grown in monolayer and in soft agar at the following levels

(IC₅₀ values in mM): A549 lung tumor at 1.35 and 2.5, and MDA-MB-435 breast tumor at 1.15 and 2.0, respectively. These positive results were also observed *in vivo*, as psammaplin A (**152**) inhibited tumor growth in the A549 lung xenograph mouse model, while also maintaining low toxicity (285). Very recently, psammaplin A (**152**) was found to inhibit mammalian aminopeptidase N (APN) that plays a key role in tumor cell invasion and angiogenesis, with an IC₅₀ value of 18 μM in a noncompetitive manner (286). Interestingly, psammaplin A potently inhibited the proliferation of several cancer and endothelial cells and this effect was dependent on the cellular amount of APN expression. Finally, psammaplin A suppressed the invasion and tube formation of endothelial cells stimulated by basic fibroblast growth factor. These data demonstrated that psammaplin A is a new inhibitor of APN and might be developed as a novel anti-angiogenic agent (286).

Geodiamolides are a group of depsipeptides with very strong cytotoxicity. Geodiamolides A (**260**), B (**261**), C (**262**), D (**263**), E (**264**), and F (**265**) exhibited very potent cytotoxicity against L1210 cell line with an ED₅₀ range of 0.0025–0.039 μg/mL (159). Comparison of the cytotoxicities of jaspamide (**259**) (157) and geodiamolide A (**260**) to F (**265**) (158,159) shows that significant variation in the three amino acid residues causes only minor changes in the levels of cytotoxicity exhibited by the peptides. By contrast, geodiamolide G (**266**), with a modified polyketide fragment, is significantly less cytotoxic than the analogue geodiamolide A (**260**) (160). Surprisingly, geodiamolide I (**268**) was completely devoid of activity (161).

Oxepin-type bromotyrosine derivatives, including psammaplysin A (**129**), B (**130**), and C (**131**) and bastadins-4 (**208**), -8 (**212**), -9 (**213**), -12 (**216**), and -14 (**218**) showed moderate cytotoxicities (95,132,133,142).

C. ANTIFOULING

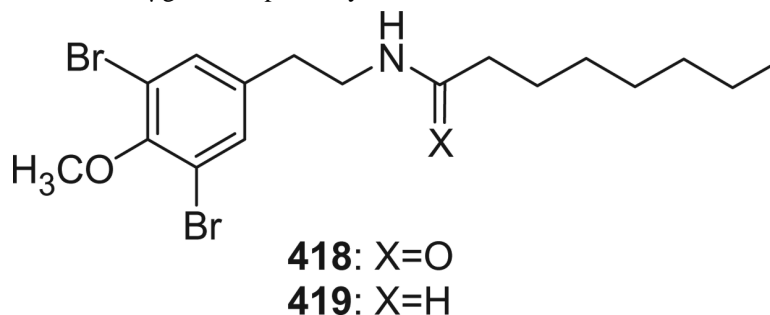
Biofouling causes serious problems in the shipping business, in aquaculture and in the cooling systems of power stations. The biofouling of ship hulls increases drag, and consequently increases fuel costs. The biofouling of fishing nets in marine aquaculture prevents a smooth flow of sea water, followed by a serious decline in the number of fish due to an insufficient oxygen supply. Metallic compounds, such as copper (I) oxide and bis(tributyltin)oxide (TBTO), have previously been used as antifouling agents. Today, however, the use of TBTO in antifouling paints is restricted in order to prevent environmental pollution. Therefore, the development of environmentally benign anti-fouling agents is essential for resolving this global problem (287). Soft-bodied benthic invertebrates are believed to have chemical defenses against predators and the overgrowth of other benthic organisms (288). Therefore, metabolites of these invertebrates are potential “environmentally-friendly” antifouling agents (289).

The Verongida sponges provide excellent examples for the use of metabolites in chemical defense (260,290). The marine sponge *Verongia aerophoba* represents an example for a wound-induced chemical defense that relies on an enzymatic conversion of inactive storage compounds into an active defense metabolite (260). Following disruption of the compartmentation (e.g. by wounding) both major components, isofistularin-3 (**80**) and aerophobin-2 (**114**), are enzymatically converted into aeroplysin-1 (**14**), which in turn gives

rise to the dienone **1** (291). Aeroplysin-1 (**14**) and dienone **1** were shown to have pronounced inhibitory activity against a number of marine organisms (bacteria, microalgae, and molluscs), which may be associated with biofouling (260). This may account for the remarkably clean surfaces of the Verongida sponges.

A bioassay system suitable for screening crude extracts against biofilm formation was developed by Yamada *et al.* (292). Interestingly, most sponges examined using this method contained anti-biofilm compounds, among which aeroplysin-1 (**14**) exhibited activity with an IC₅₀ value of 0.66 µg/cm².

Ceratinamide A (**135**), ceratinamide B (**136**), psammaplysin A (**129**), psammaplysin E (**133**), ceratinamine (**60**), and moloka'iamine (**52**) isolated from the marine sponge *Pseudoceratina purpurea*, were found to have antifouling activity (settlement and metamorphosis inhibitory activity) against cyprid larvae of the barnacle *Balanus amphitrite* with ED₅₀ values of 0.10, 2.4, 0.27, 4.8, 5.0, and 4.3 µg/mL, respectively (49,98). Ceratinamide A (**135**) and psammaplysin A (**129**) were particularly potent in the assay. Ceratinamide B (**136**), psammaplysin A (**129**), and ceratinamine (**60**) were lethal to the larvae at a concentration of 30 µg/mL, while other metabolites were not toxic at this concentration. Thus, ceratinamide A (**135**) is a promising antifouling agent. Interestingly, psammaplysin A (**129**) induced larval metamorphosis of the ascidian *Halocynthia roretzi* (98). Ceratinamine (**60**) and moloka'iamine (**52**), and 3,5-dibromo-4-methoxy-β-phenethylamine (**51**), together with several analogues, have been synthesized (197,199). 3,5-Dibromo-4-methoxy-β-phenethylamine (**51**) and its two analogues, octanoic amide (**418**) and octylamine (**419**) strongly inhibited the settlement of barnacle cyprids, with IC₅₀ values of 0.07, 0.2, and 0.008 µg/mL, respectively.



Rhodospirillum salexigens is a marine bacterium, which has adhering properties to form bacteria biofilm. Zamamistatin (**91**) exhibited significant antibacterial activity against *R. salexigens* with an inhibition zone of 21 mm at 1.6 µg/disk, and may be a valuable candidate for novel antifouling agents (75,76). 5-Bromoverongamine (**138**) was also reported to exhibit antifouling activity (100).

Due to the noteworthy absence of fouling observed on sponges of the order Verongida, a number of natural and synthetic dibromotyramine derivatives, including moloka'iamine, were selected as potential zebra mussel (*Dreissena polymorpha*) anti-foulants in our laboratory (293). The zebra mussel (ZM) re-attachment assays yielded an antifouling activity with an EC₅₀ value of 10.4 µM for moloka'iamine (**52**). Hemifistularin-3 (**108**) had

significant activity in a preliminary study against ZM attachment at a single high point concentration of 30 μM , while fistularin-3 (**79**) and aerophobin-2 (**114**) showed no antifouling activity against ZMs.

D. ENZYME ACTIVITY

Purealin (**122**) inhibited the activity of myosin Ca-ATPase and Na,K-ATPase (see Table IX) (91). However, the activity of myosin K,EDTA-ATPase was enhanced by purealin. Purealin is the first natural product which activates myosin K,EDTA-ATPase (91). A number of papers have been published about the activity of purealin (**122**) on ATPase in different modes (294–299). Purealin (**122**) modulates the ATPase activities of dephosphorylated gizzard myosin by enhancing the stability of myosin filaments against the disassembling action of ATP (294). Purealin blocks the sliding movement of sea urchin flagellar axonemes by selective inhibition of half the ATPase activity of axonemal dyneins. Purealin-sensitive ATPase activity of the dynein arms plays an essential role in generating the sliding movement of flagellar axonemes (295). Purealin activates skeletal muscle actomyosin ATPase and myosin EDTA-ATPase that enhanced the superprecipitation of actomyosin (296). Purealin binds to the myosin portion involved in actin–myosin interaction and increases the actin-activated ATPase activity of myosin (298). Purealin acts as a calmodulin antagonist in reconstituted actomyosin from chicken gizzard, resulting in the inhibition of light chain phosphorylation and the actin-activated ATPase activity of myosin (299).

Lipopurealin-A (**141**), lipopurealin-B (**142**), and lipopurealin-C (**143**) exhibited inhibitory activities on Na,K-ATPase from porcine brain and dog kidney, lipopurealin-B being the most potent inhibitor. In cardiac Na,K-ATPase all three alkaloids showed only weak activity. In addition, myosin K,EDTA-ATPase was markedly activated by purealin, whereas the enzyme was inhibited by lipopurealin-B (102). Purealidin A (**146**) showed weak inhibitory activity (22% inhibition at 10^{-4} M) on Na,K-ATPase, and had no effect on myosin K,EDTA-ATPase. These results suggest that the acryl part of purealin (**122**), lacking in purealidin A (**146**), is important for the activity of these ATPase inhibitors (104). Ianthesines B (**106**), C (**93**), and D (**107**) exhibited inhibitory activity against dog kidney Na,K-ATPase with IC_{50} values of 440, 50, and 280 μM , respectively, while ianthesine A (**105**) was inactive (>2.5 mM) (78). The amino group of the terminal α -amino acid (in **105**, **106**, and **93**) or the dipeptide moiety (in **93**) seems to be important for the activity, because the activity decreased in the order, $-\text{NH}\text{SO}_3^-$ (**93**), $-\text{NH}\text{SO}_3^-$ (**107**), NH_2 (**105**), and NMe_2 (**105**). Araplysillins-I (**99**) and -II (**100**) inhibited the purified porcine brain Na,K-ATPase with IC_{50} values of 0.5 mM and 1 mM, respectively, which is more significant than the parent alkaloids purealin (**122**) and lipopurealins (**142**) (81).

Psammaplin A (**152**), bisaprasin (**154**), psammaplin A₁ (**165**), psammaplin A₂ (**166**), aplysinellin A (**167**), and aplysinellin B (**168**) exhibited inhibitory activity against farnesyl protein transferase with IC_{50} values of 7.0, 4.2, 3.0, 4.4, 85.2, and 25.1 mM, respectively. In addition, alkaloids **152**, **154**, and **167** exhibited inhibitory activity against leucine aminopeptidase (AP-N) with IC_{50} values of 70.9, 30.2, and 2.4 mM, respectively, while other derivatives tested were inactive ($\text{IC}_{50}>100$ mM).

Recently, psammaplins were reported as potent histone deacetylase (HDAC) and DNA methyltransferase (DNMT) inhibitors (see Table X) (112). Eleven psammaplins (see Table X), isolated from the sponge *Pseudoceratina purpurea*, were tested in the histone deacetylase (HDAC) enzyme assay at concentrations ranging from 16 nM to 10 μ M, and the data obtained were compared to that of two standards, trichostatin A (300) and trapoxin A (301). There were three psammaplin derivatives whose IC₅₀ values were in a range of very potent activity (< 10 nM) and these included the following: psammaplin A (**152**) IC₅₀ = 4.2 nM, bisaprasin (**154**) IC₅₀ = 10.7 nM, and psammaplin F (**160**) IC₅₀ = 8.6 nM. In contrast, psammaplins B (**156**), C (**157**), D (**158**), G (**161**), H (**162**), and J (**164**) were only considered moderately active (IC₅₀ values >40 nM), while the other two psammaplins E (**159**) and I (**163**) were weakly active (IC₅₀ values >100 nM). These trends are mirrored in the activation of p21 promoter regions in cell-based assays (see Table X). The factors responsible for the structure–activity relationship (SAR) variations based on potency are clearly complex. It would appear that the structural features required for the best HDAC inhibition activity include the disulfide spacer linked to a hydroxyimino amide capped on each end by modified tyrosine residues. Deletion of one of the tyrosine end groups was not tolerated, but in one case it could be replaced by an oxalamic acid group (i.e. **160**).

Eight psammaplin analogues were then assessed in the DNA methyltransferase assay and the results are presented in Table X. Unfortunately, scarcity of material prevented the testing of three of the analogues, psammaplins B (**156**), C (**157**), and J (**164**). Only one alkaloid, bisaprasin (**154**), was observed to be very potent (< 10 nM) and two other alkaloids, psammaplin A (**152**) and G (**161**), were also potent. Interestingly, two of these, psammaplin A (**152**) and bisaprasin (**154**), were also potent HDAC inhibitors. Although the data set is limited, it would appear that the unifying feature for dual activity against both HDAC and DNMT is the presence of the disulfide spacer linked to a hydroxyimino amide capped on each end by aromatic moieties.

Recent findings implicate an interesting relationship between DNMT and HDAC as epigenetic modifiers in the silencing of tumor suppressor genes, but to date no single compound has been shown to exhibit dual activity for both of these distinct targets. Psammaplin A (**152**) and bisaprasin (**154**) are the first single compounds to inhibit both of these enzymes. Furthermore, while psammaplin F (**160**) is selective for HDAC, psammaplin G (**161**) is selective for DNMT. The unique structural differences between these various psammaplins make them relevant for further SAR studies. In summary, psammaplin A (**152**) and bisaprasin (**154**), are micromolar inhibitors of both HDAC and DNMT and may be useful as biomolecular probes of epigenetic gene regulation pathways. Finally, the logical next step has been taken by the Novartis group to design a synthetic compound, NVP-LAQ824 (302), based in part on the trichostatin A, trapoxin B, and psammaplin A (**152**) pharmacophores, and this HDAC inhibitor has been advanced into a Phase I anticancer clinical trial (303).

E. ANTIVIRAL ACTIVITY

Several bromotyrosine alkaloids have been reported to possess antiviral activities (see Table XI). These include moloka'iamine (**52**), mololipids (**53**), fistularin-3 (**79**) 11-ketofistularin-3 (**82**), and psammaplysin D (**132**).

Moloka'iamine (**52**) and the naturally occurring mixture mololipids (**53**) showed moderate anti-HIV activity. Moloka'iamine (**52**) showed an inhibition of 90% at 10 $\mu\text{g}/\text{mL}$ against HSV-II (42). Mololipids (**53**) exhibited selective activity against HIV-1 with an ED_{50} of 52.2 μM without cytotoxicity against human peripheral blood mononuclear cells ($\text{IC}_{50} > 100 \mu\text{g}/\text{mL}$), suggesting that this series of anti-HIV activity lipids has potential for future studies (43). A series of pure synthetic mololipids was screened for gp120 binding by analyzing the interaction of mololipid monolayers with recombinant gp120 at an air–water interface (198). None of these interacted significantly with gp120, suggesting that the action of mololipids seems unlikely by impairing HIV–glycolipid interactions on the plasma cell membrane.

Fistularin-3 (**79**) and 11-ketofistularin (**82**) showed activity against feline leukemia virus with an ED_{50} value of 22 μM (4.8 $\mu\text{g}/200 \mu\text{l}$) and 42 μM (9.3 $\mu\text{g}/200 \mu\text{l}$), respectively (71). The highest concentrations tested for cytotoxicity against FeLV were 100 $\mu\text{g}/200 \mu\text{l}$, and neither compound was toxic at this dosage. The alkaloids were less active than 3'-azido-3'-deoxythymidine (AZT, ED_{50} 0.10 μM), but were comparable to 2',3'-dideoxycytidine (ddCyd, ED_{50} 15 μM) in these assays. Fistularin-3 (**79**) also exhibited anti-HIV-1 activity with an EC_{50} value of 6.9 μM (311).

Reverse transcriptase (RT) plays a critical role in the early steps of the life of human immunodeficiency virus (HIV) (304), and for over a decade has been one of the major targets of AIDS therapy. Polycitone A (**280**) was found to be a potent general inhibitor of retroviral reverse transcriptases and cellular DNA polymerases (305). Polycitone A exhibited potent inhibitory capacity of both RNA- and DNA-directed DNA polymerases. It inhibits retroviral reverse transcriptases (RTs) of human immunodeficiency virus type 1 (HIV), murine leukemia virus (MLV) and mouse mammary tumor virus (MMTV)] as efficiently as cellular DNA polymerases of both DNA polymerases α and β and the prokaryotic Klenow fragment of *Escherichia coli* DNA polymerase I. The mode and mechanism of inhibition of the DNA-polymerase activity associated with HIV-1 RT by polycitone A (**280**) have been studied. The results suggest that the inhibitory capacity of the DNA polymerase activity is independent of the template-primer used. The RNase H function is hardly affected by this inhibitor. Polycitone A has been shown to interfere with DNA primer extension, as well as with the formation of the RT-DNA complex. Steady-state kinetic studies demonstrate that this inhibitor can be considered as an allosteric inhibitor of HIV-1 RT. The target site on the enzyme may be also spatially related to the substrate binding site, since this inhibitor behaves competitively with respect to dTTP with poly(rA) oligo(dT) as a template primer. Chemical transformation of the five phenol groups of polycitone A by methoxy groups decreased the ability to inhibit the DNA polymerase function by 40-fold. Furthermore, this analog lacks the ability to inhibit DNA primer extension as well as the formation of the RT-DNA complex (305).

F. CALCIUM CHANNEL REGULATOR

Bastadins were found to be modulators of skeletal muscle FKBP12/calcium channel complex, which selectively modulated the skeletal isoform of the ryanodine-sensitive sarcoplasmic reticulum (SR) calcium channel by a novel mechanism involving the FK506 binding protein (FKBP12)/ryanodine receptor skeletal isoform (RyR-1) complex (139). Bastadins-5 (**209**), -7 (**211**), and -19 (**223**) showed marked differences in potency and efficacy toward activation of the binding of [³H]ryanodine. In physiological salt, bastadin-5 (5 μM) increases the [³H]ryanodine binding capacity of SR membranes 5-fold, by stabilizing the high affinity conformation of RyR-1 for ryanodine without shifting the affinity of the activator site for Ca²⁺ or altering the response to caffeine or adenine nucleotides. Bastadin-5 decreases the inhibitory potency of Mg²⁺ 7-fold and high concentrations of (>100 μM) Ca²⁺ nearly 5-fold. Bastadin-5 inhibits Ca²⁺ uptake into SR vesicles and enhances Ca²⁺-induced Ca²⁺ release 8-fold. Bastadin-5 increases single-channel open dwell time, τ₁ and τ₂, 65- and 92-fold, respectively, without changing unitary conductance for Cs⁺ (450 picosiemens) or open probability. The most significant finding is that the unique actions of bastadin-5 on [³H]ryanodine binding and Ca²⁺ transport are antagonized by the immunosuppressant FK506. FK506 alone weakly enhances the binding of [³H]ryanodine, compared to bastadin-5. However, FK506 diminishes bastadin 5-induced changes in [³H]ryanodine binding and Ca²⁺ transport without altering the efficacy of adenine nucleotides. Unlike FK506, bastadin-5 does not directly promote the dissociation of FKBP12 from the RyR-1 membrane complex. However, it markedly enhances the release of FKBP12 induced by FK506. These results suggest that the bastadin-5 effector site is a novel modulatory domain on FKBP12. Bastadins represent a new class of compounds that will allow insight into the functional interactions between FKBP12 and RyR-1 (139).

Utilizing single channel analysis and measurements of Ca²⁺ flux across the sarcoplasmic reticulum, bastadin-10 (**214**) was identified as the structural congener responsible for dramatically stabilizing the open conformation of the RyR channel, possibly by reducing the free energy associated with closed to open channel transitions (G*c → o) (306). The stability of the channel open state induced by bastadin-10 sensitized the channel to activation by Ca²⁺ to such an extent that it essentially obviated regulation by physiological concentrations of Ca²⁺ and relieved inhibition by physiological Mg²⁺. These actions of bastadin-10 were produced only on the cytoplasmic face of the channel, were selectively eliminated by pretreatment of channels with FK506 or rapamycin, and were reconstituted by human recombinant FKBP12. The actions of bastadin-10 were found to be reversible. A structure–activity model is proposed by which substitutions on the Eastern and Western hemispheres of the bastarane macrocycle may confer specificity toward the RyR1–FKBP12 complex to stabilize either the closed or open channel conformation. These results indicate that RyR1–FKBP12 complexes possess a novel binding domain for phenoxycatechols and raise the possibility of molecular recognition of an endogenous ligand (306). Bastadins are now used as tools to study the calcium channel (307,308).

G. OTHER ACTIVITIES

Searching for a selective histamine-H₃ antagonist led to the isolation of verongamine (**139**) (101). Verongamine binds with an IC₅₀ of 0.5 μM to the H₃-receptor isolated from guinea

pig brain membranes (309). Verongamine also demonstrated H₃-antagonist activity in the electrical field stimulated (EFS) contracted guinea pig ileum. (310). In this assay, EFS-induced contractions are inhibited by the H-receptor agonist (*R*)- α -methyl histamine (RAM), and the effect of RAM can be blocked by H₃-antagonists. Verongamine at 1 μ g/mL blocked the effect of RAM. For comparison, aerophobin-1 (**113**) gave an H₃-receptor binding IC₅₀ of 9.0 μ M, and showed no activity in the guinea pig ileum assay. Additionally, verongamine at 1 μ g/mL has no effect against the inhibition of EFS-induced ileum contractions by the α_2 -adrenoceptor agonist clonidine. These results indicate verongamine (**139**) is a specific H₃-receptor antagonist (101). Although bromotyrosine derivatives have been reported to possess a variety of bioactivities, the detection of histamine-H₃ activity is unprecedented among sponge metabolites and marine natural products in general.

Archerine (**92**) was assessed for antihistaminic activity on histamine-induced contractions of guinea pig isolated ileum. The histamine agonist (10^{-8} – 10^{-4} M) caused a concentration-dependent contraction of the isolated organ. Archerine (**92**) at the concentration of 1.2×10^{-4} M completely abolished the 1 μ M response of histamine, while a milder effect was observed at the concentrations 1.2×10^{-5} M and 1.2×10^{-6} M. This inhibition was removed by washing the tissue with fresh medium, indicating that the antagonism produced by archerine (**92**) is reversible. This result is particularly interesting if we consider that archerine (**92**) appears not to possess all the structural features which are currently used as guidelines for the synthesis of antihistamine drugs (77).

Intravenous injection of 100 mcg/kg of *N,N,N*-trimethyl-dibromotyramine (**47**) in an anesthetized dog caused a small, transient hypertensive response (20 mm, 25 s), followed by a similar short-lived hypotensive reaction (20mm, 30 s). Large doses of **47** (1 mg/kg) caused a marked and relatively sustained rise in blood pressure (120 mm, 4.8 min), typical of that induced by 1 μ g/kg of epinephrine. This pressor effect was blocked by an *alpha* adrenergic antagonist, tolfazoline (12 mg/kg), thus characterizing **47** as an *alpha* adrenergic agent (37). When the pressor effect of **47** was blocked by tolazoline, a fall in blood pressure was observed, indicating a *beta*-adrenoreceptor mediated response. This depressive effect was blocked by propranolol (2 mg/kg), a beta-adrenergic blocker, thereby identifying a dual adrenergic effect of **47** on blood pressure. Synthetic and natural **47** caused identical responses when administered consecutively in identical doses to the same dog. Thus the possibility that the dual adrenergic activity might be due to a trace impurity seems to be ruled out (37).

N,N,N-Trimethyl-dibromotyramine (**47**) had stimulant properties on the central nervous system. Spontaneous motor activity in mice was increased 41% at a 1 mg/kg i.p. dose. A preliminary study on the smooth muscle preparations indicated that **47** had a non-specific spasmogenic response at 10 μ g/mL bath concentrations. Both atropine and antihistamine could partially antagonize this response. Although the mechanism of this action is difficult to explain at present, the quaternary structural features of **47** may possibly contribute to its spasmogenic activity in smooth muscles (37).

Ceratamines A (**249**) and B (**250**) both had IC₅₀ values of 10 μ g/mL in the cell-based antimutagenic assay. They are the first two representatives of a novel family of antimutagenic

heterocyclic alkaloids. The imidazo[4,5,d]azepine core heterocycle in the ceratamines appears to have no precedent at any oxidation level among known natural products or synthetic compounds (151).

Aplysillin A (248) weakly inhibited the binding of [¹²⁵I]-thrombin to platelet membranes with an IC₅₀ value of 20 μM (150).

VII. Conclusions

The abundance of metabolites involving the halogenation of tyrosine is an occurrence which is highly unique to the marine environment. Both the broad range of structural classes, as well as the diversity of bioactivity associated with this structural group, suggests that this group of molecules will continue to find their way into clinical applications. From the point of view of the development of novel drug leads, these molecules have a unique potential for the introduction of new drug leads and scaffolds for the generation of new drugs. This is clearly due, in part, to the good drug-like properties for this group of secondary metabolites, which, combined with the unique and abundant structural variations, suggests that the opportunities for applying these molecules to issues associated with human health has just begun.

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TABLE I

Physical-Chemical Properties of Bromotyrosine Derivatives.

	1 (3)	5 (7)	6 (7)	14 (15)	17 (16)
Appearance	Crystal	Colorless crystals	Colorless crystals	Crystal	Crystal
Molecular formula	$C_8H_7Br_2NO_3$			$C_9H_9Br_2NO_3$	$C_9H_9Br_2NO_3$
MS m/z		380, 382, 384 [M-MeO] ⁺ (8, 14, 8), 338, 340, 342, [M-BuO] ⁺ (40, 78, 39), 306, 308, 310 [M-MeOH-BuO] ⁺ (14, 27, 18)	394, 396, 398 [M-MeO] ⁺ (1, 1.5, 1), 338, 340, 342 [M-PenO] ⁺ (21, 40, 20), 306, 308, 310 [M-MeOH-PenO] ⁺ (12.5, 25, 13)	341, 339, 337 [M] ⁺ , 323, 321, 319 [M-H ₂ O] ⁺ , 240, 242 [M-H ₂ O-Br] ⁺	
MP (°C)	193–195	194–195	166–168	120–121	112–116
$[\alpha]_D$				+186° (MeOH)	-189° (c 0.5, acetone)
UV λ_{max} (MeOH) nm	257 (8000)	204 (9912)	203 (12134)	231 (3220), 284 (4915)	
IR ν_{max} (KBr) cm^{-1}	3445, 3420, 3125, 1700, 1675, 1660, 1650	3410, 3200, 1660	3390, 3185, 1668	3380, 2265, 1635, 1585	
	15:16 3:1 (11)	18 (19)	19 (7)	20 (7)	21 (20)
Appearance	Oil		Yellow crystals		
Molecular formula	$C_8H_7Br_2NO_3$	$C_3H_8Br_2O_4$	$C_{12}H_{10}Br_2O_3$	$C_{24}H_{24}Br_4N_4O_{10}$	$C_{24}H_{24}Br_4N_4O_{10}$
MS m/z	323, 325, 327 [M] ⁺ , 306, 308, 310 (2), 278, 280, 282 (3), 201, 203, 205 (100)		360, 362, 364 (49, 100, 48), 345, 347, 349 (M-Me, 15, 25, 14), 331, 333, 335 (M-29, 5, 9, 4), 317, 319, 321 (M-43, 36, 70, 35).		
MP (°C)		106–108	142–144		
$[\alpha]_D$	+30° (c 5.7, MeOH)	+22° (c 3, MeOH)		+152.5° (c 0.92, MeOH)	+160.7° (c 0.92, MeOH)
UV λ_{max} (MeOH) nm	254 (4100), 249 (4000)	281 (4900)	207 (6717), 327 (3732)	280 (10600), 231 (17400)	281 (10500), 230 (17500)
IR ν_{max} (KBr) cm^{-1}	3443, 2263, 1710, 1611	3400, 1785	CHCl ₃ 1780	3402, 1728, 1665	3350, 1732, 1662
	22:23 (3:1 mixture) (22)	24 (23)	25 (9)	26, 27, 28, 29 mixture (9)	30 (24)
Appearance	Oily mixture		Sticky semi-solid	Sticky semi-solid	Colorless needles
Molecular formula	$C_8H_7Br_2NO_3$	$C_8H_8BrNO_3$	$C_8H_8ClNO_3$	$C_8H_7BrClNO_3$	
MS m/z	VG-ZAB, EI 328 (2), 326 (4), 324 (2) (M+1), 327 (6), 325 (12), 323 (6) (M) [calcd for $C_8H_7^{79}Br_2NO_3$ 322.8790; found 322.8766 \pm 0.005], 246 (52) (M-Br), 229 (5),	EIMS: 245 (2), 175 (5), 174 (6)	EIMS 203 (3), 201 (9, M ⁺), 186 (1), 184 (3, M ⁺ -17), 161 (15), 159 (46, M ⁺ -CH ₂ CO), 134 (5), 132 (15), 133 (5), 131 (15, M ⁺ -	EIMS 219 (1), 217 (3, M ⁺), 203 (12), 201 (35), 191 (2), 189 (7), 174 (4), 172 (11), 159 (33), 157	MS 264, 262 (2.7 each, (M+1) ⁺), 263, 261 (1.4 each, M ⁺), 247, 245 (7 each, (M+1-17) ⁺), 246, 244 (1.5 each, M ⁺ -17), 235, 223 (23 each, M ⁺ -28), 218, 216 (19 each

	22:23 (3:1 mixture) (22)	24 (23)	25 (9)	26, 27, 28, 29 mixture (9)	31 (25)	30 (24)
	227 (6) (244-OH), 218 (7), 216 (7) (244-CO), 204 (40), 202 (42) (244-ketone), 176 (24), 174 (24) (202-CO), 95 (17) (174-Br), 43 (100) (O=C=NH)	C ₂ H ₂ O ₂ , 96 (21), 70 (95), 43 (100, OCNH ⁺)		(100), 182 (13), 136 (15), 123 (19), 59 (52), 44 (46), 43 (35), 39 (40)	HR: 215.9613 ± 0.01 C ₇ H ₇ BrNO ₂ , 204, 205 (5 each, 244-42), 203, 201 (16 each, 244-243) 182 (70) HR: 182.0480 ± 0.01 C ₇ H ₆ NO ₂ , 59 (100), 53 (48), 44 (61), 43 (59) 165-170	
MP (°C)		183-185				
[α] _D		+0.036° (c 0.084, MeOH)				
UV λ _{max} (MeOH) nm	255 (4000), 315 sh (100)	250 (6000), 315 (35)	238 (4100)	250 (2500), 312 (60)	242 (2200)	254 (2600)
IR ν _{max} (KBr) cm ⁻¹	(Nujol) 3400-3200, 1700, 1620	(Nujol) 3300, 1680, 1605				
	43 (35)	44 (35)	45 (35)	46 (35)	67 (21)	51 (40)
Appearance	Amorphous white solid	Amorphous solid	Amorphous solid	Amorphous solid	Solid	Colorless solid
Molecular formula	C ₁₂ H ₁₅ Br ₂ O ₃ N	C ₁₃ H ₁₇ Br ₂ O ₃ N	C ₁₃ H ₁₈ BrO ₃ N	C ₁₂ H ₁₆ BrO ₃ N	C ₁₃ H ₁₂ Br ₂ N ₂ O ₅	C ₉ H ₁₁ Br ₂ NO
MS m/z	HRMS 378.9406	HRMS 333.8839 [M ⁺ -NMe ₃]	HRMS 255.9720 [M ⁺ -NMe ₃]	HRMS 301.0323	HRMS 433.9094 MS 434, 436, 438 (M ⁺) 348, 350, 352 (M ⁺ -C ₃ H ₄ O ₃ N), 318, 320, 322 (M ⁺ -C ₃ H ₆ O ₃ N) 220-222	HRFAB: 307.9279
MP (°C)						
[α] _D		-8.33°	-9.00°	-15.00°		
UV λ _{max} (MeOH) nm	(H ₂ O) 287 (1260), 307 (1995), 281 (1250)	(H ₂ O) 277 (1263)	(H ₂ O) 277 (1260)	(H ₂ O) 287 (1257), 307 (1994), 281 (1254)	(EtOH) 274 (524), 282 (491)	224 (3.91), 284 (3.08)
IR ν _{max} (KBr) cm ⁻¹	(KBr) matrix) 3446, 1576	(KBr) matrix) 3446, 1576	(KBr) matrix) 3446, 1576	(KBr) matrix) 3446, 1576	(CHCl ₃) 3670, 3000, 1760, 1595	
	48 (38)	207 (41)	52 (42)	54 (44)	55 (45)	
Appearance	Amorphous solid	Colorless amorphous solid	Off-white powder	Pale yellow semicrystalline solid	Colorless oil	
Molecular formula	C ₁₂ H ₁₈ NBr ₂ O	C ₁₀ H ₁₁ BrN ₂ O ₃	C ₁₁ H ₁₇ Br ₂ N ₂ O	C ₁₅ H ₂₄ Br ₂ N ₂ O	C ₁₄ H ₂₂ N ₂ OBr ₂	
MS m/z	FABMS 350, 352, 354	EI 288 (6), 286 (6), 200 (99), 199 (13), 198 (100), 187 (32), 185 (32), 120 (20), 101 (10), 77 (11) HREIMS 287.9935	EIMS 354.9 (M ⁺ +H+4.1), 352.9 (M ⁺ +H+2.3), 350.9752 (M ⁺ +H, 2), 324.9 (57), 322.9 (100), 320.9 (61), 294.9 (18), 292.9 (16), 273.0 (88), 271.0 (91), 264.8 (30), 262.8 (16), 81.9 (66), 80.9 (27), 79.9 (68), 78.9 (28)	EI 406, 408, 410 (M ⁺ -2HCl, 3%; found: 406.025; C ₁₅ H ₂₄ ⁷⁹ Br ₂ N ₂ O requires 406.0255), 165 (5), 121 (54; found: 121.065; C ₈ H ₆ O requires 121.0653), 85 (64), 58 (100) FAB 407, 409, 411 ([M ⁺ -2HCl]+1)	EIMS 396, 394, 392 (1:2:1), 352, 349, 347 (1:2:1), 324, 322, 320 (1:2:1), 95, 89, 69, 53, 51, 44 HREIMS 392.0081	
MP (°C)				122-123		

	48 (38)	207 (41)	52 (42)	54 (44)	55 (45)
[α] _D					
UV λ _{max} (MeOH) nm	(EtOH) 277 (1260)	(CH ₃ OH) 212 (7762), 281 (1380), 205 (18900)	206 (28000), 284 (600)	293 (400), 448 (440)	(MeOH, HCl satd) 218 (12000), 274 (8000), 285 (1000)
IR ν _{max} (KBr) cm ⁻¹	(Dry film) 2578, 1635	(NaCl film) 3387, 3310, 1651	(NaCl) 3000, 1592, 1473, 1459, 1385, 1261, 865, 739	3000, 2940, 1632, 1454, 1256, 1043	(KBr, HCl salt) 3420, 2950, 1635, 1455, 1260, 1035
56 (45)	57 (46)	58 (46)	60 (49)	59a (47)	
Appearance	Colorless oil	Brown solid	White solid	Colorless solid	Colorless crystalline compound
Molecular formula	C ₁₄ H ₂₂ N ₂ OBr ₂	C ₁₅ H ₂₃ Br ₂ N ₂ O ₃	C ₁₅ H ₂₃ Br ₂ N ₂ O ₃	C ₁₃ H ₁₅ Br ₂ N ₃ O ₂	C ₁₅ H ₂₂ N ₂ O ₂ Br ₂
MS m/z (int)	EIMS 396, 394, 392 (1:2:1), 353, 351, 349 (1:2:1), 315, 313 (1:1), 87, 69, 58, 44 HREIMS 394.0053	FABMS 437, 439, 441 (1:2:1) HRFABMS 437.0083	FABMS 437, 439, 441 (1:2:1) HRFABMS 437.0090	FAB 404, 406, 408 (1:2:1) (-1.6 mmu)	FABMS 421, 423, 425 (1:2:1) HRFABMS 421.010534
MP (°C)	160–162	170–173		148	
[α] _D					
UV λ _{max} (MeOH) nm	(MeOH, HCl satd) 214 (14000), 276 (8000), 288 (1100)		207 (37800), 220 (12600), 276 (850)		(MeOH, HCl salt) 280 (944), 275 (950), 223 (5769)
IR ν _{max} (KBr) cm ⁻¹	(KBr, HCl salt) 3420, 2950, 1635, 1455, 1260, 1035	3300, 2720, 1720, 1620, 1480	3350, 2700, 1725, 1610 (Film) 3200, 3040, 2950, 1680, 1450, 1200, 1130	3328, 2700, 1680, 1580, 1480,	
61 (50)	62 (51)	63 (53)	64 (53)	65 (54)	67 (21)
Appearance	Amorphous solid	Colorless oil	Colorless flakes	White crystals	Solid
Molecular formula	C ₁₃ H ₁₆ Br ₂ N ₃ O ₃	C ₇ H ₅ N ₂ O ₃ Br ₂	C ₁₆ H ₂₁ Br ₂ NO ₃	C ₁₄ H ₁₈ Br ₂ NO ₃	C ₁₃ H ₁₂ Br ₂ N ₂ O ₅
MS m/z	FABMS 420, 422, 424 (1:2:1) HRFABMS 419.9568	ESIMS 479, 481, 483 (1:2:1, [M+H] ⁺), 501, 503, 505 (1:2:1, [M+Na] ⁺) HRFABMS 479.0176	EIMS 437 (0.7), 435 (1.4), 356 (1), 354 (1), 167 (1), 149 (1), 86 (8), 84 (2), 73 (3), 71 (3), 58 (100) HREIMS 432.9860	FABMS 410 (46), 408 (94), 406 (61), 325 (11), 323 (24), 321 (14), 307 (8), 305 (19), 303 (10), 244 (12), 58 (100) HRFABMS 407.9641	HRMS 433.9094 MS 434, 436, 438 (M ⁺) 348, 350, 352 (M ⁺ -C ₃ H ₄ O ₃ N), 318, 320, 322 (M ⁺ -C ₄ H ₆ O ₃ N)
MP (°C)	+3.0° (c 0.8, MeOH)	67	193–194	222–225	220–222
[α] _D		+35° (c 0.1, MeOH)	283 (880)	223 (13700), 267 (11000)	-33° (c 1.1, MeOH)
UV λ _{max} (MeOH) nm	(neat) 3365, 3280, 1675, 1453, 1206, 1138	3411, 1630, 1057	(Neat, NaCl) 2920, 2840, 2805, 2758, 1712, 1635, 1195, 950	1748 (sh, 1722, 1703) (CHCl ₃) 3670, 3000, 1760, 1595	(EtOH) 274 (524), 282 (491)
68 (58)	70 (62)	71 (63)	72 (64)	73 (61)	74 (61)
Appearance	Plates	White powder	Colorless glass	White powder	75 (65)

	68 (58)	70 (62)	71 (63)	72 (64)	73 (61)	74 (61)	75 (65)
Molecular formula	$C_{24}H_{26}Br_4N_4O_8$	$C_{24}H_{27}Br_4N_4O_{10}$	$C_{24}H_{28}Br_4N_4O_9$	$C_{24}H_{24}Br_4N_4O_9$	$C_{24}H_{24}Br_4N_4O_{10}$	$C_{24}H_{24}Br_4N_4O_{10}$	$C_{25}H_{26}Br_4N_4O_9$
MS m/z		HRFABMS 850.84 13 (-1.9 mmmu)		HRFABMS 831.8235 (-0.1 mmmu)			FABMS 841, 843, 845, 847, 849
MP (°C)	134–137 (dec.)	162–164		174.6–176.6 (dec)			
$[\alpha]_D$	+252° (acetone)	-64.2° (c 0.1, MeOH)	+189° (c 0.15)	+181.15° (c 2.17, DMSO)	+152.5°	+160.7°	
UV λ_{max} (MeOH) nm	EtOH) 234 (4.16), 284 (4.13)	282 (9400), 225 (19000), 202 (34000)	284 (11100), 233 (19750), 205 (18900)	(DMSO) 284 (11500), 262 (11600)	280.5 (10600), 231 (17400)	281 (10500), 230.5 (17500)	284 (10500), 232 (19000)
IR ν_{max} (KBr) cm^{-1}	3335, 3160, 1675, 1660, 1580, 1550	3600–3000, 1660, 1600, 1530	3400, 3350 (OH, NH), 1650 (CONH)	3600–3000, 1713, 1665, 1558, 1552, 1435, 1293, 1271, 1131, 1100, 1025	3402, 1728, 1665	3350, 1732, 1662	(KBr matrix) 3450, 1715, 1665
CD	N/A	N/A	N/A	N/A	N/A	N/A	285, +52000 250, +60,200

	76 (66)	78 (30)	79 (25)	81 (70)
Appearance	Colorless glassy solid	Colorless solid	Amorphous white solid	Amorphous white solid
Molecular formula	$C_{27}H_{32}Br_4N_4O_9$	$C_{22}H_{20}Br_2N_4O_8$	$C_{31}H_{30}Br_6N_4O_{11}$	$C_{31}H_{30}Br_6N_4O_{11}$
MS m/z	FABMS (thioglycerol+MeOH) 875 (1), 873 (2), 871 (4) [M] ⁺ , 869 (2), 867 (1), 861 (1.5), 859 (3.5), 857 (5), 855 (3.5), 853 (1.5), 322 (1.5), 320 (2.5), 318 (1.5), 297 (2.5), 295 (4.5), 293 (2.5), 281 (18), 279 (37), 277 (18), 70 (100) HRFABMS 871.97028, found 871.97930 [M] ⁺	FABMS 801, 803, 805, 807, 809	NA	FABMS 1141, 1139, 1137, 1133 ([M+Na] ⁺ , 39, 64, 100, 80, 48)
MP (°C)	NA	NA	NA	NA
$[\alpha]_D$	NA	NA	NA	+65.2° (c 1.04, acetone)
UV λ_{max} (MeOH) nm	234 (9000), 283 (4300)	260 (0.63), 230 (0.78), 210 (0.90)	+104° (c 1.67, MeOH)	(EtOH) 233 (13500), 283 (2650)
IR ν_{max} (KBr) cm^{-1}	3382, 2357, 1665, 1549, 1106, 603	NA	3395, 1655, 1602, 1550	3350, 2920, 1655, 1545
CD	NA	344.1 (2.5), 270.3 (13.8), 233.6 (24.1), 199.0 (-25.0)	NA	NA

	82 (71)	83 (63)	84 (72)	85 (72)	86 (65)
Appearance	Pale yellow; gummy solid	Unstable yellow; power	Powder	NA	NA
Molecular formula	$C_{31}H_{29}Br_6N_4O_{11}$	$C_{31}H_{30}Br_6N_4O_9$	$C_{31}H_{28}Br_6N_4O_{10}$	$C_{31}H_{30}Br_6N_4O_{10}$	$C_{31}H_{30}Br_6N_4O_{10}$
MS m/z	HRFABMS 1112.6897 (-0.6 mmmu)		EIMS 351 (2), 349 (4), 347 (2), 336 (2), 334 (4), 332 (2), 323 (4), 321 (9), 319 (5), 308 (6), 306 (12), 304 (6), 267 (6), 265 (12), 263 (6)		FABMS 1091, 1093, 1095, 1097, 1099, 1101, 1103

	82 (71)	83 (63)	84 (72)	85 (72)	86 (65)
MP (°C)	NA	NA	NA	NA	NA
[α] _D	+130° (c 0.1, MeOH)	+98.5° (c 0.10, MeOH)	NA	+136° (c 0.2, acetone)	NA
UV λ _{max} (MeOH) nm	283 (9900), 242 (14000), 225 (27000)	284 (10400), 257 (16000), 224 (26000)	280 (3400), 205 (18500)	280 (3400), 205 (18500)	284 (11000), 232 (19000)
IR ν _{max} (KBr) cm ⁻¹	3600–3200, 1720, 1660, 1590, 1525,	3450, 3350 (OH, NH), 1645 (CONH)	(Nujol) 3400 br, 1725, 1650, 1590, 1530		(KBr matrix) 3450, 1715, 1665
CD	NA	NA	NA	NA	285, +56500 250, +65200
	87 (70)	88 (70)	89:90 (74)	91 (75)	
Appearance	Amorphous off-white powder	Amorphous white powder	Noncrystalline mixture		
Molecular formula	C ₂₉ H ₂₆ N ₄ O ₁₁ Br ₆	C ₂₉ H ₂₆ N ₄ O ₁₁ Br ₆	C ₂₉ H ₂₆ N ₄ O ₉ Br ₆	C ₁₈ H ₁₈ Br ₄ N ₂ O ₆	
MS m/z	FABMS 1092, 1090, 1088, 1086, 1084, 1082, (1, 1.8, 1.8, 2, 1.8, 1.8, 1) [M+], 707 (0.8), 705 (1), 703 (0.8), 427 (10), 425 (18), 423 (10)	FABMS 1092, 1090, 1088, 1086, 1084, 1082, (1, 1.8, 1.8, 2, 1.8, 1.8, 1) [M+], 707 (1), 705 (1), 703 (1), 427 (6), 425 (10), 423 (6)	FABMS 1092, 1090, 1088, 1086, 1084, 1082 (<1) [M+], 707 (1), 705 (1), 427 (6), 425 (10), 423 (6)	FABMS 1054.68209 [M+H] ⁺	ESIMS 696.7766 [M+Na] ⁺
MP (°C)	N/A	N/A	N/A	N/A	N/A
[α] _D	-17.1° (c 1.26, acetone)	+50.0° (c 0.27, acetone)			+248° (c 0.012, CHCl ₃)
UV λ _{max} (MeOH) nm	(EtOH) 220 (12600), 250 (7740)	(EtOH) 215 (12570), 250 (7940)			
IR ν _{max} (KBr) cm ⁻¹	3360, 2930, 1750, 1660, 1600, 1540, 1260, 1095	3350, 2920, 1700, 1665, 1605, 1540, 1255, 1095, 910			
	92 (77)	93 (78)	94 (68)	95 (68)	
Appearance	Brown amorphous solid	Yellow powder	Amorphous white solid	Crystalline	
Molecular formula	C ₃₂ H ₃₆ Br ₄ N ₁₀ O ₈	C ₄₄ H ₄₃ Br ₈ N ₆ NaO ₁₆ S	C ₂₆ H ₂₁ Br ₄ N ₃ O ₈	C ₂₆ H ₂₅ Br ₄ N ₃ O ₁₀	
MS m/z	FABMS 1005, 1007, 1009, 1011, 1013 HREABMS 1008.9488	FABMS 1583 [M-Na] ⁺ , 1503 [M-SO ₃ Na]	NA	NA	
MP (°C)	NA	200 (dec.)	NA	168–171	
[α] _D	+111.4° (c 0.07, MeOH)	-96° (c 0.86, DMSO)		+93.5° (c 1.2, MeOH)	+122.7° (c 0.44, CHCl ₃)
UV λ _{max} (MeOH) nm	221 (19600), 279 (9500)	231 (2690), 283 (11900)	284 (5681), 230 (15217)	NA	
IR ν _{max} (KBr) cm ⁻¹	(KBr matrix) 3450, 1665	3700–2500, 1660, 1584, 1541, 1257, 1218, 1183, 1047, 990	3360, 1750, 1660, 1600, 1545, 1545	3360, 1750, 1740, 1660, 1600, 1545	
CD	245, +60000 285, +50000	252 (-16.0), 289 (-16.9)			
	97 (79)	98 (80)	99 (81)	101 (82)	
Appearance	Colorless oil	Amorphous white solid	White solid	Glass	

	97 (79)	98 (80)	99 (81)	101 (82)	
Molecular formula	C ₁₀ H ₁₀ Br ₂ N ₂ O ₄	C ₁₀ H ₉ Br ₂ N ₂ O ₅	C ₂₁ H ₂₃ Br ₄ N ₃ O ₅	C ₂₁ H ₂₄ Br ₃ N ₃ O ₅	
MS <i>m/z</i>	EI: 380, 382, 384 (1:2:1)	FABMS 938, 940, 942, 944, 946 (1:4:6:4:1) [M+H] ⁺	FABMS 714, 716, 718, 720, 722 (1:4:6:4:1) [M+H] ⁺	HRFABMS 635.9360	
MP (°C)		40–42	140–142	NA	
[α] _D	+86°	–38° (c 0.73, CHCl ₃)	–70° (c 0.7, MeOH)	+21° (c 0.47, CHCl ₃ –MeOH 1:1)	
UV λ _{max} (MeOH) nm	228 (8000), 290 (2000)	270 (11650)	283 (9392)	(CHCl ₃) 240 (23000), 287 (16700)	
IR ν _{max} (KBr) cm ^{–1}	3400, 2940, 1675, 1135, 1120	NA	NA	(CHCl ₃ –MeOH 1:1) 3690, 3630, 3420, 3020, 2945, 1600, 1570, 1535, 1500, 1465, 1255, 1015	
CD	248 (+4.0), 284 (+4.0)				
	102 (83)	100 (81)	102 (36)	104 (36)	105 (78)
Appearance	Colorless semisolid	Amorphous white solid	Colorless solid	Colorless solid	Colorless fine crystals
Molecular formula	C ₂₃ H ₂₅ Br ₄ N ₃ O ₇	C ₃₀ H ₅₁ Br ₄ N ₃ O ₆	C ₂₂ H ₂₄ Br ₄ N ₃ O ₇	C ₂₅ H ₂₉ Br ₄ N ₃ O ₇	C ₂₄ H ₂₇ Br ₄ N ₃ O ₇
MS <i>m/z</i>	HRFABMS 797.82940 FABMS 802 (19), 800 (67), 798 (95), 796 (67), 794 (21), 776 (28), 700 (9), 681 (14), 661 (4), 612 (33), 532 (38), 510 (100), 482 (85), 464 (42), 437 (65), 413 (48)	FABMS 938, 940, 942, 944, 946 (1:4:6:4:1) [M+H] ⁺	ESI-FTMS 761.8307 (+10.3 mmu) [M+H] ⁺	ESI-FTMS 803.8777 (–27.3 mmu) [M+H] ⁺	FABMS (Thioglycerol matrix) 786, 788, 790, 792, 794 (1:4:6:4:1) [M+H] HRFABMS 785.8661, found 785.8649 [M+H]
MP (°C)	NA	40–42	NA	NA	154–156
[α] _D	+69.0° (c 6.4, MeOH)	–38° (c 0.73, CHCl ₃)	+96.3° (c 0.19, MeOH)	+102° (c 0.067, MeOH)	–118° (c 1.02, MeOH)
UV λ _{max} (MeOH) nm	282 (5200), 208 (145000)	270 (11650)	(EtOH) 208 (8100), 284 (1200)	(EtOH) 207 (8300), 284 (1200)	210 (29500), 283 (7390)
IR ν _{max} (KBr) cm ^{–1}	3692–3026, 2933, 2853, 1649, 1643, 1545, 1400, 1384, 1281, 1095, 1044, 988, 918, 868, 765, 739, 704	NA	(NaCl) 3251 br. 2935, 1658, 1543, 1456, 1257, 989	(NaCl) 3255 br. 3058, 2933, 1771, 1631, 1542, 1456, 1257, 1024, 987	3700–2300, 1660, 1630, 1540, 1260, 1045
	106 (78)	107 (78)	108 (72)	109 (85)	110 (79)
Appearance	Colorless fine crystals	Colorless powder	Powder	Colorless amorphous solid	Colorless oil
Molecular formula	C ₂₂ H ₂₃ Br ₄ N ₃ O ₇	C ₂₂ H ₂₂ Br ₄ N ₃ O ₇ S	C ₁₈ H ₁₆ Br ₄ N ₂ O ₆	C ₂₄ H ₃₀ Br ₄ N ₃ O ₅	C ₂₃ H ₂₇ Br ₄ N ₃ O ₅
MS <i>m/z</i>	FABMS (Glycerol matrix) 758, 760, 762, 764, 766 (1:4:6:4:1) [M+H] HRFABMS 757.8348, found 757.8359 [M+H]	FABMS (Glycerol matrix) 836, 838, 840, 842, 844 (1:4:6:4:1) [M–Na] [–]	FABMS (Glycerol–MeOH–H ⁺) 676.8 (0.2%, as the centre of a cluster of ions) [MH ⁺] FABMS (3-nitrobenzyl alcohol) 698.6 (1.0% as the centre of a cluster of ions) [MNa ⁺], 658.6 (1.1% as a quintet) [MH ⁺ –H ₂ O]	FABMS 764, 762, 760, 758, 756 [M ⁺], 748, 746, 742, 740, 684, 682, 680, 678, 602, 600, 658 HRFABMS 759.8892	FABMS 742, 744, 746, 748, 750 (1:4:6:4:1) [M ⁺ +H] HRFABMS 745.8721 [M ⁺ +H] ⁺ , found 745.8776
MP (°C)	154–157	190	73–75	NA	NA
	–97° (c 0.58, MeOH)	–69° (c 0.19, MeOH)	+110° (c 0.2, acetone)	–4.5° (c 1.3, MeOH)	+6.6° (c 0.75, MeOH)

	106 (78)	107 (78)	108 (72)	109 (85)	110 (79)
UV λ_{max} (MeOH) nm	207 (45400), 283 (7300)	206 (53200), 220 (25000 sh), 282 (6760)	281 (69000), 207 (39200)	220 (100000), 284 (1000)	277 (1700), 284 (1400)
IR ν_{max} (KBr) cm^{-1}	3700–2300, 1660, 1635, 1540, 1260, 1045	3700–2500, 1662, 1596, 1541, 1258, 1217, 1046	(Nujol) 3350 br, 1660, 1590, 1540, 1270, 1220, 1095	3450, 2980, 2880, 1690, 1470, 1400, 1220, 1150	3400, 2940, 2845, 1670, 1520, 1470, 1135, 1120

	111 (79)	112 (86)	113 (69)	114 (69)	116 (79)	117(79)
Appearance	Colorless oil	Colorless oil	NA	NA	Colorless oil	Colorless oil
Molecular formula	$\text{C}_{23}\text{H}_{27}\text{Br}_4\text{N}_3\text{O}_5$	$\text{C}_{22}\text{H}_{25}\text{Br}_4\text{N}_3\text{O}_5$	$\text{C}_{15}\text{H}_{16}\text{Br}_2\text{N}_3\text{O}_4$	$\text{C}_{16}\text{H}_{19}\text{Br}_2\text{N}_5\text{O}_4$	$\text{C}_{15}\text{H}_{17}\text{Br}_2\text{N}_5\text{O}_4$	$\text{C}_{15}\text{H}_{17}\text{Br}_2\text{N}_5\text{O}_5$
MS m/z	FABMS 742, 744, 746, 748, 750 (1:4:6:4:1) $[\text{M}^+\text{H}]^+$ HREABMS 745.8721 $[\text{M}^+\text{H}]^+$, found 745.8729	ESIMS 726.85, 728.85, 730.85, 732.86, 734.85 $[\text{M}^+\text{H}]^+$ HRESIMS 728.8676 (0.8 mmu) $[\text{M}^+\text{H}]^+$	FABMS 475, 477, 479 $[\text{MH}^+]$	FABMS 504, 506, 508 $[\text{MH}^+]$	FABMS 490, 492, 494 (1:2:1) $[\text{M}^+\text{H}]^+$ HREABMS 491.9705 $[\text{M}^+\text{H}]^+$, found 491.9682	FABMS 506, 508, 510 (1:2:1) $[\text{M}^+\text{H}]^+$ HREABMS 507.9654 $[\text{M}^+\text{H}]^+$, found 507.9672
MP ($^{\circ}\text{C}$)	NA	NA	NA	NA	NA	NA
$[\alpha]_D$	+9.1 $^{\circ}$ (c 0.39, MeOH)	NA	+187 $^{\circ}$ (c 2.0, MeOH)	+139 $^{\circ}$ (c 1.9, MeOH)	+24 $^{\circ}$ (c 0.98, MeOH)	+26 $^{\circ}$ (c 0.38, MeOH)
UV λ_{max} (MeOH) nm	277 (1700), 284 (1400)	280 (3.28)	NA	NA	277 (1700), 284 (1400)	231 (6300), 284 (2400)
IR ν_{max} (KBr) cm^{-1}	3400, 2940, 2850, 1675, 1470, 1200, 1135, 1120	1736, 1655, 1591, 1542, 1458, 1390, 1257, 1044, 737	NA	NA	3400, 2930, 2845, 1680, 1540, 1430, 1200, 1135, 1125	3400, 2920, 2850, 1670, 1540, 1430, 1200, 1135, 1125

	119 (89)	120 (83)	121 (90)	122 (91)	123 (89)
Appearance	NA	Colorless oil	NA	Colorless amorphous solid	NA
Molecular formula	$\text{C}_{15}\text{H}_{18}\text{Br}_2\text{N}_5\text{O}_4$	$\text{C}_{16}\text{H}_{18}\text{Br}_2\text{N}_5\text{O}_4$	$\text{C}_{24}\text{H}_{22}\text{O}_8\text{N}_6\text{Br}_2$	$\text{C}_{27}\text{H}_{39}\text{Br}_4\text{N}_7\text{O}_7 \cdot \text{HCl}$	$\text{C}_{27}\text{H}_{32}\text{Br}_4\text{N}_7\text{O}_6$
MS m/z	FABMS 490, 492 494 $[\text{MH}^+]$	HREABMS 503.97073 FABMS 506 (53), 504 (100), 502 (55), 307 (5), 154 (50)	FABMS 681, 683, 685 (1:2:1) HREABMS 680.9940	FDMS 880, 882, 884, 886, 888 (1:4:6:4:1)	FABMS 866, 868, 870, 872, 874 $[\text{MH}^+]$
MP ($^{\circ}\text{C}$)	NA	NA	NA	NA	NA
$[\alpha]_D$	-158 $^{\circ}$ (c 1.0, MeOH)	+121.9 $^{\circ}$ (c 5.7, MeOH)	NA	-85 $^{\circ}$ (c 2.10, MeOH)	-10 $^{\circ}$ (c 1.0, MeOH)
UV λ_{max} (MeOH) nm	220 (4.47), 284 (4.08)	266 (13100), 226 (13700)	NA	NA	220 (4.54), 228 (4.11)
IR ν_{max} (KBr) cm^{-1}	3400, 1680, 1543, 1437, 1381, 1250	3654–3000, 2937, 1660, 1595, 1543, 1435, 1273, 1219, 1047, 1025, 997, 824, 765	NA	NA	3375, 1680, 1543, 1456, 1387, 1250

	124 (83)	125 (79)	126 (66)	127 (92)	128(92)
Appearance	Colorless semisolid	Colorless oil	Colorless glassy solid	NA	NA
Molecular formula	$\text{C}_{16}\text{H}_{24}\text{Br}_2\text{N}_5\text{O}_4$	$\text{C}_{15}\text{H}_{21}\text{Br}_2\text{N}_5\text{O}_4$	$\text{C}_{15}\text{H}_7\text{D}_7\text{Br}_2\text{N}_5\text{O}_5$	$\text{C}_{16}\text{H}_{19}\text{Br}_2\text{N}_5\text{O}_7$	$\text{C}_{16}\text{H}_{19}\text{Br}_2\text{N}_5\text{O}_7$

	124 (83)	125 (79)	126 (66)	127 (92)	128 (92)	
MS <i>m/z</i>	HRFABMS 510.01640 FABMS 512 (25), 510 (50), 508 (25), 451 (7), 273 (22), 219 (12), 154 (100)	FABMS 494, 496, 498 (1:2:1) [M ⁺ +H] ⁺ HRFABMS 496.0018 [M ⁺ +4H] ⁺ , found 496.0035	FABMS (Thioglycerol) 518 [M+7D-7H] ⁺ (13), 513 [M+2D-2H] ⁺ (4), 496 (8), 478 (6), 295 (23), 279 (22), 157 (60), 71 (100) HRFABMS 518.20911 [M+7D-7H] ⁺	ESIMS 524, 526, 528 (1:2:1) [M+H] ⁺	ESIMS 524, 526, 528	
MP (°C)	NA	NA	NA	NA	NA	
[α] _D	+47.0° (c 7.9, MeOH)	+27° (c 0.18, MeOH)	NA	NA	NA	
UV λ _{max} (MeOH) nm	284 (2500), 218 (4600)	228 (8600), 290 (3400)	232 (9100), 283 (4250)	229 (18500), 280 (10600)	227 (19000), 281 (10500)	
IR ν _{max} (KBr) cm ⁻¹	3588-3050, 3024, 2782, 1658, 1402, 1024, 992	3400, 2920, 1660, 1520, 1470, 1210	3500-3000, 2928, 2860, 1690-1630, 1405, 1100, 605	3450, 1730, 1715, 1665	3450, 1730, 1715, 1665	
Appearance	Colorless glass	Colorless glass	Colorless solid	Glass	Colorless oil	
Molecular formula	C ₂₁ H ₂₃ Br ₄ N ₅ O ₆	C ₂₁ H ₂₃ Br ₄ N ₅ O ₇	C ₂₂ H ₂₃ Br ₄ N ₅ O ₇	C ₂₂ H ₂₃ Br ₄ N ₅ O ₇	C ₃₆ H ₅₁ Br ₄ N ₃ O ₈	
MS <i>m/z</i>	EIMS 406 (0.4), 404 (0.4), 402 (0.4), 362 (1), 360 (2), 358 (2), 356 (1), 323 (1), 321 (2), 319 (2), 281 (2), 280 (7), 279 (6), 278 (17), 277 (4), 276 (4), 268 (1), 267 (4), 266 (2), 265 (6), 264 (1), 263 (7), 248 (5), 246 (3), 200 (6), 198 (4), 58 (100), CIMS 407, 405, 403, 361, 359, 281, 279, 277, 275, 249, 247, 233, 231, 221, 219, 193, 191, 166, 164, 125, 123, 121	EIMS 523 (9), 521 (27), 519 (26), 517 (8) overlapping 2 Br clusters, 477 (3), 475 (4), 473 (2) 2 Br cluster, 441 (6), 439 (13), 437 (6) 2 Br cluster, 423 (5), 421 (11), 419 (4) 2 Br cluster, 407 (3), 405 (4), 403 (2) 2 Br cluster, 393 (11), 391 (39), 358 (2), 356 (6), 354 (2), 283 (8), 281 (16), 279 (12), 278 (9), 276 (20), 274 (18), 272 (8) 2 Br cluster, 249 (94), 247 (97) 1 Br cluster, 235 (16), 233 (14) 1 Br cluster, 221 (24), 219 (27) 1 Br cluster, 207 (11), 205 (24), 203 (16) 2 Br cluster, 196 (9), 194 (100), 192 (17), 179 (9), 177 (18), 175 (8), 169 (4), 167 (19), 155 (45), 127 (38), 125 (43), 113 (9), 111 (12), CIMS 441, 439, 437 (2 Br), 407, 405, 403 (2 Br), 340, 338, 336 (2 Br), 249, 247 (1 Br), 221, 219 (1 Br), HRFDMS 749.8308 (M+H), C ₂₁ H ₂₃ ⁷⁹ Br ₂ ⁸¹ Br ₂ N ₅ O ₇ , calcd 749.83068	EIMS 523 (9), 521 (27), 519 (26), 517 (8) overlapping 2 Br clusters, 477 (3), 475 (4), 473 (2) 2 Br cluster, 441 (6), 439 (13), 437 (6) 2 Br cluster, 423 (5), 421 (11), 419 (4) 2 Br cluster, 407 (3), 405 (4), 403 (2) 2 Br cluster, 393 (11), 391 (39), 358 (2), 356 (6), 354 (2), 283 (8), 281 (16), 279 (12), 278 (9), 276 (20), 274 (18), 272 (8) 2 Br cluster, 249 (94), 247 (97) 1 Br cluster, 235 (16), 233 (14) 1 Br cluster, 221 (24), 219 (27) 1 Br cluster, 207 (11), 205 (24), 203 (16) 2 Br cluster, 196 (9), 194 (100), 192 (17), 179 (9), 177 (18), 175 (8), 169 (4), 167 (19), 155 (45), 127 (38), 125 (43), 113 (9), 111 (12), CIMS 441, 439, 437 (2 Br), 407, 405, 403 (2 Br), 340, 338, 336 (2 Br), 249, 247 (1 Br), 221, 219 (1 Br), HRFDMS 749.8308 (M+H), C ₂₁ H ₂₃ ⁷⁹ Br ₂ ⁸¹ Br ₂ N ₅ O ₇ , calcd 749.83068	ESIMS 523 (9), 521 (27), 519 (26), 517 (8) overlapping 2 Br clusters, 477 (3), 475 (4), 473 (2) 2 Br cluster, 441 (6), 439 (13), 437 (6) 2 Br cluster, 423 (5), 421 (11), 419 (4) 2 Br cluster, 407 (3), 405 (4), 403 (2) 2 Br cluster, 393 (11), 391 (39), 358 (2), 356 (6), 354 (2), 283 (8), 281 (16), 279 (12), 278 (9), 276 (20), 274 (18), 272 (8) 2 Br cluster, 249 (94), 247 (97) 1 Br cluster, 235 (16), 233 (14) 1 Br cluster, 221 (24), 219 (27) 1 Br cluster, 207 (11), 205 (24), 203 (16) 2 Br cluster, 196 (9), 194 (100), 192 (17), 179 (9), 177 (18), 175 (8), 169 (4), 167 (19), 155 (45), 127 (38), 125 (43), 113 (9), 111 (12), CIMS 441, 439, 437 (2 Br), 407, 405, 403 (2 Br), 340, 338, 336 (2 Br), 249, 247 (1 Br), 221, 219 (1 Br), HRFDMS 749.8308 (M+H), C ₂₁ H ₂₃ ⁷⁹ Br ₂ ⁸¹ Br ₂ N ₅ O ₇ , calcd 749.83068	HRFABMS 763.8499	HRFABMS 974.0468 [M+H]
[α] _D	-65.2° (c 0.52, MeOH)	-60.2° (c 0.63, MeOH)	NA	-57.1° (c 0.014, MeOH)	-71.4° (c 2.8, acetone)	
UV λ _{max} (MeOH) nm	229 (12700), 262 (7100 sh), 276 (4650 sh), 283 (3200 sh)	218 (28600), 256 (7000 sh), 262 (6400 sh), 277 (4000 sh), 282 (3000)	(CHCl ₃) 3420, 2940, 1670 s, 1620, 1590, 1530 s, 1450, 1250, 1140, 1110, 900	218 (17600), 255 (6700 sh), 279 (3000 sh)	210 (50900), 224 (27600 sh), (10400 sh)	
IR ν _{max} (KBr) cm ⁻¹	(CHCl ₃) 3420, 2950, 1675 s, 1660, 1540-1530, 1460, 1260, 1150, 1120, 910	(CHCl ₃) 3420, 2940, 1670 s, 1620, 1590, 1530 s, 1450, 1250, 1140, 1110, 900	(KBr smear) 3362, 2925, 2851, 1668, 1652, 1558, 1540, 1456, 1258, 1197, 1146, 1118, 1044, 1024	(CHCl ₃) 3430, 3390, 2910, 2830, 1660, 1570, 1445, 1135, 1105, 1030, 980, 950, 890	(CHCl ₃) 3430, 3390, 2910, 2830, 1660, 1570, 1445, 1135, 1105, 1030, 980, 950, 890	
Appearance	Bright yellow oil	NA	Colorless solid	Colorless solid	Colorless solid	
Molecular formula	C ₂₇ H ₂₅ Br ₄ O ₈	C ₂₂ H ₂₃ O ₆ Br ₄ N ₃	C ₂₂ H ₂₃ Br ₄ N ₅ O ₇	C ₃₅ H ₅₁ Br ₄ N ₃ O ₇	C ₃₅ H ₅₁ Br ₄ N ₃ O ₇	
MS <i>m/z</i>	FABMS 994.4 [M+H] ⁺ +C ₄ H ₁₀ O ₂ S ₂ , 840.0 [M+H].	FABMS [M+H] ⁺ 752 (22), 750 (57), 748 (100), 746 (71), 744 (23), 393 (26)	FABMS (positive, glycerol matrix) 758, 760, 762, 764, 766 [M+H] ⁺ , 780, 782, 784, 786, 788 [M]	FABMS (Positive, NBA matrix) 954, 956, 958, 960, 962 [M+H] ⁺ , 976, 977, 980, 982, 984 [M]	FABMS (Positive, NBA matrix) 954, 956, 958, 960, 962 [M+H] ⁺ , 976, 977, 980, 982, 984 [M]	
	133 (96)	134 (97)	135 (98)	136 (98)	137 (98)	

	133 (96)	134 (97)	135 (98)	136 (98)	
	HRFABMS 993.8563 [M+H] +C ₄ H ₁₀ O ₂ S ₂]		+Na ⁺ HRFABMS 783.8152 (calcd for C ₂₂ H ₂₃ ⁷⁹ Br ₂ ⁸¹ Br ₂ N ₅ O ₇ Na, +2.6 mmu)	+Na ⁺ HRFABMS 980.0320 (calcd for C ₃₆ H ₅₁ ⁷⁹ Br ₂ ⁸¹ Br ₂ N ₅ O ₇ Na, -0.4 mmu)	
MP (°C)	-80.3° (c 0.3, acetone)	NA	NA	NA	
[α] _D			-89.7° (c 0.146, MeOH)	-53.5° (c 0.263, acetone)	
UV λ _{max} (MeOH) nm	208 (53400), 224 (33300 sb), 298 (25000)	NA	(EtOH) 207 (64200), 218 (28900 sb), 255 (11000 sb)	(EtOH) 207 (51100), 219 (22700 sb), 255 (9000 sb)	
IR ν _{max} (KBr) cm ⁻¹	(CHCl ₃) 3380, 2910, 1700, 1640, 1610, 1445, 1145, 1105, 1035, 985, 950, 880	(Neat) 3450, 3300, 1660 s, 1620, 1590, 1260	(Film) 3300, 2930, 1660, 1530, 1450, 1380, 1260, 1110, 760	(Film) 3320, 2920, 2850, 1650, 1540, 1450, 1250, 1120	
	137 (99)	138 (100)	139 (101)	140 (33)	141 (102)
Appearance	NA	Oil	Yellow semisolid, oil	NA	Colorless amorphous solid
Molecular formula	C ₁₅ H ₁₇ N ₅ O ₃ Br ₂	C ₁₅ H ₁₆ N ₄ O ₃ Br ₂	C ₁₅ H ₁₈ N ₄ O ₃ Br	C ₁₄ H ₁₅ BrN ₄ O ₃	C ₃₁ H ₄₈ N ₆ O ₄ Br ₂
MS m/z	EIMS 477, 475, 473	EIMS 351, 149, 247 (2.5, 5, 2.5), 335, 333, 331 (2.5, 5, 2.5), 307, 305, 303 (50, 100, 50), 292, 290, 288 (20, 40, 20), 195 (22), 181 (31), 137 (30), 81 (80)	FABMS 381 (92), 383 (100) [M+H] ⁺ , 403 (36), 405 (38) [M+Na] ⁺ HRFABMS 381.0573	FAMS 367, 369	SIMS 727, 729, 731 (1:2:1)
MP (°C)	113–115	NA	NA	NA	94–95
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	NA	207.5 (44140)	388 (630), 289 (sh 2660), 280 (3040), 206 (33600)	387 (620), 289 (2600), 278 (3020), 207 (31000)	284 (970)
IR ν _{max} (KBr) cm ⁻¹	1538, 1372, 1107	3271, 1652, 1471, 1260	3390 br, 3231 br, 2936, 2837, 1655, 1495, 1254, 1054	3151, 1675	2930, 2850, 1675, 1520, 1450, 1250
	142 (102)	143 (102)	144 (103)	145 (103)	
Appearance	Colorless amorphous solid	Colorless amorphous solid	Colorless amorphous solid	Colorless amorphous solid	
Molecular formula	C ₃₂ H ₅₀ N ₆ O ₄ Br ₂	C ₃₃ H ₅₂ N ₆ O ₄ Br ₂	C ₃₄ H ₅₃ N ₆ O ₄ Br ₂	C ₃₆ H ₅₉ N ₆ O ₄ Br ₂	
MS m/z	SIMS 741, 743, 745 (1:2:1)	SIMS 755, 757, 759 (1:2:1)	FABMS 767, 769, 771 (1:2:1) [M+H] ⁺ HRFABMS 767.2540	FABMS 797, 799, 801 (1:2:1) [M+H] ⁺ HRFABMS 767.2956	
MP (°C)	93–95	108–110	NA	NA	
[α] _D	NA	NA	NA	NA	
UV λ _{max} (MeOH) nm	284 (930)	284 (910)	284 (1100), 274 (1400)	284 (710), 274 (1000)	
IR ν _{max} (KBr) cm ⁻¹	2930, 2850, 1675, 1540, 1455, 1260	2930, 2860, 1675, 1520, 1450	3400, 2910, 1675, 1625, 1535, 1450, 1250, 1120	3400, 2840, 1675, 1620, 1535, 1450, 1200, 1130	

	146 (104)	147 (105)	148 (103)	149 (79)	150 (79)
Appearance	Colorless amorphous solid	NA	Colorless oil	Colorless oil	Colorless oil
Molecular formula	$C_{17}H_{23}O_3N_6Br_2$	$C_{22}H_{25}N_6O_3Br_2$	$C_{14}H_{15}Br_2N_6O_3$	$C_{15}H_{18}Br_2N_5O_4$	$C_{15}H_{17}Br_2N_4O_4$
MS m/z	FABMS (Positive glycerol matrix) 559, 557, 555 (1:2:1) [M+K] ⁺ , 521, 519, 517 (1:2:1) [M+H] ⁺ , 505, 503, 501 (1:2:1) [M+H-NH ₂] ⁺ , 441, 439 (1:2:1) [M-Br] ⁺ HRFABMS 517.0241	FABMS 579, 581, 583 (1:2:1) HRFABMS 581.0366 (3.1 mmu)	459.9631	FABMS 490, 492, 494 (M ⁺ +H, 1:2:1) HRFABMS 491.9705	FABMS 475, 477, 479 (M ⁺ +H, 1:2:1) HRFABMS 476.9596
MP (°C)	NA	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ_{max} (MeOH) nm	277 (520)	286 (800), 269 (shoulder), 260 (2900), 217 (15300)	277 (1700), 284 (1400)	277 (1700), 284 (1400)	235 (2600), 290 (2800)
IR ν_{max} (KBr) cm^{-1}	(Film) 3400, 1680, 1540, 1435, 1200, 1140	3400, 1680, 1200, 1140	3400, 2920, 2845, 1680, 1520, 1470, 1200, 1135, 1120	3400, 2920, 1680, 1520, 1470, 1200, 1135, 1120	3400, 2920, 2845, 1680, 1520, 1135, 1120

	151 (89)	152 (107)	153 (107)	154 (109)	155 (110)
Appearance	NA	White powder	White powder	Colorless foam	Oil
Molecular formula	$C_{18}H_{26}Br_2N_5O_2$	$C_{22}H_{24}Br_2N_4O_6S_2$	$C_{22}H_{24}Br_2N_4O_6S_2$	$C_{44}H_{46}Br_{14}N_8O_{12}S_4$	$C_8H_{17}N_3O_4S_2$
MS m/z	502.0432	FABMS 689 (5), 687 (15), 685 (7) [M ⁺ +Na], 667 (62), 665 (100), 663 (50) [M ⁺ +H] HRFABMS 664.9560	NA	NA	EIMS 268 (18) [M ⁺], 193 (60), 134 (60) [M ⁺ -SCH ₂ CH ₂ NHCOOMe], 102 (100) [M ⁺ -SSCH ₂ CH ₂ NHCOOMe] CIMS (isobutane) 269 (100) [M ⁺ +H], 237 (18), 197 (5), 134 (80), 102 (8) HRFABMS 269.0626 (0.4 mmu)
MP (°C)	NA	172–174	NA	NA	NA
[α] _D	+17° (c 1.0, MeOH)	NA	NA	0° (c 1.0, MeOH)	NA
UV λ_{max} (MeOH) nm	285 (3.17), 330 (2.69)	(EtOH) 277 (4875)	NA	212 (110,000), 290 (14,100)	NA
IR ν_{max} (KBr) cm^{-1}	3406, 1680, 1556, 1475, 1262	3348, 1657, 1637, 1536, 1025, 679	3300 br, 1670, 1540	3400–3100 br, 2900, 1670, 1570, 1450, 1200, 1025	3630, 3547, 2960, 1724, 1630, 1525, 1255, 1052

	156 (110)	157 (110)	158 (110)	159 (112)	160 (112)
Appearance	Oil	Oil	Oil	NA	NA
Molecular formula	$C_{12}H_{13}N_3O_3BrS$	$C_{11}H_{15}N_3O_3BrS$	$C_{15}H_{20}N_3O_3BrS_2$	$C_{15}H_{19}N_4O_3S_2Br$	$C_{15}H_{18}N_3O_3S_2Br$
MS m/z	EIMS 357/359 (3) [M ⁺], 328/330 (5) [M ⁺ -HCN-2H], 298/300 (5) [M ⁺ -HSCN], 281/283 (7), 211/213 (100) [C ₈ H ₆ NOBr], 59 (30) [HSCN], CIMS (isobutane) 358/360 (21) [M ⁺ +H], 329/331 (29) [M ⁺ -HCN-H], 299/301 (35) [M ⁺ -HSCN	EIMS 379/381 (4) [M ⁺], 363/365 (2) [M ⁺ -NH ₂], 211/213 (100) [C ₈ H ₆ NOBr], CIMS (isobutane) 380/382 (32) [M ⁺ +H], 364/366 (20) [M ⁺ -NH ₂ +H], 301/303 (15) [M ⁺ -SO ₂ NH ₂ +2H].	EIMS 465/467 (5) [M ⁺], 390/392 (1) [M ⁺ -NHCOOMe-H], 331/333 (22) [M ⁺ -SCH ₂ CH ₂ NHCOOMe], 299/301 (37) [M ⁺ -SSCH ₂ CH ₂ NHCOOMe], 226/230 (40), 211/213 (31) [C ₈ H ₆ NOBr], CIMS (isobutane) 466/468 (10) [M ⁺ +H], 375/377 (3), 333/335 (8), 299/301 (35), HREIMS 465.0030 (0.2 mmu)	HRFABMS 479.0094 [M +H] ⁺ (-3.5 mmu)	HRFABMS 501.9724 [M +H] ⁺ (0.6 mmu)

	156 (110)	157 (110)	158 (110)	159 (112)	160 (112)
	+H ₂ O, 283/285 (25), HRFABMS 357.9856 (0.5 mmu)	HRFABMS 379.9913 (0.3 mmu)			
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	280 (5450)	NA	NA	206 (18070), 284 (1858)	206 (25935), 280 (2057)
IR ν _{max} (KBr) cm ⁻¹	3627, 3541, 2257, 2157, 1678, 1634, 1442, 1378, 1040	3300 br, 1670, 1540	3630, 3547, 2960, 1724, 1630, 1525, 1255, 1052	(Film) 3500–3100 br, 3327, 1668, 1539, 1420, 1358, 1287, 1221, 1010, 985	(Film) 3600–2600 br, 1647, 1527, 1424, 1390, 1287, 1219, 1047, 1019, 985

	161 (112)	162 (112)	163 (112)	164 (112)	165 (114)
Appearance	NA	NA	NA	NA	Pale yellow amorphous solid
Molecular formula	C ₁₅ H ₂₀ N ₅ O ₅ S ₂ Br	C ₁₆ H ₂₂ N ₅ O ₅ S ₂ BrNa	C ₁₂ H ₁₅ N ₂ O ₅ S ₂ Br	C ₂₂ H ₃₄ N ₄ O ₇ S ₂ Br ₂	C ₂₅ H ₃₄ Br ₂ N ₇ O ₆ S ₂
MS m/z	HRFABMS 494.0055 [M+H] ⁺ (3.4 mmu)	HRFABMS 502.0102 [M+Na] ⁺ (2.0 mmu)	HRFABMS 400.9795 [M+Na] ⁺ (1.2 mmu)	HRFABMS 700.9396 [M+Na] ⁺ (4.5 mmu)	(+)-HRFABMS 752.0381 for C ₂₅ H ₃₄ Br ₂ N ₇ O ₆ S ₂ (-2.3 mmu) (-)-HRFABMS 742.8976 for C ₂₂ H ₃₃ Br ₂ N ₄ O ₆ S ₂ (-0.3 mmu) ESIMS 743
MP (°C)	NA	NA	NA	NA	76–80
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	NA	NA	NA	NA	204 (4.73), 281 (3.88)
IR ν _{max} (KBr) cm ⁻¹	(Film) 3600–2600 br, 1666, 1631, 1596, 1531, 1437, 1408, 1354, 1290, 1220, 1145, 1043, 1025, 996	(Film) 3500–3000 br, 1660, 1531, 1419, 1384, 1360, 1260, 1231, 1037, 985	(Film) 3600–3000 br, 1654, 1531, 1501, 1420, 1361, 1284, 1043, 973	3600–2900 br, 1660, 1625, 1531, 1502, 1449, 1425, 1361, 1287, 1284, 1213, 1149, 1044	3400 br, 2925, 1655, 1530, 1485, 1250, 1230, 1040

	166 (114)	167 (114)	168 (114)	168a (114)	169 (117)	
Appearance	Pale yellow amorphous solid	Yellow amorphous solid	Yellow amorphous solid	White solid	White amorphous solid	
Molecular formula	C ₂₅ H ₃₂ Br ₂ N ₇ O ₁₂ S ₄	C ₃₁ H ₃₇ Br ₁₃ N ₄ O ₁₃ S ₃	C ₃₁ H ₃₉ Br ₁₃ N ₄ O ₁₃ S ₃	C ₃₆ H ₃₇ Br ₁₃ N ₄ O ₁₀ S ₂	C ₂₂ H ₂₄ N ₄ O ₆ S ₃ Br ₂	
MS m/z	HRFABMS 909.9285	(+)-FABMS 1068.8/1066.8, 1046.8/1044.8, 944.8/942.8 [M-SO ₃ +Na+2H] ⁺ (-)-FABMS 1044.9/1042.9 [M+2Na-H] ⁻ , 1022.9/1020.9 [M+Na] ⁻ (+)-HRFABMS 1068.7794 [M+3Na] ⁺ , 1046.8165 [M+2Na+H] ⁺	(+)-FABMS 1068.8/1066.8, 1046.8/1044.8, 944.8/942.8 [M-SO ₃ +Na+2H] ⁺ (-)-FABMS 1044.9/1042.9 [M+2Na-H] ⁻ , 1022.9/1020.9 [M+Na] ⁻ (+)-HRFABMS 1068.7794 [M+3Na] ⁺ , 1046.8165 [M+2Na+H] ⁺	(+)-FABMS 1044.7/1042.7, 1022.6/1020.6 [M+Na+H] ⁺ , 942.8/940.8 [M-SO ₃ +Na+H] ⁻ (-)-FABMS 998.7/996.8 ESIMS 998.7/996.8 (+)-HRFABMS 1044.8008 [M+2Na] ⁺	HRFABMS 990.9545 [M+H] ⁺	ESIMS 695 (46), 697 (100), 699 (60) [M+H] ⁺ , 717 (35), 719 (74), 721 (45) [M+Na] ⁺ , 466 (19), 468 (20), 363 (19), 365 (22) MALDI-TOFMS 718.9037 [M+Na] ⁺
MP (°C)	155–160	191–194	236–239	136–138	NA	
[α] _D	NA	NA	NA	NA	NA	
UV λ _{max} (MeOH) nm	204 (4.60), 281 (3.98)	204 (4.83), 291 (4.11)	205 (4.88), 280 (3.93)	NA	NA	

	166 (114)	167 (114)	168 (114)	168a (114)	169 (117)
IR ν_{\max} (KBr) cm^{-1}	3400 br, 2930, 1660, 1530, 1485, 1230, 1040	3400 br, 2925, 1660, 1565, 1270, 1230, 1040	3400 br, 2925, 1655, 1540, 1385, 1270, 1235, 1045	NA	NA
Appearance	White amorphous solid	Yellow oil	Pale tan semicrystalline solid	White semicrystalline solid	White semicrystalline solid
Molecular formula	$\text{C}_{22}\text{H}_{23}\text{N}_4\text{O}_6\text{S}_2\text{Br}_3$	$\text{C}_{44}\text{H}_{46}\text{N}_8\text{O}_{12}\text{S}_4\text{Br}_4$	$\text{C}_{23}\text{H}_{24}\text{Br}_3\text{N}_3\text{O}_4$	$\text{C}_{21}\text{H}_{24}\text{Br}_3\text{N}_3\text{O}_4$	$\text{C}_{21}\text{H}_{23}\text{Br}_4\text{N}_3\text{O}_4$
MS m/z	ESIMS 741 (25), 743 (81), 745 (100), 747 (35) [M+H] ⁺ MALDI-TOFMS 766.8495 [M+Na] ⁺	ESIMS 1323 (8), 1325 (38), 1327 (52), 1329 (43), 1331 (15) [M+H] ⁺ , 1345 (13), 1347 (54), 1349 (100), 1351 (77), 1353 (25) [M+Na] ⁺ MALDI-TOFMS 1348.9407 [M+Na] ⁺	EIMS 647, 649, 651, 653, (M ⁺ -HCl, 5%), 631, 633, 635, 637 (4), 562, 564, 566, 568 (9), 484, 486, 488 (5), 404, 406 (2), 225, 227 (35), 58 (100) FABMS 648, 650, 652, 654 [M ⁺ -HCl]+1)	FABMS 619.9380 [M+H] ⁺	FABMS 699.8480 [M+H] ⁺
MP (°C)	NA	NA	87–88.5	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ_{\max} (MeOH) nm	NA	NA	294 (3286), 266 (3850), 260 (4000), 250 (8300), 215 (26100)	222 (16700), 280 (3100)	222 (17400), 274 (2100)
IR ν_{\max} (KBr) cm^{-1}	NA	3369, 1655, 1534, 1490, 1426, 1228, 1016, 669	3427, 2922, 1632, 1454, 1256, 1053	3350, 2940, 1655, 1620, 1530, 1490, 1455	3400, 2990, 1670, 1630, 1530, 1460
Appearance	Colorless gum	NA	NA	Glass	NA
Molecular formula	$\text{C}_{36}\text{H}_{52}\text{Br}_3\text{N}_3\text{O}_5$	$\text{C}_{21}\text{H}_{23}\text{Br}_2\text{N}_3\text{O}_4$	$\text{C}_{21}\text{H}_{24}\text{Br}_3\text{N}_3\text{O}_4$	$\text{C}_{21}\text{H}_{24}\text{Br}_3\text{N}_3\text{O}_4$	$\text{C}_{20}\text{H}_{23}\text{Br}_2\text{N}_3\text{O}_3$
MS m/z	HRFABMS 844.1459 [M+H] ⁺	FABMS 588 (4), 586 (7), 584 (4) [M+H] ⁺ , 572 (5), 570 (8), 568 (5), 492 (4), 490 (4), 343 (11), 341 (10), 301 (9), 299 (9), 228 (19), 226 (21), 201 (47), 199 (57)	FABMS 668 (2), 666 (4), 664 (4), 662 (2) [M+H] ⁺ , 652 (2), 650 (4), 648 (4), 646 (2), 586 (2), 584 (1), 572 (3), 570 (4), 568 (3), 492 (1), 490 (1), 343 (8), 341 (7), 308 (2), 306 (2), 304 (3), 281 (8), 279 (13), 277 (7)	EIMS 409 (13), 407 (33), 405 (13), 307 (20), 305 (45), 303 (23), 292 (18), 290 (29), 288 (16), 187 (40), 185 (54), 183 (38), 181 (32) HRFABMS 619.9377	HRFABMS 514.0178 [M+H] ⁺
MP (°C)	NA	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ_{\max} (MeOH) nm	214 (18500), 222 (17200), 282 (2700)	NA	NA	(CHCl ₃) 240 (6750), 280 (3500)	280 (834)
IR ν_{\max} (KBr) cm^{-1}	3400, 2910, 1660, 1645, 1490, 1445	NA	NA	[CHCl ₃ -MeOH (1:1)] 3410, 3015, 2930, 1670, 1605, 1530, 1495, 1470, 1420	(Film) 1658, 1540, 1458, 1420, 1258, 1200, 1010
Appearance	NA	NA	NA	NA	NA

	180 (121)	181 (121)	182 (121)	182 (121)	183 (121)
Molecular formula	C ₂₀ H ₂₄ BrN ₃ O ₃	C ₂₃ H ₂₆ Br ₂ N ₃ O ₃	C ₂₀ H ₂₃ Br ₂ N ₃ O ₃	C ₂₁ H ₂₅ Br ₂ N ₃ O ₃	C ₂₀ H ₂₂ Br ₃ N ₃ O ₄
MS <i>m/z</i>	HRFABMS 434.1086 [M+H] ⁺	HRFABMS 578.0306 [M] ⁺	HRFABMS 512.0141 [M+H] ⁺	HRFABMS 526.0292 [M+H] ⁺	HRFABMS 609.9254 [M+H] ⁺
MP (°C)	NA	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	280 (641)	250 (5600)	282 (512)	282 (600)	282 (2600)
IR ν _{max} (KBr) cm ⁻¹	(Film) 1680, 1540, 1498, 1458, 1200, 1138, 840, 800	(Film) 1670, 1200, 1130, 800	(Film) 1678, 1200, 1138, 840, 800	1678, 1204, 1140, 840, 800	1678, 1204, 1140, 800

	185 (121)	186 (121)	187 (121)	188 (121)	189 (86)	190 (122)
Appearance	NA	NA	NA	White powder	Colorless oil	White solid
Molecular formula	C ₂₁ H ₂₄ Br ₃ N ₃ O ₄	C ₂₁ H ₂₄ Br ₃ N ₃ O ₄	C ₂₂ H ₂₆ Br ₃ N ₃ O ₄	C ₉ H ₉ NO ₃	C ₂₃ H ₂₈ Br ₃ N ₃ O ₅	C ₂₄ H ₂₈ N ₃ O ₆ Br ₃
MS <i>m/z</i>	HRFABMS 619.9391 [M+H] ⁺	HRFABMS 619.9349 [M+H] ⁺	HRFABMS 639.9457 [M+H] ⁺	NA	ESIMS 663.97, 665.96, 667.98, 669.96 [M+H] ⁺ HRESIMS 663.9763 [M+H] ⁺ (2.3 mmu)	FABMS 692, 694, 696, 698, (1:2:2:1) [M+H] ⁺ HRESIMS 694.2150 [M+H] ⁺ (-2.2 mmu)
MP (°C)	NA	NA	NA	NA	NA	190–195
[α] _D	NA	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	282 (2800)	280 (2000)	280 (1800)	NA	280 (3.26)	217 (3.65), 280 (4.78)
IR ν _{max} (KBr) cm ⁻¹	1680, 1400, 1200, 800	1678, 1202, 1138, 842, 800, 722	1670, 1200, 1135, 838, 798, 721	1694, 1650, 1600, 1480, 1452, 1430, 1282, 1200, 1132, 1120, 1072, 1020, 920, 890, 740, 688	2937, 2852, 1743, 1656, 1533, 1493, 1452, 1253, 1047, 739	3404, 2926, 1675, 1494

	191 (122)	192 (84)	192 (123)	194 (123)	195 (124)
Appearance	White solid	Colorless amorphous solid	Yellow amorphous solid	Yellow amorphous solid	White powder
Molecular formula	C ₂₂ H ₂₆ N ₃ O ₄ Br ₃	C ₂₃ H ₂₉ O ₄ N ₄ Br ₄	C ₂₈ H ₃₁ Br ₄ N ₄ O ₄	C ₂₈ H ₃₁ Br ₄ N ₄ O ₄	C ₂₄ H ₃₁ N ₃ Br ₄ O ₃ · HCl
MS <i>m/z</i>	FABMS 633, 635, 637, 639 (1:2:2:1) [M+H] ⁺ ; HRFABMS 635.7964 (-2.8 mmu)	FABMS 771, 769, 767, 765, 763 [M+Na] ⁺ , 749, 747, 745, 743, 741 [M+H] ⁺ , 669, 667, 665, 663 HRFABMS 744.8868	FABMS (glycerol matrix) 803, 805, 807, 809, 811 [M] ⁺ ; 645, 647, 649; 466, 468, 470; 411, 413, 415; 347, 349, 351 HRFABMS 806.9007 [M] ⁺ (-3.1 mmu)	FABMS 803, 805, 807, 809, 811 [M] ⁺ ; 645, 647, 649; 466, 468, 470; 426, 428, 430; 409, 411, 413 HRFABMS 806.9007 [M] ⁺ (-3.1 mmu)	DEIMS 726, 728, 730, 732, 734 (1.7); 448, 450, 452 (25:50:25); 403, 405, 407 (10:15:10); 320, 322, 324 (50:100:50)
MP (°C)	175–178	NA	NA	NA	200
[α] _D	NA	NA	NA	NA	+5.1° (c=0.013, MeOH)
UV λ _{max} (MeOH) nm	214.5 (5.12), 280.0 (4.02)	210 (23000), 285 (1600)	216 (21800), 258 (4000 sb)	214 (20600), 258 (3800 sb)	283 (7800), 276 (9400), 245 (12500)

	191 (122)	192 (84)	192 (123)	194 (123)	195 (124)
IR ν_{\max} (KBr) cm^{-1}	3350, 1670, 1200, 1137, 720	3400, 3100, 1680, 1400, 1200, 1130	NA	NA	(CHCl ₃) 3350, 1645, 1535, 1515, 1470, 1450, 1240, 980
196 (125)	197 (125)	198 (125)	199 (90)		
Appearance	Pale orange oil	Colorless amorphous solid	Colorless, amorphous solid	NA	NA
Molecular formula	C ₂₅ H ₃₃ Br ₄ N ₃ O ₃	C ₂₃ H ₃₁ N ₃ O ₃ Br ₃	C ₂₄ H ₃₃ N ₃ O ₃ Br ₃	C ₁₇ H ₂₆ N ₆ O ₃ Br ₂	C ₁₇ H ₂₆ N ₆ O ₃ Br ₂
MS m/z	CIMS 740 (22), 742 (70), 744 (100), 746 (64), 748 (20) [MH ⁺]; 696 (1), 698 (5), 700 (7), 702 (4), 704 (1) [MH ⁺ -NMe ₂]; 662 (4), 664 (10), 666 (8), 668 (2) [MH ⁺ -Br]; 582 (3), 584 (6), 586 (3) [MH ⁺ -Br ₂]; 462 (3), 464 (12), 466 (12), 468 (3), 334 (15), 336 (26), 338 (15) [C ₁₁ H ₁₄ Br ₂ NO ⁺]; 309 (12), 311 (21), 313 (8), 118 (22), EIMS 696 (1), 698 (3), 700 (7), 702 (3), 704 (1) [MH ⁺ -NMe ₂]; 462 (4), 464 (9), 466 (7), [C ₁₇ H ₂₆ Br ₂ N ₃ O ₂ ⁺]; 377 (5), 379 (6), 381 (3) [C ₁₂ H ₁₅ Br ₂ N ₂ O ₂ ⁺]; 334 (52), 336 (99), 338 (50) [C ₁₁ H ₁₄ Br ₂ NO ⁺]; 256 (20), 258 (15) [C ₁₁ H ₁₄ BrNO ⁺]; 84 (17), 58 (100) [CH ₂ NMe ₂ ⁺]	Colorless amorphous solid C ₂₃ H ₃₁ N ₃ O ₃ Br ₃ FABMS 634, 636, 638, 640 (1:3:3:1) [M+H] ⁺ HRFABMS 633.9944	Colorless, amorphous solid C ₂₄ H ₃₃ N ₃ O ₃ Br ₃ FABMS 648, 650, 652, 654 (1:3:3:1) [M+H] ⁺ HRFABMS 648.0092	NA	FABMS 521, 523, 525 (1:2:1) HRFABMS [MH ⁺] 521.0501
MP (°C)	NA	64–67	79–81	NA	NA
[α] _D	0° (c 5.0, CHCl ₃)	+21° (c 1.0, MeOH)	+16° (c 1.0 MeOH)	NA	NA
UV λ_{\max} (MeOH) nm	NA	281 (2400)	281 (2900)	NA	NA
IR ν_{\max} (KBr) cm^{-1}	1036, 1211, 1221, 1259, 1473, 1545, 1678, 2450, 2969, 3023, 3222	3425, 1655	3425, 1655	NA	NA
200 (79)	201 (127)	202 (127)	203 (127)		
Appearance	Colorless oil	White needles	White needles	Colorless gum	Colorless gum
Molecular formula	C ₃ H ₂₂ Br ₂ N ₅ O ₄	C ₂₉ H ₄₁ I ₃ N ₄ O ₄	C ₂₉ H ₄₀ I ₄ N ₄ O ₄	C ₂₈ H ₃₉ I ₃ N ₄ O ₄	C ₂₈ H ₃₉ I ₃ N ₄ O ₄
MS m/z	FABMS 494, 496, 498 (1:2:1) [M ⁺ +H] HRFABMS 496.0018	FABMS 891 (100) [MH ⁺], 643 (18), 517 (10), 430 (93), 391 (12), 304 (93), EIMS 890 (Not observed) [M], 643 (10), 517 (10), 430 (25), 304 (35), 254 (56), 142 (100), 127 (92)	FABMS 1017 (87) [MH ⁺], 643 (18), 430 (100), 391 (12), 307 (45), EIMS 1016 (Not observed) [M], 643 (30), 430 (50), 304 (100), 254 (10)	FABMS 877 (100) [MH ⁺], 629 (13), 503 (17), 430 (100), 329 (10), 290 (37), EIMS 876 (Not observed) [M], 629 (45), 503 (15), 430 (100), 304 (12), 290 (11), 142 (40), 127 (15)	FABMS 877 (100) [MH ⁺], 629 (13), 503 (17), 430 (100), 329 (10), 290 (37), EIMS 876 (Not observed) [M], 629 (45), 503 (15), 430 (100), 304 (12), 290 (11), 142 (40), 127 (15)
MP (°C)	NA	135–137	114–116	NA	NA
[α] _D	NA	-0.23° (c 0.51)	-0.20° (c 0.35)	-0.74° (c 0.24)	-0.74° (c 0.24)
UV λ_{\max} (MeOH) nm	235 (2600), 287 (700)	211 (25000), 223 (24000), 273 (5400)	207 (32000), 221 (35000), 275 (8400)	210 (40000), 222 (39000), 278 (9200)	210 (40000), 222 (39000), 278 (9200)
IR ν_{\max} (KBr) cm^{-1}	3400, 2920, 2850, 1680, 1635, 1135,	(CHCl ₃) 3368, 2935, 2883, 2855, 1672, 1600, 1518, 1500, 1491, 1479, 1463, 1447, 1441, 1416, 1278, 1272, 1254, 1050, 1020, 996	(CHCl ₃) 3368, 2938, 2882, 2855, 1674, 1614, 1602, 1522, 1464, 1416, 1264, 996	(CHCl ₃) 3367, 2940, 2861, 1671, 1522, 1492, 1463, 1264, 1260, 1255, 1050, 996, 925	(CHCl ₃) 3367, 2940, 2861, 1671, 1522, 1492, 1463, 1264, 1260, 1255, 1050, 996, 925
204 (129)	205 (129)	206 (129)	207 (129)	208 (129)	
Appearance	Colorless foam	Colorless foam	Pale yellow foam	White powder	Yellow needles
Molecular formula	C ₃₄ H ₃₀ Br ₄ N ₄ O ₈	C ₃₄ H ₂₉ Br ₅ N ₄ O ₈	C ₃₄ H ₃₀ Br ₄ N ₄ O ₈	C ₃₄ H ₂₉ Br ₄ N ₄ O ₁₁ Sn	C ₃₄ H ₂₅ Br ₅ N ₄ O ₈

	204 (129)	205 (129)	206 (129)	227 (129)	208 (129)
MS <i>m/z</i>	424 (23), 423 (11), 422 (48), 421 (6), 420 (24), 398 (24), 397 (10), 396 (13), 395 (11), 394 (8), 316 (26), 314 (25), 303 (27), 301 (25), 262 (16), 243 (9), 241 (9), 201 (17), 200 (68), 199 (19), 198 (70), 188 (26), 187 (100), 186 (31), 185 (95), 120 (25), 119 (10), 107 (19), 105 (21), 103 (15), 102 (12), 91 (18), 89 (22), 88 (10), 82 (49), 81 (17), 80 (43), 79 (16), 78 (28), 77 (76), 76 (27), 75 (25), 74 (10), 65 (15), 64 (17), 63 (43), 62 (20), 58 (11), 53 (29), 52 (21), 51 (82), 50 (33)	No molecular ion: 504 (3), 502 (10), 500 (10), 498 (3), 200 (100), 198 (100), 187 (87), 185 (87)	426 (2), 425 (6), 424 (11), 423 (10), 422 (18), 421 (4), 420 (8), 399 (6), 398 (8), 397 (13), 396 (8), 395 (9), 243 (10), 201 (24), 200 (84), 199 (26), 198 (80), 189 (12), 188 (54), 187 (100), 186 (54), 185 (100), 120 (20), 108 (12), 107 (30), 105 (14), 91 (12), 89 (10), 82 (56), 81 (27), 80 (62), 79 (22), 78 (28), 77 (64), 51 (60)	MALDI FTMS [M+Na ₂ ⁺] 1062.8130	504 (4), 502 (11), 500 (11), 498 (4), 424 (2), 422 (6), 420 (7), 418 (2), 396 (6), 394 (7), 392 (3), 342 (12), 340 (12), 82 (100), 81 (27), 80 (100), 79 (27) Found: 497.8219, C ₁₆ H ₆ ⁹⁹ Br ₃ N ₂ O ₂ requires 497.8214
MP (°C)	NA	NA	NA	NA	250 (dec)
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	220 (4.80) 282 (4.30), 288 sh (3.93)	220 sh (4.70), 280 (3.93), 193 sh (3.87)	220 (4.77), 285 (3.94)	209 (84400), 279 (5550)	210 (4.84), 288 (4.00), 315 (4.00)
IR ν _{max} (KBr) cm ⁻¹	NA	NA	NA	(ZnSe film) 3400–3000, 2921, 2852, 1660, 1531, 1486, 1424, 1262, 1234, 1180, 989	(KBr disc) 3600, 2800, 1657, 1633, 1490, 1250

	209 Tetramethyl ether (129)	210 (129)	211 (129)	228 (130)	212 (132)
Appearance	Colorless prisms	White powder	Off-white foam	Yellow solid	White film
Molecular formula	C ₃₈ H ₃₅ Br ₅ N ₄ O ₈	C ₃₄ H ₂₆ Br ₆ N ₄ O ₈	C ₃₄ H ₂₆ Br ₄ N ₄ O ₈	C ₃₄ H ₂₅ Br ₄ N ₄ O ₁₄ S ₂ N ₄ O ₂	C ₃₄ H ₂₇ Br ₅ N ₄ O ₉
HR-MS <i>m/z</i>	1073.8310	NA	NA	MALDI FTMS [M+K ₃ ⁺] 1208.6481	EIMS 504 (7.0), 502 (18.7), 500 (18.7), 498 (5.8), 342 (15.8), 340 (21.1), 199 (7.6), 199 (7.0)
MP (°C)	262–264	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	220 sh, 275	220 sh (4.69), 281 (3.47)	290 (4.18), 315 (4.19)	207 (82300), 321 (12400)	208 (5.1), 280 (3.9)
IR ν _{max} (KBr) cm ⁻¹	1670, 1565, 1520, 1495, 1455, 1043	3500–2800, 1665, 1658, 1630, 1500, 1450, 1420, 1280, 1245, 1020, 980	3600–2900, 1663, 1635, 1490, 1455, 1430, 1250, 1015, 1000, 990	(ZnSe film) 3300–2860, 1670, 1653, 1571, 1523, 1482, 1418, 1277, 1240, 1051, 1026, 1005	(Film on NaCl plate) 3340, 1700, 1660, 1590, 1530, 1490, 1450, 1420, 1360, 1280, 1240, 990

	212 Tetramethyl ether (132)	213 (132)	213 Tetramethyl ether (132)	214 (132)	215 (132)
Appearance	White powder	White powder	White powder	Colorless oil	Whitish film
Molecular formula	C ₃₇ H ₃₃ Br ₅ N ₄ O ₉	C ₃₄ H ₂₈ O ₈ N ₄ Br ₄	C ₃₄ H ₂₈ O ₉ N ₄ Br ₄	C ₃₄ H ₂₈ O ₉ N ₄ Br ₄	C ₃₄ H ₂₆ O ₈ N ₄ Br ₄
MS <i>m/z</i>	FABMS [<i>p</i> -nitrobenzyl alcohol/magic bullet (dithiothreitol/dithioerythriol) matrix] 1076.9 (33.2), 1074.9 (52.5), 1072.8 (24.7), 1070.8 (19.9). HRFABMS 1110.8194	942 (1), 940 (2), 938 (2), 936 (1) [M ⁺]	FABMS (Magic bullet matrix) +Na ⁺ , 1016 (21.1), 1018 (28.3), 1020 (26.3), 1022 (1.2). HREIMS 511.8354	NA	NA

	212 Tetramethyl ether (132)	213 (132)	213 Tetramethyl ether (132)	214 (132)	215 (132)
	(C ₃₈ H ₃₅ N ₄ O ₉) ⁷⁹ Br ₄ ⁸¹ BrNa requires 1110.8198), 1112.8194 (C ₃₈ H ₃₅ N ₄ O ₉) ⁷⁹ Br ₃ ⁸¹ Br ₂ Na requires 1112.8178), 1114.8035 (C ₃₈ H ₃₅ N ₄ O ₉) ⁷⁹ Br ₂ ⁸¹ Br ₃ Na requires 1114.8157), 1116.7491 (C ₃₈ H ₃₅ N ₄ O ₉) ⁷⁹ Br ⁸¹ Br ₄ Na requires 1116.8137)		(34.4), 513.8460 (95.8), 515.88416 (100), 517.8290 (37.5)		
MP (°C)	NA	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	NA	208 (5.1), 280 (4.0)	NA	210 (4.7), 277 (3.7)	208 (4.3), 285 (3.4), 331 (3.5)
IR ν _{max} (KBr) cm ⁻¹	NA	(Film) 3420–3200, 1710, 1660, 1620, 1585, 1450, 1420, 1360, 1230	NA	(Film) 3340 br, 1698, 1662, 1590, 1545, 1483, 1421, 1290, 1240	(Film) 3300 br, 1718, 1662, 1646, 1544, 1495, 1479, 1447, 1418, 1284, 1243

	216 Methyl ether (142)	217 (131)	217 Methyl ether (131)	226 (141)
Appearance	White amorphous solid	White powder	White powder	NA
Molecular formula	C ₃₈ H ₃₅ N ₄ O ₉ Br ₅	C ₃₄ H ₂₈ Br ₄ N ₄ O ₈	C ₃₈ H ₃₆ Br ₄ N ₄ O ₈	C ₃₄ H ₂₇ Br ₄ N ₄ O ₁₁ S
MS m/z	1096 (0.5), 1094 (2.0), 1092 (4.1), 1090 (4.2), 1088 (2.4), 1086 (0.7), 1078 (1.0), 1076 (3.7), 1074 (7.2), 1072 (6.5), 1070 (3.4), 1068 (0.8), 1065 (1.1), 1063 (2.3), 1061 (5.6), 1059 (5.3), 1057 (3.0), 1055 (0.8), 1047 (1.1), 1045 (3.2), 1043 (5.6), 1041 (5.0), 1039 (2.9), 1037 (0.7), 1015 (1.3), 1013 (2.2), 1011 (2.7), 1009 (2.1), 1007 (0.9), 648 (0.4), 632 (0.8), 630 (0.6), 602 (3.1), 600 (5.7), 598 (2.8), 592 (1.2), 590 (1.6), 571 (8.0), 569 (13.9), 567 (7.6), 551 (2.0), 549 (5.1), 547 (4.9), 545 (2.3), 536 (3.6), 532 (4.6), 530 (3.3), 438 (21.1), 436 (40.4), 434 (20.8), 412 (12.9), 411 (14.1), 410 (19.6), 409 (14.0), 408 (10.0), 342 (20.5), 340 (18.3), 318 (5.6), 316 (13.8), 314 (10.4), 276 (22.5), 261 (8.8), 169 (9.2), 115 (9.4), 82 (41.5), 80 (42.1), 31 (73.6), 29 (100.0). HREIMS 1089.8312. CIMS (Showed one extra Br) [M+Br] ⁺ 1178 (122.7), 1176 (37.3), 1174 (72.2), 1172 (92.9), 1170 (56.4), 1168 (21.8), 1166 (1.2), 1096 (21.0), 1094 (52.0), 1092 (74.2), 1090 (54.0), 1088 (22.6), 1086 (2.4)	White powder	White powder	NA
MP (°C)	NA	177–179	107–109	NA
[α] _D	NA		0.0° (c 1.52, CH ₂ Cl ₂)	NA
UV λ _{max} (MeOH) nm	NA	209 (81100), 283 (6200)	209 (76400), 276 (7450)	280 (4800), 204 (74000)
IR ν _{max} (KBr) cm ⁻¹	(Film) 3327, 2932, 2857, 1669, 1487		3413, 1666	NA

	218 (133)	219 (134)	220 (135)	221 (135)
Appearance	NA	White amorphous solid	NA	NA
Molecular formula	C ₃₈ H ₂₅ Br ₅ N ₄ O ₈	C ₃₄ H ₂₇ N ₄ O ₈ Br ₅	C ₃₄ H ₂₇ Br ₅ N ₄ O ₈	C ₃₄ H ₂₈ Br ₄ N ₄ O ₉

	218 (133)	219 (134)	220 (135)	221 (135)
MS m/z	EIMS 424 (2.4), 422 (4.5), 420 (2.5), 316 (3.4), 314 (2.6), 303 (2.7), 301 (3.1) HREIMS 421.9089	HREABMS 1016.7785 [M+H] ⁺	HREABMS 1018.7792 [M+H] ⁺	HREABMS 956.8606 [M+H] ⁺
MP (°C)	NA	NA	NA	NA
[α] _D	NA	Negative, too small to be measured	NA	NA
UV λ_{max} (MeOH) nm	284 (4.3), 292 (4.3), 314 (4.4)	NA	(Nujol) 280 (3.6)	(Nujol) 278 (4.1)
IR ν_{max} (KBr) cm^{-1}	(Nujol) 3500–3300, 1655, 1580, 1530, 1500, 1455, 1425, 1280, 1245, 1230, 1180	NA	3500–3300, 1650, 1630, 1480, 1240, 1225	3600–3100, 1660, 1640, 1490, 1470, 1285, 1220

	222 (138)	223 (139)	224 (130)	225 (140)	225 Tetramethyl ether (140)
Appearance	Colorless amorphous solid	Colorless amorphous powder	Colorless solid	Amorphous white solid	Pale yellow gum
Molecular formula	$\text{C}_{34}\text{H}_{28}\text{Br}_4\text{N}_4\text{O}_8$	$\text{C}_{34}\text{H}_{27}\text{Br}_5\text{N}_4\text{O}_8$	$\text{C}_{34}\text{H}_{28}\text{Br}_4\text{N}_4\text{O}_8$	$\text{C}_{34}\text{H}_{29}\text{N}_4\text{O}_8\text{Br}_3$	$\text{C}_{38}\text{H}_{37}\text{N}_4\text{O}_8\text{Br}_3$
MS m/z	FABMS [M ⁺ +1] 613 (4.9), 581 (1.8), 461 (5.3), 427 (1.5) HREABMS 940.8705	FABMS 1018.8	MALDI FTMS [M+Na ⁺] 958.8588	ESIMS [M+Na] ⁺ 887 (40), 885 (100), 883 (96), 881 (32) HRESIMS 886.9394, 884.9406, 882.9412, 880.9431	HRESI: 920 (24),
MP (°C)	NA	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ_{max} (MeOH) nm	NA	NA	209 (84400), 279 (5550)	279 (3.4), 3.83 (2.99)	205 (4.71)
IR ν_{max} (KBr) cm^{-1}	NA	NA	(ZnSe film) 3400–3000, 2921, 2852, 1660, 1531, 1486, 1424, 1262, 1234, 1180, 989	3422, 2925, 1743, 1654, 1697, 1490, 1380, 1235, 1044	3054, 2970, 2954, 2854, 1735, 1676, 1376,

	231 (41)	237 (41)	232:233 3:1 (41)	238 (41)
Appearance	Colorless oil	Colorless oil	Colorless solid	Colorless solid
Molecular formula	$\text{C}_{17}\text{H}_{16}\text{Br}_2\text{N}_2\text{O}_4$	$\text{C}_{18}\text{H}_{18}\text{Br}_2\text{N}_2\text{O}_4$	$\text{C}_{17}\text{H}_{15}\text{Br}_3\text{N}_2\text{O}_4$	$\text{C}_{18}\text{H}_{18}\text{Br}_3\text{N}_2\text{O}_4$
MS m/z	EIMS 474 (10), 472 (19), 470 (10), 458 (7), 456 (16), 454 (7), 256 (9), 214 (23), 213 (91), 212 (33), 211 (84), 201 (26), 200 (97), 199 (27), 198 (98), 188 (13), 187 (95), 186 (15), 185 (100), 132 (43), 120 (31), 77 (42), HREIMS 469.9437 ($\text{C}_{17}\text{H}_{16}^{81}\text{Br}_2\text{N}_2\text{O}_4$ calcd 473.9430), 471.9445 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}_2\text{N}_2\text{O}_4$ calcd 471.9457), 469.9467 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}_2\text{N}_2\text{O}_4$ calcd 473.9477)	EIMS 488 (6), 486 (13), 484 (6), 472 (6), 470 (11), 468 (6), 288 (12), 286 (12), 228 (21), 227 (97), 226 (20), 225 (100), 201 (38), 200 (30), 199 (38), 198 (27), 187 (50), 185 (53), 146 (52), 120 (18), 103 (33), 77 (38), HREIMS 487.9615 ($\text{C}_{18}\text{H}_{18}^{81}\text{Br}_2\text{N}_2\text{O}_4$ calcd 487.9593), 485.9609 ($\text{C}_{18}\text{H}_{18}^{79}\text{Br}_2\text{N}_2\text{O}_4$ calcd 485.9614), 483.9633 ($\text{C}_{18}\text{H}_{18}^{79}\text{Br}_2\text{N}_2\text{O}_4$ calcd 485.9634)	EIMS 554 (4), 552 (14), 550 (14), 548 (5), 293 (33), 291 (67), 289 (34), 267 (24), 265 (50), 263 (24), 213 (41), 212 (51), 211 (24), 198 (76), 187 (91), 185 (100), 132 (28), 120 (25), 77 (49), HREIMS 553.8549 ($\text{C}_{17}\text{H}_{15}^{81}\text{Br}_3\text{N}_2\text{O}_4$ calcd 553.8522), 551.8536 ($\text{C}_{17}\text{H}_{15}^{79}\text{Br}_3\text{N}_2\text{O}_4$ calcd 551.8542), 549.8562 ($\text{C}_{17}\text{H}_{15}^{79}\text{Br}_3\text{N}_2\text{O}_4$ calcd 549.8562), 547.8570 ($\text{C}_{17}\text{H}_{15}^{79}\text{Br}_3\text{N}_2\text{O}_4$ calcd 547.8582)	EIMS 568 (2), 566 (6), 564 (7), 562 (2), 552 (2), 550 (7), 548 (8), 546 (2), 307 (30), 305 (61), 303 (30), 292 (14), 290 (25), 288 (13), 281 (10), 279 (17), 277 (9), 271 (7), 269 (23), 267 (10), 201 (15), 200 (96), 199 (18), 198 (100), 187 (44), 185 (48), 183 (17), 181 (15), 143 (18), 120 (18), 77 (17), HREIMS 567.8672 ($\text{C}_{18}\text{H}_{18}^{81}\text{Br}_3\text{N}_2\text{O}_4$ calcd 567.8679), 565.8701 ($\text{C}_{18}\text{H}_{18}^{79}\text{Br}_3\text{N}_2\text{O}_4$ calcd 565.8699), 563.8715 ($\text{C}_{18}\text{H}_{18}^{79}\text{Br}_3\text{N}_2\text{O}_4$ calcd 563.8719), 561.8716 ($\text{C}_{18}\text{H}_{18}^{79}\text{Br}_3\text{N}_2\text{O}_4$ calcd 561.8739)
UV λ_{max} (MeOH) nm	210 (4.53), 281 (3.88)	213 (4.53), 280 (3.87)	NA	213 (4.50), 281 (3.87)

	231 (41)	237 (41)	232:233 3:1 (41)	238 (41)
IR ν_{\max} (KBr) cm^{-1}	(NaCl film) 3383, 3000, 1659, 1537, 1495, 1422, 1283, 1256	(NaCl film) 3385, 3283, 1657, 1537, 1497, 1283, 1256	(NaCl film) 3393, 1657, 1476	(NaCl film) 3300, 1661, 1537, 1497, 1472, 1422, 1260, 993
234 (41)	234a (41)	235 (41)	235a:236a (41)	
Appearance	Colorless solid	Mixture with hemibastadinol-3	Colorless solid	
Molecular formula	$\text{C}_{17}\text{H}_{17}\text{Br}_2\text{NO}_4$	$\text{C}_{19}\text{H}_{16}\text{Br}_3\text{NO}_4$	$\text{C}_{19}\text{H}_{20}\text{Br}_3\text{NO}_4$	
MS m/z	EIMS 461 (<1), 459 (0.3), 457 (>1), 443 (6), 441 (13), 439 (6), 244 (30), 242 (35), 241 (18), 227 (14), 225 (15), 201 (19), 200 (98), 199 (21), 198 (100), 187 (28), 185 (28), 120 (20), 107 (23), 77 (18) HREIMS 460.9477 ($\text{C}_{17}\text{H}_{17}^{81}\text{Br}_2\text{NO}_4$ calcd 460.9494), 458.9483 ($\text{C}_{17}\text{H}_{17}^{79}\text{Br}^{81}\text{BrNO}_4$ calcd 458.9514), 456.9507 ($\text{C}_{17}\text{H}_{17}^{79}\text{Br}_2\text{NO}_4$ calcd 456.9534)	HRFABMS [M+H] ⁺ $\text{C}_{19}\text{H}_{16}\text{Br}_3\text{NO}_4$ EIMS 541 (<1), 539 (<1), 537 (<1), 535 (<1), [M ⁺ -H ₂ O] 523 (2), 521 (7), 519 (6), 517 (2), 244 (9), 242 (10), 201 (15), 200 (100), 199 (16), 198 (100), 187 (16), 185 (17), 120 (20), 77 (13) HREIMS 540.8558 ($\text{C}_{17}\text{H}_{16}^{81}\text{Br}_3\text{NO}_4$ calcd 540.8572), 538.8586 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}^{81}\text{Br}_2\text{NO}_4$ calcd 538.8593), 536.8631 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}_2^{81}\text{BrNO}_4$ calcd 536.8612), 534.8605 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}_3\text{NO}_4$ calcd 534.8633), [M ⁺ -H ₂ O] 522.8446 ($\text{C}_{17}\text{H}_{14}^{81}\text{Br}_3\text{NO}_3$ calcd 522.8464), 518.8497 ($\text{C}_{17}\text{H}_{14}^{79}\text{Br}_2^{81}\text{BrNO}_3$ calcd 518.8504), 516.8509 ($\text{C}_{17}\text{H}_{14}^{79}\text{Br}_3\text{NO}_3$ calcd 516.8524)	HRFABMS [M+H] ⁺ $\text{C}_{19}\text{H}_{20}\text{Br}_3\text{NO}_4$ EIMS 405 (7), 403 (6), 229 (7), 227 (7), 177 (11), 149 (16), 78 (13), 77 (15) HREIMS 403.418	
MP (°C)	NA	NA	NA	NA
[α] _D	-31° (c 1.83, MeOH)	-23° (c 0.66, MeOH)	-24° (c 0.10, MeOH)	NA
UV λ_{\max} (MeOH) nm	208 (4.43), 281 (3.69)	208 (4.45), 281 (3.60)	NA	NA
IR ν_{\max} (KBr) cm^{-1}	(Film) 3381, 1643, 1541, 1495, 1420, 1289	(Film) 3387, 1651, 1497, 1279, 1256, 1057	(Film) 3381, 1643, 1539, 1478, 1279	3393, 2930, 1651, 1537, 1497, 1472, 1258
236 (41)	239 (145)	240 (145)	241 (145)	
Appearance	Mixture with hemibastadinol-2	White needles	White needles	
Molecular formula	$\text{C}_{17}\text{H}_{16}\text{Br}_3\text{NO}_4$	$\text{C}_{19}\text{H}_{17}\text{Br}_2\text{NO}_4$	$\text{C}_{19}\text{H}_{18}\text{BrNO}_4$	
MS m/z	EIMS 541 (<1), 539 (<1), 537 (<1), 535 (<1), [M ⁺ -H ₂ O] 523 (2), 521 (7), 519 (6), 517 (2), 244 (9), 242 (10), 201 (15), 200 (100), 199 (16), 198 (100), 187 (16), 185 (17), 120 (20), 77 (13) HREIMS 540.8558 ($\text{C}_{17}\text{H}_{16}^{81}\text{Br}_3\text{NO}_4$ calcd 540.8572), 538.8586 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}^{81}\text{Br}_2\text{NO}_4$ calcd 538.8593), 536.8631 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}_2^{81}\text{BrNO}_4$ calcd 536.8612), 534.8605 ($\text{C}_{17}\text{H}_{16}^{79}\text{Br}_3\text{NO}_4$ calcd 534.8633), [M ⁺ -H ₂ O] 522.8446 ($\text{C}_{17}\text{H}_{14}^{81}\text{Br}_3\text{NO}_3$ calcd 522.8464), 518.8497 ($\text{C}_{17}\text{H}_{14}^{79}\text{Br}_2^{81}\text{BrNO}_3$ calcd 518.8504), 516.8509 ($\text{C}_{17}\text{H}_{14}^{79}\text{Br}_3\text{NO}_3$ calcd 516.8524)	EIMS 484.9 (3), 482.9 (6), 480.9 (3), 177 (17), 149 (20), 134 (100), 106 (25), 78 (15), 77 (13) HREIMS 480.9526	EIMS 405 (7), 403 (6), 229 (7), 227 (7), 177 (11), 149 (16), 78 (13), 77 (15) HREIMS 403.418	
MP (°C)	NA	169–171	173–175	
[α] _D	-24° (c 0.10, MeOH)	NA	NA	NA
UV λ_{\max} (MeOH) nm	NA	(EtOH) 205 (10900), 220 (10300), 225 sh (9900), 325 (15900)	(EtOH) 206 (10800), 214 (9600), 230 sh (9400), 328 (14100)	(EtOH) 204 (13200), 227 sh (10600), 329 (14100)

	236 (41)	239 (145)	240 (145)	241 (145)
IR ν_{\max} (KBr) cm^{-1}	(NaCl film) 3381, 1643, 1539, 1478, 1279	(CHCl ₃) 3410, 3018, 2927, 2855, 1735, 1650, 1607, 1513, 1496, 1468, 1423, 1265, 1171, 1087, 909	(CHCl ₃) 3409, 3018, 1700, 1650, 1607, 1513, 1468, 1423, 1250, 1171, 1087, 1001, 949	(CHCl ₃) 3409, 3018, 2927, 2855, 1730, 1693, 1653, 1607, 1513, 1486, 1463, 1441, 1259, 1171, 1089, 1054, 1019
242 (145)	243 (146)	244 (146)	245 (146)	247 (123)
Appearance	Colorless gum	NA	NA	Yellow amorphous solid
Molecular formula	C ₁₉ H ₁₈ BrNO ₄	C ₂₃ H ₂₈ Br ₂ N ₂ O ₄	C ₂₄ H ₂₈ BrIN ₂ O ₄	C ₁₇ H ₂₂ Br ₂ N ₃ O ₂
MS m/z	EIMS 405 (8), 403 (7), 229 (8), 227 (7), 177 (12), 149 (18), 135 (9), 134 (100), 106 (21), 78 (13), 77 (16) HREIMS 403.0418	FABMS 571, 569, 567 [M+H] ⁺	FABMS 617, 615 [M+H] ⁺	FABMS 803, 805, 807, 809, 811 [M] ⁺ , 466, 468, 470, 426, 428, 430, 409, 411, 413 HRFABMS 806.9007 [M] ⁺
MP (°C)	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA
UV λ_{\max} (MeOH) nm	(EtOH) 203 (11100), 224 sh (9100), 326 (11700)	NA	NA	214 (20600), 258 sh (3800)
IR ν_{\max} (KBr) cm^{-1}	(CHCl ₃) 3413, 3018, 2935, 1710, 1650, 1607, 1513, 1466, 1425, 1248, 1168, 1087, 1001, 949	(Neat) 3286, 1635, 1542, 1515, 1455, 1256	(Neat) 3283, 1628, 1537, 1514, 1443, 1260	NA
246 (38)	248 (150)	249 (151)	250 (151)	252 (152)
Appearance	Amorphous solid	Small yellow crystals	Small yellow crystals	Yellow amorphous solid
Molecular formula	C ₁₅ H ₁₇ N ₄ O ₂ Br ₂	C ₁₇ H ₁₆ Br ₂ N ₄ O ₂	C ₁₆ H ₁₄ Br ₂ N ₄ O ₂	C ₂₂ H ₂₂ N ₃ O ₃ Br ₃
MS m/z	FABMS 443, 445, 447	HREIMS 467.9624 [M] ⁺	HREIMS 453.9460 [M] ⁺	FABMS 614, 616, 618, 620 (1:3:3:1) [M+H] ⁺ HRFABMS 615.9280 (M+H) ⁺ (+1.8 mmu)
MP (°C)	NA	236	242	NA
[α] _D	NA	NA	NA	NA
UV λ_{\max} (MeOH) nm	(EtOH) 226 (12200), 298 (32000)	NA	NA	285 (5000), 350 (1200)
IR ν_{\max} (KBr) cm^{-1}	(Dry film) 1690	NA	NA	3422, 1680
253 (153)	254 (153)	255 (153)	256 (154)	257 (154)
Appearance	Needles	White amorphous solid	White solid	White gum
Molecular formula	C ₁₈ H ₁₅ N ₂ O ₃ Br	C ₁₈ H ₁₅ N ₂ O ₃ I	C ₁₉ H ₂₁ N ₂ O ₂ Br	C ₁₉ H ₂₀ N ₂ O ₂ Br ₂
MS m/z	HRFABMS [M ⁺ +H] 387.0313	HREIMS 434.0146	HREIMS 308.1159	HREIMS 465.9891 [M ⁺]

	253 (153)	254 (153)	255 (153)	256 (154)	257 (154)
MP (°C)	178–179	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	(MeOH) 324 (8400), 290 (5000), 274 (9600), 267 (9900), 255 (10300), 205 (41400) (MeOH+NaOH), 309 (9800), 272 (8600), 266 (9900), 247 (1600), 207 (58500)	(MeOH) 325 (6600), 274 (8200), 267 (sb), 254 (9100), 230 (sb), 205 (50000) (MeOH +NaOH), 311 (8200), 274 (7600), 267 (sb), 247 (13200), 203 (79100)	(MeOH) 324 (4600), 285 (sb), 272 (5700), 266 (6100), 254 (6400), 205 (19200) (MeOH+NaOH), 218 (4600), 272 (5300), 266 (6100), 246 (8300), 205 (21400)	288 (sb), 280 (6400), 221 (30600), 208 (29000)	(DMSO) 299 (sb), 287 (2500), 279 (sb), 221 (30600), 208 (29000)
IR ν _{max} (KBr) cm ⁻¹	(CHCl ₃) 3010, 1680, 1635, 1500, 1420, 1215, 1120	(neat NaCl) 2930, 1680, 1640, 1505, 1420	NA	(CHCl ₃) 3470, 3330 br, 1605, 1500, 1460, 1445, 1420, 1285, 1260, 1055	(CHCl ₃) 3470, 3330 br, 1605, 1500, 1460, 1445, 1420, 1285, 1260, 1055

	258 (155)	259 (164)	260 (158)	261 (158)	262 (159)
Appearance	Gum	NA	Colorless prisms	Colorless crystals	Colorless glass
Molecular formula	C ₁₂ H ₁₇ NO ₅	C ₃₆ H ₄₅ IN ₄ O ₆ Br	C ₂₈ H ₄₀ IN ₃ O ₆	C ₂₈ H ₄₀ BrN ₃ O ₆	C ₂₈ H ₄₀ N ₃ O ₆ Cl
MS m/z	FABMS 256 (M+H ⁺ , 100) HRFABMS 256.11858, 256.11850	NA	FABMS 642 (100) [MH ⁺], 516 (50), 393 (15), 276 (30), 217 (50), 150 (50)	FABMS 594 (95) [MH ⁺], 516 (60), 345 (30), 267 (30), 228 (80), 150 (100) (mmu)	HREIMS 549,2603, 551.2562 (-0.2, -1.4 (mmu))
MP (°C)	NA	NA	217–218	203–204	NA
[α] _D	+25.51° (c 0.002, MeOH)	+35° (c 3.62, CHCl ₃)	+53° (c 0.04, CHCl ₃)	+101° (c 0.04, CHCl ₃)	NA
UV λ _{max} (MeOH) nm	NA	281 (5400), 290 (4100)	219 (13800), 284 (3200), 292 (3000)	214 (15400), 281 (2700), 290 (2500)	NA
IR ν _{max} (KBr) cm ⁻¹	NA	(CDCl ₃) 3400–3100, 1710, 1660, 1630	(CHCl ₃) 1725, 1670, 1655, 1630	(CHCl ₃) 3510, 3410, 1725, 1670, 1655 (sb), 1630	NA

	263 (159)	264 (159)	265 (159)	266 (164)	267 (161)
Appearance	Colorless glass	NA	NA	Colorless glass	NA
Molecular formula	C ₂₇ H ₃₈ N ₃ O ₆ I	C ₂₇ H ₃₈ N ₃ O ₆ Br	C ₂₇ H ₃₈ N ₃ O ₆ Cl	C ₂₈ H ₃₈ N ₃ O ₇ I	C ₃₄ H ₄₄ O ₇ N ₃ I
MS m/z	HREIMS 627.1798 (-0.9 mmu)	HREIMS 579.1955, 581.1909 (+1.1, -1.6 (mmu))	HREIMS 535.2449, 537.2442 (0.0, +2.2 (mmu))	HREIMS 655.1760 (M, 0.6 mmu)	EIMS 773 (48) [M] ⁺ , 706 (10), 608 (15), 552 (5), 460 (54), 413 (17), 321 (24), 276 (100), 250 (19), 162 (73), 109 (46), HREIMS 733.2199
MP (°C)	NA	NA	NA	NA	186–189
[α] _D	NA	NA	NA	NA	+19.1° (c 0.17, CHCl ₃)
UV λ _{max} (MeOH) nm	NA	NA	NA	NA	215 (12500), 280 (2800)
IR ν _{max} (KBr) cm ⁻¹	NA	NA	NA	3313, 1732, 1675, 1635	3495, 1724, 1670

	268 (161)	271 (164)	272 (164)	273 (164)	274 (164)
Appearance	NA	Colorless glass	Colorless glass	Colorless glass	Colorless glass
Molecular formula	C ₃₄ H ₄₄ O ₇ N ₃ Br	C ₂₈ H ₃₉ N ₃ O ₇ Br	C ₂₈ H ₃₉ N ₃ O ₇ Cl	C ₂₈ H ₄₀ N ₃ O ₇ I	C ₂₈ H ₃₉ N ₃ O ₇ Br
MS <i>m/z</i>	EIMS 685 (38) [M] ⁺ , 657 (10), 460 (52), 413 (24), 273 (26), 228 (100), 162 (87), 109 (59) HREIMS 685.2374	HRDCIMS 610.19509, 608.19713 (C ₂₈ H ₃₉ N ₃ O ₇ ⁸¹ Br, C ₂₈ H ₃₉ N ₃ O ₇ ⁷⁹ Br); found 610.19431, 608.19508 (-1.49, -3.38 ppm)	HRDCIMS 565.23688, 563.23981 (C ₂₈ H ₃₉ N ₃ O ₇ ³⁷ Cl, C ₂₈ H ₃₉ N ₃ O ₇ ³⁵ Cl); found 565.23956, 563.24011 (-0.5 ppm)	HREIMS 658.19892, found 658.19767 (-1.91 ppm)	HREIMS 611.20294, 609.20496 (C ₂₈ H ₄₀ N ₃ O ₇ ⁸¹ Br, C ₂₈ H ₄₀ N ₃ O ₇ ⁷⁹ Br); found 611.20371, 609.20519 (-1.3, -0.4 ppm)
MP (°C)	168–170	NA	NA	NA	NA
[α] _D	+39.3° (c=0.17, CHCl ₃)	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	214 (14000), 280 (3000)	NA	NA	NA	NA
IR ν _{max} (KBr) cm ⁻¹	(CHCl ₃) 3500, 1725, 1670	NA	NA	NA	NA

	275 (164)	276 (164)	277 (164)	278 (164)
Appearance	Colorless glass	Colorless glass	Colorless glass	Colorless glass
Molecular formula	C ₂₈ H ₃₉ N ₃ O ₇ Cl	C ₂₈ H ₄₀ O ₇ N ₃ I	C ₂₈ H ₃₉ N ₃ O ₇ Br	C ₂₇ H ₃₈ O ₇ N ₃ I
MS <i>m/z</i>	HREIMS 567.25250, 265.25549 (C ₂₈ H ₄₀ N ₃ O ₇ ³⁷ Cl, C ₂₈ H ₄₀ N ₃ O ₇ ³⁵ Cl); found 567.25184, 565.25403 (1.2, 2.6 ppm)	HREIMS 658.19892, found 658.19880 (-0.19 ppm)	HREIMS 611.20294, 609.20496 (C ₂₈ H ₄₀ N ₃ O ₇ ⁸¹ Br, C ₂₈ H ₄₀ N ₃ O ₇ ⁷⁹ Br); found 611.20374, 609.20515 (-1.3, -0.3 ppm)	HREIMS 643.17548, found 643.17539 (-0.1 ppm)
MP (°C)	NA	NA	NA	NA
[α] _D	NA	NA	NA	NA
UV λ _{max} (MeOH) nm	NA	NA	NA	NA
IR ν _{max} (KBr) cm ⁻¹	NA	NA	NA	NA

	269(164)	270 (164)	280 (167)	281 (168)	282 (167)
Appearance	Colorless glass	Colorless amorphous solid	Yellowish needles	Yellow oil	Yellowish, fluorescent oil
Molecular formula	C ₃₀ H ₄₄ N ₃ O ₆ I	C ₃₈ H ₂ Br ₈ NO ₇ · (CH ₃) ₂ CO	C ₃₀ H ₁₃ Br ₈ NO ₆	EIMS 1123 (20) [M+], 596 (55), 526 (55), 448 (15), 337 (20), 279 (55)	C ₂₄ H ₁₅ Br ₄ NO ₅
MS <i>m/z</i>	HRMS 670.2335 [MH] ⁺	FABMS 656 [M+H] ⁺	NA	NA	HRMS 719.0348
MP (°C)	NA	NA	285	NA	NA
[α] _D	+30° (c=0.027, CHCl ₃)	+5.2°	NA	NA	NA
UV λ _{max} (MeOH) nm	NA	219 (13270), 284 (4000), 292 (3000)	36 (17000), 300s (11700)	NA	400 (2000), 280 (5250) (MeOH/KOH) 515 (2800), 400 (2800), 300 (5000)
IR ν _{max} (KBr) cm ⁻¹	(Neat) 3420, 1720, 1670, 1655, 1630	NA	(CHCl ₃) 3500, 2900, 1645, 1580, 1514, 1300	(Neat) 3500, 1645, 1582, 1515	3500, 2919, 1699, 1400

	283 (167)	284 (168)	229 (41)	230 (41)
Appearance	Yellowish fluorescent oil	Yellow oil	White solid	White solid
Molecular formula	$C_{25}H_{17}Br_4NO_5$	$C_{16}H_6Br_4O_5$	$C_{20}H_{22}Br_2N_2O_4$	$C_{20}H_{21}Br_3N_2O_4$
MS m/z	HRMS 732.0619 [M+H] ⁺	HREIMS 597.6915	EIMS 516 (1), 514 (2), 512 (1), 258 (2), 257 (2), 256 (3), 255 (9), 228 (10), 227 (64), 226 (14), 225 (65), 215 (10), 214 (38), 213 (11), 212 (46), 201 (61), 199 (65), 149 (48), 146 (40), 57 (100) HREIMS 511.9948	EIMS 596 (0.4), 594 (2), 592 (2), 590 (0.4), 565 (<<1) 563 (1), 561 (1), 559 (<<1) 366 (0.3), 364 (1), 362 (0.4), 338 (0.6), 336 (2), 334 (0.7), 308 (1), 307 (10), 306 (4), 305 (20), 304 (4), 303 (10), 302 (1), 292 (5), 290 (10), 288 (5), 281 (6), 279 (14), 277 (7), 257 (2), 255 (2), 224 (2), 223 (3), 222 (3), 221 (2), 215 (15), 214 (97), 213 (16), 212 (100), 201 (30), 199 (34), 185 (4), 183 (11), 181 (8), 134 (16), 105 (17), 77 (39) HREIMS 589.9049
MP (°C)	NA	NA	NA	NA
$[\alpha]_D$	NA	NA	NA	NA
(MeOH) nm			NA	NA
(KBr) cm^{-1}	3500, 1702, 1698, 1400	(Neat) 3460, 1761, 1721, 1475	NA	NA

TABLE II

¹H and ¹³C NMR Data of Bromotyrosine Derivatives.

	1 (176)		5 (7)		6 (7)		14 (14)		15 (11)	
	¹ H	¹³ C	¹ H	acetone- <i>d</i> ₆	¹ H	acetone- <i>d</i> ₆	¹ H	¹³ C (12)	¹ H	¹³ C
1		72.8						75.8		74.2
2	7.59 s	121.5	7.20 s		7.14 s		4.10 br	87.8	7.30 d, 2.2	146.6
3		153.2					106.4			123.7
4		174.5					150.1			183.0
5		153.2					118.1		5.72 d, 2.2	57.1
6	7.59	121.5	7.20 s		7.14 s		6.34	134.9	4.44 ddd, 2.2, 2.2, 5.6	78.9
7	2.75	46.0	2.58 s		2.57 s		2.74 s	41.7	3.11 s	28.4
8		173.0					171.9			116.9
NH	2.97		6.68, 6.77 s		6.65, 6.76 s					
OMe			3.07 s		3.10 s		3.70 s	60.0		
OH			5.88 s		5.85 s		2.28		5.96 d, 5.6, 5.93 s	
1'			3.25 t		3.22 t					
2'			1.55 m		1.50 m					
3'			1.41 m		1.50 m					
4'			0.98 t		1.50 m					
5'					0.98 t					

	16 (11)		18 (19)		19 (7)		20 (7)	
	¹ H	¹³ C	¹ H	¹³ C (12)	¹ H	¹³ C	¹ H	¹³ C
1		75.5						
2	7.52 s	151.7	5.20 d, 0.7	113.4			162.0	
3		122.7		147.9			111.8	
4		183.0		120.4			150.8	
5	5.04 d, 11.2	56.1		133.2			117.5	
6	4.28 dd, 11.2, 5.0	78.4	6.36 d, 0.7	73.9	7.65 s	125.8	7.48 s	

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		16 (11)		18 (19)		19 (7)		20 (7)	
¹ H	¹³ C	¹ H	¹³ C (12)	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
acetone-d ₆	acetone-d ₆	CDCl ₃	acetone-d ₆	CDCl ₃	acetone-d ₆	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃
7	3.15 dq, 14.0	28.4	2.88 d, 18	26.3	100.7	3.67 s			
8		116.9		117.5	165.2				
9					154.3				
NH						5.82 s			
10			2.39 s	23.7					
11			2.59 s	25.2					
OMe			3.79 s	59.6		3.85 s			
OH	5.98 d, 5.0, 5.70 s		3.38						

		21 (20)		22 (22)		23 (22)		24 (23)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CDCl ₃	CDCl ₃	acetone-d ₆	DMSO-d ₆	acetone-d ₆	DMSO-d ₆	DMSO-d ₆	DMSO-d ₆	DMSO-d ₆	DMSO-d ₆
1	147.2	7.6 br	7.6 br						
2	109.1		173.9		173.5				7.1 br
3	113.7	2.92 d, 16.8 2.48 d, 16.8	42.3	2.75 d, 16.8 2.58 d, 16.8	44.1	2.60 d, 16.8 2.69 d, 16.8			172.4
3a			75.5		74.2				43.4
4	146.4	7.44 s	150.4	7.33 d, 0.6	149.2	7.28 br			73.9
5	NA		119.0		119.2				149.7
6	NA		183.7		183.9				122.2
7	103.8	5.16 d, 9.8	57.4	5.28 d, 4.2	52.7	2.82 dd, 16.4, 4.9 3.06 dd, 16.4, 4.9			188.6
7a		4.22 dd, 9.8, 1.6	68.3	4.46 brd, 4.2	63.4	4.14 brt			39.5
8	165.9								58.4
9	8.21 d, 11.4	148.9							
10	7.74 ddq, 14.3, 11.4, 1.6	144.7							
11	6.59 dq, 14.3, 7.4	128.1							
12	2.07 dd, 7.4, 1.6	19.8							
OH				5.5 br		5.6 br			5.4 br

	25 (9)		26 (9)		27 (9)		28 (9)		29 (9)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	acetone- <i>d</i> ₆	acetone- <i>d</i> ₆	5.5 br	DMSO- <i>d</i> ₆	5.5 br	5.5 br	5.6 br	5.6 br	5.6 br	5.6 br
2		176.3		173.6						
3	2.70 s	45.0	2.90 d, 16.9 2.50 d, 16.9	42.4	2.74 d, 16.9 2.59 d, 16.9	2.90 d, 16.9 2.48 d, 16.9	2.90 d, 16.9 2.48 d, 16.9	2.74 d, 16.9 2.56 d, 16.9	2.74 d, 16.9 2.56 d, 16.9	
3a		74.8		74.4						
4	7.03 d, 0.9	145.4	7.21 s	146.3	7.07 br	7.43 s	7.43 s	7.32 br	7.32 br	
5		133.0		127.4						
6		183.1		183.4						
7	3.04, 2.80 d, 16.4	41.0	5.15 d, 9.8	58.0	5.24 d, 4.1	5.06 d, 10.4	5.06 d, 10.4	5.26 d, 3.8	5.26 d, 3.8	
7a	4.14 ddd, 6.0, 5.1, 0.9	60.8	4.19 brd, 9.8	67.9	4.8 brd, 4.1	4.03 brd, 10.4	4.03 brd, 10.4	4.48 brd, 3.8	4.48 brd, 3.8	

	30 (24)		31 (25)		43 (35)		44 (35)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD
1		80.9		82.7		128.8		136.4
2					7.46 s	134.2	7.30 s	135.1
3		168.3		171.4		113.0		119.0
4	2.64 br	43.1	2.66 dd, 18.0, 1.7 2.55 dd, 18.0, 1.7	44.0		153.4		154.8
5		69.5		69.5		113.0		119.0
6	7.43 d, 2.2	156.9	7.16 d, 2.2	153.2	7.46 s, 3.12 t, 12.0	134.2	7.0 s, 3.12 t, 12.0	135.1
7		118.8		129.5	3.29	32.8	3.29	32.9
8		187.8		188.9	8.73 dd, 12.0, 3.5	81.3	3.74 dd, 12.0, 3.5	81.0
9	2.43 d, 12.5 2.31 dd, 12.5, 2.2	46.6	2.44 dd, 12.4, 1.7 2.32 dd, 12.4, 2.2	47.6		170.6		170.6
OMe								
N(Me) ₃					3.28	52.7	3.81 s	61.0
							3.30 s	52.7

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		45 (35)		46 (35)		51 (40)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
D ₂ O	CD ₃ OD	D ₂ O	CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆
1	130.5		128.0		136.7		136.7
2	7.22 d, 2.0	135.3	134.9	7.58 s	133.1		133.1
3		112.8	111.4		117.6		117.6
4		156.8	155.8		152.2		152.2
5	6.66 d, 8.5	113.9	117.8	6.65 d, 8.5	117.6		117.6
6	6.95 dd, 8.5, 2.0; 2.80 t, 12.0	131.0	130.7	6.89 dd, 8.5, 2.0; 2.80 t, 12.0	133.1		133.1
7	2.95 ^a	33.7	33.2	3.01 ^a	31.4		31.4
8	3.42 dd, 12.0, 3.7	81.9	81.6	3.52 dd, 12.0, 3.7	39.4		39.4
9		170.5	170.9				
OMe	3.54 s	57.0	3.76	60.3			
N(Me) ₃	2.96 s	53.2	52.7				

		48 (38)		207 (41)		52 (42)		54 (44)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD	CD ₃ OD
1	136.4		132.8		137.1				
2	7.69 s	134.84	130.0	7.01 dd, 2.0, 8.2	133.1	7.30 s	133.1	7.62 s	134.4
3		119.21	117.3	6.81 d, 8.2	117.5		117.5		
4		154.46	154.0		150.8		150.8		
5		119.21	110.8		117.5		117.5		
6	7.69 s	134.84	134.3	7.33 d, 2.0	133.1	7.30 s	133.1	7.62 s	
7	3.17 ddd, 17.5, 12.5, 5.5	29.04	35.0	2.72 t, 7.4	31.3	2.70 t	31.3	3.02 t, 8.0	35.2
8	3.67 ddd, 17.5, 12.5, 5.5	67.54	42.2	3.41 t, 7.4	39.6	2.92 t	39.6	3.50 t, 8.0	41.3
9			161.8		70.4	3.84 t	70.4	4.12 t, 5.5	71.7
10			164.0		27.6	1.97 m	27.6	2.30 t, 5.5, 5.5	26.4
11					36.4	3.07 t	36.4	3.22 t, 5.5	56.9
OMe	3.85 s	61.42							
N(Me) ₃	3.32 s	54.11							
NH(Me) ₂								2.91, 2.96 s	43.7, 43.6

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	55 HCl salt (45)		56 HCl salt (45)		59a (47)		57 (46)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1		NA	CD ₃ OD	NA	CD ₃ OD	CD ₃ OD	CDCl ₃	CDCl ₃
2	7.62 s		7.59 s		7.40 s	140.4	7.35 s	137.6
3						134.3		132.9
4						118.7		118.2
5						152.2		151.6
6	7.62 s		7.59 s		7.40 s	118.7	7.35 s	118.2
7	3.01 t, 8.1		3.23 t, 8.1		2.72 t, 7.5	134.3	2.65 t, 7.0	132.9
8	3.25 t, 8.1		2.94 t, 8.1		3.35 t, 7.5	35.1	3.40 q, 6.8	35.0
9	4.13 t, 5.5		4.12 t, 5.5		4.12 t, 7.5	41.4	4.05 t, 6.5	41.9
NH						71.1	4.70 brt	71.1
10	2.24 tt, 5.5, 8.4		2.30 tt, 5.5, 8.4		2.38 m	26.4	2.05 m	27.1
11	3.34 t, 8.4		3.52 t, 8.4		3.51 t, 7.5	57.0	2.75 t, 7.0	56.0
OMe							3.70 s	52.1
N(Me) ₂	2.93 s		2.96 s		3.0 s	43.72C	2.32 s	44.4
NH ₂ (Me)	2.77 s		2.72 s					
NHAc					2.01 s	22.6		
CO						173.3		156.8

	58 (46)		60 (49)		61 (50)		62 (51)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1		CD ₃ OD	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆ -TEA	CD ₃ OD
2	7.38 s	140.4	7.59 s	136.8	7.66 s	141.8	7.50 s	141.2
3		134.3		133.2		131.6		135.2 ^a
4		118.7		117.5		119.4		119.6
5		152.1		151.1		154.0		153.3
6	7.38 s	118.7	7.59 s	117.5	7.66 s	119.4	7.50 s	119.6
7	2.70 t, 7.0	134.3	7.82 t, 7.2	133.2	4.86 1H, m	69.2	2.65 t, 7.0	135.3 ^a
8	3.20 q, 6.8	42.8	3.07 t, 7.2	39.3	3.16 dd, 3.5, 1.3	46.9	3.32 m	42.8

	58 (46)		60 (49)		61 (50)		62 (51)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
9	4.05 t, 6.5	71.1	3.95 t, 5.7 9.92 br	70.6	4.04 t, 6	71.6	3.98, 4.07, m	71.1
NH								
10	2.30 m	26.4	1.99 tt, 6.1, 5.7	28.6	2.09 m	30.1	2.35, 2.70, m	30.3
11	3.50 t, 7.0	57.1	3.43 t, 6.1	36.8	3.56 t, 7	38.4	4.35 dd, 2.1, 2.7	77
12				143.0		145.2		165 ^b
13				112.4		113.1		174.1
14					1.79 s			23.8
OMe	3.65 s	52.5					3.25 s	53.6
N(Me) ₃								
NH(Me) ₂	3.00 s	44.0						
CO		159.5						
NH ₃			7.79 br					

	63 (53)		64 (53)		65 (54)		67 (21)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1		133.0		136.6		140.6		140.0
2	7.63 s	132.0	7.70 s	132.7	7.75 s	131.9	7.75 s	130.8
3		118.9		119.4		119.3		118.2
4		154.0		154.0		153.5		142.3
5		118.9		119.4		119.3		118.2
6	7.63 s	132.0	7.70 s	132.7	7.75 s	131.9	7.75 s	130.8
7	7.46 d, 16.0	141.0	7.21 d, 15.9	128.1	5.60 dd, 8.7, 4.5		5.65 dd, 8.7, 9.2	53.6 ^a
8	6.04 d, 16.0	120.1	6.44 d, 15.9	137.8	3.38 d, 9.3 3.89 d, 9.0		3.71 dd, 9.3, 11.5 4.30 dd, 7.1, 8.5	41.5
9		166.3		174.0		160.2 ^c		158.4 ^b
10	4.06 t, 6.2	72.2	4.10 t, 5.6	71.4	4.16 d, 7.1		4.15 dd, 4.5, 4.2	53.0
11	2.12 tt, 7.1, 6.2	28.2	2.25 tt, 7.8, 6.5	26.7	4.96 d, 8.7		4.96 dd, 7.1, 7.1	54.1 ^a
12	2.72 t, 7.1	56.1	3.40 t, 7.8	56.8	3.61 d, 7.1		3.52 dd, 9.0, 8.5	47.0

	63 (53)		64 (53)		65 (54)		67 (21)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
13	CDCl ₃	CDCl ₃	CD ₃ OD	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CDCl ₃	CDCl ₃
14							3.65 dd, 8.7, 8.5	157.8 ^b
NMe ₂	2.38 s	45.5	2.83 s			159.8 ^c		
OEt	4.23 d, 7.1	60.7						
OEt	1.30 t, 7.1	14.3						

	68 (58)		69 (58)		70 (62)		71 (63)	
	¹ H (820)	¹³ C (6485)	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	acetone- <i>d</i> ₆	CD ₃ OD	CDCl ₃ + DMSO- <i>d</i> ₆	1%TFA in DMSO- <i>d</i> ₆	CDCl ₃ + CD ₃ OD 4:1	CDCl ₃ + CD ₃ OD 4:1	acetone- <i>d</i> ₆	CDCl ₃
1,1'	4.18 d, 8	75.5	4.16 s	73.6	4.10 s, 4.11 s	73.9	4.16 d, 7	73.8
2,2'		114.2		113.1		113.5		113.1
3,3'		149.3		147.2		147.9		147.7
4,4'		122.7		120.8		121.8, 121.7		121.4, 121.3
5,5'	6.50 s	133.2	6.28 s	131.3	6.17 s	130.8	6.51 s	130.6
6,6'		92.6		90.3		91.9, 91.8		91.9, 91.8
7,7'	3.84 d, 18 3.14 d, 18	40.1	3.87 d, 18.5 3.02 d, 18.5	42.5	3.70, 3.71 d, 18 2.85 d, 18	39.7	3.82, 3.83, d, 18, 3.12 d, 18	38.7
8,8'		155.5		154.5		154.1		153.9
9,9'		161.6		159.0		160.3		160.0
NH	7.58 bt		7.60 b	8.10, 2H t, 6.9			7.56 brt, 6 7.81 brt, 6	
10	3.34 m	38.4	3.35 m	39.0	3.46 dd, 14, 3 3.32 dd, 14, 7	36.4	3.29 m, 3.52 m	36.2
11	1.60 m	26.1	1.69 m	71.0	3.60 m	68.1	3.79 m	68.0
12		26.1			1.73, 1.61 m	45.3	1.97, 1.60 m	45.0
13		38.4			3.55, 3.37 m	33.8	3.43 2H m	33.6
OMe	3.72 s	60.4	3.73 s	59.6	3.59 s	60.3	3.71 s	60.0
OH	5.37 d, 8						5.46, 5.47 d, 7	

	72 (64)		74 (61)		73 (61)		75 (65)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1,1'	3.94 d, 8.5 3.88 d, 8.5	73.6	4.15 d, 0.9 4.13 d, 0.9	75.5	4.14 d, 0.9 4.13 d, 0.9	75.5	4.16 s 4.14s	75.5
2,2'		113.1		114.1		114.1		114.2
3,3'		147.1		149.3		149.3		149.3
4,4'		120.9, 120.8		122.8		122.8		122.8
5,5'	6.60 s 6.57 s	131.2	6.46d, 0.9 6.47d, 0.9	132.2 133.2	6.47 d, 0.9 6.45 d, 0.9	132.2 133.2	6.46s 6.47s	132.3
6,6'		90.5, 90.2		92.6, 92.5		92.6, 92.5		92.6, 92.4
7,7'	3.60 d, 18.2 3.19 d, 18.2	39.7 39.5	3.14, 3.13 d, 18.3 3.82, 3.81 d, 18.3	40.1 40.0	3.15, 3.12 d, 18.3 3.82, 3.81 d, 18.3	40.1 40.0	3.15, 3.13 d, 18 3.82, 3.80 d, 18	40.2 40.0
8,8'		154.4, 154.1		155.1, 154.9		155.1, 154.9		155.3, 154.9
9,9'		159.1, 158.9		161.9, 161.8		161.9, 161.8		161.8
NH	8.66, 8.48 t, 5.5							
10	4.02 d, 5.7	48.5	4.43, 4.42 d, 18.8	49.9	4.43, 4.43 d, 18.8	49.9	4.12 s	49.2
11		204.4		207.8		207.8		206.2
12	2.70 2H t, 6.8	38.6	4.41 dd, 6.3, 4.9	75.7	4.40 dd, 6.3, 4.9	75.7	2.60 t, 7	37.57
13	3.34 2H m	33.8	3.66 dd, 13.9, 4.9 3.63 dd, 13.9, 6.3	43.4	3.66 dd, 13.9, 4.9 3.63 dd, 13.9, 6.3	43.4	1.88 dt, 7, 7	24.1
14							3.32 t, 7	39.6
OMe	3.63, 3.60 3H s	59.6	3.76 3H s	60.4	3.76 3H s	60.4	3.75 3H s	60.4
OH	6.41, 6.35 d, 8.5							

	76 (66)		77 (67)		78 (30)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1,1'	3.93 s	74.1	acetone-d ₆ 4.38 dd, 5, 12 4.40 dd, 5, 12	acetone-d ₆ 74.7, 74.8	DMSO-d ₆ 4.13 dd, 2.6 ^b , 3.7	DMSO-d ₆ 56.9
2,2'		113.5	5.08 d, 12; 5.06 d, 12	57.1	3.93 d, 3.5	53.0
3,3'		147.6		183.5		186.0
4,4'		121.2		122.5, 122.4		122.7
5,5'	6.57 s	131.7	7.63 s; 7.67 s	149.1, 149.2	7.49 d, 2.6	143.7
6,6'	7.47 dd, 8.6, 1.5	90.7		91.7, 91.4		84.0

	76 (66)		77 (67)		78 (30)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CD₃OD	CD₃OD	acetone-d₆	acetone-d₆	DMSO-d₆	DMSO-d₆
7,7'	3.12 d, 18 3.62 d, 18	40.0	3.31, 3.29 d, 18 3.85, 3.86 d, 18	38.2 38.1	3.68 d, 17.8 3.61 d, 17.9	43.6
8,8'		155.0		154.5, 154.3		154.9
9,9'		159.3		159.8, 159.6		158.3
10	3.08 m, 3.15 m	45.7	4.22 d, 6	49.2	3.19 br	38.6
11	3.55 m, 3.61 m	67.4, 68.9		204.7	1.50 br	26.4
12	1.28 m, 1.40 m	32.3	2.87 t, 6	39.6		
13	1.50 m, 1.60 m	25.5	3.58 dt, 6, 6	34.8		
14	3.28 m, 3.22 m	36.6				
15	1.45 m, 1.65 m	34.4				
16	3.15 m	39.4				
OMe	3.65 m	60.1				
NH	8.41 t, 6, 8.45 t, 5		7.90 t, 6		8.63 t, 5.7	
NH	8.27 t, 6; 8.21 t, 5		7.66 t, 6			
OH	6.36 s		6.03 d, 5; 6.08 d, 5			

	79 (71)		81 (70)		82 (71)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	pyridine-d₅	pyridine-d₅	DMSO-d₆ (36)	acetone-d₆	pyridine-d₅	pyridine-d₅
1,1'	4.61, 4.58 d, 7.9	74.7	3.93, 3.91 d, 7.9	73.6	4.19 m	74.7
2,2'		115.2		113.2		115.2
3,3'		148.1		147.2		148.1
4,4'		121.8		121.1		121.9
5,5'	6.62, 6.63 s	132.4	6.58, 6.56 s	131.3 131.2	6.49, 6.51 d, 1.0	132.0 132.1
6,6'		91.9		90.4		91.9
7,7'	3.47, 3.44 d, 18.2 4.40, 4.43 d, 18.2	40.3	3.61, 3.59d, 18.8 3.24, 3.19 d, 18.8	39.4	3.16, 3.19 d, 18.5 3.85, 3.83 d, 18.5	39.839.9 40.3 40.2
8,8'		155.2, 155.3		154.5		155.2, 155.8
9,9'		160.5		159.2, 159.1		160.5, 160.6
NH	9.34, 9.71 t, 5.8		8.43, 8.39, d 5.8		7.66, 7.71 t, 5.9	9.80, 9.71 t, 5.8

	79 (71)			81 (70)			82 (71)		
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H
	pyridine- <i>d</i> ₅		DMSO- <i>d</i> ₆ (36)	acetone- <i>d</i> ₆	pyridine- <i>d</i> ₅				
10	4.25, 3.98 m	44.0	3.47, 3.29 m	42.6	3.55, 3.76 m	43.4	4.97 dd, 18.0, 5.8	47.49	
11	4.76 m	69.5	4.06 m	68.1	4.25 m	69.7		201.3	
12	4.34 dd, 8.8, 5.5; 4.26 m	76.1	3.89, 3.82 m	75.4	4.05 m	75.7	4.82s	76.1	
13		152.3		151.3		152.5		152.2	
14		118.4		117.3		118.3		118.1	
15	7.92s	131.1	7.57 s	130.5	7.65 s	131.3	7.91s	131.1	
16		143.5		142.7		142.9		144.2	
17	7.92s	131.1	7.57 s	130.5	7.65 s	131.3	7.91s	131.1	
18		118.4		117.3		118.3		118.1	
19	5.29 dd, 4.3, 5.8	69.5	4.68 m, 5.2	69.4	4.90 dd, 4.3, 7.5	71.3	5.30 dd, 7.5, 4.6	70.7	
20	3.97 m 3.81 ddd, 15.3, 5.8, 4.3	48.2	3.33 d, 5.3	46.4	3.48 m 3.61 m	47.5	3.97 ddd, 5.8, 13.3, 4.6 3.81 ddd, 5.8, 13.3, 7.5	48.0	
OMe	3.63 s	59.9	3.64 s	59.7	3.71, 3.71 s	60.2	3.63 s		
11-OH	7.23 d, 5.2		5.29 d, 5.4		5.41 br s				
1,1'-OH	8.62, 8.61 d, 7.9		6.39, 6.37 d, 7.9				8.60 br s		
17-OH	7.77 d, 4.3		5.75 d, 4.6						

	83 (63)			84 (72)			85 (72)			86 (65)		
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	(CD ₃) ₂ CO	CDCl ₃	(CD ₃) ₂ CO	(CD ₃) ₂ CO	(CD ₃) ₂ CO	(CD ₃) ₂ CO	(CD ₃) ₂ CO	(CD ₃) ₂ CO	(CD ₃) ₂ CO	(CD ₃) ₂ CO	(CD ₃) ₂ CO	CD ₃ OD
1,1'	4.15d, 6 4.16d, 6	73.9 73.8	4.23 dd, 8.1, 0.9 4.18 dd, 8.1, 0.9	75.1, 75.2	4.23, 4.18 dd, 8.1, 0.9	75.1, 75.2	4.12 s 4.11 s	75.4				
2,2'		112.7		113.8		113.9		114.2				
3,3'		147.9		148.8		148.7		149.3				
4,4'		121.4		122.1		122.1		122.7				
5,5'	6.50, 6.51 d, 1	130.9	6.56, 6.52 d, 0.9	132.3	6.57, 6.52 d, 0.9	132.3	6.46, 6.44 s	132.2				
6,6'		91.8, 91.6		91.6, 91.8		92.0, 91.6		92.5				
7,7'	3.83, 3.18 d, 18 3.81, 3.15 d, 18	38.9 38.8	3.86, 3.22 d, 18.1 3.84, 3.18 d, 18.1	40.0 40.1	3.86, 3.22 d, 18.1 3.84, 3.16 d, 18.1	40.0 40.1	3.81, 3.14 d, 18 3.79, 3.09 d, 18	40.1, 40.0				
8,8'		154.1, 154.0		155.1, 155.2		154.8, 155.2		155.3, 155.1				
9,9'		159.3		160.0, 160.4		160.2, 160.0		161.7, 161.6				

	83 (63)		84 (72)		85 (72)		86 (65)	
	¹ H (CD ₃) ₂ CO	¹³ C CDCl ₃	¹ H (CD ₃) ₂ CO	¹³ C (CD ₃) ₂ CO	¹ H (CD ₃) ₂ CO	¹³ C (CD ₃) ₂ CO	¹ H CD ₃ OD	¹³ C CD ₃ OD
NH	7.78, 7.73 t, 6							
10	3.53 q, 6	37.2	3.50, 3.70 m	43.5	4.60 d, 6.0	47.5	3.62 t, 6.5	37.9
11	2.11 m	29.2	4.25 m	69.7		200.9	2.15 t, 6.5	30.6
12	4.07 t, 6	71.7	4.03 m	75.8	4.75 s	76.5	4.10 t, 6.5	71.6
13		151.3		152.0		151.2		153.6
14		118.1		118.3		118.1		119.0
15	7.50 s	132.9	7.53 s	134.1	7.57 s	134.2	7.64 s	131.7
16		137.4		139.9		140.5		143.1
17	7.50 s	132.9	7.53 s	134.1		134.2	7.64 s	131.7
18		118.1		118.3		118.1		119.0
19	2.86 t, 7	34.2	2.88 t, 7.0	34.7	2.91 t, 7.0	34.7	4.79 dd, 4.5, 7.5	72.2
20	3.60 td, 7, 6	40.4	3.58 td, 7.0, 6.0	40.9	3.58 q, 6.9	40.9	3.51, 3.46	47.6
OMe	3.71 s, 6H	60.1	3.78, 3.73 s	60.2	3.74, 3.72 s	60.2	3.76 s	60.4
OH	5.46, 5.45 d, 6							

	87 (70)		88 (70)		89 (74)		90 (74)	
	¹ H acetone-d ₆	¹³ C DMSO-d ₆	¹ H acetone-d ₆	¹³ C acetone-d ₆	¹ H DMSO-d ₆	¹³ C DMSO-d ₆	¹ H DMSO-d ₆	¹³ C DMSO-d ₆
1,1'	4.39, 4.40 d, 11.3	74.6	4.56 2H m	72.3	4.18 d, 11.4	73.3	4.29 br	72.01
2,2'	5.06, 5.07 d, 11.3	57.0, 57.1	5.27 2H m	54.8	5.19 d, 11.3	57.8	5.35	55.84
3,3'		183.7		183.6		183.8		183.39
4,4'		122.6		124.9		121.3		122.75
5,5'	7.61 s 7.64 s	149.2, 149.3	7.46 d, 1.0 7.49 d, 0.9	146.2 146.4	7.68 s 7.65 s	149.1 149.0	7.54 s	145.35
6,6'		91.7		90.8		90.5		89.38
7,7'	3.26, 3.30 d, 18.2 3.88, 3.86 d, 18.2	38.4	3.38, 3.35 d, 18.2 3.87, 3.90 d, 18.2	41.4	3.65, 3.63 d, 18 3.13, 3.10 d, 18	38.0	3.65, 3.63 d, 18 3.33, 3.30 d, 18	38.03 39.79
8,8'		154.6, 154.7		155.4, 155.5		153.9, 153.9		154.57, 153.92
9,9'		160.2		160.2		158.9		158.78
NH	7.65 br 7.67 br		7.66 br 7.68 br		8.67 dd, 11.8, 5.7 8.64 dd, 11.8, 5.7		8.67 8.64	

	87 (70)			88 (70)			89 (74)			90 (74)				
	¹ H	¹³ C	DMSO- <i>d</i> ₆	¹ H	acetone- <i>d</i> ₆	¹³ C	acetone- <i>d</i> ₆	¹ H	DMSO- <i>d</i> ₆	¹³ C	DMSO- <i>d</i> ₆	¹ H	DMSO- <i>d</i> ₆	¹³ C
10	3.53, 3.81 m	43.4	43.4	3.53, 3.80 m	43.6	43.6	3.42 m	36.3	36.3	36.3	3.42 m	36.31		
11	4.26 m	69.7	69.7	4.25 m	69.9	69.9	2.00 q, 6	29.6	29.6	29.6	2.00 q, 6	29.62		
12	4.04, 4.08 m	75.8	75.8	4.04, 4.08 m	76.0	76.0	3.95 dd, 6, 4	71.2	71.2	71.2	3.95 dd, 6, 4	71.24		
13		152.6	152.6		152.7	152.7		150.8	150.8	150.8		150.75		
14,18		118.4	118.4		118.4	118.4		117.4	117.4	117.4		117.38		
15,17	7.67 s	131.4	131.4	7.67 s	131.5	131.5	7.53 s	133.0	133.0	133.0	7.53 s	133.04		
16		143.1	143.1		143.3	143.3		133.9	133.9	133.9		133.88		
19	4.91 dd, 4.4, 7.5	71.0	71.0	4.91 ddd, 4.2, 4.2, 7.5	71.4	71.4	2.76 t, 7	33.2	33.2	33.2	2.76 t, 7	33.20		
20	3.48, 3.65 m	47.4	47.4	3.51, 3.62 m	47.4	47.4	3.42 m	34.0	34.0	34.0	3.42 m	39.79		
OH	5.97 d, 5.6 5.99 d, 5.6			4.45 d, 5.2; 5.00 d, 4.2 5.92 d, 5.6; 5.92 d, 5.6			6.77 br				6.77 br			

	91 (75)			92 (77)			93 (3:2 diastereomeric mixture) (78)		
	¹ H	¹³ C	CDCl ₃	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	DMSO- <i>d</i> ₆
1,1'	4.44 d, 5.1	77.4	77.4	4.13, 4.14 s	75.4, 75.5	75.4, 75.5	1,1'	3.96 br	73.7
2,2'		112.3	112.3		114.2	114.2	2,2'		113.0
3,3'		148.1	148.1		149.3	149.3	3,3'		147.1
4,4'		121.3	121.3		122.8	122.8	4,4'		120.6
5,5'	6.42	131.6	131.6	6.46 s	132.3	132.3	5,5'	6.54 s	131.3
6,6'		74.3	74.3		92.4, 92.5	92.4, 92.5	6,6'		90.3
7,7'	2.81 d, 1.6 2.85 d, 1.6	25.5	25.5	3.11, 3.14 d, 18.4 3.79, 3.83 d, 18.4	40.3	40.3	7,7'	3.64 d, 17.5 3.17 d, 17.5	39.4
8,8'		116.6	116.6		155.3, 155.4	155.3, 155.4	8,8'		154.3
9,9'					161.4, 161.6	161.4, 161.6	9,9'		158.9
NH	2.52 br				NH	NH	NH	8.35 m, 7.90 brd, 6.4; 8.06 br	
10,10'				3.28, 3.29 m	39.1, 40.0	39.1, 40.0	10,10'	3.40 q, 6.6	36.2
11,11'				2.07, 2.23 m; 1.80 q, 6.8	33.9, 30.1	33.9, 30.1	11,11'	2.00 q, 6.6	29.4
12,12'				3.96 t, 7.4; 2.48 t, 6.8	33.5, 23.1	33.5, 23.1	12,12'	3.96 m	71.2
13,13'					135.9, 126.1	135.9, 126.1	13,13'		150.6, 150.7, 150.8
14,14'					150.7, 149.5	150.7, 149.5	14,14'		116.7, 116.8, 116.9

	91 (75)		92 (77)		93 (3:2 diastereomeric mixture) (78)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
15,15'	CDCl ₃	CDCl ₃	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆
OH	2.45 d, 5.1	60.3	6.36 s	111.3, 126.7	7.52 s, 7.44 s	133.5
OMe	3.77 s, 3H	60.3	3.75 s	60.4	2.94 m, 2.79 m	138.0, 138.2
					2.79 m, 3.01 dd, 4.7, 13.6	36.7, 37.0
					3.87 m, 3.89 m	57.9, 57.3
					2.1	171.8, 172.5
					OH	
					20-NH	
					OMe	59.5
					15', 17'	133.5
					19'a	36.7, 36.2
					19'b	
					20'	54.5, 54.5
					21'	172.0, 172.3

	94 (68)		95a (68)		97 (79)		99 (81)		101 (82)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	4.21 s	5.87 s	5.86 s	3.92 d, 6.2	75.5	4.12s	74.1	4.32 s	60.1	60.1
2					114.2		113.5		113.4	113.4
3					149.3		148.1		147.7	147.7
4					122.7		121.9		121.1	121.1
5	6.57 s	6.34 s	6.32 s	6.58 s	132.3	6.34 s	130.9	6.30 s	131.1	131.1
6					92.6		91.9		91.7	91.7
7	3.23 d, 18.2	3.08 d, 18	3.06 d, 18	3.18 d, 18.2	40.0	3.03 d, 18.3	39.3	3.86 d, 18.5	38.7	38.7
	3.87 d, 18	3.47 d, 18	3.45 d, 18	3.60 d, 18.2		3.80 d, 18.3		2.94 d, 18.5		
8					155.2		154.2		154.0	154.0
9					163.6		159.9		159.4	159.4
10	3.40–3.60 m	3.80 m	3.57 m			3.59 t	37.7	3.55 m	38.0	38.0
		3.96 m	3.70–3.95 m							
11	4.27 m	5.28 q, 4	5.76 dd, 7, 4			2.10 tt	29.5	2.10 m	28.9	28.9

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	<u>94 (68)</u>		<u>94a (68)</u>		<u>95a (68)</u>		<u>97 (79)</u>		<u>99 (81)</u>		<u>101 (82)</u>	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
12	4.11 m		4.19 dd, 10, 4 4.24 dd, 10, 4				4.06 t		71.3		4.12 t, 5.7	73.4
13			7.50 s						151.6			153.4
14									118.5			134.4
15	7.72 m		7.54 s				7.43 s		133.3		7.39 d, 2	133.4
16			4.22 d, 4.5						137.0			112.2
17	5.68 t, 8		5.54 t, 8				7.43 s		133.3		7.09 dd, 8.4, 2	128.8
18	3.56, 4.08 t, 8		3.50, 4.00 t, 8						118.5		6.83 d, 8.4	113.3
19							2.74 t		35.9 t		2.67 t, 6.8	37.3
20							2.95 bt		42.2 t		2.94 t, 7.2	42.9
Ome	3.74 s, 3H		3.74 s, 3H				3.71 s		60.2		3.74 s	
1-OH							3.65 s		59.6			
							6.35 d, 6.2					
NH			7.10 t, 6.5 5.80 br				7.33 t				7.00 brt	

	<u>102 (83)</u>		<u>100 (81)</u>		<u>103 (36)</u>		<u>104 (36)</u>	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	4.08 s		4.08 s		3.95 s		3.93 d, 8.3	
2		75.4		73.7		113.4		113.3
3		114.1		113.4		147.2		147.3
4		149.2		147.2		121.0		121.1
5	6.37 s		122.7		6.55 s		6.56 s	
6		132.1		131.4		90.4		131.3
7	3.74, 3.03 d, 18.0		92.6		90.4		3.17, 3.60 d, 18.1	
8		40.1		39.5		154.6		154.5
9		155.1		154.6		159.2		159.1
10	3.48 m		161.6		3.41 bdd		3.36 m	
11	2.02 tt, 6.9, 13.8		37.9		36.4		2.74 t, 6.9	
12	4.01 t, 6		30.8		29.5		33.3	
13		72.3		71.3		139.0		139.0
		153.6		151.2		7.49 s		133.2

	102 (83)		100 (81)		103 (36)		104 (36)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
14	CD ₃ OD	118.9	CD ₃ OD	117.5	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆
15	7.57 s	131.7	7.44 s	7.55 s	133.9	133.9	151.1	151.1
16		142.8			136.8	136.8	117.3	117.3
17	7.57 s	131.7	7.44 s	7.55 s	133.9	133.9	74.9 s	133.2
18		118.9			117.5	117.5	3.94, 4.08 m	71.3
19	4.75 t	71.64	2.73 t	2.90 m; 3.08 bd	35.3	2.23, 2.38 m	27.8	27.8
20	3.42 brt, 7.8	47.62	3.37 dt	3.56 m	55.0	3.56 m	74.8	74.8
21		173.3	2.12m	169.9			167.1	167.1
22	1.93 s	22.7	1.25 s					
23-32			1.25 s					
33			1.54m					
OMe	3.69 s	60.4	3.72 s	59.8	3.63 s	3.63 s	59.8	59.8
Me ₂			0.87 d					
NH			7.31 t, 5.67 t	8.57 t, 5.6			8.57 t, 5.8	
⁺ NMe ₃							3.15 s	51.0

	105 (78)		106 (78)		107 (78)		108 (72)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CD ₃ OD	75.4	CD ₃ OD	75.5	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	75.2
2	4.10 s	114.2	4.07 s	114.2	3.94 br	113.1	4.18 dd, 7.8, 0.9	113.9
3		149.2		149.3		147.2		148.8
4		122.7		122.8		120.7		122.2
5	6.40 s	132.3	6.41 s	132.3	6.56 s	131.4	6.52 d, 0.9	132.3
6		92.4		92.4		90.3		91.8
7	3.09, 3.79 d, 18.2	40.2	3.09, 3.77 d, 18.2	40.2	3.65, 3.20 d, 18.2	39.4	3.83, 3.17 d, 18.2	40.1
8		155.3		155.3		154.5		155.1
9		161.4		161.6		159.0		160.4
10	3.57 t, 7.0	38.0	3.58 t, 7.0	38.0	3.40 dt, 5.8, 6.5	36.3	3.58 ddd, 13.5, 6.4, 5.8 3.45 ddd, 13.5, 7.3, 5.8	47.7

	105 (78)		106 (78)		107 (78)		108 (72)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
11	2.09 m	30.6	2.11 m	30.6	1.99 quint, 6.5	29.5	4.84 ddd, 7.3, 6.4, 3.8	71.4
12	4.02 t, 6.0	72.2	4.07 t, 6.0	72.2	3.95 m	71.2		138.5
13		153.3		153.7		150.4	7.57 s	130.9
14		119.1		119.4		116.5		111.4
15	7.57 s	134.9	7.55 s	135.0	7.53 s	134.0		150.7
16		136.9		136.6		138.8		111.4
17	7.57 s	134.9	7.55 s	135.0	7.53 s	134.0	7.57 s	130.9
18		119.1		119.4		116.5		
19	3.09 dd, 8.8, 13.9 3.17 dd, 5.2, 13.9	33.7	2.98 dd, 8.1, 14.7 3.20 dd, 4.7, 14.7	36.8	2.98 dd, 4.0, 13.0 2.86 dd, 4.0, 13.0	36.3		
20	3.74 dd, 5.2, 8.8	72.6	3.75 dd, 4.7, 8.1	57.1	3.82 br	57.2		
21		171.4		173.0		174.3		
OMe			3.72 s	60.4	3.65 s	59.6	3.72 s	60.2
NH-20					Not detected		7.69 brt, 5.8	
OH-1					6.32 br		5.48 d, 7.8	
OH-11							5.02 d, 3.8	
OH-15							3.79 s	
NH-9					8.46 t, 5.8			

	109 (84)		110 (79)		111 (79)		112 (86)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	3.91 s	73.5	3.92 d, 8.1	75.5	3.92 d, 8.2	75.5	4.04 s	75.2
2		113.0		114.2		114.2		113.8
3		147.1		149.4		149.3		148.9
4		120.8		122.8		122.8		122.5
5	6.58 s	131.2	6.59 s	132.3	6.57 s	132.3	6.36 s	132.0
6		90.2		92.5		92.4		92.0
7	3.20 d, 18.1 3.62 d, 18.1	39.1	3.23 d, 18.0 3.62 d, 18.0	40.1	3.18 d, 18.2 3.60 d, 18.2	41.4	3.73 d, 18.2 3.01 d, 18.2	39.0
8		154.4		155.3		155.2		154.8

	109 (84)		110 (79)		111 (79)		112 (86)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
9		158.9		161.6		161.6		161.2
10	3.38 m	36.1	3.41 m	37.9	3.36 m	40.1	3.42 t, 7.6	40.1
11	1.99 m	29.3	2.01 m	30.6	2.76 t, 6.9	35.1	2.76 t, 7.6	34.7
12	3.95 t, 6.3	71.3	3.97 t, 6.3	72.3		140.3		139.8
13		151.3		153.7	7.54 s	134.5	7.45 s	134.1
14		117.5		119.5		118.8		118.4
15	7.68 s	132.9	7.64 s	134.4		152.5		151.9
16		135.8		136.5		118.8		118.4
17	7.68 s	132.9	7.64 s	134.5	7.54 s	134.6	7.45 s	134.1
18		117.5		153.7		71.2	4.08 t, 5.6	71.4
19	3.05 m	26.9	2.93 t, 8.1	30.3	2.15 m	26.4	2.14 t, 6.0	28.0
20	3.50 m	64.2	3.35 m	59.2	3.40 m	57.2	3.30 t, 6.6	48.8
OMe	3.64 s	59.5	3.65 s	60.4	3.64 s	60.4	3.69 s	60.1
OH-1	6.36 m		6.36 d, 8.1		6.34 d, 8.2			
NMe							2.69 s	32.0
NH-9	8.57 t, 5.8		8.57 t, 5.8		8.58 t, 5.7			
NMe ₂ -18	3.09 s	52.3	2.78 s	43.6	2.83 s	43.7		

	113 (69)		113 acetate (69)		114 (69)		114 acetate (69)		115 (87)		116 (79)	
	¹ H	¹³ C	¹³ C	¹³ C	¹ H	¹³ C	¹³ C	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	4.26 s	74.7	CD ₃ OD/CDCl ₃	CD ₃ OD	4.14s	73.4	CD ₃ OD/CDCl ₃	CD ₃ OD	4.13 d, 0.8	75.5	3.91 d, 6.4	73.6
2		108.5				107.5				114.1		113.0
3		151.5				148.9				149.3		147.1
4		122.4				121.8				122.8		120.8
5	6.35 s	132.3			6.35 s	130.5			6.45 d, 0.9	132.2	6.58 s	131.2
6		90.6				89.7				92.4		90.2
7	3.77 d, 17.5	40.7			3.20 d, 17.5	40.0			3.12 d, 18.3	40.1	3.19 d, 18.6	39.2
	3.93 d, 17.5				3.85 d, 17.5				3.82 d, 18.3		3.61 d, 18.6	
8		155.5				153.9				155.2		154.3

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	<u>113 (69)</u>		<u>113 acetate (69)</u>		<u>114 (69)</u>		<u>114 acetate (69)</u>		<u>115 (87)</u>		<u>116 (79)</u>	
	¹ H	¹³ C	¹³ C	¹³ C	¹ H	¹³ C	¹³ C	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CD ₃ OD/CDCl ₃	CD ₃ OD	CD ₃ OD/CDCl ₃	CD ₃ OD/CDCl ₃	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆
9		160.9		159.4		161.7		158.9				
10	3.67 t, 7	40.3	3.43 t, 7	38.6	3.38 t, 6.8	39.5	3.37 brt, 6.4	37.3				
11	2.99 t, 7	27.4	2.01 t, 7	21.9	1.90 q, 7.1	22.9	2.61 t, 6.4	24.2				
12		134.6	2.67 t, 7	27.8	2.60 t, 7.1	28.9		124.1				
13	6.85 s	117.7		130.8		128.5	6.62 br	109.4				
14	7.59 s	135.9	6.47 s	108.4	6.62 s	110.3		146.9				
15				146.9		149.5						
Ome	3.86 s	60.6	3.79 s	60.3	3.77 s	60.4	3.64 s	59.6				
OH-1							6.37 d, 6.4					
NMe					2.98 s	29.5						
OCOCH ₃	NA	171.1, 20.5	NA	170.0, 20.7								
NH-9							8.63 t, 5.6					
NH-12							11.71 br					
NH-13							12.13 br					
NH-14							7.40 s					

	<u>117 (79)</u>		<u>118 (88)</u>		<u>119 (89)</u>		<u>120 (83)</u>	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD
1	3.92 d, 6.3	73.6	4.13 s	75.5	4.08 s	75.6	3.92 br	73.5
2		113.1		114.1		114.5		113.0
3		147.2		149.3		149.0		147.0
4		120.9		122.8		123.1		120.6
5	6.58 s	131.3	6.46 s	132.3	6.40 s	132.6	6.56 s	131.2
6		90.4		92.3		92.9		90.1
7	3.19 d, 18.0 3.62 d, 18.0	39.5	3.13 d, 18.3 3.81 d, 18.3	40.2	3.09 d, 18.0 3.75 d, 18.0	39.5	3.62 Abq, 18.0 3.20 Abq, 18.0	39.3
8		154.3		155.3		155.6		154.5
9		157.9		161.6		162.1		158.4
10	3.35 m	35.0	3.34-3.37 m	39.9	3.51 t, 7.0	40.5	4.16 brt, 5.1	37.9
								39.5

	117 (79)		118 (88)		119 (89)		120 (83)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	DMSO- <i>d</i> ₆	CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD
11	1.86, 1.96 m	30.2	1.65 m	29.8	2.76 t, 7.0	26.1	5.24 dt ^b	121.0
12	4.30 dd, 4.9, 7.8	56.9	1.87, 1.65 m	25.6		126.3	6.06 d, 11.4	121.8
13		174.8	4.09 dd, 5.2, 5.2	61.9	6.55 s	111.3		115.1
14		159.2		190.6		149.7		150.0
15				171.4			6.52 s	131.2
OMe	3.65 s	59.7	3.77 s	60.4	3.72 s	59.6	3.63 s	29.5
OH-1	6.36 d, 6.3				6.55 br		6.56	
NH-15							5.28 br, 5.28 br, 9.01 t, 5.4	
NH ₂								
NH-9	8.63 t, 5.1				8.75 br			
NH-12	12.5 br				11.70 s			
NH-13	9.64 br				12.30 s			
NH-14	8.96 s				7.45 s			

	121 (90)		122 (91)		123 (89)		124 (83)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H ^d	¹³ C	¹ H	¹³ C
	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆
1	3.89 d, 0.6	73.5	3.98 br	73.5	4.10 s	75.4	3.88 br	73.4
2		113.1		113.0		114.1		113.0
3		147.1		147.0		149.3		147.1
4		120.8		120.7		122.7		120.6
5	6.56 d, 0.6	131.2	6.58 br	131.2	6.40 s	132.3	6.53 s	131.2
6		90.1		90.2		92.5		90.1
7	3.12 d, 18.0 3.60 overlapped	39.4	3.24 d, 18 3.71 d, 18	39.4	3.10 d, 18.0 3.78 d, 18.0	40.2	3.62 d, 18.0 3.20 d, 18.0	39.5
8		154.4		154.4		155.3		154.4
9		158.9		158.9		161.1		158.8
10	3.40 overlapped	38.1	3.43 dt, 6, 7	36.1	3.60 t, 7.0	38.3	3.10 m	38.5
11	2.75 m	24.6	2.02 tt, 7	29.3	2.12m	30.6	1.42 m	28.2 ^c
12		120.4	3.97 t, 7	71.2	4.02 t, 7.0	72.3	1.24 m	23.3

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	121 (90)		122 (91)		123 (89)		124 (83)			
	¹ H	¹³ C	¹ H	¹³ C	¹ H ^d	¹³ C	¹ H	¹³ C		
13	CD ₃ OD	118.7	DMSO- <i>d</i> ₆	150.7	CD ₃ OD	154.1	DMSO- <i>d</i> ₆	142 m	DMSO- <i>d</i> ₆	28.0 ^c
14,14'		146.2		117.1		119.2		3.10 m		40.7
15,15'		103.1		132.8		135.0				157.2
16		149.32		136.1		136.0				
17		112.2		27.8		38.0				
18		173.2		150.7		56.0				
19		137.7		163.1		170.1				
20	7.70 s	124.2	3.42 dt, 6, 7	37.3	3.45 m	39.3				
21		128.9	2.66 t, 7	24.3	2.65 m	25.7				
22		137.0		124.1		125.9				
23	6.96	113.8	6.59 s	109.0	6.55 s	110.6				
24				146.7		149.9				
OMe	3.69	59.6	3.67 s	59.5	3.72 s	60.4		3.58 s		59.6
OH-1	6.42 br		6.48 br		6.50 br			6.56 br		
OH	10.4, 11.8, 14.4 br									
NH ₂ -18										
NH	11.95, 9.0 br								7.85 brt (NH-14)	
NH									7.35 br (NH-15)	
NH ₂	7.27 br		7.38 br		7.35 br			7.35 br		
NH-9	8.62 t, 5.7		8.57 t, 6		8.60 t, 6.0			8.46 brt, 5.4		
NH-19			8.15 t, 6		8.70 t, 6.0					
NH-22			11.74 br		11.80 s					
NH-23			12.16 br		12.35 s					

	125 (79)		126 (66)		127 (92)		128 (92)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	3.91 d, 7.9	76.3	4.10 s	76.4	3.93 d, 8.6	73.6	3.91 d, 8.2	73.6
2		114.9		115.1		113.1		113.0
3		150.1		150.2		147.2		147.1

	125 (79)		126 (66)		127 (92)		128 (92)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
4	DMSO- <i>d</i> ₆	123.5	CD ₃ OD	123.7	DMSO- <i>d</i> ₆	120.9	DMSO- <i>d</i> ₆	120.8
5	6.57 s	133.0	6.40 s	133.2	6.60 s	131.2	6.57 s	131.2
6		93.2		93.4		90.5		90.2
7	3.19 d, 18.2 3.62 d, 18.2	40.1	3.11 d, 18 3.78 d, 18	41.0	3.21 d, 18.4 3.62 d, 18.4	39.3	3.18 d, 18.3 3.61 d, 18.3	39.5
8		159.5		156.0		154.1		154.3
9		162.5		162.8		159.1		158.9
10	3.16 m	40.5	3.54 d, 4	44.7	3.99 d, 5.5	48.6	3.34 dt, 6.5, 5.9	33.8
11	1.47 m	28.3	4.45 m	78.4		205.8	2.67 t, 6.5	38.3
12	1.45 m	28.0	1.78, 2.05 m	25.7	2.61 t, 6.8	39.8		205.7
13	3.09 m	42.9	3.35 m	40.2	3.16 dt, 6.8, 4.8	35.2	3.83 d, 6.2	49.9
14		156.1		157.5		157.0		157.0
OMe	3.64 s	61.2	3.72 s	61.3	3.64 s	59.8	3.65 s	59.6
OH-1	6.34 d, 7.9				6.42 d, 8.6		6.33 d, 8.2	
OMe-14					3.50 s		3.55 s	51.5
NH-9	8.54 t, 5.8				8.64 t, 5.5		8.43 t, 5.9	
NH-13	7.44 br				7.09 t, 4.8		7.34 t, 6.2	
NH-14	7.1-7.3 4H, br							

	131 (95)		132 (96)		133 (96)		129 (94)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	7.13 s	146.7	7.17 s	146.4	7.17 s	147.3	7.01 s	146.3
2		104.5		103.6		103.5		104.3
3		149.9		149.3		149.3		149.4
4		104.4		104.1		104.1		103.9
5	3.38 d, 16.0 3.06 d, 16.0	38.3	3.45 d, 16.0 3.15 d, 16.5	37.5	3.44 d, 16.2 3.13 d, 16.2	37.4	3.37 d, 16 3.08 d, 16	38.2
6		120.9		119.9		119.9		120.4
7	4.98 s	80.4	5.07 d, 7.0	80.2	5.07 d, 7.2	80.1	4.97 s	80.2
8		158.7		158.5		158.4		158.2

	131 (95)		132 (96)		133 (96)		129 (94)		¹³ C
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	
9	CD ₃ OD	160.7	acetone-d ₆	159.1	acetone-d ₆	159.1	CD ₃ OD	160.2	DMSO-d ₆
CONH			7.84 t, 5.8		8.64 br		5.48 s		7.15 brt, 6
NH			7.26 brt, 5.3		6.02 d, 7.2				5.40 br
10	3.61 t, 6.0	38.0	3.64 q, 6.5	37.5	3.63 q, 6.6	37.9	3.61 t, 7.0	3.68 t, 6.0	39.7
11	2.14 dd, 6.0, 6.5	30.5	2.15 q, 6.0	30.4	2.14 q, 6.6	30.4	2.13 dd, 6.0, 7.0	2.10 2H	29.9
12	4.08 t, 6.0	72.2	4.10 t, 6.3	72.0	4.08 t, 6.2	72.0	4.06 t, 6.0	4.08 t, 6.0	71.9
13		154.2		152.6		152.5			153.0
14		119.4		118.4		118.6			119.1
15	7.67 s	131.6	7.60 d, 0.5	131.4	7.55 s	134.3	7.48 s	7.38 s	134.1
16		141.5		143.6		138.6			136.9
17	7.67 s	131.6	7.60 d, 0.5	131.4	7.55 s	134.3	7.48 s	7.38 s	134.1
18		119.4		118.4		118.6			119.1
19	4.92 dd, 3.0, 10	68.6	4.78 q, 5.3	72.3	3.01 t, 7.2	32.4	2.76 dd, 7.5, 7.0	2.66 t, 7.0	32.9
20	3.21 dd, 3.0, 13 3.09 dd, 10, 13	56.4	3.49 dt, 13.8, 5.1 3.37 dt, 14.0, 6.0	47.9	3.75 q, 7.0	51.2	2.96 dd, 7.5, 7.0	2.90 t, 7.0	41.5
21				174.8	7.34 d, 14.4	149.8			
22			2.14 t, 7.0	39.7		99.4			
23				26.6		197.4			
24					6.64 d, 6.3	142.6			
25			1.28 brt(H ₂₃ -H ₃₂)	27.8 (C ₂₊ -C ₃₁)	6.73 d, 6.3	142.4			
26						194.1			
32				28.6					
33			1.55 m	28.1					
34,35			0.85 d, 6.5	22.9					
OMe	3.64 s	59.3	3.64 s	59.0	3.65 s	60.0	3.64 s	3.66 s	59.3
NMe	2.73 s	33.9							
7-OH			5.99 d, 7.0		7.86 brt, 5.4				
19-OH			5.19 dd, 4.5						

	130 (94)			135 (98)			136 (98)			134 (97)		
	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	acetone-d ₆	¹ H	¹³ C	CDCl ₃
1	7.13 s	146.7	146.8	7.14s	146.8	146.8	7.17 s	147.3	147.3	7.00 s	145.4	145.4
2		104.3	104.4		104.4	104.4		103.5	103.5		103.5	103.5
3		149.8	149.9		149.9	149.9		149.3	149.3		148.5	148.5
4		104.5	104.6		104.6	104.6		104.1	104.1		104.6	104.6
5	3.38, 3.07 d	38.2	38.3	3.39, 3.07 d, 16.1	38.3	38.3	3.44, 3.13 d, 16.2	37.4	37.4	3.38, 3.09 d, 16	37.1	37.1
6		120.8	120.9		120.9	120.9		119.9	119.9		121.3	121.3
7	4.97 s	80.4	80.4	4.99 s	80.4	80.4	5.07 d, 7.2	80.1	80.1	5.03 s	78.8	78.8
8		158.7	158.8		158.8	158.8		158.4	158.4		156.7	156.7
9		160.6	160.7		160.7	160.7		159.1	159.1		158.8	158.8
CONH							8.64 br			7.26 s		
NH							6.02 d, 7.2			3.68		
10	3.62 t	38.0	38.0	3.62 t, 6.8	38.0	38.0	3.63 q, 6.6	37.9	37.9	3.68 m	37.0	37.0
11	2.10 pentet	30.5	30.6	2.13 tt, 6.0, 6.8	30.6	30.6	2.14 q, 6.6	30.4	30.4	2.08 m	29.3	29.3
12	4.07 t	72.1	72.1	4.07 t, 6.0	72.1	72.1	4.08 t, 6.2	72.0	72.0	4.05 t, 5.5	70.8	70.8
13		153.6	152.9		152.9	152.9		152.5	152.5		151.0	151.0
14		119.2	119.0		119.0	119.0		118.6	118.6		118.0	118.0
15	7.62s	134.3	134.3	7.48s	134.3	134.3	7.55 s	134.3	134.3	7.34 s	132.8	132.8
16		143.2	139.7		139.7	139.7		138.6	138.6		138.6	138.6
17	7.62 s	131.5	134.3	7.48 s	134.3	134.3	7.55 s	134.3	134.3	7.34 s	132.8	132.8
18		119.4	119.0		119.0	119.0		118.6	118.6		118.0	118.0
19	2.83 dd	72.7	35.0	2.77 t, 7.1	35.0	35.0	3.01 t, 7.2	32.4	32.4	2.73 t, 7.0	34.3	34.3
20	2.97 dd	18.4	40.0	3.44 t, 7.1	40.0	40.0	3.75 q, 7.0	51.2	51.2	2.82 t, 7.0	52.1	52.1
21			163.8	7.80 s	163.8	163.8	7.34 d, 14.4	149.8	149.8			
22								99.4	99.4			
23								197.4	197.4			
24							6.64 d, 6.3	142.6	142.6			
25							6.73 d, 6.3	142.4	142.4			
26								194.1	194.1			
NCH ₃										2.44 s	35.8	35.8
OMe	3.65 s	59.3	59.3	3.65 s	59.3	59.3	3.65 s	60.0	60.0	3.67 s	59.0	59.0

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130 (94)		135 (98)		136 (98)		134 (97)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	acetone- <i>d</i> ₆	CDCl ₃	CDCl ₃	CDCl ₃
7-OH				7.86 brt, 5.4	4.1 s		

137 (99)		138 (100)		139 (101)		140 (33)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD	0.2% TFA-H in CD ₃ OD	CD ₃ OD	CD ₃ OD + 5% CD ₃ CO ₂ D	0.2% TFA-H in CD ₃ OD	
1	126.0	137.7		112.1	112.1		130.6
2	7.46 s	134.4	7.46 s	134.8	7.42 d, 2.1	134.8	134.7
3		118.5		118.8		131.8	131.7
4		148.6		154.2		155.9	155.9
5		118.5		118.8	6.89 d, 8.4	113.1	113.1
6	7.46 s	134.4	7.46 s	134.8	7.17 dd, 8.4, 2.1	130.5	130.4
7	3.81 s	3.75 s	3.82	29.1	3.79 2YH, s	28.7	28.7
8		152.1		152.4		153.0	152.9
9		165.6		165.6		165.7	165.9
10		38.9	3.49 t, 7	40.6	3.47 t, 7.1	40.3	39.2
11		25.7	2.79 t, 7	27.9	2.77 t, 7.1	27.8	26.1
12	3.47 t	3.36 m		134.0		NA	133.4
13	2.69 t	2.58 t		110.7	6.84 br	NA	117.6
14		153.8	7.62 br	136.2	7.55 br	136.1	135.0
OMe	3.81 s	3.75 s	3.80 s	61.3	3.80 s	56.7	56.7
NH	6.50 s	6.50 s					

141 (102)		142 (102)		143 (102)		144 (103)		145 (103)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD
1		137.2		138.2		138.1		138.1	
2	7.48 s	7.48 s	134.4	7.48 s	135.3	7.46 s	135.3	7.46 s	135.3
3		118.7		119.6		119.6		119.6	
4		152.8		153.7		153.6		153.6	
5		118.7		119.6		119.6		119.6	

	141 (102)		142 (102)		143 (102)		144 (103)		145 (103)		
	¹ H	CD ₃ OD	¹ H	CD ₃ OD	¹ H	CD ₃ OD	¹ H	CD ₃ OD	¹³ C	CD ₃ OD	
6	7.48 s		7.48 s		7.48 s		7.46 s		135.3	7.46 s	135.3
7	3.83 br		3.82 br		3.83 br		3.82 s		28.9	3.82 s	28.9
8			151.9						152.9		152.9
9			165.4						166.3		166.4
10	3.47 t, 7		38.9		3.47 t, 7		3.45 t, 6.8		40.2	3.45 t, 6.8	39.9
11	2.70 t, 7		25.8		2.71 t, 7		2.66 t, 6.8		24.5	2.67 t, 6.8	24.5
12			126.0						126.2		126.4
13	6.51 s		110.7		6.51 s		6.41 s		112.0	6.46 s	111.7
14			148.5						148.3		148.5
15	4.01 t, 7		72.3		4.02 t, 7		4.00 t, 6.1		73.1	4.00 t, 6.1	73.1
16	2.04 quin, 7		30.9		2.04 quin, 7		2.03 m		31.1	2.03 tt, 6.1, 6.8	31.1
17	3.44 t, 7		37.7		3.44 t, 7		3.43 t, 7.3		38.5	3.43 t, 6.8	39.0
18			176.3						177.2		177.2
19	2.19 t, 7		37.2		2.19 t, 7		2.18 t, 7.3		38.0	2.18 t, 7.6	38.0
20	1.61 quin, 7		27.1		1.61 quin, 7		1.60 m		27.4	1.60 m	34.7-31.2
21-24	1.28 m		30.2		1.28 m		1.35-1.27 m		31.9-31.1	1.33-1.26 m	34.7-31.2
25	1.28 m		30.7		1.28 m		2.03 m		27.9	1.33-1.26 m	34.7-31.2
26	1.28 m		30.7		1.28 m		5.33 t, 5.4		131.7	1.33-1.26 m	34.7-31.2
27	1.28 m		31.0		1.28 m		5.33 t, 5.4		131.6	1.33-1.26 m	34.7-31.2
28	1.28 m		28.5		1.28 m		2.03 m		27.9	1.33-1.26 m	34.7-31.2
29	1.28 m		40.2		1.28 m		1.35-1.27 m		31.9-31.1	1.33-1.26 m	34.7-31.2
30	1.28 m		29.0		1.28 m		1.35-1.27 m		31.9-31.1	1.33-1.26 m	34.7-31.2
31	0.90 t, 7		23.1		1.28 m		1.35-1.27 m		31.9-31.1	1.33-1.26 m	34.7-31.2
32			23.1		1.28 m		1.51 m, 6.8		30.0	1.33-1.26 m	34.7-31.2
33					0.88 t, 7		0.86 d, 6.8		23.8	1.33-1.26 m	34.7-31.2
34							0.86 d, 6.8		23.8	1.33-1.26 m	29.6
35									23.8	1.33-1.26 m	27.9
36										0.89 t, 6.8	15.2

	146 (104)			147 (105)			148 (103)			149 (79)		
	¹ H	¹³ C	DMSO-d ₆	¹ H	¹³ C	DMSO-d ₆	¹ H	¹³ C	DMSO-d ₆	¹ H	¹³ C	DMSO-d ₆
1		136.4			136.5			131.4			122.0	
2	7.45 s	132.9	7.45 s		132.8	7.32 s		132.5			152.8	
3		117.4			117.0			111.9			107.6	
4		150.5			150.5			149.2			152.7	
5		117.4			117.0			111.9			105.5	
6	7.45 s	132.9	7.45 s		132.8	7.32 s		132.5	7.26 s		132.2	
7	3.75 s	27.7	3.75 s		27.9	3.69 s		27.7	3.70 s		27.0	
8		150.9			150.8			151.5			150.3	
9		163.1			163.1			163.4			164.7	
CONH							8.13 t, 5.9				8.55 t, 5.9	
NOH	12.03 s		12.09 s			11.93 s					12.19 s	
NH-9	8.15 t, 6		8.17 t, 5.4									
NH-12						11.56 br					11.55 br	
NH-13	11.77 br		11.96 br			11.98 br					11.19 br	
NH-14	12.16 br		12.33 br			7.33s					7.33 s	
NH ₂	7.83 br		7.49 s									
10	3.36 dt, 6	37.3	3.36 dt, 5.4, 6.4		37.3	3.36 dt, 5.9, 6.8		37.5	3.40 dt, 5.9, 6.9		37.6	
11	2.59 t, 6	24.4	2.61 t, 6.4		24.4	2.59 t, 6.8		24.6	2.63 t, 6.9		24.7	
12		124.3			124.2			124.5			124.2	
13	6.57 s	109.2	6.58 br		109.2	6.57 s		109.4	6.60 s		109.3	
14		146.9			147.1			147.0			146.7	
15	3.98 t, 6	70.4	4.01 5.9		70.1							
16	2.02 m	27.9	2.50 2H overlapped		31.0							
17	3.06 m	36.5	4.89 t, 7.3		58.5							
1',5'			9.20 d, 5.9		145.1							
2',4'			8.18 dt, 5.9, 7.8		128.0							
3'			8.61 t, 7.8		145.6							
OMe									3.74 s		60.0	
OH						9.77 br			10.48 br			

		150 (79)		151 (89)		152 (107)		153 (107)		154 (109)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹³ C
	DMSO-d ₆	CD ₃ OD	DMSO-d ₆	DMSO-d ₆	DMSO-d ₆	CD ₃ OD	DMSO-d ₆	DMSO-d ₆	CDCl ₃ /CD ₃ OD	DMSO-d ₆	CD ₃ OD
1		122.7		134.0							
2		155.0	7.55 s	135.2							
3		108.8		118.9							
4		154.3		154.8							
5		107.4		118.9							
6	7.26 s	134.6	7.55 s	132.5							
7	3.70 s	25.5	3.30 m	32.0							
8		151.5	4.25 dd, 12.0, 4.0	75.8							
9		167.3		166.2							
CONH	8.59 t, 5.9		9.20 t, 6.0								
NOH	12.20 s										
NH-12			11.70 s								
NH-13	14.1 br		12.25 s								
NH-14			7.25 br								
10	3.48 dt, 5.9, 6.7	39.2	3.30 m	38.7							
11	2.85 t, 6.7	25.8	2.45 m	25.2							
12		132.2		125.3							
13	7.40 s	117.7	6.42 s	110.5							
14		134.9		148.5							
OMe	3.74 s	60.8	3.82 s	61.0							
NMe			3.32 s	53.2							
OH	10.45 br										
<hr/>											
		152 (107)		153 (107)		154 (109)					
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹³ C
	CDCl ₃ /CD ₃ OD	pyridine-d ₅	CD ₃ OD	DMSO-d ₆	DMSO-d ₆	CDCl ₃ /CD ₃ OD	DMSO-d ₆	DMSO-d ₆	DMSO-d ₆	CD ₃ OD	CD ₃ OD
1,1'			132.1	128.8			128.2		Signals were not assigned		
2,2'	7.62 d, 2	7.76 d, 2	136.0	132.9	7.40 d, 2	132.5, 139.7	7.48 d, 2		8.08 t, 6; 8.05, t, 6; 7.29, d, 2; 7.00, dd, 8, 3, 2; 6.83, d, 8, 3; 6.73, d, 1.9; 6.65, d, 1.9; 3.67, s; 3.61, s; 3.44 dt, 7, 6; 3.41 dt, 7, 6; 2.81 t, 7; 2.79 t, 7		166.1, 165.8, 154.7, 153.6, 153.5, 153.0, 134.4, 133.1, 132.1, 130.6,
3,3'			112.1	108.8		108.8, 108.9					
4,4'			155.4	152.3		152.6, 152.9					

		152 (107)			153 (107)			154 (109)		
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	
CDCl ₃ /CD ₃ OD	CD ₃ OD	pyridine-d ₅	CD ₃ OD	DMSO-d ₆	DMSO-d ₆	CDCl ₃ /CD ₃ OD	DMSO-d ₆	DMSO-d ₆	CD ₃ OD	
5,5'	6.85 d, 8	6.84 d, 8	118.7	116.2	6.83 d, 8.6.87 d, 8	115.9				
6,6'	7.15 dd, 8, 2	7.26 dd, 8, 2	131.9	129.1	7.10 dd, 8, 2 7.17 dd, 8, 2	128.9, 129.1			117.0, 114.4, 110.5, 39.7	
7,7'	3.87 s	4.01 s	30.3	26.7	3.68, 3.87 s	27.5, 35.7			39.6, 38.5, 28.9, 28.7	
8,8'			154.7	151.8		151.1, 151.6				
9,9'			167.5			161.9, 163.1				
10,10'	3.63 t, 7	3.48 q, 7	41.2	38.1	3.50, 3.65 m	37.6, 38.0				
11,11'	2.87 t, 7	2.65 t, 7	40.1	37.0	2.95 m	36.6, 36.7				
OH		12, 14 br								
NH		8.56 t, 7						8.08, 8.05 t, 6		

		155 (110)			156 (110)			157 (110)			158 (110)		
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN
1			130.9		130.9		130.8		130.9		130.9		130.4
2		7.08 dd, 2.1, 8.4	130.4		130.4	7.07 dd, 1.8, 8.4	130.4		130.4	7.07 dd, 1.8, 8.4	130.4		130.4
3		6.83 d, 8.4	117.2		117.2	6.82 d, 8.4	117.1		117.1	6.82 d, 8.4	117.1		117.1
4			153.0		153.0		152.8		152.8		152.8		152.8
5			109.1		109.1		109.9		109.9		109.9		109.9
6		7.36 d, 2.1	134.1		134.1	7.35 d, 1.8	134.0		134.0	7.35 d, 2.1	134.1		134.1
7		3.76 s	28.5		28.5	3.75 s	28.5		28.5	3.76 d, 2.1	28.5		28.5
8			153.4		153.4		153.2		153.2		153.4		153.4
9		154.2	164.5		164.5		164.2		164.2		164.1		164.1
10	3.35 q, 6.3	40.7	39.7	3.65 q, 6.3	35.1	3.50 q, 6.6	39.1		39.1	3.50 q, 6.6	39.1		39.1
11	2.77 t, 6.6	38.9	34.1	3.21 t, 6.3	54.5	2.79 t, 6.6	39.0		39.0	2.79 t, 6.6	39.0		39.0
12						2.76 t, 6.3	38.2		38.2	2.76 t, 6.3	38.2		38.2
13						3.33 q, 6.3	40.6		40.6	3.33 q, 6.3	40.6		40.6
14							158.2		158.2		158.2		158.2
OMe	3.57 s		52.4			3.56 s	52.4		52.4		52.4		52.4
NH-9	5.77 br			7.37 br		7.47 t, 5.4				7.29 t, 5.4			

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		155 (110)		156 (110)		157 (110)		158 (110)	
		¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
NH-13	5.77 br	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN	CD ₃ CN
CN	111.9								
NH ₂									
		5.82 br		5.49 br					

		159 (112)		160 (112)		161 (112)		162 (112)	
		¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1		CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD	CD ₃ OD
2	7.06 dd, 8.0, 2.0	130.2	130.5	7.05 dd, 8.0, 2.0	130.5	7.01 dd, 8.0, 2.0	130.5	7.06 dd, 8.0, 2.5	130.5
3	6.75 d, 8.0	117.4	117.2	6.75 d, 8.0	117.2	6.83 d, 8.0	117.2	6.75 d, 8.5	117.2
4		154.5	153.9		153.9		153.8		153.9
5		111.0	110.6		110.6		110.6		110.6
6	7.35 d, 2.0	134.6	134.6	7.35 d, 2.0	134.6	7.28 d, 2.5	134.6	7.36 d, 2.5	134.6
7	3.78 s	28.8	28.8	3.78 s	28.8	3.69 s	28.2	3.78 s	28.8
8		153.4	153.3		153.3		153.2		153.2
9		166.0	166.0		166.0		166.0		166.0
10	3.54 t, 6.0	39.9	39.8	3.54 t, 6.0	39.8	3.42 t, 6.5	39.7	3.54 t, 7.0	39.8
11	2.84 t, 6.0	38.8	38.6	2.84 t, 6.0	38.6	2.83 t, 6.5	38.6	2.82 t, 7.0	39.4
12	2.84 t, 6.0	38.2	37.9	2.84 t, 6.0	37.9	2.83 t, 6.5	37.9	2.78 t, 7.0	38.5
13	3.53 t, 6.0	39.8	40.1	3.54 t, 6.0	40.1	3.42 t, 6.5	40.1	3.36 t, 7.0	41.0
14		162.1	161.9		161.9		161.9		159.2
15		164.0	159.2		159.2		159.2		159.2
OCH ₂ CH ₃								4.05 q, 7.0, 1.21 t, 7.0,	61.9, 15.1

		164 (112)		165 (114)		166 (114)		167 (114)	
		¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1		CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD
2	7.35 d, 2.0	129.2	130.6	7.36 d, 2.0	134.4	7.49 d, 2.0	136.1	7.34 d, 2.0	130.0
3		109.0	110.4		116.5		116.5		110.8

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	164 (112)		165 (114)		166 (114)		167 (114)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
4	CD ₃ OD	152.3	CD ₃ OD	153.7	CD ₃ OD	149.5	CD ₃ OD	154.3
5	6.75 d, 8.5	115.6	6.75 d, 8.3	117.0	7.47 d, 8.3	123.3	6.73 d, 8.3	117.3
6	7.05 dd, 8.5, 2.0	129.0	7.06 dd, 8.3, 2.0	130.3	7.21 dd, 8.3, 2.0	130.0	7.03 dd, 8.3, 2.0	130.3
7	3.78 s	27.2	3.78 s	28.7	3.86 s	29.0	3.77 s	28.7
8		151.6		153.0		152.5		153.0
9		164.6		165.8		165.6		165.9
10	3.62 m	33.5	3.51 t, 6.8	39.7 ^b	3.52 t, 6.8	39.6	3.49 t, 6.8	39.7 ^c
11	3.51 m	39.3	2.80 t, 6.8	38.6 ^a	2.80 t, 6.8	38.5	2.78 t, 6.8 ^a	38.6 ^b
12				158.6		158.6		
13			3.02 s	38.3	3.01 s	38.3		
14			3.02 s	38.3	3.01 s	38.3		
1'		129.2		130.6		136.1		127.9
2'	7.35 d, 2.0	133.0	7.49 d, 2.0	134.6	7.49 d, 2.0	134.6	7.31 d, 2.0	132.5
3'		109.0		116.5		116.5		114.6
4'		152.3		149.6		149.5		155.0
5'	6.75 d, 8.5	115.6	7.47 d, 8.8	123.3	7.47 d, 8.3	123.3		131.7
6'	7.05 dd, 8.5, 2.0	129.0	7.21 dd, 8.3, 2.0	130.0	7.21 dd, 8.3, 2.0	130.0	7.35 d, 2.0	132.2
7'	3.78 s	27.2	3.86 s	29.0	3.86 s	29.0	3.86 s	29.0
8'		151.6		152.5		152.5		153.8
9'		164.6		165.6		165.6		166.1
10'	3.22, 3.32 m	55.0	3.51 t, 6.8	39.6 ^b	3.52 t, 6.8	39.6	3.51 t, 6.8	39.6 ^c
11'	3.29 m	32.2	2.80 t, 6.8	38.5 ^a	2.80 t, 6.8	38.5	2.77 t, 6.8 ^a	38.5 ^b
1''								172.7
2''								142.5
3''							6.93 s	123.8
4''								124.1
5''							8.22 d, 2.2	134.3
6''								116.4
7''								160.2

	164 (112)		165 (114)		166 (114)		167 (114)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
8''	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD
	130.8							130.8
9''							7.65 d, 2.2	134.2

	168 (114)			168a (114)			169 (117)			170 (117)		
	¹ H	¹³ C	CDCl ₃	¹ H	¹³ C	CDCl ₃	¹ H	¹³ C	CD ₃ OD <th>¹H</th> <th>¹³C</th> <th>CD₃OD</th>	¹ H	¹³ C	CD ₃ OD
1		129.6			133.1			130.3				
2	6.81 d, 2.0	126.3	6.96 d, 1.4		126.0		7.35 d, 2.0	134.6	7.36 d, 2.0			
3		110.5			117.6			110.0				
4		143.7			144.3			153.2				153.7
5		147.5			151.2		6.74 d, 8.5	116.8	6.74 d, 8.5			117.0
6	6.18 d, 2.0	115.0	6.17 d, 1.4		114.3		7.05 dd, 8.5, 2.0	130.0	7.06 dd, 8.0, 2.0			130.6
7	3.72 s	28.3	3.71 s		25.6		3.79 s	28.0	3.76 s			28.7
8		153.1			151.7			152.8				152.8
9		166.2			163.1			165.8				166.0
10	3.51 m ^d	40.0	3.48 br		38.7		3.60 t, 7.0	39.0	3.51 t, 7.0 ^b			39.6
11	2.87 m ^d	41.1	2.48 br		38.8		2.99 7.0	37.8	2.81 7.0 ^c			38.5
1'		130.3			132.9			130.3				128.3
2'	7.32 d, 2.0	134.6	7.43 d, 1.8		134.7		7.35 d, 2.0	134.6	7.35 s			133.0
3'		113.1			117.1			110.0				112.0
4'		151.2			153.1			153.2				151.0
5'		128.4			132.0		6.74 d, 8.5	116.8				112.0
6'	6.78, d, 2.0	131.3	6.65 d, 1.8		129.6		7.05 dd, 8.5, 2.0	130.0	7.35 s			133.0
7'	3.68 br s ^d	28.7	3.63 s		28.6		3.79 s	28.0	3.78 s			28.7
8'		152.9			151.1			152.8				153.3
9'		165.4			162.7			165.8				166.0
10'	3.43 t, 6.8	39.6	3.54 t, 6.1		39.0		3.60 t, 7.0	39.0	3.50 t, 7.0 ^b			39.6
11'	2.87 t, 6.8	38.4	3.48 br		38.8		2.99 7.0	37.8	2.80 7.0 ^c			38.5
1''		171.4			166.2							

	168 (114)		168a (114)		169 (117)		170 (117)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
2''	CD ₃ OD	146.8	CDCl ₃	140.0	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD
3''	6.96 s	120.9	6.50 s	108.5				
4''		134.5		132.6				
5''	8.42 d, 2.0	135.7	8.12 d, 1.8	134.6				
6''		118.2		117.9				
7''		150.4		148.1				
8''		135.5		133.8				
9''	7.59 d, 2.0	134.1	7.67 d, 1.9	132.1				
1''-Me			3.92 s	53.5				
8,8'-Me			3.91 s, 3.85 s	63.0, 62.9				
4,4'-Me			3.61 s, 3.58 s	61.1, 60.5				
NH			7.71 br; 7.23 t, 6.3					

	171 (117)				163 (112)			
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CD ₃ OD	130.8	1'	128.7	1''	129.3	1'''	130.8
2	7.35 d, 2.0	133.3	2'	128.2	2''	134.0	2'''	133.3
3		109.5	3'	110.9	3''	113.6	3'''	109.5
4		152.8	4'	145.3	4''	152.3	4'''	152.8
5	6.74 d, 8.5	116.0	5'	145.3	5''	119.6	5'''	116.0
6	7.05 dd, 8.5, 2.0	129.2	6'	118.3	6''	129.6	6'''	129.2
7	3.78 s	27.5	7'	27.6	7''	27.9	7'''	27.5
8		152.0	8'	151.7	8''	151.5	8'''	152.0
9		164.7	9'	164.6	9''	164.6	9'''	164.7
10	3.51 t, 7.0	38.5	10'	38.5	10''	38.5	10'''	38.5
11	2.80 t, 7.0	37.4	11'	37.4	11''	37.4	11'''	37.4
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	172 (44)		173 (118)		174 (118)		175 (118)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CD ₃ OD	113.1	CD ₃ OD	112.2	CD ₃ OD	137.4	CD ₃ OD	137.4
2	7.43 d, 2.2	134.7	7.17 dd, 2.2, 8.5	130.4	7.47 s	134.5	7.14 dd, 2.0, 8.5	134.5
3		130.3	6.88 d, 8.5	113.2		113.2	6.88 d, 8.5	113.2
4		155.8		155.9		152.1		152.1
5	6.88 d, 8.5	112.1		131.8		118.6		118.6
6	7.17 dd, 2.2, 8.5	131.1	7.42 d, 2.0	134.7	7.47 s	134.5	7.47 d, 2.0	134.5
7	3.79 s	28.7	3.79 s	28.7	3.81 s	28.8	3.79 s	28.8
8		152.9		153.0		152.2		152.2
9		165.8		165.8		165.5		165.5
10	3.41 t, 7.0	41.3	3.42 t, 7.3	41.3	3.43 t, 7.2	41.3	3.42 t, 7.2	41.3
11	2.73 t, 7.0	35.2	2.75 t, 7.3	35.2	2.75 t, 7.2	35.2	2.73 t, 7.2	35.2
12		140.3		140.3		140.3		140.3
13,17	7.42 s	134.4	7.43 s	134.4	7.44 s	134.4	7.41 s	134.4
14,16		118.7		118.7		118.7		118.7
15		152.1		152.2		152.1		152.1
18	4.05 t, 5.5	71.7	4.08 t, 5.7	71.6	4.06 t, 5.8	71.6	3.99 t, 6.2	71.6
19	2.25 tt, 5.5, 7.6	26.4	2.19 tt, 5.5, 7.5	29.0	2.18 tt, 5.8, 7.8	29.0	2.03 tt, 6.2, 6.5	29.0
20	3.46 t, 7.6	56.9	3.29 t, 7.5	39.0	3.29 t, 7.8	39.0	3.41 t, 6.5	39.0
22							2.17 t, 7.3	
23							1.60 m	
24-32							1.28 16H, m 1.16 m	
33							1.51 m	
34,35							0.86 d, 6.5	
Ome	3.81 s	56.7	3.82 s	56.7	3.81 s	61.0	3.82 s	61.0
NH(CH ₃) ₂	2.93 s	43.7						

	176 acetate (119)		177 acetate (119)		178 (82)		179 (121)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CDCl ₃	132.6	CDCl ₃	132.6	CDCl ₃	135.6	CD ₃ OD	138.2

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	176 acetate (119)		177 acetate (119)		178 (82)		179 (121)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
2	7.56 d, 2		7.50 s	133.5	7.48 s	133.4	7.25 d, 7.5	130.1
3				117.8		117.7	7.20 dd, 7.3, 7.5	129.3
4				153.1		153.8	7.12 t, 7.3	127.2
5	6.80 d, 8			117.8		117.7	7.20 dd, 7.3, 7.5	129.3
6	7.2-7.5 m		7.50 s	133.5	7.48 s	133.4	7.25 d, 7.5	130.1
7	3.85 s		3.84 s	27.9	3.84 s	28.0	3.91 s	29.9
8				152.5		150.9		153.2
9				162.8		163.4		166.0
10	3.4-3.7 m		3.4-3.6 m	39.9	3.60 dt, 6.1, 5.8	37.3	2.60 t, 6.7	37.7
11	2.76 t, 7		2.74 t, 6	34.0	2.06 m	28.4	2.05 tt, 6.2, 6.7	30.7
12				135.3	4.06 t, 5.8	67.9	4.10 t, 6.2	72.2
13	7.2-7.5 m		7.38 d, 2			152.4		153.6
14				111.9		114.0		119.5
15				151.2	7.32 d, 1.8	133.3	7.51 s	134.4
16	6.80 d, 8		6.76 d, 8	113.0		111.5		137.3
17	7.02 dd, 8, 2		7.02 dd, 8, 2	129.2	7.02 dd, 8.3, 1.8	128.8	7.51 s	134.4
18	4.20 t, 6		4.14 t, 6	68.4	6.78 d, 8.6	133.2		119.5
19	1.9-2.2 m		1.9-2.2 m	28.1	2.68 t, 6.5	37.0	2.88 t, 7.5	33.3
20	3.4-3.7 m		3.4-3.6 m	38.6	2.96 t, 6.5	42.5	3.13 t, 7.5	41.5
Ome	3.86 s		3.86 s	60.6	3.82 s	60.5		
NH(CH ₃) ₂								
NH	6.60 brt, 6		6.64 t, 6		7.10 brt, 6.1			
NH	6.32 m		6.44 m					
NOH	9.80 br		10.64 br					
OCOCH ₃	1.94 s		1.94 s	23.1				
NHCOCH ₃				171.3				

	180 (121)			181 (121)			182 (121)			183 (121)		
	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD
1		138.1			138.1			138.1		137.1		
2	7.25 d, 7.5	130.0	7.25 d, 7.5		130.0	7.21 m	7.23 m	130.0	7.21 m	130.0	7.21 m	130.0
3	7.20 dd, 7.3, 7.5	129.3	7.20 dd, 7.3, 7.5		129.3	7.21 m	7.14 m	129.3	7.21 m	129.3	7.21 m	129.3
4	7.15 t, 7.3	127.2	7.12 t, 7.3		127.2	7.13 m	7.14 m	127.2	7.14 m	127.2	7.14 m	127.2
5	7.20 dd, 7.3, 7.5	129.3	7.20 dd, 7.3, 7.5		129.3	7.21 m	7.14 m	129.3	7.21 m	129.3	7.21 m	129.3
6	7.25 d, 7.5	130.0	7.25 d, 7.5		130.0	7.21 m	7.23 m	130.0	7.21 m	130.0	7.21 m	130.0
7	3.90 s	30.2	3.91 s		29.9	3.88 s	3.78 s	29.9	3.88 s	29.9	3.88 s	29.9
8		153.4			153.3			153.2		153.2		153.2
9		166.1			166.0			166.0		166.0		166.0
10	3.43 t, 6.7	37.7	3.51, t, 6.8		37.7	3.42 t, 7.2	3.32 m	41.3	3.42 t, 7.1	41.4	3.42 t, 7.1	41.4
11	2.00 tt, 6.1, 6.7	30.0	2.04 tt, 6.1, 6.8		30.7	2.73 t, 7.2	2.73 t, 6.8	35.2	2.74 t, 7.1	35.2	2.74 t, 7.1	35.2
12	4.02 t, 6.1	68.3	3.99 t, 6.1		72.3			140.3		139.1		139.1
13		155.9			153.9	7.45 s	7.48 s	134.4	7.45 s	134.4	7.45 s	134.4
14		113.4			119.6			118.7		118.7		118.7
15	7.47 d, 1.8	134.4	7.44 s		134.4			152.2		152.2		152.2
16		131.6			136.1			118.7		118.7		118.7
17	7.18 d, 1.8, 8.4	130.0	7.44 s		134.4	7.45 s	7.48 s	134.4	7.45 s	134.4	7.45 s	134.4
18	6.95 d, 8.4	115.0			119.6	4.09 t, 5.7	3.98 t, 5.9	71.6	4.10 t, 5.7	71.4	4.10 t, 5.7	71.4
19	2.88 t, 7.6	33.3	3.27 t, 7.3		36.6	2.19 tt, 5.7, 7.3	2.06 m	29.0	2.22 tt, 5.7, 7.2	33.8	2.22 tt, 5.7, 7.2	33.8
20	3.13 t, 7.6	41.9	4.83 t, 7.3		63.3	3.30 t, 7.3	3.60 m	38.9	3.32 t, 7.2	48.2	3.32 t, 7.2	48.2
21,25					146.2							
22,24					129.5							
23			8.59 t, 7.1		147.2							
NH-9							8.00 t, 5.8					
NOH-8							11.77 s					
NMe-20									2.76 s			27.1

	184 (121)		185 (121)		186 (121)		187 (121)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CD ₃ OD	130.3	CD ₃ OD	130.6	CD ₃ OD	131.8	CD ₃ OD	131.8
2	7.04 dd, 2.0, 8.3	130.6	7.03 dd, 1.7, 8.3	130.3	7.18 dd, 1.8, 8.5	130.4	7.17 dd, 2.0, 8.4	130.4
3	6.75 d, 8.3	117.1	6.75 d, 8.3	117.1	6.90 d, 8.5	113.2	6.89 d, 8.4	113.2
4		153.7		153.7		155.9		155.9
5		110.5		110.5		112.2		112.2
6	7.43 d, 2.0	134.4	7.34 d, 1.7	134.4	7.42 d, 1.8	134.4	7.42 d, 2.0	134.7
7	3.76 s	28.7	3.75 s	28.7	3.79 s	28.7	3.79 s	28.7
8		153.2		153.1		153.0		153.0
9		166.2		165.8		165.8		165.8
NMe-20				2.76 s				2.76 s
10	3.41 t, 7.1	41.4	3.42 t, 7.0	41.3	3.43 t, 7.2	41.3	3.42 t, 7.1	41.3
11	2.74 t, 7.1	35.2	2.73 t, 7.0	35.2	2.75 t, 7.2	35.2	2.74 t, 7.1	35.2
12		140.3		140.3		140.3		140.3
13	7.43 s	134.4	7.43 s	134.4	7.43 s	134.4	7.43 s	134.4
14		118.7		118.7		118.7		118.7
15		152.2		152.1		152.2		152.2
16		118.7		118.7		118.7		118.7
17	7.43 s	134.4	7.43 s	134.4	7.44 s	134.4	7.43 s	134.4
18	4.07 t, 5.7	71.6	4.06 t, 5.7	71.5	4.08 t, 5.7	71.6	4.05 t, 5.6	71.6
19	2.18 tt, 5.7, 7.2	29.0	2.21 tt, 5.7, 7.2	33.8	2.18 tt, 5.7, 7.6	29.0	2.21 tt, 5.6, 7.6	33.8
20	3.30 t, 7.2	39.0	3.34 t, 7.2	48.2	3.30 t, 7.6	38.9	3.30 t, 7.6	38.2
OMe				3.82 s		56.7		56.7

	188 (121)		189 (86)		190 (122)		191 (122)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CD ₃ OD	138.0	CD ₃ OD	131.4	DMSO-d ₆	130.4	CD ₃ OD	131.7
2	7.23 m	130.0	7.40 d, 2.0	134.4	7.38 d, 2.0	133.0	7.44 d, 2.0	7.44 d, 2.0
3	7.23 m	129.3		111.8		110.2		112.5
4	7.16 m	127.3		155.4		153.8		155.7

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	188 (121)		189 (86)		190 (122)		191 (122)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
5	7.23 m	129.3	6.85 d, 8.0	112.8	6.97 d, 8.0	112.6	6.78 d, 8.0	113.2
6	7.23 m	130.0	7.13 dd, 2.4, 8.5	130.0	7.12 dd, 2.0, 8.0	129.1	7.02 dd, 2.0, 8.0	130.4
7	3.91 s	31.0	3.76 s	28.2	3.72 s	27.8	3.76 s	28.1
8		152.2		152.6		151.8		152.7
9		166.9		165.4		163.2		165.5
10			3.39 t, 7.2	41.0	3.35 t, 7.0	41.1	3.15 t, 7.2	48.7
11			2.70 t, 6.9	34.8	2.73 t, 7.0	34.0	2.15 t, 7.2	29.0
12				139.8		139.0	4.08 t, 6.0	71.5
13			7.39 s	134.0	7.46 s	132.9		152.2
14				118.4		117.2		118.9
15				152.0		150.7	7.36 s	134.3
16				118.0		117.2		139.9
17			7.39 s	134.0	7.46	132.9	7.36 s	134.3
18			4.03 t, 5.7	70.9	3.91 t, 6.0	71.0		118.9
19			2.37 q, 6.4	25.1	2.03 t, m	28.0	2.72 t, 7.8	35.5
20			3.61 dt, 8.4, 7.6	69.0	3.38 t, 6.8	40.6	3.45 t, 7.8	41.5
21						156.5		
22					3.57 s	52.3		
23								
OMe			3.79 br	56.0	3.79 s	56.2	3.79 s	57.0
NOMe ₂			3.24 br	58.0				
NH					7.99 t, 6.0			
NMe					2.83 s	41.4	2.60 s	34.4

	192 (84)		193 (123)		194 (123)		195 (124)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1		136.4		137.9		138.0		135.7
2	7.48 s	132.9	7.49 s	134.4	7.47 s	134.6	7.41 br	134.2
3		117.2		117.8		118.5		118.6

	192 (84)		193 (123)		194 (123)		195 (124)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
4	DMSO- <i>d</i> ₆	150.5	CD ₃ OD	152.2	CD ₃ OD + TFA	152.3	CDCl ₃	152.6
5		117.2		117.8		118.5		118.6
6	7.48 s	132.9	7.49 s	134.4	7.47 s	134.6	7.41 br	134.2
7	3.74 s	27.7	3.82 s	30.7	3.81 s	30.7	3.07 dd, 13, 6, 2.95 dd, 13, 9	37.2
8		150.8		151.9		151.9	3.70 dd, 9, 6	63.9
9		163.0		165.5		165.4		169.4
10	3.34 m	49.7	3.41 t, 7.1	41.5	3.42 t, 7.1	41.5	3.53 ddd, 14, 8, 6, 3.40 dt, 14, 7	36.7
11	2.27 t	33.3	2.74 t, 7.1	35.2	2.74 t, 7.1	35.2	1.90 m	30.0
12		139.1		140.3		140.2	3.91, 3.89 m	71.1
13	7.45 s	132.9	7.43 s	134.6	7.43 s	134.4		153.9
14		117.1		118.7		118.7		118.9
15		150.4		152.4		152.3	7.46 br	133.6
16		117.1		118.7		118.7		134.7
17	7.45 s	132.9	7.43 s	134.6	7.43 s	134.4	7.46 br	133.6
18	3.97 t	70.3	4.10 t, 5.4	70.8	4.08 t, 5.8	71.6		118.9
19	2.07 m	27.7	2.60 tt, 5.4, 6.9	32.5	2.20 tt, 5.8, 7.7	29.0	3.01 m	30.2
20	3.04 m	36.5	4.99 t, 6.9	60.9	3.29 t, 7.7	38.9	3.20 m	58.9
21	3.97 t	70.4	4.80 t, 5.7	71.6	4.10 t, 5.6	70.9		
22	2.07 m	27.7	2.19 tt, 5.7, 7.7	29.0	2.60 tt, 5.6, 7.1	32.5		
23	3.04 m	36.5	3.28 t, 7.7	38.9	4.98 t, 7.1	60.8		
NOH	12.05 s							
1',5'			9.13 d, 5.8	146.4	9.13 d, 5.8	146.4		
2',4'			8.14 dd, 5.8, 7.7	129.5	8.13 dd, 5.8, 7.7	129.5		
3'			8.60 t, 7.7	147.1	8.59 t, 7.7	147.1		
NH	8.12 t							
NH ₂	7.86 br						2.82 s	43.4
NMe							2.52 s	33.1
NMe ₂							3.77 s	60.9
OMe								

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	196 (125)			197 (126)			198 (126)			199 (90)		
	¹ H	¹³ C	CD ₃ OD + CDCl ₃	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD
1		137.7			129.8			129.4		136.5		
2	7.31 s	133.2	7.47 d, 1.9		136.1	7.44 d, 1.1		136.1	7.49 s	132.9		
3		117.6			113.6			113.6		117.2		
4		152.3			157.9			157.9		150.5		
5		117.6	7.04 d, 8.5		114.5	7.04 d, 8.4		114.4		117.2		
6	7.31 s	133.2	7.20 dd, 1.9, 8.5		131.7	7.18 dd, 1.1, 8.4		131.8	7.49 s	132.9		
7	2.71 dd, 4.5, 13.8 2.94 dd, 8.8, 13.5	31.6	3.08 dd, 7.8, 14.0 2.98 dd, 7.3, 14.0		38.3	3.12 dd, 5.7, 13.6 3.05 dd, 8.6, 13.6		37.4	3.82 s	28.1		
8	3.14 dd, 4.5, 8.8	69.8	4.00 t, 7.3		56.5	3.90 m		64.9		151.0		
9		170.8			170.3			168.9		165.7		
10	3.29 dt, 2.8, 7.0	39.8	3.56 m 3.32 dd, 6.6, 13.2		42.3	3.47 m 3.38 m		42.1	3.27 m	38.9		
11	2.57, 2.54 m	34.2	2.74 t, 7.2		35.8	2.73, 2.63 m		35.8	1.56 m	27.1		
12		137.9			140.9			140.8	1.56 m	27.2		
13	7.23 s	132.8	7.51 s		135.1	7.47 s		135.1	3.17 m	41.8		
14		117.7			119.7			119.7		156.8		
15		150.9			153.2			153.2	4.09 t, 5.5	70.7		
16		117.7			119.7			119.7	1.26 m	33.6		
17	7.23 s	132.8	7.51 s		135.1	7.47 s		135.1	3.25 m	39.5		
18	3.96 t, 5.5	69.7	4.13 t, 5.6		71.9	4.12 t, 5.5		71.9				
19	2.18 m	25.4	2.32 tt, 5.6, 7.9		27.2	2.32 tt, 5.5, 7.5		27.2				
20	3.16 m	55.4	3.54 t, 7.9		57.8	3.54 t, 7.4		57.6				
21	3.74 s	60.4										
22,23	2.26 s	41.5										
24,25	2.67 s	42.9										
NH	8.67 brt											
OMe			3.91 s		57.6	3.90 s		57.6				
NMe ₂			3.00 s		44.5	3.00 s		44.4				
NMe						2.62 s		33.3				

	200 (79)		201 (127)		202 (127)		203 (127)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1		DMSO- <i>d</i> ₆		CDCl ₃		CDCl ₃		CDCl ₃
		123.7		133.7		139.1		130.9
2		155.2	7.63 d, 2.1	139.8	7.65 s	140.5	7.61 d, 2.1	140.0
3		108.2		85.7		90.3		86.1
4		153.6		156.4		157.2		157.2
5		108.2	6.72 d, 8.3	110.7		90.3	6.76 d, 8.3	111.0
6	7.31 s	135.4	7.22 dd, 2.1, 8.3	130.4	7.65 s	140.5	7.14 dd, 2.1, 8.3	130.3
7	3.70	26.7	2.78 dd, 4.9, 13.5 3.05 dd, 7.5, 13.5	31.5	2.73 dd, 4.6, 13.8 3.02 dd, 7.9, 13.8	31.0	2.63 dd, 8.7, 13.5 3.05 dd, 4.3, 13.5	37.1
8		152.6	3.13 dd, 4.9, 7.5	70.9	3.14 dd, 4.6, 7.9	69.8	3.13, dd, 8.7, 4.3	65.1
9		167.8		171.5		170.3		171.6
10	3.18 m	40.7	3.18 q, 6.6	38.8	3.20 q, 6.6	39.0	3.22 quin, 7.2	38.7
11	1.44 m	29.0	1.44 m	29.2	1.45 m	29.0	1.46 m	28.9
12	1.42 m	28.4	1.22 m	24.1	1.22 quin, 7.2	24.1	1.24 m	24.0
13	3.09 m	42.9	1.44 m	29.2	1.45 m	29.0	1.46 m	28.9
14		156.4	3.18 q, 6.6	38.9	3.20 q, 6.6	39.0	3.22 quin, 7.2	38.9
15				171.2		170.3		170.2
16			3.14 dd, 4.6, 7.8	70.4	3.14 dd, 4.6, 7.9	69.8	3.14 dd, 4.4, 7.9	69.6
17			2.72 dd, 4.6, 13.7 3.01 dd, 7.8, 13.7	30.5	2.73 dd, 4.6, 13.8 3.02 dd, 7.9, 13.8	31.0	2.73 dd, 4.4, 13.8 3.02 dd, 7.9, 13.8	31.0
18				139.9		139.1		139.0
19,23				140.4	7.65 s	140.5	7.65 s	140.5
20,22				90.1		90.3		90.2
21				157.0		157.2		157.3
4-OMe	3.74	61.7	3.81 s	56.3	3.82 s	60.7	3.81 s	56.4
21-OMe			3.84 s	60.6	3.82 s	60.7	3.86 s	60.7
8-NMe			2.33 s	42.1	2.30 s	41.9	2.28 s	34.6
18-NMe			2.30 s	42.2	2.30 s	41.9	2.30 s	41.8
NH ₂			7.1–7.3 br					
9-NH 13-NH			7.56 t, 5.9, 7.43 br					
OH			10.68, 10.12 br					

	<u>204 (129)</u>	<u>205 (129)</u>	<u>206 (129)</u>
	^H _I	^H _I	^H _I
	acetone- <i>d</i> ₆	acetone- <i>d</i> ₆	acetone- <i>d</i> ₆
1	3.65 s ^H	3.54 s ^G	3.72 s
4	7.96 t ^F	7.89 t, 6 ^E	8.00 t, 7
5	3.32 q ^E	3.25 dt, 6, 7 ^D	3.29 q, 7
6	2.62 t ^D	2.67 t, 7 ^C	2.62 t, 7
8	7.29 d, 1.9 ^A	7.28 d, 1.9 ^A	7.32 d, 1.9 ^A
11	6.86 d, 8.2 ^B	6.85 d, 8	6.85 d, 8.2
12	6.96 dd, 1.9, 8.2 ^C	6.96 dd, 1.9, 8 ^B	6.98 dd, 1.9, 8.2
16	6.87 d, 8.2 ^B	6.85 d, 8	6.85 d, 8.2
17	6.99 dd, 1.9, 8.2 ^C	6.99 dd, 1.9, 8 ^B	6.98 dd, 1.9, 8.2
19	7.31 d, 1.9 ^A	7.30 d, 1.9 ^A	7.32 d, 1.9 ^A
20	2.65 t ^D	2.60 t, 7 ^C	2.62 t, 7
21	3.27 q ^E	3.33 dt, 6, 7 ^D	3.29 q, 7
22	8.01 t ^F	8.11 t, 6 ^E	8.00 t, 7
25	3.76 s ^H	3.83 s ^G	3.72 s
27	7.51 d, 1.7	7.57 s	7.29 d, 1.9 ^A
30	6.75 d, 8.5		
31	7.15 dd, 1.7, 8.5	7.57 s	6.93 d, 1.9
36	7.13 d, 1.7	6.97 d, 1.9	7.29 d, 1.9 ^A
38	6.64 d, 1.7	6.21 d, 1.9	6.93 d, 1.9
OH-15	10.02 s	10.02s	10.02 s
OH-10	10.02 s	10.02s	10.02 s
OH-29			8.94 s
OH-34	9.85 s	10.02s	8.94 s
NOH-24	11.94 s ^G	11.75 s ^F	11.84s
NOH-2	11.83 s ^G	12.08 s ^F	11.84s

	208 (129)	208 Tetramethyl ether (129)	210 (129)	211 (129)
	¹ H	¹ H	¹ H	¹ H
	acetone-d ₆	acetone-d ₆	acetone-d ₆	acetone-d ₆
1	3.52 s ^C	signals were not assigned	3.57 s ^E	3.50 s ^D
4	10.24 d, 10.2		8.00 t, 6 ^C	10.29 d, 10
5	7.31 dd, 10.2, 14.5	7.50 2H s	3.30 m	7.34 dd, 10, 15
6	6.44 d, 14.5	7.45 d, 2	2.72 m	6.42 d, 15
8	7.63 d, 1.9	7.16 d, 2	7.65 s ^F	7.67 d, 1.9
11	6.92 d, 8.5	7.10 d, 2		6.99 d, 8.8
12	7.48 dd, 1.9, 8.5	6.80 d, 2	7.65 s ^F	7.45 dd, 1.9, 8.8
17 ¹	6.55 d, 1.9	6.24 d, 2	6.23 d, 1.7 ^{BA}	6.43 d, 2.0 ^{AB}
19 ¹	7.13 d, 1.9 ^A	Other aromatic signals are overlapped.	7.08 d, 1.7 ^{AB}	7.20 d, 2.0 ^{AB}
20	2.73 m		2.72 m	2.64 t, 6
21	3.35 m		3.30 m	3.24 q, 6
22	7.85 t, 6	4.02, 3.98, 3.94, 3.52, 3H each, s, OCH ₃	8.13 t, 6 ^C	7.85, 6
25	3.64 s ^C		3.66 s ^E	3.71 s ^D
27	7.51 s		7.64 s ^F	7.44 d, 1.9
30				6.66 d, 8.3
31	7.51 s		7.64 s ^F	7.10 dd, 1.9, 8.3
36	7.08 d, 1.9 ^A		7.04 d, 1.9 ^{AB}	7.09 d, 1.5 ^{BA}
38	6.09 d, 1.9		6.16 d, 1.9 ^{BA}	6.40 d, 1.5 ^{BA}
OH	9.85 s ^B		10.00 s	9.89 s
OH-34	10.10 s ^B		10.00 s	9.89 s
NOH	12.00 s		11.92 s ^D	12.09 s ^C
NOH-2	12.00 s		11.71 s ^D	11.99 s ^C

	228 (130)			212 (132)			212 Tetramethyl ether (132)			213 (132)		
	¹ H	¹³ C	DMSO- <i>d</i> ₆	¹ H	¹³ C	DMSO- <i>d</i> ₆	¹ H	¹³ C	NA	¹ H	¹³ C	DMSO- <i>d</i> ₆
1	3.74 s	27.8		3.57 br	27.3		3.79 br		3.54 br		27.6	
2		151.2 ^e			150.9						151.4	
3		161.2			162.8						162.9	
4	10.26 d, 10											
5	7.32 dd, 10, 14	124.1		3.40, 3.00 m	47.3		3.72, 3.38 m		3.18 q		40.9	
6	6.40 d, 14	111.4		4.63 m	70.4		4.88 m		2.62 t		34.0	
7		134.6			140.6						135.4	
8	7.62 d, 2	129.6		7.69 d, 2.0	130.2		7.69 d, 2.0		7.49 d, 2.1		132.8	
9		114.9			112.0						111.8	
10		151.3 ^e			151.8						152.4	
11	7.01 d, 8.5	122.7		6.94 d, 8.4	119.5		6.97 d, 8.0		6.75 d, 8.4		120.3	
12	7.42 dd, 8.5, 2	125.6		7.27 dd, 8.4, 2.0	126.5		7.28 dd, 8.0, 2.0		7.10 dd, 8.4, 2.1		125.7	
14		151.4			144.7						148.0	
15		139.6			143.8						143.0	
16		118.8			110.6				6.85 d, 8.1		116.5	
17	7.12 d, 2	127.2		7.13 d, 2.0	128.1		7.14 d, 2.0		6.81 dd, 8.1, 1.8		128.9	
18		137.1			131.4						130.6	
19	6.39 d, 2	116.6		6.60 d, 2.0	118.0		6.65 d, 2.0		6.73 d, 1.8		118.0	
20	2.71 t, 6	33.0		2.68 t, 6.0	33.4		2.75 m		2.67 t, 5.7		34.0	
21	3.27 m	38.7		3.40 q	39.2		3.46, 3.55		3.41 q		39.4	
22	7.85 t, 6.0						6.76 t, 6.0					
23		163.2			163.2						163.0	
24		151.0			150.4						150.4	
25	3.43 s	29.0		3.62 br	28.7		3.78 br		3.52 br		28.8	
26		133.9			137.6						137.7	
27	7.38 d, 2	132.6		7.56 s	133.5		7.52 s		7.59 s		133.1	
28		112.8			117.1						117.2	
29		151.5			145.9						145.9	
30	6.70 d, 8.5	120.2			117.1						117.2	
31	7.02 dd, 2, 8.5	129.8		7.56 s	133.5		7.52 s		7.59 s		133.1	

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	228 (130)		212 (132)		212 Tetramethyl ether (132)		213 (132)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
33		151.4		144.7				
	DMSO- <i>d</i> ₆		DMSO- <i>d</i> ₆		CDCl ₃	NA	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆
34		140.5		141.9				
35		119.0		109.7				
36	7.23 d, 2	128.1	7.07 d, 2.0	126.8	7.16 d, 2.0		7.05 d, 1.8	126.8
37		133.6		127.9				128.1
38	6.40 d, 2	117.9	6.24 d, 2.0	112.9	6.28 d, 2.0		6.22 d, 1.8	112.8
OMe					4.02 s, 4.01 s, 3.97 s, 3.70 s			
OH			5.62 d, 4.2		6.87 t, 6.0			
NH-4			7.77 t, 6.0				7.97 t, 6.0	
NH			8.00 t, 6.0				8.03 t, 5.7	
NOH	11.94, 12.13 s		11.83 br, 12.0 br				11.73, 11.96 br	
ArOH			9.8 br				10.02 br	

	213 Tetramethyl ether(132)		214 (132)		215 (132)		215 Tetramethyl ether(132)	
	¹ H	¹³ C (143)	¹ H (132)	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	3.67 br		3.61 br	27.6	3.64 br	27.3		
2				151.2		151.3		
3				162.9		161.4		
4								
5			3.30 q	47.0	7.25 dd, 14.6, 10.3	123.6	7.34 dd ^a	
6			4.62 m	70.2	6.39 d, 14.6	110.9	6.17 d, 14.7	
7				141.0		133.3		
8	7.44 d, 2.0		7.64 d, 1.7	130.6	7.52 d, sm	130.5	7.54 d, 2.7	
9				113.3		112.5		
10				151.7		152.3		
11	6.85 d, 8.0		6.91 d, 8.5	120.0	6.73 d, 8.7	119.9	6.90 d, 8.4	
12	7.03 dd, 8.3, 2.0		7.21 dd, 8.0, 2.0	126.8	7.43 dd, 8.7, 2.1	124.1	7.38 dd ^a	
14				145.0		146.7		

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	213 Tetramethyl ether(132)		214 (132)		215 (132)		215 Tetramethyl ether(132)	
	¹ H	¹³ C (143)	¹ H (132)	¹³ C (143)	¹ H	¹³ C	¹ H	¹³ C
15	CDCl ₃		DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CDCl ₃	CDCl ₃
16	6.97 d, 8.3	143.4	7.12 d, 2.1	143.4	6.87 d, 8.0	143.0	6.96 d, 8.4	143.0
17	6.91 dd, 8.3, 2.0	110.7		110.7	6.82 dd, 8.0, sm	116.7	6.90 dd ^a	116.7
18		127.7		127.7		125.8		125.8
19	6.66 d, 2.0	131.7	6.45 d, 1.8	131.7	6.72 d, sm	130.6	6.71 d, 2.1	130.6
20		117.4	2.61 t, 6.0	117.4	2.70 bt	119.1		119.1
21		33.5	3.38 q	33.5	3.43 q	33.5		33.5
22		40.6		40.6		38.5		38.5
23		163.1		163.1		162.7		162.7
24		150.8		150.8		150.1		150.1
25	3.86 br	28.5	3.61 br	28.5	3.53 br	28.9		28.9
26		134.5		134.5		137.6		137.6
27	7.53 s	133.5	7.49 d, 2.0	133.5	7.51 s	133.5	7.46 s	133.5
28		113.3		113.3		116.9		116.9
29		151.2		151.2		145.9		145.9
30		119.9	6.78 d, 8.5	119.9		116.9		116.9
31	7.53 s	129.6	7.07 dd, 8.5, sm	129.6	7.51 s	133.5	7.46 s	133.5
32		145.0		145.0		144.8		144.8
33		143.4		143.4		141.9		141.9
34		110.5		110.5		110.1		110.1
35		126.8	7.15 d, 1.9	126.8	7.07 d, 1.9	126.8	7.12 d, 2.0	126.8
36	7.19 d, 2.0	117.4	6.47 d, 1.9	117.4	6.14 d, 1.9	127.6	6.25 d, 2.0	127.6
37							4.01 s; 3.93 s; 3.92 s	
38	6.27 d, 2.0							
OMe	3.90, 3.49, 4.05, 4.00, Each s							
OH			5.64 d, 4.4					
NH-4	6.79 t, 6.0		7.78 t, 6.0		10.2 d, 10.3		8.30 d, 11.4	
NH-22	6.61 t, 6.0		7.94 t, 5.8		7.78 t, 6.0		6.58 t, 5.4	
NOH			11.87 br, 11.86 br		11.98 br, 11.97 br			
ArOH			9.78 br		10.04 br, 9.38 br			
CH ₂	3.53 q, 6.3; 3.46 q; 2.75 t; 2.73 t						3.73 br; 3.65 br; 3.58 q, 5.4; 2.82 t, 5.4	

	216 (142)		216 Tetramethyl ether (142)		227 (130)		217 (131)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CDCl ₃ 3.72 d, 12.9 3.78 d, 12.9	3.80 s	CDCl ₃ 3.73 s	3.69 s	27.8	3.40 s	27.8	DMSO-d ₆ 27.8
2					152.0		152.0	151.2
3					163.1		163.1	162.8
4	7.08 t, 6.1 ^b	6.73 t, 6.1 ^b	6.26 t, 6.1 ^b	7.89 t, 5.5				
5	3.41 m, 3.63 m	3.38 m	2.94 m, 3.32 m	3.30 m	39.9		3.20 dt, 6.6, 6.6	40.5
6	4.80 t, 6.1	4.86 dd, 5.2, 7.5	4.37 brd, 7.3	2.68 t, 7	33.7		2.54 t, 6.6	34.0
7					135.4			130.8
8	7.58 br	7.65 br	7.30–7.60 br	7.36 d, 2	132.3		6.53 d, 1.8	120.4
9					113.8			143.0
10					148.9			146.9
11				7.47 d, 8.5	121.2		6.86 d, 8.1	117.2
12	7.58 br	7.65 br	7.30–7.60 br	7.09 dd, 2, 8.5	128.6		6.81 dd, 1.8, 8.1	125.2
14					109.0			152.4
15					152.1			111.9
16				6.76 d, 8	116.2		7.48 d, 1.8	133.3
17	6.13 d, 1.8 ^c	7.08 d, 1.9 ^c	6.86 d, 1.9 ^c	6.88 dd, 2, 8	128.7			135.4
18					131.4		7.02 dd, 1.8, 8.4	129.4
19	7.03 d, 1.8 ^c	6.15 d, 1.9 ^c	6.30 d, 1.9 ^c	7.25 d, 2	132.5		6.58 d, 8.4	117.7
20	2.66 m	2.69 m	2.19 m	2.62 t, 7	33.5		2.68 t, 6.6	33.9
21	3.36 m	3.38 m	3.10, 2.94 m	3.30 m	39.8		3.37 obscured	39.9
22	7.14 t, 6.1 ^b	7.07 t, 6.1 ^b	6.70 t, 6.0 ^b	7.87 t, 5.5				
23					163.0			163.3
24					152.0			151.3
25	3.89 d, 13.0 3.81 d, 13.0	3.84 d, 13.0 3.78 d, 13.0	3.69 s	3.69 s	27.8		3.70 s	28.5
26					131.4			138.0
27	7.52 d, 1.8	7.52 d, 2.0	7.60 d, 2.0	7.22 br	132.3		7.46 s	133.2
28					112.4			117.3
29					152.2			146.2

	216 (142)		216 Tetramethyl ether (142)		227 (130)		217 (131)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
30	6.78 d, 8.4	6.65 d, 8.4	6.64 d, 8.4	128.2	6.96 d, 2	130.7	7.46 s	117.3
31	7.14 dd, 2.0, 8.4	7.14 dd, 2.0, 8.4	7.13 dd, 2.0, 8.4	130.7	6.96 d, 2	130.7	7.46 s	133.2
33				128.2		128.2		144.6
34				152.2		152.2		141.9
35				112.3		112.3		110.1
36	7.26 d, 1.8 ^d	7.29 d, 2.0 ^d	7.28 d, 2.0 ^d	132.3	7.22 br	132.3	6.93 d, 2.0	126.2
37				131.4		131.4		128.4
38	6.64 d, 1.8 ^d	6.70 d, 2.0 ^d	6.78 d, 2.0 ^d	130.7	6.97 d, 2	130.7	6.02 d, 2.0	113.2
OMe-10		4.05 s	4.00 s					
		4.01 s	3.80 s				9.39 s	
		3.89 s	3.65 s					
		3.87 s	3.58 s					
OH		3.21 br	2.70 br		10.00 s			
OH-10								
OH-24					8.90 br			
OH-34					8.90 br			
NH-4							9.97 s	
NH-22							7.82 brt, 6.6	
NOH-24							8.16 brt, 6.6	
NOH-2					11.75 s		11.93 s	
ArOH	10.73 br				11.69s		11.66 s	
OMe-34	11.27 br							

	217 Methyl ether(131)		226 (141)		218 (133)		218a (133)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	3.48 s	29.0	3.41	27.9	3.70 s	27.5	3.85 br	28.3
2		150.7		150.7		151.5		150.9
3		161.9		162.6		161.4		159.6
4	6.58 brt, 6.1		7.72 t, 5.8		10.31 d, 10.2		8.44 d, 8.4	
5	3.47 obscured	40.8	3.22 dt, 5.8, 7.0	40.3	7.45 dd, 14.3, 10.2	126.0	7.46 dd, 14.6, 8.4	124.8

	217 Methyl ether(131)		226 (141)		218 (133)		218a (133)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
6	2.71 brt, 6.0	34.5	2.54 t, 7.0	33.8	6.41 d, 14.3	110.0	6.11 d, 14.6	110.0
7		132.1		130.7		137.6		136.9
8	6.68 d, 1.5	121.2	6.50 d, 2.	120.1	7.77 s	129.5	7.57 s	129.8
9		144.3		143.0		118.1		118.5
10		149.5		146.7		145.6		146.4
11	6.96 m	113.6	6.85 d, 8.5	117.0		118.1		118.5
12	6.96 m	125.2	6.81 dd, 2.0, 8.5	125.0	7.77 s	129.5	7.57 s	129.8
14		153.1		152.3		145.0		150.4
15		112.9		111.9		141.6		144.3
16	7.45 d, 2.2	134.4	7.47 d, 2.0	133.1		110.1		118.1
17		133.7		135.4	7.00 d, 1.5	126.4	7.03 d, 2.0	126.7
18	6.94 dd, 2.2, 8.4	128.6	7.00 dd, 2.0, 8.3	129.3		130.8		135.5
19	6.64 d, 8.4	117.8	6.57 d, 8.3	117.9	6.18 d, 1.5	111.7	6.15 d, 2.0	112.5
20	2.78 brt, 6.0	34.5	2.66 t, 6.5	33.9	2.67 t, 6.5	32.8	2.72 t, 6.5	34.5
21	3.55 dt, 5.8, 6.0	40.5	3.37 dt, 6.5, 6.3	39.8	3.19 q, 6.3	38.3	3.36 bq, 6.5	39.4
22	6.76 brt, 5.8		8.10 t, 6.3		7.80 t, 5.7		6.71 t, 6.5	
23		162.0		163.1		162.9		162.3
24		150.8		151.3		150.9		150.4
25	3.89 s	28.7	3.69 s	28.4	3.59 s	28.4	3.75 br	29.2
26				137.4		134.4		132.5
27	7.51 s	136.6	7.42 s	133.1	7.46 br	133.7	7.47 d, 2.2	134.1
28		118.1		117.2		112.8		112.3
29		146.8		146.6		150.9		152.1
30		118.1		117.2	6.64 d, 8.3	119.1	6.47 d, 8.4	117.1
31	7.51 s	136.6	7.42	113.1	7.14 dd, 8.3, 1.9	130.3	7.12 dd, 8.4, 2.2	129.9
33		149.6		150.3		144.8		148.9
34		144.2		138.6		143.8		147.5
35		117.9		119.1		110.9		117.9
36	7.16 d, 2.0	127.3	6.93 s	125.9	7.20 d, 1.9	126.0	7.32 d, 2.2	129.9
37		133.0		133.6		128.3		133.0

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	217 Methyl ether (131)		226 (141)		218 (133)		218a (133)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CDCl ₃		DMSO-d ₆		DMSO-d ₆		CDCl ₃	
38	6.09 d, 2.0	114.7	5.98 s	113.5	6.40 br	117.3	6.86 d, 2.0	121.3
OMe-10	3.81 s	56.3						
C=NOH	3.48 s	62.4	11.68, 11.88					
OMe-34	4.01 s	63.3					3.83 s	61.1
NOMe-2	4.04 s	61.0					4.05 s	61.0
NOMe-24							4.10 s	63.7
OMe-15			9.35				4.03 s	63.1
10-OH								

	219 (134)		220 (135)		221 (135)		222 (138)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CDCl ₃ + 1 drop		DMSO-d ₆		DMSO-d ₆		CD ₃ OD	
1	3.71 s		3.55 s	27.4	3.52 s	27.4	3.67 s	28.7
2			11.65 s	151.4	11.77 s	151.0		153.3
3				163.0		162.9		166.0
4	6.76 t, 6.2		8.06 t, 6.0		7.77 t, 6.3			
5	3.51 m		3.28 m	40.4	2.92, 3.38 m	47.7	3.30 m	41.5
6	2.82 m		2.71 t, 6.6	33.9	4.58 m, 5.53 d, 4.4	70.5	2.55 t, 7	35.4
7				139.8		139.3		138.6
8	7.38 s		7.59 s	133.2	7.62 d, 1.9	129.8	7.39 d, 2.0	135.1
9				117.7		111.4		115.6
10				146.6		153.1		152.4
11				117.7	6.73 d, 8.5	117.4	6.82 d, 8.3	122.2
12	7.38 s		7.59 s	133.2	7.13 dd, 8.5, 1.9	126.2	7.06 dd, 8.3, 2.1	130.9
14				144.1		142.5		145.3
15				144.3		146.9		146.6
16			6.81 d, 8.2	116.6	6.83 d, 8.2	116.5		111.6
17	7.04 d, 1.9		6.67 dd, 8.2, 1.8	122.9	6.81 dd, 8.2, 1.9	126.1	7.04 d, 2.0	128.5
18				129.5		130.6		132.7
19	6.14 d, 1.9		6.17 d, 1.8	112.5	6.76 d, 1.9	112.5	6.35 d, 2.0	118.0

	219 (134)		220 (135)		221 (135)		222 (138)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CDCl ₃ + 1 drop	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CD ₃ OD	CD ₃ OD
20	2.67 m	33.3	2.67, 6.6	34.1	2.65 t, 6.3	34.1	2.66 t, 6.5	35.5
21	3.34 m	38.8	3.29 m	39.2	3.40 m	39.2	3.34 m, 7	41.7
22	7.16 t, 6.4	163.3	7.94 t, 6.0	163.0	7.95 t, 6.3	163.0		166.6
24		150.7	11.86 s	150.4	11.91 s	150.4		152.6
25	3.88 s	28.7	3.68 s	28.7	3.51 d, 12.9 3.56 d, 12.9	28.7	3.72 s	29.3
26		137.8		137.6		137.6		135.8
27	7.49 d, 2.0	133.7	7.63 s	133.6	7.58 s	133.6	7.42 d, 2.0	135.1
28		117.2		117.2		117.2		115.2
29		146.1		146.0		146.0		153.0
30	6.87 d, 8.3	117.2		117.2		117.2	6.67 d, 8.4	121.2
31	7.14 dd, 2.0, 8.3	133.7	7.63 s	133.6	7.58 s	133.6	6.94 dd, 8.5, 2.1	130.3
33		144.8		144.6		144.6		145.1
34		142.0		141.8		141.8		147.0
35		109.8		109.7		109.7		111.7
36	7.22 d, 2.0	127.0	7.07 d, 1.6	126.8	7.03 d, 1.9	126.8	7.13 d, 1.9	129.5
37		128.2		128.0		128.0		129.7
38	6.52 d, 2.0	112.8	6.15 d, 1.6	113.1	6.24 d, 1.9	113.1	6.46 d, 1.9	118.6
OH-15			9.25 s		9.36 s			
OH-34			9.99 s		9.98 s			
NOHe	11.48 br							
Ar-OH	10.17 br							

	223a (139)		224 (130)		225 (140)		225 Tetramethyl ether(140)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CDCl ₃	CDCl ₃
1	3.72 s	28.3	3.63 s	28.1	3.58 br	27.8	3.62 br	29.1
2		150.9		151.3		151.4		151.0
3		163.0		162.9		162.8		162.0
4	7.78 t, 6.8		6.75 t, 6		7.92 brt		6.62 brt	

	223a (139)		224 (130)		225 (140)		225 Tetramethyl ether(140)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
5	3.36 m	39.6	3.39 m	40.4	3.31 m	39.7	3.47 q, 6	40.9
6	2.68 t, 6.8	34.0	2.62 t, 6.5	34.4	2.61 m	33.9	2.72 6	34.6
7		136.8		131.6		130.6		132.0
8	6.76 d, 1.9	133.3	7.06 d, 2	127.5	6.62 d, 2	120.0	6.69 d, 2	121.1
9		113.2		110.3		142.9		145.0
10		151.2		144.7		146.7		149.5
11		119.9		143.2	6.96 d, 8	116.9	6.93 d, 8	125.0
12	7.09 dd, 8.3, 1.9	129.5	6.44 d, 2	117.2	6.89 dd, 8, 2	124.9	6.93 dd, 2, 8	113.5
14		145.1		151.4		152.2		153.2
15		143.4		114.1		111.9		113.0
16			7.41 d, 2	133.7	7.58 d, 2	133.1	7.43 d, 2	133.6
17	7.10 d, 1.9	127.4		136.8		135.5		135.0
18		131.8	7.06 dd, 2, 8	129.3	7.10 dd, 8, 2	129.2	6.94 dd, 2, 8	128.8
19	7.50 d, 1.9	117.4	6.84 d, 8	120.4	6.69 d, 8	117.8	6.66 d, 8	118.0
20	2.49 t, 6.8	33.2	2.77 t, 6.5	34.6	2.79 m	33.6	2.78 t, 6	34.5
21	3.16 m	40.0	3.54 m	40.2	3.50 m	39.5	3.58 q, 6	40.5
22	8.19 t, 6.8		6.97 t, 6		8.09 brt		6.67 brt	
23		162.7		163.4		163.3		162.5
24		151.1		151.9		151.7		151.5
25	3.36 s	27.6	3.88 s	28.3	3.79 br	28.4	3.87 br	28.7
26		128.3		134.5		134.5		135.0
27	6.89 d, 1.9	125.8	7.54 d, 2	134.2	7.17 dd, 8, 2	129.5	7.11 dd, 2, 8	129.4
28		110.0		114.1	6.92 d, 8	120.2	6.77 8	120.9
29		141.7		151.1		150.9		151.2
30		144.5	6.83 d, 8.5	120.2		113.3		114.2
31	5.94 d, 1.9	112.9	7.13 dd, 2, 8.5	129.3 ^c	7.53 d, 2	133.4	7.54 d, 2	134.5
32								
33		117.0		142.8		145.1		153.5
34		146.1		144.6		143.4		146.1
35		117.0		109.8		110.6		114.5

	223a (139)		224 (130)		225 (140)		225 Tetramethyl ether(140)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
36	7.46 s	133.0	7.20 d, 2	128.1	7.14 d, 2	127.2	7.21 d, 2	128.3
37		137.7		129.3		128.9		133.2
38	7.46 s	133.0	6.53 d, 2	117.8	6.44 2	117.2	6.48 d, 2	119.0
OMe-10							3.83 s	56.3
OH-10	11.91, 11.68 s		6.70 br		9.41 s			
OH-24					11.87 s			
OH-34			7.65 br		9.89 s			
NOH-24			11.24 s ^d					
NOH	9.8 br		10.89 s ^d		11.77 s			
OMe-34							3.92 s	61.0
NOMe-2							3.65 s	62.8
NOMe-24							3.99 s	63.0

	231 (41)			237 (41)			232 (41)		
	¹ H	¹³ C	pyridine- <i>d</i> ₅	¹ H	¹³ C	pyridine- <i>d</i> ₅	¹ H	¹³ C	CD ₃ OD
1			153.9	154.1	153.8				154.1
2			110.7	111.0	110.7				110.9
3	7.29 d, 2.0	7.53 s	134.3	133.8	134.2	7.29 d, 2.0	7.30 d, 2.0	134.5	
4			133.1	132.2	133.0			133.3	
5	6.95 dd, 2.0, 8.3	7.05 br	130.1	129.6	130.0	6.95 dd, 2.0, 8.3	6.96 dd, 2.0, 8.3	130.2	
6	6.77 d, 8.3	7.05 br	117.3	117.2	117.2	6.77 d, 8.3	6.78 d, 8.3	117.5	
7	2.67 t	2.87 t, 6.5	35.3	35.0	35.3	2.67 t, 7.2	2.68 t, 7.3	35.1	
8	3.38 t, 7.3	3.67 dt, 6.5, 6.5	42.0	41.5	41.9	3.40 t, 7.2	3.39 t, 7.3	42.0	
1'			153.8	154.2	155.9			151.0	
2'			110.5	111.1	112.2			112.2	
3'	7.35 d, 2.0	8.06 d, 2.1	134.5	134.5	134.8	7.43 d, 2.3	7.38 s	134.2	
4'			130.7	130.4	131.6			132.6	
5'	7.03 dd, 2.0, 8.3	7.55 dd, 2.1, 8.3	130.4	130.3	130.4	7.14 dd, 2.3, 8.4	7.38 s	134.2	
6'	6.76 d, 8.3	7.12 d, 8.3	117.1	117.2	113.2	6.89 d, 8.4		112.2	

	231 (41)		237 (41)		232 (41)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
7'	3.77 s	28.7	3.80 s	28.7	3.77 s	28.3
8'		153.3		153.1		152.9
9'		165.8		165.7		165.9
NH						
OMe-1'			3.82 s			

	233 (41)		233b (41)		234 (41)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	153.9	154.0				153.9
2	110.7	112.3				110.7
3	7.30 d, 2.0	134.2	7.31 s	133.9	7.28 d, 1.9	134.2
4		133.0		135.0		133.0
5	6.97 dd, 2.0, 8.3	130.0	7.31 s	133.9	6.92 dd, 1.9, 8.3	130.0
6	6.79 d, 8.3	117.2		112.3	6.79 d, 8.3	117.3
7	2.68 t, 7.3	35.2	2.68 t, 7.3	34.8	2.76 t, 7.0	35.2
8	3.40 t, 7.3	42.0	3.39 t, 7.3	41.7	3.51 dt, 7.0, 7.0	41.5
1'		153.8		151.0		154.0
2'		118.6		110.7		110.4
3'	7.47 s	134.5	7.36 d, 2.0	134.8	7.38 d, 2.2	135.2
4'		137.4		130.9		131.6
5'	7.47 s	134.5	7.04 dd, 2.0, 8.3	130.5	7.08 dd, 2.2, 8.4	131.0
6'		118.6	6.76 d, 8.3	117.3	6.83 d, 8.4	116.9
7'	3.82 s	28.8	3.77 s	28.6	3.81 s	40.6
8'		152.1		153.5		73.4
9'		165.3		166.2		174.3
NH					6.76 brt, 7.0	
NOMe					3.99 s	
OMe-1					3.84 s	
					8.39 t, 5.6	

	<u>238 (41)</u>		<u>233 (41)</u>		<u>233b (41)</u>		<u>234 (41)</u>	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CDCl ₃	CD ₃ OD	pyridine-d ₅	CD ₃ OD
OMe-1'	3.80 s	61.0			3.87 s			
<hr/>								
	<u>234a (41)</u>		<u>235 (41)</u>		<u>235a (41)</u>		<u>236 (41)</u>	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CDCl ₃	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD	CD ₃ OD
1				153.8				150.8
2				110.7				112.2
3	7.35 d, 2.1		7.28 d, 2.0	134.2	7.36 d, 2.0		7.31 s	133.6
4				133.1				131.9
5	7.04 dd, 2.1, 8.4		6.92 dd, 2.0, 8.0	129.9	7.05 dd, 2.0, 8.3		7.31 s	133.6
6	6.92 d, 8.4		6.80 d, 8.0	117.3				112.2
7	2.60 m		2.53 ddd, 7.0, 8.0, 14.0 2.60 ddd, 6.5, 8.5, 14.0	35.5	2.59 m			35.1
8	3.25 ddd, 7.4, 7.4, 15.0 3.41 ddd, 6.5, 7.9, 13.3		3.23 ddd, 6.5, 8.0, 15.0 3.40 ddd, 7.0, 8.5, 15.0	41.5	3.24 ddd, 6.9, 8.0, 14.6 3.42 ddd, 6.3, 8.3, 14.6			41.2
1'				150.9				153.9
2'				111.8				110.4
3'	7.42 d, 2.1		7.34 s	134.6	7.45 s		7.34 d, 2.0	135.2
4'				132.9				131.6
5'	7.15 dd, 2.1, 8.4		7.34 s	134.6	7.45 s		7.02 dd, 2.0, 8.0	130.9
6'	6.92 d, 8.4			111.8	6.92 d, 8.3		6.80 d, 8.0	116.9
7'	2.77 dd, 6.9, 14.0 2.93 dd, 4.1, 14.0		2.75 dd, 4.0, 14.0 2.88 dd, 7.0, 14.0	41.5	2.80 dd, 6.8, 14.0 2.93 dd, 4.1, 14.0			40.6
8'	4.15 dd, 4.1, 6.9		4.14 dd, 4.0, 7.0	73.3	4.17 dd, 4.1, 6.8			73.7
9'				175.8				176.2
OMe-1	3.82 s				3.80 s			
OMe-1'	3.83 s				3.83 s			

	236a (41)		239 (145)		240 (145)		241 (145)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	CD ₃ OD	NA	CDCl ₃	152.5	acetone- <i>d</i> ₆	152.8	CDCl ₃	155.0
2	7.40 s		7.48 s	118.3	7.42 s	118.8		112.3
3				129.4		130.1	7.55 d, 2.0	130.7
4				135.0		137.3		132.5
5	7.40 s		7.48 s	129.4	7.42 s	130.1	7.27 dd, 8.4, 2.0	126.4
6				118.3		118.8	6.85 d, 8.4	112.3
7	2.59 m		6.08 d, 14.6	110.7	5.95 d, 14.6	110.5	6.14 d, 14.6	113.5
8	3.24 ddd, 6.9, 8.0, 14.6 3.42 ddd, 6.3, 8.3, 14.6		7.53 dd, 11.1, 14.6	124.0	7.46 dd, 11.6, 14.6	125.9	7.49 dd, 11.4, 14.6	123.8
1'				156.9		157.2		158.9
2'			6.88 d, 8.4	115.8	6.78 d, 8.7	115.4	6.86 d, 8.6	116.4
3'			7.59 d, 8.4	132.0	7.29 d, 8.7	131.3	7.60 d, 8.6	132.5
4'				125.2		126.4		125.8
5'	7.16 dd, 2.0, 8.3		7.59 d, 8.4	132.0	7.29 d, 8.7	131.3	7.60 d, 8.6	132.5
6'	6.92 d, 8.3		6.88 d, 8.4	115.8	6.78 d, 8.7	115.4	6.86 d, 8.6	116.4
7'	2.80 dd, 6.8, 14.0 2.93 dd, 4.1, 14.0		7.13 s	122.3	6.14 s	109.9	7.12 s	121.3
8'	4.14 dd, 4.1, 6.8			145.3		148.2		147.8
9'				162.0		162.0		162.4
NH			8.45 d, 11.1		8.23 d, 11.6		8.37 d, 11.4	
OMe-1	3.83 s		3.87 s	60.7	3.85 s	60.9	3.89 s	56.6
OMe-1'	3.82 s							
OMe-8'			3.68 s	59.5	3.78 s	56.1	3.68 s	59.7
OH-1'			5.85 br		5.75 br		5.95 br	

	242 (145)		243 (146)	
	¹ H	¹³ C	¹ H	¹³ C
1	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CDCl ₃	156.4
2	acetone- <i>d</i> ₆	153.9	acetone- <i>d</i> ₆	157.1
3	7.55 d, 2.0	111.0	6.77 d, 8.1	115.9
	7.49 d, 2.0	129.5	6.92 d, 8.1	130.7
			7.04 d, 8.5	130.9

	242 (145)				243 (146)			
	¹ H	¹ H	¹³ C	DMSO- <i>d</i> ₆	¹ H	¹ H	¹³ C	acetone- <i>d</i> ₆
4			130.6				124.6	127.5
5	7.34 m	7.23 dd, 8.6, 2.1	125.7		6.92 d, 8.1	7.04 d, 8.5	130.7	130.9
6	7.01 d, 8.7	6.81 d, 8.6	112.9		6.77 d, 8.1	6.75 d, 8.5	115.9	116.1
7	6.21 d, 14.8	6.04 d, 14.6	111.8		3.47 s	3.33 s	42.9	43.1
8	7.34 m	7.41 dd, 14.6, 11.7	122.5				171.7	171.5
1'			156.0	NH-9	5.01 br	6.94 br		
2'	6.64 d, 8.5	6.74 d, 8.6	114.9	10	3.39 q, 6.2	3.42 t, 6.5	40.0	40.8
3'	7.11 d, 8.5	7.26 d, 8.6	129.4	11	2.68 t, 6.2	2.74 t, 6.5	33.6	34.8
4'			124.9	12			137.5	139.9
5'	7.11 d, 8.5	7.26 d, 8.6	129.4	13	7.18 s	7.42 s	133.0	134.1
6'	6.64 d, 8.5	6.74 d, 8.6	114.9	14			124.8	118.4
7'	5.93 s	6.13 s	105.9	15			151.8	152.3
8'			148.4	16			124.8	118.4
9'			161.7	17	7.18 s	7.42 s	133.0	134.1
NH	10.40 d, 10.0	8.22 d, 11.7		18	4.04 t, 7.5	4.04 t, 6.4	71.9	72.3
OMe-1	3.82 s	3.87 s	56.2	19	2.13 m	2.06 submerged	31.9	32.2
OMe-8'	3.66 s	3.78 s	55.6	20	3.54 q, 6.2	3.45 t, 6.5	36.1	36.6
OH-1'	9.38 br	5.75 br		21	5.80 br	7.10 br		
				22			167.9	167.5
				23	5.62 br	5.70 br	124.8	119.9
				24			151.8	149.8
				25	1.85 br	1.96 br	27.2	26.5
				26	2.13 br	2.13 br	20.1	19.6
				OH-1		8.37 s		

	244 (146)		245 (146)		247 (123)		246 (38)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1								
2	6.77 d, 8.1	135.3	6.77 d, 8.1	132.9	7.78 s	7.82 s	136.4	133.0

	<u>244 (146)</u>		<u>245 (146)</u>		<u>247 (123)</u>		<u>246 (38)</u>	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
3	6.92 d, 8.1	6.92 d, 8.1	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	119.5
4								154.5
5	6.92 d, 8.1	6.92 d, 8.1	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	119.5
6	6.77 d, 8.1	6.77 d, 8.1	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	133.0
7	3.47 s	3.47 s	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	138.4
8								124.0
9	3.39 q, 6.2	3.39 q, 6.2	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	167.5
10	2.67 t, 6.2	2.65 t, 6.2	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	39.3
11								25.9
12	7.42 d, 1.8	7.45 s	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	125.9
13								110.9
14								146.4
15								
16	7.21 d, 1.8	7.45 s	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
17	4.02 t, 7.5	4.00 t, 7.5	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
18	2.15 m	2.16 m	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
19	3.55 q, 6.2	3.56 2H	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
21	5.63 br	5.64 br	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
23	1.85 s	1.85 s	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
24	2.13 s	2.13 s	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
OMe								61.3
NH-8	5.01 br	5.01 br	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	
NH-19	5.81 br	5.82 br	CDCl ₃	CD ₃ OD + TFA	CD ₃ OD	CD ₃ OD	CD ₃ OD	

	<u>248 (150)</u>		<u>249 (151)</u>		<u>250 (151)</u>	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1	6.71 s	6.66 s	DMSO-d ₆	DMSO-d ₆	DMSO-d ₆	DMSO-d ₆
2						
3						

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	248 (150)			249 (151)			250 (151)		
	¹ H	¹³ C	DMSO-d ₆	¹ H	¹³ C	DMSO-d ₆	¹ H	¹³ C	DMSO-d ₆
4	6.65 s	118.6	116.1	4	160.5	161.2			
1'		129.7	128.3	5	121.3	121.3			
2'	7.94 d, 2.1	135.7	133.6	6	164.1	164.7			
3'		110.4	108.8	7		10.55 br			
4'		154.6	152.4	8	7.73 d, 10.0	142.9	7.14 t, 9.5		137.9
5'	6.83 d, 8.4	116.7	115.5	9	6.42 d, 10.0	100.4	6.42 d, 9.5		101.2
6'	7.72 dd, 8.4, 2.1	131.5	130.0	10		169.7			170.8
1''		129.1	128.9	11	4.23 s	35.0	4.17 s		33.9
2''	7.32 d, 1.7	127.0	124.3	12		140.2			140.1
3''		110.0	109.4	13	7.67 s	133.2	7.66 s		133.1
4''		143.9	141.9	14		116.7			116.7
5''		146.5	145.1	15		151.4			151.4
6''	7.48 d, 1.7	116.5	116.4	16		116.7			116.7
OH-4'		10.12 br		17	7.67 s	133.2	7.66 s		133.1
OH-4''		9.00 br		18	8.69		8.69		
OH-5''		9.52 br		19	3.07 d, 3.7	29.2	3.07 d, 3.7		28.9
				20	3.56 s	43.7			
				21	3.71 s	60.3	3.72 s		60.3

	251 (152)			252 (152)			253 (153)		
	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD	¹ H	¹³ C	CD ₃ OD
1		133.0	133.0						
2	7.60 d, 1.7	136.0	7.61 d, 1.7	136.1	8.67 s	139.5			
3		113.6	114.0	114.0		114.0			
4		157.0	157.1	157.1		127.9			
5	7.00 d, 7.0	114.0	7.00 d, 7.0	114.1	8.29 m	122.9			
6	7.33 dd, 1.7, 7.0	131.5	7.34 dd, 1.7, 7.0	131.6	7.25 m	123.8			
7	4.10 s	39.8	4.20 s	39.9	7.25 m	124.8			
8		160.8	160.8	160.8	7.47 m	113.1			

	251 (152)		252 (152)		253 (153)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
9		157.7		157.8		138.0
10						183.3
11	7.83 s	124.4	7.86 s	124.5		165.8
12		131.5		131.6		
13					3.51 t, 7.1	41.8
14		137.5		137.6	2.79 t, 7.1	35.2
15	8.07 s	130.9	8.12 s	131.7		132.9
16		120.2		120.3	7.38 d, 2.0	134.3
17		153.7		153.7		110.8
18		120.2		120.3		154.0
19	8.07 s	131.0	8.12 s	131.7	6.82 dd, 8.2	117.3
20					7.06 dd, 8.2, 2.0	130.1
21	4.19 s, 5.6	72.1	4.21 s, 5.6	72.5		
22	2.35 tt, 5.6, 7.9	27.2	2.30 tt, 5.6, 7.4	34.7		
23	3.57 t, 7.9	57.9	3.43 t, 7.4	49.4		
38	3.88 s	57.5	3.88 s	57.6		
OMe						
NMe ₂	3.02 s	44.5				
NMe			2.83 s	28.6		

	254 (153)		255 (153)		256 (154)		257 (154)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1								
2	8.65 s	139.6	8.67 s	139.5		26.0	50.5	24.7
3		114.0		No		50.5		49.4
4		127.9		127.8		56.7		56.1
5	8.28 m	122.9	8.29 m	123.0		57.5		56.7
6	7.25 m	123.8	7.25 s	123.8		72.0		69.9
7	7.25 m	124.8	7.25 m	124.8		112.3		110.2

	254 (153)		255 (153)		256 (154)		257 (154)	
	¹ H	¹³ C	¹ H	¹³ C	¹³ C	¹ H	¹³ C	¹³ C
8	7.45 m	113.1	7.46 m	113.1			112.4	110.9
9		138.0		138.0			113.0	112.0
10		183.3		182.9			113.0	112.1
11		166.0		165.7			119.2	113.3
13	3.49 t, 7.2	41.8	3.51 t, 7.7	42.1			119.6	120.6
14	2.76 t, 7.2	35.2	2.80 t, 7.7	35.6			122.4	123.2
15		131.0		131.0			123.6	124.4
16	7.59 d, 2.0	140.5	7.08 d, 2.0	130.8			127.4	126.4
17		84.9	6.72 d, 8.5	116.3			128.6	129.1
18		157.1		157.0			131.8	130.3
19	7.07 dd, 8.1	115.7	6.72 dd, 8.5	116.3			138.9	134.9
20	7.07 dd, 8.1, 2.0	133.3	7.08 dd, 8.5	130.8			138.2	137.9
							156.7	154.2

	258 (155)		259 (164)		260 (158)		261 (158)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1								
2		174.2		40.1		170.9		170.7
3	2.37 d, 17.4 2.19 d, 17.4	43.4	2.38 dd, 15.7, 10.8	15.7	2.32 m	42.4	2.03 dd, 14, 4	42.4
3a		81.6		175.1 ^a		43.3	2.16 d, 15	43.4
4	4.1–4.2 m	83.2		131.1		129.6		
5	6.75 d, 2.5	142.0	4.75 d, 7.1	127.8	4.93 d, 8	131.6	4.94 d, 8	131.7
6		137.8	2.23 m	29.2	2.16 m	29.0	2.16 m	29.0
6a		67.4						
7		163.4	1.32 m	43.3	1.34 m, 1.59 m	43.7	1.35 m, 1.60 m	43.8
8	4.1–4.2 m	60.6	4.62 m	70.8	4.91 m	71.0	4.88 m	71.0
9	1.24 t, 7	14.0		174.4 ^a		168.8		168.8
10	3.69 dq, 9.2, 7 3.55 dq, 9.2, 7	65.9	2.65 dd, 4.7, 15.0	39.7	4.75 dq, 8, 6.5	49.0	4.73 dq, 8, 6.5	49.0

	258 (155)		259 (164)		260 (158)		261 (158)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	DMSO- <i>d</i> ₆	DMSO- <i>d</i> ₆	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃
11	1.13 t, 7	15.4	5.26 dd, 4.7, 8.4	49.0		175.1		175.1
12				170.5 ^a	5.21 dd, 9, 8	56.7	5.20 dd, 9, 8	56.7
13			5.85 dd, 6.4, 10.2	55.5		174.4		174.4
14				168.9	4.46 dq, 8, 7	45.9	4.47 dq, 8, 7	45.9
15			4.75 m	45.8	2.95 dd, 15, 9 3.15 dd, 15, 8	32.7	2.95 dd, 15, 93.18 dd, 15, 8	32.5
16			1.12 d, 6.8	20.3		133.0		133.1
17			1.56 s	18.5	7.29 d, 2	132.2	7.30 d, 2.0	132.1
18			0.81 d, 6.5	21.9		85.1		110.0
19			1.05 d, 6.3	19.0		154.5		151.4
20				133.6	6.87 d, 9	116.1	6.95 d, 9	116.0
21			6.94 d, 8.3	127.1	7.05 dd, 9, 2	129.4	7.07 dd, 9, 2	129.5
22			6.66 d, 8.3	115.6	1.14 d, 6.5	20.4	1.13 d, 6.5	20.4
23				155.7	1.49 s	17.7	1.49 s	17.7
24			6.66 d, 8.3	115.6	0.86 d, 6.5	18.2	0.84 d, 6.5	18.2
25			6.94 d, 8.3	127.1	1.24 d, 6.5	20.6	1.22 d, 6	20.5
26			3.38 dd, 6.3, 15.2 3.24 dd, 10.5, 15.2	23.2	1.02 d, 6.5	18.7	1.02 d, 6.5	18.8
27				109.0	2.97 s	30.7	2.96 s	30.6
28				111.1	1.34 d, 7	18.8	1.33 d, 7	18.8
29				131.3				
30			7.24 d, 7.3	118.1				
31			7.13 dd, 7.3, 7.7	122.3				
32			7.10 dd, 7.3, 7.7	120.9				
33			7.56 brd, 7.3	110.6				
34				136.1				
35			2.98 s	30.8				
36			0.70 d, 6.9	17.8				
OH	5.36 br				6.27 s		6.29 s	
NH	8.14 br		6.63, 8.70 br		6.59 d, 8		6.59 d, 8	
NH			7.65 d, 8.4		6.52 d, 8		6.50 d, 8	

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	262 (159)		263 (159)		264 (159)		265 (159)	
	¹ H CDCl ₃	¹³ C CDCl ₃	¹ H CDCl ₃	¹³ C CDCl ₃	¹ H CDCl ₃	¹³ C CDCl ₃	¹ H CDCl ₃	¹³ C CDCl ₃
1		170.8		170.5		170.5		170.5
2	2.32 m	42.3	2.42 m	42.3	2.42 m	42.3	2.4 m	42.3
3	2.03 dd, 13.8, 3.6, 2.16	43.2	2.1 m	43.2	2.1 m	43.2	2.1 m	43.2
4		129.0		130.6		130.6		no ^a
5	4.93 d, 8.8	129.5	4.99 d, 8.3	131.5	4.99 d, 8.7	131.4	4.99 d, 8.7	131.4
6	2.16 m	28.9	2.21 m	29.1	2.21 m	29.1	2.21 m	29.1
7	1.36 m, 1.60 m	43.6	1.40 m, 1.69 m	43.5	1.40 m, 1.69 m	43.5	1.40 m, 1.69 m	43.5
8	4.88 m	70.9	4.86 m	71.4	4.86 m	71.4	4.86 m	71.4
9		168.7		168.2		168.2		168.2
10	4.48 dq, 7.7, 7.1	49.0	4.51 dq, 8.0, 7.1	48.9	4.52 dq, 8.0, 7.1	48.9	4.52 dq, 8.0, 7.1	48.9
11		175.1		175.8		175.8		no ^a
12	5.21 dd, 9.0, 7.3	56.6	5.08 dd, 9.0, 6.8	57.6	5.09 dd, 9.0, 6.8	57.5	5.11 dd, 9.0, 6.8	57.5
13		174.5		169.9		169.9		169.9
14	4.75 dq, 6.3, 6.3	45.8	3.77 dd, 17.6, 3.8 4.16 dq, 17.6, 1	42.2	3.77 dd, 17.9, 3.2 4.16 dq, 17.9, 4.2	42.0	3.77 dd, 18, 3.24.16 dq, 18, 4.2	42.0
15	2.92 dd, 14.7, 9.0 3.17 dd, 14.7, 7.3	32.7	2.81 dd, 14, 6.8 3.25 dd, 14, 9	32.2	2.83 dd, 14, 6.8 3.26 dd, 14, 9	32.4	2.84 dd, 14, 6.7 3.26 dd, 14, 9	32.4
16		133.0		133.4		133.4		NA
17	7.15 d, 1.7	131.5	7.15 d, 1.7	138.4	7.32 d, 2.0	132.2	7.18 d, 2.0	132.2
18		119.8		no ^a		no ^a		no ^a
19		150.2		no ^a		no ^a		no ^a
20	6.93 d, 8.3	116.3	6.90 d, 8.3	115.1	6.94 d, 8.3	116.2	6.93 d, 8.3	116.2
21	7.01 dd, 8.3, 1.7	128.8	7.08 dd, 8.3, 1.7	130.7	7.06 dd, 8.3, 2	129.7	7.01 dd, 8.3, 2	129.7
22	1.15 d, 6.7	18.7	1.16 d, 6.7	18.5	1.16 d, 6.7	18.5	1.16 d, 6.7	18.5
23	1.51 3H	17.6	1.53 d, 1	18.2	1.54 d, 1.2	18.2	1.5 d, 1.0	18.2
24	0.88 d, 6.6	20.4	0.90 d, 6.6	20.4	0.90 d, 6.7	20.4	0.91 d, 6.7	20.4
25	1.24 d, 6.3	20.5	1.25 d, 6.2	20.8	1.25 d, 6.2	20.7	1.25 d, 6.2	20.7
26	1.35 d, 7.1	18.2	1.30 d, 7.1	18.2	1.30 d, 7.1	18.2	1.30 d, 7.1	18.2
27	2.97 s	30.5	2.94 s	29.8	2.97 s	29.7	2.93 s	29.7
28	1.09 d, 6.7	18.7						

	262 (159)		263 (159)		264 (159)		265 (159)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃
OH	5.5 s		5.3 s		5.46 s		5.46 s	
NH	6.56 d, 7.7		6.60 d, 8		6.60 d, 8		6.60 d, 8	
NH	6.46 d, 6.3		6.45 dd, 3.8, 1		6.44 dd, 3.8, 1		6.44 dd, 3.8, 1	
	266 (164)		267 (161)		268 (161)		271 (164)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
	CDCl ₃	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃
1				175.0				174.9
2	2.46 m		2.55 m	40.1	2.56 m	40.1	2.45 m	
3	2.55 dd, 4, 12 2.14 t, 12		2.36, 15.2, 11.4 1.95, 15.2, 2.0	40.9	2.35, 15.2, 11.4 1.94, 15.2, 2.0	40.9	2.54 dd, 4, 13 2.14, 12	
4				133.6				133.6
5			4.82, 9.6	128.4	4.82 9.6	128.3		
6	2.95		2.28 m	29.2	2.28 m	29.2	ns ^a	
7	1.82 ddd, 3, 9, 15 1.61 ddd, 3, 11, 15		1.39, 13.6, 11.1, 4.7 1.18, 13.5, 9.4, 4.5	43.4	1.38, 13.6, 11.1, 4.7 1.19, 13.5, 9.4, 4.5	43.4	1.82 m, 1.60 m	
8	5.11 m		4.64 m	70.4	4.64 m	70.4	5.11 m	
9				170.5				170.5
10	4.51 dq, 7, 7		2.68, 15.5, 4.5 2.59, 15.5, 6.6	40.2	2.69, 15.5, 4.5 2.60, 15.5, 6.6	40.0	4.50 dq, 7, 7	
11			5.25 m	48.8	5.24 m	48.8		48.8
12	5.06 dd, 8, 9			168.4		168.4	5.06 dd, 8, 9	
13			5.38, 9.8, 6.7	56.8	5.40, 9.8, 6.7	56.7		
14	4.72 dq, 7			174.1		174.1	4.71 dq, 7, 8	
15	3.12 dd, 8, 15 2.90 dd, 9, 15		4.75 m	46.0	4.24 m	45.0	3.13 dd, 8, 15 2.90 dd, 9, 15	
16			1.16, 7.0	20.2	1.16, 7.0	20.2		
17	7.45 d, 1 s		1.60, 1.0	18.5	1.60, 1.0	18.5	7.25 d, 2	
18			0.86, 7.0	21.9	0.86, 7.0	21.9		
19			1.09, 7.0	19.1	1.08, 7.0	19.1		
20	6.88 d, 8			130.8		130.7	6.91 d, 8	
21	7.04 dd, 1, 8		7.00, 8.5	127.1	7.01, 8.5	127.1	7.02 dd, 2, 8	

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266 (164)		267 (161)		268 (161)		271 (164)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CDCl ₃		CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃ + 5% DMSO- <i>d</i> ₆	CDCl ₃	CDCl ₃
22	1.15 d, 6	6.77, 8.5	115.6	6.87, 8.5	115.6	1.14 d, 7	
23	5.90 s 5.78 s		156.6		156.6	5.90 s 5.78 s	
24	1.09 d, 7	6.77, 8.5	115.6	6.87, 8.5	115.6	1.09 d, 7	
25	1.28 d, 6	7.00, 8.5	127.1	7.01, 8.5	127.1	1.28 d, 6	
26	1.32 d, 7	3.18, 14.5, 5.7 2.86, 14.5, 9.9	31.7	3.19, 14.5, 5.7 2.88, 14.5, 9.9	31.9	1.31 d, 7	
27	2.97 s		129.6		129.2	2.96 s	
28	1.04 d, 7	7.48, 2.3	138.7	7.26, 2.3	132.7	1.03 d, 7	
29			84.2		109.7		
30			155.2		152.6		
31		6.79, 8.5	115.1	6.85, 8.5	116.4		
32		6.96, 8.5, 2.3	129.8	6.93, 8.5, 2.3	128.8		
33		2.94 s	30.3	2.92 s	30.3		
34		1.08, 7.0	18.2	1.06, 7.0	18.1		
OH		9.12 s		8.85 s			
OH		8.68 s		8.69 s			
NH-10	6.35 d, 7	7.46, 8.3		7.47, 8.3		6.21 d, 7	
NH-14	6.19 d, 7	6.78, 8.5		6.77, 8.5		6.36 d, 8	

272 (164)		273 (164)		274 (164)		275 (164)		276 (164)	
¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
CDCl ₃		CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃
1			175.5				177.6		
2	2.46 m	2.26 m	42.4	2.28 m	2.27 m	2.40 m	42.2		
3	2.54 d, 12 NA	2.17 m 1.98 dd, 3, 14	42.3	2.17 m 1.98 dd, 3, 14	2.16 m 1.98 dd, 2, 12	2.14 m 2.04 m	43.2		
4			132.9				147		
5		4.87 d, 9	131.3	4.87 d, 9	4.87 d, 9	4.93 d, 9	131.2		
6	NA	2.18 m	29.3	2.18 m	2.16 m	2.16 m	28.7		
7	NA NA	1.63 ddd, 6, 8, 14 1.39 ddd, 4, 8, 14	43.7	1.64 m 1.37 m	ns ^b 1.37 m	1.56 m 1.37 m	43.9		

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	272 (164)		273 (164)		274 (164)		275 (164)		276 (164)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
8	5.11 m	71.9	4.94 m	71.9	4.94 m	71.9	4.93 m	71.9	4.87 m	70.6
9		169.8		169.8		169.8		169.8		170.4
10	4.51 m	53.3	4.43 dq, 7, 7	53.3	4.43 m	53.3	4.43 m	53.3	4.5 dq, 7, 8	48.8
11		168.9		168.9		168.9		168.9		168.4
12	5.06 m	56.9	5.26 dd, 7, 9	56.9	5.27 dd, 7, 9	56.9	5.28 dd, 7, 9	56.9	5.16 dd, 8, 9	57.1
13		174.6		174.6		174.6		174.6		171.3
14	4.71 m	45.8	4.71 dq, 4, 9	45.8	4.71 quint, 7	45.8	4.72 quint, 6	45.8	4.71 m	52.8
15	3.14m 2.90 m	32.5	3.19 dd, 7, 15 2.89 dd, 9, 15	32.5	3.22 dd, 7, 15 2.91 dd, 9, 15	32.5	3.22 dd, 7, 15 2.93 dd, 9, 15	32.5	3.17 dd, 8, 15 2.88 dd, 9, 15	32.2
16		130.3		130.3		130.3		130.3		130.1
17	7.12s	138.2	7.46 d, 2	138.2	7.27 d, 2	138.2	7.13 d, 2	138.2	7.46 d, 2	138
18		85		85		85		85		85.3
19		154.0		154.0		154.0		154.0		154.1
20	6.91 d, 8	115.1	6.86 d, 8	115.1	6.91 d, 8	115.1	6.91 d, 8	115.1	6.88 d, 8	114.9
21	6.98 d, 8	130.4	7.03 dd, 2, 8	130.4	7.03 dd, 2, 8	130.4	7.03 dd, 2, 8	130.4	7.05 dd, 2, 8	130.1
22	1.14 d, 7	19	1.12 d, 7	19	1.12 d, 7	19	1.13 d, 7	19	1.16 d, 7	18.8
23	5.90 s 5.79 s	17.8	1.45 s	17.8	1.45 s	17.8	1.45 s	17.8	1.49 s	17.7
24	1.09 d, 7	20.5	0.86 d, 7	20.5	0.86 d, 7	20.5	0.87 d, 7	20.5	0.88 d, 7	20.4
25	1.28 d, 6	20.8	1.24 d, 6	20.8	1.23 d, 6	20.8	1.23 d, 6	20.8	1.23 d, 6	20.5
26	1.31 d, 7	63.1	3.97 dd, 4, 11 3.81 dd, 4, 11	63.1	3.97 dd, 4, 11 3.82 dm, 4, 11	63.1	3.97 dd, 4, 11 3.82 dm, 4, 11	63.1	1.32 d, 7	18.1
27	2.96 s	30.7	2.97	30.7	2.97 s	30.7	2.97 s	30.7	3.03 s	30.9
28	1.03 d, 7	18.5	1.08 d, 7	18.5	1.09 d, 7	18.5	1.09 d, 7	18.5	3.54 br	65.2
NH-10	4.51 m		7.00 d, 8		6.99 d, 8		6.98 d, 7		6.45 d, 7	
NH-14	6.37 d, 8		6.44 d, 6		6.43 d, 6		6.44 d, 6		6.67 br	

	277 (164)		278 (164)		269 (162)		270 (163)		280 (167)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
1										
2	2.41 m		2.39 m		2.23 m		2.47 m		169.7	132.0

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	277 (164)		278 (164)		269 (162)		270 (163)		280 (167)	
	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C	¹ H	¹³ C
3	2.10 m, 2.04 m	2.10 m, 2.05 m	1.98 m, 2.06 m	42.5	2.10 m	43.3				
4				133.5						
5	4.93 d, 9	4.97 d, 9	4.86 d, 8.5	132.0	4.99 d, 8.5	131.6				
6	2.15 m	2.19 m	2.06 m	29.0	2.21 m	29.1			4.57 t, 6.0	47.2
7	1.56 m, 1.37 m	1.70 m, 1.41 m	1.30 m, 1.60 m	43.6	1.78 m, 1.40 m	43.3			2.97 t, 6.0	37.1
8	4.87 m	4.88 m	4.78 sextet, 7	71.7	4.84 sextet, 6.4	71.5				132.8
9				170.0					6.89 d, 8.0	134.7
10	4.45 m	4.53 dq, 7, 8	4.25 dd, 6, 9	58.6	4.43 dd, 8.7, 7.0	58.4			6.58 d, 8.0	120.4
11				169.5						161.2
12	5.17 dd, 7, 10	5.11 dd, 7, 9	5.18 t, 7	57.2	5.13 dd, 9.8, 6.4	57.8			6.58 d, 8.0	120.4
13				174.7					6.89 d, 8.0	134.7
14	4.79 m	4.15 dd, 4, 18	4.67 quin, 6.5	46.8	4.15 dd, 18.3, 4.1 3.19 dd, 18.3, 3.4	41.9				189.7
15	3.18 dd, 7, 15 2.91 dd, 10, 15	3.24 dd, 9, 14 2.81 dd, 7, 14	2.82 dd, 14.5, 8 3.08 dd, 14.5, 8	32.2	3.25 dd, 13.2, 9.0 2.80 dd, 13.2, 6.1	32.7				132.8
16				130.5					7.62 4H, s	138.9
17	7.27 d, 2	7.50 d, 2	7.42 d, 2	138.8	7.53 d, 2.0	138.6				116.1
18				86.2						159.9
19				154.5						116.1
20	6.92 d, 8	6.89 d, 8	6.82 d, 8	115.1	6.90 d, 8.5	115.2			7.62 4H, s	138.9
21	7.03 dd, 2, 8	7.07 dd, 2, 8	7.01 d, 8	131.0	7.10 dd, 8.5, 2.0	130.9				136.0
22	1.16 d, 7	1.14 d, 7	1.09 d, 6.5	18.5	1.17 d, 6.8	18.8			7.00 4H, s	139.3
23	1.49 s	1.49 s	1.46 s	17.7	1.56 s	17.8				116.2
24	0.86 d, 6	0.89 d, 7	0.79 d, 6.5	20.5	0.90 d, 6.8	20.5				154.6
25	1.23 d, 6	1.26 d, 6	1.16 d, 6.5	20.6	1.25 d, 6.4	20.8				116.2
26	1.32 d, 7	3.91 dm, 8, 3.75 m	1.98 m	32.0	1.99 m	31.5			7.00 4H, s	139.3
27	3.03 s	2.93 s	2.97 s	30.5	2.96 s	29.7				136.0
28	3.54 br		1.04 d, 6.5	18.8	0.79 d, 6.5	18.1			7.00 4H, s	139.3
29			0.75 d, 6.5	17.8	0.75 d, 6.5	18.1				116.2
30			0.77 d, 6.5							154.6
31										116.2

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	277 (164)	278 (164)	269 (162)	270 (163)	280 (167)
32	¹ H	¹ H	¹ H	¹ H	¹ H
	CDCl ₃	CDCl ₃	CDCl ₃	CDCl ₃	DMSO-d ₆
33					7.00 4H, s
					139.3
34					189.7
					132.8
35,39					7.62 4H, s
					138.9
36,38					116.1
37					159.9
NH-10	6.46 d, 8	6.6 d, 8		6.42 d, 8.8	
NH-14	6.68 br	6.45 dd, 4, 1		6.64 t, 3.4	

	282 (167)	283 (167)	281 (168)	284 (168)
2	¹ H	¹³ C	¹ H	¹³ C
	CDCl ₃	CDCl ₃	CD ₃ OD	CDCl ₃ + CD ₃ OD
	170.0	170.0	131.2	166.6
3				
	122.6	122.6	128.0	135.2
4				
	122.6	122.4	186.0	124.9
5				
	170.0	170.0	129.0	136.2
6	3.58 t, 6	40.0	8.8' 8.00 s	
	40.0	3.85 t, 6	136.1	114.2
7	2.90 t, 6	34.0	114.0	153.7
	34.0	2.90 t, 6	162.6	114.2
8				
	129.5	129.5	114.0	136.2
9,13	7.10 d, 8	130.0	11.11'	
	130.0	7.10 d, 8	136.1	
10,12	6.85 d, 8	115.5	8.00 s	
	115.5	6.85 d, 8	136.1	
11				
	155.0	153.1	131.2	
14				
	132.9	132.5	135.9	
15,19	7.60 s	133.3	7.40	
	133.3	7.63	112.2	
16,18				
	110.2	109.0	153.5	
17				
	152.8	154.0	112.2	
20				
	132.9	132.5	135.9	
21,25	7.60 s	133.3	7.40	
	133.3	7.62	8.31 s	
22,24				
	110.2	118.2		
23				
	152.8	156.2		

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	282 (167)	283 (167)	281 (168)	284 (168)
¹ H	¹³ C	¹ H	¹ H	¹³ C
CDCl ₃	CDCl ₃	CD ₃ OD	CDCl ₃	CDCl ₃ + CD ₃ OD
26	3.94 s	61.0		

NA: not reported

^a Interchangeable signals.^c May be interchanged^d Interchangeable^b Broad signal^a Exchangeable.^b Exchangeable.^c Exchangeable.^a Coupling constants were not reported in original paper.^a Interchangeable signals.^b Interchangeable signals.^c Interchangeable signals.^b Interchangeable signals.^c Interchangeable signals.^d Shape of signal was changed in temperature-variable experiment in DMSO-*d*₆^a May be interchanged^b May be interchanged^A May be interchanged.^B May be interchanged.^C May be interchanged.^D May be interchanged.^E May be interchanged.

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F May be interchanged.

G May be interchanged.

H May be interchanged.

A May be interchanged.

B May be interchanged.

C May be interchanged.

D May be interchanged.

E May be interchanged.

F May be interchanged.

G May be interchanged.

H May be interchanged.

AB May be interchanged.

BA May be interchanged.

^aCoupling constants were not reported.

a may be interchanged.

b may be interchanged.

c may be interchanged.

^dnot observed due to limited sample size

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TABLE III

Selected ¹H-NMR Data of Bastadin Tetra-*O*-methyl Ethers (130).

Parent bastadins	-4 (208)	-5 (209)	-6 (210)	-8 (212)	-9 (213)	-11 (215)	-12 (216)	-13 (217)	-14 (218)	15 (219)	19 (223)	20 (224)
δ of MeO groups (CDCl ₃)	4.01	4.02	4.06	4.08	4.02	4.05	4.01	4.04	4.10	4.03	4.04	4.00
	4.01	3.98	4.03	4.04	4.01	4.01	4.01	4.01	4.05	4.01	4.01	3.92
	4.01	3.94	4.02	4.02	3.97	3.90	3.89	3.81	4.03	3.89	3.91	3.91
	4.01	3.52	3.61	3.92	3.70	3.49	3.87	3.48	3.83	3.73	3.61	3.72

TABLE IV

Antibacterial Activity of Bromotyrosine Derivatives.

Alkaloids	Antimicrobial activity ^a	Ref.
3-Bromoverongiaquinol (10)	Active against <i>S. f.</i> , <i>B. s.</i> ; not active against <i>A. f.</i> , <i>P. v.</i>	9
3-Bromo-5-chloroverongiaquinol (11)	Active against <i>S. l.</i> , <i>A. f.</i> , <i>P. v.</i>	9
(-)-Aeropylsinin-1 (17)	MIC 20–100 µg/mL against <i>S. a.</i> , <i>B. s.</i> , <i>M. l.</i> , <i>E. c.</i> , <i>P. a.</i>	16
(+)-Aeropylsinin-1 (14)	MIC 20–100 µg/mL against <i>S. a.</i> , <i>B. s.</i> , <i>M. l.</i> , <i>E. c.</i> , <i>P. a.</i>	16
		31
7-Bromocavernicolone (30)	Active against <i>P. c.</i> ; not active against <i>B. s.</i>	24
38	3000 µg/disk shows inhibition zone against <i>E. c.</i> 18–22 mm	31
Aeropylsinin-2 (18)	3000 µg/disk shows inhibition zone against <i>E. c.</i> <15 mm	31
Moloka'iamine (52)	Inhibit the growth of <i>B. m.</i> , <i>P. n.</i> , <i>A. m.</i> , <i>V. a.</i> , <i>F. m.</i> at 10 µg/disk	49
Aplysamine-1 (54)	Not active against <i>S. a.</i> , <i>B. s.</i> , <i>S. l.</i> , <i>E. c.</i> , <i>S. sp.</i>	44
Aplysamine 2 (172)	Not active against <i>S. a.</i> , <i>B. s.</i> , <i>S. l.</i> , <i>E. c.</i> , <i>S. sp.</i>	44
Ceratinamine (60)	Inhibit the growth of <i>B. m.</i> , <i>P. n.</i> , <i>A. m.</i> , <i>V. a.</i> , <i>F. m.</i> at 10 µg/disk	49
Aerotherionin (68)	Inhibit the growth of <i>S. a.</i> at 100 µg/disk, <i>B. s.</i> at 50 µg/disk	63
Homoaerotherionin (69)	Inhibit the growth of <i>S. a.</i> at 100 µg/disk, <i>B. s.</i> at 50 µg/disk	63
11,19-Dideoxy-fistularin 3 (83)	Inhibit the growth of <i>S. a.</i> at 25 µg/disk, <i>B. s.</i> at 10 µg/disk	63
11-Hydroxyaerotherionin (71)	Inhibit the growth of <i>S. a.</i> at 100 µg/disk, <i>B. s.</i> at 50 µg/disk	63
11-Oxo-aerotherionin (72)	MIC 30 µg/mL against <i>S. a.</i> , <i>P. a.</i> ; 10 µg/mL against <i>E. c.</i>	64
11-Epi-fistularin-3 (81)	Active against <i>B. s.</i> , <i>M. l.</i> ; not active against <i>E. c.</i>	70
Agelarin A (87)	Active against <i>B. s.</i> , <i>M. l.</i> ; not active against <i>E. c.</i>	70
Agelarin B (88)	Active against <i>B. s.</i> , <i>M. l.</i> ; not active against <i>E. c.</i>	70
Zamamistatin (91)	Active against <i>R. s.</i>	75
Aplysinamisine I (120)	Inhibit the growth of <i>S. a.</i> , <i>E. c.</i> , <i>P. a.</i> at 50–100 µg/disk	83
Aplysinamisine II (124)	Inhibit the growth of <i>S. a.</i> , <i>E. c.</i> , <i>P. a.</i> at 50–100 µg/disk	83
Aplysinamisine III (102)	Inhibit the growth of <i>S. a.</i> , <i>E. c.</i> , <i>P. a.</i> at 50–100 µg/disk	83
Purealidin B (109)	MIC 62.5 µg/mL against <i>S. a.</i> , 15.6 µg/mL against <i>B. s.</i> , 3.9 µg/mL against <i>S. l.</i>	84
Purealidin C (192)	MIC 62.5 µg/mL against <i>S. a.</i> , 15.6 µg/mL against <i>S. l.</i>	84
Araplysellin-I (99)	250 µg/disk shows inhibition zone against <i>S. a.</i> 12 mm	81
Araplysellin-II (100)	250 µg/disk shows inhibition zone against <i>S. a.</i> 7 mm	81
Anomoian A (195)	Inhibit the growth of <i>S. a.</i> at 10 µg/disk, <i>B. s.</i> at 5 µg/disk	124
Bromochelonin B (257)	Inhibit the growth of <i>B. s.</i> at 100 µg/disk	154
Purpuramine K (190)	25 µg/disk shows inhibition zone against <i>S. a.</i> 10, <i>P. a.</i> 10; <i>B. s.</i> 8; <i>C. v.</i> 7; <i>K. a.</i> 10 mm	122
Purpuramine L (191)	25 µg/disk shows inhibition zone against <i>S. a.</i> , <i>B. s.</i> 14; <i>P. a.</i> 16; <i>B. sp.</i> 12 mm	122
Psammaplina A (152)	Active against <i>S. a.</i> , <i>B. s.</i>	109
Bisaprasin (154)	Active against <i>S. a.</i> , <i>B. s.</i>	109
Psammaplina D (158)	Inhibit the growth of <i>S. a.</i> , <i>T. m.</i> at 100 µg/disk.	110
Bastadin-1 (204)	MIC: <i>S. a.</i> 6.25–12.5, <i>E. c.</i> 100, <i>N. g.</i> 50–100, <i>E. f.</i> 12.5–25 µg/disk	41
Bastadin-2 (205)	MIC: <i>S. a.</i> 6.25–12.5, <i>N. g.</i> 50–100, <i>E. f.</i> 50–100 µg/disk	41
Bastadin-3 (206)	MIC: <i>S. a.</i> 1.56–3.12, <i>N. g.</i> 0.78–1.56, <i>E. f.</i> 3.12–6.25 µg/disk	41
Bastadin-4 (208)	MIC: <i>S. a.</i> 12.5–25, <i>N. g.</i> 12.5–25, <i>E. f.</i> 50–100 µg/disk	41

Alkaloids	Antimicrobial activity ^a	Ref.
Bastadin-5 (209)	MIC: <i>S. a.</i> 12.5–25, <i>N. g.</i> 50–100, <i>E. f.</i> 50–100 µg/disk	41
Bastadin-6 (210)	MIC: <i>S. a.</i> 6.25–12.5, <i>E. f.</i> 12.5–25 µg/disk	41
207	MIC: <i>N. g.</i> 50–100 µg/disk	41
Hemibastadin 1 (231)	MIC: <i>S. a.</i> 1.56–3.12, <i>N. g.</i> 12.5–25, <i>E. f.</i> 50–100 µg/disk	41
1'-(Methoxy) hemibastadins 1 (237)	MIC: <i>S. a.</i> 6.25–12.5, <i>N. g.</i> 6.25–12.5 µg/disk	41
Hemibastadins 2 and 3 (232, 233)	MIC: <i>S. a.</i> 6.25–12.5, <i>N. g.</i> 6.25–12.5, <i>E. f.</i> 50–100 µg/disk	41
Hemibastadinol 1 (234)	MIC: <i>N. g.</i> 50–100 µg/disk	41
Hemibastadinols 2 and 3 (235, 236)	MIC: <i>N. g.</i> 50–100 µg/disk	41
Bastadin-13 (217)	MIC 6 µg/mL against <i>B. s.</i>	41

^a *Streptococcus faecalis* (*S. f.*); *Staphylococcus aureus* (*S. a.*); *Bacillus subtilis* (*B. s.*); *Micrococcus luteus* (*M. l.*); *Sarcina lutea* (*S. l.*); *Bacillus marinus* (*B. m.*); *Bacillus sphaericus* (*B. sp.*); *Escherichia coli* (*E. c.*); *Pseudomonas aeruginosa* (*P. a.*); *Neisseria gonorrhoeae* (*N. g.*); *Alcaligena faecalis* (*A. f.*); *Chromobacterium violaceum* (*C. v.*); *Klebsiella aerogenes* (*K. a.*); *Proteus vulgaris* (*P. v.*); *Vibrio alginolyticus* (*V. a.*); *Pseudomonas cichorii* (*P. c.*); *Pseudomonas nautical* (*P. n.*); *Alteromonas macleodii* (*A. m.*); *Flavobacterium marinotipicum* (*F. m.*); *Rhodospirillum salexigens* (*R. s.*); *Serratia sp.* (*S. sp.*); *Escherichia faecalis* (*E. f.*).

TABLE V

Antifungal activity of Bromotyrosine Derivatives.

Alkaloids	Antifungal activity	Ref.
Aplysamine-1 (54)	No activity	44
Aplysamine-2 (172)		
Ceratinamine (60)	No activity against <i>Candida albicans</i> , <i>Penicillium chrysogenum</i> , <i>Mortierella ramanniana</i> at 10 µg/ disk	49
Aerothionin (68)	Active against <i>C. albicans</i> at 50 µg/ disk	63
Homoaerothionin (69)	Active against <i>C. albicans</i> at 50 µg/ disk	63
11-Hydroxyaerothionin (71)	Active against <i>C. albicans</i> at 50 µg/ disk	63
11,19-Dideoxyfistularin-3 (83)	Active against <i>C. albicans</i> at 25 µg/ disk	63
77	MIC 64 µg/ml on <i>Cryptococcus neoformans</i> ATCC90113	67
11-Epi-fistularin-3 (81)	Not active toward <i>Penicillium oxalicum</i>	70
Agelorin A (87)	Not active toward <i>Penicillium oxalicum</i>	70
Agelorin B (88)	Not active toward <i>Penicillium oxalicum</i>	70
Purealidin C (192)	Modest activity against <i>C. albicans</i> , <i>Cryptococcus neoformans</i> , and <i>Paecilomyces variotii</i>	84
Anomoian A (195)	Inhibit the growth of <i>C. albicans</i> at 25 µg/disk	124
Geodiamolide A (260)	Active against <i>C. albicans</i> (MIC: 31.3 µg/ml)	158
Geodiamolide B (261)	Active against <i>C. albicans</i> (MIC: 31.3 µg/ml)	158
Psammaplins D (158)	Inhibit the growth of <i>Trichopyhton mentagrophytes</i> at 100 µg/disk.	110

TABLE VI

Antibacterial Activity against Different *Staphylococcus* Strains^a (MIC, µg/mL).

Strains	158	169	170	171	154	Meropenem
<i>S. aureus</i> KIST 1 ^b	> 25.0	3.1	12.5	> 50.0	12.5	25.0
<i>S. aureus</i> KIST 2 ^b	> 25.0	3.1	12.5	> 50.0	6.3	3.1
<i>S. aureus</i> KIST 3 ^b	> 25.0	6.3	12.5	> 50.0	6.3	50.0
<i>S. aureus</i> KIST 4 ^b	> 25.0	3.1	12.5	> 50.0	6.3	50.0
<i>S. aureus</i> 003 ^c	> 25.0	3.1	12.5	> 50.0	12.5	3.1
<i>S. aureus</i> 004 ^c	> 25.0	3.1	12.5	> 50.0	6.3	3.1
<i>S. aureus</i> Y-80-12-1109 ^d	> 25.0	6.3	12.5	> 50.0	50.0	50.0
<i>S. aureus</i> Y-80-12-1999 ^d	> 25.0	6.3	12.5	> 50.0	50.0	50.0
<i>S. aureus</i> Y-80-12-844 ^d	> 25.0	25.0	25.0	> 50.0	25.0	50.0
<i>S. epidermidis</i> 178 ^e	> 25.0	0.8	3.2	> 50.0	6.3	0.8
<i>S. epidermidis</i> 291 ^e	> 25.0	0.8	3.2	> 50.0	12.5	1.6

^a A total of 40 strains were employed for testing, and only the strains to which **169** exhibited equipotency to or higher potency than meropenem were registered.

^b Strains were obtained from KIST (Korea Institute of Science and Technology).

^c Strains were obtained from LG Chemical, Korea.

^d Strains were obtained from Yon-Sei Medical Center, Korea.

^e Ofloxacin-resistant strains.

TABLE VII

Antibiotic Activity against Several Marine Bacteria.

Compounds	Diameter of inhibitory zone (mm)										
	Isofistularin-3 (80)		Aerophobin-2 (114)		Aerophysinin-1 (14)		Dienone (1)				
Dose (µg/disk)	100	100	100	50	5	100	50	5	100	50	5
<i>Alteromonas</i> sp. NCIMB 224	-	-	11	7	-	10	9	-	-	-	-
<i>Cytophage/Flexibacter</i> sp. NCIMB 251	-	-	30	n.d.	n.d.	28	n.d.	n.d.	n.d.	n.d.	n.d.
<i>Moraxella</i> sp. NCIMB 308	-	-	22	20	-	19	16	7	-	-	-
<i>Pseudomonas fluorescens</i> NCIMB 129	-	-	8	-	-	9	7	7	-	-	-
<i>Serratia plymuthica</i> *	-	-	11	8	-	14	11	7	-	-	-
<i>Vibrio</i> sp.*	-	-	28	24	12	24	21	8	-	-	-
<i>Vibrioanguillarum</i> * NCIMB 407	-	-	27	24	11	34	21	7	-	-	-
<i>Planococcus citraus</i> ⁺ NCIMB 1495	-	-	14	n.d.	n.d.	14	n.d.	n.d.	n.d.	n.d.	n.d.

n.d.: not determined

⁺ Gram positive bacteria

* Gram negative bacteria.

TABLE VIII

Cytotoxicity of Bromotyrosine Derivatives

Alkaloids	Cytotoxicity	Ref.
Psammaplin A (152)	IC ₅₀ : K562 0.4 mM.	114
	IC ₅₀ : P388 0.3 µg/mL;	108
	ED ₅₀ : A549 0.57; SK-OV-3 0.14; SK-MEL-2 0.13; XF498 0.57; HCT15 0.68 µg/mL	117
Psammaplin D (158)	ED ₅₀ : A549 0.80; SK-OV-3 0.17; SK-MEL-2 0.20; XF498 0.60; HCT15 1.23 µg/mL	117
Bromopsammaplin A (170)	ED ₅₀ : A549 1.34; SK-OV-3 1.38; SK-MEL-2 0.90; XF498 0.92; HCT15 3.31 µg/mL	117
Bispsammaplin A (171)	ED ₅₀ : A549 1.53; SK-OV-3 1.52; SK-MEL-2 1.02; XF498 1.10; HCT15 3.35 µg/mL	117
Bisaprasin (154)	ED ₅₀ : A549 3.40; SK-OV-3 2.78; SK-MEL-2 2.94; XF498 2.44; HCT15 6.0 µg/mL	117
Psammaplin A ₁ (165)	K562: LC ₅₀ 1.9 mM	114
Psammaplin A ₂ (166)	K562: LC ₅₀ 4.2 mM	114
Aplysinellin A (167)	K562: LC ₅₀ 10.7 mM	114
Aplysinellin B (168)	K562: LC ₅₀ 7.1 mM	114
Moloka'iamine (52)	MIC: KB 50 µg/mL; LOVO 10 µg/mL;	42
	IC ₅₀ : P-388 5 µg/mL; A-549 10 µg/mL; HT-29 5 µg/mL; CV-1 10 µg/mL	49
Mololipids (53)	> 100 µM (-)	43
Ceratinamine (60)	P388 IC ₅₀ 3.4 µg/mL	49,98
<i>N,N,N</i> -Trimethyl-dibromotyramine (47)	P388 ED ₅₀ 20 µg/mL	37
11-Oxoerothionin (72)	HCT 116 (0.01-0.1 µg/mL)	64
11- <i>Epi</i> -fistularin-3 (81)	IC ₅₀ : KB > 20; BCI 5.9; ZR-75-1 4.5 µg/mL	70
11-Oxofistularin-3 (82)	100% inhibition of KB in culture at 7 µg/mL	72
Isofistularin-3 (80)	KB: 4 µg/mL active	69
Fistularin-3 (79)	ED ₅₀ : KB 4.1; PS 4.3; LE 1.3 µg/mL	68
11-Deoxyfistularin-3 (86)	LD ₅₀ : CF-7 17 µg/mL; X-17, Hela, Hep-2, RD, Lovo > 50 µg/mL	73
Aplysinamisine I (120)	IC ₅₀ : MCF-7 > 50; CCRF-CEM > 50 µg/mL; HCT116 (-).	83
Aplysinamisine II (124)	IC ₅₀ : MCF-7 > 50; CCRF-CEM > 50; HCT116 10 µg/mL.	83
Aplysinamisine III (102)	IC ₅₀ : MCF-7 30; CCRF-CEM 6; HCT116 10 µg/mL	83
Purealidin N (150)	IC ₅₀ : K1210 0.07; KB cells 0.074 µg/mL	79
Purealidin P (110)	IC ₅₀ : K1210 2.8; KB: 7.6 µg/mL	79
Purealidin Q (111)	IC ₅₀ : K1210 0.95; KB 1.2 µg/mL	79
Purealidin J (116)	> 10 µg/mL.	79
Purealidin K (117)	> 10 µg/mL	79
Purealidin L (125)	> 10 µg/mL	79
Purealidin M (149)	> 10 µg/mL	79
Purealidin O (200)	> 10 µg/mL	79
Purealidin R (97)	> 10 µg/mL	79
Aerophobin-1 (113)	> 10 µg/mL	79
Purealidin C (192)	IC ₅₀ : KB 3.2; K1210 2.4 µg/mL	84
Purealidin B (109)	-	84

Alkaloids	Cytotoxicity	Ref.
Purealidin A (146)	IC ₅₀ : L1210 1.1 µg/mL	104
Fistularin-1 (94)	ED ₅₀ : 21-35 µg/ml against KB, PS, LE	68
128	IC ₅₀ : HeLa 50 µg/mL	92
Jaspamide (259)	ED ₅₀ : larynx epithelial carcinoma 0.32 µg/mL, human embryonic lung 0.01 µg/mL	157
Geodiamolide A (260)	L1210: 0.0032 (ED ₅₀). ED ₅₀ : U373 0.016, HEY 0.043 µg/mL	158,159,169
Geodiamolide B (261)	L1210: 0.0026 (ED ₅₀).	158,159
Geodiamolide C (262)	L1210: 0.0025 (ED ₅₀).	159
Geodiamolide D (263)	L1210: 0.0039 (ED ₅₀).	159
Geodiamolide E (264)	L1210: 0.014 (ED ₅₀).	159
Geodiamolide F (265)	L1210: 0.006 (ED ₅₀).	159
Geodiamolide G (266)	ED ₅₀ : U373 7.7, HEY 8.6 µg/mL	160
Geodiamolide H (267)	TGI: HOP92 0.118, SF-268 0.153, OV Car-4 0.0186, A498 0.0948, UO-31 0.185, MDA-MB-23/ATCC 0.433 µM	161
Geodiamolide I (268)	not active	161
Bastadin-4 (208)	P-388 ED ₅₀ : 2.0 µg/mL	132
Bastadin-8 (212)	P-388 ED ₅₀ : 3.6 µg/mL, L1210 ED ₅₀ : 5 µg/mL	132, 142
Bastadin-9 (213)	P-388 ED ₅₀ : 2.7 µg/mL	132
Bastadin-12 (216)	L1210 ED ₅₀ : 5 µg/mL	142
Bastadin-14 (218)	IC ₅₀ 2 µg/mL against A-549, HT-29, P-388	133
Botryllamide D (242)	HCT116: 17 µg/mL	145
Ma'edamine A (251)	IC ₅₀ : L1210 4.3 µg/mL; KB 5.2 µg/mL	152
Ma'edamine A (252)	IC ₅₀ : L1210 3.9 µg/mL; KB 4.5 µg/mL	152
Psammaplysin A (129)	HCT116 IC ₅₀ 6 µg/mL	95
Psammaplysin B (130)	HCT116 IC ₅₀ 6 µg/mL	95
Psammaplysin C (131)	HCT116 IC ₅₀ 3 µg/mL	95
Psammaplysin E (133)	active at 5 µg/mL against KB and LoVo cells	96

TABLE IX

Enzyme Activity of Some Bromotyrosine Derivatives.

Alkaloids	Activity (IC ₅₀)					Ref.
	Tyrosine kinase (mM)	Na,K-ATPase	Myosin K,EDTA-ATPase	Farnesyl protein transferase	AP-N (mM)	
Psammaplin D (158)	2.8					110
Purealidin A (146)		22% Inhibition at 10 ⁻⁴ M	-			104
Purealin (122)			Activate			91
Lipopurealin-A (141)		30 M (brain) 20 M (kidney) 100 M (heart)				102
Lipopurealin-B (142)		6 M (brain) 10 M (kidney) > 100 M (heart)	Inhibit			102
Lipopurealin-C (143)		60 M (brain) 20 M (kidney) > 100 M (heart)				102
Araplysin-I (99)		0.5 mM (brain)				81
Araplysin-II (100)		1 mM (brain)				81
Psammaplin A (152)				7.0 mM	70.9	114
Bisaprasin (154)				4.2 mM	30.2	114
Psammaplin A ₁ (165)				3.0 mM		114
Psammaplin A ₂ (166)				4.4 mM		114
Aplysinellin A (167)				85.2 mM	2.4	114
Aplysinellin B (168)				25.1 mM		114

TABLE X

Enzyme-Based Histone Deacetylase (HDAC) and DNA Methyltransferase (DNMT) Inhibition Data, and Cell-Based p21 Promoter Activity Data, for the Psammaplins (112).

Alkaloids	HDAC enzyme inhibition IC ₅₀ (nM) ^a	cell-based fold induction activity AC ₅₀ (μM) ^b	max fold induction (22 MFI is produced at 0.5 μM)	DNMT enzyme inhibition IC ₅₀ (nM)
Psammaplin A (152)	4.2 ± 2.4	7.5	15	18.6
Psammaplin B (156)	48 ± 12	15.0	7	nt
Psammaplin C (157)	nt	nt	nt	nt
Psammaplin D (158)	44 ± 10	> 15.0	5	> 30.0
Psammaplin E (159)	327 ± 39	> 15.0	2	> 30.0
Psammaplin F (160)	2.1 ± .4	0.7	18	> 30.0
Psammaplin G (161)	18 ± 8	7.5	7	12.8
Psammaplin H (162)	79 ± 22	3.8	7	> 30.0
Psammaplin I (163)	299 ± 70	2.6	9	> 30.0
Psammaplin J (164)	20 ± 17	3.6	8	nt
Bisaprasin (154)	9 ± 5	0.7	9	3.4
Trichostatin A	14 ± 1	0.2	7.2	nt
Trapoxin A	9 ± 3	0.005	28.5	nt

^aCompounds were titrated in a 1:5 dilution series (10 μM, 2 μM, 400 nM, 80 nM, and 16 nM); averages from duplicate trials are shown, except for known HDAC inhibitors, trichostatin A and trapoxin A.

^bConcentration of compound required to produce 50% p21 promoter activity by psammaplin A (**152**).

TABLE XI

Antiviral Activity of Bromotyrosine Derivatives

Alkaloids	Antiviral activity	Ref.
Moloka'iamine (52)	Mv 1 Lu/HSV II: 10 µg/mL 92% reduced; CV-1/HSV-1 and BHK/VSV not active	42
Mololipids (53)	HIV-1 ED50 52.2 µM	43
Fistularin-3 (79)	Feline leukemia [ED ₅₀ :22 µM (4.8 µg/200 µl)]. ED ₅₀ : AZT 0.10 µM, ED ₅₀ : ddCyd 15 µM. Not active against FeLV at 100 µg/200 µl	71
11-Ketofistularin-3 (82)	Feline leukemia [ED ₅₀ :42 µM (9.3 µg/200 µl)]. ED ₅₀ : AZT 0.10 µM, ED ₅₀ : ddCyd 15 µM. Not active against FeLV at 100 µg/200 µl	71
Psammaplysin D (132)	51% inhibition at 0.1 µg/mL against Haitian RF strain of HIV-1	96

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