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Applying Mosher's Method to Acetogenins Bearing Vicinal Diols. The Absolute Configurations of Muricatetrocin C and Rollidecins A and B, New Bioactive Acetogenins from *Rollinia mucosa*

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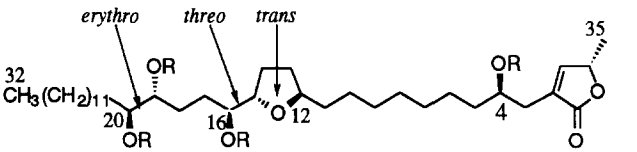
Abstract—Muricatetrocin C (**1**), rollidecin A (**2**), and rollidecin B (**3**), three new bioactive annonaceous acetogenins bearing vicinal diols, were isolated from the leaves of *Rollinia mucosa* (Annonaceae) using activity-directed fractionation. The total structural elucidations of **1–3**, including the absolute stereochemistries of the vicinal diols, were achieved by analyzing their per-Mosher ester derivatives. All three compounds showed potent and selective inhibitory effects against several human cancer cell lines. Copyright © 1996 Elsevier Science Ltd

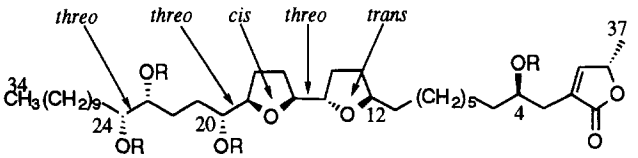
Introduction

Rollinia mucosa (Jacq.) Baill. (Annonaceae) is a tropical fruit tree native to the West Indies and Central America. Our previous search for the bioactive constituents from its leaf extracts has yielded several new and known acetogenins.[1–3] The current work reports the discovery of three additional new acetogenins, muricatetrocin C (**1**), rollidecin A (**2**) and rollidecin B (**3**). Compound **1** shares the same planar structure with muricatetrocin A and muricatetrocin B;[4] it differs from the former by having a *trans* THF ring and from the latter by having an *erythro* vicinal diol. Compounds **2** and **3** have *threo* and *erythro* vicinal diols, respectively; their common planar structure is the same as that of the parent compound of bulladecinone.[5] In the past, the only method to determine the absolute configuration of 1,2-diols in annonaceous acetogenins was by preparing their mono-Mosher ester derivatives.[4] This procedure requires some special caution to stop the reaction at the stage of mono-esterification, as well as a post-reaction separation of the mixtures of mono-Mosher esters, because acetogenins typically bear three or four hydroxyls; finally, the position of esterification in each separated mono-Mosher ester needs to be determined by appropriate EIMS methods. Thus, the amount of acetogenins required by the mono-esterification procedure is often higher than can be routinely obtained from natural sources. The method described in this paper, which aims to facilitate the direct application of Mosher's method to acetogenins bearing multiple hydroxyl groups, is considerably simpler and requires much smaller amounts of material. The stereochemistry of annonaceous acetogenins plays an important role in their bioactivities. This may be illustrated, as an additional example, by the in vitro antitumor selectivity differences reported herein between **2** and **3**.

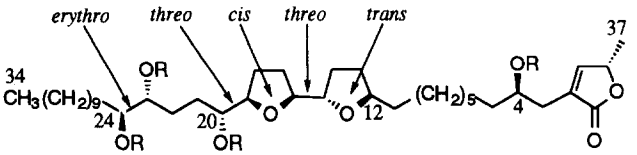
Key words: *Rollinia mucosa*, acetogenins, muricatetrocin C, rollidecin A, rollidecin B.



1: R=H; **1a**: R=TMSi; **1s**: R=(*S*)-MTPA; **1r**: R=(*R*)-MTPA



2: R=H; **2a**: R=TMSi; **2s**: R=(*S*)-MTPA; **2r**: R=(*R*)-MTPA



3: R=H; **3a**: R=TMSi; **3s**: R=(*S*)-MTPA; **3r**: R=(*R*)-MTPA

Figure 1. Structures of muricatetrocin C (**1**), rollidecin A (**2**), rollidecin B (**3**) and their respective TMSi (**1a–3a**) and Mosher ester (**1s–3s**, **1r–3r**) derivatives.

Results and Discussion

These three new acetogenins (**1–3**) were isolated from the same crude chromatographic fraction which yielded sylvaticin,[1] 12,15-*cis*-sylvaticin,[1] mucocin,[2] and rollinecins A and B.[3] Compounds **1–3** had very similar elution times on normal phase HPLC using a hexane:methanol:THF eluant system, but they were separated on a C-18 column (see Experimental).

The terminal α,β-unsaturated γ-lactone unit with a 4-OH, typical of many annonaceous acetogenins, exists in all three compounds (**1–3**); this was obvious by the comparisons of their ^{1}H and ^{13}C NMR data with those reported for known acetogenins (see Table 1).[6] The four peaks from δ 69 to 75 in each of their ^{13}C NMR spectra were suggestive of the existence of four hydroxyls in each compound as the chemical shifts of carbinyl carbons are usually located in this region.[6,7] The ^{13}C NMR signals of the THF oxymethines, on the other hand, are usually located between δ 79 and 85,[6,7] and a count of peaks in this region revealed that **1** had one THF ring and both **2** and **3** had two THF rings. This notion was supported by their ^{1}H NMR data (Table 1),[5] their HRFABMS results, as well as the preparation of their tetra-TMSi and tetra-MTPA derivatives. The planar structures of **1–3** were solved by the EIMS of their tetra-TMSi derivatives (Fig. 2). For each of these compounds, two alternative structures could possibly fit the LREIMS data. Hence, we performed HREIMS on two diagnostic fragment ions, and this information confirmed the structures as shown (see Experimental).

The ^{1}H chemical shifts were indicative of the relative stereochemistries of the hydroxyls in **1–3**. As indicated by their COSY spectra, there was only one hydroxyl flanking the THF ring(s) in each of these compounds. According to Born et al., these flanking hydroxyls should be *threo* to the THF rings because of their ^{1}H δ values (ca. δ 3.40).[8] Similarly, the ^{1}H δ values of the two carbinyl methines of a *threo* 1,2-diol should be relatively lower (ca. δ 3.40) when compared with that of an *erythro* 1,2-diol (ca. δ 3.60).[6c] Thus, the vicinal diols in **1–3** were concluded to be *erythro*, *threo* and *erythro*, respectively. The THF ring of **1** was proposed to be *trans* because of the close match of its ^{13}C NMR data with those reported for a synthetic model compound bearing the *threo/trans* relative stereochemistry.[7] Unfortunately, it was not feasible to use the same approach to assign the relative stereochemistry across the adjacent bis-THF rings in **2** and **3** due to the overlapping nature of their ^{1}H δ values (all four oxymethine protons on the THF rings resonated in the narrow region δ 3.92–3.98), and, also, due to the lack of model compounds corresponding to adjacent bis-THF rings flanked only by one hydroxyl. However, the striking similarity between the NMR data (both ^{1}H

Table 1. NMR Data for **1–3** (500 MHz for ^{1}H and 75 MHz for ^{13}C, in $CDCl_3$)

Position	Muricatetrocin C (**1**)		Rollidecin A (**2**)		Rollidecin B (**3**)	
	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1		174.6		174.6		174.6
2		131.2		131.2		131.2
3	2.40m, 2.53m	22.7–35.5	2.40m, 2.53m	22.7–35.7	2.40m, 2.53m	22.7–35.7
4	3.84m	69.9	3.84m	69.8	3.84m	69.8
5	1.40–1.50m	37.4	1.40–1.50m	37.4	1.40–1.50m	37.4
6–10	1.20–1.40m	22.7–35.5	1.20–1.40m	22.7–35.7	1.20–1.40m	22.7–35.7
11	1.40–1.60m	22.7–35.5	1.40–1.55m	22.7–35.7	1.40–1.55m	22.7–35.7
12	3.89m	79.3	3.92–3.98m	80.3	3.92–3.98m	80.2
13	1.40–2.00m	22.7–35.5	1.75–2.10m	22.7–35.7	1.75–2.10m	22.7–35.7
14	1.59m, 1.98m	22.7–35.5	1.75–2.10m	22.7–35.7	1.75–2.10m	22.7–35.7
15	3.82m	81.7	3.92–3.98m	80.7[a]	3.92–3.98m	80.8[a]
16	3.45m	74.3[a]	3.92–3.98m	81.4[a]	3.92–3.98m	81.4[a]
17	1,40–1.70m	22.7–35.5	1.75–2.10m	22.7–35.7	1.75–2.10m	22.7–35.7
18	1,40–1.70m	22.7–35.5	1.75–2.10m	22.7–35.7	1.75–2.10m	22.7–35.7
19	3.62m	74.4[a]	3.92–3.98m	82.6[a]	3.92–3.98m	82.7[a]
20	3.62m	74.7[a]	3.41m	74.6[b]	3.41m	74.6[b]
21	1,40–1.70m	22.7–35.5	1.40–1.70m	22.7–35.7	1.40–1.70m	22.7–35.7
22	1.20–1.40m	22.7–35.5	1.40–1.70m	22.7–35.7	1.40–1.70m	22.7–35.7
23	1.20–1.40m	22.7–35.5	3.54m	74.8[b]	3.39–3.42m	74.9[b]
24	1.20–1.40m	22.7–35.5	3.60m	75.4[b]	3.39–3.42m	75.6[b]
25	1.20–1.40m	22.7–35.5	1.40–1.70m	22.7–35.7	1.40–1.70m	22.7–35.7
26–31	1.20–1.40m	22.7–35.5	1.20–1.40m	22.7–35.7	1.20–1.40m	22.7–35.7
32	0.88t (7.0)	14.1	1.20–1.40m	22.7–35.7	1.20–1.40m	22.7–35.7
33	7.19m	151.8	1.20–1.40m	22.7–35.7	1.20–1.40m	22.7–35.7
34	5.06m	78.0	0.88t (J=7.0)	14.1	0.88t (J=7.0)	14.1
35	1.43d (6.9)	19.1	7.19m	151.8	7.19m	151.8
36			5.06m	78.0	5.06m	78.0
37			1.43d (J=6.9)	19.1	1.43d (J=6.9)	19.1

[a] and [b] indicate exchangeable assignments within the columns.

and ^{13}C) of **2** and **3** strongly suggested that the two acetogenins shared the same absolute stereochemical structure from C-12 through C-20.

The absolute stereochemistry of vicinal diols cannot be easily solved by a straightforward application of Mosher's method[9,10], partially because the $\delta_H(S-R)$ effects caused by the two vicinal MTPA groups may either reinforce or cancel to cause confusion. This is especially true in the case of a *threo* 1,2-diol, where, after the per-Mosher ester is made, the two MTPA groups will cancel with each other in terms of the $\delta_H(S-R)$ value and sometimes data points having the same sign (either positive or negative) may be observed on both sides of the diol.[4] However, no published work has been found actually attributing the possible irregular arrangements of the $\delta_H(S-R)$ data caused by mutual interferences from multi-MTPA groups to the fundamental invalidation of Mosher's method. To invalidate Mosher's method, MTPA groups must be compelled to assume conformations that are very much different from the ideal one as originally proposed.[9,10] According to Ohtani et al., this may happen when the steric compression becomes severe as in cases of axial-oriented MTPA groups on some rigid ring systems.[10] Fortunately, the situation is not likely to be such in annonaceous acetogenins where hydroxyls are almost always located on long, open-ended, aliphatic chains. Even in situations such as per-Mosher ester derivatives of acetogenins bearing 1,2-diols, the two vicinal MTPA groups still should be able to rotate away from each other and preserve their ideal conformations. Recently Hoye et al. reported a total synthesis of (+)-parviflorin, and determined the absolute configuration of a tetrol (bearing two terminal 1,2-diols) intermediate by preparing its *R* and *S* per-Mosher esters.[11] Having considered this, then, the mutual interferences from multi-MTPA groups ought to be explained, at least theoretically, by adding up the results from the individual MTPA groups as if they work separately. Although this ideal model would not be expected to be followed exactly in all situations, as more and more experiences are accumulated with the per-Mosher ester derivatives of annonaceous acetogenins, some rules of thumb have been found that are sometimes applicable.

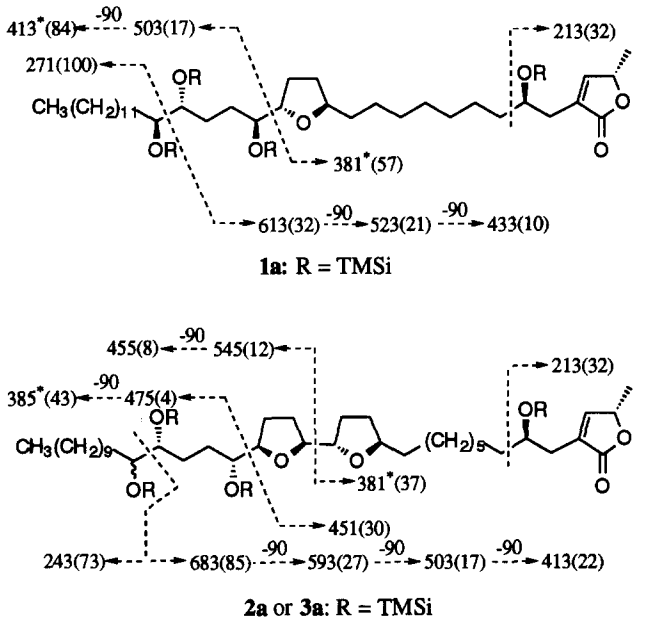


Figure 2. Some diagnostic EIMS fragment ions of **1a–3a**. Percentage intensities are indicated in parentheses (the numbers used in the lower figure is for **2a**). Peaks with asterisks have been confirmed by HREIMS.

The complexity of solving the multi-MTPA interference phenomenon partially stems from the fact that, in mono-MTPA molecules, the magnitude of $\delta_H(S-R)$ is related to the distance from the MTPA group in a way that is sensitive to the local molecular conformation surrounding the MTPA group, the details of which are characteristic of each molecule. Our experience with annonaceous acetogenins (whose conformations are largely dominated by long aliphatic chains) has been that the $\delta_H(S-R)$ magnitude is the strongest (ca. 0.13) at a proton that lies two C—C bonds away from the MTPA group, intermediately strong (ca. 0.07) at a proton that lies three or four C—C (C—O) bonds away, and relatively weak (ca. 0.03) at a proton that lies one C—C bond or five C—C (C—O) bonds away. Usually, MTPA groups assert only weak influences beyond six C—C bonds (or equivalent space distances). This trend seems to be reproducible on the aliphatic chain portion of all acetogenins we have examined so far and can be clearly illustrated with the mono-Mosher esters of gigantetrocins A and B.[4]

Tetra-Mosher ester derivatives of **1–3** were prepared, and their ^1H NMR data were assigned according to regular, single-relayed and double-relayed COSY spectra (all data points relevant to this text have been included in Table 2). For **1**, the positive value of $\delta_H(S-R)$ at H-12 (+0.09) suggested an *S* configuration at C-16, and, for **2**, the negative values of $\delta_H(S-R)$ of H-12 (−0.02), H-15 (−0.06) and H-16 (−0.09) suggested an *R* configuration at C-20. We have previously predicted that **2** and **3** shared the same structure from C-12 through C-20. This is now further supported

Table 2. Some selected ^1H NMR δ values of tetra-MTPA derivatives of compounds **1–3**

	1s	**1r**	$\Delta\delta_H(S-R)$	**2s**	**2r**	$\Delta\delta_H(S-R)$	**3s**	**3r**	$\Delta\delta_H(S-R)$
H-12	3.85	3.76	+0.09	3.91	3.93	−0.02	3.91	3.93	−0.02
H-15	3.92	3.87	+0.05	3.82	3.88	−0.06	3.84	3.88	−0.04
H-16	4.94	4.84	+0.10	3.73	3.82	−0.09	3.75	3.82	−0.07
H-19	5.02	5.17	−0.15	3.91	3.84	+0.07	3.96	3.81	+0.15

by the per-Mosher data of **3** which also pointed to an *R* configuration at the C-20 stereocenter of this molecule. These configurational assignments have reasonably assumed that in each molecule the vicinal MTPA groups were too far away from the protons being evaluated (i.e., H-12,15,16) to assert any significant influence on them. Supporting examples can be found from known acetogenins whose per-Mosher esters have been made. For example, in the tetra-Mosher esters of 12,15-*cis*-sylvaticin,[1] mucocin[2] and muricatetrocin B,[4] the $\delta_H(S-R)$ values of H-12 are consistent with the absolute configurations at the C-16 carbinol centers. When the *S* absolute configuration at C-16 was combined with the prior determined *threo/trans* relative configuration of **1** from C-16 to C-12, the absolute stereochemistry of the mono-THF ring in **1** could be readily assigned as 12*R* and 15*S*. Applying the $\delta_H(S-R)$ magnitude-distance relationship for acetogenins, as described above, we predicted that the $\delta_H(S-R)$ value of H-15 (+0.05) in **1** should be dominated by the C-19-MTPA and C-20-MTPA, and, thus, the positive value indicated that the configurations at C-19/20 were *R/S*. In this case, the effect of the C-19-MTPA reinforced that of the C-16-MTPA and the C-20-MTPA at H-15. If, on the other hand, the diol were to be 19*S*/20*R*, then the C-19-MTPA and C-20-MTPA should have combined their effects, overridden the C-16-MTPA, and given a negative $\delta_H(S-R)$ value at H-15. Similar situations can be found in the $\delta_H(S-R)$ behavior of H-15 in 28-OH bullatalicin (synonym: squamostatin-D) and bullatanocin (synonym: squamostatin-E), whose per-Mosher ester derivatives have been studied by Fujimoto's group.[7,12]

A more convincing line of supporting evidence was from the *R* and *S* per-Mosher ester data of muricatetrocin B.[4] Here, the $\delta_H(S-R)$ values of H-12 and H-15 were +0.12 and +0.02, respectively. These data were not only consistent with the structure of muricatetrocin B, but they made more sense when we considered that in this molecule the C-20-MTPA should have a cancelling effect with the C-19-MTPA and C-16-MTPA, the reason why we observed a smaller $\delta_H(S-R)$ value (+0.02) of H-15 compared with that in **1** (+0.05). Thus, the assignment of *R/S* at C-19/20 in **1** seems reasonable.

The *threo* 1,2-diol in **2** could either be *R/R* or *S/S*. If it were *S/S*, then the C-23-MTPA should have reinforced with the C-20-MTPA to override the C-24-MTPA and should have given a negative $\delta_H(S-R)$ value at H-20; however, the opposite was observed (see Table 2). Thus, the absolute configuration at C-23/C-24 of **2** should be *R/R*. Likewise, the *erythro* 1,2-diol in **3** could be either 24*S*/23*R* or 24*R*/23*S*. If it were 24*R*/23*S*, then effects of the C-24-MTPA, C-23-MTPA and C-20-MTPA should have combined to give a large negative $\delta_H(S-R)$ value at H-19. Instead, a large positive value (+0.15) was observed which suggested the 24*S*/23*R* configurations. Additional evidence was apparent when the magnitudes of the $\delta(S-R)$ values of H-19 were compared in **2** and **3**; it was more positive in **3** because in this situation the C-24-MTPA reinforced with the C-23-MTPA. In both **2** and **3** the cancelling relationship between a 1,4-MTPA pair (referring to the C-20-MTPA and C-23-MTPA) was seen. This relationship was the opposite in **1**. Another example of a 1,4-MTPA pair with a cancelling relationship could be found in the tetra-Mosher esters of 12,15-*cis*-sylvaticin where the $\delta_H(S-R)$ value of H-15 (−0.03) was dominated by the C-19-MTPA rather than by the C-16-MTPA.[1] Considering the evidence and reasoning presented above, we believe that all of the vicinal diols in **1–3** have been assigned their correct absolute stereochemistries, which can be summarized as 19*R*/20*S* in **1**, 23*R*/24*R* in **2**, and 23*R*/24*S* in **3**.

To solve the relative stereochemistries of the adjacent bis-THF rings of **2** and **3**, we analyzed the phase-sensitive NOESY spectrum of **2s** (because the four THF oxymethine ^{1}H NMR peaks were much more separated in this derivative; see Table 2) and found the cross-peak corresponding to H-16/19, but not that corresponding to H-12/15. Thus, the C-16/19 and C-12/15 THF rings were assigned as *cis* and *trans*, respectively. The relative stereochemistry at C-15/16 was chosen as *threo* by comparing the NMR data of **2** and **3** with those of cyclogonionenin,[13] trilobacin and trilobin.[14] To this point, the absolute stereochemistry from C-12 to C-20 in **2** and **3** could be established as: 12*R*, 15*S*, 16*S*, 19*R*, and 20*R*. By following the method of Hoye et al., the C-4, C-34 (in **1**) and C-36 (in **2** and **3**) stereocenters were assigned as *R*, *S*, and *S*, respectively.[15] Thus, all stereocenters in **1–3** have been assigned their absolute configurations.

Compounds **1–3** showed good bioactivity in the BST[16] (Table 3). Seven-day MTT in vitro cytotoxicity assays against six human solid tumor cell lines[17] were then performed (Table 3). Compound **1** was selectively inhibitory against PC-3 prostatic adenocarcinoma, PACA-2 pancreatic carcinoma and A-549 lung carcinoma. Compound **3** was generally more potent than **2**, and, particularly in the A-498 renal carcinoma cell line, the difference of potency was up to 10,000 times in favor of **3**. This type of stereochemistry-sensitive selectivity is not unusual within the annonaceous acetogenins. Although some encouraging results have been obtained in the course of understanding ATP depletion as the mechanism of action for this class of compound,[18,19] their extremely high bioactivities and complicated SARs[20] merit further investigations with emphases on the details of drug–receptor interactions and the development of whole animal in vivo testing models.

Experimental

Instruments

Melting points were measured on a Fisher–Johns apparatus and were not corrected. Optical rotations were taken on a Perkin–Elmer 241 polarimeter. A Perkin–Elmer 1600 FTIR spectrophotometer and a Beckman DU-7 UV spectrophotometer were used for measuring IR and UV spectra. The NMR experiments

Table 3. Bioactivities[a] of **1–3**

	BST[b] LC_{50}	A-549[c] ED_{50}	MCF-7[d] ED_{50}	HT-29[e] ED_{40}	A-498[f] ED_{50}	PC-3[g] ED_{50}	PACA-2[h] ED_{50}
1	7.6×10^{-1}	5.55×10^{-6}	3.19	1.98	3.39×10^{-2}	1.35×10^{-7}	5.69×10^{-7}
2	4.2×10^{-1}	1.04×10^{-2}	1.78	1.42	5.40×10^{-1}	1.65×10^{-4}	1.41×10^{-6}
3	2.8×10^{-1}	3.73×10^{-5}	1.32	1.69	2.28×10^{-5}	1.73×10^{-5}	3.44×10^{-6}
Adr.[i]	8.2×10^{-2}	1.57×10^{-3}	9.68×10^{-2}	1.93×10^{-2}	1.90×10^{-3}	2.81×10^{-2}	2.24×10^{-2}

[a]All results were reported in μg/mL, and all samples were tested in the same run in each cytotoxicity bioassay (c–h).
[b]Brine shrimp lethality test.
[c]Human lung carcinoma.
[d]Human breast carcinoma.
[e]Human colon adenocarcinoma.
[f]Human renal carcinoma.
[g]Human prostatic adenocarcinoma.
[h]Human pancreatic carcinoma.
[i]Adriamycin was used as the standard positive control.

were carried out on a Varian-500S (^{1}H at 500 MHz, ^{13}C at 125 MHz) or a Bruker-300 (^{1}H at 300 MHz, ^{13}C at 75 MHz) spectrometer using $CDCl_3$ as solvent and TMS as reference. HR FABMS and EIMS of TMS derivatives were taken on a Kratos MS 50 spectrometer. A Rainin system equipped with Dynamax software and a Rainin UV-1 detector (set at 230 nm) was used for all normal phase (using a 250 × 21 mm silica gel column) and reverse phase (using a 250 × 21 mm C18 column) HPLC separations.

Plant material

The leaves of *R. mucosa* (Jacq.) Baill. were collected in the Conservatory of the Missouri Botanical Garden, St Louis, Missouri; the associated plant identification numbers are: MBG no. 891568, voucher *Sherman* 285 (MO).

Extraction and purification procedures

The oven-dried (< 50 °C) pulverized leaves (1630 g) were extracted exhaustively with 95% ethanol (8000 mL × 3) and CH_2Cl_2 (8000 mL × 2 then 5000 mL × 2) at room temperature and condensed under vacuum to yield a combined extract, F001 (144 g; BST LC_{50} 2.1 μg/mL); F001 was partitioned between H_2O (1500 mL) and $CHCl_3$ (3000 mL × 3) to yield the H_2O soluble fraction (F002; 6 g; BST LC_{50} 25 μg/mL), the $CHCl_3$ soluble fraction (F003; 120 g; BST LC_{50} 0.9 μg/mL) and an insoluble interface (F004; 5 g). F003 was further partitioned between hexane (1000 mL) and 90% aq MeOH (2000 mL × 2) to yield the MeOH soluble fraction (F005; 71 g; BST LC_{50} 0.7 μg/mL) and the hexane soluble fraction (F006, 33 g; BST LC_{50} >1000 μg/mL). 68 g of F005 was fractionated on an open column (∅ = 9 cm, packed with 1.1 kg of 60–200 mesh silica gel) using $CHCl_3$–MeOH gradient elution; 29 fractions were collected. Fractions F-13 to F-16 were pooled (3.9 g; BST LC_{50} 0.14 μg/mL) and further fractionated on a second open column (∅ = 5 cm, packed with 600 g of 60–200 mesh silica gel) using hexane–acetone gradient elution. Of the 71 fractions collected, fractions F-(13, 16)-30 to F-(13, 16)-69 were subjected to repetitive reverse phase (H_2O–MeCN elution) and normal phase (hexane–THF–MeOH elution) HPLC purifications to yield **1** (15 mg), **2** (6 mg), and **3** (3 mg).

Typical procedures of chemical derivatizations

(1) Per-MPTA esters: large excess of (*R*)- or (*S*)-(α)-methoxy-(α)-trifluoromethylphenyl acetyl chloride was added to 1 mg of the starting material dissolved in 0.5 mL of CH_2Cl_2. The reaction vial was capped and kept in the refrigerator overnight. The reaction mixture was first purified over a small silica gel pipette column and then by 5% aq $NaHCO_3$ work up. Quantitative conversions were usually achieved.

(2) TMS derivatives: appropriate starting materials (50–80 μg) were treated with *N,O*-bis(trimethylsilyl)-acetamide (20 μL) and pyridine (2 μL) and heated at 70 °C for 30 min to yield the respective per-TMS derivatives.

Bioassays

The brine shrimp (*Artemia salina* Leach) test (BST) was performed as modified[16] to determine LC_{50} values in μg/mL for each partition fraction and chromatographic column pool. Seven-day MTT in vitro cytotoxicity tests against six human tumor cell lines were carried out on **1–3** at the Purdue Cancer Center, using standard protocols[17] for A-549, MCF-7, HT-29, A-498, PC-3 and PACA-2 with adriamycin as the positive control (Table 3).

Muricatetrocin C (**1**) was obtained as a white amorphous powder: mp 65–66 °C; $[\alpha]_D^{25}$ +6.3° (CH_2Cl_2); UV (MeOH) λ_{max} = 224 nm ($\varepsilon = 3.0\times10^3$); IR (dry film): 3445 (br OH), 2932, 2851, 1738, 1671, 1075 cm^{-1}; HRFABMS $(M+H)^+$ found *m/z* 597.4736, calcd 597.4730 for $C_{35}H_{64}O_7$; LREIMS of its tetra-TMS derivative (**1a**), see Figure 2; HREIMS of **1a**: for $C_{21}H_{41}O_4Si_2$ found *m/z* 413.3280, calcd 413.3271; for $C_{23}H_{45}O_2Si$ found *m/z* 381.2469, calcd 381.2461; ^{1}H and ^{13}C NMR data (see Table 1).

Rollidecin A (**2**) was obtained as a white waxy solid: mp 60–61 °C; $[\alpha]_D^{25}$ +13.0° (CH_2Cl_2); UV (MeOH) λ_{max}=222 nm ($\varepsilon=3.3\times10^3$); IR (dry film): 3441 (br OH), 2930, 2855, 1739, 1671, 1072 cm^{-1}; HRFABMS $(M+H)^+$ found *m/z* 639.4849, calcd 639.4836 for $C_{37}H_{66}O_8$; LREIMS of its tetra-TMS derivative (**2a**), see Figure 2; HREIMS of **2a**: for $C_{21}H_{37}O_4Si$ found *m/z* 381.2469, calcd 381.2461; for $C_{21}H_{45}O_2Si_2$ found *m/z* 385.2950, calcd 385.2958; ^1H and ^{13}C NMR data (see Table 1).

Rollidecin B (**3**) was obtained as a white waxy solid: mp 57–58 °C; $[\alpha]_D^{25}$ +8.8° (CH_2Cl_2); UV (MeOH) λ_{max}=224 nm ($\varepsilon=2.8\times10^3$); IR (dry film) 3445 (br OH), 2935, 2854, 1739, 1670, 1074 cm^{-1}; HRFABMS $(M+H)^+$ found *m/z* 639.4822, calcd 639.4836 for $C_{37}H_{66}O_8$; LREIMS of its tetra-TMS derivative (**3a**), see Figure 2; HREIMS of **3a**: for $C_{21}H_{37}O_4Si$ found *m/z* 381.2473, calcd 381.2461; for $C_{21}H_{45}O_2Si_2$ found *m/z* 385.2963, calcd 385.2958; ^1H and ^{13}C NMR data (see Table 1).

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