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Total Synthesis of the (+)-Antimycin A Family

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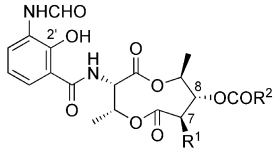
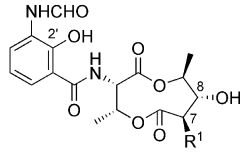
An asymmetric aldol reaction using Oppolzer's sultam has provided a practical and efficient synthetic route (15 steps, overall yield ca. 24 %) to 12 compounds of the Antimycin A family and deisovalerylblastmycin, which were obtained in pure form on a 60–300 mg scale. In the syntheses, the nine-membered dilactone ring was constructed successfully by lactonization of a 2-pyridinethiol ester bearing a TIPS group on the 8-OH by using the $(CuOTf)_2$·PhH complex.

Introduction

Antimycins have a unique nine-membered dilactone ring with one alkyl, one acyloxy, and two methyl substituents and an amide linkage connecting it to 3-formamidosalicylic acid. Thus far, over 25 antimycins, termed antimycin A_1–A_{18}, have been isolated from the *Streptomyces* strain since the first isolation in 1949 by Strong and co-workers.[1] Furthermore, deacyl antimycins such as deisovalerylblastmycin,[2] kitamycins,[3] and urauchimycins[4] have been established as derivatives with the same dilactone structure (Figure 1).



AA_1 ~ AA_{18}:
R^1 = Et, *n*Bu, *n*Hex, 1,2-dimethylpropyl, 4-methylhexyl, isopentyl
R^2 = Me, *n*Pr, *i*Pr, *n*Bu, *i*Bu, *s*Bu, isopenthy, 3-methylpentyl, Bn

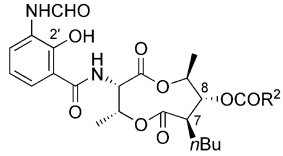


deisovalerylblastmycin: R^1 = *n*Bu
urauchimycin A: R^1 = *i*Bu
urauchimycin B: R^1 = isopentyl
kitamycin A: R^1 = *n*Hex
kitamycin B: R^1 = isopentyl

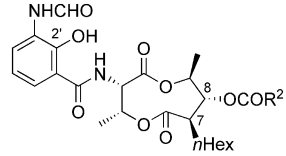
Figure 1. Structures of antimycins and deacyl antimycins.

The AA family (AAs), including deacyl antimycins, have been subjected to biological tests and some of them possess significant activities, including antifungal,[1a] insecticidal,[5] nematocidal,[1c] and anticancer[6] properties. It has also been reported that the AAs specifically inhibit the electron-transfer activity of ubiquinol in the mitochondrial respiratory chain by binding to cytochrome *c* oxidoreductase.[7] Furthermore, Hockenbery and co-workers reported the direct binding of 2′-methoxy-AA to Bcl-2 related proteins, important regulators of cell death and survival.[8] Thus, with respect to the discovery of new compounds, the investigation of the AAs is ongoing because of their characteristic biological activities.

Unfortunately, the difficulty of procuring sufficient quantities (ca. 100 mg) of pure AAs from a culture broth has hindered the systematic biological and biochemical studies of these compounds. The structural similarities of AAs have made their separation difficult and thus HPLC purification was required to isolate pure samples of each AA from a mixture. Furthermore, some of the AAs exist as an inseparable mixture of two isomers bearing a closely related acyl group. For example, antimycin A_3 (AA_3) was found to be a mixture of two compounds with a (*S*)-2-methylbutanoate or 3-methylbutanoate at the C-8 position, termed AA_{3a} and AA_{3b} (Figure 2), respectively.[9] Thus, until now, AA complexes (mixtures of AAs) have been used for biological and biochemical studies in many cases.



AA_{3a}: R_2 = (*S*)-*s*Bu
AA_{3b}: R_2 = *i*Bu
AA_{4a}: R_2 = *i*Pr
AA_{4b}: R_2 = *n*Pr
AA_9 : R_2 = Bn
AA_{11}: R_2 = isopentyl
AA_{18}: R_2 = Me
deisovalerylblastmycyin



AA_{1a}: R_2 = (*S*)-*s*Bu
AA_{1b}: R_2 = *i*Bu
AA_{2a}: R_2 = *i*Pr
AA_{2b}: R_2 = *n*Pr
AA_{15}: R_2 = isopentyl

Figure 2. Synthesized 7-buty- and 7-hexyl-AAs.

From a structural point of view, a 3-formamidosalicylic moiety is required to inhibit electron transport.[10] On the other hand, the lengths of the 7-alkyl and 8-*O*-acyl side-chains on the dilactone ring appear to affect the antifungal

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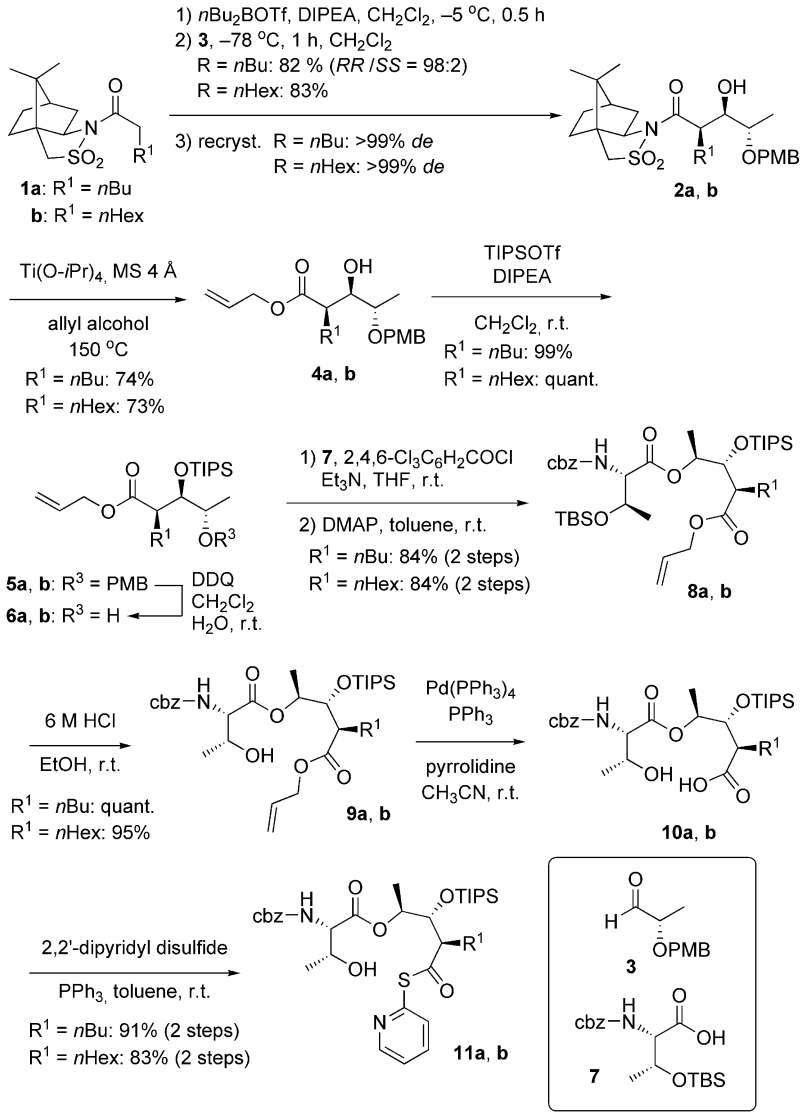
activity.[1d] This finding prompted us to carry out syntheses of AAs with different 7-alkyl and 8-*O*-acyl side-chains in sufficient amounts for future systematic biological and biochemical studies.

Several groups have previously accomplished the enantioselective total synthesis of AA_{3b} (previous name AA_3),[11a–11d] AA_{3a},[9] and AA_9[12] bearing a butyl side-chain at the C-7 position (called 7-butyl-AAs, see Figure 2). Early attempts at the asymmetric total synthesis of AA_{3a} and AA_{3b} were constrained by 1) the poor efficiency of the construction of the stereochemistry at the C-7/C-8 position, 2) the low efficiency of the cyclization to form the nine-membered dilactone ring, and 3) lengthy synthetic routes with low overall yields. Furthermore, the synthesis of other antimycins (e.g., 7-hexyl-AAs, Figure 2) has not been performed.

To overcome the problems associated with C-7/C-8 construction, several elegant methodologies have been developed towards the total[9,11] and formal[13] syntheses of AA_{3b}. Among them, the aldol reaction is the most promising methodology, and Wu and Wang recently reported that excellent stereoselectivity with high chemical yield was achieved by using Crimmins' aldol conditions in their expeditious total synthesis of AA_{3b}.[11d] Around the same time, we reported that an aldol reaction employing Oppolzer's sultam as a chiral auxiliary gave quite satisfactory results to construct the C-7 and C-8 asymmetric centers and we achieved a practical total synthesis of (+)-AA_9 that also solved the other two problems.[12]

By using this methodology, we have performed the first enantioselective synthesis of 7-hexyl-AAs, including (+)-AA_{1a}, (+)-AA_{1b}, (+)-AA_{2a}, (+)-AA_{2b}, and (+)-AA_{15} (Figure 2). In addition, we have also accomplished the enantioselective syntheses of the 7-butyl-AAs, (+)-AA_{4a}, (+)-AA_{4b}, (+)-AA_{11}, (+)-AA_{18}, and deisovalerylblastmycin (Figure 2). We report the results in detail herein.



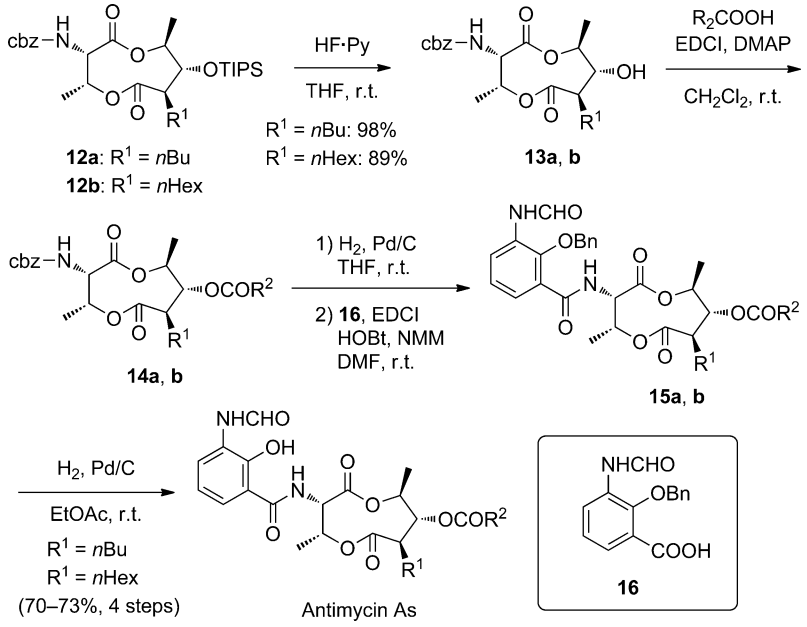
Scheme 1. Synthesis of 2-pyridinethiol ester **11a** and **11b**.

Results and Discussion

Our synthetic route is illustrated in Schemes 1 and 2. The starting materials **1a** and **1b** for 7-butyl- and 7-hexyl-AAs, respectively, were easily prepared by condensation of the corresponding auxiliary and acyl chlorides.[14] First, although the aldol reaction of **1a** with aldehyde **3**[15] was tested under exactly the same conditions as in the literature,[14] no aldol adduct was obtained at all and only polymerization of **3** was presumed (Table 1, entry 1).

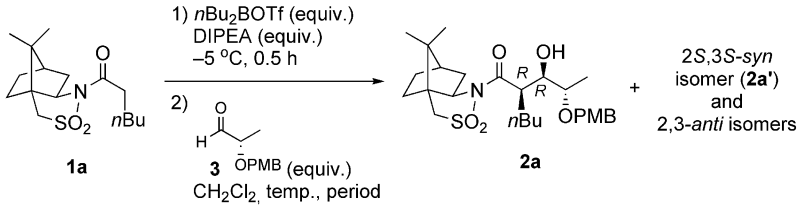
When the ratio of nBu$_2$BOTf/DIPEA was decreased from 1:1 to 2:3, **2a** and its isomers were produced in 86% yield (Table 1, entry 2). The best and most economic results were obtained with 1.5 equiv. of nBu$_2$BOTf, 2.0 equiv. of DIPEA, and 2.5 equiv. of **3** to afford **2a** with traces of other isomers in 82% yield (entry 5). The stereochemistry of the major product **2a** was confirmed by X-ray analysis to be 2*R*,3*R*.[16] In contrast, the stereochemistry of minor adducts was unclear, but we presumed that the second isomer must have the 2*S*,3*S* configuration. The ratio of **2a**/**2a′** was determined by HPLC analysis to be 98:2.

Although there was no information in the literature on the aldol reactivity/selectivity of sultam derivatives bearing a long alkyl chain such as a hexyl group at the beginning of our synthetic study,[17] we were encouraged to find that **1b** was converted into **2b** and its isomers in high yield (83%)



Scheme 2. Total synthesis of AAs.

Table 1. Sultam aldol reaction of **1a** with **3**.



Entry	Conditions 1		Conditions 2			Yield (%)
	nBu$_2$BOTf (equiv.)	DIPEA (equiv.)	Aldehyde (equiv.)	Temp. (°C)	Period (h)	
1	1.1	1.1	5.0[a]	–78	2	–
2	2.0	3.0	5.0[a]	–78	2	86
3	2.0	3.0	2.5[b]	–78	2	80
4	2.0	3.0	2.5[b]	–30	1	73
5	1.5	2.0	2.5[b]	–78	1	82
6	1.5	2.0	1.5[b]	–78	1	71

[a] Aldehyde was added dropwise over 2 h. [b] Aldehyde was added dropwise over 1 h.

and with excellent stereoselectivity under the same conditions (Scheme 1).

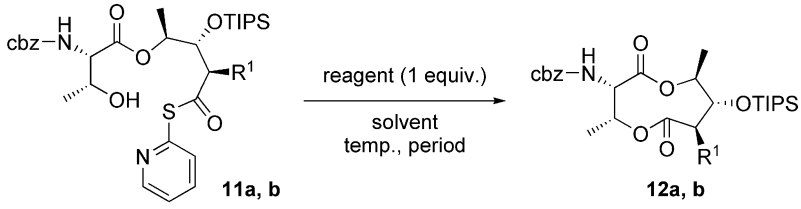
After recrystallization from *n*-hexane/EtOAc or *n*-hexane/Et_2O (63% with 99% *de* for **2a**, 79% with 99% *de* for **2b**), **2a** and **2b** were converted into allyl esters **4a** and **4b** (74 and 73% yields, respectively) by heating at 150 °C in allyl alcohol in the presence of $Ti(O\text{-}iPr)_4$ (3 equiv.) and molecular sieves 4 Å (MS 4A).[18] We decided that the hydroxy group in **4a** and **4b** should be protected at this stage and then converted into acyloxy moieties at a later stage of the practical and efficient syntheses of a wide variety of AAs.[19] The triisopropylsilyl (TIPS) group was chosen as the protecting group, which was introduced by reaction of TIPSOTf with DIPEA (>99%). After protection, the *p*-methoxybenzyl (PMB) group was removed with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to yield unstable alcohols **6a** and **6b**.[20] Without any further purification **6a** and **6b** were subsequently condensed satisfactorily with L-threonine derivative **7** under Yamaguchi conditions to afford both **8a** and **8b** in 84% yield (two steps).[21] Removal of the TBS group with 6 M HCl of **8a** and **8b** (quant. and 95%) followed by palladium(0)-catalyzed deprotection {$[Pd(PPh_3)_4]$, PPh_3, pyrrolidine}[22] of the allyl ester provided *seco*-acids **10a** and **10b**. As discussed by Wu and Wang in detail, lactonization to the nine-membered ring had been problematic for a long time.[11d] In fact, when we examined the cyclization of **10a** by using a carbodiimide-mediated reaction or Yamaguchi conditions,[21] very disappointing results were obtained. Thus, without any further purification, we treated **10a** and **10b** with 2,2′-dipyridyl disulfide/PPh_3 to obtain 2-pyridinethiol esters **11a** and **11b** in 91 and 83% yields, respectively (two steps).[23]

Although heating of **11a** at 80 °C under highly diluted conditions resulted only in decomposition (Table 2, entry 1),[23b] treatment of **11a** with 1 equiv. of $AgClO_4$ in benzene at ambient temperature gave the desired cyclic compound **12a** for the first time in 36% yield (Table 2, entry 2).[24] At a higher temperature (80 °C), the yield dramatically increased to 82% (entry 3). However, as $AgClO_4$ salts are potentially explosive, we tested other conditions for the cyclization of thiol ester **11a**. Thiol esters can be activated with copper salts as well as with silver salts[25] and the use of the copper(I) trifluoromethanesulfonate–benzene complex [$(CuOTf)_2$·PhH] led to quite a successful cyclization, giving **12a** in 88% yield when **11a** was added dropwise to a 1 mmol/L solution of the complex at 80 °C over 2 h (entry 4).

Wu and Wang reported that the efficiency of the cyclization of the precursor of AAs was strongly influenced by the protecting group at 8-OH and that the $(CuOTf)_2$·PhH complex[26] was ineffective for the cyclization of the 2-pyridinethiol ester of the *seco*-acid with an ester functionality on 8-OH.[11d] Therefore, at the present time, it is not clear why the cyclization of **11a** bearing a TIPS group on 8-OH gave an excellent yield. Compound **11b** also underwent cyclization in excellent yield to afford **12b** in 91% yield (entry 7).

The TIPS groups of lactones **12a** and **12b** were removed smoothly by using HF·Py at room temperature to provide alcohols **13a** and **13b** (98 and 89% yields, respectively), which were esterified with the carboxylic acid corresponding to the desired AAs in the presence of *N*-[3-(dimethylamino)propyl]-*N*′-ethylcarbodiimide hydrochloride (EDCI) and 4-(dimethylamino)pyridine (DMAP) in CH_2Cl_2 to give

Table 2. Lactonization of **11a** and **11b**.



11a, b **12a, b**

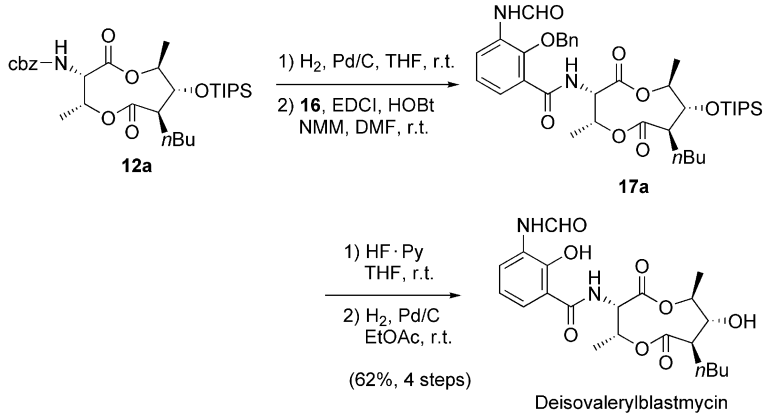
Entry	Reagent	Solvent	Temp. (°C)	Period (h)	Yield (%)
1[a]	–	toluene (1 mM)	80	2[c] then 1	–
2[a]	$AgClO_4$	benzene (0.8 mM)	r.t.	7	36
3[a]	$AgClO_4$	benzene (1 mM)	80	2	82
4[a]	$(CuOTf)_2{\cdot}C_6H_6$	benzene (1 mM)	80	2[c] then 1	88
5[a]	$(CuOTf)_2{\cdot}C_6H_6$	toluene (1 mM)	80	2[c] then 1	87
6[a]	$(CuOTf)_2{\cdot}C_6H_6$	toluene (10 mM)	80	2[c] then 1	64
7[b]	$(CuOTf)_2{\cdot}C_6H_6$	toluene (1 mM)	80	2[c] then 1	91

[a] **11a** was used. [b] **11b** was used. [c] **11a** or **11b** was added dropwise over 2 h.

esters **14a** and **14b**. Thus, the successful introduction of a wide variety of acyl moieties on 8-OH of the lactone ring can allow the present synthetic route to be used for the effective preparation for a wide variety of AAs and their derivatives. The benzyloxycarbonyl (Cbz) groups of **14a** and **14b** were removed by hydrogenolysis (Pd/C in THF) to give amines, which were successfully acylated with **16**[12] using EDCI, 1-hydroxybenzotriazole hydrate (HOBt), and *N*-methylmorpholine (NMM) in DMF to give **15a** and **15b**, respectively. Removal of the benzyl protecting groups in **15a** and **15b** by hydrogenolysis with Pd/C in ethyl acetate cleanly led to the target molecules (70–73% yields from **11a**,**b**), the physical properties of which compare well with those in the literature.

Deisovalerylblastmycin was also synthesized (Scheme 3). The Cbz group of **12a** was removed by hydrogenolysis with Pd/C and the resulting amine was successfully acylated with **16**. After deprotection of the TIPS group with HF·Py in THF, removal of the benzyl group by hydrogenolysis with Pd/C in ethyl acetate gave deisovalerylblastmycin in 64% yield (four steps).

The optical rotation data for the synthetic AAs and deisovalerylblastmycin are summarized in Table 3. The $[\alpha]_D$ values of some of the AAs have not been reported in the



Scheme 3. Total synthesis of deisovalerylblastmycin.

Table 3. Optical rotations of synthetic AAs.

	AA_{1a}	AA_{1b}	AA_{2a}	AA_{2b}
$[\alpha]_D$ (synthetic)	+ 78.4 (*c* 0.208, MeOH)	+ 70.4 (*c* 0.210, MeOH)	+ 73.4 (*c* 0.209, MeOH)	+ 72.3 (*c* 0.209, MeOH)
lit.	–	–	–	–

	AA_{3a}	AA_{3b}	AA_{4a}	AA_{4b}
$[\alpha]_D$ (synthetic)	+ 91.6 (*c* 0.320, $CHCl_3$)	+ 84.3 (*c* 1.01, $CHCl_3$)	+ 77.0 (*c* 0.208, MeOH)	+ 76.3 (*c* 0.211, MeOH)
lit.	–	+ 79.3[10d] (*c* 0.33 $CHCl_3$)	–	–

	AA_9	AA_{11}	AA_{15}	AA_{18}
$[\alpha]_D$ (synthetic)	+ 82.1 (*c* 0.171, MeOH)	+ 77.7 (*c* 0.03, MeOH)	+ 78.4 (*c* 0.150, MeOH)	+ 82.9 (*c* 0.104, MeOH)
lit.	+ 83.6[1c] (*c* 0.157, MeOH)	+ 96.7[1d] (*c*, 0.03, MeOH)	+ 76.7[1d] (*c* 0.15, MeOH)	+ 49.1[1f] (*c* 0.102, MeOH)

	Deisovalerylblastmycin
$[\alpha]_D$ (synthetic)	+ 55.1 (*c* 0.500, MeOH)
lit.	+ 37[27] (*c* 0.3, MeOH)

literature and some of the reported values are lower than those of the synthesized AAs. In addition, direct comparison of the ^{1}H NMR spectra of the synthetic samples with those of isolated compounds from the *Streptomyces* strain revealed that the compounds from nature are often contaminated to some extent and/or are a mixture of isomers because of difficulties in purification. For example, it was confirmed that AA_2 from Sigma Co. is a 2:8 mixture of AA_{2a} and AA_{2b} along with other contaminants.

Conclusion

The asymmetric aldol reaction using Oppolzer's sultam has provided a practical and efficient synthetic route (15 steps, overall yield ca. 24%) to 12 AAs and deisovalerylblastmycin, which were obtained in pure form on a 60–300 mg scale. Further synthetic studies of not only the AAs but also their analogues and an investigation of their biological activities are now in progress.

Experimental Section[28]

General: Melting points were determined with a Yanaco MP3 apparatus. Optical rotations were measured with a Jasco DIP1000 polarimeter using a 10 cm microcell. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Unity 600 (600 and 150 MHz), 500 MR (500 and 125 MHz), 400 MR (400 and 100 MHz) or Mercury 300 (300 and 75 MHz) spectrometer in $CDCl_3$. The chemical shifts are referenced relative to internal tetramethylsilane (TMS) for ^{1}H NMR and to the residual solvent signal for ^{13}C NMR ($CDCl_3$: 77.0 ppm). Mass spectra including HRMS were recorded with a JEOL MS-station 700 spectrometer. IR spectra were recorded by ATR or as neat liquid films in KBr pellets with a Jasco Model FT/IR-410 spectrophotometer. In general, reagent-grade solvents were used. Et_3N and DIPEA were distilled from CaH_2 under argon. Allyl alcohol was distilled from K_2CO_3 under argon. MS 4A was activated in a glass tube oven (200 °C, in vacuo). Analytical TLC was performed on precoated silica gel 60 F-254 plates (0.2 mm layers) on glass with a fluorescent indicator (E. Merck). Flash chromatography separations were performed on Fuji silysia BW-127ZH (53–150 μm) or Kanto Chemical Silica Gel 60 N (spherical, neutral, 63–210 μm). Reagents and solvents were commercial grades and were used without further purification unless otherwise stated. Air- and/or moisture-sensitive reactions were carried out under argon.

Octanoyl Sultam 1b: NaH (890 mg, 60% dispersion of mineral oil, 22 mmol) was added to a solution of sultam (2.17 g, 10.1 mmol) in toluene (20 mL) at 0 °C. After stirring at room temperature for 0.5 h, octanoyl chloride (4.2 mL, 22 mmol) was added at 0 °C and the mixture was stirred at ambient temperature for 27 h. The resulting mixture was quenched by the addition of 6 M aqueous NaOH and the mixture was extracted with CH_2Cl_2. The combined organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 10:1) to give the octanoyl sultam **1b** (3.48 g, quant.) as a colorless oil. $[\alpha]_D^{21}$ = –84.0 (c = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.87 (dd, J = 7.2, 5.4 Hz, 1 H), 3.50 (d, J = 13.8 Hz, 1 H), 3.42 (d, J = 13.8 Hz, 1 H), 2.81–2.61 (m, 2 H), 2.18–2.02 (m, 2 H), 1.98–1.82 (m, 3 H), 1.72–1.56 (m, 3 H), 1.46–1.22 (m, 9 H), 1.16 (s, 3 H), 0.97 (s, 3 H), 0.87 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.8, 65.0, 52.7, 48.2, 47.5, 44.4, 38.3, 35.2, 32.6, 31.4, 28.74, 28.71, 26.2, 24.2, 22.4, 20.6, 19.7, 13.9 ppm. IR (ATR): $\tilde{\nu}$ = 2925, 1694, 1327, 1211, 1133 cm^{-1}. MS (EI): m/z = 341 $[M]^+$, 326, 257 (base peak), 206, 151, 127, 57. HRMS (EI): calcd. for $C_{18}H_{31}NO_3S$ $[M]^+$ 341.2025; found 341.2021.

Aldol Adduct 2b: Dibutylboron triflate (4.4 mL, 1 M in CH_2Cl_2, 4.4 mmol) and DIPEA (1.05 mL, 6.0 mmol) were added to a solution of octanoyl sultam **1b** (1.00 g, 2.93 mmol) in CH_2Cl_2 (10 mL) at –5 °C. After stirring at –5 °C for 0.5 h and then cooling to –78 °C, a solution of aldehyde **3** (1.44 g, 7.41 mmol) in CH_2Cl_2 (5 mL) was added dropwise to the mixture over 1 h. The resulting mixture was treated with a phosphate buffer (pH 6.8) and saturated aqueous NH_4Cl and the mixture was extracted with Et_2O. The organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (toluene/EtOAc = 10:1) and subsequent recrystallizations to give the aldol adduct **2b** along with isomers (1.23 g, 83%). After recrystallization, pure **2b** was obtained in 79% yield with 99% *de* as colorless needless; m.p. 96.4–97.3 °C (*n*-hexane/Et_2O). $[\alpha]_D^{22}$ = –44.5 (c = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (dt, J = 8.7, 3.0 Hz, 2 H), 6.87 (dt, J = 9.0, 2.7 Hz, 2 H), 4.57 (d, J = 11.4 Hz, 1 H), 4.38 (d, J = 11.4 Hz, 1 H), 3.96 (dd, J = 6.3, 5.1 Hz, 1 H), 3.86 (t, J = 6.0 Hz, 1 H), 3.79 (s, 3 H), 3.58–3.38 (m, 4 H), 2.05 (br. d, J = 6.9 Hz, 2 H), 1.96–1.72 (m, 4 H), 1.60–1.10 (m, 11 H), 1.25 (d, J = 6.3 Hz, 3 H), 1.16 (s, 3 H), 0.97 (s, 3 H), 0.85 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.0, 159.0, 130.7, 129.3, 113.6, 74.1, 72.5, 69.7, 65.1, 55.2, 53.2, 48.1, 47.7, 45.7, 44.6, 38.5, 32.8, 31.6, 29.4, 27.7, 26.4, 22.5, 20.6, 19.9, 15.1, 14.0 ppm. IR (ATR): $\tilde{\nu}$ = 3499, 2928, 1662, 1511, 1331, 1246, 1209, 1132, 1066, 1035 cm^{-1}. MS (EI): m/z = 535 $[M]^+$, 414, 370, 320, 216, 194, 121 (base peak), 108. HRMS (EI): calcd. for $C_{29}H_{45}NO_6S$ $[M]^+$ 535.2967; found 535.2973.

Allyl Ester 4b: Ti(O-*i*Pr)$_4$ (275 μL, 1.1 mmol) was added to a suspension of **2b** (206 mg, 0.37 mmol, high purity was required) and activated MS 4A (406 mg) in allyl alcohol (3.8 mL) at ambient temperature and then the mixture was heated at 150 °C for 48 h. Then the resulting mixture was treated with saturated aqueous NH_4Cl and filtered through a pad of Celite. The filtrate was extracted with EtOAc and the extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 20:1 to 10:1) to give the allyl ester **4b** (103 mg, 73%) as a colorless oil. $[\alpha]_D^{23}$ = +26.9 (c = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24 (dt, J = 9.0, 2.7 Hz, 2 H), 6.87 (dt, J = 8.7, 3.0 Hz, 2 H), 5.87 (ddt, J = 17.1, 10.2, 6.0 Hz, 1 H), 5.31 (ddt, J = 17.1, 1.5, 1.5 Hz, 1 H), 5.23 (ddt, J = 10.2, 1.2, 1.2 Hz, 1 H), 4.55 (ddd, J = 5.7, 1.2, 1.2 Hz, 2 H), 4.51 (d, J = 11.1 Hz, 1 H), 4.39 (d, J = 11.4 Hz, 1 H), 3.89 (dd, J = 7.2, 5.1 Hz, 1 H), 3.80 (s, 3 H), 3.45 (qd, J = 6.0, 0.9 Hz, 1 H), 2.58 (ddd, J = 9.9, 6.9, 4.5 Hz, 1 H), 1.78–1.53 (m, 2 H), 1.35–1.15 (m, 9 H), 1.21 (d, J = 6.0 Hz, 3 H), 0.87 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.7, 159.2, 131.9, 130.2, 129.3, 118.5, 113.7, 74.7, 73.4, 70.0, 64.9, 55.1, 47.6, 31.6, 29.1, 28.1 27.3, 22.5, 14.1, 14.0 ppm. IR (ATR): $\tilde{\nu}$ = 3504, 2928, 1729, 1612, 1512, 1246, 1171, 1034 cm^{-1}. MS (CI): m/z = 378 $[M]^+$, 377, 271, 241, 224, 213, 163, 121 (base peak). HRMS (CI): calcd. for $C_{22}H_{34}O_5$ $[M]^+$ 378.2406; found 378.2379.

TIPS Ether 5b: DIPEA (145 μL, 0.83 mmol) and TIPSOTf (150 μL, 0.56 mmol) were successively added to a solution of allyl ester **4b** (103 mg, 0.27 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C. After stirring at ambient temperature for 4 h, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl and the

resulting mixture was extracted with Et_2O. The extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 20:1 to 10:1) to give the TIPS ether **5b** (148 mg, quant.) as a colorless oil. $[\alpha]_D^{24}$ = +11.9 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.22 (dt, *J* = 9.0, 2.4 Hz, 2 H), 6.85 (dt, *J* = 8.7, 2.1 Hz, 2 H), 5.85 (ddt, *J* = 17.4, 10.5, 5.7 Hz, 1 H), 5.28 (ddt, *J* = 17.4, 1.8, 1.2 Hz, 1 H), 5.20 (ddt, *J* = 10.5, 1.8, 1.2 Hz, 1 H), 4.50 (dd, *J* = 5.7, 1.5 Hz, 2 H), 4.44 (d, *J* = 11.4 Hz, 1 H), 4.38 (d, *J* = 11.4 Hz, 1 H), 4.12 (dd, *J* = 7.2, 2.7 Hz, 1 H), 3.80 (s, 3 H), 3.41 (dq, *J* = 6.3, 2.7 Hz, 1 H), 2.49 (ddd, *J* = 11.1, 7.5, 3.9 Hz, 1 H), 1.82–1.57 (m, 2 H), 1.31–1.05 (m, 29 H), 1.16 (d, *J* = 6.3 Hz, 3 H), 0.87 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.4, 158.9, 132.1, 130.8, 129.2, 118.2, 113.5, 76.5, 70.1, 64.8, 55.2, 50.5, 31.6, 29.23, 29.16, 27.8, 22.5, 18.3, 14.1, 14.0, 13.1 ppm. IR (ATR): $\tilde{\nu}$ = 2926, 1731, 1613, 1513, 1463, 1246, 1036 cm^{-1}. MS (CI): *m*/*z* = 535 $[M + H]^+$, 491, 427, 397, 357, 163, 121 (base peak). HRMS (CI): calcd. for $C_{31}H_{55}O_5Si$ $[M + H]^+$ 535.3819; found 535.3817.

Synthesis of Diester 8b

Removal of the PMB Group: Distilled water (0.5 mL) and DDQ (250 mg, 1.1 mmol) were added to a solution of **5b** (535 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at ambient temperature and the mixture was stirred for 0.5 h at same temperature. The reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ and the resulting mixture was extracted with CH_2Cl_2. The organic extracts were dried with $MgSO_4$, filtered, and concentrated to give the crude alcohol **6b**. This was then used in the following reaction without further purification.

Preparation of a Mixed Anhydride: Et_3N (560 μL, 16 mmol) and 2,4,6-trichlorobenzoyl chloride (480 μL, 3.1 mmol) were added to a solution of **7** (739 mg, 2.0 mmol) in THF (5 mL) at 0 °C. After stirring at ambient temperature for 1.5 h, the resulting mixture was filtered and concentrated to give a mixed anhydride of **7**.

Condensation of the Alcohol and the Mixed Anhydride: DMAP (191 mg, 1.6 mmol), Et_3N (140 μL, 1.00 mmol), and a solution of the mixed anhydride in toluene (5 mL) were successively added to a solution of the crude alcohol **6b** in toluene (5 mL) at 0 °C. The resulting mixture was stirred at ambient temperature for 16 h and quenched by the addition of dist. water. The resulting mixture was extracted with Et_2O and the organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 20:1) to give the diester **8b** (638 mg, 84%, two steps) as a colorless oil. $[\alpha]_D^{24}$ = +0.79 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.25 (m, 5 H), 5.89 (ddt, *J* = 17.1, 10.5, 6.0 Hz, 1 H), 5.43 (br. d, *J* = 9.9 Hz, 1 H), 5.31 (ddt, *J* = 17.1, 1.5, 1.5 Hz, 1 H), 5.23 (ddt, *J* = 10.5, 1.5, 0.9 Hz, 1 H), 5.17 (d, *J* = 12.6 Hz, 1 H), 5.05 (d, *J* = 12.3 Hz, 1 H), 4.82 (qd, *J* = 6.3, 1.8 Hz, 1 H), 4.64–4.47 (m, 2 H), 4.39 (qd, *J* = 6.3, 1.8 Hz, 1 H), 4.17 (dd, *J* = 9.9, 1.5 Hz, 1 H), 4.11 (dd, *J* = 7.8, 1.5 Hz, 1 H), 2.47 (ddd, *J* = 14.7, 7.8, 3.9 Hz, 1 H), 1.54–1.80 (m, 2 H), 1.32–1.02 (m, 29 H), 1.26 (d, *J* = 6.3 Hz, 3 H), 1.18 (d, *J* = 6.3 Hz, 3 H), 0.90–0.75 (m, 9 H), 0.85 (t, *J* = 6.6 Hz, 3 H), 0.04–0.08 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.9, 170.5, 157.0, 136.6, 132.3 128.9, 128.6, 119.2, 76.2, 74.9, 67.5, 67.1, 65.7, 60.3, 51.1, 32.0, 30.0, 29.5, 28.0, 26.1, 23.0, 21.5, 18.6, 18.2, 14.5, 13.9, 13.4, –4.0, –4.7 ppm. IR (ATR): $\tilde{\nu}$ = 2928, 1731, 1504, 1463, 1103, 1066 cm^{-1}. MS (CI): *m*/*z* = 765 $[M + H]^+$, 656, 588, 447, 397 (base peak), 223, 159, 91. HRMS (CI): calcd. for $C_{41}H_{74}NO_8Si_2$ $[M + H]^+$ 764.4953; found 764.4962.

Alcohol 9b: A 6 M aqueous HCl (290 μL) solution was added to a solution of **8b** (200 mg, 0.26 mmol) in EtOH (3.5 mL) at ambient temperature and the mixture was stirred for 24 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$. The resulting mixture was extracted with Et_2O and the organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 10:1 to 5:1) to give alcohol **9b** (105 mg, quant.) as a colorless oil. $[\alpha]_D^{22}$ = –10.9 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37–7.27 (m, 5 H), 5.91 (ddt, *J* = 17.1, 10.5, 5.7 Hz, 1 H), 5.53 (br. d, *J* = 8.4 Hz, 1 H), 5.33 (ddt, *J* = 17.4, 1.5, 1.5 Hz, 1 H), 5.24 (ddt, *J* = 10.2, 1.2, 1.2 Hz, 1 H), 5.16 (d, *J* = 12.3 Hz, 1 H), 5.09 (d, *J* = 12.0 Hz, 1 H), 5.02–4.90 (m, 1 H), 4.58 (ddd, *J* = 5.7, 1.5, 1.5 Hz, 2 H), 4.42–4.22 (m, 2 H), 4.10 (dd, *J* = 6.0, 3.6 Hz, 1 H), 2.66–2.46 (m, 1 H), 1.84–1.58 (m, 2 H), 1.40–1.02 (m, 29 H), 1.26 (d, *J* = 5.4 Hz, 3 H), 1.23 (d, *J* = 6.6 Hz, 3 H), 0.87 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.0, 170.3, 156.6, 136.2, 131.8, 128.4, 128.1, 128.0, 118.8, 76.0, 74.8, 67.7, 67.1, 65.4, 59.4, 50.5, 31.6, 29.3, 29.1, 27.7, 22.5, 19.6, 18.1, 15.3, 14.0, 12.9 ppm. IR (ATR): $\tilde{\nu}$ = 3439, 2928, 2867, 1729, 1513, 1456, 1111, 1044 cm^{-1}. MS (CI): *m*/*z* = 650 $[M + H]^+$, 606, 542, 498, 397 (base peak), 357, 269, 223. HRMS (CI): calcd. for $C_{35}H_{60}NO_8Si$ $[M + H]^+$ 650.4088; found 650.4061.

Synthesis of Pyridinethiol Ester 11b

Preparation of *seco*-Acid: $[Pd(PPh_3)_4]$ (16.9 mg, 0.015 mmol), PPh_3 (8.2 mg, 0.031 mmol), and pyrrolidine (51 μL, 0.61 mmol) were successively added to a solution of the desilylated alcohol **9b** (376 mg, 0.58 mmol) in acetonitrile (3 mL) at 0 °C. Because the alcohol was still remaining after stirring at ambient temperature for 3 h (monitored by TLC), the same amounts of the reagents were added to the mixture. After additional stirring for 4 h, the resulting mixture was treated with 6 M aqueous HCl and NaCl. The mixture was extracted with CH_2Cl_2 and the organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane/acetone = 7:1 to 5:1) to give the crude material including *seco*-acid **10b**. This was used in the next reaction without further purification.

Conversion to Pyridinethiol Ester: PPh_3 (632 mg, 2.4 mmol) and 2.2′-dipyridyl disulfide (533 mg, 2.4 mmol) were added to a solution of the crude material including *seco*-acid **10b** in toluene (3 mL) at ambient temperature and the mixture was stirred for 3 h. After concentration, the residue was purified by silica gel column chromatography (*n*-hexane/acetone = 10:1 to 5:1) to give the pyridinethiol ester **11b** (332 mg, 83%, two steps) as a pale-yellow oil. $[\alpha]_D^{23}$ = –15.6 (*c* = 1.00, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.64–8.56 (m, 1 H), 7.75 (td, *J* = 7.8, 2.1 Hz, 1 H), 7.60 (ddd, *J* = 7.8, 0.9, 0.9 Hz, 1 H), 7.42–7.26 (m, 6 H), 5.66 (br. d, *J* = 9.3 Hz, 1 H), 5.24–5.00 (m, 3 H), 4.52–4.02 (m, 3 H), 2.96–2.42 (m, 1 H), 1.88–1.66 (m, 2 H), 1.48–1.02 (m, 29 H), 1.34 (d, *J* = 6.3 Hz, 3 H), 1.24 (d, *J* = 6.3 Hz, 3 H), 0.88 (t, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.3, 170.3, 156.5, 151.0, 150.1, 137.3, 136.2, 130.1, 128.4, 128.0, 127.9, 126.2, 123.6, 76.1, 74.4, 67.6, 67.0, 59.3, 59.1, 31.5, 29.6, 29.3, 27.6, 22.6, 19.8, 18.22, 18.20, 15.4, 14.0, 13.0 ppm. IR (ATR): $\tilde{\nu}$ = 3438, 2928, 2856, 1699, 1574, 1512, 1454, 1060 cm^{-1}. MS (CI): *m*/*z* = 703 $[M + H]^+$, 659, 595, 566, 548, 447, 357, 339, 273, 236, 183, 175, 112 (base peak), 91. HRMS (CI): calcd. for $C_{37}H_{59}N_2O_7SSi$ $[M + H]^+$ 703.3812; found 703.3820.

Dilactone 12b: A solution of the pyridinethiol ester **11b** (730 mg, 1.0 mmol) in toluene (20 mL) was added dropwise to a warmed solution of $(CuOTf)_2$·PhH (567 mg, 1.0 mmol) in toluene (1 L) at 80 °C over 2 h. The resulting mixture was stirred for 1 h at the same temperature and filtered through a pad of silica gel. The filtrate was concentrated and the residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 20:1 to 10:1) to give the dilactone **12b** (476 mg, 91%) as a colorless oil. $[\alpha]_D^{24}$ = +34.7 (*c* = 1.00,

$CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.24 (m, 5 H), 5.60–5.40 (m, 2 H), 5.12 (br. s, 2 H), 4.93 (t, J = 8.7 Hz, 1 H), 4.76 (quint., J = 8.1 Hz, 1 H), 3.83 (t, J = 8.7 Hz, 1 H), 2.37 (dt, J = 15.0, 9.3 Hz, 1 H), 1.78–1.62 (m, 2 H), 1.40 (d, J = 6.3 Hz, 3 H), 1.34–1.02 (m, 29 H), 1.26 (d, J = 6.0 Hz, 3 H), 0.87 (t, J = 6.3 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.1, 170.1, 155.4, 135.9, 128.4, 128.1, 128.0, 79.0, 76.9, 70.7, 67.1, 54.7, 53.2, 31.4, 29.2, 28.9, 27.3, 22.3, 18.5, 18.1, 14.6, 13.9, 13.8 ppm. IR (ATR): $\tilde{\nu}$ = 3358, 2927, 1741, 1509, 1455, 1360, 1191, 1105, 1062, 1013 ppm. MS (CI): m/z = 592 $[M + H]^+$, 548, 484, 447 (base peak), 357, 313, 278, 236, 91. HRMS (CI): calcd. for $C_{32}H_{54}NO_7Si$ $[M + H]^+$ 592.3669; found 592.3674.

Alcohol 13b: HF·pyridine (4 mL) was added to a solution of **12b** (534 mg, 0.95 mmol) in THF (4 mL) at ambient temperature. After stirring at the same temperature for 3 h, the mixture was poured into saturated aqueous $NaHCO_3$ and the resulting mixture was extracted with EtOAc. The organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc = 10:1 to 5:1 to 2:1) to give the alcohol **13b** (336 mg, 89%) as colorless needless; m.p. 94.4–95.2 °C (*n*-hexane/CH_2Cl_2). $[\alpha]_D^{22}$ = +44.5 (c = 1.00, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.24 (m, 5 H), 5.68–5.38 (m, 2 H), 5.11 (br. s, 2 H), 4.92 (t, J = 8.4 Hz, 1 H), 4.86–4.66 (m, 1 H), 3.53 (t, J = 9.6 Hz, 1 H), 2.39 (br. s, 1 H), 2.30 (ddd, J = 11.1, 9.6, 3.3 Hz, 1 H), 1.84–1.58 (m, 2 H), 1.41 (d, J = 6.3 Hz, 3 H), 1.36–1.12 (m, 11 H), 0.86 (t, J = 6.6 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.1, 170.3, 155.6, 135.8, 128.5, 128.3, 128.0, 76.2, 70.8, 67.3, 54.9, 52.0, 31.5, 29.1, 28.9, 27.2, 22.5, 18.3, 14.8, 14.0 ppm. IR (ATR): $\tilde{\nu}$ = 3432, 3341, 2927, 1756, 1732, 1685, 1532, 1191, 1151 cm^{-1}. MS (CI): m/z = 436 $[M + H]^+$, 418, 392, 328, 273, 291, 236, 183, 91 (base peak). HRMS (CI): calcd. for $C_{23}H_{34}NO_7$ $[M + H]^+$ 436.2335; found 436.2347.

General Procedure for the Synthesis of 7-Butyl AA and 7-Hexyl AA

Acylation of Alcohol: The carboxylic acid (1.5–2.0 equiv.) corresponding to the desired AAs, EDCI (1.5–2.0 equiv.), and DMAP (0.5 equiv.) were successively added to a solution of **13a** or **13b** (0.3–0.8 mmol) in CH_2Cl_2 (3 mL) at ambient temperature. The mixture was stirred for 1–3 h and treated with dist. H_2O. The resulting mixture was extracted with EtOAc and the organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane/EtOAc) to give the crude material including ester **14a** or **14b**. This was used in the next reaction without further purification.

Removal of the Cbz Group and Amidation: A mixture of the crude ester **14a** or **14b** and Pd/C (catalytic amount) in THF (2.5 mL) was stirred under H_2 (1 atm) for 2 h in the dark. The mixture was filtered through a pad of Celite and the filtrate was concentrated. 3-Formamidosalicylic acid **16** (1.8 equiv.), EDCI (2.0 equiv.), HOBt (1 equiv.), and NMM (7.0 equiv.) were successively added to a solution of the residue in DMF (2.5 mL) at ambient temperature. After stirring for 24 h the reaction mixture was quenched by the addition of dist. H_2O and the resulting mixture was extracted with EtOAc. The organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was passed through a short column of silica gel (*n*-hexane/EtOAc) to give the crude material including amide **15a** or **15b**. This was applied in the next reaction without further purification.

Removal of the Benzyl Group: A mixture of the crude amide **15a** or **15b** and Pd/C (catalytic amount) in EtOAc (3 mL) was stirred under H_2 (1 atm) for 2 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by silica gel column chromatography (*n*-hexane/EtOAc) and recrystallization to give 7-butyl-AAs (AA_{3a}, AA_{3b}, AA_{4a}, AA_{4b}, AA_{11}, AA_{18}) or 7-hexyl-AAs (AA_{1a}, AA_{1b}, AA_{2a}, AA_{2b}, AA_{15}) (70–73%, four steps).

Antimycin $A_{1a(s)}$: Colorless needles (rotameric mixture), m.p. 157.1–158.9 °C (*n*-hexane/CH_2Cl_2). $[\alpha]_D^{24}$ = +78.4 (c = 0.208, MeOH). ^1H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.48 (s and s, total integr. 1 H), 8.79 and 8.52 (d, J = 11.5 and d, J = 1.6 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 7.8, 1.1 and br. d, J = 7.7 Hz, total integr. 1 H), 8.03 and 7.79 (br. s and br. d, J = 11.5 Hz, total integr. 1 H), 7.29 and 7.25 (br. d, J = 7.1 and dd, J = 8.4, 1.4 Hz, total integr. 1 H), 7.09 and 7.07 (br. d, J = 7.7 and br. d, J = 7.7 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.0 and t, J = 8.2 Hz, total integr. 1 H), 5.76 (dq, J = 7.8, 6.6 Hz, 1 H), 5.32 and 5.29 (t, J = 7.7 and t, J = 7.7 Hz, total integr. 1 H), 5.12 and 5.10 (t, J = 10.2 and t, J = 9.2 Hz, total integr. 1 H), 5.00 (dq, J = 9.6, 6.6 Hz, 1 H), 2.54 (ddd, J = 13.2, 11.4, 2.7 Hz, 1 H), 2.43 (sext., J = 7.1 Hz, 1 H), 1.80–1.66 (m, 2 H), 1.49 (ddq, J = 14.4, 7.8, 7.2 Hz, 1 H), 1.38–1.13 (m, 9 H), 1.32 (d, J = 6.6 Hz, 3 H), 1.29 (d, J = 6.0 Hz, 3 H), 1.19 (d, J = 7.1 Hz, 3 H), 0.95 (t, J = 7.4 Hz, 3 H), 0.86 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.2, 172.9, 170.1, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.2, 74.9, 70.9, 53.6, 50.1, 41.2, 31.4, 28.9, 28.3, 26.9, 26.5, 22.5, 17.8, 16.8, 15.0, 14.0, 11.7 ppm. IR (ATR): $\tilde{\nu}$ = 3370, 2930, 1742, 1697, 1640, 1528, 1360, 1252, 1174, 1138, 1071, 1013 cm^{-1}. MS (CI): m/z = 549 $[M + H]^+$, 521, 315, 285 (base peak), 265, 183. HRMS (CI): calcd. for $C_{28}H_{41}N_2O_9$ $[M + H]^+$ 549.2812; found 549.2807.

Antimycin A_{1b}: Colorless needles (rotameric mixture); m.p. 151.6–152.9 °C (*n*-hexane/CH_2Cl_2). $[\alpha]_D^{23}$ = +70.4 (c = 0.210, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.46 (s and s, total integr. 1 H), 8.79 and 8.52 (d, J = 11.5 and d, J = 1.6 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 7.8, 1.1 and d, J = 7.4 Hz, total integr. 1 H), 8.02 and 7.78 (br. s and br. d, J = 11.3 Hz, total integr. 1 H), 7.29 and 7.25 (d, J = 7.4 and dd, J = 8.4, 1.4 Hz, total integr. 1 H), 7.09 and 7.07 (d, J = 7.7 and d, J = 8.0 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.0 and t, J = 8.2 Hz, total integr. 1 H), 5.76 (dq, J = 7.8, 7.2 Hz, 1 H), 5.32 and 5.29 (t, J = 7.7 and t, J = 7.7 Hz, total integr. 1 H), 5.12 and 5.10 (t, J = 9.9 and t, J = 10.2 Hz, total integr. 1 H), 5.00 (dq, J = 10.2, 6.6 Hz, 1 H), 2.52 (ddd, J = 13.2, 11.4, 2.7 Hz, 1 H), 2.26 (dd, J = 6.6, 1.6 Hz, 2 H), 2.15 (sept., J = 6.6 Hz, 1 H), 1.66–1.74 (m, 1 H), 1.40–1.05 (m, 9 H), 1.31 (d, J = 6.6 Hz, 3 H), 1.30 (d, J = 6.0 Hz, 3 H), 0.99 (dd, J = 6.6, 1.6 Hz, 6 H), 0.86 (t, J = 7.1 Hz, 3 H) ppm. ^1H NMR (150 MHz, $CDCl_3$): δ = 172.9, 171.7, 170.1, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.4, 74.9, 70.9, 53.6, 50.1, 43.2, 31.5, 28.9, 28.5, 27.0, 25.5, 22.5, 22.4, 17.8, 15.0, 14.0 ppm. IR (ATR): $\tilde{\nu}$ = 3259, 2959, 1741, 1698, 1666, 1637, 1528, 1478, 1367, 1198, 1163, 1143, 1113 cm^{-1}. MS (CI): m/z = 549 $[M + H]^+$, 447, 371, 327, 285 (base peak), 265, 183, 103. HRMS (CI): calcd. for $C_{28}H_{41}N_2O_9$ $[M + H]^+$ 549.2812; found 549.2809.

Antimycin A_{2a}: Pale-yellow solid (rotameric mixture); m.p. 113.7–114.7 °C (*n*-hexane/CH_2Cl_2). $[\alpha]_D^{24}$ = +73.4 (c = 0.209, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.48 (s and s, total integr. 1 H), 8.79 and 8.52 (d, J = 11.5 and d, J = 1.6 Hz, total integr. 1 H), 8.56 and 7.34 (dd, J = 7.8, 1.1 and br. d, J = 7.7 Hz, total integr. 1 H), 8.02 and 7.78 (br. s and br. d, J = 12.1 Hz, total integr. 1 H), 7.29 and 7.25 (d, J = 8.2 and dd, J = 7.8, 1.1 Hz, total integr. 1 H), 7.09 and 7.07 (d, J = 7.7 and d, J = 8.0 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.0 and t, J = 8.2 Hz, total integr. 1 H), 5.76 (dq, J = 7.2, 7.2 Hz, 1 H), 5.32 and 5.29 (t, J = 7.7 and t, J = 7.7 Hz, total integr. 1 H), 5.11 and 5.08 (t, J = 10.2 and t, J = 9.9 Hz, total integr. 1 H), 5.00 (dq, J = 9.6, 6.0 Hz, 1 H), 2.62

(sept., J = 7.1 Hz, 1 H), 2.54 (ddd, J = 11.4, 10.2, 2.7 Hz, 1 H), 1.74–1.66 (m, 1 H), 1.40–1.10 (m, 9 H), 1.32 (d, J = 6.6 Hz, 3 H), 1.28 (d, J = 6.0 Hz, 3 H), 1.22 (dd, J = 7.2, 2.7 Hz, 6 H), 0.86 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.6, 172.9, 170.1, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.2, 74.9, 70.8, 53.6, 50.1, 34.1, 31.5, 28.9, 28.3, 27.0, 22.5, 18.9, 17.8, 15.0, 14.0 ppm. IR (ATR): $\tilde{\nu}$ = 3348, 2930, 1740, 1640, 1608, 1527, 1362, 1181, 1141, 1067. MS (CI): m/z = 535 $[M + H]^+$ (base peak), 447, 357, 303, 271, 265, 181. HRMS (CI): calcd. for $C_{27}H_{39}N_2O_9$ $[M + H]^+$ 535.2655; found 535.2662.

Antimycin A_{2b}: Colorless needles (rotameric mixture); m.p. 142.6–144.7 °C (n-hexane/CH_2Cl_2). $[\alpha]_D^{25}$ = +72.3 (c = 0.209, MeOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.48 (s and s, total integr. 1 H), 8.79 and 8.52 (d, J = 11.5 and d, J = 1.6 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 7.8, 1.1 and br. d, J = 8.0 Hz, total integr. 1 H), 8.01 and 7.78 (br. s and br. d, J = 8.0 Hz, total integr. 1 H), 7.29 and 7.25 (br. d, J = 8.2 and dd, J = 7.8, 1.4 Hz, total integr. 1 H), 7.09 and 7.07 (d, J = 7.7 and d, J = 8.0 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.0 and t, J = 8.0 Hz, total integr. 1 H), 5.75 (dq, J = 7.8, 7.8 Hz, 1 H), 5.31 and 5.29 (t, J = 7.7 and t, J = 7.7 Hz, total integr. 1 H), 5.11 and 5.10 (t, J = 9.9 and t, J = 12.6 Hz, total integr. 1 H), 4.99 (dq, J = 10.2, 6.6 Hz, 1 H), 2.52 (ddd, J = 13.2, 10.8, 2.7 Hz, 1 H), 2.36 (td, J = 7.2, 1.6 Hz, 1 H), 1.75–1.64 (m, 3 H), 1.38–1.12 (m, 9 H), 1.32 (d, J = 6.9 Hz, 3 H), 1.29 (d, J = 6.0 Hz, 3 H), 0.99 (t, J = 7.1 Hz, 3 H), 0.87 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.9, 172.3, 170.1, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.4, 74.9, 70.9, 53.6, 50.1, 36.1, 31.5, 28.9, 28.4, 27.0, 22.5, 18.3, 17.8, 15.0, 14.0, 13.7 ppm. IR (ATR): $\tilde{\nu}$ = 3351, 2929, 1739, 1673, 1636, 1610, 1526, 1205, 1163 cm^{-1}. MS (CI): m/z = 535 $[M + H]^+$ (base peak), 447, 357, 303, 271, 265, 181. HRMS (CI): calcd. for $C_{27}H_{39}N_2O_9$ $[M + H]^+$ 535.2655; found 535.2664.

Antimycin A_{3a}: Colorless needles (rotameric mixture); m.p. 173.0–174.0 °C (petroleum ether/Et_2O). $[\alpha]_D^{23}$ = +91.6 (c = 0.320, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.47 (s and s, total integr. 1 H), 8.79 and 8.51 (d, J = 11.4 and d, J = 1.2 Hz, total integr. 1 H), 8.55 and 7.38 (dd, J = 7.8, 1.2 and br. d, J = 7.2 Hz, total integr. 1 H), 7.98 and 7.78 (br. s and br. d, J = 11.4 Hz, total integr. 1 H), 7.30 and 7.25 (br. d, J = 7.2 and dd, J = 7.8, 1.2 Hz, total integr. 1 H), 7.09 and 7.07 (br. d, J = 7.2 and br. d, J = 7.2 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 7.8 and t, J = 7.8 Hz, total integr. 1 H), 5.75 (dq, J = 7.8, 6.6 Hz, 1 H), 5.31 and 5.29 (t, J = 7.8 and t, J = 7.2 Hz, total integr. 1 H), 5.11 and 5.09 (t, J = 10.2 and t, J = 10.2 Hz, total integr. 1 H), 5.00 (dq, J = 9.6, 6.6 Hz, 1 H), 2.53 (ddd, J = 12.0, 10.2, 3.6 Hz, 1 H), 2.43 (sext., J = 7.8 Hz, 1 H), 1.75–1.67 (m, 2 H), 1.50 (ddq, J = 14.4, 7.8, 7.2 Hz, 1 H), 1.40–1.05 (m, 5 H), 1.32 (d, J = 6.6 Hz, 3 H), 1.29 (d, J = 6.6 Hz, 3 H), 1.19 (d, J = 6.6 Hz, 3 H), 0.95 (dd, J = 7.8, 7.2 Hz, 3 H), 0.87 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.3, 173.0, 170.0, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.2, 74.9, 70.9, 53.6, 50.1, 41.2, 29.2, 28.1, 26.4, 22.4, 17.8, 16.8, 15.0, 13.8, 11.7 ppm. IR (neat): $\tilde{\nu}$ = 3370, 2963, 2875, 1747, 1684, 1644, 1604, 1537 cm^{-1}. MS (CI): m/z = 521 $[M + H]^+$, 419, 329, 278, 236, 91 (base peak). HRMS (CI): calcd. for $C_{26}H_{37}N_2O_9$ $[M + H]^+$ 521.2463; found 521.24988.

Antimycin A_{3b}: Colorless needles (rotameric mixture); m.p. 183.5–184.0 °C (petroleum ether/Et_2O). $[\alpha]_D^{22}$ = +84.3 (c = 1.01, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.47 (s and s, total integr. 1 H), 8.79 and 8.51 (d, J = 11.4 and d, J = 1.8 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 7.8, 1.2 and d, J = 7.8 Hz, total integr. 1 H), 7.94 and 7.76 (br. s and br. d, J = 9.5 Hz, total integr. 1 H), 7.29 and 7.24 (d, J = 7.2 and dd, J = 8.4, 1.2 Hz, total integr. 1 H), 7.07 and 7.06 (d, J = 7.8 and d, J = 11.4 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 7.8, and t, J = 7.8 Hz, total integr. 1 H), 5.73 (dq, J = 6.6, 6.6 Hz, 1 H), 5.29 and 5.28 (t, J = 7.8 and t, J = 7.2 Hz, total integr. 1 H), 5.10 and 5.09 (t, J = 10.2 and t, J = 10.2 Hz, total integr. 1 H), 4.99 (dq, J = 10.2, 6.0 Hz, 1 H), 2.51 (ddd, J = 13.8, 11.4, 3.0 Hz, 1 H), 2.26 (dd, J = 7.8, 2.4 Hz, 2 H), 2.14 (sept., J = 7.8 Hz, 1 H), 1.75–1.65 (m, 1 H), 1.45–1.10 (m, 5 H), 1.33 (d, J = 6.5 Hz, 3 H), 1.30 (d, J = 6.6 Hz, 3 H), 0.99 (dd, J = 7.2, 1.8 Hz, 6 H), 0.87 (t, J = 7.2 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 173.0, 171.7, 170.1, 169.4, 159.0, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 111.3, 75.4, 74.9, 70.9, 53.7, 50.1, 43.2, 29.2, 28.2, 25.5, 22.43, 22.40, 17.9, 15.0, 13.8 ppm. IR (neat): $\tilde{\nu}$ = 3370, 1750, 1692, 1644, 1611 cm^{-1}. MS (CI): m/z = 520 $[M]^+$, 458, 418, 264, 236, 220, 202 (base peak). HRMS (CI): calcd. for $C_{26}H_{36}N_2O_9$ $[M]^+$ 520.2421; found 520.2454.

Antimycin A_{4a}: Colorless needles (rotameric mixture); m.p. 179.3–180.4 °C (n-hexane/CH_2Cl_2). $[\alpha]_D^{25}$ = +77.0 (c = 0.208, MeOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.48 (s and s, total integr. 1 H), 8.79 and 8.52 (d, J = 11.5 and d, J = 1.6 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 7.9, 1.1 and br. d, J = 8.0 Hz, total integr. 1 H), 8.02 and 7.78 (br. s and br. d, J = 11.5 Hz, total integr. 1 H), 7.29 and 7.25 (br. d, J = 8.0 and dd, J = 8.2, 1.4 Hz, total integr. 1 H), 7.09 and 7.06 (d, J = 7.8 and d, J = 8.2 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.2 and t, J = 8.2 Hz, total integr. 1 H), 5.76 (dq, J = 7.7, 6.6 Hz, 1 H), 5.32 and 5.29 (t, J = 7.7 and t, J = 7.7 Hz, total integr. 1 H), 5.11 and 5.08 (t, J = 9.9 and t, J = 10.2 Hz, total integr. 1 H), 5.00 (dq, J = 9.6, 6.3 Hz, 1 H), 2.62 (sept., J = 7.1 Hz, 1 H), 2.54 (ddd, J = 11.4, 10.2, 3.0 Hz, 1 H), 1.75–1.65 (m, 1 H), 1.37–1.10 (m, 5 H), 1.31 (d, J = 6.6 Hz, 3 H), 1.28 (d, J = 6.6 Hz, 3 H), 1.22 (dd, J = 8.5, 2.7 Hz, 6 H), 0.88 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 175.6, 172.4, 170.1, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.2, 74.9, 70.9, 53.6, 50.1, 34.1, 29.2, 28.0, 22.4, 19.0, 17.8, 15.0, 13.8 ppm. IR (ATR): $\tilde{\nu}$ = 3369, 2956, 1745, 1687, 1642, 1528, 1363, 1180, 1141, 1067 cm^{-1}. MS (CI): m/z = 507 $[M + H]^+$, 506 $[M]^+$, 419, 265, 247, 56 (base peak). HRMS (CI): calcd. for $C_{25}H_{35}N_2O_9$ $[M + H]^+$ 507.2342; found 507.2342.

Antimycin A_{4b}: Colorless solid (rotameric mixture); m.p. 186.2–187.1 °C. $[\alpha]_D^{23}$ = +76.3 (c = 0.211, MeOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.48 (s and s, total integr. 1 H), 8.79 and 8.52 (d, J = 11.5 and d, J = 1.8 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 8.0, 0.8 and br. d, J = 8.2 Hz, total integr. 1 H), 8.03 and 7.79 (br. s and br. d, J = 8.2 Hz, total integr. 1 H), 7.29 and 7.23 (br. d, J = 8.0 and dd, J = 8.2, 1.1 Hz, total integr. 1 H), 7.09 and 7.07 (d, J = 7.4 and d, J = 8.0 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.2 and t, J = 8.0 Hz, total integr. 1 H), 5.75 (dq, J = 7.7, 6.6 Hz, 1 H), 5.32 and 5.29 (t, J = 7.8 and t, J = 7.7 Hz, total integr. 1 H), 5.11 and 5.10 (t, J = 10.2 and t, J = 10.2 Hz, total integr. 1 H), 4.99 (dq, J = 9.6, 6.3 Hz, 1 H), 2.51 (ddd, J = 12.3, 11.4, 3.0 Hz, 1 H), 2.36 (td, J = 7.4, 1.6 Hz, 2 H), 1.75–1.64 (m, 3 H), 1.40–1.15 (m, 5 H), 1.32 (d, J = 6.6 Hz, 3 H), 1.29 (d, J = 6.3 Hz, 3 H), 0.99 (t, J = 7.4 Hz, 3 H), 0.87 (t, J = 7.4 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.9, 172.3, 170.1, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.4, 74.9, 70.9, 53.6, 50.1, 36.0, 29.2, 28.1, 22.4, 18.3, 17.8, 15.0, 13.8, 13.7 ppm. IR (ATR): $\tilde{\nu}$ = 3363, 2960, 1741, 1693, 1640, 1528, 1360, 1250, 1149 cm^{-1}. MS (FAB): m/z = 507 $[M + H]^+$ (base peak), 489, 419, 265, 243, 181, 155. HRMS (FAB): calcd. for $C_{25}H_{35}N_2O_9$ $[M + H]^+$ 507.2342; found 507.2342.

Antimycin A_9: Pale-yellow solid (rotameric mixture); m.p. 151.1–151.8 °C. $[\alpha]_D^{22}$ = +82.1 (c = 0.171, MeOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.61 and 12.47 (s and s, total integr. 1 H), 8.79 and

8.50 (d, J = 11.0 Hz and br. s, total integr. 1 H), 8.55 (d, J = 10.2 Hz, 1 H), 8.11 and 7.83 (br. s and br. d, J = 10.2 Hz, total integr. 1 H), 7.40–7.25 (m, 5 H), 7.24 (dd, J = 8.0, 0.8 Hz, 1 H), 7.10 and 7.08 (d, J = 7.7 and d, J = 7.7 Hz, total integr. 1 H), 6.90 (t, J = 8.2 Hz, 1 H), 5.75 (dq, J = 7.1, 6.9 Hz, 1 H), 5.32 and 5.27 (t, J = 7.7 and t, J = 7.4 Hz, total integr. 1 H), 5.09 and 5.05 (t, J = 10.2 and t, J = 10.2 Hz, total integr. 1 H), 4.93 (dq, J = 6.6, 6.3 Hz, 1 H), 3.67 (s, 2 H), 2.49 (ddd, J = 13.2, 10.2, 2.7 Hz, 1 H), 1.62–1.54 (m, 1 H), 1.40–1.05 (m, 5 H), 1.30 (d, J = 6.6 Hz, 3 H), 1.15 (d, J = 6.3 Hz, 3 H), 0.81 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.7, 170.2, 170.0, 169.3, 159.2, 150.6, 133.0, 129.2, 128.8, 127.5, 127.4, 124.7, 120.0, 118.9, 112.5, 75.8, 74.7, 70.8, 53.5, 50.1, 41.5, 29.1, 27.9, 22.3, 17.6, 14.9, 13.7 ppm. IR (ATR): $\tilde{\nu}$ = 3372, 2957, 1745, 1688, 1642, 1530, 1364, 1182 cm^{-1}. MS (FAB): m/z = 577 [M + Na]$^+$, 555[M + H]$^+$, 413, 391, 265, 154, 55 (base peak). HRMS (FAF): calcd. for $C_{29}H_{35}N_2O_9$ [M + H]$^+$ 555.2342; found 555.2314.

Antimycin A_{11}: Colorless solid (rotameric mixture); m.p. 177.7–178.0 °C. $[a]_D^{24}$ = +77.7 (c = 0.0341, MeOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.47 (s and s, total integr. 1 H), 8.79 and 8.52 (d, J = 11.5 and d, J = 1.6 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 8.0, 0.8 and br. d, J = 7.7 Hz, total integr. 1 H), 8.01 and 7.78 (br. s and br. d, J = 11.8 Hz, total integr. 1 H), 7.29 and 7.25 (br. d, J = 7.7 and dd, J = 8.2, 1.4 Hz, total integr. 1 H), 7.09 and 7.07 (d, J = 7.7 and d, J = 7.4 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.0 and t, J = 8.0 Hz, total integr. 1 H), 5.75 (q, J = 7.7, 6.6 Hz, 1 H), 5.32 and 5.29 (t, J = 7.7 and t, J = 7.7 Hz, total integr. 1 H), 5.12 and 5.09 (t, J = 10.1 and t, J = 10.2 Hz, total integr. 1 H), 4.99 (dq, J = 9.6, 6.6 Hz, 1 H), 2.54 (ddd, J = 11.4, 10.2, 3.0 Hz, 1 H), 2.39 (td, J = 7.8, 1.1 Hz, 2 H), 1.75–1.52 (m, 4 H), 1.40–1.15 (m, 5 H), 1.32 (d, J = 6.6 Hz, 3 H), 1.29 (d, J = 6.0 Hz, 3 H), 0.92 (dd, J = 6.0, 1.1 Hz, 6 H), 0.87 (t, J = 7.1 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.9, 172.6, 170.1, 169.3, 159.1, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.4, 74.9, 70.9, 53.6, 50.1, 33.7, 32.2, 29.2, 28.1, 27.6, 22.4, 22.1, 17.8, 15.0, 13.8 ppm. IR (ATR): $\tilde{\nu}$ = 3372, 2957, 1744, 1689, 1642, 1528, 1363, 1252, 1149 cm^{-1}. MS (CI): m/z = 535 [M + H]$^+$ (base peak), 517, 419, 271, 265, 155. HRMS (CI): calcd. for $C_{27}H_{39}N_2O_9$ [M + H]$^+$ 535.2655; found 535.2653.

Antimycin A_{15}: Colorless needles (rotameric mixture); m.p. 159.4–161.7 °C (n-hexane/CH_2Cl_2). $[a]_D^{24}$ = +65.6 (c = 0.150, MeOH). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 12.63 and 12.47 (s and s, total integr. 1 H), 8.79 and 8.51 (d, J = 11.5 and d, J = 1.6 Hz, total integr. 1 H), 8.56 and 7.38 (dd, J = 7.8, 1.1 and br. d, J = 7.7 Hz, total integr. 1 H), 8.00 and 7.78 (br. s and br. d, J = 11.3 Hz, total integr. 1 H), 7.29 and 7.24 (br. d, J = 7.1 and dd, J = 7.8, 1.4 Hz, total integr. 1 H), 7.09 and 7.06 (d, J = 7.7 and d, J = 7.7 Hz, total integr. 1 H), 6.92 and 6.90 (t, J = 8.2 and t, J = 8.2 Hz, total integr. 1 H), 5.75 (dq, J = 7.2, 6.6 Hz, 1 H), 5.31 and 5.28 (t, J = 7.7 and t, J = 7.7 Hz, total integr. 1 H), 5.10 and 5.09 (t, J = 10.2 and t, J = 11.8 Hz, total integr. 1 H), 4.99 (dq, J = 9.6, 6.6 Hz, 1 H), 2.52 (ddd, J = 13.2, 11.4, 3.0 Hz, 1 H), 2.38 (dt, J = 7.2, 1.1 Hz, 1 H), 1.75–1.52 (m, 4 H), 1.40–1.15 (m, 9 H), 1.32 (d, J = 6.9 Hz, 3 H), 1.29 (d, J = 6.6 Hz, 3 H), 0.93 (dd, J = 6.0, 1.1 Hz, 6 H), 0.87 (t, J = 6.9 Hz, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 172.9, 172.3, 170.1, 169.3, 159.0, 150.6, 127.4, 124.8, 120.1, 119.0, 112.5, 75.4, 74.9, 70.9, 53.6, 50.1, 33.7, 32.2, 31.5, 28.9, 28.4, 27.6, 27.0, 22.5, 22.2, 17.8, 15.0, 14.0 ppm. IR (ATR): $\tilde{\nu}$ = 3253, 2956, 2359, 1741, 1698, 1640, 1528, 1368, 1198, 1141 cm^{-1}. MS (CI): m/z = 563 [M + H]$^+$ (base peak), 447, 385, 341, 299, 265, 247, 183. HRMS (CI): calcd. for $C_{29}H_{43}N_2O_9$ [M + H]$^+$ 563.2968; found 563.2974.

Antimycin A_{18}: Colorless needles (rotameric mixture); m.p. 198.5–199.0 °C (n-hexane/CH_2Cl_2). $[a]_D^{21}$ = +82.9 (c = 0.104, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 12.63 and 12.47 (s and s, total integr. 1 H), 8.79 and 8.51 (d, J = 11.5 and d, J = 2.0 Hz, total integr. 1 H), 8.55 and 7.38 (dd, J = 8.0, 1.0 and d, J = 7.5 Hz, total integr. 1 H), 7.99 and 7.79 (br. s and br. d, J = 12.5 Hz, total integr. 1 H), 7.29 and 7.25 (dd, J = 8.0, 1.0 and dd, J = 8.0, 1.5 Hz, total integr. 1 H), 7.10 and 7.08 (d, J = 7.5 and d, J = 10.5 Hz, total integr. 1 H), 6.92 and 6.91 (t, J = 8.0, and t, J = 9.5 Hz, total integr. 1 H), 5.75 (dq, J = 7.0, 7.0 Hz, 1 H), 5.30 and 5.29 (t, J = 7.5 and t, J = 8.5 Hz, total integr. 1 H), 5.09 and 5.08 (t, J = 10.0 and t, J = 9.5 Hz, total integr. 1 H), 4.99 (dq, J = 9.5, 6.0 Hz, 1 H), 2.25 (ddd, J = 11.5, 10.5, 3.0 Hz, 1 H), 2.14 (s, 3 H), 1.80–1.65 (m, 1 H), 1.40–1.10 (m, 5 H), 1.32 (d, J = 7.0 Hz, 3 H), 1.30 (d, J = 6.5 Hz, 3 H), 0.87 (t, J = 7.0 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.6, 169.8, 169.3, 169.1, 158.7, 150.3, 127.1, 124.5, 119.8, 118.7, 112.2, 75.4, 74.5, 70.7, 53.4, 49.8, 29.0, 27.9, 22.2, 20.5, 17.5, 14.7, 13.5 ppm. IR (ATR): $\tilde{\nu}$ = 3370, 2957, 1742, 1687, 1641, 1527, 1362, 1176, 1035 cm^{-1}. MS (CI): m/z = 479 [M + H]$^+$, 256 (base peak), 136. HRMS (CI): calcd. for $C_{23}H_{31}N_2O_9$ [M + H]$^+$ 479.2029; found 479.2023.

Synthesis of Deisovalerylblastmycin

Removal of the Cbz Group and Amidation: A mixture of diester **12a** (280 mg, 0.50 mmol) and Pd/C (catalytic amount) in THF (10 mL) was stirred under H_2 (1 atm) for 1 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated. 3-Formamidosalicylic acid **16** (124 mg, 0.46 mmol), EDCI (88 mg, 0.46 mmol), HOBt (71 mg, 0.46 mmol), and NMM (180 μL, 1.64 mmol) were successively added to a solution of the residue in DMF (2 mL) at ambient temperature. After stirring for 24 h, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl and the resulting mixture was extracted with EtOAc. The organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was passed through a short column of silica gel (n-hexane/EtOAc = 5:1 to 3:1) to give the crude amide **17a**. This was used in the next reaction without further purification.

Removal of the TIPS Group: HF·pyridine (2 mL) was added to a solution of the crude amide **17a** in THF (2 mL) at ambient temperature. After stirring at the same temperature for 3 h, the mixture was poured into saturated aqueous $NaHCO_3$ and the resulting mixture was extracted with EtOAc. The organic extracts were dried with $MgSO_4$, filtered, and concentrated. The residue was passed through a short column of silica gel (n-hexane/EtOAc = 2:1 to 1:1) to give the crude alcohol. This was used in the next reaction without further purification.

Removal of the Benzyl Group: A mixture of the crude alcohol and Pd/C (catalytic amount) in EtOAc (5 mL) was stirred under H_2 (1 atm) for 3 h. The mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified by silica gel column chromatography (n-hexane/EtOAc = 5:1 to 3:1 to 1:1) and recrystallization to give deisovalerylblastmycin (62.8 mg, 62%, four steps) as a colorless solid (rotameric mixture); m.p. 196.5–197.5 °C (n-hexane/CH_2Cl_2). $[a]_D^{21}$ = +55.1 (c = 0.500, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 12.65 and 12.50 (s and s, total integr. 1 H), 8.78 and 8.50 (d, J = 11.5 and d, J = 2.0 Hz, total integr. 1 H), 8.75 and 7.37 (dd, J = 8.0, 1.5 and d, J = 8.0 Hz, total integr. 1 H), 7.99 and 7.80 (br. s and br. d, J = 11.5 Hz, total integr. 1 H), 7.30 and 7.26 (dd, J = 8.0, 1.0 and dd, J = 8.0, 1.5 Hz, total integr. 1 H), 7.11 and 7.10 (d, J = 8.0 and d, J = 8.5 Hz, total integr. 1 H), 6.93 and 6.91 (t, J = 8.0, and t, J = 8.5 Hz, total integr. 1 H), 5.71 (dq, J = 8.0, 7.0 Hz, 1 H), 5.26 and 5.25 (t, J = 7.5 and t, J = 7.5 Hz, total integr. 1 H), 4.87 (dq, J = 10.0, 6.0 Hz, 1 H), 3.60 (t, J = 9.5 Hz, 1 H), 2.36 (ddd, J = 13.5, 11.5, 3.0 Hz, 1 H), 2.18 (br. s, 1 H), 1.85–1.65 (m, 2 H), 1.46 (d, J = 6.5 Hz, 3 H), 1.40–

1.15 (m, 4 H), 1.31 (d, J = 7.0 Hz, 3 H), 0.90 (t, J = 7.5 Hz, 3 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.0, 170.0, 169.4, 159.0, 150.6, 127.4, 124.8, 120.2, 119.0, 112.6, 77.1, 76.7, 70.7, 53.7, 52.1, 29.4, 28.6, 22.6, 18.4, 15.0, 13.9 ppm. IR (ATR): $\tilde{\nu}$ = 3333, 2957, 1735, 1679, 1642, 1528, 1363, 1254, 1190, 1160, 1043 cm^{-1}. MS (CI): m/z = 473 $[M + H]^+$ (base peak), 265, 173. HRMS (CI): calcd. for $C_{21}H_{29}N_2O_8$ $[M + H]^+$ 437.1924; found 437.1920.

Supporting Information (see footnote on the first page of this article): ^{1}H and ^{13}C NMR spectra of synthesized AAs.

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