

Total Synthesis of Mauritines A, B, C, and F: Cyclopeptide Alkaloids with a 14-Membered Paracyclophane Unit

Pierre Cristau,^[a] Taoues Temal-Laïb,^[a] Michèle Bois-Choussy,^[a] Marie-Thérèse Martin,^[a] Jean-Pierre Vors,^[b] and Jieping Zhu*^[a]

Abstract: A unified strategy for the synthesis of mauritines A (**5**), B (**6**), C (**7**), and F (**10**) has been developed based on a key intramolecular nucleophilic aromatic substitution reaction (S_NAr) for the formation of the strained 14-membered paracyclophane. It was demonstrated that the outcome of the cycloetherification is independent of the stereochemistry of the peptide

backbone and that both (1*R*)-**16** and (1*S*)-**16** cyclized smoothly to provide the corresponding macrocycle. On the other hand, dehydration of the secondary benzylic alcohol, via the phenylse-

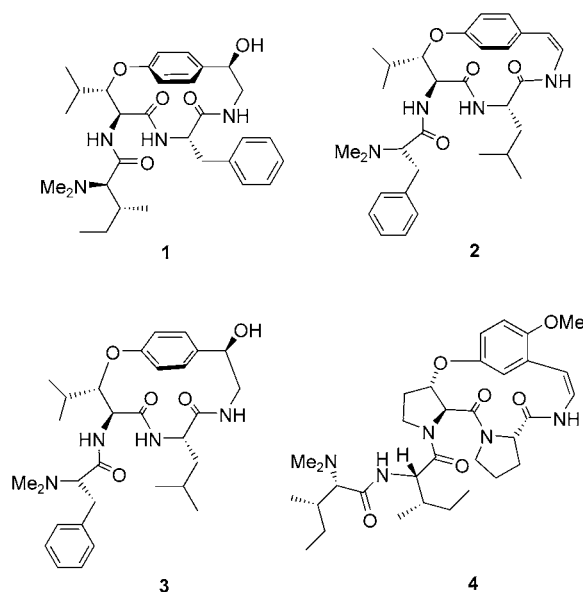
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lenide intermediate, is configuration dependent. (1*R*)-**25** underwent the two-step *syn*-elimination much more easily than (1*S*)-**22**. A modified reductive deamination procedure via the diazonium intermediate was developed. A complete assignment of proton and carbon NMR spectroscopy signals for these natural products is reported for the first time.

Introduction

Cyclopeptide alkaloids are 13-, 14-, or 15-membered macrocycles widely distributed among several plants such as *rharnaceae*, *pendaceae*, and *rubiceae*.^[1] Since the structure determination of pandamine (**1**) by Pais, Goutarel, and co-workers in 1966,^[2] the cyclopeptide alkaloid family of paracyclophanes has grown rapidly and nowadays encompasses over 200 compounds (Scheme 1). Among these, the 14-membered cyclophanes with an *endo* aryl-alkyl ether bond represent the largest subgroup and have been the research focus in the area.

Interesting biological properties such as sedative, antibacterial, and antifungal activities have been found for this



Scheme 1. Representative cyclopeptide alkaloids.

class of natural products.^[3] Sanjoinine A (frangufoline; **2**) and sanjoinine G1 (**3**) are among the most-deeply investigated compounds and the elegant work of Han's group has convincingly demonstrated that sanjoinine A (**2**) is the major bioactive component of "sanjoin", a plant seed of clinical importance in oriental medicine.^[4] However, the re-

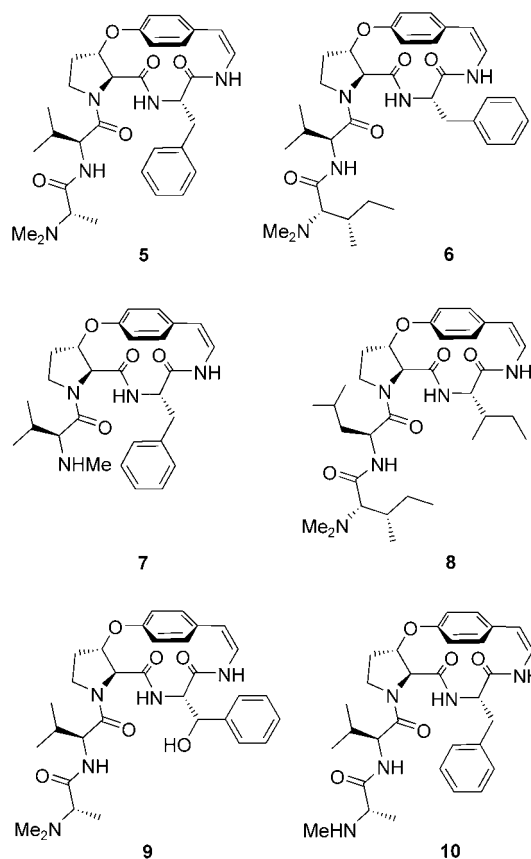
[a] Dr. P. Cristau, Dr. T. Temal-Laïb, Dr. M. Bois-Choussy, Dr. M.-T. Martin, Dr. J. Zhu
Institut de Chimie des Substances Naturelles
CNRS, 91198 Gif-sur-Yvette Cedex (France)
Fax: (+33) 169-077-247
E-mail: zhu@icsn.cnrs-gif.fr

[b] Dr. J.-P. Vors
Bayer CropScience, 14-20 Rue Pierre Baizet
69009 Lyon (France)

Supporting information for this article (experimental procedures and spectroscopic data for compounds (1*R*)-**16**, (1*S*)-**16**, (1*R*)-**20**, and (1*S*)-**20**, as well as copies of ¹H and ¹³C NMR spectra of mauritines A, B, C, and F) is available on the WWW under <http://www.chemeurj.org/> or from the author.

stricted natural availability of cyclopeptide alkaloids has not allowed systematic evaluation of their biological properties and the lack of an efficient synthetic strategy has limited, on the other hand, structure–activity relationship studies. This moderately complex structure in fact represents several synthetic challenges, including a) the construction of an aryl–alkyl ether bond under mild conditions that can be tolerated by the sensitive chiral amino acid residues; b) formation of a sensitive *Z*-enamide function, and c) formation of a strained 14-membered paracyclophane. Not surprisingly, many groups, including those of Païš,^[5] Rapoport,^[6] Schmidt,^[7] Joullié,^[8] Lipschutz,^[9] and Han,^[10] as well as our own group,^[11] have been involved in the development of new synthetic strategies.

In planning a synthesis of macrocyclic compounds, the choice of macrocyclization site and the reaction to be employed to realize this transformation is of utmost importance. For the synthesis of cyclopeptide alkaloids, diverse bond disconnections have been examined for the key ring-forming process and strategies based upon macrolactamization,^[5–8,10] intramolecular aziridine-opening reaction, intramolecular Michael addition, intramolecular aldol condensation,^[1] intramolecular amide N-alkylation,^[9] and lately, intramolecular nucleophilic aromatic substitution (S_NAr)^[11] have been investigated. However, due to the intrinsic ring strain associated with the 14-membered paracyclophane, the cyclization has turned out to be a difficult exercise. A major contribution to this field came from Schmidt and co-workers,^[7] who developed a particularly efficient carboxylic acid activation method (through a pentafluorophenyl ester) for conducting the key macrolactamization step. On the basis of this methodology, they achieved the total syntheses of zizyphine A (**4**)^[7c,e] and mucronine B at the beginning of the 1980s,^[7f,g] followed in 1991 by the 14-membered cyclopeptide alkaloid frangulanine.^[7h] This activation methodology was also featured in the total syntheses of nummularine F,^[8b,c] sanjoinine G1,^[8f,10a] and franguloline^[8h] by the groups of Joullié and Han. We have developed an alternative cyclization strategy based on an intramolecular S_NAr reaction^[12–16] and have successfully implemented it in an efficient asymmetric synthesis of sanjoinine G1.^[17] Besides being convergent, the salient feature of our approach is that two synthetic challenges associated with this molecule, namely, formation of the aryl–alkyl ether bond and macrocyclization, have been reduced to a single operation with great efficiency. In this paper, we report in detail total syntheses of mauritines A (**5**), B (**6**), C (**7**), and F (**10**; Scheme 2). We document that, by carefully tuning the peptide sequence, the previously encountered synthetic pitfall caused by *N*-*tert*-butoxycarbonyl (*N*-Boc) deprotection is readily solved, thereby leading to a more efficient synthesis.^[18] Furthermore, all the proton and carbon NMR spectroscopy signals of these natural products are attributed for the first time from detailed studies.

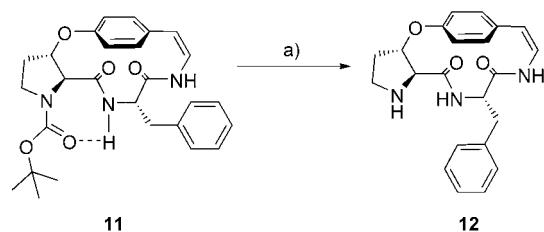


Scheme 2. Structures of mauritines A–F (**5**–**10**, respectively).

Results and Discussion

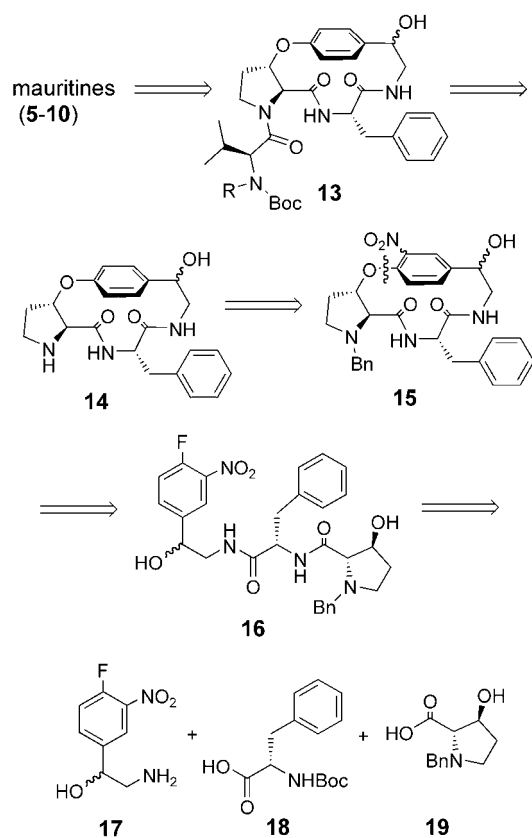
The mauritines A–F (**5**–**10**) were isolated in 1972 and 1974 by Tschesche and co-workers, from the methanol extract of the bark of the African trees *Zizyphus mauritania* Lam.^[19] The structure of these cyclopeptide alkaloids was elucidated by chemical degradation and spectroscopic studies including MS and NMR, UV, and IR spectroscopy. However, the ¹H NMR data for these natural products were only fragmentarily reported and were not attributed. The ¹³C NMR data were not available in the open literature, most probably due to the insufficient amount of natural products available from the natural resources. Fortunately, the structure of mauritine A (**5**) was determined without ambiguity by X-ray crystal analysis.^[20] Preliminary biological studies revealed that mauritines A–F (**5**–**10**) are active against the Gram-positive bacteria *Bacillus subtilis*.^[19b] Nevertheless, the limited availability of these compounds hampered systematic evaluation of their biological properties.^[21]

Our previous synthesis of mauritine A (**5**) was accomplished in 13 steps with 2.3 % overall yield.^[18] The weakness of this synthesis was the seemingly trivial *N*-Boc deprotection step (Scheme 3). Indeed, removal of the *N*-Boc function from compound **11** under a variety of conditions failed to give the desired compound **12**. After much experimentation, the procedure developed by Mann and co-workers (ZnBr₂,



Scheme 3. Removal of the *N*-Boc function, a pitfall in our first-generation synthesis of mauritine A. a) ZnBr_2 , CH_2Cl_2 , <40%.

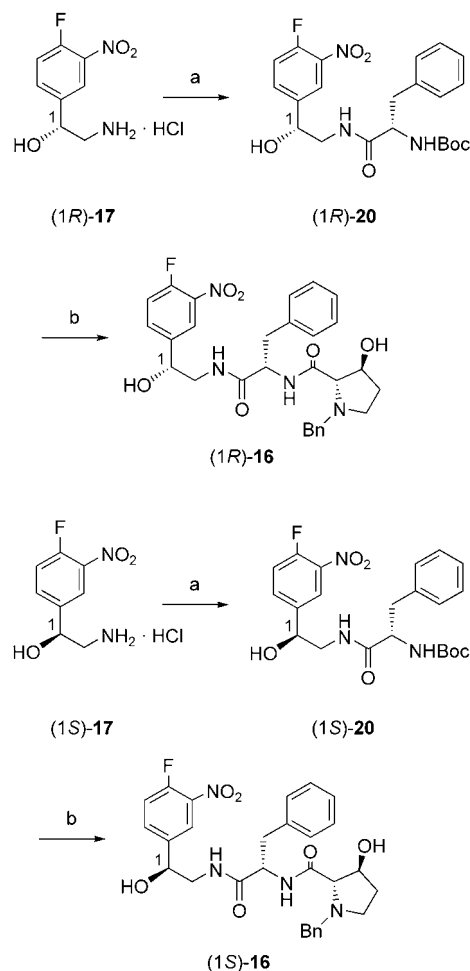
CH_2Cl_2 ^[22] was found to be the method of choice in this specific case, but the yield of the corresponding deprotected cyclophane **12** remained moderate at best (Scheme 3). It is worth noting that the same problem has been encountered in previous syntheses of franguloline.^[7h,8c] It was reasoned that the difficulty in removing this protecting group is due either to the steric hindrance around the *N*-Boc carbonyl function or to the presence of an intramolecular hydrogen bond. Based on this consideration, a slightly modified synthetic scheme was envisaged that eventually led to the development of an efficient and unified synthesis of mauritines A (**5**), B (**6**), C (**7**), and F (**10**; Scheme 4). In a forward sense, cyclization of the linear dipeptide **16** by way of an intramolecular $\text{S}_{\text{N}}\text{Ar}$ reaction would provide first the corresponding macrocycle **15** and then **14** after reductive removal of the nitro group and hydrogenolysis of the *N*-benzyl



Scheme 4. Retrosynthetic analysis of mauritines A, B, C, and F, a unified strategy. Bn = benzyl.

group. Direct *N*-acylation of the proline unit of cyclophane **14** with the *N*-Boc-protected amino acid would provide **13**. Since the *N*-Boc function in compound **13** is sterically more accessible and less prone to intramolecular hydrogen bonding, its deprotection should be much easier than that of **11**. From **13**, mauritines A, B, and F would be readily accessible by coupling with the respective amino acid. The salient feature of the present strategy is its inherent convergence, since the required acyclic precursor **16** is an intact dipeptide available in only two steps from three available building blocks: **17**, **18**, and **19** (Scheme 4).

Synthesis of the 14-membered cyclophane: To determine whether the configuration of the benzylic hydroxy group exerts any influence on the macrocyclization and subsequent dehydration steps, which are required for the introduction of the corresponding enamide function, both diastereoisomers of **16** were synthesized as depicted in Scheme 5. Cou-



Scheme 5. Synthesis of the linear dipeptides (1*R*)-**16** and (1*S*)-**16**. a) *N*-Boc-L-phenylalanine (**18**), Et_3N , EDCI, HOBT, DMF, 98% yield for (1*R*)-**20**, 93% yield for (1*S*)-**20**; b) 1. HCl, CH_3CN , 2. (2*S*,3*S*)-*N*-benzyl-2-hydroxyproline (**19**), Et_3N , EDCI, HOBT, DMF, 78% yield for (1*R*)-**16**, 95% yield for (1*S*)-**16**. EDCI = 3-(3-dimethylaminopropyl)-1-ethylcarbodiimide, HOBT = 1-hydroxy-1*H*-benzotriazole, DMF = *N,N*-dimethylformamide.

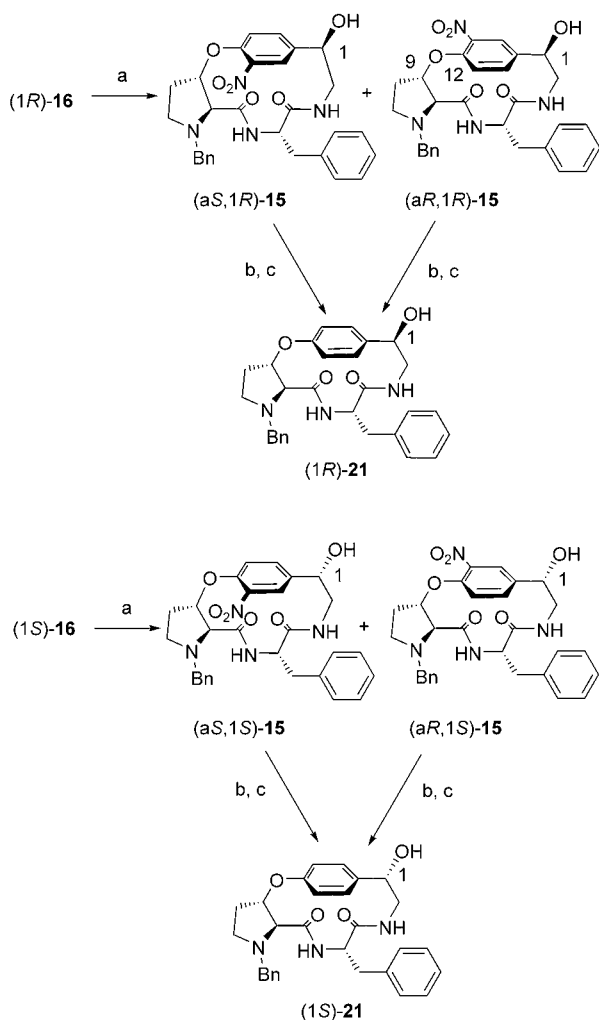
pling of (1*R*)-1-(4'-fluoro-3'-nitro)phenyl-2-amino-ethanol (1*R*)-**17**^[23] with *N*-Boc-L-phenylalanine (**18**) under classical conditions (EDCI, HOBT, DMF, room temperature) afforded (1*R*)-**20** in a 98% yield. Subsequent *N*-Boc deprotection (HCl, CH₃CN) followed by acylation with (2*S*,3*S*)-*N*-benzyl-2-hydroxyproline **19**^[24] afforded the cyclization precursor (1*R*)-**16** in a 78% yield. The same sequence applied to (1*S*)-**17** led to the formation of (1*S*)-**16** in 88% overall yield.

The key S_NAr-based cycloetherification of (1*R*)-**16** was performed in DMSO (concentration of substrate: 0.005 M) at 60 °C in the presence of TBAF and powdered 4 Å molecular sieves (Scheme 6). Under these optimized reaction conditions, the linear dipeptide (1*R*)-**16** cyclized smoothly to form the corresponding 14-membered paracyclophane in a 70% yield as a mixture of two separable atropisomers, (a*S*,1*R*)-**15** and (a*R*,1*R*)-**15**, in a ratio of 1:1.6. Atropisomer (a*S*,1*R*)-**15** was significantly more mobile on the thin-layer chromato-

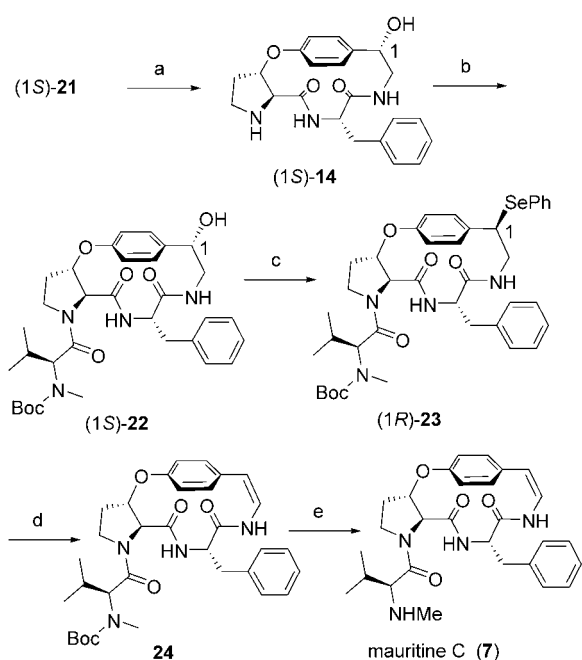
graph than its stereoisomer (a*R*,1*R*)-**15**. A strong NOE correlation observed between protons H9 and H12 for (a*R*,1*R*)-**15** was indicative of its configuration. Similarly, cyclization of (1*S*)-**16** under identical conditions proceeded efficiently to provide the paracyclophanes (a*S*,1*S*)-**15** and (a*R*,1*S*)-**15** in a 70% yield and with 1:1.4 atropoenantioselectivity (Scheme 6). These results showed that the S_NAr-based macrocyclization was independent from the configuration of the benzylic hydroxy group and thereby expanded further the synthetic utility of the method. The lack of atropodistereoselectivity was of no consequence as the planar chirality will disappear upon removal of the nitro group.

Reductive removal of the nitro group was carried out via the diazonium intermediate. The transformation was initially performed on (a*S*,1*S*)-**15** in two steps, involving a) reduction of nitro to aniline (SnCl₂, MeOH)^[25] and b) diazotization/dediazoniation with a modified Kornblum and Iffland procedure (NaNO₂, H₃PO₂, Cu₂O).^[26] Under these conditions, the desired macrocycle (1*S*)-**21** was obtained in a 43% yield. Interestingly, the intermediate aniline was obtained in much higher yield when the nitro group in **15** was subjected to catalytic hydrogenation (H₂, Pd/C, MeOH/EtOAc), instead of chemical reduction with stannous chloride.^[27] However, the aniline obtained by catalytic hydrogenation underwent deamination in only a 22% yield. Since complete removal of tin residue by liquid–liquid extraction is known to be very difficult, we hypothesized that trace amounts of tin contaminating the aniline obtained by SnCl₂ reduction might have a beneficial effect on the diazotization/dediazoniation sequence. To verify this hypothesis, the deamination of aniline obtained by hydrogenolysis was next carried out in the presence of SnCl₂·H₂O. To our delight, macrocycle (1*S*)-**21** was obtained in 70% overall yield. Application of these new conditions (Pd/C, H₂, MeOH/EtOAc, then NaNO₂, H₃PO₂, Cu₂O, SnCl₂·H₂O) to (a*S*,1*R*)-**15** and (a*R*,1*R*)-**15** afforded (1*R*)-**21** in an 80% yield (Scheme 6).

Total synthesis of mauritine C: The total synthesis of mauritine C is shown in Scheme 7. Hydrogenolysis of (1*S*)-**21** under standard conditions (Pd/C, MeOH, H₂) proceeded smoothly to provide (1*S*)-**14**. Subsequent acylation of the resulting secondary amine with *N*-Boc-*N*-methyl-L-valine under Carpino's conditions (HATU, DIPEA)^[28] afforded the fully functionalized cyclophane (1*S*)-**22** in a 71% yield over the two steps. The enamide function was introduced following the protocol of Joullié and co-workers. Thus, sequential mesylation and selenenylation (PhSeSePh, NaBH₄, EtOH) of (1*S*)-**22** furnished (1*R*)-**23**. The latter substitution reaction was hypothesized to proceed through an S_N2 mechanism. Indeed, as seen from the X-ray structure of mauritine A (**5**),^[20] the benzylic carbon is out of the plane defined by the aromatic ring due to the presence of severe ring strain. Consequently, stabilization of the possible carbocation intermediate resulting from the S_N1 mechanism is virtually nonexistent, a fact making the S_N2 mechanism more plausible. The same particular structural feature can also explain the stability of the benzylic alcohol under the hydroge-



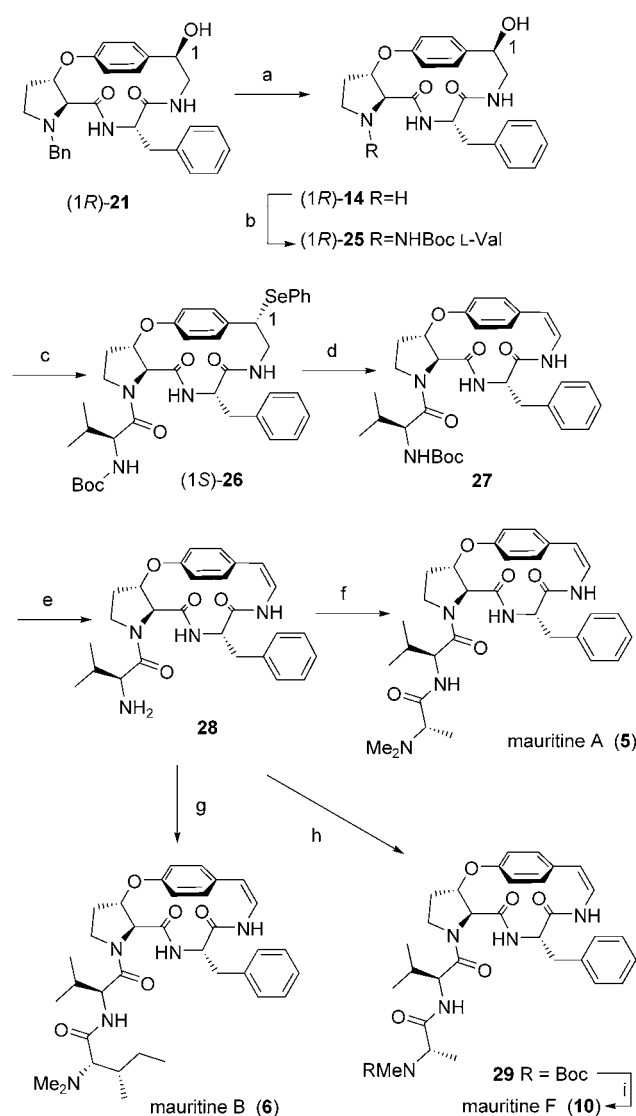
Scheme 6. S_NAr-based cycloetherification of (1*R*)-**16** and (1*S*)-**16**. a) TBAF, DMSO, powdered 4 Å molecular sieves, 60 °C, 70% yield, atropenantioselectivity of (a*S*,1*R*)-**15**/(a*R*,1*R*)-**15** = 1:1.6 and of (a*S*,1*S*)-**15**/(a*R*,1*S*)-**15** = 1:1.4; b) H₂, Pd/C, MeOH/EtOAc (1:1); c) NaNO₂, H₃PO₂, Cu₂O (0.1 equiv), SnCl₂ (0.2 equiv). TBAF = tetrabutylammonium fluoride, DMSO = dimethylsulfoxide.



Scheme 7. Synthesis of mauritine C (**7**). a) H_2 , Pd/C, MeOH, 82%; b) *N*-Boc-*N*-methyl-L-valine, HATU, DIEA, DMF, 87%; c) 1. MsCl, Et_3N , CH_2Cl_2 , 2. $(\text{PhSe})_2$, NaBH_4 , EtOH, 74%; d) 1. H_2O_2 , pyridine, CH_2Cl_2 , 2. benzene, 60°C, 48%; e) TFA, CH_2Cl_2 , 78%. HATU = *N*-[(dimethylamino)-1*H*-1,2,3-triazole[4,5-*b*]-pyridin-1-ylmethylene]-*N*-methylmethanaminium hexafluorophosphate, DIEA = *N,N*-diisopropylethylamine, Ms = mesyl = methanesulfonyl, TFA = trifluoroacetic acid.

nation conditions. Oxidation of selenide **(1R)-23** with hydrogen peroxide in dichloromethane afforded the corresponding selenoxide, which did not undergo spontaneous *syn*-elimination at room temperature. However, when a benzene solution of the selenoxide was heated to 60°C, smooth *syn*-elimination occurred to provide **24** in a 48% yield. As expected and in contrast to the *N*-Boc deprotection of compound **11** (Scheme 3), removal of the *N*-Boc function in **24** (TFA, CH_2Cl_2 , room temperature) proceeded uneventfully to provide mauritine C (**7**) in a 78% yield. It is noteworthy that the enamide function is stable under such mild acidic conditions.^[29]

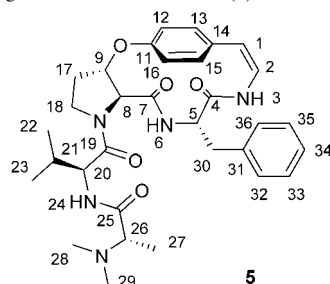
Total syntheses of mauritines A, B, and F: The synthesis of mauritines A (**5**), B (**6**), and F (**10**) was completed by starting from **(1R)-21** (Scheme 8). The proline *N*-benzyl group was first removed under hydrogenolysis conditions (Pd/C, H_2 , MeOH) and then *N*-Boc-L-valine was coupled (HATU, DIEA) to give **(1R)-25** in a 75% yield over two steps. Treatment of **(1R)-25** with mesyl chloride and triethylamine in dichloromethane afforded the corresponding mesylate, which was displaced by sodium phenyl selenide to give **(1S)-26** in a 87% yield. Oxidation with hydrogen peroxide gave the corresponding selenoxide, which underwent spontaneous *syn*-elimination at room temperature to afford the desired enamide (**27**) in a 60% yield. It has previously been reported that the two diastereomeric selenides behave differently



Scheme 8. Synthesis of mauritines A (**5**), B (**6**), and F (**10**). a) H_2 , Pd/C, MeOH, 78%; b) *N*-Boc-L-valine, HATU, DIEA, DMF, 96%; c) 1. MsCl, Et_3N , CH_2Cl_2 , 2. $(\text{PhSe})_2$, NaBH_4 , EtOH, 87%; d) H_2O_2 , pyridine, CH_2Cl_2 , 60%; e) TFA, CH_2Cl_2 ; f) *N,N*-dimethyl-L-alanine, HATU, DIEA, DMF, 59%; g) *N,N*-dimethyl-L-isoleucine, HATU, DIEA, DMF, 61%; h) *N*-Boc-*N*-methyl-L-alanine, HATU, DIEA, DMF, 79%; i) TFA, CH_2Cl_2 , 71%.

under the oxidation/elimination conditions.^[7h,8c,8f,8h] Our results unambiguously established that the selenide **(1S)-26**, which arises from the *R*-configured secondary alcohol **(1R)-14**, undergoes *syn*-elimination much more readily than a similar compound with the opposite configuration, **(1R)-23**, upon conversion into the corresponding selenoxide.

Removal of the *N*-Boc protection in **27** (TFA, CH_2Cl_2 , room temperature) provided **28** in excellent yield. Coupling of (**28**) with *N,N*-dimethyl-L-alanine or *N,N*-dimethyl-(2*S*,3*S*)-isoleucine^[30] afforded mauritine A (**5**) and mauritine B (**6**) in 59 and 61% yields, respectively. Alternatively, coupling of **28** with *N*-Boc-*N*-methyl-L-alanine followed by

Table 1. ^1H NMR and ^{13}C NMR assignments for mauritine A (**5**).^[a]

$\delta(^1\text{H})$ [ppm]	Multiplicity	No. of H atoms	Assignment	J [Hz]	$\delta(^{13}\text{C})$ [ppm]	Assignment
7.65	d	1H	H ₂₄	8.8	174.5	C ₂₅
7.15–7.26	m	6H	H ₁₆ , H _{32–36}		171.5	C ₁₉
6.99	dd	1H	H ₁₅	8.4, 1.8	170.3	C ₇
6.96	dd	1H	H ₁₂	8.1, 2.2	166.5	C ₄
6.88	dd	1H	H ₁₃	8.1, 1.8	157.3	C ₁₁
6.63	dd	1H	H ₂	10.3, 7.7	135.6	C ₃₁
6.35	d	1H	H ₆	8.4	132.4	C ₁₄
6.26	d	1H	H ₃	10.3	132.3	C ₁₅
6.21	d	1H	H ₁	7.7	130.2	C ₁₃
5.42	dt	1H	H ₉	7.0, 5.9	130.0	C ₃₂ , C ₃₆
4.52	m	1H	H ₅		128.4	C ₃₃ , C ₃₅
4.43	dd	1H	H ₂₀	8.8, 6.6	127.0	C ₃₄
4.18	m	1H	H ₁₈		125.4	C ₂
4.09	d	1H	H ₈	5.9	122.6	C ₁₂
3.41	m	1H	H _{18'}		122.4	C ₁₆
3.32	dd	1H	H ₃₀	14.0, 4.0	114.7	C ₁
2.93	q	1H	H ₂₆	7.0	83.6	C ₉
2.60	dd	1H	H _{30'}	14.0, 5.1	64.9	C ₂₆
2.51	ddd	1H	H ₁₇	12.1, 7.0, 5.5	64.1	C ₈
2.25	s	6H	H ₂₈ , H ₂₉		54.6	C ₂₀
2.13	m	1H	H _{17'}		54.0	C ₅
1.90	m	1H	H ₂₁		46.4	C ₁₈
1.18	d	3H	H ₂₇	7.0	42.4	C ₂₈ , C ₂₉
0.79	d	3H	H ₂₂ , H ₂₃	6.6	36.0	C ₃₀
0.77	d	3H	H ₂₂ , H ₂₃	6.6	31.9	C ₁₇
					31.2	C ₂₁
					19.2	C ₂₂ ^[b]
					17.9	C ₂₃ ^[b]
					12.1	C ₂₇

[a] The NMR spectra were recorded in CDCl_3 on a Bruker Avance-600 (600 MHz) spectrometer. [b] The assignment of these two signals is interchangeable.

removal of the *N*-Boc protection provided mauritine F (**10**) in 56 % overall yield.^[31]

Preliminary results of the biological screening against a variety of fungal strains were disappointing, since none of these natural products displayed exploitable antifungal activities.

Spectroscopic analysis of mauritines A, B, C, and F: The NMR data reported for mauritines A, B, C, and F were incomplete.^[19] Therefore, COSY, HMQC, HMBC, and NOESY spectra were recorded to allow the assignment of each proton and carbon NMR spectroscopy signal. The complete assignment is listed in Tables 1–4 for these natural products. This detailed NMR study also fully established the structure of our synthetic compounds.

Conclusion

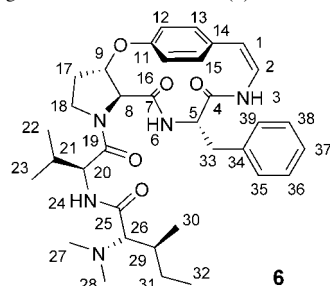
In conclusion, we have achieved the total syntheses of mauritines A (**5**), B (**6**), C (**7**), and F (**10**) in an average overall yield of about 10%. Our approach featured a key intramolecular $\text{S}_{\text{N}}\text{Ar}$ cycloetherification for the construction of the 14-membered paracyclophane. Since this macrocyclization was performed on an intact peptidic precursor, the synthesis is very convergent. Furthermore, the synthesis was divergent at a late stage that allowed us to develop a unified strategy for these natural products. Additionally, new efficient reaction conditions for the removal of the nitro group were developed in the course of this study. We also demonstrated that the deprotection problem encountered in our previous synthesis can be avoided by incorporating an additional amino acid at the N terminus. Finally, we have assigned, for the first time, all proton and carbon NMR spectroscopy signals of mauritines A (**5**), B (**6**), C (**7**), and F (**10**) in detailed studies.

Experimental Section

Compounds (aS,1R)-15 and (aR,1R)-15

15: A suspension of TBAF (5.45 mL, 1.0 M in THF) and powdered molecular sieves (3 Å, 200.0 mg, pre-dried under vacuum) in distilled DMSO (360.0 mL) was stirred at room temperature for 4 h. A solution of compound (1R)-16 (1.0 g, 1.82 mmol) in DMSO was then added in one portion. After being stirred at 60 °C for 20 h and then cooled to room temperature, the reaction mixture was diluted with water, filtered through celite, and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated under vacuum. The resulting crude oil was purified by flash chromatography (silica gel, heptanes/EtOAc (1:1)→EtOAc/MeOH (30:1)) to afford compounds (aS,1R)-15 (262 mg) and (aR,1R)-15 (415 mg) in a total yield of 70%. (aS,1R)-15: Yellow solid; m.p. 98–100 °C; $[\alpha]_{\text{D}}^{25} = -155$ ($c = 0.18$ in CHCl_3); ^1H NMR (300 MHz, CDCl_3): $\delta = 8.24$ (d, $J = 2.0$ Hz, 1H; CH arom), 7.01–7.26 (m, 12H; CH arom), 6.57 (m, 1H; NH), 5.75 (d, $J = 9.1$ Hz, 1H; NH), 5.14 (brs, 1H; CH), 4.89 (m, 1H; CH), 4.36 (ddd, $J = 14.4, 10.8, 4.0$ Hz, 1H; CH₂), 4.20 (q, $J = 8.0$ Hz, 1H; CH), 3.37 (d, $J = 12.8$ Hz, 1H; CH₂), 3.02 (d, $J = 12.8$ Hz, 1H; CH₂), 2.89 (m, 1H; CH₂), 2.78 (dd, $J = 13.4, 8.6$ Hz, 1H; CH₂), 2.70 (d, $J = 6.8$ Hz, 1H; CH), 2.67 (d, $J = 14.4$ Hz, 1H; CH₂), 2.59 (dd, $J = 13.4, 7.0$ Hz, 1H; CH₂), 2.43 (m, 1H; CH₂), 2.20 (m, 1H; CH₂), 1.99 ppm (m, 1H; CH₂); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 170.8, 169.5, 150.4, 141.6, 138.5, 137.3, 135.8, 132.0, 129.2$ (2C), 129.0 (2C),

Table 2. ^1H NMR and ^{13}C NMR assignments for mauritine B (**6**).^[a]



$\delta(^1\text{H})$ [ppm]	Multiplicity	No. of H atoms	Assignment	J [Hz]	$\delta(^{13}\text{C})$ [ppm]	Assignment
7.23–7.32	m	6H	H ₁₆ , H _{35–39}		172.4	C ₂₅
7.08	d	1H	H ₂₄	8.4	171.5	C ₁₉
7.04	dd	1H	H ₁₅	8.4, 1.9	170.6	C ₇
7.02	dd	1H	H ₁₂	8.2, 2.5	166.4	C ₄
6.94	dd	1H	H ₁₃	8.2, 1.9	157.4	C ₁₁
6.68	dd	1H	H ₂	10.4, 7.8	135.6	C ₃₄
6.33	d	1H	H ₆	8.5	132.4	C ₁₄
6.31	d	1H	H ₃	10.4	132.3	C ₁₅
6.26	d	1H	H ₁	7.8	130.3	C ₁₃
5.47	dt	1H	H ₉	6.3, 3.7	130.2	C ₃₅ , C ₃₉
4.58	m	1H	H ₅		128.4	C ₃₆ , C ₃₈
4.49	dd	1H	H ₂₀	8.4, 6.7	127.0	C ₃₇
4.24	m	1H	H ₁₈		125.4	C ₂
4.11	d	1H	H ₈	5.8	122.5	C ₁₂
3.47	m	1H	H _{18'}		122.2	C ₁₆
3.39	dd	1H	H ₃₃	14.0, 4.1	114.7	C ₁
2.64	dd	1H	H _{33'}	14.0, 5.3	83.6	C ₉
2.60	d	1H	H ₂₆	5.1	74.8	C ₂₆
2.57	m	1H	H ₁₇		64.3	C ₈
2.31	s	6H	H ₂₇ , H ₂₈		54.9	C ₂₀
2.22	m	1H	H _{17'}		54.0	C ₅
1.94	m	1H	H ₂₁		46.3	C ₁₈
1.83	m	1H	H ₂₉		43.4	C ₂₇ , C ₂₈
1.55	m	1H	H ₃₁		35.9	C ₃₃
1.24	m	1H	H _{31'}		34.6	C ₂₉
0.96	t	3H	H ₃₂	7.4	31.9	C ₁₇
0.94	d	3H	H ₃₀	6.7	30.8	C ₂₁
0.87	d	3H	H ₂₂ ^[b]	6.7	27.2	C ₃₁
0.86	d	3H	H ₂₃ ^[b]	6.7	19.4	C ₂₂ ^[c]
					18.1	C ₂₃ ^[c]
					14.6	C ₃₀
					12.2	C ₃₂

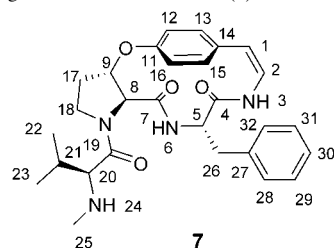
[a] The NMR spectra were recorded in CDCl_3 on a Bruker Avance-600 (600 MHz) spectrometer. [b] The assignment of these two signals is interchangeable. [c] The assignment of these two signals is interchangeable.

128.5 (2C), 128.3 (2C), 127.4, 127.1, 125.1, 124.0, 85.4, 74.8, 70.7, 58.0, 54.7, 51.7, 45.9, 42.8, 29.3 ppm; IR (CHCl_3): $\bar{\nu}$ = 3300, 3021, 1669, 1533, 1347, 1217, 1096 cm^{-1} ; high-resolution MS (CI): m/z calcd: 531.2240 [$M+H$]⁺; found: 531.2200. (a*R*,1*R*)-**15**: Yellow solid; m.p. 142 °C; $[\alpha]_D^{25}$ = –60 (c = 0.27 in CHCl_3); ^1H NMR (300 MHz, CDCl_3): δ = 7.75 (dd, J = 8.7, 1.9 Hz, 1H; CH arom), 7.45 (d, J = 1.9 Hz, 1H; CH arom), 6.97–7.32 (m, 11H; CH arom), 6.55 (m, 1H; NH), 6.24 (d, J = 9.1 Hz, 1H; NH), 5.26 (m, 1H; CH), 5.09 (d, J = 3.6 Hz, 1H; CH), 4.23–4.38 (m, 2H; CH, CH_2), 3.32 (d, J = 12.7 Hz, 1H; CH_2), 3.01 (d, J = 12.7 Hz, 1H; CH_2), 2.94 (td, J = 9.0, 3.5 Hz, 1H; CH_2), 2.88 (d, J = 7.0 Hz, 1H; CH), 2.81 (d, J = 14.0 Hz, 1H; CH_2), 2.80 (dd, J = 13.5, 7.4 Hz, 1H; CH_2), 2.67 (dd, J = 13.5, 7.7 Hz, 1H; CH_2), 2.40 (m, 1H; CH_2), 2.28 (m, 1H; CH_2), 1.90–2.12 ppm (m, 1H; CH_2); ^{13}C NMR (75 MHz, CDCl_3): δ = 170.9, 170.3, 149.9, 141.5, 137.1, 136.4, 135.7, 130.3, 129.5 (2C), 129.0 (2C), 128.5 (2C), 128.3 (2C), 127.6, 127.1, 122.7, 118.5, 82.5, 74.3, 71.3, 57.8, 54.6, 50.6, 46.8, 39.7, 28.4 ppm; IR (CHCl_3): $\bar{\nu}$ = 3387, 3301, 3021, 1670, 1534, 1507, 1361,

1220 cm^{-1} ; high-resolution MS (CI): m/z calcd: 531.2244 [$M+H$]⁺; found: 531.2235.

Compounds (a*S*,1*S*)-15** and (a*R*,1*S*)-**15**:** The cyclization of (1*S*)-**16** (1.16 mmol) was performed under identical conditions to those described for the synthesis of (1*R*)-**15**. The crude product was purified by flash chromatography (silica gel, heptanes/EtOAc (1:3) → $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20:1)) to afford compounds (a*S*,1*S*)-**15** (179 mg) and (a*R*,1*S*)-**15** (251 mg) in a total yield of 70%. (a*S*,1*S*)-**15**: Yellow solid; m.p. 126–128 °C; $[\alpha]_D^{25}$ = –151 (c = 0.15 in CHCl_3); ^1H NMR (300 MHz, CDCl_3): δ = 7.77 (dd, J = 8.5, 2.1 Hz, 1H; CH arom), 7.71 (d, J = 2.1 Hz, 1H; CH arom), 6.98–7.26 (m, 10H; CH arom), 6.83 (m, 2H; CH arom, NH), 5.52 (d, J = 9.3 Hz, 1H; NH), 5.09–5.30 (m, 2H; CH, OH), 4.89 (m, 1H; CH), 4.46 (td, J = 9.3, 7.1 Hz, 1H; CH), 3.86 (dd, J = 14.8, 5.4 Hz, 1H; CH_2), 3.48 (td, J = 14.8, 6.1 Hz, 1H; CH_2), 2.62–2.95 (m, 6H; CH, CH_2), 2.30–2.51 (m, 2H; CH_2), 2.01 ppm (m, 1H; CH_2); ^{13}C NMR (62.5 MHz, CDCl_3): δ = 172.1, 170.1, 150.7, 141.7, 139.3, 137.6, 135.5, 132.0, 129.0, 128.8 (4C), 128.2 (4C), 127.4, 126.0, 124.0, 86.3, 74.5, 71.9, 57.9, 53.3, 52.1, 49.1, 36.6, 29.8 ppm; IR (CHCl_3): $\bar{\nu}$ = 3625, 3420, 3011, 2976, 1928, 1667, 1534, 1495, 1454, 1391, 1345, 1249, 1206 cm^{-1} ; high-resolution MS (CI): m/z calcd: 531.2244 [$M+H$]⁺; found: 531.2243. (a*R*,1*S*)-**15**: Yellow solid; m.p. 116–118 °C; $[\alpha]_D^{25}$ = +13 (c = 0.2 in CHCl_3); ^1H NMR (250 MHz, CDCl_3): δ = 7.85 (d, J = 2.1 Hz, 1H; CH arom), 6.89–7.32 (m, 12H; CH arom), 6.08 (t, J = 5.8 Hz, 1H; NH), 5.94 (d, J = 9.1 Hz, 1H; NH), 5.13 (m, 1H; CH), 4.96 (m, 1H; CH), 4.54 (m, 1H; OH), 4.39 (td, J = 9.1, 7.0 Hz, 1H; CH), 3.91 (ddd, J = 14.4, 7.0, 4.1 Hz, 1H; CH_2), 3.33 (dt, J = 14.4, 5.6 Hz, 1H; CH_2), 2.71–2.90 (m, 5H; CH_2), 2.67 (d, J = 7.0 Hz, 1H; CH), 2.26–2.48 (m, 2H; CH_2), 2.00 ppm (m, 1H; CH_2); ^{13}C NMR (62.5 MHz, CDCl_3): δ = 171.7, 170.7, 144.1, 138.0, 137.5, 135.8, 131.4, 129.4, 129.2, 128.8 (4C), 128.2 (4C), 127.3, 121.9, 121.6, 86.1, 74.7, 72.1, 57.6, 53.7, 51.3, 48.1, 37.6, 29.8 ppm; IR (CHCl_3): $\bar{\nu}$ = 3404, 3024, 1669, 1534, 1507, 1498, 1363, 1227, 1206 cm^{-1} ; high-resolution MS (CI): m/z calcd: 531.2244 [$M+H$]⁺; found: 531.2264.

Compound (1*S*)-21**:** Compound (a*S*,1*S*)-**15** (51.2 mg, 0.097 mmol) was dissolved in solvent (AcOEt/MeOH (1:1); 1.5 mL), then Pd/C (10%, 5 mg) was added. The suspension was purged three times with argon and then three times with hydrogen. The reaction mixture was stirred vigorously under a hydrogen atmosphere for 2.5 h at room temperature, then filtered through celite and concentrated under vacuum. The resulting crude residue was dissolved in solvent (THF/water (3:1); 1 mL) and cooled to 0 °C. An aqueous solution of H_3PO_4 (70 μL , 50%, 0.673 mmol) was added; this was followed by successive addition of Cu_2O (1.4 mg, 0.01 mmol), SnCl_2 (3.6 mg, 0.019 mmol), and NaNO_2 (20 mg, 0.29 mmol). The reaction mixture was stirred at 0 °C for 3 h, then at room temperature for 1 h. After addition of aqueous NaOH (5%), the solution was extracted with EtOAc. The organic layer was washed with brine, dried over

Table 3. ^1H NMR and ^{13}C NMR assignments for mauritine C (**7**).^[a]

$\delta(^1\text{H})$ [ppm]	Multiplicity	No. of H atoms	Assignment	J [Hz]	$\delta(^{13}\text{C})$ [ppm]	Assignment
7.24–7.27	m	5H	H ₁₆ , H _{28–29} , H _{31–32}		174.2	C ₁₉
7.21	m	1H	H ₃₀		170.3	C ₇
7.06	dd	1H	H ₁₅	8.4, 2.1	166.6	C ₄
7.04	dd	1H	H ₁₂	8.2, 2.5	157.4	C ₁₁
6.96	dd	1H	H ₁₃	8.2, 2.1	135.6	C ₂₇
6.68	dd	1H	H ₂	10.5, 7.8	132.6	C ₁₄
6.57	d	1H	H ₆	8.4	132.4	C ₁₅
6.33	d	1H	H ₃	10.5	130.3	C ₁₃
6.26	d	1H	H ₁	7.8	129.9	C ₂₈ , C ₃₂
5.48	ddd	1H	H ₉	12.6, 7.0, 5.5	128.5	C ₂₉ , C ₃₁
4.56	m	1H	H ₅		127.0	C ₃₀
4.24	d	1H	H ₈	5.5	125.5	C ₂
3.94	dd	1H	H ₁₈	11.1, 8.2	122.7	C ₁₂
3.40	ddd	1H	H _{18'}	12.9, 11.1, 5.3	122.6	C ₁₆
3.31	dd	1H	H ₂₆	14.2, 4.5	114.7	C ₁
3.04	d	1H	H ₂₀	6.4	83.7	C ₉
2.69	dd	1H	H _{26'}	14.2, 5.2	66.4	C ₂₀
2.57	ddd	1H	H ₁₇	12.2, 7.1, 5.3	63.8	C ₈
2.29–2.32	m + s	4H	H ₂₄ , H ₂₅		54.0	C ₅
2.11	m	1H	H _{17'}		46.1	C ₁₈
1.74	m	1H	H ₂₁		36.1	C ₂₆
0.85	d	3H	H ₂₂ ^[b]	6.7	35.2	C ₂₅
0.82	d	3H	H ₂₃ ^[b]	6.7	32.1	C ₁₇
					31.7	C ₂₁
					19.4	C ₂₂ ^[c]
					18.4	C ₂₃ ^[c]

[a] The NMR spectra were recorded in CDCl_3 on a Bruker Avance-600 (600 MHz) spectrometer. [b] The assignment of these two signals is interchangeable. [c] The assignment of these two signals is interchangeable.

Na_2SO_4 , filtered, and concentrated under vacuum. The crude residue was purified by preparative TLC (silica gel, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (20:1)) to afford compound (1S)-**21** (32.6 mg, 70% yield). Compound (aR,1S)-**15** is similarly transformed into (1S)-**21**. White solid; m.p. 248°C; $[\alpha]_{\text{D}}^{25} = -77.6$ ($c = 0.12$ in CHCl_3); ^1H NMR (250 MHz, CDCl_3): $\delta = 7.58$ (dd, $J = 8.3$, 2.2 Hz, 1H; CH arom), 7.08–7.30 (m, 10H; CH arom), 7.05 (dd, $J = 8.3$, 2.6 Hz, 1H; CH arom), 6.98 (dd, $J = 8.5$, 2.6 Hz, 1H; CH arom), 6.91 (dd, $J = 8.5$, 2.2 Hz, 1H; CH arom), 5.60 (dd, $J = 8.4$, 4.2 Hz, 1H; CH), 5.50 (d, $J = 8.7$ Hz, 1H; NH), 5.13 (m, 1H; CH), 4.85 (t, $J = 6.0$ Hz, 1H; NH), 4.31 (q, $J = 8.3$ Hz, 1H; CH), 3.92 (ddd, $J = 14.2$, 8.4, 5.9 Hz, 1H; CH_2), 3.28 (ddd, $J = 14.2$, 6.2, 4.2 Hz, 1H; CH_2), 3.18 (d, $J = 12.6$ Hz, 1H; CH_2), 2.87–2.94 (m + d, $J = 12.6$ Hz, 2H; CH_2), 2.83 (dd, $J = 13.8$, 7.8 Hz, 1H; CH_2), 2.64 (dd, $J = 13.8$, 8.0 Hz, 1H; CH_2), 2.59 (d, $J = 6.5$ Hz, 1H; CH), 2.31–2.45 (m, 2H; CH_2), 1.88–1.97 ppm (m, 1H; CH_2); ^{13}C NMR (62.5 MHz, CDCl_3): $\delta = 171.5$, 170.4, 157.5, 137.5, 136.4, 135.9, 129.2, 128.8 (2C), 128.6 (2C), 128.2 (4C), 127.3, 127.2, 126.9, 121.63, 119.1, 84.6, 75.9, 72.9, 57.8, 54.4, 51.8, 47.8, 38.4, 29.8 ppm; IR (CHCl_3): $\tilde{\nu} = 3415$, 1667, 1606, 1508 cm^{-1} ; high-resolution MS (CI): m/z calcd: 486.2392 [$M+H$]⁺; found: 486.2364.

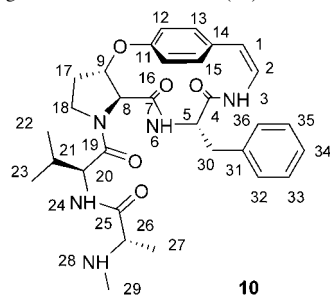
Compound (1R)-21: By the same method as that described for the synthesis of (1S)-**21**, (aS,1R)-**15** and (aR,1R)-**15** were converted into (1R)-**21** in 80 and 85% yields, respectively. White solid; m.p. 112°C; $[\alpha]_{\text{D}}^{25} = -35$ ($c = 0.15$ in CHCl_3); ^1H NMR (300 MHz, CDCl_3): $\delta = 7.48$ (m, 1H; CH arom), 7.05–7.32 (m, 11H; CH arom), 7.00 (dd, $J = 8.3$, 2.1 Hz, 1H; CH arom), 6.82 (dd, $J = 8.3$, 2.5 Hz, 1H; CH arom), 5.90 (m, 1H; NH), 5.76

(d, $J = 8.5$ Hz, 1H; NH), 5.25 (m, 1H; CH), 5.10 (d, $J = 3.5$ Hz, 1H; CH), 4.16–4.29 (m, 2H; CH, CH_2), 3.48 (d, $J = 12.0$ Hz, 1H; CH_2), 3.03 (d, $J = 12.0$ Hz, 1H; CH_2), 2.94 (m, 1H; CH_2), 2.85 (brd, $J = 13.8$ Hz, 1H; CH_2), 2.75 (dd, $J = 13.3$, 8.4 Hz, 1H; CH_2), 2.66 (dd, $J = 13.3$, 6.7 Hz, 1H; CH_2), 2.55 (d, $J = 6.7$, 1H; CH), 2.28–2.43 (m, 2H; CH_2), 1.84–1.90 ppm (m, 1H; CH_2); ^{13}C NMR (62.5 MHz, CDCl_3): $\delta = 170.9$, 170.7, 157.4, 137.6, 136.1, 135.7, 129.7 (2C), 129.1 (2C), 128.3 (4C), 128.1, 127.3 (2C), 126.9, 119.5, 116.5, 81.1, 75.8, 72.1, 57.8, 54.7, 51.0, 46.9, 40.0, 29.0 ppm; IR (CHCl_3): $\tilde{\nu} = 3020$, 1669, 1510, 1211, 1208 cm^{-1} ; high-resolution MS (CI): m/z calcd: 486.2392 [$M+H$]⁺; found: 486.2396.

Compound (1S)-14: A suspension of compound (1S)-**21** (331 mg, 0.682 mmol) and Pd/C (10%, 165 mg) in dry MeOH (7.3 mL) was purged three times with argon and hydrogen, successively. The reaction mixture was stirred at room temperature for 24 h. The purge processes was repeated twice and the reaction mixture was stirred for an additional 48 h at room temperature. The reaction mixture was filtered through celite and concentrated under vacuum. The crude residue was purified by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (50:1→20:1)) to afford compound (1S)-**14** (220 mg, 82% yield). White solid; m.p. > 250°C; $[\alpha]_{\text{D}}^{25} = +20.2$ ($c = 0.23$ in MeOH); ^1H NMR (300 MHz, CD_3OD): $\delta = 7.34$ (dd, $J = 8.8$, 2.1 Hz, 1H; CH arom), 7.07–7.24 (m, 5H; CH arom), 6.89–7.00 (m, 3H; CH arom), 5.05 (dd, $J = 16.2$, 8.1 Hz, 1H; CH), 4.56 (dd, $J = 10.2$, 6.8 Hz, 1H; CH_2), 4.04 (dd, $J = 9.4$, 6.0 Hz, 1H; CH), 3.79 (dd, $J = 13.0$, 10.0 Hz, 1H; CH_2), 3.27 (m, 1H; CH), 3.14–3.22 (m, 1H; CH_2), 2.97–3.07 (m + dd, $J = 12.6$, 6.2 Hz, 2H; CH, CH_2), 2.74 (dd, $J = 13.1$, 9.6 Hz, 1H; CH_2), 2.61 (dd, $J = 13.1$, 5.6 Hz, 1H; CH_2), 2.38–2.49 (m, 1H; CH_2), 1.96–2.09 ppm (m, 1H; CH_2); ^{13}C NMR (62.5 MHz, CD_3OD): $\delta = 172.5$, 171.7, 159.2, 138.0, 137.6, 131.2, 130.3 (2C), 129.5 (2C), 128.0, 127.8, 122.0, 117.5, 84.4, 73.9, 68.1, 56.7, 46.4, 45.1, 40.3, 32.9 ppm; IR (KBr): $\tilde{\nu} = 3404$, 3296, 1642, 1545, 1437, 1374, 1281, 1224, 1074, 1033 cm^{-1} ; high-resolution MS (ES^+): m/z calcd: 396.1923 [$M+H$]⁺; found: 396.1848.

Compound (1S)-22: *N*-Boc-*N*-methyl-L-valine (143.0 mg, 0.62 mmol), DIEA (450.0 μL , 2.58 mmol), and HATU (303.0 mg, 0.77 mmol) were successively added to a solution of (1S)-**14** (204 mg, 0.516 mmol) in dry DMF (7.0 mL) at 0°C. The reaction mixture was stirred at room temperature for 17 h, then treated with a solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated under vacuum. The crude residue was purified by flash chromatography (silica gel, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (50:1→20:1)) to afford compound (1S)-**22** (274 mg, 87% yield). White solid; m.p. 150–152°C; $[\alpha]_{\text{D}}^{25} = -149.8$ ($c = 0.35$ in CHCl_3); ^1H NMR (300 MHz, CDCl_3): mixture of two rotamers (80:20): $\delta = 7.49$ (m, 1H; CH arom), 6.98–7.24 (m, 7H; CH arom), 6.85 (m, 1H; CH arom), 6.02 (d, $J = 8.7$ Hz, 0.8H; NH), 6.00 (d, $J = 8.7$ Hz, 0.2H; NH), 5.46 (m, 1H; CH), 5.15 (m, 1H; CH), 4.75 (t, $J = 6.0$ Hz, 1H; NH), 4.45 (d, $J = 10.9$ Hz, 0.8H; CH), 4.31 (m, 1H; CH_2), 4.21 (d, $J = 10.9$ Hz, 0.2H; CH), 3.99–4.09 (m, 1H; CH), 3.93 (d, $J = 6.6$ Hz, 1H; CH), 3.76–3.88 (m, 1H; CH_2), 3.49–3.60 (m, 1H;

Table 4. ^1H NMR and ^{13}C NMR assignments for mauritine F (**10**).^[a]



$\delta(^1\text{H})$ [ppm]	Multiplicity	No. of H atoms	Assignment	J [Hz]	$\delta(^{13}\text{C})$ [ppm]	Assignment
7.74	d	1H	H ₂₄	8.9	175.1	C ₂₅
7.20–7.30	m	6H	H ₁₆ , H _{32–36}		171.4	C ₁₉
7.03	d	1H	H ₁₅	8.4	170.4	C ₇
7.00	dd	1H	H ₁₂	8.1, 2.1	166.4	C ₄
6.92	d	1H	H ₁₃	8.1	157.4	C ₁₁
6.67	dd	1H	H ₂	10.4, 7.8	135.6	C ₃₁
6.37	d	1H	H ₆	8.4	132.5	C ₁₄
6.30	d	1H	H ₃	10.4	132.4	C ₁₅
6.25	d	1H	H ₁	7.8	130.3	C ₁₃
5.47	dt	1H	H ₉	10.1, 6.7	130.1	C ₃₂ , C ₃₆
4.53–4.59	m	2H	H ₅ , H ₂₀		128.5	C ₃₃ , C ₃₅
4.18	m	1H	H ₁₈		127.1	C ₃₄
4.12	d	1H	H ₈	5.7	125.4	C ₂
3.45	m	1H	H ₁₈		122.6	C ₁₂
3.38	dd	1H	H ₃₀	14.1, 3.9	122.4	C ₁₆
3.09	q	1H	H ₂₆	6.9	114.7	C ₁
2.64	dd	1H	H ₃₀	14.1, 5.3	83.6	C ₉
2.55	m	1H	H ₁₇		64.2	C ₈
2.46	s	3H	H ₂₉		60.5	C ₂₆
2.16	m	1H	H ₁₇		54.3	C ₂₀
1.95	m	1H	H ₂₁		54.0	C ₅
1.32	d	3H	H ₂₇	6.9	46.4	C ₁₈
0.83	d	3H	H ₂₂ ^[b]	6.8	36.0	C ₃₀
0.81	d	3H	H ₂₃ ^[b]	6.8	35.2	C ₂₉
					31.9	C ₁₇
					31.2	C ₂₁
					19.9	C ₂₇
					19.2	C ₂₂ ^[c]
					17.6	C ₂₃ ^[c]

[a] The NMR spectra were recorded in CDCl_3 on the Bruker Avance-600 (600 MHz) spectrometer. [b] The assignment of these two signals is interchangeable. [c] The assignment of these two signals is interchangeable.

CH_2), 3.18–3.26 (m, 1H; CH_2), 2.91 (dd, $J=13.4$, 10.2 Hz, 1H; CH_2), 2.81 (s, 3H; CH_3), 2.71 (dd, $J=13.4$, 4.5 Hz, 1H; CH_2), 2.45–2.54 (m, 1H; CH_2), 2.07–2.22 (m, 2H; CH, CH_2), 1.48 (s, 1.8H; CH_3), 1.46 (s, 7.2H; CH_3), 0.81 (d, $J=6.6$ Hz, 3H; CH_3), 0.75 ppm (d, $J=6.6$ Hz, 3H; CH_3); ^{13}C NMR (75 MHz, CDCl_3 ; mixture of two rotamers): $\delta=171.2$, 171.1, 170.4, 169.5, 157.5, 156.4, 137.1, 136.6, 129.1, 128.8, 128.4, 127.2, 127.0, 126.7, 121.6, 118.8, 118.5, 83.4, 83.1, 80.5, 80.1, 72.7, 65.7, 65.6, 61.5, 60.0, 55.7, 55.5, 47.2, 45.6, 44.9, 38.2, 31.6, 31.4, 29.6, 29.1, 28.5, 28.4, 27.8, 19.2, 18.9, 18.5, 18.4 ppm; IR (CHCl_3): $\tilde{\nu}=3416$, 3025, 3016, 2966, 2934, 1672, 1510, 1441, 1383, 1368, 1154 cm^{-1} ; high-resolution MS (ES^+): m/z calcd: 631.3108 [$M+\text{Na}$] $^+$; found: 631.3106.

Compound (1R)-23: Et_3N (82.0 μL , 0.593 mmol) and MsCl (31.0 μL , 0.4 mmol) were added to a solution of compound (1S)-22 (60.0 mg, 99.0 μmol) in dry CH_2Cl_2 (5.0 mL) cooled to -15°C . The reaction mixture was stirred for 1 h, then concentrated under vacuum to yield the mesylated compound as a yellow solid. In a separate flask, PhSeSePh (93.0 mg, 0.297 mmol) was dissolved in dry EtOH (2 mL), and NaBH_4 (34.0 mg, 0.89 mmol) was added at 0°C . The resulting suspension was stirred at 0°C until the yellow solution became colorless. The EtOH so-

lution (2.0 mL) of mesylated compound was next added dropwise (very slowly) at 0°C to the solution of PhSeNa . The reaction mixture was stirred at 80°C for 2 h, then cooled at room temperature and concentrated under vacuum. Water was added and the mixture was extracted with EtOAc . The organic layer was washed with brine, dried over Na_2SO_4 , filtered, and concentrated under vacuum. The crude solid was purified by preparative TLC (silica gel, heptanes/ EtOAc (1:2)) to afford compound (1R)-23 (55 mg, 74% yield). White solid; $[\alpha]_D=-44.0$ ($c=0.25$ in CHCl_3); ^1H NMR (300 MHz, CDCl_3 ; mixture of two rotamers (70:30)): $\delta=7.45$ (m, 2H; CH arom), 7.29 (m, 1H; CH arom), 7.00–7.21 (m, 8H; CH arom), 6.88 (m, 2H; CH arom), 6.80 (m, 1H; CH arom), 5.87 (d, $J=8.7$ Hz, 1H; NH), 5.12 (m, 1H; CH), 4.55 (m, 1H; NH), 4.41 (d, $J=11.1$ Hz, 1H; CH), 4.14–4.26 (m, 2H; CH, CH_2), 3.91 (dd, $J=12.2$, 5.6 Hz, 1H; CH_2), 3.72–3.79 (m+d, $J=6.8$ Hz, 2H; CH), 3.53 (m, 1H; CH_2), 2.97 (dd, $J=12.2$, 5.8 Hz, 1H; CH_2), 2.68–2.77 (m+s, 5H; CH_2 , CH_3), 2.43 (m, 1H; CH_2), 2.06–2.19 (m, 2H; CH, CH_2), 1.43 (s, 2.7H; CH_3), 1.40 (s, 6.3H; CH_3), 0.73–0.78 ppm (m, 6H; CH_3); ^{13}C NMR (62.5 MHz, CDCl_3): $\delta=170.2$ (2C), 169.0, 157.6, 156.4, 136.6, 135.0 (3C), 134.5, 131.5, 129.2 (4C), 128.3 (3C), 128.1, 126.5, 121.7, 117.8, 82.9, 79.9, 66.1, 59.8, 56.4, 45.8, 45.1 (2C), 39.0, 31.4, 29.5, 28.3 (3C), 27.7, 18.8, 18.4 ppm; IR (CHCl_3): $\tilde{\nu}=3429$, 3016, 2964, 2930, 1673, 1508, 1454, 1440, 1383, 1368, 1227, 1215, 1154 cm^{-1} ; high-resolution MS (ES^+): m/z calcd: 771.2637 [$M+\text{Na}$] $^+$; found: 771.2639.

Compound 24: Pyridine (26 μL , 0.321 mmol) and H_2O_2 (39 μL , 30%, 0.382 mmol) were added successively to a solution of compound (1R)-23 (22.6 mg, 0.0302 mmol) in dry CH_2Cl_2

(1.1 mL) cooled to 0°C . The reaction mixture was stirred at 0°C for 20 min, then at room temperature for 1 h. The solution was cooled at 0°C and dimethyl sulfide (67.0 μL , 0.912 mmol) was added. The reaction mixture was stirred at 0°C for 1.5 h and concentrated under vacuum. The crude product was dissolved in benzene (1.5 mL), heated at 60°C for 2 h, concentrated under vacuum, and purified by preparative TLC (silica gel, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (30:1)) to afford compound 24 (8.5 mg, 48% yield). Colorless oil; $[\alpha]_D=-266$ ($c=0.36$ in CHCl_3); ^1H NMR (300 MHz, CD_3OD ; mixture of two rotamers (60:40)): $\delta=7.12$ –7.24 (m, 6H; CH arom), 7.00–7.03 (m, 3H; CH arom), 6.67 (d, $J=7.4$ Hz, 1H; CH), 6.11 (d, $J=7.4$ Hz, 1H; CH), 5.25 (dt, $J=10.3$, 6.6 Hz, 1H; CH), 4.46 (d, $J=11.0$ Hz, 0.6H; CH), 4.28–4.34 (m, 1.4H; CH), 4.21 (t, $J=9.2$ Hz, 0.6H; CH_2), 4.00–4.08 (m+d, $J=6.6$ Hz, 1.4H; CH, CH_2), 3.53–3.67 (m, 1H; CH_2), 2.77–2.85 (m+s, 5H; CH_2 , CH_3), 2.49–2.62 (m, 1H; CH_2), 2.09–2.24 (m, 2H; CH, CH_2), 1.50 (s, 3.6H; CH_3), 1.48 (s, 5.4H; CH_3), 0.79–0.86 ppm (m, 6H; CH_3); ^{13}C NMR (75 MHz, CD_3OD ; mixture of two rotamers): $\delta=172.7$, 171.4, 170.7, 158.9, 158.1, 157.1, 138.3, 133.4, 132.3, 130.8, 130.5, 129.4, 127.7, 126.8, 122.6, 119.9, 83.9, 83.8, 82.3, 81.6, 66.8, 62.9, 61.7, 56.4, 46.7, 46.5, 39.2, 32.7, 32.6, 30.8, 30.2, 29.2, 28.9, 28.7, 19.6, 19.1, 18.9 ppm; IR (CHCl_3): $\tilde{\nu}=3690$, 3396, 3024, 3016, 2966, 2932, 1683, 1626, 1505, 1439,

1392, 1383, 1368, 1315, 1154 cm⁻¹; high-resolution MS (ES⁺): *m/z* calcd: 613.3002 [M+Na]⁺; found: 613.3004.

Mauritine C (7): TFA (200.0 µL, 2.6 mmol) was added to a solution of compound **24** (12.5 mg, 0.0212 mmol) in dry CH₂Cl₂ (2.0 mL) cooled to 0°C. The reaction mixture was stirred at 0°C for 20 min, then at room temperature for 1 h. The solvent was removed under vacuum and the crude residue was dissolved in EtOAc. The organic layer was washed with a saturated solution of Na₂CO₃ and with brine, dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude oil was purified by flash chromatography (silica gel, CH₂Cl₂/MeOH (20:1)) to afford mauritine C (**7**; 8.1 mg, 78% yield). White solid; m.p. 70–73°C (literature value:^[13] not measured); [α]_D = -168.7 (*c* = 0.11 in MeOH; literature value:^[13] -224, *c* = 0.11 in MeOH); ¹H NMR and ¹³C NMR data: see Table 3; IR (CHCl₃): $\tilde{\nu}$ = 3396, 3024, 3018, 2960, 2930, 2875, 2855, 1689, 1626, 1505, 1229, 1215, 1212, 1204, 1098, 1083, 863, 836 cm⁻¹; high-resolution MS (ES⁺): *m/z* calcd: 491.2658 [M+H]⁺; found: 491.2640.

Compound (1R)-14: A suspension of compound (1R)-**21** (1.16 g, 2.39 mmol) and Pd/C (10%, 580 mg) in dry MeOH (26 mL) was purged three times with argon and hydrogen, successively. The reaction mixture was stirred under a hydrogen atmosphere at room temperature for 24 h during which time the system of purging was repeated twice. The suspension was filtered through celite, concentrated under vacuum, and purified by flash chromatography (silica gel, CH₂Cl₂/MeOH (20:1)) to afford compound (1R)-**14** (736 mg, 78% yield). White solid; [α]_D = +39.5 (*c* = 0.102 in DMSO); ¹H NMR (250 MHz, CD₃OD): δ = 7.38 (dd, *J* = 8.8, 2.4 Hz, 1H; CH arom), 7.06–7.24 (m, 5H; CH arom), 7.03 (dd, *J* = 8.8, 2.4 Hz, 1H; CH arom), 6.95 (dd, *J* = 8.5, 2.4 Hz, 1H; CH arom), 6.79 (dd, *J* = 8.5, 2.4 Hz, 1H; CH arom), 5.05 (dd, *J* = 16.4, 8.1 Hz, 1H; CH), 5.01 (m, 1H; CH), 4.17 (dd, *J* = 9.1, 6.1 Hz, 1H; CH), 4.09 (dd, *J* = 14.2, 4.6 Hz, 1H; CH₂), 3.28–3.35 (m under CD₃OD, 1H; CH₂), 3.12–3.25 (m + d, *J* = 7.8 Hz, 2H; CH, CH₂), 2.79–3.05 (m, 1H; CH₂), 2.75 (dd, *J* = 13.2, 9.3 Hz, 1H; CH₂), 2.62 (dd, *J* = 13.2, 6.1 Hz, 1H; CH₂), 2.35–2.49 (m, 1H; CH₂), 1.97–2.08 ppm (m, 1H; CH₂); ¹³C NMR (75 MHz, [D₆]DMSO): δ = 172.4, 169.7, 156.7, 137.2, 135.9, 129.0 (2C), 127.8 (2C), 127.4, 126.5, 126.0, 119.3, 116.6, 83.5, 70.6, 66.6, 53.3, 46.7, 44.0, (1C under [D₆]DMSO), 31.9 ppm; IR (KBr): $\tilde{\nu}$ = 3328, 3069, 3027, 2917, 2893, 2103, 1638, 1542, 1516, 1440, 1378, 1278, 1232, 1182, 1085, 1033, 854 cm⁻¹; high-resolution MS (ES⁺): *m/z* calcd: 396.1923 [M+H]⁺; found: 396.1906.

Compound (1R)-25: *N*-Boc-L-valine (256 mg, 1.18 mmol), DIEA (935.0 µL, 5.35 mmol), and HATU (630.0 mg, 1.66 mmol) were added successively to a solution of compound (1R)-**14** (423.0 mg, 1.07 mmol) in dry DMF (15.0 mL) cooled at 0°C. The reaction mixture was stirred at room temperature for 17 h, then treated with a solution of NH₄Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude oil was purified by flash chromatography (silica gel, CH₂Cl₂/MeOH (50:1→10:1)) to afford compound (1R)-**25** (611 mg, 96% yield). Pale-yellow solid; [α]_D = -121.1 (*c* = 0.19 in CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ = 7.39 (dd, *J* = 8.7, 1.8 Hz, 1H; CH arom), 7.01–7.19 (m, 6H; CH arom), 6.97 (dd, *J* = 8.5, 2.1 Hz, 1H; CH arom), 6.85 (dd, *J* = 8.4, 2.4 Hz, 1H; CH arom), 6.01 (d, *J* = 8.8 Hz, 1H; NH), 5.70 (m, 1H; NH), 5.32 (d, *J* = 9.2 Hz, 1H; NH), 5.24 (m, 1H; CH), 5.04 (brs, 1H; CH), 4.06–4.25 (m, 3H; CH, CH₂), 3.94 (m, 1H; CH), 3.82 (d, *J* = 7.2 Hz, 1H; CH), 3.59 (m, 1H; CH₂), 3.15 (m, 1H; OH), 2.83 (m, 1H; CH₂), 2.65–2.72 (m, 2H; CH₂), 2.40 (m, 1H; CH₂), 2.21 (m, 1H; CH₂), 1.95 (m, 1H; CH), 1.43 (s, 9H; CH₃), 0.93 (d, *J* = 6.8 Hz, 3H; CH₃), 0.88 ppm (d, *J* = 6.8 Hz, 3H; CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 171.7, 170.8, 169.2, 157.4, 155.9, 136.4, 135.5, 129.3 (2C), 128.3 (2C), 127.4, 127.0, 126.6, 119.9, 116.8, 80.9, 79.7, 72.1, 66.5, 56.3, 56.2, 46.9, 45.5, 39.2, 31.4 (2C), 28.4 (3C), 19.15, 17.7 ppm; IR (CHCl₃): $\tilde{\nu}$ = 3413, 3307, 3028, 3013, 2983, 2933, 2876, 1702, 1661, 1508, 1435, 1368, 1169, 1085, 1049 cm⁻¹; high-resolution MS (ES⁺): *m/z* calcd: 617.2951 [M+Na]⁺; found: 617.2967.

Compound (1S)-26: Following the procedure described for the synthesis of compound (1R)-**23**, (1S)-**26** was prepared starting from compound (1R)-**25** in 87% yield (purification by flash chromatography: silica gel, heptanes/EtOAc (1:1)). White solid; [α]_D = -176.4 (*c* = 0.62 in CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ = 7.42–7.45 (m, 2H; CH arom), 6.99–7.23 (m, 10H; CH arom), 6.95 (dd, *J* = 8.3, 2.1 Hz, 1H; CH arom), 6.80 (dd,

J = 8.1, 2.3 Hz, 1H; CH arom), 5.79 (d, *J* = 8.7 Hz, 1H; NH), 5.45 (dd, *J* = 7.5, 4.5 Hz, 1H; NH), 5.16 (m, 1H; CH), 5.12 (d, *J* = 8.9 Hz, 1H; NH), 4.71 (t, *J* = 6.8 Hz, 1H; CH), 4.18 (dd, *J* = 8.9, 6.2 Hz, 1H; CH), 3.99–4.09 (m, 3H; CH, CH₂), 3.87 (d, *J* = 6.8 Hz, 1H; CH), 3.52 (m, 1H; CH₂), 2.99 (ddd, *J* = 14.5, 6.8, 4.5 Hz, 1H; CH₂), 2.85 (dd, *J* = 13.4, 10.2 Hz, 1H; CH₂), 2.59 (dd, *J* = 13.4, 4.3 Hz, 1H; CH₂), 2.46 (m, 1H; CH₂), 2.16 (m, 1H; CH₂), 1.81 (m, 1H; CH), 1.36 (s, 9H; CH₃), 0.74–0.83 ppm (m, 6H; CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 171.7, 170.0, 169.2, 157.2, 155.8, 136.5, 134.9 (2C), 134.6, 131.0, 130.0, 129.2 (4C), 128.4 (2C), 128.3, 128.2, 126.6, 121.1, 119.6, 82.8, 79.7, 65.8, 56.2, 55.3, 45.8, 45.6, 44.3, 38.1, 31.5, 31.4, 28.4 (3C), 19.1, 17.5 ppm; IR (CHCl₃): $\tilde{\nu}$ = 3687, 3422, 3032, 3018, 3011, 2965, 2931, 2401, 2360, 2340, 1702, 1671, 1507, 1437, 1232, 1199, 1166, 1044, 927 cm⁻¹; high-resolution MS (ES⁺): *m/z* calcd: 757.2480 [M+Na]⁺; found: 757.2451.

Compound 27: Pyridine (230 µL, 2.84 mmol) and an aqueous solution of H₂O₂ (350.0 µL, 30%, 3.43 mmol) were added successively to a solution of compound (1S)-**26** (193.0 mg, 0.26 mmol) in dry CH₂Cl₂ (8.2 mL) cooled at 0°C. The reaction mixture was stirred for 1 h at 0°C, then Me₂S (380.0 µL, 5.17 mmol) was added at 0°C. The reaction mixture was stirred at room temperature for 4 h, then a large volume of EtOAc was added. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude residue was purified by flash chromatography (silica gel, heptanes/EtOAc (1:1)) and then by preparative TLC (silica gel, CH₂Cl₂/MeOH (40:1)) to afford compound **27** (90.4 mg, 60% yield). White solid; [α]_D = -181.5 (*c* = 0.24 in CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ = 7.15–7.23 (m, 6H; CH arom), 6.86–7.02 (m, 3H; CH arom), 6.62 (dd, *J* = 10.3, 7.7 Hz, 1H; CH), 6.36 (d, *J* = 8.1 Hz, 1H; NH), 6.25 (d, *J* = 10.3 Hz, 1H; NH), 6.22 (d, *J* = 7.7 Hz, 1H; CH), 5.41 (td, *J* = 10.3, 6.6 Hz, 1H; CH), 5.05 (d, *J* = 8.8 Hz, 1H; NH), 4.51 (td, *J* = 9.0, 5.0 Hz, 1H; CH), 4.20 (dd, *J* = 8.8, 7.0 Hz, 1H; CH), 4.02–4.12 (m + d, *J* = 5.9 Hz, 2H; CH, CH₂), 3.38 (m, 1H; CH₂), 3.28 (dd, *J* = 14.0, 4.4 Hz, 1H; CH₂), 2.61 (dd, *J* = 14.0, 5.1 Hz, 1H; CH₂), 2.51 (m, 1H; CH₂), 2.11 (m, 1H; CH₂), 1.79 (m, 1H; CH), 1.39 (s, 9H; CH₃), 0.77 ppm (d, *J* = 6.6 Hz, 6H; CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 170.3, 169.4, 166.5, 157.4, 154.0, 135.6, 132.6, 132.4, 130.2, 129.9 (2C), 128.6 (2C), 127.1, 125.4, 122.6, 122.5, 114.8, 83.8, 75.9, 64.1, 56.2, 54.0, 46.4, 36.2, 31.9, 31.5, 28.4 (3C), 19.2, 17.6 ppm; IR (CHCl₃): $\tilde{\nu}$ = 3395, 3018, 2930, 1692, 1626, 1502, 1369, 1163, 908, 864 cm⁻¹; high-resolution MS (ES⁺): *m/z* calcd: 599.2846 [M+Na]⁺; found: 599.2850.

Mauritine A (5): TFA (200.0 µL, 2.6 mmol) was added to a solution of compound **27** (70.0 mg, 0.12 mmol) in dry CH₂Cl₂ (1.5 mL) cooled to 0°C. The reaction mixture was stirred at 0°C for 20 min, then at room temperature for 1 h. Solvent was removed under vacuum and the resulting crude oil was dissolved in dry DMF (1.5 mL). The solution was next cooled to 0°C and *N,N*-dimethyl-L-alanine (16.0 mg, 0.13 mmol), DIEA (106.0 µL, 0.61 mmol), and HATU (71.0 mg, 0.19 mmol) were added successively. The reaction mixture was stirred at room temperature for 2 h, then treated with a solution of NH₄Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under vacuum. The resulting crude residue was purified by flash chromatography (silica gel, CH₂Cl₂/MeOH (20:1)) to afford mauritine A (**5**; 40.9 mg, 59% yield). White solid; m.p. 87–90°C (literature value:^[13] 104°C); [α]_D = -287.7 (*c* = 0.333 in MeOH; literature value:^[13] -315, *c* = 0.33 in MeOH); ¹H NMR and ¹³C NMR data: see Table 1; IR (CHCl₃): $\tilde{\nu}$ = 3393, 3027, 3022, 3015, 2992, 2963, 2939, 2873, 2834, 2790, 1732, 1689, 1626, 1599, 1505, 1434, 1373, 1246, 1099 cm⁻¹; high-resolution MS (ES⁺): *m/z* calcd: 576.3186 [M+H]⁺; found: 576.3155.

Mauritine B (6): TFA (200.0 µL, 2.6 mmol) was added to a solution of compound **27** (41.0 mg, 71.0 µmol) in dry CH₂Cl₂ (1.8 mL) cooled to 0°C. The reaction mixture was stirred at 0°C for 20 min, then at room temperature for 1 h. Solvent was removed under vacuum and the resulting crude oil was dissolved in dry DMF (1.5 mL). The solution was next cooled at 0°C and *N,N*-dimethyl-L-isoleucine (14.0 mg, 85.0 µmol), DIEA (62.0 µL, 35.5 µmol), and HATU (42.0 mg, 0.11 mmol) were added successively. The reaction mixture was stirred at room temperature for 2 h, then treated with a solution of NH₄Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under vacuum. The resulting crude residue was purified by flash chro-

matography (silica gel, CH₂Cl₂/MeOH (20:1)) to afford mauritine B (**6**; 26.7 mg, 61 % yield). Colorless oil; [α]_D = –229 (*c* = 0.332 in MeOH; literature value:^[13] –151, *c* = 0.44 in MeOH); ¹H NMR and ¹³C NMR data: see Table 2; IR (CHCl₃): $\tilde{\nu}$ = 3691, 3390, 3017, 3013, 2965, 2931, 1730, 1688, 1626, 1505, 1433, 1374 cm^{–1}; high-resolution MS (ES⁺): *m/z* calcd: 618.3655 [M+H]⁺; found: 618.3654.

Compound 29: TFA (150.0 μ L, 1.95 mmol) was added to a solution of compound **27** (20.0 mg, 0.035 mmol) in dry CH₂Cl₂ (1.5 mL) cooled to 0°C. The reaction mixture was stirred at 0°C for 20 min, then at room temperature for 1 h. Solvent was removed under vacuum and the resulting crude oil was dissolved in dry DMF (0.8 mL), then *N*-Boc-*N*-methyl-L-alanine (8.0 mg, 0.038 mmol), DIEA (31.0 μ L, 0.18 mmol), and HATU (21.0 mg, 54.0 μ mol) were added successively at 0°C. The reaction mixture was stirred at room temperature for 4 h, then treated with a solution of NH₄Cl and extracted with EtOAc. The organic layer was washed with brine, dried over Na₂SO₄, filtered, and concentrated under vacuum. The resulting crude residue was purified by preparative TLC (silica gel, heptanes/EtOAc (1:1)) to afford compound **29** (18.1 mg; 79 % yield). White solid; [α]_D = –161.2 (*c* = 0.60 in CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ = 7.15–7.28 (m, 6H; CH arom), 6.87–7.01 (m, 3H; CH arom), 6.63 (dd, *J* = 10.3, 7.7 Hz, 1H; CH), 6.37 (m, 1H; NH), 6.25 (d, *J* = 10.3 Hz, 1H; NH), 6.22 (d, *J* = 7.7 Hz, 1H; CH), 5.40 (m, 1H; CH), 4.67 (m, 1H; CH), 4.48 (m, 2H; CH), 4.06–4.16 (m+d, *J* = 5.5 Hz, 2H; CH, CH₂), 3.38 (m, 1H; CH₂), 3.30 (dd, *J* = 14.0, 4.0 Hz, 1H; CH₂), 2.74 (s, 3H; CH₃), 2.60 (dd, *J* = 14.0, 5.1 Hz, 1H; CH₂), 2.49 (m, 1H; CH₂), 2.11 (m, 1H; CH₂), 1.83 (m, 1H; CH), 1.40 (s, 9H; CH₃), 1.28 (d, *J* = 7.0 Hz, 3H; CH₃), 0.74 ppm (d, *J* = 6.6 Hz, 6H; CH₃); ¹³C NMR (75 MHz, CDCl₃): δ = 171.6, 171.1, 170.3, 166.5, 157.4 (2C), 135.4, 132.5, 132.4, 130.2, 129.9 (2C), 128.6 (2C), 127.1, 125.4, 122.5, 122.4, 114.9, 83.8, 80.7, 64.4, 64.2, 54.7, 54.0, 46.4, 36.2, 31.9, 31.5, 29.8, 28.4 (3C), 19.2, 17.7, 13.4 ppm; IR (CHCl₃): $\tilde{\nu}$ = 3395, 3017, 2969, 2933, 1685, 1626, 1505, 1436, 1392, 1369, 1324, 1221, 1205, 1160, 909 cm^{–1}; high-resolution MS (ES⁺): *m/z* calcd: 684.3373 [M+Na]⁺; found: 684.3391.

Mauritine F (10): Following the procedure described for the synthesis of mauritine C (**7**), mauritine F (**10**) was prepared from compound **29** in 71 % yield. White solid; m.p. 220–222°C (literature value:^[13] 222–225°C); [α]_D = –234 (*c* = 0.149 in MeOH; literature value:^[13] –285, *c* = 0.15 in MeOH); ¹H NMR and ¹³C NMR data: see Table 4; IR (CHCl₃): $\tilde{\nu}$ = 3651, 3394, 3024, 3018, 2991, 2966, 1689, 1626, 1505, 1227, 1208 cm^{–1}; high-resolution MS (ES⁺): *m/z* calcd: 584.2849 [M+Na]⁺; found: 584.2845.

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- For reviews, see: a) U. Schmidt, A. Lieberknecht, E. Haslinger, *The Alkaloids*, Vol. 26 (Ed.: A. Brassi), Academic Press, New York, **1985**, pp. 299–326; b) M. M. Joullié, R. F. Nutt, *Alkaloids: Chemical and Biological Perspectives*, Vol. 3 (Ed.: S. W. Pelletier), Wiley, New York, **1985**, pp. 113–168.
- M. Pais, F.-X. Jarreau, X. Lusinch, R. Goutarel, *Ann. Chim.* **1966**, 83–105.
- For reviews, see: a) H. Itokawa, K. Takeya, Y. Hitotsuyanagi, H. Morita, *The Alkaloids*, Vol. 49 (Ed.: G. A. Cordell), Academic Press, New York, **1997**, pp. 301–387; b) D. C. Gournelis, G. G. Laskaris, R. Verpoorte, *Nat. Prod. Rep.* **1997**, 14, 75–82. For a recent overview, see: c) M. Joullié, D. J. Richard, *Chem. Commun.* **2004**, 2011–2015.
- a) B. H. Han, M. H. Park, Y. N. Han, *Phytochemistry* **1990**, 29, 3315–3319; b) B. H. Han, M. H. Park, J. H. Park, *Pure Appl. Chem.* **1989**, 61, 443–448.
- a) F. Frappier, F. Rocchiccioli, F. X. Jarreau, M. Pais, *Tetrahedron* **1978**, 34, 2911–2916; b) F. Rocchiccioli, F. X. Jarreau, M. Pais, *Tetrahedron* **1978**, 34, 2917–2926.
- a) J. C. Lagarias, R. A. Houghten, H. Rapoport, *J. Am. Chem. Soc.* **1978**, 100, 8202–8209; b) D. G. Goff, J. C. Lagarias, W. C. Shih, M. P. Klein, H. Rapoport, *J. Org. Chem.* **1980**, 45, 4813–4817.
- a) U. Schmidt, H. Griesser, A. Lieberknecht, J. Talbiersky, *Angew. Chem.* **1981**, 93, 271–272; *Angew. Chem. Int. Ed. Engl.* **1981**, 20, 280–281; b) U. Schmidt, A. Lieberknecht, H. Griesser, J. Häutler, *Angew. Chem.* **1981**, 93, 272–273; *Angew. Chem. Int. Ed. Engl.* **1981**, 20, 281–282; c) U. Schmidt, A. Lieberknecht, H. Böken, H. Griesser, *Angew. Chem.* **1981**, 93, 1121–1122; *Angew. Chem. Int. Ed. Engl.* **1981**, 20, 1026–1027; d) U. Schmidt, A. Lieberknecht, H. Griesser, J. Talbiersky, *J. Org. Chem.* **1982**, 47, 3261–3264; e) U. Schmidt, A. Lieberknecht, H. Böken, H. Griesser, *J. Org. Chem.* **1983**, 48, 2680–2685; f) U. Schmidt, U. Schanbacher, *Angew. Chem.* **1983**, 95, 150–151; *Angew. Chem. Int. Ed. Engl.* **1983**, 22, 152–153; g) U. Schmidt, U. Schanbacher, *Liebigs Ann. Chem.* **1984**, 1205–1215; h) U. Schmidt, M. Zäh, A. Lieberknecht, *J. Chem. Soc. Chem. Commun.* **1991**, 1002–1004.
- a) R. F. Nutt, K.-M. Chen, M. M. Joullié, *J. Org. Chem.* **1984**, 49, 1013–1021; b) R. J. Heffner, M. M. Joullié, *Tetrahedron Lett.* **1989**, 30, 7021–7024; c) R. J. Heffner, J. Jiang, M. M. Joullié, *J. Am. Chem. Soc.* **1992**, 114, 10181–10189; d) J. Jiang, W.-R. Li, R. M. Przeglowski, M. M. Joullié, *Tetrahedron Lett.* **1993**, 34, 6705–6708; e) L. Williams, Z. Zhang, F. Shao, P. J. Carroll, M. M. Joullié, *Tetrahedron* **1996**, 52, 11673–11694; f) S. P. East, F. Shao, L. Williams, M. M. Joullié, *Tetrahedron* **1998**, 54, 13371–13390; g) S. P. East, M. M. Joullié, *Tetrahedron Lett.* **1998**, 39, 7211–7214; h) D. Xiao, S. P. East, M. M. Joullié, *Tetrahedron Lett.* **1998**, 39, 9631–9632; i) D. M. Flanagan, M. M. Joullié, *Synth. Commun.* **1990**, 20, 459–467.
- a) B. H. Lipshutz, R. W. Hungate, K. E. McCarthy, *Tetrahedron Lett.* **1983**, 24, 5155–5158; b) B. H. Lipshutz, R. W. Hungate, K. E. McCarthy, *J. Am. Chem. Soc.* **1983**, 105, 7703–7713; c) B. H. Lipshutz, B. E. Huff, K. E. McCarthy, T. A. Miller, S. M. J. Mukarram, T. J. Siahaan, W. D. Vaccaro, H. Webb, A. M. Falick, *J. Am. Chem. Soc.* **1990**, 112, 7032–7041.
- a) B. H. Han, Y. C. Kim, M. K. Park, J. H. Park, H. J. Go, H. O. Yang, D.-Y. Suh, Y.-H. Kang, *Heterocycles* **1995**, 41, 1909–1914; b) D.-Y. Suh, Y. C. Kim, Y. N. Han, B. H. Han, *Heterocycles* **1996**, 43, 2347–2351; c) Y.-A. Kim, H.-N. Shin, M.-S. Park, S.-H. Cho, S.-Y. Han, *Tetrahedron Lett.* **2003**, 44, 2557–2560.
- a) J. Zhu, T. Laib, J. Chastanet, R. Beugelmans, *Angew. Chem.* **1996**, 108, 2664–2666; *Angew. Chem. Int. Ed. Engl.* **1996**, 35, 2517–2519; b) T. Laib, J. Zhu, *Tetrahedron Lett.* **1998**, 39, 283–286.
- a) J. Zhu, *Synlett* **1997**, 133–144; b) J. S. Sawyer, *Tetrahedron* **2000**, 56, 5045–5065.
- K. C. Nicolaou, C. N. C. Boddy, S. Bräse, N. Winssinger, *Angew. Chem.* **1999**, 111, 2230–2287; *Angew. Chem. Int. Ed.* **1999**, 38, 2096–2152.
- M. Bois-Choussy, P. Cristau, J. Zhu, *Angew. Chem.* **2003**, 115, 4370–4373; *Angew. Chem. Int. Ed.* **2003**, 42, 4238–4241.
- For the synthesis of nonpeptidic macrocycles, see: G. Islas-Gonzalez, J. Zhu, *J. Org. Chem.* **1999**, 64, 914–924.
- For atropenantioselective cycloetherifications, see G. Islas-Gonzalez, M. Bois-Choussy, J. Zhu, *Org. Biomol. Chem.* **2003**, 1, 30–32.
- a) T. Laib, J. Zhu, *Tetrahedron Lett.* **1999**, 40, 83–86; b) T. Temal-Laib, J. Chastanet, J. Zhu, *J. Am. Chem. Soc.* **2002**, 124, 583–590.
- T. Laib, M. Bois-Choussy, J. Zhu, *Tetrahedron Lett.* **2000**, 41, 7645–7649.
- a) R. Tschesche, H. Wilhelm, H.-W. Fehlhaber, *Tetrahedron Lett.* **1972**, 2609–2612; b) R. Tschesche, H. Wilhelm, E. U. Kaußmann, G. Eckhardt, *Justus Liebigs Ann. Chem.* **1974**, 1694–1701.
- A. Kirfel, G. Will, *Z. Kristallogr.* **1975**, 368–383.
- Yields of extraction for the mauritines A–F = 0.001–0.09 %.
- S. C. Nigam, A. Mann, M. Taddei, C. G. Wermuth, *Synth. Commun.* **1989**, 19, 3139–3142.

- [23] T. Laib, J. Ouazzani, J. Zhu, *Tetrahedron: Asymmetry* **1998**, 9, 169–178.
- [24] Prepared in three steps from the commercially available (2*S*,3*S*)-2-hydroxyproline.
- [25] a) F. D. Bellamy, K. Ou, *Tetrahedron Lett.* **1984**, 25, 839–842; b) C. Vergne, C. M. Bois-Choussy, J. Zhu, *Synlett* **1998**, 1159–1161.
- [26] a) N. Kornblum, D. C. Iffland, *J. Am. Chem. Soc.* **1949**, 71, 2137–2143; b) E. S. Rhee, H. J. Shine, *J. Am. Chem. Soc.* **1986**, 108, 1000–1006.
- [27] Competitive N-debenzylation of the proline unit was avoided by careful TLC monitoring and by using the bi-solvent system AcOEt/MeOH.
- [28] L. A. Carpino, *J. Am. Chem. Soc.* **1993**, 115, 4397.
- [29] Enamide cleavage of franguloline under acidic conditions (2*N* HCl, 55°C) has been reported; see ref. [10b].
- [30] R. E. Bowman, H. H. Stroud, *J. Chem. Soc.* **1950**, 1342–1351.
- [31] The purities of our synthetic compounds are greater than 95% from NMR spectroscopy analysis. However, there is a discrepancy between the natural products and our synthetic compounds in the $[\alpha]_D$ value. Because ^1H NMR spectra of the natural products are unavailable, we are unable to make any comment on this point.

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