Total Syntheses of (±)-Agelasimine-A, (±)-Agelasimine-B, and (±)-Purino-diterpene and the Structure of Diacetylagelasimine-A

Masashi Ohba,* Nobuo Kawase, and Tozo Fujii

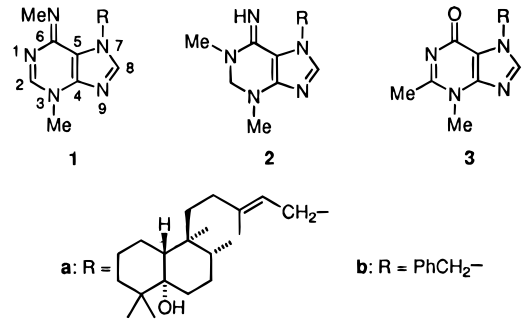
Contribution from the Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-machi, Kanazawa 920, Japan

Received March 18, 1996[⊗]

Abstract: A full account is given of the first racemic syntheses of agelasimine-A (**1a**) and agelasimine-B (**2a**), adenine-related bicyclic diterpenoids isolated from the marine sponge *Agelas mauritiana*. Central synthetic features include a highly stereoselective construction of the diol (±)-**13**, a key intermediate for their common diterpene portion, and regioselective alkylations on the adenine portions. The palladium-catalyzed cross-coupling reaction of the 9-alkyl-9-BBN derivative (±)-**17** with the 1-alkenyl triflate or halides **15a**−**c** was examined in detail as a preliminary to the preparation of the precursor (±)-**10**. The above syntheses of (±)-**1a** and (±)-**2a** have unequivocally confirmed the correctness of the structures and relative stereochemistries proposed for agelasimine-A and -B. The reaction of (±)-**1a** with acetic anhydride in pyridine afforded the monocyclic imidazole derivative (±)-**25a**, which was found to correspond to "diacetylagelasimine-A", initially assigned the purine form **26a**. A similar acetylation of (±)-**2a** led to the racemic synthesis of purino-diterpene (**3a**), an artifact separated from the acetylated mixture of the crude extract of *A. mauritiana*.

Introduction

Recent studies on biologically active metabolites of marine sponges of the genus *Agelas* revealed the presence of a number of adenine-related diterpenoids.[1−3] Most of them possess the quaternary 9-methyladeninium structures attached to diterpene portions at N7.[1] On the other hand, agelasimine-A (**1a**) and agelasimine-B (**2a**), isolated from the orange sponge *Agelas mauritiana* by Fathi-Afshar and Allen, are novel nonquaternary adenine derivatives of a bicyclic diterpene.[2] Both agelasimines display a wide range of interesting biological activities, such as cytotoxicity, inhibition of adenosine transfer into rabbit erythrocytes, Ca^{2+}-channel antagonistic action, and α_1 adrenergic blockade.[2,4] The Canadian group deduced chemical structures (**1a** and **2a**), featuring trisubstituted adenine nuclei and a diterpene portion at N7, on the basis of extensive spectral studies.[2] The main proof for these assignments came from the comparison of the spectral data of **1a** and **2a** with those of purino-diterpene (**3a**), an artifact separated by Faulkner and coworkers from the acetylated mixture of the crude extract of the same sponge (*A. mauritiana*), whose structure had been confirmed by an X-ray crystallographic analysis.[5] Recently, we have accomplished the syntheses of the *N*7-benzyl analogues **1b** and **2b** as preludes to total syntheses of **1a** and **2a**, whereby the substitution patterns proposed for the adenine moieties in **1a** and **2a** have been corroborated.[6] In this full account, we describe the syntheses of the racemic candidate structures [(±)-**1a** and (±)-**2a**], which have confirmed the correctness of the structures assigned to agelasimine-A and -B.[7a] The acetylations of (±)-**1a** and (±)-**2a** have also been investigated in connection with the origin of purino-diterpene (**3a**).[7b]



Results and Discussion

Construction of the Diterpene Portion: Stereoselective Synthesis of the Diol (±)-13. At the outset of the synthesis of the diterpene portion, a common structural unit of agelasimine-A and -B, the bicyclic enone (±)-**7** was required as a starting material (Scheme 1). We initially tried to transform (±)-3,4-dimethyl-2-cyclohexanone [(±)-**4**] to the requisite (±)-**7** via the hydroxy ketone (±)-**6**, according to the procedure of Toko-

[⊗] Abstract published in *Advance ACS Abstracts,* August 15, 1996.

(1) (a) Cullen, E.; Devlin, J. P. *Can. J. Chem.* **1975**, *53*, 1690−1691. (b) Capon, R. J.; Faulkner, D. J. *J. Am. Chem. Soc.* **1984**, *106*, 1819−1822. (c) Nakamura, H.; Wu, H.; Ohizumi, Y.; Hirata, Y. *Tetrahedron Lett.* **1984**, *25*, 2989−2992. (d) Wu, H.; Nakamura, H.; Kobayashi, J.; Ohizumi, Y.; Hirata, Y. *Tetrahedron Lett.* **1984**, *25*, 3719−3722. (e) Wu, H.; Nakamura, H.; Kobayashi, J.; Kobayashi, M.; Ohizumi, Y.; Hirata, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 2495−2504. (f) Ishida, K.; Ishibashi, M.; Shigemori, H.; Sasaki, T.; Kobayashi, J. *Chem. Pharm. Bull.* **1992**, *40*, 766−767.

(2) Fathi-Afshar, R.; Allen, T. M. *Can. J. Chem.* **1988**, *66*, 45−50.

(3) For a review on the purine alkaloids including the adenine-related diterpenoids, see: Atta-ur-Rahman; Choudhary, M. I. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1990; Vol. 38, Chapter 3.

(4) Fathi-Afshar, R.; Allen, T. M.; Krueger, C. A.; Cook, D. A.; Clanachan, A. S.; Vriend, R.; Baer, H. P.; Cass, C. E. *Can. J. Physiol. Pharmacol.* **1989**, *67*, 276−281.

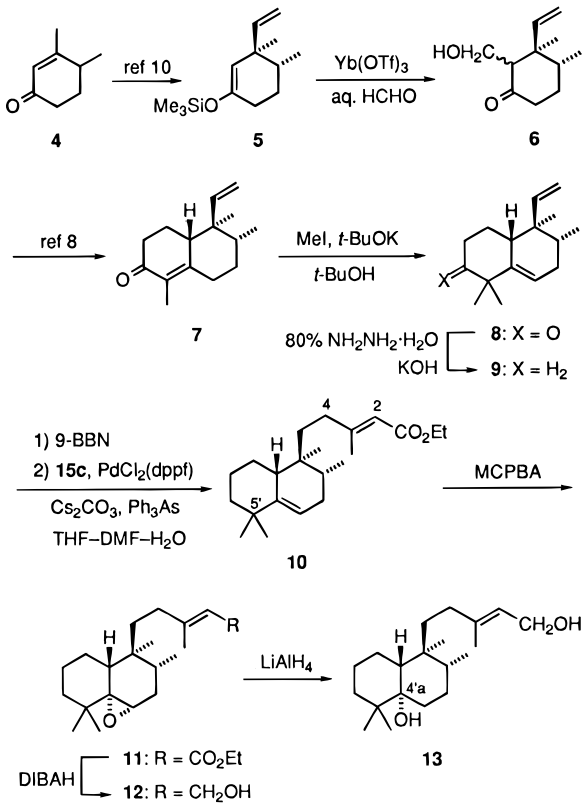
(5) Nakatsu, T.; Faulkner, D. J.; Matsumoto, G. K.; Clardy, J. *Tetrahedron Lett.* **1984**, *25*, 935−938.

(6) (a) Saito, T.; Chikazawa, J.; Nakamura, Y.; Fujii, T. *Heterocycles* **1993**, *35*, 143−146. (b) Fujii, T.; Saito, T.; Chikazawa, J.; Ohba, M.; Date, T. *Heterocycles* **1994**, *38*, 733−738. (c) Fujii, T.; Saito, T.; Chikazawa, J.; Nakamura, Y.; Ohba, M. *Chem. Pharm. Bull.* **1994**, *42*, 2461−2466.

(7) Preliminary communications: (a) Ohba, M.; Kawase, N.; Fujii, T.; Aoe, K.; Okamura, K.; Fathi-Afshar, R.; Allen, T. M. *Tetrahedron Lett.* **1995**, *36*, 6101−6104. (b) Ohba, M.; Kawase, N.; Fujii, T. *Heterocycles* **1995**, *41*, 2661−2664.

S0002-7863(96)00879-7 CCC: $12.00 © 1996 American Chemical Society

Scheme 1



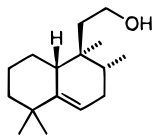
royama et al.[8] However, less satisfactory results were obtained owing to the use of cumbersome gaseous formaldehyde in the step from (±)-**4** to (±)-**6**, prompting us to switch to an alternative method. Kobayashi has recently reported that the reaction of silyl enol ethers with formaldehyde in H_2O solution (commercial formaldehyde solution) in the presence of a catalytic amount of $Yb(OTf)_3$ afforded the corresponding monohydroxymethylated adducts.[9] Under these reaction conditions, the hydroxymethylation reaction of the silyl enol ether (±)-**5**,[10] derived from (±)-**4**, was found to proceed smoothly to provide (±)-**6** as a diastereoisomeric mixture in 77% yield. Conversion of (±)-**6** into (±)-**7** was effected by following the literature procedure.[8] Methylation of (±)-**7** with MeI under thermodynamic conditions[11] furnished the deconjugated ketone (±)-**8** (83% yield), which was then subjected to the Huang-Minlon modification of the Wolff−Kishner reduction to give (±)-**9** in 93% yield.

Our effort was then focused on elongation of the side chain in (±)-**9** by exploiting the vinyl group. Several multistep elaborations devised for this purpose in similar systems have still presented significant drawbacks.[12] In an effort to achieve the above process more effectively, we envisioned the application of the palladium-catalyzed cross-coupling reaction of alkylboranes with 1-alkenyl halides developed by Suzuki and co-workers.[13] The Suzuki cross-coupling reaction seemed particularly attractive for conversion of (±)-**9** into (±)-**10** because alkylboranes are readily accessible by hydroboration of alkenes, the stereochemistry of 1-alkenyl halides is completely retained in the products, and the coupling reaction is tolerant to a wide variety of functionalities including ester. In an initial experiment, we investigated the hydroboration conditions of (±)-**9** using 9-borabicyclo[3.3.1]nonane (9-BBN) for the preparation of the 9-alkyl-9-BBN derivative, known as the best coupling partner of choice for alkylation of 1-alkenyl halides.[13b,d] The results obtained after alkaline hydrogen peroxide oxidation of the generated 9-alkyl-9-BBN derivative to form the alcohol (±)-**14** are summarized in Table 1. It may be seen that the hydroboration of (±)-**9** using 1.0 equiv of 9-BBN in THF at room temperature (entry 1) was very sluggish owing to a sterically congested environment of the vinyl group. The best result was obtained when 3.0 equiv of 9-BBN was employed in boiling THF (entry 4): the reaction proceeded regioselectively on the vinyl group of (±)-**9**, producing the alcohol (±)-**14** (after oxidation) in 82% yield.

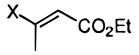
Table 1. Hydroboration−Oxidation of the Alkene (±)-**9**

	hydroboration conditions[a]			
entry	amt of 9-BBN (equiv)	temp	time (h)	(±)-**14** yield (%)
1	1.0	rt	24	8
2	3.0	rt	5	66
3	1.0	reflux	6	47
4	3.0	reflux	2	82

[a] All reactions were performed in THF and followed by oxidation with 30% aqueous H_2O_2/3 N aqueous NaOH/EtOH at 50 °C for 1 h.



14



15

a: X = OTf, **b**: X = Br, **c**: X = I

Having established the hydroboration conditions for (±)-**9**, we next tried the coupling reaction between the 9-alkyl-9-BBN derivative and the iodide **15c**[14] under conventional Suzuki's conditions[13a] [K_3PO_4, $PdCl_2$(dppf),[15] THF, DMF, 50 °C, 20 h]. However, the yield of the desired coupling product (±)-**10** was quite low (2%). To maximize the efficiency of this process, a systematic investigation was therefore undertaken by exploiting (±)-**16** as a model compound. The hydroboration of (±)-**16** itself was found to progress smoothly and selectively on the side chain, even when 1.0 equiv of 9-BBN was used in THF at room temperature, giving the alcohol (±)-**18**[16] in 93% yield after oxidation of the 9-alkyl-9-BBN (±)-**17** (which should have formed in situ) with alkaline hydrogen peroxide (Scheme 2). Next the palladium-catalyzed cross-coupling reaction of (±)-**17** employing the 1-alkenyl triflate **15a**,[17] bromide **15b**,[18] or iodide **15c**[14] was examined. The results are listed in Table 2,

(8) Tokoroyama, T.; Fujimori, K.; Shimizu, T.; Yamagiwa, Y.; Monden, M.; Iio, H. *Tetrahedron* **1988**, *44*, 6607−6622.

(9) (a) Kobayashi, S. *Chem. Lett.* **1991**, 2187−2190. (b) Kobayashi, S.; Hachiya, I. *J. Org. Chem.* **1994**, *59*, 3590−3596.

(10) Piers, E.; Marais, P. C. *J. Chem. Soc., Chem. Commun.* **1989**, 1222−1223.

(11) (a) Ringold, H. J.; Rosenkranz, G. *J. Org. Chem.* **1957**, *22*, 602−605. (b) Atwater, N. W. *J. Am. Chem. Soc.* **1960**, *82*, 2847−2852. (c) Nedelec, L.; Gasc, J. C.; Bucourt, R. *Tetrahedron* **1974**, *30*, 3263−3268.

(12) For example: (a) Iio, H.; Monden, M.; Okada, K.; Tokoroyama, T. *J. Chem. Soc., Chem. Commun.* **1987**, 358−359. (b) Piers, E.; Roberge, J. Y. *Tetrahedron Lett.* **1992**, *33*, 6923−6926. (c) Piers, E.; Breau, M. L.; Han, Y.; Plourde, G. L.; Yeh, W.-L. *J. Chem. Soc., Perkin Trans. 1* **1995**, 963−966.

(13) (a) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314−321. (b) Oh-e, T.; Miyaura, N.; Suzuki, A. *J. Org. Chem.* **1993**, *58*, 2201−2208. (c) Suzuki, A. *Pure Appl. Chem.* **1991**, *63*, 419−422. (d) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483.

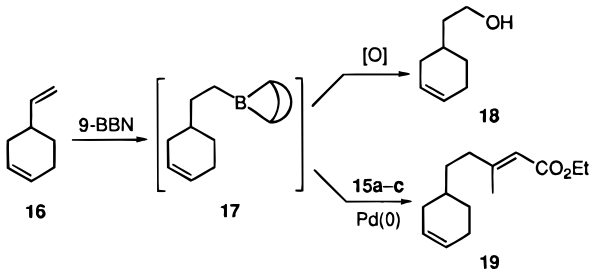
(14) Chalchat, J.-C.; Théron, F.; Vessière, R. *C. R. Acad. Sci., Ser. C* **1971**, *273*, 763−765.

(15) Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158−163.

(16) (a) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1961**, *83*, 1241−1246. (b) Kishan Reddy, Ch.; Periasamy, M. *Tetrahedron* **1992**, *48*, 8329−8336.

(17) Saulnier, M. G.; Kadow, J. F.; Tun, M. M.; Langley, D. R.; Vyas, D. M. *J. Am. Chem. Soc.* **1989**, *111*, 8320−8321.

Scheme 2



and several comments are in order. Treatment of (±)-**17**, derived from (±)-**16** and 1.1 equiv of 9-BBN, with **15c** and K_3PO_4 in the presence of $PdCl_2$(dppf) in boiling THF for 16 h produced (±)-**19** in 40% yield (entry 5). By use of 3.0 equiv of 9-BBN, however, the yield of (±)-**19** was decreased to 4% (entry 6). Similar results were obtained when the cross-coupling reactions were conducted by adding DMF and employing K_2CO_3 instead of K_3PO_4 as a base at 50 °C, but with slightly improved yields, respectively (entries 7 and 8). The decrease of yield caused by the use of excess 9-BBN is most likely due to the formation of the hydridoalkenylpalladium intermediate via transmetalation with 9-BBN, as described previously by Shibasaki and co-workers.[19] Thus, addition of H_2O to the cross-coupling reaction mixture, derived from the hydroboration of (±)-**16** with excess 9-BBN, led to the improvement of yield, presumably owing to the expected hydrolysis of the residual 9-BBN (entry 9).[19] However, the yield of (±)-**19** was still insufficient (60%). In connection with the synthesis of PGE_1, Johnson and Braun recently reported the results of their investigation on a modification of the Suzuki cross-coupling reaction: cesium carbonate in a THF−DMF−H_2O system in the presence of $PdCl_2$(dppf) and the coligand triphenylarsine accelerated the coupling reaction to proceed at room temperature.[20] Under their reaction conditions, the desired coupling product (±)-**19** was obtained in moderate yield (entry 12). Ultimately, when the hydroboration of (±)-**16** was performed with 3.0 equiv of 9-BBN, the Johnson−Braun modification gave the best results (entries 13 and 14). In the absence of H_2O or triphenylarsine, the yields of (±)-**19** decreased to a considerable extent (entries 10 and 11). The order of reactivity of the 1-alkenyl triflate and halides employed is **15c** > **15b** > **15a**, as generally observed in the Suzuki cross-coupling reaction.[13b]

With the above pilot experiment completed, we now applied the modified conditions to the 9-alkyl-9-BBN derivative prepared from (±)-**9** by treatment with 3.0 equiv of 9-BBN, succeeding in its conversion into the desired α,β-unsaturated ester (±)-**10** in 75% yield. The *E* geometry of (±)-**10** was secured from a 4% NOE enhancement observed for the C4-proton signal on irradiation of the C2-olefinic proton signal.

Direct epoxidation of (±)-**10** with *m*-chloroperoxybenzoic acid (MCPBA) in CH_2Cl_2 at 0 °C occurred on the nonconjugated endocyclic olefin, producing the monoepoxide (±)-**11** as the sole isolable isomer in 85% yield. Reduction of (±)-**11** with diisobutylaluminum hydride (DIBAH) in CH_2Cl_2−hexane at −78 °C provided the allylic alcohol (±)-**12** (87% yield), which was then subjected to the reductive cleavage of epoxide using $LiAlH_4$ in boiling THF. The hydride attack took place preferentially from the sterically less hindered carbon side of the epoxide, furnishing the diol (±)-**13** in 78% yield.[21] The relative stereochemistry of the tertiary hydroxy group at C4′a of (±)-**13** was established through a single-crystal X-ray diffraction analysis,[7a] which also confirmed those of the epoxide groups in (±)-**11** and (±)-**12**. The high stereoselectivity observed in epoxidation of (±)-**10** is probably due to access of the peracid from an orientation avoiding the axial methyl group at C5′.

Construction of the Trisubstituted Adenine Nuclei: Syntheses of (±)-Agelasimine-A and (±)-Agelasimine-B. Having successfully developed an efficient route to the diol (±)-**13**, a common candidate precursor for the diterpene portions of (±)-agelasimine-A and -B, we commenced the construction of their adenine portions according to our previous synthetic routes to the *N*7-benzyl analogues **1b** and **2b**.[6a,c] Alkylation of 3-methyladenine[22] with the unstable bromide (±)-**20**, derived from (±)-**13** via regioselective bromination of the primary hydroxy group with PBr_3, provided (±)-**21** in 65% overall yield from (±)-**13** after basification of the resulting hydrobromide salt with aqueous NaOH (Scheme 3). In a few cases, alkylation of 3-alkyladenine with alkyl halide has been shown to furnish 3,9-dialkyladenine as the minor product along with the major product 3,7-dialkyladenine.[23] The stability of (±)-**21** under alkaline conditions may rule out the possibility that the alkylated product of 3-methyladenine was not the 3,7-dialkyl derivative (±)-**21**, but the alternative 3,9-dialkyl isomer, since the latter is considered to be very unstable under the alkaline conditions employed.[24] Furthermore, the structure of (±)-**21** was confirmed by a 9% NOE enhancement of the C8-proton signal and the lack of such enhancement of the *N*3-Me signal on irradiation of the *N*7-CH_2 signal. Finally, methylation of (±)-**21** with MeI followed by basification of the resulting hydriodide salt with aqueous NaOH afforded the target molecule (±)-**1a** in 58% yield. The UV, IR, ^{1}H NMR, ^{13}C NMR, and mass spectra of synthetic (±)-**1a** proved to be virtually identical with those[2] obtained with a natural sample of agelasimine-A.

Our attention was next turned to the synthesis of another target compound, (±)-**2a**. Reduction of (±)-**21** with $NaBH_4$ afforded the 1,2-dihydro derivative (±)-**22**, which was then methylated with MeI to give the crude salt (±)-**2a**·HI. On treatment with aqueous NaOH, the crude salt furnished the desired free base (±)-**2a** in 39% overall yield [from (±)-**21**]. The 1,2-dihydro-1,3-dimethyladenine structure was assignable to (±)-**2a** on the basis of NOE experiments: 3−4% enhancements observed for the two *N*-Me signals on irradiation of the C2-proton signal revealed the proximity of these three groups. The IR, ^{1}H NMR, ^{13}C NMR, and mass spectra of synthetic (±)-**2a** were shown to be virtually superimposable on those[2] recorded for natural agelasimine-B.

Meantime, dehydrogenation of (±)-**2a** was also examined according to precedents.[6a,c,25] On oxidation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in $CHCl_3$, followed by

(18) (a) Vessière, R.; Théron, F. *C. R. Acad. Sci., Ser. C* **1965**, *260*, 597−599. (b) Théron, F.; Vessière, R. *Bull. Soc. Chim. Fr.* **1968**, 2994−3000. (c) Mavrov, M. V.; Urdaneta, N. A.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989**, 1409−1412.

(19) (a) Kondo, K.; Sodeoka, M.; Shibasaki, M. *Tetrahedron: Asymmetry* **1995**, *6*, 2453−2464. (b) Kondo, K.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 4322−4323.

(20) Johnson, C. R.; Braun, M. P. *J. Am. Chem. Soc.* **1993**, *115*, 11014−11015.

(21) For a review on reduction of epoxides to alcohols, see: Smith, J. G. *Synthesis* **1984**, 629−656.

(22) Jones, J. W.; Robins, R. K. *J. Am. Chem. Soc.* **1962**, *84*, 1914−1919.

(23) (a) Leonard, N. J.; Fujii, T. *J. Am. Chem. Soc.* **1963**, *85*, 3719. (b) Fujii, T.; Walker, G. C.; Leonard, N. J.; DeLong, D. C.; Gerzon, K. *J. Med. Chem.* **1979**, *22*, 125−129. (c) Fujii, T.; Saito, T.; Inoue, I.; Kumazawa, Y.; Leonard, N. J. *Chem. Pharm. Bull.* **1986**, *34*, 1821−1825. (d) Leonard, N. J.; Fujii, T.; Saito, T. *Chem. Pharm. Bull.* **1986**, *34*, 2037−2043.

(24) Fujii, T.; Itaya, T.; Saito, T.; Mohri, K.; Kawanishi, M.; Nakasaka, T. *Chem. Pharm. Bull.* **1989**, *37*, 1504−1513.

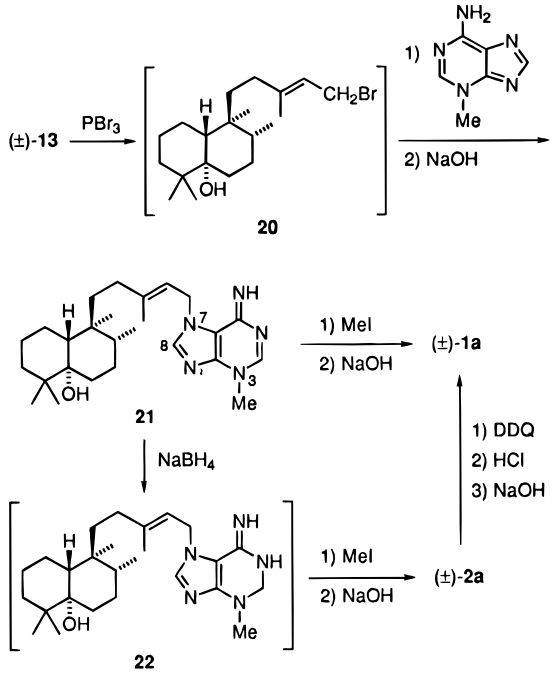
(25) Fujii, T.; Saito, T.; Nakasaka, T. *Chem. Pharm. Bull.* **1983**, *31*, 3521−3527.

Table 2. Hydroboration of the Alkene (±)-**16** with 9-BBN and Cross-Coupling Reaction of the Generated 9-Alkyl-9-BBN (±)-**17** with **15a**−**c**

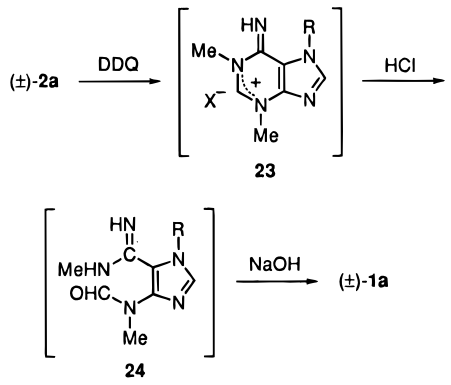
	hydroboration[a]	cross-coupling reaction[b]					
entry	amt of 9-BBN (equiv)	**15a**−**c**[b] X	method[b]	[$PdCl_2$(dppf)] (mol %)	[H_2O] (equiv mol)	[Ph_3As] (mol %)	(±)-**19** yield[c] (%)
1	1.0	OTf	C	3.2	12	11	13
2	1.1	Br	C	3.2	12	11	37
3	1.1	Br	C	10	36	11	48
4	3.0	Br	C	10	36	11	55
5	1.1	I	A	10			40
6	3.0	I	A	10			4
7	1.1	I	B[d]	10			53
8	3.0	I	B	10			14
9	3.0	I	B	10	36		60
10	3.0	I	C	10	36		62
11	3.0	I	C	10		11	46
12	1.1	I	C	10	12	11	50
13	3.0	I	C	10	12	11	75
14	3.0	I	C	10	36	11	84

[a] All reactions were carried out in THF at room temperature for 1.5 h. [b] All cross-coupling reactions were conducted using 1.1 equiv of **15a**−**c** under the following conditions, except for those indicated in the table: method A, K_3PO_4 (1.5 equiv) in boiling THF for 16 h; method B, K_2CO_3 (2.0 equiv) in THF−DMF at 50 °C for 5 h; method C, Cs_2CO_3 (1.8 equiv) in THF−DMF at room temperature for 3.5 h. [c] Isolated yields. [d] The reaction time was prolonged up to 8 h.

Scheme 3



Scheme 4



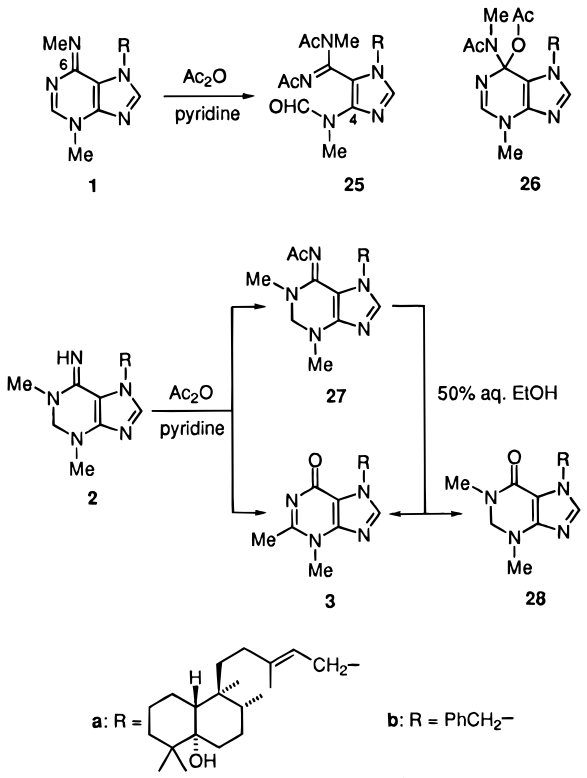
successive treatment with aqueous HCl and aqueous NaOH, (±)-**2a** gave (±)-**1a** in 43% yield. This transformation, considered to have proceeded through (±)-**23** and (±)-**24** (Scheme 4), may be suggestive of a possible biosynthetic pathway from agelasimine-B (**2a**) to agelasimine-A (**1a**).

Acetylations of (±)-1a and (±)-2a: Synthesis of (±)-Purino-diterpene and the Structure of Diacetylagelasimine-A. In connection with the structure elucidation of the above two marine sponge diterpenoids, Fathi-Afshar and Allen further reported the acetylations of **1a** and **2a** with acetic anhydride in pyridine to produce diacetylagelasimine-A and N^6-acetylagelasimine-B (**27**), respectively.[2] Diacetylagelasimine-A, although its exact nature has not been firmly established (mixture of isomers), was assigned structure **26** on the basis of ^{1}H NMR and mass spectral data.[2] However, its structure corresponds to a very reactive tetrahedral intermediate, probably difficult to isolate, in the acetolysis of the C6═NMe group in **1a**. Therefore, we first investigated the acetylation of (±)-agelasimine-A [(±)-**1a**] to check the structure of diacetylagelasimine-A.

On treatment with excess acetic anhydride in pyridine under conditions similar to those reported for **1a**,[2] (±)-**1a** afforded a 1:1 adduct of (±)-**1a** and acetic anhydride in 54% yield (Scheme 5). The ^{1}H NMR spectrum of the adduct in $CDCl_3$ at 27 °C exhibited two sets of signals, all with a 3:1 ratio of relative integral intensities, for most of the different species of protons. Similarly, two sets of signals were also observed in DMSO-d_6 at 27 °C, but they coalesced into one set at 100 °C. We have already reported that a parallel acetylation of the *N*7-benzyl congener **1b** yielded the imidazole derivative **25b**, whose structure was definitely determined on the basis of a single-crystal X-ray diffraction analysis, and that **25b** showed a similar ^{1}H NMR spectral behavior explicable in terms of *cis*−*trans* equilibration of the amide groups, most likely that of the *N*-methylformamide group at C4.[6b,c] Structure (±)-**25a** was therefore assignable to the adduct, and its formation from (±)-**1a** by acetylation may be assumed to proceed through a mechanism similar to that proposed[6c] for the benzyl analogue. In the ^{1}H NMR spectrum of (±)-**25a** in $CDCl_3$, a set of signals arising from the major geometrical isomer was found to match the data reported[2] for diacetylagelasimine-A. Thus, the structure of "diacetylagelasimine-A" obtained via a similar acetylation of agelasimine-A (**1a**) should be represented not by the proposed[2] purine form **26a** but by the monocyclic imidazole form **25a**.

Next the acetylation of (±)-agelasimine-B [(±)-**2a**] was examined. Treatment of (±)-**2a** with excess acetic anhydride in pyridine at room temperature for 1 h afforded (±)-**27a** (48% yield), whose ^{1}H NMR and mass spectral data were identical with those reported[2] for N^6-acetylagelasimine-B (Scheme 5).

Scheme 5



Interestingly, elongation of the reaction time from 1 to 50 h led to the formation of (±)-purino-diterpene [(±)-**3a**] and (±)-**27a** in 60% and 15% yields, respectively. A parallel result was obtained when the acetylation of (±)-**2a** was conducted in the absence of pyridine. Hydrolysis of (±)-**27a** in boiling 50% aqueous EtOH produced (±)-**3a** and the dihydrohypoxanthine derivative (±)-**28a** in 22% and 39% yields, respectively. The ^{1}H NMR spectral data for (±)-**3a** thus synthesized were in agreement with those reported[5] selectively for purino-diterpene (isolated from the acetylated mixture of the crude extract of *A. mauritiana*). The formation of (±)-**3a** and (±)-**28a** from (±)-**27a** may be explained in terms of a mechanism similar to that proposed[6b,c] for the *N*7-benzyl series (**27b** → **3b** + **28b**).

Conclusions

The first total syntheses of the two adenine-related bicyclic diterpenoids, agelasimine-A and agelasimine-B, have been achieved in the forms of racemic modifications through the routes featuring a highly stereoselective construction of the diol (±)-**13** and regioselective *N*-alkylations of the adenine ring. Their structures and relative stereochemistries have now been defined as shown in formulas (±)-**1a** and (±)-**2a**, respectively. The results derived from the acetylations of (±)-**1a** and (±)-**2a** have emphasized that the structure of "diacetylagelasimine-A" is **25a** instead of **26a**, and that purino-diterpene (**3a**) might have originated from agelasimine-B (**2a**) via N^6-acetylagelasimine-B (**27a**).

Experimental Section

General Methods. All melting points were determined on a Büchi model 530 capillary melting point apparatus and are corrected. TLC was performed on Merck 0.25-mm precoated silica gel plates or Merck 0.20-mm precoated aluminum oxide sheets. Chromatographic purification of products was accomplished using Merck silica gel (no. 9385) for flash chromatography,[26] Merck aluminum oxide (no. 1097) for column chromatography, and either Merck 0.50-mm precoated silica gel plates or Merck aluminum oxide (no. 1092) for preparative TLC. The ratios of solvent mixtures are shown in v/v. Air- and/or moisture-sensitive reactions were performed in oven-dried glassware under an argon or nitrogen atmosphere. Unless otherwise noted, the organic solutions obtained after extraction were concentrated under reduced pressure. UV spectra reported herein were recorded on a Hitachi 320 UV spectrophotometer on solutions in MeOH, 95% (v/v) aqueous EtOH, 80% (v/v) aqueous EtOH containing HCl at 0.1 M concentration (solvent A), 80% (v/v) aqueous EtOH (solvent N), and 80% (v/v) aqueous EtOH containing NaOH at 0.1 M concentration (solvent B). Other spectra were measured with a Shimadzu FTIR-8100 IR spectrophotometer, either a Hitachi M-80 or a JEOL JMS-SX102A mass spectrometer, and either a JEOL JNM-GSX-500 (^{1}H 500 MHz, ^{13}C 125 MHz) or a JEOL JNM-EX-270 (^{1}H 270 MHz) NMR spectrometer. Chemical shifts are reported in δ values relative to internal TMS. Elemental analyses and MS measurements were performed by Mr. Y. Itatani and his associates at Kanazawa University.

(±)-(3α,4*β*)-3-Ethenyl-2-(hydroxymethyl)-3,4-dimethylcyclohexanone [(±)-6]. To a stirred mixture of $Yb(OTf)_3$[27] (4.71 g, 7.6 mmol), commercial formaldehyde solution (190 mL), and THF (540 mL) was added a solution of (±)-*trans*-[(3-ethenyl-3,4-dimethyl-1-cyclohexen-1-yl)oxy]trimethylsilane [(±)-**5**][10] (17.06 g, 76 mmol) in THF (160 mL) over 30 min. The mixture was stirred at room temperature for 24 h, and the THF was then removed *in vacuo*. The residue, after addition of H_2O (400 mL), was extracted with CH_2Cl_2. The CH_2Cl_2 extracts were dried over anhydrous $MgSO_4$ and concentrated to leave a pale yellow oil. Distillation of the oil under reduced pressure provided a fore-run (6.00 g) as a colorless oil, bp 55−130 °C (5 mmHg), and (±)-**6** (8.14 g) as a colorless oil, bp 130−130.5 °C (5 mmHg), which was found to be a 2:1 mixture of the two possible diastereoisomers on the basis of ^{1}H NMR spectra. The IR and ^{1}H NMR spectral data for this sample were in agreement with those reported in the literature.[8] Purification of the fore-run by flash chromatography (silica gel, 3:2 hexane−EtOAc) gave an additional amount of (±)-**6**. The total yield of (±)-**6** was 10.60 g (77%).

(±)-(4aα,5α,6*β*)-5-Ethenyl-3,4,4a,5,6,7-hexahydro-1,1,5,6-tetramethyl-2(1*H*)-naphthalenone [(±)-8]. A mixture of (±)-(4aα,5α,6*β*)-5-ethenyl-4,4a,5,6,7,8-hexahydro-1,5,6-trimethyl-2(3*H*)-naphthalenone [(±)-**7**][8] (2.18 g, 10 mmol) and *t*-BuOK (1.68 g, 15 mmol) in *t*-BuOH (100 mL) was heated under reflux, and a solution of MeI (1.25 mL, 20 mmol) in *t*-BuOH (20 mL) was added dropwise over 20 min. Heating was continued for a further 30 min, and the reaction mixture was concentrated *in vacuo*. The residue, after neutralization with 1 N aqueous HCl, was partitioned between CH_2Cl_2 and H_2O. The CH_2Cl_2 extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated. Purification of the residual oil by flash chromatography (silica gel, 16:1 hexane−EtOAc) gave (±)-**8** (1.93 g, 83%) as a colorless solid, mp 48.5−52.5 °C. Recrystallization of the solid from MeOH−H_2O (2:1) afforded an analytical sample as colorless needles: mp 53.5−54.5 °C; IR (Nujol) ν_{max} 1715, 1639 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.75 (3H, s, C5-Me), 0.80 (3H, d, J = 6.8 Hz, C6-Me), 1.24 and 1.25 (6H, s each, C1-Me$_2$), 1.48−1.63 (2H, m, C4-H and C6-H), 1.78 (1H, dddd, J = 18, 11.5, 4, 2 Hz, C7-H), 1.85 (1H, dddd, J = 13.5, 5, 5, 5 Hz, C4-H), 2.06 (1H, dddd, J = 18, 5.5, 5.5, 2 Hz, C7-H), 2.33 (1H, m, C4a-H), 2.34 (1H, ddd, J = 15.5, 5, 5 Hz, C3-H), 2.48 (1H, ddd, J = 15.5, 11.5, 5 Hz, C3-H), 5.00 (1H, dd, J = 17.5, 1 Hz, CH=C*H*$_2$), 5.14 (1H, dd, J = 10.5, 1 Hz, CH=C*H*$_2$), 5.59 (1H, dd, J = 17.5, 10.5 Hz, C*H*=CH$_2$), 5.64 (1H, ddd, J = 5.5, 2, 2 Hz, C8-H); MS *m*/*z* 232 (M$^+$). Anal. Calcd for $C_{16}H_{24}O$: C, 82.70; H, 10.41. Found: C, 82.41; H, 10.71.

(±)-(1α,2*β*,8aα)-1-Ethenyl-1,2,3,5,6,7,8,8a-octahydro-1,2,5,5-tetramethylnaphthalene [(±)-9]. A mixture of (±)-**8** (5.81 g, 25 mmol), diethylene glycol (50 mL), 80% aqueous hydrazine hydrate (4.69 g, 75 mmol), and KOH (4.21 g, 75 mmol) was placed in a flask equipped with a descending condenser. The mixture was heated at 130 °C in an oil bath with stirring for 1 h. Then, the temperature of the oil bath was slowly raised to 190 °C in 1 h, and the mixture was further heated at 190 °C for 3 h to give a small amount of distillate. After cooling,

(26) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.

(27) Forsberg, J. H.; Spaziano, V. T.; Balasubramanian, T. M.; Liu, G. K.; Kinsley, S. A.; Duckworth, C. A.; Poteruca, J. J.; Brown, P. S.; Miller, J. L. *J. Org. Chem.* **1987**, *52*, 1017−1021.

the reaction mixture was poured into H_2O (150 mL), acidified with 2 N aqueous HCl, and extracted with ether. The ethereal extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated to leave a pale yellow oil. Purification of the oil by flash chromatography (silica gel, hexane) furnished (±)-**9** (5.06 g, 93%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 0.71 (3H, s, C1-Me), 0.75 (3H, d, J = 6.8 Hz, C2-Me), 1.01 and 1.07 (6H, s each, C5-Me$_2$), 0.94 (1H, m, C8-H), 1.20 (1H, ddd, J = 13, 13, 4.5 Hz, C6-H), 1.36−1.66 (5H, m, C2-H, C6-H, C7-H$_2$, C8-H), 1.74 (1H, dddd, J = 17.5, 11, 3.5, 2 Hz, C3-H), 1.90 (1H, dddd, J = 17.5, 6, 5, 2 Hz, C3-H), 1.99 (1H, m, C8a-H), 4.91 (1H, dd, J = 17.5, 1.5 Hz, CH=CH_2), 5.06 (1H, dd, J = 10.5, 1.5 Hz, CH=CH_2), 5.48 (1H, ddd, J = 6, 2, 2 Hz, C4-H), 5.55 (1H, dd, J = 17.5, 10.5 Hz, CH=CH$_2$); MS m/z 218 (M^+).

(±)-(1α,2*β*,8aα)-2-(1,2,3,5,6,7,8,8a-Octahydro-1,2,5,5-tetramethyl-1-naphthalenyl)ethanol [(±)-14]. A Typical Example (Entry 4 in Table 1). To a 0.5 M solution (3.0 mL, 1.5 mmol) of 9-BBN in THF was added dropwise a solution of (±)-**9** (109 mg, 0.50 mmol) in THF (0.5 mL) over 2 min, and the mixture was heated under reflux for 2 h. After cooling, the reaction mixture was treated with EtOH (0.9 mL), 3 N aqueous NaOH (0.6 mL), and 30% aqueous H_2O_2 (0.6 mL) at 50 °C for 1 h. The aqueous layer was saturated with K_2CO_3, separated from the organic layer, and extracted with ether. The combined organic layers were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated. Purification of the residue by flash chromatography (silica gel, 99:1 $CHCl_3$−EtOH) provided (±)-**14** (97 mg, 82%) as a colorless solid, mp 98.5−103 °C. Recrystallization of the solid from MeOH−H_2O (2:1) gave an analytical sample as colorless needles: mp 106−107 °C; ^{1}H NMR ($CDCl_3$) δ 0.66 (3H, s, C1-Me), 0.87 (3H, d, J = 6.8 Hz, C2-Me), 0.99 and 1.06 (6H, s each, C5-Me$_2$), 1.05 (1H, m, C8-H), 1.20 (1H, ddd, J = 13, 13, 4.5 Hz, C6-H), 1.37−1.64 (5H, m) and 1.69−1.88 (4H, m) (C2-H, C3-H$_2$, C6-H, C7-H$_2$, C8-H, and C1-CH$_2$), 2.13 (1H, m, C8a-H), 3.69 (2H, dt, J = 4.5, 8 Hz, CH_2OH), 5.43 (1H, ddd, J = 6, 3, 3 Hz, C4-H); HRMS m/z calcd for $C_{16}H_{28}O$ 236.2140, found 236.2137. Anal. Calcd for $C_{16}H_{28}O$: C, 81.29; H, 11.94. Found: C, 81.26; H, 11.94.

(±)-2-(3-Cyclohexenyl)ethanol [(±)-18]. To a 0.5 M solution (5.0 mL, 2.5 mmol) of 9-BBN in THF was added dropwise a solution of (±)-4-vinyl-1-cyclohexene [(±)-**16**] (270 mg, 2.5 mmol) in THF (1.5 mL) over 3 min, and the mixture was stirred at room temperature for 1.5 h. After having been treated with EtOH (1.5 mL), 6 N aqueous NaOH (0.5 mL), and 30% aqueous H_2O_2 (1.0 mL) at 50 °C for 1 h, the reaction mixture was worked up as described above for (±)-**14**. Purification of the crude oily product by flash chromatography (silica gel, 3:1 hexane−EtOAc) afforded (±)-**18**[16] (294 mg, 93%) as a colorless oil. The ^{1}H and ^{13}C NMR and IR spectral data for this sample were in agreement with those reported in the literature.[16b]

***(E)*-3-[[(Trifluoromethyl)sulfonyl]oxy]-2-butenoic Acid Ethyl Ester (15a).** According to the procedure of Keenan et al.,[28] this compound was prepared as follows. To a stirred suspension of NaH (60% oil dispersion, 300 mg, 7.5 mmol) in DMF (5 mL) at room temperature was added dropwise a solution of ethyl acetoacetate (651 mg, 5.0 mmol) in DMF (5 mL), and stirring was continued for 30 min. After addition of *N*-phenyltrifluoromethanesulfonimide (2.68 g, 7.5 mmol), the reaction mixture was stirred for a further 2 h, then diluted with ether, washed successively with saturated aqueous NH_4Cl, H_2O, and saturated aqueous NaCl, and concentrated *in vacuo*. Purification of the residual brown oil by flash chromatography (silica gel, 4:1 hexane−$CHCl_3$) provided **15a**[17] (661 mg, 50%) as a colorless oil: IR (neat) ν_{max} 1730, 1674 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.31 (3H, t, J = 7 Hz, OCH$_2$*Me*), 2.51 (3H, d, J = 0.9 Hz, C3-Me), 4.22 (2H, q, J = 7 Hz, OCH_2Me), 5.95 (1H, q, J = 0.9 Hz, C2-H); MS m/z 262 (M^+).

***(E)*-3-Bromo-2-butenoic Acid Ethyl Ester (15b).** The (*Z*)-isomer[18] (2.18 g, 11.3 mmol) was heated at 220 °C under argon in a sealed tube for 5 h. The resulting brown oil was purified by flash chromatography (silica gel, 20:1 hexane−EtOAc) to afford **15b**[18] (1.26 g, 58%) as a colorless oil: bp 83.5−84.5 °C (28 mmHg); IR (neat) ν_{max} 1720, 1634 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (3H, t, J = 7 Hz, OCH$_2$*Me*), 2.78 (3H, d, J = 1.1 Hz, C3-Me), 4.17 (2H, q, J = 7 Hz, OCH_2Me), 6.33 (1H, q, J = 1.1 Hz, C2-H); MS m/z 194 and 192 (M^+).

***(E)*-3-Iodo-2-butenoic Acid Ethyl Ester (15c).** The (*Z*)-isomer[14,29] (2.09 g, 8.7 mmol) was heated at 220 °C under argon in a sealed tube for 4 h. Purification of the resulting brown oil by flash chromatography (silica gel, 3:2 hexane−CH_2Cl_2) furnished **15c**[14] (1.44 g, 69%) as a colorless oil: bp 96−98 °C (24 mmHg); IR (neat) ν_{max} 1717, 1619 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (3H, t, J = 7 Hz, OCH$_2$*Me*), 2.98 (3H, d, J = 1.4 Hz, C3-Me), 4.16 (2H, q, J = 7 Hz, OCH_2Me), 6.63 (1H, q, J = 1.4 Hz, C2-H); MS m/z 240 (M^+).

(±)-(*E*)-5-(3-Cyclohexenyl)-3-methyl-2-pentenoic Acid Ethyl Ester [(±)-19]. A Typical Example (Entry 14 in Table 2). To a 0.5 M solution (1.8 mL, 0.9 mmol) of 9-BBN in THF was added dropwise a solution of (±)-**16** (32.5 mg, 0.30 mmol) in THF (0.4 mL) over 2 min, and the mixture was stirred at room temperature for 1.5 h. In a separate flask, a solution of the iodide **15c** (79 mg, 0.33 mmol) in DMF (0.2 mL) was added to a stirred mixture of Cs_2CO_3 (176 mg, 0.54 mmol), $PdCl_2$(dppf)[15] (25 mg, 10 mol %), Ph_3As (10 mg, 11 mol %), and DMF (1 mL). Then, H_2O (0.195 mL, 36 equiv mol) and the above THF solution of the borane were added in that order. After having been stirred at room temperature for 3.5 h, the reaction mixture was poured into H_2O (10 mL) and extracted with ether. The ethereal extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated to leave a brown oil. Purification of the oil by flash chromatography (silica gel, 3:2 hexane−CH_2Cl_2) provided (±)-**19** (56 mg, 84%) as a colorless oil: IR (neat) ν_{max} 1717, 1651 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (3H, t, J = 7 Hz, OCH$_2$*Me*), 1.20−1.30 (1H, m), 1.39−1.77 (5H, m), and 2.02−2.20 (5H, m) (C1′-H, C2′-H$_2$, C5′-H$_2$, C6′-H$_2$, C4-H$_2$, and C5-H$_2$), 2.16 (3H, d, J = 1.0 Hz, C3-Me), 4.14 (2H, q, J = 7 Hz, OCH_2Me), 5.62−5.69 (3H, m, C3′-H, C4′-H, and C2-H);[30] HRMS m/z calcd for $C_{14}H_{22}O_2$ 222.1620, found 222.1610.

(±)-[1α(*E*),2*β*,8aα]-3-Methyl-5-(1,2,3,5,6,7,8,8a-octahydro-1,2,5,5-tetramethyl-1-naphthalenyl)-2-pentenoic Acid Ethyl Ester [(±)-10]. To a 0.5 M solution (24 mL, 12 mmol) of 9-BBN in THF was added dropwise a solution of (±)-**9** (874 mg, 4.0 mmol) in THF (5 mL) over 5 min, and the mixture was heated under reflux for 2 h. In a separate flask were placed Cs_2CO_3 (2.35 g, 7.2 mmol), $PdCl_2$(dppf)[15] (327 mg, 10 mol %), Ph_3As (123 mg, 10 mol %), the iodide **15c** (1.06 g, 4.4 mmol), DMF (17 mL), and H_2O (0.86 mL, 12 equiv mol). After addition of the above THF solution of the borane, the reaction mixture was stirred at room temperature for 3 h and then worked up in a manner similar to that described above for (±)-**19**. Purification of the crude oily product by flash chromatography (silica gel, 3:2 benzene−hexane) yielded (±)-**10** (995 mg, 75%) as a colorless oil: IR (neat) ν_{max} 1717, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.64 (3H, s, C1′-Me), 0.82 (3H, d, J = 6.8 Hz, C2′-Me), 1.01 and 1.07 (6H, s each, C5′-Me$_2$), 1.04 (1H, m, C8′-H), 1.20 (1H, ddd, J = 13, 13, 4.5 Hz, C6′-H), 1.28 (3H, t, J = 7 Hz, OCH$_2$*Me*), 1.36−2.20 (12H, m, C2′-H, C3′-H$_2$, C6′-H, C7′-H$_2$, C8′-H, C8′a-H, C4-H$_2$, and C5-H$_2$), 2.19 (3H, s, C3-Me), 4.15 (2H, q, J = 7 Hz, OCH_2Me), 5.44 (1H, ddd, J = 5.5, 3, 2.5 Hz, C4′-H), 5.69 (1H, br s, C2-H);[30] MS m/z 332 (M^+).

(±)-[1α(*E*),2*β*,4*β*,4a*β*,8aα]-5-(Decahydro-4,4a-epoxy-1,2,5,5-tetramethyl-1-naphthalenyl)-3-methyl-2-pentenoic Acid Ethyl Ester [(±)-11]. A solution of (±)-**10** (389 mg, 1.17 mmol) and MCPBA (ca. 70% purity, 345 mg, 1.4 mmol) in CH_2Cl_2 (12 mL) was stirred at 0 °C for 2 h. The reaction mixture was then washed successively with 10% aqueous Na_2SO_3, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Purification of the residual oil by flash chromatography (silica gel, 3:2 CH_2Cl_2−hexane) furnished (±)-**11** (346 mg, 85%) as a colorless oil: IR (neat) ν_{max} 1717, 1647 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.69, 0.74, and 1.07 (3H each, s, C1′-Me and C5′-Me$_2$), 0.76 (3H, d, J = 6.8 Hz, C2′-Me), 1.24−1.73 (9H, m, C2′-H, C6′-H$_2$, C7′-H$_2$, C8′-H$_2$, and C5-H$_2$), 1.28 (3H, t, J = 7 Hz, OCH$_2$*Me*), 1.66 (1H, dd, J = 15.5, 12.5 Hz, C3′-H), 1.80 (1H, ddd, J = 15.5, 6, 6 Hz, C3′-H), 1.88 (1H, dd, J = 12.5, 3 Hz, C8′a-H), 1.98 (2H, dd, J = 9, 8.5 Hz, C4-H$_2$), 2.17 (3H, d, J = 1.5 Hz, C3-Me), 3.16 (1H, d, J = 6 Hz, C4′-H), 4.15 (2H, q, J =

(28) Keenan, R. M.; Weinstock, J.; Finkelstein, J. A.; Franz, R. G.; Gaitanopoulos, D. E.; Girard, G. R.; Hill, D. T.; Morgan, T. M.; Samanen, J. M.; Hempel, J.; Eggleston, D. S.; Aiyar, N.; Griffin, E.; Ohlstein, E. H.; Stack, E. J.; Weidley, E. F.; Edwards, R. *J. Med. Chem.* **1992**, *35*, 3858−3872.

(29) Piers, E.; Wong, T.; Coish, P. D.; Rogers, C. *Can. J. Chem.* **1994**, *72*, 1816−1819.

(30) For convenience, each position of the cyclohexene or naphthalene ring is indicated by a primed number.

7 Hz, OC*H*$_2$Me), 5.67 (1H, q, J = 1.5 Hz, C2-H);[30] HRMS *m*/*z* calcd for $C_{22}H_{36}O_3$ 348.2665, found 348.2666.

(±)-[1α(*E*),2*β*,4a*β*,8aα]-5-(Decahydro-4,4a-epoxy-1,2,5,5-tetramethyl-1-naphthalenyl)-3-methyl-2-penten-1-ol [(±)-12]. A solution of (±)-**11** (415 mg, 1.19 mmol) in CH_2Cl_2 (5 mL) was cooled to −78 °C, and a 0.93 M solution (4.0 mL, 3.7 mmol) of DIBAH in hexane was added dropwise over 10 min. After the mixture had been stirred at −78 °C for 45 min, the reaction was quenched by adding a 5 M solution (4 mL) of AcOH in CH_2Cl_2 at −78 °C. The resulting mixture was then stirred at room temperature, and 10% aqueous tartaric acid (5.5 mL) and H_2O (4 mL) were added. The aqueous layer was separated from the organic layer and extracted with CH_2Cl_2. The CH_2Cl_2 extracts and the above organic layer were combined, washed successively with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated to leave a colorless oil. Purification of the oil by flash chromatography (silica gel, 3:1 hexane−EtOAc) gave (±)-**12** (316 mg, 87%) as a colorless oil: IR (neat) ν_{max} 3400, 1669 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.69, 0.72, and 1.07 (3H each, s, C1′-Me and C5′-Me), 0.75 (3H, d, J = 6.8 Hz, C2′-Me), 1.15 (1H, br, OH), 1.20−1.73 (9H, m, C2′-H, C6′-H$_2$, C7′-H$_2$, C8′-H$_2$, and C5-H$_2$), 1.65 (1H, dd, J = 15.5, 12.5 Hz, C3′-H), 1.69 (3H, br s, C3-Me), 1.79 (1H, ddd, J = 15.5, 6, 6 Hz, C3′-H), 1.86 (2H, dd, J = 9, 8.5 Hz, C4-H$_2$), 1.91 (1H, dd, J = 12.5, 3 Hz, C8′a-H), 3.16 (1H, d, J = 6 Hz, C4′-H), 4.15 (2H, d, J = 7 Hz, C*H*$_2$OH), 5.42 (1H, qt, J = 1, 7 Hz, C2-H);[30] HRMS *m*/*z* calcd for $C_{20}H_{34}O_2$ 306.2559, found 306.2544.

(±)-[1α(*E*),2*β*,4a*β*,8aα]-5-(Decahydro-4a-hydroxy-1,2,5,5-tetramethyl-1-naphthalenyl)-3-methyl-2-penten-1-ol [(±)-13]. To a stirred suspension of $LiAlH_4$ (812 mg, 21.4 mmol) in THF (100 mL) was added dropwise a solution of (±)-**12** (3.28 g, 10.7 mmol) in THF (50 mL) over 10 min. After the mixture had been heated under reflux for 2 h, wet ether (50 mL) and H_2O (50 mL) were added in that order under ice-cooling. The insoluble material that resulted was removed by filtration, and the aqueous layer in the filtrate was separated from the organic layer and extracted with ether. The ethereal extracts and the above organic layer were combined, washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated to leave a colorless semisolid, which was then triturated with hexane (3 mL). The insoluble solid was collected by filtration and dried to give (±)-**13** (2.56 g, 78%), mp 132−133.5 °C. Recrystallization from hexane afforded an analytical sample as colorless prisms: mp 134.5−135 °C; IR (Nujol) ν_{max} 3455, 3340, 1671 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.81 (3H, d, J = 6.8 Hz, C2′-Me), 0.83, 0.86, and 0.99 (3H each, s, C1′-Me and C5′-Me$_2$), 1.12 (1H, br, OH), 1.19 (1H, s, OH), 1.08−1.14 (1H, m), 1.27−1.70 (13H, m), 1.18 (1H, ddd, J = 13, 13, 5 Hz), and 1.90 (1H, ddd, J = 13, 13, 4.5 Hz) (C2′-H, C3′-H$_2$, C4′-H$_2$, C6′-H$_2$, C$_7$′-H$_2$, C8′-H$_2$, C8′a-H, C4-H$_2$, and C5-H$_2$), 1.69 (3H, br s, C3-Me), 4.15 (2H, br, C*H*$_2$OH), 5.41 (1H, qt, J = 1, 7 Hz, C2-H);[30] ^{13}C NMR ($CDCl_3$) δ 16.0 (q), 16.5 (q), 17.5 (q), 21.7 (t), 22.1 (t), 24.1 (q), 24.5 (q), 26.4 (t), 32.1 (t), 32.9 (t), 36.1 (t), 36.6 (d), 37.0 (t), 38.8 (s), 38.9 (s), 41.0 (d), 59.5 (t), 76.4 (s), 123.1 (d), 140.7 (s); HRMS *m*/*z* calcd for $C_{20}H_{36}O_2$ 308.2715, found 308.2708. Anal. Calcd for $C_{20}H_{36}O_2$: C, 77.87; H, 11.76. Found: C, 77.67; H, 11.71. The relative stereochemistry of (±)-**13** was established on the basis of a single-crystal X-ray diffraction analysis.[7a]

(±)-[1α(*E*),2*β*,4a*β*,8aα]-1-[5-(3,6-Dihydro-6-imino-3-methyl-7*H*-purin-7-yl)-3-methyl-3-pentenyl]octahydro-1,2,5,5-tetramethyl-4a-(2*H*)-naphthalenol [(±)-21]. A solution of (±)-**13** (1.49 g, 4.8 mmol) in ether (100 mL) was cooled to 0 °C, and PBr_3 (0.65 g, 2.4 mmol) was added dropwise over 10 min. After the mixture had been maintained at 0 °C with stirring for 1 h, MeOH (2.2 mL) was added. The reaction mixture was then brought to room temperature, washed successively with H_2O, 5% aqueous $NaHCO_3$, and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo* to leave crude (±)-**20** (1.63 g) as a yellow oil. The oil was dissolved in $AcNMe_2$ (6 mL), and the solution was added dropwise to a stirred solution of 3-methyladenine[22] (716 mg, 4.8 mmol) in $AcNMe_2$ (18 mL) at 50 °C over 5 min. After having been stirred at 50 °C for a further 2 h, the reaction mixture was concentrated *in vacuo*. A suspension of the residue in H_2O (12 mL) was made strongly basic by addition of 10% aqueous NaOH (17 mL) and then extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with saturated aqueous NaCl, dried over anhydrous K_2CO_3, and concentrated to leave a yellow oil. Purification of the oil by column chromatography (alumina, 3:1 $CHCl_3$−MeOH) provided (±)-**21** [1.38 g, 65% from (±)-**13**] as a yellow glass: UV (95% aqueous EtOH) λ_{max} (ϵ) 224 (sh) (12 200), 280 (13 400) nm; UV (solvent A) λ_{max} (ϵ) 223 (sh) (11 000), 279 (13 700) nm; UV (solvent N) λ_{max} (ϵ) 223 (sh) (11 000), 279 (13 600) nm; UV (solvent B) λ_{max} (ϵ) 282 (11 200) nm; IR ($CHCl_3$) ν_{max} 3620, 1642 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80 (3H, d, J = 6.8 Hz, C2-Me), 0.83, 0.86, and 0.97 (3H each, s, C1-Me and C5-Me$_2$), 1.18 (1H, s, OH), 1.10 (1H, br d, J = 13 Hz), 1.23−1.68 (13H, m), 1.86 (1H, ddd, J = 12.5, 12.5, 5 Hz), and 1.96 (1H, ddd, J = 12.5, 12.5, 4.5 Hz) (C2-H, C3-H$_2$, C4-H$_2$, C6-H$_2$, C7-H$_2$, C8-H$_2$, C8a-H, C1′-H$_2$, and C2′-H$_2$), 1.79 (3H, s, C3′-Me), 3.66 (3H, s, N3″-Me), 5.15 (2H, d, J = 7 Hz, C5′-H$_2$), 5.48 (1H, t, J = 7 Hz, C4′-H), 7.51 and 7.55 (1H each, s, purine protons);[31] HRMS *m*/*z* calcd for $C_{26}H_{41}N_5O$ 439.3311, found 439.3318.

(±)-Agelasimine-A [(±)-1a]. A solution of (±)-**21** (133 mg, 0.30 mmol) and MeI (213 mg, 1.5 mmol) in $AcNMe_2$ (0.9 mL) was stirred at room temperature for 5 h. The reaction mixture was then concentrated *in vacuo*, and H_2O (1 mL) was added. The resulting mixture was brought to pH 11 by adding 10% aqueous NaOH (1 mL) and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with saturated aqueous NaCl, dried over anhydrous K_2CO_3, and concentrated. Purification of the residual oil by column chromatography (alumina, 97:3 $CHCl_3$−MeOH) furnished (±)-**1a** (79 mg, 58%) as a pale yellow glass: UV (MeOH) λ_{max} (ϵ) 223 (sh) (10 400), 287 (15 600) nm; UV (solvent A) λ_{max} (ϵ) 223 (sh) (9700), 287 (14 700) nm; UV (solvent N) λ_{max} (ϵ) 223 (sh) (9700), 287 (14 700) nm; UV (solvent B) λ_{max} (ϵ) 286 (8800) nm; HRMS *m*/*z* calcd for $C_{27}H_{43}N_5O$ 453.3467, found 453.3474. The UV (MeOH), IR ($CHCl_3$), ^{1}H NMR ($CDCl_3$), ^{13}C NMR ($CDCl_3$), and MS spectra of this sample were virtually identical with those[2] of natural agelasimine-A.

(±)-Agelasimine-B [(±)-2a]. A solution of (±)-**21** (220 mg, 0.50 mmol) in 70% aqueous MeOH was stirred at room temperature, and $NaBH_4$ (38 mg, 1.0 mmol) was added in portions. After having been stirred at room temperature for 1 h, the reaction mixture was concentrated *in vacuo*. The residual solid was partitioned between saturated aqueous K_2CO_3 and CH_2Cl_2. The CH_2Cl_2 extracts were washed with saturated aqueous K_2CO_3, dried over anhydrous K_2CO_3, and concentrated to leave crude (±)-**22** (199 mg) as a yellow foam. The total amount of the crude (±)-**22** was dissolved in $AcNMe_2$ (1 mL), and the solution, after addition of MeI (284 mg, 2.0 mmol), was stirred at room temperature for 1.5 h. The reaction mixture was concentrated *in vacuo* to leave an orange solid, to which was added H_2O (2.5 mL). The resulting mixture was brought to pH 11 by addition of 10% aqueous NaOH (2.5 mL) and extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with saturated aqueous NaCl, dried over anhydrous K_2CO_3, and concentrated. The residual yellow oil was purified by column chromatography (alumina, 99:1 $CHCl_3$−MeOH), giving (±)-**2a** [89 mg, 39% from (±)-**21**] as a pale yellow glass: UV (MeOH) λ_{max} (ϵ) 245 (sh) (7100), 327 (5400) nm; UV (solvent A) λ_{max} (ϵ) 221 (12 700), 246 (sh) (6300), 326 (5300) nm; UV (solvent N) λ_{max} (ϵ) 221 (13 100), 245 (sh) (6400), 326 (5300) nm; UV (solvent B) λ_{max} (ϵ) 240 (sh) (6400), 292 (5500) nm; HRMS *m*/*z* calcd for $C_{27}H_{45}N_5O$ 455.3624, found 455.3617. The IR ($CHCl_3$), ^{1}H NMR ($CDCl_3$), ^{13}C NMR ($CDCl_3$), and MS spectra of this sample were virtually identical with those[2] of natural agelasimine-B.

Conversion of (±)-2a into (±)-1a. A mixture of (±)-**2a** (21 mg, 0.046 mmol) and DDQ (14 mg, 0.062 mmol) in $CHCl_3$ (1 mL) was stirred at room temperature for 1 h. The reaction mixture was then concentrated *in vacuo*, and the residual brown solid was dissolved in EtOH (1 mL). The solution, after addition of 10% aqueous HCl (1 mL), was stirred at room temperature for 20 min and concentrated *in vacuo*. The residual oil was partitioned between 10% aqueous NaOH (3 mL) and CH_2Cl_2. The CH_2Cl_2 extracts were dried over anhydrous K_2CO_3 and concentrated to leave a pale yellow oil, which was purified successively by column chromatography (alumina, 20:1 $CHCl_3$−MeOH) and preparative TLC (alumina, 4:1 $CHCl_3$−MeOH), affording (±)-**1a**

(31) For convenience, each position of the naphthalene ring is indicated by an unprimed number, each carbon in the pentenyl chain by a primed number, and each skeletal atom in the purine or imidazole moiety by a doubly primed number.

(9 mg, 43%) as a slightly yellow glass. This sample was identical (by comparison of the IR and ^{1}H NMR spectra) with the one prepared from (±)-**21**.

Acetylation of (±)-Agelasimine-A. A solution of (±)-**1a** (50 mg, 0.11 mmol) and acetic anhydride (510 mg, 5.0 mmol) in pyridine (1 mL) was stirred at room temperature for 44 h. The reaction mixture was concentrated *in vacuo*, and the residual oil, after addition of H_2O (1 mL) and subsequent neutralization with $NaHCO_3$, was extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated to leave a yellow glass. Purification of the glass by flash chromatography (silica gel, 30:1 $CHCl_3$−MeOH) gave (±)-**25a** (33 mg, 54%) as a slightly yellow glass: UV (95% aqueous EtOH) λ_{max} (ϵ) 236 (sh) (10 900) nm; UV (solvent A) λ_{max} (ϵ) 236 (sh) (10 100) nm; UV (solvent N) λ_{max} (ϵ) 235 (sh) (10 500) nm; UV (solvent B) λ_{max} (ϵ) 238 (9700) nm; IR ($CHCl_3$) ν_{max} 3620, 1686, 1622 cm^{-1}; ^{1}H NMR ($CDCl_3$) (at 27 °C) [major and minor peaks (3:1 in relative integral intensity)] δ 0.803 (d, J = 6.8 Hz) and 0.795 (d, J = 6.5 Hz) (3H, C2-Me), 0.84 and 0.83 (3H), 0.86 (3H), and 0.98 (3H) (s each, C1-Me and C5-Me$_2$), 1.17 (1H, s, OH), 1.11 (1H, br d, J = 13.5 Hz) and 1.25−2.00 (15H, m) (C2-H, C3-H$_2$, C4-H$_2$, C6-H$_2$, C7-H$_2$, C8-H$_2$, C8a-H, C1′-H$_2$, and C2′-H$_2$), 1.74 (3H, s, C3′-Me), 2.16 and 2.07 (3H, s each, COMe), 2.19 and 2.25 (3H, s each, COMe), 3.16 and 3.17 (3H, s each, NMe), 3.24 and 3.37 (3H, s each, NMe), 4.59 and 4.54 (2H, d each, J = 7 Hz, C5′-H$_2$), 5.35 and 5.34 (1H, t each, J = 7 Hz, C4′-H), 7.46 and 7.42 (1H, s each, C2″-H), 8.24 and 8.19 (1H, s each, NCHO);[31] ^{1}H NMR (DMSO-d_6) (at 27 °C) [major and minor peaks (3:1 in relative integral intensity)] δ 0.73 (3H, d, J = 6.6 Hz, C2-Me), 0.77 (6H) and 0.90 (3H) (s each, C1-Me and C5-Me$_2$), 1.67 and 1.65 (3H, s each, C3′-Me), 1.99 and 1.95 (3H, s each, COMe), 2.15 and 2.13 (3H, s each, COMe), 3.03 and 3.00 (3H, s each, NMe), 3.12 and 3.23 (3H, s each, NMe), 4.56 (2H, d, J = 6.5 Hz, C5′-H$_2$), 5.24 (1H, t, J = 6.5 Hz, C4′-H), 7.81 (1H, s, C2″-H), 8.16 and 8.19 (1H, s each, NCHO);[31] ^{1}H NMR (DMSO-d_6) (at 100 °C) δ 0.75 (3H, d, J = 6.6 Hz, C2-Me), 0.79 (6H) and 0.92 (3H) (s each, C1-Me and C5-Me$_2$), 1.68 (3H, s, C3′-Me), 2.00 (3H, s, COMe), 2.13 (3H, s, COMe), 3.05 (3H, s, NMe), 3.11 (3H, s, NMe), 4.56 (2H, d, J = 6.5 Hz, C5′-H$_2$), 5.29 (1H, t, J = 6.5 Hz, C4′-H), 7.70 (1H, s, C2″-H), 8.19 (1H, s, NCHO);[31] ^{13}C NMR ($CDCl_3$) (major peaks) δ 15.9 (q), 16.8 (q), 17.4 (q), 21.7 (t), 22.1 (t), 23.8 (q), 24.0 (q), 24.4 (q), 25.3 (q), 26.3 (t), 31.5 (q), 32.0 (t), 32.9 (t), 35.5 (q), 36.0 (t), 36.5 (d), 36.8 (t), 38.7 (s), 38.9 (s), 40.9 (d), 45.3 (t), 76.2 (s), 115.9 (s), 116.8 (d), 137.4 (d), 141.9 (s), 144.3 (s), 145.5 (s), 162.2 (d), 171.6 (s), 182.1 (s); (minor peaks) δ 24.8 (q), 25.1 (q), 34.1 (q), 34.7 (q), 35.9 (d), 45.0 (t), 77.2 (s), 135.5 (d), 144.5 (s), 146.8 (s), 160.8 (d), 172.4 (s), 182.4 (s);[32] HRMS m/z calcd for $C_{31}H_{49}N_5O_4$ 555.3785, found 555.3765.

Acetylation of (±)-Agelasimine-B. (i) With Acetic Anhydride in Pyridine. A solution of (±)-**2a** (50 mg, 0.11 mmol) and acetic anhydride (510 mg, 5.0 mmol) in pyridine (1 mL) was stirred at room temperature for 1 h. The reaction mixture was then worked up as described above for (±)-**25a**, giving a crude yellow glass. Purification of the glass by flash chromatography (silica gel, 15:1 $CHCl_3$−MeOH) afforded (±)-N^6-acetylagelasimine-B [(±)-**27a**] (26 mg, 48%) as a yellow glass: UV (95% aqueous EtOH) λ_{max} (ϵ) 267 (9300), 345 (1600) nm; UV (solvent A) λ_{max} (ϵ) 256 (8400), 373 (1300) nm; UV (solvent N) λ_{max} (ϵ) 267 (9000), 345 (1500) nm; UV (solvent B) λ_{max} (ϵ) 266 (9000), 345 (1500) nm; IR ($CHCl_3$) ν_{max} 3620, 1644 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80 (3H, d, J = 6.8 Hz, C2-Me), 0.83, 0.86, and 0.98 (3H each, s, C1-Me and C5-Me$_2$), 1.20 (1H, br, OH), 1.10 (1H, br d, J = 13 Hz), 1.25−1.68 (13H, m), 1.84 (1H, ddd, J = 12.5, 12.5, 5 Hz), and 1.94 (1H, ddd, J = 12.5, 12.5, 4.5 Hz) (C2-H, C3-H$_2$, C4-H$_2$, C6-H$_2$, C7-H$_2$, C8-H$_2$, C8a-H, C1′-H$_2$, and C2′-H$_2$), 1.75 (3H, s, C3′-Me), 2.16 (3H, s, COMe), 2.96 (3H, s, NMe), 3.06 (3H, s, NMe), 4.42 (2H, s, C2″-H$_2$), 4.78 (2H, d, J = 7 Hz, C5′-H$_2$), 5.35 (1H, t, J = 7 Hz, C4′-H), 7.32 (1H, s, C8″-H);[31] HRMS m/z calcd for $C_{29}H_{47}N_5O_2$ 497.3730, found 497.3748. The ^{1}H NMR and MS spectra of (±)-**27a** were in agreement with those[2] of N^6-acetylagelasimine-B.

(32) Certain major peaks may be overlapped with minor peaks.

In a separate experiment, a similar acetylation of (±)-**2a** but with elongation of the reaction time from 1 to 50 h was carried out as described above. Purification of the crude glass by preparative TLC (silica gel, 8:1 CH_2Cl_2−EtOH) provided two compounds. The more polar product (±)-**27a** was isolated in 15% yield as a yellow glass, which was identical (by comparison of the ^{1}H NMR spectra) with the one obtained by the method described above. The less polar product (±)-**3a** was also isolated as a pale yellow solid in 60% yield. Recrystallization of the solid from EtOAc gave an analytical sample of (±)-**3a** as colorless prisms: mp 178.5−180.5 °C; UV (MeOH) λ_{max} (ϵ) 267 (11 700) nm; UV (95% aqueous EtOH) λ_{max} (ϵ) 268 (11 900) nm; UV (solvent A) λ_{max} (ϵ) 256 (10 600) nm; UV (solvent N) λ_{max} (ϵ) 267 (12 000) nm; UV (solvent B) λ_{max} (ϵ) 266 (11 800) nm; IR (Nujol) ν_{max} 3400, 1638 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 16.0 (q), 16.8 (q), 17.4 (q), 21.7 (q), 21.7 (t), 22.1 (t), 24.1 (q), 24.4 (q), 26.3 (t), 32.0 (t), 32.9 (t), 33.1 (q), 36.0 (t), 36.5 (d), 36.9 (t), 38.8 (s), 38.9 (s), 40.9 (d), 44.4 (t), 76.3 (s), 114.2 (s), 117.6 (d), 139.7 (d), 144.0 (s), 148.8 (s), 155.9 (s), 162.2 (s); HRMS m/z calcd for $C_{27}H_{42}N_4O_2$ 454.3308, found 454.3324. Anal. Calcd for $C_{27}H_{42}N_4O_2$: C, 71.33; H, 9.31; N, 12.32. Found: C, 71.14; H, 9.25; N, 12.09. The ^{1}H NMR ($CDCl_3$) spectral data for (±)-**3a** were virtually identical with those[5] reported selectively for purino-diterpene.

(ii) With Acetic Anhydride Alone. A mixture of (±)-**2a** (30 mg, 0.066 mmol) and acetic anhydride (0.25 mL, 2.6 mmol) was stirred at room temperature for 50 h. The reaction mixture was concentrated *in vacuo* to leave an orange oil. Purification of the oil by preparative TLC (silica gel, 8:1 CH_2Cl_2−EtOH) afforded (±)-**27a** (3.5 mg, 11%) as a yellow glass and (±)-**3a** (13.5 mg, 45%) as a pale yellow solid. The ^{1}H NMR spectra of these samples were identical with those of authentic samples prepared by method i, respectively.

Hydrolysis of (±)-N^6-Acetylagelasimine-B. A stirred solution of (±)-**27a** (50 mg, 0.1 mmol) in 50% aqueous EtOH (3 mL) was heated under reflux for 20 h. The reaction mixture was concentrated *in vacuo* to leave a yellow oil, which was purified by preparative TLC (silica gel, 10:1 CH_2Cl_2−EtOH) to provide two compounds. The more polar product (±)-**3a** (10 mg, 22%) was obtained as a colorless solid, which was identical with an authentic sample by comparison of the ^{1}H NMR spectrum. The less polar product (±)-**28a** (18 mg, 39%) was also isolated as a colorless glass: IR ($CHCl_3$) ν_{max} 3620, 1649 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80 (3H, d, J = 6.5 Hz, C2-Me), 0.83, 0.86, and 0.97 (3H each, s, C1-Me and C5-Me$_2$), 1.18 (1H, s, OH), 1.10 (1H, br d, J = 13.5 Hz), 1.25−1.67 (13H, m), 1.84 (1H, ddd, J = 12.5, 12.5, 5 Hz), and 1.94 (1H, ddd, J = 12.5, 12.5, 4.5 Hz) (C2-H, C3-H$_2$, C4-H$_2$, C6-H$_2$, C7-H$_2$, C8-H$_2$, C8a-H, C1′-H$_2$, and C2′-H$_2$), 1.76 (3H, s, C3′-Me), 2.91 (3H, s, NMe), 2.99 (3H, s, NMe), 4.29 (2H, s, C2″-H$_2$), 4.83 (2H, d, J = 7 Hz, C5′-H$_2$), 5.41 (1H, t, J = 7 Hz, C4′-H), 7.24 (1H, s, C8″-H);[31] HRMS m/z calcd for $C_{27}H_{44}N_4O_2$ 456.3465, found 456.3483.

Acknowledgment. This paper is dedicated to Emeritus Professor Nelson J. Leonard (University of Illinois) on the occasion of his 80th birthday in recognition of his outstanding contribution to organic chemistry and biochemistry. We thank Dr. R. Fathi-Afshar (SynPhar Laboratories Inc., Edmonton) and Professor T. M. Allen (University of Alberta) for providing us with spectral copies of their natural agelasimine-A and agelasimine-B.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of (±)-**1a**, (±)-**2a**, and (±)-**3a** and IR spectra and MS data of (±)-**1a**, (±)-**2a**, (±)-**3a**, (±)-**8**−(±)-**14**, **15a**−**c**, (±)-**19**, (±)-**21**, (±)-**25a**, (±)-**27a**, and (±)-**28a** (25 pages). See any current masthead page for ordering and Internet access instructions.

JA960879B