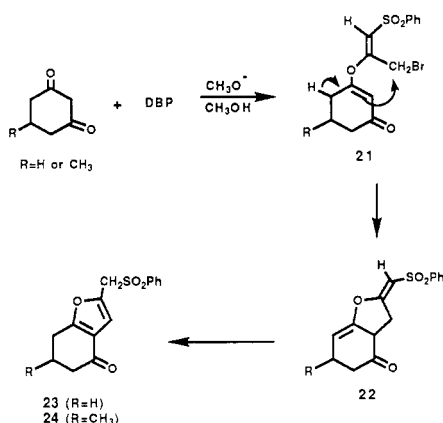


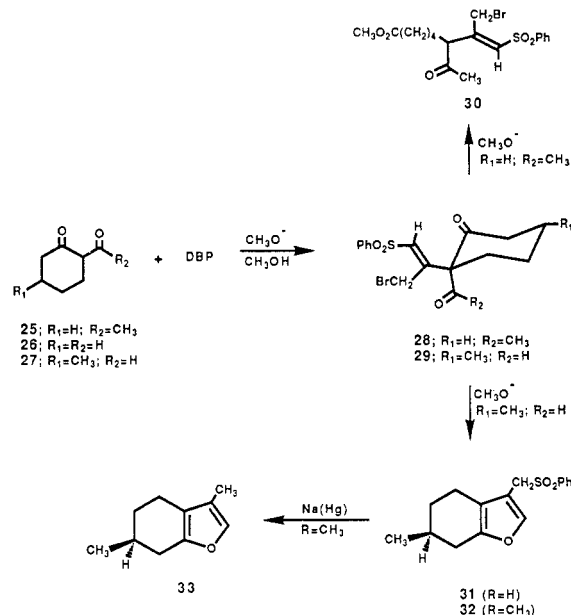
produced dihydrobenzofuranone **23** (R = H) in 85% yield. Note that in this case, the substitution pattern about the furan ring is different from that encountered with the acyclic dicarbonyl compounds. More than likely the initial step involves O-alkylation to give **21** as a transient species.<sup>18</sup> Further reaction of this material with base results in cyclization to **22**, which then undergoes a subsequent aromatization. A similar series of reactions was used to prepare furan **24**.



When 2-acetylcyclohexanone was used, employing sodium methoxide as the base, ring opening of the intermediate adduct **28** to give **30** takes precedence over deacetylation, presumably as a consequence of the stability of the anion formed. This circumstance can be avoided, however, by the use of a formyl group in place of the acetyl group to activate the cyclic ketone. Thus, DBP reacted with the sodium salt of 2-formylcyclohexanone (**26**) to give,

(18) 1,3-Cyclohexanediones preferentially alkylate on the O atom of the diketone enolate, see: Stetter, H. In *Newer Methods of Preparative Organic Chemistry*; Foerst, W., Ed.; Academic Press: New York, 1964, Vol II. Taylor, E. C.; Hanks, G. H.; McKillip, A. *J. Am. Chem. Soc.* **1968**, *90*, 2421. An alternate, but less likely, mechanism for the formation of **23** (or **24**) could involve S<sub>N</sub>2 displacement of the allylic bromide by the enolate carbon followed by cyclization and aromatization.

after treatment with potassium *tert*-butoxide, tetrahydrobenzofuran **31** in good yield. We sought to further demonstrate the utility of this approach as an entry into the vast number of 3-methyl furanoterpenoids<sup>13</sup> by employing DBP in the total synthesis of (*R*)-menthofuran (**33**).<sup>19</sup> The menthofuran precursor **32** was prepared in



the same fashion as **31**, using the commercially available (*R*)-3-methylcyclohexanone. Furan **32** was then treated with sodium amalgam to give (*R*)-menthofuran in 85% overall yield.

In conclusion, the DBP approach is a general method for the synthesis of C-2 and C-3 substituted furans. In addition to its ease of removal, the pendant sulfone at C-4 offers a convenient and versatile site for further elaboration (via alkylation<sup>20</sup> or Julia coupling<sup>21</sup>). This strategy toward furans clearly could be applied to more complex targets. We are currently investigating the scope and limitations of this protocol.

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**Supplementary Material Available:** Experimental procedures and spectroscopic data for new compounds (5 pages). Ordering information is given on any current masthead page.

(19) Tori, K.; Ueyama, M.; Horibe, I.; Tamura, Y.; Takeda, K. *Tetrahedron Lett.* **1975**, 4583.

(20) Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019.

(21) Julia, M.; Stacino, J. *Tetrahedron* **1986**, *42*, 2469.

## Total Synthesis of Mycalamides A and B

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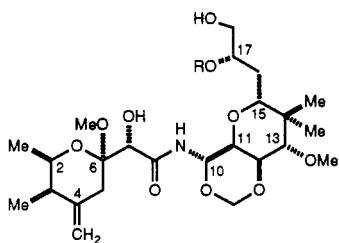
**Summary:** A total synthesis of mycalamides A (**1**) and B (**2**) was accomplished in an enantiomerically pure form, establishing unambiguously their absolute configuration.

Mycalamides A (**1**) and B (**2**) and onnamide A have recently been isolated from marine sponges.<sup>1,2</sup> Struc-

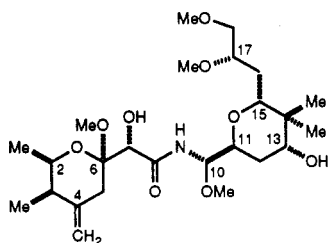
turally, they are strikingly similar to pederin (**3**), the vesicatory principle of staphylinid beetles *Paederus*.<sup>3</sup>

(1) (a) Perry, N. B.; Blunt, J. W.; Munro, M. H. G.; Pannell, L. K. *J. Am. Chem. Soc.* **1988**, *110*, 4850. (b) Perry, N. B.; Blunt, J. W.; Munro, M. H. G.; Thompson, A. M. *J. Org. Chem.* **1990**, *55*, 223.

Each of these natural products exhibits remarkable biological activity,<sup>4</sup> and we are intrigued by the acylaminal group, such as the one found at the C-10 position<sup>5</sup> of 1–3. This functional group may play an important role in the origin of the biological activity. For example, it may be activated by eliminative cleavage of the C-10 carbon–oxygen bond, and if so, the additional ring system found in mycalamides and onnamide could provide an interesting means to address the question of the process of activation and subsequent reaction in terms of stereoelectronic effects. In this paper, we report a total synthesis of mycalamides A and B as the first step toward this goal.



1: mycalamide A (R=H)  
2: mycalamide B (R=Me)



3: pederin

We chose methyl  $\alpha$ -D-glucopyranoside<sup>6</sup> as the starting material for the synthesis of right half of mycalamides because of their obvious structural similarity. With small modifications of the functional group transformations known in the carbohydrate literature, this substance was converted into the alcohol 4 ( $\alpha_D +33.3^\circ$ ,  $\text{CHCl}_3$ )<sup>7</sup> in over 65% overall yield.<sup>8</sup> A seven-step sequence of routine synthetic reactions [(1) Swern oxidation;<sup>9</sup> (2) Wittig reaction; (3)  $\text{CH}_2\text{N}_2/\text{Pd}(\text{OAc})_2/\text{Et}_2\text{O}/0^\circ\text{C}$ ,<sup>10,11</sup> (4)  $\text{H}_2/\text{Pd}$ -

(OH)<sub>2</sub> on C/EtOAc/room temperature then  $\text{H}_2/\text{PtO}_2/\text{AcOH}/\text{room temperature}$ ; (5)  $(t\text{-Bu})(\text{C}_6\text{H}_5)_2\text{SiCl}/\text{imidazole}/\text{CH}_2\text{Cl}_2/\text{room temperature}$ ; (6)  $\text{C}_6\text{H}_5\text{CH}_2\text{Br}/\text{NaH}/\text{THF}/\text{room temperature}$ ] allowed the introduction of the geminal dimethyl groups at the C-14 position in 62% overall yield, i.e. 4  $\rightarrow$  5. We planned to incorporate the C-17,18 glycol via the terminal olefin 6. As direct methods did not yield fruitful results,<sup>12</sup> 5 ( $\alpha_D +63.0^\circ$ ,  $\text{CHCl}_3$ ) was converted into 6 ( $\alpha_D +77.9^\circ$ ,  $\text{CHCl}_3$ ) in five steps [(1) Swern oxidation; (2) Horner–Emmons olefination; (3) DIBAL/ $\text{CH}_2\text{Cl}_2/-78^\circ\text{C}$ ; (4)  $\text{H}_2/\text{Rh}$  on  $\text{Al}_2\text{O}_3/\text{EtOAc}/\text{room temperature}$ ; (5)  $o\text{-O}_2\text{NC}_6\text{H}_4\text{SeCN}/\text{P}(n\text{-Bu})_3/\text{C}_6\text{H}_6/\text{room temperature}$ , followed by MCPBA treatment<sup>13</sup>] in 79% overall yield. Application of the recently developed asymmetric osmylation [ $\text{OsO}_4/\text{N},\text{N}'\text{-bis}(2,4,6\text{-trimethylbenzyl})\text{-}(S,S)\text{-1,2-diphenyl-1,2-diaminoethane}/\text{CH}_2\text{Cl}_2/-90^\circ\text{C}$ ]<sup>14</sup> gave a 6:1 mixture of the two possible glycols, which were then transformed to the corresponding carbonates and separated on silica gel to yield the desired carbonate 7 (75% overall yield;  $\alpha_D +66.7^\circ$ ,  $\text{CHCl}_3$ ) along with the corresponding undesired carbonate (13% yield). The undesired carbonate was recycled in 65% overall yield via the olefin 6.<sup>15</sup> The C-17 stereochemistry in 7 was assigned on the basis of three pieces of evidence. First, the asymmetric osmylation of 6 in the presence of the antipode of the chiral diamine yielded an inverted ratio (ca. 1:11) of the two possible glycols. Second, Sharpless asymmetric epoxidation [diethyl D-tartrate/ $\text{Ti}(i\text{-PrO})_4/t\text{-BuOOH}/\text{CH}_2\text{Cl}_2$ ]<sup>16</sup> of the allylic alcohol prepared from 5,<sup>17</sup> followed by DIBAL reduction,<sup>18</sup> yielded a ca. 1:1 mixture of the expected 1,2- and 1,3-glycols. The 1,2-glycol thus obtained was found to be identical with the major glycol which resulted in the asymmetric osmylation of 6 in the presence of the (S,S)-diamine. Third, the asymmetric osmylation using Oppolzer's chiral auxiliary<sup>19</sup> yielded a >30:1 mixture of the two possible glycols, the major product of which was correlated with 7.<sup>20</sup>

In order to construct the B ring, we needed to introduce

(11) For a large scale preparation, we used (1)  $\text{CHCl}_3/\text{aqueous NaOH}/\text{C}_6\text{H}_5\text{CH}_2(\text{Me})_3\text{N}^+\text{Cl}^-$  and (2)  $\text{Li}/\text{liquid NH}_3/-78^\circ\text{C}$  in place of the step 3 for safety reasons.

(12) These included a vinylcuprate reaction on the tosylate and iodide prepared from 5.

(13) Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* 1976, 41, 1485.

(14) Corey, E. J.; Jardine, P. D.; Virgil, S.; Yuen, P.-W.; Connell, R. D. *J. Am. Chem. Soc.* 1989, 111, 9243. For recent papers on this subject, see: (a) Hirama, M.; Oishi, T. *J. Org. Chem.* 1989, 54, 5834. Hirama, M.; Oishi, T.; Ito, S. *J. Chem. Soc., Chem. Commun.* 1989, 665. (b) Tomioka, K.; Nakajima, M.; Iitaka, Y.; Koga, K. *Tetrahedron Lett.* 1988, 29, 573. (c) Wai, J. S. M.; Marko, I.; Svendsen, J. S.; Finn, M. G.; Jacobsen, E. N.; Sharpless, K. B. *J. Am. Chem. Soc.* 1989, 111, 1123. Svendsen, J. S.; Marko, I.; Jacobsen, E. N.; Pulla Rao, Ch.; Bott, S.; Sharpless, K. B. *J. Org. Chem.* 1989, 54, 2264. (d) Annunziata, R.; Cinquini, M.; Cozzi, F.; Raimondi, L.; Stefanelli, S. *Tetrahedron Lett.* 1987, 28, 3139. (e) Tokles, M.; Snyder, J. K. *Tetrahedron Lett.* 1986, 27, 3951. (f) Yamada, T.; Narasaka, K. *Chem. Lett.* 1986, 131.

(15) This recycling was carried out in four steps, (1) 0.5 N NaOH/THF/room temperature; (2)  $\text{HC}(\text{OMe})_3/\text{PPTS}/\text{room temperature}$ ; (3) isobutyric anhydride/ $125^\circ\text{C}$ ; (4) asymmetric osmylation.

(16) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* 1980, 102, 5974. (17) This allylic alcohol was prepared from 5 in three steps [(1) Swern oxidation; (2) Horner–Emmons olefination; (3) DIBAL reduction].

(18) Finan, J. M.; Kishi, Y. *Tetrahedron Lett.* 1982, 23, 2719.

(19) (a) Vandewalle, M.; Van der Eycken, J.; Oppolzer, W.; Vulllioud, C. *Tetrahedron* 1986, 42, 4035. (b) Oppolzer, W.; Barras, J.-P. *Helv. Chim. Acta* 1987, 70, 1666.

(20) The preparation of the substrate for this asymmetric osmylation involved (1) ozonization of 6; (2) Horner–Emmons olefination; (3) basic hydrolysis; (4) acid chloride formation; and (5) coupling with Oppolzer's chiral sulfonamide. The major osmylation product with the Oppolzer's chiral auxiliary, derived from (1S)-camphor-10-sulfonyl chloride, was subjected to a five-step sequence of reactions, (1)  $(\text{MeO})_2\text{C}(\text{Me})_2/\text{camphorsulfonic acid}$ ; (2) LAH; (3) Swern oxidation; (4) MCPBA; (5) LAH, to yield the glycol corresponding to 7.

(2) Sakemi, S.; Ichiba, T.; Kohmoto, S.; Saucy, G.; Higa, T. *J. Am. Chem. Soc.* 1988, 110, 4851.

(3) (a) Cardani, C.; Ghiringhelli, D.; Mondelli, R.; Quilico, A. *Tetrahedron Lett.* 1965, 2537. (b) Matsumoto, T.; Yanagiya, M.; Maeno, S.; Yasuda, S. *Tetrahedron Lett.* 1968, 6297. (c) Furusaki, A.; Watanabe, T.; Matsumoto, T.; Yanagiya, M. *Tetrahedron Lett.* 1968, 6301.

(4) Mycalamides and onnamide are known to exhibit promising antiviral and antitumor activity: Burres, N. S.; Clement, J. J. *Cancer Res.* 1989, 49, 2935. See also the references cited in ref 1 and 2. Pederin is known to be a powerful insect toxin and a potent inhibitor of protein biosynthesis: see the references cited in ref 3.

(5) The numbering of compounds used in this paper corresponds to that of mycalamides: see structures 1 and 2.

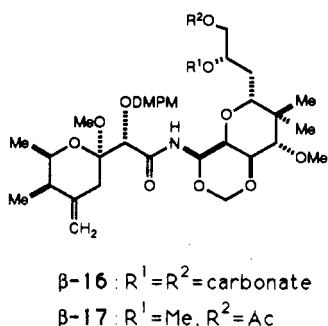
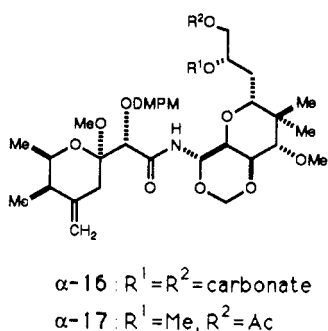
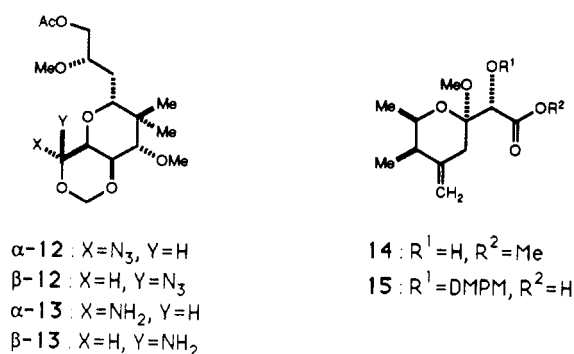
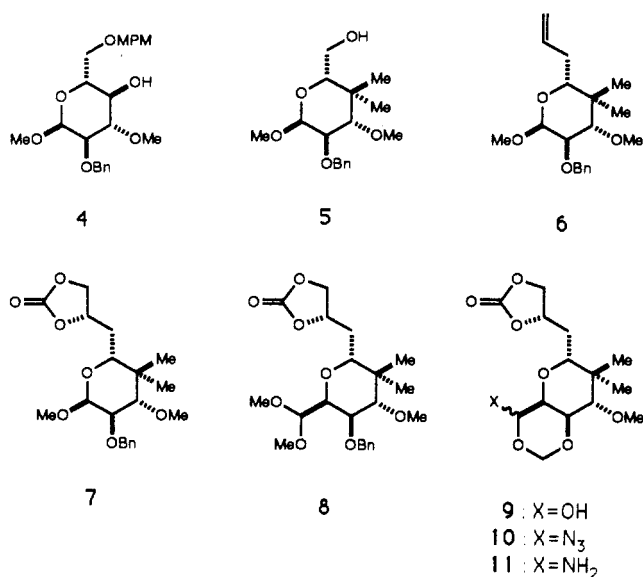
(6) Purchased from Pfanzstiehl Laboratories, Inc.

(7) Satisfactory spectroscopic data ( $^1\text{H}$  and  $^{13}\text{C}$  NMR, MS, HR MS, IR,  $[\alpha]_D$ ) were obtained for all the new compounds reported.

(8) This transformation required a six-step sequence of reactions, (1)  $4\text{-MeOC}_6\text{H}_4\text{CH}(\text{OMe})_2/p\text{-TsOH}$ ; (2)  $(n\text{-Bu})_2\text{SnO}$ , followed by  $p\text{-TsCl}/\text{NEt}_3$  treatment: cf. Munavu, R. M.; Szmant, H. H. *J. Org. Chem.* 1976, 41, 1832; (3)  $\text{MeI}/\text{Ag}_2\text{O}$ ; (4)  $\text{Na}(\text{Hg})$ ; (5)  $\text{C}_6\text{H}_5\text{CH}_2\text{Br}/\text{NaH}$ ; (6)  $\text{NaBH}_3\text{CN}/\text{TFA}$ : cf. Johansson, R.; Samuelsson, B. *J. Chem. Soc., Perkin Trans. 1* 1984, 2371.

(9) (a) Omura, K.; Swern, D. *Tetrahedron* 1978, 34, 1651. (b) Manco, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* 1978, 43, 2480.

(10) Suda, M. *Synthesis* 1981, 714.



the axially disposed aldehyde group or its equivalent at the C-11 position. This was accomplished by treatment of 7 with propargyltrimethylsilane in the presence of TMSOTf in acetonitrile,<sup>21</sup> followed by ozonization and acetalization, to furnish the dimethyl acetal 8 ( $\alpha_D +63.9^\circ$ ,

(21) For the stereochemical outcome of this type of C-glycosidation, see: Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc.* 1982, 104, 4976. Propargyltrimethylsilane was first used by Dr. Wu in these laboratories in connection with work on the conformational analysis of C-glycosides.

CHCl<sub>3</sub>) in 60% overall yield. After debenzoylation [H<sub>2</sub>/Pd(OH)<sub>2</sub> on C/EtOAc/room temperature], 8 was treated with paraformaldehyde in the presence of hydrochloric acid at 0 °C to yield the hemiacetal 9 as a C-10 diastereomeric mixture in 86% overall yield.<sup>22</sup> A standard procedure of activation (MsCl/Et<sub>3</sub>N/DMAP/CH<sub>2</sub>Cl<sub>2</sub>/-60 °C) and displacement (*n*-Bu<sub>4</sub>N<sup>+</sup>N<sub>3</sub><sup>-</sup>/CH<sub>2</sub>Cl<sub>2</sub>/-78 °C → room temperature) was applied to convert 9 into the azide 10,<sup>23</sup> a suitable precursor of the right half of mycalamide A, in 72% overall yield as a chromatographically inseparable 2:1 C-10 diastereomeric mixture. A straightforward functional group manipulation allowed for the transformation of 10 into the azide acetate 12,<sup>24</sup> a suitable precursor of the right half of mycalamide B, in five steps [(1) NaOH/aqueous *p*-dioxane/room temperature; (2) 4-MeOC<sub>6</sub>H<sub>4</sub>-(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>CCl/Hunig base/CH<sub>2</sub>Cl<sub>2</sub>/room temperature; (3) MeI/NaH/DMF/75 °C; (4) *p*-TsOH/MeOH/room temperature; (5) Ac<sub>2</sub>O/DMAP/CH<sub>2</sub>Cl<sub>2</sub>/room temperature] in 76% overall yield. The azide acetate 12 was also a 2:1 C-10 diastereomeric mixture, favoring the natural configuration. These diastereomers were separated on silica gel to give  $\alpha$ -12 and  $\beta$ -12, and both proved to be configurationally stable under a variety of conditions.

Hydrogenation (H<sub>2</sub>/Pd on C/EtOAc/room temperature) of  $\alpha$ -12 or  $\beta$ -12 yielded the expected amine  $\alpha$ -13 or  $\beta$ -13. However, neither  $\alpha$ -13 nor  $\beta$ -13 was found to be configurationally stable under acidic (camphorsulfonic acid), neutral, or basic (NH<sub>3</sub> or Et<sub>3</sub>N) conditions. The ratio of  $\alpha$ - and  $\beta$ -13 was approximately 2:1 under neutral or basic conditions while approximately 1:4, disfavoring the natural  $\alpha$ -configuration, under acidic conditions. Through the <sup>1</sup>H NMR studies, the same trend was found for the amines 11 derived from the azides 10. These experiments demonstrated that the C-10 stereochemistry of mycalamides should be addressed at the step of the amide-bond formation or thereafter.

The left half of mycalamides, 15, was prepared in two steps [(1) 3,4-(MeO)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>Cl/NaH/DMF/room temperature; (2) *n*-PrSLi/HMPA/room temperature] from 14, one of the intermediates used in Nakatas' total synthesis of pederin,<sup>25</sup> in 63% overall yield. Activation of the carboxylic acid 15 with *p*-toluenesulfonyl chloride (DMAP/CH<sub>2</sub>Cl<sub>2</sub>/room temperature)<sup>26</sup> and subsequent coupling

(22) When warmed up to room temperature, this reaction yielded the corresponding chloride, which was directly used for the next azide displacement reaction. The overall yield of this sequence was comparable with the one reported in the text but its reproducibility was not as high as the other.

(23) HR MS (FAB, NaI): calcd for C<sub>14</sub>H<sub>22</sub>N<sub>3</sub>O<sub>7</sub> (M<sup>+</sup> + H) 344.1456, found 344.1458. [ $\alpha$ ]<sub>D</sub>: +5.8° (c 0.97, CHCl<sub>3</sub>). <sup>1</sup>H NMR (major isomer, CDCl<sub>3</sub>):  $\delta$  0.95 (3 H, s, C-14 CH<sub>3</sub>), 1.21 (3 H, s, C-14 CH<sub>3</sub>), 1.70 (1 H, m, C-16 H), 2.78 (1 H, ddd, *J* = 4.5, 12.6, 14.6 Hz, C-16 H), 3.01 (1 H, d, *J* = 3.2 Hz, C-13 H), 3.41 (3 H, s, OCH<sub>3</sub>), 3.66 (1 H, dd, *J* = 3.4, 12.6 Hz, C-15 H), 3.72 (1 H, dd, *J* = 2.0, 3.2 Hz, C-12 H), 3.79 (1 H, t, *J* = 2.0 Hz, C-11 H), 4.21 (1 H, dd, *J* = 7.5, 8.5 Hz, C-18 H), 4.61 (1 H, dd, *J* = 7.8, 8.5 Hz, C-18 H), 4.69 (1 H, d, *J* = 2.0 Hz, C-10-H), 4.78 (1 H, d, *J* = 6.6 Hz, OCH<sub>2</sub>O), 4.86 (1 H, m, C-17 H), 5.20 (1 H, d, *J* = 6.6 Hz, OCH<sub>2</sub>O). IR (CCl<sub>4</sub>): 2120, 1823 cm<sup>-1</sup>.

(24) HR MS (FAB, NaI): calcd for C<sub>16</sub>H<sub>27</sub>N<sub>3</sub>O<sub>7</sub>Na (M<sup>+</sup> + Na) 396.1745, found 396.1739. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.92 (3 H, s, C-14 CH<sub>3</sub>), 1.08 (3 H, s, C-14 CH<sub>3</sub>), 1.62 (1 H, ddd, *J* = 3.0, 9.4, 14.7 Hz, C-16 H), 2.09 (3 H, s, OCOCH<sub>3</sub>), 2.26 (1 H, m, C-16 H), 3.01 (1 H, d, *J* = 3.6 Hz, C-13 H), 3.40 (3 H, s, OCH<sub>3</sub>), 3.41 (3 H, s, OCH<sub>3</sub>), 3.57 (1 H, m, C-17 H), 3.70 (1 H, m, C-15 H), 3.71 (1 H, m, C-12 H), 3.87 (1 H, m, C-11 H), 4.14 (1 H, dd, *J* = 4.9, 12.1 Hz, C-18 H), 4.36 (1 H, dd, *J* = 2.6, 12.1 Hz, C-18 H), 4.63 (1 H, d, *J* = 2.0 Hz, C-10 H), 4.77 (1 H, d, *J* = 6.5 Hz, OCH<sub>2</sub>O), 5.21 (1 H, d, *J* = 6.5 Hz, OCH<sub>2</sub>O). IR (film): 2119, 1739 cm<sup>-1</sup>.

(25) Nakata, T.; Nagao, S.; Mori, N.; Oishi, T. *Tetrahedron Lett.* 1985, 26, 6461 and 6465.

with the amines, prepared by hydrogenation of 10 or 12, yielded a mixture of  $\alpha$ -16 (38% yield)<sup>27</sup> and  $\beta$ -16 (40% yield)<sup>28</sup> or  $\alpha$ -17 (59% yield)<sup>29</sup> and  $\beta$ -17 (26% yield),<sup>30</sup> respectively. The diastereomers were readily separable by chromatography to yield stereochemically pure products. Both  $\beta$ -16 and  $\beta$ -17 were found to isomerize to the corresponding natural diastereomers upon treatment with base (*t*-BuOK/THF/reflux). It is interesting to note that  $\beta$ -16 isomerized almost exclusively to the natural diastereomer<sup>31</sup> while  $\beta$ -17 epimerized to reach a ca. 1:1 mixture of the

(26) The following reagents were tested for the activation of carboxylic acid and the order of efficiency was found as *p*-toluenesulfonyl chloride > 2,4,6-trichlorobenzene sulfonyl chloride > ethyl chloroformate > phenyl chloroformate > sulfonyl chloride > 2,4,6-triisopropylbenzenesulfonyl chloride > 2,4,6-trimethylbenzenesulfonyl chloride > methanesulfonyl chloride.

(27) HR MS (FAB, NaI): calcd for C<sub>34</sub>H<sub>49</sub>NO<sub>13</sub>Na (M<sup>+</sup> + Na) 702.3099, found 702.3116. [ $\alpha$ ]<sub>D</sub>: +72.8° (c 0.72, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (benzene-*d*<sub>6</sub>):  $\delta$  0.55 (3 H, s, C-14 CH<sub>3</sub>), 0.69 (3 H, s, C-14 CH<sub>3</sub>), 1.04 (3 H, d, *J* = 6.6 Hz, C-2 CH<sub>3</sub>), 1.07 (3 H, d, *J* = 6.9 Hz, C-3 CH<sub>3</sub>), 1.14 (1 H, dd, *J* = 10.3, 13.6 Hz, C-16 H), 1.61 (1 H, ddd, *J* = 3.2, 10.3, 13.6 Hz, C-16 H), 1.99 (1 H, dq, *J* = 2.4, 6.9 Hz, C-3 H), 2.74 (1 H, d, *J* = 14.3 Hz, C-5 H), 2.78 (1 H, d, *J* = 14.3 Hz, C-5 H), 2.87 (1 H, d, *J* = 10.4 Hz, C-13 H), 2.99 (1 H, br d, *J* = 10.3 Hz, C-15 H), 3.16 (3 H, s, C-6 OCH<sub>3</sub>), 3.24 (3 H, s, C-13 OCH<sub>3</sub>), 3.41 (1 H, dd, *J* = 7.1, 9.8 Hz, C-11 H), 3.50 (3 H, s, ArOCH<sub>3</sub>), 3.52 (3 H, s, ArOCH<sub>3</sub>), 3.56 (1 H, m, C-18 H), 3.88 (1 H, dq, *J* = 2.4, 6.6 Hz, C-2 H), 4.14 (1 H, dd, *J* = 7.1, 10.4 Hz, C-12 H), 4.15 (1 H, s, H<sub>7</sub>), 4.44 (1 H, m, C-18 H), 4.45 (1 H, m, C-17 H), 4.51 (1 H, d, *J* = 6.9 Hz, OCH<sub>2</sub>O), 4.56 (1 H, d, *J* = 6.9 Hz, OCH<sub>2</sub>O), 4.62 (1 H, d, *J* = 11.3 Hz, CH<sub>2</sub>Ar), 4.74 (1 H, d, *J* = 11.6 Hz, CH<sub>2</sub>Ar), 4.80 (1 H, s, =CH<sub>2</sub>), 4.82 (1 H, s, =CH<sub>2</sub>), 5.65 (1 H, t, *J* = 9.8 Hz, C-10 H), 6.70–6.97 (3 H, m, ArH), 7.11 (1 H, d, *J* = 9.8 Hz, NH).

(28) HR MS (FAB, NaI): calcd for C<sub>34</sub>H<sub>49</sub>NO<sub>13</sub>Na (M<sup>+</sup> + Na) 702.3099, found 702.3065. [ $\alpha$ ]<sub>D</sub>: +7.6° (c 1.01, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR (benzene-*d*<sub>6</sub>):  $\delta$  0.64 (3 H, s, C-14 CH<sub>3</sub>), 1.02 (1 H, m, C-16 H), 1.07 (3 H, d, *J* = 6.5 Hz, C-2 CH<sub>3</sub>), 1.18 (3 H, d, *J* = 7.0 Hz, C-3 CH<sub>3</sub>), 1.20 (3 H, s, C-14 CH<sub>3</sub>), 2.05 (1 H, dq, *J* = 2.6, 7.0 Hz, C-3 H), 2.32 (1 H, ddd, *J* = 7.1, 12.2, 14.1 Hz, C-16 H), 2.62 (1 H, d, *J* = 2.2 Hz, C-13 H), 2.84 (1 H, m, C-5 H), 2.86 (3 H, s, C-6 OCH<sub>3</sub>), 2.88 (1 H, d, *J* = 14.4 Hz, C-5 H), 3.10 (1 H, t, *J* = 8.4 Hz, C-18 H), 3.12 (1 H, m, C-11 H), 3.15 (1 H, dd, *J* = 2.5, 12.2 Hz, C-15 H), 3.19 (1 H, m, C-12 H), 3.28 (3 H, s, C-13 OCH<sub>3</sub>), 3.42 (3 H, s, ArOCH<sub>3</sub>), 3.53 (3 H, s, ArOCH<sub>3</sub>), 3.55 (1 H, t, *J* = 7.9 Hz, C-18 H), 3.97 (1 H, dq, *J* = 2.7, 6.5 Hz, C-2 H), 4.11 (1 H, quintet, *J* = 7.0 Hz, C-17 H), 4.40 (1 H, d, *J* = 6.6 Hz, OCH<sub>2</sub>O), 4.57 (1 H, s, C-7 H), 4.76 (1 H, d, *J* = 10.7 Hz, CH<sub>2</sub>Ar), 4.81 (1 H, s, =CH<sub>2</sub>), 4.83 (1 H, s, =CH<sub>2</sub>), 4.85 (1 H, d, *J* = 6.6 Hz, OCH<sub>2</sub>O), 4.98 (1 H, d, *J* = 10.7 Hz, CH<sub>2</sub>Ar), 5.41 (1 H, dd, *J* = 1.8, 9.6 Hz, C-10 H), 6.62–7.15 (3 H, m, ArH), 8.04 (1 H, d, *J* = 9.6 Hz, NH).

(29) HR MS (FAB, NaI): calcd for C<sub>38</sub>H<sub>55</sub>NO<sub>13</sub>Na (M<sup>+</sup> + Na) 732.3568, found 732.3570. [ $\alpha$ ]<sub>D</sub>: +38.2° (c 0.24, CCl<sub>4</sub>). <sup>1</sup>H NMR (benzene-*d*<sub>6</sub>):  $\delta$  0.80 (3 H, s, C-14 CH<sub>3</sub>), 0.87 (3 H, s, C-14 CH<sub>3</sub>), 0.92 (3 H, m, C-16 H), 1.00 (3 H, d, *J* = 6.6 Hz, C-2 CH<sub>3</sub>), 1.08 (3 H, d, *J* = 7.0 Hz, C-3 CH<sub>3</sub>), 1.65 (1 H, m, C-16 H), 1.81 (3 H, s, OCOCH<sub>3</sub>), 1.98 (1 H, dq, *J* = 2.5, 7.0 Hz, C-3 H), 2.75 (1 H, d, *J* = 14.2 Hz, C-5 H), 2.80 (1 H, d, *J* = 14.2 Hz, C-5 H), 3.02 (1 H, d, *J* = 10.4 Hz, C-13 H), 3.11 (3 H, s, OCH<sub>3</sub>), 3.28 (3 H, s, OCH<sub>3</sub>), 3.29 (3 H, s, OCH<sub>3</sub>), 3.39 (3 H, s, OCH<sub>3</sub>), 3.40 (1 H, m, H<sub>17</sub>), 3.54 (3 H, s, OCH<sub>3</sub>), 3.63 (1 H, dd, *J* = 7.0, 9.9 Hz, C-11 H), 3.89 (1 H, dq, *J* = 2.7, 6.6 Hz, C-2 H), 4.21 (1 H, s, C-7 H), 4.25 (1 H, dd, *J* = 6.9, 10.4 Hz, C-12 H), 4.47 (1 H, dd, *J* = 5.3, 12.2 Hz, C-18 H), 4.59 (1 H, dd, *J* = 2.3, 12.2 Hz, C-18 H), 4.60 (1 H, d, *J* = 7.0 Hz, OCH<sub>2</sub>O), 4.62 (1 H, d, *J* = 10.9 Hz, CH<sub>2</sub>Ar), 4.65 (1 H, d, *J* = 7.0 Hz, OCH<sub>2</sub>O), 4.76 (1 H, s, =CH<sub>2</sub>), 4.80 (1 H, s, =CH<sub>2</sub>), 4.91 (1 H, d, *J* = 10.9 Hz, CH<sub>2</sub>Ar), 5.95 (1 H, t, *J* = 9.9 Hz, C-10 H), 6.60–7.08 (3 H, m, ArH), 7.28 (1 H, d, *J* = 9.9 Hz, NH).

(30) HR MS (FAB, NaI): calcd for C<sub>36</sub>H<sub>55</sub>NO<sub>13</sub>Na (M<sup>+</sup> + Na) 732.3568, found 732.3599. [ $\alpha$ ]<sub>D</sub>: +19.8° (c 0.35, CCl<sub>4</sub>). <sup>1</sup>H NMR (benzene-*d*<sub>6</sub>):  $\delta$  0.83 (3 H, s, C-14 CH<sub>3</sub>), 1.16 (3 H, d, *J* = 6.6 Hz, C-2 CH<sub>3</sub>), 1.19 (3 H, d, *J* = 7.2 Hz, C-3 CH<sub>3</sub>), 1.29 (3 H, s, C-14 CH<sub>3</sub>), 1.68 (1 H, m, C-16 H), 1.72 (3 H, s, OCOCH<sub>3</sub>), 2.04 (1 H, dq, *J* = 2.6, 7.1 Hz, C-3 H), 2.41 (1 H, ddd, *J* = 3.9, 12.8, 15.5 Hz, C-16 H), 2.72 (1 H, d, *J* = 2.1 Hz, C-13 H), 2.85 (1 H, d, *J* = 15.3 Hz, C-5 H), 2.88 (1 H, d, *J* = 15.3 Hz, C-5 H), 2.92 (3 H, s, OCH<sub>3</sub>), 3.18 (3 H, s, OCH<sub>3</sub>), 3.26 (3 H, s, OCH<sub>3</sub>), 3.29 (1 H, m, C-11 H), 3.42 (3 H, s, OCH<sub>3</sub>), 3.48 (1 H, m, C-12 H), 3.50 (1 H, m, C-17 H), 3.51 (3 H, s, OCH<sub>3</sub>), 3.70 (1 H, dd, *J* = 2.4, 11.6 Hz, C-15 H), 3.98 (1 H, dq, *J* = 2.6, 6.6 Hz, C-2 H), 4.21 (1 H, dd, *J* = 5.9, 11.8 Hz, C-18 H), 4.35 (1 H, dd, *J* = 3.4, 11.8 Hz, C-18 H), 4.39 (1 H, d, *J* = 6.7 Hz, OCH<sub>2</sub>O), 4.41 (1 H, s, C-7 H), 4.68 (1 H, d, *J* = 11.0 Hz, CH<sub>2</sub>Ar), 4.77 (1 H, s, =CH<sub>2</sub>), 4.81 (1 H, s, =CH<sub>2</sub>), 4.87 (1 H, d, *J* = 6.7 Hz, OCH<sub>2</sub>O), 5.01 (1 H, d, *J* = 11.0 Hz, CH<sub>2</sub>Ar), 5.52 (1 H, dd, *J* = 1.9, 9.8 Hz, C-10 H), 6.60–7.13 (3 H, m, ArH), 8.09 (1 H, d, *J* = 9.8 Hz, NH).

(31) This was confirmed by starting from both the unnatural and natural C-10 diastereomers.

natural and unnatural diastereomers.<sup>31,32</sup> Mycalamides A (1)<sup>33</sup> and B (2)<sup>34</sup> were obtained from  $\alpha$ -16 and  $\alpha$ -17 in two steps [(1) *t*-BuOK/THF/room temperature for  $\alpha$ -16 and LiOH/MeOH/room temperature for  $\alpha$ -17; (2) DDQ/H<sub>2</sub>O-CH<sub>2</sub>Cl<sub>2</sub>/room temperature] in 60% and 69% overall yields, respectively. On comparison of <sup>1</sup>H and <sup>13</sup>C NMR, IR, MS, [ $\alpha$ ]<sub>D</sub>, and TLC data, the synthetic materials were found to be identical with an authentic sample of mycalamides A and B.<sup>35</sup>

The reported synthesis has a good flexibility for the preparation of various analogues of mycalamides. In this regard, it is also interesting to note that some of the intermediates should be useful for the construction of the right half of onnamide A. Lastly, it is worthwhile to point out that this synthesis has unambiguously established the absolute stereochemistry of mycalamides A and B, which had tentatively been assigned on the basis of their structural similarity to pederin.

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**Supplementary Material Available:** Experimental details for the coupling reactions to form 16 and 17 and spectroscopic data for the key intermediates and mycalamides A and B (13 pages). Ordering information is given on any current masthead page.

(32) On potassium *tert*-butoxide treatment, the carbonate group in 16 or the acetate group in 17 was hydrolyzed. It was observed that these substances decomposed slowly under the basic conditions, so epimerization was stopped at approximately 60% completion for preparative purposes to yield the epimerized natural diastereomer in 42% yield (67% corrected yield).

(33) HR MS (FAB, NaI): calcd for C<sub>24</sub>H<sub>41</sub>NO<sub>10</sub>Na (M<sup>+</sup> + Na) 526.2626, found 526.2664. [ $\alpha$ ]<sub>D</sub>: +82.4° (c 0.37, CHCl<sub>3</sub>). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.88 (3 H, s, C-14 CH<sub>3</sub>), 0.99 (3 H, s, C-14 CH<sub>3</sub>), 1.01 (3 H, d, *J* = 7.0 Hz, C-3 CH<sub>3</sub>), 1.21 (3 H, d, *J* = 6.4 Hz, C-2 CH<sub>3</sub>), 1.56 (2 H, m, C-16 H), 2.26 (1 H, dq, *J* = 2.4, 7.0 Hz, C-3 H), 2.38 (2 H, m, C-5 H), 3.31 (3 H, s, C-6 OCH<sub>3</sub>), 3.39 (1 H, dd, *J* = 6.1, 11.2 Hz, C-18 H), 3.47 (1 H, d, *J* = 10.2 Hz, C-13 H), 3.57 (3 H, s, C-13 OCH<sub>3</sub>), 3.58 (1 H, dd, *J* = 3.3, 11.2 Hz, C-18 H), 3.65 (1 H, dd, *J* = 4.5, 7.5 Hz, C-15 H), 3.75 (1 H, m, C-17 H), 3.87 (1 H, dd, *J* = 6.7, 9.6 Hz, C-11 H), 4.00 (1 H, dq, *J* = 2.7, 6.4 Hz, C-2 H), 4.24 (1 H, dd, *J* = 6.7, 10.2 Hz, C-12 H), 4.31 (1 H, s, C-7 H), 4.75 (1 H, s, =CH<sub>2</sub>), 4.86 (1 H, s, =CH<sub>2</sub>), 4.89 (1 H, d, *J* = 7.0 Hz, OCH<sub>2</sub>O), 5.15 (1 H, d, *J* = 7.0 Hz, OCH<sub>2</sub>O), 5.88 (1 H, t, *J* = 9.7 Hz, C-10 H), 7.49 (1 H, d, *J* = 9.7 Hz, NH). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  12.02 (C-3 CH<sub>3</sub>), 13.51 (C-14 CH<sub>3</sub>), 17.89 (C-2 CH<sub>3</sub>), 23.11 (C-14 CH<sub>3</sub>), 31.99 (C-16), 33.69 (C-5), 41.33 (C-3), 41.62 (C-14), 48.92 (C-6 OCH<sub>3</sub>), 61.81 (C-13 OCH<sub>3</sub>), 66.48 (C-18), 69.82 (C-2), 71.25 (C-11), 71.57 (C-17), 72.82 (C-7), 73.75 (C-10), 74.38 (C-12), 78.97 (C-15), 79.11 (C-13), 86.82 (OCH<sub>2</sub>O), 99.82 (C-6), 110.61 (=CH<sub>2</sub>), 145.56 (C-4), 171.79 (C-8). IR (film): 3100–3600, 2970, 2929, 1684, 1522, 1470, 1382, 1267, 1194, 1173, 1093, 1075, 1034, 938, 879, 670 cm<sup>-1</sup>.

(34) HR MS (FAB NaI): calcd for C<sub>26</sub>H<sub>43</sub>NO<sub>10</sub>Na (M<sup>+</sup> + Na) 540.2782, found 540.2769. [ $\alpha$ ]<sub>D</sub>: +41.2° (c 0.19, CHCl<sub>3</sub>). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.88 (3 H, s, C-14 CH<sub>3</sub>), 1.00 (3 H, s, C-14 CH<sub>3</sub>), 1.04 (3 H, d, *J* = 7.0 Hz, C-3 CH<sub>3</sub>), 1.22 (3 H, d, *J* = 6.6 Hz, C-2 CH<sub>3</sub>), 1.56 (2 H, m, C-16 H), 2.25 (1 H, d, *J* = 13.9 Hz, C-5 H), 2.28 (1 H, dq, *J* = 2.4, 7.0 Hz, C-3 H), 2.39 (1 H, d, *J* = 13.9 Hz, C-5 H), 3.21 (1 H, m, C-17 H), 3.26 (3 H, s, C-17 OCH<sub>3</sub>), 3.32 (3 H, s, C-6 OCH<sub>3</sub>), 3.43 (1 H, m, C-15 H), 3.45 (1 H, d, *J* = 10.4 Hz, C-13 H), 3.50 (1 H, dd, *J* = 5.7, 11.6 Hz, C-18 H), 3.57 (3 H, s, C-13 OCH<sub>3</sub>), 3.68 (1 H, m, C-18 H), 3.80 (1 H, dd, *J* = 6.7, 9.6 Hz, C-11 H), 3.89 (1 H, s, C-7 OH), 4.05 (1 H, dq, *J* = 2.8, 6.6 Hz, C-2 H), 4.23 (1 H, dd, *J* = 6.7, 10.4 Hz, C-12 H), 4.31 (1 H, s, C-7 H), 4.74 (1 H, s, =CH<sub>2</sub>), 4.84 (1 H, d, *J* = 7.0 Hz, OCH<sub>2</sub>O), 4.84 (1 H, s, =CH<sub>2</sub>), 5.12 (1 H, d, *J* = 7.0 Hz, OCH<sub>2</sub>O), 5.80 (1 H, t, *J* = 9.7 Hz, C-10 H), 7.52 (1 H, d, *J* = 9.9 Hz, NH). <sup>13</sup>C NMR (CDCl<sub>3</sub>):  $\delta$  12.17 (C-3 CH<sub>3</sub>), 13.70 (C-14 CH<sub>3</sub>), 17.96 (C-2 CH<sub>3</sub>), 23.20 (C-14 CH<sub>3</sub>), 29.71 (C-16), 33.68 (C-5), 41.27 (C-3), 41.45 (C-14), 48.61 (C-6 OCH<sub>3</sub>), 56.65 (C-17 OCH<sub>3</sub>), 61.80 (C-13 OCH<sub>3</sub>), 63.58 (C-18), 69.67 (C-2), 70.70 (C-11), 71.67 (C-7), 73.97 (C-10), 74.47 (C-12), 75.57 (C-15), 78.75 (C-17), 79.31 (C-13), 86.51 (OCH<sub>2</sub>O), 99.94 (C-6), 111.14 (=CH<sub>2</sub>), 145.00 (C-4), 171.75 (C-8). IR (film): 3356, 2926, 2854, 1687, 1514, 1465, 1382, 1237, 1102, 1074, 1036 cm<sup>-1</sup>.

(35) We are indebted to Professors Perry and Munro for a sample of mycalamides A and B.