was incubated in a shaker bath 2 h at 37 °C. The reaction mixture then was evaporated to dryness in vacuo, and the products were fractionated by LC using a C_{18} μ-Bondapak column (6 mm × 30 cm); the eluting solvent was H_2O–MeOH (85:15), and the flow rate was 2.8 mL/min. Two reaction products were eluted: glucose (40.1 mg) at 3.8 min and a second peak (51.7 mg) at 6.0 min, identical with **2a**: mp 141–144 °C, after recrystallization from chloroform (lit.[15] mp 143–144 °C); ORD $[\alpha]^{25}_D$ −24, $[\alpha]_{560}$ −26, $[\alpha]_{520}$ −31, $[\alpha]_{480}$ −37, $[\alpha]_{440}$ −47, $[\alpha]_{400}$ −58, $[\alpha]_{360}$ −76, $[\alpha]_{320}$ −102° (*c* 1.03, H_2O) (lit.[15] $[\alpha]^{26}_D$ −27.5°); ^{13}C NMR, in Table I.

An authentic sample of **2a**, provided by Dr. David S. Seigler, University of Illinois at Urbana-Champaign, showed the following: ORD $[\alpha]^{25}_D$ −23, $[\alpha]_{560}$ −26, $[\alpha]_{520}$ −31, $[\alpha]_{480}$ −37, $[\alpha]_{440}$ −45, $[\alpha]_{400}$ −57, $[\alpha]_{360}$ −75, $[\alpha]_{320}$ −102, $[\alpha]_{290}$ −133° (*c* 1.43, H_2O); ^{13}C NMR, in Table I.

Enzymatic Hydrolysis of 1b. **1b** (100 mg) was treated with β-glucosidase as described for **1a**. The reaction product was fractionated by LC similarly, and two reaction products were eluted: glucose (41.8 mg) at 3.8 min and a second peak, identical with **2b** (56.6 mg), at 9.4 min: mp 120–122 °C, after crystallization from water (lit.[15] mp 123.5–124.5 °C); ORD $[\alpha]^{25}_D$ −18, $[\alpha]_{560}$ −20, $[\alpha]_{520}$ −23, $[\alpha]_{480}$ −28, $[\alpha]_{440}$ −34, $[\alpha]_{400}$ −42, $[\alpha]_{360}$ −54, $[\alpha]_{320}$ −72° (*c* 0.80, H_2O) (lit.[15] $[\alpha]^{25}_D$ −19°); ^{13}C NMR, in Table I.

Authentic **2b** was obtained from a mixture of **2a** and **2b** provided by Dr. R. C. Clapp, U.S. Army Natick Development Center, and isolated originally from *Lotus australis*; 82 mg was separated by LC. Samples were injected into a 7.8 mm × 30 cm C_{18} μ-Bondapak column and eluted at 2 mL/min with H_2O–MeOH (80:20); peaks were eluted at 6.8 min (unidentified, 1.3 mg), 11.2 min (unidentified, 1.5 mg), 14.0 min (**2a**, 22.5 mg), and 18.0 min (**2b**, 55.4 mg): mp 122.5–123.0 °C, after crystallization from water; ORD $[\alpha]^{25}_D$ −16, $[\alpha]_{560}$ −18, $[\alpha]_{520}$ −23, $[\alpha]_{480}$ −28, $[\alpha]_{440}$ −34, $[\alpha]_{400}$ −42, $[\alpha]_{360}$ −53, $[\alpha]_{320}$ −73, $[\alpha]_{280}$ −104, $[\alpha]_{240}$ −160° (*c* 0.62, H_2O); ^{13}C NMR, in Table I.

Amygdalin (1d). An authentic sample of **1d** provided by Dr. David S. Seigler showed the following: ORD $[\alpha]^{25}_D$ −40, $[\alpha]_{560}$ −45, $[\alpha]_{520}$ −53, $[\alpha]_{480}$ −64, $[\alpha]_{440}$ −79, $[\alpha]_{400}$ −98, $[\alpha]_{360}$ −130, $[\alpha]_{320}$ −178, $[\alpha]_{280}$ −261° (*c* 0.33, H_2O) (lit.[9] $[\alpha]^{20}_D$ −41.9°); ^{13}C NMR, in Table I.

Gentiobiose (1c). β-Gentiobiose from Sigma Chemical Co. was used for determination of the ^{13}C NMR spectrum; see Table I.

Complete Acid Hydrolysis of 1b with Mineral Acid. A 0.012-g portion of **1b** was refluxed 3 h with 10 mL of 5% aqueous HCl. The mixture then was evaporated to dryness in vacuo and was analyzed by TLC [solvent system = 1-butanol–acetone–H_2O (4:5:1)]. The only monosaccharide detected was glucose.

Partial Hydrolysis of 1b with Mineral Acid. A 0.020-g portion of **1b** was dissolved in 10 mL of 0.5 N HCl at ambient temperature. After 1 h, the solution was evaporated to dryness in vacuo and was analyzed by LC. Sample was injected into a Waters 3.9 mm × 30 cm carbohydrate μ-Bondapak column and was eluted with MeCN–H_2O (77:23) at 2 mL/min. The following components were recorded [elution time (identity)]: 2.1 min (**2b**), 2.8 min (unidentified), 3.3 min (**1b**), 4.7 min (**2c**), 5.4 min (unidentified), 6.7 min (unidentified), 9.7 min (**1c**). Components were identified by comparison of their retention times with those of authentic reference compounds injected individually.

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Registry No. **1a**, 72229-40-4; **1a** heptaacetate, 72229-41-5; **1b**, 72229-42-6; **1b** heptaacetate, 72229-43-7; **1c**, 5996-00-9; **1d**, 29883-15-6; **2a**, 554-35-8; **2b**, 534-67-8; **2c**, 492-61-5.

The C-13 Configuration of the Bromine-Containing Diterpene Isoaplysin-20. Synthesis of Debromoisoaplysin-20 and Its C-13 Epimer

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Syntheses of the tricyclic diterpenes 13-epidebromoisoaplysin-20 (**14**) and debromoisoaplysin-20 (**15**) from methyl copalate (**3**) are described. Methyl isocopalate (**4**) prepared from **3** was converted into the corresponding alcohol **8**. By epoxidation of **8** a 1:1 mixture of isomeric epoxides was obtained; the reductive opening of the α-epoxide (**13**) afforded **14**. Hydroxylation of **4** gave the diol ester **16**, which on oxidation with dimethyl sulfoxide–acetic anhydride yielded **18a**. Transformation of **18a** into the ethylene thioketals **20** and **20a**, followed by desulfuration of the mixture to the hydroxy ester **21**, and subsequent lithium aluminium hydride reduction afforded **15**. The stereochemical features of the epoxides **9** and **13** and the diol ester **16** as well as those at C-13 of **14** and **15** were determined by analysis of their ^{13}C NMR spectra. On the basis of the comparison of the ^1H NMR signals of the methyl groups of **14** and **15** and the ones of the acetoxymethylene groups of their monoacetates **14a** and **15a** with those reported for the methyls of the bromine-containing diterpene isoaplysin-20 (**1**) and the acetoxymethylene of its monoacetate (**1a**), the stereochemistry of the natural product was established.

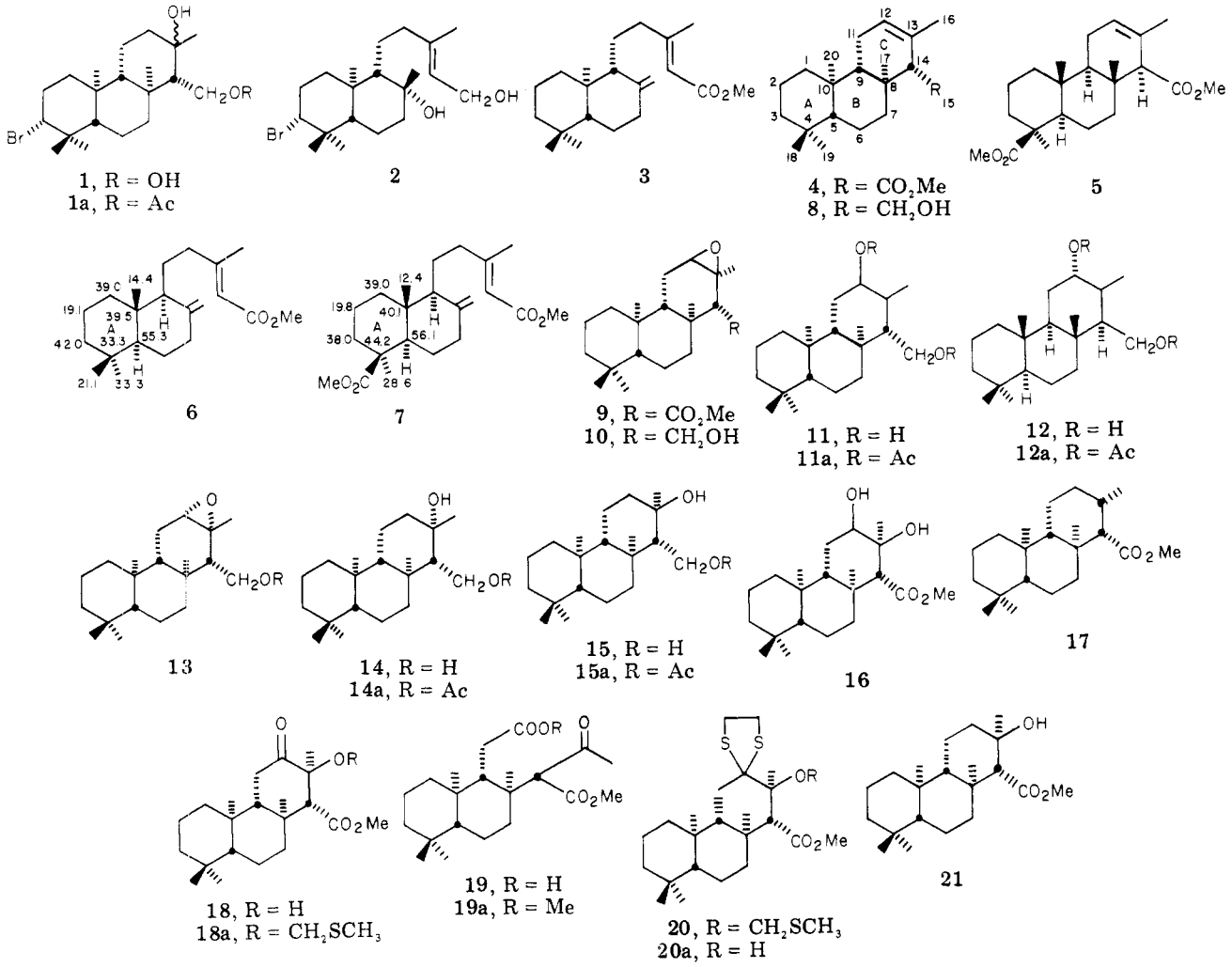
Recently Yamamura and Terada isolated from the sea hare *Aplysia kurodai* a small amount of a bromine-containing tricyclic diterpene, named isoaplysin-20 (**1**). The structure elucidation of **1** was based on the comparison of spectroscopic data with the related bicyclic diterpene aplysin-20 (**2**), also isolated from the same source, and on biogenetic considerations; the configuration at C-13, however, remained undetermined.[1,2] Since the configuration of that type of tertiary alcohol could be, on the basis of previous experience,[3] easily determined by ^{13}C NMR spectroscopy, the synthesis of debromoisoaplysin-20 and/or its C-13 epimer was planned in order to obtain enough material for carrying out these determinations, in the hope that by comparison of the available ^1H NMR data of **1** with those of the synthetic product(s) the complete stereochemistry of isoaplysin-20 could be established.

With the methyl ester of the readily available copalic acid (**3**)[4,5] as starting material and under the conditions

(1) S. Yamamura and Y. Terada, *Tetrahedron Lett.*, 2171 (1977).
(2) The numbering system used in this paper is the one reported by J. W. Rowe, "The Common and Systematic Nomenclature of Cyclic Diterpenes", Forest Products Laboratory, USDA, Madison, Wis., 1968, mentioned by D. K. Manh Duc, M. Fêtizon, and M. Kone, *Bull. Soc. Chim. Fr.*, 2351 (1975).
(3) A. S. Gupta, S. Dev, M. Sangaré, B. Septe, and G. Luckas, *Bull. Soc. Chim. Fr.*, 1879 (1976).
(4) T. Nakano and C. Djerassi, *J. Org. Chem.*, **26**, 167 (1961).

0022-3263/80/1945-0510$01.00/0

Chart I



described for the transformation of agathic into isoagathic acid,[6] the tricyclic ester, methyl isocopalate (**4**), was obtained. An exhaustive analysis of this intermediate's ^{13}C NMR spectrum was carried out in order to facilitate the general structure analysis of its derivatives. The shift assignments, listed in Table I, were made by standard chemical shift theory, analysis of the SFORD and PRFT spectra,[7] and comparison with diterpenes previously studied.[8] Confirmatory evidence for these assignments and for the stereochemistry of methyl isocopalate was obtained by comparison with the shifts of dimethyl isoagathate (**5**). Since **4** and **5** are enantiomers, except for the replacement of the methyl at C-19 of **4** by the methoxycarbonyl of **5**, it is expected that all carbon shifts, apart from the ones affected by the methoxycarbonyl group, would be very similar. That was in fact observed and, further, the differences detected in the δ values of the signals attributed to the ring A carbons of both compounds are of the same magnitude as the ones reported for similar sites of methyl copaiferate (**6**) and dimethyl agathate (**7**).[9]

Reduction of **4** with lithium aluminium hydride in refluxing ether led to isocopalol (**8**), and the next step, the regiospecific hydration of its double bond, was expected to occur smoothly by oxymercuration–demercuration. However, under standard reaction conditions (mercuric acetate, tetrahydrofuran, water, and then sodium borohydride in sodium hydroxide solution) only **8** was re-

Table I. Carbon Shifts of Methyl Isocopalate (4), 13-Epidebromoisoaplysin-20 (14), and Related Products

	4	5	8	9	13	14[a]
C-1	39.9	40.0	39.8	39.2	39.9	39.9
C-2	18.6	20.0	18.7[b]	18.2	18.1[b]	18.0[c]
C-3	41.9	37.8	41.8[c]	41.6	42.5[c]	42.1[b]
C-4	33.2	43.5	33.0	32.9	33.1	33.0
C-5	56.5	57.0	56.1	56.1	56.3	56.3
C-6	18.6	18.9	18.5[b]	18.2	18.4[b]	18.4[c]
C-7	41.9	41.8	41.4[c]	40.1	41.7[c]	41.6[b]
C-8	36.5	36.2	36.1	35.8	36.3	37.3
C-9	54.4	53.5	54.7	50.0	54.1	58.1
C-10	37.4	37.7	37.1	37.1	37.1	38.4
C-11	22.7	22.7	22.5	21.6	20.7	17.7
C-12	123.8	123.6	123.4	61.7[b]	60.4	41.9[b]
C-13	128.9	128.7	132.5	56.6	59.1	73.6
C-14	62.5	62.2	57.7	60.0[b]	55.6	59.0
C-15	173.1	172.7	60.6	172.0	60.4	60.3
C-16	21.1	21.0	21.7	22.2	22.7	30.3
C-17	15.8[b]	15.2	15.7	14.9	16.8	17.0
C-18	33.4	177.3	33.3	33.3	33.2	33.0
C-19	21.4	28.5	21.7	21.6	21.5	21.1
C-20	15.7[b]	13.5	15.7	15.6	15.6	16.1
OMe	51.0	50.7–50.9		50.8		

[a] Some MeOH was added for better solution of the compound. [b,c] The assignments for these signals may be reversed.

(5) J. R. Mahajan and G. A. L. Ferreira, *An. Acad. Brasil. Ciências*, 43, 611 (1971).
(6) S. Bory, M. Fétizon, and P. Laszlo, *Bull. Soc. Chim. Fr.*, 2310 (1963).
(7) G. C. Levy, *Acc. Chem. Res.*, 6, 161 (1973).
(8) P. M. Imamura, A. J. Marsaioli, L. E. S. Barata, and E. A. Rúveda, *Phytochemistry*, 16, 1842 (1977).
(9) B. L. Buckwalter, I. R. Burfitt, A. A. Nagel, E. Wenkert, and F. Näf, *Helv. Chim. Acta*, 58, 1567 (1975).

covered, even after 7 days of stirring at room temperature. The same result was obtained when **4** was used as starting material. The lack of reactivity of these substrates is apparently due to the unfavorable opening of the mercurium–olefin complex by the nucleophilic attack on the more substituted carbon and from the less hindered side of the double bond.

As an attractive possibility for the hydration of the double bond of **4** and/or **8**, the reductive opening of their corresponding epoxides was considered. If the opening occurs in the normal trans-diaxial way and through chairlike intermediates, an α epoxide would be necessary for obtaining a tertiary alcohol. Even though examination of models indicated that the preferential electrophilic attack by the peracid would be from the less hindered β side of the double bonds of both products, the reported influence of a homoallylic alcohol in the formation of an epoxide from the more hindered side, in a system related to **8**,[10] prompted us to study this route carefully.

Epoxidation of **4** with *m*-chloroperbenzoic acid in methylene chloride at 0 °C gave a good yield of an isomerically pure epoxide, which was shown to be the β-isomer **9**, on the basis of a comparative analysis of its ^{13}C NMR data with those of methyl isocopalate (**4**). As was previously observed in a series of steroids,[11] the introduction of the epoxide into the unsaturated ring of **4** (**4** → **9**) causes the homoallylic-positioned C-9, bearing an axial proton cis to the oxygenated function, to undergo a strong shielding effect, while the remaining homoallylic carbon, C-8, being quaternary, and the allylic ones, C-11 and C-14, are only slightly shielded. Attempted opening of epoxide **9** by lithium aluminium hydride in refluxing ether led only to isocopalol β-epoxide (**10**), but under more vigorous conditions (tetrahydrofuran and longer refluxing time) several products were produced, the major of which was the diol **11**. That the hydroxyl group at C-12 of **11** is axial follows from the half-bandwidth of the ^1H NMR signal of the adjacent proton (δ 3.90; $W_{1/2}$ = 10 Hz), and, although a comparison with an authentic sample was not carried out, it is clear, on the basis of their different physical data, that **11** and **11a** and the reported products **12** and **12a**[12] are not enantiomers, indicating that the methyl group at C-13 of **11** is equatorial.

Concordant with expectation, treatment of **8** with *m*-chloroperbenzoic acid in methylene chloride at 0 °C gave a mixture of equal amounts of two isomeric epoxides which were separated by silica gel column chromatography. One of the isomeric epoxides was readily identified as **10**, and the other as the α-isomer **13**, by analysis of its ^{13}C NMR spectrum compared with that of the parent alcohol **8**. The homoallylic carbon bearing an axial proton is, in this case, practically unaffected by the oxygenated function, in agreement with their trans relationship, while the quaternary homoallylic carbon and the allylic ones are again slightly shielded. The reductive opening of **13** with lithium aluminum hydride in refluxing ether led to **14**, one of the desired tertiary alcohols, in good yield. The ^{13}C NMR spectrum of **14** supports the proposed structure and further shows, on the basis of the signal at 30.3 ppm,[3,8] that the methyl group at C-13 is equatorial. (The carbon shifts of **5**, **8**, **9**, **13**, and **14** are listed in Table I.) At this point, the analysis of the ^1H NMR spectrum of **14**, focused on the methyl shifts, was carried out. Of the five signals attributable to these groups, those at δ 1.37 and 1.27 were assigned to the methyls at C-13 and C-8, respectively, the latter suffering a deshielding effect produced by the 1,3-diaxial interaction with the hydroxyl moiety at C-13,[13,14] and the remaining ones at δ 0.87, 0.89, and 0.92 were assigned to the methyls at C-4 and C-10. In the reported ^1H NMR spectrum of isoaplysin-20,[1] the lowest field signal, assigned to the methyl group at C-13, appears at δ 1.32. None of the remaining methyls (δ 0.93, 0.95, 0.98, 1.04), although difficult to assign unambiguously, show the deshielding effect induced by the axial hydroxyl group at C-13 on the C-8 methyl group of **14**, indicating that at the C-13 of isoaplysin-20 (**1**) the hydroxyl and methyl groups should be equatorial and axial, respectively.

A comparison of the reported ^1H NMR acetoxymethylene signals of the monoacetate **1a**—which should not be appreciably affected by the bromine at C-3—with those of **14a** was also carried out. Upon acetylation (**1** → **1a**),[1] the C-15 hydroxymethyl protons suffer a deshielding effect, appearing at δ 4.26 as a pair of doublets with coupling constants equal to 8 and 4 Hz, respectively. In the transformation of **14** into **14a**, however, the signal corresponding to the C-15 acetoxymethylene, apart from being further deshielded (δ 4.38), appears as a clean doublet (J = 4 Hz). These results which could be interpreted in terms of a different conformational preference of the acetoxymethylenes, induced by the different orientation of the hydroxyl group at C-13 of **1a** and **14a**, are in full agreement with the above observations.

With a view to obtaining more rigorous evidence in favor of the foregoing stereochemical assignment, the synthesis of debromoisoaplysin-20 (**15**) was planned. Again, methyl isocopalate (**4**) appeared suited as starting material since, as was shown in the enantiomeric series, its double bond could be stereospecifically hydroxylated to a diol with the desired stereochemistry at C-13.[2] Transformation of the secondary alcoholic function into a methylene group and reduction of the carbomethoxy moiety would then give debromoisoaplysin-20.

Methyl isocopalate was therefore hydroxylated with osmium tetraoxide in pyridine[2] to give the diol ester **16** as the sole reaction product. Although it is evident from examination of models that osmium tetraoxide should approach the double bond of **4** from the less hindered β face, it seemed interesting to confirm the stereochemistry of the cis diol by analyzing its ^{13}C NMR spectrum. Comparison of the carbon shifts of **16** with those of methyl dihydroisocopalate (**17**), obtained by catalytic hydrogenation of **4**,[2] clearly shows that the axial hydroxyl group at C-12 induces shielding effects on its γ carbons, observed only on C-9, since C-14, suffering also a β effect from the hydroxyl at C-13, appears practically unaffected. C-11, on the other hand, is deshielded, due not only to the β effect of the C-12 hydroxyl group but also to the γ anti effect of the equatorial tertiary alcohol with no γ hydrogen.[15,16] Finally a γ anti effect with a proton–proton interaction at the intervening carbons, induced by the axial C-12 hydroxyl group, can be invoked to explain the fairly high-field

(10) M. W. Lunnon and J. Mac Millan, *J. Chem. Soc., Perkin Trans. 1*, 2317 (1977).

(11) K. Tori, T. Komeno, M. Sangaré, B. Septe, B. Delpech, A. Ahond, and G. Luckas, *Tetrahedron Lett.*, 1157 (1974).

(12) The physical data reported in ref 2 for **12** and **12a** are as follows. **12**: mp 187–192 °C; $[\alpha]_D$ −3.5° (*c* 0.3, dioxane). **12a**: mp 70–72 °C; $[\alpha]_D$ −10° (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.00 and 2.05 (s, 6), 4.40 (m, 2), 4.80 (br s, 1, $W_{1/2}$ = 8.5 Hz).

(13) G. Hugel, A. C. Oehlschlager, and G. Ourisson, *Tetrahedron*, Suppl. 8, Part I, 203 (1967).

(14) The same effect has recently been reported in a very closely related system, compounds **33b** and **35**, in P. Sundararaman and W. Herz, *J. Org. Chem.*, **42**, 806 (1977).

(15) J. R. Wiseman and H. O. Krabbenhoft, *J. Org. Chem.*, **42**, 2240 (1977).

(16) The C-11 shift of **21**, 3.2 ppm downfield from the C-11 shift in **17**, confirms this observation.

shift exhibited by C-16,[17] compared with the shifts of axial methyl groups of related tertiary alcohols.[3,9,18]

It was now necessary to transform the secondary hydroxyl into a methylene group, and for this purpose, **16** was first submitted to oxidation, in the hope of obtaining the ketol **18**. The use of Jones' reagent for a short period of time, as previously described for a related transformation,[19] led only to starting material plus a mixture of minor products. For a longer period, however, a compound showing typical IR bands and ^{1}H NMR signals was obtained. This spectral information together with the ^{13}C NMR data, obtained from the analysis of the proton-noise-decoupled and SFORD spectra, allowed assignment of the structure of the oxidation product as depicted in **19**, further supported by the mass spectrum of its methyl ester **19a**. Cleavages of 1,2-diols with Jones' reagent, especially if one of the hydroxyl groups is tertiary, have previously been reported.[20] The oxidation of **16** with dimethyl sulfoxide–acetic anhydride was then considered as an attractive possibility, even though the tertiary hydroxyl group could be converted, at the same time, into a methyl thiomethyl (MTM) ether like **18a**.[21] This would not be, however, a serious disadvantage since, for the reduction of the carbonyl to a methylene group, **18a** could be transformed into a monoethylene thioketal which should be submitted to desulfuration with Raney nickel. During this step of the sequence, the MTM ether would be also removed.[21] In practice, the diol ester **16** reacted smoothly with dimethyl sulfoxide–acetic anhydride to afford crystalline **18a**, supported by its IR, ^{1}H NMR, and mass spectral data. The treatment of **18a**, without further purification, with ethanedithiol and boron trifluoride etherate in acetic acid solution yielded a reaction product that was shown by TLC to be a mixture of two components, tentatively identified as **20** and **20a** by ^{1}H NMR spectroscopy, indicating that part of the MTM ether of **18a** was cleaved during the transformation. The cleavage was complete when the crude mixture was treated with Raney nickel in refluxing ethanol for a few hours, giving pure **20a**. Further treatment under the same conditions for a longer period afforded the hydroxyl ester **21**, which, on lithium aluminum hydride reduction gave the desired product **15**. The ^{13}C NMR spectra of **21** and **15** support their structures and further show, on the basis of the signals at 24.4 and 23.8 ppm, respectively, that the methyl group at C-13 in both products is axial.[3,8,9] (The carbon shifts of **16**, **17**, **19**, **21**, and **15** are listed in Table II.)

At this point, the analysis of the ^{1}H NMR methyl shifts of **15** was also carried out. As it had been anticipated, the signal assigned to the axial methyl at C-13 appears at δ 1.33, and the C-8 methyl group, being free of the effect of the tertiary hydroxyl moiety which is equatorial in **15**, resonates with the remaining methyl groups at higher field (δ 0.82 and 0.85). The similarity of the ^{1}H NMR methyl shift pattern of **15** and the one reported for isoaplysin-20 (**1**),[1] together with the information obtained above with **14**, indicates that indeed **1** and **15** have the same configuration at C-13.

Further confirmation for this configurational assignment was obtained by analyzing the effects suffered by the C-15 hydroxymethyl protons upon acetylation. The transformation of **15** into **15a** induces deshielding of the C-15 protons and, although at 60 MHz they appear as a doublet, by recording the spectrum at 100 MHz a pair of doublets at δ 4.35 with coupling constants equal to 7.5 and 3.5 Hz and in good agreement with those reported for **1a**[1] can be observed.[22]

Table II. Carbon Shifts of Debromoisoaplysin-20 (15) and Related Products

	16[a]	17	19[b]	21	15[a]
C-1	39.3	39.8	39.4	39.9	39.8
C-2	18.3	18.6	18.1	18.5	18.4[c]
C-3	41.8	42.0	41.4	42.0	41.9
C-4	33.1	33.2	33.0	33.2	33.1
C-5	56.5	56.7	54.7	56.7	56.2
C-6	17.9	17.8	18.1	18.0	18.2[c]
C-7	41.0	41.2	34.6	41.4	41.6
C-8	36.7	37.5	42.2	37.5	37.4[d]
C-9	50.1	59.7[c]	67.0	59.9	60.1[e]
C-10	38.1	37.8	39.4	38.6	37.6[d]
C-11	25.1	16.2	30.9	19.4	18.8
C-12	74.0	34.0	180.3	43.9	43.6
C-13	72.8	31.2	203.0	72.3	74.4
C-14	60.6	60.5[c]	50.7	67.1	60.4[e]
C-15	173.0	174.0	169.2	172.8	60.5
C-16	22.6	17.2	31.9	24.4	23.8
C-17	16.0	17.0	20.3	16.3[c]	17.0
C-18	33.1	33.2	33.0	33.2	33.1
C-19	21.1	21.4	21.4	21.3	21.2
C-20	15.6	16.2	16.0	16.2[c]	16.2
OMe	50.8	50.6	51.7	50.8	

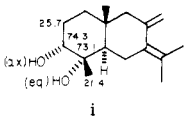
[a] Some MeOH was added for better solution of the compound. [b] The numbering system for **19** in this table is the same used for the tricyclic products for sake of clarity. [c-e] The assignments for these signals may be reversed.

Experimental Section

All melting points were determined on a Reichert hot-stage microscope and are uncorrected. Infrared spectra were measured with a Perkin-Elmer 337 spectrophotometer as solids in KBr disks. ^{1}H NMR spectra were recorded, unless otherwise indicated, in $CDCl_3$ solutions at 60 MHz on a Varian T-60 spectrometer and Me_4Si was used as an internal standard; chemical shifts are expressed in δ and coupling constants (J) and half-bandwidths ($W_{1/2}$) are given in hertz (s = singlet, d = doublet, t = triplet, m = multiplet). Unless otherwise indicated, the ^{13}C NMR spectra were recorded in $CDCl_3$ solutions on a Varian XL-100 spectrometer operating at 25.2 MHz in the Fourier transform mode; the δ values are in parts per million downfield from Me_4Si [$\delta(Me_4Si) = \delta(CDCl_3) + 76.9$]. The following abbrevations are used: PND, proton-noise-decoupled spectrum; SFORD, single-frequency off-resonance decoupled spectrum; PRFT, partially relaxed Fourier transform spectrum. Mass spectra were obtained with a Finnigan Model 1015/SL spectrometer and the high-resolution mass spectral analyses were performed with a Varian MAT Bremen Model MAT 311A instrument. Optical rotations were measured in a Carl Zeiss photoelectric polarimeter. Silica gel GF_{254} (Type 60) was utilized for thin-layer plates (TLC) and spots were

(17) T. P. Forrest and J. G. K. Webb, *Org. Magn. Reson.*, **12**, 371 (1979).

(18) Further confirmation of the shift assignments of the diol moiety and neighboring carbons of **16** was obtained by comparison with similar sites of the related system present in the sesquiterpene cuauhtemone, i, reported by K. Nakanishi, R. Crouch, I. Miura, X. Dominguez, A. Zamudio, and R. Villarreal, *J. Am. Chem. Soc.*, **96**, 609 (1974).



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visualized by staining with iodine vapor. Combustion analyses were carried out by the Analytical Laboratory of Laboratorio de Pesquisa, Rhodia (Divisão Paulinia).

Copalic Acid. This material was obtained from commerical "óleo de copaiba", following ref 4 and 5.

Methyl Isocopalate (4). A solution of copalic acid (5.39 g) in Et_2O was treated with an excess of ethereal diazomethane. The Et_2O was evaporated and the resulting oil, **3**, was treated with 98% aqueous formic acid according to ref 6 to give crystalline **4** (5.56 g): recrystallized from MeOH, mp 109–110 °C; $[\alpha]_D$ +50.9° (*c* 1.6, $CHCl_3$) (lit.[23-26] for the enantiomer: mp 104–105 °C; $[\alpha]_D$ −58°; mp 108–110 °C; mp 103–105 °C; $[\alpha]_D$ −50.4°; mp 110–111 °C; $[\alpha]_D$ −55°, respectively); IR 1730, 1250, 1185, 1165 cm^{-1}; ^1H NMR δ 0.85 (s, 3), 0.86 (s, 3), 0.92 (s, 3), 0.95 (s, 3), 1.61 (s, 3), 2.93 (m, 1), 3.68 (s, 3), 5.53 (m, 1); MS *m/e* (relative intensity) 318 (M^+, 22), 177 (100). Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.14; H, 11.06.

Isocopalol (8). $LiAlH_4$ (730 mg, 20 mmol) was gradually added to a stirred solution of **4** (2.0 g, 6.6 mmol) in anhydrous Et_2O (100 mL). After 4 h of heating at reflux, the reaction mixture was quenched as usual, washed with brine, and dried (Na_2SO_4); evaporation of the solvent gave a solid residue, which after crystallization from MeOH furnished pure **8** (1.75 g): mp 127–128 °C; $[\alpha]_D$ +13.5° (*c* 1.0, $CHCl_3$) (lit.[2,25] for the enantiomer: mp 125–126 °C; $[\alpha]_D$ −10.5°; mp 125–126 °C $[\alpha]_D$ −9°, respectively); IR 3640, 1040, 995, 840 cm^{-1}; ^1H NMR δ 0.83 (s, 6), 0.85 (s, 3), 0.88 (s, 3), 1.80 (s, 3), 3.78 (m, 1), 5.52 (m, 1); MS *m/e* (relative intensity) 290 (M^+, 26), 192 (100), 191 (66), 177 (100), 136 (34), 123 (46), 122 (72), 95 (48). Anal. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80. Found: C, 82.79; H, 12.22.

Methyl Isocopalate β-Epoxide (9). *m*-Chloroperbenzoic acid (85%, 700 mg) was added to a cold stirred solution of **4** (800 mg, 2.5 mmol) in dry CH_2Cl_2 (100 mL), and the mixture was left at 0 °C overnight. The CH_2Cl_2 solution was then washed successively with 0.1 N NaOH (3 × 30 mL) and saturated brine until neutral, dried (Na_2SO_4), and evaporated. The residue (816 mg) crystallized from $CHCl_3$–MeOH gave **9**: mp 152–154 °C; $[\alpha]_D$ +27.13° (*c* 1.0, $CHCl_3$); IR 1750, 1160, 1100, 1000 cm^{-1}; ^1H NMR δ 0.83 (s, 3), 0.85 (s, 3), 0.92 (s, 3), 1.07 (s, 3), 1.22 (s, 3), 2.37 (s, 1), 2.87 (br s, 2, $W_{1/2}$ = 6 Hz), 3.65 (s, 3); MS *m/e* (relative intensity) 334 (M^+, 3), 319 (14), 177 (84), 149 (32), 142 (80), 140 (59), 123 (67), 109 (66), 95 (91), 81 (100). Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25. Found: C, 75.31; H, 10.73.

Isocopalol β-Epoxide (10). $LiAlH_4$ (500 mg, 13 mmol) was gradually added to a stirred solution of **9** (435 mg, 1.3 mmol) in anhydrous Et_2O (60 mL). After 6 h of heating at reflux and the usual workup, **10** was obtained as a crystalline solid (400 mg) from MeOH: mp 201–203 °C; IR 3500, 1035, 990 cm^{-1}; ^1H NMR (CCl_4) δ 0.80 (s, 3), 0.83 (s, 3), 0.90 (s, 6), 1.74 (s, 3), 2.97 (m, 1), 3.6–3.9 (m, 2); MS *m/e* (relative intensity) 306 (M^+, 3), 192 (57), 191 (82), 177 (66), 123 (72), 109 (66), 95 (100). Found: M^+, *m/e* 306.2548; $C_{20}H_{34}O_2$ requires *m/e* 306.25587.

Diol 11. $LiAlH_4$ (400 mg, 10 mmol) was added to a stirred solution of **10** (400 mg, 1.3 mmol) in dry THF (60 mL). Heating at reflux for 40 h and the usual workup gave a crude product, which by TLC analyses appeared to be composed of a major component and several minor products. Application of this product to a column of silica gel (Type H) and elution with $CHCl_3$ afforded the pure diol **11** (230 mg) from MeOH: mp 174–175 °C; $[\alpha]_D$ −50.32° (*c* 1.1, $CHCl_3$); $[\alpha]_D$ −14.7° (*c* 1.05, dioxane); IR 3600 (sh), 3450, 1090, 990 cm^{-1}; ^1H NMR δ 0.85 (s, 6), 0.88 (s, 3), 0.93 (s, 3), 1.08 (d, 3, *J* = 6 Hz), 3.70 (m, 2, $W_{1/2}$ = 6 Hz), 3.90 (m, 1, $W_{1/2}$ = 10 Hz); MS *m/e* (relative intensity) 308 (M^+, 4), 191 (100), 137 (36), 123 (74), 121 (66), 109 (87), 95 (88). Found: M^+, *m/e* 308.2708; $C_{20}H_{36}O_2$ requires *m/e* 308.27152.

Diacetate 11a. The diol **11** (20 mg) was treated with acetic anhydride (0.5 mL) and pyridine (0.5 mL) overnight at room temperature. The mixture was then carefully acidified with dilute HCl (with cooling) to pH 3 and extracted with $CHCl_3$ (3 × 10 mL), and the combined $CHCl_3$ extracts were washed with H_2O until neutral, dried (Na_2SO_4), and evaporated. The residue (20 mg) recrystallized from $CHCl_3$–MeOH gave the diacetate **11a**: mp 162–163 °C; $[\alpha]_D$ −48.78° (*c* 1.3, $CHCl_3$); IR 1700, 1690, 1240, 1220, 1025, 1015 cm^{-1}; ^1H NMR δ 0.80 (s, 6), 0.85 (s, 3), 0.88 (s, 3), 0.92 (part of a doublet), 2.00 (s, 3), 2.05 (s, 3), 4.07 (dd, 2, $W_{1/2}$ = 8 Hz), 5.00 (m, 1, $W_{1/2}$ = 8 Hz); MS *m/e* (relative intensity) 332 ($M^+ - CH_3CO_2H$, 4), 273 (39), 207 (55), 191 (100), 190 (63), 135 (38). Found: $M^+ - CH_3CO_2H$, *m/e* 332.2711; $C_{22}H_{36}O_2$ requires *m/e* 332.27152.

Isocopalol α-Epoxide (13). *m*-Chloroperbenzoic acid (85%, 950 mg) was gradually added to a cold stirred solution of **8** (1 g, 3.5 mmol) in dry CH_2Cl_2 (80 mL), and the mixture was left at 0 °C overnight. The CH_2Cl_2 solution was then washed successively with 0.1 N NaOH (2 × 30 mL) and saturated brine until neutral, dried (Na_2SO_4), and evaporated. The oily residue (1.15 g), shown by analysis of its ^1H NMR spectrum to be a mixture of two isomeric epoxides in an approximate 1:1 ratio, was applied to a column of silica gel and eluted with 0.5% MeOH–$CHCl_3$ to afford **13** (374.5 mg): mp 122–124 °C; $[\alpha]_D$ +22.42° (*c* 1.1, $CHCl_3$); IR 3350, 1120, 1040, 990 cm^{-1}; ^1H NMR δ 0.84 (s, 9), 0.88 (s, 3), 1.37 (s, 3), 2.92 (m, 1), 3.83 (d, 2, *J* = 5 Hz); MS *m/e* (relative intensity) 306 (M^+, 11), 192 (53), 191 (71), 177 (74), 136 (50), 123 (80), 109 (68), 95 (100), 81 (82). Found: M^+, *m/e* 306.2548; $C_{20}H_{34}O_2$ requires *m/e* 306.25587. Elution with 1% MeOH–$CHCl_3$ afforded **10** (314.5 mg).

13-Epidebromoisoaplysin-20 (14). $LiAlH_4$ (300 mg, 7.9 mmol) was gradually added to a stirred solution of **13** (320 mg, 1 mmol) in anhydrous Et_2O (60 mL). After 6 h of heating at reflux and the usual workup, a solid residue was obtained (320 mg). Chromatography of this product on silica gel (Type H) with 1% MeOH–$CHCl_3$ afforded **14** (210 mg): mp 203–205 °C; $[\alpha]_D$ +14.58° (*c* 1, 1:1 $CHCl_3$–MeOH); IR 3330, 1250, 1090, 1030, 810 cm^{-1}; ^1H NMR δ 0.87 (s, 3), 0.89 (s, 3), 0.92 (s, 3), 1.27 (s, 3), 1.37 (s, 3), 2.53 (m, 1, $W_{1/2}$ = 8 Hz), 4.13 (m, 2, $W_{1/2}$ = 6 Hz); MS *m/e* (relative intensity) 290 ($M^+ - H_2O$, 73), 191 (35), 123 (55), 109 (64), 95 (100), 82 (58), 81 (89), 69 (100), 55 (68). Found: $M - H_2O$, *m/e* 290.2608; $C_{20}H_{34}O$ requires *m/e* 290.26095. Anal. Calcd for $C_{20}H_{36}O_2$: C, 77.87; H, 11.76. Found: C, 77.79; H, 11.45.

13-Epidebromoisoaplysin-20 Monoacetate (14a). The diol **14** (30 mg) was treated with acetic anhydride (0.5 mL) and pyridine (0.5 mL) overnight at room temperature. The mixture was then carefully acidified with dilute HCl (with cooling) to pH 3 and extracted with $CHCl_3$ (3 × 10 mL), and the combined $CHCl_3$ extracts were washed with H_2O until neutral, dried (Na_2SO_4), and evaporated. The residue (25 mg) recrystallized from MeOH gave the monoacetate **14a**: mp 179–180 °C; $[\alpha]_D$ +25.4° (*c* 1, $CHCl_3$); IR 3490, 1730, 1290, 1240, 1190, 1030 cm^{-1}; ^1H NMR δ 0.83 (s, 3), 0.87 (s, 6), 1.02 (s, 3), 1.22 (s, 3), 2.07 (s, 3), 4.38 (d, 2, *J* = 4 Hz); MS *m/e* (relative intensity) 350 (M^+, 2), 290 (90), 191 (42), 123 (54), 121 (37), 109 (65), 107 (38), 95 (100). Anal. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.42; H, 10.79.

Diol Ester 16. Osmium tetraoxide (1.025 g, 4.03 mmol) was added to a stirred solution of **4** (1.2 g, 3.77 mmol) in dry pyridine (15 mL), and the progress of the reaction was monitored by TLC. After 65 h of stirring at room temperature in the dark, a solution of sodium metabisulfite (9.0 g, 47.36 mmol) in 1:1 pyridine–H_2O (20 mL) was added. The mixture was stirred for an additional 2.5 h and extracted with EtOAc (5 × 25 mL). The combined organic extracts were washed with brine (2 × 30 mL), dried (Na_2SO_4), and evaporated, and the residue was crystallized from $CHCl_3$–MeOH to afford pure **16** (1.09 g): mp 242–245 °C with sublimation; $[\alpha]_D$ +12.69° (*c* 1.16, $CHCl_3$) (lit.[2] for the enantiomer: mp 270 °C with sublimation; $[\alpha]_D$ −17.4° (dioxane)); IR 3500, 3410, 1730, 1190 cm^{-1}; ^1H NMR δ 0.88 (s, 9), 1.17 (s, 3), 1.48 (s, 3), 2.47 (m, 2, $W_{1/2}$ = 12 Hz), 2.67 (s, 1), 3.73 (s, 3); ^1H NMR (pyridine-d_5) δ 0.82 (s, 3), 0.85 (s, 6), 1.32 (s, 3), 1.80 (s, 3), 3.17 (s, 1), 3.70 (s, 3), 3.97 (m, 1, $W_{1/2}$ = 7 Hz), 5.43 (br s, 1, exchanges with D_2O), 6.23 (br s, 1, exchanges with D_2O); MS *m/e* (relative intensity) 352 (M^+, 53), 334 (3), 279 (27), 278 (100), 191 (27), 123 (28), 117 (44), 95 (59). Anal. Calcd for $C_{21}H_{36}O_4$: C, 71.55; H, 10.29. Found: C, 71.12; H, 10.15.

Methyl Dihydroisocopalate (17). Methyl isocopalate (**4**; 250 mg, 0.79 mmol) was dissolved in a 5:1 mixture of MeOH–EtOAc

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(30 mL) and hydrogenated in the presence platinum oxide (200 mg) for 6 h at room temperature and 2 atm. After filtration of the catalyst through a Celite pad, the filtrate was concentrated to dryness; the residue (246 mg) crystallized from MeOH afforded **17** (212 mg): mp 146–148 °C; $[\alpha]_D$ +9.77° (*c* 1.59, $CHCl_3$) (lit.[2] for the enantiomer: mp 120–121 °C; $[\alpha]_D$ −42.0°); IR 1730, 1390, 1160, 1115, 1005, 760 cm^{-1}; ^1H NMR (CCl_4) δ 0.80 (s, 3), 0.83 (s, 6), 1.03 (d, 3, *J* = 7 Hz), 1.20 (s, 3), 2.17 (br s, 2), 3.58 (s, 3); MS *m/e* (relative intensity) 320 (M^+, 51), 305 (42), 192 (70), 191 (100), 137 (47), 123 (93), 109 (77), 107 (32), 101 (46), 95 (75), 82 (49), 81 (69). Anal. Calcd for $C_{21}H_{36}O_2$: C, 78.70; H, 11.32. Found: C, 78.67; H, 11.16.

Oxidations of 16. Method A. To an ice-cold solution (10 °C) of **16** (680 mg, 1.93 mmol) in acetone redistilled from $KMnO_4$ (15 mL) was added dropwise a solution of Jones' reagent[27] until a slight excess was present (0.4 mL). After 10 min of stirring, crushed ice–H_2O (ca. 30 mL) was added and the mixture was successively extracted with Et_2O (3 × 50 mL) and $CHCl_3$ (3 × 50 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated to give a residue (733 mg), which was shown by TLC (2% MeOH–$CHCl_3$) to be mainly starting material together with two other products having R_f values of 0.50 and 0.60, respectively. By crystallization of this mixture from MeOH, starting material was recovered (255 mg) and attemped separation by column chromatography of the components of the residue obtained by evaporation of the mother liquors (478 mg) was unsuccessful. This mixture was then submitted to further oxidation with an excess of Jones' reagent, followed by 30 min of stirring at room temperature and worked up as described above. Rapid chromatography of the residue (480 mg), which showed a major product on TLC (2% MeOH–$CHCl_3$), through silica gel (Type H) furnished pure **19** as a colorless oil: IR 3500–2500, 1740, 1720, 1700, 1300, 1190, 1130, 755 cm^{-1}; ^1H NMR δ 0.80 (s, 3), 0.90 (s, 6), 1.02 (s, 3), 2.20 (m, 2, $W_{1/2}$ = 16 Hz), 2.25 (s, 3), 3.5 (s, 1), 3.67 (s, 3). A solution of **19** (50 mg) in Et_2O was treated with an excess of ethereal diazomethane. Evaporation of the solvent gave **19a** as an oil, homogeneous by TLC, which solidified on standing: $[\alpha]_D$ −17.70° (*c* 2.05, $CHCl_3$); IR 1750, 1740, 1710, 1190, 1165, 1130; ^1H NMR (CCl_4) δ 0.80 (s, 3), 0.88 (s, 3), 0.92 (s, 3), 0.97 (s, 3), 2.07 (m, 2, $W_{1/2}$ = 12 Hz), 3.30 (s, 1), 3.60 (s, 3), 3.65 (s, 3); MS *m/e* (relative intensity) 380 (M^+, 2), 265 (54), 264 (100), 191 (53), 190 (81), 137 (75), 136 (94), 124 (94), 123 (81), 121 (55), 117 (52), 109 (81), 95 (55). Anal. Calcd for $C_{22}H_{36}O_5$: C, 69.44; H, 9.54. Found: C, 68.81; H, 9.26.

Method B. A mixture of **16** (1.088 g, 3.09 mmol) in Me_2SO (10 mL), predried by azeotropic distillation with benzene, and freshly distilled acetic anhydride (10 mL) was stirred for 27 h. The solvent was evaporated at reduced pressure and the residue was taken up with Et_2O (50 mL). The organic solution was washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated to afford **18a** (1.267 g) as a crystalline solid: IR 1730 (broad band), 1195, 1170, 1045, 780 cm^{-1}; ^1H NMR δ 0.83 (s, 3), 0.90 (s, 6), 1.35 (s, 3), 1.61 (s, 3), 2.20 (s, 3), 2.43 (s, 1), 2.57 (d, 1, *J* = 3 Hz), 2.83 (s, 1), 3.73 (s, 3), 4.71 (s, 2); MS *m/e* (relative intensity) 410 (M^+, 2), 363 (63), 334 (97), 275 (63), 192 (63), 191 (100), 137 (63), 95 (48).

Hydroxy Ester 21. Freshly distilled BF_3·Et_2O (1.0 mL) was added to a stirred solution of crude **18a** (500 mg, 1.22 mmol) in HOAc (10 mL) and ethanedithiol (0.6 mL). After 1 h of stirring, during which time a white precipitate separated, the reaction was complete (TLC). Crushed ice–H_2O (ca. 150 mL) was then added and the mixture was extracted with Et_2O (4 × 100 mL). The combined organic extracts were washed with brine (3 × 50 mL), dried (Na_2SO_4), and evaporated to dryness, and the ^1H NMR spectrum of the residue, showing two spots on TLC (2% MeOH–$CHCl_3$), was examined. The product appears to be a mixture of the two compounds **20** and **20a** on the basis of the singlets at δ 3.73 and 2.23, assigned to the methylene and methyl groups of the methyl thiomethyl ether moiety of **20**, the singlets at δ 1.20 and 1.67, attributed to two quaternary methyl groups of **20a**, and the broad singlet at δ 3.33, corresponding to the monoethylene thioketal group of both components. A solution of this mixture of thioketals **20** and **20a** (760 mg) in absolute EtOH (75 mL) was stirred under reflux for 8 h in the presence of Raney nickel (approximately 6 g) prepared according to ref 28. The mixture was filtered through Celite, and the filtrate was evaporated to give crystalline **20a**: IR 3450, 1740, 1720, 1195, 750 cm^{-1}; ^1H NMR δ 0.83 (s, 3), 0.88 (s, 6), 1.20 (s, 3), 1.67 (s, 3), 2.20 (d, 1, *J* = 6 Hz), 2.20 (d, 1, *J* = 8 Hz), 2.70 (br s, 1), 3.30 (br s, 4), 3.67 (s, 3). A small sample was crystallized from MeOH: mp 213–215 °C; MS *m/e* (relative intensity) 426 (M^+, 73), 398 (100), 280 (53), 171 (60), 132 (72), 131 (72), 119 (61), 118 (72), 105 (57), 95 (49).

The same procedure was repeated once more with a reaction time of 30 h. Rapid chromatography of the final residue (498 mg) through silica gel (25 g) with hexane furnished **21** (303 mg). An analytical sample was recrystallized from MeOH: mp 167–169 °C; $[\alpha]_D$ +31.32° (*c* 1.13, $CHCl_3$); IR 3420, 3390, 1740, 1720, 1215, 1195, 1145, 1130, 1005, 915 cm^{-1}; ^1H NMR δ 0.85 (s, 9), 1.10 (s, 3), 1.47 (s, 3), 2.35 (s, 1), 3.68 (s, 3); MS *m/e* (relative intensity) 336 (M^+, 13), 318 (6), 191 (45), 109 (46), 95 (100), 81 (42). Anal. Calcd for $C_{21}H_{36}O_3$: C, 74.95; H, 10.78. Found: C, 74.95; H, 10.69.

Debromoisoaplysin-20 (15). $LiAlH_4$ (130 mg, 3.4 mmol) was gradually added to a stirred solution of **21** (130 mg, 0.39 mmol) in dry THF (20 mL). After 14 h of heating at reflux and the usual workup, a solid residue was obtained. Crystallization from MeOH afforded pure **15** (103 mg): mp 191–193 °C; $[\alpha]_D$ +5.12° (*c* 1.11, $CHCl_3$); IR 3320, 1380, 1140, 1030 cm^{-1}; ^1H NMR δ 0.82 (s, 9), 0.85 (s, 3), 1.33 (s, 3), 3.00 (br s, 1), 3.93 (unresolved doublet, 2, *J* ≃ 7 Hz); MS *m/e* (relative intensity) 308 (M^+, 2), 290 (79), 275 (22), 191 (44), 137 (53), 123 (60), 121 (41), 109 (65), 95 (100), 82 (62), 81 (78). Anal. Calcd for $C_{20}H_{36}O_2$: C, 77.87; H, 11.76. Found: C, 77.79; H, 11.45.

Debromoisoaplysin-20 Monoacetate (15a). The diol **15** (40 mg) was treated with acetic anhydride (1 mL) and pyridine (1 mL) overnight at room temperature. The mixture was then carefully acidified with dilute HCl (with cooling) to pH 3 and extracted. The $CHCl_3$ extracts were washed with H_2O until neutral, dried (Na_2SO_4), and evaporated. The residue (35 mg) recrystallized from MeOH gave the monoacetate **15a**: mp 159–161 °C; $[\alpha]_D$ +3.32° (*c* 1.40, $CHCl_3$); IR 3470, 1700, 1280, 1130, 1030; ^1H NMR δ 0.83 (s, 6), 0.87 (s, 6), 1.20 (s, 3), 2.05 (s, 3), 4.35 (d, 2, *J* = 5 Hz); MS *m/e* (relative intensity) 350 (M^+, 2), 290 (74), 123 (55), 121 (38), 109 (63), 107 (40), 95 (100). Anal. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.53; H, 10.70.

Dimethyl Isoagathate (5). This material was prepared from dimethyl agathate,[29] following the procedure described in ref 6.

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