66-7; **28**, 64837-67-8; **29a**, 115-07-1; **29b**, 106-98-9; **29c**, 592-41-6; **29e**, 115-11-7; **29g**, 563-46-2; **29h**, 590-18-1; **29i**, 624-64-6; **29j**, 142-29-0; **29k**, 110-83-8; **29l**, 513-35-9; **29m**, 563-79-1; **29n**, 109-92-2; **29o**, 111-34-2; **29p**, 926-66-9; **29q**, 922-69-0; **29r**, 108-05-4; **29s**, 108-22-5; **29t**, 598-25-4; **29u**, 107-13-1; **29v**, 140-88-5; **30**, 67177-37-1; **32**, 67177-35-9; **34**, 69656-56-0; **35**, 69656-55-9; **36**, 79201-44-8; **37**, 79201-45-9; **38**, 79201-46-0; **39**, 67177-36-0; **40a**, 69665-16-3; **40b**, 69665-17-4; **42**, 32360-90-0; NMP, 550-44-7; 1,3-butadiene, 106-99-0; (*E*)-1,3-pentadiene, 2004-70-8; (*Z*,*Z*)-2,4-hexadiene, 6108-61-8; (*E*,*E*)-2,4-hexadiene, 5194-51-4; 2,5-dimethyl-2,4-hexadiene, 764-13-6.

Stereoselective Synthesis of the Enantiomer of the Novel Marine Diterpene Isoagatholactone, *ent*-13(16),14-Spongiadien-12α-ol, and the Parent Hydrocarbon Isocopalane from Methyl Isocopalate

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The stereoselective syntheses of the novel structures *ent*-isoagatholactone (**7**), *ent*-13(16),14-spongiadien-12α-ol (**8**), and the hydrocarbon isocopalane (**11**) from the ready available methyl isocopalate (**6a**) are described (see Scheme I). Methyl isocopalate (**6a**) was converted into 12,14-isocopaladiene (**27**) by $LiAlH_4$ reduction, mesylation, and elimination. A key step in the sequence was the photooxygenation of **6a** and **27**, which after reduction and chromatographic separation produced alcohols **18** and **28**, respectively. Alcohol **18** was rearranged into lactone **19** followed by reductive opening into the diol **20**, which upon oxidation produced *ent*-isoagatholactone (**7**). Alcohol **28** was in turn submitted to a second photooxygenation reaction, and the resulting unsaturated cyclic peroxide **29** was treated with ferrous sulfate to furnish **8**. Isocopalane (**11**) was obtained from **6a** when submitted to catalytic hydrogenation followed by $LiAlH_4$ reduction, mesylation, and reductive cleavage of the mesylate. The ^1H and ^{13}C NMR signal assignments for the synthesized products and intermediates are discussed.

Isoagatholactone (**1**), isolated in 1974 by Minale et al. from collections of the sponge *Spongia officinalis*,[2] was the first member of a small, but growing, group of tetracyclic diterpenes. This group now includes spongiadiol (**2a**), epispongiadiol (**3a**), spongiatriol (**2b**), epispongiatriol (**3b**), their corresponding di- and triacetates **2c**, **3c**, **2d**, and **3d**, respectively, and aplysillin (**4**), also isolated from several related species of the genus *Spongia*. These novel diterpenes possess a tetracyclic carbon skeleton not previously encountered in nature which may be formally derived from the hypothetical skeleton spongian **5**[3-5] (see Chart I).

The structural similarities of the spongian type of diterpenes with the readily available methyl isocopalate (**6a**;[6] except that methyl isocopalate is of the antipodal absolute configuration) prompted us to study its transformation into *ent*-isoagatholactone (**7**) and also into *ent*-13(16),14-spongiadien-12α-ol (**8**), as an alternative entry into the C/D ring system of this new group of natural products. If these conversions were successful, synthesis of isoagatholactone **1** and eventually of other related diterpenes, with the natural absolute configuration, would then be achieved starting with *ent*-methyl isocopalate (**9**).[7]

Although the systematic manner suggested by Kazlauskas et al.[3] for naming all members of this group of diterpenes as derived from spongian **5** is quite appropriate, we believe it necessary to establish a systematic nomenclature also for the tricyclic synthetic intermediates derived from **6a** which are, in fact, related to the natural product isoaplysin-20 (**10**).[6,8] On the assumption that the absolute configuration suggested by Yamamura et al.[8] for **10** is correct, then its carbon skeleton is **11**, common to all tricyclic derivatives of **6a**. We suggest the name isocopalane for this parent hydrocarbon. Accordingly, **10** would be 3α-bromoisocopalane-13β,15-diol.

In this paper a full report is given of the stereoselective synthesis of **7**, the enantiomer of the novel diterpene isoagatholactone (**1**), of the key intermediate **8**, and also of the hydrocarbon isocopalane (**11**).

Results and Discussion

***ent*-Isoagatholactone (7).** Our initial approach to the synthesis of *ent*-isoagatholactone (**7**) was the direct oxidation of the allylic methyl group of **6a**. However, treatment of **6a** with selenium dioxide and use of 1 and 2 mol of oxidating agent per mole of olefin in refluxing ethanol[9] led only to starting material and to a complex mixture, respectively. These results are not surprising in view of

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(2) Cimino, G.; De Rosa, D.; De Stefano, S.; Minale, L. *Tetrahedron* **1974**, *30*, 645.

(3) Kazlauskas, R.; Murphy, P. T.; Wells, R. J.; Noack, K.; Oberhänsli, W. E.; Schönholzer, P. *Aust. J. Chem.* **1979**, *32*, 867.

(4) Kazlauskas, R.; Murphy, P. T.; Wells, R. J. *Tetrahedron Lett.* **1979**, 903.

(5) On the basis of their biological activities, an ecological function has recently been proposed for some terpenoids, linear and pentacyclic sesterterpenes, isolated from *Spongia idia* (Walker, R. P.; Thompson, J. E.; Faulkner, D. J. *J. Org. Chem.* **1980**, *45*, 4976). To the best of our knowledge, the biological activities of the spongian group of diterpenes are unknown.

(6) Imamura, P. M.; Rúveda, E. A. *J. Org. Chem.* **1980**, *45*, 510.

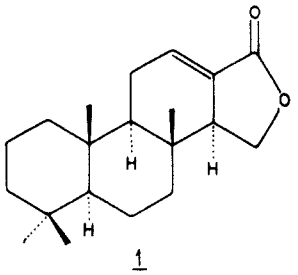
(7) Bory, S.; Manh Duc, D. K.; Fétizon, M.; Kone, M.; Trong Anh, N. *Bull. Soc. Chim. Fr.* **1975**, 2347.

(8) Yamamura, S.; Terada, Y. *Tetrahedron Lett.* **1977**, 2171.

(9) Bhalerao, U. T.; Rapaport, H. *J. Am. Chem. Soc.* **1971**, *93*, 4835.

0022-3263/81/1946-4851$01.25/0

Chart I



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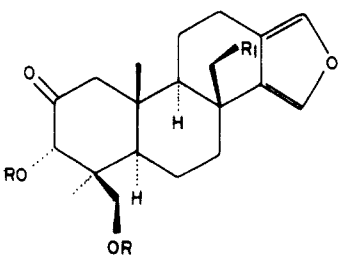
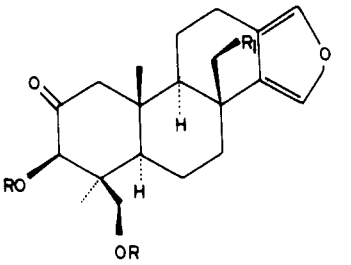
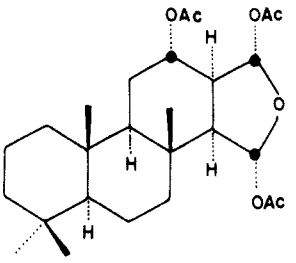


2a, R=H; R$_1$=H
2b; R=H; R$_1$=OH
2c; R=Ac; R$_1$=H
2d; R=Ac; R$_1$=OAc



3a; R=H; R$_1$=H
3b; R=H; R$_1$=OH
3c; R=Ac; R$_1$=H
3d; R=Ac; R$_1$=OAc



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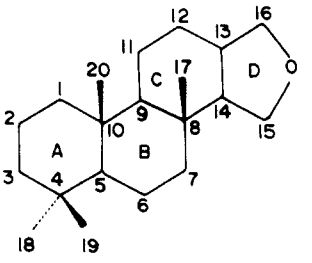

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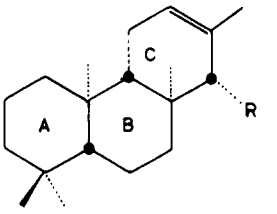
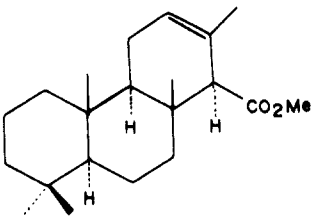


6a; R=CO$_2$Me
6b; R=CH$_2$OH
6c; R=CH$_2$OMs



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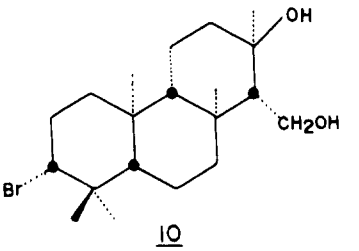
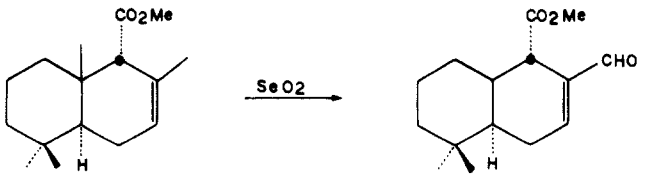


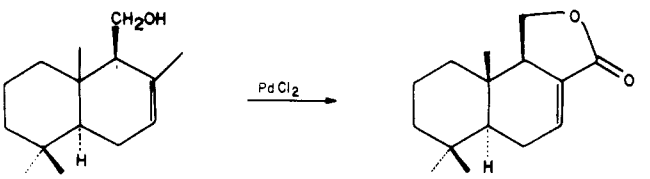
10

the recently reported[10] failure of attempts to oxidize the allylic methyl group of methyl drimentate (**12**), which has an arrangement of functional groups similar to the one present in ring C of **6a**. The lack of reactivity of the allylic methyl group can be explained by the steric hindrance produced by the pseudoequatorial carbomethoxyl, since methyl 9-epidrimenate (**13**), with a carbomethoxyl group in the pseudoaxial position, was smoothly oxidized to the corresponding aldehyde **14**. Epimerization of C-14 of **6a**



13 14

would be a serious disavantage for our synthetic plan, since, on the basis of previous equilibration studies,[7] conversion back to the original configuration, present also at C-14 of **7**, could be difficult. It was therefore decided to study the oxidation of the alcohol **6b**, with the hope that the less bulky CH_2OH group would leave the methyl group more accessible to the attack of the oxidating agent. Under the conditions described above for **6a**, **6b** also gave a complex mixture. In an attempt to transform **6b** directly into **7**, taking the transformation of bicyclofarnesol **15** into cinnamolide **16** as a model,[11] **6b** was treated with palladium



15 16

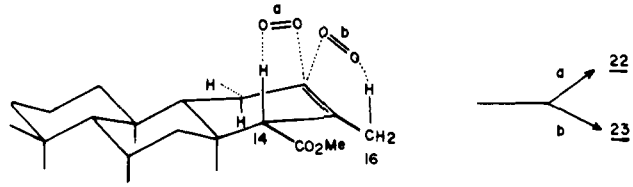
chloride in diisopropyl ether–water and heated to reflux for 48 h, but again without success. The sensitized photooxygenation of **6a** was then considered as an attractive possibility, even though it could be expected, based on the accepted mechanism of this reaction,[12,13] that the two allylic alcohols **17** and **18** should be produced. Transformation of **18** into **19** through an allylic rearrangement with simultaneous lactonization and reductive opening of the lactone ring to the diol **20**, followed by oxidation of the

(10) Ohsuka, A.; Matsukawa, A. *Chem. Lett.* **1979**, 635.

(11) Yanagawa, H.; Kato, T.; Kitahara, Y. *Synthesis* **1970**, 257.
(12) Denny, R. W.; Nickon, A. *Org. React.* **1973**, *20*, 133.
(13) For more recent publications on the mechanism of the photooxygenation reaction, see, inter alia: (a) Schulte-Elte, K. H.; Rautenstrauch, V. *J. Am. Chem. Soc.* **1980**, *102*, 1738. (b) Stephenson, L. M.; Grdina, M. B.; Orfanopoulos, M. G. *Acc. Chem. Res.* **1980**, *13*, 419.

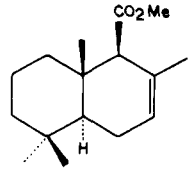
allylic alcoholic function, would then give *ent*-isoagatholactone (**7**). In practice, the photooxygenation reaction of **6a**, with hematoporphyrin as a sensitizer and a mixture of ethyl acetate and pyridine as the solvent, as previously described for a related transformation,[14] led mainly to a compound that was suspected by analysis of its IR and ^{1}H NMR spectra and confirmed by ^{13}C NMR spectroscopy to be **21**, the dehydration product of one of the possible hydroperoxides. The introduction of the enone system in **21** (going from **6a**[6] to **21**) produces typical ^{13}C NMR $\Delta\delta$ values for α- and β-carbons to the ketonic carbonyl group. On the other hand there is a clear change in ring C geometry of **21**, affecting the C-17 and C-7 chemical shifts.

The replacement of the sp^3 carbon atom at C-14 of **6a** by one of the trigonal carbons of the double bond of **21** causes an attenuation of the γ effect imposed by the pseudoequatorial C-15 on C-17, producing a downfield shift on C-17 and at the same time an increase of the γ effect induced by C-15 on C-7 which causes an upfield shift on C-7.[15] In order to minimize the production of **21**, a photooxygenation reaction in the cold, using a mixture of ethyl acetate–ethanol as solvent and methylene blue as sensitizer, was carried out. Examination of the low-field region of the ^{13}C NMR spectrum of the reaction mixture, after removal of the sensitizer and unreacted **6a** by a fast column chromatography, allowed a preliminary identification of the expected hydroperoxides on the basis of the chemical shifts and multiplicities of two sets of signals at 82.1, 126.7, 144.5, and 169.7 ppm and 84.8, 140.2, 114.1, and 171.6 ppm, attributable to C-12, C-13, C-14, and C-15 of **22** and C-12, C-13, C-16, and C-15 of **23**, respectively. By a careful silica gel column chromatography of the reduction product of the mixture of hydroperoxides, the pure allylic alcohols **17** and **18**, in a 2:1 ratio, were obtained. That, in fact, the structure and stereochemistry of the allylic alcohols are those expected from the two possible hydrogen atom abstractions, the pseudoaxial at C-14 and one of the hydrogens of the allylic methyl group, respectively, by the attack of the activated oxygen from the less hindered β face of **6a**, follows from a NMR analysis of these compounds. The ^{1}H NMR spectrum of **17** shows no olefinic protons, but the three-proton signal at δ 1.71, assigned to the vinyl methyl group at C-16, indicated the presence of a tetrasubstituted double bond, and the one-proton signal at δ 3.98 with a half-bandwidth of 8 Hz, as expected for a pseudoequatorial proton with an adjacent methylene group, suggested that the hydroxyl group at



6a

C-12 is pseudoaxial. Further support for this stereochemical assignment was obtained from the ^{1}H NMR spectrum of the epimeric alcohol **24**, easily obtained by sodium borohydride reduction of **21**, wherein the C-12 β-proton, pseudoaxial in this case, appears at δ 4.01 with a half-bandwidth of 20 Hz. Additionally, the signal of C-12 in the ^{13}C NMR spectrum of **17** appears at a higher field than the corresponding one of **24**, as expected for a pseudoaxial compared with a pseudoequatorial allylic alcohol.[16] Further, by the γ effect imposed by the hydroxyl group, C-9 of **18** appears at about 4 ppm to higher field than C-9 of **24**. Comparison of the δ values of C-12 and the trigonal carbons of **22** with those of similar sites of **17** shows the differences expected, on the basis of the reported data for the transformation of a hydroperoxide into an allylic alcohol,[17] that is, 12.8 and 2.5 ppm shielding for C-12 and C-14, respectively, and 4.5 ppm deshielding for C-13. This confirms the above attributions. It is interesting that C-14 and C-13 of **17**, even though α and β to a carbomethoxyl group, do not show the characteristic $\Delta\delta$ value of a conjugated ester. This suggests that due to the steric compression imposed by the methylene and methyl groups (C-7 and C-16 respectively) the carbomethoxyl group is somewhat less conjugated with the double bond.[18] The ^{1}H NMR spectrum of **18** shows two one-proton multiplets at δ 4.82 and 5.00, indicating the presence of a terminal double bond, and the one-proton signal at δ 4.30 with a half-bandwidth of 7 Hz suggests that the C-12 proton is pseudoequatorial. In addition, the ^{13}C NMR spectrum of **18** contains two signals with chemical shifts and multiplicities in the SFORD spectrum of 144.8 and 110.9 ppm and singlet and triplet, respectively. This is characteristic of an exocyclic methylene group. The chemical shift of C-9, also suffering a γ effect as does the same carbon of **17**, supports the pseudoaxial position of the hydroxyl group of **18**. Further confirmation for this stereochemical assignment was obtained by comparison of the ring C carbon shifts of **18** with similar sites of the related system present in 7α-hydroxymanool (**25**), previously assigned by a careful



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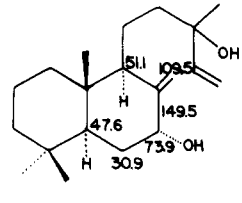

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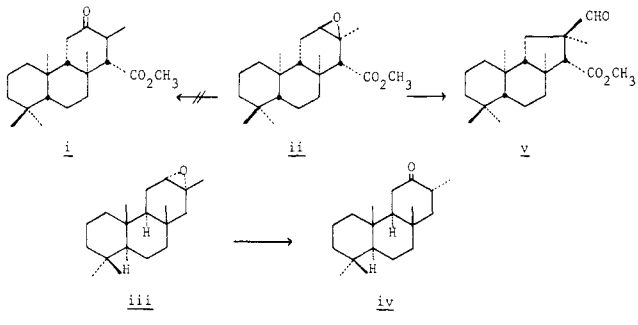
(14) Kitahara, Y.; Kato, T.; Suzuki, T.; Kanno, S.; Tanemura, M. *Chem. Commun.* **1969**, 342.

(15) In order to confirm and to extend these observations, potentially useful for the assignment of the configuration at C-14 in this group of substances, it seemed interesting to examine the ^{13}C NMR spectrum of the related substance i. An attempt to prepare i by the boron trifluoride etherate induced rearrangement of the known epoxide ii,[6] in analogy to the reported transformation of iii into iv,[7] led, however, exclusively to the aldehyde v, unambiguously identified by analysis of its IR, ^{1}H NMR, and ^{13}C NMR spectra.



(16) Tsuda, M.; Parish, E. J.; Schroepfer, G. J., Jr., *J. Org. Chem.* **1979**, *44*, 1282.

(17) El-Feraly, F. S.; Chan, Y.-M.; Capiton, G. A.; Doskotch, R. W.; Fairchild, E. H. *J. Org. Chem.* **1979**, *44*, 3952.

(18) Comparison of the differences in force constants of bond [$\Delta f_{C=O} = 0.402\ (\bar{\nu}_1^2 - \bar{\nu}_2^2)$ dyn/cm] for the C=O stretching of the ester groups, calculated by using the frequencies in the IR spectra of **17** (1723 cm^{-1}), **24** (1723 cm^{-1}), **21** (1727 cm^{-1}), and **32** (1732 cm^{-1}), measured with a Perkin-Elmer 180 spectrophotometer as Nujol mulls, with those of a characterist unconjugated (1735 cm^{-1}) and conjugated (1720 cm^{-1}) ester carbonyl showed a 60% conjugation for **17** and **24** and only a 33% for **21**, in agreement with the observed δ values for the ^{13}C NMR signals and supporting the above explanation.

Table I. Carbon Shifts of *ent*-Isogatholactone (7) and Related Products

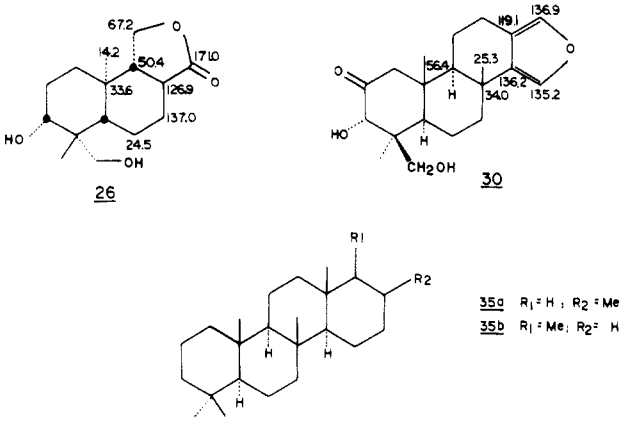
carbon	shift, ppm						
	21	17	24	18	19	20	7
C-1	38.5	39.6	39.4	39.5[a]	39.7[a]	39.7	39.8
C-2	18.1	18.5	18.3	18.4	18.3	18.8[a]	18.3
C-3	41.6	42.1	42.0	41.8	41.7	41.8	41.7
C-4	33.0	33.3	33.1	33.1	33.3	33.0	33.2
C-5	55.7	56.7	56.2	56.5	56.5	56.0	56.7
C-6	18.1	18.5	18.3	18.4	18.3	18.4[a]	18.3
C-7	37.2	38.1	38.0	39.9[a]	39.9[a]	40.9	40.7
C-8	38.8	38.1	38.0	39.9	34.4	35.6	34.5
C-9	54.4	49.9	54.0	51.5	54.1	54.2	54.4
C-10	37.0	37.1	37.0	37.1	37.4	37.2	37.3
C-11	34.1	27.7	28.4	29.0	22.4	22.5	24.2
C-12	199.6	69.3	72.0	72.6	120.8	126.9	136.2
C-13	129.4	131.2	133.0	144.8	129.4	136.5	126.8
C-14	157.4	142.0	141.0	57.3	54.1	54.9	51.2
C-15	168.1	170.5	170.0	171.7	175.1	61.0	67.2
C-16	12.5	18.5	16.2	110.9	69.7	67.1	170.0
C-17	19.4	19.8	21.5[a]	14.1	14.9	15.6[b]	14.1
C-18	33.3	33.3	33.1	33.1	33.1	33.3	33.4
C-19	21.2	21.3	21.2[a]	21.2	21.6	21.6	21.6
C-20	15.5	16.3	16.2	15.9	15.2	15.4[b]	15.3
OMe	51.3	50.8	51.0	50.7			

[a, b] The assignments for these signals within a vertical column may be reversed.

$Yb(DPM)_3$ shift study.[19] Again, comparison of the chemical shifts of the second group of signals in the ^{13}C NMR spectrum of the mixture of hydroperoxides, those at 84.8, 140.2, 114.1, and 171.6 ppm assigned to C-12 and the trigonal carbons of **23**, with those of **18** shows the expected differences between a hydroperoxide and the corresponding allylic alcohol: 12.2 and 3.2 ppm shielding for C-12 and C-16, respectively, and 4.6 ppm deshielding for C-13.[17] Treatment of **18** with sulfuric acid in aqueous dioxane afforded the lactone **19** in good yield as a crystalline solid, which on lithium aluminum hydride reduction gave the diol **20**. In the ^1H NMR spectrum of **20** the methylene protons of the 16-hydroxymethyl group appear as an AB quartet centred at δ 4.17 with J = 12 Hz and $\Delta\nu_{AB}$ = 37.1 Hz, while the protons of the 15-hydroxymethyl show a pattern of eight signals between δ 3.50 and 4.00, as expected for the AB portion of an ABX system, which simplifies into an AB quartet centred at δ 3.88 (J = 12 Hz and $\Delta\nu_{AB}$ = 20.7 Hz) upon irradiation at δ 2.18. Accordingly, the ^{13}C NMR spectrum of **20** shows two signals at 61.0 and 67.1 ppm which were unequivocally assigned to C-15 and C-16, respectively, by specific proton decoupling. In fact, irradiation at δ 4.17, the center of the AB system of the C-16 protons, transforms the triplet at 67.1 ppm into a singlet while the signal at 61.0 ppm, assigned then to C-15, remains as an asymmetric triplet. Finally, oxidation of **20** with active manganese dioxide in dichloromethane afforded *ent*-isoagatholactone (**7**), in good yield. The melting point, IR, ^1H NMR, and mass spectral data and the magnitude, but not the sign, of the optical rotations of **20** and **7** are identical with those reported for the enantiomeric compounds.[2] The ^{13}C NMR spectrum of **7**, showing ring C and D carbon shifts in complete agreement with those of comparable sites of iresin **26**,[20] supports its structure. The carbon shifts of compounds **7**, **17**–**21**, and **24** are listed in Table I.

(19) Buckwalter, B. L.; Burfitt, I. R.; Nagel, A. A.; Wenkert, E.; Näf, F. *Helv. Chim. Acta* **1975**, *58*, 1567.

(20) Wenkert, E.; Buckwalter, B. L.; Burfitt, I. R.; Gasić, M. J.; Gottlieb, H. E.; Hagaman, E. W.; Schell, F. M.; Wovkulich, P. M. In "Topics in Carbon-13 NMR Spectroscopy"; Levy, G. C., Ed., Wiley-Interscience: New York, 1976; Vol. 2.

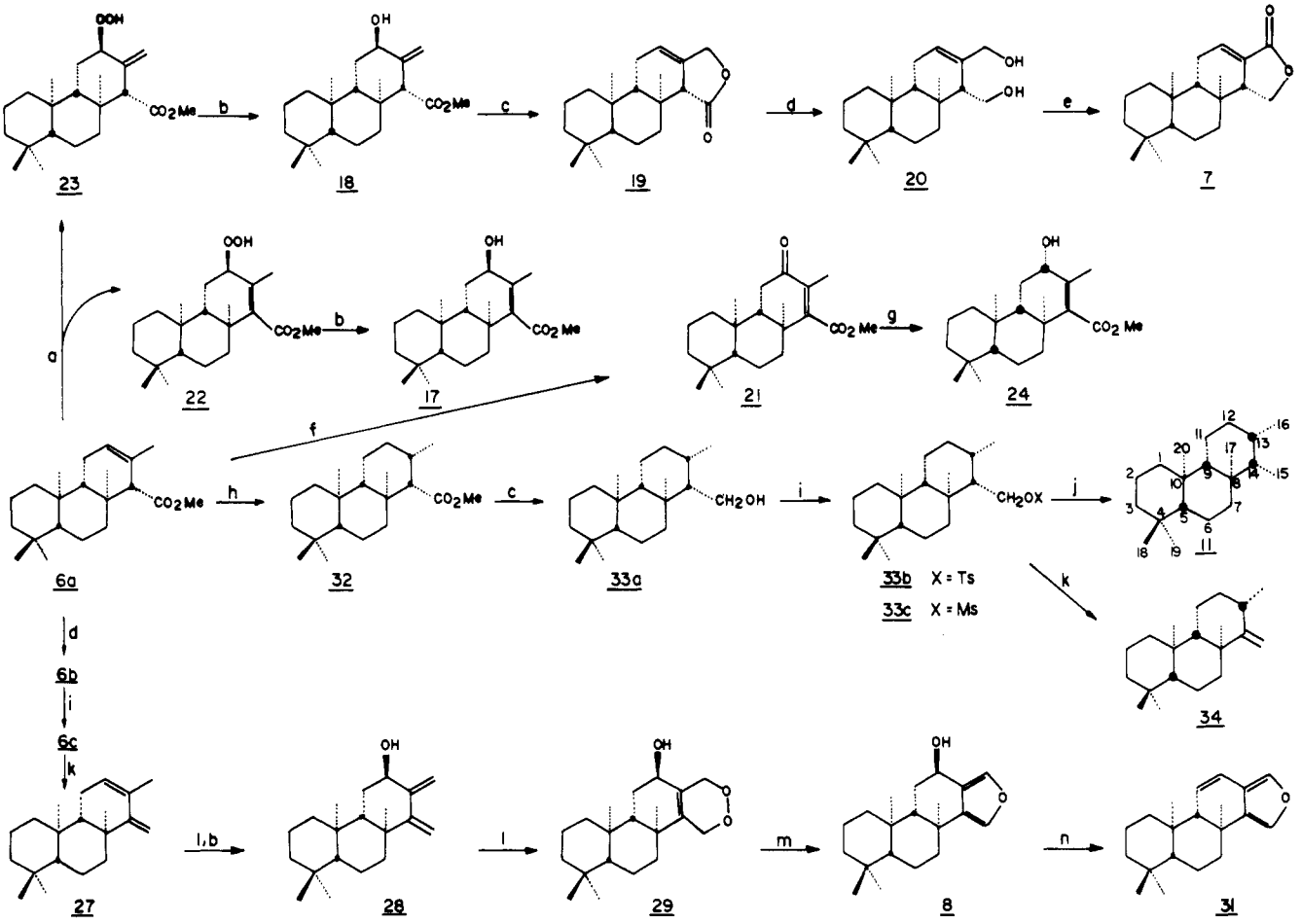


***ent*-13(16),14-Spongiadien-12α-ol (8).** Among the diterpenes with the novel spongian skeleton, aplysillin (**4**), which has several chiral centers in rings C and D, is a particularly attractive target from a synthetic organic chemistry point of view. Since only the relative stereochemistry of **4** is established, intermediate **8** (or its enantiomer) possessing a hydroxyl group with the required stereochemistry at C-12 and a furan ring which could serve as a latent equivalent to the ring D functionality of **4** appeared to be an ideal percursor. As in the case of isoagatholactone (**1**), the approach was to study the synthesis of **8** by again using methyl isocopalate (**6a**) as starting material.

In analogy to the recently reported synthesis of 3-alkylfurans developed by Herz et al.,[21] we considered that **8** could be prepared by two successive photooxygenation reactions, namely, allylic oxydation of diene **27** and Diels–Alder addition to the resulting dienol **28** to give cyclic peroxide **29** (Scheme I). The last product, on treatment with ferrous sulfate in aqueous tetrahydrofuran, would give the desired intermediate **8**. Attention was therefore turned to the preparation of **27**. Attempts to effect a simple thionyl chloride–pyridine dehydration of **6b** to produce **27** gave a complex mixture as indicated by gas chromatographic analysis. However, treatment of the mesylate **6c** with sodium ethoxide in refluxing ethanol gave smooth elimination to the diene **27**. The steric hindrance to which the pseudoequatorial mesylate at C-15 is subjected and the easy access to the allylic C-14 hydrogen by the base strongly favor elimination over substitution. The ^1H NMR spectrum of **27** contains the expected signals for the conjugated diene system present, the vinyl methyl at δ 1.78, the two-proton broadened singlet at δ 4.83, and the one-proton multiplet at δ 5.67. Further, the ^{13}C NMR spectrum exhibits four sp^2 carbon signals at 126.3, 130.8, 158.3, and 103.7 ppm attributable, on the basis of their chemical shifts and multiplicities, to C-12, C-13, C-14, and C-15, respectively. Photooxygenation and reduction of **27** under the conditions previously described,[21] afforded the oily diene alcohol **28**. That one of the hydrogens of the allylic methyl group was abstracted by the activated oxygen with concerted entry of the hydroperoxide from the less hindered β face of **27**, as in **6a**, was indicated in the ^1H NMR spectrum of **28**. The one-proton multiplet at δ 4.41 with a half-bandwidth of 8 Hz and the four-proton multiplet between δ 4.70 and 5.00 correspond to the pseudoequatorial methine proton at C-12 and to the two exocyclic methylenes, respectively. In addition, the ^{13}C NMR spectrum of **28** contains the expected signals for both exocyclic double bonds at 106.5, 158.4, 112.2, and 150.4 ppm, and, further, comparison of the chemical shifts

(21) Turner, J. A.; Herz, W. *J. Org. Chem.* **1977**, *42*, 1900.

Scheme I[a]



[a] a, $^1O_2$/methylene blue/EtOH-AcOEt (1:1); b, trimethyl phosphite; c, H_2SO_4 (6 N)-dioxane (1:13); d, $LiAlH_4$/ether; e, MnO_2/CH_2Cl_2; f, $^1O_2$/hematoporphyrin/AcOEt-pyridine (2:1)/KI, g, $NaBH_4$/MeOH; h, H_2 (2 atm)/PtO_2/MeOH-AcOEt (5:1); i, MsCl/pyridine-CH_2Cl_2 or TsCl/pyridine-CH_2Cl_2; j, NH_3(l)/Li/THF; k, EtO^-Na^+/EtOH; l, $^1O_2$/rose bengal/CH_2Cl_2-MeOH (95:5); m, $FeSO_4 \cdot 7H_2O/H_2O$; n, TsOH/benzene.

of C-12 and C-9 with those of similar sites of **18** confirms that in **28** the hydroxyl group is also pseudoaxial. Photooxygenation of **28** gave the expected peroxide **29** as a crystalline but unstable compound whose ^1H NMR signals (multiplets at δ 4.50 and 4.68), and mass spectral data (M^+ at m/e 320) were in accord with the proposed structure. Finally, treatment of **29** with ferrous sulfate in aqueous tetrahydrofuran gave the oily furan **8** in 75% yield. The ^1H NMR spectrum of **8** shows a multiplet at δ 4.85 with a half-bandwidth of 6 Hz, readily assigned to the pseudoequatorial carbinolic proton at C-12, and two signals at δ 7.07 and 7.37, characteristic of α-furan protons. Further, of the four low-field signals in the ^{13}C NMR spectrum of **8**, those at 136.1 and 135.0 ppm were assigned to C-14 and C-15, respectively, on the basis of their multiplicities from a SFORD spectrum and by comparison with the related carbons of **2a**, depicted in formula **30**. The remaining two signals, at 123.6 and 139.4 ppm, were assigned to C-13 and C-16, respectively, which, probably due to the influence of the C-12 hydroxyl group, appear deshielded compared with the analogous carbons of **2a** while the chemical shifts of C-7, C-8, and C-17 reveal a close similarity between the two compounds. Again in **8**, the signal of C-9 at 50.1 ppm confirms the pseudoaxial position of the hydroxyl group at C-12. Confirmatory evidence for the structure of **8** was obtained by its acid-catalyzed dehydration into the crystalline vinyl furan **31**. The ^1H NMR and mass spectra of **31** are identical with those published for the known degradation product of aplysillin (**4**). Unfortunately, no optical rotation was reported for the latter, which would allow establishment of the absolute stereochemistry of **4**.[4] The carbon shifts of compounds **8**, **27**, and **28** are listed in Table II.

Isocopalane (11). With the diene **27** in hand, it seemed useful to transform it into isocopalane (**11**) in order to study its spectral properties, mainly its mass spectrum. This could be useful not only because **11** has the carbon skeleton of all tricyclic derivatives depicted in this and in previous publications,[6-8] but also because of its possible presence in sediments, together with some other homologues.[22] The obvious approach for the preparation of **11** was the catalytic hydrogenation of **27**. This afforded, however, a ca. 1:1 mixture of saturated hydrocarbons which when coinjected with a mixture of isocopalane (**11**) and its C-14 epimer (prepared subsequently) afforded the same retention times.

The stepwise hydrogenation of the 1,3-diene system of **27**[23] is probably responsible for the loss of stereoselectivity observed when methyl isocopalate (**6a**) is submitted to catalitic hydrogenation.[6] This is not the case, however, for the attack of singlet oxygen, which occurs exclusively from the β face of **6a** and **27**. Another approach which appeared to be attractive involved catalytic hydrogenation of **6a**, in order to guarantee the selective generation of the chiral

(22) We thank Professor G. Ourisson for this information.
(23) Bond, C. C.; Webb, G.; Wells, P. B.; Winterbottom, J. M. *J. Chem. Soc.* **1965**, 3218.

Table II. Carbon Shifts of *ent*-13(16),14-Spongiadien-12α-ol (8), Isocopalane (11), and Related Products

	shift, ppm						
carbon	27	28	8	33a	34	11 (obsd)	11 (calcd)
C-1	39.7	39.8	39.8[b]	39.9	40.0	40.0	37.7
C-2	19.0[a]	18.8[a]	18.7[a]	18.6[a]	18.7	18.8[a]	17.6
C-3	41.9	41.8	42.0	41.8	42.0	41.6	42.2
C-4	33.1	33.2	33.3	33.2	33.3	33.3	33.9
C-5	56.2	56.5	56.7	56.5	56.5	56.7	56.2
C-6	18.6[a]	18.5[a]	18.4[a]	18.1[a]	18.7	18.2[a]	17.6
C-7	39.4	40.5	40.7[b]	42.1	40.7	42.2	37.7
C-8	37.9[b]	38.6	34.4	37.9	40.3	38.3	37.6
C-9	53.4	49.4	50.1	61.2	57.1	61.4	56.2
C-10	37.6[b]	37.6	37.0	37.6[b]	38.0	37.6	37.6
C-11	23.1	28.6	28.4	16.3	16.8	16.4	17.6
C-12	126.3	72.5	61.6	34.5	33.3	35.0	33.1
C-13	130.8	150.4	123.6	28.3	37.3	34.7	34.3
C-14	158.3	158.4	136.1	56.5	165.3	48.5	47.1
C-15	103.7	106.5	135.0	60.7	104.4	13.1	12.0
C-16	20.5	112.2	139.4	15.4	22.8	15.4	14.6
C-17	21.7	21.4	25.5	18.1	24.5	16.4	17.1
C-18	33.4	33.2	33.3	33.2	33.3	33.3	30.2
C-19	21.7	21.2	21.4	21.3	21.5	21.4	23.7
C-20	16.0	16.1	16.4	16.3	16.2	16.4	17.1

[a,b] The assignments for these signals within a vertical column may be reversed.

center at C-13, subsequent reduction of the carbomethoxyl group, and mesylation or tosylation of the corresponding primary alcohol followed by displacement of the sulfonate ester with lithium aluminum hydride (**6a** → **32** → **33a** → **33b** or **33c** → **11**). Alternatively, on the assumption of a similar reactivity to that observed for **6c**, elimination of the sulfonate ester of **33b** or **33c** under basic conditions would give **34**, which, because of its more hindered α face, would preferentially afford **11** on catalytic hydrogenation. In practice, tosylate **33b** suffered attack by the hydride at sulfur rather than carbon, regenerating exclusively the starting alcohol **33a**. Undoubtedly this is due to the steric environment of C-15.[24] Reduction with lithium in liquid ammonia of the mesylate **33c**,[25] however, afforded a product consisting of the expected hydrocarbon **11** and the starting alcohol **33a**. Pure **11** was obtained by silica gel column chromatography of the mixture. Finally, treatment of **33c** with sodium ethoxide in refluxing ethanol, in this case for a longer period than that required for the transformation of **6b** into **27**, afforded **34**. Gas chromatographic analysis of the hydrogenation product of **34** revealed that although **11** was preferentially produced, 15% of the C-14 epimer was also formed.

At this point a comparative analysis of the ^{13}C NMR spectra of **33a**, **11**, and **34** was carried out. The shift data of **33a**, based on the comparison with those reported for **32**[6] and on the known effects of the replacement of a carbomethoxyl by an alcoholic group,[26] together with the information obtained from a SFORD spectrum allowed the shift assignment of **11**. The δ values calculated by using the substituent parameters proposed by Beierbeck et al.[27] are in agreement with the above assignment. Comparison of **34** and **11** shows that in **34** C-8, C-13, C-16, and C-17 are deshielded while C-7 is shielded. Those differences can be explained by the α effect of the exocyclic double bond[28] on C-8 and C-13, by the attenuation of the γ effects imposed by C-15 on C-16 and C-17, and by an increase of the same effect of C-15 on C-7. The carbon shifts of **33a**, **11** (calculated and observed), and **34** are also listed in Table II.

The mass spectrum of **11** shows, as expected, a molecular ion peak at *m/e* 276, an important fragment at *m/e* 265, corresponding to the loss of a methyl group, and the base peak at *m/e* 191. The base peak and the ions at *m/e* 177 and 137 are characteristic of the 4,4,8,10-tetramethyldecalin system present in **11** and in many terpenes. It is worthwhile mentioning, however, that the mass spectrum of **11** contains all the ions, from the one at *m/e* 192 to those at lower mass, reported in the mass spectrum of the tetracyclic sesterterpene-derived hydrocarbon present in the lipid extracts of some Georgia and South Carolina clays, to which the tentative structures **35a** or **36b** have been assigned.[29]

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. ^1H 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 units, and coupling constants (*J*) and half-bandwidths ($W_{1/2}$) are given in hertz (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). ^{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 $|\delta(Me_4Si) = \delta(CDCl_3) + 76.9|$. Mass spectra were obtained 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 visualized by staining with anisaldehyde–sulfuric acid.[30] GC analyses were conducted by using a Finnigan Model 1015/SL gas chromatograph equipped with a FID detector and a 3 m × 2 mm 3% SE-30 glass column on Chromosorb W (100–200 mesh). Combustion analyses were carried out by the Analytical Laboratory of Laboratório de Pesquisa, Rhodia (Divisão Paulinia).

Photooxygenation of Methyl Isocopalate (6a). Method A. A solution of **6a** (500 mg, 1.57 mmol) and hematoporphyrin (29

(24) Dolby, L. J.; Rosencrantz, D. R. *J. Org. Chem.* **1963**, *28*, 1888.
(25) Dreiding, A. S.; Tomasewski, A. J. *J. Am. Chem. Soc.* **1955**, *77*, 411.
(26) Wehrli, F. W.; Wirthlin, T. "Interpretation of C-13 NMR Spectra"; Heyden and Son: New York, 1976; p 37.
(27) Beierbeck, H.; Saunders, J. K.; Ap Simon, J. W. *Can. J. Chem.* **1977**, *55*, 2813.
(28) Grover, S. H.; Stothers, J. B. *Can. J. Chem.* **1975**, *53*, 589.
(29) Scholefield, D.; Whitehurst, J. S. *J. Chem. Soc., Chem. Commun.* **1980**, 135.
(30) Stahl, E. "Thin-Layer Chromatography. A Laboratory Handbook", 2nd ed.; Springer-Verlag: West Berlin, Heidelberg, New York, 1969; p 857.

mg) in a 2:1 EtOAc–pyridine mixture (45 mL) in a vessel was irradiated with a 600-W Sylvania DYV-tungsten halogen projector lamp placed near the vessel while oxygen was bubbled through the reaction mixture. After 8 h the solvent was evaporated in vacuo, and the residue was taken up in Et_2O (5.4 mL) and MeOH (6.6 mL) and stirred with KI (1.04 g) in aqueous HOAc (9 mL) at room temperature for 4 h. Upon treatment with aqueous $NaHCO_3$ until neutral, the solution was extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed with 1 M sodium thiosulfate solution and brine, dried (Na_2SO_4), and evaporated to afford a crude product (450 mg) which after silica gel column chromatography (eluted with a 9:1 hexane–EtOAc mixture) gave pure methyl 12-oxo-13-isocopalen-15-oate (**21**; 123.2 mg, 24%) and (with a 8:2 hexane–EtOAc mixture) **18** (85.0 mg, 16%). Crystallization of **21** (MeOH) yielded material with a melting point of 108–110 °C: $[\alpha]_D$ +13.0° (*c* 1.0, $CHCl_3$); IR 3000–2850, 1740, 1690, 1640, 1240, 1050, 1020 cm^{-1}; ^1H NMR (CCl_4) δ 0.86, 0.90, and 0.96 (C-4 and C-10 Me), 1.33 (C-8 Me), 1.63 (C-13 Me), 2.31 (d, J = 2, H-11$_{ax}$), 2.46 (s, H-11$_{eq}$), 3.81 (OMe); mass spectrum, *m/e* (relative intensity) 332 (M^+, 4), 300 (4), 272 (69), 192 (12), 190 (12), 148 (61), 140 (70), 93 (100).

Anal. Calcd for $C_{21}H_{36}O_3$: C, 75.86; H, 9.70. Found: C, 75.59; H, 10.10.

Method B. A solution of **6a** (411 mg) and methylene blue (16 mg) in a 1:1 mixture of EtOH–EtOAc (90 mL) in a photooxygenation cell similar to that described by Frimer et al.,[31] cooled by circulating EtOH at 5 °C, was irradiated with a 600-W Sylvania DYV-tungsten halogen projector lamp placed near the cell and cooled with a stream of air, while oxygen was bubbled through the reaction mixture. A glass plate placed between the reaction cell and the lamp prevented premature bleaching of the dye. The progress of the reaction was monitored by TLC, and the formation of a more polar material was clearly detected, but after approximately 10 h of irradiation the reaction apparently reached a situation in which the ratio between products and starting material did not change. Trimethyl phosphite (0.2 mL) was then added, and the solvent was removed at reduced pressure. Chromatography of the crude product over silica gel (45 g) with hexane and with mixtures of hexane and increasing amounts of EtOAc resulted in the recovery of starting material **6a** (100 mg, 24%) and the isolation of the crystalline alcohols methyl 12β-hydroxy-13-(16)-isocopalen-15-oate (**18**; 85 mg, 20%) and methyl 12β-hydroxy-13-isocopalen-15-oate (**17**; 190 mg, 44%), respectively. Recrystallization of **17** from hexane afforded material with a melting point of 107–109 °C: $[\alpha]_D$ +95.6° (*c* 1.2, $CHCl_3$); IR 3450, 2990–2840, 1720, 1660, 1250, 1040 cm^{-1}; ^1H NMR δ 0.78, 0.80, and 0.83 (C-4 and C-10 Me), 1.15 (C-8 Me), 1.71 (C-13 Me), 3.72 (OMe), 3.98 (m, $W_{1/2}$ = 8, H-12); mass spectrum, *m/e* (relative intensity) 334 (M^+, 9), 319 (11), 316 (10), 276 (28), 192 (24), 191 (22), 143 (98), 142 (100), 118 (67), 109 (40).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25. Found: C, 75.43; H, 10.42.

Recrystallization of **18** from hexane afforded material with a melting point of 155–156 °C: $[\alpha]_D$ −38.9° (*c* 1.5, $CHCl_3$); IR 3560, 2990–2840, 1725, 1660, 1195, 1170, 1040, 900 cm^{-1}; ^1H NMR (CCl_4) δ 0.85, 0.87, and 0.87 (C–4 and C–10 Me), 1.00 (C–8 Me), 3,33 (br, H-14), 3.63 (OMe), 4.30 (m, $W_{1/2}$ = 7, H-12), 4.82 and 5.00 (both m, H-16); mass spectrum, *m/e* (relative intensity) 334 (M^+, 3), 316 (6), 301 (5), 192 (19), 191 (37), 149 (41), 123 (59), 112 (56), 94 (84), 81 (100).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25. Found: C, 75.13; H, 10.02.

Methyl 12α-Hydroxy-13-isocopalen-15-oate (24). $NaBH_4$ (160 mg, 4.25 mmol) was added to a stirred solution of **21** (500 mg, 1.51 mmol) in MeOH (14 mL) in an ice bath. The mixture was stirred for 30 min with cooling and then for 4 h at room temperature. A few drops of HOAc were added, and the mixture was concentrated to half the volume, diluted with H_2O (90 mL), and extracted with Et_2O (3 × 50 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a colorless oil (493 mg) which on TLC showed two spots corresponding to both epimeric alcohols. Recrystallization from hexane afforded pure **24**: 277 mg (55%); mp 142–143 °C; $[\alpha]_D$ +35° (*c* 2, $CHCl_3$); IR 3300–3160, 2960–2820, 1720, 1660, 1190, 755 cm^{-1}; ^1H NMR δ 0.71, 0.73, and 0.76 (C-4 and C-10 Me), 1.15 (C-8 Me), 1.58 (C-13 Me), 3.65 (OMe), 4.01 (m, $W_{1/2}$ = 20, H-12).

Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25. Found: C, 75.06; H, 10.22.

***ent*-12-Spongien-15-one (19).** A solution of **18** (85 mg) in a 13:1 mixture of dioxane–6 N H_2SO_4 (15 mL) was heated at 90 °C for 40 min. The mixture was then poured into crushed ice–brine (ca. 50 mL) and extracted with Et_2O (4 × 30 mL). The combined organic extracts were washed with saturated $NaHCO_3$ solution, dried (Na_2SO_4), and evaporated. The residue (90.6 mg) recrystallized from MeOH gave **19**: 68 mg (88%); mp 153–156 °C; $[\alpha]_D$ −7.6° (*c* 1.0, $CHCl_3$); IR 2990–2840, 1760, 1135, 1000 cm^{-1}; ^1H NMR (CCl_4) δ 0.85, 0.87, and 0.93 (C-4 and C-10 Me), 0.97 (C-8 Me), 4.62 (m, H-16), 5.70 (m, H-12); mass spectrum, *m/e* (relative intensity) 302 (M^+, 18), 287 (9), 192 (100), 191 (73), 177 (49).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.09; H, 10.01.

12-Isocopalene-15,16-diol (20). To a stirred mixture of $LiAlH_4$ (80 mg, 2 mmol) in anhydrous Et_2O (30 mL) was gradually added a solution of **19** (168 mg, 0.56 mmol) also in anhydrous Et_2O (20 mL) at room temperature. After 30 min of heating at reflux and the usual workup, a crystalline residue was obtained; 153 mg (89%). Recrystallization from MeOH afforded material with a melting point of 163–165 °C: $[\alpha]_D$ +16.0° (*c* 1.0, $CHCl_3$) [lit.[2] (for the enantiomer) mp 159–161 °C; $[\alpha]_D$ −16.5°]; IR 3300, 2990–2840, 985 cm^{-1}; ^1H NMR (100 MHz) δ 0.74, 0.82, and 0.88 (C-4 and C-10 Me), 0.88 (C-8 Me), 3.26 (br s, 2), 3.50–4.00 (eight signals, H-15), 4.17 (AB q, 2, $\Delta\nu_{AB}$ = 37.1 Hz, J = 12, H-16), 5.8 (m, H-12); mass spectrum, *m/e* relative intensity) 306 (M^+, 35), 288 (21), 275 (6), 258 (72), 243 (11), 192 (100), 191 (63), 177 (86).

Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found; C, 78.41; H, 11.13.

***ent*-12-Spongien-16-one (*ent*-Isoagatholactone, 7).** A mixture of **20** (190 mg, 0.62 mmol) and active MnO_2 (14 g, 0.16 mol), dried as prescribed by Goldman,[32] in CH_2Cl_2 (60 mL) was stirred for 15 h. After filtration of the mixture through a Celite pad, the filtrate and washings were concentrated to dryness. Chromatography of the crystalline residue (144 mg) on silica gel with 10% EtOAc–hexane afforded **7** (122 mg, 64%), which after recrystallization from MeOH gave material with a melting point of 153–155 °C: $[\alpha]_D$ −11.4° (*c* 0.6, $CHCl_3$) [lit.[2] (for the enantiomer) mp 153–155 °C; $[\alpha]_D$ +6.3°]; IR 2990–2840, 1760, 1690, 1230, 1210, 1010 cm^{-1}; ^1H NMR δ 0.80, 0.85, and 0.88 (C-4 and C-10 Me), 0.94 (C-8 Me), 3.97 and 4.33 (both t, J = 9, H-15), 6.77 (q, J = 3, H-12); mass spectrum, *m/e* (relative intensity) 306 (M^+, 35), 288 (21), 275 (6), 258 (72), 243 (11), 192 (100), 191 (73), 177 (49), 137 (23).

Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.42; H, 9.79.

12,14-Isocopaladiene (27). To a stirred solution of methanesulfonyl chloride (1 mL, 12.9 mmol) in a mixture of CH_2Cl_2 (7.6 mL) and pyridine (1 mL) at 0 °C was added dropwise a solution of 12-isocopalen-15-ol (**6b**;[6] 912 mg, 3.14 mmol) in CH_2Cl_2 (10 mL) and pyridine (4 mL). After 3 h at this temperature, the mixture was poured into ice–water, stirred for an additional 3-h period at room temperature, and then extracted with $CHCl_3$ (3 × 30 mL). The combined organic extracts were throughly washed with 10% HCl, aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and evaporated to yield **6c**: 1.1 g (95%); IR 2990–2840, 1360, 1170, 980, 945, 830 cm^{-1}; ^1H NMR (CCl_4) δ 0.83, 0.88, and 0.91 (C-4 and C-10 Me), 1.76 (br, C-13 Me), 2.93 (SMe), 4.23 (m, H-15), 5.53 (m, H-12).

Crude **6c** (1.0 g, 2.7 mmol) in dry THF (10 mL) was added dropwise to a solution of sodium ethoxide (from 2.3 g, 0.1 mol of sodium) in dry EtOH (50 mL). The resulting mixture was heated at reflux and the progress of the reaction was monitored by TLC. When the reaction was complete (2 h), the solvent was evaporated in vacuo, and the residue was taken up in ice–water and extracted with Et_2O (3 × 50 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), and evaporated.

(31) Frimer, A. A.; Bartlett, P. D.; Boschung, A. F.; Jewett, J. G. *J. Am. Chem. Soc.* **1977**, *99*, 7977.

(32) Goldman, I. M. *J. Org. Chem.* **1969**, *34*, 1979.

(33) Note Added in Proof: We have also completed the synthesis of (+)-isoagatholactone from (+)-manool; see Imamura, P. M.; Gonzâlez Sierra, M.; Rûveda, E. A. *J. Chem. Soc., Chem. Commun.* **1981**, 734.

The residue (959 mg) was applied to a column of silica gel and eluted with hexane to afford pure **27**: 735 mg (100%); mp 93–94 °C (hexane); $[\alpha]_D$ −130° (*c* 1.0, $CHCl_3$); IR 3090, 2990–2840, 1600, 875, 830 cm^{-1}; ^1H NMR δ 0.83, 0.86, and 0.89 (C-4 and C-10 Me), 0.96 (C-8 Me), 1.78 (d, J = 1.5, C-13 Me), 4.83 (br, H-15), 5.67 (m, H-12); mass spectrum, *m/e* (relative intensity) 272 (M^+, 61), 257 (34), 191 (16), 190 (100), 136 (44), 135 (63), 121 (42), 119 (53), 108 (51).

Anal. Calcd for $C_{20}H_{32}$: C, 88.16; H, 11.84. Found: C, 87.84; H, 11.81.

***ent*-13(16),14-Spongiadien-12α-ol (8) and *ent*-11,13-(16),14-Spongiatriene (31).** A solution of **27** (200 mg, 0.73 mmol) and rose bengal (20 mg) in a 95:5 mixture of CH_2Cl_2–MeOH (50 mL) was photooxygenated in the cell described above (procedure B). After 4 h of irradiation, trimethyl phosphite (1 mL) was added and the solvent removed in vacuo. The residue was applied to a silica gel column (30 g) and eluted sequentially with hexane and increasing amounts of EtOAc to yield starting **27** (52 mg, 26%) and 13(16),14-isocopaladien-12β-ol (**28**; 141.4 mg, 67%) as a colorless oil: $[\alpha]_D$ −197° (*c* 1.0, $CHCl_3$); IR (neat) 3340, 3080, 2990–2840, 1800, 1630, 1040, 990, 900 cm^{-1}; ^1H NMR δ 0.86, 0.93, and 0.93 (C-4 and C-10 Me), 0.98 (C-8 Me), 4.46 (m, $W_{1/2}$ = 8, H-12), 4.70–5.00 (m, H-15 and H-16); mass spectrum, *m/e* (relative intensity) 288 (M^+, 100), 270 (38), 255 (42), 191 (16), 132 (78).

The diene alcohol **28** (480 mg, 1.67 mmol) was submitted to a second photooxygenation reaction under essentially the same conditions described for **27**. After 7 h the reaction mixture was concentrated in vacuo to afford an oily product (639 mg) which upon chromatographic purification, as before, gave starting material **28** (380 mg, 79%) and 15,16-epidioxy-13-isocopalen-12β-ol (**29**; 74.4 mg, 14%); IR 3450, 3000–2840, 1035 cm^{-1}; ^1H NMR δ 0.85, 0.87, 0.90 (C-4 and C-10 Me), 1.05 (C-8 Me), 4.08 (m, $W_{1/2}$ = 10, H-12), 4.50 and 4.68 (both m, H-15 and H-16); mass spectrum, *m/e* (relative intensity) 320 (M^+, 18), 302 (41), 287 (22), 275 (70), 192 (33), 191 (24), 177 (36), 137 (100), 135 (34), 123 (58), 121 (37), 112 (62), 109 (47).

To a stirred solution of **29** (74 mg, 0.24 mmol) in peroxide-free THF (15 mL) was added a solution of $FeSO_4 \cdot 7H_2O$ (67 mg) in H_2O (10 mL). After 48 h the mixture was extracted with Et_2O (3 × 20 mL), and the combined Et_2O extracts were dried (Na_2SO_4) and concentrated, affording **8** (69.6 mg) as a crude oil. Further purification on a silica gel column (hexane–EtOAc, 92:8) gave pure **8**: 54.5 mg (75%); $[\alpha]_D$ −14.5° (*c* 2.3, $CHCl_3$); IR 3350, 2990–2840, 1480, 1045, 900, 869, 760 cm^{-1}; ^1H NMR (CCl_4) δ 0.85, 0.87, and 0.90 (C-4 and C-10 Me), 1.19 (C-8 Me), 4.85 (m, $W_{1/2}$ = 6, H-12), 7.07 (d, J = 2, H-16), 7.37 (d, J = H-15); mass spectrum, *m/e* (relative intensity) 302 (M^+, 100), 269 (62), 145 (24), 137 (32), 133 (23).

A solution of **8** (30 mg, 0.1 mmol) and *p*-toluensulfonic acid (1.5 mg) in benzene (30 mL) was stirred at reflux under a Dean–Stark trap for 1.5 h, after which time TLC analysis indicated that all **8** had disappeared. The cooled reaction mixture was then washed successively with 10% aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated, and the residue (38.4 mg) was chromatographed on an alumina column (hexane) to afford pure **31**: 14.4 mg (51%); mp 91.5–93 °C (sublimed); $[\alpha]_D$ −133.2° (*c* 1.0, $CHCl_3$); IR 3130, 3040, 3000–2840, 1480, 1030, 900, 820, 800, 780 cm^{-1}; ^1H NMR (CCl_4) δ 0.87, 0.88, and 1.05 (C-4 and C-10 Me), 1.05 (C-8 Me), 5.76 (dd, J = 10, 3, H-11), 6.43 (dd, J = 10, 3, H-12), 6.93 and 7.15 (both br, H-15 and H-16); mass spectrum, *m/e* (relative intensity) 284 (M^+, 84), 269 (58), 159 (22), 146 (25), 145 (41), 134 (41), 133 (87), 132 (100), 131 (20); found for M^+, *m/e* 284.2142 ($C_{20}H_{28}O$ requires *m/e* 284.2140).

Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.19; H, 9.40.

15-Isocopalol (33a). Methyl dihydroisocopalate **32**[6] (398 mg, 1.24 mmol) was refluxed with $LiAlH_4$ (80 mg, 2.1 mmol) in dry Et_2O (50 mL). After 5 h the reaction mixture was quenched as usual, washed with brine, and dried (Na_2SO_4). Evaporation of the solvent gave a solid residue which crystallized from hexane, affording pure **33a**: 316 mg (87%); mp 138–140 °C; $[\alpha]_D$ +11° (*c* 1.0, $CHCl_3$); IR 3360, 2990–2850, 1040, 1030 cm^{-1}; ^1H NMR (CCl_4) δ 0.85, 0.88, and 0.88 (C-4 and C-10 Me), 1.00 (low-field arm of a doublet, C-13 Me; from 0.85 to 1.00, 15), 3.69 (m, H-15); mass spectrum, *m/e* (relative intensity) 292 (M^+, 28), 277 (17), 192 (20), 191 (100), 137 (17), 123 (23).

Anal. Calcd for $C_{20}H_{36}O$: C, 82.12; H, 12.41. Found: C, 82.53; H, 12.53.

Isocopalane (11). A solution of **33a** (130 mg, 0.44 mmol) in CH_2Cl_2 (3 mL) and pyridine (2 mL) treated with methanesulfonyl chloride (0.5 mL, 6.5 mmol) as described for **6b**, afforded the corresponding mesylate **33c**: 156 mg (95%); ^1H NMR (CCl_4) δ 0.81, 0.86, and 0.86 (C-4 and C-10 Me), 0.92 (C-8 Me), 1.05 (low-field arm of a doublet C-13 Me; from 0.81 to 1.05, 15), 2.89 (S-Me), 4.22 (m, H-15).

Method A. Ammonia (30 mL) was condensed into a flame-dried, three-necked, round-bottomed flask equipped with a magnetic stirrer, dry-ice condenser, and pressure-equalizing addition funnel. Mesylate **33c** (261 mg, 0.70 mmol) in dry THF (15 mL) was added to the refluxing ammonia (−34 °C) followed by small pieces of lithium wire (50 mg, 7.2 mmol) in a stream of nitrogen. After 30 min, EtOH (5 mL) was added to the blue reaction mixture and the ammonia allowed to evaporate spontaneously. A 10% HCl solution was added to the residue until neutral, and then the mixture was extracted with Et_2O (3 × 20 mL), dried (Na_2SO_4), and evaporated, affording an oil (161 mg) which was shown to be a mixture of two components (TLC, GC). This mixture was applied to a silica gel column and eluted with hexane to yield **11**, 60.5 mg (31%). Elution with a 9:1 hexane–EtOAc mixture gave the starting alcohol **33a**, 91.1 mg (45%). Isocopalane (**11**): mp 109–110 °C (sublimed); $[\alpha]_D$ +9.3° (*c* 1.0, $CHCl_3$); IR 2990–2840, 1470, 1400, 995 cm^{-1}; ^1H NMR δ 0.77 (high-field arm of a doublet, C-14 Me), 0.87 (br, C-4, C-8, and C-10 Me), 0.95 (low-field arm of a doublet, C-13 Me), (from 0.77–0.95, 18), 1.18–1.91 (m, 18); mass spectrum, *m/e* (relative intensity) 276 (M^+, 30), 261 (16), 192 (18), 191 (100), 177 (7), 163 (8), 150 (5), 137 (16), 136 (9), 123 (25), 121 (9), 109 (30), 97 (7), 96 (10), 95 (33), 81 (16).

Anal. Calcd for $C_{20}H_{36}$: C, 86.88; H, 13.12. Found: C, 86.56; H, 12.97.

Method B. 15-Isocopalol mesylate (**33c**; 300 mg, 0.82 mmol) was treated with sodium ethoxide as described for **27** but refluxed for 48 h, yielding 14-isocopalene (**34**): 162.6 mg (72%); mp 77.5–78.5 °C (MeOH–benzene); $[\alpha]_D$ −4.1° (*c* 1.0, $CHCl_3$); IR 3060, 2990–2840, 1615, 890 cm^{-1}; ^1H NMR (CCl_4) δ 0.87, 0.88, and 0.88 (C-4 and C-10 Me), 1.05 (C-8 Me), 1.25 (d, J = 4, C-13 Me), 4.63 (H-15); mass spectrum, *m/e* 274 (M^+, 100), 259 (43), 204 (48), 191 (55), 177 (44), 137 (69), 136 (72), 123 (51), 121 (52), 109 (77), 107 (63), 95 (94).

Anal. Calcd for $C_{20}H_{34}$: C, 87.51; H, 12.49. Found: C, 87.44; H, 12.48.

Catalytic hydrogenation of **34** (20 mg, 0.07 mmol) with PtO_2 (29 mg) in EtOAc (50 mL) under 2 atm of H_2 afforded a mixture of **11** and its C-14 epimer in an 85:15 ratio (GC).

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