The Diterpenes of *Dictyota dichotoma* from the Indian Ocean

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Sixteen new diterpenes were obtained from the brown alga *Dictyota dichotoma* collected from the coast of the Indian Ocean. Fifteen of the diterpenes are novel dolabellanes and one is a new dolastane derivative. The structures of (1*S**,2*E*,4*R**,7*Z*,11*S**,12*S**)-4,12-dihydroxydolabella-2,7-dien-9-one (**2**) and (1*R**,3*E*,7*E*,9*S**,11*S**)-9-acetoxydolabella-3,7,12-trien-16-al (**13**) were determined by single-crystal X-ray diffraction analyses. The remaining compounds, (1*S**,2*E*,4*R**,7*E*,11*S**,12*S**)-4,12-dihydroxydolabella-2,7-dien-9-one (**3**), (1*S**,3*E*,7*E*,11*S**,12*S**)-12-hydroxydolabella-3,7-dien-9-one (**4**), (1*S**,3*E*,7*Z*,11*S**,12*S**)-12-hydroxydolabella-3,7-dien-9-one (**5**), the 8*R** and 8*S** isomers of (1*S**,2*E*,4*R**,6*Z*,11*S**,12*S**)-4,12-dihydroxydolabella-2,6-dien-9-one (**6** and **7**), the 8*R** and 8*S** isomers of (1*S**,3*E*,6*Z*,11*S**,12*S**)-12-hydroxydolabella-3,6-dien-9-one (**8** and **9**), (1*R**,2*R**,3*E*,7*E*,11*S**,12*S**)-2-acetoxy-12-hydroxydolabella-3,7-dien-9-one (**10**), (1*S**,3*S**,4*R**,7*E*,11*S**,12*S**)-3,4-epoxy-12-hydroxydolabella-7-en-9-one (**11**), (1*S**,3*E*,7*R**,8*R**,11*S**,12*S**)-7,8-epoxy-12-hydroxydolabella-3-en-9-one (**12**), (1*R**,3*E*,7*E*,9*S**,11*S**)-9-acetoxydolabella-3,7,12-trien-16-oic acid (**14**), (1*S**,3*E*,7*E*,11*S**,12*S**)-9-acetoxydolabella-3,7-dien-12-ol (**15**), (1*S**,3*E*,11*S**,12*S**)-9-acetoxy-7,8-epoxydolabella-3-en-12-ol (**16**), and (5*S**,8*S**,9*S**,12*S**,14*R**)-9-hydroxydolasta-1,3-dien-6-one (**17**), were all identified by interpretation of spectral data.

The cosmopolitan brown alga *Dictyota dichotoma* (Huds.) Lamouroux has been the subject of numerous chemical studies.[1] Diterpenes of many structural types have been isolated from collections of *D. dichotoma* from the Mediterranean Sea, the North Atlantic, Japan, and Australia. A collection of *D. dichotoma* from the Indian Ocean has proved to be a most prolific source of new diterpenes. We have previously reported the structural determination of dictyoxetane (**1**), a novel diterpene with a new carbon skeleton.[2] In this paper we report the structural elucidation of 15 new dolabellanes (**2**–**16**) and one new dolastane (**17**) (Chart I).

The alga *Dictyota dichotoma* was collected at Krusadai Island in the Gulf of Mannar, India. A chloroform extract of the air-dried alga was chromatographed on silica gel using eluants of increasing polarity consisting of mixtures of hexanes, benzene, ethyl acetate, and methanol. Each fraction required further chromatography on silica gel or neutral alumina using appropriate solvent mixtures to obtain fucosterol (2.9×10^{-2} % dry weight) and the 17 diterpenes listed in approximate order of increasing polarity in Table I.[3]

Table I. The Diterpenes Isolated from *D. dichotoma*, Listed in Order of Increasing Polarity

compd	yield × 10^{-3}, % dry weight	molecular formula	$[\alpha]^{23}$, deg
13	2.6	$C_{22}H_{32}O_3$	+6.7
9	2.1	$C_{20}H_{32}O_2$	+31.7
5	7.1	$C_{20}H_{32}O_2$	+7.2
15	4.3	$C_{22}H_{36}O_3$	+2.3
8	1.8	$C_{20}H_{32}O_2$	+9.4
16	1.9	$C_{22}H_{36}O_4$	−3.3
17	2.8	$C_{20}H_{30}O_2$	+160.1
4	94.1	$C_{20}H_{32}O_2$	−53.3
14	3.4	$C_{22}H_{32}O_4$	+60.2
12	2.2	$C_{20}H_{32}O_3$	−1.3
10	20.6	$C_{22}H_{34}O_4$	−73.2
1	0.7	$C_{20}H_{32}O_3$	+35.0
11	1.3	$C_{20}H_{32}O_3$	−32.7
6	0.2	$C_{20}H_{32}O_3$	+13.3
7	2.2	$C_{20}H_{32}O_3$	−52.3
2	23.5	$C_{20}H_{32}O_3$	−99.3
3	1.2	$C_{20}H_{32}O_3$	−6.5

(1*S**,2*E*,4*R**,7*Z*,11*S**,12*S**)-4,12-Dihydroxydolabella-2,7-dien-9-one (**2**) was obtained as a crystalline solid, mp 153–155 °C, $[\alpha]_D$ −99.3°, of molecular formula $C_{20}H_{32}O_3$. The IR spectrum indicated the presence of hydroxyl (3450 cm^{-1}) and α,β-unsaturated ketone (1670 cm^{-1}) groups. The α,β-unsaturated ketone gave rise to a UV absorption at 228 nm. The ^{13}C NMR spectrum contained signals at δ 206.4 (s), 139.4 (d), 138.6 (d), 136.0 (s), and 132.3 (d) assigned to the α,β-unsaturated ketone and a disubstituted olefin and at δ 84.5 (s) and 73.7 (s) due to two tertiary alcohols. In the ^1H NMR spectrum of **2**, the signal for the two olefinic protons on the disubstituted olefin appeared as a singlet at δ 5.23 (s, 2 H) while the remaining olefinic proton gave rise to a signal at δ 5.50 (dd, 1 H, J = 10.5, 5 Hz). The methyl proton signals at δ 1.96 (s), 1.28 (s), 1.17 (s), and 1.02 (d, 6 H, J = 7 Hz) were assigned to a methyl group at the α position of the α,β-unsaturated ketone, a methyl group adjacent to a tertiary alcohol, a tertiary methyl group, and an isopropyl group, respectively. The ^1H NMR spectrum also indicated that the signals for the methylene protons adjacent to the carbonyl group at δ 2.75 (dd, 1 H, J = 14, 11.5 Hz) and 2.34 (dd, 1 H, J =

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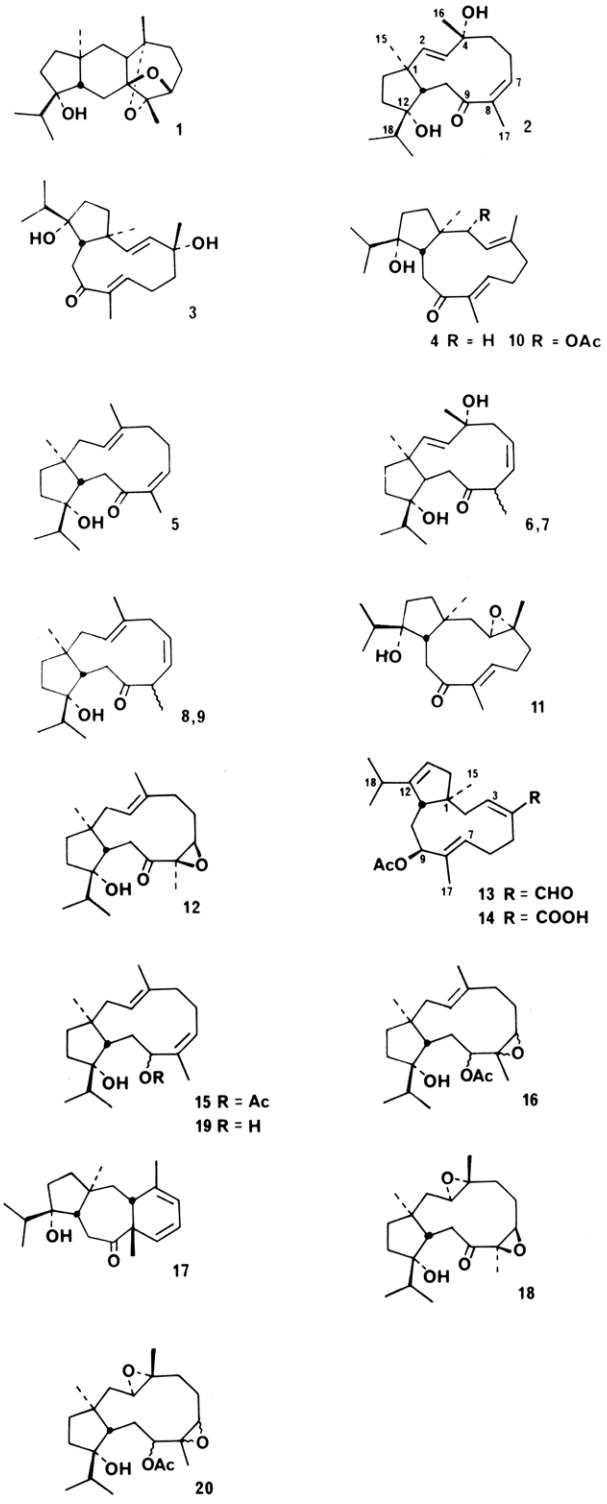
(2) Pullaiah, K. C.; Surapaneni, R. K.; Rao, C. B.; Albizati, K. F.; Sullivan, B. W.; Faulkner, D. J.; Cun-heng, H.; Clardy, J. *J. Org. Chem.* **1985**, *50*, 3665.

(3) Pullaiah, K. C. Ph.D. Thesis, Andhra University, 1984.

0022-3263/86/1951-2736$01.50/0

Chart I



14, 2 Hz) were coupled to a methine proton at δ 2.03 (dd, 1 H, J = 11.5, 2 Hz) that was not further coupled. These data suggested a 4,12-dihydroxydolabella-2,7-dien-9-one structure, but the stereochemistry could not readily be deduced.

Figure 1 is a computer-generated perspective drawing of the final X-ray model of ketone **2**. Hydrogens are omitted for clarity, and no absolute configuration is implied. The 11- and 5-membered rings are joined in a trans fashion. The double bonds between C2–C3 and C7–C8 have *E* and *Z* geometry, respectively. The carbonyl group (C9=O2) is twisted out of conjugation with the C7–C8 double bond with a C7–C8–C9–O2 torsional angle of −42°.

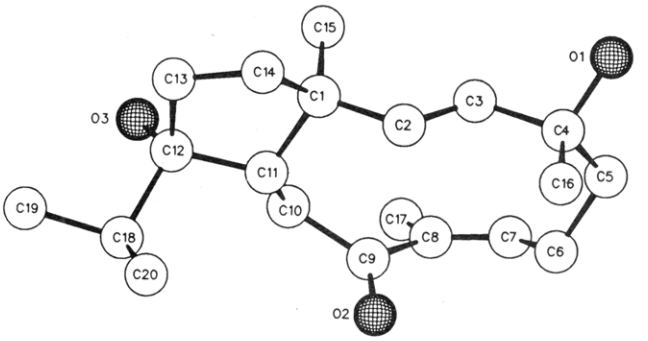


Figure 1. A computer-generated perspective drawing of the final X-ray model of ketone **2**. Hydrogens are omitted for clarity, and no absolute configuration is implied.

In general bond distances and angles agree well with accepted values.

(1*S**,2*E*,4*R**,7*E*,11*S**,12*S**)-4,12-Dihydroxydolabella-2,7-dien-9-one (**3**) is a crystalline solid, mp 212–213 °C, $[\alpha]_D$ −6.5°. Comparison of the spectral data of **3** with those of **2** revealed that they were geometrical isomers about the 7,8-olefinic bond. The ^{1}H NMR spectrum of **3** contained an olefinic proton signal at δ 6.48 (br d, 1 H, J = 9 Hz), typical of a β-proton on a *trans*-enone (cf. δ 5.50 for **2**) and two signals at δ 5.45 (d, 1 H, J = 16.5 Hz) and 5.15 (d, 1 H, J = 16.5 Hz) due to the trans-disubstituted olefin. The signal for the olefinic methyl group is at δ 1.71 (br s, 3 H), the upfield shift being due to the proximity of the methyl group to the 2,3 olefin. The structure of **3** was confirmed by the isomerization of **2** with sodium methoxide in methanol at 70 °C to obtain a 7:3 mixture of **2** and **3**.

The major metabolite from this collection of *D. dichotoma* was (1*S**,3*E*,7*E*,11*S**,12*S**)-12-hydroxydolabella-3,7-dien-9-one (**4**), which was obtained as a crystalline solid, mp 93–95 °C, $[\alpha]_D$ −53.3°. Consideration of the molecular formula, $C_{20}H_{32}O_2$, together with the ^{13}C NMR data led to the proposal that **4** was related to **3** by replacement of the allylic alcohol functionality by a trans-trisubstituted olefinic group. The presence of the *trans*-enone was indicated by the UV absorption at 235 nm (ε 7200) and the ^{1}H NMR signals at δ 1.73 (s, 3 H) and 6.35 (dd, 1 H, J = 10, 1 Hz). The trans-trisubstituted olefin gave rise to ^{1}H NMR signals at δ 1.49 (br s, 3 H) and 5.35 (dd, 1 H, J = 12, 2 Hz): the 3*E* stereochemistry is based on the observation that the C16 methyl signal appeared at δ 14.9 in the ^{13}C NMR spectrum. All other spectral data support this structural assignment.

The corresponding *cis*-enone (1*S**,3*E*,7*Z*,11*S**,12*S**)-12-hydroxydolabella-3,7-dien-9-one (**5**), was obtained as an oil, $[\alpha]_D$ +7.2°. The UV absorption at 237 nm (ε 3350) indicated the presence of the enone functionality but the ^{1}H NMR signals at δ 1.95 (br s, 3 H) and 5.58 (t, 1 H, J = 8.5 Hz) (cf. δ 1.96 and 5.50 for **2**) and the lack of a methyl signal at δ <17 in the ^{13}C NMR spectrum required the 7*Z* geometry. The remaining spectral data were all compatible with the proposed structure. The relationship between **4** and **5** was confirmed by the photolysis of **4** in benzene solution to obtain an equilibrium mixture of the *cis*- and *trans*-enones.

The alga contained four minor metabolites that were all β,γ-unsaturated ketones. One pair of compounds, **6** and **7**, had the molecular formula $C_{20}H_{32}O_3$, isomeric with **2** and **3** while a second pair, **8** and **9**, were isomeric with **4** and **5**, having the molecular formula $C_{20}H_{32}O_2$. Each of the pairs of compounds consists of two 6(*Z*)-en-9-ones that are epimeric at C8. In the ^{1}H NMR spectra of the four molecules, the $COCH(CH_3)CH{=}CHCH_2$ spin system could easily be defined by using spin-decoupling tech-

niques. The $J_{6,7}$ coupling constant of 10–11 Hz was appropriate for a cis olefinic bond and molecular models suggest that a trans olefinic bond in that position would introduce significant strain into the ring. Treatment of the enone **7** with excess sodium methoxide in methanol at 40 °C for 24 h gave a 1:1 mixture of **6** and **7** formed by equilibration at C8. When the experiment was repeated at reflux temperature for 4 h, a small quantity of the conjugated isomer **3** was obtained. These reactions confirmed the relationship between the β,γ-unsaturated ketones **7** and **6** and the α,β-unsaturated ketone **3**. In similar fashion, both **8** and **9** were converted into **4**. The stereochemistry at C8 could not be unambiguously assigned by using NOE measurements.

(1*R**,2*R**,3*E*,7*E*,11*S**,12*S**)-2-Acetoxy-12-hydroxydolabella-3,7-dien-9-one (**10**) was obtained as a crystalline solid, mp 173–174 °C, $[\alpha]_D$ −73.2°, of molecular formula $C_{22}H_{34}O_4$. The presence of the acetoxy group was indicated by an IR band at 1730 cm^{-1}, a ^1H NMR signal at δ 2.03 (s, 3 H), and ^{13}C NMR signals at δ 170.4 (s) and 21.1 (q). The α,β-unsaturated ketone gave rise to an IR band at 1660 cm^{-1}, ^1H NMR signals at δ 6.33 (br d, 1 H, J = 10.7 Hz) and 1.74 (s, 3 H), and ^{13}C NMR signals at δ 143.6 (d), 133.7 (s), 208.0 (s) and 11.8 (q). Comparison of these data with the corresponding data for enones **4** and **5** clearly indicated the 7*E* geometry. The ^{13}C NMR spectrum contained signals at 75.6 (d), 122.8 (d), and 140.6 (s) assigned to a *C*H(OAc) group and a trisubstituted olefin. Since the ^1H NMR spectrum contained two mutually coupled signals at δ 5.04 (d, 1 H, J = 10.4 Hz) and 5.25 (br d, 1 H, J = 10.4 Hz), the acetoxy group must be at C-2, adjacent to the olefinic proton. Nuclear Overhauser enhancement experiments revealed that the C-3 proton was adjacent to the C15 methyl group and the C2 proton was proximal to the C16 methyl group, as expected for the 1*R**,2*R**,3*E* geometry. As has been observed previously,[4] the functional groups on the 11-membered ring in the dolabellanes are outside and in the plane of the ring while the plane of the olefinic bonds tends to be perpendicular to the plane of the ring.

(1*S**,3*S**,4*R**,7*E*,11*S**,12*S**)-3,4-Epoxy-12-hydroxydolabella-7-en-9-one (**11**), $[\alpha]_D$ −32.7°, is a crystalline solid, mp 113–115 °C, of molecular formula $C_{20}H_{32}O_3$. Analysis of the spectral data revealed that epoxide **11** is a 3,4-epoxy derivative of ketone **4**. The ^{13}C NMR spectrum contains signals for an α,β-unsaturated ketone at δ 207.1 (s), 142.3 (d), and 135.5 (s) together with signals at δ 63.0 (d) and 61.8 (s), assigned to a trisubstituted epoxide. The signal at δ 6.55 (m, 1 H, J = 6.5, 1 Hz) in the ^1H NMR spectrum indicated the 7*E* geometry. Treatment of the ketone **4** with *m*-chloroperbenzoic acid in dry benzene gave the epoxide **11** in 81% yield together with a trace of the diepoxide. Since all reagents react from the outside of the ring system, the stereochemistry of the epoxide **11** must be 3*S**,4*R** as shown.

(1*S**,3*E*,7*R**,8*R**,11*S**,12*S**)-7,8-Epoxy-12-hydroxydolabella-3-en-9-one (**12**), $[\alpha]_D$ −1.3°, is an oil of molecular formula $C_{20}H_{32}O_3$, isomeric with epoxide **11**. The absence of the enone UV absorption suggested that epoxide **12** might be a 7,8-epoxide of either **4** or **5**. The ^{13}C NMR spectrum contained signals at δ 205.8 (s), 135.2 (s), 121.6 (d), 86.3 (s), 66.5 (d), and 62.7 (s) that were assigned to the carbons of a ketone, an olefin, a tertiary alcohol, and an epoxide, respectively. The ^1H NMR spectrum has a signal at δ 5.09 (dd, 1 H, J = 10, 5 Hz) assigned to H-3 and a signal at δ 2.96 (dd, 1 H, J = 8.5, 4.5 Hz), due to the proton on the epoxide ring. The geometry of the epoxide ring was determined by showing that the diepoxide **18**, synthesized from **12** by treatment with *m*-chloroperbenzoic acid in benzene, was identical with that prepared from ketone **5**. Assuming once more that the olefinic bonds are epoxidized on the outer face, the stereochemistries of **12** and **18** must be as drawn.

(1*R**,3*E*,7*E*,9*S**,11*S**)-9-Acetoxydolabella-3,7,12-trien-16-al (**13**), $[\alpha]_D$ +10°, was obtained as a crystalline solid, mp 163–165 °C, of molecular formula $C_{22}H_{32}O_3$. The aldehyde **13** clearly lacked the C12 tertiary alcohol functionality. The infrared spectrum contained bands at 1715, 1680, and 1630 cm^{-1} compatible with the presence of an ester and an α,β-unsaturated aldehyde. The unsaturated aldehyde moiety was responsible for the UV absorption at 229 nm (ϵ 5950). The ^{13}C NMR spectrum suggested the presence of three olefinic bonds [δ 154.7 (d), 151.5 (s), 142.5 (s), 133.2 (d), 131.5 (s), and 119.3 (d)] in addition to the aldehyde [δ 195.2 (d)] and acetate [δ 170.3 (s)] groups. The ^1H NMR spectrum contained an aldehyde proton signal at δ 9.36 (s 1 H), a signal at δ 6.53 (dd, 1 H, J = 11.5, 1.5 Hz) due to the β proton on the α,β-unsaturated aldehyde, olefinic proton signals at δ 5.30 (br s, 1 H) and 5.58 (dd, 1 H, J = 11.5, 3 Hz), and the allylic α-acetoxy proton signal at δ 5.43 (dd, 1 H, J = 10.5, 6 Hz). Even though the ^1H NMR spectrum had been almost completely assigned, ambiguities in assignment of stereochemistry required that the structure be determined by an X-ray experiment.

Figure 2 is a computer-generated perspective drawing of the final X-ray model of aldehyde **13**. Hydrogen atoms are omitted for clarity, and no absolute configuration is implied. Both ketone **2** and aldehyde **13** are shown with the same absolute configuration. The 11- and 5-membered rings are trans fused. There is a double bond at the C3–C4 position in conjugation with the aldehyde at C16. There is an *E* double bond at the C7–C8 position. All bond distances and angles agree well with generally accepted values.

(1*R**,3*E*,7*E*,9*S**,11*S**)-9-Acetoxydolabella-3,7,12-trien-16-oic acid (**14**), $[\alpha]_D$ +60.2°, is a crystalline solid, mp 152–154 °C, of molecular formula $C_{22}H_{32}O_4$. Examination of spectral data suggested that the acid **14** was related to aldehyde **13**. Oxidation of the aldehyde **13** with silver oxide and sodium cyanide in methanol gave the acid **14** in poor yield: oxidation with silver oxide in benzene did not proceed.

(1*S**,3*E*,7*E*,11*S**,12*S**)-9-Acetoxydolabella-3,7-dien-12-ol (**15**), $[\alpha]_D$ +2.3°, was obtained as an oil of molecular formula $C_{22}H_{36}O_3$. The spectral data suggested that the acetate **15** was related to either ketone **4** or ketone **5** with an acetate replacing the ketone at C9. This hypothesis was confirmed by reduction of the acetate **15** with lithium aluminum hydride in dry ether to obtain the diol **19**, which was oxidized with manganese dioxide to obtain the ketone **5**. The relative stereochemistry at C9 could not be determined from the spectral data.

(1*S**,3*E*,11*S**,12*S**)-9-Acetoxy-7,8-epoxydolabella-3-en-12-ol (**16**), $[\alpha]_D$ −3.3°, is an oil of molecular formula $C_{22}H_{36}O_4$. The ^{13}C NMR spectra indicated the presence of a secondary acetate, one olefinic bond, a tertiary alcohol, and a trisubstituted epoxide, suggesting that epoxide **16** was a monoepoxide of acetate **15**. Treatment of both epoxide **16** and acetate **15** with *m*-chloroperbenzoic acid in dry benzene gave the same diepoxide **20**. Since the ^1H NMR signal for the C9 proton is at δ 4.02 in **16** and at δ 4.85 in **15**, the epoxide must be at the 7,8 position. Considering that all functional groups must be on the outer face of the 11-membered ring, the epoxide **16** can have only

(4) Ireland, C.; Faulkner, D. J. *J. Org. Chem.* **1977**, *42*, 3157.

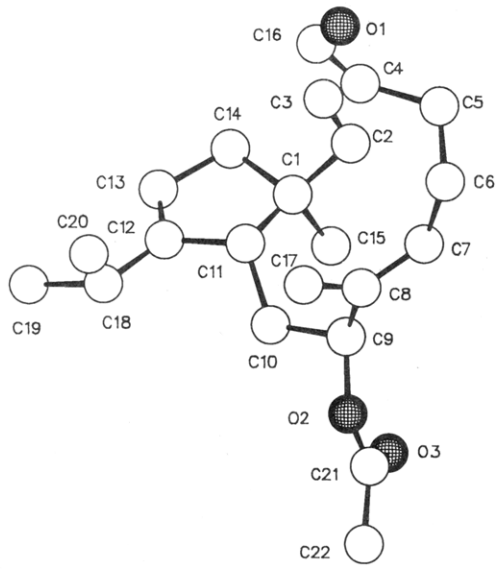
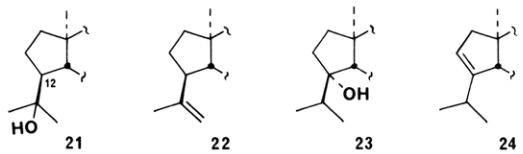


Figure 2. A computer-generated perspective drawing in the final X-ray model of aldehyde **13**. Hydrogens are omitted for clarity, and no absolute configuration is implied.

the 7*R**,8*R**,9*S** or 7*S**,8*S**,9*R** stereochemistry depending on whether acetate **15** has the 9*S** or 9*R** geometry.

(5*S**,8*S**,9*S**,12*S**,14*R**)-9-Hydroxydolesta-1,3-dien-6-one (**17**), $[\alpha]_D$ +160°, has the molecular formula $C_{20}H_{30}O_2$. The ^{13}C NMR signals at δ 213.1 (s), 136.4 (s), 126.7 (d), 121.6 (d), 117.8 (d), and 83.3 (s) were assigned to a ketone carbonyl, four olefinic carbons, and a tertiary hydroxyl carbon, respectively. The ketone **17** must therefore have three carbocyclic rings. The UV absorption at 261 nm, together with ^1H NMR signals at δ 5.60 (br d, 1 H, J = 5 Hz), 5.82 (dd, 1 H, J = 9.6, 5 Hz), and 5.96 (d, 1 H, J = 9.6 Hz) indicated the presence of a homoannular diene. The ^1H NMR spectrum also contained methyl signals at δ 1.80 (s, 3 H), 1.18 (s, 3 H), 0.96 (d, 6 H, J = 7 Hz), and 0.97 (s, 3 H). These data suggested that a hypothetical dolabella-3,5,7-trien-9-one precursor might have undergone a Cope rearrangement to obtain the dolast-1,3-dien-9-one **17**. The spectral data are completely in accord with this hypothesis. The stereochemistry of **17** was determined by observation of nuclear Overhauser enhancements of the H-14 and H-8 signals at δ 2.42 and 2.27 on irradiation of the CH_3-16 signal at δ 1.18, coupled with the observation of an enhancement of the H-4 signal at δ 5.96 on irradiation of the CH_3-20 signal at δ 1.03.

Diterpenes of the dolabellane class were first isolated from the sea hare *Dolabella californica*.[5] Since sea hares were known to obtain their secondary metabolites from dietary sources, it came as no surprise when dolabellane diterpenes were isolated from brown algae of the order Dictyotales.[6] All dolabellanes previously found in brown algae have contained either an isopropyl alcohol or isopropene side chain at C12 (**21** and **22**), while the dolabellanes **2**–**16** possess an isopropyl side chain with either an alcohol or olefin at C12 (**23** and **24**). As noted previously, dictyoxetane **1** has a unique carbon skeleton. The dolastane **17** can be related to a dolabellane precursor by a Cope rearrangement and therefore differs from other



21 **22** **23** **24**

dolastanes[7] that appear to arise by a carbonium ion initiated cyclization of the dolabellane carbon skeleton.

Experimental Section

Isolation of Diterpenes 1–17. The alga *Dictyota dichotoma* (Huds.) Lamouroux was collected by hand at Krusadai Island, Gulf of Mannar, India (9° 16′ N, 79° 12′ E) during January 1983.[8] The alga was washed with fresh water, air-dried, and powdered in a Wiley mill and the powder (1.7 kg) Soxhlet extracted with first chloroform and then methanol. Evaporation of solvent from the chloroform extract gave a dark oil (36 g), which was chromatographed on a 100–200 mesh silica gel (200 g) column (65-mm diameter) by using eluants of increasing polarity from petroleum ether (65–75 °C) through benzene and ethyl acetate to methanol. The fraction that was eluted with 10% benzene in petroleum ether contained fucosterol, mp 149 °C (400 mg). The fraction eluted with 10–20% benzene in petroleum ether was rechromatographed over silica gel by using a petroleum ether–hexane gradient to obtain fucosterol (120 mg), the aldehyde **13** (45 mg) and the β,γ-unsaturated ketone **9** (35 mg). The fraction eluted with 30% benzene in petroleum ether was rechromatographed as before to obtain, after preparative TLC on silica gel or rechromatography on 5% $AgNO_3/SiO_2$, the α,β-unsaturated ketone **5** (80 mg), the acetate **15** (30 mg), the β,γ-unsaturated ketone **8** (30 mg), the epoxy acetate **16** (32 mg), and the epoxide **12** (38 mg). The fraction eluted with 40% benzene in petroleum ether was rechromatographed on silica gel to obtain the α,β-unsaturated ketone **5** (40 mg), the acetate **15** (27 mg), the β,γ-unsaturated ketone **8** (20 mg), and the dolastane **17** (48 mg). The fraction eluted with 60% benzene in petroleum ether was rechromatographed over silica gel by using a petroleum ether/ethyl acetate gradient to obtain the α,β-unsaturated ketone **4** (15 mg) and the acid **14** (40 mg). The fraction eluted with 80% benzene in petroleum ether was rechromatographed over neutral alumina using a petroleum ether/ethyl acetate gradient to obtain impure α,β-unsaturated ketone **4** (1.35 g) and impure acid **14** (20 mg). The fraction eluted with benzene was rechromatographed over neutral alumina to obtain the α,β-unsaturated ketone **4** (100 mg), the acetate **10** (350 mg), and dictyoxetane (**1**, 17 mg). The fraction eluted with 10% ethyl acetate in benzene was rechromatographed over neutral alumina to obtain the α,β-unsaturated ketones **6** and **7** (42 mg). The fraction eluted with 20–30% ethyl acetate in benzene was repeatedly rechromatographed to obtain α,β-unsaturated ketone **3** (20 mg). The α,γ-unsaturated ketones **6** and **7** could be separated by using HPLC on Partisil with 3:1 ethyl acetate–hexane as eluant. These date are summarized in Table I.

Dictyoxetane (1): oil; $[\alpha]_D$ +35.0° (*c* 3.0, $CHCl_3$); ^1H NMR (360 MHz, C_6D_6) δ 4.25 (br d, 1 H), 2.03 (dd, 1 H, J = 2.5, 13.0 Hz), 1.90 (dd, 1 H, J = 9.5, 14.0 Hz), 1.85–1.57 (overlapping m), 1.54 (dd, 1 H, J = 3.5, 8.4 Hz), 1.29 (s, 3 H), 1.27 (s, 3 H), 1.11 (s), 0.95 (d, 3 H, J = 6.5 Hz), 0.88 (d, 3 H, J = 6.5 Hz); IR ($CHCl_3$) 3600, 3030, 1460, 1410, 1390, 1160, 1070, 1030, 1000, 910, 870 cm^{-1}; ^{13}C NMR (50 MHz, $CDCl_3$) δ 97.2 (s), 82.7 (s), 81.3 (d), 80.6 (s), 80.1 (s), 52.6 (d), 48.0 (d), 42.5 (s), 39.1 (t), 36.6 (d), 35.9 (t), 34.6 (t), 26.7 (q), 27.6 (t), 24.6 (t), 23.4 (t), 20.0 (q), 18.5 (q), 17.5 (q), 16.1 (q); HRMS, obsd m/z 320.2342, $C_{20}H_{32}O_3$ requires m/z 320.2351.

(1*S,2*E*,4*R**,7Z,11*S**,12*S**)-4,12-Dihydroxydolabella-2,7-dien-9-one (2):** mp 153–155 °C ($CHCl_3$–petroleum ether); $[\alpha]_D$ –99.3° (*c* 3.28, $CHCl_3$); UV (MeOH) 228 nm (ε 2400); IR ($CHCl_3$)

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3700, 1670, 1625 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02 (d, 6 H, J = 7 Hz), 1.17 (s, 3 H), 1.28 (s, 3 H, 1.96 (s, 3 H), 2.03 (dd, 1 H, J = 11.5, 2.0 Hz), 2.07 (m, 1 H), 2.34 (m, 1 H), 2.34 (dd, 1 H, J = 14.0, 2.0 Hz), 2.75 (dd, 1 H, J = 14.0, 11.5 Hz), 5.22 (d, 1 H, J = 14.5 Hz), 5.24 (d, 1 H, J = 14.5 Hz), 5.50 (dd, 1 H, J = 10.5, 5.0 Hz); ^{13}C NMR ($CDCl_3$) δ 206.4 (s), 139.4 (d), 138.6 (d), 136.0 (s), 132.3 (d), 84.5 (s), 73.7 (s), 52.9 (d), 46.5 (s), 40.3 (t), 39.3 (t), 36.9 (d), 35.7 (t), 35.4 (t), 25.5 (q), 23.1 (t), 20.1 (q), 18.0 (q), 18.0 (q), 17.1 (q); HRMS, obsd m/z 320.2369, $C_{20}H_{32}O_3$ requires m/z 320.2351.

(1*S,2*E*,4*R**,7*E*,11*S**,12*S**)-4,12-Dihydroxydolabella-2,7-dien-9-one (3)**: mp 212–213 °C (EtOAc–petroleum ether); $[\alpha]_D$ –6.5° (c 0.12, CH_3OH); UV (CH_3OH) 250 nm (ϵ 2020); IR ($CHCl_3$) 3500, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.48 (br d, 1 H, J = 9 Hz), 5.45 (d, 1 H, J = 16.5 Hz), 5.15 (d, 1 H, J = 16.5 Hz), 2.99 (dd, 1 H, J = 4.5, 13.5 Hz), 2.45–2.30 (overlapping m), 1.71 (br s, 3 H), 1.67–1.57 (overlapping m), 1.48 (br t, 1 H, J = 4 Hz), 1.31 (s, 3 H), 1.22 (s, 3 H), 0.97 (d, 3 H, J = 6.5 Hz), 0.78 (d, 3 H, J = 6.5 Hz); ^{13}C NMR (CD_3OD) δ 208.5 (s), 147.8 (d), 141.6 (d), 135.6 (d), 133.4 (s), 86.9 (s), 73.6 (s), 50.5 (d), 42.5, 39.6 (s), 35.7, 34.0, 32.2, 26.0 (t), 24.7 (d), 18.8, 17.9, 12.2; HRMS, obsd m/z 320.2349, $C_{20}H_{32}O_3$ requires m/z 320.2351.

(1*S,3*E*,7*E*,11*S**,12*S**)-12-Hydroxydolabella-3,7-dien-9-one (4)**: mp 93–95 °C (petroleum ether); $[\alpha]_D$ –53.3° (c 1.96, $CHCl_3$); UV (MeOH) 235 nm (ϵ 7200), 203 (6700); IR ($CHCl_3$) 3450, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.72 (d, 3 H, J = 7.0 Hz), 0.88 (d, 3 H, J = 7.0 Hz), 1.07 (s, 3 H), 1.49 (s, 3 H), 1.73 (s, 3 H), 2.14 (dd, 1 H, J = 13, 12 Hz), 2.30 (m, 3 H), 2.40 (dd, 1 H, J = 12.8, 10.8 Hz), 2.48 (m, 1 H), 2.94 (dd, 1 H, J = 12.8, 1.0 Hz), 5.35 (dd, 1 H, J = 12.1, 2.2 Hz), 6.35 (dd, 1 H, J = 10.0, 1.0 Hz); ^{13}C NMR ($CDCl_3$) δ 208.4 (s), 144.3 (d), 135.3 (s), 133.8 (s), 125.1 (d), 86.7 (s), 47.7 (d), 45.3 (s), 42.8 (t), 39.9 (t), 39.3 (t), 36.8 (t), 33.9 (d), 29.7 (t), 23.9 (t), 23.8 (q), 18.1 (q), 17.6 (q), 14.9 (q), 11.7 (q); HRMS, obsd m/e 304.2396, $C_{20}H_{32}O_2$ requires m/z 304.2402.

(1*S,3*E*,7*Z*,11*S**,12*S**)-12-Hydroxydolabella-3,7-dien-9-one (5)**: oil; $[\alpha]_D$ +7.2° (c 6.16, $CHCl_3$); UV (MeOH) 237 nm (ϵ 3350), 207 (3350); IR ($CHCl_3$) 3500, 1680, 1630, 1440, 1360, 1030 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (d, 3 H, J = 7 Hz), 1.00 (d, 3 H, J = 7 Hz), 1.11 (s, 3 H), 1.57 (br s, 3 H), 1.80 (m, 1 H), 1.95 (br s, 3 H), 2.01 (dd, 1 H, J = 8.5, 1.5 Hz), 2.12 (dd, 1 H, J = 13.0, 11.0 Hz), 2.18 (dd, 1 H, J = 15.0, 1.5 Hz) 2.22 (m, 1 H), 2.70 (dd, 1 H, J = 15.0, 8.5 Hz), 2.76 (m, 1 H), 5.02 (dd, 1 H, J = 10.5, 5.0 Hz), 5.58 (t, 1 H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 207.4 (s), 137.8 (s), 135.6 (d), 134.9 (s), 122.2 (d), 87.6 (s), 47.9 (d), 44.4 (s), 43.0 (t), 40.6 (t), 37.6 (t), 37.1 (t), 34.2 (d), 31.0 (t), 24.9 (t), 24.5 (q), 21.2 (q), 18.1 (q), 17.6 (q), 17.4 (q); HRMS, obsd m/z 304.2402, $C_{20}H_{32}O_2$ requires m/z 304.2402.

(1*S,2*E*,4*R**,6*Z*,11*S**,12*S**)-4,12-Dihydroxydolabella-2,6-dien-9-one (6)**: oil; $[\alpha]_D$ +13.3° (c 0.03, $CHCl_3$); UV (MeOH) <210 nm; IR ($CHCl_3$) 3680, 3600, 1700, 1600 cm^{-1}; ^1H NMR (C_6D_6) δ 5.75 (m, 1 H, J = 12, 9, 5, 2 Hz), 5.45 (d, 1 H, J = 16.5 Hz), 5.33 (dd, 1 H, J = 8.5, 9 Hz), 5.15 (d, 1 H, J = 16.5 Hz), 3.40 (m, 1 H), 2.45 (dd, 1 H, J = 8, 15 Hz), 2.23 (d, 1 H, J = 12 Hz), 2.17 (dd, 1 H, J = 3, 14 Hz), 2.13 (dd, 1 H, J = 4, 8 Hz), 2.00 (d, 1 H, J = 5, 12 Hz), 1.78 (m, 2 H), 1.24 (s, 3 H), 1.13 (s, 3 H), 1.00 (d, 3 H, J = 7 Hz), 0.83 (d, 3 H, J = 6.5 Hz), 0.78 (d, 3 H, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 137.6, 135.2, 131.4, 127.8, 83.9, 77.3, 53.4, 49.6, 44.8, 42.6, 38.9, 36.7, 35.1, 34.5, 28.7, 21.7, 18.2, 17.9, 17.3; HRMS, obsd m/z 302.2246 ($M^+ - H_2O$), $C_{20}H_{32}O_2$ requires m/z 302.2246.

(1*S,2*E*,4*R**,6*Z*,11*S**,12*S**)-4,12-Dihydroxydolabella-2,6-dien-9-one (7)**: oil; $[\alpha]_D$ –52.3° (c 0.3, $CHCl_3$); UV (MeOH) <210 nm; IR (CCl_4) 3570, 1720, 960, 870 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.72 (dd, 1 H, J = 10.5, 10.5 Hz), 5.45 (d, 1 H, J = 16.5 Hz), 5.40 (br m, 1 H), 5.13 (d, 1 H, J = 16.5 Hz), 3.15 (br m, 1 H), 2.35 (dd, 1 H, J = 9, 14.5 Hz), 2.21 (m, 1 H), 2.08 (dd, 1 H, J = 9, 13 Hz), 1.99 (d, 1 H, J = 14.5 Hz), 1.81 (m, 1 H), 1.55 (m, 3 H), 1.20 (s, 3 H), 1.08 (s, 3 H), 1.01 (d, 3 H, J = 7 Hz), 0.89 (d, 3 H, J = 6 Hz), 0.87 (d, 3 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 214.0 (s), 137.3 (d), 135.1 (d), 132.1 (d), 124.9 (d), 84.2 (s), 73.5 (s), 53.6 (d), 47.3 (s), 47.1 (d), 41.1 (t), 38.6 (t), 36.8 (t), 35.4 (t), 24.3 (q), 18.0 (q), 17.7 (q), 17.4 (q), 17.0 (q); HRMS, obsd m/z 320.2350, $C_{20}H_{32}O_3$ requires m/z 320.2351.

(1*S,3*E*,6*Z*,11*S**,12*S**)-12-Hydroxydolabella-3,6-dien-9-one (8)**: oil; $[\alpha]_D$ +9.4° (c 0.36, CH_3OH); UV (MeOH) <210 nm; IR (CCl_4) 3500, 1705, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.84 (dt, 1 H, J = 7.5, 10.5, 7.5 Hz), 5.52 (td, 1 H, J = 2, 8, 10 Hz), 5.24 (br d, 1 H, J = 10.5 Hz), 3.35 (m, 1 H), 2.71 (br d, 1 H), 2.58 (dd, 1 H, J = 16, 7 Hz) 2.56 (dd, 1 H, J = 6, 16 Hz), 2.25 (dd, 1 H, J = 5, 16 Hz), 2.10 (dd, 1 H, J = 13.5, 10 Hz), 2.05 (dd, 1 H, J = 5.5, 6.0 Hz), 1.82 (br s, 3 H), 1.38 (m, 2 H), 1.16 (d, 3 H, J = 7 Hz), 1.07 (s, 3 H), 0.92 (d, 3 H, J = 7 Hz), 0.90 (d, 3 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 213.4 (s), 135.0 (s), 132.5 (d), 129.8 (d), 122.8 (d), 85.8 (s), 46.5 (d), 45.4 (d), 45.3 (s), 42.4 (t), 40.2 (t), 36.1 (t), 35.6 (d), 32.5 (t), 29.5 (t), 22.6 (q), 18.0 (q), 17.9 (q), 17.6 (q), 17.2 (q); HRMS, obsd m/z 304.2397, $C_{20}H_{32}O_2$ requires m/z 304.2402.

(1*S,3*E*,6*Z*,11*S**,12*S**)-12-Hydroxydolabella-3,6-dien-9-one (9)**: oil; $[\alpha]_D$ +31.7° (c 0.36, $CHCl_3$); UV (MeOH) 213 nm (ϵ 1900); IR ($CHCl_3$) 3500, 1705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (d, 3 H, J = 7.0 Hz), 0.96 (d, 3 H, J = 7.0 Hz), 1.16 (s, 3 H), 1.22 (d, 3 H, J = 7.5 Hz), 1.44 (br s, 3 H), 2.05 (d, 1 H, J = 7.5 Hz), 2.25 (d, 1 H, J = 16.5 Hz), 2.60 (m, 2 H), 2.71 (ddd, 1 H, J = 14.5, 10.0, 1.5 Hz), 3.49 (d, 1 H, J = 7.5 Hz), 5.28 (m, 1 H), 5.55 (ddd, 1 H, J = 10.0, 7.0, 1.5 Hz), 5.78 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 213.7 (s), 136.7 (s), 134.8 (d), 127.2 (d), 122.7 (d), 86.0 (s), 48.8 (d), 47.3 (d), 45.9 (s), 42.2 (t), 40.8 (t), 38.4 (t), 36.8 (t), 36.2 (d), 33.9 (t), 20.9 (q), 17.9 (q), 17.6 (q), 17.0 (q), 15.8 (q); HRMS, obsd m/z 304.2404, $C_{20}H_{32}O_2$ requires m/z 304.2402.

(1*R,2*R**,3*E*,7*E*,11*S**,12*S**)-2-Acetoxy-12-hydroxydolabella-3,7-dien-9-one (10)**: mp 173–174 °C (10% $CHCl_3$–petroleum ether); $[\alpha]_D$ –73.2° (c 3.58, $CHCl_3$); UV (MeOH) 237 nm (ϵ 6800), 205 (4500); IR ($CHCl_3$) 3500, 1730, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.73 (d, 3 H, J = 7.0 Hz), 0.88 (d, 3 H, J = 7.0 Hz), 1.10 (s, 3 H), 1.67 (s, 3 H), 1.74 (s, 3 H), 2.04 (s, 3 H), 2.31 (m, 2 H), 2.43 (m, 1 H), 2.49 (dd, 1 H, J = 12.8, 10.8 Hz), 5.04 (d, 1 H, J = 10.4 Hz), 5.25 (br d, 1 H, J = 10.4 Hz), 6.33 (br d, 1 H, J = 10.7 Hz); ^{13}C NMR ($CDCl_3$) δ 208.0 (s), 170.4 (s), 143.6 (d), 140.6 (s), 133.7 (s), 122.8 (d), 86.2 (s), 75.6 (d), 48.4 (s), 46.3 (d), 39.4 (t), 36.4 (t), 35.4 (t), 33.9 (d), 29.6 (t), 23.7 (t), 21.1 (q), 18.0 (q), 18.0 (q), 17.5 (q), 15.6 (q), 11.8 (q); HRMS, obsd m/z 362.2456, $C_{22}H_{34}O_4$ requires m/z 362.2457.

(1*S,3*S**,4*R**,7*E*,11*S**,12*S**)-3,4-Epoxy-12-hydroxydolabella-7-en-9-one (11)**: mp 113–115 °C; $[\alpha]_D$ –32.7° (c 0.3, $CHCl_3$); UV (CH_3OH) 231 nm (ϵ 5000); IR (CCl_4) 3500, 1680, 1460, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.55 (td, 1 H, J = 1, 6.5 Hz), 3.05 (d, 1 H, J = 13.5 Hz), 2.97 (d, 1 H, J = 11 Hz), 2.55 (dd, 1 H, J = 11, 13.5 Hz), 2.46 (m, 2 H), 2.31 (dt, 1 H, J = 13.5, 3.5, 3.5 Hz), 1.78 (br s, 3 H), 1.85–1.35 (overlapping m), 1.18 (s, 3 H), 0.88 (d, 3 H, J = 6.5 Hz), 0.74 (d, 3 H, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 207.1 (s), 142.3 (d), 135.5 (s), 87.1 (s), 63.0 (d), 61.8 (s), 48.6 (d), 43.5 (t), 42.9 (s), 41.0 (t), 37.9 (t), 36.3 (t), 34.2 (d), 29.6 (t), 24.5 (t), 23.8 (q), 18.1 (q), 17.7 (q), 15.4 (q), 11.9 (q); HRMS, obsd m/z 320.2338, $C_{20}H_{32}O_3$ requires m/z 320.2351.

(1*S,3*E*,7*R**,8*R**,11*S**,12*S**)-7,8-Epoxy-12-hydroxydolabella-3-en-9-one (12)**: oil; $[\alpha]_D$ –1.3° (c 1.97, $CHCl_3$); UV (MeOH) 221 nm (sh) (ϵ 1600), 205 (3200); IR ($CHCl_3$) 3550, 1710, 1440, 1380 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (d, 3 H, J = 7 Hz), 1.01 (d, 3 H, J = 7 Hz), 1.11 (s, 3 H), 1.52 (s, 3 H), 1.67 (s, 3 H), 1.89 (m, 3 H), 2.03 (m, 1 H), 2.14 (m, 3 H), 2.46 (dd, 1 H, J = 18.5, 3.5 Hz), 2.93 (dd, 1 H, J = 18.5, 4.5 Hz), 2.96 (dd, 1 H, J = 8.5, 4.5 Hz), 5.09 (dd, 1 H, J = 10.0, 5.0 Hz); ^{13}C NMR ($CDCl_3$) δ 205.8 (s), 135.2 (s), 121.6 (d), 86.3 (s), 66.5 (d), 62.7 (s), 46.2 (d), 44.3 (s), 43.1 (t), 40.2 (t), 37.2 (t), 34.9 (d), 34.1 (t), 32.7 (t), 23.8 (q), 23.5 (t), 20.4 (q), 18.0 (q), 17.2 (q), 16.5 (q); HRMS, obsd m/z 320.2358, $C_{20}H_{32}O_3$ requires m/z 320.2351.

(1*R,3*E*,7*E*,9*S**,11*S**)-9-Acetoxydolabella-3,7,12-trien-16-al (13)**: mp 163–165 °C (5% $CHCl_3$–petroleum ether); $[\alpha]_D$ +10.0° (c 0.50, $CHCl_3$); UV (MeOH) 229 nm (ϵ 5950); IR ($CHCl_3$) 1715, 1680, 1630, 1440, 1360, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (d, 3 H, J = 7.0 Hz), 1.10 (d, 3 H, J = 7.0 Hz), 1.17 (s, 3 H), 1.45 (s, 3 H), 1.66 (ddd, 1 H, J = 14.0, 12.0, 6.0 Hz), 1.87 (ddd, 1 H, J = 14.0, 10.5, 3.0 Hz), 2.43 (dd, 1 H, J = 12.0, 3.0 Hz), 2.59 (dd, 1 H, J = 16.0, 1.5 Hz), 2.73 (ddd, 1 H, J = 12.5, 5.0, 1.5 Hz), 2.81 (dd, 1 H, J = 16.0, 11.5 Hz), 5.30 (bs, 1 H), 5.43 (dd, 1 H, J = 11.0, 6.0 Hz), 5.58 (dd, 1 H, J = 11.5, 3.0 Hz), 6.53 (dd, 1 H, J = 11.5, 1.5 Hz), 9.36 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 195.2 (d), 170.3 (s), 154.7 (d), 151.5 (s), 142.5 (s), 133.2 (d), 131.5 (s), 119.3 (d), 79.8 (d), 46.3 (t), 46.3 (d), 43.7 (s), 40.8 (t), 30.0 (t), 27.6 (t), 27.0 (d), 25.9 (q), 23.1 (t), 22.2 (q), 21.5 (q), 21.5 (q), 11.1 (q); HRMS, obsd m/z 344.2328, $C_{22}H_{32}O_3$ requires m/z 344.2351.

(1*R,3*E*,7*E*,9*S**,11*S**)-9-Acetoxydolabella-3,7,12-trien-16-oic acid (14)**: mp 152–154 °C (10% $CHCl_3$–petroleum ether); $[\alpha]_D$ +60.2° (c 2.56, $CHCl_3$); UV (MeOH) 222 nm (ϵ 5700), 207

(5550); IR ($CHCl_3$) 3300–2400 br, 1720, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (d, 3 H, J = 7 Hz), 1.06 (d, 3 H, J = 7 Hz), 1.29 (s, 3 H), 1.54 (s, 3 H), 2.01 (s, 3 H), 2.30 (br d, 1 H, J = 16 Hz), 2.64 (m, 1 H), 2.80 (br d, 1 H, J = 13 Hz), 3.18 (t, 1 H, J = 12 Hz), 5.19 (br s, 1 H), 5.23 (dd, 1 H, J = 12, 2 Hz), 5.40 (dd, 1 H, J = 10, 6 Hz), 6.03 (dd, 1 H, J = 12, 5 Hz); ^{13}C NMR (C_6D_6) δ 174.2 (s), 170.1 (s), 153.3 (s), 148.0 (d), 134.1 (s), 133.0 (d), 130.6 (s), 119.8 (d), 80.3 (d), 49.4 (t), 48.9 (d), 45.5 (s), 42.7 (t), 35.8 (t), 32.7 (t), 27.9 (q), 26.5 (d), 23.4 (t), 23.0 (q), 22.6 (q), 21.4 (q), 11.8 (q); HRMS, obsd m/z 360.2299, $C_{22}H_{32}O_4$ requires 360.2301.

(1*S,3*E*,7*E*,11*S**,12*S**)-9-Acetoxydolabella-3,7-dien-12-ol (15)**: oil; $[\alpha]_D$ +2.3° (c 0.6 $CHCl_3$); UV (MeOH) 215 nm (ϵ 1400); IR ($CHCl_3$) 3550, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (s, 3 H), 0.95 (d, 3 H, J = 7 Hz), 1.04 (d, 3 H, J = 7 Hz), 1.51 (s, 3 H), 1.60 (s, 3 H), 2.04 (s, 3 H), 2.10 (m, 2 H), 2.19 (m, 1 H), 2.32 (m, 1 H), 4.85 (d, 1 H, J = 10.6 Hz), 4.95 (t, 1 H, J = 7 Hz), 5.24 (t, 1 H, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 171.4 (s), 134.2 (s), 134.1 (s), 126.8 (d), 124.0 (d), 86.1 (s), 79.9 (d), 44.5 (s), 44.3 (t), 40.4 (t), 38.9 (t), 38.6 (t), 35.9 (d), 30.4 (t), 29.7 (t), 24.2 (t), 23.9 (t), 21.5 (q), 18.7 (q), 18.0 (q), 15.6 (q), 12.9 (q); HRMS, obsd m/z 348.2673, $C_{22}H_{36}O_3$ requires m/z 348.2664.

(1*S,3*E*,11*S**,12*S**)-9-Acetoxy-7,8-epoxydolabella-3-en-12-ol (16)**: oil; $[\alpha]_D$ -3.3° (c 2.37, $CHCl_3$); UV (MeOH) 207 nm (ϵ 2500); IR ($CHCl_3$) 3550, 1720, 1430, 1350, 1020 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.88 (d, 3 H, J = 7 Hz), 0.91 (s, 3 H), 1.02 (d, 3 H, J = 7 Hz), 1.35 (s, 3 H), 1.64 (bs, 3 H), 1.95 (dd, 1 H, J = 14.5, 9.0 Hz), 2.00 (dd, 1 H, J = 14.5, 5.0 Hz), 2.10 (s, 3 H), 2.17 (m, 1 H), 2.28 (m, 2 H), 2.75 (br s, 1 H), 2.79 (dd, 1 H, J = 10.5, 3.0 Hz), 4.02 (d, 1 H, J = 10.5 Hz), 5.04 (dd, 1 H, J = 9.0, 5.0 Hz); ^{13}C NMR ($CDCl_3$) δ 172.1 (s), 133.6 (s), 123.3 (d), 84.6 (s), 81.9 (d, 61.9 (s), 61.0 (d), 44.5 (d), 44.0 (s), 37.6 (t), 37.6 (t), 36.9 (d), 36.9 (t), 30.9 (t), 27.3 (t), 24.4 (t), 23.2 (q), 21.4 (q), 18.7 (q), 17.9 (q), 15.6 (q), 11.4 (q); HRMS, obsd m/z 364.2624, $C_{22}H_{36}O_4$ requires m/z 364.2614.

(5*S,8*S**,9*S**,12*S**,14*R**)-9-Hydroxydolasta-1,3-dien-6-one (17)**: oil; $[\alpha]_D$ +160° (c 0.76 $CHCl_3$); UV (MeOH) 261 nm (ϵ 3500), 204 (1600); IR ($CHCl_3$) 3550, 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 (s, 3 H), 0.96 (d, 6 H, J = 7 Hz), 1.18 (s, 3 H), 1.80 (s, 3 H), 2.00 (dd, 1 H, J = 13.5, 9. Hz), 2.27 (t, 1 H, J = 9.5 Hz), 2.40 (dd, 1 H, J = 11.0, 2.0 Hz), 2.70 (d, 2 H, J = 9.5 Hz), 5.60 (br d, 1 H, J = 5.0 Hz), 5.82 (dd, 1 H, J = 9.6, 5.0 Hz), 5.96 (d, 1 H, J = 9.6 Hz); ^{13}C NMR ($CDCl_3$) δ 213.1 (s), 136.4 (s), 126.7 (d), 121.6 (d), 117.8 (d), 83.3 (s), 53.2 (s), 45.7 (d), 44.4 (d), 43.3 (s), 41.4 (t), 40.1 (t), 38.2 (t), 37.5 (d), 35.8 (t), 25.1 (q), 23.3 (q), 22.1 (q), 18.4 (q), 17.6 (q); HRMS, obsd m/z 302.2248, $C_{20}H_{30}O_2$ requires m/z 302.2246.

Single-Crystal X-ray Diffraction Analysis of Ketone 2. Preliminary X-ray photographs displayed rhombohedral symmetry. Accurate lattice constants were determined by carefully determining the 2θ values for 15 reflections on an aligned diffractometer. The final cell constants were $a = b = c = 11.528$ (1) Å and $\alpha = \beta = -\gamma = 80.54$ (1)°. An experimental density indicated that the unit cell contained three molecules of composition $C_{20}H_{32}O_3$. The space group was assumed to be $R3$, and the correctness of this choice was shown by successful structure solution and refinement. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer-controlled four-circle diffractometer using graphite monochromated Cu Kα radiation (1.54178 Å) and variable speed, 1° ω-scans. A total of 1525 reflections were collected in this manner, and after corrections for Lorentz, polarization, and background effects, 1040 (68%) were judged observed ($|F_0| \geq 3\sigma(F_0)$).[9] A phasing model was found by using a multisolution tangent formula approach, and the E-synthesis from the best set showed most of the non-hydrogen atoms. This structure was extended by using tangent formula recycling[10] until the entire non-hydrogen atom framework was clear. Hydrogen atoms were located on ΔF-synthesis following partial refinement. Block diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a conventional crystalllographic residual of 0.0843 for the observed reflections.

Single-Crystal X-ray Analysis of Aldehyde 13. Preliminary X-ray photographs displayed monoclinic symmetry, and accurate lattice constants of a = 7.637 (2) Å, b = 9.761 (2) Å, c = 13.935 (3) Å, and β = 82.21 (4)° were determined as described above. Systematic extinctions, crystal density, and the presence of optical activity were accommodated by space group $P2_1$ with one molecule of composition $C_{22}H_{32}O_3$ forming the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer controlled four-circle diffractometer using graphite monochromated Cu K$\bar{\alpha}$ radiation (1.54178 Å) and variable speed, 1° ω-scans. Of the 1495 reflections collected in this fashion, 1418 (95%) were judged observed ($|F_0| \geq 3\sigma(F_0)$).[9] A phasing model was found using a multisolution weighted tangent formula approach, and the E-synthesis of the best set showed all of the non-hydrogen atoms. Hydrogens were located on a ΔF-synthesis after partial refinement of the non-hydrogen atoms. Block diagonal least-squares refinements with anisotropic non-hydrogen atoms and isotropic hydrogens have converged to a standard crystallographic residual of 0.064 for the observed reflections. Additional crystallographic details are described in the supplementary material paragraph at the end of this paper.

Isomerization of Ketone 2. A solution of the ketone **2** (4 mg) and sodium methoxide (2 mg) in methanol (1 mL) was stirred at 70 °C under dry nitrogen for 20 h. The cooled reaction mixture was partitioned between water (5 mL) and dichloromethane (2 × 10 mL). The extracts were dried over sodium sulfate, and the solvent was evaporated to obtain a yellow oil (4 mg) that was chromatographed by LC on Partisil using 1:1 hexane–ethyl acetate as eluant to obtain the ketones **2** and **3** in a 7:3 ratio.

Isomerization of Ketone 4. A solution of the ketone **4** (30 mg) in benzene (10 mL) was irradiated with UV light for 3 h. The reaction mixture was subjected to preparative TLC using 12% ethyl acetate in benzene as eluant to obtain the ketone **4** (14 mg, 46% recovery) and the ketone **5** (12 mg, 40% yield), identical in all respects with the natural product.

Isomerization of β,γ-Unsaturated Ketone 7. A solution of the β,γ-unsaturated ketone **7** (4 mg) and sodium methoxide (2 mg) in methanol was stirred at 40 °C for 24 h. Dichloromethane (20 mL) was added to the cooled solution, and the extract was washed with water (5 mL) and dried over sodium sulfate and the solvent evaporated. Examination of the product by LC on Partisil with 3:1 ethyl acetate–hexane as eluant revealed an approximately 1:1 mixture of starting material **7** and its C8 epimer **6**. The mixture of **6** and **7** was again treated with excess sodium methoxide (2 mg) in methanol (1 mL) at reflux temperature for 4 h. The cooled reaction mixture was extracted and chromatographed as before to obtain the ketone **3** (1–2 mg) and the mixture of C8 isomers **6** and **7**. The products were characterized by HPLC and ^1H spectroscopy.

Isomerization of β,γ-Unsaturated Ketone 8. A solution of the β,γ-unsaturated ketone **8** (3.6 mg) and sodium methoxide (2 mg) in methanol (1 mL) was stirred at 70 °C for 19 h. The product was treated as above to obtain the ketone **4** (2 mg) that was identified by HPLC and ^1H NMR spectroscopy.

Epoxidation of Ketone 4. *m*-Chloroperbenzoic acid (20 mg, 0.11 mmol) was added to a stirred solution of the ketone **4** (25 mg, 0.08 mmol) in dichloromethane (2 mL). After 1 h at 25 °C, dichloromethane (20 mL) was added to the reaction mixture, and the solution was washed with saturated sodium bicarbonate solution (2 × 10 mL) and brine (10 mL). The extract was dried over sodium sulfate and the solvent evaporated to obtain a white solid that was purified by LC on Partisil with 2:1 hexane/ethyl acetate as eluant to obtain the epoxide **11** (18.1 mg, 69% theo-

(9) All crystallographic calculations were done on a PRIME 9950 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were: REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson synthesis, P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; BLS78A, an anisotropic block diagonal least-squares refinement written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by K. Hirotsu and G. Van Duyne, Cornell University, 1985.

(10) Karle, J. *Acta Crystallogr., Sect. B* **1968**, *B24*, 182.

retical), identical in all respects with the natural material.

Epoxidation of Epoxide 12. A solution of *m*-chloroperbenzoic acid (8 mg, 0.044 mmol) in dry benzene (0.5 mL) was added dropwise to a stirred solution of the epoxide **11** (10 mg, 0.031 mmol) in dry benzene (1.5 mL) at 25 °C. After 5 min, the reaction mixture was diluted with ether (20 mL) and the solution washed with saturated sodium bicarbonate solutions (3 × 5 mL) and water (3 × 5 mL). The extract was dried over magnesium sulfate and the solvent removed to obtain a residue (9.5 mg) that was purified by chromatography on silica gel to obtain the bisepoxide **18** (8 mg, 76% theoretical): oil; IR 3550 (br), 2975, 1710 cm^{-1}; Anal. Calcd for $C_{20}H_{32}O_4$: C, 71.39; H, 9.5. Found: C, 71.0; H, 9.87.

Epoxidation of Ketone 5. A solution of *m*-chloroperbenzoic acid (15 mg) in dry benzene (2 mL) was added dropwise to a solution of ketone **5** (20 mg) in dry benzene and the reaction mixture treated as above. The crude product was separated by preparative TLC to obtain a 3,4-epoxide (16 mg) as the major product and the diepoxide **18**, identical in all respects with the material obtained from epoxide **11**.

Oxidation of Aldehyde 13. Silver oxide (60 mg) and sodium cyanide (3 mg) were added to a stirred solution of the aldehyde **13** (8 mg, 0.23 mmol) in methanol (4 mL) at 25 °C. After 3 h, the reaction mixture was filtered, and the product was purified by preparative TLC to obtain the acid **14** (2 mg, 24% theoretical), mp 152–153 °C, identical in all respects with the natural material.

Conversion of Acetate 15 into Ketone 5. A suspension of lithium aluminum hydride (10 mg) in dry ether was added dropwise to a stirred solution of acetate **15** (10 mg) in dry ether (2 mL). After 4 h the reaction was cautiously quenched with water followed by 2 N hydrochloric acid (10 mL). The reaction mixture was extracted with ether (5 × 10 mL), and the combined extracts were washed with water (15 mL) and dried over magnesium sulfate and the ether evaporated to obtain the diol **19** (7 mg) as a colorless oil: IR 3550 (br), 2950, 1150, 1030 cm^{-1}.

Active manganese dioxide (100 mg) was added to a stirred solution of the diol **19** (5 mg) in petroleum ether. After 3 h, the reagent was removed by filtration and the solvent evaporated, giving a residue that was purified by preparative TLC to obtain the ketone **5** (3 mg), mp 93–95 °C, identical in all respects with authentic material.

Epoxidation of Epoxy Acetate 16. A solution of *m*-chloroperbenzoic acid (13 mg) in dry benzene (2 mL) was added to a stirred solution of the epoxy acetate **16** (10 mg, 0.027 mmol) in dry benzene (2 mL) at 25 °C. After 5 min the reaction mixture was worked up as described earlier to obtain the diepoxide **20** (8 mg): mp 130 °C; IR 3500 (br), 2975 (br), 1710–1690 cm^{-1}; Anal. Calcd for $C_{22}H_{36}O_5$: C, 69.44; H, 9.54. Found: C, 69.02; H, 9.92.

Epoxidation of Acetate 15. A solution of the acetate **15** (5 mg) in dry benzene (1 mL) was treated with *m*-chlorperbenzoic acid (10 mg) as described above to obtain the diepoxide **20** (4 mg), mp 130 °C, identical in all respects with the sample prepared from epoxy acetate **16**.

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Supplementary Material Available: Tables of fractional coordinates, thermal parameters, interatomic distances, and interatomic angles for (1*S**,2*E*,4*R**,7*Z*,11*S**,12*S**)-4,12-dihydroxydolabella-2,7-dien-9-one (**2**) and for (1*R**,3*E*,7*E*,9*S**,11*S**)-9-acetoxydolabella-3,7-12-trien-16-al (**13**) (8 pages). Ordering information is given on any current masthead page.

Total Syntheses of Hirsutic Acid C and Complicatic Acid†

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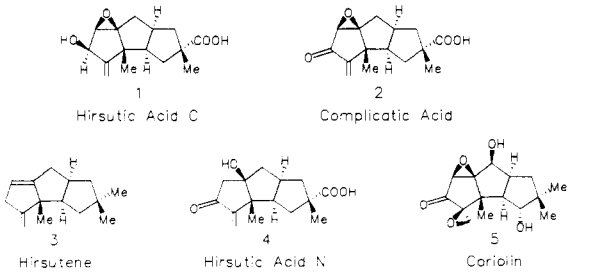
The linearly fused tricyclopentanoids hirsutic acid C (**1**) and complicatic acid (**2**) were synthesized from the methanoindene **12** in a highly stereoselective manner.

Hirsutic acid C (**1**) and an uncharacterized compound called hirsutic acid N were isolated in 1947 from fungal cultures that were thought to be the Basidiomycetes, *Stereum hirsutum*.[4] Later attempts to reisolate hirsutic acid C (**1**) from this culture were unsuccessful. Subsequently, Mellows and Mantle[5] isolated hirsutic acid C (**1**) and a related sesquiterpene, complicatic acid (**2**), from cultures of a related Basidiomycetes, *Stereum complicatum*. These authors have postulated that complicatic acid (**2**) is the same compound as hirsutic acid N.

The structure of hirsutic acid C (**1**) was originally based on spectroscopic and chemical evidence.[6] This was confirmed, and the absolute stereochemistry of **1** was determined by X-ray crystallography of the *p*-bromophenacyl derivative.[7]

Although hirsutic acid C (**1**) shows no biological activity, hirsutic acid N (aka complicatic acid (**2**) ?)[8] showed activity against *Staph. aureus* and *Str. pyogenes*.[4,5]



A large number of publications dealing with methods relating to and the total synthesis of linearly fused cyclo-

† Dedicated to Professor Samuel Danishefsky on the occasion of his election to the National Academy of Sciences.

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