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STRUCTURE AND CONFORMATION OF NEW DITERPENES BASED ON THE DOLABELLANE SKELETON FROM A *DICTYOTA* SPECIES

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Abstract—From the brown alga *Dictyota* sp. we have isolated three new diterpenes (**2**, **3** and **6**) of the dolabellane family. Their structures and conformations have been assigned on the basis of spectral studies, including proton difference decoupling and nuclear Overhauser enhancement difference spectroscopy, and chemical correlation.

Following the original isolation from the opistobranch mollusk *Dolabella californica*,[1,2] diterpenes based on the bicyclo[9.3.0] skeleton **1** (dolabellane) have been isolated from the brown seaweeds of the family Dictyotaceae[3-5] and more recently from the sea whip *Eunicea calyculata*.[6] All the dolabellane derivatives we isolated previously from *Dictyota dichotoma* show antimicrobial activity against gram-positive and/or gram-negative organisms;[3] moreover, 3(*S*), 4(*S*)-epoxy-14-oxo-1(*S*), 11(*R*),12(*S*)-dolabell-7(*E*),18-diene possesses a significant cytotoxicity and also *in vivo* activity against virus of influenza and adenovirus.[7] These observations prompted us to search further sources of dolabellane derivatives. During a collection of samples along the southern coast of Sicily by Scuba diving we observed a brown alga rather similar to but distinguishable from *Dictyota dichotoma*. TLC examination of the chloroform extract of this alga, a *Dictyota* species still awaiting for classification, showed the presence of a number of secondary metabolites, none of them identical with those synthesized by *Dictyota dichotoma*.

In the present paper we report the isolation and structure determination of three new dolabellane diterpenes, **2**, **3** and **6**.

Compound **2**, which has cytotoxic activity and is currently under investigation for *in vivo* activity against leukemia P388, was isolated in 0.1% yield from air-dried algal material and had m.p. 142–143°, $[\alpha]_D$ + 19.8°. The molecular formula was established as $C_{22}H_{34}O_3$ by high resolution mass spectrometry. Alternative losses of 18 and 60 amu from the parent ion to give peaks at *m/z* 328 and 286, respectively, indicated the presence of OH and acetoxy groups, confirmed by IR absorptions at 3600, 3490 (OH) and 1725, 1250 cm^{-1} (acetoxy). The absence of conjugated double bond system in the molecule was apparent from the UV spectrum. ^{1}H-NMR[$CDCl_3$, δ2.01 (3H, s, CH_3CO) and 5.47 (1H, dd, –C<u>H</u>OAc)] and ^{13}C-NMR (21.6, q, <u>C</u>H_3CO; 170.5 s, CH_3<u>C</u>OO; 81.0 ppm, d, <u>C</u>HOAc) data showed the acetoxy group to be attached to a secondary carbon. An AB system (δ 4.16 and 3.98, J = 11.7 Hz) in the proton spectrum of **2** moved 0.62 ppm downfield after addition of TAI; from this it was deduced that the OH is implied in a hydroxymethyl group which, on account of the values of the chemical shift of the methylene protons, must be allylic.

Since the molecular formula indicates twelve hydrogen atoms less than required for a saturated open-chain structure, four sites accounted for by the acetoxy carbonyl, a terminal and two trisubstituted double bonds (^{13}C-NMR, see Table 2), **2** must be bicyclic. The side chains of the ring system were easily identified, besides the hydroxymethyl group, as a bridgehead methyl (δ1.19, s) a vinyl methyl (δ1.50, s), and an isopropylidene group (3H, 1.65, s; 1H, 4.66, bs; 1H, 4.90, bs; allylic coupling (1.5 Hz) between methyl and terminal methylene protons). The ^{13}C-NMR spectrum confirmed these attributions (Table 2).

The complete elucidation of the gross structure of **2** was achieved by detailed analysis of the 400 MHz ^{1}H-NMR spectrum, including extensive double resonance experiments (when necessary, long-range couplings were confirmed by difference decoupling spectroscopy). The –C<u>H</u>OAc signal at δ5.47 is the X part of an AMX system whose AM-part (δ1.61, dd, J = 14.2 and 6 Hz; 1.31, dd, J = 14.2 and 11 Hz) is appropriate to a methylene attached to the single sp^3-hybridized quaternary carbon (47.1 ppm), which must also bear the bridgehead methyl, deduced from the ^{13}C-NMR spectrum. This and a long range coupling between the α-acetoxy proton and a vinyl proton at δ5.38 fixed the sequence C-1 through C-5, which could be further expanded on the basis of the following considerations.

Double resonance showed that H-5 is coupled with the allylic proton H-6′(δ2.51, dddd) and this in turn interacts with the allylic proton H-7(δ2.14, ddd). Although the signals of H-6 and H-7′ could not be fully analysed as they were strongly coupled and obscured by overlapping resonances, multiplicity of H-6′ and H-7 were only compatible with part structure =CH–CH_2–CH_2–C=, whose

Table 1. ^{1}H-NMR assignments for compounds 2, 3 and 6.§

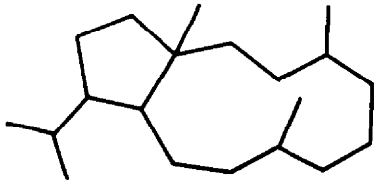
Position	2	3	6
2	1.61 (1H, dd, J = 14.2, 6)	1.59 (1H, dd, J = 14, 6)	1.64 (1H, dd, J = 13, 6)
2'	1.31 (1H, dd, J = 14.2, 11)	1.39 (1H, dd, J = 14, 10.5)	1.81 (1H, dd, J = 13, 11)
3	5.47 (1H, dd, J = 11, 6)	4.46 (1H, dd, J = 10.5, 6)	5.47 (1H, dd, J = 11, 6)
5	5.38 (1H, dd, J = 12, 3)	5.18 (1H, dd, J = 12, 3)	6.36 (1H, dd, J = 12, 4.5)
6	2.20 – 2.30*	2.15 – 2.30*	2.43* m
6'	2.51 (1H, dddd, J = 14, 12, 12, 5)	2.43 (1H, dddd, J = 14, 12, 12, 5)	3.12 (1H, dddd, J = 14, 12, 12, 5)
7	2.14 (1H, ddd, J = 12, 11.5, 5.5)	2.11 (1H, ddd, J = 12, 12, 5.2)	2.31 (1H, ddd, J = 12, 12, 5.4)
7'	2.20 – 2.30*	2.15 – 2.30*	2.41* m
9	5.21 (1H, dd, J = 11.5, 5)	5.16 (1H, dd, J = 11.5, 5)	5.33 (1H, dd, J = 11.5, 5.5)
10	1.64* m	1.63* m	1.71* m
10'	2.21 (1H, ddd, J = 12, 11.5, 1.5)	2.19 (1H, ddd, J = 12, 11.5, 1.5)	2.20 (1H, ddd, J = 12.5, 11.5, 1.5)
11'	1.40 – 1.70*	1.40 – 1.70*	1.40 – 1.65*
12	2.54 (1H, ddd, J = 12, 6, 6)	2.56 (1H, ddd, J = 12, 6, 6)	2.51 (1H, ddd, J = 12, 6, 6)
13	1.40 – 1.70*	1.40 – 1.70*	1.40 – 1.65*
14	1.40 – 1.70*	1.40 – 1.70*	1.40 – 1.65*
15	1.19 (3H, s)	1.11 (3H, s)	1.17 (3H, s)
16a	4.16 { 2H, AB system, J = 11.7	4.21 { 2H, AB system, J = 11.5	9.95 (1H, s)
16b	3.98 {	4.05 {	
17	1.50 (3H, s)	1.47 (3H, s)	1.54 (3H, s)
19	1.65 (3H, s)	1.68 (3H, s)	1.60 (3H, s)
20a	4.90 (1H, bs)	4.90 (1H, bs)	4.91 (1H, bs)
20b	4.66 (1H, bs)	4.67 (1H, bs)	4.67 (1H, bs)
–OR†	2.01 (3H, s)	2.85 (2H, bs)	2.01 (3H, s)

*Overlapped with other signals.

†R = $COCH_3$ in compounds 2 and 6; R = H in compound 3.

§^{1}H-NMR spectra were recorded at 400 MHz, $CDCl_3$. Assignments were aided by spin-decoupling and DDS experiments. TMS was used as internal standard: chemical shifts are δ values. J values are reported in Hz.

presence in the molecule was confirmed by identification of levulinic acid among the products of oxidative ozonolysis of **2**. Since this result also determined the position of the vinyl methyl at C-8, the allylic hydroxymethyl had to be located at position 4 thus completing the partial structure C-1–C-8 including the side chains. Furthermore, the vinyl methyl at C-8 is allylically coupled to the vinyl proton at δ5.21 (C-9) which is vicinally coupled to the protons of a methylene (C-10) resonating at δ1.64 (partly obscured multiplet) and 2.21 (ddd); multiplicity of the latter signal indicates that this methylene is in turn linked to a methine (C-11). At this point, only the isopropenyl group, two methylenes and a methine remained to be considered. Since the latter



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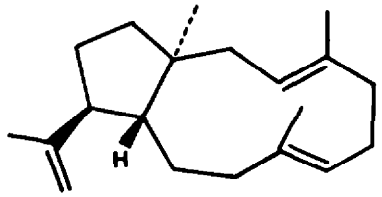

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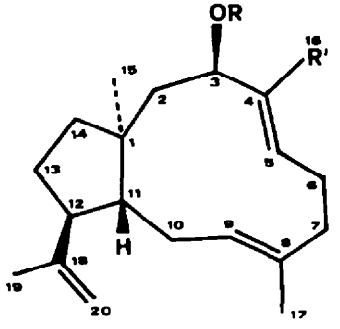

2 R = Ac, R' = CH_2OH

3 R = H, R' = CH_2OH

4 R = H, R' = CH_2OAc

5 R = Ac, R' = CH_2OAc

6 R = Ac, R' = CHO

Table 2. ^{13}C-NMR assignments for compounds 2, 3 and 6.§

Position	2		3		6	
1	47.1	s	47.1	s	47.1	s
2	29.0	t	32.8	t	29.0	t
3	81.0	d	79.1	d	77.5	d
4	135.2[a]	s	134.6[a]	s	136.3[a]	s
5	138.2	d	137.8	d	155.5	d
6	24.3[b]	t	24.2[b]	t	25.1[b]	t
7	39.7[c]	t	39.7[c]	t	39.7[c]	t
8	134.9[a]	s	134.7[a]	s	134.6[a]	s
9	126.9	d	126.8	d	127.2	d
10	28.0[b]	t	28.2[b]	t	28.1[b]	t
11	51.3	d	51.4	d	51.6	d
12	42.1	d	42.6	d	41.4	d
13	41.6[c]	t	41.8[c]	t	41.7[c]	t
14	42.6[c]	t	42.7[c]	t	42.4[c]	t
15	23.3	q	23.4	q	23.3	q
16	57.0	t	57.9	t	190.2	d
17	15.7	q	15.6	q	15.8	q
18	145.6	s	146.2	s	145.6	s
19	24.9	q	24.8	q	27.9	q
20	111.9	t	112.0	t	111.9	t
-COCH$_3$	170.5	s			170.5	s
CH$_3$CO-	21.6	q			21.3	q

§^{13}C-NMR spectra were recorded at 20.1 MHz, $CDCl_3$, ppm from TMS. Multiplicities were obtained by off-resonance decoupling. Assignments were based on comparison to models.
[a-c]Values with identical superscript within each column may be interchanged.

resonates at δ2.54 it must be allylic and therefore linked to the isopropenyl group; furthermore, on the basis of its multiplicity (ddd) it has to be connected to both C-11 methine and one of the remaining methylenes. The sequence C-1 through C-13 having been so clarified, there was only a possibility left for a regularly terpenoid structure, and this is illustrated by formula 2 (ignoring of stereochemistry).

In order to confirm that 2 possesses the dolabellane skeleton, the related diol 3 (*vide infra*) was subjected to catalytic hydrogenolysis to give a mixture of $C_{20}H_{38}$ hydrocarbons (M^+ *m/z* 278) not distinguishable in GLC on capillary column from those obtained by hydrogenation of 1(*S*),11(*R*),12(*S*)-dolabell-3(*E*),7(*E*),18-triene (7).*

The *E* nature of the C-8 double bond was indicated by the chemical shift for the Me-8 signal in the ^{13}C-NMR spectrum (15.7 ppm)[8] and confirmed by lack of nuclear Overhauser enhancement between H-9 and Me-8. Also the C-4 double bond has the *E* configuration, as results not only from lack of NOE (nuclear Overhauser enhancement) between H-5 and the hydroxymethyl protons, but also from further experiments which showed that H-3, H-5, H-9 and Me-1 are all within NOE proximity (Table 3), a situation not compatible with a *Z* configuration of C-4 double bond.

The following evidences indicate that the chiral centres at C-1, C-11 and C-12 have the same (relative) stereochemistry as in the previously reported dolabellane derivatives: (a) the magnitude of the coupling constant of $J_{11,12}$ (6 Hz) in comparison with those for $J_{12,13}$ (12 Hz)

Table 3. Results of NOEDS experiments on compound 2.*

Signal irradiated	Signal enhanced	Estimated internuclear distance
C-1 Me	H-3	2.0
	H-5	2.7
	H-9	2.5
H-3	C-1 Me	2.0
	H-5	2.3
H-5	C-1 Me	2.2
	H-3	2.3
	H-9	2.5
C-8 Me	H-6	3.0
	H-10	2.7

*Nuclear Overhauser enhancement difference spectra were performed at 400 MHz, in $CDCl_3$ solution. Estimated internuclear distances were obtained with Dreiding models and are expressed in Angstrom.

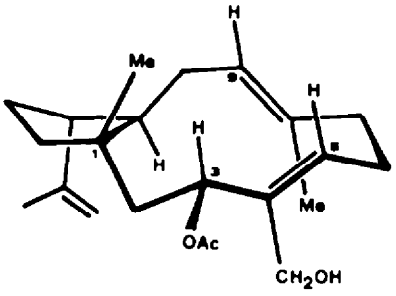

Fig. 1. Preferred conformation of compound 2.

and $J_{12,13'}$ (6 Hz) which requires a *trans* relationship between H-11 and H-12; (b) the lack of NOE between Me-1 and H-11 pointing to a *trans* ring fusion; (c) the aforementioned GLC identity of the hydrogenation products of diol 3 and 3,7,18-dolabellatriene.

Considering that the eleven-membered ring is rather rigid,[2,3] the chiral centre at C-3 was assumed to be of the R* configuration on the basis of the NOE between H-3 and Me-1 which imposes a pseudo-axial orientation for the α-acetoxy proton; further evidence for this assumption came from the value of $J_{2,3}$ (6 Hz), indicative of a pseudo-equatorial orientation of the acetoxy group,[9] and from comparison of the ^{13}C-NMR spectra of 2 and 3, which showed that the introduction of the acetate group is followed by a shift of the resonances for carbons C-3 and C-2 of +1.9 and −3.8 ppm, in agreement with the expected values for an acetate in equatorial position.[10]

The preferred conformation of metabolite 2 was studied by NOE difference spectroscopy (NOEDS)[11] and is depicted in Fig. 1. Indeed, NOEDS data (Table 3) require H-3, H-5, H-9 and Me-1 to be in pseudo-axial position and on the same face of the molecule. As a consequence, the hydromethyl and Me-8 must also be in pseudo-axial position but on the opposite face of the molecule. This is confirmed by the observation that Me-8, H-6' and H-10' are within NOE proximity. The eleven-membered ring adopts, therefore, a crown conformation analogous to that reported previously for *all-E* germacradiene systems[12,13] and the recently described 7(*S*),8(*S*)-epoxy-13-keto-1(*S*),11(*R*)-dolabell-3(*E*),12(18)-diene.[6]

Compound 3, isolated in 0.03% yield dry weight of the alga, was an optically active crystalline compound, $[\alpha]_D$ +46.4°, m.p. 104–105°. Its molecular formula $C_{20}H_{32}O_2$ was deduced by mass and ^{13}C-NMR spectra. The spectral data (Tables 1 and 2) suggested a structure closely related to that of 2 but lacking the acetate group at position 3. Confirmation was obtained by mild alkaline hydrolysis of 2, which gave a product whose physical properties (m.p., $[\alpha]_D$, IR, ^{1}H-NMR) were identical with those of 3. Furthermore, partial acetylation of 3 afforded, in addition to minor amounts of diacetate 5, two monoacetates, 2 and 4, the more polar one indistinguishable from the natural compound. The relative stereochemistry of 3 being defined by its relationship with 2, it appeared possible to establish its absolute configuration by the application of a method of asymmetric synthesis for the determination of the absolute stereochemistry of secondary alcohols. However, an inspection of a molecular model (assuming a conformation analogous to that of 2) revealed relatively small differences in size between "large" and "medium" groups in the vicinity of the chiral centre at C-3, so an inconclusive result had to be anticipated. In the event, when 3 was treated according to Mislow's method, the recovered methyl-p-tolylsulfoxide had an optical rotation opposite to that expected, but the optical yield was very low (*ca* 1%) so we attach no special significance to this apparently contrasting result. In this connection it may be noted that, in the case of the Horeau's method, a minimum value of 15% is considered significant for unambiguous assignment of absolute configuration for a secondary alcohol with a nearby polar group, such a double bond.[14] The absolute configuration remains, therefore, unsettled.

The third metabolite was isolated in 0.2% yield as a viscous oil, $[\alpha]_D$ +9.7°. The molecular formula $C_{22}H_{32}O_3$ was deduced from mass and ^{13}C-NMR spectra. IR displayed absorptions at 1725, 1250 (acetate) and 1680 cm^{-1} (α, β-unsaturated aldehyde); the latter functionality was confirmed by UV (λ_{max} 230 nm, ϵ = 8,100). These and ^{1}H and ^{13}C-NMR (Tables 1 and 2) data indicated that the new metabolite (6) is derived from 2 by replacement of the hydroxymethyl by a formyl group. Accordingly, 6 was obtained by manganese dioxide oxidation of 2 and conversely sodium borohydride reduction of 6 afforded 2. NOEDS data indicate that its conformation is not different from that of 2. A long-range coupling between the aldehyde proton and H-3 (W-coupling) suggests that the preferred conformation of the α,β-unsaturated aldehyde is s-*trans*.

EXPERIMENTAL

General procedures. Melting points were determined with a Kofler microstage and are uncorrected. MS (70 eV) were run on an AEI MS 902 instrument using a direct introduction probe. IR spectra were recorded on a Perkin-Elmer Model 684 spectrophotometer in $CHCl_3$ solutions. UV spectra were obtained on a Perkin-Elmer Model 330 instrument, in EtOH solutions. ^{1}H-NMR spectra were recorded on Bruker AM-400 (400 MHz) and Bruker WP-80 (80 MHz) FT instruments. ^{13}C-NMR spectra were recorded at 20.1 MHz on a Bruker WP-80 FT spectrometer. Both ^{1}H and ^{13}C NMR spectra were monitored in $CDCl_3$; chemical shifts are quoted in δ (ppm) from TMS used as internal standard. Optical rotations were determined with a Perkin-Elmer 141 polarimeter (1 dm tubes). GLC was effected on a Carlo Erba Fractovap 2960 capillary column gas-chromatograph equipped with a flame ionization detector. All solvents were spectral grade or distilled prior to use.

Plant material. Dictyota sp. was collected at a depth of 4–5 m along the south-east coast of Sicily, in July 1982. A specimen was deposited in the Herbarium of the Institute of Botany, Catania.

Extraction and isolation of the constituents. The air-dried and ground alga (300 g) was extracted (×3) with $CHCl_3$ and the extract evaporated to give a dark green oil (12 g). Column (5 × 120 cm) chromatography of this extract was carried out on Si gel using hexane–Et_2O gradient. Fractions of 100 ml were collected and monitored by TLC. Compounds 6, 2 and 3 were eluted in that order. The appropriate fractions were combined and further separated on a Jobin-Yvon Miniprep liquid chromatograph (Lichroprep Si 60 as packing material) using the following solvent systems: CH_2Cl_2–Me_2CO (98:2), hexane-i-PrOH (96:4), hexane-diisopropyl ether (85:15) for 2, 3 and 6, respectively.

3(R*)-*Acetoxy*-16-*hydroxy*-1(S*), 11(R*), 12(S*)-*dolabell*-4(E), 8(E), 18-*triene* (2). Compound 2 was obtained as crystals (300 mg) from hexane, m.p. 142–143°; $[\alpha]_D$ +19.8° (c = 1 in EtOH). $\nu_{max}^{CHCl_3}$ 3(cm^{-1}): 3600, 3490, 1725, 1650, 1440, 1370, 1250, 1110, 1020, 960, 890. HRMS: M$^+$ *m/z* 346.2515 obs. ($C_{22}H_{34}O_3$ requires 346.2507); *m/z*: 331, 328, 313, 286, 268, 253, 218, 200, 185, 159, 145, 131, 121, 105. For ^{1}H and ^{13}C NMR see Tables 1 and 2, respectively.

3(R*), 16-*Dihydroxy*-1(S*), 11(R*), 12(S*)-*dolabell*-4(E), 8(E), 18-*triene* (3). Crystals (100 mg), m.p. 104–105° (hexane), $[\alpha]_D$ +4.6.4° (c = 1.8 in EtOH). $\nu_{max}^{CHCl_3}$ (cm^{-1}): 3600, 3450, 1650, 1390,

1110, 1000, 895. MS *m/z*: 304, 289, 271, 268, 253, 243, 200, 185, 145, 135, 121, 100. For ^1H and ^{13}C NMR see Tables 1 and 2, respectively.

3(R*) - *Acetoxy* - 1(S*),11(R*),12(S*) - *dolabell* - 4(Z),8(E),18-trien-16-al (**6**). Viscous oil (600 mg), $[\alpha]_D$ + 9.7° (c = 1.2 in EtOH). $\nu_{max}^{CHCl_3}$ (cm^{-1}): 1725, 1680, 1450, 1370, 1250, 1110, 1020, 895. λ_{max}^{EtOH} (nm) 230 (ε = 8,100). *MS m/z*: 344, 302, 284, 269, 255, 241, 216, 201, 187, 145, 131, 121. For ^1H and ^{13}C NMR see Tables 1 and 2, respectively.

Ozonolysis of **2**. Compound **2** (5 mg) in EtOH (4 ml) was ozonized at −70° for 5 min. After elimination of excess of O_3 the EtOH soln was kept at room temp with perhydrol (30%, 0.5 ml) and aq KOH (10%, 0.5 ml). The reaction mixture was acidified with dil HCl and exhaustively extracted with Et_2O. The organic solvent was removed and the residue methylated (MeOH/HCl). Methyl levulinate was identified among the products by GLC (capillary column coated with SE-30, 25 m, 150°, carrier gas N_2, 1 ml/min).

Catalytic hydrogenolysis of **3**. Compound **3** (30 mg) in EtOH (4 ml) was hydrogenated over 10% Pd/C (10 mg) at room temp. and press. for 24 h. The catalyst was filtered and the solvent removed under vacuum leaving an oily residue whose MS showed a molecular ion at *m/z* 278 ($C_{20}H_{38}$). This material in GLC (capillary column coated with Carbowax 20 M, 25 m, 180°, carrier gas N_2, 1 ml/min) gave four peaks, which could not be separated from those of a mixture of saturated hydrocarbons ($C_{20}H_{38}$) obtained in a parallel run by hydrogenation of 1(*S*), 11(*R*), 12(*S*)-dolabell-3(*E*), 7(*E*), 18-triene, available from previous work.[4]

Basic hydrolysis of **2** *to produce* **3**. A soln of **2** (30 mg) in MeOH (5 ml) was stirred for 3 h with 0.5 ml aq. NaOH (30%) at room temp. The reaction mixture was neutralized with 1% HCl and extracted with Et_2O. The extract was washed with satd NaCl soln and the solvent evaporated. From the residue the main component was isolated by Si-gel chromatography and identified as **3**.

Acetylation of **3**. A solution of **3** (50 mg) in Et_2O was rotary evaporated in a round bottomed flask to obtain a thin film which was exposed to vapours of Ac_2O/Py in a sealed system for 30 min. The acetylated material was separated on Si-gel (hexane–Et_2O 90:10) to give in order the diacetate **5** and two monoacetates, **4** and **2**, the more polar one indistinguishable from the natural product. *Diacetate* **5**. MS: *m/z* 328 (M^+ − 60). ^{1}H-NMR ($CDCl_3$, 80 MHz): 5.48, overlapped. (–CHOAc); 4.53, 2H, AB system (J = 12 Hz), (–CH_2OAc); 2.02 and 1.99, 3H each, s, (CH_3COO–); 1.65 and 1.50, 3H each, s, (CH_3–C=); 1.20, 3H, s, (CH_3–C–). *Monoacetate* **4**. MS: *m/z* 346 (M^+), 286 (M^+–60), 268 (M^+–60–18). ^{1}H-NMR ($CDCl_3$, 80 MHz): 4.50, 2H, AB system (J = 12 Hz), (–CH_2OAc); 4.45, overlapped, (–CHOH); 2.08, 3H, s, (CH_3COO–); 1.67 and 1.55 3H each, s, (CH_3–C=); 1.08, 3H, s, (CH_3–C–).

Application of Mislow's method to **3**. **3** (50 mg) was treated with Py (240 mg) in dry Et_2O (3 ml) and added under stirring to a soln of *p*-Me–C_6H_4–SOCl (570 mg) in Et_2O (3 ml) at −15°. Conventional work-up[15] led to the isolation of a mixture of diastereomers which by reaction with methyl magnesium iodide gave a preponderance of (−)-(*S*)-methyl-p-tolylsulfoxide. Optical yield *ca* 1%.

Manganese dioxide oxidation of **2** *to produce* **6**. To a soln of **2** (20 mg) in Et_2O (30 ml) was added MnO_2 (20 mg) and the suspension was stirred at room temp. for 30 min. Evaporation of the filtered solution gave crude **6**, which was purified by chromatography on Si gel (hexane–Et_2O 60:40) to yield 15 mg of pure compound, identical in all respects to the natural aldehyde.

Sodium borohydride reduction of **6** *to produce* **2**. $NaBH_4$ (50 mg) was added to a soln of **6** (50 mg) in EtOH (10 ml) and the mixture was stirred for 1 h. After addition of H_2O (10 ml), excess reagent was destroyed by addition of 0.2 N HCl and the organic material was extracted 3x with Et_2O. The combined extracts were dried over Na_2SO_4 and evaporated *in vacuo* to yield an oil (45 mg). Chromatography of the oil on Si gel (hexane–Et_2O 50:50) gave pure **2** (38 mg). All the physical properties of the semisynthetic material were identical to those of the natural compund.

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