29. Sphinxolide, a 26-Membered Antitumoral Macrolide Isolated from an Unidentified Pacific Nudibranch

by **Graziano Guella***, **Ines Mancini**, **Giuseppe Chiasera**, and **Francesco Pietra***

Istituto di Chimica, Università di Trento, I-38050 Povo-Trento

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It is shown that an unidentified nudibranch of Hawaiian waters contains a 26-membered macrolide, sphinxolide ((−)-**1**) with potent activity against the KB cell line. The structure of sphinxolide, a 2:1 mixture of (*E*/*Z*)-isomers at the formamide moiety, is established to be (−)-**1** on the basis of extensive NMR and FAB-MS analysis, in combination with data for the products of mono- (→(−)-**2**) and diacetylation (→(+)-**3**).

1. Introduction. – Recent work with marine organisms has led to the isolation of remarkable macrolides; most of them are polymethylated, polyhydroxy(methoxy)lated, or polyether compounds, whilst a few embed contiguous isoxazole units. In general, such compounds exhibit potent biological activities.

Polymethylated and polyhydroxy(methoxy)lated marine macrolides comprise antitumoral compounds such as amphidinolide A [1a] and C [1b] isolated from cultures of the symbiotic dinoflagellate *Amphidinium* sp. and misakinolide A isolated from the marine sponge *Theonella* sp. [1c], antifungal compounds such as swinholide A isolated from the marine sponge *Theonella swinhoei* [1d], and ichtyotoxic compounds such as latrunculin A and B isolated from the sponge *Latrunculia magnifica* [1e].

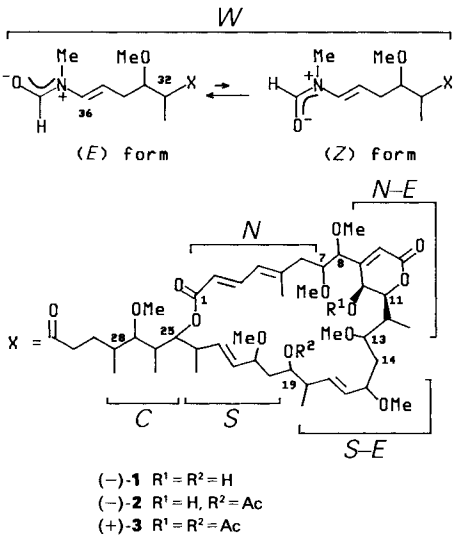
Polyether macrolides are represented by antifungal compounds such as goniodomin A isolated from the blooming dinoflagellate *Goniodoma pseudogoniaulax* [2a], by diarrhetic toxins such as pectenotoxin 1 and 2 isolated from the marine scallop *Patinopecten yessoensis* but produced by the dinoflagellate *Dinophysis fortii* [2b], and by antitumoral compounds such as bryostatin 1 isolated from the bryozoan *Bugula neritina* [2c].

Isoxazole-bearing macrolides are represented by halichondramide, an antifungal compound isolated from both the sponge *Halichondria* sp. [3a] and the nudibranch *Hexabranchus sanguineus* [3b], by ulapualide A and B, antitumoral compounds isolated from eggs of the nudibranch *Hexabranchus sanguineus* [3c], and, finally, by the structurally related kabiramide C isolated from eggs of an unidentified nudibranch [3d].

We report here on a novel antitumoral macrolide of the polymethylated and polyhydroxy(methoxy)lated type.

2. Results and Discussion. – Extensive chromatography of the organic extracts of an unidentified nudibranch of Hawaiian waters leads to a microcrystalline colourless powder, homogeneous by HPLC, the fully decoupled ^{13}C-NMR spectrum of which shows resonances in a number that depends on the solvent used, 80 in C_6D_6 and 68 in $CDCl_3$. The spectrum is composed of two similar series of signals, an intense and a weak one.

Though there is no ^{13}C-NMR-signal broadening in $CDCl_3$ between -10 and 45°, the two series of signals must be attributed to slowly equilibrating geometrical forms of an unsaturated formamide group. This group is the end portion of the side chain of the compound that we call sphinxolide ((−)-**1**[1]).



(−)-**1** $R^1 = R^2 = H$
(−)-**2** $R^1 = H$, $R^2 = Ac$
(+)-**3** $R^1 = R^2 = Ac$

2.1. *The Western Portion* W *of (−)-***1**. Double-quantum COSY [4] and double-irradiation [5] experiments are decisive in defining the western portion *W* of sphinxolide ((−)-**1**) as two slowly interconverting geometrical forms of an unsaturated amide, with an (*E*)/(*Z*) ratio of 2:1[2]). ^{13}C,^{1}H Shift-correlation experiments [9] allow the assignment of all C-atoms of *W* which is confirmed by a long-range variant of such experiments [10].

The connectivities and the configuration in fragment *W* are based on the following observations. Coupling of *H*–CO with *H*–C(36) and NOE between *Me*N and *H*–C(35) establish the fragment from the formyl group up to C(35). Double irradiation at *H*–C(35) reveals the CH_2(34) group as a *dd* with a large geminal coupling. Moreover, double-quantum COSY experiments show that *H*–C(33) is coupled with both CH_2(34) and *H*–C(32), and that the latter is also coupled with CH_3–C(32). This is confirmed by double irradiation at *H*–C(32), whereby CH_3–C(32) appears as a *s* and *H*–C(33) as a *dd*[3]). These proton connectivities are confirmed in the COSY plot of 10,19-di-*O*-acetylsphinxolide ((+)-**3**) (see below, *Fig.*) which shows *a*) that the proton at 6.50 ppm (*H*–C(36)) is correlated with *H*–CO (8.27 ppm), *H*–C(35) (5.06 ppm), and CH_2(34) (2.48 and 2.14 ppm), and *b*) that the protons CH_2(34) are correlated with *H*–C(33) (3.45 ppm) which in turn is correlated with *H*–C(32) (2.72 ppm).

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[1]) The name sphinxolide, from the mysterious Egyptian Sphinx, reflects our difficulties in defining the source and, for some time, the structure of the compound.

[2]) This phenomenon has already been encountered with other marine natural products such as halichondramide [3a,b], ulapualide [3c], kabiramide C [3d], stylocheilamide [6], and tolytoxin [7].

[3]) The analysis is aided by a ^{1}H-NMR of (−)-**1** in C_6D_6 (see *Exper. Part*). Though it is not possible to assign all signals in this solvent, the MeN signal is shifted upfield (as compared to the $CDCl_3$ solution) to a spectral zone which is not compatible with MeO groups; *H*–C(35) is shifted upfield, too, emerging neatly from all other olefinic signals. Of special value is the *H*–C(36) signal which, in C_6D_6, is shifted upfield for the (*E*) and downfield for the (*Z*) form; the latter is an indication of the (*Z*) configuration, since downfield shifts in benzene are known to occur only for protons which are spatially close to high-electron-density groups [8] such as $-O^-$ in the present case. It should also be noted that with the (*E*) form the change from $CDCl_3$ to C_6D_6 results in a 0.2-ppm downfield shift of the *H*–C(36) resonance.

At this point, the $^{13}C,^{1}H$ shift correlations [9][10] allow us to assign all C-atoms and show that *H*–C(36) is coupled with both the formyl C-atom and C(34) and that *Me*N is coupled with both C(36) and the formyl C-atom.

A large coupling between the olefinic protons suggests that the olefinic bond of fragment *W* has the (*E*) configuration. Moreover, the (*E*) configuration of the amide is assigned on the basis of a +15% NOE at *H*–C(36) on irradiation at *H*C=O. Finally, the (*Z*) configuration of the amide, where there is no NOE interrelation between *H*–C(36) and *H*C=O, is assigned on the basis that *a*) *H*–C(36), being in the conical zone of the formyl C=O, is strongly deshielded (by 0.7 ppm) with respect to the same proton in the (*E*) form, and that *b*) on irradiation at 3.05 ppm (*Me*N), there is a strong NOE at both *H*–C(35) and *H*–CO; with the (*E*) form, irradiation at 3.02 ppm (*Me*N) only results in a +7% NOE at *H*–C(35)[4]).

2.2. *Identification of Further Functional Groups.* The two series of NMR signals for sphinxolide being related to the presence of an unsaturated amide group in the (*E*) and (*Z*) configuration, analysis of the number and multiplicity of the resonances indicate that the ^{13}C-NMR spectrum of (–)-**1** is composed of 5 *s*, 28 *d*, 6 *t*, and 15 *q*; this implies the composition $C_{54}H_{85}$, not accounting for heteroatoms and H-atoms at heteroatoms. Such H-atoms show up as an intense O–H stretching band in the IR and undergo exchange with D_2O during ^{1}H-NMR experiments. The fact that on treatment with Ac_2O/pyridine, spinxolide ((–)-**1**) gives a mixture (–)-**2**/(+)-**3** of a mono- and diacetate, respectively, clarifies this point better, revealing two OH functions of markedly different reactivity[5]). A COSY contour plot for (+)-**3** is given in the *Figure*.

As to the heteroatoms, 3 *s* in the ^{13}C-NMR *(Exper. Part)* are compatible with 1 C=O and 2 COOR groups, while 10 *d* indicate 1 HC(O)–N and 9 O-bearing CH groups. This suggests that the complete molecular formula is $C_{54}H_{87}O_{15}N$, a conclusion supported by the FAB-MS data for sphinxolide ((–)-**1**) and its acetylation products *(Exper. Part)*.

The ^{13}C-NMR spectrum *(Exper. Part)* of (–)-**1** also reveals 2 *s* and 2 *d* for 2 C=CH, 8 *d* for 4 CH=CH, 6 *d* for 6 MeCH, 6 *t* for 6 CH_2, and 15 *q* for 1 *Me*N, 1 *Me*–C(olef.), 7 *Me*O, and 6 *Me*–CH.

2.3. *The Central Portion* C *of (–)*-**1**. Key to the elucidation of the central portion of (–)-**1** are the ^{1}H-NMR data.

A *dd* at 2.69 ppm (*H*–C(27)) shows homonuclear couplings with largely different ^{3}J values (9.8 and 2.4 Hz). The large coupling is with *H*–C(26) (1.93 ppm), which is assigned from its coupling with CH_3–C(26) and from its smaller coupling with *H*–C(25). The latter group is assigned on the ground that its chemical-shift values (δ(H) 5.12 and δ(C) 75.5 ppm) are compatible with substitution by the singly bonded O-atom of a lactone.

At this point, we have to admit that the weak coupling of *H*–C(27) must be with *H*–C(28). We conclude with the assignment of the signal at 3.36 ppm to *Me*O–C(27) which is based on the long-range homonuclear coupling (< 0.5 Hz and which could be derived from double irradiation at 3.36 ppm) of this group with both *H*–C(27) and CH_3–C(28).

2.4. *The Northern Portion* N *of (–)*-**1**. The presence of an $\alpha,\beta,\gamma,\delta$-unsaturated ester function is suggested by both a characteristic UV absorption band at 273 nm (ε = 32000) and an IR absorption at 1680 cm^{-1}. Confirmation of the structure and configuration is given by the NMR data.

Section C(1) to C(4) accounts for both a C-resonance at 167.2 ppm which is characteristic of an unsaturated carboxylate and an *AMX* system in the ^{1}H-NMR at 5.79, 7.52, and 6.07 ppm. The groups CH_3–C(5) and CH_2(6) can be added on the basis of allylic coupling of *H*–C(4) with both CH_3–C(5) and CH_2(6); in further support, the corresponding correlation maps can be seen in the COSY plot for diacetate (+)-**3** *(Fig.)*.

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[4]) It has been suggested that in halichondramide, which has a side chain similar to that of sphinxolide, restricted rotation occurs about the N–C(olef.) bond [3b] which corresponds to the N–C(36) bond in sphinxolide. This suggestion stemmed from observed NOE between the formyl proton and H–C(35) in halichondramide [3b]. In the case of sphinxolide, we could not observe any NOE between the formyl proton and H–C(35) so that restricted rotation must be about the HCO–N bond.

[5]) The presence of unreactive OH functions is made unlikely by the absence of signals for quaternary C-atoms in the ^{13}C-NMR spectrum of (–)-**1**.

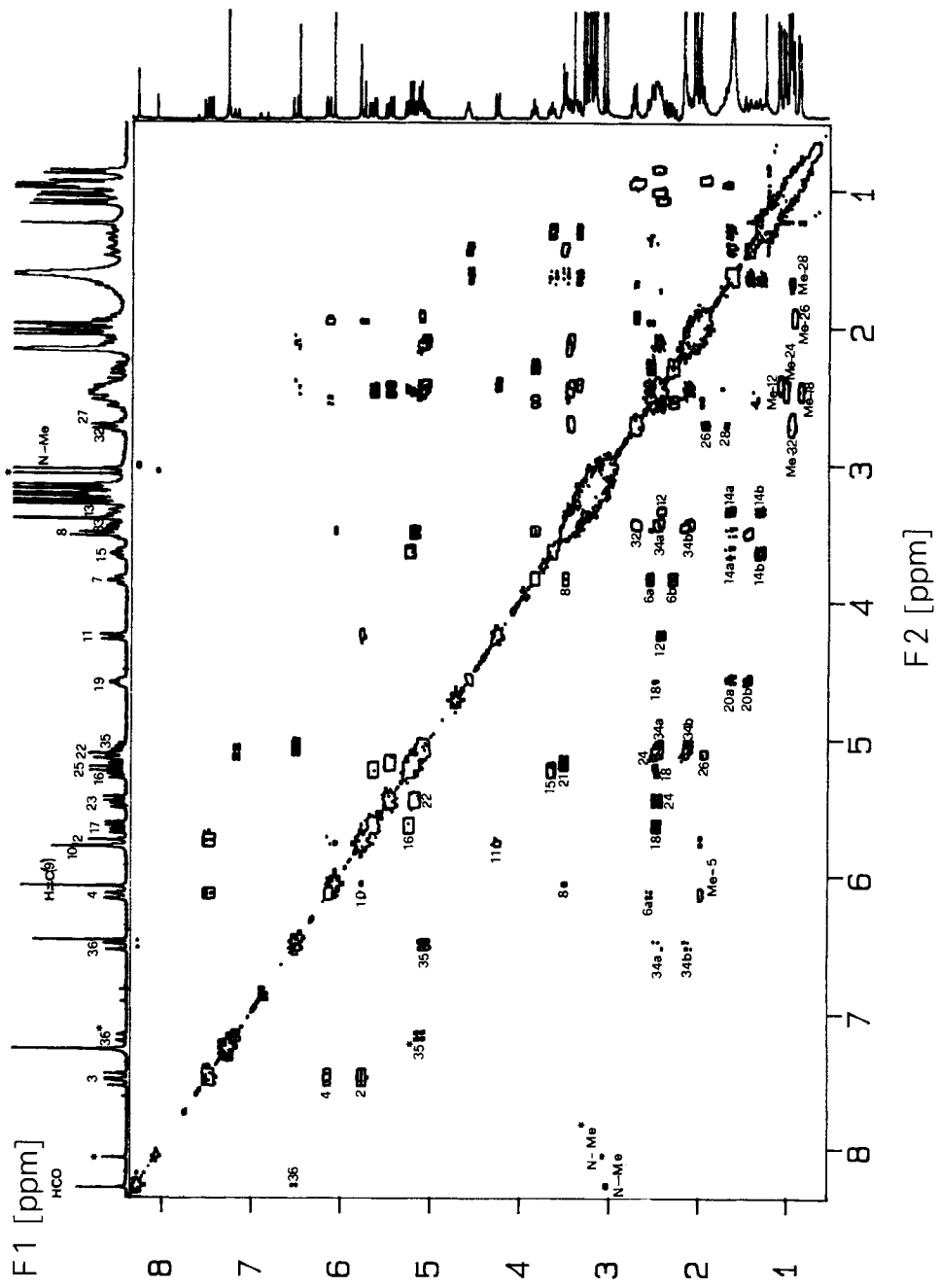

Figure. *COSY Contour plot for 10,19-di-*O*-acetylsphinxolide* ((+)-**3**). Signals for the (*Z*) form are labeled with an asterisk along the 1D ^{1}H-NMR spectrum. Numbering at the contour maps refers to the ordinate scale.

The all-*trans* configuration at the C(2)-to-C(5) diene moiety rests on a large coupling between *H*–C(2) and *H*–C(3), on a +3% NOE at *H*–C(4) on irradiation at *H*–C(2), and on a +8% NOE on *H*–C(3) on irradiation at CH_3–C(5).

2.5. *The Northeastern Portion* N-E *of (–)*-**1**. Its structure is mainly deduced from NMR data.

The MeO group appearing at 3.37 ppm in the ^{1}H-NMR spectrum can be located at C(8) on the ground that double irradiation at 3.37 ppm induces a NOE of +2% on *H*–C(sp^2) and of +4% on *H*–C(8) (3.76 ppm). The ^{1}H-NMR also reveals that *H*–C(sp^2) of fragment *N-E* is long-range coupled both with a proton deshielded by MeO (*H*–C(8)) and with a proton deshielded by OH (*H*–C(10), *dd* at 4.10 ppm). In addition, double irradiation at 3.76 ppm (*H*–C(8)) and double-quantum COSY experiments reveal that *H*–C(8) is coupled with a proton at 3.46 ppm (*H*–C(7)). No further progress can be made on the side of C(7), because the resonance at 3.46 ppm for H–C(7) is overwhelmed by other resonances.

As regards the other side, it is established that *H*–C(10) is weakly coupled with the deshielded *H*–C(11) *(dd)* which is strongly coupled with the Me-bearing C*H*(12) group (2.35 ppm *(ddq)*). This is confirmed by a positive NOE at *H*–C(11) on irradiation at 1.14 ppm (Me–C(12)).

The structure of fragment *N-E*, in particular the sequence C(7)–C(8)/C(10)–C(11)–C(12) and the presence of an OH function at C(10), are indirectly confirmed by the COSY plot of (+)–**3** *(Fig.)*, which, regarding this moiety, only differs from (–)-**1** by acetylation of the OH group.

It can be noticed *(Exper. Part)* that some ^{1}H-NMR resonances of diacetate (+)-**3** occur at markedly different field from those of both (–)-**1** and monoacetate (–)-**2**; in particular, *H*–C(10) of (–)-**2** at 5.78 ppm which is defined by a small coupling with *H*–C(11) and by a correlation map with C*H*=C(9) *(Fig.)* is shifted downfield by *ca.* 1.50 ppm with respect to *H*–C(10) of (–)-**1** and (+)-**3**.

For the C(9) moiety, see below *(Chapt. 2.8)*.

2.6. *The Southeastern Portion* S-E *of (–)*-**1**. Elucidation of the southeastern fragment *S-E* of (–)-**1** is based on double irradiation at the olefinic protons.

Thus, irradiation at the *dd* at 5.23 ppm (*H*–C(16)) reveals *trans* coupling with the proton at 5.43 ppm (*dd*; H–C(17)) and coupling with the MeO-deshielded[6]) allylic *H*–C(15) 3.52 ppm (*m*). Moreover, irradiation at 5.43 ppm reveals coupling with the *ddq* at 2.27 ppm (*H*–C(18)). The connectivities of this portion are also shown for diacetate (+)-**3** *(Fig.)*.

2.7. *The Southern Portion* S *of (–)*-**1**. Structural clarification of the southern fragment *S* of sphinxolide is based on NMR data.

Thus, irradiation at 5.52 ppm (*dd*, *H*–C(23)) reveals large couplings both with an allylic proton at 2.44 ppm (*H*–C(24)) and with another, *trans*-positioned olefinic proton at 5.14 ppm (*dd*, H–C(22)). The latter is coupled with an allylic proton (*H*–C(21)) which resonates at unusually low field (3.62 ppm). From this and from the fact that C(21) resonates at such a low field as 82.36 ppm, as established from ^{13}C,^{1}H shift-correlation experiments, we have to place a MeO group at C(21). Double irradiation at *H*–C(21), further clarifies this zone in transforming the signal of CH_2(20) to an *ABX* system and that of *H*–C(22) to a *d*.

Finally, the resonance at 1.03 ppm is assigned to CH_3–C(24) from its homonuclear coupling with *H*–C(24).

2.8. *Connection of the Fragments of (–)*-**1**. In the above partial structures, 1 keto, 1 ester, 2 *CHOMe*, 1 *CHOH*, and 3 CH_2 groups have not yet been accounted for the make up of the molecular formula $C_{54}H_{87}O_{15}N$ for sphinxolide ((–)-**1**). Location of these groups can now be defined as in structure (–)-**1** in the process of interconnecting the structural fragments. To this end, long-range ^{13}C,^{1}H shift-correlation and NOE experiments, also on the acetates (–)-**2** and (+)-**3**, are of fundamental importance, allowing the full NMR data to be established for (–)-**1**, (–)-**2**, and (+)-**3** (see *Exper. Part*).

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[6]) The presence of an MeO group at C(15) is based on the assignment of the ^{13}C-NMR signal at 82.38 ppm to C(15) from ^{13}C,^{1}H long-range shift-correlation experiments.

Interconnection of fragments *N* and *C* is based on long-range heterocoupling of *H*–C(25) with *C*(1)=O[7]). Fragments *C* and *S* can be interconnected on the basis both of long-range heterocoupling between *H*–C(26) and C(24) and of homonuclear double-resonance experiments which reveal that *H*–C(25) is long-range coupled with both CH_3–C(24) and CH_3–C(26).

To establish the connections *S*/C(19)/*S-E*/C(14)–C(13)/*N-E* of (–)-**1**, we need to examine the NMR spectra of the acetates (–)-**2** and (+)-**3**. Double irradiations with (–)-**2** and (+)-**3** reveal the coupling of *H*–C(19) which emerges neatly from the ^{1}H-NMR spectrum of these derivatives with both *H*–C(18) and 2*H*–C(20). The *S*/C(19)/*S-E* connections are confirmed by long-range homonuclear coupling between CH_3–C(18) and *H*–C(19). Fragments *S-E* and *N-E* can be joined together by the intermediacy of C(13) (OMe)–C(14) on the basis of NMR results with (+)-**3**. Here, the CH(15)–CH_2(14)–CH(13)–CH(12) fragment is clearly identified from homonuclear decoupling and COSY experiments (which are not possible with (–)-**1** owing to nearly superimposed ^{1}H-NMR resonances for *H*–C(13) and *H*–C(15)).

Fragment *N-E* of sphinxolide can now be completed by closing an α,β-unsaturated δ-lactone (see *Chapt. 2.5*). Indeed, the presence of an OH group at C(10) rules out a γ-lactone, and C(11) is not heterocoupled to any one of the MeO groups; this also defines C(11) as the C–O of one the *C*HOCOR groups[8]). The *cis* relationship between the substituents at C(10) and C(11) in the lactone ring is based on a weak homonuclear coupling between *H*–C(10) and *H*–C(11). Moreover, the allylic nature of, and steric hindrance at *HO*–C(10) is in accordance with the low reactivity of this group towards acetylating reagents (lower than for *HO*–C(19)).

Fragment *W* can be joined to fragment *C* through the C(31)(O)–CH_2(30)–CH_2(29) fragment by an indirect analysis. Thus, while fragment *W* can be extended up to C(31) on the basis of long-range heterocoupling between CH_3–C(32) and C(31)=O, there is no alternative to locate the CH_2(30)–CH_2(29) moiety between C(31) and C(28). Mutual homonuclear coupling *(Exper. Part)* demonstrates the CH_2(29)–CH_2(30) bonding.

The macrocycle can now be closed by joining together fragments *N-E* and *N*. COSY experiments with diacetate (+)-**3** reveal that CH_2(6) is correlated with a proton at 3.85 ppm, attributable to *H*–C(7). On decoupling of the latter, CH_2(6) shows up as an *AB* system, while *H*–C(8) is simplified to a br. *s*, where the broadening is due to long-range coupling with both *H*–C(10) and C*H*=C(9).

Sphinxolide ((–)-**1**) is attracting not only as complex molecular edifice, but also for its remarkably powerful activity against the KB cell line *(Exper. Part)*.

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Experimental Part

1. *General.* Reverse-phase HPLC: 25 × 1-cm column filled with *Merck-LiChroprep RP-18* (7 mμ), UV monitoring at λ 254 nm, solvent flux 5 ml·min^{-1}. Flash chromatography: *Merck-Kieselgel 60*, 15–25 mμ. TLC: *Merck-Si 60F-254* plates. M.p.: *Kofler* hot-stage microscope. Polarimetric data: *JASCO-DIP-181* digital polarimeter. UV spectra (λ_{max} in nm, ε in mol^{-1}·l·cm^{-1}): *Perkin-Elmer-Lambda-3* spectrophotometer. IR (ν_{max} in cm^{-1}): *Perkin-Elmer-337* spectrometer. NMR: *Varian-XL-300* spectrometer (^{1}H at 300 MHz, ^{13}C at 75.4 MHz), δ(ppm) rel. to $SiMe_4$ (=0 ppm), *J* in Hz. 1D ^{1}H-NMR: resolution enhancement on the FID before *Fourier* transform; for relative integration, the FID were weighted with a slight (0.5) line broadening. In the text, NOE always indicates differential NOE, whilst by irradiation, double irradiation, or decoupling, we always mean difference decoupling spectroscopy [5]; owing to the high complexity of the spectra of (–)-**1**, (–)-**2**, and (+)-**3**, normal double irradiations, even at high field, could not provide the information obtained here through differential irradiation. ^{13}C-NMR: full decoupled spectra with spectral width 16501 Hz, *ca.* 5000 scans; multiplicities from DEPT [12] or APT [13]. ^{13}C,^{1}H-NMR shift-correlation experiments [10]: spectral width 11500 Hz (2048 points)

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[7]) In analogy with the ^{1}H-NMR data for *H*–C(36) in *Footnote 3*, also the resonance for *H*–C(25) undergoes a 0.4-ppm downfield shift on changing the solvent from $CDCl_3$ to C_6D_6. This further supports the proximity of *H*–C(25) to the O-atoms at C(1).

[8]) The whole pattern of relevant NMR data (see *Exper. Part*) is in accordance with known data for α,β-unsaturated δ-lactones [11].

along the ^{13}C domain and 2680 Hz (256 time increments) along the ^{1}H domain; for each feed, 224 scans were recorded; data matrix was zero filled to 4096 × 512, and pseudo echo processing was used in both dimensions. Long-range $^{13}C,^{1}H$ shift-correlation experiments [10]: 256 × 4096 data matrix which resulted after zero filling in both dimensions in a 512 × 8192 data matrix; spectral windows, 2681 (t_1) and 16502 Hz (t_2); 1250 scans were recorded for each t_1 value with a delay of 1 s (total acquisition time 50 h); $\Delta_1 = 1/(2J_{NXH})$ and $\Delta_2 = 1/(3J_{NXH})$ durations in the sequence were 71 ms and 48 ms (setting $J_{NXH} = 7$ Hz); exponential line narrowing and *Gaussian* broadening were used prior to *Fourier* transformation in order to enhance the line shape. Double quantum filtered COSY [4a] and COSY 120° [4b]: from 2 × 512 × 2048 data matrix which resulted after zero filling in the 2nd dimension in a 2048 × 2048 data matrix; spectral width, 2363 Hz in both dimensions; acquisition times, 217 and 501 ms in the t_1 and t_2 dimensions, resp.; the *Gaussian* function was used in both dimensions prior to *Fourier* transformation; for each t_1 value, 32 scans were recorded with a delay of 1 s (total acquisition time, 14 h for double-quantum COSY and 5 h for COSY 120°). In order to quickly and automatically extract traces from 2D spectra (with $^{13}C,^{1}H$ shift-correlation and COSY experiments), we have adapted the PTRACE macro [14]; this results in automatic plotting of 1D traces on both sides of the 2D plot. FAB-MS (in *p*-nitrobenzyl alcohol): *VG-70-70-EQ* mass spectrometer provided with its own standard FAB ion source (Xe atoms of 7 KeV); in order to calculate the isotopic cluster for all the ions detected, we have devised a program based on the method of binomial expansion and useful for compounds containing polyisotopic atoms in such a high number that the isotopic cluster has a complex shape as in the FAB-MS of (−)-**2** and (+)-**3**.

2. *Collection and Isolation.* The nudibranchs were found entrapped in the nets of professional fishermen of Oahu in December 1987. The whole nudibranchs were lyophylized, and the residue (60 g) was extracted with EtOH to give 6.3 g of a viscous dark oil. Defatting was carried out by flash chromatography with a hexane/AcOEt gradient, collecting 60 fractions of 50 ml each. Fractions 30–40 were evaporated, and the residue was subjected to reverse-phase HPLC with MeCN/H_2O 55:45 to collect sphinxolide ((−)-**1**; 14 mg) as a single peak at 12.5 min. The compound proved active against the KB cell line (IC_{50} 35 pg/ml).

3. *Sphinxolide* (= *36-(*N-*Formyl*-N-*methylamino)-10,19-dihydroxy-7,8,13,15,21,27,33-heptamethoxy-5,12,18,24,26,28,32-heptamethyl-31-oxo-11,9-(2-oxo-1-oxapropan-1-yl-3-ylidene)hexatriaconta-2,4,16,22,35-pentaen-25-olide;* (−)-**1**). Colourless microcrystalline powder. M.p. (AcOEt) 90–92°. $[\alpha]_D^{25} = -10.5$ ($c = 0.15$, MeOH). UV (MeOH): 273 (32000). IR (KBr): 3430*s*, 1730–1700*vs* (unresolved), 1660*vs*, 1635*m*. ^{1}H-NMR ($CDCl_3$): 5.79 (*d*, $J(2,3) = 15.3$, H–C(2)); 7.52 (*dd*, $J(3,2) = 15.3$, $J(3,4) = 12.0$, H–C(3)); 6.07 (br. *d*, $J(4,3) = 12.0$, H–C(4)); 2.46 (*dd*, $J_{gem} = 14.9$, $J(6a,7) = 3.3$, H_a–C(6)); 2.32 (*dd*, $J_{gem} = 14.9$, $J(6b,7) = 7.2$, H_b–C(6)); 3.46 (*ddd*, $J(7,6b) = 7.2$, $J(7,8) = 6.3$, $J(7,6a) = 3.3$, H–C(7)); 3.76 (br. *d*, $J(8,7) = 6.3$, H–C(8)); 4.10 (*d*, $J(10,11) = 1.8$, H–C(10)); 4.08 (*dd*, $J(11,12) = 10.2$, $J(11,10) = 1.8$, H–C(11)); 2.35 (*ddq*, $J(12,11) = 10.2$, $J(12,13) = 3.2$, $J(12,Me) = 6.9$, H–C(12)); 3.45 (*m*, H–C(13)); 1.84 (*m*, H_a–C(14)); 1.52 (*m*, H_b–C(14)); 3.52 (*m*, H–C(15)); 5.23 (br. *dd*, $J(16,17) = 15.3$, $J(16,15) = 8.4$, H–C(16)); 5.43 (*dd*, $J(17,16) = 15.3$, $J(17,18) = 7.8$, H–C(17)); 2.27 (*ddq*, $J(18,17) = 7.8$, $J(18,19) = 7.2$, $J(18,Me) = 6.9$, H–C(18)); 3.52 (*ddd*, $J(19,20b) = 8.7$, $J(19,18) = 7.2$, $J(19,20a) = 3.9$, H–C(19)); 1.49 (*m*, H_a–C(20)); 1.42 (*m*, H_b–C(20)); 3.62 (*dt*, $J(21,22) = 8.4$, $J(21,20a) \approx J(21,20b) = 5.1$, H–C(21)); 5.14 (*dd*, $J(22,23)15.3$, $J(22,21) = 8.4$, H–C(22)); 5.52 (*dd*, $J(23,22) = 15.3$, $J(23,24) = 9.5$, H–C(23)); 2.44 (*ddq*, $J(24,23) = 9.5$, $J(24,25) = 10.1$, $J(24,Me) = 6.9$, H–C(24)); 5.12 (*dd*, $J(25,24) = 10.1$, $J(25,26) = 1.3$, H–C(25)); 1.93 (*ddq*, $J(26,27) = 9.8$, $J(26,25) = 1.3$, $J(26,Me) = 6.9$, H–C(26)); 2.69 (*dd*, $J(27,26) = 9.8$, $J(27,28) = 2.4$, H–C(27)); 1.68 (*m*, H–C(28)); 1.73 (*m*, H_a–C(29)); 1.38 (*m*, H_b–C(29)); 2.53 (*m*, H_a–C(30)); 2.45 (*m*, H_b–C(30)); 2.72 (*dq*, $J(32,33) = 9.0$, $J(32,Me) = 6.9$, H–C(32)); 3.43 (*ddd*, $J(33,32) = 9.0$, $J(33,34a) = 3.8$, $J(33,34b) = 5.1$, H–C(33)); 2.44 (*ddd*, $J_{gem} = 15.0$, $J(34a,33) = 3.9$, $J(34a,35) = 6.3$, H_a–C(34)); 2.11 (*ddd*, $J_{gem} = 15.0$, $J(34b,33) = 5.1$, $J(34b,35) = 8.1$, H_b–C(34)); 5.06 (*ddd*, $J(35,36) = 13.8$, $J(35,34a) = 6.3$, $J(35,34b) = 8.1$, H–C(35)); 6.50 (br. *d*, $J(36,35) = 13.8$, H–C(36)); 1.93 (br. *s*, Me–C(5)); 3.34 (*s*, MeO–C(7)); 3.37 (*s*, MeO–C(8)); 6.08 (br. *s*, CH=C(9)); 1.14 (*d*, $J(Me,12) = 6.9$, Me–C(12)); 3.23 (*s*, MeO–C(13)); 3.19 (*s*, MeO–C(15)); 0.84 (*d*, $J(Me,18) = 6.9$, Me–C(18)); 3.27 (*s*, MeO–C(21)); 1.03 (*d*, $J(Me,24) = 6.9$, Me–C(24)); 0.91 (*d*, $J(Me,26) = 6.9$, Me–C(26)); 3.36 (*s*, MeO–C(27)); 0.97 (*d*, $J(Me,28) = 6.9$, Me–C(28)); 0.97 (*d*, $J(Me,32) = 6.9$, Me–C(32)); 3.27 (*s*, MeO–C(33)); 3.2 (*s*, MeN); 8.7 (*s*, CHO). ^{1}H-NMR (C_6D_6; only signals for the (*E*) form of the *W* portion are reported): 2.60 (*m*, H–C(32)); 3.32 (*m*, H–C(33)); 2.13 (*ddd*, $J_{gem} = 14.7$, $J(34a,33) = 4.1$, $J(34a,35) = 6.6$, H_a–C(34)); 1.79 (*ddd*, $J_{gem} = 14.7$, $J(34b,33) = 5.1$, $J(34b,35) = 8.0$, H_b–C(34)); 4.69 (*ddd*, $J(35,36) = 13.9$, $J(35,34a) = 6.3$, $J(35,34b) = 8.0$, H–C(35)); 5.84 (br. *d*, $J(36,35) = 13.9$, H–C(36)); 0.83 (*d*, $J(Me,32) = 6.7$, Me–C(32)); 2.61 (*s*, MeN); 7.89 (*s*, CHO). ^{13}C-NMR ($CDCl_3$; assignments from short-range [8] and long-range [9] $^{13}C,^{1}H$ shift-correlation experiments; data for the (*Z*) form within brackets): 167.20 (*s*, C(1)); 120.12 (*d*, C(2)); 140.74 (*d*, C(3)); 125.46 (*d*, C(4)); 147.19 (*s*, C(5)); 40.70 (*t*, C(6)); 78.94 (*d*, C(7) or C(15)); 84.77 (*d*, C(8)); 155.42 (*s*, C(9)); 61.09 (*d*, C(10)); 83.38 (*d*, C(11)); 35.58 (*d*, C(12)); 78.55 (*d*, C(13)); 35.08 (*t*, C(14)); 82.38 (*d*, C(15) or C(7)); 131.21 (*d*, C(16)); 137.62 (*d*, C(17)); 41.89 (*d*, C(18));

82.38 (*d*, C(15) or C(7))); 131.21 (*d*, C(16)); 137.62 (*d*, C(17)); 41.89 (*d*, C(18)); 72.97 (*d*, C(19)); 39.09 (*t*, C(20)); 82.36 (*d*, C(21)); 129.64 (*d*, C(22)); 138.72 (*d*, C(23)); 40.61 (*d*, C(24)); 75.54 (*d*, C(25)); 36.47 (*d*, C(26)); 87.22 [87.14] (*d*, C(27)); 34.41 [34.36] (*d*, C(28)); 23.39 (*t*, C(29)); 41.00 [40.77] (*t*, C(30)); 213.50 [213.55] (*s*, C(31)); 48.95 [49.13] (*d*, C(32)); 82.38 (*d*, C(33)); 30.41 [30.31] (*t*, C(34)); 105.47 [107.14] (*d*, C(35)); 130.43 [126.35] (*d*, C(36)); 18.62 (*q*, *Me*–C(5)); 58.19 (*q*, *Me*O–C(7)); 57.60 (*q*, *Me*O–C(8)); 121.13 (*d*, *C*=C(9)); 164.00 (*s*, *OC*C=C(9)); 11.51 (*q*, *Me*–C(12)); 55.60 (*q*, *Me*O–C(13)); 55.90 (*q*, *Me*O–C(15)); 15.74 (*q*, *Me*–C(18)); 57.60 (*q*, *Me*O–C(21)); 17.65 (*q*, *Me*–C(24)); 9.88 (*q*, *Me*–C(26)); 61.45 [61.38] (*q*, *Me*O–C(27)); 17.44 [17.40] (*q*, *Me*–C(28)); 12.71 [12.82] (*q*, *Me*–C(32)); 57.60 [57.66] (*q*, *Me*O–C(33)); 27.54 [33.08] (*q*, MeN); 162.08 [160.77] (*d*, *C*HO). ^{13}C-NMR (C_6D_6; tentative assignments, spectral complexity much higher than in $CDCl_3$): 167.46 [167.50] (*s*, C(1)); 120.52 [120.44] (*d*, C(2)); 141.32 (*d*, C(3)); 125.71 (*d*, C(4)); 148.13 (*s*, C(5)); 40.99 (*t*, C(6)); 79.51 (*d*, C(7)); 84.00 (*d*, C(8)); 155.13 (*s*, C(9)); 61.86 (*d*, C(10)); 83.64 (*d*, C(11)); 35.94 (*d*, C(12)); 78.32 (*d*, C(13)); 35.46 (*t*, C(14)); 82.83 (*d*, C(15)); 131.98 (*d*, C(16)); 138.19 (*d*, C(17)); 40.99 (*d*, C(18)); 73.15 (*d*, C(19)); 40.38 [40.30] (*t*, C(20)); 82.61 (*d*, C(21)); 130.36 [130.26] (*d*, C(22)); 139.07 [139.19] (*d*, C(23)); 41.14 [41.10] (*d*, C(24)); 75.66 [75.76] (*d*, C(25)); 36.99 (*d*, C(26)); 87.58 [87.25] (*d*, C(27)); 34.76 [34.64] (*d*, C(28)); 23.97 [24.07] (*t*, C(29)); 43.40 [43.50] (*t*, C(30)); 211.95 [211.92] (*s*, C(31)); 49.15 [49.28] (*d*, C(32)); 83.14 [83.24] (*d*, C(33)); 30.69 [30.49] (*t*, C(34)); 104.33 [106.38] (*d*, C(35)); 130.36 [126.97] (*d*, C(36)); 18.44 (*q*, *Me*–C(5)); 56.68 (*q*, *Me*O–C(7)); 57.00 (*q*, *Me*O–C(8)); 126.86 (*d*, *C*=C(9)); 164.18 (*s*, *OC*C=C(9)); 10.96 (*q*, *Me*–C(12)); 55.37 (*q*, *Me*O–C(13)); 55.79 (*q*, *Me*O–C(15)); 17.65 (*q*, *Me*–C(18)); 58.34 [58.40] (*q*, *Me*O–C(21)); 16.63 [16.72] (*q*, *Me*–C(24)); 10.20 [10.13] (*q*, *Me*–C(26)); 61.55 [61.30] (*q*, *Me*O–C(27)); 17.86 [17.52] (*q*, *Me*–C(28)); 12.74 [12.84] (*q*, *Me*–C(32)); 57.44 [57.19] (*q*, *Me*O–C(33)); 26.95 [31.92] (*q*, MeN); 161.57 [160.50] (*d*, *C*HO).FAB-MS: 1013 ([*M* + Na]$^+$), 991 ([*M* + H]$^+$).

4. *Acetylation of (−)-***1**. A mixture of (−)-**1** (11.5 mg, 0.012 mmol), 0.5 ml of dry pyridine, and 0.5 ml of Ac_2O was stirred for 12 h at r.t. and then for further 12 h at 40°, until nearly all (−)-**1** had disappeared. Reagents in excess were evaporated, and the residue was subjected to HPLC with MeCN/H_2O 75:25 under flux gradient. Besides 5% of unreacted (−)-**1** (t_R 6.3 min), we thus obtained (−)-**2** (t_R 10.1 min; 6.5 mg, 57%) and (+)-**3** (t_R 16.6) min; 4.5 mg, 38%).

*19-*O*-Acetylsphinxolide* ((−)-**2**). Colourless microcrystalline powder. M.p. (hexane/Et_2O) 74–76°. $[\alpha]_D^{25} = -4.7$, $[\alpha]_{435}^{25} = -8.5$, $[\alpha]_{365}^{25} = -24.5$ ($c = 0.23$, $CHCl_3$). UV (MeOH): 279 (31 500). ^{1}H-NMR ($CDCl_3$): 5.78 (*d*, $J(2,3) = 15.2$, H–C(2)); 7.52 (*dd*, $J(3,2) = 15.2$, $J(3,4) = 11.7$, H–C(3)); 6.07 (br. *d*, $J(4,3) = 11.7$, H–C(4)); 2.50 (*dd*, $J_{gem} = 14.9$, $J(6a,7) = 3.5$, H_a–C(6)); 2.32 (*dd*, $J_{gem} = 14.9$, $J(6b,7) = 7.0$, H_b–C(6)); 3.46 (*ddd*, $J(7,6b) = 7.0$, $J(7,8) = 6.6$, $J(7,6a) = 3.5$, H–C(7)); 3.71 (*dd*, $J(8,7) = 6.6$, $J(8,10) = 0.8$, H–C(8)); 4.15 (br. *s*, H–C(10)); 4.05 (*dd*, $J(11,12) = 10.4$, $J(11,10) = 1.7$, H–C(11)); 2.43 (*ddq*, $J(12,11) = 10.4$, $J(12,13) = 3.5$, $J(12,Me) = 6.9$, H–C(12)); 3.43 (*m*, H–C(13)); 1.76 (*ddd*, $J_{gem} = 13.5$, $J(14a,15) = 8.4$, $J(14a,13) = 7.2$, H_a–C(14)); 1.44 (*ddd*, $J_{gem} = 13.5$, $J(14b,15) = 5.5$, $J(14b,13) = 10.5$, H_b–C(14)); 3.58 (*td*, $J(15,14a) = J(15,16) = 8.4$, $J(15,14b) = 5.5$, H–C(15)); 5.21 (br. *dd*, $J(16,17) = 15.4$, $J(16,15) = 8.5$, H–C(16)); 5.51 (*dd*, $J(17,16) = 15.4$, $J(17,18) = 8.2$, H–C(17)); 2.41 (*ddq*, $J(18,17) = 8.2$, $J(18,19) = 5.6$, $J(18,Me) = 6.9$, H–C(18)); 4.80 (*ddd*, $J(19,20a) = 8.2$, $J(19,18) = 5.6$, $J(19,20b) = 3.6$, H–C(19)); 1.67 (*ddd*, $J_{gem} = 14.9$, $J(20a,21) = 8.2$, $J(20a,19) = 7.5$, H_a–C(20)); 1.44 (*dt*, $J_{gem} = 14.9$, $J(20b,19) = J(20b,21) = 3.6$, H_b–C(20)); 3.48 (*m*, H–C(21)); 5.16 (*dd*, $J(22,23) = 15.2$, $J(22,21) = 8.2$, H–C(22)); 5.46 (*dd*, $J(23,22) = 15.2$, $J(23,24) = 9.5$, H–C(23)); 2.43 (*tq*, $J(24,23) \approx J(24,25) = 9.7$, $J(24,Me) = 6.7$, H–C(24)); 5.12 (*dd*, $J(25,24) = 10.1$, $J(25,26) = 1.5$, H–C(25)); 1.92 (*ddq*, $J(26,27) = 10.1$, $J(26,Me) = 6.9$, $J(26,25) = 1.5$, H–C(26)); 2.69 (*dd*, $J(27,26) = 10.1$, $J(27,28) = 2.0$, H–C(27)); 1.68 (*m*, H–C(28)); 1.73 (*m*, H_a–C(29)); 1.36 (*m*, H_b–C(29)); 2.45 (*m*, H_a–C(30)); 2.55 (*m*, H_b–C(30)); 2.72 (*dq*, $J(32,33) = 9.2$, $J(32,Me) = 7.0$, H–C(32)); 3.44 (*m*, H–C(33)); 2.45 (*ddd*, $J_{gem} = 14.9$, $J(34a,35) = 6.4$, $J(34a,33) = 3.6$, H_a–C(34)); 2.11 (*ddd*, $J_{gem} = 14.9$, $J(34b,35) = 8.4$, $J(34b,33) = 3.0$, H_b–C(34)); 5.06 (*ddd*, $J(35,36) = 14.1$, $J(35,34a) = 6.4$, $J(35,34b) = 8.4$, H–C(35)); 6.50 (br. *d*, $J(36,35) = 14.1$, H–C(36)); 1.95 (br. *s*, Me–C(5)); 3.38 (*s*, MeO–C(7)); 3.39 (*s*, MeO–C(8)); 6.08 (br. *s*, CH=C(9)); 1.14 (*d*, $J(Me,12) = 6.9$, Me–C(12)); 3.23 (*s*, MeO–C(13)); 3.13 (*s*, MeO–C(15)); 0.82 (*d*, $J(Me,18) = 6.9$, Me–C(18)); 3.27 (*s*, MeO–C(21)); 1.02 (*d*, $J(Me,24) = 6.7$, Me–C(24)); 0.91 (*d*, $J(Me,26) = 6.9$, Me–C(26)); 3.36 (*s*, MeO–C(27)); 0.97 (*d*, $J(Me,28) = 7.0$, Me–C(28)); 0.97 (*d*, $J(Me,32) = 7.0$, Me–C(32)); 3.27 (*s*, MeO–C(33)); 3.02 (*s*, MeN); 8.27 (*s*, CHO); 1.99 (*s*, $CH_3COOC(19)$). ^{13}C-NMR ($CDCl_3$; assignments in analogy with (−)-**1** and based on expected $\Delta\delta$'s on acetylation [15]; data for the (*Z*) form within brackets): 166.66 (*s*, C(1)); 120.38 (*d*, C(2)); 140.24 (*d*, C(3)); 125.91 (*d*, C(4)); 146.11 (*s*, C(5)); 40.65 (*t*, C(6)); 79.21 (*d*, C(7), C(11), or C(15)); 84.56 (*d*, C(8)); 155.69 (*s*, C(9)); 62.01 (*d*, C(10)); 80.76 (*d*, C(11) or C(7)); 35.21 (*d*, C(12)); 78.42 (*d*, C(13)); 35.69 (*t*, C(14)); 83.04 (*d*, C(15), C(11), or C(7)); 131.50 (*d*, C(16)); 137.36 (*d*, C(17)); 39.77 (*d*, C(18)); 74.91 (*d*, C(19)); 36.50 (*t*, C(20)); 82.45 (*d*, C(21)); 131.90 (*d*, C(22)); 137.41 (*d*, C(23)); 40.48 (*d*, C(24)); 75.42 (*d*, C(25)); 36.93 (*d*, C(26)); 87.32 [87.12] (*d*, C(27)); 34.50 [34.30] (*d*, C(28)); 23.59 (*t*, C(29)); 40.98 [40.79] (*t*, C(30)); 213.50 [213.56] (*s*, C(31)); 49.01 [49.16] (*d*, C(32)); 82.73 (*d*, C(33)); 30.55 (*t*, C(34)); 105.56 [107.17] (*d*, C(35)); 130.38

[126.41] (*d*, C(36)); 18.76 (*q*, *Me*–C(5)); 58.02 (*q*, *Me*O–C(7)); 57.88 (*q*, *Me*O–C(8)); 121.21 (*d*, *C*=C(9)); 163.76 (*s*, O*C*C=C(9)); 12.47 (*q*, *Me*–C(12)); 55.68 (*q*, *Me*O–C(13)); 55.84 (*q*, *Me*O–C(15)); 15.88 (*q*, *Me*–C(18)); 57.88 (*q*, *Me*O–C(21)); 17.96 (*q*, *Me*–C(24)); 10.19 (*q*, *Me*–C(26)); 61.36 [61.43] (*q*, *Me*O–C(27)); 17.45 [17.41] (*q*, *Me*–C(28)); 12.68 [12.80] (*q*, *Me*–C(32)); 57.70 [57.66] (*q*, *Me*O–C(33)); 27.57 [32.97] (*q*, MeN); 162.06 [160.70] (*d*, *C*HO); 21.19 (*q*, *C*H_3COOC(19)); 170.28 (*s*, CH_3*C*OOC(19)). FAB-MS: 1055 ([*M* + Na]$^+$), 1033 ([*M* + H]$^+$).

*10,19-Di-*O*-acetylsphinxolide* ((+)-**3**). Colourless microcrystalline powder. M.p. (hexane/Et_2O) 64–66°. $[\alpha]_D^{25} = +16.5$, $[\alpha]_{435}^{25} = +25.8$, $[\alpha]_{365}^{25} = +18.0$ (*c* = 0.18, $CHCl_3$). UV (MeOH): 277 (26000). ^{1}H-NMR ($CDCl_3$): 5.76 (*d*, *J*(2,3) = 15.2, H–C(2)); 7.47 (*dd*, *J*(3,2) = 15.2, *J*(3,4) = 11.7, H–C(3)); 6.15 (br. *d*, *J*(4,3) = 11.7, H–C(4)); 2.56 (*dd*, J_{gem} = 14.9, *J*(6a,7) = 2.1, H_a–C(6)); 2.30 (*dd*, J_{gem} = 14.9, *J*(6b,7) = 8.5, H_b–C(6)); 3.85 (*td*, *J*(7,6b) ≈ *J*(7,8) = 8.4, *J*(7,6a) = 2.1, H–C(7)); 3.50 (br. *d*, *J*(8,7) = 8.4, H–C(8)); 5.78 (br. *s*, H–C(10)); 4.26 (*dd*, *J*(11,12) = 10.2, *J*(11,10) = 1.7, H–C(11)); 2.43 (*m*, H–C(12)); 3.35 (*ddd*, *J*(13,14b) = 10.5, *J*(13,12) = 8.9, *J*(13,14a) = 2.0, H–C(13)); 1.66 (*ddd*, J_{gem} = 14.2, *J*(14a,15) = 8.9, *J*(14a, 13) = 2.0, H_a–C(14)); 1.33 (*ddd*, J_{gem} = 14.2, *J*(14b,13) = 10.5, *J*(14b,15) = 3.1, H_b–C(14)); 3.65 (*td*, *J*(15,14a) ≈ *J*(15,16) = 8.9, *J*(15,14b) = 3.1, H–C(15)); 5.24 (br. *dd*, *J*(16,17) = 15.2, *J*(16,15) = 8.9, H–C(16)); 5.65 (*dd*, *J*(17,16) = 15.2, *J*(17,18) = 7.2, H–C(17)); 2.48 (*ddq*, *J*(18,17) = 7.2, *J*(18,19) = 7.0, *J*(18,Me) = 6.9, H–C(18)); 4.59 (*td*, *J*(19,20a) ≈ *J*(19,18) = 7.0, *J*(19,20b) = 3.1, H–C(19)); 1.65 (*ddd*, J_{gem} = 14.7, *J*(20a,21) = 8.4, *J*(20a,19) = 7.0, H_a–C(20)); 1.46 (*ddd*, J_{gem} = 14.7, *J*(20b,21) = 3.5, *J*(20b,19) = 3.7, H_b–C(20)); 3.51 (*td*, *J*(21,22) ≈ *J*(21,20a) = 8.4, *J*(21,20b) = 3.5, H–C(21)); 5.19 (*dd*, *J*(22,23) = 15.2, *J*(22,21) = 8.5, H–C(22)); 5.46 (*dd*, *J*(23,22) = 15.2, *J*(23,24) = 9.4, H–C(23)); 2.47 (*ddq*, *J*(24,23) = 9.4, *J*(24,25) = 10.0, *J*(24,Me) = 6.9, H–C(24)); 5.12 (*dd*, *J*(25,24) = 10.0, *J*(25,26) = 1.7, H–C(25)); 1.95 (*ddq*, *J*(26,27) = 9.3, *J*(26,25) = 1.7, *J*(26,Me) = 6.9, H–C(26)); 2.71 (*dd*, *J*(27,26) = 9.6, *J*(27,28) = 2.4, H–C(27)); 1.69 (*m*, H–C(28)); 1.73 (*m*, H_a–C(29)); 1.36 (*m*, H_b–C(29)); 2.54 (*m*, H_a–C(30)); 2.45 (*m*, H_b–C(30)); 2.72 (*dq*, *J*(32,33) = 9.0, *J*(32,Me) = 6.9, H–C(32)); 3.45 (*ddd*, *J*(33,32) = 9.0, *J*(33,34a) = 3.5, *J*(33,34b) = 5.4, H–C(33)); 2.48 (*ddd*, J_{gem} = 15.0, *J*(34a,33) = 3.5, *J*(34a, 35) = 6.5, H_a–C(34)); 2.14 (*ddd*, J_{gem} = 15.0, *J*(34b,33) = 5.4, *J*(34b,35) = 8.3, H_b–C(34)); 5.06 (*ddd*, *J*(35,36) = 14.0, *J*(35,34a) = 6.5, *J*(35,34b) = 8.3, H–C(35)); 6.50 (br. *d*, *J*(36,35) = 14.0, H–C(36)); 1.97 (br. *s*, Me–C(5)); 3.21 (*s*, MeO–C(7)); 3.18 (*s*, MeO–C(8)); 6.06 (br. *s*, CH=C(9)); 1.10 (*d*, *J*(Me,12) = 7.1, Me–C(12)); 3.23 (*s*, MeO–C(13)); 3.15 (*s*, MeO–C(15)); 0.87 (*d*, *J*(Me,18) = 6.9, Me–C(18)); 3.26 (*s*, MeO–C(21)); 1.04 (*d*, *J*(Me,24) = 6.9, Me–C(24)); 0.95 (*d*, *J*(Me,26) = 6.9, Me–C(26)); 3.40 (*s*, MeO–C(27)); 0.98 (*d*, *J*(Me,28) = 6.9, Me–C(28)); 0.98 (*d*, *J*(Me,32) = 6.9, Me–C(32)); 3.29 (*s*, MeO–C(33)); 3.03 (*s*, MeN); 8.27 (*s*, CHO); 2.04 (*s*, CH_3COOC(10)); 2.02 (*s*, CH_3COOC(19)). ^{13}C-NMR ($CDCl_3$; assignments in analogy with (–)-**1** and based on the expected $\Delta\delta$'s on acetylation [15]; data for the (*Z*) form within brackets): 166.35 (*s*, C(1)); 120.58 (*d*, C(2)); 139.67 (*d*, C(3)); 125.74 (*d*, C(4)); 146.32 (*s*, C(5)); 42.74 (*t*, C(6)); 79.42 (*d*, C(7), C(11), or C(21)); 85.50 (*d*, C(8)); 152.88 (*s*, C(9)); 62.68 (*d*, C(10)); 79.68 (*d*, C(11), C(7), or C(21)); 36.11 (*d*, C(12)); 78.40 (*d*, C(13)); 36.28 (*t*, C(14)); 81.22 (*d*, C(15)); 131.10 (*d*, C(16)); 135.20 (*d*, C(17)); 38.86 (*d*, C(18)); 75.14 (*d*, C(19)); 36.12 (*t*, C(20)); 81.21 (*d*, C(21), C(11), or C(7)); 130.33 (*d*, C(22)); 136.97 (*d*, C(23)); 40.52 (*d*, C(24)); 75.40 (*d*, C(25)); 36.83 (*d*, C(26)); 87.18 (*d*, C(27)); 34.35 [34.32] (*d*, C(28)); 23.20 (*t*, C(29)); 40.91 [40.75] (*t*, C(30)); 213.60 [213.68] (*s*, C(31)); 48.92 [49.04] (*d*, C(32)); 82.28 (*d*, C(33)); 30.36 (*t*, C(34)); 105.33 [106.98] (*d*, C(35)); 130.37 [126.38] (*d*, C(36)); 18.22 (*q*, *Me*–C(5)); 58.20 (*q*, *Me*O–C(7)); 57.65 (*q*, *Me*O–C(8)); 124.50 (*d*, *C*=C(9)); 163.57 (*s*, O*C*C=C(9)); 13.34 (*q*, *Me*–C(12)); 55.67 (*q*, *Me*O–C(13)); 55.87 (*q*, *Me*O–C (15)); 15.77 (*q*, *Me*–C(18)); 57.68 (*q*, *Me*O–C(21)); 17.86 (*q*, *Me*–C(24)); 10.12 (*q*, *Me*–C(26)); 61.58 [61.55] (*q*, *Me*O–C(27)); 17.48 [17.45] (*q*, *Me*–C(28)); 12.71 [12.85] (*q*, *Me*–C(32)); 57.65 [57.69] (*q*, *Me*O–C(33)); 27.52 [33.01] (*q*, MeN); 162.09 [160.65] (*d*, *C*HO); 20.79 (*q*, *C*H_3COOC(10)); 168.15 (*s*, CH_3*C*OOC(10)); 21.18 (*q*, *C*H_3COOC(19)); 170.33 (*s*, CH_3*C*OOC(19)). FAB-MS: 1097 ([*M* + Na]$^+$), 1075 ([*M* + H]$^+$).

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