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A NEW STRAIN OF *STREPTOMYCES*: AN ANTHRACYCLINE CONTAINING A *C*-GLUCOSIDE MOIETY AND A CHIRAL DECANOL

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Key Word Index—*Streptomyces*; Actinomycetes, secondary metabolites; structural determination, anthracyclinones; 1,3-dihydroxy-6,8-decadien-5-one.

Abstract—Two new metabolites have been isolated from strain C57 of *Streptomyces* and their structure determined on the basis of chemical and NMR evidence.

INTRODUCTION

Interest in the remarkable pharmacological properties of secondary metabolites produced by *Streptomyces* species, has resulted in the isolation of many compounds over two hundred of which are anthracyclines; pyrromycines, rhodomycines and daunomycines were among the first to be isolated. Their aglycones consist of an anthraquinone chromophore with a fourth ring fused on [1]. Other products from *Streptomyces* sp. with a benz(a)anthraquinone aglycone have been isolated, such as tetrangomycin from *S. rimosus* [2], which represents the first benz (a) anthraquinone derivative isolated from a living system; vineomycine from *S. matensis*, subsp. *vineus* [3]; aquayamycin from *S. misawanensis* [4].

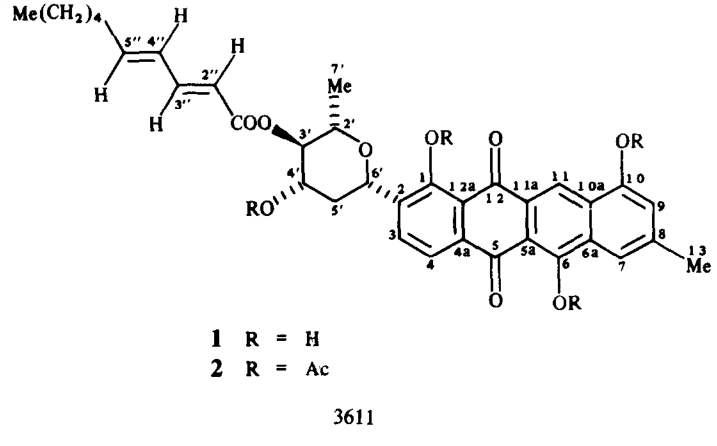
Recently galtamycinone has been obtained by acid hydrolysis of a new antibiotic, galtamycin [5]. This compound represents a new class of molecules containing a C-glucoside moiety bound to a naphthacenedione chromophore.

Strain 57 of *Streptomyces* sp has been isolated from *Camellia japonica* in the course of a screening programme for Actinomycete strains showing activity against soil phytopatogenic fungi. It has shown noteworthy activity against strains of different species of *Fusarium* and *Thielavia*, *Rhizoctonia solani* and soil saprophytes such as *Geotrichum candidum* and *Trichoderma hamatum*. This activity, which was not associated with the metabolites described herein, is strictly related to the active growth phase of the strain itself.

From strain C57 we have now isolated a new benzanthraquinone, 2-[tetrahydro-3′(deca-2″*E*,4″*E*-dienoate)-4′-hydroxy-2′-methyl-5′H-pyran-6′-yl]-1,6,10-trihydroxy-8-methyl-naphthacene-5,12-dione **1** and a new chiral decanol, 1,3-dihydroxy-6*E*,8*E*-decadien-5-one **11**. In this paper we present evidence for their structures together with some related chemical transformations.

RESULTS AND DISCUSSION

Compound **1** was obtained as a red crystalline substance, mp 232°; $[\alpha]_D$ −379.7°(*c* 0.1; pyridine). Elemental analysis and FAB mass spectrometry indicated a M_r of 600, in accordance with the formula $C_{35}H_{36}O_9$. Absorptions at 265, 300, 370 and 490 nm in the UV spectrum were consonant with the presence of a substituted 1,6-dihydroxynaphthacenequinone nucleus, whereas absorptions in the IR region at 1710 and 1685 cm^{-1} were indicative of



1 R = H
2 R = Ac

Part XXI in the series 'Secondary Mould Metabolites' For part XX see Arnone, A., Assante, G., Di Modugno, V Merlini, L. and Nasini, G (1988) *Phytochemistry* **27**, 1675.

the presence of conjugated ester and chelated quinone carbonyl groups, respectively.

Addition of D_2O to the sample caused the resonance at δ_H 14 44, 13 44, 10 94 and 5.22 in the ^1H NMR spectrum to disappear, thus identifying four hydroxy groups The formation of the tetraacetate **2** $C_{43}H_{44}O_{13}$ upon acetylation, confirmed their presence A detailed analysis of the ^1H and ^{13}C NMR spectra of **2** is fully consistent with the proton and carbon counts as illustrated in Table 1 Chemical shift criteria, as corroborated by low power specific $^1H\{^1H\}$ and $^{13}C\{^1H\}$ decoupling experiments, permitted their assignment (Tables 2 and 3)

Alkaline hydrolysis of **1** afforded two compounds, **3** and **4** The alcoholic portion **3** gave the 1,6,3′,4′-tetraacetoxy, 10-methoxy derivative **5** by treatment with diazomethane followed by acetylation and the 1,6,10,4′-tetramethoxy derivative **6** by treatment with MeI/Ag_2O, while the acidic portion **4**, namely 2*E*,4*E*-decadienoic acid, furnished upon treatment with diazomethane the corresponding methyl ester **7** (Scheme 1)

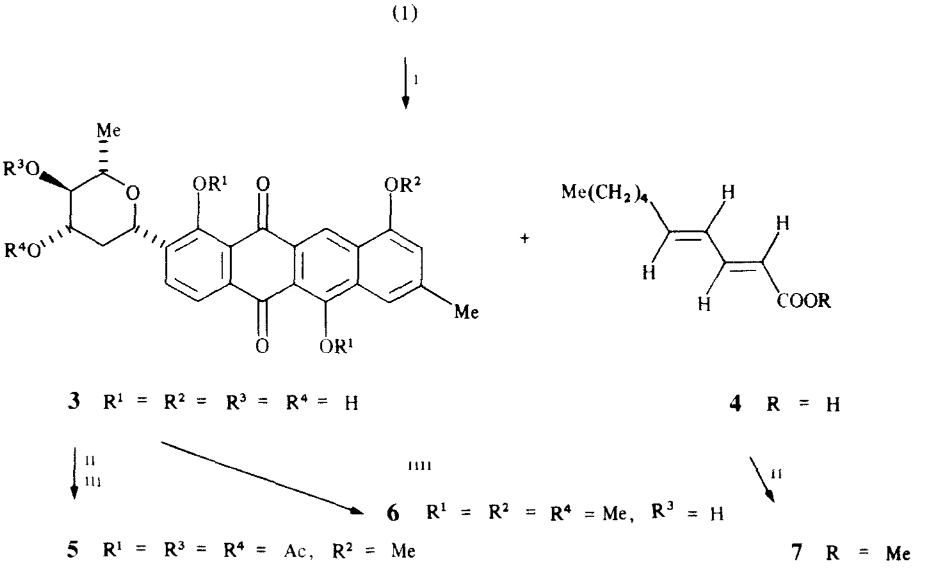
Chemical evidence, coupled with the spectral data exhibited by compounds **1**–**7** (see Tables 2, 3 and Experimental) allowed us to constitute the partial structures A–C, as shown in **8**–**10**, for **1**

The structure of partial structure A**8** was deduced from a study of the ^1H and ^{13}C NMR spectra of the abovementioned methyl 2*E*,4*E*-decadienoate **7** ($C_{11}H_{18}O_2$, $[M]^+$ *m/z* 182) Specifically, the NMR spectra of **7** showed the presence of a carbomethoxy group [δ_C = 167 76 (CO) and 51 43 (OMe)], an α-dienoic moiety and a $(CH_2)_4Me$ grouping The magnitude of the (H,H) coupling constants between H-2″, H-3″ and H-4″, H-5″ (^3J = 15 4 and 15 2 Hz) established the *E* configuration between the C-2″, C-3″ and C-4″, C-5″ double bonds

The partial structure B**9** is characterized by the number of protons which are located on oxygen-bearing carbon atoms Irradiation of the geminally coupled 5′-methylene protons resonating at δ_H 1 29 (assumed as α) and 2 29, carried out on compound **3**, caused the decoupling of the signals due to the 6′β-ethereal and the 4′β-carbinyl protons. H-4′β, in turn, presented vicinal couplings with H-3′α and with exchangeable OH-4′ proton Additionally, spin decoupling experiments revealed that the signal at δ_H 3 38 (H-2′β) was vicinally coupled to H_3-7′ and H-3′α, the

Table 1 Carbon and proton counts for compound **2** from ^{13}C and ^1H NMR data

^{13}C NMR	^1H NMR	Number of Carbons	Number of Protons
7 × Me	1 × $MeCH_2$	1	3
	1 × MeCH	1	3
	1 × Me–$\overset{\vert}{C}$=	1	3
	4 × $MeCO_2$	4	12
5 × CH_2	5 × CH_2	5	10
4 × CHOR	2 × CHOR	2	2
	2 × CHOCOR	2	2
9 × $\overset{\vert}{C}$H=	9 × $\overset{\vert}{C}$H=	9	9
8 × $\overset{\vert}{-C}$=		8	
3 × $\overset{O}{\overset{\vert}{C}}$=		3	
2 × $\underset{\vert}{\overset{\vert}{C}}$=O		2	
5 × CO_2R		5	
Total		43	44



3 $R^1 = R^2 = R^3 = R^4 = H$

4 R = H

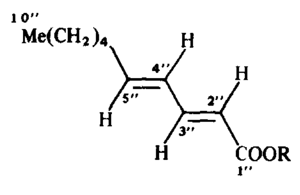
6 $R^1 = R^2 = R^4$ = Me, R^3 = H

5 $R^1 = R^3 = R^4$ = Ac, R^2 = Me

7 R = Me

Reagents i, 0 5 M KOH, ii, CH_2N_2, iii, Pyridine–Ac_2O, iiii, MeI–Ag_2O–Acetone

Scheme 1



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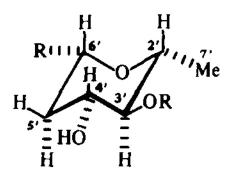

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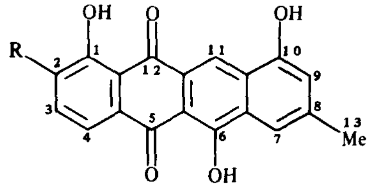

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Table 2. ^{1}H NMR chemical shifts (δ_H/ppm) and coupling constants (*J*/Hz) of compounds **1**–**3**, **5** and **6*** (300.13 MHz, TMS internal standard)

H	**1**	**2**	**3**	**5**	**6**	*J*	**1**	**2**	**3**	**5**	**6**
3	7 88†(7 82†)§	8.03	7 82	7 97	7.97	3,4	7 8	8.2	8 0	8 3	8.2
4	7.79†(7 94†)	8 27	7.75	8 25	8.10	3,6′	N.a.	0.6	0.7	0 6	0.7
7	7 56 (7.62)	7 79	7.51	7 41	7.75	4,6′	N.a.	0 4	0 4	0 4	0.5
9	6.98 (7 02)	7 37	6.95	6.81	7.08	7,9	1 5‡	1 5	1.5	1 4	1.4
11	8 44 (8 54)	8 73	8.39	9 04	8 86						
13	2.43 (2.44)	2 59	2.40	2 53	2.57	7,11	0.8‡	0 9	0.8	0.9	0.9
2′	3 66 (3.70)	3 71	3.38	3 68	3.52	7,13	0 9‡	1 1	0.9	1 0	1.0
3′	4.59 (4 74)	4 95	2 91	4 86	3.15	9,13	0 5‡	0.6	0.6	0 5	0 5
4′	3 85 (4.02)	5.20	3 55	5 16	3.42	9,OMe-10				0 2	0.2
5′α	1 40 (1 7)	1.71	1.29	1.68	1.36	2′,3′	9 5	9.5	9.1	9.7	9 2
5′β	2.45 (2.58)	2.4	2.29	2.5	2 48	2′,7′	6 1	6 2	6.1	6 1	6.1
6′	4.88 (4.94)	4.79	4 76	4 76	4 96	3′,4′	9 0	9.5	8.7	9.5	8.6
7′	1.15 (1 26)	1.30	1.29	1 31	1.35	3′,OH-3′			5.2		4 5
2″	5 96 (5 92)	5.78				4′,5′α	N a	11 5	10 8	11.5	11 0
3″	7.28 (7 33)	7 32				4′,5′β	5 0	5 0	5.2	5.1	4 9
4″	6 31 (6 33)	6 21†				4′OH-4′	5.2‖		4 7		
5″	6 31 (6.28)	6 17†				5′α,5′β	13 0	13	12.9	13	12 7
6″	2 16 (2 21)	2 19				5′α,6′	11 2	11 5	11.3	11 5	11.5
7″	1 4 (1.6)	1 45				5′β,6	2.0	N.a	2 0	N.a.	2 0
8″	1.3 (1 3)	1 3				2″,3″	15 2	15 2			
9″	1 3 (1.3)	1 3				3″,4″	9 5	N a			
10″	0 87 (0.85)	0.90				4″,5″	15 2	N.a.			
OR-1	14 44†(14.53†)	2 66†	14 42†	2.63†	3.99	5″,6″	6.5	N a.			
OR-6	13 44†(13 53†)	2 58†	13 40†	2 56†	4.08	9″,10″	6 6	6.8			
OR-10	10 94 (9 82)	2.55†	10 90	4.02	4 11						
OR-3′			5.04	2 02†	4 20						
OR-4′	5 22 (N.a.)	1.99	4 95	2 09†	3.42						

* The spectra of compounds **1** and **3**, **2** and **5**, and **6** were recorded in DMSO-d_6, CDCl$_3$, and acetone-d_6, respectively.

† Similar chemical shifts within each column may be interchanged.

§ Chemical shifts in parenthesis and coupling constants obtained in acetone-d_6

‡ Coupling constants obtained in pyridine-d_5.

‖ Coupling constants obtained in DMSO-d_6.

N a, Not assigned

latter being coupled also to the exchangeable OH-3′ proton. The large vicinal coupling values between H-2′β and H-3′α, H-3′α and H-4′β, H-4′β and H-5′α, H-5′α and H-6′β in **3** as well as in **1**, **2**, **5** and **6** (^3J = 8.7–11.5 Hz) suggest that these protons are part of a tetrahydropyran ring in which the substituents are all equatorially disposed. The sizeable NOE enhancement between the 1,3-*cis* disposed H-2′β, H-6′β (11%) and H-4′β, H-6′β (4%) in **6** confirmed as a chair the preferred conformation of this ring. Since the tetrahydropyran ring contains only one aliphatic OH in compound **1**, assigned to OH-4′ because of its vicinal coupling of 5.2 Hz with H-4′β, it follows that in **1** the ester residue **8** is placed at C-3′ Conversely, in the tetramethoxy derivative **6** the aliphatic OMe is located at C-4′ since the remaining OH-3′ proton is vicinally coupled with H-3′α.

Table 3. ^{13}C NMR data of compound **2** (75.47 MHz, $CDCl_3$, TMS as int. standard)

C	δ^*_c/ppm		$^1J_{(CH)}$/Hz	$^{>1}J_{(CH)}$/Hz
1	146.60	(*Sddd*)		8(H-3),1.5(H-4), and 4(H-6′)
2	140.94	(*Sbrdd*)		7.5(H-4) and *ca* 5(H-6′)
3	132.56	(*Dbrs*)	168	
4	126.04	(*Ds*)	168.5	
4a	136.22	(*Sd*)		8.5(H-3)
5	180.89	(*Sd*)		4(H-4)
5a	119.60	(*Sd*)		6(H-11)
6	147.82	(*Sdd*)		4(H-7) and 1.5(H-11)
6a	131.67	(*Sd*)		6(H-11)
7	120.47	(*Ddq*)	163	6(H-9) and 5.5(H_3-13)
8	141.07	(*Sq*)		6(H_3-13)
9	124.57	(*Ddq*)	163	7.5(H-7) and 5(H_3-13)
10	148.26	(*Sddd*)		1.5(H-7), 4.5(H-9), and 4.5(H-11)
10a	127.89	(*Sdd*)		6(H-7) and 6(H-9)
11	121.35	(*Ds*)	168	
11a	130.43	(*Ss*)		
12	181.07	(*Sd*)		5(H-11)
12a	124.99	(*Sd*)		6(H-4)
13	22.37	(*Qdd*)	128	4.5(H-7) and 4.5(H-9)
14	169.03†	(*Sq*)		7(H_3-15)
15	21.25†	(*Qs*)	130	
16	168.89†	(*Sq*)		7(H_3-17)
17	21.21†	(*Qs*)	130	
18	168.86†	(*Sq*)		7(H_3-19)
19	21.15†	(*Qs*)	130	
2′	75.17	(*Dm*)	142	
3′	74.17	(*Dm*)	150	
4′	72.12	(*Dm*)	*ca* 145	
5′	37.58	(*Tm*)	132.5	
6′	72.03	(*Dm*)	*ca* 148	
7′	18.03	(*Qbrs*)	125	
8′	170.38	(*Sdq*)		3(H-4′) and 6(H_3-9′)
9′	20.92†	(*Qs*)	129.5	
1″	166.33	(*Sm*)		
2″	118.27	(*Dm*)	163	
3″	146.34	(*Dm*)	*ca* 154	
4″	128.37	(*Dm*)	156	
5″	147.70	(*Dm*)	152	
6″	33.02	(*Tm*)	125	
7″	28.43	(*Tm*)	127	
8″	31.43	(*Tm*)	127	
9″	22.48	(*Tm*)	*ca* 126	
10″	13.92	(*Qm*)	123.5	

* Capital letters refer to one-bond couplings ($^1J_{CH}$) and small letters to long-range couplings ($^{>1}J_{CH}$) observed in fully ^{1}H coupled ^{13}C NMR spectrum: *S*,*s* = singlet; *D*,*d* = doublet; *T* = triplet; *Q*,*q* = quartet; *m* = multiplet; *br* = broad. C (14), C (16), C (18), C (8′) and C (15), C (17), C (19), C (9′) are respectively carbonyl and methyl carbon atoms of the 1-, 6-, 10-, and 4′-acetate groups.

† Similar chemical shifts may be interchanged.

The unassigned signals in the ^{1}H NMR spectrum of **1** are well accounted for by the presence of three phenolic OH groups, two of which chelated, one aromatic methyl group and five aromatic protons. The fine structure exhibited by these protons in compounds **2**, **3**, **5** and **6**, coupled with NOE experiments performed on the tetramethoxy derivative **6** and a detailed analysis of the long range (C, H) couplings in the ^{13}C NMR coupled spectrum of the tetraacetate **2**, permitted us assign to the fragment **10**, the 2-substituted 1,6,10-trihydroxy-8-methyl-naphthacene-5,12-dione structure. The 13-methyl protons, which served as a starting point for the structure elucidation of **10**, presented benzylic couplings to the *meta* positioned H-7 and H-9 ($^4J_{7,13} = 0.9$–1.1, $^4J_{9,13} = 0.5$–0.6 and $^3J_{7,9} = 1.4$–1.5 Hz). In addition, irradiation of H_3-13 in **6** resulted in NOE enhancement of H-7 (13%) and H-9 (9%), thus confirming their spatial proximity. H-9, in turn, was long-range coupled to the OMe resonating at δ_H 4.11, which was, therefore, located at C-10. Irradiation of the 10-OMe protons enhanced, besides H-9 (17%), a

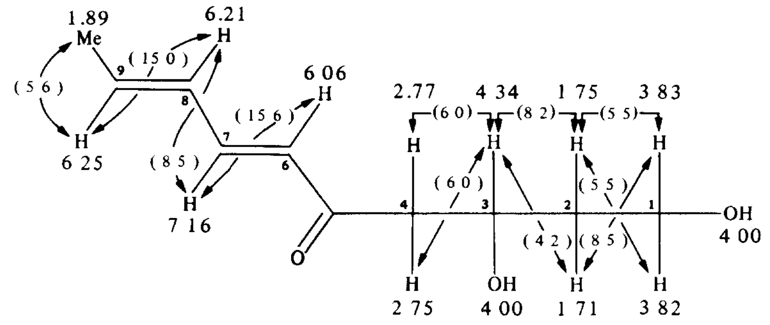


Fig 1 Chemical shifts (δ) and J (Hz) of the protons of compound **11**.

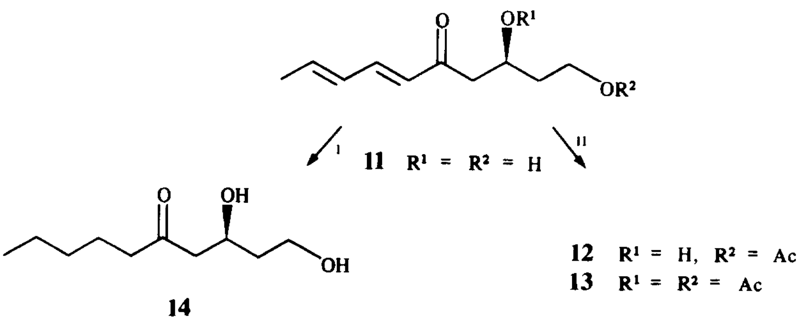
doublet signal resonating at δ_H8.86 (3%), which was assigned to the *peri* positioned H-11 The five-bond coupling of 0.9 Hz between H-7 and H-11 [6] and the reverse NOE experiments (that is, irradiation of both H-9 and H-11 led to enhancement of OMe-10 (3.5 and 0.5% respectively) confirmed these assignements The allocation of the OMe group resonating at δ4.08 at C-6 followed from the NOE observed between H-7 and OMe-6 (1.5%). The converse also occurs in the reverse experiment (6.5%). The two carbonyl carbon atoms (C-5 and C-12) resonating at δ_C 180.89 and 181.07 appeared each as a doublet in the ^{13}C NMR coupled spectrum of **2** [^3J(CH) $=4$ and 5 Hz], the three-bond couplings being removed by irradiation of the lowest field signal (H-4) of the two remaining *ortho*-coupled aromatic protons and of H-11, respectively. These findings not only indicate that H-4 and H-11 are *peri* positioned with respect to the two carbonyl groups [7] but also that the remaining chelated OH group must be placed at C-1 in **1**. The above results, in conjunction with the long range (H, H) couplings between H-6′ and H-3 and H-4 ($^4J_{3,6'}=0.7$ and $^5J_{4,6'}=0.5$ Hz) and the NOE between H-3, H-6′ (1%) in compound **6** allow the final linkage between C-2 and C-6′ to give the constitution of compound **1**, whose structure is, therefore, 2-[tetrahydro-3′(deca-2″*E*,4″*E* dienoate)-4′-hydroxy-2′-methyl-6′H-pyran-6′-yl]-1,6,10-trihydroxy-8-methyl-naphthacene-5,12-dione. It is inactive in antitumoral and antibacterial tests

The second metabolite (*S*)-1,3-dihydroxy-6*E*,8*E*-decadien-5-one **11**, $C_{10}H_{16}O_3$ ([M]$^+$, *m/z* 184), $[\alpha]_D = +23.4°$(*c* 0.3, $CHCl_3$), was revealed by the following chemical and spectroscopic evidence (Fig. 1) to be a chiral decanol which contains as partial structures a carbonyl group conjugated with a δ Me-*E*,*E*-diene moiety [λ_{max} 270 nm; ν_{max} 1635 (conj CO) and 1590 cm^{-1} (C=C)] and a 1,3-dihydroxy butyl grouping [ν_{max} 3380 cm^{-1} (OH)] which must be linked to the above mentioned CO

Chemical confirmation of the presence of two hydroxy groups was provided by acetylation of **11** to yield the monoacetate **12** and the diacetate **13** In the latter compound a characteristic downfield shift ($\Delta\delta$ 0.3–1.0 ppm) was observed for C-1 and C-3 protons which now resonate at δ4.13 and 5.35, respectively. Spin decoupling experiments also revealed that the multiplets at δ 1.75 and 1.71 assigned to H_2-2, were vicinally coupled to H_2-1 and H-3 ($^3J=4.2$–8.2 Hz) and that H-3 was adjacent to the 4-methylene protons resonating at δ2.77 and 2.75. In addition, the values of the coupling constants between the olefinic protons H-6 and H-7, H-7 and H-8, and H-8 and H-9 ($^3J=15.6$, 8.5, and 15.0 Hz, respectively) indicate that they are part of a *trans*-α,β-*trans*-γ,δ-diene system. Finally, reduction of **11** with H_2/10% Pd-C gave the tetrahydroderivative **14** which presented physical and spectroscopic properties analogous to those of the known (*S*)-1,3-dihydroxydecan-5-one [8]

EXPERIMENTAL

Mps uncorr UV absorptions were measured for solns in 95% EtOH. MS were taken at 70 eV on an instrument equipped with a FAB source NMR were recorded at 300.13 MHz for ^{1}H and 75.47 MHz for ^{13}C nuclei with TMS as int standard NOE difference spectra were obtained by subtracting alternatively right-off resonance-free induction decays (FIDS) from right-on resonance-induced FIDS NOE values (%) reported have only



11 R¹ = R² = H

12 R¹ = H, R² = Ac

13 R¹ = R² = Ac

14

Reagents i, H_2–Pd 10% / C, ii, Ac_2O–pyridine

Scheme 2.

qualitative significance Flash CC was performed on Merck silica gel (0 040–0 063 mm) TLC on Merck HF_{254} silica gel The purity of products was checked by TLC, NMR and MS, and deemed sufficient for the purposes of structural elucidation

Isolation and purification of metabolites **1** and **11** *Streptomyces* sp strain (C57) was received from Istituto di Patologia Vegetale, Facolta di Agraria, Universita di Milano Two different keys from the International Streptomyces Project [9, 10] have been used to characterize the strain

Sporophore morphology Rectiflexibiles section with very long chains of smooth surfaced spores as observed on cultures grown in oatmeal–agar and on inorganic salt starch agar

Colour of colony Aerial mycelium ascribable to the red series in colonies grown on oatmeal–agar, inorganic salt–starch agar, yeast extract–malt extract, agar and glycerol asparagine agar

Reverse of colony Distinctive over the above mentioned culture media

Soluble pigment production No melanic pigments are produced on peptone–yeast extract iron–agar

Carbohydrate utilization D-Glucose, sucrose, D-xylose, L-inositol, D-mannitol, D-fructose, rhamnose, raffinose, and L-arabinose Actinomyces are being studied in phytopathological tests The strain was maintained on PDA (potato-dextrose-agar 200-20-15 g/l) in a test tube and subcultured in shaked liquid MPGB (malt extract–peptone–glucose 4 1 4 g/l) in a 300 ml Erlenmeyer flask for 48 hr at 24 This preinoculum was used to inoculate 40 Roux flasks containing MPGA (100 ml) (malt extract–peptone–glucose–agar 4 1 4 g/l) Flasks were incubated for 10 days at 24° The flasks were then extracted twice with EtOAc containing 1% MeOH The extracts were dried (Na_2SO_4) and evapd to give a mixture of crude metabolites The mixt was chromatographed on a column of silica gel using firstly hexane–EtOAc mixts and then EtOAc–MeOH mixts and purified further by prep TLC to give metabolite **1** (600 mg) and **11** (500 mg) from 40 flasks

2-*Tetrahydro*-3′(*deca*-2″E,4″E-*dienoate*)-4′-*hydroxy*-2′-*methyl*-6′H-*pyran*-6′*yl*-1,6,10-*trihydroxy*-8-*methyl-naphthacene*-5,12-*dione*, **1** UV λ_{max} nm 265, 300, 370, 490 (ε 104 000, 20 800, 5600, 18 800), IR ν_{max}^{KBr} cm^{-1} 3450 (OH), 1710 (CO ester), 1685 (CO quinone), 1635 and 1615 (C=C), ^1H NMR see Table 2, ^{13}C NMR (DMSO) δ 187 22 s, 186 23 s, 166 01 s, 162 10 s, 158 28 s, 155 86 s, 145 32 *d*, 145 13 *d*, 141 77 s, 136 75 s, 132 85 *d*, 132 20 s, 128 20 *d*, 128 13 *s*, 125 00 s, 124 07 s, 118 93 *d*, 118 46 *d*, 116 68 *d*, 116 16 *d*, 116 11 s, 114 18 *d*, 108 67 s, 77 40 *d*, 73 58 *d*, 70 65 *d*, 68 86 *d*, 37 87 *t*, 32 25 *t*, 30 72 *t*, 27 73 *t*, 21 79 *q*, 21 79 *t*, 17 87 *q*, and 13 80 *q*

(S)-1,3-*Dihydroxy*-6E,8E-*decadien*-5-*one*, **11** Oil, EIMS *m/z* 184 (23) $[M]^+$, 169 (100), 166 (45), 149 (33), 147 (48), 96 (90), UV λ_{max} nm 270 (ε 18 000), IR $\nu_{max}^{liquid\ film}$ cm^{-1} 3380 (OH), 1635 (CO), 1590 (CH = CH), ^1H NMR see Fig 1

1,6,10,4′-*Tetraacetoxy derivative*, **2** Compound **1** (50 mg) was dissolved in 2 ml of dry pyridine and treated with Ac_2O (4 ml) The mixt was left to stand at room temp for 12 hr, poured into ice-H_2O, neutralized (satd $NaHCO_3$) and extracted with EtOAc CC gave **2** (40 mg), mp 255°, UV λ_{max} nm 255, 295, 405 (ε 85 000, 35 840, 8190), IR ν_{max}^{KBr} cm^{-1} 1770 (CO acetate), 1740 (CO ester), 1675 (CO quinone), ^1H and ^{13}C NMR see Tables 2 and 3

Methanolysis of **1** Compound **1** (500 mg) was treated with 20 ml of 0 25 M KOH in MeOH at 60° for 4 hr Evapn of solvent, dil with H_2O, neutralization and extraction with EtOAc gave after CC with hexane–EtOAc (1 1) and EtOAc–MeOH (9 1), compounds **3** (70 mg) and **4** (210 mg)

2-(*Tetrahydro*-3′,4′-*dihydroxy*-2′-*methyl*-6′H-*pyran*-6-*yl*-1,6, 10-*trihydroxy*-8-*methyl-naphthacene*-5,12-*dione*, **3** Needles, mp 295 , $[\alpha]_D$ + 189 9° (*c* 0 1, MeOH), FAB-MS *m/z* 450, UV λ_{max} nm 250 sh, 265, 290, 305 sh, 390 sh, 495 (ε 41 478, 59 478, 18 000, 12 521, 5380, 18 782), IR ν_{max}^{KBr} cm^{-1} 3430 (OH), 1615 (CO) ^1H NMR see Table 2

Deca-2E,4E-*dienoic acid*, **4** Oil, UV λ_{max} nm 253 (ε 22 938), IR $\nu_{max}^{liquid\ film}$ cm^{-1} 3420 (OH), 1695 (CO), 1650 (C = C)

10-*Methoxy*-1,6,3′,4′-*tetraacetoxy derivative* **5** Compound **3** (220 mg) in dry DMF (5 ml) was treated with excess CH_2N_2–Et_2O at 0 and allowed to stand for 2 days The resulting compound (100 mg), obtained after chromatography, was acetylated as for **1**, poured into ice -H_2O and filtered to give **5**, mp 280° (C_6H_6 -MeOH), UV λ_{max} nm 258, 300 318 443 (ε 69 600, 18 980, 7850, 8545), IR ν_{max}^{KBr} cm^{-1} 1770 and 1745 (CO acetate), 1670 (CO quinone), ^1H NMR see Table 2

1,6,10,4′-*Tetramethoxy derivative* **6** Compound **3** (100 mg) in dry Me_2CO (20 ml) was refluxed 24 hr with MeI (1 ml) and Ag_2O (100 mg) Filtration and evapn of solvent afforded **6** as a glassy solid, UV λ_{max} nm 256 285sh, 298sh, 340, 430, (ε 37 680, 12 111 10 362, 4306, 5517), IR ν_{max}^{KBr} cm^{-1} 3430 (OH), 1670 (CO) ^1H NMR see Table 2

Deca-2E,4E-*dienoic acid methyl ester*, 7 Compound **4** (70 mg) was dissolved in Et_2O (5 ml) and treated with CH_2N_2 -Et_2O at 0° overnight Evapn of solvent and prep TLC in hexane EtOAc (7 3) gave **7** as an oil MS *m/z* 182 $[M]^+$, 167, 149, 74, 59, ^1H NMR ($CDCl_3$–C_6H_6-d_6, 1 1) δ 0 87 (3H, *t*, *J* = 6 8 Hz, H_3-10″), 1 25 (4H, *m*, H_2-8″ and H_2-9″) 1 32 (2H, *m*, H_2-7″), 2 04 (2H, *br dt*, *J* = *ca* 6 5 and 7 Hz, H_2-6″), 3 61 (3H, s, OMe-1″), 5 76 (1H, *brd*, *J* = 15 4 Hz, H-2″), 5 98 (1H, *br dt*, *J* = 15 2 and 6 5, H-5″), 6 05 (1H, *br dd*, *J* = 15 2 and 9 9 Hz, H-4″), and 7 27 (1H *br dd*, *J* = 15 4 and 9 9 Hz, H-3″), ^{13}C ($CDCl_3$) δ 14 01 (*q*, C-10″), 22 49 (*t*, C-8″), 28 40 (*t*, C-7″), 31 40 (*t*, C-9″), 32 99 (*t* C-6″) 51 43 (*q*, OMe-1″), 118 67 (*d*, C-2″), 128 32 (*d*, C-4″), 145 00 (*d* C-5″), 145 43 (*d*, C-3″), and 167 76 (s, C-1″)

(S)-1-*Acetoxy*-3-*hydroxy*-6E,8E-*decadien*-5-*one*, 12 Compound **11** (100 mg) was dissolved in dry pyridine (3 ml) and treated with Ac_2O (6 ml) The soln was left to stand at 0 for 30 min, the mixt was then poured into ice-H_2O, neutralized and extracted with EtOAc Prep TLC (hexane–EtOAc 1 2) gave **12** (20 mg) and **13** (50 mg), as oils ^1H NMR ($CDCl_3$) δ 1 89 (3H *d*, *J* = 6 3 Hz, H_3-10), 1 9 (2H, *m* H_2-2), 2 08 (3H, s, Ac), 2 71 (2H, *m*, H_2-4), 3 40 (1H, *br*, OH-3), 4 22 (1H, *m* H-3) 4 26 (2H, *m*, H_2-1), 6 06 (1H, *br d*, *J* = 15 6, H-6), 6 20 (1H, *m*, H-8), 6 25 (1H *m*, H-9), and 7 18 (1H, *m*, H-7)

(S)-1,3-*Diacetoxy*-6E,8E-*decadien*-5-*one*, 13 Oil MS *m/z* 268 $[M]^+$, 250, 176, 120, 91, 60, 43, ^1H NMR ($CDCl_3$) δ 1 89 (3H, *d*, *J* = 6 3 Hz, H_3-10), 1 9 (2H, *m*, H_2-2), 2 08 and 2 06 (6H, s, 2Ac), 2 78 and 2 93 (2H, *m*, H_2-4), 4 13 (2H, *m*, H_2-1), 5 35 (1H *m*, H-3), 6 06 (1H, *br d*, *J* = 15 6 Hz, H-6), 6 20 (1H *m*, H-8), 6 25 (1H, *m*, H-9), and 7 16 (1H, *m*, H-7)

(S)-1,3-*Dihydroxy-decan*-5-*one*, **14** Decanol **11** (300 mg) was dissolved in EtOAc (25 ml) and hydrogenated in the presence of Pd 10%-C (30 mg) at 20 psi for 24 hr Filtration and evapn of solvent gave **14**[8] as an oil (200 mg) $[\alpha]_D$ + 26 ($CHCl_3$ *c* 2 6), ^1H NMR ($CDCl_3$) δ 0 89 (3H, *t*, *J* = 6 7 Hz H_3-10), 1 3 (4H, *m*, H_2-8 and H_2-9), 1 57 (2H, *m*, H_2-7), 1 68 (2H *m*, H_2-2), 2 44 (2H, *d*, *J* = 7 4 Hz, H_2-6), 2 63 (1H, *dd*, *J* = 17 2 and 7 6 Hz, H-4A), 2 60 (1H, *dd*, *J* = 17 2 and 4 6, H-4B), 3 60 and 4 00 (2H, *br*, OH-1 and OH-3), 3 79 (2H, *m*, H_2-1), and 4 30 (1H, *m*, H-3), ^{13}C ($CDCl_3$) δ 13 91 (*q*, C-10), 22 43 (*t*, C-9), 23 20 (*t*, C-7), 31 31 (*t*, C-8), 38 05 (*t*, C-2), 43 64 (*t*, C-6), 49 30 (*t*, C-4), 60 44 (*t*, C-1), 67 03 (*d*, C-3), and 212 07 (s, C-5)

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