The Absolute and Relative Configuration of the Molluscicides Ethuliacoumarin A and Isoethuliacoumarin A

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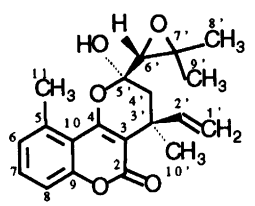
The relative and absolute configuration of ethuliacoumarin A has been established as (3′*S*,5′*R*,6′*R*) by means of an X-ray analysis based on the anomalous scattering of oxygen. The result was further confirmed by an X-ray structure determination of the (*S*)-2-methylbutanoic ester of the coumarin. An acid-catalysed conversion of ethuliacoumarin A into isoethuliacoumarin A enabled the determination of the relative and absolute configuration of this coumarin. The absolute configurations are the reverse of the arbitrarily chosen configurations previously shown in the literature.

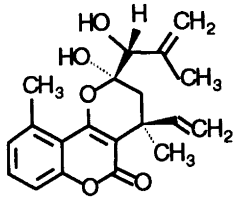
The crystals of both ethuliacoumarin A and its (*S*)-2-methylbutanoic ester are orthorhombic [$P2_12_12_1$, a = 6.9685(8), b = 20.755(1), c = 11.9252(9), Z = 4; and $P2_12_12$, a = 12.1733(5), b = 13.4935(9), c = 14.5012(9), Z = 4, respectively]. The coumarin skeletons, with the adjacent hydropyran rings of the two molecules, are very similar, but differences occur in the conformations of the allyl and oxirane side chains. In addition, inversion at the acetal carbon atom of ethuliacoumarin A takes place during the esterification reaction with the corresponding anhydride.

The aerial parts of the Egyptian plant *Ethulia conyzoides* (Asteraceae) have been used in folklore medicine as an anthelmintic agent.[1] An extract of the leaves also exhibits molluscicidal activity.[2]

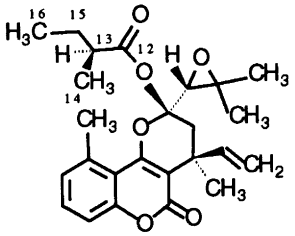
Whereas ethuliacoumarin A (**1**) is the only anthelmintic secondary constituent of *E. conyzoides*,[3] molluscicidal activity is also exhibited by isoethuliacoumarin A (**2**).[4] The structures of ethuliacoumarin A and isoethuliacoumarin A suggested in the literature[5–7] are mainly based on ^{1}H NMR spectroscopic studies.[5–7] The presence of two chiral quaternary carbons, however, makes it difficult to elucidate the relative configuration by NMR spectroscopy and the methods applied do not permit the establishment of the absolute configuration. The biological properties[4] make the coumarins interesting leads for the development of a new type of molluscicide, which can be used for the control of schistosomiasis, a major spreading disease in many tropical and subtropical countries. In order to use any compound as a lead an unequivocal establishment of the structure, including the determination of the absolute configuration, is necessary. We have fulfilled this requirement for ethuliacoumarin A by performing an X-ray structure analysis. This method permitted the establishment of the absolute configuration of the molecule using oxygen as the principal contributor to anomalous scattering. Further confirmation of the assignment of the absolute configuration was obtained by performing an X-ray structure determination on a derivative of **1** containing a chiral centre with known abso-



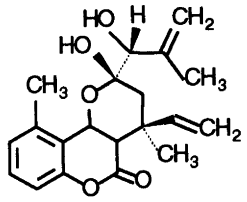
1



2a



3



2b

Scheme 1.

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lute configuration (**3**). Based on the structure of **1** and the conversion of **1** into isoethuliacoumarin A (**2**) the relative and absolute configuration of this molluscicide is also established.

Results and discussion

Chemistry. A bioassay-directed fractionation of the constituents in an extract of the aerial parts of *Ethulia conyzoides* led to the isolation of **1**.[4] The derivative **3** containing an asymmetric centre of known absolute configuration was obtained by allowing the 5′-hydroxy group react with (*S*)-2-methylbutanoic anhydride using 4-dimethylaminopyridine as a catalyst.

Comparison of different reports on the isolation of **1** and **2** from *E. conyzoides* reveals that the ratio of the yields of the two coumarins differs considerably.[3,5] These variations might be explained by dependence on the age or the variety of the plant, or **1** might be isomerized into **2** during the isolation, since we found that this isomerization is easily performed under acidic conditions. The addition of trifluoroacetic acid to a solution of **1** rapidly caused decomposition of the starting material. Three reaction products were detected by TLC but only one could be isolated. The isolated product was shown to be identical with **2**. Since this transformation must be expected to involve protonation of the oxygen of the epoxide followed by opening of the three-membered ring and elimination of a proton (Scheme 2) the absolute configuration at C-3′ and C-6′ of **1** and **2** must be identical. In contrast with previous reports our NMR spectra of **2** clearly established that two isomers were present in the solution. The presence of a cyclic hemiacetal structural unit makes it likely that the two isomers are **2a** and **2b** (Scheme 1), respectively. No similar mixture of epimers was observed in the spectra of **1**.

X-Ray structures. The atomic numbering schemes and the ORTEP drawings[8] of **1** and **3** are shown in Figs. 1 and 2. The chirality of **3** (3′*S*,5′*R*,6′*R*,13*S*) shown in Fig. 2 was chosen to conform to the known absolute configuration of the (*S*)-2-methylbutanoic ester group. Fig. 1 shows the absolute configuration of **1** as determined by the X-ray analysis (3′*S*,5′*R*,6′*R*). This determination, which is mainly based on anomalous scattering of oxygen and therefore requires careful treatment of good quality data, is supported as it is in agreement with the result of the structure determination of **3**. The X-ray analysis of the two compounds revealed that an inversion at C5′ occurs during the reaction of **1** with (*S*)-2-methylbutanoic anhydride. This inversion is probably caused by the catalyst 4-dimethylaminopyridine as indicated in Scheme 3.

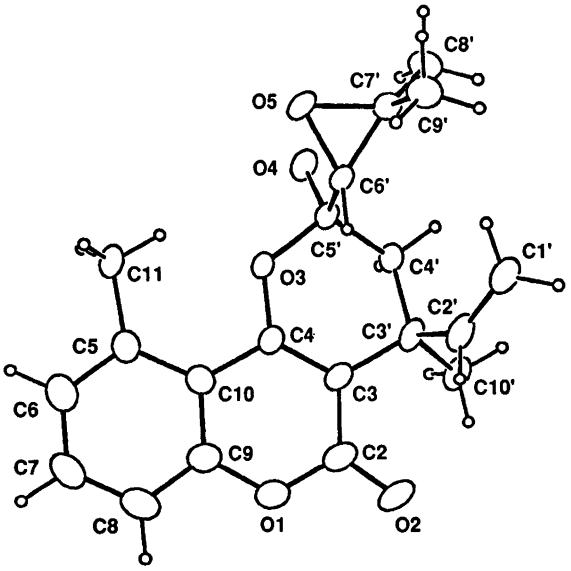


Fig. 1. ORTEP drawing of **1** with thermal ellipsoids at the 50 % probability level for non-H atoms.

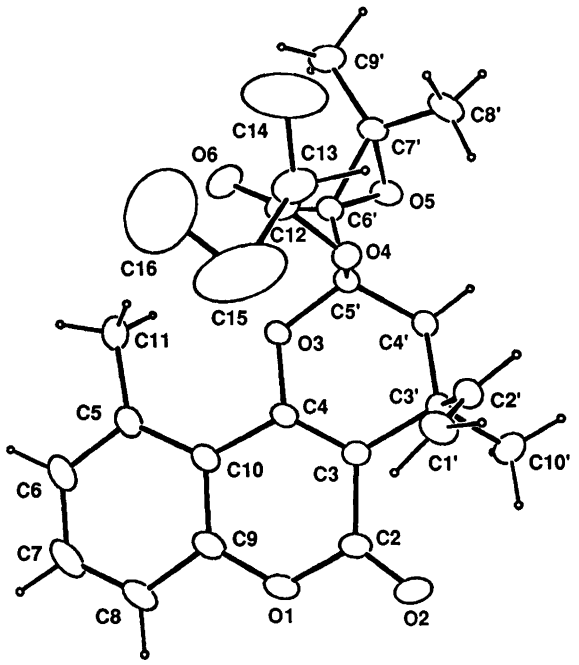
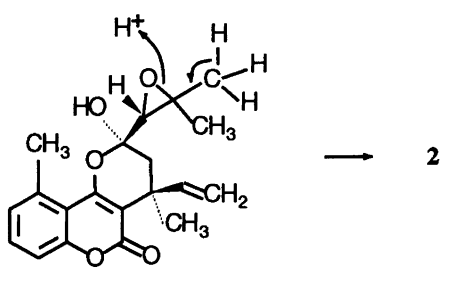
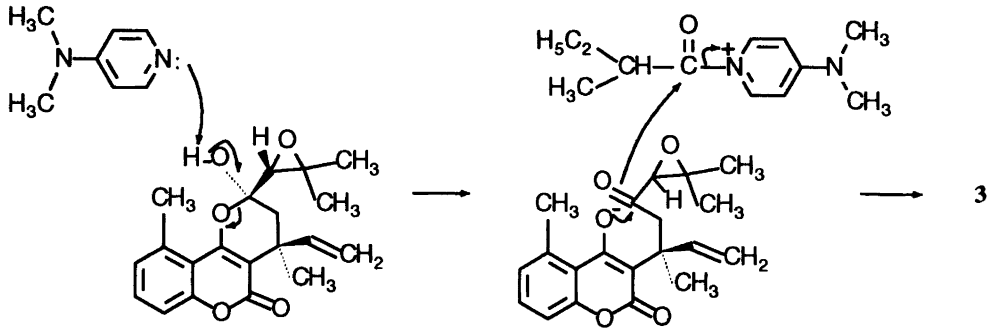


Fig. 2. ORTEP drawing of **3** with thermal ellipsoids at the 20 % probability level for non-H atoms.



1 → **2**

Scheme 2.



Scheme 3.

The overall conformations of the ring systems of **1** and **3** are similar with almost planar coumarin skeletons, and with sofa conformations of the adjacent hydropyran rings. In both compounds all atoms of this ring are in a plane, to within ± 0.05 Å, except C4′, which is displaced 0.523(2) and 0.583(3) Å in **1** and **3**, respectively, from the least-squares planes through the other five atoms of the rings. The conformations of the allyl groups at C3′ are different in the two compounds as well as those of the oxirane rings attached to C5′. The torsion angles C3–C3′–C2′–C1′ are −142.3(3) and −10.2(6)° in **1** and **3**, respectively, and the torsion angles C4′–C5′–C6′–O5 are 146.8(2) and 0.8(4)°, respectively. The twist of the oxirane ring in **3** compared with **1** may be a steric consequence of the acylation of the OH group at C5′, which further forces the allyl group to be twisted 'downward' instead of 'upward' as in **1** (see Figs. 1 and 2). Whether the conformation of the oxirane ring of **1** is determined by an intramolecular hydrogen bond (O4–H---O5) cannot be stated, because this H atom was not found in the difference electron density map. The O4---O5 distance is 2.703(2) Å, but a distance of similar length [2.796(2) Å] is found between O4 and O5 of a neighbouring molecule ($x-½, -y+½, -x+2$), so intermolecular hydrogen bonding is also possible.

The carbon atoms of the methyl and ethyl groups of the 2-methylbutanoic ester side chain of **3** have large thermal parameters, which indicate the presence of minor disorder, but it was not resolvable as a discrete disorder. The calculated values of bonds and angles involving these C-atoms should be taken with reservations, (e.g. the long C13–C15 bond and the small C13–C15–C16 angle). Good agreement was found between corresponding bonds and angles in **1** and **3** (Tables 4 and 5). No other ethuliacoumarin structures were found in the Cambridge Structural Database (CSD, January 1991).[9] The packing of the molecules in the crystals is dominated by van der Waals' forces in both structures. The possible intermolecular OH---O bond of **1** mentioned above is the only hydrogen bond found in the two crystal structures.

The first determination of the absolute configuration of **1** has been performed in this work. It should be noted that the absolute configuration established by the X-ray analyses is the reverse of that given in the literature for **1**[5] and related coumarins (for a review, see Ref. 10) in which an arbitrary choice was made.

The present study has created a basis for the use of **1** and **2** as lead structures for the development of new pesticides for control of the disease schistosomiasis. In contrast with the saponin molluscicides these coumarins also possess cercaricidal and ovicidal activity.[4]

Experimental

General methods. The NMR spectra were recorded on a Bruker AM 250 spectrometer. Standard pulse sequences (Bruker pulse program library) were used for ^{13}C–^{1}H heteronuclear correlated spectroscopy. Optical rotations were measured with a Perkin-Elmer 241 polarimeter. UV spectra were recorded in methanol with a Shimadzu 265 UV–VIS spectrophotometer. IR spectra were recorded for potassium bromide discs with a Perkin-Elmer 781 IR spectrophotometer. Column chromatography was performed over silica gel (Merck 0.063–0.200 mm) and silanised silica gel (Merck 0.063–0.200 mm, RP 2).

Isolation. Air-dried leaves of *Ethulia conyzoides L.* (500 g) collected on the banks of the Nile near Mansoura in summer 1988, identified by Dr. A. A. Arafa, Department of Botany, Mansoura University, were cut and extracted with ethanol at room temperature for 24 h. The extract was concentrated *in vacuo* to give a residue (41 g), which was taken up in toluene. The toluene solution was decolourized with charcoal, then chromatographed over silica gel using hexane, to which increasing amounts (5–50 %) of ethyl acetate were added, as the eluent to give **1** (5.6 g) and a fraction in which the more polar **2** could be detected. The fraction containing **2** was chromatographed over silanised silica gel using methanol–water (3 : 2) as the eluent to give **2** (134 mg).

Compound **1**. Colourless crystals from hexane–EtOAc, m.p. 57–60 °C, rearranging to another modification, m.p. 100–102 °C; $[\alpha]_D^{24}$ +41.9° (*c* 0.10, $CHCl_3$); IR (KBr): 3380 (m), 3080 (w), 1710 (s), 1635 (w), 1610 (s), 1600 (s), 1560 (s), 1235 (m), 900 (m) cm^{-1}. UV [methanol(log ε)]: 322

Table 1. NMR data for the 5-methylcoumarins **1**, **2** and **3**.[a]

^{1}H NMR (δ)	^{13}C NMR[b] (δ)
Compound **1**	
7.33 (1 H, dd, *J* 8.0, 7.7 Hz, H-7)	160.4, 160.0 (C-2, C-4)
7.13 (1 H, dd, *J* 8.0, 0.7 Hz, H-8)	154.0 (C-9)
7.01 (1 H, dd, *J* 7.7, 0.7 Hz, H-6)	145.1 (C-2′)
6.11 (1 H, dd, *J* 17.5, 10.7 Hz, H-2′)	137.1 (C-5)
5.13 (1 H, d, *J* 10.7 Hz, H-1$_1$′)	130.9 (C-7)
5.10 (1 H, d, *J* 17.5 Hz, H-1$_2$′)	127.5 (C-6)
4.24 (1H, s, OH)	114.8 (C-8)
3.13 (1 H, s, H-6′)	114.4 (C-10)
2.72 (3 H, s, H-11)	112.7 (C-1′)
2.22 (1 H, d, *J* 14.2 Hz, H-4$_1$′)	106.5 (C-3)
2.02 (1 H, d, *J* 14.2 Hz, H-4$_2$′)	97.2 (C-5′)
1.69 (3 H, s, H-10′)	66.5 (C-6′)
1.48 (3 H, s, H-8′)	59.4 (C-7′)
1.37 (3 H, s, H-9′)	42.0 (C-4′)
	36.0 (C-3′)
	25.2, 25.1 (C-9′, C-10′)
	24.0 (C-11)
	17.7 (C-8′)
Compound **2a**[c]	
7.34 (1 H, dd, *J* 8.0 Hz, H-7)	159.0 (C-2, C-4)
7.15 (1 H, d, *J* 8.0 Hz, H-8)	153.8 (C-9)
7.01 (1 H, d, *J* 8.0 Hz, H-6)	146.0 (C-2′)
6.11 (1 H, dd, *J* 17.5, 10.7 Hz, H-2′)	142.0 (C-7′)
5.18 (4 H, m, H-9′, H-1′)	136.6 (C-5)
4.48 (1 H, d, *J* 3 Hz, OH-6′)	130.7 (C-7)
4.37 (1 H, d, *J* 3 Hz, H-6′)	127.4 (C-6)
2.74 (3 H, s, H-11)	117.5 (C-9′)
2.26 (1 H, d, *J* 14.5 Hz, H-4$_1$′)	114.8 (C-8)
2.09 (1 H, d, *J* 14.5 Hz, H-4$_2$′)	114.5 (C-10)
1.86 (3 H, s, H-8′)	111.9 (C-1′)
1.56 (3 H, s, H-10′)	107.5 (C-3)
	99.8 (C-5′)
	80.0 (C-6′)
	40.8 (C-4′)
	35.4 (C-3′)
	24.1 (C-10′)
	23.7 (C-11)
	17.6 (C-8′)
Compound **2b**[c]	
7.35 (1 H, dd, *J* 8.0 Hz, H-7)	159.0 (C-2, C-4)
7.18 (1 H, d, *J* 8.0 Hz, H-8)	153.8 (C-9)
7.04 (1 H, d, *J* 8.0 Hz, H-6)	144.5 (C-2′)
6.20 (1 H, dd, *J* 17.5, 10.7 Hz, H-2′)	142.5 (C-7′)
5.18 (4 H, m, H-9′, H-1′)	137.1 (C-5)
4.48 (1 H, d, *J* 3 Hz, OH-6′)	131.1 (C-7)
4.30 (1 H, d, *J* 3 Hz, H-6′)	127.7 (C-6)
2.77 (3 H, s, H-11)	115.9 (C-9′)
1.91 (3 H, s, H-8′)	115.5 (C-10)
1.85 (1 H, d, *J* 15.3 Hz, H-4$_1$′)	114.8 (C-8)
1.78 (1 H, d, *J* 15.3 Hz, H-4$_2$′)	114.1 (C-1′)
1.61 (3 H, s, H-10′)	Not found (C-3)
	101.8 (C-5′)
	78.8 (C-6′)
	38.7 (C-4′)
	35.7 (C-3′)
	27.0 (C-10′)
	24.1 (C-11)
	19.3 (C-8′)

cont.

Table 1. (continued).

^{1}H NMR (δ)	^{13}C NMR[b] (δ)
Compound **3**	
7.35 (1 H, dd, *J* 8.2, 7.5 Hz, H-7)	174.3 (C-12)
7.13 (1 H, dd, *J* 8.2, 0.5 Hz, H-8)	160.2, 158.6 (C-2, C-4)
7.04 (1 H, dd, *J* 7.5, 0.5 Hz, H-6)	154.0 (C-9)
6.24 (1 H, dd, *J* 17.5, 10.7 Hz, H-2′)	143.7 (C-2′)
5.10 (1 H, dd, *J* 10.7, 0.7 Hz, H-1$_1$′)	137.4 (C-5)
5.09 (1 H, dd, *J* 17.5, 0.7 Hz, H-1$_2$′)	131.2 (C-7)
3.76 (1 H, s, H-6′)	127.8 (C-6)
2.79 (3 H, s, H-11)	114.8 (C-8)
2.37 (1 H, d, *J* 15.4 Hz, H-4$_1$′)	113.9 (C-10)
2.26 (1 H, tq, *J* 7.0 Hz, H-13)	112.2 (C-1′)
2.10 (1 H, d, *J* 15.4 Hz, H-4$_2$′)	107.9 (C-3)
1.61 (3 H, s, H-10′)	100.6 (C-5′)
1.44 (2 H, dq, *J* 7.0 Hz, H-15)	67.4 (C-6′)
1.38 (3 H, s, H-8′)	59.3 (C-7′)
1.35 (3 H, s, H-9′)	42.1 (C-4′)
1.05 (3 H, d, *J* 7.0 Hz, H-14)	40.7 (C-13)
0.61 (3 H, t, *J* 7.0 Hz, H-16)	35.1 (C-3′)
	27.2, 26.4, 25.2, 23.7 (C-11, C-9′, C-10′, C-15)
	19.0 (C-8′)
	16.1 (C-14)
	10.8 (C-16)

[a]The spectra were recorded in $CDCl_3$ with Me_4Si as an internal standard. [b]A ^{13}C–^{1}H correlated spectrum and a gated ^{13}C spectrum were used for the assignment of the signals. [c]The spectrum of **2** reveals the presence of the two epimers **2a** and **2b**. The assignments of the spectra of the two epimers may be interchanged.

(sh, 3.65), 308 (sh, 3.89), 291 (4.10), 282 (4.08) nm. NMR data are given in Table 1.

Compound **2**. Colourless crystals from methanol–water, m.p. 155–156 °C; $[\alpha]_D^{24}$ −22.7° (*c* 0.40, $CHCl_3$); IR (KBr): 3370 (m), 3070 (w), 1680 (s), 1645 (w), 1590 (s), 1550 (s), 905 (m) cm^{-1}. UV [methanol log ε)]: 321 (sh, 3.68), 308 (sh, 3.90), 292 (4.13), 283 (4.10) nm. NMR data are given in Table 1.

Preparation of **3**. A solution of **1** (200 mg), 4-dimethylaminopyridine (200 mg) and (*S*)-2-methylbutanoic anhydride[11] (240 mg) in dichloromethane (40 ml) was left for 24 h at room temperature. The mixture was concentrated *in vacuo* and the residue was chromatographed over silica gel using hexane–EtOAc (7 : 1) as the eluent to give **3** (202 mg, 81 %). Colourless crystals from hexane, m.p. 94–99 °C; $[\alpha]_D^{24}$ −40° (*c* 0.10, $CHCl_3$); IR (KBr): 3070 (w), 1745 (s), 1725 (s), 1635 (w), 1610 (s), 1600 (s), 1560 (s), 1245 (m), 1160 (s), 915 (s) cm^{-1}. UV [methanol (log ε)]: 320 (sh, 3.63), 308 (sh, 3.82), 290 (4.09), 282 (4.09) nm. NMR data are given in Table 1.

Table 2. Crystal data for **1** and **3**.

	1	**3**
Formula	$C_{20}H_{22}O_5$	$C_{25}H_{30}O_6$
Formula weight/g mol^{-1}	342.34	426.44
Space group	$P2_12_12_1$	$P2_12_12$
Melting point/°C (uncorr.)	100–102	96–99
a/Å	6.9685(8)	12.1733(5)
b/Å	20.755(1)	13.4935(9)
c/Å	11.9252(9)	14.5012(9)
V/Å^3	1724.8(2)	2382.0(2)
Z	4	4
D_c/g cm^{-3}	1.319	1.189
μ/mm^{-1}	0.73	0.65
F(000)	728	912

Conversion of **1** *into isoethuliacoumarin A* (**2**). Trifluoroacetic acid (0.5 ml) was added to a solution of **1** (500 mg) in toluene (12 ml). The solution was left for 30 min at room temperature and concentrated *in vacuo*. The residue was chromatographed over silica gel using hexane–EtOAc(5:1) as the eluent to give 68.8 mg of a product, m.p. 155–156 °C, the IR spectrum of which was superimposable on that of **2**, isolated from the plant.

X-Ray structure determinations. Crystals of **1** and **3** were obtained by slow cooling: for **1** from a solution in hexane and ethyl acetate, and for **3** from a solution in hexane. The crystals of both compounds are colourless plates. The crystal of **1** chosen for data collection was 0.08×0.22×0.38 mm and that of **3** was 0.20×0.25×0.50 mm. The data were collected on an Enraf-Nonius CAD-4 diffractometer equipped with a graphite monochromator (Cu radiation, λ = 0.5418 Å) and Nonius low-temperature device. The temperature was kept to within ±0.5 K from an estimated value of 105(5) K for the data collection of **1**. The data of **3** were collected at room temperature, because the crystals of this compound decomposed on cooling. Cell dimensions were determined by a least-squares fit of angular settings for 25 reflections (θ range 40.23–43.54°) in the case of **1**, and for 18 reflections (θ range 39.25–48.05°) in the case of **3**. A summary of crystal data is given in Table 2. The intensities were measured by the ω–2θ scan method for θ ≤

Table 3. Fractional atomic coordinates and equivalent isotropic thermal parameters[a] (Å^2) for non-hydrogen atoms of **1** amd **3**.

Atom	*x*	*y*	*z*	B_{eq}	Atom	*x*	*y*	*z*	B_{eq}
Compound **1**									
O1	0.9454(3)	0.35207(9)	0.4097(2)	2.81(3)	C4′	0.8284(3)	0.4062(1)	0.8019(2)	2.16(4)
C2	0.9509(4)	0.4001(1)	0.4892(2)	2.83(5)	C1′	1.1917(5)	0.4866(1)	0.7987(3)	3.54(5)
O2	0.9727(3)	0.45425(9)	0.4533(2)	3.95(4)	C2′	1.1112(4)	0.4664(1)	0.7074(3)	2.93(5)
C3	0.9272(3)	0.3829(1)	0.6063(2)	2.04(4)	C10′	0.7710(4)	0.4894(1)	0.6585(2)	2.92(5)
C4	0.9234(3)	0.3191(1)	0.6345(2)	1.93(4)	C5′	0.9028(3)	0.3407(1)	0.8359(2)	1.97(4)
C5	0.9337(3)	0.2007(1)	0.5720(2)	2.23(4)	O3	0.9049(3)	0.29691(7)	0.7392(1)	2.28(3)
C6	0.9339(4)	0.1588(1)	0.4821(2)	2.91(5)	O4	0.7706(3)	0.31428(8)	0.9085(2)	2.50(3)
C7	0.9372(4)	0.1802(1)	0.3715(2)	3.02(5)	C6′	1.1053(3)	0.3389(1)	0.8816(2)	1.86(4)
C8	0.9402(4)	0.2453(2)	0.3488(2)	3.06(5)	O5	1.1390(2)	0.29084(7)	0.9667(1)	2.36(3)
C9	0.9784(3)	0.2878(1)	0.4383(2)	2.53(4)	C7′	1.1659(3)	0.3591(1)	0.9945(2)	2.14(4)
C10	0.9321(3)	0.2681(1)	0.5503(2)	2.04(4)	C8′	1.0278(4)	0.3867(1)	1.0796(2)	2.90(5)
C11	0.9360(4)	0.1716(1)	0.6879(2)	2.66(4)	C9′	1.3716(4)	0.3784(1)	1.0101(2)	2.86(5)
C3′	0.9132(3)	0.4359(1)	0.6942(2)	2.36(4)					
Compound **3**									
O1	0.1560(2)	0.6264(2)	0.3570(2)	8.50(7)	C6	0.1391(3)	0.6187(3)	0.0773(3)	8.00(9)
O2	0.1883(3)	0.5639(2)	0.4937(2)	11.22(9)	C7	0.1317(3)	0.7066(3)	0.1240(4)	9.5(1)
O3	0.1707(2)	0.3568(1)	0.2310(1)	5.55(4)	C7′	0.1557(3)	0.0795(2)	0.2221(3)	6.79(8)
O4	0.3096(2)	0.2552(2)	0.2844(1)	6.09(5)	C8	0.1363(3)	0.7082(2)	0.2159(4)	8.3(1)
O5	0.0552(2)	0.1270(2)	0.2527(2)	7.38(6)	C8′	0.2196(4)	0.0308(3)	0.2968(4)	10.0(1)
O6	0.3334(2)	0.2376(2)	0.1322(2)	8.18(6)	C9	0.1485(3)	0.6195(2)	0.2633(3)	6.85(8)
C1′	0.3847(4)	0.3998(3)	0.4644(4)	9.8(1)	C9′	0.1449(4)	0.0206(3)	0.1357(3)	8.9(1)
C2′	0.3031(3)	0.3417(3)	0.4679(3)	7.37(9)	C10′	0.1104(4)	0.3603(4)	0.5155(3)	9.0(1)
C2	0.1746(4)	0.5460(2)	0.4137(3)	7.77(9)	C10	0.1554(2)	0.5296(2)	0.2184(2)	5.68(6)
C3′	0.1869(3)	0.3573(2)	0.4317(2)	6.33(8)	C11	0.1564(4)	0.4376(3)	0.0622(3)	8.4(1)
C3	0.1764(3)	0.4491(2)	0.3710(2)	5.94(7)	C12	0.3702(3)	0.2416(3)	0.2080(2)	6.93(8)
C4′	0.1480(3)	0.2691(2)	0.3733(2)	6.02(7)	C13	0.4902(4)	0.2329(4)	0.2325(3)	10.0(1)
C4	0.1686(2)	0.4435(2)	0.2786(2)	5.22(6)	C14	0.5438(6)	0.1558(6)	0.1918(8)	25.6(4)
C5′	0.1931(2)	0.2656(2)	0.2777(2)	5.40(6)	C15	0.5453(9)	0.352(1)	0.233(1)	31.5(5)
C5	0.1490(3)	0.5284(2)	0.1206(3)	6.61(8)	C16	0.5508(7)	0.327(1)	0.133(1)	32.7(7)
C6′	0.1410(3)	0.1876(2)	0.2157(2)	6.00(7)					

[a] $B_{eq} = 4/3\Sigma_i\Sigma_j\beta_{ij}\boldsymbol{a}_i\boldsymbol{a}_j$.

Table 4. Bond lengths (Å) for non-hydrogen atoms of **1** and **3**.

	1	3		1	3
O1–C2	1.377(3)	1.379(4)	C9–C10	1.398(3)	1.380(4)
O1–C9	1.377(3)	1.367(5)	C3′–C4′	1.542(3)	1.535(5)
C2–O2	1.212(3)	1.197(5)	C3′–C2′	1.527(3)	1.524(5)
C2–C3	1.451(3)	1.446(4)	C3′–C10′	1.549(3)	1.531(5)
C3–C4	1.368(3)	1.346(5)	C4′–C5′	1.511(3)	1.491(4)
C3–C3′	1.521(3)	1.525(4)	C1′–C2′	1.294(4)	1.266(6)
C4–C10	1.460(3)	1.462(4)	C5′–O3	1.467(3)	1.431(3)
C4–O3	1.337(3)	1.358(3)	C5′–O4	1.378(3)	1.429(3)
C5–C6	1.380(4)	1.376(5)	C5′–C6′	1.514(3)	1.523(4)
C5–C10	1.422(3)	1.421(5)	C6′–O5	1.443(3)	1.431(4)
C5–C11	1.508(4)	1.493(5)	C6′–C7′	1.473(3)	1.472(4)
C6–C7	1.392(4)	1.369(6)	O5–C7′	1.467(3)	1.452(4)
C7–C8	1.378(4)	1.334(7)	C7′–C8′	1.511(3)	1.487(6)
C8–C9	1.385(4)	1.388(5)	C7′–C9′	1.499(4)	1.490(6)
O4–C12		1.344(4)	C13–C14		1.36(1)
C12–O6		1.189(4)	C13–C15		1.74(2)
C12–C13		1.507(5)	C15–C16		1.49(2)

76° with $0 \le h \le 8$, $-26 \le k \le 26$, $-15 \le l \le 15$ for **1**, and $0 \le h \le 15$, $-16 \le k \le 16$, $-18 \le l \le 18$ for **3**.

Three standard reflections measured every 300 reflections showed no significant variations (less than 2 %). Intensities of 4361 reflections were measured for **1**, 3588 of which being unique (R_{int} = 0.025, based on I). Of these, 3127 reflections with $I \ge 3.0\sigma(I)$ were considered observed. Intensities of 6979 reflections were measured for **3**, 4968 being unique (R_{int} = 0.029, based on I). Of these, 2577 reflections with $I \ge 3.0\sigma(I)$ were considered observed. No absorption corrections were made. Both structures were solved by direct methods using SHELXS 86.[12] Full-matrix least-squares refinement of positional parameters for all atoms was carried out, with anisotropic temperature factors for all non-H atoms of both structures, and with H atoms included in the refinements as fixed contributions with the isotropic temperature factors fixed on the corresponding values of the atoms to which they are attached. All H atoms of **1** were located in difference electron density maps with the exception of that of the OH group at C5′, which was not included in the refinements. For **3** all H atoms were located in electron density ($\Delta\varrho$) maps, except those of the ester side chain at C5′. These H atoms were included in the refinements in their calculated positions. All other H atoms of **1** and **3** were included in the positions found in the $\Delta\varrho$ maps. The quantity minimized is $\Sigma w-(|F_o|-k|F_c|)^2$, where $w = 4F^2[\sigma^2(F^2) + (pF^2)^2]^{-1}$ and $p = 0.07$ for **1** and 0.08 for **3**. Weight analyses indicated these weighting schemes to be

Table 5. Bond angles (°) and selected torsion angles (°) for non-hydrogen atoms of **1** and **3**.

	1	3		1	3
C2–O1–C9	122.2(2)	123.4(3)	C3–C3′–C10′	111.7(2)	112.6(3)
O1–C2–O2	115.6(2)	116.2(3)	C4′–C3′–C2′	115.2(2)	111.7(3)
O1–C2–C3	118.8(2)	117.3(3)	C4′–C3′–C10′	105.7(2)	105.7(3)
O2–C2–C3	125.6(2)	126.6(3)	C2′–C3′–C10′	108.0(2)	107.2(3)
C2–C3–C4	118.5(2)	118.5(3)	C3′–C4′–C5′	116.9(2)	115.1(3)
C2–C3–C3′	119.5(2)	119.3(3)	C3′–C2′–C1′	127.8(3)	129.1(4)
C4–C3–C3′	121.9(2)	122.3(3)	C4′–C5′–O3	110.5(2)	110.1(2)
C3–C4–C10	122.2(2)	123.8(3)	C4′–C5′–O4	107.3(2)	107.8(2)
C3–C4–O3	124.4(2)	123.6(3)	C4′–C5′–C6′	116.0(2)	114.7(3)
C10–C4–O3	113.4(2)	112.6(3)	O3–C5′–O4	104.7(2)	107.8(2)
C6–C5–C10	118.5(2)	116.8(3)	O3–C5′–C6′	105.0(2)	103.6(2)
C6–C5–C11	117.4(2)	118.2(3)	O4–C5′–C6′	112.8(2)	112.6(2)
C10–C5–C11	124.1(2)	124.9(3)	C4–O3–C5′	121.5(2)	120.3(2)
C5–C6–C7	122.4(2)	123.2(4)	C5′–C6′–O5	115.0(2)	118.5(3)
C6–C7–C8	119.9(3)	120.3(4)	C5′–C6′–C7′	126.2(2)	126.7(3)
C7–C8–C9	118.4(2)	119.0(3)	O5–C6′–C7′	60.4(1)	60.0(2)
O1–C9–C8	115.2(2)	116.3(3)	C6′–O5–C7′	60.8(1)	61.4(2)
O1–C9–C10	121.5(2)	121.7(3)	C6′–C7′–O5	58.8(1)	58.6(2)
C8–C9–C10	123.4(2)	122.1(4)	C6′–C7′–C8′	122.6(2)	123.2(3)
C4–C10–C5	126.0(2)	126.4(3)	C6′–C7′–C9′	117.6(2)	117.7(3)
C4–C10–C9	116.5(2)	115.2(3)	O5–C7′–C8′	115.8(2)	114.4(3)
C5–C10–C9	117.6(2)	118.5(3)	O5–C7′–C9′	114.1(2)	114.7(3)
C3–C3′–C4′	108.1(2)	106.7(3)	C8′–C7′–C9′	115.1(2)	115.1(3)
C3–C3′–C2′	108.3(2)	112.8(3)			
C5′–O4–C12		120.2(2)	C12–C13–C14		114.9(5)
O4–C12–O6		124.2(3)	C12–C13–C15		107.7(3)
O4–C12–C13		110.5(3)	C14–C13–C15		121.4(6)
O6–C12–C13		125.4(3)	C13–C15–C16		78.6(9)
C3–C3′–C2′–C1′	−142.3(3)	−10.2(6)	C4′–C5′–C6′–O5	146.8(2)	0.8(4)
C5′–O4–C12–C13		179.9(3)	O4–C12–C13–C15		−88.5(6)
O4–C12–C13–C14		132.8(6)	C14–C13–C15–C16		52(1)

the preferred of several schemes attempted. The average and maximum values of Δ/σ in final refinement cycles are 0.01 and 0.03 for **1**, and 0.39 and 5.72 for **3**. The relatively high values of **3** are due to large thermal parameters for some of the C atoms of the ester side chain (disorder). The final error indicators are $R = 0.049$, $wR = 0.073$ for **1** and $R = 0.050$, $wR = 0.073$ for **3**. The fluctuations in the final $\Delta\varrho$ map syntheses are ± 0.3 e Å^{-3} in both structures. Scattering factors for the atoms were as implemented in the SDP program package,[13] which was used for all calculations.

The absolute configuration of **1** was determined by a procedure analogous to that described by Rogers,[14] resulting in the following R-values: $R = 0.04897$, $wR = 0.07275$, and R(reversed) = 0.04912, wR(reversed) = 0.07304. Hence the absolute configuration is established at a significance level better than 0.995 according to the Hamilton R-factor test.[15]

The final atomic parameters of **1** and **3** are listed in Table 3. Tables of anisotropic thermal parameters, hydrogen parameters, torsion angles and least-squares planes, and a listing of observed and calculated structure factors are available from the author (I.K.L.) on request. Bond lengths and angles are given in Tables 4 and 5.

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