Exciton Coupling in Circular Dichroic Spectroscopy as a Tool for Establishing the Absolute Configuration of α,β-Unsaturated Esters of Allylic Alcohols

Annette Lauridsen, Claus Cornett and S. Brøgger Christensen*

PharmaBiotec, Department of Organic Chemistry, Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen Ø, Denmark

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α,β-Unsaturated esters of allylic alcohols have been shown to exhibit exciton coupling by circular dichroic spectroscopy. This coupling permits the establishment of the absolute configuration. The method was used to prove the absolute configuration at C-2 of archangelolide. Detailed NMR spectral studies of the prepared model structures may be used as a reference for stereoisomeric guaianolides.

The allylic benzoate method has become an alternative to the Bijvoet X-ray method for determining the absolute configuration of cyclic allylic alcohols.[1,2] Esterification of an allylic alcohol with an aromatic acid yields an ester, the CD spectrum of which exhibits two Cotton effects of opposite sign (exciton split Cotton effects). This appearance originates in an exciton interaction between the two-chromphoric system consisting of the double bond and the benzoate group. Based on coupled oscillator theory, the aboslute configuration of the alcohol can be determined in a non-empirical way by the sign of the split Cotton effects. A positive sign, i.e. the component at the longer wavelength is positive and the shorter wavelength component negative, reflects a right-handed screw direction (a right-handed screwness, Fig. 1) and vice versa. The amplitude of the exciton coupling depends on (1) the spatial distance between the two coupling chromophores, (2) the difference between the wavelengths of the absorption maxima of the two chromophores, and (3) the angle between the electric transition dipole moments of the two chromophores. The choice of an appropriate aromatic acid makes it possible to obtain an observable exciton coupling and to shift the coupling to a wavelength where it is not obscured by other absorption bands. The ring structure of the alcohol defines the geometry of the two chromophores.[1,2] The method is used extensively for the determination of the chirality of allylic alcohols (for recent examples, see Refs. 3–7).

A cyclic allylic ester of an α,β-unsaturated acid is found in a number of sesquiterpene lactones e.g. thapsigargin (**1a**), trilobolide (**1b**) (Scheme 1), and archangelolide (**2a**) (Scheme 2). These esters are not hydrolysed to yield the allylic alcohol in a simple way. In principle, the α,β-unsaturated carbonyl group and the alkene should exhibit an exciton coupling and thus the chirality should be deducible from the CD spectrum.[8] In practice, however, the split Cotton effect is found at such a short wavelength that it overlaps with other bands, e.g. bands from the oxygenated γ-lactone moiety.[9] In order to verify the presence of the exciton coupling in allylic esters of α,β-unsaturated esters we decided to prepare the model compounds **4a–6c**. According to theory only the structures **4b** and **5b** should exhibit exciton coupling.

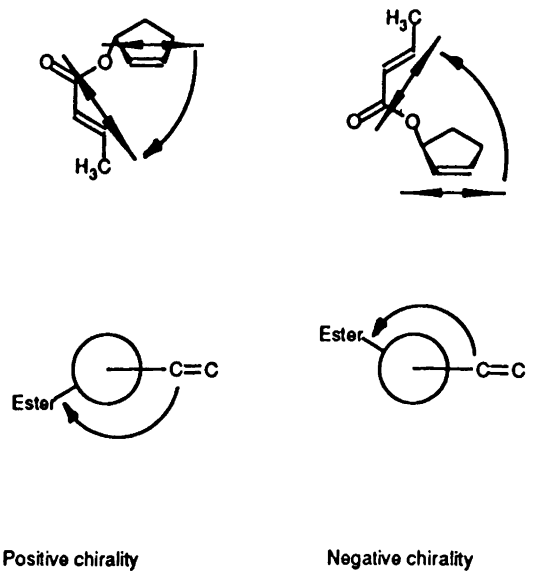
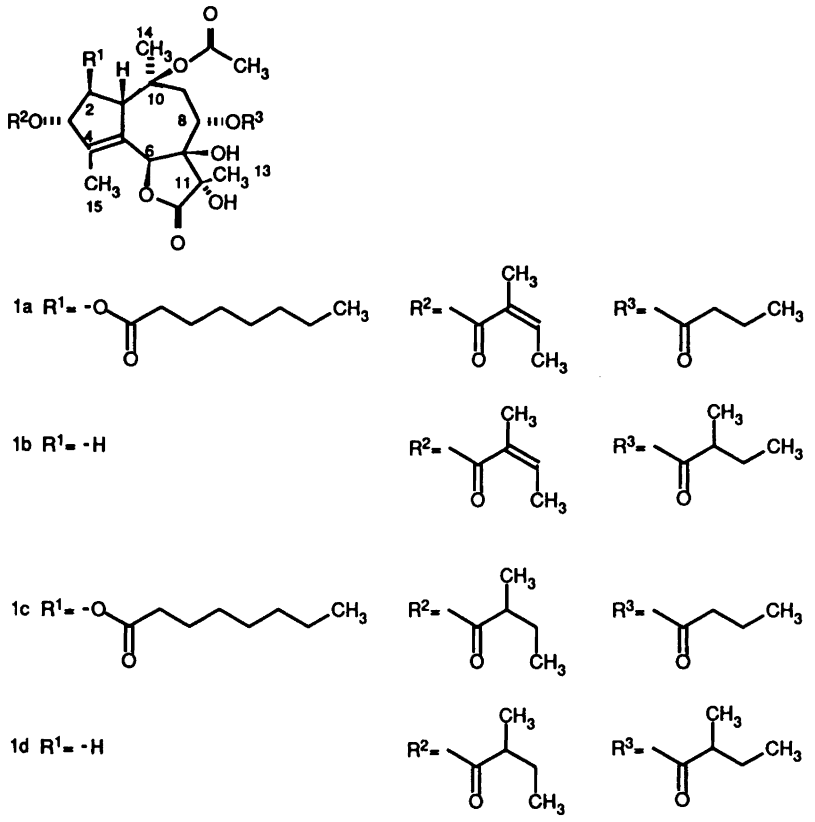
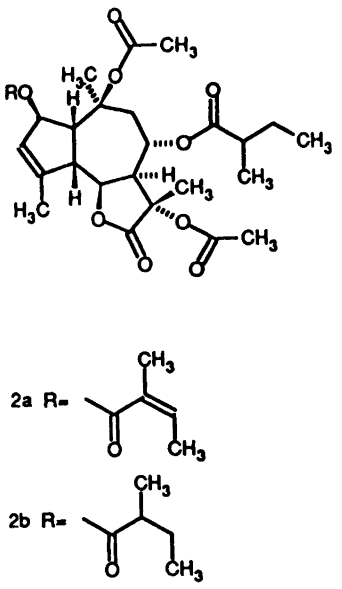


Fig. 1. Chiralities of α,β-unsaturated esters of cycloprop-2-enols.

* To whom correspondence should be addressed.



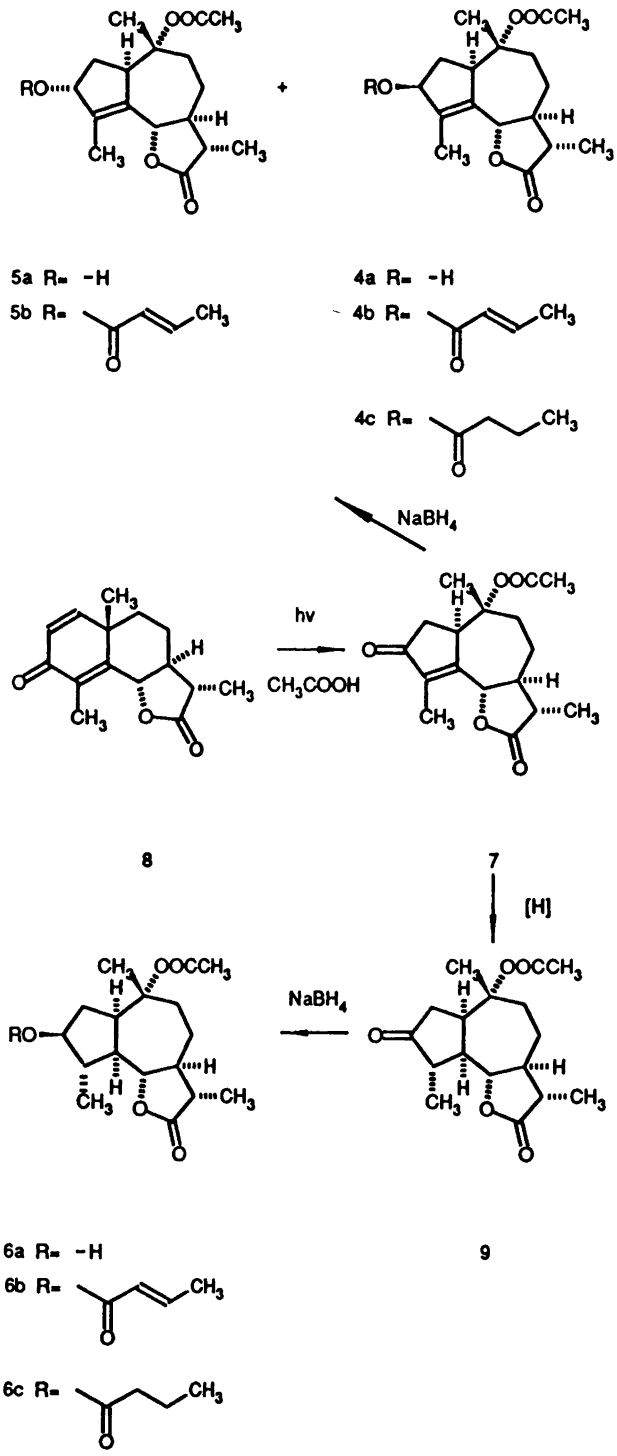
Scheme 1.



Scheme 2.

Results and discussion

Chemistry. The model compounds **4a–6c** were prepared from *O*-acetylisophotosantonin (**7**) formed by photolysis of α-santonin (**8**).[10] Reduction of the ketone with sodium borohydride afforded a mixture of the two epimeric alcohols **4a** and **5a**, which was converted into a mixture of the two esters **4b** and **5b** by reaction with 2-butenoic anhydride. The alcohol **4a**, obtained in a pure state by recrystallisation of the mixture of **4a** and **5a**, was converted into **4c**. Hydrogenation of **7** yielded **9** which was reduced with sodium borohydride. The alcohol **6a** was transformed into the esters **6b** and **6c** by reaction with 2-butenoic and butanoic anhydride, respectively. The relative configuration of C-3 of **4b** was established by means of a NOESY spectrum proving H-3 and H-1 to be *cis*. Two epimeric structures have been suggested for the major product obtained after reduction of **9** with sodium borohydride.[10,11] A NOESY experiment proved that H-3, H-1 and H-5 in **6a** are *cis* and consequently confirmed the configuration suggested by Gonzalez and Marrero.[11] The known absolute configuration of **7**[12] establishes the chirality of all the products as shown in Scheme 3. The use of 2D NMR techniques permitted a detailed assignment of the signals in the spectra of



Scheme 3.

the model compounds. In addition to correcting previous suggestions, Table 1 meets a demand for exhaustive NMR data on stereoisomeric guaianolides.

CD spectroscopy. In accordance with theory, an excition split Cotton effect was present only in the CD spectra of **4b** and **5b** (Figs. 2 and 3). Theoretically the two extrema do not need to have the same molar circular dichroism ($\Delta\varepsilon$); however, the rotational strengths, which are proportional to the integrated peak areas of the two Cotton effects, ought to be equal.[2] In this case the cut-off of the solvent prevents a measurement of the lower wavelength rotational strength. Comparison of the CD spectra obtained with those of published spectra exhibiting exciton coupling re-

Table 1. NMR data for the sesquiterpene nucleus of **4a**, **4b**, **4c**, **5b**, **6a**, **6b**, **6c**, **7** and **9**.[a]

^{1}H NMR (δ)	^{13}C NMR (δ)	^{1}H NMR (δ)	^{13}C NMR (δ)
Compound **4e**			
4.66 (1 H, dq, *J* 11.0, 1.8 Hz, H-6)	178.1 (C-12)	1.84 (1 H, m, H-7)	35.9 (C-2)
4.55 (1 H, ddq, *J* 8.0, 5.8, 1.0 Hz, H-3)	144.2, 131.2 (C-4, C-5)	1.80 (1 H, m, H-5)	34.0 (C-9)
3.77 (1 H, ddq, *J* 8.0, 6.9, 2.0 Hz, H-1)	85.5 (C-10)	1.59 (1 H, ddd, *J* 13.3, 10.8, 7.9 Hz, H-2β)	25.6 (C-8)
2.44 (1 H, ddd, *J* 13.2, 13.2, 4.1 Hz, H-9α)	81.6 (C-6)	1.47 (3 H, s, H-14)	24.5 (C-14)
2.40 (1 H, ddd, *J* 14.2, 8.0, 8.0 Hz, H-2α)	77.8 (C-3)	1.40 (1 H, dddd, *J* 12.8, 10.7, 8.0, 5.3 Hz, H-8β)	17.9 (C-15)
2.21 (1 H, dq, *J* 12.0, 6.8 Hz, H-11)	51.3, 49.0 (C-1, C-7)	1.21 (3 H, d, *J* 7.0 Hz, H-13)	13.0 (C-13)
2.18 (1 H, m, H-8α)	41.5 (C-11)	1.13 (3 H, d, *J* 6.8 Hz, H-15)	
1.99–1.91 (2 H, m, H-7, H-9β)	37.4 (C-9)		
1.89 (3 H, ddd, *J* 2.0, 1.8, 1.0 Hz, H-15)	34.7 (C-2)		
1.58 (1 H, ddd, *J* 14.2, 6.9, 5.8 Hz, H-2β)	25.2 (C-8)	Compound **6b/6c**[d]	
1.39 (1 H, dddd, *J* 14.8, 13.2, 11.2, 3.5 Hz, H-8β)	20.2 (C-14)	1.71 (1 H, ddd, *J* 7.6, 6.9, 6.9 Hz, H-3)	178.3 (C-12)
1.22 (3 H, d, *J* 6.8 Hz, H-13)	12.3, 12.4 (C-13, C-15)	4.17 (1 H, dd, *J* 10.3, 10.3 Hz, H-6)	86.2 (C-10)
1.20 (3 H, s, H-14)		2.90 (1 H, ddd, *J* 11.2, 8.3, 8.3 Hz, H-1)	86.6 (C-6)
		2.40 (1 H, ddd, *J* 13.6, 7.6, 7.6 Hz, H-2α)	79.5 (C-3)
Compound **4b/4c**[b]		2.32 (1 H, m, H-9α)	51.2 (C-5)
5.56 (1 H, ddq, *J* 8.3, 5.9, 1.2 Hz, H-3)	177.9 (C-12)	2.30 (1 H, m, H-4)	49.1 (C-7)
4.65 (1 H, dq, *J* 10.8, 1.6 Hz, H-6)	141.2, 133.5 (C-4, C-5)	2.22 (1 H, m, H-11)	46.2 (C-4)
3.83 (1 H, m, H-1)	86.3 (C-10)	2.08 (1 H, m, H-9β)	43.8, 43.2 (C-1, C-11)
2.55 (1 H, ddd, *J* 14.8, 8.3, 8.3 Hz, H-2α)	81.2 (C-6)	1.99 (1 H, m, H-8α)	33.6 (C-9)
2.41 (1 H, ddd, *J* 13.5, 13.5, 3.8 Hz, H-9α)	79.7 (C-3)	1.89 (1 H, m, H-7)	32.9 (C-2)
2.21 (1 H, m, H-11)	52.1, 48.9 (C-1, C-7)	1.83 (1 H, ddd, *J* 10.4, 8.4, 5.6 Hz, H-5)	25.6, 25.1 (C-8, C-14)
2.20 (1 H, m, H-8α)	41.5 (C-11)	1.57 (1 H, ddd, *J* 13.6, 11.4, 7.4 Hz, H-2β)	18.5 (C-15)
2.02 (1 H, m, H-7)	37.9 (C-9)	1.50 (3 H, s, H-14)	13.2 (C-13)
1.98 (1 H, m, H-9β)	32.0 (C-2)	1.40 (1 H, m, H-8β)	
1.85 (3 H, ddd, *J* 2.2, 1.6, 1.2 Hz, H-15)	25.2 (C-8)	1.21 (3 H, d, *J* 6.9 Hz, H-13)	
1.61 (1 H, ddd, *J* 14.8, 7.6, 5.9 Hz, H-2β)	19.9 (C-14)	1.12 (3 H, d, *J* 7.2 Hz, H-15)	
1.38 (1 H, dddd, *J* 14.6, 13.5, 11.0, 3.8 Hz, H-8β)	12.7 (C-15)		
1.23 (3 H, d, *J* 6.8 Hz, H-13)	12.4 (C-13)	Compound **7**[c,e]	
1.20 (3 H, s, H-14)		4.83 (1 H, dq, *J* 10.6, 1.6 Hz, H-6)	206.8 (C-3)
		4.16 (1 H, ddq, *J* 5.8, 3.1, 2.2 Hz, H-1)	176.9 (C-12)
Compound **5b**[b]		2.62 (1 H, ddd, *J* 13.7, 13.7, 4.6 Hz, H-9α)	160.7 (C-5)
5.63 (1 H, dd, *J* 8.0, 2.7 Hz, H-3)	178.2 (C-12)	2.51 (1 H, dd, *J* 19.4, 5.8 Hz, H-2α)	143.2 (C-4)
4.58 (1 H, dq, *J* 10.8, 1.6 Hz, H-6)	141.2, 135.6 (C-4, C-5)	2.41 (1 H, dd, *J* 19.4, 3.1 Hz, H-2β)	85.4 (C-10)
4.09 (1 H, m, H-1)	86.6 (C-10)	2.34 (1 H, dq, *J* 12.2, 6.7 Hz, H-11)	81.1 (C-6)
2.50–2.10 (3 H, m, H-2a, H-7, H-11)	82.0 (C-6)	2.20 (1 H, m, H-7)	48.2 (C-7)
2.42 (1 H, ddd, *J* 13.4, 13.4, 4.3 Hz, H-9α)	81.1 (C-3)	2.19 (1 H, m, H-9β)	47.2 (C-1)
2.20 (1 H, m, H-8α)	53.3, 49.0 (C-1, C-7)	2.09 (1 H, m, H-8α)	41.2 (C-11)
1.95 (1 H, m, H-9β)	41.6 (C-11)	1.90 (3 H, dd, *J* 2.2, 1.6 Hz, H-15)	37.9 (C-9)
1.89 (3 H, dd, *J* 2.0, 1.6 Hz, H-15)	38.3 (C-9)	1.47 (1 H, dddd, *J* 14.1, 13.7, 10.7, 3.6 Hz, H-8β)	36.7 (C-2)
1.58 (1 H, m, H-2b)	32.4 (C-2)	1.29 (3 H, d, *J* 6.7 Hz, H-13)	25.3 (C-8)
1.39 (1 H, dddd, *J* 14.5, 13.4, 11.2, 3.8 Hz, H-8β)	25.2 (C-8)	1.10 (3 H, s, H-14)	19.9 (C-14)
1.23 (3 H, d, *J* 6.7 Hz, H-13)	19.8 (C-14)		12.3 (C-13)
1.11 (3 H, s, H-14)	13.6 (C-15)		9.3 (C-15)
	12.4 (C-13)	Compound **9**[d]	
Compound **6a**[c]		4.09 (1 H, dd, *J* 10.0, 10.0 Hz, H-6)	218.3 (C-3)
4.25 (1 H, dd, *J* 10.2, 10.2 Hz, H-6)	178.3 (C-12)	3.30 (1 H, dt, *J* 8.7, 8.7 Hz, H-1)	177.8 (C-12)
3.75 (1 H, ddd, *J* 7.9, 7.1, 7.1 Hz, H-3)	86.6 (C-10)	2.49 (1 H, m, H-4)	85.9 (C-10)
2.92 (1 H, ddd, *J* 10.8, 8.7, 8.7 Hz, H-1)	84.3 (C-6)	2.43 (1 H, m, H-9α)	84.2 (C-6)
2.32 (1 H, m, H-9α)	77.1 (C-3)	2.40 (2 H, d, *J* 8.7 Hz, H-2α, H-2β)	50.5, 48.4, 48.3, 43.2 (C-1, C-4, C-5, C-7)
2.22 (1 H, m, H-11)	51.0 (C-5)	2.25 (1 H, m, H-5)	42.9 (C-11)
2.19 (1 H, m, H-2α)	49.3 (C-7)	2.22 (1 H, m, H-11)	39.4 (C-2)
2.15 (1 H, m, H-9β)	46.9 (C-4)	2.10 (1 H, m, H-8α)	33.7 (C-9)
1.98 (1 H, m, H-4)	45.2 (C-1)	2.02 (1 H, m, H-9β)	26.0 (C-8)
1.95 (1 H, m, H-8α)	42.8 (C-11)	1.96 (1 H, m, H-7)	24.5 (C-14)
		1.42 (1 H, m, H-8β)	15.9 (C-15)
		1.42 (3 H, s, H-14)	13.1 (C-13)
		1.25 (3 H, d, *J* 7.1 Hz, H-13)	
		1.22 (3 H, d, *J* 6.8 Hz, H-15)	

[a]The spectra were recorded in $CDCl_3$ with Me_4Si as an internal standard. The signals due to the acyl groups were as expected. [b]A NOESY spectrum was used for the assignment of the signals. [c]A COSY spectrum, a NOESY spectrum and a ^{13}C–^1H correlated spectrum were used for the assignment of the signals. [d]A COSY and a NOESY spectrum were used for the assignment of the signals. [e]The assignments of C-8 and C-14 given in Ref. 19 have been interchanged.

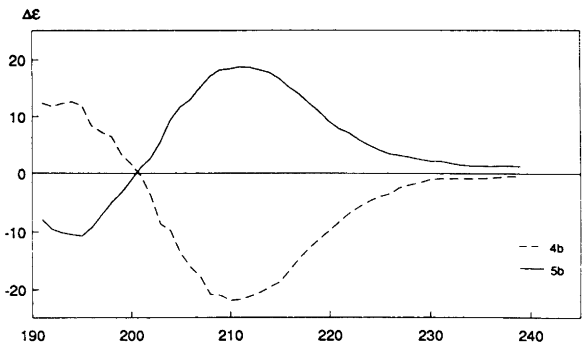


Fig. 2. CD spectra of compounds **4b** and **5b**.

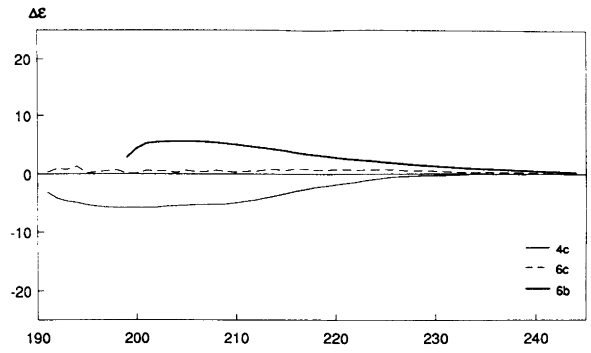


Fig. 3. CD spectra of compounds **4c**, **6c** and **6b**.

veals a close resemblance.[1,2] Inspection of Dreiding stereomodels of the two compounds reveals that the cyclopentene ring is nearly planar implying that the screwness defined by the two chromophores of **4b** will be almost a mirror image of that defined by the chromophores of **5b** in spite of the fact that the two products are not enantiomeric. Thus, the observation that the spectra of **4b** and **5b** look almost like spectra of two antipodes must reflect that the exciton coupling is the major contribution to the CD spectra. An interpretation of the chiralities of **4b** and **5b** based on the CD spectra requires that the direction of the transition moments in the chromophores be established. This direction has not been rigorously determined in α,β-unsaturated esters but it is assumed to fall into the long axis of the chromophore,[2,13] which means that it will form a small angle with the C–O bond of the allylic alcohol. Fortunately this implies, that the screwness defined by the α,β-unsaturated carbonyl group and the double bond will be of the same sign, irrespective of the conformation of the ester group. The above considerations lead to the conclusion that the chirality of a 2,3-cyclopentenol can be deduced with confidence from the chirality of the exciton coupling in an α,β-unsaturated ester of the alcohol; a conclusion which is confirmed by the fact that the chiralities deduced from the CD spectrum of **4b** and **5b** agree with those established by chemical and NMR spectroscopic means.

The configuration at C-2 in archangelolide (**2a**) was not established originally.[14] In later publications O-2 was stated to be β disposed but no argument was given.[15,16] Overlapping signals make ^{1}H NMR spectroscopy inappropriate for the determination of the configuration at C-2. In contrast, CD spectroscopy should be suitable for this problem. No excition coupling can be seen in the CD spectrum of **2a** (Fig. 4), which is in accordance with a previous report.[14] In order to see whether this was due to an overlap of other bands, e.g. a band from the oxygenated γ-lactone moiety,[9] the CD spectrum of the dihydro derivative **2b** was recorded (Fig. 4). An exciton coupling can be recognized in the difference spectrum (**2a**−**2b**) (Fig. 4). The small Δε values of the Cotton effects compared with those observed in the spectra of **4b** and **5b** is explained by the enhanced difference between the wavelengths of the absorption maxima of the two chromophores of **2a**. The above deduction is based on the assumption that subtraction of the spectrum of **2b** from that of **2a** yields the exciton split Cotton effect. As discussed below this cannot be the case. The spectrum of **2b** is a summation of the contributions from the allylic saturated ester group and the remaining ester groups including the oxygenated lactone. In the spectrum of **2a** the contribution from the allylic ester group is an exciton split Cotton effect. This implies that the subtraction of the spectrum of **2b** from the spectrum of **2a** yields a result corresponding to the exciton coupling minus the contribution to the spectrum of **2b** of the saturated allylic ester. This fault, however, is permissible since the allylic saturated ester makes only a minor contribution to the CD spectrum (compare Fig. 3). The above argument leads to the conclusion that the chirality of C-2 in archangelolide can be determined as that depicted in formula **2a** from the sign of the exciton coupling as visualized in the difference spectrum (**2a**–**2b**).

The CD spectra of thapsigargin (**1a**), dihydrothapsigargin (**1c**), trilobolide (**1b**), and dihydrotrilobolide (**1d**) have previously been recorded in order to correlate the absolute configuration of **1a** with that of **1b**.[17,18] Subtraction of the spectrum of **1c** from that of **1a** and that of **1d** from that of **1b** reveals a negative exciton chirality in both cases. Thus, the CD data confirm that the formulae **1a** and **1b** depict the previously established chirality of C-3.

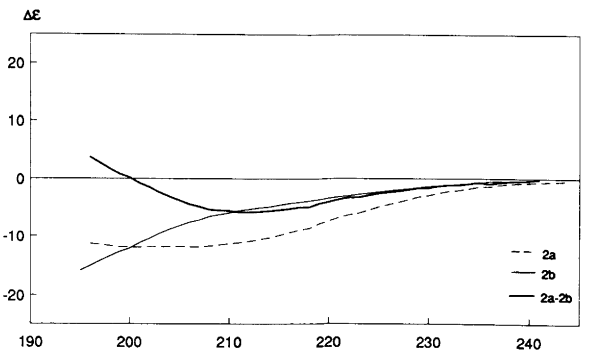


Fig. 4. CD spectra of archangelolide (**2a**) and dihydroarchangelolide (**2b**), and the difference spectrum (**2a**−**2b**).

Experimental

General methods. The NMR spectra were recorded on a Bruker AM 250 spectrometer. Standard pulse sequences (Bruker pulse program library) were used for 2D spectra: COSY, NOESY, and ^{13}C–^{1}H heteronuclear correlated spectroscopy. COSY and NOESY were used in the phase-sensitive mode (TPPI). Optical rotations were measured with a Perkin-Elmer 241 polarimeter. UV spectra were recorded in acetonitrile with a Shimadzu 265 UV spectrophotometer. Electron impact mass spectra (MS) were recorded with a Varian-Mat 711 spectrometer at 70 eV. The CD spectra were recorded in acetonitrile. Column chromatography (CC) was performed over silica gel (Merck 0.06–0.200 mm). HPLC was performed by means of a Waters 6000 A pump, a combined RI–UV detector (Knauer dual 61.00), and a prepacked LiChrosorb RP 18 column, 8×250 mm, particle size 5 μm (Knauer).

Preparation of **4a** *and* **5a**. Sodium borohydride (0.25 g) was added to a solution of **7**[10] in methanol (15 ml) and the mixture was left to stir for 30 min at 0 °C. The reaction mixture was acidified with 0.1 M hydrochloric acid (15 ml) and concentrated to half the volume *in vacuo*. The residue was extracted with diethyl ether. The ether phase was washed with water, dried, and concentrated *in vacuo* to give a gum, which was purified by CC using toluene–ethyl acetate (1:1) as the eluent to give a mixture of **4a** and **5a** (648 mg, 65 %). Crystallization from ethyl acetate yielded 380 mg (38 %) of **4a** as colourless crystals, m.p. 140 °C, $[\alpha]_D^{25}$ +21.1° (*c* 1.0, $CHCl_3$). NMR data are given in Table 1.

Preparation of **4b** *and* **5b**. A solution of the mixture of **4a** and **5a** (70 mg), 4-dimethylaminopyridine (60 mg), and 2-butenoic anhydride (70 μl) in dichloromethane (3 ml) was left for 75 min at room temperature. To the solution was added diethyl ether (10 ml) and the organic phase was washed with 1 M hydrochloric acid and 1 M sodium carbonate, dried, and concentrated *in vacuo*. The residue was purified by CC using toluene–ethyl acetate (19:1) as the eluent to give a mixture of **4b** and **5b** (21 mg, 24 %). The esters **4b** and **5b** were separated by HPLC using methanol–water (2:1) as the eluent to yield **4b** (11.7 mg, 14 %) and **5b** (3.1 mg, 4 %) as amorphous powders. **4b**: UV: λ_{max} 204 nm (log ε 4.37). MS: *m/z* 316.167957 [$C_{19}H_{24}O_4$, M^+ – CH_3COOH] (14 %), 248 (26 %), 230 [M^+ – CH_3COOH – C_3H_5COOH] (100 %), 215 [M^+ – CH_3COOH – C_3H_5COOH – CH_3] (76 %), 69 [$C_3H_5CO^+$] (81 %), 43 [CH_3CO^+] (52 %). NMR data are given in Table 1. **5b**: UV: λ_{max} 203 nm (log ε 4.25). MS: *m/z* 316.167957 [$C_{19}H_{24}O_4$, M^+ – CH_3COOH] (17 %), 248 (44 %), 230 [M^+ – CH_3COOH – C_3H_5COOH] (100 %), 215 [M^+ – CH_3COOH – C_3H_5COOH – CH_3] (82 %), 69 [$C_3H_5CO^+$] (89 %), 43 [CH_3CO^+] (68 %). NMR data are given in Table 1.

Preparation of **4c**. A solution of **4a** (21 mg), 4-dimethylaminopyridine (11 mg) and butyric acid (20 μl) was stirred for 10 min at 0 °C. To the solution was added *N,N'*-dicyclohexylcarbodiimide and the mixture was left for 4 h at 0 °C, 16 h at 5 °C and filtered. Diethyl ether (10 ml) was added to the filtrate and the solution was washed with 1 M hydrochloric acid and 1 M sodium carbonate, dried and concentrated. The residue was purified by CC using toluene–ethyl acetate (5:1) as the eluent to give **4c** (16 mg, 59 %) as an amorphous powder. UV: λ_{max} 199 nm (log ε 4.05). MS: *m/z* 318.183281 [$C_{19}H_{26}O_4$, M^+ – CH_3COOH] (19 %), 248 (59 %), 230 [M^+ – CH_3COOH – C_3H_7COOH] (100 %), 215 [M^+ – CH_3COOH – C_3H_7COOH – CH_3] (80 %), 71 [$C_3H_7CO^+$] (47 %), 43 [CH_3CO^+] (80 %). NMR data are given in Table 1.

Preparation of **9**. Palladium-on-charcoal (10 %, 150 mg) was added to a solution of **7** (500 mg) in ethyl acetate (25 ml), and the mixture was left overnight in a hydrogen atmosphere at a pressure of 3 atm. The mixture was filtered and the filtrate concentrated *in vacuo*. Purification of the residue by CC using toluene–ethyl acetate (6:1) as the eluent yielded **9** (277 mg, 55 %), m.p. 163–164 °C (ethyl acetate), $[\alpha]_D^{25}$ −25.5° (*c* 1.1, $CHCl_3$). {Ref. 10: m.p. 164.5–165.5 °C, $[\alpha]_D^{24}$ −26.6° (*c* 1.0)}. NMR data are given in Table 1.

Preparation of **6a**. Compound **6a** was prepared by reduction of **9** (340 mg) with sodium borohydride as described for the preparation of **4a** and **5a**. The crude reaction product was purified by CC using toluene–ethyl acetate (3:1) as the eluent to give **6a** (103 mg, 30 %). Recrystallization from tetrachloromethane of an analytical sample yielded **6a** as colourless crystals, m.p. 109–111 °C, $[\alpha]_D^{25}$ −20.3° (*c* 1.0, $CHCl_3$). {Ref. 10: m.p. 108–109 °C, $[\alpha]_D^{24}$ −24° (*c* 0.85); Ref. 11: m.p. 104–105 °C, $[\alpha]_D^{24}$ – 25° (*c* 0.88)}.

Preparation of **6b**. 100 mg of **6a** were butenoylated as described for the mixture of **4a** and **5a** to give 43 mg (35 %) of **6b** as an amorphous powder, UV: λ_{max} 204 nm (log ε 4.26). MS: *m/z* 378 [M^+] (0.1 %), 336 [M^+ – CH_2CO] (3 %), 318.183281 [$C_{19}H_{26}O_4$, M^+ – CH_3COOH] (8 %), 292 [M^+ – C_3H_5COOH] (2 %), 249 (47 %), 232 [M^+ – CH_3COOH – C_3H_5COOH] (100 %), 176 (27 %), 159 (50 %), 69 [$C_3H_5CO^+$] (90 %), 43 [CH_3CO^+](66 %). NMR data are given in Table 1.

Preparation of **6c**. 50 mg of **6a** were butanoylated as described for **4a** to give 38 mg (62 %) of **6c** as an amorphous powder, UV: λ_{max} 191 nm (log ε 3.79). MS: *m/z* 338 [M^+ – CH_2CO] (5 %), 320.201251 [$C_{19}H_{28}O_4$, M^+ – CH_3COOH] (6 %), 292 [M^+ – C_3H_7COOH] (13 %), 249 (36 %), 232 [M^+ – CH_3COOH – C_3H_7COOH] (100 %), 177 (42 %), 159 (57 %), 152 (64 %), 71 [$C_3H_7CO^+$] (60 %), 43 [CH_3CO^+] (76 %). NMR data are given in Table 1.

Preparation of **2b**. Palladium-on-charcoal (10%, 10 mg) was added to a solution of archangelolide **2a** (50 mg) in methanol (3 ml) and the mixture was left for 30 min in a hydrogen atmosphere. The mixture was filtered and the filtrate concentrated *in vacuo* to give **2b** (43 mg, 86%). UV: λ_{max} 195 nm (log ε 3.93).

UV data for archangelolide (**2a**): λ_{max} 196 (log ε 4.09) and λ_{max} 215 (log ε 3.93). ^{1}H NMR: the signals originating in the sesquiterpene nucleus of **2b** matched closely the corresponding signals of **2a**. The signals originating in the acyl groups were as expected.

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