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New Applications of the CD Exciton Chirality Method. Stereochemical Assignment of Organic Compounds Containing Carboxylic Acid Groups

Anne Fischbeck, Nana Bartke, and **Hans-Ulrich Humpf***

Institut für Lebensmittelchemie, Westfälische Wilhelms-Universität Münster, 48149 Münster, Germany

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Summary. CD exciton chirality methods are described for the stereochemical assignment of organic compounds containing carboxylic acid groups. Using the chromophoric combination 2-naphthoate or 2-anthroate and 9-anthrylmethyl group the absolute stereochemistry of α- and β-hydroxy carboxylic acids can be deduced from a single CD measurement. Furthermore, as demonstrated with cyclic and acylic dicarboxylic acids, the direct esterification of sterically hindered carboxyl groups with 2-naphthol also allows the stereochemical assignment *via* CD spectroscopy.

Keywords. Exciton chirality method; Circular dichroism; Carboxylic acid groups; Anthryldiazomethane; Stereochemistry.

Introduction

The exciton chirality circular dichroism (CD) method is a microscale procedure to determine the absolute configuration and conformation of organic molecules and has been widely used in the field of organic chemistry and natural product analysis [1–3]. The CD exciton chirality method is based on the through space coupling of two or more chromophores in chiral substrates giving rise to a bisignate circular dichroism curve. The signs of these split *Cotton* effects (couplets) establish the absolute sense of twist of the electric transition moments in a nonempirical manner. If the spacial orientation of the transition dipoles of two chromophores is clockwise (looking from the chromophore in front to the chromophore in back as shown in Fig. 1A or Fig. 2A), defined as positive chirality (Fig. 1B), the CD shows a positive first *Cotton* effect at higher wavelength and a negative *Cotton* effect at lower wavelength and *vice versa*.

* Corresponding author. E-mail: humpf@uni-muenster.de

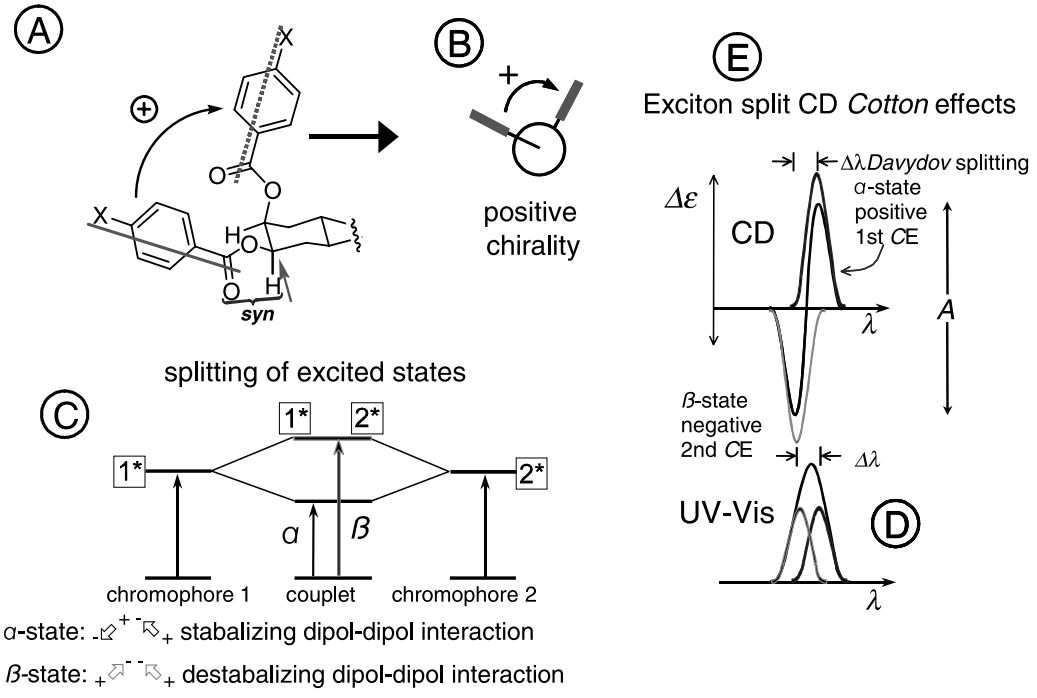


Fig. 1. Exciton coupling of two identical chromophores

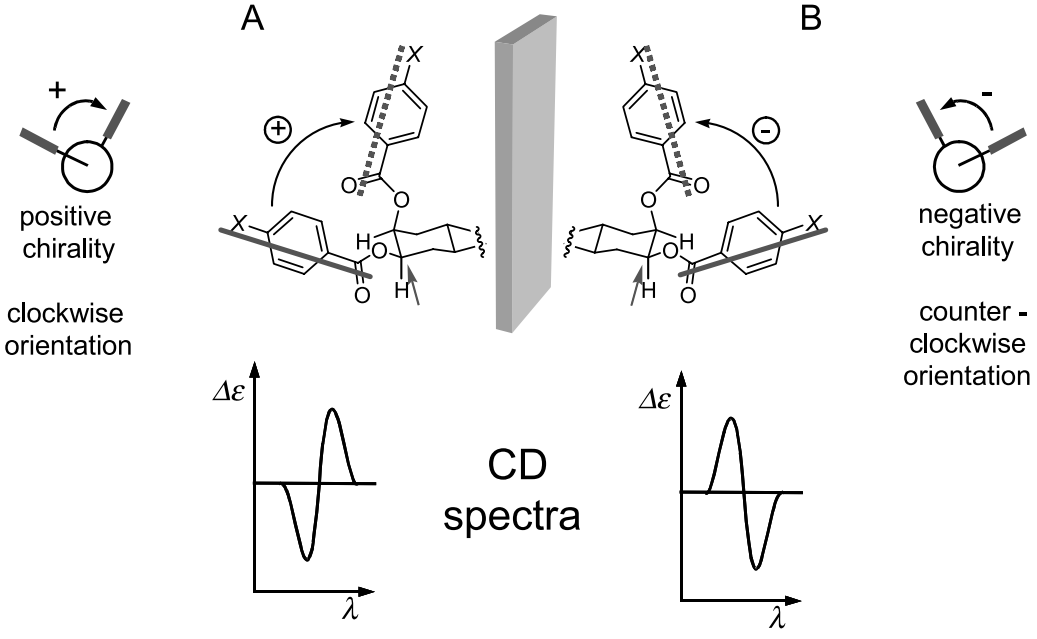


Fig. 2. Clockwise (A) and counter-clockwise (B) orientation of two identical exciton coupling chromophores leading to positive (A) and negative chirality (B) and to mirror image CD spectra

When the electric transition moments of two (or more) chromophores interact, the energy levels of the excited state split and a stabilized dipole–dipole interaction at a lower energy level (α-state) and the destabilized dipole–dipole interaction at a higher energy level (β-state) is observed (Fig. 1C). In the UV-Vis spectra the excited states are observed as a red shifted α-state (stabilized dipole–dipole interaction) and a blue shifted β-state (destabilized dipole–dipole interaction) and the signal appears as a single absorption maximum with double intensity (Fig. 1D). In cases where the energy difference between the α- and the β-state is substantial, the UV-Vis spectra show two maxima. In the CD-spectrum the α- and the β-state is reflected by a positive and a negative *Cotton* effect (*C*E) resulting in the typical bisignate or split CD curves with a positive first *C*E at higher wavelength and a negative second *C*E at lower wavelength (Figs. 1E and 2A).

The corresponding mirror image compound with a counterclockwise orientation of the two chromophores (negative chirality) results in a mirror image CD curve with a negative first *C*E at higher wavelength and a positive second *C*E at lower wavelength (Fig. 2B). The amplitude of a CD spectrum, which is defined as the distance between the peak and through of a split CD curve, is (i) inversely proportional to the square of the interchromophoric distance; (ii) proportional to the absorption coefficient of their chromophores; and (iii) depending on the interchromophoric projection angle with a maximum at approximately 70° and minima at 0° and 180° [1, 2].

Any chromophore with large ε-value and known direction of the electric transition moment μ is useful for exciton chirality (Fig. 3). 4-Substituted benzoate chromophores are widely used for exciton coupling and the direction of the electric transition moment is along the long axis of the molecule and almost parallel to the C–O bond (see Fig. 1A). Although there might be free rotation around the two C–O bonds, ester bonds are known to be *s-trans* (see Fig. 1A) and furthermore X-ray data and calculations show that the ester carbonyl is *syn* with respect to the

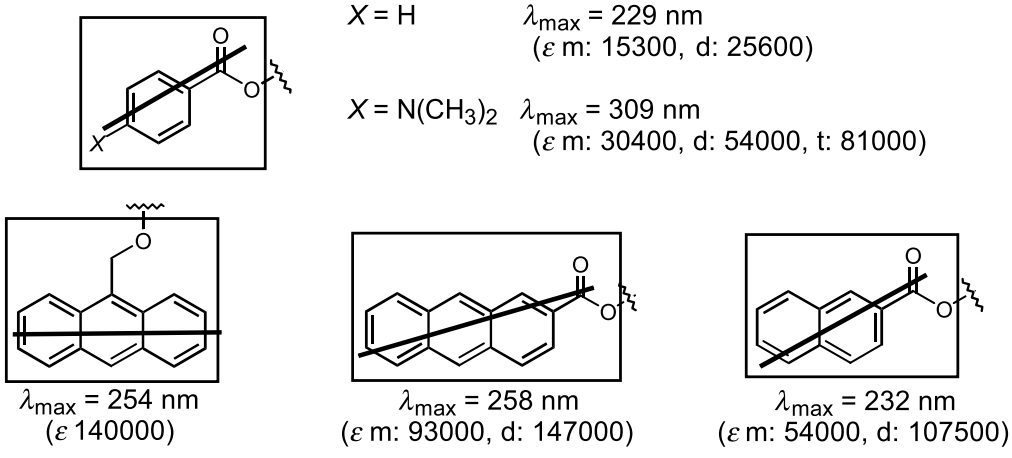


Fig. 3. Various chromophores useful for exciton chirality applications; also shown are the ε-values for the corresponding mono-, di-, and tri-derivatives (bold lines represent the direction of the transition dipoles); ε is the unit of $mol^{-1}\,dm^3\,cm^{-1}$

methane hydrogen [1, 2]. Other powerful chromophores are the 2-naphthoate, the 2-anthroate, and the 9-anthrylmethyl group (Fig. 3) [4, 5, 16, 17]. These chromophores are highly fluorescent and they enhance the sensitivity of CD detection limits and therefore facilitate microscale measurements. Fluorescent chromophores are also useful for exciton coupling fluorescence/CD applications [6, 7]. The chromophore can be introduced by O- or N-acylation or could already be preexisting in the molecule (*e.g.*, enone, diene, *etc*. [8]). Exciton chirality can also be extended to nondegenerate systems consisting of two different chromophores. For example, the bichromophoric 9-anthroate/4-methoxycinnamate derivatives of 1,2-polyols result in characteristic CD spectra for each stereochemical pattern [2]. In case of different chromophores exciton coupling is still observed even when the absorption maxima of the chromophores are 100 nm apart [1].

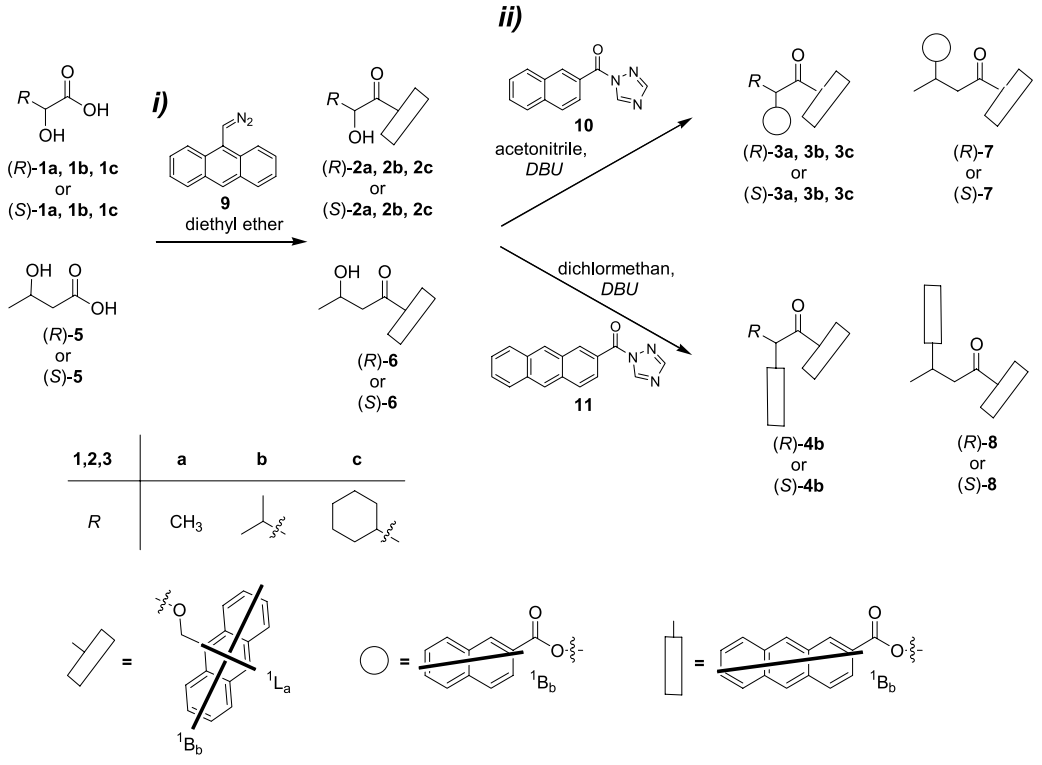
In recent years, studies have focused on extending the applicability of the exciton chirality method to unexplored areas by developing chromophores with red shifted and/or intense absorption maxima [9], intramolecular stacking properties such as porphyrins and zinc porphyrins [10–13], and chromophores which are useful for fluorescence CD [6, 7]. The methods developed so far are most commonly applied to compounds bearing two or more hydroxyl or amino groups that may easily be derivatized with an exciton-coupling chromophore. There is also an increasing interest developing exciton chirality methods for other functional groups such as carboxylic acid [16–18] and sulfanyl groups [19] as well as monoamines and monoalcohols [11–15].

In this paper we summarize our results on the stereochemical assignment of organic compounds containing carboxylic acid groups and present a new chromophoric combination for the stereochemical assignment of α- and β-hydroxy carboxylic acids. Carboxylic acid moieties and related structural units are widespread in bioactive natural products and play important roles in fundamental biochemical processes (*i.e.*, lactic acid, sphingolipids), in anticancer drugs (*i.e.*, taxol^{TM} side chain), and in antibiotics (*i.e.*, amphotericin B). Furthermore, chiral α-hydroxy acids are important building blocks for the synthesis of optically active glycols [20], halo esters [21], epoxides [22], and amino acids [23]. For the synthesis of α-hydroxy functionalized carboxylic acids several enzymatic [24–28] and chemical [29–32] methods have been described. The stereochemical assignment of the α-hydroxy acid moiety as well as other carboxylic acid groups still remains a difficult task.

Results and Discussion

Stereochemical Assignment of α- and β-Hydroxy Carboxylic Acids

The application of the exciton chirality method to α- and β-hydroxy carboxylic acids requires two chromophores suitable for exciton coupling. The ''bichromophoric'' exciton coupled CD method utilizes two different types of chromophores which are selectively introduced at two different types of hydroxyls or other functional groups. We have recently demonstrated this method with a series of α- and β-hydroxy carboxylic acids **1** and **5** with different side chains as model compounds (Scheme 1) [16, 17]. Using 9-anthryldiazomethane (**9**) carboxyl groups of α- and



Scheme 1

β-hydroxy carboxylic acids can be selectively derivatized to the corresponding 9-anthrylmethylesters **2** and **6** (Scheme 1). The chromophoric reagent **9** has been developed as fluorescent marker for HPLC analysis of fatty acids [33, 34]. It is commercially available or can also be easily synthesized [17, 35], stored for several months, and used whenever needed. Since **9** is highly reactive, the derivatization of carboxyl groups proceeds very fast (<30 min) and the reaction can be easily followed by the color change from light yellow to red. Different solvents can be used for this reaction and even water is useful for amino acids or polar fatty acids. According to Scheme 1 the chiral hydroxy carboxylic acids **1a**–**1c** and **5** were derivatized with **9** to the corresponding esters **2a**–**2c** and **6** in approximately 80–90% yield. The remaining secondary hydroxyl group in α- (**2a**–**c**) or β-position (**6**) was derivatized with the 2-naphthoate or the 2-anthroate chromophore (Scheme 1, ii). Subsequent treatment of the anthrylmethylesters **2a**–**2c** and **6** with either 2-naphthoyltriazole (**10**) [16, 17] or 2-anthroyltriazole (**11**) gave the bichromophoric derivatives **3a**–**3c** and **7** and **4b**, **8** (Scheme 1, ii). Due to the intense absorption of the 9-anthrylmethyl group ($\varepsilon = 140000\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) as well as the 2-naphthoate ($\varepsilon = 54000\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and the 2-anthroate ($\varepsilon = 93000\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) chromophore, the chromophoric derivatives are highly fluorescent, facilitating easy purification on small scale. The CD and UV spectra of **3a**, **3b**, **3c**, **7**, and **4b**, **8** are shown in Figs. 4 and 5.

In (*R*)-**3a** the long axis ^1B_b transition (Scheme 1) of the 9-anthrylmethyl chromophore with its quite intense absorption couples with the ^1B_b band of

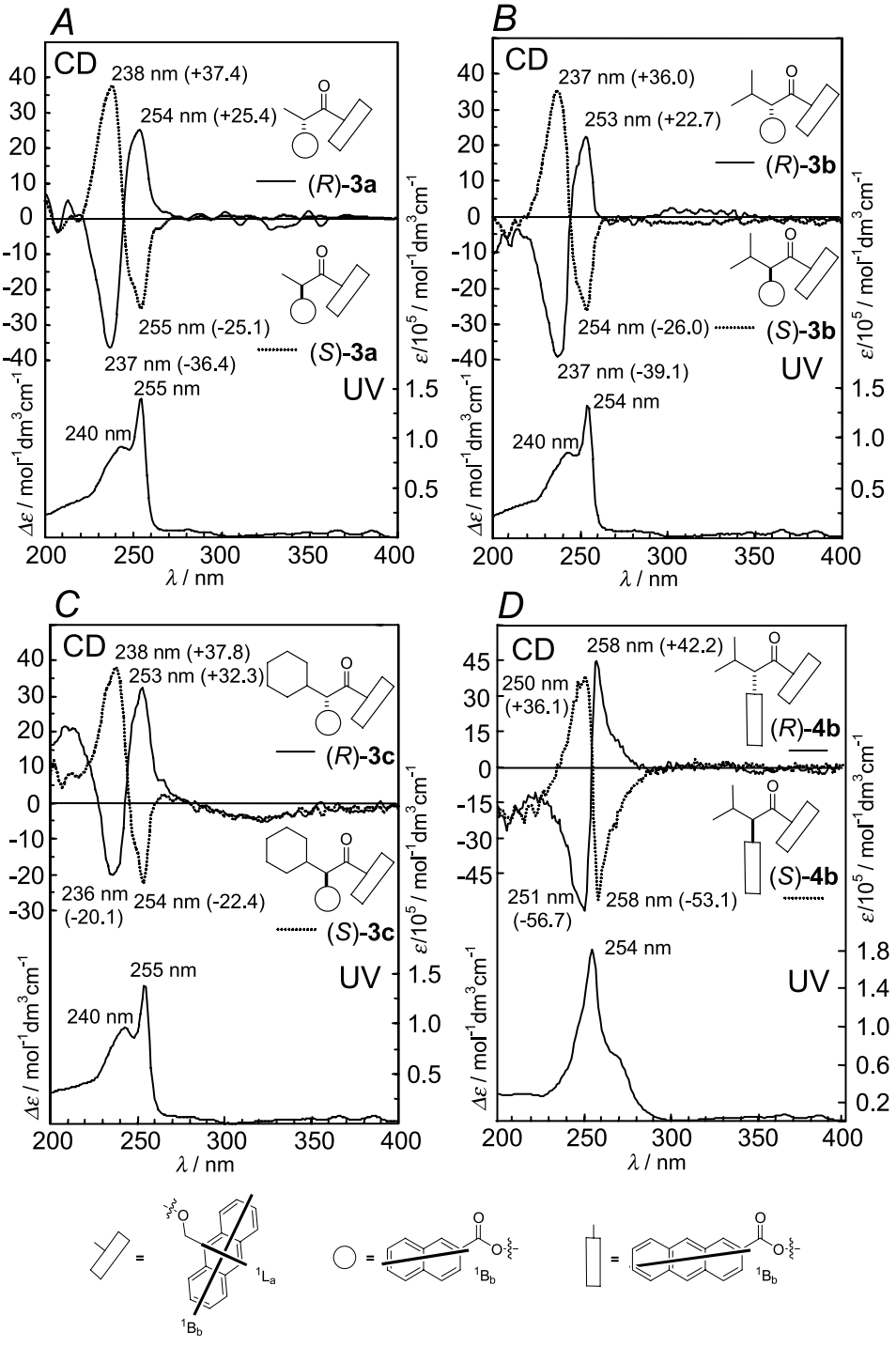


Fig. 4. UV and CD spectra of bichromophoric derivatives **3a**, **3b**, **3c**, and **4b** in acetonitrile (1-cm cell); the bold lines represent the direction of the transition dipoles

the 2-naphthoate chromophore to give a positive split CD curve with extrema at 254 nm ($\Delta\varepsilon = +25.4\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and 237 nm ($\Delta\varepsilon = -36.4\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and an amplitude A of +61.8. From this positive CD we can conclude that the

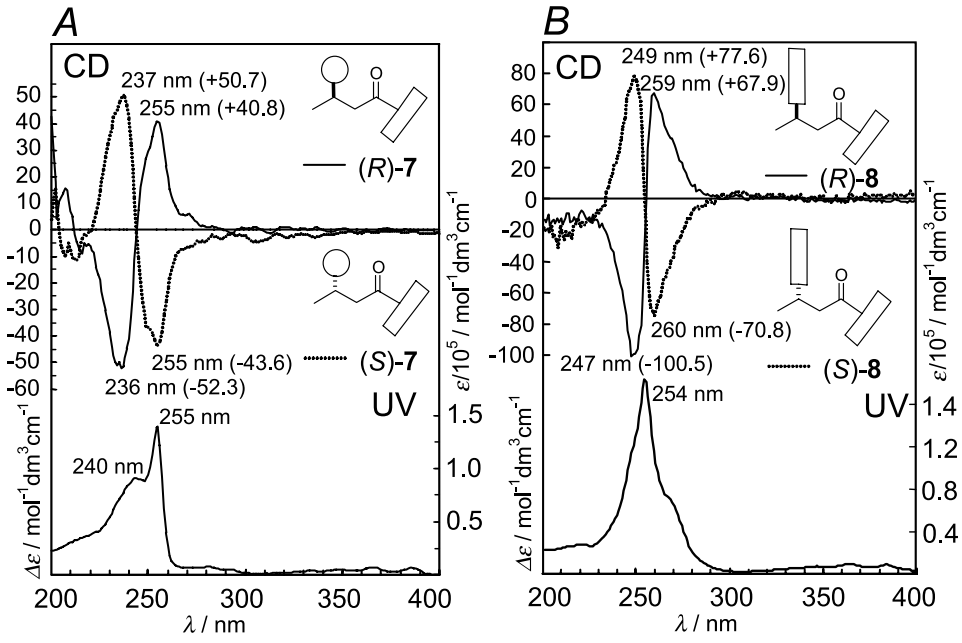


Fig. 5. UV and CD spectra of bichromophoric derivatives **7** and **8** in acetonitrile (1-cm cell); the bold lines represent the direction of the transition dipoles

electric transition dipoles (^1B_b) of the 9-anthrylmethyl chromophore and the 2-naphthoate constitute a positive chirality. The corresponding enantiomer (*S*)-**3a** exhibits a mirror image CD curve with a negative *Cotton* effect at 255 nm ($\Delta\varepsilon = -25.1\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and a positive *C*E at 238 nm ($\Delta\varepsilon = +37.4\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$), amplitude $A = -62.5$. All other bichromophoric derivatives of various α-hydroxy carboxylic acids (**3b**, **3c**) revealed similar CD spectra with a positive bisignate CD couplet for the (*R*)-configured compounds and a negative couplet for the (*S*)-configured compounds (see Figs. 4B and 4C) [17]. These data clearly demonstrate that the absolute stereochemistry of α-hydroxy carboxylic acids can be deduced from a single CD measurement. Since exciton coupling depends on the interchromophoric distance and the torsion angle between the transition dipoles of the chromophores, the resulting CD curves are determined by the conformation of the chromophoric derivatives. Therefore one would expect that the group (methyl, isopropyl, cyclohexyl; Scheme 1) attached to the α-carbon affects the amplitude of the bisignate CD curve. However, as shown with chromophoric derivatives **3a**–**3c**, the amplitude of the resulting CD spectra is not much affected by the group at the chiral center. For example, the enantiomer (*S*)-**3a** ($A = -62.5$) with the relatively small methyl group yielded almost the same amplitude as (*S*)-**3c** ($A = -60.2$) with the large bulky cyclohexyl group at the chiral center. Thus, the preferred sense of twist between the 9-anthrylmethyl and the 2-naphthoate follows the same CD pattern and is not affected by the substituent attached to the stereogenic center. If the CD curve of the bichromophoric derivative shows positive chirality (positive first *C*E at longer wavelength), the α-hydroxy carboxylic acid has (*R*) configuration and *vice versa*. These results were also confirmed by calculations of the low energy conformation of **3**. The obtained projection angels

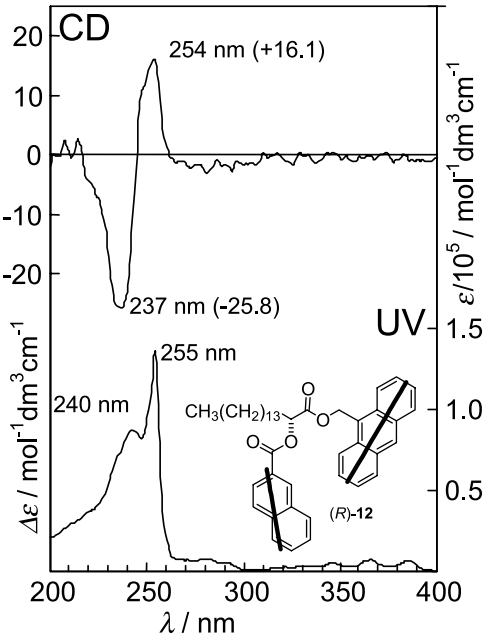


Fig. 6. UV and CD spectra of bichromophoric diester (*R*)-**12** in acetonitrile (1-cm cell); the bold lines represent the direction of the transition dipoles

between the two transition dipoles of the chromophores are in very good agreement with the experimental data [17].

The presented method is also useful for the stereochemical assignment of β-hydroxy carboxylic acids. As a representative example Fig. 5A shows the CD spectra of the bichromophoric derivative of 3-hydroxybutanoic acid (**7**). Again, the (*R*)-configured compound (*R*)-**7** gave a positive split CD curve with extrema at 255 ($\Delta\varepsilon = +40.8\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and 236 nm ($\Delta\varepsilon = -52.3\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$), whereas the corresponding enantiomer (*S*)-**7** revealed a mirror image CD (Fig. 5A).

Besides the model compound shown in Figs. 4 and 5, this method was intensively applied to various long chain α- and β-hydroxy carboxylic acids and the results were confirmed in many cases by other methods [36–39]. As a representative example Fig. 6 shows the CD of the bichromophoric diester of 2-hydroxypalmitic acid (*R*)-**12**, which was obtained by kinetic resolution through lipase-catalyzed enantioselective acetylation [38].

In order to increase the amplitude of the CD spectra and therefore the sensitivity of the method we tested the use of the 2-anthroate chromophore for the derivatization of the hydroxy group instead of the 2-naphthoate (Scheme 1). As example the obtained CD spectra of bichromophoric derivatives **4b** and **8** are shown in Figs. 4D and 5B. The CD spectra of **4b** can be directly compared with **3b** and as can be seen in Figs. 4B and 4D the enantiomers of both compounds gave similar CD spectra whereas the amplitudes are increased almost 2-fold in the case of **4b**. The amplitude *A* of (*R*)-**4b** and (*S*)-**4b** is +98.9 and −89.2, whereas (*R*)-**3b** and (*S*)-**3b** gave an amplitude *A* of +61.8 and −62. Similar results were observed for the bichromophoric derivatives of 3-hydroxybutanoic acid (*R*)-**8** and (*S*)-**8**.

When the 9-anthrylmethyl/2-naphthoate combination in **7** (Fig. 5A) is replaced by the 9-anthrylmethyl/2-anthroate pair, the amplitudes of the resulting bichromophoric derivatives **8** (Fig. 5B) are almost two times larger.

Stereochemical Assignment of Other Carboxylic Acid Groups

Although **9** is an excellent reagent, it is very bulky and not useful for sterically hindered carboxylic acid groups. Therefore it was necessary to develop a different strategy based on the direct esterificaton of carboxylic acid groups with 2-naphthol (**17**, $\lambda_{max} = 222\,nm$, $\varepsilon = 54000\,mol^{-1}\,dm^3\,cm^{-1}$, *Me*CN). For the derivatization of carboxylic acid groups in a one-pot reaction in quantitative yield *N*,*N*-bis(2-oxo-3-

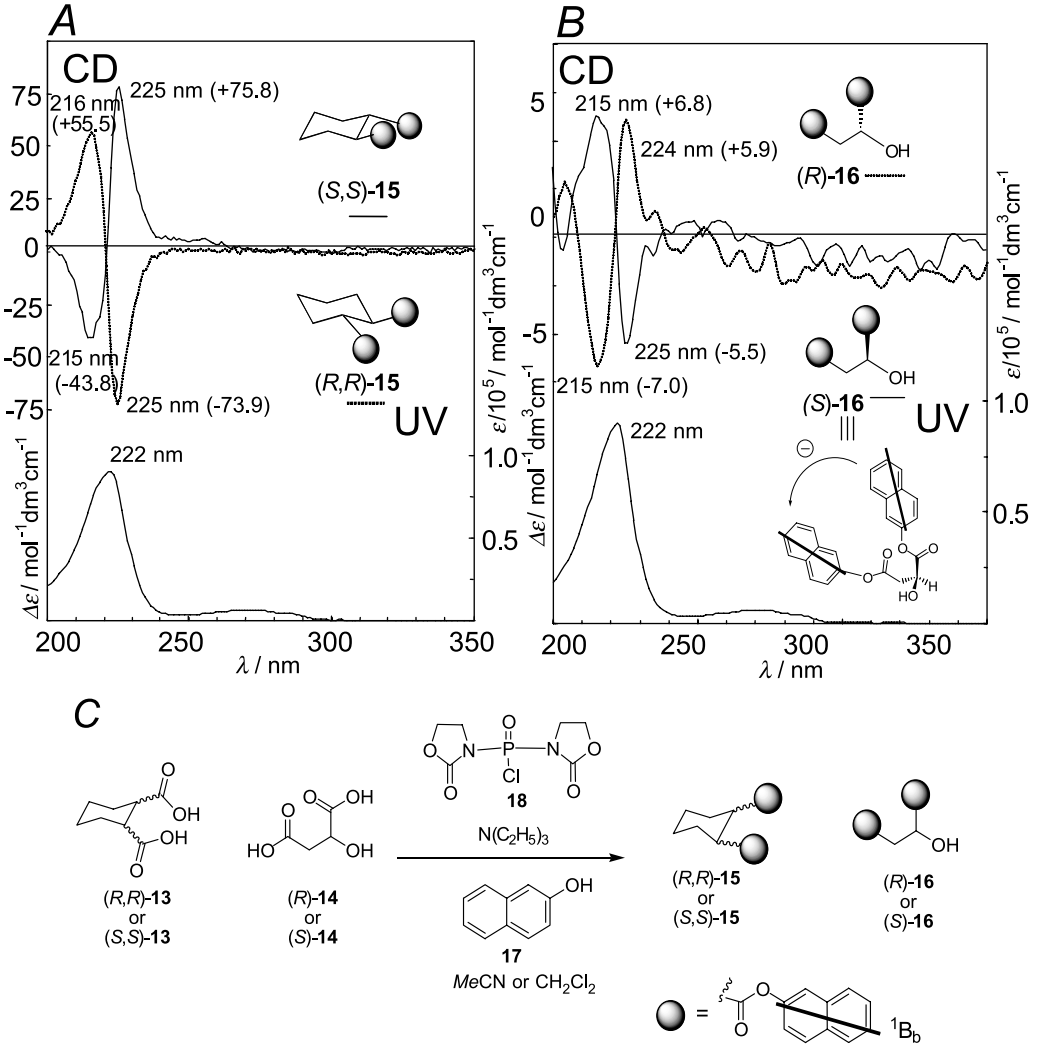


Fig. 7. UV and CD spectra of (A) (*R*,*R*)- and (*S*,*S*)-cyclohexanedicarboxylic acid dinaphthylester **15** and (B) (*R*)- and (*S*)-malic acid dinaphthylester **16** in acetonitrile (1-cm cell); (C) chromophoric derivatization of *trans*-cyclohexane

oxazolidinyl)phosphorodiamidic chloride (**18**) was used for the activation of the carboxyl group (Fig. 7C) [40]. According to Fig. 7C this method was used for the derivatization of *trans*-cyclohexanedicarboxylic acid (**13**) and malic acid (**14**). The corresponding UV and CD spectra are shown in Fig. 7. For the (1*R*,2*R*)-dinaphthylester (*R,R*)-**15** (dashed line) the interaction between the ^1B_b bands of the two chromophores gives rise to a negative split CD curve with extrema at 225 nm ($\Delta\varepsilon = -73.9\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and 216 nm ($\Delta\varepsilon = +55.5\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and an amplitude A of -129.4, thus establishing a negative chirality and reflecting a counterclockwise orientation of the interacting transition dipoles. The enantiomer (*S,S*)-**15** (Fig. 7A, solid line) revealed a curve of similar shape but opposite *Cotton* effects (*C*E) at 225 nm ($\Delta\varepsilon = +75.8\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and 215 nm ($\Delta\varepsilon = -43.8\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$), amplitude $A = +119.6$.

The dinaphthylester *of* (*R*)- *and* (*S*)-**14** revealed also mirror image CD spectra with an amplitude A of -12.3 for (*S*)-**16** and of $+12.8$ for its enantiomer (*R*)-**16** (Fig. 7B). The relatively small A values observed for (*R*)-**16** and (*S*)-**16** can be explained by the free rotation and the mixture of conformational isomers. However, calculations of the preferred minimum energy conformation are in good agreement with the experimental results, demonstrating the usefulness of this method [40].

Another possible reagent for the derivatization of carboxylic acid groups is naphthyldiazomethane (**19**, $\lambda_{max} = 223$ nm, $\varepsilon = 60000\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$, Fig. 8B). However as can be seen from the following example the obtained CD effects are relatively weak compared to the corresponding 2-naphthylesters. The diterpene

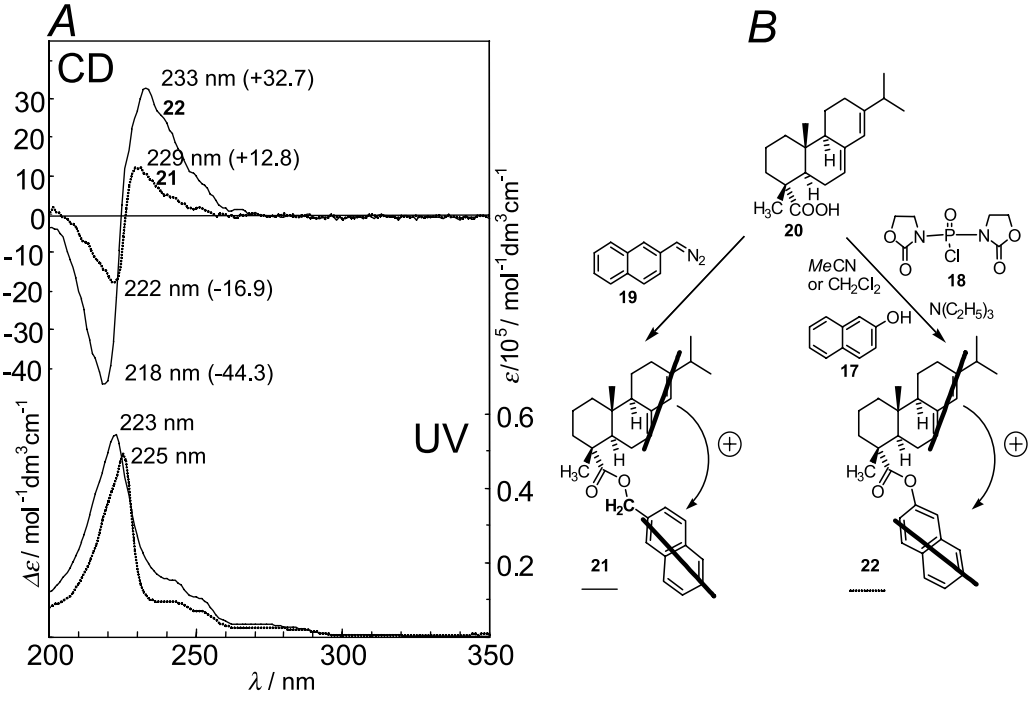


Fig. 8. (A) UV and CD spectra of abietic acid derivatives **21** and **22** in acetonitrile (1-cm cell); (B) conversion of abietic acid **20** to the corresponding 2-naphthylmethylester **21** and the naphthylester **22**; the bold lines represent the direction of the transition dipoles

abietic acid (**20**) which is a well known major constituent of gum or wood resin, was used as model compound. The molecule consists of the typical hydrophenantrene system and contains an (*R*) configured carboxylic group in position 1 (Fig. 8B). This group was either derivatized with **17** as described above to yield the mononaphthylester **22** or with **19** to yield the 2-naphthylmethylester **21** (Fig. 8B). For exciton coupling at least two chromophores are required and in the case of abietic acid the ^1B_b band of the napthyl or 2-naphthylmethyl group interacts with the diene moiety at *ca.* 235 nm ($\Delta\varepsilon = 21500\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$, *Me*CN) already preexisting in the molecule. The resulting CD spectra are shown in Fig. 8A. The CD of **22** is characterized by a positive CD couplet with extrema at 233 nm ($\Delta\varepsilon = +32.7\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$) and 218 nm ($\Delta\varepsilon = -44.3\,\mathrm{mol^{-1}\,dm^3\,cm^{-1}}$), constituting a positive chirality, just as expected from the orientation of the two transition moments as the structure in Fig. 8B demonstrates. The amplitude *A* of +77.0 is about 2.5-fold larger compared to that of **21** (*A* value of +29.7). These data clearly show that with compounds having a fixed conformation the naphthyl derivatives generally yield stronger CD effects than the corresponding naphthylmethylesters, which have greater conformational flexibility due to the additional CH_2-group. This method has been recently applied for the stereochemical assignment of the tricarballylic acid side chain of fumonisins, a class of mycotoxins with carcinogenic activity [41, 42].

Conclusion

The two-step derivatization using the 9-anthrylmethyl- and the 2-naphthoate or 2-anthroate chromophore provides a general method for the absolute configurational assignment of α- and β-hydroxy carboxylic acids. The chromophoric combination 9-anthrylmethyl-/2-naphthoate or 9-anthrylmethyl-/2-anthroate leads to strong bisignate mirror image CD curves with *A* values ranging from −149 to +168 for α- and β-hydroxy carboxylic acid enantiomers. The preferred sense of twist between the 9-anthrylmethyl- and the 2-naphthoate or 2-anthroate group follows the same CD pattern: negative chirality: (*S*) configuration, positive chirality: (*R*) configuration. This general principle was also demonstrated with various long chain α- and β-hydroxy carboxylic acids.

The presented one-step method using **18** for the activation of the carboxyl group was shown to be a potent and effective way for the esterification of carboxylic acids with 2-naphthol, achieving conversion to the naphthylesters under mild conditions and in high yield. It enables the circular dichroism exciton chirality method to be utilized for the stereochemical assignment of carboxyl groups, a moiety that is often encountered in natural products, but for which only very few CD approaches have been developed so far.

Experimental

All solvents and chemicals used for reaction were of reagent grade and were purchased from Fluka, Sigma-Aldrich (Deisenheim, Germany) or Merck (Darmstadt, Germany). 9-Anthryldiazomethane (**9**) was purchased from Serva, (Heidelberg, Germany). Anhydrous solvents were percolated over molecular sieve or freshly distilled. ^{1}H NMR spectra were recorded in $CDCl_3$ on a

Bruker DPX-400 spectrometer and are reported in ppm (δ) relative to $CHCl_3$ (7.26 ppm) as internal reference. ESI-MS: Quattro LC (Waters-Micromass, Manchester, UK) with nanospray. MALDI-TOF: LAZARUS III DE time of flight mass spectrometer (constructed by *H. Luftmann*, Institut für Organische Chemie, Münster, Germany) operated at 19 kV with delayed extraction and a path length of 2 m. A N_2 laser was used to generate the primary beam at 337 nm with a pulse width of 3 ns. Exact mass determination: MicroTof (Bruker Daltonics, Bremen, Germany) with loop injection, calibration with sodium formiat cluster. UV-Vis and CD spectra were recorded in acetonitrile on a Perkin Elmer Lambda 40 spectrophotometer and a JASCO J-600 spectropolarimeter in a 1 cm cell.

2-Anthroyltriazole (**11**, $C_{17}H_{11}N_3O$)

1,1′-Carbonylbis-1,2,4-triazol (162 mg, 1 mmol) was added to a solution of 200 mg 2-anthroic acid (0.9 mmol) in 5 cm^3 anhydrous *Me*CN at room temperature and the mixture was stirred overnight to afford a yellow slurry. The reaction mixture was concentrated under reduced pressure, dissolved in 50 cm^3 diethyl ether, and quickly washed with aqueous $NaHCO_3$ (10%, 2×10 cm^3) and 8 cm^3 brine and then dried ($NaSO_4$). The organic layer was concentrated under reduced pressure to give 90 mg **11** as a yellow solid (37%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.65$ (m, 2H), 8.02 (d, $J = 10.0$ Hz, 2H), 8.19 (d, $J = 8.0$ Hz, 2H), 8.27 (d, $J = 8.0$ Hz, 1H), 8.47 (s, 1H), 8.73 (s, 1H), 8.92 (s, 1H), 9.08 (s, 1H), 9.52 (s, 1H) ppm; ESI-MS: $m/z = 274$ $[M + H]^+$.

*General Two Step Synthesis of Chromophoric Derivatives **4** and **8***

To a solution of 5 mg hydroxy acid in 0.5 cm^3 dry methanol a solution of 1.2 equiv of **9**/COOH group in 2.0 cm^3 dry methanol was added dropwise. The reaction mixture was stirred at room temperature for 30 min, concentrated under reduced pressure and the product purified by prep. TLC (silica gel 60 F_{254}, Merck). Solvent system: diethyl ether:*n*-pentane (1:1), yield 30–90%. The anthrylmethylester (**2b** and **6**, 3–9 mg) was then treated with 1.2 equivalents **11** and a catalytic amount of *DBU* dissolved in 1 cm^3 CH_2Cl_2 at room temperature for 12 h. The reaction mixture was concentrated and purified by prep. TLC as described above, yielding (*R*)-**4b**, (*S*)-**4b**, (*R*)-**8**, and (*S*)-**8**.

9′-Anthrylmethyl 2(R)-(2″-anthroyloxy)-3-methylbutanoate ((*R*)-**4b**, $C_{35}H_{28}O_4$)

Yield 58%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.05$ (d, 6H), 2.36 (m, 1H), 5.22 (d, $J = 4.8$ Hz, 1H), 6.24 (d, $J = 12.8$ Hz, 1H), 6.36 (d, $J = 12.4$ Hz, 1H), 7.51 (m, 7H), 8.04 (m, 5H), 8.36 (d, $J = 8.8$ Hz, 2H), 8.48 (s, 1H), 8.53 (d, $J = 8.4$ Hz, 2H), 8.80 (s, 1H) ppm; ESI-MS: $m/z = 535$ $[M + Na]^+$, 567 $[M + Na–CH_3OH]^+$; HRMS: $m/z =$ calcd for $C_{35}H_{28}O_4Na$ $[M + Na]^+$ 535.18853, found 535.1880; CD (acetonitrile): λ_{max} ($\Delta\varepsilon$) = 258 (+42.2), 251 (−56.7) nm ($mol^{-1}\,dm^3\,cm^{-1}$).

9′-Anthrylmethyl 2(S)-(2″-anthroyloxy)-3-methylbutanoate ((*S*)-**4b**, $C_{35}H_{28}O_4$)

Yield 68%; ^{1}H NMR and MS are the same as for (*R*)-**4b**; CD (acetonitrile): $\lambda_{max}(\Delta\varepsilon) = 258$ (−53.1), 250 (+36.1) $nm\,mol^{-1}\,dm^3\,cm^{-1}$).

9′-Anthrylmethyl 3(R)-(2″-anthroyloxy)butanoate ((*R*)-**8**, $C_{34}H_{26}O_4$)

Yield 49%; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.46$ (d, $J = 6.4$ Hz, 3H), 2.85 (m, 2H), 5.61 (m, 1H), 6.28 (s, 2H), 7.40 (m, 5H), 7.83 (m, 4H), 8.06 (m, 3H), 8.30 (m, 4H), 8.46 (d, $J = 8.8$ Hz, 2H) ppm; MALDI-TOF: $m/z = 498$ M^+; MicroTof: $m/z =$ calcd for $C_{34}H_{26}O_4Na$ $[M + Na]^+$ 521.17288, found 521.1723; CD (acetonitrile): λ_{max} ($\Delta\varepsilon$) = 259 (+67.9), 247 (−100.5) nm ($mol^{-1}\,dm^3\,cm^{-1}$).

9′-Anthrylmethyl 3(S)-(2″-anthroyloxy)butanoate ((*S*)-**8**, $C_{34}H_{26}O_4$)

Yield 65%; ^{1}H NMR and MS are the same as for (*R*)-**8**; CD (acetonitrile): λ_{max} ($\Delta\varepsilon$) = 260 (−70.8), 249 (+77.6) nm ($mol^{-1}\,dm^3\,cm^{-1}$).

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