Microscale Determination of the Absolute Configuration of α-Aryl-Substituted Alcohols by the CD Exciton Chirality Method

Waldemar Adam,[†] Zoltan Lukacs,[†,‡] Kirsten Viebach,[‡] Hans-Ulrich Humpf,*[,‡] Chantu R. Saha-Möller,[†] and Peter Schreier[‡]

Contribution from the Institutes of Organic Chemistry and Food Chemistry, University of Würzburg, Am Hubland, D-97074 Würzburg, Germany

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The absolute configurations of a broad spectrum of aryl alcohols **1** have been determined for the first time by the CD exciton chirality method. The configurational assignment is additionally verified by computer modeling and lipase-catalyzed acetylation of the racemic alcohols. The CD-spectroscopic data have revealed that the *S* enantiomers of the benzoate derivatives **2** display a positive first Cotton effect and the *R* enantiomers a negative one at around 228 nm. Thus, the sense of the first Cotton effect of the benzoate derivative **2** allows a reliable assignment of the absolute configuration of the corresponding alcohol **1**.

Introduction

Chiral properties of optically active substances are of vital importance for their biological and pharmacological activity; however, enantiomerically pure or enriched natural products are often accessible only in very small amounts. Therefore, the determination of their absolute configurations requires sensitive methods, which are suitable for small-scale analysis. Several methods are described in the literature that take advantage of the formation of diastereomers to determine the configuration of secondary alcohols;[1] however, they all do have limitations in their applicability and sensitivity. In taking a more direct approach, the CD exciton chirality method[2] provides a convenient analytical tool for the microscale ($<4 \times 10^{-5}$ M) determinination of the absolute configurations of chiral compounds in solution, provided they contain two or more chromophores. The signs of the CD curves for bichromophoric derivatives are defined nonempirically by the absolute twist between the electric transition moments of the interacting chromophores, which gives rise to a bisignate circular dichroism curve.[2]

The CD exciton chirality method may also be applied to systems with different chromophores (nondegenerate systems). One of these chromophores may already be contained in the molecule, such as the double bonds in enes[3] or dienes,[4] and the other chromophore is subsequently introduced by derivatization. The applicability of this sensitive method for the determination of the absolute configuration has already been demonstrated for a variety of substrates,[2] e.g., 1,2- and 1,3-polyols,[5] amines,[6] 2-hydroxy acids,[7] and allylic or homoallylic alcohols.[3]

Our preliminary study on the biocatalytic oxidation of arylalkanes with bacteria, isolated from topsoil by a selective screening procedure, has shown that the corresponding hydroxylated products were formed in high enantiomeric excess (ee > 90%).[8] The absolute configurations of most of the α-aryl-substituted alcohols produced in this microbial transformation of the arylalkanes are not known. Since laboratory-scale biotransformations provide only small amounts of these optically active alcohols, the assignment of their absolute configuration is usually not feasible by traditional means. Therefore, we have applied the CD exciton chirality method for this purpose. Herewithin we report the first microscale determination of the absolute configurations for a broad set of α-arylated alcohols.

Results and Discussion

At least two chromophores are required in a substrate for the determination of the absolute configuration by the CD exciton chirality method. Since the benzoyl group ($\lambda_{max} = 229$ nm, $\epsilon = 15\,300$ M^{-1} cm^{-1}) has already been successfully employed as a second chromophore for the configurational assignment of allylic and homoallylic alcohols,[3] the aryl alcohols **1** were converted to the corresponding benzoate derivatives **2** with benzoyltriazole in quantitative yields (Scheme 1) to facilitate the exciton-coupled CD measurements.

To demonstrate the applicability of this method, the alcohols **1a**, **1b**, and **1j** were used in enantiomerically

* Corresponding author. E-mail: humpf@pzlc.uni-wuerzburg.de. Fax: +49-931-8885484.

† Institute of Organic Chemistry.

‡ Institute of Food Chemistry.

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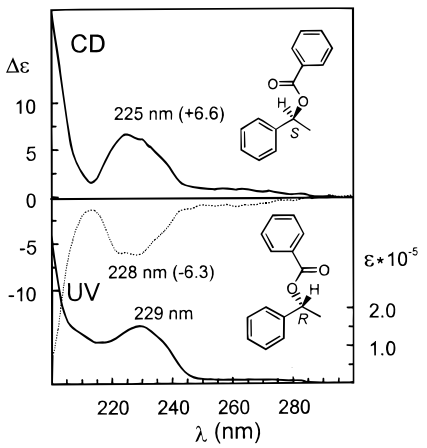
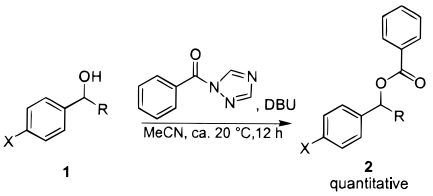


Figure 1. CD and UV spectra of (*R*)- and (*S*)-(1-phenyl)-1-ethyl benzoate (**2a**) in acetonitrile.

Scheme 1. Preparation of the Benzoate Derivatives 2 of the Aryl-Substituted Alcohols 1



	R	X
a	CH_3	H
b	C_2H_5	H
c	C_2H_5	Br
d	$CH{=}CH_2$	H
e	$C(CH_3)_3$	H
f	*n*-C_4H_9	H
g	$CH_2CH(CH_3)_2$	H
h	*n*-C_5H_{11}	H
i	*n*-C_6H_{13}	H
j	*n*-C_9H_{19}	H

pure form, while the other substrates **1c**−**i** were employed as racemic mixtures. The enantiomerically pure bichromophoric reference compounds **2a**, **2b**, and **2j** were directly used for the CD measurements. As representative examples, the UV and CD spectra of substrate **2a** are shown in Figure 1. The CD spectrum of (*S*)-**2a** revealed a positive Cotton effect at 225 nm ($\Delta\epsilon = +6.6$) and the *R* enantiomer showed a negative one at 228 nm ($\Delta\epsilon = -6.3$).[9] The CD spectra of the benzoate **2a** arose from the exciton coupling between the transition moments of the two chromophores, namely the phenyl and benzoate groups. In particular, the ^1L_a transition of the phenyl group (ca. 210 nm), which is polarized along the long axis of the chromophore, couples with the ^1L_a transition band of the benzoate at ca. 230 nm. If the two axes of the benzoate and phenyl chromophores possess the sense of a right-handed screw, the first Cotton effect is positive, which is observed for the *S*-configured benzoate **2a**. Since the exciton chirality depends on the conformation of the molecule, computer calculations with Macromodel 5.0 [10] were performed with the modified Allinger MM2 force field to assess the preferred conformation of the benzoate derivative **2a** (Figure 2).

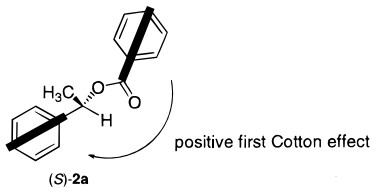


Figure 2. Favored conformation of (*S*)-(1-phenyl)-1-ethyl benzoate (**2a**) assessed by computational studies with Macromodel 5.0[10] (— indicates transition dipole).

From a local-energy minimization and a Monte Carlo conformational search it could be seen that the hydrogen atom is positioned in the same plane as the phenyl ring; thus, the transition bands of the benzoate chromophore and the phenyl ring are oriented in a clockwise sense to each other in the *S* enantiomer and counterclockwise in the *R* enantiomer of the benzoate **2a** (Figure 2). This results in a positive first Cotton effect for the *S* benzoates and a negative one for the *R* benzoates of **2a** at around 228 nm, which is in very good agreement with our experimental results (Figure 1).

The enantiomerically pure reference compounds **2a**, **2b**, and **2j** have shown that the *R* enantiomers generally display a negative first Cotton effect, whereas the *S* enantiomers display a positive first Cotton effect at wavelengths around 228 nm (Table 1, entries 1−4 and 17). The second Cotton effect at wavelengths below 210 nm was not observed because the CD is perturbed by solvent effects and other electronic transitions.[3c] Since the first Cotton effect at ca. 228 nm is well-separated and not perturbed by other bands, this reflects the chirality sense of the substance in a straightforward manner and it is not necessary to consider the second Cotton effect below 210 nm. Additionally, the perturbation of the second Cotton effect is not unusual for exciton chirality measurements. For the benzoates of allylic and homoallylic alcohols, the second Cotton effect was also not observed, and their configurational assignment has been based on the first one at around 228 nm.[3]

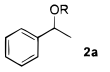
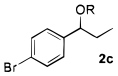
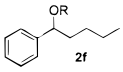
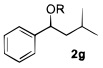
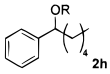
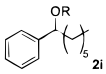
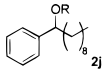
The other alcohols **1c**−**g** were employed as racemic mixtures. After esterification, the enantiomers of the benzoates **2c**−**g** were separated on a chiral, analytical HPLC column and the CD measurements were applied directly on the collected fractions (Table 1). The use of racemates offers several advantages: First, the racemic alcohols **1** are readily available in sufficient quantities according to standard preparative procedures; second, after separation of the enantiomers of the corresponding benzoates, both opposing Cotton effects may be recorded and thereby additional verification of the results is possible.

It is significant to note that alkyl chains up to 10 carbon atoms, as in the case of the benzoate **2j** (Table 1, entry 17), and substitution of the phenyl ring in the *para* position (**2c**, entries 5 and 6) do not affect the sense of the Cotton effect (Figure 3). For the *p*-bromo-substituted alcohol **1c**, the UV maximum is red-shifted to 221 nm

(9) The corresponding alcohols (*R*)-**1a** and (*S*)-**1a** did not show any Cotton effect around 228 nm.

(10) All calculations were carried out with MM2 force field in $CHCl_3$; at least 1000 conformers were searched for each simulation.

Table 1. CD Data in Acetonitrile[12] and Absolute Configurations of the Benzoates 2

entry	substrate[a]	enantiomer[b]	CD effect λ[c][nm]	CD effect Δε[d]	config[e]
1	 **2a**	1[f]	228	- 6.3	*R*
2		2[f]	225	+ 6.6	*S*
3	 **2b**	1[f]	228	- 7.1	*R*
4		2[f]	229	+ 7.4	*S*
5	 **2c**	1	233	+ 10.0	*S*
6		2	232	- 10.9	*R*
7	 **2d**	1	223	+ 3.6	*S*
8		2	224	- 3.6	*R*
9	 **2e**	1	229	- 2.1	*R*
10		2	228	+ 10.3	*S*
11	 **2f**	2[g]	223	+ 3.5	*S*
12	 **2g**	2[g]	224	- 6.2	*R*
13	 **2h**	[h]	224	+ 9.6	*S*
14			225	- 4.9	*R*
15	 **2i**	[h]	225	+ 6.5	*S*
16			227	- 3.7	*R*
17	 **2j**	[f]	226	+ 9.3	*S*

[a] R = COC_6H_5. [b] Number indicates the elution order of the enantiomers on the chiral HPLC column. [c] Maximum of first Cotton effect. [d] The amplitude values of the enantiomers may vary because fractions collected from the chiral HPLC were not enantiomerically pure. [e] Determined by CD spectroscopy and verified by lipase-catalyzed kinetic resolution of the alcohols. [f] Enantiomerically pure authentic reference. [g] Due to impurities, it was not possible to determine the CD effect of both enantiomers. [h] Elution order cannot be given because the benzoates could not be separated; alcohols were separated first and then benzoylated.

(data not shown) relative to that of the unsubstituted phenyl alcohols, which display a maximum at around 210 nm. Accordingly, in the case of the benzoate **2c**, the first Cotton effect was observed at 233 nm ($\Delta\epsilon = +10.0$) for the *S* enantiomer and at 232 nm ($\Delta\epsilon = -10.9$) for the *R* enantiomer (Figure 3), while for the unsubstituted benzoates the first Cotton effects were observed at 223−229 nm. Additionally, the second Cotton effect of **2c** is shifted to ca. 215 nm, away from the strongly perturbed region below 210 nm; thus, a split-CD curve was obtained for this derivative (Figure 3). Furthermore, the allylic double bond in **2d** did not alter the sign of the Cotton effect for the *R* and *S* enantiomers (entries 7 and 8), which demonstrates the versatility of this analytical method. The additional minor Cotton effect, which derives from the coupling between the double bond and the benzoate groups has the opposite sense in comparison to the major Cotton effect between the phenyl and the benzoate groups; however, this minor Cotton effect is significantly

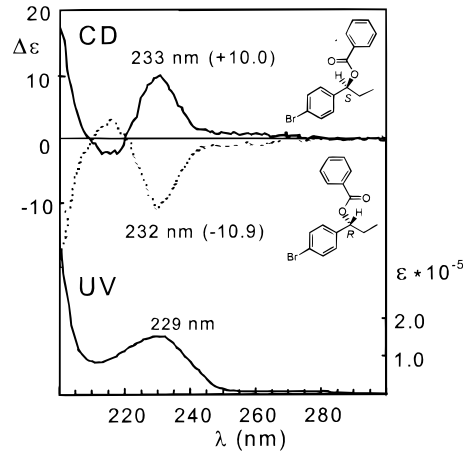


Figure 3. CD and UV spectra of (*R*)- and (*S*)-[1-(*p*-bromo)-phenyl]-1-propyl benzoate (**2c**) in acetonitrile.

Table 2. Multidimensional Gas Chromatography (MDGC) of the Chiral Alcohols 1

entry	alcohol	chiral column[a]	config[b]
1	**1a**	*β*	*R*
2	**1b**	*β*	*R*
3	**1c**	*γ*	*R*
4	**1d**	*β*	*R*
6	**1e**	ethyl	*S*
9	**1f**	*β*	*R*
10	**1g**	ethyl	*S*
11	**1h**	*β*	*S*
12	**1i**	ethyl	*S*

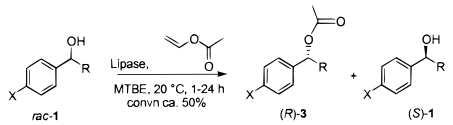
[a] First separation on an achiral DB-Wax column; alcohol peak was transferred to a chiral column: *β*, heptakis(2,6-*O*-dimethyl-3-*O*-pentyl)-*β*-cyclodextrin; ethyl, heptakis(2,3-*O*-diethyl-6-*tert*-butyldimethylsilyl)-*β*-cyclodextrin; *γ*, heptakis(2,6-*O*-dimethyl-3-*O*-pentyl)-*γ*-cyclodextrin. [b] Configurations of the first eluting enantiomer.

weaker. Thus, the overall Cotton effect of **2d** is diminished compared to that of the saturated derivative **2b**, but the usual pattern of a positive Cotton effect for the *S* and a negative one for the *R* enantiomer is preserved. These results were additionally verified by employing the enantiomerically pure *R* and *S* isomers of **1d**.

To elucidate the absolute configurations of the alcohols obtained by microbial transformations of arylalkanes,[8] it was necessary to determine the elution order of the enantiomers of the alcohols by multidimensional gas chromatography (MDGC) on chiral cyclodextrin columns. After hydrolysis of the respective enantiomers of the benzoates **2c**−**i**, which were initially separated by chiral HPLC, the enantiomerically pure free alcohols were analyzed by chiral MDGC (Table 2). Since the absolute configurations of the corresponding benzoates were known from CD spectroscopy and hydrolysis proceeded under retention of the absolute configuration, the elution orders of the enantiomers of the alcohols **1** were obtained by chiral GC analysis. The absolute configurations of the alcohols formed in the biotransformations of the aryl alkanes were subsequently disclosed by comparison with the GC elution order.

For the additional verification of the CD-spectral results, the lipase-catalyzed kinetic resolution of the racemic alcohols **1** was carried out by acetylation with vinyl acetate in MTBE (Scheme 2). The configurations of the remaining alcohols are either literature-known or may be assessed by the well-established empirical model

Scheme 2. Lipase-Catalyzed Kinetic Resolution of Racemic Alcohols 1



for the recognition of secondary alcohols by lipases.[11] The *R* enantiomers of the alcohols are converted under kinetic resolution preferably to their acetate, and therefore, the remaining alcohols are *S*-configured. The enantiomeric excess of the unreacted alcohol was determined by chiral HPLC and MDGC and hereby the elution order of the enantiomers was obtained simultanously. The latter results are in excellent agreement with the configurational assignment by the exciton chirality method.

Finally, the sensitivity of this method could be increased ca. 3-fold when the 2-naphthoate chromophore ($\lambda_{max} = 232$ nm, $\epsilon = 54\,000$ M^{-1} cm^{-1}) was used instead of the benzoate one ($\epsilon = 15\,300$ M^{-1} cm^{-1}). The increased extinction coefficient allowed employment of even lower amounts of the substrates. The sign of the Cotton effects for the enantiomers of the 2-naphthoate derivatives relative to the respective benzoates did not change. In the case of the 2-naphthoate derivatives of the alcohol **1b**, the *R* enantiomer showed a negative first Cotton effect at 234 nm ($\Delta\epsilon = -22.5$) and the *S* enantiomer a positive one at 234 nm ($\Delta\epsilon = +20.5$).

In summary, we have demonstrated for the first time that the CD exciton chirality method may be extended to the arylated alcohols **1** for the determination of their absolute configurations. The results obtained from CD spectroscopy were additionally verified by computer modeling of the benzoate derivatives **2** and by lipase-catalyzed acetylation of the racemic alcohols **1**. Thus, it was established that the first Cotton effect of the benzoate derivatives **2** at around 228 nm permits the unambiguous assignment of the absolute configurations of the corresponding alcohols **1**. Additional functionalities such as a double bond or a substitutent in the *para* position of the phenyl ring of the alcohols **1** do not adversely perturb the CD measurements. However, with the introduction of any new functionalities, the influence on the equilibrium of the various possible conformers has to be taken into account. Nevertheless, the variety of substrates applied in this study demonstrates the versatility of the CD method and its usefulness in organic chemistry.

Experimental Section

General Aspects. ^{1}H NMR spectra were recorded on a Bruker WM 400 (Bruker, Ettlingen, Germany) spectrometer in $CDCl_3$ and are reported in ppm (δ) relative to $CDCl_3$ as internal reference; coupling constants (J) are given in hertz (Hz). UV−vis spectra were recorded on a UV 2101 PC UV/VIS scanning spectrophotometer (Shimadzu, Kyoto, Japan); CD spectra were measured on a JASCO J-600 (JASCO, Gross-Umstadt, Germany) in a 1-cm cuvette, by using acetonitrile or *n*-hexane as solvent. Gas chromatographic analysis was performed on a Siemens SiChromat (Siemens, München, Germany) multidimensional gas chromatography (MDGC) system, supplied with two ovens (independent temperature control) and equipped with two flame-ionization detectors (FID) and a "live-switching" coupling device. Preseparation was achieved on an achiral J&W DB WAX column (30 m × 0.25 mm, $d_f = 0.25$ μm; J&W Scientific, Folsom, CA). Subsequently, the peak was cut out and transferred to a chiral column for separation of the enantiomers: heptakis(2,6-*O*-dimethyl-3-*O*-pentyl)-β-cyclodextrin column (β), heptakis(2,6-*O*-dimethyl-3-*O*-pentyl)-γ-cyclodextrin column (γ), heptakis-(2,3-*O*-diethyl-6-*tert*-butyl-dimethylsilyl)-β-cyclodextrin column (ethyl), heptakis(2,3-*O*-diacetyl-6-*tert*-butyl-dimethylsilyl)-β-cyclodextrin column (ac).

Mass spectrometry was conducted on a MD 800 mass spectrometer coupled with a Fisons GC 8000 (Fisons, Mainz-Kastel, Germany); HPLC analysis was performed on an instrument that consisted of a Knauer 64A HPLC pump (Knauer, Berlin, Germany), a UV detector (Knauer, Berlin, Germany), and a Chiralyzer (IBZ Messtechnik, Hannover, Germany), with detection at 220 nm. Chiralcel OD-H, Chiralcel OB-H, and Chiralpak AS columns (all from J. T. Baker B. V., Deventer, NL) were used for chiral HPLC analysis. Authentic references were obtained from Sigma-Aldrich (Sigma-Aldrich, Deisenhofen, Germany). The alcohols **2c** and **2f**−**i** were prepared by Grignard reactions of the respective aldehydes according to standard literature procedures.[13]

General Procedure for Benzoylation of Aryl Alcohols. Under an argon atmosphere, 1 mmol of alcohol **1** and 1.2 mmol of benzoyltriazole[3c] were dissolved in approximately 5 mL of dry acetonitrile and 1.3 mmol of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) were added to the solution. The reaction mixture was stirred for 12 h at room temperature (approximately 20 °C). The crude mixture was purified by preparative thin-layer chromatography (8:2 pentane:ethyl ether) to afford the benzoylated derivatives **2** in quantitative yields. The 2-naphthoate derivatives were obtained analogously by employing 2-naphthoylimidazole (Sigma-Aldrich, Deisenhofen, Germany).

General Procedure for the Lipase-Catalyzed Kinetic Resolution of Aryl Alcohols. Alcohol **1** (0.1 mmol) and 10 mg of lipase (Chirazyme L1, Boehringer, Mannheim, Germany) were added to a solution of 0.4 mmol of vinyl acetate in 1 mL of *tert*-butyl methyl ether. The mixture was stirred for 1−24 h, depending on the alcohol used, at room temperature (approximately 20 °C) and the enzyme was separated by centrifugation. The supernatant was analyzed by chiral HPLC and multidimensional gas chromatography (MDGC). The acetate **3** was characterized by GC−MS.

(1-Phenyl)ethan-1-ol (1a). MDGC: DB-Wax, 100 to 240 °C (10 °C/min); β, 80 °C (15 min isothermal) to 200 °C (2 °C/min).

(*R*)- and (*S*)-(1-Phenyl)-1-ethyl Benzoate (2a). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, $J = 7.36$ Hz, 2H), 7.57 (t, $J = 7.32$ Hz, 1H), 7.38 (m, 7H), 6.15 (q, 1H), 1.69 (d, $J = 6.6$ Hz, 3H). CD (acetonitrile): 228 nm, $\Delta\epsilon = -6.3$ (*R* enantiomer); 225 nm, $\Delta\epsilon = +6.6$ (*S* enantiomer).

(1-Phenyl)propan-1-ol (1b). MDGC: DB-Wax, 80 to 240 °C (10 °C/min); β, 60 °C (15 min isothermal) to 200 °C (2 °C/min).

(*R*)- and (*S*)-(1-Phenyl)-1-propyl Benzoate (2b). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, $J = 6.96$ Hz, 2H), 7.44 (m, 8H), 5.92 (t, $J = 7.0$ Hz, 1H), 2.07 (m, 2H), 0.97 (t, $J = 7.72$ Hz, 3H). CD (acetonitrile): 228 nm, $\Delta\epsilon = -7.1$ (*R* enantiomer); 229 nm, $\Delta\epsilon = +7.4$ (*S* enantiomer).

(1-Phenyl)-1-propyl 2-Naphthoate. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (s, 1H), 8.11 (d, 1H), 7.98 (d, 1H), 7.89 (d, 2H), 7.60 (t, 1H), 7.52 (t, 1H), 7.48 (d, 2H), 7.36 (t, 2H), 7.31 (t, 1H), 6.0 (t, $J = 7.14$ Hz, 1H), 2.12 (m, 1H), 2.02 (m, 1H), 1.02 (t, $J = 7.08$ Hz, 3H). CD (acetonitrile): 234 nm, $\Delta\epsilon = -22.5$ (*R* enantiomer); 234 nm, $\Delta\epsilon = +20.5$ (*S* enantiomer).

[1-(*p*-Bromo)phenyl]propan-1-ol (1c). MDGC: DB-Wax, 100 to 240 °C (10 °C/min); γ, 80 °C (21 min isothermal) to 200 °C (2 °C/min).

(11) Burgess, K.; Jennings, L. *J. Am. Chem. Soc.* **1991**, *113*, 6129−6139.

(12) CD measurement of **2h** in *n*-hexane (data not shown) revealed almost the same CD curves with slight differences in λ_{max} and amplitudes; for this reason, the CD spectra of all other compounds were not measured in *n*-hexane.

(13) March, J. *Advanced Organic Chemistry*, 3rd ed.; John Wiley & Sons: New York, 1985; pp 816−822.

[1-(*p*-Bromo)phenyl]-1-propyl Benzoate (2c). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 6.96 Hz, 2H), 7.58 (t, J = 7.32 Hz, 1H), 7.47 (q, 4H), 7.29 (t, J = 8.44 Hz, 2H), 5.86 (t, J = 6.64 Hz, 1H), 1.96 (m, 2H), 0.95 (t, J = 7.36 Hz, 3H). CD (acetonitrile): 232 nm, $\Delta\epsilon = -10.9$ (*R* enantiomer); 233 nm, $\Delta\epsilon = +10.0$ (*S* enantiomer).

[1-(*p*-Bromo)phenyl]-1-propyl Acetate (3c). GC−MS: *m*/*z* (%) 256 (0.01), 229 (55), 227 (57), 216 (29), 214 (31), 199 (11), 198 (32), 197 (12), 196 (33), 187 (94), 186 (14), 185 (100), 171 (33), 169 (35), 157 (23), 118 (31), 117 (91), 116 (20), 115 (51), 90 (12), 89 (13), 78 (16), 77 (45), 76 (18), 75 (18), 51 (19), 43 (83).

(1-Phenyl)-2-propen-1-ol (1d). MDGC: DB-Wax, 80 to 240 °C (5 °C/min); β, 80 °C (27 min isothermal) to 200 °C (1 °C/min).

(1-Phenyl)-2-propenyl Benzoate (2d). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 5.88 Hz, 2H), 7.58 (t, J = 7.68 Hz, 1H), 7.46 (t, J = 6.6 Hz, 4H), 7.39 (t, J = 7 Hz, 2H), 7.33 (d, J = 7.36 Hz, 1H), 6.52 (m, 1H), 6.14 (m, 1H), 5.41 (d, J = 8.9 Hz, 1H), 5.31 (d, J = 10.28 Hz, 1H). CD (acetonitrile): 224 nm, $\Delta\epsilon = -3.6$ (*R* enantiomer); 223 nm, $\Delta\epsilon = +3.6$ (*S* enantiomer).

(1-Phenyl)-2-propenyl Acetate (3d). GC−MS: *m*/*z* (%) 176 (1), 134 (71), 133 (21), 117 (28), 116 (63), 115 (100), 105 (27), 91 (16), 77 (20), 51 (12), 43 (51).

2,2 Dimethyl-1-phenylpropan-1-ol (1e). MDGC; DB-Wax: 60 to 240 °C (4 °C/min); ethyl: 60 °C (34 min isothermal) to 200 °C (2 °C/min).

2,2 Dimethyl-1-phenyl-1-propyl Benzoate (2e). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, J = 6.64 Hz, 2H), 7.60 (t, J = 7.32 Hz, 1H), 7.50 (t, J = 7.72 Hz, 2H), 7.39 (d, J = 6.96 Hz, 2H), 7.31 (m, 3H), 5.75 (s, 1H), 1.07 (s, 9H). CD (acetonitrile): 229 nm, $\Delta\epsilon = -2.1$ (*R* enantiomer); 228 nm, $\Delta\epsilon = +10.3$ (*S* enantiomer).

(1-Phenyl)pentan-1-ol (1f). MDGC: DB-Wax, 100 to 240 °C (5 °C/min); β, 80 °C (24 min isothermal) to 200 °C (2 °C/min).

(1-Phenyl)-1-pentyl Benzoate (2f). ^{1}H NMR (250 MHz, $CDCl_3$): δ 8.10 (d, J = 6.7 Hz, 2H), 7.57 (t, J = 7.33 Hz, 1H), 7.38 (m, 7H), 5.99 (t, J = 6.1 Hz, 1H), 2.00 (m, 2H), 1.37 (m, 4H), 0.90 (t, J = 6.73 Hz, 3H). CD (acetonitrile): 223 nm, $\Delta\epsilon = +3.5$ (*S* enantiomer).

(1-Phenyl)-1-pentyl Acetate (3f). GC−MS: *m*/*z* (%) 206 (18), 165 (19), 164 (93), 150 (11), 149 (87), 146 (25), 131 (11), 118 (26), 117 (92), 115 (37), 108 (37), 107 (100), 105 (56), 104 (82), 103 (21), 92 (14), 91 (88), 79 (76), 78 (31), 77 (76), 65 (16), 51 (25), 43 (84), 41 (26).

3-Methyl-1-phenylbutan-1-ol (1g). MDGC: DB-Wax, 80 to 240 °C (5 °C/min); ethyl, 80 °C (24 min isothermal) to 200 °C (1 °C/min).

3-Methyl-1-phenyl-1-butyl Benzoate (2g). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 7.0 Hz, 2H), 7.56 (t, J = 7.32 Hz, 1H), 7.45 (t, J = 7.72 Hz, 4H), 7.35 (t, J = 6.96 Hz, 2H), 7.30 (d, J = 6.96 Hz, 1H), 6.07 (m, 1H), 1.75 (m, 2H), 1.12 (m, 1H), 1.00 (d, J = 6.24 Hz, 3H), 0.98 (d, J = 6.24 Hz, 3H). CD (acetonitrile): 224 nm, $\Delta\epsilon = -6.2$ (*R* enantiomer).

(1-Phenyl)hexan-1-ol (1h). MDGC: DB-Wax, 80 to 240 °C (10 °C/min); β, 80 °C (18 min isothermal) to 200 °C (2 °C/min).

(1-Phenyl)-1-hexyl Benzoate (2h). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.12, 2H), 7.52 (t, J = 6.6 Hz, 1H), 7.38 (m, 7H), 5.98 (t, J = 6.96 Hz, 1H), 2.04 (m, 1H), 1.87 (m, 1H), 1.43 (m, 2H), 1.25 (m, 4H), 0.87 (t, J = 7.0 Hz, 3H). CD (acetonitrile): 225 nm, $\Delta\epsilon = -4.9$ (*R* enantiomer); 224 nm; $\Delta\epsilon = +9.6$ (*S* enantiomer).

(1-Phenyl)-1-hexyl Acetate (3h). GC−MS: *m*/*z* (%) 220 (4), 178 (35), 149 (28), 117 (28), 107 (100), 105 (13), 104 (37), 91 (30), 79 (16), 77 (14), 43 (59), 41 (6).

(1-Phenyl)heptan-1-ol (1i). MDGC: DB-Wax, 100 to 240 °C (5 °C/min); ethyl, 100 °C (28 min isothermal) to 200 °C (2 °C/min).

(1-Phenyl)-1-heptyl Benzoate (2i). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, J = 8.09 Hz, 2H), 7.56 (t, J = 7.36 Hz, 1H), 7.44 (q, 4H), 7.35 (t, J = 7.35 Hz, 2H), 7.29 (d, J = 6.99 Hz, 1H), 5.97 (t, J = 6.98 Hz, 1H), 2.05 (m, 1H), 1.9 (m, 1H), 1.25 (m, 8H), 0.86 (t, J = 6.62 Hz, 3H). CD (acetonitrile): 227 nm, $\Delta\epsilon = -3.7$ (*R* enantiomer); 225 nm, $\Delta\epsilon = +6.5$ (*S* enantiomer).

(1-Phenyl)-1-heptyl Acetate (3i). GC−MS: *m*/*z* (%) 234 (3), 192 (34), 149 (31), 117 (26), 107 (100), 104 (46), 91 (33), 79 (17), 77 (15), 43 (57).

(1-Phenyl)-1-decyl Benzoate (2j). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.9 (dd, J = 7.33 Hz, 2H), 7.37 (t, J = 7.33 Hz, 1H), 7.15 (m; 7H), 5.8 (t, J = 6.86 Hz, 1H), 1.74 (m, 2H), 1.09 (m, 14H), 0.68 (t, J = 6.4 Hz, 3H). CD (acetonitrile): 226 nm, $\Delta\epsilon = +9.3$ (*S* enantiomer).

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