Enantioselective Synthesis of 3-Aryl-3-hydroxypropanoic Esters as Subunits for Chiral Liquid Crystals

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Abstract:

Chiral liquid crystals (LCs) with their unique optical and mechanical properties are perspective functional soft materials for fundamental science and advanced technological applications. Herein, we introduce the chiral 3-aryl-3-hydroxypropanoic ester moiety as a versatile building block for the preparation of LC compounds. Three chiral subunits differing in aromatic part were obtained through asymmetric transfer hydrogenation using Ru(II) complexes in 98 - >99% *ee*. Chiral LC compounds of diverse topologies were further prepared without deterioration of the *ee* during the synthesis. Mesomorphic behavior of rod-shaped, bent-shaped flexible dimeric, and polycatenar LCs is consistent with their topology - chiral nematic and smectic phases were identified, as well as rarely observed twist grain boundary A and blue phases. The utilization of synthetic chiral building blocks offers the possibility of fine-tuning the intermolecular interactions by subtle changes in the molecular structure, as well as the preparation of corresponding racemic forms. This paves the way for the study of self-organization and the structure-property relationship in chiral soft materials.

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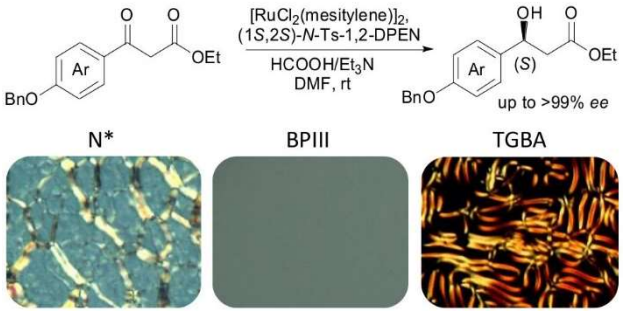


Introduction

Chirality, *i.e.* the geometric property of an object not being superimposable on its mirror image, is an important research topic in a wide range of scientific and technological areas, especially in soft materials due to their huge potential for applications in diverse fields.[1,2] Liquid crystals (LCs) are dynamic functional soft materials that share the anisotropic properties of the crystalline state and the fluidity of a liquid. Molecular shape, microsegregation of incompatible parts and specific molecular interactions drive the process of self-assembly and self-organization toward the formation of various LC phases.[3,4] The introduction of chirality into LCs results in various chiral liquid crystalline phases such as the cholesteric, chiral smectic, twist grain boundary (TGB), and blue phases (BP), each with unique properties.[5,6] Despite the variety of the known chiral LC structures, chirality is mainly introduced by the incorporation of readily available cholesterol unit[7–10] or chiral precursors bearing a methyl group at the chiral centre.[7,11,12] Both chiral subunits suffer from several limitations. The structural variations of cholesterol-based materials are limited due to their monofunctional structure which allows extension only *via* esterification of the 3-hydroxy group, and there are no readily available racemic modifications. Both limitations reduce the possibility for fine-tuning of specific properties of the material[7] and prevent comparison of the mesomorphic behaviour between the

enantiomer and corresponding racemic mixture which is not always unequivocal.[13,14] The chiral subunit with the methyl group at the stereogenic centre is derived either from chiral alcohols or lactic acid and it is often used in terminal chains or spacer of flexible dimer molecules.[7,15] The methyl group causes branching which disrupts lateral interactions and destabilizes LC behaviour, which is particularly pronounced for bent-shaped dimers.[16,17] Since LC behaviour depends on the terminal chain length, a limited number of available adequate chiral alcohols represents a drawback to their use. The elongation of the terminal chain can be achieved only by the successive addition of a single carbon synthon which includes several synthetic steps.[18] Furthermore, partial racemization takes place during the synthesis resulting in the lower enantiomeric purity of the target chiral material.[18,19]

Our work aimed to develop a versatile chiral building block for liquid crystals that enables the preparation of molecules of various topologies and does not possess methyl branching. In terms of requirements, the chiral 3-aryl-3-hydroxypropanoic ester subunit has several advantages. The hydroxyl group is less spacious than the methyl group allowing for better interactions between aromatic mesogenic units. The stereogenic center is positioned near the rigid aromatic fragment which reduces its conformational freedom, contributes to shortening the pitch length of the chiral nematic phase, and increases the helical twisting power.[20,21] Importantly, our synthetic strategy provides chiral subunits with the variable aromatic moiety in high enantiomeric purity. We illustrate its applicability in the design and synthesis of chiral molecules of various shapes by preparing examples of rod-shaped, bent-shaped flexible dimeric and policatenar molecules (Figure 1). The utilization of synthetic rather than naturally occurring chiral building blocks offers the possibility to tune intermolecular interactions by subtle changes in chemical structure, which affects overall thermal behavior and liquid-crystalline characteristics.

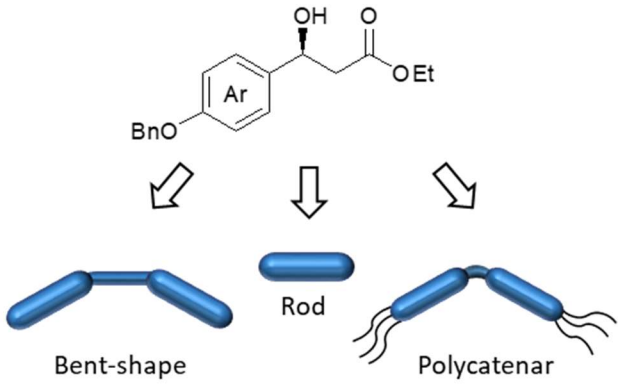
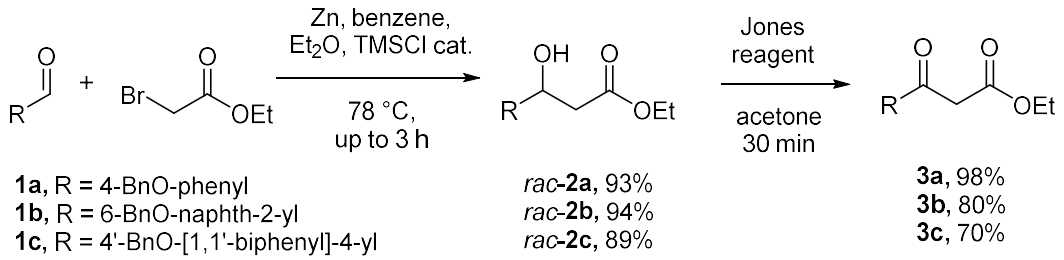


Figure 1. Schematic presentation of chiral subunit and its applicability in the design of chiral molecules of various shapes

Results and discussion

As a first step toward the preparation of the designed chiral LCs, we had to envisage the synthesis of orthogonally protected derivatives of chiral 3-aryl-3-hydroxypropanoic ester in both chiral and racemic forms. After consideration of the several available pathways leading to chiral 3-aryl-3-hydroxypropanoic esters,[22–25] we decided on an approach utilizing asymmetric transfer hydrogenation (ATH) of β-ketoesters. Ever since the pioneering work of Noyori and Ikariya,[26] catalytic ATH of ketones using Ru(II) complexes has become a widely used method for the synthesis of different chiral secondary alcohols, and a large number of catalytic systems have been developed so far.[27–30] Therefore, variations in both catalyst and ligand, could easily allow for a better reaction optimization with regard to enantioselectivity.

Synthesis. The synthesis started with the Reformatsky reaction of 4-(benzyloxy)benzaldehyde (**1a**), 6-(benzyloxy)-2-naphthaldehyde (**1b**), or 4'-(benzyloxy)-[1,1'-biphenyl]-4-carbaldehyde (**1c**), with ethyl bromoacetate. Racemic 3-aryl-3-hydroxypropanoic acid esters *rac*-**2a-c** were obtained in 89-94% yield. In the next step, Jones oxidation of *rac*-**2a-b** gave 3-aryl-3-ketoesters **3a-c** in 70-98% yield (Scheme 1).

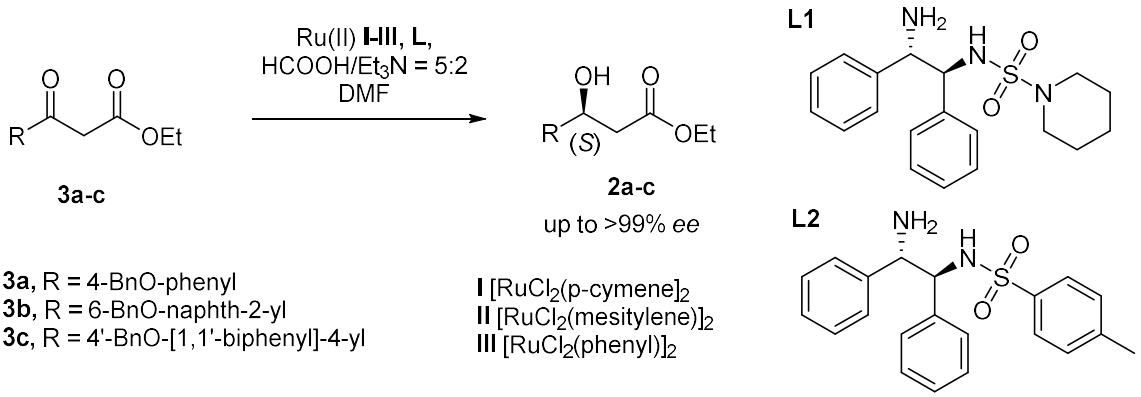


Scheme 1. Synthesis of β-ketoesters **3a-c** in two steps from corresponding aldehydes

In asymmetric transfer hydrogenation reactions, several ruthenium $[RuCl_2(\eta^6\text{-arene})]_2$ precursors **I-III**, with arene being *p*-cymene, mesitylene or benzene respectively, were tested in combination with (1*S*,2*S*)-*N*-(piperidyl-*N*-sulfonyl)-1,2-DPEN[31] (**L1**) or (1*S*,2*S*)-(+)-*N*-Ts-1,2-DPEN[26] (**L2**) ligand. The metal complexes were prepared by heating the metal precursor with the ligand (1.2 equiv. to the metal) at 80 °C in DMF. Reactions were carried in DMF using an azeotropic mixture of HCO_2H and Et_3N (5:2) as a hydrogen donor at either 40 °C or room temperature (Table 1). Initially, all the reactions were conducted with a 10 mol% catalyst at 40 °C to determine optimal precursor/ligand pairs. Catalysts with ligand **L2** performed somewhat better than catalysts with ligand **L1** in terms of enantioselectivity in all tested cases. For all three substrates, the best results were obtained using a combination of mesitylene precatalyst and **L2** ligand. In the case of naphthyl (**3b**), and biphenyl (**3c**) substrates, catalyst loading can successfully be lowered to 2 mol% with no impact on enantioselectivity and accompanied by somewhat longer reaction times up to 24 h (Table 1, entries 18 and 28). Interestingly, for phenyl substituted substrate **3a**, lowering to 2 mol% of catalyst resulted in incomplete conversion (95%) even after 48 h (Table 1, entry 9). Conducting the reaction at room temperature instead of 40 °C, resulted in a small increase in enantioselectivity for all substrates. In the case of substrate **3a**, the best results were obtained with 5 mol% catalyst at room temperature, giving product **2a** in 82% yield and >99% *ee* (Table 1, entry 8). For the substrates **3b** and **3c**, the best results were obtained with 2 mol% catalyst at room temperature, giving products **2b** and **2c** in 89% yield, 98% *ee* (Table 1, entry 19), and in 80% yield, 99% *ee* (Table 1, entry 29),

respectively. As reported in the literature, ATH of ethyl benzoylacetate with the same catalyst/ligand system gives the product with (*S*) configuration.[31] Therefore, we presumed that the absolute configuration of the generated chiral centre in products **2a-c** is also (*S*) and this configuration was unambiguously confirmed in compound **2b** by X-ray analysis.[32] Furthermore, when using (1*R*,2*R*)-(-)-*N*-Ts-1,2-DPEN as a ligand instead of (1*S*,2*S*)-**L2**, opposite enantiomer (*R*)-**2b** was obtained in 98% *ee* (Table 1, entry 20).

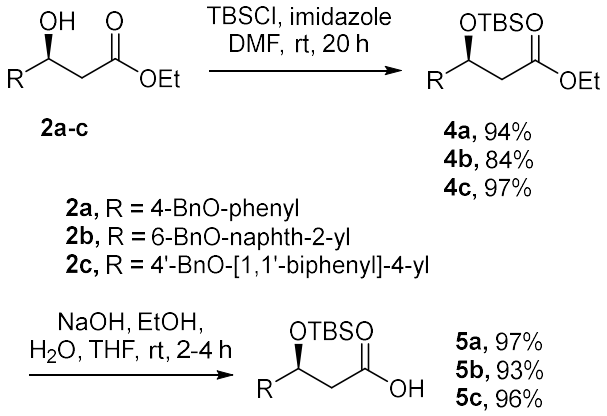
Table 1. Optimization of the reaction conditions for the ATH reaction



Entry	Substrate	$[RuCl_2(\eta^6\text{-arene})]_2$ (mol%)	Ligand	Time (h)	Conversion (%)[a]	Yield (%)	*ee* (%)[b]
1	**3a**	*p*-cymene (10 mol%)	**L1**	48	70	31	38
2	**3a**	mesitylene (10 mol%)	**L1**	24	95	81	90
3	**3a**	benzene (10 mol%)	**L1**	24	100	92	92
4	**3a**	*p*-cymene (10 mol%)	**L2**	48	90	70	82
5	**3a**	mesitylene (10 mol%)	**L2**	3	100	97	97
6	**3a**	benzene (10 mol%)	**L2**	24	95	73	93
7	**3a**	mesitylene (5 mol%)	**L2**	24	100	88	98
8[c]	**3a**	**mesitylene (5 mol%), rt**	**L2**	**24**	**100**	**82**	**>99**
9	**3a**	mesitylene (2 mol%)	**L2**	48	95	69	98
10[c]	**3a**	mesitilyene (2 mol%), rt	**L2**	48	93	78	99
11	**3b**	*p*-cymene (10 mol%)	**L1**	24	100	87	90
12	**3b**	mesitylene (10 mol%)	**L1**	3	100	92	95
13	**3b**	benzene (10 mol%)	**L1**	3	100	94	89
14	**3b**	mesitylene (10 mol%)	**L2**	2	100	81	97
15	**3b**	benzene (10 mol%)	**L2**	3	100	82	91
16	**3b**	mesitylene (5 mol%)	**L2**	3	100	90	98
17[c]	**3b**	mesitylene (5 mol%), rt	**L2**	24	100	73	98
18	**3b**	mesitylene (2 mol%)	**L2**	24	100	80	98
19[c]	**3b**	**mesitylene (2 mol%), rt**	**L2**	**24**	**100**	**89**	**98**
20[c]	**3b**	**mesitylene (2 mol%), rt**	**L2**[d]	**24**	**100**	**86**	**98**[e]
21	**3c**	*p*-cymene (10 mol%)	**L1**	24	100	91	88
22	**3c**	mesitylene (10 mol%)	**L1**	3	100	82	97
23	**3c**	benzene (10 mol%)	**L1**	3	100	89	93
24	**3c**	mesitylene (10 mol%)	**L2**	2	100	81	98
25	**3c**	benzene (10 mol%)	**L2**	3	100	82	94
26	**3c**	mesitylene (5 mol%)	**L2**	24	100	92	98
27[c]	**3c**	mesitylene (5 mol%), rt	**L2**	24	100	83	98
28	**3c**	mesitylene (2 mol%)	**L2**	24	100	74	98
29[c]	**3c**	**mesitylene (2 mol%), rt**	**L2**	**24**	**100**	**80**	**99**

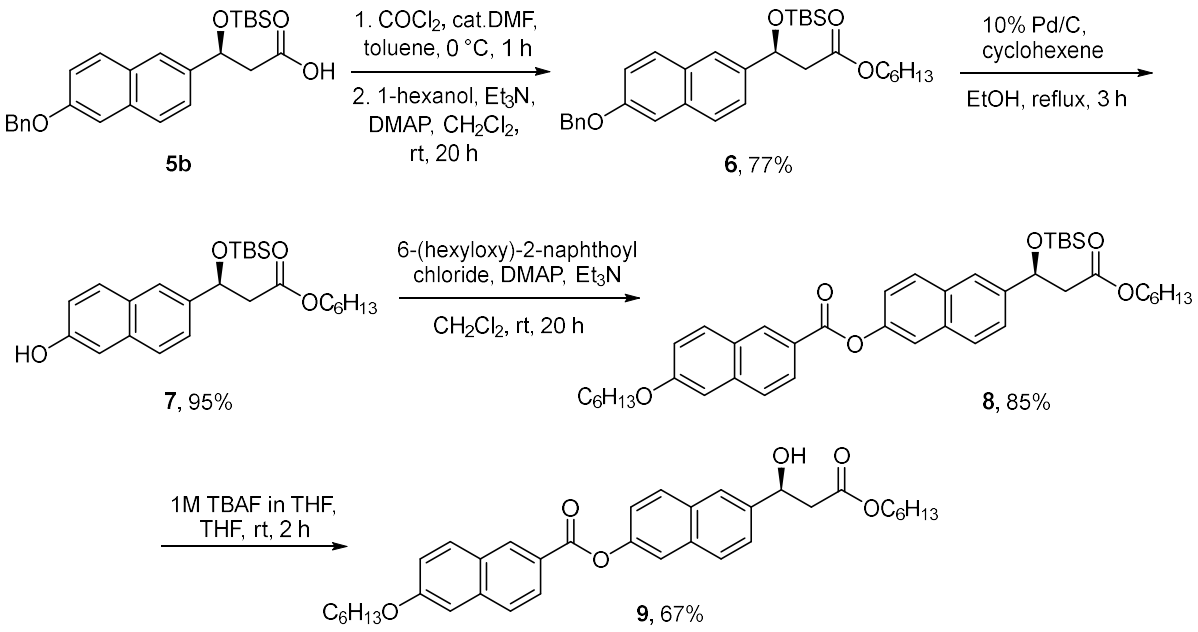
[a] Determined by HPLC on InfinityLab Poroshell 120 EC-C18 column in MeOH/H_2O gradient; [b] Determined by HPLC on Chiralcel OD-3 and Chiralpak IA; [c] room temperature instead of 40 °C; [d] (1*R*,2*R*)-(-)-*N*-Ts-1,2-DPEN was used instead of (1*S*,2*S*); [e] opposite (*R*) enantiomer obtained.

To obtain synthetically useful precursors for all envisaged compounds, the hydroxy group was protected using *tert*-butyldimethylsilyl chloride (TBSCl) to obtain orthogonally protected esters **4a-c** in 84-97% yield, which were then subjected to base hydrolysis to obtain acids **5a-c** (Scheme 2).



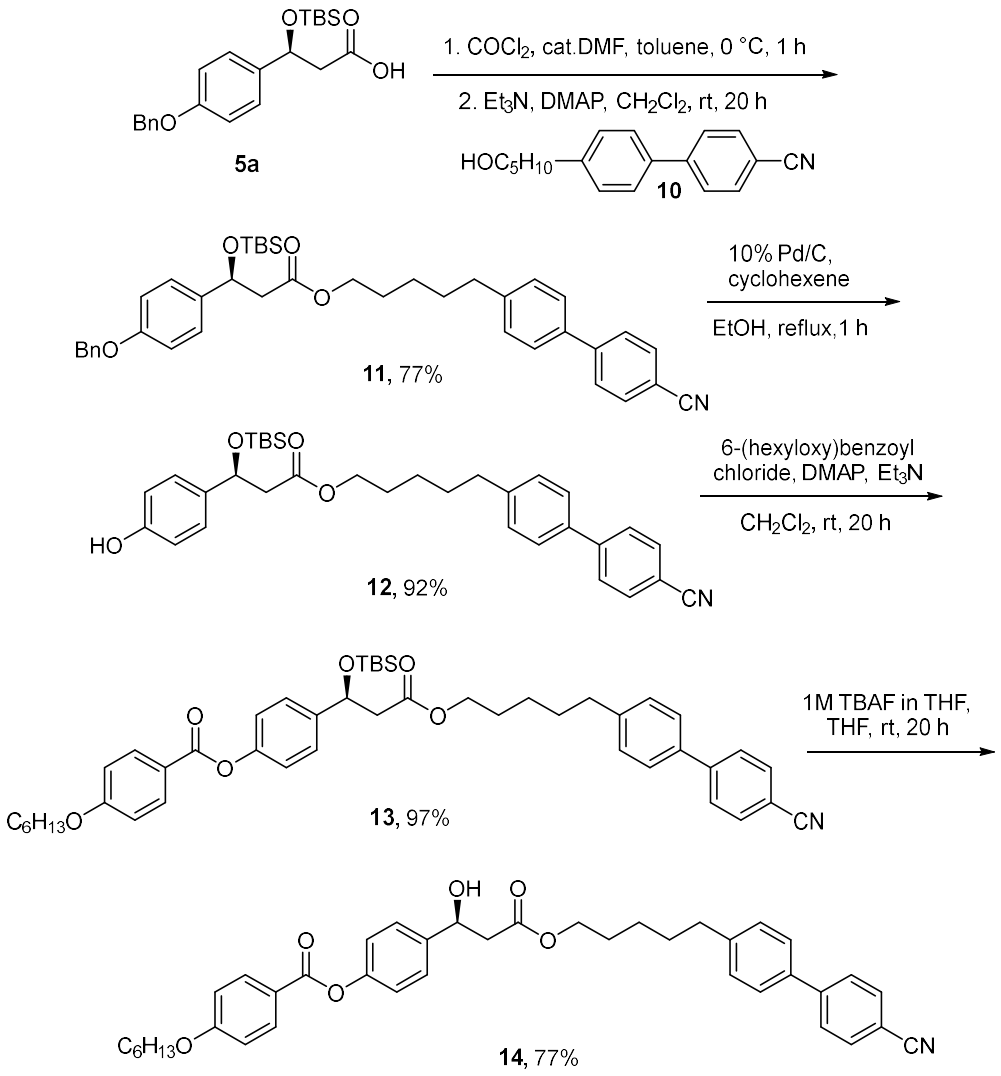
Scheme 2. Protection of hydroxy group and subsequent ester hydrolysis to obtain **5a-c**

We proceeded with the synthesis of rod-shaped, bent-shaped flexible dimeric and policatenar molecules to evaluate the applicability of the prepared chiral subunit. As a first step in obtaining rod-shaped final compound **9** (Scheme 3), chiral acid **5b** was converted in a one-pot procedure to acyl halogenide and then esterified using 1-hexanol to obtain ester **6** in 77% yield. The benzyl protecting group was removed by transfer hydrogenation with 10% Pd/C and cyclohexene as a hydrogen donor in 95% yield. Alcohol **7** was used for esterification of 6-(hexyloxy)-2-naphthoic acid to provide diester **8** in 85% yield. In the final step of the synthesis, TBS protecting group was removed using TBAF, and compound **9** was obtained in 67% yield (Scheme 3).



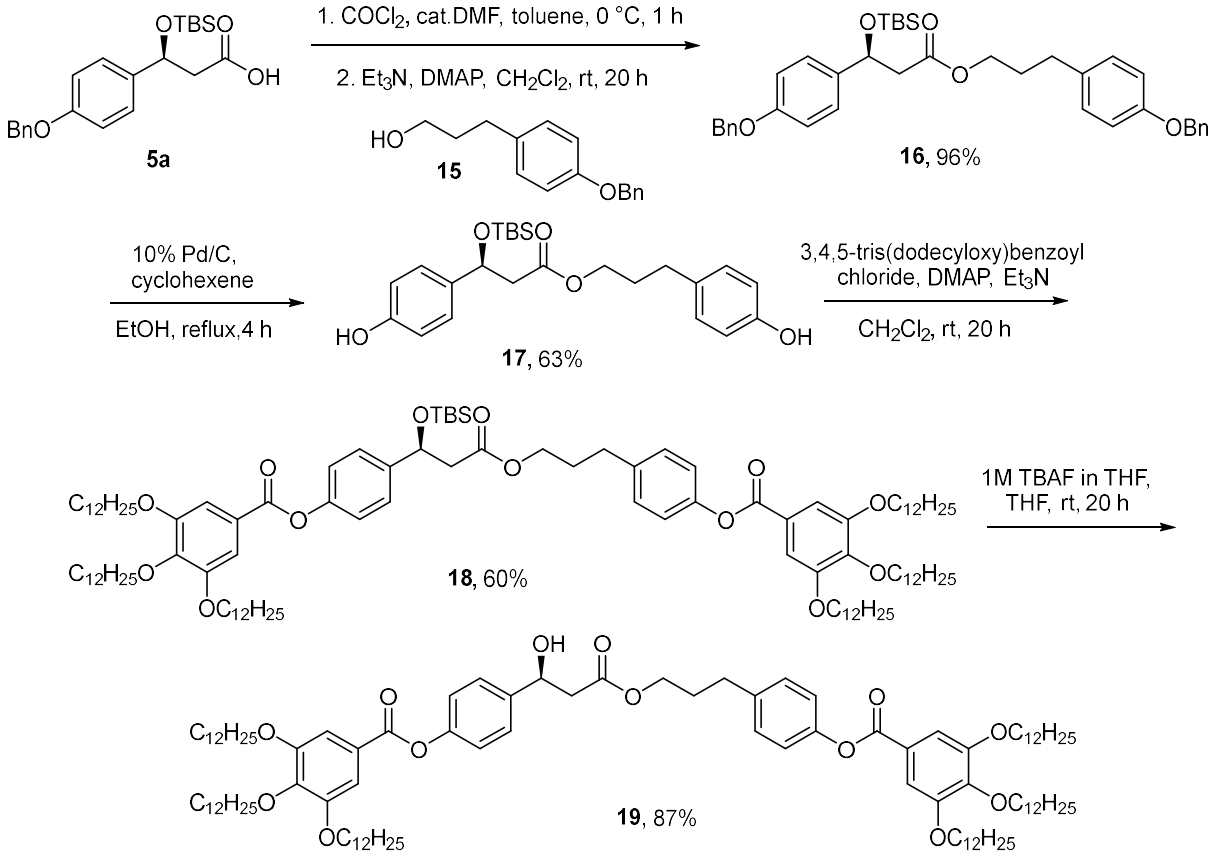
Scheme 3. Synthesis of rod-shaped final compound **9**

Bent-shaped flexible dimer **14** was synthesized using a similar strategy (Scheme 4). Alcohol **10**[33] was prepared as described in the literature and used for the esterification of chiral acid **5a** to obtain compound **11** in 77 % yield. Removal of benzyl protecting group using transfer hydrogenation with 10% Pd/C and cyclohexene gave alcohol **12** in 92% yield. Synthesis was continued with the esterification of 6-(hexyloxy)-2-naphthoic acid using alcohol **12**, followed by the removal of the TBS protecting group to obtain the final compound **14**. The same reaction sequence was repeated on racemic acid *rac*-**5a**, and *rac*-**14** was prepared for comparison to chiral compound **14**. The enantiomeric purity of **14** was determined to be 99% which confirmed that there is no deterioration in *ee* during the synthesis.



Scheme 4. Synthesis of bent-shaped flexible dimer **14**

By adopting a molecular design for polycatenar molecules, with the known ability to form columnar phases,[34] we prepared a hexacatenar bent-shaped dimer **19** (Scheme 5) Alcohol **15**[35] was used for esterification of chiral acid **5a**, and ester **16** was obtained in 96% yield. The deprotection of two benzyl groups using transfer hydrogenation with Pd/C and cyclohexene provided diol **17** in 63% yield. Diol **17** was used for double esterification of 3,4,5-tris(dodecyloxy)benzoic acid[36] and diester **18** was obtained in 60% yield. In the last step, deprotection of the TBS group gave the final compound **19** in 87% yield.



Scheme 5. Synthesis of a hexacatenar bent-shaped dimer **19**

Mesophase characterization of 9, 14, *rac*-14 and 19. All prepared compounds display mesomorphic properties. The transition temperatures and corresponding enthalpies are presented in Table S1. Incorporation of the chiral naphthyl-3-hydroxypropanoate moiety in the typical rod-shaped molecule **9** resulted in a chiral nematic material. The enantiotropic chiral nematic phase (N*) was identified by the characteristic fan-like and oily streaks textures (Figure 2a). In addition, two monotropic phases were observed just before crystallization. On cooling from the N* phase, the short-lived filamentary growth suggested the presence of a transient twist grain boundary A (TGBA) phase[37] (Figure 2b) which turned into the pseudo-isotropic texture of the SmA* phase. The TGB phase is presumably a result of the competition between a helical macrostructure, formed by strongly chiral systems, and the requirement for the formation of a lower energy layered structure.[38] It was suggested that the chirality of the helical macrostructure can be increased by the reduction in the conformation flexibility of the chiral

centre and the extension of the rigid aromatic fragment within a chiral molecule.[20,21] The chiral naphthyl-3-hydroxypropanoate derivative **9** has both structural elements – conformational freedom of the stereogenic centre is reduced due to the neighboring aromatic moiety, and the rigid mesogenic unit possesses two naphthyl fragments. As we have shown during the synthesis, both aromatic fragments can be easily altered, which allows further investigation of the structure-property relationship or the discovery and elucidation of novel modifications of the TGB phases.

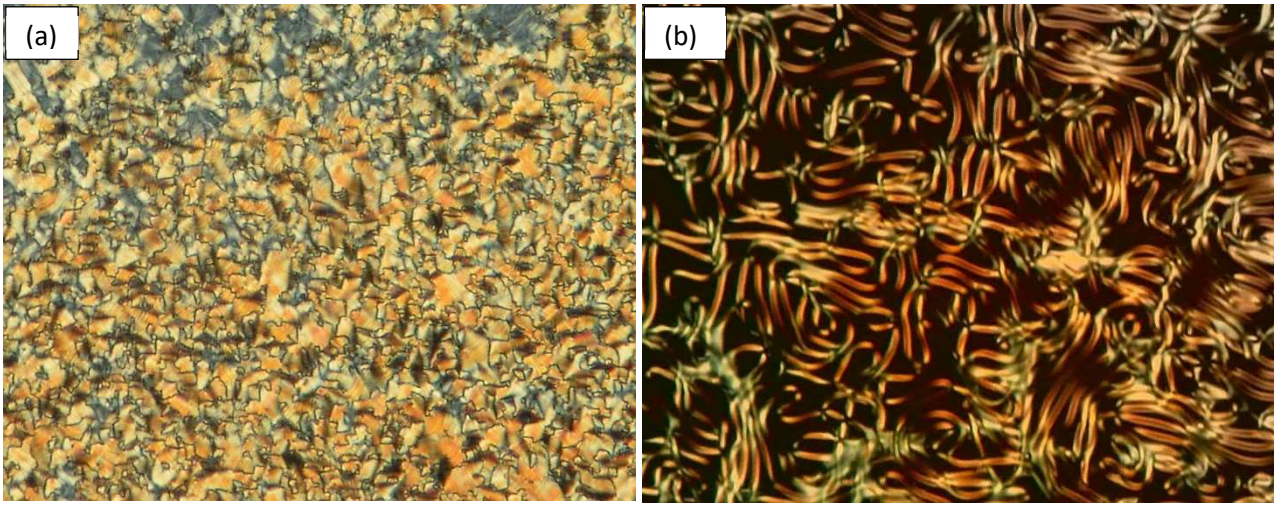


Figure 2. Optical textures of **9** obtained on cooling. (a) fan-like and oily streaks textures of the N* phase at 124 °C, (b) filamentary texture of the TGBA phase at 108 °C.

Changing the geometry of the molecule into a bent shape in which the stereogenic centre is positioned in the spacer resulted in monotropic polymorphic behavior. On cooling the isotropic liquid of the chiral dimer **14**, a mesophase appears at 51 °C with a bluish foggy texture without any distinctive structure (Figure 3a). Such a texture is reported for the blue phase BPIII.[37] Upon further cooling the BPIII changed to a smectic phase without the appearance of the N* phase.

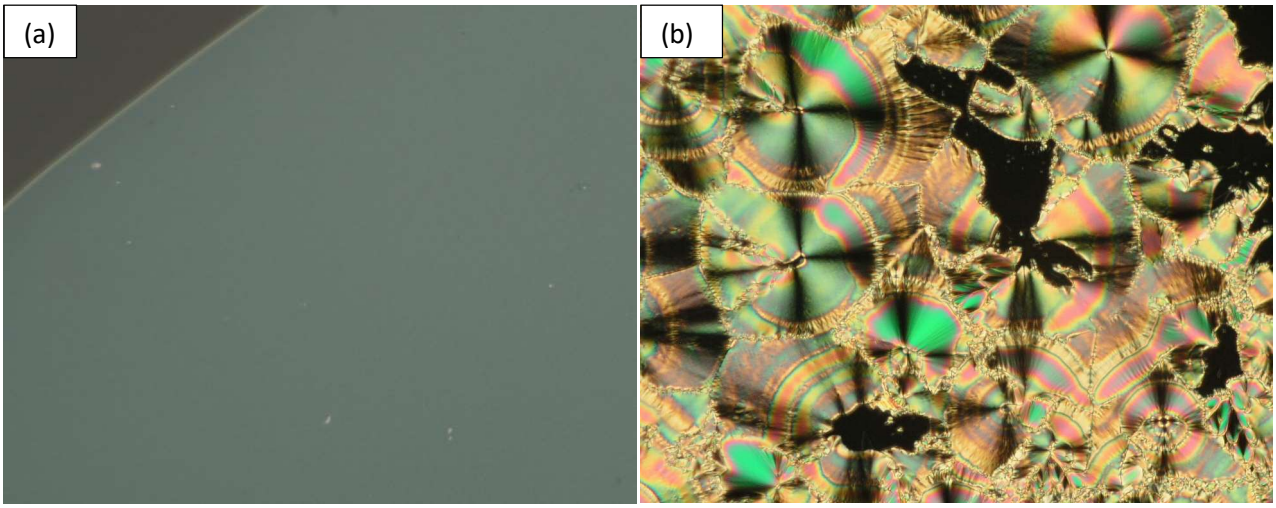


Figure 3. Optical textures of **14** obtained on cooling. (a) bluish foggy texture of the BPIII phase at 51 °C, (b) fan-shaped texture of the smectic phase at 40 °C

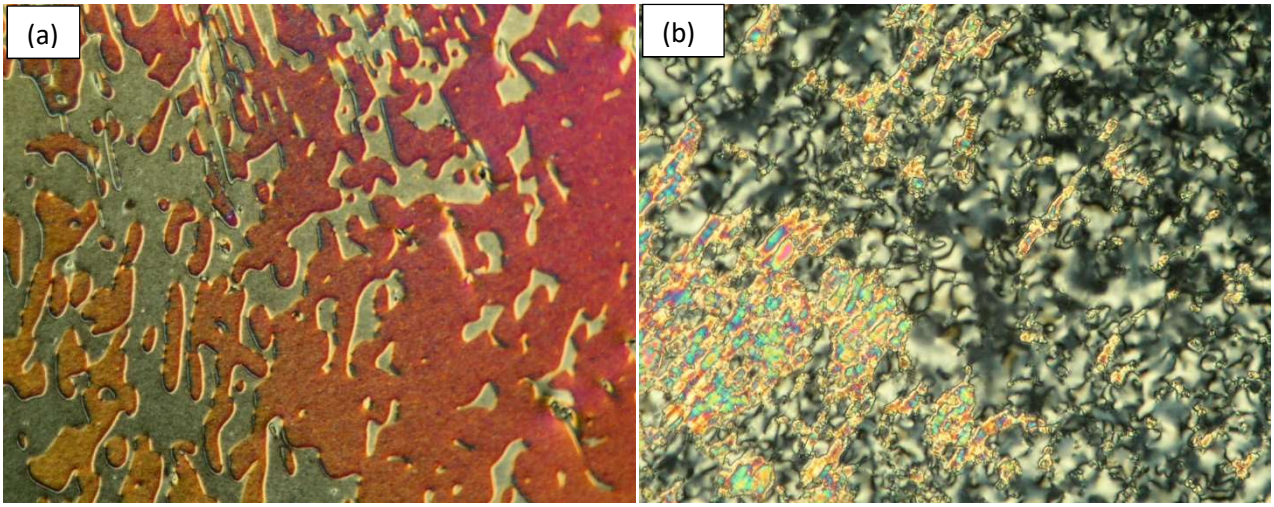


Figure 4. Optical textures of *rac*-**14** obtained on cooling. (a) marble texture of the N phase at 47 °C, (b) focal-conic and schlieren-like texture with two and four brushes of the intercalated SmC phases at 31 °C.

Growth of the fan-shaped texture and the presence of pseudo-isotropic regions implies the smectic A or chiral anticlinic smectic C phase (SmC_A*)[37] (Figure 3b). Investigation of the corresponding racemic dimer *rac*-**14** reveals the presence of the monotropic nematic phase characterized by typical marble texture followed by the smectic phase. On cooling, from the N

to smectic phase a very small focal-conic texture developed (Figure 4a). Shearing the sample led to a schlieren-like texture with two and four brushes (Figure 4b) which have also been observed in intercalated SmC phases of mesogenic twins.[39–41] The presence of two-point defects in the schlieren texture indicates that the phase has an anticlinic structure.[41] Although rapid crystallization prevents X-ray investigation, optical microscopy observation strongly supports identification of the smectic phase as SmC_A. Consequently, the smectic phase of the corresponding chiral dimer **14** is tentatively assigned as SmC_A*. The observed behavior is unusual. For a single material, blue phase is normally found in a very narrow temperature range (a few degrees) between the isotropic liquid and a chiral nematic (N*) phase. To date, two exceptions were reported.[13,14] U-shaped binaphthyl mesogenic derivative displays direct BPIII to SmA transition[14] while bent-core 4-cyanoresorcinols with two branched chiral terminal chains show BPIII to M (mesophase with unidentified structure) transition.[13] In both cases a comparison of the mesomorphic properties of enantiopure with the corresponding racemic compound showed that the BPIII phase is replaced by the nematic phase in the racemic material. It is interesting to note that previously reported materials significantly differ in shape and source of chirality, making the flexible dimer **14** a novel structural motif for which this unusual phase sequence was observed.

The third example represents a successful modification of the chemical structure which leads to the columnar organization. According to the observed mosaic texture (Figure 5), the liquid-crystalline phase of hexacatenar dimer **19** was identified as columnar hexagonal (Col_h). The addition of six alkoxy chains at the periphery of bent-shaped dimers results in microsegregation induced by the incompatible space-filling requirements of the aromatic and alkyl parts of the molecules. This is the classical behaviour of polycatenars[42,43] confirming that the structure of the bent-shaped flexible dimers can be varied in a similar way as bent-core mesogens to obtain columnar organization.

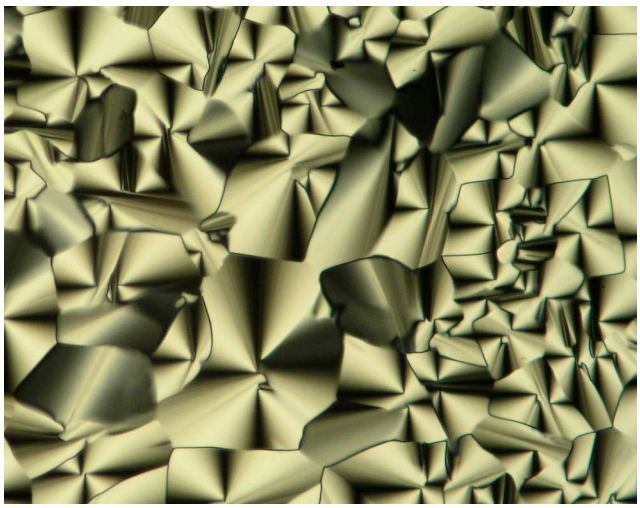


Figure 5. Mosaic optical texture of the columnar phase of **19** obtained on cooling at 25 °C.

Conclusion

Here we report the synthesis and evaluation of the chiral 3-aryl-3-hydroxypropanoic ester subunit as a building block for chiral liquid crystals. The chiral phenyl, naphthyl, and biphenyl subunits are obtained through asymmetric transfer hydrogenation using Ru(II) complexes in >99%, 98%, and 99% *ee*, respectively. Liquid crystalline compound **14** synthesized from 3-phenyl-3-hydroxypropanoic ester **2a** exhibits the enantiomeric purity of 99%, confirming no deterioration of the *ee* during the synthesis. The appropriate material design leads to different molecular topologies and thus different self-organization. The examples of rod-shaped (**9**), bent-shaped flexible dimeric (**14**), and polycatenar materials (**19**) show mesomorphic behavior consistent with their shape. In addition to the expected chiral nematic and smectic phase, compounds **9** and **14** exhibit rarely observed TGBA and BPIII phases, respectively. These results confirm that the chiral 3-aryl-3-hydroxypropanoic ester subunit can be successfully used in the synthesis of LC materials. Furthermore, the synthetic strategy allows variations in the aryl moiety and also the preparation of corresponding racemic forms, both of which have a

profound effect on LC properties.[44,45] Our chiral building blocks have great potential for molecular engineering of liquid crystals and other functional materials which can be used for the study of new chiral structures with complex architecture and for tuning specific physical properties.

Experimental Section

General Methods. All reactions were conducted under an argon atmosphere unless stated otherwise. THF, benzene and Et_2O were dried following standard methods. The commercial grade reagents and solvents were used without further purification. TLC was performed on aluminum-baked silica plates (60 F254, Merck). UV light (254 nm) or phosphomolybdic acid reagent was used for visualizing. Column chromatography was performed on silica gel (Silicagel 60, 70–230 mesh, Merck) or flash silica gel (Silicagel 60, 230-400 mesh, Merck). ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded on a Bruker AV 300 and 600 spectrometers in $CDCl_3$ or d_6-DMSO. Chemical shifts (δ) are given in ppm referenced to TMS or solvent. Coupling constants are given in Hz. Chemical purity and reaction progress were monitored by HPLC on an Agilent 1260 Infinity instrument on an InfinityLab Poroshell 120 EC-C18, 4.6 x 100 mm, 2.7 μ column with DAD detector, 0.5 mL/min flow. The optical purity of the formed products was determined by chiral HPLC analysis on Agilent 1260 Infinity instrument on Daicel Chiralcel OD-3 (4.6 x 250 mm, 3 μ) and Chiralpak IA (4.6 x 250 mm, 5 μ) columns. Optical rotations were measured using Optical Activity AA-10 automatic polarimeter. Melting points were determined with an Electrothermal 9100 apparatus in open capillaries and are uncorrected. High resolution mass spectrometry (HRMS) was performed on 4800 Plus MALDI TOF/TOF Analyzer (CHCA matrix). Optical textures were determined using an Olympus BX51 polarizing microscope equipped with a Linkam TH600 hot stage and PR600 temperature controller and Olympus camera EP50. The phase transition temperatures and corresponding

enthalpies were determined from thermograms recorded on Perkin-Elmer Diamond DSC, operated at scanning rates of 5 °C min^{-1}. X-ray data collection was performed on Oxford Diffraction Xcalibur Nova R diffractometer with a microfocusing Cu tube (λ = 1.54179 Å). (1*S*,2*S*)-(+)-*N*-*p*-Tosyl-1,2-diphenylethylenediamine **L2**, $[RuCl_2(p\text{-cymene})]_2$ **I**, $[RuCl_2(mesitylene)]_2$ **II** and $[RuCl_2(C_6H_6)]_2$ **III**, were obtained from commercial sources. (1*S*,2*S*)-*N*-(Piperidyl-*N*-sulfonyl)-1,2-diphenylethylenediamine **L1** was prepared according to the literature procedure.[31] Compound **1a** is commercially available. Compounds **1b**,[46] **1c**,[47] **10**,[33] and **15**,[35] are known compounds and were prepared according to literature procedures.

Experimental Procedures. *General reaction procedure A - Ethyl 3-(4-(benzyloxy)phenyl)-3-hydroxypropanoate (rac-***2a***)*.[48] Powdered zinc (0.8 g, 12.2 mmol) was placed in a dry three-necked flask under argon, and the flask was fitted with a reflux condenser and a dropping funnel. A solution of ethyl bromoacetate (0.55 mL, 5 mmol), 4-benzyloxybenzaldehyde **1a** (1.29 g, 6.1 mmol) and TMSCl (30 μL) in a mixture of dry benzene (8 mL) and dry diethyl ether (1 mL) was placed in a dropping funnel. 1 mL of the solution was added to the zinc and the mixture was heated to reflux until the reaction starts. The rest of the solution is added dropwise and the mixture was refluxed for another 30 min. After cooling, the mixture is diluted with MTBE (30 mL) and a 10% aqueous solution of H_3PO_4 (20 mL) is added. Layers were separated and the water layer was extracted with MTBE (2 x 20 mL). Combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude ester was purified using silica gel column chromatography (DCM/EtOAc = 9:1) to obtain product *rac*-**2a** (1.40 g, 93%) as a white solid. *mp* = 73.1-73.6 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.26 (t, *J* = 7.1 Hz, 3H), 2.67 (dd, *J* = 16.3, 3.6 Hz, 1H), 2.75 (dd, *J* = 16.3, -9.3 Hz, 1H), 3.16 (d, *J* = 3.4 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 5.06 (s, 2H), 5.06-5.09 (m, 1H), 6.96 (d, *J* = 8.7 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 7.31-7.34 (m, 1H), 7.35-7.40 (m, 2H), 7.40-

7.45 (m, 2H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ 14.2, 43.3, 60.8, 69.9, 70.0, 114.9, 127.0, 127.4, 128.0, 128.6, 135.0, 136.9, 158.4, 172.5.

*Ethyl 3-(6-(benzyloxy)naphthalen-2-yl)-3-hydroxypropanoate (rac-***2b***)*. According to the general procedure A, starting from 6-hydroxy-2-naphthaldehyde **1b** (4.67 g, 18 mmol) and ethyl bromoacetate (1.80 mL, 16 mmol), and after silica gel column chromatography (DCM/EtOAc = 9:1), compound *rac*-**2b** was prepared as a white solid (5.25 g, 94%). *mp* = 105.7-106.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 3H), 2.77 (dd, J = 16.3, 3.8 Hz, 1H), 2.83 (dd, J = 16.3, 9.1 Hz, 1H), 3.34 (d, J = 3.4 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 5.17 (s, 2H), 5.26 (dt, J = 9.0, 3.6 Hz, 1H), 7.18-7.28 (m, 2H), 7.30-7.36 (m, 1H), 7.36-7.42 (m, 2H), 7.44 (dd, J = 8.5, 1.8 Hz, 1H), 7.46-7.53 (m, 2H), 7.71 (d, J = 8.5 Hz, 1H), 7.73 (d, J = 8.9 Hz, 1H), 7.75-7.78 (m, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 14.2, 43.3, 60.9, 70.1, 70.4, 107.1, 119.4, 124.3, 124.4, 127.3, 127.6, 128.0, 128.6, 128.8, 129.6, 134.1, 136.8, 137.8, 156.9, 172.5. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{22}H_{22}O_4Na$: 373.1416, found: 373.1422.

*Ethyl 3-(4'-(benzyloxy)-[1,1'-biphenyl]-4-yl)-3-hydroxypropanoate (rac-***2c***)*. According to the general procedure A, starting from 4'-(benzyloxy)-[1,1'-biphenyl]-4-carbaldehyde **1c** (1.1 g, 3.8 mmol) and ethyl bromoacetate (0.35 mL, 3.2 mmol), and after silica gel column chromatography (DCM/EtOAc = 9:1), compound *rac*-**2c** was prepared as a white solid (1.07 g, 89%). *mp* = 154.5-155.0 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.28 (t, J = 7.2 Hz, 3H), 2.75 (dd, J = 16.4, 3.8 Hz, 1H), 2.80 (dd, J = 16.4, 9.1 Hz, 1H), 3.26 (d, J = 3.5 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 5.11 (s, 2H), 5.17 (dt, J = 8.9, 3.6 Hz, 1H), 7.05 (d, J = 8.7 Hz, 2H), 7.38-7.43 (m, 4H), 7.44-7.47 (m, 2H), 7.52 (d, J = 8.8 Hz, 2H), 7.54 (d, J = 8.3 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 14.2, 43.2, 60.9, 70.10, 70.12, 115.2, 126.1, 126.9, 127.5, 128.0, 128.1, 128.6, 133.5, 136.9, 140.3, 140.9, 158.4, 172.5. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{24}H_{24}O_4Na$: 399.1572, found: 399.1562.

*General reaction procedure B - Ethyl 3-(4-(benzyloxy)phenyl)-3-oxopropanoate (***3a***).*[49] To a solution of hydroxyester *rac*-**2a** (2.65 g, 8.82 mmol) in acetone (50 mL), cooled to 0 °C, Jones reagent was added dropwise until red-brown color persisted. The mixture was stirred for another 30 min. The solvent was evaporated, water was added (50 mL), and the mixture was extracted with CH_2Cl_2 (3 x 30 mL). Organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude ketoester was purified using silica gel column chromatography (CH_2Cl_2) to obtain product **3a** (2.63 g, 98%) as a white solid. *mp* = 60.5-61.6 °C. ^{1}H NMR (600 MHz, DMSO) δ 1.17 (t, J = 7.1 Hz, 3H), 3.82-4.45 (m, 4H), 5.22 (s, 2H), 7.14 (d, J = 8.9 Hz, 2H), 7.32-7.37 (m, 1H), 7.38-7.43 (m, 2H), 7.44-7.50 (m, 2H), 7.93 (d, J = 8.9 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, DMSO) δ 14.0, 45.3, 60.5, 69.5, 114.8, 127.8, 128.0, 128.5, 128.9, 130.8, 136.7, 162.6, 167.8, 191.7. NMR data is given for keto form, traces of enol form are also visible in NMR.

*Ethyl 3-(6-(benzyloxy)naphthalen-2-yl)-3-oxopropanoate (***3b***).* According to the general procedure B, starting from hydroxyester *rac*-**2b** (1.70 g, 4.85 mmol) and after silica gel column chromatography (CH_2Cl_2) product **3b** (1.34 g, 80%) was obtained as a white solid. *mp* = 98.5-99.1 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 4.08 (s, 2H), 4.23 (q, J = 7.1 Hz, 2H), 5.20 (s, 2H), 7.22-7.25 (m, J = 2.5 Hz, 1H), 7.29 (dd, J = 8.9, 2.5 Hz, 1H), 7.32-7.39 (m, 1H), 7.39-7.45 (m, 2H), 7.45-7.52 (m, 2H), 7.76 (d, J = 8.6 Hz, 1H), 7.87 (d, J = 8.9 Hz, 1H), 7.98 (dd, J = 8.6, 1.8 Hz, 1H), 8.37 (s, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 14.1, 46.0, 61.5, 70.2, 107.1, 120.2, 124.6, 127.4, 127.6, 127.9, 128.2, 128.7, 130.5, 131.4, 131.6, 136.3, 137.5, 159.2, 167.7, 192.1. NMR data is given for keto form, only traces of enol form are visible in NMR.

*Ethyl 3-(4'-(benzyloxy)-[1,1'-biphenyl]-4-yl)-3-oxopropanoate (***3c***).* According to the general procedure B, starting from hydroxyester *rac*-**2c** (1.43 g, 3.8 mmol) and after silica gel column chromatography (CH_2Cl_2) product **3c** (1.0 g, 70%) was obtained as a white solid. *mp* = 151.6-

152.2 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.27 (t, J = 7.1 Hz, 3H), 4.01 (s, 2H), 4.23 (q, J = 7.1 Hz, 2H), 5.13 (s, 2H), 7.03-7.15 (m, 2H), 7.31-7.38 (m, 1H), 7.37-7.43 (m, 2H), 7.44-7.48 (m, 2H), 7.53-7.60 (m, 2H), 7.66 (d, J = 8.5 Hz, 2H), 7.99 (d, J = 8.5 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 14.1, 46.0, 61.5, 70.1, 115.4, 126.8, 127.5, 128.1, 128.4, 128.7, 129.2, 132.3, 134.2, 136.7, 145.9, 159.2, 167.6, 192.0. NMR data is given only for major keto form, both keto and enol form are visible in NMR in 5.5 : 1 ratio respectively.

General reaction procedure C for asymmetric transfer hydrogenation. A mixture of [($RuCl_2$(η^6-mesitylene)]$_2$ (**II**) (5 or 2 mol%) and the chiral ligand (**L2**) (6 or 3 mol%) was heated in DMF (1 mL) at 80 °C for 20 min under argon. The solution was cooled to room temperature. A mixture of HCO_2H and Et_3N, 5:2 molar ratio (0.3 mL) followed by the solution of ketone (0.35 mmol) in DMF (1 mL) were added. The reaction mixture was stirred at room temperature for 24 h. The mixture was partitioned between water (10 mL) and MTBE (20 mL). The organic layer was washed with water (10 mL), and brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude ester was purified using silica gel column chromatography (CH_2Cl_2/EtOAc = 9:1).

Ethyl (S)-3-(4-(benzyloxy)phenyl)-3-hydroxypropanoate (**2a**), yield 82%, NMR given above for the racemic compound. *ee* > 99%, Chiralpak IA, *n*-hexane/ethanol = 95:5, 220 nm, 1 ml/min, t_R(minor) = 48.6 min, t_R(major)= 50.3 min. $[\alpha]_D^{20°C}$ = -26.3 (*c* 0.57, CH_2Cl_2).

Ethyl (S)-3-(6-(benzyloxy)naphthalen-2-yl)-3-hydroxypropanoate (**2b**), yield 89%, NMR given above for the racemic compound. *ee* = 98%, Chiralcel OD-3, *n*-hexane/2-propanol = 90:10, 220 nm, 1 ml/min, t_R(major)= 14.6 min, t_R(minor)= 15.1 min. $[\alpha]_D^{20°C}$ = -26.0 (*c* 1.0, $CHCl_3$). Compound **2b** was crystallized from 2-propanol for X-ray analysis.

Ethyl (S)-3-(4'-(benzyloxy)-[1,1'-biphenyl]-4-yl)-3-hydroxypropanoate (**2c**), yield 80%, NMR given above for the racemic compound. *ee* = 99%, Chiralcel OD-3, *n*-hexane/ethanol = 95:5, 254 nm, 1 ml/min, t_R(major)= 23.7 min, t_R(minor)= 26.5 min. $[\alpha]_D^{20°C}$ = -21.9 (*c* 0.82, $CHCl_3$).

*General reaction procedure D - Ethyl (S)-3-(4-(benzyloxy)phenyl)-3-((tert-butyldimethylsilyl)oxy)propanoate (***4a***).* Compound **2a** (340 mg, 1.13 mmol), TBSCl (204 mg, 1.4 mmol), and imidazole (123 mg, 1.8 mmol) in DMF (5 ml) were stirred overnight at room temperature. The mixture was partitioned between 5% aqueous solution of NH_4Cl (20 mL) and MTBE (20 mL). Layers were separated and water layer was extracted with MTBE (2 x 10 mL). Combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Crude product was purified using silica gel column chromatography (CH_2Cl_2) to obtain compound **4a** (439 mg, 94%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.18 (s, 3H), 0.01 (s, 3H), 0.84 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H), 2.51 (dd, J = 14.5, 4.3 Hz, 1H), 2.71 (dd, J = 14.5, 9.1 Hz, 1H), 4.10-4.14 (m, 2H), 5.05 (s, 2H), 5.10 (dd, J = 9.1, 4.2 Hz, 1H), 6.92 (d, J = 8.7 Hz, 2H), 7.26 (d, J = 8.9 Hz, 2H), 7.30-7.49 (m, 5H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ -5.1, -4.5, 14.3, 18.2, 25.8, 46.7, 60.6, 70.2, 71.9, 114.7, 127.2, 127.7, 128.1, 128.7, 136.8, 137.2, 158.3, 171.4. According to the same procedure, racemic compound *rac*-**4a** was prepared starting from 4 g of *rac*-**2a** in 96% yield.

*Ethyl (S)-3-(6-(benzyloxy)naphthalen-2-yl)-3-((tert-butyldimethylsilyl)oxy)propanoate (***4b***).* According to the general procedure D, starting from compound **2b** (1.10 g, 3.1 mmol), and after silica gel column chromatography (CH_2Cl_2) compound **4b** (1.22 g, 84%) was obtained as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ: -0.17 (s, 3H), 0.05 (s, 3H), 0.87 (s, 9H), 1.25 (t, J = 7.1 Hz, 3H), 2.61 (dd, J = 14.6, 4.1 Hz, 1H), 2.80 (dd, J = 14.6, 9.2 Hz, 1H), 3.91-4.45 (m, 2H), 5.18 (s, 2H), 5.25-5.34 (m, 1H), 7.20-7.25 (m, 2H), 7.33-7.36 (m, 1H), 7.39-7.43 (m, 2H), 7.47 (dd, J = 8.6, 1.7 Hz, 1H), 7.48-7.50 (m, 2H), 7.70 (d, J = 5.9 Hz, 1H), 7.71 (s, 1H), 7.74 (d, J = 8.8 Hz, 1H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ: -5.1, -4.5, 14.3, 18.2, 25.8, 46.6, 60.6, 70.2, 72.5, 107.3, 119.4, 124.6, 124.8, 127.2, 127.7, 128.2, 128.8, 128.9, 129.6, 134.2, 137.0, 139.6, 156.9, 171.3. HRMS (MALDI) *m/z*, ([M+Na]$^+$): calcd. for $C_{28}H_{36}O_4SiNa$: 487.2281, found: 487.2267.

Ethyl (S)-3-(4'-(benzyloxy)-[1,1'-biphenyl]-4-yl)-3-((tert-butyldimethylsilyl)oxy)propanoate (**4c**). According to the general procedure D, starting from compound **2c**, and after silica gel column chromatography (CH_2Cl_2) compound **4c** (0.74 g, 97%) was obtained as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.14 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 1.26 (t, J = 7.1 Hz, 3H), 2.57 (dd, J = 14.5, 4.2 Hz, 1H), 2.76 (dd, J = 14.5, 9.2 Hz, 1H), 4.05-4.22 (m, 2H), 5.11 (s, 2H), 5.19 (dd, J = 9.1, 4.1 Hz, 1H), 7.04 (d, J = 8.7 Hz, 1H), 7.30-7.57 (m, 11H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ -5.2, -4.6, 14.2, 18.1, 25.7, 46.5, 60.5, 70.1, 72.0, 115.1, 126.3, 126.5, 127.5, 128.0, 128.0, 128.6, 133.6, 137.0, 139.9, 142.6, 158.3, 171.2.

*General reaction procedure E - (S)-3-(4-(Benzyloxy)phenyl)-3-((tert-butyldimethylsilyl)oxy)propanoic acid (***5a***).* Ester **4a** (430 mg, 1.04 mmol) was dissolved in a mixture of EtOH, H_2O and THF (5:1:2, 16 mL). NaOH (0.4 g, 10.4 mmol) was added and the mixture was stirred at room temperature for 2 - 4 h. After completion of the reaction as indicated by HPLC, the mixture was evaporated, MTBE (30 mL) was added, followed by a 10% aqueous solution of H_3PO_4 (30 mL). Layers were separated, and the water layer was extracted with MTBE (2 x 20 mL). Combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product **5a** (389 mg, 97%) was used directly in the next step without further purification. ^{1}H NMR (600 MHz, d_6-DMSO) δ -0.17 (s, 3H), -0.01 (s, 3H), 0.80 (s, 9H), 2.44-2.55 (m, 2H), 5.04 (dd, J = 9.1, 4.3 Hz, 1H), 5.07 (s, 2H), 6.93-7.00 (m, 2H), 7.24-7.29 (m, 2H), 7.30-7.35 (m, 1H), 7.36-7.42 (m, 2H), 7.43-7.45 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, d_6-DMSO) δ -5.1, -4.8, 17.8, 25.6, 46.0, 69.2, 71.4, 114.4, 126.9, 127.7, 127.8, 128.4, 136.3, 137.1, 157.6, 171.8. According to the same procedure, racemic compound *rac*-**5a** was prepared starting from 1 g of *rac*-**4a** in quantitative yield.

*(S)-3-(6-(Benzyloxy)naphthalen-2-yl)-3-((tert-butyldimethylsilyl)oxy)propanoic acid (***5b***)*

According to the general procedure E, starting from compound **4b** (1.21 g, 2.6 mmol), crude product **5b** (1.05 g, 93%) was obtained and used directly in the next step without further

purification. ^{1}H NMR (300 MHz, d_6-DMSO) δ -0.18 (s, 3H), 0.01 (s, 3H), 0.79 (s, 9H), 2.51-2.68 (m, 2H), 5.17-5.26 (m, 3H), 7.23 (dd, J = 8.9, 2.5 Hz, 1H), 7.29-7.54 (m, 7H), 7.67-7.88 (m, 3H), 12.23 (s, 1H). ^{13}C{^{1}H} NMR (75 MHz, d_6-DMSO) δ -5.1, -4.8, 17.9, 25.6, 45.9, 69.3, 72.1, 107.2, 118.9, 124.2, 124.6, 126.9, 127.8, 127.9, 128.2, 128.4, 129.4, 133.7, 136.9, 139.2, 156.3, 171.8. HRMS (MALDI) *m/z*, ([M+Na]$^{+}$): calcd. for $C_{26}H_{32}O_4SiNa$: 459.1968, found: 459.1970.

*(S)-3-(4'-(Benzyloxy)-[1,1'-biphenyl]-4-yl)-3-((tert-butyldimethylsilyl)oxy)propanoic acid (***5c***).* According to the general procedure E, starting from ester **4c** (0.57 g, 1.2 mmol), crude product **5c** (0.52 g, 96%) was obtained and used directly in the next step without further purification. ^{1}H NMR (600 MHz, $CDCl_3$) δ -0.12 (s, 3H), 0.07 (s, 3H), 0.87 (s, 9H), 2.68 (dd, J = 15.0, 4.1 Hz, 1H), 2.81 (dd, J = 15.0, 8.9 Hz, 1H), 5.11 (s, 2H), 5,20 (dd, J = 8.9, 4.0 Hz, 1H), 7.04-7.06 (m, 2H), 7.31-7.37 (m, 1H), 7.38-7.42 (m, 4H), 7.45-7.48 (m, 2H), 7.51-7.55 (m, 4H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ -5.26, -4.6, 18.1, 25.7, 45.8, 70.1, 71.7, 115.2, 126.2, 126.6, 127.5, 128.0, 128.1, 128.6, 133.5, 137.0, 140.1, 141.9, 158.4, 176.1.

*Hexyl (S)-3-(6-(benzyloxy)naphthalen-2-yl)-3-((tert-butyldimethylsilyl)oxy)propanoate (***6***).* Carboxylic acid **5b** (610 mg, 1.4 mmol) was suspended in dry toluene (5 mL) under argon and the solution was cooled to 0 °C. Oxalyl chloride (360 µL 4.2 mmol) was added followed by DMF (1 drop). The mixture was stirred for 1 hour at room temperature, solvent was evaporated, and the residue dissolved in CH_2Cl_2 (10 mL). This solution was added dropwise to a premixed solution of 1-hexanol (2 mL), Et_3N (1.95 mL, 14 mmol) and DMAP (68 mg, 0.56 mmol) in CH_2Cl_2 (5 mL). Reaction mixture was stirred overnight at room temperature. Water (30 mL) was added and the mixture extracted with MTBE (3 x 20 mL). Organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Crude product was purified using silica gel column chromatography (CH_2Cl_2/*n*-hexane = 8:2) to obtain ester **6** (0.56 g, 77%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.18 (s, 3H), 0.04 (s, 3H),

0.68-0.99 (s, 12H), 1.14-1.43 (m, 6H), 1.53-1.62 (m, 2H), 2.61 (dd, *J* = 14.5, 4.4 Hz, 1H), 2.80 (dd, *J* = 14.5, 9.0 Hz, 1H), 3.93-4.13 (m, 2H), 5.17 (s, 2H), 5.28 (dd, *J* = 9.0, 4.3 Hz, 1H), 7.16-7.27 (m, 2H), 7.31-7.53 (m, 6H), 7.63-7.78 (m, 3H). $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) δ -5.1, -4.5, 14.1, 18.2, 22.7, 25.7, 25.9, 28.7, 31.6, 46.6, 64.9, 70.2, 72.5, 107.3, 119.3, 124.6, 124.8, 127.2, 127.7, 128.2, 128.8, 128.9, 129.6, 134.2, 137.1, 139.6, 156.9, 171.4. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{32}H_{44}O_4SiNa$: 543.2907, found: 543.2915.

*Hexyl (S)-3-((tert-butyldimethylsilyl)oxy)-3-(6-hydroxynaphthalen-2-yl)propanoate (**7**).* Ester **6** (530 mg, 1.0 mmol) was dissolved in absolute ethanol (3 mL) under argon, cyclohexene (3 mL) was added followed by 10% Pd/C (40 mg). The mixture was stirred under reflux for 3 h, cooled to room temperature, filtered over celite and the filtrate was concentrated under reduced pressure. Crude product was purified using silica gel column chromatography (CH_2Cl_2/EtOAc = 9:1) to obtain alcohol **7** (0.3 g, 95%) as a white solid. *mp* = 66.0-66.9 °C. $[\alpha]_D^{25}$ = - 43.0 (*c* 1.72, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ -0.18 (s, 3H), 0.04 (s, 3H), 0.81-0.94 (m, 12H), 1.17-1.39 (m, 6H), 1.54-1.65 (m, 2H), 2.63 (dd, *J* = 14.5, 4.4 Hz, 1H), 2.82 (dd, *J* = 14.5, 9.0 Hz, 1H), 3.71-4.39 (m, 1H), 5.28 (dd, *J* = 9.0, 4.4 Hz, 1H), 5.65 (bs, 1H), 7.10 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.13 (d, *J* = 2.5 Hz, 1H), 7.44 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.67 (d, *J* = 1.7 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ -5.1, -4.5, 14.1, 18.2, 22.6, 25.7, 25.8, 28.7, 31.6, 46.6, 65.0, 72.5, 109.6, 118.1, 124.7, 124.9, 126.8, 128.6, 129.9, 134.3, 139.3, 153.8, 171.8. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{25}H_{38}O_4SiNa$: 453.2437, found: 453.2424.

*(S)-6-(1-((tert-Butyldimethylsilyl)oxy)-3-(hexyloxy)-3-oxopropyl)naphthalen-2-yl 6-(hexyloxy)-2-naphthoate (**8**).* 6-(Hexyloxy)-2-naphthoic acid (140 mg, 0.52 mmol) was suspended in dry toluene (5 mL) under argon and the solution was cooled to 0 °C. Oxalyl chloride (220 µL 2.6 mmol) was added followed by DMF (1 drop). The mixture was stirred for 1 hour at room temperature, solvent was evaporated, and the residue dissolved in CH_2Cl_2 (5

mL). This solution was added dropwise to a premixed solution of compound **7** (250 mg, 0.57 mmol), Et_3N (0.7 mL, 5.7 mmol) and DMAP (25 mg) in CH_2Cl_2 (5 mL). Reaction mixture was stirred overnight at room temperature. Water (30 mL) was added and the mixture extracted with MTBE (3 x 20 mL). Organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Crude product was purified using silica gel column chromatography (CH_2Cl_2) to obtain ester **8** (300 mg, 85%) as a white solid. *mp* = 78.8-79.4 °C. $[\alpha]_D^{25}$ = - 28.3 (*c* 0.67, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ -0.15 (s, 3H), 0.06 (s, 3H), 0.68-1.04 (m, 15H), 1.17-1.45 (m, 10H), 1.43-1.69 (m, 4H), 1.76-2.04 (m, 2H), 2.64 (dd, *J* = 14.6, 4.4 Hz, 1H), 2.83 (dd, *J* = 14.6, 9.0 Hz, 1H), 4.00-4.15 (m, 4H), 5.33 (dd, *J* = 8.9, 4.3 Hz, 1H), 7.14-7.29 (m, 2H), 7.40 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.54 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.71 (d, *J* = 2.3 Hz, 1H), 7.76-7.83 (m, 3H), 7.85-7.93 (m, 2H), 8.19 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.74 (d, *J* = 1.8 Hz, 1H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ -5.0, -4.5, 14.1, 14.2, 18.2, 22.7, 22.8, 25.7, 25.8, 25.9, 28.7, 29.3, 31.6, 31.7, 46.5, 64.9, 68.4, 72.5, 106.6, 118.8, 120.3, 121.8, 124.5, 124.6, 125.0, 126.3, 127.2, 128.0, 128.1, 129.6, 131.1, 131.4, 131.9, 133.6, 137.8, 141.7, 149.0, 159.6, 165.8, 171.3. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{42}H_{56}O_6SiNa$: 707.3744, found: 707.3734.

*(S)-6-(3-(Hexyloxy)-1-hydroxy-3-oxopropyl)naphthalen-2-yl 6-(hexyloxy)-2-naphthoate (***9***)*

Compound **8** (280 mg, 0.41 mmol) was dissolved in THF (1 mL). TBAF (1M solution in THF, 0.5 mL, 0.5 mmol) was added and the mixture was stirred for 2 h at room temperature. Water (10 mL) was added, and the mixture extracted with CH_2Cl_2 (3 x 10 mL). Organic extracts were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude product was purified first using silica gel column chromatography (CH_2Cl_2 to CH_2Cl_2/EtOAc = 9:1) and then recrystallized (*i*Pr_2O/n-hexane = 2:1) to obtain compound **9** (156 mg, 67%) as a white solid (broad mp range due to the exhibition of LC properties; see Table S1). $[\alpha]_D^{25}$ = -16.7 (*c* 0.66, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.89 (t, *J* = 6.8 Hz, 3H), 0.91-0.97 (m,

3H), 1.25-1.43 (m, 10H), 1.48-1.54 (m, 2H), 1.59-1.64 (m, 2H), 1.84-1.90 (m, 2H), 2.62-3.06 (m, 2H), 3.45 (d, *J* = 3.6 Hz, 1H), 4.10-4.15 (m, 4H), 5.31 (dt, *J* = 8.1, 4.0 Hz, 1H), 7.18 (d, *J* = 2.5 Hz, 1H), 7.23 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.41 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.51 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.72 (d, *J* = 2.3 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.88-7.98 (m, 3H), 8.18 (dd, *J* = 8.6, 1.8 Hz, 1H), 8.73 (d, *J* = 1.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 14.1, 14.2, 22.6, 22.8, 25.7, 25.9, 28.6, 29.3, 31.5, 31.7, 43.4, 65.3, 68.4, 70.5, 106.6, 118.8, 120.3, 121.9, 124.4, 124.5, 124.6, 126.3, 127.2, 127.9, 128.3, 129.7, 131.1, 131.5, 131.9, 133.6, 137.8, 139.9, 149.1, 159.6, 165.8, 172.6. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{36}H_{42}O_6Na$: 593.2879, found: 593.2870.

*5-(4'-Cyano-[1,1'-biphenyl]-4-yl)pentyl (S)-3-(4-(benzyloxy)phenyl)-3-((tert-butyldimethylsilyl)oxy)propanoate (***11***).* Carboxylic acid **5a** (500 mg, 1.3 mmol) was suspended in dry toluene (10 mL) under argon. Oxalyl chloride (0.34 mL, 3.9 mmol) and DMF (1 drop) were added. The mixture was stirred for 1 hour at room temperature and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 (8 mL) and this solution was added to a premixed solution of **10** (410 mg, 1.5 mmol), Et_3N (1.8 mL, 13 mmol) and DMAP (50 mg) in CH_2Cl_2 (3 mL). The reaction mixture was stirred overnight at room temperature. Water was added (30 mL), layers were separated and the aqueous layer extracted with CH_2Cl_2 (2 x 30 mL). Combined organic extracts were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Crude product was purified using silica gel column chromatography (CH_2Cl_2) to obtain **11** (630 mg, 77%) as a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ -0.18 (s, 3H), 0.01 (s, 3H), 0.84 (s, 9H), 1.37-1.42 (m, 2H), 1.63-1.70 (m, 4H), 2.52 (dd, *J* = 14.6, 4.4 Hz, 1H), 2.65-2.69 (m, 2H), 2.72 (dd, *J* = 14.6, 9.1 Hz, 1H), 4.01-4.10 (m, 2H), 5.04 (s, 2H), 5.09 (dd, *J* = 9.0, 4.4 Hz, 1H), 6.89-6.94 (m, 2H), 7.23-7.26 (m, 2H), 7.27-7.29 (m, 2H), 7.30-7.35 (m, 1H), 7.35-7.40 (m, 2H), 7.41-7.44 (m, 2H), 7.49-7.52 (m, 2H), 7.65-7.67 (m, 2H), 7.69-7.72 (m, 2H). $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ -5.1, -4.5, 18.2,

25.7, 25.9, 28.6, 31.1, 35.6, 46.6, 64.6, 70.2, 72.0, 110.7, 114.7, 119.2, 127.2, 127.3, 127.6, 127.7, 128.1, 128.7, 129.3, 132.7, 136.7, 136.8, 137.1, 143.4, 145.7, 158.4, 171.4. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{40}H_{47}NO_4SiNa$: 656.3172, found: 656.3170. Racemic compound *rac*-**11** was prepared according to the same procedure starting from 0.5 g of *rac*-**5a** in 56% yield.

*5-(4'-Cyano-[1,1'-biphenyl]-4-yl)pentyl (S)-3-((tert-butyldimethylsilyl)oxy)-3-(4-hydroxyphenyl)propanoate (***12***).* Ester **11** (280 mg, 0.44 mmol) was dissolved in absolute ethanol (6 mL) under argon. Cyclohexene (6 mL) and 10% Pd/C (94 mg) were added. The mixture was stirred under reflux for 1 hour, cooled to room temperature and filtered over celite. The filtrate was concentrated under reduced pressure and purified using silica gel column chromatography (CH_2Cl_2/EtOAc = 9:1) affording **12** (220 mg, 92%) as a colourless oil. $[\alpha]_D^{20°C}$ = -31.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ -0.18 (s, 3H), 0.00 (s, 3H), 0.83 (s, 9H), 1.36-1.42 (m, 2H), 1.63-1.70 (m, 4H), 2.51 (dd, *J* = 14.5, 4.4 Hz, 1H), 2.65-2.68 (m, 2H), 2.72 (dd, *J* = 14.5, 9.0 Hz, 1H), 4.02-4.10 (m, 2H), 5.07 (dd, *J* = 9.0, 4.4 Hz, 1H), 5.23 (bs, 1H), 6.77 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.67 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 8.5 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ -5.1, -4.5, 18.2, 25.7, 25.8, 28.6, 31.1, 35.5, 46.6, 64.6, 72.0, 110.7, 115.2, 119.2, 127.3, 127.4, 127.6, 129.3, 132.7, 136.4, 136.7, 143.4, 145.7, 155.2, 171.6. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{33}H_{41}NO_4SiNa$: 566.2703, found: 566.2709. Racemic compound *rac*-**12** was prepared according to the same procedure starting from 170 mg of *rac*-**11** in 87% yield.

*(S)-4-(1-((tert-Butyldimethylsilyl)oxy)-3-((5-(4'-cyano-[1,1'-biphenyl]-4-yl)pentyl)oxy)-3-oxopropyl)phenyl 4-(hexyloxy)benzoate (***13***).* 6-(Hexyloxy)-2-benzoic acid (110 mg, 0.5 mmol) was suspended in dry toluene (5 mL) under argon and the solution was cooled to 0 °C. Oxalyl chloride (130 µL, 1.5 mmol) was added followed by DMF (1 drop). Mixture was stirred for 1 hour at room temperature, solvent was evaporated, and the residue dissolved in CH_2Cl_2 (3 mL)

and added to a premixed solution of compound **12** (300 mg, 0.55 mmol), Et_3N (0.70 mL, 5.0 mmol) and DMAP (25 mg) in CH_2Cl_2 (8 mL). The reaction mixture was stirred overnight, water was added (20 mL) and extracted with CH_2Cl_2 (2 x 10 mL). Combined organic layers were washed with brine and dried over Na_2SO_4, filtered and concentrated under reduced pressure. Product **13** (360 mg, 97%) was obtained after silica gel column chromatography (CH_2Cl_2) as a colourless oil. $[\alpha]_D^{20°C}$ = -22.2 (*c* 0.45, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ -0.14 (s, 3H), 0.04 (s, 3H), 0.86 (s, 9H), 0.92 (t, 3H), 1.34-1.38 (m, 4H), 1.38-1.44 (m, 2H), 1.45-1.51 (m, 2H), 1.66-1.71 (m, 4H), 1.80-1.84 (m, 2H), 2.56 (dd, *J* = 14.7, 4.3 Hz, 1H), 2.66-2.69 (m, 2H), 2.74 (dd, *J* = 14.7, 9.0 Hz, 1H), 4.04 (t, *J* = 6.6 Hz, 2H), 4.04-4.11 (m, 2H), 5.17 (dd, *J* = 9.0, 4.2 Hz, 1H), 6.96 (d, *J* = 8.9 Hz, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 8.6 Hz, 2H), 8.12 (d, *J* = 8.9 Hz, 2H).^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ -5.1, -4.5, 14.2, 18.2, 22.7, 25.7, 25.79, 25.84, 28.6, 29.2, 31.1, 31.7, 35.6, 46.6, 64.7, 68.5, 71.9, 110.7, 114.5, 119.2, 121.6, 121.7, 127.0, 127.3, 127.6, 129.3, 132.4, 132.7, 136.7, 141.6, 143.4, 145.7, 150.5, 163.7, 165.0, 171.3. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{46}H_{57}NO_6SiNa$: 770.3853, found: 770.3859. Racemic compound *rac*-**13** was prepared according to the same procedure starting from 90 mg of *rac*-**12** in 69% yield.

*(S)-4-(3-((5-(4'-Cyano-[1,1'-biphenyl]-4-yl)pentyl)oxy)-1-hydroxy-3-oxopropyl)phenyl 4-(hexyloxy)benzoate (***14***).* Compound **13** (350 mg, 0.47 mmol) was dissolved in THF (15 mL) and TBAF (1M solution in THF, 0.21 mL, 0.21 mol) was added. The mixture was stirred overnight at room temperature, concentrated under reduced pressure and purified using silica gel column chromatography (CH_2Cl_2/EtOAc = 9:1) and then crystallized from 2-propanol to obtain product **14** (230 mg, 77%) as a white solid (broad mp range due to the exhibition of LC properties; see Table S1). *ee* = 99%, Chiralcel OD-3, *n*-hexane/ethanol = 90:10, 220 nm, 1 mL/min, t_R(major) = 25.4 min, t_R(minor) = 28.6 min. $[\alpha]_D^{20}$ = -11.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR

(600 MHz, $CDCl_3$): δ 0.90-0.94 (m, 3H), 1.33-1.38 (m, 4H), 1.38-1.43 (m, 2H), 1.45-1.51 (m, 2H), 1.67-1.72 (m, 4H), 1.79-1.86 (m, 2H), 2.67-2.69 (m, 2H), 2.70-2.79 (m, 2H), 3.24 (d, J = 3.5 Hz, 1H), 4.04 (t, J = 6.6 Hz, 2H), 4.15 (t, J = 6.6 Hz, 1H), 5.15 (dt, J = 8.3, 3.8 Hz, 1H), 6.96 (d, J = 8.9 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 8.2 Hz, 2H), 7.42 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 8.2 Hz, 2H), 7.65 (d, J = 8.4 Hz, 2H), 7.70 (d, J = 8.5 Hz, 2H), 8.13 (d, J = 8.9 Hz, 2H).$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 14.2, 22.7, 25.6, 25.8, 28.5, 29.2, 31.0, 31.7, 35.5, 43.5, 65.0, 68.5, 70.0, 110.7, 114.5, 119.2, 121.5, 122.0, 126.9, 127.3, 127.6, 129.3, 132.4, 132.7, 136.8, 140.0, 143.3, 145.6, 150.7, 163.7, 165.1, 172.5. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{40}H_{43}NO_6Na$: 656.2988, found: 656.2972. Racemic compound *rac*-**14** was prepared in 71% yield according to the same procedure starting from 80 mg of *rac*-**13**.

*3-(4-(Benzyloxy)phenyl)propyl (S)-3-(4-(benzyloxy)phenyl)-3-((tert-butyldimethylsilyl)oxy)propanoate (***16***).* Carboxylic acid **5a** (287 mg, 0.74 mmol) was suspended in anhydrous toluene (7 mL) under argon. Oxalyl chloride (90 µL, 0.97 mmol) was added followed by DMF (1 drop). The mixture was stirred for 1.5 h at room temperature. The solvent was evaporated and the residue dissolved in CH_2Cl_2 (3 mL). This solution was added to a premixed solution of alcohol **15** (100 mg, 0.41 mmol), Et_3N (0.4 mL, 2.9 mmol), and DMAP (7 mg) in CH_2Cl_2 (2 mL). The reaction mixture was stirred overnight at room temperature. Water (20 mL) was added and the mixture was extracted with MTBE (3 × 20 mL). Combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude compound was purified using silica gel column chromatography (CH_2Cl_2) to obtain product **16** (243 mg, 96 %) as a colourless oil. ^1H NMR (300 MHz, $CDCl_3$) δ -0.17 (s, 3H), -0.01 (s, 3H), 0.83 (s, 9H), 1.84-1.94 (m, 2H), 2.50-2.60 (m, 3H), 2.74 (dd, J = 15 Hz, 9 Hz, 1H), 4.06 (td, J = 6.8 Hz, 2.6 Hz, 2H), 5.02 (s, 4H), 5.10 (dd, J = 9 Hz, 4.6 Hz, 1H), 6.87-6.94 (m, 4H), 7.04-7.08 (m, 2H), 7.24-7.44 (m, 12H). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ -5.2, -4.6, 18.1, 25.7, 30.4, 31.3, 46.4, 63.8, 70.0, 70.1, 71.8, 114.5, 114.8, 127.1,

127.4, 127.5 (2C), 127.9, 128.0, 128.6, 129.3, 133.6, 136.6, 137.0, 137.2, 157.1, 158.2, 171.3. HRMS (MALDI) *m/z*, ([M+K]$^+$): calcd. for $C_{38}H_{46}O_5SiK$: 649.2752, found: 649.2730.

*3-(4-Hydroxyphenyl)propyl (S)-3-((tert-butyldimethylsilyl)oxy)-3-(4-hydroxyphenyl)propanoate (***17***).* Compound **16** (227 mg, 0.37 mmol) was dissolved in absolute ethanol (8 mL), cyclohexene (8 mL) and 10% Pd/C (80 mg) were added. The mixture was stirred under reflux for 4 h, cooled to room temperature, filtered over celite and the filtrate was concentrated under reduced pressure. The crude product was purified using silica gel column chromatography (CH_2Cl_2/EtOAc = 9:1) to obtain product **17** (100 mg, 63%) as a colourless oil. ^{1}H NMR (300 MHz, d_6-DMSO) δ -0.22 (s, 3H), -0.04 (s, 3H), 0.77 (s, 9H), 1.75-1.85 (m, 2H), 2.47-2.66 (m, 4H), 3.89-4.04 (m, 2H), 4.99 (dd, J = 9.0 Hz, 4.4 Hz, 1H), 6.66 (d, J = 8.4 Hz, 2H), 6.70 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 8.4 Hz, 2H), 7.14(d, J = 8.5 Hz, 2H), 9.14 (bs, 1H), 9.33 (bs, 1H). ^{13}C{^{1}H} NMR (d_6-DMSO) δ -5.3, -4.8, 17.7, 25.5, 30.0, 30.5, 45.6, 63.3, 71.6, 114.9, 115.0, 127.0, 129.0, 131.0, 133.9, 155.4, 156.7, 170.4. HRMS (MALDI) *m/z*, ([M+Na]$^+$): calcd. for $C_{24}H_{34}O_5SiNa$: 453.2073, found: 453.2094.

*(S)-4-(3-((3-((tert-Butyldimethylsilyl)oxy)-3-(4-((3,4,5-tris(dodecyloxy)benzoyl)oxy)phenyl)propanoyl)oxy)propyl)phenyl 3,4,5-tris(dodecyloxy)benzoate (***18***).* 3,4,5-Tris(dodecyloxy) benzoic acid[36] (784 mg, 1.16 mmol) was suspended in anhydrous toluene (5 mL) under argon. Oxalyl chloride (130 µL, 1.5 mmol) was added followed by DMF (1 drop). The mixture was stirred for 3 h at room temperature. The solvent was evaporated and the residue dissolved in CH_2Cl_2 (5 mL). This solution was added to a premixed solution of diol **17** (100 mg, 0.23 mmol), Et_3N (0.33 mL, 2.3 mmol) and DMAP (5 mg) in CH_2Cl_2 (3 mL). The reaction mixture was stirred overnight at room temperature. Water (10 mL) was added and the mixture was extracted with MTBE (3 × 10 mL). Combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Crude compound was purified using silica gel column chromatography (CH_2Cl_2/MTBE =

500:1) to obtain product **18** (242 mg, 60%) as a colourless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ -0.13 (s, 3H), 0.05 (s, 3H), 0.86-0.90 (m, 27H), 1.26-1.38 (m, 96H), 1.44-1.51 (m, 12H), 1.72-1.79 (m, 4H), 1.79-1.87 (m, 8H), 1.94-2.01 (m, 2H), 2.59 (dd, *J* = 14.8, 4.1 Hz, 1H), 2.68-2.74 (m, 2H), 2.77 (dd, *J* = 14.8, 9.2 Hz, 1H), 4.02-4.06 (m, 12H), 4.07-4.17 (m, 2H), 5.20 (dd, *J* = 9.1 Hz, 4.0 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.40 (s, 4H), 7.42 (d, *J* = 8.6 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ -5.1, -4.5, 14.3, 18.2, 22.84, 22.85, 25.8, 26.21, 26.23, 29.4, 29.5, 29.6, 29.73, 29.78, 29.81, 29.85, 29.88, 29.91, 30.3, 30.5, 31.8, 32.07, 32.09, 46.5, 64.0, 69.4, 71.8, 73.7, 108.67, 108.69, 121.76, 121.81, 124.0, 124.1, 127.1, 129.5, 138.9, 141.8, 143.1, 143.2, 149.4, 150.5, 153.09, 153.11, 165.2, 165.3, 171.3. HRMS (MALDI) *m/z*, ($[M+Na]^+$): calcd. for $C_{110}H_{186}O_{13}SiNa$: 1766.3560, found: 1766.3597.

*(S)-4-(3-((3-Hydroxy-3-(4-((3,4,5-tris(dodecyloxy)benzoyl)oxy)phenyl)propanoyl) oxy)propyl)phenyl 3,4,5-tris(dodecyloxy)benzoate (***19***).* To the solution of compound **18** (242 mg, 0.14 mmol) in THF (5.6 mL) TBAF (1M solution in THF, 0.2 mL, 0.2 mmol) was added. The reaction mixture was stirred at room temperature overnight and monitored by TLC (CH_2Cl_2/MTBE = 500:1). The solvent was evaporated and the crude product purified using silica gel column chromatography (CH_2Cl_2/MTBE = 500:1) to obtain product **19** (197 mg, 87%) as a white solid (broad mp range due to the exhibition of LC properties; see Table S1). $[\alpha]_D^{20}$ = -5.0 (*c* 1.1 $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84-0.92 (m, 18H), 1.26-1.39 (m, 96H), 1.42-1.53 (m, 12H), 1.71-1.87 (m, 12H), 1.96-2.05 (m, 2H), 2.70-2.78 (m, 4H), 4.02-4.08 (m, 12H), 4.19 (t, *J* = 6.5 Hz, 2H), 5.17 (dd, *J* = 7.5 Hz, 5.2 Hz, 1H), 7.10-7.25 (m, 6H), 7.39-7.47 (m, 6H), OH not visible. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 14.1, 22.7, 26.08, 26.10, 29.33, 29.38, 29.41, 29.59, 29.65, 29.67, 29.71, 29.75, 30.1, 30.4, 31.6, 31.94, 31.96, 43.3, 64.2, 69.3, 69.9, 73.6, 108.6, 121.7, 121.9, 123.8, 123.9, 126.9, 129.34, 138.6, 140.1, 143.1, 149.3, 150.6,

153.0, 165.0, 165.2, 172.4. HRMS (MALDI) *m/z*, ([M+Na]$^+$): calcd. for $C_{104}H_{172}O_{13}Na$: 1652.2696, found: 1652.2690.

Supporting Information. The Supporting Information is available free of charge at https://pubs.acs.org/doi and includes ^{1}H NMR and ^{13}C{^{1}H} NMR spectra for compounds **1** - **19**, chiral HPLC chromatograms for compounds **2a-c** and **14**, LC characterization and DSC data for compounds **9**, **14**, *rac*-**14** and **19**, and X-ray crystallography of **2b** (PDF); and FAIR data, including the primary NMR FID files for compounds **1-19** (ZIP).

Accession Codes CCDC 2184469 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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