



Synthesis of optically active derivatives of bicyclic chiral diols with C₂ symmetry

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ABSTRACT

This paper reports efficient procedures for the preparation of optically active dibromide, diazide, diamine, and unsaturated diesters derived from a chiral bicyclic diol with C₂ symmetry namely (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethanol **3**. Esterification of **3** with saturated and unsaturated carboxylic acids and acids chlorides leads to the corresponding normal-, olefinic- and acetylenic diesters in average yields of 81%. Also more efficient techniques for the preparation of starting diol **3** in higher yields as well as for a very simple separation of DCU (*N,N'*-dicyclohexylurea) from reactions carried out following the DCC/DMAP method are described.

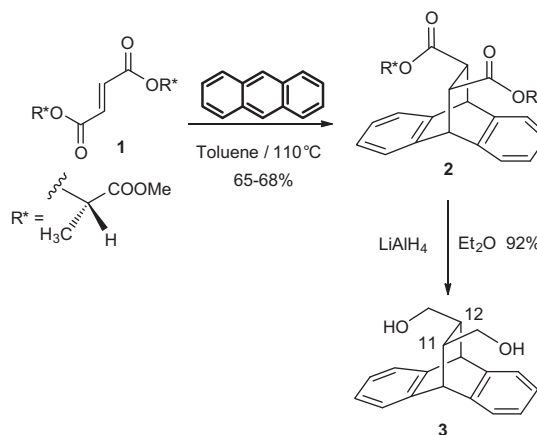
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1. Introduction

Chiral dihydroethano- and ethenoanthracene derivatives are versatile organic molecules with C₂ symmetry which have been used in synthetic and biological applications. They have also been used as chiral ligands in enantioselective reactions, attached to a metal as catalytically active species, and as chiral polymer's precursors.^{1,2} At present, we are interested in reactions that involve the use of C₂ symmetrical substrates as precursors for the synthesis of optically active molecules with potential biological activity. Thus, we have reported the physical characteristics of a series of new TADDOL derived unsaturated esters^{3a} and the use of these diesters in the synthesis of macrodiolides via cyclohydrostanation reactions.^{3b} In this context, we considered it convenient to synthesize a series of derivatives of the chiral diol (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethanol **3**, and to study some of their reactions.

2. Results and discussion

Diol **3** was prepared using a variation of a synthetic route that involves an asymmetric carbo-Diels–Alder reaction as the key step, as shown in Scheme 1.⁴ The use of (*S*)-(-)-methyl lactate instead of (*S*)-(-)-ethyl lactate used initially and, especially, small variations in the experimental techniques enabled us to increase the global yield of the synthesis. Thus using fumarate **1** in a ratio 1/anthracene = 1:3.5 (originally 1:5), after 4 days of reaction (6 in the original paper) diester **2** was obtained enantiomerically pure in yields of 65–68% after recrystallization from ethyl acetate/hexane (original paper 50–60%). Then, diester **2** was reduced with LiAlH₄ in boil-



Scheme 1. Synthesis of bicyclic chiral diol **3**.

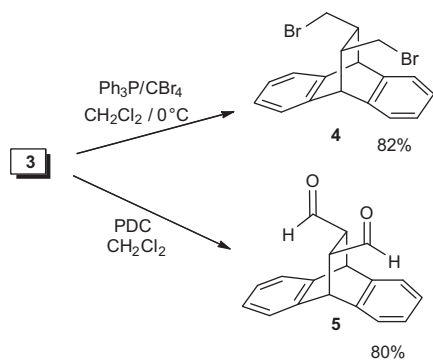
ing ether leading to the chiral diol **3** with 92% yield of pure compound. The increase in the yield (in the original paper 75%) was achieved simply by increasing the amount of LiAlH₄.

Bromination of diol **3** with carbon tetrabromide in the presence of triphenylphosphine in dichloromethane afforded the new (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethylene dibromide **4** in 82% yield (Scheme 2).

On the other hand, oxidation of diol **3** with pyridinium dichromate (PDC) in anhydrous dichloromethane took place with retention of configuration to give the new dialdehyde (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarbaldehyde **5**, in 80% yield (Scheme 2).

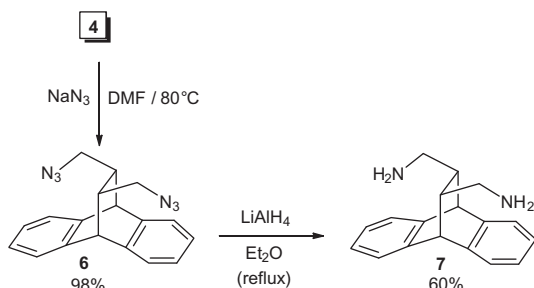
We then attempted the synthesis of diamine **7** via the reaction between chiral dibromide **4** and potassium phthalimide (Gabriel synthesis). Reaction of compound **4** with sodium azide in dry

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Scheme 2. Synthesis of new derivatives **4** and **5** starting from diol **3**.

dimethylformamide (DMF) at 80 °C gave the new diazide **6** in excellent yield (98%).⁵ Then, reduction of **6** with LiAlH₄ (Scheme 3) in refluxing ether afforded (11*R*,12*R*)-diamine **7** in 60% yield.⁶



Scheme 3. Synthesis of chiral diamine **7** via diazide **6**.

Diamine **7** was previously obtained by resolution of the brucine salt of the carboxylic acid precursor and has been tested as a chemosensitizer against chloroquine resistant *Plasmodium falciparum*, responsible for Malaria.⁷

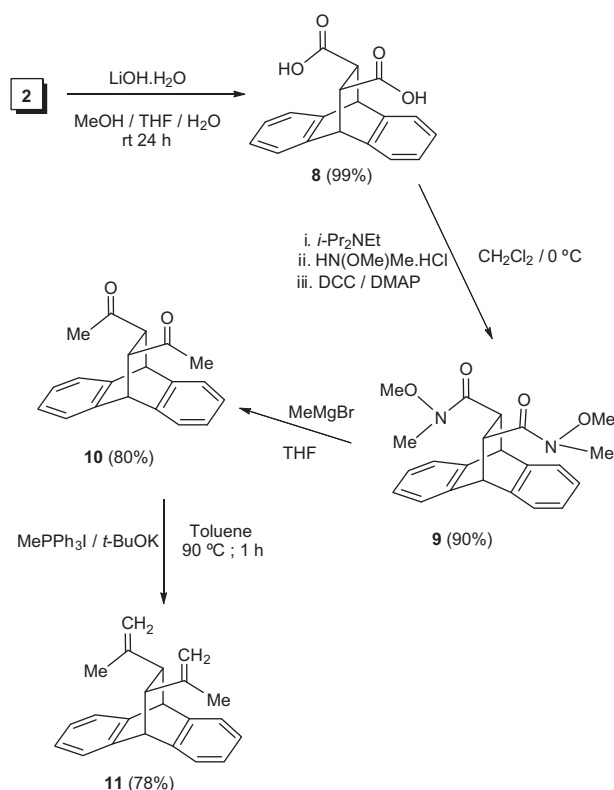
Another target of our synthetic studies was the synthesis of (11*R*,12*R*)-9,10-dihydro-11,12-diisopropenyl-9,10-ethaneanthracene **11**. The starting material for this synthesis was the diacid **8** which was quantitatively obtained by hydrolysis of the corresponding diester **2** (Scheme 4).⁸ Without further purification, compound **8** was treated with ethyldiisopropylamine, *N,O*-dimethylhydroxylamine hydrochloride, DCC, and a catalytic amount of DMAP, to give the new Weinreb's amide (11*R*,12*R*)-dicarboxamide **9** in 90% yield.

Addition of methylmagnesium bromide to diamide **10** gave (11*R*,12*R*)-diketone **10** (80%), which upon treatment with a mixture of methylphosphonium iodide and potassium *tert*-butoxide led to the new (11*R*,12*R*)-diene **11** in an average 78% yield.

We also carried out studies on the synthesis of unsaturated esters of **3**, which could serve as precursors of macrocycles. The only known example of this type of compounds is **16**.²

We first studied the esterification of benzoic and phenylacetic acids with diol **3** using the *N,N'*-dicyclohexylcarbodiimide (DCC)/4-(*N,N*-dimethylamino) pyridine (DMAP) method (Method A, Scheme 5). Dibenzate **12** and diphenylacetate **13** were obtained in excellent yields. These compounds were also prepared in similar yields from the corresponding acid chlorides (Method B).

These results led us to undertake the synthesis of unsaturated esters of **3** by means of the DCC/DMAP method (Method A, Scheme 6). The reactions were carried out by mixing diol **3** in dry CH₂Cl₂ with DCC, *p*-toluenesulfonic acid (TsOH), and DMAP, followed by the addition of the unsaturated acids. The resulting di-



Scheme 4. Synthesis of optically active (11*R*,12*R*)-derivatives **9–11**.

ters were obtained in good yields except for the case of compounds **15** and **20** which could only be prepared by Method B.

On the other hand, the reaction of the lithium alkoxide of **3** with the corresponding acyl chloride provided the corresponding (11*R*,12*R*)-unsaturated diesters as shown in Scheme 6 (Method B) in good to excellent yields. These reactions were carried out by mixing **3** (in THF) with BuLi (in hexane) and then adding the acid chlorides to the mixture at 0 °C. The reaction mixtures were then heated at reflux and finally left at rt for 12 h. As shown in Scheme 6, these reactions lead in all cases to the corresponding diesters as the only products. The average global yield of these reactions, after purification, was around 83%.

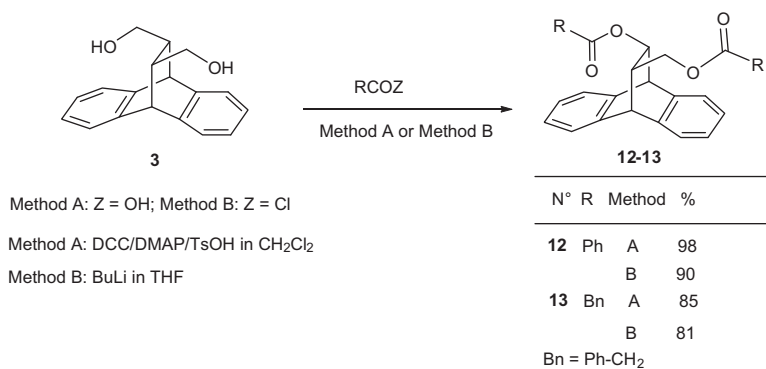
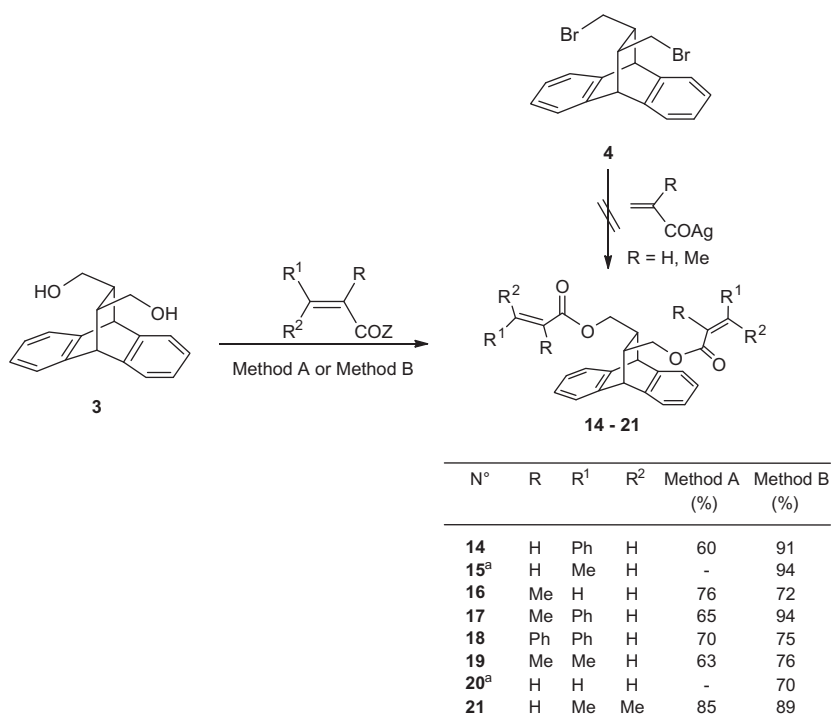
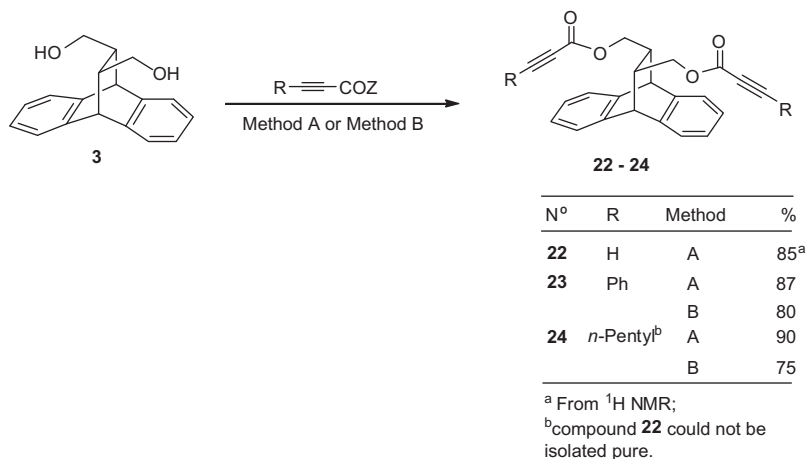
Attempts to accomplish the esterification reaction between the dibromide **4** and the silver salts of the unsaturated acids were unsuccessful (Scheme 6).

We then studied the esterification of propyn-, octyn-, and phenylpropynoic acids with diol **3** using the DCC/DMAP method. These reactions were carried out as described above for the case of substituted propenoic acids, and provided the (11*R*,12*R*)-acetylenic diesters **22–24** as the only products in good yields (Scheme 7).

The new unsaturated esters were obtained in an average yield of around 86%. The esterification of phenyl propynoyl- and octynoyl chlorides using Method B led to the corresponding diesters **23** and **24** in high yields, as shown in Scheme 7. Attempts to obtain similar acetylenic esters using TADDOL were unsuccessful.⁸

3. Conclusion

Several compounds with C₂ symmetry derived from (11*R*,12*R*)-9,10-dihydro-9,10-ethaneanthracene-11,12-dimethanol **3** were successfully prepared. These compounds would be useful starting materials for the synthesis of biologically active molecules, new catalysts, macrocycles, and polymers.

Scheme 5. Synthesis of unsaturated diesters **12** and **13**.Scheme 6. Synthesis of unsaturated diesters **14–21**.Scheme 7. Synthesis of acetylenic diesters **22–24**.

4. Experimental

4.1. General methods

THF was distilled from sodium benzophenone under nitrogen; CH_2Cl_2 was distilled from P_2O_5 under nitrogen. All reagents used were of analytical reagent grade. NMR spectra: ^1H NMR (CDCl_3 , δ), ^{13}C NMR (70 MHz, CDCl_3 , δ) were obtained using a Bruker ARX 300 instrument. Infrared spectra were recorded with a Nicolet Nexus FT spectrometer. Mass spectra were obtained using a Finnigan MAT Incos 50 Galaxy System (DIP-MS) and, the high resolution spectra, with a Finnigan MAT 900 with E/B configuration at Cologne University (Germany). Melting points were determined on a Kofler hot stage and are uncorrected. Specific rotations were measured with a Polar L- μP , IBZ Messtechnik. All spectra of compounds **2–5**, **7–13**, and **16–17** are reported from isolated products of both methods (A and B).

4.2. Synthesis of (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethanol **3**

4.2.1. Bis[(*S*)-1-methyloxycarbonyl-ethyl]-(11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylate **2**

The reaction between the fumarate of (*S*)-methyl lactate **1** and anthracene was carried out according to Ref. 4 in toluene at 110 °C. The following variations of the original technique were performed: ratio **1**/anthracene = 1:3.5 (original paper 1:5); reaction time 4 days (originally 6 days). Under these reaction conditions, diastereomerically pure compound **2** was obtained in 60–68% yield (original paper 50–60%) by recrystallization from ethyl acetate/hexane.

4.2.2. Reduction of **2**

To a suspension of LiAlH_4 (4.07 g, 107.18 mmol) in dry diethyl ether (125 mL), under atmosphere of argon and at room temperature, was added dropwise a solution of diester **2** (10.0 g, 21.44 mmol) in dry diethyl ether (100 mL) with vigorous stirring. The mixture was heated at reflux for 1 h and then stirred at room temperature for 3 h, and cooled down to 0 °C. Water (60 mL) was added dropwise with stirring. After acidifying with 1 M HCl, the aqueous layer was extracted with diethyl ether (3 \times 50 mL) and the combined organic extracts were washed with a satd NaCl solution and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the crude product was purified by column chromatography (Silica Gel 60, hexane– Et_2O , 50:50) to give **3** (5.26 g, 19.73 mmol, 92% yield) as a white powder, mp: 123–125 °C.

4.3. Synthesis of (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethylene dibromide **4**

To a solution of **3** (81.0 g, 3.75 mmol) in dry CH_2Cl_2 (15 mL) under argon, was added CBr_4 (3.11 g, 9.38 mmol) and the mixture was stirred vigorously at rt for 15 min. The mixture was cooled down to 0 °C and Ph_3P (2.95 g, 11.26 mmol) was added. Then the reaction mixture was stirred for 3 h at rt. The solvent was distilled off under reduced pressure and the white residue was purified by percolation through Silica Gel 60 (hexane– Et_2O , 90:10) to give **4** (1.21 g, 3.08 mmol, 82%) as a white powder; mp: 170–172 °C; $[\alpha]_{\text{D}}^{23} = -4.8$ (c 0.30, CH_2Cl_2); ^1H NMR: 1.67–1.82 (m, 2H), 2.75 (dd, 2H, $^3J = 8.7$ Hz, $^2J = 10.5$ Hz), 3.13 (dd, 2H, $^3J = 5.6$ Hz, $^2J = 10.5$ Hz), 4.73 (s, 2H), 6.99–7.33 (m, 8H); ^{13}C NMR: 36.76, 47.86, 49.20, 124.36, 125.93, 126.67, 126.98, 139.99, 142.76; IR (KBr) ν : 3064, 3037, 3021, 2971, 2897, 2847, 1456, 1231, 1021, 753, 551 cm^{-1} ; MS: m/z (%) 392 (10), 314 (11), 313 (55), 312

(11), 311 (55), 259 (9), 257 (9), 178 (100), 152 (5), 53 (28). Elemental Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{Br}_2$: C, 55.13; H, 4.11. Found: C, 55.19; H, 4.18.

4.4. Synthesis of (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarbaldehyde **5**

To a solution of **3** (0.10 g, 0.37 mmol) in dry CH_2Cl_2 (10 mL) under argon, was added PDC (1.125 g, 3 mmol) and the mixture was stirred vigorously 12 h at rt. The solvent was distilled off under reduced pressure and the white residue was purified by percolation through Silica Gel 60 (hexane– EtOAc , 70:30) to give **5** (0.08 g, 0.30 mmol, 80%) as a white powder; mp: 132–134 °C; $[\alpha]_{\text{D}}^{23} = -5.3$ (c 1.00, CH_2Cl_2); ^1H NMR: 2.75–2.93 (m, 2H); 4.53 (d, 2H); 6.75–7.26 (m, 8H); 9.82 (s, 2H); ^{13}C NMR: 45.36, 53.46, 125.16, 126.93, 140.62, 143.35, 197.15; IR (KBr) ν : 3010, 2990, 2987, 2930, 2864, 2783, 1953, 1910, 1736, 1452, 1416, 1280, 1234, 1020, 803, 752, 703, 653 cm^{-1} . Elemental Anal. Calcd for $\text{C}_{18}\text{H}_{14}\text{O}_2$: C, 82.42; H, 5.38. Found: C, 82.58; H, 5.29.

4.5. Synthesis of (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethanazide **6**

To a solution of **4** (0.20 g, 0.51 mmol) in dry DMF under argon, was added NaN_3 (0.10 g, 1.53 mmol). The mixture was heated at 80 °C for 4 h and then was warmed up to rt. After quenching with water (5 mL), the organic layer was separated and the aqueous layer was extracted with CHCl_3 (3 \times 10 mL). The combined organic extracts were washed once with satd NaCl solution and then dried with anhydrous Na_2SO_4 . The solvent was removed under reduced pressure to give **6** (0.16 g, 0.50 mmol, 98%) as a yellowish solid, mp: 88–90 °C; $[\alpha]_{\text{D}}^{23} = -20.4$ (c 1.02, CH_2Cl_2) which can be used without further purification. ^1H NMR: 2.07 (s, 2H); 2.26–2.54 (m, 4H); 4.78 (s, 2H); 6.83–7.17 (m, 8H); ^{13}C NMR: 39.96, 46.37, 52.24, 122.16, 123.26, 125.15, 125.92, 126.21, 141.07, 143.28.

4.6. Synthesis of (11*R*,12*R*)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethanamine **7**

To a suspension of LiAlH_4 (0.17 g, 4.48 mmol) in dry diethyl ether (5 mL), under atmosphere of argon, and at rt, was added dropwise a and with vigorous stirring a solution of **6** (0.14 g, 0.44 mmol) in dry diethyl ether (5 mL). The mixture was heated at reflux for 2 h and then stirred at rt for 8 h. After cooling to 0 °C water (5 mL) was added dropwise. The organic layer was washed once with HCl 10% (10 mL) and water (10 mL) and the aqueous layer was extracted with Et_2O (3 \times 10 mL). The combined organic extracts were dried with anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the crude product was purified by column chromatography (Silica Gel 60, hexane– Et_2O , 50:50) to give **7** (0.07 g, 0.26 mmol, 60%) as a white solid; mp (hydrochloride): 185–187 °C (lit.⁹ 187–188 °C); ^1H NMR: 1.83 (s, 4H); 2.03–2.41 (m, 6H); 4.07 (s, 2H); 6.79–7.21 (m, 8H); ^{13}C NMR: 47.60, 46.57, 46.14, 122.98, 123.26, 124.91, 125.01, 125.32, 125.64, 125.72, 125.85, 143.41, 143.67.

4.7. Synthesis of (11*R*,12*R*)-9,10-dihydro-*N,N*-dimethyl- \dot{N} , \dot{N} -dimethoxy-9,10-ethanoanthracene-11,12-dicarboxamide **9**

To a solution of **8** (0.128 g, 0.44 mmol) in dry CH_2Cl_2 (10 mL) under argon and at 0 °C, was consecutively added DIPEA (0.18 mL, 0.13 g, 1.05 mmol), $\text{HN}(\text{OMe})\text{Me}$ (0.10 g, 1.05 mmol), DCC (0.19 g, 0.91 mmol) and DMAP (0.05 g, 0.37 mmol). The mixture was stirred for 2 h at 0 °C, and then was warmed up to rt. After stirring during 12 h, the reaction was quenched with water (5 mL). The organic layer was separated and the aqueous layer was

extracted with Et₂O (2 × 15 mL). The combined organic extracts were dried with anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (Silica Gel 60, hexane–EtOAc, 90:10) to give **9** (0.15 g, 0.39 mmol, 90%) as a white powder; mp: 165–167 °C; $[\alpha]_D^{23} = -120.3$ (c 2.00, dioxane); ¹H NMR: 2.11 (s, 2H); 2.54 (s, 3H); 2.57 (s, 3H); 3.42 (s, 6H); 4.39 (s, 2H); 6.76–7.29 (m, 8H); ¹³C NMR: 32.76, 33.63, 45.62, 46.35, 61.13, 122.18, 125.26, 126.02, 140.27, 142.59, 172.46; IR (KBr) ν : 3066, 3034, 2964, 2898, 1950, 1911, 1689, 1452, 1418, 1233, 1021, 804, 752, 652 cm⁻¹. Elemental Anal. Calcd for C₂₂H₂₄N₂O₄: C, 69.46; H, 6.36. Found: C, 69.58; H, 6.46.

4.8. Synthesis of (11R,12R)-11,12-diacetyl-9,10-dihydro-9,10-ethanoanthracene 10

To cooled (0 °C) solution of **9** (0.128 g, 0.44 mmol) in dry THF (6 mL) was added under argon a solution 3 M of MeMgBr (0.70 mL, 0.26 g, 2.19 mmol) in dry diethyl ether. The mixture was stirred for 15 min at 0 °C, and then warmed up to rt. After quenching with NH₄Cl (5 mL), the organic layer was separated and the aqueous layer was extracted with EtOAc (5 × 10 mL). The combined organic extracts were dried with anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (Silica Gel 60, hexane–EtOAc, 60:40) to give **10** (0.08 g, 0.29 mmol, 80%) as a white powder; mp: 160–162 °C; $[\alpha]_D^{23} = -15.3$ (c 1.02, CH₂Cl₂); ¹H NMR: 2.12 (s, 6H); 3.36 (s, 2H); 4.52 (s, 2H); 6.83–7.24 (m, 8H); ¹³C NMR: 30.50, 48.26, 53.46, 120.12, 126.03, 126.47, 139.95, 142.63, 207.62; IR (KBr) ν : 3025, 2955, 1740, 1454, 1171, 1095, 1042, 763, 751 cm⁻¹. Elemental Anal. Calcd for C₂₀H₁₈O₂: C, 82.73; H, 6.25. Found: C, 82.79; H, 6.18.

4.9. Synthesis of (11R,12R)-9,10-dihydro-11,12-diisopropenyl-9,10-ethanoanthracene 11

To a solution of MePPh₃I (3.04 g, 7.52 mmol) in dry toluene (30 mL) under argon was added K^tBuO (0.78 g, 7.0 mmol). The mixture was heated at 90 °C for 30 min and then cooled down to rt. A solution of **10** (0.16 g, 0.54 mmol) in dry toluene (15 mL) was then added. After 15 min the mixture was heated at 90 °C for 1 h. The mixture was cooled to rt and the reaction was quenched with water (40 mL). The organic layer was separated and the aqueous layer was extracted with hexane–Et₂O (70:30, 2 × 20 mL). The combined organic extracts were washed once with H₂O and satd NaCl solution, and then dried with anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (Silica Gel 60, hexane–EtOAc, 60:40) to give **11** (0.12 g, 0.42 mmol, 78%) as a yellowish oil; $[\alpha]_D^{23} = -10.3$ (c 1.01, CH₂Cl₂); ¹H NMR: 1.48 (s, 6H); 2.73 (s, 2H); 4.15 (s, 2H); 4.32 (s, 2H); 4.59 (s, 2H); 6.91–7.24 (m, 8H); ¹³C NMR: 22.40, 48.77, 50.84, 111.23, 122.55, 125.17, 125.96, 126.37, 140.66, 144.06, 147.15; IR (film) ν : 3067, 3021, 2945, 1637, 1615, 1461, 1406, 1187, 1058, 987, 813, 756 cm⁻¹; HRMS (ESI) m/z calcd for C₂₂H₂₂ [M]⁺ 286.4160, found: 286.4159.

4.10. Esterifications of carboxylic acids with 3

Method A: Ratio **3**/acid/DCC/DMAP/TsOH = 1.0:2.2:3.1:0.4:0.4.

Method B: Ratio **3**/BuLi/acid chloride = 1.0:2.4:3.0.

4.10.1. Method A—typical procedure: synthesis of (11R,12R)-9,10-dihydro-9,10-ethanoanthracene-11,12-di methyl bis(benzoate) 12

To a solution of **3** (0.25 g, 0.94 mmol) in dry CH₂Cl₂ (10 mL) under argon and at rt, was added consecutively DCC (0.60 g,

2.91 mmol), *p*-toluenesulfonic acid (TsOH) (0.06 g, 0.37 mmol) and DMAP (0.05 g, 0.37 mmol). After 15 min stirring, the mixture was cooled down to 0 °C and a solution of benzoic acid (0.25 g, 2.06 mmol) in dry CH₂Cl₂ (5 mL) was added slowly. The mixture was warmed up to rt and then stirred for 12 h. The separation of DCU and some unreacted **3** was carried out by percolation of the crude reaction mixture through a fritted Büchner funnel containing two layers of about 1 cm deep each (the lower of silica gel and the upper of Celite). The layers were washed with CH₂Cl₂ (3 × 5 mL). The solvent of the combined filtrates was removed under reduced pressure and the crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 80:20) to give **12** (0.44 g, 0.93 mmol, 98%) as a white powder; mp: 58–60 °C; $[\alpha]_D^{23} = -11.2$ (c 1.01, CH₂Cl₂); ¹H NMR: 1.87–2.00 (m, 2H), 3.80 (dd, 2H, ³J = 8.2 Hz, ²J = 11.1 Hz), 4.06 (dd, 2H, ³J = 5.3 Hz, ²J = 11.1 Hz), 4.27 (s, 2H), 6.94–7.50 (m, 8H), 7.86–8.01 (m, 10H); ¹³C NMR: 43.06, 46.65, 67.59, 124.04, 125.93, 126.79, 128.87, 130.19, 133.40, 140.73, 143.56, 166.81; IR (film) ν : 3068, 3037, 3021, 2948, 2893, 1720, 1600, 1448, 1274, 1114, 1072, 1025, 909, 757, 707 cm⁻¹; MS: m/z (%) 474 (29), 352 (13), 230 (12), 215 (17), 202 (15), 178 (100), 152 (20), 105 (98), 77 (83), 51 (24); HRMS (ESI) m/z calcd for C₃₂H₂₆O₄ [M]⁺ 474.1831, found: 474.183.

4.10.2. Method B—typical procedure: synthesis of (11R,12R)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethyl bis(phenylethanoate) 13

A solution of **1** (0.25 g, 0.94 mmol) in dry THF (10 mL) was cooled to 0 °C under argon. Then, a 1.35 M solution of *n*-BuLi in hexane (1.70 mL, 2.25 mmol) was added slowly with a syringe. The mixture was stirred at rt for 30 min and then cooled to 0 °C. Phenylacetyl chloride (0.44 g, 2.84 mmol) was then added slowly. A white precipitate (LiCl) formed immediately. The mixture was refluxed for 1 h and then stirred 12 h at rt. After quenching with a saturated solution of NaHCO₃ (ca. 20 mL), the organic layer was separated and the aqueous layer was extracted with Et₂O (3 × 10 mL). The combined organic extracts were washed once with H₂O and satd NaCl solution, and then dried with anhydrous Na₂SO₄. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 85:15) to give **13** (0.38 g, 0.76 mmol, 81%) as a yellowish oil; $[\alpha]_D^{23} = -22.1$ (c 1.04, CH₂Cl₂); ¹H NMR: 1.40–1.62 (m, 2H), 3.39 (dd, 2H, ³J = 8.7 Hz, ²J = 11.1 Hz), 3.54 (s, 4H), 3.69 (dd, 2H, ³J = 5.5 Hz, ²J = 11.1 Hz), 3.91 (s, 2H), 6.91–7.34 (m, 18H); ¹³C NMR: 42.02, 42.59, 45.99, 67.26, 123.87, 125.80, 126.42, 126.66, 127.64, 129.11, 129.73, 134.62, 140.43, 143.22, 171.52; IR (neat) ν : 3060, 3025, 2944, 1740, 1495, 1456, 1254, 1142, 1006, 761, 719, 691 cm⁻¹; MS: m/z (%) 502 (4), 215 (5), 202 (5), 178 (100), 152 (5), 118 (4), 91 (83), 65 (10); HRMS (ESI) m/z calcd for C₃₄H₃₀O₄ [M]⁺ 502.2144, found: 502.214.

4.10.3. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethyl bis((E)-3-phenylpro penoate) 14

Method B. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 80:20) to give **14** (0.95 g, 1.8 mmol, 91%) as a white solid, mp: 60–62 °C; $[\alpha]_D^{23} = +18.7$ (c 1.06, CH₂Cl₂); ¹H NMR: 1.78–1.88 (m, 2H), 3.72 (dd, 2H, ³J = 8.1 Hz, ²J = 11.5 Hz), 3.90 (dd, 2H, ³J = 5.4 Hz, ²J = 11.5 Hz), 4.23 (s, 2H), 6.38 (d, 2H, ³J = 16.0 Hz), 6.99–7.51 (m, 18H), 7.60 (d, 2H, ³J = 16.0 Hz); ¹³C NMR: 41.56, 45.07, 65.89, 116.88, 122.51, 124.51, 125.30, 126.08, 127.14, 127.88, 129.30, 133.39, 139.31, 141.95, 144.12, 165.65; IR (film) ν : 3060, 3021, 2944, 2889, 1709, 1639, 1448, 1305, 1169, 765, 734 cm⁻¹; MS: m/z (%) 526 (13), 498 (20), 378 (33), 348 (20), 230 (18), 215 (12), 202 (11), 178 (100), 152 (11), 131 (93), 103 (83), 77 (46), 51 (8); HRMS (ESI) m/z calcd for C₃₆H₃₀O₄ [M]⁺ 526.2144, found: 526.214.

Elemental Anal. Calcd for $C_{36}H_{30}O_4$: C, 82.11; H, 5.74. Found: C, 82.00; H, 5.69.

4.10.4. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethano anthracene-11,12-dimethyl bis((E)-2-butenate) 15

Method B. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 70:30) to give **15** (0.35 g, 0.88 mmol, 94%) as a yellowish dense oil, $[\alpha]_D^{23} = -13.7$ (c 1.00, CH₂Cl₂); ¹H NMR: 1.79 (dd, 6H, ⁴J = 1.5 Hz, ³J = 6.3 Hz), 2.01–2.09 (m, 2H), 3.57 (dd, 2H, ³J = 8.6 Hz, ²J = 11.1 Hz), 3.78 (dd, 2H, ³J = 5.7 Hz, ²J = 11.1 Hz), 4.17 (s, 2H), 5.77 (dq, 2H, ³J = 15.7 Hz, ³J = 6.3 Hz), 6.87 (dq, 2H, ³J = 15.7 Hz, ⁴J = 1.5 Hz), 6.96–7.23 (m, 8H); ¹³C NMR: 18.46, 42.94, 46.53, 66.95, 122.96, 123.9, 125.89, 126.41, 126.68, 140.61, 143.45, 145.39, 166.61; IR (neat) ν: 3072, 3041, 3017, 2940, 2913, 1720, 1654, 1460, 1441, 1258, 1177, 1099, 959, 839, 757, 730 cm⁻¹; MS: *m/z* (%) 402 (13), 178 (100), 69 (32); HRMS (ESI) *m/z* calcd for $C_{26}H_{26}O_4$ [M]⁺: 402.1831, found: 402.183.

4.10.5. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethyl bis((E)-2-methyl-3-phenylpropenoate) 17

Method B. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 70:30) to give **17** (0.49 g, 0.88 mmol, 94%) as a white solid, mp: 73–75 °C; $[\alpha]_D^{23} = +7.3$ (c 1.06, CH₂Cl₂); ¹H NMR: 1.81–1.89 (m, 2H), 2.01 (s, 6H), 3.69 (dd, 2H, ³J = 8.1 Hz, ²J = 11.3 Hz), 3.92 (dd, 2H, ³J = 5.5 Hz, ²J = 11.3 Hz), 4.19 (s, 2H), 6.99 (m, 2H), 7.11–7.34 (m, 8H), 7.60 (s, 10H); ¹³C NMR: 14.61, 43.11, 46.75, 67.77, 124.04, 126.02, 126.63, 126.82, 128.86, 130.22, 136.36, 139.71, 140.76, 143.54, 168.73; IR (KBr) ν: 3060, 3017, 2951, 2889, 1701, 1631, 1491, 1445, 1250, 1196, 1114, 909, 757, 730, 699 cm⁻¹; MS: *m/z* (%) 554 (3), 230 (25), 215 (20), 202 (9), 178 (100), 152 (9), 145 (70), 117 (73), 91 (49), 77 (4); HRMS (ESI) *m/z* calcd for $C_{38}H_{34}O_4$ [M]⁺: 554.2457, found: 554.245. Elemental Anal. Calcd for $C_{38}H_{34}O_4$: C, 82.28; H, 6.18. Found: C, 82.36; H, 6.24.

4.10.6. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethyl bis((E)-2,3-diphenyl-2-propenoate) 18

Method B. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 81:15) to give **18** (0.48 g, 0.70 mmol, 75%) as a white solid, mp: 69–71 °C; $[\alpha]_D^{23} = -4.1$ (c 1.06, CH₂Cl₂); ¹H NMR: 1.52–1.63 (m, 2H), 3.46 (dd, 2H, ³J = 7.5 Hz, ²J = 11.2 Hz), 3.65 (dd, 2H, ³J = 4.7 Hz, ²J = 11.2 Hz), 3.89 (s, 2H), 6.90–7.40 (m, 28H), 7.75 (s, 2H); ¹³C NMR: 42.54, 46.13, 67.70, 123.86, 125.84, 126.45, 126.65, 128.30, 128.68, 129.14, 129.57, 130.13, 131.17, 133.05, 135.03, 136.64, 140.57, 140.85, 143.21, 167.71; IR (film) ν: 3052, 3021, 2951, 2889, 1709, 1627, 1491, 1445, 1250, 1165, 909, 761, 734, 707, 687 cm⁻¹; MS: *m/z* (%) 678 (4), 277 (14), 230 (23), 215 (17), 207 (40), 202 (11), 178 (100), 152 (28), 77 (12); HRMS (ESI) *m/z* calcd for $C_{48}H_{38}O_4$ [M]⁺: 678.2770, found: 678.276. Elemental Anal. Calcd for $C_{48}H_{38}O_4$: C, 84.93; H, 5.64. Found: C, 85.02; H, 5.68.

4.10.7. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethano anthracene-11,12-dimethyl bis((E)-2-methyl-2-butenate) 19

Method B. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 80:20) to give **19** (0.31 g, 0.71 mmol, 76%) as a yellowish dense oil; $[\alpha]_D^{23} = -18.8$ (c 1.00, CH₂Cl₂); ¹H NMR (300 MHz, CDCl₃) δ (ppm) 1.85–2.06 (m, 14H), 3.79 (dd, 2H, ³J = 8.1 Hz, ²J = 11.2 Hz), 4.06 (dd, 2H, ³J = 5.3 Hz, ²J = 11.2 Hz), 4.39 (s, 2H), 6.71 (m, 2H), 6.92–7.40 (m, 8H); ¹³C NMR (300 MHz, CDCl₃) δ (ppm) 12.41, 14.73, 42.88, 46.57, 67.13, 123.87, 125.81, 126.6, 128.5, 137.89, 140.06, 140.73, 141.95, 143.46, 168.12; IR (neat) ν: 3068, 3017, 2924, 2854, 1713, 1650, 1456, 1266, 1142, 1076, 761, 734 cm⁻¹; MS: *m/z* (%) 430 (25),

330 (6), 230 (6), 215 (7), 202 (5), 178 (100), 152 (7), 83 (57), 55 (52); HRMS (ESI) *m/z* calcd for $C_{28}H_{30}O_4$ [M]⁺: 430.2144, found: 430.214.

4.10.8. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethano anthracene-11,12-dimethyl bis(propenoate) 20

Method B. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 70:30) to give **20** (3.87 g, 10.33 mmol, 70%) as a white solid, mp: 92–94 °C; $[\alpha]_D^{23} = -19.2$ (c 1.00, CH₂Cl₂); ¹H NMR: 1.68–1.82 (m, 2H), 3.61 (dd, 2H, ³J = 7.6 Hz, ²J = 11.3 Hz), 3.83 (dd, 2H, ³J = 4.8 Hz, ²J = 11.3 Hz), 4.17 (s, 2H), 5.73 (dd, 2H, ²J = 1.5 Hz, ³J = 10.0 Hz), 6.05 (dd, 2H, ²J = 1.5 Hz, ³J = 10.5 Hz), 6.30 (dd, 2H, ³J = 10 Hz, ³J = 10.5 Hz), 6.94–7.30 (m, 8H); ¹³C NMR: 42.85, 46.35, 67.15, 123.94, 125.93, 126.54, 126.78, 128.78, 131.36, 140.58, 143.37, 166.25; IR (KBr) ν: 3068, 3041, 3017, 2955, 2893, 1732, 1631, 1468, 1410, 1297, 1270, 1192, 1188, 1056, 982, 908, 811, 757, 730 cm⁻¹; MS: *m/z* (%) 374 (13), 215 (2), 202 (3), 178 (100), 152 (3), 97(3), 83 (3), 55 (20); HRMS (ESI) *m/z* calcd for $C_{24}H_{22}O_4$ [M]⁺: 374.1518, found: 374.152. Elemental Anal. Calcd for $C_{24}H_{22}O_4$: C, 76.99; H, 5.92. Found: C, 77.08; H, 5.98.

4.10.9. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethanoanthracene-11,12-dimethyl bis((E)-3-methyl-2-butenate) 21

Method B. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 75:25) to give **21** (0.34 g, 0.84 mmol, 89%) as a yellowish dense oil, $[\alpha]_D^{23} = -18.9$ (c 1.00, CH₂Cl₂); ¹H NMR: 1.68–1.70 (m, 2H), 1.78 (s, 6H), 2.06 (s, 6H), 3.50 (dd, 2H, ³J = 7.4 Hz, ²J = 11.3 Hz), 3.75 (dd, 2H, ³J = 5.2 Hz, ²J = 11.3 Hz), 4.17 (s, 2H), 5.62 (s, 2H), 6.91–7.24 (m, 8H); ¹³C NMR: 20.63, 27.75, 43.03, 46.43, 66.34, 116.36, 123.90, 125.88, 126.40, 126.64, 140.75, 143.48, 157.27, 166.71; IR (neat) ν: 3064, 3037, 3021, 2944, 2909, 1709, 1650, 1445, 1227, 1142, 1076, 912, 846, 757, 730 cm⁻¹; MS: *m/z* (%) 430 (6), 178 (100), 152 (2), 83 (19), 55 (8), HRMS (ESI) *m/z* calcd for $C_{28}H_{30}O_4$ [M]⁺: 430.2144, found: 430.214.

4.10.10. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethano anthracene-11,12-dimethyl bis(phenylpropynoate) 23

Method A. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 70:30) to give **23** (0.77 g, 1.47 mmol, 87%) as a yellowish dense oil; $[\alpha]_D^{23} = +7.4$ (c 0.98, CH₂Cl₂); ¹H NMR: 1.92–2.10 (m, 2H), 3.91 (dd, 2H, ³J = 8.9 Hz, ²J = 11.3 Hz), 4.14 (dd, 2H, ³J = 5.4 Hz, ²J = 11.3 Hz), 4.48 (s, 2H), 7.17–7.83 (m, 18H); ¹³C NMR: 42.62, 46.07, 68.33, 81.00, 87.25, 120.00, 124.13, 126.07, 126.68, 126.97, 129.04, 131.17, 133.48, 140.33, 143.12, 154.20 ppm; IR (neat) ν: 3064, 3017, 2920, 2850, 2221, 1709, 1487, 1456, 1281, 1184, 1165, 905, 757, 730, 687 cm⁻¹; MS: *m/z* (%) 552 (18), 231 (2), 202 (4), 178 (100), 152 (3), 129(30), 102(3), 75 (4); HRMS (ESI) *m/z* calcd for $C_{36}H_{26}O_4$ [M]⁺: 522.1831, found: 522.183.

4.10.11. Synthesis of (11R,12R)-9,10-dihydro-9,10-ethano anthracene-11,12-dimethyl bis(2-octynoate) 24

Method A. The crude product was purified by column chromatography (Silica Gel 60, hexane–Et₂O, 80:20) to give **24** (0.43 g, 0.85 mmol, 90%) as a yellowish dense oil, $[\alpha]_D^{23} = -8.1$ (c 1.00, CH₂Cl₂); ¹H NMR: 0.83 (t, 6H), 1.15–1.38 (m, 8H), 1.44–1.58 (m, 4H), 1.62–1.73 (m, 2H), 2.24 (t, 4H), 3.53 (dd, 2H, ³J = 8.4 Hz, ²J = 11.3 Hz), 3.80 (dd, 2H, ³J = 5.1 Hz, ²J = 11.3 Hz), 4.19 (s, 2H), 6.94–7.31 (m, 8H); ¹³C NMR: 14.24, 19.11, 22.46, 27.60, 31.44, 42.56, 45.96, 67.98, 73.46, 90.64, 123.95, 125.92, 126.59, 126.78, 140.39, 143.22, 154.00; IR (neat) ν: 3068, 3045, 3021, 2928, 2858, 2229, 1712, 1460, 1235, 1080, 955, 746, 726, 629 cm⁻¹; MS: *m/z* (%) 510 (7), 231(6), 215 (8), 202 (6), 178 (100), 152 (5),

123 (18), 93 (6), 79 (6), 67 (24), 55 (24); HRMS (ESI) m/z calcd for $C_{34}H_{38}O_4$ $[M]^+$ 510.2770, found: 510.277.

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