CHAPTER 2
EXPERIMENTAL

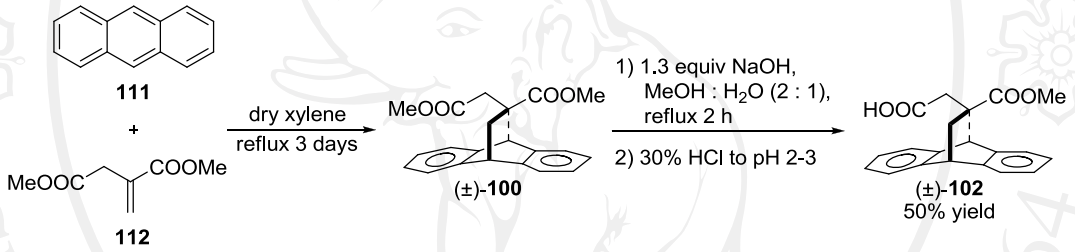
General Methods

All reaction were carried out under nitrogen atmosphere. Unless otherwise noted, meterials were obtained from commercial suppliers and used without further purification. Melting points were determined by using a Gallenkamp Electrothermal apparatus and were uncorrected. Optical rotations were measured in $CHCl_3$ on an Atago AP-300 polarimeter. Infrared spectra were recorded on a FT-IR model TENSER 27 (Bruker) spectrometer and absorption frequencies were reported in reciprocal centimeters (cm^{-1}). Mass spectra (electrospray ionization mode, ESI-MS) were recorded on a micromass Q-TOF2^{Tm} (Waters) spectrometer. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker DRX 400 MHz spectrometers and chemical shifts were given in ppm downfield from tetramethylsilane (TMS). All NMR spectra were measured in $CDCl_3$ and chemical shift were reported as δ-values in parts per million (ppm) relative to residue $CHCl_3$ as internal reference (^{1}H: δ 7.26, ^{13}C: δ 77.00) and coupling constants (*J* values) were reported in hertz (Hz). Peak multiplicities are indicated as follows: *s* (singlet), *d* (doublet), *t* (triplets), *dt* (doublet of triplets), *ddd* (doublet of doublet of doublets) and *m* (multiplet). Flash column chromatography was performed employing Merck silica gel 60 and Merck silica gel 60H. Preparative thin layer chromatography (PLC) plates were carried out using Merck silica gel 60 PF_{254}. Analytical thin layer chromatography was performed with Merck silica gel 60 F_{254} aluminum plates. Solvents were dried over CaH_2 and distilled before used. Tetrahydrofuran (THF) was freshly distilled from sodium and benzophenone ketyl under nitrogen. Diisopropylamine was distilled over CaH_2 and stored under nitrogen. *n*-Butyllithium was purchased from Fluka and Across as solution in hexane and titrated periodically according to the 2,5-dimethoxybenzyl alcohol method. Pyrrolidine, piperidine and triethylamine were died over CaH_2 and freshly distilled before used. Benzyl bromide was distillated under reduce pressure for later used.

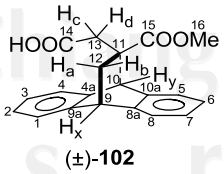
Enantiomeric excesses were determined by ^{1}H-NMR spectroscopy using the chiral lanthanide shift reagent, tris[3-(haptafluoropropylhydroxymethylene)-*d*-camphorato]praseodymium(III), $Pr(hfc)_3$. The calculation of %yield of all products was based on the isolated product as pure compounds and ^{1}H-NMR spectroscopy technique.

2.1 Preparation and resolution of both enantiomerically pure dimethyl itaconate–anthracene adducts ((+)-(11*S*)-100 and (–)-(11*R*)-100)

2.1.1 Preparation of (±)-11-carbomethoxy-11-carboxylmethyl-9,10-dihydro-9,10-ethanoanthracene ((±)-100)



A mixture of anthracene (**111**) (169.04 g, 0.95 mol) and dimethyl itaconate (**112**) (100.00 g, 0.63 mol) in dried xylene (800 mL) was heated under reflux for 3 days to obtain dimethyl itaconate–anthracene adduct ((±)-**100**) racemic form. After that, the compound (±)-**100** was refluxed with sodium hydroxide (1.3 equiv) in solution of MeOH:H_2O (2:1) for 2 hours. The crude reaction mixture adjusted to pH 2-3 by 30% HCl solution, then extracted with CH_2Cl_2 (3 times). The combined organic portion were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was crystallized from CH_2Cl_2/hexane to give (±)-11-carbomethoxy-11-carboxylmethyl-9,10-dihydro-9,10-ethanoanthracene ((±)-**102)**, as a monoacid–anthracene adduct in 50% yield (100.3791 g) and 100% conversion from the starting material.



(±)-102

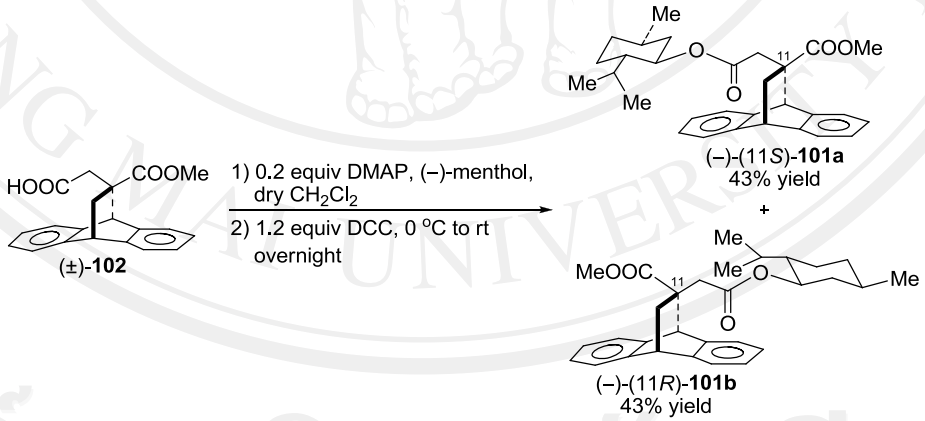
Table 13 Data of the monoacid–anthracene adduct (±)-**100**

Physical properties	
White solid Melting point (m.p.) 208.4–209.7 °C (from CH_2Cl_2/hexane)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3019	C–H stretching of aromatic
3453	–OH stretching of acid
2950, 2853	$-CH_2$, $-CH_3$ stretching
1740	C=O stretching
1645	C=C stretching
1434, 1343	$-CH_2$, $-CH_3$ bending
1254, 1115	C–O stretching
768	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.47, 2.78, 4.13	*ABX* system, (J = 13.1, 3.0, 2.4 Hz), 3H, H_a, H_b, H_x
1.96	*d* (J = 16.5 Hz), 1H, H_c or H_d
2.94	*d* (J = 16.5 Hz), 1H, H_c or H_d
3.44	*s*, 3H, $COOCH_3$-16
4.33	*s*, 1H, H_y
6.99–7.33	*m*, 8H, ArH

Table 13 Data of the monoacid–anthracene adduct (±)-**100** (continued)

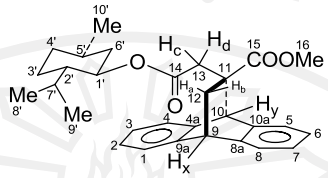
^{13}C-NMR (100 MHz) in $CDCl_3$	
36.82 (CH_2-12), 40.09 (CH-9), 44.15 (CH_2-13), 50.10 (C_q-11), 52.25 (CH_2-16), 52.87 (CH-10), 123.36, 123.59, 124.26, 125.76, 125.79, 125.82, 126.56, 126.76 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 139.52, 140.01, 142.83, 143.63 (C_q-ArH-4a, 8a, 9a,10a), 174.75 (Cq-15), 176.28 (C_q-14)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{20}H_{18}O_4$	322.1205 (M^+)
Lock mass of $C_{12}H_{14}N_4O_4SNa$	333.0633 $(M+Na)^+$
Calc. for $C_{20}H_{18}O_4Na$	345.1103 $(M+Na)^+$
Found for $C_{20}H_{18}O_4Na$	345.1106 $(M+Na)^+$

2.1.2 Preparation of (–)-11-carbomethoxy-11-[(–)-menthoxyacetyl]-9,10-dihydro-9,10-ethanoanthracenes ((–)-(11*S*)-101a and (–)-(11*R*)-101b)



The racemic monoacid–anthracene adduct (±)-**102** (22.25 g, 0.069 mol), DMAP (0.2 equiv, 1.69 g, 13.80 mmol) and (–)-menthol (1.2 equiv, 16.18 g, 103.54 mmol) in dry CH_2Cl_2 were treated with DCC (1.2 equiv, 17.10 g, 82.81 mmol) at 0 °C for overnight. The mixture was filtered. The solution was washed with H_2O and saturated NaCl solution, dried over $MgSO_4$, filtered and concentrated in *vacuo*. The crude product was purified by crystallization to obtain monomenthyl–anthracene

adduct in two diastereomers which are (–)-(11*S*)-**101a** in 43% yield (13.6705 g) from CH_2Cl_2/hexane and (–)-(11*S*)-**101b** in 43% yield (13.6700 g) from MeOH.



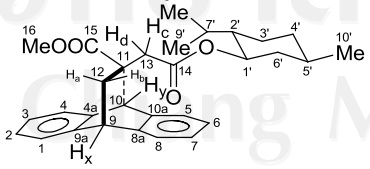
(–)-(11*S*)-**101a**

Table 14 Data of the monomenthyl–anthracene adduct (–)-**101a**

Physical properties	
White solid Melting point (m.p.) 185.3–186.8 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{28.0}$ = –14.21° (*c* = 0.219, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3025	C–H stretching of aromatic
2950, 2886	$-CH_2$, $-CH_3$ stretching
1729	C=O stretching of ester
1638	C=C stretching of aromatic
1459, 1371	$-CH_2$, $-CH_3$ bending
1221, 1196	C–O stretching of ester
747	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
0.70	*d* (*J* = 7.0 Hz), 3H, H-methyl
0.76–1.96	*m*, 9H, H-menthyl
0.84	*d* (*J* = 6.6 Hz), 3H, H-methyl
0.85	*d* (*J* = 7.0 Hz), 3H, H-methyl

Table 14 Data of the monomenthyl–anthracene adduct (–)-**101a** (continued)

Chemical shift (δ, ppm)	Type of protons
1.48, 2.82, 4.32	*ABX* system, (J = 13.0, 3.0, 2.4 Hz), 3H, H_a, H_b, H_x
1.94	*d* (J = 16.2 Hz), 1H, H_c or H_d
2.92	*d* (J = 16.2 Hz), 1H, H_c or H_d
3.47	*s*, 3H, $COOCH_3$-16
4.35	*s*, 1H, H_y
4.60	*ddd* (J = 10.9, 10.9, 4.4 Hz), 1H, H-1′
7.03–7.31	*m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
16.05, 20.75, 21.93, 23.16, 25.97, 31.31, 34.11, 40.48 (C-menthyl), 36.99 (CH_2-12), 44.14 (CH-9), 44.97 (CH_2-13), 50.23 (C_q-11), 52.04 (CH_3-16), 52.97 (CH-10), 74.59 (CH-1′), 123.31, 123.53, 124.21, 124.93, 125.70, 126.44, 126.57, 127.54 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 139.74, 140.17, 142.81, 143.69 (C_q-ArH-4a, 8a, 9a,10a), 170.63 (C_q-14), 174.74 (C_q-15)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{30}H_{36}O_4$	460.2614 (M^+)
Lock mass of $C_{32}H_{42}NO_2$	472.3215 $(M+H)^+$
Calc. for $C_{30}H_{36}O_4Na$	483.2511 $(M+Na)^+$
Found for $C_{30}H_{36}O_4Na$	483.2506 $(M+Na)^+$



(–)-(11*R*)-**101b**

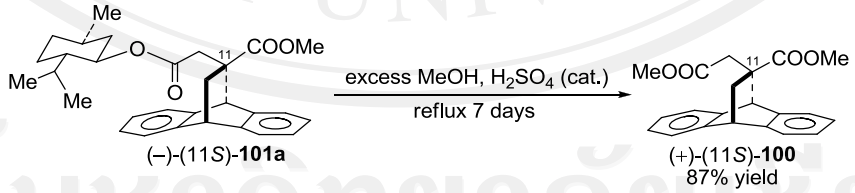
Table 15 Data of the monomenthyl–anthracene adduct (–)-**101b**

Physical properties	
White solid Melting point (m.p.) 102.1–103.1 °C (from MeOH) $[\alpha]_{589}^{28.7}$ = –61.35° (c = 0.163, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3040	C–H stretching of aromatic
2953, 2869	$–CH_2$, $–CH_3$ stretching
1727	C=O stretching of ester
1459, 1308	$–CH_2$, $–CH_3$ bending
1389, 1370	$–CH_3$ bending
1175, 1063	C–O stretching of ester
766	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
0.67	*d* (J = 7.0 Hz), 3H, H-methyl
0.78–1.94	*m*, 9H, H-menthyl
0.87	*d* (J = 7.0 Hz), 3H, H-methyl
0.90	*d* (J = 6.6 Hz), 3H, H-methyl
1.45, 2.80, 4.31	*ABX* system, (J = 13.0, 3.1, 2.4 Hz), 3H, H_a, H_b, H_x
1.96	*d* (J = 15.8 Hz), 1H, H_c or H_d
2.95	*d* (J = 15.8 Hz), 1H, H_c or H_d
3.47	*s*, 3H, $COOCH_3$-16
4.34	*s*, 1H, H_y

Table 15 Data of the monomenthyl–anthracene adduct (–)-**101b** (continued)

Chemical shift (δ, ppm)	Type of protons
4.58 7.03–7.30	*ddd* (*J* = 10.9, 10.9, 4.4 Hz), 1H, H-1′ *m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
15.95, 20.79, 21.96, 23.10, 25.87, 31.32, 34.13, 44.91 (C-menthyl), 36.64 (CH_2-12), 40.66 (CH_2-13), 44.13 (CH-9), 50.43 (C_q-11), 52.02 (CH_3-16), 53.01 (CH-10), 74.66 (CH-1′), 123.29, 123.59, 124.19, 125.73, 125.78, 126.47, 126.63, (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 139.62, 140.23, 142.80, 143.77 (C_q-ArH-4a, 8a, 9a,10a), 170.45 (C_q-15), 174.74 (C_q-14)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{30}H_{36}O_4$ Lock mass of $C_{32}H_{42}NO_2$ Calc. for $C_{30}H_{36}O_4Na$ Found for $C_{30}H_{36}O_4Na$	460.2614 (M^+) 472.3215 $(M+H)^+$ 483.2511 $(M+Na)^+$ 483.2506 $(M+Na)^+$

2.1.3 Preparation of optically active (+)-(11*S*)-11-carbomethoxy-11-methoxyacetyl-9,10-dihydro-9,10-ethanoanthracene (+)-(11*S*)-100

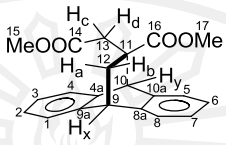


(–)-(11*S*)-**101a**

(+)-(11*S*)-**100**
87% yield

The monomenthyl–anthracene adduct (–)-(11*S*)-**101a** (11.3138 g, 24.58 mmol) was dissolved in excess anhydrous MeOH (800 mL). The solution was added conc. H_2SO_4 (10 mL) as a catalyst and then heated to reflux (7 days). The crude reaction mixture was neutralized with aqueous NaOH solution, then extracted with CH_2Cl_2 (3 times). The combined organic portion were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was crystallized from CH_2Cl_2/hexane to

give optically active (+)-(11*S*)-11-carbomethoxy-11-methoxyacetyl-9,10-dihydro-9,10-ethanoanthracene, dimethyl–itaconate anthracene adduct ((+)-(11*S*)-**100**) in 87% yield (7.1595 g), 100% conversion from the starting material.



(±)-**100**

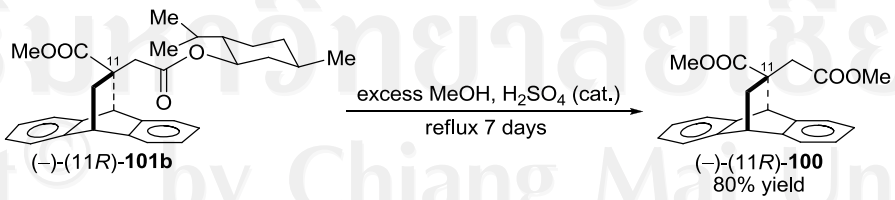
Table 16 Data of the dimethyl-itaconate anthracene adduct (+)-(11*S*)-**100**

Physical properties	
White solid Melting point (m.p.) 138.0–140.0 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{24.8}$ = +38.74° (*c* = 0.327, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3000	C–H stretching of aromatic
2951, 2850	$–CH_2$, $–CH_3$ stretching
1740	C=O stretching of ester
1460	C=C stretching of aromatic
1463, 1427	$–CH_2$, $–CH_3$ bending
1353	$–CH_3$ bending
1196	C–O stretching of ester
767	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.46, 2.81, 4.31	*ABX* system, (*J* = 13.0, 3.0, 2.6 Hz), 3H, H_a, H_b, H_x
1.97	*d* (*J* = 16.1 Hz), 1H, H_c or H_d

Table 16 Data of the dimethyl–itaconate anthracene adduct (+)-(11*S*)-**100** (continued)

Chemical shift (δ, ppm)	Type of protons
2.92	*d* (*J* = 16.1 Hz), 1H, H_c or H_d
3.47	*s*, 3H, $COOCH_3$-17
3.57	*s*, 3H, $COOCH_3$-15
3.46	*s*, 1H, H_y
7.03–7.31	*m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
36.72 (CH_2-12), 44.07 (CH-9), 44.33 (CH_2-12), 50.30 (C_q-11), 51.59 (CH_3-15), 52.15 (CH_3-17), 52.79 (CH-10), 123.29, 123.54, 124.23, 125.72, 126.46, 126.62 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 139.62, 140.09, 142.83, 143.65 (C_q-ArH-4a, 8a, 9a, 10a), 171.47 (C_q-14), 174.84 (C_q-16)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{21}H_{20}O_4$	336.1362 (M^+)
Lock mass of $C_{12}H_{14}N_4O_4SNa$	333.0633 $(M+Na)^+$
Calc. for $C_{21}H_{21}O_4$	337.1440 $(M+H)^+$
Found for $C_{21}H_{21}O_4$	337.1433 $(M+H)^+$

2.1.4 Preparation of optically active (–)-(11*R*)-11-carbomethoxy-11-methoxyacetyl-9,10-dihydro-9,10-ethanoanthracene ((–)-(11*R*)-100)

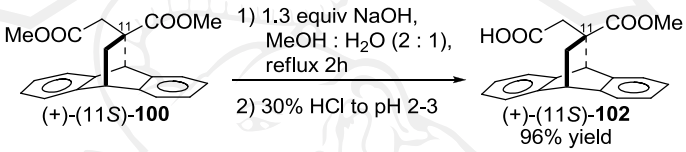


Dimethyl-itaconate anthracene adduct (–)-(11*R*)-**100** was prepared according to general procedure 2.1.3, adduct (–)-(11*R*)-**101b** (10.55 g, 22.92 mmol) provided optically active adduct (–)-(11*R*)-**100** in 80% yield (6.1684 g), 100% conversion from

the starting material as white solid, m.p. 140.1–143.2 °C, ($[\alpha]_{589}^{24.4}$ = –37.62° (*c* = 0.443, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 16).

2.2 Synthesis of both enantiomerically pure monoacid–anthracene adducts (+)-(11*S*)-102 and (–)-(11*R*)-102

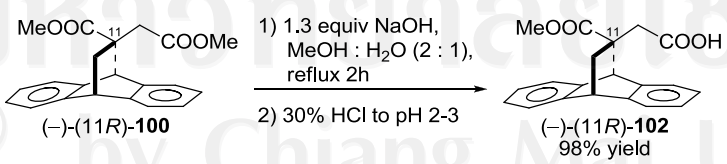
2.2.1 Synthesis of enantiomeric (+)-(11*S*)-11-carbomethoxy-11-carboxyl methyl-9,10-dihydro-9,10-ethanoanthracene ((+)-(11*S*)-102)



(+)-(11*S*)-**100** → (+)-(11*S*)-**102** 96% yield

Compound (+)-(11*S*)-**102** (5.1048 g, 15.19 mmol) was refluxed with sodium hydroxide (0.79 g, 19.70 mmol) in solution of MeOH:H_2O (2:1) for 2 hours. The crude reaction mixture adjusted to pH 2-3 by 30% HCl solution, then extracted with CH_2Cl_2 (3 times). The combined organic portion were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was crystallized from CH_2Cl_2/hexane to give (+)-(11*S*)-11-carbomethoxy-11-carboxylmethyl-9,10-dihydro-9,10-ethano anthracene, enantiomeric monoacid–anthracene adduct (+)-(11*S*)-**102** in 96% yield (4.7198 g) and 100% conversion from the starting material as white crystals, m.p. 148.2–149.8 °C, ($[\alpha]_{589}^{27.6}$ = +45.45° (*c* = 0.176, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 13).

2.2.2 Synthesis of enantiomeric (–)-(11*R*)-11-carbomethoxy-11-carboxyl methyl-9,10-dihydro-9,10-ethanoanthracene ((–)-(11*R*)-102)



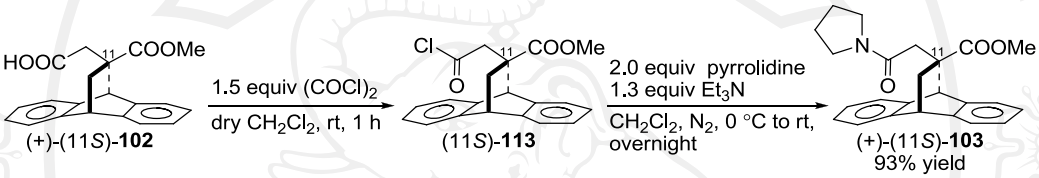
(–)-(11*R*)-**100** → (–)-(11*R*)-**102** 98% yield

Monoacid–anthracene adduct (–)-(11*R*)-**102** was prepared according to typical procedure 2.2.1, adduct (–)-(11*R*)-**100** (6.0567 g, 18.01 mmol) and sodium hydroxide (0.94 g, 23.40 mmol) provided the optically active adduct (–)-(11*R*)-**102** in

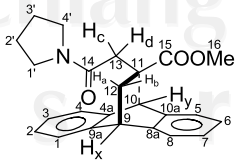
98% yield (5.7136 g), 100% conversion from the starting material as white solid, m.p. 152.8–154.1 °C, ($[\alpha]_{589}^{24.9}$ = –40.45° (*c* = 0.356, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 13).

2.3 Synthesis of both enantiomerically pure amide–anthracene adducts (+)-(11*S*)-103, (–)-(11*R*)-103, (+)-(11*S*)-104 and (–)-(11*R*)-104

2.3.1 Synthesis of (+)-(11*S*)-11-carbomethoxy-11-pyrrolidinylacetyl-9,10-dihydro-9,10-ethanoanthracene ((+)-(11*S*)-103)



Oxalyl chloride (1.5 equiv, 0.65 mL, 7.76 mmol) was added slowly under nitrogen gas to a solution of monoacid–anthracene adduct (+)-(11*S*)-**102** (1.6473 g, 5.11 mmol) in dry CH_2Cl_2 (15 mL) at room temperature and stirred for 1 h. Then, the excess oxalyl chloride and CH_2Cl_2 were evaporated to dryness by a rotary evaporator to give acid chloride–anthracene adduct (11*S*)-**113**. CH_2Cl_2 (15 mL) was added to the adduct (11*S*)-**113** under nitrogen gas at room temperature. The solution mixture was cooled down to 0 °C by an ice bath, then pyrrolidine (2.0 equiv, 0.84 mL, 10.22 mmol) and Et_3N (1.3 equiv, 0.93 mL, 6.64 mmol) were added. The reaction mixture was stirred at room temperature for overnight. After that, the resulting solution was washed with H_2O (3 times) and the combined organic portions were dried ($MgSO_4$), filtered and concentrated in vacuo. Purification of residue by flash column chromatography (acetone/EtOAc/hexane = 1:2:7 as eluent) gave the (+)-(11*S*)-11-carbomethoxy-11-pyrrolidinylacetyl-9,10-dihydro-9,10-ethanoanthracene, pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** in 93% yield (1.7907 g), 100% conversion from the starting material.



(+)-(11*S*)-**103**

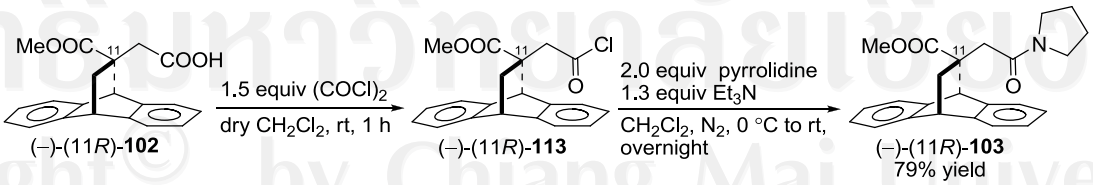
Table 17 Data of the pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103**

Physical properties	
White solid Melting point (m.p.) 162.3–163.5 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{29.6}$ = +54.47° (*c* = 0.235, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3064, 3019	C–H stretching of aromatic
2951, 2869	$–CH_2$, $–CH_3$ stretching
1742	C=O stretching of ester
1711	C=O stretching of amide
1636	C=C stretching of aromatic
1431, 1340	$–CH_2$, $–CH_3$ bending
1192	C–N stretching of amide
1066	C–O stretching of ester
768	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.44, 2.88, 4.30	*ABX* system, (*J* = 13.2, 3.1, 2.4 Hz), 3H, H_a, H_b, H_x
1.68–1.86	*m*, 4H, H-2′, H-3′
1.90	*d*, (*J* = 16.3), 1H, H_c or H_d
2.29	*d*, (*J* = 16.3), 1H, H_c or H_d
2.99	*dt*, (*J* = 10.2, 6.7 Hz), 1H, H-1′
3.18	*dt*, (*J* = 10.2, 6.7 Hz), 1H, H-1′
3.41–3.26	*m*, 2H, H-4′

Table 17 Data of the pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (continued)

Chemical shift (δ, ppm)	Type of protons
3.39	*s*, 1H, $COOCH_3$-16
4.32	*s*, 1H, H_y
7.00–7.33	*m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
24.27 (CH_2-2′), 25.93 (CH_2-3′), 37.35 (CH_2-12), 44.32 (CH-9), 45.39 (CH_2-13), 45.41 (CH_2-1′), 46.27 (CH_2-4′), 50.17 (C_q-11), 51.95 (CH_3-16), 53.35 (CH-10), 123.30, 123.47, 124.17, 125.37, 125.51, 125.58, 126.29, 126.40 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 140.31, 140.42, 142.99, 143.97 (C_q-4a, 8a, 9a, 10a), 168.69 (C_q-14), 175.95 (C_q-15)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{24}H_{25}NO_3$	375.1834 (M^+)
Lock mass of $C_{21}H_{27}NO_4Na$	380.1826 $(M+Na)^+$
Calc. for $C_{24}H_{26}NO_3$	376.1913 $(M+H)^+$
Found for $C_{24}H_{26}NO_3$	376.1912 $(M+H)^+$

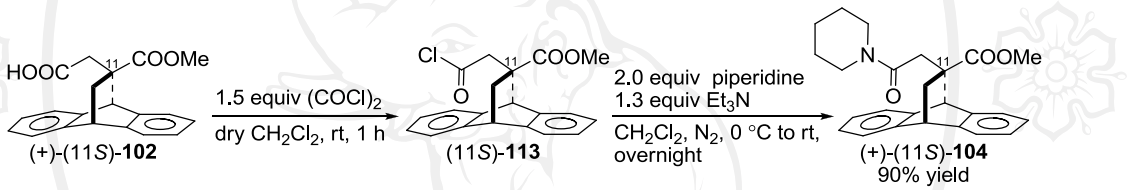
2.3.2 Synthesis of (–)-(11*R*)-11-carbomethoxy-11-pyrrolidinylacetyl-9,10-dihydro-9,10-ethanoanthracene ((–)-(11*R*)-103)



Pyrrolidinyl amide–anthracene adduct (–)-(11*R*)-**103** was prepared according to typical procedure 2.3.1, adduct (–)-(11*R*)-**102** (1.0012 g, 3.11 mmol), oxalyl chloride (1.5 equiv, 0.39 mL, 4.66 mmol), pyrrolidine (2.0 equiv, 0.51 mL, 6.21

mmol) and Et_3N (1.3 equiv, 0.56 mL, 4.04 mmol). Purification of the crude product by flash column chromatography (acetone/EtOAc/hexane = 1:2:7 as eluent) gave the (−)-(11*S*)-11-carbomethoxy-11-pyrrolidinylacetyl-9,10-dihydro-9,10-ethanoanthracene, pyrrolidinyl amide–anthracene adduct (−)-(11*R*)-**103** in 79% yield (1.1660 g), 100% conversion from the starting material as white solid, m.p. 167.6–169.6 °C, ($[\alpha]_{589}^{28.6}$ = –57.03° (*c* = 0.263, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 17).

2.3.3 Synthesis of (+)-(11*S*)-11-carbomethoxy-11-piperidinylacetyl-9,10-dihydro-9,10-ethanoanthracene ((+)-(11*S*)-104)



Pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**104** was prepared according to typical procedure 2.3.1, adduct (+)-(11*S*)-**102** (1.9878 g, 6.17 mmol), oxalyl chloride (1.5 equiv, 0.78 mL, 9.25 mmol), piperidine (2.0 equiv, 1.22 mL, 12.33 mmol) and Et_3N (1.3 equiv, 1.12 mL, 8.02 mmol). Purification of the crude product by flash column chromatography (EtOAc/hexane = 4:6 as eluent) gave the (+)-(11*S*)-11-carbomethoxy-11-pyrrolidinylacetyl-9,10-dihydro-9,10-ethanoanthracene, piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** in 90% yield (2.1539 g), 100% conversion from the starting material.

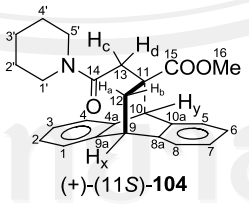


Table 18 Data of the piperidinyl amide–anthracene adduct (+)-(11*S*)-**104**

Physical properties
White solid Melting point (m.p.) 188.8–190.5 °C (from CH_2Cl_2/hexane)

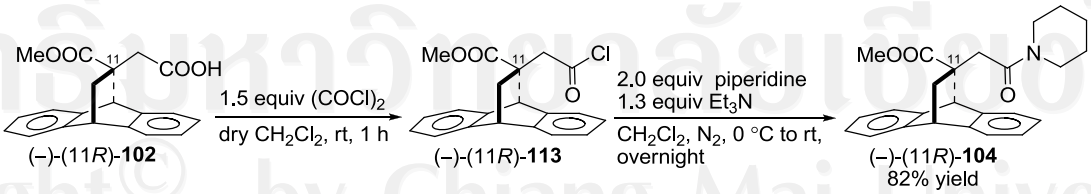
Table 18 Data of the piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (continued)

Physical properties	
$[\alpha]_{589}^{29.1}$ = +55.56° (*c* = 0.279, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3026, 3002	C–H stretching of aromatic
2948, 2855	$–CH_2$, $–CH_3$ stretching
1742	C=O stretching of ester
1721	C=O stretching of amide
1643	C=C stretching of aromatic
1431, 1340	$–CH_2$, $–CH_3$ bending
1257	C–N stretching of amide
1188	C–O stretching of ester
748	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.41, 2.87, 4.29	*ABX* system, (*J* = 13.3, 3.0, 2.5 Hz), 3H, H_a, H_b, H_x
1.32–1.70	*m*, 6H, H-2′, H-3′, H-4′
1.94	*d*, (*J* = 16.2), 1H, H_c or H_d
2.98	*d*, (*J* = 16.2), 1H, H_c or H_d
3.01–3.07	*m*, 1H, H-1′
3.08–3.21	*m*, 1H, H-1′
3.23–3.36	*m*, 1H, H-5′
3.38	*s*, 1H, $COOCH_3$-16

Table 18 Data of the piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (continued)

Chemical shift (δ, ppm)	Type of protons
3.45–3.58	*m*, 1H, H-5′
4.29	*s*, 1H, H_y
6.96–7.36	*m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
24.39, 25.46, 26.19 (CH_2-2′, 3′, 4′), 37.47 (CH_2-12), 42.56 (CH_2-5′), 44.11 (CH_2-13), 44.38 (CH-9), 46.39 (CH_2-1′), 50.41 (C_q-11), 51.94 (CH_3-16), 53.53 (CH-10), 123.36, 123.51, 124.15, 125.35, 125.58, 125.61, 126.62, 126.44 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 140.38, 140.47, 143.04, 144.03 (C_q-4a, 8a, 9a, 10a), 168.52 (C_q-14), 175.98 (C_q-15)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{25}H_{27}NO_3$	389.1991 (M^+)
Lock mass of $C_{21}H_{27}NO_4Na$	380.1826 $(M+Na)^+$
Calc. for $C_{25}H_{28}NO_3$	390.2096 $(M+H)^+$
Found for $C_{25}H_{28}NO_3$	390.2065 $(M+H)^+$

2.3.4 Synthesis of (–)-(11*R*)-11-carbomethoxy-11-piperidinylacetyl-9,10-dihydro-9,10-ethanoanthracene (–)-(11*R*)-104

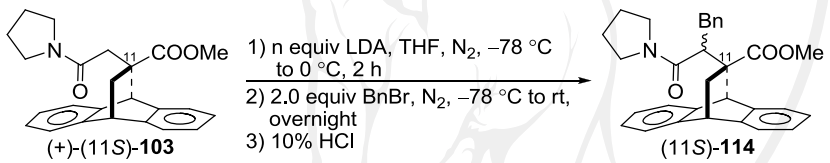


Pyrrolidinyl amide–anthracene adduct (–)-(11*R*)-**104** was prepared according to typical procedure 2.3.1, adduct (–)-(11*R*)-**102** (0.9016 g, 2.80 mmol), Oxalyl chloride (1.5 equiv, 0.36 mL, 4.20 mmol), piperidine (2.0 equiv, 0.55 mL, 5.59 mmol)

and Et_3N (1.3 equiv, 0.51 mL, 3.64 mmol). Purification of the crude product by flash column chromatography (EtOAc/hexane = 4:6 as eluent) gave the (–)-(11*R*)-11-carbomethoxy-11-pyrrolidinylacetyl-9,10-dihydro-9,10-ethanoanthracene, piperidinyl amide–anthracene adduct (–)-(11*R*)-**104** in 82% yield (0.8968 g), 100% conversion from the starting material as white solid, m.p. 197.7–199.8 °C, ($[\alpha]_{589}^{28.7}$ = –55.56° (*c* = 0.225, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 18).

2.4 Synthesis of both enantiomerically pure pyrrolidinyl amide–anthracene adduct derivatives [(11*S*)-114, (11*R*)-114, (11*S*)-115 and (11*R*)-115]

2.4.1 Synthesis of (11*S*)-11-[2′-benzyl-1′-pyrrolidinylacetyl]-11-carbo methoxy-9,10-dihydro-9,10-ethanoanthracene ((11*S*)-144)



2.4.1.1 By using 1.2 equivalence of lithium diisopropylamide (LDA)

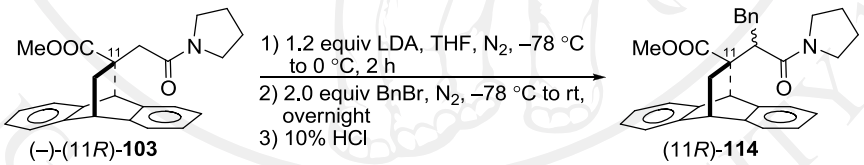
To a 100 mL round-buttomed flask equipped with a magnetic bar, fitted with a three-way stopcock and a nitrogen inlet. *n*-Butyllithium (1.87 mL, 2.28 mmol, 1.2 M in hexane) was added to a stirring solution of diisopropylamine (0.39 mL, 2.70 mmol) in THF (3 mL) at –78 °C and the reaction mixture was stirred at 0 °C for 1 hour. To the LDA solution at –78 °C, a solution of optically pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (0.7124 g, 1.90 mmol) in THF (5 mL) was added at –78 °C and left stirring at 0 °C for 2 hours. Benzyl bromide (2.0 equiv, 0.45 mL, 3.80 mmol) was added to the reaction mixture at –78 °C then stirred for additional 15 mins and continued stirring at 0 °C to room temperature for overnight. The reaction mixture was quenched with 10% HCl. After that, the resulting solution was extracted with CH_2Cl_2 (3 times). The combined organic portions were dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of residue by flash column chromatography (EtOAc/acetone/hexane = 1:1:8 as eluent) gave two diastereomeric benzylpyrrolidinyl amide–anthracene adducts (11*S*)-**114**, (11*S*)-11-[2′-benzyl-1′-

pyrrolidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene which cannot be isolated by flash column chromatography in 93% yield (0.3996 g), 53% conversion from the starting material.

2.4.1.2 By using 2.5 equivalence of lithium diisopropylamide (LDA)

Prepared according to typical procedure 2.4.1.1, optically pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (0.7124 g, 1.90 mmol), LDA (4.01 mL, 4.90 mmol, 1.2 M in hexane, 2.5 equiv, 0.82 mL, 5.88 mmol) in THF (6 mL) and benzyl bromide (2.0 equiv, 0.47 mL, 3.92 mmol). Purification of the crude product by flash column chromatography (EtOAc/Acetone/hexane = 1:1:8 as eluent) gave two diastereomeric benzylpyrrolidinyl amide–anthracene adducts (11*S*)-**114**, (11*S*)-11-[2′-benzyl-1′-pyrrolidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene which cannot be isolated by flash column chromatography in 57% yield (0.3996 g), 93% conversion from the starting material.

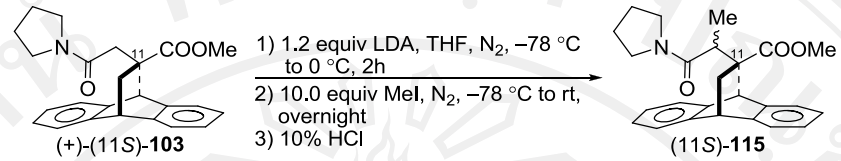
2.4.2 Synthesis of (11*R*)-11-[2′-benzyl-1′-pyrrolidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene ((11*R*)-114)



(–)-(11*R*)-**103** (11*R*)-**114**

Prepared according to typical procedure 2.4.1.1, optically pyrrolidinyl amide–anthracene adduct (**–**)-(11*R*)-**103** (0.9986 g, 2.74 mmol), LDA (2.69 mL, 2.29 mmol, 1.2 M in hexane, 1.2 equiv, 0.55 mL, 3.95 mmol) in THF (4 mL) and benzyl bromide (2.0 equiv, 0.65 mL, 5.48 mmol). Purification of the crude product by flash column chromatography (EtOAc/Acetone/hexane = 1:1:8 as eluent) gave two diastereomeric benzylpyrrolidinyl amide–anthracene adducts (11*R*)-**114**, (11*R*)-11-[2′-benzyl-1′-pyrrolidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene which cannot be isolated by flash column chromatography in 58% yield (0.7371 g), 91% conversion from the starting material as white solid.

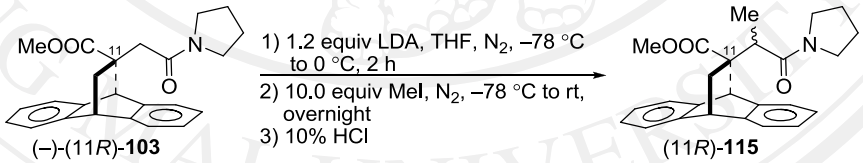
2.4.3 Synthesis of (11*S*)-11-[2′-methyl-1′-pyrrolidinylacetyl]-11-carbo methoxy-9,10-dihydro-9,10-ethanoanthracene ((11*S*)-115)



(+)-(11*S*)-**103** (11*S*)-**115**

Prepared according to typical procedure in 2.4.1.1, optically pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (0.7269 g, 1.94 mmol), LDA (1.91 mL, 2.32 mmol, 1.2 M in hexane, 1.2 equiv, 0.39 mL, 2.79 mmol) in THF (3.5 mL) and methyl iodide (10.0 equiv, 1.21 mL, 19.36 mmol). Purification of the crude product by flash column chromatography (EtOAc/Acetone/hexane = 1:1:8 as eluent) gave two diastereomeric methylpyrrolidinyl amide–anthracene adducts (11*S*)-**115**, (11*S*)-11-[2′-methyl-1′-pyrrolidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene in 86% yield (0.6379 g) from NMR technique, 100% conversion from the starting material. The starting material and the products cannot be isolated.

2.4.4 Synthesis of (11*R*)-11-[2′-methyl-1′-pyrrolidinylacetyl]-11-carbo methoxy-9,10-dihydro-9,10-ethanoanthracene ((11*R*)-115)

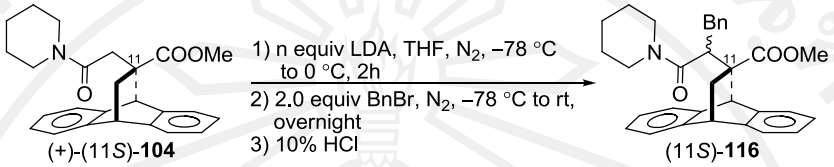


(–)-(11*R*)-**103** (11*R*)-**115**

Prepared according to typical procedure in 2.4.1.1, optically pyrrolidinyl amide–anthracene adduct (–)-(11*R*)-**103** (1.0026 g, 2.67 mmol), LDA (2.63 mL, 3.20 mmol, 1.2 M in hexane, 1.2 equiv, 0.54 mL, 3.85 mmol) in THF (4 mL) and methyl iodide (10.0 equiv, 1.67 mL, 26.70 mmol). Purification of the crude product by flash column chromatography (EtOAc/Acetone/hexane = 1:1:8 as eluent) gave two diastereomeric methylpyrrolidinyl amide–anthracene adducts (11*R*)-**115**, (11*R*)-11-[2′-methyl-1′-pyrrolidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene in 54% yield (0.5657 g) from NMR technique, 60% conversion from the starting material as white solid. The starting material and the products cannot be isolated.

2.5 Synthesis of both enantiomerically pure piperidinyl amide–anthracene adduct derivative (11*S*)-116, (11*R*)-116, (11*S*)-117 and (11*R*)-117

2.5.1 Synthesis of (11*S*)-11-[2′-benzyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene ((11*S*)-116)



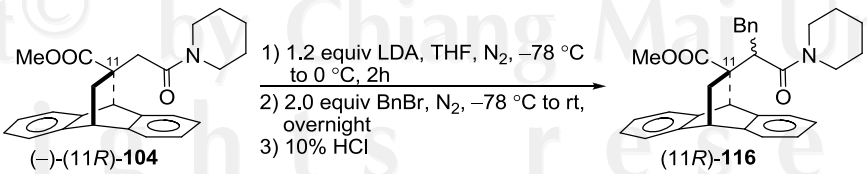
2.5.1.1 By using 1.2 equivalence of lithium diisopropylamide (LDA)

Prepared according to typical procedure in 2.4.1.1, optically piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (0.7113 g, 1.83 mmol), LDA (1.80 mL, 2.19 mmol, 1.2 M in hexane, 1.2 equiv, 0.37 mL, 2.63 mmol) in THF (3 mL) and benzyl bromide (2.0 equiv, 0.43 mL, 3.65 mmol). Purification of the crude product by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave two diastereomeric benzylpiperidinyl amide–anthracene adducts (11*S*)-**116**, (11*S*)-11-[2′-benzyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene which cannot be isolated by flash column chromatography in 98% yield (0.6687 g), 79% conversion from the starting material.

2.5.1.2 By using 2.5 equivalence of lithium diisopropylamide (LDA)

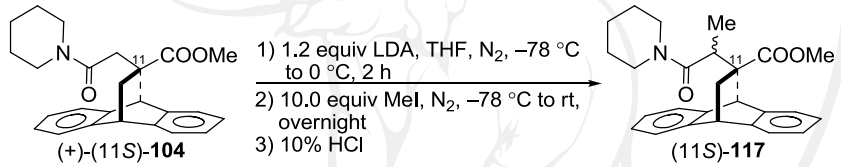
Prepared according to typical procedure in 2.4.1.1, optically piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (0.8387 g, 2.15 mmol), LDA (4.40 mL, 5.38 mmol, 1.2 M in hexane, 2.5 equiv, 0.90 mL, 6.46 mmol) in THF (6.5 mL) and benzyl bromide (2.0 equiv, 0.51 mL, 4.31 mmol). This reaction gave the complex mixture which cannot be purified.

2.5.2 Synthesis of (11*R*)-11-[2′-benzyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene ((11*R*)-116)



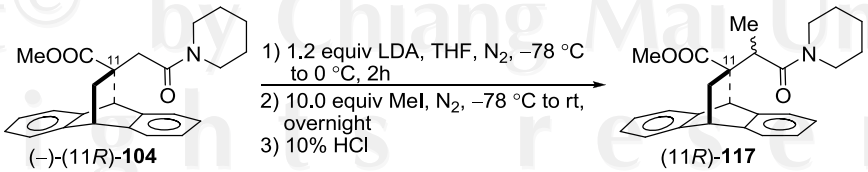
Prepared according to typical procedure in 2.4.1.1, optically piperidinyl amide–anthracene adduct (**–**)-(11*R*)-**104** (0.9946 g, 2.55 mmol), LDA (2.53 mL, 3.10 mmol, 1.2 M in hexane, 1.2 equiv, 0.52 mL, 3.71 mmol) in THF (4 mL) and benzyl bromide (2.0 equiv, 0.61 mL, 5.16 mmol). Purification of the crude product by flash column chromatography (EtOAc/Acetone/hexane = 1.5:8.5 as eluent) gave two diastereomeric benzylpiperidinyl amide–anthracene adducts (11*R*)-**116**, (11*R*)-11-[2′-benzyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene which cannot be isolated by flash column chromatography in 61% yield (0.7246 g), 89% conversion from the starting material as white solid.

2.5.3 Synthesis of (11*S*)-11-[2′-benzyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene ((11*S*)-117)



Prepared according to typical procedure in 2.4.1.1, optically piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (0.9940 g, 2.55 mmol), LDA (2.51 mL, 3.06 mmol, 1.2 M in hexane, 1.2 equiv, 0.51 mL, 3.67 mmol) in THF (4 mL) and methyl iodide (10.0 equiv, 1.59 mL, 25.52 mmol). Purification of the crude product by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave two diastereomeric methylpiperidinyl amide–anthracene adducts (11*S*)-**117**, (11*S*)-11-[2′-methyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10- in 65% yield (0.6745 g) from NMR technique, 72% conversion from the starting material. The starting material and the products cannot be isolated.

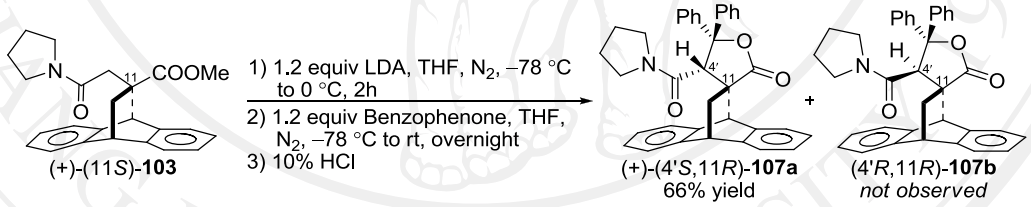
2.5.4 Synthesis of (–)-(11*R*)-11-[2′-methyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene ((11*R*)-117)



Prepared according to typical procedure in 2.4.1.1, optically piperidinyl amide–anthracene adduct (**–**)-(11*R*)-**104** (0.9997 g, 2.57 mmol), LDA (2.52 mL, 3.08 mmol, 1.2 M in hexane, 1.2 equiv, 0.52 mL, 3.70 mmol) in THF (4 mL) and methyl iodide (10.0 equiv, 1.60 mL, 25.67 mmol). Purification of the crude product by flash column chromatography (EtOAc/Acetone/hexane = 1:1:8 as eluent) gave two diastereomeric methylpiperidinyl amide–anthracene adducts (11*R*)-**117**, (11*R*)-11-[2′-methyl-1′-piperidinylacetyl]-11-carbomethoxy-9,10-dihydro-9,10-ethanoanthracene in 59% yield (0.6314 g) from NMR technique, 87% conversion from the starting material as white solid. The starting material and the products cannot be isolated.

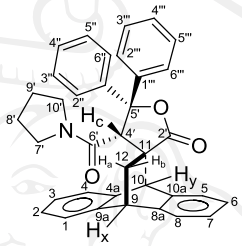
2.6 Synthesis of diastereomerically pure spiro–lactone anthracene adducts (4′*S*,11*R*)-107a, (4′*R*,11*R*)-107b, (4′*S*,11*R*)-108a and (4′*R*,11*R*)-108b]

2.6.1 Synthesis of diastereomeric tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene ((+)-(4′*S*,11*R*)-107a and (4′*R*,11*R*)-107b)



To a 100 mL round-buttomed flask equipped with a magnetic stirrer bar, fitted with a three-way stopcock and nitrogen inlet. *n*-Butyllithium (2.47 mL, 3.25 mmol, 1.3 M in hexane) was added to a stirring solution of diisopropylamine (0.55 mL, 3.90 mmol) in THF (3 mL) at –78 °C and the reaction mixture was stirred at 0 °C for 1 hour. To the LDA solution at –78 °C, a solution of optically pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (1.0157 g, 2.71 mmol) in THF (5 mL) was added at –78 °C and left stirring at 0 °C for 2 hours. The solution of benzophenone (1.2 equiv, 0.5915 g, 3.25 mmol) in THF (5 mL) was added to the reaction mixture at –78 °C then stirred for additional 15 minutes and continued stirring at 0 °C to room temperature for overnight. The reaction mixture was quenched with 10% HCl. After that, the resulting solution was extracted with CH_2Cl_2 (3 times). The combined

organic portions were dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of residue by flash column chromatography (CH_2Cl_2/EtOAc/hexane = 1:2:7 as eluent) gave spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a**, (+)-(4′*S*,11*R*)-tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethano anthracene in 66% yield (0.4683 g), 50% conversion from the starting material. On the other hand, adduct (4′*R*,11*R*)-**107b** was be not observed in this reaction.



(+)-(4′*S*,11*R*)-**107a**

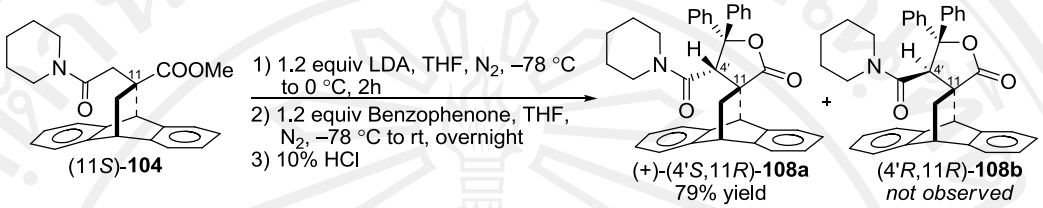
Table 19 Data of the spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a**

Physical properties	
White solid Melting point (m.p.) 288.5–288.9 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{28.9}$ = +87.44° (*c* = 0.215, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3064, 3019	C–H stretching of aromatic
2924, 2852	$-CH_2$ stretching
1779	C=O stretching of ester
1728	C=O stretching of amide
1633	C=C stretching of aromatic
1438	$-CH_2$ bending
1158	C–N stretching of amide
1001	C–O stretching of ester
703	C–H bending of aromatic (out of plane)

Table 19 Data of the spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (continued)

NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.49–1.35	*m*, 1H, H-9′
1.52, 1.56, 4.13	*ABX* system, (*J* = 13.6, 2.3, 2.0 Hz), 3H, H_a, H_b, H_x
1.63–1.77	*m*, 3H, H-8′, H-9′
2.23–2.34	*m*, 1H, H-7′
2.63–2.74	*m*, 1H, H-10′
2.97–3.13	*m*, 1H, H-7′
3.21–3.37	*m*, 1H, H-10′
3.26	*s*, 1H, H_c
5.11	*s*, 1H, H_y
6.95–7.49	*m*, 18H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
24.70 (CH_2-9′), 25.83 (CH_2-8′), 42.68 (CH_2-12), 44.09 (CH-9), 45.46 (CH_2-10′), 46.58 (CH_2-7′), 47.93 (CH-10), 50.89 (C_q-11), 61.92 (CH-4′), 86.74 (C_q-5′), 121.99, 123.84, 124.51, 125.22, 125.59, 125.79, 125.83, 125.93, 126.34, 127.44, 127.82, 127.98, 128.71 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2″, 3″, 4″, 5″, 6″, 2‴, 3‴, 4‴, 5‴, 6‴), 139.78, 140.19, 141.39, 143.43, 143.48 (C_q-4a, 8a, 9a ,10a, 1″, 1‴), 166.85 (CH-6′), 176.88 (CH-2′)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{36}H_{31}NO_3$	525.2304 (M^+)
Lock mass of $C_{28}H_{37}N_5O_7Na$	578.2591 $(M+Na)^+$
Calc. for $C_{36}H_{31}NO_3Na$	548.2202 $(M+Na)^+$
Found for $C_{36}H_{31}NO_3Na$	548.2202 $(M+Na)^+$

2.6.2 Synthesis of diastereomeric tetrahydro-4′-carbopiperidinyl-5′,5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene ((+)-(4′*S*,11*R*)-108a and (4′*R*,11*R*)-108b)



Prepared according to typical procedure in 2.6.1, piperidinyl amide–anthracene adduct (+)-(11*S*)-**10**4 (1.0015 g, 2.57 mmol), LDA (2.35 mL, 3.08 mmol, 1.3 M in hexane, 1.2 equiv, 0.52 mL, 3.70 mmol) in dry THF (5 mL) and benzophenone (1.2 equiv, 0.5623 g, 3.08 mmol). Purification of the crude product by flash column chromatography (CH_2Cl_2/EtOAc/hexane = 1:2:7 as eluent) gave spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**108a**, (+)-(4′*S*,11*R*)-tetrahydro-4′-carbopiperidinyl-5′,5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethano anthracene in 79% yield (0.6243 g), 57% conversion from the starting material. On the other hand, adduct (4′*R*,11*R*)-**108b** was be not observed in this reaction.

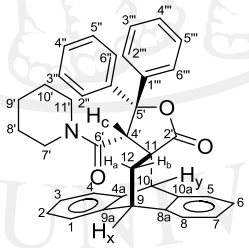

(+)-(4'S,11R)-**108a**

Table 20 Data of the spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**108a**

Physical properties
White solid Melting point (m.p.) 274.1–274.8 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{29.0}$ = +98.43° (*c* = 0.254, $CHCl_3$)

Table 20 Data of the spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**108a** (continued)

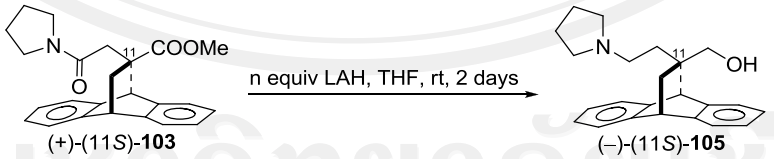
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3070, 3023	C–H stretching of aromatic
2930, 2848	$–CH_2$ stretching
1790	C=O stretching of ester and amide
1629	C=C stretching of aromatic
1448	$–CH_2$ bending
1226	C–N stretching of amide
1144	C–O stretching of ester
703	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
0.81–0.96	*m*, 1H, H-8′ or H-9′ or H-10′
1.17–1.31	*m*, 1H, H-8′ or H-9′ or H-10′
1.32–1.46	*m*, 4H, H-8′ or H-9′ or H-10′
1.50, 1.55, 4.09	*ABX* system, (J = 13.1, 3.1, 2.4 Hz), 3H, H_a, H_b, H_x
2.63–2.75	*m*, 1H, H-7′
2.78–2.90	*m*, 1H, H-7′
3.01–3.12	*m*, 1H, H-11′
3.16–3.29	*m*, 1H, H-11′
3.56	*s*, 1H, H_c
5.04	*s*, 1H, H_y
6.38–7.81	*m*, 18H, ArH

Table 20 Data of the spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**108a** (continued)

^{13}C-NMR (100 MHz) in $CDCl_3$	
23.95, 24.67, 24.99 (CH_2-8′, 9′, 10′), 41.94 (C_q-11), 42.68 (CH_2-12), 44.12 (CH-9), 46.79 (CH_2-7′), 48.09 (CH-10), 51.64 (C_q-11), 58.95 (CH-4′), 86.68 (C_q-5′), 122.07, 123.77, 124.79, 125.53, 125.68, 125.71, 125.89, 126.31, 126.70, 127.47, 127.51, 127.82, 128.04, 128.72 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2″, 3″, 4″, 5″, 6″, 2‴, 3‴, 4‴, 5‴, 6‴), 139.96, 140.10, 141.25, 142.36, 143.39, 143.61 (C_q-4a, 8a, 9a ,10a, 1″, 1‴), 167.02 (CH-6′), 176.93 (CH-2′)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{37}H_{33}NO_3$	539.2460 (M^+)
Lock mass of $C_{28}H_{37}N_5O_7Na$	578.2591 $(M+Na)^+$
Calc. for $C_{37}H_{33}NO_3Na$	562.2358 $(M+Na)^+$
Found for $C_{37}H_{33}NO_3Na$	562.2348 $(M+Na)^+$

2.7 Reduction reaction of both enantiomerically pure (pyrrolidinyl or piperidinyl) amide–anthracene adducts

2.7.1 Synthesis of (–)-(11*S*)-11-hydroxymethylene-11-(2″-pyrrolidinylethyl) -9,10-dihydro-9,10-ethanoanthracene ((–)-(11*S*)-105)

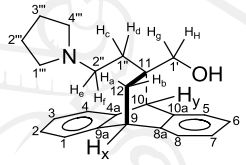


(+)-(11*S*)-**103** (–)-(11*S*)-**105**

2.7.1.1 By using 5 equivalence of lithium aluminium hydride (LAH)

To a 100 mL round-bottomed flask equipped with a magnetic bar and a septum cap and nitrogen inlet. The solution of pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (0.1083 g, 0.29 mmol) in THF (5 mL) was added to a cooled (–78 °C) solution of LAH (5.0 equiv, 0.0547 g, 1.44 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 2 days and then quenched by

dropwise addition of acetone (1 mL). After that, the resulting solution was extraction with CH_2Cl_2 (3 times). The combined organic portions were dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–anthracene adduct (–)-(11*S*)-**105**, (–)-(11*S*)-11-hydroxymethylene-11-(2′′-pyrrolidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 64% yield (0.0614 g), 100% conversion from the starting material.



(–)-(11*S*)-**105**

Table 21 Data of *N*,*O* TADDOLs–like anthracene adduct (–)-(11*S*)-**105**

Physical properties	
White solid Melting point (m.p.) 162.8–164.2 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{28.8}$ = –24.24° (*c* = 0.165, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3064, 3020	C–H stretching of aromatic
2936, 2812	–CH_2 stretching
1449	–CH_2 bending
1139	C–N stretching of amine
1062	C–O stretching of alcohol
756	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.09–1.40	*m*, 4H, H_a, H_b, H_c, H_d

Table 21 Data of *N,O* TADDOLs–like anthracene adduct (–)-(11*S*)-**105** (continued)

Chemical shift (δ, ppm)	Type of protons
1.68–1.86	*m*, 4H, H-2‴, H-3‴
2.25	*ddd*, (*J* = 12.8, 6.4, 2.9 Hz), 1H, H_e or H_f
2.48–2.66	*m*, 4H, H-1‴, H-4‴
2.74	*d*, (*J* = 11.7 Hz), 1H, H_g or H_h
2.84	*ddd*, (*J* = 12.8, 10.2, 2.6 Hz), 1H, H_e or H_f
3.11	*d*, (*J* = 11.7 Hz), 1H, H_g or H_h
4.19	*t*, (*J* = 2.4 Hz), 1H, H_x
4.38	*s*, 1H, H_y
5.88	*s*, 1H, -OH
6.93–7.45	*m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
23.33 (CH_2-2‴,3‴), 38.35 (CH_2-12), 39.46 (CH_2-1″), 44.57 (CH-9), 44.94 (C_q-11), 48.63 (CH-10), 51.25 (CH_2-2″), 53.54 (CH_2-1‴, 4‴), 68.93 (CH_2-1′), 122.87, 123.31, 124.90, 125.34, 125.50, 125.57, 125.64, 125.67 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 142.12, 142.30, 143.10, 144.70 (C_q-4a, 8a, 9a, 10a)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{23}H_{27}NO$	333.2093 (M^+)
Lock mass of $C_{21}H_{27}NO_4Na$	380.1826 $(M+Na)^+$
Calc. for $C_{23}H_{28}NO$	334.2171 $(M+H)^+$
Found for $C_{23}H_{28}NO$	334.2172 $(M+H)^+$

2.7.1.2 By using 10 equivalence of lithium aluminium hydride (LAH)

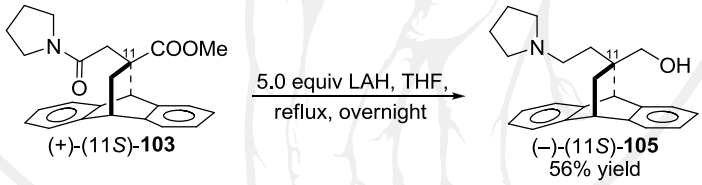
Prepared according to typical procedure in 2.7.1.1, optically pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (0.1001 g, 0.27 mmol), LAH (10.0 equiv, 0.1012 g, 2.67 mmol) in THF (5 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N,O*

TADDOLs–anthracene adduct (–)-(11*S*)-**105**, (–)-(11*S*)-11-hydroxymethylene-11-(2′′-pyrrolidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 50% yield (0.0440 g), 100% conversion from the starting material.

2.7.1.3 By using 15 equivalence of lithium aluminium hydride (LAH)

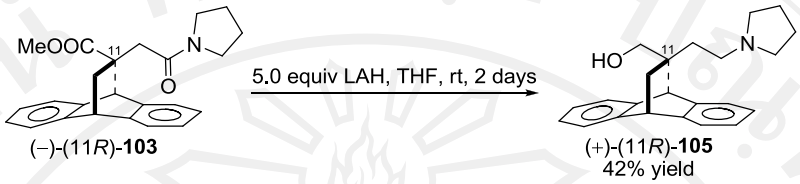
Prepared according to typical procedure in 2.7.1.1, optically pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (0.1065 g, 0.28 mmol), LAH (15.0 equiv, 0.1615 g, 4.25 mmol) in THF (5 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–anthracene adduct (–)-(11*S*)-**105**, (–)-(11*S*)-11-hydroxymethylene-11-(2′′-pyrrolidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 42% yield (0.0401 g), 100% conversion from the starting material.

2.7.1.4 By using 5 equivalence of lithium aluminium hydride (LAH) and refluxing overnight



To a 100 mL round-bottomed flask equipped with a magnetic stirrer and a septum cap and nitrogen inlet. The solution of pyrrolidinyl amide–anthracene adduct (+)-(11*S*)-**103** (0.2622 g, 0.70 mmol) in THF (10 mL) was added to a solution of LAH (5.0 equiv, 0.1325 g, 3.49 mmol) in THF (10 mL) and the mixture was heated to reflux for overnight. The crude reaction was quenched by dropwise addition of acetone (2 mL). After that, the resulting solution was extraction with CH_2Cl_2 (3 times). The combined organic portions were dried over $MgSO_4$, filtered and concentrated in vacuo. Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–like anthracene adduct (–)-(11*S*)-**105**, (–)-(11*S*)-11-hydroxymethylene-11-(2′′-pyrrolidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 56% yield (0.1285 g), 100% conversion from the starting material.

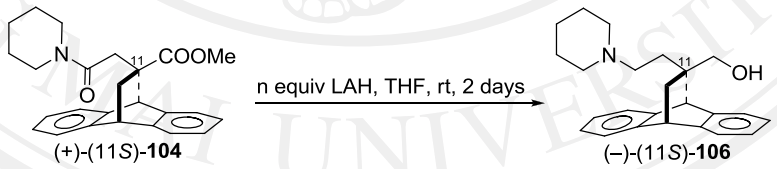
2.7.2 Synthesis of (+)-(11*R*)-11-hydroxymethylene-11-(2″-pyrrolidinyl ethyl)-9,10-dihydro-9,10-ethanoanthracene ((+)-(11*R*)-105)



(−)-(11*R*)-**103** (+)-(11*R*)-**105** 42% yield

Prepared according to typical procedure in 2.7.1.1, optically pyrrolidinyl amide–anthracene adduct (−)-(11*S*)-**103** (0.1892 g, 0.50 mmol), LAH (5.0 equiv, 0.1343 g, 3.54 mmol) in THF (5 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–anthracene adduct (+)-(11*S*)-**105**, (+)-(11*S*)-11-hydroxymethylene-11-(2″-pyrrolidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 42% yield (0.0700 g), 100% conversion from the starting material as white crystals, m.p. 167.6–169.6 °C, ($[\alpha]_{589}^{25.4}$ = +32.43° (*c* = 0.185, CH_2Cl_2)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 21).

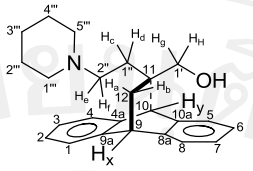
2.7.3 Synthesis of (−)-(11*S*)-11-hydroxymethylene-11-(2″-piperidinylethyl)-9,10-dihydro-9,10-ethanoanthracene ((−)-(11*S*)-106)



(+)-(11*S*)-**104** (−)-(11*S*)-**106**

2.7.3.1 By using 5 equivalence of lithium aluminium hydride (LAH)

Prepared according to typical procedure in 2.7.1.1, optically piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (0.1005 g, 0.26 mmol), LAH (5.0 equiv, 0.0489 g, 1.29 mmol) in THF (5 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–anthracene adduct (−)-(11*S*)-**106**, (−)-(11*S*)-11-hydroxymethylene-11-(2″-piperidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 54% yield (0.0485 g), 100% conversion from the starting material.



(–)-(11*S*)-**106**

Table 22 Data of *N*,*O* TADDOLs–like anthracene adduct (**–**)-(11*S*)-**106**

Physical properties	
White solid Melting point (m.p.) 162.8–164.6 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{25.4}$ = –13.99° (*c* = 0.225, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3064, 6024	C–H stretching of aromatic
2936, 2842	–CH_2 stretching
1463, 1362	–CH_2 bending
1126	C–N stretching of amide
1066	C–O stretching of ester
763	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.09–1.34	*m*, 6H, H_a, H_b, H_c, H_d, H-3‴
1.53–1.72	*m*, 4H, H-2‴, H-4‴
2.17	*ddd*, (*J* = 13.3, 6.8, 2.7 Hz), 1H, H_e or H_f
2.22–2.67	*m*, 4H, H-1‴, H-5‴
2.55	*ddd*, (*J* = 13.3, 9.5, 2.6 Hz), 1H, H_e or H_f
2.72	*d*, (*J* = 11.8 Hz), 1H, H_g or H_h
3.08	*d*, (*J* = 11.8 Hz), 1H, H_g or H_h
4.19	*t*, (*J* = 2.6 Hz), 1H, H_x

Table 22 Data of *N*,*O* TADDOLs–like anthracene adduct (**–**)-(11*S*)-**106** (continued)

Chemical shift (δ, ppm)	Type of protons
4.34 6.94–7.43	*s*, 1H, H_y *m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$	
25.44 (CH_2-2′′′,4′′′), 29.70 (CH_2-3′′′), 36.07 (CH_2-12), 39.48 (CH_2-1′′), 44.62 (CH-9), 45.08 (C_q-11), 49.14 (CH-10), 54.19 (CH_2-2′′), 54.39 (CH_2-1′′′, 5′′′), 68.39 (CH_2-1′), 122.87, 123.33, 124.98, 125.35, 125.59, 125.61, 125.65, 125.70 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 142.15, 142.37, 143.10, 143.72 (C_q-4a, 8a, 9a, 10a)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{24}H_{29}NO$ Lock mass of $C_{21}H_{27}NO_4Na$ Calc. for $C_{24}H_{39}NO$ Found for $C_{24}H_{30}NO$	347.2249 (M^+) 380.1826 $(M+Na)^+$ 348.2327 $(M+H)^+$ 348.2322 $(M+H)^+$

2.7.3.2 By using 10 equivalence of lithium aluminium hydride (LAH)

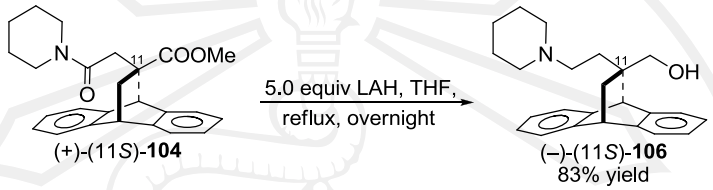
Prepared according to typical procedure in 2.7.1.1, optically piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (0.0983 g, 0.25 mmol), LAH (10.0 equiv, 0.0958 g, 2.52 mmol) in THF (5 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–anthracene adduct (**–**)-(11*S*)-**106**, (**–**)-(11*S*)-11-hydroxymethylene-11-(2′′-piperidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 67% yield (0.0586 g), 100% conversion from the starting material.

2.7.3.3 By using 15 equivalence of lithium aluminium hydride (LAH)

Prepared according to typical procedure in 2.7.1.1, optically piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (0.1016 g, 0.26 mmol), LAH (15.0 equiv, 0.1485 g, 3.91 mmol) in THF (5 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O*

TADDOLs–anthracene adduct (−)-(11*S*)-**106**, (−)-(11*S*)-11-hydroxymethylene-11-(2′′-piperidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 63% yield (0.0574 g), 100% conversion from the starting material.

2.7.3.4 By using 5 equivalence of lithium aluminium hydride (LAH) and refluxing overnight

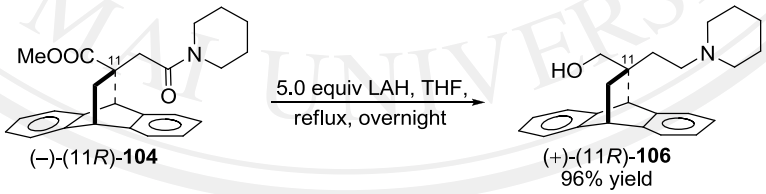


(+)-(11*S*)-**104**

(−)-(11*S*)-**106**
83% yield

Prepared according to typical procedure in 2.7.1.4, optically piperidinyl amide–anthracene adduct (+)-(11*S*)-**104** (0.2199 g, 0.56 mmol), LAH (5.0 equiv, 0.0955 g, 2.52 mmol) in THF (10 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–anthracene adduct (−)-(11*S*)-**106**, (−)-(11*S*)-11-hydroxymethylene-11-(2′′-piperidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 83% yield (0.1639 g), 100% conversion from the starting material.

2.7.4 Synthesis of (+)-(11*S*)-11-hydroxymethylene-11-(2′′-piperidinylethyl)-9,10-dihydro-9,10-ethanoanthracene [(+)-(11*S*)-106]



(−)-(11*R*)-**104**

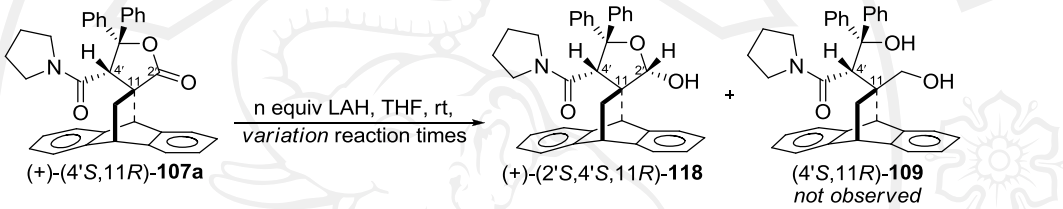
(+)-(11*R*)-**106**
96% yield

Prepared according to typical procedure in 2.7.1.4, optically piperidinyl amide–anthracene adduct (−)-(11*S*)-**104** (0.2014 g, 0.52 mmol), LAH (5.0 equiv, 0.0981 g, 2.59 mmol) in THF (10 mL). Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave *N*,*O* TADDOLs–anthracene adduct (+)-(11*S*)-**106**, (+)-(11*S*)-11-hydroxymethylene-11-(2′′-piperidinylethyl)-9,10-dihydro-9,10-ethanoanthracene in 96% yield (0.1724 g), 100% conversion from the starting material as white crystals, m.p. 197.7–199.8 °C, ($[\alpha]_{589}^{25.1}$

= +15.47° (*c* = 0.237, CH_2Cl_2)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 22).

2.8 Reduction reaction of diastereomerically pure spiro–lactone anthracene adducts (4′*S*,11*R*)-107a and (4′*S*,11*R*)-108a

2.8.1 Synthesis of compound (2′*S*,4′*S*,11*R*)-114a by variation of the stoichiometric amount of lithium aluminium hydride (LAH) as a nucleophile and reaction times



2.8.1.1 By using 7 equivalence of lithium aluminium hydride (LAH) and stirring 3 hours

Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (0.0956 g, 0.18 mmol), LAH (7.0 equiv, 0.0483 g, 1.27 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 3 hours. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2′*S*,4′*S*,11*R*)-**118**, tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene in 83% yield (0.0798 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**109** was be not observed in this reaction.

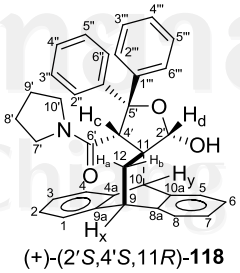


Table 23 Data of adduct (+)-(2′*S*,4′*S*,11*R*)-**118**

Physical properties	
White solid Melting point (m.p.) 274.3–275.4 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{25.8}$ = +123.47° (*c* = 0.162, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3022	C–H stretching of aromatic
2948, 2873	$–CH_2$ stretching
1614	C=O stretching of amide
1444, 1325	$–CH_2$ bending
1173	C–N stretching of amide
1026	C–O stretching of ester
761	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.32, 1.47, 4.11	*ABX* system, (*J* = 13.2, 2.9,2.6 Hz), 3H, H_a, H_b, H_x
1.55–1.73	*m*, 2H, H-9′
1.77–1.96	*m*, 2H, H-8′
2.41–2.54	*m*, 1H, H-10′
2.79–2.89	*m*, 1H, H-7′
3.28–3.44	*m*, 2H, H-7′ and H-10′
3.32	*s*, 1H, H_c
4.49	*d*, (*J* = 12.4 Hz), 1H, H_d
4.71	*s*, 1H, H_y
6.61–7.62	*m*, 18H, ArH
8.22	*d*, (*J* = 12.4 Hz), 1H, -OH

Table 23 Data of adduct (+)-(2′*S*,4′*S*,11*R*)-**118** (continued)

^{13}C-NMR (100 MHz) in $CDCl_3$	
24.22 (CH_2-9′), 26.09 (CH_2-8′), 44.34 (CH-9), 44.75 (CH_2-12), 46.45 (CH_2-10′), 47.05 (CH-10), 47.60 (CH_2-7′), 56.89 (C_q-11), 63.51 (CH-4′), 92.03 (C_q-5′), 106.36 (CH-2′), 122.45, 123.50, 123.88, 125.08, 125.49, 125.74, 125.88, 125.95, 126.25, 126.34, 126.64, 126.87, 127.39, 128.18 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2′′, 3′′, 4′′, 5′′, 6′′, 2′′′, 3′′′, 4′′′, 5′′′, 6′′′), 140.38, 141.40, 143.15, 144.48, 147.36 (C_q-4a, 8a, 9a, 10a, 1′′, 1′′′), 170.36 (CH-6′)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{36}H_{33}NO_3$	527.2406 (M^+)
Lock mass of $C_{28}H_{37}N_5O_7Na$	578.2591 $(M+Na)^+$
Calc. for $C_{36}H_{33}NO_3Na$	550.2358 $(M+Na)^+$
Found for $C_{36}H_{33}NO_3Na$	550.2358 $(M+Na)^+$

2.8.1.2 By using 7 equivalence of lithium aluminium hydride (LAH) and stirring 6 hours

Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (0.1046 g, 0.20 mmol), LAH (7.0 equiv, 0.05 g, 1.39 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 6 hours. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2′*S*,4′*S*,11*R*)-**118**, tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene in 90% yield (0.0945 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**109** was be not observed in this reaction.

2.8.1.3 By using 7 equivalence of lithium aluminium hydride (LAH) and stirring 24 h

Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (0.1065 g, 0.20 mmol), LAH (7.0 equiv, 0.0538 g, 1.42 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for overnight. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2′*S*,4′*S*,11*R*)-**118**, tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene in 71% yield (0.0762 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**109** was be not observed in this reaction.

2.8.1.4 By using 7 equivalence of lithium aluminium hydride (LAH) and stirring 3 days

Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (0.1104 g, 0.21 mmol), LAH (7.0 equiv, 0.0558 g, 0.15 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 3 days. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2′*S*,4′*S*,11*R*)-**118**, tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene in 64% yield (0.0709 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**109** was be not observed in this reaction.

2.8.1.5 By using 20 equivalence of lithium aluminium hydride (LAH) and stirring 24 h

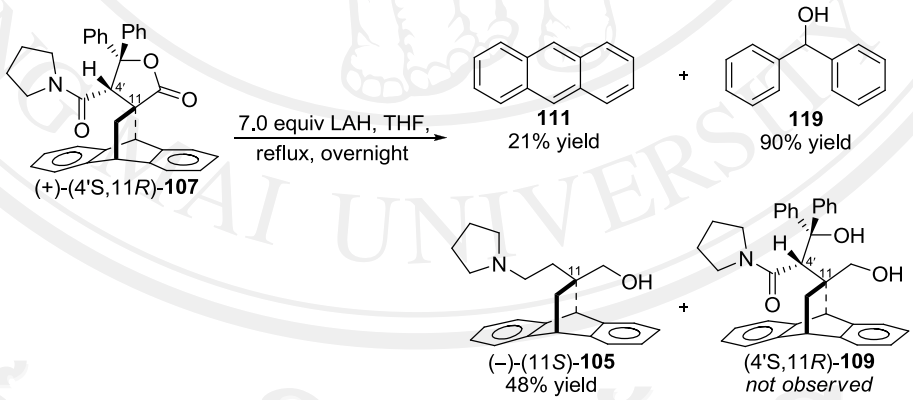
Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (0.1086 g, 0.21 mmol), LAH (20.0 equiv, 0.1568 g, 4.13 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for overnight. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2′*S*,4′*S*,11*R*)-**118**, tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-

9,10-dihydro-9,10-ethanoanthracene in 76% yield (0.0826 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**109** was be not observed in this reaction.

2.8.1.6 By using 20 equivalence of lithium aluminium hydride (LAH) and stirring 3 days

Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (0.0915 g, 0.17 mmol), LAH (20.0 equiv, 0.1321 g, 3.48 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 3 days. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2′*S*,4′*S*,11*R*)-**118**, tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene in 83% yield (0.0760 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**109** was be not observed in this reaction.

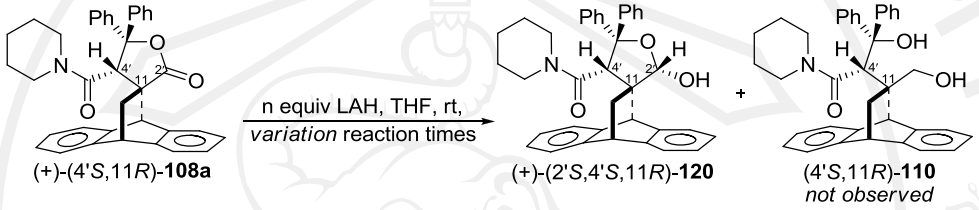
2.8.1.7 By using 7 equivalence of lithium aluminium hydride (LAH) and refluxing overnight



Prepared according to typical procedure in 2.7.1.4, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**107a** (0.1021 g, 0.19 mmol), LAH (7.0 equiv, 0.0515 g, 1.36 mmol) in THF (5 mL). The reaction mixture was heated to reflux for overnight. Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave anthracene (**111**) in 21% yield (0.0074 g), diphenylmethanol (**119**) in 90% yield (0.0326) and *N*,*O* TADDOLs–anthracene

adduct (–)-(11*R*)-**105** in 48% yield (0.0313 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**109** was be not observed in this reaction.

2.8.2 Synthesis of compound (2*S*′,4′*S*,11*R*)-114b by variation of the stoichiometric amount of lithium aluminium hydride (LAH) as a nucleophile and reaction times



2.8.2.1 By using 7 equivalence of lithium aluminium hydride (LAH) and stirring 3 days

Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**108a** (0.1024 g, 0.19 mmol), LAH (7.0 equiv, 0.05 g, 1.33 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 3 days. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2*S*′,4′*S*,11*R*)-**120**, tetrahydro-4′-carbopiperilidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene in 78% yield (0.0800 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**110** was be not observed in this reaction.

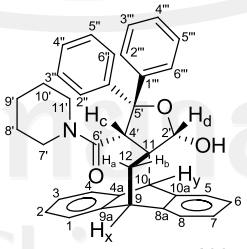

(+)-(2′*S*,4′*S*,11*R*)-**120**

Table 24 Data of adduct (+)-(2′*S*,4′*S*,11*R*)-**120**

Physical properties	
White solid Melting point (m.p.) 259.7–259.9 °C (from CH_2Cl_2/hexane) $[\alpha]_{589}^{25.7}$ = +148.05° (*c* = 0.154, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3022	C–H stretching of aromatic
2940, 2858	$–CH_2$ stretching
1606	C=O stretching of amide
1445, 1334	$–CH_2$ bending
1250	C–N stretching of amide
1070	C–O stretching of ester
760	C–H bending of aromatic (out of plane)
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.08–1.24	*m*, 1H, H-8′
1.31, 1.49, 4.10	*ABX* system, (*J* = 13.2, 2.8,2.6 Hz), 3H, H_a, H_b, H_x
1.43–1.66	*m*, 5H, H-8′, 9′, 10′
2.83–2.99	*m*, 1H, H-11′
3.11–3.21	*m*, 2H, H-7′, 11′
3.30–3.46	*m*, 1H, H-7′
3.59	*s*, 1H, H_c
4.46	*d*, (*J* = 12.4 Hz), 1H, H_d
4.67	*s*, 1H, H_y
6.96–7.50	*m*, 18H, ArH
8.33	*d*, (*J* = 12.4 Hz), 1H, -OH

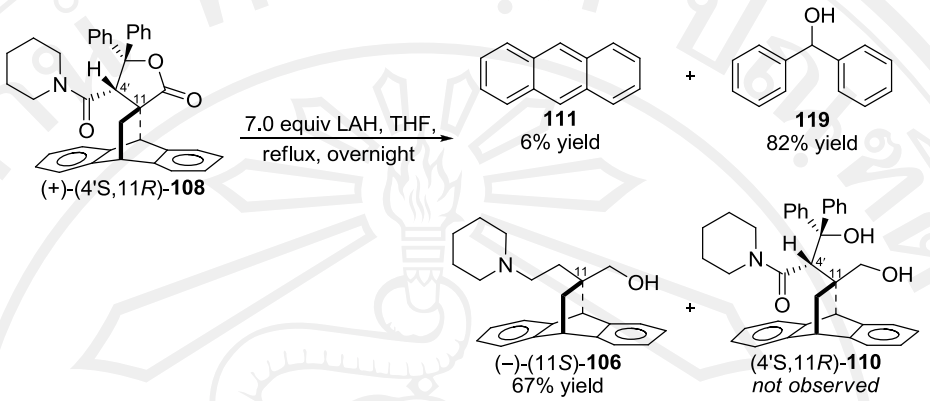
Table 24 Data of adduct (+)-(2′*S*,4′*S*,11*R*)-**120** (continued)

^{13}C-NMR (100 MHz) in $CDCl_3$	
23.97, 24.75, 25.39 (CH_2-8′, 9′, 10′), 42.98 (CH_2-7′), 44.40 (CH-9), 45.51 (CH_2-12), 47.09 (CH-10), 47.92 (CH_2-11′), 57.32 (C_q-11), 60.62 (CH-4′), 92.12 (C_q-5′), 106.57 (CH-2′), 122.49, 123.32, 124.43, 125.37, 125.56, 125.82, 125.90, 126.10, 125.45, 126.60, 126.71, 126.91, 127.27, 128.17 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2″, 3″, 4″, 5″, 6″, 2‴, 3‴, 4‴, 5‴, 6‴), 140.70, 141.22, 142.99, 143.83, 144.60, 147.61 (C_q-4a, 8a, 9a ,10a, 1″, 1‴), 170.12 (CH-6′)	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{37}H_{35}NO_3$	541.2617 (M^+)
Lock mass of $C_{28}H_{37}N_5O_7Na$	578.2591 $(M+Na)^+$
Calc. for $C_{37}H_{35}NO_3Na$	564.6685 $(M+Na)^+$
Found for $C_{37}H_{35}NO_3Na$	564.6685 $(M+Na)^+$

2.8.2.2 By using 20 equivalence of lithium aluminium hydride (LAH) and stirring 3 days

Prepared according to typical procedure in 2.7.1.1, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**108a** (0.1084 g, 0.20 mmol), LAH (20.0 equiv, 0.1527 g, 4.02 mmol) in THF (5 mL). The reaction mixture was stirred at room temperature for 3 days. Purification of residue by flash column chromatography (EtOAc/hexane = 1.5:8.5 as eluent) gave adduct (+)-(2′*S*,4′*S*,11*R*)-**120**, tetrahydro-4′-carbopyrrolidinyl-5′,5′-diphenyl-2′-hydroxy-2′-furan-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene in 55% yield (0.5927 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**110** was be not observed in this reaction.

2.8.2.3 By using 7 equivalence of lithium aluminium hydride (LAH) and refluxing overnight



Prepared according to typical procedure in 2.7.1.4, optically spiro–lactone anthracene adduct (+)-(4′*S*,11*R*)-**108a** (0.1032 g, 0.19 mmol), LAH (7.0 equiv, 0.0508 g, 1.34 mmol) in THF (5 mL). The reaction mixture was heated to reflux for overnight. Purification of residue by flash column chromatography (MeOH/EtOAc/hexane = 1:4:5 as eluent) gave anthracene (**111**) in 6% yield (0.0022 g), diphenylmethanol (**119**) in 82% yield (0.0288) and *N*,*O* TADDOLs–anthracene adduct (–)-(11*R*)-**106** in 67% yield (0.0445 g), 100% conversion from the starting material. On the other hand, adduct (4′*S*,11*R*)-**110** was be not observed in this reaction.