CHAPTER 2

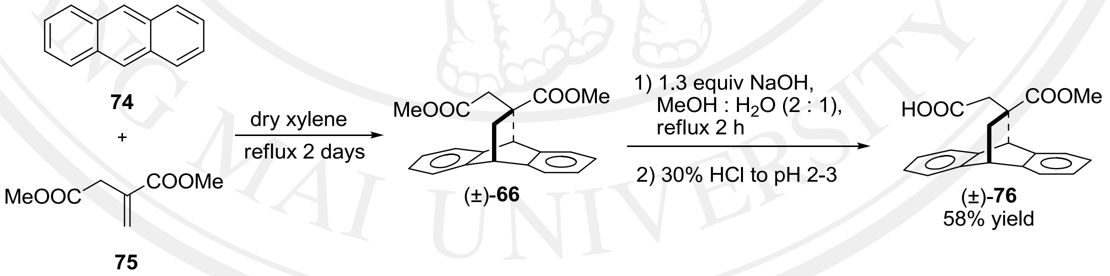
EXPERIMENTAL

General Methods

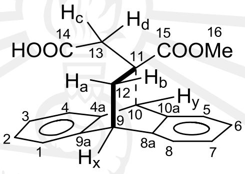
The ^1H and ^{13}C NMR spectra were recorded on Bruker DRX 400 MHz spectrometers and chemical shifts were given in ppm downfield from tetramethylsilane (TMS). All NMR spectra were measured in $CDCl_3$ and chemical shifts were reported as δ-values in parts per million (ppm) relative to residue $CHCl_3$ as internal reference (^1H: 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* (triplet), *q* (quartet), *qn* (quintet) and *m* (multiplet). Optical rotations were measured in $CHCl_3$ on an Atago AP-300 polarimeter. Melting points were determined by using a Gallenkamp Electrothermal apparatus and were uncorrected. 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-TOF-2^{Tm} (Waters) spectrometer. 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}. All experiments which are sensitive to moisture and air were carried out under nitrogen or argon. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Solvent 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. Hexamethylphospharamide (HMPA) was distillated under reduce pressure for later used. Ethyl bromide was dried over CaH_2 and distilled before used. The calculation of %yield of all products was based on the isolated products as pure compounds and ^1H NMR spectroscopy technique.

2.1 Resolution of enantiomeric dimethyl itaconate–anthracene adducts (+)-(11*S*)-66 and (–)-(11*R*)-66

2.1.1 Synthesis of (±)-11-carbomethoxy-11-carboxylmethyl-9,10-dihydro-9,10-ethanoanthracene [(±)-76]



A mixture of anthracene **74** (173.87 g, 0.9755 mol) and dimethyl itaconate **75** (102.89 g, 0.6504 mol) in dried xylene (800 mL) was heated under reflux for 3 days to obtain dimethyl itaconate–anthracene adduct in racemic form (±)-**66**. After that, compound (±)-**64** was hydrolyzed by 1.3 equiv NaOH in MeOH:H_2O (2:1) for 2 hours. The crude reaction mixture was adjusted to pH 2-3 by 30% hydrochloric acid solution, then extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and evaporated to dryness. The crude product was recrystallized from CH_2Cl_2/hexane to give (±)-monoacid adduct, *(±)-11-Carbomethoxy-11-carboxylmethyl-9,10-dihydro-9,10-ethanoanthracene* [(±)-**76**] in 58% yield (120.8154 g), and 100% conversion from the starting material.



(±)-**76**

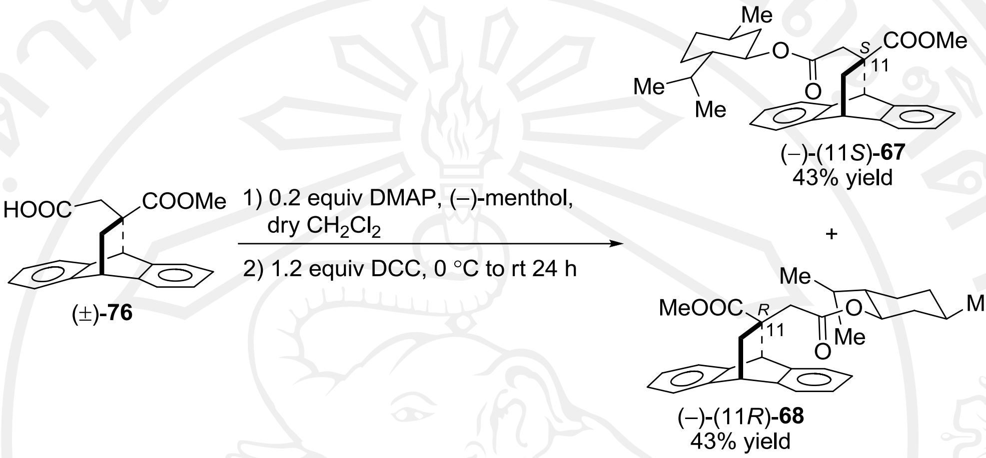
Table 16 Data of the monoacid adduct (±)-**76**

Physical properties	
white crystal 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 of ester
1645	C=C stretching of aromatic
1343, 1434	$-CH_2$, $-CH_3$ bending
1115, 1254	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
1.47, 2.79, 4.31	*ABX* system, (*J* = 13.1, 3.0, 2.4 Hz), 3H, H_a, H_b, H_x
1.97	*d* (*J* = 16.6 Hz), 1H, H_c

Table 16 Data of the monoacid adduct (±)-**76** (continued)

NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (*δ*, ppm)	Type of protons
2.96	*d* (*J* = 16.6 Hz), 1H, H_d
3.45	*s*, 3H, $COOCH_3$-16
4.30	*s*, 1H, H_y
7.04-7.30	*m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
36.74 (CH_2-12), 44.01 (CH-9), 44.66 (CH_2-13), 50.01 (C_q-11), 52.23 (CH_3-16), 52.8 1 (CH-10), 123.31, 123.55, 123.84, 124.19, 125.71, 125.74, 125.78, 126.51 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 139.45, 139.93, 142.76, 143.55 (C_q-ArH-4a, 8a, 9a, 10a), 174.70 (C_q-15), 176.85 (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 $C_{20}H_{18}O_4Na$	345.1103 $(M+Na)^+$

2.1.2 (–)-11-Carbomethoxy-11-[(–)-menthoxyacetyl]-9,10-dihydro-9,10-ethanoanthracenes [(–)-(11*S*)-67 and (–)-(11*R*)-68]

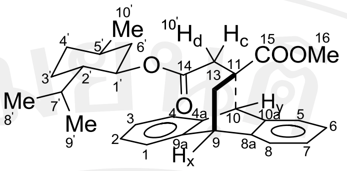


(±)-**76**

(–)-(11*S*)-**67**
43% yield

(–)-(11*R*)-**68**
43% yield

A mixture of the monoacid adduct (±)-**76** (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 24 h. The mixture was filtered and extracted with CH_2Cl_2. The solution was washed with H_2O and saturated NaCl solution, dried over $MgSO_4$, filtered and evaporated to dryness. The crude product was recrystallized to obtain monomenthyl adduct in two diastereoisomer forms which are (–)-(11*S*)-**67** in 43% yield (13.6705 g) from CH_2Cl_2/hexane and (–)-(11*R*)-**68** in 43% yield (13.6700 g) from CH_2Cl_2/MeOH.



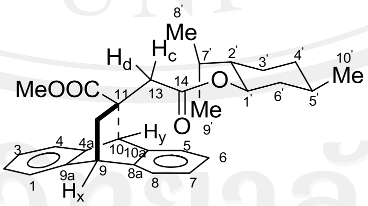
(–)-(11*S*)-**67**

Table 17 Data of monomenthyl adduct (–)-(11*S*)-**67**

Physical properties	
white powder melting point (m.p.) 185.3–186.8 °C (from CH_2Cl_2/hexane) specific rotation, $[\alpha]_D^{34.3}$ = –144.93° (*c* = 0.109, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3025	C–H stretching of aromatic
2866, 2950	$–CH_2$, $–CH_3$ stretching
1729	C=O stretching of ester
1638	C=C stretching of aromatic
1459, 1371	$–CH_2$, $–CH_3$ bending
1196, 1221	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
0.76-1.96	*m*, 9H, H-menthyl
0.89	*d* (*J* = 7.0 Hz), 3H, H-methyl
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
2.92	*d* (*J* = 16.2 Hz), 1H, H_d
3.47	*s*, 3H, $COOCH_3$-16
4.35	*s*, 1H, H_y

Table 17 Data of monomenthyl adduct (–)-(11*S*)-**67** (continued)

NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
2.92	*d* (J = 16.2 Hz), 1H, 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, CH-1'
7.03-7.31	m, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
16.05, 20.75, 21.93, 23.16, 25.97, 31.31, 34.11, 40.81 (C-menthyl), 36.99 (CH_2-12), 44.14 (CH-10), 44.97 (CH_2-13), 50.23 (C_q-11), 52.04 (CH_3-16), 52.97 (CH-9), 74.59 (CH-1'), 123.31, 123.53, 124.21, 125.70, 126.44, 126.57, 139.74, 140.17, 142.81, 143.69 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 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 $C_{32}H_{41}NO_2$	472.3215 $(M+H)^+$
Calc. for $C_{30}H_{36}O_4Na$	483.2511 $(M+Na)^+$
Found for $C_{30}H_{36}O_4Na$	483.2511 $(M+Na)^+$



(–)-(11*R*)-**68**

Table 18 Data of monomenthyl adduct (–)-(11*R*)-**68**

Physical properties
white crystals

Table 18 Data of monomenthyl adduct (–)-(11*R*)-**68** (continued)

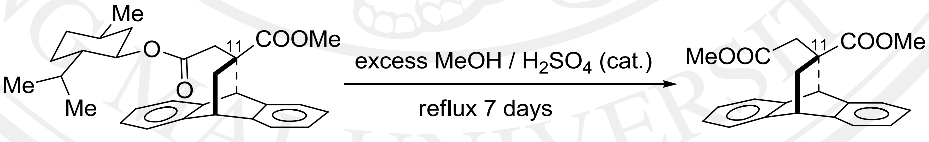
Physical properties	
melting point (m.p.) 102.1–103.1 °C (from methanol) specific rotation, $[\alpha]_D^{29.2}$ = –82.23° (c = 0.231, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3040	C–H stretching of aromatic
2953, 2869	$–CH_2$, $–CH_3$ stretching
1727	C=O stretching of ester
1459, 1308	$–CH_2$, $–CH_3$ bending
1370, 1389	$–CH_3$bending
1063, 1175	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
2.95	*d* (J = 15.8 Hz), 1H, H_d
3.47	*s*, 3H, $COOCH_3$-16
4.34	*s*, 1H, H_y
4.58	*ddd* (J = 10.9, 10.9, 4.4 Hz), 1H, CH-1'
7.03-7.30	*m*, 8H, ArH

Table 18 Data of monomenthyl adduct (−)-(11*R*)-**68** (continued)

<table>
<tr><th colspan="2">^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)</th></tr>
<tr><td colspan="2">15.96, 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), 46.8, 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, 139.62, 140.23, 142.80, 143.77 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8), 170.45 (C_q-15), 174.74 (C_q-14)</td></tr>
<tr><td colspan="2">Mass spectrometry (ESI-MS)</td></tr>
<tr><td>Molecular weight</td><td>m/z</td></tr>
<tr><td>Calc. of $C_{30}H_{36}O_4$</td><td>460.2614 (M^+)</td></tr>
<tr><td>Lock mass of $C_{32}H_{41}NO_2$</td><td>472.3215 $(M+H)^+$</td></tr>
<tr><td>Calc. for $C_{30}H_{36}O_4Na$</td><td>483.2511 $(M+Na)^+$</td></tr>
<tr><td>Found for $C_{30}H_{36}O_4Na$</td><td>483.2511 $(M+Na)^+$</td></tr>
</table>

2.1.3 Preparation of optically active 11-carbomethoxy-11-methoxyacetyl-9,10-dihydro-9,10-ethanoanthracene [(+)-(11*S*)-66]

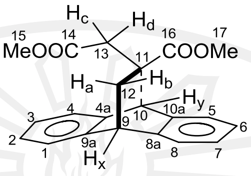
Typical procedure



(−)-(11*S*)-**67**

(+)-(11*S*)-**66**
83% yield

To a solution of adduct (−)-(11*S*)-**67** (34.4855 g, 74.87 mmol) in excess anhydrous MeOH (3000 mL) was added conc. H_2SO_4 (40 mL) as catalyst and the mixture was heated to reflux for 7 days. The crude reaction mixture was adjusted by aqueous NaOH solution, then extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and evaporated to dryness. The precipitate was recrystallized from CH_2Cl_2/hexane to give optically active *11-carbomethoxy-11-methoxyacetyl-9,10-dihydro-9,10-ethanoanthracene* [(+)-(11*S*)-**66]** in 83% yield (20.9429 g), 100% conversion.



(+)-(11*S*)-**66**

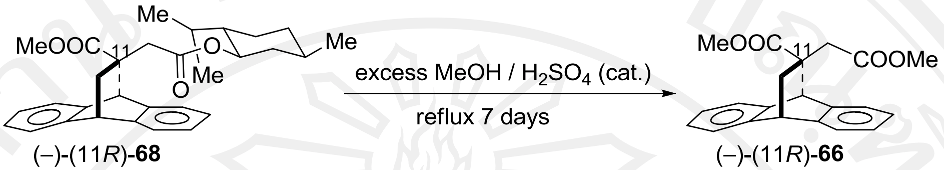
Table 19 Data of optically active dimethyl itaconate–anthracene adduct (+)-(11*S*)-**66**

Physical properties	
white crystals melting point (m.p.) 138.0–140.0°C (CH$_2$Cl$_2$/hexane) [lit.[25] m.p. 154–155°C CH$_2$Cl$_2$/hexane)] specific rotation, $[\alpha]_D^{27.2}$ = +80.83° (c = 0.141, 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
1436, 1353	–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$_c$

Table 19 Data of optically active dimethyl itaconate–anthracene adduct (+)-(11*S*)-**66** (continued)

NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
2.92	*d* (J = 16.1 Hz), 1H, H_d
3.47	*s*, 3H, $COOCH_3$-17
3.57	*s*, 3H, $COOCH_3$-15
4.36	*s*, 1H, H_y
7.03-7.31	*m*, 8H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
36.72 (CH_2-12), 44.07 (CH-9), 44.33 (CH_2-13), 50.30 (C_q-11), 51.59 (CH_3-15), 52.15 (CH_3-17), 52.79 (CH-10), 123.28, 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 $C_{21}H_{20}O_4Na$	359.1259 $(M+Na)^+$
Found for $C_{21}H_{20}O_4Na$	359.1259 $(M+Na)^+$

2.1.4 Preparation of optically active 11-carbomethoxy-11-methoxyacetyl-9,10-dihydro-9,10-ethanoanthracene [(–)-(11*R*)-66]



(–)-(11*R*)-**68**

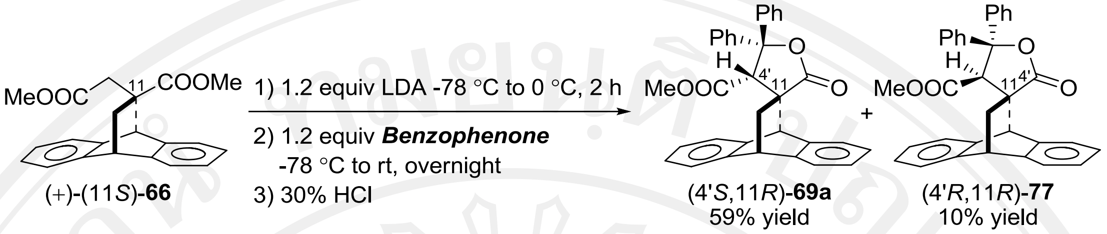
(–)-(11*R*)-**66**
80% yield

Prepared according to typical procedure 2.1.3, adduct (–)-(11*R*)-**68** (10.55 g, 22.92 mmol) provided optically active adduct [(–)-(11*R*)-**66**] in 80% yield (6.1684 g), 100% conversion as white crystals, m.p. 140.1–143.2°C, ($[\alpha]^{30.6}_{589}$ = –83.62° (*c* = 0.110, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 19).

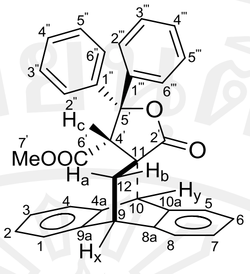
2.2 Syntheses of both enantiomerically pure forms of tetrahydro-4′-carbomethoxy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes and derivatives [(4′*S*,11*R*)-69a, (4′*R*,11*R*)-77, (4′*R*,11*S*)-69a and (4′*S*,11*S*)-77]

Typical procedure

2.2.1 Synthesis of enantiomeric tetrahydro-4′-carbomethoxy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes [(4′*S*,11*R*)-69a, (4′*R*,11*R*)-77]



To a 100 mL round-bottomed flask equipped with a magnetic stirrer bar, fitted with a three-way stopcock and nitrogen inlet. *n*-Butyllithium (14.0 mL, 18.42 mmol, 1.4 M in hexane) was added to a stirring solution of diisopropylamine (3.1 mL, 22.12 mmol) in dry THF (30 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 dimethyl itaconate–anthracene adduct (+)-(11*S*)-**66** (5.1633g, 15.35 mmol) in THF (15 mL) was added at –78 °C and left stirring at 0 °C for 2 hours. The solution of benzophenone (3.6646 g, 20.11 mmol) in THF 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 resultant mixture was quenched with 10% hydrochloric acid solution and extraction three times with CH_2Cl_2. The combined organic extracts were washed with H_2O, dried over $MgSO_4$, filtered and evaporated to dryness. The crude product was purified by flash column chromatography (silica gel, EtOAc : CH_2Cl_2 : hexane = 0.5 : 1 : 8.5 as eluent) and preparative thin layer chromatography (PLC, EtOAc : CH_2Cl_2 : hexane = 0.5 : 1 : 8.5 as developing solvent) afforded two diastereomer spiro–lactones, *tetrahydro-4′-carbomethoxy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes*, (4′*S*,11*R*)-**69a** in 59% yield (4.0498 g) as the major isomer and (4′*R*,11*R*)-**77** in 10% yield (0.7167 g) as the minor isomer, 93% conversion from the starting material.



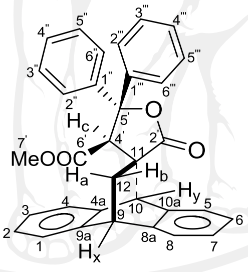
(4'S,11R)-**69a**

Table 20 Data of major spiro–lactone diastereomer (4′S,11R)-**69a**

Physical properties	
white crystals melting point (m.p.) 274.0–275.1 °C (CH_2Cl_2/hexane) specific rotation, $[\alpha]_D^{33.7}$ = +88.87° (c = 0.117, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrationss
3026	C–H stretching of aromatic
2940, 2800	$–CH_2$, $–CH_3$ stretching
1785, 1737	C=O stretching of ester
1600	C=C stretching of aromatic
1450, 1345	$–CH_2$, $–CH_3$ bending
1159	C–O stretching of ester
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.41, 1.58, 4.12	*ABX* system (J = 13.1, 3.1, 2.6 Hz), 3H, H_a, H_b, H_x
3.30	*s*, 3H, $COOCH_3$-7'
3.40	*s*, 1H, H_c
4.70	*s*, 1H, H_y
7.00-7.48	*m*, 18H, ArH

Table 20 Data of major spiro–lactone diastereomer (4′*S*,11*R*)-**69a** (continued)

^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
43.13 (CH_2-12), 44.18(CH-9), 48.35 (CH-10), 50.76 (C_q-11), 51.63 (CH-4'), 65.04 (CH_3-7'), 86.63 (C_q-5'), 123.01, 124.48, 125.64, 125.77, 125.86, 126.36, 126.52, 126.93, 127.50, 128.22, 128.30, 128.73, 129.59 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2'', 3'', 4'', 5'', 6'', 2''', 3''', 4''', 5''', 6'''), 140.33, 140.92, 141.60, 143.88, 143.99, 144.37 (C_q-ArH-4a, 8a, 9a, 10a, 1'', 1'''), 170.88 (C_q-6'), 177.31 (C_q-2')	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{33}H_{26}O_4$	486.1831 (M^+)
Lock mass of $C_{32}H_{41}NO_2$	472.3215 $(M+H)^+$
Calc. for $C_{33}H_{26}O_4Na$	509.1729 $(M+Na)^+$
Found for $C_{33}H_{26}O_4Na$	509.1729 $(M+Na)^+$



(4'*R*,11*R*)-**77**

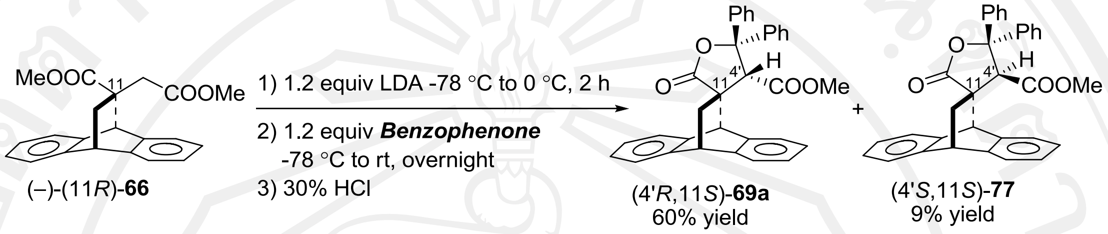
Table 21 Data of minor spiro–lactone diastereomer (4′*R*,11*R*)-**77**

Physical properties	
white crystals melting point (m.p.) 222.1–224.1°C (CH_2Cl_2/hexane) specific rotation, $[\alpha]_D^{32.2}$ = +51.61° (*c* = 0.127, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrationss
3026	C–H stretching of aromatic

Table 21 Data of minor diastereomer (4′*R*,11*R*)-**77** (continued)

IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrationss
2950, 2850	$–CH_2$,$–CH_3$ stretching
1785, 1741	C=O stretching of ester
1600	C=C stretching of aromatic
1450, 1342	$–CH_2$, $–CH_3$ bending
1219	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
1.52, 2.43, 4.29	*ABX* system (*J* = 13.2, 3.5, 2.7 Hz), 3H, H_a, H_b, H_x
3.07	*s*, 3H, $COOCH_3$-7'
3.72	*s*, 1H, H_c
3.92	*s*, 1H, H_y
6.83-7.84	*m*, 18H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
38.52 (CH_2-12), 43.76 (CH-9), 48.66 (CH-4'), 51.40 (CH_3-7'), 52.86 (C_q-11), 62.35 (CH-10), 86.50 (C_q-5'), 123.15, 123.81, 124.54, 124.99, 125.22, 125.49, 125.94, 126.81, 126.96, 127.39, 128.14, 128.58, 129.28, 130.09 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2'', 3'', 4'', 5'', 6'', 2''', 3''', 4''', 5''', 6'''), 138.24,138.78, 142.00, 142.99, 144.12, 144.43 (C_q-ArH-4a, 8a, 9a, 10a, 1'', 1'''), 170.07 (C_q-6'), 175.69 (C_q-2')	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{33}H_{26}O_4$	486.1831 (M^+)
Lock mass of $C_{32}H_{41}NO_2$	472.3215 $(M+H)^+$
Calc. for $C_{33}H_{26}O_4Na$	509.1729 $(M+Na)^+$
Found for $C_{33}H_{26}O_4Na$	509.1729 $(M+Na)^+$

2.2.2 Synthesis of enantiomeric of tetrahydro-4′-carbomethoxy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes [(4′*R*,11*S*)-69a and (4′*S*,11*S*)-77]



Prepared according to typical procedure 2.2.1, adduct (−)-(11*R*)-**66** (4.2815 g, 12.73 mmol), LDA (3.0 mL, 21.41 mmol, 1.2 equiv, 12.0 mL, 15.28 mmol) and benzophenone (3.0166 g, 16.55 mmol, 1.2 equiv). Purification the crude product by flash column chromatography (silica gel, EtOAc : CH_2Cl_2 : hexane = 0.5 : 1 : 8.5 as eluent) and PLC (silica gel, EtOAc : CH_2Cl_2 : hexane = 0.5 : 1 : 8.5 as developing solvent) afforded two diastereomers, *tetrahydro-4′-carbomethoxy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes*, (4′*R*,11*S*)-**69a** in 60% yield (3.3938 g) as the major isomer and (4'*S*,11*S*)-**77** in 9% yield (0.5058 g) as the minor isomer, 91% conversion from the starting material.

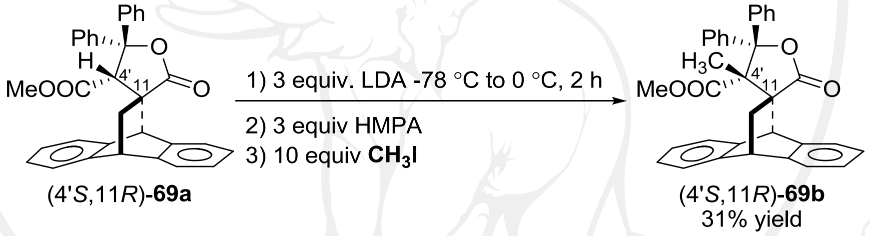
Compound (4′*R*,11*S*)-**69a**: White crystals; m.p. 278.4–279.1 °C (from CH_2Cl_2/hexane); ($[\alpha]_D^{29.4}$ = –171.51° (c = 0.155, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 20).

Compound (4′*S*,11*S*)-**77**: White crystals; m.p. 231.0–231.8 °C (from CH_2Cl_2/hexane); ($[\alpha]_D^{25.1}$ = –2.24° (c = 1.088, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 21).

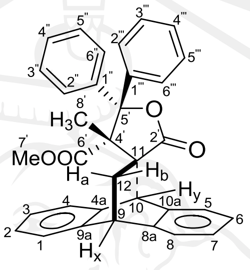
2.3 Syntheses of both enantiomerically pure forms of tetrahydro-4′-carbomethoxy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes derivatives [(4'*S*,11*R*)-69b, (4'*S*,11*R*)-69c, (4'*R*,11*S*)-69b and (4'*R*,11*S*)-69c]

Typical procedure

2.3.1 Synthesis of enantiomeric of tetrahydro-4′-carbomethoxymethyl-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes [(4′*S*,11*R*)-69b]



To a 100 mL round-bottomed flask equipped with a magnetic stirrer bar, fitted with a three-way stopcock and nitrogen inlet. *n*-Butyllithium (7.90 mL, 10.41 mmol, 1.4 M in hexane) was added to a stirring solution of diisopropylamine (4.50 mL, 32.11 mmol) in dry THF (20 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 adduct [(4′*S*,11*R*)-**69a**] (1.6891 g, 3.47 mmol) in THF (15 mL) was added at –78 °C followed by HMPA (1.80 mL, 10.35 mmol) and left stirring at 0 °C for 2 hours. Methyl iodide (2.2 mL, 35.34 mmol, 10.0 equiv) 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 resultant mixture was quenched with 10% hydrochloric acid solution and extraction three times with CH_2Cl_2. The combined organic extracts were washed with H_2O, dried over $MgSO_4$, filtered and evaporated to dryness. Purification the crude product by flash column chromatography (silica gel, EtOAc : hexane = 1 : 9 as eluent) afforded *tetrahydro-4′-carbomethoxymethy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes*, (4′*S*,11*R*)-**69b** in 31% yield (0.5312 g), 99% conversion from the starting material.



(4′*S*,11*R*)-**69b**

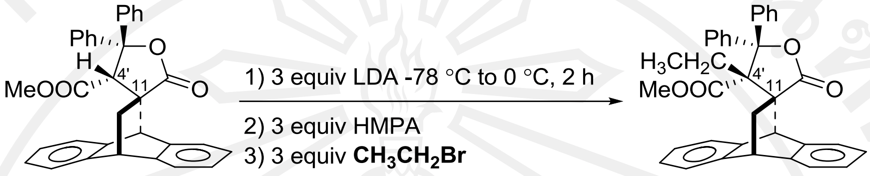
Table 22 Data of methyl spiro–lactone adduct (4′*S*,11*R*)-**69b**

Physical properties	
white crystals melting point (m.p.) 199.5–200.9 °C (CH_2Cl_2/hexane) specific rotation, $[\alpha]_D^{31.9}$ = +179.01° (c = 0.105, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3026	C–H stretching of aromatic
2947, 2820	$-CH_2$, $-CH_3$ stretching
1727	C=O stretching of ester
1600	C=C stretching of aromatic
1460, 1302	$-CH_2$, $-CH_3$ bending
1223	C–O stretching of ester
766	C–H bending of aromatic (out of plane)

Table 22 Data of methyl spiro–lactone adduct (4′*S*,11*R*)-**69b** (continued)

NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
2.13, 2.89, 4.24	*ABX* system (*J* = 12.6, 3.5, 2.2 Hz), 3H, H_a, H_b, H_x
2.97	*s*, 3H, CH_3-8'
3.17	*s*, 3H, $COOCH_3$-7'
5.10	*s*, 1H, H_y
6.92-7.29	*m*, 18H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
42.40 (CH_2-12), 44.37 (CH_3-9), 50.84 (CH-10), 51.36 (CH_3-8'), 52.19 (CH3-7'), 54.52 (C_q-11), 122.46, 123.84, 124.80, 124.85, 125.47, 126.09, 126.38, 127.19, 127.60, 127.82, 127.94, 128.17, 128.78 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2'', 3'', 4'', 5'', 6'', 2''', 3''', 4''', 5''', 6'''), 137.47 (C_q-11), 137.17, 138.52, 139.39, 140.73, 141.89, 143.16, 144.85, 146.54 (C_q-ArH-4a, 8a, 9a, 10a, 1'', 1'''), 168.61 (C_q-6'), 172.43 (C_q-2')	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{34}H_{28}O_4$	500.1988 (M+)
Lock mass of $C_{32}H_{41}NO_2$	472.3215 (M+H)+
Calc. for $C_{34}H_{28}O_4Na$	523.1886 $(M+Na)^+$
Found for $C_{34}H_{28}O_4Na$	523.1886 $(M+Na)^+$

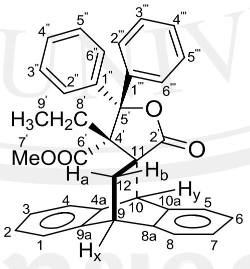
2.3.2 Synthesis of enantiomeric of tetrahydro-4′-carbomethoxyethyl-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes [(4′*S*,11*R*)-69c]



(4'*S*,11*R*)-**69a**

(4'*S*,11*R*)-**69c**
18% yield

Prepared according to typical procedure 2.3.1, adduct (4′*S*,11*R*)-**69a** (1.6717 g, 3.44 mmol) in THF (15 mL), LDA solution (7.80 mL, 10.27 mmol, 3.0 equiv, 4.50 mL, 32.11 mmol), HMPA (1.80 mL, 10.35 mmol) and ethyl bromide (0.80 mL, 10.79 mmol, 3.0 equiv). Purification of the crude product by flash column chromatography (silica gel, EtOAc : hexane = 1 : 9 as eluent) and PLC (silica gel, EtOAc : hexane = 1 : 9 as developing solvent) afforded afforded *tetrahydro-4′-carbomethoxyethy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes,* (4′*S*,11*R*)-**69c** in 18% yield (0.3215 g), 100% conversion from the starting material



(4'*S*,11*R*)-**69c**

Table 23 Data of ethyl spiro–lactone adduct (4′*S*,11*R*)-**69c**

Physical properties
white powder melting point (m.p.) 185.4–186.8 °C (CH_2Cl_2/hexane)

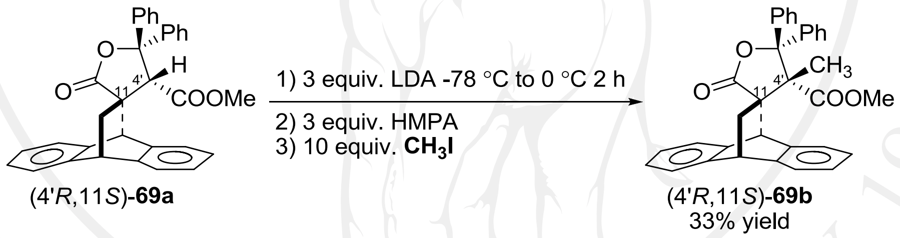
Table 23 Data of ethyl spiro–lactone adduct (4′*S*,11*R*)-**69c** (continued)

Physical properties	
specific rotation, $[\alpha]_{D}^{33.0}$ = +260.55° (c = 0.105, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
$\nu_{\max}$ (cm^{-1})	Type of vibrations
3057	C–H stretching of aromatic
2947, 2890	$–CH_2$, $–CH_3$ stretching
1726	C=O stretching of ester
1600	C=C stretching of aromatic
1457, 1365	$–CH_2$, $–CH_3$ bending
1228	C–O stretching of ester
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
0.99	*t* (J = 7.5 Hz), 3H, CH_3-9'
2.11, 2.83, 4.23	*ABX* system (J = 12.7, 3.5, 2.3 Hz), 3H, H_a, H_b, H_x
2.99	*s*, 3H, CH_3-7'
3.41-3.53	*m*, 2H, CH_2-8'
5.14	*s*, 1H, H_y
6.94-7.30	*m*, 18H, Ar-H
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
13.72 (CH_3-9'), 42.82 (CH-12), 44.42 (CH-9), 50.89 (CH-10), 51.28 (CH_3-7'), 54.47 (C_q-11), 61.14 (CH_2-8'), 122.46, 123.68, 124.51, 124.85, 125.30, 126.06, 126.32, 127.17, 127.49, 127.79, 127.82, 127.98, 128.08, 128.94 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2'', 3'', 4'', 5'', 6'', 2''', 3''', 4''', 5''', 6'''), 137.47, 138.75, 139.56, 140.67, 142.18, 143.37, 145.19, 146.56 (C_q-ArH-4a, 8a, 9a, 10a, 1'', 1'''), 168.66 (C_q-6'), 172.32 (C_q-2')	

Table 23 Data of ethyl spiro–lactone adduct (4′*S*,11*R*)-**69c** (continued)

Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{35}H_{30}O_4$	514.2144 (M^+)
Lock mass of $C_{32}H_{41}NO_2$	472.3215 $(M+H)^+$
Calc. for $C_{35}H_{30}O_4Na$	537.2042 $(M+Na)^+$
Found for $C_{35}H_{30}O_4Na$	537.2042 $(M+Na)^+$

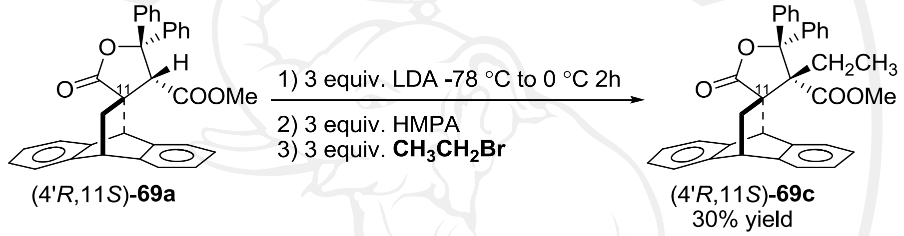
2.3.3 Synthesis of enantiomeric of tetrahydro-4′-carbomethoxymethyl-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracene [(4′*R*,11*S*)-69b]



Prepared according to typical procedure 2.3.1, adduct (4'*R*,11*S*)-**69a** (1.5890 g, 3.27 mmol) in THF (15 mL), LDA solution (7.40 mL, 9.75 mmol, 3.0 equiv, 4.50 mL, 32.11 mmol), HMPA (1.70 mL, 9.77 mmol, 3.0 equiv) and methyl iodide (2.10 g, 33.73 mmol, 10.0 equiv). Purification of the crude product by flash column chromatography (silica gel, EtOAc : hexane = 1 : 9 as eluent) and PLC (silica gel, EtOAc : hexane = 1 : 9 as developing solvent) afforded *tetrahydro-4′-carbomethoxymethy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes*, (4′*R*,11*S*)-**69b** in 33% yield (0.5421 g), 99% conversion from the starting material**.**

Compound (4′*R*,11*S*)-**69b**: White crystals; m.p. 198.0–201.0 °C (from CH_2Cl_2/hexane); ($[\alpha]_D^{30.2}$ = –59.99° (*c* = 0.120, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 22).

2.3.4 Synthesis of enantiomeric of tetrahydro-4′-carbomethoxyethyl-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethano anthracenes [(4′*R*,11*S*)-69c]



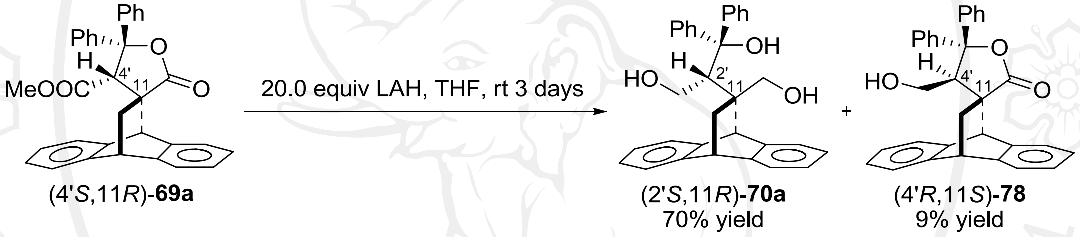
Prepared according to typical procedure 2.3.1, adduct (4′*R*,11*S*)-**69a** (2.0203 g, 4.15 mmol) in THF (15 mL), LDA solution (9.50 mL, 12.51 mmol, 3.0 equiv, 5.50 mL, 39.24 mmol), HMPA (2.20 mL, 12.65 mmol, 3.0 equiv) and ethyl bromide (1.00 mL, 13.49 mmol). Purification of the crude product by flash column chromatography (silica gel, EtOAc : hexane = 1 : 9 as eluent) and PLC (silica gel, EtOAc : hexane = 1 : 9 as developing solvent) afforded *tetrahydro-4′-carbomethoxyethy-5′-diphenyl-2′-furanone-3′-spiro-11-9,10-dihydro-9,10-ethanoanthracenes*, (4′*R*,11*S*)-**69c** in 18% yield (0.3819 g), 100% conversion from the starting material**.**

Compound (4′*R*,11*S*)-**69c**: White crystals; m.p. 186.1–187.8 °C (from CH_2Cl_2/hexane); ($[\alpha]_D^{29.8}$ = –322.89° (*c* = 0.116, $CHCl_3$)). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 23).

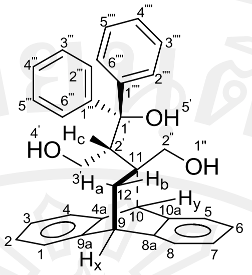
2.4 Syntheses of both enantiomerically pure forms of 11-hydroxymethylene-11-(2′-(1′,3′-dihydroxy-1′,1′-diphenylpropyl))-9,10-dihydro-9,10-ethano anthracenes [(2′*S*,11*R*)-70a and (2′*R*,11*S*)-70a]

Typical procedure

2.4.1 Synthesis of optically active of 11-hydroxymethylene-11-(2′-(1′,3′-dihydroxy-1′,1′-diphenylpropyl))-9,10-dihydro-9,10-ethano anthracene [(2′*S*,11*R*)-70a]



To a 100 mL two-necked round-bottomed flask equipped with a magnetic stirrer and a septum cap and nitrogen inlet. The solution of major product (4′*R*,11*S*)-69a (2.0598 g, 4.23 mmol) in THF (20 mL) was added to a cooled (–78 °C) solution of LAH (3.3419 g, 84.6 mmol, 20 equiv) in THF (20 mL). The reaction mixture was stirred at room temperature for 3 days and then quenched by dropwise addition of acetone (10 mL). After that, the resulting solution was extracted three times with EtOAc and the combined organic portions were dried, filtered and concentrated *in vacuo*. Purification of the residue by flash column chromatography (EtOAc/hexane = 1 : 9 as eluent) afforded two compounds : (2′*S*,11*R*)-70a in 70% yield (1.3602 g) as the major product and (4′*R*,11*S*)-78 in 9% yield (0.1769 g) as the minor products, 100% conversion from the starting material.



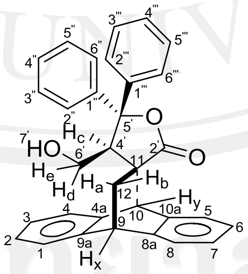
(2'*S*,11*R*)-**70a**

Table 24 Data of triol TADDOL–anthracene adduct (2′*S*,11*R*)-**70a**

Physical properties	
white solid melting point (m.p.) 202.7–204.2 °C (CH_2Cl_2/hexane) specific rotation, $[\alpha]_D^{32.0}$ = –60.55° (c = 0.142, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3386	O–H stretching of alcohol
3020	C–H stretching of aromatic
2948, 2890	$–CH_2$, $–CH_3$ stretching
1600	C=C stretching of aromatic
1461, 1376	$–CH_2$, $–CH_3$ bending
1034, 1167	C–O stretching of alcohol
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
0.52 1.36, 3.91	*ABX* system (*J* = 13.5, 3.0, 2.6 Hz), 3H, H_a, H_b, H_x
2.25	*s*, 1H, H_c
2.55, 4.25	*d*, *A*B system (*J* = 8.7 Hz), 2H, CH_2-2"
2.60	*s*, 1H, OH-1"
3.97, 4.51	*d*, (*J* = 12.9 Hz), 2H, CH_2-3'
4.69	*s*, 1H, H_y

Table 24 Data of triol TADDOL–anthracene adduct (2′*S*,11*R*)-**70a** (continued)

NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (*δ*, ppm)	Type of protons
4.97 5.69 7.05-7.36	*s*, 1H, OH-4' *s*, 1H, OH-5' *m*, 18H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
38.26 (CH_2-12), 44.67 (CH-9), 48.36 (C_q-11), 49.66 (CH-10), 52.93 (CH-2'), 61.61 (CH_2-3'), 66.48 (CH_2-2"), 82.34 (C_q-1'), 122.55, 123.26, 123.33, 124.73, 124.79, 125.43, 125.62, 126.03, 126.09, 126.17, 126.31, 126.54, 127.67, 128.27, (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2''', 3''', 4''', 5''', 6''', 2'''', 3'''', 4'''', 5'''', 6''''), 140.48, 141.57, 142.64, 144.92, 146.01, 149.62 (C_q-ArH-4a, 8a, 9a, 10a, 1''', 1'''')	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{32}H_{30}O_3$ Lock mass of $C_{32}H_{41}NO_2$ Calc. for $C_{32}H_{30}O_3Na$ Found for $C_{32}H_{30}O_3Na$	462.2195 (M^+) 472.3215 $(M+H)^+$ 485.2093 $(M+Na)^+$ 485.2093 $(M+Na)^+$



(4'*R*,11*S*)-**78**

Table 25 Data of reduced compound (4′*R*,11*S*)-**78**

Physical properties	
white crystals	

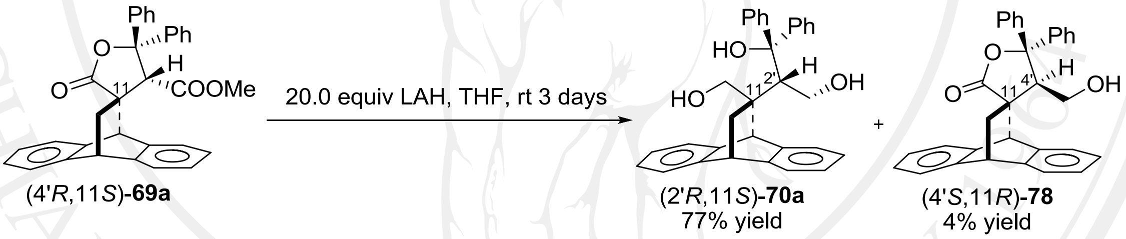
Table 25 Data of reduced compound (4′*R*,11*S*)-**78** (continued)

Physical properties	
melting point (m.p.) 195.9–196.5 °C (CH_2Cl_2/hexane) specific rotation, $[\alpha]_D^{32.0}$ = +200.25° (*c* = 0.097, $CHCl_3$)	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
3484	O–H stretching of alcohol
3019, 3058	C–H stretching of aromatic
2924, 2851	$–CH_2$, $–CH_3$ stretching
1767	C=O stretching of ester
1469, 1373	$–CH_2$, $–CH_3$ bending
1173	C–O stretching of ester
1030	C–O stretching of alcohol
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
1.16, 2.18, 4.02	*ABX* system (*J* = 13.4, 3.0, 2.4 Hz), 3H, H_a, H_b, H_x
3.01	*s*, 1H, alcohol
3.41	*s*, 1H, H_c
3.67, 3.84	*d*, *AB* system (*J* = 8.7 Hz), 2H, H_e, H_d
4.05	*s*, 1H, H_y
6.58-7.47	*m*, 18H, ArH
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
33.74 (CH_2-12), 44.06 (CH-9), 49.05 (C_q-11), 53.41 (CH-10), 57.14 (CH-4'), 76.68 (CH_2-6'), 80.79 (C_q-1'), 123.15, 124.80, 125.18, 125.65, 125.98,126.27, 126.41, 126.61, 126.72, 127.04, 127.25, 128.09, 128.61 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2'', 3'', 4'', 5'', 6'', 2''', 3''', 4''', 5''', 6'''), 140.00, 140.33, 143.60, 144.08, 144.36, 144.58 (C_q-ArH-4a, 8a, 9a, 10a, 1'', 1'''), 177.08 (C_q-2')	

Table 25 Data of reduced compound (4′*R*,11*S*)-**78** (continued)

Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{33}H_{28}O_3$	458.1882 (M^+)
Lock mass of $C_{32}H_{26}N_4O_2S$	472.3215 $(M+H)^+$
Calc. for $C_{32}H_{26}O_3Na$	481.1780 $(M+Na)^+$
Found for $C_{32}H_{26}O_3Na$	481.1780 $(M+Na)^+$

2.4.2 Synthesis of optically active of 11-hydroxymethylene-11-(2′-(1′,3′-dihydroxy-1′,1′-diphenylpropyl))-9,10-dihydro-9,10-ethanoanthracene [(2′*R*,11*S*)-70a]

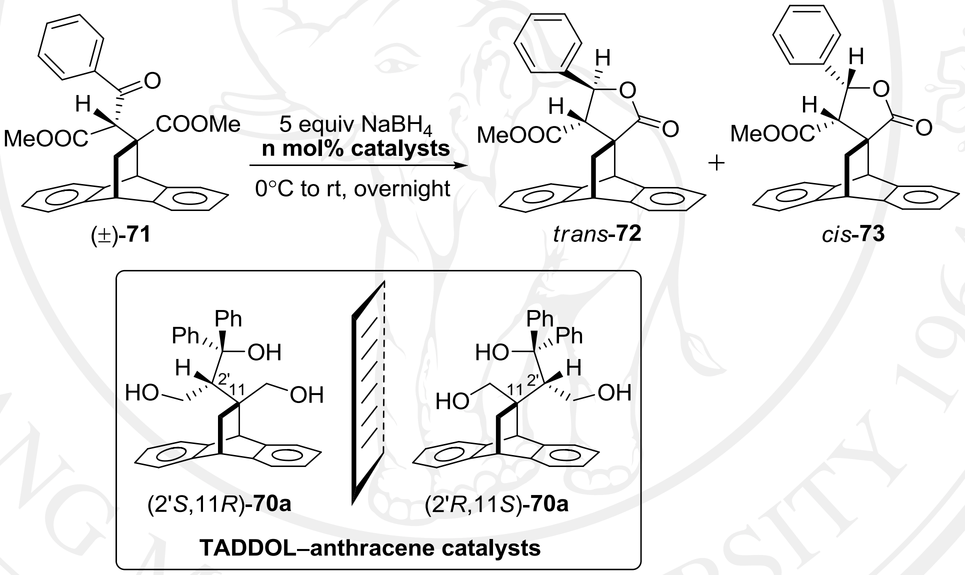


Prepared according to typical procedure 2.4.1, adduct (4′*R*,11*S*)-**69a** (2.3050 g, 4.74 mmol) and LAH (3.7338 g, 98.38 mmol). Usual workup and purification of the crude product by flash column chromatography (silica gel, EtOAc : hexane = 1.0 : 9.0 as eluent) afforded two compounds: (2′*R*,(11*S*)-**70a** in 77% yield (1.6765 g) as the major product and (4′*S*,11*R*)-**78** in 4% yield (0.0776 g) as the minor products, 100% conversion from the starting material.

Compound (2′*R*,11*S*)-**70a**: White crystals; m.p. 184.0.6–187.0 °C (from CH_2Cl_2/hexane); $[\alpha]^{30.3}_{589}$ = +310.17° (*c* = 0.127, $CHCl_3$). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 24).

Compound (4′*S*,11*R*)-**78**: White crystals; m.p. 197.0–198.6 °C (from CH_2Cl_2/hexane); $[\alpha]_D^{25.3}$ = –234.92° (*c* = 0.249, $CHCl_3$). IR, ^1H, ^{13}C NMR and mass spectral data are identical to previously reported data (Table 25).

2.5 Study the effect of the triol TADDOL–anthracene catalysts (2′*S*,11*R*)-70a and (2′*R*,11*S*)-70a for reduction reaction of 11-carbomethoxy-11-(1′-benzoyl)methoxyacetyl-9,10-dihydro-9,10- ethanoanthracene [(±)-71]

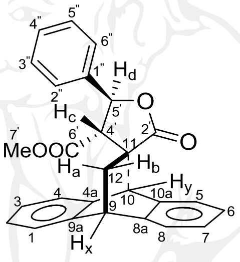


2.5.1 Reduction of *β*-keto ester (±)-71 in the presence of TADDOL–anthracene catalyst (2′*S*,11*R*)-70a

Typical procedure

2.5.1.1 1 mol% of TADDOL–anthracene catalyst (2′*S*,11*R*)-**70a**

To a 100 mL round-bottomed flask fitted with a three-way stopcock and nitrogen inlet. A cooled (0°C) solution of *β*-keto ester adduct (±)-**71** (0.1055 g, 0.23 mmol) and compound (2′*S*,11*R*)-**70a** (0.0017 g, 2.30 μmol, 1 mol%) in THF (6 mL) was added $NaBH_4$ (56.00 mg, 1.48 mmol). The reaction mixture was stirred at 0°C to room temperature for overnight and then quenched by the dropwise addition of acetone (1 mL). The resulting solution was extracted three times with CH_2Cl_2 and the combined organic portions were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 32% yield (0.0303 g) and 15% yield (0.0139 g) respectively, 99% conversion from the starting material.



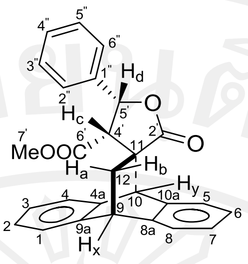
trans-**72**

Table 26 Data of *trans*-isomer **72**

Physical properties	
white crystals m.p. 228.9-229.9°C [lit.[21] m.p. 220-221°C (CH_2Cl_2/hexane)]	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
2951, 2870	$–CH_2$, $–CH_3$ stretching
1774	C=O stretching of ester
1459	$–CH_2$, $–CH_3$ bending
1205	C–O stretching of ester

Table 26 Data of *trans*-isomer **72** (continued)

NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
2.11, 2.55, 4.38	*ABX* system (J = 12.5, 3.0, 2.4 Hz), 3H, H_a, H_b, H_x
2.96	*s*, 3H, $COOCH_3$-7'
3.05	*d* (J = 10.2 Hz), 1H, H_c
4.66	*s*, 1H, H_y
6.05	*d* (J = 10.2 Hz), 1H, H_d
7.05-7.44	*m*, 13H, ArH-1, 2, 3, 4, 5, 6, 7, 8, 2", 3", 4", 5", 6"
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
37.41 (CH_2-12), 43.82 (CH-9), 46.67 (CH-10), 51.45 (C_q-11), 51.82 (CH_3-7'), 59.02 (CH-4'), 78.35 (CH-5'), 123.18, 123.44, 124.79, 125.16, 125.97, 126.32, 126.60, 126.68, 127.61, 128.64, 128.86 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2", 3", 4", 5", 6"), 137.19, 137.79, 139.89, 143.32 (C_q-ArH-4a, 8a, 9a, 10a), 168.11 (C_q-2"), 175.98 (C_q-6")	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{28}H_{24}O_4$	422.1518 (M^+)
Lock mass of $C_{32}H_{41}NO_2$	472.3215 $(M + H)^+$
Calc. for $C_{56}H_{43}O_8$	843.2985 $(M – H)^+$
Found for $C_{56}H_{43}O_8$	843.2943 $(M – H)^+$



cis-**73**

Table 27 Data of *cis*-isomer **73**

Physical properties	
white crystals m.p. 220.0-221.0°C [lit.[21] m.p. 220-221°C (CH_2Cl_2/hexane)]	
IR spectroscopy (Evaporated thin film)	
ν_{max} (cm^{-1})	Type of vibrations
2951	$–CH_2$, $–CH_3$ stretching
1795	C=O stretching of ester
1454	$–CH_2$, $–CH_3$ bending
1143	C–O stretching of ester
NMR spectroscopy	
^{1}H-NMR (400 MHz) in $CDCl_3$	
Chemical shift (δ, ppm)	Type of protons
2.20, 2.26, 4.49	*ABX* system (*J* = 12.4, 3.1, 2.3 Hz), 3H, H_a, H_b, H_x
2.54	*d* (*J* = 5.6 Hz), 1H, H_c
3.28	*s*, 3H, $COOCH_3$-7'
4.77	*s*, 1H, H_y
5.51	*d* (*J* = 5.6 Hz), 1H, H_d
6.97 – 7.56	*m*, 13H, ArH-1, 2, 3, 4, 5, 6, 7, 8, 2'', 3'', 4'', 5'', 6''
^{13}C-NMR (100 MHz) in $CDCl_3$ (ppm)	
40.78 (CH_2-12), 43.75 (CH-9), 46.87 (CH-10), 50.87 (C_q-11), 51.36 (CH_3-7'), 61.03(CH-4'), 76.89 (CH-5'), 123.96, 124.35, 125.36, 125.97, 125.99, 126.25, 126.76, 127.46, 128.20, 128.46 (CH-ArH-1, 2, 3, 4, 5, 6, 7, 8, 2'', 3'', 4'', 5'', 6''),	

Table 27 Data of *cis*-isomer **73** (continued)

^{13}C-NMR (100 MHz) in CDCl$_3$ (ppm)	
139.33, 140.65, 142.01, 143.27 (C$_q$-ArH-4a, 8a, 9a, 10a), 168.28 (C$_q$-2''), 176.74 (C$_q$-6'')	
Mass spectrometry (ESI-MS)	
Molecular weight	m/z
Calc. of $C_{28}H_{24}O_4$	422.1518 (M$^+$)
Lock mass of $C_{32}H_{41}NO_2$	472.3215 (M + H)$^+$
Calc. for $C_{56}H_{43}O_8$	843.2985 (M – H)$^+$
Found for $C_{56}H_{43}O_8$	843.2943 (M – H)$^+$

2.5.1.2 1 mol% of TADDOL–anthracene catalyst (2′*S*,11*R*)-**70a** in THF:H_2O (4:0.5)

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1027 g, 0.23 mmol), compound (2′*S*,11*R*)-**70a** (0.0013 g, 2.81 μmol, 1 mol%) in a solution of THF and H_2O (4.5 mL, 4 : 0.5) and $NaBH_4$ (0.0445 g, 1.18 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) 47% yield (0.0450 g) and 11% yield (0.0105 g) respectively, 100% conversion from the starting material.

2.5.1.3 5 mol% of TADDOL–anthracene catalyst (2′*S*,11*R*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1016 g, 0.23 mmol), compound (2′*S*,11*R*)-**70a** (0.0057 g, 0.01 mmol, 5 mol%) in THF (6 mL) and $NaBH_4$ (0.0429 g, 1.13 mmol). Purification of the crude product by

PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 24% yield (0.0227 g) and 20% yield (0.016 g) respectively, 83% conversion from the starting material.

2.5.1.4 10 mol% of TADDOL–anthracene catalyst (2′*S*,11*R*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1067 g, 0.24 mmol), compound (2′*S*,11*R*)-**70a** (0.0116 g, 0.03 mmol, 10 mol%) in THF (6 mL) and $NaBH_4$ (0.0631 g, 1.67 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 10% yield (0.0096 g) and 25% yield (0.0250 g) respectively, 100% conversion from the starting material.

2.5.1.5 15 mol% of TADDOL–anthracene catalyst (2′*S*,11*R*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1002 g, 0.23 mmol), compound (2′*S*,11*R*)-**70a** (0.0175 g, 0.04 mmol, 15 mol%) in THF (6 mL) and $NaBH_4$ (0.0464 g, 1.23 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 43% yield (0.0362 g) and 13% yield (0.0106 g) respectively, 89% conversion from the starting material.

2.5.1.6 20 mol% of TADDOL–anthracene catalyst (2′*S*,11*R*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1013 g, 0.23 mmol), compound (2′*S*,11*R*)-**70a** (0.0228 g, 0.05 mmol, 20 mol%) in THF (6 mL) and $NaBH_4$ (0.0545 g, 1.44 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 35% yield (0.0299 g) and 13% yield (0.0112 g) respectively, 89% conversion from the starting material.

2.5.2 Reduction of *β*-keto ester (±)-71 in the presence of TADDOL–anthracene catalyst (2′*R*,11*S*)-70a

2.5.2.1 1 mol% of TADDOL–anthracene catalyst (2′*R*,11*S*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1063 g, 0.24 mmol), compound (2′*R*,11*S*)-**70a** (0.0016 g, 3.46 μmol, 1 mol%) in THF (6 mL) and $NaBH_4$ (0.0642 g, 1.70 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 40% yield (0.0655 g) and 2% yield (0.0022 g) respectively, 100% conversion from the starting material.

2.5.2.2 1 mol% of TADDOL–anthracene catalyst (2′*R*,11*S*)-**70a** in THF:H_2O (4:0.5)

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1255 g, 0.28 mmol), compound (2′*R*,11*S*)-**70a** (0.0015 g, 3.24 μmol, 1 mol%) in a solution of THF and H_2O (4.5 mL, 4:0.5) and $NaBH_4$ (0.0458 g, 1.21 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 5% yield (0.0062 g) and 7% yield (0.0087 g) respectively, 100% conversion from the starting material.

2.5.2.3 5 mol% of TADDOL–anthracene catalyst (2′*R*,11*S*)-**70a**

Prepared according to typical procedure in 2.3.1.1, *β*-keto diester adduct (±)-**71** (0.1474 g, 0.33 mmol), compound (2′*R*,11*S*)-**68** (0.0077 g, 0.02 mmol, 5 mol%) in THF (6 mL) and $NaBH_4$ (0.0687 g, 1.82 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 39% yield (0.0530 g) and 16% yield (0.0219 g) respectively, 100% conversion from the starting material.

2.5.2.4 10 mol% of TADDOL–anthracene catalyst (2′*R*,11*S*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.11194 g, 0.27 mmol), compound (2′*R*,11*S*)-**68** (0.0137 g, 0.03 mmol, 10 mol%) in THF (6 mL) and $NaBH_4$ (0.0746 g, 1.97 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 40% yield (0.0444 g) and 16% yield (0.0175 g) respectively, 100% conversion from the starting material.

2.5.2.5 15 mol% of TADDOL–anthracene catalyst (2′*R*,11*S*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1030 g, 0.23 mmol), compound (2′*R*,11*S*)-**70a** (0.0199 g, 0.04 mmol, 15 mol%) in THF (6 mL) and $NaBH_4$ (0.0458 g, 1.21 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 50% yield (0.0475 g) and 16% yield (0.0155 g) respectively, 100% conversion from the starting material.

2.5.2.6 20 mol% of TADDOL–anthracene catalyst (2′*R*,11*S*)-**70a**

Prepared according to typical procedure in 2.5.1.1, *β*-keto diester adduct (±)-**71** (0.1325 g, 0.30 mmol), compound (2′*R*,11*S*)-**70a** (0.0288 g, 0.06 mmol, 5 mol%) in THF (6 mL) and $NaBH_4$ (0.0729 g, 1.93 mmol). Purification of the crude product by PLC using EtOAc : hexane = 1 : 9 as developing solvent afforded two diastereomeric spiro–lactones, *tetrahydro-4'-carbomethoxy-5'-phenyl-2'-furanone-3'-spiro-11-9,10-dihydro-9,10-ethanoanthracenes* (*trans*-**72** and *cis*-**73**) in 46% yield (0.0562 g) and 13% yield (0.0157 g) respectively, 100% conversion from the starting material.