

## Supporting Information

### Absolute Stereochemistry of Allylic Alcohols, Amines and Other Ene Moieties: A Microscale Cross Metathesis / Exciton Chirality Protocol

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#### Materials and General Procedures

Anhydrous dichloromethane was dried and distilled from  $\text{CaH}_2$ . Acetonitrile used for CD and UV-vis measurements were Optima grade. Unless otherwise noted, materials were obtained from a commercial supplier and were used without further purification. Grubbs' second generation ruthenium catalyst, tricyclohexylphosphine [1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazol-2-ylidene][benzylidene]ruthenium (IV) dichloride **1** is commercially available from Strem Chemicals. Prostaglandin A<sub>1</sub> ethyl ester and Corey lactone diol **4** were purchased from Cayman Chemical. (*R*)-2-Aminobut-3-en-1-ol, benzoate salt was purchased from Acros Organics. All reactions were performed in predried glassware under Ar. Olefin metathesis reaction was first optimized at a 50 mg level of the sample and scaled down further at an 1 mg ~  $\mu\text{g}$  level of the sample. Purification was performed either by column chromatography using ICN silica gel (32-63 mesh) or by preparative TLC using silica gel plate, 60 F-254, 0.25 mm, E. Merck.  $^1\text{H}$  NMR spectra were obtained on Bruker DMX 300 or 400 MHz spectrometers and are reported in parts per million (ppm) relative to TMS ( $\delta$ ), with coupling constants (*J*) in Hertz (Hz). Low- and high- resolution FAB mass spectra were measured on a JEOL JMS-DX303 HF mass spectrometer using a glycerol matrix and Xe ionizing gas. UV-vis spectra were recorded on a Perkin-Elmer Lambda 40 spectrophotometer, and reported as  $\lambda_{\text{max}}$  [nm] ( $\epsilon_{\text{max}}$  [Lmol<sup>-1</sup>cm<sup>-1</sup>]). The CD spectra were recorded on JASCO-810 spectrophotometer. The CD spectra were measured in millidegrees and normalized into  $\Delta\epsilon_{\text{max}}$  [Lmol<sup>-1</sup>cm<sup>-1</sup>]. Molecular modeling calculations were executed with MacroModel 7.1 package (Schrodinger, Inc., Portland, OR) including Maestro 3.0 as GUI, on a Dell Precision 330 workstation.

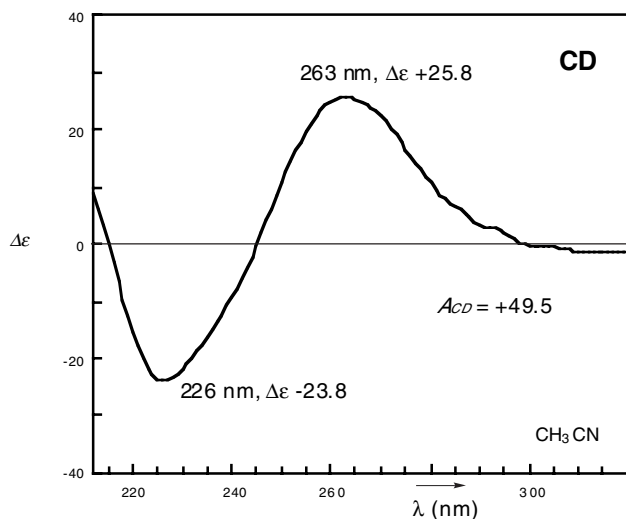
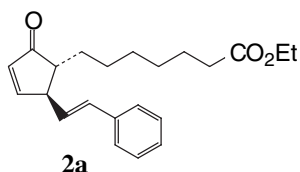
#### Styryl ketone (2a) and styryl *p*-phenylbenzoate (3b).

To a solution of prostaglandin A<sub>1</sub> ethyl ester (100  $\mu\text{g}$ , 270 nmol) in dichloromethane (1 mL) was added Grubbs' second generation ruthenium catalyst **1** (53  $\mu\text{g}$ , 63 nmol) and styrene (310 nL, 2.7  $\mu\text{mol}$ ) at room temperature, and the mixture was stirred at 40 °C for 2 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by preparative thin layer chromatography on silica gel (25 % ethyl acetate

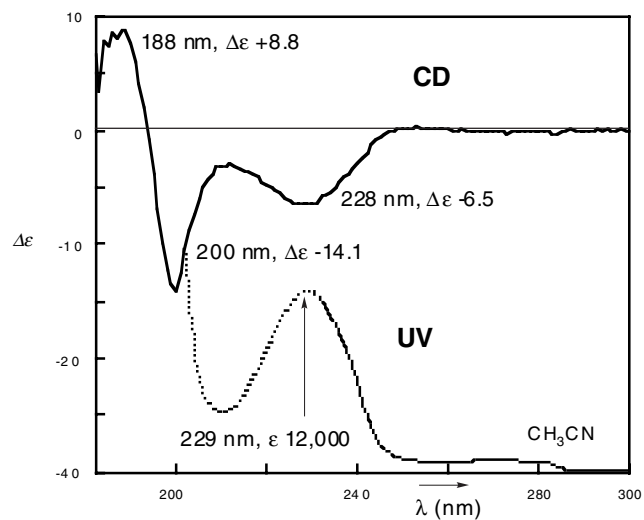
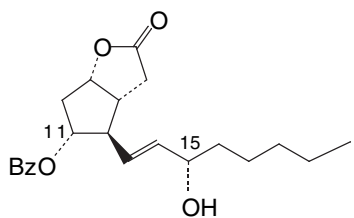
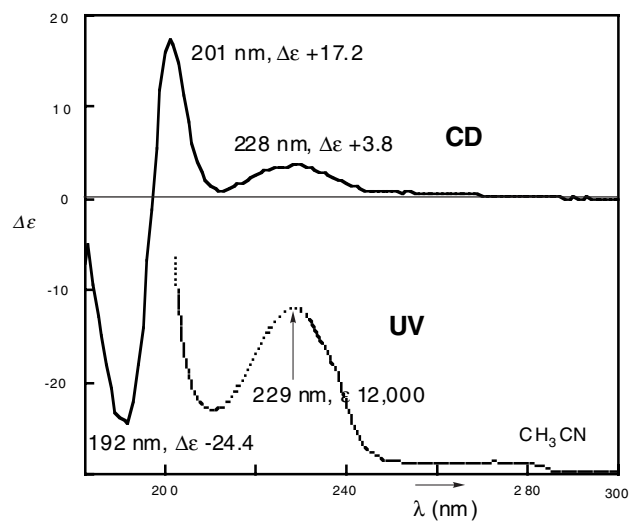
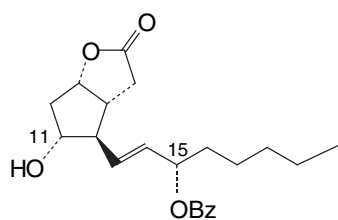
in hexane) to afford the desired styryl ketone **2a** (85 %) and styryl alcohol **2b** (89 %) as yellow oils. The above mentioned procedure of olefin metathesis was first optimized at an 1 mg level of the sample, and the yields for **2a** and **2b** were calculated: Data for **2a**; UV (MeCN) 253 nm ( $\epsilon$  17,000);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  1.22-1.62 (m, 12H) including 1.24 (t, 3H,  $J$  = 7.2 Hz), 1.80-1.88 (m, 1H), 2.15-2.19 (m, 1H), 2.26 (t, 2H,  $J$  = 7.5 Hz), 3.40 (brdd, 1H,  $J$  = 8.4, 2.2 Hz), 4.11 (q, 2H,  $J$  = 7.1 Hz), 6.11 (dd, 1H,  $J$  = 15.8, 8.4 Hz), 6.22 (dd, 1H,  $J$  = 5.6, 2.0 Hz), 6.50 (d, 1H,  $J$  = 15.8 Hz), 7.23-7.37 (m, 5H), 7.54 (dd, 1H,  $J$  = 5.7, 2.5 Hz); HRFABMS calcd for  $\text{C}_{22}\text{H}_{29}\text{O}_3$   $[\text{M}+\text{H}]^+$  341.2117, found 341.2118.

To a solution of the styryl alcohol **2b** (50  $\mu\text{g}$ , 240 nmol) obtained above in dichloromethane (1 mL) was added *p*-phenylbenzoic acid (53  $\mu\text{g}$ , 270 nmol), EDC (80  $\mu\text{g}$ , 420 nmol), and DMAP (36  $\mu\text{g}$ , 290 nmol) at room temperature, and the mixture was stirred for 15 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by preparative thin layer chromatography on silica gel (25 % ethyl acetate in hexane) to afford the styryl benzoate **3b** (80 %) as a white solid: CD ( $\text{CHCl}_3$ ) 275 nm,  $\Delta\epsilon$  +9.8, 250 nm,  $\Delta\epsilon$  -9.4 ( $A_{\text{CD}}$  = +19.2); UV (MeCN) 265 nm ( $\epsilon$  30,000);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  0.89 (t, 3H,  $J$  = 6.9 Hz), 1.25-1.57 (m, 6H), 1.77-1.96 (m, 2H), 5.68 (dt, 1H,  $J$  = 6.8, 6.8 Hz), 6.26 (dd, 1H,  $J$  = 15.9, 7.2 Hz (7.2 Hz in  $\text{CD}_3\text{CN}$ ), 6.71 (d, 1H,  $J$  = 16.0 Hz), 7.25 (d, 1H,  $J$  = 5.4 Hz), 7.31 (dd, 2H,  $J$  = 7.8, 7.8 Hz), 7.38-7.41 (m, 3H), 7.47 (dd, 2H,  $J$  = 7.9, 7.9 Hz), 7.63 (d, 2H,  $J$  = 7.2 Hz), 7.67 (d, 2H,  $J$  = 8.2 Hz), 8.15 (d, 2H,  $J$  = 8.2 Hz); HRFABMS calcd for  $\text{C}_{27}\text{H}_{28}\text{O}_2$   $[\text{M}]^+$  384.2090, found 384.2097.

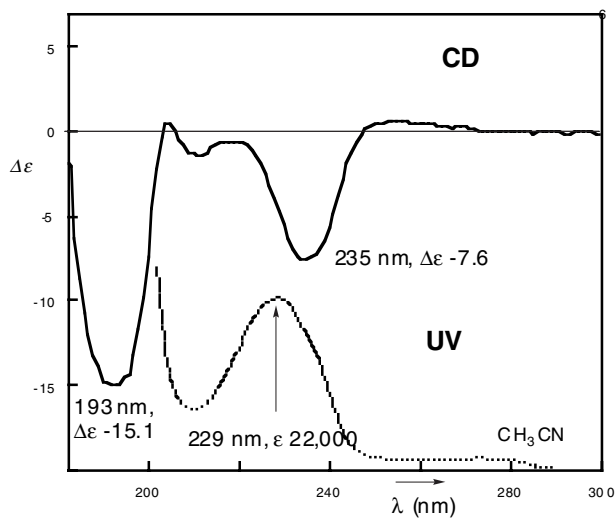
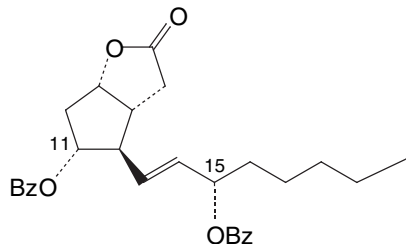
#### CD spectrum of **2a** (after subtraction of CE of $\text{PGA}_1$ ethyl ester).



# CD spectra of C-15 allylic and C-11 homoallylic monobenzoates.



### CD spectrum of C-11, 15 dibenzoate.



### Styryl *p*-phenylbenzoate (**6a**).

To a solution of Corey lactone diol **4** (10  $\mu$ g, 37 nmol) in dichloromethane (0.5 mL) was added Grubbs' second generation ruthenium catalyst **1** (20  $\mu$ g, 24 nmol) and styrene (1 drop) at room temperature, and the mixture was stirred at 40  $^{\circ}$ C for 1 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by preparative thin layer chromatography on silica gel (25 % ethyl acetate in hexane) to afford the styryl alcohols **5a** (66 %) and **2b** (63 %) as yellow oils, which were respectively acylated without further purification. The above mentioned olefin metathesis was optimized first at a 50 mg and an 1 mg level of the sample and the yields for **5a** and **2b** were calculated.

To a solution of the styryl alcohol **5a** obtained (100  $\mu$ g, 410 nmol) in dichloromethane (1 mL) was added *p*-phenylbenzoic acid (89  $\mu$ g, 450 nmol), EDC (130  $\mu$ g, 700 nmol), and DMAP (60  $\mu$ g, 490 nmol) at room temperature, and the mixture was stirred for 18 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by preparative thin layer chromatography on silica gel (33 % ethyl acetate in hexane) to afford the desired styryl *p*-phenylbenzoate **6a** (170  $\mu$ g, quant.) as a white solid: UV (MeCN) 264 nm ( $\epsilon$  30,000);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  2.30 (ddd, 1H,  $J$  = 15.6, 5.2, 2.0 Hz), 2.56-2.72 (m, 2H), 2.87-2.92 (m, 3H), 5.12 (ddd, 1H,  $J$  = 4.8, 4.8, 4.8 Hz), 5.37 (ddd, 1H,  $J$  = 11.6, 5.6, 5.6 Hz), 6.09 (dd, 1H,  $J$  = 15.6, 7.2 Hz),

6.55 (d, 1H,  $J = 16.0$  Hz), 7.22-7.25 (m, 1H), 7.29-7.40 (m, 5H), 7.47 (dd, 2H,  $J = 5.6, 5.6$  Hz), 7.61 (d, 2H,  $J = 6.8$  Hz), 7.66 (d, 2H,  $J = 8.4$  Hz), 8.10 (d, 2H,  $J = 8.8$  Hz); HRFABMS calcd for  $C_{28}H_{25}O_4$   $[M+H]^+$  425.1753, found 425.1775.

***p*-Methoxystyryl *p*-dimethylaminobenzoate (8a) and *p*-methoxystyryl *p*-methoxycinnamate (8b).**

To a solution of Corey lactone diol **4** (100  $\mu$ g, 370 nmol) in dichloromethane (1 mL) was added Grubbs' second generation ruthenium catalyst **1** (36  $\mu$ g, 42 nmol) and *p*-methoxystyrene (500 nL, 3.7  $\mu$ mol) at room temperature, and the mixture was stirred at 40 °C for 3 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by preparative thin layer chromatography on silica gel (25 % ethyl acetate in hexane) to afford the *p*-methoxystyryl alcohol **7b** (73 %) as a yellow oil and crude **7a** which was again purified by preparative thin layer chromatography on silica gel (67 % ethyl acetate in hexane, 61 % as a white solid). *p*-Methoxystyryl alcohols **7a** and **7b** were acylated without further purification, respectively. The above mentioned procedure of olefin metathesis was first optimized at a 50 mg level of the sample and the yields for **7a** and **7b** were calculated.

To a solution of the *p*-methoxystyryl alcohol **7a** thus obtained (9.5 mg, 35  $\mu$ mol) in acetonitrile (1 mL) was added *p*-dimethylaminobenzoylimidazole (7.8 mg, 36  $\mu$ mol), and DBU (5.3  $\mu$ L, 36  $\mu$ mol) at room temperature. After the reaction mixture was stirred for 3 h at this temperature,  $H_2O$  was added, and the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over  $Na_2SO_4$ , filtered and concentrated *in vacuo* to give the crude products, which were purified by column chromatography on silica gel (from 40 % to 67 % ethyl acetate in hexane) to afford the *p*-methoxystyryl *p*-dimethylaminobenzoate **8a** (13 mg, 89 %) as a white solid: UV (MeCN) 310 nm ( $\epsilon$  27,700), 264 nm ( $\epsilon$  21,300);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  2.24 (ddd, 1H,  $J = 15.4, 4.6, 1.4$  Hz), 2.54-2.65 (m, 2H), 2.84-2.93 (m, 3H), 3.03 (s, 6H), 3.80 (s, 3H), 5.11 (ddd, 1H,  $J = 5.0, 5.0, 5.0$  Hz), 5.29 (ddd, 1H,  $J = 10.4, 5.3, 5.3$  Hz), 5.92 (dd, 1H,  $J = 15.8, 7.2$  Hz), 6.46 (d, 1H,  $J = 15.9$  Hz), 6.64 (d, 2H,  $J = 9.0$  Hz), 6.84 (d, 2H,  $J = 8.7$  Hz), 7.27 (d, 2H,  $J = 8.9$  Hz), 7.86 (d, 2H,  $J = 8.9$  Hz); HRFABMS calcd for  $C_{25}H_{28}NO_5$   $[M+H]^+$  422.1967, found 422.1950.

To a solution of the *p*-methoxystyryl alcohol **7b** obtained above (4.0 mg, 17  $\mu$ mol) in dichloromethane (2 mL) was added *p*-methoxycinnamic acid (3.3 mg, 19  $\mu$ mol), EDC (5.6 mg, 29  $\mu$ mol), and DMAP (2.5 mg, 20  $\mu$ mol) at room temperature, and the mixture was stirred for 33 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by preparative thin layer chromatography on silica gel (25 % ethyl acetate in hexane) to afford the corresponding *p*-methoxystyryl *p*-methoxycinnamate **8b** (6.2 mg, 92 %) as a yellow oil: UV (MeCN) 307 nm ( $\epsilon$  23,700), 298 nm ( $\epsilon$  23,900), 269 nm ( $\epsilon$  22,700);  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  0.89 (t, 3H,  $J = 6.8$  Hz), 1.26-1.42 (m, 6H), 1.67-1.85 (m, 2H), 3.80 (s, 3H), 3.84 (s, 3H), 5.51 (dt, 1H,  $J = 6.8, 6.8$  Hz), 6.05 (dd, 1H,  $J = 15.9, 7.4$  Hz (7.2 Hz in  $CD_3CN$ ), 6.33 (d, 1H,  $J = 15.9$  Hz), 6.59 (d, 1H,  $J = 15.9$  Hz), 6.84 (d, 2H,  $J = 8.7$  Hz), 6.90 (d, 2H,  $J = 8.7$  Hz), 7.32 (d, 2H,  $J = 8.7$  Hz), 7.48 (d, 2H,  $J = 8.7$  Hz), 7.65 (d, 1H,  $J = 16.0$  Hz); HRFABMS calcd for  $C_{25}H_{30}O_4$   $[M]^+$  394.2144, found 394.2138.

## Styryl naphthimides.

To a solution of (*R*)-2-aminobut-3-en-1-ol, benzoate salt **9** (30 mg, 140  $\mu$ mol) in pyridine (1 mL) was added 2,3-naphthalenedicarboxylic acid anhydride (31 mg, 160  $\mu$ mol) at room temperature.<sup>1</sup> After the reaction mixture was stirred at 80 °C for 10 h, saturated aqueous CuSO<sub>4</sub> solution was added, and the resulting mixture was extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated *in vacuo* to give the crude products, which were purified by column chromatography on silica gel (from 25 % to 50 % ethyl acetate in hexane) to give the corresponding naphthimide (31 mg, 81 %) as a white solid: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.86 (brs, 1H), 4.02 (dd, 1H, *J* = 11.7, 4.3 Hz), 4.21 (dd, 1H, *J* = 11.6, 7.6 Hz), 5.00-5.05 (m, 1H), 5.285-5.295 (m, 1H), 5.32-5.33 (m, 1H), 6.21 (ddd, 1H, *J* = 17.2, 10.3, 6.9 Hz), 7.68-7.72 (m, 2H), 8.02-8.06 (m, 2H), 8.32 (s, 2H); HRFABMS calcd for C<sub>16</sub>H<sub>14</sub>NO<sub>3</sub> [M+H]<sup>+</sup> 268.0974, found 268.0989.

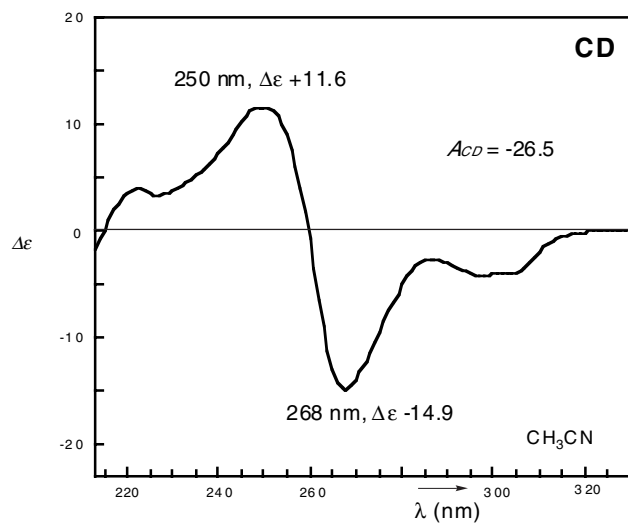
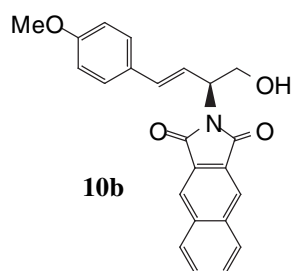
### Styryl naphthimide (**10a**, X = H).

To a solution of the naphthimide obtained above (6 mg, 22  $\mu$ mol) in dichloromethane (1 mL) was added Grubbs' second generation ruthenium catalyst **1** (4.3 mg, 5.1  $\mu$ mol) and styrene (X = H) (26  $\mu$ L, 220  $\mu$ mol) at room temperature, and the mixture was stirred at 40 °C for 10 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by column chromatography on silica gel (from 25 % to 40 % ethyl acetate in hexane) to give the desired styryl naphthimide **10a** (X = H) (6.5 mg, 84 %) as a yellow oil: CD (MeCN) 266 nm,  $\Delta\epsilon$  -18.4, 245 nm  $\Delta\epsilon$  +10.5 (*A<sub>CD</sub>* = -28.9); UV (MeCN) 260 nm ( $\epsilon$  52,000); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>)  $\delta$  2.68 (dd, 1H, *J* = 8.6, 3.9 Hz), 4.03-4.12 (m, 1H), 4.25 (m, 1H), 5.16 (ddd, 1H, *J* = 7.4, 7.4, 4.6 Hz), 6.61 (dd, 1H, *J* = 15.9, 7.1 Hz), 6.69 (d, 1H, *J* = 15.9 Hz), 7.19-7.51 (m, 5H), 7.65-7.70 (m, 2H), 8.01-8.05 (m, 2H), 8.31 (s, 2H); HRFABMS calcd for C<sub>22</sub>H<sub>18</sub>NO<sub>3</sub> [M+H]<sup>+</sup> 344.1286, found 344.1305.

### *p*-Methoxystyryl naphthimide (**10b**, X = -OMe).

To a solution of the naphthimide (10  $\mu$ g, 37 nmol) in dichloromethane (1 mL) was added Grubbs' second generation ruthenium catalyst **1** (20  $\mu$ g, 24 nmol) and *p*-methoxystyrene (X = OMe) (1 drop) at room temperature, and the mixture was stirred at 40 °C for 12 h. The reaction mixture was concentrated *in vacuo* to give the crude products which were purified by preparative thin layer chromatography on silica gel (25 % ethyl acetate in hexane) to afford to give the desired *p*-methoxystyryl naphthimide **10b** (X = OMe) (61 %) as a yellow oil. The procedure of olefin metathesis was first optimized at a 2 mg level of the sample and the yield for **10b** (X = OMe) was calculated: UV (MeCN) 260 nm ( $\epsilon$  54,000); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  2.69 (brs, 1H), 3.79 (s, 3H), 4.07 (dd, 1H, *J* = 4.4, 11.6 Hz), 4.23 (brs, 1H), 5.14 (ddd, 1H, *J* = 4.8, 7.6, 7.6 Hz), 6.50 (dd, 1H, *J* = 16.0, 8.0 Hz (7.6 Hz in CD<sub>3</sub>CN), 6.66 (d, 1H, *J* = 16.0 Hz), 6.83 (d, 2H, *J* = 8.8 Hz), 7.34 (d, 2H, *J* = 8.8 Hz), 7.69-7.72 (m, 2H), 8.04-8.07 (m, 2H), 8.34 (s, 2H); HRFABMS calcd for C<sub>23</sub>H<sub>20</sub>NO<sub>4</sub> [M+H]<sup>+</sup> 374.1392, found 374.1402.

### CD spectrum of 10b.



### Reference

1. Kawamura, A.; Berova, N.; Dirsch, V.; Mangoni, A.; Nakanishi, K.; Schwartz, G.; Bielawska, A.; Hannun, Y.; Kitagawa, I. *Bioorg. Med. Chem.* **1996**, *4*, 1035-1043.