

Supporting Information

Enantioselective Photocycloaddition Mediated by Chiral Brønsted Acids: Asymmetric Synthesis of the Rocaglamides

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I) Experimental Section

a) General Information:

¹H NMR spectra were recorded at 400 MHz at ambient temperature with CDCl₃ as solvent unless otherwise stated. ¹³C NMR spectra were recorded at 75 or 100 MHz at ambient temperature with CDCl₃ as solvent unless otherwise stated. (¹H NMR and ¹³C of TADDOLs derivatives were recorded on a 400 MHz Bruker DPX Spectrometer. The ¹³C resonance frequency is 100 MHz). Chemical shifts are reported in parts per million relative to CDCl₃ (¹H, δ 7.24; ¹³C, δ 77.0), DMSO-d₆ (¹H, δ 2.49; ¹³C, δ 39.7) or CD₃OD (¹H, δ 3.35, 4.78; ¹³C, δ 49.3). Data for ¹H NMR are reported as follows: chemical shift, integration, multiplicity (app = apparent, par obs = partially obscure, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants. All ¹³C NMR spectra were recorded with complete proton decoupling.

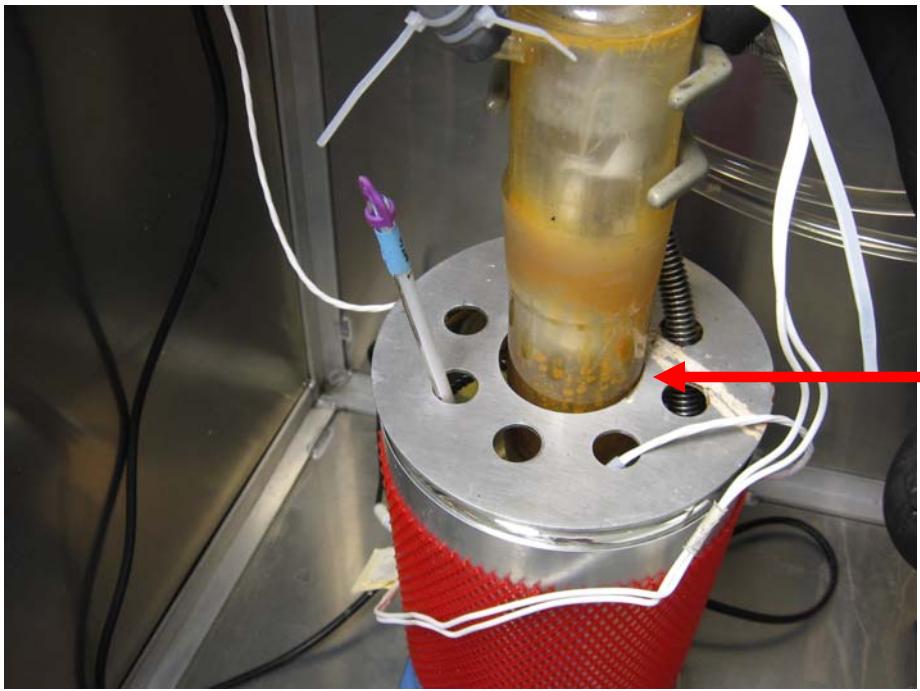
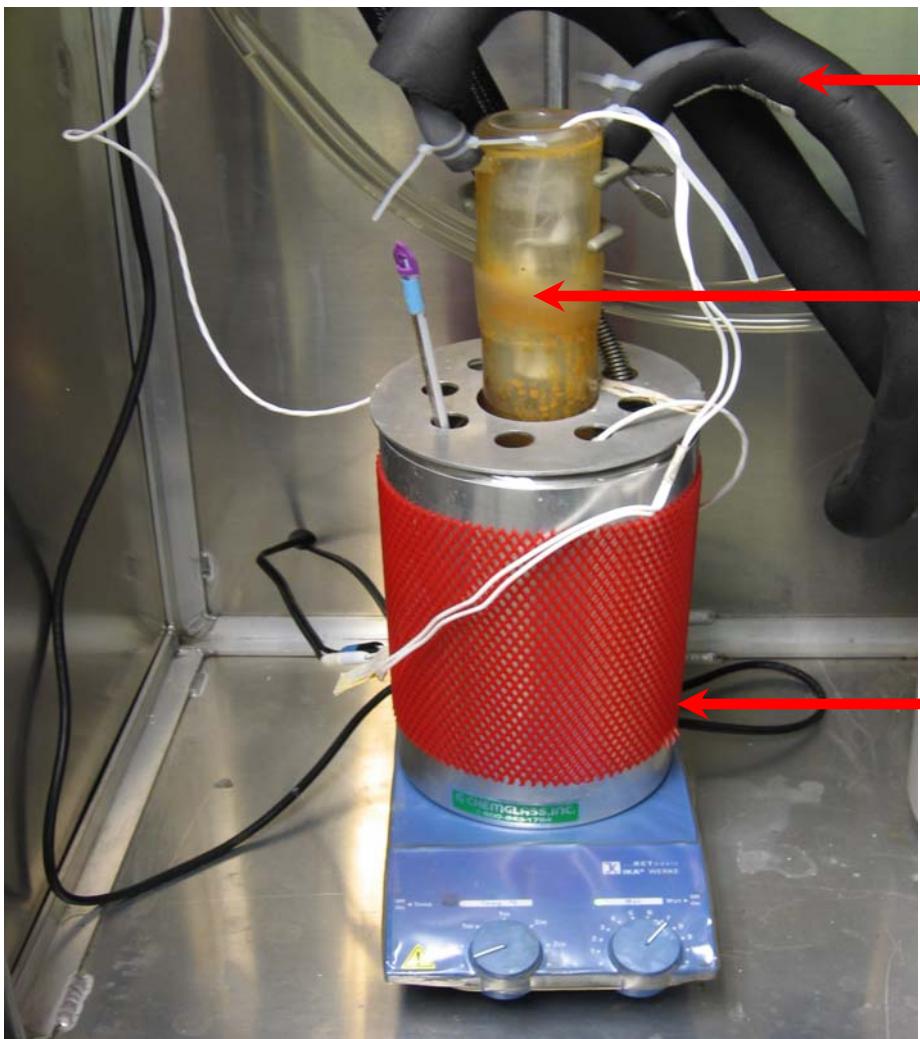
Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. The comparison of OH stretching frequencies (S34) were recorded Thermo/Nicolet Nexus 470 FT-IR. The sample cell was a Crystal Labs model SL-3 FTIR NaCl 0.1 mm pathlength cell.

Low and high-resolution mass spectra were obtained in the Boston University Mass Spectrometry Laboratory using a Waters Q-TOF API US.

HPLC analyses are performed using an Agilent 1100 series HPLC (Chiracel OD, Column No. OD00CE-AI015 and Regis, Pirkle Covalent (R,R) Whelk-01 column). Melting points were recorded on a Mel-Temp apparatus (Laboratory Devices). Analytical thin layer chromatography was performed using 0.25 mm silica gel 60-F plates. Flash chromatography was performed using 200-400 mesh silica gel (Scientific Absorbents, Inc.). Yields refer to chromatographically and spectroscopically pure materials, unless otherwise stated.

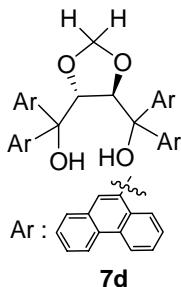
Methylene chloride, acetonitrile, methanol, and benzene were purified by passing through two packed columns of neutral alumina (Innovative Technology, Inc, Newburyport, MA).

Photochemistry experiments were performed using a Hanovia 450 W medium pressure mercury lamp housed in quartz immersion coded with a Thermo Neslab-ULT 80 system circulator. Pyrex test tubes (16 x 100 mm) were mounted on a support approximately 0.5 cm from the immersion well lamp. A uranium filter ($\text{h}\nu > 350 \text{ nm}$) was obtained from James Glass (Hanover, MA). All other reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise noted.



b) Detailed procedures for the preparation of TADDOL derivatives

Compounds **7a** and **7b** were purchased from Strem and used without purification. Compounds **7c**, was prepared according to a literature reference.^{S1}



Preparation of **7d** from (S, S)-dimethyl tartrate. (S, S)-methylene- α - α - α' - α' -tetraphenanthren-9-yl-1,3-dioxolane-4,5-dimethanol **7d**.

To a solution of *L*-dimethyltartrate (1g, 5.6 mmol, 1 equiv) in EtOAc (10 mL) was added dimethoxymethane (600 μ L, 6.7 mmol, 1.2 equiv) and BF₃.Et₂O (1.78 mL, 14 mmol, 2.5 equiv). The resulting mixture was then refluxed for 7 h. The reaction was then cooled to rt and carefully quenched with saturated NaHCO₃. The organic layer was then washed with water (2 X 10 mL) and brine (1 X 10 mL). After drying over

MgSO₄, filtration, and concentration *in vacuo*, the resulting yellow oil was purified on silica gel (90:10, hexane:EtOAc) to afford 0.94 g (5 mmol, 86 %) of dimethyl 2,3-*O*-methylene-*L*-tartrate as a colorless oil which was spectroscopically identical to a previous reported compound.^{S2} A solution 0.8 g of dimethyl 2,3-*O*-methylene-*L*-tartrate (4.2 mmol) in THF (5 mL) was added dropwise to solution of (phenanthren-9-yl)magnesium bromide (21 mmol, prepared from 5.41 g of 9-bromophenanthrene and 0.50 g of Mg powder and catalytic amount of iodine) in THF (80 mL) at rt. The reaction mixture was then stirred at rt for 12 h. The reaction was quenched by careful addition of saturated NH₄Cl. The organic layer was separated and the aqueous layer extracted twice with ether (2 X 50 mL). After the combined organic layers were dried using MgSO₄, the solvent was removed *in vacuo* to afford a yellow oil. Purification *via* flash chromatography (80:20 hexanes/EtOAc) afforded a white solid which was then submitted to precipitation using benzene/hexane (1/1, ca, 60 mL). and dried under high *vacuum* for 5 h. 2.54 g (3 mmol, 72 %) of **7d** was isolated as a white solid.

White solid: mp 237-239°C;

$[\alpha]_D^{22} = +343^\circ$ ($c = 1.04$, CHCl₃);

IR ν_{\max} (film): 3550, 3060, 2888, 1496, 1448, 1108, 1056, 958 cm⁻¹;

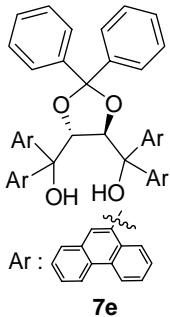
¹H NMR (400 MHz, DMSO-d₆, 421 K) δ 8.80-8.10 (8 H, m), 7.90 (1 H, s), 7.70-6.70 (9 H, m), 6.20 (1 H, s), 4.70 (1 H, s) ppm;

¹³C NMR (100 MHz, DMSO-d₆, 421 K) δ 139.3, 131.9, 131.6, 131.5, 131.0, 130.8, 130.7, 129.8, 129.6, 129.2, 128.6, 128.3, 127.8, 127.5, 127.4, 127.2, 126.2, 126.1, 125.8, 125.7, 123.9, 123.5, 123.2, 123.1, 98.6, 83.3 ppm;

LRMS (APPI+) m/z calculated for C₆₁H₄₂O₄ 838.98 found 821.30 (M-18).

^{S1} Cuenca, A.; Medio-Simon, M.; Aguilar, G. A.; Weibel, D.; Beck, A. K.; Seebach, D. *Helv. Chim. Acta*. **2000**, 83, 3153-3162.

^{S2} Beck, A. K.; Bastani, B.; Plattner, D. A.; Petter, W.; Seebach, D.; Braunschweiger, H.; Gysi, P.; La Vecchia, L. *Chimia*, **1991**, 45, 238-241.



(S, S)-diphenyl- α - α - α' - α' -tetraphenanthren-9-yl-1,3-dioxolane-4,5-dimethanol 7e To a 50 mL round-bottomed flask equipped with a distillation apparatus was added *L*-dimethyl tartrate (0.5 g, 2.8 mmol, 1 equiv), dimethoxydiphenylmethane (0.66 g, 3.1 mmol, 1.1 equiv) and a catalytic amount of *p*-TsOH following by 15 mL of anhydrous benzene. The resulting mixture was refluxed until the azeotrope benzene-water was removed (\sim 80°C). After cooling the mixture to room temperature, the solution was diluted in EtOAc and the organic layer was washed with a saturated NaHCO₃ solution (1 X 15 mL),

water (1 X 15 mL), and brine (1 X 15 mL). The organic layer was dried over MgSO₄, filtered, and evaporated in *vacuo* to afford a brown oil. The resulting oil is then purified *via* flash chromatography (90:10, hexane:EtOAc) to afford diphenyl acetal tartrate (0.578 g, 1.60 mmol, 60 %) as a white solid which was spectroscopically identical to a previous reported compound.^{S3} A solution 0.72 g of 2,2-diphenyl-[1,3]dioxolane-4,5-dicarboxylic acid dimethyl ester (2.0 mmol, 1 equiv) in THF (10 mL) was added dropwise to solution of (phenanthren-9-yl)magnesium bromide (10 mmol, 5 equiv) prepared from 2.7 g of 9-bromophenanthrene and 0.25 g of Mg powder and catalytic amount of iodine) in THF (40 mL) at rt. The reaction mixture was then stirred at rt for 12 h. The reaction was quenched by careful addition of a saturated NH₄Cl. The organic layer was separated and the aqueous layer extracted twice with ether (2 X 50 mL). After the combined organic layers were dried using MgSO₄, the solvent was removed in *vacuo* to afford a yellow oil. Purification *via* flash chromatography (80:20 hexanes/EtOAc) afforded a white solid which was then submitted to recrystallization using benzene/hexanes (1/1 ca, 40 mL). After drying under high *vacuum* for 5 h, 1.48 g (1.5 mmol, 75 %) of 7e was isolated as a white solid.

White solid: mp 314-317°C;

$[\alpha]_D^{22} = +519^\circ$ (c = 1.3, CHCl₃);

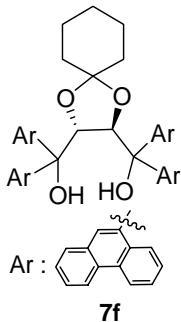
IR ν_{max} (film): 3548, 3060, 1497, 1450, 1223, 1103, 896 cm⁻¹;

¹H NMR (400 MHz, DMSO-d₆, 421 K) δ 8.70-8.20 (6 H, m), 7.80 (1 H, s), 7.70-7.50 (6 H, m), 7.30-7.10 (4 H, m), 7.0-6.70 (6 H, m) ppm;

¹³C (100 MHz, DMSO-d₆, 421 K) δ 143.9, 139.8, 138.2, 131.9, 131.8, 131.7, 131.6, 131.3, 131.0, 130.9, 129.8, 129.6, 129.4, 129.0, 128.9, 128.3, 128, 127.9, 127.8, 127.5, 127.3, 126.4, 126.1, 126.0, 125.9, 125.6, 125.5, 123.6, 123.4, 123.3, 123.1, 111.3, 84.9, 81.8 ppm;

HRMS (APPI+) m/z calculated for C₇₃H₅₀O₄ 991.1757 found 1013.3808 (M+Na).

^{S3} a) Altava, B.; Burguete, M. I.; Garcia-Verdugo, E.; Luis, S. V.; Miravet, J. F.; Vincent, M. J.; *Tetrahedron: Asymmetry* **2000**, *11*, 4885-4893. b) Irrure, J.; Alonso-Alija, C.; Piniella, J. F.; Alvarez-Larena, A. *Tetrahedron: Asymmetry* **1992**, *3*, 1591-1596.



Preparation of 7f from (S, S)-dimethyl tartrate. (S, S)-cyclohexyl- α - α '- α '-tetraphenanthren-9-yl-1,3-dioxolane-4,5-dimethanol 7f.

To a solution of *L*-dimethyltartrate (2 g, 11.2 mmol, 1 equiv) in EtOAc (10 mL) was added cyclohexanone (1.39 mL, 13.5 mmol, 1.2 equiv) and BF₃.Et₂O (3.54 mL, 28 mmol, 2.5 equiv). The resulting mixture was then refluxed for 7 h. The reaction was then cooled to rt and carefully quenched with a solution of a saturated aqueous NaHCO₃. The organic layer was then washed with water (2 X 10 mL) and brine (1 X 10 mL). After drying over MgSO₄, filtration, and

concentration *in vacuo*, the resulting yellow oil was purified on silica gel (90:10, hexane:EtOAc) to afford 2.17 g (8 mmol, 75 %) of dimethyl 2,3-*O*-cyclohexene-*L*-tartrate as an colorless oil which was spectroscopically identical to previous reported compound.^{S2} A solution 1.00 g of dimethyl 2,3-*O*-cyclohexene-*L*-tartrate (3.87 mmol, 1 equiv) in THF (10 mL) was added dropwise to solution of (phenanthren-9-yl)magnesium bromide (19.4 mmol, 5 equiv, (prepared from 4.98 g of 9-bromophenanthrene and 0.46 g of Mg powder and catalytic amount of iodine in THF (70 mL) at rt.) The reaction mixture was then stirred at rt for 12 h. The reaction was quenched by careful addition of a saturated NH₄Cl solution. The organic layer was separated and the aqueous layer was extracted twice with ether (2 X 50 mL). After the combined organic layers were dried using MgSO₄, the solvent was removed *in vacuo* to afford a yellow oil. Purification *via* flash chromatography (80:20 hexanes/EtOAc) afforded a white solid which was then precipitated using methanol/CH₂Cl₂ (1/1, ca, 40 mL). After drying under high *vacuum* for 5 h, 1.61 g (1.77 mmol, 46 %) of 7f was isolated as a white solid.

White solid: mp 275-277°C;

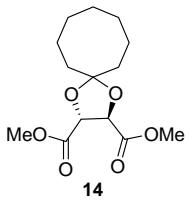
$[\alpha]_D^{22} = +79^\circ$ (c = 2.0, CHCl₃);

IR ν_{\max} (film): 3566, 3369, 3061, 2934, 2856, 1443, 1218, 1111, 1051, 896 cm⁻¹;

¹H NMR (400 MHz, DMSO-d₆, 406 K) δ 8.8-8.7 (12 H, m), 8.33-8.27 (4 H, m), 8.08 (2 H, m), 7.95 (2 H, m), 7.60 (10 H, m), 7.3 (4 H, m), 7.06 (1 H, m), 6.78 (1 H, m), 5.05 (2 H, s), 0.95 (4 H, m), 0.55 (2 H, m), 0.23 (2 H, m) ppm;

¹³C NMR (100 MHz, DMSO-d₆, 406 K) δ 141.3, 138.8, 132.6, 131.9, 131.8, 131.5, 131.0, 129.8, 129.7, 129.5, 128.3, 128.0, 127.8, 127.7, 127.4, 126.6, 126.4, 126.3, 126.1, 125.6, 123.7, 123.4, 123.3, 111.2, 82.4, 81.1, 49.5, 36.8, 25.0, 24.2 ppm;

HRMS (APPI+) m/z calculated for C₆₆H₅₀O₄ 907.1008 found 929.3607 (M+Na).



Dimethyl 2,3-O-cyclooctyl-L-tartrate 14. To a solution of *L*-dimethyltartrate (1.5 g, 8.43 mmol, 1 equiv) in EtOAc (10 mL) was added cyclooctanone (1.22 mL, 9.27 mmol, 1.1 equiv) and $\text{BF}_3\cdot\text{Et}_2\text{O}$ (2.67 mL, 21.08 mmol, 2.5 equiv). The resulting mixture was then refluxed for 7 h. The reaction was then cooled at rt and carefully quenched with a solution of a saturated NaHCO_3 . The organic layer was then washed with water (2 X 10 mL) and brine (1 X 10 mL). After drying over MgSO_4 , filtration, concentration *in vacuo*, the resulting yellow oil was purified on silica gel (90:10, hexane:EtOAc) to afford 2.10 g (7.3 mmol, 87 %) of dimethyl 2,3-O-cyclooctene-*L*-tartrate **14** as a colorless oil

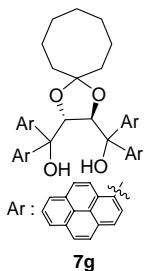
$$[\alpha]_D^{22} = -0.23^\circ (\text{c} = 1.4, \text{CHCl}_3)$$

IR ν_{max} (film): 2924, 2849, 1755, 1440., 1271, 1108, 966 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 4.63 (2H, s), 3.68 (6H, s), 1.77 (3H, m), 1.50-1.42 (11H, m) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 118.2, 76.9, 52.8, 34.7, 27.9, 24.5, 22.1 ppm;

HRMS (EI) m/z calculated for $\text{C}_{14}\text{H}_{22}\text{O}_6$ 286.1416 found 309.1427 ($\text{M}+\text{Na}$).



Preparation of (S, S)-cyclooctyl-a-a-a'-a'-tetraphenanthren-9-yl-1,3-dioxolane-4,5-dimethanol 7g. A solution 0.33 g of dimethyl 2,3-O-cyclooctene-*L*-tartrate **13** (1.15 mmol) in THF (5 mL) was added dropwise to solution of (pyren-1-yl)magnesium bromide (5.77 mmol, prepared from 1.62 g of 1-bromopyrene and 0.14 g of Mg powder and catalytic amount of iodine in THF (15 mL) at rt). The reaction mixture was then stirred at rt for 24 h. The reaction was quenched by careful addition of saturated aqueous NH_4Cl . The organic layer was separated and the aqueous layer was extracted twice with ether (2 X 50 mL). After the combined organic layers were dried using MgSO_4 , the solvent was removed *in vacuo* to afford a yellow oil. Purification *via* flash chromatography (80:20 hexanes/EtOAc) afforded a white solid which was then precipitated using toluene/hexane (1/1, ca, 30 mL). After drying under high *vacuum* for 5 h, 0.30 g (0.29 mmol, 25 %) of **7g** was isolated as a yellow white powder.

Yellow white powder: mp 286°C;

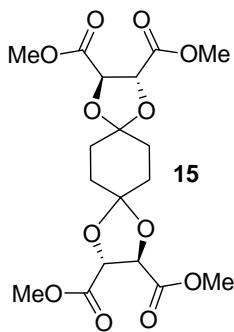
$$[\alpha]_D^{22} = -89^\circ (\text{c} = 1.2, \text{CHCl}_3);$$

IR ν_{max} (film): 3560, 3352, 3041, 2923, 1456, 1213, 1112, 1050, 976 cm^{-1} ;

^1H NMR (400 MHz, DMSO-d_6 , 406 K) δ 9.10 (1 H, m), 8.60 (1 H, m), 8.40-7.80 (14 H, m), 7.50 (1 H, m), 7.30 (1 H, m), 5.80 (1 H, s), 1.20-0.5 (8 H, m) ppm;

^{13}C (100 MHz, DMSO-d_6 , 406 K) δ 142.1, 139.9, 131.9, 131.7, 131.6, 131.5, 131.0, 130.7, 130.1, 128.5, 128.2, 128.0, 126.8, 126.7, 126.6, 126.3, 126.2, 125.8, 125.6, 125.3, 125.2, 125.0, 124.7, 114.1, 82.6, 81.3, 35.7, 27.8, 24.9, 22.2 ppm;

HRMS (APPI+) m/z calculated for $\text{C}_{76}\text{H}_{54}\text{O}_4$ 1031.2396 found 1053.4226 ($\text{M}+\text{Na}$).



1,4,9,12-Tetraoxa-dispiro[4.2.4.2]tetradecane-2,3,10,11-tetracarboxylic acid tetramethyl ester 15. To a solution of *L*-dimethyltartrate (6.675 g, 37.50 mmol, 2.1 equiv) in EtOAc (10 mL) was added cyclohexanedione (2 g, 17.85 mmol, 1.1 equiv) and BF₃.Et₂O (4.97 mL, 39.27 mmol, 2.2 equiv). The resulting mixture was then refluxed for 7 h. The reaction was then cooled to rt and carefully quenched with a solution of a saturated NaHCO₃ solution. The organic layer was then washed with water (2 X 10 mL) and brine (1 X 10 mL). After drying over

MgSO₄, filtration, concentration *in vacuo*, the resulting yellow oil was purified on silica gel (90:10, hexane:EtOAc) to afford 4.50 g (10.4 mmol, 64 %) of 1,4,9,12-Tetraoxa-dispiro[4.2.4.2]tetradecane-2,3,10,11-tetracarboxylic acid tetramethyl ester **15** as a white solid

White solid mp 75-77°C;

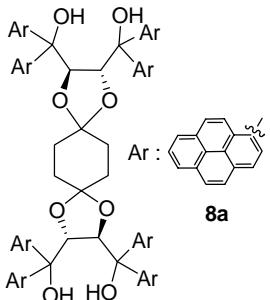
$[\alpha]_D^{22} = -20^\circ$ (c = 1.2, CHCl₃);

IR ν_{\max} (film): 2954, 1758, 1440, 1379, 1223, 1122, 969 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 4.78 (1 H, s), 3.78 (3 H, s), 1.90 (2 H, s) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 170.1, 113.4, 76.9, 52.8, 32.7 ppm;

HRMS (EI) m/z calculated for C₁₈H₂₄O₁₂ 432.1268 found 455.0861 (M+Na).



Preparation of 7b from (S, S)-dimethyl tartrate. (S,S,S,S)-(2)-trans,trans-2,3,10,11-Tetrakis(hydroxydiphenyl-1-ylmethyl)-1,4,9,12-tetraoxadispiro[4.2.4.2]tetradecane 8a. A solution 0.46 g of 1,4,9,12-Tetraoxa-dispiro[4.2.4.2]tetradecane-2,3,10,11-tetracarboxylic acid tetramethyl ester (1.07 mmol, 1 equiv) in THF (5 mL) was added dropwise to solution of (pyren-1-yl)magnesium bromide (10.68 mmol) (prepared from 3 g of 1-bromopyrene and 0.256 g of Mg powder and catalytic amount of iodine in THF (35 mL) at rt). The reaction mixture was then stirred at rt for 24 h. The reaction was quenched by careful addition of a saturated aqueous 1

NH₄Cl. The organic layer was separated and the aqueous layer was extracted twice with ether (2 X 50 mL). After the combined organic layers were dried using MgSO₄, the solvent was removed *in vacuo* to afford a yellow oil. Purification *via* flash chromatography (80:20 hexanes/EtOAc) afforded a white solid which was then submitted twice to precipitation using toluene/hexane (1/1, ca, 30 mL). After drying under high *vacuum* for 5h, 0.60 g (0.35 mmol, 21 %) of **8a** was isolated as a yellow-white solid.

Yellow-white solid: mp 322⁰C;

$[\alpha]_D^{22} = +86^\circ$ (c = 1.1, CHCl₃);

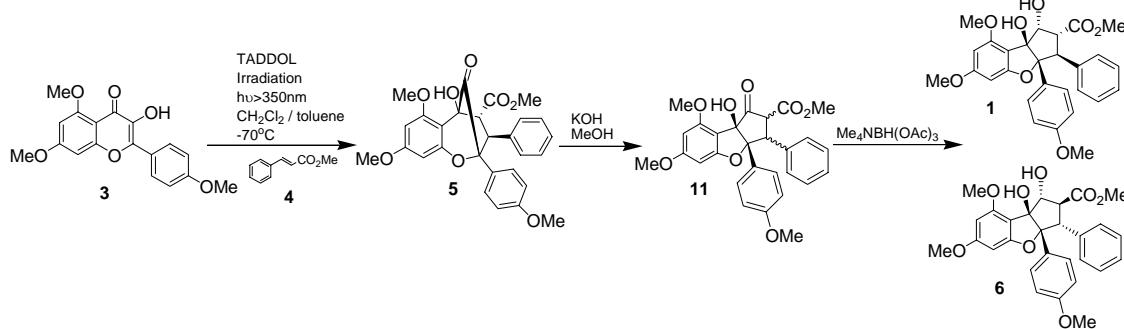
IR ν_{max} (film): 3564, 3354, 3041, 2954, 1378, 1131, 1052, 844 cm⁻¹;

¹H NMR (400 MHz, DMSO-d₆, 421 K) δ 9-7 (72 H, m), 5.80 (4 H, m), 1.48-0.33 (8 H, m) ppm;

¹³C NMR (100 MHz, DMSO-d₆, 421 K) δ 141.6, 139.8, 131.4, 130.8, 130.6, 129.8, 128.2, 128.0, 127.8, 127.7, 126.5, 126.2, 125.6, 125.4, 125.3, 125.2, 124.9, 124.3, 110.6, 82.9, 81.6, 33.7 ppm;

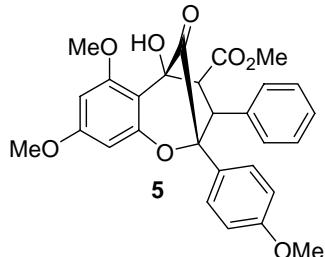
LRMS (APPI+) m/z calculated for C₁₄₂H₈₈O₈ 1920.6479 found 1884.60 (M-2 x H₂O).

c) General procedures for the enantioselective photocycloaddition reaction and preparation of methyl rocaglate



Irradiation of 3-Hydroxyflavone 3 and methyl cinnamate 4 in the presence of TADDOL 7g. To a 16 x 150 mm test tube was added 3-hydroxyflavone 3 (100 mg, 0.30 mmol) and methyl cinnamate 4 (250 mg, 1.54 mmol) and TADDOL derivative 7g (315 mg, 0.31 mmol) in 3 ml of anhydrous CH_2Cl_2 and 7 ml of anhydrous toluene. After degassing with argon for 5 min, the mixture was irradiated for 10h at -70°C using a Hanovia UV lamp uranium filter. The solution was concentrated in *vacuo* to afford a yellow oil. The resulting residue was then triturated with 10 mL of MeOH to precipitate of a yellow-white solid corresponding to the TADDOL derivative 7g. After filtration, the filtrate was dried under *vacuum* to afford a yellow oil and near quantitative recovery of the TADDOL 7g (92 %). Purification *via* flash chromatography (60:40 hexanes/EtOAc) afforded 87 mg (0.26 mmol, 58 %) of trimethoxy cyclopenta[bc]benzopyran 5 (as a diastereomeric mixture of *endo/exo* cyclopenta[bc]benzopyrans) as a white solid.

Trimethoxy cyclopenta[bc]benzopyran 5.



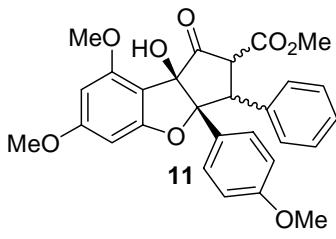
White solid: mp 83-85°C;

IR ν_{max} (film): 3475, 3013, 2943, 2832, 1786, 1737, 1611, 1590, 1510, 1450, 1255, 1146, 1094, 828 cm^{-1} ;

^1H MR (400 MHz, CDCl_3) δ 7.54-7.52 (2 H, d, $J = 8.8$ Hz), 7.25-7.23 (2 H, d, $J = 8.8$ Hz), 7.17-7.49 (2 H, m), 7.10-7.04 (6 H, m), 6.85-6.82 (2 H, m), 6.64-6.60 (4 H, m), 6.19-6.18 (1 H, d, $J = 2$ Hz), 6.18-6.17 (1 H, d, $J = 2$ Hz), 6.11-6.10 (1 H, d, $J = 2$ Hz), 6.08-6.07 (1 H, d, $J = 2$ Hz), 4.49-4.47 (1 H, d, $J = 9.2$ Hz), 4.191-4.168 (1 H, d, $J = 9.2$ Hz), 3.94 (1 H, s), 3.84 (3 H, s), 3.83 (3 H, s), 3.77 (4 H, m), 3.75 (3 H, s), 3.71 (3 H, s), 3.66 (4 H, m), 3.62 (3 H, s), 3.55 (3 H, s), 3.29 (1 H, s);

^{13}C NMR (75 MHz, CDCl_3) δ 205.5, 170.7, 170.6, 161.9, 161.3, 158.8, 158.6, 158.4, 153.6, 152.8, 139.9, 138.1, 130.1, 129.8, 128.9, 128.7, 128.2, 127.8, 127.9, 127.0, 126.5, 125.6, 113.6, 112.7, 112.6, 107.7, 106.5, 97.9, 95.5, 94.4, 94.3, 93.6, 93.4, 92.7, 88.7, 83.6, 81.04, 80.7, 62.4, 57.6, 56.1, 55.9, 55.4, 55.3, 55.1, 54.5, 53.4, 52.2, 51.8 ppm;

HRMS (CI/ NH_3) m/z calculated for $\text{C}_{28}\text{H}_{26}\text{O}_8$ 490.1628 found 491.1739 ($\text{M}+\text{H}$).



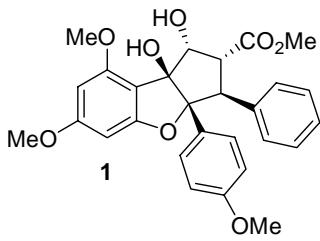
Keto rocaglate 11. To a solution of aglain **5** (87 mg, 0.18 mmol, 1 equiv) in MeOH (10 mL) was added a solution of NaOMe (24 mg, 0.44 mmol, 2.5 equiv) in MeOH (2 mL) at rt. The resulting solution was stirred for 20 min at 60°C. After quenching the reaction with saturated aqueous NH₄Cl, 10 mL of EtOAc was then added, and the organic layer was washed with water (2 X 5 mL) and brine (5 mL). The

organic layer was dried over MgSO₄, filtered, and concentrated *in vacuo* to afford 83 mg (0.17 mmol, 95 %) of crude ketol shift product **11** (as a diastereomeric mixture of *endo/exo* keto rocaglates) as yellow oil which was used without further purification.

IR ν_{\max} (film): 3501, 3006, 2947, 2926, 2839, 1762, 1734, 1615, 1513, 1450, 1440, 1255, 1213, 1146, 1033, 1076 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.34-7.32 (2 H, d, *J* = 6.8 Hz), 7.20-7.19 (2 H, m), 7.09-6.86 (15 H, m), 6.65 (2 H, d, *J* = 8.8 Hz), 6.51 (2 H, d, *J* = 6.8 Hz), 6.33 (1 H, d, *J* = 1.6 Hz), 6.17 (1 H, d, *J* = 1.6 Hz), 6.13 (1 H, d, *J* = 1.6 Hz), 6.12 (1 H, d, *J* = 1.6 Hz), 6.05 (1 H, d, *J* = 1.6 Hz), 6.00 (1 H, d, *J* = 1.6 Hz), 4.46 (1 H, s), 4.42 (1 H, d, *J* = 14.8 Hz), 4.36 (1 H, d, *J* = 14.8 Hz), 4.22 (1 H, d, *J* = 13.6 Hz), 4.04 (1 H, d, 13.6 Hz), 3.84 (3 H, s), 3.08-3.79 (9 H, m), 3.77 (9 H, m), 3.70 (6 H, m), 3.64 (6 H, m), 3.57 (3 H, s), 3.30 (1 H, s), 3.01 (1 H, s) ppm;

HRMS (EI) m/z calculated for C₂₈H₂₆O₈ 490.1628 found 490.9634 (M+H).



Endo methyl rocaglate 1. To a solution of 264 mg (1.00 mmol, 6 equiv) of Me₄NBH(OAc)₃ and 112 μ L (0.5 mmol, 10 equiv) of acetic acid in 3 mL of CH₃CN was added a solution of 82 mg (0.17 mmol, 1 equiv) of the crude ketol shift **11** product in 1 mL of CH₃CN. The resulting green-blue solution was stirred for 3 h at rt before being quenched with 4 mL of saturated aqueous NH₄Cl. The solution was then

treated with 3mL of a 3 M aqueous solution of sodium/potassium tartrate and stirred at rt for 30 min. The aqueous solution was extracted with CH₂Cl₂ (2 X 5 mL). The combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated *in vacuo*. Purification on silica gel (40/60, hexanes/EtOAc) afforded 50 mg (0.10 mmol, 61 %) of the corresponding *endo* methyl rocaglate **1** and 13 mg (0.03 mmol, 16 %) of the corresponding *exo* methyl rocaglate **6**.

Recrystallization of **1** (50 mg) from benzene (600 μ L) / hexanes (100 μ L) afforded 86% (43 mg) recovery of enantiomerically enriched **1** (94% ee) isolated from the mother liquor.

Chiral HPLC analysis of *endo* methyl rocaglate was performed using Regis, Pirkle Covalent (*R*, *R*) Whelk-01 column. Conditions: Gradient, 10 to 60% *i*-PrOH/hexanes, for 30 min, 0.8 mL/min, 210 nm. t = 17.90 min (-)-methyl rocaglate, t = 22.26 min (+)-methyl rocaglate, ee = 94%

White solid: mp 92-93°C;

$[\alpha]_D^{22} = -42^\circ$ (c = 0.98, CHCl₃)^{S4} (94% ee)

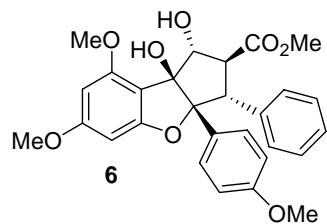
IR ν_{max} (film): 3013, 2954, 2926, 2853, 1734, 1615, 1517, 1457, 1433, 1262, 1195, 1150, 1031, 832 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.09 (2 H, d, J = 9.2 Hz), 7.05-7.03 (3 H, m), 6.84 (2 H, m), 6.65 (2 H, d, J = 9.2 Hz), 6.27 (1 H, d, J = 2 Hz), 6.1 (1 H, d, J = 2 Hz), 5.01 (1 H, dd, J = 6.4, 1.2 Hz), 4.28 (1 H, d, J = 14.4 Hz), 3.80 (1 H, dd, J = 14.4, 6.4 Hz), 3.86 (3 H, s), 3.82 (3 H, s), 3.69 (3 H, s), 3.63 (3 H, s), 3.50 (1 H, s), 1.81 (1 H, br) ppm;

¹³C NMR (75 MHz, CDCl₃) δ 170.5, 164.1, 160.9, 158.8, 157.0, 137.0, 129.0, 128.4, 127.8, 127.7, 126.5, 112.7, 107.7, 101.9, 93.7, 92.7, 89.5, 79.6, 60.4, 55.8, 55.1, 55.0, 51.9, 50.6 ppm;

HRMS (CI/NH₃) m/z calculated for C₂₈H₂₈O₈ 492.1784 found 493.1891 (M+H).

***Exo* methyl rocaglate 6.**



Foamy yellow solid mp: 84-85°C.

IR ν_{max} (film): 3031, 3006, 2958, 2936, 2846, 1730, 1636, 1430, 1307, 1258, 1132, 103 cm⁻¹;^{ss}

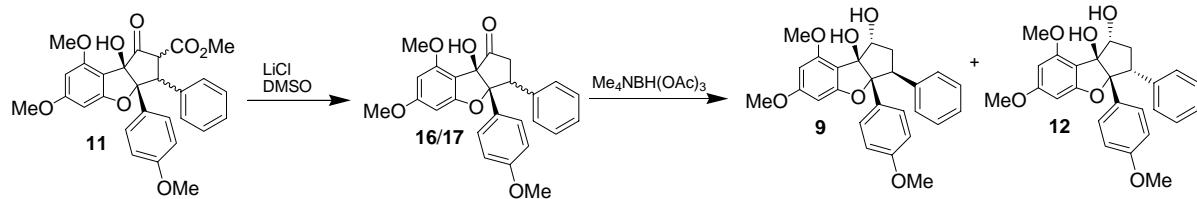
¹H NMR (400 MHz, CDCl₃) δ 7.34 (2 H, d, *J* = 8.8 Hz), 7.17-1.15 (3 H, m), 6.95-6.94 (2 H, m), 6.87 (2 H, d, *J* = 8.8 Hz), 6.12 (1 H, d, *J* = 1.6 Hz), 6.06 (1 H, d, *J* = 1.6 Hz), 4.76 (1 H, dd, *J* = 10.2, 1.6 Hz), 4.02 (1 H, d, *J* = 12.8 Hz), 3.82 (3 H, s), 3.78 (3 H, s), 3.77 (3 H, s), 3.60 (3 H, s), 3.23 (1 H, dd, *J* = 12.8, 10.2 Hz), 1.81 (1 H, s) ppm;

¹³C NMR (75 MHz, CDCl₃) δ 173.1, 164.1, 162.0, 159.4, 157.9, 135.0, 129.1, 128.4, 128.0, 127.3, 119.7, 113.6, 105.1, 99.5, 92.6, 91.4, 88.8, 83.9, 55.8, 55.8, 55.4, 54.8, 52.3, 50.9 ppm;

HRMS (CI/NH₃) m/z calculated for C₂₈H₂₈O₈ 492.1784 found 493.1891 (M+H).

^{ss} Kraus, G. A.; Sy, J. O. *J. Org. Chem.* **1989**, *54*, 77-83

d) Detailed procedures for the preparation of rocaglaol

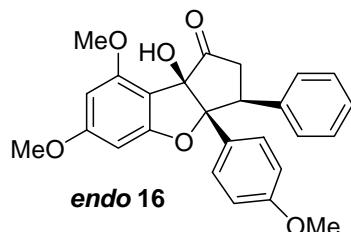


Endo/exo cyclopentanone derivatives: Keto rocaglate **11** intermediate (30 mg, 0.061 mmol, 1 equiv) was dissolved in DMSO (1 mL). 4 mg of lithium chloride was added (0.091 mmol, 1.5 equiv) followed by 5 μ L of water (0.182 mmol, 3 equiv). The resulting mixture was heated at 100°C for 12 h. After cooling the reaction to rt, water (6 mL) was added and the reaction mixture extracted with ethyl acetate (3 X 5 mL). The combined organic layers were washed once with brine (5 mL), dried over MgSO₄, and filtered. The solvent was removed *in vacuo* and the resulting white solid purified *via* silica gel (40/60, hexanes/EtOAc) to afford 18 mg (69 %, 0.042 mmol) of a 4/1 mixture of *endo/exo* **16/17** as a white solid.

White solid: mp 152°C;

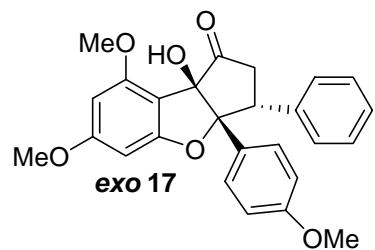
IR ν_{max} (film): 3466, 3013, 2940, 2840, 1749, 1609, 1509, 1458, 1345, 1249, 1148, 1036, 998, 812, 756 cm⁻¹;

HRMS (CI/NH₃) m/z calculated for C₂₆H₂₄O₆ 432.1573 found 433.1636 (M+H).



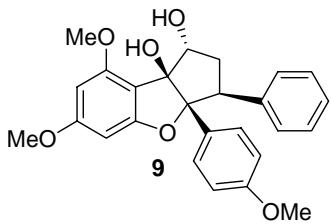
¹H NMR (400 MHz, CDCl₃) δ 7.09 (3 H, m), 6.96 (4 H, m), 6.68 (2 H, d, *J* = 8.8 Hz), 6.34 (1 H, d, *J* = 1.6 Hz), 6.1 (1 H, d, *J* = 1.6 Hz), 3.80 (1 H, m), 3.84 (3 H, s), 3.81 (3 H, s), 3.69 (3 H, s), 3.00 (2 H, m) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 210.9, 164.9, 161.4, 159.0, 158.7, 137.5, 128.3, 128.2, 128.2, 128.1, 128.0, 127.0, 113.4, 101.5, 98.8, 89.9, 89.0, 55.9, 55.8, 55.7, 48.8, 40.1 ppm;



¹H NMR (400 MHz, CDCl₃) δ 7.33 (2 H, d, J = 8.8 Hz), 7.23 (3 H, m), 7.05 (2H, m), 6.88 (2 H, d, J = 8.8 Hz), 6.14 (1 H, d, J = 2 Hz), 6.00 (1 H, d, J = 2 Hz), 4.05 (1 H, m), 3.78 (3 H, s), 3.77 (3 H, s), 3.76 (3 H, s), 2.60 (1 H, m) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 209.7, 164.4, 162.5, 159.4, 158.4, 136.0, 129.1, 128.9, 128.3, 128.3, 128.1, 126.1, 113.5, 106.7, 92.6, 88.6, 87.2, 55.8, 55.8, 55.6, 50.9, 39.4 ppm;



Endo Rocaglaol 9. To a solution of Me₄NBH(OAc)₃ (66 mg, 0.25 mmol, 6 equiv) and 26 μ L (0.4 mmol, 10 equiv) of acetic acid in 3 mL of CH₃CN was added a solution of 18 mg (0.04 mmol, 1 equiv) of the crude **16/17** in 1 mL of CH₃CN. The resulting green-blue solution was stirred for 3 h at rt before being quenched with 2 mL of saturated aqueous NH₄Cl. The solution was then treated with 1 mL of a 3 M aqueous solution of sodium/potassium tartrate and stirred at rt for 30 min. The aqueous solution was extracted with CH₂Cl₂ (2 X 5 mL). The combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated *in vacuo*. Purification on silica gel (40/60, hexanes/EtOAc) afford 12 mg (0.027 mmol, 66 %) of the corresponding *endo* rocaglaol **9** as a colorless oil and 3 mg (0.007 mmol, 16 %) of the corresponding *exo* rocaglaol **12** as a colorless oil.

Recrystallization of **9** (50 mg) from CH₂Cl₂ (500 μ L) / isooctane (100 μ L) afforded 79 % (39 mg) recovery of enantiomerically enriched **9** (96 %) isolated from the mother liquor. (*endo* rocaglaol **9** crystallizes as a centrosymmetric racemate)

Chiral HPLC analysis of *endo* rocaglaol **9** was performed using ChiralCel OD column. Conditions: Gradient, 0 to 18% i-PrOH/hexanes, for 50 min, 0.6 mL/min, 210 nm. t = 52.4 min (-)-rocaglaol, t = 56.7 min (+)-rocaglaol, ee = 96 %.

$$[\alpha]_D^{22} = -96^\circ \text{ (c = 0.44, CHCl}_3\text{)}^{s4} \text{ (96% ee)}$$

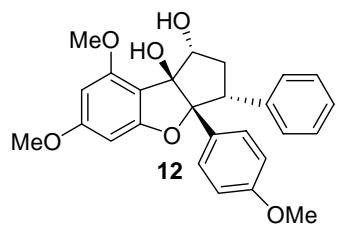
IR ν_{max} (film): 3496, 3008, 2940, 2841, 1607, 1509, 1456, 1337, 1300, 1294, 1204, 1148, 1120, 817 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.09 (5 H, m), 6.97 (2 H, d, *J* = 9.2 Hz), 6.6 (2 H, d, *J* = 8.8 Hz), 6.27 (1 H, d, *J* = 2 Hz), 6.13 (1 H, d, *J* = 2 Hz), 4.80 (1 H, d, *J* = 6 Hz), 3.9 (1 H, dd, *J* = 14.4, 6.8 Hz), 3.88 (3 H, s), 3.82 (3 H, s), 3.69 (3 H, s), 3.30, (1 H, brs), 2.73 (1 H, ddd, *J* = 14.4, 13.6, 6.0 Hz), 2.18 (1 H, dd, *J* = 13.6, 6.8 Hz) 1.56 (1 H, brs) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 163.8, 160.9, 158.5, 156.9, 138.5, 128.8, 127.9, 127.5, 126.6, 126.1, 112.6, 107.6, 103.4, 94.7, 92.3, 89.3, 78.9, 55.6, 55.6, 55.0, 53.1, 36.3 ppm;

HRMS (CI/NH₃) m/z calculated for C₂₆H₂₆O₆ 434.1729 found 435.1713 (M+H).

***Exo* Rocaglaol 12**



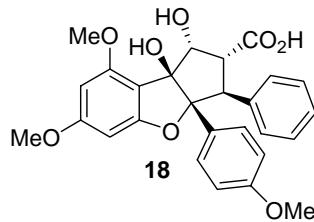
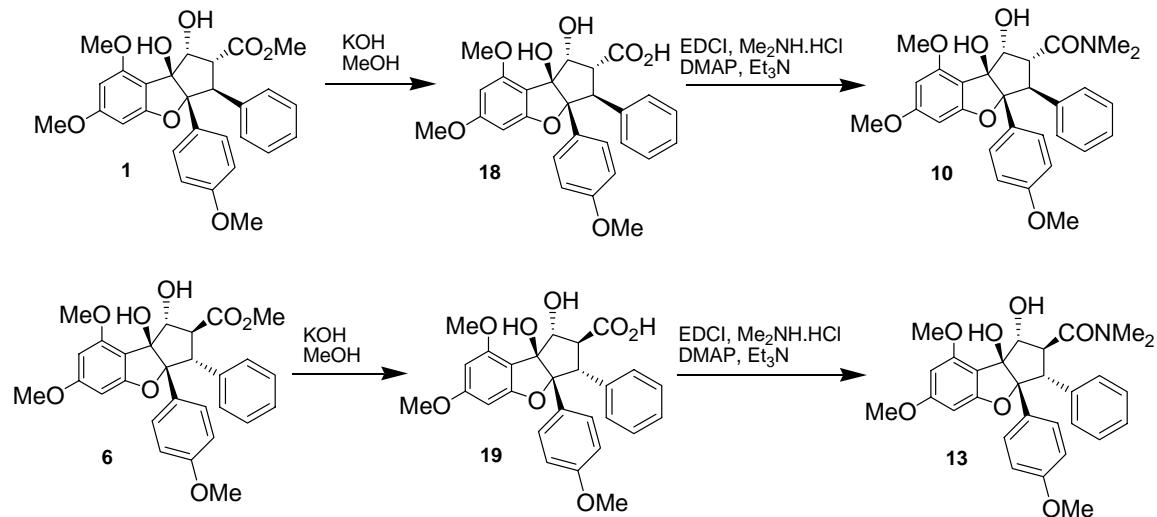
IR ν_{max} (film): 3473, 3005, 2928, 2851, 1739, 1606, 1507, 1456, 1248, 1178, 1037, 757 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 7.32 (2 H, d, $J = 7.6$ Hz), 7.16 (3 H, m), 6.98 (2 H, m), 6.87 (1 H, d, $J = 7.6$ Hz), 6.13 (1 H, d, $J = 2$ Hz), 6.06 (1 H, d, $J = 2$ Hz), 4.66 (1 H, dd, $J = 11.2$, 6 Hz), XX, 3.82 (3 H, s), 3.78 (3 H, s), 3.76 (3 H, s), 2.45, (1 H, ddd, $J = 11.2$, 6, 5.2 Hz), 2.09 (1 H, ddd, m), 2.77 (1 H, dd, $J = 5.2$, 1.2 Hz) ppm;

^{13}C NMR (100 MHz, CDCl_3) δ 164.0, 162.5, 160.2, 159.1, 158.0, 137.8, 129.7, 129.0, 128.4, 127.9, 126.8, 113.6, 106.2, 101.0, 92.6, 92.5, 88.7, 81.4, 55.8, 55.4, 50.8, 34.4 ppm;

HRMS (CI/ NH_3) m/z calculated for $\text{C}_{26}\text{H}_{26}\text{O}_6$ 434.1729 found 435.1780 ($\text{M}+\text{H}$).

e) Detailed procedures for the preparation of rocaglamide



Endo rocaglic acid **18**. To a solution of 50 mg (0.097 mmol, 1 equiv) of *endo* methyl rocaglate **1** in MeOH (1.5 mL) was added 22 mg (0.39 mmol, 4 equiv) of potassium hydroxide. The resulting yellow solution was stirred for 12 h at 44°C before being quenched with 2 mL of 1N HCl. The aqueous solution was then extracted with EtOAc (2 X 5 mL). The combined organic layer was dried over MgSO₄ and filtered. The solvent was removed in *vacuo* to offer a crude solid which was recrystallized using CHCl₃ to afford 46 mg (96 %, 0.09 mmol) of **18** as a white solid.

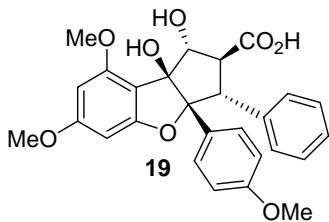
White solid: mp 110-111°C;
 $[\alpha]_D^{22} = -18^\circ$ (c = 1.16, CHCl₃)

IR ν_{max} (film): 3489, 3015, 2935, 2843, 1715, 1607, 1508, 1457, 1249, 1215, 1148, 1121, 756 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.06 (5 H, m), 6.86 (2 H, m), 6.65 (2 H, d, *J* = 8.8 Hz), 6.26 (1 H, d, *J* = 2 Hz), 6.09 (1 H, d, *J* = 2 Hz), 5.03 (1 H, d, *J* = 6.4 Hz), 4.23 (1 H, d, *J* = 14 Hz), 3.89 (1 H, dd, *J* = 14, 6.8 Hz) 3.83 (3 H, s), 3.81 (3 H, s), 3.69 (3 H, s) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 175.4, 164.4, 161.0, 158.9, 157.2, 136.9, 129.1, 128.2, 128.1, 128.0, 127.9, 126.8, 126.5, 112.9, 107.7, 102.0, 93.8, 92.9, 89.7, 79.6, 55.9, 55.3, 55.0, 50.5 ppm;

HRMS(Cl/NH₃) m/z calculated for C₂₆H₂₆O₆ 478.1628 found 478.1668.



***Exo* rocaglic acid **19**.** Following the previous procedure using 30 mg (0.06 mmol, 1 equiv) of *exo* methyl rocaglate **6** in MeOH (1.5 mL) and 17 mg (0.30 mmol, 5 equiv) of potassium hydroxide. 27 mg (0.056 mmol, 89 %) of *exo* rocaglic acid **19** was isolated as a white solid.

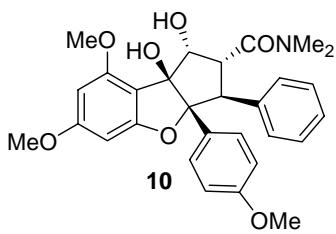
White solid: mp 258-259 °C;

IR ν_{max} (film): 3446, 2941, 1709, 1603, 1506, 1456, 1250, 1198, 1125, 1006, 907 cm^{-1} ;

^1H NMR (400 MHz, CD₃OD) δ 7.33 (2 H, d, J = 8.8 Hz), 7.14 (3 H, m), 6.99 (2 H, m), 6.15 (2 H, s), 4.70 (1 H, d, J = 10.4 Hz), 3.92 (1 H, d, J = 12.8 Hz), 3.79 (3 H, s), 3.78 (3 H, s), 3.78 (3 H, s), 3.12 (1 H, dd, J = 12.8, 10.4 Hz) ppm;

^{13}C NMR (100 MHz, CD₃OD) δ 176.5, 165.2, 163.1, 160.5, 160.2, 136.8, 131.5, 130.4, 129.6, 128.7, 128.0, 113.9, 106.8, 100.6, 93.4, 92.3, 89.1, 85.2, 56.4, 56.1, 55.9, 55.7, 52.3 ppm;

HRMS(Cl/NH₃) m/z calculated for C₂₆H₂₆O₆ 478.1628 found.478.1635



Endo rocaglamide 10. To a solution of 33 mg (0.069 mmol, 1 equiv) of *endo* rocaglic acid **18** in DMF (2 mL) was added dimethylamine hydrochloride (7 mg, 0.08 mmol, 1.2 equiv) and DMAP (9.1 mg, 0.08 mmol, 1.2 equiv). After cooling the reaction mixture to 0°C, EDCI (13 mg, 0.08 mmol, 1.2 equiv) was added portionwise over a 5 min period. The mixture was stirred at 0°C for 30 min. A solution of triethylamine (11

μL, 0.08 mmol, 1.2 equiv) was then added and the reaction mixture stirred for an additional 1 h at 0°C and 12 h at rt before being quenched with 1 mL of 1N HCl solution and diluted with water. The aqueous solution was then extracted twice with CH₂Cl₂ (2 X 10 mL). The collected organic layer was washed with brine (1 X 10 mL). After drying over MgSO₄, and filtration, the organic solvent was removed *in vacuo* to afford a yellow oil which was then purified using silica gel chromatography (95/05, CH₂Cl₂/MeOH) to afford 22 mg (0.045 mmol, 65 %) of rocaglamide **10** as a white solid.

Chiral HPLC analysis of *endo* rocaglamide **10** was obtained using Chiracel OD column. Conditions: Gradient, 10 to 60% *i*-PrOH/hexanes, for 40 min, 1 mL/min, 210 nm. t = 26.29 min (+)-rocaglamide, t = 32.77 min (-)-rocaglamide, ee = 94 %

White solid: mp 117-118°C;

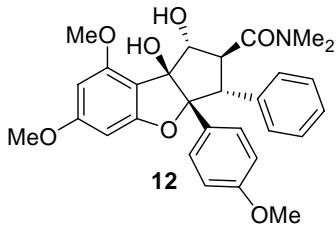
$$[\alpha]_D^{22} = -99^\circ \text{ (c = 0.13, CHCl}_3\text{)}^{s4} \text{ (94% ee)}$$

IR ν_{max} (film): 3475, 2938, 2841, 1718, 1619, 1506, 1457, 1336, 1251, 1199, 1147, 1121, 1036, 997 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.09 (2 H, d, *J* = 8.7 Hz), 7.00 (3H, m), 6.84 (2 H, m), 6.65 (2H, d, *J* = 8.7 Hz), 6.25 (1 H, d, *J* = 2.1 Hz), 6.08 (1 H, d, *J* = 2.1 Hz), 4.92 (1 H, d, *J* = 6.6 Hz), 4.53 (1 H, d, *J* = 13.5 Hz), 4.04 (1 H, dd, *J* = 13.5, 6.6 Hz), 3.83 (3 H, s), 3.81 (3 H, s), 3.44 (1 H, s), 3.29 (3 H, s), 2.92 (3 H, m), 0.90 (1 H, s) ppm;

¹³C NMR (100 MHz, CDCl₃) δ 169.5, 163.9, 161.1, 158.6, 157.2, 137.6, 128.8, 127.8, 127.7, 127.6, 127.1, 126.3, 112.7, 107.6, 101.7, 94.0, 92.5, 89.3, 78.6, 77.9, 55.9, 55.7, 55.1, 47.7, 37.1, 35.8 ppm;

HRMS (CI/NH₃) m/z calculated for C₂₉H₃₁NO₇ 505.2101 found 506.1982(M+H)



***Exo* rocaglamide** Following the same experimental procedure for compound **10**, to 35 mg (0.07 mmol, 1 equiv) of *exo* rocaglic acid **18** in DMF (2 mL) was added 14 mg (0.09 mmol, 1.2 equiv) of EDCI, 10 mg (0.09 mmol, 1.2 equiv) of DMAP, 7.1 mg (0.09, 1.2 equiv) of dimethylamine hydrochloride and 13 μ L (0.09 mmol, 1.2 equiv) of triethylamine. After purification

using silica gel chromatography (95/05, CH₂Cl₂/MeOH), 27 mg (0.056 mmol, 63 %) of the *exo* rocaglamide **12** was isolated as a white solid.

White solid: mp 181-182 °C;

IR ν_{max} (film): 3478, 2932, 2846, 1731, 1622, 1506, 1457, 1253, 1204, 1147, 1127, 1036, 912 cm⁻¹,^{ss}

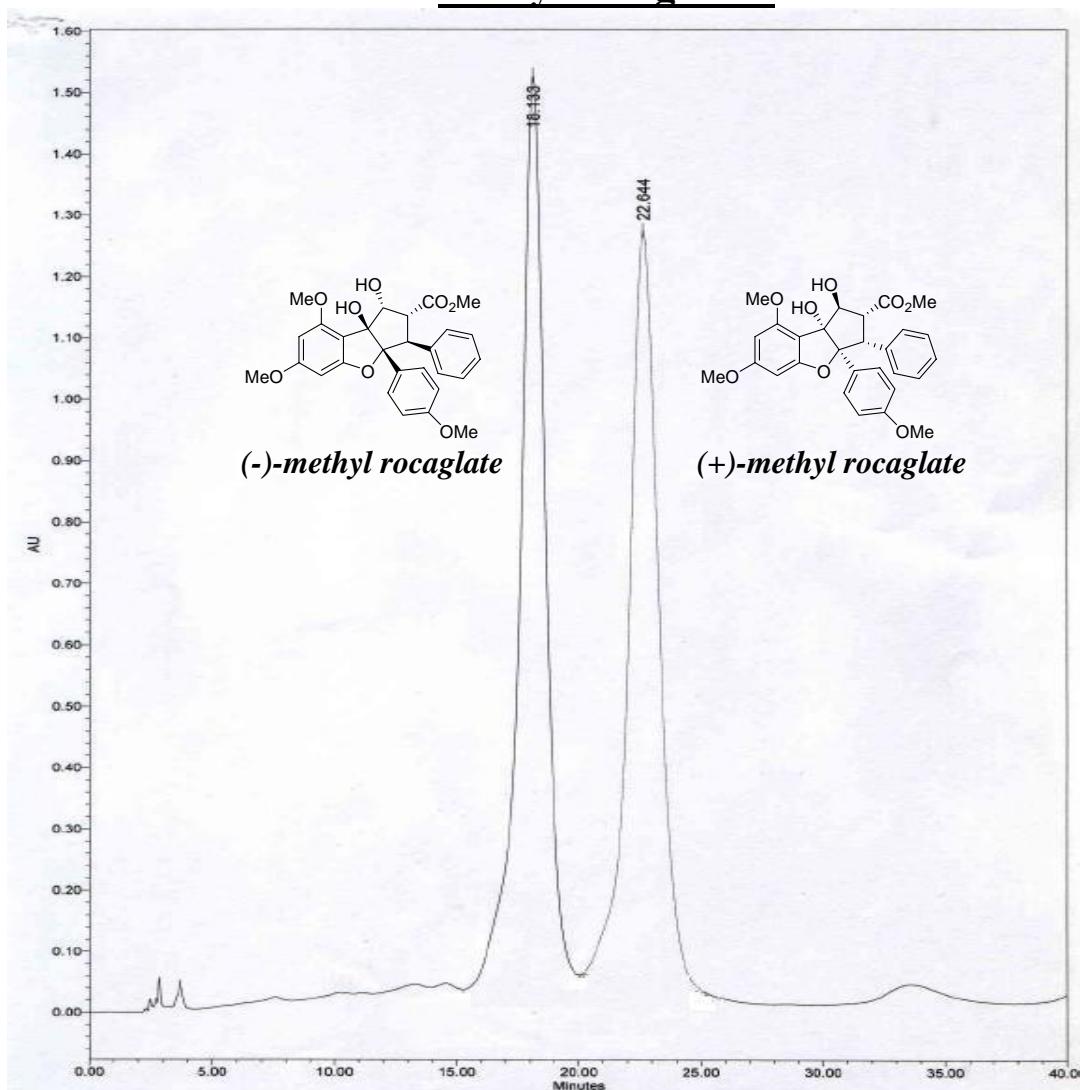
¹H NMR (400 MHz, CDCl₃) δ 7.40 (2 H, d, *J* = 8.8 Hz), 7.16 (3 H, m), 7.01 (2 H, m), 6.88 (2 H, d, *J* = 8.8 Hz), 6.20 (1 H, d, *J* = 2 Hz), 6.10 (1 H, d, *J* = 2 Hz), 4.82 (1 H, d, *J* = 10 Hz), 4.24 (1 H, d, *J* = 12.4 Hz), 3.83 (3 H, s), 3.82 (3 H, s), 3.79 (3 H, s), 3.56 (1 H, dd, *J* = 10, 12.4 Hz), 2.99 (3 H, s), 2.87 (3 H, s), 2.00 (1 H, br s) ppm,^{ss}

¹³C NMR (100 MHz, CDCl₃) δ 171.7, 163.9, 162.2, 159.4, 158.1, 135.9, 129.5, 129.3, 128.6, 128.1, 127.3, 113.6, 105.9, 100.2, 92.6, 91.9, 88.8, 84.9, 55.9, 55.8, 55.4, 55.0, 47.5, 37.7, 36.2 ppm;^{ss}

HRMS (CI/NH₃) m/z calculated for C₂₉H₃₁NO₇ 505.2101 found 506.2194 (M+H)

II) Chiral HPLC analyses

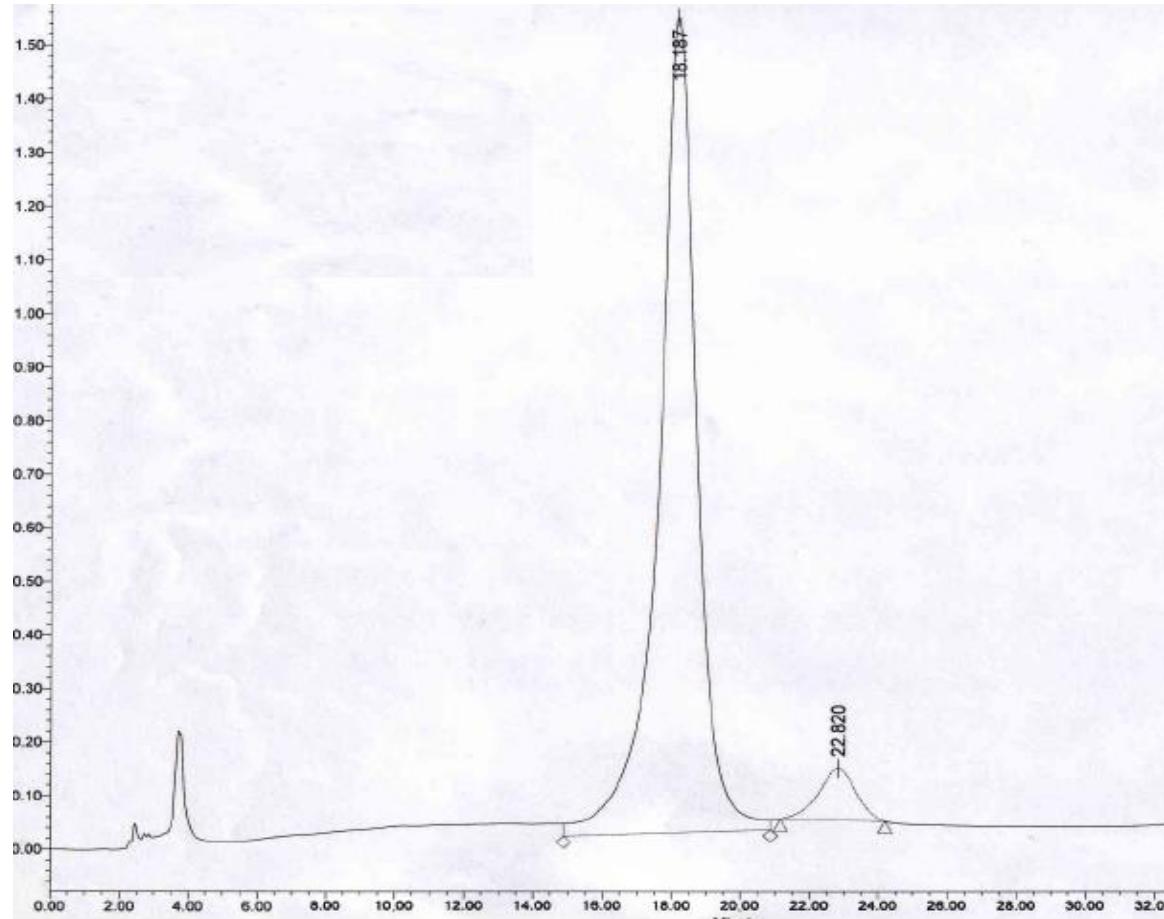
methyl rocaglate 1



Chiral HPLC trace of racemic methyl rocaglate **1**

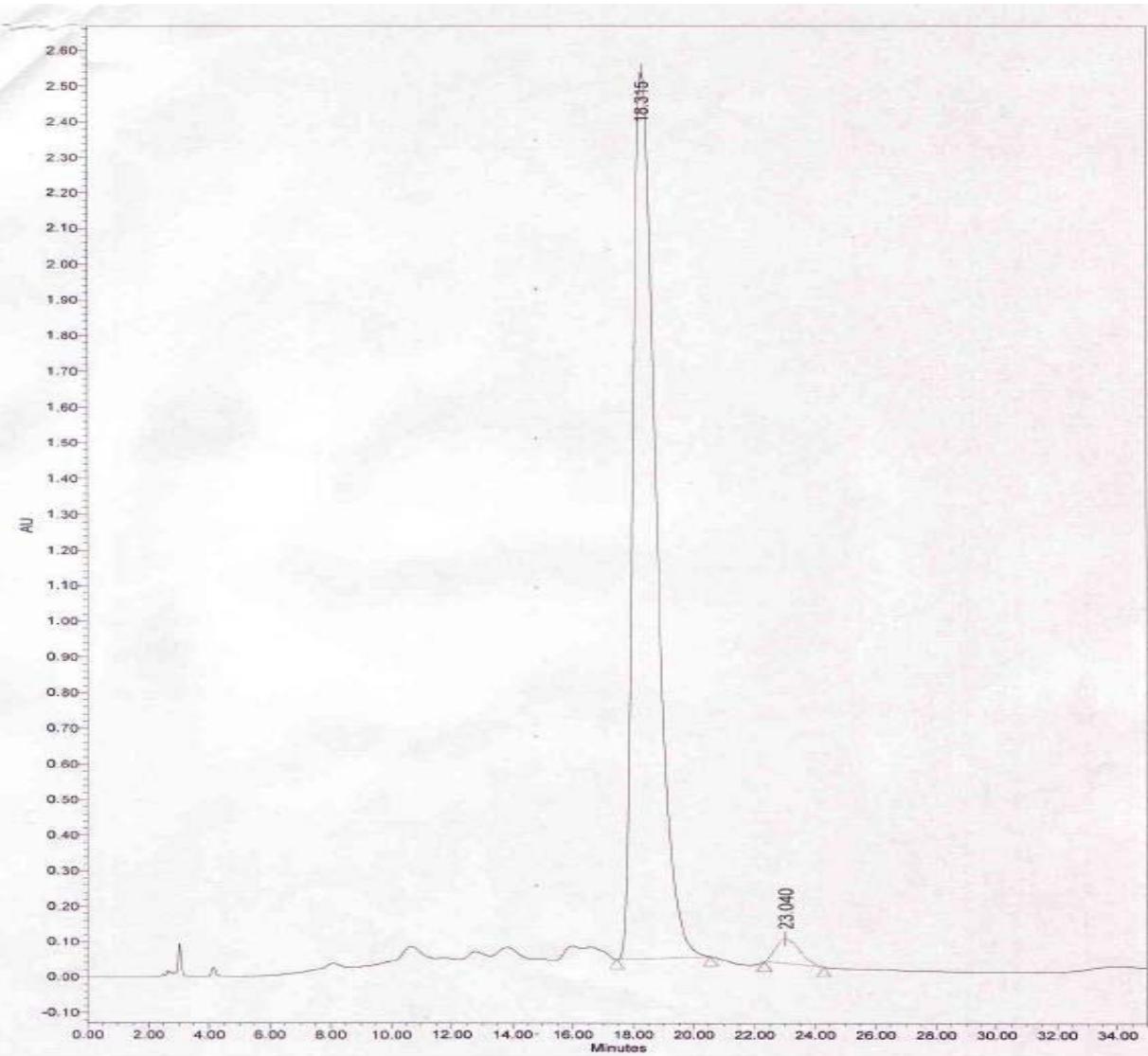
Column : Regis, Pirkle Covalent (R, R) Whelk-01.

Conditions: Gradient, 10 to 60% *i*-PrOH/hexanes for 30 min, 0.8 mL/min, 210 nm
t = 17.90 min (-)-methyl rocaglate, t = 22.26 min (+)-methyl rocaglate



Chiral HPLC trace of methyl rocaglate **1** obtained using TADDOL derivative **7g**
Column : Regis, Pirkle Covalent (R, R) Whelk-01.

Conditions: Gradient, 10 to 60% *i*-PrOH/hexanes, for 30 min, 0.8 mL/min, 210 nm
 $t = 17.90$ min (-)-methyl rocaglate, $t = 22.26$ min (+)-methyl rocaglate
ee = 82 %



Chiral HPLC trace of methyl rocaglate **1** obtained from the mother liquor after recrystallization using benzene/hexanes

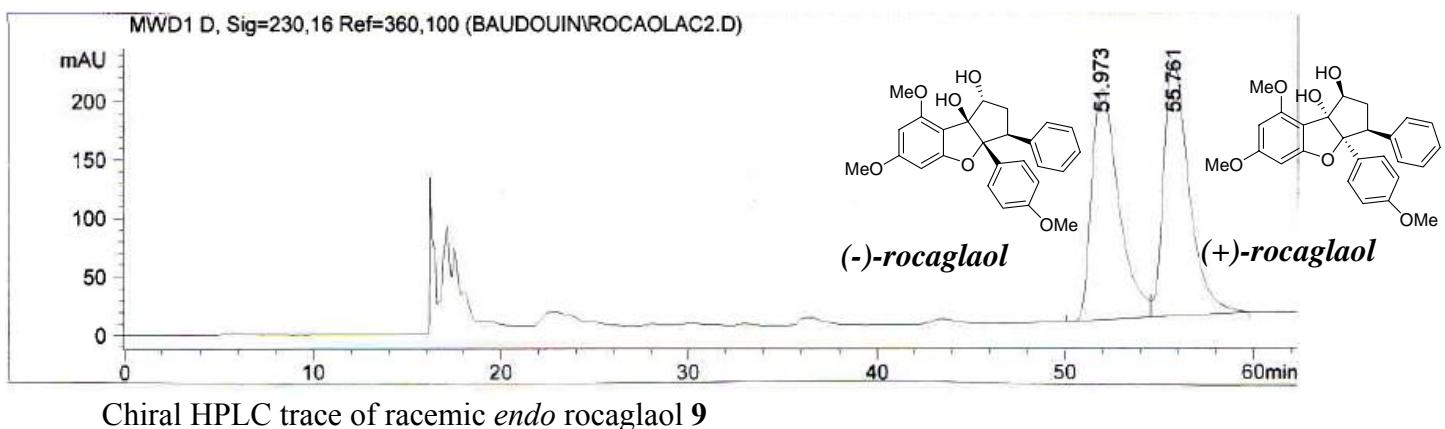
Column: Regis, Pirkle Covalent (R, R) Whelk-01.

Conditions: Gradient, 10 to 60% *i*-PrOH/hexanes, for 30 min, 0.8 mL/min, 210 nm

$t = 17.90$ min (-)-methyl rocaglate, $t = 22.26$ min (+)-methyl rocaglate

ee = 94 %

Rocaglaol 9

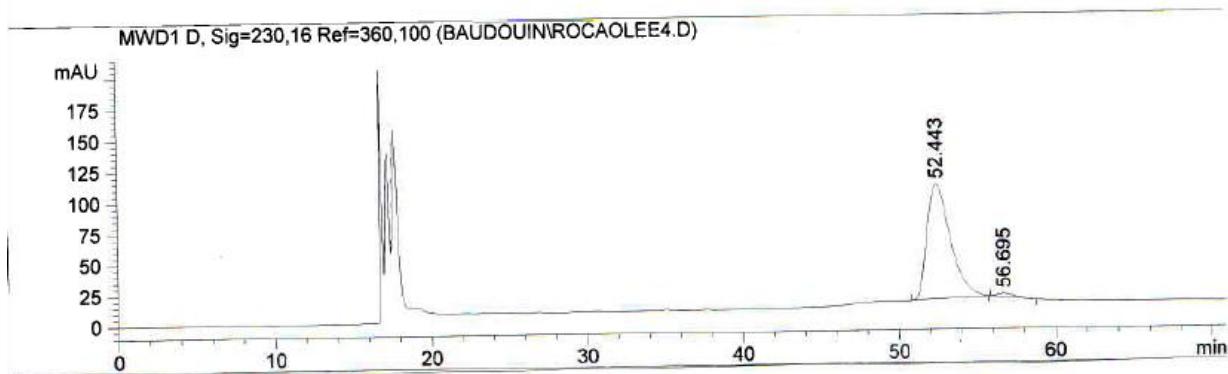


Chiral HPLC trace of racemic *endo* rocaglaol **9**

Column: ChiralCel OD.

Conditions: Gradient, 0 to 18% i-PrOH/hexanes, for 50 min, 0.6 mL/min, 230 nm.

t = 52.4 min (-)-rocaglaol, t = 56.7 min (+)-rocaglaol.



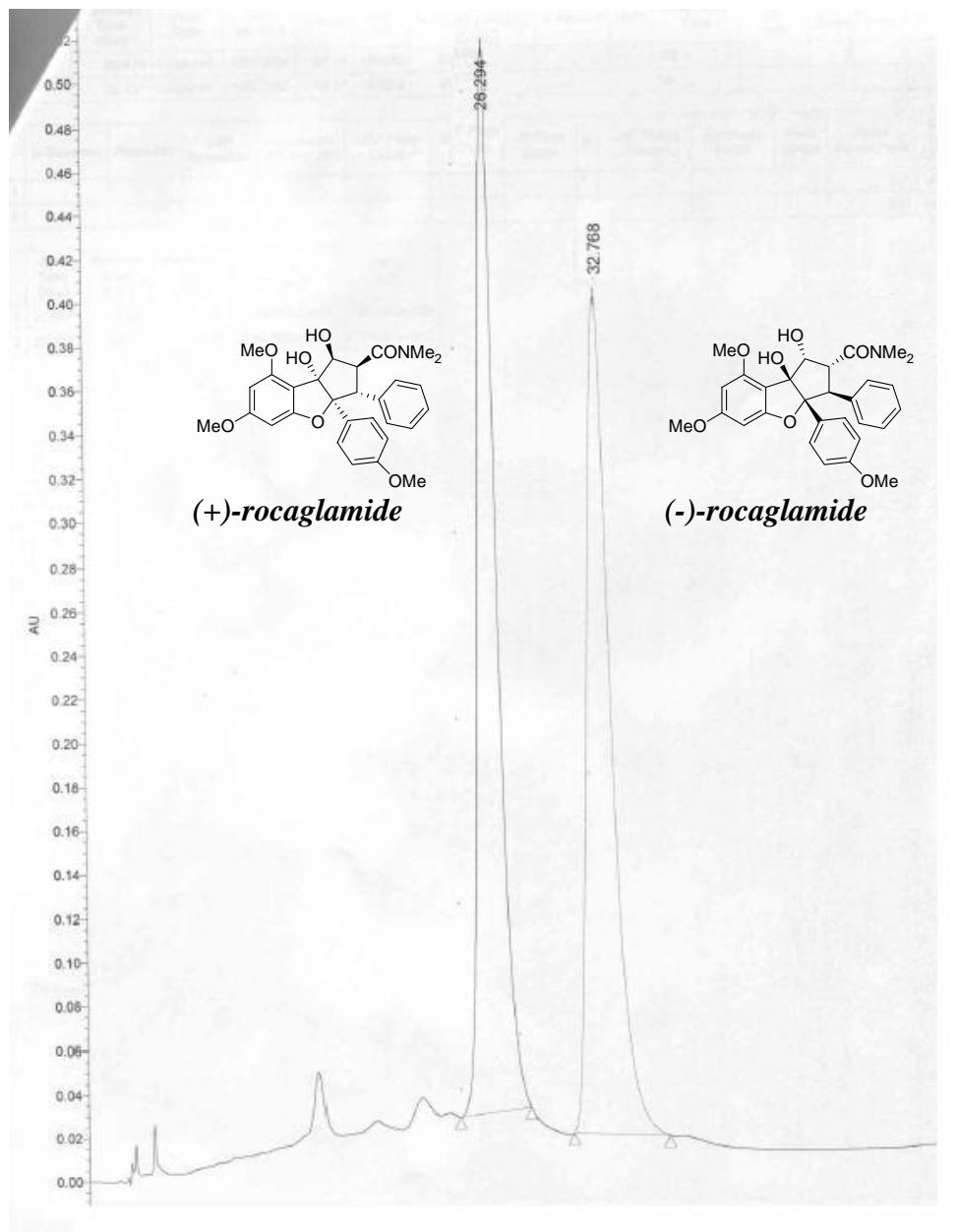
Chiral HPLC trace of *endo* rocaglaol **9** obtained from the mother liquor after recrystallization using CH₂Cl₂/isooctane

Column: ChiralCel OD.

Conditions: Gradient, 0 to 18% i-PrOH/hexanes, for 50 min, 0.6 mL/min, 230 nm.

t = 52.4 min (-)-rocaglaol, t = 56.7 min (+)-rocaglaol, ee = 96%

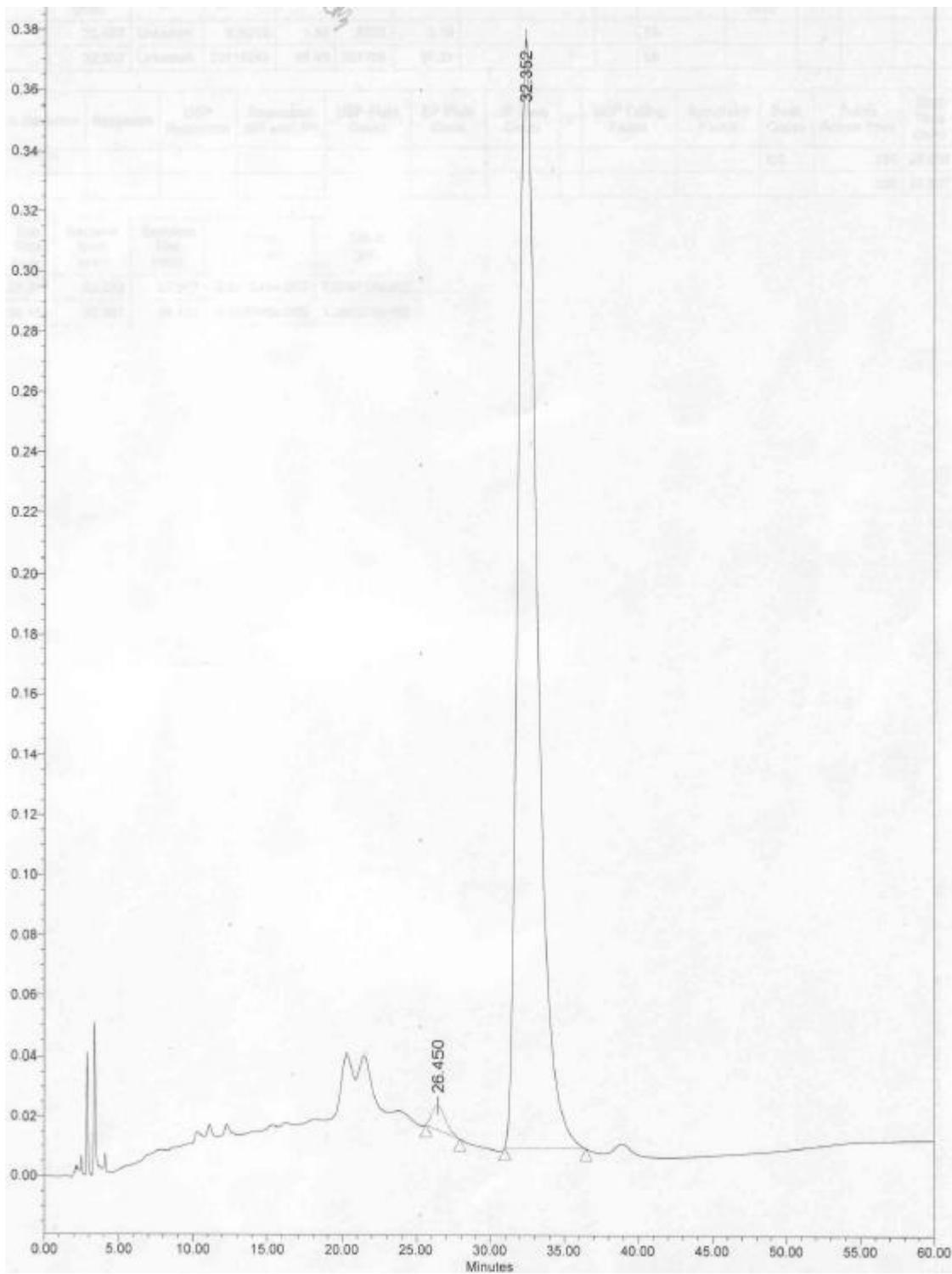
Rocaglamide 10



Chiral HPLC trace of racemic *endo* rocaglamide **10**

Column: ChiralCel OD.

Conditions: Gradient, 10 to 60% *i*-PrOH/hexanes, for 40 min, 1 mL/min, 210 nm.
t = 26.29 min (+)-rocaglamide, t = 32.77 min (-)-rocaglamide



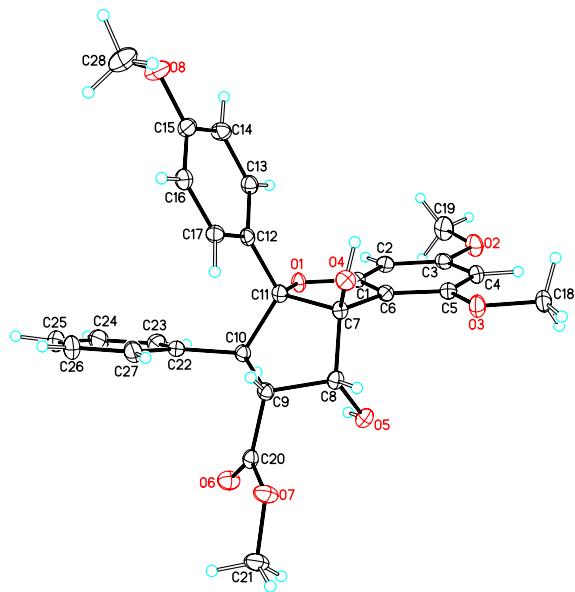
Chiral HPLC trace of a *endo* rocaglamide **10**

Column: ChiralCel OD.

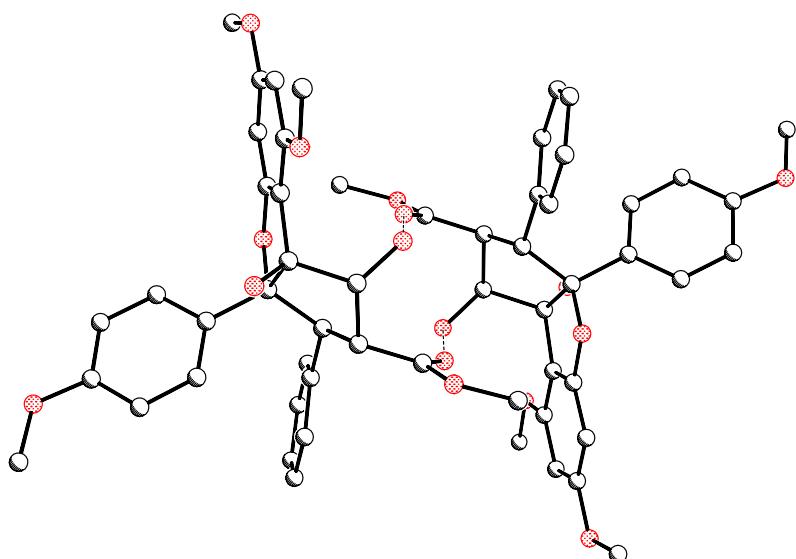
Conditions: Gradient, 10 to 60% *i*-PrOH/hexanes, for 40 min, 1 mL/min, 210 nm.
 $t = 26.45$ min (+)-rocaglamide, $t = 32.35$ min (-)-rocaglamide, ee = 94%

III) X-ray crystallographic Data

a) X-ray crystallographic data for **1**



Crystals of compound **1** suitable for x-ray analysis were obtained by slow evaporation from benzene / hexanes. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 604104). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).



Unit cell representation for the centrosymmetric racemate **1**

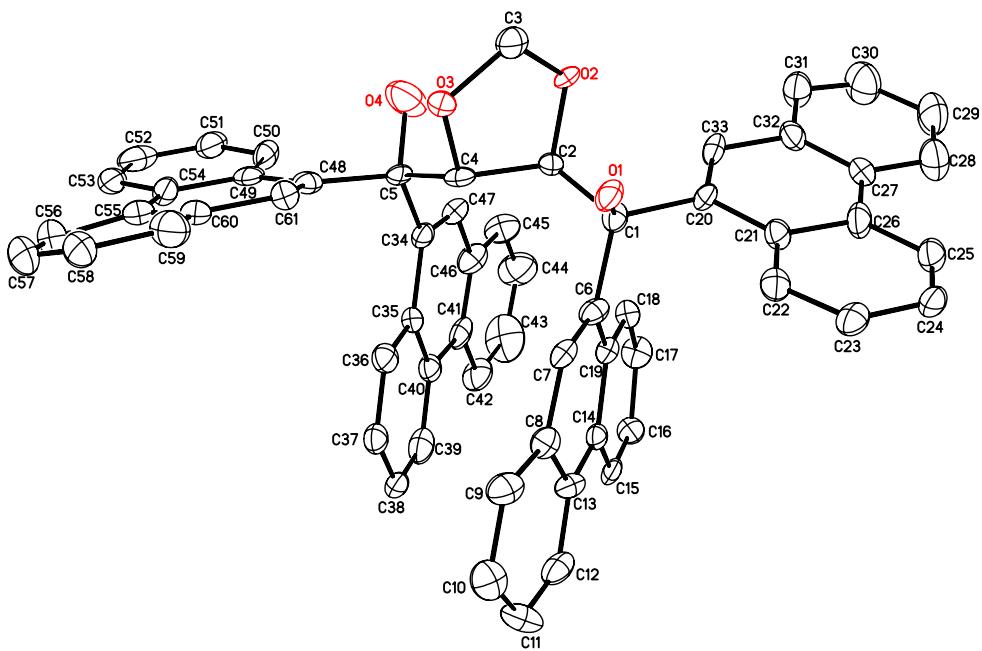
Table 1: Crystal data and structure refinement for 1.

Identification code	1
Empirical formula	C28 H28 O8
Formula weight	492.50
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 10.0768(14) Å b = 10.4422(7) Å c = 12.5172(8) Å
Volume	1157.17(19) Å ³
Z	2
Density (calculated)	1.413 Mg/m ³
Absorption coefficient	0.104 mm ⁻¹
F(000)	520
Crystal size	0.20 x 0.20 x 0.15 mm ³
Theta range for data collection	1.84 to 26.58°
Index ranges	-12<=h<=12, -12<=k<=13, -15<=l<=15
Reflections collected	25370
Independent reflections	4719 [R(int) = 0.0311]
Completeness to theta = 26.58°	97.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9846 and 0.9796
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	4719 / 0 / 393
Goodness-of-fit on F ²	1.097
Final R indices [$>2\sigma(I)$]	R1 = 0.0360, wR2 = 0.0934
R indices (all data)	R1 = 0.0507, wR2 = 0.0991
Largest diff. peak and hole	0.251 and -0.230 e.Å ⁻³

Table 2: Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for derivative 1. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	2050(1)	-1930(1)	-3057(1)	19(1)
O(2)	2595(1)	223(1)	-5826(1)	29(1)
O(3)	740(1)	2264(1)	-2722(1)	25(1)
O(4)	-302(1)	-31(1)	-1899(1)	22(1)
O(5)	3408(1)	1568(1)	-541(1)	23(1)
O(6)	4668(1)	-5(1)	1331(1)	26(1)
O(7)	3328(1)	1389(1)	2005(1)	27(1)
O(8)	-3740(1)	-5969(1)	-4191(1)	33(1)
C(1)	1984(1)	-893(1)	-3506(1)	18(1)
C(2)	2428(1)	-946(1)	-4468(1)	20(1)
C(3)	2255(1)	146(1)	-4857(1)	21(1)
C(4)	1708(2)	1246(1)	-4297(1)	22(1)
C(5)	1293(1)	1254(1)	-3330(1)	20(1)
C(6)	1423(1)	153(1)	-2933(1)	18(1)
C(7)	1080(1)	-130(1)	-1934(1)	18(1)
C(8)	2095(1)	807(1)	-633(1)	18(1)
C(9)	2295(1)	-232(1)	4(1)	18(1)
C(10)	2461(2)	-1519(1)	-938(1)	18(1)
C(11)	1347(1)	-1662(1)	-2164(1)	17(1)
C(12)	-9(1)	-2808(1)	-2679(1)	18(1)
C(13)	-504(2)	-3741(1)	-3884(1)	21(1)
C(14)	-1751(2)	-4772(2)	-4364(1)	25(1)
C(15)	-2531(1)	-4900(1)	-3642(1)	23(1)
C(16)	-2075(2)	-3974(1)	-2450(1)	22(1)
C(17)	-831(1)	-2942(1)	-1991(1)	20(1)
C(18)	526(2)	3369(1)	-3142(1)	28(1)
C(19)	3034(2)	-945(2)	-6489(1)	34(1)
C(20)	3564(1)	365(1)	1160(1)	19(1)
C(21)	4506(2)	2100(2)	3134(1)	30(1)
C(22)	2507(1)	-2807(1)	-640(1)	20(1)
C(23)	3310(2)	-3700(2)	-1090(1)	27(1)
C(24)	3402(2)	-4892(2)	-834(1)	33(1)
C(25)	2691(2)	-5204(2)	-133(1)	35(1)
C(26)	1911(2)	-4318(2)	336(1)	33(1)
C(27)	1822(2)	-3119(2)	94(1)	27(1)
C(28)	-4639(2)	-6075(2)	-3517(2)	40(1)

b) X-ray crystallographic data for TADDOL 7d



Crystals of compound **7d** suitable for x-ray analysis were obtained by slow evaporation from CH₂Cl₂ / isoctane. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 604103). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Table 3: Crystal data and structure refinement for TADDOL 7d.

Identification code	TADDOL 7d		
Empirical formula	C125 H90 CL6 O8		
Formula weight	1932.67		
Temperature	173(2) K		
Wavelength	0.71073 Å		
Crystal system	Monoclinic		
Space group	C2		
Unit cell dimensions	a = 25.6030(13) Å	α= 90°.	
	b = 16.0366(10) Å	β= 99.148(2)°.	
	c = 27.6197(16) Å	γ = 90°.	
Volume	11196.0(11) Å ³		
Z	4		
Density (calculated)	1.147 Mg/m ³		
Absorption coefficient	0.208 mm ⁻¹		
F(000)	4024		
Crystal size	0.40 x 0.15 x 0.10 mm ³		
Theta range for data collection	1.49 to 21.49°.		
Index ranges	-26<=h<=22, -16<=k<=16, -28<=l<=28		
Reflections collected	34127		
Independent reflections	12712 [R(int) = 0.0450]		
Completeness to theta = 21.49°	100.0 %		
Absorption correction	Semi-empirical from equivalents		
Max. and min. transmission	0.9795 and 0.9214		
Refinement method	Full-matrix least-squares on F ²		
Data / restraints / parameters	12712 / 1 / 1252		
Goodness-of-fit on F ²	1.075		
Final R indices [I>2sigma(I)]	R1 = 0.0768, wR2 = 0.2166		
R indices (all data)	R1 = 0.0912, wR2 = 0.2298		
Absolute structure parameter	0.08(12)		
Largest diff. peak and hole	0.682 and -0.451 e.Å ⁻³		

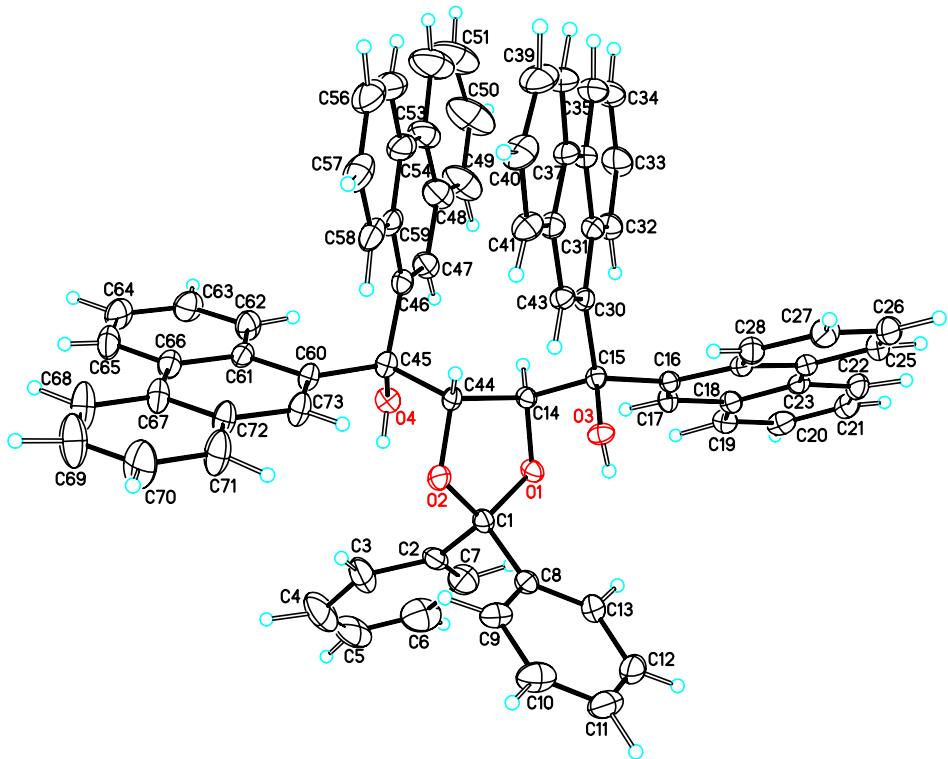
Table 4: Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for TADDOL 7d. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	2968(2)	713(3)	3787(2)	40(1)
O(2)	2091(2)	936(3)	4245(2)	34(1)
O(3)	2781(2)	571(3)	4860(2)	39(1)
O(4)	1947(2)	-273(4)	5072(2)	76(2)
O(5)	3056(2)	11360(3)	264(2)	34(1)
O(6)	2238(2)	10439(3)	-198(2)	30(1)
O(7)	2935(2)	10136(3)	-592(2)	30(1)
O(8)	2062(2)	10228(3)	-1309(1)	26(1)
C(1)	2523(3)	157(4)	3663(2)	36(2)
C(2)	2250(3)	112(4)	4117(2)	29(2)
C(3)	2465(3)	1270(5)	4632(3)	45(2)
C(4)	2620(3)	-194(4)	4587(2)	33(2)
C(5)	2344(2)	-760(4)	4923(2)	29(2)
C(6)	2751(3)	-711(4)	3543(3)	35(2)
C(7)	3281(3)	-804(5)	3641(2)	37(2)
C(8)	3542(3)	-1550(5)	3530(3)	38(2)
C(9)	4087(3)	-1655(5)	3670(3)	50(2)
C(10)	4344(3)	-2393(5)	3547(3)	58(2)
C(11)	4036(3)	-2980(5)	3246(3)	56(2)
C(12)	3493(3)	-2874(5)	3119(3)	50(2)
C(13)	3221(3)	-2205(5)	3251(3)	38(2)
C(14)	2664(3)	-2104(4)	3173(2)	31(2)
C(15)	2333(3)	-2753(5)	2946(2)	39(2)
C(16)	1801(3)	-2716(5)	2887(3)	38(2)
C(17)	1567(3)	-2013(5)	3057(3)	44(2)
C(18)	1864(3)	-1366(5)	3258(2)	40(2)
C(19)	2418(3)	-1359(4)	3328(2)	34(2)
C(20)	2156(3)	538(4)	3209(2)	36(2)
C(21)	2375(3)	723(5)	2766(3)	40(2)
C(22)	2901(3)	659(4)	2727(3)	41(2)
C(23)	3080(3)	878(5)	2296(3)	45(2)
C(24)	2736(4)	1168(5)	1894(3)	51(2)
C(25)	2221(4)	1209(5)	1917(3)	49(2)
C(26)	2004(3)	1005(5)	2334(3)	51(2)
C(27)	1440(3)	1085(5)	2360(3)	46(2)
C(28)	1068(4)	1329(6)	1948(3)	69(3)
C(29)	554(4)	1429(8)	1996(4)	85(3)
C(30)	372(4)	1253(7)	2440(4)	82(3)
C(31)	726(3)	1058(5)	2835(3)	58(2)
C(32)	1274(3)	952(4)	2802(3)	44(2)
C(33)	1646(3)	667(5)	3232(2)	38(2)
C(34)	2094(3)	-1506(4)	4634(2)	33(2)
C(35)	2401(3)	-2201(5)	4483(2)	35(2)
C(36)	2964(3)	-2203(5)	4551(3)	41(2)
C(37)	3241(3)	-2844(5)	4406(2)	39(2)
C(38)	2978(3)	-3540(5)	4160(3)	47(2)
C(39)	2435(4)	-3552(5)	4094(3)	53(2)
C(40)	2142(3)	-2908(5)	4244(2)	39(2)
C(41)	1557(3)	-2913(5)	4131(3)	45(2)
C(42)	1280(4)	-3579(6)	3893(3)	59(2)
C(43)	735(5)	-3510(9)	3794(4)	100(4)
C(44)	464(4)	-2837(8)	3906(4)	83(3)
C(45)	721(3)	-2216(6)	4140(3)	55(2)
C(46)	1268(3)	-2247(6)	4257(3)	51(2)
C(47)	1564(3)	-1542(5)	4502(3)	46(2)
C(48)	2708(3)	-1032(4)	5407(3)	36(2)

C(49)	2486(3)	-1519(4)	5769(3)	41(2)
C(50)	1964(3)	-1682(5)	5751(3)	44(2)
C(51)	1766(4)	-2097(5)	6122(3)	54(2)
C(52)	2109(5)	-2376(6)	6510(4)	64(3)
C(53)	2613(5)	-2268(5)	6550(3)	64(3)
C(54)	2837(4)	-1829(5)	6187(3)	52(2)
C(55)	3404(4)	-1623(5)	6237(3)	54(2)
C(56)	3806(4)	-1951(6)	6614(3)	70(3)
C(57)	4314(5)	-1730(8)	6660(4)	88(4)
C(58)	4483(3)	-1160(6)	6346(3)	59(2)
C(59)	4127(3)	-849(6)	5955(3)	62(2)
C(60)	3583(3)	-1106(5)	5900(3)	48(2)
C(61)	3212(3)	-806(5)	5480(3)	45(2)
C(62)	2612(3)	11810(4)	-15(2)	31(2)
C(63)	2366(3)	11198(4)	-431(2)	31(2)
C(64)	2568(3)	9791(4)	-327(2)	36(2)
C(65)	2746(2)	10916(4)	-776(2)	25(2)
C(66)	2466(2)	10850(4)	-1316(2)	25(2)
C(67)	2239(3)	12082(4)	331(2)	31(2)
C(68)	2437(3)	12569(4)	778(2)	33(2)
C(69)	2975(3)	12734(4)	940(3)	38(2)
C(70)	3150(3)	13110(4)	1367(3)	36(2)
C(71)	2798(3)	13376(5)	1670(3)	45(2)
C(72)	2271(3)	13284(4)	1517(2)	38(2)
C(73)	2073(3)	12877(4)	1070(3)	38(2)
C(74)	1509(3)	12728(4)	928(2)	35(2)
C(75)	1116(3)	13123(5)	1167(3)	49(2)
C(76)	584(3)	12924(6)	1027(3)	61(2)
C(77)	429(3)	12372(5)	636(3)	50(2)
C(78)	782(3)	11987(5)	400(3)	42(2)
C(79)	1345(3)	12180(4)	530(3)	39(2)
C(80)	1730(2)	11858(4)	262(2)	29(2)
C(81)	2843(3)	12586(4)	-242(2)	30(2)
C(82)	3386(3)	12666(4)	-203(2)	34(2)
C(83)	3630(3)	13353(5)	-388(2)	37(2)
C(84)	4207(3)	13381(6)	-321(3)	64(3)
C(85)	4423(3)	14042(6)	-517(3)	59(2)
C(86)	4137(3)	14702(6)	-729(3)	61(2)
C(87)	3601(3)	14707(5)	-770(3)	50(2)
C(88)	3322(3)	14002(4)	-622(2)	37(2)
C(89)	2760(3)	13951(4)	-681(2)	31(2)
C(90)	2436(3)	14567(4)	-929(3)	41(2)
C(91)	1884(3)	14486(5)	-1006(3)	39(2)
C(92)	1651(3)	13793(5)	-851(2)	37(2)
C(93)	1957(3)	13171(4)	-600(2)	34(2)
C(94)	2521(2)	13200(4)	-498(2)	26(2)
C(95)	2213(2)	11659(4)	-1520(2)	26(2)
C(96)	2527(3)	12375(4)	-1650(2)	30(2)
C(97)	3070(2)	12398(4)	-1546(2)	25(2)
C(98)	3350(3)	13077(5)	-1679(2)	35(2)
C(99)	3082(3)	13739(4)	-1920(2)	32(2)
C(100)	2560(3)	13734(4)	-2012(2)	33(2)
C(101)	2254(3)	13053(4)	-1887(2)	30(2)
C(102)	1665(2)	13087(4)	-1978(2)	27(2)
C(103)	1387(3)	13725(4)	-2202(2)	36(2)
C(104)	846(3)	13750(5)	-2259(3)	48(2)
C(105)	558(3)	13115(5)	-2095(3)	48(2)
C(106)	845(3)	12426(5)	-1862(3)	40(2)
C(107)	1402(2)	12427(4)	-1807(2)	26(2)
C(108)	1683(3)	11714(4)	-1594(2)	30(2)
C(109)	2864(3)	10490(4)	-1654(2)	29(2)

C(110)	2656(3)	10294(4)	-2171(2)	31(2)
C(111)	2114(3)	10277(4)	-2363(3)	36(2)
C(112)	1940(3)	10035(5)	-2838(3)	41(2)
C(113)	2295(3)	9831(5)	-3143(3)	48(2)
C(114)	2824(3)	9838(5)	-2975(2)	40(2)
C(115)	3028(3)	10075(4)	-2489(2)	35(2)
C(116)	3578(2)	10045(4)	-2305(2)	32(2)
C(117)	3979(3)	9873(5)	-2599(3)	53(2)
C(118)	4499(4)	9823(6)	-2391(3)	60(2)
C(119)	4648(3)	9898(6)	-1908(3)	57(2)
C(120)	4286(3)	10087(5)	-1608(3)	50(2)
C(121)	3756(2)	10187(4)	-1787(2)	32(2)
C(122)	3377(2)	10394(4)	-1485(2)	26(2)
Cl(1)	725(1)	8904(2)	-925(1)	94(1)
Cl(2)	651(1)	10710(2)	-803(1)	85(1)
Cl(3)	4407(3)	2022(5)	4643(3)	225(3)
Cl(4)	4262(2)	126(4)	4714(2)	157(2)
Cl(5)	5433(2)	9364(4)	-440(2)	183(2)
Cl(6)	5713(1)	10774(2)	248(1)	104(1)
C(1S)	1042(3)	9798(6)	-684(3)	69(3)
C(2S)	3971(8)	1193(15)	4773(8)	203(10)
C(3S)	5875(5)	9928(14)	-49(5)	169(9)

c) X-ray crystallographic data for TADDOL 7e



Crystals of compound **7e** suitable for x-ray analysis were obtained by slow evaporation from CH₂Cl₂ / isoctane. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 604102). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Table 5: Crystal data and structure refinement for TADDOL 7e

Identification code	TADDOL 7e	
Empirical formula	C73 H50 O4	
Formula weight	991.13	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 10.2354(6) Å b = 18.0628(10) Å c = 16.1878(9) Å	$\alpha = 90^\circ$. $\beta = 103.189(3)^\circ$. $\gamma = 90^\circ$.
Volume	2913.9(3) Å ³	
Z	2	
Density (calculated)	1.130 Mg/m ³	
Absorption coefficient	0.069 mm ⁻¹	
F(000)	1040	
Crystal size	0.60 x 0.50 x 0.40 mm ³	
Theta range for data collection	1.71 to 28.28°	
Index ranges	-13<=h<=13, -23<=k<=17, -21<=l<=21	
Reflections collected	40710	
Independent reflections	12810 [R(int) = 0.0305]	
Completeness to theta = 28.28°	99.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9730 and 0.9599	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	12810 / 1 / 882	
Goodness-of-fit on F ²	1.043	
Final R indices [I>2sigma(I)]	R1 = 0.0453, wR2 = 0.1207	
R indices (all data)	R1 = 0.0506, wR2 = 0.1237	
Absolute structure parameter	1.6(7)	
Largest diff. peak and hole	0.242 and -0.291 e.Å ⁻³	

Table 6: Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for TADDOL 7e. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O(1)	3690(1)	756(1)	7554(1)	24(1)
O(2)	5689(1)	670(1)	7170(1)	26(1)
O(3)	5638(1)	476(1)	9043(1)	22(1)
O(4)	3745(1)	-166(1)	5978(1)	25(1)
C(1)	4646(2)	1168(1)	7230(1)	23(1)
C(2)	4004(2)	1495(1)	6365(1)	28(1)
C(3)	4767(2)	1541(2)	5755(1)	46(1)
C(4)	4237(3)	1874(2)	4977(2)	64(1)
C(5)	2958(3)	2170(2)	4827(1)	62(1)
C(6)	2226(3)	2116(2)	5425(2)	61(1)
C(7)	2723(2)	1785(1)	6199(1)	42(1)
C(8)	5224(2)	1804(1)	7826(1)	26(1)
C(9)	6520(2)	2035(1)	7881(1)	32(1)
C(10)	7030(2)	2633(1)	8401(1)	44(1)
C(11)	6226(3)	3008(1)	8841(1)	46(1)
C(12)	4922(3)	2783(1)	8775(1)	41(1)
C(13)	4428(2)	2173(1)	8270(1)	34(1)
C(14)	4162(1)	19(1)	7771(1)	19(1)
C(15)	4614(1)	-69(1)	8752(1)	19(1)
C(16)	3478(1)	74(1)	9220(1)	19(1)
C(17)	2224(1)	252(1)	8788(1)	22(1)
C(18)	1139(1)	373(1)	9199(1)	22(1)
C(19)	-141(2)	570(1)	8722(1)	27(1)
C(20)	-1186(2)	685(1)	9103(1)	31(1)
C(21)	-975(2)	600(1)	9982(1)	32(1)
C(22)	263(2)	409(1)	10461(1)	30(1)
C(23)	1353(2)	289(1)	10079(1)	23(1)
C(24)	2697(2)	112(1)	10563(1)	23(1)
C(25)	2980(2)	40(1)	11454(1)	32(1)
C(26)	4240(2)	-94(1)	11919(1)	35(1)
C(27)	5300(2)	-159(1)	11512(1)	33(1)
C(28)	5070(2)	-99(1)	10644(1)	26(1)
C(29)	3761(2)	25(1)	10137(1)	21(1)
C(30)	5280(1)	-831(1)	8964(1)	20(1)
C(31)	4557(2)	-1521(1)	8948(1)	23(1)
C(32)	3138(2)	-1564(1)	8692(1)	29(1)
C(33)	2466(2)	-2228(1)	8687(1)	39(1)
C(34)	3193(2)	-2874(1)	8938(1)	42(1)
C(35)	4545(2)	-2851(1)	9179(1)	38(1)
C(36)	5275(2)	-2188(1)	9204(1)	27(1)
C(37)	6722(2)	-2175(1)	9473(1)	27(1)
C(38)	7505(2)	-2806(1)	9782(1)	39(1)
C(39)	8887(2)	-2755(1)	9998(1)	44(1)
C(40)	9542(2)	-2102(1)	9909(1)	40(1)
C(41)	8817(2)	-1475(1)	9628(1)	29(1)
C(42)	7399(2)	-1505(1)	9420(1)	25(1)
C(43)	6647(2)	-846(1)	9171(1)	22(1)
C(44)	5332(1)	-75(1)	7320(1)	20(1)
C(45)	4931(2)	-513(1)	6466(1)	23(1)
C(46)	4542(2)	-1309(1)	6657(1)	26(1)
C(47)	3217(2)	-1485(1)	6485(1)	32(1)
C(48)	2741(2)	-2210(1)	6590(1)	43(1)
C(49)	1338(3)	-2350(2)	6411(2)	61(1)
C(50)	878(4)	-3063(2)	6480(2)	82(1)
C(51)	1798(4)	-3644(2)	6689(2)	88(1)

C(52)	3160(4)	-3517(2)	6890(2)	73(1)
C(53)	3659(3)	-2784(1)	6852(1)	48(1)
C(54)	5076(2)	-2611(1)	7074(1)	41(1)
C(55)	6060(3)	-3156(2)	7395(2)	57(1)
C(56)	7384(3)	-2999(2)	7630(2)	56(1)
C(57)	7836(3)	-2278(2)	7558(1)	48(1)
C(58)	6909(2)	-1728(1)	7262(1)	37(1)
C(59)	5524(2)	-1875(1)	6993(1)	30(1)
C(60)	6023(2)	-493(1)	5955(1)	24(1)
C(61)	5761(2)	-816(1)	5104(1)	25(1)
C(62)	4512(2)	-1134(1)	4708(1)	34(1)
C(63)	4304(2)	-1436(1)	3912(1)	40(1)
C(64)	5327(2)	-1443(1)	3475(1)	40(1)
C(65)	6543(2)	-1136(1)	3843(1)	38(1)
C(66)	6798(2)	-817(1)	4649(1)	29(1)
C(67)	8094(2)	-507(1)	5026(1)	33(1)
C(68)	9190(2)	-500(2)	4625(2)	55(1)
C(69)	10406(2)	-186(2)	5018(2)	62(1)
C(70)	10611(2)	119(2)	5817(2)	55(1)
C(71)	9568(2)	115(2)	6236(2)	47(1)
C(72)	8308(2)	-192(1)	5837(1)	33(1)
C(73)	7241(2)	-184(1)	6275(1)	31(1)

IV) Infrared spectrum of TADDOL derivatives: Comparison of OH stretching frequencies.

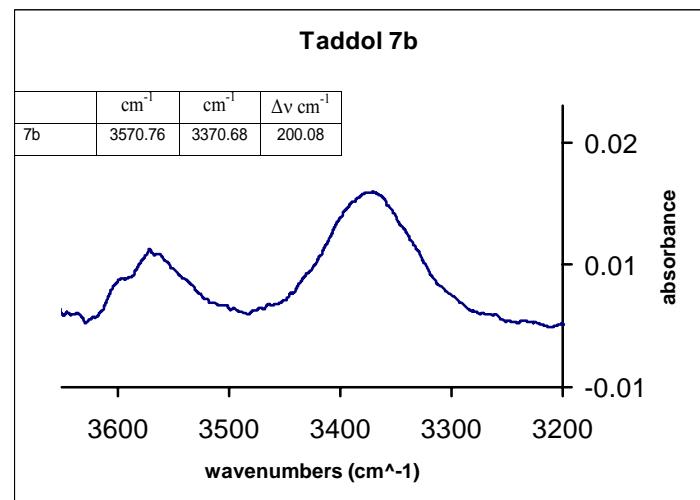
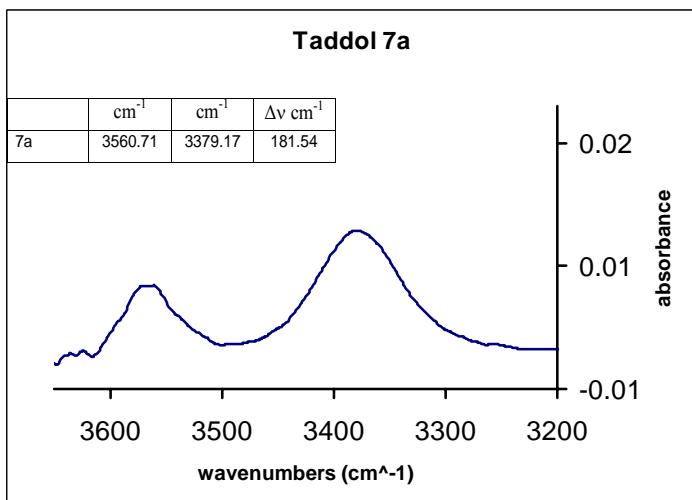
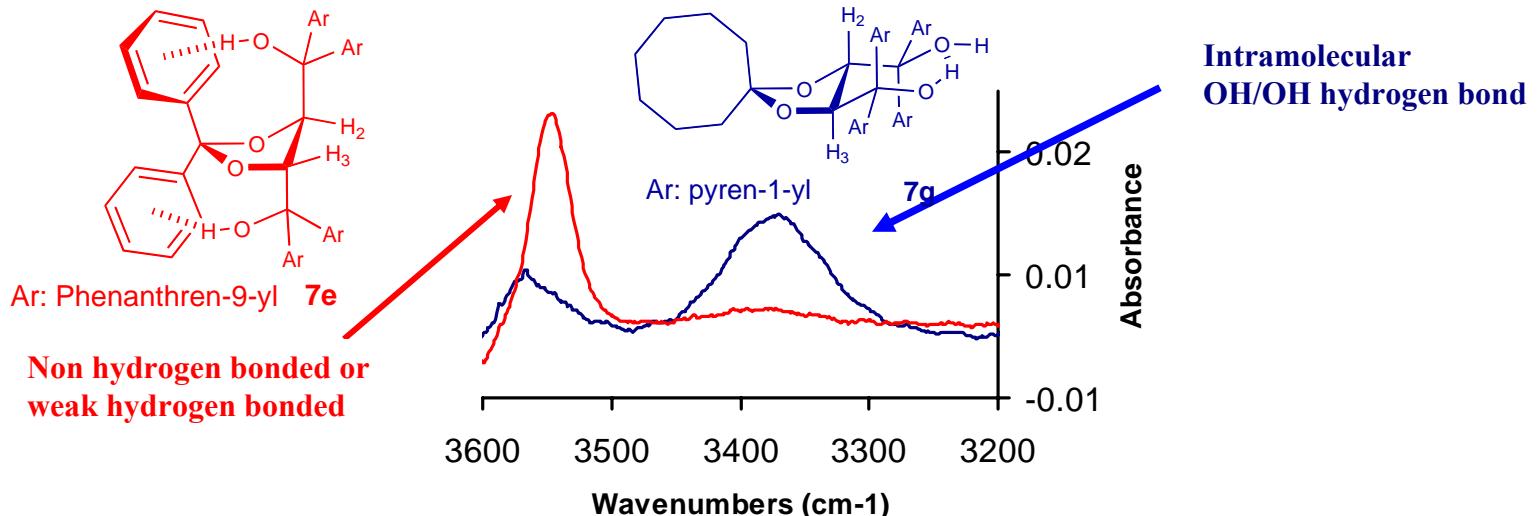


Figure 1. IR spectrum for TADDOL 7a (5 mM in CH_2Cl_2).

Figure 2. IR spectrum for TADDOL 7b (5 mM in CH_2Cl_2).

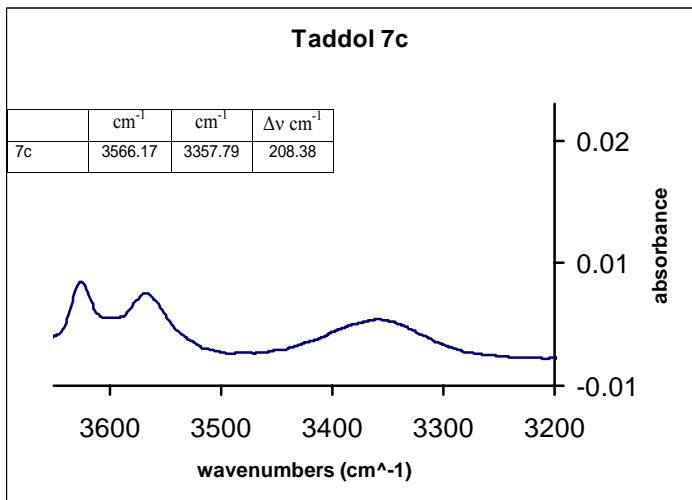


Figure 3. IR spectrum for TADDOL 7c (5 mM in CH_2Cl_2).

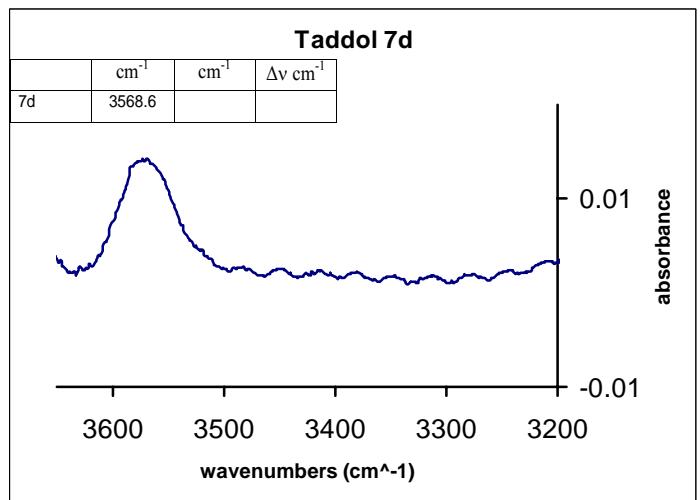


Figure 4. IR spectrum for TADDOL 7d (5 mM in CH_2Cl_2).

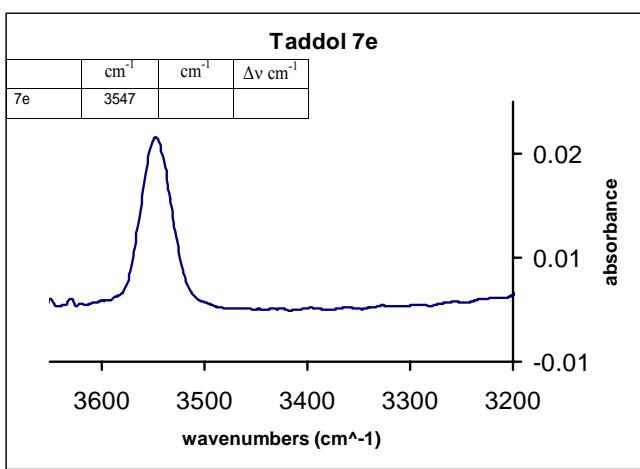


Figure 5. IR spectrum for TADDOL 7e (5 mM in CH₂Cl₂).

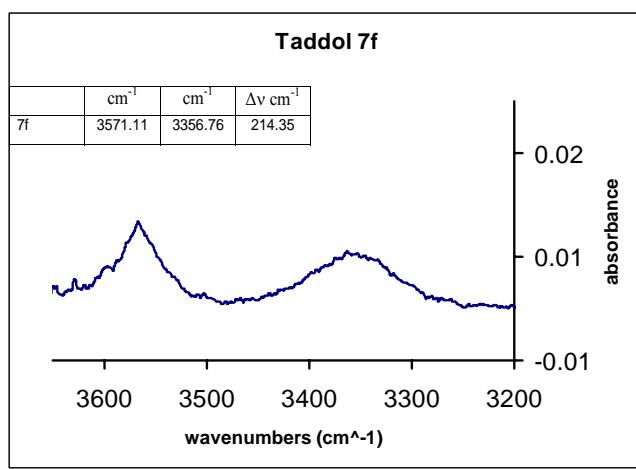


Figure 6. IR spectrum for TADDOL 7f (5 mM in CH₂Cl₂).

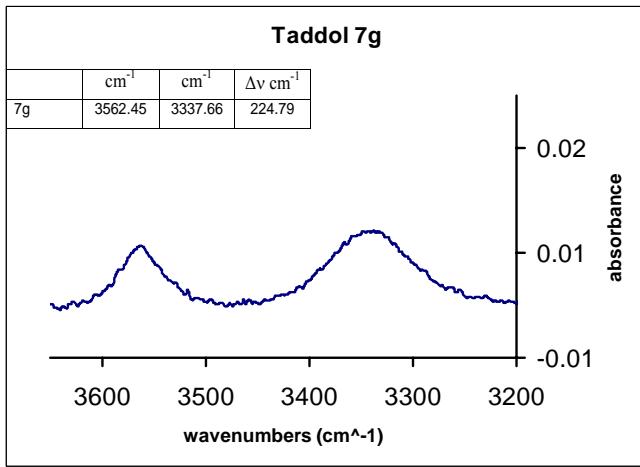


Figure 7. IR spectrum for TADDOL 7g (5 mM in CH₂Cl₂).

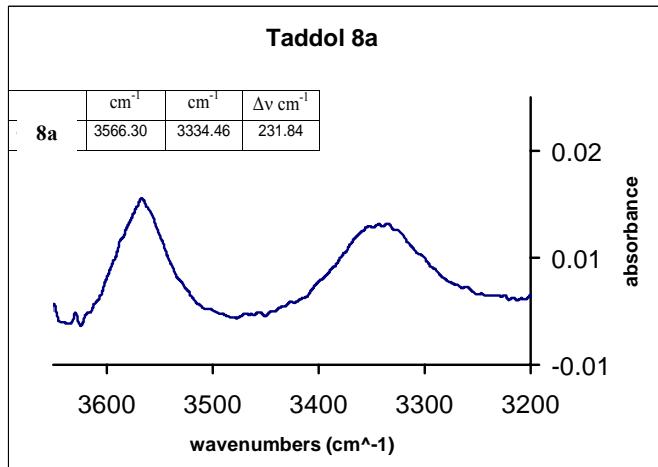
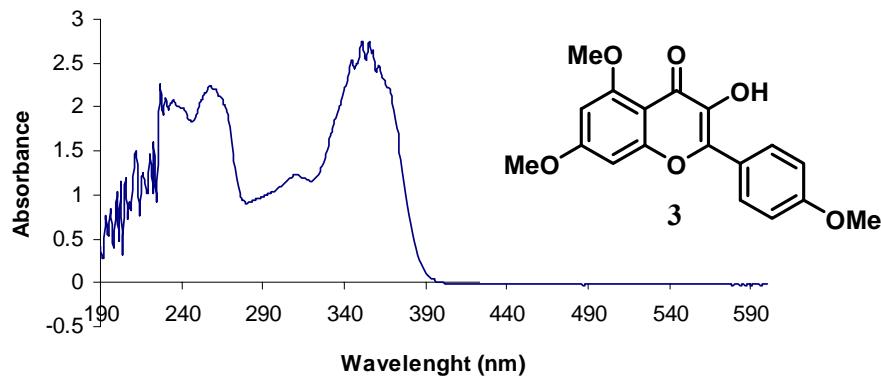


Figure 8. IR spectrum for TADDOL 8a (5 mM in CH₂Cl₂).

V) UV spectra of TADDOL 7g, 8a, and 3-hydroxyflavone 3

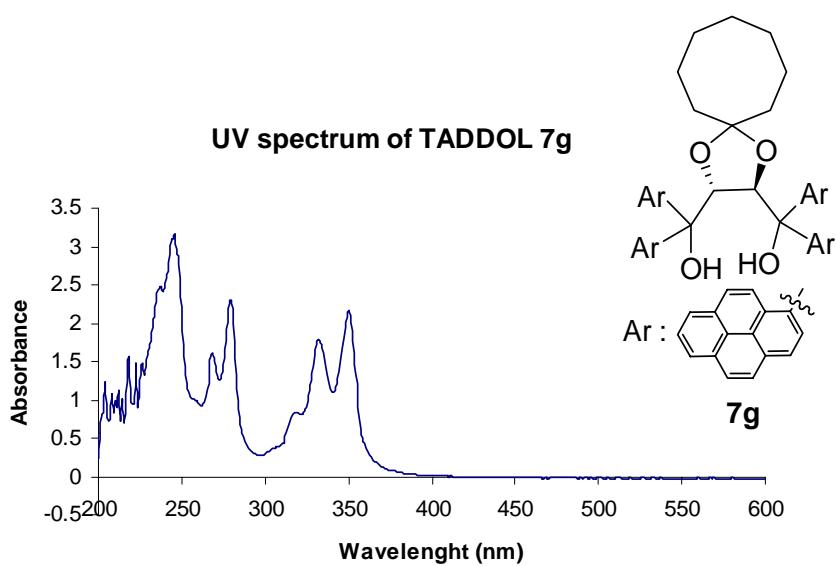
UV spectrum of 3-hydroxyflavone 3



Conditions (in CH_2Cl_2):

$C = 0.058 \text{ mmol/L}$
 $\text{At } 350 \text{ nm, } A = 2.749$
 $\varepsilon_{3-\text{HF}} = 47.4 \text{ L mmol}^{-1} \text{ cm}^{-1}$

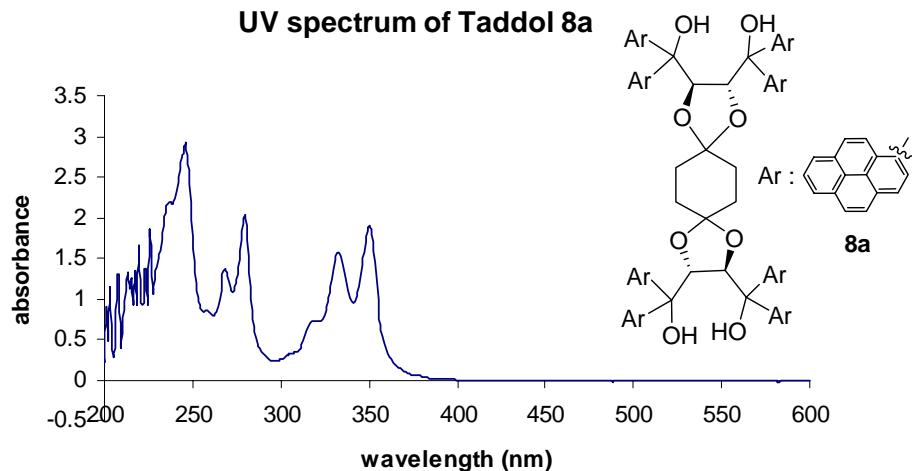
UV spectrum of TADDOL 7g



Conditions (in CH_2Cl_2):

$C = 0.013 \text{ mmol/L}$
 $\text{At } 350 \text{ nm, } A = 2.159$
 $\varepsilon_{7g} = 166 \text{ L mmol}^{-1} \text{ cm}^{-1}$

UV spectrum of Taddol 8a



Conditions (in CH_2Cl_2):

$C = 0.006 \text{ mmol/L}$
 $\text{At } 350 \text{ nm, } A = 1.898$
 $\varepsilon_{8a} = 316 \text{ L mmol}^{-1} \text{ cm}^{-1}$

VI) Calculation of the Electrostatic Potential Surface for Oxidopyrylium 2

A representative conformer of oxidopyrylium **2** and an atom numbering scheme is shown in Figure 9. The starting geometry for this structure was taken as the lowest energy conformer obtained from a semi-empirical AM1 conformational search in Spartan '04 (V1.0.1). These coordinates were then subjected to a geometry optimization using the B3LYP/6-31+G* level of theory. The calculated Mulliken charges are listed in Table 7. The computed electrostatic potential surfaces are shown for the bond density (Figure 10) and for the molecular surface (Figure 11).

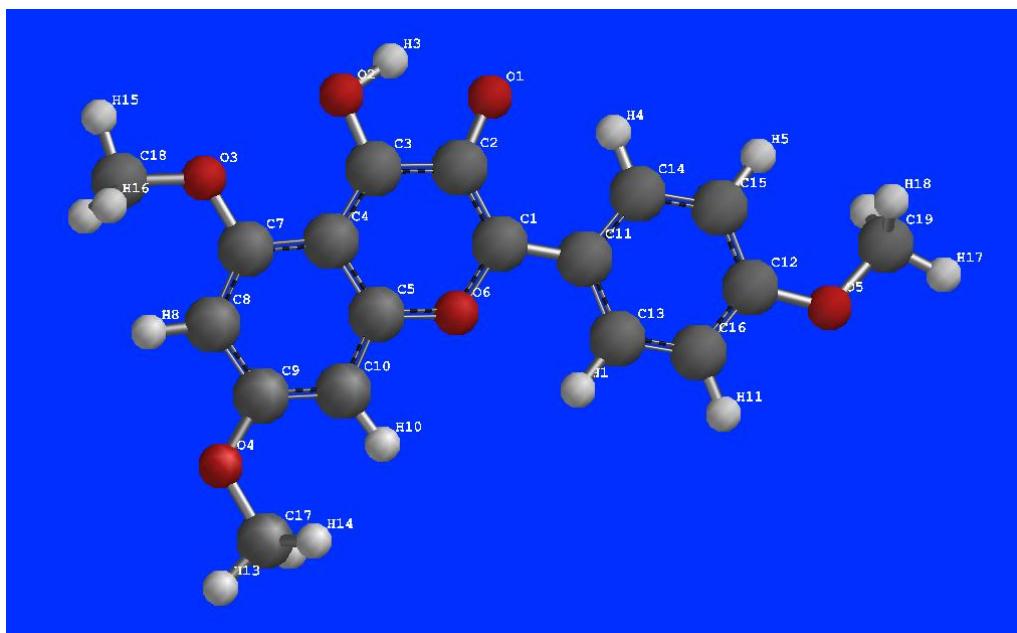


Figure 9: B3LYP/6-31+G* optimized oxidopyrylium **2** conformer and atom numbering scheme.

Table 7: Mulliken Net Atomic Charges for oxidopyrylium **2**.

Atom	Charge (a.u.)				
1 C	0.370796	15 C	-0.200187	29 H	0.208862
2 O	-0.388925	16 C	-0.263012	30 H	0.214690
3 C	0.196969	17 C	-0.265586	31 H	0.208849
4 C	0.559595	18 C	-0.333266	32 C	-0.353403
5 C	0.287949	19 H	0.192272	33 H	0.210147
6 C	-0.061044	20 H	0.259758	34 H	0.219831
7 C	-0.345369	21 H	0.179486	35 H	0.210243
8 C	0.233470	22 H	0.188205	36 O	-0.390238
9 H	0.194281	3 O	-0.771206	37 C	-0.363681
10 C	-0.528585	24 O	-0.641061	38 H	0.205382
11 H	0.195594	25 H	0.549197	39 H	0.208070
12 C	0.351866	26 O	-0.375264	40 H	0.205494
13 C	0.277154	27 O	-0.389735		
14 C	0.112142	28 C	-0.369741		
				Sum of atomic charges =	0.000000

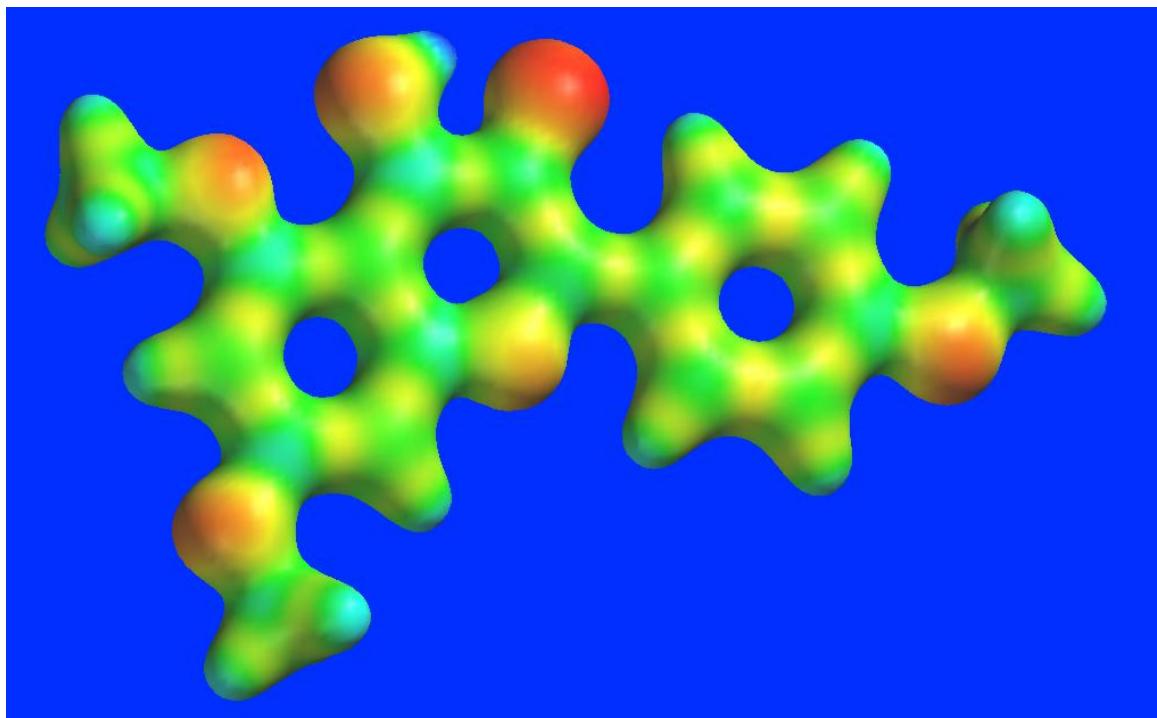


Figure 11. Electrostatic potential map (bond density) for oxidopyrylium **2**

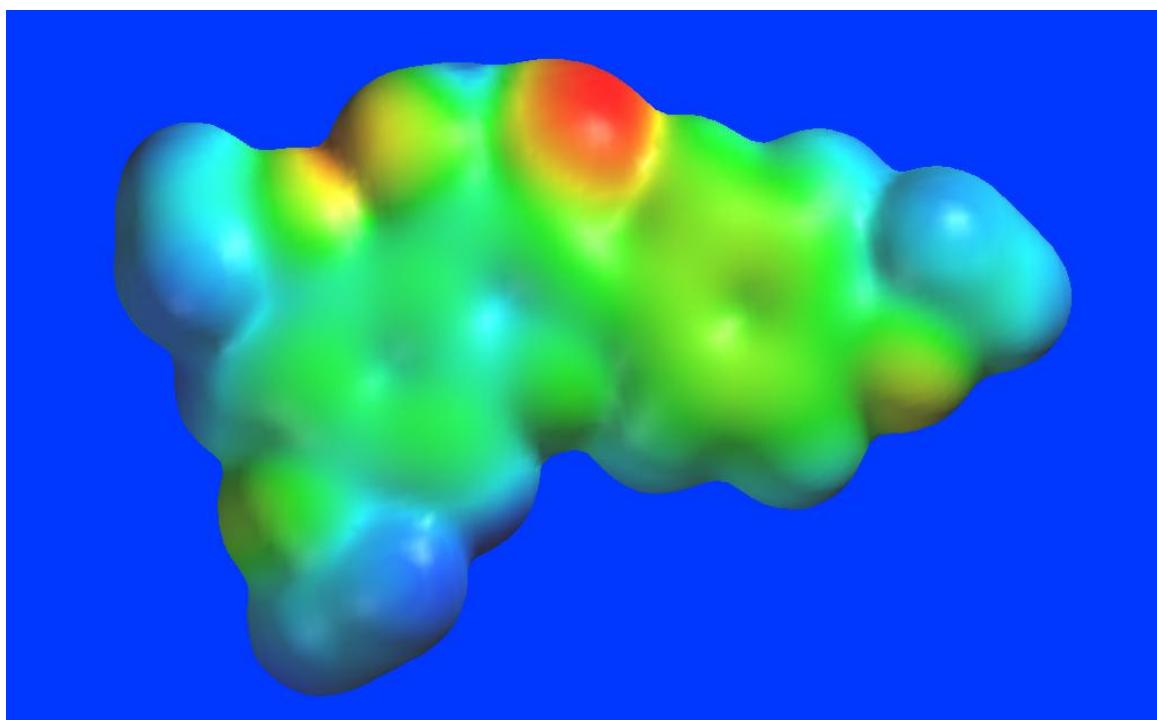
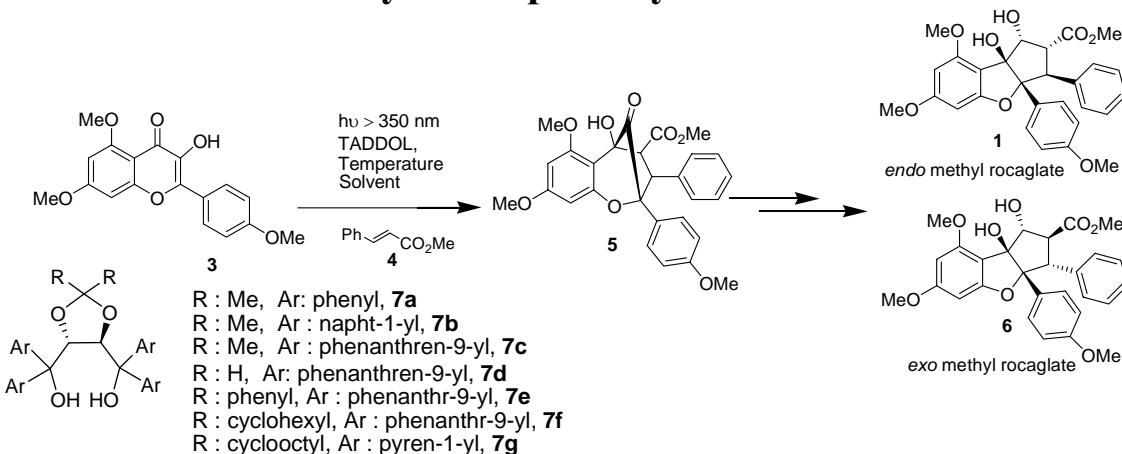


Figure 12. Electrostatic potential map (molecular surface) for oxidopyrylium **2**

VII) Influence of temperature, solvent and stoichiometry on the enantioselectivity of the photocycloadditon



Influence of the temperature

entry	additive	temperature	Solvent	yield of 5 , % ^b	yield of 1 / 6 , % ^c	ee of 1 / 6 , % ^d
1 ^a	7a	0°C	Toluene	60	41 / 15	7 / 5
2 ^a	7b	0°C	Toluene	61	49 / 7	25 / 18
3 ^a	7a	-70°C	Toluene/CH ₂ Cl ₂ 2/1	51	35 / 4	15 / 7
4 ^a	7b	-70°C	Toluene/CH ₂ Cl ₂ 2/1	92	52 / 9	40 / 36

^a Reactions conducted with 1 equiv of 3-HF, 1 equiv of additive, and 5 equiv. of methyl cinnamate. ^b

Isolated yield. ^c Isolated yield for the α -ketol rearrangement/ reduction sequence. ^d Determined by chiral HPLC

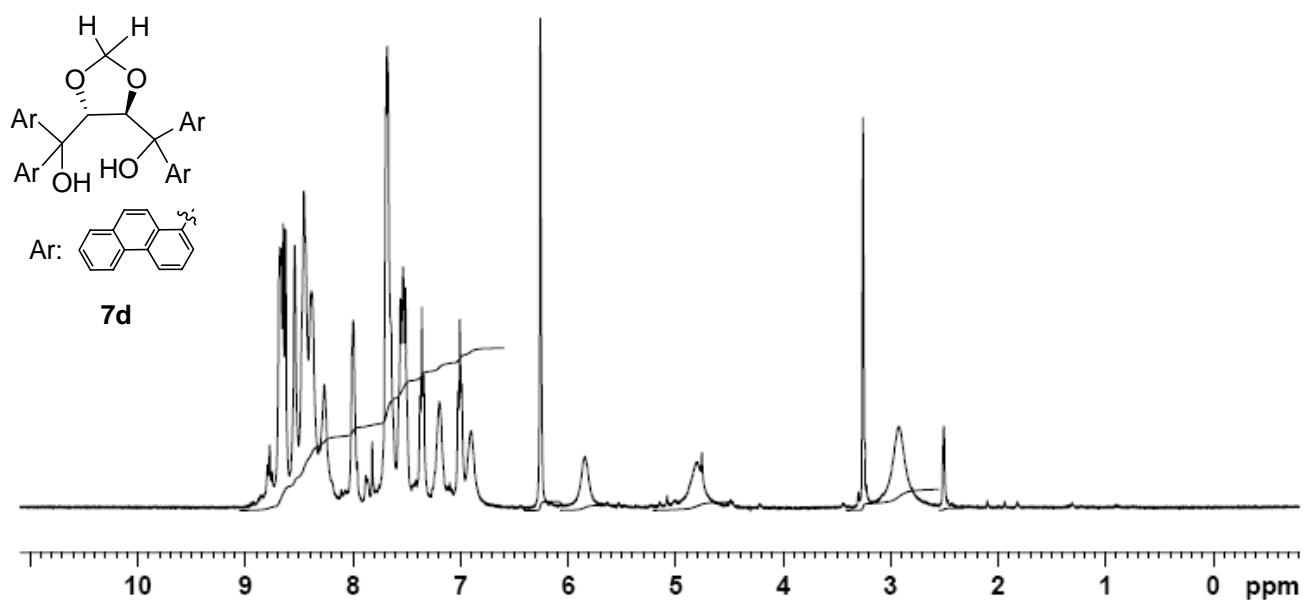
Influence of stoichiometry and concentration.

entry	additive	Conditions	Concentration of 3	Equiv of 4	yield of 5 , % ^a	yield of 1 / 6 , % ^b	ee of 1 / 6 , % ^c
5	7c 1 equiv	Toluene/CH ₂ Cl ₂ , -70°C 2/1	0.03 M	5	90	71 / 14	60 / 58
6	7c 1 equiv	CH ₂ Cl ₂ , -70°C	0.03 M	1.5	56	66 / 28	54 / 48
7	7c 1 equiv	CH ₂ Cl ₂ , -70°C	0.1 M	1.5	70	67 / 15	55 / 48
8	7c 1 equiv	CH ₂ Cl ₂ , -70°C	0.2 M	1.5	59	64 / 17	45 / 43
9	7f 1 equiv	Toluene/CH ₂ Cl ₂ , -70°C 2/1	0.03 M	5	79	67 / 19	70 / 47
10	7f 2 equiv	Toluene/CH ₂ Cl ₂ , -70°C 2/1	0.03 M	5	92	47 / 15	71 / 50

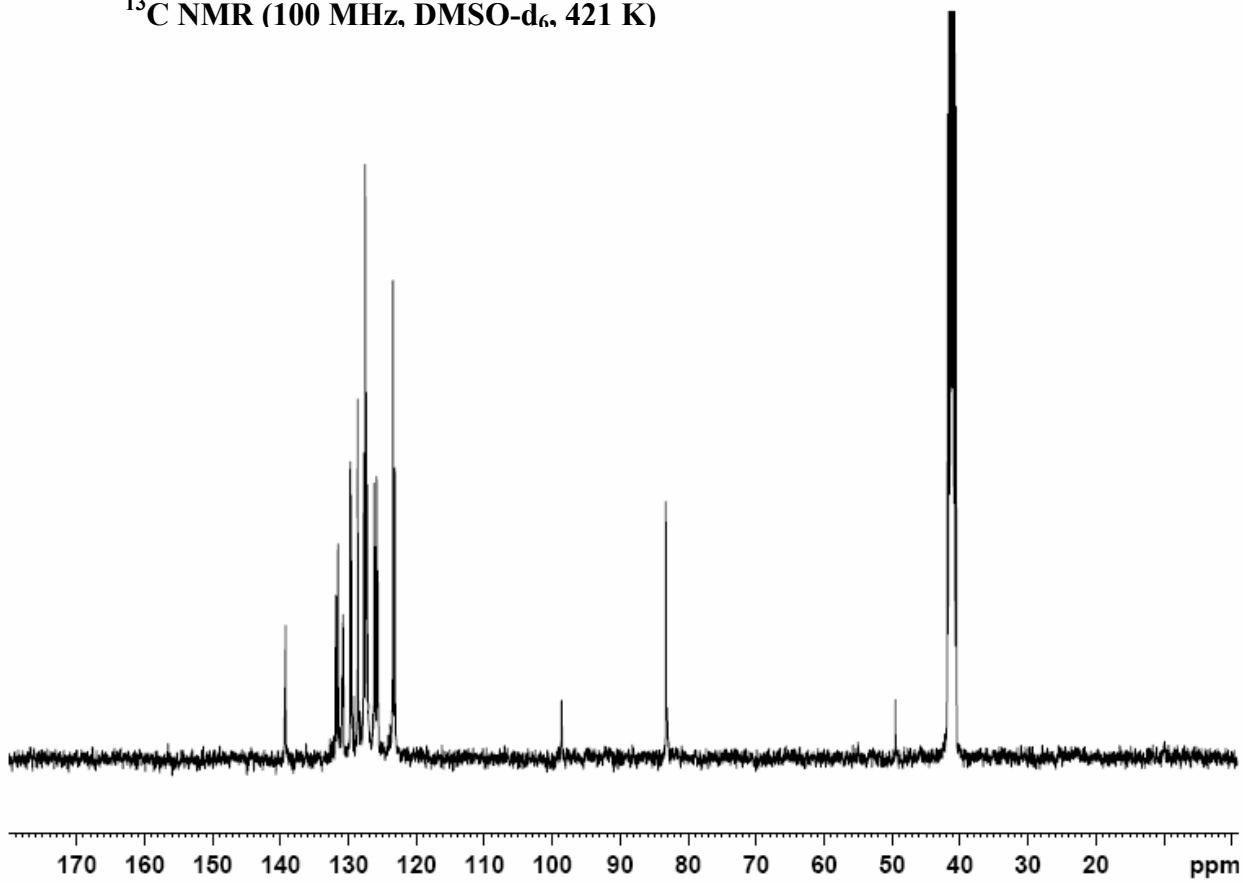
^a Isolated yield. ^b Isolated yield for the α -ketol rearrangement/ reduction sequence. ^c Determined by chiral HPLC

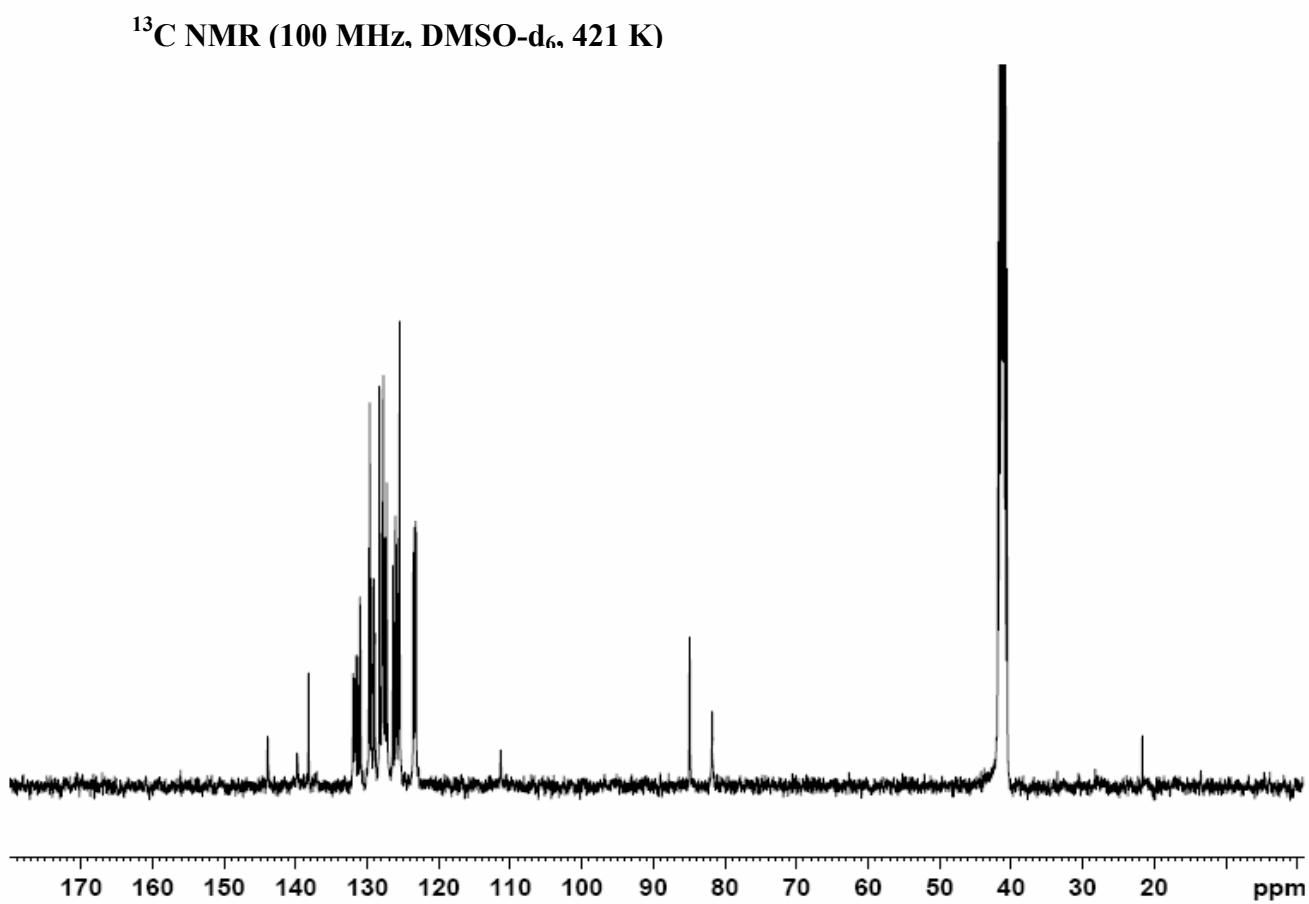
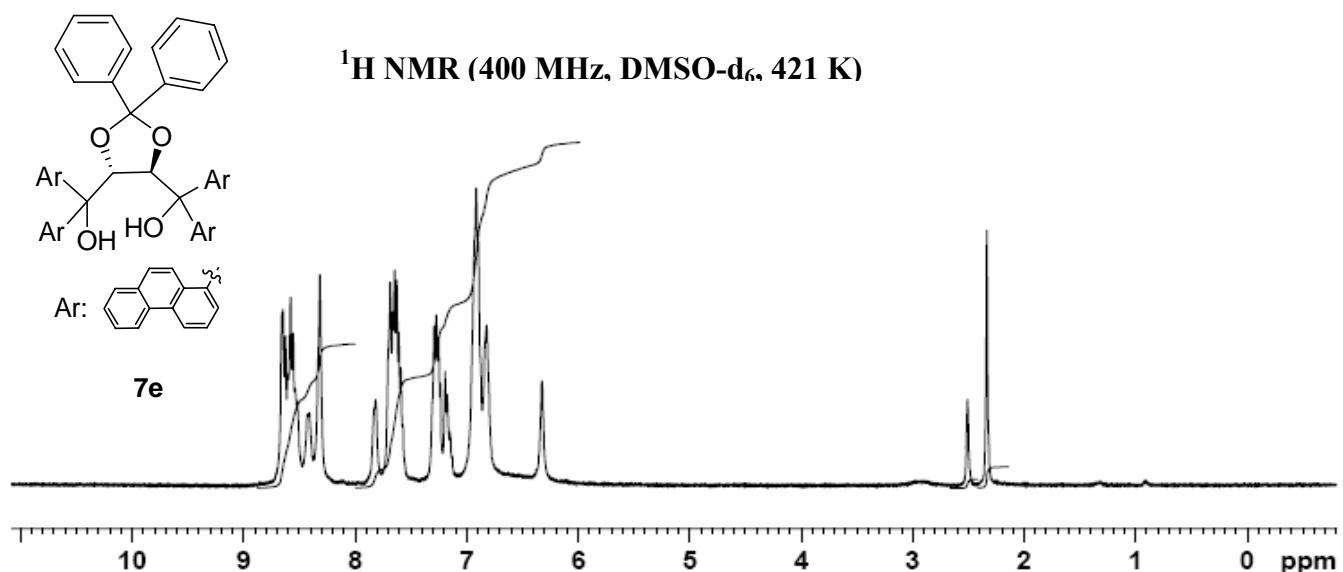
VII) ^1H and ^{13}C NMR spectra

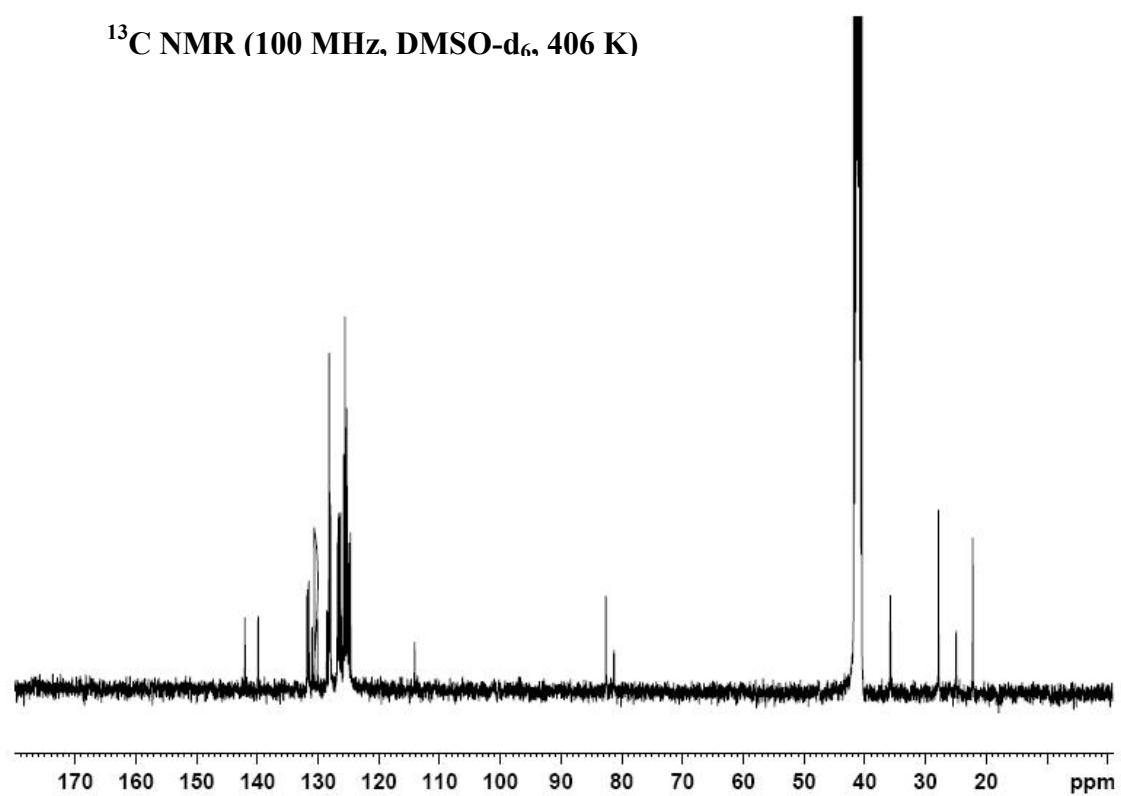
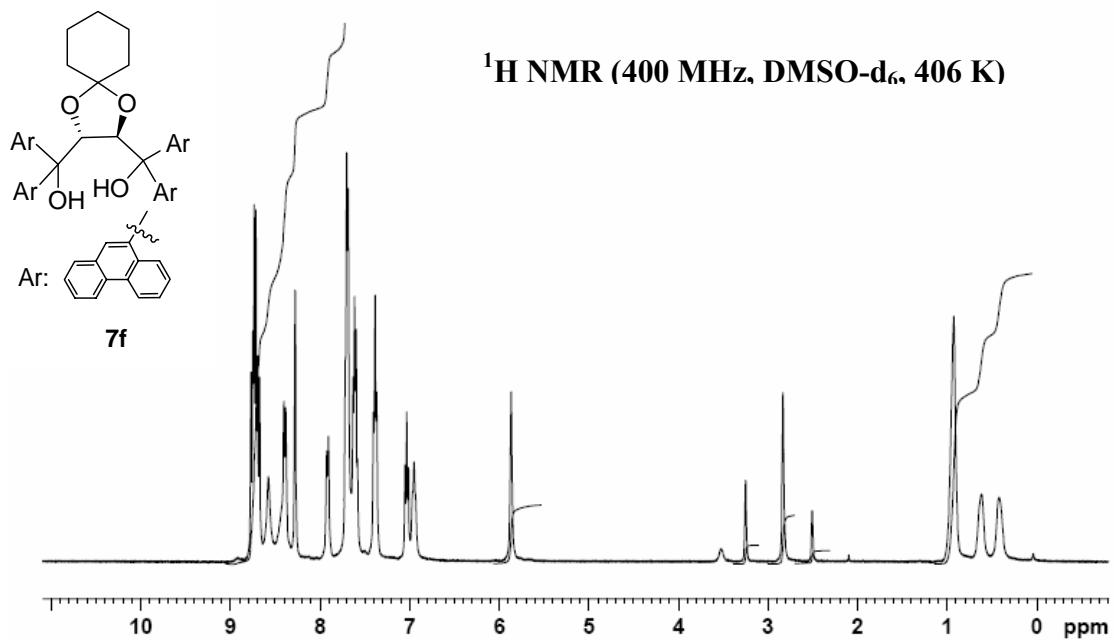
^1H NMR (400 MHz, DMSO-d₆, 421 K)

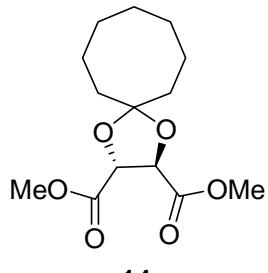


^{13}C NMR (100 MHz, DMSO-d₆, 421 K)



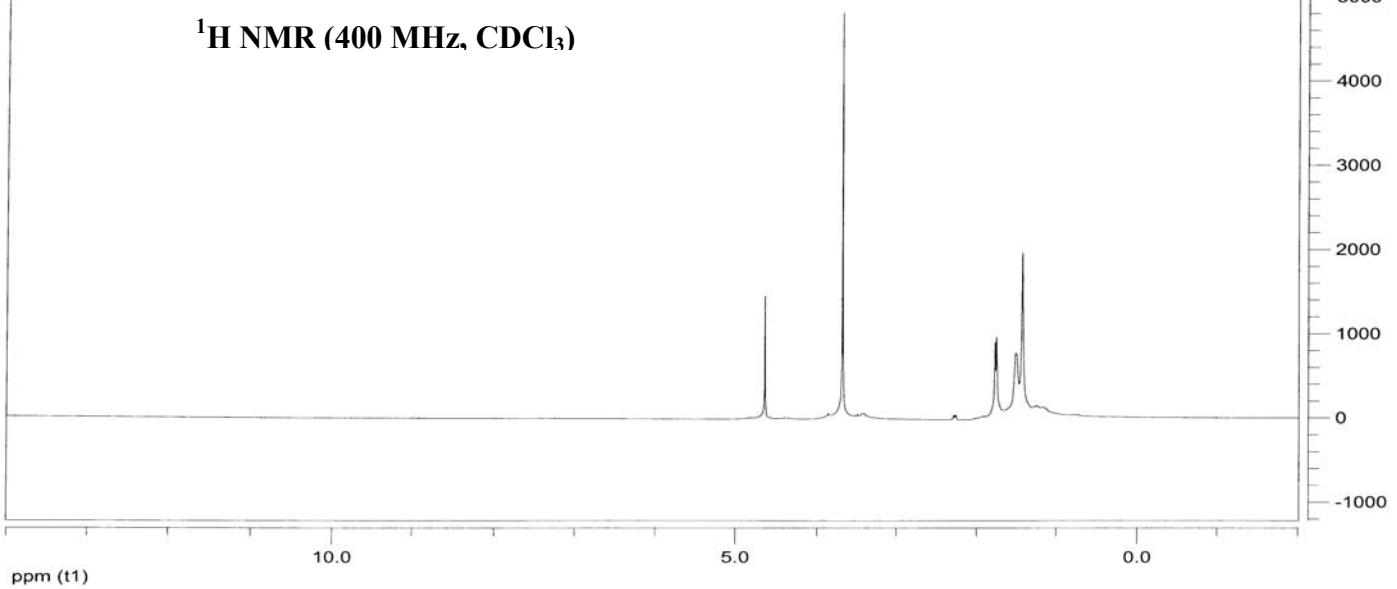




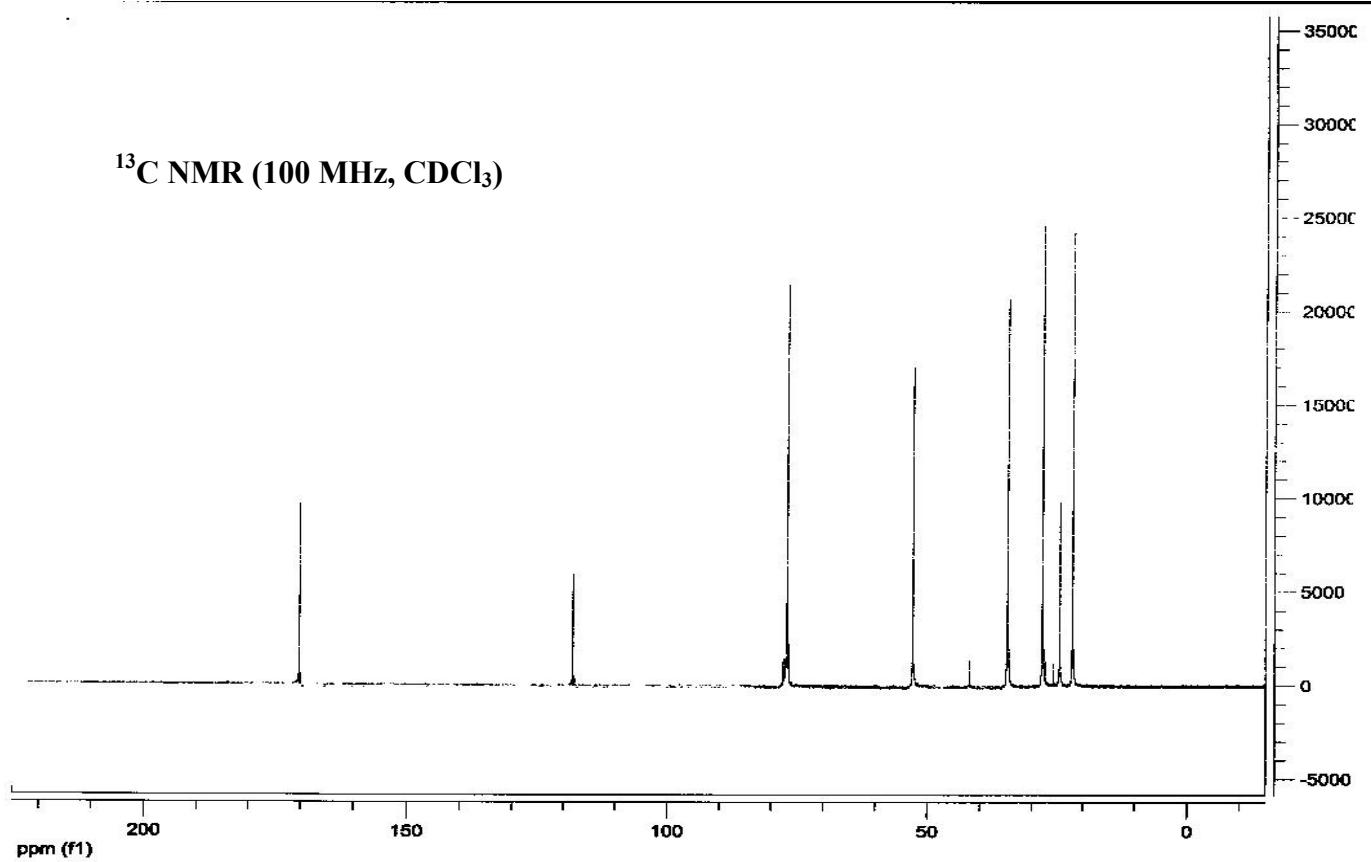


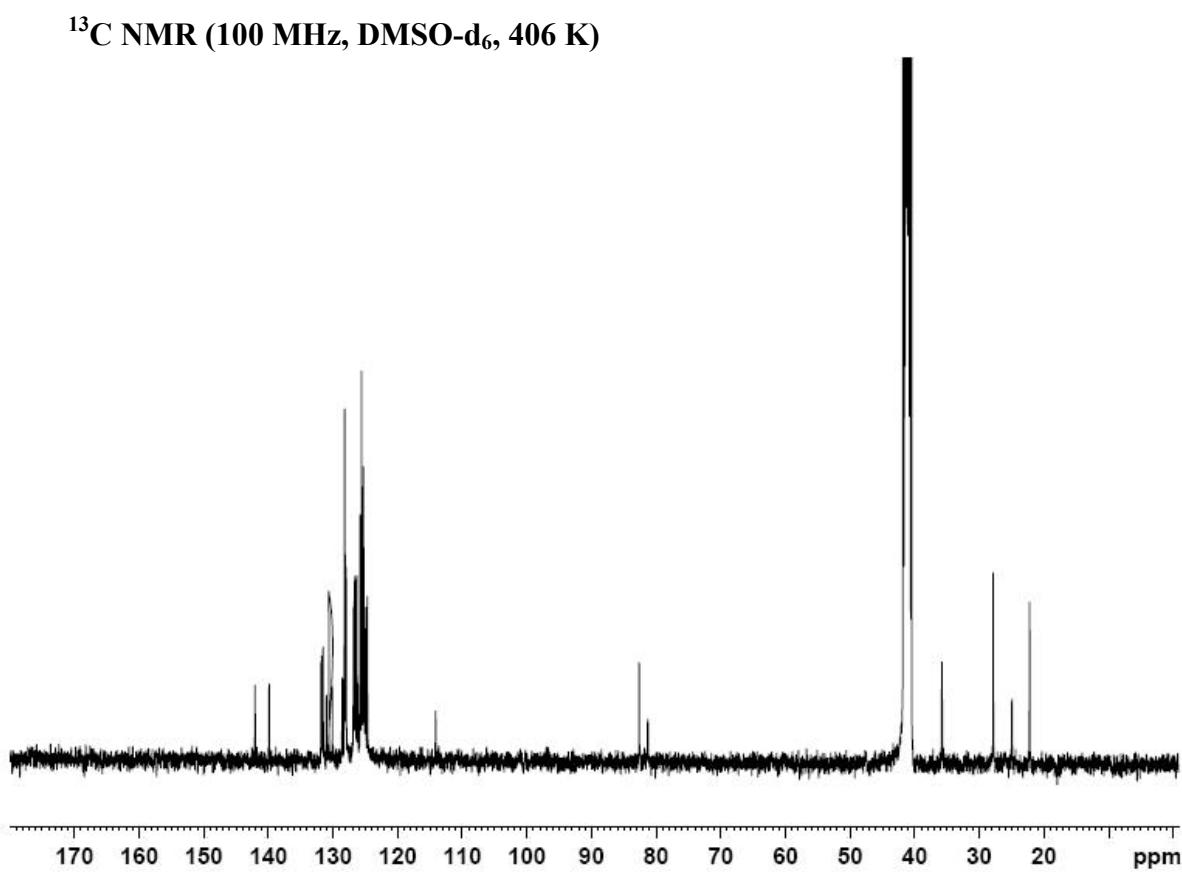
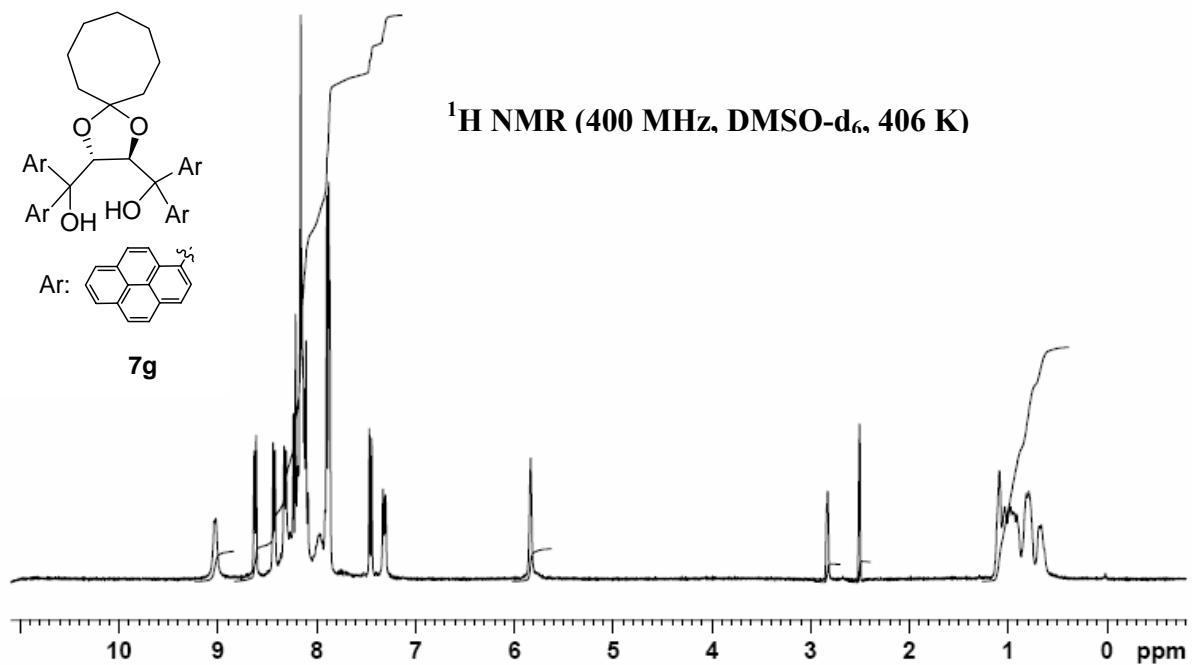
14

^1H NMR (400 MHz, CDCl_3)

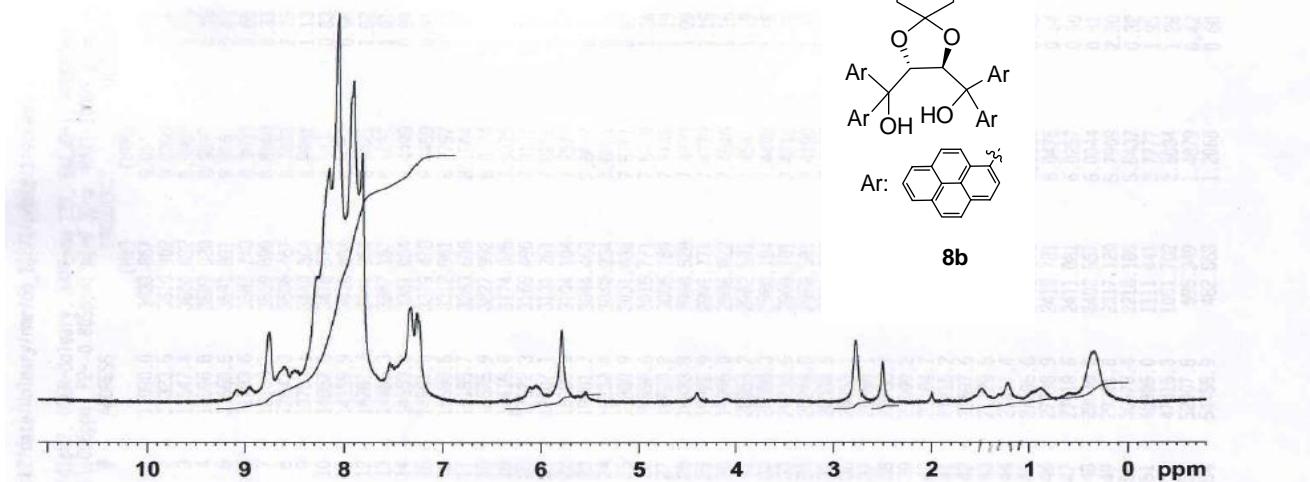


^{13}C NMR (100 MHz, CDCl_3)

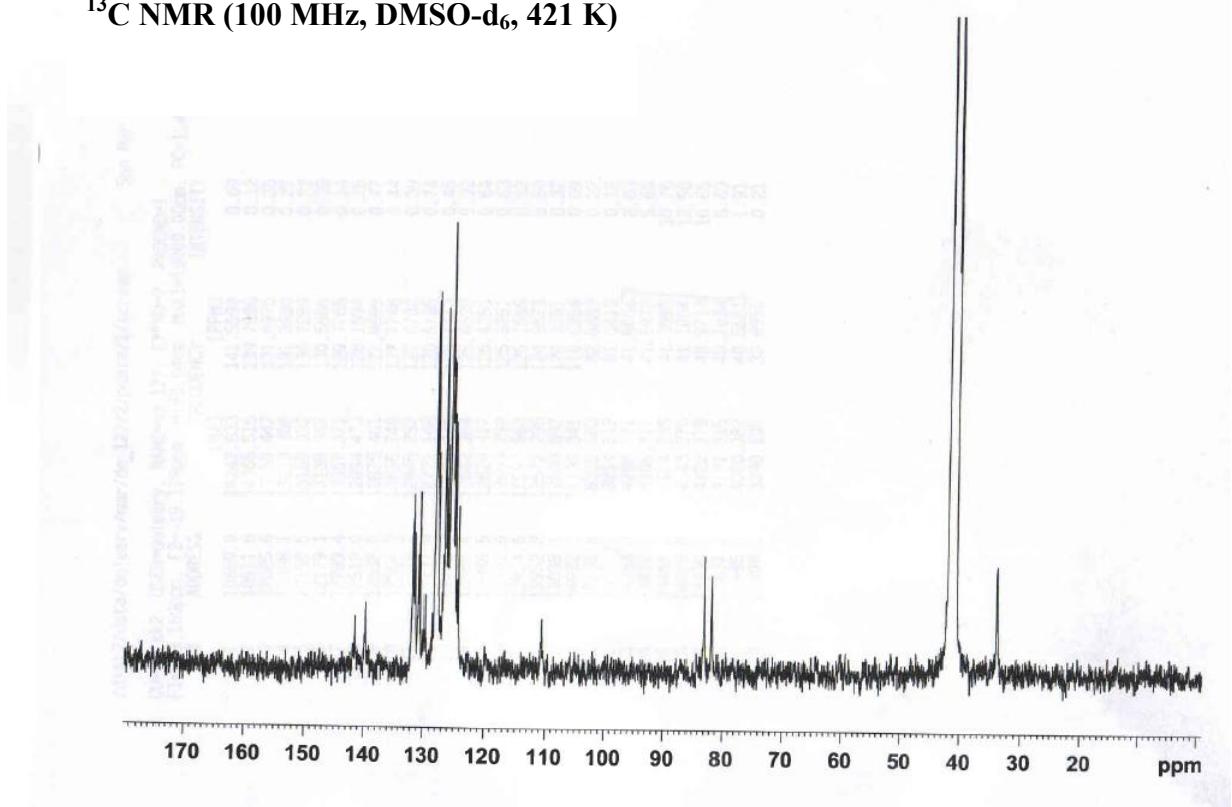


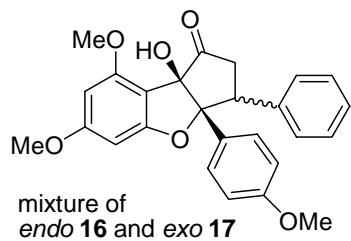


¹H NMR (400 MHz, DMSO-d₆, 421 K)

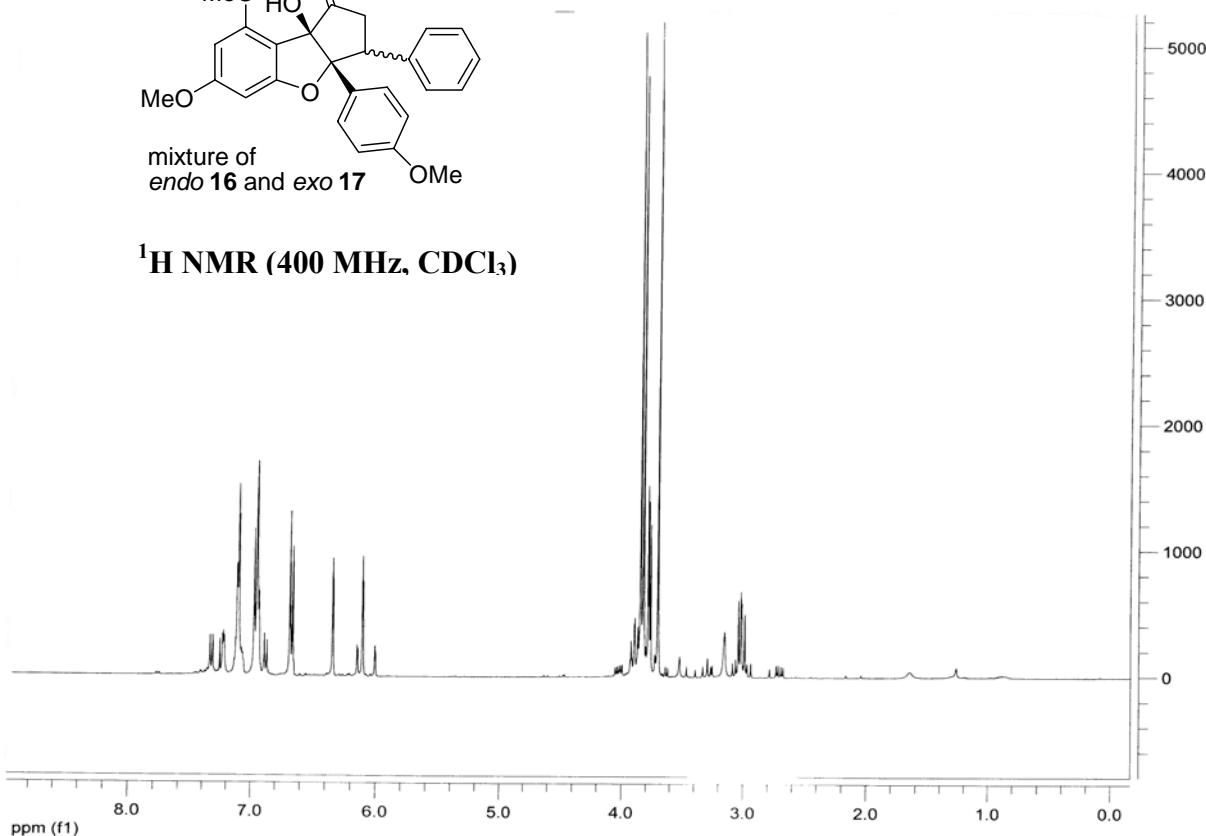


¹³C NMR (100 MHz, DMSO-d₆, 421 K)

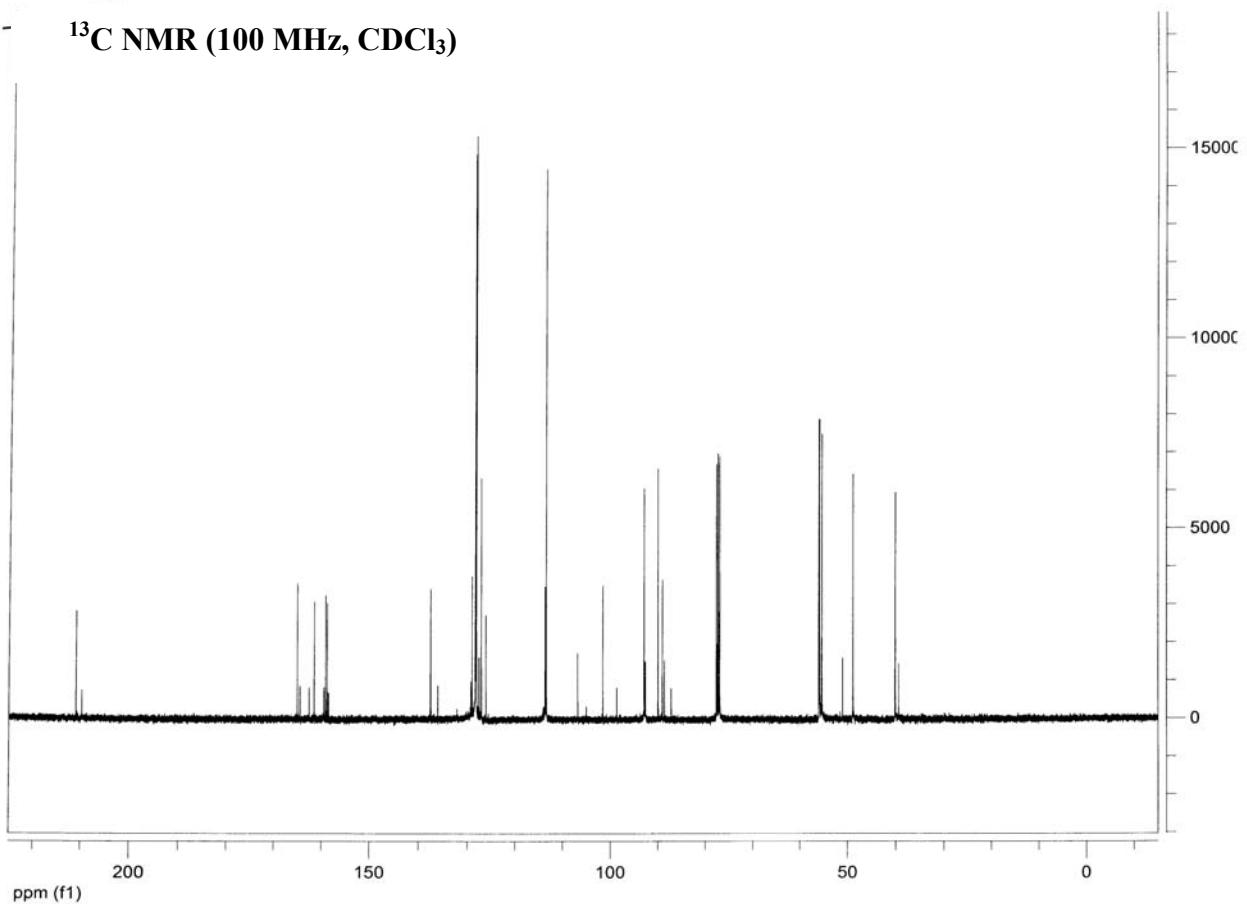


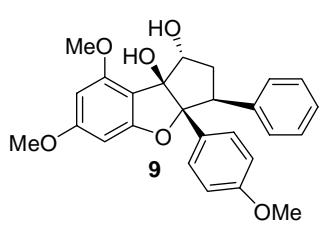


¹H NMR (400 MHz, CDCl₃)

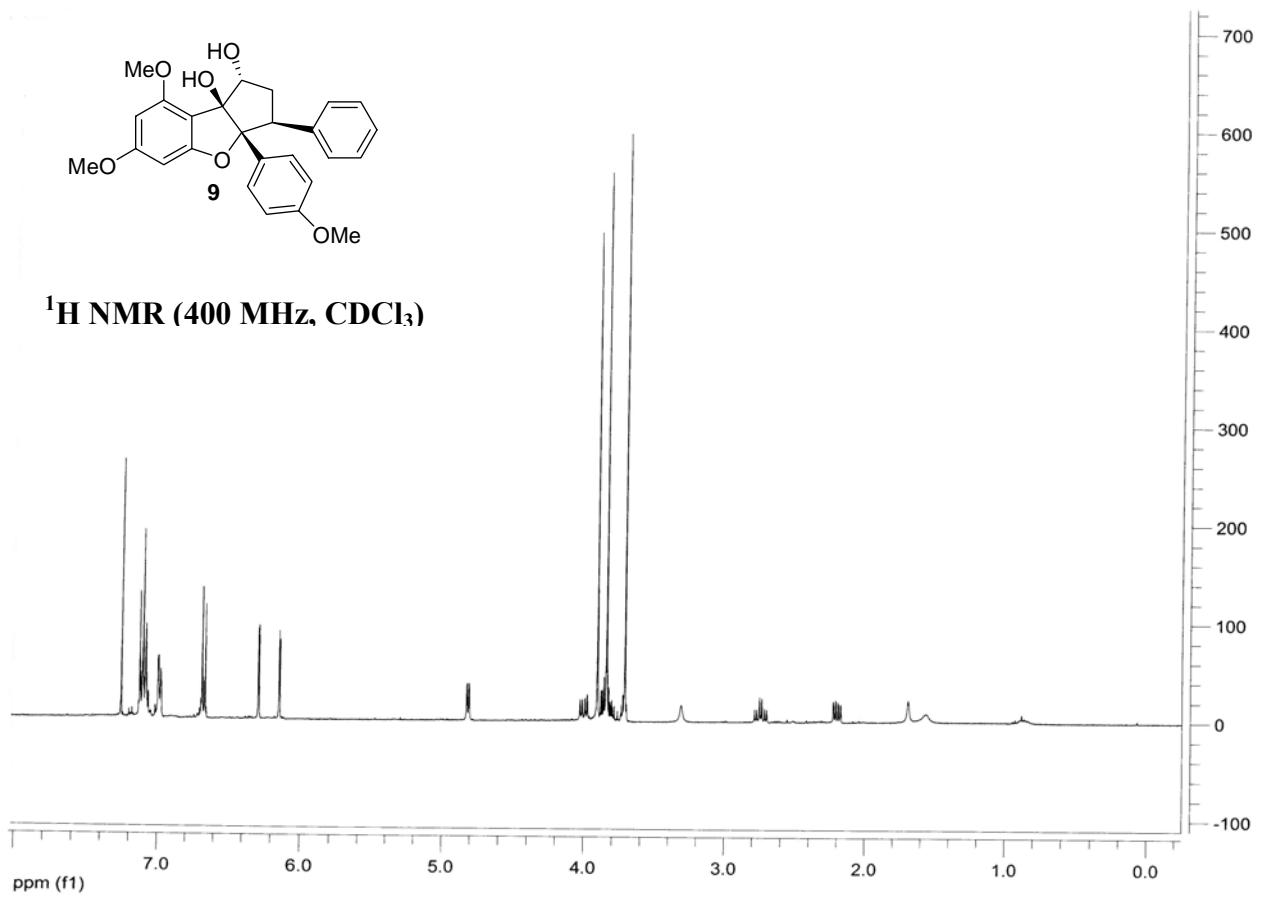


¹³C NMR (100 MHz, CDCl₃)

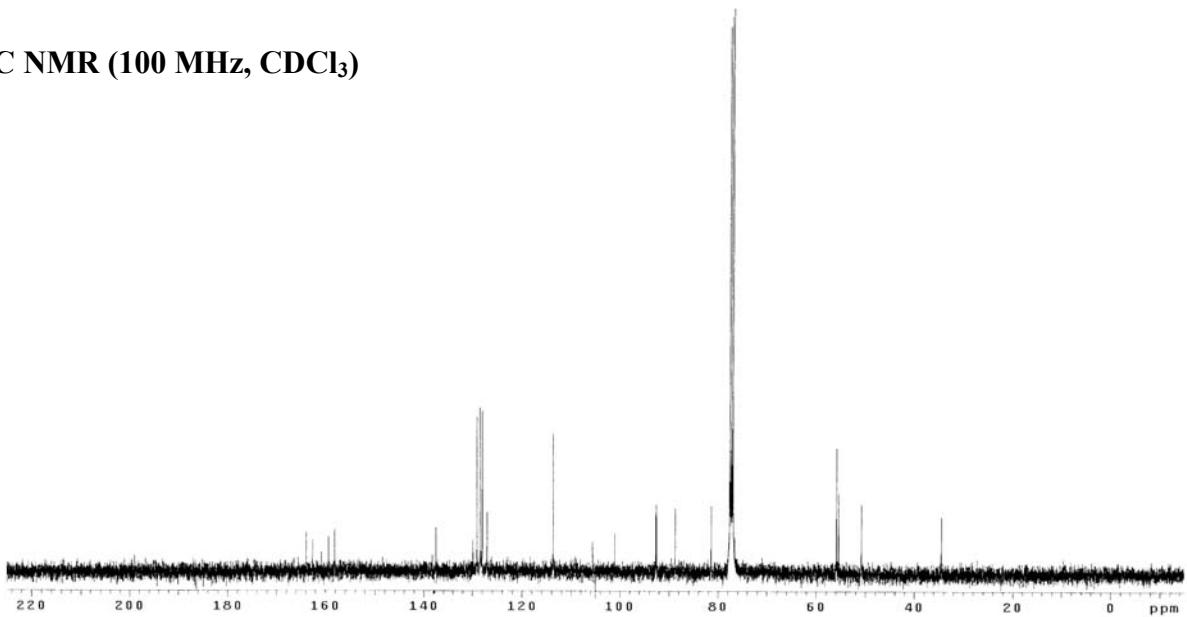


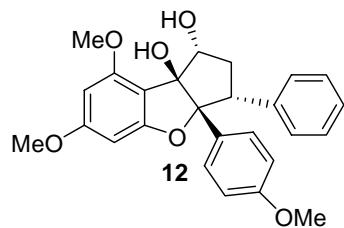


¹H NMR (400 MHz, CDCl₃)

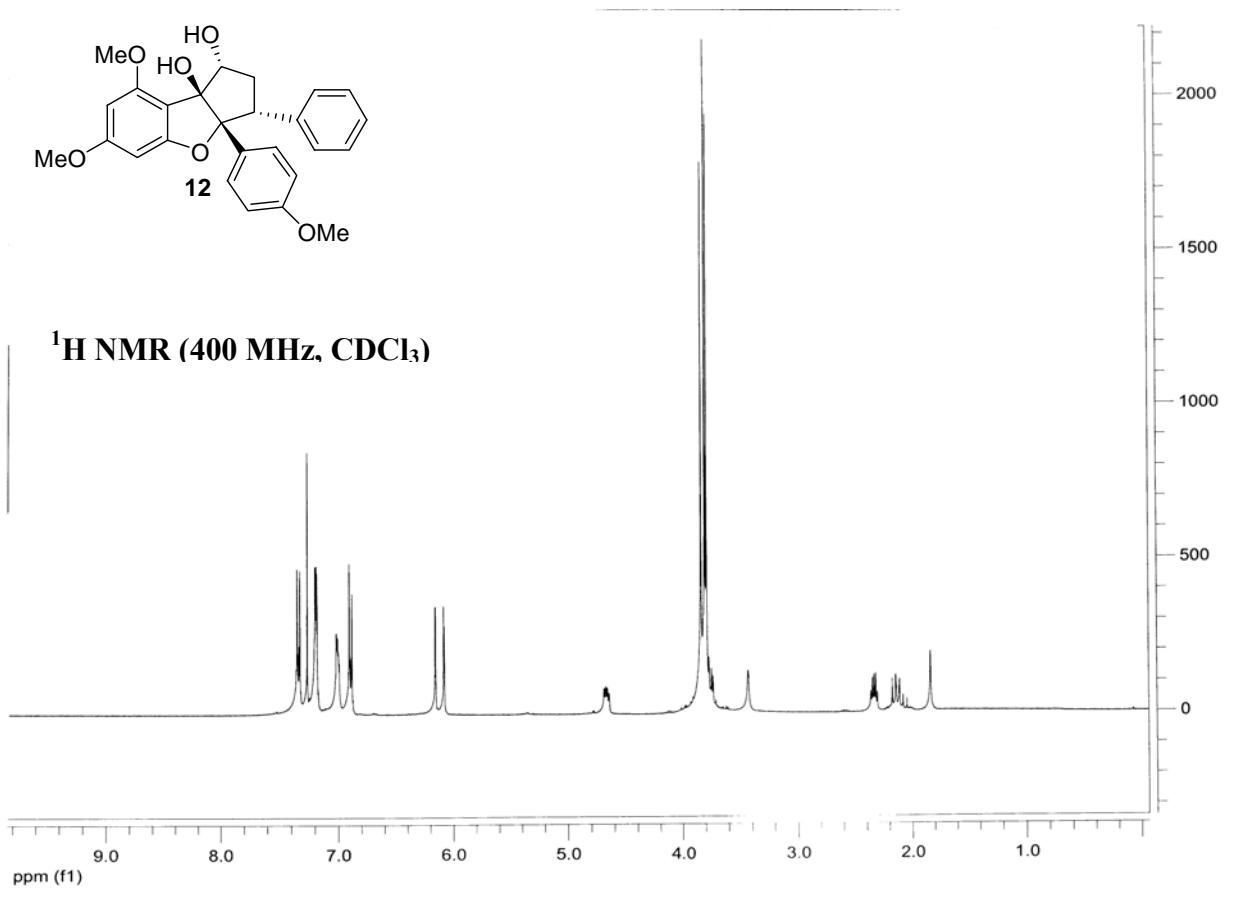


¹³C NMR (100 MHz, CDCl₃)

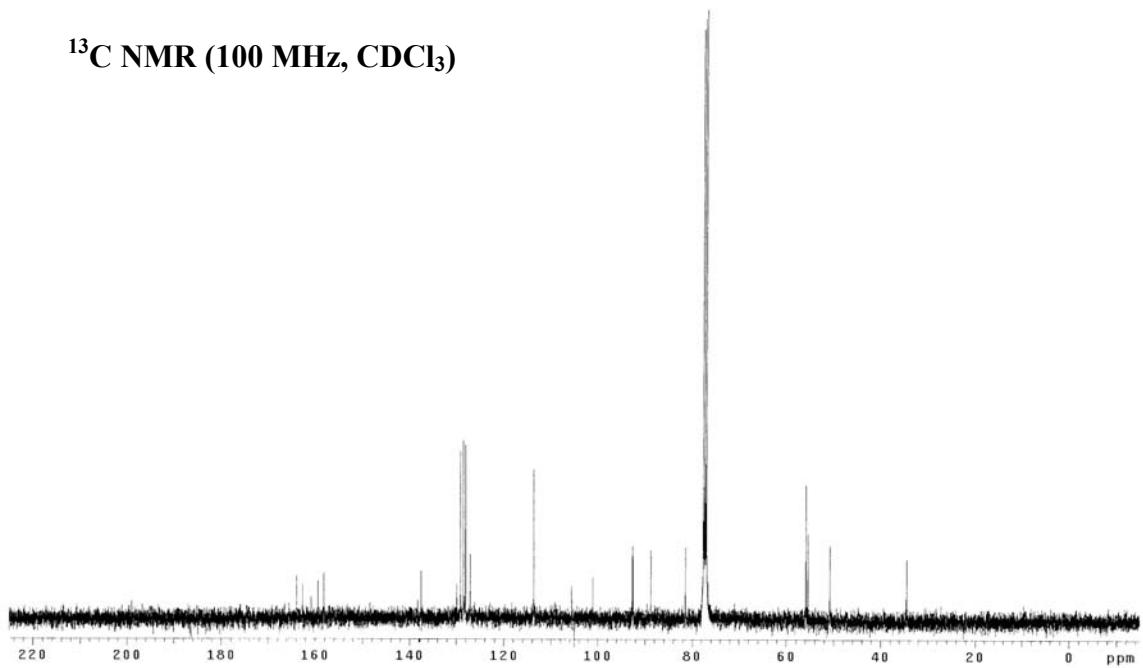


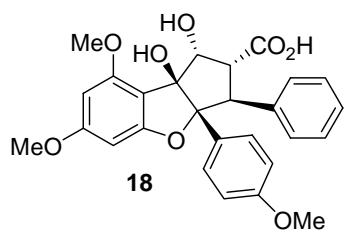


¹H NMR (400 MHz, CDCl₃)

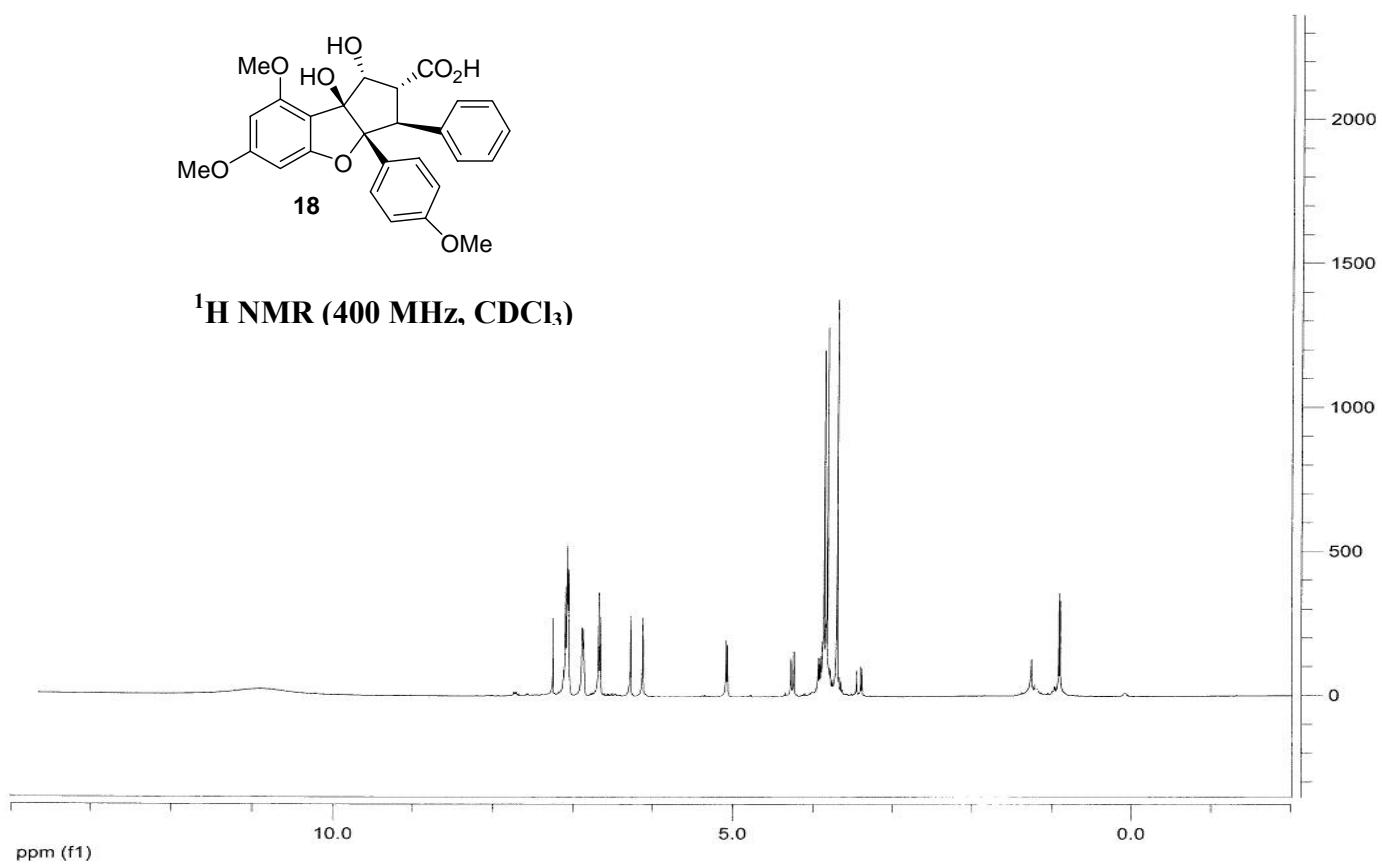


¹³C NMR (100 MHz, CDCl₃)

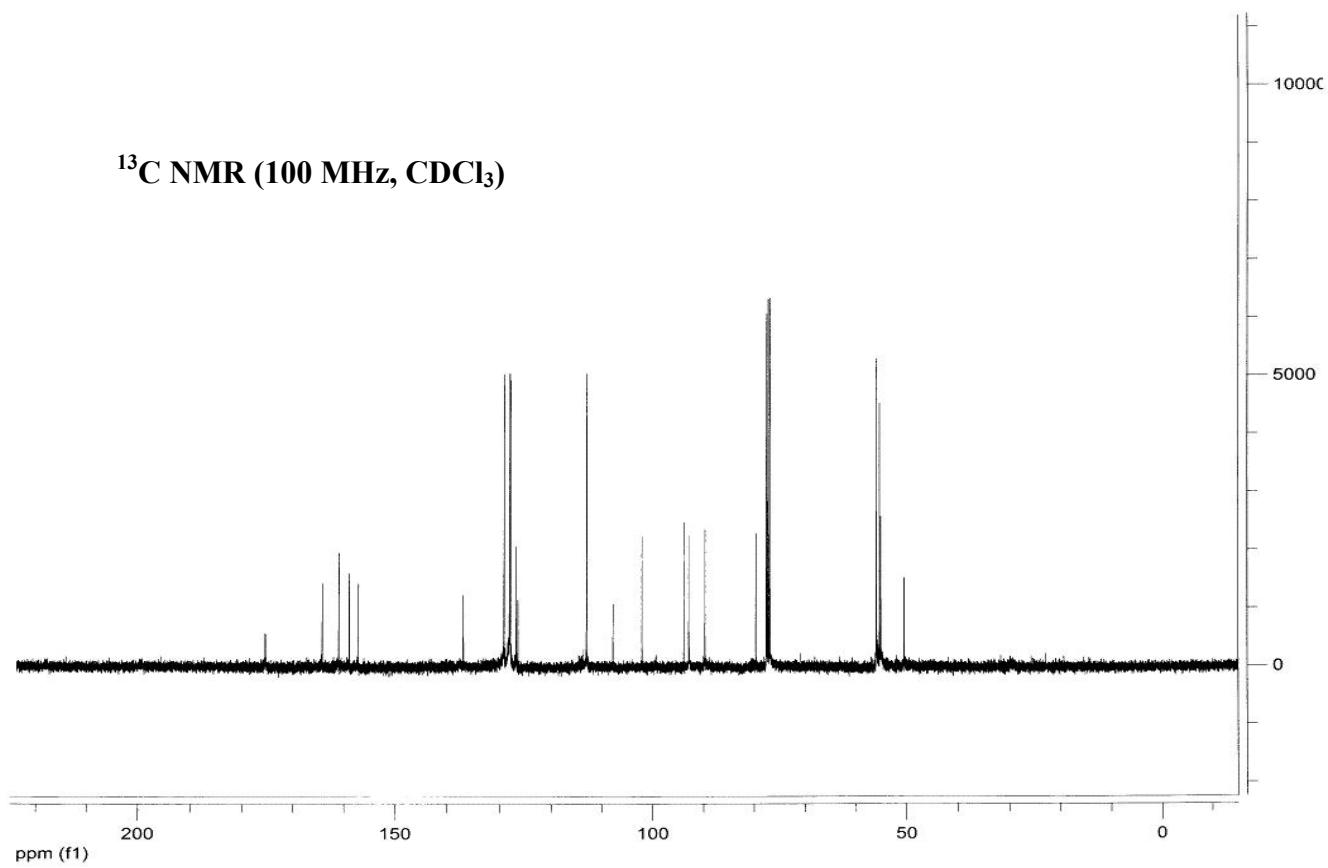


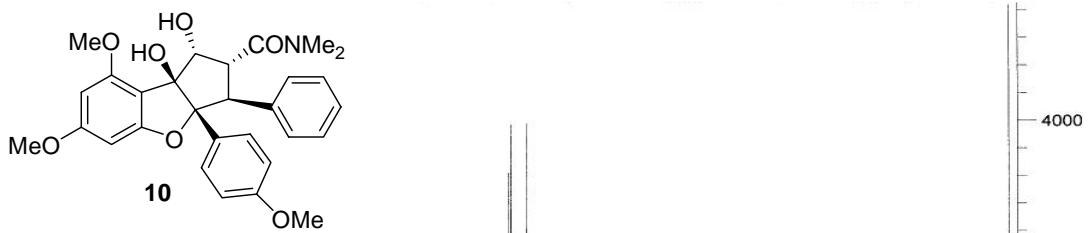


^1H NMR (400 MHz, CDCl_3)

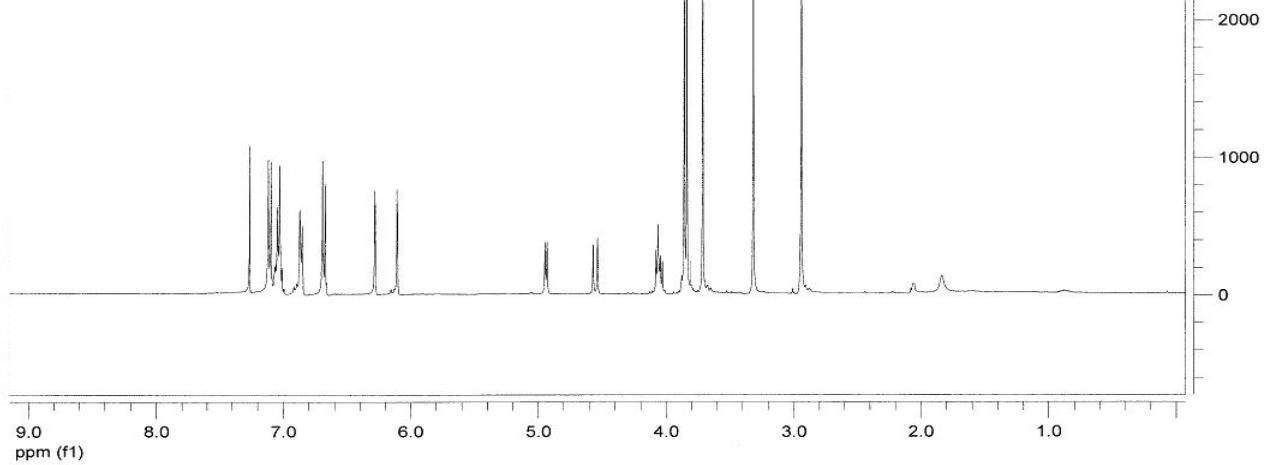


^{13}C NMR (100 MHz, CDCl_3)

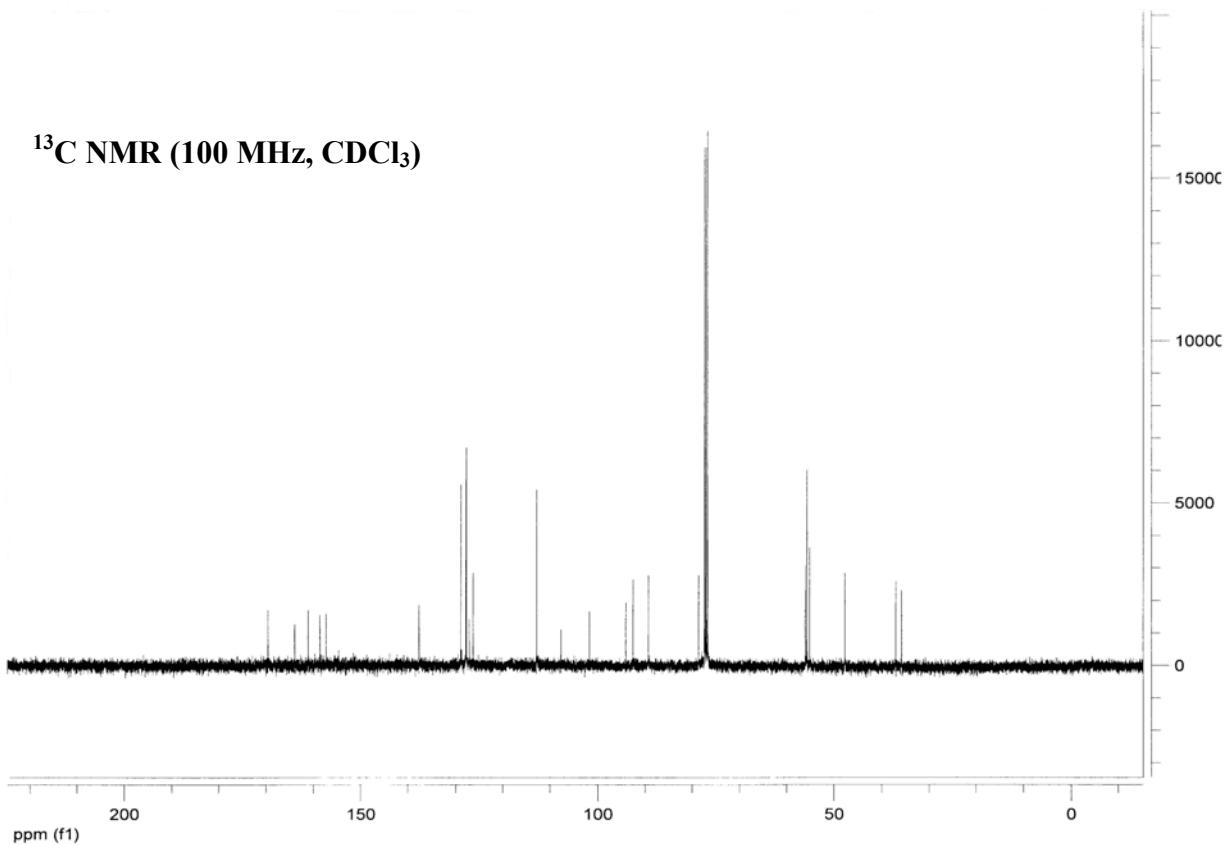


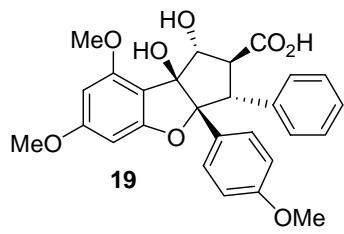


¹H NMR (400 MHz, CDCl₃)

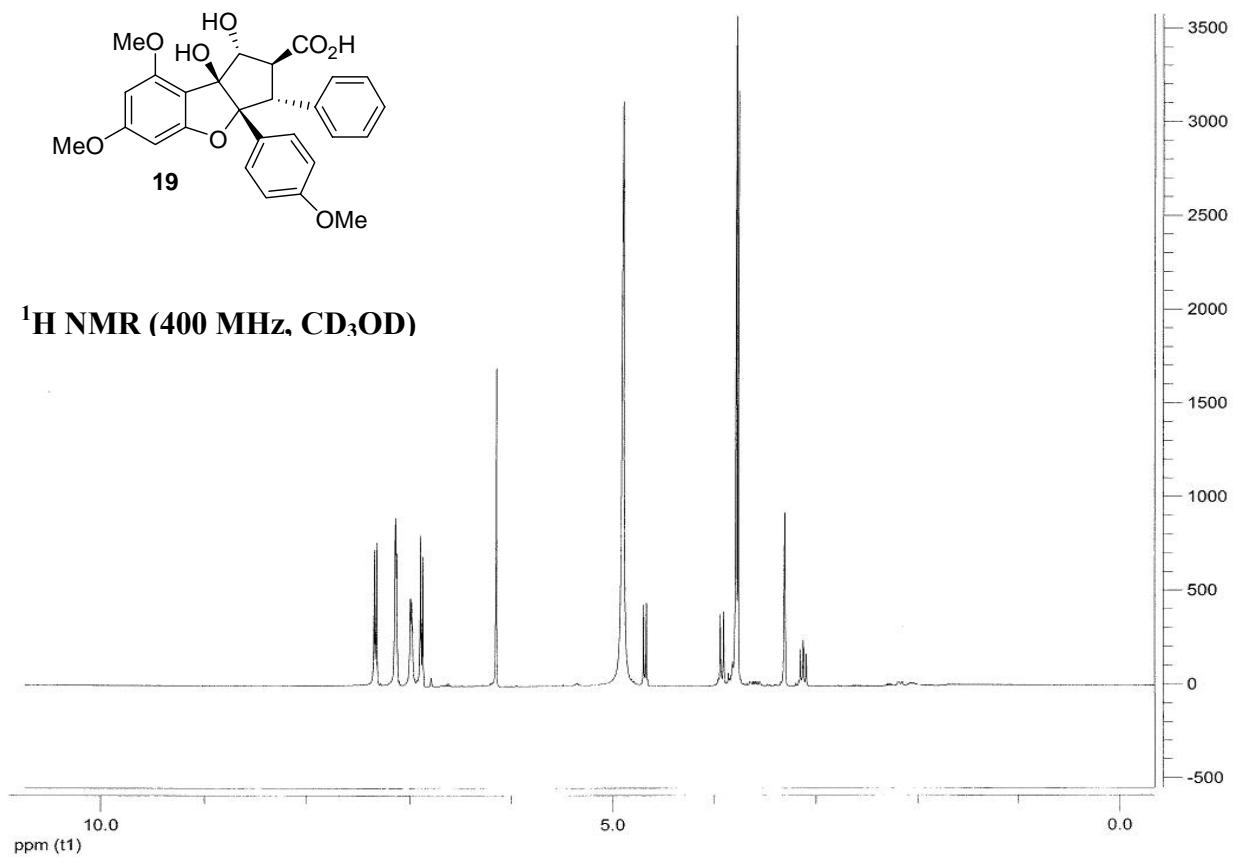


¹³C NMR (100 MHz, CDCl₃)

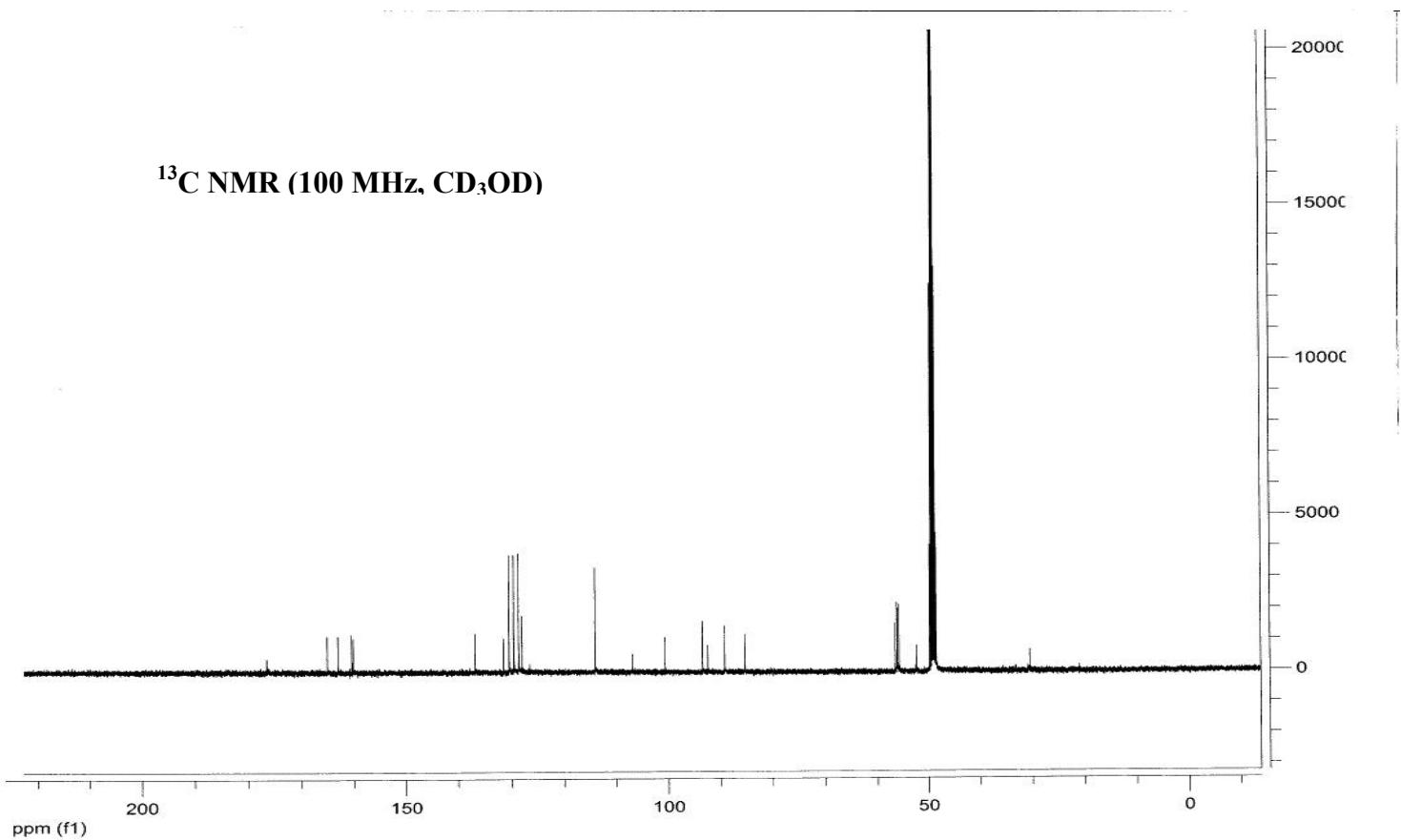


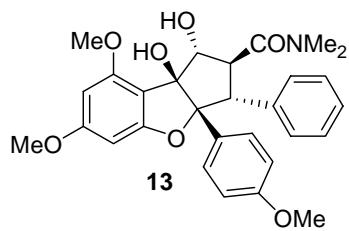


¹H NMR (400 MHz, CD₃OD)

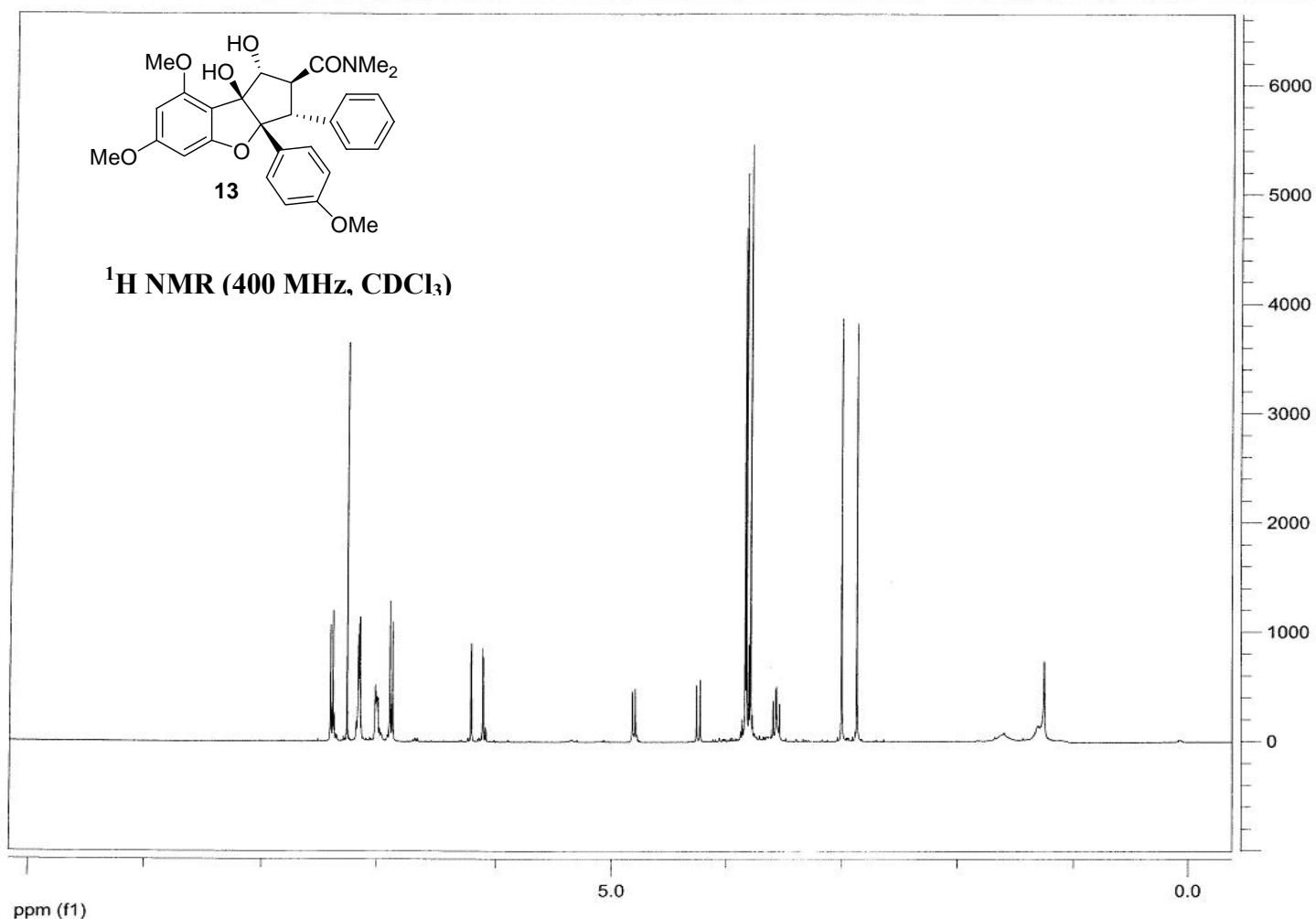


¹³C NMR (100 MHz, CD₃OD)





^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (75 MHz, CDCl_3)

