

# Enantioselective Total Syntheses of Kuwanon X, Kuwanon Y, and Kuwanol A

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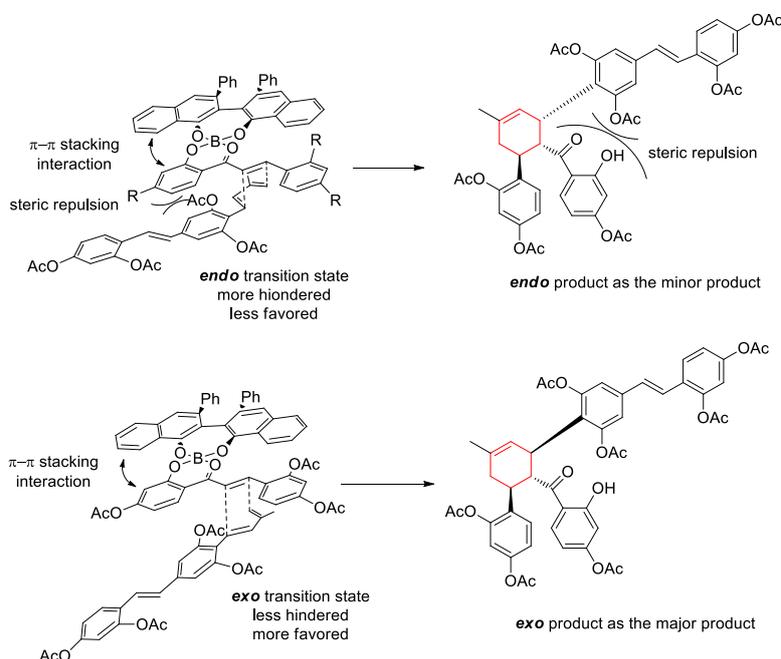
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## Supporting Information

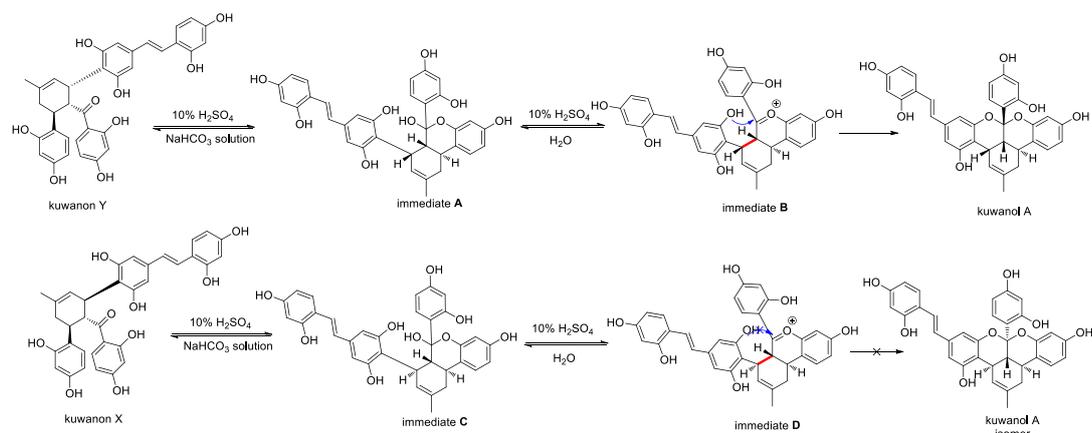
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## I) The Proposed Mechanism for the *Exo*-selective Asymmetric Diels-Alder Cycloaddition.



This Diels-Alder reaction features high enantioselectivity and *exo* selectivity which can be explained by the two transition states. The chiral ligand blocks the  $\alpha$ -face of the dienophile in both *endo* and *exo* transition states, so the diene could only approach the dienophile by its less hindered  $\beta$ -face. Because of the steric hindrance between the acetyl group and the phenyl group, the less hindered *exo* transition state is more favored to show *exo* selectivity in this asymmetric Diels-Alder cycloaddition.

## II) Proposed Explanation for the *Endo*-selective Acid-induced ketalization.



When kuwanon X was used as the substrate to do the acid-induced ketalization reaction, we could detect the existence of immediate C. But this immediate C was very unstable. After quenching the reaction by saturated  $NaHCO_3$  aqueous solution, this immediate C disappeared and only the kuwanon X was recovered. Based on this results, we proposed the mechanism for the ketalization of kuwanons X and Y.

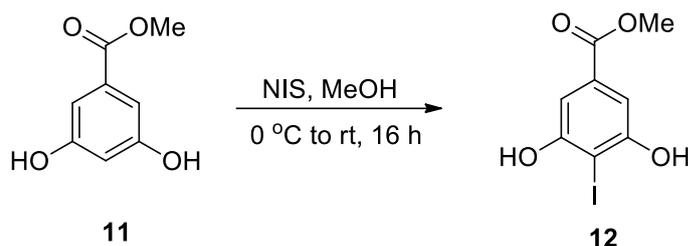
In immediate B, the phenolic hydroxyl group and the oxonium ion are oriented in the same direction, so the oxonium ion will be accessible to the hydroxyl group and then ketalized natural product can be obtained. As to immediate D, the oxonium ion is too far for the hydroxyl group to attack, so the new six-member ring can't be formed.

### III) Experimental Section

#### a) General information:

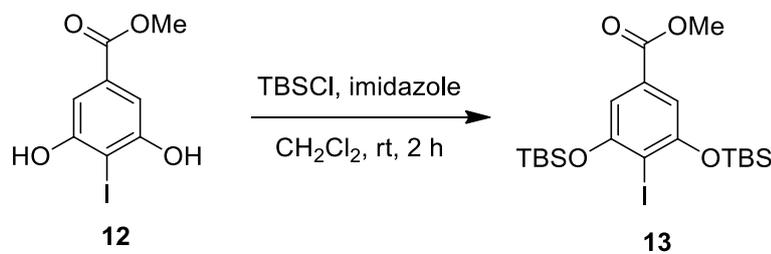
<sup>1</sup>H NMR spectra were recorded on a Varian 400 MHz spectrometer at ambient temperature with CDCl<sub>3</sub> as the solvent unless otherwise stated. <sup>13</sup>C NMR spectra were recorded on a Varian 100 MHz spectrometer (with complete proton decoupling) at ambient temperature; The NMR spectra of Kuwanon X were recorded on a Bruker spectrometer (<sup>1</sup>H at 500 MHz and <sup>13</sup>C at 125 MHz). Chemical shifts are reported in parts per million relative to chloroform (<sup>1</sup>H, δ 7.26; <sup>13</sup>C, δ 77.10), acetone-*d*<sub>6</sub> (<sup>1</sup>H, δ 2.05; <sup>13</sup>C, δ 29.8), DMSO-*d*<sub>6</sub> (<sup>1</sup>H, δ 2.5; <sup>13</sup>C, δ 39.5). Data for <sup>1</sup>H NMR are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad) and coupling constants (Hz). Infrared spectra were recorded on a Thermo Fisher FT-IR200 spectrophotometer. High-resolution mass spectra were obtained at Peking University Mass Spectrometry Laboratory using a Bruker APEX IV FTMS Flash chromatography. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm and are recorded as [α]<sub>D</sub><sup>25</sup> (concentration in grams/100 mL solvent). The samples were analyzed by HPLC/MS on a Waters Auto Purification LC/MS system (3100 Mass Detector, 2545 Binary Gradient Module, 2767 Sample Manager, and 2998 Photodiode Array (PDA) Detector). The system was equipped with a Waters C18 5μm SunFire separation column (150\*4.6 mm), equilibrated with HPLC grade water (solvent A) and HPLC grade methanol (solvent B) with a flow rate of 1.0 mL/min at rt. Chiral HPLC analysis was performed on an Agilent 1200 series (CHIRALCEL AD-H, Column No. ADH0CE-MK114). 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. Yields refer to chromatographically and spectroscopically pure materials, unless otherwise stated. All reagents were used as supplied by Sigma-Aldrich, J&K and Alfa Aesar Chemicals. Methylene chloride, Methanol and N,N-dimethylformamide were distilled from calcium hydride; tetrahydrofuran was distilled from sodium/benzophenone ketyl prior to use. All reactions were carried out in oven-dried glassware under an argon atmosphere unless otherwise noted.

## b) Detailed experimental procedures



### Methyl 3,5-dihydroxy-4-iodobenzoate (**12**)<sup>1</sup>

To a solution of **11** (1.50 g, 8.92 mmol) in MeOH (10 mL), a solution of NIS (2.11g, 9.37 mmol) in MeOH (10 mL) was added slowly at 0 °C. The reaction mixture was slowly warmed to room temperature while mixing. After 16 h the reaction mixture was diluted with ice water and quenched by saturated Na<sub>2</sub>SO<sub>3</sub>, then extracted with EtOAc. The combined organic layers were washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. After purification by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>/EtOAc = 5:1), the title compound **12** was obtained as white solid in a yield of 2.54 g (8.64 mmol, 97%) with the same spectroscopic data as those previously reported.



### Methyl 3,5-bis((tert-butyl)dimethylsilyloxy)-4-iodobenzoate (**13**)

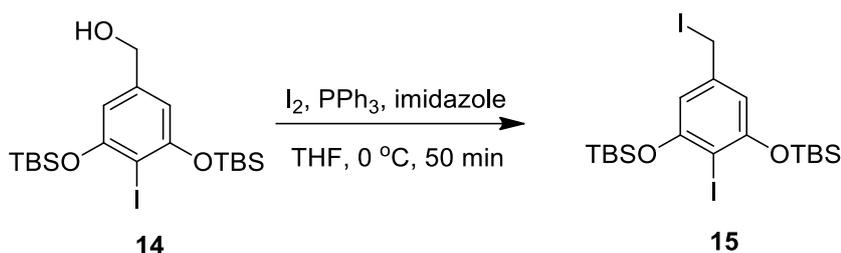
To a solution of **12** (2.00 g, 6.80 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (40 mL), imidazole (2.78g, 40.8 mmol) and TBSCl (3.08 g, 20.4 mmol) was added sequentially at room temperature. After mixing for 2 h, full conversion was obtained, as observed by TLC. The reaction mixture was quenched by water, extracted with CH<sub>2</sub>Cl<sub>2</sub> and washed by brine. The organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. After purification by flash column chromatography (petroleum ether/EtOAc = 10:1), the title compound **13** was obtained as white solid in a yield of 3.47 g (6.64 mmol, 98%). Mp: 94-96 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.09 (s, 2H), 3.89 (s, 3H), 1.07 (s, 18H), 0.304(s, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 166.5, 156.8, 131.0, 111.8, 94.4, 52.3, 25.9, 18.4, -4.0; IR (neat): ν<sub>max</sub> (cm<sup>-1</sup>) = 2929, 2857, 1722, 1571, 1417, 1250, 1095, 835, 782; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>20</sub>H<sub>35</sub>IO<sub>4</sub>Si<sub>2</sub>: 523.1191, found: 523.1200.



### (3,5-Bis((tert-butyl)dimethylsilyloxy)-4-iodophenyl)methanol (**14**)

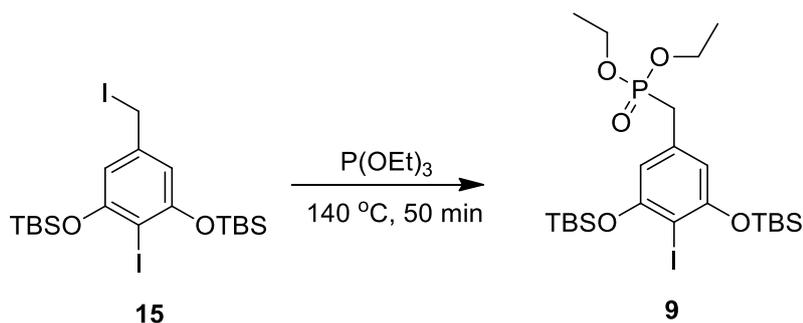
1 (a) Berliner, M. A.; Cordi, E. M.; Dunetz, J. R.; Price, K. E. *Org. Process Res. Dev.* **2010**, *14*, 180. (b) Chiummiento, L.; Funicello, M.; Lopardo, M. T.; Lupattelli, P.; Choppin, S.; Colobert, F. *Eur. J. Org. Chem.* **2012**, 188.

To a solution of **13** (2.00 g, 3.83 mmol) in THF (15 mL), DIBAL (8.42 mL, 1 M in THF) was added slowly at °C. The reaction mixture was kept at °C for 2 h and then quenched by MeOH. The resulting mixture was stirred for 1 h after adding saturated solution of potassium sodium tartrate and extracted with EtOAc. The combined organic layers was washed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo*. After purification by flash column chromatography (petroleum ether/EtOAc = 6:1), the title compound **14** was obtained as white solid in a yield of 1.80 g (3.64 mmol, 95%). Mp: 74-76 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.47 (d, *J* = 0.8 Hz, 2H), 4.56 (d, *J* = 6.0 Hz, 2H), 1.68-1.58(m, 1H), 1.06 (s, 18H), 0.28 (s, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.9, 142.4, 109.7, 86.2, 64.7, 25.1, 18.4, -3.9; IR (neat): ν<sub>max</sub> (cm<sup>-1</sup>) = 3318, 2929, 2857, 1568, 1422, 1254, 1092, 825, 780; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>19</sub>H<sub>35</sub>IO<sub>3</sub>Si<sub>2</sub>: 495.1242, found: 495.1240.



**((2-Iodo-5-(iodomethyl)-1, 3-phenylene)bis(oxy))bis(tert-butyl dimethylsilyl) ether (15)**

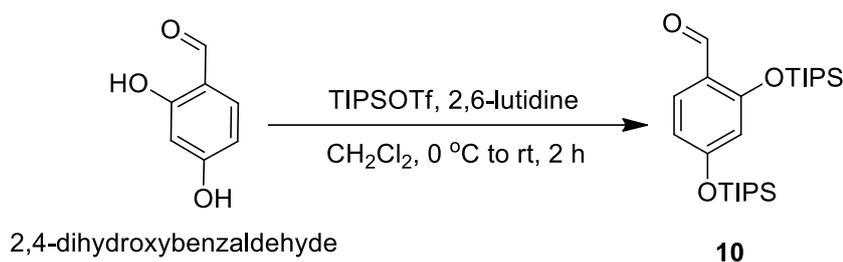
To a solution of **14** (1.80 g, 3.64 mmol) in THF (20 mL), imidazole (0.297 g, 4.38 mmol) and PPh<sub>3</sub> (1.05 g, 4.00 mmol) were added at room temperature. The reaction mixture was cooled to 0 °C, and I<sub>2</sub> (1.02 g, 4.00 mmol) in THF (5 mL) was added slowly over 20 min. The reaction was kept at 0 °C for another 30 min and then quenched by a few drops of water. The resulting mixture was concentrated *in vacuo* to get the crude product. After purification by flash column chromatography (petroleum ether/EtOAc = 50:1), the title compound **15** was obtained as white solid in a yield of 2.06 g (3.41 mmol, 94%). Mp: 84-86 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.46 (s, 2H), 4.31 (s, 2H), 1.07 (s, 18H), 0.29 (s, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.8, 140.3, 111.8, 87.0, 25.9, 18.4, 4.9, -4.0; IR (neat): ν<sub>max</sub> (cm<sup>-1</sup>) = 2929, 2856, 1568, 1423, 1258, 1232, 1106, 1074, 823, 778; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>19</sub>H<sub>34</sub>I<sub>2</sub>O<sub>2</sub>Si<sub>2</sub>: 605.0260, found: 605.0261.



**Diethyl 3, 5-bis((tert-butyl dimethylsilyl)oxy)-4-iodobenzylphosphonate (9)**

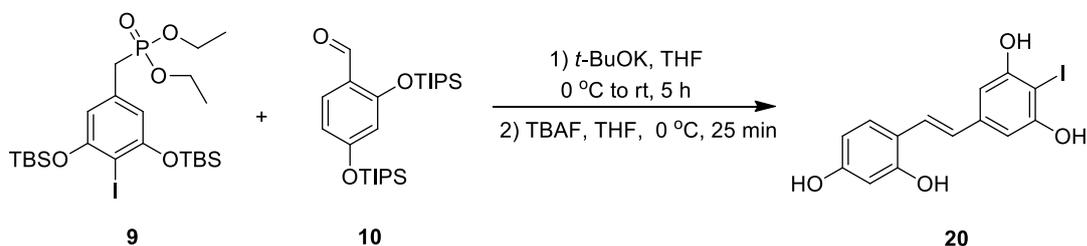
The compound **15** (4.10 g, 6.79 mmol) and P(OEt)<sub>3</sub> (5 ml) were added to a sealed tube, and the mixture was heated to 140 °C for 50 min. After cooled to room temperature, the reaction mixture was purified directly by flash column chromatography (petroleum ether/EtOAc = 20:1 to 5:1) to afford the title compound **9** as white solid in a yield of 4.13 g (6.72 mmol, 99%). Mp: 64-66 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.43 (d, *J* = 2.4 Hz, 2H), 4.02 (m, 4H), 3.04 (s, 1H), 2.99 (s, 1H), 1.25 (t, *J* = 7.2 Hz, 6H), 1.06 (s, 18H), 0.28 (s, 12H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 156.6, 156.5, 132.8, 132.7, 113.0, 112.9, 85.6, 85.5, 62.1, 62.0, 34.1, 32.8, 25.9, 18.3, 16.4, 16.3, -4.1; IR (neat): ν<sub>max</sub> (cm<sup>-1</sup>) = 2929, 2857, 1567, 1423,

1251,1230, 1083, 1025, 823, 776; HRMS (ESI)  $[M+H]^+$  calculated for  $C_{23}H_{44}IO_5PSi_2$ : 615.1582, found: 615.1579.



### 2, 4-Bis((triisopropylsilyloxy)benzaldehyde) (10)

To a solution of 2, 4-dihydroxybenzaldehyde (5.00 g, 36.2 mmol) in  $CH_2Cl_2$  (150 mL) was added 2, 6-lutidine (13.5 mL, 116 mmol) at 0 °C, after stirring for 5 min, TIPSOTf (23.4 mL, 86.9 mmol) was added dropwise at 0 °C. The reaction mixture was allowed to stir at room temperature for 2 h and then diluted with water. The resulting mixture was extracted with  $CH_2Cl_2$  and washed by brine. The organic layers were dried over  $Na_2SO_4$  and concentrated *in vacuo*. After purification by flash column chromatography (petroleum ether/EtOAc = 40:1), the title compound **10** was obtained as yellow oil in a yield of 14.8 g (32.8 mmol, 91%).  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  10.37 (d,  $J = 0.8$  Hz, 1H), 7.71 (d,  $J = 8.4$  Hz, 1H), 6.52 (ddd,  $J = 0.8, 2.0, 8.4$  Hz, 1H), 6.35 (d,  $J = 2.0$  Hz, 1H), 1.36-1.22 (m, 6H), 1.16-1.05 (m, 36H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  188.7, 163.0, 161.1, 129.8, 121.3, 114.4, 110.4, 18.1, 17.8, 17.7, 17.6, 13.0, 12.6, 12.3; IR (neat):  $\nu_{max}$  ( $cm^{-1}$ ) = 2943, 2866, 1685, 1591, 1273, 1185, 995, 880, 670; HRMS (ESI)  $[M+H]^+$  calculated for  $C_{25}H_{46}O_3Si_2$ : 451.3058, found: 451.3051.

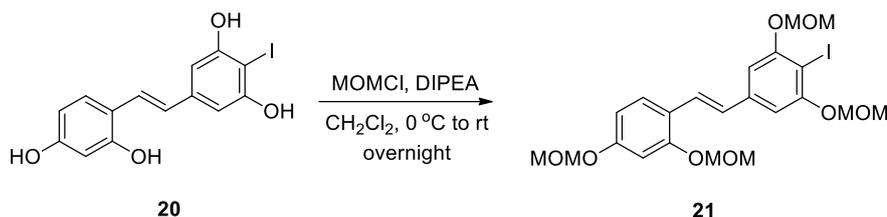


### (E)-5-(2, 4-dihydroxystyryl)-2-iodobenzene-1, 3-diol (20)

To a solution of **9** (0.450 g, 0.732 mmol) and **10** (1.48 g, 3.29 mmol) in THF (8 mL) was added *t*-BuOK (0.246 g, 2.20 mmol) at 0 °C. The reaction mixture was slowly warmed to room temperature and quenched by water after 5 h. The resulting mixture was extracted with EtOAc and the combined organic layers was washed by brine, dried over  $Na_2SO_4$  and concentrated *in vacuo* to get an oil mixture. The mixture was filtrated through a pad of silica gel (petroleum ether) to afford the crude product before being used directly in the next step.

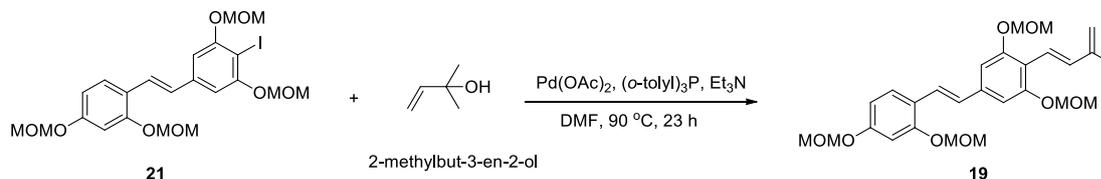
The crude product was dissolved in THF (8 mL) and TBAF (4.39 mL, 4.39 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 25 min at 0 °C and quenched by saturated  $NH_4Cl$  solution. The resulting mixture was extracted with EtOAc, and the combined organic layers were washed by brine, dried over  $Na_2SO_4$  and concentrated *in vacuo* to afford the crude product. After purification by flash column chromatography (petroleum ether/EtOAc = 1:1), the title compound **20** was obtained as gray foams in a yield of 0.182 g (0.492 mmol, 67%).  $^1H$  NMR (400 MHz, acetone- $d_6$ )  $\delta$  8.77 (br.s, 2H), 8.59 (br.s, 1H), 8.39 (br.s, 1H), 7.41 (d,  $J = 8.8$  Hz, 1H), 7.37 (d,  $J = 16.4$  Hz, 1H), 6.87 (d,  $J = 16.4$  Hz, 1H), 6.67 (s, 2H), 6.44 (d,  $J = 2.4$  Hz, 1H), 6.38 (dd,  $J = 2.4, 8.4$  Hz, 1H);  $^{13}C$  NMR (100 MHz, acetone- $d_6$ )  $\delta$  159.3, 158.8, 157.0, 141.4, 128.3, 125.1, 125.0, 117.0, 108.5, 104.8, 103.5, 73.0; IR (neat):  $\nu_{max}$  ( $cm^{-1}$ ) =

3331, 1586, 1516, 1421, 1264, 1164, 1035, 972, 821; HRMS (ESI)  $[M+H]^+$  calculated for  $C_{14}H_{11}IO_4$ : 370.9775, found: 370.9776.



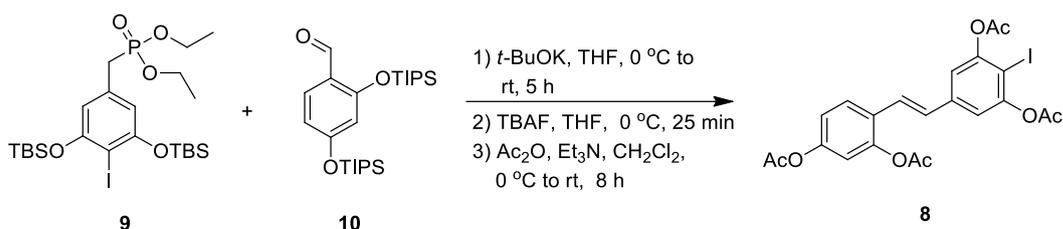
**(E)-5-(2,4-bis(methoxymethoxy)styryl)-2-iodo-1,3-bis(methoxymethoxy)benzene (21)**

To a solution of **20** (113 mg, 0.305 mmol) and DIPEA (303  $\mu$ L, 1.83 mmol) in  $CH_2Cl_2$  (1.5 mL) was added MOMCl (102  $\mu$ L, 1.34 mmol) dropwise at 0  $^{\circ}C$ , the resulting mixture was slowly warmed to room temperature and stirred overnight. After quenched by water, the mixture was extracted with  $CH_2Cl_2$ . The combined organic layers were washed by brine, dried over  $Na_2SO_4$  and concentrated *in vacuo* to afford the crude product. After purification by flash column chromatography (petroleum ether/ $CH_2Cl_2$  = 1:1), the title compound **21** was obtained as white solid in a yield of 80.8 mg (0.148 mmol, 48%). Mp: 129-131  $^{\circ}C$ ;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.49 (d,  $J$  = 8.8 Hz, 1H), 7.38 (d,  $J$  = 16.4 Hz, 1H), 6.94 (d,  $J$  = 16.4 Hz, 1H), 6.91 (s, 2H), 6.84 (d,  $J$  = 2.4 Hz, 1H), 6.72 (dd,  $J$  = 2.4, 8.4 Hz, 1H), 5.30 (s, 4H), 5.24 (s, 2H), 5.18 (s, 2H), 3.55 (s, 6H), 3.53 (s, 3H), 3.49 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  158.2, 157.5, 155.8, 140.4, 127.5, 126.9, 124.5, 120.9, 109.6, 106.7, 104.0, 95.1, 94.5, 79.0, 56.6, 56.4, 56.2; IR (neat):  $\nu_{max}$  ( $cm^{-1}$ ) = 2953, 2905, 1569, 1265, 1151, 1043, 1007, 921; HRMS (ESI)  $[M+H]^+$  calculated for  $C_{22}H_{27}IO_8$ : 547.0823, found: 547.0828.



**5-((E)-2,4-bis(methoxymethoxy)styryl)-1,3-bis(methoxymethoxy)-2-((E)-3-methylbuta-1,3-dien-1-yl)benzene (19)**

To a solution of **21** (100 mg, 0.183 mmol) and 2-methylbut-3-en-2-ol (95.7  $\mu$ L, 0.915 mmol) in DMF (0.75 mL) was added (*o*-tolyl) $_3P$  (11.1 mg, 0.0366 mmol) and  $Et_3N$  (31.8  $\mu$ L, 0.229 mmol). The solution was bubbled with Argon for 30 min and then  $Pd(OAc)_2$  (2.1 mg, 0.00915 mmol) was added. The resulting mixture was heated to 90  $^{\circ}C$  for 23 h and then cooled down to the room temperature. The reaction mixture was diluted with EtOAc and washed by brine. The combined organic layers were dried over  $Na_2SO_4$  and concentrated *in vacuo* to afford the crude product. After purification by flash column chromatography (petroleum ether/EtOAc = 15:1), the title compound **19** was obtained as yellow solid in a yield of 67.8 mg (0.140 mmol, 76%). Mp: 104-106  $^{\circ}C$ ;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.50 (d,  $J$  = 8.4 Hz, 1H), 7.35 (d,  $J$  = 16.4 Hz, 1H), 7.34 (d,  $J$  = 16.4 Hz, 1H), 6.95 (s, 2H), 6.93 (d,  $J$  = 15.2 Hz, 1H), 6.86 (d,  $J$  = 16.8 Hz, 1H), 6.84 (d,  $J$  = 2.4 Hz, 1H), 6.73 (dd,  $J$  = 2.4, 8.4 Hz, 1H), 5.28 (s, 4H), 5.24 (s, 2H), 5.18 (s, 2H), 5.08 (s, 1H), 5.06 (s, 1H), 3.52 (s, 9H), 3.49 (s, 3H), 2.01 (s, 3H);  $^{13}C$  NMR (100 MHz,  $CDCl_3$ )  $\delta$  158.0, 156.2, 155.7, 143.7, 138.2, 135.8, 127.5, 127.3, 123.6, 121.3, 120.0, 116.7, 116.3, 109.6, 107.0, 104.0, 95.1, 95.0, 94.6, 56.4, 56.3, 56.2, 18.4; IR (neat):  $\nu_{max}$  ( $cm^{-1}$ ) = 2952, 2905, 1592, 1557, 1432, 1261, 1207, 1151, 1077, 1043, 1010, 922; HRMS (ESI)  $[M+H]^+$  calculated for  $C_{27}H_{34}O_8$ : 486.2248, found: 486.2254.

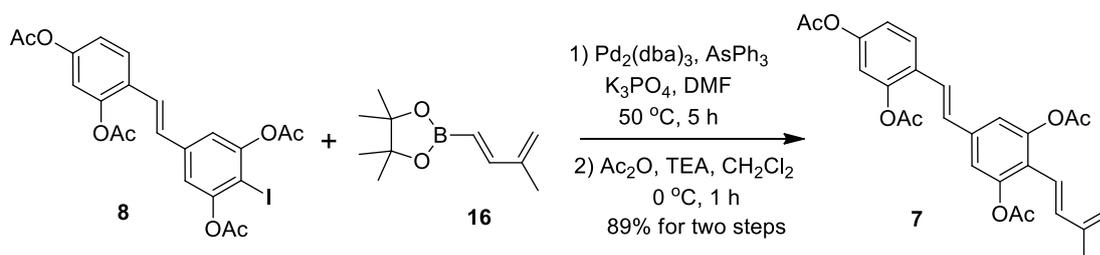


#### (E)-4-(3,5-diacetoxy-4-iodostyryl)-1,3-phenylene diacetate (**8**)

To a solution of **9** (1.51 g, 2.46 mmol) and **10** (5.00 g, 11.1 mmol) in THF (24 mL) was added *t*-BuOK (0.830 g, 7.39 mmol) at 0 °C. The reaction mixture was slowly warmed to room temperature and quenched by water after 5 h. The resulting mixture was extracted with EtOAc and the combined organic layers was washed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to get an oil mixture. The mixture was filtrated through a pad of silica gel (petroleum ether) to afford the crude product before being used directly in the next step.

The crude product was dissolved in THF (24 mL) and TBAF (14.8 mL, 14.8 mmol) was added dropwise at 0 °C. The reaction mixture was stirred for 25 min and quenched by saturated NH<sub>4</sub>Cl solution. The resulting mixture was extracted with EtOAc, and the combined organic layers were washed by brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to afford the crude product.

The crude product from second step and Et<sub>3</sub>N (4.10 mL, 29.5 mmol) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (24 mL) at 0 °C, and then Ac<sub>2</sub>O (1.39 mL, 14.8 mmol) was added slowly. The resulting mixture was warmed to room temperature slowly. After 8 h, the reaction mixture was diluted with water and extracted with EtOAc. The combined organic layers were washed by saturated NH<sub>4</sub>Cl solution, followed by saturated NaHCO<sub>3</sub> solution and brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to afford the crude product. After purification by flash column chromatography (petroleum ether/EtOAc = 5:1), the title compound **8** was obtained as white solid in a yield of 0.754 g (1.40 mmol, 57% in three steps). Mp: 165-167 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.59 (d, *J* = 8.8 Hz, 1H), 7.09 (s, 2H), 7.08 (d, *J* = 16.4 Hz, 1H), 7.02 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.95 (d, *J* = 1.6 Hz, 1H), 6.93 (d, *J* = 16.4 Hz, 1H), 2.39 (s, 6H), 2.35 (s, 3H), 2.29 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 168.9, 168.7, 168.3, 152.7, 150.6, 148.5, 139.4, 128.6, 127.2, 126.8, 124.1, 119.5, 118.3, 116.4, 87.1, 21.2, 21.1, 21.0; IR (neat): ν<sub>max</sub> (cm<sup>-1</sup>) 1764, 1367, 1181, 1144, 1037, 894, 725; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>22</sub>H<sub>19</sub>IO<sub>8</sub>: 539.0203, found: 539.0211.



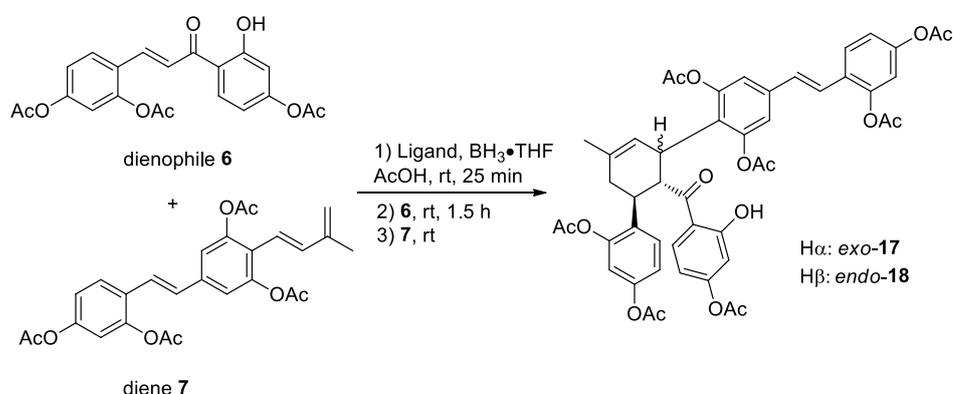
#### 4-((E)-3,5-diacetoxy-4-((E)-3-methylbuta-1,3-dien-1-yl)styryl)-1,3-phenylene diacetate (**7**)

To a solution of **8** (181 mg, 0.336 mmol) and **16**<sup>2</sup> (261 mg, 1.35 mmol) in DMF (5 mL) was added AsPh<sub>3</sub> (14.4 mg, 0.0471 mmol) and K<sub>3</sub>PO<sub>4</sub> (714 mg, 3.36 mmol). The solution was bubbled with Argon for 30 min and then Pd<sub>2</sub>(dba)<sub>3</sub> (21.6 mg, 0.0235 mmol) was added. The resulting mixture was heated to 50 °C for 5 h and then filtrated through a pad of celite. The filtrate was diluted with EtOAc and washed by brine. The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to afford the

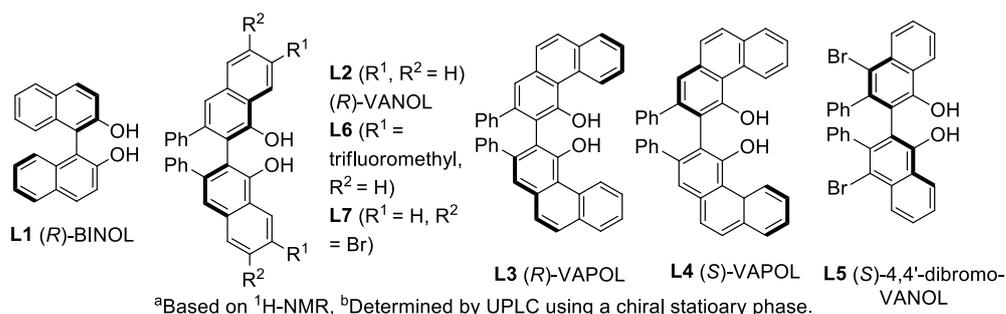
<sup>2</sup> Known Compound **16** was synthesized according to literature : Cannillo, A.; Norsikian, S.; Retailleau, P.; Dau, M. T. H.; Iorga, B. I.; Beau, J. *Chem. Eur. J.* **2013**, *19*, 9127.

crude product.

The crude product and Et<sub>3</sub>N (0.467 ml, 3.36 mmol) were dissolved in CH<sub>2</sub>Cl<sub>2</sub> (6 mL) at 0 °C, and then Ac<sub>2</sub>O (0.190 mL, 2.02 mmol) was added slowly. The reaction was kept at 0 °C for 1 h and then quenched by water. The mixture was extracted with EtOAc and washed by brine. The combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated *in vacuo* to afford the crude product. After purification by flash column chromatography (petroleum ether/EtOAc = 5:1), the title compound **7** was obtained as yellow solid in a yield of 143 mg (0.299 mmol, 89%). Mp: 144-146 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.59 (d, *J* = 8.4 Hz, 1H), 7.08 (s, 2H), 7.04, (d, *J* = 16.0 Hz, 1H), 7.02 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.95 (d, *J* = 2.0 Hz, 1H), 6.93 (d, *J* = 16.0 Hz, 1H), 6.90 (d, *J* = 16.8 Hz, 1H), 6.29 (d, *J* = 16.4 Hz, 1H), 5.12 (s, 1H), 5.10 (s, 1H), 2.35 (s, 3H), 2.30 (s, 6H), 2.27 (s, 3H), 1.92 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 168.8, 168.7, 168.6, 150.3, 149.2, 148.3, 142.0, 137.8, 137.0, 129.1, 127.1, 127.0, 123.4, 123.0, 119.4, 118.7, 118.5, 117.9, 116.3, 20.9, 20.8, 20.7, 17.9; IR (neat): ν<sub>max</sub> (cm<sup>-1</sup>) 1765, 1426, 1370, 1186, 1043, 1016; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>27</sub>H<sub>26</sub>O<sub>8</sub>: 479.1700, found: 479.1708.

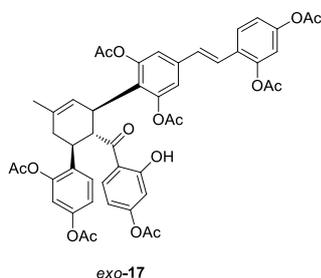


entry	ligands	time (h)	yield (%)	endo/exo <sup>a</sup>	ee(%) <sup>b</sup> endo/exo
1	<b>L1</b>	23	95	1:4.2	70/13
2	<b>L2</b>	24	70	1:5.3	94/81
3	<b>L3</b>	21	69	1:11.4	50/96
4	<b>L4</b>	21	79	1:13.0	53/97
5	<b>L5</b>	22	60	1:3.1	0/1
6	<b>L6</b>	20	42	1:7.0	81/63
7	<b>L7</b>	28	80	1:3.5	96/63



### General procedure for the asymmetric Diels-Alder reaction

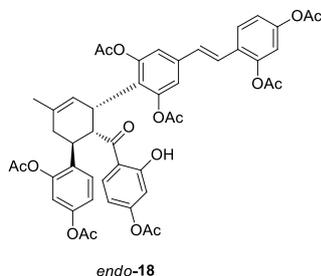
To a solution of ligand (2.5 eq) in THF (0.2 M) was added  $\text{BH}_3\cdot\text{THF}$  (1.2 eq) and AcOH (1.2 eq) sequentially. The resulting mixture was stirred at room temperature for 25 min, and then concentrated to dryness and further dried under high vacuum at room temperature for 30 min. The resulting solid was dissolved in dry THF (0.1 M), and then pre-activated 5 Å molecular sieve (20 weight equiv to **6**) and the dienophile **6** (1.0 eq) were added to the solution. The resulting solution was stirred at room temperature for 1.5 h before the diene **7** (1.05 eq) was added to the reaction mixture. When full conversion was obtained, as observed by TLC, the reaction mixture was quenched by addition of  $\text{H}_2\text{O}$  (15.0 eq) and filtered through a pad of celite. The celite was further washed with EtOAc, and the organic filtrates were collected and concentrated *in vacuo*. The crude product was filtrated through a pad of silica gel to get the mixture of *exo*-**17** and *endo*-**18** before determination of the ratio of *endo/exo* by NMR. Further purification was achieved by flash column chromatography (petroleum ether/EtOAc = 5:1 to 2:1), the *exo*-**17** and *endo*-**18** were obtained as yellow solid in a total yield of 42-95%.



### *Exo*-**17**

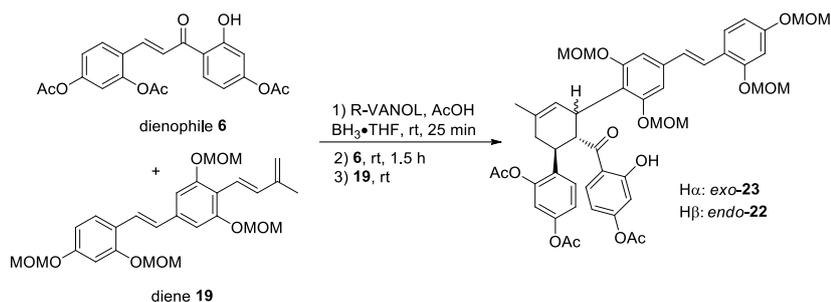
To a solution of *S*-VAPOL (56.3 mg, 0.105 mmol) in THF (0.2 mL) was added  $\text{BH}_3\cdot\text{THF}$  (50.2  $\mu\text{L}$ , 0.0502 mmol) and AcOH (2.9  $\mu\text{L}$ , 0.0502 mmol) sequentially. The resulting mixture was stirred at room temperature for 25 min, and then concentrated to dryness and further dried under high vacuum at room temperature for 30 min. The resulting solid was dissolved in dry THF (0.4 mL), and then pre-activated 5 Å molecular sieve (332 mg) and the dienophile **6** (16.6 mg, 0.0418 mmol) were added to the solution. The resulting solution was stirred at room temperature for 1.5 h before the diene **7** (21.0 mg, 0.0439 mmol) was added to the reaction mixture. The reaction mixture was quenched by addition of  $\text{H}_2\text{O}$  (11.3  $\mu\text{L}$ , 15.0 eq) after 21 h and filtered through a pad of celite. The celite was further washed with EtOAc, and the organic filtrates were collected and concentrated *in vacuo*. The crude product was filtrated through a pad of silica gel to get the mixture of *exo*-**17** and *endo*-**18** before determination of the ratio of *endo/exo* by NMR. Further purification was achieved by flash column chromatography (petroleum ether/EtOAc = 5:1 to 2:1) to afford the *exo*-**17** as yellow solid in a yield of 26.1 mg (0.0298 mmol, 71%) and *endo*-**18** as yellow solid in a yield of 2.7 mg (0.00308 mmol, 7%). Mp: 129-131 °C;  $[\alpha]_D^{25}$  -227 (c 0.10 MeOH);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  12.30 (s, 1H), 7.56 (d,  $J$  = 8.4 Hz, 1H), 7.33 (d,  $J$  = 9.2 Hz, 1H), 7.17 (d,  $J$  = 8.4 Hz, 1H), 6.99 (dd,  $J$  = 2.0, 8.4 Hz, 1H), 6.96 (s, 1H), 6.92 (d,  $J$  = 16.4 Hz, 1H), 6.92 (d,  $J$  = 2.0 Hz, 1H), 6.84-6.78 (m, 4H), 6.49 (d,  $J$  = 2.0 Hz, 1H), 6.29 (dd,  $J$  = 2.0, 8.8 Hz, 1H), 5.36 (s, 1H), 4.29 (br.s, 1H), 4.05 (d,  $J$  = 9.6 Hz, 1H), 3.74 (br.s, 1H), 2.41 (s, 3H), 2.33 (s, 3H), 2.32 (s, 3H), 2.28 (s, 4H), 2.27 (s, 4H), 2.19 (s, 3H), 2.17 (s, 3H), 1.78 (s, 3H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  207.7, 169.2, 168.9, 168.8, 168.7, 168.5, 168.0, 163.8, 156.4, 150.3, 150.0, 149.3, 149.1, 148.4, 148.3, 137.4, 132.8, 131.9, 130.8, 129.0, 127.1, 127.0, 126.0, 123.2, 123.1, 119.5, 119.4, 119.3, 118.3, 118.2, 116.4, 116.3, 112.0, 110.3, 48.4, 39.5, 37.4, 35.6, 23.2, 21.1, 21.0, 21.0, 20.9, 20.8; IR (neat):  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 1766, 1632, 1368, 1183, 1145, 1013, 902, 729; HRMS (ESI)  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{48}\text{H}_{44}\text{O}_{16}$ : 877.2702, found: 877.2691. The *exo*-isomer **17** (*S*-VAPOL as chiral ligand): 97% *ee* (HPLC conditions:

Chiralcel AD-H column, hexane/*i*-PrOH = 60/40, 1.0 mL/min,  $\lambda$  = 280 nm,  $t_R$  (major) = 21.6 min,  $t_R$  (minor) = 13.4 min). The enantiomer of *exo*-isomer **17** (*R*-VAPOL as chiral ligand): -95% *ee* (HPLC conditions: Chiralcel AD-H column, hexane/*i*-PrOH = 60/40, 1.0 mL/min,  $\lambda$  = 280 nm,  $t_R$  (major) = 11.3 min,  $t_R$  (minor) = 18.7 min).



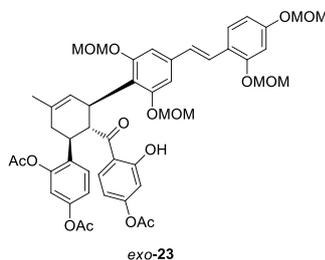
### **Endo-18**

To a solution of *R*-VANOL (283 mg, 0.646 mmol) in THF (1.2 mL) was added BH<sub>3</sub>•THF (310  $\mu$ L, 0.310 mmol) and AcOH (17.7  $\mu$ L, 0.310 mmol) sequentially. The resulting mixture was stirred at room temperature for 25 min, and then concentrated to dryness and further dried under high vacuum at room temperature for 30 min. The resulting solid was dissolved in dry THF (2.4 mL), and then pre-activated 5Å molecular sieve (2.06 g) and the dienophile **6** (103 mg, 0.258 mmol) were added to the solution. The resulting solution was stirred at room temperature for 1.5 h before the diene **7** (130 mg, 0.271 mmol) was added to the reaction mixture. The reaction mixture was quenched by addition of H<sub>2</sub>O (69.8  $\mu$ L, 15.0 eq) after 24 h and filtered through a pad of celite. The celite was further washed with EtOAc, and the organic filtrates were collected and concentrated *in vacuo*. The crude product was filtrated through a pad of silica gel to get the mixture of *exo*-**17** and *endo*-**18** before determination of the ratio of *endo/exo* by NMR. Further purification was achieved by flash column chromatography (petroleum ether /EtOAc = 5:1 to 2:1) to afford the *exo*-**17** as yellow solid in a yield of 138 mg (0.158 mmol, 61%) and *endo*-**18** as yellow solid in a yield of 24 mg (0.0274 mmol, 11%). Mp: 122-124 °C;  $[\alpha]_D^{26}$  + 92 (c 0.095 MeOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  12.58 (s, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.41 (d, *J* = 8.8 Hz, 1H), 7.26 (d, *J* = 8.4 Hz, 1H), 7.01 (d, *J* = 2.4 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 6.93-6.88 (m, 4H), 6.81 (d, *J* = 16.4 Hz, 1H), 6.64 (br.s, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 6.27 (dd, *J* = 2.0, 8.8 Hz, 1H), 5.34 (s, 1H), 3.90 (m, 1H), 3.83 (dd, *J* = 4.8, 6.0 Hz, 1H), 3.73 (m, 1H), 3.10 (dd, *J* = 7.2, 19.2 Hz, 1H), 2.34 (s, 3H), 2.28 (s, 6H), 2.23 (m, 1H), 2.19 ((s, 3H), 2.17 (br.s, 3H), 2.14 (s, 3H), 1.87 (s, 3H), 1.75 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  206.6, 169.1, 168.9, 168.8, 168.2, 163.9, 156.2, 150.3, 149.5, 148.4, 148.3, 137.5, 134.4, 134.0, 131.4, 129.1, 128.0, 127.2, 127.1, 125.1, 123.1, 120.8, 119.6, 119.5, 118.6, 116.4, 116.3, 112.1, 110.6, 46.3, 33.9, 33.7, 32.6, 23.4, 21.1, 21.1, 21.0, 20.9; IR (neat):  $\nu_{\max}$  (cm<sup>-1</sup>) 1768, 1634, 1498, 1369, 1193, 1146, 1015, 904; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>48</sub>H<sub>44</sub>O<sub>16</sub>: 877.2702, found: 877.2715. The *endo*-isomer **18** (*R*-VANOL as chiral ligand): 94% *ee* (HPLC conditions: Chiralcel AD-H column, hexane/*i*-PrOH = 70/30, 1.0 mL/min,  $\lambda$  = 280 nm,  $t_R$  (major) = 27.4 min,  $t_R$  (minor) = 23.5 min). The *endo*-isomer **18** (*R*-6, 6'-dibromo-VANOL as chiral ligand): 96% *ee* (HPLC conditions: Chiralcel AD-H column, hexane/*i*-PrOH = 70/30, 1.0 mL/min,  $\lambda$  = 280 nm,  $t_R$  (major) = 25.4 min,  $t_R$  (minor) = 21.9 min).



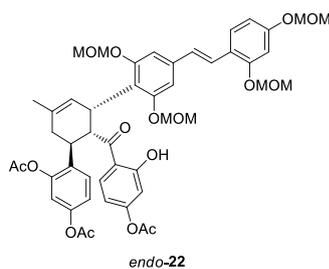
### *Exo*-23 and *Endo*-22

To a solution of *R*-VANOL (55.1 mg, 0.126 mmol) in THF (0.3 mL) was added BH<sub>3</sub>·THF (60.3  $\mu$ L, 0.0603 mmol) and AcOH (3.5  $\mu$ L, 0.0603 mmol) sequentially. The resulting mixture was stirred at room temperature for 25 min, and then concentrated to dryness and further dried under high vacuum at room temperature for 30 min. The resulting solid was dissolved in dry THF (0.5 mL), and then pre-activated 5 Å molecular sieve (400 mg) and the dienophile **6** (20 mg, 0.0523 mmol) were added to the solution. The resulting solution was stirred at room temperature for 1.5 h before the diene **19** (26.9 mg, 0.0553 mmol) was added to the reaction mixture. After 23 h, the reaction mixture was quenched by addition of H<sub>2</sub>O (13.6  $\mu$ L, 15.0 eq) and filtered through a pad of celite. The celite was further washed with EtOAc, and the organic filtrates were collected and concentrated *in vacuo*. The crude product was filtrated through a pad of silica gel to get the mixture of *exo*-**23** and *endo*-**22** before determination of the ratio of *endo/exo* by NMR (*endo/exo* = 1:1.2). Further purification was achieved by flash column chromatography (petroleum ether/EtOAc = 5:1 to 1:1) to afford the *exo*-**23** as light yellow solid in a yield of 20.5 mg (0.0232 mmol, 47%) and *endo*-**22** as light yellow solid in a yield of 18.7 mg (0.0211 mmol, 42%).



### *Exo*-23

Mp: 51-53 °C; [ $\alpha$ ]<sub>D</sub><sup>22</sup> + 260 (c 0.18 MeOH); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  12.44 (s, 1H), 7.45 (d, *J* = 8.8 Hz, 1H), 7.34 (d, *J* = 8.8 Hz, 1H), 7.22 (d, *J* = 14.0 Hz, 1H), 7.18 (d, *J* = 6.8 Hz, 1H), 6.84-6.80 (m, 5H), 6.70 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.67 (s, 1H), 6.44 (d, *J* = 2.4 Hz, 1H), 6.27 (dd, *J* = 2.4, 8.8 Hz, 1H), 5.35 (s, 1H), 5.30 (d, *J* = 6.0 Hz, 1H), 5.24 (d, *J* = 7.2 Hz, 1H), 5.22 (s, 2H), 5.17 (s, 2H), 4.96 (d, *J* = 6.0 Hz, 1H), 4.87 (d, *J* = 6.4 Hz, 1H), 4.54 (d, *J* = 10.0 Hz, 1H), 4.47 (s, 1H), 3.78 (d, *J* = 6.8 Hz, 1H), 3.61 (s, 3H), 3.52 (s, 3H), 3.48 (s, 3H), 3.37 (s, 3H), 2.43 (s, 3H), 2.26 (d, *J* = 4.4 Hz, 2H), 2.20 (s, 3H), 2.17 (s, 3H), 1.74 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  208.8, 169.2, 168.9, 168.2, 163.5, 158.0, 156.7, 156.1, 155.8, 155.7, 149.0, 148.6, 138.7, 131.4, 131.1, 127.6, 127.3, 124.6, 123.4, 121.3, 119.3, 118.6, 116.4, 111.8, 110.2, 109.6, 106.5, 104.1, 95.2, 94.9, 94.6, 56.5, 56.4, 56.2, 56.0, 48.1, 38.3, 23.2, 21.3, 21.2, 21.1, 19.2; IR (neat):  $\nu_{\text{max}}$  (cm<sup>-1</sup>) 1767, 1632, 1599, 1500, 1194, 1151, 1042, 1013, 923; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>48</sub>H<sub>52</sub>O<sub>16</sub>: 885.3328, found: 885.3310. The *exo*-**23** (*R*-VANOL as chiral ligand): -76% *ee* (HPLC conditions: Chiralcel AD-H column, hexane/*i*-PrOH = 72/28, 1.0 mL/min,  $\lambda$  = 280 nm, *t<sub>R</sub>* (major) = 6.5 min, *t<sub>R</sub>* (minor) = 8.5 min).



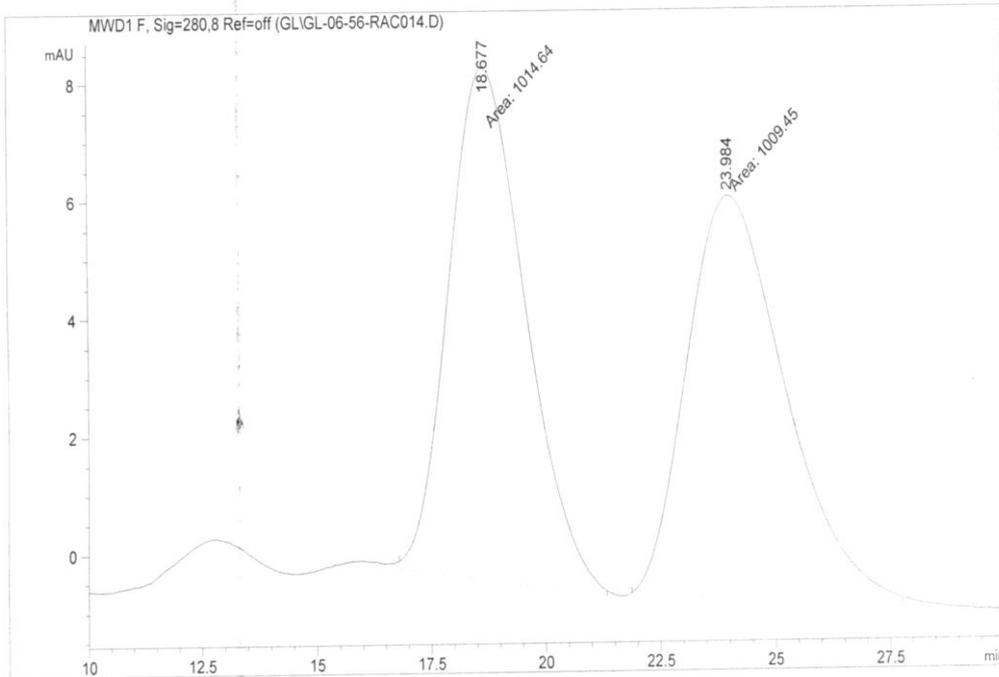
***Endo-22***

Mp: 53-55 °C;  $[\alpha]_D^{26} + 215$  (c 0.095 MeOH);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  12.26, 7.67 (d,  $J = 8.8$  Hz, 1H), 7.45 (d,  $J = 8.8$  Hz, 1H), 7.25 (d,  $J = 4.4$  Hz, 1H), 7.22 (d,  $J = 3.6$  Hz, 1H), 6.89 (dd,  $J = 2.4, 8.4$  Hz, 1H), 6.86-6.81(m, 3H), 6.75(s, 2H), 6.70 (dd,  $J = 2.4, 8.4$  Hz, 1H), 6.54 (d,  $J = 2.4$  Hz, 1H), 6.49 (dd,  $J = 2.0, 8.8$  Hz, 1H), 5.52 (d,  $J = 2.8$  Hz, 1H), 5.22 (s, 2H), 5.17 (s, 2H), 4.86 (br.s, 2H), 4.54 (br.s, 1H), 4.16 (dd,  $J = 6.4, 8.8$  Hz, 1H), 4.08 (dd,  $J = 7.6, 14.8$  Hz, 1H), 3.51 (s, 3H), 3.49 (s, 3H), 3.33 (br.s, 6H), 2.54 (dd,  $J = 6.4, 18.4$  Hz, 1H), 2.25 (s, 3H), 2.24 (s, 6H), 2.18 (d,  $J = 7.6$  Hz, 1H), 1.82 (s, 3H);  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )  $\delta$  206.2, 169.2, 169.1, 168.5, 163.6, 157.9, 155.9, 155.7, 148.9, 148.7, 138.8, 135.1, 132.3, 131.0, 127.8, 127.7, 127.4, 123.5, 122.5, 121.4, 119.3, 118.7, 117.5, 116.3, 112.2, 110.8, 109.6, 104.0, 95.1, 94.7, 94.6, 56.4, 56.2, 56.0, 49.5, 36.7, 34.6, 31.9, 23.5, 21.2, 21.1; IR (neat):  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 1766, 1598, 1501, 1196, 1152, 1042, 1012, 921; HRMS (ESI)  $[\text{M}+\text{H}]^+$  calculated for  $\text{C}_{48}\text{H}_{52}\text{O}_{16}$ : 885.3328, found: 885.3320. The *endo-22* (*R*-VANOL as chiral ligand): 90% *ee* (HPLC conditions: Chiralcel AD-H column, hexane/*i*-PrOH = 82/18, 1.0 mL/min,  $\lambda = 280$  nm,  $t_R$  (major) = 19.0 min,  $t_R$  (minor) = 15.5 min).

Data File D:\DATA\GL\GL-06-56-RAC014.D  
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**Endo- product 18 racemic**



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Area Percent Report  
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Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

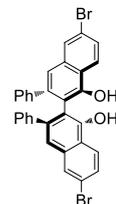
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.677	MM	1.9425	1014.64062	8.70548	50.1282
2	23.984	MM	2.4561	1009.45081	6.84989	49.8718

Totals : 2024.09143 15.55537

=====  
\*\*\* End of Report \*\*\*

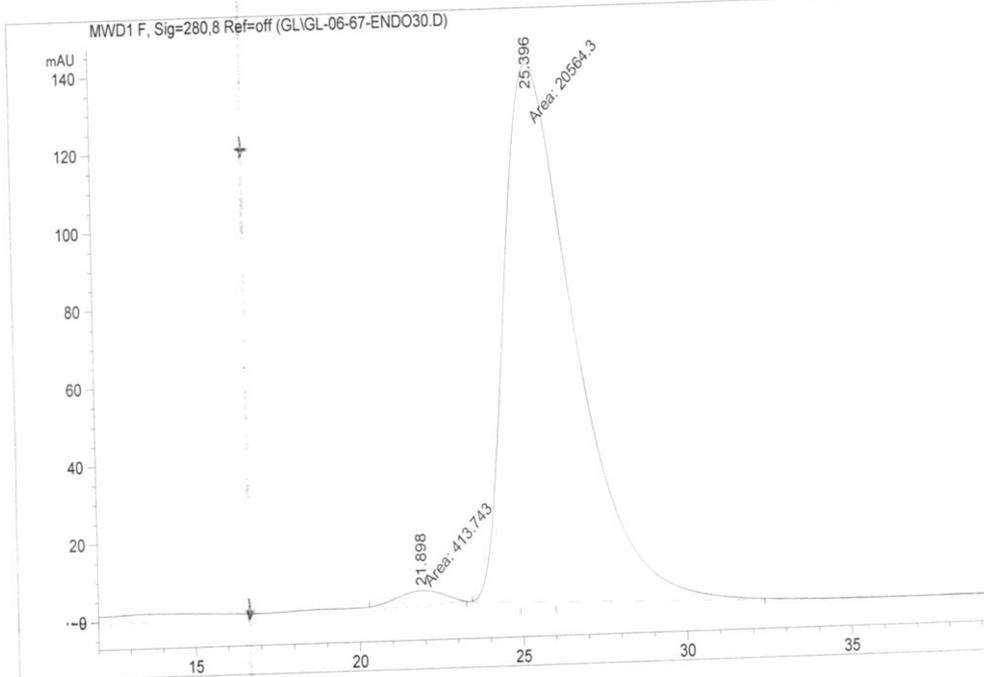
Data File D:\DATA\GL\GL-06-67-ENDO30.D  
 Sample Name: GL-06-67-endo-1

Acq. Operator : gl  
 Acq. Instrument : 仪器 1  
 Injection Date : 6/29/2015 6:27:54 PM  
 Location : Vial 1  
 Inj Volume : 15 µl  
 Acq. Method : D:\METHODS\70HEX.M  
 Last changed : 7/7/2014 11:03:25 AM by lichao  
 Analysis Method : D:\METHODS\90HEX.M  
 Last changed : 8/6/2015 10:15:13 PM by gl  
 (modified after loading)  
 Sample Info : gl-06-67-1-endo-70%hex AD



**Endo-product 18**

L7 R-6,6'-dibromo-VANOL



=====  
 Area Percent Report  
 =====

Sorted By : Signal  
 Multiplier: : 1.0000  
 Dilution: : 1.0000  
 Use Multiplier & Dilution Factor with ISTDs

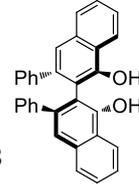
Signal 1: MWD1 F, Sig=280,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.898	MM	1.3012	413.74319	3.85268	1.9723
2	25.396	MM	2.4748	2.05643e4	138.49269	98.0277
Totals :				2.09780e4	142.34537	

=====  
 \*\*\* End of Report \*\*\*

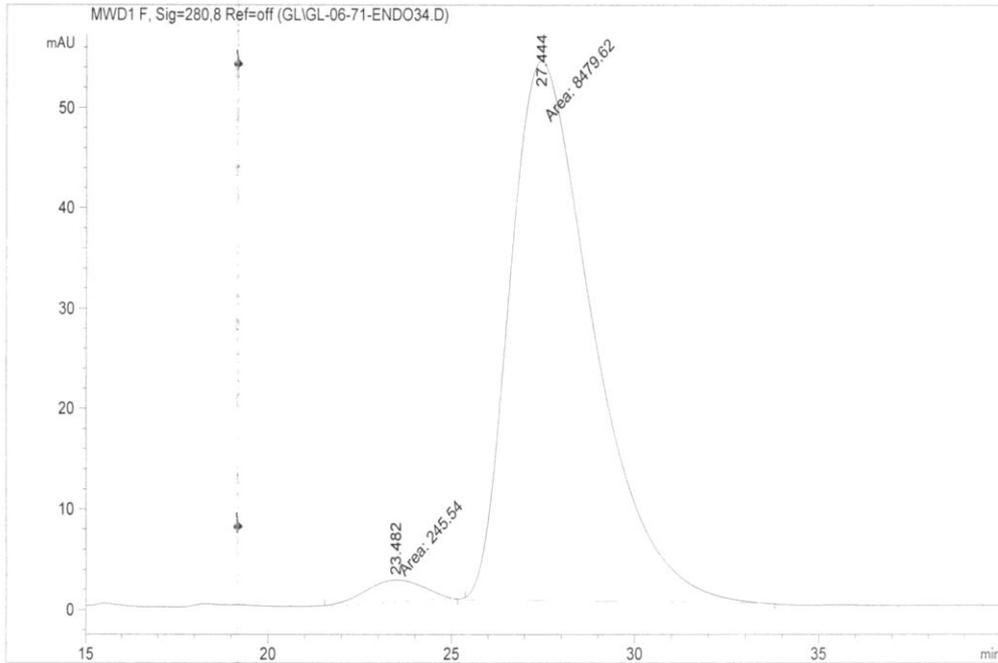
Sample Name: GL-06-71-endo-1

=====  
Acq. Operator : gl  
Acq. Instrument : 仪器 1 Location : Vial 1  
Injection Date : 7/4/2015 10:52:51 PM Inj Volume : 20 µl  
  
Acq. Method : D:\METHODS\50HEX.M  
Last changed : 7/4/2015 10:42:20 PM by gl  
(modified after loading)  
Analysis Method : D:\METHODS\90HEX.M  
Last changed : 8/6/2015 10:25:58 PM by gl  
(modified after loading)  
Sample Info : gl-06-71-endo-1-70%hex AD



Endo-product 18

R-VANOL



=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.482	MM	1.8483	245.54012	2.21408	2.8142
2	27.444	MM	2.6305	8479.61816	53.72617	97.1858

Totals : 8725.15828 55.94025

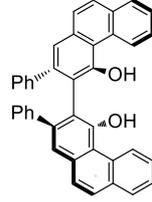
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\*\*\* End of Report \*\*\*



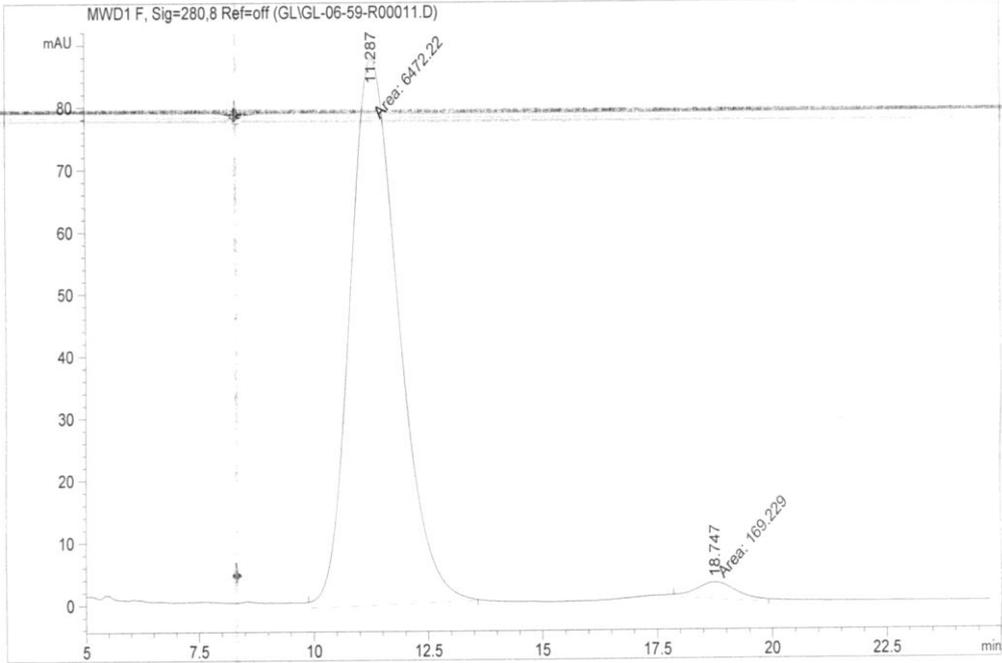
Data File D:\DATA\GL\GL-06-59-R00011.D  
Sample Name: GL-06-59-R-exo-

Acq. Operator : gl  
Acq. Instrument : 仪器 1  
Injection Date : 6/18/2015 10:37:08 PM  
Location : Vial 1  
Inj Volume : 10 µl  
Acq. Method : D:\METHODS\90HEX.M  
Last changed : 6/18/2015 10:20:37 PM by gl  
(modified after loading)  
Analysis Method : D:\METHODS\90HEX.M  
Last changed : 8/6/2015 10:39:12 PM by gl  
(modified after loading)  
Sample Info : gl-06-59-R-exo60%hex AD

Exo-product 17



R-VAPOL



=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

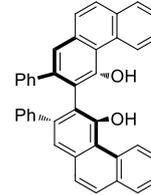
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.287	MM	1.2280	6472.21729	87.83923	97.4519
2	18.747	MM	1.0476	169.22887	2.69224	2.5481

Totals : 6641.44615 90.53147

=====  
\*\*\* End of Report \*\*\*

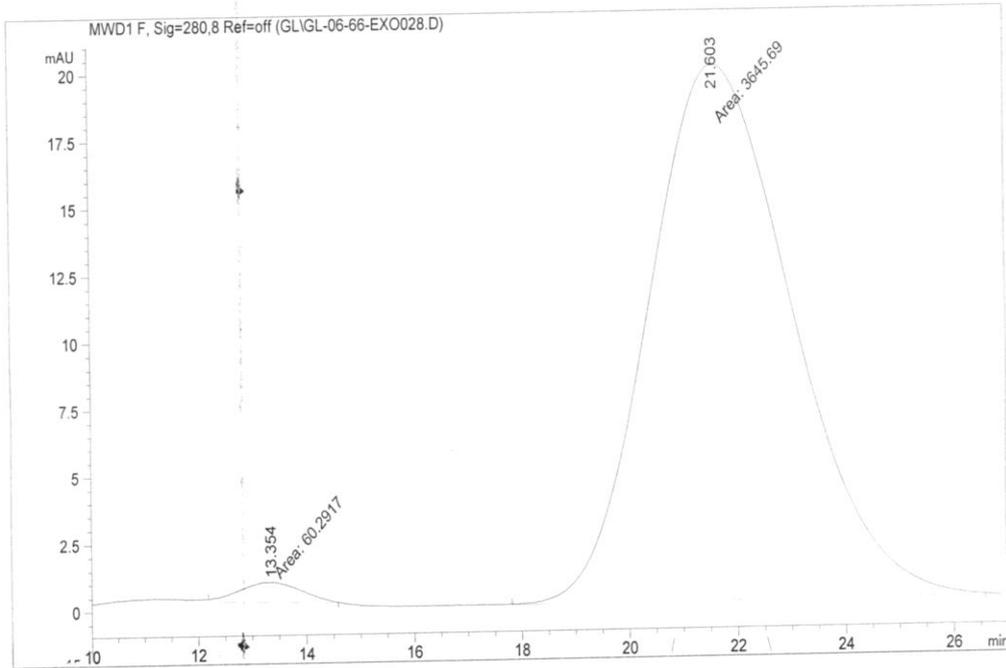
Data File D:\DATA\GL\GL-06-66-EXO028.D  
Sample Name: GL-06-66-exo

=====  
Acq. Operator : gl  
Acq. Instrument : 仪器 1  
Injection Date : 6/28/2015 3:24:51 PM  
Location : Vial 1  
Inj Volume : 20 µl  
Acq. Method : D:\METHODS\50HEX.M  
Last changed : 6/28/2015 3:22:40 PM by gl  
(modified after loading)  
Analysis Method : D:\METHODS\90HEX.M  
Last changed : 8/6/2015 10:31:56 PM by gl  
(modified after loading)  
Sample Info : gl-06-66-exo-60%hex AD



S-VAPOL

Exo-product 17



=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.354	MM	1.8363	60.29174	7.51987e-1	1.6269
2	21.603	MM	3.0397	3645.69482	19.98943	98.3731

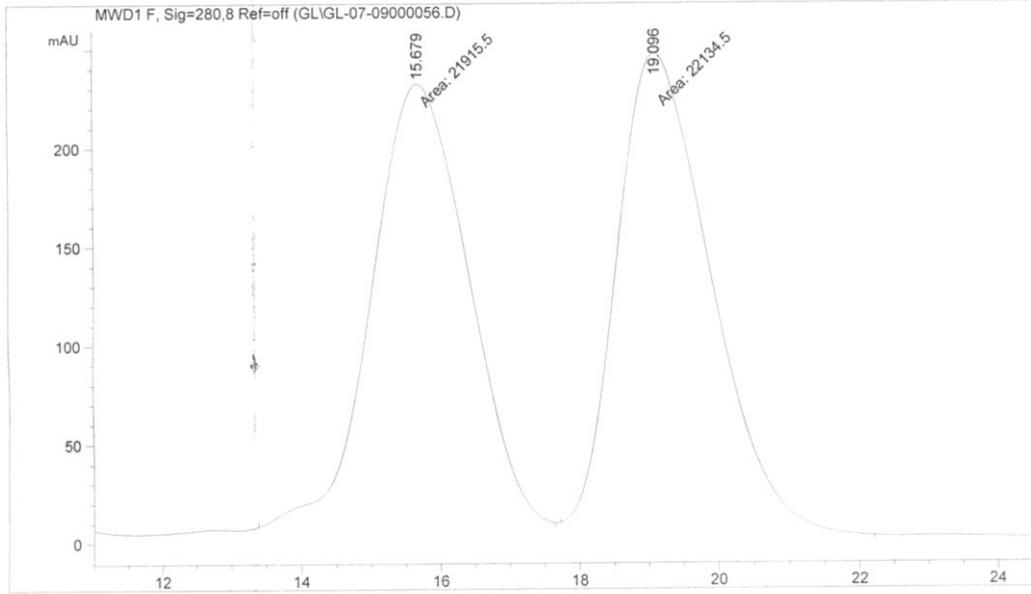
Totals : 3705.98656 20.74141

=====  
\*\*\* End of Report \*\*\*

Data File D:\DATA\GL\GL-07-09000056.D  
Sample Name: gl-07-09-rac-endo-1

=====  
Acq. Operator : gl  
Acq. Instrument : 仪器 1  
Injection Date : 8/3/2015 8:11:14 PM  
Location : Vial 1  
Inj Volume : 10 µl  
Acq. Method : D:\METHODS\70HEX.M  
Last changed : 8/3/2015 8:09:06 PM by gl  
(modified after loading)  
Analysis Method : D:\METHODS\90HEX.M  
Last changed : 8/19/2015 4:36:59 PM by gl  
(modified after loading)  
Sample Info : gl-07-09-rac-endo-823-AD  
=====

**Endo-product 22 racemic**



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Area Percent Report  
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Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

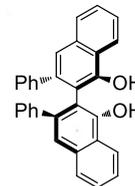
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.679	MM	1.6184	2.19155e4	225.69235	49.7514
2	19.096	MM	1.5339	2.21345e4	240.49763	50.2486

Totals : 4.40501e4 466.18999

=====  
\*\*\* End of Report \*\*\*

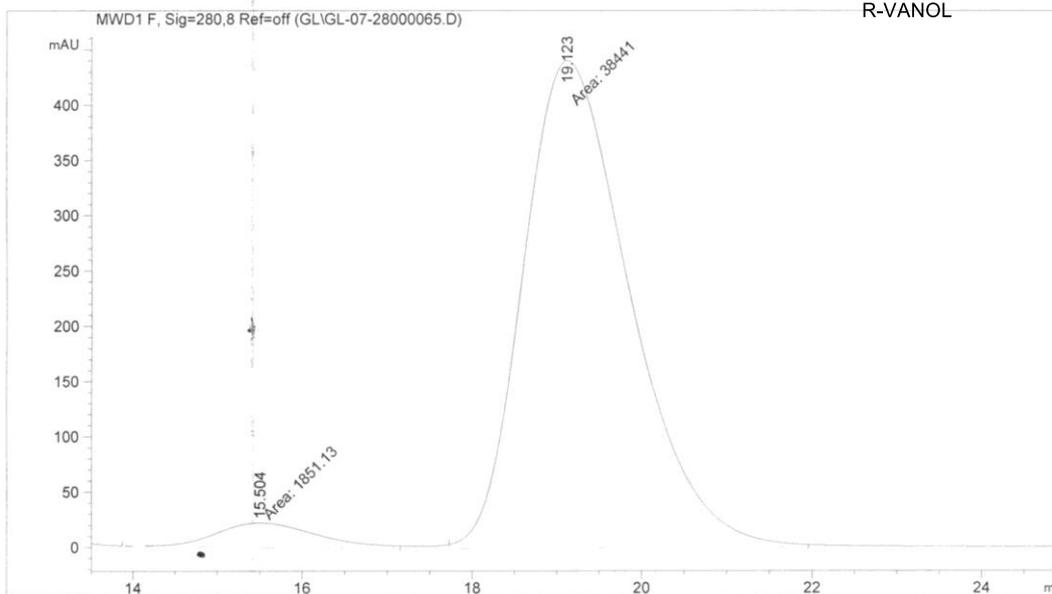
Data File D:\DATA\GL\GL-07-28000065.D  
Sample Name: gl-07-28-endo

=====  
Acq. Operator : gl  
Acq. Instrument : 仪器 1  
Injection Date : 8/24/2015 3:43:03 PM  
Location : Vial 1  
Inj Volume : 20 µl  
Acq. Method : D:\METHODS\90HEX.M  
Last changed : 8/24/2015 3:41:02 PM by gl  
(modified after loading)  
Analysis Method : D:\METHODS\90HEX.M  
Last changed : 9/1/2015 10:54:37 PM by gl  
(modified after loading)  
Sample Info : gl-07-28-endo-82%-AD



Endo-product 22

R-VANOL



=====  
Area Percent Report  
=====

Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

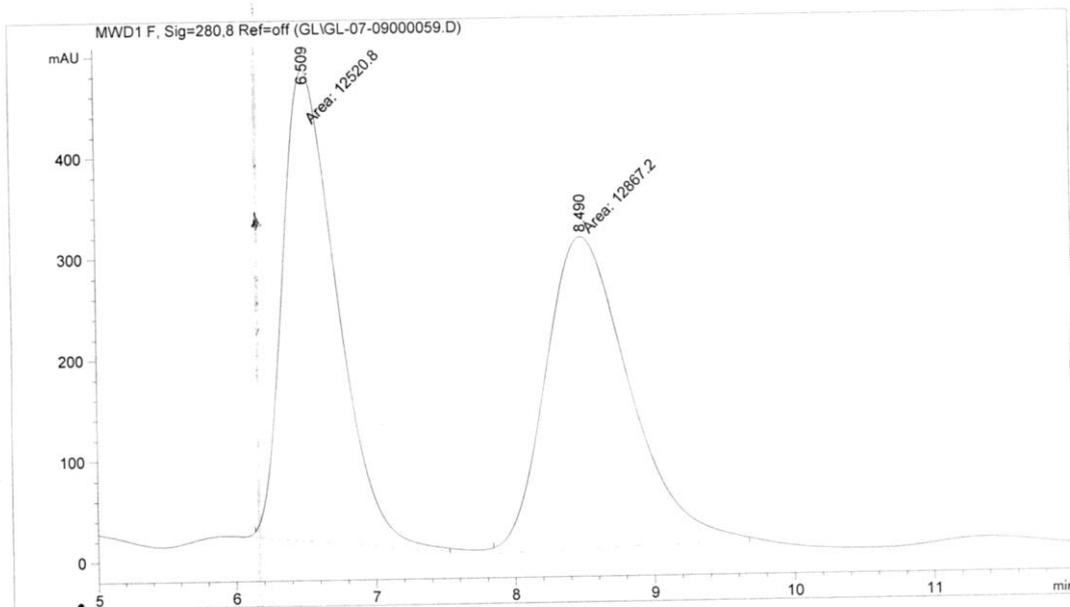
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.504	MM	1.3867	1851.13086	22.24936	4.5943
2	19.123	MM	1.4516	3.84410e4	441.36026	95.4057
Totals :				4.02921e4	463.60962	

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\*\*\* End of Report \*\*\*  
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Data File D:\DATA\GL\GL-07-09000059.D  
Sample Name: gl-07-09-exo

=====  
Acq. Operator : gl  
Acq. Instrument : 仪器 1 Location : Vial 1  
Injection Date : 8/3/2015 11:26:54 PM Inj Volume : 20 µl

=====  
Acq. Method : D:\METHODS\90HEX.M  
Last changed : 8/3/2015 11:39:33 PM by gl  
(modified after loading)  
Analysis Method : D:\METHODS\90HEX.M  
Last changed : 9/1/2015 10:57:29 PM by gl **exo-product 23 racemic**  
(modified after loading)  
Sample Info : gl-07-09-rac-exo-72%-AD



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Area Percent Report  
=====

Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.509	MM	0.4479	1.25208e4	465.86890	49.3178
2	8.490	MM	0.6943	1.28672e4	308.87372	50.6822

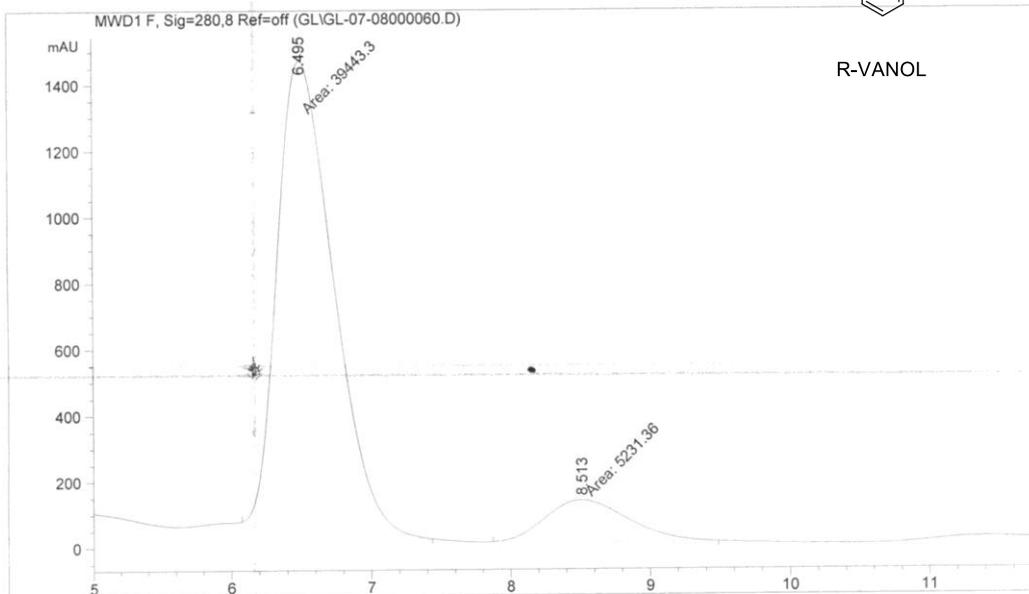
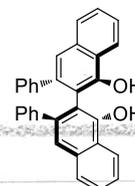
Totals : 2.53879e4 774.74261

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\*\*\* End of Report \*\*\*

Data File D:\DATA\GL\GL-07-08000060.D  
Sample Name: gl-07-08-exo

=====  
Acq. Operator : gl  
Acq. Instrument : 仪器 1 Location : Vial 1  
Injection Date : 8/4/2015 12:05:33 AM Inj Volume : 20 µl  
Acq. Method : D:\METHODS\90HEX.M  
Last changed : 8/4/2015 12:18:01 AM by gl  
(modified after loading)  
Analysis Method : D:\METHODS\90HEX.M  
Last changed : 9/1/2015 10:57:29 PM by gl  
(modified after loading)  
Sample Info : gl-07-08-exo-728-AD

exo-product 23



=====  
Area Percent Report  
=====

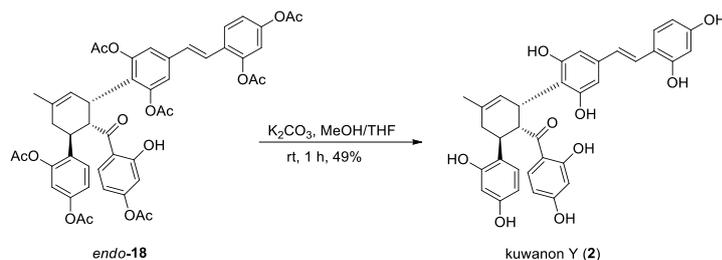
Sorted By : Signal  
Multiplier: : 1.0000  
Dilution: : 1.0000  
Use Multiplier & Dilution Factor with ISTDs

Signal 1: MWD1 F, Sig=280,8 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.495	MM	0.4631	3.94433e4	1419.59570	88.2901
2	8.513	MM	0.6947	5231.35840	125.50135	11.7099

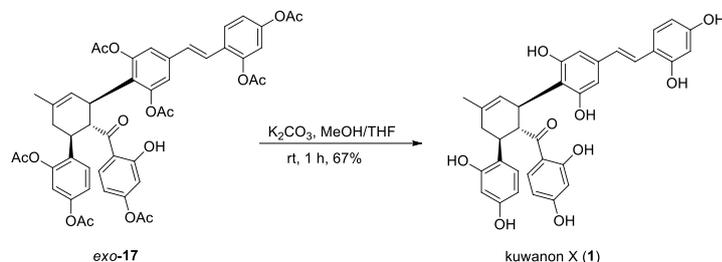
Totals : 4.46747e4 1545.09705

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\*\*\* End of Report \*\*\*



### Kuwanon Y (2)

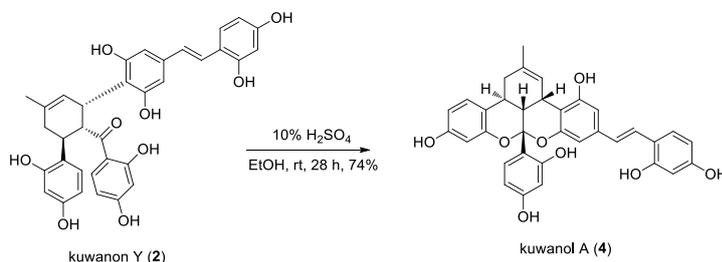
To a solution of *endo*-**18** (42.2 mg, 0.0482 mmol) in THF (0.6 mL) and MeOH (1.2 mL) was added  $K_2CO_3$  (66.5 mg, 0.482 mmol) at room temperature. The reaction was quenched by 10% HCOOH aqueous solution after 1 h, and the resulting mixture was extracted with EtOAc. The combined organic layers were washed by saturated  $NaHCO_3$  solution, followed by brine, dried over  $Na_2SO_4$ , and concentrated *in vacuo*. After purification by flash column chromatography ( $CH_2Cl_2/MeOH = 95:5$ ), kuwanon Y (**2**) was obtained as an amorphous solid in a yield of 13.8 mg (0.0237 mmol, 49%).  $[\alpha]^{25}_D +153$  (c 0.129 EtOH);  $^1H$  NMR (400 MHz, acetone- $d_6$ )  $\delta$  12.60 (s, 1H), 8.75 (br.s, 1H), 8.51 (d,  $J = 9.2$  Hz, 1H), 8.47 (br.s, 1H), 8.31 (br.s, 1H), 8.10 (br.s, 1H), 7.81 (br.s, 2H), 7.35 (d,  $J = 8.4$  Hz, 1H), 7.22 (d,  $J = 16.4$  Hz, 1H), 6.98 (d,  $J = 8.4$  Hz, 1H), 6.76 (d,  $J = 16.4$  Hz, 1H), 6.50 (d,  $J = 2.4$  Hz, 1H), 6.43 (s, 2H), 6.40 (d,  $J = 2.4$  Hz, 1H), 6.36 (dd,  $J = 2.4, 6.8$  Hz, 1H), 6.34 (dd,  $J = 2.4, 6.0$  Hz, 1H), 6.30 (dd,  $J = 2.4, 8.4$  Hz, 1H), 6.23 (d,  $J = 2.4$  Hz, 1H), 5.76 (s, 1H), 4.61 (dd,  $J = 4.0, 5.2$  Hz, 1H), 4.10 (s, 1H), 3.74 (dd,  $J = 3.2, 3.6$  Hz, 1H), 2.48 (d,  $J = 18.0$  Hz, 1H), 2.20 (dd,  $J = 2.4, 16.4$  Hz, 1H), 1.92 (s, 3H);  $^{13}C$  NMR (100 MHz, acetone- $d_6$ )  $\delta$  209.6, 167.0, 165.8, 158.9, 157.8, 157.5, 156.7, 156.3, 139.1, 135.0, 133.7, 128.7, 128.1, 125.9, 124.6, 123.8, 121.9, 117.3, 114.8, 113.7, 108.6, 108.3, 107.4, 106.5, 103.5, 103.4, 47.9, 36.2, 33.1, 32.4, 23.8; IR (neat):  $\nu_{max}$  ( $cm^{-1}$ ) 3293, 1685, 1597, 1517, 1443, 1256, 1212, 1166, 1031, 970, 839; HRMS (ESI)  $[M+H]^+$  calculated for  $C_{34}H_{30}O_9$ : 583.1963, found: 583.1967.



### Kuwanon X (1)

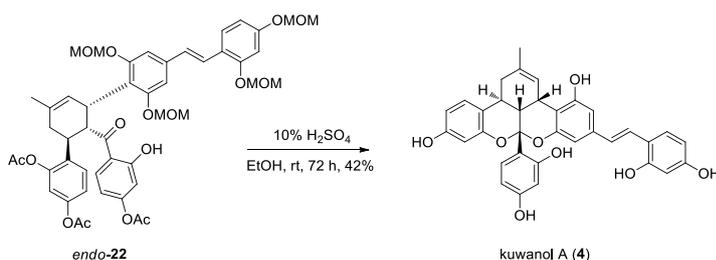
To a solution of *exo*-**17** (107 mg, 0.122 mmol) in THF (0.7 mL) and MeOH (1.4 mL) was added  $K_2CO_3$  (169 mg, 1.22 mmol) at room temperature. The reaction was quenched by 10% HCOOH aqueous solution after 1 h, and the resulting mixture was extracted with EtOAc. The combined organic layers were washed by saturated  $NaHCO_3$  solution, followed by brine, dried over  $Na_2SO_4$ , and concentrated *in vacuo*. After purification by flash column chromatography ( $CH_2Cl_2/MeOH = 95:5$ ), kuwanon X (**1**) was obtained as an amorphous solid in a yield of 48.1 mg (0.0826 mmol, 68%).  $[\alpha]^{25}_D -274$  (c 0.050 MeOH);  $^1H$  NMR (500 MHz, DMSO- $d_6$ , 120 °C)  $\delta$  12.80 (s, 1H), 9.64 (br.s, 1H), 8.91 (br.s, 1H), 8.77 (br.s, 1H), 8.39 (s, 1H), 8.33 (s, 2H), 8.24 (s, 1H), 7.58 (d,  $J = 9.0$  Hz, 1H), 7.20 (d,  $J = 8.5$  Hz, 1H), 7.0 (d,  $J = 16.5$  Hz, 1H), 6.71 (d,  $J = 8.5$  Hz, 1H), 6.59 (d,  $J = 16.5$  Hz, 1H), 6.30 (d,  $J = 2.5$  Hz, 1H), 6.27 (s, 2H), 6.23 (dd,  $J = 2.0, 8.0$  Hz, 1H), 6.10 (d,  $J = 2.5$  Hz, 1H), 5.99 (dd,  $J = 2.5, 8.5$  Hz, 1H), 5.94 (dd,  $J = 2.5, 8.5$  Hz, 1H), 5.90 (d,  $J = 2.5$  Hz, 1H), 5.20 (s, 1H), 4.76 (t,  $J = 10.5$  Hz, 1H), 4.31 (d,  $J = 8.0$  Hz, 1H), 3.52 (td,  $J = 5.0, 11.5$  Hz, 1H), 2.40 (br. d,  $J = 12.5$  Hz, 1H), 2.05 (dd,  $J = 4.5, 17.0$  Hz, 1H), 1.67 (s, 3H);  $^{13}C$

NMR (125 MHz, DMSO-*d*<sub>6</sub>, 120 °C)  $\delta$  208.2, 163.6, 163.2, 157.4, 155.7, 155.4, 155.3, 154.9, 136.6, 132.2, 130.6, 128.0, 126.4, 124.5, 124.4, 122.5, 120.5, 115.6, 114.5, 114.2, 106.9, 106.3, 105.8, 104.4, 102.7, 101.3, 45.5, 38.3, 37.0, 36.7, 22.0; IR (neat):  $\nu_{\max}$  (cm<sup>-1</sup>) 3365, 2924, 1698, 1613, 1454, 1368, 1232, 973, 669; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>34</sub>H<sub>30</sub>O<sub>9</sub>: 583.1963, found: 583.1970.



### Kuwanol A (4)

To a solution of **2** (12.2 mg, 0.0210 mmol) in EtOH (6 mL), 10% H<sub>2</sub>SO<sub>4</sub> aqueous solution (1.2 mL) was added dropwise. The reaction mixture was stirred at room temperature for 28 h and then quenched by saturated NaHCO<sub>3</sub> solution. The resulting mixture was extracted with EtOAc, washed by brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. After purification by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 96:4), kuwanol A (**4**) was obtained as an amorphous solid in a yield of 8.7 mg (0.0154 mmol, 73%).  $[\alpha]_D^{26} +394$  (c 0.111 MeOH); <sup>1</sup>H NMR (400 MHz, acetone-*d*<sub>6</sub>)  $\delta$  8.53 (br.s, 1H), 8.43-8.35 (m, 3H), 8.25 (br.s, 1H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.32 (d, *J* = 16.4 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.13 (dd, *J* = 0.8, 8.8 Hz, 1H), 6.88 (d, *J* = 16.4 Hz, 1H), 6.64 (d, *J* = 1.6 Hz, 1H), 6.61 (d, *J* = 1.6 Hz, 1H), 6.49 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.45 (s, 1H), 6.43 (d, *J* = 2.0 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 6.37 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.35 (d, *J* = 2.8 Hz, 1H), 6.23 (dd, *J* = 2.4, 8.8 Hz, 1H), 3.47 (s, 1H), 3.29 (dd, *J* = 5.6, 12.0 Hz, 1H), 2.98 (td, *J* = 5.2, 11.6 Hz, 1H), 2.70 (dd, *J* = 5.6, 17.2 Hz, 1H), 2.03-2.01 (m, 1H), 1.77 (s, 3H); <sup>13</sup>C NMR (100 MHz, acetone-*d*<sub>6</sub>)  $\delta$  159.8, 159.1, 157.7, 157.6, 157.5, 156.9, 154.1, 153.4, 139.4, 133.3, 130.3, 128.3, 127.8, 125.6, 124.4, 123.2, 117.6, 117.2, 117.1, 111.9, 109.7, 108.4, 107.1, 107.0, 106.8, 104.6, 103.9, 103.5, 102.5, 37.2, 36.2, 35.1, 28.4, 23.9; IR (neat):  $\nu_{\max}$  (cm<sup>-1</sup>) 3332, 2923, 1686, 1609, 1510, 1456, 1258, 1166, 1149, 1125, 1020, 969; HRMS (ESI) [M+H]<sup>+</sup> calculated for C<sub>34</sub>H<sub>28</sub>O<sub>8</sub>: 565.1857, found: 565.1862.



### Kuwanol A (4)

To a solution of *endo-22* (15.1 mg, 0.0170 mmol) in EtOH (3.75 mL), 10% H<sub>2</sub>SO<sub>4</sub> aqueous solution (0.75 mL) was added dropwise at room temperature. The reaction mixture was stirred for 72 h and then quenched by saturated NaHCO<sub>3</sub> solution. The resulting mixture was extracted with EtOAc, washed by brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated *in vacuo*. After purification by flash column chromatography (CH<sub>2</sub>Cl<sub>2</sub>/MeOH = 96:4), kuwanol A (**4**) was obtained as an amorphous solid in a yield of 4.0 mg (0.00709 mmol, 42%).

#### IV) Comparison of Natural and Synthetic Kuwanons X and Y, Kuwanol A

##### NMR data comparison of natural and synthetic kuwanon X

<sup>1</sup>H NMR (Hz) DMSO-*d*<sub>6</sub> 120 °C

Natural ( 270 MHz)	Synthetic (500 MHz)	Natural ( 270 MHz)	Synthetic (500 MHz)
13.11(s, 1H, 21°C)	12.80 (s, 1H)	6.27 (s, 2H)	6.27 (s, 2H)
-	9.64 (br.s, 1H)	6.23 (dd, <i>J</i> = 2.6, 8.5, 1H)	6.23 (dd, <i>J</i> = 2.0, 8.0, 1H)
-	8.91 (br.s, 1H)	6.11 (d, <i>J</i> = 2.1, 1H)	6.10 (d, <i>J</i> = 2.5, 1H)
-	8.77 (br.s, 1H)	6.00 (dd, <i>J</i> = 2.5, 8.8, 1H)	5.99 (dd, <i>J</i> = 2.5, 8.5, 1H)
-	8.39 (br.s, 1H)	5.94 (dd, <i>J</i> = 2.1, 8.3, 1H)	5.94 (dd, <i>J</i> = 2.5, 8.5, 1H)
-	8.33 (br.s, 2H)	5.90 (d, <i>J</i> = 2.5, 1H)	5.90 (d, <i>J</i> = 2.5, 1H)
-	8.24 (br.s, 1H)	5.20 (br.s, 1H)	5.20 (br.s, 1H)
7.59 (d, <i>J</i> = 8.8, 1H)	7.58 (d, <i>J</i> = 9.0, 1H)	4.78 (br.t, <i>J</i> = 10.0, 1H)	4.76 (br.t, <i>J</i> = 10.5, 1H)
7.21 (d, <i>J</i> = 8.5, 1H)	7.20 (d, <i>J</i> = 8.5, 1H)	4.30 (br.d, <i>J</i> = 10.0, 1H)	4.31 (br.d, <i>J</i> = 8.0, 1H)
6.99 (d, <i>J</i> = 16.0, 1H)	7.00 (d, <i>J</i> = 16.5, 1H)	3.50 (ddd, <i>J</i> = 5.0, 10.0, 13.0, 1H)	3.52 (td, <i>J</i> = 5.0, 11.5, 1H)
6.71 (d, <i>J</i> = 8.3, 1H)	6.71 (d, <i>J</i> = 8.5, 1H)	2.38 (dd, <i>J</i> = 13.0, 16.0, 1H)	2.40 (br.d, <i>J</i> = 12.5, 1H)
6.56 (d, <i>J</i> = 16.0, 1H)	6.59 (d, <i>J</i> = 16.5, 1H)	2.05 (dd, <i>J</i> = 5.0, 16.0, 1H)	2.05 (dd, <i>J</i> = 4.5, 17.0, 1H)
6.31 (d, <i>J</i> = 2.6, 1H)	6.30 (d, <i>J</i> = 2.5, 1H)	1.67 (s, 3H)	1.67 (s, 3H)

<sup>13</sup>C NMR (Hz) DMSO-*d*<sub>6</sub> 120°C\*

Natural ( 67.5 MHz)	Synthetic (125 MHz)	Natural ( 67.5 MHz)	Synthetic (125 MHz)
208.9	208.7	121.1	121.0
164.2	164.1	116.2	116.1
163.9	163.7	115.2	115.0
158.1	157.9	114.9	114.7
156.4	156.2	107.6	107.4
156.0	155.9	107.0	106.8
155.9	155.8	106.4	106.3
155.6	155.4	105.0	104.9
137.2	137.1	103.4	103.2
132.9	132.7	102.0**	101.8
131.2	131.1	46.1	46.0
128.7	128.5	39.0	38.8
127.1	126.9	37.7	37.5
125.2	125.0	37.4	37.2
125.1	124.9	22.7	22.5
123.1	123.0		

\*Date shown for synthetic kuwanon X has been referenced to DMSO-*d*<sub>6</sub> (δ 40.0) for comparison

\*\*Chemical shift of this carbon was recorded as 102.0 in 'Hano, Y.; Tsubura, H.; Nomura, T. *Heterocycles* **1986**, 24, 2603' but 120.0 in 'Hirakura, K.; Hano, Y.; Fukai, T. *Chem. Pharm. Bull.* **1985**, 33, 1088.'

$[\alpha]_D$  of Natural and Synthetic Kuwanon X

Natural Kuwanon X	Synthetic Kuwanon X
$[\alpha]^{21}_D$ -322 (c=0.049 in MeOH)	$[\alpha]^{25}_D$ -274 (c=0.050 in MeOH)

### NMR data comparison of natural and synthetic kuwanon Y

$^1\text{H}$  NMR (Hz) acetone- $d_6$

Natural	Synthetic (400 MHz)	Natural	Synthetic (400 MHz)
-	12.60 (br.s, 1H)	6.40 (d, $J = 2.0$ , 1H)	6.40 (d, $J = 2.4$ , 1H)
-	8.75 (br.s, 1H)	6.36 (dd, $J = 2.0$ , 8.0, 1H)	6.36 (dd, $J = 2.4$ , 6.8, 1H)
8.52 (d, $J = 8.0$ , 1H)	8.51 (d, $J = 9.2$ , 1H)	6.35 (dd, $J = 2.0$ , 8.0, 1H)	6.34 (dd, $J = 2.4$ , 6.0, 1H)
-	8.47 (br.s, 1H)	6.30 (dd, $J = 2.0$ , 8.0, 1H)	6.30 (dd, $J = 2.4$ , 8.4, 1H)
-	8.31 (br.s, 1H)	6.24 (d, $J = 2.0$ , 1H)	6.23 (d, $J = 2.4$ , 1H)
-	8.10 (br.s, 1H)	5.76 (s, 1H)	5.76 (s, 1H)
-	7.81 (br.s, 2H)	4.60 (dd, $J = 4.0$ , 5.0, 1H)	4.61 (dd, $J = 4.0$ , 5.2, 1H)
7.34 (d, $J = 8.0$ , 1H)	7.35 (d, $J = 8.4$ , 1H)	4.11 (d, $J = 5.0$ , 1H)	4.10 (s, 1H)
7.22 (d, $J = 16.0$ , 1H)	7.22 (d, $J = 16.4$ , 1H)	3.75 (dd, $J = 3.0$ , 4.0, H)	3.74 (dd, $J = 3.2$ , 3.6, H)
6.98 (d, $J = 8.0$ , 1H)	6.98 (d, $J = 8.4$ , 1H)	2.49 (d, $J = 18.0$ , 1H)	2.48 (d, $J = 18.0$ , 1H)
6.77 (d, $J = 16.0$ , 1H)	6.76 (d, $J = 16.4$ , 1H)	2.19 (dd, $J = 3.0$ , 18.0, 1H)	2.20 (dd, $J = 2.4$ , 16.4, 1H)
6.50 (d, $J = 2.0$ , 1H)	6.50 (d, $J = 2.4$ , 1H)	1.92 (s, 3H)	1.92 (s, 3H)
6.44 (s, 2H)	6.43 (s, 2H)		

$^{13}\text{C}$  NMR (Hz) acetone- $d_6$

Natural	Synthetic (100 MHz)	Natural	Synthetic (100 MHz)
208.6	209.6	121.6	121.9
166.2	167.0	116.9	117.3
165.1	165.8	114.3	114.8
158.3	158.9	113.3	113.7
157.1	157.8	108.2	108.6
156.8	157.5	107.9	108.3
156.0	156.7	107.0	107.4
155.6	156.3	106.1	106.5
138.5	139.1	103.2	103.5
134.4	135.0	103.1	103.4
133.3	133.7	47.8	47.9
128.2	128.7	36.0	36.2
127.6	128.1	33.1	33.1
125.5	125.9	32.4	32.4
124.1	124.6	23.7	23.8
123.3	123.8		

$[\alpha]_D$  of Natural and Synthetic Kuwanon Y

Natural Kuwanon Y	Synthetic Kuwanon Y
$[\alpha]^{22}_D$ +172 (c=0.129 in EtOH)	$[\alpha]^{25}_D$ +153 (c=0.129 in EtOH)

## NMR data comparison of natural and synthetic kuwanon A

<sup>1</sup>H NMR (Hz) acetone-*d*<sub>6</sub>

Natural (400 MHz)	Synthetic (400 MHz)	Natural (400 MHz)	Synthetic (400 MHz)
-	8.53 (br.s, 1H)	6.43 (d, <i>J</i> = 2.4, 1H)	6.43 (d, <i>J</i> = 2.0, 1H)
-	8.43-8.35 (m, 3H)	6.40 (d, <i>J</i> = 2.4, 1H)	6.39 (d, <i>J</i> = 2.4, 1H)
-	8.25 (br.s, 1H)	6.38 (dd, <i>J</i> = 2.4, 8.4, 1H)	6.37 (dd, <i>J</i> = 2.4, 8.4, 1H)
7.39 (d, <i>J</i> = 8.4, 1H)	7.39 (d, <i>J</i> = 8.8, 1H)	6.35 (d, <i>J</i> = 2.4, 1H)	6.35 (d, <i>J</i> = 2.8, 1H)
7.32 (d, <i>J</i> = 16.5, 1H)	7.32 (d, <i>J</i> = 16.4, 1H)	6.23 (dd, <i>J</i> = 2.4, 8.6, 1H)	6.23 (dd, <i>J</i> = 2.4, 8.8, 1H)
7.23 (d, <i>J</i> = 8.6, 1H)	7.23 (d, <i>J</i> = 8.4, 1H)	3.47 (dd, <i>J</i> = 5.0, 5.9, 1H)	3.47 (s, 1H)
7.13 (d, <i>J</i> = 8.4, 1H)	7.13 (dd, <i>J</i> = 0.8, 8.8, 1H)	3.30 (dd, <i>J</i> = 5.9, 11.9, 1H)	3.29 (dd, <i>J</i> = 5.6, 12.0, 1H)
6.88 (d, <i>J</i> = 16.5, 1H)	6.88 (d, <i>J</i> = 16.4, 1H)	3.00 (ddd, <i>J</i> = 5.0, 11.9, 12.0, 1H)	2.98 (td, <i>J</i> = 5.2, 11.6, 1H)
6.64 (d, <i>J</i> = 1.5, 1H)	6.64 (d, <i>J</i> = 1.6, 1H)	2.70 (dd, <i>J</i> = 5.0, 17.1, 1H)	2.70 (dd, <i>J</i> = 5.6, 17.2, 1H)
6.62 (d, <i>J</i> = 1.5, 1H)	6.61 (d, <i>J</i> = 1.6, 1H)	2.00 (dd, <i>J</i> = 12.0, 17.1, 1H)	2.03-2.01 (m, 1H)
6.49 (dd, <i>J</i> = 2.4, 8.4, 1H)	6.49 (dd, <i>J</i> = 2.4, 8.4, 1H)	1.77 (s, 3H)	1.77 (s, 3H)
6.44 (d, <i>J</i> = 5.0, 1H)	6.45 (s, 1H)		

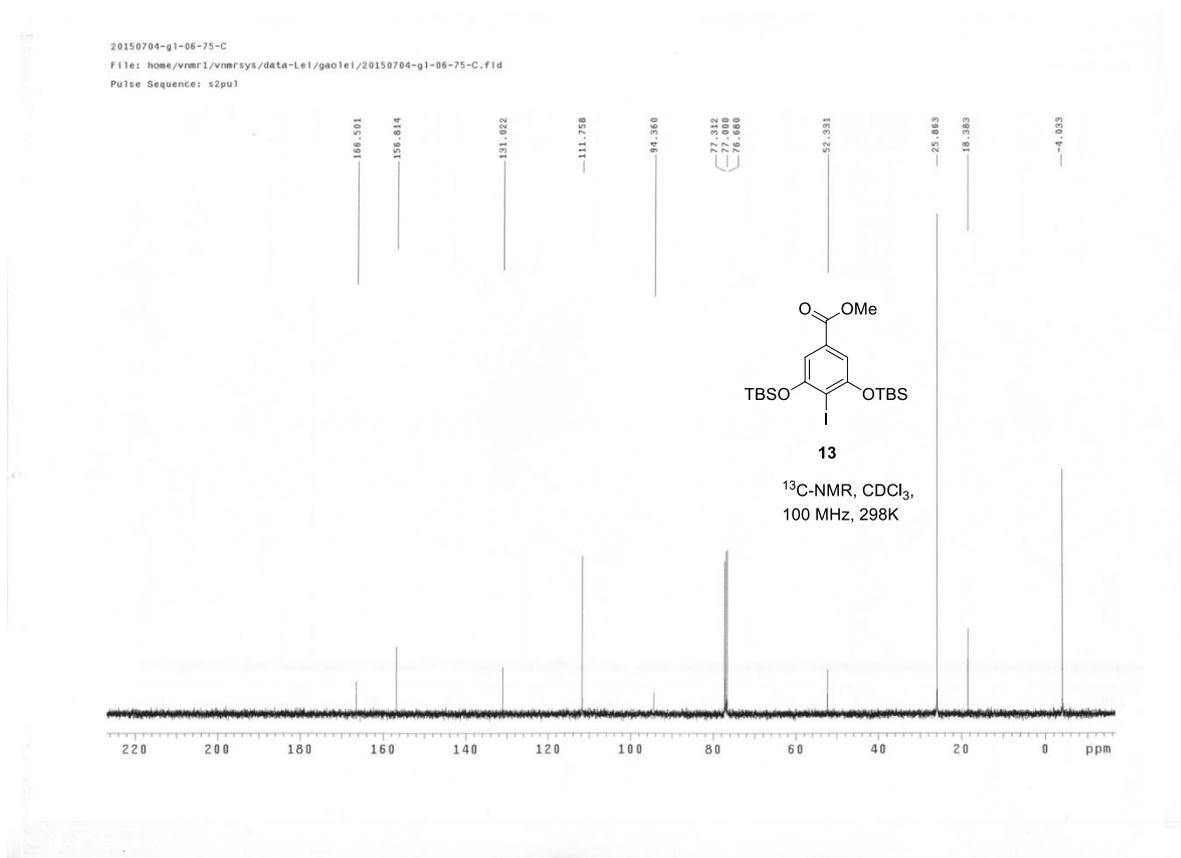
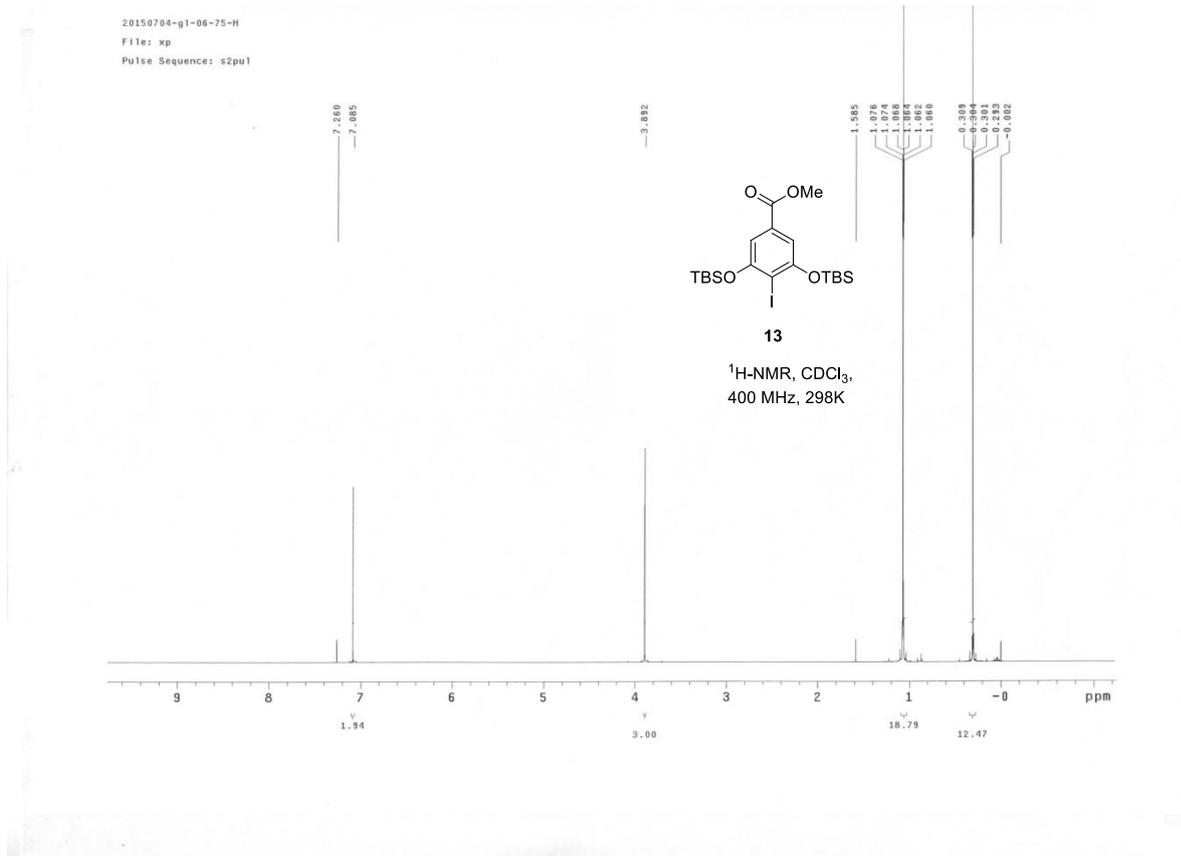
<sup>13</sup>C NMR (Hz) acetone-*d*<sub>6</sub>

Natural	Synthetic (100 MHz)	Natural	Synthetic (100 MHz)
159.3	159.8	116.7	117.2
158.4	159.1	116.6	117.1
157.2	157.7	111.4	111.9
157.0	157.6	109.3	109.7
156.9	157.5	108.0	108.4
156.9	156.9	106.7	107.1
153.4	154.1	106.7	107.0
152.5	153.4	106.4	106.8
138.8	139.4	104.2	104.6
132.7	133.3	103.5	103.9
129.7	130.3	103.2	103.5
127.8	128.3	102.1	102.5
127.2	127.8	37.2	37.2
125.1	125.6	36.1	36.2
124.0	124.4	35.0	35.1
122.7	123.2	28.4	28.4
117.1	117.6	23.8	23.9

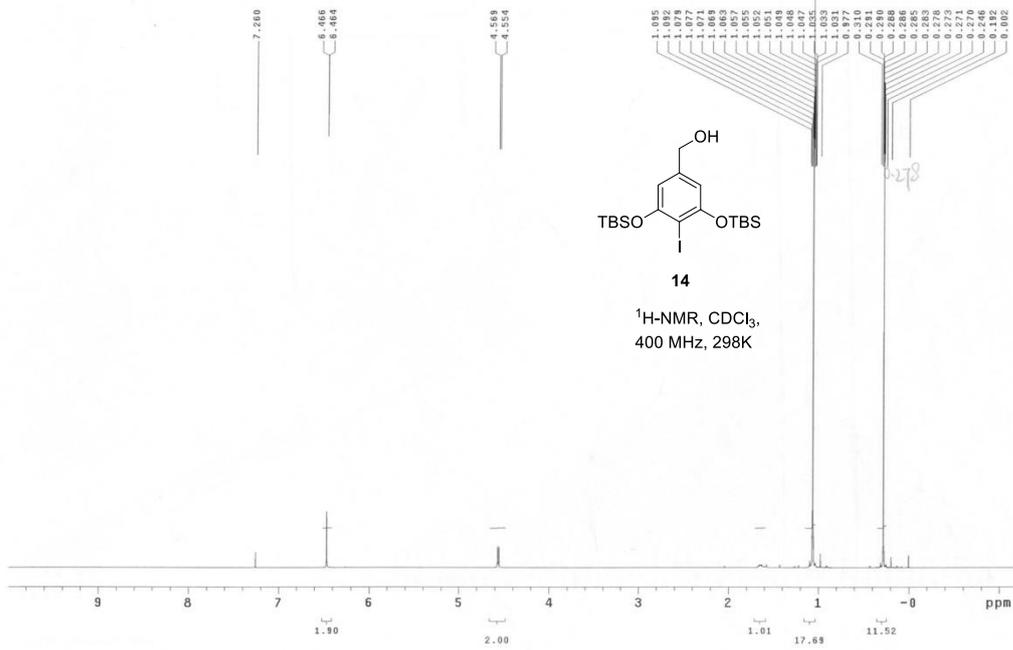
[α]<sub>D</sub> of Natural and Synthetic Kuwanon A

Natural Kuwanol A	Synthetic Kuwanol A
[α] <sup>24</sup> <sub>D</sub> +557 (c=0.111 in MeOH)	[α] <sup>26</sup> <sub>D</sub> +394 (c=0.111 in MeOH)

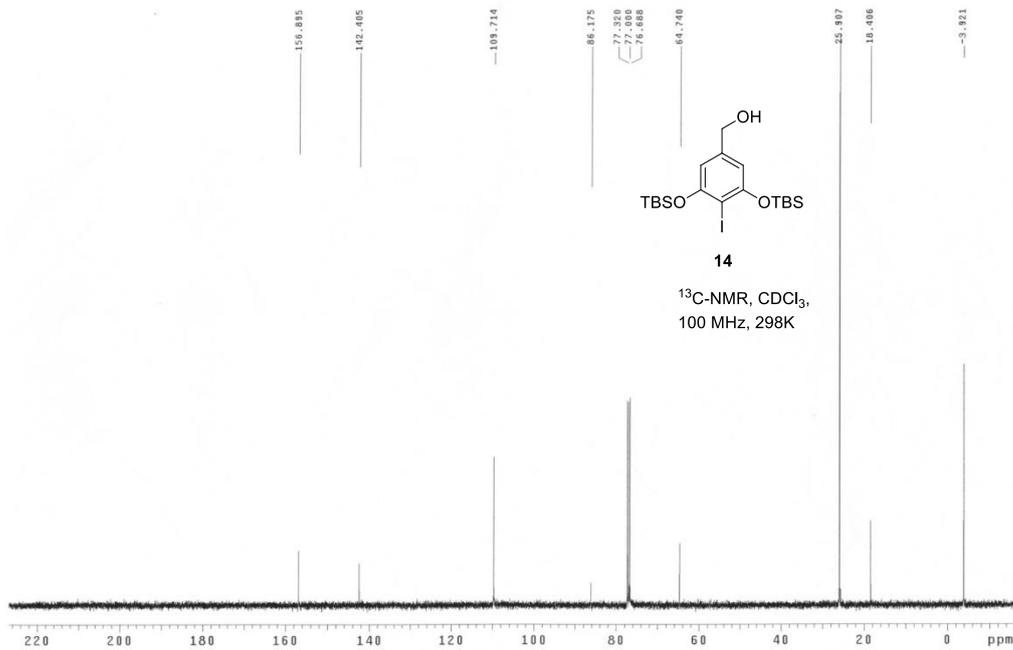
# V) $^1\text{H}$ , $^{13}\text{C}$ NMR Spectra



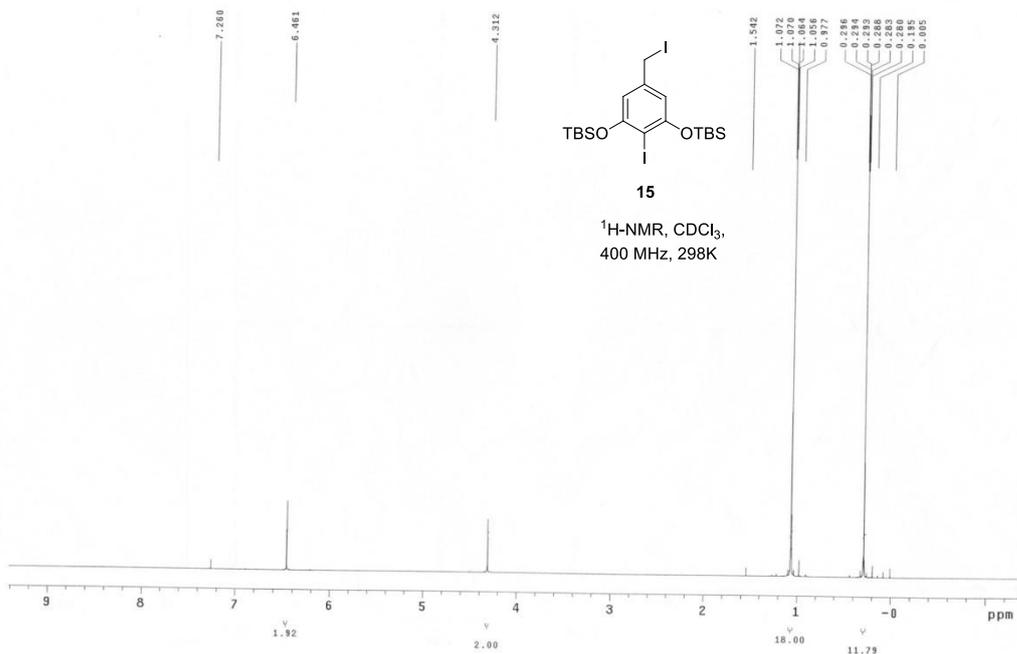
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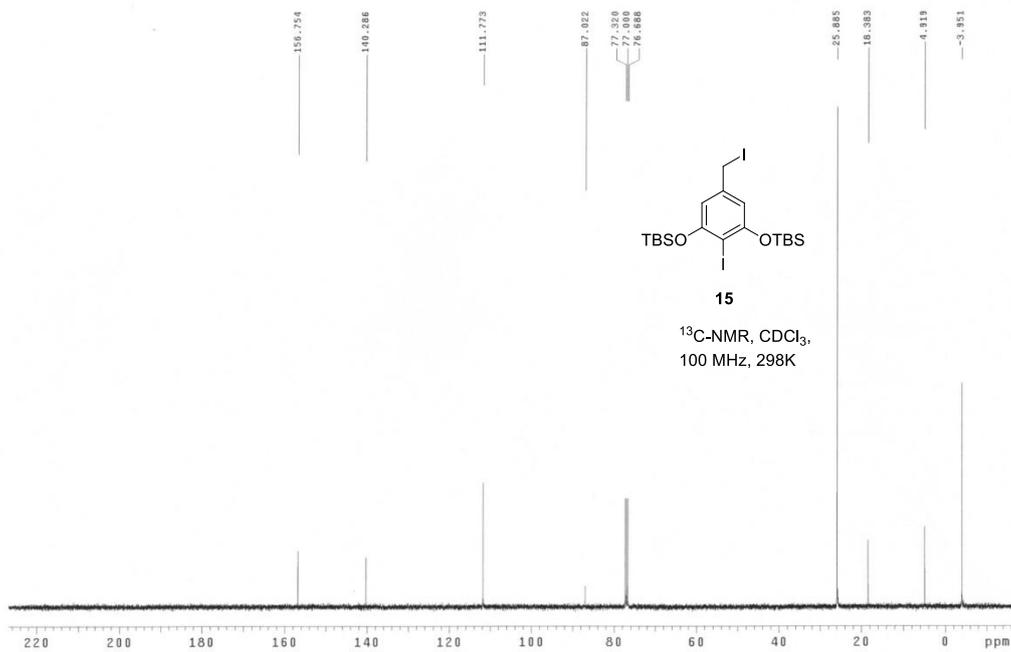
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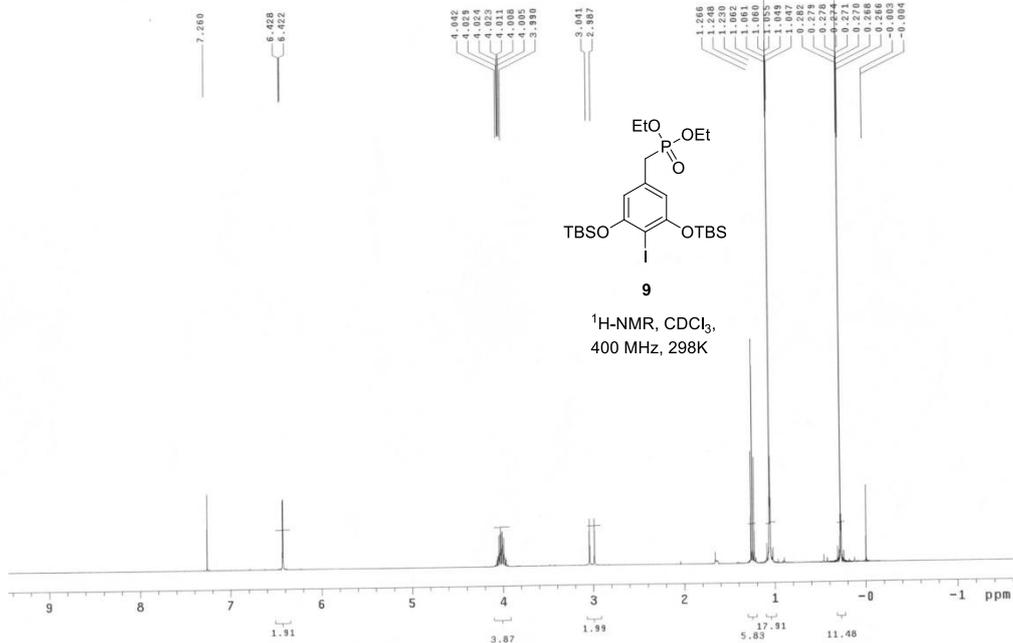
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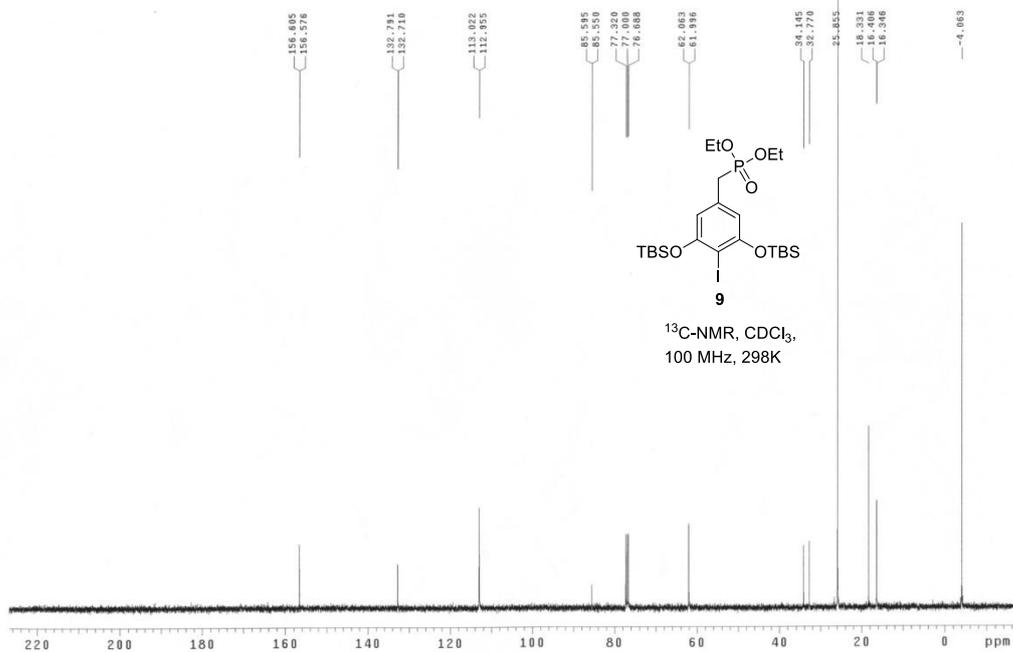
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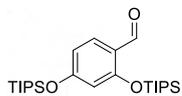
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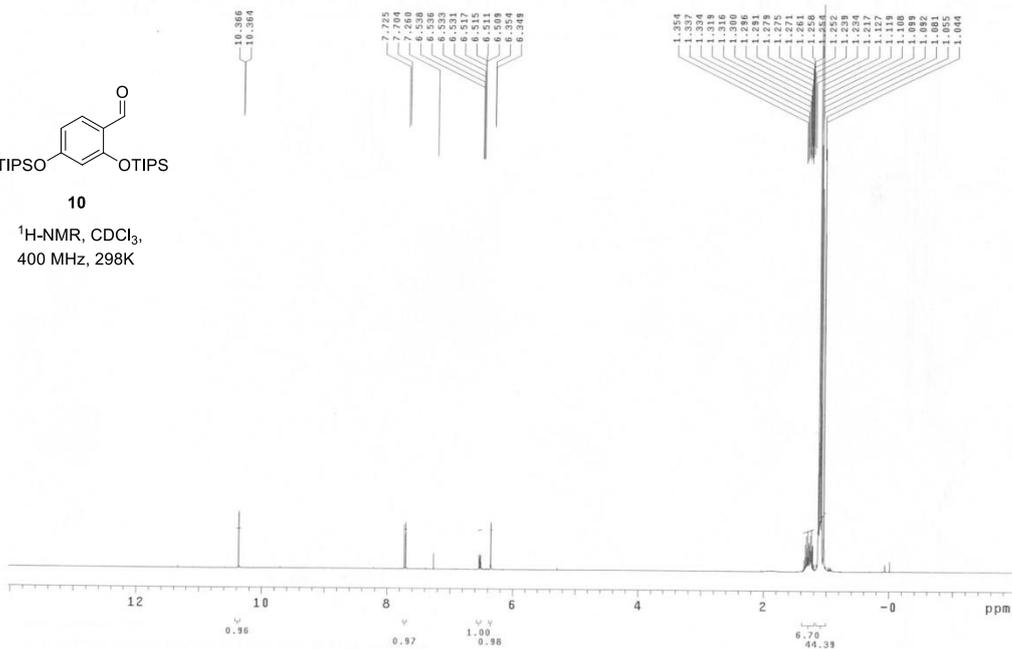
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10

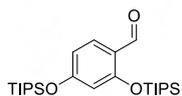
<sup>1</sup>H-NMR, CDCl<sub>3</sub>,  
400 MHz, 298K



20150702-g1-06-10-C

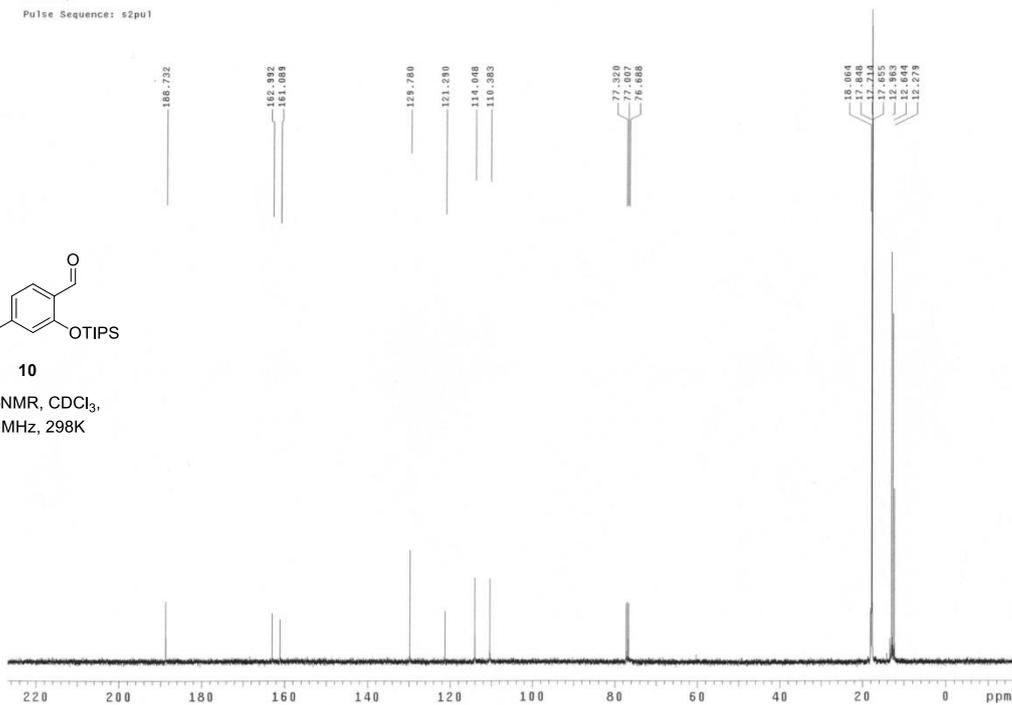
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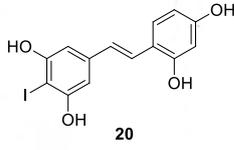


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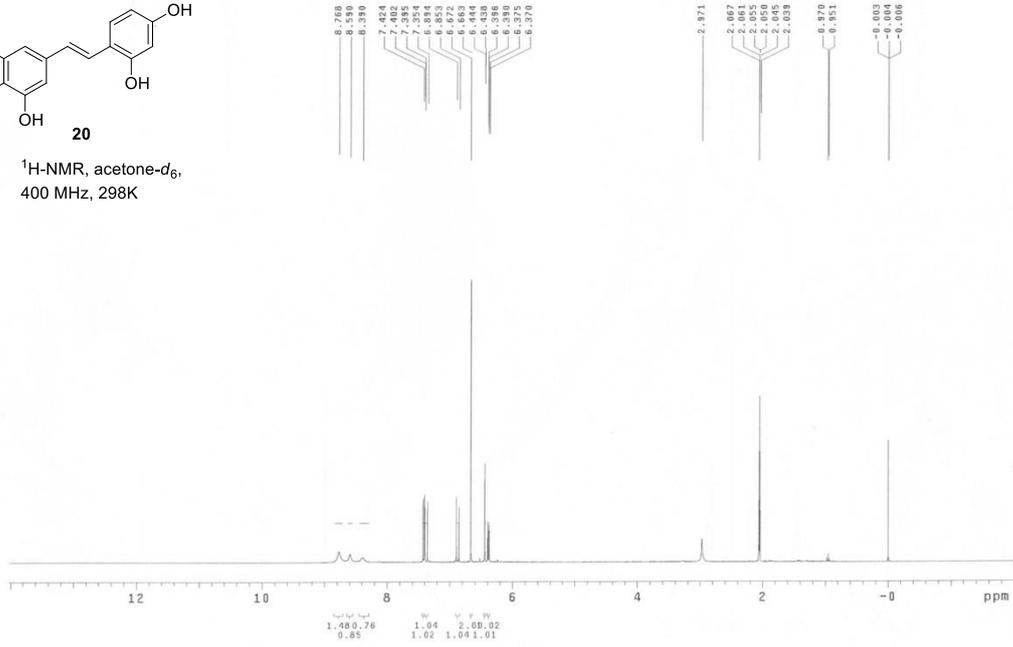
<sup>13</sup>C-NMR, CDCl<sub>3</sub>,  
100 MHz, 298K



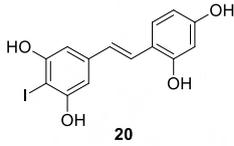
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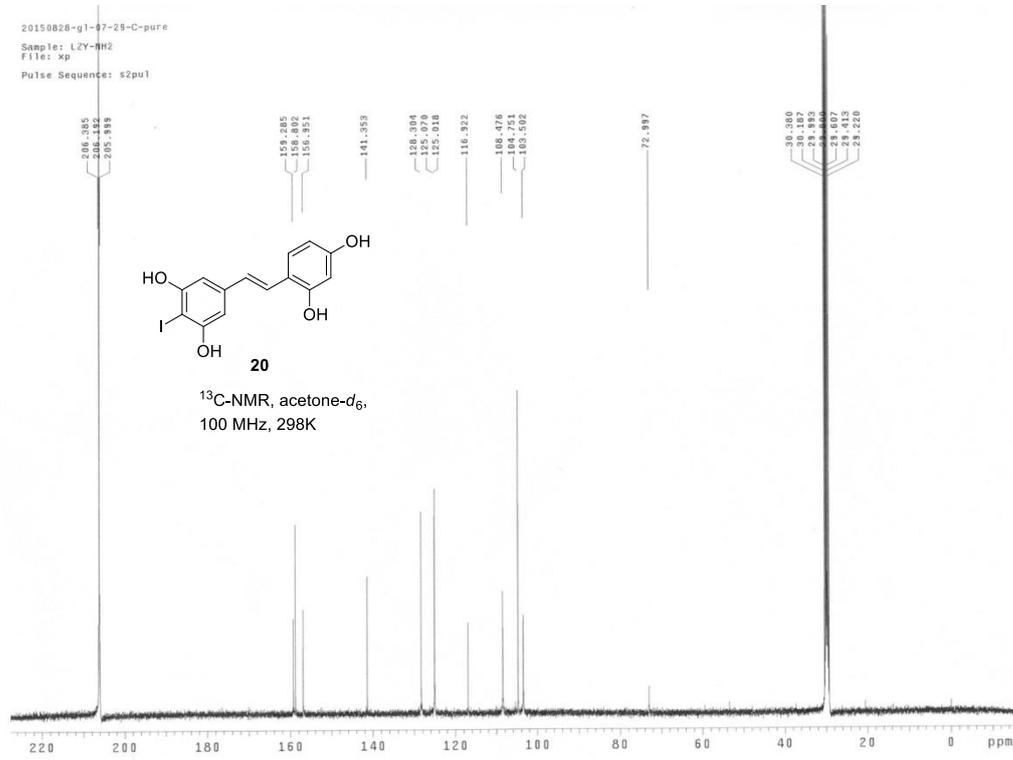
<sup>1</sup>H-NMR, acetone-d<sub>6</sub>,  
400 MHz, 298K

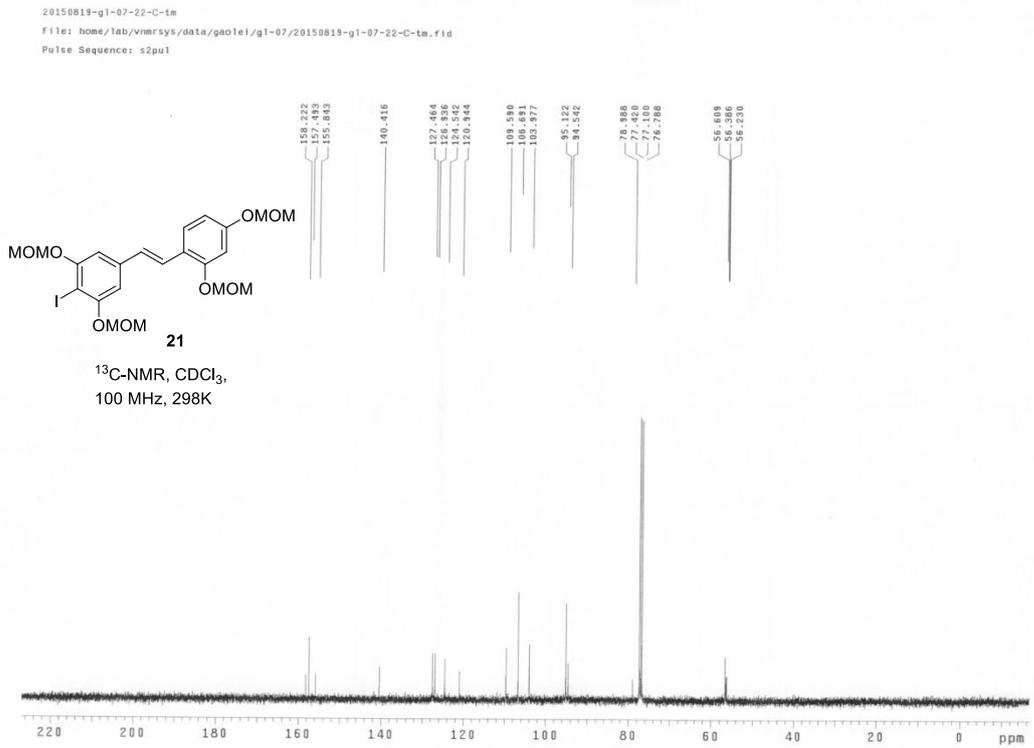
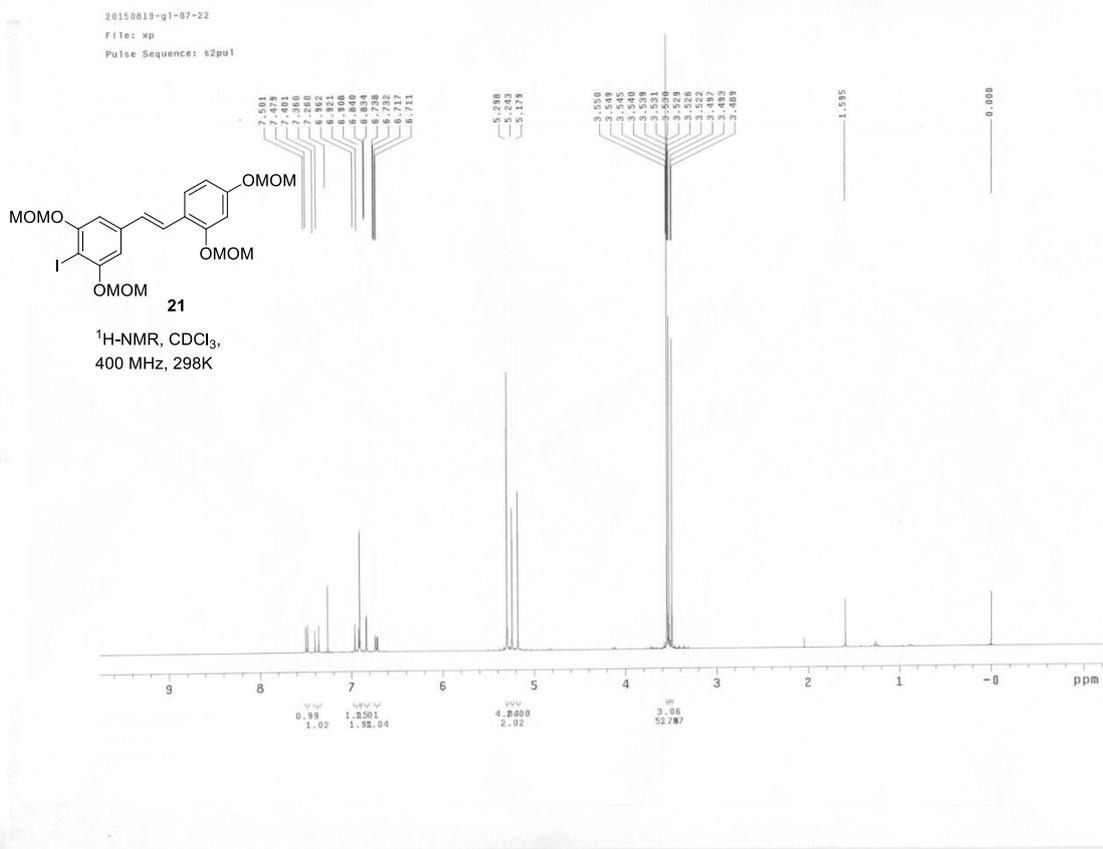


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Pulse Sequence: s2pu1

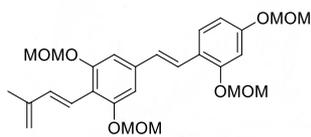


<sup>13</sup>C-NMR, acetone-d<sub>6</sub>,  
100 MHz, 298K

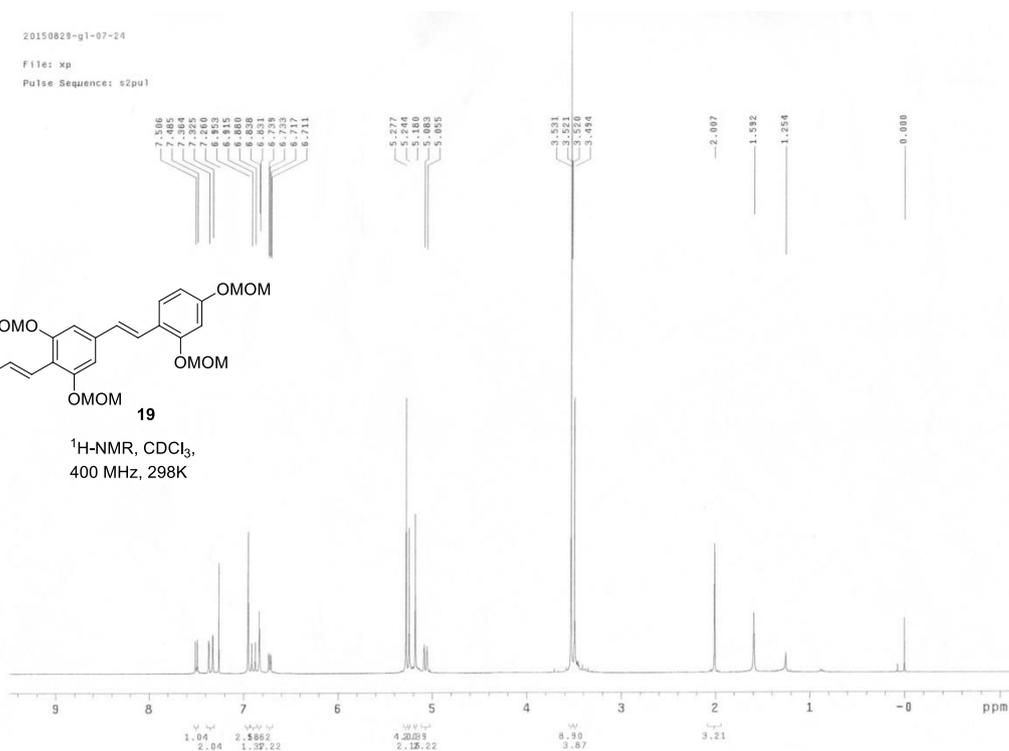




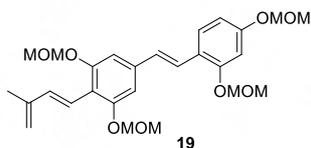
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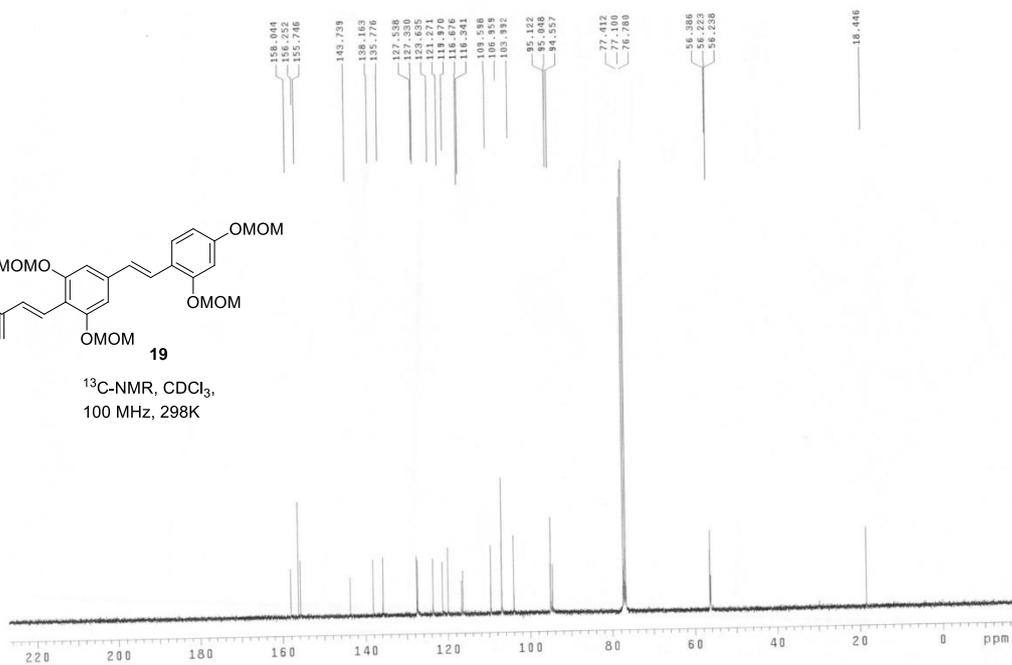
<sup>1</sup>H-NMR, CDCl<sub>3</sub>,  
400 MHz, 298K



20150828-g1-07-24-C  
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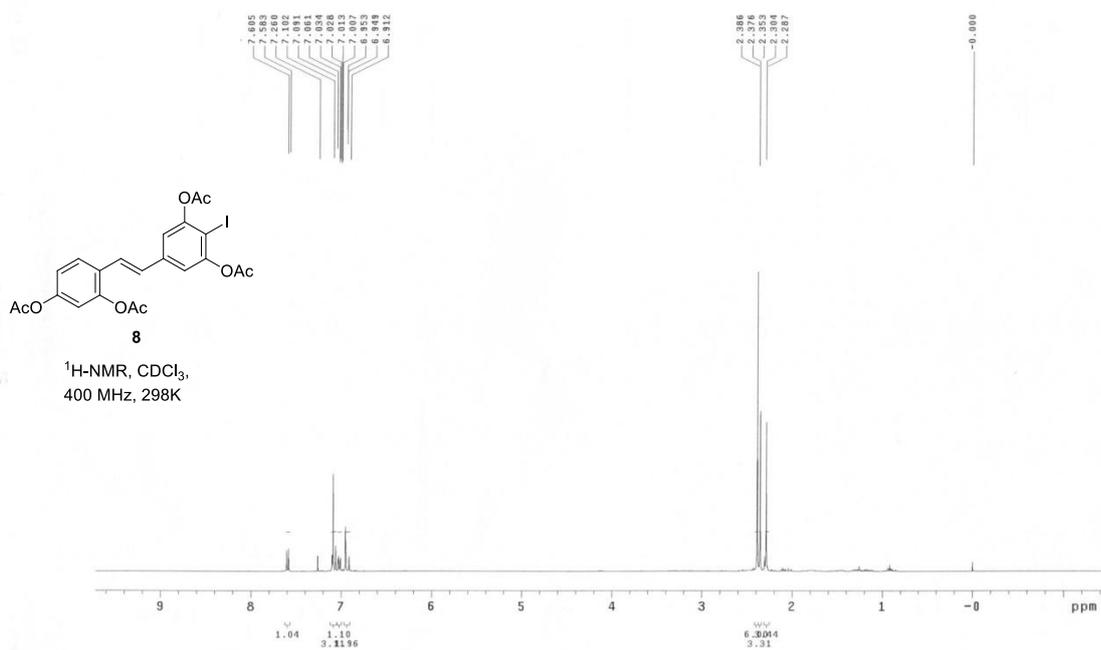
<sup>13</sup>C-NMR, CDCl<sub>3</sub>,  
100 MHz, 298K



20150707-g1-06-77-H-1

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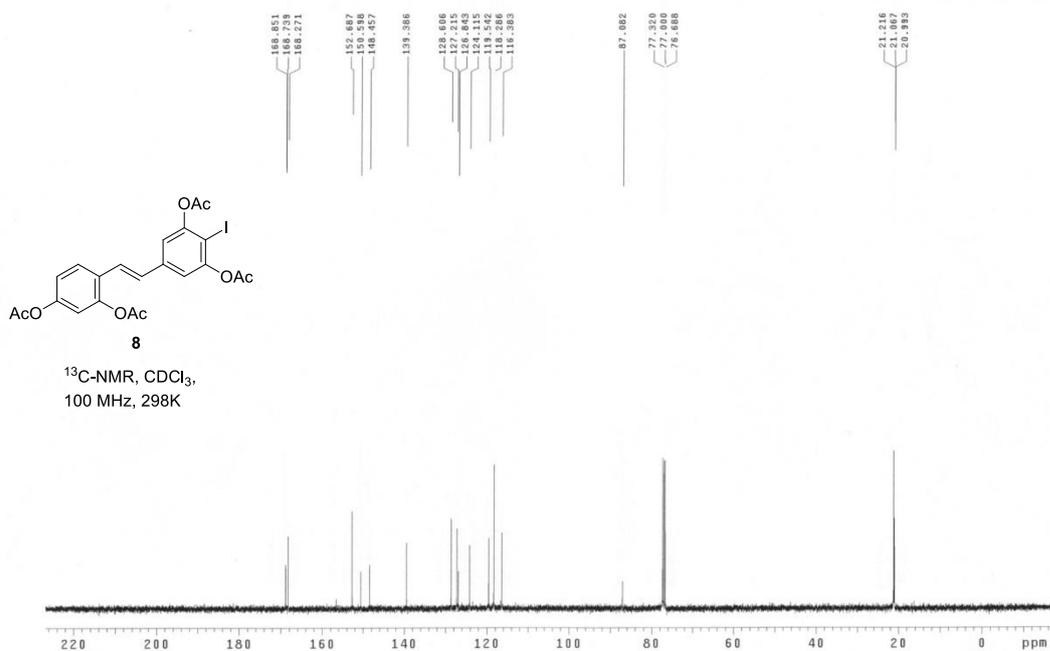
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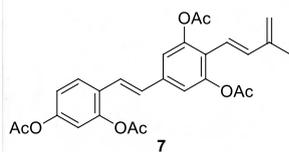
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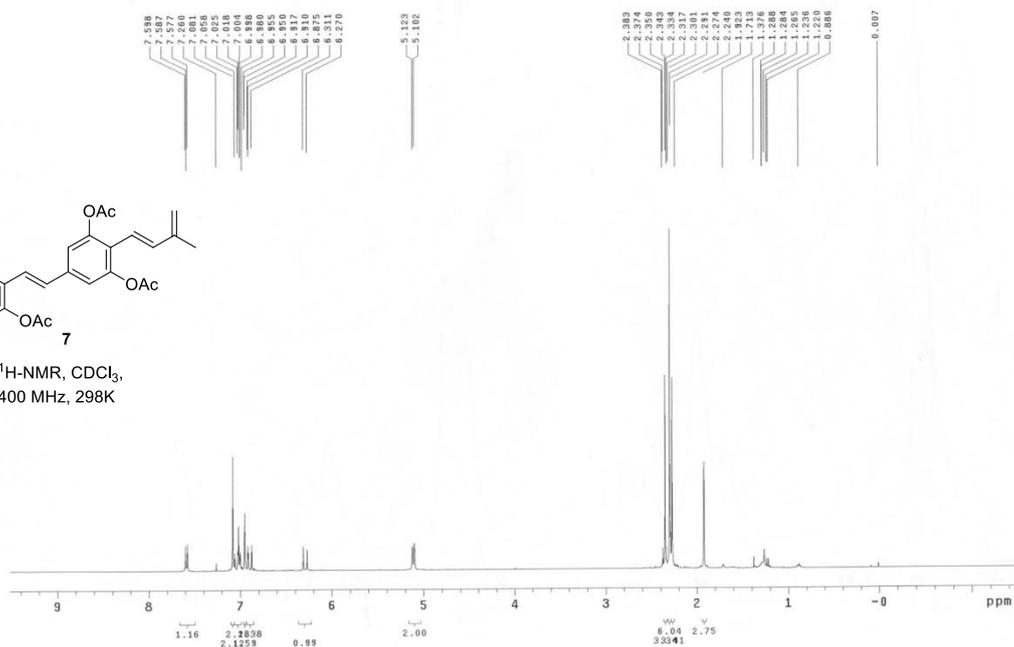
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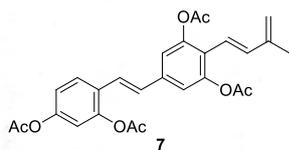
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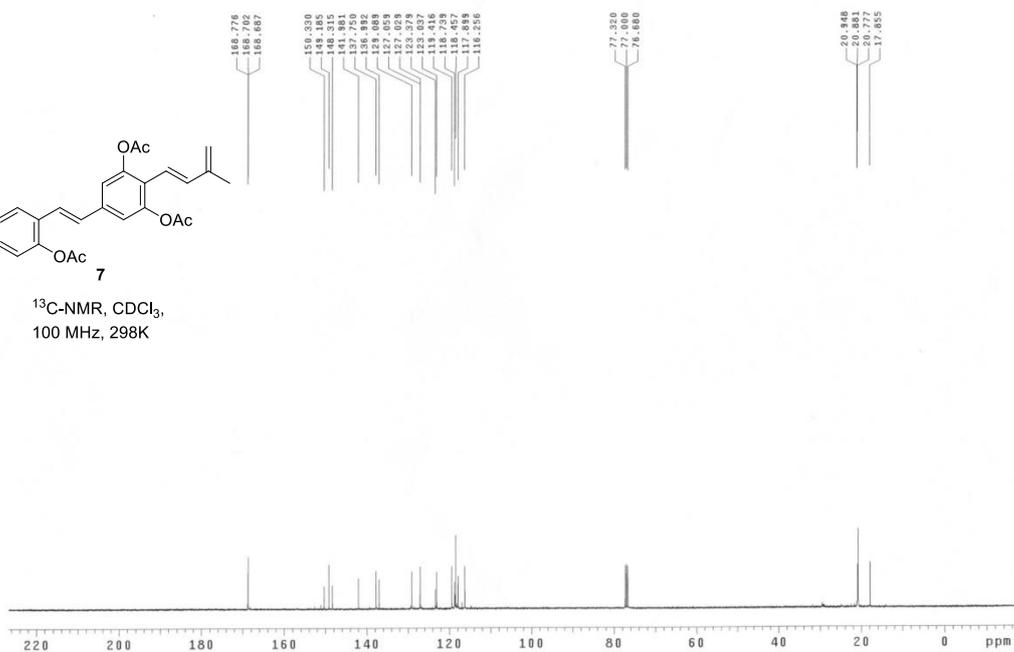
<sup>1</sup>H-NMR, CDCl<sub>3</sub>,  
400 MHz, 298K



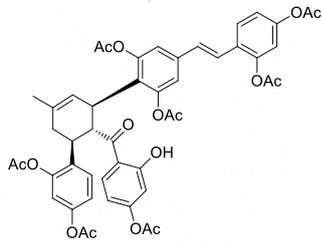
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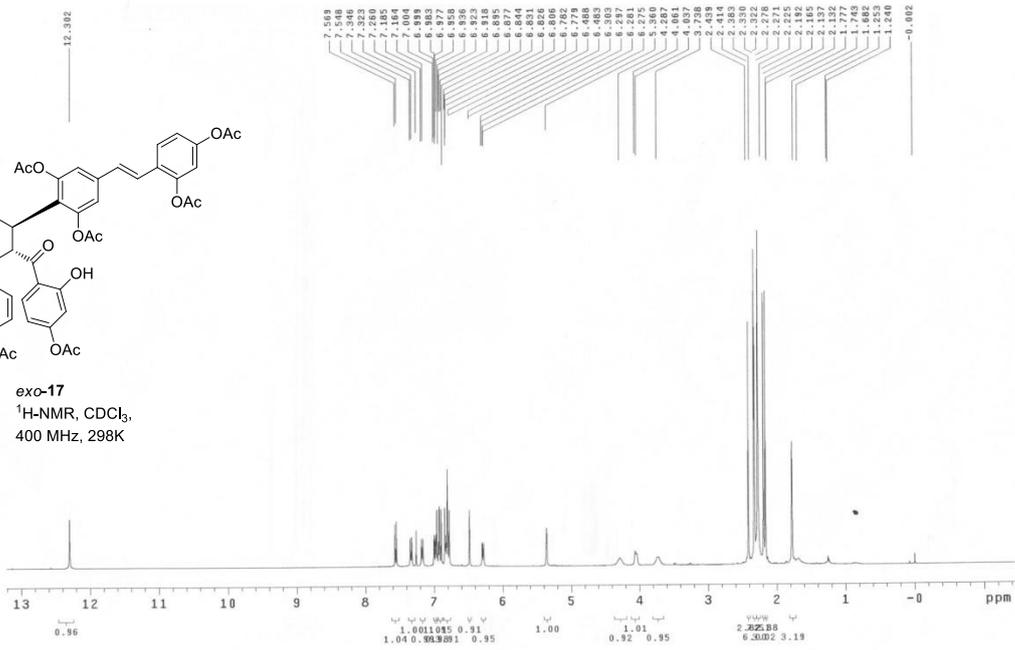
<sup>13</sup>C-NMR, CDCl<sub>3</sub>,  
100 MHz, 298K



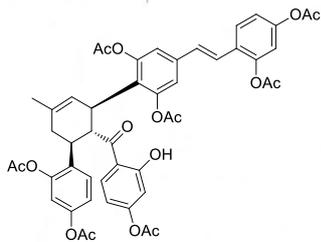
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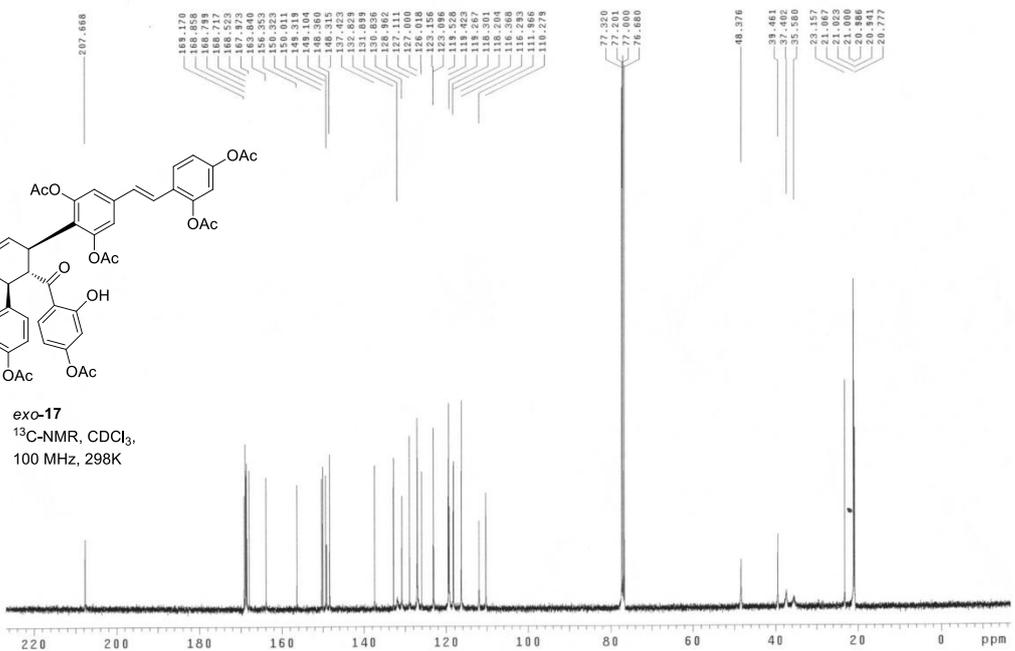
exo-17  
<sup>1</sup>H-NMR, CDCl<sub>3</sub>,  
 400 MHz, 298K

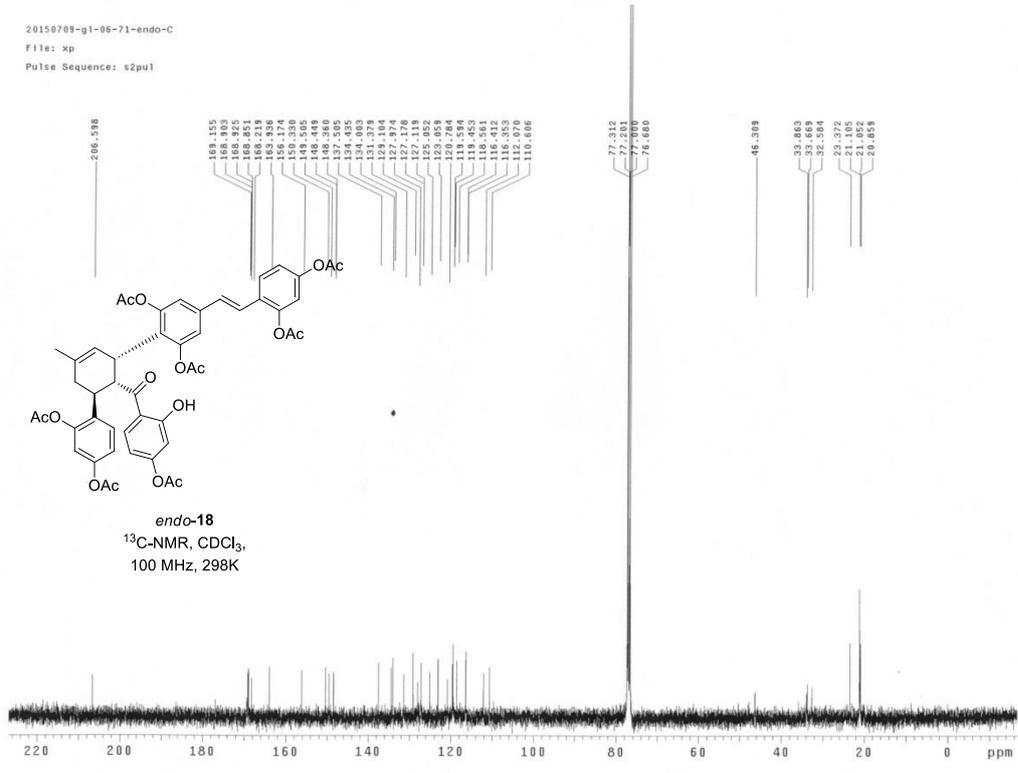
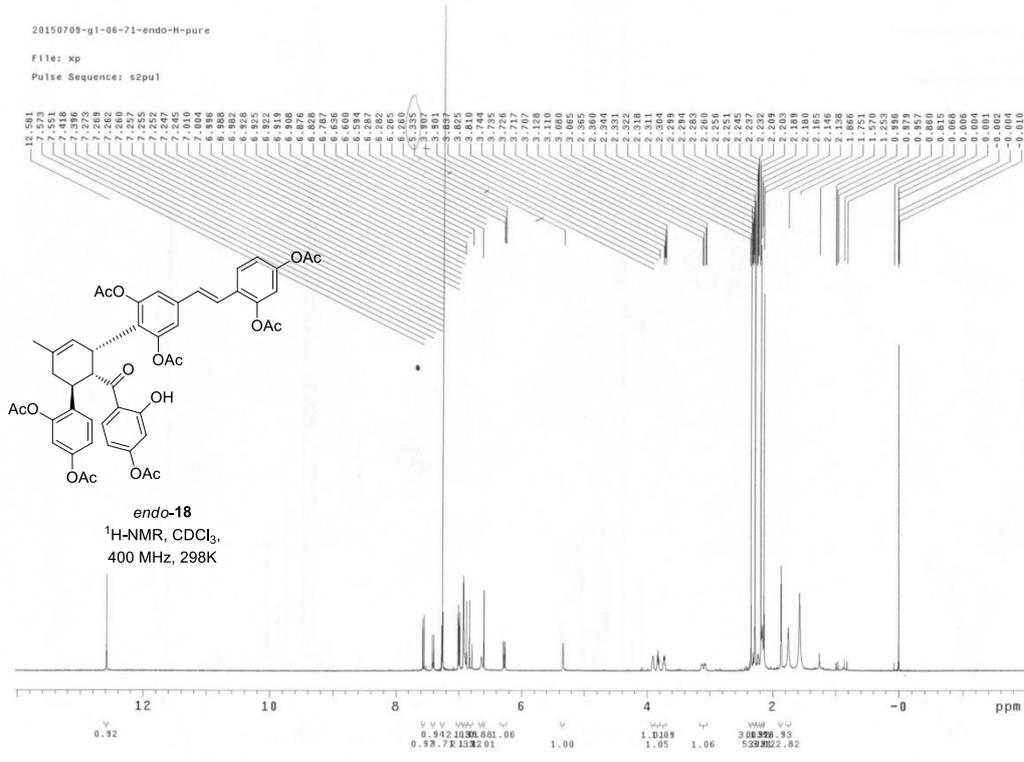


20150711-g1-06-71-exo-H-C-1  
 File: xp  
 Pulse Sequence: s2pu1

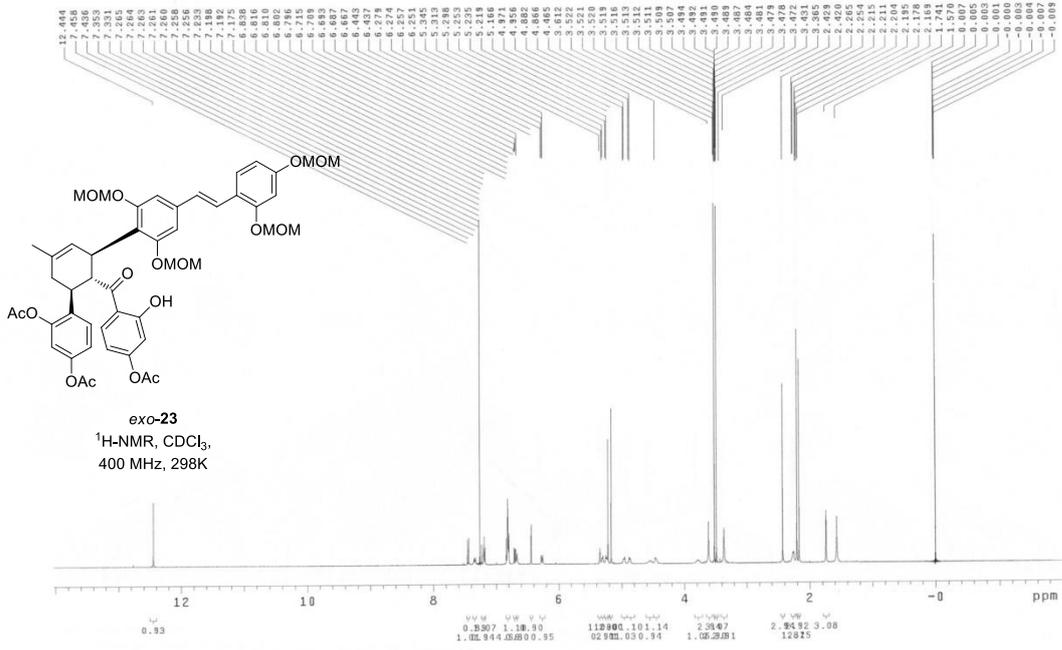


exo-17  
<sup>13</sup>C-NMR, CDCl<sub>3</sub>,  
 100 MHz, 298K

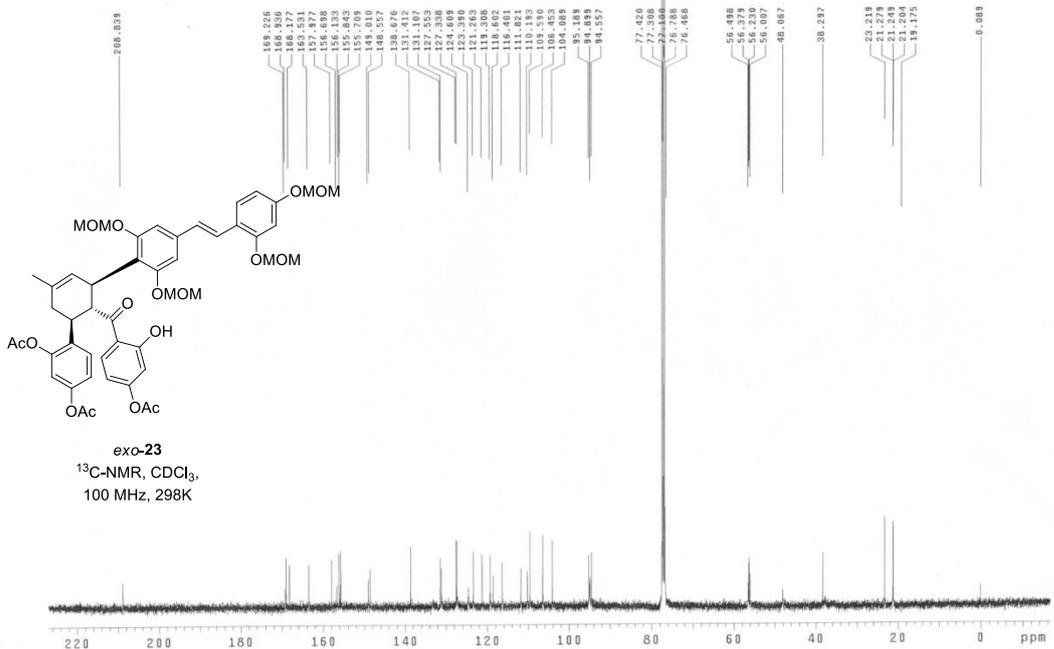




20150826-g1-07-28-exo-H  
 File: home/lab/vnmrsys/data/gaote1/g1-07-20150826-g1-07-28-exo-H.fid  
 Pulse Sequence: s2pul



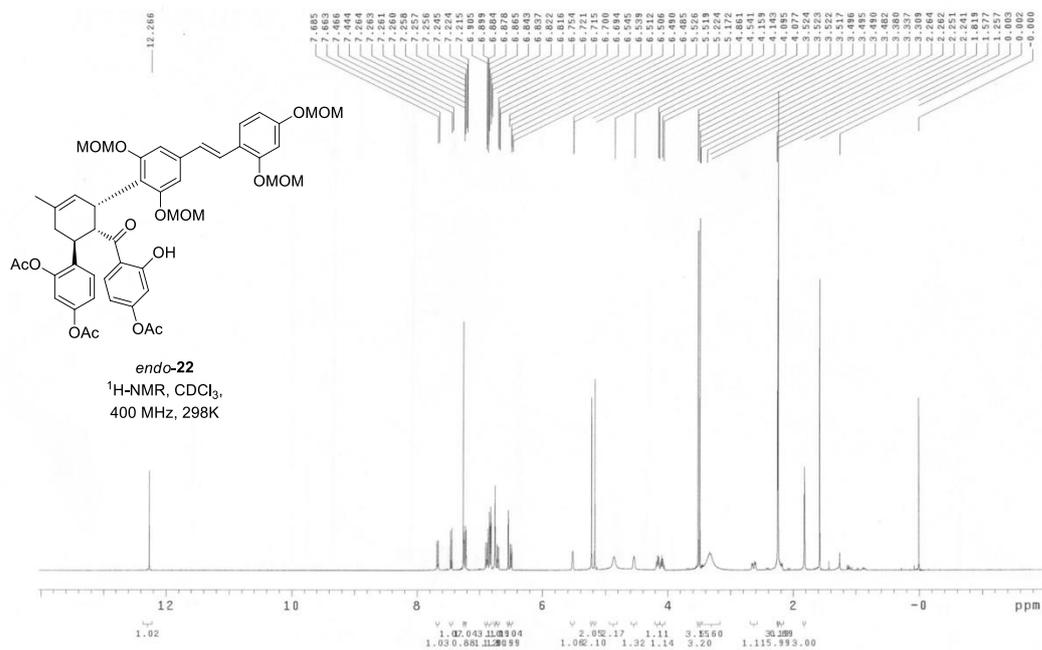
20150826-g1-07-28-exo-C  
 File: home/lab/vnmrsys/data/gaote1/g1-07-20150826-g1-07-28-exo-C.fid  
 Pulse Sequence: s2pul



20150828-g1-07-28-endo-1

File: home/lab/vnmrsvs/data/gaolet/g1-07/20150824-g1-07-28-endo-1.fid

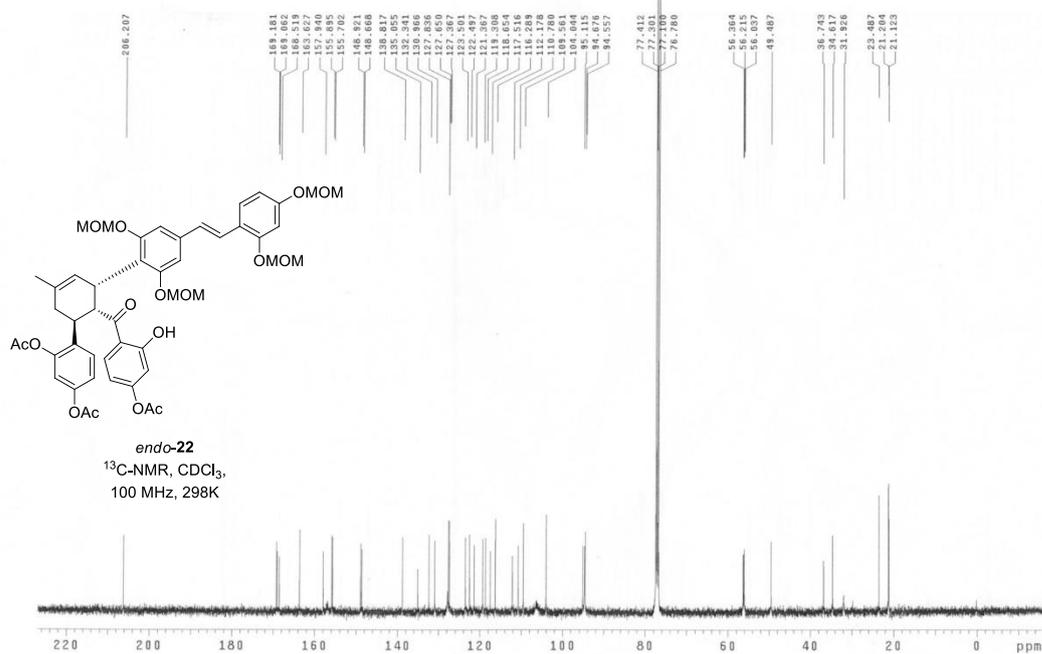
Pulse Sequence: s2pu1



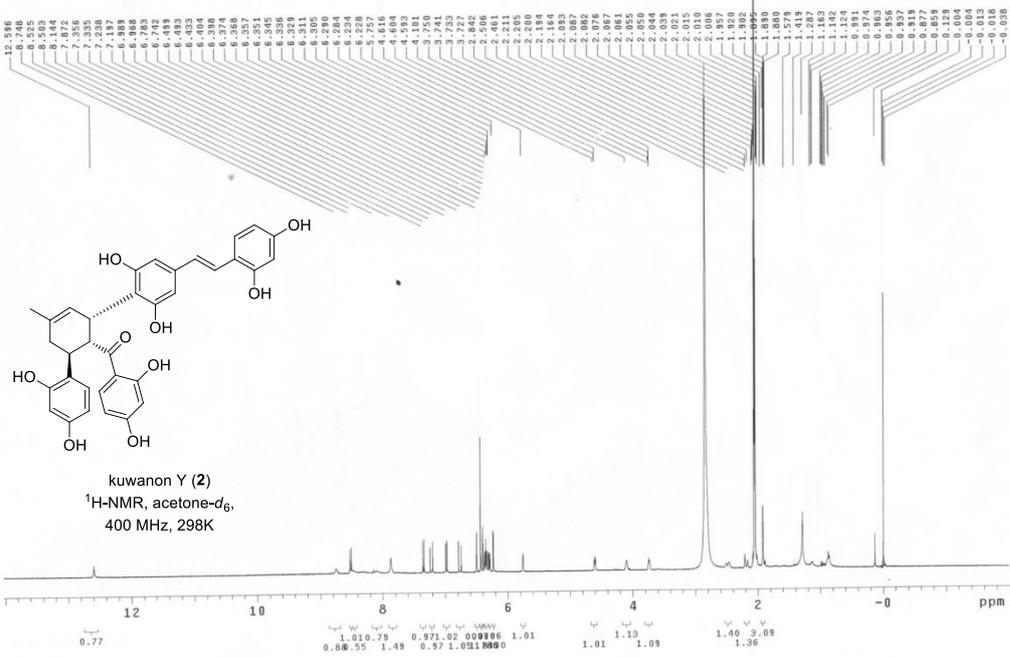
20150825-g1-07-28-endo-C-4

File: home/lab/vnmrsvs/data/gaolet/20150825-g1-07-28-endo-C-4.fid

Pulse Sequence: s2pu1



20150705-g1-06-80-kuwanonY-H  
File: xp  
Pulse Sequence: s2pu1



20150711-g1-06-78-kuwanonY-C  
File: home/lab/vnmrsys/data/gaolei/g1-06/20150711-g1-kuwanonY-C.fid  
Pulse Sequence: s2pu1

