Total Synthesis of (-)-Blepharocalyxin D and Analogues

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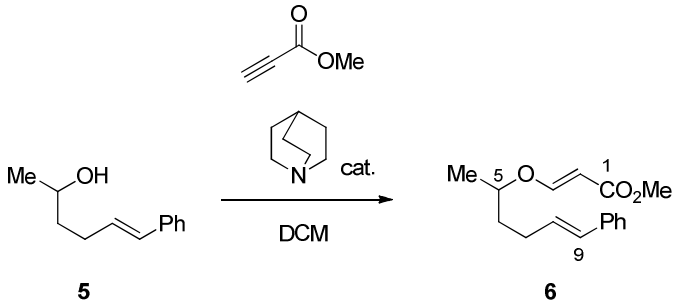
General Experimental

All commercially available compounds were used without further purification. Anhydrous solvents were obtained by passing through a modified Grubbs system of alumina columns, manufactured by Anhydrous Engineering. Routine monitoring of reactions was performed using precoated Merck-Keiselgel 60 F_{254} aluminium backed TLC plates. The spots were visualised by UV_{254} light and/or dipping the plates in potassium permanganate, phosphomolybdic acid or vanillin solutions followed by heating. All air or moisture sensitive reactions were carried out in flame-dried glassware under a positive pressure of nitrogen using standard syringe/septa techniques. Flash column chromatography[1] was performed using silica gel (obtained from Fluorochem Ltd. or Sigma-Aldrich) as the adsorbent. Petroleum ether is of the 40-60 °C boiling point range.

Melting points were determined on an electrothermal apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer in the solid or liquid state. ^{1}H and ^{13}C-NMR spectra were recorded using either Jeol ECP 400 (^{1}H: 400 MHz; ^{13}C: 101 MHz); a Jeol Lambda 300 (^{1}H: 300 MHz; ^{13}C: 76 MHz); a Varian 400 (^{1}H: 400 MHz; ^{13}C: 101 MHz). ^{1}H and ^{13}C NMR spectra were referenced to the residual *protio* solvent. All chemical shifts (δ) are reported in ppm and coupling constants (*J*) are in Hertz (Hz) and are reported to the nearest half integer. DEPT 135, COSY and HSQC NMR spectra were routinely used to definitively assign the signals of ^{1}H and ^{13}C-NMR spectra. Chemical ionisation (CI) mass spectra were recorded on a VG Autospec mass spectrometer. Electrospray (ESI) mass spectra were recorded on a VG Quattro mass spectrometer. Methane was the ionisation gas used for chemical ionisation.

Experimental Procedures

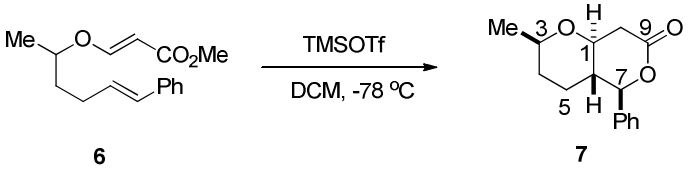
Methyl (2*E*, 8*E*)-5-methyl-9-phenyl-4-oxanona-2,8-dienoate 6



5 **6**

Methyl propiolate (0.23 mL, 2.59 mmol, 1.2 eq.) in dry DCM (20 mL) was added dropwise over a period of 3 h to a solution of alcohol **5** (380 mg, 2.16 mmol, 1.0 eq.) and quinuclidine (9 mg, cat.) in dry DCM (15 mL) at room temperature under nitrogen. Upon complete addition the reaction was stirred for 5 h before addition of a 5% v/v aqueous solution of acetic acid (5 mL). The solution was stirred vigorously for 0.5 h and the layers were separated. The aqueous phase was extracted with DCM (2 x 25 mL). The combined organic phases were washed with a saturated aqueous solution of $NaHCO_3$ (30 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Purification by flash column chromatography eluting with 5% EtOAc in petrol gave *enol-ether* **6** (330 mg, 59%); ν_{max} (neat)/cm^{-1} 2980, 2949, 1737, 1241, 1211, 1132, 1046, 750; δ_H (400 MHz, $CDCl_3$) 1.31 (3H, d, *J* 6.5, CH_3), 1.70 (1H, dddd, *J* 14.0, 9.0, 7.0, 5.0, 6-*H*H), 1.86 (1H, m, 6-H*H*), 2.22-2.36 (2H, m, 7-H_2), 3.71 (3H, s, OCH_3), 4.12 (1H, m, 5-H), 5.27 (1H, d, *J* 12.5, 2-H), 6.18 (1H, dt, *J* 15.5 and 7.0, 8-H), 6.41 (1H, br d, *J* 15.5, 9-H), 7.19-7.24 (1H, m, Ar-H), 7.28-7.36 (4H, m, Ar-H), 7.56 (1H, d, *J* 12.5, 3-H); δ_C (100 MHz, $CDCl_3$) 20.0 (CH_3), 28.7 (C-7), 35.8 (C-6), 51.0 (OCH_3), 79.0 (C-5), 96.9 (C-2), 126.0 (2 x C-Ar), 127.1 (C-Ar), 128.5 (2 x C-Ar), 129.1 (C-8), 130.8 (C-9), 137.4 (C-Ar), 162.1 (C-3), 168.5 (C-1); Found (CI) 261.1495 $[MH]^+$ ($C_{16}H_{21}O_3$ requires 261.490)

(±)-(1*α*, 6*β*)-3*β* -Methyl-7*β* -phenyl-2,8-dioxabicyclo[4.4.0]decan-9-one 7

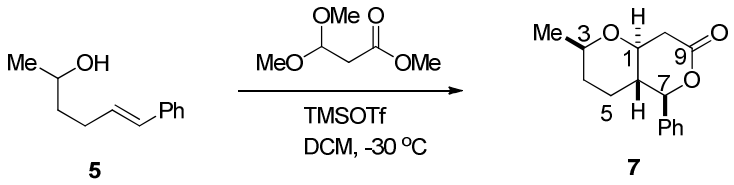


6 **7**

Method 1

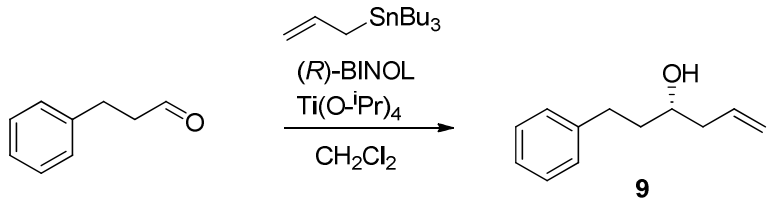
TMSOTf (0.42 mL, 2.30 mmol, 2.0 eq.) was added dropwise to a stirred solution of enol-ether **6** (300 mg, 1.15 mmol, 1.0 eq.) in dry DCM (20 mL) at -78 ^{o}C under argon. After 1.5 h the reaction was quenched with saturated aqueous $NaHCO_3$ (20 mL) and the layers were separated. The aqueous phase was extracted with DCM (3 x 30 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. Recrystallisation from EtOAc gave *lactone* **7** (195 mg, 69%) as a colorless crystalline solid; M.p. 160-162 ^{o}C; ν_{max} (neat)/cm^{-1} 2977, 2941, 2919, 2882, 1730, 1084; δ_H (500 MHz, $CDCl_3$) 1.21 (3H, d, *J* 6.5, CH_3), 1.23-1.28 (2H, m, 4-*H*H and 5-*H*H), 1.44 (1H, m, 4-H*H* or 5-H*H*), 1.65-1.72 (2H, m, 4-H*H* or 5-H*H* and 6-H), 2.66 (1H, dd, *J* 18.0 and 11.0, 10-H_{ax}), 3.11 (1H, dd, *J* 18.0 and 6.0, 10-H_{eq}), 3.55 (1H, m, 3-H), 3.65 (1H, ddd, *J* 11.0, 10.0 and 6.0, 1-H), 4.82 (1H, d, *J* 10.5, 7-H), 7.28-7.30 (2H, m, Ar-H), 7.36-7.41 (3H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 21.6 (CH_3), 25.3 and 32.4 (C-4 and C-5), 37.5 (C-10), 43.5 (C-6), 73.7 and 74.1 (C-1 and C-3), 84.5 (C-7), 127.1 (2 x C-Ar), 128.6 (2 x C-Ar), 128.9 (C-Ar), 136.9 (C-Ar), 169.4 (C-9); Found (CI) 247.1379 $[MH]^+$ ($C_{15}H_{19}O_3$) requires 247.1334; Elemental Analysis Calc. (%) for $C_{15}H_{18}O_3$: C 73.15, H 7.37, Found C 72.98, H 7.09.

Method 2



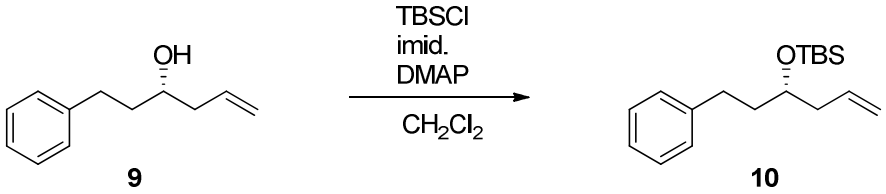
TMSOTf (0.39 mL, 2.19 mmol, 2.0 eq.) was added dropwise to a stirred solution of alcohol **5** (193 mg, 1.1 mmol, 1.0 eq.) and methyl 3,3-dimethoxypropionate (0.46 mL, 3.29 mmol, 3 eq.) in dry DCM (15 mL) at -30 ^{o}C under nitrogen. After 1 h saturated aqueous $NaHCO_3$ (15 mL) was added and the phases were separated. The aqueous phase was extracted with DCM (2 x 15 mL) and the combined organic phases were dried over $MgSO_4$ and the solvent removed *in vacuo*. Purification by flash column chromatography eluting with 10-40% EtOAc in petrol gave lactone **7** (182 mg, 67%) as a colorless crystalline solid; spectroscopic data as above.

(*S*)-1-Phenylhex-5-en-3-ol 9



Titanium isopropoxide (1.1 ml, 1.08 g, 3.80 mmol) was added dropwise to a suspension of (*R*)-1,1'-bi-2-naphthol (1.09 g, 3.80 mmol) and 4Å molecular sieve powder in CH_2Cl_2 (75 ml) under N_2 turning the suspension bright red. The resulting suspension was refluxed for 1 h before cooling to room temperature. 3-Phenylpropanal (5 ml, 5.09 mg, 37.97 mmol) was added and stirred for 10 minutes. The reaction was cooled to -78 °C and allyltributyltin (12.8 ml, 13.83 mg, 41.77 mmol) was added slowly. After stirring for 10 minutes the reaction was placed in a -20 °C freezer under N_2 for 80 h. The mixture was warmed to room temperature and saturated aqueous sodium hydrogen carbonate (8 ml) was added and reaction was stirred for 1 hr. $MgSO_4$ was added and stirred for 10 minutes, then filtered and the resulting red solution was concentrated *in vacuo*. The crude material was purified by column chromatography using 5% ethyl acetate in petroleum ether 40-60 as the eluent to yield alcohol **9** as a yellow oil (5.53 g, 31.39 mmol, 83% yield). $[\alpha]_D^{22}$ -25.0 (*c*. 2.0 $CHCl_3$) lit $[\alpha]_D^{25}$ -30 (*c*. 2.0, $CHCl_3$) δ_H ($CHCl_3$, 400MHz) 1.61 – 1.67 (1H, br s, OH), 1.76 – 1.84 (2H, m, 4-H_2), 2.19 (1H, m, 2-H*H*), 2.34 (1H, m, 2-*H*H), 2.69 (1H, m, 1-H*H*), 2.82 (1H, m, 1-*H*H), 3.68 (1H, m, 3-H), 5.16 (2H, m, 6-H_2), 5.83 (1H, m, 5-H), 7.15 – 7.34 (5H, m, Ar). δ_c ($CHCl_3$, 100MHz) 32.2 (C-2), 38.5 (C-1), 42.2 (C-4), 70.0 (C-3), 118.5 (C-6), 126.0, 128.5, 128.6, 134.7 (C-5), 142.2 (*i*-Ar). Spectroscopic data in accordance with literature data.[1]

(*S*)- 3-*tert*-Butyldimethylsilyloxy-1-phenylhex-5-ene 10

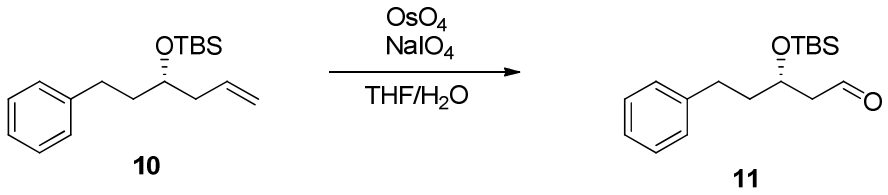


Alcohol **9** (1.28 g, 7.30 mmol) was dissolved in anhydrous CH_2Cl_2 (15 ml) and *tert*-butyldimethylsilylchloride (1.31 g, 8.75 mmol), imidazole (1.49 g, 21.86 mmol) and 4-DMAP (90 mg, 0.73 mmol) were added and stirred at room temperature for 16 h under N_2. Water (20 ml) was added and the mixture was extracted with CH_2Cl_2 (2 x 20 ml). The combined organic fractions were dried over $MgSO_4$ and concentrated *in vacuo* then purified by column chromatography using 1% ethyl acetate in petroleum ether 40-60 as the eluent to yield silyl ether **10** as a yellow oil (1.66 g, 5.72 mmol, 78% yield). $[\alpha]_D^{21}$ -9.0 (*c*. 1.0 $CHCl_3$) δ_H (400 MHz, $CDCl_3$) 0.06 (3H, s, CH_3Si), 0.07 (3H, s, CH_3Si), 0.92 (8H, s, $(CH_3)_3CSi$), 1.69 – 1.83 (2H, m, 2-H_2), 2.28 (2H, t, *J* 6, 4-H_2), 2.59 (1H, m, 1-*H*H), 2.72 (1H, m, 1-H*H*),

3.77 (1H, quin, *J* 6.0 3-H), 4.93 – 5.15 (2H, m, 6-H_2), 5.74 (1H, m, 5-H), 7.16 – 7.21 (3H, m), 7.24 – 7.31 (2H, m); δ_C ($CHCl_3$, 100MHz) -4.3 (CH_3CSi), -4.5 (CH_3CSi), 18.1 ($(CH_3)_3CSi$), 25.9 ($(CH_3)_3CSi$), 31.8 (C-1), 38.7 (C-2), 41.9 (C-4), 71.6 (C-3), 116.8 (C-6), 125.6, 128.3, 128.4, 135.1 (C-4), 142.6 (*i*-Ar).

Spectroscopic data in accordance with literature data.[2]

(*S*)- 3-*tert*-Butyldimethylsilyloxy-5-phenyl-pentanal 11

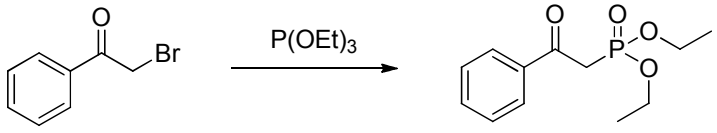


10 **11**

Silyl ether **174** (581 mg, 2 mmol) was dissolved in a THF/H_2O mixture (1:1, 40 ml) and sodium periodate (1.93 g, 9 mmol) and osmium tetroxide (1 crystal) were added and the reaction was stirred under N_2 for 3 hrs. Water (30 ml) was added and mixture was extracted with ethyl acetate (3 x 40 ml). The combined organic fractions were dried over $MgSO_4$ and concentrated *in vacuo*. The crude material was purified by column chromatography using 2% ethyl acetate in petroleum ether 40-60 as the eluent to yield aldehyde **173** as a yellow oil (475 mg, 1.62 mmol, 81% yield). $[\alpha]_D^{20}$ +5.0 (*c*. 1.0 $CHCl_3$) δ_H (400 MHz, $CDCl_3$) 0.06 (3 H, s, CH_3Si), 0.09 (3H, s, CH_3Si), 0.90 (9H, s, $(CH_3)_3CSi$), 1.82 – 1.94 (2H, m, 4-H_2), 2.57 – 2.61 (2H, m, 2-H_2), 2.62 – 2.73 (2H, m, 5-H_2), 4.26 (1H, p, *J* 6, 3-H), 7.15 – 7.24 (2H, m, Ar), 7.25 – 7.33 (3H, m, Ar), 9.82 (1H, dd, *J* 3, 2, 1-H);. δ_C ($CDCl_3$, 100MHz) -4.5 (CH_3CSi), 18.1 ($(CH_3)_3CSi$), 25.9 ($(CH_3)_3CSi$), 31.6 (C-5) 39.7 (C-2), 50.9 (C-4), 67.9 (C-3), 126.1 (*p*-Ar), 128.4, 128.6, 141.8 (*i*-Ar), 202.1 (C-1).

Spectroscopic data in accordance with literature data (racemic).[3]

Diethyl 2-oxo-2-phenylethylphosphonate 12



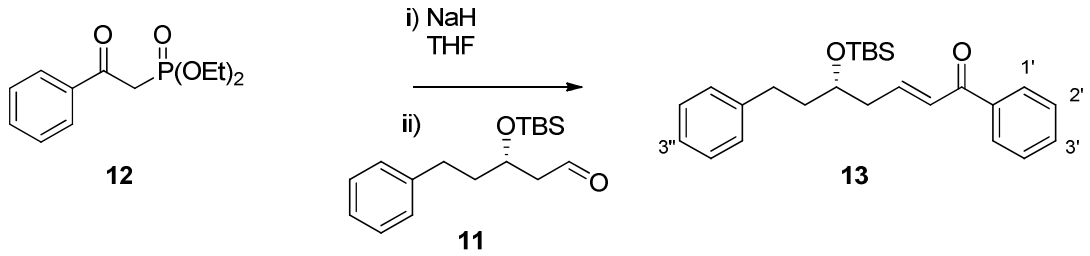
12

Bromoacetophenone (5 g, 25.12 mmol) and triethylphosphite (4.17 g, 25.12 mmol) were heated to 110 °C and refluxed for 24 h. The resulting crude black oil was purified by column chromatography using 80% ethyl acetate in petroleum ether 40-60 as the eluent to yield phosphonate **12** as a yellow oil (4.19 g, 16.34 mmol, 65% yield). δ_H (400 MHz, $CDCl_3$) 1.26 (6H, t, *J* 7, $P(OCH_2CH_3)$), 3.63 (2H, d, *J* 23, 1-H_2), 4.12

(4H, p, *J* 7, P(OC*H*$_2$CH$_3$)), 7.42 – 7.50 (2H, m, Ar), 7.57 (1H, m, *p*-Ar), 7.98 – 8.02 (2H, m, Ar);. δ_C (100 MHz, $CDCl_3$) 16.3 (d, *J* 6.5, P(OCH$_2$*C*H$_3$)), 38.6 (d, *J* 130.0, P(O*C*H$_2$CH$_3$)), 62.7 (d, *J* 6.5, C-1), 128.7, 129.1, 133.8 (*p*-Ar), 136.6 (d, *J* 2, *i*-Ar), 192.1 (d, *J* 6.5, C-2).

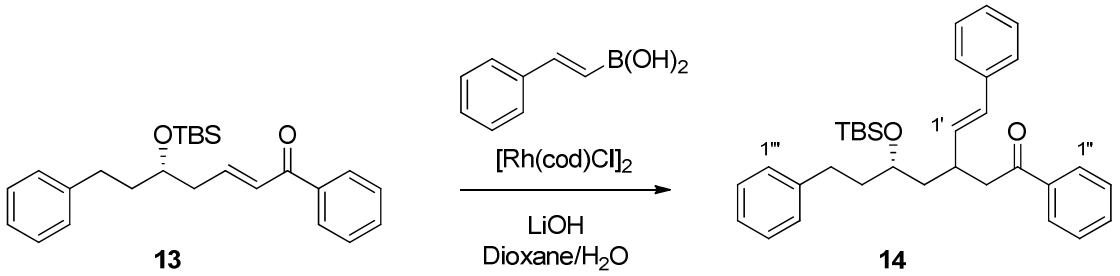
Spectroscopic data in accordance with literature data.[4]

(*5S, 2E)*-5-*tert*-Butyldimethylsilyloxy-1,7-diphenylhept-2-en-1-one 13



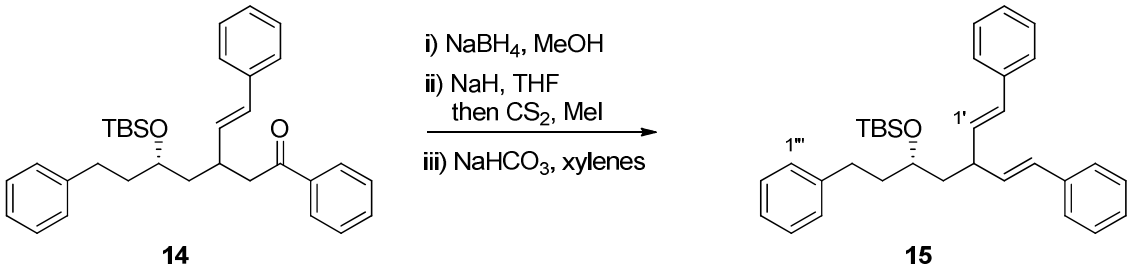
Sodium hydride (91 mg, 2.27 mmol) was suspended in anhydrous THF (10 ml) and cooled to 0 °C. Phosphonate **12** (500 mg, 1.95 mmol) in THF (4 ml) was added dropwise and stirred for 0.5 h until the suspension became a solution. Aldehyde **11** (475 mg, 1.62 mmol) in THF (9 ml) was added and the reaction was warmed to room temperature and stirred for 18 h. Water (30 ml) was added to quench the reaction and the mixture was extracted with ethyl acetate (3 x30 ml). The combined organic fractions were dried over $MgSO_4$ and concentrated *in vacuo*. The crude material was purified by column chromatography using 2% ethyl acetate in petroleum ether 40-60 as the eluent to yield *ketone* **13** as a yellow oil (361 mg, 0.92 mmol, 65% yield, $[\alpha]_D^{20}$ +3.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 2954, 2928, 2856, 1671, 1622, 1253, 1089, 986, 814, 774, 969; δ_H (400 MHz, $CDCl_3$) 0.05 (3H, s, CH_3Si), 0.08 (3H, s, CH_3Si), 0.91 (9H, s, $(CH_3)_3CSi$), 1.76 – 1.86 (2H, m, 6-H_2), 2.53 (2H, ddd, *J* 8, 6, 1.5, 4-H_2), 2.60 – 2.79 (2H, m, 7-H_2), 3.92 (1H, p, *J* 6, 5-H), 6.90 (1H, dt, *J* 15.5, 1.5, 2-H), 7.06 (1H, dt, *J* 15.5, 8, 3-H), 7.15 – 7.21 (2H, m, Ar), 7.22 – 7.33 (3H, m, Ar), 7.43 – 7.50 (2H, m, Ar, 2'-H), 7.54 (1H, m, 3'-H), 7.92 (2H, dd, *J* 8.4, 1.4, 1'-H); δ_C ($CDCl_3$, 100MHz) -4.4 (*C*H_3CSi), 18.1 ((CH$_3$)$_3$*C*Si), 25.8 ((*C*H$_3$)$_3$CSi), 31.7 (C-7), 39.2 (C-6), 40.8 (C-4), 70.9 (C-5), 125.8 (C-3''), 128.0 (C-2), 128.3, 128.4, 128.50, 128.51, 132.6 (C-3'), 137.9, 142.1, 146.1 (C-3), 190.5 (C-1); HRMS (CI) calc for $C_{25}H_{34}O_2Si$ [M+H] 395.2406 found 395.2397

(*5S, 1'E*)-5-*tert*-Butyldimethylsilyloxy-1,7-diphenyl-3-(phenylethenyl)-heptan-1-one 14



Ketone **13** (345 mg, 0.87 mmol) was dissolved in a 10:1 mixture of 1,4-dioxane and water (5.5 ml) and phenylvinylboronic acid (259 mg, 1.75 mmol), $[Rh(cod)Cl]_2$ (21 mg, 0.04 mmol) and lithium hydroxide (21 mg, 0.87 mmol) were added and stirred for 16 h at room temperature. Et_2O (20 ml) and water (20 ml) were added and stirred for 5 minutes. The phases were separated and the aqueous phase was extracted with Et_2O (2 x 20 ml). The combined organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. The crude material was purified by column chromatography using 2% ethyl acetate in petroleum ether 40-60 as the eluent to yield *ketone* **14** as a yellow oil (407 mg, 0.82 mmol, 94% yield) as a mixture of diastereomers. ν_{max}/cm^{-1} 2928, 1685, 1448, 1253, 1060, 966, 834, 773, 767; δ_H (400 MHz, $CDCl_3$) 0.00 – 0.13 (6H, m, CH_3Si), 0.90 & 0.93 (9H, s, $((CH_3)_3CSi)$, 1.67 – 2.01 (4H, m, 4-H_2 & 6-H_2), 2.89 – 2.56 (2H, m, 7-H_2), 3.22 – 3.00 (3H, m, 2-H_2 & 3-H), 3.82 (1H, m, 5-H), 6.09 (1H, m, 1'-H), 6.39 (1H, m, 2'-H), 7.11 – 7.26 (2H, m, Ar), 7.29 – 7.34 (4H, m, Ar), 7.48 (2H, m, Ar), 7.58 (1H, m, Ar), 7.96 (2H, dd, *J* 8.0, 1.5, Ar); δ_C (100 MHz, $CDCl_3$) -4.3 (CH_3Si), -4.2 (CH_3Si), -4.1 (CH_3Si), -3.9 (CH_3CSi), 18.2 ($(CH_3)_3CSi$), 18.2 ($(CH_3)_3CSi$), 26.1 ($(CH_3)_3CSi$), 26.1 ($(CH_3)_3CSi$), 31.2 (C-7), 31.4 (C-7), 35.9, 36.2, 38.2, 40.0, 42.4, 42.46, 44.8, 45.5, 69.9 (C-5), 70.0 (C-5), 125.7, 125.8, 126.3, 127.3, 128.2, 128.3, 128.46, 128.47, 128.48, 128.55, 128.59, 128.60, 128.7, 130.6, 130.9, 133.0, 133.1, 133.15, 133.4, 137.4, 137.5, 142.5, 142.8, 198.9 (C-1), 199.2 (C-1); HRMS (ESI) calc for $C_{33}H_{42}O_2SiNa$ [M+Na] 521.2846 found 521.2836.

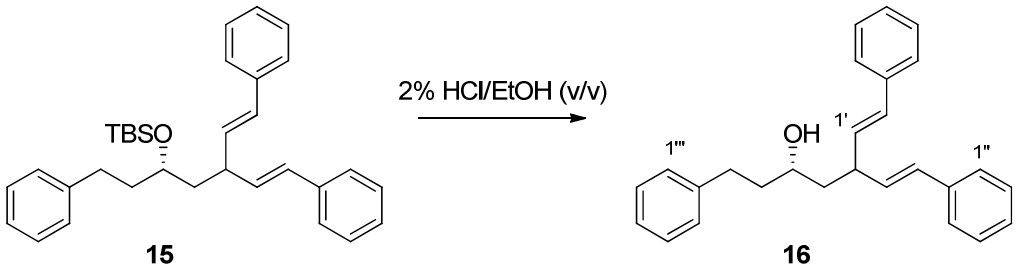
(*3S, 6E, 1'E*)-3-*tert*-Butyldimethylsilyloxy-1,7-diphenyl-5-(phenylethenyl)-hept-6-ene 15



Ketone **14** (200 mg, 0.4 mmol) was dissolved in methanol (10 ml) and sodium borohydride (32 mg, 0.8 mmol) was added and the reaction was stirred for 0.5 h. Saturated ammonium chloride solution (10 ml) was added and the mixture was extracted with ethyl acetate (3 x 10 ml). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. The resulting crude oil was dissolved in anhydrous

THF (10 ml) under N_2. Sodium hydride (48 mg, 1.2 mmol, 60% in mineral oil) was added and the reaction was stirred for 0.5 h before carbon disulfide (168 µl, 213 mg, 2.8 mmol) and iodomethane (103 µl, 227 mg, 1.6 mmol) were added and the reaction was stirred for 70 h. Water (20 ml) was added and the mixture was extracted with ethyl acetate (3 x 20 ml). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* and then purified by column chromatography using 2% ethyl acetate in petroleum ether as the eluent to yield xanthate (168 mg, 0.28 mmol) as a colorless oil. The xanthate was dissolved in xylene (5 ml), sodium hydrogen carbonate (119 mg, 1.42 mmol) was added and the mixture was heated to reflux for 6 hrs. The solvent was removed *in vacuo*, CH_2Cl_2 (5ml) was added and filtered and the filtrate was concentrated *in vacuo* to give *silyl ether* **15** as a pale yellow oil (131 mg, 0.27 mmol, 68% yield over three steps). $[\alpha]_D^{22}$ -41.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 3060, 3025, 2927, 2855, 1448, 1253, 1071, 966; δ_H (400 MHz, $CDCl_3$) 0.05 (3H, s, CH_3Si), 0.07 (3H, s, CH_3Si), 0.94 (9H, s, $((CH_3)_3CSi)$), 1.70 – 1.95 (4H, m, 2-H_2 & 4-H_2), 2.67 (2H, m, 7-H), 3.21 (1H, p, *J* 7.5, 5-H), 3.84 (1H, dq, *J* 7, 5, 3-H), 6.13 (1H, dd, *J* 16.0, 7.5, 6-H), 6.19 (1H, dd, *J* 16.0, 7.5, 1'-H), 6.38 (1H, d, *J* 16.0, 7-H), 6.43 (1H, d, *J* 16.0, 2'-H), 7.39 – 7.11 (15H, m, Ar); δ_C (100 MHz, $CDCl_3$) -4.2 (CH_3Si), -4.0 (CH_3Si), 18.1 ($(CH_3)_3CSi$), 26.0 ($(CH_3)_3CSi$), 31.2 (C-1), 39.2 (C-2), 42.4 (C-4), 42.7 (C-5), 69.7 (C-3), 125.7, 126.1, 127.1, 127.2, 128.3, 128.5, 129.6 (C-7), 130.2 (C-2'), 132.7 (C-6), 133.1 (C-1'), 137.4, 137.5, 142.5; HRMS (ESI) calc for $C_{33}H_{42}OSiNa$ [M+Na] 505.2897 found 505.2883.

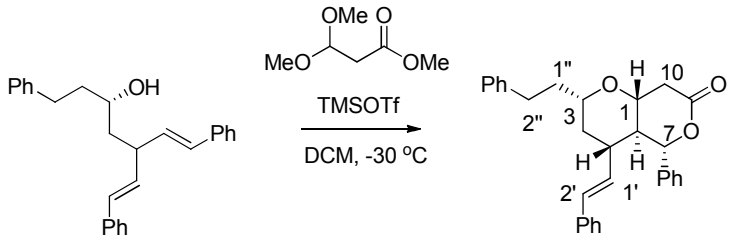
(*5S, 6E, 1'E*)- 1,7-Diphenyl-5-(phenylethenyl)hept-6-en-3-ol 16



Silyl ether **15** (121 mg, 0.25 mmol) was dissolved in 2% HCl/EtOH (v/v) (5 ml) and stirred for 5 h. The reaction mixture was poured into ethyl acetate (20 ml) and water (20 ml), the phases were separated and the aqueous phase was extracted with ethyl acetate (2 x 20 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo*, and purified by column chromatography using 20% ethyl acetate in petroleum ether 40-60 as the eluent to yield *alcohol* **16** as a yellow oil (83 mg, 0.225 mmol, 90% yield). $[\alpha]_D^{21}$ -8.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 3356, 3081, 3059, 2919, 2851, 1494, 1448, 964, 744, 692; δ_H (400 MHz, $CDCl_3$) 1.64 (1H, br s, OH), 1.75 – 1.98 (4H, m, 2-H_2 & 4-H_2), 2.68 (1H, m, 1-*H*H), 2.84 (1H, m, 1-H*H*), 3.37 (1H, p, *J* 8, 5-H), 3.82 (1H, m, 3-H), 6.19 (1H, dd, *J* 16, 8, 6-H), 6.28 (1H, dd, *J* 16, 8, 1'-H), 6.49 (1H, d, *J* 16, 7-H), 6.53 (1H, d, *J* 16, 2'-H), 7.10 – 7.57 (15H, m, Ar); δ_C (100 MHz, $CDCl_3$) 32.3 (C-

1), 39.7 (C-2), 42.9 (C-4), 43.6 (C-5), 69.6 (C-3), 126.0, 126.30, 126.33, 127.39, 127.43, 128.53, 128.57, 128.68, 128.69, 129.9 (C-7), 130.7 (C-2'), 132.2 (C-6), 133.1 (C-1'), 137.4, 137.5, 142.2; HRMS (ESI) calc for $C_{27}H_{28}ONa$ [M+Na] 391.2032 found 391.2049.

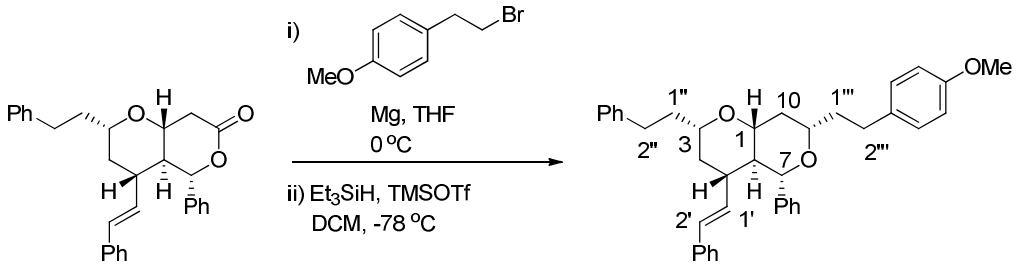
(-)-(1*R*, 3*S*, 5*S*, 6*S*, 7*S*)-3-Phenylethyl-7-phenyl-5((*E*)-phenethenyl)-2,8-dioxabicyclo[4.4.0]decan-9-one 17



16 **17**

TMSOTf (82 µL, 0.45 mmol, 2.0 eq.) was added dropwise to a stirred solution of alcohol **16** (83 mg, 0.23 mmol, 1.0 eq.) and methyl 3,3-dimethoxypropionate (0.13 mL, 0.90 mmol, 4.0 eq.) in dry DCM (15 mL) at -30 ^{o}C under argon. After 1 h saturated aqueous $NaHCO_3$ was added (15 mL) and the layers were separated. The aqueous phase was extracted with DCM (2 x 15 mL) and the combined organic phases were dried over $MgSO_4$ and the solvent removed *in vacuo*. Purification by flash column chromatography eluting with 10-30% EtOAc in petrol gave *lactone* **17** (45 mg, 45%) as a yellow oil; $[\propto]_D^{20}$ -61.8 (*c* 2.2 $CHCl_3$); ν_{max} (neat)/cm^{-1} 3024, 2918, 2854, 1736, 1495, 1455, 1344, 1237, 752; δ_H (400 MHz, $CDCl_3$) 1.38 (1H, dt, *J* 13.5, 11.5, 4-H_{ax}), 1.64 (1H, ddd, *J* 13.5, 4.0, 2.0, 4-H_{eq}), 1.76 (1H, m, 1'-*H*H), 1.88 (1H, m, 1"-H*H*), 1.97 (1H, q, *J* 10.5, 6-H), 2.34 (1H, m, 5-H), 2.68-2.83 (2H, m, 2"-H_2), 2.74 (1H, dd, *J* 18.0, 12.0, 10-H_{ax}), 3.14 (1H, dd, *J* 18.0, 5.0, 10-H_{eq}), 3.50 (1H, m, 3-H), 3.70 (1H, ddd, *J* 12.0, 10.5, 5.0, 1-H), 4.97 (1H, d, *J* 10.5, 7-H), 5.16 (1H, dd, *J* 16.0, 9.0, 1'-H), 5.97 (1H, d, *J* 16.0, 2'-H), 6.74 (2H, m, Ar-H), 7.09 (1H, m, Ar-H), 7.11-7.14 (3H, m, Ar-H), 7.18-7.25 (7H, m, Ar-H), 7.31 (2H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 31.4 (C-2"), 37.2, 37.4 (C-10 and C-1"), 39.1 (C-4), 42.4 (C-5), 47.8 (C-6), 73.4 (C-1), 75.5 (C-3), 85.3 (C-7), 125.8 (C-Ar), 125.9 (C-Ar), 127.0 (C-Ar), 128.0 (C-Ar), 128.39 (C-Ar), 128.43 (C-Ar), 128.5 (C-Ar), 128.9 (C-Ar), 129.4 (C-2'), 132.1 (C-1'), 136.7 (C-Ar), 137.9 (C-Ar), 141.7 (C-Ar), 168.9 (C-9); Found (ESI) 461.2101 $[MNa]^+$ ($C_{30}H_{30}O_3Na$ requires 461.2087).

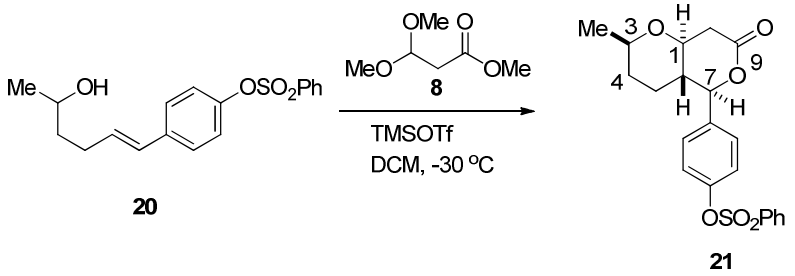
(-)-(1*R*, 3*S*, 5*S*, 6*S*, 7*S*, 9*S*)-9-(4-Methoxyphenyl)-3-phenylethyl-7-phenyl-5((*E*)-phenethenyl)-2,8-dioxabicyclo[4.4.0]decane 240



17 **18**

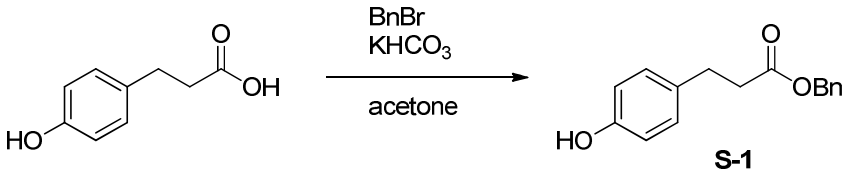
Methoxyphenethyl bromide (1 ml, 1376 mg, 6.40 mmol) was added to a solution of vacuum dried magnesium (171 mg, 7.04) in tetrahydrofuran (6.4 ml). A single crystal of iodine was added and the reaction mixture was warmed to initial reaction. On cooling to room temperature the magnesium was seen to be consumed. 1 ml of the resulting solution was added slowly to a solution of lactone **17** (43 mg, 0.09 mmol, 1.0 eq.) in dry Et_2O (5 ml) under argon at 0 ^oC. After 3 h saturated aqueous NH_4Cl was added (10 ml) and the phases separated. The aqueous phase was extracted with Et_2O (3 x 15 ml) and the combined organic phases washed with brine (25 ml) and dried over $MgSO_4$. The solvent was removed *in vacuo* and purification by flash column chromatography eluting with 5-20% EtOAc in petrol gave the lactol intermediate (36 mg, 70%) which was used in the next step directly. TMSOTf (17 µl, 0.094 mmol, 1.5 eq.) was added dropwise to a solution of the lactol (36 mg, 0.063 mmol, 1.0 eq.) and triethylsilane (0.1 ml, 0.63 mmol, 10.0 eq.) in dry DCM (5 ml) under argon at -78 ^oC. After 0.75 h a saturated aqueous solution of $NaHCO_3$ (15 ml) was added and the phases separated. The aqueous phase was extracted with DCM (2 x 20 ml) and the combined organic phases dried over $MgSO_4$. The solvent was removed *in vacuo* and purification by flash column chromatography eluting with 2-10% EtOAc in petrol gave *bicycle* **18** (24 mg, 68%) as a white crystalline solid; M.p. 133-135 ^oC; $[\propto]_D^{20}$ -100.0 (*c* 1.2 $CHCl_3$); ν_{max} (neat)/cm^{-1} 3024, 2941, 2893, 2850, 1609, 1513, 1247, 1067, 1030, 742, 688; δ_H (400 MHz, $CDCl_3$) 1.32 (1H, m, 4-*H*H), 1.56 (1H, m, 4-H*H*), 1.66-2.00 (6H, m, 6-H, 10-H_{ax}, 1"-H_2 and 1"'-H_2), 2.08 (1H, ddd, *J* 12.5, 4.5, 2.0, 10-H_{eq}), 2.22 (1H, m, 5-H), 2.66 (1H, t, *J* 8.0, 2"-H_2 or 2"'-H_2), 2.69 (2H, m, 2"-H_2 or 2"'-H_2), 3.38 (1H, ddd, *J* 11.5, 9.5, 4.5, 1-H), 3.47 (1H, m, 3-H), 3.55 (1H, m, 9-H), 3.80 (3H, s, OCH_3), 4.02 (1H, d, *J* 10.0, 7-H), 5.15 (1H, dd, *J* 15.5, 9.0, 1'-H), 5.82 (1H, d, *J* 15.5, 2'-H), 6.73 (2H, m, Ar-H), 6.83 (2H, d, *J* 9.0, Ar-H), 6.99 (1H, m, Ar-H), 7.08-7.23 (11H, m, Ar-H), 7.29-7.32 (3H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 30.4, 31.6 (C-2" and C-2"'), 37.6, 37.7 (C-1" and C-1"'), 38.1 (C-10), 40.3 (C-4), 41.9 (C-5), 50.6 (C-6), 55.2 (OCH_3), 75.0, 75.7 (C-3 and C-9), 79.1 (C-1), 83.4 (C-7), 113.7 (C-Ar), 125.7 (C-Ar), 125.8 (C-Ar), 126.5 (C-Ar), 127.8 (C-Ar), 127.89 (C-Ar), 127.94 (C-Ar), 128.2, 128.3 (C-2' and C-Ar), 128.5 (C-Ar), 129.4 (C-Ar), 134.13, 134.14 (C-1' and C-Ar), 137.4 (C-Ar), 140.9 (C-Ar), 142.1 (C-Ar), 157.6 (C-Ar); Found (ESI) 581.3033 $[MNa]^+$ ($C_{39}H_{42}O_3Na$ requires 581.3026). Elemental Analysis Calc. (%) for $C_{39}H_{42}O_3$: C 83.83, H 7.58, Found 83.34, H 7.47.

(±)-(1*α*, 6*β*)-3*β* -Methyl-7*β* -(4-benzenesulfonyloxyphenyl)-2,8-dioxabicyclo[4.4.0]decan-9-one 21



TMSOTf (0.21 mL, 1.19 mmol, 2.0 eq.) was added dropwise to a stirred solution of alcohol **20** (197 mg, 0.59 mmol, 1.0 eq.) and methyl 3,3-dimethoxypropionate **8** (0.34 mL, 2.37 mmol, 4.0 eq.) in dry DCM (15 mL) at -30 ^{o}C under argon. After 1 h saturated aqueous $NaHCO_3$ (15 mL) was added and the phases were separated. The aqueous phase was extracted with DCM (2 x 15 mL) and the combined organic phases were dried over $MgSO_4$ and the solvent removed *in vacuo*. Purification by flash column chromatography eluting with 10-50% EtOAc in petrol followed by recrystallisation from EtOAc gave *lactone* **21** (222 mg, 93%) as a white crystalline solid; M.p. 143-145 ^{o}C; ν_{max} (neat)/cm^{-1} 2952, 2857, 1736, 1365, 1176, 1153, 1089, 866, 847, 751; δ_H (400 MHz, $CDCl_3$) 1.17-1.27 (2H, m, 4-*H*H and 5-*H*H), 1.20 (3H, d, *J* 6.0, CH_3), 1.38 (1H, m, 4-H*H*), 1.59 (1H, m, 6-H), 1.67 (1H, m, 5-H*H*), 2.63 (1H, dd, *J* 18.0, 11.0, 10-H_{ax}), 3.09 (1H, dd, *J* 18.0, 6.0, 10-H_{eq}), 3.53 (1H, dqd, *J* 11.0, 6.0, 2.0, 3-H), 3.63 (1H, ddd, *J* 11.0, 10.0, 6.0, 1-H), 4.79 (1H, d, *J* 11.0, 7-H), 7.02 (2H, d, *J* 8.5, Ar-H), 7.22 (2H, d, *J* 8.5, Ar-H), 7.54 (2H, m, Ar-H), 7.69 (1H, m, Ar-H), 7.84 (2H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 21.5 (CH_3), 25.1 (C-4), 32.3 (C-5), 37.3 (C-10), 43.4 (C-6), 73.6 (C-3), 73.9 (C-1), 83.5 (C-7), 122.6 (C-Ar), 128.4 (C-Ar), 128.5 (C-Ar), 129.2 (C-Ar), 134.4 (C-Ar), 135.2 (C-Ar), 136.0 (C-Ar), 149.7 (C-Ar), 169.1 (C-9); Found (ESI) 425.1021 $[MNa]^+$ ($C_{21}H_{22}O_6SNa$ requires 425.1029).

Benzyl 3-(4'-hydroxyphenyl)propionate S-1

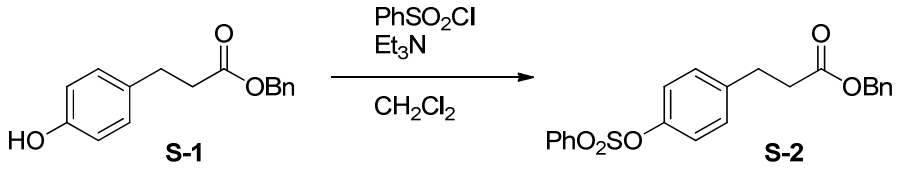


Acid (5.0 g, 30.09 mmol), benzyl bromide (4.3 ml, 36.11 mmol) and potassium hydrogen carbonate (4.52 g, 45.14 mmol) were suspended in acetone (30 ml) and heated to reflux for 18 h. After cooling to room

temperature, the acetone was removed *in vacuo* and CH_2Cl_2 (20 ml) and water (20 ml) were added. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 20 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 20% ethyl acetate in petroleum ether 40-60 as the eluent to yield benzyl ester **S-1** as a pale yellow oil (7.68 g, 29.95 mmol, 99% yield). δ_H (400 MHz, $CDCl_3$) 2.64 (2H, t, *J* 8, 2-H_2), 2.90 (2H, t, *J* 8, 3-H_2), 5.10 (2H, s, OC*H*$_2$Ph), 6.73 (2H, d, *J* 8.5, Ar), 7.04 (2H, d, *J* 8.5, Ar), 7.28 – 7.38 (5H, m, OCH_2*Ph*); δ_C (100 MHz, $CDCl_3$) 30.1 (C-3), 36.2 (C-2), 66.3 (OCH_2), 115.3, 128.2, 128.5, 129.4, 132.6, 135.9, 153.9, 172.8 (C-1).

Spectroscopic data in accordance with literature data.[5]

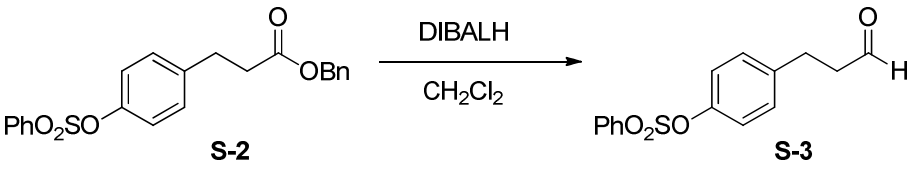
Benzyl 3-(4'-benzenesulfoxyphenyl)propionate S-2



Benzenesulfonyl chloride (3.82 ml, 5.29 g, 29.95 mmol) and triethylamine (4.31 ml, 3.03 g, 29.95 mmol) were added dropwise sequentially to a stirring solution of benzyl ester **S-1** (7.68 g, 29.95 mmol) in CH_2Cl_2 (50 ml) under N_2 at 0 °C. Once both additions were complete, the reaction mixture was warmed to room temperature and stirred for 18 h. Saturated ammonium chloride solution (50 ml) was added and the biphasic mixture was stirred for 5 minutes. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 50 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 20% ethyl acetate in petroleum ether 40-60 as the eluent to yield benzyl ester **S-2** as a pale yellow solid (10.69 g, 26.97 mmol, 90% yield). mp 60-62°C; δ_H (301 MHz, $CDCl_3$) 2.63 (2H, t, *J* 8, 2-H_2), 2.92 (2H, t, *J* 8, 3-H_2), 5.09 (2H, s, OC*H*$_2$Ph)), 6.86 (2H, d, *J* 8.5, Ar), 7.08 (2H, d, *J* 8.5, Ar), 7.26 – 7.39 (5H, m, OCH_2*Ph*), 7.47 – 7.56 (2H, m, OSO_2*Ph*), 7.65 (1H, m, OSO_2*Ph*), 7.79 – 7.86 (2H, m, OSO_2*Ph*); δ_C (76 MHz, $CDCl_3$) 30.3 (C-3), 35.7 (C-2), 66.5 (O*C*H_2Ph), 122.4, 128.3, 128.4, 128.6, 128.7, 129.2, 129.6, 134.3, 135.9, 139.6, 148.1, 172.4 (C-1).

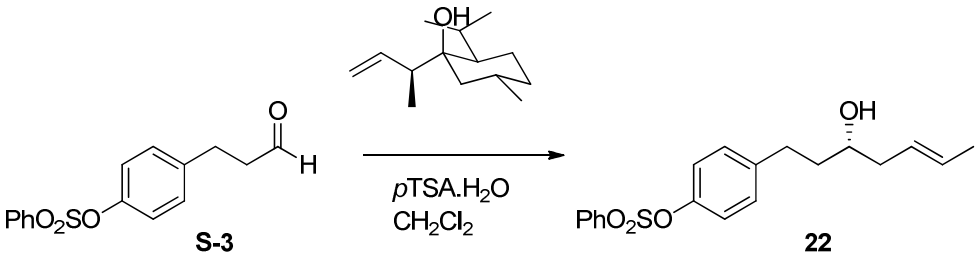
Spectroscopic data in accordance with literature data. [5]

3-(4'-(Benzenesulfoxyphenyl)propional S-3



Diisobutylaluminium hydride (6.62 ml, 1M in hexanes) was added dropwise to a stirring solution of benzyl ester **S-2** (2.5 g, 6.31 mmol) in CH_2Cl_2 (40 ml) under N_2 at -78 °C. The reaction was stirred for 6 h at -78 °C then quenched by addition of saturated Rochelle's salt solution (100 ml) and stirred until the phases separated. The reaction mixture was extracted with CH_2Cl_2 (2 x 100 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 20 – 30% ethyl acetate in petroleum ether 40-60 as the eluent to yield *aldehyde* **S-3** as a colorless oil (1.78 g, 6.15 mmol, 98% yield). ν_{max}/cm^{-1} 2924, 2852, 1720 (CHO), 1503, 1370, 1198, 1177, 1149, 1092, 863; δ_H (400 MHz, $CDCl_3$) 2.79 (2H, td, *J* 8, 1, 2-H_2), 2.95 (2H, t, *J* 8, 3-H_2), 6.92 (2H, d, *J* 8.5, Ar), 7.12 (2H, d, *J* 8.5, Ar), 7.53 – 7.60 (2H, m, OSO_2*Ph*), 7.70 (1H, m, OSO_2*Ph*), 7.84 – 7.89 (2H, m, OSO_2*Ph*), 9.83 (1H, t, *J* 1, 1-H). δ_C (101 MHz, $CDCl_3$) 27.5 (C-3), 45.2 (C-2), 122.6, 128.6, 129.3, 129.6, 139.7, 148.1, 201.0 (C-1). HRMS (ESI) calc for $C_{15}H_{14}O_4SNa$ [M+Na] 313.0505 found 313.0503.

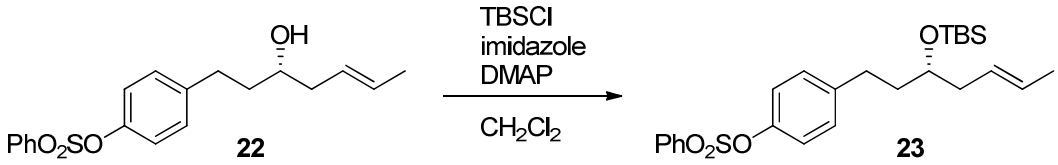
(*S, E*) 1-(4'-Benzenesulfoxyphenyl)-hept-5-en-3-ol 22



Nokami reagent (1.20 g, 5.86 mmol) and *para* toluenesulfonic acid hydrate (54 mg, 0.28 mmol) were added to a solution of aldehyde **S-3** (825 mg, 2.85 mmol) in CH_2Cl_2 (20 ml) under N_2. The reaction mixture was stirred for 20 h. Water (20 ml) was added and the phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 20 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 5 – 30% ethyl acetate in petroleum ether 40-60 as the eluent to yield *alcohol* **22** as a colorless oil (969 mg, 2.79 mmol, 98% yield). $[\alpha]_D^{20}$ -11.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 3401, 2917, 1501, 1371, 1198, 1149, 866; δ_H (400 MHz, $CDCl_3$) 1.65 – 1.75 (5H, m, 7-H_3 & 4-H_2), 2.08 (1H, m, 2-H*H*), 2.25 (1H, m, 2-*H*H), 2.62 (1H, m, 1-*H*H), 2.76 (1H, m, 1-H*H*), 3.55 (1H, m, 3-H), 5.40 and 5.55 (each 1H, each m, 5-H & 6-H), 6.87 (2H, d, *J* 8.5, Ar), 7.10 (2H, d, *J* 8.5, Ar), 7.49 – 7.55 (2H, m, OSO_2*Ph*), 7.63 – 7.69 (1H, m, OSO_2*Ph*), 7.81 – 7.86 (2H, m, OSO_2*Ph*);

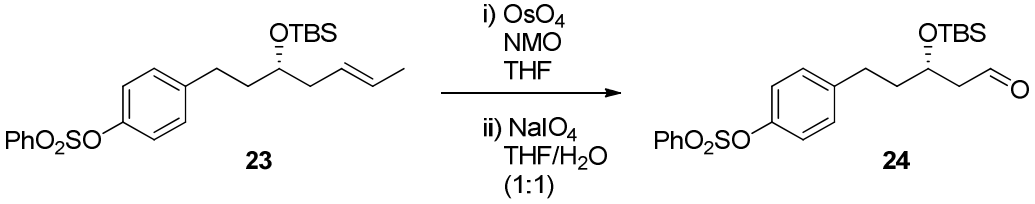
δ_C (101 MHz, $CDCl_3$) 18.1 (C-7), 31.4 (C-1), 38.1 (C-4), 40.9 (C-2), 69.9 (C-3), 122.1, 126.7, 128.5, 129.1, 129.4, 129.5, 134.1, 135.5, 141.3, 147.6. HRMS (ESI) calc for $C_{19}H_{22}O_4SNa$ [M+Na] 369.1131 found 369.1118.

(*S, E*) 1-(4'-(benzenesulfoxy)phenyl)-3-(*tert*butyldimethyl)silyloxy-hept-5-ene 23



Alcohol **22** (1.61 g, 4.65 mmol) was dissolved in anhydrous CH_2Cl_2 (40 ml) and TBDMSCl (842 mg, 5.58 mmol), imidazole (950 mg, 13.96 mmol) and DMAP (57 mg, 0.46 mmol) were added. The reaction mixture was stirred for 40 h under a balloon of argon. Water (20 ml) was added and the reaction mixture was stirred for a further 5 minutes. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 20 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 1% ethyl acetate in petrol as the eluent to give *TBS ether* **23** (1.78 g, 83% yield) as a yellow oil. $[\alpha]_D^{20}$ -7.0 (*c.* 1.0 $CHCl_3$) ν_{max}/cm^{-1} 2953, 2928, 1502, 1375, 1200, 1151, 864, 832 δ_H (400 MHz, $CDCl_3$) 0.03 (3H, s, CH_3Si), 0.04 (3H, s, CH_3Si), 0.90 (9H, s, $(CH_3)_3CSi$), 1.52 – 1.77 (5H, m, 2-H_2 & 7-H_3), 2.16 (2H, t, *J* 5, 4-H_2), 2.53 (1H ddd, *J* 14, 11, 5.5, 1-H*H*), 2.67 (1H, ddd, *J* 14, 11, 6, 1*H*H), 3.67 (1H, p, *J* 6, 3-H), 5.25 – 5.54 (2H, m, 5-H & 6-H), 6.87 (2H, d, *J* 9, Ar), 7.07 (2H, d, *J* 9, Ar), 7.52 (2H, t, *J* 7.5, OSO_2*Ph*), 7.66 (1H, tt, *J* 7.5, 1.5, OSO_2*Ph*), 7.84 (2H, dd, *J* 8.5, 1.5, OSO_2*Ph*); δ_C (101 MHz, $CDCl_3$) -4.6 (*C*H_3CSi), -4.3 (*C*H_3CSi), 18.0 (C-7), 18.1 ($(CH_3)_3$*C*Si), 25.9 (($C H_3$)$_3$CSi), 31.1 (C-1), 38.4 (C-2), 40.6 (C-4), 71.8 (C-3), 122.1, 127.3 (C-6), 127.4 (C-5), 128.5, 129.0, 129.4, 134.1, 135.5, 141.9, 147.5; HRMS (ESI) calc for $C_{25}H_{34}O_4SSiNa$ [M+Na] 483.1995, found 483.1987

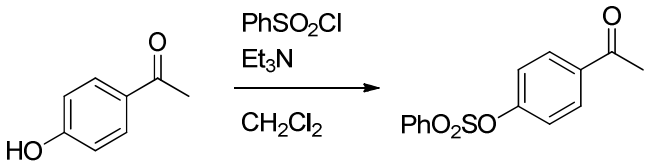
(*S*)-5-(4'-Benzenesulfoxyphenyl)-3-(*tert*butyldimethylsilyloxy)-pentanal 24



N-Methyl morpholine-*N*-oxide (153 mg, 1.13 mmol) and osmium tetroxide (1 crystal) were added to a stirring solution of silyl ether **23** (260 mg, 0.56 mmol) in THF (5 ml) and stirred for 0.75 h. The reaction was quenched with the addition of saturated sodium sulfite solution (10 ml). The resulting biphasic mixture was extracted with ethyl acetate (3 x 30 ml) and the combined organic phases were dried over

$MgSO_4$ and concentrated *in vacuo* to give a yellow oil. The crude oil was dissolved in THF (10 ml) and water (10 ml) and $NaIO_4$ (232 mg, 1.27 mmol) was added and stirred for 2 h, after which additional $NaIO_4$ (232 mg, 1.27 mmol) was added and stirred for a further 1 h. The reaction was quenched with the addition of saturated sodium hydrogen carbonate solution (10 ml). The resulting biphasic mixture was extracted with ethyl acetate (3 x 30 ml), the combined organic phases dried over $MgSO_4$ and concentrated *in vacuo* to give *aldehyde* **24** (247.7 mg, 98% yield) as a yellow oil. $[\alpha]_D^{20}$ -5.0, ν_{max}/cm^{-1} 2953, 2929, 2856, 1723, 1502, 1373, 1199, 1178, 1150, 1092, 864, 863; δ_H (400 MHz, $CDCl_3$) 0.05 (3H, s, CH_3Si), 0.07 (3H, s, CH_3Si), 0.89 (9H, s, $(CH_3)_3CSi$), 1.75 – 1.85 (2H, m, 4-H_2), 2.49 – 2.72 (4H, m, 2-H_2 & 5-H_2), 4.22 (1H, p, *J* 6, 3-H), 6.88 (2H, d, *J* 8.5, Ar), 7.07 (2H, d, *J* 8.5, Ar), 7.53 (2H, dd, *J* 8, 7, OSO_2*Ph*), 7.66 (1H, m, OSO_2*Ph*), 7.84 (2H, dd, *J* 8.5, 1, OSO_2*Ph*), 9.80 (1H, t, *J* 2, 1-H); δ_C (101 MHz, $CDCl_3$) -4.6 (*C*H_3Si), -4.5 (*C*H_3Si), 18.0 ($(CH_3)_3$*C*Si), 25.7 ($(CH_3)_3$CSi), 30.8 (C-5), 39.3 (C-4), 50.8 (C-2), 67.5 (C-3), 122.3, 128.5, 129.1, 129.3, 134.1, 135.5, 140.9, 147.7, 201.7 (C-1). HRMS (ESI) calc for $C_{23}H_{32}O_5SSiNa$ [M+Na] 471.1632, found 471.1633.

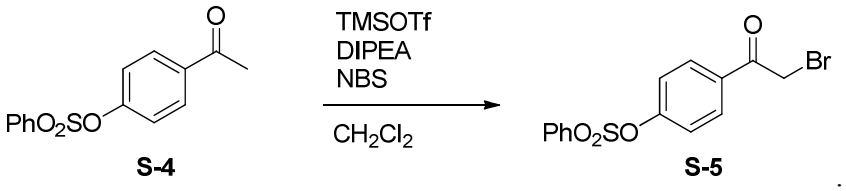
4'-Benzenesulfoxyacetophenone S-4



S-4

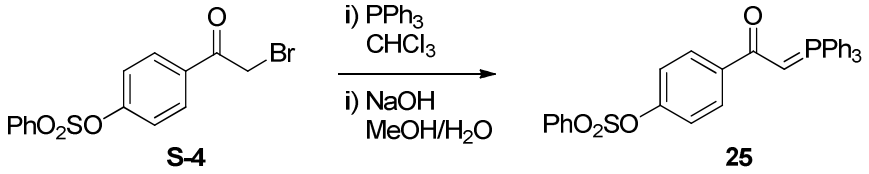
4'-Hydroxyacetophenone (2.5 g, 18.36 mmol) was dissolved in anhydrous CH_2Cl_2 (50 ml) under N_2 and cooled to 0 °C. Benzenesulfonyl chloride (2.34 ml, 3.24 g, 18.36 mmol) and triethylamine (2.55 ml, 1.86 g, 18.36 mmol) were added dropwise and the reaction was warmed to room temperature and stirred for 16 h. Water (50 ml) was added and mixture was extracted with CH_2Cl_2 (2 x 30 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 30% ethyl acetate in petroleum ether 40-60 as the eluent to yield *sulfonate* **S-4** as a colorless oil (4.70 g, 16.99 mmol, 93% yield). ν_{max}/cm^{-1} 3069, 3006, 3963, 1683, 1595, 1374, 1200, 1151, 859, 846, 752, 577, 559; δ_H (400 MHz, $CDCl_3$) 2.57 (3H, s, CH_3), 7.02 – 7.14 (2H, m, Ar), 7.50 – 7.57 (2H, m, OSO_2*Ph*), 7.69 (1H, m, OSO_2*Ph*), 7.82 – 7.86 (2H, m, OSO_2*Ph*), 7.87 – 7.92 (2H, m, Ar); δ_C (100 MHz, $CDCl_3$) 26.7 (CH_3), 122.6, 128.5, 129.40, 129.42, 130.2, 134.6, 135.2, 135.8, 153.0, 196.7 (C=O); HRMS (ESI) calc for $C_{14}H_{12}O_4SNa$ [M+Na] 299.0348 found 299.0336

2-Bromo-4'-benzenesulfoxyacetophenone S-5



Sulfonate **S-4** (4.70 g, 16.99 mmol) was dissolved in anhydrous CH_2Cl_2 (50 ml) under N_2 and cooled to 0 °C. *N,N*-Diisopropylethylamine (3.7 ml, 21.24 mmol) and TMSOTf (3.69 ml, 20.39 ml) were added dropwise and the mixture was stirred for 0.5 hr. *N*-Bromosuccinimide (3.63 g, 20.39 mmol) was added and mixture was warmed to room temperature and stirred for 3 h. The reaction mixture was washed sequentially with saturated ammonium chloride solution (40 ml) and saturated sodium hydrogen carbonate solution (40 ml), dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 30% ethyl acetate in petroleum ether 40-60 as the eluent to yield *sulfonate* **S-5** as a pale yellow oil which crystallized on standing to give dark yellow crystals (5.29 g, 14.88 mmol, 88% yield). mp 69-71 °C ν_{max}/cm^{-1} 3073, 1698, 1595, 1364, 1180, 1153, 835, 747, 564; δ_H (400 MHz, $CDCl_3$) 4.38 (2H, s, 2-CH_2), 7.06 – 7.17 (2H, m, Ar), 7.50 – 7.59 (2H, m, OSO_2*Ph*), 7.68 (1H, m, OSO_2*Ph*), 7.80 – 7.87 (2H, m, OSO_2*Ph*), 7.87 – 8.02 (2H, m, Ar); δ_C (100 MHz, $CDCl_3$) 30.4 (C-2), 122.7, 128.4, 129.3, 130.8, 132.6, 134.6, 135.1, 153.4, 189.9 (C-1); HRMS (ESI) calc for $C_{14}H_{11}O_4SBrNa$ [M+Na] 376.9454 found 376.9460.

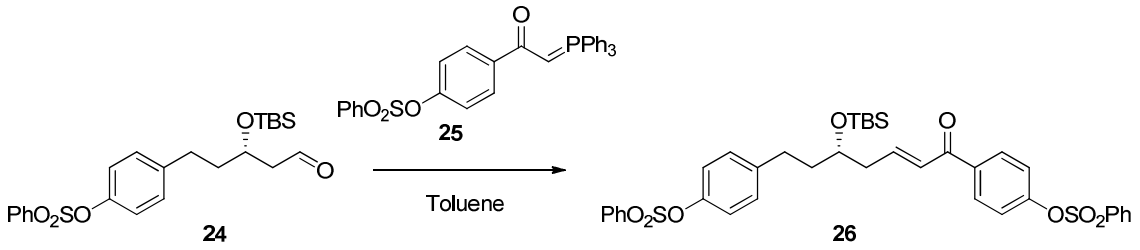
Triphenyl-(4-((benzenesulfoxy)benzoyl)-2'-methylenephosphorane 25



Triphenylphosphine (738 mg, 2.81 mmol) was added to a stirring solution of acetophenone **S-4** (1000 mg, 2.81 mmol) in chloroform (15 ml) and stirred for 18 hrs. The solvent was removed *in vacuo* and resulting solid was triturated with diethyl ether (20 ml). The resulting solid was dissolved in methanol/water (20 ml 1:1 v/v), sodium hydroxide (112 mg, 2.81 mmol) was added and stirred for 3 hrs. The precipitate was filtered and washed with water before drying for 60 hrs in a vacuum oven to yield *ylide* **25** as a colorless solid (1.1 g, 2.05 mmol, 73%). mp 166-168 °C; ν_{max}/cm^{-1} 3059, 1591, 1522, 1437, 1373, 1103, 689; δ_H (400 MHz, $CDCl_3$) 4.35 (1H, d, *J* 21, 2'-H), 6.93 (2H, d, *J* 9, Ar), 7.41 – 7.60 (10H, m, Ar), 7.62 – 7.72 (8H, m, Ar), 7.77 – 7.83 (2H, m, Ar), 7.86 (2H, d, *J* 9, Ar); δ_C (101 MHz, $CDCl_3$) 51.3 (d, *J* 111, C-2'), 121.5, 126.3, 127.2, 128.3, 128.4, 128.5, 128.6, 128.9, 129.0, 129.1, 131.9, 131.9, 132.0, 132.1, 132.2,

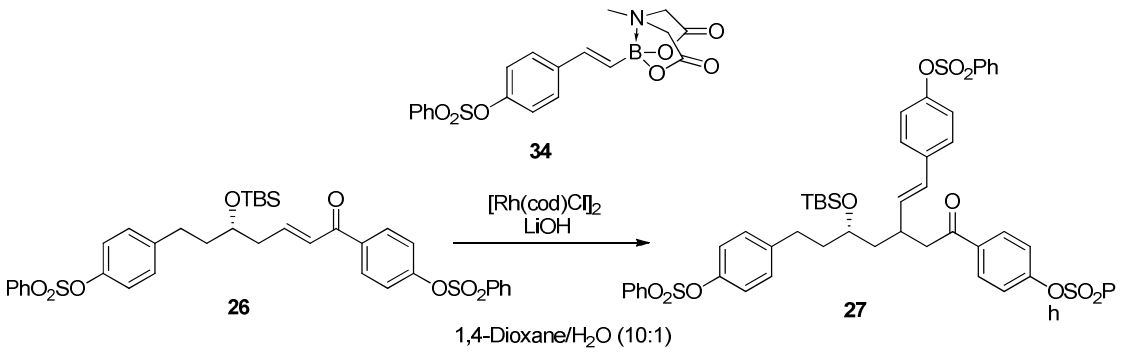
132.2, 133.0, 133.1, 133.1, 134.1, 135.3, 140.3, 140.4, 150.3, 183.3 (C-1'). HRMS (CI) calc for $C_{32}H_{26}O_4PS$ [M+H] 537.1289, found 537.1285

(*5S, 2E*)-5-(*tert*-Butyldimethyl)silyloxy-1,7-di(4'-(benzenesulfoxy)phenylhept-2-en-1-one 26



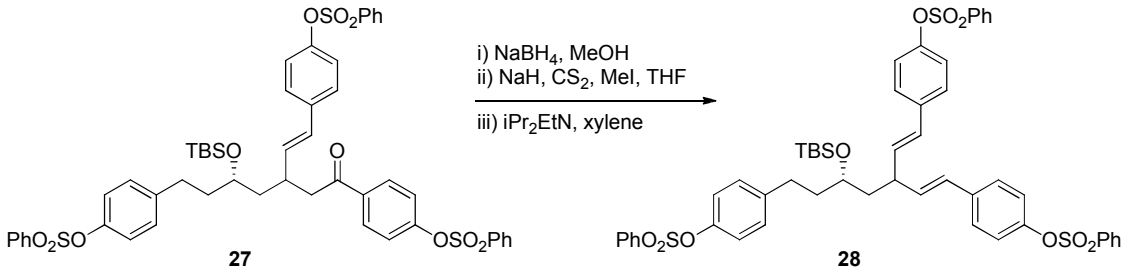
Ylide **25** (275.6 mg, 0.51 mmol) and aldehyde **24** (115 mg, 0.26 mmol) were dissolved in toluene (10 ml) and heated to reflux for 20 h. After cooling to room temperature, solvent was removed *in vacuo* and the mixture was purified by column chromatography using 20 % ethyl acetate in petrol as the eluent to give *enone* **26** as a yellow oil (165 mg, 0.23 mmol, 91%). $[\alpha]_D^{20}$ -3.0 (*c*. 1.0 $CHCl_3$), ν_{max}/cm^{-1} 2952, 2928, 1671, 1620, 1501, 1449, 1374, 1199, 1178, 1150, 861, 833; δ_H (400 MHz, $CDCl_3$) 0.03 (3H, s, CH_3Si), 0.05 (3H, s, CH_3Si), 0.88 (9H, s, $(CH_3)_3CSi$), 1.68 – 1.77 (2H m, 6-H_2), 2.45 – 2.51 (2H, m, 4-H_2), 2.57 (1H, m, 7-H*H*), 2.68 (1H, m, 7-*H*H), 3.87 (1H, p, *J* 6, 5-H), 6.81 – 6.91 (2H, m, Ar), 7.00 – 7.15 (3H, m, Ar & 3-H), 7.47 – 7.62 (4H, m, OSO_2*Ph*), 7.60 – 7.76 (2H, m, OSO_2*Ph*), 7.74 – 7.92 (3H, m, OSO_2*Ph* & 2-H);. δ_C (101 MHz, $CDCl_3$) -4.5 (CH_3CSi), -4.3 (CH_3CSi), 18.1 ($(CH_3)_3CSi$), 25.8 ($(CH_3)_3CSi$), 31.1 (C-7), 38.9 (C-6), 40.8 (C-4), 70.7 (C-5), 122.2, 122.5, 128.4, 128.5, 129.3, 130.2, 134.1, 134.5, 135.5, 136.5, 141.2, 146.6, 152.6, 188.8 (C-1) HRMS (ESI) calc for $C_{37}H_{42}O_8S_2SiNa$ [M+Na] 706.1982, found 706.1983.

(*5S, 2E*)-3-(4'Benzenesulfoxyphenyl)ethynyl-5-(*tert*-butyldimethyl)silyloxy-1,7-di(4'-(benzenesulfoxy)phenylheptanone 27



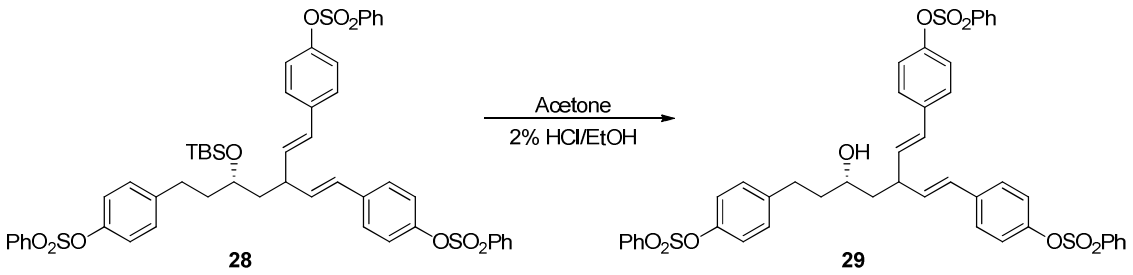
MIDA boronate **34** (843 mg, 2.03 mmol) was suspended in 1,4-dioxane (20 ml) and 1M sodium hydroxide solution (10 ml) was added and stirred for 1 h. pH7 phosphate buffer (20 ml) was added and mixture was extracted with ethyl acetate (3 x 20 ml). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* until ~5ml 1,4-dioxane remained. Dioxane solution of boronic acid was added to a 1,4-dioxane solution (25 ml) of enone **26** (718 mg, 1.02 mmol), $[Rh(cod)Cl]_2$ (25 mg, 0.05 mmol) and lithium hydroxide (24 mg, 1.02 mmol) and heated to reflux for 3 hrs. On cooling to room temperature water (30 ml) was added and the reaction mixture was extracted with ethyl acetate (3 x 30 ml). The combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo* and purified by column chromatography using 20% ethyl acetate in petrol as the eluent to yield *ketone* **27** (886 mg, 0.92 mmol, 90%). ν_{max}/cm^{-1} 3008, 2957, 2856, 1751, 1501, 1346, 1199, 1176, 1148, 857, 732; δ_H (400 MHz, C_6D_6) -0.05, 0.01, 0.03 (6H, s, CH_3Si), 0.94, 0.95 (9H, s, (CH_3)CSi), 1.51 – 1.81 (4H, m), 2.34 - 2.52 (2H, m), 2.55 – 2.69 (2H, m), 2.89 – 3.14 (1H, m, 3-H), 3.59 – 3.74 (1H, m, 5-H), 5.85, 5.87 (1H, ddd, *J* 16, 7), 6.16, 6.25 (1 H, d, *J* 16), 6.73 – 6.95 (20H, m, Ar), 7.55 (2H, dd, *J* 9, 3, Ar), 7.57 – 7.69 (5H, m, Ar); δ_C (101 MHz, C_6D_6) -4.6, -4.5, -4.5, -4.2 (CH_3Si), 17.9, 17.9 ((CH_3)*C*Si), 25.8, 25.8 ((CH_3)CSi), 30.3, 30.4, 35.0 (C-3), 35.4 (C-3), 37.8, 39.4, 41.9, 43.9, 44.6, 69.6 (C-5), 69.7 (C-5), 122.4, 122.4, 122.6, 122.7, 127.0, 127.0, 128.2, 128.3, 128.3, 128.7, 128.7, 128.8, 128.9, 128.9, 129.1, 129.3, 129.4, 129.6, 129.7, 133.4, 133.5, 133.5, 133.5, 133.8, 133.8, 134.2, 134.5, 135.5, 135.5, 135.7, 135.7, 135.9, 135.9, 136.2, 136.2, 141.2, 141.5, 148.0, 148.9, 152.8, 152.9, 195.8 (C-1), 195.9 (C-1); HRMS (ESI) calc for $C_{51}H_{54}O_{11}S_3SiNa$ [M+Na] 989.2490 found 989.2497.

(*3S, 6E, 1'E*)-5-(4'Benzenesulfoxyphenyl)ethenyl-5-(*tert*-butyldimethyl)silyloxy-1,7-di(4'-(benzenesulfoxy)phenylhept-6-ene 28



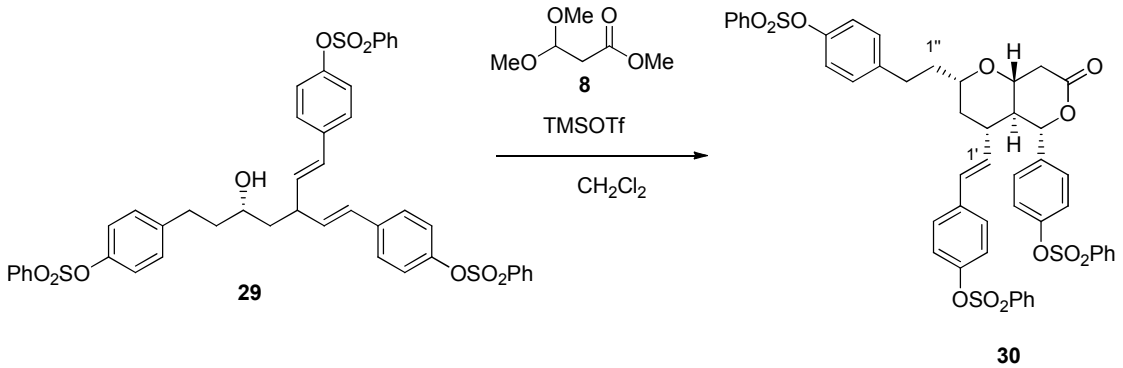
Ketone **27** (684 mg, 0.71 mmol) and sodium borohydride (53 mg, 1.41 mmol) were dissolved in methanol (35 ml) and stirred for 1 h at which point additional sodium borohydride (53 mg, 1.41 mmol) was added and stirred for a further 0.5 h. The reaction was quenched with 1M HCl (30 ml) and extracted with ethyl acetate (3 x 30 ml). The combined organic fractions were dried over $MgSO_4$ and concentrated *in vacuo*. The resulting oil was dissolved in THF (20 ml) under N_2 and NaH (848.5 mg, 21.21 mmol) was added. After 1 hr CS_2 (2.98 ml, 49.50 mmol) and MeI (1.82 ml, 28.29 mmol) were added and heated to 50 °C for 1 hr. The reaction was quenched with the addition of 1M HCl (20 ml) and the reaction was extracted with ethyl acetate (3 x 30 ml). The combined organic fractions were dried over $MgSO_4$, concetrated *in vacuo* and purified by column chromatography using 20% ethyl acetate in petrol as the eluent to yield a xanthate as a yellow oil. The yellow oil was used immediately and was dissolved in dry xylene (10 ml) under N_2. Hunigs base (few drops) was added and reaction heated to reflux for 24 h. After cooling to room temperature xylene and Hunig's base were removed *in vacuo* to give *diene* **28** (410 mg, 0.43 mmol, 61%) as a brown oil. $[\alpha]_D^{21}$ -8.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 2927, 2855, 1500, 1372, 1198, 1177, 1149, 862, 833, 747, 685, 578; δ_H (400 MHz, C_6D_6) -0.05 (3H, s, CH_3Si), 0.00 (3H, s, CH_3Si), 0.96 (9H, s, (CH_3)CSi), 1.52 – 1.84 (4H, m, 2-H_2 & 4-H_2), 2.45 (2H, t, *J* 7, 1-H_2), 3.07 (1H, p, *J* 7, 5-H), 3.67 (1H, p, *J* 7, 3-H), 5.81 – 5.87 (1H, dd, *J* 16, 7, 1'-H), 5.90 (1H, dd, *J* 16, 7, 6-H), 6.16 (1, d, *J* 16, 2'-H), 6.22 (1H, d, *J* 16, 7-H), 6.65 – 6.99 (21H, m, Ar), 7.54 – 7.77 (6H, m, Ar); δ_C (101 MHz, C_6D_6) -4.4 (CH_3Si), -4.3 (CH_3Si), 17.9 ((CH_3)*C*Si), 25.8 ((*C*H_3)CSi), 30.4 (C-1), 38.8 (C-2), 42.1 (C-4), 42.7 (C-5), 69.4 (C-3), 122.4, 122.7, 122.7, 127.1, 128.3, 128.3, 128.7, 128.7, 129.3, 133.3, 133.4, 133.4, 133.4, 133.7, 135.8, 136.0, 136.2, 136.2, 141.1, 148.0, 148.9, 149.0; HRMS (ESI) calc for $C_{51}H_{54}O_{10}S_3SiNa$ [M+Na] 973.2540 found 973.2535.

(*3S, 6E, 1'E*)-5-(4'Benzenesulfoxyphenyl)ethenyl-1,7-di(4'-(benzenesulfoxyphenyl)hept-6-en-3-ol 29



TBS ether **28** (410 mg, 0.43 mmol) was suspended in 2% HCl/ethanol (30 ml), acetone (2 ml) was added to aid solubility and the reaction was stirred for 18 h after which HCl (0.6 ml) was added and the reaction was stirred for a further 1 h. Water (20 ml) and ethyl acetate (30 ml) were added and the mixture was extracted with ethyl acetate (3 x 30 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 30-40% ethyl acetate in petrol as the eluent to give *alcohol* **29** (295 mg, 0.35 mmol, 82%). $[\alpha]_D^{23}$ -5.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 3566, 3067, 2925, 2855, 1500, 1449, 1368, 1197, 1176, 1148, 1091, 861, 747, 685, 578; δ_H (400 MHz, C_6D_6) 1.32 – 1.62 (4H, m, 2-H_2 & 4-H_2), 2.32 (1H, m, 1-H*H*), 2.47 (1H, m, 1-*H*H), 3.13 (1H, p, *J* 7, 5-H), 3.40 (1H, m, 3-H), 5.81 (1H, dd, *J* 16, 7, 1'-H), 5.91 (1H, dd, *J* 16, 7, 6-H), 6.13 (1H, d, *J* 16, 2'-H), 6.20 (1H, d, *J* 16, 7-H), 6.61 – 7.00 (21H, m, Ar), 7.55 – 7.80 (6H, m, Ar); δ_C (101 MHz, C_6D_6) 31.1 (C-1), 39.4 (C-2), 42.4 (C-4), 43.1 (C-5), 68.3 (C-3), 122.3, 122.6, 122.7, 127.1, 127.1, 128.3, 128.3, 128.7, 128.7, 129.4, 132.9, 133.4, 133.4, 133.4, 133.9, 135.8, 135.8, 136.0, 136.2, 136.3, 141.1, 148.0, 148.9, 148.9; HRMS (ESI) calc for $C_{45}H_{40}O_{10}S_3Na$ [M+Na] 859.1678 found 859.1712.

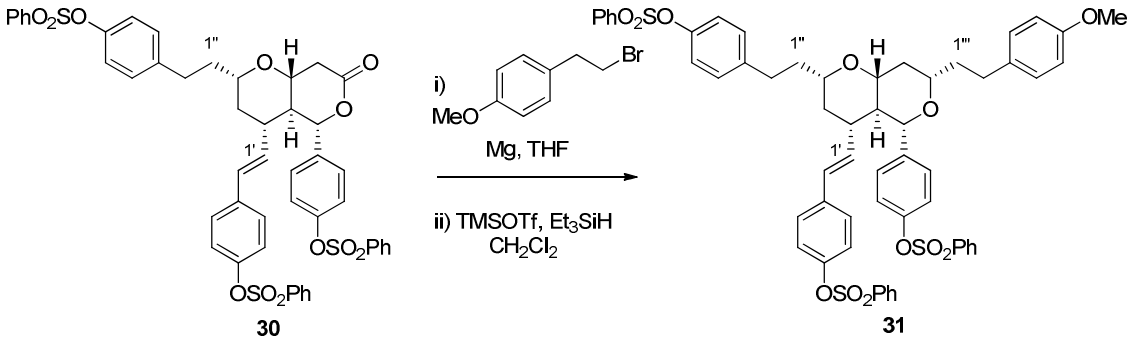
(-)-(1*R*, 3*S*, 5*S*, 6*S*, 7*S*)-3-(*p*-Benzenesulfoxyphen)ethyl-5-(*E*)-(*p*-benzenesulfoxyphen)ethynyl-7-(*p*-*b*enzenesulfoxy)phenyl-2,8-dioxabicyclo[4.4.0]decan-9-one 30



Trimethylsilyl trifluoromethanesulfonate (77 µl, 0.43 mmol) was added to a stirring solution of alcohol **29** (179 mg, 0.21 mmol) and methyl 3,3-dimethoxypropanoate **8** (121 µl, 0.86 mmol) in CH_2Cl_2 (20 ml) at -30 °C under N_2. The reaction mixture was stirred for 1.5 h before being quenched by the addition of water (20 ml). The phases were separated and the aqueous phase was washed with CH_2Cl_2 (2 x 30 ml).The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column

chromatography using 30-50% ethyl acetate in petrol as the eluent to yield *lactone* **30** as a pale yellow oil (142 mg, 0.16 mmol, 75%). m.p. $[\alpha]_D^{21}$ -20.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 2924, 2854, 1738, 1501, 1369, 1198, 1177, 1149, 1091, 862, 749, 685; δ_H (400 MHz, $CDCl_3$) 1.32 (1H, m, 4-*H*H), 1.59 (1H, ddd, *J* 13.5, 4, 2, 4-H*H*), 1.63 – 1.85 (2H, m, 1"-H_2), 1.88 (1H, q, *J* 10, 6-H), 2.32 (1H, m, 5-H), 2.54 – 2.84 (3H, m, 2"-H_2 & 10-H_{ax}), 3.11 (1 H, dd, *J* 18, 5.5, 10-H_{eq}), 3.45 (1H, m, 3-H), 3.67 (1H, ddd, *J* 11.5, 10, 5.5, 1-H), 4.94 (1H, d, *J* 10, 7-H), 5.07 (1H, dd, *J* 16, 9, 1'-H), 5.94 (1H, d, *J* 16, 2'-H), 6.70 (2H, d, *J* 8.5, Ar), 6.82 (3H, dd, *J* 15, 8.5, Ar), 6.92 (2H, d, *J* 8.5, Ar), 7.10 (2H, d, *J* 8.5, Ar), 7.16 (2 H, d, *J* 8.5, Ar), 7.48 – 7.60 (7H, m, Ar), 7.65 – 7.77 (5H, m, Ar), 7.86 (4H, m, Ar); δ_C (101 MHz, $CDCl_3$) 30.7 (C-2"), 37.0 (C-1"), 37.2 (C-10), 39.0 (C-4), 42.3 (C-5), 47.6 (C-6), 73.2 (C-3), 75.4 (C-1), 84.1 (C-7), 122.2, 122.3, 122.4, 126.7, 128.4, 128.4, 128.4, 128.5 (C-2'), 129.1, 129.1, 129.2, 129.3, 129.5, 130.0, 132.9 (C-1') 134.2, 134.3, 134.3, 135.2, 135.3, 135.4, 135.5, 137.1, 140.8, 147.7, 148.6, 149.6, 168.5 (C-9); HRMS (ESI) calc for $C_{48}H_{42}O_{12}S_3Na$ [M+Na] 929.1730, found 929.1702.

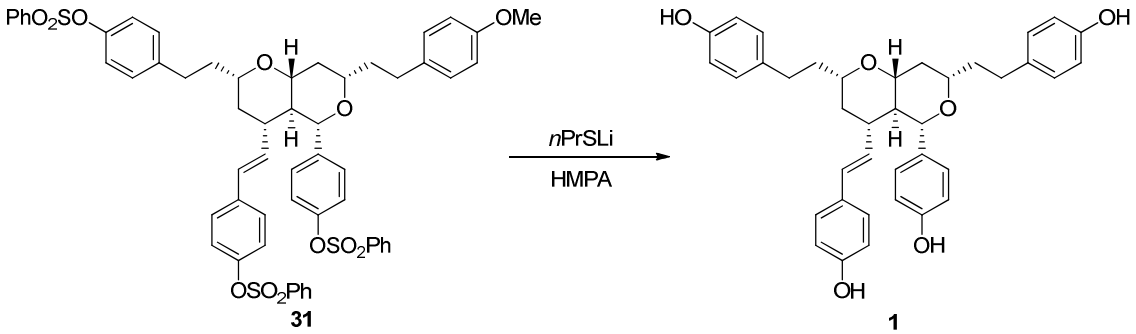
(–)-(1*R*, 3*S*, 5*S*, 6*S*, 7*S*, 9*S*)- 3α, 9α-di(*p*-Benzenesulfoxyphen)ethyl-5α-(*E*)-(*p*-benzenesulfoxyphen)ethynyl-7α-(*p-b*enzenesulfoxy)phenyl-2,8-dioxabicyclo[4.4.0]decane 31



Methoxyphenethyl bromide (1 ml, 1376 mg, 6.40 mmol) was added to a solution of vacuum dried magnesium (171 mg, 7.04) in tetrahydrofuran (6.4 ml). A single crystal of iodine was added and the reaction mixture was warmed to initial reaction. On cooling to room temperature the magnesium was seen to be consumed. 1 ml of the resulting solution was added slowly to a solution of lactone **30** (275 mg, 0.303 mmol) in tetrahydrofuran (20 ml) at 0 °C. The reaction was warmed to room temperature and stirred for 4 h before the reaction mixture was quenched with saturated ammonium chloride (30 ml) and extracted with ethyl acetate (3 x 50 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 20-50% ethyl acetate in petrol as the eluent to give *lactol* (168 mg, 0.161 mmol, 53%) as a pale yellow oil. Lactol was dissolved in dichloromethane (20 ml) and triethylsilane (258 µl, 1.61 mmol) was added. The reaction mixture was cooled to -78 °C and TMSOTf (44µl, 0.242 mmol) was added dropwise. The reaction was stirred at -78 °C for 1 h before quenching with saturated ammonium chloride (30 ml) and extracting with

dichloromethane (3 x 30 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and filtered through a silica plug using 60% ethyl acetate in petrol as the eluent to give *bicycle* **31** (131 mg, 0.128 mmol, 42% over two steps, 76% from lactol) as a pale yellow oil. $[\alpha]_D^{22}$ -41.0 (*c*. 1.0 $CHCl_3$); ν_{max}/cm^{-1} 2930, 1501, 1449, 1371, 1198, 1176, 1149, 863. δ_H (500 MHz, $CDCl_3$) 1.26 (1H, m, 4-H*H*), 1.45 (1H, m, 4-*H*H), 1.54 – 1.64 (3H, m, 6-H, 10-*H*H & 1”-H*H*), 1.72 – 1.83 (2H, m, 1” *H*H & 1”’-*H*H), 1.89 (1H, m, 1”’-H*H*) 2.01 (1H, m, 10-H*H*), 2.17 (1H, m, 5-H), 2.54 – 2.73 (4H, m, 2”-H & 2”’-H), 3.30 (1H, m, 1-H), 3.35 (1H, m, 3-H), 3.49 (1H, m, 9-H), 3.78 (3H, s, C*H*$_3$O) 3.95 (1H, d, *J* 10, 7-H), 5.01 (1H, dd, *J* 16, 9.0, 1’-H), 5.75 (1H, d, *J* 16, 2’-H), 6.65 (2H, d, *J* 8, Ar), 6.79 (4H, dd, *J* 12, 8, Ar), 6.88 (4H, d, *J* 8, Ar), 7.06 (5H, dd, *J* 11, 8, Ar), 7.51 (8H, m, Ar), 7.58 – 7.68 (4H, m, Ar), 7.73 (2H, d, *J* 8, Ar), 7.82 (6H, t, *J* 8, Ar); δ_C (101 MHz, $CDCl_3$) 30.3 & 30.9 (C-2” & C-2”’), 37.3 (C-1”), 37.6 (C-1”’), 37.9 (C-10), 40.2 (C-4), 42.0 (C-5), 50.6 (C-6), 55.2 (MeO), 75.0 (C-9), 75.4 (C-3), 78.8 (C-1), 82.3 (C-7), 113.7, 122.1, 122.2, 126.5, 127.1 (C-2’), 128.3, 128.4, 128.4, 128.5, 129.1, 129.1, 129.1, 129.3, 129.4, 129.5, 133.9, 134.1, 134.1, 134.2, 134.2, 134.9 (C-1’), 135.4, 135.5, 135.7, 136.0, 140.0, 141.1, 147.6, 148.3, 148.9, 157.7; HRMS (ESI) calc for $C_{57}H_{54}O_{12}S_3Na$ [M+Na] 1049.2669, found 1049.2632.

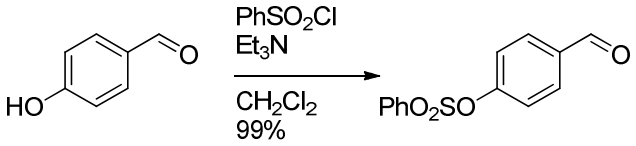
(–)-Blepharocalyxin D 1



n-Butyllithium (1.90 ml, 3 mmol, 1.58 M in hexanes) was added dropwise to a solution of propanethiol (272 µl, 3 mmol) in HMPA (2 ml) under N_2 at 0 °C. After 1hr, the reaction mixture was warmed to room temperature and the hexane was removed *in vacuo*. To the resulting solution of lithium propanethiolate, a solution of bicycle **35** (20 mg, 0.019 mmol) in HMPA (1 ml) was added slowly. The reaction mixture was heated to 180 °C for 30 minutes before cooling to room temperature. Water (20 ml) was added and the mixture was extracted with ethyl acetate (3 x 20 ml). The combined organic fractions were dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography using 50% ethyl acetate in hexane to give (–)-blepharocalyxin D **1** (9.6 mg, 0.016 mmol, 85%) as a pale yellow solid. $[\alpha]_D^{21}$ -79.2 (*c*. 0.23 MeOH); lit.[6] $[\alpha]_D^{22}$ -77.1 (*c*. 0.11 MeOH); δ_H (Acetone-D_6, 400MHz) 1.08 (1H, m, 4-*H*H), 1.50 – 1.81 (7H, m, 1”-H_2, 1”’-H_2, 4-H*H*, 6-H & 10-*H*H), 2.00 (1H, ddd, *J* 12, 4.0, 1.5, 10-H*H*), 2.22 (1H, m, 5-H), 2.49 – 2.67 (4H, m, 2”-H_2 & 2”’-H_2), 3.36 (1H, m, 1-H), 3.42 – 3.63 (2H, m, 3-H & 9-H), 3.99 (1H, d,

J 10, 7-H), 5.06 (1H, dd, *J* 16, 8.5, 1'-H), 5.82 (1H, d, *J* 16, 2'-H), 6.50 – 6.69 (4H, m, Ar), 6.69 – 6.78 (5H, m, Ar), 6.87 – 7.08 (5H, m, Ar), 8.37 – 8.58 (2H, m, Ar); δ_C (Acetone-D_6, 126MHz) 30.4 & 30.5 (C-2" & C-2"'), 38.1 & 38.2 (C-1" & C-1"'), 38.4 (C-10), 40.6 (C-4), 41.6 (C-5), 51.2 (C-6), 74.6, 75.4, 79.1 (C-1), 82.7 (C-7), 114.6, 114.7, 115.0, 115.1, 126.9, 127.0 (C-2'), 129.2, 129.3, 129.7, 132.1 (C-2'), 132.7, 132.8, 132.9, 155.4, 155.5, 156.0, 156.9. HRMS (ESI) calc for $C_{38}H_{40}O_6Na$ [M+Na] 615.2713, found 615.2717.

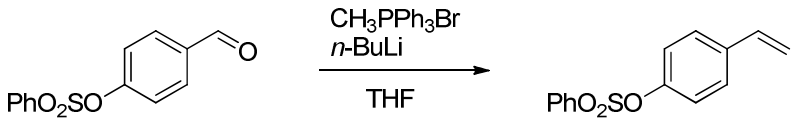
4-(Benzenesulfoxy)benzaldehyde 32



32

4-Hydroxybenzaldehyde (2.5g, 20.47 mmol) was suspended in CH_2Cl_2 (35 ml) under N_2 and cooled to 0 °C. Benzenesulfonyl chloride (2.6 ml, 20.47 mmol) and triethylamine (2.8 ml, 20.47 mmol) were added dropwise, the reaction was warmed to room temperature and stirred for 2 hrs. 1M HCl (30 ml) was added and the reaction mixture was washed with 1M HCl (2 x 30 ml). The organic phase was dried over $MgSO_4$ and concentrated *in vacuo* to give aldehyde **32** (5.34 g, 20.36 mmol, 99%) as a colorless solid mp 78-79 °C, lit mp 81-82 °C[6]; δ_H (400 MHz, $CDCl_3$) 7.09 – 7.24 (2H, m, Ar), 7.48 – 7.60 (2H, m, OSO_2*Ph*), 7.68 (1H, m, OSO_2*Ph*), 7.78 – 7.88 (4H, m, OSO_2*Ph* & Ar), 9.97 (1H, s, 1-H); δ_C (101 MHz, $CDCl_3$) 123.0, 128.4, 129.3, 131.3, 134.6, 134.9, 135.1, 153.7, 190.6 (C-1).
Spectroscopic data in accordance with literature data.[7]

(4'-Benzenesulfoxyphenyl)ethene 33

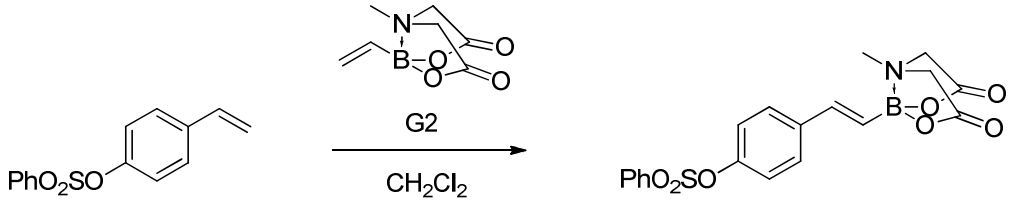


32 **33**

n-Butyllithium (5 ml, 7.85 mmol, 1.57 M in hexanes) was added dropwise to a stirring suspension of methyltriphenylphosphonium bromide (2.73 g, 7.63 mmol) in THF (30 ml) at -78 °C under N_2. After stirring for 0.5 hr, a solution of aldehyde **32** (1.00 g, 3.81 mmol) in THF (10 ml) was added slowly. The reaction was allowed to warm to room temperature overnight then quenched with saturated ammonium chloride (60 ml) and was extracted with diethyl ether (3 x 50 ml). The combined organic phases were dried over $MgSO_4$, concentrated *in vacuo* and purified by flash chromatography using 2% ethyl acetate in petrol as the eluent to yield *styrene* **33** as a colorless oil (603 mg, 2.32 mmol, 61%). ν_{max}/cm^{-1} 3069, 1501, 1372, 1199, 1178, 862, 848; δ_H (400 MHz, $CDCl_3$) 5.27 (1H, d, *J* 11, 2-H*H*), 5.69 (1H, d, *J* 17.5. 2-*H*H),

6.65 (1H, dd, *J* 17.5, 11, 1-H), 6.93 (2H, d, *J* 8.5), 7.31 (2H, d, *J* 8.5), 7.53 (2H, tt, *J* 8, 1, OSO_2Ph), 7.67 (1H, tt, *J* 8, 1, OSO_2Ph), 7.84 (2H, dd, *J* 8, 1, OSO_2Ph); δ_C (101 MHz, $CDCl_3$) 115.0 (C-2), 122.4, 127.3, 128.5, 129.1, 134.2, 135.3, 135.4 (C-1), 136.6, 148.9; HRMS (ESI) calc for $C_{14}H_{12}O_3SNa$ [M+Na] 283.0399 found 283.0409.

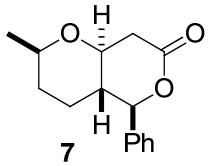
4'-Benzenesulfoxyphenethyl boronic acid MIDA boronate 34



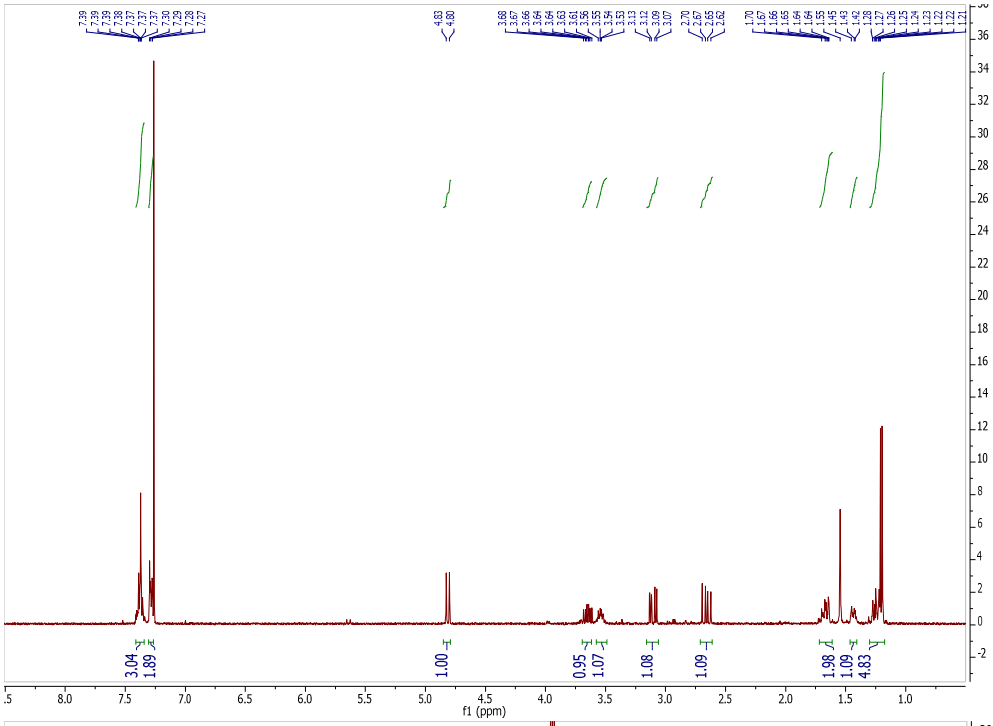
33 **34**

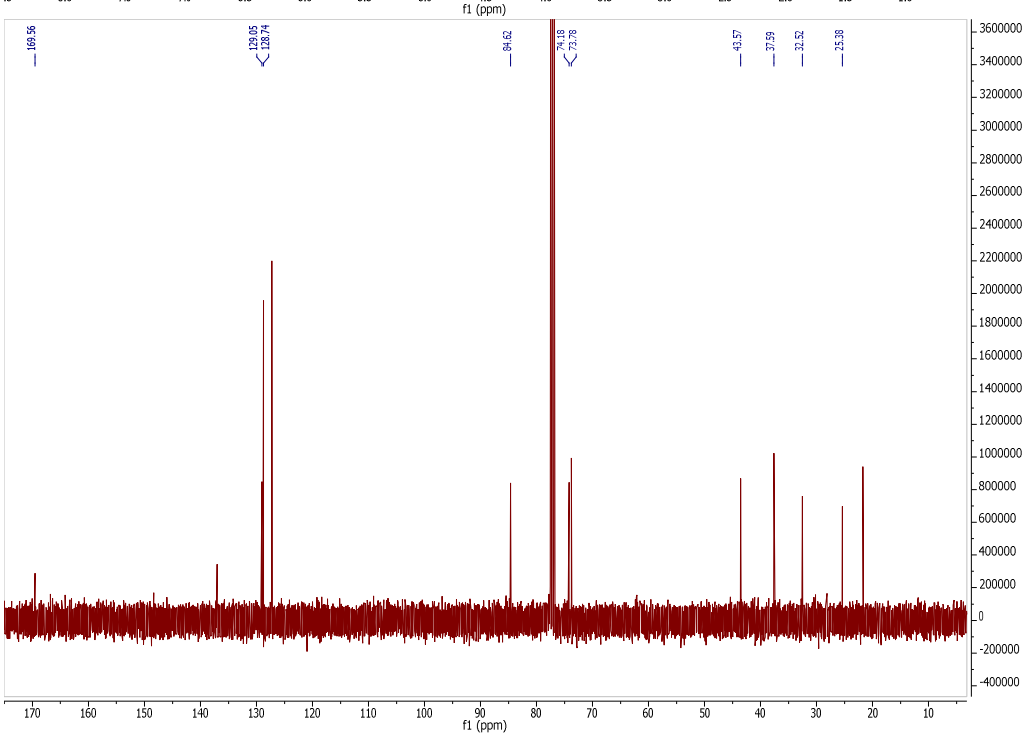
Styene **33** (559 mg, 2.15 mmol), vinyl boronic acid MIDA boronate (260 mg, 1.42 mmol) and Grubbs 2nd generation catalyst (121 mg, 0.14 mmol) were combined in CH_2Cl_2 (20 ml) and heated under reflux for 24 hrs. After cooling to room temperature, solvent was removed *in vacuo* and the residue was purified by column chromatography using 20% acetonitrile in diethyl ether as the eluent to yield *boronate* **34** (457 mg, 1.10 mmol, 77%). mp 174-176 °C; ν_{max}/cm^{-1} 3008, 2963, 1769, 1750, 1503, 1345, 1196, 1174, 1146, 1027, 852; δ_H (400 MHz, acetone) 3.06 (3H, s, CH_3), 4.08 (2H, d, *J* 17), 4.26 (2H, d, *J* 17), 6.35 (1H, d, *J* 18), 6.91 (1H, d, *J* 18), 7.00 (2H, d, *J* 8.5, Ar), 7.51 (1H, d, *J* 8.5, Ar), 7.62 – 7.72 (2H, m, OSO_2Ph), 7.82 (1H, m, OSO_2Ph), 7.84 – 7.91 (2H, m, OSO_2Ph); HRMS (CI) calc for $C_{19}H_{19}BNO_7S$ [M+H] 416.0975 found 416.0965.

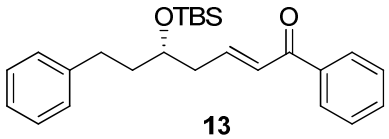
NMR Spectra of novel compounds



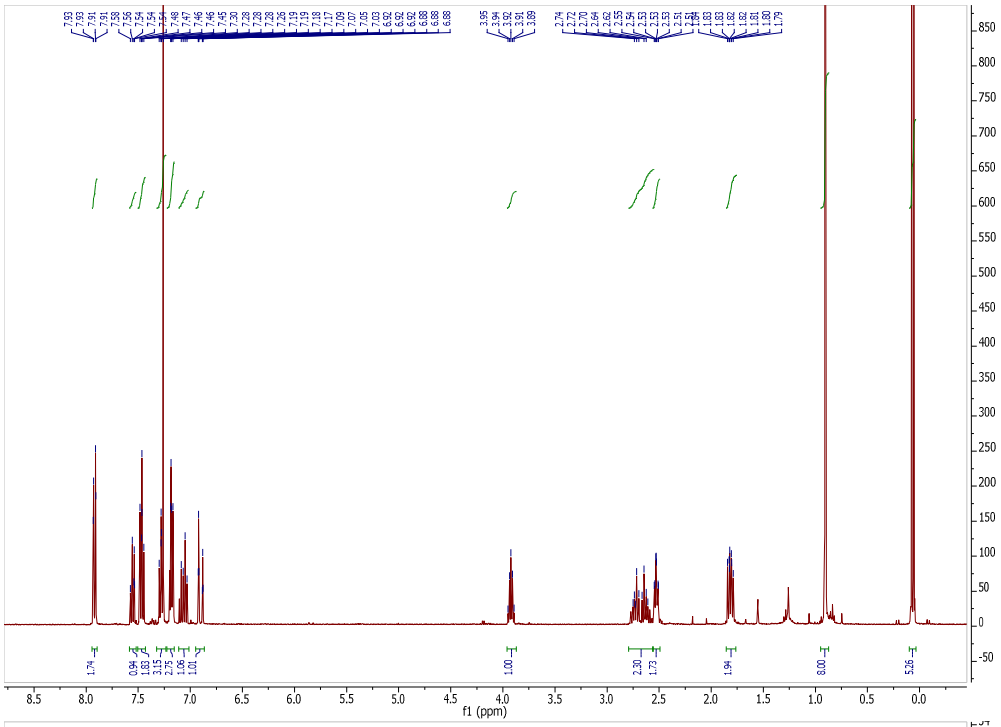
7

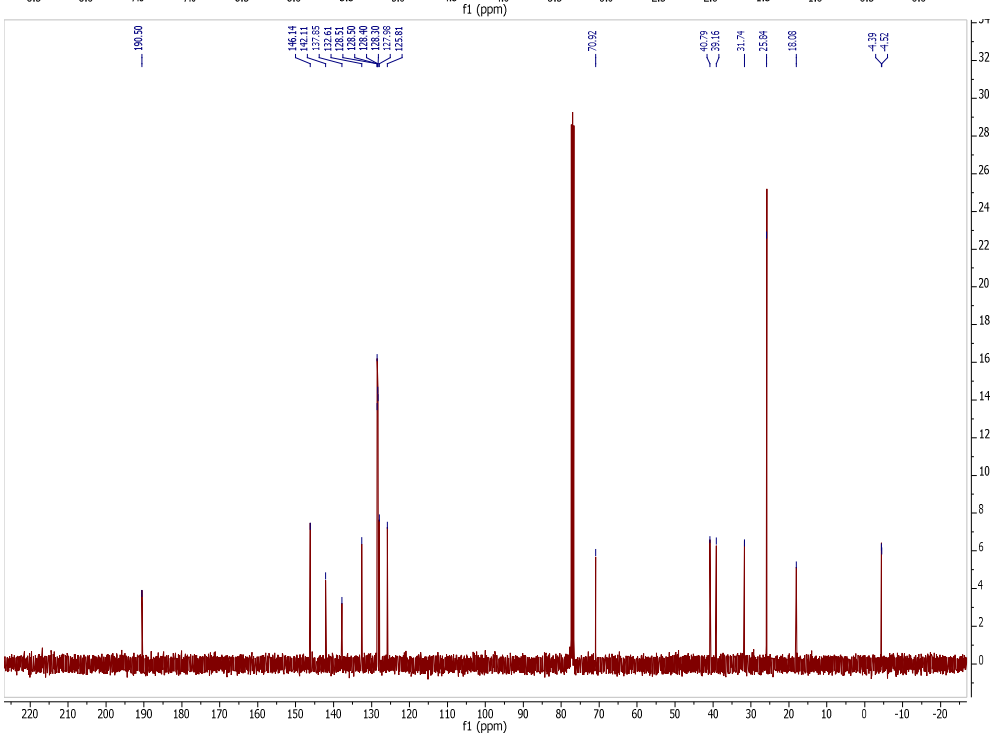


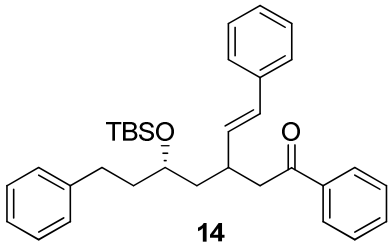




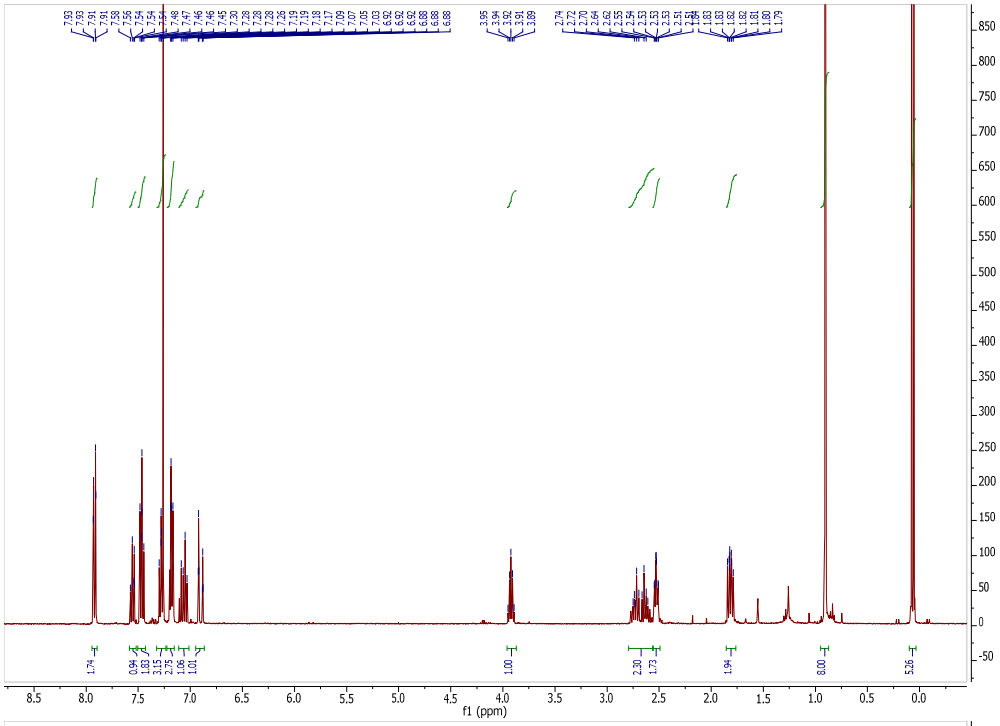
13

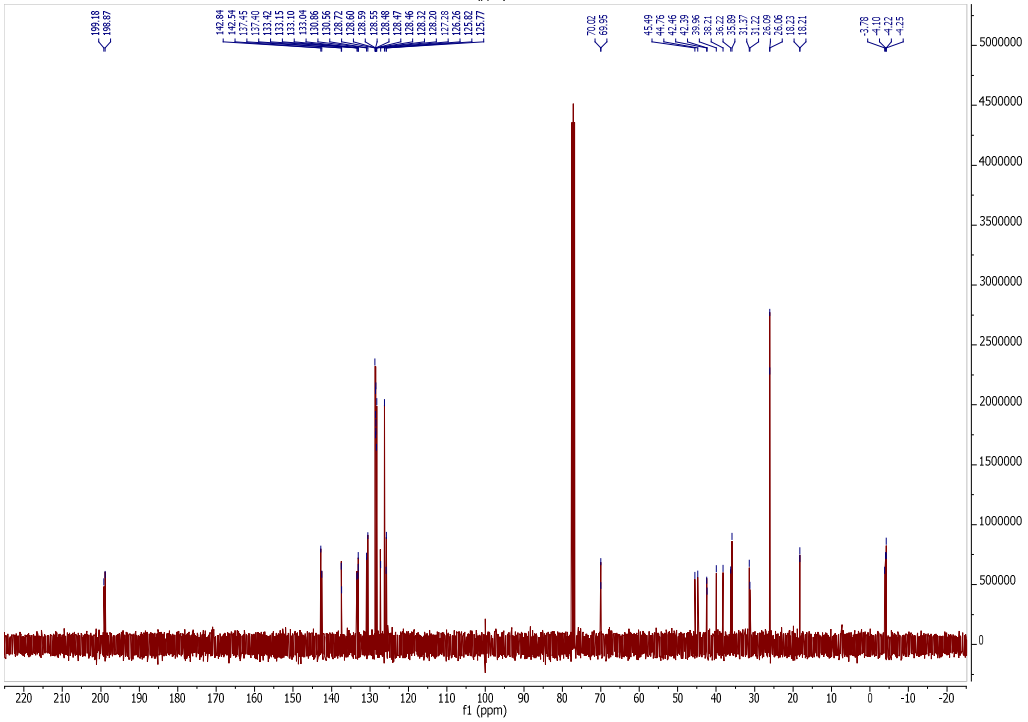


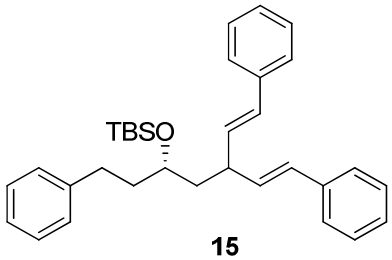




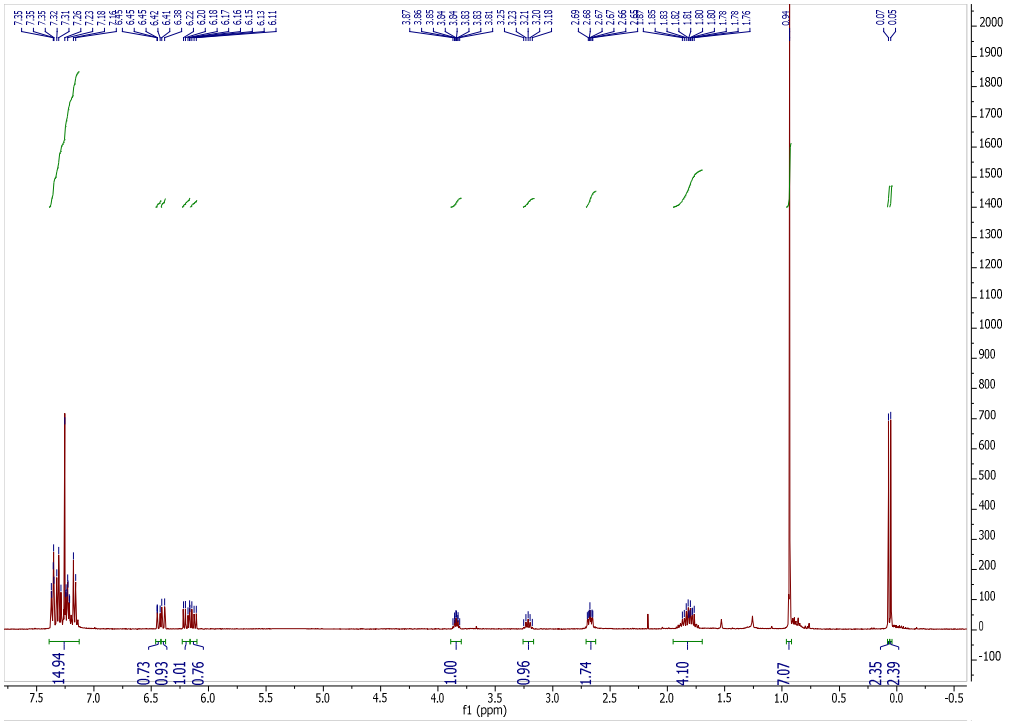
14






TBSO

15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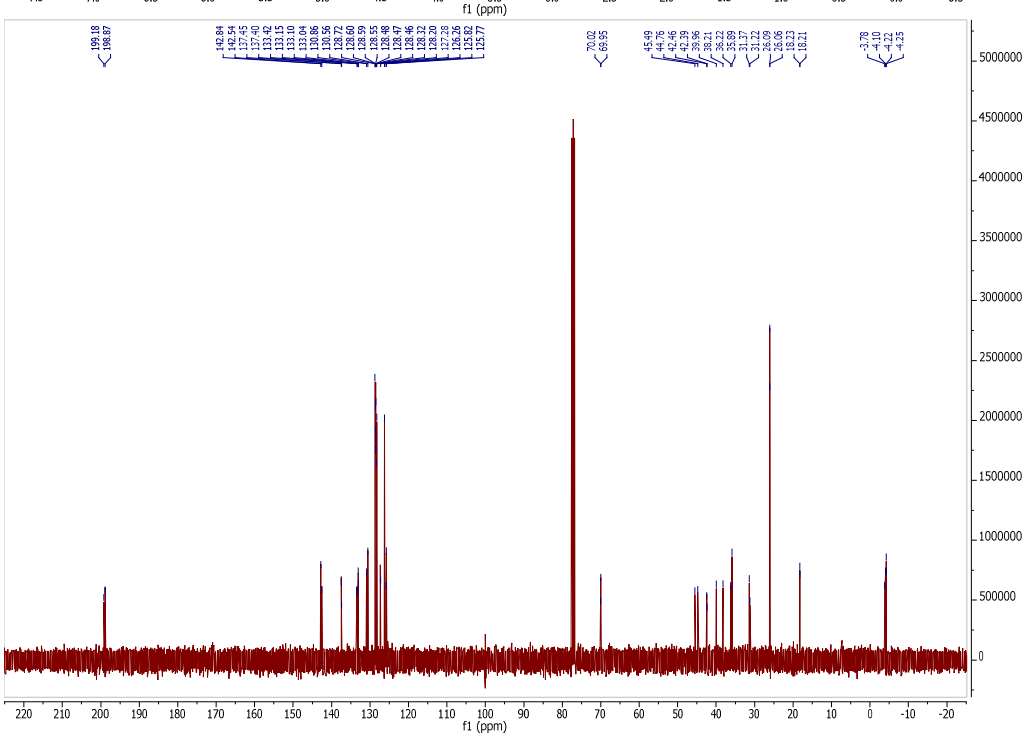
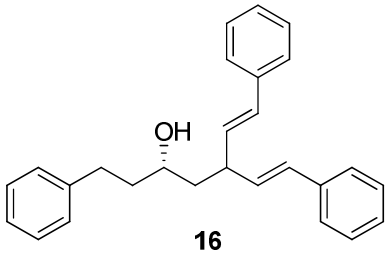
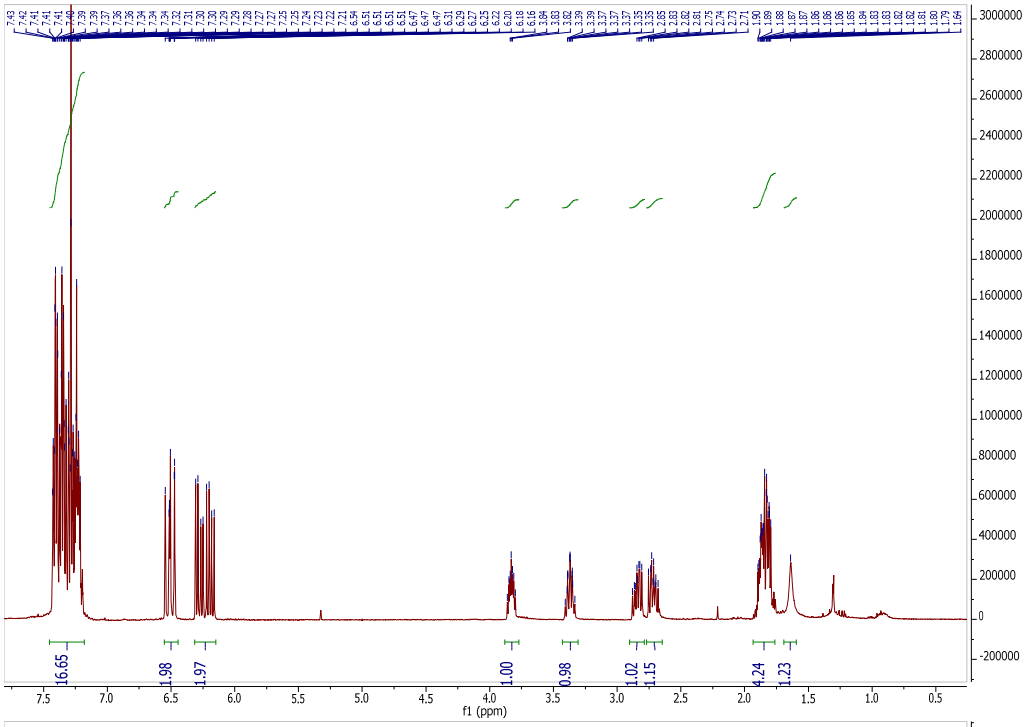
0.93
1.01
0.76
1.00
0.96
1.74
4.10
7.07
2.35
2.39
f1 (ppm)


f1 (ppm)


OH

16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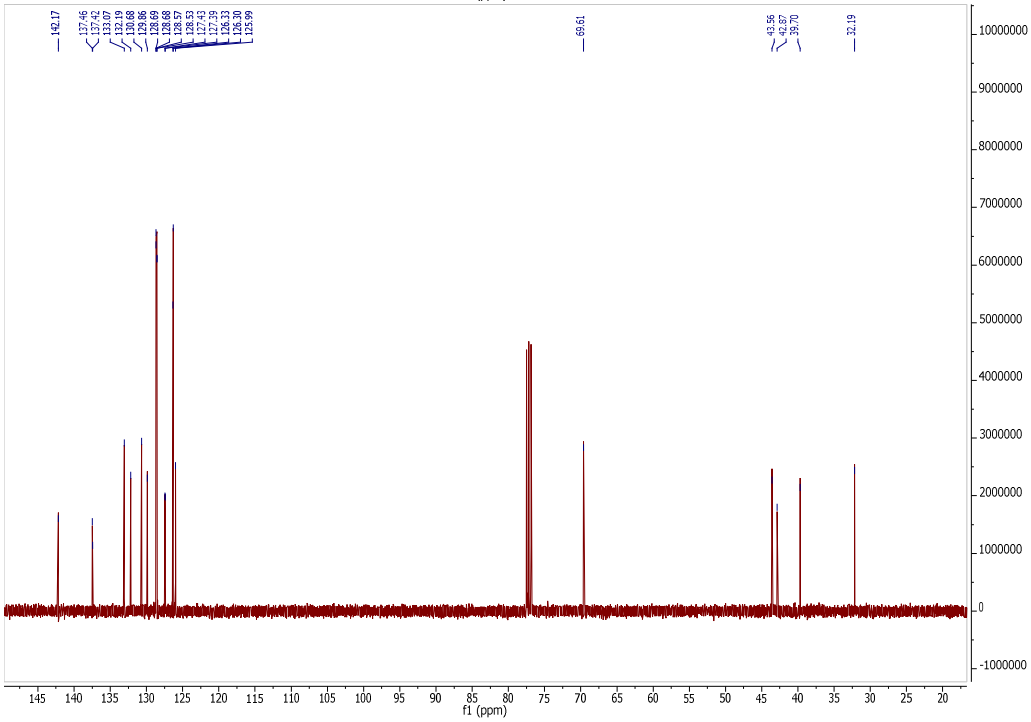
1.00
0.98
1.02
1.15
4.24
1.23
f1 (ppm)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132.19
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128.69
128.68
128.57
128.53
127.43
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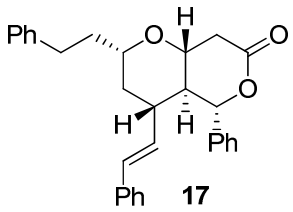
42.87
39.70
32.19
f1 (ppm)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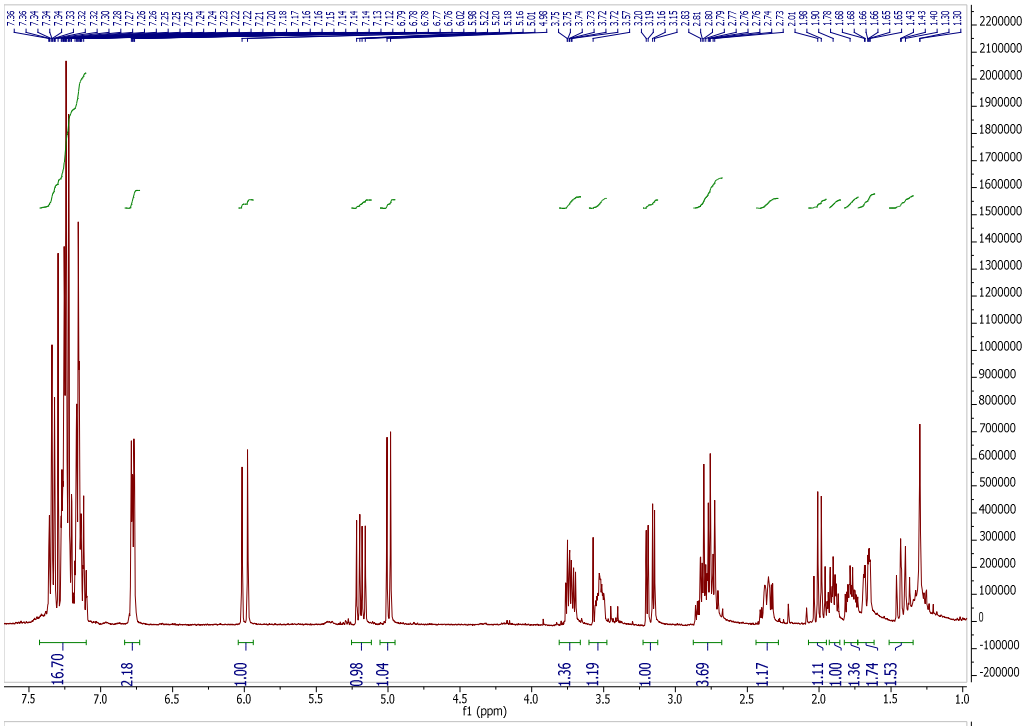
H
O
O
H
H
Ph
Ph

17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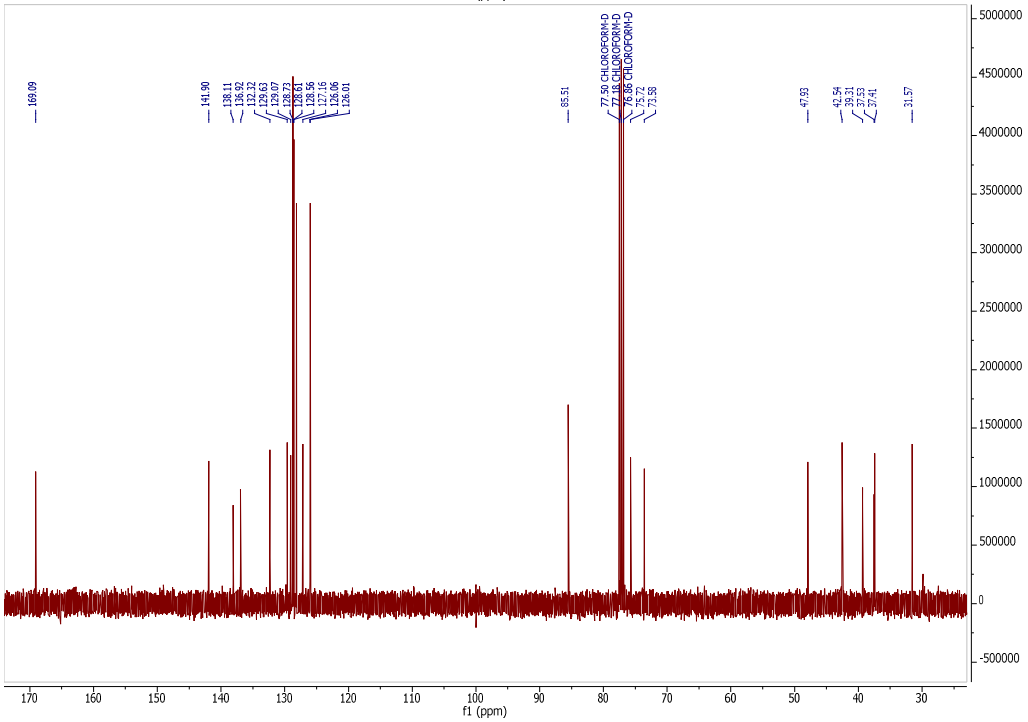
0.98
1.04
1.36
1.19
1.00
3.69
1.17
1.11
1.00
1.36
1.74
1.53
f1 (ppm)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132.12
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128.73
128.61
128.56
127.16
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85.51
77.50 CHLOROFORM-D
77.18 CHLOROFORM-D
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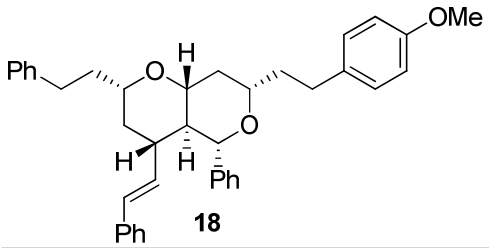
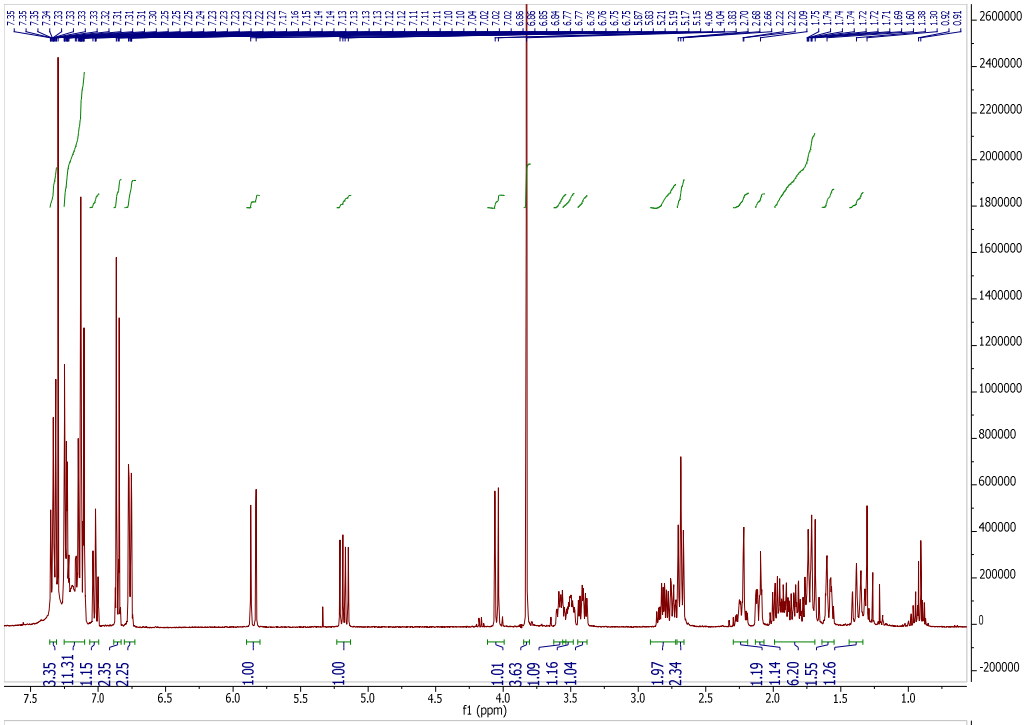
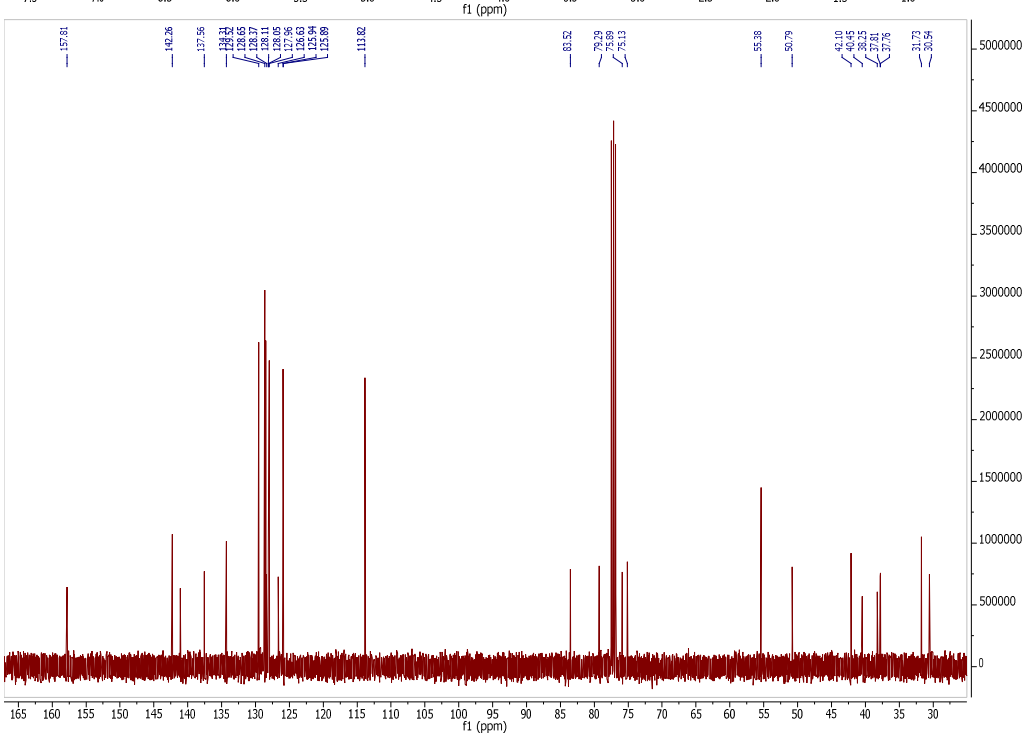
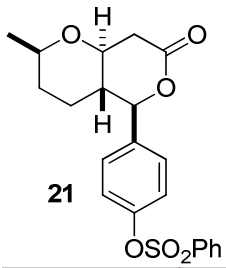
f1 (ppm)


OMe
Ph
O
H
O
H
H
Ph
Ph

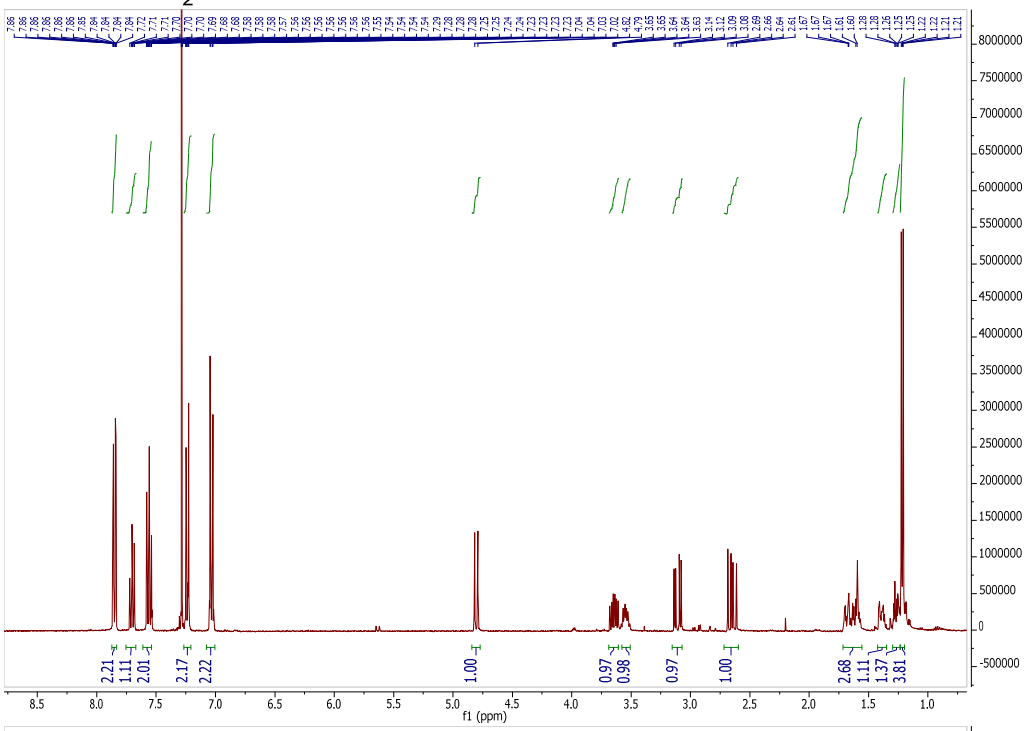
18

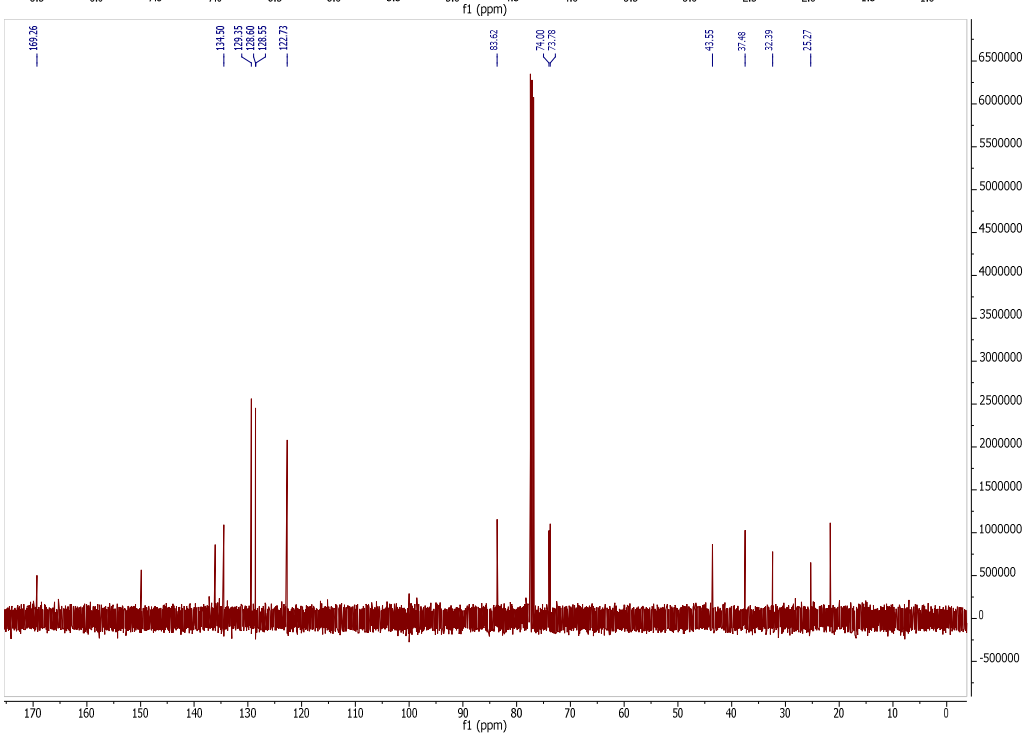

3.35
11.31
1.15
2.35
2.25
1.00
1.00
1.01
3.63
1.09
1.16
1.04
1.97
2.34
1.19
1.14
6.20
1.55
1.26
f1 (ppm)

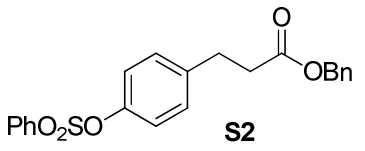

157.81
142.26
137.56
113.82
83.52
79.29
75.89
75.13
55.38
50.79
42.10
40.45
38.25
37.81
37.76
31.73
30.54
f1 (ppm)


H
O
O
O
H
OSO2Ph

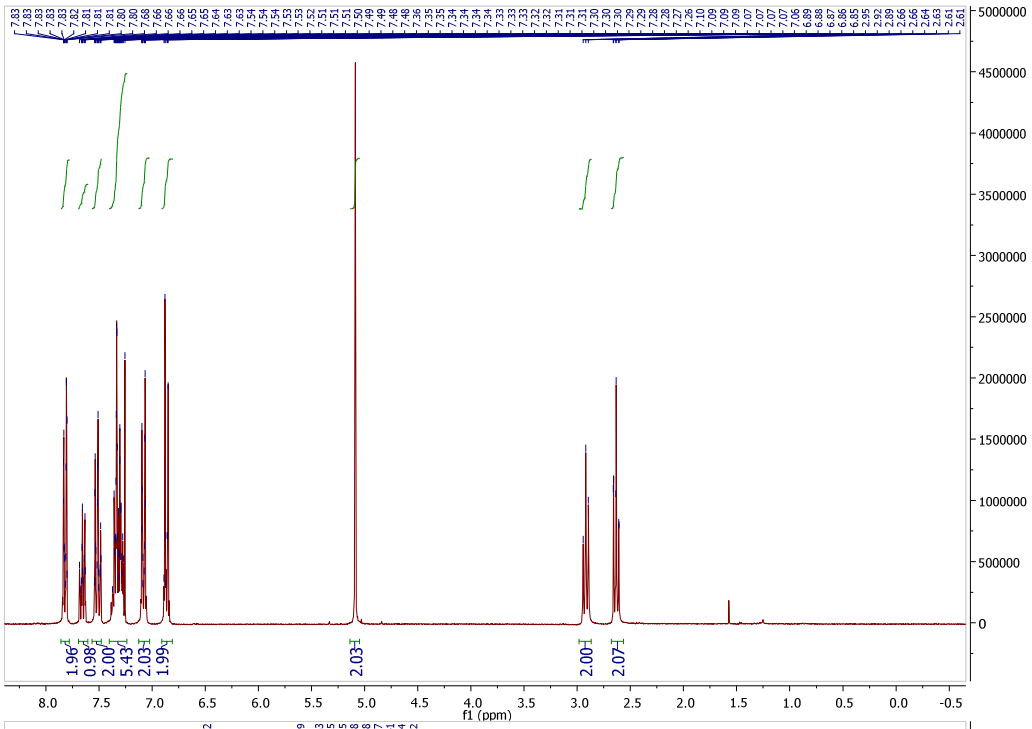
21

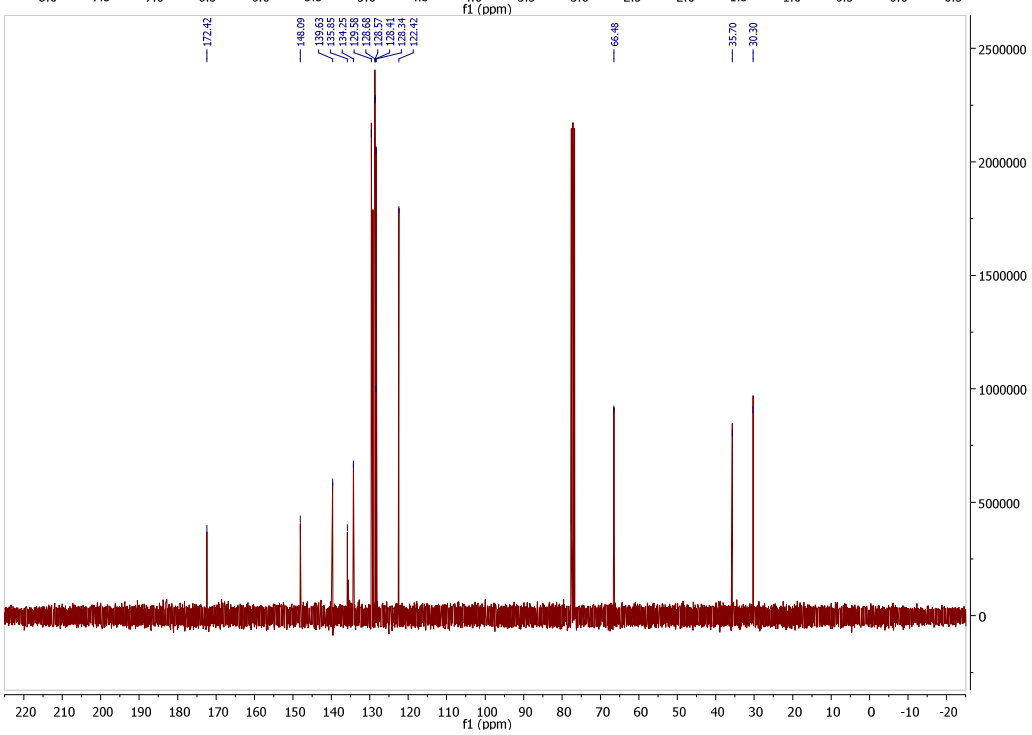

2.21
1.11
2.01
2.17
2.22
1.00
0.97
0.98
0.97
1.00
2.68
1.11
1.37
3.81
f1 (ppm)

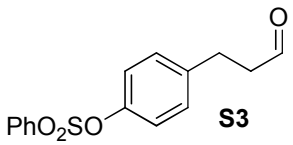

169.26
134.50
129.35
128.60
128.55
122.73
83.62
74.00
73.78
43.55
37.48
32.39
25.27
f1 (ppm)


O
OBn
PhO2SO

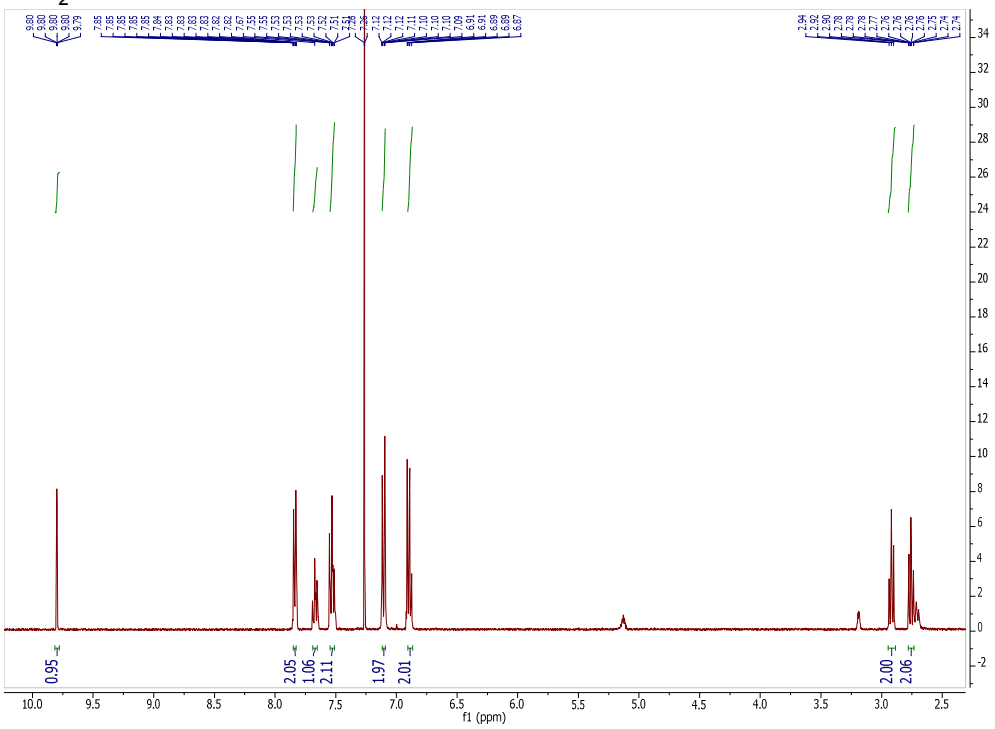
S2

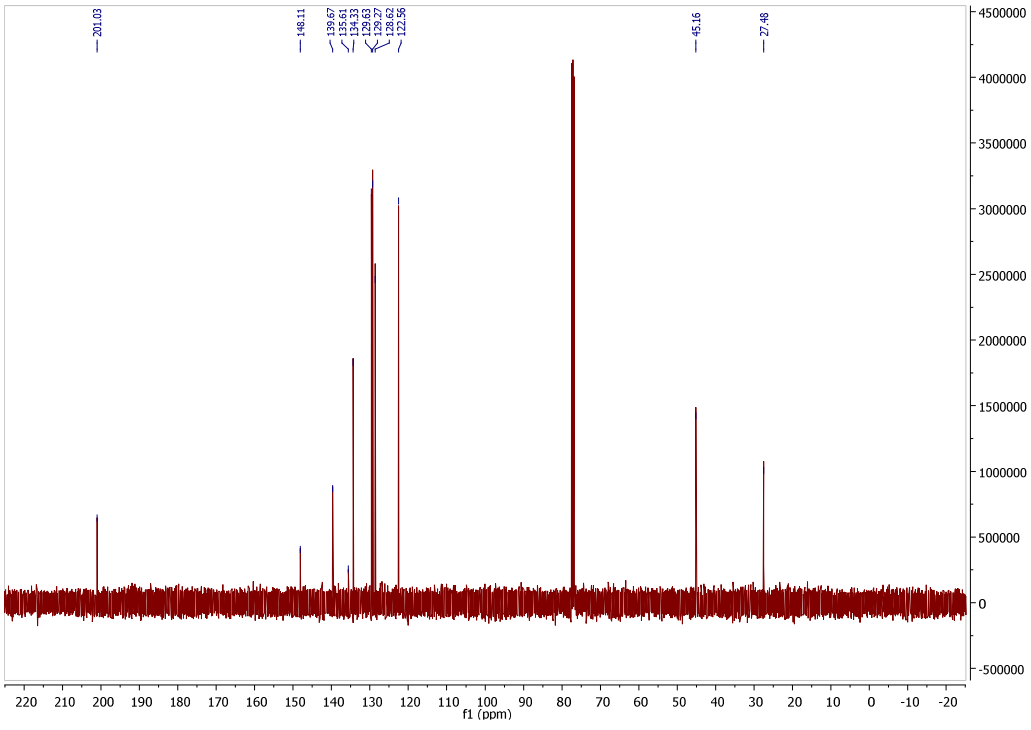

1.96
0.98
2.00
5.43
2.03
1.99
2.03
2.00
2.07
f1 (ppm)

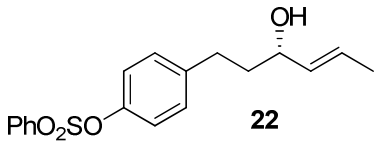

172.42
148.09
139.63
135.85
134.25
129.58
128.68
128.57
128.41
128.34
122.42
66.48
35.70
30.30
f1 (ppm)


O
PhO2SO

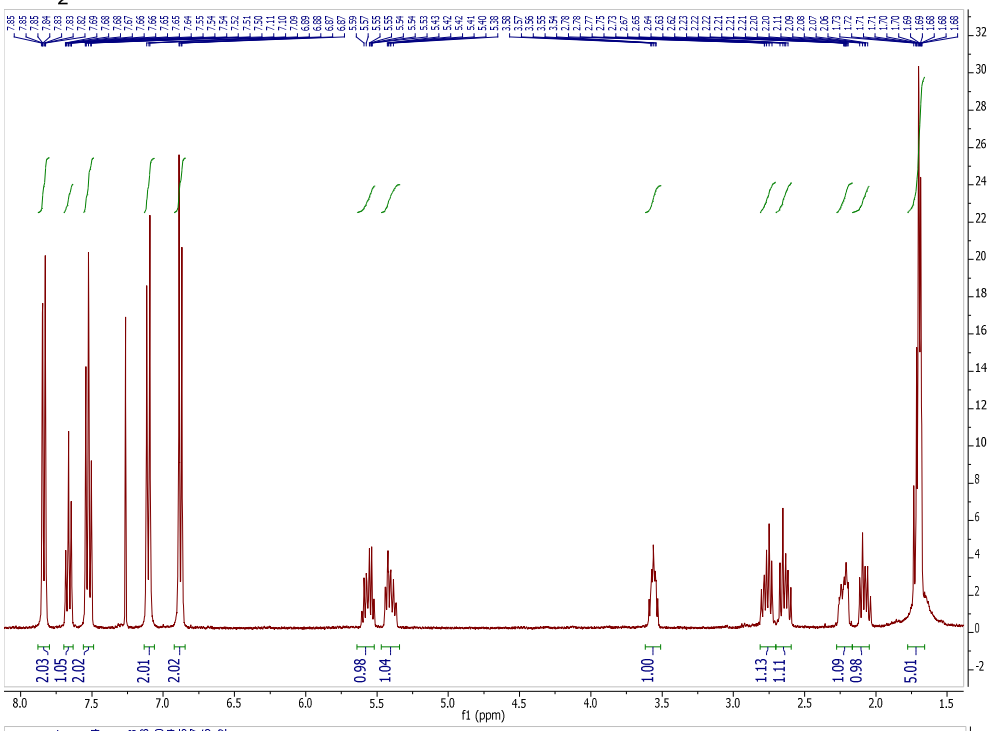
S3

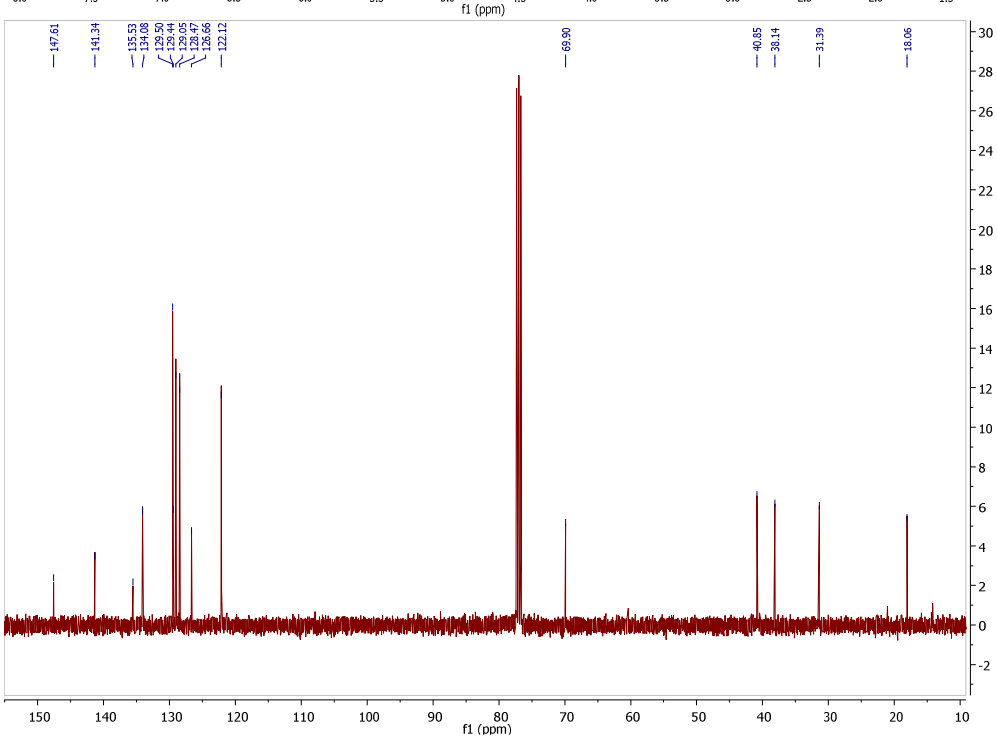

0.95
2.05
1.06
2.11
1.97
2.01
2.00
2.06
f1 (ppm)

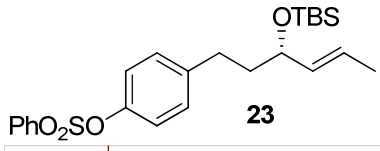

201.03
148.11
139.67
135.61
134.33
129.63
129.27
128.62
122.56
45.16
27.48
f1 (ppm)


OH
PhO2SO

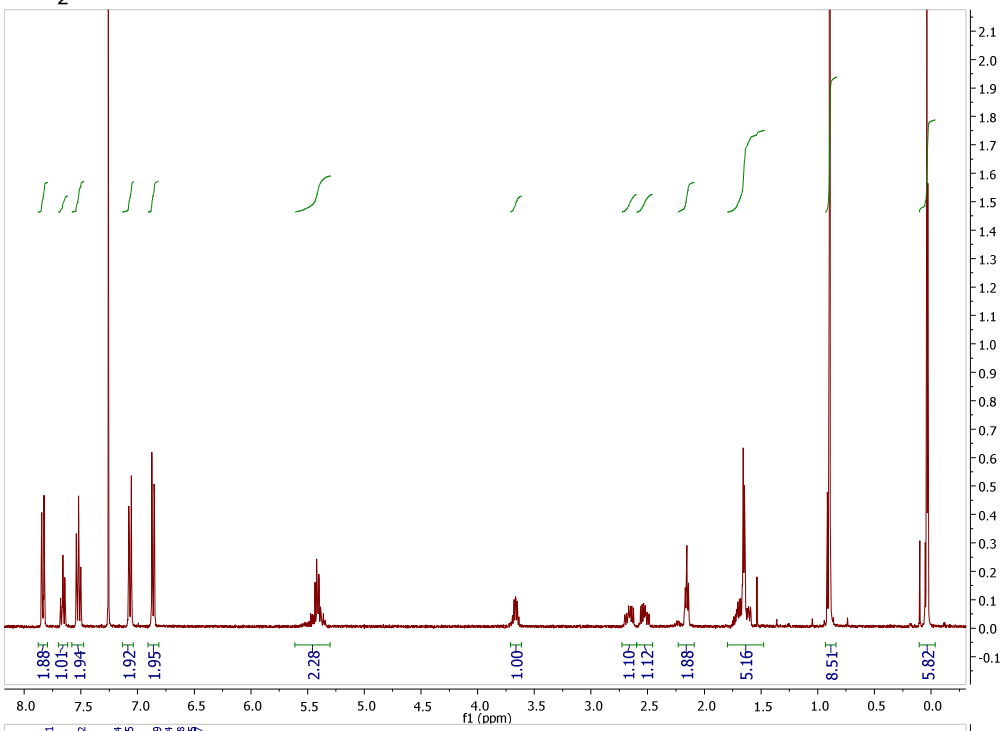
22

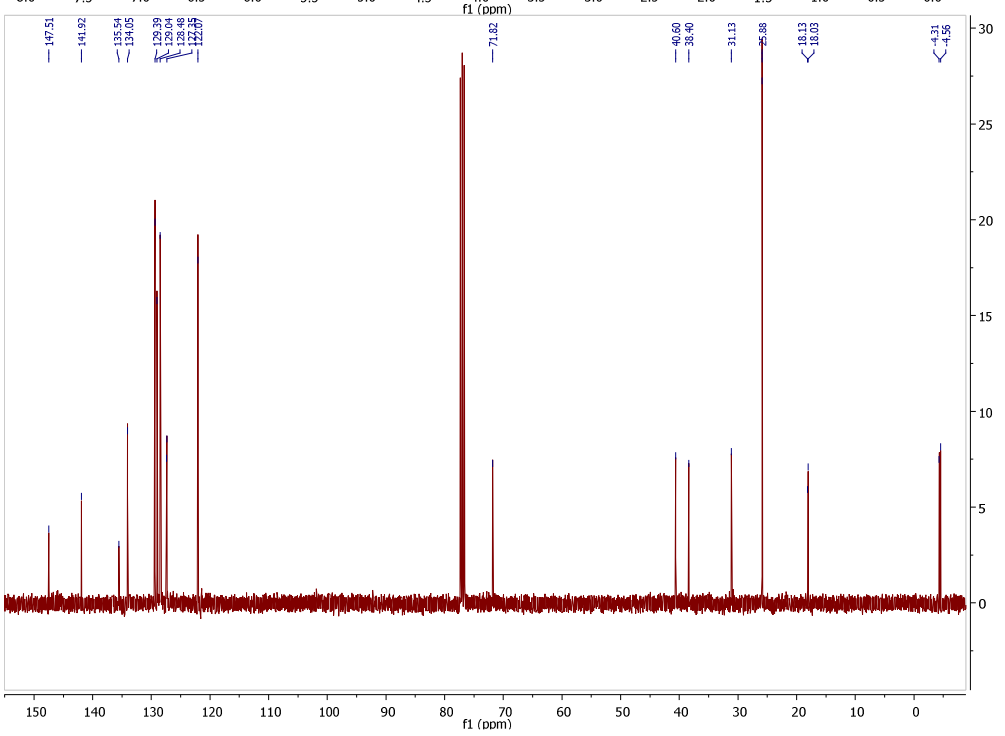

2.03
1.05
2.02
2.01
2.02
0.98
1.04
1.00
1.13
1.11
1.09
0.98
5.01
f1 (ppm)

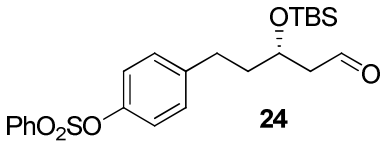

147.61
141.34
135.53
134.08
129.50
129.44
129.05
128.47
126.66
122.12
69.90
40.85
38.14
31.39
18.06
f1 (ppm)


OTBS
PhO2SO

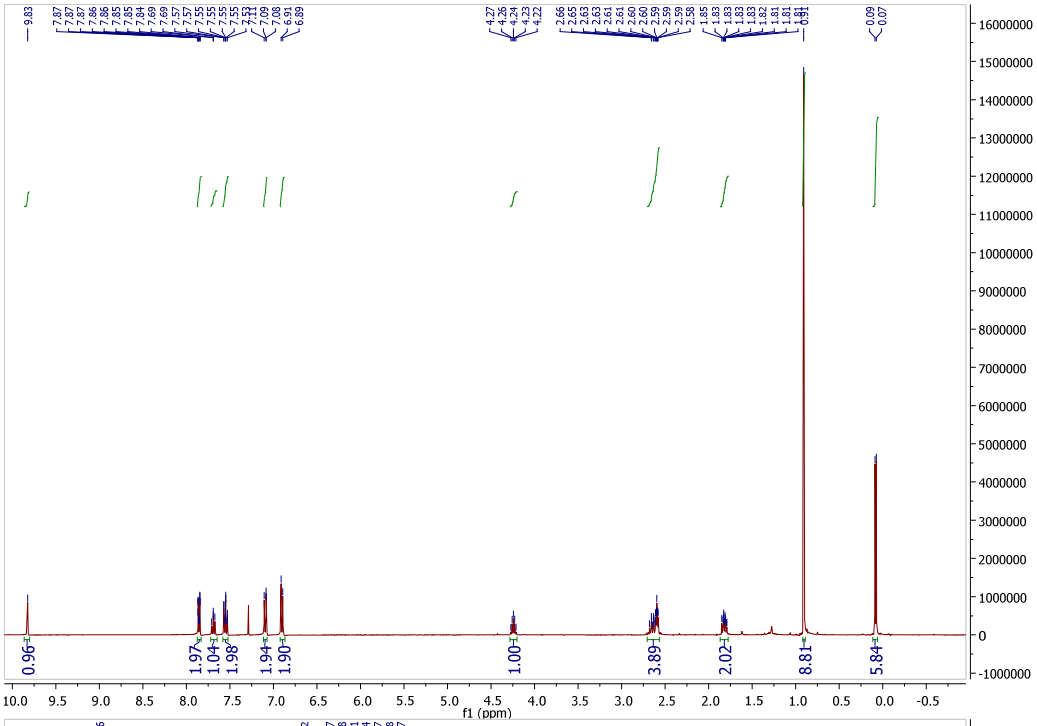
23

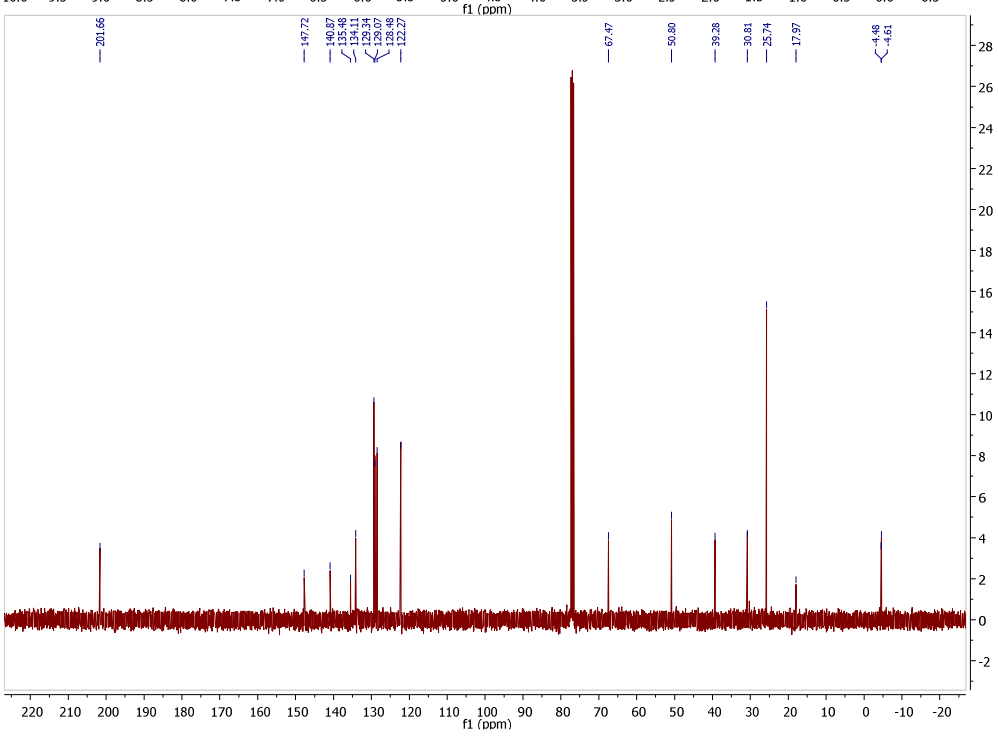

1.88
1.01
1.94
1.92
1.95
2.28
1.00
1.10
1.12
1.88
5.16
8.51
5.82
f1 (ppm)

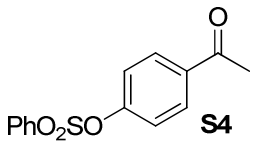

147.51
141.92
135.54
134.05
129.39
129.04
128.48
127.45
122.07
71.82
40.60
38.40
31.13
25.88
18.13
18.03
-4.31
-4.56
f1 (ppm)


OTBS
O
PhO2SO

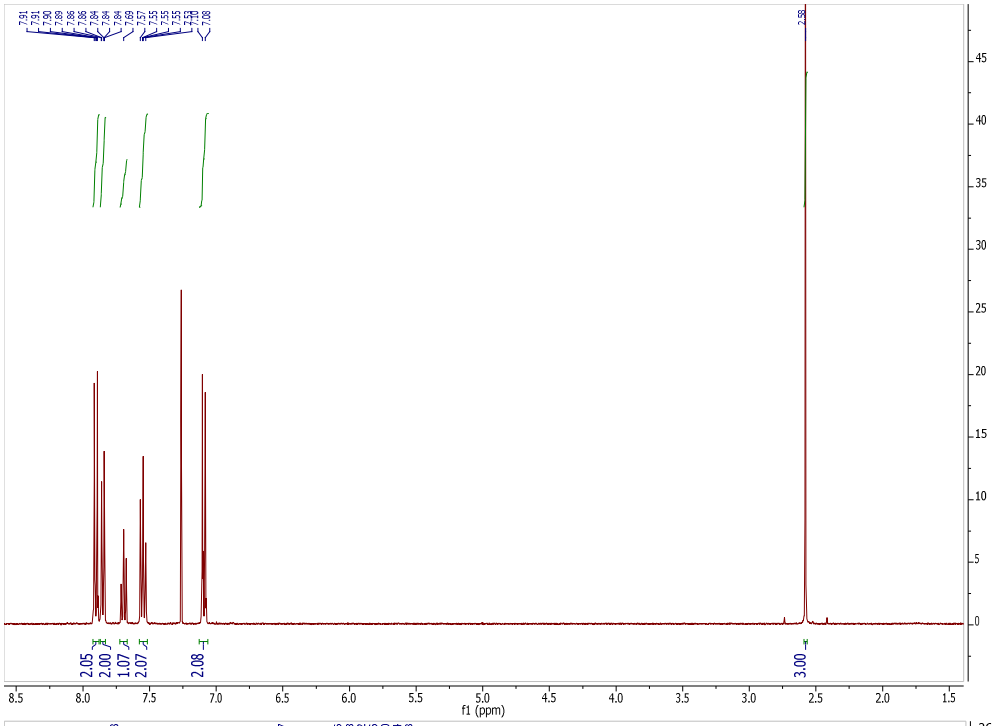
24

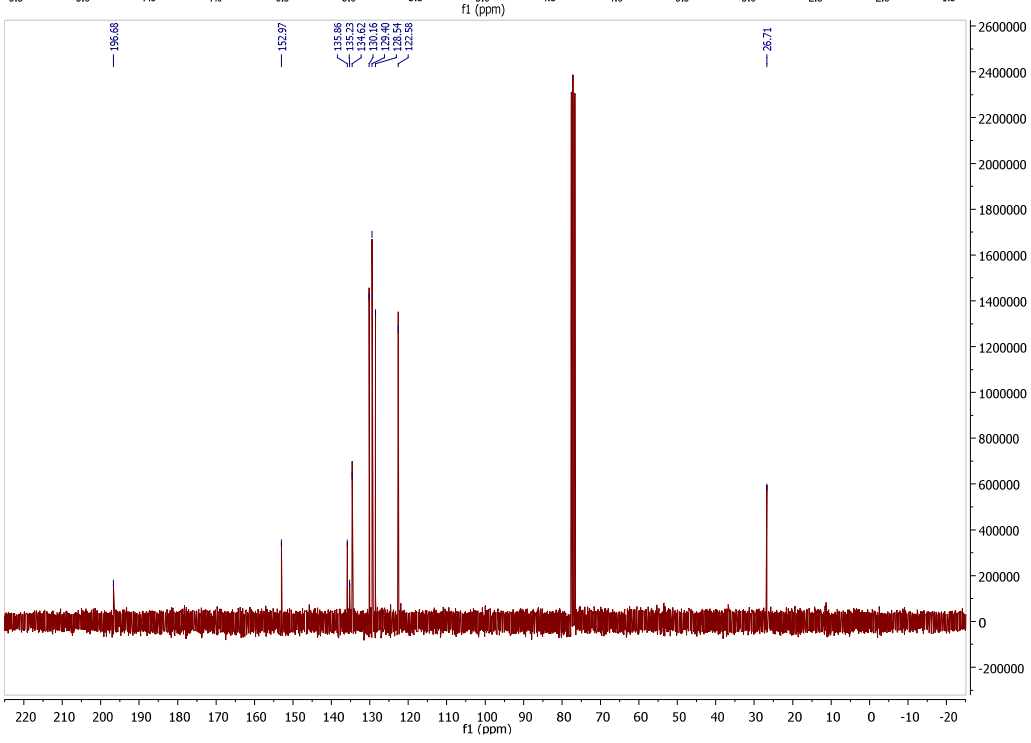

9.83
7.87
7.87
7.87
7.86
7.86
7.85
7.85
7.84
7.69
7.69
7.57
7.57
7.55
7.55
7.55
7.55
7.11
7.11
7.09
7.08
6.91
6.89
4.27
4.26
4.24
4.23
4.22
2.66
2.65
2.63
2.63
2.61
2.61
2.60
2.60
2.59
2.59
2.59
2.58
1.85
1.83
1.83
1.83
1.82
1.81
1.81
0.91
0.91
0.09
0.07
0.96
1.97
1.04
1.98
1.94
1.90
1.00
3.89
2.02
8.81
5.84
f1 (ppm)

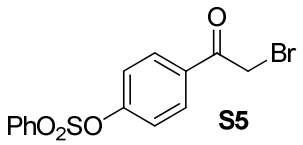

201.66
147.72
140.87
135.48
134.11
129.34
129.07
128.48
122.27
67.47
50.80
39.28
30.81
25.74
17.97
4.48
4.61
f1 (ppm)


O
PhO2SO

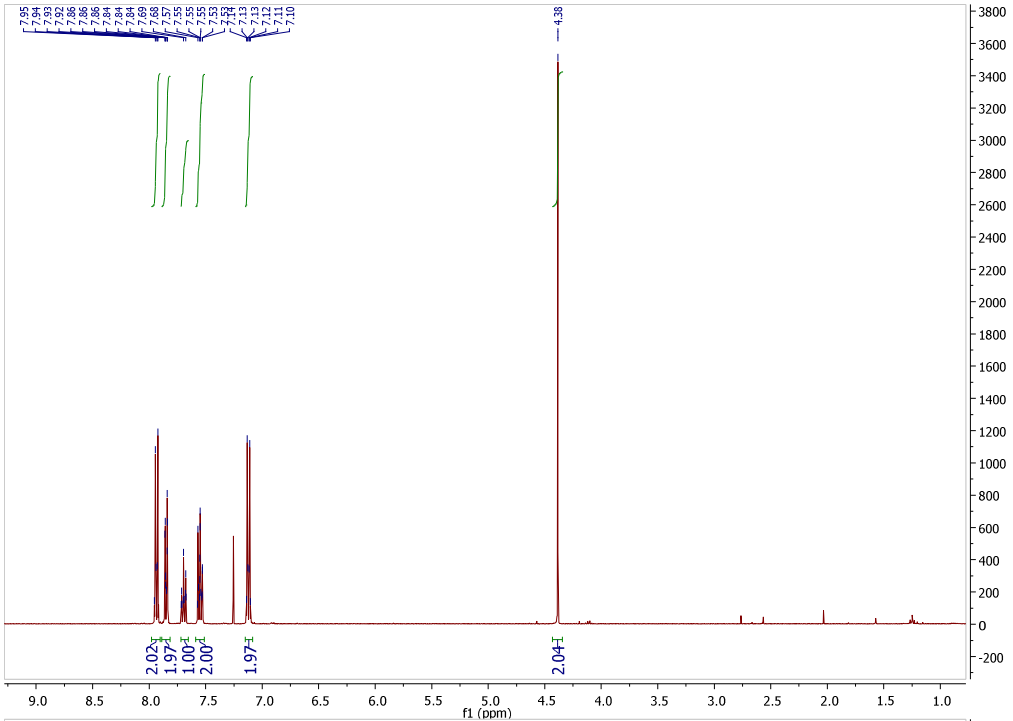
S4

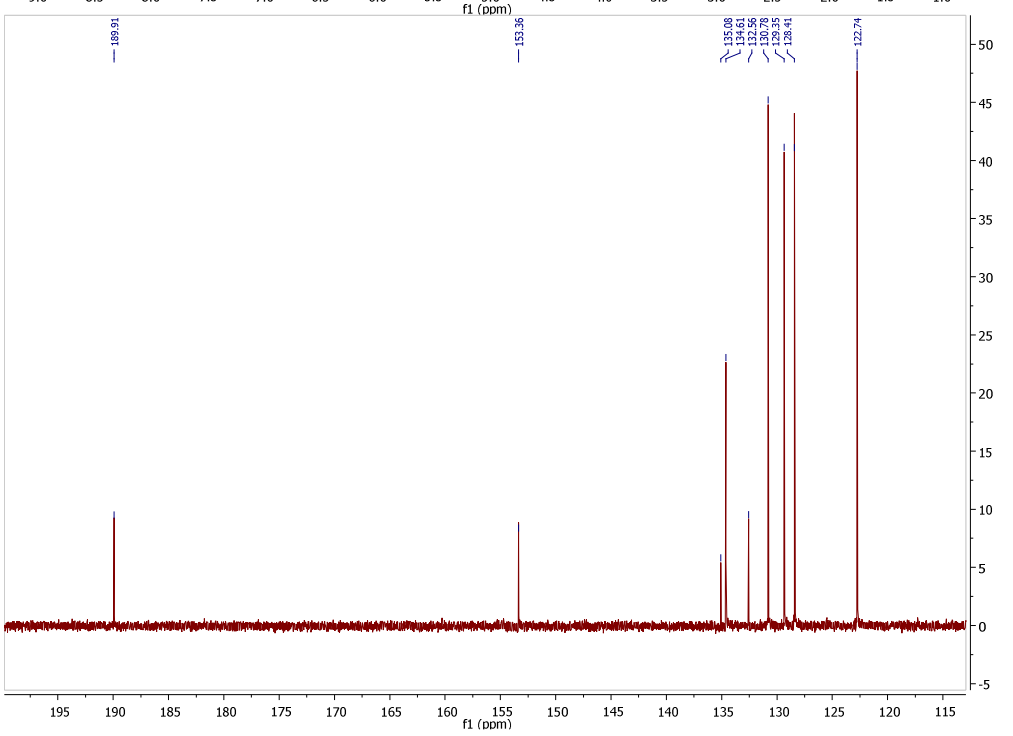

7.91
7.91
7.90
7.89
7.88
7.88
7.86
7.84
7.84
7.69
7.57
7.55
7.55
7.53
7.10
7.08
2.58
2.05
2.00
1.07
2.07
2.08
3.00
f1 (ppm)

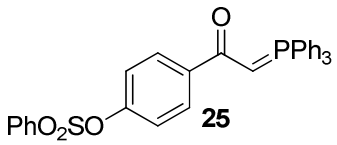

196.68
152.97
135.86
135.23
134.62
130.45
129.40
128.54
122.58
26.71
f1 (ppm)


O
Br
PhO2SO

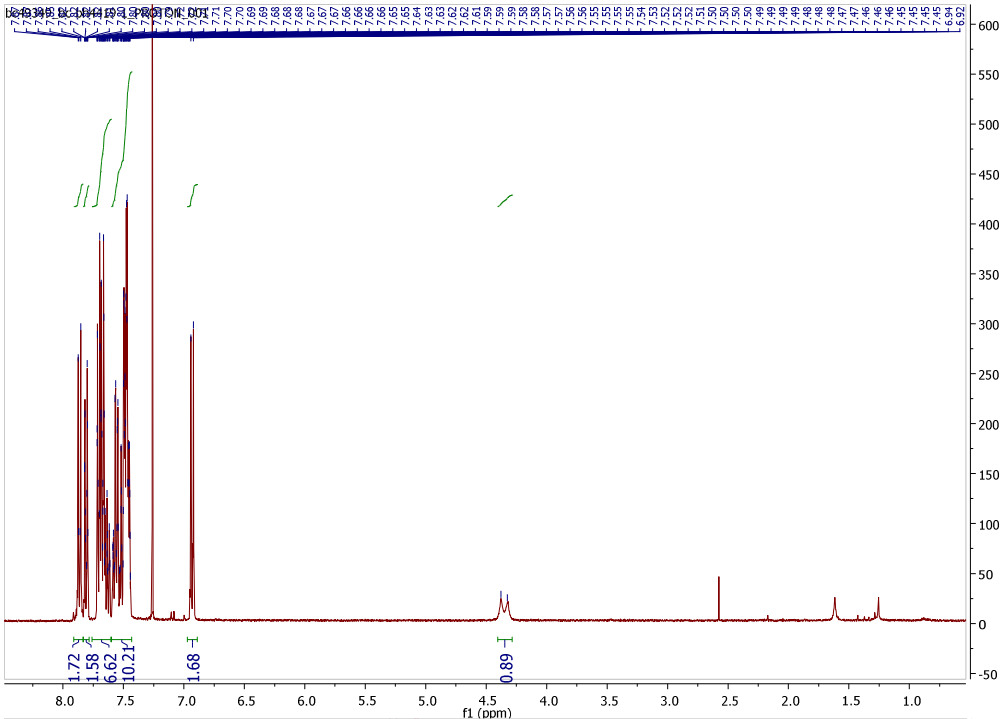
S5

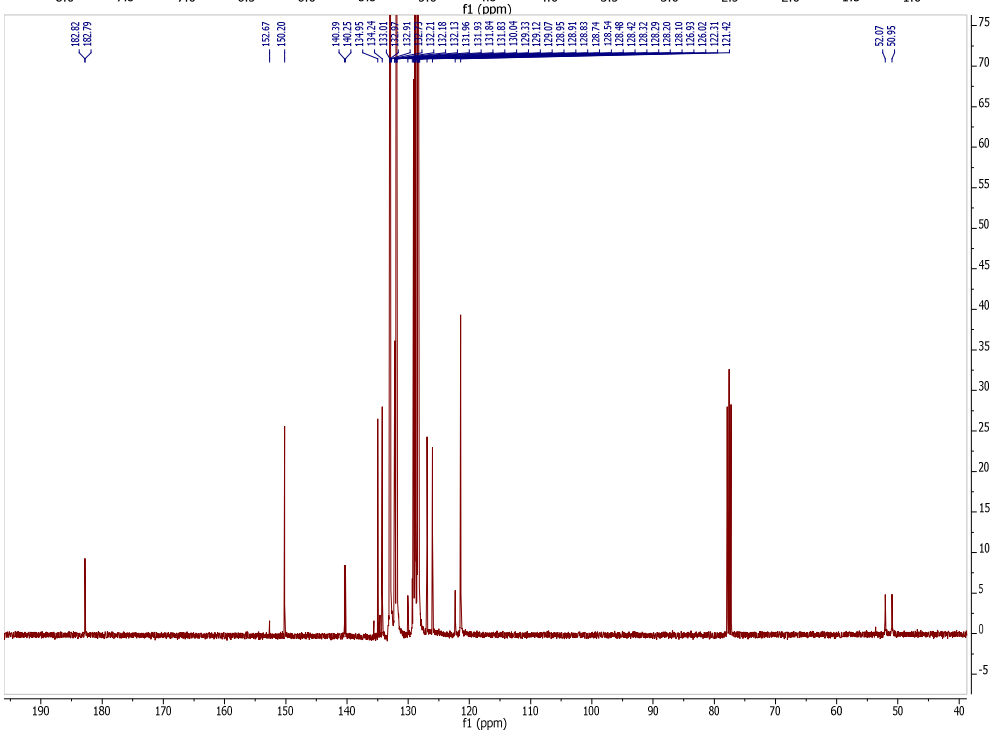

7.95
7.94
7.93
7.92
7.86
7.86
7.86
7.84
7.84
7.84
7.69
7.68
7.57
7.55
7.55
7.55
7.53
7.14
7.13
7.12
7.11
7.10
4.38
2.02
1.97
1.00
2.00
1.97
2.04
f1 (ppm)

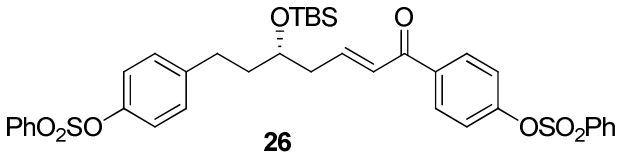

189.91
153.36
135.08
134.61
132.56
130.20
129.35
128.41
122.74
f1 (ppm)


O
PPh3
PhO2SO

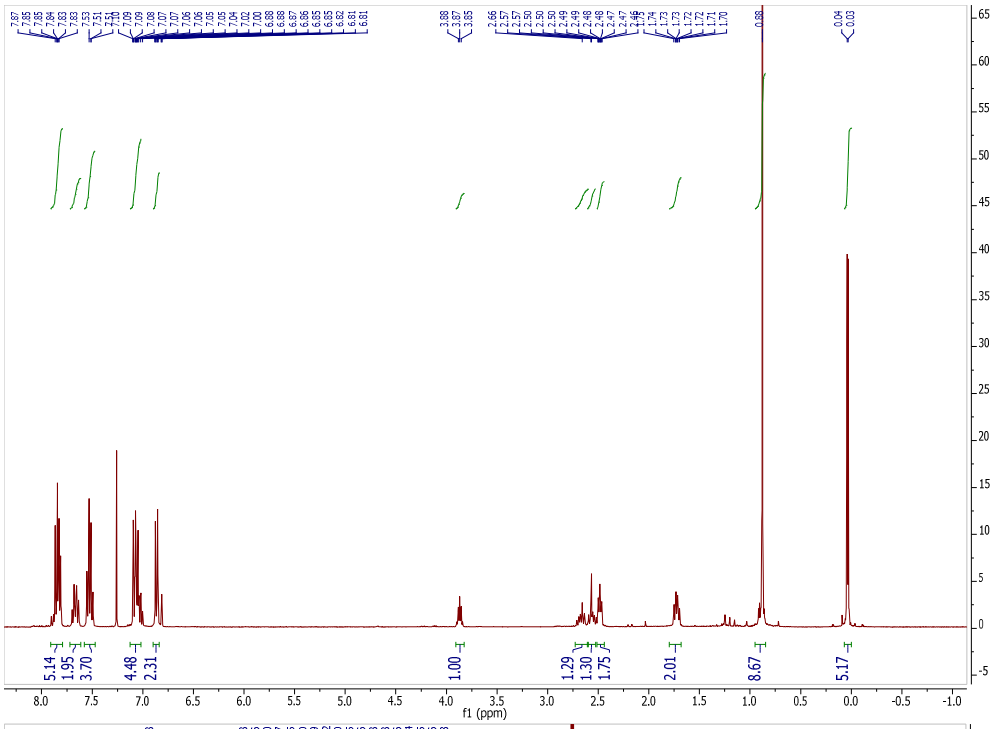
25

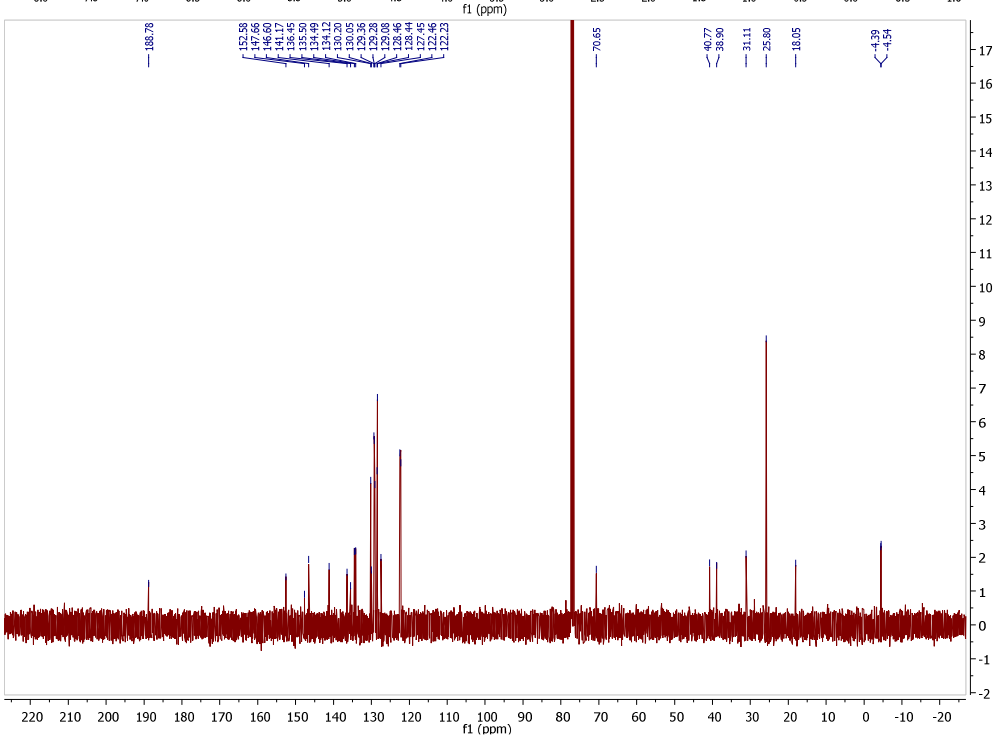

1.72
1.58
6.62
10.21
1.68
0.89
f1 (ppm)

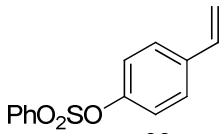

182.82
182.79
152.67
150.20
140.39
140.25
134.45
134.24
133.01
57.07
56.95
f1 (ppm)


OTBS
O
PhO2SO
OSO2Ph

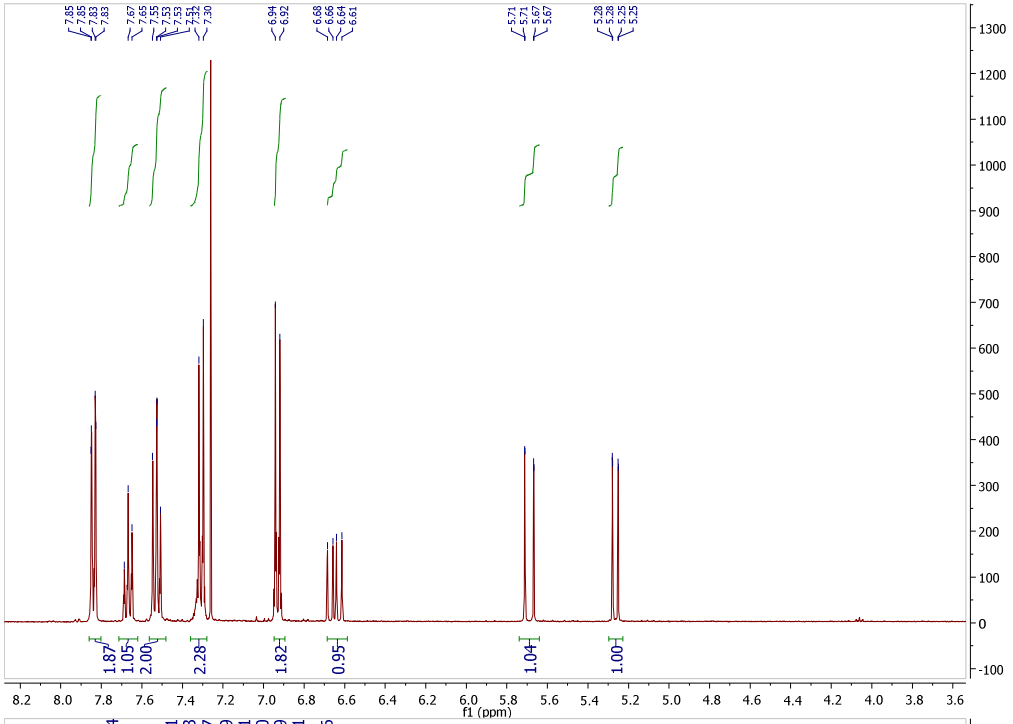
26

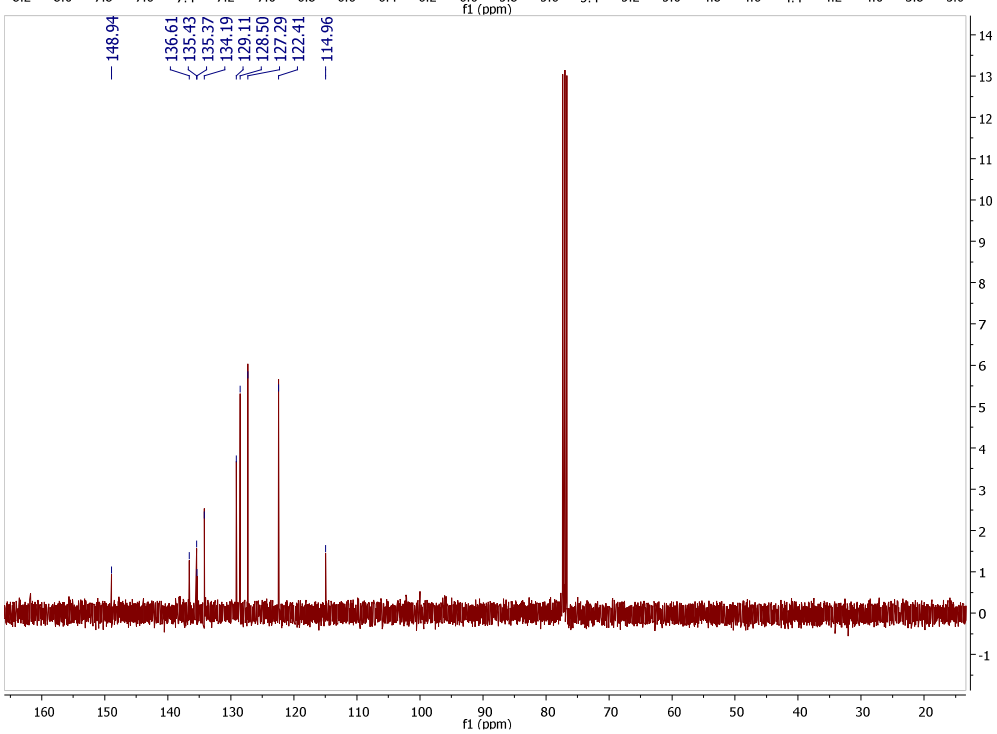

5.14
1.95
3.70
4.48
2.31
1.00
1.29
1.30
1.75
2.01
8.67
5.17
f1 (ppm)

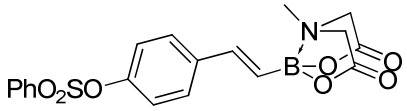

188.78
152.58
147.66
146.60
141.17
136.45
135.56
134.49
134.12
130.20
130.05
129.36
129.28
128.08
128.46
128.44
127.45
122.46
122.23
70.65
40.77
38.90
31.11
25.80
18.05
-4.39
-4.54
f1 (ppm)


PhO2SO

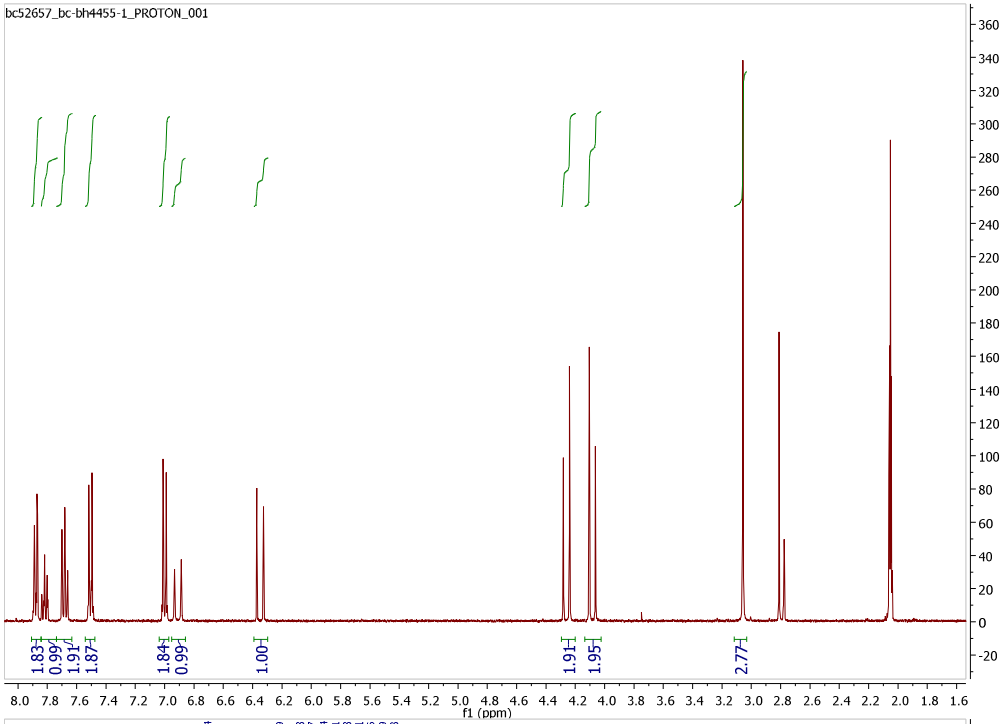
33

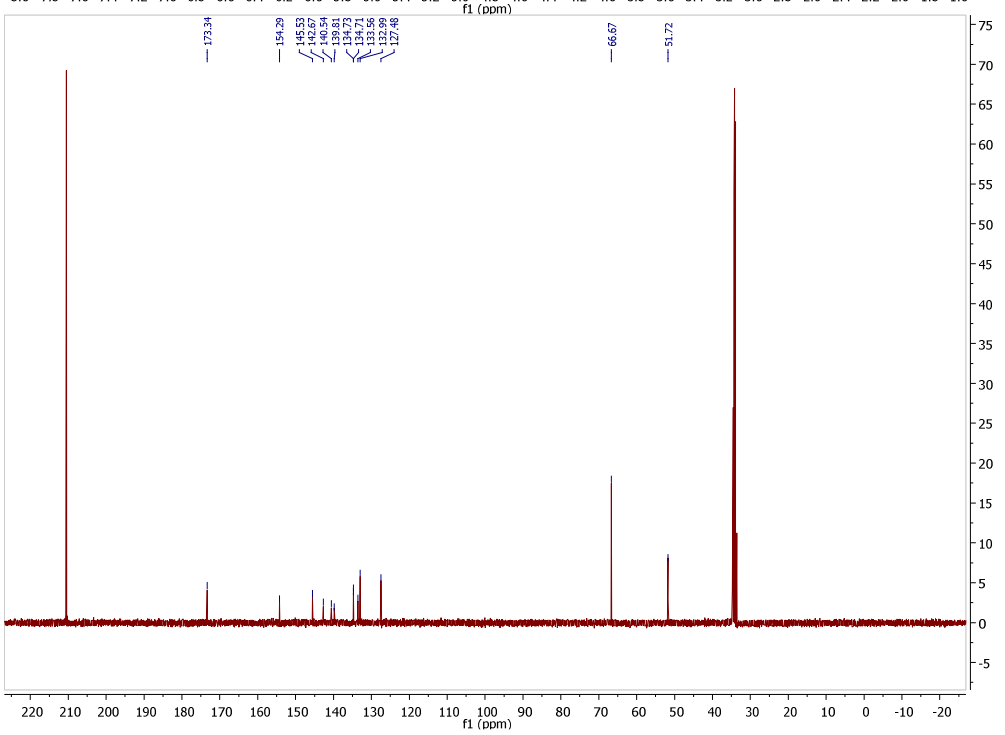

7.85
7.85
7.83
7.83
7.67
7.65
7.55
7.53
7.51
7.51
7.32
7.30
6.94
6.92
6.68
6.66
6.64
6.61
5.71
5.71
5.67
5.67
5.28
5.28
5.25
5.25
1.87
1.05
2.00
2.28
1.82
0.95
1.04
1.00
f1 (ppm)

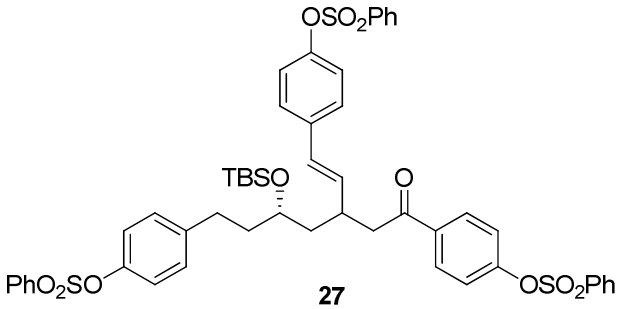

148.94
136.61
135.43
135.37
134.19
129.11
128.50
127.29
122.41
114.96
f1 (ppm)


PhO2SO
N
B
O
O
O
O

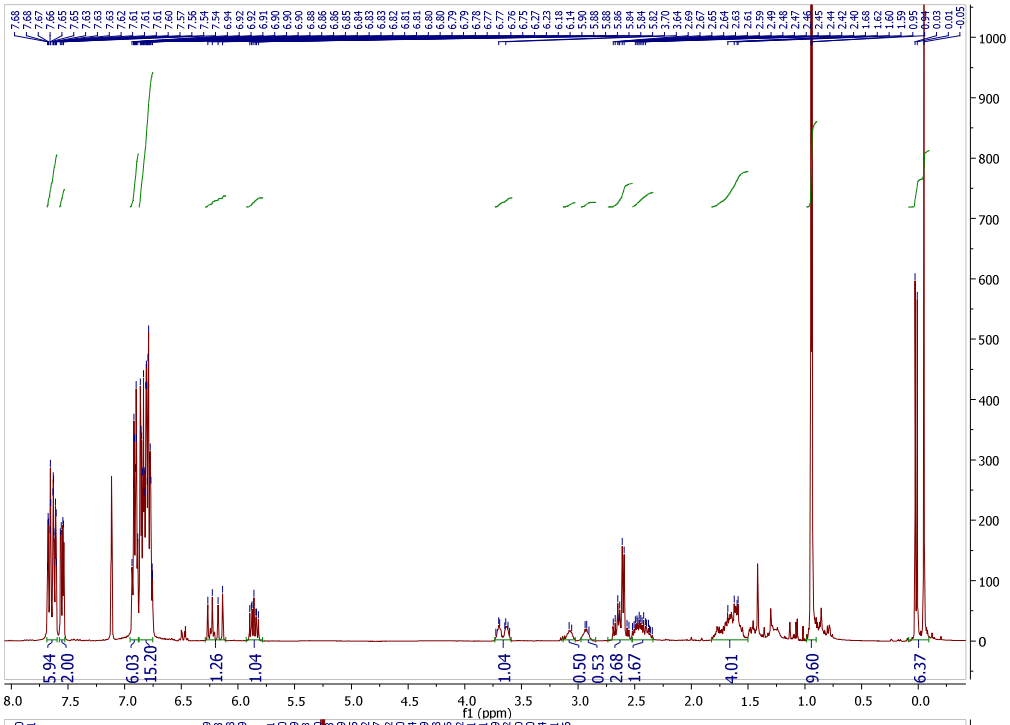
34

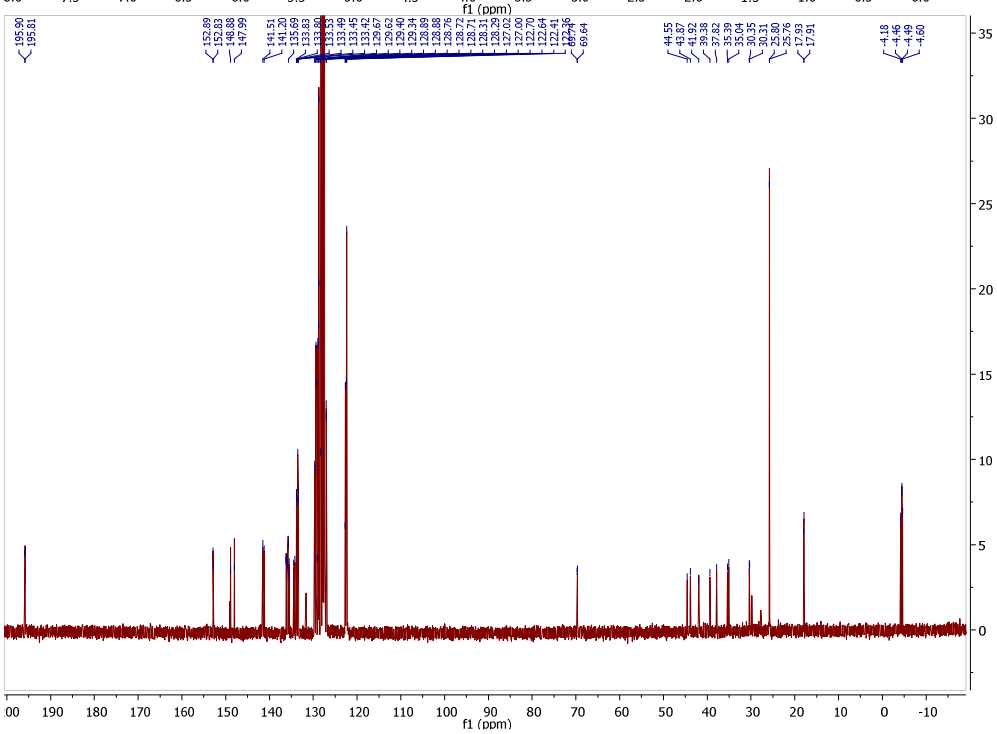

bc52657_bc-bh4455-1_PROTON_001
1.83
0.99
1.91
1.87
1.84
0.99
1.00
1.91
1.95
2.77
f1 (ppm)

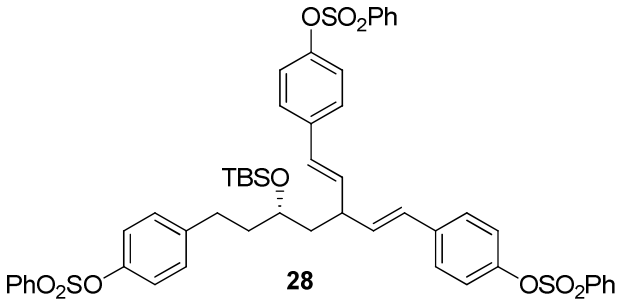

173.34
154.29
145.53
142.67
140.54
139.81
134.73
134.71
133.56
132.99
127.48
66.67
51.72
f1 (ppm)



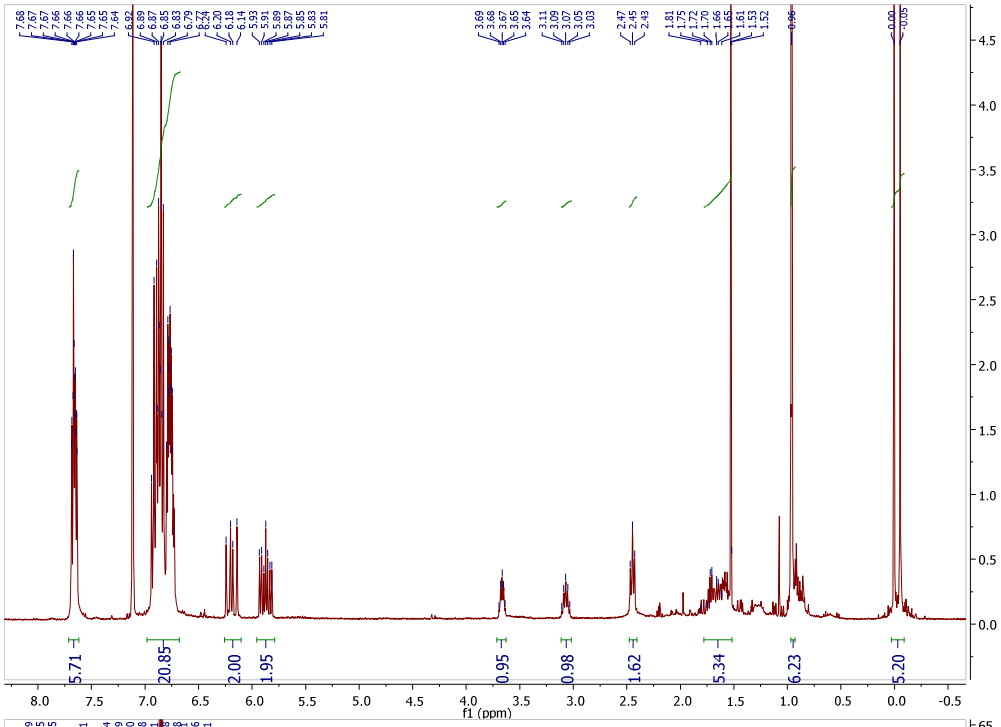
27

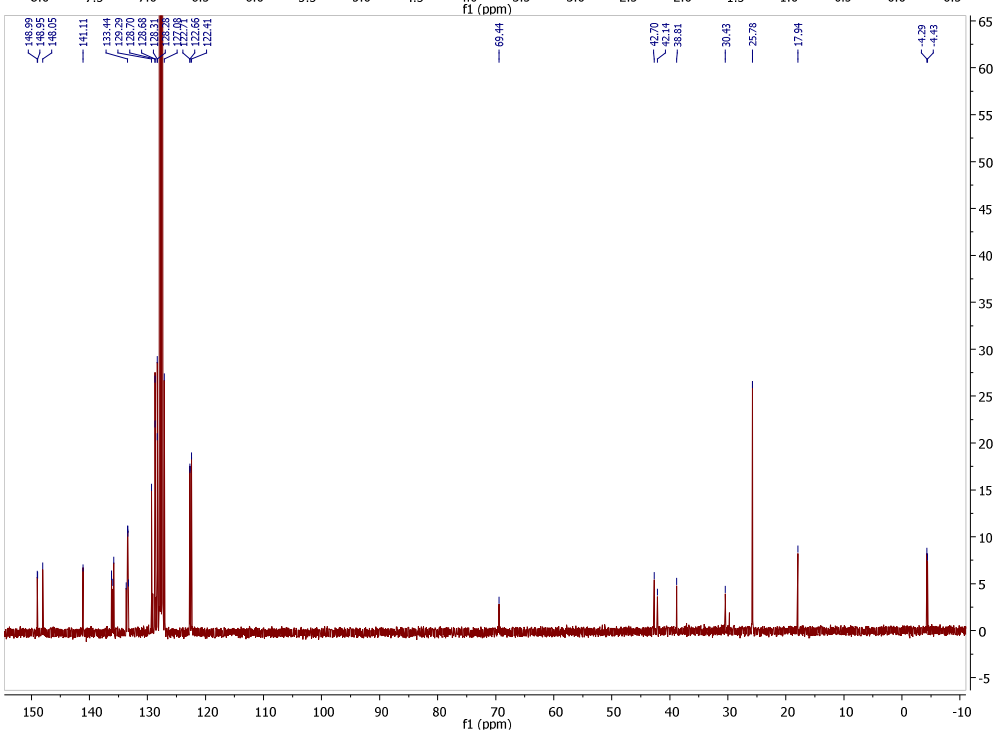


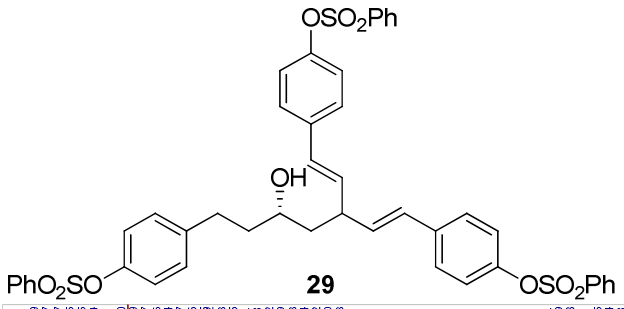



OSO2Ph
TBSO
PhO2SO
OSO2Ph

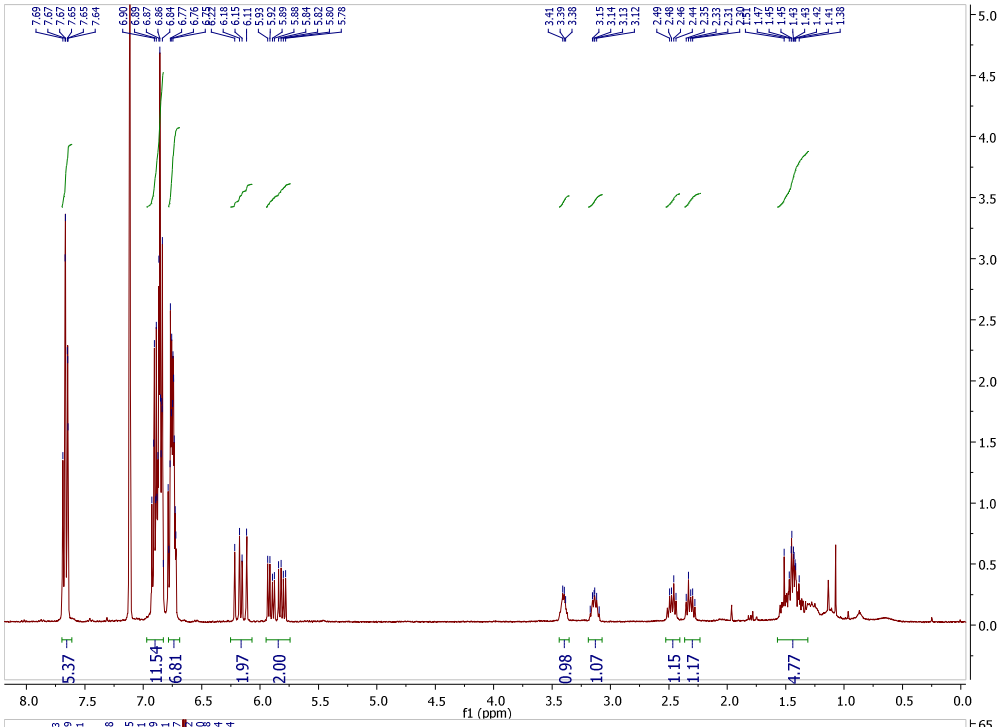
28

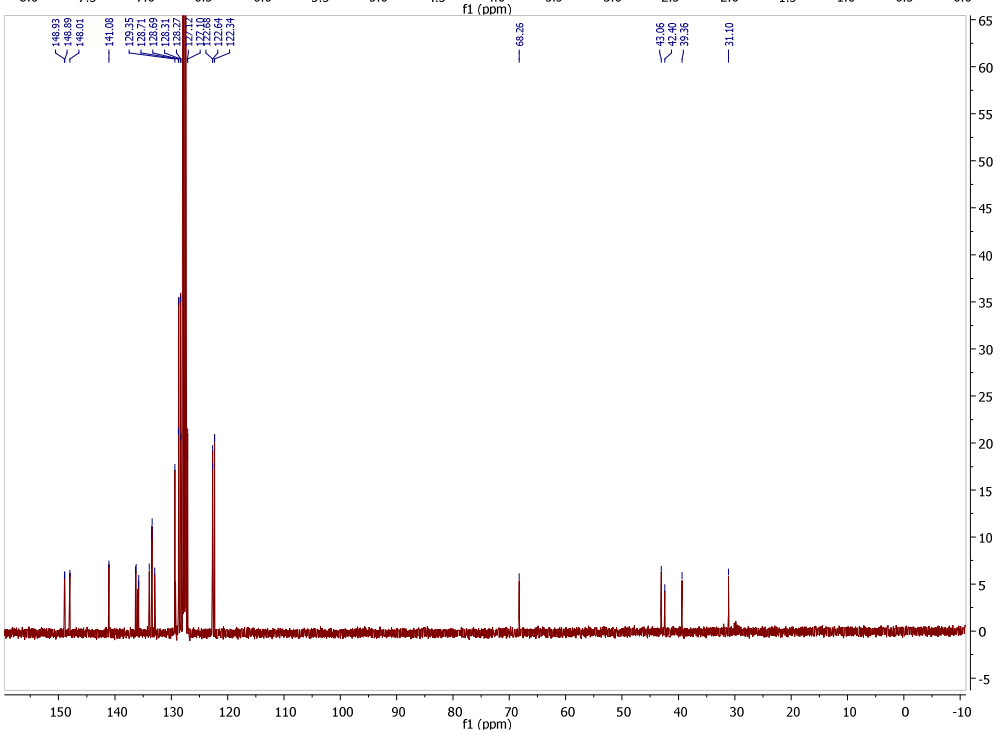

5.71
20.85
2.00
1.95
0.95
0.98
1.62
5.34
6.23
5.20
f1 (ppm)

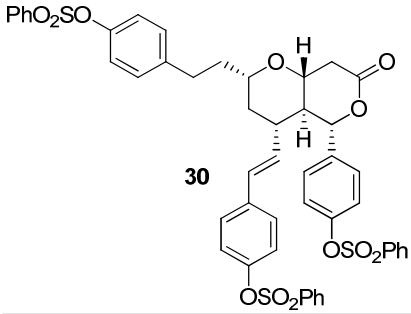

148.99
148.95
148.05
141.11
133.44
129.29
128.70
128.68
128.31
69.44
42.70
42.14
38.81
30.43
25.78
17.94
-4.29
-4.43
f1 (ppm)


OSO2Ph
OH
PhO2SO
OSO2Ph

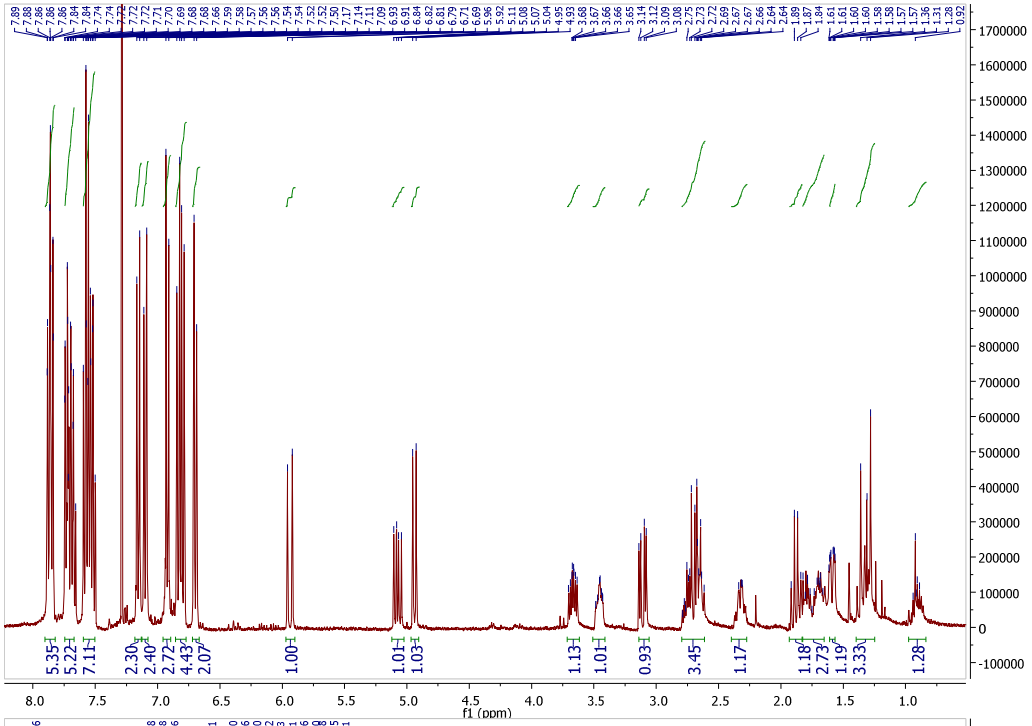
29

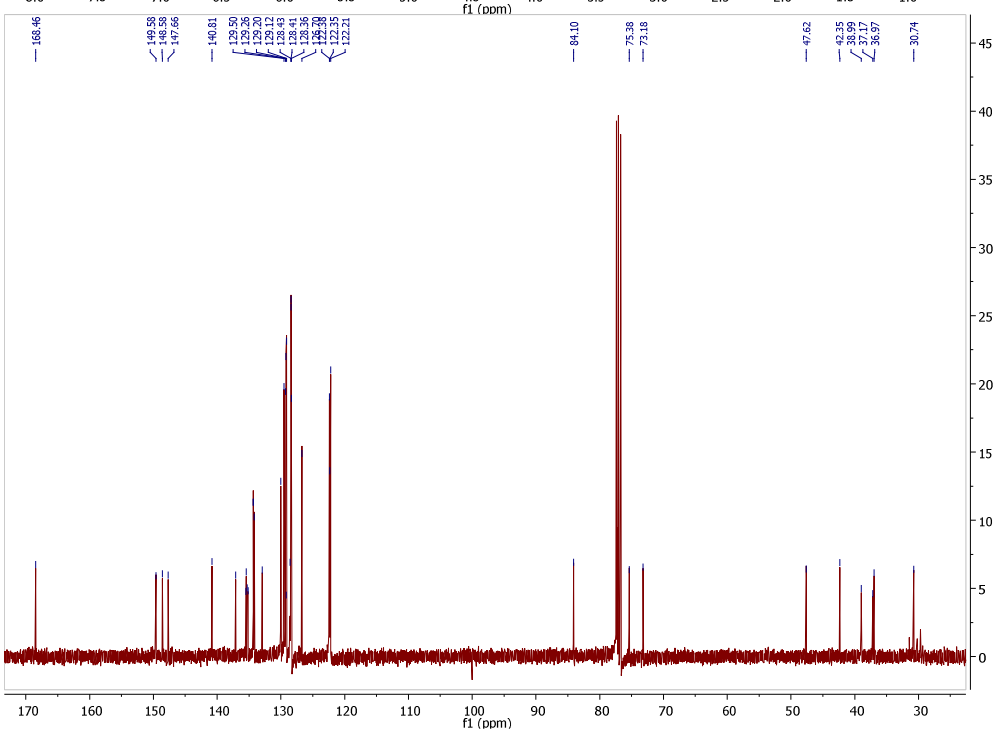

5.37
11.54
6.81
1.97
2.00
0.98
1.07
1.15
1.17
4.77
f1 (ppm)

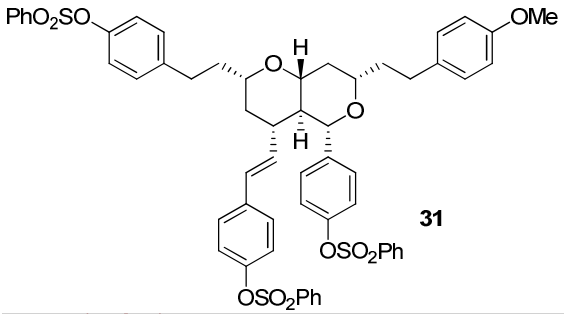

148.93
148.89
148.01
141.08
129.35
128.71
128.69
128.31
128.27
127.41
127.10
122.64
122.34
68.26
43.06
42.90
39.36
31.10
f1 (ppm)



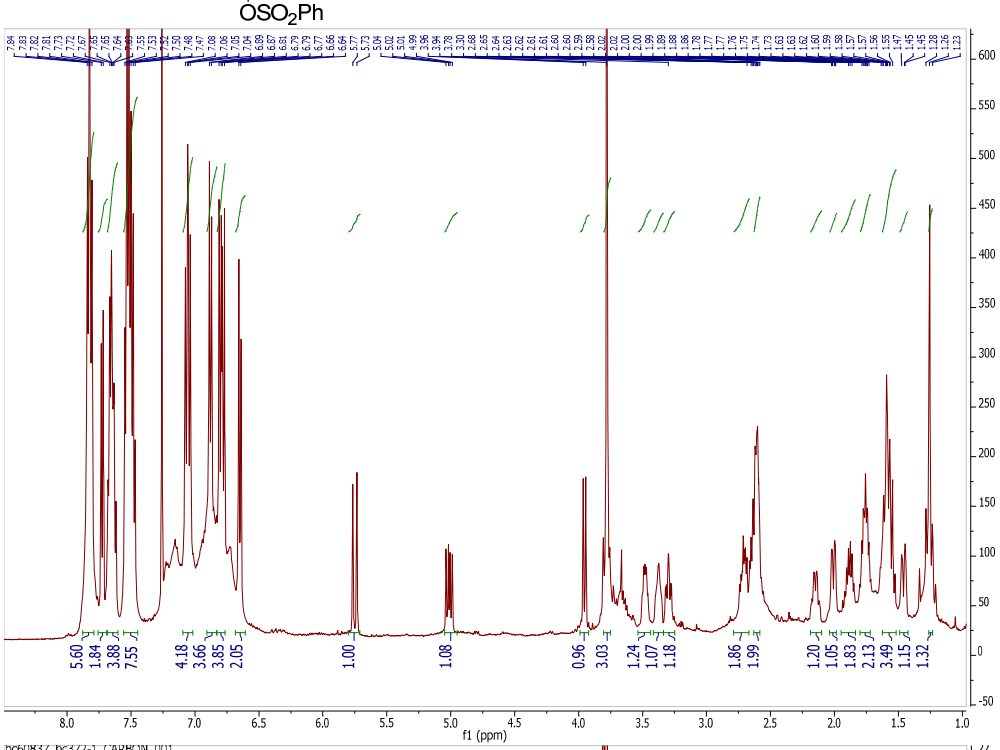
30

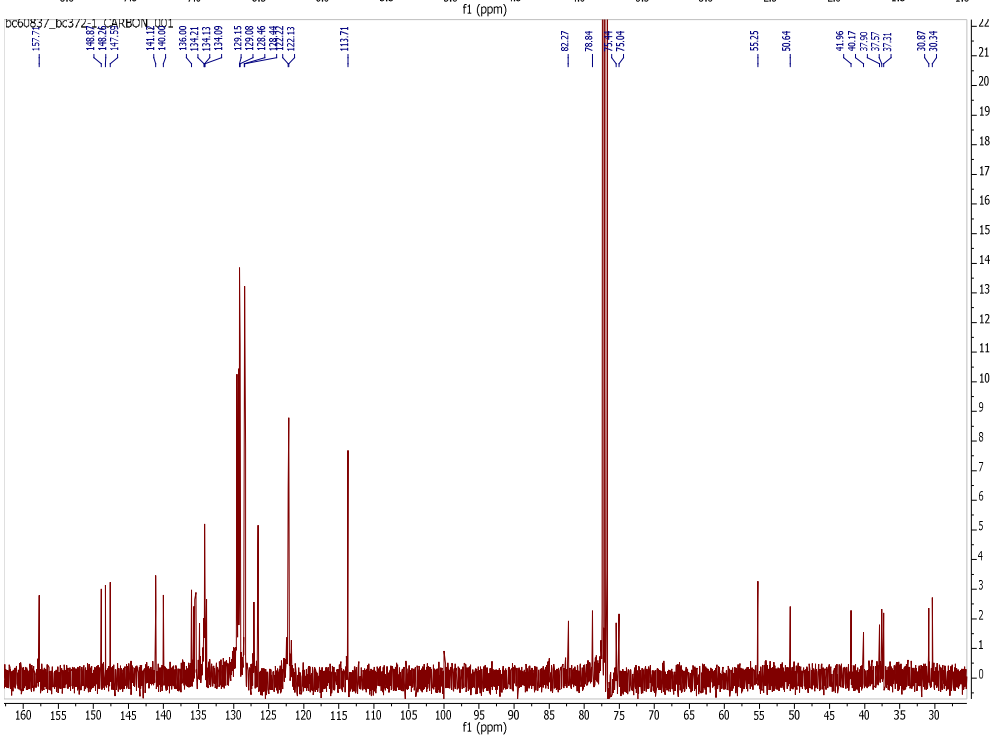


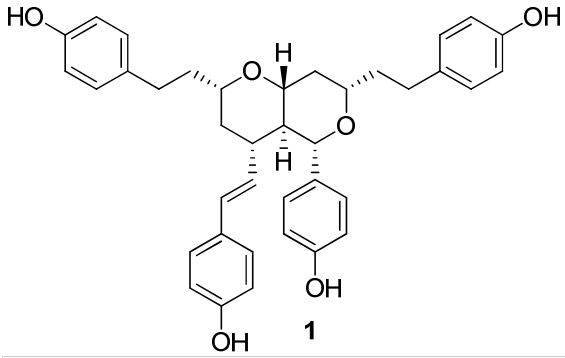



PhO2SO
OMe
H
O
O
H
OSO2Ph
OSO2Ph

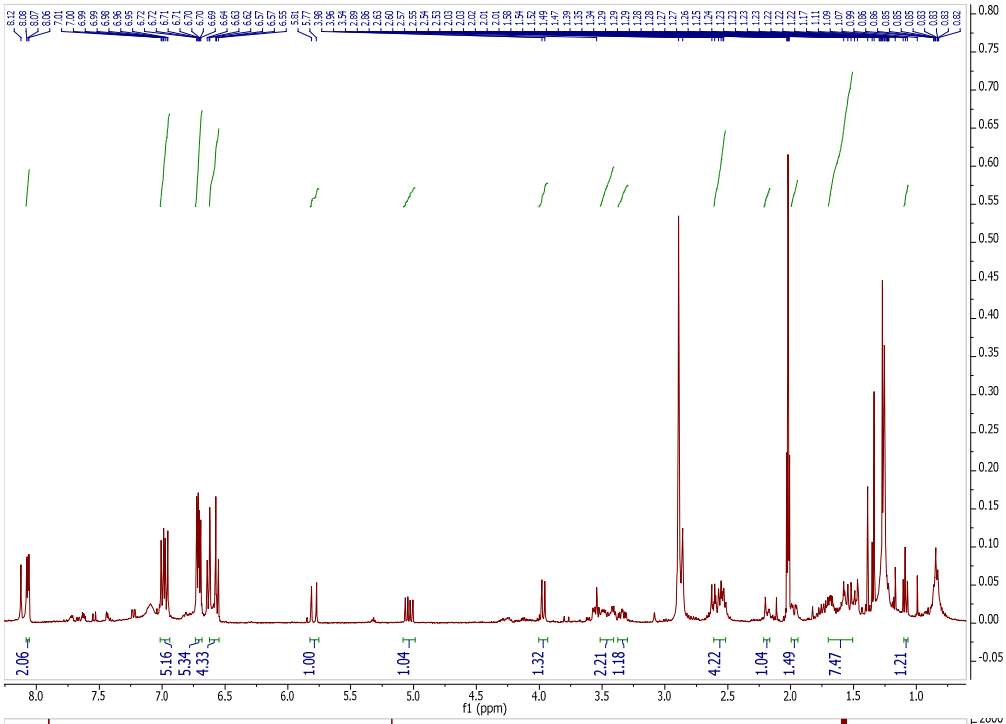
31

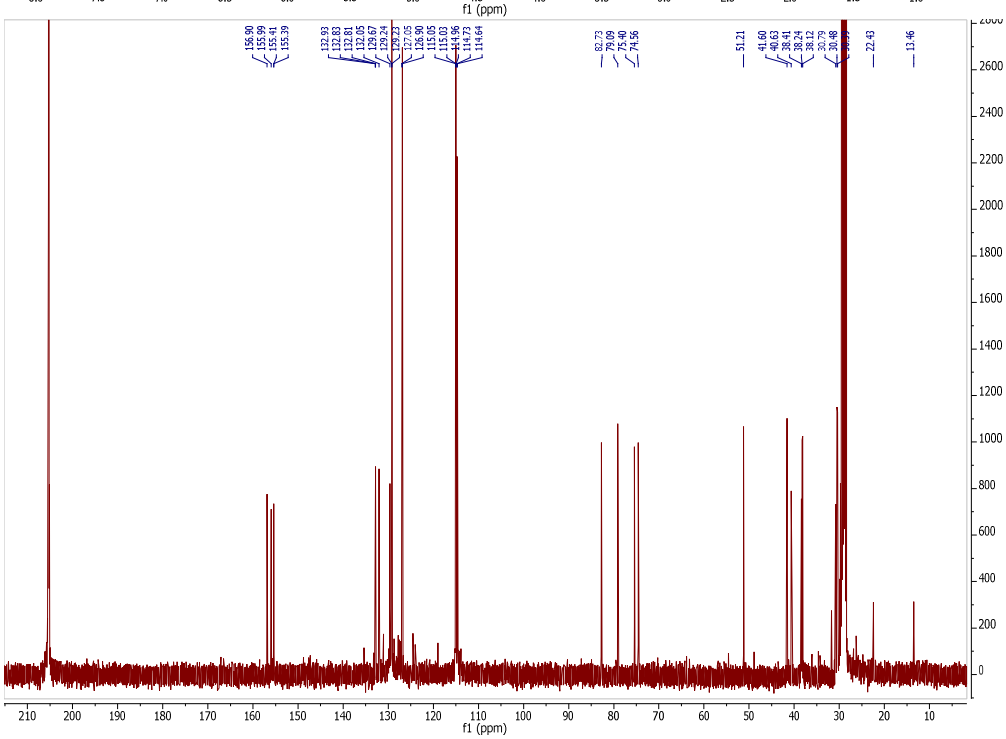

5.60
1.84
3.88
7.55
4.18
3.66
3.85
2.05
1.00
1.08
0.96
3.03
1.24
1.07
1.18
1.86
1.99
1.20
1.05
1.83
2.13
3.49
1.15
1.32
f1 (ppm)


DC60837_DC372_1_CARBON_01
157.74
148.84
148.74
147.59
141.17
140.92
136.00
134.21
134.13
134.09
129.15
129.08
128.96
128.84
122.22
122.13
113.71
82.27
78.84
77.49
75.04
55.25
50.64
41.96
40.07
37.50
37.37
37.31
20.87
20.74
f1 (ppm)


HO
OH
H
O
O
H
OH
OH

1


2.06
5.16
5.34
4.33
1.00
1.04
1.32
2.21
1.18
4.22
1.04
1.49
7.47
1.21
f1 (ppm)


156.90
155.58
155.41
155.39
132.93
132.83
132.61
130.45
129.47
129.24
129.23
127.05
126.90
115.05
115.03
114.96
114.73
114.64
82.73
79.09
75.40
74.56
51.21
41.60
40.63
38.41
38.24
38.12
30.70
30.48
22.43
13.46
f1 (ppm)

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