

# The Synthesis of Optically Active Calix[4]arenes with One or Three Substituents on the Methylene Bridges.

Vijayagopal Gopalsamuthiram, Rui H. Huang and William D.Wulff\*

Department of Chemistry, Michigan State University, East Lansing, MI 48824

wulff@chemistry.msu.edu

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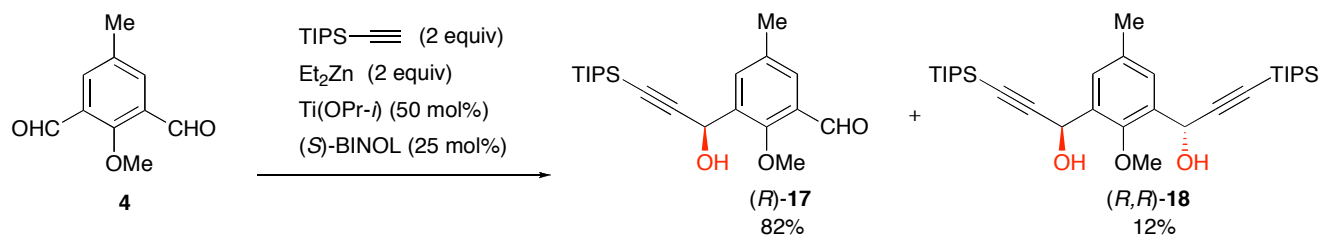
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## General Experimental

All reactions were run using either oven-dried or flame-dried glassware under an inert atmosphere of argon. Chemicals used were reagent grade and used as supplied except where noted. The following solvents were distilled from the listed drying agents: Tetrahydrofuran (Na, benzophenone), diethyl ether (Na, benzophenone), toluene (Na), dichloromethane (CaH<sub>2</sub>). Anhydrous 1,2 dichloroethane was purchased from Aldrich and used under an atmosphere of argon. Molecular sieves (4Å) 1/16" pellets were dried in an oven for 2-3 days at 125-140 °C prior to use. Silver nitrate (99.9995 % Ag) was purchased from Strem chemicals. Chromatographic purifications were performed on Merck silica gel grade (230-400 mesh) by step gradient elution method starting from 5 % ethyl acetate / hexanes unless otherwise mentioned and TLC's were performed on plastic backed TLC plates from Silicycles. The general solvent systems used were either a combination of ethyl acetate / hexanes or dichloromethane / hexanes unless otherwise specified. Compounds were visualized by dipping the TLC plate in a solution of KMnO<sub>4</sub> followed by heating with a heat-gun. <sup>1</sup>H NMR data were obtained either on a Varian 300 MHz or 500 MHz instrument and are reported in parts per million (δ) relative to tetramethyl silane (0.00 ppm) or chloroform (7.24 ppm) for spectra run in CDCl<sub>3</sub> and multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), dt (doublet of triplets) and br (broad). <sup>13</sup>C NMR data were obtained on a Varian 300 MHz or 500 MHz instrument and are reported in δ relative to CDCl<sub>3</sub> (77 ppm). Infrared spectra were recorded on a Perkin Elmer FT IR instrument and the peaks are reported in cm<sup>-1</sup> with indicated relative intensities: s (strong), m (medium), w (weak), brs (broad and strong). 1-D NOE experiments and NOESY experiments were performed on a Varian 600 MHz NMR instrument. Mass spectral data and elemental analysis were obtained from Michigan State University Biochemistry Mass spectrometry facility and in-house analysis facility. The mass spectra were obtained using direct probe EI using chloroform as solvent on a JEOL AX-505 double focusing mass spectrometer. FAB spectra using 2-nitrobenzyl alcohol as solvent were obtained on a JEOL HX-110 double focusing mass spectrometer in the positive ionization mode. Data are reported in the form of *m/z* (intensity relative to base peak = 100). 2,6-Diformyl-4-methyl anisole was prepared by Swern oxidation of 2,6-bis-hydroxymethyl-4-methyl anisole following literature procedure<sup>1</sup>. The synthesis of carbene complex **11** was reported in an earlier communication.<sup>2</sup> Organo-lithium reagents were purchased from Aldrich and titrated to a known concentration following the procedure of Gilman.<sup>3</sup> The indicated reaction temperatures are of the oil bath temperature monitored by a digital temperature controller. The reactions were often monitored for completion by quenching an aliquot of the reaction mixture in ether/water and ethereal layer was subjected to GC/MS analyses on Saturn 2000R mass spectrometer and

3800GC using chrome-pack capillary column. Melting points were recorded on Thomas Hoover capillary melting point apparatus using 1.5-1.8×90mm capillary tubes. Optical rotation measurements were made on a Perkin Elmer 141 polarimeter at 589 nm (Sodium D Line) using 1dm cells. Specific rotations are reported in degrees per decimeter at 25°C and the concentration is given in grams per 100 mL.

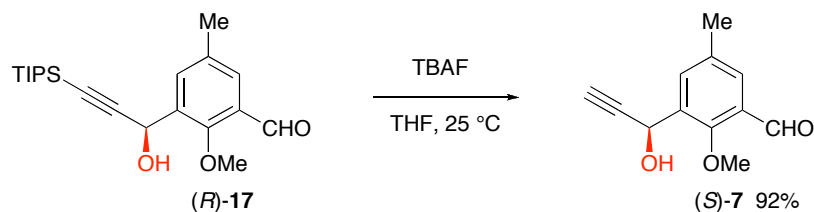
### Synthesis of the Propargyl Alcohol (*R*)-17.



In a flame dried three-necked round-bottomed flask filled with argon was added triisopropylsilyl acetylene (4.5 mL, 20 mmol). Toluene (10 mL) and diethyl zinc (1.1 M in toluene, 18 mL, 19.8 mmol) were added and the resulting solution was refluxed for 5 h upon which time the resulting solution turned grey in color. (*S*)-BINOL (0.572 g, 2 mmol) in 20 mL of dichloromethane which had been pre-dried over anhydrous 4Å molecular sieves was added to this grey solution and after stirring for 15 min, titanium *iso*-propoxide (1.5 mL, 5 mmol) was added via syringe. The solution turned deep red and stirring was continued for another 1h. Aldehyde **4**<sup>1</sup> (1.78 g, 10 mmol) in dichloromethane (20 mL) was added and the reaction was monitored by GC/MS for completion. Saturated aqueous ammonium chloride (80 mL) was added to quench the reaction. After extraction with dichloromethane (100 mL), drying over anhydrous magnesium sulfate, and evaporation of the solvent, the crude mixture of products was obtained as a yellow oil which were separated by column chromatography (5% to 15% ethylacetate / hexanes) on silica gel to afford 3.0 g (8.2 mmol, 82 %) of (*R*)-**17** as a yellow oil along with 0.63 g (1.16 mmol, 11.6 %) of the bis-alkynol (*R,R*)-**18**. The meso isomer of **18** co-eluted with BINOL and thus its yield was not determined. The absolute configuration was determined after desilylation to give (*S*)-**7** as described below. R<sub>f</sub> for (*R*)-**17** (85/15 hexanes/ethylacetate) = 0.34. Spectral data for (*R*)-**17**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 1.06 (s, 21H), 2.35 (s, 3H), 2.52 (d, 1H, *J* = 5.5 Hz), 3.99 (s, 3H), 5.78 (d, 1H, *J* = 6.0 Hz), 7.62 (d, 1H, *J* = 2.5Hz), 7.78 (d, 1H, *J* = 2.0 Hz), 10.31 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 11.19, 18.59, 20.72, 63.68, 65.73, 90.76, 103.34, 128.90, 129.67, 132.93, 134.48, 136.95, 159.15, 189.82; IR (neat) 3429, 2988, 2943, 2172, 1689, 1606, 1587, 1477 cm<sup>-1</sup>; mass

spectrum  $m/z$  (% rel.intensity) 360  $M^+$  (2), 343 (47), 318 (100), 303 (30), 288 (50), 260 (13). Anal calcd for  $C_{21}H_{32}O_3Si$ : C, 69.95; H, 8.95. Found: C, 69.49; H, 9.11.

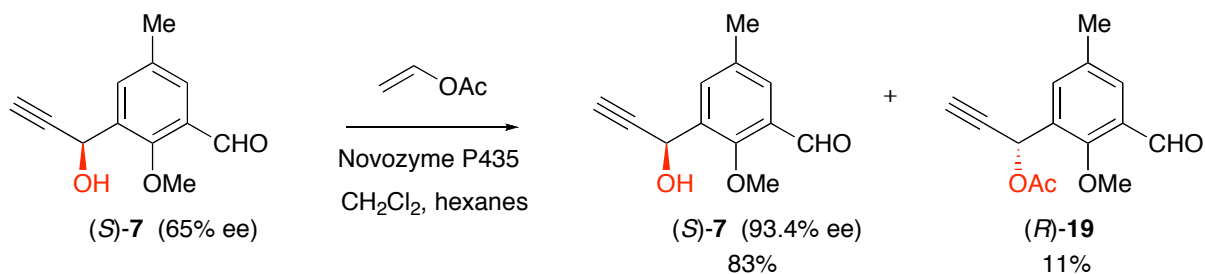
### Desilylation of Propargyl Alcohol (*R*)-17 to give the Propargyl Alcohol Aldehyde (*S*)-7.



To a flame-dried 100 mL flask was added 2.95 g (8.2 mmol) of (*R*)-17 and 35 mL of ether followed by dropwise addition of 5 equiv of *tetra*-butylammonium fluoride (1M in tetrahydrofuran). The resulting solution was stirred for 4 h at room temperature. Aqueous workup followed by removal of the organic solvent afforded the crude product which was purified by silica-gel chromatography (50% ethyl acetate/hexanes) to afford 1.54 g (7.5 mmol, 92 %) of (*S*)-7 as a yellow solid;  $R_f$  (1/1 hexanes/ethyl acetate) = 0.69, mp 60-62°C. Spectral data for (*S*)-7:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  2.36 (s, 3H), 2.65 (d, 1H,  $J = 2.1$  Hz), 2.74 (s, 1H), 3.98 (s, 3H), 5.72 (dd, 1H,  $J = 3.6, 2.4$  Hz), 7.62 (d, 1H,  $J = 2.1$ Hz), 7.66 (d, 1H,  $J = 2.4$  Hz), 10.29 (s, 1H);  $^{13}\text{CNMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  20.97, 59.73, 65.85, 75.14, 83.61, 129.24, 130.37, 134.64, 135.06, 135.20, 189.71, 1  $\text{sp}^2$  C not located; IR (neat) 3425, 3289, 2910, 2875, 2100, 1609, 1479, 1088  $\text{cm}^{-1}$ ; mass spectrum FAB in NBA  $m/z$  (% rel intensity) 204  $M^+$  (Not found), 187 (94), 173 (20), 115 (15), 93 (40); HRMS calcd for  $C_{12}H_{12}O_3$  ( $M^+$ -17)  $m/z$  187.0759, meas 187.076.

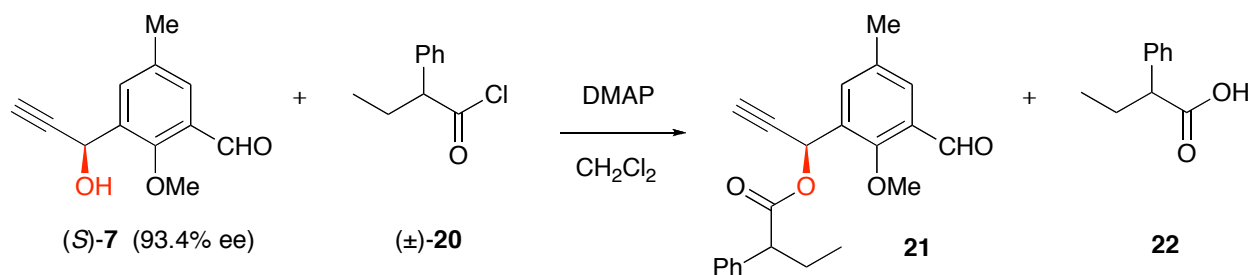
Racemic alkynol 7 was prepared following a similar sequence from aldehyde 4 using (*rac*)-BINOL followed by desilylation. HPLC Analysis of (*S*)-7 revealed the enantiomeric excess to be 65.4 % (Chiralpak AS column, 94:6 hexane:*i*-PrOH to 85:15 hexane:*i*-PrOH, 254 nm, flow rate 0.5 mL/min); Retention times (*S*)-7 = 47.09 min, (*R*)-7 = 42.99. The assignment of the major enantiomer as (*S*) is consistent with the direction of addition of phenylacetylene to benzaldehyde with the same procedure developed by Pu,<sup>4</sup> with the enhancement of the optical purity of (*S*)-7 by kinetic resolution with Novozyme 435 described below, and with the method of Horeau for the determination of the configuration of secondary alcohols by partial resolution also described below.<sup>5</sup>

### Enrichment of the Optical Purity of Propargyl Alcohol Aldehyde (**S**)-7.



To 1.54 g (7.54 mmol) of (*S*)-7 (65% ee) in a round bottomed flask was added dichloromethane and hexanes (1/3 ratio, 45 mL) followed by the addition of 1.5 mL of vinyl acetate. Novozyme 435 (300 mg) was added with vigorous stirring and the reaction mixture was left at room temperature overnight. Removal of the resin by filtration and evaporation of the solvent under reduced pressure afforded the crude product. Purification by silica-gel chromatography gave 1.27 g (6.26 mmol, 83%) of (*S*)-7 in 93.4% ee (determined as described above) as a yellow solid and 0.196 g (0.80 mmol, 10.6%) of (*R*)-19 as white solid. Mp of (*R*)-19 = 52-54°C. The enantiomeric purity of the acetate was not determined. Spectral data for (*R*)-19: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 2.10 (s, 3H), 2.37 (s, 3H), 2.63 (d, 1H, *J* = 2.5 Hz), 3.92 (s, 3H), 6.72 (d, 1H, *J* = 2.0 Hz), 7.65 (d, 1H, *J* = 2.5 Hz), 7.69 (d, 1H, *J* = 2.5 Hz), 10.29 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 20.70, 20.91, 59.40, 65.40, 75.39, 80.04, 128.95, 130.48, 130.96, 134.79, 135.68, 158.48, 169.32, 189.29; IR (neat) 3292, 2938, 2861, 2753, 2257, 2125, 1745, 1686, 1606, 1481 cm<sup>-1</sup>; Mass spectrum *m/z* (% rel intensity) 246 M<sup>+</sup> (3), 231 (14), 187 (100), 115 (!2). Anal calcd for C<sub>14</sub>H<sub>14</sub>O<sub>4</sub>: C, 68.28; H, 5.73. Found: C, 68.19; H, 5.68. Specific rotation of (*S*)-7: [α]<sub>D</sub> -5.0 (c 1.02 *i*-PrOH) on 93.4% ee material.

### The Absolute Configuration of Propargyl Alcohol Aldehyde (**S**)-7 Determined by Horeau's Method.<sup>5</sup>



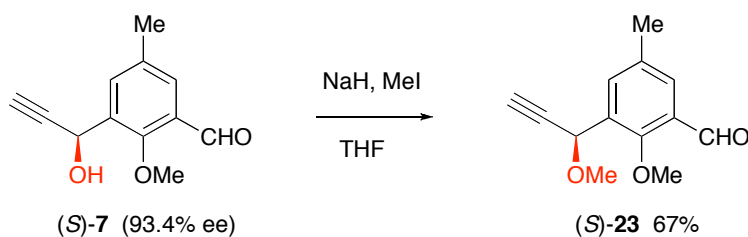
The alcohol (*S*)-7 (93.4% ee, 0.204 g, 1 mmol) and N,N-dimethyl amino pyridine (25 mg, 0.20 mmol) were transferred to a 25 mL three-necked round-bottomed flask and CH<sub>2</sub>Cl<sub>2</sub> (2 mL) was added. To this solution was added racemic 2-phenylbutyryl chloride **20** (0.35 mL, 2 mmol) and the resultant mixture stirred at ambient

temperature for 15 h. After 15 h, pyridine was removed under high vacuum and the residue was dissolved in dichloromethane (50 mL) and the organic layer was washed with saturated aqueous sodium bicarbonate (100 mL). Removal of the solvent under reduced pressure afforded the ester **21** as an oil and as a 2.26:1 mixture of inseparable diastereomers in 96% yield (0.336 g, 0.96 mmol). The aqueous layer was acidified to pH ~ 3 and then extracted with dichloromethane (4×50 mL). Drying the organic layer over anhydrous magnesium sulfate followed by removal of the solvent afforded 2-phenylbutanoic acid **22** (26 mg, 0.16 mmol, 16%) as an oil. Further acidification followed by extraction with dichloromethane did not afford any more carboxylic acid. The specific rotation of the acid was recorded in two different solvents and the results are tabulated below (Table 1). Based on the sign of the optical rotation of the isolated carboxylic acid and adopting Horeau's rule, the absolute configuration of the propargylic alcohol **7** can be assigned as the (*S*)-isomer. Spectral data for **21** (2.2:1) mixture of diastereomers:  $R_f$  (85/15 hexanes/ethyl acetate) = 0.32;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  0.86-0.91 (m, 4H), 1.76-1.84 (m, 2H), 2.07-2.14 (m, 2H), 2.20 (s, 3H), 2.33 (s, 1.4 H), 2.54 (d, 0.4 H,  $J = 2.0$  Hz), 2.61 (d, 0.9 H,  $J = 2.0$  Hz), 3.50 (t, 0.45 H,  $J = 8.0$  Hz), 3.51 (t, 0.9 H,  $J = 7.5$  Hz), 3.70 (s, 3H), 3.84 (s, 1.41H), 6.67 (d, 0.9H,  $J = 2.5$  Hz), 6.70 (d, 0.41 H,  $J = 2.5$  Hz), 7.19-7.23 (m, 4H), 7.25 (d, 0.71 H,  $J = 1.5$  Hz), 7.26 (d, 0.32 H,  $J = 2.0$  Hz), 7.28–7.29 (m, 2H), 7.30 (d, 0.58 H,  $J = 2.0$  Hz), 7.56-7.58 (m, 1.3H), 7.64 (d, 0.4 H,  $J = 2.5$  Hz), 10.23 (s, 0.9 H), 10.29 (s, 0.39 H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  12.04, 12.07, 20.64, 20.71, 26.49, 26.58, 53.08, 53.31, 59.67, 59.72, 65.19, 65.34, 75.39, 75.45, 79.73, 80.04, 127.32, 127.36, 128.02, 128.55, 128.78, 128.91, 129.97, 130.26, 131.01, 131.06, 134.62, 134.72, 134.96, 135.53, 138.17, 138.25, 158.39, 158.51, 172.29, 172.33, 189.37 (3 aryl carbons not seen); IR (neat) 3285, 2967, 2936, 2876, 1741, 1891, 1604, 1589, 1479  $\text{cm}^{-1}$ ; mass spectrum  $m/z$  (% rel.intensity) 350  $\text{M}^+$  (10), 320 (20), 203 (20), 187 (40), 119 (55), 91 (100), HRMS calcd for  $\text{C}_{22}\text{H}_{22}\text{O}_4$   $m/z$  350.1518, meas 350.1517.

**Table 1. Optical Rotations of Isolated 2-Phenyl Butanoic Acid**

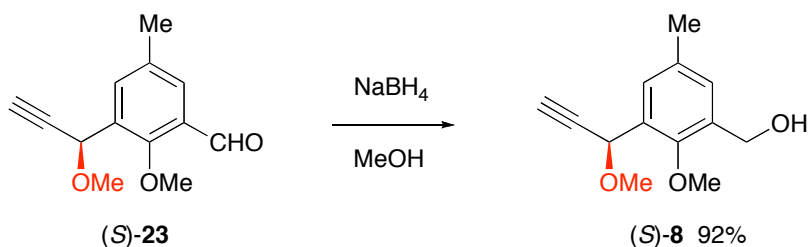
Solvent	Concentration	Specific rotation	Literature value of Optically pure ( <i>l</i> )-2-phenyl butanoic acid	Optical Purity
Toluene	0.9	-15.1 °	-93 °	16.34 %
Chloroform	1.0	-11.4°	-74.8 °	15.3 %

### Preparation of Propargyl Ether Aldehyde (**S**-23).



To a pre-weighed flame dried three necked 250 mL round bottomed flask was added 0.53 g (13.2 mmol) sodium hydride (60% dispersion in oil) and pentane (15 mL) was added. The resulting slurry was stirred at ambient temperature for 15 minutes. Most of the pentane was carefully removed using a syringe such that the NaH precipitate was not disturbed and the residual solvent was removed under vacuum to afford 318 mg of sodium hydride. Tetrahydrofuran (45 mL) was added to this flask under argon and then (**S**)-7 (2.10 g, 10.31 mmol, 93.4% ee) was slowly added over 5 minutes. Upon completion of the addition, the yellow slurry was stirred for another 45 min. Iodomethane (1.06 mL, 17.0 mmol) was added and the reaction was allowed to stir overnight. Ether (30 mL) was added and the reaction was worked up by addition of saturated aqueous ammonium chloride solution (25 mL). The product was extracted with ether (150 mL) and the organic layer was washed with water (150 mL). After drying over anhydrous magnesium sulfate and removal of ether under reduced pressure, the product was purified by silica gel chromatography (15% ethyl acetate/hexanes) to afford 1.51 g (6.91 mmol, 67 %) of (**S**)-23 as a colorless oil;  $R_f$  (85/15 hexanes/ethyl acetate) = 0.43. Spectral data for (**S**)-23:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  2.37 (s, 3H), 2.65 (d, 1H,  $J = 2.5$  Hz), 3.49 (s, 3H), 3.94 (s, 3H), 5.40 (d, 1H,  $J = 2.0$  Hz), 7.64 (s, 1H), 7.73 (s, 1H), 10.32 (s, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  20.64, 56.42, 65.38, 66.39, 75.60, 81.05, 128.76, 129.77, 132.56, 134.63, 135.56, 158.62, 189.52; IR (neat) 3285, 2938, 2826, 2753, 2114, 1693, 1589, 1479  $\text{cm}^{-1}$ ; mass spectrum  $m/z$  (% rel intensity) 219 ( $\text{M}^+ + 1$ , 22), 218 ( $\text{M}^+$ , 33), 203 (36), 187 (100), 140 (44), 123 (36); HRMS calcd for  $\text{C}_{13}\text{H}_{15}\text{O}_3$   $m/z$  219.1021, meas 219.1020. Specific rotation:  $[\alpha]_D +15.4$  ( $c$  1.06  $\text{CHCl}_3$ ) on material prepared from (**S**)-7 that was 93.4% ee.

### Reduction of Aldehyde (**S**)-23 to give Alcohol (**S**)-8.



The aryl aldehyde **23** (1.52 g, 6.94 mmol, 93.4% ee) was dissolved in methanol (0.22 M) and transferred to a clean 100 mL round-bottomed flask. Sodium borohydride (1.1 equiv) was added portion-wise and the exothermic reaction was allowed to subside before addition of the next portion. After addition, the resultant mixture was stirred at room temperature for 3-4 h. Aqueous workup was followed by three-fold extraction with ether and removal of solvent under reduced pressure afforded 1.41 g (6.38 mmol, 92%) of the benzyl alcohol (**S**)-**8** as an oil;  $R_f$  (1/1 hexanes/ethyl acetate) = 0.44. Spectral data for (**S**)-**8**:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  2.31 (s, 3H), 2.59 (d, 1H,  $J = 2.5$  Hz), 3.46 (s, 3H), 3.91 (s, 3H), 4.52 (s, 2H), 5.32 (d, 1H,  $J = 2.0$  Hz), 7.19 (d, 1H,  $J = 2.5$  Hz), 7.40 (d, 1H,  $J = 2.0$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  20.43, 27.49, 56.11, 62.58, 66.66, 74.90, 81.24, 129.73, 130.69, 131.54, 132.30, 134.33, 153.30; IR (neat) 3431, 3287, 2937, 2828, 2114, 1728, 1595, 1481  $\text{cm}^{-1}$ ; mass spectrum  $m/z$  (% rel intensity) 220 ( $\text{M}^+$ , 68) 203 (44), 189 (100), 159 (26), HRMS calcd for  $\text{C}_{13}\text{H}_{16}\text{O}_3$   $m/z$  220.1099, meas 220.1098. Specific rotation:  $[\alpha]_{\text{D}} +20.6$  ( $c$  0.58  $\text{CHCl}_3$ ) on material prepared from (**S**)-**7** (93.4% ee).

### Conversion of Alcohol (**S**)-8 to Bromide (**S**)-9.

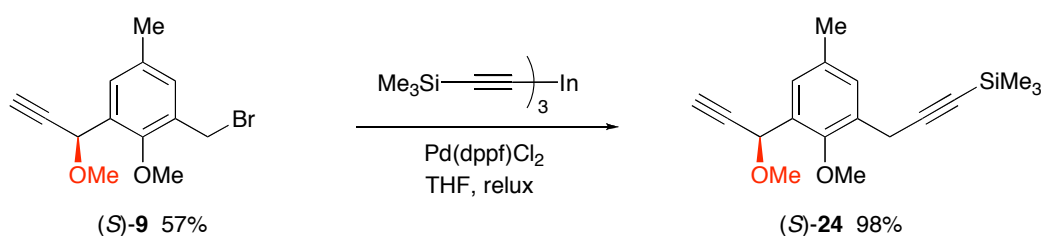


The benzyl alcohol **8** (1.4 g, 6.36 mmol, 93.4% ee) was dissolved in 15 mL of dichloromethane in a 100 mL three-necked round-bottomed flask and *p*-toluene sulfonyl chloride (0.72 g, 3.75 mmol) was added followed by pyridine (0.3 mL, 3.75 mmol). The reaction was monitored for completion by TLC and excess dichloromethane (50 mL) was added. The organic layer was washed with 2 N HCl (50 mL) followed by saturated aqueous sodium



bicarbonate and brine solution (50 mL each). Drying over anhydrous magnesium sulfate followed by removal of the solvent under reduced pressure afforded the crude tosylate as a solid that was immediately taken onto the next step. The crude benzyl tosylate was dissolved in N,N-dimethyl formamide (15 mL) in a 100 mL flask and anhydrous lithium bromide (0.26 g, 3.0 mmol) was added. The resultant mixture was heated to 50 °C and stirred for 3-4 h. Water (50 mL) was added and the reaction mixture was extracted with ether (50 mL). Drying over anhydrous magnesium sulfate was followed by removal of the solvent and afforded the crude product which was purified by silica-gel chromatography (10% ethyl acetate/hexanes) to give a 57% yield (1.00 g, 3.55 mmol) of the bromide (*S*)-**9** as colorless oil;  $R_f$  (9/1 hexanes/ethyl acetate) = 0.39. Spectral data for (*S*)-**9**:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  2.31 (s, 3H), 2.59 (d, 1H,  $J = 2.1\text{Hz}$ ), 3.45 (s, 3H), 3.82 (s, 3H), 4.68 (s, 2H), 5.34 (d, 1H,  $J = 2.4\text{Hz}$ ), 7.16 (d, 1H,  $J = 2.4\text{Hz}$ ), 7.39 (d, 1H,  $J = 2.1\text{Hz}$ );  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  20.87, 56.38, 61.10, 62.85, 66.99, 75.13, 81.72, 128.79, 130.48, 131.41, 133.62, 134.49, 153.40; IR (neat) 3290, 2942, 2824, 2114, 1734, 1591, 1483, 1435  $\text{cm}^{-1}$ ; mass spectrum  $m/z$  (% rel intensity) 282  $\text{M}^+$  (12,  $^{79}\text{Br}$ ), 284 (11,  $^{81}\text{Br}$ ) (15), 258 (45,  $^{79}\text{Br}$ ), 238 (85,  $^{79}\text{Br}$ ), 203 (90), 171 (100), 128 (65), 69 (45); HRMS calcd for  $\text{C}_{13}\text{H}_{15}^{79}\text{BrO}_2$   $m/z$  282.0255, meas 282.0254. Specific rotation:  $[\alpha]_D +8.6$  ( $c$  0.62  $\text{CHCl}_3$ ) on material prepared from (*S*)-**7** (93.4% ee).

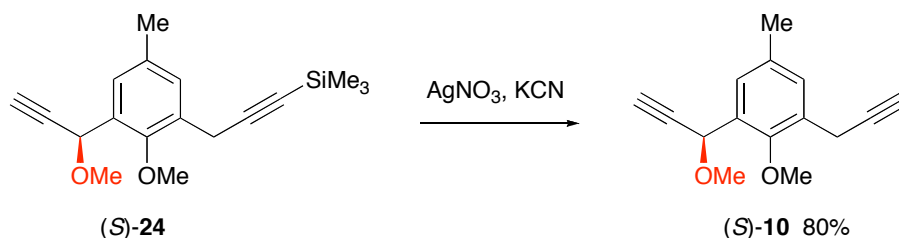
#### Preparation of Mono-Methoxy Diyne (*S*)-**24**.



Trimethylsilylethynyllithium<sup>6</sup> (6 mmol) was prepared by addition of *n*-butyllithium (2.4 mL, 2.5 M in hexanes, 6 mmol) to trimethylsilylacetylene (0.85 mL, 6 mmol) in tetrahydrofuran (10 mL) in a 100 mL flame-dried round-bottom flask under argon at  $-78\text{ }^\circ\text{C}$ . The resulting solution was allowed to warm to room temperature for 10 to 15 min. Indium(III) chloride (0.444 g, 2 mmol) was added to a three-necked 100 mL round bottom flask and dried under vacuum with a heat gun. Positive argon pressure was then established and THF (10 mL) was added. The resulting solution was cooled to  $-78\text{ }^\circ\text{C}$  and trimethylsilylethynyllithium was added drop-wise via syringe. The mixture was subsequently warmed to room temperature. The benzyl halide (*S*)-**9** (1.00 g, 3.55 mmol, 93.4% ee) and  $\text{Pd(dppf)Cl}_2$  (80 mg, 0.098 mmol) were introduced into a flame-dried three-necked 100 mL round-bottomed

flask and THF (20 mL) was added. The solution of trialkynylindium reagent was added to this flask under refluxing conditions and the reaction was continued until the disappearance of the starting material was determined as monitored by GCMS. The reaction was then quenched by the addition of 10 mL of methanol and the solvent was removed under vacuum. Ether (100 mL) was added and the organic layer was washed with 10% hydrochloric acid (2 x 50 mL), saturated aqueous sodium bicarbonate (2 x 50 mL) and saturated aqueous sodium chloride solution (2 x 50 mL). The resulting solution was filtered through a pad of silica gel to remove any inorganic impurities and upon concentration under reduced pressure the crude product was obtained. The trimethylsilylated alkyne (*S*)-**24** was thus obtained in 98% yield (1.04 g, 3.46 mmol);  $R_f$  (19/1 hexanes/dichloromethane) = 0.42. Spectral data for (*S*)-**24**:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  0.13 (s, 9H), 2.31 (s, 3H), 2.57 (d, 1H,  $J = 2.1$  Hz), 3.44 (s, 3H), 3.60 (s, 2H), 3.77 (s, 3H), 5.32 (d, 1H,  $J = 2.1$ Hz), 7.28 (s, 1H), 7.33 (s, 1H);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  0.29, 20.71, 21.19, 56.63, 62.53, 67.43, 75.27, 82.11, 87.00, 104.67, 128.03, 129.79, 131.33, 134.52, 153.34, 1  $\text{sp}^2$  C not located; IR (neat) 3289, 2959, 2899, 2822, 2175, 1482, 1435  $\text{cm}^{-1}$ ; Anal calcd for  $\text{C}_{18}\text{H}_{24}\text{O}_2\text{Si}$  C, 71.95; H, 8.05. Found C, 72.19; H, 8.06. Specific rotation:  $[\alpha]_D +13.1$  ( $c$  0.45  $\text{CHCl}_3$ ) on material prepared from (*S*)-**11** (93.4 % ee).

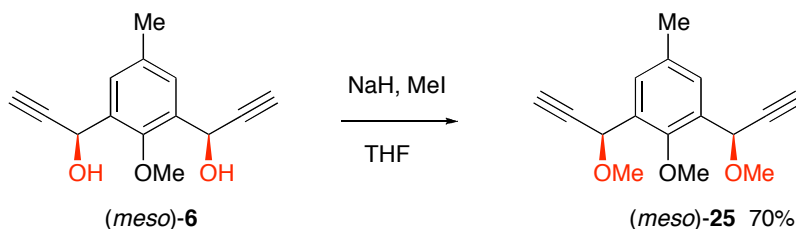
#### Preparation of Mono-Propargyl Ether Diyne (*S*)-**10**.



The mono-silyated diene (*S*)-**24** (1.04 g, 3.48 mmol, 93.4% ee) was dissolved in 20 mL of ethanol in a 100 mL round-bottomed flask and transferred to a 100 mL round-bottomed flask shielded from light containing silver nitrate (0.67 g, 4 mmol) in aqueous ethanol (2/1 EtOH/ $\text{H}_2\text{O}$ , 12 mL) and the resultant mixture was stirred overnight. Potassium cyanide (1.1 g, 17.4 mmol) in 2 mL of  $\text{H}_2\text{O}$  was then slowly added dropwise and the resultant solution stirred at room temperature for 2 h. The reaction was then diluted with water (75 mL) and extracted with ether (100 mL). Removal of the solvent under vacuum afforded the crude product that was purified by silica-gel chromatography (5% ethyl acetate in hexanes) to afford 0.633 g (80%) of diene (*S*)-**10** as oil;  $R_f$  (19/1 hexanes/ethyl acetate) = 0.23. Spectral data for (*S*)-**10**:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  2.14 (t, 1H,  $J = 2.7$  Hz), 2.32 (s, 3H), 2.58

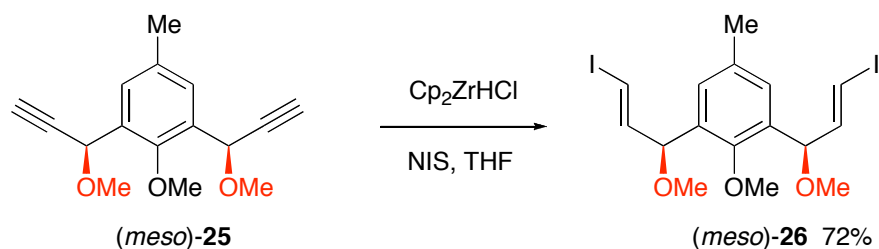
(d, 1H,  $J = 2.1$  Hz), 5.33 (d, 1H,  $J = 2.4$  Hz), 7.29 (s, 1H), 7.34 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  19.04, 20.91, 56.37, 62.72, 67.15, 70.24, 75.07, 81.79, 81.98, 127.95, 129.23, 130.93, 131.19, 134.41, 153.04; IR ( $\text{CDCl}_3$ ) 3292, 2946, 2826, 2118, 1479, 1433  $\text{cm}^{-1}$ ; mass spectrum  $m/z$  (% rel intensity) 228 ( $\text{M}^+$ , 30), 197 (50), 154 (100), 136 (60); HRMS calcd for  $\text{C}_{15}\text{H}_{16}\text{O}_2$   $m/z$  228.1150, meas 228.1151. Specific rotation:  $[\alpha]_{\text{D}} +3.5$  ( $c$  0.43  $\text{CHCl}_3$ ) on material obtained from (*S*)-**7** (93.4 % ee).

### Preparation of the bis-Propargyl Ether *meso*-**25**.



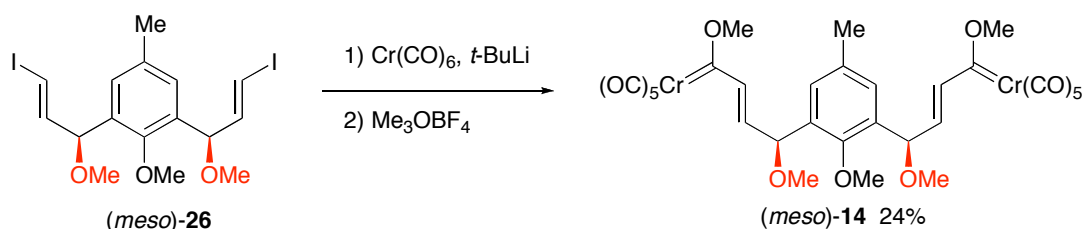
To a pre-weighed flame dried three necked 100 mL round bottomed flask was added 250 mg sodium hydride (60% dispersion in oil) and then pentane (10 mL) was added. The resulting slurry was stirred at ambient temperature for 15 minutes. The pentane was then removed using a syringe and the residual solvent was removed under vacuum to leave 156 mg of sodium hydride. Tetrahydrofuran (20 mL) was added to this flask under argon and then the (*meso*)-alkynol **6**<sup>7</sup> (0.598 g, 2.6 mmol) was slowly added over 5 minutes. Upon completion of the addition, the yellow slurry was stirred for another 45 min. Iodomethane (0.7 mL) was added and the reaction was left overnight. Ether (25 mL) was added and the reaction was worked up by addition of saturated ammonium chloride solution (15 mL). The product was extracted with ether (100 mL) and the organic layer was washed with water (100 mL). Drying over anhydrous magnesium sulfate, removal of ether under reduced pressure and purification by silica gel chromatography gave *meso*-**25** in 70% yield (0.46 g, 1.82 mmol);  $R_f = 0.37$  (hexanes / ethyl acetate = 85 / 15). Spectral data for *meso*-**25**:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz)  $\delta$  2.34 (s, 3H), 2.58 (d, 2H,  $J = 2.5$  Hz), 3.44 (s, 6H), 3.84 (s, 3H), 5.35 (d, 2H,  $J = 2.0$  Hz), 7.44 (s, 2H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz)  $\delta$  20.93, 56.28, 63.57, 67.01, 75.12, 81.74, 129.85, 131.42, 134.60, 153.16; IR (neat) 3290, 2990, 2939, 2903, 2824, 2114, 1730, 1664, 1591, 1481  $\text{cm}^{-1}$ ; mass spectrum FAB in NBA  $m/z$  (% rel intensity) 258 (50), 227 (100), 154 (100), 136 (60), HRMS calcd for  $\text{C}_{16}\text{H}_{18}\text{O}_3$   $m/z$  258.1256, meas 258.1257.

### Preparation of bis-vinyl iodide (*meso*)-26



Newly purchased or freshly prepared<sup>8</sup> Schwartz reagent (3.1 g, 12 mmol) and a stir bar were placed in a flame-dried 100 mL round-bottomed flask under nitrogen and shielded from light with foil and then 20 mL of freshly distilled tetrahydrofuran was added. To this freshly prepared Schwartz reagent was added diyne (*meso*)-25 (774 mg, 3 mmol) and the mixture was stirred at room temperature for 1 h. N-Iodosuccinimide (2.7 g, 12 mmol) was subsequently added and stirring continued for 4 h. The reaction was quenched by pouring the mixture into saturated sodium bicarbonate solution (40 mL). A solution of 10 % ethyl acetate/hexanes (100 mL) was added and the organic layer separated and washed with brine (40 mL), dried over anhydrous magnesium sulfate. After filtration through a bed of Celite atop a short plug of silica gel with 10 % ethyl acetate/hexanes the solvents were removed to give the crude product as an oil. Purification by column chromatography on silica gel (5 % ethyl acetate / hexanes) afforded the desired vinyl iodide (*meso*)-26 (1.10 g, 2.16 mmol) in 72 % yield as a light-yellow solid. Mp 104-106°C. Spectral data for (*meso*)-26: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 2.30 (s, 3H), 3.29 (s, 6H), 3.68 (s, 3H), 4.91 (d, 2H, *J* = 6.5 Hz), 6.42 (d, 2H, *J* = 14.5 Hz), 6.65 (dd, 2H, *J* = 14.5, 6.5 Hz), 7.11 (s, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 21.04, 56.59, 62.93, 78.79, 79.20, 128.34, 132.25, 135.03, 145.35, 153.48; IR (neat) 2982, 2930, 2822, 1605, 1477, 1432, 1338, 1277 cm<sup>-1</sup>. Anal calcd for C<sub>16</sub>H<sub>20</sub>I<sub>2</sub>O<sub>3</sub> C, 37.38; H, 3.92. Found C, 37.55; H, 3.88.

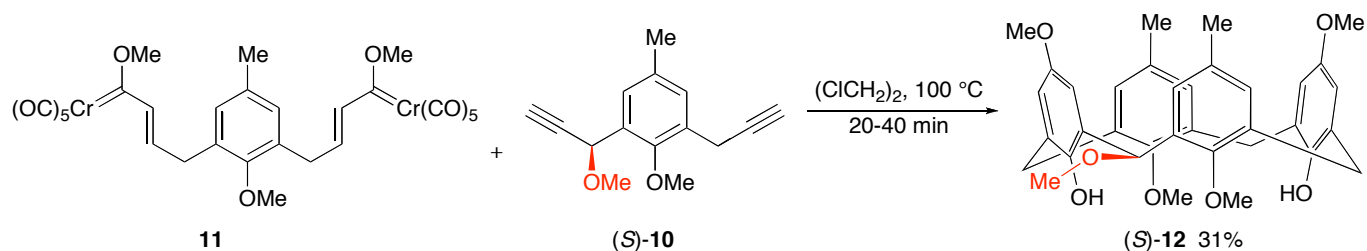
### Preparation of Bis-Carbene complex (*meso*)-14



To a solution of the (*meso*)-vinyl iodide **26** (0.91 g, 1.77 mmol), chromium hexacarbonyl (1.59 g, 7.14 mmol) in tetrahydrofuran (60 mL) was added *tert*-butyl lithium (4 equiv) dropwise at -78°C and the resultant dark red suspension was stirred at this temperature for 30 min. The reaction was then warmed up to room temperature and

stirred for 4 h. The solvent was evaporated under vacuum and water/ dichloromethane (1:1, 50 mL) was added and then trimethyl oxonium tetrafluoroborate (6.5 equiv) was added and the mixture stirred for 30 min. The organic layer (150 mL) was washed with water (2 x 50 mL) and dried over anhydrous magnesium sulfate. After filtration the solvent was removed and the crude product was purified by silica-gel chromatography (15 % ethyl acetate / hexanes) to give the bis-carbene complex (310 mg, 0.424 mmol, 24 % yield) as a deep-red oil.  $R_f$  (ethyl acetate / hexanes = 85/15) = 0.30. Spectral data for (*meso*)-**14**:  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  2.25 (s, 3H), 3.34 (s, 6H), 3.76 (s, 3H), 4.71 (s, 6H), 5.08 (d, 2H,  $J = 5.1$  Hz), 6.07 (dd, 2H,  $J = 15.0, 5.7$  Hz), 7.10 (s, 2H), 7.52 (d, 2H,  $J = 15.0$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 125 MHz) 20.87, 56.98, 62.96, 66.57, 76.18, 128.90, 130.84, 132.10, 135.39, 141.96, 153.46, 216.41, 223.98, 337.01; IR (neat) 2934, 2828, 2060, 1917, 1605, 1477, 1452, 1275, 1228  $\text{cm}^{-1}$ ; mass spectrum  $m/z$  (% rel. intensity) 729.9 ( $\text{M}^+$ , 2.8), 698.9 (3.5), 589.9 (64), 450.0 (100), 418.9 (28), 179.1 (40), HRMS calcd for  $\text{C}_{30}\text{H}_{26}\text{Cr}_2\text{O}_{15}$   $m/z$  730.0082, meas 730.0080.

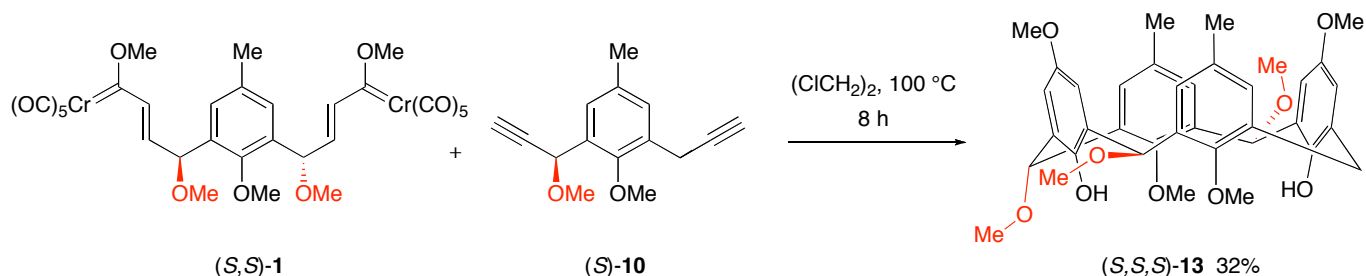
**General Procedure for the Synthesis of Calixarenes: Illustrated for 5,17-dimethyl-2(*S*),11,23,26,28-pentamethoxy-25,27-dihydroxycalix[4]arene (*S*)-12.**



A mixture of the bis-carbene complex **11**<sup>2</sup> (0.122 g, 0.183 mmol) and diyne (*S*)-**10** (93% ee, 0.043 g, 0.183 mmol) in 72 mL of 1,2-dichloroethane was introduced into a 250 mL pear shaped single-necked flask in which the 14/20 joint was replaced by a T-shaped high vacuum Teflon valve. The solution was deoxygenated by the freeze-thaw method (3 cycles,  $-196$  to  $25$   $^{\circ}\text{C}$ ) and then backfilled with argon at ambient temperature. The flask was sealed and then heated at  $100$   $^{\circ}\text{C}$  for 0-40 min during which time the deep red solution turned yellow. The flask was cooled to room temperature and the yellow solution was stirred overnight exposed to air to facilitate demetalation. The solvent was removed from the resulting dark brown mixture and the residue was dissolved in ethyl acetate (50 mL) and then filtered through a short pad of silica gel. The silica gel pad was rinsed several times with ethyl acetate and the combined organic layer was stripped of solvent to give the crude calixarene. TLC analysis of the crude material revealed only one spot corresponding to the product and examination of the  $^1\text{H NMR}$  spectrum

indicated no other side products. Purification of the product by silica-gel chromatography (50% ethyl acetate/hexanes) afforded the calix[4]arene pentamethyl ether (*S*)-**12** in 31% yield (0.032 g, 0.057 mmol) as an off-white solid; mp 270-273 °C. Spectral data for (*S*)-**12**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 2.03 (s, 6H), 3.22 (d, 1H, *J* = 12.6 Hz), 3.32 (d, 2H, *J* = 13.2 Hz), 3.44 (s, 3H), 3.72 (s, 3H), 3.74 (s, 3H), 3.94 (s, 3H), 3.98 (s, 3H), 4.11 (d, 1H, *J* = 12.3 Hz), 4.14 (d, 1H, *J* = 13.2 Hz), 4.35 (d, 1H, *J* = 12.9 Hz), 5.94 (s, 1H), 6.58 (d, 2H, *J* = 3.0 Hz), 6.60 (d, 1H, *J* = 3.0 Hz), 6.65 (d, 1H, *J* = 3.0 Hz), 6.72 (s, 1H), 6.75 (d, 2H, *J* = 5.5 Hz), 6.90 (d, 1H, *J* = 2.0 Hz), 6.96 (d, 1H, *J* = 3.0 Hz), 7.59 (s, 1H), 7.69 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz) δ 20.86, 21.02, 31.03, 31.82, 31.95, 55.78, 55.81, 57.36, 63.51, 63.74, 73.83, 108.12, 113.42, 114.00, 114.32, 126.87, 128.36, 128.73, 129.41, 129.63, 130.06, 130.49, 130.92, 132.07, 132.37, 133.22, 134.36, 134.56, 134.88, 145.79, 146.78, 150.87, 151.04, 152.25, 152.91; IR (CH<sub>2</sub>Cl<sub>2</sub>) 3333, 2943, 2829, 1603, 1461, 1433, 1346 cm<sup>-1</sup>; mass spectrum *m/z* (% rel intensity) 570 (100), 539 (60), 507 (92), 475 (52), 154 (64), HRMS calcd for C<sub>35</sub>H<sub>38</sub>O<sub>7</sub> 570.2616, meas 570.2618. Specific rotation: [α]<sub>D</sub> -5.4 (*c* 0.91, CHCl<sub>3</sub>) on material prepared from (*S*)-**10** of 93.4% ee. The calix[8]arene is present only in insignificant amounts as indicated by the relative intensities of molecular ion peaks corresponding to the monomer and dimer (100/0.4). Calixarene (*S*)-**12** was also characterized by X-ray diffraction as described below.

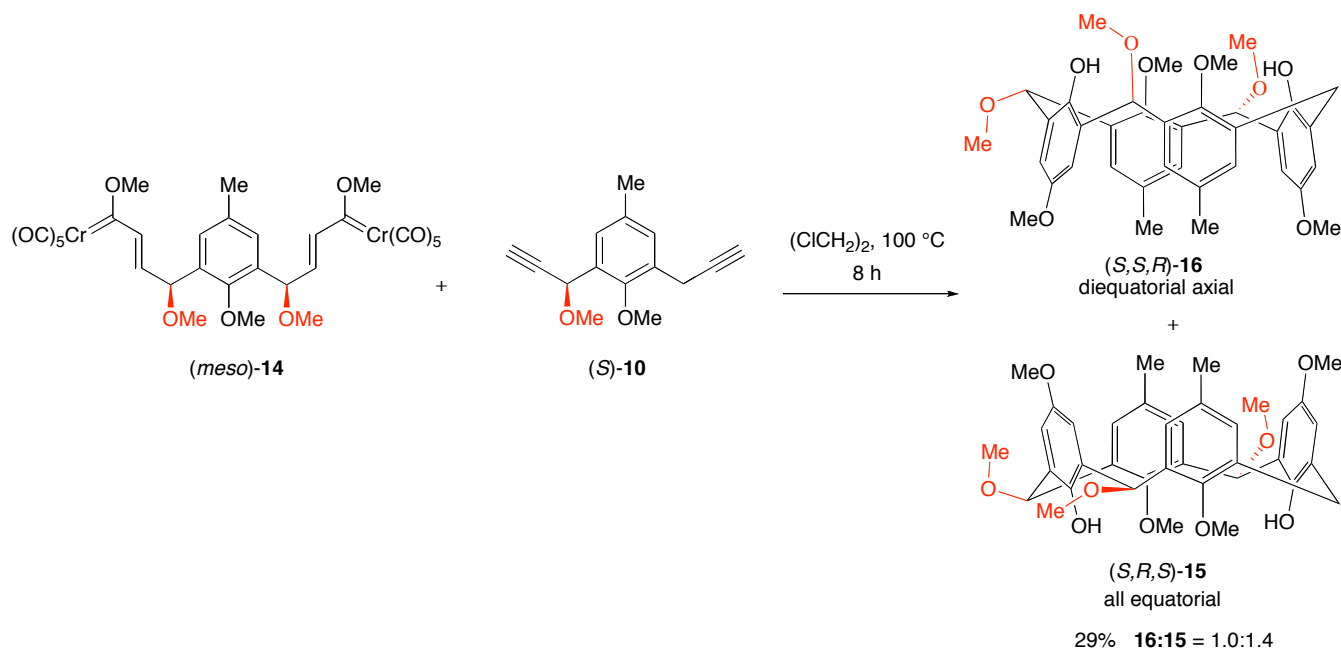
*Preparation of 5,17-Dimethyl-2(R),8(R),14(R),11,23,26,28-heptamethoxy-25,27-dihydroxycalix[4]arene-(S,S,S)-13.*



A solution of chiral bis-carbene complex (*S,S,S*)-**1** (0.216 g, 0.29 mmol, 97.8% ee)<sup>7</sup> and chiral alkyne (*S,S,S*)-**10** (0.11 g, 0.48 mmol, 93.4% ee) in 118 mL of 1,2-dichloroethane was prepared for reaction according to the general procedure for the preparation of (*S*)-**12** described above. The reaction mixture was then heated at 100 °C for 8 h. Work up according to the general procedure followed by purification in 25% ethyl acetate/hexanes afforded the heptamethyl ether (*S,S,S*)-**13** in 32 % yield (0.058 g, 0.093 mmol) as a white solid; mp 105-108 °C, *R*<sub>f</sub> = 0.3 (1/1 hexanes/ethyl acetate). TLC analysis of the crude material revealed only one spot corresponding to the product and examination of the <sup>1</sup>H NMR spectrum indicated no other side products. Spectral data for (*S,S,S*)-**13**: <sup>1</sup>H NMR

(CDCl<sub>3</sub>, 500 MHz)  $\delta$  2.07 (s, 6H), 3.35 (d, 1H,  $J = 13.0$  Hz), 3.38 (s, 3H), 3.43 (s, 3H), 3.44 (s, 3H), 3.73 (s, 3H), 3.74 (s, 3H), 3.99 (s, 3H), 4.00 (s, 3H), 4.09 (d, 1H,  $J = 13.0$  Hz), 5.04 (s, 1H), 6.00 (s, 1H), 6.05 (s, 1H), 6.53 (d, 1H,  $J = 2.5$  Hz), 6.57 (d, 1H,  $J = 3.0$  Hz), 6.66 (d, 1H,  $J = 2.0$  Hz), 6.78 (d, 1H,  $J = 2.0$  Hz), 6.92 (d, 1H,  $J = 3.0$  Hz), 6.99 (d, 1H,  $J = 2.0$  Hz), 7.01 (d, 1H,  $J = 3.0$  Hz), 7.08 (d, 1H,  $J = 2.0$  Hz), 7.81 (s, 1H); <sup>13</sup>C NMR (125 MHz)  $\delta$  20.96, 21.08, 29.69, 32.10, 55.76, 55.81, 57.16, 57.25, 57.41, 63.64, 64.42, 73.18, 108.45, 110.45, 114.11, 114.59, 126.36, 126.78, 128.14, 128.99, 129.54, 130.35, 131.03, 131.33, 132.31, 132.52, 134.46, 134.49, 135.01, 136.74, 145.81, 145.90, 150.88, 151.05, 152.09, 153.03 (one carbon missing); IR (neat) 3312, 2934, 2826, 1607, 1482, 1435, 1236 cm<sup>-1</sup>; mass spectrum FAB in NBA ( $m/z$ , % rel intensity) 630 M<sup>+</sup> (20), 567 (40), 535 (90), 294 (80), 263 (100), HRMS calcd for C<sub>37</sub>H<sub>42</sub>O<sub>9</sub> 630.2829, measd 630.2832. Specific rotation:  $[\alpha]_D -16.2$  ( $c$  1.61, CHCl<sub>3</sub>). No detectable amount of a calix[8]arene was observed by mass spectra. The enantiomeric purity of the calix[4]arene was found to be 100% ee by HPLC analysis (Chiralcel OD column, 254 nm, 99.5:0.5 hexanes:*i*-PrOH to 95:5 hexanes:*i*-PrOH, retention time = 8.35 min). Analyses using other chiral HPLC columns did not show the presence of any other small peaks due to the enantiomer.

5,17-dimethyl-2(*S*),8(*R*),11,14(*R*),23,26,28-heptamethoxy-25,27-dihydroxy calixarene (*S,S,R*)-**16** and 5,17-dimethyl-2(*R*),8(*S*),11,14(*R*),23,26,28-heptamethoxy-25,27-dihydroxy calixarene (*S,R,S*)-**15**.



A mixture of bis-carbene complex (*meso*)-**14** (0.137 g, 0.188 mmol) and chiral alkyne (*S*)-**10** (0.048 g, 0.211 mmol, 93.4 % ee) in 118 mL of 1,2-dichloroethane was subjected to the freeze-thaw degassing according to

the general procedure. The reaction mixture was then heated at 100°C for 8 h. Work up according to the general procedure followed by purification by silica gel chromatography with 25 % ethylacetate/hexanes as eluent afforded a mixture of two calix[4]arenes in a 1.36:1.0 ratio in 29 % yield (0.034 g, 0.055 mmol) as light yellow solid. TLC analysis of the crude reaction mixture revealed only one spot corresponding to the product mixture and examination of the crude <sup>1</sup>H NMR indicated no other side products were formed other than the two calix[4]arenes. Melting point of the purified mixture is 165-168°C. The mixture was analyzed by HPLC which indicated the presence of a mixture of two compounds in a ratio of 1.36:1 (R001086C5 Silica column, 254 nm, hexanes / i-PrOH 99.5/ 0.5 to 95/ 5, flow rate 0.5 mL/min, retention time for **16** = 46.15 min and **15** = 55.13 min). The 1.36:1 mixture of **16** to **15** was purified again by gradual elution and thereby **16** could be separated from **15** which was still obtained as an enriched mixture (ratio 4.1:1). R<sub>f</sub> for **16** (hexanes / ethylacetate = 1/1) = 0.62. Spectral data for **16**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 2.03 (s, 3H), 2.09 (s, 3H), 3.29 (d, 1H, J = 13.0 Hz), 3.38 (s, 3H), 3.44 (s, 3H), 3.46 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H), 3.93 (s, 6H), 4.09 (d, 1H, J = 12.5 Hz), 5.05 (s, 1H), 5.80 (s, 2H), 6.60 (d, 1H, J = 3.0 Hz), 6.69 (s, 2H), 6.79 (s, 1H), 6.86 (s, 1H), 6.93 (s, 1H), 6.99 (d, 1H, J = 2.7 Hz), 7.10 (s, 1H) (OH protons not located); <sup>13</sup>C NMR (125 MHz) of **16** δ 14.16, 20.71, 21.05, 29.67, 30.74, 55.74, 55.76, 57.12, 57.33, 57.53, 64.32, 74.15, 107.61, 114.16, 125.80, 127.64, 131.31, 132.77, 133.86, 134.52, 145.41, 151.96, 152.39, 152.88 (13 carbons not located); Spectral data for **15** was extracted from the spectrum of a mixture of **15** and **16** with the aid of a pure sample of **16**: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz) δ 2.07 (s, 3H), 2.08 (s, 3H), 3.42 (s, 3H), 3.43 (s, 3H), 3.72 (s, 3H), 3.73 (s, 3H), 3.74 (s, 3H), 3.99 (s, 3H), 4.04 (s, 3H), 5.69 (s, 1H), 5.91 (s, 1H), 5.93 (s, 1H), 6.58 (d, 1H, J = 3.0 Hz), 6.75 (s, 1H), 6.86 (s, 1H), 6.91 (s, 1H), 6.92 (s, 1H), 6.96 (s, 2H), 6.98 (s, 1H), 7.40 (s, 1H), 7.81 (s, 1H) (2 methylene H's not located); <sup>13</sup>C NMR (125 MHz) δ 21.13, 21.26, 31.56, 31.75, 56.98, 60.38, 63.35, 63.71, 63.87, 73.44, 73.60, 73.86, 108.17, 108.39, 109.15, 114.32, 126.62, 128.55, 130.44, 130.75, 130.79, 131.38, 131.58, 132.25, 133.80, 134.35, 134.64, 135.37, 135.69, 144.27, 145.57, 149.94, 150.25, 150.74, 153.02, 153.81 (1 C not located); IR of mixture (neat) 3350, 2932, 2828, 1604, 1491, 1435, 1346, 1234 cm<sup>-1</sup>; mass spectrum of mixture; FAB in NBA *m/z* (% rel.intensity) 630.2 (10), 567.2 (16), 535.1 (40), 197.1 (30), 135.1 (72); HRMS calcd for C<sub>37</sub>H<sub>42</sub>O<sub>9</sub> 630.2829 meas 630.2832. Specific rotation was taken on the 1.36:1 mixture of diastereomers **16** and **15** that was derived from (*S*)-**10** (93 % ee): [α]<sub>D</sub> - 3.2° (c = 1.7 in CHCl<sub>3</sub>). The structures of the two conformers are tentatively assigned as the diequatorial axial **16** and all equatorial **15** respectively based on the chemical shifts of the methine hydrogens. The equatorial methine proton and the two axial protons are located at 5.05 ppm and 5.80 ppm in **16** whereas the axial protons in **15** are observed at 5.69, 5.91 and 5.93 ppm respectively.



### X-Ray Diffraction Data for Calix[4]arene (*S*)-12.

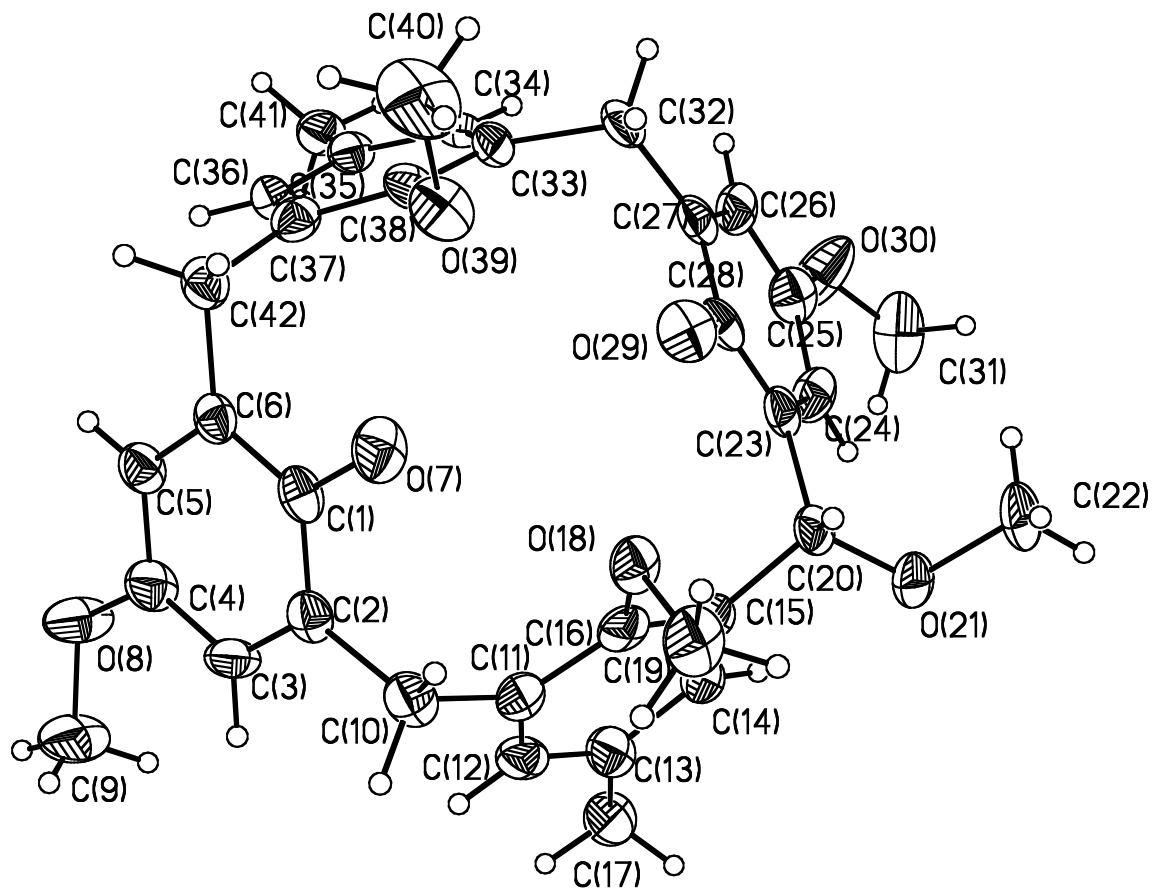


Figure 1. ORTEP plot for Calix[4]arene (*S*)-12. Only one of the two molecules in the unit cell is shown.

Table 1. Crystal data and structure refinement for (*S*)-12

Identification code	wf060905
Empirical formula	C71 H78 Cl2 O14
Formula weight	1226.23
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P1
Unit cell dimensions	a = 11.190(2) Å b = 11.396(2) Å c = 14.071(3) Å alpha = 108.80(3) deg. beta = 96.93(3) deg. gamma = 107.54(3) deg.
Volume	1571.8(5) Å <sup>3</sup>
Z	1
Density (calculated)	1.295 Mg/m <sup>3</sup>
Absorption coefficient	0.170 mm <sup>-1</sup>
F(000)	650
Crystal size	0.4 x 0.2 x 0.1 mm
Theta range for data collection	1.58 to 28.32 deg.
Index ranges	-14 ≤ h ≤ 14, -14 ≤ k ≤ 15, -18 ≤ l ≤ 18
Reflections collected / unique	19128 / 14123 [R(int) = 0.0436]
Completeness to theta = 28.32	94.9%
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	14123 / 3 / 784
Goodness-of-fit on F <sup>2</sup>	0.724
Final R indices [I > 2σ(I)]	R1 = 0.0547, wR2 = 0.1271
R indices (all data)	R1 = 0.1196, wR2 = 0.1525
Absolute structure parameter	-0.01(8)
Largest diff. peak and hole	0.344 and -0.386 e.Å <sup>-3</sup>

Table 2. Atomic coordinates ( × 10<sup>4</sup>), equivalent isotropic displacement parameters (Å<sup>2</sup> × 10<sup>3</sup>), and occupancies for (*S*)-12

x	y	z	U(eq)	Occ.	
C(1)	-172(4)	-896(4)	-2204(3)	29(1)	1
C(2)	1167(4)	-260(4)	-1882(3)	30(1)	1
C(3)	1855(4)	-121(5)	-2624(3)	35(1)	1
C(4)	1236(4)	-580(5)	-3651(3)	37(1)	1
C(5)	-105(4)	-1208(4)	-3969(3)	32(1)	1
C(6)	-824(4)	-1365(4)	-3256(3)	28(1)	1
O(7)	-824(3)	-1088(3)	-1458(2)	41(1)	1
O(8)	1848(3)	-480(4)	-4432(2)	55(1)	1
C(9)	3232(5)	-26(7)	-4155(4)	66(2)	1
C(10)	1855(5)	333(4)	-737(3)	37(1)	1
C(11)	2010(4)	1770(4)	-222(3)	32(1)	1
C(12)	2970(4)	2795(5)	-336(3)	36(1)	1
C(13)	3109(4)	4119(5)	84(3)	37(1)	1
C(14)	2195(4)	4434(4)	620(3)	32(1)	1

C(15)	1230(4)	3458(4)	771(3)	31(1)	1
C(16)	1186(4)	2146(4)	390(3)	31(1)	1
C(17)	4199(4)	5204(5)	0(4)	46(1)	1
O(18)	266(3)	1187(3)	593(2)	33(1)	1
C(19)	755(5)	990(5)	1506(3)	44(1)	1
C(20)	214(4)	3804(4)	1311(3)	28(1)	1
O(21)	816(2)	5090(2)	2097(2)	34(1)	1
C(22)	-2(4)	5392(4)	2786(3)	44(1)	1
C(23)	-927(4)	3735(4)	535(3)	28(1)	1
C(24)	-920(4)	4899(4)	402(3)	36(1)	1
C(25)	-1959(4)	4877(4)	-246(3)	38(1)	1
C(26)	-2990(4)	3693(4)	-805(3)	35(1)	1
C(27)	-2984(4)	2514(4)	-717(3)	30(1)	1
C(28)	-1947(4)	2557(4)	-22(3)	29(1)	1
O(29)	-2051(3)	1370(3)	80(2)	39(1)	1
O(30)	-2068(4)	5976(3)	-418(3)	69(1)	1
C(31)	-1332(6)	7234(5)	298(4)	64(2)	1
C(32)	-4054(4)	1219(4)	-1385(3)	32(1)	1
C(33)	-3739(4)	559(4)	-2408(3)	29(1)	1
C(34)	-3770(4)	1125(4)	-3153(3)	30(1)	1
C(35)	-3432(4)	620(4)	-4076(3)	29(1)	1
C(36)	-2974(4)	-424(4)	-4221(3)	28(1)	1
C(37)	-2898(4)	-995(4)	-3484(3)	30(1)	1
C(38)	-3334(4)	-505(4)	-2600(3)	30(1)	1
O(39)	-3256(3)	-1080(3)	-1859(2)	42(1)	1
C(40)	-4434(5)	-2173(5)	-2010(5)	68(2)	1
C(41)	-3515(4)	1213(4)	-4893(3)	35(1)	1
C(42)	-2285(4)	-2023(4)	-3624(3)	33(1)	1
C(1A)	-1665(4)	1078(4)	-7001(3)	29(1)	1
C(2A)	-2699(4)	-90(4)	-7615(3)	28(1)	1
C(3A)	-2724(4)	-1270(4)	-7509(3)	33(1)	1
C(4A)	-1746(4)	-1305(4)	-6823(3)	34(1)	1
C(5A)	-713(4)	-138(4)	-6257(3)	32(1)	1
C(6A)	-653(4)	1058(4)	-6309(3)	28(1)	1
O(7A)	-1536(3)	2284(3)	-7049(2)	36(1)	1
C(8A)	-1723(3)	-2431(3)	-6676(2)	46(1)	1
C(9A)	-2847(5)	-3579(5)	-7133(4)	54(1)	1
C(10A)	-3800(4)	-96(4)	-8357(3)	32(1)	1
C(11A)	-4799(4)	286(4)	-7796(3)	28(1)	1
C(12A)	-5750(4)	-655(4)	-7609(3)	33(1)	1
C(13A)	-6660(4)	-333(4)	-7083(3)	31(1)	1
C(14A)	-6526(4)	979(4)	-6675(3)	34(1)	1
C(15A)	-5572(4)	1976(4)	-6813(3)	27(1)	1
C(16A)	-4759(4)	1584(4)	-7424(3)	27(1)	1
C(17A)	-7758(5)	-1403(5)	-6980(4)	52(1)	1
O(18A)	-3847(2)	2547(3)	-7655(2)	31(1)	1
C(19A)	-4360(5)	2700(5)	-8569(3)	42(1)	1
C(20A)	-5374(4)	3429(4)	-6287(3)	27(1)	1
O(21A)	-6618(2)	3544(3)	-6453(2)	36(1)	1
C(22A)	-6529(5)	4860(5)	-6293(4)	57(1)	1
C(23A)	-4737(4)	3922(4)	-5141(3)	26(1)	1
C(24A)	-5515(4)	3760(4)	-4443(3)	30(1)	1
C(25A)	-4923(4)	4144(4)	-3407(3)	30(1)	1
C(26A)	-3604(4)	4714(4)	-3069(3)	27(1)	1
C(27A)	-2825(4)	4898(4)	-3742(3)	25(1)	1
C(28A)	-3410(4)	4496(4)	-4786(3)	25(1)	1
O(29A)	-2709(3)	4660(3)	-5496(2)	35(1)	1

O(30A)	-5588(3)	4001(3)	-2657(2)	47(1)	1
C(31A)	-6949(4)	3509(6)	-2969(4)	51(1)	1
C(32A)	-1376(4)	5510(4)	-3329(3)	27(1)	1
C(33A)	-769(4)	4463(4)	-3479(3)	23(1)	1
C(34A)	-772(4)	3822(4)	-2793(3)	26(1)	1
C(35A)	-324(4)	2788(4)	-2946(3)	22(1)	1
C(36A)	28(4)	2315(4)	-3872(3)	24(1)	1
C(37A)	71(3)	2933(4)	-4581(3)	22(1)	1
C(38A)	-284(4)	4032(4)	-4348(3)	25(1)	1
O(39A)	-175(3)	4762(3)	-4992(2)	30(1)	1
C(40A)	995(4)	5895(4)	-4618(3)	44(1)	1
C(41A)	-222(4)	2194(4)	-2146(3)	29(1)	1
C(42A)	427(4)	2358(4)	-5596(3)	31(1)	1
Cl(1)	2266(2)	7789(1)	256(1)	78(1)	1
Cl(2)	2373(2)	6721(2)	-1859(1)	126(1)	1
C(100)	1402(6)	6746(7)	-1021(4)	91(2)	1

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

Table 3. Bond lengths [Å] and angles [deg] for (S)-12.

C(1)-O(7)	1.386(5)
C(1)-C(2)	1.395(6)
C(1)-C(6)	1.416(5)
C(2)-C(3)	1.391(6)
C(2)-C(10)	1.526(6)
C(3)-C(4)	1.377(6)
C(4)-O(8)	1.380(5)
C(4)-C(5)	1.396(6)
C(5)-C(6)	1.381(5)
C(6)-C(42)	1.520(6)
O(8)-C(9)	1.435(6)
C(10)-C(11)	1.507(6)
C(11)-C(12)	1.397(6)
C(11)-C(16)	1.402(6)
C(12)-C(13)	1.384(6)
C(13)-C(14)	1.405(6)
C(13)-C(17)	1.500(6)
C(14)-C(15)	1.390(6)
C(15)-C(16)	1.400(6)
C(15)-C(20)	1.521(6)
C(16)-O(18)	1.389(5)
O(18)-C(19)	1.447(5)
C(20)-O(21)	1.416(5)
C(20)-C(23)	1.541(5)
O(21)-C(22)	1.444(4)
C(23)-C(28)	1.378(6)
C(23)-C(24)	1.396(6)
C(24)-C(25)	1.377(6)
C(25)-O(30)	1.387(5)
C(25)-C(26)	1.389(6)
C(26)-C(27)	1.390(6)

C(27)-C(28)	1.403(6)
C(27)-C(32)	1.505(6)
C(28)-O(29)	1.379(5)
O(30)-C(31)	1.381(6)
C(32)-C(33)	1.531(5)
C(33)-C(38)	1.378(6)
C(33)-C(34)	1.398(6)
C(34)-C(35)	1.388(6)
C(35)-C(36)	1.399(6)
C(35)-C(41)	1.517(5)
C(36)-C(37)	1.397(5)
C(37)-C(38)	1.400(6)
C(37)-C(42)	1.499(6)
C(38)-O(39)	1.407(5)
O(39)-C(40)	1.452(6)
C(1A)-O(7A)	1.363(5)
C(1A)-C(2A)	1.395(6)
C(1A)-C(6A)	1.411(6)
C(2A)-C(3A)	1.392(6)
C(2A)-C(10A)	1.513(6)
C(3A)-C(4A)	1.389(6)
C(4A)-C(8A)	1.371(5)
C(4A)-C(5A)	1.381(6)
C(5A)-C(6A)	1.371(6)
C(6A)-C(42A)	1.527(6)
C(8A)-C(9A)	1.407(5)
C(10A)-C(11A)	1.531(6)
C(11A)-C(12A)	1.383(5)
C(11A)-C(16A)	1.385(6)
C(12A)-C(13A)	1.397(6)
C(13A)-C(14A)	1.370(6)
C(13A)-C(17A)	1.508(6)
C(14A)-C(15A)	1.388(6)
C(15A)-C(16A)	1.398(5)
C(15A)-C(20A)	1.512(6)
C(16A)-O(18A)	1.410(5)
O(18A)-C(19A)	1.429(5)
C(20A)-O(21A)	1.435(4)
C(20A)-C(23A)	1.523(5)
O(21A)-C(22A)	1.414(5)
C(23A)-C(28A)	1.382(5)
C(23A)-C(24A)	1.409(5)
C(24A)-C(25A)	1.391(5)
C(25A)-C(26A)	1.371(5)
C(25A)-O(30A)	1.387(5)
C(26A)-C(27A)	1.385(5)
C(27A)-C(28A)	1.396(5)
C(27A)-C(32A)	1.511(5)
C(28A)-O(29A)	1.368(4)
O(30A)-C(31A)	1.412(5)
C(32A)-C(33A)	1.513(5)
C(33A)-C(34A)	1.385(5)
C(33A)-C(38A)	1.403(5)
C(34A)-C(35A)	1.380(5)
C(35A)-C(36A)	1.394(5)
C(35A)-C(41A)	1.498(5)
C(36A)-C(37A)	1.392(5)

C(37A)-C(38A)	1.379(5)
C(37A)-C(42A)	1.523(5)
C(38A)-O(39A)	1.405(4)
O(39A)-C(40A)	1.427(5)
Cl(1)-C(100)	1.758(5)
Cl(2)-C(100)	1.696(6)
O(7)-C(1)-C(2)	117.1(4)
O(7)-C(1)-C(6)	121.8(4)
C(2)-C(1)-C(6)	121.1(4)
C(3)-C(2)-C(1)	118.4(4)
C(3)-C(2)-C(10)	120.7(4)
C(1)-C(2)-C(10)	120.8(4)
C(4)-C(3)-C(2)	121.2(4)
C(3)-C(4)-O(8)	124.7(4)
C(3)-C(4)-C(5)	120.2(4)
O(8)-C(4)-C(5)	115.2(4)
C(6)-C(5)-C(4)	120.4(4)
C(5)-C(6)-C(1)	118.7(4)
C(5)-C(6)-C(42)	119.0(4)
C(1)-C(6)-C(42)	122.2(4)
C(4)-O(8)-C(9)	116.2(3)
C(11)-C(10)-C(2)	112.6(3)
C(12)-C(11)-C(16)	116.5(4)
C(12)-C(11)-C(10)	121.9(4)
C(16)-C(11)-C(10)	121.6(4)
C(13)-C(12)-C(11)	123.7(4)
C(12)-C(13)-C(14)	117.6(4)
C(12)-C(13)-C(17)	122.3(4)
C(14)-C(13)-C(17)	120.1(4)
C(15)-C(14)-C(13)	121.1(4)
C(14)-C(15)-C(16)	118.9(4)
C(14)-C(15)-C(20)	120.5(4)
C(16)-C(15)-C(20)	120.6(4)
O(18)-C(16)-C(15)	118.8(4)
O(18)-C(16)-C(11)	119.5(4)
C(15)-C(16)-C(11)	121.7(4)
C(16)-O(18)-C(19)	112.6(3)
O(21)-C(20)-C(15)	107.9(3)
O(21)-C(20)-C(23)	111.6(3)
C(15)-C(20)-C(23)	111.0(3)
C(20)-O(21)-C(22)	111.7(3)
C(28)-C(23)-C(24)	119.8(4)
C(28)-C(23)-C(20)	121.5(4)
C(24)-C(23)-C(20)	118.7(4)
C(25)-C(24)-C(23)	119.8(4)
C(24)-C(25)-O(30)	124.7(4)
C(24)-C(25)-C(26)	120.5(4)
O(30)-C(25)-C(26)	114.7(4)
C(25)-C(26)-C(27)	120.3(4)
C(26)-C(27)-C(28)	118.7(4)
C(26)-C(27)-C(32)	120.1(4)
C(28)-C(27)-C(32)	121.2(4)
C(23)-C(28)-O(29)	123.7(4)
C(23)-C(28)-C(27)	120.8(4)
O(29)-C(28)-C(27)	115.5(4)
C(31)-O(30)-C(25)	119.3(4)

C(27)-C(32)-C(33)	111.6(3)
C(38)-C(33)-C(34)	118.2(4)
C(38)-C(33)-C(32)	123.2(4)
C(34)-C(33)-C(32)	118.4(4)
C(35)-C(34)-C(33)	121.5(4)
C(34)-C(35)-C(36)	118.3(4)
C(34)-C(35)-C(41)	121.0(4)
C(36)-C(35)-C(41)	120.6(4)
C(37)-C(36)-C(35)	121.8(4)
C(36)-C(37)-C(38)	117.3(4)
C(36)-C(37)-C(42)	120.0(4)
C(38)-C(37)-C(42)	122.6(4)
C(33)-C(38)-C(37)	122.6(4)
C(33)-C(38)-O(39)	120.0(4)
C(37)-C(38)-O(39)	117.2(4)
C(38)-O(39)-C(40)	112.9(4)
C(37)-C(42)-C(6)	110.6(3)
O(7A)-C(1A)-C(2A)	123.2(4)
O(7A)-C(1A)-C(6A)	115.9(4)
C(2A)-C(1A)-C(6A)	120.8(4)
C(3A)-C(2A)-C(1A)	118.3(4)
C(3A)-C(2A)-C(10A)	119.7(4)
C(1A)-C(2A)-C(10A)	121.9(4)
C(4A)-C(3A)-C(2A)	121.6(4)
C(8A)-C(4A)-C(5A)	117.2(4)
C(8A)-C(4A)-C(3A)	124.3(4)
C(5A)-C(4A)-C(3A)	118.5(4)
C(6A)-C(5A)-C(4A)	122.4(4)
C(5A)-C(6A)-C(1A)	118.3(4)
C(5A)-C(6A)-C(42A)	121.6(4)
C(1A)-C(6A)-C(42A)	120.0(4)
C(4A)-C(8A)-C(9A)	117.6(3)
C(2A)-C(10A)-C(11A)	111.1(3)
C(12A)-C(11A)-C(16A)	117.5(4)
C(12A)-C(11A)-C(10A)	120.7(4)
C(16A)-C(11A)-C(10A)	121.7(4)
C(11A)-C(12A)-C(13A)	122.1(4)
C(14A)-C(13A)-C(12A)	117.9(4)
C(14A)-C(13A)-C(17A)	121.4(4)
C(12A)-C(13A)-C(17A)	120.7(4)
C(13A)-C(14A)-C(15A)	122.7(4)
C(14A)-C(15A)-C(16A)	117.0(4)
C(14A)-C(15A)-C(20A)	121.9(4)
C(16A)-C(15A)-C(20A)	121.1(4)
C(11A)-C(16A)-C(15A)	122.4(4)
C(11A)-C(16A)-O(18A)	118.7(4)
C(15A)-C(16A)-O(18A)	118.9(4)
C(16A)-O(18A)-C(19A)	112.5(3)
O(21A)-C(20A)-C(15A)	107.3(3)
O(21A)-C(20A)-C(23A)	112.1(3)
C(15A)-C(20A)-C(23A)	110.0(3)
C(22A)-O(21A)-C(20A)	112.5(3)
C(28A)-C(23A)-C(24A)	119.9(3)
C(28A)-C(23A)-C(20A)	120.8(3)
C(24A)-C(23A)-C(20A)	119.3(3)
C(25A)-C(24A)-C(23A)	118.9(4)
C(26A)-C(25A)-O(30A)	115.7(3)

C(26A)-C(25A)-C(24A)	120.3(4)
O(30A)-C(25A)-C(24A)	124.0(4)
C(25A)-C(26A)-C(27A)	121.5(4)
C(26A)-C(27A)-C(28A)	118.6(4)
C(26A)-C(27A)-C(32A)	119.2(3)
C(28A)-C(27A)-C(32A)	122.2(3)
O(29A)-C(28A)-C(23A)	117.1(3)
O(29A)-C(28A)-C(27A)	122.1(3)
C(23A)-C(28A)-C(27A)	120.7(4)
C(25A)-O(30A)-C(31A)	116.8(3)
C(27A)-C(32A)-C(33A)	111.9(3)
C(34A)-C(33A)-C(38A)	117.8(4)
C(34A)-C(33A)-C(32A)	120.2(4)
C(38A)-C(33A)-C(32A)	121.8(3)
C(35A)-C(34A)-C(33A)	122.1(4)
C(34A)-C(35A)-C(36A)	117.6(3)
C(34A)-C(35A)-C(41A)	121.2(4)
C(36A)-C(35A)-C(41A)	121.2(4)
C(37A)-C(36A)-C(35A)	122.5(4)
C(38A)-C(37A)-C(36A)	117.3(4)
C(38A)-C(37A)-C(42A)	122.0(3)
C(36A)-C(37A)-C(42A)	120.6(4)
C(37A)-C(38A)-C(33A)	122.1(3)
C(37A)-C(38A)-O(39A)	120.4(3)
C(33A)-C(38A)-O(39A)	117.5(3)
C(38A)-O(39A)-C(40A)	112.1(3)
C(37A)-C(42A)-C(6A)	110.3(3)
Cl(2)-C(100)-Cl(1)	111.9(3)

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Symmetry transformations used to generate equivalent atoms.

Table 4. Anisotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ) for (*S*)-**12**.

U11	U22	U33	U23	U13	U12
C(1)	39(3)	31(2)	29(2)	16(2)	19(2)
C(2)	39(3)	34(2)	26(2)	14(2)	9(2)
C(3)	24(2)	54(3)	32(2)	18(2)	6(2)
C(4)	36(3)	53(3)	30(2)	19(2)	14(2)
C(5)	37(3)	42(3)	27(2)	15(2)	11(2)
C(6)	31(2)	22(2)	32(2)	9(2)	11(2)
O(7)	43(2)	48(2)	32(2)	18(1)	14(1)
O(8)	29(2)	106(3)	29(2)	30(2)	12(1)
C(9)	29(3)	127(5)	38(3)	28(3)	18(2)
C(10)	44(3)	50(3)	31(2)	21(2)	12(2)
C(11)	37(3)	44(3)	20(2)	14(2)	2(2)
C(12)	29(2)	55(3)	27(2)	19(2)	7(2)
C(13)	39(3)	51(3)	30(2)	21(2)	13(2)
C(14)	36(3)	38(2)	23(2)	12(2)	8(2)
C(15)	33(2)	45(3)	19(2)	14(2)	5(2)
C(16)	32(2)	43(3)	20(2)	16(2)	1(2)
C(17)	39(3)	57(3)	41(3)	18(2)	18(2)
O(18)	43(2)	41(2)	23(1)	17(1)	10(1)



C(19)	59(3)	54(3)	33(2)	29(2)	18(2)	24(3)
C(20)	33(2)	37(2)	20(2)	14(2)	13(2)	15(2)
O(21)	43(2)	41(2)	22(1)	12(1)	12(1)	16(1)
C(22)	64(3)	54(3)	27(2)	19(2)	26(2)	30(2)
C(23)	37(3)	38(3)	21(2)	13(2)	16(2)	21(2)
C(24)	44(3)	37(3)	23(2)	10(2)	8(2)	8(2)
C(25)	50(3)	42(3)	33(2)	20(2)	15(2)	24(2)
C(26)	40(3)	46(3)	20(2)	11(2)	7(2)	19(2)
C(27)	33(3)	42(3)	26(2)	15(2)	19(2)	21(2)
C(28)	36(3)	39(3)	29(2)	20(2)	23(2)	22(2)
O(29)	42(2)	43(2)	40(2)	24(2)	11(2)	15(2)
O(30)	102(3)	36(2)	47(2)	12(2)	-25(2)	19(2)
C(31)	112(5)	50(3)	47(3)	23(3)	30(3)	42(3)
C(32)	29(2)	47(3)	27(2)	15(2)	17(2)	18(2)
C(33)	26(2)	33(2)	28(2)	9(2)	14(2)	9(2)
C(34)	17(2)	36(2)	32(2)	10(2)	5(2)	9(2)
C(35)	24(2)	39(2)	24(2)	14(2)	8(2)	8(2)
C(36)	28(2)	29(2)	28(2)	8(2)	10(2)	12(2)
C(37)	26(2)	30(2)	29(2)	11(2)	6(2)	3(2)
C(38)	27(2)	38(3)	33(2)	20(2)	15(2)	11(2)
O(39)	48(2)	48(2)	45(2)	32(2)	23(2)	19(2)
C(40)	66(4)	57(3)	95(4)	46(3)	49(3)	13(3)
C(41)	33(2)	42(3)	32(2)	16(2)	8(2)	16(2)
C(42)	35(2)	26(2)	38(2)	11(2)	14(2)	12(2)
C(1A)	31(2)	36(3)	25(2)	13(2)	14(2)	15(2)
C(2A)	33(2)	37(2)	19(2)	12(2)	13(2)	15(2)
C(3A)	39(3)	40(3)	23(2)	9(2)	13(2)	19(2)
C(4A)	44(3)	37(3)	25(2)	10(2)	12(2)	21(2)
C(5A)	35(3)	44(3)	25(2)	13(2)	13(2)	25(2)
C(6A)	23(2)	40(3)	19(2)	9(2)	10(2)	11(2)
O(7A)	31(2)	39(2)	37(2)	17(1)	3(1)	9(1)
C(8A)	54(2)	39(2)	47(2)	17(2)	2(2)	21(2)
C(9A)	61(3)	41(3)	55(3)	21(2)	4(3)	11(2)
C(10A)	33(2)	39(2)	21(2)	7(2)	5(2)	12(2)
C(11A)	30(2)	36(2)	15(2)	8(2)	3(2)	9(2)
C(12A)	36(3)	30(2)	25(2)	7(2)	6(2)	8(2)
C(13A)	29(2)	38(3)	18(2)	9(2)	4(2)	2(2)
C(14A)	31(2)	55(3)	19(2)	12(2)	11(2)	21(2)
C(15A)	20(2)	45(3)	16(2)	13(2)	4(2)	12(2)
C(16A)	25(2)	41(3)	17(2)	14(2)	7(2)	12(2)
C(17A)	49(3)	48(3)	48(3)	12(2)	21(3)	4(2)
O(18A)	29(2)	44(2)	24(1)	19(1)	11(1)	12(1)
C(19A)	54(3)	57(3)	21(2)	19(2)	10(2)	23(2)
C(20A)	24(2)	39(2)	22(2)	13(2)	6(2)	17(2)
O(21A)	32(1)	55(2)	30(1)	18(1)	6(1)	25(1)
C(22A)	58(3)	68(3)	62(3)	30(3)	16(2)	41(3)
C(23A)	30(2)	33(2)	20(2)	9(2)	7(2)	17(2)
C(24A)	28(2)	42(3)	23(2)	11(2)	9(2)	19(2)
C(25A)	26(2)	47(3)	22(2)	13(2)	11(2)	18(2)
C(26A)	31(2)	31(2)	20(2)	10(2)	3(2)	14(2)
C(27A)	27(2)	28(2)	23(2)	9(2)	5(2)	15(2)
C(28A)	29(2)	28(2)	23(2)	12(2)	7(2)	13(2)
O(29A)	28(2)	61(2)	23(1)	24(1)	10(1)	17(1)
O(30A)	30(2)	87(2)	25(2)	22(2)	12(1)	20(2)
C(31A)	34(3)	87(4)	35(3)	27(3)	14(2)	20(3)
C(32A)	27(2)	32(2)	21(2)	10(2)	6(2)	9(2)
C(33A)	16(2)	28(2)	23(2)	8(2)	4(2)	9(2)

C(34A)	22(2)	37(2)	16(2)	11(2)	5(2)	6(2)
C(35A)	18(2)	26(2)	24(2)	12(2)	4(2)	6(2)
C(36A)	24(2)	27(2)	22(2)	8(2)	8(2)	11(2)
C(37A)	13(2)	31(2)	22(2)	11(2)	4(2)	6(2)
C(38A)	24(2)	27(2)	22(2)	13(2)	4(2)	5(2)
O(39A)	32(2)	36(2)	23(1)	18(1)	6(1)	8(1)
C(40A)	44(3)	50(3)	38(2)	26(2)	13(2)	6(2)
C(41A)	30(2)	39(2)	23(2)	16(2)	9(2)	15(2)
C(42A)	24(2)	45(3)	26(2)	14(2)	9(2)	12(2)
Cl(1)	95(1)	69(1)	46(1)	15(1)	-20(1)	18(1)
Cl(2)	75(1)	194(2)	58(1)	35(1)	14(1)	-5(1)
C(100)	73(4)	112(5)	48(3)	10(3)	-3(3)	5(4)

The anisotropic displacement factor exponent takes the form:

$$-2 \pi^2 [ h^2 a^2 U_{11} + \dots + 2 h k a^* b^* U_{12} ]$$

Table 5. Hydrogen coordinates (  $\times 10^4$ ), isotropic displacement parameters ( $\text{\AA}^2 \times 10^3$ ), and occupancies for (S)-**12**.

x	y	z	U(eq)	Occ.	
H(3A)	2749	291	-2422	42	1
H(5A)	-518	-1523	-4664	39	1
H(7)	-1601	-1468	-1724	62	1
H(9A)	3558	-12	-4754	100	1
H(9B)	3495	-616	-3897	100	1
H(9C)	3569	854	-3630	100	1
H(10A)	1366	-178	-386	44	1
H(10B)	2700	262	-669	44	1
H(12A)	3550	2574	-717	43	1
H(14A)	2237	5311	878	38	1
H(17A)	4747	4824	-368	69	1
H(17B)	4692	5823	681	69	1
H(17C)	3858	5657	-366	69	1
H(19A)	87	318	1611	66	1
H(19B)	1026	1808	2097	66	1
H(19C)	1477	712	1416	66	1
H(20C)	-111	3164	1633	33	1
H(22A)	434	6270	3306	66	1
H(22B)	-190	4758	3112	66	1
H(22C)	-792	5348	2400	66	1
H(24A)	-215	5687	751	44	1
H(26A)	-3688	3689	-1240	42	1
H(29)	-1424	1484	515	59	1
H(31A)	-1526	7885	78	97	1
H(31B)	-433	7370	357	97	1
H(31C)	-1526	7322	958	97	1
H(32A)	-4847	1379	-1527	38	1
H(32B)	-4189	622	-1015	38	1
H(34A)	-4023	1856	-3027	35	1

H(36A)	-2713	-746	-4824	34	1
H(40A)	-4331	-2523	-1482	102	1
H(40B)	-4610	-2860	-2677	102	1
H(40C)	-5139	-1859	-1970	102	1
H(41A)	-3847	1914	-4667	52	1
H(41B)	-4080	535	-5529	52	1
H(41C)	-2670	1564	-5000	52	1
H(42A)	-2519	-2600	-4349	39	1
H(42B)	-2604	-2565	-3235	39	1
H(10C)	-3414	-2054	-7908	40	1
H(10D)	-33	-165	-5824	38	1
H(10E)	-2253	2300	-7234	55	1
H(10F)	-2706	-4294	-6976	81	1
H(10G)	-3050	-3823	-7869	81	1
H(10H)	-3552	-3405	-6865	81	1
H(11A)	-4213	-975	-8898	39	1
H(11B)	-3463	528	-8679	39	1
H(11C)	-5785	-1529	-7841	39	1
H(11D)	-7097	1211	-6291	41	1
H(11E)	-8274	-1005	-6584	79	1
H(11F)	-7418	-1878	-6635	79	1
H(11G)	-8283	-2009	-7655	79	1
H(11H)	-3710	3369	-8692	62	1
H(11I)	-5091	2963	-8482	62	1
H(11J)	-4625	1871	-9148	62	1
H(12B)	-4814	3947	-6607	32	1
H(12E)	-7382	4886	-6423	85	1
H(12F)	-6068	5157	-6755	85	1
H(12G)	-6078	5432	-5591	85	1
H(12H)	-6411	3402	-4670	36	1
H(12I)	-3224	4984	-2371	32	1
H(12J)	-1981	4681	-5297	52	1
H(13A)	-7303	3447	-2391	77	1
H(13B)	-7247	2644	-3512	77	1
H(13C)	-7223	4102	-3216	77	1
H(13D)	-1174	6050	-2597	32	1
H(13E)	-1010	6087	-3680	32	1
H(13F)	-1087	4097	-2210	31	1
H(13G)	242	1559	-4021	29	1
H(14B)	1032	6364	-5078	66	1
H(14C)	1719	5612	-4585	66	1
H(14D)	1020	6473	-3940	66	1
H(14E)	-497	2649	-1562	44	1
H(14F)	659	2283	-1928	44	1
H(14G)	-761	1270	-2436	44	1
H(14H)	1220	2196	-5458	37	1
H(14I)	571	2992	-5933	37	1
H(20A)	988	5850	-1051	110	1
H(20B)	731	7053	-1228	110	1

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## References

- 1) Morgan, B.; Dolphin, D. *J. Org. Chem.* **1987**, *52*, 5367.
- 2) Gopalsamuthiram V.; Wulff, W. D. *J. Am. Chem. Soc.* **2004**, *126*, 13936
- 3) Gilman, H.; Cartledge, F.K. *J. Organomet. Chem.* **1964**, *2*, 447
- 4) Moore, D.; Pu, L. *Org. Lett.* **2002**, *4*, 1855
- 5) Horeau, A. in "Stereochemistry: Fundamentals and Methods" Kagan, H. B., ed.; vol 3, George Thieme, Stuttgart, 1977, p. 51.
- 6) Suzuki, M.; Kimura, Y.; Terashima, S. *Chem. Pharm. Bull.* **1986**, *34*, 1531
- 7) Gopalsamuthiram, V.; Predeus, A.; Huang, R.; Wulff, W.D. *J. Am. Chem. Soc.* **2009**, *131*, 18018.
- 8) Lipshutz, B. H.; Keil, R.; Ellsworth, E. L. *Tetrahedron Lett.* **1990**, *31*, 7257.