

Supporting Information

Computer-Aided Design of Chiral Ligands. Part III. A Novel Ligand for Asymmetric Allylation Designed Using Computational Techniques

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Computational Protocols. Calculations were performed on SGI workstations using an R-4000 or R-10,000 processor. Interactive fragment mapping with our previously described method¹ was used for the positioning of functional groups around transition states to identify optimal locations. For the 3-D database searching, the CAVEAT^{2,3} program was used along with the TRIAD (a database of tricyclic ring structures) and ILIAD (a database of acyclic structures) databases. Visualization of CAVEAT input and output was accomplished using a MacroModel interface. The Cambridge Structural Database and the CAS three-dimensional database were obtained separately and also used. CAVEAT databases were constructed using metals and lone pairs as searchable elements in addition to nonmetallic atoms as previously described.³ Also, vectors which possessed tips oriented towards each other were allowed.³ The features described above are available in the CAVEAT 2.2b release.

Once a ligand was identified, it was appended to the transition state and extensive Monte Carlo conformational searching was performed using forcefield methods (MM2*) to evaluate all the possible conformational isomers. Calculations of boron transition states were initially performed with MM2* parameters for the boron allylation reaction⁴ in MacroModel 4.0/6.0.⁵ Additional MM2* parameters⁶ were introduced to allow boronate calculations. Results consistent with the enol boronate MNDO calculations of Gennari and Todeschini⁷ were observed. The searches produced a number of structures incorporating *si* and *re* facial attack of the aldehyde.

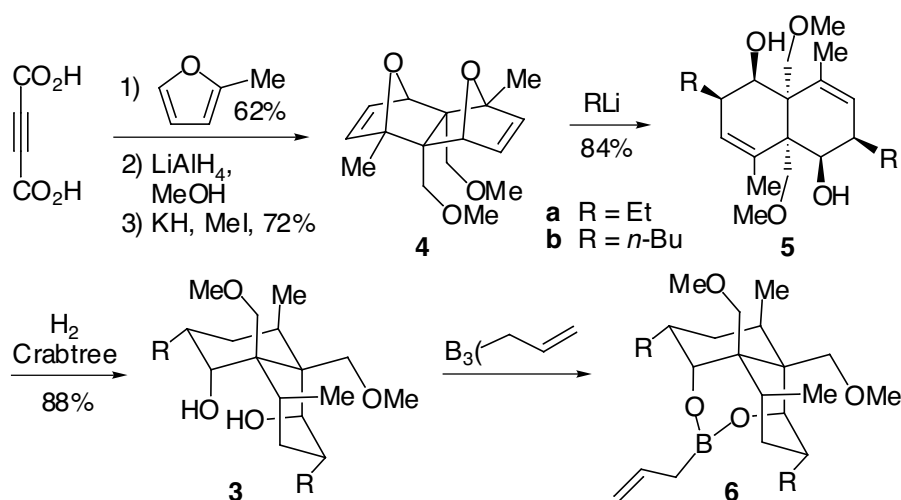
Subsequently, AM1 and HF calculations were performed using all the transition structure *re* and *si* geometries from MacroModel within 4.0 kcal/mol of the global minimum. Semi-empirical AM1 calculations were performed using Spartan 5.0⁸ while HF calculations employing 3-21G* and 6-31G* basis sets were performed using Spartan 5.0 or Gaussian98.⁹ A Boltzmann distribution at the reaction temperature (195 K) was used to calculate the π -facial selectivity for the attack on the aldehyde component at each level of theory (i.e., corresponding to the *si:re* ratio).

In previous studies, HF calculations using 3-21G basis sets were used to generate the transition states for related reactions and were found to be reliable.^{4,10} Due to the large number of transition states that we need to analyze to fully examine all the conformational isomers, we used HF/3-21G* or HF/6-31G* methods. For each reaction, 20-30 transition structures, each with approximately 30 heavy atoms, were optimized. All transition structure structures were confirmed as a true saddle points on the potential energy surface as characterized by the presence of one large imaginary frequency ($\sim 400\text{ cm}^{-1}$). The imaginary frequency corresponds to bond breaking and formation expected for the allylation reaction coordinate.

General Experimental Considerations. Unless otherwise noted, all non-aqueous reactions were carried out under an atmosphere of dry N₂ in dried glassware. When necessary, solvents and reagents were dried prior to use. Diethyl ether and dichloromethane were de-oxygenated by purging with N₂ and then dried by passing through activated alumina. Tetrahydrofuran and toluene were distilled from sodium and hexanes from calcium hydride. DMF was distilled from CaH₂ under reduced pressure and oxalyl chloride was distilled prior to use.

Analytical thin layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica-gel 60-F plates. Preparative thin layer chromatography was performed on EM Reagents 1.00 mm silica-gel plates. Visualization was accomplished with UV light. Chromatography on silica gel was performed using a forced flow of the indicated solvent system on EM Reagents Silica Gel 60 (230-400 mesh).¹¹ Conversions and enantiomeric excesses for the allylation reactions were measured using a Waters 600 high performance liquid chromatography (HPLC) with UV detection at 254 nm and a Daicel Chiralpak AD column (0.46 cm x 25 cm). ¹H NMR spectra were recorded on Bruker AM-500 (500 MHz) or AM-250 (250 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane (0 ppm) or from the solvent resonance (CDCl₃ 7.26 ppm, CD₂Cl₂ 5.30 ppm, DMSO-d₆ 2.49 ppm, D₂O 4.80 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants, and number of protons. Proton decoupled ¹³C NMR spectra were recorded on a Bruker AM-500 (125 MHz) spectrometer. Chemical shifts are reported in ppm from tetramethylsilane (0 ppm) or from the solvent resonance (CDCl₃ 77.36 ppm). Mass spectra were obtained on a low resonance Micromass Platform LC in electron spray mode and high resonance VG autospec with an ionization mode of either CI or ES. IR spectra were taken on a Perkin-Elmer FT-IR spectrometer using a thin film on NaCl plates. Melting points were obtained on Thomas Scientific Unimelt apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer Polarimeter 341 with a sodium lamp and are reported as follows [α]^T _{λ} , (c g/100 mL solvent).

Compounds **4** and **5b** were prepared according to the procedure of Lautens and Fillion.¹² Characterization data for these compounds are in agreement with reported literature values.



Bis-alkene 5a. To a solution of ethyl iodide (2.2 mL, 26.9 mmol) in Et₂O (60 mL) at -78 °C was added *t*-BuLi (43 mL, 53.8 mmol, 1.2 M in pentane) dropwise with stirring. The solution became cloudy and white. The reaction was allowed to stir at -78 °C for 45 min, then at ambient for 90 min. The mixture was then returned to -78 °C, and transferred via cannula to a stirred solution of the bis-oxabicyclo **4** (750 mg, 2.69 mmol) in Et₂O (100 mL). The reaction was allowed to stir at -78 °C for 1 h,

then at 0 °C for 90 min. The solution was quenched with saturated NH₄Cl (50 mL), and the aqueous fraction was extracted with CH₂Cl₂ (4 x 50 mL). The combined organic fractions were dried (MgSO₄), filtered and concentrated. Purification by flash chromatography (3:1 hexanes:EtOAc) afforded **5a** (827 mg, 91%) as a white solid: *R*_f = 0.35 (SiO₂, 3:1 hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 5.44 (s, 2H), 3.97 (s, 2H), 3.74-3.71 (d + s, 10 Hz, 2H + 2H), 3.28-3.24 (d + s, 10 Hz, 2H + 6H), 1.85 (brs, 2H), 1.80 (s, 6H), 1.51 (quintet, 7.4 Hz, 2H), 1.39 (quintet, 7.4 Hz, 2H), 0.95 (t, 7.4 Hz, 6H); ¹³C NMR (500 MHz, CDCl₃) δ 133.9, 127.2, 75.0, 70.2, 58.7, 50.0, 38.2, 24.6, 19.1, 11.6.

Diol 3a. To [Cy₃PIr(COD)py]PF₆ (32 mg, 0.040 mmol) was added a solution of **5a** (676 mg, 2.00 mmol) in CH₂Cl₂ (70 mL). The atmosphere was purged and the reaction was left stirring under an atmosphere of H₂ overnight. The reaction mixture was concentrated *via* rotary evaporation. Purification by flash chromatography (3:1 hexanes:EtOAc) yielded **3a** (663 mg, 98%) as a white solid. *R*_f = 0.40 (SiO₂, 3:1 hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 3.93 (d, 6.9 Hz, 2H), 3.42 (d, 9.3 Hz, 2H), 3.37 (d, 8.0 Hz, 2H), 3.26 (s, 6H), 3.20 (d, 9.3 Hz, 2H), 2.06-1.98 (m, 2H + 2H), 1.57 (m, 2H), 1.40 (septet, 7.3 Hz, 2H), 1.26 - 1.20 (m, 2H + 2H), 1.09 (d, 7.4 Hz, 6H), 0.91 (t, 7.4 Hz, 6H); ¹³C NMR (500 MHz, CDCl₃) δ 74.7, 73.3, 58.8, 46.6, 34.7, 34.3, 32.4, 25.6, 21.3, 11.7.

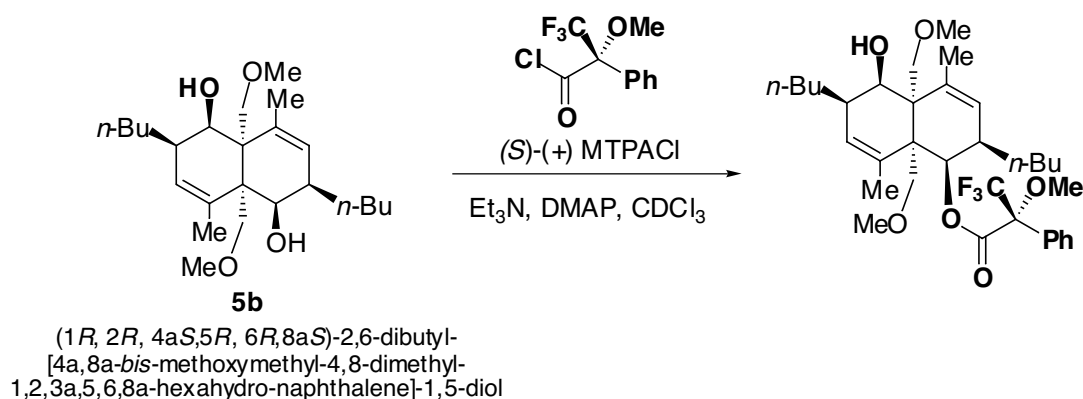
Resolution of racemic diol 3a. Resolution was carried out using a Daicel semi-prep Chiralpak AD column (10 x 250 mm) and a Waters differential refractometer detector. Purified racemic diol (100 mg) was dissolved in 10 mL of eluent (5 % *i*-PrOH/hexanes). A 900 μL aliquot was injected at a flow rate of 2.4 mL/min: *t*_R(-)-**3a** = 10.7, *t*_R(+)-**3a** = 12.3 min.

Diol 3b. To [Cy₃PIr(COD)py]PF₆ (38 mg, 0.0468 mmol) was added to a solution of **5b** (925 mg, 2.35 mmol) in CH₂Cl₂ (40 mL). The atmosphere was purged and the reaction was left stirring under an atmosphere of H₂ overnight. The reaction mixture was concentrated *via* rotary evaporation. Purification by flash chromatography (3:1 hexanes:EtOAc) yielded **3b** (933 mg, 2.45 mmol, 100%) as a white solid. An analytical sample was recrystallized from CH₂Cl₂ to give colorless crystals suitable for X-ray analysis (see below). The X-ray structure established that the relative configuration and the preferred conformational form of **3b** are those illustrated above. mp 114-116 °C; *R*_f = 0.49 (SiO₂, 3:1 hexanes:EtOAc); ¹H NMR (500 MHz, CDCl₃) δ 3.88 (s, 2H), 3.39 (d, 9.2 Hz, 2H), 3.23 (s, 6H), 3.17 (d, 9.4 Hz, 2H), 2.55 (brs, 2H), 2.02-1.96 (m, 4H), 1.71-1.60 (m, 2H), 1.35-1.15 (m, 16H), 1.05 (d, 7.4 Hz, 6H), 0.87 (m, 6H); ¹³C NMR (500 MHz, CDCl₃) δ 75.0, 73.3, 58.7, 46.3, 34.7, 32.7, 32.5, 32.0, 29.2, 22.8, 21.3, 14.1.

Resolution of racemic diol 3b. Resolution was carried out using a Daicel semi-prep Chiralpak AD column (10 x 250 mm) and a Waters differential refractometer detector. Purified racemic diol (500 mg) was dissolved in 10% *i*-PrOH/hexanes (4.0 mL). The eluent was 2.5% *i*-PrOH/hexanes, the flow rate was 2.4 mL/min, and 400 μL injections were used. With multiple overlapping runs, one gram of racemic material was resolved in five hours: *t*_R(-)-**3b** = 10.8 min, *t*_R(+)-**3b** = 13.2 min. The second fraction has [*α*]_D²⁰ = +5.76 (c = 0.050, CHCl₃, 100% ee).

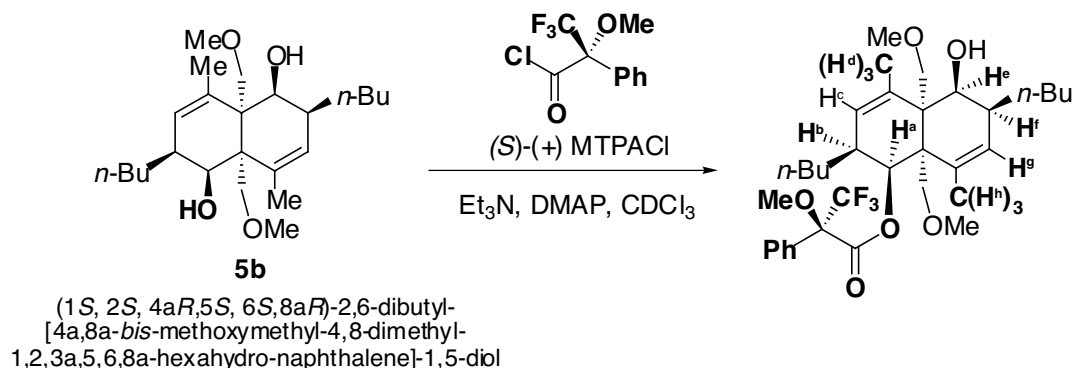
Absolute configuration of diol 3b via Mosher ester analysis of 5b. Compound **5b** was resolved using CSP HPLC (5% *i*-PrOH/hexanes; $t_R(-)\text{-5b} = 9.2$, $t_R(+)\text{-5b} = 13.3$ min) as described above for **3a**. Each enantiomer of **5b** was converted to the corresponding Mosher ester. Microscale Mosher esterifications were performed following the procedure of Ward and Rhee.¹³ (*R*)-(+)-MTPA (2.1 equivalents) was dissolved in hexanes. DMF (2.1 equivalents) and oxalyl chloride (4.2 equivalents) were added and the mixture stirred for 2 h. The clear, colorless supernatant was extracted from an oily, yellow residue (DMFCl) using a syringe, filtered through a glass wool plug, and concentrated *via* rotary evaporation to give a clear, colorless oil ((*S*)-(+)-MTPACl).¹⁴

In a vial, a solution of the diol (1.0 equivalent) was mixed with DMAP (few crystals), CDCl_3 (0.5 mL), and Et_3N (3.0 equivalents). This solution was added dropwise to the MTPACl and stirred overnight, giving a clear, yellow solution which was directly analyzed by NMR.



Note: HPLC studies shows that hydrogenation of this enantiomer of **5a** gives (-)-**3a**.

Mosher ester of (1*R*, 2*R*, 4*aS*, 5*R*, 6*R*, 8*aS*)-**5b**: ^1H NMR (CDCl_3 , 500 MHz) δ 7.59-7.61 (m, 2H, Ph), 7.37-7.41 (m, 3H, Ph), 5.61 (d, $J = 3.7$ Hz, 1H, $\text{RR}'\text{CH}(\text{OC}(=\text{O})\text{CR}_3''')$), 5.39 (d, $J = 1.2$ Hz, 2H, vinyl), 3.74-3.80 (m, 3H, $\text{RCH}_2\text{OMe} + \text{RR}'\text{CH}(\text{OH})$), 3.64-3.68 (m, 1H, ROH), 3.42 (d, $J = 8.9$ Hz, 1H, RCH_2OMe), 3.20-3.34 (m, 10H, $\text{ROCH}_3 + \text{RCH}_2\text{OMe}$), 2.16 (br s, 1H, $\text{RR}'\text{CH}(n\text{-Bu})$), 1.93 (br s, 1H, $\text{RR}'\text{CH}(n\text{-Bu})$), 1.85 (dd, $J = 2.1, 1.1$ Hz, 3H, ring methyl), 1.75 (dd, $J = 2.1, 1.0$ Hz, 3H, ring methyl), 1.04-1.46 (m, 12H, nBu), 0.92 (t, $J = 7.2$ Hz, 3H, *n*-Bu methyl), 0.77 (t, $J = 7.3$ Hz, 3H, *n*-Bu methyl).

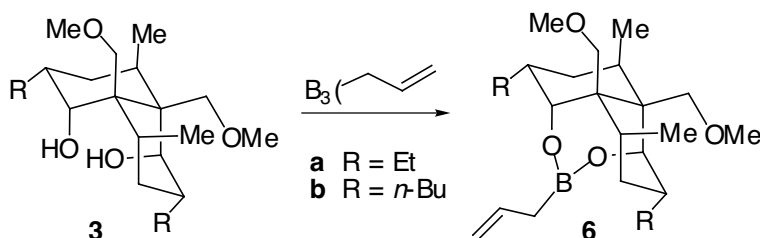


Mosher ester of (1*S*, 2*S*, 4*aR*, 5*S*, 6*S*, 8*aR*)-**5b**: ^1H NMR (CDCl_3 , 500 MHz) δ 7.58 (d, $J = 7.2$ Hz 2H, Ph), 7.34-7.41 (m, 3H, Ph), 5.56 (d, $J = 2.6$ Hz, 1H, $\text{RR}'\text{CH}(\text{OC}(=\text{O})\text{CR}_3''')$), 5.46 (d, $J = 1.0$ Hz, 1H,

RC(Me)=CHCH n -Bu)CH(OC(=O)CR $_3$ 'R''), 4.77 (d, J = 0.9 Hz, 1H, RC(Me)=CHCH(n -Bu)CH(OH)R'), 3.77 (d, J = 8.9 Hz, 3H, RCH $_2$ OMe), 3.66 (d, J = 9.1 Hz, 1H, RCH $_2$ OMe), 3.55 (d, J = 1.5 Hz, 3H, RR'C(=O)C(OCH $_3$)(CF $_3$)(Ph)), 3.53 (d, J = 3.3 Hz, 1H, ROH), 3.48 (d, J = 12.4 Hz, 1H, RR'CH(OH)), 3.37 (d, J = 8.9 Hz, 1H, RCH $_2$ OMe), 3.25 (s, 3H, RCH $_2$ OCH $_3$), 3.23 (s, 3H, RCH $_2$ OCH $_3$), 3.20 (d, J = 9.1 Hz, 1H, RCH $_2$ OMe), 2.22 (br s, 1H, RR'CH(n -Bu)), 1.83 (dd, J = 1.2, 1.0 Hz, 3H, ring methyl), 1.69 (br s, 1H, RR'CH(n -Bu)), 1.56 (dd, J = 1.2, 1.1 Hz, 3H, ring methyl), 1.12-1.48 (m, 12H, n -Bu), 0.89 (overlapping d, J = 10.4 Hz, 3H, n -Bu methyl and dd, J = 14.6, 10.7 Hz, 3H, n -Bu methyl).

Table S1. Coupled protons for the Mosher ester of (1*S*, 2*S*, 4*aR*, 5*S*, 6*S*, 8*aR*)-**5b** from the 500 MHz COSY.

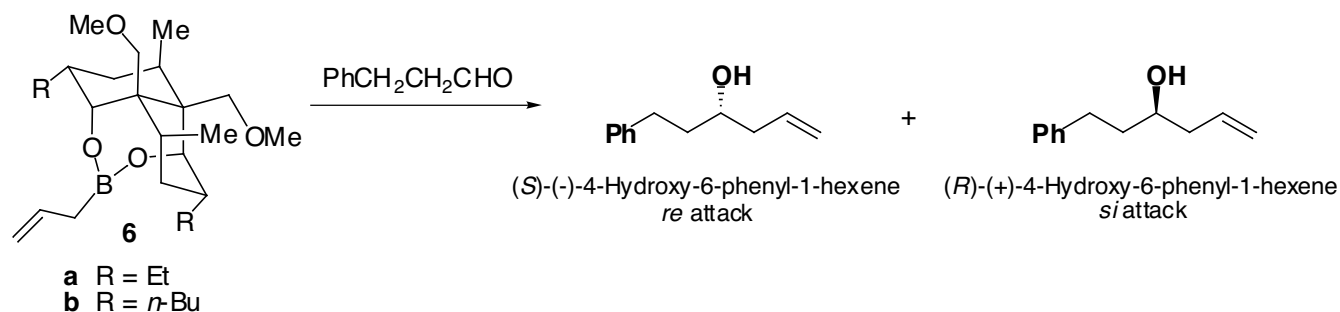
Proton	^1H - ^1H COSY*
a	b
b	a, c
c	b, d
d	c
e	f
f	e, g
g	f, h
h	g



General Procedure for the Preparation of Allylboronates.¹⁵ To a solution of triallylborane¹⁶ (0.597 mmol, 1.18 equivalents) in THF (0.5 mL) in a Schlenk flask was added dropwise the appropriate amount of ligand (0.50 mmol, 1.00 equivalents) dissolved in THF (1.5 mL). The solution was stirred at room temperature for 2 h and then heated to reflux for 1.5 h. After cooling to room temperature, the solvent was removed *in vacuo*.

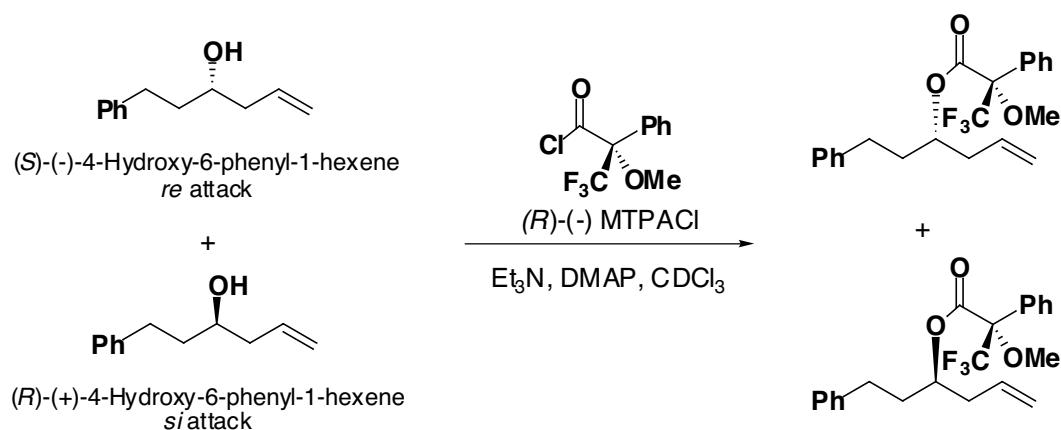
(1*R*, 5*R*, 6*R*, 8*R*, 9*R*, 10*R*, 11*R*, 13*R*)-3-Allyl-6,13-diethyl-9,10-bis-methoxymethyl-8,11-dimethyl-2,4-dioxo-3-bora-tricyclo[7.4.0.0^{5,10}]tridecane (**6a**). ^1H NMR: CDCl $_3$, 500 MHz; δ 5.87-5.96 (m, 1H, H $_2$ C=CHR), 4.80-4.90 (m, 2H, H $_2$ C=CHR), 4.24 (d, J = 7.9 Hz, 1H, RR'CH(OBR $_2$ '')), 3.48 (d, J = 9.4 Hz, 1H, RCH $_2$ OMe), 3.21-3.26 (m, 4H, RCH $_2$ OMe + RCH $_2$ OCH $_3$), 2.10 (q, J = 7.4 Hz, 1H, RR'CH(Et)), 1.66-1.71 (m, 2H, allylic methylene), 1.49-1.62 (m, 1H, RR'CH(CH $_3$)), 1.32-1.40 (m, 2H, ring methylene), 1.10 (d, J = 6.6 Hz, 3H, RCH $_2$ CH $_3$), 0.89 (t, J = 7.3 Hz, 2H, RCH $_2$ CH $_3$); ^{13}C NMR (CDCl $_3$, 125 MHz); δ 11.5, 22.4, 25.6, 33.7, 35.1, 35.4, 45.9, 58.9, 72.7, 81.5, 111.7, 137.2; ^{11}B NMR (CDCl $_3$, 64.2 MHz) δ 31.5.

(1*R*, 5*R*, 6*R*, 8*R*, 9*R*, 10*R*, 11*R*, 13*R*)-3-Allyl-6,13-dibutyl-9,10-bis-methoxymethyl-8,11-dimethyl-2,4-dioxo-3-bora-tricyclo[7.4.0.0^{5,10}] tridecane (**6b**). ¹H NMR (CDCl₃, 500 MHz) δ 5.87-5.96 (m, 1H, H₂C=CHR), 4.81-4.92 (m, 2H, H₂C=CHR), 4.23 (s, 1H, RR'CH(OBR₂')), 3.43-3.51 (d, 1H, RCH₂OMe), 3.15-3.30 (m, 4H, RCH₂OMe and ROCH₃), 2.05-2.15 (m, 1H, α to nBu in ring), 1.75-1.90 (m, 1H, α to Me in ring), 1.71-1.72 (d, 2H, allylic), 1.55-1.65 (m, 1H, nBu), 1.20-1.45 (m, 5H, nBu), 1.11 (d, *J* = 7.6 Hz, 3H, RR'CHCH₃), 0.89 (t, *J* = 6.9 Hz, 3H, nBu CH₃); ¹³C NMR (CDCl₃, 125 MHz) δ 14.1, 22.4, 22.8, 29.0, 32.5, 33.1, 34.1, 35.2, 46.0, 58.9, 72.7, 81.7, 112.7, 137.2; ¹¹B NMR (CDCl₃, 64.2 MHz) δ 30.4.



General Procedure for the Boron Allylation of Dihydrocinnamaldehyde.^{13,14} A solution of the allylboronate (0.354 mmol) in toluene (0.5 mL) was added to flame-dried Schlenk flask containing 4Å molecular sieves (powdered, 50 wt relative to the ligand). At -78 °C hydrocinnamaldehyde (72.5 μL, 0.551 mmol, 1.56 equivalents), dissolved in toluene (~0.5 mL), was added dropwise over 30 min. After overnight at -78 °C, a solution of NaBH₄ (23.0 mg, 0.610 mmol, 1.70 equivalents) in EtOH (~2 mL) was added to consume any remaining aldehyde; the aldehyde greatly complicates the HPLC analysis. After stirring at room temperature for 1.5 h, the reaction mixture was poured into H₂O (10 mL), extracted with Et₂O (4 x 10 mL), dried (MgSO₄), concentrated *in vacuo.*, and chromatographed to afford 4-hydroxy-6-phenyl-1-hexene identical to that reported previously:¹⁷ ¹H NMR (CDCl₃, 500 MHz) δ 7.26-7.30 (m, 2H, Ph), 7.16-7.23 (m, 3H, Ph), 5.78-5.88 (m, 1H, H₂C=CHR), 5.13-5.17 (m, 2H, H₂C=CHR), 3.64-3.72 (m, 1H, RR'CH(OH)), 3.68-3.88 (m, 2H, PhCH₂R), 2.16-2.37 (m, 2H, H₂C=CHCH₂R), 1.77-1.83 (m, 2H, PhCH₂CH₂R), 1.59 (d, *J* = 4.2 Hz, ROH); ¹³C NMR (CDCl₃, 125 MHz) δ 32.0, 38.4, 42.0, 69.9, 118.1, 125.8, 128.27, 128.33, 128.37, 134.6, 142.0.

The enantiomeric excess was determined by chiral HPLC while the configuration was determined by Mosher ester analysis (see below) and confirmed by comparison of the optical rotation to literature values: CSP HPLC (OD, 99:1 hexanes:*i*-PrOH, 0.8 mL/min) *t_R*(*S*) = 19.9 min, *t_R*(*R*) = 33.2 min; [*α*]_D²² = -10.6 (*c* = 2.30, 39% ee (*S*), C₆D₆); [*α*]_D²² = -8.3 (*c* = 2.49, 39% ee (*S*), CHCl₃); [*α*]_D²² (lit¹⁸) = +16.9 (*c* = 1.0, 80% ee (*R*), CHCl₃); [*α*]_D²⁵ (lit¹⁹) = -21.6 (*c* = 1.19, 95% ee (*S*), CHCl₃); [*α*]_D²³ (lit²⁰) = +11.1 (*c* = 3.14, 53% ee (*R*), CHCl₃).



Diagnostic ¹H NMR Peaks for the Mosher Esters of the Two Enantiomers of 4-Hydroxy-6-phenyl-1-hexene. The Mosher Ester of 4-hydroxy-6-phenyl-1-hexene were prepared as described above for **5b**: ¹H NMR (CDCl₃, 500 MHz) δ 7.20-7.33 (m, Ph, (S) enantiomer), 7.11-7.21 (m, Ph, (R) enantiomer), 5.70-5.80 (m, 1H, H₂C=CHR, (S) enantiomer), 5.60-5.70 (m, 1H, H₂C=CHR, (R) enantiomer), 5.10-5.14 (m, 1H, H₂C=CHR, (S) enantiomer), 5.08-5.10 (m, 1H, H₂C=CHR, (S) enantiomer), 5.03-5.06 (m, 1H, H₂C=CHR, (R) enantiomer), 5.00-5.03 (m, 1H, H₂C=CHR, (R) enantiomer).

X-ray Structure Determination of 3b. Compound **3b**, C₂₄H₄₆O₄, crystallizes in the monoclinic space group C2/c (systematic absences hkl: h+k=odd and h0l: l=odd) with a=22.2227(4)Å, b=14.6662(2)Å, c=14.8727(2)Å, β=93.5920(10)°, V=4837.83(13)Å³, Z=8 and d_{calc}=1.095 g/cm³. X-ray intensity data were collected on a Rigaku R-Axis IIC area detector employing graphite-monochromated Mo-Kα radiation (λ=0.71069 Å) at a temperature of 200°K. Indexing was performed from a series of 1° oscillation images with exposures of 8 minutes per frame. A hemisphere of data was collected using 10° oscillation angles with exposures of 15 minutes per frame and a crystal-to-detector distance of 82 mm. Oscillation images were processed using bioteX,²¹ producing a listing of unaveraged F² and σ(F²) values which were then passed to the teXsan²² program package for further processing and structure solution on a Silicon Graphics O2 computer. A total of 18456 reflections were measured over the ranges 5.48 ≤ 2θ ≤ 50.68°, -26 ≤ h ≤ 26, -17 ≤ k ≤ 17, -16 ≤ l ≤ 17 yielding 4378 unique reflections (R_{int} = 0.0285). The intensity data were corrected for Lorentz and polarization effects but not for absorption.

The structure was solved by direct methods (SIR92²³). The alkyl chain C22-C23-C24 chain was disordered by a rotation about the C9-C21 bond; the two contributing disorder models had relative populations of 70:30. Refinement was by full-matrix least squares based on F² using SHELXL-93.²⁴ All reflections were used during refinement (F²'s that were experimentally negative were replaced by F² = 0). The weighting scheme used was w=1/[σ²(F_o²) + 0.0617P² + 5.3153P] where P = (F_o² + 2F_c²)/3. Non-hydrogen atoms were refined anisotropically and hydrogen atoms were refined using a

“riding” model except for the two hydroxyl hydrogens which were included as constant contributions to the structure factors and were not refined. Refinement converged to $R_1=0.0634$ and $wR_2=0.1552$ for 4079 reflections for which $F > 4\sigma(F)$ and $R_1=0.0689$, $wR_2=0.1590$ and $GOF = 1.167$ for all 4378 unique, non-zero reflections and 287 variables.²⁵ The maximum Δ/σ in the final cycle of least squares was 0.013 and the two most prominent peaks in the final difference Fourier were +0.353 and -0.450 e/Å³.

Table S1 lists cell information, data collection parameters, and refinement data. Final positional and equivalent isotropic thermal parameters are given in Table S2. Anisotropic thermal parameters are in Table S3. Tables S4 and S5 list bond distances and bond angles. Figure S1 is an ORTEP²⁶ representation of the molecule with 30% probability thermal ellipsoids displayed.

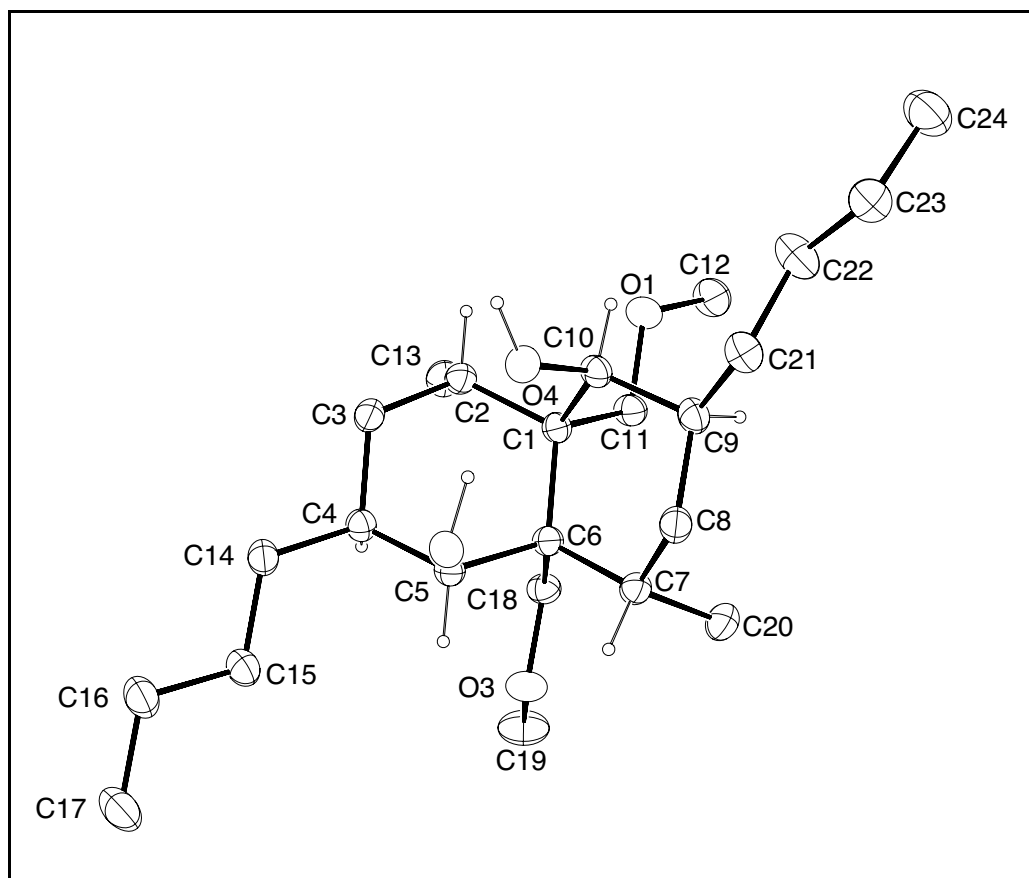


Figure S1. ORTEP drawing of **3b** with 30% probability thermal ellipsoids.

Table S1. Summary of Structure Determination of **3b**

Formula:	C ₂₄ H ₄₆ O ₄
Formula weight:	398.61
Crystal class:	monoclinic
Space group:	C2/c (#15)
Z	8
Cell constants:	
	a 22.2227(4) Å
	b 14.6662(2) Å
	c 14.8727(2) Å
	β 93.592(1) °
	V 4837.83(13) Å ³
μ	0.72 cm ⁻¹
crystal size, mm	0.42 x 0.36 x 0.14
D _{calc}	1.095 g/cm ³
F(000)	1776
Radiation:	Mo-Kα (λ=0.71069 Å)
2θ range	5.48 – 50.68 °
hkl collected:	-26 ≤ h ≤ 26; -17 ≤ k ≤ 17; -16 ≤ l ≤ 17
No. reflections measured:	18456
No. unique reflections:	4378 (R _{int} =0.0285)
No. observed reflections	4079 (F>4σ)
No. reflections used in refinement	4378
No. parameters	287
R indices (F>4σ)	R ₁ =0.0634 wR ₂ =0.1552
R indices (all data)	R ₁ =0.0689 wR ₂ =0.1590
GOF:	1.167
Final Difference Peaks, e/Å ³	+0.353, -0.450

Table S2. Refined Positional Parameters for Compound **3b**.

Atom	x	y	z	U _{eq} , Å ²
C1	0.13200(8)	0.37934(13)	0.07581(13)	0.0315(4)
C2	0.11113(9)	0.33957(14)	-0.02001(13)	0.0357(5)
H2	0.1013	0.3929	-0.0579	0.047
C3	0.05290(9)	0.2834(2)	-0.02081(13)	0.0370(5)
H3a	0.0193	0.3245	-0.0143	0.049
H3b	0.0468	0.2536	-0.0789	0.049
C4	0.05244(9)	0.21116(14)	0.05297(13)	0.0337(4)
H4	0.0856	0.1686	0.0447	0.045
C5	0.06305(8)	0.25624(13)	0.14489(13)	0.0313(4)
H5	0.0652	0.2071	0.1897	0.042
C6	0.12364(8)	0.31028(13)	0.15714(13)	0.0313(4)
C7	0.12543(9)	0.35760(14)	0.25307(13)	0.0347(5)
H7	0.1016	0.3181	0.2904	0.046
C8	0.09450(9)	0.45121(14)	0.25373(14)	0.0382(5)
H8a	0.0512	0.4423	0.2476	0.051
H8b	0.1040	0.4799	0.3117	0.051
C9	0.11255(9)	0.51536(14)	0.17990(14)	0.0372(5)
H9	0.1564	0.5230	0.1868	0.049
C10	0.09761(8)	0.47134(13)	0.08809(14)	0.0337(4)
H10	0.1106	0.5137	0.0422	0.045
C11	0.19925(9)	0.4053(2)	0.07457(14)	0.0373(5)
H11a	0.2133	0.4293	0.1329	0.050
H11b	0.2229	0.3516	0.0625	0.050
C12	0.26737(10)	0.5019(2)	0.0081(2)	0.0556(7)
H12a	0.2719	0.5440	-0.0405	0.083
H12b	0.2934	0.4504	0.0011	0.083
H12c	0.2780	0.5316	0.0644	0.083
C13	0.15870(10)	0.2863(2)	-0.0694(2)	0.0453(5)
H13a	0.1942	0.3231	-0.0732	0.068
H13b	0.1427	0.2712	-0.1290	0.068
H13c	0.1689	0.2313	-0.0369	0.068
C14	-0.00689(9)	0.1575(2)	0.04491(14)	0.0391(5)
H14a	-0.0399	0.2000	0.0507	0.052
H14b	-0.0115	0.1315	-0.0151	0.052
C15	-0.01306(10)	0.0813(2)	0.1129(2)	0.0448(5)
H15a	0.0195	0.0381	0.1072	0.060
H15b	-0.0090	0.1067	0.1731	0.060
C16	-0.07246(11)	0.0312(2)	0.1010(2)	0.0514(6)
H16a	-0.0763	0.0056	0.0407	0.068
H16b	-0.1050	0.0746	0.1061	0.068
C17	-0.07921(14)	-0.0445(2)	0.1686(2)	0.0670(8)
H17a	-0.1169	-0.0751	0.1558	0.100
H17b	-0.0782	-0.0192	0.2282	0.100
H17c	-0.0467	-0.0872	0.1648	0.100
C18	0.17363(9)	0.23722(14)	0.15862(14)	0.0375(5)
H18a	0.1742	0.2086	0.0999	0.050
H18b	0.2126	0.2656	0.1722	0.050
C19	0.20776(13)	0.1023(2)	0.2289(2)	0.0650(8)
H19a	0.1974	0.0559	0.2707	0.098
H19b	0.2458	0.1289	0.2486	0.098
H19c	0.2106	0.0759	0.1703	0.098
C20	0.18775(10)	0.3656(2)	0.3039(2)	0.0469(6)

H20a	0.2060	0.3064	0.3092	0.070
H20b	0.1831	0.3901	0.3629	0.070
H20c	0.2129	0.4054	0.2714	0.070
C21	0.08414(11)	0.6094(2)	0.1888(2)	0.0462(5)
H21a	0.0840	0.6250	0.2522	0.061
H21b	0.0425	0.6069	0.1649	0.061
C22	0.1168(3)	0.6848(4)	0.1398(5)	0.060(2)
H22a	0.1599	0.6779	0.1531	0.079
H22b	0.1091	0.6765	0.0754	0.079
C23	0.0992(2)	0.7791(2)	0.1636(3)	0.0614(10)
H23a	0.1035	0.7863	0.2285	0.082
H23b	0.0571	0.7885	0.1446	0.082
C24	0.1370(2)	0.8505(3)	0.1200(4)	0.0781(13)
H24a	0.1210	0.9100	0.1310	0.117
H24b	0.1362	0.8398	0.0563	0.117
H24c	0.1778	0.8471	0.1451	0.117
C22'	0.0985(6)	0.6776(9)	0.1174(11)	0.055(4)
H22'	0.0767	0.7335	0.1281	0.073
H22b'	0.0834	0.6541	0.0593	0.073
C23'	0.1644(3)	0.7007(6)	0.1121(7)	0.059(2)
H23a'	0.1861	0.6459	0.0973	0.079
H23b'	0.1804	0.7213	0.1709	0.079
C24'	0.1758(4)	0.7738(5)	0.0428(7)	0.061(2)
H24a'	0.2162	0.7964	0.0528	0.091
H24b'	0.1478	0.8229	0.0485	0.091
H24c'	0.1707	0.7482	-0.0166	0.091
O1	0.20703(6)	0.47212(11)	0.00688(10)	0.0442(4)
O2	0.01124(6)	0.31053(9)	0.16230(9)	0.0350(3)
O3	0.16296(7)	0.17024(11)	0.22483(10)	0.0452(4)
O4	0.03324(6)	0.46181(10)	0.07453(10)	0.0389(4)
H2a	0.0119	0.3688	0.1274	0.070
H4a	0.0115	0.4915	0.0292	0.070

$$U_{eq}=1/3[U_{11}(aa^*)^2+U_{22}(bb^*)^2+U_{33}(cc^*)^2+2U_{12}aa^*bb^*\cos\gamma+2U_{13}aa^*cc^*\cos\beta+2U_{23}bb^*cc^*\cos\alpha]$$

Table S3. Refined Thermal Parameters (U's) for **3b**.

Atom	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
C1	0.0266(9)	0.0342(10)	0.0337(10)	0.0022(8)	0.0012(7)	-0.0039(8)
C2	0.0349(10)	0.0399(11)	0.0323(10)	0.0024(9)	0.0022(8)	-0.0037(9)
C3	0.0358(11)	0.0422(11)	0.0325(10)	-0.0009(9)	-0.0021(8)	-0.0048(9)
C4	0.0317(10)	0.0344(10)	0.0350(10)	-0.0009(8)	0.0023(8)	-0.0025(8)
C5	0.0271(9)	0.0331(10)	0.0337(10)	0.0015(8)	0.0022(7)	-0.0008(8)
C6	0.0268(9)	0.0348(10)	0.0323(10)	0.0038(8)	0.0011(7)	-0.0011(8)
C7	0.0329(10)	0.0396(11)	0.0315(10)	0.0015(8)	0.0005(8)	-0.0042(9)
C8	0.0381(11)	0.0407(11)	0.0358(11)	-0.0040(9)	0.0011(8)	-0.0056(9)
C9	0.0338(10)	0.0348(11)	0.0428(12)	-0.0012(9)	0.0006(8)	-0.0056(9)
C10	0.0272(10)	0.0333(10)	0.0405(11)	0.0037(9)	0.0004(8)	-0.0040(8)
C11	0.0288(10)	0.0416(11)	0.0415(11)	0.0064(9)	0.0026(8)	-0.0031(9)
C12	0.0373(12)	0.068(2)	0.062(2)	0.0108(13)	0.0055(11)	-0.0196(12)
C13	0.0446(12)	0.0536(14)	0.0389(12)	-0.0039(10)	0.0110(9)	-0.0035(11)
C14	0.0379(11)	0.0397(11)	0.0392(11)	-0.0036(9)	0.0001(9)	-0.0076(9)
C15	0.0436(12)	0.0446(13)	0.0463(13)	0.0003(10)	0.0041(10)	-0.0121(10)
C16	0.0495(14)	0.0483(14)	0.057(2)	-0.0026(11)	0.0052(11)	-0.0159(11)
C17	0.071(2)	0.055(2)	0.076(2)	0.0049(14)	0.012(2)	-0.0260(14)
C18	0.0327(10)	0.0411(11)	0.0386(11)	0.0068(9)	0.0012(8)	0.0008(9)
C19	0.068(2)	0.059(2)	0.069(2)	0.0218(14)	0.0096(14)	0.0250(14)
C20	0.0441(12)	0.0547(14)	0.0405(12)	-0.0001(10)	-0.0080(9)	-0.0051(11)
C21	0.0481(13)	0.0395(12)	0.0513(13)	-0.0029(10)	0.0043(10)	-0.0023(10)
C22	0.056(4)	0.039(2)	0.084(4)	0.002(3)	0.008(3)	-0.005(2)
C23	0.069(2)	0.051(2)	0.063(2)	0.003(2)	-0.007(2)	-0.005(2)
C24	0.073(3)	0.055(2)	0.103(4)	0.018(2)	-0.019(2)	-0.017(2)
C22'	0.049(7)	0.025(4)	0.090(10)	-0.002(5)	0.013(7)	-0.006(4)
C23'	0.035(4)	0.045(5)	0.097(7)	0.021(4)	-0.008(4)	-0.008(4)
C24'	0.054(5)	0.036(4)	0.091(7)	0.023(4)	-0.003(4)	-0.015(4)
O1	0.0320(8)	0.0508(9)	0.0499(9)	0.0144(7)	0.0035(6)	-0.0111(7)
O2	0.0270(7)	0.0376(8)	0.0410(8)	-0.0010(6)	0.0051(6)	-0.0009(6)
O3	0.0419(8)	0.0450(9)	0.0488(9)	0.0152(7)	0.0049(7)	0.0082(7)
O4	0.0263(7)	0.0431(8)	0.0465(8)	0.0025(7)	-0.0030(6)	0.0005(6)

The form of the anisotropic displacement parameter is:

$$\exp[-2\pi^2(a^2U_{11}h^2+b^2U_{22}k^2+c^2U_{33}l^2+2b^*c^*U_{23}kl+2a^*c^*U_{13}hl+2a^*b^*U_{12}hk)].$$

Table S4. Bond Distances (Å) in **3b**.

C1-C11	1.543(3)	C1-C10	1.567(3)	C1-C2	1.582(3)
C1-C6	1.597(3)	C2-C3	1.533(3)	C2-C13	1.538(3)
C3-C4	1.526(3)	C4-C5	1.524(3)	C4-C14	1.533(3)
C5-O2	1.437(2)	C5-C6	1.563(3)	C6-C18	1.543(3)
C6-C7	1.585(3)	C7-C8	1.536(3)	C7-C20	1.540(3)
C8-C9	1.519(3)	C9-C21	1.526(3)	C9-C10	1.528(3)
C10-O4	1.439(2)	C11-O1	1.423(2)	C12-O1	1.409(2)
C14-C15	1.519(3)	C15-C16	1.511(3)	C16-C17	1.512(4)
C18-O3	1.421(2)	C19-O3	1.407(3)	C21-C22'	1.507(12)
C21-C22	1.532(6)	C22-C23	1.486(8)	C23-C24	1.514(5)
C22'-C23'	1.511(12)	C23'-C24'	1.520(10)		

Table S5. Bond Angles (°) in **3b**.

C11-C1-C10	105.6(2)	C11-C1-C2	108.0(2)	C10-C1-C2	107.8(2)
C11-C1-C6	108.9(2)	C10-C1-C6	112.1(2)	C2-C1-C6	114.0(2)
C3-C2-C13	109.2(2)	C3-C2-C1	113.9(2)	C13-C2-C1	116.5(2)
C4-C3-C2	114.3(2)	C5-C4-C3	109.7(2)	C5-C4-C14	112.1(2)
C3-C4-C14	110.2(2)	O2-C5-C4	108.8(2)	O2-C5-C6	113.1(2)
C4-C5-C6	114.1(2)	C18-C6-C5	105.3(2)	C18-C6-C7	108.3(2)
C5-C6-C7	107.4(2)	C18-C6-C1	109.5(2)	C5-C6-C1	111.9(2)
C7-C6-C1	114.0(2)	C8-C7-C20	108.5(2)	C8-C7-C6	114.3(2)
C20-C7-C6	116.5(2)	C9-C8-C7	114.2(2)	C8-C9-C21	111.6(2)
C8-C9-C10	109.4(2)	C21-C9-C10	113.0(2)	O4-C10-C9	108.9(2)
O4-C10-C1	112.8(2)	C9-C10-C1	112.8(2)	O1-C11-C1	109.8(2)
C15-C14-C4	116.0(2)	C16-C15-C14	113.2(2)	C15-C16-C17	113.6(2)
O3-C18-C6	109.8(2)	C22'-C21-C9	115.6(7)	C22'-C21-C22	19.7(6)
C9-C21-C22	113.6(3)	C23-C22-C21	114.7(5)	C22-C23-C24	112.4(4)
C21-C22'-C23'	115.7(9)	C22'-C23'-C24'	113.4(7)	C12-O1-C11	111.2(2)
C19-O3-C18	111.8(2)				

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Stretching Interactions (STR):

1 B3 - C3	1.5800	4.0000	0.0000	0000	0000
1 B3 - H1	1.1960	4.6000	0.0000	0000	0000
1 B3 - O3	1.5360	6.2000	1.3000	0000	0000
1 B3 - O2	1.5910	5.5000	0.0000	0000	0000

Bending Interactions (BND):

2 C3 - B3 - H1	118.2000	0.3000	0000	0000	0000
2 C3 - B3 - C3	118.2000	0.3000	0000	0000	0000
2 C3 - B3 - O3	112.2000	0.1000	0000	0000	0000
2 C2 - O3 - B3	120.2000	0.3000	0000	0000	0000
2 H1 - C3 - B3	111.0000	0.3000	0000	0000	0000
2 C3 - C3 - B3	115.2000	0.3000	0000	0000	0000

Torsional Interactions (TOR):

4 C2 - O3 - B3 - C3	0.0000	0.0000	0.3000	0000	0000	0000	0000
4 H1 - C3 - B3 - C3	0.0000	0.0000	0.2000	0000	0000	0000	0000
4 O0 - C3 - B3 - O0	0.0000	0.0000	0.3000	0000	0000	0000	0000
4 O0 - O3 - B3 - O0	0.0000	0.0000	0.5000	0000	0000	0000	0000

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$$wR_2 = \{ \sum w (F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2 \}^{1/2}$$

$$GOF = \{ \sum w (F_o^2 - F_c^2)^2 / (n - p) \}^{1/2}$$

where n = the number of reflections and p = the number of parameters refined.

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