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Applications of Asymmetric Allylation Reactions
Towards Natural Product Synthesis

Philip R. Harsh

Thesis submitted to the Eberly College of Arts and Sciences at West Virginia University
in partial fulfillment of the requirements for the degree of

Master of Science
in
Chemistry

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ABSTRACT

Applications of Asymmetric Allylation Reactions Towards Natural Product Synthesis

Philip R. Harsh

A short asymmetric synthesis of (*R*)-(+)-Goniothalamine oxide was developed and synthesized using a Leighton asymmetric allylation reaction and Grubbs ring-closing metathesis. (*R*)-(+)-Goniothalamine oxide is a styryl lactone that exhibits anti-cancer activity against a variety of cancer cell lines including MCF-7, T47D, and MDA-MB-231. The methodology of asymmetric allylation is also demonstrated on intermediates of RK-397, which is a 32-membered oxopolyene macrolide with anti-cancer activity.

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CHAPTER OUTLINE

CHAPTER I:

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CHAPTER I

1.1 Introduction: Previous Asymmetric Allylation Reactions

Asymmetric allylation reactions have been the focus of several research groups for the past few decades. Throughout this period, the groups of Brown, Keck, Roush, and Leighton have most notably developed various asymmetric allylation reagents that have shown to add allyl groups with high enantioselectivity for a variety of aldehydes. Scheme 1 shows a generic asymmetric allylation of an achiral aldehyde where the chiral reagent selectively forms one of the two possible enantiomeric homoallylic alcohols.

Scheme 1: *Generic Chiral Allylation Reaction*

The reaction conditions of each type of asymmetric allylation reaction are quite different in several aspects including: catalytic vs. stoichiometric, chiral reagents vs. chiral Lewis acid, and reaction conditions (time/temperature). Outlined in Scheme 2 are the different reaction types and conditions for the most common asymmetric allylation reagents.

Scheme 2: Common Asymmetric Allylation Reactions

BROWN

CARREIRA/GAUTHIER

ROUSH

KECK

LEIGHTON

Brown was one of the first to recognize the potentiality of this reaction. Brown and co-workers explored the asymmetric allylation reactions using a chiral allylborane reagent, Ipc₂Ballyl (Scheme 3). The Brown reagent, Ipc₂Ballyl, is made by a three-step procedure that begins with the hydroboration of the natural product α -pinene, from which it draws its chirality.¹

Scheme 3: *Brown Asymmetric Allylation*

The Brown allylation of achiral aldehydes, in general, affords secondary homoallylic alcohols with high enantioselectivity (85-99 %ee) for a variety of substrates. The reaction can be dependent upon temperature under $-78\text{ }^{\circ}\text{C}$ being the most common reaction condition. Similarly, it is important to generate the Brown reagent without the presence of any magnesium salts, which can lower the enantioselectivity/reactivity of the reaction. Thus in the absence of magnesium salts, the typical allylborylation of an aldehyde can occur almost instantaneously at $-78\text{ }^{\circ}\text{C}$.

Brown also showed that the allylation of aldehydes proceeded through a chair-like Zimmerman-Traxler transition state. Thus *E*-substituted allyl reagents give *anti*-homoallylic alcohols and *Z*-substituted reagents give *syn*-homoallylic alcohols. Figure 1 shows Brown's proposed transition state for the allylation where the R-group of the aldehyde occupies the equatorial position allowing minimal steric interactions between the axial isopinocampheyl (Ipc) ligands and the allyl group.²

Figure 1: *Transition State of Brown Allylation*

At about the same time as the Brown group, the Roush group also developed an asymmetric allylation reagent. Roush and coworkers utilized a boron-based reagent for

asymmetric allylation reactions; however, it is quite different in many aspects from the Brown reaction. Scheme 4 shows a typical asymmetric allylation of an aldehyde with the Roush's allyl boronate complex.

Scheme 4: *Roush Asymmetric Allylation*

The allyl boronate reagent that Roush employs in the allylation reaction is considerably more stable than the allyl-diisopinocampheyl reagent that Brown used. This has very important advantages for allowing the reagent to be purified by distillation, if necessary. The major downfall of the Roush's allylation reaction is that it produces homoallylic alcohols with lower enantioselectivities (70-90 %ee) compared to Brown's. The enantioselectivities are diminished by the presence of water and thus the addition of 4 Å molecular sieves is important to achieve the highest stereoselectivity.³

Figure 2: *Transition State of Roush Asymmetric Allylation*

Roush proposed that the selectivity in the allylborylation reactions was due to the favored transition state that minimized the lone-pair/lone-pair interactions between the aldehyde and the ester carbonyl. Figure 2 shows these transition states and the desired enantioselective product.³

Leighton discovered that silicon could also be used as an allylation reagent when it was constrained in a five-membered ring by 1,2-aminoalcohols, 1,2-diols, and 1,2-diamines. He suggests this is due to the increased Lewis acidity imparted by the heteroatoms and ring strain. His hypothesis is supported by the fact that the simple trichloroallylsilane has insufficient Lewis acidity for uncatalyzed allylation of aldehydes. Scheme 5 outlines a typical Leighton allylation using a chiral silicon 1,2-diamine reagent.

Scheme 5: *Leighton Asymmetric Allylation*

Leighton and coworkers optimized the silicon reagent (shown in reaction above) by replacing an original benzyl groups with a para-substituted bromo-benzyl groups. This transformation of the silicon reagent was very important to increase the enantioselectivity (90-99 %ee) and yields (70-95%) for the allylation of aliphatic, aromatic, and conjugated aldehydes.⁴ Leighton and coworkers extended applications of the reagent by applying onto chiral aldehydes. Scheme 6 outlines a typical Leighton allylation using both enantiomers of the silicon reagent (**1**) on a chiral substrate. Thus,

Leighton methodology demonstrates high reagent control over substrate control for aldehydes with chiral centers in the beta-position.⁴

Scheme 6: *Leighton Allylation of Chiral Aldehydes*

Keck and Carreira research groups have explored the development of a catalytic asymmetric allylation reaction. The key difference between the approaches of these two research groups is that Keck employs an allyl-tin based reagent while Carreira uses an allyl-silane reagent. The scheme 7 shows the two catalytic asymmetric allylation reactions to give homoallylic alcohols.^{5,6,7}

Scheme 7: Keck and Carreira Catalytic Asymmetric Allylations

CARREIRA/GAUTHIER

KECK

Both reactions are catalytic in chiral Lewis acids, which are generated by the titanium specie and the chiral ligand (BINOL) that is available commercially in both enantiomers. It is important to note that in Carreira allylation reactions, the addition of a small amount of CH_3CN is important to keep the polymeric TiF_4 soluble. The enantioselectivities for both reactions are competitive with each other with enantioselectivities in the range of 70 to 95 %.

Another important factor to mention about each of the reactions is the toxicity of the tin reagent compared to silicon reagent. The health effects of tin can range from acute to long term depending on the exposure and type of the tin reagent one is exposed to. Triethylstannane has been recognized as the most dangerous form of tin due to the short hydrogen bonds. Tin compounds become considerably less toxic as the hydrogen bond is lengthened.⁸ Health effects that are associated with tin are: liver damage, brain damage, and malfunction of the immune system.⁸

Silicon, on the other hand, is relatively less harmful to humans. Silicon concentrates in no particular organ of the body but is found in the skin and tissues. Silicon may cause health affects including: respiratory tract infection and irritation of skin and eyes.⁹

1.2 Previous approaches to Goniotalamin oxide/analogues

There have been several syntheses of Goniotalamin and Goniotalamin oxide derivatives. Goniotalamin was first isolated in 1967 from the bark of *Cryptocarya caloneura* and was assigned to have (*S*)-stereochemistry.¹⁰ However, the stereochemistry was revised many years later to the (*R*) configuration. Several derivatives of Goniotalamin have been discovered from a variety of tropical/subtropical plants including; *Cryptocarya moschata*,¹¹ *Bryonopsis laciniosa*,¹² and various *Goniotalamus*¹³ species. These natural products have shown cytotoxicity on a variety of cells lines including: MCF-7, T47D, and MDA-MB-231 (breast carcinoma); HeLa (human cervical carcinoma); HL-60 (leukemia carcinoma); Caov-3 (ovarian carcinoma). Figure (3) shows a variety of Goniotalamin-based derivatives.¹⁴

Figure 3: *Goniotalamin-Based Derivatives*

There are two total syntheses of (*R*)-(+)-goniothalamine and (*R*)-(+)-goniothalamine oxide that have been recently reported by Marko and Bose respectively.^{14,15} Note that several other research groups have synthesized Goniothalamine and Goniothalamine analogues but the emphasis of this thesis will be on the two syntheses mentioned above with relevance to their work.¹⁵ Marko and coworkers, employed a sulfoxide-modified Julia olefination starting from optically pure glycidol ether. In contrast, Bose and coworkers utilized a ring-closing metathesis and Jacobsen's hydrolytic kinetic resolution of a racemic epoxide.

In 2006, Marko and coworkers completed the total synthesis of (*R*)-(+)-goniothalamine and (*R*)-(+)-goniothalamine oxide in five and six steps (51-55% overall yield) respectively (Scheme 8).

Scheme 8: Retrosynthesis Analysis of Marko's Synthesis

(R)-(+)-goniothalamin was completed by a connection at the C6-C7 bond by employing a sulfoxide modified Julia olefination on aldehyde 4 and sulfoxide 3. The aldehyde 4 was assembled from the protected diene 2 by a ring closing metathesis. Ring opening and acylation of the optically pure protected glycidol 1 afforded the protected diene 2. (R)-(+)-goniothalamin oxide 6 was accomplished by epoxidation of (R)-(+)-goniothalamin 5.¹⁴

Bose's synthesis (Scheme 9) achieved the natural products of (R)-(+)-goniothalamin and (R)-(+)-goniothalamin oxide in six steps with 65% overall yield.

Scheme 9: Retrosynthesis Analysis of Bose's Synthesis

Bose synthesized the two natural products shown in Scheme 9 by a ring closing metathesis of triene **4** using Grubbs' 1st generation catalyst. The triene **4** was afforded by an acylation of alcohol **3** which was synthesized from the chiral epoxide **2**. The chiral epoxide **2** was furnished by using an olefination followed by epoxidation of *trans*-cinnamaldehyde **1** followed by a Jacobsen hydrolytic kinetic resolution (HKR) of the racemic epoxide. The downfall of using Jacobsen HKR is that half of the starting epoxide is converted to a chiral epoxide with the opposite stereochemistry of the natural product.¹⁶ Compound **6** was synthesized by using Jacobsen's epoxidation from **5**.

1.3 Total synthesis of (R)-(+)-goniothalamin oxide

Our approach for the total synthesis of (R)-(+)-goniothalamin oxide is much similar to Bose's synthesis, in that we go through the same homoallylic alcohol. The retrosynthesis in Scheme 10 shows the similarities and the differences in the two syntheses.

Scheme 10: Retrosynthetic Approach Towards (R)-(+)-goniothalamin oxide

Our route to (R)-(+)-goniothalamin oxide also relies upon a ring-closing metathesis of the diene **4** using the Grubbs I catalyst. Acylation of the secondary alcohol of epoxide **3a** could afford the diene **4** that would be used in the ring-closing metathesis. Epoxide **3a** could be prepared by a Leighton allylation of *trans*-cinnamaldehyde **1** followed by an diastereoselective epoxidation of the internal double bond of the allyl-product **2**.

Scheme 11: Stereoselective Synthesis of Epoxide **3a & **3b****

The total synthesis of (*R*)-(+)-goniothalamine oxide was accomplished by using commercially available starting material *trans*-cinnamaldehyde **1**. Enantioselective allylation of *trans*-cinnamaldehyde **1** was completed using the (*S,S*)-Leighton reagent **7** to furnish secondary alcohol **2** in 95% yield with excellent stereoselectivity. The stereoselective epoxidation of the internal double bond was completed by using VO(acac)₂/*t*-BuOOH in refluxing benzene to diastereoselectively furnish the undesired product (**3b**) in the ratio of 10:1 (Scheme 11). However, the desired product (**3a**) could be furnished at a greater yield and higher diastereoselectivity using a *m*CPBA epoxidation of **2**.

It is important to note that the mixture of diastereomers were inseparable by flash chromatography at this point, but could be cleanly separated following the acylation reaction (Scheme 12).

Scheme 12: Acylation of epoxides

Thus, the mixture of epoxides was acylated using acrylic acid, DMAP/DCC in CH₂Cl₂ (70% yield). The mixture of acylated products **4a/4b** was then easily separated by flash chromatography to give two pure diastereomers. The (1*R*,2'*S*,3'*S*) diastereomer

4a was used to complete the total synthesis of (*R*)-(+)-goniothalamine oxide by means of a ring-closing metathesis (Scheme 13), which was induced upon exposure of **4a** to the Grubbs 1st generation catalyst.

Scheme 13: Ring-Closing Metathesis of Diene **4a**

The other diastereomer (1*R*,2'*S*,3'*S*)-**4b** was also subject to a ring-closing metathesis using Grubbs 1st generation catalyst (Grubbs I) to give the diastereomeric product of (*R*)-(+)-goniothalamine oxide **6** (Scheme 14). This diastereomer could be prepared in a slightly higher yield replacing the diastereoselective directed epoxidation of **2** with an unselective *m*CPBA epoxidation.

Scheme 14: Ring-Closing Metathesis of Diene **4b**

The total synthesis of (*R*)-(+)-goniothalamine oxide **5** and (1*R*,2'*S*,3'*S*)-3-phenyloxiran-2-yl)-5,6-dihydro-2*H*-pyran-2-one **6** were completed in four steps in 35% and 33% overall yield respectively. Both syntheses provide material with physical and spectral data that matched the data reported in the literature.¹⁴

CHAPTER II

2.1 Background of Oxopolyene Macrolide Antibiotic RK-397

RK-397 (Figure 4) is a 32-membered oxopentaene macrolide antibiotic that was isolated and characterized from a Japanese soil bacterium in 1993 by Osada and co-workers.¹⁶ The macrolide processes antifungal properties along with potent oncotoxicity in a variety of cancer cell lines.¹⁷ Due to this interesting activity and the unique structure of RK-397, many research groups have completed total and formal syntheses of this compound including: McDonald¹⁸, Denmark¹⁹, Sammakia²⁰ and O'Doherty.²⁰

Figure 4: *RK-397, 32-membered oxopentaene antibiotic*

O'Doherty's formal synthesis of RK-397 utilizes two dienoate asymmetric hydration reaction sequences (**7** to **6** and **8** to **5**) to set the initial asymmetry of the convergent synthesis. In addition, several highly diastereoselective reactions were used to control the remaining stereocenters of RK-397. These reactions included two reagent controlled Leighton allylation reactions, as well as three substrate controlled intramolecular hydration reactions and one substrate controlled aldol reaction (**4** + **5** to **3**, Scheme 15).²¹

Scheme 15: Retrosynthesis of RK-397

In addition to developing new reaction sequences for the practical syntheses of biologically important molecules, the O'Doherty group has also been interested in

developing a *de novo* asymmetric approach to stereochemically complex chiral molecules by using an asymmetric catalysis to install all the chiral centers from achiral starting materials (i.e., **7** and **8**, Scheme 15). If the two Leighton allylation reactions in the O'Doherty route could be replaced with catalytic asymmetric allylation reactions, then this route to RK-397 would become truly a *de novo* asymmetric approach. Thus, we decided to try to incorporate the newly developed Krische asymmetric allylation as an alternative to the two Leighton allylation reactions. At the outset, it was decided this reaction would be conducted in collaboration with the Krische group.

Scheme 16: *Synthesis of Leighton Allylation Intermediates Towards RK-397*

Outlined in Scheme 16 are the two key sequences (**a** and **b**) that contain the relevant Leighton allylation steps. In addition, to having the advantage of replacing stoichiometric reagents with catalytic reagents, the incorporation of two Krische allylation reactions will eliminate the need for two additional oxidation reactions.

2.2 Outline of Krische Catalytic Asymmetric Allylation

Krische and coworkers have developed a transfer hydrogenation/allylation reaction that employs an iridium catalyst generated in situ to couple allyl acetate to allylic, aliphatic, and benzylic alcohols to furnish homoallylic alcohol products with high levels of asymmetric induction (Scheme 17).²²

Scheme 17: *Ir-Catalyzed Transfer Hydrogenative Allylation of Allylic Alcohols*

The Ir-catalyzed transfer hydrogenative allylation of alcohols shown above is very important in the synthesis of a wide range of diverse natural product architectures. By using this type of catalytic asymmetric allylation reaction, one is able to eliminate the stoichiometric amount of metallic waste that is associated with other types of asymmetric allylations and oxidation/reductions steps that may occur in a total synthesis. In addition, by eliminating the use of an oxidation steps it also reduces the amount of waste generated. Thus the Krische allylation could be a very valuable tool towards the total or formal synthesis of a natural product.

2.3 Synthesized Intermediates for Krische Allylation and Future Work

A series of alcohol intermediates, aldehyde standards and homoallylic alcohol products were synthesized in preparation for the Krische collaboration (scheme 18 and 19). The two homoallylic alcohols **13** and **14** were prepared from Dibal-H reduction of the known esters **9** and **11** (Scheme 18). Samples of 300 mg of **13** and 150 mg of **14** were prepared and sent to the Krische labs at the University of Texas-Austin.

Scheme 18: *Synthesized Alcohols*

Scheme 19: *Synthesized Aldehydes*

Because the Krische allylation reaction generates aldehyde intermediate, the two aldehydes **6** and **15** were prepared by MnO_2 and Dess-Martin oxidation respectively (scheme 19). Finally, the two aldehydes were asymmetrically allylated to prepare samples of the two sets of two diastereomeric homoallylic alcohols **10a** and **10b** as well as **12a** and **12b** using the enantiomeric Leighton reagents (Scheme 20). Thus samples of 10 mg of **10a**, 15 mg of **10b**, 10 mg of **12a** and 10 mg of **12b** were prepared and sent to the Krische labs at the University of Texas-Austin. These efforts are on going and will be reported in due course.

Scheme 20: *Leighton Allylation Products*

Conclusion:

In conclusion, a short total synthesis of (R)-(+)-Goniothalamine Oxide has been completed using a Leighton asymmetric allylation reaction and a Grubbs ring-closing metathesis. Also intermediate alcohols and aldehydes of RK-397 were synthesized for a collaboration to complete a catalytic asymmetric allylation.

CHAPTER III

Experimental Section

3.1 General Information: Instrumentation, Materials, Manipulation

^1H and ^{13}C NMR spectra were recorded on a 600 or 270 MHz spectrometer. Chemical shifts are reported relative to internal tetramethylsilane (δ 0.00 ppm) or CDCl_3 (δ 7.26 ppm) or CD_3OD (δ 4.89 ppm) for ^1H NMR and CDCl_3 (δ 77.1 ppm) or CD_3OD (δ 49.15 ppm) for ^{13}C NMR. Infrared (IR) spectra were obtained on a FT-IR spectrometer. Optical rotations were measured with a digital polarimeter in the solvent specified. Melting points were determined with a standard melting point apparatus and are uncorrected. Flash column chromatography was performed on 60-200 mesh silica gel. Analytical thin-layer chromatography was performed with precoated glass-backed plates and visualized by quenching of fluorescence and by charring after treatment with *p*-anisaldehyde or phosphomolybdic acid (PMA) or potassium permanganate stain (KMnO_4). R_f values are obtained by elution in the stated solvent ratios (v/v). Ether, THF, methylene chloride and triethylamine were dried by passing through activated alumina column with argon gas pressure. Commercial reagents were used without purification unless otherwise noted. Air and/ or moisture- sensitive reactions were carried out under an atmosphere of argon/nitrogen using oven-dried glassware and standard syringe/septa techniques. HPLC analyses were carried out using a chiral column eluting (flow rate = 1.0 mL/min) with Argon-degassed HPLC grade solvents. Detection was done by UV.

(3*R*,*E*)-1-Phenylhexa-1,5-dien-3-ol (2):

To a solution of *E*-cinnamaldehyde **1** (478 mg, 3.62 mmol) in 5 mL of CH₂Cl₂ at -10 °C was added (*S,S*)-Leighton Reagent (1.0 g, 1.81 mmol) in 4 mL of CH₂Cl₂ at -10 °C. After stirring for 5 min the solution was stored in a freezer for 20 hrs. The reaction was quenched with 1N HCl (10%), sat. NH₄Cl aqueous solution, and then diluted with EtOAc then passed through celite. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated to afford the crude product. Flash chromatography on silica gel (8:2 (v/v) hexane/EtOAc) provided compound **2** (600 mg, 95% yield) as a yellow oil. *R_f* = 0.37 (8:2 (v/v) hexane/EtOAc). Spectral data gave a satisfactory match to previous reports.²³ $[\alpha]_D^{25} = 30^\circ$ (*c* 1.6, CHCl₃); IR (neat, cm⁻¹) 3348, 1640, 1493, 964, 913, 746, 691; ¹H NMR (CDCl₃, 600 MHz) 7.39 (m, 2H), 7.32 (m, 2H), 7.24 (m, 1H), 6.62 (d, *J* = 15.6 Hz, 1H), 6.18 (dd, *J* = 15.6, 6.6 Hz, 1H), 5.87 (dddd, *J* = 17.4, 10.2, 7.2, 7.2 Hz, 1H), 5.19 (m, 2H), 4.37 (dd, 6.6, 6.6 Hz, 1H), 2.42 (m, 2H), 1.85 (s, 1H); ¹³C NMR (CDCl₃, 600 MHz) δ 136.6, 134.0, 131.5, 130.4, 128.5, 127.6, 126.4, 118.5, 71.7, 42.0; HRMS (CI) calcd for [C₁₂H₁₄O + Na]⁺: 197.0945, Found: 197.0942

(1R,2'S,3'S)-3'-phenyloxiran-2'-yl)but-3-en-1-ol (3a):

To a solution of product (1*R,E*)-1-phenylhexa-1,5-dien-3-ol **2** (150 mg, 0.861 mmol) in 7 mL of benzene was added VO(acac)₂ (3 mg, 12 μmol) to produce a green colored solution. After 10 min of stirring *t*-BuOOH (85 mg, 0.947 mmol) was added to the solution which was accompanied by a color change to a pale yellow/orange color. The reaction was quenched with a sat. NaHCO₃ aqueous solution. The layers were separated. The aqueous layer was extracted with EtOAc and the combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated to afford crude product. Flash chromatography on silica gel (9:1 (v/v) hexane/EtOAc) provided compound **3a** (119 mg, 71% yield) as a colorless oil. Spectral data gave a satisfactory match to previous reports.²⁴ *R*_f = 0.30 (8:2 (v/v) hexanes:EtOAc); [α]_D²⁵ = 26 ° (*c* 0.4, CHCl₃); IR (neat, cm⁻¹) 3439, 1642, 917; ¹H NMR (CDCl₃, 270 MHz) 7.32 (m, 5H), 5.90 (ddt, *J* = 16.8, 10.2, 7.2, 7.2 Hz, 1H), 5.17 (m, 2H), 3.99 (dddd, *J* = 4.8, 4.8, 4.0, 4.0 Hz, 1H), 3.97 (d, *J* = 1.8 Hz, 1H), 3.10 (dd, *J* = 3.0, 1.8 Hz, 1H), 2.35(m, 2H), 2.03(m, 1H); ¹³C NMR (CDCl₃, 600 MHz) δ 136.8, 133.4, 128.5, 128.3, 125.7, 118.4, 68.3, 64.2, 55.0, 37.9; HRMS (CI) calcd for [C₁₂H₁₄O₂ + Na]⁺: 213.0894, Found: 213.0892

(1R,2'S,3'S)-3'-phenyloxiran-2'-yl)but-3-enyl acrylate (4a):

To a solution of product (1R,2'S,3'S)-3'-phenyloxiran-2'-yl)but-3-en-1-ol **3a** (120 mg, 0.629 mmol) in 10 mL of CH₂Cl₂ was added acrylic acid (188 mg, 2.61 mmol), DCC (538 mg, 2.61 mmol), and DMAP (4 mg) at room temperature. After stirring for 6 hrs the reaction was diluted with ether, passed through celite, and extracted with 1M aqueous NaHSO₄ and then sat. aqueous NaHCO₃. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated. Flash chromatography on silica gel (9.5:0.5 (v/v) hexanes/EtOAc) provided compound **4a** (92.2 mg, 60% yield) as a colorless oil. R_f = 0.59 (8:2 (v/v) hexanes:EtOAc); $[\alpha]_D^{25}$ = 61° (*c* 0.4, CHCl₃); IR (neat, cm⁻¹) 1731, 1240, 1186, 1046; ¹H NMR (CDCl₃, 600 MHz) 7.30 (m, 5H), 6.43 (dd, *J* = 17.3, 1.5 Hz, 1H), 6.12 (dd, *J* = 17.1, 10.4 Hz, 1H), 5.84 (m, 2H), 5.16 (m, 2H), 4.99 (ddd, *J* = 7.2, 5.2, 3.2 Hz), 3.94 (d, *J* = 2.0 Hz, 1H), 3.07 (dd, *J* = 5.7, 2.0 Hz, 1H), 2.57 (m, 2H); ¹³C NMR (CDCl₃, 600 MHz) δ 165.3, 136.6, 132.4, 131.3, 128.5, 128.3, 128.1, 125.6, 118.5, 72.1, 61.8, 57.3, 35.8 HRMS (CI) calcd for [C₁₂H₁₄O₂ + Na]⁺: 267.0999, Found: 267.0997

(R)-(+)-goniothalamine oxide (5):

To a solution of product (1R,2'S,3'S)-3'-phenyloxiran-2'-yl)but-3-enyl acrylate **4a** (25 mg, 0.10 mmol) in 7 mL of CH₂Cl₂ was added Grubbs (I) catalyst (8 mg, 0.010 mmol) at room temperature. After stirring for 4 hrs at reflux the reaction was concentrated. Flash chromatography on silica gel (7:3 (v/v) hexane:EtOAc) provided compound **5** (17 mg, 77% yield) as a dark oil. (Note: Color caused by Grubbs catalyst) $R_f = 0.086$ (8:2 (v/v) hexanes:EtOAc). Spectral data gave a satisfactory match to previous reports.²⁵ $[\alpha]^{25}_D = 100^\circ$ (c 0.4, CHCl₃); IR (neat, cm⁻¹) 1724, 1247, 1041, 815; ¹H NMR (CDCl₃, 600 MHz) 7.34(m, 5H), 6.94 (ddd, $J = 8.7, 4.9, 3.7$ Hz, 1H), 6.08 (ddd, $J = 9.6, 3.7, 1.7$, 1H), 4.45 (ddd, $J = 9.1, 5.8, 5.8$ Hz, 1H), 3.89 (d, $J = 1.9$ Hz, 1H), 3.27 (dd, $J = 5.6, 1.9$ Hz, 1H), 2.59 (m, 2H); ¹³C NMR (CDCl₃, 600 MHz) δ 163.7, 144.2, 135.7, 128.7, 128.6, 125.7, 121.6, 77.1, 61.5, 57.3, 25.9 HRMS (CI) calcd for [C₁₂H₁₄O₂ + Na]⁺: 217.0786 Found: 217.0865

(1R,2'R,3'R)-3'-phenyloxiran-2'-yl)but-3-enyl acrylate (4b**):**

To a solution of product (1R,2'R,3'R)-3'-phenyloxiran-2'-yl)but-3-en-1-ol **3b** (120 mg, 0.629 mmol) in 10 mL of CH₂Cl₂ was added acrylic acid (188 mg, 2.61 mmol), DCC (538 mg, 2.61 mmol), and DMAP (4 mg) at room temperature. After stirring for 6 hrs the reaction was diluted with ether, passed through celite, and extracted with 1M aqueous NaHSO₄ and then sat. aqueous NaHCO₃. The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄, and concentrated. Flash chromatography on silica gel (9.5:0.5 (v/v) hexanes/EtOAc) provided compound **4b** (92.2 mg, 60% yield) as a colorless oil. *R_f* = 0.58 (8:2 (v/v) hexanes:EtOAc); IR (neat, cm⁻¹) 1731, 1406, 1373, 1240, 1186, 1046, 984; ¹H NMR (CDCl₃, 270 MHz) 7.29 (m, 5H), 6.48 (dd, *J* = 17.3, 1.5 Hz, 1H), 6.17 (dd, *J* = 17.0, 7.0 Hz, 1H), 5.83 (m, 2H), 5.14 (m, 1H), 4.98 (dd, *J* = 12.6, 6.7, 1H), 3.79 (d, *J* = 2.0 Hz, 1H), 3.17 (dd, *J* = 5.9, 2.0 Hz, 1H), 2.54 (m, 2H); ¹³C NMR (CDCl₃, 600 MHz) δ 165.6, 136.5, 132.4, 131.6, 128.7, 128.6, 128.4, 125.8, 119.1, 73.1, 62.7, 56.7, 36.2

(R)-6-((2R,3R)-3-phenyloxiran-2-yl)-5,6-dihydro-2H-pyran-2-one (6):

To a solution of product (1R,2'R,3'R)-3'-phenyloxiran-2'-yl)but-3-enyl acrylate **4b** (25 mg, 0.10 mmol) in 7 mL of CH₂Cl₂ was added Grubbs (I) catalyst (8 mg, 0.010 mmol) at room temperature. After stirring for 4 hrs at reflux the reaction was concentrated. Flash chromatography on silica gel (7:3 (v/v) hexane:EtOAc) provided compound **6** (17 mg, 77% yield) as a dark oil. *R_f* = 0.087 (8:2 (v/v) hexanes:EtOAc); IR (neat, cm⁻¹) 1724, 1386, 1247, 1041, 815, 698; ¹H NMR (CDCl₃, 270 MHz) 7.33(m, 5H), 6.92 (ddd, *J* = 8.7, 5.4, 3.0 Hz, 1H), 6.08 (ddd, 9.9, 2.6, 1.7 1H), 4.68 (ddd, *J* = 8.7, 4.7, 3.7 Hz, 1H), 4.08 (d, *J* = 1.9 Hz, 1H), 3.24 (dd, *J* = 3.7, 1.9 Hz, 1H), 2.62 (m, 2H); ¹³C NMR (CDCl₃, 600 MHz) δ 162.8, 143.9, 135.9, 128.6, 128.6, 125.7, 121.6, 75.1, 62.1, 55.0, 26.2

(-)-(E,4S,5S)-Ethyl 5-(*tert*-butyldimethylsilyloxy)-4,6-dimethylhept-2-enoate (9):

The δ -hydroxy enoate (200 mg, 1.0mmol) was added to a flask with CH_2Cl_2 (1.0 mL) followed by addition of 2,6-lutidine (233 μL , 2.0 mmol). The mixture was allowed to cool to 0°C in an ice bath. Then TBSOTF (253 μL , 1.1 mmol) was added slowly via syringe and the reaction was allowed to warm to RT and stir 2 hours. The reaction was then quenched with the addition of Et_2O (4mL) followed by washing with a saturated aqueous solution of CuSO_4 (1 mL). The layers were separated and the organic layer was washed with brine (1.5mL). The organics were then dried over Na_2SO_4 and concentrated *en vacuo*. The crude mixture was purified immediately by flash column chromatography over silica gel (5% CH_2Cl_2 /5% Et_2O /Hexanes) to yield TBS-protected enoate **9** (276 mg, 88%) as a clear, colorless oil. Spectral data gave a satisfactory match to previous reports.²⁶ $[\alpha]_D^{25} = -27$ ($c = 1.5$, CH_2Cl_2); ^1H NMR (CDCl_3 , 270 MHz) δ 6.97 (dd, $J = 15.8, 7.9$ Hz, 1H), 5.76 (d, $J = 15.8$ Hz, 1H), 4.18 (q, $J = 7.2$ Hz, 2H), 3.37 (dd, $J = 4.9, 4.9$ Hz, 1H), 2.51 (m, 1H), 1.71 (m, 1H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.03 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.87 (d, $J = 6.7$ Hz, 3H), 0.85 (d, $J = 6.7$ Hz, 3H), 0.04 (s, 3H), 0.03 (s, 3H). HRMS (ESI) calcd for $[\text{C}_{17}\text{H}_{34}\text{O}_3\text{Si} + \text{Na}]^+$: 337.2175 Found: 337.2180.

(-)-(E,4S,5S)-5-(tert-butyldimethylsilyloxy)-4,6-dimethylhept-2-en-1-ol (13):

The ester **9** (2.13 g, 6.78 mmol) was dissolved in THF (6.8 ml) and cooled to -78°C . Next was added 2.2 equiv Dibal-H (14.91 ml of 1M hexane solution) via syringe. The reaction was allowed to stir at -78°C for 35 min when determined complete by TLC (UV, anisaldehyde stain). The reaction was then quenched by the addition of acetone (3 ml) which was pre-cooled to match the temp of the reaction. The reaction was allowed to stir for 5 min then warmed to room temp at which time aqueous 20 wt% Na, K-tartrate (30 ml) was added with rapid stirring. This two phase solution was allowed to stir rapidly until the phases separated easily upon stopping the stirring. The layers were separated and the aqueous layer was extracted with Et₂O (3 x 15ml). The organics were collected and washed with 15 ml of brine and dried over Na₂SO₄ followed by concentration *en vacuo*. This procedure required no further purification and produced allylic alcohol **13** (1.623 g, 89%) as a clear, colorless oil. Spectral data gave a satisfactory match to previous reports.²⁷ ¹H NMR (CDCl₃, 270 MHz) δ 5.64 (m, 2H), 4.10 (dd, $J = 5.4, 5.4$ Hz, 2H), 3.27 (dd, $J = 5.4, 4.3$ Hz, 1H), 2.36 (m, 1H), 1.73 (m, 1H), 1.24 (dd, $J = 5.7, 5.7$ Hz, OH, 1H), 0.99 (d, $J = 6.9$ Hz, 3H), 0.90 (s, 9H), 0.87 (d, $J = 6.7$ Hz, 3H), 0.86 (d, $J = 6.7$ Hz, 3H), 0.03 (s, 3H), 0.02 (s, 3H). $[\alpha]_{\text{D}}^{24} = -13.5$ ($c = 2.6$, CH₂Cl₂);

(-)-(E,4S,5S)-5-(tert-butyldimethylsilyloxy)-4,6-dimethylhept-2-enal (6):

The allylic alcohol **13** (1.33 g, 4.89) was dissolved in CH₂Cl₂ (15 ml) followed by the addition of 10 mass equivalent of MnO₂ (13.3 g) in one portion. The reaction was allowed to stir at RT for 4 days until determined complete by TLC (UV, KMnO₄). The mixture was filtered through celite and concentrated *en vacuo*. This procedure required no further purification and produced enal **6** (987 mg, 87.5%) as a clear, colorless oil. Spectral data gave a satisfactory match to previous reports.²⁸ ¹H NMR (CDCl₃, 270 MHz) δ 9.53 (dd, *J* = 7.9 Hz, 1H), 6.92 (dd, *J* = 15.8, 7.9 Hz, 1H), 6.13 (d, *J* = 15.8, 8.1 Hz, 1H), 3.45 (dd, *J* = 4.9, 4.9 Hz, 1H), 2.64 (m, 1H), 1.73 (m, 1H), 1.08 (d, *J* = 6.9 Hz, 3H), 0.91 (s, 9H), 0.89 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.7 Hz, 3H), 0.09 (s, 3H), 0.04 (s, 3H). $[\alpha]_D^{24} = -48.4$ (*c* = 1.2, CH₂Cl₂).

(-)-(E,4R,7S,8S)-8-(tert-butyldimethylsilyloxy)-7,9-dimethyldeca-1,5-dien-4-ol (10a):

A solution of enal **6** (6.00 g, 22.2 mmol) in CH₂Cl₂ (75 mL) was cooled to -15° C in a salt-ice bath and was added via cannula to a separate RBF containing allyl silane [(S,S)-Leighton reagent] (28.6 g, 51.48 mmol) in CH₂Cl₂ (75 mL) at -15° C. The reaction was then placed in the freezer and allowed to react for 5 days. The reaction mixture was then diluted with EtOAc (100 mL) and filtered through a plug of Celite to remove the white precipitate that had formed after several minutes stirring with EtOAc. The filtrate was then washed with sat. aq. NaHCO₃ (75 mL) and brine (75 mL). The organics were then dried over Na₂SO₄. After concentration the crude mixture was purified immediately by silica gel column chromatography (5% EtOAc/Hexanes) to yield 5.80 g (84%) of acetone **10a**. The minor isomer (from the ca 10% enantiomer) was isolated in a mixture with other products. Spectral data gave a satisfactory match to previous reports.²⁹ R_f = 0.60 (1:4 EtOAc:Hexanes), $[\alpha]_D^{25}$ = -13 (c = 0.9, CH₂Cl₂); IR (neat, cm⁻¹) 3345 (br), 2960, 2930, 2856, 1634, 1473, 1260, 1113, 1055, 1005, 975, 856, 775; ¹H NMR (CDCl₃, 600 MHz) δ 5.79 (m, 1H), 5.62 (dd, J = 15.0, 7.8 Hz, 1H), 5.44 (dd, J = 15.0, 7.2 Hz, 1H), 5.12 (m, 2H), 4.12 (m, 1H), 3.25 (dd, J = 6.0, 4.2 Hz, 1H), 2.30 (m, 3H), 1.73 (m, 1H), 1.56 (d, J = 4.0 Hz, 1H), 0.98 (d, J = 6.6 Hz, 3H), 0.89 (s, 9H), 0.87 (d, J = 6.7 Hz, 3H), 0.83 (d, J = 6.7 Hz, 3H), 0.03 (s, 6H); ¹³C NMR (CDCl₃, 150 MHz) δ 136.1, 134.4, 131.1, 117.9, 80.9, 72.2, 42.0, 41.3, 31.5, 26.0, 20.5, 17.4, 16.7, -3.5, -3.8. HRMS (ESI) calcd for [C₁₈H₃₆O₂Si + Na]⁺: 335.2382 Found: 335.2385.

(4S,7S,8S,E)-8-(tert-butyldimethylsilyloxy)-7,9-dimethyldeca-1,5-dien-4-ol (10b):

A solution of enal **6** (0.07 g, 0.259 mmol) in CH₂Cl₂ (5 mL) was cooled to –15° C in a salt-ice bath and was added via cannula to a separate RBF containing allyl silane [(*R,R*)-Leighton reagent] (0.286 g, 0.517 mmol) in CH₂Cl₂ (5 mL) at –15° C. The reaction was then placed in the freezer and allowed to react for 3 days. The reaction mixture was then diluted with EtOAc (50 mL) and filtered through a plug of Celite to remove the white precipitate that had formed after several minutes stirring with EtOAc. The filtrate was then washed with sat. aq. NaHCO₃ (20 mL) and brine (25 mL). The organics were then dried over Na₂SO₄. After concentration the crude mixture was purified immediately by silica gel column chromatography (5% EtOAc/Hexanes) to yield 0.080g (86%) of acetone **10b**. The minor isomer (from the ca 10% enantiomer) was isolated in a mixture with other products. Spectral data gave a satisfactory match to previous reports.²⁵ R_f = 0.60 (1:4 EtOAc:Hexanes), $[\alpha]_D^{25}$ = – 13 (c = 0.9, CH₂Cl₂); IR (neat, cm^{–1}) 3353 (br), 2957, 2929, 2857, 1642, 1472, 1251, 1112, 1050, 1005, 974, 857, 834, 771; ¹H NMR (CDCl₃, 600 MHz) δ 5.80 (m, 1H), 5.62 (dd, J = 15.0, 7.8 Hz, 1H), 5.44 (dd, J = 15.0, 7.2 Hz, 1H), 5.12 (m, 2H), 4.12 (m, 1H), 3.25 (dd, J = 6.0, 4.2 Hz, 1H), 2.30 (m, 3H), 1.73 (m, 1H), 1.56 (d, J = 4.0 Hz, 1H), 0.98 (d, J = 6.6 Hz, 3H), 0.89 (s, 9H), 0.87 (d, J = 6.7 Hz, 3H), 0.83 (d, J = 6.7 Hz, 3H), 0.03 (s, 6H); ¹³C NMR (CDCl₃, 150 MHz) δ 135.9, 134.3, 130.7, 118.0, 80.7, 71.8, 42.0, 40.7, 31.6, 26.1, 20.5, 18.4, 17.4, 16.4.

(–)-Ethyl 2-((2*R*,4*S*,6*R*)-6-((*E*,3*S*,4*S*)-4-(*tert*-butyldimethylsilyloxy)-3,5-dimethylhex-1-enyl)-2-phenyl-1,3-dioxan-4-yl)acetate (11**):**

To a solution of the alcohol (5.2 g, 13.5 mmol) and benzaldehyde (1.51 mL, 15.0 mmol) in THF (42 mL) was added the *t*-BuOK (151 mg, 1.35 mmol). The reaction mixture was stirred for 15 min. The addition of *t*-BuOK and benzaldehyde was repeated for 3 times every 15 min and then the reaction mixture was quenched with 35 mL pH=7 buffer solution, extracted with Et₂O (3 x 100 mL), dried (Na₂SO₄), and concentrated under reduced pressure. The crude product was purified using silica gel flash chromatography eluting with 10% EtOAc/hexane to give 4.23 g (8.64 mmol, 64%) of colorless oil acetal **11**. R_f = 0.70 (1:4 EtOAc:Hexanes), $[\alpha]_D^{25} = -8$ ($c = 1.0$, CH₂Cl₂); IR (neat, cm⁻¹) 2957, 2929, 2856, 1736, 1472, 1370, 1339, 1251, 1149, 1095, 1051, 1025, 974, 938, 857, 835, 772, 697; ¹H NMR (CDCl₃, 600 MHz) δ 7.50 (m, 2H), 7.33 (m, 3H), 5.76 (dd, $J = 15.0$, 7.8 Hz, 1H), 5.60 (s, 1H), 5.50 (dd, $J = 15.0$, 7.2 Hz, 1H), 4.34 (m, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 3.29 (dd, $J = 5.4$, 4.2 Hz, 1H), 2.73 (dd, $J = 15.6$, 7.2 Hz, 1H), 2.51 (dd, $J = 15.6$, 6.0 Hz, 1H), 2.34 (m, 1H), 1.75 (m, 1H), 1.74 (m, 1H), 1.56 (m, 1H), 1.26 (t, $J = 7.2$ Hz, 3H), 1.00 (d, $J = 6.6$ Hz, 3H), 0.91 (s, 9H), 0.89 (d, $J = 6.6$ Hz, 3H), 0.85 (d, $J = 6.6$ Hz, 3H), 0.04 (s, 6H); ¹³C NMR (CDCl₃, 150 MHz) δ 170.7, 138.4, 136.5, 128.6, 128.2, 128.1, 126.1, 100.6, 80.7, 77.2, 73.1, 60.5, 41.0, 40.7, 36.7, 31.6, 26.1, 20.5, 18.4, 17.6, 15.9, 14.1, -3.5, -3.7; HRMS (ESI) calcd for [C₂₈H₄₆O₅Si + Na]⁺: 513.3006 Found: 513.2982.

(-)-2-((2*R*,4*S*,6*R*)-6-((*E*,3*S*,4*S*)-4-(*tert*-butyldimethylsilyloxy)-3,5-dimethylhex-1-enyl)-2-phenyl-1,3-dioxan-4-yl)acetaldehyde (15):

To a solution of alcohol **14** (40mg, 0.089mmol) is stirred at room temperature in DCM (3mL) under an inert atmosphere and the periodinane (99mg, 0.134mmol) is added in one portion. The reaction is stirred until completion (TLC, about 2 hours) then quenched with sodium thiosulphate (saturated solution), extracted 3 times with ethyl acetate, washed with brine, dried over magnesium sulphate, filtered and concentrated in vacuum. The curde product was purified using silica gel flash chromatography eluting with 30% EtOAc/Hexanes to yield about 36mg (90%) of colorless oil aldehyde **15**. $R_f = 0.50$ (1:4 EtOAc:Hexanes), $[\alpha]_D^{25} = -8.4$ ($c = 1.0$, CH_2Cl_2); IR (neat, cm^{-1}) 2957, 2929, 2856, 1724, 1472, 1385 1360, 1251, 1183, 1096, 1050, 1022, 973, 938, 855, 835, 771, 697 672; ^1H NMR (CDCl_3 , 600 MHz) δ 9.86 (t, $J = 1.8$ Hz, 1H), 7.50 (m, 2H), 7.33 (m, 3H), 5.76 (dd, $J = 15.6, 7.8$ Hz, 1H), 5.60 (s, 1H), 5.51 (dd, $J = 15.6, 5.4$ Hz, 1H), 4.43 (m, 1H), 4.36 (m, 1H), 3.29 (dd, $J = 5.4, 4.2$ Hz, 1H), 2.82 (dd, $J = 16.8, 7.2$ Hz, 1H), 2.62 (dd, $J = 16.8, 5.4$ Hz, 1H), 2.34 (m, 1H), 1.74 (m, 1H), 1.72 (m, 1H), 1.60 (m, 1H), 1.00 (d, $J = 7.2$ Hz, 3H), 0.91 (s, 9H), 0.89 (d, $J = 7.2$ Hz, 3H), 0.85 (d, $J = 7.2$ Hz, 3H), 0.04 (s, 6H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 200.2, 138.2, 136.7, 128.7, 128.1, 128.0, 126.1, 100.7, 80.7, 77.2, 71.7, 49.3, 40.7, 36.8, 31.6, 26.1, 20.5, 18.4, 17.6, 15.9, -3.5, -3.7; HRMS (ESI) calcd for $[\text{C}_{26}\text{H}_{42}\text{O}_4\text{Si} + \text{Na}]^+$: 469.2745 Found: 469.2750.

(-)-(S)-1-((2R,4R,6R)-6-((E,3S,4S)-4-(tert-butyldimethylsilyloxy)-3,5-dimethylhex-1-enyl)-2-phenyl-1,3-dioxan-4-yl)pent-4-en-2-ol (12a).

A solution of aldehyde **15** (10 mg, 0.022 mmol) in CH₂Cl₂ (1 mL) was cooled to –15° C in a salt-ice bath and was added *via* cannula to a separate RBF containing allyl silane [(*R,R*)-Leighton reagent] (16 mg, 0.067 mmol) in CH₂Cl₂ (1 mL) at –15° C. The reaction was then placed in the freezer and allowed to react for 2 h. The reaction mixture was then diluted with EtOAc (5 mL) and filtered through a plug of Celite to remove the white precipitate that had formed after several minutes stirring with EtOAc. The filtrate was then washed with sat. aq. NaHCO₃ (10 mL) and brine (10 mL). The organics were then dried over Na₂SO₄. After concentration the crude mixture was purified immediately by silica gel column chromatography (10% EtOAc/5% MeOH/Hexanes) to yield 10 mg (90%) of homoallylic alcohol **12a**. [α]_D²⁵ = – 2.3 (*c* = 1.0, CH₂Cl₂); IR (neat, cm^{–1}) 3441 (br), 2955, 2930, 2856, 1472, 1461, 1385, 1337, 1251, 1215, 1097, 1052, 1022, 974, 914, 857, 835, 772, 697, 673; ¹H NMR (CDCl₃, 600 MHz) δ 7.50 (m, 2H), 7.33 (m, 3H), 5.84 (m, 1H), 5.75 (dd, *J* = 15.6, 7.8 Hz, 1H), 5.59 (s, 1H), 5.52 (dd, *J* = 15.6, 6.6 Hz, 1H), 5.13 (m, 2H), 4.33 (ddd, *J* = 9.6, 6.6, 1.8 Hz, 1H), 4.20 (dddd, *J* = 10.8, 8.4, 3.0, 3.0 Hz, 1H), 4.04 (m, 1H), 3.29 (dd, *J* = 5.4, 4.2 Hz, 1H), 2.34 (m, 1H), 2.26 (m, 2H), 1.71 (m, 4H), 1.61 (m, 1H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.91 (s, 9H), 0.89 (d, *J* = 7.2 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.04 (s, 6H); ¹³C NMR (CDCl₃, 150 MHz) δ 138.6, 136.4, 134.7, 128.6, 128.4, 128.1, 126.1, 118.0, 100.7, 80.7, 77.5, 74.0, 67.0, 42.2, 42.1, 40.7, 37.0, 31.6, 26.1, 20.5, 18.4, 17.6, 15.9, –3.5, –3.7; HRMS (ESI) calcd for [C₂₉H₄₈O₄Si + Na]⁺: 511.3214 Found: 511.3220.

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Appendix

¹³C NMR, 600 MHz
CDCl₃

¹H NMR, 600 MHz
CDCl₃

¹³C NMR, 600 MHz
CDCl₃

^{13}C NMR, 600 MHz
 CDCl_3

¹H NMR, 270 MHz
CDCl₃

¹³C NMR, 600 MHz
CDCl₃

270 MHz, ^1H NMR, CDCl_3

99 S

X : parts per Million : 1H

C:\pel_data\spectra\K397 ester.sp

270 MHz, ^1H NMR, CDCl_3

L9 S

X : parts per Million : ^1H

270 MHz, ^1H NMR, CDCl_3

89 S

X : parts per Million : ^1H

9.5638
9.5345
9.5052

7.2598
6.9572
6.9250
6.8986

6.1360
6.1309
6.1067

5.5954
5.5631
5.2950

3.6364
3.4591
3.4423

2.6687
2.6489
2.6438

2.1075
2.1031
2.0394
1.7544
1.7383
1.7288

1.1083
1.0834
0.9193
0.9134
0.8943
0.8548
0.8299

0.0929
0.0607
0.0445
0.0336

¹³C NMR, 67.5 MHz
CDCl₃

¹³C NMR, 67.5 MHz
CDCl₃

PH1H1-8-28-08

Archive directory: /export/home/vnmr1/vnmr.sys/data
Sample directory:
File: PROTON

Pulse Sequence: szpul

Solvent: CDCl₃
Temp: 28.0 C / 301.1 K
INNOVA-600 "inova600"

Relax. delay 1.000 sec
Pulse 30.0 degrees
Acq. time 4.000 sec
Width 9594.6 Hz
16 repetitions
OBSERVE H1 599.6669940 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 131072
Total time 1 min, 20 sec

¹H NMR 600 MHz
CDCl₃

¹H NMR 600 MHz
CDCl₃