Fleming−Tamao Oxidation and Masked Hydroxyl Functionality: Total Synthesis of (+)-Pramanicin and Structural Elucidation of the Antifungal Natural Product (−)-Pramanicin

Anthony G. M. Barrett,*,† John Head,‡ Marie L. Smith,† Nicholas S. Stock,† A. J. P. White,† and D. J. Williams†

Department of Chemistry, Imperial College of Science, Technology and Medicine, South Kensington, London SW7 2AZ, United Kingdom, and Celltech Therapeutics, 216 Bath Road, Slough, Berkshire SL1 4EN, United Kingdom

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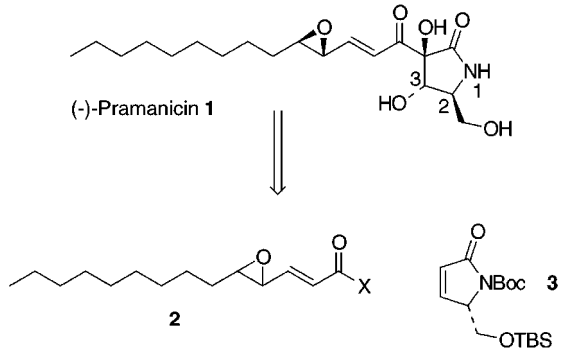
The total synthesis of (+)-pramanicin (**41b**) is reported, thereby establishing the relative and absolute stereochemistry of the naturally occurring antifungal agent. The key steps involve (i) conjugate addition of the diethyl((diethylamino)diphenylsilyl)zincate to a suitably protected γ-lactam **3** and quenching of the resultant enolate with the α,β-unsaturated γ,δ-epoxy aldehyde **2** (X = H), (ii) Ni(acac)$_2$-catalyzed hydroxylation of a β-dicarbonyl array, and (iii) Fleming−Tamao oxidation to reveal the masked C-3 hydroxyl group.

Introduction

(−)-Pramanicin (**1**) contains a highly functionalized γ-lactam-based headgroup with a functionalized lipophilic side chain. Isolated from a fungus belonging to the *Stagonospora* species, **1** shows moderate activity toward a variety of fungal pathogens but notable activity against the acapsular form of *Cryptococcus neoformans*, with an MIC of 62 nM.[1] This microorganism has been implicated as a causative agent of meningitis in AIDS patients, and therefore pramanicin poses an interesting target for synthesis. Schwartz and co-workers, employing a variety of NMR and mass spectral techniques and chemical transformations, established that the epoxide entity possessed the *trans*-stereochemistry and that the C-4 hydroxyl and C-2 hydroxymethyl groups were *trans* to the C-3 alcohol. Nonetheless, these authors did not establish the absolute stereochemistry of the molecule nor the relative stereochemistry of the epoxide to the γ-lactam stereocenters. The biosynthetic origins of pramanicin have been defined by Harrison and co-workers, who showed the incorporation of acetate and serine into the antibiotic.[2]

Retrosynthetically, pramanicin can be divided into two components, the protected γ-lactam **3** derived from L-glutamic acid and an appropriate side chain coupling partner, **2** (Scheme 1). It was envisaged that addition of a silyl cuprate or zincate in a 1,4-fashion to lactam **3** would proceed with *anti*-stereoselectivity on steric grounds, thus defining the absolute configuration of the silyl residue at C_3 and thereby, on Fleming−Tamao oxidation, the configuration of the resultant alcohol. In the Michael addition reaction, trapping of the enolate in situ with a side chain electrophile, **2**, would furnish the carbon backbone of the natural product in a "one-pot" procedure.

Scheme 1



Such a convergent procedure should be amenable for the elaboration of analogues for bioassay.

Results and Discussion

Synthesis of the γ-Lactam and Side Chain Units. The γ-lactam **3**, which was synthesized from L-glutamic acid (**4**) via alcohol **5** following literature procedures[3] but with minor workup modifications as noted in the Experimental Section, was obtained in multigram quantities (Scheme 2). A double Wadsworth−Emmons strategy[4] was used in the elaboration of the epoxy acyl chloride **2c**. Thus, homologation of decanal (**6**) using methyl (diethylphosphono)acetate followed by reduction using DIBAl-H gave allylic alcohol **8** which was epoxidized with *m*-CPBA, and subsequently oxidized to the corresponding aldehyde using Dess−Martin periodinane.[5] A second Wadsworth−Emmons homologation afforded the racemic methyl ester **2a** which was formed with complete *E*-selectivity. This was hydrolyzed to the carboxylic acid **2b** using potassium

† Imperial College of Science, Technology and Medicine.
‡ Celltech Therapeutics.

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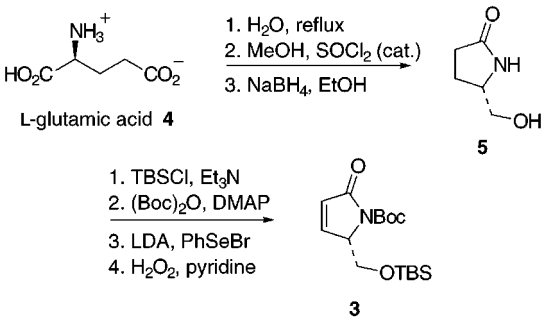
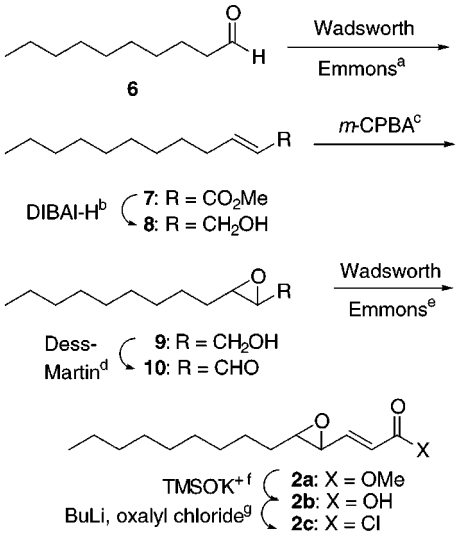
Scheme 2



Reagents and Conditions: see reference 3 and experimental section

Scheme 3

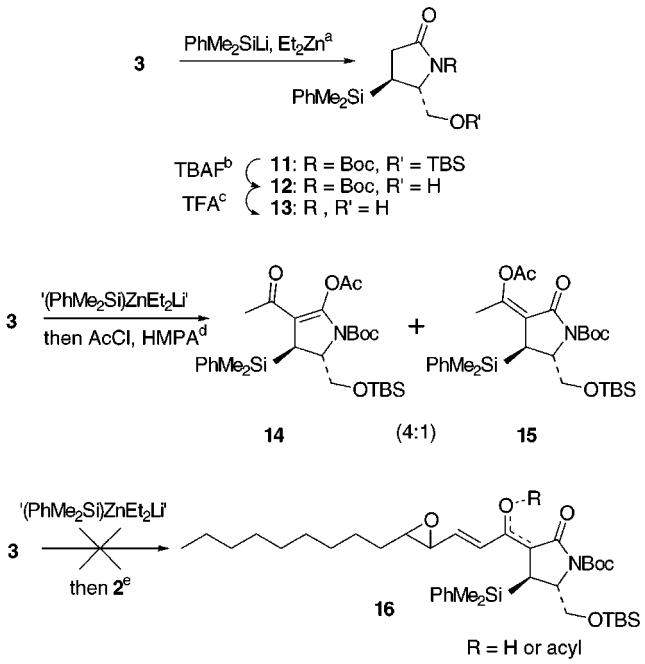


Reagents and Conditions: (a) $(EtO)_2P(O)CH_2CO_2Me$, NaH, THF -78°C to 25°C (99%); (b) DIBAl-H, Et_2O, -78°C to 25°C (92%); (c) *m*-CPBA, CH_2Cl_2, 25°C (96%); (d) Dess-Martin periodinane, CH_2Cl_2 , 25°C (93%); (e) $(EtO)_2P(O)CH_2CO_2Me$, NaH, THF -78°C to 25°C (92%); (f) TMSOK$^+$, THF, 25°C (79%); (g) *n*-BuLi, THF, -78°C then oxalyl chloride, -78°C to 25°C (60%) as judged by MeOH/Et_3N quench to afford ester **2a** (60% recovery).

trimethylsilanolate in THF[6] and subsequently converted into the acyl chloride **2c** by deprotonation with *n*-BuLi and reaction with oxalyl chloride (Scheme 3). The extent of conversion of acid **2b** into chloride **2c** was quantified by quenching an aliquot with methanol and triethylamine and isolation of the resulting methyl ester **2a**. This procedure gave the acid chloride **2c** with minimum levels of impurities.

Michael Addition of (Dimethylphenylsilyl)lithium and Diethylzinc to Lactam 3. Initially the Michael addition of lithium diethyl(dimethylphenylsilyl)zincate[7] to the lactam **3** was examined to produce the corresponding masked hydroxy lactam system. Such conjugated

Scheme 4



Reagents and Conditions: (a) $PhMe_2SiLi$, Et_2Zn, THF, -78°C (99%); (b) TBAF, THF (85%); (c) TFA, CH_2Cl_2 (90%); (d) $PhMe_2SiLi$, Et_2Zn, THF, -78°C then freshly distilled AcCl (4 eq.), HMPA, -78°C to 25°C (99%); (e) $PhMe_2SiLi$, Et_2Zn, THF, -78°C then **2c**, HMPA.

addition reactions are amply precedented,[7,8] and the subsequent silane Fleming−Tamao oxidation is well documented.[9] Addition of the phenyldimethylsilylzincate to lactam **3** proceeded in quantitative yield, affording the silane **11** as a single diastereoisomer (Scheme 4). Confirmation of the stereochemical outcome of this reaction was made through deprotection of the Boc and TBS residues, furnishing the crystalline amido alcohol **13** which was obtained as crystals suitable for an X-ray structure determination (Figure 1). With the knowledge that the 1,4-addition of a silyl zincate proceeded stereoselectively, attention was focused on trapping the enolate in situ with an acid halide or equivalent electrophile. For simplicity, acetyl chloride was chosen as a model trapping reagent. Following the procedure of Tanaka,[10] excess acetyl chloride was added to the lactam enolate, formed from the addition of lithium diethyl(dimethylphenylsilyl)-zincate to **3**, with HMPA as cosolvent. A near quantitative yield of a mixture of the doubly acetylated compounds **14** and **15** was isolated in a 4:1 ratio, giving good indication that *C*-acylation had occurred initially. However, disappointingly, introduction of acyl chloride **2c** with or without HMPA as cosolvent afforded none of the

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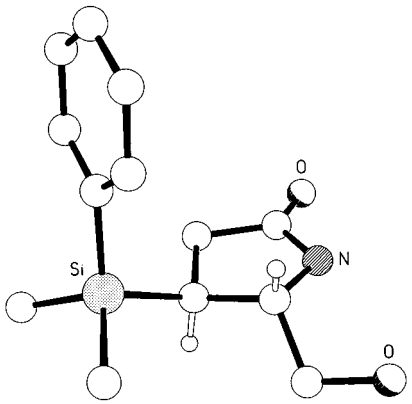


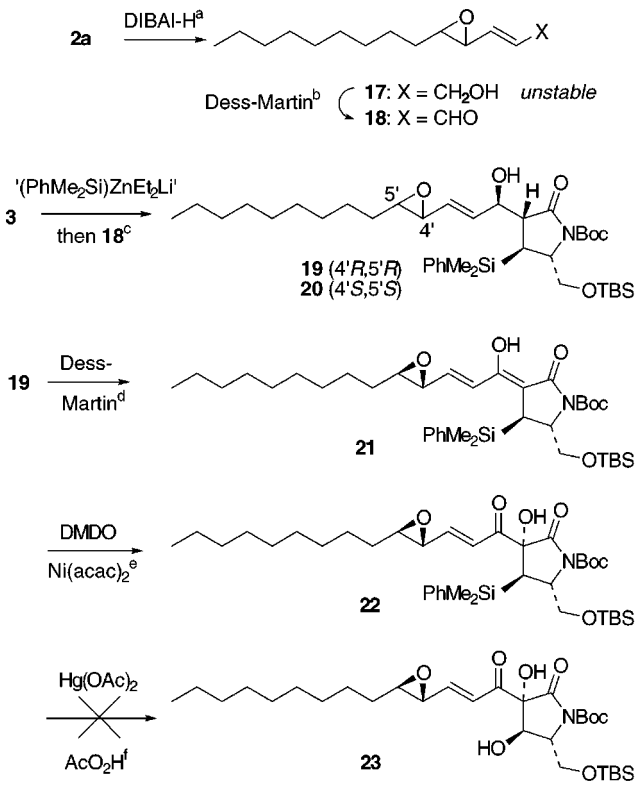
Figure 1. Molecular structure and absolute stereochemistry of **13**.

desired β-diketone derivative **16**; only intractable mixtures of materials resulted (Scheme 4).

In light of the failure to utilize **2c**, attention was directed to the use of the aldehyde **2** (X = H) as the coupling partner. Aldehyde **18** was readily synthesized from the methyl ester **2a** via reduction with DIBAl-H and immediate oxidation with Dess−Martin periodinane. The intermediate allylic alcohol **17** was unstable to prolonged standing. Sequential addition of lithium diethyl(dimethylphenylsilyl)zincate and the aldehyde **18** to the lactam **3** gave the adducts **19** and **20** as a 1:1 mixture of diastereoisomers in an excellent 85% yield (Scheme 5). The two diastereoisomers **19** and **20** were separated by chromatography, and their structures were determined by comparison with model aldol adducts and by alternative syntheses (vide infra). The isolation of only two discrete products, from the racemic epoxy aldehyde **18** and isolation of **20** exclusively, from the aldol reaction using (4*S*,5*S*)-**18** were consistent with a highly diastereoselective addition of the aldehyde to the enolate. The stereochemistry of adducts **19** and **20** was determined by the synthesis of the model compounds **24** and **27**, using acetaldehyde and crotonaldehyde to quench the enolate, respectively (Scheme 6), two single-crystal X-ray structure determinations, and comparisons by ^{1}H NMR spectroscopy. Global deprotection of adducts **24** and **27** resulted in formation of the crystalline amido diols **26** and **29**, the structures of which were elucidated by single-crystal X-ray analysis, thereby unambiguously determining the stereochemical outcome of the aldol reactions (Figure 2). It is reasonable to suggest that the key aldol reaction giving rise to the pramanicin precursors **19** and **20** and model adducts **24** and **27** involved a Zimmerman−Traxler type model (Scheme 6). This places the alkyl chain of the aldehyde in a pseudoequatorial position, thus minimizing unfavorable steric interactions.

Oxidation of the aldol adduct **20** to produce the β-diketone **21** was examined. Initially, several preparations of manganese dioxide[11] were examined as oxidants since the aldol hydroxyl was allylic but were unsuccessful. Oxidation using sodium acetate buffered PCC[12] led

Scheme 5



Reagents and Conditions: (a) DIBAl-H, Et_2O, 78°C to 25°C; (b) Dess-Martin periodinane, CH_2Cl_2 (72% over both steps); (c) $PhMe_2SiLi$, Et_2Zn, THF, -78°C then **18**, THF, -78°C to 25°C (85% 1:1 mixture of **19** and **20**); (d) Dess-Martin periodinane, CH_2Cl_2, 0°C; (e) dimethyldioxirane, $Ni(acac)_2$ (cat.), acetone, water, 10°C (80% over both steps); (f) $Hg(OAc)_2$, AcO_2H, AcOH, 25°C.

to degradation, and the use of TPAP[13] yielded only baseline material by TLC analysis. Fortunately, Dess−Martin periodinane effected the oxidation under mild conditions to afford the diketone **21**, which proved unstable to chromatography on both silica and alumina. Stereoselective hydroxylation of dione **21** was accomplished using dimethyldioxirane in the presence of a nickel(II) acetylacetonate catalyst at subambient temperature.[14] This gave the hydroxy dione **22** in an excellent 80% yield over both steps. Presumably, the stereochemistry of this hydroxylation reaction follows from steric congestion by the adjacent phenyldimethylsilyl moiety, thus forcing oxidation from the opposite face. At this stage there only remained the need to carry out the key Fleming−Tamao oxidation to unmask the silyl residue as a hydroxyl. Fleming and others have developed a wide range of reagents to accomplish this transformation, with the mildest being the use of mercury(II) acetate in the presence of peracetic acid.[9] Much to our disappointment, reaction of silane **22** under these conditions yielded multiple degradation products. The use of the phenyldimethylsilyl residue to mask the key alcohol was abandoned in favor of a more readily oxidizable silyl

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(14) Adam, W.; Smerz, A. K. *Tetrahedron* **1996**, *52*, 5799.

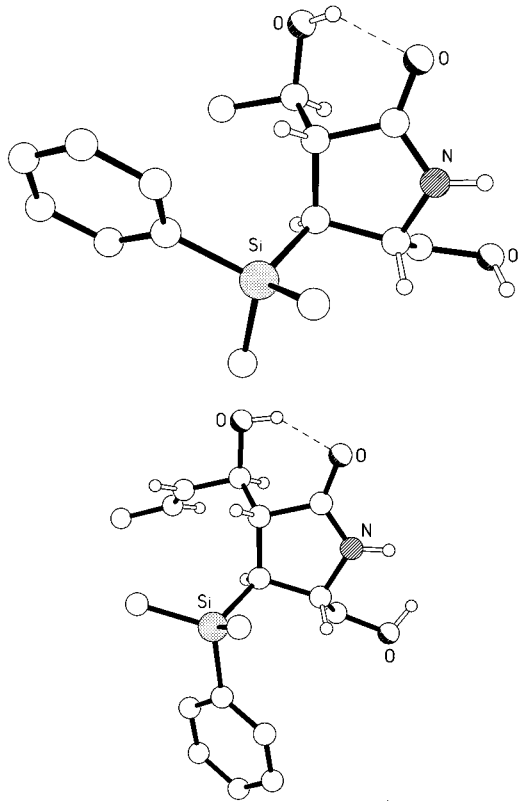
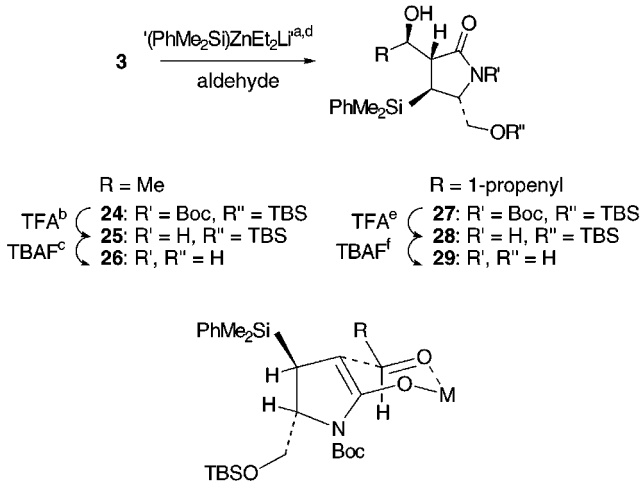


Figure 2. Molecular structures and absolute stereochemistries of (a, top) **26** and (b, bottom) **29**.

Scheme 6



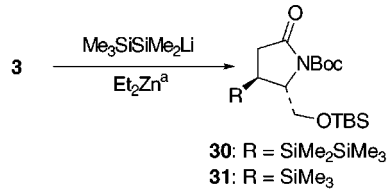
Transition state model

Reagents and Conditions: (a) $PhMe_2SiLi$, Et_2Zn, THF, -78°C then acetaldehyde (74%); (b) TFA, CH_2Cl_2 (84%); (c) TBAF, THF (91%); (d) $PhMe_2SiLi$, Et_2Zn, THF, -78°C then crotonaldehyde; (e) TFA , CH_2Cl_2 (53%); (f) TBAF, THF (78%).

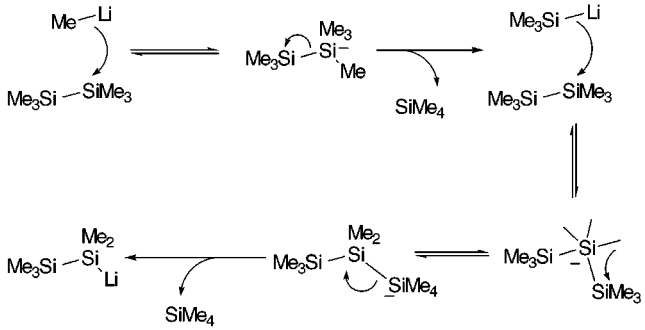
entity. However, the lithium diethyl(dimethylphenylsilyl)zincate had played an important role in developing the one-pot silyl addition/coupling protocol and subsequent oxidative elaboration of the natural product framework.

Michael Addition of (Pentamethyldisilyl)lithium and Diethylzinc to Lactam 3. The pentamethyldisilanyl anion has recently attracted attention due to its inherent "soft" nature and the possibility of the oxidation of silanes formed from its reactions with electrophiles under mild conditions.[15] Krohn has employed this silyl entity as a masked hydroxyl group in the synthesis of the antibiotic (±)-rabelomycin,[16] prompting us to investigate the viability of this surrogate alcohol within our approach to pramanicin. Preliminary efforts at introducing this silyl entity by Michael addition to the lactam **3** using the procedure described by Krohn[16] were unsuccessful and gave intractable mixtures of products. Reaction of the pentadimethylsilanyl anion, generated by the reported procedure from hexamethyldisilane (1.6 equiv) and methyllithium (1 equiv), with diethylzinc and subsequent addition of the lactam **3** gave the desired disilane **30** and the undesired trimethylsilane **31** with the silane **31** predominating. The formation of the undesired adduct **31** was significantly suppressed by the use of 2 equiv of hexamethyldisilane in the initial reaction with methyllithium (Scheme 7). The importance of reaction stoichiometry on the balance between the formation of pentamethyldisilyllithium and trimethylsilyllithium is consistent with the mechanism of lithiation in Scheme 7.

Scheme 7



possible mechanism for formation of pentamethyldisilyl anion



Reagents and Conditions: (a) $Me_3SiSiMe_3$ (2 eq.), MeLi (1 eq.), THF, HMPA, 0°C, 20 min. then Et_2Zn, THF, -78°C (76% with <5% of **31**).

The enantiomerically pure aldehyde (4*R*,5*R*)-**18** was prepared following the methods in Scheme 3 but using Sharpless epoxidation[17] to elaborate the epoxy alcohol (2*R*,3*R*)-**9** and thereby control the absolute stereochemistry of the process. (2*R*,3*R*)-**9** was obtained in high enantiomeric excess (>95%) as judged by conversion of the aldehyde **10** and (2*S*,3*R*)-**10** into the diastereoisomeric imidazolidines **32a** and **32b** under the protocol of Alexakis[18] and subsequent ^{1}H NMR analysis. A single

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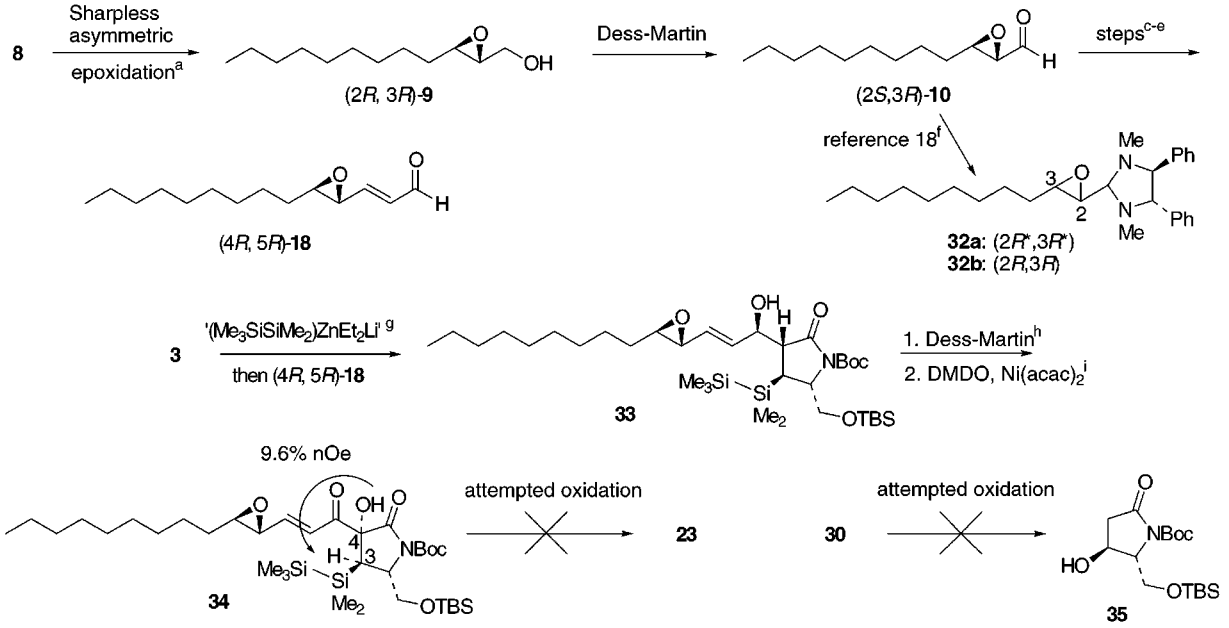
Scheme 8



Reagents and Conditions: (a) $Ti(O^iPr)_4$ (cat.), D-(-)-DIPT (cat.), *t*-BuOOH, DCM, 4A mol. sieves, CH_2Cl_2, -30°C, 15 hrs, (86% ee>95%); (b) Dess-Martin periodinane, CH_2Cl_2 (97%); (c) $(EtO)_2P(O)CH_2CO_2Me$, NaH, THF, -78°C (95%); (d) DIBAl-H, Et_2O, -78°C; (e) Dess-Martin periodinane, CH_2Cl_2 (74% over two steps); (f) *(S,S)*-N,N'-dimethyl-1,2-diphenyl ethylene diamine, Et_2O, 4A mol sieves; (g) $Me_3SiSiMe_3$ (2 eq.), MeLi (1 eq.), HMPA, 0°C then Et_2Zn, THF, -78°C followed by addition of (4*R*,5*R*)-**18** (60%); (h) Dess-Martin periodinane, CH_2Cl_2, 0°C; (i) dimethyldioxirane, $Ni(acac)_2$ (cat.), acetone, water, 0°C (61% over two steps).

recrystallization gave enantiomerically pure (2*R*, 3*R*)-**9**. Pentamethyldisilyllithium was prepared using the optimized procedure and converted into the corresponding zincate. Michael addition to the unsaturated lactam **3** and in situ trapping with the enantiomerically pure aldehyde (4*R*,5*R*)-**18** afforded the *β*-hydroxylactam **33** in 60% yield, as a single diastereoisomer. Sequential Dess−Martin periodinane and dimethyldioxirane oxidation catalyzed by $Ni(acac)_2$ of the aldol adduct **33** gave disilane **34** as a single diastereoisomer in 61% over both steps (Scheme 8). The ^1H NMR spectrum of the disilane **34** proved suitable for ^1H NMR NOE analysis. A 9.6% enhancement was observed in the signal for the *γ*-lactam C-3 proton upon irradiation of the hydroxyl proton of the tertiary alcohol, thereby confirming that the desired stereochemistry had been established. At this stage only the key Fleming−Tamao oxidation remained to be carried out. Unfortunately and much to our bitter disappointment, attempted oxidation of the disilane **34** or the model **30** under diverse and varied conditions gave only complex mixtures of products. The use of potassium or tetrabutylammonium fluoride in the presence of 3-chloroperoxybenzoic acid[15,19] afforded none of the desired alcohol. No traces of the possible siloxane[19] or silanol were evident (Scheme 8). Attempted Si−Si cleavage of the disilane **34** under Krohn conditions to produce the corresponding silanol for further oxidation[20] was not attempted. Such powerful Lewis acid acidic reagents indeed would be inappropriate for the delicate disilane **34**. Since all attempts at oxidizing the disilane entity in the advanced intermediate **34** failed, attention was focused on utilizing a yet more readily oxidizable silane.

Michael Addition of ((Diethylamino)diphenylsilyl)lithium and Diethylzinc to Lactam 3 and Completion of the Total Synthesis of (+)-Pramanicin. The disclosure by Tamao on the synthesis and utility of aminosilyllithium reagents as masked hydroxide anions[21] prompted us to examine these reagents in the synthesis of pramanicin. ((Diethylamino)diphenylsilyl)lithium is readily generated by the direct metalation of the silyl chloride with lithium metal in THF and has been converted into the corresponding Grignard and cuprate reagents.[21] In an extension of this chemistry, we have converted the organolithium reagent into lithium diethyl((diethylamino)diphenylsilyl)zincate for conjugate addition to the unsaturated lactam **3**. Complexation of an aliquot of freshly prepared ((diethylamino)diphenylsilyl)-lithium to diethylzinc and subsequent addition to lactam **3** followed by ethanolysis gave the desired conjugate adduct **36** in good yield (64%) as a single diastereoisomer. Furthermore, this silane **36** could be readily oxidized in near quantitative yield using peracetic acid, hydrogen peroxide, or 3-chloroperoxybenzoic acid as oxidants, with KHF_2 in DMF at ambient temperature to furnish alcohol **35** (Scheme 9).[20] Utilization of lithium diethyl((diethylamino)diphenylsilyl)zincate in our Michael addition/aldol sequence using (4*R*,5*R*)-**18** afforded the *β*-hydroxylactam **37a** (50%), after ethanolysis, as a single diastereoisomer accompanied by a small quantity of the corresponding silanol (10%). Dess−Martin periodinane and $Ni(acac)_2$-catalyzed dimethyldioxirane oxidations proceeded uneventfully to provide the silane **38a** in excellent overall yield (71%). Finally and much to our relief, oxidation of

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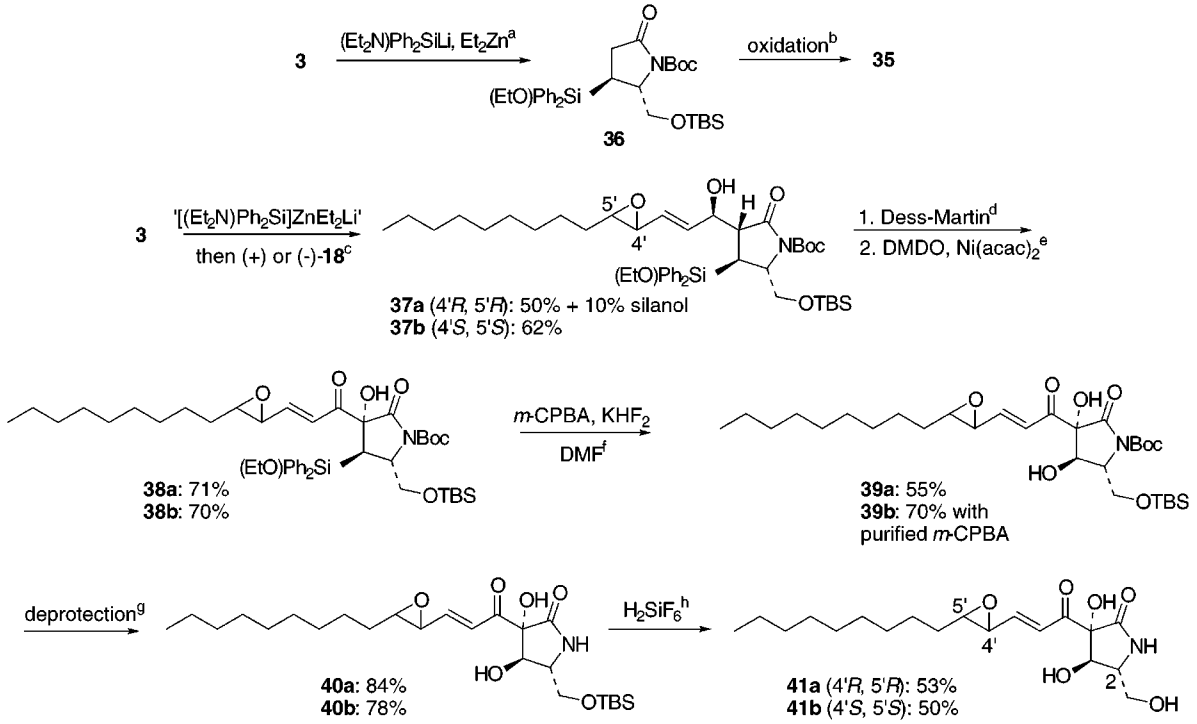
Scheme 9



Reagents and Conditions: (a) $(Et_2N)Ph_2SiLi$, Et_2Zn, THF, -78°C then EtOH/NH_4Cl, (64%); (b) *m*-CPBA or H_2O_2 or AcO_2H, KHF_2, DMF (94%); (c) $(Et_2N)Ph_2SiLi$, Et_2Zn, THF, -78°C followed by (4'*R*,5'*R*)-**18** for **37a** or (4'*S*,5'*S*)-**18** for **37b**, -78°C to 25°C then EtOH/NH_4Cl; (d) Dess-Martin periodinane, CH_2Cl_2, 0°C; (e) dimethyldioxirane, $Ni(acac)_2$, acetone, water, 0°C; (f) *m*-CPBA, KHF_2, DMF, 0°C to 25°C; (g) **39a**: SiO_2, 0.1 mmHg, 40°C, **39b**: TFA, CH_2Cl_2, 0°C to 25°C; (h) H_2SiF_6, MeCN, 0°C to 25°C.

the silane **38a** was achieved using 3-chloroperoxybenzoic acid as the oxidant to give diol **39a**. However, the reaction proceeded in only moderate yield (55%) despite the apparent efficiency of reaction by TLC analysis.

Deprotection of the Boc group in lactam **39a** was accomplished using either the standard conditions of trifluoroacetic acid in dichloromethane or the procedure of Apelqvist, whereby Boc-protected amides can be deprotected using silica gel at low pressure.[22] Initial attempts at deprotection of the *tert*-butyldimethylsilyl ether **40a** using tetrabutylammonium fluoride resulted only in extensive decomposition. However, the use of fluorosilicic[23] acid in this deprotection successfully gave lactam **41a**, albeit in moderate yield (55%). Yet at this point we were thwarted once again. Comparison of the ^1H NMR spectra of lactam **41a** with a sample of authentic (−)-pramanicin revealed very subtle differences in the resonances associated with the epoxide ring system (Figure 3). We were forced to admit we had prepared the wrong diastereoisomer for (−)-pramanicin and that the natural product probably had an epoxide with the 4′*S*,5′*S*-configuration. To test this hypothesis and to hopefully complete the synthesis, we sought to prepare diastereoisomer **41b** using the enantiomeric aldehyde (4*S*,5*S*)-**18**. This was accomplished in a fashion similar to that described for enantiomer (4*R*,5*R*)-**18** but using a more succinct route to the aldehyde, via direct homologation of aldehyde (2*R*,3*S*)-**10** with (formylmethylene)triphenylphosphorane (Scheme 10).[24] Increased yields (70%) for the Fleming−Tamao oxidation of the ethoxydiphenylsilane **39b** were achieved with the use of purified 3-chloroperoxybenzoic acid.[25] The use of alternative oxidants such as hydrogen peroxide or peracetic acid, reagents that proved successful with the model compound **35**, gave complex product mixtures.

Diastereoisomer **41b** was identical by ^1H and ^{13}C NMR with authentic pramanicin (see Figure 3), and while the Merck group[1] established the relative stereochemistry of the γ-lactam ring of the natural product and that the side chain epoxide was *trans*, they did not establish the stereochemistry of the side chain relative to the lactam entity. In their paper, pramanicin was depicted (arbitrarily) as *ent*-**41a**. This work clearly establishes the relative stereochemistry to be as in isomer **41b**. However, the optical rotation of diastereoisomer **41b** ($[\alpha]^{25}_D$ = +28.8°, *c* 0.21 in MeOH) is of sign opposite that reported for authentic pramanicin ($[\alpha]^{25}_D$ = −31.5°, *c* 0.21 in MeOH) and thus indicates the absolute stereochemistry of pramanicin to be that of **1**. After completion of this work, Harrison and co-workers published further findings into the biosynthesis of pramanicin.[26] They have demonstrated, via isotope labeling experiments, the incorporation of L-serine during the biosynthetic pathway and gratifyingly corroborated our synthetic findings by confirming the 2*S*-configuration of the natural product.

Experimental Section

General Procedures. Unless otherwise stated, solvents and amine bases were dried by distillation under N_2 or Ar,

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(25) Schwartz, N. N.; Blumbergs, J. H. *J. Org. Chem.* **1964**, *29*, 1976.
(26) Duspara, P.; Jenkins, S. I.; Hughes, D. W.; Harrison, P. H. M. *J. Chem. Soc., Chem. Commun.* **1998**, 2643.

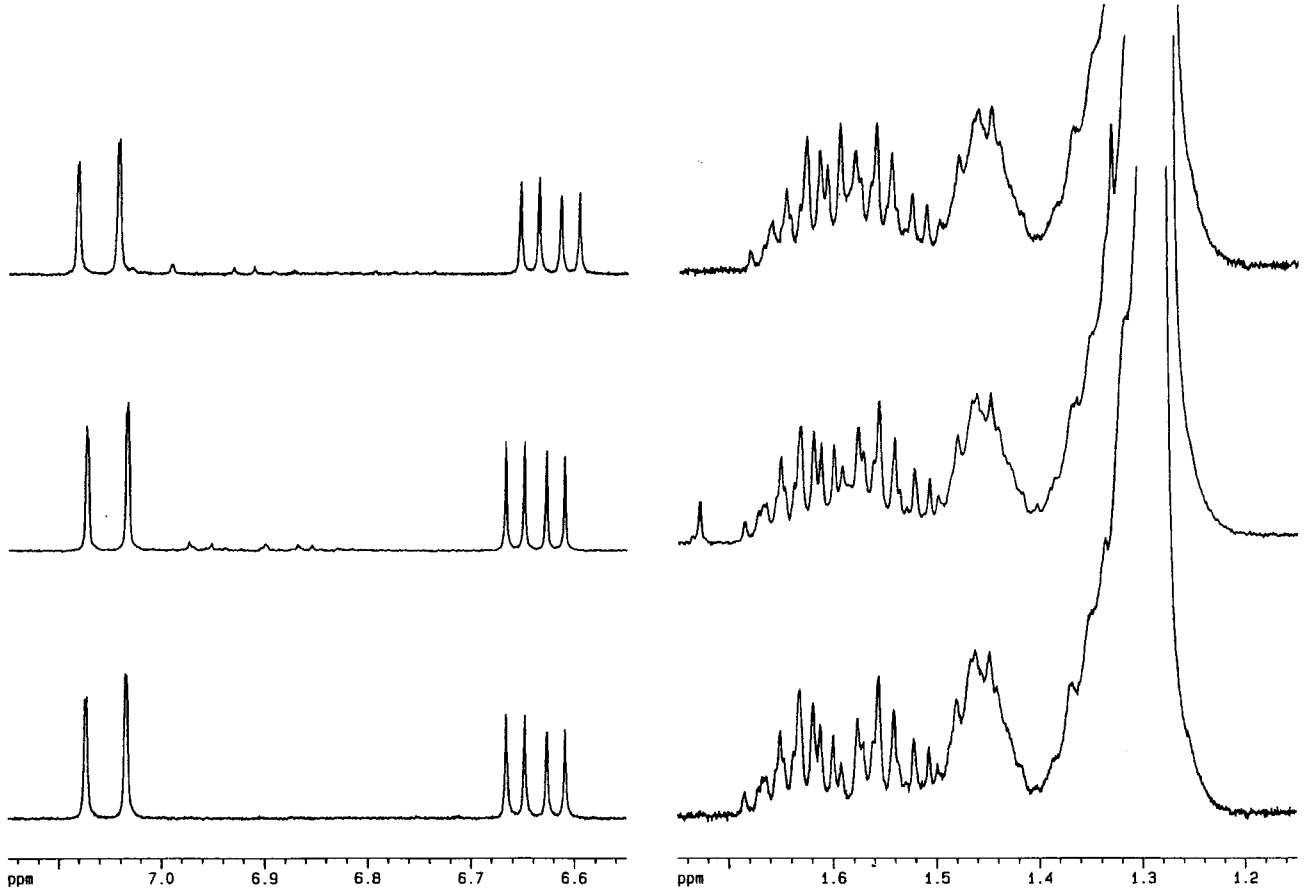
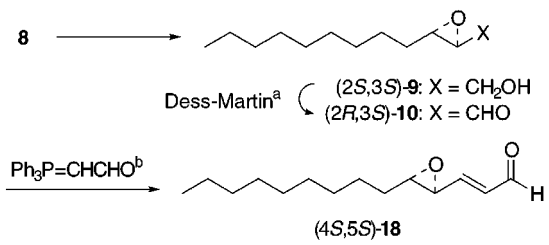


Figure 3. ^{1}H NMR (400 MHz, CD_3OD) correlation spectra of **41a** (top), **41b** (middle), and **1** showing olefinic resonances and protons α to the epoxide ring system.

Scheme 10



Reagents and Conditions: (a) Dess-Martin periodinane, CH_2Cl_2 (97%); (b) Ph_3P=CHCHO, PhMe, reflux (95%).

from Na (PhMe), sodium benzophenone ketyl (Et_2O), potassium benzophenone ketyl (THF), CaH_2 (CH_2Cl_2, DMF, MeCN, Et_3N, pentane, HMPA), and Mg (MeOH, EtOH). All other reagents were used as received from commercial sources. All reactions were performed in oven-dried (160 °C) glassware under N_2 or Ar. Chromatography and chromatographed refers to flash column chromatography on BDH 40−63 μM grade silica gel (eluants are given in parentheses). Analytical thin-layer chromatography (TLC) was performed on precoated glass-backed plates (Merck Kieselgel 60 F_{254}) and visualized with ceric molybdate or potassium permanganate stains.

(+)-Methyl (2*S*)-5-Oxopyrrolidine-2-carboxylate. Using a modification of the procedure reported by Tamm:[3] L-Glutamic acid (25.00 g, 0.194 mol) in H_2O (125 mL) was heated under reflux for 48 h, after which the solvent was evaporated and the residue azeotropically dried with MeOH. The resulting colorless crystalline material was suspended in dry MeOH (100 mL) and freshly distilled $SOCl_2$ added dropwise until complete dissolution occurred (~1 mL). The solution was stirred at room temperature for 48 h when solid $NaHCO_3$ was added until neutral pH was obtained. The solvent was rotary evaporated and the residue azeotropically dried with MeOH at 40 °C. Extraction of the residue with hot CH_2Cl_2 and rotary evaporation yielded (+)-methyl (2*S*)-5-oxopyrrolidine-2-carboxylate (27.70 g, 99%).

(+)-(2*S*)-2-(Hydroxymethyl)-5-pyrrolidinone (5). Using a modification of the reported procedure: [3] $NaBH_4$ (2.20 g, 58.2 mmol) was added to (+)-methyl-(2*S*)-5-oxopyrrolidine-2-carboxylate (5.00 g, 34.9 mmol) in dry EtOH (200 mL) at room temperature. After 3 h, Me_2CO (10 mL) was added, and after a further 30 min, the mixture was acidified using concentrated HCl (4.30 mL, 233 mmol) with cooling, not permitting the pH to fall below 3.5. The solvent was evaporated and the residue chromatographed (EtOAc−MeOH, 4:1) and recrystallized from Me_2CO to give **5** (3.25 g, 81%) as a colorless solid.

(*E*)-Methyl 2-Dodecenoate (7).[27] $(EtO)_2P(O)CH_2CO_2Me$ (8.26 mL, 0.045 mol) was added dropwise to a suspension of NaH (60% dispersion in mineral oil; 1.80 g, 0.045 mol) in THF (100 mL) at 0 °C, and the mixture was allowed to warm to room temperature with stirring for 30 min. The solution was cooled to −78 °C and decanal (**6**) (5.65 mL, 0.030 mol) added. The mixture was allowed to warm to room temperature, after which it was diluted with Et_2O, washed with H_2O, and dried ($MgSO_4$). Filtration, rotary evaporation, and chromatography (hexanes−Et_2O, 95:5) gave **7** (6.32 g, 99%) as a colorless oil: (R_f = 0.43); IR (film) 2927, 2856, 1728, 1659 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (1H, dt, J = 15.6, 7.0 Hz), 5.83 (1H, dt, J = 15.6, 1.5 Hz), 3.74 (3H, s), 2.20 (2H, ddt, J = 8.5, 7.0, 1.5 Hz), 1.45 (2H, m), 1.28 (12H, br s), 0.90 (3H, t, J = 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2, 149.8, 120.8, 51.3, 32.2, 31.9, 29.5, 29.4, 29.3, 29.1, 28.0, 22.7, 14.1; MS(CI) *m/e* $(M + NH_4)^+$ 230, $(M + H)^+$ 213; HRMS(CI) calcd for $C_{13}H_{28}$-

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NO_2 $(M + NH_4)^+$ 230.2120, found $(M + NH_4)^+$ 230.2130. Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.62; H, 11.64.

(*E*)-Dodec-2-en-1-ol (8).[28] DIBAl-H (1 M in hexanes; 32.00 mL, 0.032 mol) was added dropwise to a solution of **7** (2.67 g, 0.0125 mol) in Et_2O at 0 °C. After 2 h the mixture was cooled to −78 °C, quenched with MeOH (5 mL), and allowed to warm to room temperature. After 1 h, the mixture was diluted with CH_2Cl_2, washed with brine, and dried ($MgSO_4$). Chromatography (hexanes−Et_2O, 2:1) yielded **8** (2.13 g, 92%) as a colorless oil: (R_f = 0.39); IR (film) 3338, 2924, 2854, 1670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.66 (2H, m), 4.08 (2H, d, J = 5.0 Hz), 2.04 (2H, m), 1.38 (2H, m), 1.27 (12H, br s), 0.89 (3H, t, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.6, 128.8, 63.8, 32.2, 31.9, 29.6, 29.5, 29.3, 29.20, 29.17, 22.7, 14.1; MS(CI) *m/e* $(M + NH_4)^+$ 202; HRMS(CI) calcd for $C_{12}H_{28}NO$ $(M + NH_4)^+$ 202.2171, found $(M + NH_4)^+$ 202.2164. Anal. Calcd for $C_{12}H_{24}O$: C, 78.20; H, 13.12. Found: C, 78.42; H, 12.91.

2,3-Epoxydodecan-1-ol (9).[29] 3-Chloroperbenzoic acid (50−60%; 1.00 g, 5.79 mmol) was added to a solution of **8** (0.15 g, 1.36 mmol) in CH_2Cl_2 (10 mL). After 1 h at room temperature, the solution was diluted with CH_2Cl_2 and washed with aqueous Na_2CO_3, dried ($MgSO_4$), and rotary evaporated. Chromatography (hexanes−Et_2O, 2:1) gave **9** (261 mg, 96%) as a colorless solid: (R_f = 0.24); IR (DRIFTS) 3141, 2954, 2925, 2850 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.93 (1H, ddd, J = 12.6, 5.3, 2.3 Hz), 3.62 (1H, ddd, J = 12.6, 7.3, 4.6 Hz), 2.95 (2H, m), 1.99 (1H, app. t, J = 6.3 Hz), 1.58 (2H, m), 1.27−1.49 (14H, m), 0.89 (3H, t, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 61.8, 58.6, 56.1, 31.9, 31.6, 29.5, 29.4, 29.3, 25.9, 22.7, 14.1; MS(CI) *m/e* $(M + NH_4)^+$ 218, $(M + H)^+$ 201; HRMS(CI) calcd for $C_{12}H_{28}NO_2$ $(M + NH_4)^+$ 218.2120, found $(M + NH_4)^+$ 218.2131. Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.08. Found: C, 71.77; H, 11.81.

(+)-(2*R*,3*R*)-2,3-Epoxydodecan-1-ol [(2*R*,3*R*)-9)]. To a suspension of crushed 4 Å molecular sieves in CH_2Cl_2 (30 mL) cooled to −25 °C were added redistilled D-(−)-DIPT (0.150 mL; 0.713 mmol) and $Ti(O^iPr)_4$ (0.143 mL, 0.484 mmol) followed by a solution of **8** (1.19 g; 6.46 mmol) in CH_2Cl_2 (5 mL) via cannula. The reaction mixture was allowed to stir for 12 h. After the mixture was cooled to −35 °C, *t*-BuOOH (5−6 M in decane; 2.34 mL) was added dropwise and the reaction mixture slowly warmed to −30 °C. After 15 h at −30 °C, 30% aqueous NaOH saturated with NaCl (0.64 mL) was added followed by dilution with Et_2O (7.9 mL). The mixture was allowed to warm to 10 °C, and after a further 10 min, $MgSO_4$ (0.64 g) and Celite (0.079 g) were added. After further stirring for 30 min, the mixture was filtered through a short pad of Celite washing with Et_2O, and the combined washings were rotary evaporated to yield a colorless solid. Chromatography (hexanes−Et_2O, 2:1) afforded (2*R*,3*R*)-**9** (1.02 g, 86%): R_f = 0.24; $[\alpha]^{25}_D$ = +31.3° (*c* = 1, $CHCl_3$), recrystallized (hexanes) to give (0.76 g, 59%) of epoxide, $[\alpha]^{26}_D$ = +32.3° (*c* = 1, $CHCl_3$); mp 57−59 °C. Spectroscopic data were identical to those reported for racemic **9**.

(−)-(2*S*,3*S*)-2,3-Epoxydodecan-1-ol [(2*S*,3*S*)-9].[30] Prepared as for (2*R*,3*R*)-**9**, $[\alpha]^{25}_D$ = −31.7° (*c* = 1, $CHCl_3$).

2,3-Epoxydodecanal (10). Dess−Martin periodinane (0.225 g, 0.53 mmol) was added to a solution of **9** (0.100 g, 0.50 mmol) in CH_2Cl_2 (15 mL). After 40 min, the mixture was diluted with Et_2O and quenched by the addition of saturated aqueous $NaHCO_3$ (12 mL) and saturated aqueous $Na_2S_2O_3$ (3 mL). After dissolution of the precipitate that was formed, the mixture was washed with aqueous $NaHCO_3$ and H_2O, dried ($MgSO_4$), filtered, and rotary evaporated to yield a colorless solid. Chromatography (hexanes−Et_2O, 9:1) gave **10** (0.92 g, 93%) as a colorless crystalline material: R_f = 0.27; mp 34−35 °C; IR (film) 3033, 2912, 2859, 1739, 1714 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.01 (1H, d, J = 6.3 Hz), 3.23 (1H, ddd, J = 7.3, 5.7, 1.9 Hz), 3.13 (1H, dd, J = 6.3, 1.9 Hz), 1.65 (2H, m), 1.48 (2H, m), 1.28 (12H, br s), 0.89 (3H, t, J = 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.5, 59.2, 56.8, 31.9, 31.2, 29.4, 29.2, 25.8, 22.7, 14.1; MS(CI) *m/e* $(M + NH_4)^+$ 216, $(M + H)^+$ 199; HRMS(CI) calcd for $C_{12}H_{26}NO_2$ $(M + NH_4)^+$ 216.1964, found $(M + NH_4)^+$ 216.1973. Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.66; H, 10.91.

(−)-(2*S*,3*R*)-2,3-Epoxydodecanal [(2*S*,3*R*)-10]. Prepared as for **10** from (2*R*,3*R*)-**9**, $[\alpha]^{25}_D$ = −63.6° (*c* = 1, $CHCl_3$).

(+)-(2*R*,3*S*)-2,3-Epoxydodecanal [(2*R*,3*S*)-10]. Prepared as for **10** from (2*S*,3*S*)-**9**, $[\alpha]^{25}_D$ = +63.4° (*c* = 1, $CHCl_3$).

(*E*)-Methyl 4,5-Epoxy-2-tetradecenoate (2a). $(EtO)_2P(O)CH_2CO_2Me$ (0.56 mL, 3.06 mmol) was added to a suspension of NaH (60% dispersion in mineral oil; 0.122 g, 3.06 mmol) in THF (25 mL) at 0 °C. After 1 h at room temperature, the mixture was cooled to −78 °C when **10** (0.405 g, 2.04 mmol) in THF (5 mL) was added dropwise via cannula. The mixture was maintained at −78 °C for 30 min and allowed to warm to room temperature. After 2 h, the mixture was diluted with Et_2O, washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated to afford a colorless oil. Chromatography (hexanes−Et_2O (95:5) gave **2a** (477 mg, 92%) as a colorless oil: R_f = 0.28; IR (film) 2952, 2925, 2856, 1723, 1657 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.70 (1H, dd, J = 15.7, 7.0 Hz), 6.13 (1H, d, J = 15.7 Hz), 3.76 (3H, s), 3.21 (1H, dd, J = 7.0, 1.9 Hz), 2.89 (1H, ddd, J = 7.5, 5.5, 1.9 Hz), 1.61 (2H, m), 1.46 (2H, m), 1.28 (12H, br s), 0.89 (1H, t, J = 6.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 145.2, 123.0, 61.6, 56.3, 51.7, 31.91, 31.87, 29.5, 29.34, 29.28, 25.8, 22.7, 14.1; MS(CI) *m/e* $(M + NH_4)^+$ 272, $(M + H)^+$ 255; HRMS(CI) calcd for $C_{15}H_{30}NO_3$ $(M + NH_4)^+$ 272.2226, found $(M + NH_4)^+$ 272.2207. Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30; Found: C, 70.79; H, 10.16.

(+)-(4*R*,5*R*)-Methyl 4,5-Epoxy-2-tetradecenoate [(4*R*,5*R*)-2a]. Prepared as for **2a** from (2*S*,3*R*)-**10**, $[\alpha]^{25}_D$ = +13.8° (*c* = 1, $CHCl_3$), mp 30−32 °C.

(*E*)-4,5-Epoxytetradec-2-en-1-ol (17). DIBAl-H (1 M in hexanes; 8.65 mL, 8.65 mmol) was added dropwise to **2a** (1.00 g, 3.93 mmol) in Et_2O (60 mL) at −78 °C. After 70 min, TLC analysis showed the complete consumption of starting material, and the reaction was quenched by the careful addition of saturated aqueous Na_2SO_4 (20 mL). After being stirred for 20 min, the mixture was filtered through a pad of Celite and the organic phase separated, dried ($MgSO_4$), filtered, and evaporated to dryness to afford a colorless solid. This was used immediately without further purification.

(*E*)-(4*R*,5*R*)-4,5-Epoxytetradec-2-en-1-ol [(4*R*,5*R*)-17]. Prepared as for **17** and used directly without further purification due its instability.

(*E*)-4,5-Epoxytetradec-2-enal (18). Dess−Martin periodinane (450 mg, 1.06 mmol) was added to **17** (200 mg, 0.884 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After being warmed to room temperature, the mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (12 mL) and saturated aqueous $Na_2S_2O_3$ (3 mL). After dissolution of the precipitate that formed, the mixture was washed with aqueous $NaHCO_3$, dried ($MgSO_4$), filtered, and rotary evaporated to dryness to yield a colorless solid. Chromatography (hexanes−Et_2O, 4:1) afforded **18** (193 mg, 97%): R_f = 0.38; IR (film) 3019, 2923, 2853, 2728, 1691, 1641 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.57 (1H, d, J = 7.6 Hz), 6.55 (1H, dd, J = 15.6, 6.9 Hz), 6.42 (1H, dd, J = 15.6, 7.6 Hz), 3.33 (1H, dd, J = 6.9, 2.0 Hz), 2.96 (1H, ddd, J = 7.6, 5.6, 2.0 Hz), 1.66 (2H, m), 1.48 (2H, m), 1.28 (12H, br s), 0.89 (3H, t, J = 6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.5, 153.1, 133.5, 62.0, 56.2, 31.9, 29.5, 29.33, 29.28, 25.8, 22.7, 14.1; MS(CI) *m/e* $(M + NH_4)^+$ 242; HRMS(CI) calcd for $C_{14}H_{28}NO_2$ $(M + NH_4)^+$ 242.2120, found $(M + NH_4)^+$ 242.2121. Anal. Calcd for $C_{14}H_{24}O_2$: C, 74.95; H, 10.78; Found: C, 74.72; H, 10.76.

(+)-(*E*)-(4*R*,5*R*)-4,5-Epoxytetradec-2-enal [(4*R*,5*R*)-18]. Prepared as in the synthesis described for **18**, from (4*R*,5*R*)-**17**, $[\alpha]^{25}_D$ = +20.6° (*c* = 1, $CHCl_3$), mp 41−43 °C.

(−)-(*E*)-(4*S*,5*S*)-4,5-Epoxytetradec-2-enal [(4*S*,5*S*)-18]. (2*R*,3*S*)-**10** (450 mg, 2.27 mmol) was added to a stirred suspension of $Ph_3P{=}CHCHO$ (691 mg, 2.27 mmol) in PhMe (15 mL). The suspension was heated to reflux for 12 h and rotary evaporated and the residue extracted with hexane. The

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(29) Lambertus, T.; Waander, P. P.; Stokkingreef, E. H. M.; Zwanenburg, B. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 332.

organic phase was rotary evaporated and chromatographed (hexanes−Et_2O, 6:1) to give (4*S*,5*S*)-**18** (483 mg, 95%), R_f = 0.15. Spectroscopic data were obtained identical to those reported for **18**.

(*E*)-4,5-Epoxy-2-tetradecenoic Acid (2b). To ester **2a** (0.500 g, 1.97 mmol) in THF (20 mL) was added Me_3SiOK (0.31 g, 2.17 mmol). After 3 h, aqueous citric acid (0.5 M; 10 mL) was added, and after a further 2 h, the mixture was washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. The resulting colorless solid was chromatographed (hexanes−Et_2O, 1:2) to give acid **2b** (371 mg, 79%): R_f = 0.49; mp 86−88 °C; IR (DRIFTS) 3500−3000, 2927, 2852, 1693, 1660 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.82 (1H, dd, J = 15.5, 6.9 Hz), 6.13 (1H, d, J = 15.5 Hz), 3.25 (1H, dd, J = 6.9, 1.7 Hz), 2.91 (1H, ddd, J = 7.3, 5.6, 1.7 Hz), 1.63 (2H, m), 1.47 (2H, m), 1.28 (12H, br s), 0.90 (3H, t, J = 6.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 147.7, 122.5, 61.8, 56.1, 31.91, 31.88, 29.5, 29.34, 29.29, 25.8, 22.7, 14.1; MS(CI) *m/e* $(M + NH_4)^+$ 258; HRMS(CI) calcd for $C_{14}H_{28}NO_3$ $(M + NH_4)^+$ 258.2069, found $(M + NH_4)^+$ 258.2067. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07; Found: C, 69.91; H, 10.04.

(*E*)-4,5-Epoxy-2-tetradecenoyl Chloride (2c). To a suspension of **2b** (100 mg, 0.416 mmol) in THF (5 mL) at −78 °C was added *n*-BuLi in hexanes (2.3 M; 180 μL, 0.416 mmol). The solution was allowed to warm to 0 °C and cooled to −78 °C, after which freshly distilled $(COCl)_2$ (36.3 μL, 0.416 mmol) was added. The acid chloride **2c** was used directly but was quantified by the addition of Et_3N (200 μL) and MeOH (500 μL) followed by aqueous workup, yielding ester **2a** (63 mg, 60%) and starting acid **2b**.

(Dimethylphenylsilyl)lithium. Following the original procedure by Gilman:[31] Li metal (1.00 g, 0.144 mol) was added to $PhMe_2SiCl$ (4.92 mL, 0.0293 mol) in THF (50 mL). After being stirred for 5 h, the claret solution was transferred via filter cannula to a storage bottle. The solution was analyzed using the double titration method described by Whitesides et al.[32] as follows: H_2O (10 mL) was added to the silyllithium reagent (1 mL) and the mixture titrated using 0.1 M HCl (3.85 mL) with phenolphthalein as indicator. To determine the excess base content, the silyllithium reagent (1 mL) was added to dibromoethane (2 mL) followed by H_2O (10 mL) and the resultant aqueous layer titrated using 0.1 M HCl (0.58 mL) using phenolphthalein as indicator. These titrations showed the (dimethylphenylsilyl)lithium solution in THF to be 0.33 M.

(−)-*tert*-Butyl (2*R*,3*S*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3-(dimethylphenylsilyl)-5-oxopyrrolidine-1-carboxylate (11). (Dimethylphenylsilyl)lithium in THF (0.438 M; 1.80 mL, 0.788 mmol) was added to an ice-cooled solution of Et_2Zn in hexanes (1 M; 0.780 mL, 0.780 mmol) in THF (10 mL). After 5 min, the mixture was cooled to −78 °C, and **3** (0.05 g, 0.152 mmol) in THF (2 mL) was added via cannula when the solution instantly changed color from red to yellow. After 5 min, saturated aqueous $NaHCO_3$ (10 mL) was added and the mixture allowed to warm to room temperature. The solution was diluted with Et_2O, washed with H_2O, dried ($MgSO_4$), filtered, and evaporated to dryness. Chromatography (hexanes−Et_2O, 6:1) gave **11** (336 mg, 95%) as a colorless solid: R_f = 0.16; $[\alpha]^{25}_D$ = −31.7° (c = 1, $CHCl_3$); mp 57−59 °C; IR (film) 3071, 3050, 2955, 2930, 2858, 1790, 1752, 1712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (2H, m), 7.36 (3H, m), 4.04 (1H, ddd, J = 4.4, 2.4, 2.2 Hz), 3.83 (1H, dd, J = 10.2, 4.4 Hz), 3.50 (1H, dd, J = 10.2, 2.4 Hz), 2.88 (1H, dd, J = 18.0, 11.4 Hz), 2.30 (1H, dd, J = 18.0, 3.0 Hz), 1.70 (1H, ddd, J = 11.4, 3.0, 2.4, Hz), 1.48 (9H, s), 0.86 (9H, s), 0.32 (3H, s), 0.31 (3H, s), 0.01 (3H, s), 0.00 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.4, 150.0, 135.8, 133.7, 129.7, 128.1, 82.6, 64.7, 60.4, 34.0, 28.1, 25.9, 18.9, 18.2, −5.3, −5.4, −5.5; MS(CI) *m/e* 464 $(M + H)^+$; HRMS(CI) calcd for $C_{24}H_{42}NO_4Si_2$ $(M + H)^+$ 464.2652, found $(M + H)^+$ 464.2641. Anal. Calcd for $C_{24}H_{41}NO_4Si_2$: C, 62.16; H, 8.91; N, 3.02. Found: C, 62.15; H, 8.87; N, 2.87.

(+)-*tert*-Butyl (2*R*,3*S*)-2-(Hydroxymethyl)-3-(dimethylphenylsilyl)-5-oxopyrrolidine-1-carboxylate (12). Bu_4NF in THF−H_2O (5:1) (1 M; 140 μL, 0.140 mmol) was added to **11** (59 mg, 0.127 mmol) in THF (2 mL) at 0 °C. After 10 min, rotary evaporation and chromatography (hexanes−Et_2O, 1:9) gave **12** (37 mg, 85%) as a colorless oil: R_f = 0.20; $[\alpha]^{25}_D$ = +52.4° (c = 1, $CHCl_3$); IR (film) 3216, 3071, 2979, 2956, 2903, 1741, 1700 cm^{-1}; ^1H (400 MHz, $CDCl_3$) δ 7.49 (2H, m), 7.37 (3H, m), 5.76 (1H, br s), 3.94 (1H, d, J = 8.5 Hz), 3.71−3.80 (2H, m), 2.47 (1H, dd, J = 17.3, 6.8 Hz), 2.24 (1H, dd, J = 17.3, 8.9 Hz), 1.52 (1H, m), 1.47 (9H, s), 0.37 (3H, s), 0.36 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 153.1, 135.6, 133.8, 129.9, 128.2, 82.8, 70.2, 54.7, 31.7, 30.3, 27.7, 22.6, −4.7, −5.1; MS(CI) *m/e* 367 $(M + NH_4)^+$, 350 $(M + H)^+$; HRMS(CI) calcd for $C_{18}H_{28}NO_4Si$ $(M + H)^+$ 350.1788, found $(M + H)^+$ 350.1783. Anal. Calcd for $C_{18}H_{27}NO_4Si$: C, 61.86; H, 7.79; N, 4.01. Found: C, 61.79; H, 7.51; N, 3.85.

(+)-(2*R*,3*S*)-3-(Dimethylphenylsilyl)-2-(hydroxymethyl)-5-pyrrolidinone (13). A solution of **12** (55 mg, 0.157 mmol) in $CHCl_3$ (5 mL) was added to silica gel (40−63 μm mesh; 300 mg), and the slurry was dried in vacuo and heated under high vacuum (~0.1 mmHg) at 50 °C for 12 h. After cooling, the solid was extracted with EtOAc and the extracts evaporated to give **13** (35 mg, 90%) as a colorless solid which was recrystallized from Et_2O to furnish colorless crystals suitable for X-ray analysis: R_f = 0.39 (EtOAc−MeOH, 95:5); $[\alpha]^{25}_D$ = +52.6° (c = 1, $CHCl_3$); mp 79−80 °C; IR (film) 3324, 2954, 2904, 2864, 1965, 1888, 1674, 1643 cm^{-1}; ^1H NMR 400 (MHz, $CDCl_3$) δ 7.47 (2H, m), 7.35 (3H, m), 7.17 (1H, br s), 3.64 (1H, m), 3.44 (1H, dd, J = 11.4, 2.7 Hz), 3.35 (1H, br s), 3.25 (1H, dd, J = 11.4, 7.3 Hz), 2.43 (1H, dd, J = 17.4, 10.7 Hz), 2.22 (1H, dd, J = 17.4, 9.2 Hz), 1.50 (1H, m), 0.33 (3H, s), 0.32 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 136.0, 133.8, 129.7, 128.1, 66.5, 58.5, 32.6, 22.0, −4.7, −5.1; MS(CI) *m/e* 267 $(M + NH_4)^+$, 250 $(M + H)^+$; HRMS(CI) calcd for $C_{13}H_{20}NO_2Si$ $(M + H)^+$ 250.1263, found $(M + H)^+$ 250.1263. Anal. Calcd for $C_{13}H_{19}NO_2Si$: C, 62.61; H, 7.68; N, 5.62. Found: C, 62.41; H, 7.83; N, 5.68. Crystal data for **13**: $C_{13}H_{19}NO_2Si$, M = 249.4, triclinic, $P1$ (no. 1), a = 6.685(3) Å, b = 6.704(3) Å, c = 33.510(6) Å, α = 93.97(2)°, β = 90.82(2)°, γ = 111.01(4)°, V = 1397.3(9) $Å^3$, Z = 4 (there are four crystallographically independent molecules in the asymmetric unit), D_c = 1.185 g cm^{-3}, μ(Cu Kα) = 14.1 cm^{-1}, F(000) = 536, T = 293 K; clear plates, 0.30 × 0.15 × 0.03 mm, Siemens P4/RA diffractometer, ω-scans, 4858 independent reflections, F^2 refinement, R_1 = 0.095, wR_2 = 0.225, 3471 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 124°$], and 566 parameters. The absolute structure was determined by use of the Flack parameter [x^+ = 0.11(10), x^- = 0.89(10)]. CCDC 132032.

(−)-*tert*-Butyl (2*R*,3*S*)-5-Acetoxy-4-acetyl-2-[(*t*-butyldimethylsiloxy)methyl]-3-(dimethylphenylsilyl)-2,3-pyrroline-1-carboxylate (14) and (−)-*tert*-Butyl (2*R*,3*S*)-4-(1-Acetoxyethylidene)-2-[(*t*-butyldimethylsiloxy)methyl]-3-(dimethylphenylsilyl)-5-oxopyrrolidine-1-carboxylate (15). $PhMe_2SiLi$ in THF (0.484M; 0.94 mL, 0.458 mmol) was added with stirring to ice-cooled Et_2Zn in hexanes (1 M; 0.46 mL, 0.460 mmol) in THF (3 mL) under Ar. After 10 min, the solution was cooled to −78 °C when **3** (150 mg, 0.458 mmol) in THF (2 mL) was added via cannula. After a further 5 min at −78 °C, freshly distilled AcCl (0.13 mL; 1.83 mmol) in HMPA (0.6 mL) was added via cannula, washing in the residue with THF (1 mL). The mixture was allowed to warm to room temperature, diluted with Et_2O, washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (hexanes−Et_2O, 6:1) gave **14** and **15** (249 mg, 99%) in a 4:1 ratio, respectively. Data for **14**: R_f = 0.18; $[\alpha]^{25}_D$ = −113.2° (c = 1, $CHCl_3$); IR (film) 3071, 2955, 2930, 2857, 1780, 1764, 1739, 1714, 1677 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (2H, m), 7.36 (3H, m), 3.98 (1H, dd, J = 7.3, 3.2 Hz), 3.62 (1H, dd, J = 9.3, 3.2 Hz), 3.40 (1H, dd, J = 9.3, 7.3 Hz), 2.56 (1H, s), 2.39 (3H, s), 2.05 (3H, s), 1.46 (9H, s), 0.86 (9H, s), 0.36 (3H, s),

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0.33 (3H, s), 0.01 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 166.4, 153.4, 150.2, 135.9, 133.7, 129.6, 128.0, 121.1, 82.6, 64.3, 57.5, 28.7, 28.1, 25.8, 21.0, 18.2, 16.8, −4.4, −4.7, −5.5, −5.7; MS(CI) *m/e* 548 $(M + H)^+$; HRMS(CI) calcd for $C_{28}H_{46}NO_6Si_2$ $(M + H)^+$ 548.2864, found $(M + H)^+$ 548.2875. Data for **15**: R_f = 0.13; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (2H, m), 7.37 (3H, m), 3.96 (1H, dd, J = 7.5, 3.3 Hz), 3.66 (1H, dd, J = 9.6, 3.3 Hz), 3.40 (1H, dd, J = 9.6, 7.5 Hz), 2.50 (1H, s), 2.25 (3H, s), 1.68 (3H, s), 1.45 (9H, s), 0.88 (9H, s), 0.41 (3H, s), 0.40 (3H, s), 0.02 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 164.0, 149.8, 149.4, 135.2, 134.0, 129.7, 128.0, 119.8, 82.5, 64.1, 57.4, 28.2, 28.0, 25.8, 20.9, 19.8, 18.1, −4.7, −4.9, −5.4, −5.6; MS-(CI) *m/e* 548 $(M + H)^+$; HRMS(CI) calcd for $C_{28}H_{46}NO_6Si_2$ $(M + H)^+$ 548.2864, found $(M + H)^+$ 548.2879.

(+)-*tert*-Butyl (2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-3-(dimethylphenylsilyl)-4-[(*E*)-(4*R*,5*R*)-epoxytetradec-(1*R*)-hydroxy-2-enyl]-5-oxopyrrolidine-1-carboxylate (19) and (−)-*tert*-butyl (2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy) methyl]-3-(dimethylphenylsilyl)-4-[(*E*)-(4*S*,5*S*)-epoxytetradec-(1*R*)-hydroxy-2-enyl]-5-oxopyrrolidine-1-carboxylate (20). $PhMe_2SiLi$ in THF (0.451 M; 0.686 mL, 0.310 mmol) was added to Et_2Zn in hexanes (1 M; 0.310 mL, 0.310 mmol) in THF (4 mL) at 0 °C. After 5 min, the solution was cooled to −78 °C when **3** (100 mg, 0.305 mmol) in THF (4 mL) was added via cannula. After a further 5 min, **18** (70.6 mg, 0.315 mmol) in THF (4 mL) was added via cannula and the mixture allowed to warm to room temperature over 30 min. The mixture was quenched by the addition of saturated aqueous $NaHCO_3$ (5 mL) followed by H_2O (5 mL). The solution was diluted with Et_2O, and the organic phase was washed with H_2O, dried ($MgSO_4$), and filtered. Rotary evaporation and chromatography (hexane−Et_2O, 3:1) gave **19** and **20** (179 mg, 85%) as a separable 1:1 mixture of diastereoisomers. Data for **19**: R_f = 0.11; $[\alpha]^{25}_D$ = +9.5° (c = 1, $CHCl_3$); IR (film) 3444, 3070, 2957, 2928, 2856, 1779, 1723 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (2H, m), 7.39 (3H, m), 5.50 (1H, dd, J = 15.5, 6.9 Hz), 5.45 (1H, dd, J = 15.5, 6.9 Hz), 4.32 (1H, app. t, J = 8.3 Hz), 4.29 (1H, s), 4.00 (1H, m), 3.83 (1H, dd, J = 10.2, 4.3 Hz), 3.41 (1H, dd, J = 10.2, 2.3 Hz), 2.98 (1H, dd, J = 6.9, 2.0 Hz), 2.81 (1H, ddd, J = 7.6, 5.6, 2.0 Hz), 2.41 (1H, dd, J = 8.6, 4.6 Hz), 1.57 (2H, m), 1.49 (9H, s), 1.40 (1H, dd, J = 4.6, 3.0 Hz), 1.28−1.43 (14H, m), 0.88 (12H, m), 0.35 (3H, s), 0.34 (3H, s), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 149.6, 135.2, 134.1, 133.8, 129.9, 128.2, 83.5, 77.2, 74.0, 65.0, 60.5, 59.4, 57.6, 49.7, 32.1, 31.9, 29.6, 29.52, 29.49, 29.3, 28.0, 26.0, 22.7, 21.1, 18.5, 14.1, −5.1, −5.4; MS(CI) *m/e* 688 $(M + H)^+$; HRMS(CI) calcd for $C_{38}H_{66}NO_6Si_2$ $(M + H)^+$ 688.4429, found $(M + NH_4)^+$ 688.4447. Anal. Calcd for $C_{38}H_{65}NO_6Si_2$: C, 66.33; H, 9.52; N, 2.04. Found: C, 66.45; H, 9.56; N, 2.03. Data for **20**: R_f = 0.21; $[\alpha]^{25}_D$ = −24.1° (c = 1, $CHCl_3$); IR (film) 3473, 3070, 3050, 2955, 2928, 2857, 1779, 1723 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (2H, m), 7.35 (3H, m), 5.34 (2H, m), 4.37 (1H, s), 4.32 (1H, ddd, J = 8.8, 4.7, 2.4 Hz), 3.99 (1H, m), 3.88 (1H, dd, J = 10.4, 3.7 Hz), 3.34 (1H, dd, J = 10.4, 1.9 Hz), 2.89 (1H, m), 2.78 (1H, ddd, J = 7.6, 5.5, 2.1 Hz), 2.38 (1H, dd, J = 9.0, 4.7 Hz), 1.56 (2H, m), 1.48 (9H, s), 1.41 (2H, m), 1.34 (1H, dd, J = 4.7, 3.0 Hz), 1.25 (12H, br s), 0.87 (3H, t, J = 6.7 Hz), 0.85 (9H, s), 0.33 (3H, s), 0.32 (3H, s), 0.02 (3H, s), 0.01 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.5, 149.5, 135.1, 134.8, 134.0, 131.8, 129.8, 128.2, 83.5, 74.1, 64.9, 60.3, 59.5, 57.9, 49.2, 32.0, 31.9, 29.51, 29.47, 29.4, 29.3, 28.0, 26.0, 25.8, 22.7, 21.1, 18.5, 14.1, −5.4, −5.6; MS(CI) *m/e* 688 $(M + H)^+$; HRMS(CI) calcd for $C_{38}H_{66}NO_6Si_2$ $(M + H)^+$ 688.4429, found $(M + H)^+$ 688.4441. Anal. Calcd for $C_{38}H_{65}NO_6Si_2$: C, 66.33; H, 9.52; N, 2.04. Found: C, 66.05; H, 9.29; N, 1.96.

(*E*)-*tert*-Butyl (2*R*,3*S*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-3-(dimethylphenylsilyl)-4-[(*E*)-(4*R*,5*R*)-epoxy-1-hydroxytetradec-2-enylidene]-5-oxopyrrolidine-1-carboxylate (21). Dess−Martin periodinane (55 mg, 0.130 mmol) was added to **20** (80.0 mg, 0.116 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The mixture was allowed to warm to room temperature when saturated aqueous $NaHCO_3$ (3 mL) and saturated aqueous $Na_2S_2O_3$ (3 mL) were added. After dissolution of the emulsion formed, the organic phase was separated and the aqueous layer extracted with CH_2Cl_2. The combined organic phase was dried ($MgSO_4$), filtered, and rotary evaporated to yield **21** as a viscous pale yellow oil which was not purified due to its instability toward chromatographic supports.

(+)-*tert*-Butyl (2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-3-(dimethylphenylsilyl)-4-[(*E*)-(4*R*,5*R*)-epoxy-1-oxo-tetradec-2-en-1-yl]-4-hydroxy-5-oxopyrrolidine-1-carboxylate (22). $Ni(acac)_2$ (1.4 mg, 5.4 μmol) in H_2O (0.5 mL) and freshly prepared dimethyldioxirane in Me_2CO (0.1 M; 1 mL) were added to crude **21** (30.0 mg, 43.7 μmol) in Me_2-CO (1 mL) at 10 °C. Further additions of dimethyldioxirane in Me_2CO (0.1 M; 2 × 0.5 mL) were made at 1 h intervals until TLC analysis indicated complete reaction after 3 h. After rotary evaporation, the residue was dissolved in CH_2Cl_2, washed with H_2O, and dried ($MgSO_4$). Rotary evaporation and chromatography (hexanes−Et_2O, 6:1) gave **22** (24.5 mg 80%) as a colorless oil: R_f = 0.14; $[\alpha]^{25}_D$ = +25.3° (c = 1, $CHCl_3$); IR (film) 3444, 3070, 3049, 2954, 2927, 2856, 1786, 1726, 1687, 1624 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (2H, m), 7.32 (3H, m), 6.91 (1H, d, J = 15.6 Hz), 6.49 (1H, dd, J = 15.6, 7.5 Hz), 4.51 (1H, s), 4.19 (1H, app dt, J = 6.5, 1.0 Hz), 4.14 (1H, dd, J = 11.0, 2.2 Hz), 3.14 (1H, dd, J = 7.5, 1.8 Hz), 3.13 (1H, dd, J = 11.0, 0.9 Hz), 2.82 (1H, ddd, J = 7.4, 5.8, 1.8 Hz), 2.01 (1H, d, J = 6.5 Hz), 1.52−1.65 (2H, m), 1.50 (9H, s), 1.31−1.48 (2H, m), 1.27 (12H, br s), 0.88 (3H, t, J = 6.6 Hz), 0.83 (9H, s), 0.41 (3H, s), 0.31 (3H, s), −0.03 (3H, s), −0.07 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.7, 171.8, 149.7, 145.8, 137.3, 134.0, 129.4, 127.9, 125.5, 125.2, 85.3, 83.7, 61.7, 61.6, 59.1, 56.9, 34.0, 31.9, 31.8, 30.3, 29.5, 29.34, 29.26, 28.0, 25.8, 22.7, 18.2, 14.1, −2.8, −3.7, −5.69, −5.73; MS(EI) *m/e* 701 $(M^{\bullet+})$; HRMS(EI) calcd for $C_{38}H_{63}NO_7Si_2$ $(M^{\bullet+})$ 701.4143, found $(M^{\bullet+})$ 701.4147. Anal. Calcd for $C_{38}H_{63}NO_7Si_2$:,C, 65.01; H, 9.04; N, 2.00. Found: C, 65.01; H, 9.17; N, 2.06.

(−)-*tert*-Butyl (2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-3-(dimethylphenylsilyl)-4-((1*R*)-hydroxyethyl)-5-oxopyrrolidine-1-carboxylate (24). $PhMe_2SiLi$ (0.484 M in THF; 0.95 mL, 0.460 mmol) was added to ice-cooled Et_2Zn in hexanes (1 M; 0.46 mL, 0.460 mmol) in THF (3 mL). After 5 min, the ruby-colored solution was cooled to −78 °C when **3** (150 mg, 0.458 mmol) in THF (3 mL) was added via cannula. After a further 5 min, precooled (0 °C) CH_3CHO (26 μL, 0.465 mmol) in THF (2 mL) was added via cannula. The mixture was allowed to warm to room temperature, when saturated aqueous $NaHCO_3$ (5 mL) was added. The solution was diluted with Et_2O, washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. The resultant oil was chromatographed (hexanes−Et_2O, 3:1) to afford **24** (172 mg, 74%) as a colorless oil: R_f = 0.18; $[\alpha]^{25}_D$ = −14.7° (c = 1, $CHCl_3$); IR (film) 3492, 3070, 3050, 2956, 2930, 2858, 1779, 1721 cm^{-1}; ^{1}H NMR 300 MHz ($CDCl_3$) δ 7.50 (2H, m), 7.37 (3H, m), 4.13 (1H, br s), 4.02 (1H, m), 3.98 (1H, dq, J = 8.6, 6.3), 3.79 (1H, dd, J = 10.2, 4.6 Hz), 3.42 (1H, dd, J = 10.2, 2.3 Hz), 2.31 (1H, dd, J = 8.6, 4.6 Hz), 1.50 (9H, s), 1.39 (1H, dd, J = 4.3, 3.0 Hz), 1.04 (3H, d, J = 6.3 Hz), 0.88 (9H, s), 0.38 (3H, s), 0.37 (3H, s), 0.04 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.7, 149.7, 135.2, 133.8, 129.9, 128.2, 83.3, 76.7, 69.5, 64.9, 59.3, 51.1, 28.0, 26.0, 21.4, 20.9, 18.5, −5.2, −5.5; MS(CI) *m/e* 508 $(M + H)^+$; HRMS-(CI) calcd for $C_{26}H_{46}NO_5Si_2$ $(M + H)^+$ 508.2915, found $(M + H)^+$ 508.2924.

(+)-(2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3-(dimethylphenylsilyl)-4-((1*R*)-hydroxyethyl)-5-pyrrolidinone (25). TFA (0.20 mL) was added to **24** (96 mg, 0.189 mmol) in CH_2Cl_2 (3 mL), and after 2 h, saturated aqueous $NaHCO_3$ (3 mL) was added and the mixture diluted with CH_2-Cl_2. The organic layer was washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. The resulting oil was chromatographed (hexanes−Et_2O, 1:2) to yield **25** (63 mg, 84%) as a colorless oil: R_f = 0.26; $[\alpha]^{25}_D$ = +28.3° (c = 1, $CHCl_3$); IR (film) 3444, 3233, 2955, 2929, 2885, 2857, 1687 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 7.51 (2H, m), 7.39 (3H, m), 6.22 (1H, br s), 3.73 (1H, dq, J = 8.3, 6.3), 3.50 (1H, m), 3.29 (1H, dd, J = 9.9, 4.0 Hz), 3.21 (1H, dd, J = 9.9, 8.3 Hz), 2.26 (1H, dd, J = 8.3, 6.0 Hz), 1.10 (1H, m), 1.06 (3H, d, J = 6.3 Hz), 0.85 (9H, s), 0.40 (3H, s), 0.39 (3H, s), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.2, 135.7, 133.9, 129.9, 128.2, 70.5, 68.4,

56.5, 48.7, 25.9, 24.2, 21.1, 18.3, −4.6, −5.5, −5.6; MS(CI) *m/e* 408 $(M + H)^+$; HRMS(CI) calcd for $C_{21}H_{38}NO_3Si_2$ $(M + H)^+$ 408.2390, found $(M + H)^+$ 408.2402. Anal. Calcd for $C_{21}H_{37}NO_3Si_2$: C, 61.87; H, 9.15; N, 3.44. Found: C, 61.80; H, 9.20; N, 3.29.

(+)-(2*R*,3*S*,4*R*)-3-(Dimethylphenylsilyl)-2-(hydroxymethyl)-4-((1*R*)-hydroxyethyl)-5-pyrrolidinone (26). Bu_4NF in THF/H_2O (1 M; 0.08 mL, 80 μmol) was added to **25** (31.1 mg, 76.3 μmol) in THF (2 mL) at 0 °C and the mixture allowed to warm to room temperature. After 1.5 h, the mixture was diluted with EtOAc, washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. The resulting solid was chromatographed (EtOAc) to give **26** (20.0 mg, 91%) as a colorless solid (R_f = 0.28); this was recrystallized from Et_2O to produce crystals for X-ray analysis: mp 108−109.5 °C; $[\alpha]^{25}_D$ = +4.6° (*c* = 0.28, $CHCl_3$); IR (film) 3322, 3070, 2956, 2930, 2894, 1957, 1854, 1820, 1682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (2H, m), 7.38 (3H, m), 7.31 (1H, br s), 5.19 (1H, br s), 4.35 (1H, br s), 3.67 (1H, dq, *J* = 6.4, 3.8 Hz), 3.55−3.60 (2H, m′s), 3.20 (1H, dd, *J* = 12.2, 3.5 Hz), 2.29 (1H, dd, *J* = 5.7, 3.8 Hz), 1.39 (1H, dd, *J* = 5.7, 4.6 Hz), 1.27 (3H, d, *J* = 6.4 Hz), 0.34 (3H, s), 0.33 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.6, 135.6, 133.8, 129.8, 128.2, 72.0, 64.9, 56.2, 49.3, 25.8, 20.9, −5.3, −5.7; MS(CI) *m/e* 294 $(M + H)^+$; HRMS(CI) calcd for $C_{15}H_{24}NO_3Si$ $(M + H)^+$ 294.1525, found $(M + H)^+$ 294.1522. Anal. Calcd for $C_{15}H_{23}NO_3Si$: C, 61.40; H, 7.90; N, 4.77. Found: C, 61.57; H, 8.12; N, 4.61. Crystal data for **26**: $C_{15}H_{23}NO_3Si$, *M* = 293.4, monoclinic, *C*2 (no. 5), *a* = 12.768(1) Å, *b* = 7.829(1) Å, *c* = 16.750(1) Å, β = 96.72(1)°, *V* = 1662.8(2) $Å^3$, *Z* = 4, D_c = 1.172 g cm^{-3}, μ(Cu Kα) = 13.0 cm^{-1}, *F*(000) = 632, *T* = 293 K; clear platy needles, 0.30 × 0.13 × 0.03 mm, Siemens P4/PC diffractometer, ω-scans, 1501 independent reflections, F^2 refinement, R_1 = 0.046, wR_2 = 0.117, 1314 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 128°$], and 182 parameters. The absolute structure was unambiguously determined by a combination of *R*-factor tests [$R_1^+ = 0.0461$, $R_1^- = 0.0466$] and by use of the Flack parameter [$x^+ = 0.01(15)$, $x^- = 0.99(15)$]. CCDC 132033.

***tert*-Butyl (2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3-(dimethylphenylsilyl)-4-[(*E*)-(1*R*)-hydroxybut-2-en-1-yl]-5-oxopyrrolidine-1-carboxylate (27).** $PhMe_2SiLi$ in THF (0.484 M; 0.95 mL, 0.460 mmol) was added to ice-cooled Et_2Zn in hexanes (1 M; 0.46 mL, 0.460 mmol) in THF (3 mL). After 5 min, the ruby-colored solution was cooled to −78 °C when **3** (150 mg, 0.458 mmol) in THF (3 mL) was added via cannula. Following a further 5 min, precooled (0 °C) $CH_3CH{=}CHCHO$ (42 μL, 0.465 mmol) in THF (2 mL) was added via cannula. The mixture was allowed to warm to room temperature when saturated aqueous $NaHCO_3$ (5 mL) was added. The solution was diluted with Et_2O, washed with H_2O, dried ($MgSO_4$), filtered, and evaporated to dryness. The resultant oil was chromatographed (hexanes−Et_2O, 3:1) to afford **27** with an inseparable unidentified aldehyde contaminant: R_f = 0.21; ^1H NMR (300 MHz $CDCl_3$) δ 7.47 (2H, m), 7.39 (3H, m), 5.67 (1H, dq, *J* = 15.2, 6.6 Hz), 5.01 (1H, ddq, *J* = 15.2, 8.3, 1.3 Hz), 4.24 (1H, app t, *J* = 8.6 Hz), 4.23 (1H, s), 4.00 (1H, m), 3.80 (1H, dd, *J* = 9.9, 4.6 Hz), 3.44 (1H, dd, *J* = 9.9, 2.3 Hz), 2.40 (1H, dd, *J* = 8.9, 4.6 Hz), 1.65 (3H, dd, *J* = 6.6, 1.3 Hz), 1.51 (9H, s), 1.41 (1H, dd, *J* = 4.6, 3.0 Hz), 0.90 (9H, s), 0.34 (3H, s), 0.33 (3H, s), 0.06 (3H, s), 0.05 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 149.7, 135.4, 133.9, 131.4, 129.8, 129.6, 128.1, 83.4, 76.6, 65.0, 59.4, 49.6, 28.0, 26.0, 21.2, 18.5, 17.7, −5.2, −5.4; MS(CI) *m/e* 534 $(M + H)^+$; HRMS(CI) calcd for $C_{28}H_{48}NO_5Si_2$ $(M + H)^+$ 534.3071, found $(M + H)^+$ 534.3087.

(+)-(2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3-(dimethylphenylsilyl)-4-[(*E*)-(1*R*)-hydroxybut-2-en-1-yl]-5-pyrrolidinone (28). TFA (0.2 mL) was added to **27** (126 mg, 0.236 mmol) in CH_2Cl_2 (7 mL). After 2 h at room temperature, saturated aqueous $NaHCO_3$ (5 mL) was added and the mixture diluted with CH_2Cl_2. The separated organic phase was dried ($MgSO_4$), filtered, and evaporated to dryness. Chromatography (hexanes−Et_2O, 1:2) gave **28** (54.6 mg, 53%) as a colorless solid: R_f = 0.21; mp 84−86 °C; $[\alpha]^{25}_D$ = +52.9° (*c* = 1, $CHCl_3$); IR (film) 3439, 3212, 3070, 2955, 2929, 2897, 2857, 1686 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (2H, m), 7.40 (3H, m), 6.47 (1H, br s), 5.66 (1H, dq, *J* = 15.2, 6.6 Hz), 5.11 (1H, ddq, *J* = 15.2, 7.9, 1.3 Hz), 3.99 (1H, app. t, *J* = 8.6 Hz), 3.50 (1H, m), 3.28 (1H, dd, *J* = 9.9, 4.0 Hz), 3.21 (1H, dd, *J* = 9.9, 7.9 Hz), 2.35 (1H, dd, *J* = 8.6, 6.0 Hz), 1.65 (3H, dd, *J* = 6.6, 1.3 Hz), 1.09 (1H, app. t, *J* = 5.6 Hz), 0.86 (9H, s), 0.36 (3H, s), 0.34 (3H, s), −0.01 (3H, s), −0.02 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.2, 135.9, 133.9, 131.4, 129.7, 129.3, 128.2, 76.4, 68.3, 56.6, 47.4, 23.7, 18.3, 17.7, −4.6, −5.4, −5.5; MS(CI) *m/e* 434 $(M + H)^+$; HRMS(CI) calcd for $C_{23}H_{40}NO_3Si_2$ $(M + H)^+$ 434.2547, found $(M + H)^+$ 434.2553.

(+)-(2*R*,3*S*,4*R*)-3-(Dimethylphenylsilyl)-4-[(*E*)-(1*R*)-hydroxybut-2-en-1-yl]-2-(hydroxymethyl)-5-pyrrolidinone (29). Bu_4NF in THF/H_2O (1.0 M; 0.12 mL, 0.120 mmol) was added to **28** (47.3 mg, 0.109 mmol) in THF (3 mL) at 0 °C. The solution was allowed to warm to room temperature, and after 2 h, the mixture was diluted with EtOAc, washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (EtOAc) gave **29** (27.2 mg, 78%) as a colorless crystalline solid which was recrystallized from Et_2O to provide crystals for X-ray analysis: mp 135−136 °C; R_f = 0.32; $[\alpha]^{25}_D$ = +12.7° (*c* = 0.39, $CHCl_3$); IR (film) 3333, 3070, 2954, 2915, 2889, 1682, 1590 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.48 (2H, m), 7.40 (3H, m), 7.22 (1H, br s), 5.52 (2H, m), 4.98 (1H, d, *J* = 2.2 Hz), 3.91 (2H, m), 3.53 (2H, m), 3.21 (1H, m), 2.41 (1H, app t, *J* = 5.7 Hz), 1.65 (3H, d, *J* = 5.0 Hz), 1.35 (1H, app t, *J* = 5.0 Hz), 0.35 (3H, s), 0.33 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.9, 135.6, 133.9, 131.2, 129.8, 128.8, 128.2, 76.8, 65.9, 56.2, 48.6, 24.7, 17.8, −5.2, −5.6; MS(CI) *m/e* 320 $(M + H)^+$; HRMS(CI) calcd for $C_{17}H_{26}NO_3Si$ $(M + H)^+$ 320.1681, found $(M + H)^+$ 320.1677. Crystal data for **29**: $C_{17}H_{25}NO_3Si$, *M* = 319.5, monoclinic, $P2_1$ (no. 4), *a* = 8.541(1) Å, *b* = 7.839(1) Å, *c* = 13.986(1) Å, β = 104.21(1)°, *V* = 907.7(1) $Å^3$, *Z* = 2, D_c = 1.169 g cm^{-3}, μ(Cu Kα) = 12.3 cm^{-1}, *F*(000) = 344, *T* = 293 K; clear prisms, 0.20 × 0.17 × 0.13 mm, Siemens P4/PC diffractometer, ω-scans, 1622 independent reflections, F^2 refinement, R_1 = 0.046, wR_2 = 0.114, 1475 independent observed absorption corrected reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 128°$], and 200 parameters. The absolute structure was unambiguously determined by a combination of *R*-factor tests [$R_1^+ = 0.0460$, $R_1^- = 0.0468$] and by use of the Flack parameter [$x^+ = 0.16(13)$, $x^- = 0.84(13)$]. CCDC 132034.

(−)-*tert*-Butyl (2*R*,3*S*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3-(1,1,2,2,2-pentamethyldisilyl)-5-oxopyrrolidine-1-carboxylate (30). MeLi in hexanes (1.4 M; 221 μL, 0.31 mmol) was added to hexamethyldisilane (0.125 mL, 0.61 mmol) in HMPA (0.8 mL) at 0 °C. After 20 min, THF (2 mL) was added and the resulting solution transferred via cannula to Et_2Zn in hexanes (1 M; 0.31 mL, 0.31 mmol) in THF (2 mL) cooled to 0 °C. After a further 5 min, the zincate solution was cooled to −78 °C when **3** (100 mg, 0.305 mmol) in THF (3 mL) was added via cannula. The mixture changed color from brown to pale yellow instantaneously and was allowed to warm to room temperature over 15 min. Saturated aqueous $NaHCO_3$ (5 mL) was added and the mixture diluted with Et_2O, washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (hexanes−Et_2O, 6:1) gave **30** (106 mg, 76%) as a low-melting crystalline solid: R_f = 0.24; mp 32−33 °C; $[\alpha]^{25}_D$ = −27.7° (*c* = 1, $CHCl_3$); IR (film) 2952, 2895, 2859, 1791, 1753, 1712 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.03 (1H, m), 3.88 (1H, dd, *J* = 10.2, 4.3 Hz), 3.60 (1H, dd, *J* = 10.2, 2.3 Hz), 2.93 (1H, dd, *J* = 18.2, 11.2 Hz), 2.25 (1H, dd, *J* = 18.2, 3.0 Hz), 1.59 (1H, app dt, *J* = 11.2, 2.6 Hz), 1.53 (9H, s), 0.88 (9H, s), 0.09 (9H, s), 0.06 (6H, s), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7, 150.0, 82.7, 64.9, 61.1, 34.6, 28.1, 25.9, 18.7, 18.2, −1.8, −5.47, −5.51, −5.9, −6.1; MS(CI) *m/e* 460 $(M + H)^+$; HRMS(CI) calcd for $C_{21}H_{46}NO_4Si_3$ $(M + H)^+$ 460.2735, found $(M + H)^+$ 460.2778. Anal. Calcd for $C_{21}H_{45}NO_4Si_3$: C, 54.85; H, 9.86; N, 3.05. Found: C, 54.65; H, 9.61; N, 2.89. Data for TMS adduct **31**: R_f = 0.21; ^1H NMR (300 MHz, $CDCl_3$) δ 4.02 (1H, m), 3.91 (1H, dd, *J* = 10.2, 4.3 Hz), 3.59 (1H, dd, *J* = 10.2, 2.3 Hz), 2.91 (1H, dd, *J* = 18.0, 11.4 Hz), 2.27 (1H, dd, *J* = 18.0, 3.2 Hz), 1.55 (9H, s), 1.47 (1H, app dt, *J* = 11.4, 2.7 Hz), 0.89 (9H, s), 0.04−0.07 (15H, m's); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 82.8, 64.8, 60.5, 33.9, 28.1, 25.9, 19.2, 18.2, 1.0, −3.8, −5.47, −5.51; MS(CI) *m/e* 402 (M

+ H)$^+$; HRMS(CI) calcd for $C_{19}H_{40}NO_4Si_2$ (M + H)$^+$ 402.2496, found (M + H)$^+$ 402.2512.

(4*S*,5*S*)-1,3-Dimethyl-2-(2,3-epoxydodecyl)-4,5-diphenylimidazolidine (32a). (*S*,*S*)-*N*,*N*′-Dimethyl-1,2-diphenylethylenediamine (48 mg, 0.200 mmol) and 4 Å molecular sieves (~250 mg) were added to **10** (30 mg, 0.151 mmol) in Et_2O (3 mL). After 30 min at room temperature, no aldehyde was present (TLC). The mixture was filtered through Celite and rotary evaporated: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.05−7.32 (20H, m), 3.78 (1H, d, J = 8.6 Hz), 3.68 (1H, d, J = 8.6 Hz), 3.49−3.60 (4H, m), 2.97−3.07 (3H, m), 2.90 (1H, m), 2.45 (3H, s), 2.42 (3H, s), 2.37 (6H, s), 1.45−1.80 (8H, m), 1.28 (24H, br s), 0.89 (6H, t, J = 6.7 Hz).

(4*S*,5*S*)-1,3-Dimethyl-2-((2*R*,3*R*)-epoxydodecyl)-4,5-diphenylimidazolidine (32b). (*S*,*S*)-*N*,*N*′-Dimethyl-1,2-diphenylethylenediamine (80 mg, 0.330 mmol) and 4 Å molecular sieves (~250 mg) were added to (2*S*,3*R*)-**10** (58 mg, 0.292 mmol) in Et_2O (5 mL). After 30 min at room temperature no aldehyde was present (TLC). The mixture was filtered through Celite and rotary evaporated. The residue was then analyzed by ^{1}H NMR (270 MHz, $CDCl_3$). This was compared to the ^{1}H NMR of the imidazoline obtained from the reaction between **10** and (*S*,*S*)-*N*,*N*′-dimethyl-1,2-diphenylethylenediamine. Only one diastereoisomer is visible in the case of **32b**: ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.05−7.32 (10H, m), 3.77 (1H, d, J = 8.5 Hz), 3.60 (1H, d, J = 6.1 Hz), 3.53 (1H, d, J = 8.5 Hz), 2.96−3.07 (2H, m), 2.42 (3H, m), 2.38 (3H, s), 1.45−1.80 (4H, m), 1.28 (12H, br s), 0.89 (3H, t, J = 6.7 Hz).

(+)-*tert*-Butyl (2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-4-[(*E*)-(4*R*,5*R*)-epoxytetradec-(1*R*)-hydroxy-2-en-1-yl]-3-(1,1,2,2,2-pentamethyldisilyl)-5-oxopyrrolidine-1-carboxylate (33). MeLi in hexanes (1.4 M; 221 μL, 0.31 mmol) was added to a solution of hexamethyldisilane (0.125 mL, 0.6 mmol) in HMPA (0.8 mL) at 0 °C. After 20 min, THF (2 mL) was added and the resulting solution added via cannula to Et_2-Zn in hexanes (1 M; 0.31 mL, 0.31 mmol) in THF (2 mL) at 0 °C. After a further 5 min, this solution was cooled to −78 °C when **3** (100 mg, 0.30 mmol) in THF (2 mL) was added via cannula. Subsequently, (4*R*,5*R*)-**18** (70.0 mg, 0.32 mmol) in THF (2 mL) was added via cannula and the mixture allowed to warm to room temperature and quenched by the addition of saturated aqueous $NaHCO_3$. The mixture was washed with H_2O, dried ($MgSO_4$), and rotary evaporated. Chromatography (hexanes−Et_2O, 3:1) gave **33** (123 mg, 60%) as a colorless oil: R_f = 0.23; $[\alpha]^{25}_D$ = +14.0° (c = 1, $CHCl_3$); IR (film) 3480, 2953, 2928, 2857, 1780, 1722 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (1H, dd, J = 15.5, 7.6 Hz), 5.59 (1H, dd, J = 15.5, 8.0 Hz), 4.39 (1H, s), 4.40 (1H, m), 3.96 (2H, m), 3.56 (1H, dd, J = 8.7, 1.4 Hz), 3.10 (1H, dd, J = 8.0, 2.1 Hz), 2.82 (1H, ddd, J = 7.6, 5.4, 2.0 Hz), 2.35 (1H, dd, J = 8.8, 4.4 Hz), 1.55 (9H, s), 1.34 (1H, dd, J = 4.4, 2.5 Hz), 1.27−1.52 (16H, m), 0.90 (9H, s), 0.89 (3H, t, J = 7.1 Hz), 0.07−0.11 (21H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 149.6, 134.0, 130.6, 83.6, 73.9, 65.2, 60.6, 60.4, 57.6, 50.6, 32.1, 31.9, 29.54, 29.50, 29.4, 29.3, 28.0, 26.0, 25.9, 22.7, 21.2, 18.5, 14.1, −1.7, −5.1, −5.3, −5.6; MS(CI) *m/e* 701 (M + NH_4)$^+$ 684 (M + H)$^+$; HRMS(CI) calcd for $C_{35}H_{70}NO_6Si_3$ (M + NH_4)$^+$ 684.4511, found (M + NH_4)$^+$ 684.4518. Anal. Calcd for $C_{35}H_{69}NO_6Si_3$: C, 61.44; H, 10.17; N, 2.05. Found: C, 61.26; H, 10.33; N, 1.85.

(+)-*tert*-Butyl (2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-4-[(*E*)-(4*R*,5*R*)-epoxy-1-oxotetradec-2-en-1-yl]-4-hydroxy-3-(1,1,2,2,2-pentamethyldisilyl)-5-oxopyrrolidine-1-carboxylate (34). Dess−Martin periodinane (80 mg, 188.6 μmol) was added to **33** (62 mg, 90.9 μmol) in CH_2Cl_2 (9.5 mL) at 0 °C. The mixture was allowed to warm to room temperature when saturated aqueous $Na_2S_2O_3$ (3 mL) and saturated aqueous $NaHCO_3$ (3 mL) were added and the mixture stirred vigorously for 1 h. The organic layer was separated, washed twice with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), and rotary evaporated to yield the dione. This compound was unstable on silica or prolonged exposure to atmospheric conditions and was used without further purification. Ni(acac)$_2$ (1.4 mg) in H_2O (0.5 mL) followed by freshly prepared dimethyldioxirane in Me_2CO (0.1 M; 1.0 mL, 0.1 mmol) was added to the crude dione (32 mg, 46.9 μmol) in Me_2CO (1 mL) at 0 °C. Further quantities (0.5 mL) of dimethyldioxirane solution were added at 1 h intervals until TLC analysis indicated complete consumption of starting material. Rotary evaporation gave an oil which was dissolved in CH_2Cl_2, extracted with H_2O, and dried ($MgSO_4$). Rotary evaporation and chromatography (hexanes−Et_2O, 6:1) gave **34** (20 mg 61%) over two steps: R_f = 0.26; $[\alpha]^{25}_D$ = +5.3° (c = 1, $CHCl_3$); IR (film) 3443, 2954, 2929, 2857, 1784, 1725, 1623 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (1H, d, J = 15.6 Hz), 6.64 (1H, dd, J = 15.6, 7.8 Hz), 4.99 (1H, s), 4.32 (1H, dd, J = 11.0, 2.0 Hz), 4.20 (1H, m), 3.47 (1H, dd, J = 11.0, 1.2 Hz), 3.27 (1H, dd, J = 7.8, 1.9 Hz), 2.93 (1H, ddd, J = 7.6, 5.7, 1.9 Hz), 1.69 (1H, d, J = 4.2 Hz), 1.61 (2H, m), 1.54 (9H, s), 1.45 (2H, m), 1.28 (12H, m), 0.92 (9H, s), 0.89 (3H, t, J = 6.9 Hz), 0.04−0.11 (21H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.6, 171.7, 149.9, 146.0, 126.3, 85.1, 83.8, 77.2, 63.2, 61.4, 59.5, 57.1, 35.9, 31.93, 31.85, 29.5, 29.4, 29.3, 28.0, 25.9, 25.8, 22.7, 18.4, 14.1, −1.2, −2.4, −2.9, −5.5, −5.6; MS(EI) *m/e* 697 (M$^{\bullet+}$); HRMS(EI) calcd for $C_{35}H_{67}NO_7Si_3$ (M$^{\bullet+}$) 697.4225, found (M$^{\bullet+}$) 697.4205. Anal. Calcd for $C_{35}H_{67}NO_6Si_3$: C, 60.21; H, 9.67; N, 2.01. Found: C, 60.36; H, 9.66; N, 2.26.

Chloro(diethylamino)diphenylsilane. Following the literature procedure:[33] Freshly distilled Et_2NH (11.7 mL, 110 mmol) in THF (10 mL) was added dropwise over a period of 30 min to a solution of freshly distilled Et_3N (15.5 mL, 110 mmol) and redistilled Ph_2SiCl_2 (20.7 mL, 100 mmol) in dry THF (150 mL) in a Schlenk flask. The mixture was allowed to stir for 12 h when dry hexane (100 mL) was added and the suspension filtered. Rotary evaporation and distillation of the filtrate gave $(Et_2N)Ph_2SiCl$ (20.2 g, 71%): bp 120 °C (0.45 mmHg); ^{1}H NMR (270 MHz, $CDCl_3$) δ 7.79 (4H, m), 7.43 (6H, m), 2.95 (4H, q, J = 6.9 Hz), 1.07 (6H, t, J = 6.9 Hz).

(Diethylamino)diphenylsilyllithium. Following the literature procedure:[34] Li wire (0.5−1.0% Na content; 0.2 g) cut into small pieces was added to $(Et_2N)Ph_2SiCl$ (1.0 mL, 3.73 mmol) in THF (15 mL) and the mixture stirred vigorously for 5 min, and then cooled to 0 °C. The solution underwent color changes from blue-green to purple, then to green, and eventually to brown over a 3 h period, after which the (diethylamino)-diphenylsilyllithium was used directly and without filtration, assuming a concentration of 0.233 M (complete lithiation).

(−)-*tert*-Butyl (2*R*,3*S*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-3-(ethoxydiphenylsilyl)-5-oxopyrrolidine-1-carboxylate (36). $(Et_2N)Ph_2SiLi$ in THF (0.233 M; 2 mL, 0.460 mmol) was added to Et_2Zn in hexanes (1 M; 0.46 mL, 0.460 mmol) in THF (3 mL) at 0 °C. After 10 min, the solution was cooled to −78 °C when **3** (150 mg, 0.458 mmol) in THF (3 mL) was added. The mixture was stirred for a further 5 min and subsequently quenched with a slurry of NH_4Cl in absolute ethanol for 24 h. The mixture was diluted with Et_2O, washed with H_2O, separated, and dried ($MgSO_4$). Rotary evaporation and chromatography (hexanes−Et_2O, 4:1) gave **36** (163 mg, 64%): R_f = 0.21; $[\alpha]^{25}_D$ = −11.6° (c = 1, $CHCl_3$); IR (film) 3071, 3050, 2955, 2930, 2859, 1788, 1753, 1713 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (4H, m), 7.45 (6H, m), 4.25 (1H, m), 3.88 (1H, dd, J = 10.2, 4.6 Hz), 3.76 (2H, q, J = 6.9 Hz), 3.64 (1H, dd, J = 10.2, 2.3 Hz), 2.94 (1H, dd, J = 18.2, 11.2 Hz), 2.54 (1H, dd, J = 18.2, 3.3 Hz), 2.24 (1H, app dt, J = 11.2, 3.0 Hz), 1.43 (9H, s), 1.20 (3H, t, J = 6.9 Hz), 0.91 (9H, s), 0.06 (3H, s), 0.05 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 149.6, 135.1, 134.9, 132.1, 132.1, 130.5, 128.3, 128.2, 128.0, 82.3, 64.5, 59.6, 33.3, 28.0, 25.9, 18.3, 17.5, −5.48, −5.52; MS(CI) *m/e* 556 (M + H)$^+$; HRMS(CI) calcd for $C_{30}H_{46}NO_5Si_2$ (M + H)$^+$ 556.2915, found (M + H)$^+$ 556.2934. Anal. Calcd for $C_{30}H_{45}NO_5Si_2$: C, 64.82; H, 8.16; N, 2.52. Found: C, 65.08; H, 8.12; N, 2.85.

(−)-*tert*-Butyl (2*R*,3*S*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-4-hydroxy-5-oxopyrrolidine-1-carboxylate (35). KHF_2 (20.0 mg, 0.256 mmol) and 3-chloroperbenzoic acid (55−86%; 100.0 mg, ~3.0 equiv (assuming 70% purity)) was added to **36** (58.0 mg, 0.104 mmol) in DMF (3 mL). After 1.5 h, the mixture was diluted with Et_2O, washed with saturated aque-

(33) Tamao, K.; Nakajo, E.; Ito, Y. *Tetrahedron* **1988**, *44*, 3997.
(34) Tamao, K. Kawachi, A.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 3989.

ous $NaHCO_3$, dried, and rotary evaporated. The resulting colorless solid was chromatographed (hexanes−Et_2O, 1:2) to afford **35** (34.0 mg, 94%): $R_f = 0.29$; mp 141−143 °C; $[\alpha]^{25}_D = -47.9°$ ($c = 1$, $CHCl_3$); IR (DRIFTS) 3491, 2957, 2865, 1772, 1723, 1690 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.38 (1H, m), 4.05 (1H, m), 3.86 (1H, dd, $J = 10.7$, 3.8 Hz), 3.82 (1H, dd, $J = 10.7$, 2.3 Hz), 2.95 (1H, dd, $J = 18.0$, 6.0 Hz), 2.36 (1H, d, $J = 18.0$ Hz), 1.94 (1H, d, $J = 3.5$ Hz), 1.53 (9H, s), 0.86 (9H, s), 0.03 (3H, s), 0.02 (3H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ 172.8, 150.0, 83.1, 68.0, 67.5, 62.4, 42.7, 28.1, 25.8, 18.2, −5.6; MS-(CI) *m/e* 363 $(M + NH_4)^+$, 346 $(M + H)^+$; HRMS(CI) calcd for $C_{16}H_{35}N_2O_5Si$ $(M + NH_4)^+$ 363.2315, found $(M + NH_4)^+$ 363.2322. Anal. Calcd for $C_{16}H_{31}NO_5Si$: C, 55.62; H, 9.04; N, 4.05. Found: C, 55.82; H, 9.13; N, 4.12.

***tert*-Butyl (2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-4-[(*E*)-(4*R*,5*R*)-epoxytetradec-(1*R*)-hydroxy-2-en-1-yl]-3-(ethoxydiphenylsilyl)-5-oxopyrrolidine-1-carboxylate (37a).** $(Et_2N)Ph_2SiLi$ (0.233 M; 3.0 mL, 0.70 mmol) was added to Et_2Zn in hexanes (1 M; 0.7 mL, 0.70 mmol) in THF (7.5 mL) at −10 °C. After 20 min, the solution was cooled to −78 °C when **3** (229 mg, 0.70 mmol) in THF (7 mL) was added via cannula. An instantaneous color change occurred, from green-brown to pale yellow, and following 5 min of stirring, (4*R*,5*R*)-**18** (157 mg, 0.70 mmol) in THF (7 mL) was added via cannula. The mixture was allowed to warm to room temperature, when a slurry of NH_4Cl in absolute EtOH (∼20 mL) was added and stirring continued for 12 h. The suspension was diluted with Et_2O and washed with H_2O and the aqueous layer extracted with Et_2O. The combined organic phases were dried ($MgSO_4$), filtered, and rotary evaporated. Chromatography (hexanes−Et_2O, 3:1) gave **37a** (273 mg, 50%) as a colorless oil and 55 mg (10%) of the corresponding silanol, also as a colorless oil. Data for **37a**: $R_f = 0.13$; IR (film) 3474, 3071, 3050, 2928, 2857, 1780, 1722 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (4H, m), 7.46 (6H, m), 5.67 (1H, dd, $J = 15.5$, 6.6 Hz), 5.45 (1H, dd, $J = 15.5$, 7.8 Hz), 4.47 (1H, m), 4.40 (1H, d, $J = 2.9$ Hz), 4.14 (1H, m), 3.94 (1H, dd, $J = 10.6$, 3.8 Hz), 3.72 (2H, q, $J = 7.0$ Hz), 3.47 (1H, dd, $J = 10.6$, 1.9 Hz), 2.99 (1H, dd, $J = 7.8$, 2.0 Hz), 2.82 (1H, m), 2.76 (1H, app t, $J = 6.9$ Hz), 2.06 (1H, dd, $J = 6.4$, 4.6 Hz), 1.55 (2H, m), 1.46 (9H, s), 1.27−1.40 (14H, m), 1.19 (3H, t, $J = 7.0$ Hz), 0.90 (9H, s), 0.89 (3H, t, $J = 7.0$ Hz), 0.05 (6H, s); ^{13}C NMR (75 MHz $CDCl_3$) δ 175.4, 149.6, 135.2, 134.6, 131.6, 131.2, 130.8, 130.7, 128.3, 83.2, 73.5, 63.9, 60.3, 59.9, 58.5, 57.8, 49.3, 32.1, 31.9, 30.3, 29.6, 29.5, 29.3, 28.0, 26.0, 25.9, 22.7, 19.9, 18.5, 18.2, 14.1, −5.3, −5.4; MS(FAB$^+$) *m/e* 780 $(M + H)^+$; HRMS(FAB$^+$) calcd for $C_{44}H_{70}NO_7Si_2$ $(M + H)^+$ 780.4691, found $(M + H)^+$ 780.4688. Data for corresponding silanol $(HO)Ph_2SiR$ (see the text): $R_f = 0.40$ (hexanes−Et_2O, 1:1); IR (film) 3422, 3071, 3051, 2955, 2928, 2856, 1775, 1721, 1590 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 (4H, m), 7.43 (6H, m), 5.69 (1H, dd, $J = 15.6$, 7.0 Hz), 5.50 (1H, dd, $J = 15.6$, 7.3 Hz), 4.45 (1H, m), 4.15 (1H, m), 3.94 (1H, d, $J = 1.6$ Hz), 3.86 (1H, dd, $J = 10.5$, 3.8 Hz), 3.37 (1H, dd, $J = 10.5$, 1.8 Hz), 2.98 (1H, dd, $J = 7.2$, 2.0 Hz), 2.87 (1H, ddd, $J = 7.4$, 5.7, 2.0 Hz), 2.79 (1H, app t, $J = 7.4$ Hz), 1.98 (1H, dd, $J = 7.8$, 5.7 Hz), 1.55 (2H, m), 1.26−1.49 (14H, m′s), 1.46 (9H, s), 0.88 (9H, s), 0.86 (3H, t, $J = 6.7$ Hz), 0.03 (3H, s), 0.02 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 162.9, 149.7, 134.6, 134.6, 134.1, 133.6, 130.6, 130.5, 128.3, 83.4, 73.4, 63.7, 60.5, 58.7, 57.3, 49.2, 31.93, 31.86, 29.51, 29.48, 29.4, 29.3, 28.0, 26.0, 25.8, 22.7, 20.8, 18.5, 14.1, −5.38, −5.43; MS(FAB$^+$) *m/e* 752 $(M + H)^+$. Anal. Calcd for $C_{42}H_{65}NO_7Si_2$: C, 67.07; H, 8.71; N, 1.86. Found: C, 66.76; H, 8.52; N, 1.78.

(−)-*tert*-Butyl (2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-4-[(*E*)-(4*R*,5*R*)-epoxy-1-oxotetradec-2-en-1-yl]-3-(ethoxydiphenylsilyl)-4-hydroxy-5-oxopyrrolidine-1-carboxylate (38a). Dess−Martin periodinane (106 mg, 0.250 mmol) was added to **37a** (150 mg, 0.192 mmol) in CH_2Cl_2 (60 mL) at 0 °C. After the mixture was warmed to room temperature over 1 h, saturated aqueous $NaHCO_3$ (15 mL) and saturated aqueous $Na_2S_2O_3$ (15 mL) were added. The two-phase mixture was rapidly stirred until complete dissolution of the white precipitate in the CH_2Cl_2 layer. The organic phase was separated, washed with H_2O, dried ($MgSO_4$), filtered, and rotary evaporated to yield a pale yellow oil. Due to the compound's instability toward chromatographic supports, it was used without further purification. The crude dione (108 mg, 0.139 mmol), split into three separate reaction vessels, was dissolved in Me_2CO (0.5 mL each), and the solutions were cooled to 0 °C. $Ni(acac)_2$ (4 mg, 15.6 μmol) in H_2O (0.35 mL) was added to each solution, after which freshly prepared dimethyldioxirane (1.5 mL) was added, and the solutions were allowed to warm to room temperature slowly. After 2.5 h, TLC analysis indicated complete reaction, and the three solutions were combined and rotary evaporated. The residue was dissolved in CH_2Cl_2, washed with H_2O, dried ($MgSO_4$), filtered, evaporated, and chromatographed (hexanes−Et_2O, 4:1) to furnish **38a** (108 mg, 71% over both steps) as a colorless oil: $R_f = 0.19$; $[\alpha]^{25}_D = -6.1°$ ($c = 1$, $CHCl_3$); IR (film) 3448, 3072, 3050, 2956, 2928, 2857, 1962, 1897, 1786, 1726, 1687, 1624 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (2H, dd, $J = 7.6$, 1.7 Hz), 7.57 (2H, dd, $J = 7.6$, 1.7 Hz), 7.41 (6H, m), 6.93 (1H, d, $J = 15.5$ Hz), 6.33 (1H, dd, $J = 15.5$, 7.6 Hz), 4.69 (1H, s), 4.49 (1H, d, $J = 6.6$ Hz), 4.24 (1H, dd, $J = 11.0$, 2.1 Hz), 3.66 (2H, m), 3.42 (1H, dd, $J = 11.0$, 0.8 Hz), 3.12 (1H, dd, $J = 7.6$, 1.7 Hz), 2.81 (1H, ddd, $J = 7.3$, 5.9, 1.7 Hz), 2.54 (1H, d, $J = 6.6$ Hz), 1.58 (2H, m), 1.47 (9H, s), 1.28−1.46 (14H, m), 1.13 (3H, t, $J = 6.9$ Hz), 0.91 (12H, m), 0.05 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 171.4, 149.7, 145.3, 135.6, 135.0, 133.4, 132.9, 130.2, 130.1, 127.9, 127.8, 125.6, 85.3, 83.6, 62.0, 61.4, 59.6, 58.4, 57.0, 33.1, 32.0, 31.9, 30.3, 29.5, 29.4, 29.3, 28.0, 25.9, 22.7, 18.4, 18.1, 14.1, −5.5; MS(FAB$^+$) *m/e* 793 $(M^{\bullet+})$; HRMS(FAB$^+$) calcd for $C_{44}H_{67}NO_8Si_2$ $(M^{\bullet+})$ 793.4405, found $(M^{\bullet+})$ 793.4408. Anal. Calcd for $C_{44}H_{67}NO_8Si_2$: C, 66.54; H, 8.50; N, 1.76. Found: C, 66.34; H, 8.37; N, 1.64.

(−)-*tert*-Butyl (2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-3,4-dihydroxy-4-[(*E*)-(4*R*,5*R*)-epoxy-1-oxotetradec-2-en-1-yl]-5-oxopyrrolidine-1-carboxylate (39a). KHF_2 (13 mg, 166.5 μmol) and 3-chloroperbenzoic acid (assumed 70% activity; 50 mg, 203 μmol) were sequentially added to **38a** (52 mg, 65.5 μmol) in DMF (4 mL) at 0 °C. The mixture was allowed to warm to room temperature, and after 1.5 h, the solution was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and H_2O, dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was chromatographed (hexanes−Et_2O, 3:2) to afford **39a** (21 mg, 55%) as a colorless oil: $R_f = 0.25$; $[\alpha]^{25}_D = -1.3°$ ($c = 0.61$, $CHCl_3$); IR (film) 3454, 2955, 2928, 2856, 1784, 1732, 1694, 1627 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.12 (1H, d, $J = 15.5$ Hz), 6.78 (1H, dd, $J = 15.5$, 7.3 Hz), 5.12 (1H, br s), 4.32 (1H, d, $J = 3.0$ Hz), 4.15 (1H, dd, $J = 10.6$, 4.0 Hz), 4.05 (1H, m), 3.98 (1H, dd, $J = 10.6$, 2.0 Hz), 3.91 (1H, br s), 3.28 (1H, dd, $J = 7.3$, 1.7 Hz), 2.93 (1H, ddd, $J = 7.0$, 5.6, 1.7 Hz), 1.63 (2H, m), 1.56 (9H, s), 1.45 (2H, m), 1.29 (12H, m), 0.91 (9H, s), 0.90 (3H, t, $J = 6.9$ Hz), 0.12 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.5, 169.7, 149.6, 146.8, 126.2, 84.3, 82.4, 75.9, 64.2, 61.9, 61.3, 56.8, 32.0, 31.9, 30.3, 29.5, 29.34, 29.31, 28.0, 25.8, 22.7, 18.3, 14.1, −5.6.

(+)-(2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3,4-dihydroxy-4-[(*E*)-(4*R*,5*R*)-epoxytetradec-2-en-1-oxy]-5-oxopyrrolidine (40a). Carbamate **39a** (13.0 mg, 22.9 μmol) in EtOAc (∼3 mL) was added to silica gel (40−63 mesh; 300 mg) and the slurry dried in vacuo. The silica gel was placed under high vacuum (0.1 mmHg) at 40 °C for 12 h, cooled, and extracted with EtOAc, and the filtrate was rotary evaporated. Chromatography (hexanes−diethyl ether, 1:2) afforded **40a** (9 mg, 84%) as a colorless solid: $R_f = 0.19$; mp 123−125 °C; $[\alpha]^{25}_D = +70.0°$ ($c = 0.27$, $CHCl_3$); IR (film) 3338, 2954, 2925, 2855, 1722, 1685, 1626 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 7.05 (1H, dd, $J = 15.7$, 0.8 Hz), 6.62 (1H, dd, $J = 15.7$, 7.1 Hz), 4.23 (1H, d, $J = 7.2$ Hz), 3.86 (1H, dd, $J = 11.1$, 2.7 Hz), 3.68 (1H, dd, $J = 11.1$, 4.4 Hz), 3.46 (1H, ddd, $J = 7.2$, 4.4, 2.7 Hz), 3.32 (1H, m), 2.92 (1H, ddd, $J = 7.1$, 5.1, 1.9 Hz), 1.62 (1H, m), 1.55 (1H, m), 1.45 (2H, m), 1.29 (12H, br s), 0.92 (9H, s), 0.89 (3H, t, $J = 7.0$ Hz), 0.10 (3H, s), 0.09 (3H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 198.0, 174.8, 145.2, 127.9, 88.2, 78.4, 62.9, 62.5, 60.2, 57.8, 33.1, 30.7, 30.5, 30.5, 27.0, 26.4, 23.8, 19.2, 14.5, −5.3, −5.4; MS(FAB$^+$) *m/e* 484 $(M + H)^+$; HRMS-(FAB$^+$) calcd for $C_{25}H_{46}NO_6Si$ $(M + H)^+$ 484.3094, found $(M + H)^+$ 484.3090.

(+)-(2*R*,3*R*,4*R*)-3,4-Dihydroxy-4-[(*E*)-(4*R*,5*R*)-epoxy-1-oxotetradec-2-en-1-yl]-2-(hydroxymethyl)-5-pyrrolidinone (41a). Aqueous H_2SiF_6 (20−25%; 2 μL) was added to **40a** (9 mg, 18.6 μmol) in MeCN (1 mL) at 0 °C. The mixture was allowed to warm to room temperature, and after 3 h, the solution was diluted with EtOAc, washed with H_2O, and dried (Na_2SO_4). The organic phase was rotary evaporated and the residue chromatographed (freshly redistilled EtOAc) to afford **41a** (3.6 mg, 53%) as a colorless solid: R_f = 0.15; mp 108−110 °C; $[\alpha]^{25}_D$ = +44.6° (c = 0.24, $CHCl_3$); IR (film) 3341, 2924, 2854, 1704, 1626 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.06 (1H, dd, J = 15.7, 0.5 Hz), 6.62 (1H, dd, J = 15.7, 7.2 Hz), 4.15 (1H, d, J = 7.2 Hz), 3.79 (1H, dd, J = 11.6, 2.8 Hz), 3.54 (1H, dd, J = 11.6, 5.3 Hz), 3.47 (1H, ddd, J = 7.2, 5.3, 2.8 Hz), 3.32 (1H, m), 2.92 (1H, ddd, J = 7.2, 5.1, 2.0 Hz), 1.62 (1H, m), 1.55 (1H, m), 1.45 (2H, m), 1.29 (12H, br s), 0.89 (3H, t, J = 7.0 Hz); 13C NMR (100 MHz, CD_3OD) δ 197.9, 175.0, 145.1, 128.0, 88.1, 78.9, 62.8, 62.0, 60.2, 57.8, 33.1, 30.7, 30.52, 30.45, 27.0, 23.7, 14.4.

(−)-*tert*-Butyl (2*R*,3*S*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-4-[(*E*)-(4*S*,5*S*)-epoxytetradec-(1*R*)-hydroxy-2-en-1-yl]-3-(ethoxydiphenylsilyl)-5-oxopyrrolidine-1-carboxylate (37b). Prepared in a fashion identical to that of **37a** employing (4*S*,5*S*)-**18**: R_f = 0.18; $[\alpha]^{25}_D$ = −25.2° (c = 1, $CHCl_3$); IR (film) 3474, 3071, 3050, 2955, 2928, 2856, 1780, 1722, 1590 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (4H, m), 7.47 (6H, m), 5.50 (1H, dd, J = 15.5, 7.3 Hz), 5.39 (1H, dd, 15.5, 7.6 Hz), 4.46 (1H, m), 4.41 (1H, d, J = 1.3 Hz), 4.20 (1H, m), 3.95 (1H, dd, J = 10.6, 3.3 Hz), 3.74 (2H, q, J = 6.9 Hz), 3.48 (1H, dd, J = 10.6, 1.7 Hz), 2.93 (1H, dd, J = 7.6, 2.0 Hz), 2.82 (1H, ddd, J = 7.3, 5.3, 2.0 Hz), 2.71 (1H, dd, J = 8.3, 5.3 Hz), 1.91 (1H, dd, J = 5.3, 3.6 Hz), 1.55 (2H, m), 1.45 (9H, s), 1.29−1.43 (14H, m′s), 1.19 (3H, t, J = 6.9 Hz), 0.89 (12H, m), 0.05 (3H, s), 0.04 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 149.5, 135.2, 135.1, 135.0, 131.7, 131.6, 131.3, 130.7, 128.3, 83.2, 73.9, 64.4, 60.3, 59.7, 58.6, 58.0, 48.6, 32.0, 31.9, 29.53, 29.48, 29.4, 29.3, 27.9, 26.0, 25.8, 22.7, 20.3, 18.5, 18.2, 14.1, −5.4; MS(FAB+) m/e 780 (M + H)$^+$; HRMS(CI) calcd for $C_{44}H_{70}NO_7Si_2$ (M + H)$^+$ 780.4691, found (M + H)$^+$ 780.4653. Anal. Calcd for $C_{44}H_{69}NO_7Si_2$: C, 67.74; H, 8.91; N, 1.80. Found: C, 67.52; H, 8.64; N, 1.73.

(−)-*tert*-Butyl (2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-4-[(*E*)-(4*S*,5*S*)-epoxy-1-oxotetradec-2-en-1-yl]-3-(ethoxydiphenylsilyl)-4-hydroxy-5-oxopyrrolidine-1-carboxylate (38b). Prepared in a manner identical to that reported for the (4,5)-epimer, **38a**: R_f = 0.20; $[\alpha]^{25}_D$ = −35.7° (c = 1, $CHCl_3$); IR (film) 3442, 3072, 3050, 2956, 2928, 2856, 1787, 1726, 1688, 1625 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (2H, dd, J = 7.8, 1.3 Hz), 7.56 (2H, dd, J = 7.8, 1.3 Hz), 7.38 (6H, m), 6.80 (1H, d, J = 15.5 Hz), 6.37 (1H, dd, J = 15.5, 7.2 Hz), 4.71 (1H, s), 4.46 (1H, d, J = 6.6 Hz), 4.23 (1H, dd, J = 11.1, 2.1 Hz), 3.62 (2H, m), 3.41 (1H, dd, J = 11.1, 1.1 Hz), 3.06 (1H, dd, J = 7.2, 1.7 Hz), 2.79 (1H, ddd, J = 7.4, 5.5, 1.7 Hz), 2.54 (1H, d, J = 6.6 Hz), 1.57 (2H, m), 1.45 (9H, s), 1.26−1.43 (14H, m's), 1.11 (3H, t, J = 6.9 Hz), 0.89 (9H, s), 0.88 (3H, t, J = 7.2 Hz), 0.03 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 171.2, 149.7, 145.3, 135.5, 135.0, 133.5, 132.8, 130.1, 129.9, 127.83, 127.76, 125.2, 85.3, 83.6, 61.9, 61.6, 59.6, 58.3, 56.6, 32.8, 32.0, 31.9, 30.3, 29.7, 29.5, 29.4, 29.3, 27.9, 25.8, 22.7, 18.3, 18.0, 14.1, −5.6; MS(EI) m/e 793 (M$^{\bullet+}$); HRMS(EI) calcd for $C_{44}H_{67}NO_8Si_2$ (M$^{\bullet+}$) 793.4405, found (M$^{\bullet+}$) 793.4368.

(−)-*tert*-Butyl (2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)-methyl]-3,4-dihydroxy-4-[(*E*)-(4*S*,5*S*)-epoxy-1-oxotetradec-2-en-1-yl]-5-oxopyrrolidine-1-carboxylate (39b). KHF_2 (9.1 mg, 116.5 μmol) and purified 3-chloroperbenzoic acid (99%; 24.1 mg, 139.8 μmol) were added to **38b** (37 mg, 46.6 μmol) in dry DMF (2.6 mL) at 0 °C. The mixture was allowed to warm to room temperature and, after 1.5 h, diluted with Et_2O. The solution was washed with saturated aqueous $NaHCO_3$ and H_2O, dried ($MgSO_4$), and rotary evaporated to leave a colorless oil. Chromatography (hexanes−Et_2O, 3:2) gave **39b** (19 mg, 70%) as a colorless oil: R_f = 0.17; $[\alpha]^{25}_D$ = −17.7° (c = 0.44, $CHCl_3$); IR (film) 3448, 2956, 2928, 2856, 1785, 1730, 1691, 1628 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (1H, d, J = 15.5 Hz), 6.80 (1H, dd, J = 15.5, 6.9 Hz), 5.00 (1H, br s), 4.31 (1H, d, J = 3.6 Hz), 4.14 (1H, dd, J = 10.2, 4.3 Hz), 4.04 (1H, m), 3.98 (1H, dd, J = 10.2, 8.3 Hz), 3.78 (1H, br s), 3.28 (1H, dd, J = 6.9, 1.7 Hz), 2.93 (1H, ddd, J = 7.3, 5.6, 1.7 Hz), 1.62 (2H, m), 1.56 (9H, s), 1.45 (2H, m), 1.29 (12H, m), 0.91 (9H, s), 0.90 (3H, t, J = 6.9 Hz), 0.12 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.4, 169.7, 149.5, 146.7, 126.0, 84.3, 82.4, 76.2, 75.8, 64.0, 62.0, 61.2, 56.6, 32.0, 31.9, 29.7, 29.6, 29.5, 29.34, 29.27, 28.0, 25.82, 25.76, 22.7, 18.2, 14.1, −5.60, −5.63; MS(EI) m/e 583 (M$^{\bullet+}$); HRMS(EI) calcd for $C_{30}H_{53}NO_8Si$ (M$^{\bullet+}$) 583.3540, found (M$^{\bullet+}$) 583.3529. Anal. Calcd for $C_{30}H_{53}NO_8Si$: C, 61.72; H, 9.15; N, 2.40. Found: C, 61.61; H, 9.26; N, 2.29.

(2*R*,3*R*,4*R*)-2-[(*tert*-Butyldimethylsiloxy)methyl]-3,4-dihydroxy-4-[(*E*)-(4*S*,5*S*)-epoxy-1-oxotetradec-2-en-1-yl]-5-pyrrolidinone (40b). TFA (70 μL) was added to **39b** (18.7 mg, 32.0 μmol) in CH_2Cl_2 (4 mL) at 0 °C and the mixture allowed to warm to room temperature. After 3 h, the solution was diluted with CH_2Cl_2, washed with saturated aqueous $NaHCO_3$ and H_2O, dried ($MgSO_4$), filtered, and rotary evaporated. The resulting solid was chromatographed (hexane−Et_2O, 1:2) to yield **40b** (12.1 mg, 78%): R_f = 0.22; ^{1}H NMR (400 MHz, CD_3OD) δ 7.04 (1H, d, J = 15.7 Hz), 6.64 (1H, dd, J = 15.7, 7.1 Hz), 4.22 (1H, d, J = 7.2 Hz), 3.86 (1H, dd, J = 11.1, 2.7 Hz), 3.68 (1H, dd, J = 11.1, 4.5 Hz), 3.46 (1H, ddd, J = 7.2, 4.5, 2.7), 3.32 (1H, m), 2.92 (1H, ddd, J = 6.3, 5.1, 2.0 Hz), 1.62 (1H, m), 1.56 (1H, m), 1.46 (2H, m), 1.29 (12H, br s), 0.92 (9H, s), 0.89 (3H, t, J = 7.0 Hz), 0.10 (3H, s), 0.09 (3H, s); ^{13}C NMR (75 MHz, CD_3OD) δ 196.6, 173.5, 143.8, 126.5, 86.8, 77.1, 61.5, 61.3, 58.9, 56.4, 31.7, 29.2, 29.1, 29.0, 25.6, 25.0, 22.3, 17.8, 13.0, −6.7, −6.8; MS(EI) m/e 483 (M$^{\bullet+}$); HRMS(EI) calcd for $C_{25}H_{45}NO_6Si$ (M$^{\bullet+}$) 483.3016, found (M$^{\bullet+}$) 483.3017.

(+)-(2*R*,3*R*,4*R*)-3,4-Dihydroxy-4-[(*E*)-(4*S*,5*S*)-epoxy-1-oxotetradec-2-en-1-yl]-2-(hydroxymethyl)-5-pyrrolidinone, (+)-Pramanicin (41b). Prepared in a manner identical to that stated for **41a** to afford **41b** in 50% yield: R_f = 0.14 (EtOAc); $[\alpha]^{25}_D$ = +28.1° (c = 0.21, MeOH); IR (film) 3333, 2924, 2854, 1709, 1688, 1626 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 7.05 (1H, dd, J = 15.6, 0.5 Hz), 6.63 (1H, dd, J = 15.6, 7.1 Hz), 4.14 (1H, d, J = 7.2 Hz), 3.79 (1H, dd, J = 11.6, 2.9 Hz), 3.54 (1H, dd, J = 11.6, 5.4 Hz), 3.47 (1H, ddd, J = 7.2, 5.4, 2.9 Hz), 3.31 (1H, m), 2.93 (1H, ddd, J = 6.2, 5.0, 2.0 Hz), 1.62 (1H, m), 1.58 (1H, m), 1.45 (2H, m), 1.29 (12H, br s), 0.89 (3H, t, J = 6.9 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 197.9, 175.0, 145.2, 127.9, 88.1, 78.9, 62.9, 62.0, 60.2, 57.8, 33.1, 30.8, 30.7, 30.53, 30.46, 27.0, 23.8, 14.5.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of **2a**, **2b**, **10**−**15**, **18**−**20**, **22**, **24**−**31**, **33**−**36**, and **37**−**41a,b** and X-ray crystallographic data for **13**, **26**, and **29**. This material is available free of charge via the Internet at http://pubs.acs.org.

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