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Total Synthesis of Epothilone E and Related Side-chain Modified Analogues via a Stille Coupling Based Strategy†

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Abstract—A Stille coupling strategy has been utilized to complete a total synthesis of epothilone E from vinyl iodide **7** and thiazole-stannane **8h**. The central core fragment **7** and its *trans*-isomer **11** were prepared from triene **15** using ring-closing metathesis (RCM), and were subsequently coupled to a variety of alternative stannanes to provide a library of epothilone analogues **18a–o** and **19a–o**. The Stille coupling approach was then used to prepare epothilone B analogues from the key macrolactone intermediate **24** which was itself synthesized by a macrolactonization based strategy.

Introduction

The epothilones (**1–5**, Fig. 1)[1,2] have elicited widespread interest and excitement in both biological and chemical arenas due to their potent cytotoxicity, and more importantly, the mechanism by which they exert this effect. Like Taxol™, the epothilones promote the polymerization of α- and β-tubulin subunits and stabilize the resulting microtubule assembly.[1–4] Since microtubules play an important role in many cellular processes, including cell division, disruption of their regular behavior is detrimental and can ultimately result in cell death. Recent biological studies[3] have revealed that the epothilones are more potent than Taxol™, and more significantly, that they retain activity against both Taxol™-resistant and other multidrug-resistant cell lines. These important biological properties, coupled with their interesting and novel molecular structures have made the epothilones the target of numerous synthetic endeavors.[5–10] These studies have culminated in the total synthesis of epothilones A,[5a,c,6a–e,7] B,[5b,c,6c,e] C,[5a,c,6a–e,7] D[5b,c,6c,e] and E[6f] and of a large number of related analogues.[9,10]

We recently reported, in a preliminary communication,[6f] the first total synthesis of epothilone E (**3**) by a strategy in which the key step was a Stille coupling[11] between vinyl iodide **7** and the thiazole moiety (**8h**, Fig. 2a). The macrolactone core fragment **7**, which was prepared via ring-closing olefin metathesis (RCM),[12,13] could subsequently be used to provide convenient and flexible access to a variety of side-chain modified epothilone analogues (**9**) for biological evaluation (Fig. 2b). The RCM reaction used to access **7** also provided *trans*-macrolactone (**11**, Fig. 2b) which could serve as an alternative template for the Stille coupling process and provide an additional array of analogues of **10**.

We now wish to report a full account of the synthetic efforts involved in this work and to present an extension of the Stille coupling protocol to the synthesis of a number of side-chain modified analogues of epothilone B.

Results and Discussion

The chemical synthesis of the requisite vinyl iodides **7** and **11** is delineated in Scheme 1. Asymmetric allylboration of aldehyde **12**[14] [(+)-Ipc_2B(allyl), Et_2O, −100°C] using Brown's methodology[15] provided the enantiopure alcohol **13** in 91% yield. Subsequent coupling (DCC, 4-DMAP, toluene, 0 to 25°C) with a 3:2 mixture of alcohols **14a** and **14b** used in our previous synthesis of epothilone A[6a,d] afforded metathesis precursor **15a** (49% yield) and its readily separable 6*S*,7*R* diastereoisomer (**15b**, 33% yield, not shown). In an analogous fashion to our previous studies,[6a,c,d,f,10f] RCM was achieved using the ruthenium initiator

Key words: Epothilones; synthesis; Stille coupling; anticancer agents.
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† This paper is dedicated with admiration and respect to the memory of Sir Derek H. R. Barton.

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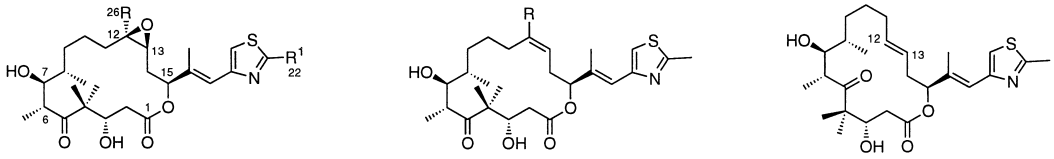


Figure 1. Structures and numbering of epothilones A–E and C12,13-*trans*-epothilone C.

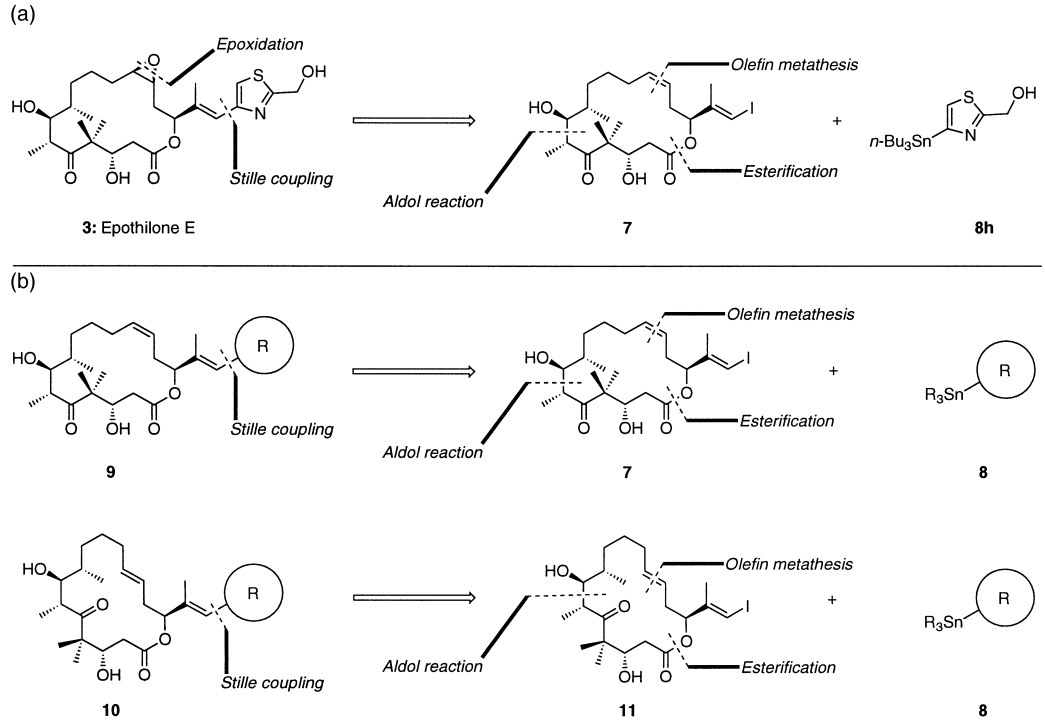


Figure 2. (a) Retrosynthetic analysis and strategy for the total synthesis of epothilone E (**3**) and (b) side-chain modified analogues of epothilone C (**9**) and its $\Delta^{12,13}$*trans*-isomer (**10**).

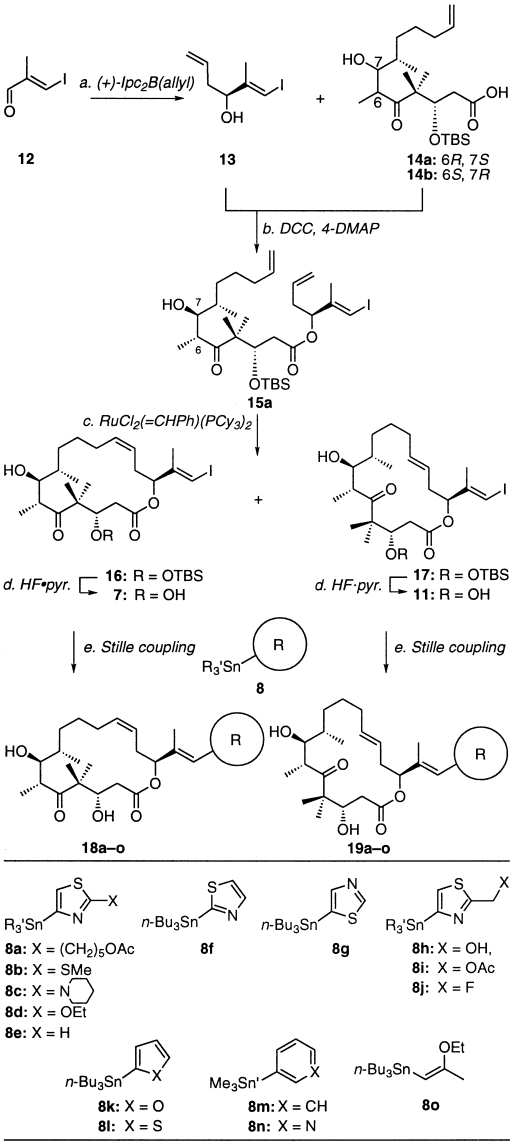
$[RuCl_2(=CHPh)(PCy_3)_2]$[13] (CH_2Cl_2, 25°C) to provide the *Z*- and *E*-macrolactones **16** (35%) and **17** (30%). Separation and subsequent deprotection (HF•pyr., THF, 25°C) of the individual isomers provided pure core structures **7** (84%) and **11** (85%), setting the stage for the all-important Stille coupling reaction.

The stannane coupling partners used in the Stille reaction are shown in Scheme 1. Thiazole stannanes **8k, 8l**, and **8o** were obtained from commercial sources, whereas stannanes **8e–8g**[16] and **8m,n**[17] were prepared using established procedures. The remaining coupling partners **8a–d, 8h–j**, and additional stannanes **8p–r** were prepared from readily accessible 2,4-dibromothiazole[18] (**20**) via monobromides **21** as outlined in Schemes 2 and 3. Thus, formation of thiazole **21a** (Scheme 2) was achieved via a three-step process commencing with a Sonogashira coupling[19] between dibromide **20** and pentyn-1-ol [$Pd(PPh_3)_4$, CuI, *i*-Pr_2NH, 70°C] to give an intermediate alkyne in 83% yield. Catalytic hydrogenation (H_2, PtO_2, EtOH, 25°C) and subsequent esterification (Ac_2O, pyr., CH_2Cl_2, 25°C) afforded the desired monobromide (**21a**) in 83% yield for two steps. Sulfide **21b** was obtained in 92% yield by replacing the 2-bromo substituent of **20** with the thiomethyl moiety using sodium thiomethoxide (EtOH, 25°C). Alternatively, reaction of dibromide **20** with piperidine at 50°C afforded thiazole **21c** in a quantitative yield. Finally, the ethoxy and methoxy thiazoles **21d** and **21p** were prepared by treating dibromide **20** with NaOH in ethanol and methanol, respectively. Bromides (**21a–c,p**) were then transformed to the desired trimethylstannanes (**8a–c,p**) with hexamethylditin under palladium catalyzed conditions ($Pd(PPh_3)_4$, toluene, 80–100°C), whereas tri-*n*-butylstannane **8d** was obtained from ethoxybromide **21d** by halogen–metal exchange (*n*-BuLi, Et_2O, −78°C) and subsequent trapping with tri-*n*-butyltin chloride in 98% yield.

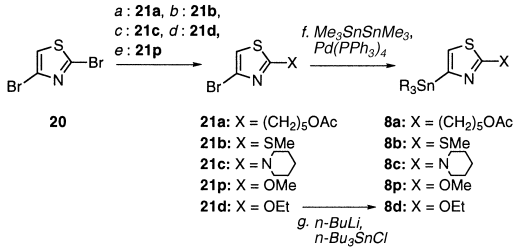
The synthesis of stannanes (**8h–j** and **8q–r**) was also achieved from the common precursor **20** (Scheme 3). Thus, palladium catalyzed alkenylation [*n*-$Bu_3SnCH{=}CH_2$, $Pd(PPh_3)_4$, toluene, 100°C] of 2,4-dibromothiazole **20** afforded monobromide **21q**, which underwent halogen–

metal exchange (*n*-BuLi, Et_2O, −78°C) and subsequent quenching with tri-*n*-butyltin chloride to furnish the desired stannane **8q**. Reduction of the intermediate vinyl bromide **21q** (H_2, PtO_2, EtOH, 25°C) provided access to ethyl thiazole **21r**, which was converted into stannane **8r** in an identical manner to that described for **8q**. The synthesis of stannanes **8h–j** was achieved via the key hydroxymethyl thiazole **21h**. This alcohol was itself obtained from dibromide **20** in a two-step process involving lithiation (*n*-BuLi, Et_2O, −78°C) and subsequent quenching with DMF to give intermediate aldehyde **22**, which was then reduced ($NaBH_4$, MeOH, 25°C) to furnish the desired alcohol **21h** in 63% overall yield. Conversion of **21h** into stannane **8h** required a three-step sequence involving protection of the hydroxyl group (TBSCl, imidazole, CH_2Cl_2, 96%), stannylation (i. *n*-BuLi, Et_2O, −78°C; ii. *n*-Bu_3SnCl, 85%) and subsequent deprotection (TBAF, THF, 25°C, 95%). Fluorination of the resulting stannane **8h** (DAST, CH_2Cl_2, −78°C) provided direct access to stannane **8j** in 57% yield. Esterification of the key alcohol **21h** (4-DMAP, Ac_2O, EtOAc, 25°C) afforded acetate **21i** which was converted into stannane **8i** with hexamethylditin [$Pd(PPh_3)_4$, toluene, 100°C] in 41% overall yield.

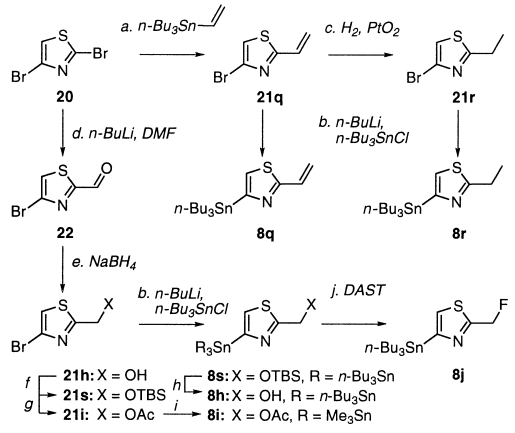
With the necessary components in hand, the critical Stille couplings could now be investigated. In the event, two alternative sets of reaction conditions proved



Scheme 1. Synthesis of common intermediates **7** and **11** and desoxyepothilones **18a–o** and **19a–o**. Reagents and conditions: (a) 1.3 equiv of (+)-Ipc_2B(allyl), Et_2O, −100°C, 0.5 h, 91%; (b) 2.0 equiv of **13**, 1.5 equiv of DCC, 1.5 equiv of 4-DMAP, toulene, 0→25°C, 12 h, 49% of **15a** plus 33% of its (6*S*,7*R*)-diastereoisomer **15b**; (c) 10 mol% of $RuCl_2(=CHPh)(PCy_3)_2$, CH_2Cl_2, 25°C, 30 h, 35% of **16** plus 30% of **17**; (d) 25% v/v HF•pyr. in THF, 25°C, 30 h, 84% of **7**; 85% of **11**; (e) procedure A: 2.0 equiv of **8**, 5–10 mol% $Pd(PPh_3)_4$, toulene, 90–100°C, 15–40 min, 39–88%; procedure B: 2.0–2.2 equiv of **8**, 20–30 mol% $Pd(MeCN)_2Cl_2$, DMF, 25°C, 12–33 h, 49–94%. TBS = *tert*-butyldimethylsilyl; DCC = dicyclohexylcarbodiimide; 4-DMAP = 4-dimethylaminopyridine; pyr. = pyridine.



Scheme 2. Preparation of stannanes **8a–d** and **8p**. Reagents and conditions: (a) i. 1.2 equiv of $HC{\equiv}C(CH_2)_3OH$, 0.05 equiv of $Pd(PPh_3)_4$, 0.1 equiv of CuI, *i*-Pr_2NH, 70°C, 2 h, 83%; ii. H_2, 0.1 equiv of PtO_2, EtOH, 25°C, 4 h, 100%; iii. 2.0 equiv of Ac_2O, 3.0 equiv of pyr., CH_2Cl_2, 25°C, 83%; (b) 3.0 equiv of NaSMe, EtOH, 25°C, 2 h, 92%; (c) piperidine (0.1 M), 50°C, 8 h, 100%; (d) 13 equiv of NaOH, EtOH, 25°C, 30 h, 91%; (e) 13 equiv of NaOH, MeOH, 25°C, 16 h, 82%; (f) 5–10 equiv of $Me_3SnSnMe_3$, 5–10 mol% of $Pd(PPh_3)_4$, toulene, 80–100°C, 0.5–3 h, 81–100%; (g) 1.1 equiv of *n*-BuLi, 1.2 equiv of *n*-Bu_3SnCl, −78→25°C, 30 min, 98%.



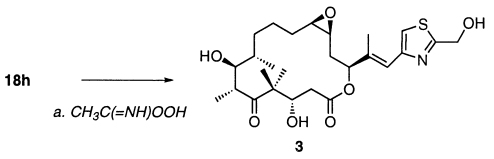
Scheme 3. Preparation of stannanes **8h–j** and **8q–s**. Reagents and conditions: (a) 1.05 equiv of *n*-$Bu_3SnCH{=}CH_2$, toluene, 100°C, 21 h, 83%; (b) 1.1–1.2 equiv of *n*-BuLi, 1.2–1.25 equiv of *n*-Bu_3SnCl, −78→25°C, 1 h, 28–85%; (c) H_2, 0.15 equiv of PtO_2, EtOH, 25°C, 4 h, 84%; (d) 1.2 equiv of *n*-BuLi, 2.0 equiv of DMF, −78→25°C, 2 h; (e) 1.9 equiv of $NaBH_4$, MeOH, 25°C, 30 min, 63% for two steps; (f) 1.3 equiv of TBSCl, 2.0 equiv of imidazole, CH_2Cl_2, 25°C, 0.5 h, 96%; (g) 1.2 equiv of 4-DMAP, 3.2 equiv of Ac_2O, EtOAc, 25°C, 5 min, 91%; (h) 1.2 equiv of TBAF, THF, 25°C, 20 min, 95%; (i) 10 equiv of $Me_3SnSnMe_3$, 7 mol% of $Pd(PPh_3)_4$, toulene, 100°C, 25 min, 45%; (j) 1.1 equiv of DAST, CH_2Cl_2, −78→25°C, 10 min, 57%. DAST = diethylamino sulfurtrifluoride; TBAF = tetra-*n*-butylammonium fluoride.

adequate (Scheme 1). Procedure A involved heating a toluene solution of the desired vinyl iodide (**7** or **11**) with the appropriate stannane **8** in the presence of catalytic $Pd(PPh_3)_4$ at 90–100°C for between 15 and 40 min. This protocol was used to couple stannanes **8a–c, 8e–i**, and **8n**. The remaining stannanes, **8d, 8j–m**, and **8o**[20] were coupled using an alternative, milder method, procedure B, in which a mixture of vinyl iodide (**7** or **11**) and stannane **8** in DMF was treated with $Pd(MeCN)_2Cl_2$ at 25°C.

The coupling of vinyl iodide **7** and stannane **8h** provided macrolactone **18h** which served as the precursor to the natural epothilone E (**3**) (Scheme 4). The total synthesis was completed by epoxidation with in situ generated methylperoxycarboximidic acid[21] (H_2O_2, $KHCO_3$, MeCN, MeOH, 25°C) furnishing epothilone E (**3**) (66% based on 50% conversion), which exhibited identical physical characteristics (^1H and ^{13}C NMR) to those kindly provided by Professor G. Höfle GBF, Braunshweig, Germany.

At this stage, we postulated that the Stille coupling approach could be extended to provide facile access to a variety of side-chain modified analogues of epothilone B (**2**). The impetus for this development was twofold. Firstly, epothilone B is the most active of the epothilones and, therefore, warranted further investigation. Secondly, the C26 position of this compound has already proven to be a fertile site for modification,[9b,10a,b] and we felt that analogues possessing a combination of these two variables could be interesting for further biological evaluation. The retrosynthetic analysis of epothilone analogues possessing these dual modifications is shown in Figure 3 and requires the preparation of the crucial vinyl iodide core fragment **24**. A macrolactonization strategy similar to that used in our synthesis of epothilone B[6b,c,e] and a variety of epothilone analogues[10a–c,e] was thought to be most suitable for this task.

The synthesis began from the vinyl iodide **13** (Scheme 5) which we had used in the preparation of epothilone E and related analogues (Scheme 1). Protection of the allylic hydroxyl group (TBSCl, imidazole, DMF, 0 to 25°C) afforded silyl ether **25** (84%) which was transformed into aldehyde **26** by a two-step dihydroxylation–glycol-cleavage sequence (OsO_4, NMO, THF/*t*-BuOH/H_2O, 0 to 25°C; then $NaIO_4$, MeOH/H_2O, 0°C, 82% for two steps). A stereocontrolled Wittig reaction with



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Scheme 4. Synthesis of epothilone E (**3**). Reagents and conditions: (a) 30 equiv of H_2O_2, 60 equiv of CH_3CN, 10 equiv of $KHCO_3$, MeOH, 25°C, 6 h, 66% (based on 50% conversion).

the stabilized ylide **27**[22] (benzene, reflux) afforded ester **28** as a single geometrical isomer in 98% yield. Reduction of the latter compound (DIBAL, THF, −78°C) afforded alcohol **29**, which was protected as the triphenylmethyl (trityl) derivative **30** (TrCl, 4-DMAP, DMF, 80°C, 95%). Elaboration of the terminal olefin was then achieved by selective hydroboration–oxidation to give alcohol **31** (9-BBN, THF, 0°C; then NaOH, H_2O_2, 0°C) which was transformed further into diiodide **32** (I_2, imidazole, Ph_3P, 0°C) in 92% overall yield. Introduction of the C8 stereocenter was then achieved using an Ender's alkylation protocol[23] (SAMP hydrazone of propionaldehyde, LDA, THF, 0°C; then −100°C and add **32** in THF) resulting in the formation of SAMP hydrazone **33** in 71% yield. Conversion to nitrile **34** (MMPP, MeOH/phosphate buffer pH 7, 0°C, 89%)[23e] and ensuing reduction (DIBAL, toluene, −78°C) afforded the desired aldehyde **35** in 88% yield.

The transformation of aldehyde **35** into the desired epothilone macrocyclic core **24** is summarized in Scheme 6. Aldol reaction of ketone **36**, previously used in our synthesis of epothilone B and related analogues[6e,10a–c,e] (LDA, THF, −78 to −40°C) and aldehyde **35**, afforded alcohols **37** and **38** in 66% overall yield, with modest selectivity for the desired 6*R*,7*S* diastereoisomer (**37**). Separation and silylation (TBSOTf, 2,6-lutidine, CH_2Cl_2, −20 to 0°C) of the correct aldol product **37** provided tris-silyl ether **39** in 90% yield. Selective removal of the primary silyl ether protecting group (HF•pyr. in pyr./THF, 0°C) afforded alcohol **40** (84%), which was oxidized to acid **42** via aldehyde **41** by a two-step procedure [Swern oxidation; then $NaClO_2$, 2-methyl-2-butene, NaH_2PO_4, *t*-BuOH/H_2O, 25°C, 98% for two steps). Removal of the C15 silicon protecting group (TBAF, THF, 0 to 25°C) provided hydroxy-acid **43** (95%) and laid the foundation for the macrolactonization process. This key step was achieved under

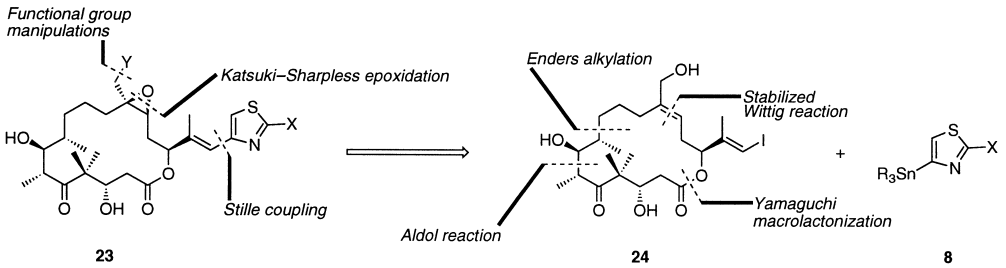

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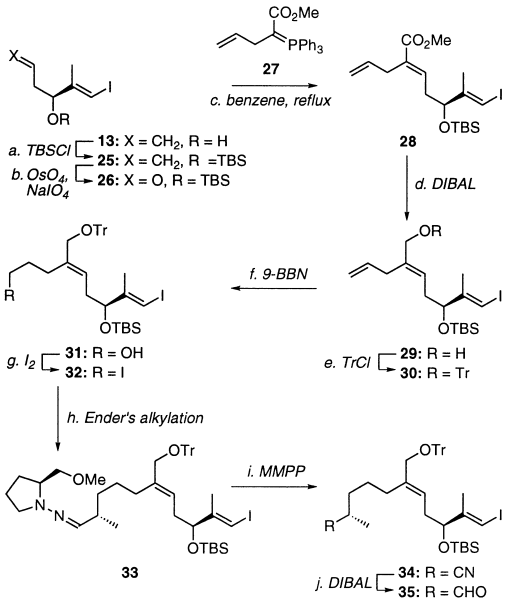
Figure 3. Retrosynthetic analysis of epothilone analogues possessing modified C-26 and side-chain moieties.

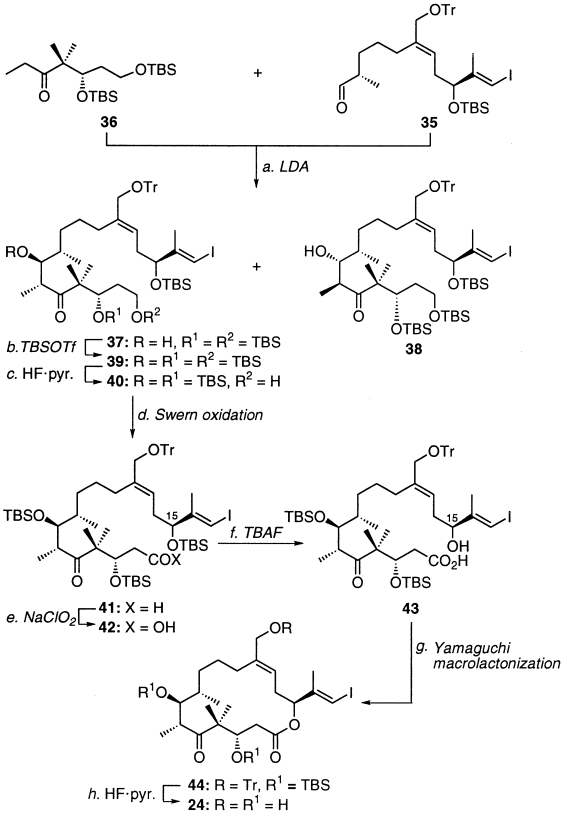
Yamaguchi conditions[24] (2,4,6-trichlorobenzoylchloride, Et_3N, THF; then add to a solution of 4-DMAP in toluene, 0.005 M, 75°C) to give the protected epothilone core **44** in 84% yield. Global deprotection (HF•pyr., THF, 0 to 25°C, 86%) completed the synthesis of the key vinyl iodide intermediate **24**.

With intermediate **24** in hand, the Stille coupling protocol could then be employed to attach the desired heterocyclic moiety. The mild procedure B, employing $Pd(MeCN)_2Cl_2$ was thought to be the most practical and efficient process and was utilized in the preparation of C26 hydroxy epothilones **45–48** (Scheme 7) from the vinyl iodide **24** and the appropriate stannanes **8** (see Schemes 2 and 3). Unfortunately, these conditions were not suitable for the coupling of **24** and vinyl stannane **8q** (see Scheme 3). Recourse to the alternative procedure A provided access to the desired epothilone **49**, albeit, in poor yield.

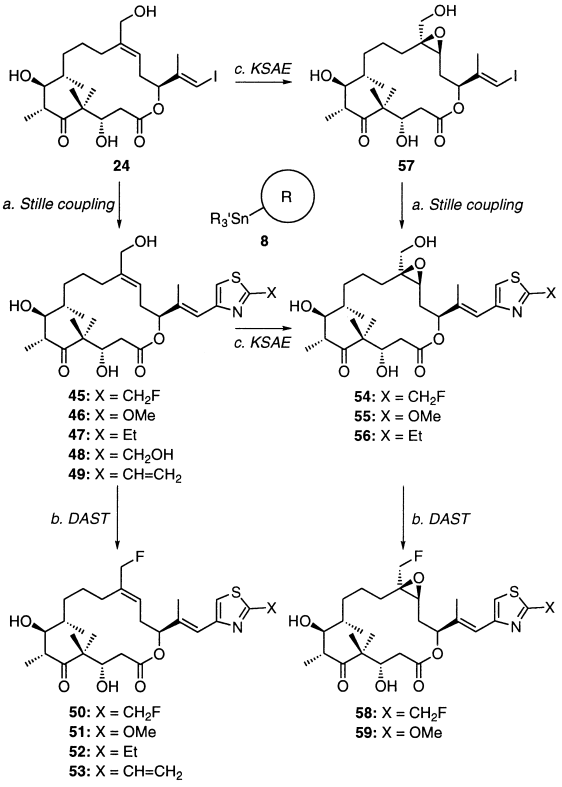
The presence of the C26 hydroxy functionality provided a convenient handle for further elaboration of the epothilone products. For example, the C26 alcohols **45–47** and **49** were treated with DAST (CH_2Cl_2, −78°C) to furnish fluorinated epothilone analogues **50–53** in moderate yields as shown in Scheme 7. Alternatively, asymmetric epoxidation of substrates **45** and **46** under Katsuki–Sharpless conditions[25] [(+)-DET, Ti(*i*-PrO)$_4$, *t*-BuOOH, 4Å molecular sieves, CH_2Cl_2, −40°C] afforded epothilones **54** and **55**, respectively. Subsequent treatment with DAST (CH_2Cl_2, −78°C) provided additional analogues **58** and **59**, again in moderate yield. At this juncture, a more efficient approach to epoxides such as **54** and **55** was envisaged in which asymmetric epoxidation of vinyl iodide **24** could provide a common intermediate, which could then serve as a substrate for the Stille coupling. Despite initial reservations concerning the compatibility of the epoxide functionality with the Stille conditions, the epoxide **57** required for this approach was prepared from olefin **24** in 81% yield as described for the synthesis of **45** and **46**. To our pleasant surprise, application of the standard coupling procedure B, using stannane **8r**, resulted in the successful preparation of epothilone analogue **56** (73% yield based on 70% conversion).



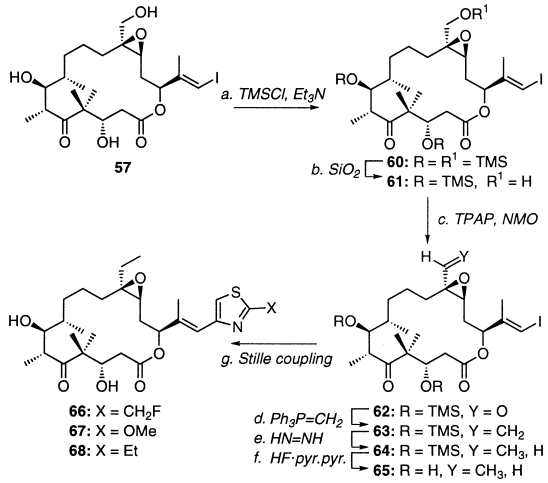
Scheme 5. Stereoselective synthesis of aldehyde **35**. Reagents and conditions: (a) 1.7 equiv of TBSCl, 2.8 equiv of imidazole, DMF, 0→25°C, 7 h, 84%; (b) i. 1.0 mol% OsO_4, 1.1 equiv of NMO, THF:*t*-BuOH:H_2O (5:5:1), 0→25°C, 13 h, 89%; ii. 6.0 equiv of $NaIO_4$, MeOH:H_2O (2:1), 0°C, 30 min, 92%; (c) 2.4 equiv of **27**, benzene, reflux, 1.2 h, 98%; (d) 3.0 equiv of DIBAL, THF, −78°C, 2.5 h, 100%; (e) 1.4 equiv of TrCl, 1.7 equiv of 4-DMAP, DMF, 80°C, 21 h, 95%; (f) 1.4 equiv of 9-BBN, THF, 0°C, 9 h; then 3 N aqueous NaOH and 30% H_2O_2, 0°C, 1 h, 95%; (g) 2.6 equiv of I_2, 5.0 equiv of imidazole, 2.5 equiv of Ph_3P, Et_2O:MeCN (3:1), 0°C, 45 min, 97%; (h) 1.3 equiv of SAMP hydrazone from propionaldehyde, 1.4 equiv of LDA, THF, 0°C, 16 h; then −100°C and add 1.0 equiv of **32** in THF, −100→−20°C, 20 h, 71%; (i) 2.5 equiv of MMPP, MeOH:phosphate buffer pH 7 (1:1), 0°C, 3.5 h, 89%; (j) 3.0 equiv of DIBAL, toluene, −78°C, 1 h, 88%. 9-BBN = 9-borabicyclo[3.3.1]nonane; DIBAL = diisobutylaluminium hydride; LDA = lithium diisopropylamide; NMO = 4-methylmorpholine *N*-oxide; SAMP = (*S*)-(−)-1-amino-2-(methoxymethyl)pyrrolidine; MMPP = monoperoxyphthalic acid, magnesium salt; Tr = triphenylmethyl.



Scheme 6. Stereoselective synthesis of vinyl iodide **24**. Reagents and conditions: (a) 1.45 equiv of LDA, THF, −78°C, then 1.4 equiv of **36** in THF, −78°C, 1.5 h then; −40°C, 0.5 h; then 1.0 equiv of **35** in THF at −78°C (66% combined yield, ca. 1.5:1 ratio of **37:38**); (b) 3.2 equiv of TBSOTf, 4.3 equiv of 2,6-lutidine, CH_2Cl_2, −20→0°C, 2.5 h, 90%; (c) HF•pyr. in pyr., THF, 0°C, 3 h, 84%; (d) 2.0 equiv of $(COCl)_2$, 4.0 equiv of DMSO, 6.0 equiv of Et_3N, CH_2Cl_2, −78→0°C, 1.5 h, 98%; (e) 5.0 equiv of $NaClO_2$, 75 equiv of 2-methyl-2-butene, 2.5 equiv of NaH_2PO_4, *t*-BuOH:H_2O (4.5:1), 25°C, 40 min, 100%; (f) 6.0 equiv of TBAF, THF, 0→25°C, 19 h, 95%; (g) 6.0 equiv of Et_3N, 2.4 equiv of 2,4,6-trichlorobenzoylchloride, THF, 0°C, 1.5 h; then add to a solution of 2.2 equiv of 4-DMAP in toluene (0.005 M based on **43**), 75°C, 2.5 h, 84%; (h) 25% v/v HF•pyr. in THF 0→25°C, 15 h, 86%.



Scheme 7. Synthesis of epothilone analogues **54–56** and **58, 59** and desoxyepothilones **45–49** and **50–53**. Reagents and conditions: (a) procedure A: 1.7 equiv of **8q**, 13 mol% $Pd(PPh_3)_4$, toluene, 100°C, 2 h, 15%; procedure B: 1.5–2.0 equiv of **8**, 10–20 mol% $Pd(MeCN)_2Cl_2$, DMF, 25°C, 15–33 h, 41–56%; (b) 1.05–1.4 equiv of DAST, CH_2Cl_2, −78°C, 10 min, 26–58%; (c) 0.5 equiv of (+)-DET, 0.5 equiv of Ti(*i*-PrO)$_4$, 2.2 equiv of *t*-BuOOH, −40°C, CH_2Cl_2, 4 Å molecular sieves, 1–2 h, 52–89%. DET = diethyl tartrate.



Scheme 8. Synthesis of C26-substituted epothilones **66–68**. Reagents and conditions: (a) 15 equiv of Et_3N, 8.0 equiv of TMSCl, DMF, 25°C, 12 h; (b) silica gel, CH_2Cl_2, 25°C, 12 h, 98% for two steps; (c) 3.0 equiv of NMO, 10 mol% TPAP, CH_2Cl_2, 25°C, 40 min, 90%; (d) 9.7 equiv of $Ph_3P^+CH_3Br^-$ (mixture with $NaNH_2$), THF, −5°C, 65% (e) 25 equiv of H_2NNH_2, 16 equiv of H_2O_2, EtOH, 0°C, 3 h; (f) HF•pyr.pyr. in THF, 0→25°C, 2 h, 75% for two steps; (g) 1.7–2.3 equiv of **8**, 20–30 mol% $Pd(MeCN)_2Cl_2$, DMF, 25°C, 15–23 h, 52–79%. TPAP = tetrapropylammonium perruthenate; TMS = trimethylsilyl.

The success of the Stille coupling strategy on substrates possessing an epoxide moiety indicated that epothilones **66–68** could be accessed from a common intermediate **65** as outlined in Scheme 8. Preparation of the desired template (**65**) was achieved by a six-step sequence, which started with global protection of triol **57** (TMSCl, Et_3N, DMF, 25°C). Selective deprotection, using silica gel (CH_2Cl_2, 25°C, 98% for two steps), revealed the C26 primary hydroxyl functionality which was then oxidized (TPAP, NMO, 4Å molecular sieves, CH_2Cl_2, 25°C)[26] to furnish aldehyde **62** in 90% yield. Methylenation[27] using methyl triphenylphosphonium bromide (Schlosser's 'instant ylid' mix, THF, −5°C) furnished olefin **63** (65%) which underwent reduction with in situ generated diimide[28] (H_2NNH_2, H_2O_2, EtOH, 0°C) to give intermediate **64**. Deprotection of the remaining silyl ethers (HF•pyr. in pyr./THF, 0°C) afforded the desired vinyl iodide **65** in 75% yield for two steps. The Stille coupling procedure B described above was then used to access epothilones **66–68** in moderate yields (Scheme 8).

Conclusion

The chemistry described herein relies on a Stille coupling approach to construct a series of epothilone analogues with diversity at the side-chain or at both the side chain and C26 site from a common macrocyclic intermediate. The synthesized epothilones are under biological evaluation and their tubulin polymerization and cytotoxicity properties will be reported in due course.

Experimental

General techniques

All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions, unless otherwise noted. Tetrahydrofuran (THF) and diethyl ether (ether) were distilled from sodium benzophenone, and dichloromethane (CH_2Cl_2), benzene (PhH), and toluene from calcium hydride. Anhydrous solvents were also obtained by passing them through commercially available activated alumina columns. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. All solutions used in work up procedures were saturated unless otherwise noted. All reagents were purchased at highest commercial quality and used without further purification unless otherwise stated.

All reactions were monitored by thin-layer chromatography carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as visualizing agent and 7% ethanolic phosphomolybdic acid or *p*-anisaldehyde solution and heat as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Preparative thin-layer chromatography separations were carried out on 0.25, 0.50, or 1 mm E. Merck silica gel plates (60F-254).

NMR spectra were recorded on Bruker DRX-600, AMX-500, AMX-400, or AC-250 instruments and

calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; band, several overlapping signals; b, broad. IR spectra were recorded on a Perkin–Elmer 1600 series FT-IR spectrometer. Optical rotations were recorded on a Perkin–Elmer 241 polarimeter. High resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer under fast atom bombardment (FAB) conditions.

Vinyl iodide 13. Allylmagnesium bromide (183 mL, 1 M in ether, 183 mmol, 1.3 equiv) was added dropwise, over 45 min, to a solution of (−)-$(Ipc)_2$BOMe (58.0 g, 183 mmol, 1.3 equiv) in ether (800 mL) at 0°C, and the resulting pale-gray slurry was allowed to warm to 25°C over 1 h. The ether was removed under reduced pressure and pentane (800 mL) was added to the residual solid. The resulting slurry was stirred at 25°C for 10 min and then the solids were allowed to settle over 30 min. The clear supernatant was then transferred carefully to a separate flask via cannula. This process was repeated four times (200 mL of pentane each) and the resulting solution was added dropwise, over 1 h, to a solution of aldehyde **12**[14] at −100°C. After 1 h at −100°C, MeOH (10 mL) was added and the mixture was allowed to warm to 25°C over 40 min. Saturated $NaHCO_3$ (125 mL) and H_2O_2 (50 mL of a 50% aqueous solution) were then added and the mixture was left to warm to 25°C over 12 h. The layers were separated and the aqueous phase was extracted with EtOAc (3×500 mL). The combined organic phases were washed with saturated aqueous NH_4Cl (500 mL), dried (Na_2SO_4), and concentrated under reduced pressure. Flash column chromatography (silica gel, 25% ether in hexanes) furnished vinyl iodide **13** (26.7 g, 80%). R_f = 0.31 (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ −18.4 (*c* 9.0, $CHCl_3$); IR (film) ν_{max} 3358, 3077, 2977, 2914, 1642, 1619, 1433, 1379, 1279, 1048, 997, 918 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.26 (s, 1H, IC*H* =C(CH_3)), 5.70 (dddd, *J* = 17.0, 10.0, 7.0, 7.0 Hz, 1H, CH_2=C*H*), 5.11 (dd, *J* = 17.0, 1.5 Hz, 1H, CH_2=CH), 5.10 (dd, *J* = 10.0, 1.5 Hz, 1H, CH_2=CH), 4.17 (dd, *J* = 7.5, 5.5 Hz, 1H, C*H*OH), 2.47 (bs, 1H, OH), 2.33 (ddd, *J* = 14.0, 7.0, 5.5 Hz, 1H, CH_2CH=), 2.26 (ddd, *J* = 14.0, 7.5, 7.0 Hz, 1H, CH_2CH=), 1.79 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 148.9, 133.6, 118.4, 78.5, 75.3, 39.6, 20.0.

Triene 15a and its 6*S*,7*R* diastereoisomer 15b. A solution of ketoacids **14** (414 mg, 1.0 mmol, 1.0 equiv) (ca. 3:2 ratio **14a:14b**), 4-(dimethylamino)pyridine (4-DMAP, 183 mg, 1.5 mmol, 1.5 equiv) and alcohol **13** (476 mg, 2.0 mmol, 2.0 equiv) in toluene (2.0 mL, 0.5 M) was cooled to 0°C and then treated with 1,3-dicyclohexylcarbodiimide (DCC, 309 mg, 1.5 mmol, 1.5 equiv). The reaction mixture was stirred at 25°C for 12 h, then concentrated under reduced pressure and the residue was partitioned between EtOAc (50 mL) and water (10 mL). The organic layer was separated, washed with saturated aqueous NH_4Cl (5 mL) and water (5 mL), and dried ($MgSO_4$). Evaporation of the solvents followed by flash column chromatography of the residue (silica gel, 15% EtOAc in hexanes) furnished trienes **15a** (318 mg, 49%) and **15b** (214 mg, 33%). **15a**: R_f = 0.60 (silica gel, 18% EtOAc in hexanes); $[\alpha]_D^{22}$ −16.1 (*c* 0.40, $CHCl_3$); IR (film) ν_{max} 3420, 2930, 2857, 1739, 1685, 1463, 1383, 1290, 1254, 1167, 1091, 995, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.33 (s, 1H, IC*H*=C(CH_3)), 5.86–5.78 (m, 1H, CH_2C*H*=CH_2), 5.68–5.58 (m, 1H, CH_2C*H*=CH_2), 5.31 (dd, *J* = 7.0, 7.0 Hz, 1H, CHOCO), 5.09 (dd, *J* = 16.5, 2.0 Hz, 1H, CH_2CH=CH_2), 5.06 (dd, *J* = 9.5, 2.0 Hz, 1H, CH_2CH=CH_2), 4.99 (dd, *J* = 17.0, 2.0 Hz, 1H, CH_2CH=CH_2), 4.92 (dd, *J* = 10.5, 2.0 Hz, 1H, CH_2CH=CH_2), 4.37 (dd, *J* = 5.5, 4.0 Hz, 1H, $(CH_3)_2$CC*H*(OTBS)), 3.37 (s, 1H, C*H*OH), 3.30–3.26 (s, 1H, CHO*H*), 3.28 (q, *J* = 7.0 Hz, 1H, CH_3C*H*(C=O)), 2.79 (dd, *J* = 17.0, 5.5 Hz, 1H, CH_2COO), 2.43 (dd, *J* = 17.0, 4.0 Hz, 1H, CH_2COO), 2.43–2.33 (m, 2H), 2.11–1.98 (m, 2H), 1.81 (s, 3H, ICH=CCH_3), 1.81–1.72 (m, 1H), 1.58–1.40 (m, 2H), 1.37–1.27 (m, 1H), 1.20–1.05 (m, 1H), 1.19 (s, 3H, C(CH_3)$_2$), 1.10 (s, 3H, C(CH_3)$_2$), 1.03 (d, *J* = 6.5 Hz, 3H, CH_3CH(C=O)), 0.87 (s, 9H, SiC(CH_3)$_3$(CH_3)$_2$), 0.83 (d, *J* = 7.0 Hz, 3H, CH_3CHCH_2), 0.10 (s, 3H, SiC(CH_3)$_3$(CH_3)$_2$), 0.04 (s, 3H, SiC(CH_3)$_3$(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 221.8, 170.7, 144.7, 139.1, 132.4, 118.3, 114.2, 81.2, 77.0, 74.6, 73.4, 53.8, 41.3, 40.1, 37.1, 35.4, 34.2, 32.4, 26.1, 25.9, 22.0, 20.1, 19.8, 18.1, 15.3, 9.7, −4.4, −4.8; HRMS (FAB), calcd for $C_{30}H_{53}IO_5Si$ ($M+Cs^+$) 781.1761, found 781.1770. **15b**: R_f = 0.36 (silica gel, 17% EtOAc in hexanes); $[\alpha]_D^{22}$ −20.4 (*c* 0.83, $CHCl_3$); IR (film) ν_{max} 3512, 3076, 2932, 2858, 1740, 1690, 1465, 1381, 1290, 1254, 1171, 1089, 986, 916, 835 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.33 (s, 1H, IC*H*=C(CH_3)), 5.80 (dddd, *J* = 17.0, 10.0, 6.5, 6.5 Hz, 1H, CH_2C*H*=CH_2), 5.63 (dddd, *J* = 17.0, 10.0, 7.0, 7.0 Hz, 1H, CH_2C*H*=CH_2), 5.31 (dd, *J* = 7.0, 7.0 Hz, 1H, CHOCO), 5.11–5.06 (m, 2H, CH_2CH=CH_2), 5.01 (dd, *J* = 17.0, 2.0 Hz, 1H, CH_2CH=CH_2), 4.96 (dd, *J* = 10.0, 1.0 Hz, 1H, CH_2CH=CH_2), 4.46 (dd, *J* = 6.5, 4.0 Hz, 1H, $(CH_3)_2$CC*H*(OTBS)), 3.41 (m, 1H, C*H*OH) 3.33 (s, 1H, OH), 3.21 (qd, *J* = 7.0, 2.0 Hz, 1H, CH_3C*H*(C=O)), 2.46–2.30 (m, 4H), 2.12–1.98 (m, 2H), 1.81 (s, 3H, ICH=CCH_3), 1.60–1.33 (m, 5H), 1.15 (s, 3H, C(CH_3)$_2$), 1.11 (s, 3H, C(CH_3)$_2$), 1.03 (d, *J* = 7.0 Hz, 3H, CH_3CH(C=O)), 0.99 (d, *J* = 6.5 Hz, 3H, CH_3CHCH_2) 0.86 (s, 9H, SiC(CH_3)$_3$(CH_3)$_2$), 0.08 (s, 3H, SiC(CH_3)$_3$(CH_3)$_2$), 0.04 (s, 3H, SiC(CH_3)$_3$(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 221.0, 170.8, 144.7, 138.7, 132.4, 118.3, 114.6, 81.2, 77.0, 74.8, 72.6, 53.9, 41.4, 40.1, 37.1, 35.3, 33.9, 32.1, 26.0, 25.9, 21.9, 20.1, 19.7, 18.2, 15.6, 10.7, −4.3, −4.7; HRMS (FAB), calcd for $C_{30}H_{53}IO_5Si$ ($M+Cs^+$) 781.1761, found 781.1735.

Macrolactones 16 and 17. To a solution of triene **15a** (649 mg, 1.0 mmol, 1.0 equiv) in CH_2Cl_2 (250 mL, 0.004 M) was added bis(tricyclohexylphosphine)benzylidine ruthenium dichloride ($RuCl_2$(=CHPh)(PCy_3)$_2$) (82 mg, 0.10 mmol, 0.1 equiv) and the reaction mixture was stirred at 25°C for 30 h. After completion of the reaction (established by TLC), the solvent was removed under reduced pressure and the crude products were purified by flash column chromatography (silica gel, 20% EtOAc in hexanes) to give *cis*-hydroxy lactone **16** (217 mg, 35%) and *trans*-hydroxy lactone **17** (186 mg, 30%). **16**: R_f = 0.47 (silica gel, 18% EtOAc in hexanes);

$[\alpha]_D^{22}$ −44.5 (*c* 0.40, $CHCl_3$); IR (thin film) ν_{max} 3416, 2929, 2856, 1745, 1694, 1463, 1384, 1254, 1158, 1096, 1067, 980, 828, 778 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.37 (s, 1H, IC*H*=C(CH_3)), 5.45 (ddd, *J* = 10.5, 10.5, 2.0 Hz, 1H, C*H*=$CHCH_2$), 5.30 (ddd, *J* = 10.5, 10.5, 4.0 Hz, 1H, C*H* = $CHCH_2$), 5.08 (d, *J* = 10.5 Hz, 1H, CHOCO), 4.07 (dd, *J* = 6.5, 6.5 Hz, 1H, $(CH_3)_2CCH$ (OTBS)), 3.94–3.90 (m, 1H, C*H*OH($CHCH_3$)), 3.03 (qd, *J* = 6.5, 3.0 Hz, 1H, CH_3CH(C=O)), 2.98 (bs, 1H, OH), 2.77 (d, *J* = 6.5 Hz, 1H, CH_2COO), 2.76 (d, *J* = 6.5 Hz, 1H, CH_2COO), 2.69 (ddd, *J* = 14.5, 11.0, 11.0 Hz, 1H, =CHC*H*$_2$CHO), 2.33–2.24 (m, 1H), 2.05–1.92 (m, 2H), 1.86 (s, 3H, ICH=CC*H*$_3$), 1.81–1.72 (m, 1H), 1.68–1.58 (m, 1H), 1.47–1.40 (m, 1H), 1.28–1.08 (m, 2H), 1.19 (s, 3H, C(CH_3)$_2$), 1.18 (s, 3H, C(CH_3)$_2$), 1.13 (d, *J* = 6.5 Hz, 3H, C*H*$_3$CH(C=O)), 1.01 (d, *J* = 7.0 Hz, 3H, C*H*$_3$$CHCH_2$), 0.82 (s, 9H, SiC(C*H*$_3$)$_3$($CH_3$)$_2$), 0.12 (s, 3H, SiC($CH_3$)$_3$(C*H*$_3$)$_2$), 0.07 (s, 3H, SiC($CH_3$)$_3$(C*H*$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 217.6, 170.5, 145.8, 134.9, 123.3, 80.1, 77.4, 76.2, 73.2, 53.6, 43.1, 39.0, 38.8, 33.6, 31.6, 28.4, 27.9, 26.2, 24.8, 23.0, 20.6, 18.7, 16.5, 14.2, −3.5, −5.2; HRMS (FAB), calcd for $C_{28}H_{49}IO_5Si$ ($M + Cs^+$) 753.1448, found 753.1458. **17**: R_f = 0.53 (silica gel, 18% EtOAc in hexanes); $[\alpha]_D^{22}$ −21.0 (*c* 0.40, $CHCl_3$); IR (thin film) ν_{max} 3384, 2927, 2856, 1743, 1693, 1462, 1384, 1255, 1160, 1095, 836, 777 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.33 (s, 1H, IC*H*=C(CH_3)), 5.42 (ddd, *J* = 15.5, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 5.23 (ddd, *J* = 15.5, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 5.23 (d, *J* = 7.5 Hz, 1H, CHOCO), 4.26 (dd, *J* = 8.5, 3.5 Hz, 1H, $(CH_3)_2CCH$(OTBS)), 3.81–3.77 (m, 1H, C*H*OH($CHCH_3$)), 3.07 (qd, *J* = 7.0, 3.5 Hz, 1H, CH_3CH(C=O)), 3.04 (bs, 1H, OH), 2.71 (dd, *J* = 16.5, 8.5 Hz, 1H, CH_2COO), 2.65 (dd, *J* = 16.5, 3.5 Hz, 1H, CH_2COO), 2.43–2.30 (m, 2H), 2.13–2.00 (m, 2H), 1.87–1.78 (m, 1H), 1.86 (s, 3H, ICH=CC*H*$_3$), 1.76–1.66 (m, 1H), 1.64–1.52 (m, 1H), 1.40–1.30 (m, 2H), 1.18 (s, 3H, C(CH_3)$_2$), 1.17 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH(C=O)), 1.12 (s, 3H, C(CH_3)$_2$), 0.99 (d, *J* = 7.0 Hz, 3H, C*H*$_3$$CHCH_2$), 0.85 (s, 9H, SiC(C*H*$_3$)$_3$($CH_3$)$_2$), 0.13 (s, 3H, SiC(C*H*$_3$)$_3$(C*H*$_3$)$_2$), 0.01 (s, 3H, SiC($CH_3$)$_3$(C*H*$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.8, 169.9, 145.0, 134.6, 124.5, 78.9, 76.4, 74.4, 74.0, 54.3, 42.5, 40.3, 38.7, 36.1, 32.8, 32.6, 26.3, 22.0, 21.4, 18.7, 16.2, 13.8, −3.7, −4.6; HRMS (FAB), calcd for $C_{28}H_{49}IO_5Si$ ($M + Cs^+$) 753.1148, found 753.1456.

***cis*-Macrolactone diol 7.** To a solution of iodide **16** (305 mg, 0.491 mmol) in THF (8.2 mL, 0.06 M) at 25°C was added HF•pyr. (2.7 mL) and the resulting solution was stirred at the same temperature for 27 h. The reaction was then quenched by careful addition to a mixture of saturated aqueous $NaHCO_3$ (100 mL) and EtOAc (100 mL), and the resulting two-phase mixture was stirred at 25°C for 2 h. The extracts were then separated and the organic layer was washed with saturated aqueous $NaHCO_3$ (100 mL) and brine (100 mL), and then dried ($MgSO_4$). Purification by flash column chromatography (silica gel, 20→50% EtOAc in hexanes) furnished diol **7** (208 mg, 84%). R_f = 0.21 (silica gel, 25% EtOAc in hexanes); $[\alpha]_D^{22}$ −53.1 (*c* 1.37, $CHCl_3$); IR (thin film) ν_{max} 3499, 2930, 1732, 1688, 1469, 1379, 1259, 1149, 1093, 1048, 1006, 732 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.43 (s, 1H, IC*H*=C(CH_3)), 5.44 (ddd, *J* = 10.5, 10.5, 4.5 Hz, 1H, C*H*=$CHCH_2$), 5.34 (dd, *J* = 9.5, 2.0 Hz, 1H, CHOCO), 5.32 (ddd, *J* = 10.5, 10.5, 5.5 Hz, 1H, C*H* = $CHCH_2$), 4.07 (ddd, *J* = 11.0, 6.0, 3.0 Hz, 1H, $(CH_3)_2CCH$(OH)), 3.73 (ddd, *J* = 2.5, 2.5, 2.5 Hz, 1H, C*H*OH($CHCH_3$)), 3.10 (qd, J = 7.0, 2.5 Hz, 1H, CH_3CH(C=O)), 2.84 (d, *J* = 2.5 Hz, 1H, $CH(CH_3)CHOHCH(CH_3)$), 2.66 (ddd, *J* = 15.0, 9.5, 9.5 Hz, 1H, =CHC*H*$_2$CHO), 2.51 (dd, *J* = 15.5, 11.0 Hz, 1H, CH_2COO), 2.42 (dd, *J* = 15.5, 3.0 Hz, 1H, CH_2COO), 2.35 (d, *J* = 6.0 Hz, 1H, $(CH_3)_2CHOH$), 2.21–2.12 (m, 2H), 2.05–1.97 (m, 1H), 1.88 (s, 3H, ICH=C(C*H*$_3$)), 1.76–1.70 (m, 1H), 1.70–1.62 (m, 1H), 1.32 (s, 3H, C(CH_3)$_2$), 1.18 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH(C=O)), 1.10 (s, 3H, C(CH_3)$_2$), 1.35–1.05 (m, 3H), 0.99 (d, *J* = 7.0 Hz, 3H, C*H*$_3$$CHCH_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 219.9, 170.0, 145.3, 133.8, 124.0, 80.2, 77.3, 74.1, 72.8, 52.7, 42.0, 38.8, 38.4, 32.5, 31.2, 27.5, 27.4, 22.2, 20.8, 19.7, 15.5, 13.6; HRMS (FAB), calcd for $C_{22}H_{35}IO_5$ ($M + Cs^+$) 639.0584, found 639.0557.

***trans*-Macrolactone diol 11.** A solution of iodide **17** (194 mg, 0.313 mmol) in THF (5.2 mL, 0.06 M) was treated with HF•pyr. (1.7 mL) according to the procedure described for the preparation of diol **7** to afford, after flash column chromatography (silica gel, 20→50% EtOAc in hexanes), diol **11** (134 mg, 85%). R_f = 0.16 (silica gel, 25% EtOAc in hexanes); $[\alpha]_D^{22}$ −20.0 (*c* 1.15, $CHCl_3$); IR (film) ν_{max} 3478, 2930, 1732, 1693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.37 (d, *J* = 1.5 Hz, 1H, IC*H*=C(CH_3)), 5.35 (ddd, *J* = 14.5, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 5.24 (ddd, *J* = 14.5, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 5.17 (dd, *J* = 6.5, 3.5 Hz, 1H, CHOCO), 4.41 (dd, *J* = 8.0, 3.5 Hz, 1H, $(CH_3)_2CCH$(OTBS)), 3.85 (bs, 1H, C*H*OH($CHCH_3$)), 3.38 (bs, 1H, CHO*H*($CHCH_3$)), 3.18 (qd, *J* = 7.0, 6.5 Hz, 1H, CH_3CH(C=O)), 2.68–2.34 (m, 4H), 2.44 (s, 3H, CH_3Ar), 2.19–2.11 (m, 1H), 1.96 (s, 3H, ICH = C(C*H*$_3$)), 1.99–1.93 (m, 1H), 1.67–1.52 (m, 2H), 1.48–1.42 (m, 1H), 1.31–0.99 (m, 2H), 1.22 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH(C=O)), 1.14 (s, 3H, C(CH_3)$_2$), 1.09 (s, 3H, C(CH_3)$_2$), 1.02 (d, *J* = 7.0 Hz, 3H, C*H*$_3$$CHCH_2$), 0.84 (s, 9H, SiC(C*H*$_3$)$_3$($CH_3$)$_2$), 0.08 (s, 3H, SiC($CH_3$)$_3$(C*H*$_3$)$_2$), −0.01 (s, 3H, SiC($CH_3$)$_3$(C*H*$_3$)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 218.3, 170.1, 160.9, 137.5, 136.3, 135.2, 134.6, 125.0, 115.8, 77.1, 75.1, 74.1, 54.0, 43.6, 40.7, 38.4, 35.3, 32.9, 30.9, 26.8, 26.1, 23.2, 21.8, 18.4, 16.8, 16.2, 14.6, 13.7, −3.9, −4.5; HRMS (FAB), calcd for $C_{22}H_{35}IO_5$ ($M + Cs^+$) 639.0584, found 639.0606.

Bromothiazole 21a. To a solution of 2,4-dibromothiazole **20**[18] (400 mg, 1.6 mmol, 1.0 equiv) in *i*-Pr_2NH (3.0 mL, 0.5 M) was added 4-pentyn-1-ol (270 mg, 3.2 mmol, 2.0 equiv), $Pd(PPh_3)_4$ (95 mg, 0.082 mmol, 0.05 equiv), and CuI (30 mg, 0.16 mmol, 0.1 equiv). The reaction mixture was then heated at 70°C for 2 h and, after cooling to 25°C, the solvents were removed under reduced pressure. Flash column chromatography (silica gel, 10→75% EtOAc in hexanes) furnished alkyne **69** (326 mg, 83%). R_f = 0.50 (silica gel, 100% ether); IR (film) ν_{max} 3377, 3118, 2933, 2876, 2230, 1458, 1258, 1206, 1075 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (s,

1H, ArH), 3.79 (t, $J=6.0$ Hz, 2H, CH_2OH), 2.60 (t, $J=7.0$ Hz, 2H, $CH_2(CH_2)_2OH$), 1.98 (bs, 1H, OH), 1.87 (tt, $J=7.0$, 6.0 Hz, 2H, CH_2CH_2OH); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 150.0, 125.2, 117.7, 97.2, 73.5, 61.1, 30.4, 15.9; HRMS (FAB), calcd for C_8H_8NOS ($M+H^+$) 245.9588, found 245.9597.

A solution of alkyne **69** (70 mg, 0.280 mmol, 1.0 equiv) and PtO_2 (6.5 mg, 0.028 mmol, 0.1 equiv) in EtOH (2 mL) was stirred at 25°C under an atmosphere of hydrogen for 4 h. Subsequent filtration through a short plug of silica gel, eluting with EtOAc, and removal of the solvents under reduced pressure furnished alcohol **70** (70 mg, 100%). $R_f=0.40$ (silica gel, 100% ether); IR (film) ν_{max} 3356, 3122, 2929, 2858, 1480, 1257, 1056 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.07 (s, 1H, ArH), 3.64 (t, $J=6.5$ Hz, 2H, CH_2OH), 3.00 (t, $J=7.5$ Hz, 2H, $CH_2(CH_2)_4OH$), 1.81 (tt, $J=8.0$, 7.5 Hz, 2H, $CH_2(CH_2)_3OH$), 1.74 (bs, 1H, OH), 1.60 (tt, $J=7.0$, 6.5 Hz, 2H, CH_2CH_2OH), 1.46 (tt, $J=8.0$, 7.0 Hz, $CH_2(CH_2)_2OH$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 142.1, 124.1, 115.7, 62.5, 33.4, 32.2, 29.4, 25.1; HRMS (FAB), calcd for $C_8H_{12}BrNOS$ ($M+H^+$) 249.9901, found 249.9907.

A solution of alcohol **70** (25 mg, 0.100 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL, 0.1 M), was treated with pyridine (16 μL, 0.200 mmol, 2.0 equiv) and Ac_2O (28 μL, 0.299 mmol, 3.0 equiv). The resulting mixture was stirred at 25°C until the completion of the reaction was established by TLC. The mixture was then partitioned between water (10 mL) and CH_2Cl_2 (10 mL) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2×10 mL) and the combined extracts were concentrated under reduced pressure and purified by flash column chromatography (silica gel, 10→40% ether in hexanes) to furnish the desired bromothiazole **21a** (24 mg, 83%). $R_f=0.60$ (silica gel, 50% ether in hexanes); IR (film) ν_{max} 3116, 2940, 2861, 1736, 1480, 1366, 1243, 1047, 888 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.08 (s, 1H, ArH), 4.05 (t, $J=6.5$ Hz, 2H, CH_2OAc), 2.99 (t, $J=7.5$ Hz, 2H, $CH_2(CH_2)_4OAc$), 2.03 (s, 3H, $COCH_3$), 1.81 (tt, $J=8.0$, 7.5 Hz, 2H, $CH_2(CH_2)_3OAc$), 1.66 (tt, $J=8.0$, 6.5 Hz, 2H, CH_2CH_2OAc), 1.45 (tt, $J=8.0$, 7.5 Hz, 2H, $CH_2(CH_2)_2OAc$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 172.1, 137.1, 124.1, 115.7, 64.1, 33.3, 29.3, 28.2, 25.3, 20.9; HRMS (FAB), calcd for $C_{10}H_{14}BrNO_2S$ ($M+H^+$) 292.0007, found 292.0016.

2-Thiomethyl-4-bromothiazole 21b. 2,4-Dibromothiazole **20**[18] (82 mg, 0.34 mmol, 1.0 equiv) was dissolved in ethanol (2.3 mL, 0.15 M) and treated with sodium thiomethoxide (75 mg, 1.02 mmol, 3.0 equiv). The reaction mixture was stirred at 25°C for 2 h, upon which time completion of the reaction was established by ^1H NMR. The mixture was poured into water (5 mL) and extracted with ether (2×5 mL). The combined organic extracts were dried ($MgSO_4$), the solvents evaporated, and the residue purified by flash column chromatography (silica gel, 5% EtOAc in hexanes) to furnish 2-thiomethyl-4-bromothiazole **21b** (77 mg, 92%). $R_f=0.58$ (silica gel, 10% EtOAc in hexanes); IR (film) ν_{max} 3118, 2926, 1459, 1430, 1388, 1242, 1040, 966, 876, 818 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.07 (s, 1H, ArH), 2.69 (s, 3H, SCH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 167.9, 124.2, 115.5, 16.6; GC–MS (EI), calcd for $C_4H_4BrNS_2$ (M^+) 209/211, found 209/211.

2-Piperidinyl-4-bromothiazole 21c. 2,4-Dibromothiazole **20**[18] (184 mg, 0.76 mmol, 1.0 equiv) was dissolved in piperidine (1.5 mL, 0.5 M) and the reaction mixture heated at 50°C for 8 h, upon which time completion of the reaction was indicated by TLC. The mixture was poured into water (5 mL) and extracted with ether (2×5 mL). After drying the combined organic fractions ($MgSO_4$), evaporation of the solvents, and purification by flash column chromatography (silica gel, 5% EtOAc in hexanes) furnished 2-piperidinyl-4-bromothiazole **21c** (188 mg, 100%). $R_f=0.52$ (silica gel, 10% EtOAc in hexanes); mp 66°C (EtOAc–hexanes); IR (film) ν_{max} 3088, 2940, 2852, 1530, 1482, 1447, 1263 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.35 (s, 1H, ArH), 3.42 (bt, $J=5.5$ Hz, 4H, $CH_2(CH_2CH_2)_2N$), 1.66–1.62 (m, 6H, $CH_2(CH_2CH_2)_2N$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.8, 121.5, 102.8, 49.1, 24.9, 23.9; HRMS (FAB), calcd for $C_8H_{11}BrN_2S$ ($M+H^+$) 246.9904, found 246.9910.

2-Ethoxy-4-bromothiazole 21d. To a solution of 2,4-dibromothiazole **20**[18] (58 mg, 0.239 mmol, 1.0 equiv) in EtOH (2.4 mL, 0.1 M) was added NaOH (122 mg, 3.05 mmol, 12.8 equiv) and the resulting solution was stirred at 25°C until TLC indicated the disappearance of dibromide (ca. 30 h). The resulting yellow solution was then partitioned between ether (10 mL) and saturated aqueous NH_4Cl (10 mL) and the layers were separated. The aqueous layer was extracted with ether (10 mL) and the combined organic extracts were washed with brine (20 mL), dried ($MgSO_4$) and concentrated carefully under reduced pressure. Flash column chromatography (silica gel, 17% ether in hexanes) furnished 2-ethoxy-4-bromothiazole **21d** as a volatile oil (45 mg, 91%). $R_f=0.58$ (silica gel, 17% ether in hexanes); IR (film) ν_{max} 3125, 2983, 2936, 2740, 1514, 1480, 1392, 1360, 1277, 1234, 1080, 1018, 897, 823 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1H, ArH), 4.48 (q, $J=7.0$ Hz, 2H, CH_3CH_2), 1.43 (t, $J=7.0$ Hz, 3H, CH_3CH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 174.2, 118.5, 107.8, 68.3, 14.3; GC–MS (EI), calcd for C_4H_4BrNSO (M^+) 193/195, found 193/195.

2-Methoxy-4-bromothiazole 21p. To a solution of 2,4-dibromothiazole **20**[18] (253 mg, 1.04 mmol, 1.0 equiv) in MeOH (10.5 mL, 0.1 M) was added NaOH (555 mg, 13.9 mmol, 13.3 equiv) and the resulting solution was stirred at 25°C until TLC indicated the disappearance of dibromide (ca. 16 h). The resulting yellow solution was then partitioned between ether (10 mL) and saturated aqueous NH_4Cl (10 mL) and the layers were separated. The aqueous phase was extracted with ether (10 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated carefully under reduced pressure. Flash column chromatography (silica gel, 10% ether in hexanes) furnished 2-methoxy-4-bromothiazole **21p** as a volatile oil (138 mg, 82%). $R_f=0.56$ (silica gel, 17% ether in hexanes); IR (film) ν_{max} 3125, 2952, 2752, 1524,

1520, 1481, 1417, 1277, 1238, 1081, 982, 884, 819 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 1H, ArH), 4.09 (s, 3H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 174.8, 118.5, 108.4, 58.8; GC–MS (EI), calcd for C_5H_6BrNSO (M^+) 207/209, found 207/209.

2-Hydroxymethyl-4-bromothiazole 21h. To a solution of 2,4-dibromothiazole **20**[18] (50 mg, 0.206 mmol, 1.0 equiv) in anhydrous ether (2.0 mL, 0.1 M) at −78°C, was added *n*-BuLi (154 μL, 1.6 M in hexanes, 0.247 mmol, 1.2 equiv), and the resulting solution was stirred at the same temperature for 30 min. DMF (32 μL, 0.412 mmol, 2.0 equiv) was then added at −78°C and, after being stirred at −78°C for 30 min, the reaction mixture was slowly warmed up to 25°C over a period of 2 h. Hexane (2.0 mL) was added and the resulting mixture was passed through a short silica gel cake eluting with 30% EtOAc in hexanes. The solvents were evaporated to give the crude aldehyde **22** (50 mg), which was used directly in the next step.

To a solution of aldehyde **22** (50 mg) in methanol (2.0 mL) at 25°C, was added sodium borohydride (15 mg, 0.397 mmol, 1.9 equiv), and the resulting mixture was stirred at the same temperature for 30 min. EtOAc (1.0 mL) and hexane (2.0 mL) were added, and the mixture was passed through a short silica gel cake eluting with EtOAc. The solvents were then evaporated and the crude product was purified by flash column chromatography (silica gel, 20→50% EtOAc in hexanes) to furnish 2-hydroxymethyl-4-bromothiazole **21h** (25 mg, 63% over two steps). R_f = 0.16 (silica gel, 18% EtOAc in hexanes); IR (film) ν_{max} 3288, 3122, 2922, 2855, 1486, 1447, 1345, 1250, 1183, 1085, 1059, 967, 893 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.20 (s, 1H, ArH), 4.93 (s, 2H, CH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 173.0, 124.4, 117.0, 61.8; HRMS (FAB), calcd for C_4H_4BrNOS ($M+H^+$) 193.9275, found 193.9283.

2-(*tert*-Butyldimethylsilyloxymethyl)-4-bromothiazole 21s. To a solution of alcohol **21h** (59 mg, 0.304 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL, 0.3 M) was added imidazole (62 mg, 0.608 mmol, 2.0 equiv), followed by *tert*-butyldimethylchlorosilane (69 mg, 0.456 mmol, 1.3 equiv) at 25°C. After 30 min at 25°C, the reaction mixture was quenched with MeOH (100 μL) and then passed through silica gel eluting with CH_2Cl_2. Evaporation of solvents gave the desired silyl ether **21s** (90 mg, 96%). R_f = 60 (silica gel, 10% EtOAc in hexanes); IR (film) ν_{max} 2943, 2858, 1489, 1465, 1355, 1254, 1193, 1108, 887, 841, 780 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 1H, ArH), 4.93 (s, 2H, CH_2), 0.94 (s, 9H, $SiC(CH_3)_3(CH_3)_2$), 0.12 (s, 6H, $SiC(CH_3)_3(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 174.5, 124.2, 116.4, 62.9, 25.7, 18.2, −5.5; HRMS (FAB), calcd for $C_{10}H_{18}BrNOSSi$ ($M+H^+$) 308.0140, found 308.0151.

2-Acetoxymethyl-4-bromothiazole 21i. To a solution of alcohol **21h** (37 mg, 0.191 mmol, 1.0 equiv) in EtOAc (2.0 mL, 0.1 M) was added Ac_2O (58 μL, 0.618 mmol, 3.2 equiv) followed by 4-DMAP (28 mg, 0.227 mmol, 1.2 equiv) and the resulting mixture was stirred at 25°C for 5 min. The reaction mixture was then washed with brine (2.0 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 17→50% EtOAc in hexanes) furnished alcohol 2-acetoxymethyl-4-bromothiazole **21i** (41 mg, 91%). R_f = 0.27 (silica gel, 17% EtOAc in hexanes); IR (film) ν_{max} 3119, 2954, 1747, 1485, 1435, 1373, 1224, 1038, 890, 836 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.26 (s, 1H, ArH), 5.35 (s, 2H, CH_2OAc), 2.16 (s, 3H, CH_3CO); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.0, 165.7, 125.0, 118.1, 62.1, 20.5; HRMS (FAB), calcd for $C_6H_6BrNO_2S$ ($M+H^+$) 235.9381, found 235.9390.

2-Vinyl-4-bromothiazole 21q. To a solution of 2,4-dibromothiazole **20**[18] (437 mg, 1.80 mmol, 1.0 equiv) in toluene was added tri-*n*-butyl(vinyl)tin (552 μL, 1.89 mmol, 1.05 equiv) followed by $Pd(PPh_3)_4$ (208 mg, 0.180 mmol, 0.1 equiv) and the resulting mixture was heated at 100°C. After 21 h, the mixture was cooled and purified directly by flash column chromatography (silica gel, 0→9% ether in hexanes) to afford 2-vinyl-4-bromothiazole **21q** as an oil (285 mg, 83%). R_f = 0.50 (silica gel, 17% ether in hexanes); IR (film) ν_{max} 3121, 1470, 1259, 1226, 1124, 1082, 975, 926, 887, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.13 (s, 1H, ArH), 6.86 (dd, J = 17.5, 11.0 Hz, 1H, $CH{=}CH_2$), 6.09 (d, J = 17.5 Hz, 1H, $CHCH_2$), 5.59 (d, J = 10.5 Hz, 1H, $CHCH_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 167.7, 129.5, 125.6, 120.8, 116.2; GC–MS (EI), calcd for C_5H_4BrNS (M^+) 189/191, found 189/191.

2-Ethyl-4-bromothiazole 21r. To a solution of 2-vinyl-4-bromothiazole **21q** (279 mg, 1.47 mmol, 1.0 equiv) in EtOH (15 mL, 0.1 M) was added PtO_2 (50 mg, 0.220 mmol, 0.15 equiv) and the resulting mixture was stirred under an atmosphere of hydrogen at 25°C for 4 h. Subsequent filtration through a short plug of silica gel, eluting with EtOAc, and careful concentration under reduced pressure furnished 2-ethyl-4-bromothiazole **21r** (238 mg, 84%). R_f = 0.63 (silica gel, CH_2Cl_2); IR (film) ν_{max} 3122, 2974, 2932, 1483, 1456, 1245, 1181, 1090, 1040, 956, 884, 831 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.08 (s, 1H, ArH), 3.03 (q, J = 7.5 Hz, 2H, CH_2CH_3), 1.37 (t, J = 7.5 Hz, 3H, CH_2CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 174.1, 124.1, 115.6, 27.1, 13.8; GC–MS (EI), calcd for C_5H_6BrNS (M^+) 191/193, found 191/193.

Stannane 8a. A solution of bromothiazole **21a** (7.5 mg, 0.026 mmol, 1.0 equiv) in degassed toluene (260 mL, 0.1 M), was treated with hexamethylditin (54 μL, 0.26 mmol, 10 equiv) and $Pd(PPh_3)_4$ (3.0 μg, 0.0026 mmol, 0.1 equiv) and the mixture was heated at 100°C for 3 h. The reaction mixture was cooled to 25°C and purified by flash column chromatography (silica gel; pretreated with Et_3N, 50% ether in hexanes) to afford the desired stannane **8a** (9.1 mg, 93%). R_f = 0.60 (silica gel, 50% ether in hexanes); IR (film) ν_{max} 2922, 2851, 1737, 1461, 1381, 1238, 1043 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.23 (s, 1H, ArH), 4.07 (t, J = 6.5 Hz, 2H, CH_2OAc), 3.09 (t, J = 8.0 Hz, 2H, $CH_2(CH_2)_4OAc$), 2.05 (s, 3H, $COCH_3$), 1.83 (tt, J = 8.0, 7.5 Hz, 2H, $CH_2(CH_2)_3OAc$), 1.67 (tt, J = 8.0, 6.5 Hz, 2H, CH_2CH_2OAc), 1.47 (tt, J = 8.0, 7.5 Hz, 2H,

$CH_2(CH_2)_2OAc$), 0.34 (s, 9H, $Sn(CH_3)_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 172.2, 142.1, 124.7, 117.9, 64.2, 33.0, 30.0, 29.5, 28.2, 25.4, −9.1.

2-Thiomethyl-4-trimethylstannylthiazole 8b. To a solution of bromothiazole **21b** (51 mg, 0.24 mmol, 1.0 equiv) in degassed toluene (4.9 mL, 0.1 M) was added hexamethylditin (498 μL, 2.4 mmol, 10 equiv) and $Pd(PPh_3)_4$ (14 mg, 0.012 mmol, 0.05 equiv) and the reaction mixture was heated at 80°C for 3 h according to the procedure described for the synthesis of stannane **8a** to afford, after flash column chromatography (silica gel, 5% Et_3N in hexanes), stannane **8b** (71 mg, 100%). $R_f = 0.67$ (silica gel; pretreated with Et_3N, 10% EtOAc); IR (film) ν_{max} 2981, 2924, 1382, 1030, 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.25 (s, 1H, ArH), 2.70 (s, 3H, SCH_3), 0.32 (s, 9H, $Sn(CH_3)_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.4, 160.2, 124.9, 17.2, −8.9; HRMS (FAB), calcd for $C_7H_{13}NS_2Sn$ ($M+H^+$) 295.9588, found 295.9576.

2-Piperidinyl-4-trimethylstannylthiazole 8c. A solution of bromothiazole **21c** (64 mg, 26 mmol, 1.0 equiv) in degassed toluene (5.2 mL, 0.05 M) was treated with hexamethylditin (540 μL, 2.6 mmol, 10 equiv) and $Pd(PPh_3)_4$ (15 mg, 0.013 mmol, 0.05 equiv) and heated at 80°C for 3 h according to the procedure described for the synthesis of stannane **8a** to afford, after flash column chromatography (silica gel; pretreated with Et_3N, hexanes), stannane **8c** (86 mg, 100%). $R_f = 0.67$ (silica gel, 10% EtOAc in hexanes containing Et_3N); IR (film) ν_{max} 2935, 2854, 1511, 1449, 1259, 771 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.58 (s, 1H, ArH), 3.48 (bt, $J = 5.0$ Hz, 4H, $CH_2(CH_2CH_2)_2N$), 1.70–1.60 (m, 6H, $CH_2(CH_2CH_2)_2N$), 0.29 (s, 9H, $Sn(CH_3)_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 173.4, 156.6, 113.9, 50.2, 25.3, 24.3, −9.0; HRMS (FAB), calcd for $C_{11}H_{20}N_2SSn$ ($M+H^+$) 333.0447, found 333.0358.

2-Methoxy-4-trimethylstannylthiazole 8p. To a solution of bromothiazole **21p** (147 mg, 0.758 mmol, 1.0 equiv) in degassed toluene (7.6 mL, 0.1 M) was added hexamethylditin (785 μL, 3.79 mmol, 5.0 equiv) and $Pd(PPh_3)_4$ (88 mg, 0.076 mmol, 0.1 equiv) and the reaction mixture was heated at 100°C for 30 min according to the procedure described for the synthesis of stannane **8a** to afford, after flash column chromatography (silica gel, 5% Et_3N in hexanes), stannane **8p** (170 mg, 81%). $R_f = 0.49$ (silica gel; pretreated with Et_3N, 17% ether in hexanes); IR (film) ν_{max} 2985, 2948, 2915, 1512, 1414, 1259, 1234, 1219, 1087, 988 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.72 (s, 1H, ArH), 4.07 (s, 3H, OCH_3), 0.32 (s, 9H, $Sn(CH_3)_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 176.0, 154.5, 117.9, 58.5, −9.1; HRMS (FAB), calcd for $C_7H_{13}NOSSn$ ($M+H^+$) 279.9818, found 279.9810.

2-Acetoxymethyl-4-trimethylstannylthiazole 8i. To a solution of bromothiazole **21i** (41 mg, 0.174 mmol, 1.0 equiv) in degassed toluene (1.7 mL, 0.1 M) was added hexamethylditin (307 μL, 1.74 mmol, 10 equiv) and $Pd(PPh_3)_4$ (15 mg, 0.013 mmol, 0.07 equiv) and the reaction mixture was heated at 100°C for 25 min according to the procedure described for the synthesis of stannane **8a** to afford, after flash column chromatography (silica gel, hexanes containing 5% Et_3N), stannane **8i** (25 mg, 45%). $R_f = 0.33$ (silica gel; pretreated with Et_3N, 17% EtOAc in hexanes); IR (film) ν_{max} 2974, 2915, 1745, 1437, 1374, 1229, 1031 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 1H, ArH), 5.45 (s, 2H, CH_2OAc), 2.15 (s, 3H, $COCH_3$) 0.37 (s, 9H, $Sn(CH_3)_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.3, 165.0, 160.1, 126.9, 62.5, 20.8, −8.9; HRMS (FAB), calcd for $C_9H_{15}NO_2SSn$ ($M+H^+$) 321.9924, found 321.9939.

2-(*tert*-Butyldimethylsilyloxymethyl)-4-tri-*n*-butylstannylthiazole 8s. To a solution of bromothiazole **21s** (20 mg, 0.065 mmol, 1.0 equiv) in ether (1.0 mL, 0.07 M) at −78°C, was added *n*-BuLi (49 mL, 1.6 M in hexanes, 0.078 mmol, 1.2 equiv) and the resulting mixture was stirred at −78°C for 10 min. Tri-*n*-butyltin chloride (23 μL, 0.078 mmol, 1.2 equiv) was then added, the solution stirred at −78°C for 10 min, and then slowly warmed to 25°C over a period of 1 h. The reaction mixture was diluted with hexane (2.0 mL), and passed through silica gel eluting with 20% EtOAc in hexanes. Flash column chromatography (silica gel; pretreated with Et_3N, 5% ether in hexanes) furnished the desired stannane **8s** (35 mg, 85%). $R_f = 0.36$ (silica gel, 5% EtOAc in hexanes); IR (film) ν_{max} 2955, 2928, 2856, 1464, 1353, 1255, 1185, 1103, 1081, 1006, 841 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.08 (s, 1H, ArH), 4.98 (s, 2H, CH_2OTBS), 1.75–1.57 (m, 6H, CH_3CH_2), 1.44–1.31 (m, 6H, $CH_3CH_2CH_2$), 1.26–1.09 (m, 6H, $CH_3(CH_2)_2CH_2$), 0.94 (s, 9H, $SiC(CH_3)_3(CH_3)_2$), 0.91 (t, $J = 7.0$ Hz, 9H, CH_3), −0.02 (s, 6H, $SiC(CH_3)_3(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 173.2, 159.1, 125.3, 63.5, 29.0, 27.3, 25.8, 18.3, 13.7, 10.1, −5.4; HRMS (FAB), calcd for $C_{22}H_{45}NOSSiSn$ ($M+H^+$) 520.2093, found 520.2074.

2-Hydroxymethyl-4-tri-*n*-butylstannylthiazole 8h. To a solution of silyl ether **8s** (20 mg, 0.039 mmol, 1.0 equiv) in THF (1.0 mL, 0.04 M) was added TBAF (46 mL, 1.0 M in THF, 0.046 mmol, 1.2 equiv) and the reaction mixture was stirred at 25°C for 20 min. Hexane (2.0 mL) was added, and the mixture passed through silica gel eluting with EtOAc. Evaporation of solvents gave the desired alcohol **8h** (15 mg, 95%). $R_f = 0.09$ (silica gel, 20% ether in hexanes); IR (film) ν_{max} 3209, 2956, 2923, 2855, 1461, 1342, 1253, 1174, 1064, 962 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 1H, ArH), 4.99 (s, 2H, CH_2OH), 3.64 (bs, 1H, OH), 1.62–1.45 (m, 6H, CH_3CH_2), 1.38–1.27 (m, 6H, $CH_3CH_2CH_2$), 1.19–1.02 (m, 6H, $CH_3(CH_2)_2CH_2$), 0.88 (t, $J = 7.0$ Hz, 9H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.7, 159.1, 125.7, 61.7, 28.9, 27.1, 13.6, 10.1; HRMS (FAB), calcd for $C_{16}H_{31}NOSSn$ ($M+H^+$) 406.1228, found 406.1237.

2-Fluoromethyl-4-tri-*n*-butylstannylthiazole 8j. To a solution of alcohol **8h** (90 mg, 0.223 mmol, 1.0 equiv) in CH_2Cl_2 (2.2 mL, 0.1 M) at −78°C was added DAST (32 μL, 0.242 mmol, 1.1 equiv) and the solution was stirred at this temperature for 10 min. After quenching with saturated aqueous $NaHCO_3$ (2 mL) the mixture was allowed to warm to 25°C, and then partitioned

between CH_2Cl_2 (15 mL) and saturated aqueous $NaHCO_3$ (15 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2×15 mL). The combined organic extracts were washed with brine (40 mL), dried ($MgSO_4$), and concentrated under reduced pressure. Flash column chromatograpahy (silica gel; pretreated with Et_3N, 17% ether in hexanes) furnished stannane **8j** (52 mg, 57%). R_f = 0.59 (silica gel, 17% ether in hexanes); IR (film) ν_{max} 2956, 2925, 2870, 2863, 1464, 1376, 1358, 1184, 1084, 1023, 874, 807 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (s, 1H, ArH), 5.69 (d, J = 47.5 Hz, 2H, CH_2F), 1.58–1.52 (m, 6H, CH_3CH_2), 1.36–1.29 (m, 6H, $CH_3CH_2CH_2$), 1.14–1.07 (m, 6H, $CH_3(CH_2)_2CH_2$), 0.88 (t, J = 7.5 Hz, 9H, CH_3): ^{13}C NMR (100.6 MHz, C_6D_6) δ 165.0 (d, J = 88 Hz), 160.1, 127.4, 80.5 (d, J = 676 Hz), 29.4, 27.6, 13.9, 10.5; HRMS (FAB), calcd for $C_{16}H_{30}FNSSn$ ($M+H^+$) 408.1183, found 408.1169.

2-Ethoxy-4-tri-*n*-butylstannylthiazole 8d. A solution of bromothiazole **21d** (82 mg, 0.394 mmol, 1.0 equiv) in ether (3.9 mL, 0.1 M) was treated with *n*-BuLi (289 μL, 1.5 M in hexanes, 0.433 mmol, 1.1 equiv) and tri-*n*-butyltin chloride (128 μL, 0.473 mmol, 1.2 equiv) according to the procedure described for the synthesis of stannane **8s**, to yield, after column chromatography (silica gel; pretreated with Et_3N, hexanes), stannane **8d** (161 mg, 98%). IR (film) ν_{max} 2956, 2927, 2870, 2851, 1504, 1472, 1258, 1257, 1232, 1211, 1082, 1023, 960, 894, 872 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.65 (s, 1H, ArH), 4.43 (q, J = 7.0 Hz, 2H, CH_3CH_2O), 1.61–1.53 (m, 6H, CH_3CH_2), 1.43 (t, J = 7.0 Hz, 3H, CH_3CH_2O), 1.37–1.30 (m, 6H, $CH_3CH_2CH_2$), 1.08–1.04 (m, 6H, $CH_3(CH_2)_2CH_2$), 0.89 (t, J = 7.5 Hz, 9H, CH_3); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 175.7, 155.3, 118.3, 68.5, 29.0, 27.2, 14.5, 13.7, 10.1; HRMS (FAB), calcd for $C_{17}H_{33}NOSSn$ ($M+H^+$) 418.1380, found 418.1396.

2-Vinyl-4-tri-*n*-butylstannylthiazole 8q. A solution of bromothiazole **21q** (191 mg, 1.00 mmol, 1.0 equiv) in ether (14.0 mL, 0.07 M), was treated with *n*-BuLi (804 μL, 1.5 M in hexanes, 1.20 mmol, 1.2 equiv) and tri-*n*-butyltin chloride (341 μL, 1.26 mmol, 1.25 equiv) according to the procedure described for the synthesis of stannane **8s** to yield, after column chromatography (silica gel; pretreated with Et_3N, hexanes), stannane **8q** (112 mg, 28%). R_f = 0.63 (silica gel, 17% ether in hexanes); IR (film) ν_{max} 2956, 2925, 2870, 2850, 1459, 1377, 1205, 1080, 981, 913, 868 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (s, 1H, ArH), 7.02 (dd, J = 17.5, 11.0 Hz, 1H, $CH=CH_2$), 6.00 (d, J = 17.5 Hz, 1H, $CH=CH_2$), 5.52 (d, J = 11.0 Hz, 1H, $CH=CH_2$), 1.61–1.53 (m, 6H, CH_3CH_2), 1.37–1.27 (m, 6H, $CH_3CH_2CH_2$), 1.13–1.10 (m, 6H, $CH_3(CH_2)_2CH_2$), 0.88 (t, J = 7.5 Hz, 9H, CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 167.7, 160.3, 131.0, 124.7, 119.5, 29.0, 27.2, 13.6, 10.1; HRMS (FAB), calcd for $C_{17}H_{31}NSSn$ ($M+H^+$) 402.1279, found 402.1290.

2-Ethyl-4-tri-*n*-butylstannylthiazole 8r. To a solution of bromothiazole **21r** (238 mg, 1.24 mmol, 1.0 equiv) in ether (12.0 mL, 0.1 M) at −78°C, was added *n*-BuLi (909 μL, 1.5 M in hexanes, 1.36 mmol, 1.1 equiv) and tri-*n*-butyltin chloride (403 μL, 1.49 mmol, 1.2 equiv) according to the procedure described for the synthesis of stannane **8s** to yield, after column chromatography (silica gel; pretreated with Et_3N, hexanes), stannane **8r** (357 mg, 72%). R_f = 0.64 (silica gel, CH_2Cl_2); IR (film) ν_{max} 2956, 2925, 2870, 2852, 1464, 1376, 1292, 1174, 1072, 1033, 953, 875 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18 (s, 1H, ArH), 3.10 (q, J = 7.6 Hz, 2H, CH_3CH_2Ar), 1.60–1.50 (m, 6H, CH_3CH_2), 1.39 (t, J = 7.6 Hz, 3H, CH_3CH_2Ar), 1.36–1.30 (m, 6H, $CH_3CH_2CH_2$), 1.13–1.08 (m, 6H, $CH_3(CH_2)_2CH_2$), 0.88 (t, J = 7.3 Hz, 9H, CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 172.9, 158.9, 124.5, 29.1, 27.0, 26.6, 14.7, 13.7, 10.1; HRMS (FAB), calcd for $C_{17}H_{33}NSSn$ ($M+H^+$) 404.1434, found 404.1416.

***cis*-Macrolactone 18h.** A solution of vinyl iodide **7** (10.0 mg, 0.020 mmol, 1.0 equiv), stannane **8h** (16.0 mg, 0.040 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (2.1 mg, 0.002 mmol, 0.1 equiv) in degassed toluene (200 μL, 0.1 M) was heated at 100°C for 20 min. The reaction mixture was then poured into saturated aqueous $NaHCO_3$–NaCl (5 mL) and extracted with EtOAc (2×5 mL). After drying the combined organic extracts (Na_2SO_4), evaporation of the solvents and purification by preparative thin-layer chromatography (500 μm silica gel plate, 50% EtOAc in hexanes), furnished macrolactone **18h** (7.5 mg, 76%). R_f = 0.29 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −44.2 (*c* 0.60, $CHCl_3$); IR (thin film) ν_{max} 3387, 2925, 2859, 1730, 1688, 1508, 1461, 1256, 1183, 1150, 1061, 980, 755 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.12 (s, 1H, ArH), 6.61 (s, 1H, $CH=C(CH_3)$), 5.45 (ddd, J = 10.5, 10.5, 4.5 Hz, 1H, $CH=CHCH_2$), 5.38 (ddd, J = 10.5, 10.5, 5.0 Hz, 1H, $CH=CHCH_2$), 5.31 (d, J = 8.5 Hz, 1H, CHOCO), 4.92 (d, J = 4.0 Hz, 2H, CH_2OH), 4.23 (ddd, J = 11.5, 5.5, 2.5 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.75–3.71 (m, 1H, $CHOH(CHCH_3)$), 3.32 (d, J = 5.5 Hz, 1H, $C(CH_3)_2CHOH$), 3.25 (t, J = 4.0 Hz, 1H, CH_2OH), 3.13 (qd, J = 7.0, 2.0 Hz, 1H, $CH_3CH(C=O)$), 3.03 (d, J = 2.0 Hz, 1H, $CH_3CHCH(OH)CHCH_3$), 2.68 (ddd, J = 15.0, 9.5, 9.5 Hz, 1H, $CH=CHCH_2CHO$), 2.50 (dd, J = 15.0, 11.5 Hz, 1H, CH_2COO), 2.35 (dd, J = 15.0, 2.5 Hz, 1H, CH_2COO), 2.31–2.24 (m, 1H, $CH=CHCH_2CHO$), 2.24–2.16 (m, 1H), 2.09 (s, 3H, $CH=CCH_3$), 2.06–1.98 (m, 1H), 1.82–1.73 (m, 1H), 1.72–1.62 (m, 1H), 1.39–1.17 (m, 3H), 1.33 (s, 3H, $C(CH_3)_2$), 1.19 (d, J = 7.0 Hz, 3H, $CH_3CH(C=O)$), 1.08 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.5, 170.3, 169.9, 152.3, 139.0, 133.5, 124.9, 118.9, 116.5, 78.4, 74.2, 72.2, 61.8, 53.4, 41.7, 39.3, 38.6, 32.4, 31.7, 27.5, 27.4, 22.8, 18.4, 16.0, 15.5, 13.5; HRMS (FAB), calcd for $C_{26}H_{39}NO_6S$ ($M+Cs^+$) 626.1552, found 626.1530.

Epothilone E (3). To a solution of macrolactone **18h** (10.0 mg, 0.020 mmol, 1.0 equiv) in methanol (600 μL, 0.03 M) was added acetonitrile (32 μL, 0.606 mmol, 30 equiv), $KHCO_3$ (10 mg, 0.102 mmol, 5 equiv) and hydrogen peroxide (27 μL, 35% w/w in water, 0.303 mmol, 15 equiv) and the reaction mixture stirred at 25°C for 3 h. Additional acetonitrile (32 μL, 0.606 mmol, 30 equiv), $KHCO_3$ (10 mg, 0.102 mmol, 5 equiv), and hydrogen peroxide (27 μL, 35% w/w in water, 0.303

mmol, 15 equiv) were then added and stirring was continued for a further 3 h. The reaction mixture was then passed directly through a short plug of silica gel, eluting with ether, and the filtrate was concentrated under reduced pressure. Preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes) furnished unreacted starting material **18h** (5.0 mg, 50%) and epothilone E (**3**) (3.4 mg, 33%). $R_f = 0.56$ (silica gel, 66% EtOAc in hexanes); $[\alpha]_D^{22} = -27.5$ (*c* 0.20, $CHCl_3$); IR (film) ν_{max} 3413, 2928, 2867, 1731, 1689, 1462, 1375, 1257, 1152, 1061, 978, 756 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.13 (s, 1H, ArH), 6.61 (s, 1H, C*H*=CCH$_3$), 5.46 (dd, *J* = 8.1, 2.4 Hz, 1H, CHOCO), 4.94 (d, *J* = 5.2 Hz, 2H, C*H*$_2$OH), 4.16–4.12 (m, 1H, (CH$_3$)$_2$CC*H*(OH)), 3.82–3.78 (m, 1H, C*H*OH(CHCH$_3$)), 3.66 (bs, 1H, OH), 3.23 (qd, *J* = 6.8, 5.2 Hz, 1H, CH$_3$C*H*(C=O)), 3.04 (ddd, *J* = 8.1, 4.5, 4.5 Hz, 1H, CH$_2$C*H*(O)CHCH$_2$), 2.91 (ddd, *J* = 7.3, 4.5, 4.1 Hz, 1H, CH$_2$C*H*(O)CHCH$_2$), 2.61 (t, *J* = 5.2 Hz, 1H, CH$_2$O*H*), 2.55 (dd, *J* = 14.7, 10.4 Hz, 1H, CH$_2$COO), 2.48 (bs, 1H, OH), 2.45 (dd, *J* = 14.7, 3.2 Hz, 1H, CH$_2$COO), 2.14–2.07 (m, 1H, C*H*$_2$CH(O)CHCH$_2$), 2.11 (s, 3H, CH=CC*H*$_3$), 1.91 (ddd, *J* = 15.1, 8.1, 8.1 Hz, 1H, C*H*$_2$CH(O)CHCH$_2$), 1.78–1.66 (m, 2H, C*H*$_2$CH(O)CHCH$_2$), 1.52–1.38 (m, 5H), 1.36 (s, 3H, C(CH$_3$)$_2$), 1.18 (d, 3H, *J* = 6.8 Hz, C*H*$_3$CH(C=O)), 1.10 (s, 3H, C(CH$_3$)$_2$), 1.01 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CHCH$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.0, 170.6, 169.9, 152.3, 137.6, 119.8, 117.0, 76.7, 74.8, 73.6, 62.3, 57.5, 54.4, 52.7, 43.6, 38.9, 36.2, 31.4, 30.4, 27.0, 23.7, 21.3, 21.0, 17.2, 15.6, 14.3; HRMS (FAB), calcd for $C_{26}H_{39}NO_7S$ ($M + H^+$) 510.2525, found 510.2539.

***cis*-Macrolactone 18a.** A solution of vinyl iodide **7** (5.0 mg, 0.010 mmol, 1.0 equiv), stannane **8a** (7.4 mg, 0.020 mmol, 2.0 equiv), and $Pd(PPh_3)_4$ (2.0 mg, 0.002 mmol, 0.1 equiv) in degassed toluene (200 μL, 0.1 M) was heated at 90°C for 15 min according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 75% ether in hexanes), macrolactone **18a** (4.8 mg, 82%). $R_f = 0.30$ (silica gel, 75% ether in hexanes); $[\alpha]_D^{22}$ −34.0 (*c* 0.20, $CHCl_3$); IR (thin film) ν_{max} 3455, 2921, 2852, 1733, 1688, 1461, 1370, 1245, 1046, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 1H, ArH), 6.61 (s, 1H, C*H*=C(CH$_3$)), 5.45 (ddd, *J* = 10.5, 10.5, 4.5 Hz, 1H, C*H*=CHCH$_2$), 5.39 (ddd, *J* = 10.5, 10.5, 4.5 Hz, 1H, C*H*=CHCH$_2$), 5.29 (dd, *J* = 10.5, 2.5 Hz, 1H, CHOCO), 4.26 (dd, *J* = 10.5, 2.5 Hz, 1H, (CH$_3$)$_2$CC*H*OH), 4.07 (t, *J* = 6.5 Hz, 1H, CH$_2$OAc), 3.75–3.72 (m, 1H, C*H*OH(CHCH$_3$)), 3.42 (bs, 1H, OH), 3.14 (qd, *J* = 7.0, 2.5 Hz, 1H, CH$_3$C*H*(C=O)), 2.99 (t, *J* = 7.5 Hz, 2H, C*H*$_2$(CH$_2$)$_4$OAc), 2.70 (ddd, *J* = 15.0, 10.0, 10.0 Hz, 1H, CH=CHC*H*$_2$), 2.50 (dd, *J* = 15.0, 11.5 Hz, 1H, CH$_2$COO), 2.34 (dd, *J* = 15.0, 2.5 Hz, 1H, CH$_2$COO), 2.31–2.24 (m, 2H), 2.25–2.18 (m, 2H), 1.90–1.20 (m, 3H), 2.10 (s, 3H, CH=C(C*H*$_3$)), 2.05 (s, 3H, COCH$_3$), 1.85 (tt, *J* = 8.0, 6.5 Hz, 2H, C*H*$_2$(CH$_2$)$_3$OAc), 1.68 (tt, *J* = 7.5, 7.0 Hz, 2H, C*H*$_2$CH$_2$OAc), 1.48 (tt, *J* = 8.0, 7.0 Hz, 2H, C*H*$_2$(CH$_2$)$_2$OAc), 1.34 (s, 3H, C(CH$_3$)$_2$), 1.19 (d, *J* = 7.0 Hz, 3H, CH$_3$CH(C=O)), 1.09 (s, 3H, C(CH$_3$)$_2$), 1.01 (d, *J* = 7.5 Hz, 3H, CH$_3$CHCH$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.6, 171.2, 170.4, 152.0, 138.6, 133.4, 132.1, 125.1, 119.4, 115.4, 78.5, 74.1, 72.3, 64.2, 53.4, 41.6, 39.3, 38.6, 33.1, 32.4, 31.8, 29.7, 29.4, 28.2, 27.6, 27.5, 25.4, 22.7, 18.5, 15.9, 15.5, 13.5; HRMS (FAB), calcd for $C_{25}H_{37}NO_5S$ ($M + Cs^+$) 724.2284, found 724.2310.

***trans*-Macrolactone 19a.** A solution of vinyl iodide **11** (5.0 mg, 0.010 mmol, 1.0 equiv), stannane **8a** (7.4 mg, 0.020 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (2.0 mg, 0.001 mmol, 0.1 equiv) in degassed toluene (200 μL, 0.1 M) was heated at 100°C for 15 min according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 75% ether in hexanes), lactone **19a** (4.9 mg, 84%). $R_f = 0.25$ (silica gel, 75% ether in hexanes); $[\alpha]_D^{22}$ −14.6 (*c* 0.50, $CHCl_3$); IR (thin film) ν_{max} 3483, 2925, 2855, 1733, 1691, 1462, 1369, 1245, 1042, 976 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.00 (s, 1H, ArH), 6.57 (s, 1H, C*H*=C(CH$_3$)), 5.53 (ddd, *J* = 15.0, 7.5, 7.5 Hz, 1H, C*H*=CHCH$_2$), 5.40 (dd, *J* = 6.0, 6.0 Hz, 1H, CHOCO), 5.39 (ddd, *J* = 15.0, 7.5, 7.5 Hz, 1H, C*H*=CHCH$_2$), 4.18 (ddd, *J* = 10.5, 2.5, 2.5 Hz, 1H, (CH$_3$)$_2$CC*H*(OH)), 4.07 (t, *J* = 7.0 Hz, 2H, CH$_2$OAc), 3.76–3.73 (m, 1H, C*H*OH(CHCH$_3$)), 3.26–3.22 (m, 1H), 3.24 (qd, *J* = 7.0, 2.0 Hz, 1H, CH$_3$C*H*(C=O)), 3.00 (t, *J* = 8.0 Hz, 2H, C*H*$_2$(CH$_2$)$_4$OAc), 2.70 (bs, 1H, OH), 2.56 (dd, *J* = 15.5, 10.5 Hz, 1H, CH$_2$COO), 2.48–2.44 (m, 2H), 2.47 (dd, *J* = 15.5, 2.5 Hz, 1H, CH$_2$COO), 2.22–2.14 (m, 1H), 2.09 (s, 3H, CH=C(C*H*$_3$)), 2.05 (s, 3H, COCH$_3$), 2.02–1.94 (m, 1H), 1.83 (tt, *J* = 8.0, 7.5 Hz, 2H, C*H*$_2$(CH$_2$)$_3$OAc), 1.70–1.20 (m, 4H), 1.69 (tt, *J* = 7.0, 6.5 Hz, 2H, C*H*$_2$CH$_2$OAc), 1.48 (tt, *J* = 7.5, 6.5 Hz, 2H, C*H*$_2$(CH$_2$)$_2$OAc), 1.30 (s, 3H, C(CH$_3$)$_2$), 1.19 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CH(C=O)), 1.08 (s, 3H, C(CH$_3$)$_2$), 0.99 (d, *J* = 7.0 Hz, 3H, C*H*$_3$CHCH$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.0, 170.6, 169.9, 152.0, 137.1, 134.3, 127.8, 125.8, 119.9, 115.7, 77.8, 75.7, 72.4, 64.2, 52.6, 43.4, 38.8, 37.8, 36.3, 33.2, 32.4, 30.7, 28.3, 27.3, 25.4, 21.0, 20.7, 16.3, 16.1, 15.4, 14.8; HRMS (FAB), calcd for $C_{32}H_{49}NO_7S$ ($M + Cs^+$) 724.2284, found 724.2308.

***cis*-Macrolactone 18b.** A solution of vinyl iodide **7** (9.2 mg, 0.018 mmol, 1.0 equiv), stannane **8b** (10.7 mg, 0.036 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (2.1 mg, 0.0018 mmol, 0.1 equiv) in degassed toluene (180 μL, 0.1 M) was heated at 100°C for 40 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 75% ether in hexanes), macrolactone **18b** (4.1 mg, 44%). $R_f = 0.50$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −38.6 (*c* 0.21, $CHCl_3$); IR (thin film) ν_{max} 3444, 2925, 1732, 1682, 1259, 1037, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 1H, C*H*=C(CH$_3$)), 6.52 (bs, 1H, ArH), 5.45 (ddd, *J* = 10.5, 10.5, 4.0 Hz, 2H, C*H*=CHCH$_2$), 5.39 (ddd, *J* = 10.5, 10.5, 4.0 Hz, 1H, C*H*=CHCH$_2$), 5.29 (d, *J* = 8.0 Hz, 1H, CHOCO), 4.20 (ddd, *J* = 11.0, 5.5, 2.5 Hz, 1H, (CH$_3$)$_2$CC*H*(OH)), 3.75–3.73 (m, 1H, C*H*OH(CHCH$_3$)), 3.13 (qd, *J* = 6.5, 2.0 Hz, 1H, CH$_3$C*H*(C=O)), 2.98 (d, *J* = 2.0 Hz, 1H, CHO*H*(CHCH$_3$)), 2.93 (d, *J* = 5.5 Hz, 1H, (CH$_3$)$_2$CCH(O*H*)), 2.71 (ddd, *J* = 15.0, 10.0, 10.0 Hz 1H, CH=CHCH$_2$), 2.70 (s, 3H, SCH$_3$), 2.51 (dd, *J* = 15.5, 11.5 Hz, 1H, CH$_2$COO), 2.30 (dd, *J* = 15.0,

2.5 Hz, 1H, CH_2COO), 2.28–2.16 (m, 2H), 2.13 (d, J = 1.0 Hz, 3H, CH=C(CH_3)), 2.06–1.98 (m, 1H), 1.79–1.60 (m, 2H), 1.40–1.06 (m, 3H), 1.33 (s, 3H, $C(CH_3)_2$), 1.19 (d, J = 7.0 Hz, 3H, CH_3CH(C=O)), 1.09 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.4, 170.4, 165.7, 152.7, 138.6, 133.5, 124.9, 119.1, 115.9, 78.8, 74.1, 72.6, 53.2, 41.8, 39.2, 38.6, 32.5, 31.7, 27.6, 27.5, 22.6, 19.0, 16.7, 15.6, 15.6, 13.5; HRMS (FAB), calcd for $C_{26}H_{39}NO_5S_2$ ($M + Cs^+$) 642.1324, found 642.1345.

***trans*-Macrolactone 19b.** A solution of vinyl iodide **11** (6.9 mg, 0.014 mmol, 1.0 equiv), stannane **8b** (8.2 mg, 0.028 mmol, 2.0 equiv), and $Pd(PPh_3)_4$ (1.6 mg, 0.0014 mmol, 0.1 equiv) in degassed toluene (140 μL, 0.1 M) was heated at 100°C for 40 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 75% ether in hexanes), macrolactone **19b** (5.0 mg, 72%). R_f = 0.47 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −32.9 (*c* 0.35, $CHCl_3$); IR (film) ν_{max} 3488, 2928, 1728, 1692, 1259, 1036, 800, 757 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (s, 1H, ArH), 6.48 (s, 1H, C*H*=C(CH_3)), 5.53 (ddd, J = 15.0, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 5.40 (d, J = 8.0 Hz, 1H, CHOCO), 5.39 (ddd, J = 15.0, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 4.12 (ddd, J = 11.0, 2.5, 2.5 Hz, 1H, $(CH_3)_2$CC*H*OH), 3.77–3.74 (m, 1H, C*H*OH($CHCH_3$)), 3.24 (m, 1H, CH=CHCH_2), 3.07 (m, 1H, CH_3C*H*(C=O)), 2.70 (s, 3H, SCH_3), 2.61 (d, J = 3.5 Hz, 1H, CHO*H*($CHCH_3$)), 2.59–2.44 (m, 5H), 2.19–2.12 (m, 1H), 2.13 (s, 3H, CH=C(CH_3)), 2.02–1.94 (m, 1H), 1.70–1.55 (m, 2H), 1.48–1.41 (m, 1H), 1.29 (s, 3H, $C(CH_3)_2$), 1.18 (d, J = 7.0 Hz, 3H, CH_3CH(C=O)), 1.08 (s, 3H, $C(CH_3)_2$), 0.99 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.0, 170.6, 165.6, 152.8, 137.5, 134.3, 125.9, 119.4, 116.2, 78.0, 75.6, 72.6, 52.5, 43.4, 38.7, 37.8, 36.5, 32.4, 30.6, 27.3, 21.4, 20.6, 16.7, 16.3, 15.5, 14.7; HRMS (FAB), calcd for $C_{26}H_{39}NO_5S_2$ ($M + Cs^+$) 642.1324, found 642.1298.

***cis*-Macrolactone 18c.** A solution of vinyl iodide **7** (7.0 mg, 0.014 mmol, 1.0 equiv), stannane **8c** (9.2 mg, 0.028 mmol, 2.0 equiv), and $Pd(PPh_3)_4$ (0.8 mg, 0.0007 mmol, 0.05 equiv) in degassed toluene (140 μL, 0.1 M) was heated at 100°C for 40 min according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 75% ether in hexanes) macrolactone **18c** (5.4 mg, 72%). R_f = 0.32 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −48.5 (*c* 0.40, $CHCl_3$); IR (thin film) ν_{max} 3452, 2930, 2857, 1731, 1685, 1531, 1451, 1256 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.36 (bs, 1H, ArH), 6.35 (s, 1H, C*H*=C(CH_3)), 5.41 (ddd, J = 11.0, 11.0, 5.0 Hz, 1H, C*H*=$CHCH_2$), 5.39 (ddd, J = 11.0, 11.0, 5.0 Hz, 1H, C*H*=$CHCH_2$), 5.23 (d, J = 9.5 Hz, 1H, CHOCO), 4.27 (d, J = 10.5 Hz, 1H, $(CH_3)_2$CC*H*(OH)), 3.73–3.72 (m, 1H, C*H*OH($CHCH_3$)), 3.60 (bs, 1H, OH), 3.45 (bt, 4H, J = 5.5 Hz, $CH_2(CH_2CH_2)_2N$), 3.14 (qd, J = 7.0, 2.0 Hz, 1H, CH_3C*H*(C=O)), 3.11 (bs, 1H, OH), 2.67 (ddd, J = 15.5, 10.0, 10.0 Hz, 1H, CH=CHCH_2), 2.47 (dd, J = 15.0, 2.5 Hz, 1H, CH_2COO), 2.30 (dd, J = 15.5, 2.5 Hz, 1H, CH_2COO), 2.28–2.17 (m, 2H), 2.10 (d, J = 1.0 Hz, 3H, CH=C(CH_3)), 2.06–1.97 (m, 1H), 1.80–1.60 (m, 2H), 1.70–1.56 (m, 6H, $CH_2(CH_2CH_2)_2N$), 1.39–1.08 (m, 3H), 1.32 (s, 3H, $C(CH_3)_2$), 1.18 (d, J = 6.5 Hz, 3H, CH_3CH(C=O)), 1.07 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.5 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.7, 170.9, 170.4, 148.8, 137.8, 133.2, 125.3, 119.9, 105.0, 78.7, 74.0, 72.3, 55.6, 49.6, 41.5, 39.5, 38.5, 32.4, 31.9, 27.6, 27.4, 25.1, 24.1, 22.9, 18.3, 15.8, 15.5, 13.4; HRMS (FAB), calcd for $C_{30}H_{47}N_2O_5S$ ($M + H^+$) 547.3206, found 547.3187.

***trans*-Macrolactone 19c.** A solution of vinyl iodide **11** (6.0 mg, 0.012 mmol, 1.0 equiv), stannane **8c** (7.9 mg, 0.024 mmol, 2.0 equiv), and $Pd(PPh_3)_4$ (0.7 mg, 0.0006 mmol, 0.05 equiv) in degassed toluene (120 μL, 0.1 M) was heated at 100°C for 40 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 75% ether in hexanes), macrolactone **19c** (2.9 mg, 44%). R_f = 0.56 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −23.8 (*c* 0.21, $CHCl_3$); IR (film) ν_{max} 3421, 2928, 2856, 1729, 1692, 1531, 1450, 1256 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.37 (s, 1H, C*H*=CCH_3), 6.31 (s, 1H, ArH), 5.51 (ddd, J = 15.0, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 5.40 (ddd, J = 15.0, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 5.38 (dd, J = 8.0, 3.0 Hz, 1H, CHOCO), 4.12 (ddd, J = 6.0, 2.5, 2.5 Hz, 1H, $(CH_3)_2$C C*H*OH), 3.76 (q, J = 3.5 Hz, 1H, C*H*OH($CHCH_3$)), 3.45 (bt, 4H, J = 5.5 Hz, $CH_2(CH_2CH_2)_2N$), 3.30 (d, J = 4.0 Hz, 1H, CH_3C*H*(C=O)), 3.25–3.20 (m, 1H, CH=CHCH_2), 2.61 (d, J = 3.5 Hz, 1H, CHO*H*($CHCH_3$)), 2.54 (dd, J = 15.0, 10.5 Hz, 1H, CH_2COO), 2.49–2.41 (m, 4H), 2.18–2.13 (m, 1H), 2.13 (d, J = 1.5 Hz, 3H, CH=C(CH_3)), 2.02–1.93 (m, 2H), 1.69–1.65 (m, 6H, $CH_2(CH_2CH_2)_2N$), 1.48–1.43 (m, 3H), 1.29 (s, 3H, $C(CH_3)_2$), 1.18 (d, J = 7.0 Hz, 3H, CH_3CH(C=O)), 1.07 (s, 3H, $C(CH_3)_2$), 0.98 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.2, 170.6, 149.3, 135.9, 134.0, 126.1, 120.7, 105.9, 78.2, 75.4, 72.4, 55.7, 49.5, 43.2, 38.8, 38.0, 36.5, 32.4, 30.9, 29.9, 27.4, 25.1, 24.1, 20.8, 16.1, 15.2, 14.6; HRMS (FAB), calcd for $C_{30}H_{47}N_2O_5S$ ($M + H^+$) 547.3206, found 547.3222.

***cis*-Macrolactone 18d.** A solution of vinyl iodide **7** (14 mg, 0.028 mmol, 1.0 equiv), stannane **8d** (14 mg, 0.055 mmol, 2.0 equiv), and $Pd(MeCN)_2Cl_2$ (2.0 mg, 0.008 mmol, 0.3 equiv) in degassed DMF (280 μL, 0.1 M) was stirred at 25°C for 20 h. The resulting mixture was then concentrated under reduced pressure, filtered through silica, eluting with EtOAc, and purified by preparative thin-layer chromatography (250 μm silica gel plate, 50% ether in hexanes) to furnish macrolactone **18d** (12.5 mg, 89%). R_f = 0.30 (silica gel, 66% ether in hexanes); $[\alpha]_D^{22}$ −70.2 (*c* 0.63, $CHCl_3$); IR (thin film) ν_{max} 3501, 2934, 1732, 1688, 1526, 1472, 1386, 1232, 1150, 1091, 1007 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.47 (s, 1H, ArH), 6.33 (s, 1H, C*H*=C(CH_3)), 5.43 (ddd, J = 10.5, 10.5, 3.5 Hz, 1H, C*H*=$CHCH_2$), 5.37 (ddd, J = 10.5, 10.5, 4.5 Hz, 1H, C*H*=$CHCH_2$), 5.26 (dd, J = 9.5, 1.5 Hz, 1H, CHOCO), 4.44 (q, J = 7.0 Hz, 2H, CH_3CH_2O), 4.18 (ddd, J = 11.0, 5.5, 2.5 Hz, 1H, $(CH_3)_2$CC*H*(OH)), 3.73 (m, 1H, C*H*OH($CHCH_3$)), 3.12 (qd, J = 7.0, 2.0 Hz, 1H, CH_3C*H*(C=O)), 2.98 (d,

J = 1.5 Hz, 1H, OH), 2.95 (d, J = 5.5 Hz, 1H, OH), 2.69 (ddd, J = 15.0, 10.0, 10.0 Hz, 1H, CH=CHCH_2CHO), 2.49 (dd, J = 15.5, 11.5 Hz, 1H, CH_2COO), 2.36 (dd, J = 15.5, 2.5 Hz, 1H, CH_2COO), 2.23–2.16 (m, 3H), 2.11 (s, 3H, CH=C(CH_3)), 2.04–1.98 (m, 1H), 1.77–1.71 (m, 1H), 1.70–1.61 (m, 1H), 1.42 (t, J = 7.0 Hz, 3H, C$H_3$$CH_2$O), 1.38–1.16 (m, 2H), 1.31 (s, 3H, C(CH_3)$_2$), 1.17 (d, J = 7.0 Hz, 3H, CH_3CH(C=O)), 1.08 (s, 3H, C(CH_3)$_2$), 0.99 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 220.3, 173.4, 170.4, 146.7, 137.6, 133.4, 125.0, 119.8, 109.1, 79.0, 74.1, 72.6, 67.7, 53.1, 41.8, 39.2, 38.5, 32.5, 31.7, 27.5, 27.5, 22.6, 19.1, 15.6, 15.3, 14.5, 13.5; HRMS (FAB), calcd for $C_{27}H_{41}NO_6S$ (M + Cs^+) 640.1709, found 640.1732.

***trans*-Macrolactone 19d.** A solution of vinyl iodide **11** (14 mg, 0.028 mmol, 1.0 equiv), stannane **8d** (23 mg, 0.055 mmol, 2.0 equiv), and $Pd(MeCN)_2Cl_2$ (2.0 mg, 0.008 mmol, 0.3 equiv) in degassed DMF (280 μL, 0.1 M) was stirred at 25°C for 20 h, according to the procedure described for the synthesis of macrolactone **18d** to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **19d** (12 mg, 86%). R_f = 0.27 (silica gel, 66% ether in hexanes); $[\alpha]_D^{22}$ −28.0 (*c* 0.48, $CHCl_3$); IR (thin film) ν_{max} 3495, 2930, 1732, 1690, 1526, 1472, 1233, 1017, 976 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.50 (s, 1H, ArH), 6.30 (s, 1H, C*H*=C(CH_3)), 5.57–5.51 (m, 1H, C*H*=$CHCH_2$), 5.42–5.36 (m, 1H, C*H*=$CHCH_2$), 5.37 (dd, J = 9.0, 2.5 Hz, 1H, CHOCO), 4.46 (q, J = 7.0 Hz, 2H, CH_3CH_2O), 4.10 (ddd, J = 10.5, 3.5, 3.0 Hz, 1H, (CH_3)$_2$CC*H*(OH)), 3.76–3.73 (m, 1H, C*H*OH($CHCH_3$)), 3.23 (qd, J = 7.0, 4.5 Hz, 1H, CH_3C*H*(C=O)), 3.07 (d, J = 3.5 Hz, 1H, OH), 2.57–2.38 (m, 3H), 2.56 (dd, J = 15.5, 10.5 Hz, 1H, CH_2COO), 2.47 (dd, J = 15.5, 2.5 Hz, 1H, CH_2COO), 2.18–2.16 (m, 1H), 2.13 (s, 3H, CH=C(CH_3)), 2.03–1.94 (m, 1H), 1.70–1.55 (m, 2H), 1.48–1.41 (m, 1H), 1.44 (t, J = 7.0 Hz, 3H, C$H_3$$CH_2$O), 1.29 (s, 3H, C($CH_3$)$_2$), 1.27–1.16 (m, 1H), 1.18 (d, J = 7.0 Hz, 3H, CH_3CH(C=O)), 1.08 (s, 3H, C(CH_3)$_2$), 0.98 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 220.0, 173.3, 170.6, 146.8, 136.4, 134.1, 126.1, 120.2, 109.5, 78.3, 75.5, 72.6, 67.7, 52.4, 43.4, 38.7, 37.8, 36.6, 32.4, 30.7, 27.4, 21.2, 20.5, 16.2, 15.0, 14.7, 14.5; HRMS (FAB), calcd for $C_{27}H_{41}NO_6S$ (M + Cs^+) 640.1709, found 640.1731.

***cis*-Macrolactone 18e.** A solution of vinyl iodide **7** (5.1 mg, 0.010 mmol, 1.0 equiv), tri-*n*-butylstannane **8e**[16] (7.5 mg, 0.020 mmol, 2.0 equiv), and $Pd(PPh_3)_4$ (1.1 mg, 0.001 mmol, 0.10 equiv) in degassed toluene (100 μL, 0.1 M) were heated at 100°C for 20 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **18e** (3.2 mg, 70%). R_f = 0.42 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −30.4 (*c* 0.35, $CHCl_3$); IR (thin film) ν_{max} 3438, 2927, 2857, 1730, 1688, 1463, 1383, 1294, 1254, 1151, 1090, 1050, 980, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, J = 2.0 Hz, 1H, NCHS), 7.20 (d, J = 2.0 Hz, 1H, NCHC), 6.70 (s, 1H, C*H*=C(CH_3)), 5.46 (ddd, J = 10.5, 10.5, 4.0 Hz, 1H, C*H*=$CHCH_2$), 5.39 (ddd, J = 10.5, 10.5, 5.0 Hz, 1H, C*H*=$CHCH_2$), 5.33 (dd, J = 9.5, 1.5 Hz, 1H, CHOCO), 4.22 (dd, J = 11.5, 2.5 Hz, 1H, (CH_3)$_2$CC*H*(OH)), 3.75–3.73 (m, 1H, C*H*OH($CHCH_3$)), 3.14 (qd, J = 7.0, 2.0 Hz, 1H, CH_3C*H*(C=O)), 3.05 (d, J = 5.5 Hz, 1H, CHO*H*($CHCH_3$)), 3.00 (s, 1H, C(CH_3)$_2$CHO*H*), 2.73 (ddd, J = 15.0, 9.5, 9.5 Hz, 1H, CH=CHCH_2CHO), 2.51 (dd, J = 15.5, 11.5 Hz, 1H, CH_2COO), 2.38 (dd, J = 15.5, 2.5 Hz, 1H, CH_2COO), 2.31–2.24 (m, 1H, CH=CHCH_2CHO), 2.24–2.16 (m, 1H), 2.13 (s, 3H, CH=C(CH_3)), 2.07–1.99 (m, 1H), 1.81–1.73 (m, 1H), 1.71–1.61 (m, 1H), 1.41–1.16 (m, 3H), 1.33 (s, 3H, C(CH_3)$_2$), 1.19 (d, J = 7.0 Hz, 3H, CH_3CH(C=O)), 1.09 (s, 3H, C(CH_3)$_2$), 1.00 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.5, 170.4, 153.4, 152.0, 138.8, 133.5, 124.9, 119.2, 116.2, 78.6, 74.1, 72.6, 53.2, 41.8, 39.2, 38.6, 32.5, 31.7, 27.6, 27.5, 22.6, 18.9, 15.7, 15.5, 13.5; HRMS (FAB), calcd for $C_{25}H_{37}NO_5S$ (M + Cs^+) 596.1447, found 596.1430.

***trans*-Macrolactone 19e.** A solution of vinyl iodide **11** (5.1 mg, 0.010 mmol, 1.0 equiv), tri-*n*-butylstannane **8e**[16] (7.5 mg, 0.020 mmol, 2.0 equiv), and $Pd(PPh_3)_4$ (1.1 mg, 0.002 mmol, 0.10 equiv) in degassed toluene (100 μL, 0.1 M) was heated at 100°C for 20 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **19e** (3.4 mg, 74%). R_f = 0.47 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −34.9 (*c* 0.35, $CHCl_3$); IR (thin film) ν_{max} 3437, 2928, 2858, 1728, 1692, 1464, 1379, 1253, 1151, 1045, 975, 756 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, J = 1.5 Hz, 1H, NCHS), 7.21 (d, J = 1.5 Hz, 1H, NCHC), 6.66 (s, 1H, C*H*=C(CH_3)), 5.53 (ddd, J = 14.5, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 5.42 (dd, J = 5.5, 5.5 Hz, 1H, CHOCO), 5.39 (ddd, J = 14.5, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 4.19 (ddd, J = 10.0, 3.5, 2.5 Hz, 1H, (CH_3)$_2$CC*H*(OH)), 3.74 (dd, J = 6.5, 3.5 Hz, 1H, C*H*OH($CHCH_3$)), 3.26 (qd, J = 7.0, 6.5 Hz, 1H, CH_3C*H*(C=O)), 3.08 (d, J = 3.5 Hz, 1H, OH), 2.71 (d, J = 3.5 Hz, 1H, OH), 2.57 (dd, J = 15.0, 10.0 Hz, 1H, CH_2COO), 2.52–2.44 (m, 2H, CH=CHCH_2CHO), 2.50 (dd, J = 15.0, 2.5 Hz, 1H, CH_2COO), 2.22–2.14 (m, 1H), 2.12 (s, 3H, CH=C(CH_3)), 2.02–1.92 (m, 1H), 1.69–1.56 (m, 2H), 1.51–1.43 (m, 1H), 1.36–1.16 (m, 2H), 1.29 (s, 3H, C(CH_3)$_2$), 1.18 (d, J = 7.0 Hz, 3H, CH_3CH(C=O)), 1.07 (s, 3H, C(CH_3)$_2$), 0.98 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.0, 170.4, 153.4, 151.9, 137.7, 134.4, 125.7, 119.5, 116.3, 77.7, 75.8, 72.5, 52.5, 43.6, 38.8, 37.8, 36.3, 32.5, 30.6, 27.3, 21.2, 20.6, 16.4, 15.6, 14.8; HRMS (FAB), calcd for $C_{25}H_{37}NO_5S$ (M + Cs^+) 596.1447, found 596.1431.

***cis*-Macrolactone 18f.** A solution of vinyl iodide **7** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8f**[16] (7.5 mg, 0.020 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (1.1 mg, 0.001 mmol, 0.10 equiv) in degassed toluene (100 μL, 0.1 M) was heated at 100°C for 20 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 50% EtOAc in hexanes),

macrolactone **18f** (3.9 mg, 84%). $R_f = 0.18$ (silica gel, 33% EtOAc in hexanes); $[\alpha]_D^{22}$ −78.9 (*c* 0.35, $CHCl_3$); IR (thin film) ν_{max} 3380, 2930, 1734, 1687, 1464, 1374, 1297, 1251, 1146, 1054, 1008, 979, 755 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, $J = 3.5$ Hz, 1H, NC*H*CHS), 7.34 (d, $J = 3.5$ Hz, 1H, NCHC*H*S), 6.90 (s, 1H, C*H*=C(CH_3)), 5.46 (ddd, $J = 10.5$, 10.0, 4.5 Hz, 1H, C*H*=$CHCH_2$), 5.38 (ddd, $J = 10.5$, 10.0, 5.0 Hz, 1H, C*H*=$CHCH_2$), 5.32 (d, $J = 9.5$ Hz, 1H, CHOCO), 4.25 (dd, $J = 11.0$, 2.5 Hz, 1H, $(CH_3)_2CCH$(OH)), 3.73 (d, $J = 2$ Hz, 1H, C*H*OH($CHCH_3$)), 3.23 (bs, 1H, OH), 3.13 (qd, $J = 6.5$, 2.0 Hz, 1H, CH_3CH(C=O)), 3.01 (bs, 1H, OH), 2.66 (ddd, $J = 15.0$, 10.0, 10.0 Hz, 1H, CH=CHCH_2CHO), 2.52 (dd, $J = 15.5$, 11.0 Hz, 1H, CH_2COO), 2.37 (dd, $J = 15.5$, 2.5 Hz, 1H, CH_2COO), 2.34–2.27 (m, 1H, CH=CHCH_2CHO), 2.25–2.15 (m, 1H), 2.18 (s, 3H, CH=C(CH_3)), 2.07–2.00 (m, 1H), 1.95–1.85 (m, 1H), 1.80–1.73 (m, 1H), 1.73–1.63 (m, 1H), 1.40–1.10 (m, 2H), 1.34 (s, 3H, $C(CH_3)_2$), 1.19 (d, $J = 6.5$ Hz, 3H, CH_3CH(C=O)), 1.08 (s, 3H, $C(CH_3)_2$), 0.99 (d, $J = 7.5$ Hz, 3H, C$H_3$$CHCH_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.5, 170.2, 164.8, 142.6, 142.2, 133.8, 124.6, 119.2, 119.1, 78.0, 74.2, 72.4, 53.3, 41.8, 39.1, 38.6, 32.5, 31.6, 27.5, 27.5, 22.7, 18.7, 16.7, 15.4, 13.6; HRMS (FAB), calcd for $C_{25}H_{37}NO_5S$ ($M + Cs^+$) 596.1447, found 596.1468.

***trans*-Macrolactone 19f.** A solution of vinyl iodide **11** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8f**[16] (7.1 mg, 0.020 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (1.1 mg, 0.001 mmol, 0.1 equiv) in degassed toluene (100 μL, 0.1 M) was heated at 100°C for 40 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **19f** (4.1 mg, 88%). $R_f = 0.42$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −53.7 (*c* 0.35, $CHCl_3$); IR (thin film) ν_{max} 3380, 2928, 1732, 1690, 1463, 1373, 1250, 1135, 1053, 1017, 974, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, $J = 3.5$ Hz, 1H, NC*H*CHS), 7.34 (d, $J = 3.5$ Hz, 1H, NCHC*H*S), 6.86 (s, 1H, C*H*=C(CH_3)), 5.51 (ddd, $J = 15.0$, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 5.41 (dd, $J = 7.5$, 3.5 Hz, 1H, CHOCO), 5.34 (ddd, $J = 15.0$, 7.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 4.24 (dd, $J = 10.0$, 2.5 Hz, 1H, $(CH_3)_2CCH$(OH)), 3.74 (d, $J = 4.5$ Hz, 1H, C*H*OH($CHCH_3$)), 3.26 (qd, $J = 7.0$, 4.5 Hz, 1H, CH_3CH(C=O)), 3.11 (bs, 1H, OH), 2.95 (bs, 1H, OH), 2.57 (dd, $J = 15.5$, 10.0 Hz, 1H, CH_2COO), 2.52–2.40 (m, 2H, CH=CHCH_2CHO), 2.50 (dd, $J = 15.5$, 2.5 Hz, 1H, CH_2COO), 2.23–2.15 (m, 1H), 2.17 (s, 3H, CH=C(CH_3)), 2.00–1.92 (m, 1H), 1.66–1.58 (m, 2H), 1.53–1.44 (m, 1H), 1.38–1.15 (m, 2H), 1.29 (s, 3H, $C(CH_3)_2$), 1.19 (d, $J = 7.0$ Hz, 3H, CH_3CH(C=O)), 1.07 (s, 3H, $C(CH_3)_2$), 0.98 (d, $J = 7.0$ Hz, 3H, C$H_3$$CHCH_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 219.9, 170.5, 164.5, 142.7, 141.1, 134.9, 125.1, 119.5, 119.1, 76.9, 76.1, 72.4, 52.5, 43.7, 38.8, 37.6, 35.9, 32.5, 30.5, 27.1, 21.0, 20.8, 16.6, 16.6, 14.9; HRMS (FAB), calcd for $C_{25}H_{37}NO_5S$ ($M + Cs^+$) 596.1447, found 596.1430.

***cis*-Macrolactone 18g.** A solution of vinyl iodide **7** (10 mg, 0.020 mmol, 1.0 equiv), stannane **8g**[16] (10 mg, 0.040 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (2.5 mg, 0.002 mmol, 0.1 equiv) in degassed toluene (200 μL, 0.1 M) was heated at 100°C for 40 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **18g** (6.5 mg, 73%). $R_f = 0.24$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −29.3 (*c* 0.15, $CHCl_3$); IR (thin film) ν_{max} 3224, 2922, 2853, 1721, 1682, 1460, 1254, 1089, 1050, 991, 884, 807, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H, NCHS), 7.82 (s, 1H, NCHC), 6.75 (s, 1H, C*H*=C(CH_3)), 5.46 (ddd, $J = 10.5$, 10.5, 3.5 Hz, 1H, C*H*=$CHCH_2$), 5.39 (ddd, $J = 10.5$, 10.5, 4.5 Hz, 1H, C*H*=$CHCH_2$), 5.34 (dd, $J = 8.5$, 3.5 Hz, 1H, CHOCO), 4.14–4.08 (m, 1H, $(CH_3)_2CCH$(OH)), 3.76–3.72 (m, 1H, C*H*OH($CHCH_3$)), 3.12 (qd, $J = 7.0$, 2.0 Hz, 1H, CH_3CH(C=O)), 2.87 (bs, OH), 2.73 (ddd, $J = 15.0$, 10.5, 8.5 Hz, 1H, CH=CHCH_2CHO), 2.52 (dd, $J = 15.5$, 10.5 Hz, 1H, CH_2COO), 2.44 (dd, $J = 15.5$, 3.0 Hz, 1H, CH_2COO), 2.39–2.34 (m, 1H), 2.26–2.13 (m, 2H), 2.08–1.95 (m, 2H), 2.00 (s, 3H, CH=C(CH_3)), 1.77–1.15 (m, 3H), 1.33 (s, 3H, $C(CH_3)_2$), 1.18 (d, $J = 7.0$ Hz, 3H, CH_3CH(C=O)), 1.09 (s, 3H, $C(CH_3)_2$), 0.99 (d, $J = 7.0$ Hz, 3H, C$H_3$$CHCH_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.0, 170.2, 152.3, 143.3, 137.0, 133.6, 124.4, 121.4, 116.6, 78.6, 74.1, 72.6, 53.2, 41.8, 39.2, 38.6, 32.5, 31.7, 27.6, 27.5, 22.6, 18.9, 15.7, 15.5, 13.5; HRMS (FAB), calcd for $C_{25}H_{37}NO_5S$ ($M + Na^+$) 486.2290, found 486.2278.

***trans*-Macrolactone 19g.** A solution of vinyl iodide **11** (12 mg, 0.024 mmol, 1.0 equiv), stannane **8g**[16] (12 mg, 0.047 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (3.0 mg, 0.002 mmol, 0.1 equiv) in degassed toluene (250 μL, 0.1 M) was heated at 100°C for 40 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **19g** (8.5 mg, 76%). $R_f = 0.25$ (silica gel, 66% EtOAc in hexanes); $[\alpha]_D^{22}$ −15.9 (*c* 0.33, $CHCl_3$); IR (film) ν_{max} 3419, 2932, 1734, 1728, 1691, 1466, 1375, 1252, 1149, 1043, 1008, 975, 881 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.80 (s, 1H, NCHS), 7.83 (s, 1H, NCHC), 6.72 (s, 1H, C*H*=C(CH_3)), 5.57 (ddd, $J = 15.0$, 7.5, 6.0 Hz, 1H, C*H*=$CHCH_2$), 5.42 (dd, $J = 9.0$, 3.5 Hz, 1H, CHOCO), 5.38 (ddd, $J = 15.0$, 8.0, 7.0 Hz, 1H, C*H*=$CHCH_2$), 4.09 (ddd, $J = 10.5$, 3.5, 3.0 Hz, 1H, $(CH_3)_2CCH$OH), 3.78–3.72 (m, 1H, C*H*OH($CHCH_3$)), 3.23 (qd, $J = 6.5$, 4.5 Hz, 1H, CH_3CH(C=O)), 2.90 (d, $J = 4.0$ Hz, 1H, OH), 2.58 (dd, $J = 15.0$, 10.5 Hz, 1H, CH_2COO), 2.52 (dd, $J = 15.0$, 3.0 Hz, 1H, CH_2COO), 2.20 (m, 2H), 2.05–1.94 (m, 1H), 1.72–1.64 (m, 1H), 1.64–1.55 (m, 1H), 1.48–1.37 (m, 1H), 1.35–1.16 (m, 3H), 1.30 (s, 3H, $C(CH_3)_2$), 1.19 (d, $J = 6.5$ Hz, 3H, CH_3CH(C=O)), 1.09 (s, 3H, $C(CH_3)_2$), 0.98 (d, $J = 7.0$ Hz, 3H, C$H_3$$CHCH_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 219.8, 170.5, 152.4, 143.3, 136.7, 134.4, 133.9, 125.7, 116.6, 77.9, 75.3, 72.7, 52.2, 43.4, 38.5, 37.6, 36.7, 32.2, 30.6, 27.2, 21.5, 20.3, 16.1, 15.3, 14.5; HRMS (FAB), calcd for $C_{25}H_{37}NO_5S$ ($M + Cs^+$) 486.2290, found 486.2487.

***trans*-Macrolactone 19h.** A solution of vinyl iodide **11** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8h** (8.0 mg,

0.020 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (1.1 mg, 0.001 mmol, 0.1 equiv) in degassed toluene (100 μL, 0.1 M) was heated at 100°C for 20 min according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **19h** (4.3 mg, 88%). $R_f = 0.20$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −31.5 (*c* 0.60, $CHCl_3$); IR (thin film) ν_{max} 3410, 2930, 1726, 1692, 1463, 1374, 1255, 1180, 1064, 973 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.13 (s, 1H, ArH), 6.60 (s, 1H, C*H*=C(CH_3)), 5.48 (ddd, *J* = 15.0, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 5.40 (dd, *J* = 5.5, 5.5 Hz, 1H, CHOCO), 5.35 (ddd, *J* = 5.0, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 4.91 (d, *J* = 7.0 Hz, 2H, CH_2OH), 4.23 (ddd, *J* = 9.5, 3.5, 3.0 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.74 (ddd, *J* = 7.0, 5.0, 2.5 Hz, 1H, C*H*OH($CHCH_3$)), 3.34 (t, *J* = 7.0 Hz, 1H, CH_2OH), 3.26 (qd, *J* = 7.0, 7.0 Hz, 1H, $CH_3CH(C=O)$), 3.05 (d, *J* = 3.5 Hz, 1H, $C(CH_3)_2CHOH$), 3.00 (d, *J* = 5.0 Hz, 1H, $CH_3CHCH(OH)CHCH_3$), 2.56 (dd, *J* = 15.5, 9.5 Hz, 1H, CH_2COO), 2.47 (dd, *J* = 15.5, 3.0 Hz, 1H, CH_2COO), 2.58–2.45 (m, 1H, CH=$CHCH_2CH$), 2.24–2.16 (m, 1H, CH=$CHCH_2CH$), 2.08 (s, 3H, CH=CCH_3), 1.98–1.90 (m, 1H), 1.63–1.56 (m, 2H), 1.54–1.46 (m, 1H), 1.41–1.30 (m, 1H), 1.27 (s, 3H, $C(CH_3)_2$), 1.20 (d, *J* = 7.0 Hz, 3H, $CH_3CH(C=O)$), 1.07 (s, 3H, $C(CH_3)_2$), 0.99 (d, *J* = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 219.6, 170.4, 169.7, 158.1, 152.4, 137.5, 134.7, 125.3, 116.3, 76.8, 76.3, 72.2, 61.8, 53.5, 44.0, 39.1, 37.6, 35.8, 32.6, 30.2, 27.1, 21.0, 20.9, 16.7, 15.9, 15.1; HRMS (FAB), calcd for $C_{26}H_{39}NO_6S$ ($M + Cs^+$) 626.1552, found 626.1536.

***cis*-Macrolactone 18i.** A solution of vinyl iodide **7** (7.9 mg, 0.016 mmol, 1.0 equiv), stannane **8i** (10.0 mg, 0.031 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (1.8 mg, 0.002 mmol, 0.1 equiv) in degassed toluene (150 μL, 0.1 M) was heated at 100°C for 40 min according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes), macrolactone **18i** (5.0 mg, 60%). $R_f = 0.33$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −58.6 (*c* 0.14, $CHCl_3$); IR (thin film) ν_{max} 3466, 2927, 1740, 1687, 1464, 1375, 1224, 1047, 1008, 977 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.15 (m, 1H, ArH), 6.61 (s, 1H, C*H*=C(CH_3)), 5.45 (ddd, *J* = 10.5, 10.5, 4.0 Hz, 1H, C*H*=$CHCH_2$), 5.41–5.35 (m, 1H, C*H*=$CHCH_2$), 5.35 (s, 2H, CH_2OAc), 5.31–5.29 (m, 1H, CHOCO), 4.20 (m, 1H, $(CH_3)_2CCH(OH)$), 3.74 (m, 1H, C*H*OH($CHCH_3$)), 3.13 (qd, *J* = 6.5, 2.0 Hz, 1H, $CH_3CH(C=O)$), 3.03–2.96 (m, 2H, OH), 2.70 (ddd, *J* = 15.0, 10.0, 10.0 Hz, 1H, CH=$CHCH_2CHO$), 2.51 (dd, *J* = 15.0, 11.5 Hz, 1H, CH_2COO), 2.38 (dd, *J* = 15.0, 2.5 Hz, 1H, CH_2COO), 2.28–2.23 (m, 1H), 2.22–2.14 (m, 2H), 2.16 (s, 3H, $COCH_3$), 2.11 (s, 3H, CH=C(CH_3)), 2.05–1.98 (m, 1H), 1.79–1.72 (m, 1H), 1.71–1.64 (m, 1H), 1.39–1.15 (m, 2H), 1.33 (s, 3H, $C(CH_3)_2$), 1.19 (d, *J* = 7.0 Hz, 3H, $CH_3CH(C=O)$), 1.09 (s, 3H, $C(CH_3)_2$), 1.00 (d, *J* = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 220.5, 170.4, 163.6, 152.7, 139.2, 133.6, 124.9, 119.1, 117.6, 116.5, 78.5, 74.1, 72.5, 62.4, 53.2, 41.8, 39.2, 38.6, 32.5, 31.7, 29.7, 27.5, 27.5, 22.6, 18.8, 15.7, 15.5, 13.5; HRMS (FAB), calcd for $C_{28}H_{41}NO_7S$ ($M + Cs^+$) 668.1658, found 668.1679.

***trans*-Macrolactone 19i.** A solution of vinyl iodide **11** (11.0 mg, 0.022 mmol, 1.0 equiv), stannane **8i** (14.0 mg, 0.044 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (2.5 mg, 0.002 mmol, 0.1 equiv) in degassed toluene (210 μL, 0.1 M) was heated at 100°C for 40 min according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes), unreacted vinyl iodide **11** (2.5 mg, 36%) and macrolactone **19i** (4.5 mg, 39%). $R_f = 0.30$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −33.7 (*c* 0.18, $CHCl_3$); IR (thin film) ν_{max} 3497, 2933, 1739, 1694, 1506, 1456, 1374, 1225, 1046, 976 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.16 (s, 1H, ArH), 6.58 (s, 1H, C*H*=C(CH_3)), 5.56–5.50 (m, 1H, C*H*=$CHCH_2$), 5.41–5.35 (m, 2H, C*H*=$CHCH_2$ and CHOCO), 5.36 (s, 2H, CH_2OAc), 4.15 (dd, *J* = 10.5, 2.5 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.75–3.73 (m, 1H, C*H*OH($CHCH_3$)), 3.24 (qd, *J* = 7.0, 4.5 Hz, 1H, $CH_3CH(C=O)$), 3.10 (m, 1H, OH), 2.62 (m, 1H, OH), 2.56 (dd, *J* = 15.0, 10.5 Hz, 1H, CH_2COO), 2.48 (dd, *J* = 15.0, 3.0 Hz, 1H, CH_2COO), 2.47–2.43 (m, 2H), 2.20–2.14 (m, 1H), 2.16 (s, 3H, $COCH_3$), 2.10 (d, *J* = 1.5 Hz, 3H, CH=C(CH_3)), 2.01–1.94 (m, 1H), 1.69–1.55 (m, 2H), 1.49–1.41 (m, 1H), 1.30–1.15 (m, 2H), 1.29 (s, 3H, $C(CH_3)_2$), 1.18 (d, *J* = 7.0 Hz, 3H, $CH_3CH(C=O)$), 1.07 (s, 3H, $C(CH_3)_2$), 0.98 (d, *J* = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.0, 170.6, 163.6, 152.7, 138.0, 134.4, 125.8, 119.4, 117.7, 116.5, 77.8, 75.7, 72.5, 62.5, 52.5, 43.5, 38.7, 37.8, 36.4, 32.4, 30.7, 29.7, 27.3, 21.1, 20.6, 16.3, 15.6, 14.7; HRMS (FAB), calcd for $C_{28}H_{41}NO_7S$ ($M + Cs^+$) 668.1658, found 668.1681.

***cis*-Macrolactone 18j.** A solution of vinyl iodide **7** (12.5 mg, 0.025 mmol, 1.0 equiv), stannane **8j** (20 mg, 0.049 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (1.5 mg, 0.006 mmol, 0.2 equiv) in degassed DMF (250 μL, 0.1 M) was stirred at 25°C for 20 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 67% ether in hexanes) macrolactone **18j** (9 mg, 74%). $R_f = 0.32$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −65.3 (*c* 0.45, $CHCl_3$); IR (thin film) ν_{max} 3406, 2924, 2852, 1732, 1682, 1455, 1366, 1263, 1192, 1148, 1096, 1043, 983, 881 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (s, 1H, ArH), 6.62 (s, 1H, C*H*=C(CH_3)), 5.60 (d, *J* = 47.0 Hz, 2H, CH_2F), 5.45 (ddd, *J* = 10.5, 10.5, 4.0 Hz, 1H, C*H*=$CHCH_2$), 5.38 (ddd, *J* = 10.0, 10.0, 5.0 Hz, 1H, C*H* = $CHCH_2$), 5.31 (dd, *J* = 10.0, 1.5 Hz, 1H, CHOCO), 4.19 (ddd, 1H, *J* = 11.0, 5.0, 2.5 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.73 (m, 1H, C*H*OH($CHCH_3$)), 3.13 (qd, *J* = 7.0, 2.0 Hz, 1H, $CH_3CH(C=O)$), 2.97 (d, *J* = 2.0 Hz, 1H, OH), 2.93 (d, *J* = 5.5 Hz, 1H, OH), 2.71 (ddd, *J* = 15.0, 10.0, 10.0 Hz, 1H, CH=$CHCH_2CHO$), 2.51 (dd, *J* = 15.5, 11.5 Hz, 1H, CH_2COO), 2.39 (dd, *J* = 15.5, 2.0 Hz, 1H, CH_2COO), 2.29–2.22 (m, 1H), 2.22–2.16 (m, 1H), 2.11 (d, *J* = 1.0 Hz, 3H, CH=C(CH_3)), 2.06–1.99 (m, 1H), 1.77–1.71 (m, 1H), 1.69–1.62 (m, 1H), 1.38–1.16 (m, 3H), 1.32 (s, 3H, $C(CH_3)_2$), 1.18 (d, *J* = 7.0 Hz, 3H, $CH_3CH(C=O)$),

1.08 (s, 3H, $C(CH_3)_2$), 1.00 (d, $J=7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 220.4, 160.3, 170.4, 153.0, 139.3, 133.6, 124.8, 119.1, 117.9, 80.5 (d, $J=676$ Hz) 78.6, 74.1, 72.6, 53.1, 41.9, 39.2, 38.6, 32.5, 31.7, 27.5, 27.5, 22.6, 19.0, 15.6, 15.5, 13.6; HRMS (FAB), calcd for $C_{26}H_{38}FNO_5S$ ($M+Cs^+$) 628.1509, found 628.1530.

***trans*-Macrolactone 19j.** A solution of vinyl iodide **11** (15 mg, 0.030 mmol, 1.0 equiv), stannane **8j** (27 mg, 0.066 mmol, 2.2 equiv) and $Pd(MeCN)_2Cl_2$ (1.5 mg, 0.006 mmol, 0.2 equiv) in degassed DMF (300 μL, 0.1 M) was stirred at 25°C for 20 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes) macrolactone **19j** (11 mg, 75%). $R_f=0.17$ (silica gel, 33% ether in hexanes); $[\alpha]_D^{22}$ −37.1 (*c* 0.55, $CHCl_3$); IR (thin film) ν_{max} 3508, 2934, 1730, 1690, 1505, 1461, 1428, 1366, 1251, 1196, 1150, 1041, 977 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.22 (s, 1H, ArH), 6.58 (s, 1H, $CH=C(CH_3)$), 5.61 (d, $J=47.0$ Hz, 2H, CH_2F), 5.55–5.50 (m, 1H, $CH=CHCH_2$), 5.41–5.35 (m, 2H, $CH=CHCH_2$ and CHOCO), 4.15 (ddd, $J=10.0$, 3.5, 3.0 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.75–3.73 (m, 1H, $CHOH(CHCH_3)$), 3.24 (qd, $J=7.0$, 4.5 Hz, 1H, $CH_3CH(C=O)$), 3.05 (d, $J=4.0$ Hz, 1H, OH), 2.62 (d, $J=4.0$ Hz, 1H, OH), 2.56 (dd, $J=15.0$, 10.5 Hz, 1H, CH_2COO), 2.49 (dd, $J=15.5$, 2.5 Hz, 1H, CH_2COO), 2.49–2.44 (m, 2H), 2.20–2.13 (m, 1H), 2.10 (s, 3H, $CH=C(CH_3)$), 2.01–1.93 (m, 1H), 1.67–1.56 (m, 2H), 1.49–1.43 (m, 1H), 1.31–1.17 (m, 2H), 1.28 (s, 3H, $C(CH_3)_2$), 1.18 (d, $J=6.5$ Hz, 3H, $CH_3CH(C=O)$), 1.07 (s, 3H, $C(CH_3)_2$), 0.98 (d, $J=7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 219.9, 170.5, 163.5, 153.0, 138.2, 134.4, 125.7, 119.3, 118.0, 80.6 (d, $J=675$ Hz), 77.7, 75.7, 72.5, 52.4, 43.6, 38.7, 37.7, 36.4, 32.4, 30.6, 27.3, 21.2, 20.6, 16.4, 15.5, 14.8; HRMS (FAB), calcd for $C_{26}H_{38}FNO_5S$ ($M+Cs^+$) 628.1509, found 628.1487.

***cis*-Macrolactone 18k.** A solution of vinyl iodide **7** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8k** (7.1 mg, 0.020 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (0.5 mg, 0.002 mmol, 0.2 equiv) in degassed DMF (100 μL, 0.1 M) was stirred at 25°C for 12 h according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 33% EtOAc in hexanes) to furnish macrolactone **18k** (3.9 mg, 87%). $R_f=0.53$ (silica gel, 33% EtOAc in hexanes); $[\alpha]_D^{22}$ −45.8 (*c* 0.45, $CHCl_3$); IR (thin film) ν_{max} 3500, 2929, 1730, 1689, 1463, 1378, 1296, 1253, 1154, 1088, 1047, 1013, 980, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39, (d, $J=2.0$ Hz, 1H, ArH), 6.41 (dd, $J=3.0$, 2.0 Hz, 1H, ArH), 6.37 (s, 1H, $CH=C(CH_3)$), 6.30 (d, 1H, $J=3.0$ Hz, ArH), 5.44 (ddd, $J=10.5$, 10.5, 3.5 Hz, 1H, $CH=CHCH_2$), 5.38 (ddd, $J=10.5$, 10.5, 5.0 Hz, 1H, $CH=CHCH_2$), 5.32 (dd, $J=9.5$, 1.5 Hz, 1H, CHOCO), 4.14–4.07 (m, 1H, $(CH_3)_2CCH(OH)$), 3.76–3.74 (m, 1H, $CHOH(CHCH_3)$), 3.13 (qd, $J=6.5$, 2.5 Hz, 1H, $CH_3CH(C=O)$), 2.87 (bs, 1H, OH), 2.72 (ddd, $J=15.0$, 10.0, 10.0 Hz, 1H, $CH=CHCH_2CHO$), 2.53 (dd, $J=15.5$, 11.0 Hz, 1H, CH_2COO), 2.50 (bs, 1H, OH), 2.44 (dd, $J=15.5$, 3.0 Hz, 1H, CH_2COO), 2.25–2.15 (m, 1H), 2.07–1.98 (m, 1H), 2.04 (s, 3H, $CH=C(CH_3)$), 1.78–1.71 (m, 1H), 1.70–1.61 (m, 1H), 1.39–1.16 (m, 3H), 1.32 (s, 3H, $C(CH_3)_2$), 1.18 (d, $J=6.5$ Hz, 3H, $CH_3CH(C=O)$), 1.10 (s, 3H, $C(CH_3)_2$), 1.00 (d, $J=7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.2, 170.3, 152.4, 141.6, 134.2, 133.6, 124.7, 115.7, 111.3, 109.8, 79.1, 74.1, 72.9, 52.8, 42.2, 39.0, 38.6, 32.6, 31.7, 27.7, 27.6, 22.3, 19.9, 15.6, 15.1, 13.7; HRMS (FAB), calcd for $C_{26}H_{38}O_6$ ($M+Cs^+$) 579.1723, found 579.1705.

***trans*-Macrolactone 19k.** A solution of vinyl iodide **11** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8k** (7.1 mg, 0.020 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (0.5 mg, 0.002 mmol, 0.2 equiv) in degassed DMF (100 μL, 0.1 M) was stirred at 25°C for 12 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 33% EtOAc in hexanes) macrolactone **19k** (4.1 mg, 92%). $R_f=0.44$ (silica gel, 33% EtOAc in hexanes); $[\alpha]_D^{22}$ −18.8 (*c* 0.44, $CHCl_3$); IR (thin film) ν_{max} 3518, 2929, 1728, 1692, 1463, 1375, 1255, 1153, 1075, 1016, 975, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.40 (s, 1H, ArH), 6.41 (dd, $J=3.0$, 1.5 Hz, 1H, ArH), 6.33 (s, 1H, $CH=C(CH_3)$), 6.31 (d, $J=3.0$ Hz, 1H, ArH), 5.55 (ddd, $J=14.5$, 7.0, 7.0 Hz, 1H, $CH=CHCH_2$), 5.38 (dd, $J=9.0$, 4.0 Hz, 1H, CHOCO), 5.43–5.34 (m, 1H, $CH=CHCH_2$), 4.10–4.05 (m, 1H, $(CH_3)_2CCH(OH)$), 3.78–3.72 (m, 1H, $CHOH(CHCH_3)$), 3.24 (qd, $J=7.0$, 6.5 Hz, 1H, $CH_3CH(C=O)$), 2.93 (d, $J=3.5$ Hz, 1H, OH), 2.57 (dd, $J=15.5$, 10.5 Hz, 1H, CH_2COO), 2.50 (dd, $J=15.5$, 2.5 Hz, 1H, CH_2COO), 2.47–2.37 (m, 2H), 2.19–2.0 (m, 1H), 2.04–1.95 (m, 1H), 2.03 (s, 3H, $CH=C(CH_3)$), 1.71–1.61 (m, 2H), 1.48–1.39 (m, 1H), 1.38–1.32 (m, 1H), 1.29 (s, 3H, $C(CH_3)_2$), 1.27–1.20 (m, 3H), 1.18 (d, $J=7.0$ Hz, 3H, $CH_3CH(C=O)$), 1.08 (s, 3H, $C(CH_3)_2$), 0.98 (d, $J=7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.2, 170.6, 152.3, 141.7, 134.3, 133.8, 126.1, 115.6, 111.3, 109.8, 78.2, 75.4, 72.7, 52.3, 43.5, 38.6, 37.8, 36.8, 32.4, 30.8, 27.4, 21.5, 20.4, 16.3, 15.2, 14.7; HRMS (FAB), calcd for $C_{26}H_{38}O_6$ ($M+Cs^+$) 579.1723, found 579.1707.

***cis*-Macrolactone 18l.** A solution of vinyl iodide **7** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8l** (7.5 mg, 0.020 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (0.5 mg, 0.002 mmol, 0.2 equiv) in degassed DMF (100 μL, 0.1 M) was stirred at 25°C for 12 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 33% EtOAc in hexanes), macrolactone **18l** (4.1 mg, 88%). $R_f=0.49$ (silica gel, 33% EtOAc in hexanes); $[\alpha]_D^{22}$ −34.0 (*c* 0.40, $CHCl_3$); IR (thin film) ν_{max} 3498, 2928, 2858, 1729, 1688, 1462, 1377, 1251, 1152, 1089, 1048, 1008, 978, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29, (dd, $J=3.5$, 3.5 Hz, 1H, $SCHCHCH$), 7.03 (d, $J=3.5$ Hz, 2H, ArH), 6.73 (s, 1H, $CH=C(CH_3)$), 5.45 (ddd, $J=10.5$, 10.5, 3.0 Hz, 1H, $CH=CHCH_2$), 5.39 (ddd, $J=10.5$, 10.5, 5.0 Hz, 1H, $CH=CHCH_2$), 5.37 (dd, $J=10.5$, 2.5 Hz, 1H, CHOCO),

4.10 (ddd, J = 10.5, 5.5, 2.5 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.77–3.74 (m, 1H, $CHOH(CHCH_3)$), 3.14 (qd, J = 7.0, 2.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.88 (bs, 1H, OH), 2.76 (ddd, J = 14.0, 10.5, 10.5 Hz, 1H, $CH{=}CHCH_2CHO$), 2.53 (dd, J = 16.0, 10.5 Hz, 1H, CH_2COO), 2.46 (bs, 1H, OH), 2.45 (dd, J = 16.0, 2.5 Hz, 1H, CH_2COO), 2.25–2.15 (m, 2H), 2.04–1.97 (m, 1H), 2.04 (s, 3H, $CH{=}CCH_3$), 1.78–1.70 (m, 1H), 1.70–1.55 (m, 1H), 1.42–1.15 (m, 3H), 1.32 (s, 3H, $C(CH_3)_2$), 1.18 (d, J = 7.0 Hz, 3H, $CH_3CH(C{=}O)$), 1.10 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.2, 170.4, 139.9, 133.8, 133.6, 127.9, 126.9, 125.6, 124.8, 120.6, 79.4, 74.1, 73.0, 52.8, 42.1, 39.1, 38.6, 32.6, 31.8, 27.7, 27.6, 22.3, 19.9, 15.6, 15.1, 13.7; HRMS (FAB), calcd for $C_{26}H_{38}O_5S$ ($M + Na^+$) 485.2338, found 485.2321.

***trans*-Macrolactone 19l.** A solution of vinyl iodide **11** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8l** (7.5 mg, 0.020 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (0.5 mg, 0.002 mmol, 0.2 equiv) in degassed DMF (100 μL, 0.1 M) was stirred at 25°C for 12 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 18% EtOAc in hexanes) macrolactone **19l** (4.4 mg, 94%). R_f = 0.31 (silica gel, 18% EtOAc in hexanes); $[\alpha]_D^{22}$ −12.9 (c 0.45, $CHCl_3$); IR (thin film) ν_{max} 3495, 2928, 2928, 1727, 1692, 1462, 1374, 1251, 1150, 1044, 1012, 975, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (dd, J = 4.0, 2.5 Hz, 1H, $SCHCHCH$), 7.04 (d, J = 4.0 Hz, 1H, ArH), 7.03 (d, J = 2.5 Hz, 1H, ArH), 6.70 (s, 1H, $CH{=}C(CH_3)$), 5.56 (ddd, J = 14.5, 7.0, 7.0 Hz, 1H, $CH{=}CHCH_2$), 5.43 (dd, J = 9.5, 2.5 Hz, 1H, CHOCO), 5.40 (ddd, J = 14.5, 8.5, 5.0 Hz, 1H, $CH{=}CHCH_2$), 4.07 (ddd, J = 10.5, 3.0, 2.5 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.78–3.74 (m, 1H, $CHOH(CHCH_3)$), 3.23 (qd, J = 7.0, 4.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.93 (d, J = 3.5 Hz, 1H, OH), 2.57 (dd, J = 15.5, 10.5 Hz, 1H, CH_2COO), 2.50 (dd, J = 15.5, 2.5 Hz, 1H, CH_2COO), 2.52–2.37 (m, 2H), 2.19–2.10 (m, 1H), 2.05–1.97 (m, 1H), 2.02 (s, 3H, $CH{=}C(CH_3)$), 1.70–1.63 (m, 1H), 1.63–1.57 (m, 1H), 1.16–1.15 (m, 3H), 1.29 (s, 3H, $C(CH_3)_2$), 1.18 (d, J = 7.0 Hz, 3H, $CH_3CH(C{=}O)$), 1.08 (s, 3H, $C(CH_3)_2$), 0.98 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.0, 170.6, 139.8, 134.2, 133.4, 127.9, 126.9, 126.1, 125.6, 120.7, 78.6, 75.4, 72.8, 52.3, 43.4, 38.6, 37.8, 37.0, 32.4, 30.7, 27.4, 21.6, 20.4, 16.3, 15.1, 14.7; HRMS (FAB), calcd for $C_{26}H_{38}O_5S$ ($M + Cs^+$) 595.1494, found 595.1511.

***cis*-Macrolactone 18m.** A solution of vinyl iodide **7** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8m**[17] (4.8 mg, 0.020 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (0.5 mg, 0.002 mmol, 0.2 equiv) in degassed DMF (100 μL, 0.1 M) was stirred at 25°C for 12 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 33% EtOAc in hexanes), macrolactone **18m** (3.9 mg, 86%). R_f = 0.49 (silica gel, 33% EtOAc in hexanes); $[\alpha]_D^{22}$ −28.8 (c 0.40, $CHCl_3$); IR (thin film) ν_{max} 3498, 2930, 1729, 1688, 1462, 1379, 1298, 1254, 1152, 1089, 1047, 1008, 754 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.31 (m, 2H, ArH), 7.30–7.21 (m, 3H, ArH), 6.58 (s, 1H, $CH{=}C(CH_3)$), 5.46 (ddd, J = 10.5, 10.5, 4.0 Hz, 1H, $CH{=}CHCH_2$), 5.42 (ddd, J = 10.5, 10.5, 4.5 Hz, 1H, $CH{=}CHCH_2$), 5.38 (dd, J = 9.5, 1.5 Hz, 1H, CHOCO), 4.12 (ddd, J = 11.0, 5.5, 3.0 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.79–3.74 (m, 1H, $CHOH(CHCH_3)$), 3.13 (qd, J = 7.0, 2.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.89 (d, J = 2.5 Hz, 1H, $CHOH(CHCH_3)$), 2.77 (ddd, J = 15.5, 10.0, 10.0 Hz, 1H, $CH{=}CHCH_2CHO$), 2.54 (dd, J = 15.5, 11.0 Hz, 1H, CH_2COO), 2.50 (d, J = 5.5 Hz, 1H, $(CH_3)_2CCH(OH)$), 2.45 (dd, J = 15.5, 3.0 Hz, 1H, CH_2COO), 2.28–2.17 (m, 2H), 2.08–1.98 (m, 1H), 1.93 (s, 3H, $CH{=}C(CH_3)$), 1.81–1.71 (m, 1H), 1.71–1.67 (m, 1H), 1.42–1.16 (m, 3H), 1.31 (s, 3H, $C(CH_3)_2$), 1.18 (d, J = 7.0 Hz, 3H, $CH_3CH(C{=}O)$), 1.10 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.2, 170.4, 136.9, 136.0, 133.5, 129.0, 128.2, 127.1, 126.8, 124.9, 79.3, 74.1, 72.9, 52.8, 42.1, 39.1, 38.6, 32.6, 31.7, 27.7, 27.6, 22.3, 19.9, 15.6, 14.5, 13.7; HRMS (FAB), calcd for $C_{28}H_{40}O_5$ ($M + Cs^+$) 589.1930, found 589.1944.

***trans*-Macrolactone 19m.** A solution of vinyl iodide **11** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8m**[17] (4.8 mg, 0.020 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (0.5 mg, 0.002 mmol, 0.2 equiv) in degassed DMF (100 μL, 0.1 M) was stirred at 25°C for 12 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 18% EtOAc in hexanes) macrolactone **19m** (4.1 mg, 89%). R_f = 0.32 (silica gel, 18% EtOAc in hexanes); $[\alpha]_D^{22}$ −3.8 (c 0.40, $CHCl_3$); IR (thin film) ν_{max} 3518, 2930, 1728, 1692, 1461, 1374, 1256, 1174, 1073, 1043, 1012, 975, 755 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.31 (m, 2H, ArH), 7.27–7.21 (m, 3H, ArH), 6.55 (s, 1H, $CH{=}C(CH_3)$), 5.51 (ddd, J = 14.5, 7.0, 7.0 Hz, 1H, $CH{=}CHCH_2$), 5.44 (dd, J = 9.0, 3.0 Hz, 1H, CHOCO), 5.42 (ddd, J = 14.5, 7.0, 7.0 Hz, 1H, $CH{=}CHCH_2$), 4.08 (ddd, J = 10.0, 3.0, 2.5 Hz, 1H, $(CH_3)_2CCH(OH)$), 3.78–3.73 (m, 1H, $CHOH(CHCH_3)$), 3.24 (qd, J = 7.0, 4.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.96 (d, J = 3.0 Hz, 1H, OH), 2.59 (dd, J = 15.0, 10.0 Hz, 1H, CH_2COO), 2.51 (dd, J = 15.0, 2.5 Hz, 1H, CH_2COO), 2.50–2.42 (m, 2H), 2.20–2.12 (m, 1H), 2.05–1.94 (m, 1H), 1.90 (s, 3H, $CH{=}C(CH_3)$), 1.70–1.64 (m, 1H), 1.65–1.55 (m, 1H), 1.48–1.40 (m, 1H), 1.30–1.10 (m, 1H), 1.29 (s, 3H, $C(CH_3)_2$), 1.17 (d, J = 7.0 Hz, 3H, $CH_3CH(C{=}O)$), 1.08 (s, 3H, $C(CH_3)_2$), 0.97 (d, J = 7.0 Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.0, 170.7, 136.8, 135.6, 134.1, 129.0, 128.2, 127.1, 126.8, 126.3, 78.4, 75.4, 72.7, 52.4, 43.4, 38.6, 37.8, 36.9, 32.4, 30.8, 27.5, 21.5, 20.4, 16.3, 14.7, 14.5; HRMS (FAB), calcd for $C_{28}H_{40}O_5$ ($M + Cs^+$) 589.1930, found 589.1948.

***cis*-Macrolactone 18n.** A solution of vinyl iodide **7** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8n**[17] (4.8 mg, 0.020 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (1.1 mg, 0.001 mmol, 0.10 equiv) in degassed toluene (100 μL, 0.1 M) was heated at 100°C for 20 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 66% EtOAc in hexanes),

macrolactone **18n** (1.9 mg, 42%). $R_f = 0.24$ (silica gel, 3% MeOH in $CHCl_3$); $[\alpha]_D^{22}$ −20.0 (*c* 0.08, $CHCl_3$); IR (thin film) ν_{max} 3417, 2926, 1730, 1687, 1463, 1414, 1377, 1252, 1148, 1011, 979, 754 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.55–8.50 (m, 1H, ArH), 8.50–8.44 (m, 1H, ArH), 7.58 (d, $J = 8.0$ Hz, 1H, ArH), 7.31–7.23 (m, 1H, ArH), 6.54 (s, 1H, C*H*=C(CH_3)), 5.47 (ddd, $J = 10.5$, 10.5, 3.5 Hz, 1H, C*H*=$CHCH_2$), 5.41 (ddd, $J = 10.5$, 10.5, 5.0 Hz, 1H, C*H*=$CHCH_2$), 5.36 (dd, $J = 10.0$, 2.0 Hz, 1H, CHOCO), 4.16 (m, 1H, $(CH_3)_2CCH(OH)$), 3.78–3.74 (m, 1H, C*H*OH($CHCH_3$)), 3.13 (qd, $J = 7.0$, 2.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.89 (d, $J = 2.5$ Hz, 1H, OH), 2.76 (ddd, $J = 15.0$, 10.0, 10.0 Hz, 1H, CH=CHCH_2CHO), 2.53 (dd, $J = 15.5$, 11.0 Hz, 1H, CH_2COO), 2.45 (dd, $J = 15.5$, 2.5 Hz, 1H, CH_2COO), 2.28–2.17 (m, 2H), 2.08–2.00 (m, 1H), 1.93 (s, 3H, CH=C(CH_3)), 1.79–1.73 (m, 1H), 1.71–1.63 (m, 1H), 1.40–1.15 (m, 3H), 1.33 (s, 3H, $C(CH_3)_2$), 1.18 (d, $J = 7.0$ Hz, 3H, $CH_3CH(C{=}O)$), 1.10 (s, 3H, $C(CH_3)_2$), 1.00 (d, $J = 7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.1, 170.3, 150.1, 147.8, 138.6, 136.0, 133.6, 124.7, 123.3, 123.1, 78.9, 74.1, 73.0, 52.9, 42.1, 39.2, 38.6, 32.6, 31.6, 27.6, 27.6, 22.4, 19.7, 15.6, 14.6, 13.7; HRMS (FAB), calcd for $C_{27}H_{40}NO_5$ ($M + H^+$) 458.2906, found 458.2923.

***trans*-Macrolactone 19n.** A solution of vinyl iodide **11** (5.1 mg, 0.010 mmol, 1.0 equiv), stannane **8n**[17] (4.8 mg, 0.020 mmol, 2.0 equiv) and $Pd(PPh_3)_4$ (1.1 mg, 0.002 mmol, 0.10 equiv) in degassed toluene (100 μL, 0.1 M) was heated at 100°C for 20 min, according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (500 μm silica gel plate, 66% EtOAc in hexanes), macrolactone **19n** (2.1 mg, 46%). $R_f = 0.11$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −12.9 (*c* 0.07, $CHCl_3$); IR (film) ν_{max} 3418, 2924, 2855, 1729, 1693, 1461, 1375, 1251, 1153, 1048, 975, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.56 (bm, 1H, ArH), 8.48 (bm, 1H, ArH), 7.58 (d, $J = 7.5$ Hz, 1H, ArH), 7.35–7.25 (m, 1H, ArH), 6.50 (s, 1H, C*H*=C(CH_3)), 5.58 (ddd, $J = 15.0$, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 5.43 (dd, $J = 7.5$, 3.5 Hz, 1H, CHOCO), 5.41 (ddd, $J = 15.0$, 7.5, 7.5 Hz, 1H, C*H*=$CHCH_2$), 4.09 (ddd, $J = 10.5$, 3.5, 3.5 Hz, 1H, $(CH_3)_2CCHOH$), 3.77–3.74 (m, 1H, C*H*OH($CHCH_3$)), 3.23 (qd, $J = 7.0$, 4.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.89 (d, 1H, OH), 2.60 (dd, $J = 15.5$, 10.5 Hz, 1H, CH_2COO), 2.52 (dd, $J = 15.5$, 3.0 Hz, 1H, CH_2COO), 2.52–2.45 (m, 2H), 2.20–2.13 (m, 1H), 2.05–1.97 (m, 1H), 1.91 (s, 3H, CH=C(CH_3)), 1.71–1.52 (m, 2H), 1.48–1.40 (m, 1H), 1.30 (s, 3H, $C(CH_3)_2$), 1.18 (d, $J = 7.0$ Hz, 3H, $CH_3CH(C{=}O)$), 1.09 (s, 3H, $C(CH_3)_2$), 0.97 (d, $J = 7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 219.9, 170.6, 150.1, 147.8, 139.2, 138.3, 135.9, 134.4, 125.9, 123.3, 123.0, 78.0, 75.4, 72.8, 52.4, 43.4, 38.6, 37.8, 36.8, 32.4, 30.8, 27.4, 26.4, 21.5, 20.4, 16.2, 14.6; HRMS (FAB), calcd for $C_{27}H_{40}NO_5$ ($M + H^+$) 458.2906, found 458.2927.

***cis*-Macrolactone 18o.**[20] A solution of vinyl iodide **7** (16.5 mg, 0.033 mmol, 1.0 equiv), stannane **8o** (22 μL, 0.065 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (1.0 mg, 0.004 mmol, 0.1 equiv) in degassed DMF (330 μL, 0.1 M) was stirred at 25°C for 33 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes) unreacted vinyl iodide **7** (3.4 mg, 21%) and macrolactone **18o**[20] (7 mg, 51%). $R_f = 0.33$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −48.4 (*c* 0.64, $CHCl_3$); IR (thin film) ν_{max} 3494, 2932, 1737, 1688, 1622, 1464, 1364, 1300, 1249, 1226, 1150, 1090, 1049, 1006, 976 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.29 (s, 1H, C*H*=C(CH_3)), 5.47 (ddd, $J = 10.5$, 10.5, 5.0 Hz, 1H, C*H*=$CHCH_2$), 5.32 (ddd, $J = 10.0$, 10.0, 5.0 Hz, 1H, C*H*=$CHCH_2$), 5.15 (dd, $J = 9.5$, 1.5 Hz, 1H, CHOCO), 4.13 (m, 1H, $(CH_3)_2CCH(OH)$), 3.72 (m, 1H, C*H*OH($CHCH_3$)), 3.12 (qd, $J = 7.0$, 2.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.87 (bs, 1H, OH), 2.61 (ddd, $J = 15.0$, 10.0, 10.0 Hz, 1H, CH=CHCH_2CHO), 2.50 (dd, $J = 15.5$, 11.0 Hz, 1H, CH_2COO), 2.42 (dd, $J = 15.5$, 3.0 Hz, 1H, CH_2COO), 2.36 (m, 1H), 2.23–2.12 (m, 2H), 2.22 (s, 3H, $COCH_3$), 2.14 (d, $J = 1.0$ Hz, 3H, CH=C(CH_3)), 2.05–2.00 (m, 1H), 1.76–1.72 (m, 1H), 1.69–1.61 (m, 2H), 1.38–1.15 (m, 2H), 1.34 (s, 3H, $C(CH_3)_2$), 1.19 (d, $J = 7.0$ Hz, 3H, $CH_3CH(C{=}O)$), 1.09 (s, 3H, $C(CH_3)_2$), 0.99 (d, $J = 7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 219.9, 198.8, 170.0, 152.9, 134.0, 124.0, 123.1, 78.0, 74.1, 72.8, 52.9, 42.0, 39.1, 38.4, 32.3, 31.9, 31.1, 27.4, 22.3, 19.2, 17.4, 15.7, 15.4, 13.5; HRMS (FAB), calcd for $C_{24}H_{38}O_6$ ($M + Cs^+$) 555.1723, found 555.1729.

***trans*-Macrolactone 19o.**[20] A solution of vinyl iodide **11** (17 mg, 0.034 mmol, 1.0 equiv), stannane **8o** (23 μL, 0.068 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (1.1 mg, 0.004 mmol, 0.1 equiv) in degassed DMF (340 μL, 0.1 M) was stirred at 25°C for 20 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plate, 50% EtOAc in hexanes) unreacted vinyl iodide **11** (2.3 mg, 14%) and macrolactone **19o**[20] (7 mg, 49%). $R_f = 0.31$ (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −15.5 (*c* 0.64, $CHCl_3$); IR (thin film) ν_{max} 3500, 2937, 1732, 1688, 1622, 1472, 1428, 1361, 1250, 1220, 1164, 1043, 1011, 974 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.24 (s, 1H, C*H*=C(CH_3)), 5.56–5.50 (m, 1H, C*H*=$CHCH_2$), 5.35–5.29 (m, 1H, C*H*=$CHCH_2$), 5.23 (dd, $J = 9.0$, 2.5 Hz, 1H, CHOCO), 4.14–4.09 (m, 1H, $(CH_3)_2CCH(OH)$), 3.74–3.72 (m, 1H, C*H*OH($CHCH_3$)), 3.22 (qd, $J = 7.0$, 4.5 Hz, 1H, $CH_3CH(C{=}O)$), 2.74 (d, $J = 4.5$ Hz, 1H, OH), 2.56 (dd, $J = 15.0$, 10.0 Hz, 1H, CH_2COO), 2.51 (dd, $J = 15.0$, 3.0 Hz, 1H, CH_2COO), 2.46 (m, 1H), 2.46–2.31 (m, 2H), 2.22 (s, 3H, $COCH_3$), 2.20–2.12 (m, 1H), 2.13 (s, 3H, CH=C(CH_3)), 2.02–1.95 (m, 1H), 1.69–1.56 (m, 2H), 1.46–1.22 (m, 2H), 1.30 (s, 3H, $C(CH_3)_2$), 1.17 (d, $J = 7.5$ Hz, 3H, $CH_3CH(C{=}O)$), 1.08 (s, 3H, $C(CH_3)_2$), 0.97 (d, $J = 7.0$ Hz, 3H, CH_3CHCH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 219.9, 198.7, 170.3, 152.8, 134.9, 125.2, 123.0, 77.1, 75.5, 72.8, 52.4, 43.4, 38.6, 37.6, 36.4, 32.2, 32.0, 30.7, 27.1, 21.4, 20.3, 16.2, 15.9, 14.6; HRMS (FAB), calcd for $C_{24}H_{38}O_6$ ($M + Cs^+$) 555.1723, found 555.1703.

Silyl ether 25. To a solution of alcohol **13** (12.96 g, 54.4 mmol, 1.0 equiv), in DMF (180 mL, 0.3 M) at 0°C,

was added imidazole (10.2 g, 150.0 mmol, 2.8 equiv) followed by TBSCl (13.5 g, 89.8 mmol, 1.7 equiv). After warming to 25°C over 7 h, the solvent was removed under reduced pressure and the resulting oil was partitioned between ether (200 mL) and saturated aqueous NH_4Cl (200 mL). The aqueous layer was extracted with ether (200 mL) and the combined organic extracts were washed with brine (550 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 0→5% EtOAc in hexanes) furnished silyl ether **25** as an oil (16.03 g, 84%). $R_f = 0.48$ (hexanes); $[\alpha]_D^{22}$ −17.5 (*c* 1.65, $CHCl_3$); IR (thin film) ν_{max} 2954, 2928, 2857, 1472, 1361, 1278, 1252, 1082, 914, 836, 776, 677 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.16 (s, 1H, C*H*=CCH_3), 5.74–5.66 (m, 1H, C*H*=CH_2), 5.03 (bm, 1H, CH=C*H*$_2$), 5.01 (s, 1H, CH=C*H*$_2$), 4.16 (dd, *J* = 6.5, 6.5 Hz, 1H, C*H*OTBS), 2.25 (m, 2H, CH_2=CHC*H*$_2$), 1.77 (s, 3H, CH=C(C*H*$_3$)), 0.88 (s, 9H, $SiC(CH_3)_3$), 0.04 (s, 3H, $Si(CH_3)_2$), −0.01 (s, 3H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 149.9, 134.4, 117.0, 77.5, 77.2, 41.0, 25.7, 19.6, 18.2, −4.8, −5.1.

Aldehyde 26. To a solution of olefin **25** (16.0 g, 45.3 mmol, 1.0 equiv) in a mixture of THF (206 mL), *t*-BuOH (206 mL) and H_2O (41 mL) at 0°C was added 4-methylmorpholine *N*-oxide (NMO) (5.84 g, 49.8 mmol, 1.1 equiv) followed by OsO_4 (5.2 mL, 2.5% w/v in *t*-BuOH, 0.453 mmol, 0.01 equiv). The mixture was stirred vigorously for 13 h at 25°C and then quenched with saturated aqueous Na_2SO_3 (125 mL). The resulting solution was stirred for 2 h and then partitioned between EtOAc (150 mL) and water (150 mL). The organic phase was separated and the aqueous phase was extracted with EtOAc (2×200 mL). The combined organic extracts were dried ($MgSO_4$), filtered, and the solvents were removed under reduced pressure. Flash column chromatography (silica gel, 50→90% ether in hexanes) provided unreacted starting material (1.0 g, 6%) and the desired diols as a ca. 1:1 mixture of diastereoisomers (15.5 g, 89%). $R_f = 0.44$ (silica gel, 50% EtOAc in hexanes); IR (thin film) ν_{max} 3387, 2952, 2928, 1252, 1080, 837, 777 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.28 and 6.26 (singlets, 1H total, C*H*=C(CH_3)), 4.47–4.42 (m, 1H, CHOSi), 3.86–3.76 (m, 1H, C*H*OH), 3.61–3.55 and 3.49–3.39 (m, 2H total, C*H*$_2$OH), 3.33 and 3.15 (2 doublets, *J* = 2.0 and 3.5 Hz, 1H total, CHO*H*), 2.46 and 2.45 (triplets, *J* = 5.5 and 5.5 Hz, CH_2O*H*), 1.78 and 1.76 (singlets, 3H total), 1.63–1.60 and 1.58–1.53 (m, 2H total, CH_2), 0.88 and 0.87 (singlets, 9H total, $SiC(CH_3)_3$), 0.08 and 0.07 (singlets, 3H total, $Si(CH_3)_2$), 0.01 and 0.00 (singlets, 3H total, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 149.5, 149.1, 78.7, 77.8, 77.1, 76.6, 74.6, 70.5, 68.6, 66.8, 66.5, 38.6, 38.1, 25.6, 20.5, 19.2, 18.0, 17.9, −4.9, −5.1, −5.4, −5.5; HRMS (FAB), calcd for $C_{13}H_{27}IO_3Si$ ($M + Na^+$) 409.0672, found 409.0662.

The diols (obtained as described above) (23.3 g, 60.2 mmol, 1.0 equiv) were dissolved in a mixture of MeOH (400 mL) and water (200 mL) and the solution was cooled to 0°C. $NaIO_4$ (77.2 g, 361.1 mmol, 6.0 equiv) was then added portionwise over 5 min, and the resulting slurry was vigorously stirred for 30 min at 25°C. After completion of the reaction, the mixture was partitioned between CH_2Cl_2 (500 mL) and water (500 mL) and the organic phase was separated. The aqueous layer was extracted with CH_2Cl_2 (500 mL) and the combined organic extracts were washed with brine (1 L), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 17→50% ether in hexanes) provided aldehyde **26** as an oil (19.6 g, 92%). $R_f = 0.35$ (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ −34.1 (*c* 2.8, $CHCl_3$); IR (thin film) ν_{max} 2954, 2928, 2885, 2856, 1728, 1471, 1279, 1254, 1091, 838, 777, 677 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.73 (dd, *J* = 2.5, 2.5 Hz, 1H, CHO), 6.34 (s, 1H, C*H*=CCH_3), 4.70 (dd, *J* = 8.0, 4.0 Hz, 1H, CHOSi), 2.68 (ddd, *J* = 16.0, 8.3, 2.5 Hz, 1H, (CHO)C*H*$_2$), 2.44 (ddd, *J* = 16.0, 4.0, 2.5 Hz, 1H, (CHO)C*H*$_2$), 1.80 (s, 3H, CH=CC*H*$_3$), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.05 (s, 3H, $Si(CH_3)_2$), 0.01 (s, 3H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.5, 148.7, 78.9, 72.5, 49.6, 25.7, 19.8, 18.0, −4.9, −5.3; HRMS (FAB), calcd for $C_{12}H_{23}IO_2Si$ ($M + Na^+$) 377.0410, found 377.0402.

Methyl ester 28. A mixture of aldehyde **26** (19.6 g, 55.2 mmol, 1.0 equiv) and stabilized ylide **27** (50.2 g, 134.0 mmol, 2.4 equiv) [prepared from 4-bromo-1-butene by: i. phosphonium salt formation; ii. anion formation with KHMDS; and iii. quenching with MeO-C(O)Cl)][22] in benzene (550 mL, 0.1 M) was heated at reflux for 1.5 h. After cooling to 25°C, the mixture was filtered and the solvent was removed under reduced pressure. Flash column chromatography (silica gel, 9→17% ether in hexanes) furnished methyl ester **28** (24.5 g, 98%). $R_f = 0.37$ (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ −7.25 (*c* 1.6, $CHCl_3$); IR (thin film) ν_{max} 3078, 2952, 2920, 2856, 1720, 1462, 1434, 1276, 1253, 1208, 1084, 836, 776, 672 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.81 (dd, *J* = 7.4, 7.4 Hz, 1H, C*H*=$CCOOCH_3$), 6.22 (s, 1H, C*H*=CCH_3), 5.83–5.75 (m, 1H, C*H*=CH_2), 4.99–4.98 (m, 1H, CH=C*H*$_2$), 4.96 (m, 1H, CH=C*H*$_2$), 4.22 (dd, *J* = 7.5, 5.1 Hz, 1H, CHOSi), 3.72 (s, 3H, $COOCH_3$), 3.05 (d, *J* = 6.0 Hz, 2H, C*H*$_2$C(CO_2Me)), 2.40 (ddd, *J* = 15.0, 7.5, 7.5 Hz, 1H, C*H*$_2$CHOSi), 2.33 (ddd, *J* = 15.0, 7.5, 5.1 Hz, 1H, C*H*$_2$CHOSi), 1.77 (s, 3H, CH=C(C*H*$_3$)), 0.85 (s, 9H, $SiC(CH_3)_3$), 0.02 (s, 3H, $Si(CH_3)_2$), −0.02 (s, 3H, $Si(CH_3)_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 167.6, 149.6, 139.5, 135.2, 131.1, 115.2, 78.1, 76.3, 51.7, 35.6, 31.0, 25.6, 19.6, 18.1, −5.0, −5.2; HRMS (FAB), calcd for $C_{18}H_{31}IO_3Si$ ($M + Cs^+$) 583.0142, found 583.0159.

Allylic alcohol 29. Methyl ester **28** (24.5 g, 54.3 mmol, 1.0 equiv) was dissolved in THF (280 mL, 0.2 M) and the solution was cooled to −78°C. DIBAL (163.0 mL, 1 M in CH_2Cl_2, 163.0 mmol, 3.0 equiv) was added dropwise at −78°C over 50 min, and the reaction mixture was then stirred for a further 80 min. The reaction mixture was quenched with saturated aqueous sodium–potassium tartrate (150 mL) and the resulting mixture was allowed to warm up to 25°C over 16 h. The organic layer was separated and the aqueous phase was extracted with ether (3×250 mL). The combined organic extracts were washed with brine (650 mL), dried

($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 17→50% ether in hexanes) furnished alcohol **29** (22.9 g, 100%). $R_f = 0.11$ (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ −7.25 (*c* 1.6, $CHCl_3$); IR (thin film) ν_{max} 3346, 3078, 2954, 2928, 2857, 1637, 1471, 1361, 1276, 1252, 1078, 1005, 836, 775, 674, 558 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.16 (s, 1H, C*H*=C(CH_3)), 5.81–5.73 (m, 1H, C*H*=CH_2), 5.45 (dd, *J* = 6.5, 6.5 Hz, 1H, C*H*=CCH_2OH), 5.03 (m, 2H, CH=CH_2), 4.16 (dd, *J* = 6.5, 6.5 Hz, 1H, CHOSi), 4.02 (d, *J* = 4.5 Hz, 2H, CH_2OH), 2.85 (dd, *J* = 15.0, 5.1 Hz, 1H, CH_2CH=CH_2), 2.84 (dd, *J* = 15.0, 5.0 Hz, 1H, CH_2CH=CH_2), 2.27 (ddd, *J* = 15.0, 6.5, 6.5 Hz, 1H, CH_2CHOSi), 2.25 (ddd, *J* = 15.0, 6.5, 6.5 Hz, 1H, CH_2CHOSi), 1.78 (s, 3H, CH=C(CH_3)), 0.88 (s, 9H, SiC(CH_3)$_3$), 0.02 (s, 3H, Si(CH_3)$_2$), −0.02 (s, 3H, Si(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 149.9, 138.3, 135.5, 123.3, 115.5, 77.5, 76.6, 66.9, 34.4, 32.5, 25.6, 19.5, 18.0, −5.0, −5.2; HRMS (FAB), calcd for $C_{17}H_{31}IO_2Si$ ($M + Cs^+$), 555.0192, found 555.0177.

Triphenylmethyl ether 30. Alcohol **29** (23.5 g, 55.7 mmol, 1.0 equiv) was dissolved in DMF (300 mL, 0.15 M) and 4-DMAP (11.3 g, 92.5 mmol, 1.7 equiv) and trityl chloride (22.1 g, 79.3 mmol, 1.4 equiv) were added. The reaction mixture was stirred at 80°C for 21 h, cooled to room temperature and the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, 5→30% ether in hexanes) to afford the required ether **30** as an oil (35.3 g, 95%). $R_f = 0.88$ (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ −0.74 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3058, 2927, 2854, 1488, 1470, 1448, 1250, 1082, 836, 702, 632 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.45–7.43 (m, 5H, Ph), 7.32–7.21 (m, 10H, Ph), 6.19 (s, 1H, C*H*=CCH_3), 5.61 (m, 2H, C*H*=CH_2 and CH=CH_2), 4.87 (m, 2H, CH=CH_2 and C*H*=(C)CH_2OTr), 4.19 (dd, *J* = 6.8, 6.8 Hz, 1H, CHOSi), 3.46 (s, 2H, CH_2OTr), 2.78 (dd, *J* = 15.4, 6.7 Hz, 1H, CH_2CH=CH_2), 2.73 (dd, *J* = 15.4, 6.3 Hz, 1H, CH_2CH=CH_2), 2.33 (ddd, *J* = 14.5, 6.8, 6.8 Hz, 1H, CH_2CHOSi), 2.31 (ddd, *J* = 14.5, 6.8, 6.8 Hz, 1H, CH_2CHOSi), 1.80 (s, 3H, CH=C(CH_3)), 0.87 (s, 9H, SiC(CH_3)$_3$), 0.04 (s, 3H, Si(CH_3)$_2$), 0.00 (s, 3H, Si(CH_3)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 150.2, 144.3, 136.1, 135.6, 128.7, 127.7, 126.8, 122.5, 115.2, 86.6, 77.4, 67.0, 34.6, 33.0, 25.8, 19.7, 18.0, −4.9, −5.0; HRMS (FAB), calcd for $C_{36}H_{45}IO_2Si$ ($M + Cs^+$) 797.1288, found 797.1309.

Alcohol 31. Olefin **30** (35.3 g, 53.1 mmol, 1.0 equiv) was dissolved in THF (53 mL, 1.0 M) and the solution was cooled to 0°C. Compound 9-BBN (149 mL, 0.5 M in THF, 74.5 mmol, 1.4 equiv) was added dropwise over 1.5 h, and the resulting mixture was stirred for 9 h at 0°C. Aqueous NaOH (106 mL of a 3 N solution, 319.0 mmol, 6.0 equiv) was added, followed by aqueous H_2O_2 (32 mL, 30% w/w in water, 319.0 mmol, 6.0 equiv). Stirring was continued for 1 h at 0°C, after which time the reaction mixture was diluted with ether (500 mL) and water (500 mL). The organic layer was separated and the aqueous phase was extracted with ether (2×500 mL). The combined organic extracts were washed with brine (1 L), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 9→50% ether in hexanes) furnished alcohol **31** (34.6 g, 95%). $R_f = 0.54$ (silica gel, 60% ether in hexanes); $[\alpha]_D^{22}$ −3.5 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3380, 3058, 3032, 2926, 2855, 1489, 1449, 1278, 1251, 1078, 835, 706, 632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47–7.45 (m, 5H, Ph), 7.32–7.22 (m, 10H, Ph), 6.22 (s, 1H, C*H*=C(CH_3)), 5.58 (dd, *J* = 7.1, 7.1 Hz, 1H, C=C*H*CH_2), 4.22 (dd, *J* = 6.8, 6.0 Hz, 1H, CHOSi), 3.52 (bm, 2H, CH_2OH), 3.50 (s, 2H, CH_2OTr), 2.33 (dd, *J* = 14.5, 6.8, 6.8 Hz, 1H, CH_2CHOSi), 2.28 (ddd, *J* = 14.5, 6.8, 6.8 Hz, 1H, CH_2CHOSi), 2.14 (m, 2H, C$H_2CH_2CH_2$OH), 1.82 (s, 3H, CH=CCH_3), 1.46 (m, 2H, CH_2CH_2OH), 0.90 (s, 9H, SiC(CH_3)$_3$), 0.06 (s, 3H, Si(CH_3)$_2$), 0.02 (s, 3H, Si(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 150.2, 144.2, 137.9, 128.5, 127.8, 126.9, 122.2, 86.6, 77.5, 77.3, 67.1, 62.5, 34.6, 31.2, 25.7, 19.8, 18.2, −4.9, −5.0; HRMS (FAB), calcd for $C_{36}H_{47}IO_3Si$ ($M + Cs^+$) 815.1394, found 815.1430.

Iodide 32. A solution of alcohol **31** (34.6 g, 50.73 mmol, 1.0 equiv) in a mixture of ether (380 mL) and MeCN (127 mL) was cooled to 0°C. Imidazole (17.3 g, 253.7 mmol, 5.0 equiv) and PPh_3 (33.3 g, 126.8 mmol, 2.5 equiv) were then added and the mixture was stirred until all the solids had dissolved. Iodine (33.5 g, 131.9 mol, 2.6 equiv) was added and the mixture was stirred for 45 min at 0°C. The reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (150 mL) and the layers were separated. The aqueous phase was then extracted with ether (2×250 mL) and the combined organic extracts were washed with brine (750 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 5→9% ether in hexanes) furnished iodide **32** (39.2 g, 97%). $R_f = 0.88$ (silica gel, 60% ether in hexanes); $[\alpha]_D^{22}$ −2.9 (*c* 2.6, $CHCl_3$); IR (thin film) ν_{max} 3057, 2926, 2855, 1481, 1448, 1251, 1083, 939, 836, 774, 706, 632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49–7.45 (m, 5H, Ph), 7.33–7.23 (m, 10H, Ph), 6.23 (s, 1H, C*H*=CCH_3), 5.67 (dd, *J* = 7.2, 7.1 Hz, 1H, CH_2C=C*H*), 4.22 (dd, *J* = 6.8, 6.8 Hz, 1H, CHOSi), 3.51 (s, 2H, CH_2OTr), 3.07 (dd, *J* = 7.1, 7.0 Hz, 2H, CH_2I), 2.34 (ddd, *J* = 14.5, 6.8, 6.8 Hz, 1H, CH_2CHOSi), 2.25 (ddd, *J* = 14.5, 6.8, 6.8 Hz, CH_2CHOSi), 2.13 (m, 2H, C$H_2CH_2CH_2$I), 1.84 (s, 3H, CH=CCH_3), 1.75 (m, 2H, CH_2CH_2CH_2I), 0.90 (s, 9H, SiC(CH_3)$_3$), 0.07 (s, 3H, Si(CH_3)$_2$), 0.02 (s, 3H, Si(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 150.1, 144.1, 136.9, 128.6, 127.9, 126.9, 126.3, 86.7, 77.6, 77.2, 67.3, 34.7, 32.1, 25.8, 19.9, 18.2, 6.8, −4.9, −5.0; HRMS (FAB), calcd for $C_{36}H_{46}I_2O_2Si$ ($M + Cs^+$) 925.0411, found 925.0450.

Hydrazone 33. The SAMP hydrazone of propionaldehyde[23] (5.6 g, 32.76 mmol, 1.3 equiv) in THF (16 mL), was added to a freshly prepared solution of LDA at 0°C (diisopropylamine (5.0 mL, 35.28 mmol, 1.4 equiv) was added to *n*-BuLi (22.0 mL, 1.6 M in hexanes, 35.28 mmol, 1.4 equiv) in 32 mL of THF at 0°C). After stirring at that temperature for 16 h, the resulting yellow solution was cooled to −100°C, and a solution of iodide **32** (20.0 g, 25.23 mmol, 1.0 equiv) in THF

(32 mL) was added dropwise over a period of 2 h. The mixture was allowed to warm to −20°C over 20 h, and then poured into saturated aqueous NH_4Cl (50 mL) and extracted with ether (3×100 mL). The combined organic extract was dried ($MgSO_4$), filtered and evaporated. Purification by flash column chromatography on silica gel (5→50% ether in hexanes) provided hydrazone **33** (15.0 g, 71%) as a yellow oil. R_f = 0.63 (silica gel, 40% ether in hexanes); $[\alpha]_D^{22}$ −22.7 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3057, 2927, 2854, 1489, 1448, 1251, 1078, 940, 836, 775, 706, 668, 632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46–7.44 (m, 5H, Ph), 7.31–7.21 (m, 10H, Ph), 6.40 (d, *J* = 6.5 Hz, 1H, N=CH), 6.21 (s, 1H, C*H*=CCH$_3$), 5.50 (dd, *J* = 7.0, 7.0 Hz, 1H, CH$_2$C=C*H*), 4.20 (dd, *J* = 6.0, 6.0 Hz, 1H, CHOSi), 3.54 (dd, *J* = 9.2, 3.5 Hz, 1H, C*H*$_2$OCH$_3$), 3.45 (s, 2H, CH$_2$OTr), 3.41 (dd, *J* = 9.5, 7.0 Hz, 1H, C*H*$_2$OCH$_3$), 3.37 (s, 3H, CH$_2$OC*H*$_3$), 3.32–3.30 (m, 2H, CH$_2$N), 2.60–2.55 (m, 1H), 2.34–2.20 (m, 3H), 2.04–1.95 (m, 1H), 1.98–1.73 (m, 5H), 1.82 (s, 3H, CH=CC*H*$_3$), 1.38–1.21 (m, 4H), 0.96 (d, *J* = 6.9 Hz, 3H, CHC*H*$_3$), 0.89 (s, 9H, SiC(CH$_3$)$_3$), 0.06 (s, 3H, Si(CH$_3$)$_2$), 0.01 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 150.2, 144.3, 138.5, 128.6, 127.7, 126.8, 121.3, 86.5, 77.4, 74.7, 67.0, 63.5, 59.2, 50.4, 37.0, 35.5, 34.6, 28.8, 26.5, 25.9, 25.8, 22.1, 19.8, 18.9, 18.2, −4.9, −5.0; HRMS (FAB), calcd for $C_{45}H_{63}IN_2O_3Si$ (M + Cs^+) 967.2707, found 967.2740.

Nitrile 34. Monoperoxyphthalic acid magnesium salt (MMPP·6H_2O, 80%, 52.4 g, 84.8 mmol, 2.5 equiv) was added portionwise over 10 min to a rapidly stirred solution of hydrazone **33** (28.3 g, 33.9 mmol, 1.0 equiv) in a mixture of MeOH (283 mL), THF (100 mL) and pH 7 phosphate buffer (283 mL) at 0°C. The mixture was stirred at 0°C for 1.5 h and then more THF (120 mL) was added in two portions over 30 min to help dissolve the starting material. After stirring for a further 1.5 h the reaction mixture was poured into a saturated aqueous solution of $NaHCO_3$ (750 mL) and the product was extracted with ether (750 mL) and then EtOAc (2×750 mL). The combined organic extracts were washed with brine (1 L), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 9→20% ether in hexanes) furnished nitrile **34** as a colorless oil (21.8 g, 89%). R_f = 0.44 (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ +2.9 (*c* 1.2, $CHCl_3$); IR (thin film) ν_{max} 3057, 2928, 2855, 2238, 1490, 1448, 1252, 1081, 836, 775, 707, 632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47–7.45 (m, 5H, Ph), 7.33–7.23 (m, 10H, Ph), 6.22 (s, 1H, C*H*=CCH$_3$), 5.56 (dd, *J* = 6.8, 6.8 Hz, 1H, CH$_2$C=C*H*), 4.21 (dd, *J* = 6.8, 6.8 Hz, 1H, CHOSi), 3.49 (s, 2H, CH$_2$OTr), 2.48 (m, 1H, C*H*(CH$_3$)), 2.29 (ddd, *J* = 14.5, 6.8, 6.8 Hz, 1H, C*H*$_2$CHOSi), 2.24 (ddd, *J* = 14.5, 6.8, 6.8 Hz, 1H, C*H*$_2$CHOSi), 2.07 (m, 2H, C*H*$_2$(C)CH$_2$OTr)), 1.82 (s, 3H, CH=CC*H*$_3$), 1.58–1.23 (m, 4H), 1.24 (d, *J* = 7.0 Hz, 3H, CHC*H*$_3$), 0.90 (s, 9H, SiC(CH$_3$)$_3$), 0.07 (s, 3H, Si(CH$_3$)$_2$), 0.0 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 150.0, 144.1, 137.6, 128.6, 127.8, 126.9, 122.7, 122.5, 86.5, 77.4, 76.7, 34.6, 33.7, 31.5, 27.8, 25.7, 25.5, 25.2, 22.6, 19.7, 18.1, 17.8, 14.1, −4.9, −5.0; HRMS (FAB), calcd for $C_{39}H_{50}INO_2Si$ (M + Cs^+) 852.1710, found 852.1738.

Aldehyde 35. Nitrile **34** (7.01 g, 9.74 mmol, 1.0 equiv) was dissolved in toluene (195 mL, 0.05 M) and cooled to −78°C. DIBAL (29.2 mL, 1.0 M in toluene, 29.2 mmol, 3.0 equiv) was added dropwise at −78°C over 10 min. The reaction mixture was stirred at −78°C until completion was verified by TLC (1 h). Methanol (10 mL) and HCl (10 mL, 1.0 N in water) were added sequentially and the resulting mixture was brought up to 0°C over 1 h. Ether (250 mL) and water (250 mL) were added and the layers were separated. The aqueous phase was extracted with ether (2×250 mL) and the combined organic extracts were washed with brine (500 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 17→33% ether in hexanes) afforded aldehyde **35** as an oil (6.18 g, 88%). R_f = 0.51 (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ +2.0 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3057, 2927, 2855, 1726, 1490, 1448, 1251, 1081, 836, 775, 707, 632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.51 (d, *J* = 1.9 Hz, 1H, CHO), 7.46–7.45 (m, 5H, Ph), 7.32–7.22 (m, 10H, Ph), 6.20 (s, 1H, C*H*=CCH$_3$), 5.54 (dd, *J* = 7.0, 7.0 Hz, 1H, CH$_2$C=C*H*), 4.20 (dd, *J* = 6.5, 6.0 Hz, 1H, CHOSi), 3.47 (s, 2H, CH$_2$OTr), 2.34–2.20 (m, 3H, C*H*$_2$CHOSi and C*H*(CH$_3$)), 2.04 (m, 2H, C*H*$_2$(C)CH$_2$OTr), 1.82 (s, 3H, CH=CC*H*$_3$), 1.66 (m, 1H), 1.30–1.19 (m, 3H), 1.02 (d, *J* = 7.0 Hz, 3H, CHC*H*$_3$), 0.89 (s, 9H, SiC(CH$_3$)$_3$), 0.06 (s, 3H, Si(CH$_3$)$_2$), 0.00 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 205.0, 150.1, 144.2, 138.0, 128.6, 127.8, 126.9, 122.1, 86.6, 77.5, 67.1, 46.1, 34.6, 30.3, 28.6, 25.8, 25.6, 19.8, 18.2, 13.2, −4.9, −5.0; HRMS (FAB), calcd for $C_{39}H_{51}IO_3Si$ (M + Cs^+) 855.1707, found 855.1672.

tris-(Silylethers) 37 and 38. A solution of ketone **36**[6e] (1.20 g, 2.99 mmol, 1.4 equiv) in THF (4.3 mL) was added dropwise over 5 min to a freshly prepared solution of LDA (diisopropylamine (424 μL, 3.03 mmol, 1.45 equiv) was added to *n*-BuLi (2.00 mL, 1.52 M in hexanes, 3.04 mmol, 1.45 equiv) at 0°C, and after 5 min THF (4.3 mL) was added at −78°C. After stirring for 1.5 h at −78°C, the solution was allowed to warm up to −40°C over a period of 30 min. The reaction mixture was then cooled to −78°C, and a solution of aldehyde **35** (1.51 g, 2.09 mmol, 1.0 equiv) in THF (12.5 mL) was added dropwise over 15 min. The resulting mixture was stirred for 1 h at −78°C, and then quenched by dropwise addition of AcOH (3.1 mL of a 1 M solution in THF, 3.10 mmol, 1.5 equiv). The mixture was then warmed to 25°C and partitioned between ether (25 mL) and saturated aqueous NH_4Cl (25 mL). The aqueous phase was extracted with ether (3×25 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 4→20% ether in hexanes) provided unreacted ketone (502 mg, 42%), undesired aldol product **38** (705 mg, 27%) and a mixture of desired aldol product **37** and unreacted aldehyde **35** (1.136 g, (ca. 9:1 ratio of **37**:**35** by ^1H NMR)) (i.e. 39% yield of **37**). This mixture was used directly in the next step. **37**: (major) (obtained as a colorless oil from a mixture containing **35**, by flash column chromatography (silica gel, 10→17% EtOAc in hexanes)). R_f = 0.22 (silica gel, 10% ether in hexanes); $[\alpha]_D^{22}$ −20.0 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3486,

2954, 2928, 2856, 1682, 1472, 1448, 1253, 1090, 994, 836, 775, 706, 668, 632 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.45–7.43 (m, 5H, Ph), 7.30–7.19 (m, 10H, Ph), 6.19 (s, 1H, C*H*=CCH$_3$), 5.51 (dd, *J* = 7.0, 6.9 Hz, 1H, C=C*H*CH$_2$), 4.18 (dd, *J* = 6.3, 6.2 Hz, 1H, CHOSi), 3.88 (dd, *J* = 7.5, 2.6 Hz, 1H, CHOSi), 3.65 (m, 1H, CH$_2$OSi), 3.59 (m, 1H, CH$_2$OSi), 3.46 (d, *J* = 11.2 Hz, 1H, CH$_2$OTr), 3.43 (d, *J* = 11.2 Hz, 1H, CH$_2$OTr), 3.27 (m, 1H, CH$_3$C*H*(C=O)), 3.22 (d, *J* = 9.3 Hz, 1H, C*H*OH), 2.32–2.18 (m, 2H, C=CHC*H*$_2$CHOSi), 2.00 (m, 2H, C*H*$_2$(C)CH$_2$OTr), 1.80 (s, 3H, CH=C(C*H*$_3$)), 1.66 (m, 2H), 1.46 (m, 2H), 1.27 (m, 1H, C*H*(CH$_3$), 1.19 (s, 3H, C(CH$_3$)$_2$), 1.07 (s, 3H, C(CH$_3$)$_2$), 0.99 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)), 0.89 (s, 9H, SiC(CH$_3$)$_3$), 0.87 (s, 9H, SiC(CH$_3$)$_3$), 0.86 (s, 9H, SiC(CH$_3$)$_3$), 0.71 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)), 0.10 (s, 3H, Si(CH$_3$)$_2$), 0.07 (s, 3H, Si(CH$_3$)$_2$), 0.04 (s, 3H, Si(CH$_3$)$_2$), 0.03 (s, 6H, Si(CH$_3$)$_2$), −0.01 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 222.1, 150.1, 144.1, 138.6, 128.5, 127.6, 126.7, 121.1, 86.4, 77.4, 74.8, 74.1, 67.1, 60.4, 54.0, 41.2, 37.9, 35.4, 34.7, 33.0, 29.2, 26.2, 26.0, 25.9, 25.7, 23.0, 20.6, 19.8, 18.4, 18.3, 18.2, 15.4, 9.6, −3.5, −3.9, −4.7, −4.8, −5.1; HRMS (FAB), calcd for $C_{60}H_{97}IO_6Si_3$ (M + Cs^+) 1257.4692, found 1257.4639. **38**: (minor) colorless oil; R_f = 0.38 (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ −11.9 (*c* 2.9, $CHCl_3$); IR (thin film) ν_{max} 3501, 2954, 2930, 2856, 1682, 1469, 1254, 1088, 836, 776, 705, 670 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46–7.44 (m, 5H, Ph), 7.31–7.21 (m, 10H, Ph), 6.21 (s, 1H, C*H*=C(CH$_3$)), 5.52 (dd, *J* = 7.0, 6.9 Hz , 1H, C=C*H*CH$_2$), 4.20 (dd, *J* = 6.5, 6.5 Hz, 1H, CHOSi), 3.88 (dd, *J* = 7.5, 2.5 Hz, 1H, CHOSi), 3.67 (m, 1H, CH$_2$OSi), 3.60 (m, 1H, CH$_2$OSi), 3.46 (s, 2H, CH$_2$OTr), 3.30–3.21 (m, 2H, C*H*OH, CH$_3$CH(C=O)), 2.30–2.25 (m, 2H, C=CHC*H*$_2$CHOSi), 2.05–1.93 (m, 2H, C*H*$_2$C(CH$_2$OTr)=CH), 1.81 (s, 3H, CH=C(C*H*$_3$)), 1.63 (m, 1H, C*H*(CH$_3$)), 1.45 (m, 2H), 1.24 (m, 2H), 1.19 (s, 3H, C(CH$_3$)$_2$), 1.05 (s, 3H, C(CH$_3$)$_2$), 1.01 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)), 0.89 (s, 9H, SiC(CH$_3$)$_3$), 0.88 (obscured d, 3H, CH(C*H*$_3$)), 0.88 (s, 18H, SiC(CH$_3$)$_3$), 0.11 (s, 3H, Si(CH$_3$)$_2$), 0.07 (s, 3H, Si(CH$_3$)$_2$), 0.06 (s, 3H, Si(CH$_3$)$_2$), 0.04 (s, 6H, Si(CH$_3$)$_2$), 0.01 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 221.8, 150.1, 144.2, 138.6, 128.7, 127.8, 126.9, 121.6, 86.5, 77.4, 77.3, 75.0, 74.0, 67.1, 60.5, 53.9, 53.4, 41.6, 37.8, 35.4, 34.7, 32.9, 29.0, 26.1, 25.9, 25.7, 23.2, 20.2, 19.8, 18.3, 18.2, 18.1, 15.4, 10.5, −3.7, −4.1, −4.9, −5.0, −5.3; HRMS (FAB), calcd for $C_{60}H_{97}IO_6Si_3$ (M + Cs^+) 1257.4692, found 1257.4749.

tetra-(Silylether) 39. Alcohol **37** (1.136 g of a 9:1 mixture with aldehyde **35**, 0.933 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (5.0 mL), cooled to −20°C and treated with 2,6-lutidine (470 μL, 4.04 mmol, 4.3 equiv) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (695 μL, 3.03 mmol, 3.2 equiv). The mixture was then stirred for 2.5 h with slow warming to 0°C. The reaction was then quenched with saturated aqueous $NaHCO_3$ (25 mL) and the aqueous phase was extracted with ether (3×25 mL). The combined organic extracts were washed with brine (250 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 4→9% ether in hexanes) furnished tetra-(silylether) **39** as a colorless oil (1.04 g, 90%). R_f = 0.91 (silica gel, 20% ether in hexanes); $[\alpha]_D^{22}$ −16.8 (*c* 0.7, $CHCl_3$); IR (thin film) ν_{max} 3058, 2951, 2856, 1693, 1471, 1253, 1079, 1004, 836, 706 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.46–7.43 (m, 5H, Ph), 7.29–7.19 (m, 10H, Ph), 6.19 (s, 1H, C*H*=CCH$_3$), 5.49 (dd, *J* = 7.0, 7.0 Hz, 1H, C=C*H*CH$_2$), 4.18 (dd, *J* = 6.3, 6.1 Hz, 1H, CHOSi), 3.85 (dd, *J* = 7.6, 2.5 Hz, 1H, CHOSi), 3.70 (dd, *J* = 6.7, 2.0 Hz, 1H, CHOSi), 3.67 (ddd, *J* = 9.6, 4.8, 4.8 Hz, 1H, CH$_2$OSi), 3.59 (ddd, *J* = 9.7, 7.9. 7.9 Hz, 1H, CH$_2$OSi), 3.45 (d, *J* = 11.2 Hz, 1H, CH$_2$OTr), 3.42 (d, *J* = 11.2 Hz, 1H, CH$_2$OTr), 3.08 (qd, *J* = 6.8, 6.8 Hz, 1H, CH$_3$C*H*(C=O)), 2.27 (ddd, *J* = 14.4, 7.2, 7.2 Hz, 1H, C=CHC*H*$_2$CHOSi), 2.23 (ddd, *J* = 14.5, 6.2, 6.2 Hz, 1H, C=CHC*H*$_2$CHOSi), 1.97 (m, 2H, C*H*$_2$C(CH$_2$OTr)=CH), 1.79 (s, 3H, CH=C(C*H*$_3$)), 1.57 (m, 1H), 1.46 (m, 1H), 1.25 (m, 3H), 1.17 (s, 3H, C(CH$_3$)$_2$), 1.01 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)), 0.95 (s, 3H, C(CH$_3$)$_2$), 0.87 (s, 18H, SiC(CH$_3$)$_3$), 0.86 (s, 18H, SiC(CH$_3$)$_3$), 0.09–0.03 (m, 24H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.2, 150.2, 144.3, 138.7, 128.6, 127.7, 126.8, 121.5, 86.5, 77.5, 77.4, 77.3, 74.0, 67.1, 60.9, 53.6, 45.1, 38.7, 38.0, 34.6, 31.0, 29.3, 26.5, 26.2, 26.1, 25.9, 25.8, 24.4, 19.7, 19.5, 18.5, 18.3, 18.2, 18.1, 17.5, 15.1, −3.6, −3.7, −3.8, −4.0, −4.9, −5.0, −5.2, −5.3; HRMS (FAB), calcd for $C_{66}H_{111}IO_6Si_4$ (M + Cs^+) 1371.5557, found 1371.5523.

Alcohol 40. To a solution of tetra-silyl ether **39** (180 mg, 0.145 mmol) in THF (1.5 mL) at 0°C was added HF•pyr. in pyr./THF mixture (prepared from a stock solution containing 420 μL HF•pyr., 1.14 mL pyr. and 2.00 mL THF) (1.5 mL) and the resulting solution was stirred for 2 h at 0°C. More HF•pyr. in the pyr./THF mixture (0.5 mL) was then added and stirring was continued for additional 1 h at 0°C. The reaction was quenched by careful addition of saturated aqueous $NaHCO_3$ and the product was extracted with EtOAc (3×25 mL). The combined organic extracts were then dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel 30% ether in hexanes) furnished alcohol **40** as a pale yellow oil (137 mg, 84%). R_f = 0.36 (silica gel, 40% ether in hexanes); $[\alpha]_D^{22}$ −26.0 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3422, 2928, 2855, 1690, 1490, 1471, 1448, 1360, 1252, 1086, 1004, 986, 836, 774, 706 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.44–7.42 (m, 5H, Ph), 7.29–7.20 (m, 10H, Ph), 6.19 (s, 1H, C*H*=CCH$_3$), 5.49 (dd, *J* = 7.1, 7.1 Hz, 1H, C=C*H*CH$_2$), 4.17 (dd, *J* = 6.2, 6.0 Hz, 1H, CHOSi), 4.03 (dd, *J* = 6.6, 3.7 Hz, 1H, CHOSi), 3.73 (dd, *J* = 7.2, 1.7 Hz, 1H, CHOSi), 3.65 m, 2H, C*H*$_2$OH), 3.45 (d, *J* = 11.7 Hz, 1H, CH$_2$OTr), 3.42 (d, *J* = 11.7 Hz, 1H, CH$_2$OTr), 3.06 (qd, *J* = 6.9, 6.9 Hz, 1H, CH$_3$CH(C=O)), 2.28 (ddd, *J* = 14.7, 7.3, 7.3 Hz, 1H, C=CHC*H*$_2$CHOSi), 2.22 (ddd, *J* = 14.7, 6.3, 6.3 Hz, 1H, C=CHC*H*$_2$CHOSi), 1.98 (m, 2H, C*H*$_2$C(CH$_2$OTr)=CH), 1.79 (s, 3H, CH=C(C*H*$_3$)), 1.56 (m, 2H), 1.24 (m, 3H), 1.18 (s, 3H, C(CH$_3$)$_2$), 1.03 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)), 0.97 (s, 3H, C(CH$_3$)$_2$), 0.87 (3 singlets, 27H, SiC(CH$_3$)$_3$), 0.81 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)), 0.10 (s, 3H, Si(CH$_3$)$_2$), 0.04 (s, 9H, Si(CH$_3$)$_2$), 0.03 (s, 3H, Si(CH$_3$)$_2$), 0.00 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 219.2, 150.0, 144.1, 138.5, 128.5, 127.6, 126.7, 121.4, 86.4, 77.5, 77.4, 77.3, 73.1, 67.2, 60.2, 53.7, 45.2, 38.6, 38.4, 34.7, 30.9, 29.4, 26.6, 26.3,

26.1, 25.8, 25.0, 19.8, 18.6, 18.4, 17.9, 17.8, 15.7, −3.4, −3.6, −3.7, −3.8, −4.7, −4.8; HRMS (FAB), calcd for $C_{60}H_{97}IO_6Si_3$ ($M+Cs^+$) 1257.4692, found 1257.4780.

Aldehyde 41. To a solution of oxalyl chloride (150 μL, 1.72 mmol, 2.0 equiv) in CH_2Cl_2 (10 mL) at 78°C was added dropwise DMSO (247 μL, 3.48 mmol, 4.0 equiv). After stirring for 10 min at −78°C, a solution of alcohol **40** (960 mg, 0.853 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added dropwise. The resulting solution was stirred at −78°C for 1 h, and then Et_3N (714 μL, 5.12 mmol, 6.0 equiv) was added and the reaction mixture was allowed to warm up to 25°C over 30 min. Water (30 mL) was added, and the product was extracted with ether (3×40 mL). The combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Flash column chromatography (silica gel, 17→50% ether in hexanes) furnished aldehyde **41** as a colorless oil (943 mg, 98%). R_f = 0.74 (silica gel, 40% ether in hexanes); $[\alpha]_D^{22}$ −10.8 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 2928, 2855, 1728, 1690, 1471, 1448, 1260, 1252, 1085, 987, 836, 774, 706 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.74 (dd, *J* = 2.4, 1.5 Hz, 1H, CHO), 7.44–7.42 (m, 5H, Ph), 7.29–7.20 (m, 10H, Ph), 6.19 (s, 1H, C*H*=CCH$_3$), 5.49 (dd, *J* = 7.0, 6.8 Hz, 1H, C=C*H*CH$_2$), 4.44 (dd, *J* = 6.3, 5.0 Hz, 1H, CHOSi), 4.18 (dd, *J* = 6.9, 6.4 Hz, 1H, CHOSi), 3.70 (dd, *J* = 7.2, 1.8 Hz, 1H, CHOSi), 3.45 (d, *J* = 11.4 Hz, 1H, CH$_2$OTr), 3.42 (d, *J* = 11.4 Hz, 1H, CH$_2$OTr), 3.05 (qd, *J* = 7.0, 7.0 Hz, 1H, CH$_3$C*H*(C=O)), 2.49 (ddd, *J* = 17.0, 4.5, 1.4 Hz, C*H*$_2$CHO), 2.38 (ddd, *J* = 17.0, 5.4, 2.8 Hz, 1H, C*H*$_2$CHO), 2.27 (ddd, *J* = 14.0, 7.1, 7.1 Hz, 1H, C=CHC*H*$_2$CHOSi), 2.23 (ddd, *J* = 14.5, 6.5, 6.5 Hz, 1H, C=CHC*H*$_2$CHOSi), 1.98 (m, 2H, C*H*$_2$C(CH$_2$OTr)=CH), 1.79 (s, 3H, CH=C(C*H*$_3$)), 1.27 (m, 4H), 1.19 (s, 3H, C(CH$_3$)$_2$), 1.12 (m, 1H), 1.00 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)), 0.98 (s, 3H, C(CH$_3$)$_2$), 0.87 (s, 27H, Si(CH$_3$)$_3$), 0.80 (d, *J* = 6.7 Hz, 3H, CH(C*H*$_3$)), 0.07 (s, 3H, Si(CH$_3$)$_2$), 0.04 (s, 3H, Si(CH$_3$)$_2$), 0.03 (s, 3H, Si(CH$_3$)$_2$), 0.03 (s, 3H, Si(CH$_3$)$_2$), 0.02 (s, 3H, Si(CH$_3$)$_2$), 0.00 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.4, 201.1, 150.2, 144.25, 138.6, 128.6, 127.7, 126.8, 121.5, 86.5, 77.5, 77.4, 77.3, 71.3, 67.1, 53.4, 49.5, 45.1, 38.6, 34.6, 30.8, 29.2, 26.2, 25.9, 25.7, 24.0, 19.7, 18.8, 18.4, 18.1, 18.0, 17.7, 15.4, −3.6, −3.7, −4.1, −4.4, −4.9, −5.0; HRMS (FAB), calcd for $C_{60}H_{95}IO_6Si_3$ ($M+Cs^+$) 1255.4536, found 1255.4561.

Carboxylic acid 42. To a solution of aldehyde **41** (943 mg, 0.839 mmol, 1.0 equiv) in *t*-BuOH (38.5 mL) and H_2O (8.4 mL) was added 2-methyl-2-butene (31.5 mL, 2 M in THF, 63.0 mmol, 75 equiv), NaH_2PO_4 (250 mg, 2.08 mmol, 2.5 equiv) followed by $NaClO_2$ (380 mg, 4.20 mmol, 5.0 equiv) and the resulting mixture was stirred at 25°C for 40 min. The volatiles were then removed under reduced pressure and the residue was partitioned between EtOAc (40 mL) and brine (40 mL) and the layers separated. The aqueous phase was then extracted with EtOAc (3×40 mL), and the combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Flash column chromatography (silica gel, 60% ether in hexanes) furnished carboxylic acid **42** as an oil (956 mg, 100%). R_f = 0.47 (silica gel, 40% ether in hexanes); $[\alpha]_D^{22}$ −19.6 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3389, 2930, 2856, 1711, 1469, 1254, 1085, 988, 835, 775, 705 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.44–7.43 (m, 5H, Ph), 7.29–7.20 (m, 10H, Ph), 6.19 (s, 1H, C*H*=CCH$_3$), 5.49 (dd, *J* = 7.3, 7.1 Hz, 1H, C=C*H*CH$_2$), 4.34 (dd, *J* = 6.4, 3.3 Hz, 1H, CHOSi), 4.18 (dd, *J* = 6.2, 6.2 Hz, 1H, CHOSi), 3.72 (dd, *J* = 7.2, 1.7 Hz, 1H, CHOSi), 3.45 (d, *J* = 11.4 Hz, 1H, CH$_2$OTr), 3.41 (d, *J* = 11.4 Hz, 1H, CH$_2$OTr), 3.07 (qd, *J* = 7.0, 7.0 Hz, 1H, CH$_3$C*H*(C=O)), 2.46 (dd, *J* = 16.3, 3.1 Hz, 1H, C*H*$_2$CO$_2$H), 2.32–2.18 (m, 3H, C*H*$_2$CO$_2$H and C=CHC*H*$_2$CHOSi), 1.97 (m, 2H, C*H*$_2$C(CH$_2$OTr)=CH), 1.80 (s, 3H, CH=C(C*H*$_3$)), 1.31–1.19 (m, 5H), 1.19 (s, 3H, C(CH$_3$)$_2$), 1.02 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)), 0.99 (s, 3H, C(CH$_3$)$_2$), 0.87 (s, 27H, Si(CH$_3$)$_3$), 0.80 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)), 0.07, (s, 3H, Si(CH$_3$)$_2$), 0.04 (s, 3H, Si(CH$_3$)$_2$), 0.04 (s, 3H, Si(CH$_3$)$_2$), 0.03 (s, 3H, Si(CH$_3$)$_2$), 0.02 (s, 3H, Si(CH$_3$)$_2$), 0.00 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.2, 176.7, 150.2, 144.2, 138.6, 128.6, 127.7, 126.8, 121.5, 86.5, 77.6, 77.4, 77.3, 73.5, 67.1, 53.4, 45.2, 40.0, 38.5, 34.6, 30.8, 29.3, 26.2, 26.0, 25.8, 23.7, 19.7, 19.1, 18.5, 18.1, 17.7, 15.6, −3.6, −3.7, −4.3, −4.6, −4.9, −5.0; HRMS (FAB), calcd for $C_{60}H_{95}IO_7Si_3$ ($M+Cs^+$) 1271.4485, found 1271.4550.

Hydroxy acid 43. A solution of carboxylic acid **42** (956 mg, 0.839 mmol, 1.0 equiv) in THF (17 mL) at 0°C was treated with TBAF (5.0 mL, 1.0 M in THF, 5.00 mmol, 6.0 equiv) and the mixture was allowed to warm to 25°C over 19 h. The reaction was then quenched by the addition of saturated aqueous NH_4Cl (40 mL) and the product was extracted with EtOAc (3×40 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 5% MeOH in CH_2Cl_2) furnished hydroxy acid **43** as a yellow oil (817 mg, 95%). R_f = 0.27 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]_D^{22}$ −11.4 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3364, 3057, 2938, 2856, 1712, 1694, 1469, 1254, 1086, 1053, 988, 836, 776, 734, 705 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.43–7.42 (m, 5H, Ph), 7.30–7.21 (m, 10H, Ph), 6.32 (s, 1H, C*H*=C(CH$_3$)), 5.46 (dd, *J* = 7.2, 7.2 Hz, 1H, C=C*H*CH$_2$), 4.35 (dd, *J* = 6.3, 3.2 Hz, 1H, C*H*OH), 4.21 (dd, *J* = 6.4, 6.3 Hz, 1H, CHOSi), 3.73 (dd, *J* = 7.3, 1.2 Hz, 1H, CHOSi), 3.52 (d, *J* = 12.1 Hz, 1H, CH$_2$OTr), 3.48 (d, *J* = 12.1 Hz, 1H, CH$_2$OTr), 3.06 (m, 2H, CH$_3$C*H*(C=O) and OH), 2.45 (dd, *J* = 16.4, 3.0 Hz, 1H, C*H*$_2$CO$_2$H), 2.35 (m, 2H, C=CHC*H*$_2$CHOH), 2.29 (dd, *J* = 16.4, 6.5 Hz, 1H, C*H*$_2$CO$_2$H), 2.07–1.94 (m, 2H, C*H*$_2$C(CH$_2$OTr)=CH), 1.85 (s, 3H, CH=C(C*H*$_3$)), 1.71 (m, 1H), 1.39 (m, 1H, C*H*(CH$_3$)), 1.27 (m, 3H), 1.18 (s, 3H, C(CH$_3$)$_2$), 1.02 (obscured d, 3H, CH(C*H*$_3$)), 1.02 (s, 3H, C(CH$_3$)$_2$), 0.87 (s, 18H, Si(CH$_3$)$_3$), 0.81 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)), 0.09 (s, 3H, Si(CH$_3$)$_2$), 0.07 (s, 3H, Si(CH$_3$)$_2$), 0.04 (s, 3H, Si(CH$_3$)$_2$), 0.02 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.1, 176.5, 149.1, 144.2, 140.7, 128.6, 127.7, 126.9, 120.3, 86.7, 78.5, 77.5, 76.1, 73.4, 67.1, 53.5, 53.0, 45.1, 40.0, 38.6, 33.4, 30.9, 29.2, 26.5, 26.2, 26.0, 25.6, 25.3, 23.7, 20.1, 19.9, 19.0, 18.5, 18.2, 17.6, 15.8, 13.5, −3.6, −3.7, −4.3, −4.6; HRMS (FAB), calcd for $C_{54}H_{81}IO_7Si_2$ ($M+Cs^+$) 1157.3620, found 1157.3669.

Macrolactone 44. To a solution of hydroxy acid **43** (1.06 g, 1.04 mmol, 1.0 equiv) in THF (15 mL, 0.07 M) was added Et_3N (870 μL, 6.24 mmol, 6.0 equiv) and 2,4,6-trichlorobenzoyl chloride (390 μL, 2.50 mmol, 2.4 equiv). The reaction mixture was stirred at 0°C for 1.5 h, and then added slowly over a period of 2 h via a syringe pump to a solution of 4-DMAP (280 mg, 2.29 mmol, 2.2 equiv) in toluene (208 mL, 0.005 M based on **43**) at 75°C. The mixture was stirred at that temperature for an additional 0.5 h and was then concentrated under reduced pressure. The resulting residue was filtered through a plug of silica gel eluting with 50% ether in hexanes. Flash column chromatography (silica gel, 17% ether in hexanes) furnished macrolactone **44** as a colorless foam (877 mg, 84%). R_f = 0.19 (10% ether in hexanes); $[\alpha]_D^{22}$ −7.4 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 2929, 2855, 1742, 1695, 1468, 1381, 1253, 1156, 1065, 985, 834, 774, 733, 706 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.44–7.42 (m, 5H, Ph), 7.29–7.20 (m, 10H, Ph), 6.39 (s, 1H, C*H*=CCH$_3$), 5.51 (dd, *J* = 9.5, 6.8 Hz, 1H, C=C*H*CH$_2$), 5.07 (d, *J* = 9.3 Hz, 1H, CHOCO), 4.02 (d, *J* = 9.2 Hz, 1H, CHOSi), 3.82 (d, *J* = 8.9 Hz, 1H, CHOSi), 3.46 (d, *J* = 11.5 Hz, 1H, CH$_2$OTr), 3.42 (d, *J* = 11.5 Hz, 1H, CH$_2$OTr), 2.95 (dq, *J* = 8.7, 7.0 Hz, 1H, CH$_3$CH(C=O)), 2.72 (m, 2H, C=CHC*H*$_2$CHO and CH$_2$COO), 2.54 (dd, *J* = 16.2, 9.7 Hz, 1H, CH$_2$COO), 2.29 (m, 1H, C=CHC*H*$_2$CHO), 2.12 (dd, *J* = 14.3, 5.1 Hz, 1H, C*H*$_2$C(CH$_2$OTr)=CH), 1.98 (m, C*H*$_2$C(CH$_2$OTr)=CH), 1.88 (s, 3H, CH=C(C*H*$_3$)), 1.44–1.23 (m, 5H), 1.18 (s, 3H, C(CH$_3$)$_2$), 1.10 (s, 3H, C(CH$_3$)$_2$), 1.07 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)), 0.92 (s, 9H, Si(CH$_3$)$_3$), 0.82 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)), 0.72 (s, 9H, Si(CH$_3$)$_3$), 0.08 (s, 3H, Si(CH$_3$)$_2$), 0.05 (s, 3H, Si(CH$_3$)$_2$), 0.05 (s, 3H, Si(CH$_3$)$_2$), −0.32 (s, 3H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 216.0, 171.7, 147.0, 145.0, 142.9, 129.5, 128.6, 127.8, 120.2, 87.3, 81.0, 78.8, 76.6, 67.5, 54.2, 48.8, 41.0, 40.1, 38.4, 33.6, 32.4, 32.2, 29.6, 28.0, 27.2, 26.9, 25.3, 23.5, 21.2, 19.5, 19.3, 18.6, 15.0, −2.5, −2.8, −3.0, −4.8; HRMS (FAB), calcd for $C_{54}H_{79}IO_6Si_2$ (M + Cs^+) 1139.3514, found 1139.3459.

Triol 24. To a solution of macrolactone **44** (608 mg, 0.604 mmol, 1.0 equiv) in THF (45 mL) at 0°C was added HF•pyr. (15 mL). The resulting mixture was allowed to warm up to 25°C over 15 h and was then cooled to 0°C and quenched by careful addition of saturated aqueous $NaHCO_3$ (50 mL). The product was then extracted with EtOAc (3×50 mL), and the combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Flash column chromatography (silica gel, 60% EtOAc in hexanes) furnished triol **24** as a colorless foam (280 mg, 86%). R_f = 0.32 (silica gel, 60% EtOAc in hexanes); $[\alpha]_D^{22}$ −32.1 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3413, 2923, 2857, 1731, 1686, 1461, 1379, 1259, 1148, 1046, 737 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.43 (s, 1H, C*H*=CCH$_3$), 5.38 (dd, *J* = 9.7, 5.4 Hz, 1H, C=C*H*CH$_2$), 5.29 (dd, *J* = 8.8, 1.9 Hz, 1H, CHOCO), 4.08 (m, 1H, C*H*OH), 4.06 (d, *J* = 13.0 Hz, 1H, C*H*$_2$OH), 4.00 (d, *J* = 13.0 Hz, 1H, C*H*$_2$OH), 3.69 (dd, *J* = 3.5. 3.4 Hz, 1H, C*H*OH), 3.12 (qd, *J* = 6.9, 3.1 Hz, 1H, CH$_3$C*H*(C=O)), 2.76 (bs, 1H, OH), 2.67 (ddd, *J* = 15.0, 9.7, 9.7 Hz, 1H, C=CHC*H*$_2$CHO), 2.45 (dd, *J* = 15.4, 10.6 Hz, 1H, CH$_2$COO), 2.38 (bs, 1H, OH), 2.33 (dd, *J* = 15.4, 3.0 Hz, 1H, CH$_2$COO), 2.21 (m, 2H, C*H*$_2$C(CH$_2$OH)=CH), 2.06 (m, 1H, C=CHC*H*$_2$CHO), 1.87 (s, 3H, CH=C(C*H*$_3$)), 1.71 (m, 1H), 1.66 (m, 1H), 1.32 (s, 3H, C(CH$_3$)$_2$), 1.29–1.24 (m, 3H), 1.17 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)), 1.08 (s, 3H, C(CH$_3$)$_2$), 0.99 (d, *J* = 7.0 Hz, 3H, CH(C*H*$_3$)); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.1, 170.0, 145.3, 142.4, 120.7, 80.5, 77.6, 74.0, 72.9, 66.1, 53.0, 42.2, 39.3, 38.0, 31.8, 31.6, 28.0, 25.7, 22.5, 20.7, 19.2, 16.0, 13.6; HRMS (FAB), calcd for $C_{23}H_{37}IO_6$ (M + Cs^+) 669.0689, found 669.0711.

Macrolactone 45. A solution of vinyl iodide **24** (55 mg, 0.103 mmol, 1.0 equiv), stannane **8j** (84 mg, 0.207 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (4 mg, 0.015 mmol, 0.15 equiv) in degassed DMF (1 mL, 0.1 M) was stirred at 25°C for 33 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 80% EtOAc in hexanes), starting vinyl iodide **24** (21 mg, 39%) and macrolactone **45** (30 mg, 56%). R_f = 0.48 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −48.3 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3372, 2924, 2860, 1731, 1682, 1454, 1384, 1252, 1148, 1040, 979, 735 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.21 (s, 1H, ArH), 6.61 (s, 1H, C*H*=CCH$_3$), 5.58 (d, *J* = 47.0 Hz, 2H, CH$_2$F), 5.45 (dd, *J* = 9.8, 5.3 Hz, 1H, C=C*H*CH$_2$), 5.26 (dd, *J* = 9.4, 2.0 Hz, 1H, CHOCO), 4.23 (dd, *J* = 10.9, 2.4 Hz, 1H, C*H*OH), 4.08 (d, *J* = 13.1 Hz, 1H, C*H*$_2$OH), 4.01 (d, *J* = 13.1 Hz, 1H, C*H*$_2$OH), 3.70 (dd, *J* = 4.2, 2.7 Hz, 1H, C*H*OH), 3.16 (qd, *J* = 6.8, 2.6 Hz, 1H, CH$_3$C*H*(C=O)), 2.94 (bs, 1H, OH), 2.69 (ddd, *J* = 15.2, 9.6, 9.6 Hz, 1H, C=CHC*H*$_2$CHO), 2.46 (dd, *J* = 14.8, 10.9 Hz, 1H, CH$_2$COO), 2.36–2.24 (m, 2H, C*H*$_2$C(CH$_2$OH)=CH), 2.30 (dd, *J* = 14.8, 2.6 Hz, 1H, CH$_2$COO), 2.09 (s, 3H, CH=C(C*H*$_3$)), 2.07 (m, 1H, C=CHC*H*$_2$CHO), 1.77–1.58 (m, 5H), 1.33 (s, 3H, C(CH$_3$)$_2$), 1.17 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)), 1.06 (s, 3H, C(CH$_3$)$_2$), 1.00 (d, *J* = 7.0 Hz, 3H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.1, 170.1, 152.6, 141.9, 139.4, 121.4, 118.8, 117.7, 86.8, 81.0, 79.8, 78.7, 73.9, 72.4, 66.3, 53.4, 41.9, 39.6, 38.0, 32.0, 31.8, 28.1, 22.7, 18.4, 16.1, 15.8, 13.5; HRMS (FAB), calcd for $C_{22}H_{40}FNO_6S$ (M + Cs^+) 658.1615, found 658.1644.

Macrolactone 46. A solution of vinyl iodide **24** (32 mg, 0.060 mmol, 1.0 equiv), stannane **8p** (28 mg, 0.101 mmol, 1.7 equiv) and $Pd(MeCN)_2Cl_2$ (1.7 mg, 0.07 mmol, 0.1 equiv) in degassed DMF (650 μL, 0.1 M) was stirred at 25°C for 20 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 80% EtOAc in hexanes), starting vinyl iodide **24** (6 mg, 19%) and macrolactone **46** (17 mg, 54%). R_f = 0.37 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −48.7 (*c* 0.15, $CHCl_3$); IR (thin film) ν_{max} 3402, 2931, 2874, 1731, 1686, 1533, 1458, 1420, 1383, 1242, 1150, 1048, 1007, 979 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.50 (s, 1H, ArH), 6.36 (s, 1H, C*H*=CCH$_3$), 5.45 (dd, *J* = 10.0, 5.0 Hz, 1H, C=C*H*CH$_2$), 5.23 (dd, *J* = 9.5, 1.5 Hz, 1H, CHOCO), 4.24 (bd, *J* = 11.0 Hz, 1H, C*H*OH), 4.11–3.68 (m, 1H, C*H*$_2$OH), 4.07 (s, 3H, OCH$_3$), 4.01 (d,

J = 13.0 Hz, 1H, CH_2OH), 3.71 (dd, J = 4.0, 2.5 Hz, 1H, CHOH), 3.30 (bs, 1H, OH), 3.16 (qd, J = 7.0, 2.5 Hz, 1H, CH_3CH(C=O)), 3.00 (bs, 1H, OH), 2.68 (ddd, J = 15.0, 10.0, 9.5 Hz, 1H, C=CHCH_2CHO), 2.46 (dd, J = 15.0, 11.0 Hz, 1H, CH_2COO), 2.30–2.20 (m, 2H, CH_2C(CH_2OH)=CH), 2.29 (dd, J = 15.0, 3.0 Hz, 1H, CH_2COO), 2.11–2.04 (m, 1H, C=CHCH_2CHO), 2.11 (s, 3H, CH=C(CH_3)), 1.83–1.61 (m, 4H), 1.41–1.25 (m, 1H), 1.33 (s, 3H, C(CH_3)$_2$), 1.18 (d, J = 7.0 Hz, 3H, CH(CH_3)), 1.07 (s, 3H, C(CH_3)$_2$), 1.01 (d, J = 7.0 Hz, 3H, CH(CH_3)); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.4, 174.1, 170.3, 146.4, 141.9, 138.0, 121.8, 119.5, 109.2, 79.0, 73.8, 72.4, 66.2, 58.5, 53.5, 41.7, 39.6, 37.8, 32.0, 31.6, 28.0, 25.4, 22.8, 18.1, 15.9, 15.4, 13.2; HRMS (FAB), calcd for $C_{27}H_{41}NO_7S$ ($M + Cs^+$) 656.1658, found 656.1675.

Macrolactone 47. A solution of vinyl iodide **24** (41 mg, 0.076 mmol, 1.0 equiv), stannane **8r** (61 mg, 0.151 mmol, 2.0 equiv) and $Pd(MeCN)_2Cl_2$ (4 mg, 0.015 mmol, 0.2 equiv) in degassed DMF (760 μL, 0.1 M) was stirred at 25°C for 21h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 80% EtOAc in hexanes), starting vinyl iodide **24** (6 mg, 15%) and macrolactone **47** (20.5 mg, 51%). R_f = 0.41 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −86.0 (c 0.25, $CHCl_3$); IR (thin film) ν_{max} 3387, 2968, 2936, 2874, 1733, 1685, 1458, 1381, 1253, 1149, 1050, 1003, 912 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (s, 1H, ArH), 6.63 (s, 1H, CH=CCH$_3$), 5.43 (dd, J = 9.0, 5.5 Hz, 1H, C=CHCH$_2$), 5.25 (dd, J = 8.5, 2.0 Hz, 1H, CHOCO), 4.32 (ddd, J = 11.0, 5.5, 2.5 Hz, 1H, CHOH), 4.12–4.07 (m, 2H, CH_2OH and OH), 4.02 (d, J = 11.0 Hz, 1H, CH_2OH), 3.69 (dd, J = 2.0, 2.0 Hz, 1H, CHOH), 3.16 (qd, J = 7.0, 2.5 Hz, 1H, CH_3CH(C=O)), 3.08 (bs, 1H, OH), 2.98 (q, J = 7.0 Hz, 2H, CH_2CH$_3$), 2.61 (ddd, J = 15.0, 9.0, 9.0 Hz, 1H, C=CHCH_2CHO), 2.46 (dd, J = 14.5, 11.0 Hz, 1H, CH_2COO), 2.38 (dd, J = 15.0, 4.0 Hz, 1H, CH_2C(CH_2OH)=CH), 2.31–2.25 (m, 1H, CH_2C(CH_2OH)=CH), 2.23 (dd, J = 14.5, 2.5 Hz, 1H, CH_2COO), 2.17–2.07 (m, 1H, C=CHCH_2CHO), 2.04 (s, 3H, CH=C(CH_3)), 1.97 (bs, 1H, OH), 1.78–1.61 (m, 3H), 1.38–1.23 (m, 2H), 1.37 (q, J = 7.0 Hz, 3H, CH_2CH_3), 1.35 (s, 3H, C(CH_3)$_2$), 1.18 (d, J = 7.0 Hz, 3H, CH(CH_3)), 1.05 (s, 3H, C(CH_3)$_2$), 1.01 (d, J = 7.0 Hz, 3H, CH(CH_3)); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.7, 172.0, 170.3, 151.7, 141.8, 138.7, 121.8, 119.2, 114.9, 78.1, 73.9, 71.8, 66.2, 53.8, 41.5, 39.6, 38.0, 31.8, 31.6, 27.8, 26.7, 25.2, 22.9, 17.4, 16.1, 15.7, 14.0, 13.2; HRMS (FAB), calcd for $C_{28}H_{43}NO_6S$ ($M + Na^+$) 544.2709, found 544.2724.

Macrolactone 48. A solution of vinyl iodide **24** (26 mg, 0.048 mmol, 1.0 equiv), stannane **8h** (29 mg, 0.072 mmol, 1.5 equiv) and $Pd(MeCN)_2Cl_2$ (1.5 mg, 0.006 mmol, 0.1 equiv) in degassed DMF (480 μL, 0.1 M) was stirred at 25°C for 15 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, EtOAc), starting vinyl iodide **24** (10.5 mg, 40%) and macrolactone **48** (10.5 mg, 41%). R_f = 0.27 (silica gel, EtOAc); $[\alpha]_D^{22}$ −43.0 (c 0.14, $CHCl_3$); IR (thin film) ν_{max} 3388, 2924, 2851, 1732, 1682, 1462, 1384, 1251, 1185, 1150, 1067 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (s, 1H, ArH), 6.63 (s, 1H, CH=CCH$_3$), 5.45 (dd, J = 9.0, 6.0 Hz, 1H, C=CHCH$_2$), 5.27 (bd, J = 7.0 Hz, 1H, CHOCO), 4.29 (dd, J = 11.0, 2.5 Hz, 1H, CHOH), 4.09 (d, J = 13.0 Hz, 1H, CH_2OH), 4.00 (d, J = 13.0 Hz, 1H, CH_2OH), 3.68 (dd, J = 4.0, 2.5 Hz, 1H, CHOH), 3.15 (qd, J = 6.5, 2.5 Hz, 1H, CH_3CH(C=O)), 2.99 (bs, 1H, OH), 2.65 (ddd, J = 15.0, 9.0, 9.0 Hz, 1H, C=CHCH_2CHO), 2.46 (dd, J = 14.5, 11.0 Hz, 1H, CH_2COO), 2.39–2.33 (m, 1H, CH_2C(CH_2OH)=CH), 2.26 (dd, J = 14.5, 2.5 Hz, 1H, CH_2COO), 2.26–2.20 (m, 1H, CH_2C(CH_2OH)=CH), 2.14–2.10 (m, 1H, C=CHCH_2CHO), 2.07 (s, 3H, CH=C(CH_3)), 1.99–1.61 (m, 4H), 1.42–1.24 (m, 2H), 1.33 (s, 3H, C(CH_3)$_2$), 1.16 (d, J = 7.0 Hz, 3H, CH(CH_3)), 1.04 (s, 3H, C(CH_3)$_2$), 1.00 (d, J = 7.0 Hz, 3H, CH(CH_3)); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.5, 170.3, 170.2, 152.1, 141.9, 139.0, 121.5, 118.9, 116.4, 78.4, 73.9, 72.0, 66.2, 61.9, 53.6, 41.7, 39.6, 37.9, 31.8, 31.6, 29.7, 28.1, 25.4, 22.9, 17.7, 15.8, 13.2; HRMS (FAB), calcd for $C_{27}H_{41}NO_7S$ ($M + Cs^+$) 656.1658, found 656.1677.

Macrolactone 49. A solution of vinyl iodide **24** (37 mg, 0.069 mmol, 1.0 equiv), stannane **8q** (47 mg, 0.117 mmol, 1.7 equiv) and $Pd(PPh_3)_4$ (10 mg, 0.009 mmol, 0.13 equiv) in degassed toluene (780 μL, 0.1 M) was heated at 100°C for 2 h according to the procedure described for the synthesis of macrolactone **18h**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 80% EtOAc in hexanes), macrolactone **49** (5.5 mg, 15%). R_f = 0.35 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −48.1 (c 0.27, $CHCl_3$); IR (thin film) ν_{max} 3403, 2930, 2873, 1732, 1686, 1462, 1381, 1291, 1266, 1250, 1149, 1004, 980, 937 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.04 (s, 1H, ArH), 6.85 (dd, J = 17.5, 11.0 Hz, 1H, CH=CH$_2$), 6.61 (s, 1H, CH=CCH$_3$), 6.05 (d, J = 17.5 Hz, 1H, CH=CH_2), 5.56 (d, J = 11.0 Hz, 1H, CH=CH_2), 5.45 (dd, J = 10.0, 5.5 Hz, 1H, C=CHCH$_2$), 5.26 (dd, J = 9.5, 2.0 Hz, 1H, CHOCO), 4.29 (ddd, J = 11.0, 6.0, 2.5 Hz, 1H, CHOH), 4.09 (dd, J = 13.0, 6.5 Hz, 1H, CH_2OH), 4.02 (dd, J = 13.0, 6.0 Hz, 1H, CH_2OH), 3.71 (ddd, J = 4.5, 2.5, 2.5 Hz, 1H, CHOH), 3.54 (d, J = 6.0 Hz, 1H, OH), 3.17 (qd, J = 7.5, 2.0 Hz, 1H, CH_3CH(C=O)), 3.02 (d, J = 2.0 Hz, 1H, OH), 2.68 (ddd, J = 15.0, 10.0, 9.0 Hz, 1H, C=CHCH_2CHO), 2.45 (dd, J = 14.5, 11.0 Hz, 1H, 3H, CH_2COO), 2.37–2.31 (m, 1H, CH_2C(CH_2OH)=CH), 2.30–2.24 (m, 1H, CH_2C(CH_2OH)=CH), 2.28 (dd, J = 15.0, 3.5 Hz, 1H, CH_2COO), 2.14–2.07 (m, 1H, C=CHCH_2CHO), 2.09 (d, J = 1.0 Hz, 1H, CH=C(CH_3)), 1.79–1.60 (m, 4H), 1.39–1.25 (m, 2H), 1.35 (s, 3H, C(CH_3)$_2$), 1.18 (d, J = 7.0 Hz, 3H, CH(CH_3)), 1.07 (s, 3H, C(CH_3)$_2$), 1.02 (d, J = 7.0 Hz, 3H, CH(CH_3)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 221.4, 171.2, 166.9, 153.6, 142.8, 140.2, 130.9, 122.6, 121.1, 120.0, 116.7, 79.3, 74.7, 73.0, 67.1, 54.5, 42.5, 40.5, 38.7, 32.8, 32.5, 28.8, 26.2, 23.7, 18.7, 16.7, 14.1, 14.0; HRMS (FAB), calcd for $C_{28}H_{41}NO_6S$ ($M + Cs^+$) 652.1709, found 652.1693.

Fluoride 50. A solution of triol **45** (3.6 mg, 0.007 mmol, 1.0 equiv) in CH_2Cl_2 (10 μL, 0.07 M) at −78°C

was treated with DAST (11 μL of a 0.7 M solution in CH_2Cl_2, 0.08 mmol, 1.1 equiv) and the mixture was stirred at −78°C for 10 min. The reaction was then quenched by the addition of saturated aqueous $NaHCO_3$ (500 μL) and the mixture was allowed to warm to 25°C. The product was then partitioned between saturated aqueous $NaHCO_3$ (5 mL) and CH_2Cl_2 (5 mL) and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2×5 mL) and the combined organic extracts were dried ($MgSO_4$) and then concentrated under reduced pressure. Preparative thin-layer chromatography (250 μm silica gel plate, 40% EtOAc in hexanes) furnished fluoride **50** (2.1 mg, 58%). R_f = 0.39 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −34.4 (*c* 0.09, $CHCl_3$); IR (thin film) ν_{max} 3413, 2919, 2849, 1725, 1684, 1465, 1381, 1290, 1250, 1150, 1041, 979, 872 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.22 (s, 1H, ArH), 6.62 (s, 1H, C*H*=CCH$_3$), 5.60 (d, *J* = 47.0 Hz, 2H, ArC*H*$_2$F), 5.56–5.52 (m, 1H, C=C*H*CH$_2$), 5.27 (dd, *J* = 9.5, 2.0 Hz, 1H, CHOCO), 4.79 (dd, *J* = 47.9, 10.8 Hz, 1H, CH=CC*H*$_2$F), 4.71 (dd, *J* = 47.9, 10.8 Hz, 1H, CH=CC*H*$_2$F), 4.24 (dd, *J* = 10.9, 2.6 Hz, 1H, C*H*OH), 3.70 (dd, *J* = 4.3, 2.5 Hz, 1H, C*H*OH), 3.15 (qd, *J* = 6.8, 2.5 Hz, 1H, CH$_3$C*H*(C=O)), 3.00–2.85 (m, 1H, OH), 2.71 (m, 1H, C=CHC*H*$_2$CHO), 2.46 (dd, *J* = 14.9, 11.0 Hz, 1H, CH$_2$COO), 2.38–2.29 (m, 2H, C*H*$_2$C(CH$_2$OH)=CH), 2.30 (dd, *J* = 14.9, 2.8 Hz, 1H, CH$_2$COO), 2.15–2.09 (m, 1H, C=CHC*H*$_2$CHO), 2.11 (d, *J* = 1.0 Hz, CH=C(C*H*$_3$)), 1.80–1.50 (m, 4H), 1.37–1.29 (m, 2H), 1.33 (s, 3H, C(CH$_3$)$_2$), 1.18 (d, *J* = 6.8 Hz, 3H, CH(C*H*$_3$)), 1.06 (s, 3H, C(CH$_3$)$_2$), 1.01 (d, *J* = 7.1 Hz, 3H, CH(C*H*$_3$)); HRMS (FAB), calcd for $C_{27}H_{39}F_2NO_5S$ (M + H$^+$) 528.2595, found 528.2610.

Fluoride 51. A solution of triol **46** (8.2 mg, 0.016 mmol, 1.0 equiv) in CH_2Cl_2 (200 μL, 0.04 M) at −78°C was treated with DAST (2.5 μL, 0.019 mmol, 1.2 equiv) and the resulting mixture was stirred at −78°C for 10 min according to the procedure described for the synthesis of fluoride **50**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 30% EtOAc in hexanes), fluoride **51** (3.5 mg, 43%). R_f = 0.57 (silica gel, 60% EtOAc in hexanes); $[\alpha]_D^{22}$ −41.7 (*c* 0.11, $CHCl_3$); IR (thin film) ν_{max} 3418, 2925, 2852, 1734, 1686, 1535, 1461, 1415, 1383, 1334, 1241, 1150, 1045, 976 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.51 (s, 1H, ArH), 6.37 (s, 1H, C*H*=CCH$_3$), 5.55–5.51 (m, 1H, C=C*H*CH$_2$), 5.22 (dd, *J* = 10.0, 2.0 Hz, 1H, CHOCO), 4.81 (dd, *J* = 48.0, 11.0 Hz, 1H, CH=CC*H*$_2$F), 4.71 (dd, *J* = 48.0, 11.0 Hz, 1H, CH=CC*H*$_2$F), 4.26 (dd, *J* = 11.0, 2.5 Hz, 1H, C*H*OH), 4.09 (s, 3H, CH$_3$O), 3.71 (dd, *J* = 4.5, 2.0 Hz, 1H, C*H*OH), 3.17 (qd, *J* = 7.0, 2.5 Hz, 1H, CH$_3$C*H*(C=O)), 3.01–2.95 (m, 1H, OH), 2.76–2.68 (m, 1H, C=CHC*H*$_2$CHO), 2.47 (dd, *J* = 14.5, 11.0 Hz, 1H, CH$_2$COO), 2.37–2.27 (m, 2H, C*H*$_2$C(CH$_2$OH)=CH), 2.29 (dd, *J* = 14.5, 2.5 Hz, 1H, CH$_2$COO), 2.17–2.11 (m, 1H, C=CHC*H*$_2$CHO), 2.14 (s, 3H, CH=C(C*H*$_3$)), 1.80–1.50 (m, 4H), 1.40–1.22 (m, 2H), 1.34 (s, 3H, C(CH$_3$)$_2$), 1.19 (d, *J* = 7.0 Hz, 3H, CH(C*H*$_3$)), 1.08 (s, 3H, C(CH$_3$)$_2$), 1.03 (d, *J* = 7.0 Hz, 3H, CH(C*H*$_3$)); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 220.3, 174.1, 170.1, 146.1, 138.1, 125.9, 125.8, 119.4, 109.1, 86.2 (d, *J* = 660 Hz), 78.5, 73.7, 72.4, 58.5, 53.3, 41.6, 39.5, 37.8, 32.0, 31.6, 29.6, 27.6, 25.1, 22.8, 18.0, 15.7, 13.1; HRMS (FAB), calcd for $C_{27}H_{40}FNO_6S$ (M + H$^+$) 526.2639, found 526.2625.

Fluoride 52. A solution of triol **47** (12.5 mg, 0.024 mmol, 1.0 equiv) in CH_2Cl_2 (500 μL, 0.05 M) at −78°C was treated with DAST (250 μL, 0.1 M in CH_2Cl_2, 0.025 mmol, 1.05 equiv) and the resulting mixture was stirred at −78°C for 10 min according to the procedure described for the synthesis of fluoride **50**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 60% EtOAc in hexanes), fluoride **52** (5.1 mg, 41%). R_f = 0.19 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −68.6 (*c* 0.22, $CHCl_3$); IR (thin film) ν_{max} 3504, 2969, 2935, 2877, 1736, 1687, 1461, 1369, 1290, 1250, 1148, 1068, 1044, 1008, 976 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.98 (s, 1H, ArH), 6.60 (s, 1H, C*H*=CCH$_3$), 5.56–5.52 (m, 1H, C=C*H*CH$_2$), 5.23 (dd, *J* = 10.0, 2.0 Hz, 1H, CHOCO), 4.80 (dd, *J* = 48.0, 10.5 Hz, 1H, CH=CC*H*$_2$F), 4.71 (dd, *J* = 48.0, 10.5 Hz, 1H, CH=CC*H*$_2$F), 4.33 (ddd, *J* = 11.0, 5.5, 2.5 Hz, 1H, C*H*OH), 3.71 (ddd, *J* = 5.0, 2.5, 2.0 Hz, 1H, C*H*OH), 3.71 (d, *J* = 6.0 Hz, 1H, CHO*H*), 3.17 (qd, *J* = 7.0, 2.0 Hz, 1H, CH$_3$C*H*(C=O)), 3.07 (m, 1H, OH), 4.51 (q, *J* = 7.5 Hz, 2H, C*H*$_2$CH$_3$), 2.70 (ddd, *J* = 15.0, 10.0, 2.0 Hz, 1H, C=CHC*H*$_2$CHO), 2.45 (dd, *J* = 14.5, 11.0 Hz, 1H, CH$_2$COO), 2.39–2.28 (m, 2H, C*H*$_2$C(CH$_2$OH)=CH), 2.26 (dd, *J* = 14.5, 2.5 Hz, 1H, CH$_2$COO), 2.17–2.10 (m, 1H, C=CHC*H*$_2$CHO), 2.08 (d, *J* = 1.5 Hz, 3H, CH=C(C*H*$_3$)), 1.80–1.67 (m, 3H), 1.39 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$), 1.39–1.24 (m, 2H), 1.35 (s, 3H, C(CH$_3$)$_2$), 1.19 (d, *J* = 7.0 Hz, 3H, CH(C*H*$_3$)), 1.07 (s, 3H, C(CH$_3$)$_2$), 1.03 (d, *J* = 7.0 Hz, 3H, CH(C*H*$_3$)); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 220.7, 172.0, 170.3, 151.6, 138.9, 138.1, 126.1 (d, *J* = 46 Hz), 119.5, 115.2, 86.3 (d, *J* = 658 Hz), 78.2, 73.8, 72.2, 53.7, 41.5, 39.7, 37.9, 32.3, 31.6, 27.7, 26.8, 25.1, 23.0, 17.6, 15.9, 15.8, 14.0, 13.1; HRMS (FAB), calcd for $C_{28}H_{42}FNO_5S$ (M + Cs$^+$) 656.1822, found 656.1843.

Fluoride 53. A solution of triol **49** (6.0 mg, 0.0115 mmol, 1.0 equiv) in CH_2Cl_2 (1.5 mL, 0.01 M) at −78°C was treated with DAST (25 μL, 0.08 M in CH_2Cl_2, 0.016 mmol, 1.1 equiv) and the resulting mixture was stirred at −78°C for 10 min according to the procedure described for the synthesis of fluoride **50**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 50% EtOAc in hexanes), fluoride **53** (3.0 mg, 50%). R_f = 0.50 (silica gel, 50% EtOAc in hexanes); $[\alpha]_D^{22}$ −12.4 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3408, 2926, 2851, 1732, 1682, 1462, 1384, 1292, 1250, 1150, 1068, 974 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.04 (s, 1H, ArH), 6.86 (dd, *J* = 17.4, 10.8 Hz, 1H, C*H*=CH$_2$), 6.59 (s, 1H, C*H*=CCH$_3$), 6.05 (d, *J* = 17.5 Hz, 1H, CH=C*H*$_2$), 5.55 (d, *J* = 11.0 Hz, 1H, CH=C*H*$_2$) 5.57–5.51 (m, 1H, C=C*H*CH$_2$), 5.25 (d, *J* = 10.0 Hz, 1H, CHOCO), 4.79 (dd, *J* = 48.0, 10.7 Hz, 1H, CH=CC*H*$_2$F), 4.71 (dd, *J* = 48.0, 10.7 Hz, 1H, CH=CC*H*$_2$F), 4.28 (dd, *J* = 10.6, 1.6 Hz, 1H, C*H*OH), 3.70 (m, 1H, C*H*OH), 3.33–3.25 (m, 1H, CHO*H*), 3.16 (qd, *J* = 7.0, 2.1 Hz, 1H, CH$_3$C*H*(C=O)), 2.98 (m, 1H, OH), 2.75–2.66 (m, 1H, C=CHC*H*$_2$CHO), 2.46 (dd, *J* = 14.6, 11.0 Hz, 1H, CH$_2$COO), 2.37–2.27 (m, 2H, C*H*$_2$C(CH$_2$OH)=CH), 2.28 (dd, *J* = 14.6, 2.6 Hz, 1H, CH$_2$COO), 2.15–2.08 (m,

1H, C=CHCH_2CHO), 2.11 (s, 3H, CH=C(CH_3)), 1.80–1.64 (m, 3H), 1.43–1.27 (m, 2H), 1.34 (s, 3H, C(CH_3)$_2$), 1.18 (d, J = 6.8 Hz, 3H, CH(CH_3)), 1.07 (s, 3H, C(CH_3)$_2$), 1.03 (d, J = 7.0 Hz, 3H, CH(CH_3)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.9, 170.5, 166.3, 152.9, 139.3, 138.7 (d, J = 54 Hz), 130.2, 126.1 (d, J = 43 Hz), 120.4, 119.4, 116.1, 86.3 (d, J = 659 Hz), 78.3, 73.8, 72.3, 53.5, 41.5, 39.5, 37.8, 32.1, 31.6, 29.6, 27.5, 25.1, 22.8, 17.7, 15.7, 13.0; HRMS (FAB), calcd for $C_{28}H_{40}FNO_5S$ (M + H$^+$) 522.2689, found 522.2704.

Epoxide 54. To a solution of allylic alcohol **45** (25.4 mg, 0.049 mmol, 1.0 equiv) and 4 Å molecular sieves in CH_2Cl_2 (0.50 mL) at −40°C was added dropwise (+)-diethyl-D-tartrate (41 μL, 0.59 M in CH_2Cl_2, 0.024 mmol, 0.5 equiv) followed by titanium isopropoxide (55 μL, 0.35 M in CH_2Cl_2, 0.019 mmol, 0.4 equiv). After 1 h at that temperature, *t*-butyl hydroperoxide (22 μL of a 5 M solution in decane, 0.110 mmol, 2.2 equiv) was added and the reaction mixture was stirred at −30°C for 2 h. The reaction mixture was then filtered through Celite into saturated aqueous Na_2SO_4 (10 mL), eluting with EtOAc (10 mL). The resulting biphasic mixture was then stirred for 1 h and the layers were separated. The aqueous phase was extracted with EtOAc (3×10 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Preparative thin-layer chromatography (250 μm silica gel plates, 80% EtOAc in hexanes) furnished epoxide **54** (13.5 mg, 52%). R_f = 0.23 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −55.4 (*c* 0.06, $CHCl_3$); IR (thin film) ν_{max} 3425, 2929, 2862, 1732, 1688, 1456, 1367, 1292, 1258, 1195, 1149, 1040, 980 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.22 (s, 1H, ArH), 6.62 (s, 1H, CH=CCH$_3$), 5.59 (d, J = 47.0 Hz, 2H, ArCH_2F), 5.46 (dd, J = 6.7, 3.4 Hz, 1H, CHOCO), 4.14–4.09 (m, 1H, CHOH), 3.89 (d, J = 6.4 Hz, 1H, OH), 3.76 (bs, 1H, CHOH), 3.72 (d, J = 12.1 Hz, 1H, CH_2OH), 3.56 (dd, J = 12.1, 7.5 Hz, 1H, CH_2OH), 3.33 (qd, J = 6.8, 5.3 Hz, 1H, CH_3CH(C=O)), 3.16 (dd, J = 6.3, 6.1 Hz, 1H, C(O)CHCH$_2$CHO), 2.55 (dd, J = 14.1, 10.2 Hz, 1H, CH_2COO), 2.50 (bs, 1H, OH), 2.41 (dd, J = 14.1, 3.1 Hz, 1H, CH_2COO), 2.11 (s, 3H, CH=C(CH_3)), 2.10–1.97 (m, 2H, C(O)CHCH_2CHO), 1.91–1.81 (m, 2H, CH_2C(CH_2OH)), 1.74–1.60 (m, 3H), 1.50–1.30 (m, 2H), 1.34 (s, 3H, C(CH_3)$_2$), 1.18 (d, J = 6.8 Hz, 3H, CH(CH_3)), 1.06 (s, 3H, C(CH_3)$_2$), 0.99 (d, J = 7.0 Hz, 3H, C(CH_3)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.0, 170.3, 163.5 (d, J = 93 Hz), 152.6, 137.5, 119.3, 118.2, 80.5 (d, J = 675 Hz), 76.4, 74.6, 73.2, 63.8, 63.3, 56.9, 52.7, 39.1, 36.6, 31.2, 31.0, 28.1, 22.4, 20.9, 20.6, 17.5, 15.8, 14.2; HRMS (FAB), calcd for $C_{27}H_{40}FNO_7S$ (M + H$^+$) 542.2588, found 542.2575.

Epoxide 55. To a solution of allylic alcohol **46** (22 mg, 0.042 mmol, 1.0 equiv) and 4 Å molecular sieves in CH_2Cl_2 (420 μL) at −40°C was added dropwise (+)-diethyl-D-tartrate (4 μL, 0.021 mmol, 0.5 equiv), followed by titanium isopropoxide (5 μL, 0.016 mmol, 0.4 equiv) and after 1 h at this temperature, *t*-butyl hydroperoxide (18 μL of a 5 M solution in decane, 0.092 mmol, 2.2 equiv) according to the procedure described for the synthesis of epoxide **54** to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 80% EtOAc in hexanes), epoxide **55** (16 mg, 70%). R_f = 0.25 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −44.8 (*c* 1.4, $CHCl_3$); IR (thin film) ν_{max} 3435, 2959, 2935, 2877, 1732, 1689, 1534, 1459, 1421, 1371, 1338, 1241, 1174, 1039, 980 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.51 (s, 1H, ArH), 6.35 (s, 1H, CH=CCH$_3$), 5.40 (dd, J = 7.0, 3.0 Hz, 1H, CHOCO), 4.11 (ddd, J = 10.0, 6.5, 3.0 Hz, 1H, CHOH), 4.07 (s, 3H, CH_3O), 3.88 (d, J = 6.0 Hz, 1H, OH), 3.77–3.74 (m, 1H, CHOH), 3.73 (dd, J = 12.5, 4.0 Hz, 1H, CH_2OH), 3.57 (dd, J = 12.5, 8.0 Hz, 1H, CH_2OH), 3.32 (qd, J = 7.0, 5.0 Hz, 1H, CH_3CH(C=O)), 3.16 (dd, J = 7.0, 5.5 Hz, 1H, C(O)CHCH$_2$CHO), 2.54 (dd, J = 14.5, 10.0 Hz, 1H, CH_2COO), 2.50 (bs, 1H, OH), 2.40 (dd, J = 14.5, 3.5 Hz, 1H, CH_2COO), 2.13 (s, 3H, CH=C(CH_3)), 2.12–2.05 (m, 1H, C(O)CHCH_2CHO), 2.03–1.95 (m, 2H), 1.90–1.82 (m, 1H, CH_2C(CH_2OH)), 1.75–1.60 (m, 2H), 1.50–1.20 (m, 3H), 1.35 (s, 3H, C(CH_3)$_2$), 1.16 (d, J = 7.0 Hz, 3H, CH(CH_3)), 1.07 (s, 3H, C(CH_3)$_2$), 0.99 (d, J = 7.0 Hz, 3H, 74.5, 73.1, 63.8, 63.4, 60.4, 58.4, 57.1, 52.7, 43.4, 39.1, 36.4, 31.2, 30.9, 28.1, 22.2, 21.0, 20.3, 17.3, 15.4, 14.0; HRMS (FAB), calcd for $C_{27}H_{41}NO_8S$ (M + Cs$^+$) 672.1607, found 672.1584.

Fluoride 58. A solution of triol **54** (5.0 mg, 0.009 mmol, 1.0 equiv) in CH_2Cl_2 (1 mL, 0.01 M) at −78°C was treated with DAST (20 μL of a 0.1 M solution in CH_2Cl_2, 0.025 mmol, 1.05 equiv) according to the procedure described for the synthesis of fluoride **50**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 60% EtOAc in hexanes), fluoride **58** (2.0 mg, 41%). R_f = 0.22 (silica gel, 50% EtOAc in hexanes); IR (thin film) ν_{max} 3402, 2954, 2923, 2853, 1732, 1688, 1462, 1378, 1262, 1185, 1149, 1082, 1031, 980 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (s, 1H, ArH), 6.63 (s, 1H, CH=CCH$_3$), 5.60 (d, J = 47.0 Hz, 2H, ArCH_2F), 5.47 (dd, J = 7.0, 3.0 Hz, 1H, CHOCO), 4.39 (dd, J = 47.5, 10.5 Hz, 1H, C(O)CH_2F), 4.30 (dd, J = 47.5, 10.5 Hz, 1H, C(O)CH_2F), 4.13 (ddd, J = 9.5, 6.5, 3.0 Hz, 1H, CHOH), 3.75 (dd, J = 5.0, 5.0 Hz, 1H, CHOH), 3.74 (d, J = 7.0 Hz, 1H, OH), 3.31 (qd, J = 7.0, 6.0 Hz, 1H, CH_3CH(C=O)), 3.02 (dd, J = 6.0, 6.0 Hz, 1H, CH(O)CH_2CHO), 2.56 (dd, J = 14.0, 10.0 Hz, 1H, CH_2COO), 2.46 (brs, 1H, OH), 2.42 (dd, J = 14.0, 4.0 Hz, 1H, CH_2COO), 2.13 (s, 3H, CH=C(CH_3)), 2.10–1.97 (m, 3H), 1.95–1.87 (m, 1H), 1.90–1.82 (m, 1H), 1.75–1.63 (m, 2H), 1.50–1.20 (m, 2H), 1.36 (s, 3H, C(CH_3)$_2$), 1.16 (d, J = 7.0 Hz, 3H, CH(CH_3)), 1.08 (s, 3H, C(CH_3)$_2$), 1.01 (d, J = 7.0 Hz, 3H, C(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 221.5, 170.4, 163.7, 152.7, 137.4, 119.5, 118.4, 85.2 (d, J = 700 Hz), 80.6 (d, J = 675 Hz), 76.3, 74.3, 73.4, 60.2, 52.6, 43.3, 38.9, 36.5, 31.0, 30.9, 27.1, 22.2, 20.8, 20.6, 17.2, 15.7, 13.9; MS (electrospray), calcd for $C_{27}H_{39}F_2NO_6S$ (M + H$^+$) 544, found 544.

Fluoride 59. A solution of triol **55** (15 mg, 0.028 mmol, 1.0 equiv) in CH_2Cl_2 (280 μL, 0.1 M) at −78°C was treated with DAST (5 μL, 0.038 mmol, 1.4 equiv) according to the procedure described for the synthesis of fluoride **50**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, 50% EtOAc

in hexanes), fluoride **59** (4.0 mg, 26%). $R_f = 0.42$ (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −29.4 (*c* 0.33, $CHCl_3$); IR (thin film) ν_{max} 3492, 2960, 2928, 2874, 2865, 1738, 1732, 1693, 1682, 1537, 1462, 1455, 1422, 1384, 1241, 1144, 980 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.52 (s, 1H, ArH), 6.35 (s, 1H, C*H*=CCH_3), 5.41 (dd, *J* = 7.0, 3.5 Hz, 1H, CHOCO), 4.40 (dd, *J* = 47.5, 10.5 Hz, 1H, CH_2F), 4.30 (dd, *J* = 47.5, 10.5 Hz, 1H, CH_2F), 4.14 (ddd, *J* = 10.0, 7.0, 3.5 Hz, 1H, C*H*OH), 4.08 (s, 3H, CH_3O), 3.80 (d, *J* = 7.0 Hz, 1H, OH), 3.78 (dd, *J* = 3.5, 3.5 Hz, 1H, C*H*OH), 3.31 (qd, *J* = 7.0, 5.0 Hz, 1H, CH_3CH(C=O)), 3.01 (dd, *J* = 7.0, 5.5 Hz, 1H, C(O)C*H*CH_2CHO), 2.55 (dd, *J* = 14.5, 10.0 Hz, 1H, CH_2COO), 2.53 (bs, 1H, OH), 2.40 (dd, *J* = 14.5, 3.5 Hz, 1H, CH_2COO), 2.14 (s, 3H, CH=C(CH_3)), 2.12–2.15–1.90 (m, 3H), 1.73–1.70 (m, 1H), 1.55–1.24 (m, 5H), 1.36 (s, 3H, $C(CH_3)_2$), 1.17 (d, *J* = 6.5 Hz, 3H, CH(CH_3)), 1.09 (s, 3H, $C(CH_3)_2$), 1.00 (d, *J* = 7.0 Hz, 3H, $C(CH_3)_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.1, 173.9, 170.2, 146.3, 135.7, 120.0, 109.8, 85.8, 85.2 (d, *J* = 695 Hz), 65.8, 61.5 (d, *J* = 82 Hz), 58.4, 57.3 (d, *J* = 27 Hz), 52.7, 43.3, 39.2, 36.5, 31.1, 31.0, 27.3, 22.2, 21.2, 20.4, 17.3, 15.4, 13.9; HRMS (FAB), calcd for $C_{27}H_{40}FNO_7S$ ($M + Cs^+$) 674.1564, found 674.1594.

Epoxide 57. To a solution of allylic alcohol **24** (81 mg, 0.151 mmol, 1.0 equiv) and 4 Å molecular sieves in CH_2Cl_2 (1.25 mL) at −40°C was added dropwise (+)-diethyl-D-tartrate (13 μL, 0.076 mmol, 0.5 equiv), followed by titanium isopropoxide (18 μL, 0.060 mmol, 0.4 equiv) and after 1 h at this temperature, *t*-butyl hydroperoxide (66 μL of a 5 M solution in decane, 0.330 mmol, 2.2 equiv) according to the procedure described for the synthesis of epoxide **54** to yield, after flash column chromatography (silica gel, 80% EtOAc in hexanes), epoxide **57** (74 mg, 89%). $R_f = 0.34$ (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −32.5 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3455, 2959, 2931, 2877, 1733, 1689, 1465, 1377, 1289, 1257, 1147, 1040, 979, 912 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.46 (s, 1H, C*H*=CCH_3), 5.48 (dd, *J* = 4.9, 4.7 Hz, 1H, CHOCO), 4.00 (bm, 1H, C*H*OH), 3.75 (dd, *J* = 5.6, 3.4 Hz, 1H, C*H*OH), 3.71 (d, *J* = 12.5 Hz, 1H, CH_2OH), 3.64 (bs, 1H, OH), 3.56 (d, *J* = 12.5 Hz, 1H, CH_2OH), 3.32 (qd, *J* = 6.7, 6.7 Hz, 1H, CH_3CH(C=O)), 3.09 (dd, *J* = 6.3, 6.2 Hz, 1H, C(O)C*H*CH_2CHO), 2.52 (dd, *J* = 14.3, 9.8 Hz, 1H, CH_2COO), 2.43 (dd, *J* = 14.3, 3.4 Hz, 1H, CH_2COO), 2.28 (bs, 1H, OH), 1.95 (m, 2H, C(O)CHCH_2CHO), 1.86 (s, 3H, CH=C(CH_3)), 1.79 (m, 1H, CH_2C(CH_2OH)), 1.67 (m, 1H), 1.61 (m, 1H), 1.46 (m, 2H), 1.33 (s, 3H, $C(CH_3)_2$), 1.24 (m, 2H), 1.15 (d, *J* = 6.8 Hz, 3H, CH(CH_3)), 1.06 (s, 3H, $C(CH_3)_2$), 0.98 (d, *J* = 7.0 Hz, 3H, $C(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.2, 170.2, 143.7, 80.4, 75.3, 75.1, 73.6, 63.8, 63.0, 56.2, 52.2, 44.1, 38.7, 36.7, 31.6, 30.8, 30.7, 27.6, 22.7, 21.5, 21.3, 17.5, 14.6; HRMS (FAB), calcd for $C_{23}H_{37}IO_7$ ($M + Na^+$) 575.1483, found 575.1462.

Epoxide 56. A solution of vinyl iodide **57** (20 mg, 0.036 mmol, 1.0 equiv), stannane **8r** (29 mg, 0.072 mmol, 1.5 equiv) and $Pd(MeCN)_2Cl_2$ (2.0 mg, 0.004 mmol, 0.1 equiv) in degassed DMF (360 μL, 0.1 M) was stirred at 25°C for 20 h, according to the procedure described for the synthesis of lactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, EtOAc), starting vinyl iodide **57** (6 mg, 30%) and macrolactone **56** (10 mg, 51%). $R_f = 0.23$ (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −60.0 (*c* 0.14, $CHCl_3$); IR (thin film) ν_{max} 3414, 2969, 2933, 2872, 1736, 1687, 1458, 1373, 1293, 1258, 1150, 980, 914 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 1H, ArH), 6.61 (s, 1H, C*H*=CCH_3), 5.43 (dd, *J* = 8.0, 3.0 Hz, 1H, CHOCO), 4.20 (ddd, *J* = 9.5, 6.5, 3.0 Hz, 1H, C*H*OH), 4.04 (d, *J* = 6.5 Hz, 1H, OH), 3.77 (dd, *J* = 4.0, 4.0 Hz, 1H, C*H*OH), 3.74 (dd, *J* = 12.5, 4.0 Hz, 1H, CH_2OH), 3.57 (dd, *J* = 12.5, 8.0 Hz, 1H, CH_2OH), 3.32 (qd, *J* = 7.0, 4.5 Hz, 1H, CH_3CH(C=O)), 3.16 (dd, *J* = 7.5, 5.0 Hz, 1H, C(O)C*H*CH_2CHO), 3.01 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 2.56 (bs, 1H, OH), 2.54 (dd, *J* = 14.0, 10.0 Hz, 1H, CH_2COO), 2.38 (dd, *J* = 14.0, 3.0 Hz, 1H, CH_2COO), 2.14 (ddd, *J* = 15.0, 4.5, 3.0 Hz, 1H, C(O)CHCH_2CHO) 2.11 (s, 3H, CH=C(CH_3)), 2.02–1.96 (m, 1H, C(O)CHCH_2CHO), 1.93–1.84 (m, 1H), 1.74–1.71 (m, 1H), 1.55–1.25 (m, 5H), 1.40 (t, *J* = 8.0 Hz, 3H, CH_3CH_2), 1.37 (s, 3H, $C(CH_3)_2$), 1.17 (d, *J* = 7.0 Hz, 3H, CH(CH_3)), 1.08 (s, 3H, $C(CH_3)_2$), 1.01 (d, *J* = 7.0 Hz, 3H $C(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.4, 172.0, 170.5, 151.5, 137.2, 119.7, 115.5, 76.4, 74.1, 72.7, 63.8, 63.5, 57.3, 53.1, 42.9, 39.2, 36.4, 31.4, 30.9, 28.3, 26.8, 21.9, 21.2, 19.5, 17.1, 15.9, 14.0, 13.6; HRMS (FAB), calcd for $C_{28}H_{43}NO_7S$ ($M + Na^+$) 560.2658, found 560.2640.

bis-Silylether 61. To a solution of triol **57** (83 mg, 0.150 mmol, 1.0 equiv) in DMF (1.5 mL, 0.1 M) was added Et_3N (315 μL, 2.26 mmol, 15 equiv) followed by TMSCl (152 μL, 1.20 mmol, 8 equiv) and the mixture was stirred at 25°C for 12 h. The mixture was then concentrated under reduced pressure and the resulting oil was partitioned between ether (10 mL) and water (10 mL) and the layers were separated. The aqueous layer was extracted with ether (3×10 mL) and the combined extracts were dried ($MgSO_4$), concentrated under reduced pressure and then filtered through a short plug of silica gel. The resulting filtrate was concentrated, dissloved in CH_2Cl_2 (5 ml) and silica gel (1 g) was added. The resulting slurry was stirred at 25°C for 12 h, filtered, concentrated and finally passed through a short plug of silica gel to afford the bis-silylether **61** as a foam (103 mg, 98%). $R_f = 0.48$ (silica gel, 60% Et_2O in hexanes); $[\alpha]_D^{22}$ −19.1 (*c* 0.23, $CHCl_3$); IR (thin film) ν_{max} 3408, 2956, 1746, 1698, 1454, 1383, 1250, 1156, 1113, 1060, 1021, 985, 898, 841, 752 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.44 (s, 1H, ArH), 5.37 (dd, *J* = 9.0 Hz, 1H, CHOCO), 4.01 (dd, *J* = 10.5, 2.5 Hz, 1H, C*H*OH), 3.86 (d, *J* = 10.0 Hz, 1H, CHOSi), 3.79 (dd, *J* = 12.5, 4.5 Hz, 1H, CH_2OH), 3.49 (ddd, *J* = 12.5, 10.5, 8.5 Hz, 1H, CH_2OH), 3.39 (m, 1H, OH), 3.09 (dd, *J* = 10.5, 3.5 Hz, 1H, C*H*(O)CH_2CHO), 2.97 (qd, *J* = 6.5, 4.0 Hz, 1H, CH_3C*H*(C=O)), 2.74 (dd, *J* = 16.5, 10.5 Hz, 1H, CH_2COO), 2.67 (dd, *J* = 16.0, 2.5 Hz, 1H, CH_2COO), 2.18–2.15 (m, 1H, CH(O)CH_2CHO), 1.95–1.82 (m, 2H), 1.82 (s, 3H, CH_3C=C), 1.68–1.40 (m, 4H), 1.24 (m, 2H), 1.18 (s, 3H, $C(CH_3)_2$), 1.11 (s, 3H, $C(CH_3)_2$), 1.06 (d, *J* = 6.5 Hz, 3H, CH(CH_3)), 0.95 (d,

J = 7.0 Hz, 3H, CH(CH_3)), 0.14 (s, 9H, (CH_3)$_3$Si), 0.06 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 214.8, 170.8, 145.4, 81.4, 80.6, 76.2, 74.5, 64.0, 63.4, 58.1, 53.2, 48.3, 40.0, 35.6, 32.9, 31.4, 28.7, 24.5, 23.4, 23.3, 19.6, 19.5, 17.9, 0.9, 0.3; HRMS (FAB), calcd for $C_{29}H_{53}IO_7Si_2$ ($M + Cs^+$) 829.1429, found 829.1459.

Aldehyde 62. To a suspension of alcohol **61** (20 mg, 0.029 mmol, 1.0 equiv) and 4 Å molecular sieves in CH_2Cl_2 (0.25 mL) was added NMO (10 mg, 0.085 mmol, 3.0 equiv) followed by TPAP (1 mg, 0.003 mmol, 0.1 equiv). The resulting slurry was stirred at 25°C for 40 min and then filtered through a short plug of silica to afford aldehyde **62** (18 mg, 90%). R_f = 0.66 (silica gel, 60% Et_2O in hexanes); IR (thin film) ν_{max} 2956, 2913, 2851, 1732, 1698, 1454, 1383, 1250, 1156, 1113, 1021, 987, 895, 841, 750 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (s, 1H, CH=O), 6.51 (s, 1H, ArH), 5.46 (dd, J = 7.9, 3.4 Hz, 1H, CHOCO), 3.81 (d, J = 8.3 Hz, 1H, CHOSi), 3.32 (dd, J = 8.5, 4.2 Hz, 1H, CHOSi), 3.04 (qd, J = 7.1, 7.1 Hz, 1H CH_3CH(C=O)), 2.65 (dd, J = 15.6, 8.3 Hz, 1H, CH_2COO), 2.59 (dd, J = 15.6, 4.1 Hz, 1H, CH_2COO), 2.21 (ddd, J = 15.2, 3.8, 3.8 Hz, 1H, CH(O)CH_2CHO), 2.06–1.97 (m, 2H), 1.87 (s, 3H, CH_3C=CH), 1.87–1.80 (m, 1H), 1.62–1.56 (m, 1H), 1.51–1.41 (m, 2H), 1.27–1.21 (obscured m, 2H), 1.15 (s, 3H, C(CH_3)$_2$), 1.08 (s, 3H, C(CH_3)$_2$), 1.08 (d, J = 6.2 Hz, 3H, CH(CH_3)), 0.96 (d, J = 6.9 Hz, 3H, CH(CH_3)), 0.13 (s, 9H, (CH_3)$_3$Si), 0.05 (s, 9H, (CH_3)$_3$Si); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 216.2, 198.7, 170.7, 144.9, 81.7, 79.6, 75.0, 74.2, 64.1, 57.7, 53.3, 47.5, 40.0, 36.0, 31.8, 31.0, 29.5, 25.3, 22.9, 22.7, 21.9, 19.9, 19.2, 17.1, 0.4, 0.0; HRMS (FAB), calcd for $C_{29}H_{51}IO_7Si_2$ ($M + Cs^+$) 827.1272, found 827.1304.

Olefin 63. Methyltriphenylphosphonium bromide (104 mg of a mixture with sodium amide (Aldrich), 0.250 mmol, 9.7 equiv) in THF (2.0 mL) was added portionwise to a solution of aldehyde **62** (18.0 mg, 0.026 mmol, 1.0 equiv) in THF (0.5 mL) at −5°C until the completion of the reaction was established by TLC. Saturated aqueous NH_4Cl (1 mL) was added and the product was extracted with ether (3×2 mL) dried ($MgSO_4$) and then concentrated under reduced pressure. Flash column chromatography (silica gel, 15% ether in hexanes) furnished olefin **63** (11.7 mg, 65%). R_f = 0.50 (silica gel, 20% Et_2O in hexanes); $[\alpha]_D^{22}$ −17.9 (c 0.2, $CHCl_3$); IR (thin film) ν_{max} 2954, 2923, 1747, 1698, 1456, 1382, 1250, 1156, 1113, 1021, 986, 889, 841, 750 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.44 (s, 1H, ArH), 6.00 (dd, J = 17.0, 10.0 Hz, 1H, CH=CH_2), 5.36 (dd, J = 9.0, 2.0 Hz, 1H, CHOCO), 5.29 (dd, J = 17.5, 1.5 Hz, 1H, CH_2=CH), 5.14 (dd, J = 10.5, 1.5 Hz, 1H, CH_2=CH), 4.12 (dd, J = 9.0, 5.0 Hz, 1H, CHOSi), 3.85 (d, J = 9.5 Hz, 1H, CHOSi), 3.04 (qd, J = 9.0, 7.0 Hz, 1H, CH_3CH(C=O)), 2.85 (dd, J = 9.5, 4.0 Hz, 1H, CH(O)CCH=CH_2), 2.73 (dd, J = 16.0, 10.0 Hz, 1H, CH_2COO), 2.65 (dd, J = 16.0, 2.5 Hz, 1H, CH_2COO), 2.12 (ddd, J = 15.0, 4.0, 2.0 Hz, 1H, CH_2CH(O), 1.93–1.78 (3H, m), 1.84 (s, 3H, CH = CCH_3), 1.65–1.20 (m, 5H), 1.19 (s, 3H, C(CH_3)$_2$), 1.11 (s, 3H, C(CH_3)$_2$), 1.08 (d, J = 6.5 Hz, 3H, CH(CH_3)), 0.95 (d, J = 7.0 Hz, 3H, CH(CH_3)), 0.14 (s, 9H, (CH_3)$_3$Si), 0.07 (9H, s, (CH_3)$_3$Si), ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 215.2, 170.6, 145.4, 136.7, 116.0, 81.2, 80.2, 75.7, 74.7, 63.6, 63.3, 53.3, 48.0, 39.4, 35.9, 33.4, 31.0, 30.3, 29.3, 24.3, 23.6, 22.7, 19.8, 19.5, 17.6, 0.7, 0.3; HRMS (FAB), calcd for $C_{30}H_{53}IO_6Si_2$ ($M + Cs^+$) 825.1480, found 825.1450.

Macrolactone 65. A solution of olefin **63** (15 mg, 0.022 mmol, 1.0 equiv) in EtOH (1.0 mL) was treated with hydrazine (17 μL, 0.500 mmol, 25.0 equiv) and H_2O_2 (25 μL, 30% w/w in water, 0.370 mmol, 16.0 equiv) and the resulting mixture stirred at 0°C for 3 h. The mixture was then partitioned between ether (4 mL) and water (2 mL) and the layers were separated. The aqueous layer was extracted with ether (3×4 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure to give macrolactone **64** as a foam (15.0 mg) which was dissolved in THF (1.5 mL) and treated with HF•pyr. in pyr./THF (600 μL) and the mixture was stirred at 0°C for 2 h. The reaction mixture was then quenched with saturated aqueous $NaHCO_3$ (5 mL) and was extracted with EtOAc (3×3 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. Flash column chromatography (silica gel, 80% ether in hexanes) furnished macrolactone **65** (9.4 mg, 75%). R_f = 0.06 (silica gel, 60% Et_2O in hexanes); $[\alpha]_D^{22}$ −19.3 (c 0.33, $CHCl_3$); IR (thin film) ν_{max} 3416, 2954, 2926, 2872, 1734, 1689, 1456, 1384, 1287, 1256, 1149, 1084, 978, 892 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.46 (s, 1H, CH=CCH_3), 5.48 (dd, J = 5.0, 5.0 Hz, 1H, CHOCO), 4.03 (bm, 1H, CHOH), 3.76 (bm, 2H, CHOH and OH), 3.34 (qd, J = 6.5, 6.5 Hz, 1H, CH_3CH(C=O)), 2.73 (dd, J = 6.5, 6.5 Hz, 1H, CH(O)CCH_2CH_3), 2.54 (dd, J = 14.5, 10.0 Hz, 1H, CH_2COO), 2.44 (dd, J = 14.5, 8.5 Hz, 1H, CH_2COO), 2.29 (bs, 1H, OH), 1.96–1.85 (m, 2H), 1.89 (s, 3H, CH_3C=CH), 1.70–1.40 (m, 5H), 1.31–1.24 (m, 4H), 1.35 (s, 3H, C(CH_3)$_2$), 1.19 (d, J = 6.5 Hz, 3H, CH(CH_3)), 1.07 (s, 3H, C(CH_3)$_2$), 0.99 (d, J = 7.0 Hz, 3H, CH(CH_3)), 0.91 (t, J = 7.5 Hz, 3H, CH_3CH_2) ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.5, 170.3, 143.8, 80.2, 75.4, 73.8, 63.8, 59.1, 52.1, 44.1, 38.6, 36.4, 31.0, 30.5, 29.7, 29.2, 28.8, 22.8, 21.7, 21.3, 20.1, 17.4, 14.6, 8.8; HRMS (FAB), calcd for $C_{24}H_{39}IO_6$ ($M + Cs^+$) 683.0846, found 683.0870.

Macrolactone 66. A solution of vinyl iodide **65** (9.4 mg, 0.017 mmol, 1.0 equiv), stannane **8j** (10 mg, 0.036 mmol, 2.1 equiv) and $Pd(MeCN)_2Cl_2$ (1.0 mg, 0.004 mmol, 0.2 equiv) in degassed DMF (250 μL, 0.07 M) was stirred at 25°C for 15 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, EtOAc) macrolactone **66** (4.6 mg, 52%). R_f = 0.40 (silica gel, 80% EtOAc in hexanes); $[\alpha]_D^{22}$ −30.0 (c 0.17, $CHCl_3$); IR (thin film) ν_{max} 3432, 2967, 2933, 2872, 1736, 1689, 1458, 1384, 1256, 1151, 1067, 1038, 979, 905, 733 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (s, 1H, ArH), 6.62 (s, 1H, CH=CCH_3), 5.59 (d, J = 47.1 Hz, 2H, CH_2F), 5.46 (dd, J = 6.3, 3.7 Hz, 1H, CHOCO), 4.15 (d, J = 8.8 Hz, 1H, CHOH), 3.98 (bs, 1H, OH), 3.77 (brs, 1H, CHOH), 3.35 (qd, J = 6.6, 4.8 Hz, 1H, CH_3CH(C=O)), 2.82 (dd, J = 6.1, 6.1 Hz, 1H, CH(O)CCH_2CH_3), 2.56 (dd, J = 14.0,

9.9 Hz, 1H, CH_2COO), 2.48 (bs, 1H, OH), 2.41 (dd, J = 14.0, 3.0 Hz, 1H, CH_2COO), 2.13 (s, 3H, CH=C(CH_3)), 2.04 (ddd, J = 15.1, 5.9, 4.0 Hz, 1H, $CH_2CH(O)CCH_2CH_3$), 2.00–1.94 (m, 1H, $CH_2CH(O)CCH_2CH_3$), 1.78–1.24 (m, 9H), 1.36 (s, 3H, $C(CH_3)_2$), 1.17 (d, J = 7.0 Hz, 3H, $CH(CH_3)$), 1.07 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.0 Hz, 3H, $CH(CH_3)$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.5, 170.5, 163.7, 152.8, 137.8, 119.2, 118.2, 81.2, 79.8, 74.8, 73.3, 64.1, 59.9, 52.6, 43.5, 38.9, 36.4, 31.5, 30.7, 29.2, 28.9, 22.4, 20.7, 20.6, 17.3, 15.7, 14.1, 8.7; HRMS (FAB), calcd for $C_{28}H_{42}FNO_6S$ ($M+Cs^+$) 672.1771, found 672.1793.

Macrolactone 67. A solution of vinyl iodide **65** (11 mg, 0.020 mmol, 1.0 equiv), stannane **8p** (14 mg, 0.034 mmol, 1.7 equiv) and $Pd(MeCN)_2Cl_2$ (1.0 mg, 0.004 mmol, 0.2 equiv) in degassed DMF (250 μL, 0.08 M) was stirred at 25°C for 20 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, Et_2O) macrolactone **67** (8.5 mg, 79%). R_f = 0.68 (silica gel, Et_2O); $[\alpha]_D^{22}$ −44.7 (*c* 0.08 $CHCl_3$); IR (thin film) ν_{max} 3442, 2964, 2934, 1732, 1683, 1536, 1461, 1422, 1384, 1241, 1150, 1070, 979, 906, 732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.52 (s, 1H, ArH), 6.36 (s, 1H, C*H*=CCH_3), 5.41 (dd, J = 7.0, 3.3 Hz, 1H, CHOCO), 4.15 (ddd, J = 10.3, 7.0, 3.7 Hz, 1H, C*H*OH), 4.08 (s, 3H, OCH_3), 3.99 (bd, J = 6.3 Hz, 1H, OH), 3.77 (bm, 1H, C*H*OH), 3.34 (qd, J = 6.6, 4.8 Hz, 1H, CH_3CH(C=O)), 2.81 (dd, J = 6.6, 5.9 Hz, 1H, C*H*(O)CCH_2CH_3), 2.55 (dd, J = 14.2, 10.1 Hz, 1H, CH_2COO), 2.52 (bs, 1H, OH), 2.39 (dd, J = 14.0, 2.9 Hz, 1H, CH_2COO), 2.14 (s, 3H, CH=C(CH_3)), 2.05 (ddd, J = 15.1, 5.5, 4.0 Hz, 1H, $CH_2CH(O)CCH_2CH_3$), 1.98–1.92 (m, 1H, $CH_2CH(O)CCH_2CH_3$), 1.80–1.70 (m, 2H), 1.58–1.39 (m, 5H), 1.30–1.24 (m, 2H), 1.17 (d, J = 7.0 Hz, 3H, $CH(CH_3)$), 1.08 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.0 Hz, 3H, $CH(CH_3)$), 0.91 (t, J = 7.4 Hz, 3H, CH_3CH_2); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.5, 174.1, 170.5, 146.5, 136.3, 119.8, 109.7, 74.6, 73.3, 64.2, 60.1, 58.4, 52.7, 43.4, 39.1, 36.4, 31.6, 30.8, 29.4, 28.9, 22.6, 22.4, 21.0, 20.4, 17.2, 15.5, 14.0, 8.7; HRMS (FAB), calcd for $C_{28}H_{43}NO_7S$ ($M+Cs^+$) 670.1815, found 670.1837.

Macrolactone 68. A solution of vinyl iodide **65** (5.8 mg, 0.011 mmol, 1.0 equiv), stannane **8r** (10 mg, 0.025 mmol, 2.3 equiv) and $Pd(MeCN)_2Cl_2$ (1.0 mg, 0.004 mmol, 0.3 equiv) in degassed DMF (100 μL, 0.1 M) was stirred at 25°C for 23 h, according to the procedure described for the synthesis of macrolactone **18d**, to yield, after preparative thin-layer chromatography (250 μm silica gel plates, Et_2O) macrolactone **68** (3.7 mg, 65%). R_f = 0.45 (silica gel, Et_2O); $[\alpha]_D^{22}$ −33.3 (*c* 0.09, $CHCl_3$); IR (thin film) ν_{max} 3406, 2954, 2924, 2872, 1736, 1692, 1454, 1384, 1254, 1150, 1071, 979 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (s, 1H, ArH), 6.60 (s, 1H, C*H*=CCH_3), 5.42 (dd, J = 7.9, 3.1 Hz, 1H, CHOCO), 4.33 (bs, 1H, C*H*OH), 4.24 (bd, J = 9.6 Hz, 1H, OH), 3.76 (bm, 1H, C*H*OH), 3.32 (qd, J = 6.8, 4.3 Hz, 1H, CH_3CH(C=O)), 3.01 (q, J = 7.6 Hz, 2H, $ArCH_2CH_3$), 2.82 (dd, J = 7.4, 4.8 Hz, 1H, C*H*(O)CH_2), 2.60 (bs, 1H, OH), 2.54 (dd, J = 13.6, 10.3 Hz, 1H, CH_2COO), 2.35 (dd, J = 14.0, 2.9 Hz, 1H, CH_2COO), 2.10–2.05 (obscured m, 1H, $CH_2CH(O)CCH_2CH_3$), 2.09 (s, 3H, CH=C(CH_3)), 1.96–1.90 (m, 1H, $CH_2CH(O)CCH_2CH_3$), 1.80–1.67 (m, 2H), 1.66–1.25 (m, 7H), 1.38 (s, 3H, $C(CH_3)_2$), 1.16 (d, J = 7.0 Hz, 3H $CH(CH_3)$), 1.07 (s, 3H, $C(CH_3)_2$), 1.00 (d, J = 7.0 Hz, 3H $CH(CH_3)$), 0.92 (t, J = 7.4 Hz, 3H, CH_3CH_2), 0.91 (t, J = 7.5 Hz, 3H, CH_3CH_2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.7. 170.6, 115.4, 74.1, 72.6, 64.4, 60.4, 53.2, 42.7, 39.2, 36.3, 31.8, 30.8, 29.7, 28.9, 28.7, 27.8, 26.8, 22.7, 22.0, 21.3, 19.4, 17.5, 17.0, 16.0, 14.1, 14.0, 13.6, 8.6; HRMS (FAB), calcd for $C_{29}H_{45}NO_6S$ ($M+Cs^+$) 668.2022, found 668.2042.

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