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Total Synthesis of 26-Hydroxy-Epothilone B and Related Analogs *via* a Macrolactonization Based Strategy†

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Abstract: The chemical synthesis of a series of 26-substituted epothilones B is described. Fully protected 26-hydroxydesoxy-epothilone B (**7**), prepared via the macrolactonization strategy, served as a common precursor to the designed epothilones described. The synthesized compounds were members of a large epothilone library whose biological screening led to the identification of a number of highly potent antitumor agents.

INTRODUCTION

The discovery of the epothilones (isolated from the myxobacteria *sorangium cellulosum* strain 90)[1] and the recognition of their tubulin-binding mechanism[2] of action marked the beginning of a new era in the search for novel anti-cancer drugs. In addition to the natural products,[3] epothilones A-E (**1-5**, **Figure 1**), a large number of analogs[4,5] have been synthesized and evaluated. The chemical biology of epothilones has also recently been reviewed.[6,7]

Due to the higher potency of epothilone B as a tubulin polymerization and cytotoxic agent, the synthesis of epothilone analogs with substitution at C26 assumed high priority in our laboratories. In a preliminary communication,[4a] we disclosed the chemical synthesis of 26-hydroxy epothilone B (**6**, **Figure 1**), and a number of derivatives thereof, together with relevant biological data. In this article, we describe the details of the total synthesis of a series of C26-substituted epothilones *via* a macrolactonization based strategy, starting from a readily available intermediate previously used for the total synthesis of epothilone B.[3g] A facile and rapid entry into the 26-hydroxy epothilone series would require a common intermediate as close to the final target molecules as possible and which would be readily accessible in a stereocontrolled manner.

† This paper is dedicated with affection and respect to our colleague and friend Professor Madeleine M. Joullié in celebration of her forty years of distinguished research and teaching at the University of Pennsylvania.

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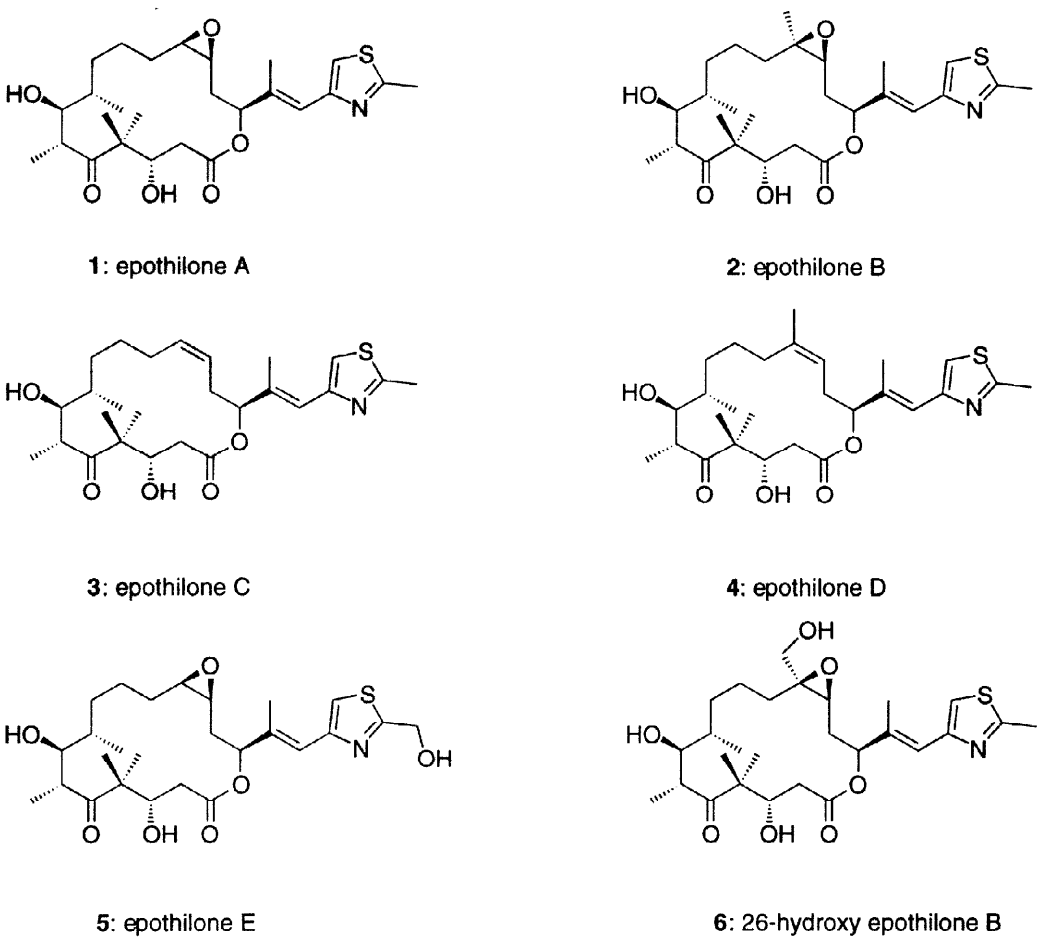
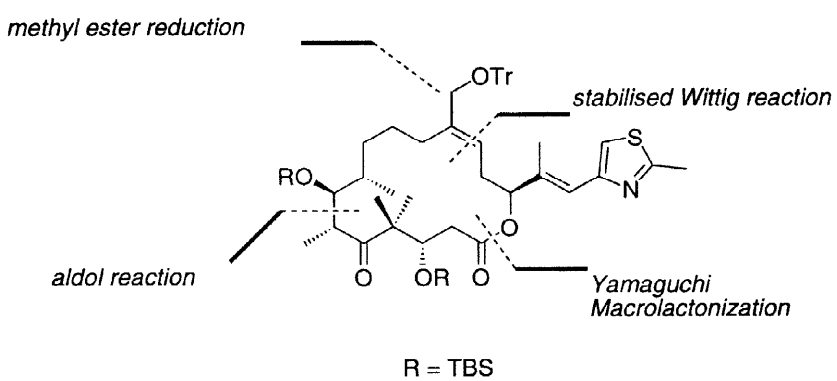


Figure 1. Structures of epothilones A-E (**1-5**) and 26-hydroxy epothilone B (**6**).

Designed compound **7** (**Figure 2**) fulfills these criteria. Its construction was envisioned to proceed along the path previously charted in these laboratories for epothilone B[3g] and would involve (a) a stabilized ylid



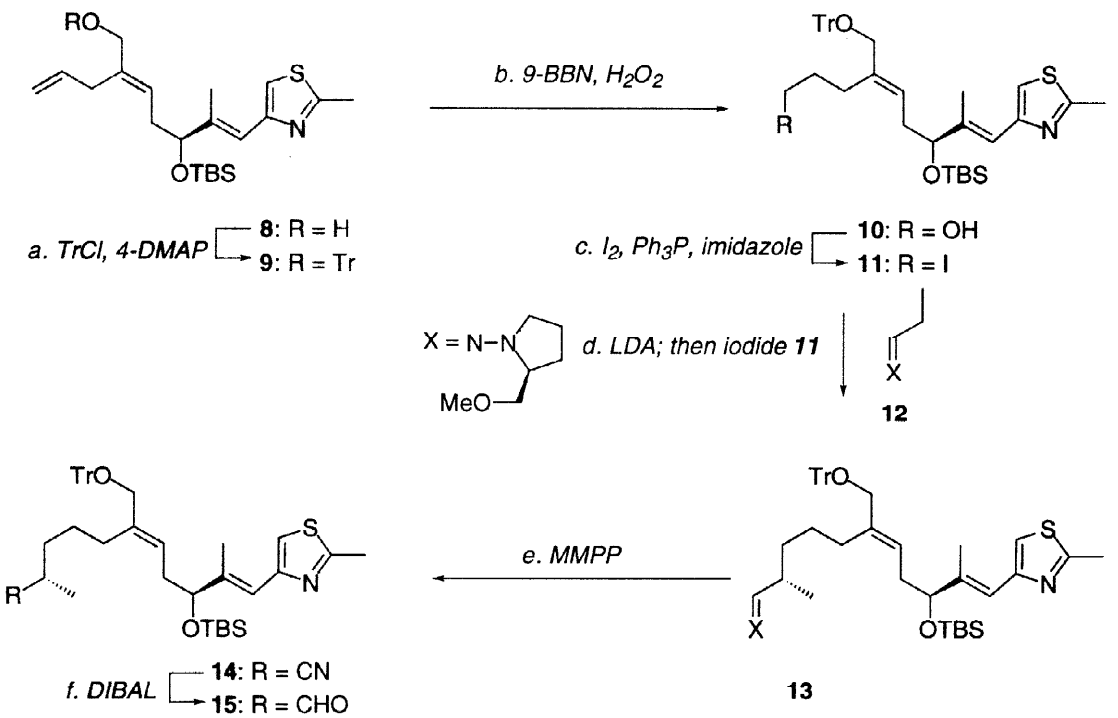
7: fully protected 26-hydroxydesoxy epothilone B

Figure 2. Fully protected 26-hydroxydesoxy epothilone B (**7**) and strategic bond disconnections.

condensation to install the C12,13 double bond geometry and simultaneously provide the C26 carbon; (b) an aldol condensation to form the C6,7 bond; and (c) a Yamaguchi-type macrolactonization to form the macrocyclic skeleton.

RESULTS AND DISCUSSION

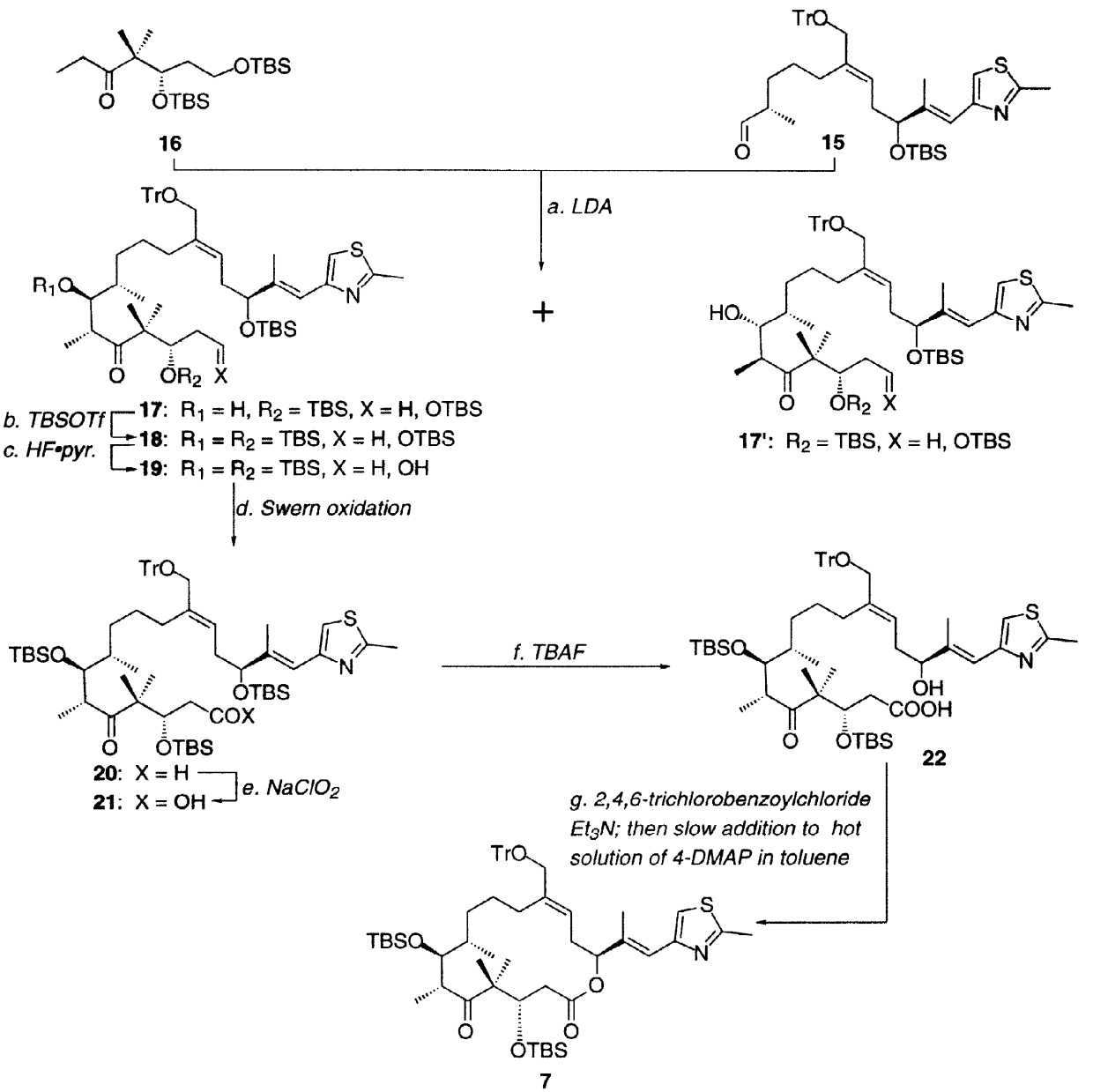
The execution of the synthesis of **7** is depicted in **Schemes 1** and **2**. The required key intermediate aldehyde **15** was prepared from the previously described[3g] allylic alcohol **8** as shown in **Scheme 1**.



Scheme 1. Stereoselective synthesis of aldehyde **15**. Reagents and conditions: (a) 1.0 equiv. of trityl chloride, 1.0 equiv. of 4-DMAP, DMF, 70 °C, 1 h, 99%; (b) 1.2 equiv. of 9-BBN, THF, 0 °C, 2 h; then 3 N aqueous NaOH, then 30% H_2O_2, 3 h, 94%; (c) 1.5 equiv. of I_2, 3.0 equiv. of imidazole, 1.5 equiv. of Ph_3P, Et_2O:MeCN (3:1), 0 °C, 0.5 h, 90%; (d) 1.3 equiv. of **12**, 1.3 equiv. of LDA, THF, 0 °C, 14 h; then 1.0 equiv. of **11** in THF, −100 → −20 °C, 10 h, 94% based on 70% conversion; (e) 2.5 equiv. of monoperoxyphthalic acid, magnesium salt (MMPP), MeOH:phosphate buffer pH 7 (1:1), 0 °C, 1 h, 91%; (f) 2.0 equiv. of DIBAL, toluene, −78 °C, 1 h, 97%. 4-DMAP = 4-dimethylaminopyridine; 9-BBN = 9-borabicyclo[3.3.1]nonane; LDA = lithium diisopropylamide; DIBAL = diisobutylaluminium hydride.

The first task was the selection of a suitable group for the protection of the primary hydroxyl functionality at C26. A triphenylmethyl (trityl, Tr) group was judged to be most useful for this purpose, and indeed served admirably throughout the course of the synthesis. Protection of **8** as a trityl ether (trityl chloride, 4-DMAP, DMF; for abbreviations, see legends in **Schemes**) furnished **9** in 99% yield. Regioselective hydroboration of **9** employing 9-BBN, and an ensuing basic hydrogen peroxide work-up led to primary alcohol **10** in 94% yield,

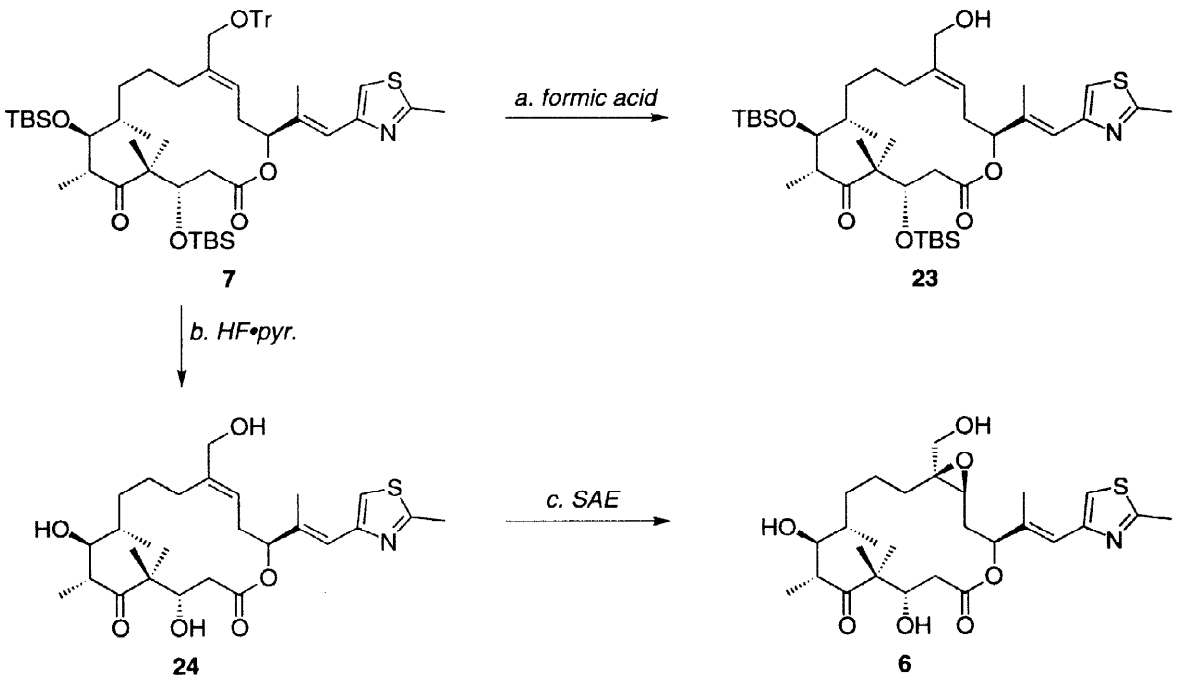
which was converted to iodide **11** by the action of Ph_3P, iodine and imidazole in the mixed solvent system of MeCN:Et_2O (3:1, 90% yield).



Scheme 2. Stereoselective synthesis of fully protected 26-hydroxydesoxy epothilone B **7**. Reagents and conditions: **(a)** 1.2 equiv. of LDA, THF, 0 °C, 15 min; then 1.2 equiv. of **16** in THF, −78 → −60 °C, 1 h; then 1.0 equiv. of **15** in THF at −78 °C, (85 % combined yield, *ca* .3 : 1 ratio of **17**:**17'**); (b) 1.2 equiv. of TBSOTf, 2.0 equiv. of 2,6-lutidine, CH_2Cl_2, 0 °C, 2 h, 92%; (c) HF•pyr. in pyridine, THF, 0 → 25 °C, 4 h, 74%; (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, 99%; (e) 3.0 equiv. of $NaClO_2$, 4.0 equiv. of 2-methyl-2-butene, 1.5 equiv. of NaH_2PO_4, *t*-BuOH:H_2O (5:1), 25 °C, 2 h, 99%; (f) 6.0 equiv. of TBAF, THF, 25 °C, 8 h, 89%; (g) 1.3 equiv. of 2,4,6-trichlorobenzoylchloride, 2.2 equiv. of Et_3N, THF, 0 °C, 1 h; then add to a solution of 2.2 equiv. of 4-DMAP in toluene (0.005 M based on **22**), 75 °C, 1 h, 75%; TBAF = tetra *n*-butylammonium fluoride.

Stereoselective alkylation of SAMP hydrazone **12**,[8] *via* its lithio derivative (LDA, THF, –78 → 0 °C), with iodide **11** (–100 → –20 °C, 94% yield, based on *ca.* 70% conversion) led to hydrazone **13**. The transformation of **13** to nitrile **14** proceeded smoothly under the influence of MMPP[8c,9] (91% yield), and reduction of the latter with DIBAL in toluene at –78 °C provided the key aldehyde **15** in excellent yield (97%). The coupling of the C1-C6 ketone fragment **16**[3g] with the C7-C15 aldehyde **15** *via* a *syn*-selective aldol reaction (LDA, –78 °C) as shown in **Scheme 2**, furnished compound **17** along with its (6*S*,7*R*)-diastereoisomer **17′** (85% total yield, *ca.* 3:1 ratio in favor of **17**). Chromatographic purification (silica gel, 20% Et_2O in hexanes), followed by silylation (TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 92% yield) gave tetra(silyl)ether **18**. The use of buffered pyridinium hydrofluoride (HF•pyr.) in THF[10] permitted selective desilylation of the primary TBS group of **18** giving **19** (74% yield), which was sequentially oxidized to aldehyde **20** [$(COCl)_2$, DMSO, Et_3N, 99%], and thence to carboxylic acid **21** ($NaClO_2$, 99%). Selective desilylation at C15 was achieved by the use of TBAF in THF, providing the hydroxy-acid **22** in 89% yield. The latter compound was in turn subjected to the macrolactonization conditions described by Yamaguchi,[11] allowing isolation of the lactone **7** in 75% yield.

Having secured a facile route to lactone **7**, we were faced with a number of choices regarding the further manipulation of this intermediate. Initial explorations employing formic acid in ether[12] demonstrated that we could selectively expose the key C26-hydroxyl moiety whilst retaining the TBS ethers at C3 and C7 leading to compound **23** in 69% yield (**Scheme 3**).

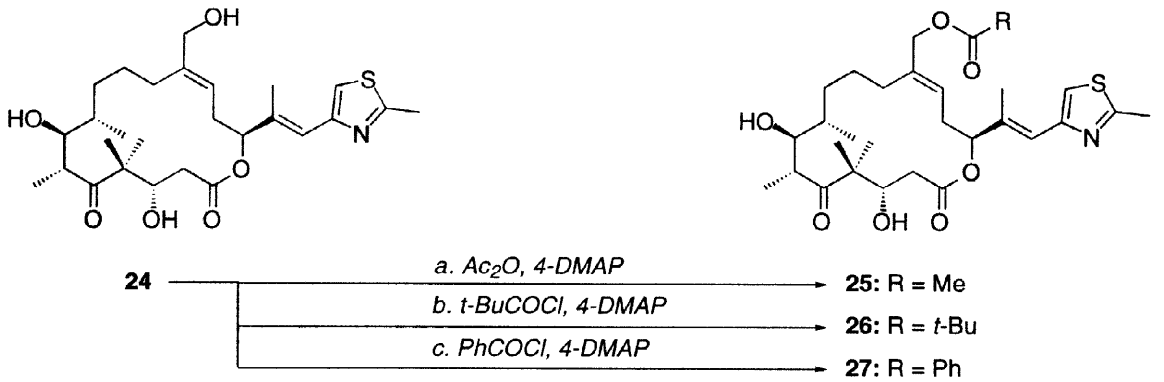


Scheme 3. Synthesis of 26-hydroxydesoxy epothilone B (**24**) and 26-hydroxy epothilone B (**6**). Reagents and conditions: (a) 50% formic acid in Et_2O, –10 °C, 5 h, 69%; (b) 30% HF•pyr. (by volume) in THF, 0 → 25 °C, 36 h, 78%; (c) 0.25 equiv. of (+)-diethyl-L-tartrate, 0.2 equiv. of Ti(*i*-OPr)$_4$, 2.0 equiv. of *t*-BuOOH, –30 °C, 2 h, 76% (d.e. >95%).

Alternatively, treatment of **7** with HF•pyr. in THF promoted concomitant cleavage of both the silyl groups and the trityl moiety, leading to **24** in 78% yield. We were pleased to find that using the conditions of

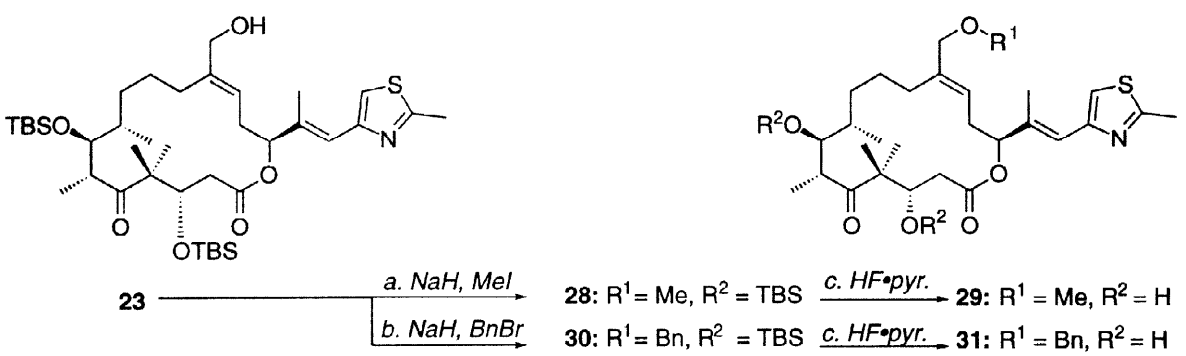
Sharpless[13] [(+)-diethyl-L-tartrate, Ti(^{i}OPr)$_4$, *t*-BuOOH], allylic alcohol **23** was readily converted to 26-hydroxyepothilone B (**6**) in 76% yield and excellent diasteroeselectivity (d.e. >95% as judged by ^{1}H NMR spectroscopy). With these intermediates at hand, a plethora of 26-substituted epothilones came within reach.

Reaction of allylic alcohol **24** with either simple acid anhydrides (e.g. acetic anhydride) or acid chlorides (e.g. pivaloyl chloride or benzoyl chloride) provided the corresponding esters in high yield (**25**, 85%; **26**, 93%; **27**; 90%, **Scheme 4**).



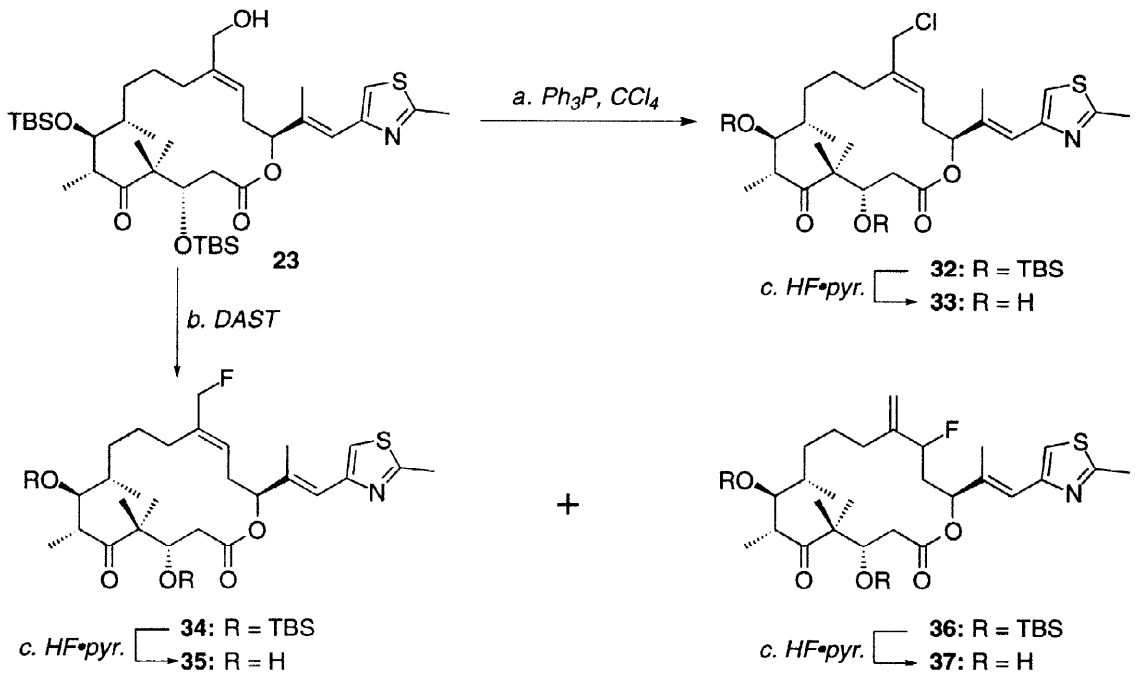
Scheme 4. Synthesis of 26-ester-desoxy epothilones **25-27**. Reagents and conditions: (a) 1.1 equiv. of Ac_2O, 1.1 equiv of 4-DMAP, EtOAc, 0→25 °C, 0.5 h, 85 %; (b) 3.0 equiv. of pivaloyl chloride, 4.0 equiv. of Et_3N, 0.1 equiv. of 4-DMAP, CH_2Cl_2, 0 °C, 0.5 h, 93% ; (c) 3.0 equiv. of benzoyl chloride, 4.0 equiv. of Et_3N, 0.1 equiv. of 4-DMAP, CH_2Cl_2, 0 °C, 0.5 h, 90%.

To further investigate the effects of steric bulk at C26 on biological activity, we next targeted the methyl ether **29** and the bulkier benzyl ether **31** (**Scheme 5**). Formation of the sodium anion of alcohol **23** was achieved using sodium hydride in DMF or THF. Quenching with either methyl iodide or benzyl bromide provided the intermediate ethers **28** and **30**, respectively, which were deprotected under our standard conditions (HF•pyr./THF), to afford **29** and **31** in high yield (89 and 87%).



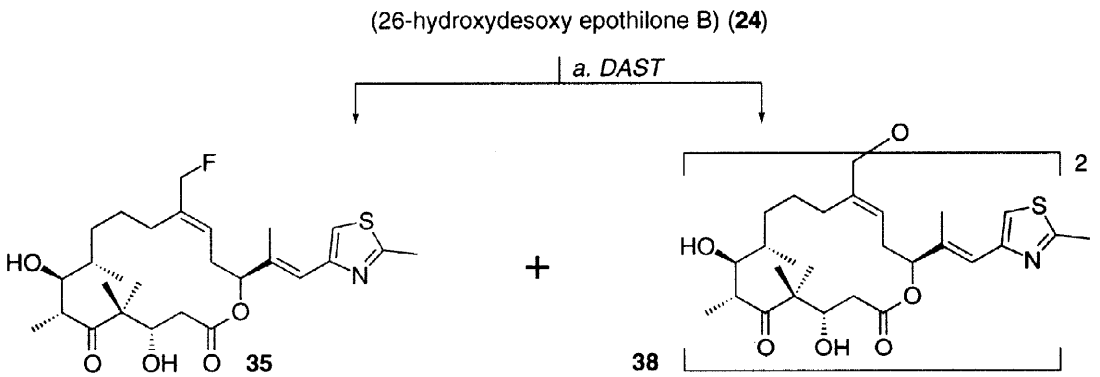
Scheme 5. Synthesis of 26-ether-desoxy epothilones **29** and **31**. Reagents and conditions: (a) 1.1 equiv. of NaH, 20 equiv. of MeI, DMF, 0 °C, 1 h, 65%; (b) 1.1 equiv. of NaH, 20 equiv. of BnBr, THF, 0 → 25 °C, 1 h, 40%; (c) 30% HF•pyr. (by volume) in THF, 0 → 25 °C, 24 h, 89% of **29**, 87% of **31**.

We were also interested in the effect of introducing halogen substituents at C26, as these groups, and fluorine in particular, frequently have a profound effect on the biological activity of a compound. Refluxing **23** in carbon tetrachloride with triphenylphosphine (**Scheme 6**) gave **32** (85%), with ensuing silyl deprotection (HF•pyr.) yielding allylic chloride **33** (74%). Alternatively, upon exposure to DAST in CH_2Cl_2 at –78 °C, allylic alcohol **23** afforded a 3:1 mixture of fluorides **34** and **36** (the latter arising from S_N2' attack).



Scheme 6. Synthesis of 26-chloro- and 26-fluoro-epothilones **33**, **35** and **37**. Reagents and conditions: (a) 4.0 equiv. of Ph_3P, CCl_4, 75 °C, 24 h, 85%; (b) 1.2 equiv. of DAST, CH_2Cl_2, –78 °C, 55% of **34**, 21% of **36**; (c) 30% HF•pyr. (by volume) in THF, 0 → 25 °C, 24 h, 86% of **33**, 74% of **35**, 84% of **37**. DAST = diethylamino sulfurtrifluoride.

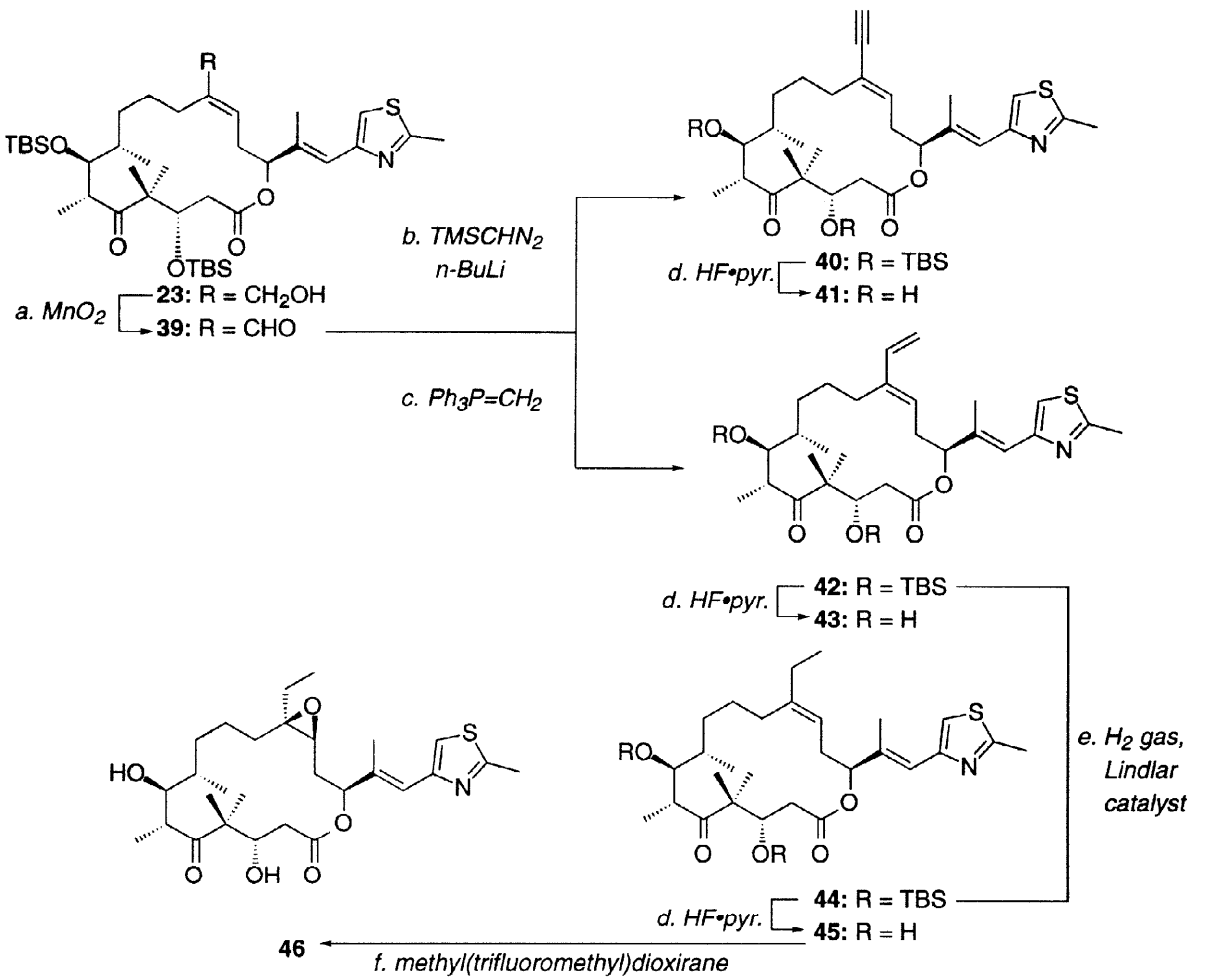
As previously, deprotection of these products gave a high yield of allylic fluorides **35** and **37** (74 and 84%, respectively). Interestingly, when the triol **24** was exposed to the same fluorination conditions (**Scheme 7**),



Scheme 7. Synthesis of epothilone analogs **35** and **38**. Reagents and conditions: (a) 1.2 equiv. of DAST, CH_2Cl_2, –78 °C, 65% of **35**, 12% of **38**. DAST = diethylamino sulfurtrifluoride.

35 was the major product obtained (65%), with no evidence for the formation of the undesired S_N2' derived component. One can perhaps postulate that the silyl ethers of **23** force the macrocycle to adopt a conformation which is more predisposed towards this mode of nucleophilic attack. Another unanticipated observation from this reaction was the isolation of a small amount of dimeric compound **38** (12%), presumably arising from attack of allylic alcohol **24** upon the activated hydroxyl group at a faster rate than the fluoride ion.

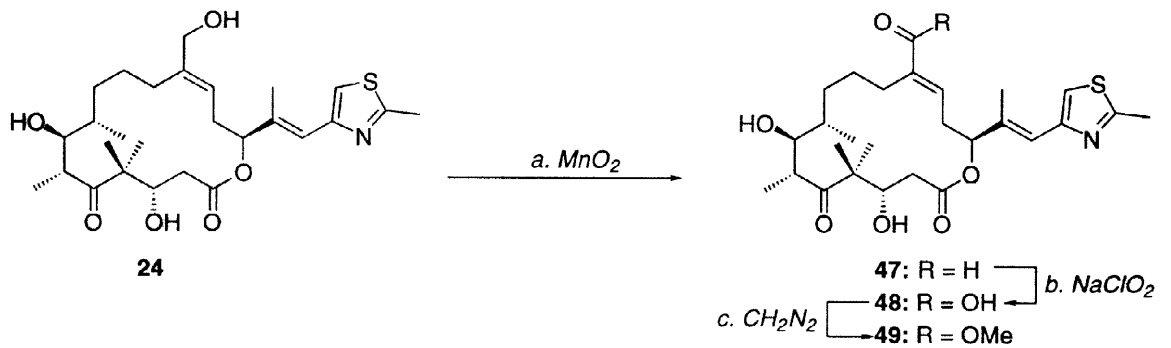
To probe the tolerance of the epothilone binding site for both saturated and unsaturated alkyl substituents, we decided to prepare compounds with ethyl, ethylene and acetylene appendages at C12. Towards this end, allylic alcohol **23** was exposed to excess MnO_2 in ether to give enal **39** (85%, **Scheme 8**).



Scheme 8. Synthesis of C26-substituted epothilones **41**, **43**, **45** and **46**. Reagents and conditions: (a) 5.0 equiv. of MnO_2, Et_2O, 25 °C, 3 h, 85%; (b) 1.5 equiv. trimethylsilyl diazomethane, then 1.3 equiv. *n*-BuLi (1.5 M in hexanes), THF, −78 → 0 °C, 1h, 75%; (c) 2.0 equiv. of $Ph_3P^+CH_3Br^-$, 2.0 equiv. of LiHMDS (1.0 M in THF, THF, 0 °C, 0.5 h, 85%; (d) 30% HF•pyr. (by volume) in THF, 0 → 25 °C, 24 h, 91% of **41**, 85% of **43**, 75% of **45**; (e) H_2 gas, Lindlar catalyst, EtOAc, 25 °C, 15 min, 50%; (f) methyl(trifluoromethyl)dioxirane, MeCN, 0 °C, 58% of **46** and 19% of corresponding C12,13 diastereoisomer **46'**.

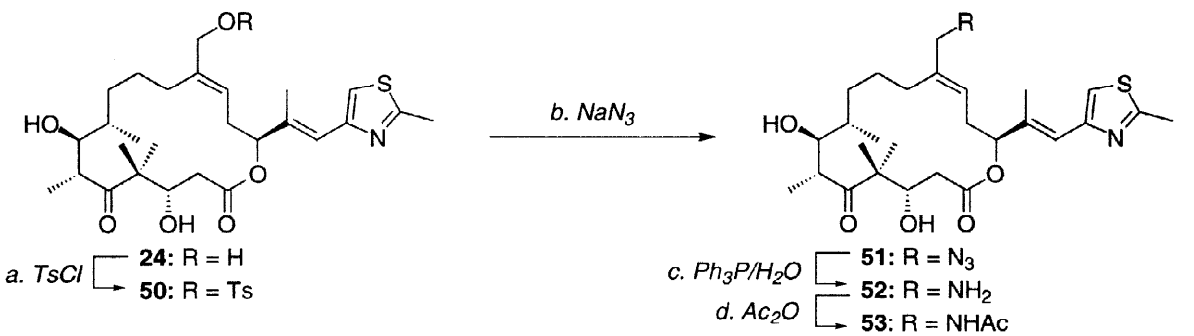
Subsequent Wittig methylenation using the ylid derived from methyl triphenylphosphonium bromide and LiHMDS gave conjugated diene **42** (85% yield). Alternatively, treatment of aldehyde **39** with the anion derived from trimethylsilyl diazomethane[14] gave acetylene **40** in good yield (75%). These unsaturated analogs (**40** and **42**) were then desilylated as before to afford **41** (91%) and **43** (85%), respectively. Careful hydrogenation of **42** in the presence of Lindlar catalyst provided **44**, albeit in moderate yield (50%). Following desilylation of **44** (75%), diol **45** was epoxidised using methyl(trifluoromethyl)dioxirane in MeCN[15] to give epoxide **46** along with its C12,C13 diastereoisomer in 75% total yield (*ca.* 2:1 ratio in favor of **46**). The major diastereoisomer from this reaction (**46**) gave crystals suitable for X-ray analysis and allowed conformation of the facial selectivity of the epoxidation process (see ORTEP drawing, **Figure 3**).

In addition to the esters described above, we also wished to investigate the activities of the reverse esters (i.e. α,β-unsaturated ester systems). Oxidation of allylic alcohol **24** to enal **47** was efficiently achieved in a similar fashion as for **23** → **39**, by reaction with MnO_2 in ether (**Scheme 9**).



Scheme 9. Synthesis of analogs **47-49**. Reagents and conditions: (a) 5.0 equiv. of MnO_2, Et_2O, 25 °C, 3 h, 85%; (b) 5.0 equiv. of $NaClO_2$, 70 equiv. of 2-methyl-2-butene, 2.5 equiv. of NaH_2PO_4, *t*-BuOH:H_2O (5:1), 0 °C, 0.5 h, 98%; (c) CH_2N_2, Et_2O, 0 °C, 80%.

Further oxidation by $NaClO_2$ provided carboxylic acid derivative **48** which was esterified by exposure to diazomethane in ether to give methyl ester **49**. The preparation and testing of an amide derivative was also considered important, and by selective tosylation (70%) of **24** (**Scheme 10**), followed by displacement of the

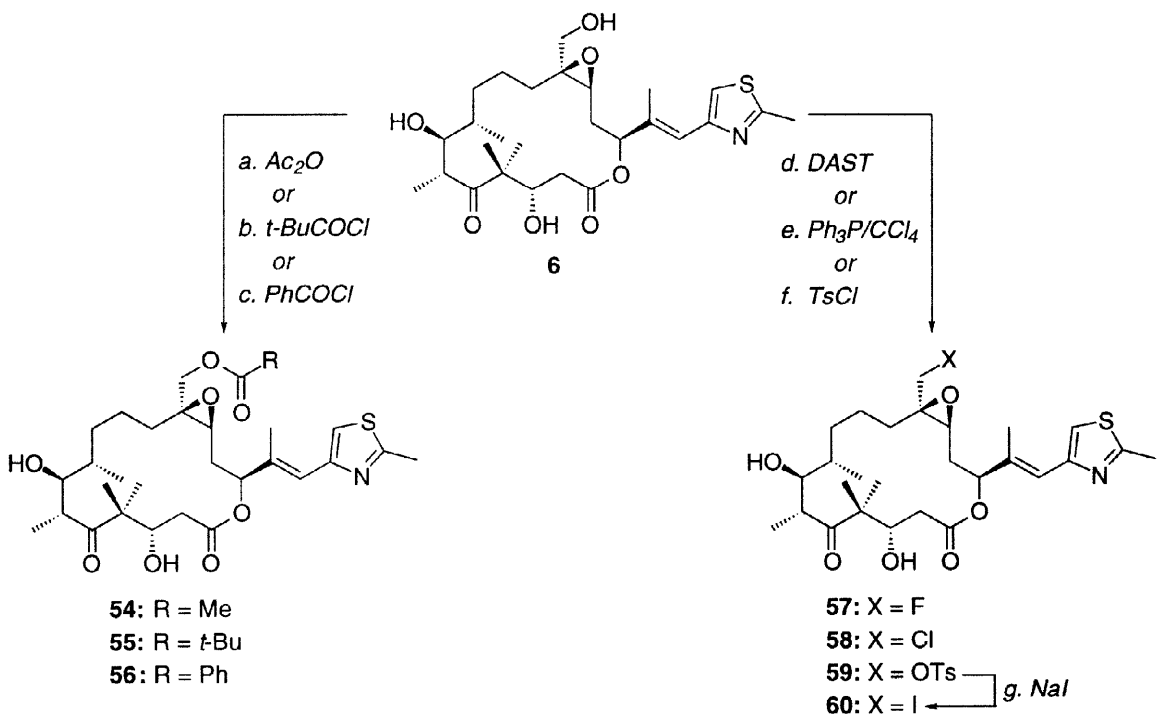


Scheme 10. Synthesis of analogs **50-53**. Reagents and conditions: (a) 3.0 equiv. of TsCl, 2.0 equiv. of Et_3N, 0.1 equiv. of 4-DMAP, CH_2Cl_2, 0 °C, 1 h, 70%; (b) 3.0 equiv. of NaN_3, DMF, 25 °C, 10 h, 75%; (c) 2.0 equiv. of Ph_3P, 3.0 equiv. of H_2O, THF, 60 °C, 8 h, 70%; (d) 1.1 equiv. of Ac_2O, CH_2Cl_2, 10 min, 98%.

resulting tosylate **50** with sodium azide in DMF and reduction of the resulting azide **51** with triphenylphosphine in the presence of water, we were able to isolate the highly sensitive amine **52** (70% yield). This was immediately exposed to acetic anhydride in CH_2Cl_2 to provide the acetamide **53** (98%).

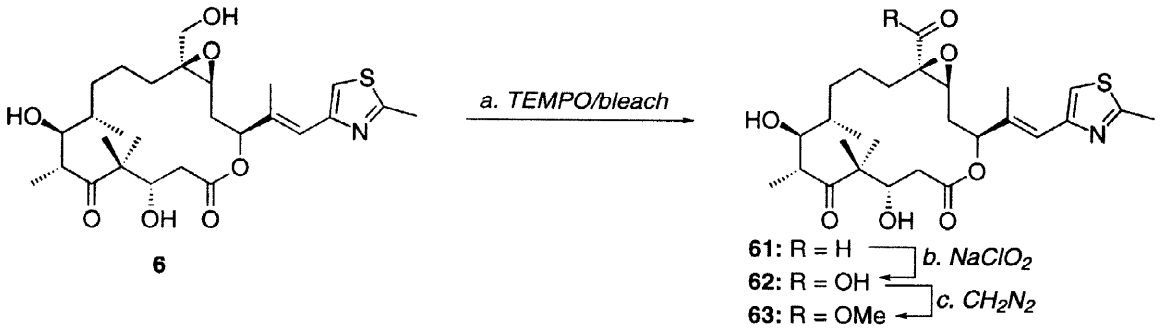
The epothilone analogs so far described (with the exception of **46**) lacked the C12,13 oxirane functionality, and even though the latter could conceivably be introduced by non-selective epoxidation (as in the case of **46**), we sought to define procedures for the controlled construction of the corresponding epoxides. Epoxide **6** served well as a central intermediate for the synthesis of numerous epothilone analogs as shown in **Schemes 11** and **12**.

Thus, selective esterification of **6** with Ac_2O, *t*-BuCOCl, or PhCOCl under standard conditions (see **Scheme 11**) proceeded smoothly to afford compounds **54** (90%), **55** (90%) and **56** (85%), respectively. We were pleased to find that selective halogenation of epoxy triol **6** proved relatively straightforward. The reaction of **6** with DAST proved surprisingly efficient, affording epoxy fluoride **57** (65%) as long colorless needles, which were subjected to single crystal X-ray confirming its absolute stereochemistry (see ORTEP drawing in **Figure 3**). The corresponding chloride **58** was also efficiently prepared from the same intermediate by the use of triphenylphosphine in CCl_4:CH_3CN (3:1, 85% yield). Tosylation of the primary alcohol of **6** provided tosylate **59** in 85% yield and was followed by displacement with sodium iodide in acetone to afford epoxy iodide **60** in 85% yield.



Scheme 11. Synthesis of analogs **54-60**. Reagents and conditions: (a) 1.1 equiv. of Ac_2O, 1.0 equiv. of 4-DMAP, EtOAc, 0 °C, 0.5 h, 90%; (b) 3.0 equiv. of pivaloyl chloride, 4.0 equiv. of Et_3N, 0.05 equiv. of 4-DMAP, CH_2Cl_2, 0 °C, 0.5 h, 90%; (c) 1.2 equiv. of benzoyl chloride, 4.0 equiv. of Et_3N, 0.05 equiv. of 4-DMAP, CH_2Cl_2, 0 °C, 0.5 h, 85%; (d) 1.1 equiv. of DAST, CH_2Cl_2, −78 °C, 10 min, 65%; (e) 4.0 equiv. of Ph_3P, CCl_4:CH_3CN (3:1), 25 °C, 1 h, 85%; (f) 3.0 equiv. of TsCl, 2.0 equiv. of Et_3N, 0.1 equiv of 4-DMAP, CH_2Cl_2, 0 °C, 1 h 85%; (g) 3.0 equiv. of NaI, $CH_3C(O)CH_3$, 55 °C, 2 h, 90%.

Our next important goal was the chemoselective oxidation of the primary alcohol of **6** to give aldehyde **61 (Scheme 12)** which would, hopefully, by further oxidation, permit access to the corresponding carboxylic



Scheme 12. Synthesis of analogs **61-63**. Reagents and conditions: (a) 5.0 equiv. of TEMPO (0.008 M solution in CH_2Cl_2), 1.0 equiv. of NaOCl (0.035 M solution in 5% aqueous $NaHCO_3$), 0.1 equiv. of KBr (0.2 M aqueous solution), CH_2Cl_2, 0 °C, 0.5 h, 90%; (b) 5.0 equiv. of $NaClO_2$, 70 equiv. of 2-methyl-2-butene, 2.5 equiv. of NaH_2PO_4, *t*-BuOH:H_2O (5:1), 0 °C, 0.5 h, 95%; (c) CH_2N_2, EtOAc:Et_20 (2:1), 0 °C, 2 h, 90%.

acid and esters thereof. Initial attempts using TPAP/NMO[16] proved disappointing, with the majority of material being lost to heteroatom oxidation in the thiazole ring. A much more satisfactory outcome was obtained by employing the stabilized radical source TEMPO with bleach as the stoichiometric re-oxidant.[17] This remarkably mild procedure delivered aldehyde **61** in 90% yield.

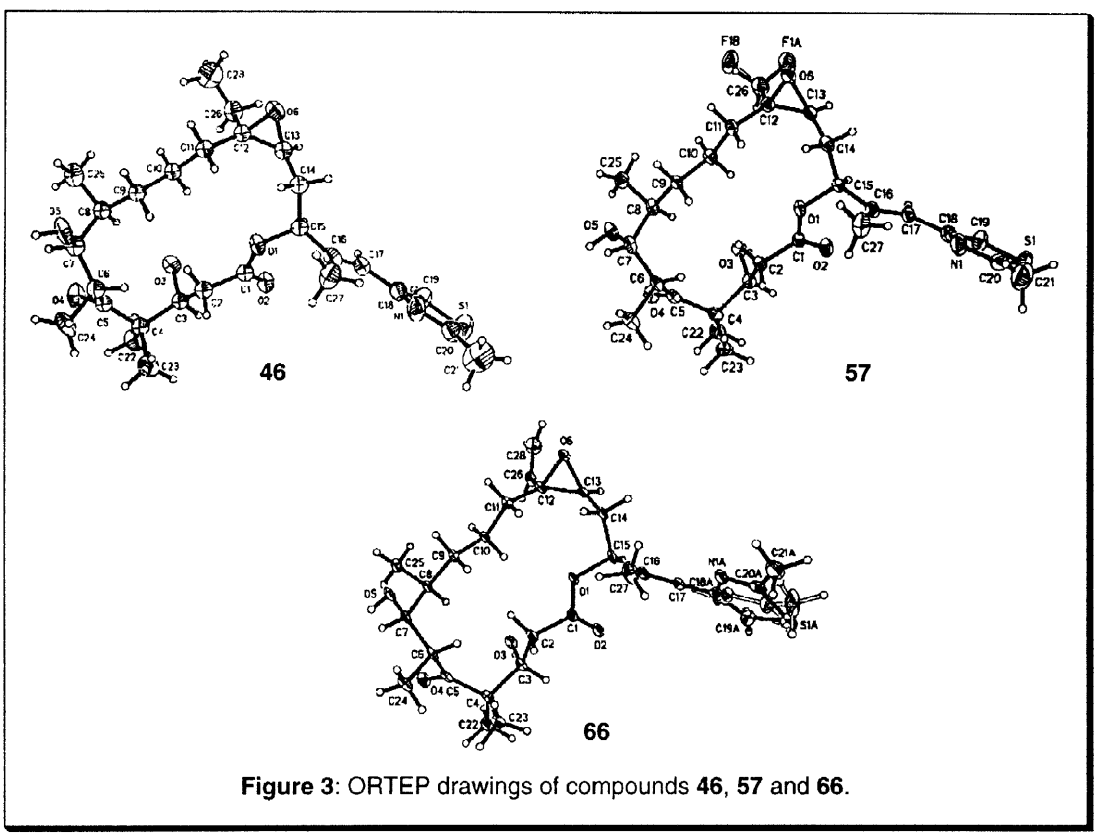
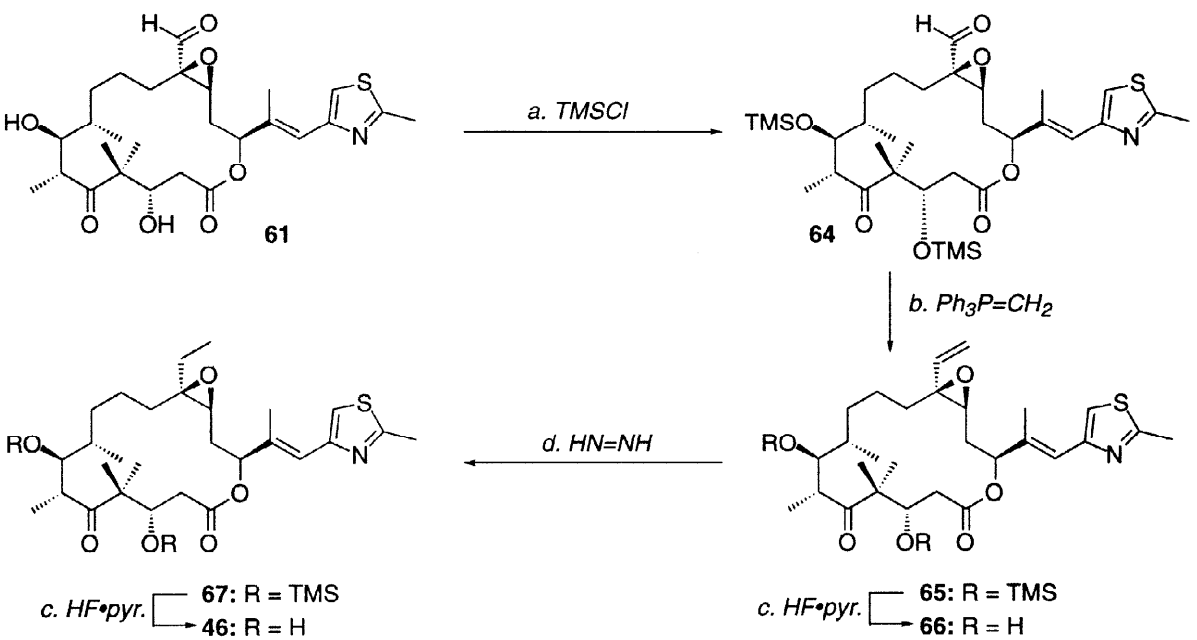


Figure 3: ORTEP drawings of compounds **46**, **57** and **66**.

Further oxidation employing sodium chlorite then provided the highly sensitive carboxylic acid **62** (95%), which was subsequently esterified with diazomethane giving methyl ester **63** (90%). In the light of these results, we reasoned that we should also be able to access the allylic epoxide **66** (**Scheme 13**). Protection of the C3 and C7 hydroxyls of **61** as TMS ethers gave **64** (90%), and subsequent Wittig methylenation as described previously delivered **65** in good yield (75%). Finally, desilylation using buffered HF•pyr. afforded **66** in excellent yield (97%). The latter compound proved highly crystalline and once more we were able to confirm its structure by X-ray crystallographic analysis (ORTEP drawing, **Figure 3**).

As discussed above, we had prepared the ethyl analog **46** *via* epoxidation of the corresponding olefin system **45** (**Scheme 8**), albeit with modest selectivity. If selective hydrogenation of the terminal olefin of **65** (**Scheme 13**) would prove to be feasible, we could secure a new route to this compound. Initial results utilizing palladium catalysts were disappointing, with epoxide ring-opened products predominating. However, by employing diimide, prepared *in situ* from hydrazine and hydrogen peroxide in ethanol,[18] we were able to convert **65** to **67** in 90% yield, and, thence, to **46** by standard desilylation (97% yield).



Scheme 13. Synthesis of epothilones **66** and **46**. Reagents and conditions: (a) 3.5 equiv. of TMSCl, 5.5 equiv. of Et_3N, CH_2Cl_2, 0 → 25 °C, 12 h, 90%; (b) 2.0 equiv. of $Ph_3P^+CH_3Br^-$, 2.0 equiv. of NaHMDS, THF, 0 → 25 °C, 75%; (c) HF•pyr. in pyridine, THF, 0 → 25 °C, 3 h, 97% of **66**, 75% of **46**; (d) 25 equiv. of H_2NNH_2, 16 equiv. of 30% H_2O_2, EtOH, 90%.

CONCLUSION

In this article we described synthetic studies culminating in the chemical synthesis of a variety of C26-substituted epothilone analogs, several of which have already demonstrated high levels of biological activity.[4a,7] The synthetic strategies developed in this program may provide facile entries into a new generation of designed epothilones for further chemical biology studies.

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EXPERIMENTAL SECTION

General Techniques. For a detailed description of general experimental techniques employed see ref. 3f.

Compound 9. Tritylation of Alcohol 8. Alcohol **8** (80.0 g, 0.2 mol) was dissolved in DMF (2 L, 0.1 M) and 4-DMAP (35.0 g, 0.29 mol, 1.4 equiv.) and trityl chloride (68 g, 0.24 mol, 1.2 equiv.) were added. The reaction mixture was stirred at 70 °C for 1 h, cooled to room temperature and the solvent was removed under reduced pressure. The resulting residue was filtered through a pad of silica gel to give the protected alcohol **9** as a yellowish oil (133 g, 99%): R_f = 0.68 (silica gel, 60% ether in hexanes); $[\alpha]^{22}_D$ +9.3 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 2928, 2855, 1490, 1447, 1253, 1077, 836, 775, 703 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.49-7.30 (m, 5 H, Ph), 7.28-7.10 (m, 10 H, Ph), 6.85 (s, 1 H, SCH=C), 6.47 (s, 1 H, C*H*=CCH_3), 5.80-5.60 (m, 2 H, C*H*=CH_2, CH_2C*H*=CCH_2OTr), 4.86 (dd, *J* = 17.1, 1.6 Hz, 1 H, CH=CH_2), 4.80 (dd, *J* = 17.1, 1.4 Hz, 1 H, CH=CH_2), 4.11 (dd, *J* = 6.5, 6.3 Hz, 1 H, CHOSi), 3.47 (s, 2 H, CH_2OTr), 2.85-2.70 (m, 2 H, CH_2CH=CH_2), 2.68 (s, 3 H, N=C(S)CH_3), 2.48-2.15 (m, 2 H, CH_2CHOSi), 1.99 (s, 3 H, CH=CCH_3), 0.89 (s, 9 H, $SiC(CH_3)_3$), 0.01 (s, 3 H, $Si(CH_3)_2$), 0.00 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.2, 153.1, 145.9, 144.2, 142.3, 135.5, 128.6, 127.9, 127.8, 126.7, 123.6, 118.7, 115.1, 115.0, 86.4, 78.5, 67.1, 34.9, 33.0, 25.8, 19.1, 18.2, 13.9, –4.7, –4.9; FAB HRMS (NBA/CsI) *m/e* 768.2286, M + Cs^+ calcd for $C_{40}H_{49}NO_2SSi$ 768.2308.

Primary Alcohol 10. Selective Hydroboration of Olefinic Compound 9. Compound **9** (1.1 g, 2.91 mmol) was dissolved in THF (3.0 mL, 1.0 M) and the solution was cooled to 0 °C. 9-BBN (7.0 mL, 0.5 M solution in THF, 3.5 mmol, 1.2 equiv.) was added, and the reaction mixture was stirred for 2 h at 0 °C. Aqueous NaOH (7.0 mL, 3 N solution, 21.0 mmol, 7.2 equiv.) was added with stirring, followed by H_2O_2 (2.4 mL, 30%, aqueous solution). Stirring was continued for 0.5 h at 0 °C, after which time the reaction mixture was diluted with ether (30 mL). The organic solution was separated and the aqueous phase was extracted with ether (2 x 15 mL). The combined organic layer was washed with brine (2 x 5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. Flash column chromatography (silica gel, 50 → 80% ether in hexanes) furnished primary alcohol **10** (1.3 g, 94%): R_f = 0.19 (silica gel, 60% ether in hexanes); $[\alpha]^{22}_D$ +0.4 (*c* 2.0, $CHCl_3$); IR (thin film) ν_{max} 3385, 2927, 2855, 1490, 1448, 1253, 1075, 836, 775, 707 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57-7.45 (m, 5 H, Ph), 7.30-7.20 (m, 10 H, Ph), 6.89 (s, 1 H, SCH=C), 6.50 (s, 1 H, C*H*=CCH_3), 5.67 (dd, *J* = 7.2, 7.1 Hz, 1 H, C=C*H*CH_2), 4.23 (dd, *J* = 6.5, 6.0 Hz, 1 H, CHOSi), 3.51-3.48 (m, 2 H, CH_2OH), 3.50 (s,

2 H, CH_2OTr), 2.69 (s, 3 H, N=C(S)CH_3), 2.48-2.33 (m, 2 H, CH_2CHOSi), 2.14 (dd, J = 8.0, 7.4 Hz, 2 H, $CH_2CH_2CH_2OH$), 2.04 (s, 3 H, CH=CCH_3), 1.59-1.50 (m, 2 H, CH_2CH_2OH), 0.92 (s, 9 H, $SiC(CH_3)_3$), 0.10 (s, 3 H, $Si(CH_3)_2$), 0.05 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.3, 153.9, 145.1, 143.4, 138.3, 129.5, 128.8, 128.7, 128.1, 124.1, 119.5, 116.1, 87.5, 79.4, 68.2, 63.2, 36.1, 32.1, 28.0, 25.7, 20.0, 19.1, 15.1, –3.7, –3.9; FAB HRMS (NBA/CsI) *m/e* 786.2390, M + Cs^+ calcd for $C_{40}H_{51}NO_3SSi$ 786.2413.

Iodide 11. A solution of alcohol **10** (129.5 g, 0.2 mmol) in ether: MeCN (1.2 L, 3:1, 0.1 M) was cooled to 0 °C. Imidazole (67.5 g, 1.0 mol, 5.0 equiv.), Ph_3P (130.0 g, 0.5 mol, 2.5 equiv.), and iodine (131.0 g, 0.51 mol, 2.6 equiv.) were sequentially added and the mixture was stirred for 0.5 h at 0 °C. A saturated aqueous solution of $Na_2S_2O_3$ (500 mL) was added, followed by the addition of ether (1 L). The organic phase was washed with brine (500 mL), dried ($MgSO_4$), and the solvents were removed under vacuum. Flash column chromatography (silica gel, 5% ether in hexanes) gave pure iodide **11** (136.0 g, 90%) as a colorless oil: R_f = 0.75 (silica gel, 60% ether in hexanes); $[\alpha]^{22}_D$ +10.4 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 2926, 2854, 1470, 1447, 1074, 835, 775, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44-7.42 (m, 5 H, Ph), 7.29-7.21 (m, 10 H, Ph), 6.89 (s, 1 H, SCH=C), 6.49 (s, 1 H, C*H*=CCH$_3$), 5.60 (dd, J = 7.3, 7.1 Hz, 1 H, CH_2C=C*H*), 4.18 (dd, J = 6.5, 6.3 Hz, 1 H, CHOSi), 3.46 (s, 2 H, CH_2OTr), 3.05 (dd, J = 7.1, 7.0 Hz, 2 H, CH_2I), 2.69 (s, 3 H, N=C(S)CH_3), 2.48-2.25 (m, 2 H, CH_2CHOSi), 2.17-2.09 (m, 1 H, $CH_2CH_2CH_2I$), 2.03 (s, 3 H, CH=CCH_3), 1.80-1.74 (m, 2 H, $CH_2CH_2CH_2I$), 1.40-1.25 (m, 2 H, CH_2CH_2I), 0.89 (s, 9 H, $SiC(CH_3)_3$), 0.07 (s, 3 H, $Si(CH_3)_2$), 0.02 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.3, 153.9, 145.0, 143.5, 137.2, 129.5, 128.6, 127.7, 125.4, 119.7, 116.1, 87.5, 79.3, 68.4, 36.1, 33.2, 30.4, 26.7, 20.1, 19.1, 14.9, 7.6, –3.7, –3.9; FAB HRMS (NBA/CsI) *m/e* 896.1462, M + Cs^+ calcd for $C_{40}H_{50}INO_2SSi$ 896.1431.

Hydrazone 13. Alkylation of SAMP Hydrazone 12 with Iodide 11. SAMP hydrazone **12** (337 mg, 0.2 mmol, 1.3 equiv.) in THF (2.5 mL), was added to a freshly prepared solution of LDA at 0 °C [diisopropylamine (277 mL, 0.20 mmol, 1.3 equiv.) was added to *n*-BuLi (1.39 mL, 1.6 M solution in hexanes, 0.20 mmol, 1.3 equiv.) in 2.5 mL of THF at 0 °C] at 0°C. After stirring at that temperature for 14 h, the resulting yellow solution was cooled to –100 °C, and a solution of iodide **11** (0.5 g, 0.99 mmol, 1.0 equiv.) in THF (3 mL) was added dropwise over a period of 5 min. The mixture was allowed to warm to –20 °C over 10 h, and then poured into saturated aqueous NH_4Cl solution (5 mL) and extracted with ether (3 x 25 mL). The combined organic extracts were dried ($MgSO_4$), filtered and evaporated. Purification by flash column chromatography on silica gel (20 → 40% ether in hexanes) provided hydrazone **13** (380 mg, 94%, de > 98% by ^1H NMR) as a yellow oil: R_f = 0.44 (silica gel, 60% ether in hexanes); $[\alpha]^{22}_D$ –15.1 (*c* 1.1, $CHCl_3$); IR (thin film) ν_{max} 2953, 2874, 1727, 1598, 1491, 1448, 1374, 1235, 1078, 836, 775, 706, 632 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44-7.40 (m, 5 H, Ph), 7.27-7.18 (m, 10 H, Ph), 6.89 (s, 1 H, SCH=C), 6.48 (s, 1 H, C*H*=CCH$_3$), 6.39 (d, J = 6.5 Hz, 1 H, CNH), 5.60 (dd, J = 6.7, 6.7 Hz, 1 H, CH_2C=C*H*), 4.16 (dd, J = 6.9, 5.7 Hz, 1 H, CHOSi), 3.53 (dd, J = 9.2, 3.8 Hz, 1 H, CH_2OCH_3), 3.44 (s, 2 H, CH_2OTr), 3.39 (dd, J = 9.2, 7.0 Hz, 1 H, CH_2OCH_3), 3.35 (s, 3 H, CH_2OCH_3), 3.34-3.27 (m, 2 H, CH_2N), 2.69 (s, 3 H, N=C(S)CH_3), 2.57-2.53 (m, 1 H), 2.40-2.27 (m, 3 H), 2.25-2.15 (m, 1 H), 2.03 (s, 3 H, CH=CCH_3), 1.79-1.72 (m, 1 H), 1.95-1.75 (m, 4 H), 1.35-1.20 (m, 4 H), 0.98 (d, J = 6.9 Hz, 3 H, CHCH_3), 0.89 (s, 9 H, $SiC(CH_3)_3$), 0.07 (s, 3 H, $Si(CH_3)_2$), 0.02 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.2, 154.1, 145.2, 143.3, 138.8, 129.5,

128.6, 127.7, 123.4, 119.7, 116.1, 87.4, 79.5, 75.7, 68.2, 64.4, 60.1, 51.3, 37.9, 36.5, 36.0, 35.9, 29.7, 27.5, 26.8, 23.0, 20.1, 19.7, 19.1, 14.9, –3.7, –3.9; FAB HRMS (NBA/CsI) *m/e* 938.3760, M + Cs^+ calcd for $C_{49}H_{67}N_3O_3SSi$ 938.3727.

Nitrile 14. Monoperoxyphthalic acid magnesium salt (MMPP•$6H_2O$, 76 g, 0.15 mol, 2.5 equiv.) was added in several portions to a rapidly stirred solution of hydrazone **13** (39.6 g, 49 mmol, 1.0 equiv.) in a mixture of MeOH, pH 7 phosphate buffer and THF (1:1:0.6, 800 mL) at 0 °C. The mixture was stirred at 0 °C until the reaction was complete by TLC (*ca.* 1 h). The resulting suspension was placed in a separating funnel along with ether (600 mL) and saturated aqueous $NaHCO_3$ solution (500 mL). The organic layer was separated and the aqueous phase was extracted with ether (500 mL). The combined organic solution was washed with water (250 mL) and brine (250 mL), dried ($MgSO_4$) and concentrated. Flash column chromatography (silica gel, 40% ether in hexanes) afforded nitrile **14** (31.1g, 91%) as a colorless oil: R_f = 0.49 (silica gel, 40% ether in hexanes); $[\alpha]^{22}_D$ +12.5 (*c* 2, $CHCl_3$); IR (thin film) ν_{max} 2929, 2874, 1491, 1448, 1253, 1077, 835, 775, 706 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45-7.40 (m, 5 H, Ph), 7.29-7.19 (m, 10 H, Ph), 6.91 (s, 1 H, SCH=C), 6.51 (s, 1 H, C*H*=CCH_3), 5.63 (dd, *J* = 7.2, 7.2 Hz, 1 H, CH_2C=C*H*), 4.19 (dd, *J* = 6.8, 5.6 Hz, 1 H, CHOSi), 3.47 (s, 2 H, CH_2OTr), 2.70 (s, 3 H, N=C(S)CH_3), 2.48-2.42 (m, 1 H), 2.41-2.34 (m, 1 H), 2.33-2.28 (m, 1 H), 2.12-2.06 (m, 2 H), 2.05 (s, 3 H, CH=CC*H*$_3$), 1.55-1.45 (m, 1 H), 1.45-1.37 (m, 2 H), 1.35-1.29 (m, 1 H), 1.21 (d, *J* = 7.0 Hz, 3 H, CHC*H*$_3$), 0.91 (s, 9 H, $SiC(CH_3)_3$), 0.09 (s, 3 H, $Si(CH_3)_2$), 0.03 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 165.2, 153.9, 145.2, 143.1, 137.9, 129.5, 128.6, 127.7, 124.7, 124.3, 123.7, 119.7, 116.1, 87.4, 79.4, 68.2, 36.1, 34.7, 29.4, 26.8, 26.5, 26.2, 20.1, 19.1, 18.7, 14.9, –3.7, –3.9; FAB HRMS (NBA/NaI) *m/e* 713.3599, M + Na^+ calcd for $C_{43}H_{54}N_2O_2SSi$ 713.3573.

Aldehyde 15. Nitrile **14** (32.9 g, 47.6 mmol) was dissolved in toluene (1 L) and cooled to –78 °C. DIBAL (143 mL, 1.0 M solution in toluene, 143 mmol, 3.0 equiv.) was added dropwise at –78 °C and the reaction mixture was stirred at that temperature until its completion was verified by TLC (*ca.* 1 h). Methanol (150 mL) and aqueous HCl (150 mL, 1.0 N solution) were sequentially added and the resulting mixture was brought up to 0 °C and stirred at that temperature for 30 min. Ether (500 mL) and water (200 mL) were added, and the organic layer was separated. The aqueous phase was extracted with ether (2 x 500 mL) and the combined organic solution was washed with brine (500 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. Flash column chromatography (silica gel, 30% ether in hexanes) furnished pure aldehyde **15** (32.2 g, 97%): R_f = 0.46 (silica gel, 30% ether in hexanes); $[\alpha]^{22}_D$ +10.3 (*c* 3.2, $CHCl_3$); IR (thin film) ν_{max} 2928, 2874, 1724, 1449, 1254, 1068, 837, 701 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.51 (d, *J* = 1.8 Hz, 1 H, CHO), 7.45-7.42 (m, 5 H, Ph), 7.28-7.19 (m, 10 H, Ph), 6.90 (s, 1 H, SCH=C), 6.49 (s, 1 H, C*H*=CCH_3), 5.60 (dd, *J* = 7.0, 7.0 Hz, 1 H, CH_2C=C*H*), 4.17 (dd, *J* = 6.5, 6.0 Hz, 1 H, CHOSi), 3.46 (s, 2 H, CH_2OTr), 2.69 (s, 3 H, N=C(S)CH_3), 2.40-2.33 (m, 1 H), 2.32-2.27 (m, 1 H), 2.25-2.16 (m, 1 H), 2.08-2.04 (m, 2 H), 2.03 (s, 3 H, CH=CC*H*$_3$), 1.66-1.55 (m, 2 H), 1.30-1.19 (m, 2 H), 0.98 (d, *J* = 7.0 Hz, 3 H, CHC*H*$_3$), 0.90 (s, 9 H, $SiC(CH_3)_3$), 0.08 (s, 3 H, $Si(CH_3)_2$), 0.02 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 205.9, 165.2, 153.9, 145.1, 143.2, 138.3, 129.5, 128.6, 127.7, 124.3, 119.6, 116.1, 87.4, 79.4, 68.2, 47.1, 36.0, 31.2, 29.4, 26.7, 26.5, 20.1, 19.1, 14.9, 14.0, –3.7, –3.9; FAB HRMS (NBA/CsI) *m/e* 826.2753, M + Cs^+ calcd for $C_{43}H_{55}NO_3SSi$ 826.2726.

tris(Silylethers) 17 and 17′. Aldol Reaction of Ketone 16 with Aldehyde 15. A solution of ketone **16** (270 mg, 0.67 mmol, 1.2 equiv.) in THF (1.5 mL) was added dropwise to a freshly prepared solution of LDA [diisopropylamine (94 mL, 0.67 mmol) was added to *n*-BuLi (0.43 mL, 1.6 M solution in hexanes, 0.67 mmol) in 2.5 mL of THF at 0 °C] in THF (2.5 mL) at –78 °C. After stirring for 15 min at –78 °C, the solution was allowed to warm to –60 °C over a period of 1 h. The reaction mixture was cooled to –78 °C, and a solution of aldehyde **15** (244 mg, 0.56 mmol, 1.0 equiv.) in THF (1.0 mL) was added dropwise. The resulting mixture was stirred for 15 min at –78 °C, and then quenched by dropwise addition of saturated aqueous NH_4Cl solution (2 mL). The aqueous phase was extracted with ether (3 x 5 mL) and the combined organic layer was dried ($MgSO_4$) and concentrated. Purification by flash column chromatography (silica gel, 20% ether in hexanes) provided pure aldol products **17**: and **17′** (85% total yield, *ca.* 3:1 by ^1H NMR). **17**: Colorless oil; R_f = 0.41 (silica gel, 20% ether in hexanes); $[\alpha]^{22}_D$ –19.0 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3503, 2953, 2858, 1683, 1465, 1386, 1254, 1089, 998, 836, 775, 735, 705 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.48-7.41 (m, 5 H, Ph), 7.31-7.19 (m, 10 H, Ph), 6.89 (s, 1 H, SCH=C), 6.52 (s, 1 H, C*H*=CCH_3), 5.61 (dd, *J* = 7.0, 6.9 Hz , 1 H, C=C*H*CH_2), 4.19 (dd, *J* = 6.3, 6.2 Hz, 1 H, CHOSi), 3.91 (dd, *J* = 7.4, 2.6 Hz, 1 H, CHOSi), 3.71-3.65 (m, 1 H, $CH(CH_3)$C*H*OH), 3.67 (ddd, *J* = 9.9, 7.4. 7.4 Hz, 1 H, CH_2OSi), 3.47 (s, 2 H, CH_2OTr), 3.31-3.24 (m, 2 H, CH_2OSi, C(O)C*H*(CH_3)), 2.69 (s, 3 H, N=$C(CH_3)$S), 2.43-2.37 (m, 1 H, C=CHC*H*$_2$CHO), 2.36-2.30 (m, 1 H, C=CHC*H*$_2$CHO), 2.08-2.04 (m, 2 H, C*H*$_2$C(CH_2OTr)=CH), 2.05 (s, 3 H, CH=C(C*H*$_3$)), 1.74-1.63 (m, 2 H), 1.54-1.43 (m, 2 H), 1.40-1.30 (m, 1 H), 1.22 (s, 3 H, $C(CH_3)_2$), 1.09 (s, 3 H, $C(CH_3)_2$), 1.03 (d, *J* = 6.9 Hz, 3 H, CH(C*H*$_3$)), 0.92 (s, 18 H, 2 x $SiC(CH_3)_3$), 0.90 (s, 9 H, $SiC(CH_3)_3$), 0.74 (d, *J* = 6.7 Hz, 3 H, CH(C*H*$_3$)), 0.14 (s, 3 H, $Si(CH_3)_2$), 0.09 (s, 6 H, $Si(CH_3)_2$), 0.05 (s, 6 H, $Si(CH_3)_2$), 0.04 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 222.7, 164.5, 153.5, 144.6, 142.6, 138.4, 128.9, 128.1, 127.8, 126.9, 122.7, 118.9, 115.2, 86.5, 78.7, 74.8, 74.1, 67.3, 60.3, 53.8, 41.2, 37.7, 35.2, 34.9, 32.7, 28.9, 25.9, 25.7, 25.6, 25.3, 22.7, 20.2, 18.9, 18.1, 18.0, 17.9, 15.0, 13.7, 9.7, –4.1, –4.4, –4.9, –5.2, –5.6; FAB HRMS (NBA/CsI) *m/e* 1228.5800, M + Cs^+ calcd for $C_{64}H_{101}NO_6SSi_3$ 1228.5712.

***tetra*(Silylether) 18.** Compound **17** (15.4 g, 14.4 mmol) was dissolved in CH_2Cl_2 (500 mL), cooled to 0 °C and treated with 2,6-lutidine (6.0 mL, 50.0 mmol, 3.5 equiv.) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (6.6 mL, 29.0 mmol, 2.0 equiv.). After stirring for 2 h at 0 °C, the reaction mixture was quenched with aqueous HCl (50 mL, 1.0 N solution) and the aqueous phase was extracted with CH_2Cl_2 (3 x 200 mL). The combined organic solution was washed with brine (250 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 3% ether in hexanes) provided *tetra*(silylether) **18** (16.2 g, 95%) as a colorless oil. R_f = 0.51 (silica gel, 10% ether in hexanes); $[\alpha]^{22}_D$ –13.9 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 2932, 2858, 1694, 1466, 1386, 1254, 1081, 942, 836, 776, 736 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.57-7.48 (m, 5 H, Ph), 7.46-7.19 (m, 10 H, Ph), 6.91 (s, 1 H, SCH=C), 6.52 (s, 1 H, C*H*=CCH_3), 5.59 (dd, *J* = 7.0, 7.0 Hz , 1 H, C=C*H*CH_2), 4.19 (dd, *J* = 6.4, 6.0 Hz, 1 H, CHOSi), 3.88 (dd, *J* = 7.6, 2.5 Hz, 1 H, CHOSi), 3.73 (dd, *J* = 6.8, 2.1 Hz, 1 H, CHOSi), 3.67 (ddd, *J* = 9.7, 4.8, 4.8 Hz, 1 H, CH_2OSi), 3.59 (dt, *J* = 9.7, 7.8 Hz, 1 H, CH_2OSi), 3.47 (d, *J* =11.5 Hz, 1 H, CH_2OTr), 3.45 (d, *J* =11.5 Hz, 1 H, CH_2OTr), 3.11 (dq, *J* = 6.8, 6.8 Hz, 1 H, C(O)C*H*(CH_3)), 2.70 (s, 3 H, N=$C(CH_3)$S), 2.41-2.35 (m, 1 H, C=CHC*H*$_2$CHO), 2.35-2.29 (m, 1 H, C=CHC*H*$_2$CHO), 2.08-2.04 (m, 2 H, C*H*$_2$C(CH_2OTr)=CH), 2.06 (s, 3

H, CH=C(C*H*$_3$)), 1.62-1.56 (m, 1 H), 1.52-1.44 (m, 1 H), 1.36-1.24 (m, 4 H), 1.19 (s, 3 H, C(CH$_3$)$_2$), 1.10-1.05 (m, 1 H), 1.04 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.98 (s, 3 H, C(CH$_3$)$_2$), 0.92 (s, 9 H, SiC(CH$_3$)$_3$), 0.91 (s, 9 H, SiC(CH$_3$)$_3$), 0.89 (s, 9 H, SiC(CH$_3$)$_3$), 0.88 (s, 9 H, SiC(CH$_3$)$_3$), 0.82 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.10 (s, 6 H, Si(CH$_3$)$_2$), 0.07 (s, 3 H, Si(CH$_3$)$_2$), 0.06 (s, 3 H, Si(CH$_3$)$_2$), 0.05 (s, 6 H, Si(CH$_3$)$_2$), 0.04 (s, 6 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, CDCl$_3$) δ 218.7, 164.5, 153.5, 144.5, 142.5, 138.3, 128.8, 127.8, 126.9, 122.9, 118.9, 115.2, 86.4, 78.6, 76.7, 74.0, 67.3, 60.8, 53.5, 44.8, 38.6, 37.9, 34.9, 30.9, 29.1, 26.0, 25.9, 25.7, 25.6, 25.4, 24.2, 19.2, 18.9, 18.2, 18.1, 18.0, 17.9, 17.2, 14.8, 13.7, –3.3, –3.9, –4.1, –4.3, –4.9, –5.2, –5.5, –5.6; FAB HRMS (NBA/CsI) *m/e* 1342.6698, M + Cs$^+$ calcd for $C_{70}H_{115}NO_6SSi_4$ 1342.6577.

Alcohol 19. Selective Removal of the Primary TBS of 18. To a cooled (0 °C) solution of the silyl ether **18** (21.0 g, 17.7 mmol) in THF (175 mL) was added HF•pyr. in pyridine/THF mixture [prepared from a stock solution containing 42 mL HF•pyridine, 114 mL pyridine and 200 mL THF] (256 mL) and the resulting solution allowed to warm to room temperature. After stirring for 3 h, the reaction was diluted with EtOAc and quenched by careful addition of saturated aqueous NaHCO$_3$ solution. The layers were separated and the aqueous phase was extracted with ether (3 x 300 mL). The combined organic extracts were then dried (MgSO$_4$), filtered and concentrated *in vacuo*. Flash chromatography gave the alcohol **19** as a pale yellow oil (14.2 g, 74%): R_f = 0.37 (silica gel, 60% ether in hexanes); $[\alpha]^{22}_D$ –7.6 (*c* 0.5, CHCl$_3$); IR (thin film) ν_{max} 3405, 2932, 2857, 1691, 1465, 1384, 1254, 1084, 988, 836, 774, 734, 705 cm^{-1}; ^{1}H NMR (600 MHz, CDCl$_3$) δ 7.49-7.31 (m, 5 H, Ph), 7.28-7.20 (m, 10 H, Ph), 6.91 (s, 1 H, SCH=C), 6.53 (s, 1 H, C*H*=CCH$_3$), 5.61 (dd, *J* = 7.0, 6.9 Hz, 1 H, C=C*H*CH$_2$), 4.21 (dd, *J* = 6.8, 5.6 Hz, 1 H, CHOSi), 4.06 (dd, *J* = 6.3, 3.9 Hz, 1 H, CHOSi), 3.76 (dd, *J* = 7.2, 2.0 Hz, 1 H, CHOSi), 3.65 (t, *J* = 6.1 Hz, 2 H, C*H*$_2$OH), 3.49 (d, *J* =11.6 Hz, 1 H, CH$_2$OTr), 3.46 (d, *J* =11.6 Hz, 1 H, CH$_2$OTr), 3.11 (dq, *J* = 7.0, 7.0 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.71 (s, 3 H, N=C(CH$_3$)S), 2.44-2.37 (m, 1 H, C=CHC*H*$_2$CHO), 2.35-2.29 (m, 1 H, C=CHC*H*$_2$CHO), 2.08-2.04 (m, 2 H, C*H*$_2$C(CH$_2$OTr)=CH), 2.06 (s, 3 H, CH=C(C*H*$_3$)), 1.61-1.57 (m, 2 H), 1.44-1.21 (m, 5 H), 1.20 (s, 3 H, C(CH$_3$)$_2$), 1.06 (d, *J* = 6.9 Hz, 3 H, CH(C*H*$_3$)), 1.02 (s, 3 H, C(CH$_3$)$_2$), 0.93 (s, 9 H, SiC(CH$_3$)$_3$), 0.92 (s, 9 H, SiC(CH$_3$)$_3$), 0.90 (s, 3 H, SiC(CH$_3$)$_3$), 0.84 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.13 (s, 3 H, Si(CH$_3$)$_2$), 0.11 (s, 3 H, Si(CH$_3$)$_2$), 0.08 (s, 3 H, Si(CH$_3$)$_2$), 0.07 (s, 3 H, Si(CH$_3$)$_2$), 0.06 (s, 3 H, Si(CH$_3$)$_2$), 0.05 (s, 3 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, CDCl$_3$) δ 219.4, 164.3, 153.1, 144.3, 142.3, 138.0, 128.7, 127.7, 126.7, 122.8, 118.7, 115.1, 86.4, 78.6, 77.4, 73.1, 67.3, 60.1, 53.7, 44.9, 38.6, 38.2, 35.0, 30.8, 29.2, 26.5, 26.2, 25.9, 25.8, 24.8, 19.1, 18.4, 18.2, 18.1, 17.8, 17.5, 15.5, 14.0, –3.7, –3.8, –3.9, –4.0, –4.7, –4.9; FAB HRMS (NBA/CsI) *m/e* 1228.5725, M + Cs$^+$ calcd for $C_{64}H_{101}NO_6SSi_3$ 1228.5712.

Aldehyde 20. Oxidation of Alcohol 19. To a solution of oxalyl chloride (2.22 mL, 25 mmol, 2.0 equiv.) in CH$_2$Cl$_2$ (100 mL) was added dropwise DMSO (3.6 mL, 51 mmol, 4.0 equiv.) at –78 °C. After stirring for 15 min at –78 °C, a solution of alcohol **19** (13.6 g, 12.7 mmol, 1.0 equiv.) in CH$_2$Cl$_2$ (20 mL) was added dropwise at –78 °C over a period of 5 min. The solution was stirred at –78 °C for 30 min, and then Et$_3$N (10.7 mL, 76 mmol, 6.0 equiv.) was added. The reaction mixture was allowed to warm to 0 °C over a period of 30 min and then ether (200 mL) was added, followed by saturated aqueous NH$_4$Cl solution (400 mL). The organic phase was separated and the aqueous phase was extracted with ether (2 x 300 mL). The combined organic solution was dried (MgSO$_4$), filtered and concentrated under reduced pressure. Purification

by flash column chromatography (silica gel, 20% ether in hexanes) provided aldehyde **20** (13.5 g, 99%) as a colorless oil: R_f = 0.77 (silica gel, 40% ether in hexanes); $[\alpha]^{22}_D$ –6.8 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 2943, 2849, 1725, 1690, 1466, 1384, 1255, 1091, 985, 832, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.76 (dd, *J* = 2.5, 1.5 Hz, 1 H, CHO), 7.47-7.43 (m, 5 H, Ph), 7.28-7.19 (m, 10 H, Ph), 6.89 (s, 1 H, SCH=C), 6.51 (s, 1 H, C*H*=CCH$_3$), 5.58 (dd, *J* = 7.1, 7.0 Hz, 1 H, C=C*H*CH$_2$), 4.45 (dd, *J* = 5.4, 4.5 Hz, 1 H, CHOSi), 4.19 (dd, *J* = 6.9, 6.6 Hz, 1 H, CHOSi), 3.73 (dd, *J* = 7.1, 2.0 Hz, 1 H, CHOSi), 3.48 (d, *J* = 11.5 Hz, 1 H, CH_2OTr), 3.46 (d, *J* = 11.5 Hz, 1 H, CH_2OTr), 3.08 (dq, *J* = 7.0, 6.8 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.51 (ddd, *J* = 16.8, 4.5, 1.5 Hz, 1 H, C*H*$_2$CHO), 2.39 (ddd, *J* = 16.8, 5.4, 2.5 Hz, 1 H, C*H*$_2$CHO), 2.38-2.29 (m, 2 H, C=CHC*H*$_2$CHO), 2.08-2.04 (m, 2 H, C*H*$_2$C(CH$_2$OTr)=CH), 2.05 (s, 3 H, CH=C(C*H*$_3$)), 1.61-1.57 (m, 2 H), 1.44-1.23 (m, 3 H), 1.20 (s, 3 H, C(CH$_3$)$_2$), 1.02 (d, *J* = 6.9 Hz, 3 H, CH(C*H*$_3$)), 1.00 (s, 3 H, C(CH$_3$)$_2$), 0.91 (s, 9 H, SiC(CH$_3$)$_3$), 0.89 (s, 9 H, SiC(CH$_3$)$_3$), 0.88 (s, 3 H, SiC(CH$_3$)$_3$), 0.82 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.09 (s, 3 H, Si(CH$_3$)$_2$), 0.08 (s, 3 H, Si(CH$_3$)$_2$), 0.05 (s, 3 H, Si(CH$_3$)$_2$), 0.04 (s, 3 H, Si(CH$_3$)$_2$), 0.03 (s, 6 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.8, 201.4, 164.5, 153.5, 144.6, 142.5, 138.3, 128.8, 127.8, 126.9, 122.9, 118.9, 115.2, 86.5, 78.6, 77.5, 71.4, 67.3, 53.2, 49.4, 44.9, 38.5, 34.9, 30.7, 29.1, 26.3, 25.9, 25.7, 23.8, 18.9, 18.6, 18.2, 17.9, 17.8, 17.3, 15.1, 13.8, –3.9, –4.1, –4.5, –4.7, –4.9, –5.2; FAB HRMS (NBA/CsI) *m/e* 1226.5630, M + Cs^+ calcd for $C_{64}H_{99}NO_6SSi_3$ 1226.5555.

Carboxylic Acid 21. Oxidation of Aldehyde 20. Aldehyde **20** (13.4 g, 12.6 mmol) *t*-BuOH (570 mL), isobutylene (472 mL, 2 M solution in THF, 0.94 mol), H_2O (120 mL), $NaClO_2$ (5.7 g, 63 mmol, 5.0 equiv.) and NaH_2PO_4 (3.78 g, 31 mmol, 2.5 equiv.) were combined and stirred at room temperature for 2 h. The reaction mixture was concentrated under reduced pressure and the residue was subjected to flash column chromatography (silica gel, 6% MeOH in CH_2Cl_2) to afford carboxylic acid **21** (13.6 g, 99%): R_f = 0.55 (silica gel, 5% MeOH in CH_2Cl_2); IR (thin film) ν_{max} 2932, 2857, 1711, 1465, 1365, 1254, 1083, 988, 836, 775 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.48-7.39 (m, 5 H, Ph), 7.28-7.17 (m, 10 H, Ph), 6.91 (s, 1 H, SCH=C), 6.61 (s, 1 H, C*H*=CCH$_3$), 5.60 (dd, *J* = 7.1, 7.1 Hz , 1 H, C=C*H*CH$_2$), 4.38 (dd, *J* = 6.8, 3.1 Hz, 1 H, CHOSi), 4.23 (dd, *J* = 7.9, 4.8 Hz, 1 H, CHOSi), 3.72 (dd, *J* = 6.2, 2.0 Hz, 1 H, CHOSi), 3.49 (d, *J* = 11.6 Hz, 1 H, CH_2OTr), 3.46 (d, *J* = 11.6 Hz, 1 H, CH_2OTr), 3.10 (dq, *J* = 6.8, 6.6 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.45 (dd, *J* = 16.3, 2.0 Hz, 1 H, C*H*$_2$COOH), 2.40-2.29 (m, 3 H, C*H*$_2$COOH, C=CHC*H*$_2$CHO), 2.17-2.09 (m, 1 H, C*H*$_2$C(CH$_2$OTr)=CH), 2.04-1.99 (m, 1 H, C*H*$_2$C(CH$_2$OTr)=CH), 2.01 (s, 3 H, CH=C(C*H*$_3$)), 1.37-1.23 (m, 5 H), 1.16 (s, 3 H, C(CH$_3$)$_2$), 1.07 (s, 3 H, C(CH$_3$)$_2$), 1.04 (d, *J* = 6.7 Hz, 3 H, CH(C*H*$_3$)), 0.90 (s, 9 H, SiC(CH$_3$)$_3$), 0.88 (s, 18 H, 2 x SiC(CH$_3$)$_3$), 0.81 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.10 (s, 3 H, Si(CH$_3$)$_2$), 0.09 (s, 3 H, Si(CH$_3$)$_2$), 0.08 (s, 3 H, Si(CH$_3$)$_2$), 0.06 (s, 3 H, Si(CH$_3$)$_2$), 0.03 (s, 3 H, Si(CH$_3$)$_2$), 0.02 (s, 3 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.5, 176.4, 165.2, 153.1, 144.6, 143.3, 138.5, 128.9, 127.8, 126.9, 123.0, 118.6, 114.9, 86.4, 78.7, 77.1, 73.4, 67.3, 53.6, 44.5, 39.9, 38.9, 34.9, 31.2, 30.9, 29.0, 26.3, 26.0, 25.8, 25.7, 23.2, 18.7, 18.5, 18.2, 17.9, 17.2, 16.7, 15.3, 13.8, –4.1, –4.2, –4.5, –4.6, –4.8, –5.0, –5.2; FAB HRMS (NBA/CsI) *m/e* 1242.5610, M + Cs^+ calcd for $C_{64}H_{99}NO_7SSi_3$ 1242.5504.

Hydroxy Acid 22. Selective Desilylation of tris(Silyl) Ether 21. A solution of tris(silyl) ether **21** (13.5g, 12.4 mmol) in THF (100 mL) at 0 °C was treated with TBAF (75.6 mL, 1.0 M solution in THF, 75.6 mmol, 6.0 equiv.) and then allowed to warm to 25 °C. After stirring for 10 h at that temperature, the reaction

mixture was diluted with EtOAc (200 mL) and washed with saturated aqueous NH_4Cl solution (100 mL). The aqueous solution was extracted with EtOAc (4 x 100 mL) and the combined organic phase was washed with brine (100 mL), dried ($MgSO_4$) and concentrated. The crude mixture was purified by flash column chromatography (silica gel, 5% MeOH in CH_2Cl_2) to provide hydroxy acid **22** (10.8 g, 89%) as a yellow oil: R_f = 0.39 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –4.2 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3354, 2931, 2860, 1707, 1461, 1361, 1255, 1085, 1049, 985, 826, 773, 732, 703 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.47-7.39 (m, 5 H, Ph), 7.29-7.19 (m, 10 H, Ph), 6.92 (s, 1 H, SCH=C), 6.65 (s, 1 H, C*H*=CCH$_3$), 5.56 (dd, *J* = 7.2, 7.2 Hz , 1 H, C=C*H*CH$_2$), 4.38 (dd, *J* = 6.4, 3.3 Hz, 1 H, C*H*OH), 4.21 (dd, *J* = 6.6, 6.3 Hz, 1 H, CHOSi), 3.74 (dd, *J* = 5.2, 2.0 Hz, 1 H, CHOSi), 3.55 (d, *J* =11.9 Hz, 1 H, CH$_2$OTr), 3.51 (d, *J* =11.9 Hz, 1 H, CH$_2$OTr), 3.09 (dq, *J* = 6.9, 6.8 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.47 (dd, *J* = 16.4, 3.3 Hz, 1 H, C*H*$_2$COOH), 2.44-2.41 (m, 2 H, C=CHC*H*$_2$CHO), 2.30 (dd, *J* = 16.4, 6.4 Hz, 1 H, C*H*$_2$COOH), 2.16-2.12 (m, 1 H, C*H*$_2$C(CH$_2$OTr)=CH), 2.07-1.99 (m, 1 H, C*H*$_2$C(CH$_2$OTr)=CH), 2.04 (s, 3 H, CH=C(C*H*$_3$)), 1.33-1.23 (m, 5 H), 1.17 (s, 3 H, C(CH$_3$)$_2$), 1.06 (s, 3 H, C(CH$_3$)$_2$), 1.04 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.88 (s, 9 H, SiC(CH$_3$)$_3$), 0.87 (s, 9 H, SiC(CH$_3$)$_3$), 0.83 (d, *J* = 6.9 Hz, 3 H, CH(C*H*$_3$)), 0.09 (s, 3 H, Si(CH$_3$)$_2$), 0.08 (s, 3 H, Si(CH$_3$)$_2$), 0.05 (s, 3 H, Si(CH$_3$)$_2$), 0.03 (s, 3 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 218.4, 176.3, 165.3, 152.8, 144.5, 142.2, 140.4, 128.8, 127.9, 127.0, 121.8, 119.1, 115.4, 86.7, 77.3, 77.2, 73.5, 67.4, 53.6, 44.7, 39.9, 38.8, 33.5, 31.1, 28.9, 26.4, 25.9, 25.8, 25.4, 23.2, 18.9, 18.6, 18.2, 17.9, 16.9, 15.5, 14.2, –4.1, –4.2, –4.5, –4.9; FAB HRMS (NBA/CsI) *m/e* 1228.4705, M + Cs^+ calcd for $C_{58}H_{85}NO_7SSi_2$ 1228.4640.

Lactone 7. Macrolactonization of Hydroxy Acid 22. A solution of hydroxy acid **22** (3.75 g, 3.87 mmol, 1.0 equiv..) in THF (50 mL, 0.07 M) was treated at 0 °C with Et_3N (3.24 mL, 23.2 mmol, 6.0 equiv.) and 2,4,6-trichlorobenzoyl chloride (1.45 mL, 9.3 mmol, 2.4 equiv.). The reaction mixture was stirred at 0 °C for 1 h, and then added slowly over a period of 2 h *via* syringe pump to a solution of 4-DMAP (104 mg, 8.51 mmol, 2.2 equiv.) in toluene (900 mL, 0.005 M based on **22**) at 75 °C and stirred at that temperature for 1 h. The reaction mixture was concentrated under reduced pressure to a small volume and filtered through silica gel. The residue was washed with 40% ether in hexanes, and the resulting solution was concentrated. Purification by flash column chromatography (silica gel, 20% ether in hexanes) furnished lactone **7** (2.76 g, 75%) as a colorless oil: R_f = 0.27 (20% ether in hexanes); $[\alpha]^{22}_D$ –7.3 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 2932, 2860, 1740, 1695, 1466, 1383, 1254, 1158, 1101, 1049, 910, 834, 773, 735 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.47-7.42 (m, 5 H, Ph), 7.29-7.19 (m, 10 H, Ph), 6.96 (s, 1 H, SCH=C), 6.57 (s, 1 H, C*H*=CCH$_3$), 5.56 (dd, *J* = 7.5, 6.4 Hz , 1 H, C=C*H*CH$_2$), 5.00 (d, *J* = 9.9 Hz, 1 H, CHOCO), 4.00 (d, *J* = 9.8 Hz, 1 H, CHOSi), 3.83 (d, *J* = 9.9 Hz, 1 H, CHOSi), 3.49 (d, *J* =11.2 Hz, 1 H, CH$_2$OTr), 3.46 (d, *J* =11.2 Hz, 1 H, CH$_2$OTr), 2.98 (dq, *J* = 7.1, 6.6 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.81-2.73 (m, 2 H, C=CHC*H*$_2$CHO, CH$_2$COO), 2.71 (s, 3 H, N=C(CH$_3$)S), 2.60 (dd, *J* = 16.3, 9.9 Hz, 1 H, CH$_2$COO), 2.44-2.38 (m, 1 H, C=CHC*H*$_2$CHO), 2.20 (dd, *J* = 14.0, 6.0 Hz, 1 H, C*H*$_2$C(CH$_2$OTr)=CH), 2.13 (s, 3 H, CH=C(C*H*$_3$)), 2.03-2.00 (m, 1 H, C*H*$_2$C(CH$_2$OTr)=CH), 1.46-1.37 (m, 3 H), 1.29-1.24 (m, 2 H), 1.16 (s, 3 H, C(CH$_3$)$_2$), 1.09 (s, 3 H, C(CH$_3$)$_2$), 1.08 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.94 (s, 9 H, SiC(CH$_3$)$_3$), 0.83 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.72 (s, 9 H, SiC(CH$_3$)$_3$), 0.09 (s, 3 H, Si(CH$_3$)$_2$), 0.06 (s, 6 H, Si(CH$_3$)$_2$), 0.05 (s, 3 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 215.6, 171.4, 164.9, 152.8, 144.5, 142.1, 138.8, 128.8, 127.9, 127.1, 120.3, 119.7, 116.2, 86.4, 79.6, 76.1, 66.7, 53.3, 48.0, 39.1, 37.3, 32.1, 31.3, 28.5, 26.9, 26.2, 25.8, 24.1, 19.1, 18.4, 18.3, 17.5, 15.1, 13.9, 13.8, –3.6, –3.9, –4.0, –

6.1; FAB HRMS (NBA/CsI) *m/e* 1110.4598, M + Cs^+ calcd for $C_{58}H_{83}NO_6SSi_2$ 1110.4534.

Alcohol 23. Lactone **7** (1.0 g, 1.0 mmol) was dissolved in Et_2O (20 mL) and the solution was cooled to –10 °C. Formic acid (20 mL) was added over a 15 min period and the mixture was stirred for 10 min at –10 °C, and then for 3 h at –5 °C. Water (20 mL) and then solid $NaHCO_3$ were sequentially added until cessation of effervescence. The layers were separated and the aqueous phase extracted with Et_2O (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography (silica gel, 50% ether in hexanes) furnished alcohol **23** (508 mg, 69%): R_f = 0.35 (silica gel, 60% ether in hexanes); $[\alpha]^{22}_D$ –21.2 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3417, 2933, 2857, 1741, 1695, 1466, 1383, 1253, 1194, 1158, 1101, 1066, 1018, 986, 834, 775, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.56 (s, 1 H, C*H*=CCH$_3$), 5.47 (dd, *J* = 9.4, 6.7 Hz , 1 H, C=C*H*CH$_2$), 5.01 (d, *J* = 9.8 Hz, 1 H, CHOCO), 4.13 (d, *J* = 12.8 Hz, 1 H, C*H*$_2$OH), 4.03 (d, *J* = 9.8 Hz, 1 H, CHOSi), 3.98 (d, *J* =12.8 Hz, 1 H, C*H*$_2$OH), 3.87 (d, *J* =9.1 Hz, 1 H, CHOSi), 3.02 (dq, *J* = 7.1, 6.6 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.76 (d, *J* = 16.5 Hz, 1 H, C*H*$_2$COOH), 2.75-2.70 (m, 1 H, C=CHC*H*$_2$CHO), 2.69 (s, 3 H, N=C(CH$_3$)S), 2.64 (dd, *J* = 16.3, 9.8 Hz, 1 H, CH$_2$COO), 2.49-2.35 (m, 1 H, C=CHC*H*$_2$CHO), 2.17 (dd, *J* = 14.1, 6.5 Hz, 1 H, C*H*$_2$C(CH$_2$OH)=CH), 2.10 (s, 3 H, CH=C(C*H*$_3$)), 2.00-1.96 (m, 1 H, C*H*$_2$C(CH$_2$OH)=CH), 1.72-1.64 (m, 2 H), 1.58-1.44 (m, 3 H), 1.18 (s, 3 H, C(CH$_3$)$_2$), 1.12 (s, 3 H, C(CH$_3$)$_2$), 1.09 (d, *J* = 6.7 Hz, 3 H, CH(C*H*$_3$)), 0.96 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.93 (s, 9 H, SiC(CH$_3$)$_3$), 0.82 (s, 9 H, SiC(CH$_3$)$_3$), 0.10 (s, 3 H, Si(CH$_3$)$_2$), 0.09 (s, 3 H, Si(CH$_3$)$_2$), 0.06 (s, 3 H, Si(CH$_3$)$_2$), –0.15 (s, 3 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 215.7, 171.5, 164.9, 152.7, 142.7, 138.6, 120.4, 119.8, 116.3, 79.5, 76.4, 66.5, 53.3, 48.1, 39.1, 37.3, 31.9, 31.3, 27.9, 27.2, 26.1, 25.9, 24.2, 19.2, 18.4, 18.3, 17.6, 14.7, –2.2, –3.9, –4.0, –5.9;

Lactone 24. Desilylation of lactone 7. To a solution of lactone **7** (611 mg, 0.61 mmol, 1.0 equiv.) in THF (45 mL) was added HF•pyr. (15 mL) at 0 °C. After stirring at room temperature for 24 h, the reaction mixture was quenched at 0 °C by careful addition of saturated aqueous $NaHCO_3$ solution (50 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a crude oil which was subjected to preparative thin layer chromatography (silica gel, 5% methanol in CH_2Cl_2) to give the triol lactone **24** (240 mg, 78%): R_f = 0.43 (silica gel, 80% EtOAc in hexanes); $[\alpha]^{22}_D$ –81.8 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3406, 2934, 2857, 1731, 1686, 1460, 1377, 1256, 1048, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.92 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.45 (dd, *J* = 7.5, 7.1 Hz, 1 H, C=C*H*CH$_2$), 5.23 (dd, *J* = 7.8, 1.9 Hz, 1 H, CHOCO), 4.29 (d, *J* = 11.0 Hz, 1 H, C*H*OH), 4.09 (d, *J* = 12.9 Hz, 1 H, C*H*$_2$OH), 4.01 (d, *J* =12.9 Hz, 1 H, C*H*$_2$OH), 3.70 (bs, 1 H, C*H*OH), 3.17 (dq, *J* = 6.9, 2.3 Hz, 1 H, C(O)C*H*(CH$_3$)), 3.01 (bs, 1 H, OH), 2.69 (s, 3 H, N=C(CH$_3$)S), 2.53 (ddd, *J* = 16.0, 7.5, 7.5 Hz, 1 H, C=CHC*H*$_2$CHO), 2.45 (dd, *J* = 14.5, 11.0 Hz, 1 H, CH$_2$COO), 2.36-2.30 (m, 1 H, C=CHC*H*$_2$CHO), 2.27-2.20 (m, 1 H, C*H*$_2$C(CH$_2$OH)=CH), 2.17 (dd, *J* = 14.5, 2.5 Hz, 1 H, CH$_2$COO), 2.10-2.03 (m, 1 H, C*H*$_2$C(CH$_2$OH)=CH), 1.96 (s, 3 H, CH=C(C*H*$_3$)), 1.70-1.60 (m, 2 H), 1.30 (s, 3 H, C(CH$_3$)$_2$), 1.28-1.19 (m, 3 H), 1.12 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.99 (s, 3 H, C(CH$_3$)$_2$), 0.95 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 221.2, 170.5, 165.3, 151.9, 141.8, 138.6, 121.5, 118.9, 115.4, 77.7, 74.0, 71.4, 65.7, 53.7, 41.3, 39.4, 37.8, 31.3, 27.5, 24.9, 22.6, 22.4, 18.5, 16.9, 15.9, 15.4, 13.1; FAB HRMS (NBA/CsI) *m/e* 640.1688, M + Cs^+ calcd for $C_{27}H_{41}NO_6S$ 640.1709.

Epoxide 6. Sharpless Epoxidation of Lactone 24. To a solution of allylic alcohol **24** (224 mg, 44 μmol, 1.0 equiv.) and 4 Å molecular sieves (40 mg) in CH_2Cl_2 (0.5 mL) at –30 °C was added dropwise (+)-diethyl-L-tartrate (19 μL, 11 mmol, 0.25 equiv.) and titanium isopropoxide (26 μL, 8.8 mmol, 0.2 equiv.) in CH_2Cl_2 (4 mL). After 1 h, *t*-butyl hydroperoxide (180 μL, 88 mmol, 5 M in decane, 2.0 equiv.) was added and the reaction mixture was stirred at –30 °C for 2 h. The reaction mixture was then filtered through celite. The filtrate was diluted with EtOAc (3 mL) and washed with aqueous saturated sodium sulfate solution (4 mL). The layers were separated and the aqueous phase was extracted with EtOAc (3 x 3 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a crude oil which was subjected to column chromatography (silica gel, 5% methanol in CH_2Cl_2) to give the triol epoxide **6** (159 mg, 71%): R_f = 0.51 (silica gel, EtOAc); $[\alpha]^{22}_D$ –55.6 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3446, 2931, 2857, 1731, 1689, 1461, 1377, 1256, 1056, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH_3), 5.42 (dd, *J* = 4.3, 2.6 Hz, 1 H, CHOCO), 4.24 (bs, 1 H, OH), 4.18 (dd, *J* = 10.5, 2.8 Hz, 1 H, C*H*OH), 3.74 (d, *J* = 5.6 Hz, 1 H, C*H*OH), 3.72 (d, *J* = 12.5 Hz, 1 H, CH_2OH), 3.56 (d, *J* = 12.5 Hz, 1 H, CH_2OH), 3.31 (dd, *J* = 6.7, 4.8 Hz, 1 H, C*H*OCH_2), 3.13 (dq, *J* = 6.8, 5.3 Hz, 1 H, C(O)C*H*(CH_3)), 2.68 (s, 3 H, N=C(CH_3)S), 2.64 (bs, 1 H, OH), 2.53 (dd, *J* = 14.5, 10.5 Hz, 1 H, CH_2COO), 2.35 (dd, *J* = 14.5, 2.8 Hz, 1 H, CH_2COO), 2.11-2.08 (m, 1 H, OCHCH_2CHO), 2.06 (s, 3 H, CH=C(CH_3)), 1.99-1.95 (m, 1 H, OCHCH_2CHO), 1.87-1.85 (m, 1 H, CH_2C(CH_2OH)OCH), 1.69-1.65 (m, 1 H, CH_2C(CH_2OH)OCH), 1.50-1.36 (m, 4 H), 1.35 (s, 3 H, C(CH_3)$_2$), 1.30-1.18 (m, 1 H), 1.15 (d, *J* = 6.8 Hz, 3 H, CH(CH_3)), 1.06 (s, 3 H, C(CH_3)$_2$), 0.98 (d, *J* = 7.0 Hz, 3 H, CH(CH_3)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.1, 170.3, 164.9, 151.5, 137.1, 119.6, 116.0, 76.8, 74.2, 72.7, 63.8, 63.5, 57.2, 53.1, 43.1, 39.2, 36.5, 31.4, 30.9, 28.3, 22.1, 21.3, 19.7, 19.2, 17.3, 16.0, 13.8; FAB HRMS (NBA/NaI) *m/e* 546.2520, M + Na^+ calcd for $C_{27}H_{41}NO_7S$ 546.2501.

Acetate 25. Selective Esterification of Alcohol 24 with Acetic Anhydride. To a stirred solution of alcohol **24** (25.0 mg, 0.032 mmol) in EtOAc (1.0 mL, 0.03 M) at 0 °C, was added acetic anhydride (15 μL, 0.16 mmol, 5.0 equiv.) and 4-DMAP (4.3 mg, 0.035 mmol, 1.1 equiv.). The solution was stirred for 0.5 h at 0 °C, filtered over silica gel and concentrated *in vacuo*. Purification by preparative thin layer chromatography (5% MeOH in CH_2Cl_2) provided pure **25** (16.3 mg, 85% based on 60% conversion): R_f = 0.45 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –65.4 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3394, 2932, 1734, 1689, 1461, 1377, 1247, 1025 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.95 (s, 1 H, SCH=C), 6.58 (s, 1 H, C*H*=CCH_3), 5.46 (dd, *J* = 8.5, 4.2 Hz, 1 H, $AcOCH_2C$=C*H*CH_2), 5.24 (d, *J* = 8.5 Hz, 1 H, CH_2COOCH), 4.54 (d, *J* = 12.1 Hz, 1 H, AcOCH_2C=CH), 4.41 (d, *J* = 12.1 Hz, 1 Hz, 1 H, AcOCH_2C=CH), 4.30 (d, *J* = 10.2 Hz, 1 H, $(CH_3)_2$CC*H*OH), 3.70 (s, 1 H, C*H*OH), 3.58 (bs, 1 H, OH), 3.16 (dq, *J* = 13.4, 2.5 Hz, 1 H, C(O)C*H*CH_3), 3.01 (s, 1 H, OH), 2.69 (s, 3 H, N=C(CH_3)S), 2.65 (obscured m, 1 H, CH_2CH=CCH_2OAc), 2.47 (dd, *J* = 14.3, 11.0 Hz, 1 H, CH_2COOCH), 2.38-2.32 (m, 1 H), 2.28 (dd, *J* = 14.3, 2.5 Hz, CH_2COOCH), 2.29-2.24 (m, 1 H, CH_2($AcOCH_2$)C=CHCH_2), 2.06 (s, 3 H, CH=CCH_3), 2.05 (s, 3 H, CH=CCH_2OOCCH_3), 1.76-1.63 (m, 3 H), 1.34 (s, 3 H, C(CH_3)$_2$), 1.32-1.22 (m, 4 H), 1.19 (d, *J* = 6.7 Hz, 3 H, CH(CH_3)), 1.06 (s, 3 H, C(CH_3)$_2$), 1.00 (d, *J* = 7.1 Hz, 3 H, CH(CH_3)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.3, 170.7, 165.0, 151.6, 138.6, 136.8, 124.7, 119.1, 115.6, 78.0, 73.9, 72.0, 67.4, 53.7, 41.6, 39.7, 38.1, 32.1, 31.6, 28.3, 25.3, 23.0, 21.1, 19.1, 17.7, 16.1, 15.8, 13.3; FAB HRMS (NBA/CsI) *m/e* 682.1836, M + Cs^+ calcd for $C_{32}H_{49}NO_7S$ 682.1815.

Pivaloate 26. Selective Esterification of Triol 24 with Pivaloyl Chloride. To a stirred solution of triol **24** (6.0 mg, 0.011 mmol) in CH_2Cl_2 (0.4 mL, 0.03 M) at 0 °C, was added triethylamine (8 μL, 0.055 mmol, 5.0 equiv.), pivaloyl chloride (2.1 μL, 0.17 mmol, 1.5 equiv.) and 4-DMAP (0.2 mg, 0.1 equiv.). The solution was stirred for 0.5 h and the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution. The layers were separated and the aqueous phase extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (60% EtOAc in hexanes) provided pure **26** (6.3 mg, 93%): R_f = 0.70 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –69.6 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3395, 2965, 1733, 1728, 1460, 1383, 1285, 1153, 1023 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.94 (s, 1 H, SCH=C), 6.58 (s, 1 H, C*H*=CCH$_3$), 5.43 (dd, *J* = 9.5, 5.5 Hz, 1 H, PivOCH$_2$C=C*H*CH$_2$), 5.24 (d, *J* = 9.1 Hz, 1 H, CH$_2$COOC*H*), 4.52 (d, *J* = 12.8 Hz, 1 H, PivOC*H*$_2$C=CH), 4.40 (d, *J* = 12.9 Hz, 1 H, PivOC*H*$_2$C=CH), 4.28 (d, *J* = 10.6 Hz, 1 H, (CH$_3$)$_2$CC*H*OH), 3.71 (dd, *J* = 4.2, 2.5 Hz, 1 H, C*H*OH), 3.49 (bs, 1 H, OH), 3.17 (dq, *J* = 13.4,.4, 2.5 Hz, 1 H, C(O)C*H*CH$_3$), 2.95 (bs, 1 H, OH), 2.68 (s, 3 H, N=C(CH$_3$)S), 2.65 (ddd, *J* = 15.1, 9.7, 9.5 Hz, 1 H, C*H*$_2$CH=CCH$_2$OPiv), 2.45 (dd, *J* = 14.5, 11.0 Hz, 1 H, C*H*$_2$COOCH), 2.38-2.32 (m, 1 H), 2.28 (dd, *J* = 14.5, 2.5 Hz, C*H*$_2$COOCH), 2.25-2.22 (m, 1 H, C*H*$_2$(PivOCH$_2$)C=CHCH$_2$), 2.06 (s, 3 H, CH=CC*H*$_3$), 1.76-1.69 (m, 2 H), 1.34 (s, 3 H, C(CH$_3$)$_2$), 1.32-1.22 (m, 4 H), 1.19 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 1.18 (s, 9 H, OOCC(CH$_3$)$_3$), 1.06 (s, 3 H, C(CH$_3$)$_2$), 1.00 (d, *J* = 7.1 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.2, 178.0, 170.1, 164.9, 151.7, 138.5, 137.3, 123.7, 119.3, 115.7, 78.2, 74.0, 72.2, 67.3, 53.6, 41.8, 39.7, 38.9, 38.0, 32.2, 31.7, 28.3, 27.3, 27.2, 25.3, 22.9, 19.1, 18.1, 16.0, 15.9, 13.4; FAB HRMS (NBA/CsI) *m/e* 724.2310, M + Cs^+ calcd for $C_{32}H_{49}NO_7S$ 724.2284.

Benzoate 27. Selective Esterification of Triol 24 with Benzoyl Chloride. To a stirred solution of triol **24** (6.0 mg, 0.011 mmol) in CH_2Cl_2 (0.4 mL, 0.03 M) at 0 °C, was added triethylamine (8 μL, 0.055 mmol, 5.0 equiv.), benzoyl chloride (1.6 μL, 0.14 mmol, 1.2 equiv.) and 4-DMAP (0.2 mg, 0.1 equiv.). The solution was stirred for 0.5 h and the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution. The layers were separated and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (60% EtOAc in hexanes) provided pure **27** (6.5 mg, 90%): R_f = 0.55 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –62.9 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3420, 2932, 1721, 1452, 1379, 1272, 1109 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.2, 1.1 Hz, 2 H, Ph), 7.54 (m, 1 H, CH Ph), 7.42 (dd, *J* = 8.2, 7.2 Hz, 2 H, Ph), 6.90 (s, 1 H, SCH=C), 6.57 (s, 1 H, C*H*=CCH$_3$), 5.58 (dd, *J* = 8.7, 6.0 Hz, 1 H, BzOCH$_2$C=C*H*CH$_2$), 5.26 (d, *J* = 8.7 Hz, 1 H, CH$_2$COOC*H*), 4.80 (d, *J* = 12.8 Hz, 1 H, BzOC*H*$_2$C=CH), 4.67 (d, *J* = 12.6 Hz, 1 H, BzOC*H*$_2$C=CH), 4.29 (d, *J* = 10.8 Hz, 1 H, (CH$_3$)$_2$CC*H*OH), 3.69 (s, 1 H, C*H*OH), 3.49 (bs, 1 H, OH), 3.15 (dq, *J* = 13.4, 2.5 Hz, 1 H, C(O)C*H*CH$_3$), 2.94 (bs, 1 H, OH), 2.68 (s, 3 H, N=C(CH$_3$)S), 2.69-2.62 (obscured m, 1 H, C*H*$_2$CH=CCH$_2$OAc), 2.45 (dd, *J* = 14.5, 11.1 Hz, 1 H, C*H*$_2$COOCH), 2.42-2.36 (m, 1 H), 2.35-2.27 (m, 1 H), 2.25 (dd, *J* = 14.6, 2.5 Hz, C*H*$_2$COOCH), 2.20-2.14 (m, 1 H), 2.06 (s, 3 H, CH=CC*H*$_3$), 1.76-1.69 (m, 3 H), 1.34 (s, 3 H, C(CH$_3$)$_2$), 1.42-1.27 (m, 3 H), 1.19 (d, *J* = 6.6 Hz, 3 H, CH(C*H*$_3$)), 1.05 (s, 3 H, C(CH$_3$)$_2$), 0.98 (d, *J* = 7.0 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.3, 170.0, 166.2, 164.9, 151.7, 138.4, 136.9, 132.9, 130.1, 129.5, 128.3, 124.8, 119.3,

115.6, 78.0, 74.0, 72.1, 68.0, 53.7, 41.7, 39.7, 38.1, 32.1, 31.7, 28.6, 25.4, 22.9, 19.1, 17.9, 16.1, 15.9, 13.4; FAB HRMS (NBA/CsI) *m/e* 668.1682, M + Cs^+ calcd for $C_{28}H_{41}NO_7S$ 668.1658.

Methyl Ether 28. Etherification of Alcohol 23 with Methyl Iodide. To a stirred solution of alcohol **23** (15.0 mg, 20.4 μmol) in DMF (0.4 mL) at 0 °C was added MeI (25 μL, 0.41 mmol, 20 equiv.) followed by NaH (60% suspension in oil, 1.0 mg, 1.0 equiv.). After stirring for 30 min, the reaction mixture was quenched by the addition of saturated aqueous NH_4Cl solution (1 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 x 2 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (40% Et_2O in hexanes) provided pure **28** (9.4 mg, 62%): R_f = 0.61 (silica gel, 40% Et_2O in hexanes); $[\alpha]^{22}_D$ –16.3 (*c* 0.5, $CHCl_3$); IR (thin film) ν_{max} 2932, 2857, 1741, 1695, 1465, 1381, 1253, 1191, 1158, 1100, 834, 115 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.57 (s, 1 H, C*H*=CCH$_3$), 6.54 (dd, *J* = 9.4, 6.6 Hz, 1 H, C=C*H*CH$_2$), 5.00 (bd, *J* = 9.2 Hz, CHOCO), 4.03 (m, 1 H, CHOSi), 4.02 (d, *J* = 11.8 Hz, 1 H, C*H*$_2$OMe), 3.88 (d, *J* = 9.0 Hz, 1 H, CHOSi), 3.63 (d, *J* = 11.8 Hz, 1 H, C*H*$_2$OMe), 3.01 (dq, *J* = 8.8, 7.0 Hz, 1 H, C(O)C*H*CH$_3$), 2.82-2.61 (m, 4 H, C=CHC*H*$_2$CHO and CH$_2$COO), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.38 (m, 1 H, C*H*$_2$C(CH$_2$OH)=CH), 2.17 (dd, *J* = 14.6, 6.7 Hz, C*H*$_2$C(CH$_2$OH)=CH), 2.11 (s, 3 H, CH=CC*H*$_3$), 1.93 (m, 1 H, C*H*(CH$_3$), 1.69 (m, 1 H), 1.58-1.46 (m, 3 H), 1.18 (s, 3 H, C(CH$_3$)$_2$), 1.12 (s, 3 H, C(CH$_3$)$_2$), 1.01 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.96 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.93 (s, 9 H, SiC(CH$_3$)$_3$), 0.83 (s, 9 H, SiC(CH$_3$)$_3$), 0.11 (s, 3 H, Si(CH$_3$)$_2$), 0.10 ((s, 3 H, Si(CH$_3$)$_2$), 0.06 (s, 3 H, Si(CH$_3$)$_2$), –0.14 (s, 3 H, Si(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 215.4, 171.3, 164.8, 152.5, 141.3, 138.5, 122.0, 119.7, 116.2, 79.5, 76.1, 76.0, 57.7, 53.3, 39.2, 32.0, 28.1, 27.2, 26.2, 26.0, 24.2, 19.1, 18.5, 18.4, 17.7, 15.1, –3.4. –3.7, –3.8, –5.7;

Methyl Ether 29. Desilyilation of 28. Methyl ether **29** (5.3 mg, 85%) was obtained from compound **28** (9.2 mg, 12.3 μmol) according to the procedure described above for **24**. **29**: R_f = 0.48 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –64.0 (*c* 0.5, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 6.95 (s, 1 H, SCH=C), 6.58 (s, 1 H, C*H*=CCH$_3$), 5.43 (dd, *J* = 10.2, 4.9 Hz, 1 H, CH$_3$OCH$_2$C=C*H*CH$_2$), 5.22 (d, *J* = 8.2 Hz, 1 H, CH$_2$COOC*H*), 4.29 (d, *J* = 9.1 Hz, 1 H, (CH$_3$)$_2$CC*H*OH), 3.91 (d, *J* = 11.7 Hz, 1 H, CH$_3$OC*H*$_2$C=CH), 3.71 (d, *J* = 2.1 Hz, 1 H, C*H*OH), 3.69 (d, *J* = 11.8 Hz, 1 H, CH$_3$OC*H*$_2$C=CH), 3.58 (bs, 1 H, OH), 3.27 (s, 3 H, CH$_2$OC*H*$_3$), 3.16 (dq, *J* = 13.7, 2.0 Hz, 1 H, C(O)C*H*CH$_3$), 3.05 (s, 1 H, OH), 2.68 (s, 3 H, N=C(CH$_3$)S), 2.65 (obscured m, 1 H, C*H*$_2$CH=CCH$_2$OCH$_3$), 2.47 (dd, *J* = 14.5, 11.1 Hz, 1 H, C*H*$_2$COOCH), 2.33-2.29 (m, 1 H), 2.26 (dd, *J* = 14.4, 2.5 Hz, C*H*$_2$COOCH), 2.06 (s, 3 H, CH=CC*H*$_3$), 2.07-2.04 (m, 1 H), 1.76-1.63 (m, 3 H), 1.34 (s, 3 H, C(CH$_3$)$_2$), 1.32-1.22 (m, 4 H), 1.17 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 1.06 (s, 3 H, C(CH$_3$)$_2$), 1.01 (d, *J* = 7.1 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.4, 170.2, 164.9, 151.6, 139.1, 127.4, 123.7, 119.2, 115.6, 78.5, 76.0, 73.8, 72.2, 57.9, 53.7, 41.6, 39.7, 38.2, 32.4, 31.8, 28.1, 25.3, 27.2, 22.9, 19.1, 17.9, 16.0, 15.9, 13.2; FAB HRMS (NBA/CsI) *m/e* 654.1885, M + Cs^+ calcd for $C_{28}H_{43}NO_6S$ 654.1865.

Benzyl Ether 30. Etherification of Alcohol 23 with Benzyl Bromide. To a stirred solution of **23** (45.0 mg, 61.1 μmol) in THF (1.5 mL) at –15 °C was added sequentially tetra-*n*-butylammonium iodide (0.5 mg), benzyl bromide (130 μL, 0.74 mmol, 25 equiv.) and sodium hydride (60% suspension in oil, 5.0 mg, 123

mmol, 2.0 equiv.). The reaction mixture was then slowly allowed to warm to room temperature over 3.5 h. Saturated aqueous NH_4Cl solution (1 mL)was then added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 2 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (40% Et_2O in hexanes) provided pure **30** (20.2 mg, 40%); R_f = 0.65 (silica gel, 40% Et_2O in hexanes); $[\alpha]^{22}_D$ –14.0 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 2954, 2930, 2886, 2856, 1741, 1696, 1471, 1383, 1254, 1200, 1158, 1101, 1067, 1019, 985, 940, 913, 874, 835, 775, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.32 (m, 4 H, Ph), 7.28 (obscured m, 1 H, Ph), 6.96 (s, 1 H, SCH=C), 6.56 (s, 1 H, C*H*=CCH$_3$), 5.48 (dd, *J* = 9.6, 6.5 Hz, 1 H, C=C*H*CH$_2$), 5.01 (d, *J* = 9.6 Hz, 1 H, CHOCO), 4.50 (d, *J* = 11.9 Hz, 1 H, OC*H*$_2$Ph), 4.39 (d, *J* = 11.9 Hz, 1 H, OC*H*$_2$Ph), 4.07 (d, *J* = 11.9 Hz, 1 H, C*H*$_2$OBn), 4.03 (d, *J* = 9.4 Hz, 1 H, CHOSi), 3.87 (d, *J* = 8.9 Hz, 1 H, CHOSi), 3.76 (d, *J* = 11.9 Hz, C*H*$_2$OBn), 3.01 (dq, *J* = 8.6, 6.8 Hz, 1 H, C(O)C*H*CH$_3$), 2.78 (m, 2 H, C=CHC*H*$_2$CHO and CH$_2$COO), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.64 (dd, *J* = 16.3, 9.9 Hz, 1 H, CH$_2$COO), 2.39 (m, 1 H, C=CHC*H*$_2$CHO), 2.18 (m, 1 H, C*H*$_2$C(CH$_2$OBn)=CH), 2.11 (s, 3 H, CH=C(C*H*$_3$)), 2.00 (m, 1 H, C=CHC*H*$_2$CHO), 1.68 (m, 1 H, C*H*(CH$_3$)), 1.63-1.45 (m, 4 H), 1.18 (s, 3 H, C(CH$_3$)$_2$), 1.11 (s, 3 H, C(CH$_3$)$_2$), 1.09 (d, *J* = 6.7 Hz, 3 H, CH(C*H*$_3$)), 0.94 (d, *J* = 6.1 Hz, CH(C*H*$_3$)), 0.94 (s, 9 H, SiC(CH$_3$)$_3$), 0.80 (s, 9 H, SiC(CH$_3$)$_3$), 0.10 (s, 3 H, Si(CH$_3$)$_2$), 0.08 (s, 3 H, Si(CH$_3$)$_2$), 0.06 (s, 3 H, Si(CH$_3$)$_2$), –0.16 (s, 3 H, Si(CH$_3$)$_2$);)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 214.9, 170.9, 164.5, 152.2, 141.1, 138.3, 128.2, 127.8, 127.4, 122.0, 119.5, 116.0, 79.4, 76.1, 73.4, 71.8, 53.4, 48.1, 39.4, 37.7, 33.2, 31.6, 28.4, 27.3, 26.4, 26.2, 24.4, 24.2, 19.2, 18.7, 18.6, 17.9, 15.3, –3.1, –3.4, –3.5, –5.4; FAB HRMS (NBA/CsI) *m/e* 958.3940, M + Cs^+ calcd for $C_{46}H_{75}NO_6SSi_2$ 958.3908.

Benzyl Ether 31. Desilylation of 30. Benzyl ether **31** (9.7 mg, 90%) was obtained from compound **30** (15.0 mg, 18.1 μmol) according to the procedure described above for **24**. **31**: R_f = 0.48 (silica gel, 80% Et_2O in hexanes); $[\alpha]^{22}_D$ –91.6 (*c* 0.5, $CHCl_3$); IR (thin film) ν_{max} 3411, 2929, 1732, 1684, 1454, 1384, 1294, 1251, 1186, 1149, 1088, 1008, 979, 912, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.32-7.30 (m, 4 H, Ph), 7.28 (m, 1 H, Ph), 6.95 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.46 (dd, *J* = 9.9, 4.8 Hz, C=C*H*CH$_2$), 5.24 (dd, *J* = 8.9, 1.1 Hz, 1 H, CHOCO), 4.47 (d, *J* = 11.9 Hz, 1 H, OC*H*$_2$Ph), 4.41 (d, *J* = 11.9 Hz, 1 H, OC*H*$_2$Ph), 4.28 (bd, *J* = 10.4 Hz, 1 H, C*H*OH), 3.99 (d, *J* = 11.8 Hz, 1 H, C*H*$_2$OBn), 3.81 (d, *J* = 11.8 Hz, 1 H, C*H*$_2$OBn), 3.67 (bs, 1 H, CHOH), 3.57 (bs, 1 H, OH), 3.14 (dq, *J* = 6.9, 2.2 Hz, 1 H, C(O)C*H*CH$_3$), 2.99 (bs, 1 H, OH), 2.69 (obscured m, 1 H, C=CHC*H*$_2$CHO), 2.68 (s, 3 H, N=C(CH$_3$)S), 2.44 (dd, *J* = 14.6, 11.2 Hz, 1 H, CH$_2$COO), 2.32 (m, 1 H, C*H*$_2$C(CH$_2$OBn)=CH), 2.28 (m, 1 H, C*H*$_2$C(CH$_2$OBn)=CH), 2.24 (dd, *J* = 14.6, 2.6 Hz, CH$_2$COO), 2.11 (m, 1 H, C=CHC*H*$_2$CHO), 2.06 (s, 3 H, CH=C(C*H*$_3$)), 1.71 (m, 1 H, C*H*(CH$_3$)), 1.58 (m, 1 H), 1.33 (s, 3 H, C(CH$_3$)$_2$), 1.32-1.23 (m, 3 H), 1.17 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 1.05 (s, 3 H, C(CH$_3$)$_2$), 0.98 (d, *J* = 7.0 Hz, 3 H, C(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.4, 170.1, 139.2, 138.2, 128.3, 127.7, 127.5, 123.8, 78.5, 73.8, 73.5, 72.1, 72.0, 53.7, 41.6, 39.7, 38.2, 32.3, 31.8, 28.2, 25.3, 23.0, 19.1, 17.9, 16.1, 15.9, 13.3; FAB HRMS (NBA/CsI) *m/e* 730.2206, M + Cs^+ calcd for $C_{34}H_{47}NO_6S$ 730.2178.

Chloride 32. Chlorination of Compound 23. To a stirred solution of **23** (3.4 mg, 4.6 μmol) in CCl_4 was added Ph_3P (5.0 mg, 18.4 μmol, 4.0 equiv.). The reaction mixture was refluxed for 12 h and then cooled to room temperature. The solvent was removed *in vacuo* and the residue was purified by preparative thin layer chromatography (20% Et_2O in hexanes) to give **32** (3.0 mg, 85%): R_f = 0.44 (silica gel, 20% Et_2O in hexanes);

$[\alpha]^{22}_D$ –25.4 (*c* 0.5, $CHCl_3$); IR (thin film) ν_{max} 2933, 2857, 1742, 1695, 1466, 1383, 1466, 1383, 1254, 1186, 1158, 1099, 1019, 985, 834, 775, 733 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.56 (s, 1 H, C*H*=CCH_3), 5.57 (dd, *J* = 9.6, 6.5 Hz, C=C*H*CH_2), 5.03 (bd, *J* = 9.4 Hz, 1 H, CHOCO), 4.15 (d, *J* = 11.1 Hz, 1 H, CH_2Cl), 4.03 (bd, *J* = 9.7 Hz, CHOSi), 3.92 (d, *J* = 11.1 Hz, CH_2Cl), 3.88 (s, *J* = 8.9 Hz, 1 H, CHOSi), 3.00 (dq, *J* = 8.7, 6.8 Hz, C(O)C*H*CH_3), 2.77 (m, 1 H, CH_2COO), 2.72 (m, 1 H, C=CHC*H*$_2$CHO), 2.70 (s, 3 H, N=C(CH_3)S), 2.63 (dd, *J* = 16.4, 9.8 Hz, 1 H, CH_2COO), 2.41 (m, 1 H, C=CHC*H*$_2$CHO), 2.17 (m, 2 H, C*H*$_2$C(CH_2Cl)=CH), 2.11 (s, 3 H, CH=C(C*H*$_3$)), 1.72 (m, 1 H, C*H*(CH_3)), 1.50 (m, 1 H), 1.21-1.04 (m, 3 H), 1.18 (s, 3 H, C(CH_3)$_2$), 1.12 (s, 3 H, C(CH_3)$_2$), 1.09 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.97 (d, *J* = 6.9 Hz, 3 H, CH(C*H*$_3$)), 0.93 (s, 9 H, SiC(CH_3)$_3$), 0.83 (s, 9 H, SiC(CH_3)$_3$), 0.10 (s, 3 H, Si(CH_3)$_2$), 0.99 (s, 3 H, Si(CH_3)$_2$), 0.07 (s, 3 H, Si(CH_3)$_2$), –0.15 (s, 3 H, Si(CH_3)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 214.8, 170.8, 164.5, 152.2, 140.5, 137.8, 124.8, 119.9, 116.2, 79.8, 53.4, 49.4, 39.4, 32.5, 31.5, 27.8, 27.0, 26.4, 26.2, 24.4, 24.2, 19.3, 18.7, 18.6, 17.9, 15.2, –3.1, –3.4, –3.5, –5.4; FAB HRMS (NBA/CsI) *m/e* 886.3138, M + Cs^+ calcd for $C_{39}H_{68}ClNO_5SSi_2$ 886.3100.

Chloride 33. Desilylation of 32. Chloride **33** (9.3 mg, 92%) was obtained from compound **32** (15.0 mg, 19.9 μmol) according to the procedure described above for **24**. **33**: R_f = 0.77 (silica gel, Et_2O); $[\alpha]^{22}_D$ –71.4 (*c* 0.5, $CHCl_3$); IR (thin film) ν_{max} 3387, 2922, 1731, 1682, 1383, 1259, 1086, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.58 (s, 1 H, C*H*=CCH_3), 5.55 (dd, *J* = 10.0, 5.1 Hz, C=C*H*CH_2), 5.23 (dd, *J* = 8.2, 1.1 Hz, CHOCO), 4.28 (bd, *J* = 10.4 Hz, C*H*OH), 4.10 (d, *J* = 11.4 Hz, CH_2Cl), 3.95 (d, *J* = 11.4 Hz, CH_2Cl), 3.61 (bs, 1 H, C*H*OH), 3.58 (bs, 1 H, OH), 3.14 (dq, *J* = 6.8, 2.4 Hz, C(O)C*H*CH_3), 3.02 (bs, 1 H, OH), 2.68 (s, 3 H, 3 H, N=C(CH_3)S), 2.66 (m, 1 H, C=CHC*H*$_2$CHO), 2.45 (dd, *J* = 14.6, 11.2 Hz, CH_2COO), 2.33 (m, 2 H, C*H*$_2$C(CH_2Cl)=CH), 2.27 (dd, *J* = 14.6, 2.6 Hz, CH_2COO), 2.26 (m, 1 H, C=CHC*H*$_2$CHO), 2.06 (s, 3 H, CH=C(C*H*$_3$)), 1.79-1.62 (m, 2 H), 1.37-1.28 (m, 3 H), 1.33 (s, 3 H, C(CH_3)$_2$), 1.17 (d, *J* = 6.9 Hz, CH(C*H*$_3$)), 1.06 (s, 3 H, C(CH_3)$_2$), 1.01 (d, *J* = 7.1 Hz, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.3, 170.0, 165.0, 151.6, 138.7, 126.6, 119.4, 115.7, 78.1, 73.9, 72.2, 53.7, 49.2, 41.7, 39.7, 38.1, 32.6, 31.8, 27.7, 25.0, 23.0, 19.1, 18.0, 16.0, 15.9, 13.3; FAB HRMS (NBA/CsI) *m/e* 658.1394, M + Cs^+ calcd for $C_{27}H_{40}ClNO_5S$ 658.1370.

Fluorides 34 and 36. To a stirred solution of allylic alcohol **23** (33 mg, 0.46 mmol) in CH_2Cl_2 (0.5 mL) at –78 °C was added DAST (7.4 mL, 0.56 mmol, 1.2 equiv.). After stirring for 5 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution (0.5 mL) and warmed to room temperature. The layers were separated and the aqueous phase was extracted with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a crude oil which was subjected to preparative thin layer chromatography (silica gel, 20% Et_2O in hexanes) to give the fluorides **34** (55%) and **36** (21%). **34**: R_f = 0.74 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –18.4 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 2932, 2871, 2856, 1741, 1695, 1465, 1381, 1252, 1156, 1098, 1019, 984, 834, 775, 733, 670 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.57 (s, 1 H, C*H*=CCH_3), 5.55 (m, 1 H, C=C*H*CH_2), 5.03 (dd, *J* = 9.8, 0.7 Hz, 1 H, CHOCO), 4.87 (dd, *J* = 48.4, 10.5 Hz, 1 H, CH_2F), 4.66 (dd, *J* = 47.4, 10.5 Hz, 1 H, CH_2F), 4.04 (d, *J* = 9.4 Hz, 1 H, CHOSi), 3.88 (d, *J* = 9.1 Hz, 1 H, CHOSi), 3.00 (dq, *J* = 8.6, 7.0 Hz, 1 H, C(O)C*H*(CH_3), 2.77 (obscured m, 1 H, C=CHC*H*$_2$CHO), 2.71 (s, 3 H, N=C(CH_3)S), 2.65 (dd, *J* = 16.2, 10.1 Hz, 1 H,

C=CHCH_2CHO), 2.43, (dd, J = 12.2, 10.4 Hz, CH_2COO), 2.20 (m, 1 H, CH_2C(CH_2F)=CH), 2.12 (s, 3 H, CH=C(CH_3)), 2.05 (m, 1 H, CH_2COO), 2.01 (m, 1 H, CH_2C(CH_2OH)=CH), 1.71 (m, 1 H, CH(CH_3)), 1.63 (m, 1 H), 1.57 (m, 3 H), 1.19 (s, 3 H, C(CH_3)$_2$), 1.13 (s, 3 H, C(CH_3)$_2$), 1.09 (d, J = 6.8 Hz, 3 H, CH(CH_3)), 0.96 (d, J = 6.9 Hz, 3 H, CH(CH_3)), 0.93 (s, 9 H, SiC(CH_3)$_3$), 0.83 (s, 9 H, SiC(CH_3)$_3$), 0.10 (s, 6 H, Si(CH_3)$_2$), 0.07, (s, 3 H, Si(CH_3)$_2$), –0.14 (s, 3 H, Si(CH_3)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) 215.1, 171.0, 164.7, 152.3, 138.1, 123.9, 123.7, 119.9, 116.2, 86.9, 85.8, 79.1, 76.0, 53.4, 48.1, 39.4, 37.6, 32.0, 31.5, 28.0, 27.2, 26.3, 26.1, 24.4, 24.0, 19.2, 18.6, 18.5, 17.8, 15.2, –3.3, –3.6, –3.7, –5.6; FAB HRMS (NBA/CsI) *m/e* 870.3432, M + Cs^+ calcd for $C_{39}H_{68}FNO_5SSi_2$ 870.3395. **36**: R_f = 0.77 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ +0.67 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 2928, 2855, 1741, 1695, 1472, 1253, 1084, 1020, 987, 836, 775, 668 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.60 (s, 1 H, CH=CCH_3), 5.59 (dd, J = 11.2, 1.0 Hz, 1 H, CHOCO), 5.28 (bd, J = 59 Hz, 1 H, CHF), 5.04 (s, 1 H, C=CH_2), 4.89 (s, 1 H, C=CH_2), 4.24 (bs, 1 H, CHOSi), 4.00 (d, J = 9.4 Hz, CHOSi), 2.97 (dq, J = 8.8, 7.1 Hz, 1 H, C(O)CH(CH_3), 2.70 (s, 3 H, N=C(CH_3)S) 2.49 (dd, J = 14.6, 5.7 Hz, 1 H, CH_2COO), 2.26 (m, 3 H, CH_2COO and CHFCH_2), 2.12 (s, 3 H, CH=C(CH_3)), 2.07 (m, 2 H, (CH_2=C)CH_2), 1.72 (m, 1 H, CH(CH_3)), 1.66-1.48 (m, 4 H), 1.22 (s, 3 H, C(CH_3)$_2$), 1.17 (s, 3 H, C(CH_3)$_2$), 1.09 (d, J = 6.8 Hz, 3 H, CH(CH_3)), 0.91 (d, J = 6.9 Hz, 3 H, CH(CH_3)), 0.90 (s, 9 H, SiC(CH_3)$_3$), 0.87 (s, 9 H, SiC(CH_3)$_3$), 0.12 (s, 3 H, SiC(CH_3)$_2$), 0.06, (s, 3 H, SiC(CH_3)$_2$), 0.06, (s, 3 H, SiC(CH_3)$_2$), 0.03 (s, 3 H, SiC(CH_3)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 215.9, 170.5, 164.7, 152.4, 137.0, 121.0, 116.6, 109.3, 109.2, 90.9, 54.0, 39.8, 39.7, 34.3, 27.1, 26.1, 26.0, 24.5, 19.2, 18.3, 18.1, 15.1, –3.4, –3.85, –4.0, –5.4; FAB HRMS (NBA/CsI) *m/e* 870.3361, M + Cs^+ calcd for $C_{39}H_{68}FNO_5SSi_2$ 870.3395.

Fluoride 35: Desilylation of 34. Fluoride **35** (7.4 mg, 74%) was obtained from compound **34** (14 mg, 19.7 μmol) according to the procedure described above for **24**. **35**: R_f = 0.31 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –74.0 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3417, 2935, 1732, 1682, 1508, 1469, 1385, 1301, 1250, 1066, 1037, 982 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.59 (s, 1 H, CH=CCH_3), 5.52 (m, 1 H, FCH_2C=CH), 5.23 (dd, J = 10.0, 1.5 Hz, CHOCO), 4.81 (dd, J = 47.5, 10.5 Hz, 1 H, CH_2F), 4.67 (dd, J = 47.5, 10.5 Hz, 1 H, CH_2F), 4.30 (bd, J = 10.0 Hz, 1 H, CHOH), 3.69 (bd, J = 2.0 Hz, 1 H, CHOH), 3.57 (bs, 1 H, OH), 3.16 (dq, J = 7.0, 2.0 Hz, 1 H, C(O)CH(CH_3), 3.04 (bs, 1 H, OH), 2.73 (obscured m, 1 H, C=CHCH_2CHO), 2.69 (s, 3 H, N=C(CH_3)S), 2.44 (dd, J = 14.4, 11.3 Hz, 1 H, CH_2COO), 2.32 (m, 2 H, CH_2C(CH_2F)=CH and C=CHCH_2CHO), 2.25 (dd, J = 14.4, 2.0 Hz, 1 H, CH_2COO), 2.12 (m, 1 H, CH_2C(CH_2F)=CH), 2.07 (s, 3 H, CH=C(CH_3)), 1.76 (m, 1 H, CH(CH_3)), 1.68 (m, 1 H), 1.41-1.22 (m, 3 H), 1.34 (s, 3 H, C(CH_3)$_2$), 1.18 (d, J = 7.0 Hz, 3 H, CH(CH_3)), 1.06 (s, 3 H, C(CH_3)$_2$), 1.01 (d, J = 7.0 Hz, 3 H, CH(CH_3)); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.5, 170.1, 165.1, 151.6, 138.7, 138.1, 138.0, 126.0, 125.9, 119.3, 115.6, 86.8, 85.5, 78.1, 73.7, 72.0, 53.6, 41.4, 39.5, 37.8, 32.1, 31.5, 27.6, 25.0, 22.8, 18.9, 17.6, 15.8, 15.7, 13.0; FAB HRMS (NBA/CsI) *m/e* 642.1690, M + Cs^+ calcd for $C_{27}H_{40}FNO_5S$ 642.1666.

Fluoride 37. Desilylation of 36. Fluoride **37** (4.0 mg, 84%) was obtained from compound **36** (7 mg, 9.5 μmol) by the procedure described above for **24**. **37**: R_f = 0.22 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –26.4 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3418, 2935, 1732, 1682, 1385, 1301, 1256, 1067, 1038 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.57 (s, 1 H, SCH=C), 6.57 (s, 1 H, CH=CCH_3), 5.38 (dd, J = 11.1, 1.1 Hz, 1 H,

CHOCO), 5.08 (s, 1 H, C=CH_2), 4.98 (dd, J = 48.4, 9.2 Hz, 1 H, CHF), 4.93 (s, 1 H, C=CH_2), 4.33 (bd, J = 10.9 Hz, 1 H, C*H*OH), 3.69 (bd, J = 6.1 Hz, 1 H, C*H*OH), 3.26 (m, 2 H, CHFCH_2), 3.03 (bs, 1 H, OH), 2.68 (s, 3 H, N=C(CH_3)S), 2.46 (dd, J = 11.0, 10.4 Hz, 1 H, CH_2COO), 2.39 (dd, J = 11.0, 2.4 Hz, 1 H, CH_2COO), 2.21 (m, 1 H, C(O)C*H*(CH_3), 2.03, (s, 3 H, CH=C(CH_3)), 1.78 (m, 1 H, C*H*(CH_3)), 1.72 (m, 1 H), 1.48-1.22 (m, 3 H), 1.37 (s, 3 H, C(CH_3)$_2$), 1.09 (d, J = 6.8 Hz, CH(CH_3)), 1.05 (s, 3 H, C(CH_3)$_2$), 0.93 (d, J = 7.1 Hz, 3 H, C(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.4, 169.9, 165.0, 151.6, 147.0, 146.9, 138.3, 119.0, 115.8, 110.3, 110.2, 90.7, 89.3, 75.8, 71.8, 53.8, 41.4, 40.0, 39.8, 39.2, 35.4, 35.1, 30.8, 29.2, 23.4, 21.2, 18.9, 17.6, 16.0, 15.5, 11.2; FAB HRMS (NBA/CsI) *m/e* 642.1691, M + Cs^+ calcd for $C_{27}H_{40}FNO_5S$ 642.1666.

Fluoride 35 and Dimeric Epothilone 38. To a solution of allylic alcohol **24** (27 mg, 53.2 μmol, 1.0 equiv.) in CH_2Cl_2 (1.5 mL) at –78 °C was added DAST (8 μL, 58.5 μmol). After stirring for 5 min, the reaction mixture was quenched by the careful addition of saturated aqueous $NaHCO_3$ solution (1.0 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 1 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo* to give a residue which was subjected to preparative thin layer chromatography (silica gel, 50% EtOAc in hexanes) to give fluoride **35** (17.7 mg, 65%) whose spectroscopic data were identical to those described above and dimeric species **38** (3.2 mg, 12%): **38**: R_f = 0.43 (silica gel, 80% EtOAc in hexanes); $[\alpha]^{22}_D$ –48.9 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3398, 2924, 2851, 1737, 1731, 1687, 1681, 1502, 1455, 1383, 1292, 1262, 1148, 1084, 979, 882, 735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (s, 2 H, SCH=C), 6.59 (s, 2 H, C*H*=CCH_3), 5.40 (dd, J = 10.0, 4.5 Hz, 2 H, C=C*H*CH_2), 5.22 (dd, J = 9.0, 1.0 Hz, 2 H, CHOCO), 4.29 (bd, J = 10.5 Hz, 2 H, C*H*OH), 3.91 (d, J = 12.0 Hz, 2 H, CH_2OCH_2), 3.69 (bs, OH), 3.67 (d, J = 12.0 Hz, 2 H, CH_2OCH_2), 3.15 (dq, J = 7.0, 2.0 Hz, 2 H, C(O)C*H*(CH_3)), 3.09 (bs, 2 H, OH), 2.68 (s, 3 H, N=C(CH_3)S), 2.67 (obscured m, 1 H, C=CHCH_2CHO), 2.45 (dd, J = 14.5, 11.0 Hz, 2 H, CH_2COO), 2.27 (m, 4 H, CH_2C(CH_2OCH_2)=CH and C=CHCH_2CHO), 2.26 (dd, J = 14.5, 2.5 Hz, 1 H, CH_2COO) 2.06 (m, 1 H, CH_2C(CH_2OH)=CH), 2.04 (s, 3 H, CH=C(CH_3)), 2.27-2.20 (m, 1 H, CH_2C(CH_2OH)=CH), 1.78 (m, 1 H, C(*H*)CH_3), 1.71, (m, 1 H), 1.34 (s, 3 H, C(CH_3)$_2$), 1.33-1.21 (m, 3 H), 1.17 (d, J = 7.0 Hz, 3 H, CH(CH_3)), 1.06 (s, 3 H, C(CH_3)$_2$), 1.00 (d, J = 7.0 Hz, 3 H, CH(CH_3)); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.6, 170.4, 165.1, 151.8, 139.2, 139.1, 124.0, 119.3, 115.7, 78.5, 73.8, 73.3, 72.2, 53.6, 41.5, 39.6, 38.1, 32.3, 31.8, 28.1, 25.2, 22.9, 19.0, 17.9, 16.1, 16.0, 13.3; FAB HRMS (NBA/CsI) *m/e* 997.5247, M + Cs^+ calcd for $C_{54}H_{80}N_2O_{11}S_2$ 997.5281.

Aldehyde 39. Oxidation of allylic alcohol 23. To a stirred solution of **23** (9.8 mg, 13.3 μmol, 1.0 equiv.) in Et_2O (1.0 mL) at room temperature was added in several portions solid MnO_2 (6.0 mg, 69 μmol, 5 equiv.). After stirring for 3 h, the reaction mixture was filtered through silica gel, eluting with 50% Et_2O in hexanes, to give enal **39** as a colorless foam (8.3 mg, 85%). R_f = 0.47 (silica gel, 60% Et_2O in hexanes); $[\alpha]^{22}_D$ –6.1 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 2927, 2855, 1743, 1693, 1463, 1254, 1156, 1020, 836, 775, 668 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.36 (s, 1 H, CHO), 6.99 (s, 1 H, SCH=C), 6.62 (s, 1 H, C*H*=CCH_3), 6.49 (dd, J = 9.0, 6.4 Hz, 1 H, CHO=C*H*), 5.36 (bm, 1 H, CHOCO), 4.11 (bm, 1 H, CHOSi), 3.88 (d, J = 9.0 Hz, CHOSi), 2.98 (m, 2 H, C(O)C*H*(CH_3) and C=CHCH_2CHO), 2.71 (s, 3 H, N=C(CH_3)S), 2.71 (obscured m, 1 H, C=CHCH_2CHO), 2.66 (bd, J = 14.6 Hz, 1 H, CH_2COO), 2.58 (dd, J = 14.7, 8.0 Hz, 1 H, CH_2COO), 2.31-2.24 (m, 2 H, CH_2C(CHO)=CH), 2.17 (s, 3 H, CH=C(CH_3)), 1.74 (m, 1 H, C*H*(CH_3)), 1.56 (m, 1 H), 1.36-

1.17 (m, 3 H), 1.16 (s, 3 H, $C(CH_3)_2$), 1.12 (s, 3 H, $C(CH_3)_2$), 1.09 (d, J = 6.8 Hz, 3 H, $CH(CH_3)$), 0.93 (d, J = 6.8 Hz, 3 H, $CH(CH_3)$), 0.92 (s, 9 H, $SiC(CH_3)_3$), 0.82 (s, 9 H, $SiC(CH_3)_3$), 0.08 (s, 6 H, $Si(CH_3)_2$), 0.05 (s, 3 H, $Si(CH_3)_2$), –0.1 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 215.4, 195.2, 170.8, 164.9, 152.1, 147.6, 147.0, 137.0, 120.5, 116.7, 77.6, 75.4, 65.3, 53.5, 40.1, 37.8, 32.9, 31.5, 27.0, 26.2, 26.0, 25.1, 24.7, 19.2, 18.5, 18.4, 17.9, 15.1, –3.4, –3.5, –3.8, –5.5; FAB HRMS (NBA/CsI) *m/e* 866.3304, M + Cs^+ calcd for $C_{39}H_{67}NO_6SSi_2$ 866.3282.

Alkyne 40. To a stirred solution of TMS-diazomethane (28 μL, 2.0 M solution in THF, 56 μmol, 1.3 equiv.) in THF (0.5 mL) at –78 °C was added *n*-BuLi (33 μL, 1.5 M solution in hexanes, 49.5 μmol) and the mixture was stirred for 30 min. A solution of aldehyde **39** (28 mg, 38.14 μmol, 1.0 equiv.) was then added dropwise over 5 min. The reaction was stirred at –78 °C for one hour and then at 0 °C for 30 min. Saturated aqueous NH_4Cl (2.0 mL) was added and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 2 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (20% Et_2O in hexanes) provided pure alkyne **40** (21.0 mg, 75%): R_f = 0.71 (silica gel, 60% Et_2O in hexanes); $[\alpha]^{22}_D$ –37.6 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 2929, 2855, 1742, 1697, 1472, 1383, 1303, 1252, 1180, 1158, 1102, 1067, 1019, 984, 938, 917, 876, 835, 775, 734 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.57 (s, 1 H, CH=CCH_3), 5.91 (dd, J = 10.0, 7.1 Hz, C=$CHCH_2$), 5.03 (bd, J = 9.9 Hz, 1 H, CHOCO), 4.02 (d, J = 9.7 Hz, 1 H, CHOSi), 3.88 (d, J = 8.7 Hz, 1 H, CHOSi), 2.98 (dq, J = 8.6, 6.9 Hz, C(O)$CH(CH_3)$), 2.81-2.74 (m, 2 H, CH_2COO and C=$CHCH_2CHO$), 2.78 (s, 1 H, CCH), 2.68 (dd J = 16.4, 10.2 Hz, CH_2COO), 2.67 (s, 3 H, N=$C(CH_3)$S), 2.46 (m, 1 H, C=$CHCH_2CHO$), 2.20 (m, 1 H, $CH_2C(CCH)$=CH), 2.10 (s, 3 H, CH=$C(CH_3)$), 1.92 (m, 2 H, $CH_2C(CCH)$=CH and CH_2CH_2), 1.61 (m, 1 H, $CH(CH_3)$), 1.49 (m, 1 H), 1.26 (m, 2 H), 1.18 (s, 3 H, $C(CH_3)_2$), 1.14 (s, 3 H, $C(CH_3)_2$), 1.08 (d, J = 6.7 Hz, $CH(CH_3)$), 0.97 (d, J = 6.7 Hz, $CH(CH_3)$), 0.93 (s, 9 H, $SiC(CH_3)_3$), 0.84 (s, 9 H, $SiC(CH_3)_3$), 0.10 (s, 3 H, $Si(CH_3)_2$), 0.09 (s, 3 H, $Si(CH_3)_2$), 0.07 (s, 3 H, $Si(CH_3)_2$), -0.07 (s, 3 H, $Si(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 215.0, 171.1, 164.7, 152.3, 137.9, 132.3, 119.9, 116.3, 85.1, 78.8, 76.4, 75.6, 53.4, 39.1, 32.6, 31.1, 30.7, 27.7, 26.3, 26.2, 24.6, 24.2, 19.3, 18.6, 18.5, 17.8, 15.2, 14.2, –3.4, –3.6, 3.7, –5.7; FAB HRMS (NBA/CsI) *m/e* 862.3368, M + Cs^+ calcd for $C_{40}H_{67}NO_5SSi_2$ 862.3333.

Alkyne 41. Deprotection of 40. Alkyne **41** (5.0 mg, 91%) was obtained from compound **41** (8.0 mg, 10.9 μmol) according to the procedure described above for **24**. **41**: R_f = 0.55 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –94.6 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3288, 2925, 1732, 1683, 1505, 1455, 1384, 1261, 1149, 1047, 979, 736, 668 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.60 (s, 1 H, CH=CCH_3), 5.92 (dd, J = 10.1, 5.4 Hz, C=$CHCH_2$), 5.25 (dd, J = 9.6, 1.7 Hz, CHOCO), 4.29 (dd, J = 11.0, 0.9 Hz, 1 H, $CHOH$), 3.71(bs, 1 H, $CHOH$), 3.57 (bs, 1 H, OH), 3.12 (dq, J = 18.0, 6.8 Hz, 1 H, C(O)$CH(CH_3)$), 3.06 (bs, 1 H, OH), 2.79 (s, 1 H, CCH), 2.72 (m, 2 H, C=$CHCH_2CHO$), 2.68 (s, 3 H, N=$C(CH_3)$S), 2.47 (dd, J = 14.7, 11.3 Hz, CH_2COO), 2.34 (m, 2 H, $CH_2C(CCH)$=CH), 2.29 (dd, J = 14.7, 2.7 Hz, CH_2COO), 2.07 (obscured m, 1 H, CH_2CH_2), 2.06 (s, 3 H, CH=$C(CH_3)$), 1.79 (m, 2 H, $CH(CH_3)$ and CH_2CH_2), 1.37-1.21 (m, 2 H), 1.33 (s, 3 H, $C(CH_3)_2$), 1.19 (d, J = 7.9 Hz, 3 H, $CH(CH_3)$), 1.06 (s, 3 H, $C(CH_3)_2$), 1.00 (d, J = 7.1 Hz, 3 H, $C(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 215.7, 170.1, 165.1, 158.5, 151.7, 138.3, 134.4, 125.0, 119.5, 115.8, 84.6,

77.9, 75.7, 74.2, 72.1, 53.6, 41.9, 39.5, 32.7, 30.3, 25.6, 23.0, 19.0, 17.7, 16.0, 15.3, 13.4; FAB HRMS (NBA/CsI) *m/e* 634.1625, M + Cs^+ calcd for $C_{28}H_{39}NO_5S$ 634.1603.

Diene 42. Wittig Olefination of Aldehyde 39. To a stirred suspension of methyl triphenylphosphonium bromide (60.0 mg, 168 μmol, 20 equiv.) in THF (1.0 mL) at 0 °C was added a solution of LiHMDS (160 μL, 1.0 M solution in THF, 160 μmol, 0.67 mmol, 19.0 equiv.) and the bright yellow solution was stirred for an additional 30 min. To a stirred solution of **39** (6.0 mg, 8.2 mmol, 1.0 equiv.) in THF (0.5 mL) at 0 °C was added an aliquot (250 μL, 5.0 equiv.) of the ylid solution. Methanol (0.1 mL) was added and the solvents were removed *in vacuo*. Purification by preparative thin layer chromatography (40% Et_2O in hexanes) provided diene **42** (5.1 mg, 85%) R_f = 0.71 (silica gel, 60% Et_2O in hexanes); $[\alpha]^{22}_D$ –40.0 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 2931, 2856, 1742, 1695, 1466, 1383, 1254, 1186, 1157, 1098, 1020, 987, 873, 834, 775 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.57 (s, 1 H, C*H*=CCH_3), 6.20 (dd, *J* = 17.6, 11.0 Hz, 1 H, C*H*$_2$=CH=C=CH), 5.47 (dd, *J* = 10.0, 6.5 Hz, 1 H, CH_2=CH=C=C*H*), 5.19 (obscured m, 1 H, CHOCO), 5.13 (d, *J* = 17.6 Hz, 1 H, CH_2=C*H*=C=CH), 4.97 (d, *J* = 11.0 Hz, 1 H, CH_2=C*H*=C=CH), 4.11 (bd, *J* = 9.2 Hz, 1 H, CHOSi), 3.87 (d, *J* = 8.9 Hz, 1 H, CHOSi), 3.03 (dq, *J* = 8.0, 6.4 Hz, 1 H, C(O)C*H*(CH_3)), 2.77 (ddd, *J* = 19.5, 9.7, 9.7 Hz, 1 H, C=CHC*H*$_2$CHO), 2.71 (s, 3 H, N=C(CH_3)S), 2.64 (m, 2 H, C*H*$_2$C=CH and CH_2COO), 2.13 (s, 3 H, CH=C(C*H*$_3$)), 1.74 (m, 1 H, C*H*(CH_3)), 1.58 (m, 2 H), 1.37-1.22 (m, 2 H), 1.17 (s, 3 H, C(CH_3)$_2$), 1.11 (s, 3 H, C(CH_3)$_2$), 1.09 (d, *J* = 6.7 Hz, 6 H, 2 x CH(C*H*$_3$)), 0.93 (s, 9 H, SiC(CH_3)$_3$), 0.82 (s, 9 H, SiC(CH_3)$_3$), 0.10 (s, 3 H, Si(CH_3)$_2$), 0.07 (s, 3 H, Si(CH_3)$_2$), 0.06 (s, 3 H, Si(CH_3)$_2$), –0.12 (s, 3 H, Si(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 215.4, 170.9, 164.5, 152.3, 142.6, 139.8, 125.9, 119.7, 116.1, 112.1, 79.1, 79.0, 75.5, 53.4, 47.7, 39.9, 37.4, 32.9, 31.3, 29.6, 27.9, 26.9, 26.2, 26.0, 24.4, 19.1, 18.5, 18.3, 17.7, 15.0, –3.4, –3.8, –3.9, –5.6; FAB HRMS (NBA/CsI) *m/e* 864.3523, M + Cs^+ calcd for $C_{40}H_{69}NO_5SSi_2$ 864.3489.

Diene 43. Deprotection of 42. Diene **43** (3.0 mg, 85%) was obtained from compound **34** (5.0 mg, 6.8 μmol) according to the procedure described above for **24**. **43**: R_f = 0.49 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –17.4 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3502, 2928, 1733, 1687, 1507, 1463, 1383, 1295, 1256, 1183, 1150, 1081, 1012, 984, 903, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.62 (s, 1 H, C*H*=CCH_3), 6.23 (dd, *J* = 17.5, 10.5 Hz, 1 H, C*H*$_2$=CH=C=CH), 5.45 (dd, *J* = 10.0, 5.0 Hz, 1 H, CH_2=CH=C=C*H*), 5.25 (dd, *J* = 7.5, 1.2 Hz, 1 H, CHOCO), 5.16 (d, *J* = 17.5 Hz, 1 H, CH_2=C*H*=C=CH), 5.00 (d, *J* = 11.0 Hz, 1 H, CH_2=C*H*=C=CH), 4.35 (d, *J* = 9.5 Hz, 1 H, C*H*OH), 3.70 (d, *J* = 2.0 Hz, 1 H, C*H*OH), 3.19 (dq, *J* = 7.0, 2.5 Hz, 1 H, C(O)C*H*(CH_3)), 3.01 (bs, 1 H, OH), 2.73 (ddd, *J* = 20.0, 10.0, 10.0 Hz, 1 H, C=CHC*H*$_2$CHO), 2.70 (s, 3 H, N=C(CH_3)S), 2.44 (dd, *J* = 14.0, 10.5 Hz, CH_2COO), 2.43-2.26 (m, 3 H, C=CHC*H*$_2$CHO and C*H*$_2$C=CH), 2.23 (dd, *J* = 14.0, 2.5 Hz, 1 H, CH_2COO), 2.01 (s, 3 H, CH=C(C*H*$_3$)), 1.77-1.60 (m, 2 H), 1.44-1.22 (m, 3 H), 1.36 (s, 3 H, C(CH_3)$_2$), 1.17 (d, *J* = 6.7 Hz, 3 H, CH(C*H*$_3$)), 1.06 (s, 3 H, C(CH_3)$_2$), 1.02 (d, *J* = 7.0 Hz, C(CH_3)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.7, 171.1, 166.4, 151.7, 141.1, 139.6, 127.7, 119.2, 115.6, 112.2, 78.5, 73.5, 72.0, 53.7, 41.4, 39.8, 37.7, 33.0, 31.4, 29.7, 26.6, 25.9, 22.9, 18.9, 17.3, 15.9, 12.9; FAB HRMS (NBA/CsI) *m/e* 636.1779, M + Cs^+ calcd for $C_{28}H_{41}NO_5S$ 636.1760.

Compound 44. Hydrogenation of 42. To a stirred solution of diene **42** (18.0 mg, 24.6 μmol) in EtOAc (1.5 mL) was added Lindlar catalyst (5.0 mg). Air was purged from the flask by vacuum before the introduction of a hydrogen atmosphere. After stirring vigorously for 50 min, the solution was filtered through celite and concentrated *in vacuo*. Purification by preparative thin layer chromatography (20% Et_2O in hexanes) gave pure **44** (9.0 mg, 50%): R_f = 0.88 (silica gel, 60% Et_2O in hexanes); $[\alpha]^{22}_D$ –26.7 (*c* 3.0, $CHCl_3$); IR (thin film) ν_{max} 2950, 2845, 1738, 1691, 1461, 1378, 1247, 1153, 1096, 1012, 981, 829, 772 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.57 (s, 1 H, C*H*=CCH$_3$), 5.17 (dd, *J* = 8.4, 7.9 Hz, 1 H, C=C*H*CH$_2$), 5.00 (bd, *J* = 10.1 Hz, 1 H, CHOCO), 4.04 (bd, *J* = 9.8 Hz, 1 H, CHOSi), 3.89 (d, *J* = 9.0 Hz, 1 H, CHOSi), 3.03 (dq, *J* = 8,8, 7.0 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.80 (d, *J* = 15.8 Hz, 1 H, CH$_2$COO), 2.71 (s, 3 H, N=C(CH$_3$)S), 2.68 (obscured m, 2 H, CH$_2$COO and C=CHC*H*$_2$CHO), 2.02 (m, 1 H, C=CHC*H*$_2$CHO), 1.77 (s, 3 H, CH=C(C*H*$_3$)), 2.11-1.98 (m, 2 H, C*H*$_2$C=CH), 2.01 (q, *J* = 7.5 Hz, 2 H, C*H*$_2$CH$_3$), 1.81 (m, 1 H, C*H*(CH$_3$)), 1.74-1.49 (m, 4 H), 1.19 (s, 3 H, C(CH$_3$)$_2$), 1.13 (s, 3 H, C(CH$_3$)$_2$), 1.10 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.98 (d, *J* = 6.9 Hz, 3 H, CH(C*H*$_3$)), 0.98 (t, *J* = 7.4 Hz, 3 H, CH$_2$C*H*$_3$), 0.95 (s, 9 H, SiC(CH$_3$)$_3$), 0.84 (s, 9 H, SiC(CH$_3$)$_3$), 0.11 (s, 3 H, Si(CH$_3$)$_2$), 0.07 (s, 6 H, Si(CH$_3$)$_2$), –0.12 (s, 3 H, Si(CH$_3$)$_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 215.1, 171.1, 164.5, 152.4, 145.9, 138.7, 119.2, 117.2, 115.8, 79.8, 76.1, 53.3, 48.1, 39.1, 37.5, 32.3, 31.3, 29.9, 28.7, 27.4, 26.2, 26.0, 24.2, 19.3, 19.1, 18.6, 18.5, 15.2, 12.3, –3.4, –3.8, –3.9, –5.8; FAB HRMS (NBA/CsI) *m/e* 866.3671, M + Cs^+ calcd for $C_{40}H_{71}NO_5SSi_2$ 866.3646.

Compound 45. Deprotection of 44. Compound **45** (2.6 mg, 75%) was obtained from compound **44** (5.0 mg, 6.8 μmol) according to the procedure described above for **24**: **45**: R_f = 0.34 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –64.3 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3454, 2987, 2928, 1728, 1583, 1504, 1460, 1375, 1296, 1251, 1186, 1151, 1047, 977, 749 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.22 (dd, *J* = 8.5, 1.1 Hz, 1 H, CHOCO), 5.13 (dd, *J* = 10.1, 4.7 Hz, 1 H, C=C*H*CH$_2$), 4.31 (d, *J* = 10.7 Hz, 1 H, C*H*OH), 3.72 (bs, 1 H, OH), 3.55 (d, *J* = 4.8 Hz, 1 H, C*H*OH), 3.17 (dq, *J* = 6.8, 2.2 Hz, 1 H, C(O)C*H*(CH$_3$)), 3.03 (bs, 1 H, OH), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.66 (ddd, *J* = 15.1, 10.1, 10.1 Hz, 1 H, C=CHC*H*$_2$CHO), 2.45 (dd, *J* = 14.6, 11.2 Hz, 1 H, CH$_2$COO), 2.29 (m, 2 H, C=CHC*H*$_2$CHO and CH$_2$COO), 2.07 (s, 3 H, CH=C(C*H*$_3$)), 2.05-1.91 (m, 2 H, C*H*$_2$C=CH), 2.08 (s, 3 H, CH=C(C*H*$_3$)), 1.99 (q, *J* = 7.5 Hz, 2 H, C*H*$_2$CH$_3$), 1.76 (m, 1 H, C*H*(CH$_3$)), 1.64 (m, 1 H), 1.39-1.26 (m, 3 H), 1.35 (s, 3 H, C(CH$_3$)$_2$), 1.19 (d, *J* = 6.5 Hz, 3 H, CH(C*H*$_3$)), 1.07 (s, 3 H, C(CH$_3$)$_2$), 1.02 (d, *J* = 7.0 Hz, 3 H, CH(C*H*$_3$)), 0.969 (t, *J* = 7.5 Hz, 3 H, CH$_2$C*H*$_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.7, 170.3, 143.9, 119.1, 115.4, 78.8, 73.8, 72.0, 53.5, 41.4, 39.6, 38.0, 32.4, 31.6, 29.7, 28.7, 25.3, 22.8, 18.9, 17.7, 15.9, 15.7, 13.1, 12.6; FAB HRMS (NBA) *m/e* 506.2956, M + H^+ calcd for $C_{28}H_{43}NO_5S$ 506.2940.

Epoxides 46 and 46′. Epoxidation of 45. To a stirred solution of olefin **45** (31.0 mg, 61.3 μmol, 1.0 equiv.) in MeCN (4 mL) at 0 °C was added sequentially disodium EDTA solution (1.2 mL,0.4 mM solution in water, 0.48 μmol) and 1,1,1-trifluoromethyl acetone (2.0 mL, 14.2 mmol, 120 equiv.). A mixture of solid oxone:$NaHCO_3$ (800 mg:180 mg) was then added potionwise until the reaction was judged to be complete by TLC. The reaction mixture was treated with excess Me_2S (100 μL) and water (500 μL) and was then extracted with EtOAc (4 x 2 mL). The combined organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Purification by preparative thin layer chromatography (70% EtOAc in hexanes) provided pure epoxides **46**

(18.4 mg, 58%) and its diastereomeric epoxide **46′** (6.1 mg, 19%); **46**: R_f = 0.30 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –45.6 (*c* 0.8, $CHCl_3$); IR (thin film) ν_{max} 3466, 2959, 2876, 1730, 1683, 1459, 1370, 1253, 1146, 1063, 975, 887, 751, 663 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.60 (s, 1 H, C*H*=CCH$_3$), 5.42 (dd, *J* = 7.4, 2.8 Hz, 1 H, CHOCO), 4.36 (bs, 1 H, OH), 4.22 (bs, 1 H, C*H*OH), 3.76 (bs, 1 H, C*H*OH), 3.33 (dq, *J* = 6.8, 6.8 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.82 (dd, *J* = 7.2, 5.0 Hz, 1 H, C*H*(O)CCH$_2$CH$_3$), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.65 (bs, 1 H, OH), 2.54 (dd, *J* = 13.8, 10.4 Hz, 1 H, CH$_2$COO), 2.35 (dd, *J* = 13.8, 3.0 Hz, 1 H, CH$_2$COO), 2.09 (s, 3 H, CH=C(C*H*$_3$)), 2.03 (obscured m, 1 H, (CH$_2$CH$_3$)COCHC*H*$_2$CHO), 1.94 (ddd, *J* = 15.1, 7.6 Hz, 1 H, (CH$_2$CH$_3$)COCHC*H*$_2$CHO), 1.88-1.69 (m, 3 H), 1.60 (m, 2 H, C*H*$_2$CH$_3$), 1.63-1.34 (m, 4 H), 1.37 (s, 3 H, C(CH$_3$)$_2$), 1.16 (d, *J* = 6.9 Hz, 3 H, CH(C*H*$_3$)), 1.07 (s, 3 H, C(CH$_3$)$_2$), 1.00 (d, *J* = 7.0 Hz, CH(C*H*$_3$)), 0.91 (t, *J* = 7.5 Hz, 3 H, CH$_2$C*H*$_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.6, 170.5, 165.1, 151.6, 137.2, 119.4, 116.0, 76.4, 74.2, 72.6, 64.2, 60.2, 53.0, 42.8, 39.0, 36.2, 31.7, 30.6, 29.4, 28.6, 22.0, 21.1, 19.5, 19.0, 17.0, 15.9, 13.6, 8.6; FAB HRMS (NBA/CsI) *m/e* 654.1890, M + H^+ calcd for $C_{28}H_{43}NO_6S$ 654.1865. **46′**: R_f = 0.28 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –18.0 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3466, 2956, 2867, 1729, 1690, 1458, 1380, 1252, 1147, 1047, 886, 792, 731 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.98 (s, 1 H, SCH=C), 6.61 (s, 1 H, C*H*=CCH$_3$), 5.67 (d, *J* = 9.1 Hz, 1 H, CHOCO), 4.17 (bd, *J* = 10.7 Hz, 1 H, C*H*OH), 4.06 (bs, 1 H, C*H*OH), 3.82 (bs, 1 H, OH), 3.33 (dd, *J* = 7.1, 7.1 Hz, 1 H, C(O)C*H*(CH$_3$)), 3.05 (dd, *J* = 10.8, 3.2 Hz, 1 H, C*H*(O)CCH$_2$CH$_3$), 2.89 (bs, 1 H, OH), 2.72 (s, 3 H, N=C(CH$_3$)S), 2.47 (dd, *J* = 12.1, 12.1 Hz, 1 H, CH$_2$COO), 2.42 (dd, *J* = 12.2, 2.4 Hz, 1 H, CH$_2$COO), 2.12 (s, 3 H, CH=C(C*H*$_3$)), 2.09 (m, 1 H, (CH$_2$CH$_3$)COCHC*H*$_2$CHO), 1.85 (m, 4 H, (CH$_2$CH$_3$)C(O)CHC*H*$_2$CHO, C*H*(CH$_3$) and C*H*$_2$CH$_3$), 1.50-1.39 (m, 3 H), 1.37 (s, 3 H, C(CH$_3$)$_2$), 1.31-1.13 (m, 3 H), 1.09 (d, *J* = 7.0 Hz, 3 H, CH(C*H*$_3$)), 1.04 (s, 3 H, C(CH$_3$)$_2$), 0.93 (d, *J* = 6.5 Hz, 3 H, CH(C*H*$_3$)), 0.88 (t, *J* = 7.5 Hz, 3 H, CH$_2$C*H*$_3$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 222.5, 170.4, 169.2, 153.7, 138.0, 119.4, 116.3, 76.3, 74.2, 70.8, 65.5, 63.3, 51.7, 42.4, 38.7, 38.1, 33.1, 32.0, 28.4, 28.3, 22.1, 21.1, 18.8, 18.6, 16.0, 15.2, 12.3, 9.2; FAB HRMS (NBA/CsI) *m/e* 654.1887, M + H^+ calcd for $C_{28}H_{43}NO_6S$ 654.1865.

Aldehyde 47. Selective Oxidation of Triol 24. To a solution of alcohol **24** (25 mg, 49 μmol) in Et_2O (1.0 mL, 0.05 M) at 25 °C, was added MnO_2 (21 mg, 0.24 mmol, 5.0 equiv.). The resulting suspension was stirred for 3 h, filtered over celite and the solvent removed under reduced pressure. Purification by preparative thin layer chromatography (5% MeOH in CH_2Cl_2) provided pure aldehyde **47** (22.2 mg, 89%): R_f = 0.50 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –82.2 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3449, 2934, 1735, 1683, 1460, 1378, 1254, 1150, 1047 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.38 (s, 1 H, CHO), 6.99 (s, 1 H, SCH=C), 6.65 (s, 1 H, C*H*=CCH$_3$), 6.44 (dd, *J* = 9.8, 5.4 Hz, 1 H, CHOC=C*H*CH$_2$), 5.40 (d, *J* = 7.5 Hz, 1 H, CH$_2$COOC*H*), 4.30 (m, 1 H), 3.74 (d, *J* = 6.1 Hz, 1 H, C*H*OH), 3.65 (bs, 1 H, OH), 3.15 (dq, *J* = 6.8, 2.3 Hz, 1 H, C(O)C*H*CH$_3$), 2.98 (s, 1 H, OH), 2.95 (ddd, *J* = 15.3, 9.7, 9.6 Hz, 1 H, C*H*$_2$CH=CCHO), 2.69 (s, 3 H, N=C(CH$_3$)S), 2.64 (ddd, *J* = 15.3, 7.5, 5.4 Hz, 1 H, C*H*$_2$CH=CCHO), 2.44 (dd, *J* = 14.3, 11.2 Hz, 1 H, C*H*$_2$COOCH), 2.45-2.37 (m, 1 H), 2.23 (dd, *J* = 14.3, 2.5 Hz, 1 H, C*H*$_2$COOCH), 2.25-2.16 (m, 1 H), 2.11 (s, 3 H, CH=CC*H*$_3$), 1.88-1.79 (m, 2 H), 1.35 (s, 3 H, C(CH$_3$)$_2$), 1.32-1.22 (m, 4 H), 1.16 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 1.05 (s, 3 H, C(CH$_3$)$_2$), 0.99 (d, *J* = 7.0 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.4, 194.8, 170.0, 165.3, 151.4, 148.7, 145.7, 137.8, 119.8, 116.1, 77.3, 73.5, 72.0, 53.7, 41.6, 39.6, 33.3,

31.3, 25.4, 24.6, 22.9, 19.0, 17.4, 16.0, 15.9, 12.9; FAB HRMS (NBA/CsI) *m/e* 638.1526, M + Cs^+ calcd for $C_{27}H_{39}NO_6S$ 638.1552.

Carboxylic Acid 48. Oxidation of Aldehyde 47. Aldehyde **47** (12 mg, 0.024 mmol), *t*-BuOH (1.0 mL), isobutylene (0.75 mL, 2 M solution in THF, 0.15 mmol), H_2O (0.2 mL), $NaClO_2$ (10 mg, 0.14 mmol, 6.0 equiv.) and NaH_2PO_4 (7 mg, 0.07 mmol, 3.0 equiv.) were combined and stirred at 0 °C for 1 h. The reaction mixture was concentrated under reduced pressure and the residue was subjected to flash column chromatography (silica gel, 6% MeOH in CH_2Cl_2) to afford pure carboxylic acid **48** (11.8 mg, 98%): R_f = 0.50 (silica gel, 10% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –51.0 (*c* 0.6, $CHCl_3$); ^1H NMR (600 MHz, CD_3OD) δ 7.23 (s, 1 H, SCH=C), 6.78 (dd, *J* = 9.1, 6.6 Hz, 1 H, HOOCC=C*H*CH_2), 6.64 (s, 1 H, C*H*=CCH_3), 5.39 (d, *J* = 8.3 Hz, 1 H, CH_2COOCH), 4.33 (dd, *J* = 9.6, 4.7 Hz, 1 H, C*H*OH), 3.63 (dd, *J* = 6.7, 3.0 Hz, 1 H, C*H*OH), 3.24 (dq, *J* = 13.3, 6.6 Hz, 1 H, C(O)C*H*CH_3), 3.20 (dd, *J* = 14.7, 7.2 Hz, 1 H, CH_2COO), 2.84 (ddd, *J* = 15.2, 9.0, 8.9 Hz, 1 H, CH_2CH=CCOOH), 2.69 (s, 3 H, N=C(CH_3)S), 2.55 (ddd, *J* = 15.1, 6.5, 2.3 Hz, 1 H, CH_2CH=CCHO), 2.44-2.33 (m, 4 H), 1.47-1.15 (obscured m, 3 H), 1.30 (s, 3 H, C(CH_3)$_2$), 1.17 (d, *J* = 6.8 Hz, 3 H, CH(CH_3)), 0.99 (d, *J* = 7.0 Hz, 3 H, CH(CH_3)), 0.98 (s, 3 H, C(CH_3)$_2$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 219.7, 171.6, 170.9, 166.8, 153.1, 139.1, 138.2, 136.6, 120.3, 117.6, 79.3, 76.9, 72.1, 54.9, 48.2, 45.4, 40.4, 38.3, 33.8, 31.2, 28.4, 27.9, 23.1, 19.4, 18.7, 17.7, 15.8, 9.3; FAB HRMS (NBA/CsI) *m/e* 654.1478, M + Cs^+ calcd for $C_{27}H_{39}NO_6S$ 654.1502.

Ester 49. Esterification of Carboxylic Acid 48. To a solution of acid **48** (13 mg, 0.024 mmol) in EtOAc (0.5 mL, 0.05 M) at 0 °C, was added CH_2N_2 (solution in Et_2O, excess). The solution was stirred for 15 min, excess CH_2N_2 was removed by bubbling argon, and the solvent was removed under reduced pressure. Purification by preparative thin layer chromatography (60% EtOAc in hexanes) provided pure ester **49** (12.5 mg, 95%): R_f = 0.60 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –65.9 (*c* 0.4, $CHCl_3$); IR (thin film) ν_{max} 3442, 2936, 1712, 1441, 1289, 1260, 1191, 1146, 1047 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.70 (dd, *J* = 10.6, 5.0 Hz, 1 H, CH_3OOCC=C*H*CH_2), 6.61 (s, 1 H, C*H*=CCH_3), 5.29 (d, *J* = 6.8 Hz, 1 H, CH_2COOCH), 4.25 (b, 1 H), 3.72 (s, 1 H, $COOCH_3$), 3.74-3.70 (obscured, 1 H, C*H*OH), 3.54 (bs, 1 H, OH), 3.15 (dq, *J* = 6.7, 2.8 Hz, 1 H, C(O)C*H*CH_3), 2.99 (s, 1 H, OH), 2.95 (ddd, *J* = 15.3, 10.4, 10.1 Hz, 1 H, CH_2CH=CCHO), 2.68 (s, 3 H, N=C(CH_3)S), 2.44 (dd, *J* = 14.3, 11.2 Hz, 1 H, CH_2COOCH), 2.33-2.25 (m, 1 H), 2.23 (dd, *J* = 14.3, 2.5 Hz, 1 H, CH_2COOCH), 2.08 (s, 3 H, CH=CCH_3), 1.83-1.69 (m, 3 H), 1.44-1.35 (m, 1 H), 1.34 (s, 3 H, C(CH_3)$_2$), 1.34-1.22 (m, 3 H), 1.17 (d, *J* = 6.8 Hz, 3 H, CH(CH_3)), 1.05 (s, 3 H, C(CH_3)$_2$), 1.00 (d, *J* = 7.1 Hz, 3 H, CH(CH_3)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.3, 169.9, 167.7, 165.1, 151.5, 138.4, 137.0, 135.0, 119.7, 115.8, 77.8, 73.6, 72.2, 53.7, 51.8, 41.6, 39.8, 37.8, 33.5, 31.7, 27.3, 26.4, 22.9, 19.1, 17.6, 16.1, 16.0, 13.1; FAB HRMS (NBA/CsI) *m/e* 744.1998, M + Cs^+ calcd for $C_{27}H_{39}NO_6S$ 744.1971.

Azide 51. Tosylation of 24 and Displacement with Sodium Azide. To a stirred solution of alcohol **50** (5.0 mg, 9.9 μmol) in CH_2Cl_2 (0.5 mL) at 0 °C was added Et_3N (4 μL, 28.5 μmol, 3.0 equiv.) followed by tosyl chloride (2.5 mg, 14.2 μmol) and 4-DMAP (1.0 mg, 8.8 μmol, 1.0 equiv.). The reaction mixture was warmed to room temperature and was stirred for 2 h before saturated aqueous NH_4Cl (0.5 mL) was added.

The layers were separated and the aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic extracts were combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was dissolved in DMF (0.5 mL) and NaN_3 (2.0 mg, 29.7 μmol, 3.0 equiv.) was added in one portion. The reaction mixture was stirred for 10 h, before being poured into saturated aqueous NH_4Cl solution (2 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 x 2 mL). The combined organic extracts were, dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (5% MeOH in CH_2Cl_2) provided azide **51**: R_f = 0.50 (silica gel, 80% EtOAc in hexanes); IR (thin film) ν_{max} 3403, 2931, 2101, 1732, 1688, 1504, 1463, 1383, 1252, 1154, 1064, 1009, 979, 737 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.95 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.45 (dd, J = 10.1, 5.1 Hz, 1 H, C=C*H*CH$_2$), 5.24 (dd, J = 9.6, 1.6 Hz, 1 H, CHOCO), 4.31 (bd, J = 10.7 Hz, 1 H, C*H*OH), 3.71 (d, J = 13.2 Hz, 1 H, C*H*$_2$N$_3$), 3.70 (obscured m, 2 H, C*H*OH and OH), 3.64 (d, J = 13.2 Hz, 1 H, C*H*$_2$N$_3$), 3.14 (dq, J = 6.8, 2.1 Hz, 1 H, C(O)C*H*CH$_3$), 3.08 (bs, 1 H, OH), 2.68 (obscured m, 2 H, C=CHC*H*$_2$CHO), 2.67 (s, 3 H, N=C(CH$_3$)S), 2.43 (dd, J = 14.5, 3.4 Hz, CH$_2$COO), 2.41-2.29 (2 H, m, C*H*$_2$C(CN$_3$)=CH), 2.25 (dd, J = 14.5, 2.6 Hz, 1 H, CH$_2$COO), 2.06 (s, 3 H, CH=CC*H*$_3$), 1.62 (m, 1 H, C*H*(CH$_3$), 1.59 (m, 1 H), 1.38-1.14 (m, 3 H), 1.32 (s, 3 H, C(CH$_3$)$_2$), 1.17 (d, J = 6.8 Hz, 3 H, CH(C*H*$_3$)), 1.05 (s, 3 H, C(CH$_3$)$_2$), 1.00 (d, J = 7.1 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.4, 170.1, 165.0, 151.6, 138.5, 136.5, 126.4, 119.2, 115.7, 78.1, 73.8, 72.1, 56.8, 53.8, 41.5, 39.7, 38.1, 32.4, 31.7, 29.2, 25.2, 23.0, 19.1, 18.0, 16.0, 15.8, 13.2.

Amine 52. Reduction of Azide 51. To a stirred solution of **51** (4.0 mg, 7.7 μmol) in a mixed solvent system of THF:H_2O (1:1, 0.5 mL) was added Ph_3P (4.0 mg, 15.4 mmol, 2.0 equiv.). After heating to 60 °C for 8 h, the reaction mixture was poured into brine (2 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 x 2 mL). The combined organic extracts were dried ($MgSO_4$), filtered and evaporated *in vacuo*. Purification by preparitive thin layer chromatography (EtOAc) of the resulting residue gave amine **52** (2.7 mg. 70%): R_f = 0.26 (silica gel, EtOAc); $[\alpha]^{22}_D$ –69.8 (*c* 0.2, $CHCl_3$); ^1H NMR (600 MHz, CD_3OD) δ 7.21 (s, 1 H, SCH=C), 6.58 (s, 1 H, C*H*=CCH$_3$), 5.42 (dd, J = 8.0, 8.0 Hz, 1 H, C=C*H*CH$_2$), 5.27 (dd, J = 9.1, 1.1 Hz, 1 H, CHOCO), 4.27 (dd, J = 10.1, 3.9 Hz, 1 H, C*H*OH), 3.64 (dd, J = 6.8, 3.0 Hz, 1 H, C*H*OH), 3.23 (m, 3 H, C(O)C*H*CH$_3$ and C=CHC*H*$_2$CHO), 2.76 (ddd, J = 18.4, 9.3, 9.3 Hz, 1 H, C*H*$_2$C(CH$_2$NH$_2$)=CH), 2.68 (s, 3 H, N=C(CH$_3$)S), 2.41 (dd, J = 6.2, 2.2 Hz, 1 H, CH$_2$COO), 2.34 (m, 1 H, C*H*$_2$C(CH$_2$OH)=CH), 2.08 (m, 2 H, C*H*$_2$C(CH$_2$OH)=CH) and CH$_2$COO), 2.06 (s, 3 H, CH=CC*H*$_3$), 1.71 (m, 1 H, C*H*(CH$_3$)), 1.48 (m, 1 H), 1.42-1.28 (m, 3 H), 1.31 (s, 3 H, C(CH$_3$)$_2$), 1.18 (d, J = 6.8 Hz, 3 H, C*H*(CH$_3$), 1.00 (d, J = 6.9 Hz, 3 H, C*H*(CH$_3$), 0.99 (s, 3 H, C(CH$_3$)$_2$); ^{13}C NMR (150.9 MHz, C_6D_6) δ 219.4, 170.2, 164.6, 153.1, 138.7, 128.4, 120.3, 119.7, 116.3, 78.8, 74.3, 72.3, 54.0, 42.4, 40.2, 38.3, 32.4, 31.7, 29.4, 26.0, 23.0, 18.9, 18.7, 16.4, 16.0, 14.0.

Acetamide 53. Acetylation of Amine 52. To a stirred solution of amine **52** (5.0 mg, 9.9 μmol) in CH_2Cl_2 (0.5 mL) was added Et_3N (3.0 μL, 19.8 μmol, 2.0 equiv.), followed by Ac_2O (1.0 μL, 9.9 μmol, 1.0 equiv.). After stirring for 10 min, the solvent was removed *in vacuo* and the residue was purified by preparative thin layer chromatography (50% EtOAc in hexanes) to give amide **53** (5.4 mg, 99%): R_f = 0.81 (silica gel, EtOAc); $[\alpha]^{22}_D$ –75.2 (*c* 0.2, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 6.95 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.54 (bs, 1 H, NH), 5.30 (dd, J = 8.7, 8.5 Hz, 1 H, C=C*H*CH$_2$), 5.26 (dd, J = 8.1, 2.2

Hz, 1 H, CHOCO), 4.31 (bd, J = 10.1 Hz, 1 H, OH), 3.95 (dd, J = 16.2, 7.0 Hz, 1 H, C*H*OH), 3.69 (bs, 1 H, OH), 3.58 (dd, J = 15.9, 5.1 Hz, 1 H, CHOH), 3.21 (dq, J = 6.9, 2.6 Hz, 1 H, C(O)C*H*CH_3), 2.68 (s, 3 H, N=C(CH_3)S), 2.59 (m, 1 H, C=CHC*H*$_2$CHO), 2.47 (dd, J = 14.3, 10.8 Hz, 1 H, CH_2COO), 2.38 (m, 1 H, C=CHC*H*$_2$CHO), 2.15 (m, 1 H, C*H*$_2$C(CNH(Ac))=CH), 2.27 (dd, J = 14.4, 2.1 Hz, CH_2COO), 2.08 (m, 1 H, C*H*$_2$C(CNH(Ac))=CH), 1.81 (m, 1 H), 1.73 (m, 1 H, C*H*(CH_3)), 1.64 (m, 1 H), 1.35 (m, 1 H), 1.17 (d, J = 6.9 Hz, 3 H, C*H*(CH_3), 1.04 (s, C(CH_3)$_2$), 0.99 (d, J = 7.0 Hz, 3 H, C*H*(CH_3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.3, 170.2, 170.0, 164.9, 151.9, 138.0, 120.8, 119.1, 115.7, 77.9, 74.1, 71.6, 60.4, 53.7, 44.4, 41.8, 39.5, 37.9, 31.6, 31.4, 29.1, 25.4, 25.0, 23.4, 22.8, 21.1, 19.2, 18.0, 16.1, 15.9, 14.3, 13.5.

Compound 54. Esterification of Alcohol 6. Compound **54** (10 mg, 90%) was obtained from compound **6** (11 mg, 0.021 mmol) according to the procedure described above for **25**: R_f = 0.50 (silica gel, 80% EtOAc in hexanes); $[\alpha]^{22}_D$ –48.2 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3394, 2932, 1734, 1689, 1461, 1377, 1247, 1025 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.43 (dd, J = 7.6, 3.0 Hz, 1 H, CH_2COOC*H*), 4.20 (bs, 2 H, (CH_3)$_2$CC*H*OH, OH), 4.19 (d, J = 12.2 Hz, 1 H, AcOC*H*$_2$COCH), 3.95 (d, J = 12.2 Hz, 1 H, AcOC*H*$_2$COCH), 3.76 (bs, 1 H, C*H*OH), 3.29 (dq, J = 7.0, 4.0 Hz, 1 H, C(O)C*H*CH_3), 2.98 (dd, J = 7.5, 4.6 Hz, 1 H, AcOCH$_2$COC*H*), 2.69 (s, 3 H, N=C(CH_3)S), 2.65 (bs, 1 H, OH), 2.54 (dd, J = 14.0, 10.3 Hz, 1 H, C*H*$_2$COOCH), 2.38 (dd, J = 14.0, 2.9 Hz, 1 H, C*H*$_2$COOCH), 2.12 (ddd, J = 15.1, 4.0, 3.9 Hz, 1 H, AcOCH$_2$COCHC*H*$_2$CHO), 2.08 (s, 3 H, CH=CC*H*$_3$), 2.05 (s, 3 H, C*H*$_3$COOCH$_2$COCH), 1.97-1.87 (m, 2 H), 1.77-1.70 (m, 1 H), 1.53-1.42 (m, 4 H), 1.36 (s, 3 H, C(CH_3)$_2$), 1.16 (d, J = 6.9 Hz, 3 H, CH(C*H*$_3$)), 1.08 (s, 3 H, C(CH_3)$_2$), 0.99 (d, J = 7.0 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.3, 170.3, 165.1, 151.5, 137.2, 119.7, 116.1, 76.4, 73.6, 72.7, 66.4, 65.9, 61.3, 58.4, 53.2, 42.7, 39.3, 36.3, 31.4, 31.1, 29.8, 28.5, 21.8, 21.5, 20.9, 19.6, 19.2, 17.1, 16.0, 15.4, 13.4; FAB HRMS (NBA/CsI) *m/e* 698.1786, M + Cs$^+$ calcd for $C_{29}H_{43}NO_8S$ 698.1764.

Compound 55. Esterification of Alcohol 6. Compound **55** (10.4 mg, 90%) was obtained from compound **6** (10.0 mg, 0.019 mmol) according to the procedure described above for **26**: R_f = 0.70 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –51.2 (*c* 0.2, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.42 (dd, J = 7.6, 2.8 Hz, 1 H, CH_2COOC*H*), 4.21 (obscured bs, 1 H), 4.21 (d, J = 12.2 Hz, 1 H, PivOC*H*$_2$COCH), 4.12 (bs, 1 H), 3.92 (d, J = 12.2 Hz, 1 H, PivOC*H*$_2$COCH), 3.76 (bs, 1 H, C*H*OH), 3.29 (dq, J = 6.9, 4.5 Hz, 1 H, C(O)C*H*CH_3), 2.97 (dd, J = 7.3, 4.9 Hz, 1 H, PivOCH$_2$COC*H*), 2.69 (s, 3 H, N=C(CH_3)S), 2.58 (obscured bs, 1 H, OH), 2.54 (dd, J = 14.0, 10.3 Hz, 1 H, C*H*$_2$COOCH), 2.37 (dd, J = 14.0, 3.1 Hz, 1 H, C*H*$_2$COOCH), 2.12 (ddd, J = 15.1, 4.0, 3.9 Hz, 1 H, PivOCH$_2$COCHC*H*$_2$CHO), 2.09 (s, 3 H, CH=CC*H*$_3$), 1.98-1.87 (m, 2 H), 1.74-1.62 (m, 2 H), 1.53-1.42 (m, 3 H), 1.36 (s, 3 H, C(CH_3)$_2$), 1.17 (s, 9 H, CO_2C(CH_3)$_3$), 1.16 (d, J = 6.9 Hz, 3 H, CH(C*H*$_3$)), 1.08 (s, 3 H, C(CH_3)$_2$), 0.99 (d, J = 7.0 Hz, 3 H, CH(C*H*$_3$)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.7, 178.1, 170.6, 165.1, 151.8, 137.3, 119.8, 116.2, 76.2, 74.0, 72.8, 66.2, 61.3, 58.0, 53.0, 42.9, 39.0, 38.8, 36.2, 31.2, 30.7, 28.3, 27.0, 21.7, 21.1, 19.5, 19.0, 17.0, 15.8, 13.5; FAB HRMS (NBA/CsI) *m/e* 740.2253, M + Cs$^+$ calcd for $C_{32}H_{49}NO_8S$ 740.2233.

Compound 56. Esterification of Alcohol 6. Compound **56** (7.7 mg, 75%) was obtained from compound **6** (8.5 mg, 0.016 mmol) according to the procedure described above for **27**: R_f = 0.60 (silica gel, 60%

EtOAc in hexanes); $[\alpha]^{22}_D$ –39.2 (*c* 0.3, $CHCl_3$); IR (thin film) ν_{max} 3352, 2962, 1724, 1453, 1272, 1112, 718 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 8.2, 1.1 Hz, 2 H, Ph), 7.55 (m, 1 H, Ph), 7.41 (dd, *J* = 8.0, 7.7 Hz, 2 H, Ph), 6.94 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH_3), 5.45 (dd, *J* = 7.4, 3.1 Hz, 1 H, CH_2COOCH), 4.45 (d, *J* = 12.1 Hz, 1 H, $BzOCH_2COCH$), 4.21 (obscured bs, 1 H), 4.19 (d, *J* = 12.0 Hz, 1 H, $BzOCH_2COCH$), 4.11 (bs, 1 H), 3.73 (bs, 1 H, C*H*OH), 3.30 (dq, *J* = 6.9, 4.3 Hz, 1 H, C(O)C*H*CH_3), 3.10 (dd, *J* = 7.1, 5.1 Hz, 1 H, $BzOCH_2COCH$), 2.69 (s, 3 H, N=$C(CH_3)$S), 2.54 (bs, 1 H, OH), 2.47 (dd, *J* = 13.9, 10.4 Hz, 1 H, CH_2COOCH), 2.34 (dd, *J* = 13.9, 3.1 Hz, 1 H, CH_2COOCH), 2.13 (ddd, *J* = 15.6, 4.5, 3.8 Hz, 1 H, $BzOCH_2COCHCH_2CHO$), 2.09 (s, 3 H, CH=CCH_3), 2.04-1.95 (m, 2 H), 1.74-1.42 (m, 5 H), 1.35 (s, 3 H, $C(CH_3)_2$), 1.14 (d, *J* = 6.9 Hz, 3 H, $CH(CH_3)$), 1.05 (s, 3 H, $C(CH_3)_2$), 0.97 (d, *J* = 7.0 Hz, 3 H, $CH(CH_3)$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 221.1, 171.1, 166.8, 165.9, 152.4, 134.0, 130.5, 129.3, 120.5, 117.0, 77.2, 74.8, 73.6, 68.1, 62.2, 59.5, 54.3, 54.0, 43.7, 40.1, 37.2, 32.2, 32.0, 29.7, 22.9, 22.2, 22.1, 20.5, 20.1, 18.1, 16.9, 14.4; FAB HRMS (NBA/CsI) *m/e* 760.1950, M + Cs^+ calcd for $C_{34}H_{45}NO_8S$ 760.1920.

Compound 57. Selective Fluorination of Triol 6. To a stirred solution of **6** (20.4 mg, 38.9 μmol) in CH_2Cl_2 (1.5 mL) at –78 °C was added DAST (6.2 μL, 46.7 μmol, 1.2 equiv.). After stirring for 5 min, the reaction mixture was quenched by the addition of saturated aqueous $NaHCO_3$ solution (2 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 2 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (silica gel, 5% methanol in CH_2Cl_2) provided **57** (9.0 mg, 90%) as a colorless solid (13.3 mg, 65%): R_f = 0.33 (silica gel, 60% EtOAc in hexanes); Mp 94-96 °C (Et_2O); $[\alpha]^{22}_D$ –50.3 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3487, 2958, 1732, 1688, 1504, 1455, 1376, 1254, 1151, 1008, 980, 914, 733 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.98 (s, 1 H, SCH=C), 6.60 (s, 1 H, C*H*=CCH_3), 5.44 (dd, *J* = 7.5, 3.5 Hz, 1 H, CHOCO), 4.48 (dd, *J* = 47.5, 10.5 Hz, 1 H, CH_2F), 4.24 (dd, *J* = 47.5, 10.5 Hz, 1 H, CH_2F), 4.21 (obscured m, 1 H, C*H*OH), 4.13 (bs, 1 H, OH), 3.77 (bs, 1 H, C*H*OH), 3.31 (dq, *J* = 7.0, 6.5 Hz, C(O)C*H*CH_3), 3.01 (dd, *J* = 7.0, 5.0, Hz, 1 H, FCH_2COCH), 2.70 (s, 3 H, N=$C(CH_3)$S), 2.64 (bs, 1 H, OH), 2.55 (dd, *J* = 14.0, 3.1 Hz, 1 H, CH_2COO), 2.36 (dd, *J* = 14.0, 2.5 Hz, 1 H, CH_2COO), 2.19-1.91 (m, 2 H, $FCH_2COCHCH_2CHO$), 1.73 (m, 1 H, $CH(CH_3)$), 1.61-1.22 (m, 6 H), 1.37 (s, 3 H, $C(CH_3)_2$), 1.17 (d, *J* = 7.0 Hz, $CH(CH_3)$), 1.08 (s, 3 H, $C(CH_3)_2$), 1.00 (d, *J* = 6.5 Hz, 3 H, $C(CH_3)_2$); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 220.4, 170.3, 165.1, 151.5, 137.0, 119.7, 116.1, 85.8, 84.4, 76.6, 73.8, 72.7, 61.6, 61.4, 57.3, 57.2, 52.9, 42.7, 39.0, 36.2, 31.1, 30.8, 27.2, 21.7, 21.1, 19.5, 19.0, 17.0, 15.8, 13.4; FAB HRMS (NBA/CsI) *m/e* 658.1640, M + Cs^+ calcd for $C_{27}H_{40}FNO_6S$ 658.1615.

Compound 58. Selective Chlorination of Triol 6. Compound **58** (8.2 mg, 75%) was obtained from compound **6** (9.0 mg, 0.017 mmol) according to the procedure described above for **32**: **58**: R_f = 0.55 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –51.2 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3440, 2930, 1732, 1383, 1070, cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.98 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH_3), 5.42 (dd, *J* = 7.7, 3.1 Hz, 1 H, CH_2COOCH), 4.21 (d, *J* = 8 Hz, 1 H), 4.05 (bs, 1 H), 3.76 (dd, *J* = 4.3, 4.3 Hz, 1 H, C*H*OH), 3.56 (d, *J* = 11.6 Hz, 1 H, $ClCH_2COCH$), 3.42 (d, *J* = 11.6 Hz, 1 H, $ClCH_2COCH$), 3.29 (dq, *J* = 7.0, 4.4 Hz, 1 H, C(O)C*H*CH_3), 2.97 (dd, *J* = 7.3, 4.9 Hz, 1 H, $ClCH_2COCH$), 2.69 (s, 3 H, N=$C(CH_3)$S), 2.61 (bs, 1 H, OH), 2.53 (dd, *J* = 14.0, 10.3 Hz, 1 H, CH_2COOCH), 2.33 (dd, *J* = 14.1, 3.0 Hz, 1 H, CH_2COOCH), 2.13 (ddd, *J* =

15.6, 4.7, 3.4 Hz, 1 H, $ClCH_2COCHCH_2CHO$), 2.09 (s, 3 H, $CH{=}CCH_3$), 2.04-1.95 (m, 2 H), 1.74-1.35 (m, 5 H), 1.35 (s, 3 H, $C(CH_3)_2$), 1.14 (d, J = 6.9 Hz, 3 H, $CH(CH_3)$), 1.07 (s, 3 H, $C(CH_3)_2$), 0.97 (d, J = 6.8 Hz, 3 H, $CH(CH_3)$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.2, 170.2, 163.2, 160.4, 157.7, 133.9, 120.0, 116.2, 76.2, 74.1, 72.8, 62.4, 60.8, 53.1, 49.1, 43.0, 39.2, 36.7, 31.6, 30.8, 28.1, 22.7, 21.9, 21.4, 19.8, 19.1, 17.2, 16.0, 14.2; FAB HRMS (NBA) *m/e* 542.2361, M + H^+ calcd for $C_{27}H_{40}NO_6S$ 542.2343.

Compound 60. Tosylation of Alcohol 6 and Displacement with Sodium Iodide. To a stirred solution of alcohol **6** (5.0 mg, 9.5 μmol) in CH_2Cl_2 (0.5 mL) at 0 °C was added Et_3N (4 μL, 28.5 μmol, 3.0 equiv.) followed by tosyl chloride (2.5 mg, 14.2 μmol) and 4-DMAP (1.0 mg, 8.8 μmol, 1.0 equiv.). The reaction mixture was warmed to room temperature and stirred for 2 h before saturated aqueous NH_4Cl (0.5 mL) was added. The layers were separated and the aqueous phase was extracted with EtOAc (3 x 2 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was then dissolved in acetone (0.5 mL) and treated with NaI (2.8 mg, 19 μmol, 2.0 equiv.). After stirring at room temperature for 12 h, the solvent was removed *in vacuo* and the residue was purified by preparative thin layer chromatography (50% EtOAc in hexanes) to provide pure iodide **60** (6.6 mg, 90%): R_f = 0.62 (silica gel, 60% EtOAc in hexanes); $[\alpha]^{22}_D$ –27.8 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3410, 2964, 2926, 2851, 1732, 1682, 1634, 1441, 1384, 1256, 1149, 1084, 974, cm^{-1}; ^1H NMR (600 MHz, C_6D_6) δ 6.64 (s, 1 H, SCH=C), 6.41 (s, $CH{=}CCH_3$), 5.31 (dd, J = 7.6, 3.1 Hz, 1 H, CHOCO), 4.15 (dd, J = 10.1, 2.3 Hz, 1 H, $CHOH$), 3.74 (dd, J = 4.4, 4.4 Hz, 1 H, $CHOH$), 3.08 (dq, J = 6.1, 6.1 Hz, 1 H, $C(O)CHCH_3$), 2.78 (d, J = 10.4 Hz, 1 H, CH_2I), 2.64 (d, J = 10.4 Hz, 1 H, CH_2I), 2.61 (dd, J = 7.1, 5.2 Hz, 1 H, ICH_2COCH), 2.40 (dd, J = 14.3, 10.4 Hz, 1 H, CH_2COO), 2.21 (dd, J = 14.3, 3.0 Hz, 1 H, CH_2COO), 2.15 (s, 3 H, $N{=}C(CH_3)S$), 1.96 (s, 3 H, $CH{=}CCH_3$), 1.91 (m, 1 H, $ICH_2COCHCH_2CHO$), 1.74 (m, 3 H, $ClCH_2COCHCH_2CHO$, $CH(CH_3)$ and CH_2), 1.42-1.09 (m, 6 H), 1.03 (s, 3 H, $C(CH_3)_2$), 1.02 (d, J = 7.0 Hz, 3 H, $CH(CH_3)$), 0.94 (s, 3 H, $C(CH_3)_2$), 0.87 (d, J = 7.0 Hz, 3 H, $CH(CH_3)$); ^{13}C NMR (150.9 MHz, C_6D_6) δ 219.3, 170.0, 164.8, 161.2, 152.7, 137.3, 120.0, 116.7, 76.5, 75.0, 73.1, 64.9, 63.8, 62.2, 53.2, 43.8, 39.6, 36.6, 32.8, 30.6, 30.1, 22.6, 21.5, 20.1, 18.9, 17.5, 15.9, 14.5, 13.0; FAB HRMS (NBA/) *m/e* 766.0644, M + H^+ calcd for $C_{27}H_{40}INO_6S$ 766.0675.

Epoxy Aldehyde 61. Oxidation of Alcohol 6. To a solution of alcohol **6** (12 mg, 22.9 mmol, 1.0 equiv.) in CH_2Cl_2 (250 mL, 0.1 M) was added, at 0 °C, TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy, free radical) (6 mg, 38 mmol, 1.5 equiv.), KBr (10 mL, 2.3 mmol, 0.2 M aqueous solution, 0.1 equiv.), and NaOCl (0.065 mL, 25.2 mmol, 0.035 M , 4% solution in water, 1.1 equiv.). After stirring for 0.5 h, the organic layer was dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification by preparative thin layer chromatography (silica gel, 5% methanol in CH_2Cl_2) provided aldehyde **61** (9.0 mg, 90%) as a colorless oil: R_f = 0.88 (silica gel, 80% EtOAc in hexanes); $[\alpha]^{22}_D$ –0.2 (*c* 0.1, $CHCl_3$); IR (thin film) ν_{max} 3480, 2966, 2931, 1730, 1689, 1461, 1380, 1254, 1184, 1149, 1069, 1013, 980, 912, 732 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.83 (s, 1 H, CHO), 7.01 (s, 1 H, SCH=C), 6.67 (s, 1 H, $CH{=}CCH_3$), 5.57 (dd, J = 5.5, 5.3 Hz, 1 H, CHOCO), 4.23 (bs, 1 H, $CHOH$), 4.06 (bs, 1 H, OH), 3.77 (bs, 1 H, $CHOH$), 3.34 (dq, J = 6.9, 3.9 Hz, 1 H, $C(O)CH(CH_3)$), 3.30 (dd, J = 6.7, 5.2 Hz, 1 H, $CHOCH_2$), 2.71 (s, 3 H, $N{=}C(CH_3)S$), 2.61-2.59 (m, 1 H, $OCHCH_2CHO$), 2.60 (dd, J = 14.0, 10.0 Hz, 1 H, CH_2COO), 2.44 (dd, J = 14.0, 3.4 Hz, 1 H, CH_2COO), 2.14 (ddd, J = 14.3, 5.2, 5.2 Hz, 1 H, $OCHCH_2CHO$), 2.12 (s, 3 H, $CH{=}C(CH_3)$), 2.10-2.02 (m, 1 H,

CH_2C(CHO)OCH), 1.81-1.73 (m, 2 H), 1.62-1.58 (m, 1 H), 1.45-1.38 (m, 2 H), 1.37 (s, 3 H, C(CH_3)$_2$), 1.35-1.29 (m, 1 H), 1.14 (d, J = 6.9 Hz, 3 H, CH(CH_3)), 1.07 (s, 3 H, C(CH_3)$_2$), 0.97 (d, J = 7.0 Hz, 3 H, CH(CH_3)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.7, 198.8, 170.1, 165.2, 151.6, 136.8, 119.8, 116.5, 75.2, 73.7, 72.9, 63.9, 56.8, 52.7, 42.7, 38.6, 36.5, 30.6, 30.5, 23.4, 21.8, 20.2, 19.9, 19.1, 16.7, 16.2, 13.4; FAB HRMS (NBA/CsI) *m/e* 654.1478, M + Cs^+ calcd for $C_{27}H_{39}NO_7S$ 654.1502.

Carboxylic Acid 62. Oxidation of Aldehyde 61. Aldehyde **61** (13.0 mg, 24.9 mmol, 1 equiv.). *t*-BuOH (1.2 mL), 2-methyl-2-butene (1.0 mL. 1 mmol, 2 M solution in THF, 70.0 equiv.), H_2O (270 mL, 0.02M), $NaClO_2$ (14.0 mg, 155 mmol, 6.0 equiv.) and NaH_2PO_4 (9.6 mg, x.xx mmol, 3 equiv.) were combined and stirred at 0 °C for 30 min. The reaction mixture was concentrated under reduced pressure and the residue was subjected to flash column chromatography (silica gel, 5% MeOH in CH_2Cl_2) to afford carboxylic acid **62** (12.6 mg, 95%): R_f = 0.61 (silica gel, 20% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –41.5 (*c* 0.6, MeOH); IR (thin film) ν_{max} 3450, 2929, 2854, 1758, 1670, 1461, 1380, 1254, 1183, 1149, 1070, 1012, 980, 912, 725 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD) δ 7.20 (s, 1 H, SCH=C), 6.64 (s, 1 H, C*H*=CCH$_3$), 5.41 (dd, J = 5.9, 2.9 Hz, 1 H, CHOCO), 4.43 (dd, J = 9.5, 4.0 Hz, 1 H, C*H*OH), 3.67 (dd, J = 6.9, 2.8 Hz, 1 H, C*H*OH), 3.36 (dq, J = 6.8, 6.7 Hz, 1 H, C(O)C*H*(CH$_3$)), 3.16 (bs, 1 H, C*H*OCH$_2$), 2.67 (s, 3 H, N=C(CH$_3$)S), 2.55 (dd, J = 15.4, 4.1 Hz, 1 H, CH$_2$COO), 2.49 (dd, J = 15.4, 9.5 Hz, 1 H, CH$_2$COO), 2.15-2.08 (m, 1 H, OCHCH_2CHO), 2.07 (s, 3 H, CH=C(CH_3)), 2.07-2.02 (m, 2 H, OCHCH_2CHO, CH_2C(COOH)OCH), 1.75-1.64 (m, 2 H), 1.59-1.52 (m, 1 H), 1.51-1.40 (m, 2 H), 1.38-1.33 (m, 1 H), 1.32 (s, 3 H, C(CH_3)$_2$), 1.15 (d, J = 6.8 Hz, 3 H, CH(CH_3)), 1.01 (s, 3 H, C(CH_3)$_2$), 0.97 (d, J = 6.7 Hz, 3 H, CH(CH_3)); ^{13}C NMR (150.9 MHz, CD_3OD) δ 220.1, 171.5, 166.3, 152.8, 138.3, 119.7, 117.2, 77.0, 76.8, 71.2, 59.2, 54.0, 45.2, 39.7, 36.1, 32.6, 28.9, 28.1, 22.7, 21.1, 19.4, 18.2, 17.4, 15.3, 15.2; FAB HRMS (NBA) *m/e* 538.2497, M + H^+ calcd for $C_{27}H_{39}NO_8S$ 538.2475.

Methylester 63. Methylester **63** (12 mg, 90%) was prepared from carboxylic acid **62** (13 mg, 24.2 mmol) by reaction with diazomethane according to the procedure described above for **49**: R_f = 0.44 (silica gel, 5% MeOH in CH_2Cl_2); $[\alpha]^{22}_D$ –39.7 (*c* 0.3, $CDCl_3$); IR (thin film) ν_{max} 3514, 2958, 2854, 1737, 1690, 1447, 1380, 1263, 1198, 1156, 1065, 981, 732 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.97 (s, 1 H, SCH=C), 6.61 (s, 1 H, C*H*=CCH$_3$), 5.49 (dd, J = 5.7, 3.9 Hz, 1 H, CHOCO), 4.23 (bs, 1 H, C*H*OH), 3.92 (bs, 1 H, C*H*OH), 3.76 (bs, 1 H, OH), 3.72 (s, 3 H, CO_2CH_3), 3.30 (dq, J = 6.7, 2.6 Hz, 1 H, C(O)C*H*(CH$_3$)), 3.28 (dd, J = 6.2, 6.0 Hz, 1 H, C*H*OCH$_2$), 2.69 (s, 3 H, N=C(CH$_3$)S), 2.61 (bs, 1 H, OH), 2.57 (dd, J = 14.2, 10.2 Hz, 1 H, CH$_2$COO), 2.42 (dd, J = 14.2, 3.2 Hz, 1 H, CH$_2$COO), 2.10 (s, 3 H, CH=C(CH_3)), 2.08 (ddd, J = 15.1, 6.2, 3.9 Hz, 1 H, OCHCH_2CHO), 2.03 (ddd, J = 15.1, 6.0, 6.0 Hz, 1 H, OCHCH_2CHO), 1.96-1.91 (m, 1 H, CH_2C(COOMe)OCH), 1.87-1.83 (m, 1 H, CH_2C(COOMe)OCH), 1.77-1.72 (m, 1 H), 1.65-1.57 (m, 2 H), 1.56-1.45 (m, 2 H), 1.35 (s, 3 H, C(CH_3)$_2$), 1.13 (d, J = 7.0 Hz, 3 H, CH(CH_3)), 1.07 (s, 3 H, C(CH_3)$_2$), 0.96 (d, J = 7.0 Hz, 3 H, CH(CH_3)); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 220.4, 170.6, 170.2, 164.9, 151.6, 136.1, 119.7, 116.4, 75.7, 73.9, 72.9, 60.7, 58.9, 52.9, 52.7, 42.8, 38.9, 35.9, 31.2, 30.3, 27.3, 21.7, 20.8, 20.2, 19.2, 16.8, 16.1, 13.4; FAB HRMS (NBA) *m/e* 552.2650, M + H^+ calcd for $C_{28}H_{41}NO_8S$ 552.2631.

Aldehyde 64. TMS Silylation of Diol 61. To a stirred solution of **61** (63.0 mg, 120.1 μmol, 1.0 equiv.) in CH_2Cl_2 (1.3 mL) at 0 °C was added Et_3N (101 μL, 660 μmol, 5.5 equiv.) followed by TMSCl (58

μL, 420 μmol, 3.5 equiv.). The reaction mixture was allowed to warm to room temperature and stirred for 12 h. Saturated aqueous $NaHCO_3$ solution (2 mL) was added and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (3 x 2 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Flash column chromatography (silica gel, 40% Et_2O in hexanes) then gave pure **64** (67 mg, 90%); R_f = 0.45 (silica gel, 60% Et_2O in hexanes); $[\alpha]^{22}_D$ +7.4 (*c* 0.5, $CDCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1 H, CHO), 6.98 (s, 1 H, C*H*=CCH$_3$), 5.40 (dd, *J* = 7.8, 2.9 Hz, 1 H, CHOCO), 4.23 (dd, *J* = 8.0, 4.0 Hz, 1 H, C*H*OH), 3.81 (d, *J* = 8.5 Hz, 1 H, C*H*OH), 3.29 (dd, *J* = 8.4, 4.3 Hz, 1 H, C(O)C*H*CH$_2$), 3.04 (dq, *J* = 8.1, 8.1 Hz, 1 H, C(O)C*H*(CH$_3$)), 2.70 (s, 3 H, N=C(CH$_3$)S), 2.69-2.51 (m, 2 H, CH$_2$COO), 2.29 (ddd, *J* = 15.1, 3.8, 3.8 Hz, 1 H, C(O)C*H*$_2$CHO), 2.12 (s, 3 H, CH=C(C*H*$_3$)), 2.08 (m, 4 H, C(O)C*H*$_2$CHO, C*H*$_2$C(CHO) and C*H*(CH$_3$)), 1.84 (m, 1 H), 1.67-1.22 (m, 3 H), 1.06 (s, 6 H, C(CH$_3$)$_2$), 1.04 (d, *J* = 7.0 Hz, CH(C*H*$_3$)), 0.96 (d, *J* = 6.8 Hz, CH(C*H*$_3$)), 0.13 (s, 9 H, Si(CH$_3$)$_3$), 0.12 (s, 9 H, Si(CH$_3$)$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 215.6, 198.4, 170.6, 165.0, 152.0, 136.4, 121.1, 117.1, 79.7, 76.0, 75.3, 64.1, 58.4, 53.4, 47.5, 45.8, 40.0, 36.1, 32.4, 31.0, 25.4, 22.8, 22.7, 22.6, 19.4, 19.2, 17.3, 14.5, 0.7, 0.4.

Olefin 65. Wittig Olefination of 64. Compound **65** (43 mg, 75.2 μmol, 75%) was prepared from **64** (67 mg, 100 μmol) according to the procedure described above for **42**: R_f = 0.31 (silica gel, 30% Et_2O in hexanes); $[\alpha]^{22}_D$ –14.0 (*c* 0.3, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.53 (s, 1 H, C*H*=CCH$_3$), 6.01 (dd, *J* = 17.0, 10.7 Hz, 1 H, C*H*$_2$=CH), 5.28 (dd, *J* = 17.0, 1.5 Hz, 1 H, CH$_2$=C*H*), 5.27 (obscured m, 1 H, CHOCO), 5.12 (dd, *J* = 10.7, 1.5 Hz, 1 H, C*H*$_2$=CH), 4.09 (dd, *J* = 8.7, 2.4 Hz, 1 H, C*H*OH), 3.85 (d, *J* = 9.3 Hz, C*H*OH), 3.05 (dq, *J* = 9.2, 6.8 Hz, 1 H, C(O)C*H*CH$_3$), 2.90 (dd, *J* = 9.7, 4.0 Hz, 1 H, C(O)CH), 2.76 (dd, *J* = 16.1, 10.1 Hz, 1 H, CH$_2$COO), 2.69 (s, 3 H, N=C(CH$_3$)S), 2.68 (dd, *J* = 16.1, 2.7 Hz, 1 H, CH$_2$COO), 2.20 (ddd, *J* = 15.2, 3.9, 1.8 Hz, 1 H, C(O)CHC*H*$_2$), 2.09 (s, 3 H, CH=C(C*H*$_3$)), 1.96 (ddd *J* = 15.2, 9.7, 9.7 Hz, 1 H, C(O)CHC*H*$_2$), 1.81 (m, 1 H, C*H*(CH$_3$)), 1.67 (m, 1 H), 1.64-1.47 (m, 3 H), 1.31-1.26 (m, 3 H), 1.15 (s, 3 H, C(CH$_3$)$_2$), 1.09 (s, 3 H, C(CH$_3$)$_2$), 1.06 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.95 (d, *J* = 6.8 Hz, 3 H, CH(C*H*$_3$)), 0.13 (s, 9 H, Si(CH$_3$)$_3$), 0.06 (s, 9 H, Si(CH$_3$)$_3$); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 214.9, 170.7, 164.7, 152.1, 137.2, 136.8, 120.5, 116.8, 115.8, 80.4, 76.0, 63.9, 63.7, 53.4, 48.1, 39.4, 35.9, 33.9, 31.1, 24.2, 19.6, 19.3, 17.8, 14.4, 0.9, 0.6; FAB HRMS (NBA/CsI) *m/e* 796.2472, M + Cs^+ calcd for $C_{34}H_{57}NO_5SSi_2$ 796.2500.

Compound 66. Desilylation of 65. To a stirred solution of **65** (70.0 mg, 0.10 mmol), in THF (10 mL) at 0 °C was added HF•pyridine:pyridine:THF mixture (3 mL, prepared from a stock solution containing 0.42 mL HF•pyridine, 1.14 mL pyridine and 2.0 mL THF). After stirring for 7 h, the reaction mixture was quenched by the addition of water (6 mL) and solid $NaHCO_3$. The layers were separated and the aqueous phase was extracted with EtOAc (3 x 6 mL). The combined organic extracts were combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (50% EtOAc in hexanes) provided pure **66** (53 mg, 97%): R_f = 0.52 (silica gel, 60% EtOAc in hexanes); Mp 94-96 °C (Et2O); $[\alpha]^{22}_D$ –54.9 (*c* 0.2, $CHCl_3$); IR (thin film) ν_{max} 3460, 2965, 1734, 1689, 1253, 1149, 980, 914, 733 cm^{-1}; ^1H NMR (600 MHz, C_6D_6) δ 6.70 (s, 1 H, SCH=C), 6.42 (s, 1 H, C*H*=CCH$_3$),5.71 (dd, *J* = 17.1, 10.9 Hz, 1 H, C*H*$_2$=CH), 5.47 (dd, *J* = 3.5, 2.9 Hz, 1 H, CHOCO), 5.35 (d, *J* = 17.1 Hz, 1 H, CH$_2$=C*H*), 4.96 (d, *J* = 10.8 Hz, 1 H, C*H*$_2$=CH), 4.28 (bs, 1 H, C*H*OH), 3.93 (bs, 1 H, C*H*OH), 3.84 (bs, 1 H, OH), 3.23 (dq, *J* = 6.7, 4.4

Hz, 1 H, C(O)C*H*CH_3), 2.81 (dd, J = 5.9, 5.9 Hz, 1 H, C(O)CH), 2.47 (bs, 1 H, OH), 2.38 (dd, J = 14.0, 10.1 Hz, 1 H, CH_2COO), 2.20 (dd, J = 14.0, 2.6 Hz, 1 H, CH_2COO), 2.19 (s, 3 H, N=C(CH_3)S), 2.02 (s, 3 H, CH=C(C*H*$_3$)), 1.82 (m, 2 H, C(O)CHC*H*$_2$), 1.72 (m, 1 H), 1.65 (m, 1 H), 1.58-1.41 (m, 4 H), 1.32 (m, 1 H), 1.11 (s, 3 H, $C(CH_3)_2$), 1.07 (d, J = 6.9 Hz, 3 H, CH(C*H*$_3$)), 0.96 (s, 3 H, $C(CH_3)_2$), 0.95 (d, J = 7.0 Hz, 3 H, $C(CH_3)_2$): ^{13}C NMR (150.9 MHz, C_6D_6) δ 219.4, 170.0, 164.7, 152.9, 138.5, 137.1, 119.6, 116.6, 115.5, 76.6, 74.8, 73.2, 63.0, 62.6, 53.2, 43.5, 39.4, 36.4, 32.0, 30.6, 30.0, 22.6, 20.8, 20.3, 18.9, 17.3, 16.1, 14.1; FAB HRMS (NBA) *m/e* 520.2748, M + H^+ calcd for $C_{28}H_{41}NO_6S$ 520.2733.

TMS Ether 67. Diimide reduction of 65. To a stirred solution of TMS ether **65** (20 mg, 30.1 μmol) in EtOH (2 mL) at 0 °C was added sequentially hydrazine (33.2 μL, 1 mmol, 33 equiv.) and 30% H_2O_2 (50 μL, 0.5 mmol, 16 equiv.). After stirring for 3 h at 0 °C, the reaction mixture was quenched by the addition of water (1 mL) and Et_2O (2 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3 x 2 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. Purification by preparative thin layer chromatography (40% Et_2O in hexanes) provided pure **66** (20 mg, 90%): R_f = 0.37 (silica gel, 40% Et_2O in hexanes); $[\alpha]^{22}_D$ –14.7 (*c* 1.2, $CHCl_3$); IR (thin film) ν_{max} 2949, 2894, 1737, 1692, 1457, 1379, 1250, 1194, 1155, 1110, 1015, 971, 887, 842, 747, 630 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.96 (s, 1 H, SCH=C), 6.59 (s, 1 H, C*H*=CCH$_3$), 5.24 (d, J = 9.4 Hz, 1 H, CHOCO), 4.02 (dd, J = 10.6, 2.0 Hz, 1 H, CHOSi), 3.89 (d, J = 9.8 Hz, 1 H, CHOSi), 3.30 (dq J = 13.5, 9.8 Hz, 1 H, C(O)C*H*CH_3), 2.85 (dd, J = 10.2, 3.5 Hz, 1 H, (Et(CO)C*H*), 2.79 (dd, J = 16.2, 10.7 Hz, 1 H, CH_2COO), 2.72 (dd, J = 16.2, 2.1 Hz, 1 H, CH_2COO), 2.70 (s, 3 H, N=C(CH_3)S), 2.20 (ddd, J = 13.9, 3.7, 1.1 Hz, 1 H, (Et(CO)CHC*H*$_2$), 2.09 (s, 3 H, CH=C(C*H*$_3$)), 1.91 (m, 3 H, (Et(CO)CHC*H*$_2$ and C*H*$_2$CH$_3$), 1.80 (m, 1 H, C*H*$_2$(CO)), 1.67 (m, 1 H, C*H*(CH_3)), 1.57 (m, 1 H, C*H*$_2$(CO)), 1.43-1.27 (m, 4 H), 1.16 (s, 3 H, $C(CH_3)_2$), 1.11 (s, 3 H, $C(CH_3)_2$), 1.07 (d, J = 6.7 Hz, 3 H, CH(C*H*$_3$)), 0.98 (d, J = 6.9 Hz, 3 H, CH(C*H*$_3$)), 0.95 (t, J = 7.4 Hz, 3 H, CH_2CH_3), 0.15 (s, 9 H, $Si(CH_3)_3$), 0.07 (s, 9 H, $Si(CH_3)_3$); (125.7 MHz, $CDCl_3$) δ 214.9, 171.0, 164.7, 152.1, 137.5, 120.5, 116.7, 80.6, 76.7, 76.2, 64.9, 62.2, 53.1, 48.2, 39.0, 35.6, 33.8, 31.2, 29.6, 29.0, 27.8, 24.5, 24.1, 23.2, 19.5, 19.1, 17.8, 14.1, 7.9, 0.7, 0.3; FAB HRMS (NBA) *m/e* 666.3658, M + H^+ calcd for $C_{34}H_{59}NO_6SSi_2$ 666.3680.

Compound 46. Deprotection of 67. Compound **46** (43 mg, 75.2 μmol, 75%) was prepared from **67** (67 mg, 100 μmol) according to the procedure described above for **66**. The product from this reaction displayed spectroscopic data identical to those reported above for **46**.

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