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An Unusual Reversal of Stereoselectivity in a Boron Mediated Aldol Reaction: Enantioselective Synthesis of the C_1–C_6 Segment of the Epothilones

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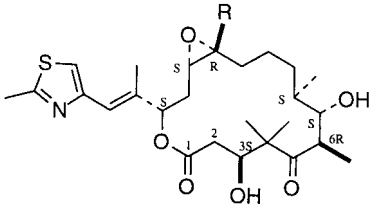
Abstract—Enantioselective syntheses of differentially protected C_1–C_6 fragments, (3*S*)-3-hydroxy-4,4-dimethyl-5-oxoheptanoic acid **4**, (5*S*)-7-[1,1-bis(methylethyl)-2-methyl-1-silapropoxy]-5-hydroxy-4,4-dimethylheptan-3-one **5** and (4*S*)-2-(2,2-dimethyl-1,3-dioxan-4-yl)-2-methylpentan-3-one **23**, common to both epothilones A and B, are reported. © 2000 Elsevier Science Ltd. All rights reserved.

Epothilone B (**1**) and epothilone A (**2**) (Fig. 1) belong to a new class of macrolides with Taxol® like antitumor activity and were first isolated by Höfle et al. from the myxobacterium *Sorangium cellulosum*.[1] Apart from the increase in potency over Taxol® against multiple drug resistant cancer cell lines, the antifungal activity and novel molecular architecture of the epothilones make them interesting synthetic targets.[2,3] Accordingly, in a short period of time several total syntheses[4–11] and communications of syntheses in progress have been reported.[12–21]

Retrosynthetic analysis of the epothilones indicated to us that synthons **3** and **4** could serve as key intermediates once appropriately protected (Scheme 1). We have previously reported the synthesis of the suitably protected C_7–C_{15} fragment **3**.[18] Herein we wish to report the efficient enantioselective synthesis of the C_1–C_6 synthons **4**, **5** and **23**.



1 Epothilone B, R = Me
2 Epothilone A, R = H

Figure 1.

The pioneering work of Evans on chiral oxazolidinones led to the development of enantioselective aldol reactions to construct β-hydroxy carbonyl compounds.[22,23] The C_1–C_6 synthons **4** and **5**, with their β-hydroxy carbonyl functionality, appeared to be the best candidates for the enantioselective aldol reaction protocol. Although enantioselective aldol condensations using *N*-acetyloxazolidinones via their boron enolates are known to give poor enantioselection,[22] we anticipated higher enantioselectivity by employing more bulky aldehydes **7**† and **8**[24] (Scheme 2). In each case, however, the reaction of the boron enolate of **9**, obtained using 9-borobicyclo[3.3.1]-non-9-yl triflate (9-BBN-OTf) and diisopropyl ethylamine (DIPEA), with the aldehydes **7** and **8** resulted in a 1:1 diastereomeric mixture of aldol adducts.

Since the oxazolidinone **9** did not show any stereodifferentiation we reacted oxazolidinone **10** with the aldehyde **7**, under standard conditions[22] (i.e. 1 equiv. of the oxazolidinone, 1.1 equiv. of the boryl triflate and 1.2 equiv. of diisopropyl ethylamine in methylene chloride at −78°C), via the enolate obtained using 9-borobicyclo-[3.3.1]-nonyl triflate (9-BBN-OTf). The crude product was desulfurized by

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† The aldehyde **7** was synthesized from the known 3,3-dimethyl-4-oxohex-1-ene **33** by ketalization to afford 2-(1,1-dimethylprop-2-enyl)-2-ethyl-1,3-dioxolane **34**, followed by ozonolysis.

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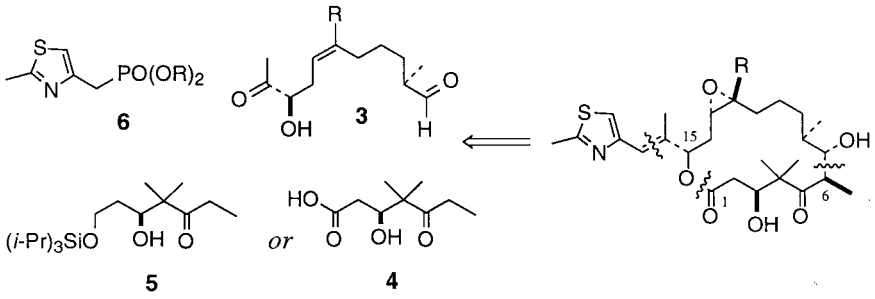
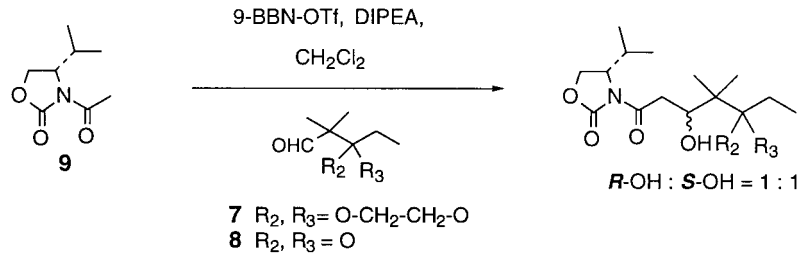


Scheme 1.



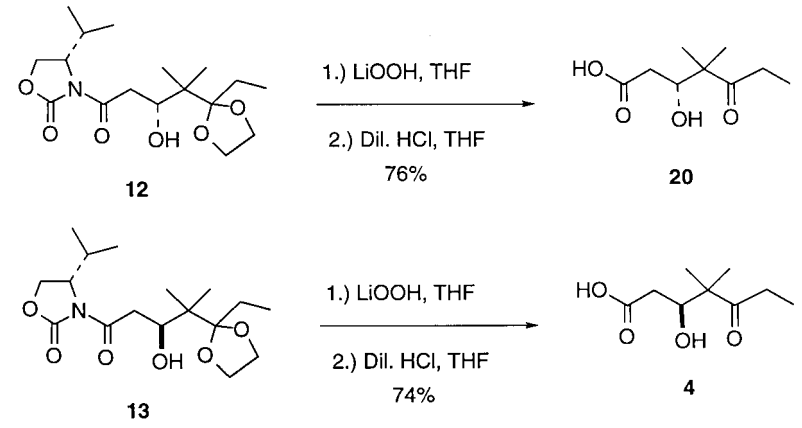
Scheme 2.

Raney nickel treatment affording the adducts **12** and **13** in a 67:33 ratio (Table 1, entry 1). The major product as per literature analogy[22] was assumed to be the *S*-isomer, but hydrolysis of the adduct **12** liberated the acid **20** (Scheme 3), which showed opposite optical rotation when compared to the reported *S*-isomer **4**,[15] indicating it has opposite stereochemistry. X-Ray crystallographic structure determination of **12** revealed it was indeed the *R*-isomer (Fig. 2).

On the other hand when the same reaction was carried out using dibutylboron triflate (Bu_2B-OTf) the expected isomer **13** was obtained as a major product, with a reversal of isomeric ratio (36:64) (Table 1, entry 2).[25] Hydrolysis of

Table 1.

Entry	Imide	Aldehyde	Boryl triflate	Ratio of R-OH:S-OH	Yield (%)
1.	**10**	7	9-BBN-OTf	**12**:**13**=67:33	64
2.	**10**	7	Bu_2B-OTf	**12**:**13**=36:64	66
3.	**11**	7	9-BBN-OTf	**14**:**15**=33:67	69
4.	**11**	7	Bu_2B-OTf	**14**:**15**=63:37	70
5.	**10**	8	9-BBN-OTf	**16**:**17**=77:23	67
6.	**10**	8	Bu_2B-OTf	**16**:**17**=23:77	70
7.	**11**	8	9-BBN-OTf	**18**:**19**=24:76	66
8	**11**	8	Bu_2B-OTf	**18**:**19**=77:23	68
9.	**10**	21	9-BBN-OTf	**23**:**24**=68:32	24
10.	**10**	22	9-BBN-OTf	**25**:**26**= 4:96	41



Scheme 3.

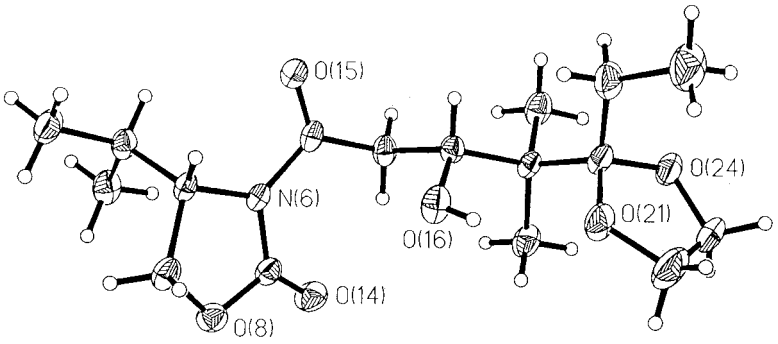
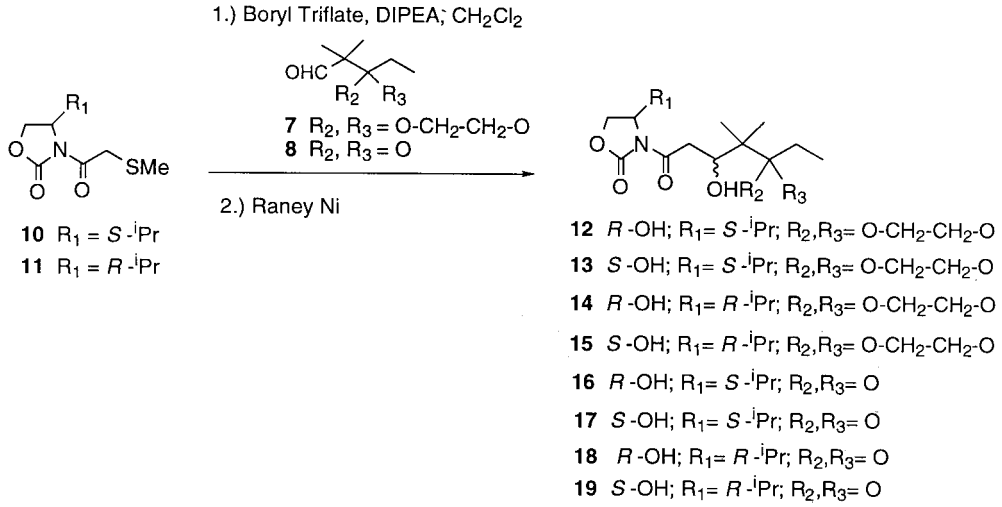


Figure 2. View of adduct **12** showing configuration of the hydroxyl group containing atom O(16). Thermal ellipsoids are drawn at the 50% probability level.



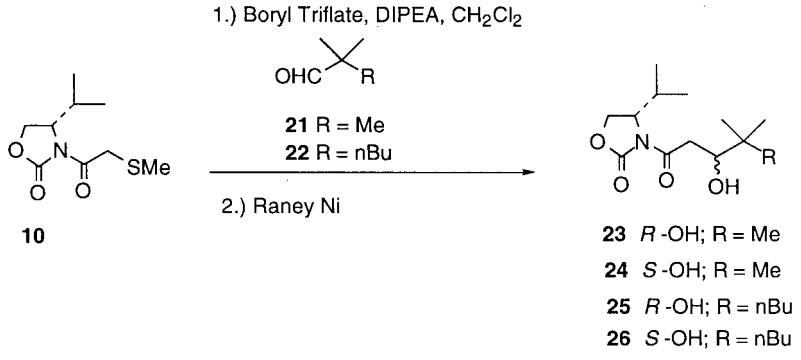
Scheme 4.

the adduct **13** yielded the required hydroxy acid **4** in 74% yield (Scheme 3).

Reversal in selectivity is not expected with a change from 9-BBN-OTf to Bu_2BOTf, as both are known to generate (*Z*)-enolates under these conditions.[22,26–28] Identical results were obtained when the oxazolidinone **11** was reacted with the aldehyde **7**. The generality of this reaction is further established by employing the aldehyde **8**, resulting in a similar reversal of stereoselectivity with the change in ligands on boron (Scheme 4, Table 1).

To check the steric contribution of the aldehydes in these reversals of selectivity, we had reacted the relatively less bulky trimethylacetaldehyde **21** and valeraldehyde **22** with the oxazolidinone **10** using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate. In the case of aldehyde **21** the reaction did result in a reversal of selectivity yielding **23** and **24** in a 68:32 ratio. On the other hand, the reaction employing valeraldehyde **22** showed no reversal of selectivity affording the adducts **25** and **26** in 4:96 ratio (Scheme 5, Table 1).[25] This observation points to the fact that the steric nature of the aldehyde is also an important factor and only bulky aldehydes exhibit this reversal in selectivity.

Apart from numerous reports indicating that both 9-BBN-OTf and Bu_2B-OTf form only (*Z*)-enolates under these



Scheme 5.

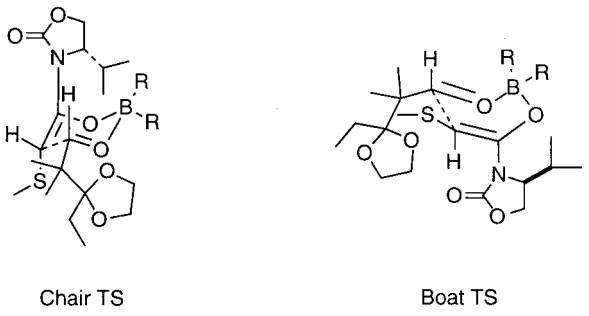


Figure 3.

conditions,[22,26–28] the reversal in selectivity can not be due to formation of an (*E*)-enolate as both the enolates are expected to give the same isomer after Raney nickel treatment. One plausible explanation for the reversal of product ratio is the existence of a predominant boat transition state for 9-BBN enolates resulting in the opposite stereoselectivity. Although it is not clear why 9-BBN derived enolates appear to proceed predominantly via the boat transition state, the severe steric interaction between the pseudoaxial thiomethyl group with the dimethyl dioxolane chain of the aldehyde in the chair transition state may be the main factor favoring a boat transition state (Fig. 3).[29,30]

In support of our proposed boat transition state hypothesis we calculated the *cis*/*trans* ratio of the thiomethyl containing intermediates in the reaction of **10** with the aldehyde **8** and found it to be 30:70. The *anti* isomer **27** formed as a major isomer along with the evans *syn* isomer **28** and non-evans *syn* isomer **29** in 70:23:7 ratio.[31] Formation of the *anti* isomer **27** as a major product is a clear indication of a possible boat transition state (Figs. 4 and 5).

With the adduct **15** in hand we focused our attention on converting it into the required ketoalcohol **5**. Thus lithium borohydride reduction of **15** followed by deketalization using dilute aqueous HCl resulted in production of the keto-diol **30**, which on selective silylation with (*i*-Pr)$_3$SiOTf and 2,6-lutidine afforded the synthon **5** as shown in Scheme 6.

In an attempt to increase the yield of **5**, we sought to rearrange the sequence of synthetic operations as shown in Scheme 7. Reductive cleavage of the chiral auxiliary of **15** as before with $LiBH_4$ followed, however, by selective primary alcohol silylation furnished the mono-alcohol **31**

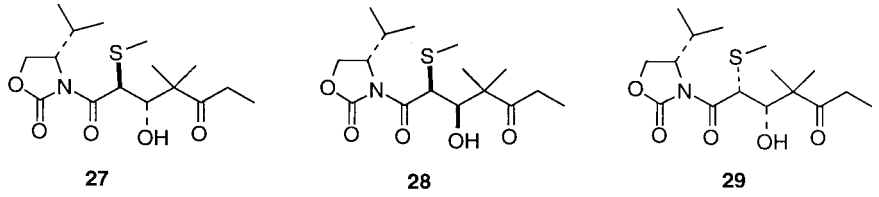


Figure 4.

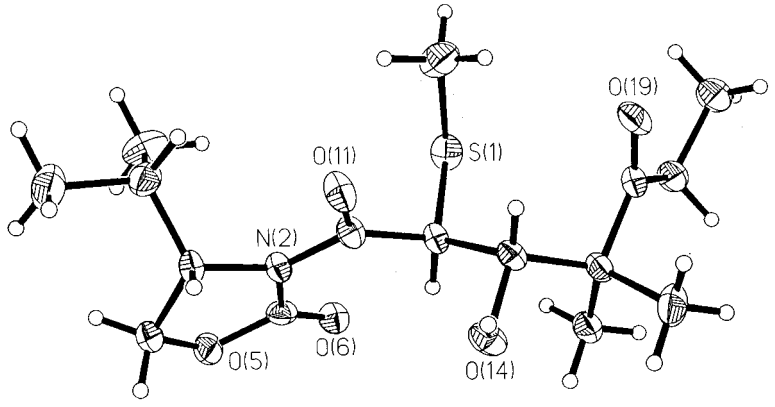
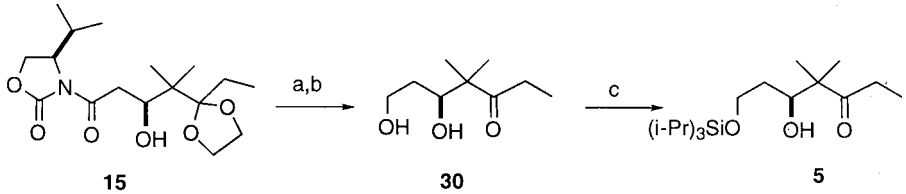
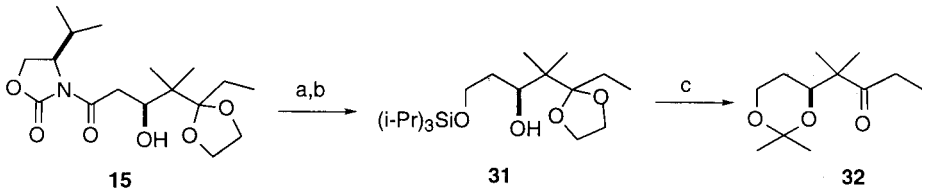


Figure 5. Absolute Configuration of isomer **27** showing the *trans* configuration of the thiomethyl group and the hydroxyl group at O(14). Thermal ellipsoids are drawn at the 50% probability level.



Scheme 6. (a) $LiBH_4$, THF, 0°C; (b) 1N HCl, 22°C; (c) (*i*-Pr)$_3$SiOTf, CH_2Cl_2, 2,6-Lutidine, 22°C (36% from **15**).



Scheme 7. (a) $LiBH_4$, THF, 0°C; (b) $(i\text{-Pr})_3SiOTf$, CH_2Cl_2, DMAP, imidazole, 22°C (66% from **15**); (c) $PdCl_2(CH_3CN)_2$, acetone, 22°C (69%).

in 66% unoptimized overall yield. During the attempted selective removal of the dioxolane protecting group under mild conditions, we encountered the serendipitous formation of the ketal derivative **32**, another equivalent of the aldol fragment **4**. Thus upon treatment of **31** with Pd(II) in acetone,[32] scission of the dioxolanyl protecting group did indeed occur but presumably was followed by unexpected loss of the TIPS ether with subsequent ketalization by solvent with Pd(II) acting as a Lewis acid giving **32** in respectable yield.

The ketal **32** had spectroscopic properties in accord with its reported NMR, IR and optical rotation.[7] With the C_1–C_6 and C_7–C_{15} fragments of epothilone A prepared, completion of the total synthesis is at hand.

Experimental

All solvents were purchased as HPLC grade and where appropriate were distilled from CaH_2 and stored over 4Å molecular sieves prior to use. Solvent and reagent transfers were accomplished via dried syringe, and all reactions were routinely conducted under an inert atmosphere unless otherwise indicated. Flash chromatography was accomplished using silica gel (SAI, 32–63 μm). All NMR analysis were conducted in $CDCl_3$ and referenced to chloroform at δ 7.27. ^1H NMR spectra were recorded either on Bruker DRX 300, 400 or 500 spectrometers operating at 300, 400, 500 MHz, respectively. ^{13}C NMR were recorded either on Bruker DRX 300, 400 or 500 spectrometers operating at 75.4, 100.6, 125.7 MHz, respectively. HRMS were obtained on a Bruker Bioapex I 3T FTMS using ESI interface. Optical rotations were recorded on Jasco DIP-370 digital polarimeter. IR spectra were recorded on a Perkin–Elmer 1610 FT spectrometer.

2-(1,1-Dimethylprop-2-enyl)-2-ethyl-1,3-dioxolane 34. To a solution of 3,3-dimethyl-4-oxohex-1-ene **33**[33] (12.6 g, 100 mmol) in 300 ml of benzene was added diethylene glycol (12.4 g, 200 mmol) and pyridinium *p*-toluene sulfonate (1 g), and the mixture was refluxed, using a Dean–Stark apparatus, for 30 h. The reaction mixture was washed with sodium bicarbonate, water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent afforded the crude product which was distilled under reduced pressure to give the pure ketal **34** (11.7 g, 69%). IR (thin film): ν_{max} 2974, 2886, 1637, 1465, 1414, 1376, 1218, 1146, 1066, 913, 689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.96 (dd, J=17.6, 10.7 Hz, 1H), 4.96 (dd, J=13.1, 1.5 Hz, 1H), 4.92 (dd, J=6.5, 1.5 Hz, 1H), 3.97 (dt, J=3.0, 2.0 Hz, 2H), 3.94 (dt, J=3.0, 2.0 Hz, 2H), 1.65 (q, J=7.4 Hz, 2H), 0.97 (s, 6H), 0.77 (t, J=7.4 Hz, 3H); ^{13}C NMR: (100.6 MHz, $CDCl_3$) δ 145.2, 115.3, 111.8, 66.8, 46.4, 27.7, 22.3, 7.5; FAB HRMS *m/z* 171.1382, $(MH)^+$ calcd for $C_{10}H_{19}O_2$ 171.1385.

2-(2-Ethyl-1,3-dioxolan-2-yl)-2-methyl propanal 7. Ozone was bubbled through a solution of the ketal **34** (11.05 g, 65 mmol) in methanol (30 ml) at −78°C until the solution became slightly blue in color. Excess ozone was flushed out with a stream of argon and to the crude ozonide was added dimethyl sulfide (15 ml). The reaction mixture was allowed to warm to rt. After stirring for 3 h, water was added, and the solution was extracted with ethyl acetate. The organic layer was washed with water and brine and dried over anhydrous sodium sulfate. Evaporation of the solvent gave the crude product which was purified by column chromatography (silica gel, 3% ethyl acetate in hexanes) to afford the pure aldehyde **7** (7.93 g, 71%). IR (thin film): ν_{max} 2979, 2891, 1731, 1466, 1393, 1150, 1095, 1059, 932, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.65 (s, 1H), 4.01 (dt, 3.3, 1.8 Hz, 2H), 3.97 (dt, J=3.3, 1.8 Hz, 2H), 1.61 (q, J=7.4 Hz, 2H), 1.03, (s, 3H), 1.03 (s, 3H), 0.80 (t, J=7.4 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 205.3, 113.5, 66.5, 55.0, 28.7, 17.8, 7.3; FAB HRMS *m/z* 173.1150, $(MH)^+$ calcd for $C_9H_{17}O_3$ 173.1177.

Aldol condensation of the oxazolidinone 9 with aldehyde 7. To a solution of the oxazolidinone **9** (342 mg, 2 mmol) in dry methylene chloride (3 ml) at 0°C was added 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate (594 mg, 2.2 mmol) followed by diisopropylethyl amine (310 mg, 2.4 mmol), and the mixture was stirred for 30 min. The resulting slurry was cooled to −78°C, and the aldehyde **7** (378 mg, 2.2 mmol) in methylene chloride (1 ml) was added. After stirring for 1 h the solution was allowed to warm to rt. Stirring was continued for an additional 2 h. The reaction was quenched with buffer (pH 7), extracted with ether and the solvent was evaporated. The crude material obtained was dissolved in methanol (4 ml) and hydrogen peroxide (112 mg, 3.3 mmol) was added at 0°C. After stirring for 2 h, water was added, and the solution was extracted with ethyl acetate. The organic layer was washed with water, brine, dried over anhydrous sodium sulfate and evaporated. The crude product obtained was purified by column chromatography over (silica gel, 25% ethyl acetate in hexanes) to afford the pure adducts **12** (212 mg, 31%) and **13** (206 mg, 30%).

(4*S*)-3-[(3*R*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-hydroxy-4-methylpentanoyl]-4-(methylethyl)-1,3-oxazolidin-2-one 12. $[\alpha]_D^{22}$=+93.0 (*c*=1.0, $CHCl_3$); IR (thin film): ν_{max} 3507, 2969, 2888, 1780, 1702, 1387, 1303, 1202, 1150, 1062, 924, 710 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 4.37 (dt, J=7.5, 3.7 Hz, 1H), 4.04–4.28 (m, 3H), 3.89–3.99 (m, 4H), 3.76

(dd, J=1.6, 1.6 Hz, 1H), 3.07 (dd, J=14.7, 10.2 Hz, 1H), 2.86 (ddd, J=14.5, 2.3, 2.3 Hz, 1H), 2.0–2.35 (m, 1H), 1.79 (dq, 14.4, 7.2 Hz, 1H), 1.68 (dq, J=14.4, 7.2 Hz 1H), 0.86 (s, 3H), 0.84 (s, 3H), 0.80 (d, J=7.4 Hz, 3H), 0.78 (t, J=7.3 Hz, 3H), 0.78 (d, J=7.4 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 172.6, 154.6, 117.4, 72.6, 67.5, 66.8, 63.8, 58.9, 46.6, 38.4, 28.9, 27.8, 21.8, 18.2, 16.5, 15.1, 8.0; FAB HRMS m/z 344.2070, $(MH)^+$ calcd for $C_{17}H_{30}NO_6$ 344.2073.

(4*S*)-3-[(3*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-hydroxy-4-methylpentanoyl]-4-(methylethyl)-1,3-oxazolidin-2-one 13. $[\alpha]_D^{22}$=+11.0 (c=1.21, $CHCl_3$); IR (thin film): ν_{max} 3508, 2969, 2889, 1780, 1701, 1468, 1387, 1303, 1204, 1062, 924, 711 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$) δ 4.42 (dt, J=6.4, 3.2 Hz, 1H), 4.11–4.27 (m, 3H), 3.95–4.06 (m, 4H), 3.79 (dd, J=1.7, 1.7 Hz, 1H), 3.26 (dd, J=15.1, 10.3 Hz, 1H), 2.84 (ddd, J=15.0, 2.3, 1.6 Hz, 1H), 2.32–2.44 (m, 1H), 1.86 (dq, J=14.3, 7.2 Hz, 1H), 1.73 (dq, J=14.3, 7.2 Hz, 1H), 0.93 (s, 3H), 0.88 (s, 3H), 0.86 (d, J=7.0 Hz, 3H), 0.84 (t, J=7.3 Hz, 3H), 0.84 (d, J=7.0 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 172.3, 154.0, 116.8, 72.3, 67.0, 66.4, 63.1, 58.5, 46.2, 37.9, 28.1, 27.3, 21.1, 17.8, 16.4, 14.4, 7.5; FAB HRMS m/z 344.2097, $(MH)^+$ calcd for $C_{17}H_{30}NO_6$ 344.2073.

Aldol condensation of the oxazolidinone 9 with aldehyde 8. To a solution of the oxazolidinone **9** (342 mg, 2 mmol) in dry methylene chloride (3 ml) at 0°C was added 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate (594 mg, 2.2 mmol) followed by diisopropylethyl amine (310 mg, 2.4 mmol) and the mixture was stirred for 30 min. The slurry was cooled to −78°C and aldehyde **8** (282 mg, 2.2 mmol) in methylene chloride (1 ml) was added. After stirring for 1 h, the solution was allowed to warm to rt. Stirring was continued for another 2 h, and the reaction was quenched with buffer (pH 7), extracted with ether, and the solvent was evaporated. The crude material obtained was dissolved in methanol (4 ml) and hydrogen peroxide (112 mg, 3.3 mmol) was added at 0°C. After stirring for 2 h, excess water was added and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated. The crude product obtained was purified by column chromatography (silica gel, 25% ethyl acetate in hexanes) to afford the pure adducts **16** (173 mg, 29%) and **17** (180 mg, 30%).

1-[(4*S*)-4-Methylethyl-2-oxo-1,3-oxazolidin-3-yl]-(3*R*)-3-hydroxy-4,4-dimethyl heptane-1,5-dione 16. $[\alpha]_D^{22}$=+83.2 (c=0.7, $CHCl_3$); IR (thin film): ν_{max} 3513, 2968, 2937, 1779, 1699, 1387, 1205, 771, 703 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$) δ 4.42 (dt, J=7.5, 3.4 Hz, 1H), 4.16–4.35 (m, 3H), 3.17 (bs, 1H), 3.06 (dd, J=16.3, 2.6 Hz, 1H), 2.94 (dd, J=16.3, 10.0 Hz, 1H), 2.53 (dq, J=7.2, 2.4 Hz, 2H), 2.27–2.40 (m, 1H), 1.17 (s, 3H), 1.13 (s, 3H), 1.00 (t, J=7.1 Hz, 3H), 0.89 (d, J=7.0 Hz, 3H), 0.86 (d, J=7.0 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 216.2, 172.2, 154.0, 72.4, 63.4, 58.3, 50.9, 37.8, 31.0, 28.4, 21.4, 19.3, 17.8, 14.6, 7.7; FAB HRMS m/z 300.1816, $(MH)^+$ calcd for $C_{15}H_{26}NO_5$ 300.1811.

1-[(4*S*)-4-Methylethyl-2-oxo-1,3-oxazolidin-3-yl]-(3*S*)-3-hydroxy-4,4-dimethyl heptane-1,5-dione 17. $[\alpha]_D^{22}$=+28.0 (c=1.35, $CHCl_3$); IR (thin film): ν_{max} 3512, 2969, 2878, 1780, 1699, 1468, 1388, 1206, 1100, 1059, 972 cm^{-1}; ^{1}H NMR: (300 MHz, $CDCl_3$) δ 4.43 (dt, J=7.5, 3.5 Hz, 1H), 4.17–4.33 (m, 3H), 3.24 (d, J=5.0 Hz, 1H), 3.06 (dd, J=15.6, 9.5 Hz, 1H), 2.97 (dd, J=15.6, 3.1 Hz, 1H), 2.54 (dq, J=7.0, 1.3 Hz, 2H), 2.28–2.44 (m, 1H), 1.19 (s, 3H), 1.13 (s, 3H), 1.01 (t, J=7.0 Hz, 3H), 0.90 (d, J=6.9 Hz, 3H), 0.86 (d, J=6.9 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 215.9, 172.5, 154.1, 72.6, 63.5, 58.5, 51.0, 37.7, 31.1, 28.3, 21.3, 19.5, 17.9, 14.6, 7.7; FAB HRMS m/z 300.1799, $(MH)^+$ calcd for $C_{15}H_{26}NO_5$ 300.1811.

General procedure for the aldol reaction of thiomethyl-oxazolidinones with the aldehydes

To a solution of the thiomethyloxazolidinone (2 mmol) in dry methylene chloride (3 ml) at 0°C was added boryltriflate (2.2 mmol) followed by diisopropylethyl amine (310 mg, 2.4 mmol), and the mixture was stirred for 30 min. The slurry was cooled to −78°C, and the aldehyde (2.2 mmol) in methylene chloride (1 ml) was added. After stirring for 1 h, the solution was allowed to warm to rt. Stirring was continued for 2 h and the reaction was quenched with buffer (pH 7), extracted with ether and the solvent was evaporated. The resulting crude material was dissolved in methanol (4 ml) and hydrogen peroxide (112 mg, 3.3 mmol) was added at 0°C. After stirring for 2 h, excess water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated. The product obtained was dissolved in acetone (10 ml) and Raney nickel was added (1 g, 50% slurry in water). The resultant mixture was stirred at 60°C for 45 min and filtered through a pad of celite. The filter aid was washed with acetone and the solvent evaporated to give the desulfurized product, which was purified by column chromatography (silica gel, 25% ethyl acetate in hexanes) to give the aldol adducts.

Aldol condensation of thiomethyloxazolidinone 10 with the aldehyde 7 using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate. Condensation of the oxazolidinone **10** with the aldehyde **7** using the 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **12** (302 mg, 44%) and **13** (137 mg, 20%).

Aldol condensation of thiomethyloxazolidinone 10 with the aldehyde 7 using dibutylboron trifluoromethanesulfonate. Condensation of the oxazolidinone **10** with the aldehyde **7** using dibutylboron trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **12** (172 mg, 25%) and **13** (281 mg, 41%).

Aldol condensation of thiomethyloxazolidinone 11 with the aldehyde 7 using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate. Condensation of the oxazolidinone **11** with the aldehyde **7** using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **14** (151 mg, 22%) and **15** (322 mg, 47%).

(4*R*)-3-[(3*R*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-hydroxy-4-methylpentanoyl]-4-(methylethyl)-1,3-oxazolidin-2-one 14. $[\alpha]_D^{22}=-12.3$ (c=1.1, $CHCl_3$); IR (thin film): ν_{max} 3508, 2970, 2886, 1780, 1700, 1468, 1387, 1303, 1205, 1150, 1061, 971, 925 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 4.40 (dt, J=7.5, 3.7 Hz, 1H), 4.10–4.31 (m, 4H), 3.96–4.05 (m, 4H), 3.79 (bs, 1H), 3.27 (dd, J=15.1, 10.2 Hz, 1H), 2.85 (dd, J=15.1, 2.4 Hz, 1H), 2.29–2.46 (m, 1H), 1.87 (dq, J=14.5, 7.3 Hz, 1H), 1.74 (dq, J=14.5, 7.3 Hz, 1H), 0.94 (s, 3H), 0.89 (s, 3H), 0.87 (d, J=7.2 Hz, 3H), 0.85 (t, J=7.3 Hz, 3H), 0.84 (d, J=7.2 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 172.3, 154.0, 116.8, 72.3, 67.0, 66.4, 63.1, 58.5, 46.2, 37.9, 28.1, 27.3, 21.1, 17.8, 16.4, 14.4, 7.5; FAB HRMS m/z 344.2094, $(MH)^+$ calcd for $C_{17}H_{30}NO_6$ 344.2073.

(4*R*)-3-[(3*S*)-4-(2-Ethyl-1,3-dioxolan-2-yl)-3-hydroxy-4-methylpentanoyl]-4-(methylethyl)-1,3-oxazolidin-2-one 15. $[\alpha]_D^{22}=-92.6$ (c=1.06, $CHCl_3$); IR (thin film): ν_{max} 3502, 2969, 2892, 1780, 1702, 1388, 1303, 1202, 1063, 924 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 4.45 (dt, J=7.1, 3.8 Hz, 1H), 4.10–4.35 (m, 4H), 3.95–4.09 (m, 4H), 3.88 (bs, 1H), 3.15 (dd, J=14.7, 10.3 Hz, 1H), 2.95 (dd, J=14.7, 2.1 1H), 2.32–2.40 (m, 1H), 1.87 (dq, J=14.5, 7.2 Hz, 1H), 1.77 (dq, J=14.5, 7.2 Hz, 1H), 0.94 (s, 3H), 0.92 (s, 3H), 0.89 (d, J=6.9 Hz, 3H), 0.88 (t, J=7.0 Hz, 3H), 0.87 (d, J=6.9 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 172.1, 154.1, 116.9, 72.1, 67.0, 66.4, 63.3, 58.4, 46.1, 38.0, 28.4, 27.3, 21.3, 17.8, 16.0, 14.7, 7.5; FAB HRMS m/z 344.2078, $(MH)^+$ calcd for $C_{17}H_{30}NO_6$ 344.2073.

Aldol condensation of thiomethyloxazolidinone 11 with the aldehyde 7 using dibutylboron trifluoromethanesulfonate. Condensation of the oxazolidinone **11** with the aldehyde **7** using the dibutylboron trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **14** (309 mg, 45%) and **15** (171 mg, 25%).

Aldol condensation of thiomethyloxazolidinone 10 with the aldehyde 8 using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate. Condensation of the oxazolidinone **10** with the aldehyde **8** using the 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **16** (317 mg, 53%) and **17** (84 mg, 14%).

Aldol condensation of thiomethyloxazolidinone 10 with the aldehyde 8 using dibutylboron trifluoromethanesulfonate. Condensation of the oxazolidinone **10** with the aldehyde **8** using dibutylboron trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **16** (102 mg, 17%) and **17** (317 mg, 53%).

Aldol condensation of thiomethyloxazolidinone 11 with the aldehyde 8 using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate. Condensation of the oxazolidinone **11** with the aldehyde **8** using the 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **18** (96 mg, 16%) and **19** (299 mg, 50%).

1-[(4*R*)-4-Methylethyl-2-oxo-1,3-oxazolidin-3-yl]-(3*R*)-3-hydroxy-4,4-dimethyl heptane-1,5-dione 18. $[\alpha]_D^{22}=-29.0$ (c=1.2, $CHCl_3$); IR (thin film): ν_{max} 3521, 2969, 2878, 1780, 1699, 1468, 1387, 1302, 1207, 1101, 1059, 1022, 972, 775 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 4.38 (dt, J=8.4, 3.3 Hz, 1H), 4.12–4.26 (m, 3H), 3.26 (d, J=5.1 Hz, 1H), 2.99 (dd, J=16.4, 9.9 Hz, 1H), 2.92 (dd, J=16.4, 2.7 Hz, 1H), 2.49 (dq, J=7.1, 2.9 Hz, 2H), 2.25–2.36 (m, 1H), 1.13, (s, 3H), 1.06 (s, 3H), 0.95 (t, J=7.1 Hz, 3H), 0.85 (d, J=7.0 Hz, 3H), 0.81 (d, J=7.0 Hz, 3H); ^{13}C NMR: (100.6 MHz, $CDCl_3$) δ 216.2, 172.8, 15.5, 72.9, 63.9, 58.9, 51.4, 38.1, 31.5, 28.7, 21.6, 19.9, 18.2, 15.0, 8.1; FAB HRMS m/z 300.1808, $(MH)^+$ calcd for $C_{15}H_{26}NO_5$ 300.1811.

1-[(4*R*)-4-Methylethyl-2-oxo-1,3-oxazolidin-3-yl]-(3*S*)-3-hydroxy-4,4-dimethyl heptane-1,5-dione 19. $[\alpha]_D^{22}=-84.0$ (c=2.25, $CHCl_3$); IR (thin film): ν_{max} 3513, 2966, 2360, 1781, 1700, 1467, 1387, 1206, 1059, 971 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 4.44 (dt, J=8.2, 3.4 Hz, 1H), 4.34 (ddd, J=10.3, 3.9, 1.8 Hz, 1H), 4.28 (dd, J=9.0, 8.9 Hz, 1H), 4.21 (dd, J=9.1, 3.0 Hz, 1H), 3.16 (d, J=4.8 Hz, 1H), 3.09 (dd, J=16.3, 2.2 Hz, 1H), 2.98 (dd, J=16.3, 10.3 Hz, 1H), 2.56 (dq, J=7.2, 4.0 Hz, 2H), 2.32–2.42 (m, 1H), 1.20 (s, 3H), 1.16 (s, 3H), 1.03 (t, J=7.1 Hz, 3H), 0.92 (d, J=7.0 Hz, 3H), 0.89 (d, J=7.0 Hz, 3H); ^{13}C NMR: (100.6 MHz, $CDCl_3$) δ 216.5, 172.5, 154.2, 72.7, 63.7, 58.6, 51.1, 38.1, 31.3, 28.6, 21.8, 19.6, 18.1, 14.9, 8.0; FAB HRMS m/z 300.1800, $(MH)^+$ calcd for $C_{15}H_{26}NO_5$ 300.1811.

Aldol condensation of thiomethyloxazolidinone 11 with the aldehyde 8 using dibutylboron trifluoromethanesulfonate. Condensation of the oxazolidinone **11** with the aldehyde **8** using the dibutylboron trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **18** (305 mg, 51%) and **19** (102 mg, 17%).

Aldol condensation of thiomethyloxazolidinone 10 with the aldehyde 21 using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate. Condensation of the oxazolidinone **10** with the aldehyde **21** using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **23** (85 mg, 17%) and **24** (38 mg, 7%).

(4*S*)-3-[(3*R*)-3-Hydroxy-4,4-dimethylpentanoyl]-4-(methylethyl)-1,3-oxazolidin-2-one 23. $[\alpha]_D^{22}=133.4$ (c=1, $CHCl_3$); IR (thin film): ν_{max} 3549, 2962, 2874, 1782, 1697, 1373, 1183, 1059, 1021, 752 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 4.43 (dt, J=8.2, 3.3 Hz, 1H), 4.26 (dd, J=9.0, 8.9 Hz, 1H), 4.20 (dd, J=9.0, 2.9 Hz, 1H), 3.75 (d, J=10.6 Hz, 1H), 3.14 (dd, J=16.7, 1.7 Hz, 1H), 2.94 (dd, J=16.6, 10.6 Hz, 1H), 2.71 (b, 1H), 2.30 - 2.39 (m, 1H), 0.93 (s, 9H), 0.90 (d, J=7.0 Hz, 3H), 0.86 (d, J=7.0 Hz, 3H); ^{13}C NMR: (100.6 MHz, $CDCl_3$) δ 173.8, 154.5, 75.8, 63.9, 58.8, 38.3, 34.9, 28.8, 26.0, 18.3, 15.1; FAB HRMS m/z 258.1704, $(MH)^+$ calcd for $C_{13}H_{23}NO_4$ 258.1705.

(4*S*)-3-[(3*S*)-3-Hydroxy-4,4-dimethylpentanoyl]-4-(methylethyl)-1,3-oxazolidin-2-one 24. $[\alpha]_D^{22}=38.4$ (c=1.1,

$CHCl_3$); IR (thin film): ν_{max} 3529, 2961, 2873, 1781, 1695, 1387, 1202, 774, 695 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 4.44 (dt, J=7.5, 3.5 Hz, 1H), 4.30 (dd, J=9.0, 8.9 Hz, 1H), 4.22 (dd, J=9.0, 3.2 Hz, 1H), 3.72 (dd, J=8.0, 4.8 Hz, 1H), 3.07 (d, J=3.3 Hz, 1H), 3.05 (s, 1H), 2.33 - 2.41 (m, 1H), 0.94 (s, 9H), 0.92 (d, J=7.0 Hz, 3H), 0.88 (d, J=7.0 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 173.4, 75.8, 63.4, 58.5, 37.7, 34.6, 28.3, 25.5, 17.8, 14.6; FAB HRMS *m/z* 258.1701, $(MH)^+$ calcd for $C_{13}H_{23}NO_4$ 258.1705.

Aldol condensation of thiomethyloxazolidinone 10 with the aldehyde 22 using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate. Condensation of the oxazolidinone **10** with the aldehyde **22** using 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate following the general procedure described above resulted in the formation of the adducts **25** and **26**.

(4*S*)-3-[(3*S*)-3-Hydroxy heptanoyl]-4-(methylethyl)-1,3-oxazolidin-2-one 26. (211 mg, 41%). $[\alpha]_D^{22}$=41.1 (c=1, $CHCl_3$); IR (thin film): ν_{max} 3527, 2959, 2932, 1780, 1697, 1387, 1206, 1058, 972, 711 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 4.40 (dt, J=7.9, 3.4 Hz, 1H), 4.24 (dd, J=9.0, 8.9 Hz, 1H), 4.17 (dd, J=9.0, 3.1 Hz, 1H), 4.00 (tt, J=5.7, 5.7 Hz, 1H) 3.02 (d, J=6.0 Hz, 2H), 2.9–3.1(b, 1H), 2.27–2.40 (m, 1H), 1.25–1.59 (m, 6H), 0.87 (d, J=7.0 Hz, 3H), 0.88 (t, J=6.8 Hz, 3H), 0.83 (d, J=7.0 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 172.7, 154.0, 67.9, 63.4, 58.2, 42.4, 36.2, 28.2, 27.4, 22.4, 17.7, 14.5, 13.8; FAB HRMS *m/z* 258.1703, $(MH)^+$ calcd for $C_{13}H_{23}NO_4$ 258.1705.

Thiomethyl hydroxy adducts 27, 28 and 29. Condensation of the oxazolidinone **10** with the aldehyde **8** using the 9-borobicyclo[3.3.1]nonyl trifluoromethanesulfonate following the general procedure described above but without Raney nickel treatment resulted in the formation of the adducts **27** (324 mg, 47%), **28** (114 mg, 16%) and **29** (38 mg, 5%).

1-[(4*S*)-4-Methylethyl-2-oxo-1,3-oxazolidin-3-yl]-(2*S*,3*R*)-3-hydroxy-2-thiomethyl-4,4-dimethyl heptane-1,5-dione 27. $[\alpha]_D^{22}$=65.7 (c=1.2, $CHCl_3$); IR (thin film): ν_{max} 3501, 2969, 1778, 1694, 1373, 1304, 1206, 1102, 969, 710 cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 4.94 (d, J=6.1 Hz, 1H), 4.47 (dt, J=8.3, 3.0 Hz, 1H), 4.34 (dd, J=8.8, 8.7 Hz, 1H), 4.31 (d, J=6.1 Hz, 1H), 4.21 (dd, J=8.8, 3.0 Hz, 1H), 3.57 (b, 1H), 2.71 (dq, J=18.6, 7.0, 1H), 2.48 (dq, J=18.6, 7.0, 1H), 2.24–2.37 (m, 1H), 2.01 (s, 3H), 1.27 (s, 3H), 1.10 (s, 3H), 0.96 (t, J=7.0 Hz, 3H), 0.92 (d, J=7.0 Hz, 3H), 0.91 (d, J=7.0 Hz, 3H); ^{13}C NMR: (100.6 MHz, $CDCl_3$) δ 214.9, 171.2, 153.8, 78.0, 63.7, 58.5, 51.7, 43.3, 32.5, 29.0, 24.1, 20.1, 18.2, 15.1, 13.4, 8.1; FAB HRMS *m/z* 346.1688, $(MH)^+$ calcd for $C_{16}H_{27}NO_5S$ 346.1688.

1-[(4*S*)-4-Methylethyl-2-oxo-1,3-oxazolidin-3-yl]-(2*S*,3*S*)-3-hydroxy-2-thiomethyl-4,4-dimethyl heptane-1,5-dione 28. $[\alpha]_D^{22}$=60.8 (c=1.1, $CHCl_3$); IR (thin film): ν_{max} 3507, 2969, 1775, 1694, 1372, 1204, 1100, 974, 772, 710 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 4.92 (d, J=8.8 Hz, 1H), 4.23–4.36 (m, 2H), 4.07–4.18 (m, 2H), 3.17 (d, J=3.1 Hz, 1H), 2.48 (q, J=7.1 Hz, 1H), 2.16–2.24 (m, 1H), 2.02 (s, 3H), 1.17 (s, 3H), 0.98 (s, 3H), 0.89 (t, J=7.1 Hz, 3H), 0.85 (d, J=6.9 Hz, 3H), 0.84 (d, J=6.9 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 215.4, 168.8, 153.4, 71.2, 63.3, 58.1, 51.5, 46.2, 31.4, 28.4, 21.3, 20.1, 17.6, 14.7, 12.4, 7.7; FAB HRMS *m/z* 346.1684, $(MH)^+$ calcd for $C_{16}H_{27}NO_5S$ 346.1688.

1-[(4*S*)-4-Methylethyl-2-oxo-1,3-oxazolidin-3-yl]-(2*R*,3*R*)-3-hydroxy-2-thiomethyl-4,4-dimethyl heptane-1,5-dione 29. $[\alpha]_D^{22}$=69.3 (c=1, $CHCl_3$); IR (thin film): ν_{max} 3476, 2968, 2925, 2359, 1775, 1692, 1374, 1316, 1202, 1100, 973, cm^{-1}; ^1H NMR: (400 MHz, $CDCl_3$) δ 4.99 (d, J=8.6 Hz, 1H), 4.40 (dt, J=8.2, 3.1 Hz, 1H), 4.29, (dd, J=9.0, 9.0 Hz, 1H), 4.25 (d, J=3.3 Hz, 1H), 4.22 (dd, J=9.0, 2.8 Hz, 1H), 3.26 (d, J=3.4 Hz, 1H), 2.56 (q, J=7.1 Hz, 2H), 2.32–2.42 (m, 1H), 2.08 (s, 3H), 1.21 (s, 3H), 1.08 (s, 3H), 0.99 (t, J=7.1 Hz, 3H), 0.91 (d, J=7.0 Hz, 3H), 0.90 (d, J=7.0 Hz, 3H); ^{13}C NMR: (100.6 MHz, $CDCl_3$) δ 215.8, 169.4, 154.0, 72.5, 63.4, 59.3, 51.7, 31.7, 28.6, 22.1, 20.7, 18.4, 14.7, 13.4, 8.2; FAB HRMS *m/z* 346.1691, $(MH)^+$ calcd for $C_{16}H_{27}NO_5S$ 346.1688.

(3*R*)-3-Hydroxy-4,4-dimethyl-5-oxoheptanoic acid 20. To a solution of the adduct **12** (172 mg, 0.5 mmol) in THF (7 ml) and water (2 ml) at 0°C was added lithium hydroxide (24 mg, 1 mmol) followed by hydrogen peroxide (51 mg, 1.5 mmol). The mixture was stirred while allowing it to warm to rt. Stirring was continued for 4 h at rt. The mixture was acidified with 1N HCl (2 ml) and further stirred for 2 h. Excess water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated. The crude product obtained was purified by column chromatography (silica gel, 40% ethyl acetate in hexanes) to yield the pure acid **20** (72 mg, 76%). $[\alpha]_D^{22}$=+26.0 (c=1.85, $CHCl_3$); IR (thin film): ν_{max} 3352, 2976, 2939, 1704, 1566, 1414, 1246, 1083, 1032, 973, 886 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 4.23 (dd, J=9.4, 2.8 Hz, 1H), 2.38–2.59 (m, 4H), 1.15 (s, 3H), 1.12 (s, 3H), 1.00 (t, J=7.1 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 216.7, 177.1, 72.6, 50.7, 36.5, 31.2, 21.4, 19.4, 7.6; FAB HRMS *m/z* 189.1131, $(MH)^+$ calcd for $C_9H_{17}O_4$ 189.1127.

(3*S*)-3-Hydroxy-4,4-dimethyl-5-oxoheptanoic acid 4. Hydrolysis of the adduct **13** (172 mg, 0.5 mmol) following the procedure described above yielded the acid **4** (70 mg, 74%).

(5*S*)-7-[1,1-Bis(methylethyl)-2-methyl-1-silapropoxy]-5-hydroxy-4,4-dimethyl heptan-3-one 5. To a solution of the imide **15** (172 mg, 0.5 mmol) in dry THF (5 ml) was added lithium borohydride (24 mg, 1.1 mmol) at 0°C. The reaction was allowed to warm to rt. After stirring for 4 h, 1N HCl (2 ml) was added, and the stirring was continued for an additional 2 h. Water was added to the reaction and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated to give the crude product as a viscous liquid. The product was dissolved in dry methylene chloride (3 ml), imidazole (51 mg, 0.75 mmol), DMAP (7 mg, 0.057 mmol) and triisopropylsilyl chloride (97 mg, 0.5 mmol) were added. After stirring overnight, excess water was added to the reaction mixture and extracted with ethyl acetate. The

organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated. The crude product was purified by column chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the pure silylether **5** (60 mg, 36%). $[\alpha]_D^{22}=-4.1°$ (c=1.0, $CHCl_3$); IR (thin film): ν_{max} 3501, 2942, 2867, 1704, 1452, 1400, 1095, 882, 658 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 4.00 (ddd, J=10.0, 3.9, 2.0 Hz, 1H), 3.95 (ddd, J=10.0, 4.7, 4.7 Hz, 1H), 3.60 (d, J=2.3 Hz, 1H), 2.59 (dq, J=18.2, 7.2 Hz, 1H), 2.50 (dq, J=18.2, 7.2 Hz, 1H), 1.52–1.56 (m, 2H), 1.14 (s, 3H), 1.10 (s, 3H), 1.07–0.99 (m, 21H), 1.01 (t, J=7.2 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ 216.4, 76.6, 63.3, 51.5, 33.4, 31.2, 21.0, 19.6, 17.8, 11.6, 7.7; FAB HRMS m/z 331.2646, $(MH)^+$ calcd for $C_{18}H_{39}O_3Si$ 331.2668.

(3*S*)-1-[1,1-Bis(methylethyl)-2-methyl-1-silapropoxy]-4-(2-ethyl-1,3-dioxolan-2-yl)-4-methylpentan-3-ol 22. To a stirred solution of the imide **15** (258 mg, 0.75 mmol) in dry THF (5 ml) was added lithium borohydride (36 mg, 1.65 mmol) at 0°C. The reaction was allowed to warm to rt. After stirring for 4 h, the reaction was quenched with aqueous ammonium chloride solution and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated to give a viscous liquid. The product was dissolved in dry methylene chloride (3 ml), imidazole (77 mg, 1.13 mmol), DMAP (10 mg, 0.08 mmol) and triisopropylsilyl chloride (145 mg, 0.75 mmol) were added. After stirring overnight, water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated. The crude product obtained was purified by column chromatography (silica gel, 7% ethyl acetate in hexanes) to afford the pure silylether **22** (185 mg, 66%). $[\alpha]_D^{22}=-31.3$ (c=1.82, $CHCl_3$); IR (thin film): ν_{max} 3529, 2942, 2866, 1465, 1384, 1150, 1093, 1065, 952, 923, 882, 658 cm^{-1}; ^1H NMR: (300 MHz, $CDCl_3$) δ 3.96–4.10 (m, 4H), 3.83–3.92 (m, 3H), 1.86 (dq, J=14.6, 7.3 Hz, 1H), 1.75 (dq, J=14.6, 7.3 Hz, 1H), 1.44–1.62 (m, 2H), 1.00–1.15 (m, 21H), 0.90 (s, 3H), 0.88 (s, 3H), 0.87 (t, J=7.4 Hz, 3H); ^{13}C NMR: (75.4 MHz, $CDCl_3$) δ 117.7, 72.9, 67.5, 66.8, 61.9, 46.6, 35.1, 27.7, 21.9, 18.3, 16.5, 12.3, 8.0; FAB HRMS m/z 375.2958, $(MH)^+$ calcd for $C_{20}H_{43}O_4Si$ 375.2930.

(4*S*)-2-(2,2-Dimethyl-1,3-dioxan-4-yl)-2-methylpentan-3-one 23. Bis(acetonitrile)dichloropalladium(II) (29.5 mg, 0.1 mmol) was added to a solution of the silyl ether **22** (187 mg, 0.5 mmol) in dry acetone (5 ml), and the mixture was stirred overnight at rt. Water was added to the reaction mixture and extracted with ethyl acetate. The organic layer was washed with water and brine, dried over anhydrous sodium sulfate and evaporated. The crude product obtained was purified by column chromatography (silica gel, 10% ethyl acetate in hexanes) to afford the pure ketal **23** (74 mg, 69%).

Crystal structure determination for adduct 12. Crystals were obtained by crystallization from hexane. A colorless crystal of **12** with the dimensions 0.07×0.08×0.8 mm was measured on a Bruker P4 diffractometer using CuKα radiation (λ=1.54178 Å). Crystal data: $C_{17}H_{29}NO_6$, M=343.41, monoclinic space group $P2_1$, a=11.892(1) Å, b=6.424(1) Å, c=13.247(1) Å, β=115.41(1)°, V=914.1(2) $Å^3$, Z=2, D_c=1.25 g/cm^3, F (000)=372, μ(CuKα)=0.78 mm^{-1}. A total of 1881 reflections were collected at room temperature in the range of $4°<2\theta<114°$ of which 1517 reflections are unique and 1262 reflections $(R)_{(int)}$=0.040, observed with $I > 2\sigma(I)$. The structure was solved by direct methods and refined by least squares procedure within the SHELXL program system. The final residuals were wR_2=0.1595 and R_1=0.0624. The maximum and minimum peaks in the final electron density difference map were 0.22 and −0.24 e/$Å^3$, respectively. The absolute configuration was determined from the known configuration of the isopropyl group.

Crystal structure determination for major isomer 27. Crystals were obtained by crystallization from hexane/methylene chloride. A colorless crystal of **27** with the dimensions 0.04×0.07×0.4 mm was measured on a Bruker P4 diffractometer using CuKα radiation (λ=1.54178 Å). Crystal data: $C_{16}H_{27}NO_5S$, M=345.45, monoclinic space group $P2_1$, a=9.728(1) Å, b=9.387(1) Å, c=10.364(1) Å, β=96.68(1)°, V=940.0(2) $Å^3$, Z=2, D_c=1.22 g/cm^3, F(000)=372, μ(CuKα)=1.73 mm^{-1}. A total of 1862 reflections were collected at room temperature in the range of $4°<2\theta<114°$ of which 1364 reflections are unique and 1172 reflections $(R)_{(int)}$=0.040, observed with $I > 2\sigma(I)$. The structure was solved by direct methods and refined by least squares procedure within the SHELXL program system. The extinction coefficient used was 0.0049(15). The final residuals for the 1172 observed reflections were wR_2=0.1437 and R_1=0.0494. The maximum and minimum peaks in the final electron density difference map were 0.20 and −0.20 e/$Å^3$, respectively. The absolute configuration was determined from a second data set on the same crystal in which 2787 reflections were collected. The correct absolute configuration gave a Flack parameter of −0.0184(894) and an R_1=0.0955 for 1358 reflections after merging. The other enantiomer gave a Flack parameter of 0.9793(932) and a higher R_1=0.0990 for the 1358 reflections after merging.

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