Bioorganic & Medicinal Chemistry Letters, Vol.3, No.11, pp. 2171-2176, 1993
Printed in Great Britain

0960-894X/93 $6.00 + .00

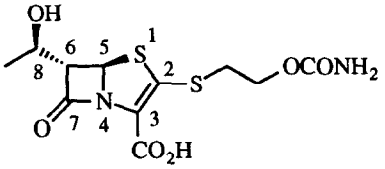
NOVEL, STEREOSELECTIVE SYNTHESES OF PENEM ANTIBIOTICS: EFFICIENT, FORMAL SYNTHESES OF SCH 34343

Donald Hou,* Janet L. Mas, Tze-Ming Chan, Yee-Shing Wong and Martin Steinman
Schering-Plough Research Institute
Kenilworth, NJ 07033
and
Andrew T. McPhail
Paul M. Gross Chemical Laboratory, Duke University
Durham, N.C. 27708

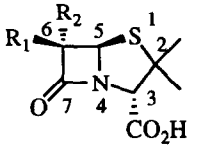
(*Received* 1 *April* 1993)

Abstract. Novel, stereoselective syntheses of (3*S*, 4*R*, 5*R*)-1-(allyloxycarbonyl)methyl-3-[1-hydroxyethyl]-4-β-naphthoxy(thiocarbonyl)thio-2-azetidinone (**13**) and (3*S*, 4*R*, 5*R*, 3'*S*, 4'*R*, 5'*R*)-4,4'-dithio-bis-1-(allyloxycarbonyl)methyl-3-[-1-hydroxyethyl]-2-azetidinone (**22**), key intermediates in the synthesis of the penem antibiotic Sch 34343, were developed starting from readily available 6-aminopenicillanic acid. Advantages of these routes include 1) the highly stereospecific introduction of the hydroxyethyl sidechain with the desired (*R*)-configuration and 2) the retention of the sulfur of the starting material.

Sch 34343 (**1**) is a member of the penem antibiotic group and possesses potent antimicrobial activity against both aerobic and anaerobic Gram-positive and Gram-negative organisms (excluding *Pseudomonas*), is stable to β-lactamases and is bactericidal.[1] Several syntheses have been developed for Sch 34343[1,2] starting from 6-aminopenicillanic acid (**2**). However, introduction of a 6-[(1*R*)-hydroxyethyl] group via an aldol condensation on 6,6-dibromopenicillanic acid (**3**),[3] readily prepared from **2**,[4] provides a mixture of stereoisomers and the sulfur of **2** is not retained in the synthetic sequence. It occurred to us that anhydropenicillins[5] may be more useful starting materials for penem synthesis for the following reasons.[6,7] DiNinno *et al.*[3a] have shown that aldol condensation of the β-enolate of **3** with acetaldehyde affords solely the C-8 (*R*) stereoisomer and that reaction of the α-enolate leads to a mixture of the C-8 (*R*) and C-8 (*S*) stereoisomers. Inspection of molecular models suggested that for anhydropenicillins the interactions that are present in **3** between the substituents at C-6 with the C-2 β-methyl group would be attenuated. This would lead to higher stereoselectivity in the aldol condensation if the enolate is formed from the β-face with greater selectivity than with **3**.[8] Secondly, cleavage of the S-C(O) bond of the anhydropenicillin would retain the sulfur and permit its incorporation into the target penem, avoiding additional steps for its removal and reintroduction.[9] This paper describes the stereospecific conversion of **2** to advanced intermediates for the synthesis of Sch 34343.

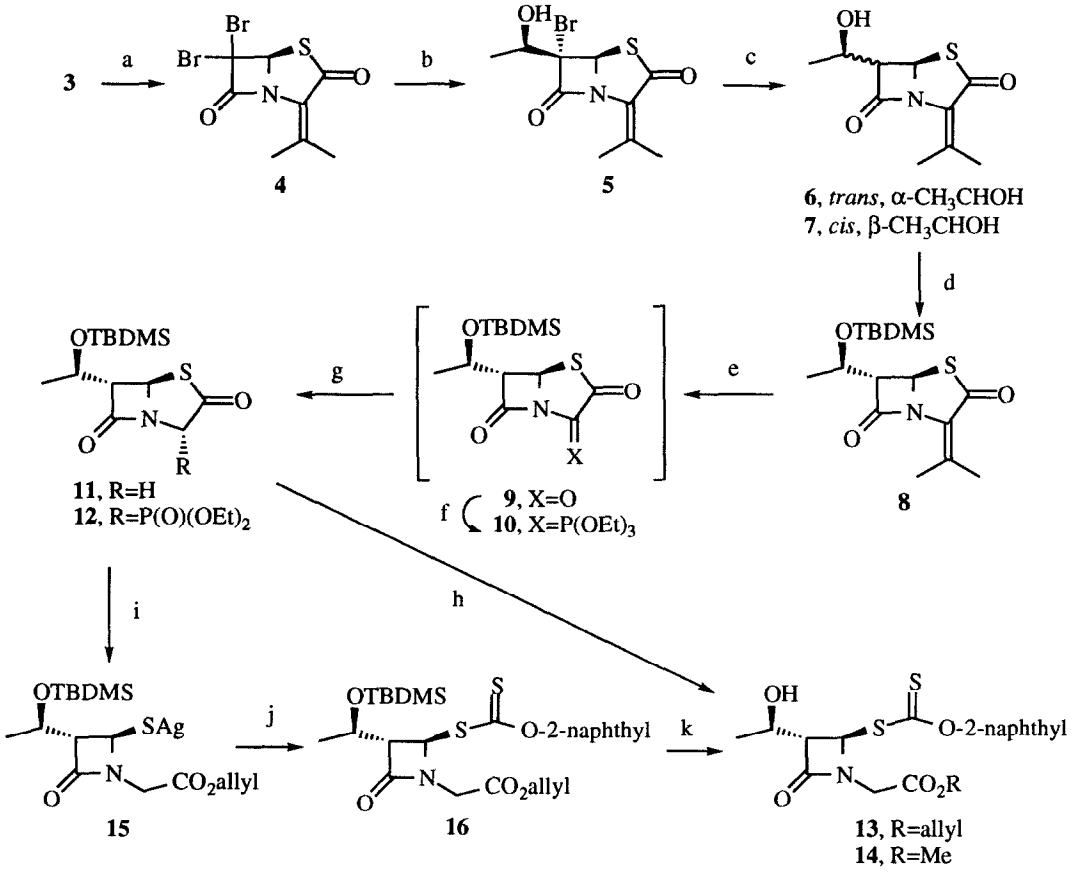


1 (Sch 34343)



2, R_1=NH_2, R_2=H
3, R_1, R_2=Br

Scheme 1



(a) $SOCl_2$, 4 eq pyridine, CH_2Cl_2, 0°C, 93% (b) 1) EtMgBr, THF, -78°C 2) 1.2 eq CH_3CHO, -78°C, 93% (c) Zn, NH_4OAc, MeOH, 0°C, 76% (d) TBDMSCl, pyridine, DMF, 97% (e) O_3, EtOAc, -78°C (not isolated) (f) $P(OEt)_3$, 5 eq, -78°C→RT (not isolated) (g) HOAc, H_2O, 42% (**8** → **11**) (h) 1) allyl alcohol or MeOH, conc. HCl 2) **NCCT**, 10% (i) AgIm, allyl alcohol, CH_3CN (j) **NCCT**, CH_2Cl_2, 62% (**11** → **16**) (k) HOAc/THF/H_2O (3:1:1), 70°C, 86%.

Clayton[4a] has previously described the synthesis of **3** from **2** and the conversion of **3** to anhydropenicillin **4**, in modest yield, via rearrangement of the mixed anhydride of **3** (Scheme 1). It was found that by proceeding through the acid chloride[5] the rearrangement went very well to afford **4** in 93% yield.[10] Of note is that pyridine is sufficient for the rearrangement to proceed in this case since Wolfe *et al.*[5] reported that addition of the more basic triethylamine is necessary to effect rearrangement. In this case triethylamine afforded **4** together with a significant amount of 6-α-bromoanhydropenicillin. Aldol condensation of **4** with acetaldehyde afforded a single product in 93% yield, which was expected to be 6-β-[(1*R*)-hydroxyethyl] **5** based on literature precedents.[3] Reduction with zinc then yielded a mixture of *trans* and *cis* isomers **6** and **7** in

a 15.5:1 ratio. Recrystallization (2 crops) afforded pure *trans* **6** in 75% yield. The absolute stereochemistry of **6** was determined unambiguously by single crystal X-ray analysis (See Figure 1) indicating it to be the desired 6-α-[(1*R*)-hydroxyethyl] isomer.[11]

Attention was next focused on converting **6** to an advanced intermediate suitable for conversion to Sch 34343. Silylation using TBDMSCl afforded silyl ether **8** in 97% yield. Removal of the *iso*-propylidene group was accomplished by a two-step procedure.[12] Ozonolysis gave tricarbonyl **9** (not isolated) and subsequent treatment with $P(OEt)_3$ followed by hydrolysis of the intermediate phosphorane **10** (not isolated) then afforded thiolactone **11** and phosphonate **12**[13] in 42% and 10% yield, respectively. Monitoring of the two-step sequence using ^1H, ^{13}C and ^{31}P NMR showed that formation of **9** proceeded cleanly at -70°C but that phosphorane formation occurred at an appreciable rate only at 0°C or higher (about 3 h at 12°C). Alcoholysis of the S-C(O) bond of thiolactone **11** under basic conditions (morpholine, triethylamine) were unsuccessful. However, acid catalyzed transesterification with allyl alcohol or MeOH and further reaction of the respective intermediate thiols with *O*-2-naphthalenyl carbonochloridothioate (**NCCT**) gave allyl ester **13** and methyl ester **14** in 10% and 32% yield (unoptimized), with the expected concomitant loss of the TBDMS protecting group. More successful was use of silver imidazolate to cleave the S-C(O) bond, which in the presence of allyl alcohol afforded crude silver salt **15**.[14,15] Subsequent treatment with **NCCT** then gave **16** in 62% overall yield for the two steps. Removal of the TBDMS group afforded **13** in 86% yield.[16] Since both **13**[2b] and **16**[17] have been converted to Sch 34343, these routes constitute formal syntheses of Sch 34343.

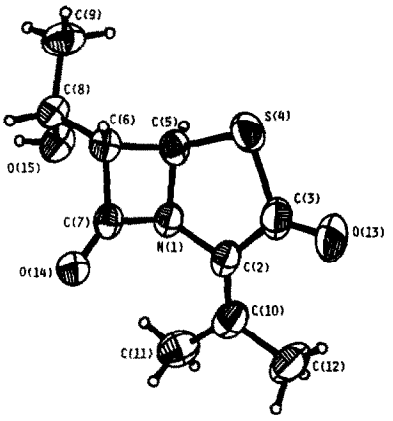
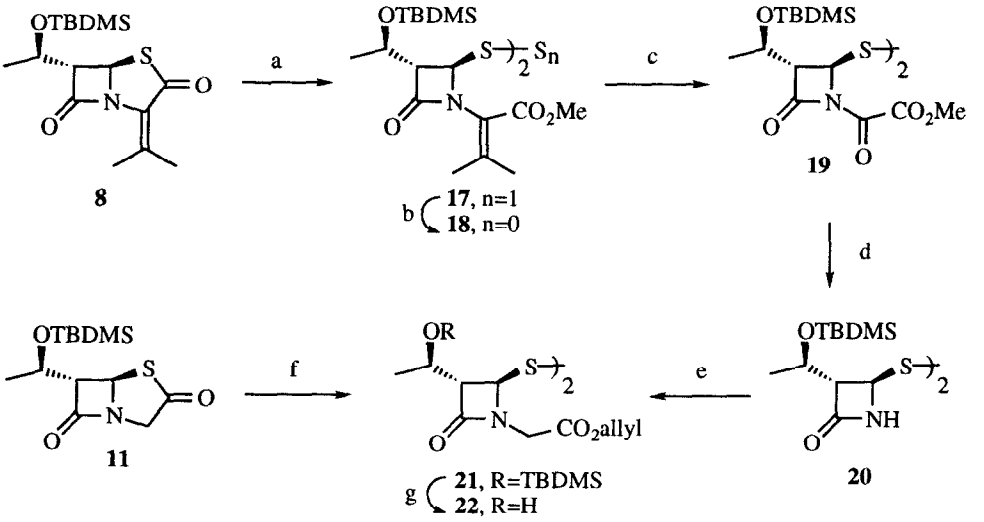


Figure 1. ORTEP diagram (50% probability ellipsoids) showing the solid-state conformation of **6**; small circles represent hydrogen atoms.

Although the cleavage of the S-C(O) bond of thiolactone **6** with silver imidazolate worked well, the conversion of **8**→**11** proceeded in only modest yields. Therefore, an alternative method for cleavage of the S-C(O) bond was developed using an earlier intermediate (Scheme 2). Treatment of **8** with CuCl in the presence of oxygen and MeOH gave two products, which were identified as the symmetrical trisulfide **17** and disulfide **18** (≈1:5 ratio). Trisulfide **17** could be converted to disulfide **18** upon treatment with PPh_3[18] to give disulfide **18** in 86% overall yield. Control experiments indicated that the additional sulfur in trisulfide **18** comes from the starting material and is the result of both C(5)-S and S-C(O) bond cleavages. Removal of the nitrogen side-chain was accomplished by a two-step sequence. Ozonolysis afforded *bis*-oxalimide **19** in 90% yield, which was then treated with NH_4OH to complete removal of the side-chain to give **20** in 88% yield. Alkylation with allyl iodoacetate gave **21** in 72% yield. Alternatively, disulfide **21** was also prepared from **11** by copper-catalyzed cleavage of the S-C(O) bond in the presence of allyl alcohol in 73% yield. Finally, removal of the TBDMS group afforded the key intermediate **22** in 89% yield.[16] As with **13** and **16** this constitutes a formal synthesis of Sch 34343 since **22** is a known intermediate for its synthesis.[2b]

Scheme 2



(a) CuCl, 0.56 eq, O_2, MeOH, 50°C (b) PPh_3, CH_3CN, RT, combined yield for (a) and (b) is 86% (c) 1) O_3, CH_2Cl_2, -78°C 2) Me_2S, RT, 90% (d) 5% NH_4OAc, Et_2O, RT, 88% (e) 2.4 eq NaH, 4 eq allyl iodoacetate, THF, -30°C, 72% (f) 1 eq CuCl, allyl alcohol, 55°C, 73% (g) HOAc/THF/H_2O (3:1:1), 70°C, 89%.

To summarize, two routes were developed starting from **2** that intersect known intermediates (**13**, **16** and **22**) for the synthesis of Sch 34343. Notable advantages of these short routes include the highly stereoselective introduction of the 6-(*R*)-hydroxyethyl sidechain and the retention of the C-5 sulfur of **2**. Furthermore, these routes are applicable to the synthesis of other penems.

Acknowledgment. The authors (DH) are grateful to Drs. N. I. Carruthers and S. W. McCombie for helpful discussions during the course of this work, to the Physical and Chemical Research Development Group for obtaining optical rotations, mass spec and microanalysis results, to Dr. J. J. Kaminski for molecular modeling calculations of the epimers of phosphonate **12** and to Mrs. J. Nocka for help in naming the compounds.

References and Notes

1. Ganguly, A. K.; Afonso, A.; Girijavallabhan, V. M.; McCombie, S. *J. Antimicrobial Chemotherapy* **1985**, *15*, *Suppl. C.*, 1.
2. (a) McCombie, S. W.; Ganguly, A. K. *Medicinal Research Reviews* **1988**, *8*, 393 and references cited therein. (b) Gala, D.; Chiu, J. S.; Ganguly, A. K.; Girijavallabhan, V. M.; Jaret, R. S.; Jenkins, J. K.; McCombie, S. W.; Nyce, P. L.; Rosenhouse, S.; Steinman, M. *Tetrahedron* **1992**, *48*, 1175.
3. (a) DiNinno, F.; Beattie, T. R.; Christensen, B. G. *J. Org. Chem.* **1977**, *42*, 2960. (b) Aimetti, J. A.; Kellogg, M. S. *Tetrahedron Lett.* **1979**, *20*, 3805.
4. (a) Clayton, J. P. *J. Chem. Soc. (C)* **1969**, 2123. (b) For an improved procedure, see Volkmann, R. A.; Carroll, R. D.; Drolet, R. B.; Elliot, M. L.; Moore, B. S. *J. Org. Chem.* **1982**, *47*, 3344.
5. Wolfe, S.; Godfrey, J. C.; Holdrege, C. T.; Perron, Y. G. *Can. J. Chem.* **1968**, *46*, 2549.

6. This work is part of Schering-Plough Corp. *Eur. Pat. Appl.* EP 255,278 (*C. A.* **109:** P92652j) and covers subsequent *U.S. Patents* 4,767,853 (August 30, 1988); 4,876,338 (October 24, 1989); 4,948,885 (August 14, 1990) and 5,053,502 (October 1, 1991).
7. While this work was in progress, workers at Bristol-Myers reported similar results for the conversion of 6,6-dibromopenicillanic acid to 6-[(1*R*)-hydroxyethyl]anhydropenicillin **6**. See Martel, A.; Daris, J.-P.; Bachand, C.; Menard, M. *Can. J. Chem.* **1987**, *65*, 2179.
8. Work at Pfizer showed that higher C-8 (*R*) stereochemistry could be achieved in the aldol condensation by increasing the amount of β-face selectivity and minimizing the steric effect of the β-methyl group using penicillin based substrates. See Brown, B. B.; Volkmann, R. A. *Tetrahedron Lett.* **1986**, *27*, 1545.
9. For a different approach for retention of the sulfur of 6-aminopenicillanic acid for penem synthesis, see Alpegiani, M.; Bedeschi, A.; Giudici, F.; Perrone, E.; Franceschi, G. *J. Am. Chem. Soc.* **1985**, *107*, 6398.
10. Analytical samples were prepared by flash chromatography and/or recrystallization except for compounds **9** and **10**, which were not fully characterized. ^{1}H NMR's for compounds **3** and **4** were consistent with those reported in Reference 4a. ^{1}H NMR's for compounds **5**, **6**, **7** and **8** were in agreement with those reported in Reference 7. **9**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.12 (s, 3H), 0.14 (s, 3H), 0.86 (s, 9H), 1.34 (d, 3H, *J* = 7 Hz), 4.30 (m, 1H), 4.56 (m, 1H), 5.70 (d, 1H, *J* = 3.7 Hz); ^{13}C NMR (100.2 MHz, CD_3COCD_3) δ -5.5, -4.0, 18.4, 21.7, 25.9, 50.4, 65.0, 69.8, 156.9, 164.2, 189.8 **10**: ^{13}C NMR (100.2 MHz, CD_3COCD_3) δ 166.9 (d, $^1J_{PC}$ = 119.4), 175.4, 189.4 (d, $^2J_{PC}$ = 37.3 Hz); ^{31}P (161.2 MHz, CD_3COCD_3, 85% H_3PO_4 as external standard) δ 36.4. **11**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.87 (s, 9H), 1.27 (d, 3H, *J* = 6.2 Hz), 3.44 (dd, 1H, *J* = 0.9, 16.8 Hz), 3.53 (dd, 1H, *J* = 1.5, 4.4 Hz), 4.30 (m, 1H), 4.37 (d, 1H, *J* = 16.8 Hz), 5.37 (s, 1H); ^{13}C NMR (100.2 MHz, CD_3COCD_3) δ -5.0, -4.2, 18.4, 22.5, 26.0, 54.0, 63.4, 65.8, 72.5, 171.0, 205.2; IR ($CHCl_3$) 1768, 1725 cm^{-1}; mp 65-66°C (Et_2O/pet ether); $[\alpha]_D^{25}$ +161.5° (*c* 0.997, $CHCl_3$); Anal. Calcd for $C_{13}H_{23}O_3SSi$: C, 51.79; H, 7.69; N, 4.65; S, 10.63. Found: C, 51.78; H, 7.58; N, 4.62; S, 10.64. **12**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.077 (s, 3H), 0.087 (s, 3H), 0.88 (s, 9H), 1.27 (d, 3H, *J* = 6.3 Hz), 1.35 (m, 6H), 3.56 (m, 1H), 4.26 (m, 4H), 4.32 (m, 1H), 4.72 (dd, 1H, *J* = 0.5, 16.9 Hz), 5.48 (dd, 1H, *J* = 1.6, 3.4 Hz); ^{13}C NMR (100.2 MHz, CD_3COCD_3) δ -4.9, -4.4, 16.6 (d, $^3J_{PC}$ = 2.5 Hz), 16.7 (d, $^3J_{PC}$ = 2.5 Hz), 18.5, 22.4, 26.1, 64.1 (d, $^2J_{PC}$ = 6.6 Hz), 64.2 (d, $^2J_{PC}$ = 6.6 Hz), 63.0 (d, $^1J_{PC}$ = 156.4 H), 62.7, 65.4, 72.8 (d, $^3J_{PC}$ = 2.8 Hz), 170.5 (d, $^3J_{PC}$ = 9.6 Hz), 200.5 (d, $^2J_{PC}$ = 4.1 H). ^{31}P (161.2 MHz, CD_3COCD_3, 85% H_3PO_4 as external standard) δ 11.7. ^{1}H NMR, IR and TLC for **13** were consistent with those reported in Reference 2b. **14**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.20 (d, 3H, *J* = 7 Hz), 2.15 (br s, 1H), 3.28 (m, 1H), 3.44 (s, 3H), 3.72 (d, 1H, *J* = 17 Hz), 4.18 (d, 1H, *J* = 17 Hz), 4.21 (m, 1H), 5.76 (m, 1H), 7.00-7.76 (m, 7H); IR ($CHCl_3$) 3500 (br), 1765, 1750 cm^{-1}; MS (FAB, glycerol) *m/e* 406 $(M+1)^+$. ^{1}H NMR for **15** was consistent with that reported in Reference 14. **16**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.12 (d. 6H), 0.91 (s, 9H), 1.34 (d, 3H, *J* = 6.1 Hz), 3.37 (dd, 1H, *J* = 2.5, 6.0 Hz), 3.96 (d, 1H, *J* = 17.8 Hz), 4.28 (d, 1H, *J* = 17.8 Hz), 5.89 (d, 1H, *J* = 2.6 Hz), 7.25-8.00 (br m, 7H); IR (Neat, NaCl plates) 1765, 1740 cm^{-1}; MS (FAB, thioglycerol) *m/e* 546 $(M+1)^+$, 488 $(M-t\text{-}Bu)^+$, 326 (100%, M—SC(S)O-naphthyl)$^+$; $[\alpha]_D^{25}$ +80.1° (*c* 1.171, $CHCl_3$); Anal. Calcd for $C_{27}H_{35}NO_5S_2Si$: C, 59.42; H, 6.46; N, 2.57; S, 11.75. Found: C, 59.50; H, 6.38; N, 2.52; S, 11.51. **17**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.07 (s, 6H), 0.85 (s, 18H), 1.23 (d, 6H, *J* = 6.3 Hz), 1.94 (s, 6H), 2.23 (s, 6H), 3.29 (dd, 2H, *J* = 2.5, 3.9 Hz), 3.74 (s, 6H), 4.29 (m, 2H), 5.4 (d, 2H, *J* = 2.5 Hz); IR ($CHCl_3$) 1750, 1716 cm^{-1}; MS (FAB, glycerol)

m/e 777 $(M)^+$. **18**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.07 (s, 6H), 0.09 (s, 6H), 0.88 (s, 18H), 1.33 (d, 6H, *J* = 6.3 Hz), 1.94 (s, 6H), 2.21 (s, 6H), 3.40 (dd, 2H, *J* = 2.2, 6.1 Hz), 3.72 (s, 6H), 4.26 (m, 2H), 5.14 (d, 2H, *J* = 2.2 Hz); mp 124-125°C (EtOH); IR ($CHCl_3$) 1750, 1715 cm^{-1}; MS (FAB, glycerol) *m/e* 745 $(M)^+$; $[\alpha]_D^{25}$ -105.7° (*c* 1.042, $CHCl_3$); Anal. Calcd for $C_{34}H_{60}N_2O_8S_2Si_2$: C, 54.80; H, 8.12; N, 3.76; S, 8.60. Found: C, 54.75; H, 8.05; N, 3.77; S, 8.71. **19**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.01 (s, 6H), 0.06 (s, 6H), 0.81 (s, 18H), 1.25 (d, 6H, *J* = 6.4 Hz), 3.62 (t, 2H, *J* = 2.8 Hz), 3.91 (s, 6H), 4.36 (m, 2H), 5.37 (d, 2H, *J* = 2.8 Hz); mp 147.5-148.5°C (Et_2O/pet ether); IR ($CHCl_3$) 1805, 1752, 1705 cm^{-1}; MS (FAB, glycerol) *m/e* 693 $(M)^+$; $[\alpha]_D^{25}$ -124.4° (*c* 1.013, $CHCl_3$); Anal. Calcd for $C_{28}H_{48}N_2O_{10}S_2Si_2$: C, 48.53; H, 6.98; N, 4.04; S, 9.25. Found: C, 48.70; H, 7.04; N, 3.85; S, 9.41. **20**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.057 (s, 6H), 0.064 (s, 6H), 0.86 (s, 18H), 1.24 (d, 6H, *J* = 6.2 Hz), 3.29 (dd, 2H, *J* = 2.0, 4.4 Hz), 4.22 (m, 2H), 4.79 (d, 2H, *J* = 2.1 Hz), 6.52 (br s, 2H); mp 130.5-132°C (Et_2O/pet ether); IR ($CHCl_3$) 1760 cm^{-1}; MS (FAB, glycerol) *m/e* 520 $(M+H)^+$; $[\alpha]_D^{25}$ +208.9° (*c* 1.000, $CHCl_3$); Anal. Calcd for $C_{22}H_{44}N_2O_4S_2Si_2$: C, 50.73; H, 8.51; N, 5.38; S, 12.31. Found: C, 50.49; H, 8.38; N, 5.30; S, 12.51. **21**: ^1H NMR (200 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.08 (s, 6H), 0.86 (s, 18H), 1.27 (d, 6H, *J* = 6.4 Hz), 3.34 (dd, 2H, *J* = 1.9, 5.1 Hz), 3.78 (d, 2H, *J* = 18.0 Hz), 4.28 (d, 2H, *J* = 18.0 Hz), 4.62 (d, 4H, *J* = 6.0 Hz), 5.04 (d, 2H, *J* = 1.9 Hz), 5.85 (m, 2H); MS (FAB, glycerol) *m/e* 717 $(M+1)^+$. **22**: ^1H NMR and TLC were consistent with those reported in Reference 2b.

11. *Crystal data:* $C_{10}H_{13}NO_3S$; MW = 227.28, orthorhombic, space group $P2_12_12_1(D_2^4)$, *a* = 11.350(1) Å, *b* = 19.841(2) Å, *c* = 4.946(1) Å, *V* = 1113.8(4) $Å^3$, *Z* = 4, $D_{calcd.}$ = 1.355 g cm^{-3}, μ(CuKα radiation, λ = 1.5418 Å) = 24.5 cm^{-1}. Intensity data (+*h*,+*k*,+*l*; 1367 non-equivalent reflections) were recorded on an Enraf-Nonius CAD-4 diffractometer [CuKα radiation, graphite monochromator; ω-2θ scans, θ_{max} = 75°] from a crystal of dimensions 0.06 x 0.08 x 0.80 mm. The crystal structure was solved by direct methods (MULTAN11/82). Full-matrix least-squares refinement (Enraf-Nonius SDP) of atomic positional and thermal parameters (anisotropic C, N, O, S; isotropic H) converged (max. shift:esd = 0.02) at R = 0.033 (R_w = 0.046) over 1180 reflections with $I > 3.0\sigma(I)$. The absolute stereochemistry was assigned by use of the anomalous scattering of Cu Kα radiation. X-ray crystallographic data for **6** have been deposited with the Cambridge Crystallographic Data Centre.
12. Perrone, E.; Alpegiani, M.; Bedeschi, A.; Giudici, F.; Franceschi, G. *Tetrahedron Lett.* **1984**, *25*, 2399.
13. The diethyl phosphonate group was determined to have the *S* stereochemistry (α-face) by difference nOe experiments and comparison of hydrogen bond distances for each epimer as determined by molecular modeling [SYBYL (Tripos Associates) and Macromodel, Version 3.5 (W. C. Still)].
14. For an alternative synthesis of **15** see Leanza, W. J.; DiNinno, F.; Muthard, D. A.; Wilkening, R. R.; Wildonger, K. J.; Ratcliffe, R. W.; Christensen, B. G. *Tetrahedron* **1983**, *39*, 2505.
15. Initial attempts to cleave the S-C(O) bond using $AgNO_3$/MeOH, with or without bases (pyridine, morpholine or K_2CO_3) present were unsuccessful. Contrast this to the results reported for cleavage of 4-thioacetylazetidinones using $AgNO_3$/MeOH. See Lattrell, R. *Liebigs Ann. Chem.* **1974**, 1937.
16. Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.
17. Girijavallabhan, V. M.; Ganguly, A. K.; Pinto, P. A.; Versace, R. W. Schering-Plough Corp. *U.S. Patent* 4,503,064 (*C. A.* **103**: 215072f; March 5, 1985) and subsequent *U. S. Patent* 4,530,793 (July 23, 1985).
18. (a) Harpp, D. N.; Smith, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 6045. (b) Schonbert, A. *Chem. Ber.* **1935**, *68*, 163.