Highly Diastereoselective Aldol Reactions of Cobalt-complexed and Uncomplexed Propynals with *O*-Silyl Ketene *O,S*-Ketals: Highly Stereoselective Divergent Formal Syntheses of the β-Lactam Antibiotics (±)-PS-5 and (±)-*epi*-PS-5[1]

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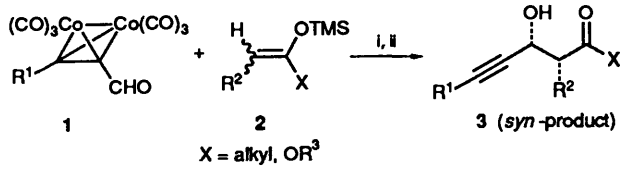
Treatment of a cobalt-complexed propynal derived from 3-trimethylsilylprop-2-ynal with *O*-silyl ketene *O,S*-ketals afforded the *syn*-aldol products exclusively, whereas the uncomplexed substrate 3-trimethylsilylprop-2-ynal provided the *anti*-ones exclusively or in a highly diastereoselective manner. These newly developed aldol reactions could be successfully applied to highly stereoselective formal syntheses of the carbapenem antibiotics (±)-PS-5 and (±)-6-*epi*-PS-5.

Propynal–hexacarbonyldicobalt complexes **1**[2,3] have recently been found to be excellent substrates for *syn*-selective aldol reaction with silyl nucleophiles **2** under the Mukaiyama conditions.[4] The reaction proceeded in a highly stereoselective manner regardless of the geometry of the starting silyl nucleophiles **2**, to give products *syn*-**3** (Scheme 1). Trimethylsilyl (TMS) enol ethers **2** (X = alkyl; both cyclic and acyclic)[2a] as well as cyclic *O*-TMS ketene ketals **2** (X = OR^3)[2b] could serve as suitable silyl nucleophiles in this aldol reaction. However, only moderate to good *syn*-selectivity (*syn*:*anti* = 60–90:40–10)[2b] was achieved when *O*-TMS ketene ketals **2** (X = OR^3) derived from propionates (acyclic ketals) were employed instead of cyclic ketals.



Scheme 1 *Reagents:* i, Lewis acid; ii, CAN

The present study was, therefore, initiated to try to improve the *syn*-selectivity in the aldol reaction of the cobalt complex **1** with acyclic *O*-silyl ketene ketal species. We describe herein (i) an exclusive formation of the *syn*-isomers from the aldol reaction between the cobalt complex **4** and *O*-silyl ketene *O,S*-ketals **5**, (ii) a highly *anti*-selective aldol reaction of the propynal **8** with ketals **5** and (iii) their successful application to highly stereoselective divergent syntheses of the β-lactam antibiotics (±)-PS-5 **33** and (±)-6-*epi*-PS-5 **34**.

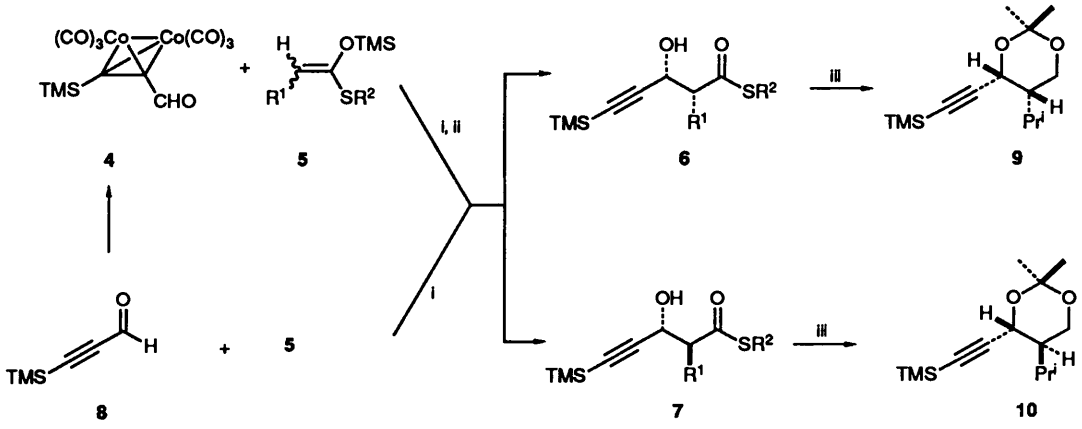
Results and Discussion

Aldol Reaction of the Cobalt-complexed Propynal **4** *and Uncomplexed Propynal* **8** *with Acyclic* O-*Silyl Ketene* O,S-*Ketals* **5**.—Recently, Gennari *et al.*[5,6] have disclosed the effectiveness of *O*-silyl ketene *O,S*-ketals for stereoselective carbon–carbon bond formation, and have developed a highly diastereoselective aldol reaction. We were attracted by their results[5,6] because *O*-silyl ketene *O,S*-ketals could be regarded as equivalent to the corresponding *O*-silyl ketene ketals. The aldol products prepared from the reaction with *O*-silyl ketene *O,S*-ketals will be handled in the same way as those from *O*-silyl ketene ketals in further elaboration. Accordingly, our programme aimed at an improvement in the degree of *syn*-selectivity was started to examine the reaction of the complex **4** with *O*-silyl ketene *O,S*-ketals **5**. The required substrates **5** were prepared according to Gennari's procedure.[5,7] The ratio of the *E*-and *Z*-isomers of the ketals **5** was determined by ^{1}H NMR spectroscopy.

In our previous paper,[2b] it became apparent that the most efficient Lewis acid for the aldol reaction of the complex **1** with silyl nucleophiles was titanium(IV) tetrachloride from the stereoselective point of view. Hence, we chose again $TiCl_4$ as a Lewis acid for the present study. The aldol reaction was carried out as follows. To a solution of the complex **4**[2b] and (*E*)-1-(*tert*-butylthio)-1-trimethylsiloxyprop-1-ene **5a** (*E*:*Z* >98:<2) in dry methylene dichloride was added dropwise a solution of $TiCl_4$ in CH_2Cl_2 at −78 °C to give the cobalt-complexed aldol product. The cobalt-complexed aldol condensation product was subsequently treated with cerium(IV) ammonium nitrate (CAN)[8] in methanol at 0 °C to afford, after chromatographic purification, the pure *syn*-isomer **6a** (Scheme 2)† in 90% yield, which was apparently free from the corresponding *anti*-isomer **7a** (^{1}H NMR spectrum; Table 1; entry 1). The complete diastereocontrol resulting in exclusive formation of the *syn*-isomer **6a** with satisfactory chemical yield was realized. This result is in marked contrast to the case[2b] of the reaction between complex **4** and (*E*)-*O*-TMS ketene ketal prepared from methyl propionate where only moderate *syn*-selectivity was observed (*syn*:*anti* 75:25). This promising preliminary result made us investigate the reaction of complex **4** with other *O*-silyl ketene *O,S*-ketals **5**. The *Z*-congener, (*Z*)-**5a** (*E*:*Z* 5:95), was exposed to the complex **4** under the identical conditions as described for (*E*)-**5a** to furnish exclusively the *syn*-isomer **6a** in 84% yield.

Variation of the substituent on the sulfur atom from *tert*-butyl to phenyl (**5a** → **5b**) in the *O,S*-ketals **5** didn't affect the degree of the *syn*-selectivity (entry 3). Furthermore, upon treatment with (*Z*)-**5c** (*E*:*Z* 5:95) having an ethyl appendage, the complex **4** yielded the *syn*-product **6c** in 93% yield (entry 6). However, it became apparent that $TiCl_4$ was no longer useful in the reaction of complex **4** with (*E*)-**5c** (*E*:*Z* >98:<2) which gave a mixture of the *syn* and *anti* isomers in the ratio 63:37 in 81% yield (entry 4). This was quite unexpected judging from the results observed through entries 1–3 and 6 in Table 1. The low diastereoselectivity found with $TiCl_4$ in the case of (*E*)-**5c** (entry 4) could fortunately be overcome by changing the Lewis acid to boron trifluoride–diethyl ether, which brought about complete *syn*-stereocontrol to afford the *syn*-isomer **6c** exclusively in 89% yield (entry 5). We are as yet still uncertain about the effectiveness of BF_3·OEt_2 over $TiCl_4$ in this specific

† *Syn* and *anti* Stereochemistry refers, throughout this paper, to that depicted in structures **6** and **7**, respectively.



Scheme 2 *Reagents:* i, Lewis acid; ii, CAN; iii, $LiAlH_4$ (LAH)

Table 1 Aldol reaction of cobalt-complexed propynal **4** and uncomplexed propynal **8** with *O*-silyl ketene *O,S*-ketals **5** in the presence of $TiCl_4$

Entry	Aldehyde	Ketal 5	R^1	R^2	*E*:*Z*[a]	Yield (%)[b]	Product	Ratio[a]
1	**4**	**a**	Me	Bu^t	>98:<2	90	**6a**:**7a**	>98:<2[c]
2	**4**	**a**	Me	Bu^t	5:95	84	**6a**:**7a**	>98:<2[c]
3	**4**	**b**	Me	Ph	<2:>98	89	**6b**:**7b**	>98:<2[c]
4	**4**	**c**	Et	Bu^t	>98:<2	81	**6c**:**7c**	63:37
5	**4**	**c**	Et	Bu^t	>98:<2	89[d]	**6c**:**7c**	>98:<2[c]
6	**4**	**c**	Et	Bu^t	5:95	93	**6c**:**7c**	>98:<2[c]
7	**4**	**d**	Pr^i	Bu^t	<2:>98	[e]		
8	**8**	**a**	Me	Bu^t	>98:<2	87	**6a**:**7a**	5:95
9	**8**	**a**	Me	Bu^t	5:95	86	**6a**:**7a**	4:96
10	**8**	**b**	Me	Ph	<2:>98	87	**6b**:**7b**	<2:>98[f]
11	**8**	**c**	Et	Bu^t	>98:<2	74	**6c**:**7c**	<2:>98[f]
12	**8**	**c**	Et	Bu^t	5:95	92	**6c**:**7c**	<2:>98[f]
13	**8**	**d**	Pr^i	Bu^t	<2:>98	70	**6d**:**7d**	27:73[g]

[a] Determined by NMR spectra unless otherwise stated. [b] Yields of products isolated by chromatography. [c] No *anti*-isomer could be detected by NMR spectroscopy. [d] BF_3-OEt_2 was employed instead of $TiCl_4$. [e] No reaction took place. [f] No *syn*-isomer could be detected by NMR spectroscopy. [g] Ratio of each isomer isolated by chromatography.

case. It should be mentioned that no reaction took place and that the starting aldehyde **4** was completely recovered when the *O,S*-ketal **5d** bearing a branched substituent on the double bond was submitted to the standard aldol conditions. Use of various Lewis acids and/or increasing the reaction temperature were fruitless. It may be that steric congestion between the isopropyl group and the cobalt-complexed triple-bond moiety would lead to recovery of the starting material.

Stereochemical assignment[9] of those *syn*-isomers **6** as well as the *anti*-ones **7** (*vide infra*) was made by careful ^1H NMR spectral analysis of the propynyl protons of each isomer by comparison of their chemical-shift value and magnitude of the vicinal coupling constant. The propynyl protons of the *syn*-isomers **6** appeared at lower field with smaller vicinal coupling constants compared with those of the corresponding *anti*-isomers **7**. This phenomenon is in good agreement with literature precedent.[9] The above ^1H NMR considerations allowed us to determine conveniently the stereochemical relationship between α- and β-positions of the aldol condensation products. In addition, transformation of aldol products **6a,c** and **7a,c** into β-lactams **19,20** and **21,22**, respectively, established their stereochemistry unambiguously (*vide infra*).

Exclusive formation of the *syn*-isomers **6** in the reaction of the cobalt-complexed propynal **4** with *O*-silyl ketene *O,S*-ketals **5** could be tentatively rationalised in terms of synclinal transition states[10] *via* the fluxional putative intermediates which might arise from co-ordination of the aldehyde oxygen with Lewis acid (Fig. 1). The *O,S*-ketals **5** would synclinally approach the electrophilic centre of the putative cationic intermediates where the hydrogen atom on the double bond of the *O,S*-ketals should be placed on the most sterically demanding position of the cationic intermediate to minimise interference with the bulky cobalt moiety (T_1 and T_2).[10] The bulk of the cobalt complex would therefore govern the stereochemical outcome and give rise to the exclusive production of the *syn*-isomers **6**. In the case of compound **5d**, an approach to the aldehyde counterpart would be prevented because of repulsion with the bulky isopropyl group. Although we overrode the low *syn*-selectivity observed in the reaction of the complex **1** with *O*-silyl ketene ketals by replacement of the latter with its *O,S*-congeners, there is still uncertainty about the role of the sulfur atom† in the occurrence of high *syn*-selectivity.

We previously reported[2] that uncomplexed propynals, upon treatment with silyl nucleophiles under Mukaiyama conditions[4] as a control experiment, afforded the aldol products nonselectively or the *anti*-isomers preodominantly depending on the structure of silyl nucleophiles. The uncomplexed propynals, in contrast to the corresponding cobalt-complexed ones, could hardly be expected to be suitable substrates for our stereoselective aldol reaction. As mentioned earlier, however, Gennari *et al.*[5–7] have presented some successful examples of the *anti*-selective aldol reaction of several kinds of aldehydes with *O*-silyl ketene *O,S*-ketals. We became interested in their results that would provide us with an opportunity to develop the *anti*-selective aldol reaction of

† Gennari[6] interpreted this superiority of *O*-silyl ketene *O,S*-ketals over *O*-silyl ketene ketals in the aldol reaction in terms of electronic properties which for the former are more similar to those of silyl enol ethers derived from the corresponding ketones.

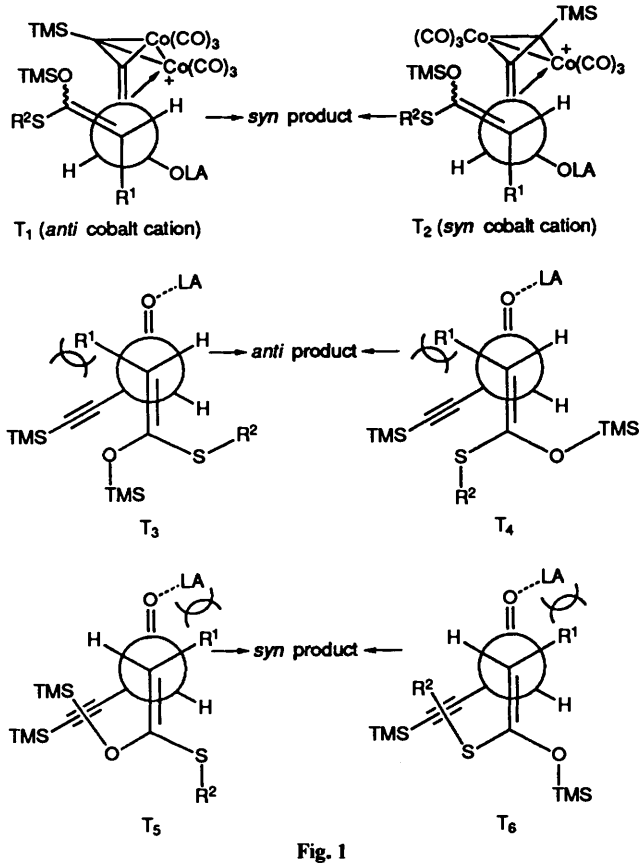


Fig. 1

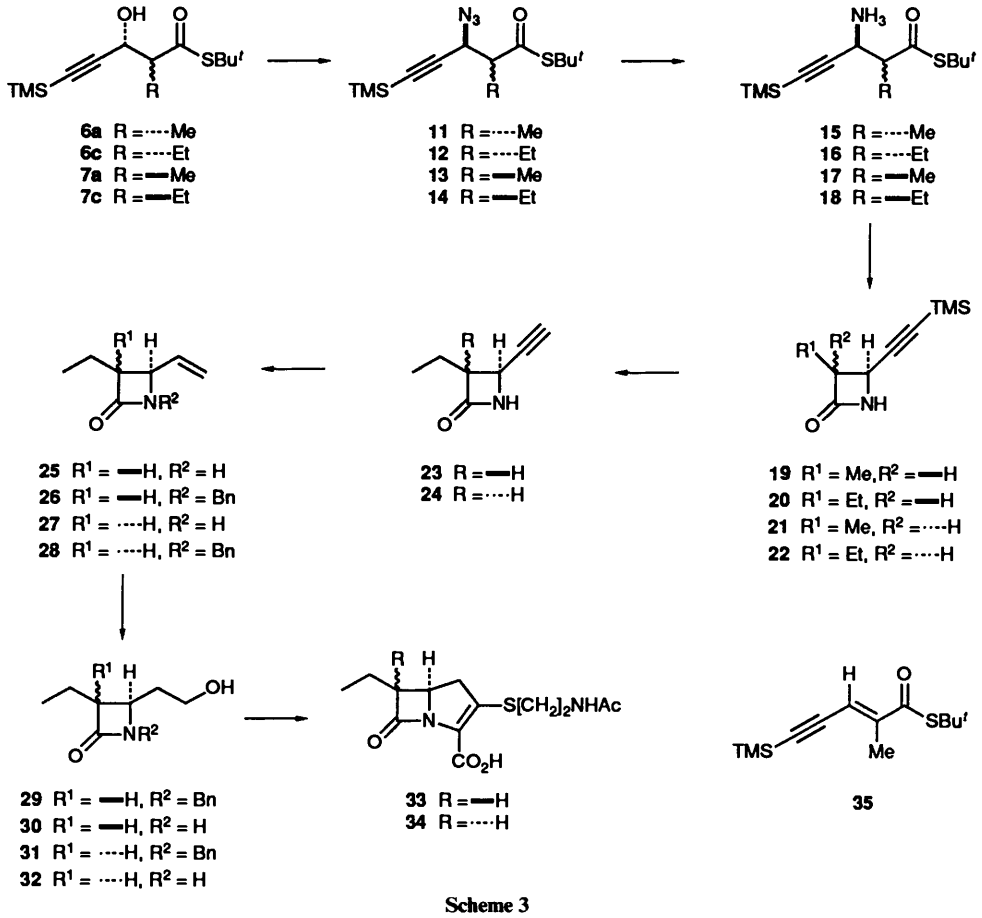
propynals. If propynals can serve as ideal substrates for our purpose, we might well be able to prepare independently the *syn*- and *anti*-isomers in a highly diastereoselective manner from propynals with or without cobalt complexation.

The aldol reaction between the propynal **8** and the *O,S*-ketals **5** was performed under the standard conditions except for treatment with CAN to furnish the *anti*-isomers **7** exclusively or in a highly *anti*-selective manner (Table 1, entries 8–13). In the case of the isopropyl derivative (entry 13), the reaction proceeded in 70% yield, but the *anti*-selectivity was rather lower (*anti*:*syn* 73:27). The *syn*- and *anti*-isomers **6d** and **7d** could be isolated in pure form by column chromatography. The propynyl protons of each isomer **6d** and **7d** resonated at δ 4.60 and 4.42, respectively, in their ^{1}H NMR spectra. The relationship of those chemical-shift values stands in line with literature precedent.[9] However, the vicinal coupling constant between the α- and β-proton of the *syn*-isomer **6d** was found to be *J* 6.9 Hz, whereas that of the *anti*-isomer **7d** showed a smaller value, *J* 4.4 Hz. The magnitude of the vicinal coupling constant of those propynyl protons are in disagreement with the empirical rule wherein the β-proton of the *syn*-isomer should have a smaller coupling constant than that of the corresponding *anti*-isomer. In order to confirm the stereochemistry of those aldol products **6d** and **7d**, we converted them into the ketals **9** and **10**, respectively by consecutive treatment with lithium aluminium hydride (LAH) in tetrahydrofuran (THF) and 2,2-dimethoxypropane in the presence of toluene-*p*-sulfonic acid (*p*-TsOH). The propynyl proton of ketal **9** derived from the *syn*-isomer **6d** appeared at δ 4.76 with a smaller coupling constant (*J* 5.5 Hz) which should be attributed to an axial–equatorial coupling. On the other hand, the larger coupling constant (*J* 11 Hz) due to an axial–axial coupling at δ 4.52 could be recognised in the ^{1}H NMR spectrum of the ketal **10**. Thus, the stereochemical relationship between the α- and β-position in the aldol products **6d** and **7d** was unambiguously established.

The results summarised in Table 1 (entries 8–13) are in good agreement with prediction based on Gennari's results.[5,6] The stabilised propynyl cation species[10] assumed to occur in the reaction of the cobalt-complexed propynal (Fig. 1, T_1 and T_2) cannot any longer be taken as an intermediate in the case of uncomplexed propynals. The high *anti*-selectivity obtained here may be best explained by the intermediacy of acyclic, staggered transition states with antiperiplanar alignment of silyl nucleophiles (Fig. 1, T_3–T_6) as Heathcock[11] and Gennari[5,6] had already proposed. It is worth mentioning the stability of these four possible transition states (T_3–T_6) in Fig. 1. There are unfavourable nonbonding gauche interactions between the triple bond of the propynal **8** and the alkyl substituent on the double bond of the *O,S*-ketals **5** in the transition states T_3 and T_4. More serious interference of the propynyl moiety with the fairly bulky $SiMe_3$ or *tert*-butyl group of the *O,S*-ketal should be expected in the transition states T_5 and T_6 where another enormous destabilising factor can be predicted. Namely, there is an interaction between the appendage on the double bond of the *O,S*-ketal with the Lewis acid co-ordinated with the aldehyde oxygen and being forced *trans* to the propynyl part. These considerations putatively provided the clue for our understanding of the observed preferential formation of the *anti*-isomers **7**. The low *anti*-selectivity in the case of substrate **5d** would reflect the fact that the bulkier the alkyl substituent (R^1) on the double bond of the *O,S*-ketal becomes, the more serious is the nonbonding interaction between the propynyl moiety and R^1 in the transition states T_3 and T_4. It should be stated that the cobalt-complexed propynyl moiety of the aldehyde counterpart plays the most important role in producing the *syn*-isomers selectively. On the other hand, sterically bulky $SiMe_3$ and/or *tert*-butyl groups on the hetero atoms of the *O,S*-acetals **5**, as well as co-ordination of the Lewis acid with aldehyde oxygen, might govern the stereochemical course, resulting in the exclusive formation of the *anti*-aldol products.

Formal Total Syntheses of (±)-*PS*-5 *and* (±)-6-epi-*PS*-5.—(±)-PS-5 **33**, a representative carbapenem antibiotic, has been isolated from *Streptomyces cremeus* subsp. *auratilis* A 271[12] and *Streptomyces fulvovirides* A 933[13] and shown to possess antimicrobial activity involving inhibitory activity against β-lactamases. An unnatural 6-*epi*-isomer, (±)-6-*epi*-PS-5 **34**[14] was reported, in comparison with PS-5 **33**, to be less potent against gram-positive organism, but more effective against gram-negative bacteria.

We were motivated to synthesize the β-lactams **30**[15] and **32**,[14] both of which had already been converted into (±)-PS-5 **33** and (±)-6-*epi*-PS-5 **34**, respectively, by taking advantage of our newly developed aldol reaction of the cobalt-complexed and uncomplexed propynals. At the outset, transformation of the aldol condensation products **6a** and **7a** into β-lactams **19** and **21** involving introduction of the amino functionality at the β-position, followed by ring closure was investigated. The *syn*-product **6a** was exposed to Mitsunobu conditions[16] with phthalimide, diethyl azodicarboxylate (DEAD) and triphenylphosphine to give the dehydrated product **35** instead of the desired amino derivative. Production of compound **35** was predictable from the consideration that compound **6a** has a β-hydroxy ketone structure which should be susceptible to β-elimination by treatment with base. The geometry of product **35** is so far not manifest since a nuclear Overhauser effect (NOE) experiment could barely give sufficient corroborative information, although compound **35** was isolated as a pure, single isomer. We postulated that the occurrence of elimination might be mainly due to the steric bulk and basicity of the phthalimide. Hoping to obtain an increase in substitution over elimination, we changed the amino nucleophile for azide.



Scheme 3

Three azido compounds were examined. The best result was obtained with hydrazoic acid[16,17] in benzene to give the *anti*-β-azido compound **11** with complete inversion of stereochemistry at the β-position in 86% yield (Scheme 3). The enyne **35** could not be detected in the reaction mixture.

Diphenyl phosphoroazidate[16,18] and trimethylsilyl azide[16] also yielded the desired compound **11**, but the enyne **35** was the main product. Similar treatment of the *anti*-isomer **7a** furnished the *syn*-β-azido derivative **13** in 77% yield. Reduction of the azido group in compound **11** was realized by treatment with triphenylphosphine and water[19] to afford the amino derivative **15** in 82% yield. In addition, both dibutyltin dihydride[20] and propane-1,3-dithiol[21] were found to be effective for the above conversion, resulting in the production of compound **15** in 51 and 72% yield, respectively. Conversion of azide **13** into the reduced product **17** (76%) proceeded with triphenylphosphine and water[19] without any difficulty. The β-amino derivatives **15** and **17** underwent ring closure by successive exposure to trimethylsilyl chloride and triethylamine, and *tert*-butylmagnesium chloride[22] in dry THF to give the corresponding β-lactams **19**[23] and **21**[23] in 87 and 70% yield, respectively. We had therefore developed an efficient and convenient way to synthesize the β-lactams **19** and **21** from the corresponding aldol products **6a** and **7a**. It is noteworthy that no isomerization occurred during these processes.

The above method was successively applied to the preparation of the β-lactam analogues **20** and **22** having an ethyl substituent at the C-3 position of the lactam ring. Introduction of an azido functionality[16,17] at the β-position of hydroxy compounds **6c** and **7c**, followed by reduction[19] and ring construction,[22] led to the formation of β-lactams **20**[23] and **22**[23] in 56 and 52% overall yield, respectively. Upon treatment with tetrabutylammonium fluoride (TBAF) in THF, the silane **20** gave compound **23** in 86% yield, which was subsequently hydrogenated in the presence of Lindlar catalyst to furnish the olefin derivative **25** in 90% yield. The *cis*-lactam **22** was similarly desilylated (quantitative) to compound **24**, which was in turn half-hydrogenated to afford olefinic lactam **27** in 88% yield. At this point the olefins **25** and **27** seemed to be directly convertible into the target alcohols **30**[15] and **32**,[14] respectively. However, hydroboration–oxidation of compound **25** under various conditions gave only an intractable mixture. Therefore, we protected the nitrogen of lactams **25** and **27** with a benzyl group (**26**, 80%; **28**, 81%). The next step was the introduction of an hydroxy at the end of the double bond. Exposure of compound **26** to disiamylborane[24] at 0 °C, followed by oxidation with a system composed of hydrogen peroxide and sodium hydroxide afforded, as expected, the alcohol **29** in 75% yield. 9-Borabicyclo[3.3.1]nonane also worked, but was less useful in this reaction. The *cis*-analogue **28** was hydroborated and oxidised under the identical conditions to give compound **31** in 68% yield. The second and final step was to remove the protecting group on the nitrogen atom. The deprotection was realized by treatment of compounds **29** and **31** with sodium in liquid ammonia at −78 °C to provide the desired alcohols **30**[15] and **32**[14] in 82 and 77% yield, respectively. Since these two alcohols **30**[15] and **32**[14] had already been independently transformed into (±)-PS-5 **33** and (±)-6-*epi*-PS-5 **34**, the present syntheses of β-lactams **30** and **32** amount to formal syntheses of carbapenems (±)-PS-5 and (±)-6-*epi*-PS-5.

In summary, we developed not only a highly *syn*-selective aldol reaction of the cobalt-complexed propynal with *O*-silyl ketene *O*,*S*-ketals, but also a highly *anti*-selective aldol condensation between the propynal and *O*-silyl ketene *O*,*S*-ketals. Furthermore, on the basis of our newly developed aldol reactions, we succeeded in a highly diastereoselective divergent

synthesis of the β-lactam antibiotics (±)-PS-5 and (±)-6-*epi*-PS-5.

Experimental

M.p.s were determined on a Yanagimoto micro melting-apparatus and are uncorrected. IR spectra were measured with a JASCO A-102 spectrometer for solutions in $CHCl_3$, mass spectra with a Hitachi M-80 mass spectrometer, ^1H NMR spectra with JEOL EX-270, JEOL JNM-GX 400 and 500 spectrometers for solutions in $CDCl_3$ and using either tetramethylsilane as internal standard for compounds that have no silyl group or $CHCl_3$ (δ 7.26) for compounds possessing the silyl group, ^{13}C NMR spectra with JEOL EX-270 and JEOL JNM-GX 500 spectrometers for solutions in $CDCl_3$ with $CDCl_3$ (δ_C 77.0) as internal reference. All *J* values are in Hz. CH_2Cl_2 was freshly distilled from CaH and THF from sodium/benzophenone prior to use. Aldol reactions were performed in oven-dried glassware under an inert atmosphere of nitrogen. Silica gel (silica gel 60, 230–400 mesh, Nacalai Tesque) was used for chromatography. Organic extracts were dried over anhydrous Na_2SO_4. The starting *O*-silyl ketene *O,S*-ketals **5** were prepared according to Gennari's procedure. The cobalt-complexed propynal **4** was synthesized from the propynal **8** by our method.[2] Light petroleum refers to the fraction boiling in the range 30–70 °C.

General Procedure for the Aldol Reaction of Cobalt-complexed Propynal **4** *with* O-*Silyl Ketene* O,S-*Ketals* **5**.—To a solution of compound **4** (1 mmol) and the *O*-silyl ketene *O,S*-ketal **5** (1.5 mmol) in dry CH_2Cl_2 (5 cm^3) was added dropwise a solution of $TiCl_4$ in dry CH_2Cl_2 (1 mol dm^{-3} solution; 1.2 mol equiv.) over a period of 10 min at −78 °C. The stirred reaction mixture was kept at the same temperature for *ca.* 30 min until consumption of the starting complex **4** (monitored by TLC), and was then quenched by addition of saturated aq. ammonium chloride (1 cm^3). The reaction mixture was washed successively with water and brine, dried, and concentrated. The residue was dissolved in methanol (5 cm^3). CAN (4 mol equiv.) was added portionwise to the stirred methanol solution at 0 °C, the mixture was stirred for *ca.* 30 min (monitored by TLC) and the methanol was evaporated off. The residue was diluted with water (3 cm^3) and extracted with ethyl acetate several times. The combined extracts were washed successively with water and brine, dried, and evaporated to dryness. Chromatography of the residue with hexane–ethyl acetate (40:1) gave the aldol products. The yield and ratio of each isomer are listed in Table 1 (entries 1–7).

S-tert-*Butyl* (2R*,3R*)-3-*Hydroxy*-2-*methyl*-5-(*trimethylsilyl*)*pent*-4-*ynethioate* **6a**. The solid syn-*product* **6a** had m.p. 37–38.5 °C (from hexane) (Found: M^+ + 1, 273.1282. $C_{13}H_{25}O_2SSi$ requires *m/z*, 273.1343); ν_{max}/cm^{-1} 3470 (OH), 2175 (C≡C) and 1660 (C=O); δ_H 4.61 (1 H, dd, *J* 4.6 and 5.5, 3-H), 2.78 (1 H, dq, *J* 4.6 and 6.9, CH), 2.74 (1 H, d, *J* 5.5, OH), 1.47 (9 H, s, Bu^t), 1.32 (3 H, d, *J* 6.9, Me) and 0.61 (9 H, s, TMS); δ_C 203.29, 103.60, 90.67, 64.17, 53.70, 48.40, 29.74, 12.61 and −0.22; *m/z* 273 (M^+ + 1, 1.8%), 216 (97), 154 (67), 99 (65), 75 (100) and 57 (99).

S-*Phenyl* (2R*,3R*)-3-*Hydroxy*-2-*methyl*-5-(*trimethylsilyl*)*pent*-4-*ynethioate* **6b**. The solid syn-*product* **6b** had m.p. 43.5–44 °C (from hexane) (Found: C, 61.6; H, 6.9%; M^+, 292.0932. $C_{15}H_{20}O_2SSi$ requires C, 61.60; H, 6.89%; *M*, 292.0952); ν_{max}/cm^{-1} 3600 and 3340 (OH), 2180 (C≡C) and 1685 (C=O); δ_H 7.47–7.40 (5 H, m, Ph), 4.70 (1 H, d, *J* 4.4, 3-H), 3.02 (1 H, dq, *J* 4.4 and 7.3, CH), 2.54 (1 H, br s, OH), 1.45 (3 H, d, *J* 7.3, Me) and 0.19 (9 H, s, TMS); δ_C 200.37, 134.51, 129.56, 129.22, 127.02, 103.35, 91.18, 64.03, 53.43, 12.49 and −0.23; *m/z* 292 (M^+, 1.8%), 127 (52), 110 (100), 99 (97), 75 (100) and 57 (72).

S-tert-*Butyl* (2R*,3R*)-2-*Ethyl*-3-*hydroxy*-5-(*trimethylsilyl*)*pent*-4-*ynethioate* **6c**. The syn-*product* **6c** was an oil (Found: M^+ + 1, 287.1459. $C_{14}H_{27}O_2SSi$ requires *m/z* 287.1499); ν_{max}/cm^{-1} 3575 and 3500 (OH), 2160 (C≡C) and 1660 (C=O); δ_H 4.49 (1 H, t-like, *J* 6.0, 3-H), 2.63 (1 H, d, *J* 5.0, OH), 2.59 (1 H, ddd, *J* 5.0, 6.0 and 9.2, CH), 1.87–1.71 (2 H, m, CH_2), 1.45 (9 H, Bu^t), 0.97 (3 H, t, *J* 7.3, Me) and 0.14 (9 H, s, TMS); δ_C 202.07, 103.84, 90.85, 63.52, 61.49, 48.49, 29.67, 21.45, 11.85 and −0.25; *m/z* 287 (M^+ + 1, 0.5%), 230 (100), 215 (16), 201 (6.5), 75 (5.0) and 57 (7.0).

General Procedure for the Aldol Reaction of the Propynal **8** *with* O-*Silyl Ketene* O,S-*Ketals* **5**.—To a solution of compound **8** (1 mmol) and the *O*-silyl ketene *O,S*-ketal **5** (1.5 mmol) in dry CH_2Cl_2 (5 cm^3) was added dropwise a solution of $TiCl_4$ in dry CH_2Cl_2 (1 mol dm^{-3}; 1.2 mol equiv.) over a period of 10 min at −78 °C. The reaction mixture was stirred for *ca.* 30 min (monitored by TLC), quenched by addition of saturated aq. ammonium chloride (1 cm^3) and diluted with water. Extraction with ethyl acetate, followed by usual work-up, afforded the aldol products. The yield and ratio of each isomer are summarised in Table 1 (entries 8–13).

S-tert-*Butyl* (2R*,3S*)-3-*Hydroxy*-2-*methyl*-5-(*trimethylsilyl*)*pent*-4-*ynethioate* **7a**. The solid anti-*product* **7a** had m.p. 40–42 °C (from hexane) (Found: M^+ + 1, 273.1323. $C_{13}H_{25}O_2SSi$ requires *m/z*, 273.1343); ν_{max}/cm^{-1} 3475 (OH), 2180 (C≡C) and 1660 (C=O); δ_H 4.45 (1 H, t, *J* 6.9, 3-H), 2.80 (1 H, quin-like, *J* 6.9, CH), 2.65 (1 H, d, *J* 6.9, OH), 1.47 (9 H, s, Bu^t), 1.27 (3 H, d, *J* 7.3, Me) and 0.17 (9 H, s, TMS); δ_C 203.26, 104.27, 90.95, 64.93, 54.14, 48.47, 29.74, 15.04 and −0.23; *m/z* 273 (M^+ + 1, 18%), 216 (33), 154 (29), 123 (24), 99 (31), 75 (59) and 457 (100).

S-*Phenyl* (2R*,3S*)-3-*Hydroxy*-2-*methyl*-5-(*trimethylsilyl*)*pent*-4-*ynethioate* **7b**. The anti-*product* **7b** was an oil (Found: C, 61.75; H, 6.9%; M^+, 292.0977. $C_{15}H_{20}O_2SSi$ requires C, 61.60; H, 6.89%; *M*, 292.0952); ν_{max}/cm^{-1} 3590 and 3350 (OH), 2170 (C≡C) and 1690 (C=O); δ_H 7.45–7.41 (5 H, m, Ph), 4.55 (1 H, t-like, *J* 6.9, 3-H), 3.05 (1 H, quin-like, *J* 6.9, CH), 2.62 (1 H, d, *J* 6.9, OH), 1.38 (3 H, d, *J* 6.9, Me) and 0.19 (9 H, s, TMS); δ_C 200.49, 134.43, 129.56, 129.23, 127.17, 103.83, 91.55, 64.94, 53.96, 15.05 and −0.23; *m/z* 292 (M^+, 0.6%), 110 (100), 99 (45), 75 (100) and 57 (33).

S-tert-*Butyl* (2R*,3S*)-2-*Ethyl*-3-*hydroxy*-5-(*trimethylsilyl*)*pent*-4-*ynethioate* **7c**. The solid anti-*product* **7c** had m.p. 40.5–41 °C (from hexane) (Found: C, 58.7; H, 9.2. $C_{14}H_{26}O_2SSi$ requires C, 58.69; H, 9.15%); ν_{max}/cm^{-1} 3400 (OH), 2175 (C≡C) and 1650 (C=O); δ_H 4.44 (1 H, dd, *J* 6.4 and 8.2, 3-H), 2.79 (1 H, d, *J* 6.4, OH), 2.63 (1 H, quin-like, *J* 8.2, CH), 1.81–1.69 (2 H, m, CH_2), 1.48 (9 H, s, Bu^t), 0.98 (3 H, t, *J* 7.5, Me) and 0.17 (9 H, s, TMS); δ_C 203.40, 104.58, 90.66, 63.61, 60.76, 48.72, 29.69, 23.13, 11.52 and −0.20; *m/z* 287 (M^+ + 1, 2.3%), 230 (98), 168 (64), 137 (38), 75 (100) and 57 (82).

S-tert-*Butyl* (2R*,3R*)- *and* (2R*,3S*)-3-*Hydroxy*-2-*isopropyl*-5-(*trimethylsilyl*)*pent*-4-*ynethioates* **6d** *and* **7d**. The solid syn-*product* **6d** had m.p. 65.5–66.5 °C (from hexane) (Found: M^+ +1, 301.1706. $C_{15}H_{29}O_2SSi$ requires *m/z*, 301.1656); ν_{max}/cm^{-1} 3590 (OH), 2175 (C≡C) and 1670 (C=O); δ_H 4.60 (1 H, dd, *J* 6.0 and 6.9, 3-H), 2.59 (1 H, t, *J* 6.9, CH), 2.29–2.25 (1 H, m, CH), 2.22 (1 H, br s, OH), 1.49 (9 H, s, Bu^t), 1.08 (3 H, d, *J* 6.9, Me), 1.00 (3 H, d, *J* 6.9, Me) and 0.16 (9 H, s, TMS); δ_C 200.57, 104.19, 91.26, 65.50, 62.29, 48.58, 29.67, 27.68, 21.53, 19.45 and − 0.24; *m/z* 301 (M^+ + 1, 0.3%), 224 (57), 169 (51), 93 (53), 73 (69) and 57 (100). The anti-*product* **7d** was an oil (Found: M^+ + 1, 301.1616); ν_{max}/cm^{-1} 3450 (OH), 2160 (C≡C) and 1645 (C=O); δ_H 4.42 (1 H, dd, *J* 4.4 and 10, 3-H), 3.20 (1 H, d, *J* 10, OH), 2.37 (1 H, dd, *J* 4.4 and 8.8, CH), 2.20 (1 H, d-hept, *J* 8.8 and 6.4, CH), 1.49 (9 H, s, Bu^t), 1.01 (3 H, d, *J* 6.4, Me), 1.00 (3 H, d, *J* 6.4, Me) and 0.16 (9 H, s, TMS); δ_C 204.20, 104.83, 90.32, 64.91, 62.11, 48.94, 29.61, 27.98, 20.69 and

−0.19; *m/z* 301 (M^+ + 1, 3.0%), 244 (21), 169 (34), 99 (25), 73 (49), 57 (100) and 41 (32).

(4R*,5S*)-5-*Isopropyl*-2,2-*dimethyl*-4-*trimethylsilylethynyl*-1,3-*dioxane* **9**.—LAH (77.4 mg, 2.04 mmol) was added to a solution of compound **6d** (304.4 mg, 1.01 mmol) in dry THF (5.0 cm^3) at room temperature. After being stirred for 1 h, the reaction mixture was quenched by addition of a small amount of water at 0 °C followed by 10% aq. sodium hydroxide. The resulting precipitates were filtered off by suction and the filtrate was dried and evaporated. The residue was dissolved in 2,2-dimethoxypropane (1.5 cm^3) and *p*-TsOH (10.4 mg) was added. The reaction mixture was stirred at room temperature for 1 h and then diluted with saturated aq. ammonium chloride and extracted with ethyl acetate. The extract was washed successively with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane–ethyl acetate (40:1) to give the *title compound* **9** (126 mg, 49%) as an oil; ν_{max}/cm^{-1} 2170 (C≡C); δ_H 4.76 (1 H, dd, *J* 0.9 and 5.5, 4-H), 3.87 (1 H, dd, *J* 9.2 and 12, C*H*HO), 3.83 (1 H, ddd, *J* 0.9, 4.6 and 12, CH*H*O), 1.79–1.56 (2 H, m, 2 × CH), 1.62 and 1.35 (3 H, each, s, 2-Me_2), 0.95 (3 H, d, *J* 6.4, Me), 0.93 (3 H, d, *J* 6.4, Me) and 0.16 (9 H, s, TMS); δ_C 104.07, 98.97, 92.61, 64.74, 60.45, 43.54, 28.48, 26.92, 23.73, 20.37, 19.98 and −0.35.

(4R*,5R*)-5-*Isopropyl*-2,2-*dimethyl*-4-*trimethylsilylethynyl*-1,3-*dioxane* **10**.—Similar treatment of the *anti*-product **7d** (107 mg, 0.35 mmol) with LAH (51 mg, 1.30 mmol) and 2,2-dimethoxypropane (2.0 cm^3) afforded the *title compound* **10** (55 mg, 70%) as an oil; ν_{max}/cm^{-1} 2170 (C≡C); δ_H 4.52 (1 H, d, *J* 11, 4-H), 3.77 (1 H, dd, *J* 4.9 and 12, C*H*HO), 3.71 (1 H, dd, *J* 10 and 12, CH*H*O), 1.96 (1 H, d-hept, *J* 3.9 and 6.8, C*H*Me_2), 1.82–1.76 (1 H, m, CH), 1.41 (6 H, s, 2-Me_2), 0.97 (3 H, d, *J* 6.8, Me), 0.91 (3 H, d, *J* 6.8, Me) and 0.15 (9 H, s, TMS); δ_C 103.67, 98.76, 90.51, 64.13, 60.14, 45.06, 28.80, 26.72, 20.56, 19.89, 17.64 and − 0.22; chemical ionisation mass *m/z* 239 ($M^+ - CH_3$, 0.08%), 73 (2.3), 57 (2.3) and 41 (100).

S-tert-*Butyl* (E)-2-*Methyl*-5-(*trimethylsilyl*)*pent*-2-*en*-4-*ynethioate* **35**.—To a solution of compound **6a** (123 mg, 0.45 mmol), phthalimide (72 mg, 0.49 mmol) and triphenylphosphine (131 mg, 0.50 mmol) in dry THF (4 cm^3) was added DEAD (92 mg, 0.53 mmol) at room temperature. The reaction mixture was stirred at room temperature for 2 h. THF was evaporated off and the residue was chromatographed with hexane–CH_2Cl_2 (3:1) to furnish the *title compound* **35** (99 mg, 74%) as an oil (Found: M^+, 254.1178. $C_{13}H_{22}OSSi$ requires *M*, 254.1159); ν_{max}/cm^{-1} 2150 (C≡C) and 1640 (C=O); δ_H 6.51 (1 H, br s, vinylic H), 2.07 (3 H, d, *J* 1.5, Me), 1.48 (9 H, s, Bu^t) and 0.21 (9 H, s, TMS); δ_C 193.22, 147.86, 116.35, 108.34, 101.11, 48.06, 29.79, 15.21 and −0.24; *m/z* 254 (M^+, 1.6%), 239 (3.5), 198 (8.4), 165 (100), 97 (37) and 57 (12).

S-tert-*Butyl* (2R*,3S*)-3-*Azido*-2-*methyl*-5-(*trimethylsilyl*)-*pent*-4-*ynethioate* **11**.—*Method A*. To a solution of compound **6a** (607 mg, 2.23 mmol) and triphenylphosphine (713 mg, 2.72 mmol) in dry benzene (15 cm^3) were successively added a solution of hydrazoic acid in benzene (~4% solution; 5 cm^3, 4.65 mmol) and DEAD (0.4 cm^3, 2.54 mmol) at room temperature. After being stirred for 1 h, the reaction mixture was diluted with water and extracted with ethyl acetate. The extract was washed with brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–ethyl acetate (100:1) gave the anti-*azido compound* **11** (572 mg, 86%) as a yellow oil (Found: C, 52.5; H, 7.8; N, 13.95. $C_{13}H_{23}N_3OSSi$ requires C, 52.49; H, 7.79; N, 14.12%); ν_{max}/cm^{-1} 2175 (C≡C), 2100 (N_3) and 1670 (C=O); δ_H 4.35 (1 H, d, *J* 9.3, 3-H), 2.72 (1 H, dq, *J* 9.3 and 6.8, CH), 1.47 (9 H, s, Bu^t), 1.25 (3 H, d, *J* 6.8, Me) and 0.19 (9 H, s, TMS); δ_C 200.44, 98.06, 94.40, 55.66, 52.80, 48.53, 29.71, 15.24 and −0.21; *m/z* 241 [$M^+ - (CH_3)_2C{=}CH_2$, 26%], 142 (12), 124 (15), 97 (40), 73 (21) and 57 (100).

Method B. To a solution of compound **6a** (24.3 mg, 0.089 mmol), diphenyl phosphoroazidate (49.5 mg, 0.18 mmol) and triphenylphosphine (45.9 mg, 0.17 mmol) in dry THF (6.0 cm^3) at −60 °C was added DEAD (37.2 mg, 0.21 mmol). After being stirred for 2 h, the reaction mixture was warmed to room temperature. THF was evaporated off and the residue was purified by preparative TLC (PLC) with hexane–CH_2Cl_2(2:1) to provide title compound **11** (13.4 mg, 50%) and compound **35** (7.1 mg, 32%).

Method C. To a solution of compound **6a** (49.9 mg, 0.18 mmol), trimethylsilyl azide (0.10 cm^3, 0.75 mmol) and triphenylphosphine (58.9 mg, 0.22 mmol) in dry benzene (2.0 cm^3) at 0 °C was added DEAD (0.10 cm^3, 0.64 mmol). After being stirred for 2 h, the reaction mixture was warmed to room temperature. Benzene was evaporated off and the residue was purified by PLC with hexane–CH_2Cl_2 (2:1) to provide compound **11** (14.9 mg, 64%) and compound **35** (30.2 mg, 27%).

S-tert-*Butyl* (2R*,3R*)-3-*Azido*-2-*methyl*-5-(*trimethylsilyl*)-*pent*-4-*ynethioate* **13**.—According to Method A described for compound **11**, the title product **13** (284 mg, 77%) was obtained by treatment of compound **7a** (338 mg, 1.24 mmol) with triphenylphosphine (348 mg, 1.33 mmol), hydrazoic acid (~4% benzene solution; 2 cm^3, 1.86 mmol) and DEAD (0.25 cm^3, 1.60 mmol). The syn-*azido compound* **13** was a yellow oil (Found: M^+ + 1, 298.1474. $C_{13}H_{24}N_3OSSi$ requires *m/z*, 298.1408); ν_{max}/cm^{-1} 2175 (C≡C), 2100 (N_3) and 1670 (C=O); δ_H 4.34 (1 H, d, *J* 7.3, 3-H), 2.76 (1 H, quint-like, *J* 6.9, CH), 1.46 (9 H, s, Bu^t), 1.26 (3 H, d, *J* 6.8, Me) and 0.19 (9 H, s, TMS); δ_C 200.00, 98.16, 93.99, 55.24, 53.17, 48.37, 29.71, 13.49 and −0.22; *m/z* 298 (M^+ + 1, 0.5), 241 (40), 142 (39), 124 (43), 97 (100), 73 (90) and 57 (99); δ_C 199.98, 98.19, 94.00, 55.28, 53.20, 48.37, 29.72, 13.47 and −0.21.

S-tert-*Butyl* (2R*,3S*)-3-*Amino*-2-*methyl*-5-(*trimethylsilyl*)-*pent*-4-*ynethioate* **15**.—*Method A*. Triphenylphosphine (538 mg, 2.05 mmol) was added to a solution of azide **11** (284 mg, 0.95 mmol) in dry THF (10 cm^3) at room temperature. The reaction mixture was stirred for 15 h at the same temperature. Water (0.15 cm^3) was added and the mixture was stirred for 24 h at room temperature before being diluted with water and extracted with ethyl acetate. The extract was washed with brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–ethyl acetate (10:1) provided the *amino thioester* **15** (213 mg, 82%) as a solid, m.p. 56–57 °C (from light petroleum) (Found: C, 57.4; H, 9.3; N, 5.2. $C_{13}H_{25}NOSSi$ requires C, 57.51; H, 9.28; N, 5.16%) (Found: M^+ + 1, 272.1505. $C_{13}H_{26}NOSSi$ requires *m/z*, 272.1503); ν_{max}/cm^{-1} 3380 and 3310 (NH), 2175 (C≡C) and 1670 (C=O); δ_H 3.78 (1 H, d, *J* 8.8, 3-H), 2.62 (1 H, dq, *J* 8.8 and 6.8, CH), 1.50 (2 H, br s, NH_2), 1.46 (9 H, s, Bu^t), 1.24 (3 H, d, *J* 6.8, Me) and 0.13 (9 H, s, TMS); δ_C 202.55, 107.09, 88.41, 55.46, 48.20, 47.25, 29.77, 15.70 and −0.09; *m/z* 272 (M^+ + 1, 2.1%), 214 (27), 153 (28), 126 (100), 98 (38) and 57 (25).

Method B. A solution of dibutyltin dihydride (51.2 mg, 0.22 mmol) in dry benzene (0.9 cm^3) was added to a solution of compound **11** (20.3 mg, 0.068 mmol) in dry benzene (0.5 cm^3) at room temperature. After the mixture had been stirred overnight at ambient temperature, benzene was evaporated off. The residue was purified by PLC with hexane–diethyl ether (2:1) to afford compound **15** (9.5 mg, 51%).

Method C. To a solution of compound **11** (30.3 mg, 0.10 mmol) in dry methanol (1.0 cm^3) were added triethylamine

(0.10 cm^3, 0.72 mmol) and propane-1,3-dithiol (0.05 cm^3, 0.50 mmol) successively at room temperature. After removal of solvent, the residue was diluted with water and then extracted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–ethyl acetate (5:1) provided compound **15** (20.0 mg, 72%).

S-tert-*Butyl* (2R*,3R*)-3-*Amino*-2-*methyl*-5-(*trimethylsilyl*)-*pent*-4-*ynethioate* **17**.—According to Method A described for compound **15**, the *title compound* **17** (340 mg, 76%) was obtained by treatment of azide **13** (488 mg, 1.64 mmol) with triphenylphosphine (538 mg, 2.05 mmol) and water (0.5 cm^3). The syn-*amino compound* **17** was an oil (Found: C, 57.1; H, 9.1; N, 5.4. $C_{13}H_{25}NOSSi$ requires C, 57.51; H, 9.28; N, 5.16%); ν_{max}/cm^{-1} 3380 and 3320 (NH), 2170 (C≡C) and 1670 (C=O); δ_H 3.84 (1 H, d, *J* 5.5, 3-H), 2.67 (1 H, dq, *J* 5.5 and 6.8, CH), 1.51 (2 H, br s, NH_2), 1.44 (9 H, s, Bu^t), 1.24 (3 H, d, *J* 6.8, Me) and 0.12 (9 H, s, TMS); δ_C 201.95, 106.88, 87.79, 54.36, 47.96, 46.50, 29.75, 12.73 and −0.10; *m/z* 254 (M^+ − OH, 0.5%), 214 (7.6), 153 (4.5), 126 (100), 98 (6.9) and 57 (5.4).

(3R*,4S*)-3-*Methyl*-4-(*trimethylsilylethynyl*)*azetidin*-2-*one* **19**.[23]—To a solution of amine **15** (71 mg, 0.26 mmol) in dry THF (2.5 cm^3) at −78 °C were added trimethylamine (0.05 cm^3, 0.36 mmol) and trimethylsilyl chloride (0.05 cm^3, 0.39 mmol). The reaction mixture was warmed to room temperature and, after being stirred for 1 h at room temperature, was recooled to −78 °C, and a solution of *tert*-butylmagnesium chloride (2 mol dm^{-3} in THF; 0.05 cm^3, 1.00 mmol) was added. The reaction mixture was again warmed to room temperature and stirred for 15 h. The reaction mixture was quenched by addition of water and extracted with ethyl acetate. The extract was washed with brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–ethyl acetate (7:1) gave the *title compound* **19** (41 mg, 87%) as a solid, m.p. 75.5–76.5 °C (from light petroleum) (Found: C, 59.6; H, 8.3; N, 7.6. $C_9H_{15}NOSi$ requires C, 59.62; H, 8.34; N, 7.73%); ν_{max}/cm^{-1} 3400 (NH), 2160 (C≡C) and 1760 (C=O); δ_H 6.40 (1 H, br s, NH), 3.84 (1 H, d, *J* 2.3, 4-H), 3.28 (1 H, ddq, *J* 0.9, 2.3 and 7.3, 3-H), 1.34 (3 H, d, *J* 7.3, Me) and 0.15 (9 H, s, TMS); δ_C 170.69, 102.77, 90.60, 55.36, 45.52, 12.84 and −0.31; *m/z* 182 (M^+ + 1, 0.15%), 138 (57), 123 (100), 110 (9.3) and 83 (5.6).

(3R*,4R*)-3-*Methyl*-4-(*trimethylsilylethynyl*)*azetidin*-2-*one* **21**.[23]—According to the procedure described for compound **19**, its stereoisomer **21** (12 mg, 70%) was obtained by treatment of amine **17** (24.5 mg, 0.09 mmol) with triethylamine (0.02 cm^3, 0.14 mmol), trimethylsilyl chloride (0.02 cm^3, 0.16 mmol) and *tert*-butylmagnesium chloride (2 mol dm^{-3} THF solution; 0.40 cm^3, 0.80 mmol). The *azetidinone* **21** was an oil (Found: M^+ + 1, 182.0945. $C_9H_{16}NOSi$ requires *m/z* 182.0989); ν_{max}/cm^{-1} 3370 (NH), 2160 (C≡C) and 1740 (C=O); δ_H 6.00 (1 H, br s, NH), 4.35 (1 H, d, *J* 5.0, 4-H), 3.41 (1 H, ddq, *J* 1.4, 5.0 and 7.8, 3-H), 1.34 (3 H, d, *J* 7.8, Me) and 0.18 (9 H, s, TMS); δ_C 170.85, 100.96, 92.63, 50.07, 43.45, 10.84 and −0.25; *m/z* 182 (M^+ + 1, 1.4%), 138 (39), 123 (100), 110 (10) and 83 (3.7).

S-tert-*Butyl* (2R*,3S*)-3-*Amino*-2-*ethyl*-5-(*trimethylsilyl*)-*pent*-4-*ynethioate* **16**.—According to the procedure for the preparation of compound **15** from compound **6a**, compound **6c** (492 mg, 1.71 mmol) was treated with triphenylphosphine (801 mg, 3.05 mmol), hydrazoic acid (~4% benzene solution; 7.5 cm^3, 6.98 mmol) and DEAD (0.5 cm^3, 3.00 mmol) to give the crude azide product **12**, which was subsequently reduced with triphenylphosphine (787 mg, 3.00 mmol) and water (5.0 cm^3) to afford, after chromatography with hexane–ethyl acetate (20:1), the *title amine* **16** (333 mg, 68%) as a solid, m.p. 48.0–49.0 °C (from light petroleum) (Found: M^+ + 1, 286.1652. $C_{14}H_{28}NOSSi$ requires *m/z*, 286.1659); ν_{max}/cm^{-1} 3380 and 3310 (NH), 2175 (C≡C) and 1670 (C=O); δ_H 3.75 (1 H, d, *J* 8.8, 3-H), 2.50 (1 H, dt, *J* 8.8 and 4.9, CH), 1.82–1.65 (2 H, m, CH_2), 1.50 (2 H, br s, NH_2), 1.48 (9 H, s, Bu^t), 0.96 (3 H, t, *J* 7.3, Me) and 0.16 (9 H, s, TMS); δ_C 202.32, 107.44, 88.29, 62.16, 48.45, 46.31, 29.72, 23.99, 11.46 and −0.09; *m/z* 286 (M^+ + 1, 0.05%), 126 (100), 98 (6.6) and 57 (5.6).

S-tert-*Butyl* (2R*,3R*)-3-*Amino*-2-*ethyl*-5-(*trimethylsilyl*)-*pent*-4-*ynethioate* **18**.—According to the procedure for the preparation of compound **15** from hydroxy ester **6a**, compound **7c** (700 mg, 2.44 mmol) was treated with triphenylphosphine (1.4 g, 5.34 mmol), hydrazoic acid (~4% benzene solution; 5.0 cm^3, 4.65 mmol) and DEAD (0.50 cm^3, 3.18 mmol) to give the crude azide **14**, which was subsequently reduced with triphenylphosphine (1.40 g, 5.34 mmol) and water (5.0 cm^3) to afford the *title compound* **18** (513 mg, 74%) as an oil (Found: C, 58.7; H, 9.5; N, 4.9. $C_{14}H_{27}NOSSi$ requires C, 58.89; H, 9.53; N, 4.91%); ν_{max}/cm^{-1} 3380 and 3310 (NH), 2175 (C≡C) and 1670 (C=O); δ_H 3.74 (1 H, d, *J* 6.8, 3-H), 2.49 (1 H, ddd, *J* 4.4, 6.8 and 8.1, CH), 1.83–1.66 (2 H, m, CH_2), 1.59 (2 H, br s, NH_2), 1.46 (9 H, s, Bu^t), 0.96 (3 H, t, *J* 7.8, Me) and 0.14 (9 H, s, TMS); δ_C 201.45, 106.96, 87.93, 62.05, 48.18, 45.95, 29.71, 21.80, 11.83 and −0.11; *m/z* 286 (M^+ + 1, 0.1%), 126 (100), 98 (5.9) and 57 (4.3).

(3R*,4S*)-3-*Ethyl*-4-(*trimethylsilylethynyl*)*azetidin*-2-*one* **20**.[23]—According to the procedure for the preparation of compound **19**, the amine **16** (286 mg, 1.00 mmol) was treated with triethylamine (0.20 cm^3, 1.40 mmol), trimethylsilyl chloride (0.20 cm^3, 1.60 mmol) and *tert*-butylmagnesium chloride (1.9 mol dm^{-3} THF solution; 2.0 cm^3, 3.80 mmol) to furnish the *title compound* **20** (162 mg, 83%) as a solid m.p. 79.5–80.5 °C (from light petroleum) (Found: M^+, 195.1057. $C_{10}H_{17}NOSi$ requires *M*, 195.1078); ν_{max}/cm^{-1} 3410 (NH), 2180 (C≡C) and 1760 (C=O); δ_H 5.90 (1 H, br s, NH), 3.93 (1 H, d, *J* 2.4, 4-H), 3.29–3.22 (1 H, m, 3-H), 1.89–1.69 (2 H, m, CH_2), 1.05 (3 H, t, *J* 7.3, Me) and 0.18 (9 H, s, TMS); δ_C 170.17, 103.07, 90.30, 61.94, 43.33, 21.28, 10.86 and −0.32; *m/z* 195 (M^+, 0.07%), 152 (30), 137 (100) and 110 (4.6).

(3R*,4R*)-3-*Ethyl*-4-(*trimethylsilylethynyl*)*azetidin*-2-*one* **22**.[23]—According to the procedure for the preparation of lactam **19**, amine **18** (291 mg, 1.02 mmol) was treated with triethylamine (0.20 cm^3, 1.40 mmol), trimethylsilyl chloride (0.20 cm^3, 1.60 mmol) and *tert*-butylmagnesium chloride (1.9 mol dm^{-3} THF solution; 2.0 cm^3, 3.80 mmol) to furnish the *title compound* **22** (138 mg, 70%) as a solid, m.p. 68.0–69.0 °C (from light petroleum) (Found: $M^+ - CH_3$, 180.0879. $C_9H_{14}NOSi$ requires *m/z* 180.0844): ν_{max}/cm^{-1} 3400 (NH), 2160 (C≡C) and 1745 (C=O); δ_H 6.46 (1 H, br s, NH), 4.31 (1 H, d, *J* 5.5, 4-H), 3.20 (1 H, ddt, *J* 1.4, 5.5 and 6.9, 3-H), 1.88–1.74 (2 H, m, CH_2), 1.04 (3 H, t, *J* 7.3, Me) and 0.15 (9 H, s, TMS); δ_C 170.57, 101.19, 92.15, 56.86, 42.73, 19.89, 11.54 and −0.35; *m/z* 195 (M^+, 0.06%), 152 (37), 137 (100) and 110 (9.5).

(3R*,4S*)-3-*Ethyl*-4-*ethynylazetidin*-2-*one* **23**.—To a solution of compound **20** (162 mg, 0.83 mmol) in dry THF (10 cm^3) at −78 °C was added TBAF (1.0 mol dm^{-3} THF solution; 1.2 cm^3, 1.20 mmol). The reaction mixture was gradually warmed to room temperature, then was diluted with water and extracted with ethyl acetate. The extract was washed successively with water and brine, and concentrated to dryness. Chromatography of the residue with hexane–ethyl acetate (3:1) afforded the *title compound* **23** (88 mg, 86%) as an oil; ν_{max}/cm^{-1} 3410 (NH), 3310 (HC≡), 2125 (C≡C) and 1765 (C=O); δ_H 6.59 (1 H, br s, NH), 3.90 (1 H, t, *J* 2.4, 4-H), 3.25 (1

H, dddd, *J* 1.0, 2.4, 6.3 and 8.3, 3-H), 2.44 (1 H, d, *J* 2.4, C≡CH), 1.86–1.66 (2 H, m, CH_2) and 1.02 (3 H, t, *J* 7.3, Me); δ_C 170.09, 81.48, 73.43, 61.83, 42.65, 21.27 and 10.92; *m/z* 97 ($M^+ - C_2H_2$, 0.17%), 95 (1.8), 79 (100), 65 (20) and 55 (21).

(3R*,4R*)-3-*Ethyl*-4-*ethynylazetidin*-2-*one* **24**.—Similar treatment of compound **22** (100 mg, 0.51 mmol) with TBAF (1.0 mol dm^{-3} THF solution; 0.7 cm^3, 0.70 mmol) gave the *title compound* **24** (62.9 mg, 100%) as an oil; ν_{max}/cm^{-1} 3400 (NH), 3300 (HC≡), 2110 (C≡C) and 1755 (C=O); δ_H 6.70 (1 H, br s, NH), 4.31 (1 H, dd, *J* 2.3 and 5.0, 4-H), 3.22 (1 H, dddd, *J* 1.8, 5.0, 6.9 and 8.7, 3-H), 2.25 (1 H, d, *J* 2.3, C≡CH), 1.89–1.73 (2 H, m, CH_2) and 1.03 (3 H, t, *J* 7.3, Me); δ_C 170.63, 79.44, 75.07, 56.60, 42.07, 19.89 and 11.54; *m/z* 95 ($M^+ - CO$, 2.0%), 79 (100), 65 (19) and 55 (21).

(3R*,4R*)-3-*Ethyl*-4-*vinylazetidin*-2-*one* **25**.—A solution of compound **23** (142 mg, 1.15 mmol) in hexane–methanol (20:1; 12 cm^3) was hydrogenated over Lindlar catalyst (17 mg) under hydrogen at atmospheric pressure for 30 min (monitored by TLC) at room temperature. The catalyst was removed by suction and the filtrate was concentrated. Chromatography of the residue with hexane–ethyl acetate (3:1) provided the *vinyl compound* **25** (130 mg, 90%) as an oil; ν_{max}/cm^{-1} 3420 (NH) and 1760 (C=O); δ_H 6.43 (1 H, br s, NH), 5.91 (1 H, ddd, *J* 6.9, 10 and 17, vinylic H), 5.26 (1 H, dt, *J* 10 and 0.9, vinylic H), 5.13 (1 H, dt, *J* 17 and 0.9, vinylic H), 3.78 (1 H, ddt, *J* 2.3, 6.9 and 0.9, 4-H), 2.81 (1 H, dddd, *J* 0.9, 2.3, 6.0 and 8.2, 3-H), 1.85–1.64 (2 H, m, CH_2) and 1.00 (3 H, t, *J* 7.3, Me); δ_C 170.86, 137.47, 116.44, 59.95, 56.09, 21.29 and 11.20; *m/z* 126 ($M^+ + 1$, 13%), 82 (95), 67 (100) and 57 (30).

(3R*,4S*)-3-*Ethyl*-4-*vinylazetidin*-2-*one* **27**.—Similar reduction of compound **24** (151 mg, 1.23 mmol) with Lindlar catalyst (17 mg) under hydrogen (1 atm) gave the *title compound* **27** (136 mg, 88%) as an oil (Found: M^+, 125.0874. $C_7H_{11}NO$ requires *M*, 125.0830); ν_{max}/cm^{-1} 3400 (NH) and 1750 (C=O); δ_H 5.89 (1 H, ddd, *J* 6.9, 10 and 17, vinylic H), 5.78 (1 H, br s, NH), 5.32 (1 H, dt, *J* 17 and 1.0, vinylic H), 5.30 (1 H, dt, *J* 10 and 1.0, vinylic H), 4.22 (1 H, ddt, *J* 5.4, 6.9 and 1.0, 4-H), 3.27–3.18 (1 H, m, 3-H), 1.81–1.43 (2 H, m, CH_2) and 0.99 (3 H, t, *J* 7.3, Me); δ_C 170.05, 134.74, 118.57, 56.84, 53.58, 18.75 and 11.99; *m/z* 126 ($M^+ + 1$, 3.3%), 82 (70), 67 (100) and 55 (24).

(3R*,4R*)-1-*Benzyl*-3-*ethyl*-4-*vinylazetidin*-2-*one* **26**.—Sodium hydride (60% oil dispersion; 55 mg, 1.43 mmol) was added to a stirred solution of compound **25** (136 mg, 1.09 mmol) in dry THF (8 cm^3) at 0 °C. After the mixture had been stirred for 15 min, benzyl bromide (0.25 cm^3, 2.10 mmol) was added and the reaction mixture was stirred for an additional hour at room temperature. The reaction was quenched by addition of water and extracted with chloroform. The extract was washed successively with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane–ethyl acetate (10:1) to afford the *title compound* **26** (186 mg, 80%) as an oil (Found: M^+, 215.1277. $C_{14}H_{17}NO$ requires *M*, 215.1308); ν_{max}/cm^{-1} 1730 (C=O); δ_H 7.35–7.22 (5 H, m, Ph), 5.76 (1 H, ddd, *J* 8.3, 10 and 16, vinylic H), 5.24 (1 H, dd, *J* 0.9 and 16, vinylic H), 5.20 (1 H, dd, *J* 0.9 and 10, vinylic H), 4.67 and 3.95 (2 H, ABq, *J* 15, benzylic H), 3.55 (1 H, dd, *J* 1.8 and 8.3, 4-H), 2.86 (1 H, ddd, *J* 1.8, 6.0 and 7.8, 3-H), 1.79 (1 H, ddq, *J* 6.0, 16 and 7.3, C*H*Me), 1.65 (1 H, ddq, *J* 7.8, 16 and 7.3, C*H*Me) and 0.96 (3 H, t, *J* 7.3, Me); δ_C 169.63, 136.09, 136.05, 128.61, 128.33, 127.50, 118.95, 59.36, 58.70, 44.26, 21.21 and 11.21; *m/z* 215 (M^+, 0.6%), 91 (19), 82 (100) and 67 (69).

(3R*,4S*)-1-*Benzyl*-3-*ethyl*-4-*vinylazetidin*-2-*one* **28**.—Similar treatment of compound **27** (141 mg, 1.12 mmol) with sodium hydride (60% oil dispersion; 54 mg, 1.36 mmol) and benzyl bromide (0.25 cm^3, 2.10 mmol) gave the *title compound* **28** (196 mg, 81%) as an oil (Found: M^+, 215.1279. $C_{14}H_{17}NO$ requires *M*, 215.1308); ν_{max}/cm^{-1} 1730 (C=O); δ_H 7.38–7.20 (5 H, m, Ph), 5.73 (1 H, ddd, *J* 8.2, 10 and 17, vinylic H), 5.30 (1 H, d, *J* 10, vinylic H), 5.27 (1 H, d, *J* 17, vinylic H), 4.65 and 3.97 (2 H, ABq, *J* 15, benzylic H), 3.97 (1 H, dd, *J* 5.3 and 8.2, 4-H), 3.15 (1 H, ddd, *J* 5.3, 7.3 and 8.8, 3-H), 1.86–1.60 (2 H, m, CH_2) and 0.97 (3 H, t, *J* 7.2, Me); δ_C 170.17, 136.03, 133.30, 128.59, 128.34, 127.47, 120.61, 56.97, 55.85, 44.15, 18.64 and 12.04; *m/z* 215 (M^+, 0.4%), 91 (29), 82 (100) and 67 (60).

(3R*,4R*)-1-*Benzyl*-3-*ethyl*-4-(2-*hydroxyethyl*)*azetidin*-2-*one* **29**.—To a solution of disiamylborane in dry THF (2.5 cm^3; 2 mol dm^{-3})[24] at 0 °C was added a solution of the vinyl compound **26** (237 mg, 1.10 mmol) in dry THF (5 cm^3). The reaction mixture was stirred at room temperature for 1 h and then aq. 20% sodium hydroxide (2 cm^3) and aq. 35% hydrogen peroxide (2 cm^3) were added to the reaction mixture, which was then stirred for an additional hour and extracted with ethyl acetate. The extract was then washed successively with water and brine, dried, and concentrated to dryness. Chromatography of the residue with hexane–ethyl acetate (1:1) afforded the *alcohol* **29** (193 mg, 75%) as an oil (Found: M^+, 233.1415. $C_{14}H_{19}NO_2$ requires *M*, 233.1415); ν_{max}/cm^{-1} 3400 (OH) and 1730 (C=O); δ_H 7.36–7.24 (5 H, m, Ph), 4.63 and 4.11 (2 H, ABq, *J* 15, benzylic H), 3.68–3.59 (2 H, m, CH_2OH), 3.28 (1 H, ddd, *J* 2.3, 5.0 and 8.3, 4-H), 2.82 (1 H, ddd, *J* 2.3, 5.5 and 7.8, 3-H), 1.97–1.58 (4 H, m, 2 × CH_2) and 0.99 (3 H, t, *J* 7.3, Me); δ_C 170.28, 136.25, 128.74, 128.09, 127.60, 59.54, 57.31, 55.34, 44.29, 35.38, 21.48 and 11.47; *m/z* 233 (M^+, 20%), 133 (21), 91 (100), 82 (100) and 67 (67).

(3R*,4S*)-1-*Benzyl*-3-*ethyl*-4-(2-*hydroxyethyl*)*azetidin*-2-*one* **31**.—Similar treatment of vinyl compound **28** (202 mg, 0.94 mmol) with disiamylborane, followed by oxidation with a system composed of hydrogen peroxide and aq. 20% sodium hydroxide, gave the *title alcohol* **31** (148 mg, 68%) as an oil (Found: M^+, 233.1416); ν_{max}/cm^{-1} 3420 (OH) and 1720 (C=O); δ_H 7.37–7.23 (5 H, m, Ph), 4.61 and 4.18 (2 H, ABq, *J* 15, benzylic H), 3.67 (1 H, q, *J* 6.3, 4-H), 3.60 (2 H, t, *J* 6.6, CH_2OH), 3.10 (1 H, ddd, *J* 6.3, 6.6 and 9.2, 3-H), 1.87–1.52 (4 H, m, 2 × CH_2) and 1.10 (3 H, t, *J* 7.4, Me); δ_C 171.23, 136.44, 128.72, 127.94, 127.53, 60.20, 54.03, 52.63, 44.64, 32.22, 18.73 and 12.55; *m/z* 233 (M^+, 6.2%), 133 (9.0), 91 (50), 82 (100) and 67 (38).

(3R*,4R*)-3-*Ethyl*-4-(2-*hydroxyethyl*)*azetidin*-2-*one* **30**.[15]—Sodium (8.9 mg, 0.39 mmol) was added to liquid ammonia (~2 cm^3) at −78 °C, to which a solution of compound **29** (46.5 mg, 0.20 mmol) in dry THF (2 cm^3) was subsequently added. The reaction mixture was stirred at the same temperature for 1 h. Solid ammonium chloride was added to the reaction mixture, which was then gradually warmed to room temperature. The precipitate was filtered off by suction and the filtrate was concentrated to leave a residue, which was chromatographed with ethyl acetate to provide the *title compound* **30** (23 mg, 82%) as an oil (Found: M^+, 143.0924. $C_7H_{13}NO_2$ requires *M*, 143.0944); ν_{max}/cm^{-1} 3410 (NH and OH) and 1740 (C=O); δ_H 6.50 (1 H, br s, NH), 3.79–3.68 (2 H, m, CH_2O), 3.45 (1 H, ddd, *J* 2.4, 4.9 and 7.8, 4-H), 2.75 (1 H, dddd, *J* 2.0, 2.4, 5.9 and 8.3, 3-H), 2.53 (1 H, br s, OH), 1.92–1.62 (4 H, m, 2 × CH_2) and 1.01 (3 H, t, *J* 7.3, Me); δ_C 171.30, 60.43, 58.41, 52.81, 37.30, 21.37 and 11.38; *m/z* 144 ($M^+ + 1$, 2.0%), 82 (100), 67 (80), 55 (39) and 41 (57).

(3R*,4S*)-3-*Ethyl*-4-(2-*hydroxyethyl*)*azetidin*-2-*one* **32**.[14]—Similar treatment of compound **31** (48 mg, 0.21 mmol) with sodium (9.5 mg, 0.43 mmol) in liquid ammonia gave the *title*

compound **32** (22 mg, 77%) as an oil (Found: M^+, 143.0910); ν_{max}/cm^{-1} 3400 (NH and OH) and 1730 (C=O); δ_H 6.00 (1 H, br s, NH), 3.88–3.73 (3 H, 4-H and CH_2OH), 3.16 (1 H, ddt, *J* 1.5, 5.4 and 7.3, 3-H), 1.87–1.72 (4 H, m, 2 × CH_2) and 1.07 (3 H, t, *J* 7.3, Me); δ_C 171.57, 61.20, 55.00, 50.44, 33.08, 18.23 and 12.54; *m/z* 144 ($M^+ + 1$, 2.1%), 82 (98), 67 (100), 55 (38) and 41 (50).

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Paper 2/05449C
Received 12*th October* 1992
Accepted 27*th October* 1992