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On the Possibility of Carbamate-directed Hydroboration. An Approach to the Asymmetric Synthesis of 1-Aminocyclopentane-1,3-dicarboxylic Acid

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Abstract

Hydroboration (using BH_3) of 1-substituted 3-cyclopentenes **3**, **9** and **17** and an enantioselective synthesis of the excitatory amino acid 1-aminocyclopentane-1,3-dicarboxylic acid *via* asymmetric hydroboration [90% de, 45% ee using (+)-IpcBH$_2$] of cyclopentene **17** are described. © 1999 Elsevier Science Ltd. All rights reserved.

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Association between a reagent and a functional group in a substrate prior to reaction of the reagent with a functional group elsewhere in the substrate is a useful control element for stereoselective synthesis.[1] Selectivity in the hydroboration of alkenes can often be rationalised on the basis of the favoured product arising from minimisation of non-bonded steric interactions between the hydroborating agent and the alkene in the transition state.[2] Studies by Brown and coworkers indicate that hydroborations occur by a dissociative mechanism involving free, uncomplexed or monomeric hydroborating agents. Although progress has been made in directed transition metal catalysed hydroboration,[1,3] developing functional groups which are generally able to direct uncatalysed hydroboration by preassociation remains a challenge for synthesis. However, there are isolated reports of (uncatalysed) hydroborations where the observed selectivity has been explained by such a directing effect of a polar functional group.[1] House and Melillo suggested that a regiocontrolled alkene hydroboration with BH_3 in THF arose from prior coordination to an ester group.[4] Wilt and Narutis implicated π-complexation between borane and an aryl substituent in the hydroboration of *syn*-7-arylnorbornenes.[5] Zweifel and coworkers invoked ether complexation in the hydroboration of a conjugated alkyne.[6] Intramolecular ether coordination was proposed by Suzuki and coworkers to account for the poor regioselectivity seen in the

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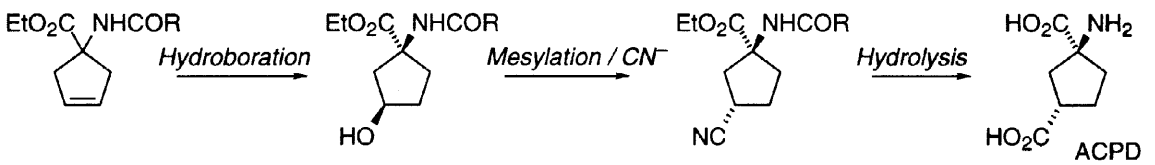
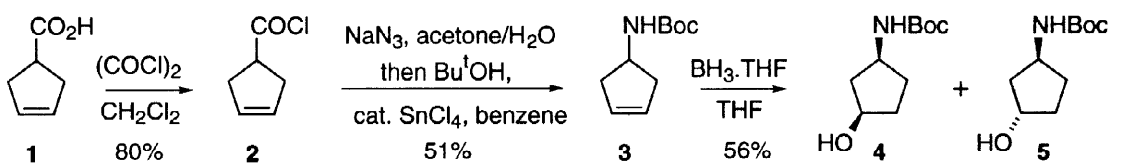
hydroboration of a terminal alkene using BH_3.THF; dicyclohexylborane was found to give a better yield of the desired primary alcohol.[7] Although hydroboration results have been reported which are not consistent with possible alkoxy direction,[8] Panek and coworkers have recently found a strong effect using BH_3.DMS in THF which relies on ester reduction *in situ* prior to (intramolecular) hydroboration from the intermediate dialkoxyborane; interestingly the corresponding unsaturated alcohol showed no selectivity on hydroboration.[9] Diastereoselectivity originating from prior substrate-reagent association might be anticipated to be effected by the coordinative ability of the solvent used.[1] Indeed Sibi and Li have observed such an effect in the reaction of an allylic carbamate with BH_3.THF followed by oxidative work-up, where the anti : syn ratio in the 1,2-aminoalcohol product altered slightly in moving from THF [94:6 (anti : syn)] to ether (92 : 8) to CH_2Cl_2 (86 : 14); the 1,2- : 1,3-regioselectivity also changed from 95 : 5 in THF or ether to 77 : 33 in CH_2Cl_2 (using BH_3.Me_2S was found to give about the same regio- and stereoselectivity as BH_3.THF).[10] In the context of developing new, stereocontrolled approaches to cyclic aminoalcohols and, especially, an asymmetric synthesis of the excitatory amino acid 1-aminocyclopentane-1,3-dicarboxylic acid (ACPD)[11] (eq. 1), we became interested in the possibility of using a protected amine to direct hydroboration and detail our studies on these topics in this paper.[12]



(1)

The Boc group was chosen for amine protection after consideration of its potential directing effect together with its demonstrated tolerance in hydroborations of acyclic unsaturated Boc-protected amines.[10,13] In order to first examine solely the effect of the NHBoc group on hydroboration diastereoselectivity, Boc-protected cyclopent-3-enamine **3** was prepared for study from the acid **1**[14] *via* the acid chloride **2**[15] and a subsequent Curtius rearrangement (NaN_3, acetone/H_2O, 5 °C, 30 min, then Bu^tOH, 4Å molecular sieves, cat. $SnCl_4$,[16] benzene, reflux, 5.5 h, 51% yield from **2**) (eq. 2).

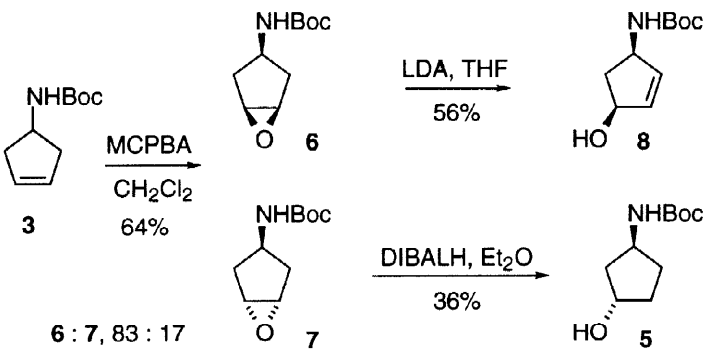


(2)

Reaction of cyclopentene **3** with BH_3.THF or BH_3.Me_2S (1 equiv., 0 °C to 25 °C, 17 h) in different solvents followed by standard oxidative work-up (1 M NaOH, 30% H_2O_2) was found to give ratios of alcohols **4** and **5** indicating a similar diastereoselectivity dependence on solvent to that found by Sibi and Li, although the effect was more pronouced in the present work [BH_3.THF in THF (cis : trans, 23 : 77); BH_3.Me_2S in ether (29 : 71), in CH_2Cl_2 (46 : 54)]. The diastereoselectivity can also be compared with that reported for hydroboration of 4-methylcyclopentene using BH_3.THF in THF, which gave 3-methylcyclopentanol (cis :

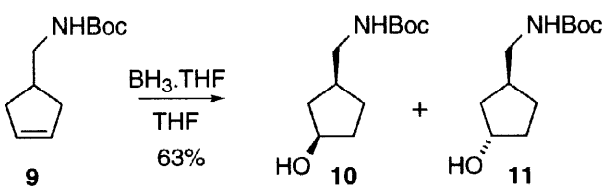
trans, 17 : 83)].[17] Our results suggest a weak coordinative directing effect (in CH_2Cl_2) of the NHBoc group which, however, is not able to overide its steric (and any electronic) effect.

The relative stereochemistry of alcohols **4** and **5** was established as follows. Epoxidation of **3** gives an 83 : 17 mixture of epoxides **6** and **7** which were separated (eq. 3).[18] The major epoxide isomer was rearranged using LDA to an allylic alcohol whose spectral data matched that recently reported[19] for the cis isomer **8** (cis stereochemistry unambiguous, since it arises from a nitroso hetero Diels-Alder cycloaddition with cyclopentadiene); the data were not consistent with that reported for the corresponding trans allylic alcohol.[20] In particular, CH_2 signals in the ^1H NMR spectra are diagnostic (centered at δ 2.7 and 1.5 for the cis allylic alcohol **8** and δ 2.2 and 1.9 for the trans allylic alcohol). The minor epoxide isomer, which could now be assigned as the trans isomer **7**, was ring-opened with DIBALH to give an alcohol whose spectral data matched that found for the predominant isomer (i.e. **5**)[21] arising from hydroboration of **3**, but did not match the data for the minor isomer (i.e. **4**)[22] from hydroboration of **3**. In particular, NH signals in the ^1H NMR spectra are diagnostic (centered at δ 5.2 and 4.5 for the cis alcohol **4** and trans alcohol **5**, respectively).



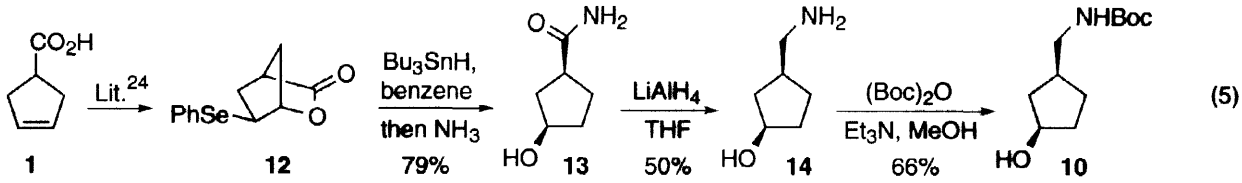
(3)

The Boc-protected (cyclopent-3-ene)methylamine **9**[23] was also briefly examined to study the effect of changing the distance between the alkene and the NHBoc group: a ratio cis : trans, 22 : 78 was observed in THF (eq. 4).



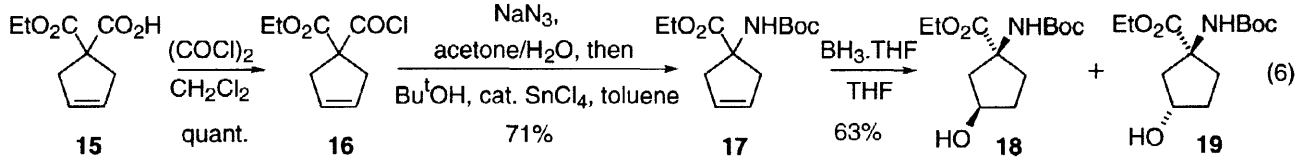
(4)

The relative stereochemistry of alcohols **10** and **11** was established as follows. The selenolactone **12**,[24] (prepared from acid **1**) was deselenated and subsequently ring-opened with ammonia to give the hydroxyamide **13** which was then reduced[25] and the resultant amine **14** Boc-protected to give an alcohol **10** (eq. 5), whose spectral data matched that found for the minor isomer arising from hydroboration of **9**, but did not match the data for the major isomer from hydroboration of **9**. ^1H NMR signals for $CHCH_2NH$ (centered at δ 2.1 and 4.8 for the cis alcohol **10** and δ 2.3 and 4.6 for the trans alcohol **11**) are useful for differentiating the isomers.



(5)

For our projected ACPD synthesis (eq. 1) the issue of hydroboration diastereoselectivity with cyclopentene **17** was next examined. Cyclopentene **17** was prepared from the half-acid ester **15**[14,26] *via* the acid chloride **16**[26] and a subsequent Curtius rearrangement (71% yield from **15**) (eq. 6).

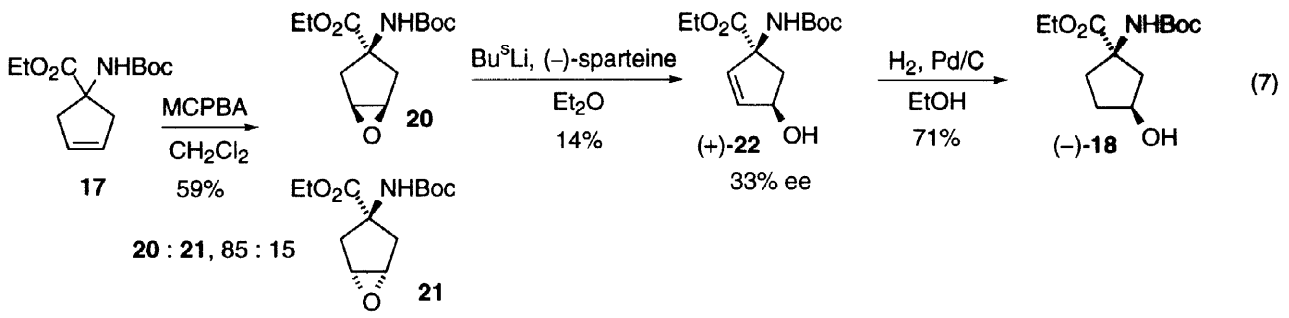


(6)

Using HPLC to follow the course of the hydroboration of cyclopentene **17** with BH_3.THF (1 equiv., THF, 0 °C, then standard oxidative work up) showed that the alkene **17** was consumed within 6 min, and the diastereomeric ratio of alcohols **18/19** at this stage was 77 : 23 (**18** : **19**). However, the ratio then rose [after 30 min: 84 : 16 (**18** : **19**)] to 95 : 5 (**18** : **19**) after 17 h. Hydroboration usually only becomes reversible on heating to over 160 °C.[2c] Therefore, our observations suggest preferential further reaction of the intermediate(s) derived from hydroboration cis to the ester, possibly by selective activation of the ester group to reduction through formation of an intramolecular Lewis acid-base complex between boron and the ester group. Although no byproducts were isolated which could be assigned as arising from this process, the total isolated yield of alcohols **18/19** did decrease with time (84% after 10 min, 73% after 30 min). From a practical standpoint, it is preferable to allow the selective removal of the minor isomer to proceed (at the expense of overall yield), since chromatographic separation of the two alcohols is difficult when there is a larger proportion of the alcohol **19** present, leading to a reduction in overall isolated yield of pure **18**. In order to examine whether hydroboration was potentially occuring *via* prior formation of a covalent (N-B) complex between BH_3 and the cyclopentene **17**, the rate of evolution of H_2 (presumably arising from reaction of BH_3 with the NH) was monitored (using an inverted buret); approximately 20% of the theoretical maximum volume of H_2 was evolved in 6 min (80% evolution was observed after 20 h) - indicating that formation of such a complex is unlikely to play a significant role in influencing the diastereoselectivity.

The relative stereochemistry of alcohols **18** and **19** was established as follows. Epoxidation of **17** gives an 85 : 15 mixture of epoxides **20** and **21** which were separated (eq. 7). The structure of the minor epoxide **21** (trans epoxide and carbamate groups) was secured by X-ray crystallographic analysis (fig. 1). The major epoxide isomer **20** was rearranged using Bu^sLi/(−)-sparteine[27] to give an allylic alcohol (+)-**22** {33% ee [determined by ^1H NMR using (+)-2,2,2-trifluoro-1-(9-anthryl)ethanol (TFE)]},[28] which was hydrogenated to give an alcohol (−)-**18** whose spectral data matched that found for the major isomer from hydroboration of **17**, but the data did not match that found for the minor isomer from

hydroboration of **17**. In particular, NH signals in the ^{1}H NMR spectra are diagnostic (centered at δ 5.8 and 5.1 for the cis alcohol **18** and trans alcohol **19**, respectively).



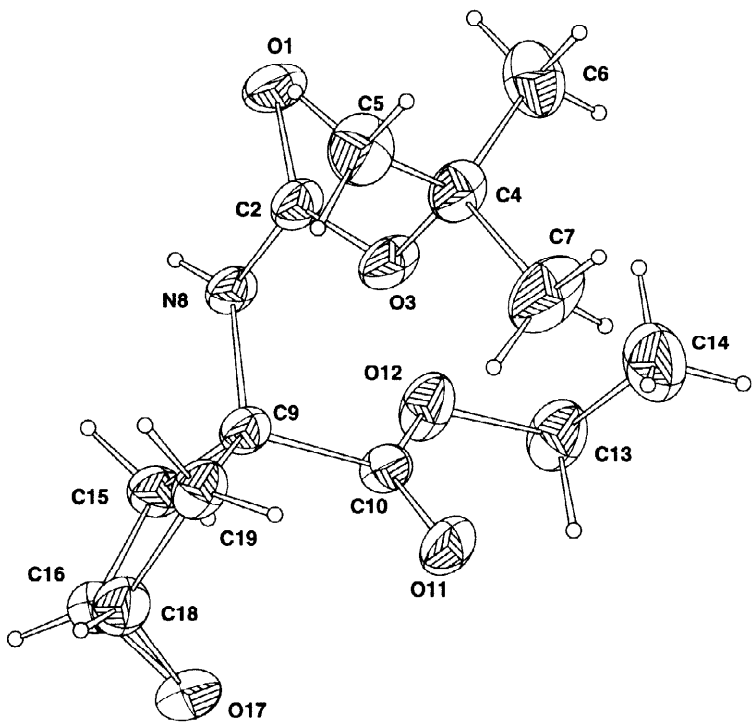
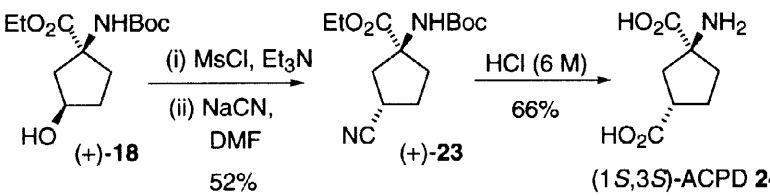


Fig. 1. Molecular structure of epoxide **21** (thermal ellipsoids are at the 50% level)

Reaction of cyclopentene **17** with the most commonly used reagent for asymmetric hydroboration of cis 1,2-disubstituted alkenes, (–)-Ipc$_2$BH[2,29] (3 equiv., THF, 0 °C to room temperature, 17 h) followed by oxidation gave, after careful chromatography pure samples of alcohols **18** {34%, racemic [determined by ^{1}H NMR using (–)-TFE)]} and (+)-**19** (4%, 63% ee) (**18** : **19** = 81 : 19 by HPLC analysis of the crude reaction mixture). However, reaction of cyclopentene **17** with (–)-IpcBH$_2$[2,30] (1 equiv., THF, 0 °C to room temperature, 17 h) gave the alcohol (–)-**18** in 42% yield and 34% ee (**18** : **19** = 95 : 5 by HPLC analysis of the crude reaction mixture). 34% ee was also obtained in diglyme under otherwise indentical conditions. No reaction was observed in ether, or on lowering the reaction temperature to −60 °C with THF as solvent. Within the scope of this study the best conditions were found to be using (–)-IpcBH$_2$ (2.3 equiv., THF, −40 °C, 72 h) which gave (–)-**18** in 77% yield and

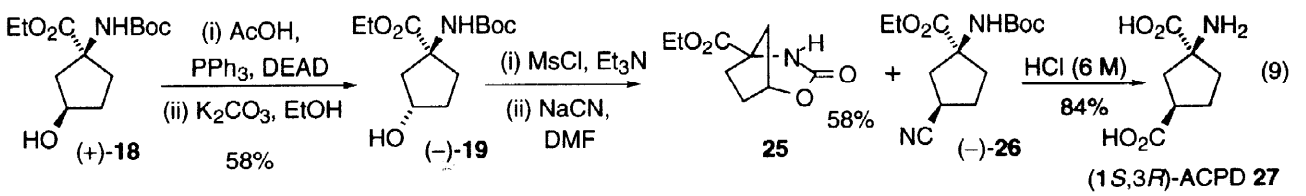
47% ee [similarly using (+)-IpcBH$_2$ gave (+)-**18** in 74% yield and 48% ee]. None of alcohol **19** was detected at the end of these latter reactions. However, control experimental established that, as with BH_3, this was due to preferential removal during the reaction of the intermediate(s) derived from hydroboration cis to the ester (after 1 h, **18** : **19** = 87 : 13, after 21 h, 93 : 7). Attempts to improve on the ee of **18** obtained with IpcBH$_2$ by using dilongifolylborane (Lgf$_2$BH)[31] or transition-metal catalysed hydroboration[3,32] were unsuccessful; reaction of cyclopentene **17** with Lgf$_2$BH (4 equiv., THF, 25 °C, 48 h) gave the alcohol (−)-**18** in 20% yield and 49% ee (**18** : **19** = 67 : 33 by ^{1}H NMR analysis of the crude reaction mixture); treatment of cyclopentene **17** with catecholborane in the presence of [RhCl(COD)] and (*S*,*S*)-(+)-DIOP in THF gave the alcohol **18** in 33% yield and 5% ee and the alcohol **19** in 19% yield and 6% ee (**18** : **19** = 50 : 50 by ^{1}H NMR analysis of the crude reaction mixture).

Alcohol (+)-**18** (45% ee) was converted to (1*S*,3*S*)-ACPD **24** {$[\alpha]_D^{23}$ +2.0 (*c* 0.41 in H_2O), lit.[11a] $[\alpha]_D^{20}$ +8.4 (*c* 1.0 in H_2O)} *via* mesylation (MsCl, Et_3N, CH_2Cl_2, 0 °C to room temperature, 17 h, 87%) and reaction with NaCN (3 equiv., DMF, 80 °C, 17 h) to give cyanide (+)-**23** (60% yield), followed by hydrolysis (6 M HCl, reflux, 4 h) and ion-exchange [Dowex 50WX8-100, 2 M aq. NH_3, 66% from (+)-**23**)] (eq. 8).



(8)

Alcohol (+)-**18** (45% ee) could also be converted into (1*S*,3*R*)-ACPD **27** {$[\alpha]_D^{23}$ −3.9 (*c* 0.26 in H_2O), lit.[11a] $[\alpha]_D^{20}$ −6.9 (*c* 1.0 in H_2O)} by the same sequence of transformations after first forming the inverted alcohol (−)-**19** (AcOH, PPh_3, DEAD, THF, 77%, then K_2CO_3, EtOH, 76%) (eq. 9). However, the major product in the reaction of the mesylate with NaCN was the bicyclic carbamate **25**.



(9)

In summary, hydroboration of the simple cyclopentene **3** with BH_3 in THF occurs mainly trans to the carbamate group, however the diastereoselectivity is reduced in CH_2Cl_2 suggesting the emergence a weak carbamate directive effect. With alkene **17** hydroboration occurs preferentially cis to the carbamate group in the presence of ester functionality. This may be due to differential steric effects of the two functional groups and/or a preferential directing effect by the carbamate group. Asymmetric hydroboration of alkene **17** gives alcohol (+)-**18** (in up to 48% ee) which can be converted to ACPDs **24** and **27**.

EXPERIMENTAL

All reactions requiring anhydrous conditions were conducted in flame-dried apparatus under an atmosphere of argon. Syringes and needles for the transfer of reagents were dried at 140 °C and allowed to cool in a desiccator over P_2O_5 before use. Ethers were distilled from sodium benzophenone ketyl; (chlorinated) hydrocarbons, and amines from CaH_2. Internal reaction temperatures are reported unless stated otherwise. Reactions were monitored by TLC using commercially available glass-backed plates, pre-coated with a 0.25 mm layer of silica containing a fluorescent indicator (Merck). Column chromatography was carried out on Kieselgel 60 (40-63 μm). Light petroleum refers to the fraction with bp 40-60 °C. Melting points (mp) are uncorrected. $[\alpha]_D$ Values are given in 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded as thin films unless stated otherwise. Peak intensities are specified as strong (s), medium (m) or weak (w). ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ unless stated otherwise with Varian Gemini 200, Bruker AC200, Bruker AC250, Bruker WH300, Bruker DPEX400, Bruker AM500 or Bruker AMX500 spectrometers. Chemical shifts are reported relative to $CHCl_3$ [δ_H 7.26, δ_C(central line of t) 77.0]. Coupling constants (J) are given in Hz. HPLC analysis was performed by the Glaxo Wellcome Physical Sciences Unit (Stevenage) using an Inertsil ODS-2 column (4.6 mm x 150 mm) on a Capital HPLC machine (Broxburn, Scotland). Detection was at 215 nm at 40 °C, with a flow rate of 1.0 cm^3 min^{-1}.

Cyclopent-3-ene carbonyl chloride **2**. $(COCl)_2$ (3.90 cm^3, 44.7 mmol) was added to a cooled (ice-water bath) solution of the carboxylic acid **1**[14] (4.13 g, 36.8 mmol) in CH_2Cl_2 (40 cm^3). DMF (1 drop) was added, giving some effervesence, and the reaction mixture was stirred with cooling for 1.5 h, then allowed to warm to room temperature and stirred for a further 3.5 h. Purification by distillation [120 °C/15 mbar (lit.[15] 95-96 °C/55 mmHg) gave a colourless oil, the acid chloride **2** (3.84 g, 80%); δ_H(200 MHz) 5.67 (2 H, s, 2 x CH=), 3.65-3.50 (1 H, m, CH) and 2.92-2.65 (4 H, m, 2 x CH_2).

N-Boc Cyclopent-3-enamine **3**. A solution of the acid chloride **2** (3.84 g, 29.4 mmol) in acetone (9 cm^3) was added dropwise to a cooled (3 °C) solution of NaN_3 (2.96 g, 45.5 mmol) in H_2O (9 cm^3) whilst maintaining the reaction temperature below 6 °C. After 30 min the reaction mixture was extracted with benzene (4 x 15 cm^3) and the combined organic extracts were dried ($MgSO_4$) to give a solution of the azide [ν_{max}/cm^{-1}(benzene) 2137, 1716]. 4Å Molecular sieves (5 g) and Bu^tOH (28 cm^3, 0.29 mmol) were added successively to the reaction mixture which was then heated to reflux. After 4.5 h IR analysis indicated complete conversion to the isocyanate [ν_{max}/cm^{-1} (benzene) 2268, 1716]. $SnCl_4$ (0.21 cm^3, 1.8 mmol) was then added to the solution at room temperature and the reaction mixture was heated to reflux. After 1 h IR analysis indicated complete reaction of the isocyanate [ν_{max}/cm^{-1} (benzene) 1716]. The reaction mixture was then stored at 5 °C. After 10 d the reaction mixture was filtered, the sieves were washed with EtOAc and the combined filtrates were evaporated under reduced pressure to give a yellow solid. Purification by column chromatography (30% ether/light petroleum) gave a white solid, the cyclopentene **3** (2.75 g, 51%); R_f 0.77 (50% EtOAc/light petroleum); Found: C, 65.76; H, 9.49; N, 7.64. $C_{10}H_{17}NO_2$ requires C, 65.54; H, 9.35; N, 7.64%; mp 70-72 °C (from EtOAc/light petroleum); ν_{max}/cm^{-1}

(KBr) 3336s, 3053w, 3015w, 2980m, 2928m, 2854w, 1703s, 1680s, 1542s, 1452w, 1365m, 1288m, 1269m, 1175s, 1052m and 686m; δ_H(200 MHz) 5.72 (2 H, s, 2 x CH=), 4.71 (1 H, brs, NH), 4.37-4.15 (1 H, m, CH), 2.71 (2 H, dd, *J* 7.4 and 15.3, 2 x H of CH_2), 2.16 (2 H, dd, *J* 3.9 and 15.2, 2 x H of CH_2) and 1.43 (9 H, s, 3 x Me); δ_C(50 MHz) 155.5 (C=O, quat.), 128.8 (2 x CH=), 79.1 (C, quat.), 50.0 (CHN), 40.4 (2 x CH_2) and 28.4 (3 x Me); *m/z* (CI) 184 [$(M + H)^+$, 20%], 145 (100), 128 (20), 84 (55), 58 (25), 52 (48), 44 (42) and 36 (23) [Found: $(M + H)^+$, 184.1338. $C_{10}H_{18}NO_2$ requires *M*, 184.1338].

N-Boc cis- and trans-3-Aminocyclopentan-1-ols **4** and **5**. BH_3.THF (1 mol dm^{-3} in THF; 0.55 cm^3, 0.55 mmol) was added to a cooled (ice-water bath) solution of the cyclopentene **3** (0.10 g, 0.5 mmol) in THF (0.6 cm^3). The reaction mixture was allowed to warm to room temperature and stirred overnight. Water was added (1 cm^3), followed by aq. H_2O_2 (30% w/w; 0.19 cm^3, 1.7 mmol) and aq. NaOH (1 mol dm^{-3}; 0.55 cm^3, 0.55 mmol). The mixture was extracted with ether (3 x 5 cm^3), then saturated with K_2CO_3 and extracted with THF (10 cm^3). The combined organic extracts were washed with brine (20 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. ^1H NMR analysis (400 MHz, benzene d_6) of the NH signals at δ 5.17 and 4.25 and the CHN signals at δ 3.87 and 3.78 of this crude product gave cis alcohol **4** : trans alcohol **5** = 23 : 77. The residue was purified by column chromatography (gradient elution, 25-75% ether/light petroleum). First to elute was a semi-solid, the cis alcohol **4** (23 mg, 21%); R_f 0.24 (50% EtOAc/light petroleum); ν_{max}/cm^{-1} (KBr) 3442s, 3378s, 2969s, 2874w, 1690s, 1510s, 1460w, 1432w, 1392w, 1367m, 1352m, 1333w, 1254s, 1175s, 1111m, 1072w, 1059m, 1020w, 986w, 960w and 942w; δ_H(500 MHz) 5.17 (1 H, brs, NH), 4.45-4.30 (1 H, m, C*H*OH), 4.14-3.93 (1 H, m, C*H*NH), 2.18 (1 H, brs, OH), 2.16-1.98 (2 H, m, H of 2-CH_2 and H of 4-CH_2), 1.86-1.73 (3 H, m, H of 4-CH_2 and 5-CH_2), 1.73-1.63 (1 H, m, H of 2-CH_2) and 1.49 (9 H, s, 3 x Me); δ_C(125 MHz) 155.5 (C=O, quat.), 79.0 (C, quat.), 73.2 (CHO), 50.8 (CHN), 42.5 (2-CH_2), 34.3 (5-CH_2), 31.5 (4-CH_2) and 28.3 (3 x Me); *m/z* (EI) 145 (11%), 84 (22), 72 (18), 59 (26), 57 (100), 43 (53) and 41 (68); *m/z* (CI) 202 [$(M + H)^+$, 100%] [Found: $(M + H)^+$, 202.1443. $C_{10}H_{20}NO_3$ requires *M*, 202.1443]. Second to elute was a white solid, the trans alcohol **5** (39 mg, 35%); R_f 0.16 (50% EtOAc/light petroleum); Found: C, 59.84; H, 9.25; N, 6.79. $C_{10}H_{19}NO_3$ requires C, 59.68; H, 9.51; N, 6.96%; mp 84-85 °C (from ether/light petroleum); ν_{max}/cm^{-1}(KBr) 3342s, 2967m, 1682s, 1534s, 1452w, 1364m, 1311m, 1268m, 1252m, 1178s, 1106m, 1011s and 843w; δ_H(500 MHz) 4.57 (1 H, brs, NH), 4.46-4.37 (1 H, m, CHO), 4.27-4.07 (1 H, m, CHN), 2.43-2.29 (1 H, m, H of 5-CH_2), 2.26-1.97 (3 H, m, H of 2-CH_2, H of 4-CH_2 and OH), 1.73-1.56 (2 H, m, H of 2-CH_2 and H of 4-CH_2), 1.47 (9 H, s, 3 x Me) and 1.46-1.36 (1 H, m, H of 5-CH_2); δ_C(125 MHz) 155.9 (C=O, quat.), 79.7 (C, quat.), 72.6 (CHO), 50.9 (CHN), 43.5 (2-CH_2), 34.2 (4-CH_2), 31.7 (5-CH_2) and 28.9 (3 x Me); *m/z* (EI) 72 (16%), 59 (30), 57 (100), 56 (28), 43 (37) and 41 (42); *m/z* (CI) 219 [$(M + NH_4)^+$ 10%], 102 (100) [Found: $(M + NH_4)^+$, 219.1709. $C_{10}H_{23}N_2O_3$ requires *M*, 219.1709]

N-Boc (1R,3r,5S)- and (1R,3s,5S)-6-Oxabicyclo[3.1.0]hexan-3-amines **6** and **7**. Peracetic acid (36-40% w/v in acetic acid; 3.4 cm^3, 20 mmol) was added dropwise to a cooled (ice-water bath) solution of the cyclopentene **3** (1.50 g, 8.2 mmol), Na_2CO_3 (5.2 g, 49 mmol) and

NaOAc (10 mg) in CH_2Cl_2 (60 cm^3) and the reaction mixture was then allowed to warm to room temperature. After 6 d the mixture was filtered, the solid material washed with CH_2Cl_2 (20 cm^3) and the combined filtrates washed with saturated aq. $NaHCO_3$ (3 x 100 cm^3), brine (100 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. ^1H NMR analysis of the epoxide signals at δ 3.45 and 3.37 of the residue gave cis epoxide **6** : trans epoxide **7** = 83 : 17. The residue was purified by column chromatography (1% MeOH/CH_2Cl_2). First to elute was an amorphous solid, the cis epoxide **6** (0.81 g, 50%); R_f 0.68 (5% MeOH/CH_2Cl_2); ν_{max}/cm^{-1} (KBr) 3446m, 2977m, 2929m, 1713s, 1493s, 1392m, 1367m, 1344m, 1247m, 1172s, 1069s, 943m and 833m; δ_H(200 MHz) 5.06-4.86 (1 H, m, NH), 4.24-4.04 (1 H, m, CHN), 3.54 (2 H, s, 2 x CHO), 2.07-1.98 (2 H, m, 2 x H of CH_2), 1.98-1.89 (2 H, m, 2 x H of CH_2) and 1.40 (9 H, s, 3 x Me); δ_C(125 MHz) 155.5 (C=O, quat.), 79.4 (C, quat.), 57.5 (2 x CHO) 46.7 (CH), 36.5 (2 x CH_2) and 28.8 (3 x Me); *m/z* (CI) 200 [$(M + H)^+$, 48%], 161 (47), 144 (100) and 100 (45) [Found: $(M + H)^+$, 200.1287. $C_{10}H_{18}NO_3$ requires *M*, 200.1287]. Second to elute was an amorphous solid, the trans epoxide **7** (0.23 g, 14%); R_f 0.58 (5% MeOH/CH_2Cl_2); ν_{max}/cm^{-1} (KBr) 3359s, 3042w, 3010w, 2961w, 2924m, 2853m, 1684s, 1533s, 1396w, 1289m, 1259m, 1173s, 1082m and 833m; δ_H(200 MHz) 4.46-4.26 (1 H, m, NH), 3.90-3.70 (1 H, m, CHN), 3.48 (2 H, s, 2 x CHO), 2.50 (2 H, dd, *J* 7.7 and 14.0, 2 x H of 2-CH_2), 1.44 (9 H, s, 3 x Me) and 1.36-1.04 (2 H, m, 2 (H of 2-CH_2); δ_C(125 MHz) 155.1 (C=O, quat.), 79.4 (C, quat.), 55.5 (2 x CHO), 46.5 (CHN), 34.3 (2 x CH_2) and 28.4 (3 x Me).

N-Boc cis-4-Aminocyclopent-2-en-1-ol **8**. Bu^nLi (2.3 mol dm^{-3} in hexanes; 0.65 cm^3, 1.5 mmol) was added to a cooled (ice-water bath) solution of diisopropylamine (0.23 cm^3,1.8 mmol) in THF (3.8 cm^3). After 30 min a solution of the cis epoxide **6** (100 mg, 0.5 mmol) in THF (1.3 cm^3) was added dropwise to the stirred reaction mixture Cooling was maintained for 2.5 h before warming to room temperature and stirring overnight. MeOH (1 cm^3) was then added and the mixture concentrated under reduced pressure. The residue was pre-absorbed onto silica and purified by column chromatography (gradient elution, 50-100% ether/light petroleum) to give a colourless oil, the allylic alcohol **8** (56 mg, 56%); R_f 0.29 (50% EtOAc/light petroleum); ν_{max}/cm^{-1} 3350s, 2977s, 2934m, 1716s, 1694s, 1538s, 1505s, 1393m, 1367m, 1333m, 1254m, 1169s, 1059s, 992m and 860m; δ_H(400 MHz) 5.97-5.88 (1 H, m, CH=), 5.84-5.76 (1 H, m, =CH), 5.03 (1 H, d, *J* 8.1, NH), 4.70-4.59 (1 H, m, C*H*OH), 4.47-4.35 (1 H, m, CHN), 3.43 (1 H, brs, OH), 2.66 (1 H, ddd, *J* 8.0 and 14.4, H of CH_2), 1.59-1.42 (1 H, m, H of CH_2) and 1.42 (9 H, s, 3 x Me); δ_C(100 MHz) 155.3 (C=O, quat.), 136.0 (CH=), 134.2 (=CH), 79.5 (C, quat.), 75.1 (CHOH), 54.8 (CH), 41.3 (CH_2) and 28.4 (3 x Me); *m/z* (ES) 222 [$(M + Na)^+$, 12%], 200 [$(M + H)^+$, 7%], 198 (8), 182 (13), 126 (100) and 121 (30); *m/z* (CI) 219 [$(M + NH_4)^+$, 12%], 200 [$(M + H)^+$, 100] and 181 (74) [Found: $(M + H)^+$, 200.1279. $C_{10}H_{18}NO_3$ requires *M*, 200.1287].

N-Boc trans-3-Aminocyclopentan-1-ol **5**. DIBALH (1 mol dm^{-3} in hexanes; 0.6 cm^3, 0.6 mmol) was added to a solution of the trans epoxide **7** (20 mg, 0.1 mmol) in ether (0.6 cm^3) and the reaction mixture stirred for 3 h at room temperature. Aq. NaOH (1 mol dm^{-3}; 0.6 cm^3) was added and the quenched mixture stirred for 30 min before filtering off the

precipitate which had formed. The solids were washed with ether (25 cm^3), the washings combined with the original filtrate and concentrated under reduced pressure. The residue was pre-absorbed onto silica and purified by column chromatography (gradient elution, 50-60% ether/light petroleum) to give the trans alcohol **5** (7.1 mg, 36%).

N-Boc (Cyclopent-3-ene)methylamine **9**. Et_3N (0.36 cm^3, 2.6 mmol) and di-*tert*-butyl dicarbonate (0.57 g, 2.6 mmol) were added successively to a solution of (cyclopent-3-ene)methylamine[23] (0.23 g, 2.4 mmol) in MeOH (3.2 cm^3). After heating at 50 °C for 1 h the mixture was concentrated to dryness under reduced pressure and the residue partitioned between EtOAc (20 cm^3) and aq. HCl (2 mol dm^{-3}; 20 cm^3). The organic extract was washed with saturated aq. $NaHCO_3$ (20 cm^3), water (20 cm^3) and brine (20 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. Purification of the residue by column chromatography (50% ether/light petroleum) gave a colourless oil, the carbamate **9** (0.175 g, 38%); R_f 0.63 (50% ether/light petroleum); ν_{max}/cm^{-1} 3354m, 3055w, 2978m, 2929m, 1694s, 1520s, 1455w, 1391m, 1366m, 1250m and 1174s; δ_H(200 MHz) 5.62 (2 H, s, CH=CH), 4.71 (1 H, brs, NH), 3.14-2.93 (2 H, m, CH_2N), 2.56-2.25 (3 H, m, CH and 2 x H of CH_2), 2.15-1.87 (2 H, m, 2 x H of CH_2) and 1.41 (9 H, s, 3 x Me); δ_C(50 MHz) 156.1 (C=O, quat.), 129.5 (CH=CH), 78.9 (C, quat.), 45.6 (CH_2N), 37.1 (CH), 36.5 (2 x CH_2) and 28.4 (3 x Me); *m/z* (APCI) 198 [$(M + H)^+$, 3%], 189 (12) and 142 (100).

N-Boc cis- and trans-3-(Aminomethyl)cyclopentan-1-ols **10** and **11**. Following the procedure for the preparation of **4** and **5**, using BH_3.THF (1 mol dm^{-3} in THF; 0.82 cm^3, 0.82 mmol) and the carbamate **9** (0.161 g, 0.82 mmol) gave a residue which was purified by column chromatography (gradient elution, 25-100% ether/light petroleum) to give a colourless oil, an inseparable mixure of the the cis alcohol **10** and the trans alcohol **11** (0.11 g, 63%, 22 : 78 respectively by ^1H NMR); R_f 0.23 (50% EtOAc/light petroleum); ν_{max}/cm^{-1}(KBr) 3350s, 2959s, 1694s, 1538s, 1366m, 1251m and 1171s; δ_H(500 MHz) 4.82 (0.22 H, brs, NH of **10**), 4.57 (0.78 H, brs, NH of **11**), 4.43-4.36 (0.78 H, m, C*H*OH of **11**), 4.36-4.27 (0.22 H, m, C*H*OH of **10**), 3.16-2.97 (2 H, m, C*H*$_2$NH), 2.32 (0.78 H, quintet, *J* 7.6 and 15.5, C*H*CH_2NH of **11**), 2.14 (0.22 H, quintet, *J* 7.1 and 14.3, C*H*CH_2NH of **10**), 2.07-1.99 (0.22 H, m, H of 2-CH_2 of **10**), 1.99-1.88 (1.6 H, m, 4-CH_2 of **11**), 1.85-1.74 (0.8 H, m, H of 2-CH_2 of **11**), 1.74-1.65 (0.3 H, m, 4-CH_2 of **10** and 5-CH_2 of **10**), 1.65-1.55 (0.8 H, m, H of 2-CH_2 of **11**), 1.44 (9 H, s, 3 x Me) and 1.37-1.20 (2 H, m, 5-CH_2 of **11** and H of 2-CH_2 of **10**); δ_C(125 MHz) 156.5 (C=O, quat.), 79.6 (C, quat.), 74.0 (CHO), 45.8 (CH), 40.5 (CH_2), 38.3 (CH_2), 35.4 (CH_2), 28.9 (3 x Me) and 28.2 (CH_2); *m/z* (EI) 159 (16%), 142 (24), 97 (27), 81 (28), 80 (40), 59 (70), 57 (100) and 41 (83); *m/z* (CI) 216 [$(M + H)^+$, 5%], 177 (56), 114 (100), 96 (63), 82 (65), 58 (70), 52 (97) and 44 (94) [Found: $(M + H)^+$, 216.1608. $C_{11}H_{22}NO_3$ requires *M*, 216.1600].

cis-3-Hydroxycyclopentane-1-formamide **13**. Tributyltin hydride (0.11 cm^3, 0.41 mmol) and AIBN (spatula tip) were added successively to a solution of the selenolactone **12**[24] (100 mg, 0.37 mmol) in benzene (1.7 cm^3) and the reaction mixture heated under reflux. After 4 h the reaction was cooled to room temperature, aq. NH_3 (35% w/w; 0.25 cm^3, 5 mmol) was

added and the mixture heated under reflux. After 2.5 h the reaction was allowed to cool to room temperature and stirred overnight. The mixture was then concentrated under reduced pressure and azeotroped with benzene (5 x 4 cm^3). The residue was pre-absorbed onto silica and purified by column chromatography (gradient elution, 5-100% EtOAc/light petroleum then 100% MeOH)to give a white solid, the amide **13** (38 mg, 79%); R_f 0 (50% EtOAc/light petroleum); mp 90-95 °C; ν_{max}/cm^{-1} (KBr) 3356s, 3192m, 2960w, 1662s, 1631s, 1415m, 1348w, 1092w and 986w; δ_H(200 MHz) 4.87 (3 H, s, NH_2 and OH), 4.21 (1 H, quintet, *J* 4.5 and 9.7, CHO), 2.75 (1 H, quintet, *J* 8.2 and 15.6, CH) and 2.16-1.52 (6 H, m, 3 x CH_2); δ_C(50 MHz) 180.8 (C=O, quat.), 72.8 (CHO), 42.7 (CH), 38.2 (CH_2), 34.8 (CH_2) and 27.5 (CH_2).

cis-3-(Aminomethyl)cyclopentan-1-ol **14**. A solution of the amide **13** (38 mg, 0.3 mmol) in THF (2 cm^3) was added dropwise to a cooled (ice-water bath) solution of $LiAlH_4$ (50 mg, 1.3 mmol) in THF (0.4 cm^3) and the reaction mixture was then heated to reflux. After 7.5 h the reaction mixture was cooled with an ice-water bath and a mixture of THF (0.45 cm^3) and water (0.45 cm^3) added. After allowing to warm to room temperature over 15 min the mixture was filtered, the solids washed with ether (30 cm^3) and the combined filtrates concentrated under reduced pressure. The residue was extracted with $CHCl_3$, dried (Na_2SO_4) and concentrated under reduced pressure to give a colourless oil, the amine **14** (17 mg, 50%); R_f 0 (50% EtOAc/light petroleum); ν_{max}/cm^{-1} (KBr) 3360s, 2927s, 1666w, 1600m, 1454m, 1348m, 1075m and 1010m; δ_H(200 MHz) 4.27-4.08 (1 H, m, CHO), 3.06-2.43 (5 H, m, NH_2, CH_2N and OH), 2.36-1.92 (2 H, m, CH_2), 1.92-1.60 (3 H, m, CH_2 and CH) and 1.60-1.16 (2 H, m, CH_2); δ_C(50 MHz) 72.7 (CHO), 45.2 (CH_2), 39.8 (CH_2), 38.9 (CHN), 36.4 (CH_2) and 26.2 (CH_2).

N-Boc cis-3-(Aminomethyl)cyclopentan-1-ol **10**. Et_3N (23 x 10^{-3} cm^3, 0.17 mmol) was added to a solution of the amine **14** (17 mg, 0.15 mmol) and di-*t*-butyl dicarbonate (35.4 mg, 0.16 mmol) in MeOH (0.21 cm^3) and the reaction mixture heated at 50 °C for 1 h. The reaction mixture was then allowed to cool to room temperature and stirred for a further 2 h before concentrating under reduced pressure. The residue was pre-absorbed onto silica and purified by column chromatography (50% ether/pentane) to give a colourless oil, the carbamate **10** (21 mg, 66%); R_f 0.28 (50% EtOAc/light petroleum); ν_{max}/cm^{-1} (KBr) 3350s, 2958s, 1704s, 1670s, 1538s, 1458m, 1392m, 1366m, 1254m, 1171m and 1009w; δ_H(200 MHz) 4.85 (1 H, brs, NH), 4.40-4.23 (1 H, m, CHO), 3.30-3.01 (2 H, m, CH_2N), 2.24-1.85 (3 H, m, H of 2-CH_2, CH and OH), 1.85-1.61 (3 H, m, H of 4-CH_2 and H of 5-CH_2), 1.56-1.45 (1 H, m, H of 4-CH_2), 1.44 (9 H, s, 3 x Me) and 1.37-1.20 (2 H, m, H of 2-CH_2); δ_C(50 MHz) 156.3 (C=O, quat.), 79.1 (C, quat.), 73.4 (CHO), 45.6 (CH_2), 39.2 (2-CH_2), 38.1 (CHN), 35.3 (5-CH_2), 28.4 (3 x Me) and 27.4 (4-CH_2); *m/z* (EI) 158 (12), 142 (16), 114 (31), 100 (28), 97 (25), 85 (26), 84 (35) and 83 (54); *m/z* (CI) 216 [$(M + H)^+$, 46), 177 (84), 160 (56), 116 (59), 114 (100), 100 (36), 98 (76) and 96 (47) [Found: $(M + H)^+$, 216.1601. $C_{11}H_{22}NO_3$ requires *M*, 216.1600].

Ethyl 1-(Chloroformyl)cyclopent-3-ene-1-carboxylate **16**. Oxalyl chloride (1.20 cm^3, 13.8 mmol) was added to a cooled (ice-water bath) solution of the carboxylic acid **15**[14,26] (2.00 g, 10.9 mmol) in CH_2Cl_2 (20 cm^3). DMF (1 drop) was added, giving some effervesence, and the reaction mixture was stirred for 15 min before warming to room temperature and stirring for a further 2 h. The reaction mixture was then concentrated under reduced pressure to give a colourless oil, the acid chloride **16** (2.21 g, 100%); R_f 0.06 (30% ether/light petroleum); ν_{max}/cm^{-1} 3000m, 2960m, 1810s, 1755s, 1450m, 1256m, 1225m and 1080m; δ_H(200 MHz) 5.63 (2 H, s, 2 x CH=), 4.28 (2 H, q, *J* 7.1, CH_2O), 3.20-2.95 (4 H, m, 2 x CH_2) and 1.31 (3 H, t, *J* 7.1, Me).

N-Boc Ethyl 1-Aminocyclopent-3-ene-1-carboxylate **17**. A solution of the acid chloride **16** (17.9 g, 90 mmol) in acetone (28.5 cm^3) was added dropwise to a cooled (3 °C) solution of NaN_3 (8.9 g, 0.14 mol) in H_2O (28.5 cm^3), maintaining the reaction temperature below 6 °C. After 30 min the reaction mixture was extracted with toluene (4 x 36 cm^3) and the combined organic extracts were dried ($MgSO_4$) to give a solution of the azide [ν_{max}/cm^{-1} (toluene) 2138, 1747, 1714]. 3Å Molecular sieves (20 g) were added, followed by *t*-BuOH (85 cm^3, 0.89 mol) and the reaction mixture was heated to reflux. After 2 h IR analysis indicated complete conversion to the isocyanate [ν_{max}/cm^{-1}(toluene) 2269, 1733]. $SnCl_4$ (0.62 cm^3, 5.3 mmol) was added and the reaction mixture heated to reflux. After 1 h IR analysis indicated complete reaction of the isocyanate [ν_{max}/cm^{-1}(diffuse reflectance) 1732]. The reaction mixture was then stirred at room temperature for 17 h, then filtered, the sieves were washed with EtOAc (200 cm^3) and the combined filtrates concentrated under reduced pressure to give an orange solid which was pre-absorbed onto silica and purified by column chromatography (30% ether/cyclohexane) to give a white solid, the carbamate **17** (16.1 g, 71%); R_f 0.71 (50% EtOAc/light petroleum); Found: C, 61.07; H, 8.30; N. 5.49. $C_{13}H_{21}NO_4$ requires C, 61.16; H, 8.29; N, 5.49%; mp 76-78 °C (EtOAc/light petroleum); ν_{max}/cm^{-1} 3367m, 2979m, 2933m, 1713s, 1513m, 1445m, 1367m, 1221s and 1170s; δ_H(200 MHz) 5.61 (2 H, s, 2 x CH=), 5.18 (1 H, s, NH), 4.17 (2 H, q, *J* 7.1, CH_2O), 3.02 (2 H, d, *J* 15.9, 2 x H of CH_2), 2.57 (2 H, d, *J* 16.1, 2 x H of CH_2), 1.40 (9 H, s, 3 x Me) and 1.23 (3 H, t, *J* 7.1, Me); δ_C(50 MHz) 174.2 (C=O, quat.), 154.9 (C=O, quat.), 127.6 (2 x CH=), 79.7 (C, quat.), 64.1 (C, quat.), 61.4 (CH_2O), 44.8 (2 x CH_2), 28.2 (3 x Me) and 14.1 (Me); *m/z* (EI) 82 (15%) 59 (30), 57 (100), 43 (31), 41 (44); *m/z* (CI) 256 [$(M + H)^+$, 25%], 217 (55), 200 (32), 199 (31), 156 (100), 84 (27), 52 (50) and 44 (50) [Found: $(M + H)^+$, 256.1549. $C_{13}H_{22}NO_4$ requires *M*, 256.1549].

N-Boc Ethyl cis- and trans-1-Amino-3-hydroxycyclopent-3-ene-1-carboxylates **18** and **19**. BH_3.THF (1 mol dm^{-3} in THF; 2.0 cm^3, 2.0 mmol) was added to a cooled (ice-water bath) solution of the alkene **17** (0.50 g, 2.0 mmol) in THF (3.0 cm^3). The reaction mixture was allowed to warm to room temperature and stirred overnight. Water was added (2.0 cm^3), followed by aq. H_2O_2 (30% w/w; 0.67 cm^3, 6.0 mmol) and aq. NaOH (1 mol dm^{-3}; 1.2 cm^3, 1.2 mmol). The mixture was extracted with ether (3 x 10 cm^3), then saturated with K_2CO_3 and extracted with THF (10 cm^3). The combined organic extracts were washed with brine (10 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. HPLC analysis (0.1% aq.

H_3PO_4 for 2 min, then to 100% of 95% aq. MeCN + 0.1% H_3PO_4 over 40 min) gave **18** : **19** = 94.1 : 5.9 (t_R major, 20.7 min; t_R minor, 20.2 min). ^1H NMR (400 MHz) analysis of the NH signals at δ 5.81 and 5.07 gave **18** : **19** = 96 : 4. The residue was purified by column chromatography (25-75% ether/light petroleum). First to elute was the cis alcohol **18** (0.32 g, 58%) R_f 0.26 (50% EtOAc/light petroleum); ν_{max}/cm^{-1} 3370s, 2978s, 1694s, 1504m, 1455w, 1392w, 1367m, 1253m, 1169s and 1035m; δ_H(200 MHz) 5.81 (1 H, brs, NH), 4.63 (1 H, brs, OH), 4.34 (1 H, brs, C*H*-OH), 4.16 (2 H, q, *J* 7.1, CH_2O), 2.45 (1 H, dd, *J* 6.0 and 14.9, H of 2-CH_2), 2.38-2.20 (1 H, m, H of CH_2), 2.17-1.79 (4 H, m, 2 x H of CH_2 and CH_2), 1.39 (9 H, s, 3 x Me) and 1.23 (3 H, t, *J* 7.1, Me); δ_C(125 MHz) 174.1 (C=O, quat.), 154.0 (C=O, quat.), 79.4 (C, quat.), 72.4 (CHOH), 63.8 (C, quat.), 61.0 (CH_2O), 45.9 (CH_2), 35.0 (CH_2), 34.1 (CH_2), 27.5 (3 x Me) and 13.2 (Me); *m/z* (thermospray filament +ve ion) 274 [$(M + H)^+$, 98%], 174 (100) [Found: $(M + H)^+$, 274.1645. $C_{13}H_{24}NO_5$ requires *M*, 274.1654]. Second to elute was a mixture of products. This mixture was further purified by dissolving in ether (20 cm^3) and washing with dilute aq. sodium bisulphite solution (2 x 20 cm^3), water (20 cm^3) and brine (20 cm^3). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure to give a residue which was purified by column chromatography (75% ether/cyclohexane) to give a colourless oil, the trans alcohol **19** (28 mg, 5%); R_f 0.18 (50% EtOAc/cyclohexane); ν_{max}/cm^{-1} (diffuse reflectance) 3347m, 2979m, 2944m, 1714s, 1689s, 1504m, 1455w, 1392w, 1367m, 1283m, 1253m, 1170s, 1092m and 1037m; δ_H(250 MHz) 5.07 (1 H, brs, NH), 4.44 (1 H, brs, C*H*-OH), 4.27-4.15 (2 H, m, CH_2O), 2.90 (1 H, d, *J* 7.5, OH), 2.54-2.29 (2 H, m, CH_2), 2.24-2.03 (2 H, m, CH_2), 1.94-1.67 (2 H, m, CH_2), 1.44 (9 H, s, 3 x Me) and 1.28 (3 H, t, *J* 7.0, Me); δ_C(63 MHz) 175.9 (C=O, quat.), 155.2 (C=O, quat.), 80.1 (C, quat.), 73.1 (CHO), 65.0 (C, quat.), 61.9 (CH_2O), 47.2 (CH_2), 34.9 (CH_2), 28.3 (3 x Me), 26.9 (CH_2) and 14.1 (Me); *m/z* (thermospray filament +ve ion) 274 [$(M + H)^+$, 50%], 218 (100) and 173 (4) [Found: $(M + H)^+$, 274.1648. $C_{13}H_{24}NO_5$ requires *M*, 274.1654].

N-Boc Ethyl (1R,3r,5S)- and (1R,3s,5S)-3-Amino-6-oxabicyclo[3.1.0]hexane-3-carboxylates **20** and **21**. MCPBA (50% w/w pure; 11.13 g, 32.2 mmol) was added to a cooled (ice-water bath) solution of the alkene **17** (6.86 g, 26.9 mmol) in CH_2Cl_2 (70 cm^3) and the reaction mixture was then allowed to warm to room temperature and stirred overnight. The reaction mixture was then diluted with CH_2Cl_2 (100 cm^3), washed with saturated aq. $NaHCO_3$ (6 x 200 cm^3) and brine (200 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. ^1H NMR analysis of the epoxide signals at δ 3.60 and 3.54 of the residue gave cis (epoxide and carbamate groups) epoxide **20** : trans epoxide **21** = 85 : 15. The residue was then pre-absorbed onto silica and purified by column chromatography (18% EtOAc/light petroleum). First to elute was a mixture of the cis epoxide **20** and 3-chlorobenzoic acid which was dissolved in ether (200 cm^3) and stirred vigorously with saturated aq. $NaHCO_3$ (200 cm^3). After 17 h the organic layer was washed with saturated aq. $NaHCO_3$ (5 x 200 cm^3), brine (200 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to give a wax, the cis epoxide **20** (4.04 g, 55 %); R_f 0.53 (50% EtOAc/light petroleum); Found: C, 57.51; H, 7.73; N, 5.00. $C_{13}H_{21}NO_5$ requires C, 57.55; H, 7.80; N, 5.16%; mp 60-63 °C; ν_{max}/cm^{-1} (KBr) 3323m, 2968m, 2935m, 1733s, 1712s, 1525s, 1459w, 1430w, 1368m, 1322m, 1288s, 1250m, 1230s, 1175s, 1080m and 859s; δ_H(200 MHz) 5.05 (1 H, brs, NH), 4.15 (2 H, q, *J* 7.2,

CH_2O), 3.59 (2 H, s, 2 x CHO), 2.43 (2 H, d, *J* 15.3, 2 x H of CH_2), 2.24 (2 H, d, *J* 15.3, 2 x H of CH_2), 1.38 (9 H, s, 3 x Me) and 1.21 (3 H, t, *J* 7.1, Me); δ_C(50 MHz) 172.2 (C=O, quat.), 154.5 (C=O, quat.), 79.8 (C, quat.), 62.1 (C, quat.), 61.6 (CH_2O), 56.9 (2 x CHO), 38.6 (2 x CH_2), 28.2 (3 x Me) and 14.1 (Me); *m/z* (EI) 142 (55), 98 (65), 57 (100) and 41 (37); *m/z* (CI) 272 [$(M + H)^+$,15%], 216 (35), 198 (22), 172 (25), 156 (100), 82 (22), 74 (23) and 46 (27) [Found: $(M + H)^+$, 272.1498. $C_{13}H_{22}O_5N$ requires *M*, 272.3214]; Second to elute was a mixture of the cis and trans epoxides which was recrystallised from ether/pentane (1 : 2, 15 cm^3) to give colourless crystals, the trans epoxide **21** (300 mg, 4%); R_f 0.41 (50% EtOAc/light petroleum); Found: C, 58.54; H, 8.01; N, 5.18. $C_{13}H_{21}NO_5$ requires C, 57.55; H, 7.80; N, 5.16%; mp 113-115 °C (ether/pentane); ν_{max}/cm^{-1}(KBr) 3263m, 3068m, 2981m, 2963m, 2934m, 1745s, 1703s, 1427w, 1394m, 1368m, 1316w, 1234w, 1201m, 1162m, 1101m, 1081m and 845m; δ_H(200 MHz) 5.12 (1 H, brs, NH), 4.20 (2 H, q, *J* 7.1, CH_2O), 3.57 (2 H, s, 2 x CHO), 2.89 (2 H, d, *J* 14.8, 2 x H of CH_2), 2.07 (2 H, d, *J* 14.8, 2 x H of CH_2), 1.42 (9 H, s, 3 x Me) and 1.27 (3 H, t, *J* 7.1, Me); δ_C(50 MHz) 173.0 (C=O, quat.), 154.5 (C=O, quat.), 80.0 (C, quat.), 63.8 (C, quat.), 61.7 (CH_2O), 56.7 (2 x CHO), 38.7 (2 x CH_2), 28.2 (3 x Me) and 14.1 (Me); *m/z* (EI) 198 (6%), 142 (23), 98 (42), 57 (100), 49 (37) and 41 (57). *m/z* (CI) 272 [$(M + H)^+$, 7%], 233 (60), 216 (100), 198 (70), 172 (40), 74 (75), 52 (87) and 44 (65) [Found: $(M + H)^+$. 272.1498, $C_{13}H_{22}NO_5$ requires *M*, 272.3214].

X–Ray structure determination of epoxide 21

Crystal data. $C_{13}H_{21}NO_5$, $M = 271.31$. Monoclinic, $a = 6.1810(2)$, $b = 17.3990(11)$, $c = 13.4480(9)$ Å, $\beta = 91.299(4)°$, $V = 1445.9(1)$ $Å^3$ (by least-squares refinement of images on 90 frames, $\lambda = 0.71069$ Å), spacegroup $P2_1/c$ (C^5_{2h}, No. 14), $Z = 4$, $D_{calc} = 1.246$ g cm^{-3}. Colourless prism, crystallised from a solution of cyclohexane-toluene-diisopropyl ether (1:1:1) at room temperature. Crystal dimensions: 1.5 × 0.25 × 0.2 mm, μ (Mo-Kα) = 9.00 cm^{-1}. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). Any request to the CCDC for the material should quote the full literature citation.

Data collection and processing. Enraf-Nonius DIP2000 diffractometer, using the Enraf-Nonius DIP2000 Xpress control software, MoKα radiation; 3085 unique reflections measured ($0 \leq \theta \leq 27°$), 2172 reflections observed, $I > 6\sigma(I)$, [merging $R = 0.041$]. The diffraction data was processed using the DIP2000 DENZO suite of software.[33] Multiscan absorption correction was performed within the interframe scaling using the SCALEPACK software.[33]

Structure analysis and refinement. Direct methods (SIR 92).[34] Full-matrix least squares refinement with the hydrogen atoms placed geometrically and robust resistant 3 term (2.29, 0.504, 1.62) Chebyschev polynomial weighting scheme.[35] Final *R*, R_W and S values are 0.0493, 0.0530 and 0.9659. Unobserved reflections were not included. Programs used and the source of scattering factor data are given in ref. 36. 173 Parameters were refined, the maximum electron density in the difference map (ρ_{max}) was 0.34 $eÅ^{-3}$ and ρ_{min} −0.26 $eÅ^{-3}$. Standard deviations in bond lengths and angles range from 0.002 to 0.004 Å and 0.1 to 0.4°.

N-Boc Ethyl (1S,4R)-1-Amino-4-hydroxycyclopent-2-ene-1-carboxylate **22**. Bu^{s}Li (0.7 mol dm^{-3} in cyclohexane; 0.68 cm^3, 0.48 mmol) and (–)-sparteine (0.21 cm^3, 0.91 mmol) were added successively to pre-cooled ether (1.5 cm^3) at –78 °C. After 1.5 h the cis epoxide **20** (100 mg, 0.37 mmol) in ether (0.4 cm^3) was added dropwise over 10 min, maintaining the temperature at –78 °C, and the reaction mixture then warmed to room temperature. After 17 h the reaction mixture was cooled to 0 °C, HCl (2 mol dm^{-3}; 2 cm^3) was added and the organic layer separated. The aqueous layer was then re-extracted with ether (2 x 2 cm^3) and the combined organic layers washed with brine (5 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography (20% EtOAc/pentane). First to elute was unreacted epoxide **20** (24 mg, 24%). Second to elute was a colourless oil, the allylic alcohol **22** (14 mg, 14%, 18% based on recovered epoxide **20**); R_f 0.26 (50% EtOAc/light petroleum); $[\alpha]_D^{20}$ +15.9 (*c* 0.56 in $CHCl_3$); ^{1}H NMR analysis with (+)-TFE shows splitting of the alkene signal at δ 6.20 to give 33% ee; ν_{max}/cm^{-1} (KBr) 3371m, 2979w, 2929w, 1733s, 1703s, 1532w, 1454w, 1369m, 1258m, 1176m, 1055s and 808w; δ_H(500 MHz) 6.25-6.15 (1 H, m, CH=), 6.00 (1 H, brs, OH), 5.59 (1 H, d, *J* 5.3, =CH), 4.94-4.69 (1 H, m, CHO), 4.50 (1 H, brs, NH), 4.35-4.09 (2 H, m, CH_2O), 2.94 (1 H, dd, *J* 7.6 and 14.8, H of CH_2), 2.06 (1 H, d, *J* 14.7, H of CH_2), 1.43 (9 H, s, 3 x Me) and 1.26 (3 H, t, *J* 7.1, Me); δ_C(125 MHz) 173.2 (C=O, quat.), 154.3 (CO, quat.), 138.8 (CH=), 131.5 (CH=), 80.3 (C, quat.), 76.0 (CHO), 69.1 (C, quat.), 62.3 (CH_2), 45.0 (CH_2), 28.3 (3 x Me) and 14.0 (Me); *m/z* (EI), 154 (17%), 142 (76), 98 (65), 57 (100) and 41 (63); *m/z* (CI) 272 [(M + H)$^+$, 5%], 154 (37), 139 (24), 82 (19), 74 (32), 58 (36), 52 (100), 44 (75) and 36 (41) [Found: (M + H)$^+$, 272.1498. $C_{13}H_{22}NO_5$ requires 272.1498].

N-Boc Ethyl (1S,4R)-1-Amino-4-hydroxycyclopentane-1-carboxylate **18**. Palladium on charcoal (10%, 2.9 mg) was added to a solution of the allylic alcohol **22** (10.5 mg, 39 mmol) in EtOH (2 cm^3). The reaction mixture was flushed with hydrogen 3 times before being left under a hydrogen balloon for 8 h. The mixture was then evacuated and air introduced, the solid material was filtered off and washed with ether (10 cm^3). The filtrate was concentrated under reduced pressure, pre-absorbed onto silica and purified by column chromatography (50% ether/light petroleum) to give a colourless oil, the cis alcohol **18** (7.5 mg, 71%); R_f 0.22 (50% EtOAc/light petroleum); $[\alpha]_D^{23}$ –2.4 (*c* 0.75 in $CHCl_3$).

N-Boc Ethyl (1R,3S)-1-Amino-4-hydroxycyclopentane-1-carboxylate **18.** $BF_3.Et_2O$ (1.22 cm^3, 9.6 mmol) was added dropwise to a solution of [(+)-IpcBH$_2$]$_2$TMEDA (Fluka, 2.00 g, 4.8 mmol) in THF (6.8 cm^3). After stirring for 1 h the white precipitate which had formed was filtered off with suction into a pre-cooled (–40 °C) flask under a stream of argon. The precipitate was washed with cold (–40 °C) THF (3 x 1.2 cm^3) and the washings combined with the original filtrate. The alkene **17** (0.51 g, 2.0 mmol) in THF (3 cm^3) was added dropwise to this cold solution and the reaction mixture stirred at –40 °C for 72 h. Water was added (5 cm^3), followed by aq. H_2O_2 (30% v/v; 1.63 cm^3, 14.4 mmol) and aq. NaOH (1 mol dm^{-3}; 4.8 cm^3, 4.8 mmol). The oxidised solution was extracted with ether (3 x 30 cm^3), then saturated with K_2CO_3 and extracted with THF (50 cm^3). The organic extracts were combined, washed with brine (80 cm^3), dried ($MgSO_4$) and concentrated under reduced

pressure. The trans alcohol **19** could not be detected in this residue by ^{1}H NMR (400 MHz) analysis in the NH region. The residue was pre-absorbed onto silica and purified by column chromatography (gradient elution, 25-50% ether/light petroleum) to give a colourless oil, the cis alcohol **18** (0.40 g, 77%); $[\alpha]_D^{20}$ −3.6 (*c* 1 in $CHCl_3$); ^{1}H NMR analysis with (−)-TFE shows splitting of the 2-C*H*H signal at δ 2.40 to give 47% ee.

N-Boc Ethyl (1S,3R)-1-Amino-4-hydroxycyclopentane-1-carboxylate **18**

Following the procedure for the preparation of *(1R,3S)*-**18**, using $BF_3.Et_2O$ (0.61 cm^3, 4.8 mmol), $[(-)\text{-IpcBH}_2]_2$TMEDA[28] (1.00 g, 2.4 mmol) and alkene **17** (0.26 g, 1.0 mmol) gave the cis alcohol **18** (201 mg, 74%); $[\alpha]_D^{20}$ +2.9 (*c* 1 in $CHCl_3$); ^{1}H NMR analysis with (−)-TFE shows splitting of the 2-C*H*H signal at δ 2.42 to give 48% ee.

N-Boc Ethyl (1S,3S)-1-Amino-3-cyanocyclopent-3-ene-1-carboxylate **23**. Et_3N (0.11 cm^3, 0.8 mmol), followed by freshly distilled MsCl (42 x 10^{-3} cm^3, 0.5 mmol) was added to a cooled (ice-water bath) solution of (1*S*,3*R*)-alcohol **18** ($[\alpha]_D^{23}$ +3.5, 46% ee, 67 mg, 0.2 mmol) in CH_2Cl_2 (1.2 cm^3). The reaction mixture was stirred at room temperature overnight and then diluted with CH_2Cl_2 (15 cm^3), washed with ice-water (15 cm^3), cold (ice-water bath) aq. HCl (2 mol dm^{-3}; 15 cm^3), saturated aq. $NaHCO_3$ (15 cm^3) and brine (15 cm^3) and then dried ($MgSO_4$) and concentrated under reduced pressure to give a colourless oil, the mesylate (75 mg, 87%); R_f 0.39 (50% EtOAc/light petroleum); ν_{max}/cm^{-1} 3379s, 2963s, 1738s, 1700s, 1514m, 1504m, 1455m, 1367s, 1259s, 1168s, 1077m, 1019m and 893m; δ_H(200 MHz) 5.31-5.19 (1 H, m, NH), 5.14 (1 H, brs, CH), 4.17 (2 H, q, *J* 7.1 CH_2O), 3.00 (3 H, s, $MeSO_2$), 2.80 (1 H, dd, *J* 6.6 and 15.3, H of CH_2), 2.39-2.02 (5 H, m, H of CH_2 and 2 x CH_2), 1.43 (9 H, s, 3 x Me) and 1.25 (3 H, t, *J* 7.4, Me). NaCN (31 mg, 0.63 mmol) was added to a solution of the mesylate in DMF (3.6 cm^3) and the reaction mixture heated at 80 °C overnight. After cooling to room temperature the reaction mixture was poured into water (20 cm^3) and extracted with ether (20 cm^3). The aqueous layer was re-extracted with ether (20 cm^3) and the combined organic extracts washed with water (2 x 30 cm^3), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was pre-absorbed onto silica and purified by column chromatography (gradient elution, 10-50% ether/light petroleum) to give a white solid, the (1*S*,3*S*) nitrile **23** (36 mg, 60%); R_f 0.63 (50% EtOAc/light petroleum); $[\alpha]_D^{23}$ +2.2 (*c* 1.0 in $CHCl_3$); mp 104-105 °C; ν_{max}/cm^{-1}(KBr) 3294s, 2976m, 2358m, 1731s, 1674s, 1530s, 1446m, 1367m, 1300s, 1240m, 1169m and 1092m; δ_H(200 MHz) 5.13 (1 H, brs, NH), 4.35-4.16 (2 H, m, CH_2O), 3.30-3.06 (1 H, m, CH-CN), 2.57 (2 H, d, *J* 9.0, 2 x H of CH_2), 2.39-1.94 (4 H, m, CH_2 and 2 x H of CH_2), 1.44 (9 H, s, 3 x Me) and 1.31 (3 H, t, *J* 7.1, Me); δ_C(125 MHz) 173.1 (C=O, quat.), 154.8 (C=O, quat.), 121.8 (CN, quat.), 80.4 (C, quat.), 65.2 (C, quat.), 62.1 (CH_2O), 40.8 (CH_2), 37.0 (CH_2), 30.2 (CH_2), 28.3 (3 x Me), 27.1 (CH) and 14.1 (Me); *m/z* (thermospray filament +ive ion) 300 [(M + NH_4)$^+$, 25%], 283 [(M + H)$^+$, 67%] and 244 (100); *m/z* (APCI), 227 (15%), 183 (100), 122 (6) and 109 (74) [Found: (M + H)$^+$, 283.1680. $C_{14}H_{23}N_2O_4$ requires *M*, 283.1658].

(1S,3S)-1-Aminocyclopentane-1,3-dicarboxylic acid **24**. (1*S*,3*S*)-nitrile **23** (20 mg, 71 (mol) was suspended in aq. HCl (6 mol dm^{-3}; 6 cm^3) and the mixture heated at reflux. After 4

h the reaction mixture was allowed to cool to room temperature, concentrated under reduced pressure and the residue was dissolved in water and purified by ion-exchange chromatography (Dowex 50WX8-100, eluted with aq. NH_3 (2 mol dm^{-3}), followed by evaporation under reduced pressure and freeze-drying to give a white solid, the amino acid **24** (8.1 mg, 66%); $[\alpha]_D^{23}$ +2.0 (*c* 0.41 in H_2O) {lit.,[11a] $[\alpha]_D^{20}$ +8.4 (*c* 1.0 in H_2O)}; $[\alpha]_D^{23}$ +5.7 (*c* 0.35 in 6 mol dm^{-3} HCl) {lit.,[11a] $[\alpha]_D^{20}$ +24.5 (*c* 1.0 in 6 mol dm^{-3} HCl)}; ν_{max}/cm^{-1}(KBr) 3438s, 1616m and 1399m; δ_H(500 MHz, D_2O) 2.95-2.86 (1 H, m, CH), 2.37-2.23 (2 H, m, CH_2), 2.15-2.02 (2 H, m, CH_2), 1.97-1.87 (1 H, m, H of CH_2) and 1.85-1.75 (1 H, m, H of CH_2); δ_C(125 MHz, D_2O) 181.5 (C=O, quat.), 177.6 (C=O, quat.), 67.1 (C, quat.), 45.6 (CH), 40.0 (CH_2), 36.3 (CH_2) and 29.8 (CH_2).

N-Boc Ethyl (1S,3S)-trans-1-Amino-3-hydroxycyclopent-3-ene-1-carboxylate **19**. Acetic acid (0.11 cm^3, 1.9 mmol) was added to a solution of (1*S*,3*R*)-alcohol **18** ($[\alpha]_D^{23}$ +2.9, 48% ee; 0.18 g, 0.6 mmol) and PPh_3 (0.50 g, 1.9 mmol) in THF (5 cm^3). A solution of DEAD (0.30 cm^3, 1.9 mmol) in THF (1.4 cm^3) was added dropwise to this mixture and the reaction mixture stirred at room temperature for 3 h. Concentration under reduced pressure gave a residue which was redissolved in CH_2Cl_2 (20 cm^3), washed with saturated aq. $NaHCO_3$ (20 cm^3) and brine (20 cm^3), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was pre-absorbed onto silica and purified by column chromatography (gradient elution, 25-40% ether/light petroleum) to give a colourless oil, the acetate (0.16 g, 77%); R_f 0.62 (50% EtOAc/light petroleum); $[\alpha]_D^{22}$ −3.0 (*c* 1 in $CHCl_3$); ν_{max}/cm^{-1} 3363m, 2980s, 1738s, 1699s, 1520s, 1505s, 1456m, 1367s, 1246s, 1169m, 1097w and 1038m; δ_H(200 MHz) 5.29-5.14 (1 H, m, CHO), 5.00 (1 H, brs, NH), 4.17 (2 H, q, *J* 7.2, CH_2O), 2.46-2.05 (4 H, m, 2 x CH_2), 2.01 (3 H, s, Me), 1.96-1.74 (2 H, m, CH_2), 1.40 (9 H, s, 3 x Me) and 1.25 (3 H, t, *J* 7.2, Me); δ_C(125 MHz) 173.6 (C=O quat.), 170.8 (C=O, quat.), 155.0 (C=O, quat.), 80.0 (C, quat.), 74.9 (CHO), 64.8 (C, quat.), 61.5 (CH_2O), 43.3 (CH_2), 35.2 (CH_2), 31.2 (CH_2), 28.2 (3 x Me), 21.2 (Me) and 14.1 (Me); *m/z* (EI) 182 (16%), 126 (51), 108 (18), 82 (100), 57 (98) and 43 (75); *m/z* (CI) 333 [$(M + NH_4)^+$, 13%], 316 [$(M + H)^+$, 23], 277 (100), 260 (24), 259 (50), 218 (54), 216 (46) and 182 (26) [Found: $(M + H)^+$. 316.1760. $C_{15}H_{26}NO_6$ requires *M*, 316.1760]. K_2CO_3 (0.35 g, 2.5 mmol) was added to a solution of the above acetate in EtOH (2.3 cm^3) and the reaction mixture stirred at room temperature overnight. Concentration under reduced pressure gave a residue which was partitioned between ether (15 cm^3) and aq. HCl (2 mol dm^{-3}, 15 cm^3). The aqueous layer was re-extracted with ether (2 x 15 cm^3), the combined organic extracts were washed with brine (30 cm^3), dried ($MgSO_4$) and concentrated under reduced pressure to give a colourless oil, the trans alcohol **19** (0.11 g, 76 %, 58% from **18**); $[\alpha]_D^{22}$ −1.5 (*c* 1 in $CHCl_3$); ^1H NMR analysis with (−)-TFE shows splitting of the *Me*CH_2O signal at δ 1.31 to give 44% ee.

N-Boc Ethyl (1S,3R)-1-Amino-3-cyanocyclopent-3-ene-1-carboxylate **26** *and Ethyl (1S,5R)-2-aza-4-oxa-3-oxobicyclo[3.2.1]octane-1-carboxylate* **25**. Following the procedure for the preparation of the (1*S*,3*S*) nitrile **23**, using Et_3N (0.11 cm^3, 0.79 mmol), MsCl (31 x 10^{-3} cm^3, 0.4 mmol) and (1*S*,3*S*)-alcohol **19** (0.10 g, 0.37 mmol) in CH_2Cl_2 (1.8 cm^3) gave a mesylate (0.101 g, 78%); R_f 0.41 (50% EtOAc/light petroleum); ν_{max}/cm^{-1} 3377s, 2980s,

1732s, 1514m, 1367m, 1170m, 1096w and 1010w; δ_H(200 MHz) 5.36-5.19 (1 H, m, CHO), 5.13 (1 H, m, NH), 4.28-4.11 (2 H, m, CH_2O), 3.02 (3 H, s, $MeSO_2$), 2.74-2.46 (2 H, m, CH_2), 2.44-1.85 (4 H, m, 2 x CH_2), 1.42 (9 H, s, 3 x Me) and 1.27 (3 H, t, *J* 7.2, Me). Treatment of the mesylate as before with NaCN (42 mg, 0.9 mmol) in DMF (11 cm^3) at 80 °C overnight gave a residue which was pre-absorbed onto silica and purified by column chromatography (gradient elution, 10-100% ether/light petroleum, EtOAc). First to elute was a colourless oil, the nitrile **26** (29 mg, 35%); R_f 0.56 (50% EtOAc/light petroleum); $[\alpha]_D^{20}$ −13.4 (*c* 1.4 in $CHCl_3$); ν_{max}/cm^{-1} 3370s, 2980s, 2241m, 2142w, 1736s, 1514m, 1367m, 1256m and 1176m; δ_H(200 MHz) 5.08 (1 H, brs, NH), 4.28-4.11 (2 H, m, CH_2O), 3.17-2.98 (1 H, m, CH-CN), 2.88-2.72 (1 H, m, H of CH_2), 2.42-1.97 (5 H, m, H of CH_2 and 2 x CH_2), 1.44 (9 H, s, 3 x Me) and 1.27 (3 H, t, *J* 7.2, Me); δ_C(125 MHz) 173.3 (C=O, quat.), 154.9 (C=O, quat.), 122.1 (CN, quat.), 80.4 (C, quat.), 65.1 (C, quat.), 61.9 (CH_2O), 41.0 (CH_2), 37.0 (CH_2), 29.6 (CH_2), 28.2 (3 x Me), 27.3 (CH) and 14.1 (Me); *m/z* (EI) 109 (54), 86 (17), 84 (30), 59 (25), 57 (100), 49 (48) and 41 (53); *m/z* (CI) 300 [$(M + NH_4)^+$, 13%], 283 [$(M + H)^+$, 17], 244 (100), 226 (33), 190 (23), 185 (68), 183 (45), 109 (24) and 46 (47) [Found: $(M + H)^+$, 283.1658. $C_{14}H_{23}N_2O_4$ requires *M*, 283.1658]. Second to elute was an amorphous white solid, the bicyclic carbamate **25** (33 mg, 58%); R_f 0.08 (50% EtOAc/light petroleum); $[\alpha]_D^{24}$ −4.0 (*c* 0.55 in $CHCl_3$); ν_{max}/cm^{-1}(KBr) 3432m, 2962w, 1710s, 1400m, 1372w, 1291m, 1249m, 1219m, 1184w and 1080m; δ_H(200 MHz) 6.05 (1 H, brs, NH), 4.94-4.86 (1 H, m, CHO), 4.29 (2 H, q, *J* 7.0, CH_2O), 2.36-2.14 (2 H, m, 3 x CH_2) and 1.32 (3 H, t, *J* 7.2, Me); δ_C(100 MHz) 170.4 (C=O, quat.), 152.3 (C=O, quat.), 79.0 (CH), 63.3 (C, quat.), 62.4 (CH_2O), 39.8 (CH_2), 38.2 (CH_2), 31.8 (CH_2) and 14.0 (Me); *m/z* (EI) 199 (M^+, 5%), 82 (48), 55 (63), 54 (37), 49 (49), 43 (72), 41 (100) and 39 (67) [Found: M^+, 199.0845. $C_9H_{13}NO_4$ requires *M*, 199.0845].

(1S,3R)-1-Aminocyclopentane-1,3-dicarboxylic acid **27**. Following the procedure for the preparation of **24**, using (1*S*,3*R*) nitrile **26** (10 mg, 35 (mol) and HCl (6 mol dm^{-3}, 6 cm^3) at reflux for 5 h gave a white solid, the amino acid **27** (5.1 mg, 84%); $[\alpha]_D^{23}$ −3.9 (*c* 0.26 in H_2O) {lit.,[11a] $[\alpha]_D^{20}$ −6.9 (*c* 1.0 in H_2O)}; $[\alpha]_D^{20}$ −6.0 (*c* 0.24 in 6 mol dm^{-3} HCl) {lit.,[11a] $[\alpha]_D^{20}$ -10.1 (*c* 1.0 in 6 mol dm^{-3} HCl)}; ν_{max}/cm^{-1} (KBr) 3437s, 3125s, 1586s, 1397s and 1225m; δ_H(200 MHz, D_2O) 3.04-2.97 (1 H, m, CH), 2.33 (1 H, dd, *J* 8.6 and 14.5, H of CH_2), 2.24-2.12 (2 H, m, 2 x H of CH_2), 2.02 (1 H, dd, *J* 5.5 and 14.5, H of CH_2) and 1.97-1.87 (2 H, m, 2 x H of CH_2); δ_C(125 MHz, D_2O) 184.5 (C=O, quat.), 177.9 (C=O, quat.), 67.4 (C, quat.), 47.0 (CH), 40.2 (CH_2), 36.3 (CH_2) and 30.6 (CH_2).

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