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Synthetic Approaches to (1*S*,3*R*)-3-Aminomethyl-2,2,3-trimethylcyclopentylmethanol and (1*S*,3*R*)-3-Amino-2,2,3-trimethylcyclopentylmethanol from (+)-Camphoric Acid

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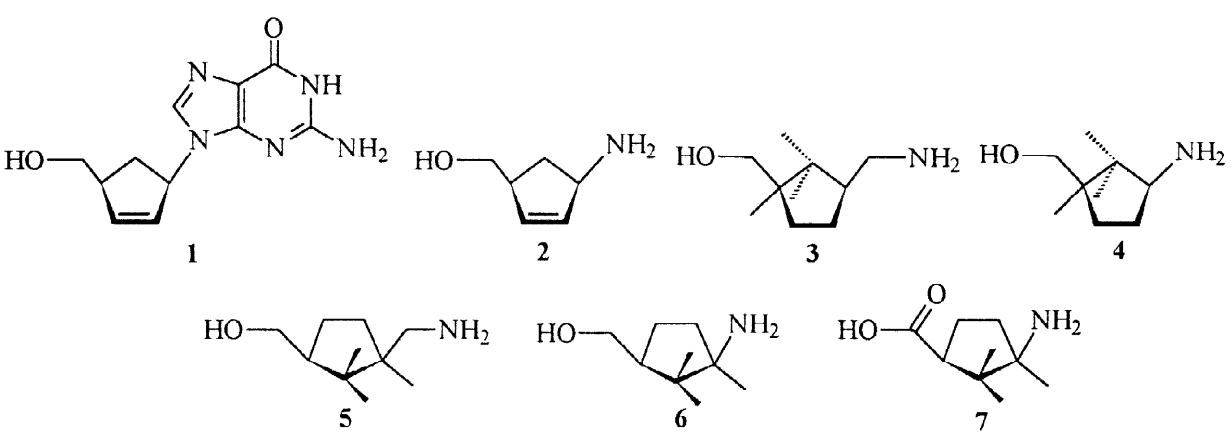
Abstract: The title aminomethyl (**5**) and amino (**6**) alcohols, which are of interest as intermediates in the synthesis of carbocyclic analogues of nucleosides, were prepared from (+)-camphoric acid *via* methyl (1*S*,3*R*)-3-carbamoyl-2,3,3-trimethylcyclopentane carboxylate (**8**). Direct reduction of **8** gave **5** in 26% yield. Amino alcohol **6** was prepared in 11-53% overall yields by several approaches, each involving oxidative degradation of **8** followed by a reduction step. © 1998 Elsevier Science Ltd. All rights reserved.

The interesting biological activity shown by carbocyclic analogues of nucleosides (CANs) such as carbovir (**1**) has spurred the search for new analogues as potential antineoplastic and antiviral agents.[1] Like many CANs, carbovir is prepared by constructing the heterocyclic base about an amino alcohol precursor, in this specific case the aminocyclopentenylmethanol **2**.[2] The general applicability of this approach has led to increased interest in cyclopentylamines as key synthetic intermediates for preparation of CANs.[3]



We are currently investigating the relationship between the biological activity of CANs and various structural and configurational features of their amino alcohol moiety.[4] To this end, we have previously prepared the amino alcohols **3**[4] and **4**[5] and also some carbocyclic analogues of guanosine.[6] In the present work, we describe the synthesis of **5** and **6**, which are isomeric with **3** and **4**, respectively, and will serve as precursors for

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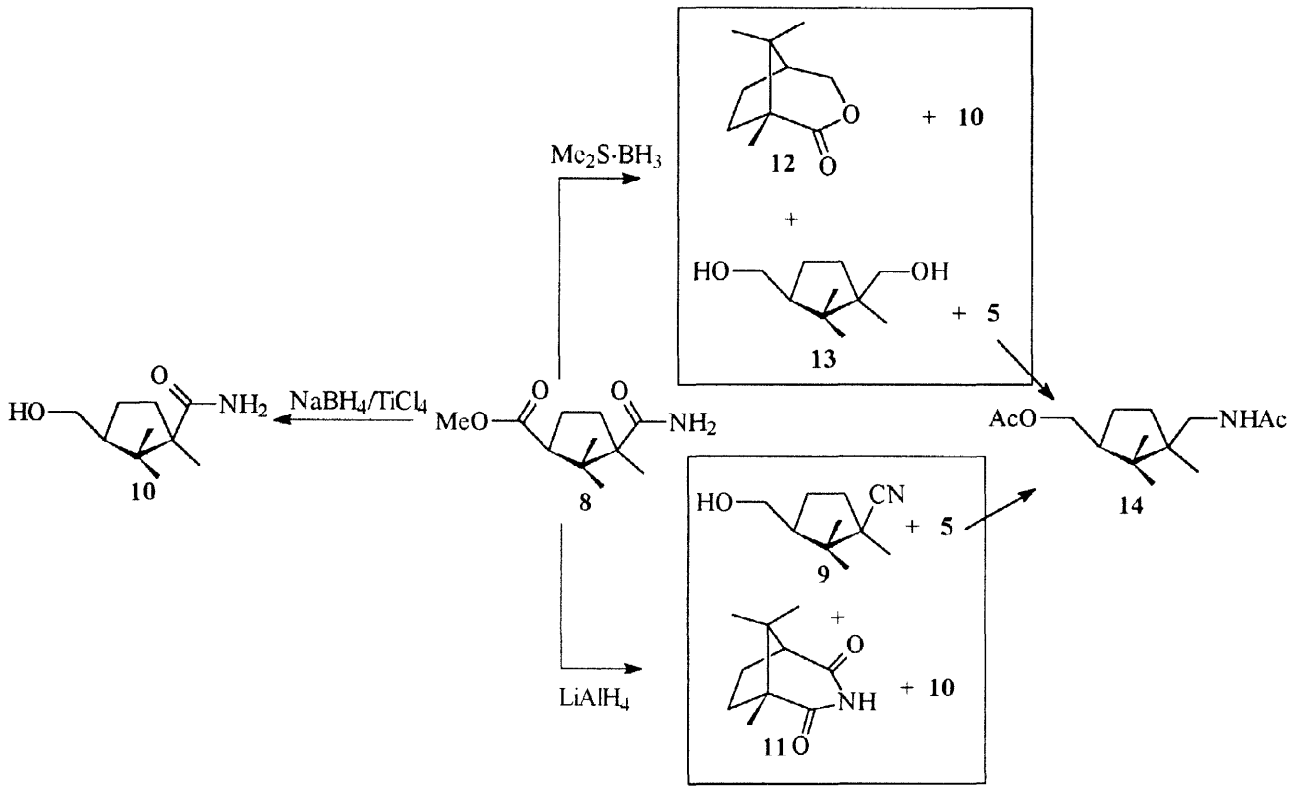
the synthesis of novel CANs. We also optimized the synthesis of amino acid 7, which is both an intermediate in the synthesis of 6 and a potential GABA agonist.[7]

RESULTS AND DISCUSSION

The common precursor, methyl (1*S*,1*R*)-3-carbamoyl-2,2,3-trimethylcyclopentane carboxylate (**8**), was easily prepared from (+)-camphoric acid by the method of Boeckman *et al.*[8]



Scheme 1

Conversion of **8** into amino alcohol **5** (Scheme 1) required simultaneous reduction of the amide and ester carbonyls, for which the traditional reagents $NaBH_4/TiCl_4$,[9] $(CH_3)_2S{\cdot}BH_3$,[10] and $LiAlH_4$[11] were assayed under diverse conditions in an attempt to optimize the yield of **5**. Table 1 lists the results, which varied greatly as regards both the nature and yield of the compound(s) isolated. In most cases compound **5** was not isolated or was isolated with one or more of compounds **9-13.**

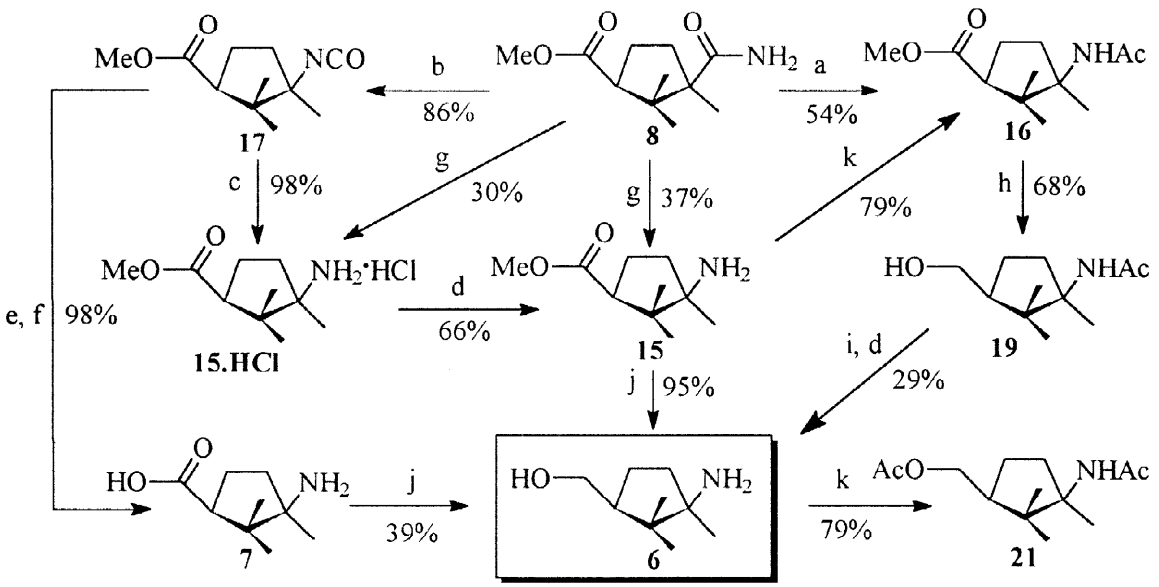
Poor or zero yields of **5** were obtained using $NaBH_4/TiCl_4$ or $(CH_3)_2S{\cdot}BH_3$ as reducing agent: reaction of **8** with $TiCl_4$-activated $NaBH_4$ gave hydroxy amide **10** as the only isolated product; and reaction of **8** with $(CH_3)_2S{\cdot}BH_3$ gave **10** and a slightly lower yield of **5** (entry 2). Increasing the reaction time gave **5** as the major product, but in slightly lower yield (entry 3). Attempts at increasing the yield of **5** by allowing the dimethyl sulfide liberated to distil from the reaction mixture during the reaction[10c] afforded an even lower yield of **5**, together with minor amounts of (+)-α-campholide (**12**)[12] and diol **13**[13] (entry 4). Formation of **12** is attributable to nucleophilic attack of the amide group by the alkoxide initially formed in the ester reduction step, followed by BH_3-promoted elimination of ammonia. Subsequent reduction of **12** would give **13**.

Table 1. Reduction of Carbamoyl Ester **8**

Entry	Reagent	Reductant/**8**	Solvent	T	t	Result*
1	$NaBH_4/TiCl_4$	2.6/6.3	$(CH_3OCH_2)_2$	18	20	**10** (21%)
2	$(CH_3)_2S{\cdot}BH_3$	2.9	THF	66	5	**5** (21%) + **10** (26%)
3	$(CH_3)_2S{\cdot}BH_3$	2.9	THF	66	22	**5** (17%) + **10** (7%)
4	$(CH_3)_2S{\cdot}BH_3$	2.2	THF	66	1	**5** (11%) + **12** (8%) + **13**(9%)
5	$LiAlH_4$	2.3	THF (11)	66	20	**9** (22%) + **10** (18%)
6	$LiAlH_4$	7.5	THF (54)	66	40	**9** (38%) + **5** (12%)
7	$LiAlH_4$	7.5	THF (75)	66	96	**11** (40%)
8	$LiAlH_4$	7.5	THF (100)	66	17	**5** (26%)

*Yields are for isolated products after purification by standard techniques.

With $LiAlH_4$ as reducing agent, the ester group was usually reduced, in most cases with concurrent dehydration and/or reduction of the amide group. The outcome of the reaction was greatly influenced by dilution of the reagents. At low dilution, hydroxy nitrile **9** was the major product, the result of dehydration of the amide by $LiAlH_4$, as has been observed previously for sterically hindered amides.[14] To our surprise, longer reaction times at slightly higher dilution gave (+)-camphorimide **11** as the major product.[15] The best yield of amino alcohol **5** was obtained using a high reductant/reactant ratio and high dilution conditions (entry 8 in Table 1).



a) $Pb(AcO)_4$, AcOH, reflux; b) $Pb(AcO)_4$, toluene, reflux; c) 2N HCl, dioxane, r.t.; d) Amberlite IRA-400(OH); e) 2N HCl, dioxane, reflux; f) Dowex 50 x 8-200, H_2O, NH_4OH; g) PIFA, CH_3CN, H_2O, 25°C; h) $LiBH_4$, THF, reflux; i) 2N HCl, EtOH reflux; j) $LiAlH_4$, THF, reflux; k) Ac_2O, py, 25°C.

Scheme 2

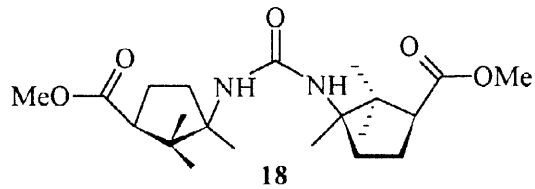
Several routes to amino alcohol **6** were explored (Scheme 2). In all cases, the first step was oxidative degradation of the carboxamide group of **8**. In the first instance, lead tetraacetate in refluxing acetic acid was used as oxidant,[16] which gave mixtures of diverse products (Table 2).

Table 2. Oxidative Degradation of Carbamoyl Ester **8** with $Pb(OAc)_4$/Acetic Acid

Entry (n°)	Time	Result*
1	22 min	**15** (7%) + **16** (2%) + **17** (52 %)
2	35 min	**15** (20%) + **18** (21%)
3	2 h	**15** (37%) + **16** (34%)
4	14 h	**15** (9%) + **16** (54%)
5	24 h	**16** (54%)

*Yields are for isolated products after purification by standard techniques.

The main oxidation products isolated were the amino ester **15** and/or its acetyl derivative **16**, in some cases together with isocyanate **17** or urea **18**. The pattern of products seemed to depend heavily on the reaction time. Very short reaction times gave mainly **17**, which is consistent with the mechanism proposed for this oxidation.[17] Hydrolysis of **17** would give amino ester **15**, which at intermediate reaction times could add to **17** to give significant amounts of **18** (entry 2 in Table 2). Longer reaction times gave mainly **16**, which would have formed by acylation of **15** and/or acetolysis of **18**.



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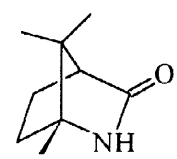

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Oxidative degradation of **8** with lead tetraacetate under anhydrous conditions, using toluene as solvent, gave isocyanate **17** as the only product. Partial hydrolysis of **17** with 2N HCl gave excellent yields of **15·HCl** when carried out at room temperature, or of the fully hydrolysed product **7·HCl** when carried out for 2 h at reflux. Isolation of the free bases **15** and **7** was easily achieved by ion-exchange chromatography using basic or acidic ion-exchange resin, respectively.

Oxidative degradation of **8** with [*I,I*-bis(trifluoroacetoxy)iodo]benzene (PIFA)[18] led directly to **15·HCl**, though in considerably lower yields than obtained by oxidation with lead tetraacetate followed by hydrolysis. In some assays, **7·HCl** was also detected in the reaction mixture.

The next step in the conversion of **8** to **5** was reduction of the remaining carbonyl group. Use of $LiBH_4$ to selectively reduce the ester group[19] of **16** led to fair yields of the hydroxy acetamide **19**. However, **19** proved highly resistant to a variety of hydrolysis conditions (Table 3), which was attributed to steric hindrance at the carbon bearing the acetamido group. The best yield of **6** was obtained by refluxing a mixture of **19** in ethanolic HCl for 240 h (entry 4 in Table 3).

Table 3. Hydrolysis of Hydroxy Acetamide **19**

Entry	Reagent	Time (h)	Temperature (°C)	Result*
1	$Ba(OH)_2$	192	100	**19** (88%)
2	2N HCl	7	100	**19** (50%)**
3	2N HCl	18	100	**6** (6%)**
4	2N HCl + EtOH	240	90	**6** (29%)**

*Yields are for isolated products after purification by standard techniques. **The remaining product was an intractable tar.

Reduction of amino acid **7** with $LiAlH_4$ in refluxing THF for 5.5 h, followed by the customary work-up (treatment with dilute NaOH and then chromatographic separation), gave pure amino alcohol **6** in 39% yield. A small amount of lactam **20** (15%) was also isolated. The yield of **6** was not significantly improved by adding triethanolamine in the hydrolysis step.[20]

Attempts to reduce **15·HCl** by refluxing it with lithium triethylborohydride in THF for 24 h also gave lactam **20**, this time as major product (55%). By contrast, reduction of free **15** with $LiAlH_4$ gave amino alcohol **6** in almost quantitative yield.

EXPERIMENTAL

Melting points were measured on a Reichert Kofler thermopan and are uncorrected; Na-D line polarimetry was carried out at 25°C in a Perkin-Elmer 241 polarimeter; infrared spectra were recorded in a Perkin-Elmer FTIR 1640 spectrometer; ^1H NMR and ^{13}C NMR spectra were recorded in a Bruker AMX 300 spectrometer; and mass spectra were recorded in a Kratos MS-59 spectrometer. Silica gel (230 mesh) was purchased from Merck. All other chemicals used were of reagent grade and were obtained from Aldrich Chemical Co. Methyl (1*S*,3*R*)-3-carbamoyl-2,2,3-trimethylcyclopentanecarboxylate (**8**) was prepared by the method reported by Boeckman *et al.*[8]

(1*R*,3*S*)-3-Hydroxymethyl-1,2,2-trimethylcyclopentanecarbonitrile (9) and (1*R*,3*S*)-3-hydroxymethyl-1,2,2-trimethylcyclopentanecarboxamide (10). To a cooled (0°C) suspension of $LiAlH_4$ (0.41 g, 10.75 mmol) in dry THF (25 mL) was added, dropwise, a solution of **8** (1 g, 4.69 mmol) in THF (25 mL). The suspension was refluxed for 20 h, and then cooled and treated with wet Et_2O and water. The organic solvents were eliminated using a rotary evaporator, the solids were filtered out, and the aqueous filtrate was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and then evaporated, which left 0.70 g of a doughy residue. Chromatography of this residue on silica gel (20 g), using 8:2 CH_2Cl_2/MeOH as eluant, gave **9** (170 mg, 22%) and **10** (160 mg, 18%), in both cases as white solids. Compound **9** was recrystallized from hexane to obtain an analytical sample. M.p. 88-90°C. IR (KBr): 3512, 2973, 2236, 1658, 1461, 1374, 1036, 798 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.79-3.73 (m, 1H, 3-CHH), 3.62-3.56 (m, 1H, 3-CHH), 2.30-2.17 (m, 1H), 2.08-1.95 (m, 2H), 1.82-1.73 (m, 1H), 1.57-1.47 (m, 2H, 1H after D_2O exch.), 1.32 (s, 3H, CH_3), 1.09 (s, 6H, 2 CH_3). ^{13}C NMR ($CDCl_3$) δ: 124.49 (CN), 64.90 (3-CH_2), 48.38 (C3), 46.65 (C1), 45.94 (C2), 35.94 (C5), 26.02 (C4), 23.71 (CH_3), 22.05 (CH_3), 21.33 (CH_3). EIMS *m/z* (%): 167 (6, M^+), 152 (11), 138 (13), 137 (19), 136 (18), 123 (17), 122 (100), 110 (12), 109 (58), 108 (11), 107 (13), 97 (16), 96 (21), 95 (47), 94

(14), 84 (10), 83 (17), 82 (18), 81 (16), 79 (13), 76 (11), 70 (24), 69 (26), 68 (57), 67 (39), 55 (23), 53 (14). Calcd. for $C_{10}H_{17}NO$ (167.25): C, 71.81; H, 10.24; N, 8.37. Found: C, 72.01; H, 10.11; N, 8.23.

Compound **10** was recrystallized from EtOAc to obtain an analytical sample. M.p. 136-137°C. $[\alpha]_D^{25}$ +84.2 (*c* 1, MeOH). IR (KBr): 3348, 3185, 2965, 1676, 1603, 1458, 1406, 1095, 1058, 1023, 756 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 5.53 (bs, 2H, D_2O exch., NH_2), 3.75 (dd, 1H, *J* = 10.13, 5.28 Hz, 3-CHH), 3.55 (dd, 1H, *J* = 10.13, 8.22 Hz, 3-CHH), 2.40-2.30 (m, 1H), 2.13-1.93 (m, 2H), 1.72 (bs, 1H, D_2O exch., OH), 1.56-1.41 (m, 2H), 1.22 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 0.83 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6) δ: 177.57 (CO), 63.00 (3-CH_2), 55.62 (C3), 48.83 (C1), 44.18 (C2), 32.40 (C5), 25.09 (C4), 23.30 (CH_3), 21.62 (CH_3), 19.58 (CH_3). EIMS *m/z* (%): 185 (2, M^+), 167 (3), 154 (8), 124 (13), 123 (28), 109 (10), 95 (9), 86 (100), 81 (15), 73 (28), 69 (25), 67 (25), 58 (15), 57 (10), 55 (25), 53 (10). Calcd. for $C_{10}H_{19}NO_2$ (185.26): C, 64.83; H, 10.34; N, 7.56. Found: C, 64.99; H, 10.52; N, 7.42.

(1*S*,3*R*)-3-Aminomethyl-2,2,3-trimethylcyclopentylmethanol (5). *Method A.* To a dispersion of $LiAlH_4$ (1.33 g, 35 mmol) in dry THF (135 mL) was added a solution of **8** (1 g, 4.69 mmol) in THF (335 mL). The mixture was refluxed for 17 h, whereupon the reaction was quenched and worked up as described above for the preparation of **9** and **10**, this time extracting the aqueous filtrate with three 150 mL portions of EtOAc. After drying of the combined extracts over anhydrous Na_2SO_4 and evaporation of the solvent, there remained 0.61 g of a colourless oil, which was chromatographed on silica gel (20 g), using 8:2 CH_2Cl_2/MeOH as eluant. Compound **5** (210 mg, 26%) was isolated as a white solid, which was recrystallized from EtOAc to obtain an analytical sample. M.p. 88-90°C. $[\alpha]_D^{25}$ +40.3 (*c* 0.43, MeOH). IR (KBr): 3334, 2968, 1576, 1493, 1451, 1377, 1323, 1055, 1022, 992 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.73 (dd, 1H, *J* = 10.24, 5.40 Hz, 1-CHH), 3.52 (dd, 1H, *J* = 10.24, 8.40 Hz, 1-CHH), 2.61 (s, 2H, 3-CH_2), 2.17-2.06 (m, 1H), 1.99-1.87 (m, 1H), 1.66-1.56 (m, 1H), 1.48-1.26 (m, 5H, 2H after D_2O exch.), 0.98 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.75 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 65.49 (1-CH_2), 50.88 (C1), 49.23 (3-CH_2), 49.03 (C2), 44.54 (C3), 35.06 (C4), 25.77 (C5), 24.14 (CH_3), 20.58 (CH_3), 18.84 (CH_3). EIMS *m/z* (%): 171 (1, M^+), 153 (5), 140 (21), 125 (51), 123 (100), 122 (22), 109 (20), 107 (29), 95 (32), 83 (17), 81 (61), 79 (18), 70 (30), 69 (29), 67 (40), 58 (45), 57 (40), 56 (22), 55 (48), 53 (18). Calcd. for $C_{10}H_{21}NO$ (171.28): C, 70.12; H, 12.36; N, 8.18. Found: C, 70.37; H, 12.29; N, 7.97.

Method B. A solution of amido ester **8** (1.75 g, 8.21 mmol) in THF (3.5 mL) was stirred at reflux under argon. From a syringe, 10.2M $(CH_3)_2S{\cdot}BH_3$ (2.33 mL, equiv. to 23.8 mmol) was added dropwise, causing the mixture to bubble vigorously. After 5 h at reflux, the mixture was cooled in ice and treated with excess methanol (1.45 mL) and then HCl-saturated Et_2O (7.11 mL) and stirred for 15 min at 0°C followed by 30 min at room temperature. The solvent was eliminated *in vacuo*, and the gelatinous white residue (2.47 g) was dissolved in MeOH (35 mL) and passed through a column of Amberlite IRA-400(OH) (50 mL), which was eluted with methanol. The eluate (50 mL) was concentrated under reduced pressure, and the resulting oil (1.26 g) was chromatographed on silica gel (30 g), using 9:1 CH_2Cl_2/MeOH followed by MeOH as eluants. First to elute was the hydroxy amide **10** (390 mg, 26%), followed by compound **5** (300 mg, 21%). The physical and spectroscopic data for these compounds were as listed above.

(1*S*,3*R*)-3-(Acetylaminomethyl)-2,2,3-trimethylcyclopentylmethyl acetate (14). A mixture of **5** (300 mg, 1,75 mmol) in Ac_2O (2 mL) and pyridine (2 mL) was stirred at room temperature for 24 h. The mixture was

concentrated to dryness and the solid obtained was dissolved in CH_2Cl_2 (20 mL) and washed with saturated $NaHCO_3$ and H_2O. The organic layer was separated, dried (Na_2SO_4) and concentrated to an oily residue (0.33 g) which was chromatographed on silica gel (7.5 g) 1:2 hexane/EtOAc as eluant. Ester **14** (290 mg, 65%) was isolated as a colourless oil. An analytical sample was obtained by bulb-bulb distillation in a Kugelrohr apparatus (oven temp. 117-120 °C/0.01 Torr). $[\alpha]_D^{25}$ +25.3 (*c* 0.55, MeOH). IR (film): 3318, 2967, 1740, 1653, 1559, 1458, 1374, 1240, 1150, 1033 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 5.47 (bs, 1H, D_2O exch., NH), 4.07 (dd, 1H, *J* = 10.84, 6.34 Hz, 1-CHH), 3.98 (dd, 1H, *J* = 10.84, 7.97 Hz, 1-CHH), 3.25 (dd, 1H, *J* = 13.40, 6.56 Hz, 3-CHH), 3.18 (dd, 1H, *J* = 13.40, 5.74 Hz, 3-CHH), 2.25-2.14 (m, 1H), 2.02 (s, 3H, CH_3CO), 1.97 (s, 3H, CH_3CO), 1.94-1.81 (m, 1H), 1.72-1.61 (m, 1H), 1.42-1.26 (m, 2H), 0.95 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.80 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 171.61 (CO), 170.50 (CO), 66.69 (1-CH_2), 48.12 (C3), 46.61 (C1), 46.08 (3-CH_2), 44.75 (C2), 34.96 (C4), 25.43 (C5), 23.87 (CH_3), 23.60 (CH_3), 21.40 (CH_3CO), 21.20 (CH_3CO), 18.97 (CH_3). EIMS *m/z* (%): 255 (6, M^+), 212 (5), 196 (17), 182 (14), 152 (5), 136 (38), 124 (12), 123 (100), 122 (14), 121 (43), 107 (16), 98 (12), 95 (23), 93 (18), 81 (38), 73 (39), 72 (25), 70 (28), 69 (12), 67 (20), 55 (15). Calcd. for $C_{14}H_{25}NO_3$ (255.35): C, 65.85; H, 9.87; N, 5.49. Found: C, 65.37; H, 10.02 ; N, 5.61.

Oxidative degradation of 8. Preparation of methyl (1*S*,3*R*)-3-amino-2,2,3-trimethylcyclopentane carboxylate (15), methyl (1*S*,3*R*)-3-acetylamino-2,2,3-trimethylcyclopentane carboxylate (16), methyl (1*S*,3*R*)-isocyanato-2,3,3-trimethylcyclopentanecarboxylate (17), and (1*R*,1'*R*,3*S*,3'*S*)-*N*,*N*'-bis(3-methoxycarbonyl-1,2,2-trimethylcyclopentyl)urea (18). *Method A*. A suspension of **8** (1 g, 4.69 mmol) and $Pb(OAc)_4$ (3.12 g, 7.04 mmol) in AcOH (16 mL) was heated at reflux for between 22 min and 24 h. The solvent was distilled from the reaction mixture under reduced pressure, and the dark brown residue was dissolved in cold 1:1 CH_2Cl_2/H_2O (50 mL) and neutralized with saturated $NaHCO_3$ solution. The white solid formed was filtered out, washed with CH_2Cl_2 (15 mL) and discarded, and the aqueous layer of the filtrate and washings was separated and extracted with CH_2Cl_2 (2 × 25 mL) and EtOAc (2 × 25 mL). This extract and the organic layer above were combined, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The oily residue obtained was chromatographed on silica gel (25 g), using 7:3 CH_2Cl_2/MeOH as eluant. For the 2 h reaction, first to elute from the chromatography column was **16** (360 mg, 34%), which was isolated as an oil that crystallized spontaneously. Next eluted **15** (320 mg, 37%), which was isolated as a colourless oil.

Compound **15.** An analytical sample was obtained by bulb-bulb distillation in a Kugelrohr apparatus (oven temp. 60-65°C/0.01 Torr). $[\alpha]_D^{25}$ +52.86° (*c* 1.05, MeOH). IR (film): 3373, 2968, 2877, 1728, 1458, 1436, 1198, 1176 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.69 (s, 3H, OCH_3), 2.72 (dd, 1H, *J* = 9.45, 8.07 Hz, 1-H), 2.19-2.09 (m, 1H), 1.81-1.68 (m, 3H), 1.45 (bs, 2H, D_2O exch., NH_2), 1.06 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 176.30 (CO), 62.57 (C3), 53.30 (C1), 51.86 (OCH_3), 47.12 (C2), 39.26 (C4), 24.99 (CH_3), 24.38 (CH_3), 22.42 (C5), 19.77 (CH_3). EIMS *m z* (%): 185 (1, M^+), 154 (6), 126 (5), 111 (6), 110 (9), 109 (12), 98 (12), 97 (7), 95 (9), 85 (6), 84 (12), 83 (10), 71 (31), 70 (100), 69 (22), 67 (9), 59 (5), 58 (71), 57 (21), 56 (7), 55 (15), 53 (6). Calcd. for $C_{10}H_{19}NO_2$ (185.26): C, 64.83; H, 10.34; N, 7.56. Found: C, 64.65; H, 10.52; N, 7.67.

Compound **16**. An analytical sample of **16** was obtained by recrystallization from hexane. M.p. 62-64°C. $[\alpha]_D^{25}$ +73.9 (*c* 1.01, MeOH). IR (KBr): 3340, 2973, 1733, 1721, 1653, 1541, 1508, 1438, 1374, 1308, 1173, 1086, 777 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 6.06 (bs, 1H, D_2O exch., NH), 3.69 (s, 3H, OCH_3), 2.71 (dd, 1H, *J* = 9.36, 7.50 Hz, 1-H), 2.29-2.23 (m, 1H), 2.09-1.87 (m, 3H), 1.95 (s, 3H, CH_3CO), 1.41 (s, 3H, CH_3), 1.09 (s, 3H, CH_3),

0.91 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 177.12 (OCO), 170.36 (NCO), 66.18 (C3), 53.40 (C1), 52.14 (OCH_3), 48.31 (C2), 36.31 (C4), 26.41 ($\underline{C}H_3CO$), 25.02 (CH_3), 24.59 (C5), 19.67 (CH_3), 19.64 (CH_3). EIMS *m/z* (%): 227 (40, M^+), 184 (30), 168 (17), 167 (79), 154 (35), 153 (14), 126 (21), 125 (11), 124 (13), 113 (28), 112 (81), 110 (26), 109 (22), 108 (17), 99 (20), 98 (36), 93 (13), 84 (15), 83 (12), 71 (55), 70 (100), 69 (19), 67 (17), 60 (12), 58 (20), 57 (32), 55 (20). Calcd. for $C_{12}H_{21}NO_3$ (227.30): C, 63.41; H, 9.31; N, 6.16. Found: C, 63.28; H, 9.43; N, 5.94.

For the 35 min reaction, elution of urea **18** (192 mg, 21%) was followed by elution of compound **15** (173 mg, 20%). An analytical sample of **18** was obtained by recrystallization from MeOH. M.p. 142-144°C. $[\alpha]_D^{25}$ +53.99 (*c* 1.49, MeOH). IR (KBr): 3586, 3398, 2973, 1732, 1654, 1551, 1438, 1376, 1353, 1178, 1090 cm^{-1}. ^1H-NMR ($CDCl_3$) δ: 4.71 (bs, 2H, D_2O exch., 2 × NH), 3.69 (s, 6H, 2 × OCH_3), 2.70 (dd, 2H, J = 9.53, 7.44 Hz, 3-H+3'-H), 2.21-2.00 (m, 4H), 1.96-1.82 (m, 4H), 1.40 (s, 6H, 2 × CH_3), 1.11 (s, 6H, 2 × CH_3), 0.89 (s, 6H, 2 × CH_3). ^{13}C-NMR ($CDCl_3$) δ: 177.05 (2 × CO_2), 158.42 (NCON), 65.33 (C1+C1'), 53.36 (C3+C3'), 52.08 (2 × OCH_3), 48.78 (C2+C2'), 37.02 (C5+C5'), 25.85 (2 × CH_3), 24.03 (C4+C4'), 21.14 (2 × CH_3), 19.92 (2 × CH_3). EIMS *m/z* (%): 396 (16, M^+), 281 (4), 227 (2), 212 (3), 185 (34), 184 (13), 169 (26), 154 (27), 137 (34), 110 (17), 109 (54), 95 (12), 84 (16), 83 (15), 71 (24), 70 (100), 69 (17), 67 (17), 59 (11), 58 (16), 57 (16), 55 (16). Calcd. for $C_{21}H_{36}N_2O_6$ (396.52): C, 63.61; H, 9.15; N, 7.06. Found: C, 63.45; H, 9.44; N, 6.81.

For the 22 min reaction, the combined CH_2Cl_2 layers were quickly dried (Na_2SO_4) and concentrated *in vacuo*, to leave an oily residue which was identified (IR, ^1H NMR) as **17** (see below, *Method B*). The combined EtOAc layers gave, after the chromatographic work-up, **16** and **15**.

Method B. A solution of **8** (10 g, 46.89 mmol) in dry toluene (250 mL) at reflux was treated with a single portion of $Pb(OAc)_4$ (20.60 g, 46.90 mmol) and the resulting suspension was refluxed for a further 30 min. The reaction mixture was cooled and added to cold 4N HCl (300 mL) and stirred briefly. The solids were filtered out and discarded, and the organic layer of the filtrate was separated, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. A yellow oil was isolated and identified as compound **17** (8.49 g, 86%). An analytical sample was obtained by bulb-bulb distillation (oven temp., 50-55°C/ 0.1 Torr). $[\alpha]_D^{25}$ +20.91 (*c* 0.99, MeOH). IR (film): 2976, 2258, 1735, 1458, 1436, 1380, 1357, 106, 1175 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.70 (s, 3H, OCH_3), 2.65 (dd, 1H, J = 9.37, 7.32 Hz, 1-H), 2.31-2.20 (m, 1H), 2.12-2.01 (m, 1H), 1.86-1.72 (m, 2H), 1.33 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 0.92 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 174.63 (OCO), 122.62 (NCO), 69.40 (C3), 52.04 (C1), 51.90 (OCH_3), 48.04 (C2), 38.47 (C4), 25.79 (CH_3), 23.82 (CH_3), 22.44 (C5), 21.21 (CH_3). EIMS *m/z* (%): 211 (23, M^+), 183 (43), 170 (16), 168 (100), 152 (17), 151 (55), 137 (29), 136 (22), 124 (61), 123 (20), 115 (70), 110 (24), 109 (57), 108 (22), 97 (92), 96 (65), 93 (26), 92 (23), 83 (67), 82 (27), 81 (20), 69 (33), 67 (32), 59 (20), 58 (31), 55 (31), 53 (21). Calcd. for $C_{11}H_{17}NO_3$ (211.26): C, 62.54; H, 8.11; N, 6.63. Found: C, 62.73; H, 8.32; N, 6.54.

Method C. Compound **8** (1.43 g, 6.70 mmol) was added in a single portion to a solution of PIFA (2.90 g, 6.74 mmol) in CH_3CN (10.5 mL) and distilled H_2O (10.5 mL) and stirred at room temperature for 5.5 h. The reaction mixture was diluted with water (125 mL) and treated with 12N HCl, and the aqueous phase was separated and washed with Et_2O (125 mL). The aqueous layer was concentrated under reduced pressure, and the yellow solid (0.95 g) obtained was recrystallized twice from an EtOH/Et_2O solvent pair, affording **15·HCl**

(451 mg, 30%). An analytical sample was obtained by further recrystallization from EtOH/Et_2O. M.p. 181-183°C. IR (KBr): 3419, 3042, 2985, 1732, 1644, 1526, 1458, 1429, 1382, 1369, 1322, 1201, 1154, 1016 cm^{-1}. ^1H NMR (DMSO-d_6) δ: 8.21 (bs, 3H, D_2O exch., NH_3^+), 3.62 (s, 3H, OCH_3), 2.81 (dd, 1H, J = 9.36, 8.02 Hz, 1-H), 2.04-1.97 (m, 2H), 1.83-1.66 (m, 2H), 1.24 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 0.81 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6) δ: 173.82 (CO), 64.37 (C3), 51.92 (C1 or OCH_3), 51.78 (OCH_3 or C1), 46.09 (C2), 34.38 (C4), 22.58 (CH_3), 22.22 (C5), 21.95 (CH_3), 20.00 (CH_3). The **15·HCl** (400 mg, 1.80 mmol) was dissolved in MeOH (15 mL) and passed through a column of Amberlite IRA-400(OH) (11 mL), eluting with MeOH. The eluate (65 mL) was concentrated under reduced pressure, affording **15** (220 mg, 66%) as an oil identical to that obtained by *Method A*.

Methyl (1*S*,3*R*)-3-acetylamino-2,2,3-trimethylcyclopentanecarboxylate (16). Compound **16** could also be prepared by reacting **15** (320 mg, 1.73 mmol) with acetic anhydride (1.59 mL, 16.83 mmol) in pyridine (1.36 mL). Reaction conditions and work-up were as described for preparation of **14**, except that chromatography used 7:3 EtOAc/hexane as eluant. Compound **16** (310 mg, 79%) was isolated as a solid identical to that obtained by *Method A*.

Methyl (1*S*,3*R*)-3-amino-2,2,3-trimethylcyclopentanecarboxylate hydrochloride (15·HCl). The hydrochloride of **15** (**15·HCl**) could also be prepared by treating **17** (1 g, 4.73 mmol) with a mixture of dioxan (25 mL) and 2N HCl (40 mL) at room temperature for 2 h. Evaporation of the solvent afforded **15·HCl** (1.03 g, 98%) as a white solid identical to that obtained by *Method C*.

(1*S*,3*R*)-3-Amino-2,2,3-trimethylcyclopentanecarboxylic acid (7). A solution of **17** (4.50 g, 21.3 mmol) in a mixture of dioxan (112 mL) and 2N HCl (180 mL) was refluxed for 2 h. Evaporation of the solvent afforded **7·HCl** (4.33 g, 98%) as a white solid. An analytical sample was obtained by recrystallization from an EtOH/Et_2O solvent pair. M.p. 251-253°C. IR (KBr): 2981, 1724, 1586, 1505, 1380, 1179, 1153. ^1H NMR (DMSO-d_6) δ: 12.41 (bs, 1H, D_2O exch., CO_2H), 8.05 (bs, 3H, D_2O exch, NH_3^+), 2.72 (dd, 1H, J = 8.90, 7.84 Hz, 1-H), 2.05-1.96 (m, 2H), 1.82-1.67 (m, 2H), 1.22 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 0.86 (s, 3H, CH_3). ^{13}C NMR (DMSO-d_6) δ: 175.48 (CO), 64.64 (C3), 52.26 (C1), 45.87 (C2), 34.53 (C4), 23.07 (CH_3), 22.21 (C5), 21.96 (CH_3), 19.70 (CH_3).

A solution of **7·HCl** (4.30 g, 20.7 mmol) in water (36 mL) was isolated on a column of Dowex 50WX8-200(H^+) (43.5 mL of resin, 74 mL of water). The column was eluted with water until the eluate had pH < 6, and then with 14M NH_4OH (750 mL). Concentration of the ammoniacal eluate under reduced pressure gave 7 (3.47 g, 98%). An analytical sample was prepared by recrystallization from an EtOH/Et_2O solvent pair. M.p. ≥ 276°C (decomp). $[\alpha]_D^{25}$ +51.69° (*c* 1.42, H_2O). IR (KBr): 3060, 2965, 2880, 2518, 2202, 1718, 1664, 1654, 1623, 1558, 1284. ^1H NMR (D_2O) δ: 2.51 (dd, 1H, J = 9.20, 4.32 Hz, 1-H), 2.07-1.72 (m, 4H), 1.12 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.86 (s, 3H, CH_3). ^{13}C NMR (D_2O) δ: 185.51 (CO), 67.23 (C3), 59.13 (C1), 46.92 (C2), 36.54 (C4), 27.36 (CH_3), 25.01 (C5), 18.97 (CH_3), 18.09 (CH_3). EIMS *m/z* (%): 171 (1, M^+), 156 (1), 138 (1), 126 (3), 110 (6), 109 (4), 98 (8), 95 (17), 84 (13), 82 (4), 71 (28), 70 (100), 69 (15), 68 (4), 67 (9), 58 (10), 57 (25), 56 (13), 55 (8), 53 (7). Calcd. for $C_9H_{17}NO_2$ (171.24): C, 63.13; H, 10.01; N, 8.18. Found: C, 63.35; H, 9.89; N, 8.23.

(1*R*,3*S*)-*N*-(3-Hydroxymethyl-1,2,2-trimethylcyclopentyl)acetamide (19). A suspension of $LiBH_4$ (0.17 g, 7.72 mmol) in dry THF (26 mL) was refluxed for 1 h. The mixture was cooled to 40°C, a solution of **16** (500

mg, 2.20 mmol) in dry THF (25 mL) was added dropwise, and the mixture was refluxed for 4 h. The reaction was quenched by addition of iced water (100 mL) and the THF was removed using a rotary evaporator. The aqueous mixture was extracted with CH_2Cl_2 (3 × 100 mL), and the extracts were combined, dried over anhydrous Na_2SO_4 and evaporated to dryness. The doughy residue (0.32 g) was chromatographed on silica gel (10 g), using 4:1 EtOAc/hexane as eluant. Hydroxy amide **19** (300 mg, 68%) was isolated as a white solid. An analytical sample was obtained by recrystallization from a hexane/EtOAc solvent pair. M.p. 102-104°C. $[\alpha]_D^{25}$ +65.7 (*c* 0.97, MeOH). IR (KBr): 3244, 2974, 1648, 1549, 1378, 1319, 1036, 1018 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 6.01 (bs, 1H, D_2O exch., NH), 3.71-3.57 (m, 2H, 3-CH_2), 2.27 (t, 1H, D_2O exch., J = 4.55 Hz, OH), 2.09-1.78 (m, 4 H), 1.90 (s, 3H, CH_3CO), 1.52-1.39 (m, 1H), 1.36 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 0.87 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 170.35 (CO), 65.50 (3-CH_2), 64.33 (C1), 49.05 (C3), 46.32 (C2), 35.84 (C5), 25.66 (CH_3), 24.88 (CH_3), 24.38 (C4), 20.38 ($\underline{C}H_3CO$), 18.69 (CH_3). EIMS *m/z* (%): 199 (7, M^+), 184 (4), 168 (1), 156 (11), 140 (71), 126 (14), 125 (17), 122 (17), 112 (54), 111 (20), 107 (27), 99 (14), 98 (23), 97 (16), 96 (16), 82 (54), 71 (40), 70 (100), 69 (19), 60 (14), 58 (23), 57 (38), 55 (14), 53 (10). Calcd. for $C_{11}H_{21}NO_2$ (199.29): C, 66.30; H, 10.62; N, 7.03. Found: C, 66.57; H, 10.55; N, 6.89.

(1*S*,3*R*)-3-Amino-2,2,3-trimethylcyclopentylmethanol (6). *Method A.* A solution of **19** (220 mg, 1.10 mmol) in a mixture of 2N HCl (4 mL) and EtOH (4 mL) was refluxed for 10 days. The solvent was evaporated and any water remaining in the residue was removed by azeotropic co-distillation with toluene (2 × 25 mL). The dark-coloured solid residue was dissolved in MeOH (10 mL) and passed through a column of Amberlite IRA-420(OH) (8 mL), eluting with MeOH. The eluate (35 mL) was concentrated under reduced pressure to afford an ochre solid (100 mg), which was chromatographed on silica gel (5 g), using 1:1 CH_2Cl_2/MeOH as eluant. Amino alcohol **6** (50 mg, 29%) was isolated as a white solid. An analytical sample was obtained by recrystallization from EtOAc. M.p. 132-134°C. $[\alpha]_D^{25}$ +13.94 (*c* 0.18, MeOH). IR (KBr): 3312, 2957, 2870, 2641, 1616, 1508, 1458, 1158, 1129, 1025, 1004, 915 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 3.66 (dd, 1H, J = 11.03, 1.40 Hz, 1-C$\underline{H}$H), 3.39 (dd, 1H, J = 11.03, 3.12 Hz, 1-CH$\underline{H}$), 1.92-1.79 (m, 4H), 1.55 (b, 3H, D_2O exch., NH_2 + OH), 1.47-1.41 (m, 1H), 1.15 (s, 3H, CH_3), 0.96 (s, 3H, CH_3), 0.90 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 62.36 (1-CH_2), 61.00 (C3), 51.61 (C1), 47.53 (C2), 39.07 (C4), 29.57 (CH_3), 25.94 (CH_3), 22.64 (C5), 18.12 (CH_3). EIMS *m/z* (%): 157 (1, M^+), 142 (1), 127 (4), 126 (2), 114 (2), 109 (2), 98 (4), 96 (4), 95 (17), 84 (8), 79 (3), 77 (2), 71 (21), 70 (100), 69 (16), 67 (5), 58 (9), 57 (18), 56 (7), 55 (4), 53 (3). Calcd. for $C_9H_{19}NO$ (157.25): C, 68.74; H, 12.18; N, 8.91. Found: C, 68.93; H, 12.34; N, 8.74.

Method B. Amino acid **7** (4.00 g, 23.36 mmol) was added in two portions to a cooled (0°C), stirred suspension of $LiAlH_4$ (2.22 g, 58.5 mmol) in dry THF (56 mL) under argon. The suspension was refluxed for 5 h, and then its was stirred vigorously, cooled to 0°C and quenched by slow, successive addition from a dropping funnel of water (95 mL), 1N NaOH (47 mL) and CH_2Cl_2 (142 mL). After a further 30 min stirring, the solids were filtered out and washed with CH_2Cl_2 (500 mL), and the two layers of the filtrate were separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 150 mL), and the extracts were combined with the organic layer and washings, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting solid residue (2.54 g) was chromatographed on silica gel (80 g), using 1:1 CH_2Cl_2/MeOH as eluant. First to elute was **20**[8] (520 mg, 15%), followed by **6** (1.45 g, 39%), which was isolated as a white solid identical to that obtained by *Method A*.

Method C. A solution of **15** (500 mg, 2.70 mmol) in dry THF (18 mL) was added to a cooled (0°C) suspension of $LiAlH_4$ (3.40 g, 90.91 mmol) in dry THF (16 mL) stirring under argon, and the suspension was refluxed for 3 h. The vigorously stirred suspension was cooled to 0°C and then quenched by slow, successive addition from a dropping funnel of wet ether and water. The solids formed were filtered out and washed with CH_2Cl_2 (100 mL), and the organic layer of the filtrate was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL), and these extracts and the organic layer and washings were combined, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Amino alcohol **6** (403 mg, 95%) was isolated as a white solid identical to that obtained by *Methods A* and *B*.

(1*S*,3*R*)-3-Acetylamino-2,2,3-trimethylcyclopentylmethyl acetate (21). Amino alcohol **6** (140 mg, 0.89 mmol) was stirred with Ac_2O (4 mL) in dry pyridine (4 mL). Reaction conditions and work-up were as described for preparation of **14.** Compound **22** (170 mg, 79%) was isolated as a yellow oil. An analytical sample was obtained by chromatography on silica gel (8 g), using 1:2 EtOAc/hexane as eluant. $[\alpha]_D^{25}$ +62.50 (*c* 0.94, MeOH). IR (film): 3325, 2969, 1742, 1655, 1541, 1369, 1244, 1034 cm^{-1}. ^1H NMR ($CDCl_3$) δ: 5.38 (bs, 1H, D_2O exch., NH), 4.07 (dd, 1H, *J* = 10.88, 6.52 Hz, 1-C<u>H</u>H), 3.99 (dd, 1H, *J* = 10.88, 7.76 Hz, 1-CH<u>H</u>), 2.16-1.81 (m, 4H), 2.02 (s, 3H, CH_3CO), 1.92 (s, 3H, CH_3CO), 1.41-1.30 (m, 1H), 1.33 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 0.82 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 171.54 (CO), 170.01 (CO), 66.67 (1-CH_2), 65.47 (C3), 46.05 (C1), 45.12 (C2), 36.43 (C4), 24.84 (CH_3), 24.74 (CH_3), 23.33 (C5), 21.76 (<u>C</u>H_3CO), 21.38 (<u>C</u>H_3CO), 18.83 (CH_3). EIMS *m/z* (%): 241 (12, M^+), 198 (4), 184 (4), 182 (7), 181 (18), 166 (5), 156 (4), 139 (12), 138 (49), 125 (18), 124 (12), 122 (32), 112 (56), 107 (35), 99 (21), 98 (18), 96 (26), 71 (40), 70 (100), 69 (18), 60 (12), 58 (17), 57 (36), 55 (10), 53 (8). Calcd. for $C_{13}H_{23}NO_3$ (241.33): C, 64.70; H, 9.61; N, 5.80. Found: C, 64.54; H, 9.75; N, 6.02.

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12. a) (1*R*)-(+)-1,8,8-Trimethyl-3-oxabicyclo[3.2.1]octan-2-one (**12**): M.p. 210-211°C (lit.[12b] m.p. 210-211°C). ^{1}H RMN ($CDCl_3$) δ: 4.47 (ddd, 1H, *J* = 10.73, 2.98, 1.77 Hz, 4*exo*-H), 4.10 (d, *J* = 10.73 Hz, 4*endo*-H), 2.19-2.03 (m, 2H), 1.92-1.68 (m, 3H), 1.17 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 0.97 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 177.28 (CO), 74.43 (C4), 54.08 (C1), 44.99 (C5), 42.63 (C8), 36.51 (C7), 27.35 (C6), 22.79 (CH_3), 20.30 (CH_3), 14.66 (CH_3). EIMS *m/z* (%): 168 (12, M^+), 155 (10), 153 (10), 137 (12), 110 (11), 109 (100), 95 (20), 83 (18), 81 (16), 69 (25), 68 (10), 67 (23), 55 (18). Calcd. for $C_{10}H_{16}O_2$ (168.23): C, 71.39; H, 9.59. Found: C, 71.28; H 9.72. b) Kayser, M. M.; Morand, P., *Can. J. Chem.* **1978**, 56, 1524-1532.

13. a) (1*R*,3*S*)-(+)-(3-Hydroxymethyl-1,2,2-trimethylcyclopentylmethanol (**13**): M.p. 133-135°C (lit.[13b] m.p. 133-134°C). ^{1}H NMR ($CDCl_3$) δ: 3,74 (dd, 1H, *J* = 10.23, 5.29 Hz, 3-CHH), 3.59 and 3.47 (AB system, 2H, *J* = 10.73 Hz, 1-CH_2), 3.52 (dd, 1H, *J* =10.23, 8.27 Hz, 3-CHH), 2.14-1.89 (m, 2H), 1.66-1.55 (m, 1H), 1.43-1.30 (m, 2H), 1.19 (bs, 2H, D_2O exch., OH), 1.03 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 0.79 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 69.62 (1-CH_2), 65.37 (3-CH_2), 50.94 (C3), 49.23 (C1), 44.40 (C2), 34.14 (C5), 25.92 (C4), 24.61 (CH_3), 20.82 (CH_3), 18.92 (CH_3). EIMS *m/z* (%): 157 (1, M^+-CH_3), 154 (3, M^+-H_2O), 139 (73), 123 (100), 121 (32), 111 (16), 109 (23), 96 (15), 95 (32), 93 (22), 85 (42), 84 (18), 83 (27), 82 (22), 81 (67), 79 (22), 71 (47), 69 (57), 68 (25), 67 (45), 58 (34), 57 (41), 55 (59), 53 (21). Calcd. for $C_{10}H_{20}O_2$ (172.27): C, 69.72; H, 11.70. Found: C, 69.65; H 11.87. b) Johnson, T. H.; Klein, K.C., *J. Org. Chem.* **1979**, 44, 461-462.

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15. a) (1*R*)-(+)-1,8,8-Trimethyl-3-azabicyclo[3.2.1]octane-2,4-dione (**11**): M.p. 249-250 °C (lit.[15b,c] m.p. 248°C); $[\alpha]_D^{25}$ +5.81 (*c* 0.98, MeOH) (lit[15b,c] $[\alpha]_D^{25}$ +1.6 in $HCCl_3$); IR (KBr): 3210, 3087, 2966, 1728, 1687, 1366, 1317, 1268, 1230, 1192, 1102 cm^{-1}. ^{1}H NMR ($CDCl_3$) δ: 7.70 (bs, 1H, D_2O exch., NH), 2.62 (d, 1H, *J* = 6.92 Hz, 5-H), 2.29-2.17 (m, 1H), 2.06-1.80 (m, 3H), 1.18 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.99 (s, 3H, CH_3). ^{13}C NMR ($CDCl_3$) δ: 178.70 (CO), 176.67 (CO), 56.49 (C5), 54.32 (C1), 45.53 (C8), 34.70 (C7), 25.72 (C6), 22.30 (CH_3), 19.81 (CH_3), 13.61 (CH_3). EIMS *m/z* (%): 181 (46, M^+), 166 (28), 138 (27), 125 (16), 124 (12), 123 (17), 112 (11), 110 (29), 109 (15), 96 (13), 95 (100), 93 (11), 85 (23), 83 (66), 82 (10), 79 (13), 77 (12), 70 (12), 69 (37), 67 (30), 55 (42), 53 (18). Calcd. for $C_{10}H_{15}NO_2$ (181.23): C, 66.27; H, 8.34; N, 7.73. Found: C, 66.33; H, 8.74; N, 7.81. b) Bredt, J.; Wornast, K., *Justus Liebig Ann. Chem.* **1903**, 328, 338-348. c) Evans, W. C., *J. Chem. Soc.* **1910**, 97, 2234-2237.

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