Diversity-Oriented Synthesis of Aminocyclohexitols from Garner's Aldehyde

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Received: 25.09.2012; Accepted after revision: 10.12.2012

Abstract: A short and efficient synthetic route to three stereoisomeric aminocyclohexane tetrols of the quercitol type has been developed from L-serine, which featured stereoselective allylation, stereocontrolled dihydroxylation, and ring-closing metathesis as key steps.

Key words: allylation, carbocycles, dihydroxylation, metathesis, stereoselective synthesis

Carbasugars have received considerable attention as mimics of natural sugars, a property associated with drug development related to a myriad of diseases including diabetes, viral and bacterial infections, immunological disorders, and cancer.[1] Amino-substituted carbasugars, also known as aminocyclohexitols, are distinctly important since the protonated amino group mimics the oxonium ion structure in the transition state of a glycosidase reaction.[2] Several naturally occurring aminocyclohexitol derivatives such as valienamine (**1**),[3] validamine (**2**),[4] valiolamine (**3**),[5] and synthetic modifications thereof, for example, voglibose (**4**)[6] (Figure 1) have provided impetus for further search of new aminocarbasugar derivatives. Thus, several elegant synthetic methodologies directed towards the development of new entities as well as classical targets have been reported.[7] Three general concepts, which have emerged from these studies for the design of glycomimetics include: (i) N-alkylation of aminocarbasugars;[8] (ii) variation of ring size to fine tune the hydrophobic-hydrophylic balance;[9] and (iii) use of stereoisomeric compounds[10] to address the fundamental difference prevalent in sugars. Although great advances have been made, the need for the development of a common synthetic route that would encompass the three broad objectives stated above, for the ultimate preparation of distinguished aminocarbasugars from a common starting material does exist.

Our synthetic strategy (Scheme 1) towards the synthesis of new aminocarbasugar derivatives involves elaboration of the α-chiral aldehyde of the type **I** (obtainable from Garner's aldehyde[11]), having two points of stereochemical diversity, with suitable organometallic reagent having a terminal alkenyl residue to induce two further degrees of diversities, namely, chain length variation and variation in the stereogenicity of the newly created stereocenter. The diene **II**, thus obtainable, on ring-closing metathesis (RCM) should deliver the carbocyclic template **III** on which functional group manipulation of the alkene part would create further diversity in the substitution pattern as well as their steric disposition leading to the aminocarbasugar derivative **IV** with six different points of diversity all together. We have recently reported[12] a stereodivergent synthesis of three stereoisomeric aminocyclopentitol derivatives from the aldehyde **I**. We were interested to develop our methodology further as a general platform to access new compounds. Herein, we describe a synthesis of three aminocyclohexitol derivatives as a partial realization of our stated objectives.

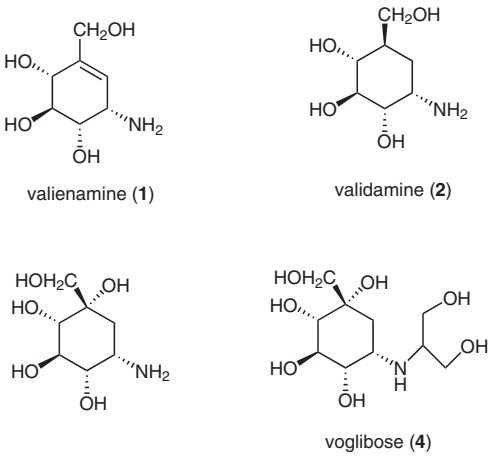
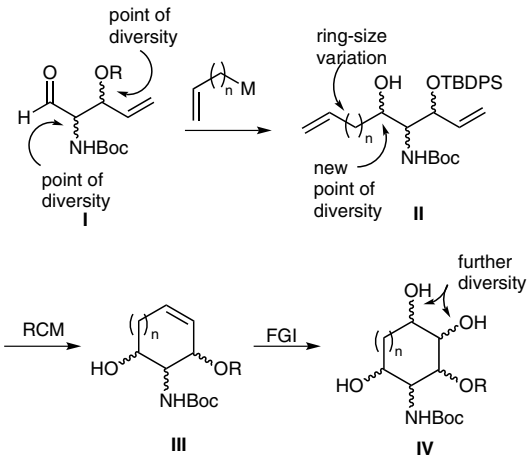


Figure 1 Selected examples of aminocyclohexitol derivatives

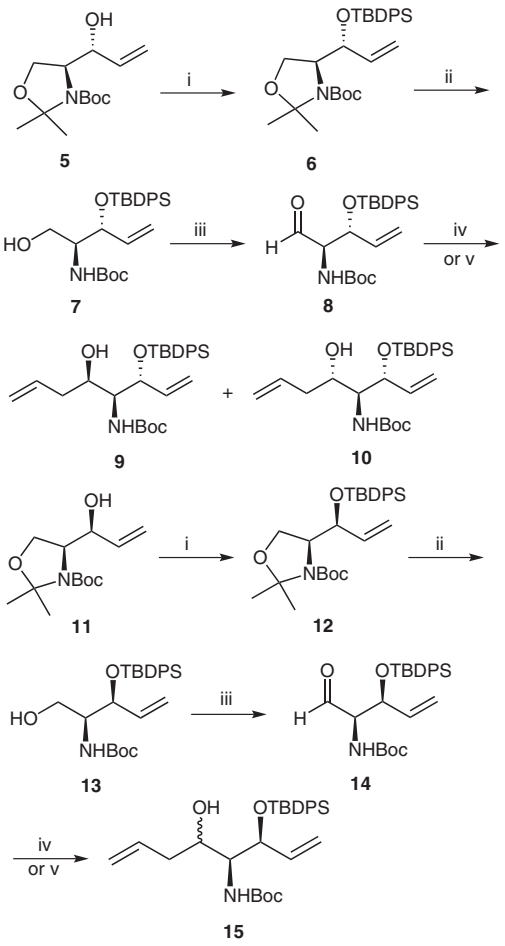


Scheme 1 Synthetic planning for aminocarbasugars

SYNTHESIS 2013, 45, 0536–0544
Advanced online publication: 09.01.2013
DOI: 10.1055/s-0032-1317962; Art ID: SS-2012-Z0754-OP

Our synthesis started from the known[13] allyl alcohol **5**, which was protected as its TBDPS ether **6** under standard conditions. Hydrolytic deprotection of the oxazolidine unit in the latter provided the primary alcohol **7**, which was smoothly oxidized to the aldehyde **8** using Dess–Martin periodinane[14] following precedence[15] for similar conversion (Scheme 2). The latter proved to be essentially pure and could be preserved at –20 °C for days without any appreciable damage as could be seen from repeated optical rotation and spectroscopic measurement. However, for practical reasons, it was used as such in the next step. Thus, addition of allylzinc bromide to the aldehyde **8** under controlled conditions provided a separable mixture of alcohols **9** and **10** with modest selectivity[16] in favor of **9** in a combined yield of 93%. On the other hand, addition of allylmagnesium bromide to the aldehyde **8** produced the *syn*-alcohol **9** with somewhat better selectivity (~2.3:1) but in lesser yield (69%). Configuration of the newly created stereocenter in each of the alcohols **9** and **10** was not determined at this stage, but followed from synthetic work described later. Similarly, the known allyl alcohol **11** was converted to the required aldehyde **14** over three identical steps in a combined yield of 73%. Similar addition of allylzinc bromide to **14** indeed proceeded well, but the product was obtained as a mixture (~3:1) of epimeric alcohols **15** (93%), which could not be separated at this stage. On the other hand, use of allylmagnesium bromide produced a mixture of alcohols **15** in a lower yield (73%) but with a better isomeric composition (~5.6:1) in the same sense (Scheme 2). However, the exact nature of the diastereoselection could not be deciphered at this stage. The dienes **9** and **10** were then separately subjected to ring-closing metathesis with Grubbs' catalyst benzylidene bistricyclohexylphosphinoruthenium(IV) dichloride (**16**). Pleasingly, the corresponding cyclohexene derivatives **17** and **23** (Scheme 3) were obtained in excellent yields. Compound **17** on hydrogenation in the presence of tetrabutylammonium fluoride provided the cycloalkane **20**, which was found to be devoid of any symmetry as judged from number of signals in its ^{13}C NMR spectrum. This led to the establishment of the configuration at the free hydroxyl bearing carbon as shown. Dihydroxylation of the alkene **17** proved to be exceedingly facile and gave only one product **18** in 95% yield.

The latter was converted into the acetonide **21** as the only product, and thence to the diol **22** after simple deprotection of the TBDPS ether. Compound **22** was found to be suitable for single crystal X-ray analysis. The crystal structure[17] is depicted in Figure 2, which clearly establishes the relative stereochemistry of the stereogenic centers in the molecule. Further deprotection of the TBDPS group from the triol **18** then delivered the targeted tetrol **19** in an overall yield of 38% over seven steps from **5**. Similar treatment of the diene **10** provided quick access to the epimeric cyclohexenol **23** under comparable conditions. Hydrogenation of the latter resulted in the symmetric diol **26** and hence the stereochemistry at the carbinol carbon in



Scheme 2 *Reagents and conditions*: (i) TBDPSCl, imidazole, CH_2Cl_2, **6** (98%), **12** (97%); (ii) *p*-TsOH, MeOH, **7** (80%), **13** (77%); (iii) Dess–Martin periodinane, CH_2Cl_2, **8** (97%), **14** (98%); (iv) allylzinc bromide,NH_4Cl, THF, **9** (57%), **10** (36%), **15** (93%); (v) allylmagnesium bromide, THF, **9** (48%), **10** (21%), **15** (73%).

the starting diene **10** was indirectly established as shown. Dihydroxylation of the alkene **23** also proved to be a highly diastereoselective as well as high-yielding reaction leading to the triol **24**.The stereochemistry of the dihydroxylation reaction was surmised from the belief that it took place *anti* to the bulky OTBDPS group. Deprotection of the TBDPS group from **24** then neatly afforded the desired tetrol derivative **25** in an overall yield of 23% over seven steps from **5** (Scheme 3).

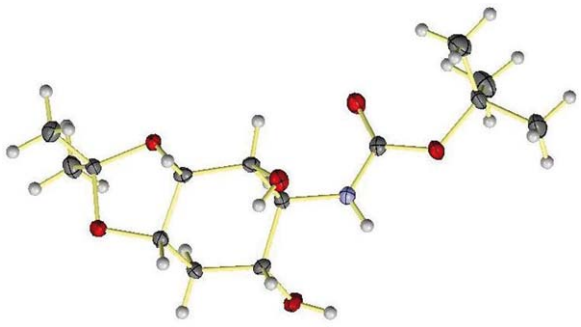
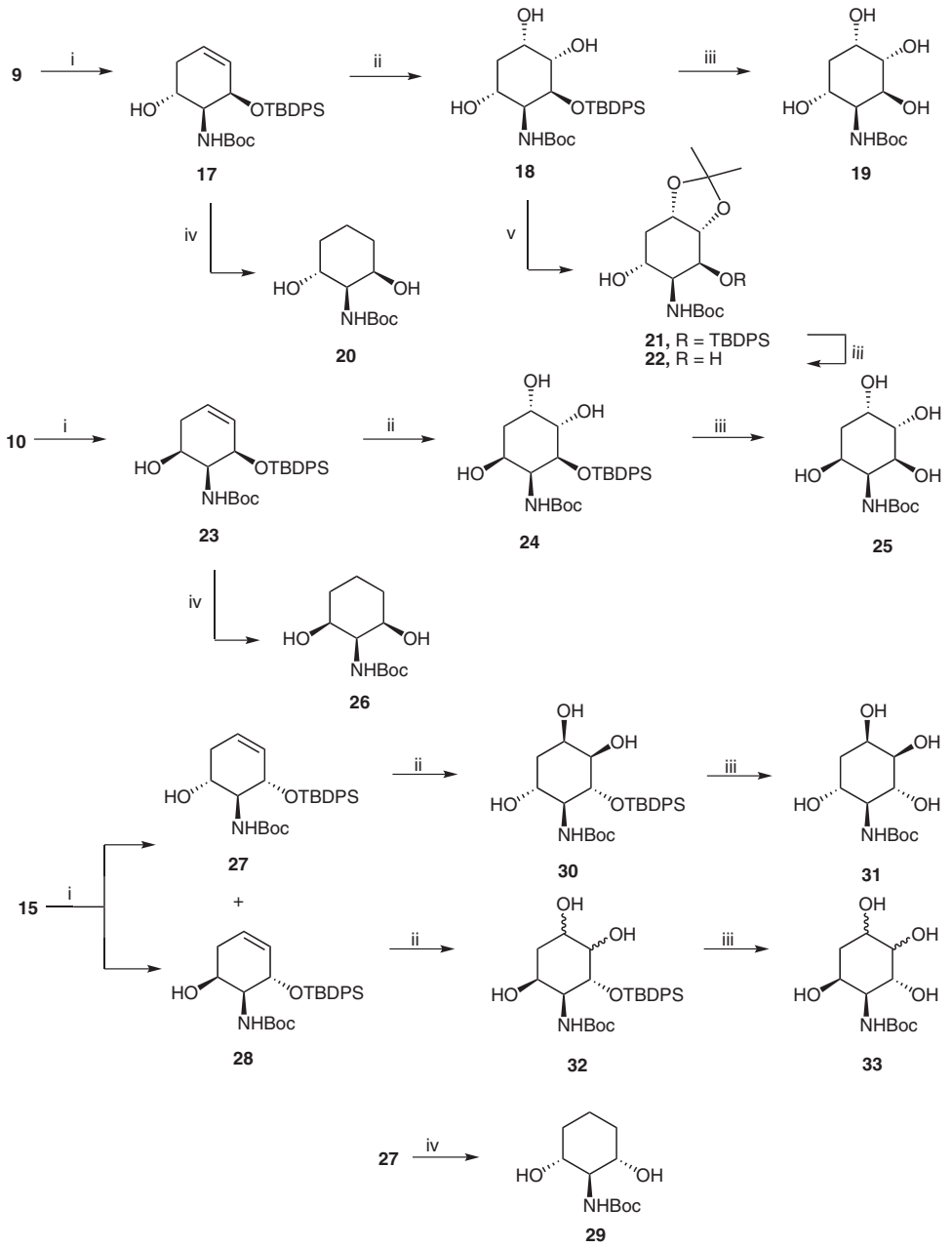


Figure 2 ORTEP plot of compound **22**

We then became interested to carry forward the mixture of dienes **15** with the hope that the products will be separable at some stage down the line. Pleasingly, ring-closing metathesis of the mixture **15** neatly provided a separable mixture of the corresponding cycloalkenes **27** and **28**.The stereochemical identity of the major product **27** was revealed from its conversion to the symmetric diol **29** through the one-pot protocol involving hydrogenation and TBDPS removal. Dihydroxylation of the hydroxyalkene **27** delivered only one isomer in this instance too and the stereochemistry of the resulting triol **30** followed from similar arguments. Final removal of the TBDPS group then provided the tetrol **31** in an overall yield of 44% over seven steps from **11** (Scheme 3).

On the other hand, dihydroxylation of the isomeric cyclohexene **28** proved to be high-yielding but nonselective. Moreover, the isomeric diols **32** resisted purification by conventional means in our hands. Removal of the TBDPS group from this diol mixture provided the corresponding tetrol derivatives **33** also as an inseparable mixture (Scheme 3).

In short, we have developed a convenient route to three stereoisomeric aminocyclohexitol derivatives from a common starting material and using a common set of transformations involving easily available reagents and simple reaction conditions. The targeted compounds **19**, **25**, and **31** were obtained in good overall yields and high



Scheme 3 *Reagents and conditions*: (i) catalyst **16** (5 mol%), CH_2Cl_2, **17** (95%), **23** (94%), **27** (70%), **28** (23%); (ii) OsO_4, NMMO, acetone–H_2O, **18** (97%), **24** (95%), **30** (96%), **32** (94%); (iii) TBAF·H_2O, THF, **19** (96%), **22** (96%), **25** (93%), **31** (97%), **33** (91%); (iv) H_2, Pd/C, THF, and then TBAF·H_2O, THF, **20** (94%), **26** (93%), **29** (96%); (v) 2,2-dimethoxypropane, *p*-TsOH, CH_2Cl_2, 96%.

optical purity. Although several aminocyclitol derivatives are known, quercitol like aminocyclitols are less documented.[18] This diversity oriented approach[19] may therefore complement to those existing in the literature and hence find application.

Optical rotations were measured in spectroscopic grade $CHCl_3$ on a Rudolph Autopol IV polarimeter at 25 °C and the $[\alpha]_D$ values are recorded in units of 10^{-1} deg cm^2 g^{-1}. IR spectra were recorded on a PerkinElmer Spectrum-1 spectrophotometer. Liquid samples were sandwiched between two KBr plates and solid samples were pelleted with KBr. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer purchased through a DST-FIST grant. Data for rotamers are presented within parentheses wherever appropriate. Chemical shifts are recorded relative to residual solvent peak. Mass spectra were recorded on a JEOL-JMS 600 instrument from I. I. C. B., Kolkata or IACS, Kolkata. Petroleum ether (PE) refers to the fraction boiling in the range 60–80 °C. Silica gel (60–120, 100–120, or 200–230 mesh) for column chromatography was purchased from Spectrochem, India.

***tert*-Butyl (*S*)-4-[(*R*)-1-(*tert*-Butyldiphenylsilyloxy)allyl]-2,2-dimethyloxazolidine-3-carboxylate (6) and *tert*-Butyl (*S*)-4-[(*S*)-1-(*tert*-Butyldiphenylsilyloxy)allyl]-2,2-dimethyloxazolidine-3-carboxylate (12)**

To a stirred solution of the *anti*-allyl alcohol **5** (1.03 g, 4 mmol) in CH_2Cl_2 (3 mL) was added imidazole (0.40 gm, 6 mmol, 1.5 equiv). After 5 min, TBDPSCl (1.15 mL, 4.4 mmol, 1.1 equiv) was added slowly at r.t. and the resulting reaction mixture was stirred for 4 h at r.t. The mixture was then diluted with EtOAc (60 mL) and the EtOAc layer was washed successively with aq 1 N HCl (50 mL), H_2O (50 mL), and brine (50 mL), and dried (Na_2SO_4). It was filtered and the filtrate was concentrated in vacuo to leave to leave a yellowish crude oil, which on purification by silica gel chromatography using 5% EtOAc in hexane afforded **6** as a syrupy liquid (1.94 g, 98%); $[\alpha]_D$ –18.2 (c = 0.74, $CHCl_3$).

IR (KBr): 2976, 2933, 1704, 1474, 1385, 1366, 1257, 1175, 1112, 822 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66–7.63 (1 H, m), 7.59–7.57 (3 H, m), 7.36–7.26 (6 H, m), 5.67–5.56 (1 H, m), 4.67 (1 H, dt, J = 10.4, 4.8 Hz), 5.55 (1 H, dd, J = 16.8, 6.8 Hz), 4.26 (1 H, t, J = 7.6 Hz), 4.08–3.99 (1 H, m), 3.84–3.83 (2 H, m), 1.45–1.32 (15 H, m), 0.97 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.8 (153.1), 138.1, 136.0, 135.9, 134.2, 133.7, 129.6, 129.5 (129.4), 127.4 (127.3), 117.3 (116.7), 94.3 (93.8), 79.9 (79.8), 76.2, 65.1 (64.6), 62.0 (61.8), 28.4, 27.1 (26.7), 24.8, 23.1, 19.4.

Anal. Calcd for $C_{29}H_{41}NO_4Si$: C, 70.26; H, 8.34; N, 2.83. Found: C, 70.06; H, 8.57; N, 2.98.

12

Similarly, compound **12** was prepared from alcohol **11**; yield: 1.93 g (97%); colorless liquid; $[\alpha]_D$ –20.94 (c = 0.55, $CHCl_3$).

IR (KBr): 1703, 1428, 1389, 1366, 1257, 1173, 1106, 1075, 822 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.61 (4 H, m), 7.43–7.35 (6 H, m), 5.88–5.81 (1 H, m), 5.07 (1 H, d, J = 10.0 Hz), 4.93 (1 H, d, J = 17.2 Hz), 4.61 (1 H, t, J = 5.2 Hz), 4.35 (1 H, d, J = 9.2 Hz), 3.99–3.92 (2 H, m), 1.62–1.42 (6 H, m), 1.20 (9 H, m), 1.06 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 151.8, 136.2, (136.0), 135.8, 133.8, 133.6, 129.8 (129.7), 127.6, 127.4, 117.7 (117.4), 94.8 (93.7), 79.9 (79.7), 73.6, 63.4 (63.2), 61.0 (60.5), 28.3, 27.0 (26.4), 24.6, 23.1, 19.4.

Anal. Calcd for $C_{29}H_{41}NO_4Si$: C, 70.26; H, 8.34; N, 2.83. Found: C, 70.13; H, 8.40; N, 2.93.

***tert*-Butyl (2*S*,3*R*)-3-(*tert*-Butyldiphenylsilyloxy)-1-hydroxypent-4-en-2-ylcarbamate (7) and *tert*-Butyl (2*S*,3*S*)-3-(*tert*-Butyldiphenylsilyloxy)-1-hydroxypent-4-en-2-ylcarbamate (13)**

To a stirred solution of **6** (990 mg, 2 mmol) in MeOH (6 mL) was added a catalytic amount of *p*-TsOH (114 mg, 0.6 mmol, 0.3 equiv) and the reaction mixture was stirred at r.t. for 2 h by which time the reaction was complete. The mixture was then quenched with sat. aq $NaHCO_3$ (20 mL) and extracted with EtOAc (2 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The crude residue was purified by column chromatography over silica gel using 30% EtOAc in hexane as eluent to give the alcohol **7** as a colorless viscous liquid (1.94 g, 98%); $[\alpha]_D$ +8.2 (c = 0.95, $CHCl_3$).

IR (KBr): 3436, 2963, 2858, 1697, 1505, 1366, 1171, 1112, 1050, 933, 821 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.55 (4 H, m), 7.38–7.27 (6 H, m), 5.72 (1 H, ddd, J = 17.2, 10.4, 6.8 Hz), 5.00–4.97 (3 H, m), 4.34 (1 H, t, J = 4 Hz), 3.79 (1 H, dd, J = 11.2, 4.4 Hz), 3.54–3.48 (2 H, m), 1.41 (1 H, br s), 1.33 (9 H, s), 1.01 (9 H, s).

13C NMR (100 MHz, $CDCl_3$): δ = 156.1, 136.8, 136.0, 135.9, 133.1, 133.0, 130.1, 130.0, 127.8, 127.6, 117.4, 79.5, 76.4, 62.7, 56.3, 28.3, 27.1, 19.4.

MS (TOFMS ES+): m/z = 478 (M + Na).

Anal. Calcd for $C_{26}H_{37}NO_4Si$: C, 68.53; H, 8.18; N, 3.07. Found: C, 68.68; H, 8.37; N, 2.91.

13

Similarly, compound **13** was prepared from **12**; yield: 1.40 g (77%); colorless liquid; $[\alpha]_D$ –13.62 (c = 0.92, $CHCl_3$).

IR (KBr): 3445, 2962, 1696, 1498, 1428, 1391, 1366, 1249, 1171, 1112, 1084, 1027, 999, 927, 821, 740 cm^{-1}.

^{1}H NMR (400 Mz, CDCl3): δ = 7.68–7.63 (4 H, m), 7.47–7.35 (6 H, m), 5.86–5.82 (1 H, m), 5.03–4.86 (3 H, m), 4.31–4.29 (1 H, m), 3.68–3.57 (3 H, m), 2.1 (1 H, br s), 1.43 (9 H, s), 1.1 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 136.6, 135.6, 135.4, 132.9, 132.6, 129.5, 129.3, 127.3, 127.0, 116.9, 79.2, 73.7, 62.7, 56.3, 27.8, 26.6, 18.9.

MS (TOFMS ES+): m/z = 578 (M + Na).

Anal. Calcd for $C_{26}H_{37}NO_4Si$: C, 68.53; H, 8.18; N, 3.07. Found: C, 68.76; H, 8.39; N, 3.12.

***tert*-Butyl (2*R*,3*R*)-3-(*tert*-Butyldiphenylsilyloxy)-1-oxopent-4-en-2-ylcarbamate (8) and *tert*-Butyl (2*R*,3*S*)-3-(*tert*-Butyldiphenylsilyloxy)-1-oxopent-4-en-2-ylcarbamate (14)**

To a stirred solution of the alcohol **7** (455 mg, 1 mmol) in anhyd CH_2Cl_2 (5 mL) was added solid Dess–Martin periodinane (551 mg, 1.3 mmol, 1.3 equiv). The resulting mixture was stirred for 0.5 h at r.t. It was then diluted with Et_2O (30 mL) and quenched with aq 0.5 M NaOH (30 mL). The mixture was stirred for 15 min and the aqueous phase was extracted with Et_2O (2 × 25 mL). The combined organic extracts were washed with aq 0.5 M NaOH (20 mL), H_2O (20 mL), and brine (20 mL), dried (Na_2SO_4), filtered, and the filtrate was concentrated under reduced pressure to provide the crude aldehyde **8** as a colorless oil (440 mg, 97%); $[\alpha]_D$ –53.2 (c = 1.35, $CHCl_3$).

IR (KBr): 2963, 2859, 1715, 1496, 1392, 1366, 1167, 1112, 1027, 938, 822, 740 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.64 (1 H, s), 7.60–7.52 (6 H, m), 7.36–7.18 (9 H, m), 5.89 (1 H, ddd, J = 17.2, 10.8, 6.4 Hz), 5.21 (1 H, d, J = 17.2 Hz), 5.13–5.07 (2 H, m), 4.57 (1 H, br s), 4.22 (1 H, t, J = 6.8 Hz), 1.43 (9 H, s), 0.98 (15 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 154.25, 135.2, 134.9, 134.8, 131.9, 129.0, 128.9, 126.7, 126.6, 126.5, 116.7, 78.8, 74.2, 63.8, 27.2, 25.9, 25.7, 18.4.

MS (TOFMS ES+): m/z = 476 (M + Na).

14
Similarly, compound **14** was prepared from **13**; yield: 444 mg (98%); colorless liquid; $[\alpha]_D$ –46.1 (c = 1.25, $CHCl_3$).

IR (KBr): 2857, 1716, 1494, 1367, 1168, 1113, 933, 822, 741 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.58 (1 H, s), 7.59–7.53 (5 H, m), 7.38–7.28 (8 H, m), 5.89 (1 H, ddd, J = 17.2, 10.0, 7.2 Hz), 5.12 (1 H, d, J = 8.0 Hz, NH), 4.95 (1 H, d, J = 10.4 Hz), 4.88 (1 H, d, J = 17.2 Hz), 4.62 (1 H, t, J = 3.2 Hz), 4.27 (1 H, dd, J = 8.0, 3.6 Hz), 1.39 (9 H, s), 0.99 (11 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.5, 155.0, 135.5, 135.3, 135.1, 132.1, 129.6, 129.4, 127.3, 127.0, 117.8, 79.6, 73.5, 63.7, 27.8, 26.5, 18.9.

MS (TOFMS ES+): m/z = 476 (M + Na).

***tert*-Butyl (3*R*,4*S*,5*R*)-3-(*tert*-Butyldiphenylsilyloxy)-5-hydroxyhepta-1,6-dien-4-ylcarbamate (9) and *tert*-Butyl (3*R*,4*S*,5*S*)-3-(*tert*-Butyldiphenylsilyloxy)-5-hydroxyhepta-1,6-dien-4-ylcarbamate (10)**
Method A: To a solution of aldehyde **8** (680 mg, 1.5 mmol) in a mixture of THF (6 mL) and sat. aq NH_4Cl (4 mL) were added allyl bromide (0.76 mL, 9 mmol) followed by Zn dust (588 mg, 9 mmol). The mixture was stirred at r.t. for 6 h and then extracted with EtOAc (2 × 30 mL). The combined organic extracts were washed successively with aq 1 M HCl (25 mL), H_2O (50 mL), and brine (50 mL), and dried (Na_2SO_4). It was filtered and the filtrate was concentrated in vacuo to leave a pale yellow crude product, which was purified by flash chromatography on silica gel using 15% EtOAc in hexane as eluent to provide the dienes in the order **9** (414 mg, 56%) followed by **10** (276 mg, 37%) each as a colorless liquid.

9
$[\alpha]_D$ +8.84 (c = 1.05, $CHCl_3$).

IR (KBr): 3446, 2934, 1715, 1644, 1500, 1367, 1170, 1109, 1074, 926, 824, 929, 704 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.62 (4 H, m), 7.46–7.34 (6 H, m), 5.77 (2 H, ddd, J = 17.2, 10.4, 6.8 Hz), 5.16–5.06 (3 H, m), 5.0–4.94 (2 H, m,), 4.47 (1 H, t, J = 3.6 Hz), 4.17 (1 H, t, J = 6.8 Hz), 3.46 (1 H, dd, J = 9.2, 3.6 Hz), 3.13 (1 H, s), 2.26 (1 H, dt, J = 14.0, 6.8 Hz), 2.154 (1 H, dt, J = 17.2, 6.8 Hz), 1.40 (9 H, s), 1.08 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 137.2, 136.1, 136.0, 134.4, 132.9, 132.6, 130.1, 129.9, 127.8, 127.6, 117.7, 117.4, 79.2, 78.4, 69.3, 56.6, 38.4, 28.4, 27.1, 19.4.

MS (TOFMS ES+): m/z = 518 (M + Na).

Anal. Calcd for $C_{29}H_{41}NO_4Si$: C, 70.26; H, 8.16; N, 2.83. Found: C, 70.11; H, 8.33; N, 2.71.

10
$[\alpha]_D$ –5.4 (c = 1.63, $CHCl_3$).

IR (KBr): 3437, 2933, 1717, 1642, 1501, 1366, 1171, 1111, 1041, 727, 704 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.69 (2 H, d, J = 6.4 Hz), 7.67 (2 H, d, J = 6.8 Hz), 7.63–7.34 (6 H, m), 5.86–5.84 (1 H, m), 5.79–5.71 (1 H, m), 5.28 (1 H, d, J = 16.8 Hz), 5.17 (1 H, d, J = 10.4 Hz), 5.08 (2 H, dd, J = 9.2, 4.4 Hz), 5.03 (1 H, s), 4.62 (2 H, d, J = 2.4 Hz), 3.59 (1 H, t, J = 8.0 Hz), 3.48 (1 H, d, J = 4.8 Hz), 2.24–2.21 (1 H, m), 2.05 (1 H, q, J = 7.2 Hz), 1.42 (9 H, s), 1.09 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.1, 136.4, 136.1, 135.9, 134.6, 133.6, 133.3, 130.1, 129.9, 129.7, 127.9, 127.7, 118.4, 117.4, 79.3, 73.4, 71.1, 58.9, 38.3, 28.4, 27.1, 26.9, 19.4.

MS (TOFMS ES+): m/z = 518 (M + Na).

Anal. Calcd for $C_{29}H_{41}NO_4Si$: C, 70.26; H, 8.16; N, 2.83. Found: C, 70.47; H, 8.20; N, 2.98.

Method B: To a stirred solution of the aldehyde **8** (453 mg, 1 mmol) in anhyd THF (6 mL) was added allylmagnasium bromide (1 M solution in Et_2O, 3 mL, 3 mmol, 3 equiv) dropwise at –78 °C. The mixture was then allowed to warm slowly to –30 °C and stirred at that temperature for 4 h. It was quenched with sat. aq NH_4Cl (15 mL) and allowed to come to r.t., diluted with H_2O (20 mL), and extracted with EtOAc (2 × 50 mL). The combined organic layers were washed successively with H_2O (50 mL) and brine (50 mL), and dried (Na_2SO_4). It was filtered and the filtrate was concentrated under reduced pressure to leave a pale yellow crude product, which was purified by flash column chromatography over silica gel using 15% EtOAc in hexane as eluent to provide the homoallylic alcohols **9** (244 mg, 49%) followed by **10** (98 mg, 20%) each as a colorless liquid.

Epimeric Mixture of Alcohols 15
Similarly, the epimeric mixture of alcohols **15** was prepared from the aldehyde **14** following Method A and B as detailed for the preparation of the dienes **9** and **10**; yield of **15**: Method A: 94%; Method B: 76%; colorless liquid. Selectivity: Method A: *syn*/*anti* = 3:1; Method B: *syn*/*anti* = 5.5:1.

IR (KBr): 3442, 2934, 1700, 1643, 1499, 1428, 1366, 1170, 1109, 1180, 925, 854, 703 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 7.71–7.64 (6 H, m), 7.45–7.34 (8 H, m), 5.83–5.76 (2 H, m), 5.14–5.02 (3 H, m), 4.98–4.86 (3 H, m), 4.57 (1 H, d, J = 7.2 Hz), 4.32 (1 H, t, J = 6.4 Hz), 3.98 (1 H, br s), 3.60 (1 H, br s), 3.51 (1 H, d, J = 6.8 Hz), 2.36–2.1 (2 H, m), 1.47 and 1.44 (9 H, s), 1.08 and 1.06 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 156.0, 137.6, 137.2, 136.1, 136.0, 134.9, 134.3, 133.7, 133.5, 133.2, 130.0, 129.9, 127.9, 127.7, 127.6, 127.5, 118.1, 118.0, 117.3, 79.5,79.3, 76.2, 74.1, 70.5, 70.1, 58.5, 57.6, 39.0, 38.4, 28.4, 27.1, 27.0, 19.5, 19.4.

MS (TOFMS ES+): m/z = 518 (M + Na).

RCM of the Dienes 9, 10, and 15: Formation of the Cycloalkenes 17, 23, 27, and 28; General Procedure
To a stirred solution of the appropriate diene (0.50 mmol) in degassed anhyd CH_2Cl_2 (0.01 M, 50 mL) was added Grubbs' catalyst **16** (21 mg, 5 mol%) and the homogenous mixture was refluxed for 16 h under an argon atmosphere. The solvent was removed in vacuo and the residual mass was purified by flash column chromatography over silica gel using 30% EtOAc in hexane as eluent to give the appropriate cyclohexene.

***tert*-Butyl (1*S*,2*R*,6*R*)-2-(*tert*-Butyldiphenylsilyloxy)-6-hydroxycyclohex-3-enylcarbamate (17)**
Yield: 221 mg (95%); colorless liquid; $[\alpha]_D$ –101.53 (c = 0.75, $CHCl_3$).

IR (KBr): 3445, 2932, 1700, 1503, 1367, 1242, 1170, 1106, 1066, 956, 762, 704 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 7.68–7.63 (4 H, m), 7.45–7.26 (6 H, m), 5.60 (1 H, ddd, J = 7.2, 4.8, 2.4 Hz), 5.32–5.26 (2 H, m), 5.29 (1 H, t, J = 4.0 Hz), 5.03 (1 H, t, J = 4.8 Hz), 3.58 (1 H, t, J = 8.4 Hz), 2.62 (1 H, td, J = 18.0, 4.8 Hz), 2.50 (1 H, br s), 2.05 (1 H, dd, J = 17.6, 9.2 Hz), 1.45 (9 H, s), 1.25 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 136.0, 135.8, 133.7, 133.1, 130.0, 129.8, 128.1, 127.9, 127.5, 127.4, 79.7, 68.8, 66.9, 56.6, 34.6, 28.4, 27.1, 19.5.

MS (TOFMS ES+): m/z = 490 (M + Na).

Anal. Calcd for $C_{27}H_{37}NO_4Si$: C, 69.34; H, 7.97; N, 2.99. Found: C, 69.21; H, 8.09; N, 2.85.

***tert*-Butyl (1*S*,2*R*,6*S*)-2-(*tert*-Butyldiphenylsilyloxy)-6-hydroxycyclohex-3-enylcarbamate (23)**
Yield: 219 mg (94%); colorless liquid; $[\alpha]_D$ –12.73 (c = 1.16, $CHCl_3$).

IR (KBr): 3441, 2932, 1700, 1499, 1429, 1367, 1240, 1168, 1110, 1050, 854, 761, 703 cm^{-1}.

^1H NMR (400Mz, $CDCl_3$): δ = 7.66–7.64 (4 H, m), 7.47–7.37 (6 H, m), 5.66 (1 H, dd, *J* = 10, 6.4 Hz), 5.44–5.42 (2 H, m), 4.44 (1 H, d, *J* = 8.8 Hz), 4.38 (1 H, br s), 3.80–3.73 (2 H, m), 2.30 (2 H, br s), 1.45 (9 H, s), 1.08 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 135.8, 135.7, 133.0, 132.6, 130.2, 130.0, 127.9, 127.8, 127.6, 127.0, 79.8, 69.2, 68.6, 54.0, 32.5, 28.4, 26.9, 19.3.

MS (TOFMS ES+): *m*/*z* = 490 (M + Na).

Anal. Calcd for $C_{27}H_{37}NO_4Si$: C, 69.34; H, 7.97; N, 2.99. Found: C, 69.51; H, 8.12; N, 3.08.

***tert*-Butyl (1*S*,2*S*,6*R*)-2-(*tert*-Butyldiphenylsilyloxy)-6-hydroxycyclohex-3-enylcarbamate (27)**
Yield from the mixture **15** (prepared via route A): 163 mg (70%); yield from the mixture **15** (prepared via Method B): 184 mg (78%); colorless liquid; mp 128–130 °C; $[\alpha]_D$ +6.32 (*c* = 1.14, $CHCl_3$).

IR (KBr): 3417, 3327, 1680, 1527, 1365, 1320, 1250, 1171, 1106, 1064, 981, 703 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 7.65–7.62 (4 H, m), 7.46–7.39 (7 H, m), 6.55 (1 H, d, *J* = 9.2 Hz), 5.39 (1 H, dd, *J* = 10.0, 4.8 Hz), 5.05 (1 H, d, *J* = 10.0 Hz), 4.63 (1 H, d, *J* = 5.6 Hz), 4.33 (1 H, d, *J* = 6.4 Hz), 3.38 (1 H, q, *J* = 9.6 Hz), 2.22 (1 H, td, *J* = 18, 12.4 Hz), 1.95 (1 H, dd, *J* = 16.8, 11.6 Hz), 1.40 (10 H, s), 0.98 (10 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.4, 136.0, 133.6, 133.0, 130.0, 129.9, 129.7, 128.9, 128.0, 127.7, 127.6, 125.8, 80.0, 71.9, 70.1, 59.8, 34.1, 28.3, 29.7, 26.9, 19.3.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{27}H_{37}NO_4Si$ + Na: 490.2390; found: 490.2356 (M + Na).

***tert*-Butyl (1*S*,2*S*,6S)-2-(*tert*-Butyldiphenylsilyloxy)-6-hydroxycyclohex-3-enylcarbamate (28)**
Yield from the mixture **15** (prepared via route A): 54 mg (23%); yield from the mixture **15** (prepared via Method B): 33 mg (14%); colorless liquid; $[\alpha]_D$ +32.2 (*c* = 1.2, $CHCl_3$).

IR (KBr): 3445, 2932, 1700, 1503, 1367, 1242, 1170, 1106, 1066, 956, 762, 704 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 7.66–7.62 (4 H, m), 7.47–7.40 (6 H, m), 5.12 (1 H, d, *J* = 8.8 Hz), 5.46 (1 H, d, *J* = 9.2 Hz), 5.22 (1 H, d, *J* = 10.0 Hz), 4.73 (1 H, d, *J* = 2.8 Hz), 4.25 (1 H, br s), 3.91 (1 H, br s), 3.73 (1 H, dt, *J* = 13.6, 6.8 Hz), 2.26 (1 H, br d, *J* = 17.2 Hz), 2.04 (1 H, dd, *J* = 18.4, 6.8 Hz), 1.38 (9 H, s), 1.0 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 136.3, 136.0, 135.9, 134.0, 133.3, 130.0, 129.9, 129.6, 127.6, 127.4, 126.7, 79.8, 69.8, 67.5, 57.1, 34.7, 28.3, 27.0, 19.3.

MS (TOFMS ES+): *m*/*z* = 490 (M + Na).

Anal. Calcd for $C_{27}H_{37}NO_4Si$: C, 69.34; H, 7.97; N, 2.99. Found: C, 69.47; H, 7.84; N, 3.15.

Dihydroxylation: Formation of the Triols 18, 24, 30, and 32; General Procedure
To a stirred solution of the appropriate cyclohexene (467 mg, 1 mmol) in acetone–H_2O (5:1, 6 mL) were added *N*-methylmorpholine *N*-oxide (NMMO; 234 mg, 2 mmol, 2 equiv), followed by OsO_4 (12.7 mg, 5 mol% in H_2O) at r.t., and the resulting mixture was stirred for 24 h. It was quenched with sat. aq $Na_2S_2O_5$ (15 mL). Solvent was removed in vacuo and the residual mass was extracted with EtOAc (2 × 50 mL). The combined organic extracts were washed with brine (30 mL) and dried (Na_2SO_4). It was filtered and the filtrate was concentrated under reduced pressure to leave a pale yellow crude product, which on purification by column chromatography over silica gel using 60% EtOAc in hexane provided the required triol as a viscous foamy liquid.

***tert*-Butyl (1*S*,2*S*,3*S*,4*S*,6*R*)-2-(*tert*-Butyldiphenylsilyloxy)-3,4,6-trihydroxycyclohexylcarbamate (18)**
Yield: 486 mg (97%); $[\alpha]_D$ –10.3 (*c* = 1.1, $CHCl_3$).

IR (KBr): 3419, 2931, 2859, 1696, 1590, 1513, 1367, 1171, 1111, 1023, 759, 702 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 7.59–7.55 (4 H, m), 7.50–7.40 (6 H, m), 5.54 (1 H, d, *J* = 7.6 Hz), 4.62 (1 H, d, *J* = 3.6 Hz), 4.53 (1 H, d, *J* = 5.6 Hz), 4.37 (1 H, d, *J* = 6.8 Hz), 3.96 (1 H, s), 3.83 (1 H, dq, *J* = 11.2, 6.8 Hz), 3.66 (1 H, ddd, *J* = 16.0, 10.4, 5.6 Hz), 1.78 (1 H, td, *J* = 11.6, 6.8 Hz), 1.61 (1 H, q, *J* = 11.6 Hz), 1.28 (9 H, s), 1.02 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 135.9, 135.8, 133.1, 132.7, 130.1, 130.0, 127.9, 79.7, 74.1, 71.8, 67.8, 66.9, 54.8, 36.0, 28.3, 27.1, 19.4.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{27}H_{39}NO_6Si$ + Na: 524.2444; found: 524.2442 (M + Na).

***tert*-Butyl (1*S*,2*S*,3*S*,4*S*,6*S*)-2-(*tert*-Butyldiphenylsilyloxy)-3,4,6-trihydroxycyclohexylcarbamate (24)**
Yield: 476 mg (95%); $[\alpha]_D$ –16.4 (*c* = 1.0, $CHCl_3$).

IR (KBr): 3444, 2929, 1694, 1504, 1392, 1168, 1112, 1070, 1024, 703 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 7.65–7.63 (4 H, m), 7.48–7.38 (6 H, m), 5.20 (1 H, br s), 4.21 (1 H, br s), 4.15 (1 H, br s), 3.92 (1 H, d, *J* = 3.2 Hz), 3.83 (1 H, d, *J* = 3.2 Hz), 3.66 (1 H, br s), 2.26 (1 H, br s), 2.0–1.97 (1 H, m), 1.9 (1 H, dt, *J* = 12.0, 2.8 Hz), 1.39 (9 H, s), 1.10 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 135.9, 132.2, 130.4, 130.2, 128.0, 127.9, 79.8, 75.4, 71.5, 70.1, 64.3, 50.1, 35.0, 28.3, 27.0, 19.2.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{27}H_{39}NO_6Si$ + Na: 524.2444; found: 524.2441 (M + Na).

***tert*-Butyl (1*S*,2*R*,3*R*,4*R*,6*R*)-2-(*tert*-Butyldiphenylsilyloxy)-3,4,6-trihydroxycyclohexylcarbamate (30)**
Yield: 481 mg (96%); $[\alpha]_D$ –34.9 (*c* = 1.1, $CHCl_3$).

IR (KBr): 3419, 2931, 2859, 1696, 1590, 1513, 1367, 1171, 1111, 1023, 759, 702 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 7.75–7.73 (2 H, m), 7.67 (2 H, d, *J* = 6.4 Hz), 7.39–7.36 (6 H, m), 4.39 (1 H, d, *J* = 6.4 Hz), 4.07 (1 H, br s), 3.76–3.66 (3 H, m), 3.57–3.48 (2 H, m), 2.41 (1 H, br s), 2.18–2.15 (br s, 2 H), 1.35 (9 H, s), 1.1 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 136.0, 135.6, 133.6, 132.0, 130.3, 128.2, 128.1, 80.0, 75.3, 73.7, 70.1, 67.4, 59.4, 35.5, 28.2, 27.0, 19.5.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{27}H_{39}NO_6Si$ + Na: 524.2444; found: 524.2473 (M + Na).

Diastereomeric Mixture of Triols 32
Yield: 471 mg (94%); $[\alpha]_D$ –20.6 (*c* = 1.1, $CHCl_3$).

IR (KBr): 3403, 2931, 1690, 1511, 1428, 1392, 1367, 1249, 1169, 1112, 834, 703 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 7.60–7.58 (5 H, m), 7.50–7.41 (7.5 H, m), 5.65 (1 H, d, *J* = 9.6 Hz), 5.04 (1.2 H, br s), 4.64 (1.2 H, d, *J* = 6.0 Hz), 4.56 (1.26 H, d, *J* = 6.0 Hz), 3.95 (1.26 H, br s), 3.85–3.81 (3.7 H, m), 3.52 (1.5 H, m), 1.63 (2.5 H, d, *J* = 7.2 Hz), 1.33 (11 H, s), 1.01 (11 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 136.0, 135.6, 133.9, 132.5, 130.1, 130.0, 128.0, 127.9, 79.6, 75.1, 72.2, 70.1, 56.8, 32.2, 28.3, 27.0, 19.5.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{27}H_{39}NO_6Si$ + Na: 524.2444; found: 524.2447 (M + Na).

Deprotection of TBDPS Ethers: Formation of the Tetrols 19, 25, 31, and 33; General Procedure

To a stirred solution of the appropriate triol (202 mg, 0.40 mmol) in anhyd THF (4 mL), was added Bu_4NF (157 mg, 0.60 mmol, 1.5 equiv) at r.t. and stirring was continued for 4 h at r.t. The reaction mixture was concentrated under reduced pressure and the residual mass was purified by column chromatography over silica gel using 8% MeOH in $CHCl_3$ as eluent to give the corresponding tetrol.

***tert*-Butyl (1*S*,2*S*,3*S*,4*S*,6*R*)-2,3,4,6-Tetrahydroxycyclohexylcarbamate (19)**

Yield: 102 mg (96%); colorless amorphous powder; mp 156–158 °C; $[\alpha]_D$ –56.3 (*c* = 0.53, MeOH).

IR (KBr): 3395, 1682, 1665, 1528, 1333, 1306, 1249, 1175, 1030, 989, 905 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 5.85 (1 H, d, *J* = 7.6 Hz), 4.81 (1 H, br s), 4.61 (1 H, br s,), 4.39–4.34 (2 H, br d), 3.66–3.58 (4 H, m), 1.68 (1 H, br d, *J* = 10.4 Hz), 1.58 (1 H, q, *J* = 11.2 Hz), 1.37 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.3, 79.1, 77.4, 72.1, 71.7, 65.5, 54.6, 36.9, 28.2.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{11}H_{21}NO_6$ + Na: 286.1267; found: 286.1266 (M + Na).

***tert*-Butyl (1*S*,2*S*,3*S*,4*S*,6*S*)-2,3,4,6-Tetrahydroxycyclohexylcarbamate (25)**

Yield: 99 mg (93%); colorless powder; mp 144–146 °C; $[\alpha]_D$ –8.7 (*c* = 0.66, MeOH).

IR (KBr): 3395, 1682, 1665, 1528, 1333, 1306, 1249, 1175, 1030, 989, 905 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 6.02 (1 H, d, *J* = 9.6 Hz), 4.60–4.48 (3 H, m), 4.17 (1 H, d, *J* = 5.2 Hz), 3.80 (1 H, br s), 3.67 (1 H, br s), 3.52 (3 H, br s), 1.57 (2 H, d, *J* = 4.4 Hz), 1.27 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.2, 79.1, 73.0, 71.9, 68.5, 63.1, 49.7, 34.8, 28.2.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{11}H_{21}NO_6$ + Na: 286.1267; found: 286.1265 (M + Na).

***tert*-Butyl (1*S*,2*R*,3*R*,4*R*,6*R*)-2,3,4,6-Tetrahydroxy-cyclohexylcarbamate (31)**

Yield: 103 mg (97%); colorless powder; mp 196–198 °C; $[\alpha]_D$ –38.4 (*c* = 0.65, MeOH).

IR (KBr): 3484, 3345, 1690, 1527, 1457, 1393, 1333, 1284, 1167, 1078, 1006, 863 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 6.41 (1 H, d, *J* = 6.8 Hz, NH), 4.50 (1 H, br s), 4.39–4.38 (3 H, m), 3.76 (1 H, br s), 3.54 (1 H, br s), 3.34 (1 H, br s), 3.15 (1 H, d, *J* = 7.6 Hz), 3.04 (1 H, q, *J* = 8.4 Hz), 1.84 (1 H, br d, *J* = 12.8 Hz), 1.38 (9 H, s), 1.32–1.28 (1 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 77.0, 75.2, 70.8, 67.6, 66.4, 60.2, 37.8, 28.3.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{11}H_{21}NO_6$ + Na: 286.1267; found: 286.1265 (M + Na).

Diastereomeric Mixture of Tetrols 33

Yield (combined): 96 mg (91%); colorless powder; mp 152–154 °C.

IR (KBr): 3482, 2924, 1688, 1664, 1540, 1416, 1369, 1244, 1164, 1131, 1019, 952 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 6.40 (0.5 H, d, *J* = 8.4 Hz, NH), 6.02 (1 H, br s), 4.84–4.73 (3 H, m), 4.50 (2 H, br s), 4.40 (0.5 H, br s), 4.36–4.34 (1 H, m), 4.16–4.15 (0.5 H, br s), 3.77 (3 H, br s), 3.63 (1 H, br s), 3.17 (2 H, m), 1.85 (1 H, m), 1.72 (2 H, br d), 1.38 (16 H, s), 1.17 (1 H, t, *J* = 7.2 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 155.2, 79.1, 77.6, 75.1, 70.8, 67.6, 66.4, 48.6, 38.7, 33.2, 28.3, 28.2, 23.0, 13.4.

HRMS (TOFMS ES+): *m*/*z* calcd for $C_{11}H_{21}NO_6$ + Na: 286.1267; found: 286.1269 (M + Na).

One-Pot Hydrogenation and Removal of TBDPS Ether: Formation of the Diols 20, 26, and 29; General Procedure

To a stirred solution of the appropriate olefin (0.25 mmol) in anhyd THF (4 mL) was added 10% Pd/C (20 mg) followed by Bu_4NF (98 mg, 0.37 mmol, 1.5 equiv) and the heterogeneous mixture was stirred for 6 h at r.t. under H_2 atmosphere. It was then filtered through a Celite bed and the filtrate was concentrated under reduced pressure to leave a crude viscous residual mass, which was directly purified by column chromatography over silica gel using 55% EtOAc in hexane as eluent to give the corresponding aminodiol compound.

***tert*-Butyl (2*R*,6*R*)-2,6-dihydroxycyclohexylcarbamate (20)**

Yield: 55 mg (94%); colorless powder; mp 134–136 °C; $[\alpha]_D$ –46.0 (*c* = 0.92, $CHCl_3$).

IR (KBr): 3408, 3289, 1663, 1539, 1368, 1253, 1178, 1070, 1004 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 5.23 (1 H, br s), 4.13 (1 H, s), 3.74–3.67 (1 H, m), 3.38 (1 H, t, *J* = 12.4 Hz), 2.65 (1 H, br s), 2.06–2.03 (1 H, m), 1.82–1.78 (2 H, m), 1.68–1.64 (3 H, m), 1.46 (9 H, s), 1.32–1.29 (1 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 80.0, 70.0, 69.7, 59.2, 33.7, 31.9, 28.4, 18.1.

MS (TOFMS ES+): *m*/*z* = 254 (M + Na).

Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 57.24; H, 9.01; N, 5.91.

***tert*-Butyl (1*S*,2*R*,6*S*)-2,6-Dihydroxycyclohexylcarbamate (26)**

Yield: 53 mg (93%); colorless liquid; mp 90–92 °C.

IR (KBr): 3370, 3289, 1670, 1533, 1372, 1291, 1248, 1178, 1038, 1012, 957 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 5.48 (1 H, br s), 4.03 (2 H, d, *J* = 3.8 Hz), 3.54 (1 H, br s), 2.95 (2 H, br s), 1.92–1.85 (3 H, m), 1.65–1.54 (3 H, m), 1.46 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 79.7, 70.7, 53.4, 31.6, 28.4, 13.4.

MS (TOFMS ES+): *m*/*z* = 254 (M + Na).

Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 57.01; H, 9.03; N, 5.95.

***tert*-Butyl (1*R*,2*R*,6*S*)-2,6-Dihydroxycyclohexylcarbamate (29)**

Yield: 56 mg (96%); colorless powder; mp 176–178 °C.

IR (KBr): 3434, 3306, 1655, 1558, 1449, 1368, 1321, 1170, 1042, 1022, 946 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 4.89 (1 H, br s), 3.42–3.35 (2 H, m), 3.25–3.19 (1 H, m), 2.93 (2 H, br s), 2.05–2.00 (2 H, m), 1.76–1.71 (1 H, m), 1.46 (9 H, s), 1.40–1.23 (3 H, m).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 157.0, 77.6, 71.2, 63.2, 34.5, 28.8, 20.4.

MS (TOFMS ES+): *m*/*z* = 254 (M + Na).

Anal. Calcd for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 57.23; H, 9.31; N, 6.18.

***tert*-Butyl (3a*S*,4*S*,5*S*,6*R*,7a*S*)-4-(*tert*-Butyldiphenylsilyloxy)-6-hydroxy-2,2-dimethylhexahydrobenzo[*d*][1,3]dioxol-5-ylcarbamate (21)**

To a stirred solution of the aminotriol **18** (200 mg, 0.40 mmol) in anhyd CH_2Cl_2 (2 mL), was added 2,2-dimethoxypropane (0.20 mL, 1.60 mmol, 4 equiv), followed by a catalytic amount *p*-TsOH at r.t. under N_2 atmosphere. The resulting solution was stirred for 0.5 h. After completion of reaction, it was quenched with solid $NaHCO_3$ (0.5 g) and the solvent was removed in vacuo. The crude mass was

purified by column chromatography over silica gel using 10% EtOAc in hexane as eluent to give the single acetonide **21** as a colorless oily liquid (207 mg, 96%); $[\alpha]_D$ –5.9 (*c* = 1.32, $CHCl_3$).

IR (KBr): 3427, 2930, 1701, 1504, 1367, 1219, 1171, 1112, 1051, 740, 703 cm^{-1}.

^1H NMR (400 Mz, $CDCl_3$): δ = 7.66–7.62 (4 H, m), 7.47–7.38 (6 H, m), 4.82 (1 H, br s), 4.35 (1 H, q, *J* = 6.4 Hz), 4.16 (1 H, br s), 4.0–3.97 (1 H, m), 3.85 (1 H, q, *J* = 5.2 Hz), 3.70 (1 H, dt, *J* = 7.6, 2.8 Hz), 2.85 (1 H, br s), 2.35 (1 H, td, *J* = 10.0, 4.8 Hz), 1.88 (1 H, br s), 1.40 (9 H, s), 1.38 (3 H, s), 1.16 (3 H, s), 1.10 (9 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 135.8, 135.7, 133.0, 132.8, 130.2, 130.1, 128.0, 127.9, 108.8, 79.7, 76.6, 72.3, 72.2, 68.8, 55.8, 34.2, 28.3, 27.5, 27.1, 26.9, 25.1, 19.4.

MS (TOFMS ES^+): *m*/*z* = 564 (M + Na).

Anal. Calcd for $C_{30}H_{43}NO_6Si$: C, 66.51; H, 8.00; N, 2.59. Found: C, 66.38; H, 8.11; N, 2.72.

***tert*-Butyl (3a*R*,4*S*,5*S*,6*R*,7a*S*)-4,6-Dihydroxy-2,2-dimethylhexahydrobenzo[*d*][1,3]dioxol-5-ylcarbamate (22)**

To a stirred solution of the TBDPS ether **21** (108 mg, 0.2 mmol) in anhyd THF (2 mL), Bu_4NF (80 mg, 0.30 mmol, 1.5 equiv) was added at r.t. and stirring was continued for 4 h at r.t. The reaction mixture was concentrated under reduced pressure and the residual mass was purified by column chromatography over silica gel using 60% EtOAc in PE as eluent to give the diol **22** as a colorless solid (58 mg, 96%); mp 166–168 °C ($CHCl_3$–MeOH); $[\alpha]_D$ –39.2 (*c* = 1.1, MeOH).

IR (KBr): 3470, 3375, 3422, 2977, 1682, 1519, 1391, 1460, 1370, 1245, 1170, 1042 cm^{-1}.

^1H NMR (400 Mz, DMSO-d_6): δ = 6.13 (1 H, d, *J* = 7.6 Hz, NH), 5.10 (1 H, d, *J* = 4 Hz, OH), 4.47 (1 H, d, *J* = 5.2 Hz), 4.20 (1 H, q, *J* = 7.2 Hz), 3.97 (1 H, t, *J* = 5.2 Hz), 3.90 (1 H, br s), 3.58–3.46 (2 H, m), 2.03 (1 H, td, *J* = 10.8, 4.8 Hz), 1.54 (1 H, dq, *J* = 9.2, 4.8 Hz), 1.42 (3 H, s), 1.39 (9 H, s), 1.24 (3 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 108.2, 78.1, 77.8, 72.5, 68.7, 64.3, 55.8, 37.3, 28.7, 28.6, 26.5.

MS (TOFMS ES^+): *m*/*z* = 326 (M + Na).

Anal. Calcd for $C_{14}H_{25}NO_6$: C, 55.43; H, 8.31; N, 4.62. Found: C, 55.61; H, 8.53; N, 4.50.

Acknowledgment

Financial assistance from DST, New Delhi (Grant No. SR/S1/OC-35/2009), is gratefully acknowledged. We are also thankful to CSIR (New Delhi) for a fellowship to A.B.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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