An Efficient Synthesis of Aminocyclopentitols via the Stereoselective Amination of Polybenzyl Ethers Using Chlorosulfonyl Isocyanate

In Su Kim, Qing Ri Li, Jae Koo Lee, Sang Hwi Lee, Jae Kyung Lim, Ok Pyo Zee, Young Hoon Jung*

College of Pharmacy, Sungkyunkwan University, Suwon 440-746, Korea
Fax +82(31)2907773; E-mail: yhjung@skku.ac.kr

Received 4 April 2007

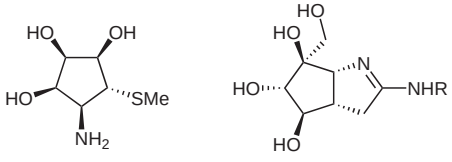
Abstract: An efficient stereoselective route for the preparation of stereoisomeric aminocyclopentitols **3**–**5** was achieved using a six-step sequence starting from the corresponding D-sugars. Key steps of the synthesis of the title compounds involved the regioselective and diastereoselective amination of cinnamylic 1,2-*anti*- or 1,2-*syn*-tribenzyl ethers using chlorosulfonyl isocyanate (CSI), intramolecular olefin metathesis, and diastereoselective dihydroxylation.

Key words: aminocyclopentitol, chlorosulfonyl isocyanate, amination, mannostatin, dihydroxylation

Glycosidases are involved in a wide range of important biological processes, such as intestinal digestion, the post-translational processing of glycoproteins, and the lysosomal catabolism of glycoconjugates.[1] Inhibitors of these enzymes have received much attention and are currently being used for treating diabetes,[2] viral infections (e.g., HIV and influenza),[3] malaria,[4] and cancer.[5] The majority of these inhibitors are iminosugars, in which an oxygen atom in a monosaccharide is replaced by a nitrogen atom, and they have been often found in natural plants and microorganisms. While these iminosugars and their derivatives have been extensively studied, the development of aminocyclopentitol analogues as glycosidase inhibitors has received little attention.

The aminocyclopentitols have been found in a number of natural products, e.g. mannostatin A (**1**)[6] and trehazoline (**2**).[7] In particular, mannostatin A (**1**), isolated from the soil microorganism *Streptoverticillus* is the most potent and specific class II α-mannosidase inhibitor reported to date,[8] which stimulated us to develop an efficient synthetic route for the manufacture of various aminocyclopentitol analogues as new α-mannosidase inhibitors (Figure 1).

Recently, we described a new method for the regioselective and diastereoselective introduction of an N-protected



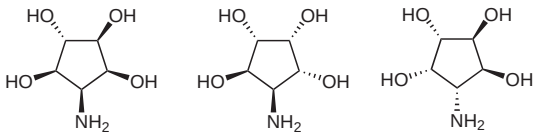
1 **2** (R = α-Glc)

Figure 1 Mannostatin A (**1**) and trehazoline (**2**)

SYNLETT 2007, No. 11, pp 1711–1714
Advanced online publication: 25.06.2007
DOI: 10.1055/s-2007-984518; Art ID: U02907ST

amine group into various allylic ethers using CSI[9] and demonstrated the application of this methodology to the total synthesis of polyhydroxylated alkaloids.[10] As a part of our ongoing investigation of iminosugars, we considered preparing aminocyclopentitol precursors with a 3-amino-1,2-diol functional group assembly.

We report herein a convenient synthetic route for the preparation of stereoisomeric 5-amino-1,2,3,4-cyclopentanetetrols **3**–**5** via the regioselective and stereoselective amination of polybenzyl ethers using CSI (Figure 2). In addition, we describe interesting results for the diastereoselective dihydroxylation of olefin in polyfunctionalized carbocycles **10a**–**c**.



3 **4** **5**

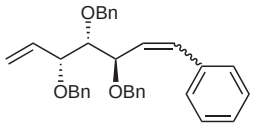
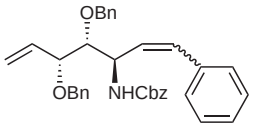
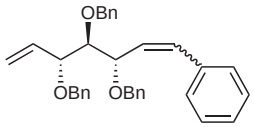
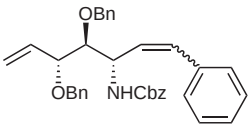
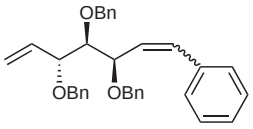
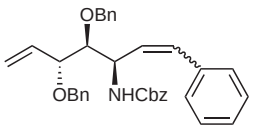
Figure 2 Structure of various aminocyclopentitols

In initial studies, we investigated the regioselectivity and diastereoselectivity of the reactions of stereoisomeric tribenzyl ethers **6a**–**c** with CSI, which were prepared from commercially available D-sugars (D-lyxose, D-ribose and D-arabinose), to provide the corresponding products **7a**–**c** (Table 1).

As shown in entries 1 and 2, treatment of 1,2-*anti*-tribenzyl ethers **6a** and **6b** with CSI in toluene at 0 °C furnished the corresponding 1,2-*anti*-amino alcohols **7a** and **7b** with excellent diastereoselectivities of 24:1 and 18:1, respectively, in favor of the 1,2-*anti*-isomer. However, the reaction of 1,2-*syn*-tribenzyl ethers **6c** with CSI afforded the desired 1,2-*syn*-amino alcohol **7c** as a major product with moderate diastereoselectivity of 1:5 in a 72% combined yield (entry 3). Table 1 shows that the stereochemistries of major products **7a**–**c** were identical to those of the corresponding substrates **6a**–**c**. These results can be interpreted by the neighboring group effect leading to the retention of the original configuration via a double configuration inversion.[10,11]

The carbocycles **10a**–**c** were straightforwardly prepared in high overall yields (27–33%) from the benzyl-protected lactols **8a**–**c** using a five-step sequence, as shown in Scheme 1. The Wittig olefination of **8a**–**c** using the DMSO anion[12] and benzyltriphenylphosphonium

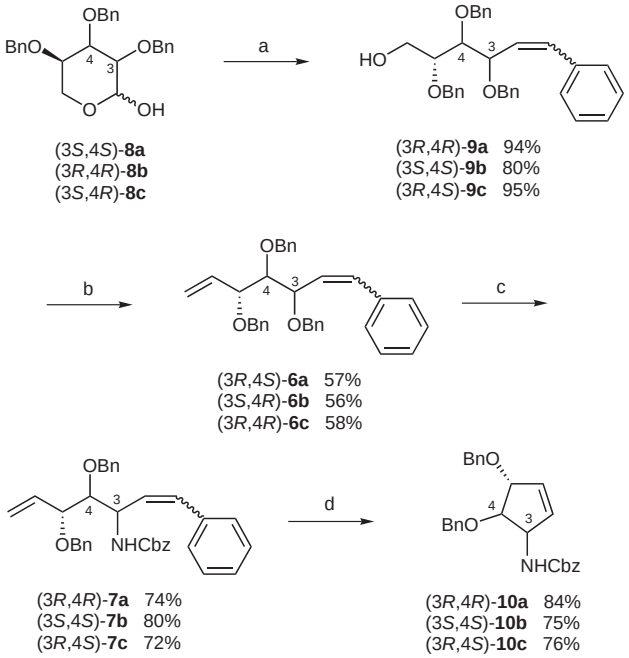
Table 1 Diastereoselective CSI Reactions of Various Cinnamylic Polybenzyl Ethers **7a–c**

Entry	Substrate	Product	Yield (%)[a]	Ratio (*anti*/*syn*)[b]
1	 **6a**	 **7a**	74	24:1
2	 **6b**	 **7b**	80	18:1
3	 **6c**	 **7c**	72	1:5

[a] Isolated yield of pure materials.
[b] Isomeric ratio as determined by ^{1}H NMR analysis.

chloride in THF at 45 °C afforded the alcohols **9a–c** in high yields. Oxidation of the alcohols **9a–c** with Dess–Martin reagent yielded the corresponding aldehydes, which were then subjected to the Wittig reaction using NaHMDS and methyltriphenylphosphonium bromide, to furnish the dienic compounds **6a–c**. Reactions between the polybenzyl ethers **6a–c** and CSI were carried out in toluene at 0 °C. These were followed by desulfonylation using aqueous 25% sodium sulfite solution, to furnish the cinnamylic amine products **7a–c** with high diastereoselectivity.[13] Finally, treatment of **7a–c** with second-generation Grubbs' catalyst [$(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh][14] in toluene at 80 °C provided the carbocyclic compounds **10a–c** in good yields.[15]

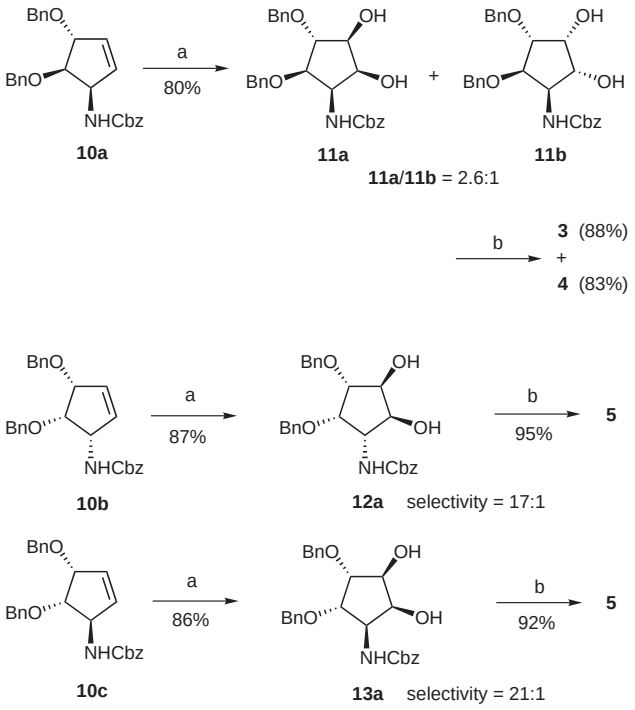
Next, we investigated the dihydroxylation of the stereoisomeric cyclic allylic amines **10a–c** using a catalytic amount of OsO_4 in 80% acetone (Scheme 2).[16] Ratios of stereoisomers were determined by HPLC analysis of the inseparable reaction mixture, and the relative configurations of **11a**–**13a** and **11b** were assigned by NOE studies of the isolated pure materials obtained by additional purification processes, involving introduction and removal of the acetonide group.[17] In all cases, dihydroxylation occurred preferentially from the *anti*-direction with respect to the allylic benzyloxy group at C-4 to give **11a**–**13a** as major products, although the level of diastereoselectivity depended upon the ring substitution pattern. Interestingly, osmylation of **10b** with its bottom face completely shielded by three substituents did not produce a higher level of diastereoselectivity than that observed for **10c**. The excellent diastereoselectivity (21:1) of **10c** could be explained by steric interaction between the bulky benzyloxy groups at C-4/C-5 and the oxidant (OsO_4), the directing ability of the NHCO group[18] (as reasonably good hydrogen donor), and allylic strain[19] in the five-membered ring system. Finally, hydrogenolysis of the diols **11a**–**13a** and **11b** with



Scheme 1 *Reagents and conditions*: (a) NaH, DMSO, $BnPPh_3Cl$, THF, 45 °C; (b) (i) Dess–Martin periodinane, CH_2Cl_2, 0 °C; (ii) NaHMDS, $MePPh_3Br$, THF, 0 °C; (c) (i) CSI, Na_2CO_3, toluene, 0 °C; (ii) 25% Na_2SO_3, r.t.; (d) $(IMesH_2)(PCy_3)(Cl)_2Ru$=CHPh (5 mol%), toluene, 80 °C.

10% Pd/C and 6 N HCl in methanol followed by purification using ion-exchange resin provided the free amines **3**–**5** as viscous liquids.[20]

In conclusion, an efficient stereoselective route for the preparation of stereoisomeric aminocyclopentitols **3**–**5** was accomplished from the readily available D-sugars via the regio- and diastereoselective amination of polybenzyl ethers using chlorosulfonyl isocyanate, intramolecular olefin metathesis leading to carbocyclic ring skeleton



Scheme 2 *Reagents and conditions*: (a) cat. OsO_4, 50% NMO, 80% acetone, r.t.; (b) (i) 2,2-dimethoxypropane, PPTS, CH_2Cl_2, r.t.; (ii) separation; (iii) *p*-TsOH, MeOH, 40 °C; (iv) 10% Pd/C, H_2, 6 N HCl, MeOH, r.t.; (v) DOWEX-50WX8 (H^+ form, 0.5 M NH_4OH as eluent).

formation, and diastereoselective dihydroxylation. Moreover, we have provided useful information for the dihydroxylation of olefins in 1-amino-4,5-diol cyclopentenes. Currently, we are preparing other aminocyclitols and aminocyclopentitols for evaluation as potent α-mannosidase inhibitors.

Acknowledgment

This research was supported by the Seoul Research and Business Development (Seoul R&BD) Program (#10541), and by the Brain Korea 21 (BK21) Program.

References and Notes

(1) (a) Asano, N. *Curr. Top. Med. Chem.* **2003**, *3*, 471. (b) Elbein, A. D. *FASEB J.* **1991**, *5*, 3055. (c) Asano, N.; Nash, R. J.; Molyneux, R. J.; Fleet, G. W. J. *Tetrahedron: Asymmetry* **2000**, *11*, 1645.

(2) (a) Somsak, L.; Nagya, V.; Hadady, Z.; Docsa, T.; Gergely, P. *Curr. Pharm. Des.* **2003**, *9*, 1177. (b) Johnson, P. S.; Lebovitz, H. E.; Coniff, R. F.; Simonson, D. C.; Raskin, P.; Munera, C. L. *J. Clin. Endocrinol. Metab.* **1998**, *83*, 1515.

(3) (a) Greimel, P.; Spreitz, J.; Stutz, A. E.; Wrodnigg, T. M. *Curr. Top. Med. Chem.* **2003**, *3*, 513. (b) Fleet, G. W. J.; Karpas, A.; Dwek, R. A.; Fellows, L. E.; Tyms, A. S.; Peturrson, S.; Namgoong, S. K.; Ramsden, N. G.; Smith, P. W.; Son, J. C.; Wilson, F.; Witty, D. R.; Jacob, G. S.; Rademacher, T. W. *FEBS Lett.* **1988**, *237*, 128. (c) Gruters, R. A.; Neefjes, J. J.; Tersmette, M.; de Goede, R. E. Y.; Tulp, A.; Huisman, H. G.; Miedema, F.; Ploegh, H. L. *Nature (London)* **1987**, *330*, 74.

(4) Bitonti, A. J.; Sjoersma, A.; McCann, P. P. Eur. Patent Appl. EP423728, **1991**.

(5) (a) Nishimura, Y. *Curr. Top. Med. Chem.* **2003**, *3*, 575. (b) Ostrander, G. K.; Scribner, N. K.; Rohrschneider, L. R. *Cancer Res.* **1988**, *48*, 1091. (c) Tsuruoka, T.; Fukuyasu, H.; Ishii, M.; Usui, T.; Shibahara, S.; Inouye, S. *J. Antibiot.* **1996**, *49*, 155.

(6) For a recent review of synthetic and biological features of the mannostatins, see: Berecibar, A.; Grandjean, C.; Siriwardena, A. *Chem. Rev.* **1999**, *99*, 779.

(7) (a) Ando, O.; Nakajima, M.; Hamano, K.; Itoi, K.; Takahashi, S.; Takamatsu, Y.; Sato, A.; Enokita, R.; Haruyama, H. *J. Antibiot.* **1993**, *46*, 1116. (b) Ando, O.; Satake, H.; Itoi, K.; Sato, A.; Nakajima, M.; Takahashi, S.; Haruyama, H. *J. Antibiot.* **1991**, *44*, 1165.

(8) Aoyagi, T.; Yamamoto, T.; Kojiri, K.; Morishima, H.; Nagai, M.; Hamada, M.; Takeuchi, T.; Umezawa, H. *J. Antibiot.* **1989**, *42*, 883.

(9) (a) Kim, J. D.; Kim, I. S.; Hua, J. C.; Zee, O. P.; Jung, Y. H. *Tetrahedron Lett.* **2005**, *46*, 1079. (b) Jung, Y. H.; Kim, J. D. *Arch. Pharm. Res.* **2005**, *28*, 382. (c) Kim, J. D.; Zee, O. P.; Jung, Y. H. *J. Org. Chem.* **2003**, *68*, 3721. (d) Kim, J. D.; Han, G.; Zee, O. P.; Jung, Y. H. *Tetrahedron Lett.* **2003**, *44*, 733. (e) Jung, Y. H.; Kim, J. D. *Arch. Pharm. Res.* **2003**, *26*, 667. (f) Kim, J. D.; Han, G.; Jeong, L. S.; Park, H.-J.; Zee, O. P.; Jung, Y. H. *Tetrahedron* **2002**, *58*, 4395. (g) Kim, J. D.; Lee, M. H.; Han, G.; Park, H.; Zee, O. P.; Jung, Y. H. *Tetrahedron* **2001**, *57*, 8257. (h) Jung, Y. H.; Kim, J. D. *Arch. Pharm. Res.* **2001**, *24*, 371. (i) Kim, J. D.; Lee, M. H.; Lee, M. J.; Jung, Y. H. *Tetrahedron Lett.* **2000**, *41*, 5073. (j) Jung, Y. H.; Kim, J. D. *Arch. Pharm. Res.* **2000**, *23*, 574.

(10) (a) Kim, I. S.; Oh, J. S.; Zee, O. P.; Jung, Y. H. *Tetrahedron* **2007**, *63*, 2622. (b) Kim, I. S.; Ji, Y. J.; Jung, Y. H. *Tetrahedron Lett.* **2006**, *47*, 7289. (c) Kim, I. S.; Zee, O. P.; Jung, Y. H. *Org. Lett.* **2006**, *8*, 4101. (d) Kim, I. S.; Kim, J. D.; Ryu, C. B.; Zee, O. P.; Jung, Y. H. *Tetrahedron* **2006**, *62*, 9349. (e) Kim, J. D.; Kim, I. S.; Jin, C. H.; Zee, O. P.; Jung, Y. H. *Org. Lett.* **2005**, *7*, 4025.

(11) (a) Krow, G. R.; Yuan, J.; Lin, G.; Sonnet, P. E. *Org. Lett.* **2002**, *4*, 1259. (b) Roberts, D. D. *J. Org. Chem.* **1997**, *62*, 1857. (c) Winstein, S.; Allred, E.; Heck, R.; Grick, R. *Tetrahedron* **1958**, *3*, 1.

(12) (a) For a recent review of Wittig olefination, see: Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863. (b) Choi, W. J.; Park, J. K.; Yoo, S. J.; Kim, H. O.; Moon, H. R.; Chun, M. W.; Jung, Y. H.; Jeong, L. S. *J. Org. Chem.* **2001**, *66*, 6490.

(13) Characterization data for **7a**–**c**:
7a: (*Z*:*E* = 2.5:1, *anti*:*syn* = 24:1); $[\alpha]_D^{30}$ –14.9 (*c* = 1.0, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 3.50–3.53 (t, *J* = 4.5 Hz, 0.71 H), 3.60–3.61 (br, 0.29 H), 3.91–4.01 (m, 1 H), 4.32 (d, *J* = 11.5 Hz, 0.29 H), 4.33 (d, *J* = 12.0 Hz, 0.71 H), 4.60–4.77 (m, 3.29 H), 5.01–5.15 (m, 4.13 H), 5.29 (d, *J* = 17.0 Hz, 0.29 H), 5.38 (d, *J* = 10.0 Hz, 0.29 H), 5.53 (t, *J* = 10.0, 12.0 Hz, 0.71 H), 5.70–5.84 (m, 1.71 H), 5.90–5.99 (m, 0.29 H),6.00 (dd, *J* = 7.5, 15.5 Hz, 0.29 H), 6.52 (d, *J* = 15.5 Hz, 0.29 H), 6.53 (d, *J* = 15.5 Hz, 0.71 H), 7.23–7.36 (m, 20 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 49.69, 66.67, 70.64, 73.65, 81.66, 81.94, 119.76, 120.06, 126.80, 127.51, 127.94, 127.99, 128.09, 128.17, 128.40, 128.55, 128.66, 128.69, 132.55, 132.85, 134.88, 135.12, 136.58, 137.05, 138.14, 138.33, 155.99. HRMS (FAB): *m*/*z* [M + H^+] calcd for $C_{35}H_{36}NO_4$: 534.2644; found: 534.2639.
7b: (*Z*:*E* = 2.6:1, *anti*:*syn* = 18:1); $[\alpha]_D^{25}$ –79.6 (*c* = 0.1, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$): δ = 3.68–3.73 (br, 0.56 H), 3.80 (t, *J* = 7.0 Hz, 0.72 H), 3.88–3.92 (m, 0.72 H), 4.29 (d, *J* = 11.5 Hz, 0.28 H), 3.39 (d, *J* = 11.5 Hz, 0.72 H), 4.47 (d, *J* = 11.5 Hz, 0.28 H), 4.54 (d, *J* = 11.5 Hz, 0.72 H),

4.57 (d, *J* = 11.5 Hz, 0.28 H), 4.61 (d, *J* = 11.5 Hz, 0.72 H), 4.63 (d, *J* = 11.5 Hz, 0.28 H), 4.67 (d, *J* = 11.5 Hz, 0.72 H), 4.89 (br, 0.28 H), 5.06–5.16 (m, 2 H), 5.25 (t, *J* = 8.0 Hz, 0.72 H), 5.35–5.44 (m, 3 H), 5.76 (dd, *J* = 10.0, 10.5 Hz, 0.72 H), 5.85–5.94 (m, 1 H), 6.17 (dd, *J* = 8.0, 15.5 Hz, 0.28 H), 6.49 (d, *J* = 15.5 Hz, 0.28 H), 6.63 (d, *J* = 10.5 Hz, 0.72 H), 7.03–7.46 (m, 20 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 50.32, 66.87, 70.47, 70.53, 74.49, 81.12, 81.34, 83.20, 83.50, 119.70, 120.25, 126.78, 127.53, 127.60, 127.85, 128.01, 128.15, 128.23, 128.37, 128.58, 128.65, 128.68, 128.76, 128.90, 132.74, 132.82, 136.18, 136.58, 138.25, 155.60. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{35}H_{36}NO_4$: 534.2644; found: 534.2640.

7c: (*Z*:*E* = 2.8:1, *anti*:*syn* = 1:5); [a]$_D^{25}$ +1.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.56 (t, *J* = 7.5 Hz, 0.74 H), 3.71 (dd, *J* = 3.5, 6.5 Hz, 0.26 H), 3.88–3.93 (m, 1 H), 4.30 (d, *J* = 11.5 Hz, 0.26 H), 4.45–4.64 (m, 3.46 H), 4.76 (d, *J* = 11.5 Hz, 0.26 H), 4.91–4.93 (br, 0.26 H), 5.09–5.14 (m, 2.74 H), 5.31–5.64 (m, 3 H), 5.84 (dd, *J* = 10.0, 11.0 Hz, 0.74 H), 5.84–5.87 (m, 1 H), 6.18 (dd, *J* = 8.0, 16.0 Hz, 0.26 H), 6.53 (d, *J* = 11.0 Hz, 0.74 H), 6.56 (d, *J* = 16.0 Hz, 0.26 H), 7.06–7.49 (m, 20 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 54.78, 66.88, 70.52, 74.50, 74.66, 81.11, 83.47, 120.33, 126.06, 126.81, 127.82, 127.87, 127.97, 128.14, 128.17, 128.27, 128.35, 128.53, 128.67, 128.69, 128.72, 128.79, 132.76, 136.18, 136.86, 137.01, 138.30, 155.80. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{35}H_{36}NO_4$: 534.2644; found: 534.2654.

(14) For recent reviews of ring-closing metathesis, see: (a) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18. (b) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012.

(15) Characterization data for **10a**–**c**:
10a: [α]$_D^{29}$ –32.9 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.09 (br t, *J* = 5.5 Hz, 1 H), 4.52–4.61 (m, 5 H), 4.90–4.93 (br, 1 H), 5.12 (s, 2 H), 5.19 (d, *J* = 7.5 Hz, 1 H), 5.95 (d, *J* = 6.0 Hz, 1 H), 6.03 (d, *J* = 5.5 Hz, 1 H), 7.27–7.40 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.67, 66.99, 71.92, 72.79, 82.56, 86.81, 128.00, 128.09, 128.17, 128.22, 128.34, 128.61, 128.67, 128.72, 128.74, 132.89, 134.65, 136.76, 137.77, 138.37, 156.37. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{27}H_{28}NO_4$: 430.2018; found: 430.2020.
10b: [α]$_D^{25}$ –79.6 (*c* = 0.1, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.02 (t, *J* = 5.5 Hz, 1 H), 4.30 (dd, *J* = 2.5, 5.0 Hz, 1 H), 4.64 (d, *J* = 12.0 Hz, 1 H), 4.65 (d, *J* = 12.0 Hz, 1 H), 4.69–4.71 (br, 1 H), 4.72 (d, *J* = 12.0 Hz, 1 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 5.12 (s, 2 H), 5.29 (d, *J* = 9.0 Hz, 1 H), 6.05 (dd, *J* = 2.0, 6.0 Hz, 1 H), 6.09 (dd, *J* = 3.0, 6.0 Hz, 1 H), 7.27–7.38 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 54.65, 66.88, 72.31, 72.58, 78.42, 80.03, 127.86, 127.90, 128.02, 128.05, 128.22, 128.61, 128.69, 133.06, 135.08, 136.90, 138.30, 138.79, 156.36. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{27}H_{28}NO_4$: 430.2018; found: 430.2013.
10c: [α]$_D^{29}$ +6.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.02 (t, *J* = 5.5 Hz, 1 H), 4.30 (dd, *J* = 2.5, 5.0 Hz, 1 H), 4.64 (d, *J* = 12.0 Hz, 1 H), 4.65 (d, *J* = 12.0 Hz, 1 H), 4.70–4.73 (br m, 2 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 5.12 (s, 2 H), 5.28 (d, *J* = 9.0 Hz, 1 H), 6.05 (dd, *J* = 1.5, 6.0 Hz, 1 H), 6.08 (dd, *J* = 2.5, 6.5 Hz, 1 H), 7.27–7.41 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 54.65, 66.87, 72.31, 72.58, 78.44, 80.03, 127.84, 127.90, 128.01, 128.03, 128.21, 128.60, 128.69, 133.05, 135.08, 136.91, 138.30, 143.67, 156.35. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{27}H_{28}NO_4$: 430.2018; found: 430.2019.

(16) (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3947. (b) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, *24*, 3943. (c) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *17*, 1973.

(17) Characterization data for **11a**–**13a** and **11b**:
11a: [α]$_D^{23}$ +1.0 (*c* = 0.22, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.92–4.25 (m, 5 H), 4.46 (d, *J* = 11.0 Hz, 1 H), 4.53 (d, *J* = 12.0 Hz, 1 H), 4.57 (d, *J* = 11.0 Hz, 1 H), 4.65 (d, *J* = 12.0 Hz, 1 H), 5.11 (d, *J* = 12.5 Hz, 1 H), 5.16 (d, *J* = 12.5 Hz, 1 H), 5.54–5.59 (br, 1 H), 7.22–7.36 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 53.83, 67.33, 72.06, 72.71, 73.41, 80.22, 82.63, 88.40, 128.04, 128.09, 128.24, 128.39, 128.45, 128.71, 128.78, 128.81, 136.52, 137.20, 137.92, 154.56. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{27}H_{30}NO_6$: 464.2073; found: 464.2068.
11b: [α]$_D^{22}$ –18.2 (*c* = 0.08, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.58–1.64 (br, 1 H), 2.84–2.88 (br, 1 H), 3.86 (dd, *J* = 4.0, 4.5 Hz, 1 H), 3.93 (t, *J* = 6.5 Hz, 1 H), 4.01–4.21 (m, 3 H), 4.78 (d, *J* = 11.5 Hz, 1 H), 4.52–4.60 (m, 2 H), 4.71 (d, *J* = 11.5 Hz, 1 H), 5.12 (s, 2 H), 5.52 (br s, 1 H), 7.24–7.48 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 57.16, 67.41, 69.13, 72.46, 73.06, 77.49, 80.21, 82.78, 128.22, 128.28, 128.33, 128.42, 128.49, 128.79, 136.41, 137.42, 137.57, 157.66. HRMS (FAB): *m*/*z* [M + Na$^+$] calcd for $C_{27}H_{29}NO_6Na$: 486.1893; found: 486.1896.
12a: [α]$_D^{23}$ +7.3 (*c* = 0.44, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.82 (br s, 1 H), 3.09 (br s, 1 H), 3.91–3.99 (m, 3 H), 4.17 (dd, *J* = 4.5, 5.5 Hz, 1 H), 4.23 (br d, *J* = 3.0 Hz, 1 H), 4.52 (d, *J* = 12.0 Hz, 1 H), 4.68 (d, *J* = 12.0 Hz, 1 H), 4.76 (d, *J* = 12.0 Hz, 1 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 5.14 (d, *J* = 12.5 Hz, 1 H), 5.10 (d, *J* = 12.5 Hz, 1 H), 5.62 (d, *J* = 6.0 Hz, 1 H), 7.27–7.40 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 58.34, 67.35, 72.63, 73.27, 73.59, 76.42, 77.58, 84.59, 127.94, 128.01, 128.21, 128.37, 128.50, 128.69, 128.76, 128.82, 136.45, 138.04, 138.29, 157.59. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{27}H_{30}NO_6$: 464.2073; found: 464.2083.
13a: [α]$_D^{29}$ –2.5 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.98–3.22 (br, 2 H), 3.90–3.98 (br m, 2 H), 4.21–4.26 (br m, 3 H), 4.51 (d, *J* = 11.7 Hz, 1 H), 4.71 (d, *J* = 12.0 Hz, 1 H), 4.79 (d, *J* = 12.0 Hz, 1 H), 4.82 (d, *J* = 11.7 Hz, 1 H), 5.17 (s, 2 H), 5.63 (br d, *J* = 5.7 Hz, 1 H), 7.23–7.65 (m, 15 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 58.41, 67.34, 72.66, 73.31, 73.61, 76.46, 77.52, 84.55, 127.91, 127.98, 128.17, 128.34, 128.47, 128.66, 128.74, 128.80, 136.44, 138.00, 138.29, 157.69. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_{27}H_{30}NO_6$: 464.2073; found: 464.2072.

(18) Donohoe, T. J.; Blades, K.; Moore, P. R.; Waring, M. J.; Winter, J. J. G.; Helliwell, M.; Newcombe, N. J.; Stemp, G. *J. Org. Chem.* **2002**, *67*, 7946.

(19) Poli, G. *Tetrahedron Lett.* **1989**, *30*, 7385.

(20) Characterization data for **3**–**5**:
3: [α]$_D^{23}$ +6.3 (*c* = 0.79, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 3.22 (t, *J* = 3.0 Hz, 1 H), 3.73 (dd, *J* = 4.0, 7.5 Hz, 1 H), 3.80 (dd, *J* = 3.0, 7.5 Hz, 1 H), 3.91–3.94 (m, 2 H). ^{13}C NMR (125 MHz, D_2O): δ = 51.91, 73.32, 75.91, 76.01, 83.35. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_5H_{12}NO_4$: 150.0766; found: 150.0766.
4: [α]$_D^{23}$ –11.9 (*c* = 0.23, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 3.35 (t, *J* = 8.0 Hz, 1 H), 3.86–3.92 (m, 2 H), 3.99 (t, *J* = 4.5 Hz, 1 H), 4.07 (dd, *J* = 6.0, 8.0 Hz, 1 H). ^{13}C NMR (125 MHz, D_2O): δ = 56.37, 71.18, 73.37, 74.80, 76.84. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_5H_{12}NO_4$: 150.0766; found: 150.0767.
5: [α]$_D^{22}$ –2.3 (*c* = 1.0, MeOH). ^{1}H NMR (500 MHz, D_2O): δ = 3.46 (t, *J* = 6.0 Hz, 1 H), 3.96 (t, *J* = 5.0 Hz, 1 H), 4.00 (dd, *J* = 6.0, 6.5 Hz, 1 H), 4.19 (t, *J* = 7.0 Hz, 1 H), 4.22 (dd, *J* = 4.5, 5.5 Hz, 1 H). ^{13}C NMR (125 MHz, D_2O): δ = 57.19, 67.83, 71.83, 73.85, 76.39. HRMS (FAB): *m*/*z* [M + H$^+$] calcd for $C_5H_{12}NO_4$: 150.0766; found: 150.0767.