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Homochiral rigid γ-amino acid glycosides from aucubin

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Abstract—Two homochiral glucosylated hydroxy γ-amino acids **7** and **11** were synthesized by chiral pool synthesis in eight steps from the natural iridoid aucubin.

1. Introduction

For several decades, the discovery of new medicinal chemistry leads has almost exclusively relied upon the isolation of bioactive natural products from plant extracts, microbiological fermentations or animal sources. More recently, the advent of combinatorial chemistry permitted the intentional creation of chemical libraries, which can be screened for a variety of biological activities in the course of high throughput screening programs. Such libraries should include a large number of diverse molecules bearing substituents and functional groups in a well-defined three-dimensional relationship. In this context, the preparation of novel rigid scaffolds from small homochiral natural products appears a promising approach, which renews the interest in the secondary metabolites of living organisms.

In nature, amino acids and carbohydrates are the major building blocks used to generate molecular diversity. Their combination in glycopeptides and glycoproteins plays an important role in intercellular recognition phenomena, including metastasis, adhesion, infection, and inflammation. Consequently, the interest of various types of sugar-amino acid hybrids and conjugates as scaffolds to build up libraries for improved drug discovery has been recently emphasized.[1–6] The aim of this work is the synthesis of glycosides of rigid homochiral hydroxyamino acids from the naturally abundant iridoid glycoside aucubin **1**,[7] in order to provide new structural scaffolds possessing three different functional groups in addition to the sugar unit.

We have recently shown that the hydroxy group at C-6 on the aucubin aglycone could be selectively epimerized,[8] or converted into an amino group,[9] and that the cyclopentano[*c*]pyran basic core could be easily rearranged into various other fused systems, including bicyclo[3.1.0]hexane,[10,11] 8,9-diazatricyclo[4.4.0.0^{1,5}]-decane,[12] and cyclopenta[*c*]furan.[9,10] These results permitted us to conceive an access to hydroxy γ-amino acids derived from the cyclopenta[*c*]pyran and cyclopenta[*c*]furan skeletons, with conservation of the sugar unit (Scheme 1).

2. Results and discussion

Starting from 2′,3′,4′,6′,10-penta-*O*-pivaloylaucubin **2**, readily obtained from aucubin **1** in four steps and 30% overall yield, introduction of the amino group was ensured by a modified Mitsunobu reaction involving phthalimide as nitrogen donor.[13] (6*R*)-Phthalimidoperpivaloylbarstioside **3** was obtained in 81% yield under those conditions.[9] Compound **3** was the key intermediate in the syntheses of both cyclopenta[*c*]pyran and cyclopenta[*c*]furan derivatives. Our approach further involved oxidation of an aldehyde function, obtained either by substitution or by rearrangement, to elaborate the carboxylic acid group present in the target molecules.

Obtainment of a γ-amino acid in the cyclopentano[*c*]pyran series implied introduction of a carbonyl group at C-4 of **3**. For this purpose, a Vilsmeier reaction, which takes advantage of the activation of position 4 toward electrophilic attack, appeared particularly

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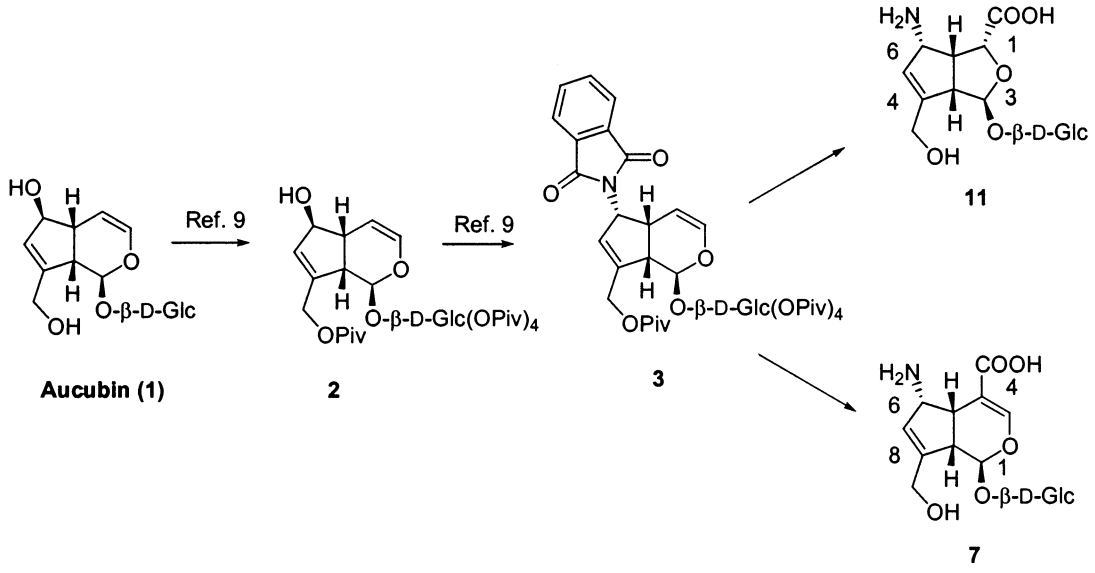
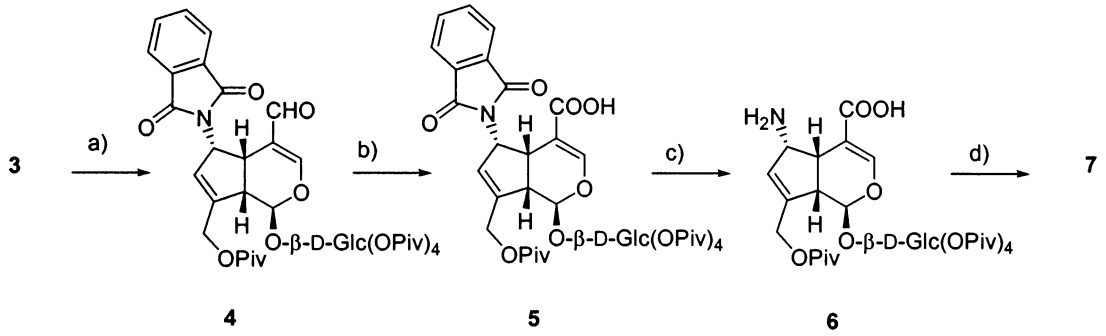


Scheme 1.

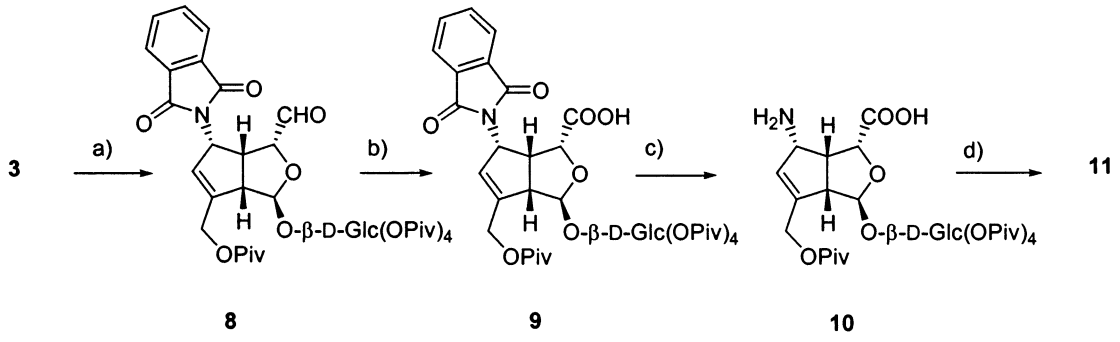
attractive. Indeed, it had been previously shown to give excellent results in terms of yield, when performed on hexa-*O*-acetylaucubin and related substrates.[14] Thus, treatment of **3** with dimethylformamide and phosphoryl chloride in dichloromethane in the presence of 4 Å molecular sieves provided the aldehyde **4**[15] in 60% yield. Oxidation of the carbonyl group of **4**, by use of potassium dichromate in acetic acid,[16] afforded the corresponding carboxylic acid **5**[17] in 50% yield. Deprotection of the amino group with hydrazine in ethanol[18] gave **6**[19] in 82% yield. Final removal of the pivaloyl protecting groups was obtained upon treatment of **6** with lithium hydroxide in aqueous acetonitrile, giving the desired glucosylated hydroxy γ-amino acid **7**[19] in 85% yield (Scheme 2).

We envisaged an entry to the cyclopenta[*c*]furan series through oxidation of the dihyropyran double bond of **3** to a iodolactol, followed by rearrangement of this latter in alkaline medium into the corresponding tetrahydrofuran carbaldehyde.[9] Accordingly, reaction of **3** with NIS in aqueous acetonitrile, followed by addition of toluene, 0.1 M aqueous potassium hydrogenocarbonate, and tetrabutylammonium bromide to the resulting iodolactols solution, gave the desired carbaldehyde **8**[9] in 80% yield. The same reaction sequence which permitted conversion of **4** to **7** was then applied to **8**. It successively involved: (i) potassium dichromate oxidation to the carboxylic acid **9**;[20] (ii) hydrazine deprotection to the amino compound **10**,[20] and (iii) lithium hydroxide saponification of the pivaloyl groups to give the fully deprotected glucosylated hydroxy γ-amino acid **11**[20] (Scheme 3).

The metabolic instability of most natural *O*-linked glycopeptides appears as an inherent limitation, which severely hampers the biological evaluation of these materials and their possible consideration as potential drugs. In order to overcome these drawbacks, synthetic mimics must prove more stable than the model compounds towards glycosidases catalyzed hydrolysis. Accordingly, the two fully deprotected glucosylated amino acids **7** and **11** were tested for possible hydrolysis in the presence of α-glucosidase from *Bacillus stearothermophilus* (4 mU/ml) and β-D-glucosidase from almonds (60 mU/ml). In both cases, no hydrolysis could be observed after 4 h incubation at 37°C.



Scheme 2. *Reagents and conditions*: (a) DMF, $POCl_3$, CH_2Cl_2, 4 Å sieves, 60%; (b) $K_2Cr_2O_7$, AcOH, 50%; (c) NH_2NH_2, EtOH, 82%; (d) LiOH, CH_3CN/H_2O, 85%.



Scheme 3. *Reagents and conditions*: (a) NIS, CH_3CN/H_2O then $KHCO_3$, Bu_4NBr, toluene, 80%; (b) $K_2Cr_2O_7$, AcOH, 50%; (c) NH_2NH_2, EtOH, 82%; (d) LiOH, CH_3CN/H_2O, 85%.

3. Conclusion

In summary, two homochiral glycosylated hydroxyamino acids **7** and **11** were synthesized in good yield from the natural iridoid aucubin. Both possess three points of chemical diversity in addition to the sugar unit. Interestingly, the dihedral angles between the amino and carboxylic groups are significantly different in these two conformationally constrained compounds. Consequently, both appear as rigid scaffolds suitable for further development in combinatorial chemistry, particularly in the fields of glycopeptides and glycopeptide mimics.

References

1. Schweizer, F. *Angew. Chem., Int. Ed.* **2002**, *41*, 230–252.
2. Stöckle, M.; Voll, G.; Günther, R.; Lohof, E.; Locardi, E.; Gruner, S.; Kessler, H. *Org. Lett.* **2002**, *4*, 2501–2504.
3. Koviach, J. L.; Chappell, M. D.; Halcomb, R. L. *J. Org. Chem.* **2001**, *66*, 2318–2326.
4. Jobron, L.; Hummel, G. *Angew. Chem., Int. Ed.* **2000**, *39*, 1620–1624.
5. St. Hilaire, P. M.; Lowary, T. L.; Meldal, M.; Bock, K. *J. Am. Chem. Soc.* **1998**, *120*, 13312–13320.
6. Suhara, Y.; Hildreth, J. E. K.; Ichikawa, Y. *Terahedron Lett.* **1996**, *37*, 1575–1578.
7. Bourquelot, E.; Herissey, H. *Compt. Rend. Acad. Sci.* **1902**, *134*, 1441–1443.
8. Cachet, X.; Deguin, B.; Koch, M.; Makhlouf, K.; Tillequin, F. *J. Nat. Prod.* **1999**, *62*, 400–402.
9. Mouriès, C.; Deguin, B.; Koch, M.; Tillequin, F. *Helv. Chim. Acta* **2003**, *86*, in press.
10. Cachet, X.; Deguin, B.; Tillequin, F.; Rolland, Y.; Koch, M. *Helv. Chim. Acta* **2000**, *83*, 2812–2822.
11. Chiaroni, A.; Riche, C.; Cachet, X.; Deguin, B.; Koch, M.; Tillequin, F. *Acta Cryst.* **2000**, *C56*, 358–359.
12. Cachet, X.; Deguin, B.; Tillequin, F.; Koch, M.; Chiaroni, A. *Heterocycles* **2002**, *57*, 523–528.
13. Chong, J. M.; Park, S. B. *J. Org. Chem.* **1992**, *57*, 2220–2227.
14. Jensen, S. R.; Kirk, O.; Nielsen, B. J. *Tetrahedron* **1987**, *43*, 1949–1954.
15. Compound **4**: Mp 103°C (recrystallized from cyclohexane/AcOEt, 7:3); $[\alpha]_D^{20}=-25.6$ (*c* 1.05, $CHCl_3$); ESI-MS $m/z=946$ $(M+Na)^+$. Anal. calcd for $C_{49}H_{65}NO_{16}$: C, 63.69; H, 7.09; N, 1.52 Found: C, 63.75; H, 7.08; N, 1.52%; IR (film) *v* 2971, 2928, 2862, 1722, 1635, 1480, 1282, 1143, 721 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 8.74 (s, 1H, C*H*O), 7.40 (m, 2H, H-ar.), 6.80 (m, 2H, H-ar.), 6.57 (d, $J=1$, 1H, H-3), 6.05 (d, $J=8$, 1H, H-1), 5.86 (*br.* d, $J=9.5$, 1H, H-6), 5.43 (m, 1H, H-7), 5.30 (t, $J=9$, 1H, H-3′), 5.26 (dd, $J=8$, 9, 1H, H-2′), 5.14 (t, $J=9$, 1H, H-4′), 5.10 (d, $J=15$, 1H, H-10a), 4.88 (d, $J=15$, 1H, H-10b), 4.60 (d, $J=8$, 1H, H-1′), 4.17 (dd, $J=12.5$, 1.5, 1H, H-6′a), 4.00 (dd, $J=12.5$, 5.5, 1H, H-6′b), 3.23 (td, $J=9.5$, 8, 1H, H-5), 2.99 (ddd, $J=9$, 5.5, 1.5, 1H, H-5′), 2.54 (*br.* t, $J=8$, 1H, H-9), 1.30–1.00 (45H, 15 CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 189.3 (C-11), 178.2, 177.2, 176.3 (5 *C*=O Piv), 167.9 (2 *C*=O Pht.), 162.4 (C-3), 142.9 (C-8), 133.9 (2 *C*-ar.), 131.6 (2 *C*-ar.), 125.2 (C-7), 123.2 (2 *C*-ar), 118.7 (C-4), 98.4 (C-1), 98.2 (C-1′), 72.6 (C-5′), 72.0 (C-3′), 70.7 (C-2′), 67.7 (C-4′), 61.9 (C-6′), 61.5 (C-10), 55.9 (C-6), 46.2 (C-9), 33.9 (C-5), 29.6 (5 $C(CH_3)_3$), 27.0 (15 CH_3).
16. Nightingale, D. V.; Wagner, W. S. *J. Org. Chem.* **1960**, *25*, 32–34.
17. Compound **5**: Mp 133°C (recrystallized from CH_2Cl_2); $[\alpha]_D^{20}=-9$ (*c* 1, $CHCl_3$); (ESI-MS) m/z 962 $(M+Na)^+$. Anal. calcd for $C_{49}H_{65}NO_{17}$: C, 62.61; H, 6.97; N, 1.49. Found: C, 62.27; H, 6.64; N, 1.26%; IR (film) *v* 3254, 2974, 2936, 2909, 2874, 1735, 1725, 1638, 1481, 1461, 1399, 1368, 1330, 1282, 1206, 1140, 1075, 1038, 943, 721 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 7.95–7.79 (m, 4H, H-ar), 7.50 (d, $J=1.5$, 1H, H-3), 6.10 (d, $J=8$, 1H, H-1), 5.82 (*br.* s, 1H, H-7), 5.77 (*br.* d, $J=8.5$, 1H, H-6), 5.57 (t, $J=9.5$, 1H, H-3′), 5.32 (d, $J=8$, 1H, H-1′), 5.30 (t, $J=9.5$, 1H, H-4′), 5.14 (dd, $J=8$, 9.5, 1H, H-2′), 5.05 (*br.* s, 2H, H-10a, H-10b), 4.35 (dd, $J=12$, 1.5, 1H, H-6′a), 4.28 (dd, $J=12$, 5.5, 1H, H-6′b), 4.18 (ddd, $J=9.5$, 5.5, 1.5, 1H, H-5′), 3.73 (td, $J=8.5$, 1.5, 1H, H-5), 3.00 (*br.* t, $J=8.5$, 1H, H-9), 1.30–1.00 (5 s, 45H, 15 CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 178.2, 177.6, 177.3, 176.6, 176.5 (*C*=O Piv), 171.0 (C-11), 168.5 (2 *C*=O Pht.), 155.4 (C-3), 143.5 (C-8), 133.9 (2 *C*-ar), 131.6 (2 *C*-ar.), 124.9 (C-7), 123.1 (2 *C*-ar), 104.5 (C-4), 98.4 (C-1′), 97.6 (C-1), 72.6 (C-3′), 72.3 (C-5′), 70.9 (C-2′), 67.8 (C-4′), 62.0 (C-10), 61.8 (C-6′), 56.7 (C-6), 46.3 (C-9), 38.7 (5 $C(CH_3)_3$), 35.5 (C-5), 27.5 (15 CH_3).
18. Ing, H. R.; Manske, R. H. F. *J. Chem. Soc.* **1926**, 2348–2351.
19. **Compound 6**: Glassy solid; $[\alpha]=-34$ (*c* 0.03, $CHCl_3$); ESI-MS $m/z=832$ $(M+Na)^+$. Anal calcd for $C_{41}H_{63}NO_{15}$:

C, 60.80; H, 7.84; N, 1.73. Found: C, 60.16; H, 7.79; N, 1.75%; IR (film) ν 2963, 2924, 1744, 1724, 1639, 1534, 1480, 1398, 1367, 1273, 1234, 1111, 1076, 1037, 955, 889, 804 cm^{-1}; ^1H NMR (300 MHz, $CD_3OD/CDCl_3$) δ 8.50 (s, 1H, H-3), 5.88 (*br*.s, 1H, H-7), 5.45 (t, $J=9.5$, 1H, H-3′), 5.32 (t, $J=9.5$, 1H, H-4′), 5.14 (dd, $J=8$, 9.5, 1H, H-2′), 5.13 (d, $J=8$, 1H, H-1′), 4.99 (d, $J=9$, 1H, H-1), 4.93 (d, $J=15$, 1H, H-10a), 4.82 (*br*.d, $J=15$, 1H, H-10b), 4.50 (m, 1H, H-6), 4.32 (dd, $J=12.5$, 1.5, 1H, H-6′a), 4.26 (ddd, $J=9.5$, 3, 1.5 Hz, 1H, H-5′), 4.16 (dd, $J=12.5$, 3, 1H, H-6′b), 3.92 (*br*.d, $J=9$, 1H, H-9), 3.10 (*br*.t, $J=8.5$, 1H, H-5), 1.30–1.00 (5 s, 45H, 15 CH_3); ^{13}C NMR (75 MHz, $CDCl_3/CD_3OD$) 179.0, 178.4, 178.0, 176.9 (5 *C*=O Piv, C-11), 153.2 (C-3), 145.3 (C-8), 126.7 (C-7), 110.3 (C-4), 98.7 (C-1′), 97.7 (C-1), 72.8 (C-3′), 72.6 (C-5′), 71.2 (C-2′), 67.7 (C-4′), 62.2 (C-10), 61.4 (C-6′), 58.1 (C-6), 47.3 (C-9), 39.3 (C-5), 39.1 (5 $C(CH_3)_3$), 27.5 (15 CH_3). **Compound 7**: Amorphous powder. $[\alpha]_D^{20}=-15$ (*c* 0.9, H_2O); ESI-MS $m/z=390$ $(M+H)^+$, 412 $(M+Na)^+$. Anal. calcd for $C_{16}H_{23}NO_{10}$: C, 49.36; H, 5.95; N, 3.6. Found: C, 49.45; H, 5.95; N, 3.81%; IR (KBr) ν 3412, 2920, 2914, 1746, 1642, 1528, 1463, 1320, 1273, 1038, 991; ^1H NMR (300 MHz, D_2O) δ 7.30 (d, $J=1.5$, 1H, H-3), 5.29 (*br*.s, 1H, H-7), 4.92 (d, $J=8.5$, 1H, H-1), 4.68 (d, $J=8$, 1H, H-1′), 4.39 (*br*.d, $J=8$, 1H, H-6), 4.31 (*br*. d, $J=16$, 1H, H-10a), 4.12 (*br*.d, $J=16$, 1H, H-10b), 3.71 (dd, $J=12.5$, 1.5, 1H, H-6′a), 3.51 (dd, $J=12.5$, 5.5, 1H, H-6′b), 3.38–3.16 (m, 5H, H-9, H-3′, H-4′, H-5′, H-2′), 2.72 (*br*.t, $J=8$, 1H, H-5); ^{13}C NMR (75 MHz, CD_3OD/D_2O) 175.4 (C-11), 153.5 (C-3), 153.0 (C-8), 123.8 (C-7), 110.4 (C-4), 99.8 (C-1′), 99.1 (C-1), 77.3, 76.8, 73.8, 70.6 (C-3′, C-4′, C-2′, C-5′), 61.8 (C-6′), 60.8 (C-10), 58.6 (C-6), 46.8 (C-9), 38.7 (C-5).

20. **Compound 9**: Glassy solid; $[\alpha]_D^{20}=-48.05$ (*c* 0.33, $CHCl_3$); ESI-MS $m/z=950$ $(M+Na)^+$. Anal. calcd for $C_{48}H_{65}NO_{17}$: C, 62.12; H, 7.06; N, 1.51. Found: C, 62.10; H, 7.02; N, 1.49%; IR (film) ν 3254, 2972, 2935, 2874, 1774, 1740, 1716, 1480, 1461, 1398, 1367, 1336, 1282, 1141, 719 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85, 7.72 (2 m, 4H, H-ar), 6.18 (m, 1H, H-5), 5.90 (s, 1H, H-3), 5.40 (m, 1H, H-6), 5.37 (t, $J=9.5$, 1H, H-3″), 5.16 (t, $J=9.5$, 1H, H-4″), 5.15 (dd, $J=8$, 9.5, 1H, H-2″), 5.02 (d, $J=8$, 1H, H-1″), 4.78 (*br*.s, 2H, H-4′a, H-4′b), 4.75 (d, $J=6.5$, 1H, H-1), 4.22 (dd, $J=12.5$, 1.5, 1H, H-6″a), 4.09 (dd, $J=12.5$, 4.5, 1H, H-6″b), 3.80 (ddd, $J=9.5$, 4.5, 1.5, 1H, H-5″), 3.45 (q, $J=6.5$, 1H, H-6a), 3.32 (m, 1H, H-3a), 1.30–1.00 (5 s, 45H, 15 CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) 178.0, 177.8, 177.0, 176.3 (5 *C*=O Piv), 173.1 (*C*OOH), 168.6 (2 *C*=O Pht.), 136.2 (C-4), 134.1 (2 C-ar), 131.8 (2 C-ar.), 128.8 (C-5), 123.4 (2 C-ar), 102.0 (C-3), 96.9 (C-1″), 79.3 (C-1), 73.1 (C-3″), 72.1 (C-5″), 69.9 (C-2″), 67.6 (C-4″), 61.5 (C-4′, C-6″), 61.0 (C-6), 57.7 (C-3a), 48.8 (C-6a), 38.9 (5 $C(CH_3)_3$), 27.2 (15 CH_3). **Compound 10**: Mp 210°C decomp. (recrystallized from CH_3CN/H_2O, 1:1); $[\alpha]_D^{20}=-26$ (*c* 0.03, $CHCl_3$); ESI-MS $m/z=798$ $(M+H)^+$, 820 $(M+Na)^+$. Anal. calcd for $C_{40}H_{63}NO_{15}$: C, 60.21; H, 7.96; N, 1.76. Found: C, 59.47; H, 7.51; N, 1.50%; IR (film) ν 3455, 3194, 2971, 2936, 2909, 2874, 1741, 1596, 1480, 1460, 1398, 1367, 1280, 1140, 1061, 1036, 965 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.77 (m, 1H, H-5), 5.55 (s, 1H, H-3), 5.28 (t, $J=9.5$, 1H, H-3″), 5.18 (t, $J=9.5$, 1H, H-4″), 5.15 (d, $J=8$, 1H, H-1″), 4.98 (dd, $J=8$, 9.5, 1H, H-2″), 4.79 (*br*.d, $J=15$, 1H, H-4′a), 4.58 (*br*.d, $J=15$, 1H, H-4′b), 4.39 (m, 1H, H-6), 4.31 (*br*.d, $J=7.5$, 1H, H-1), 4.23 (*br*.d, $J=12.5$, 1H, H-6″a), 4.07 (dd, $J=12$, 3.5, 1H, H-6″b), 3.91 (*br*.d, $J=9.5$, 1H, H-5″), 3.30 (*br*.d, $J=7.5$, 1H, H-3a), 3.10 (q, $J=7.5$, 1H, H-6a), 1.30–1.00 (5 s, 45H, 15 CH_3); ^{13}C (75 MHz, $CDCl_3$) 178.1, 177.9, 177.2, 176.9, 176.1 (5 *C*=O Piv, C-1′), 141.3 (C-4), 125.8 (C-5), 100.5 (C-3), 95.7 (C-1″), 79.1 (C-1), 72.2 (C-3″), 71.9 (C-5″), 70.9 (C-2″), 67.5 (C-4″), 61.35 (C-6″), 60.9 (C-4′), 57.9 (C-3a), 54.5 (C-6), 46.8 (C-6a), 38.7 (5 $C(CH_3)_3$), 27.1 (15 CH_3). **Compound 11**: Glassy solid; $[\alpha]_D^{20}=-33$ (*c* 0.1, H_2O); ESI-MS $m/z=400$ $(M+Na)^+$. Anal. calcd for $C_{15}H_{23}NO_{10}$: C, 47.74; H, 6.14; N, 3.71. Found: C, 47.68; H, 5.13; N, 3.04%; IR (KBr) ν 3407, 2918, 2318, 2313, 1651, 1587, 1412, 1307, 1069, 1011, 958 cm^{-1}; ^1H NMR (300 MHz, CD_3OD/D_2O) δ 5.93 (m, 1H, H-5), 5.81 (s, 1H, H-3), 4.96 (d, $J=8$, 1H, H-1″), 4.72 (*br*.d, $J=4.5$, 1H, H-6), 4.59 (d, $J=7$, 1H, H-1), 4.48 (d, $J=15$, 1H, H-4′a), 4.38 (d, $J=15$, 1H, H-4′b), 4.08 (dd, $J=12.5$, 1.5, 1H, H-6″a), 3.88 (dd, $J=12.5$, 5.5, 1H, H-6″b), 3.70–3.40 (m, 5H, H-3a, H-6a, H-3″, H-4″, H-5″, H-2″); ^{13}C NMR (75 MHz, CD_3OD/D_2O) 179.7 (C-1′), 147.8 (C-4), 124.1 (C-5), 105.7 (C-3), 101.5 (C-1″), 80.2 (C-1), 77.3, 76.7, 74.0, 70.4 (C-3″, C-4″, C-2″, C-5″), 61.7 (C-6″), 59.6 (C-4′), 58.4 (C-3a), 57.1 (C-6), 48.2 (C-6a).