Expeditious Stereoselective Synthesis of L-Iminosugar Precursors via a Mitsunobu Reaction

Antoine Bussière, Véronique Barragan-Montero,* Khalid Oumzil, Jean-Yves Winum, Jean-Louis Montero*

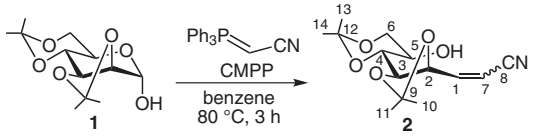
Institut des Biomolécules Max Mousseron (IBMM) UMR 5247 CNRS-UM1-UM2 Bâtiment de Recherche Max Mousseron, Ecole Nationale Supérieure de Chimie de Montpellier, 8 Rue de l'Ecole Normale, 34296 Montpellier Cedex, France
Fax +33(4)67144343; E-mail: jean-louis.montero@univ-montp2.fr; E-mail: vbarragan@univ-montp2.fr
Received 19 December 2008

Abstract: An efficient stereoselective synthesis of L-imino-*C*-gulosides is disclosed. Starting from the 2,3:4,6-di-*O*-isopropylidene-D-mannopyranose the synthetic pathway involves first a Wittig reaction with CMPP to introduce the carbon at the pseudo-anomeric position, followed by a Michael reaction under ultrasound activation to introduce the nitrogen center, and finally a Mitsunobu reaction for the ring closure leading to the *C*-iminosugar from the L-series.

Key words: carbohydrates, azasugars, stereoselective, Mitsunobu reaction, glycosidase

Among carbohydrate mimetics, iminosugars (or azasugars), in which the endocyclic oxygen of the sugar is replaced by a nitrogen atom, attract considerable attention. Nojirimycin, a natural azasugar isolated from *Streptomyces* filtrate, was found to inhibit α- and β-glucosidase.[1] Extended researches have enlarged the range of biological activities of azasugars and demonstrated that those low-molecular-weight compounds are powerful inhibitors of a variety of glycosidases. As a consequence, the therapeutical potentials of natural or synthetic azasugars are remarkable.[2–5] Compared to azasugars, aza-*C*-glycosides, which possess a C-linked aglycon, have shown to improve the selectivity of the inhibitors. Moreover, they offer the possibility of further functionalization and/or elongation in search of improved biological activities, inhibitory properties depending also on the nature of the substituents on the nitrogen atom. Since several decades, various synthetic methods focusing on azasugars and aza-*C*-glycosides have been developed.[6–15] Interest in finding simple and general ways to synthesize such carbohydrate mimetics has, of course, been prompted by their remarkable properties.

The second aspect of our research deals with L-sugars. While D-sugars are abundant, L-sugars are rare and expensive. Moreover, the latter play important roles in therapy, and efforts are needed to develop the synthesis of these valuable sugars.[16–21] In this work, we were interested to find a direct and potentially general approach to aza-*C*-glycosides from the L-series using a strategy developed by our group. Thus, as part of our program devoted to develop new synthetic routes to sugar derivatives, we have recently published a powerful cascade sequence using (cyanomethylene)trimethylphosphorane (CMMP) for the synthesis of carba-*C*-glycosides.[22] However, in order to prepare azahexopyranoses using a comparable approach, a one-pot reaction could not be envisaged, and the conversion had to be separated into three sequential steps. The reaction involves (a) a ring-opening process with the aim to free the hemiacetal hydroxyl group; (b) nucleophile addition at the anomeric position in order to introduce the nitrogen with a variety of substituents, and (c) a ring closure (Scheme 1 and Scheme 2).

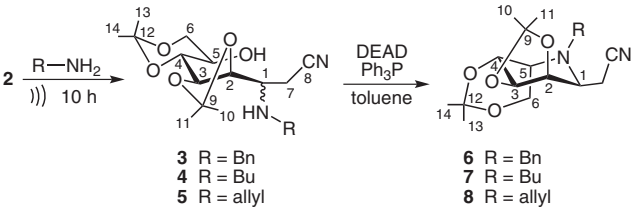


Scheme 1

To access the L-azahexopyranose system, we focused the methodology on mannose, using 2,3:4,6-di-*O*-isopropylidene-D-mannopyranose (**1**) as starting material. In order to achieve the ring opening, a Wittig reaction between (cyanomethylene)triphenylphosphorane (CMPP, more stable than CMMP) and the protected sugar – but free at the anomeric position – was performed under reflux in benzene for 3 hours. An improved and easy procedure to synthesize CMPP was previously described by Wasserman et al.[23] The equilibrium between the open and cyclic forms allowed CMPP to react on the aldehyde. The *Z*-isomer **2** was obtained as the main product[24] (*Z*/*E* = 7:3) with no ring closure being observed during the reaction nor during the purification.[25] In this compound, the conjugation of the alkene with the nitrile group allowed an intermolecular Michael addition of nucleophiles. In this case, three different amines were used to explore the reaction as described in Scheme 2. Michael addition of amines without an activating system gives very low yields, and many methods have been reported in the literature such as the use of amberlyst 15,[26] β-cyclodextrin,[27] cerium(IV) ammonium nitrate,[28] borax,[29] and ultrasound irradiation.[30] Our thought was to find a better procedure in order to achieve the reaction under more convenient conditions with a low rate of byproducts and subsequent ease of purification. Therefore, ultrasound activation seemed highly promising (Scheme 2). The *Z*-isomer and the amine were placed in an ultrasound bath for 10 hours to give exclusively (according to the amine involved in the reaction)

SYNLETT 2009, No. 6, pp 0978–0980
Advanced online publication: 16.03.2009
DOI: 10.1055/s-0028-1088209; Art ID: G39508ST

compounds **3**, **4**, and **5** in high yields.[31] These resulting compounds presented a free hydroxy group on the pseudo-C5 position and a secondary amine at the pseudo-anomeric center. At this stage, the stereochemistry of C1 could not be assigned. The two entities were engaged in an intramolecular Mitsunobu reaction which allowed the ring closure. The substitution of the activated hydroxyl group by the amine proceeded with a complete inversion of configuration. Thus, the L-enantiomer, a L-gulose derivative, was selectively obtained in 70% yield (Scheme 2) in each case.[32] It is worth pointing out that compounds **6**, **7**, and **8** are α-anomers, as indicated by NMR experiments (J_{1-2} close to 2 Hz). This implies that compounds **3**, **4**, and **5** possess an *S*-configuration for C1.



Scheme 2

In summary, we have developed a simple and efficient stereoselective synthesis of aza-*C*-gulosides of the L-series starting from a D-sugar. Compared to published methodologies, our strategy allows in few steps the preparation of a L-iminosugar with a variety of substituents on the nitrogen atom and an aglycon moiety that can be modified. The application of this methodology is currently being extended to other monosaccharides, with emphasis on the preparation of new heterosugars.

Acknowledgment

We thank the Ministère de l'Enseignement Supérieur et de la Recherche for a Doctoral fellowship (A. B.).

References and Notes

(1) Inouye, S.; Tsuruoka, T.; Nida, T. *J. Antibiot.* **1966**, *19*, 288.
(2) Borges de Melo, E.; da Silveira Gomes, A.; Carvalho, I. *Tetrahedron* **2006**, *62*, 10277.
(3) Suganuma, R.; Walden, C. M.; Butters, T. D.; Platt, F. M.; Dwek, R. A.; Yanagimachi, R.; Van der Spoel, A. C. *Biol. Reprod.* **2005**, *72*, 805.
(4) Zou, W. *Curr. Top. Med. Chem.* **2005**, *5*, 1363.
(5) *Iminosugars: From Synthesis to Therapeutic Applications*; Compain, P.; Martin, O. R., Eds.; John Wiley and Sons, Ltd.: Chichester, **2007**.
(6) McDonnell, C.; Cronin, L.; O'Brien, J. L.; Murphy, P. V. *J. Org. Chem.* **2004**, *69*, 3565.
(7) Songa, X.; Hollingsworth, R. I. *Tetrahedron Lett.* **2007**, *48*, 3115.
(8) La Ferla, B. L.; Bugada, P.; Cipolla, L.; Peri, F.; Nicotra, F. *Eur. J. Org. Chem.* **2004**, 2451.
(9) Myers, W. H.; Robertson, G. J. *J. Am. Chem. Soc.* **1943**, *65*, 8.
(10) Jones, J. K. N.; Szarek, W. A. *Can. J. Chem.* **1963**, *41*, 636.
(11) Hanessian, S.; Haskell, T. H. *J. Org. Chem.* **1963**, *28*, 2604.
(12) Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 495.
(13) Behr, J.-B.; Plantier-Royon, R. *Recent Res. Dev. Org. Chem.* **2006**, *10*, 23.
(14) Afarinkia, K.; Bahar, A. *Tetrahedron: Asymmetry* **2005**, *16*, 1239.
(15) Ruiz, M.; Ruanova, T. M.; Blanco, O.; Nunez, F.; Pato, C.; Ojea, V. *J. Org. Chem.* **2008**, *73*, 2240.
(16) Aguilar, M.; Diaz-Perez, P.; Garcia-Moreno, M. I.; Ortiz Mellet, C.; Garcia Fernandez, J. M. *J. Org. Chem.* **2008**, *73*, 1995; and references cited therein.
(17) Takahashi, H.; Shida, T.; Hitomi, Y.; Iwai, Y.; Miyama, N.; Nishiyama, K.; Sawada, D.; Ikegami, S. *Chem. Eur. J.* **2006**, *12*, 5868.
(18) Joseph, C. C.; Regeling, H.; Zwanenburg, B.; Chittenden, G. J. F. *Carbohydr. Res.* **2002**, *337*, 1083.
(19) Pandey, G.; Bharadwaj, K. C.; Khan, M. I.; Shashidhara, K. S.; Puranik, V. G. *Org. Biomol. Chem.* **2008**, *6*, 2587.
(20) Pearson, M. S. M.; Mathé-Allainmat, M.; Fargeas, V.; Lebreton, J. *Eur. J. Org. Chem.* **2005**, 2159.
(21) Shitara, E.; Nishimura, Y.; Kojima, F.; Takeuchi, T. *Bioorg. Med. Chem.* **2000**, *8*, 343.
(22) Bussiere, A.; Barragan-Montero, V.; Toupet, L.; Clavel, C.; Montero, J.-L. *Lett. Org. Chem.* **2006**, *3*, 654.
(23) Wasserman, H. H.; Petersen, A. K. *Tetrahedron Lett.* **1997**, *38*, 953; and references cited therein.
(24) **Synthesis of Compound 2**
To a solution of 2,3:4,6-Di-*O*-isopropylidene-D-manno-pyranose (1 equiv, 23 mmol, 6 g) in anhyd benzene was added(cyanomethylene) triphenylphosphorane (3 equiv, 69 mmol, 21 g). The mixture was stirred and refluxed under argon atmosphere for 3 h. The reaction mixture was diluted with CH_2Cl_2 (200 mL) and washed twice with brine (50 mL). The organic layer was dried over anhyd Na_2SO_4 for 30 min and concentrated under vacuum to give pale yellowish oil. The crude was chromatographed on SiO_2 (PE–Et_2O, 5:5) to afford the two isomers (6.5 g, 70% for *Z*-isomer) as colorless oils. R_f = 0.16 (*Z*-isomer, major), 0.08 (*E*-isomer, minor; PE–Et_2O, 5:5). ^{1}H NMR (400 MHz, acetone-d_6): δ (*Z*-isomer) = 6.81 (dd, J_{1-7} = 11.26 Hz, J_{1-2} = 8.00 Hz, H_1), 5.77 (dd, J_{7-1} = 11.27 Hz, J_{7-2} = 1.30 Hz, H_7), 5.16 (dt, J_{2-1} = 7.85 Hz, J_{2-3} = 7.80 Hz, J_{2-7} = 1.27 Hz, H_2), 4.72 (dd, J_{3-2} = 7.48 Hz, J_{3-4} = 1.45 Hz, H_3), 4.29 (d, J_{OH-5} = 6.01 Hz, –OH), 3.81–3.70 (m, H_5, H_{6a}), 3.58 (dd, *J* = 10.16, 9.07 Hz, H_{6a}), 3.48 (dd, J_{4-5} = 9.17 Hz, J_{4-3} = 1.43 Hz, H_4), 1.48, 1.41, 1.37, 1.31 (4 s, 12 H, H_{10}, H_{11}, H_{13}, H_{14}). ^{13}C NMR (100 MHz, acetone-d_6): δ (*Z*-isomer) = 153.45 (C_1), 117.16 (C_8), 111.70 (C_9), 102.34 (C_7), 99.90 (C_{12}), 77.87 (C_2), 77.64 (C_3), 74.44 (C_4), 66.48 (C_6), 63.94 (C_5), 30.09, 27.90, 26.89, 19.96 (C_{10}, C_{11}, C_{13}, C_{14}). MS (ESI$^+$): *m/z* = 306.22 [M + Na]$^+$.
(25) Nicotra, F.; Ronchetti, F.; Russo, G.; Toma, L. *Tetrahedron Lett.* **1984**, *25*, 5697.
(26) Das, B.; Chowdhury, N. *J. Mol. Catal. A.: Chem.* **2007**, *263*, 212.
(27) Surendra, K.; Krishnaveni, N. S.; Sridhar, R.; Rao, K. R. *Tetrahedron Lett.* **2006**, *47*, 2125.
(28) Duan, Z.; Xuan, X.; Li, T.; Yang, C.; Wu, Y. *Tetrahedron Lett.* **2006**, *47*, 5433.
(29) Hussain, S.; Bharadwaj, S. K.; Chaudhuri, M. K.; Kalita, H. *Eur. J. Org. Chem.* **2007**, 374.
(30) Yang, J.-M.; Ji, S.-J.; Gu, D.-G.; Shen, Z.-L.; Wang, S.-Y. *J. Organomet. Chem.* **2005**, *690*, 2989.
(31) **Typical Procedure for the Synthesis of Compounds 3–5**
Compound **2** (1 equiv) was dissolved in dry amine in excess. The mixture was placed in an ultrasound bath under an argon atmosphere for 10 h. The unreacted amine was removed under reduced pressure and the byproducts removed by flash chromatography on SiO_2 (PE–Et_2O, 8:2) to afford

compounds **3**, **4**, or **5** as colorless oils in 80% yield.
Compound **3**: R_f = 0.11 (PE–Et_2O, 8:2). ^{1}H NMR (400 MHz, acetone-d_6): δ = 7.46–7.19 (m, 5 H, H_c, H_d, H_e), 4.48 (dd, J_{3-2} = 6.29 Hz, J_{3-4} = 1.55 Hz, H_3), 4.28 (dd, J_{2-1} = 8.85 Hz, J_{2-3} = 6.29 Hz, H_2), 4.22 (d, J_{OH-5} = 5.88 Hz, OH), ν_0 = 3.82 (ABq, 2 H, ν_A = 4.03, ν_B = 3.87, Δν = 64.2 Hz, J_{AB} = 14.0 Hz, H_a), 3.79–3.68 (m, H_5, H_{6a}), 3.63–3.50 (m, H_{6b}), 3.61 (dd, J_{4-5} = 8.93 Hz, J_{4-3} = 1.57 Hz, H_4), 3.33 (ddd, J_{1-2} = 8.92 Hz, J_{1-7b} = 5.18 Hz, J_{1-7a} = 4.49 Hz, H_1), 2.81 (dd, J_{7a-7b} = 17.39 Hz, J_{7a-1} = 4.44 Hz, H_{7a}) 2.58 (dd, J_{7b-7a} = 17.40 Hz, J_{7b-1} = 5.29 Hz, H_{7b}), 1.48, 1.33, 1.23, 1.20 (4 s, 12 H, H_{10}, H_{11}, H_{13}, H_{14}). ^{13}C NMR (100 MHz, acetone-d_6): δ = 142.55 (C_b), 130.07 and 129.87 (2 C, C_c, C_d), 128.55 (C_e), 119.67 (C_8), 110.31 (C_9), 99.82 (C_{12}), 80.65 (C_2), 75.79 (C_3), 74.44 (C_4), 66.48 (C_6), 63.92 (C_5), 53.73 (C_1), 52.16 (C_a), 29.98, 27.75, 27.20, 20.03 (4C, C_{10}, C_{11}, C_{13}, C_{14}), 22.03 (C_7). MS (ESI$^+$): *m/z* = 391.13 [M + H]$^+$, 413.13 [M + Na]$^+$. MS (ESI$^-$): *m/z* = 425.46 [M + Cl]$^-$.
Compound **4**: R_f = 0.28 (Et_2O). ^{1}H NMR (400 MHz, acetone-d_6): δ = 4.48 (dd, J_{3-2} = 6.26 Hz, J_{3-4} = 1.56 Hz, H_3), 4.20 (dd, J_{2-1} = 8.53 Hz, J_{2-3} = 6.26 Hz, H_2), 3.84–3.67 (m, H_4, H_5, H_{6a}), 3.64–3.56 (m, H_{6b}), 3.28 (ddd, J_{1-2} = 8.52 Hz, J_{1-7b} = 5.54 Hz, J_{1-7a} = 4.52 Hz, H_1), 2.73 (dd, J_{7a-7b} = 17.31 Hz, J_{7a-1} = 4.53 Hz, H_{7a}), 2.55 (dd, J_{7b-7a} = 17.32 Hz, J_{7b-1} = 5.54 Hz, H_{7b}), 2.78–2.70 (m, H_{9a}), 2.68–2.61 (m, H_{9b}), 1.49–1.32 (m, H_{10}, H_{11}), 1.50, 1.48, 1.33, 1,32 (4 s, 12 H, H_{14}, H_{15}, H_{17}, H_{18}), 0.91 (t, J_{12-11a} = 7.20, J_{12-11b} = 7.20 Hz, H_{12}). ^{13}C NMR (100 MHz, acetone-d_6): δ = 119.83 (C_8), 110.15 (C_{13}), 99.91 (C_{16}), 80.26 (C_2), 75.83 (C_3), 74.45 (C_4), 66.57 (C_6), 64.07 (C_5), 55.36 (C_1), 48.30 (C_9), 34.09 (C_{10}), 30.15, 27.75, 27.13, 20.45 (4 C, C_{14}, C_{15}, C_{17}, C_{18}), 21.95 (C_{11}), 15.25 (C_{12}). MS (ESI$^+$): *m/z* = 357.31 [M + H]$^+$, 379.33 [M + Na]$^+$. MS (ESI$^-$): *m/z* = 355.36 [M – H]$^-$, 391.28 [M + Cl]$^-$.
Compound **5**: R_f = 0.08 (PE–Et_2O, 9:1). ^{1}H NMR (400 MHz, acetone-d_6): δ = 5.90 (dddd, $J_{10-11trans}$ = 17.29 Hz, $J_{10-11cis}$ = 10.33 Hz, J = 6.15 Hz, J = 5.19 Hz, H_{10}), 5.25 (qd, $J_{11trans-10}$ = 17.29 Hz, J = 1.80, 1.80, 1.79 Hz, $H_{11trans}$), 5.08 (ddd, $J_{11cis-10}$ = 10.34 Hz, J = 3.42 Hz, J = 1.48 Hz, H_{11cis}), 4.48 (dd, J_{3-2} = 6.28 Hz, J = 1.57 Hz, H_3), 4.24 (dd, J = 8.68 Hz, J_{2-3} = 6.27 Hz, H_2), 3.82–3.55 (m, 4 H, H_4, H_5, H_{6a}, H_{6b}), 3.47–3.29 (m, 3 H, H_1, H_{9a}, H_{9b}), 2.75 (dd, J_{7a-7b} = 17.35 Hz, J = 4.49 Hz, H_{7a}), 2.55 (dd, J_{7b-7a} = 17.35 Hz, J = 5.41 Hz, H_{7b}), 1.48, 1.32 (2 d, 12 H, H_{13}, H_{14}, H_{16}, H_{17}). ^{13}C NMR (100 MHz, acetone-d_6): δ = 139.48 (C_{10}), 119.76 (C_8), 116.70 (C_{11}), 110.26 (C_{12}), 99.90 (C_{15}), 80.52 (C_2), 75.85 (C_3), 74.52 (C_4), 66.54 (C_6), 63.96 (C_5), 53.15 (C_1), 51 (C_9), 30.16, 27.74, 27.74, 20.34 (C_{13}, C_{14}, C_{15}, C_{17}), 22.26 (C_7). MS (ESI$^+$): *m/z* = 341.27 [M + H]$^+$, 363.29 [M + Na]$^+$.

(32) **Typical Procedure for the Synthesis of Compounds 6–8**
Compounds **3**, **4**, or **5** (1 equiv) and Ph_3P (2 equiv) were dissolved in a minimum amount of dry toluene. The mixture was stirred under argon at r.t. DEAD (2 equiv, 2.56 mmol, 1.2 mL) was added dropwise, and the mixture was stirred further 3 h. The crude product was purified by chromatography on SiO_2 (PE–Et_2O, 7:3) to afford compounds **6**, **7**, or **8** in 70% yield.

Compound **6**: R_f = 0.2 (PE–Et_2O, 7:3); $[\alpha]_D$ +5.86 (*c* 1, $HCCl_3$, 25 °C). ^{1}H NMR (400 MHz, acetone d_6): δ = 7.42 (m, 2 H, H_c), 7.30 (m, 2 H, H_d), 7.23 (m, 1 H, H_e), 4.43 (dd, J_{3-4} = 2.5 Hz, J_{3-2} = 8.0 Hz, H_3), 4.25 (dd, J_{4-3} = 2.7 Hz, J_{4-5} = 5.6 Hz, H_4), 4.23 (dd, J_{2-1} = 2.1 Hz, J_{2-3} = 8.1 Hz, H_2), ν_0 = 3.99 (ABq, 2 H, ν_A = 4.13, ν_B = 3.85, Δν = 112.3 Hz, J_{AB} = 14.3 Hz, H_a), 3.85 (ddd, J_{1-2} = 2.2 Hz, J_{1-7b} = 7.3 Hz, J_{1-7a} = 7.4 Hz, H_1), 3.38 (dd, J_{6a-5} = 6.1 Hz, J_{6a-6b} = 11.7 Hz, H_{6a}), 3.33 (dd, J_{6b-5} = 6.4 Hz, J_{6b-5} = 11.8 Hz, H_{6b}), 2.99 (dd, J_{7a-1} = 7.7 Hz, J_{7a-7b} = 17.0 Hz, H_{7a}), 3.00 (ddd, J_{5-6a} = 6.3 Hz, J_{5-6b} = 6.4 Hz, J_{5-4} = 5.7 Hz, H_5), 2.91 (dd, J_{7b-1} = 7.2 Hz, J_{7b-7a} = 17.0 Hz, H_{7b}), 1.61 (s, CH_3), 1.38 (d, J = 0.4 Hz, CH_3), 1.30 (s, CH_3), 1.30 (s, CH_3). ^{13}C NMR (100 MHz, acetone-d_6): δ = 143.17 (C_b), 130.49, 129.94 ($C_{ortho/meta}$), 128.71 (C_{para}), 120.32 (C_8), 110.60 (C_9), 101.23 (C_{12}), 75.99 (C_3), 73.64 (C_4), 65.87 (C_2), 63.77 (C_6), 56.87 (C_a), 56.15 (C_5), 53.49 (C_1), 27.67, 27.25, 24.44, 22.68 (C_{10}, C_{11}, C_{13}, C_{14}), 19.81 (C_7). MS (ESI$^+$): *m/z* = 373.32 [M + H]$^+$, 395.28 [M + Na]$^+$, 411.18 [M + K]$^+$, 767.57 [2 M + Na]$^+$.
Compound **7**: R_f = 0.6 (PE–Et_2O, 8:2); $[\alpha]_D$ +6.52 (*c* 1, $HCCl_3$, 25 °C). ^{1}H NMR (400 MHz, acetone-d_6): δ = 4.38 (dd, J_{3-4} = 26.0 Hz, J_{3-2} = 8.0 Hz, H_3), 4.26 (dd, J_{4-3} = 2.6 Hz, J_{4-5} = 5.6 Hz, H_4), 4.15 (dd, J_{2-1} = 2.2 Hz, J_{2-3} = 8.0 Hz, H_2), 3.78 (dd, J_{6a-5} = 6.2 Hz, J_{6a-6b} = 11.7 Hz, H_{6a}), 3.69 (ddd, J_{1-2} = 2.2 Hz, J_{1-7a} = 7.7 Hz, J_{1-7b} = 8.4 Hz, H_1), 3.56 (dd, J_{6b-5} = 6.6 Hz, J_{6b-6a} = 11.7 Hz, H_{6b}), 3.05 (q, J_{5-4} = J_{5-6a} = J_{5-6b} = 6.1 Hz, H_5), 2.86–2.64 (m, 4 H, H_{7a}, H_{7b}, H_{9a}, H_{9b}), (s, 3 H, CH_3), 1.41–1.20 (m, 4 H, H_{10a}, H_{10b}, H_{11a}, H_{11b}), 1.47, 1.36, 1.33, 1.30 (4 s, 12 H, H_{14}, H_{15}, H_{17}, H_{18}). ^{13}C NMR (100 MHz, acetone-d_6): δ = 120.20 (C_8), 110.46 (C_{13}), 101.13 (C_{16}), 75.97 (C_3), 73.47 (C_2), 65.69 (C_4), 64.57 (C_6), 57.07 (C_5), 53.58 (C_1), 52.66 (C_9), 35.35 (C_{10}), 27.60, 27.08, 24.47, 22.85 (C_{14}, C_{15}, C_{17}, C_{18}), 21.60 (C_{11}), 19.81 (C_7), 15.38 (C_{12}). MS (ESI$^+$): *m/z* = 339.36 [M + H$^+$], 361.26 [M + Na]$^+$, 699.47 [2 M + Na]$^+$.
Compound **8**: R_f = 0.28 (PE–Et_2O, 8:2); $[\alpha]_D$ +8.34 (*c* 1, $HCCl_3$, 25 °C). ^{1}H NMR (400 MHz, acetone-d_6): δ = 5.76 (dddd, $J_{10-11trans}$ = 17.19 Hz, $J_{10-11cis}$ = 10.07 Hz, J_{10-9b} = 7.99 Hz, J_{10-9a} = 4.40 Hz, H_{10}), 5.15 (dtd, $J_{11trans-10}$ = 17.21 Hz, J = 2.03 Hz, $J_{11trans-11cis}$ = 1.11 Hz, $H_{11trans}$), 5.00 (dtd, $J_{10-11cis}$ = 10.07 Hz, J = 1.88 Hz, $J_{11cis-9a}$ = 1.87 Hz, $J_{11cis-11trans}$ = 0.92 Hz, H_{11cis}), 4.37 (dd, J_{3-2} = 7.94 Hz, J_{3-4} = 2.60 Hz, H_3), 4.25 (dd, J_{4-5} = 5.27 Hz, J_{4-3} = 2.60 Hz, H_4), 4.17 (dd, J_{2-3} = 7.95 Hz, J_{2-1} = 2.12 Hz, H_2), 3.78 (td, J = 8.17 Hz, J_{1-2} = 1.94 Hz, J = 1.94 Hz, H_1), 3.74 (dd, J_{6a-6b} = 11.82 Hz, J = 5.63 Hz, H_{6a-6b}), 3.60 (tdd, J_{9a-9b} = 14.88 Hz, J_{9a-10} = 4.12 Hz, $J_{9a-11cis}$ = 1.87 Hz, J = 1.87 Hz, H_{9a}), 3.57 (dd, J_{6b-6a} = 11.76 Hz, J = 5.85 Hz, H_{6a-6b}), 3.26 (tdd, J_{9b-9a} = 14.88 Hz, J_{9b-10} = 7.99 Hz, J = 1.04, 1.04 Hz, H_{9b}), 2.99 (q, J_{5-4} = 5.59 Hz, J_{5-6a} = 5.59 Hz, J_{5-6b} = 5.59 Hz, H_5), 2.84 (d, J = 0.65 Hz, H_{7a}), 2.82 (s, H_{7b}), 1.50, 1.37, 1.34, 1.30 (4 d, 12 H, J = 0.58 Hz, H_{13}, H_{14}, H_{16}, H_{17}). ^{13}C NMR (100 MHz, acetone-d_6): δ = 140.93 (C_{10}), 120.04 (C_8), 116.88 (C_{11}), 110.53 (C_{12}), 101.04 (C_{15}), 75.88 (C_3), 73.75 (C_2), 66.04 (C_4), 64.51 (C_6), 55.81 (C_9), 55.67 (C_5), 53.38 (C_1), 28.07, 27.20, 24.50, 22.38 ($C_{14,}$ C_{13}, C_{16}, C_{17}), 19.77 (C_7). MS (ESI$^+$): *m/z* = 323.27 [M + H]$^+$, 345.21 [M + Na]$^+$, 361.20 [M + K]$^+$.