

Efficient Preparation and Characterization of Carbohydrate Based Monomers. D-mannose Derivatives

L. M. Stefan, A. M. Pană, M. Silion, M. Bălan, G. Bandur, and L. M. Rusnac

Abstract— The field of polymeric biomaterials is very important from the socio-economical viewpoint. Synthetic carbohydrate polymers are being increasingly investigated as biodegradable, biocompatible and biorenewable materials. The aim of this study was to synthesize and characterize some derivatives based on D-mannose. D-mannose was chemically modified to obtain 1-O-allyl-2,3:5,6-di-O-isopropylidene-D-mannofuranose and 1-O-(2',3'-epoxy-propyl)-2,3:5,6-di-O-isopropylidene-D-mannofuranose.

The chemical structure of the resulting compounds was characterized by FT-IR and NMR spectroscopy, and by HPLC-MS.

Keywords—D-mannose, biopolymers, spectroscopy, synthesis.

1. INTRODUCTION

THE last decade has been a time of intense efforts in the field of biodegradable polymers. Polymers are some of the most widely used materials in our everyday life. Their applications include: food and cosmetic industries, agriculture, drug delivery systems, bioadhesives, ocular devices, and materials for orthopedic applications [1]-[3]. Non-biodegradability of the most commercially available plastics has caused many environmental problems (common plastics often decompose over hundreds of years). Ecological and economical concerns have attracted great interest towards

renewable resources [4]. Facing the problems of environmental concerns and limits of fossil resources, there has been a growing trend in using carbohydrates as raw materials in polymers synthesis due to their inherent biodegradability and availability. Carbohydrate-based polymers are potential “green” materials capable to substitute polymers based on petrochemical resources [5], [6].

The term “glycopolymers” includes both natural and artificial polymers grafted on carbohydrates and polymers derived from chemically modified sugars; it includes not only linear polymers but also branched polymers and dendrimers [7], [8].

Glycopolymers can be classified into three groups (fig. 1): polymers containing carbohydrate moieties attached to side polymeric chains, polymers containing carbohydrate units in the main polymeric chain and reticulated polymers where the carbohydrates are included into the hydrocarbon matrix [9].

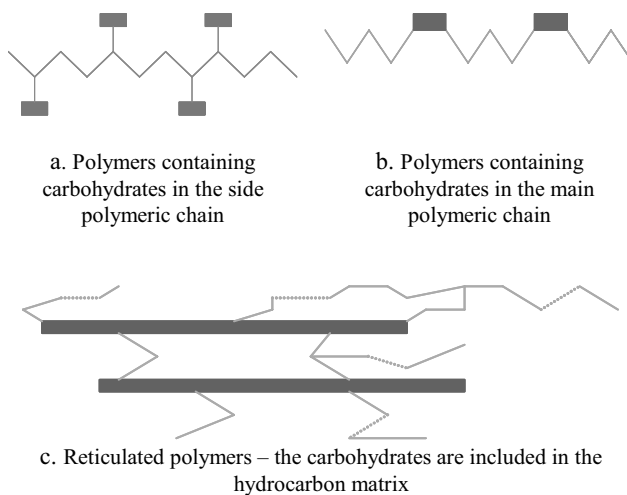


Fig. 1 The classification of glycopolymers [9]

In accordance with our continuing interest to obtain biodegradable polymers, in this study we report the results obtained in the synthesis and characterization of some D-mannose derivatives, namely 1-O-allyl-2,3:5,6-di-O-isopropylidene-D-mannofuranose (3) and 1-O-(2',3'-

epoxy-propyl)-2,3:5,6-di-O-isopropylidene-D-mannofuranose

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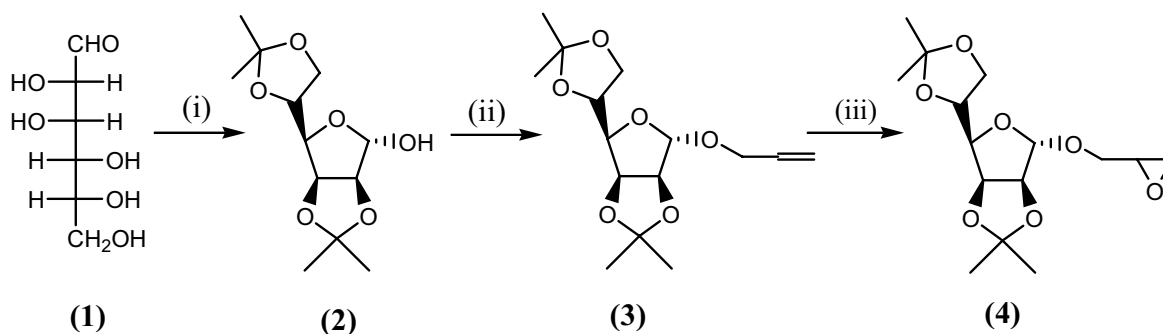
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(4). The infrared and NMR analyses confirmed the structure of the synthesized compound, and additionally their molecular weight was confirmed by HPLC-MS analysis. The synthesis

of these derivatives based on D-mannose (1) was achieved according to Scheme 1.



Scheme 1. Preparation of 1-O-(2',3'-epoxy-propyl)-2,3:5,6-di-O-isopropylidene-D-mannofuranose: i) acetone, H₂SO₄, 0°C – r.t., 5h; ii) AllCl, NaH, DMF; iii) meta-chloroperoxybenzoic acid;

II. EXPERIMENTAL

The key intermediate, diacetone mannose was obtained according to the literature. White crystals; mp=122-125°C. [10], [11]. The diacetone mannose derivative 2 was allylated with allyl chloride (AllCl) under basic catalysis (NaH) in anhydrous DMF. The excess catalyst was neutralized with excess MeOH [12], [13]. The product was purified by silicagel column chromatography (hexane:ethyl acetate = 6:1) to obtain 3 as a colorless syrup in 85% yield.

The synthesis of (4) was achieved using meta-chloroperoxybenzoic acid (MCPBA) at low temperature: 1-O-allyl-2,3:5,6-di-O-isopropylidene-D-mannofuranose 3 (1.00 g, 3.33 mmol) in 5 mL chloroform was cooled to 0°C. MCPBA (2.29 g, 13.27 mmol, 4 equiv.) was added at once. The reaction mass was stirred vigorously at room temperature. After 24 hours the reaction mixture was diluted with chloroform, washed with brine, dried over Na₂SO₄, and concentrated under vacuum. The product was purified by silicagel column chromatography (hexane:ethyl acetate = 2:1) to obtain 4 as a syrup in 85% yield.

III. MATERIALS AND METHODS

D-(+)-mannose (98%), cyclohexane, chloroform, ethyl acetate, hexane, allyl chloride (AC) (98%), sodium hydride, sulfuric acid and acetone were purchased from Merck. meta-chloroperoxybenzoic acid (MCPBA) (77%) was purchased from Aldrich, sodium bicarbonate from ChimoPar, sodium hydroxide and sodium sulfate from Acros Organics. All this materials were used without further purification.

All syntheses were monitored using thin-layer chromatography (TLC) performed on silica gel plates, Merk, DC-Autofolien Kiesegel 60 F 254, using different eluants.

FT-IR Analysis. The FTIR spectra were recorded on a Jasco FT/IR-410 spectrometer. The IR analyses were done using KBr pellets.

NMR-Spectroscopy. The NMR spectra were recorded on a Bruker Avance DRX 400 spectrometer using TMS as reference and CDCl₃ as solvent.

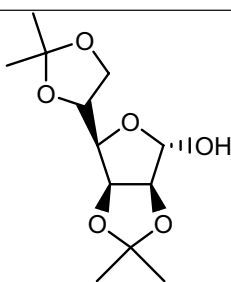
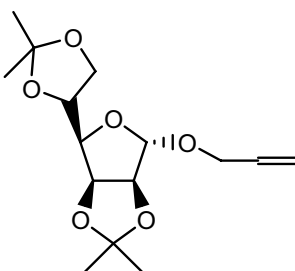
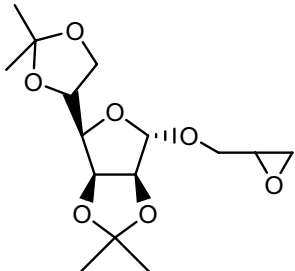
HPLC-MS Analysis. Mass spectrometry experiments were performed using a quadrupole time-of-flight mass spectrometer, equipped with an electrospray ion source (Agilent 6520 Accurate Mass Q-ToF LC/MS). The samples were dissolved in a chloroform/methanol 6:4 (v/v) mixture. The solutions were introduced into the ESI source via a syringe pump at a flow-rate of 0.2 mL/min. The electrospray interface was set in positive ionization mode with the capillary voltage at 4000 V and a heat source of 325°C, in full scan spectra (m/z 100–1000). Nitrogen was used as a drying (7 L/min) and nebulizing gas (35 psi). Data were collected and processed using a MassHunter Workstation software.

IV. RESULTS AND DISCUSSION

A. FT-IR Results

Table 1 presents the IR spectra of diacetone mannofuranose (2), 1-O-allyl-2,3:5,6-di-O-isopropylidene-D-mannofuranose (3) and 1-O-(2',3'-epoxy-propyl)-2,3:5,6-di-O-isopropylidene-D-mannofuranose (4).

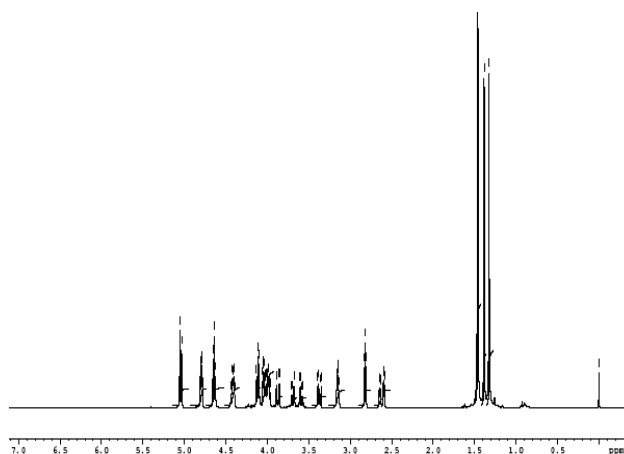
TABLE I
 THE FTIR SPECTRA OF THE D-MANNOSE DERIVATIVES PRESENT IN SCHEME 1

Compound	Band frequency (cm ⁻¹)	Assignment
 2,3:5,6-di-O-isopropylidene-D-mannofuranose	3435.56 2986.23; 2949.59; 2901.38; 2872.45 838.88; 776.20; 687.49	Alcoholic O–H stretch Aliphatic C–H stretching Out of plane γ vibrations for aliphatic C–H stretching
 1-O-allyl-2,3:5,6-di-O-isopropylidene-D-mannofuranose	3082.65; 1648.84 2991.05; 2937.06; 2890.77 1457.92; 1374.03; 1259.29 850.45; 758.85; 686.53	=CH ₂ asymmetric stretching; C=C bond stretching Aliphatic C–H stretching C–O stretching of the ether groups Out of plane γ vibrations for aliphatic C–H stretching
 1-O-(2',3'-epoxy-propyl)-2,3:5,6-di-O-isopropylidene-D-mannofuranose	3054.69; 915.05 2979.48; 2937.04; 2895.59 1454.06; 1374.03; 1264.11 851.41; 752.10; 718.35	Epoxy group stretching Aliphatic C–H stretching C–O stretching of the ether groups Out of plane γ vibrations for aliphatic C–H stretching

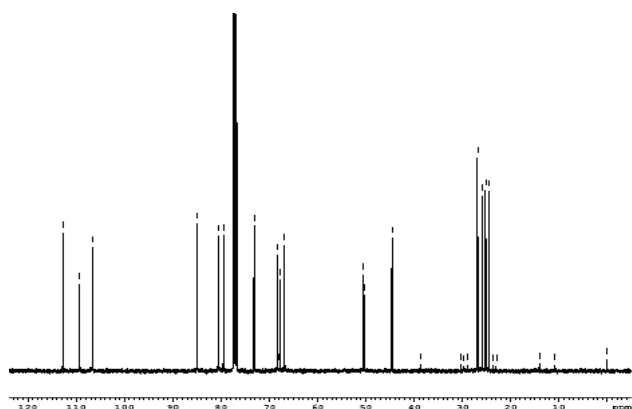
Allylation of 2 was readily proven from the FTIR spectra. The intense O–H bond stretching absorption band at 3435 cm⁻¹ has disappeared in the product 3 spectrum. The medium intensity signal characteristic to =CH₂ asymmetric stretching appears at about 3082 cm⁻¹, while the $\nu_{C=C}$ absorption band around 1650 cm⁻¹ marks the presence of the C=C double bond. The FTIR spectrum of 4 confirms the oxidation of the C=C double bond. The signals assigned to the characteristic bands of epoxy group appears at 3054 cm⁻¹ and 915 cm⁻¹. In addition, the intense signal at about 1650 cm⁻¹ characteristic to the C=C bond has disappeared.

B. NMR-Spectroscopy

The NMR spectroscopy also confirmed the structure of the epoxidated product 4. The ¹H-NMR spectrum of 4 is shown in fig. 2. The spectrum shows the characteristic signals for the isopropylidene CH₃ protons between 1.2 and 1.5 ppm, thus proving that this protective group has not been lost during epoxidation. The protons from the sugar ring display signals between 4.4 and 5.0 ppm. The signals of the protons in the epoxy group are placed between 2.5 and 3.2 ppm. The methylene attached to the epoxy ring display signals between 3.3 – 3.8 ppm.

Fig. 2 The ^1H -NMR spectrum of 4

The ^{13}C -NMR spectrum of 4 is shown in fig. 3 and confirms its structure as well. The isopropylidene CH_3 can be found at about 25 ppm, while the two C atoms in the epoxy group are expressed by signals between 44 and 50 ppm. The three acetal C atoms (one in the glucose moiety and two in the isopropylidene protecting groups) appear between 106 and 112 ppm, while the signals for the other sugar C atoms and the methylene attached to the epoxy ring are displayed between 67 and 85 ppm.

Fig. 3 The ^{13}C -NMR spectrum of 4

C. HPLC-MS Analysis

Additionally, The HPLC-MS analysis was performed in order to confirm the molecular weight of 3 and 4. The products were detected as Na and H adducts. The mass spectrum for compound 3 is presented in Fig. 4. The base peak is observed at $m/z = 323.07$ and is associated with the presence of the single-charge sodium adduct $[\text{M}+\text{Na}]^+$. Another ion of $m/z = 363.10$ is also detectable and can be attributed to the sodium adduct $[\text{M}+\text{C}_3\text{H}_4+\text{Na}]^+$.

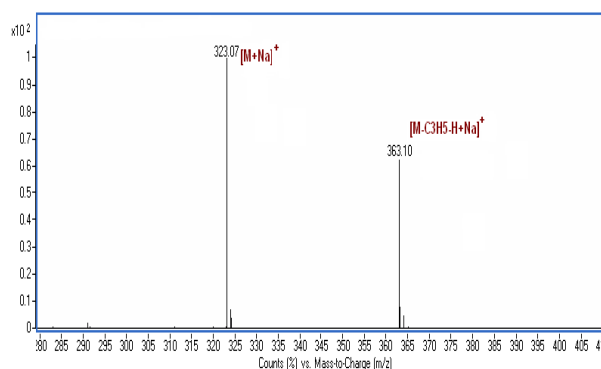


Fig. 4 The HPLC-MS spectrum of 3

Fig. 5 displays the mass spectrum for compound 4. It shows that the most abundant ion corresponds to the $[\text{M}+\text{Na}]^+$ single-charge sodium adduct at $m/z = 339.07$. The peak observed at $m/z = 317.09$ is associated with the presence of the hydrogen adduct $[\text{M}+\text{H}]^+$. The peaks accompanying the base peak are $[\text{M}+\text{C}_3\text{H}_6\text{O}_2+\text{Na}]^+$ at $m/z = 729.29$ and $[2(\text{M}+\text{C}_3\text{H}_6\text{O}_2)+\text{Na}]^+$ at $m/z = 803.41$, corresponding to an adduct of two EpDAM molecules with sodium and $\text{C}_3\text{H}_6\text{O}_2$. Also an additional peak can be observed at $m/z = 413.18$ and is attributed to $[\text{M}+\text{C}_3\text{H}_6\text{O}_2+\text{Na}]^+$.

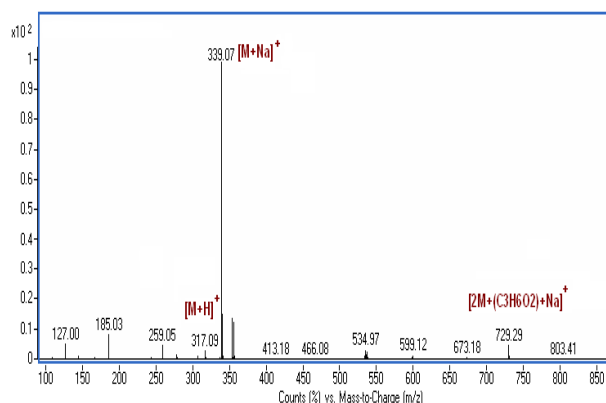


Fig. 5 The HPLC-MS spectrum of 4

V. CONCLUSION

Two derivatives of D-mannose were successfully synthesized and analyzed using FTIR and NMR (^1H -NMR and ^{13}C -NMR) spectroscopy and HPLC-MS. The FTIR and NMR spectroscopy results confirmed the structures of these compounds. The HPLC-MS analysis confirmed the molecular weights of 3 and 4. The synthesis of these D-mannose derivatives (in high yields, 85% for each step) is part of our work to obtain biodegradable polymers. Polymer materials derived from carbohydrates are potentially biodegradable and they lead to minimum environmental pollution.

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REFERENCES

- [1] G. Swift, "Opportunities for Environmentally Degradable Polymers", *Journal of Macromolecular Science, Part A*, 32:4, 1995, pp. 641-651.
- [2] J. P. Jain, M. Sokolsky, N. Kumar and A.J. Domb, "Fatty Acid Based Biodegradable Polymer", *Polymer Reviews*, 48:1, 2008, pp. 156-191.
- [3] A. Steinbüchel, "Use of Biosynthetic, Biodegradable Thermoplastics and Elastomers from Renewable Resources: The Pros and Cons", *Journal of Macromolecular Science, Part A*, 32:4, 1995, pp. 653-660.
- [4] M. Khalid, C. T. Ratnam, C.A. Luqman, A. Salmiaton, T.S.Y. Choong, and H. Jalaludin, "Thermal and Dynamic Mechanical Behavior of Cellulose- and Oil Palm Empty Fruit Bunch (OPEFB)-Filled Polypropylene Biocomposites", *Polymer-Plastics Technology and Engineering*, 48:12, 2009 pp. 1244-1251.
- [5] S. G. Tan, W. S. Chow, "Biobased Epoxidized Vegetable Oils and Its Greener Epoxy Blends: A Review", *Polymer-Plastics Technology and Engineering*, 49:15, 2010, pp. 1581-1590.
- [6] X. L. Wang, K. K. Yang, and Y. Z. Wang, "Properties of Starch Blends with Biodegradable Polymers", *Polymer Reviews*, 43:3, 2003, 385-409.
- [7] M. Okada, "Molecular design and synthesis of glycopolymers", *Progress In Polymer Science*, 26, 2001, pp. 67-104.
- [8] V. Ladmiraal, E. Melia, D. M. Haddleton, "Synthetic glycopolymers: An overview", *European Polymer Journal*, 40, 2004, pp. 431-449.
- [9] A. M. Pană, L. Rusnac, G. Bandur, E. Şişu, V. Badea, M. Silion, "Synthesis and Characterization of New Glycopolymers Based on Monosachharides and Maleic Anhydride I. Glucose derivatives", *Materiale Plastice, Bucureşti*, 47(1), 2010.
- [10] S. Hanessian, *Preparative Carbohydrate Chemistry*, CRC Press, 1997, pp. 8-19.
- [11] V. K. Rajput, B. Mukhopadhyay, *Tetrahedron Letters*, 47, 2006, pp. 5939.
- [12] H. M. I. Osborn, Academic Press, 2002, pp. 50.
- [13] A. M. Pană, L. Rusnac, G. Bandur, C. Deleanu, M. Balan, M. Silion, "Synthesis and Characterization of New Glycopolymers Based on Monosachharides and Maleic Anhydride II. Mannose derivatives", *Materiale Plastice, Bucureşti*, 47(3), 2010.