(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 October 2016 (20.10.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/166682 A1

(51) **International Patent Classification**:
C07H 1/00 (2006.01) ***C08G 64/32*** (2006.01)

(21) **International Application Number**:
PCT/IB2016/052108

(22) **International Filing Date**:
13 April 2016 (13.04.2016)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
62/146,723 13 April 2015 (13.04.2015) US

(71) **Applicant**: **KING ABDULLAH UNIVERSITY OF SCIENCE AND TECHNOLOGY** [SA/SA]; 4700 King Abdullah University of Science and Technology, Thuwal, 23955-6900 (SA).

(72) **Inventors**: **GNANOU, Yves**; 4700 King Abdullah University of Science and Technology, Thuwal, 23955-6900 (SA). **PATI, Debasis**; 4700 King Abdullah University of Science and Technology, Thuwal, 23955-6900 (SA). **FENG, Xiaoshuang**; 4700 King Abdullah University of Science and Technology, Thuwal, 23955-6900 (SA). **HADJICHRISTIDIS, Nikolaos**; 4700 King Abdullah University of Science and Technology, Thuwal, 23955-6900 (SA).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*

WO 2016/166682 A1

(54) **Title**: USE OF CO2 FOR THE SYNTHESIS OF CYCLIC GLYCOCARBONATES AND LINEAR POLYGLYCOCARBONATES BY POLYCONDENSATION FROM GLYCANS

(57) **Abstract**: Provided herein are methods for synthesizing cyclic carbonates, glycocarbonates, and polyglycocarbonates by reacting polyol glycans with carbon dioxide. Synthesis can include selective polycondensation of polyol glycan hydroxyl moieties.

USE OF CO2 FOR THE SYNTHESIS OF CYCLIC GLYCOCARBONATES AND LINEAR POLYGLYCOCARBONATES BY POLYCONDENSATION FROM GLYCANS

BACKGROUND

[0001] Polycarbonates comprise a broad class of durable materials widely used both as commodity plastics and engineering plastics due to a number of advantageous features including temperature resistance, impact resistance and optical properties. Polycarbonates are utilized throughout the electronics, construction, data storage, automotive, aeronautical, security, medical and telecommunications industries, among others. Polycarbonates are primarily synthesized from bisphenol A (BPA) and phosgene, which account for an annual production of about 1 billion kilograms. Many other polycarbonate synthesis mechanisms exist, with the underlying commonality being a synthetic scheme involving a diol (i.e., a compound comprising two hydroxyl groups, or polyol, and phosgene, phosgene derivatives, or isocyanates.

[0002] All such synthetic methods are detrimental to the environment and the health and safety of workers due to the toxic nature of the phosgene, phosgene derivatives, and isocyanates. Further, BPA is a harmful pollutant, even in spite of its low soil half-life, and has been linked to numerous adverse health effects.

SUMMARY

[0003] In general, this disclosure describes synthesis of cyclic glycocarbonates and linear polyglycocarbonates from glycans using carbon dioxide (CO_2). In particular, this disclosure describes synthesis of cyclic glycocarbonates from mannose, galactose monosaccharide and lactose disaccharides, and synthesis of linear polyglycocarbonates from glucose. Also demonstrated herein is selective polycondensation of various glucose derivatives to produce the linear polyglycocarbonates.

[0004] The details of one or more examples are set forth in the accompanying drawings and the description below. Other features, objects, and advantages will be apparent from the description and drawings, and from the claims.

[0005]

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] The accompanying drawings illustrate non-limiting example embodiments of the invention.

[0007] **FIG. 1** illustrates an overview of green synthesis of cyclic or linear polycarbonates directly from CO_2, according to one or more embodiments of this disclosure.

[0008] **FIGS. 2A-B** illustrates infrared spectra of glycocarbonates, according to one or more embodiments of this disclosure.

[0009] **FIG. 2C** illustrates a ^{13}C spectrum of cyclic mannose carbonate acetate, according to one or more embodiments of this disclosure.

[0010] **FIG. 3** illustrates a ^{13}C spectrum of cyclic galactose carbonate acetate, according to

[0011] **FIG. 4** illustrates a ^{13}C spectrum of cyclic Lactose carbonate acetate, according to one or more embodiments of this disclosure.

[0012] **FIG. 5** illustrates an infrared spectra of linear polyglycocarbonates, according to one or more embodiments of this disclosure.

[0013] **FIG. 6A** illustrates MALDI-TOF data of linear polyglycocarbonate acetate, according to one or more embodiments of this disclosure.

[0014] **FIG. 6B** illustrates a gel permeation chromatogram of linear polyglycocarbonates acetate, according to one or more embodiments of this disclosure.

[0015] **FIG. 6C** illustrates a gel permeation chromatogram of oligomer small fractions from a reaction mixture, according to one or more embodiments of this disclosure.

[0016] **FIG. 6D** illustrates a ^{1}H spectrum of linear polyglycocarbonate acetate, according to one or more embodiments of this disclosure.

[0017] **FIG. 6E** illustrates a ^{13}C spectrum of linear polyglycocarbonate acetate, according to one or more embodiments of this disclosure.

[0018] **FIG. 7A** illustrates a gel permeation chromatogram of Linear poly-(methyl 4 and 6 benzylidine) glucocarbonates and a α-methyl 4 and 6 benzylidine glucopyranoside monomer, according to one or more embodiments of this disclosure.

[0019] **FIG. 7B** illustrates a ^{13}C spectrum of linear poly-(methyl 4 and 6 benzylidine) glucocarbonates, according to one or more embodiments of this disclosure.

[0020] **FIG. 7C** illustrates a ^{13}C spectrum of linear poly-methyl 4 and 6 benzylidine glycocarbonates, according to one or more embodiments of this disclosure.

[0021] **FIG. 8A** illustrates a gel permeation chromatogram of Linear poly-(1,2,3-tri-O-methyl) 4 and 6 glucocarbonates and α-methyl 2 and 3 dimethyl 4 and 6 dihydroxyls glucopyranoside monomers, according to one or more embodiments of this disclosure.

[0022] **FIG. 8B** illustrates a ^{13}C spectrum of linear poly-(methyl 3 and 4 di-O-methyl) glycocarbonates, according to one or more embodiments of this disclosure.

DETAILED DESCRIPTION

[0023] The present invention is described with reference to the attached figures, wherein like reference numerals are used throughout the figures to designate similar or equivalent elements. The figures are not drawn to scale and they are provided merely to illustrate the invention. Several aspects of the invention are described below with reference to example applications for illustration. It should be understood that numerous specific details, relationships, and methods are set forth to provide an understanding of the invention. One skilled in the relevant art, however, will readily recognize that the invention can be practiced without one or more of the specific details or with other methods. In other instances, well-known structures or operations are not shown in detail to avoid obscuring the invention. The present invention is not limited by the illustrated ordering of acts or events, as some acts may occur in different orders and/or concurrently with other acts or events. Furthermore, not all illustrated acts or events are required to implement a methodology in accordance with the present invention.

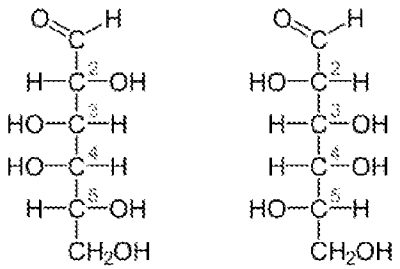
[0024] The methods and compositions disclosed herein provide an alternative to conventional methods for synthesizing cyclic carbonates, glycocarbonates, and polyglycocarbonates, which use toxic phosgene, phosgene derivatives or isocyanates and synthetic reagents. There exists a need for environmentally friendly processes for synthesizing cyclic carbonates and/or glycocarbonates -which have a detrimental effect on environment and when used for the large-scale production. In particular, this disclosure provides novel methods for synthesizing cyclic carbonates, glycocarbonates, and polyglycocarbonates using CO_2. Further disclosed herein are novel methods for synthesizing cyclic carbonates, glycocarbonates, and polyglycocarbonates using naturally occurring glycans. The ability to use naturally occurring glycans as synthesis reactants offers the opportunity to obviate environmental and safety hazards germane to synthetic reagents, while also providing a more cost effective alternative.

[0025] As used herein, “polycarbonates” refers to a general class of monomers and polymers containing a carbonate moiety.

[0026] As used herein, “polyol” refers to a compound comprising two or more hydroxyl groups. An example of a polyol includes bisphenol A (BPA), among many others.

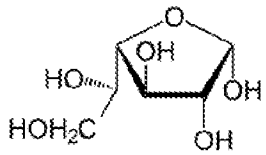
[0027] As used herein, “hexose” generally refers to a class of monosaccharides characterized by six carbon atoms and a chemical formula of $C_6H_{12}O_6$. Hexoses having an aldehyde functional group at position 1 are classified as aldohexoses, whereas hexoses having

a ketone functional group at position 2 are classified as ketohexoses. Aldohexoses include four chiral centers allowing for 16 stereoisomers, or 8 pairs of L-/D- enantiomers. The 8 aldohexose enantiomer pairs include allose, altrose, galactose, glucose, gulose, idose, mannose, and talose. Hexose molecules are polyols. In both open chain and heterocyclic, hemiacetal aldohexoses, the L-/D- distinction is determined by the orientation of the hydroxyl group at position 5. For example, open-chain D-Galactose and L-Galactose have the following structures:

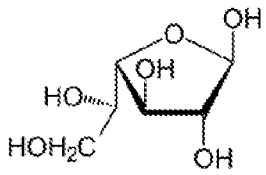


D-Galactose L-Galactose

[0028] Open-chain aldohexoses can convert to heterocylic forms upon nucleophillic addition between the aldehyde function group at position 1 the hydroxyl group at position 4 or position 5. A reaction at position 4 yields α and β steriosiomsers of furanose, a five-membered cyclic, wherein the α and β stereoisomers are differentiated by the hydroxyl orientation at the anomeric carbon. For example, α-D-Galactofuranose has the following structure:

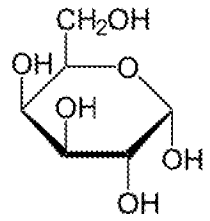


while β-D-Galactofuranose has the following structure:

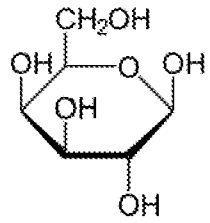


[0029] Reaction at position 5 yields yields α and β sterioisomers of pyranose, a six-membered cyclic, wherein the α and β stereoisomers are differentiated by the hydroxyl

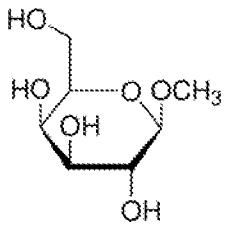
orientation at the anomeric carbon. For example, α -D-Galactopyranose has the following structure:



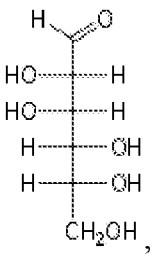
while β-D-Galactopyranose has the following structure:



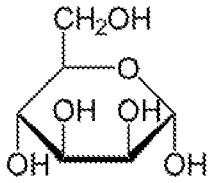
[0030] Converting the anomeric hydroxyl group of a pyranose molecule to an OC_n group forms a pyranoside. For example, D- β -methyl galactopyranoside has the following structure:



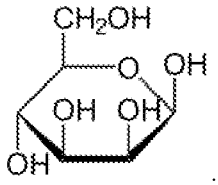
[0031] In another example, open-chain D-mannose has the following structure:



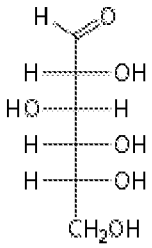
while heterocyclic α -D-Mannopyranose has the following structure:



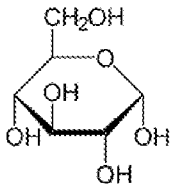
and heterocyclic β-D-Mannopyranose has the following structure:



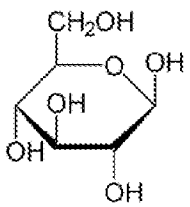
[0032] In another example, open-chain D-glucose has the following structure:



while heterocyclic α -D-Glucopyranose has the following structure:

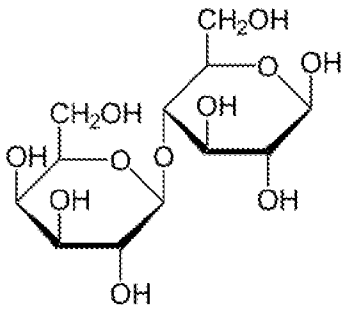


and heterocyclic β-D-Glucopyranose has the following structure:



[0033] As used herein, the term "glycan", or the prefix "glyco-" refers to a molecule containing one or more saccharide moieties. Similarly, the term "glycoside" refers to any molecule in which a saccharide group, or glycone, is bonded through its anomeric carbon to another group, or a glycone, via a glycosidic bond. The glycone can comprise one or more saccharide groups. The glycosidic bond can be formed by oxygen, nitrogen, or carbon. Hexose, as described above, constitutes a class of glycosides. In another example, D- β - methyl galactopyranoside and D-lactose are glycopyranosides.

[0034] Lactose refers to a disaccharide comprising galactose and glucose moieties. An example of lactose is lactopyranose, which is formed via glycosidic bonding between β-galactopyranose and the 4 position of α-glucopyranose and/or β-glucopyranose. Accordingly, "α-lactose" and "β-lactose" refer to anomeric form of the glucopyranose ring. For example, β-lactose has the following structure:



The glycosidic bonding of β-galactopyranose with glucopyranose classifies lactose as a pyranoside.

[0035] Figure 1 illustrates a non-limiting overview of green synthesis of cyclic or linear polycarbonates directly from CO_2. As provided herein, methods for synthesizing glycocarbonates can comprise reacting a polyol glycan with carbon dioxide. A polyol can comprise 2 hydroxyl, groups, 3 hydroxyl groups, 4 hydroxyl groups, 5 hydroxyl groups, or more than 5 hydroxyl groups. In some embodiments, two hydroxyl groups which form the carbonate moiety are substituents of adjacent carbons atoms of the polyol glycan. In some such embodiments, the two hydroxyl groups are cis relative to each other. In other such embodiments, the two hydroxyl groups are trans relative to each other. In some embodiments, two hydroxyl groups which form the carbonate moiety are substituents of non-adjacent carbon atoms of the polyol glycan. In some such embodiments, the two hydroxyl groups are cis relative to each other. In other such embodiments, the two hydroxyl groups are trans relative to each other.

[0036] The glycan can comprise an open chain or closed chain structure. In some embodiments, the polyol glycan can comprise hexose. In other embodiments, the polyol glycan can comprise a pyranose moiety. In some such embodiments, the polyol glycan can comprise a polysaccharide moiety. In other embodiments, the polyol glycan can comprise a pyranoside. In some embodiments, the glyan can comprise a monosaccharide, disaccharide, oligosaccharide, or polysaccharide.

[0037] In some embodiments, the polyol glycan can comprise glycan derivatives. Glycan derivatives can include α-Methyl 3 and 4 di-O-methyl 2 and 6 dihydroxyls glucopyranoside, α-Methyl 2 and 4 di-O-methyl 3 and 6 dihydroxyls glucopyranoside, and other like saccharides, including disaccharides and trisaccharides.

[0038] In some embodiments, reacting can occur in the presence of one or more solvents. A non-limiting list of suitable solvents can include dibromomethane, dimethylformamide, ionic liquids, or combinations thereof. Further examples of solvents include ethers, such as triglycol dimethyl ether, tetrahydrofuran and dimethyl sulfoxide. An example of a suitable ionic liquid includes 1-Butyl-3-methylimidazolium hexafluorophosphate. Additionally, ionic liquids can include Imidazolium based ionic liquids with different counter ions, such as 3-Methyl-(4-9)-(fluoro)imidazolium Bis[(trifluoromethyl)sulfonyl]imide, 1-hexyl-3-methylimidazolium tris(penta fluoro propyl)trifluoro phosphate and 1-pentyl-3-methyl imidazolium tris(nona fluoro butyl)] trifluoro-phosphate etc. Ionic liquids can include ammonium based ionic liquids with different counter ions, such as choline bis(trifluoromethylsulfonyl)imide, tetrabutyl ammonium docusate, peg-5-cocomonium methylsulphate etc. (ref: J. Phys. Chem. B, Vol. 111, No. 30, 2007). A further example of ionic liquids includes super based derived protonic ionic liquids, such as Methyl-triaza bicycloundacane (MTBD) and trifluoroethanol [MTBDH+] [TFE-] (ref: Angew. Chem. Int. Ed. 2010, 49, 5978 –5981). Examples of ionic liquids include polyionic liquids, such as poly(1-[(2-methacryloyloxy)ethyl]-3-butylimidazoliums, poly(1-ethyl-3-vinyl-imidazolium) bis(trifluoromethylsulfonyl) imide, N,N-dimetyl-N,N-diallylammonium bis(trifluoromethylsulfonyl) imide and poly(diallyldimethylammonium chloride) solution(Electrochimica Acta, doi:10.1016/j.electacta.2015.03.038)].

[0039] In some embodiments, reacting can be conducted in the presence of a catalyst. A non-limiting list of suitable catalysts can include 1,8-diazabicyclo[5.4.0]undec-7-ene. Further examples of catalysts include carbene, phosphagene bases and earth metal salts (LiCl,

LiBr, LiOTf, $LiPF_6$ etc.). Further, methods as provided herein are free of phosgene, phosgene derivatives, and isocyanates.

[0040] In some embodiments, reacting occurs at a pressure between about 1 bar and about 20 bar. In other embodiments, reaction occurs at a pressure between about 2.5 bar and about 15 bar. In other embodiments, reacting occurs at a pressure between about 5 bar and about 10 bar. In some embodiments herein, reacting can occur between about 60 °F and about 80 °F, between about 65 °F and about 75 °F. In some embodiments, reacting occurs at room temperature, or about 68 °F. In other embodiments, reacting can occur at about 70 °F. In some embodiments, reacting occurs over a period of about 12 hours, about 24 hours, about 36 hours, about 48 hours, about 60 hours, about 72 hours, about 84 hours, or about 96 hours.

[0041] In some embodiments, methods further comprises selectively protecting one or more hydroxyl moieties of the polyol glycan before reacting, wherein the polyol glycan comprises at least three hydroxyl moieties. The number of protected hydroxyl moieties can be selected such that two hydroxyl moieties remain unprotected. For example, two hydroxyl moieties of a polyol glycan having four hydroxyl moieties can be protected before reacting. Protecting can include methylating.

[0042] In some embodiments, cyclic and linear polyglycocarbonates can be obtained via cyclization and/or polycondensation by reacting commercially available D-α-methyl mannose, galactose monosaccharides, D-Lactose disaccharides and glucose with organo base diazabycyclo undecene (DBU) and CO_2.

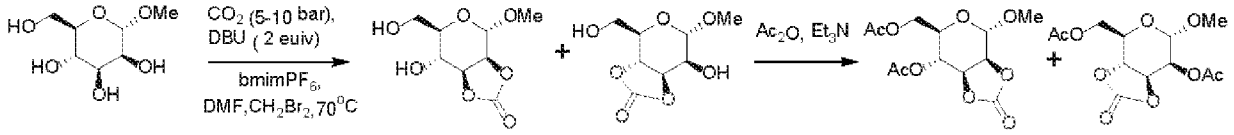
[0043] In other embodiments, cyclic glycocarbonates and linear polyglycocarbonates can be synthesized from glycans through reaction with CO_2. In one such embodiment, cyclic glycocarbonates can be synthesized from mannose and galactose monosaccharides and lactose disaccharides by cyclization of their cis dihydroxyls (e.g., 2 & 3 cis-dihydroxyls in mannose, 3 & 4 cis-dihydroxyls in galactose and lactose). In other embodiments, linear polyglycocarbonates can be synthesized from glucose by polycondensation of the alternate trans (2, 3 and 4) hydroxyls with CO_2. In other embodiments, linear polyglycocarbonates can be synthesized by selective polycondensation of various glucose derivatives by selectively leaving two hydroxyls free and protecting one or more remaining hydroxyl groups. In some embodiments cyclic glycocarbonates can be conjugated to amine/thiol functionalized materials to increase their hydrophilicity and glycans specificity towards biological recognitions.

[0044] The synthesis methodology described herein can further be extended to the other polyhydroxyls compounds to synthesize cyclic carbonates or linear polycarbonates.

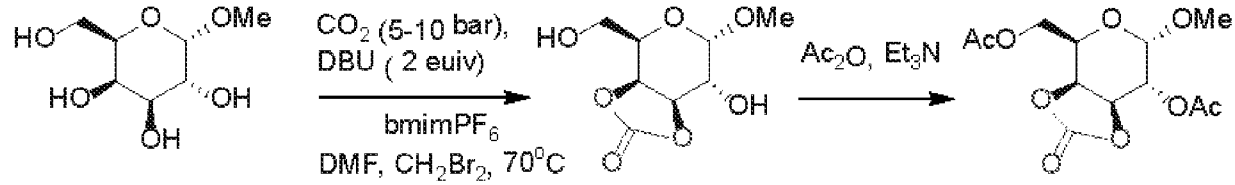
EXAMPLES:

Example 1: Synthesis of cyclic glycocarbonates and acetylated cyclic glycocarbonates from α-methyl glycopyranosides

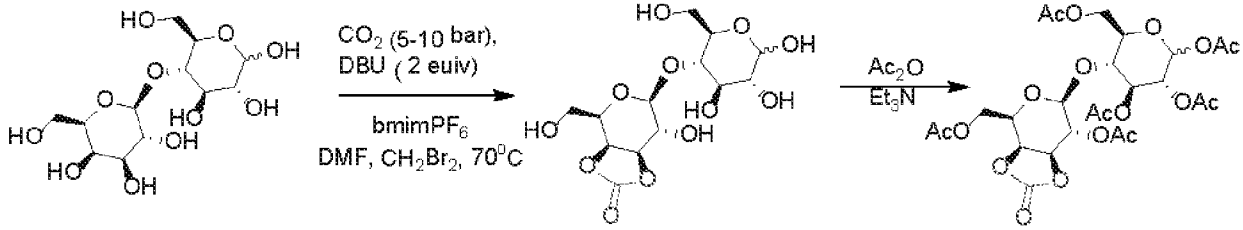
[0045] In this example, cyclic glycocarbonates and acetylated cyclic glycocarbonates were synthesized from the following respective glycopyranosides: D-α-methyl mannopyranoside, D-α-methyl galactopyranoside, and D-lactose pyranose in three separate procedures. The synthetic scheme for cyclic α-methyl mannopyranoside carbonate and subsequently cyclic α-methyl mannoseopyranoside carbonate acetate is shown below in Scheme 1A:



[0046] The synthetic scheme for cyclic α-methyl galactopyranoside carbonate and subsequently cyclic α-methyl galactopyranoside carbonate acetate is shown below in Scheme 1B:



[0047] The synthetic scheme for lactopyranoside cyclic carbonate and subsequently lactopyranoside cyclic carbonate acetate is shown below in Scheme 1C:



[0048] In each procedure, 5.15 mmol of glycopyranoside was deposited in an autoclave in addition to 2 molar equivalents (10.30 mmol) of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 4 molar equivalents (20.60 mmol) of dibromomethane (CH_2Br_2). Next, 2 mL of dimethyl formamide (DMF) was added to the reaction mixture to solubilize the starting materials and 2 mL of ionic liquid 1-Butyl-3-methylimidazolium hexafluorophosphate ($bmimPF_6$) was added to increase the solubility of CO_2 in the reaction medium. The autoclave was then charged with CO_2 at the pressure of 5-10 bar and stirred at room temperature for 1 hour. The temperature of the autoclave was then raised to 70 °C and subsequently stirred for 20 hours, whereafter the CO_2 was released from the reaction mixture. The reaction products were transferred into a round bottom flask and the synthesized cyclic glycocarbonates were analyzed by infrared spectroscopy (IR). Figure 2A illustrates the infrared spectra of each respective cyclic glycocarbonate. The peak observed at 1800 cm^{-1} indicates the presence of the cyclic glycocarbonates.

[0049] Next, 20 mL of freshly distilled anhydrous dichloromethane was added to each round bottom flask containing the cyclic glycocarbonates, along with 5 molar equivalents of trimethylamine (Et_3N) and 2.5 molar equivalents of acetic anhydride (Ac_2O). The mixtures were stirred for 12 hours to obtain the acetylated cyclic glycocarbonates. After the complete acetylation of the cyclic glycocarbonates, the reaction mixtures were washed with 1 (N) hydrochloric acid, followed by distilled water and brine solution. Finally, the reaction mixture was dried on anhydrous sodium sulphate and the solvent was removed under vacuum. The desired cyclic glycocarbonates were isolated by silica gel column chromatography purification using a 2:1 ratio of hexane and ethyl acetate (EtOAc) as the mobile phase. Figure 2B illustrates the infrared spectra of each respective cyclic glycocarbonate acetate. The peak observed at 1800 cm^{-1} further confirmed the cyclic structures.

[0050] As shown in Scheme 1A, the 2 and 3 cis-hydroxyls of the methyl mannopyranoside and the 3 and 4 trans-hydroxyls of the methyl mannopyranoside underwent cyclization to produce stable cyclic carbonate with an overall 90% yield. The cyclic structure was further confirmed by H and C coupling NMR experiments. Figure 2C illustrates a ^{13}C spectrum of cyclic mannose carbonate acetate. Notably, the peak at 153 ppm confirms the cyclic structure

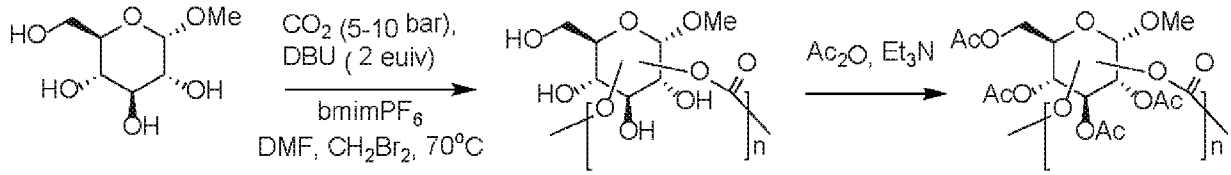
[0051] As shown in Scheme 1B, the 3 and 4 cis-hydroxyls α-methyl galactopyranoside underwent cyclization to produce stable cyclic carbonate with a 70% yield. The cyclic structure was further confirmed by H and C coupling NMR experiments. Figure 3

illustrates a ^{13}C spectrum of cyclic galactose carbonate acetate. Notably, the peak at 153 ppm confirms the cyclic structure.

[0052] As shown in Scheme 1C, the 3 and 4 cis-dihydroxyls of the galactose moiety in the D-lactose underwent cyclization to produce cyclic carbonate with a 50% yield. The cyclic structure was further confirmed by H and C coupling NMR experiments. Figure 4 illustrates a ^{13}C spectrum of cyclic Lactose carbonate acetate. Notably, the peak at 153 ppm confirms the cyclic structure.

Example 2: Synthesis of linear polyglycocarbonates and acetylated linear polyglycocarbonates from glucose

[0053] In this example, linear polyglycocarbonates and acetylated linear polyglycocarbonates were synthesized from α-methyl glucopyranoside; the synthetic scheme is shown below in Scheme 2:



[0054] First, 5.15 mmol of α-methyl glucopyranoside was deposited in an autoclave, in addition to 2 molar equivalents (10.30 mmol) of DBU and 4 molar equivalents (20.60 mmol) of dibromomethane. Next, 2 mL of DMF was added to the reaction mixture to solubilize the starting materials. Further 2 mL of ionic liquid $bmimPF_6$ was added to increase of CO_2 solubility in the reaction medium. Then, the autoclave was charged with CO_2 at the pressure of 5-10 bar and stirred at room temperature for 1 hour. The temperature of the autoclave was raised to 70 °C and subsequently stirred for 72 hours, whereafter the CO_2 was released from the reaction mixture. The reaction products were transferred into a round bottom flask and the synthesized linear glycocarbonates were tested by infrared spectroscopy (IR). Figure 5 illustrates the infrared spectra of the linear glycocarbonate. The peak observed at 1747 cm^{-1} indicates the presence of the linear glycocarbonates. Because the alternating 2, 3 and 4 hydroxyls of α-methyl glucopyranoside are trans to each other, formation of linear carbonates is favored over cyclization.

[0055] Next, 20 mL of freshly distilled anhydrous dichloromethane was added to the round bottom flask containing the linear glycocarbonates, along with 5 molar equivalents of

triethylamine and 2.5 molar equivalents of acetic anhydride. The mixture was stirred for 12 hours to obtain the acetylated linear glycocarbonates. After the complete acetylation of the linear polyglycocarbonates, the reaction mixture was washed with 1 (N) hydrochloric acid, followed by distilled water and brine solution was given. Finally, the reaction mixture was dried on anhydrous sodium sulphate and the solvent was removed under vacuum. Figure 5 illustrates the infrared spectra of the synthesized acetylated linear glycocarbonates, with a peak observed at 1747 cm^{-1} due to the presence of the linear glycocarbonates.

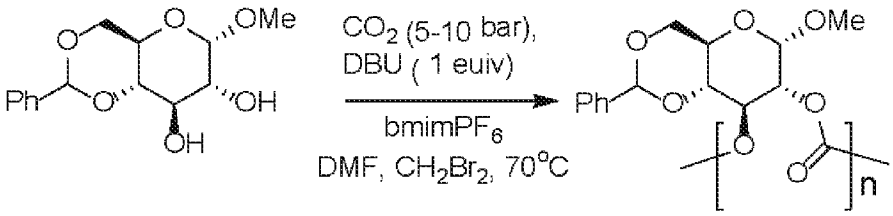
[0056] The molecular weight and linear structure were further confirmed by H and C coupling NMR experiments. Figure 6A illustrates MALDI-TOF data of linear polyglycocarbonate acetate in the crude reaction mixture. The results show formations ranging from small oligomeric mixtures (di, tri, tetra *etc.*) to higher molecular weight linear polyglycocarbonates, up to about 7 kDa. The peak to peak distance of the molecular ion peaks defines a difference of 305 Da, which is characteristic of the linear polyglycocarbonates without branching or crosslinking.

[0057] The acetylated products of the linear polyglycocarbonates, particularly the small oligomeric mixtures (di, tri tetra *etc.*), were further isolated by column chromatography purification using a 2:1 ratio of hexane and ethyl acetate (EtOAc) as eluent. Further analysis was performed using GPC and ^{1}H and ^{13}C NMR spectroscopy. Figure 6B illustrates a gel permeation chromatogram of the acetylated linear polyglycocarbonates. Figure 6C illustrates a gel permeation chromatogram of oligomer small fractions from the reaction mixture. The gel permeation chromatogram showed about 90% consumption of the monomers after 72 hours. Figure 6D illustrates a ^{1}H spectrum of the linear polyglycocarbonate acetate products. Broadened peaks were observed for the higher molecular weight polyglycocarbonates. Figure 6E illustrates a ^{13}C spectrum of the linear polyglycocarbonate acetate products. Significant multi-peaks were observed at about 154-155 ppm for the mixed carbonates or oligomeric mixtures. These data confirm that the exclusively linear polyglycocarbonate reaction products contain a mixture of oligomeric and higher molecular weight polyglycocarbonates and the absence of branching and crosslinking.

Example 3: Synthesis of linear polyglycocarbonates from α-methyl 4 and 6 benzylidine 2 and 3 dihydroxyls glycans:

[0058] In this example, linear polyglycocarbonates were synthesized from α-methyl 4 and 6 benzylidine 2 and 3 dihydroxyls glycans. α-Methyl 4 and 6 benzylidine glucopyranosides were chosen as a model compound to follow the progress of the reaction

where only two free hydroxyls (free 2-OH and 3-OH hydroxyls) can participate in the polycondensation reaction. The synthetic scheme is shown below in Scheme 3:



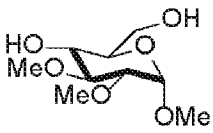
[0059] First, 3.54 mmol of α-methyl 4 and 6 benzylidine glucopyranosides was deposited in an autoclave, in addition to 1 molar equivalent (3.54 mmol) of DBU and 2 molar equivalents (7.08 mmol) dibromomethane. Next, 2 mL of DMF was added to the reaction mixture to solubilize the starting materials. Further 1 mL of ionic liquid bmimPF_6 was added to increase the solubility of CO_2 in the reaction medium. Then, the autoclave was charged with CO_2 at the pressure of 5-10 bar and stirred at room temperature for 1 hour. The temperature of the autoclave was raised to 70 °C and stirred for 48 hours, whereafter CO_2 was released from the reaction mixture. The reaction products were transferred into a round bottom flask and the synthesized linear polyglycocarbonates were tested by infrared spectroscopy (IR). Figure 5 illustrates the infrared spectra of the linear glycocarbonate. The peak observed at 1747 cm^{-1} indicates the presence of the linear glycocarbonates. The product was isolated in dichloromethane simultaneously washing with 1 (N) HCl and brine solution. The dichloromethane solution was dried over anhydrous sodium sulphate and solvent was removed under vacuum.

[0060] Following purification of the products by methods described in previous examples, the product was then characterized by GPC and ^{13}C NMR spectroscopy. Figure 7A illustrates a gel permeation chromatogram of the linear poly-(methyl 4 and 6 benzylidine) glucocarbonates and α-methyl 4 and 6 benzylidine glucopyranoside monomer acetylated linear polyglycocarbonates. Although the monomer is shown to be completely consumed, the reaction did not progress to higher molecular weights. Figures 7B-C illustrate ^{13}C spectra of linear poly-(methyl 4 and 6 benzylidine) glucocarbonates. Three different 154-155 ppm ^{13}C peaks for the mixed carbonates are observed, indicating self-condensation of 2-OH and 3-OH and the cross condensation among 2 and 3.

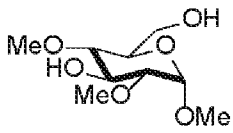
Example 4: Synthesis of linear polyglycocarbonates from 4 and 6 dihydroxyls glycans

[0061] Inherently, all hydroxyl substituents of a carbohydrate form a reactivity hierarchy. For example, when all hydroxyl groups attached to C-2, C-3, C-4 and C-6 in methyl-glucopyranoside have an equatorial orientation, the general order of reactivity

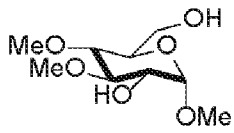
towards nucleophilicity to form O-linkages is: 6-OH >>3-OH >>2-OH >>4-OH. Based on this concept and the disclosure herein, polycondensation can selectively be triggered by protecting specific hydroxyls. Suitable substrate glycans derivatives must 1) include a free primary hydroxyl group, and 2) a free hydroxyl at position 2, 3, or 4 (e.g., free hydroxyl groups at positions 6 and 4, positions 6 and 3, or positions 6 and 2) with all other hydroxlys protected. Scheme 4 illustrates a non-limiting list of suitable glycans with selectively available and protected hydroxyl groups:



4 and 6 dihydroxyl

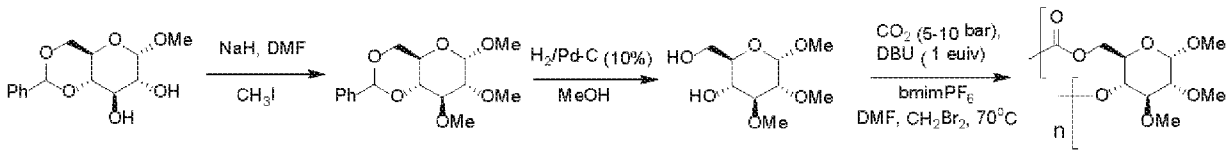


3 and 6 dihydroxyl



2 and 6 dihydroxyl

[0062] In this example, linear polyglycocarbonates are synthesized from CO_2 and α-Methyl 3 and 4 di-*O*-methyl 4 and 6 dihydroxyls glucopyranoside; the synthetic scheme is shown below in Scheme 5:



[0063] First, 7.08 mmol of α-methyl 4 and 6 benzylidine glucopyranosides was taken in a round bottom flask and 20 mL anhydrous DMF was added to the reaction mixture. Sodium hydride in 2.5 molar equivalents (17.71 mmol) was added to the reaction mixture under inert condition and stirred for 30 minutes. Next, 10 mL of DMF and 2.5 molar equivalents (17.71 mmol) of methyl iodide were added to the reaction mixture and stirred for 12 hours to obtain 1, 2 and 3 trimethyl 4 and 6 benzylidine glucopyranoside. Then the reaction mixture was diluted with dichloromethane and washed with 1 (N) HCl to remove the undesired salts. The organic layer was dried over anhydrous sodium sulfate and solvent was removed under vacuum. The compound was characterized by ^{13}C and ^{1}H NMR. The 1, 2 and 3 trimethyl 4 and 6 benzylidine glucopyranoside was hydrogenated at 30 bar hydrogen gas pressure with 10% Pd-C for 16 h in methanol to remove the bezylidine group. The completion of the reaction was confirmed by TLC and 1, 2 and 3 methyl glycopyranoside was isolated and characterized by ^{1}H and ^{13}C NMR.

[0064] Next, 4.5 mmol of α- 1, 2 and 3 trimethyl glycopyranoside, 1 molar equivalent (4.5 mmol) of DBU and 2 molar equivalents (9 mmol) of dibromomethane were added to an autoclave, whereafter 1 mL of anhydrous DMF and 1 mL of bmimPF6 was added to the reaction mixture to increase the solubility of the starting materials and CO_2 respectively. CO_2

was charged to the autoclave at the pressure of 10 bar. Then the reactor was stirred for 1hour at room temperature. Subsequently, the reaction mixture was increased to 70°C and stirred for 48 hours. The reaction mixture was then taken from the reactor and tested with infrared spectroscopy to confirm the formation of polycarbonates. The reaction mixture was diluted with ethyl acetate and simultaneously washed with 1 (N) HCl, water and brine solution. The ethyl acetate layer was dried over anhydrous sodium sulphate and solvent was removed under vacuum. The reaction mixture was characterized by GPC, ^{1}H and ^{13}C NMR.

[0065] Figure 5 illustrates the infrared spectra of the products, with a peak observed at 1747 cm^{-1} due to the presence of the linear glycocarbonates. The reaction mixture was then purified to remove undesired components and the reaction products were analyzed by GPC and 1H and 13C NMR spectroscopy. Figure 8A illustrates a gel permeation chromatogram of the linear poly-(1,2,3-tri-*O*-methyl) 4 and 6 glucocarbonates and α-methyl 2 and 3 dimethyl 4 and 6 dihydroxyls glucopyranoside monomer. Chloroform was used as eluent at the 1 mL/min flow at room temperature. The GPC results clearly show the progress of the reaction, but not to an extent of more than tetramers or oligomers, even though only a small amount of unreacted monomer could be detected in the reaction mixture. Figure 8B illustrates the ^{13}C spectrum of linear poly-(methyl 3 and 4 di-O-methyl) glycocarbonates, which shows multiple peaks at about 154-155 ppm, indicating the formation of mixed carbonates.

[0066] Similar results are expected for synthesizing linear polyglycocarbonates from CO_2 and α-Methyl 3 and 4 di-*O*-methyl 2 and 6 dihydroxyls glucopyranoside, and/or α-Methyl 2 and 4 di-*O*-methyl 3 and 6 dihydroxyls glucopyranoside.

WHAT IS CLAIMED IS:

1. A method for making glycocarbonates, the method comprising reacting a polyol glycan with carbon dioxide.

2. The method of claim 1, wherein the polyol glycan comprises hexose.

3. The method of claim 1, wherein the polyol glycan comprises a pyranose moiety.

4. The method of claim 1, wherein the polyol glycan comprises a pyranoside.

5. The method of claim 1, wherein the polyol glycan comprises a polysaccharide moiety.

6. The method of claim 1, wherein the polyol glycan comprises a glycan derivative.

7. The method of claim 1, wherein reaction occurs in the presence of one or more solvents.

8. The method of claim 7, wherein the one or more solvents can comprise dibromomethane, dimethylformamide, an ionic liquid, or combinations thereof.

9. The method of claim 8, wherein the ionic liquid comprises 1-Butyl-3-methylimidazolium hexafluorophosphate.

10. The method of claim 1, further comprising selectively protecting one or more hydroxyl moieties of the polyol glycan before reacting, wherein the polyol glycan comprises at least three hydroxyl moieties.

11. The method of claim 10, wherein protecting comprises methylating.

12. The method of claim 1, wherein reacting is conducted in the presence of a catalyst.

13. The method of claim 12, wherein the catalyst comprises 1,8-diazabicyclo[5.4.0]undec-7-ene.

14. The method of claim 1, wherein the method is free of phosgene, phosgene derivatives, and isocyanates.

15. The method of claim 1, wherein reacting is conducted at a pressure between about 1 bar and about 20 bar.

16. The method of claim 1, wherein reacting is conducted at a temperature of between about 60 °F and 80 °F.

17. The method of claim 1, wherein the glycocarbonates comprise linear polyglycocarbonates.

18. The method of claim 1, wherein the glycocarbonates comprise cyclic glycocarbonates.

19. A method for making cyclic carbonates or linear polycarbonates, the method comprising reacting a polyhydroxyl compound with carbon dioxide.

20. The method of claim 19, wherein the method is free of phosgene, phosgene derivatives, and isocyanates.

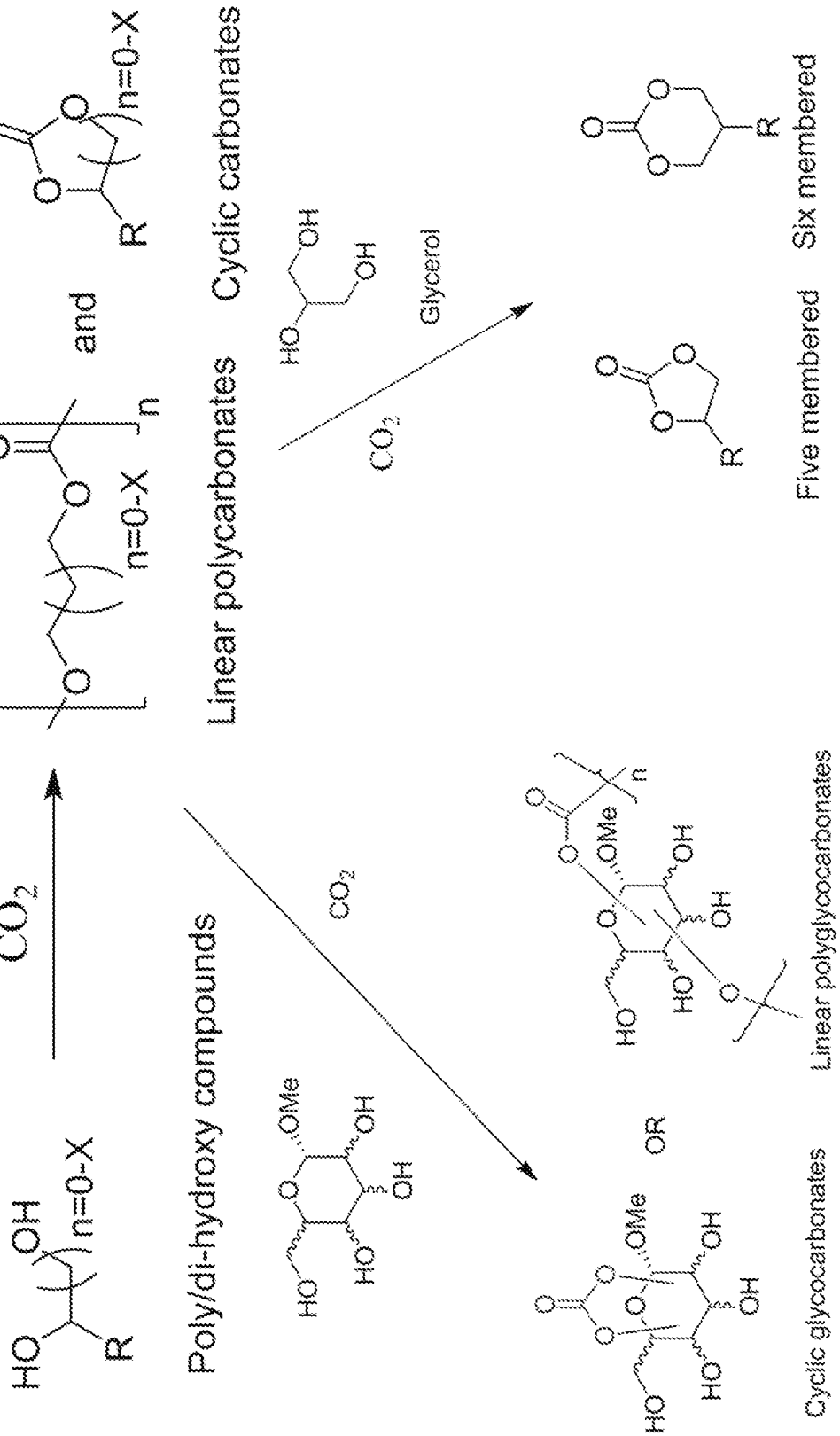

CO2
Poly/di-hydroxy compounds
Linear polycarbonates
and
Cyclic carbonates
CO2
Glycerol
Five membered
Six membered
CO2
Cyclic glycocarbonates
Linear polyglycocarbonates

FIG 1

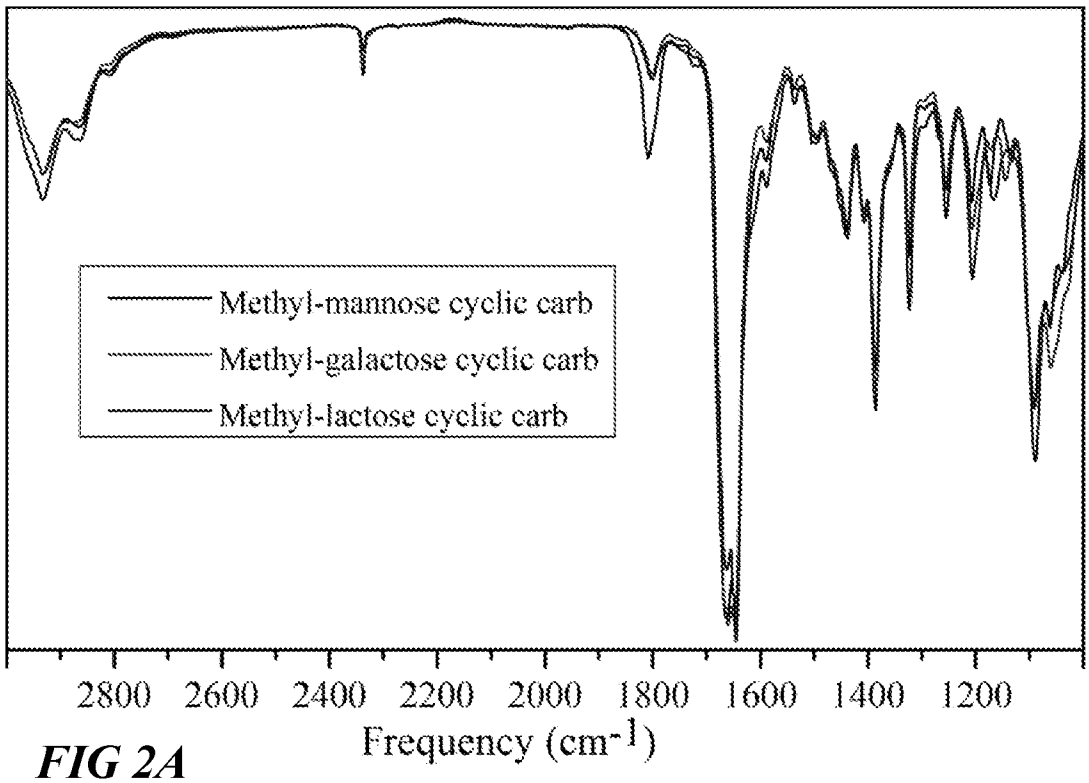

Methyl-mannose cyclic carb
Methyl-galactose cyclic carb
Methyl-lactose cyclic carb
2800 2600 2400 2200 2000 1800 1600 1400 1200
Frequency (cm-1)

FIG 2A

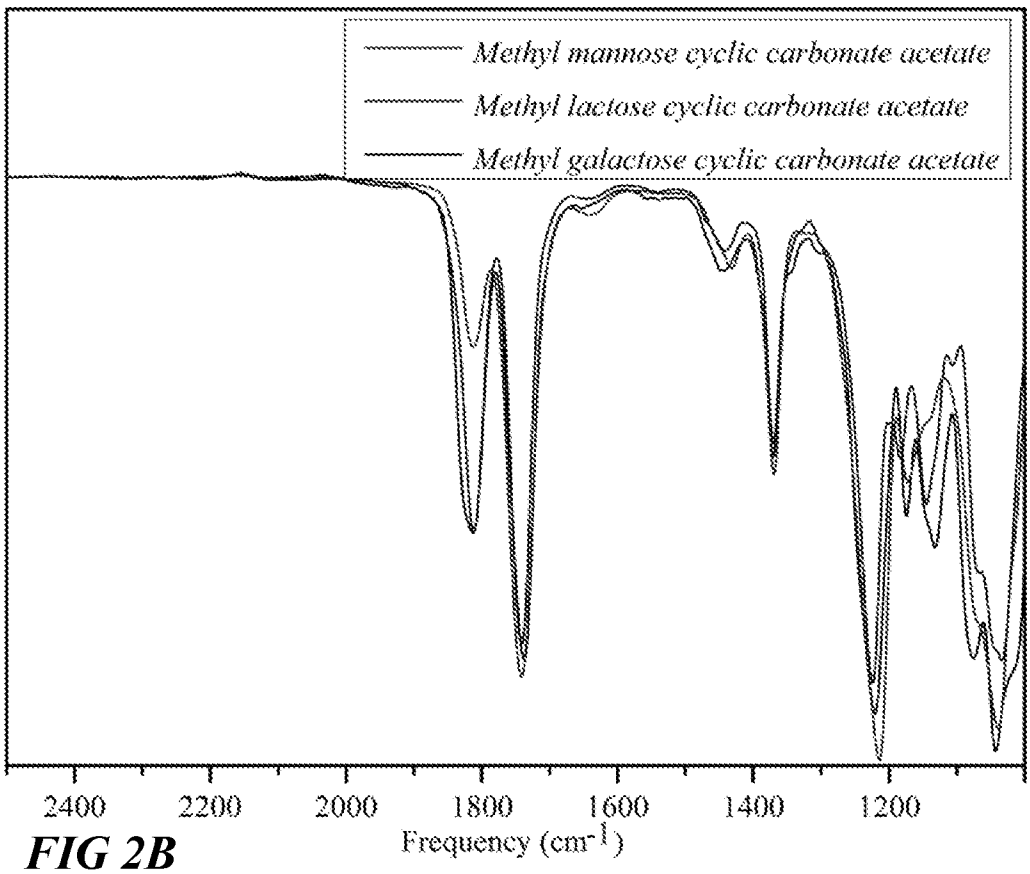

Methyl mannose cyclic carbonate acetate
Methyl lactose cyclic carbonate acetate
Methyl galactose cyclic carbonate acetate
2400 2200 2000 1800 1600 1400 1200
Frequency (cm-1)

FIG 2B

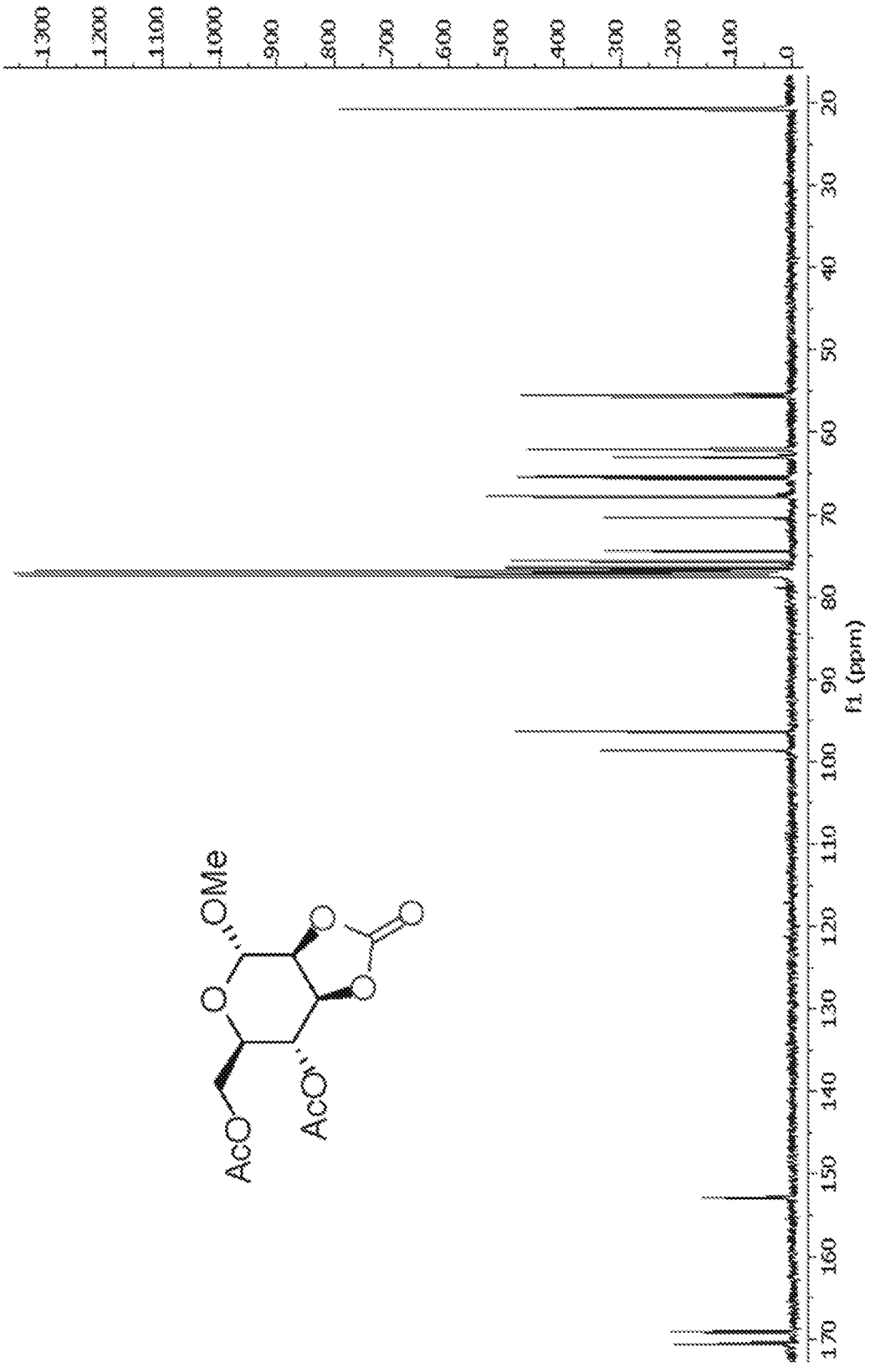


FIG 2C

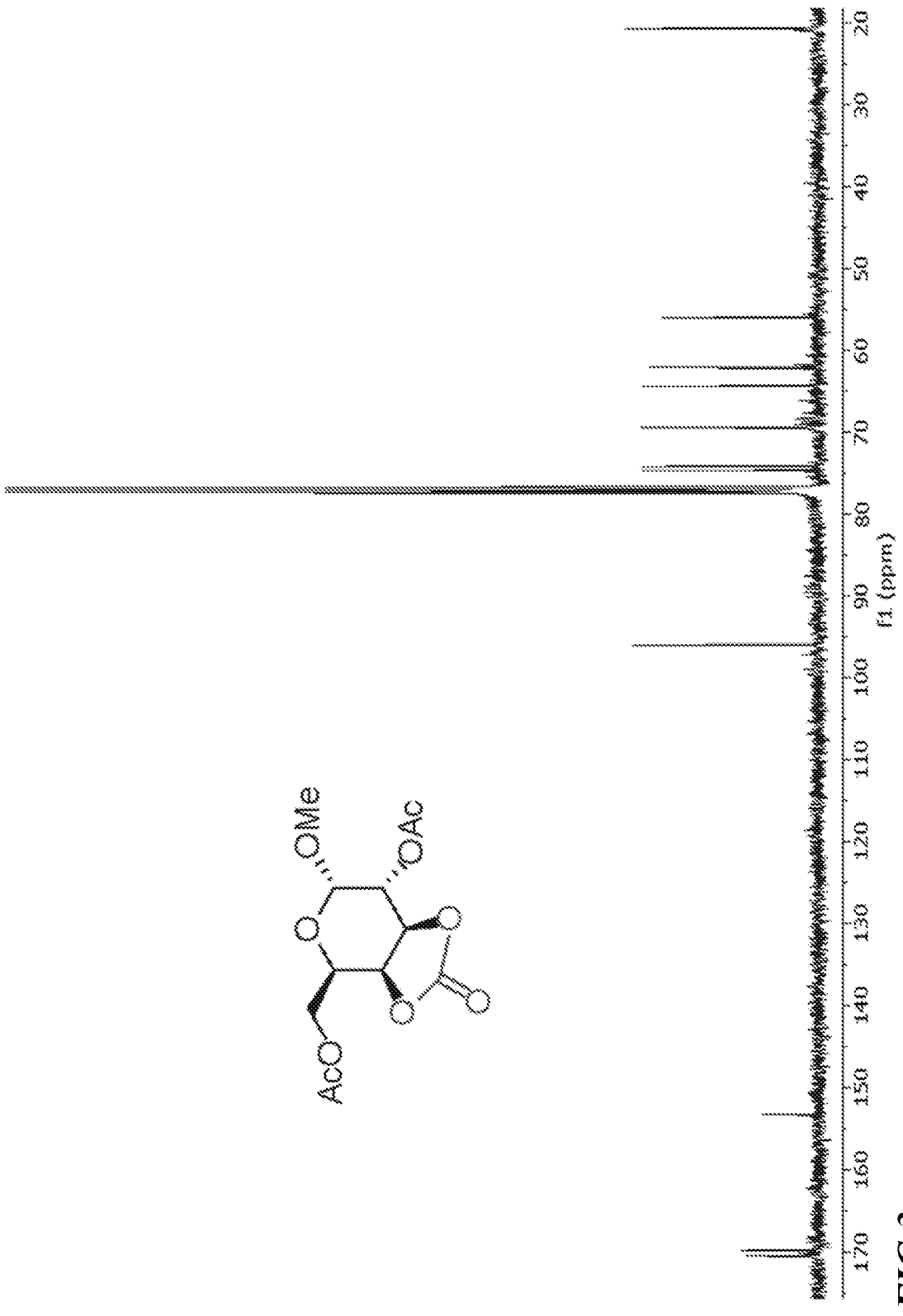

OMe
OAc
AcO
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

FIG 3

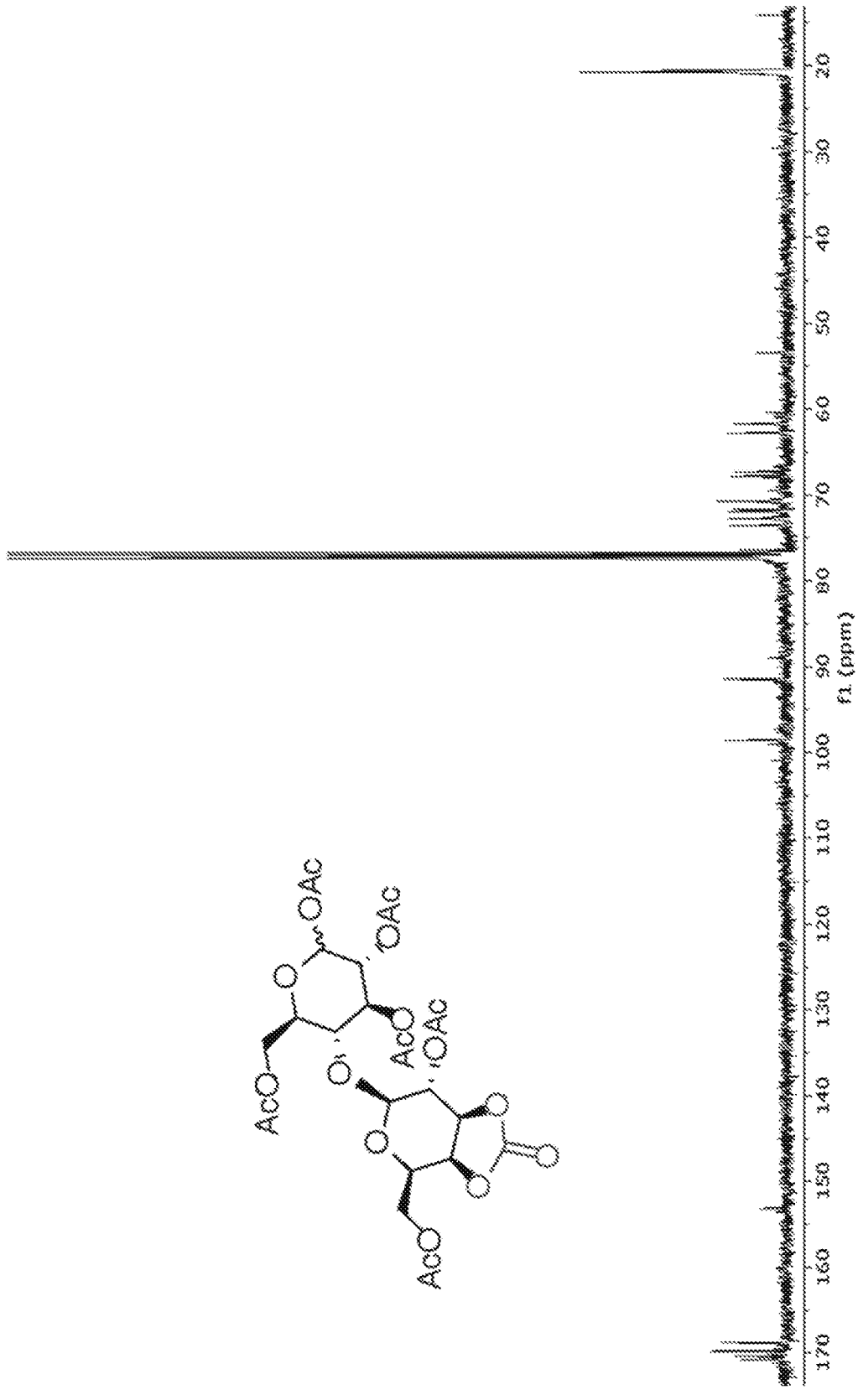

AcO
OAc
OAc
AcO
OAc
AcO
O
O
O
O
O
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

FIG 4

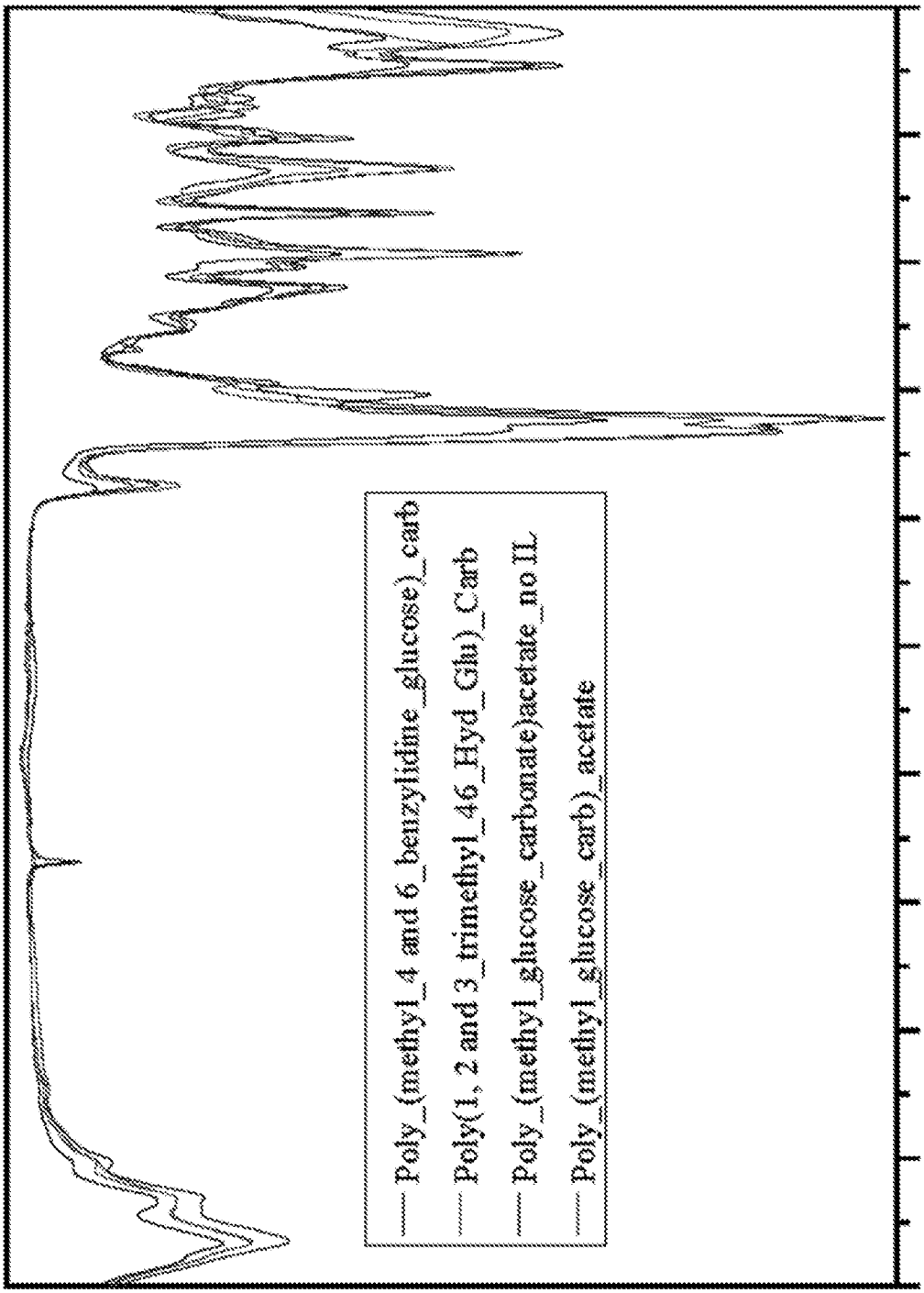

Poly_(methyl_4 and 6_benzylidine_glucose)_carb
Poly(1, 2 and 3_trimethyl_46_Hyd_Glu)_Carb
Poly_(methyl_glucose_carbonate)acetate_no IL
Poly_(methyl_glucose_carb)_acetate
2800
2600
2400
2200
2000
1800
1600
1400
1200
Frequency (cm-1)

FIG 5

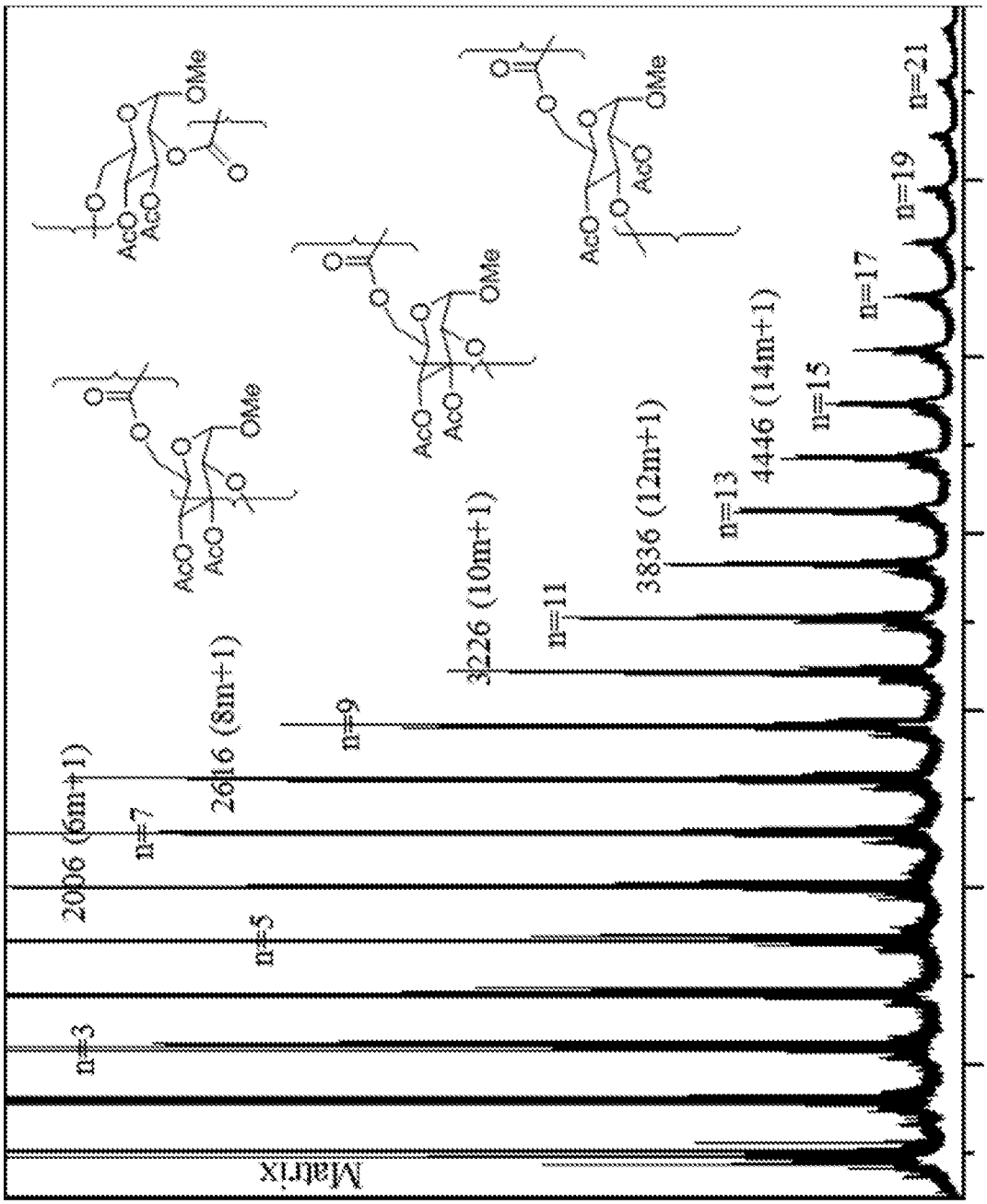

Matrix
n=3
n=5
2006 (6m+1)
n=7
2616 (8m+1)
n=9
3226 (10m+1)
n=11
3836 (12m+1)
n=13
4446 (14m+1)
n=15
n=17
n=19
n=21
1000
2000
4000
5000
6000
m/z
AcO
OMe

FIG 6A

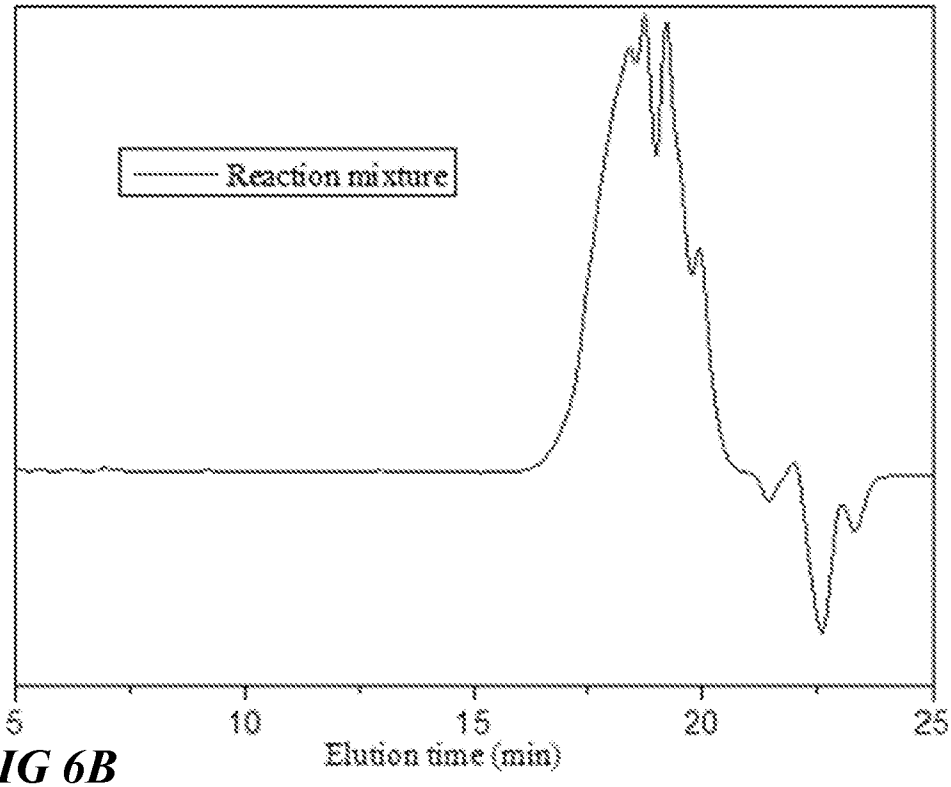

Reaction mixture
5
10
15
20
25
Elution time (min)

FIG 6B

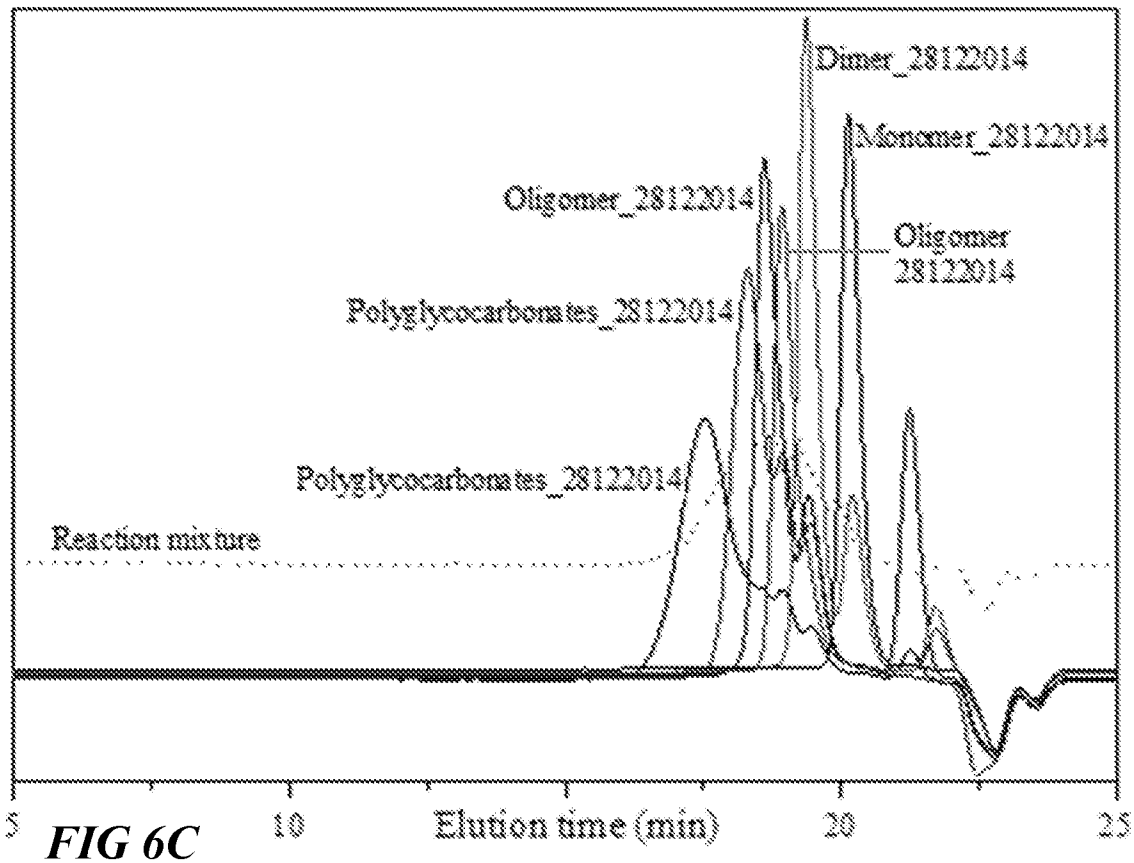

Dimer_28122014
Monomer_28122014
Oligomer_28122014
Oligomer 28122014
Polyglycocarbonates_28122014
Polyglycocarbonates_28122014
Reaction mixture
5
10
Elution time (min)
20
25

FIG 6C

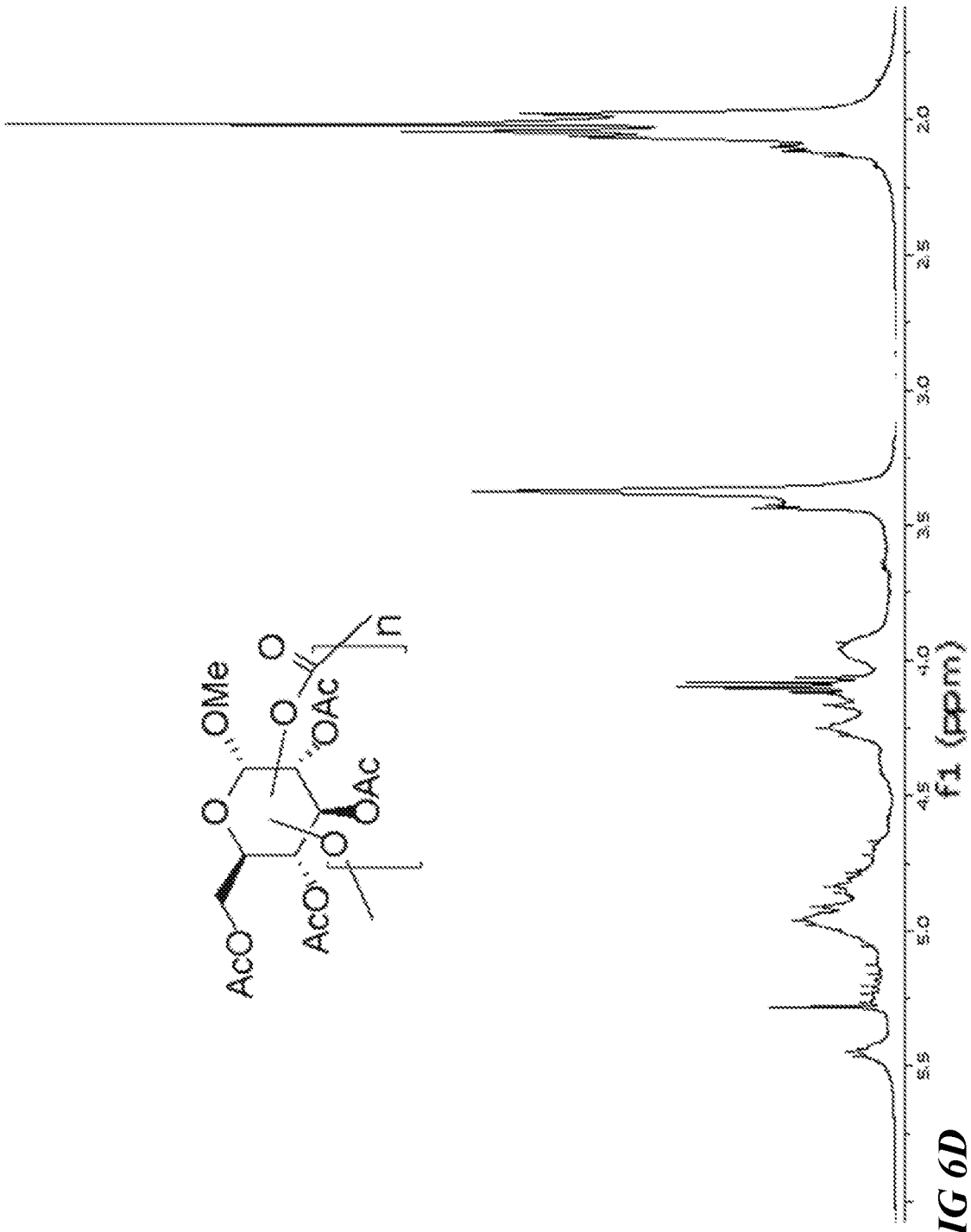


FIG 6D

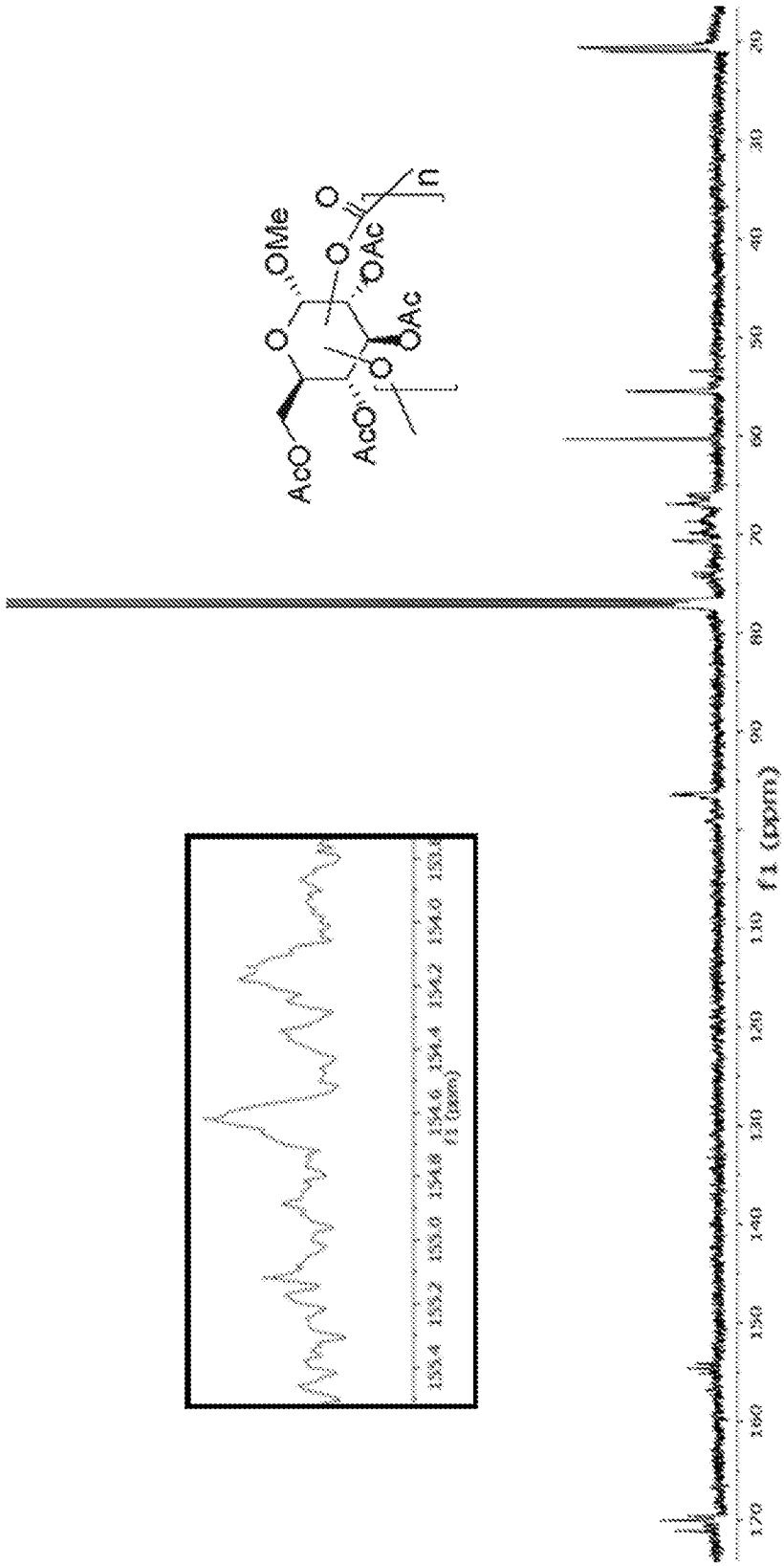


FIG 6E

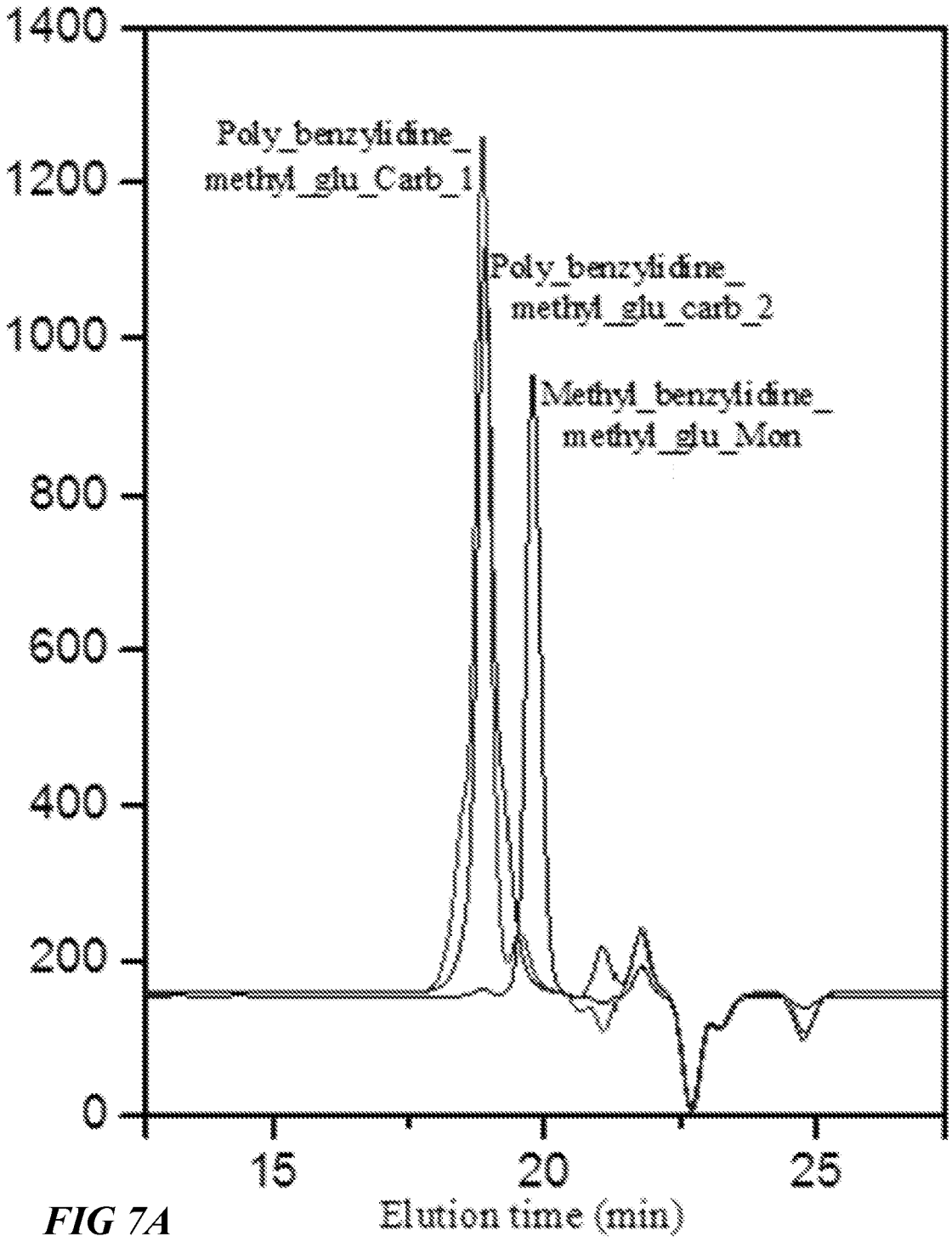

1400
1200
1000
800
600
400
200
0
Poly_benzylidine_
methyl_glu_Carb_1
Poly_benzylidine_
methyl_glu_carb_2
Methyl_benzylidine_
methyl_glu_Mon
15
20
25
Elution time (min)

FIG 7A

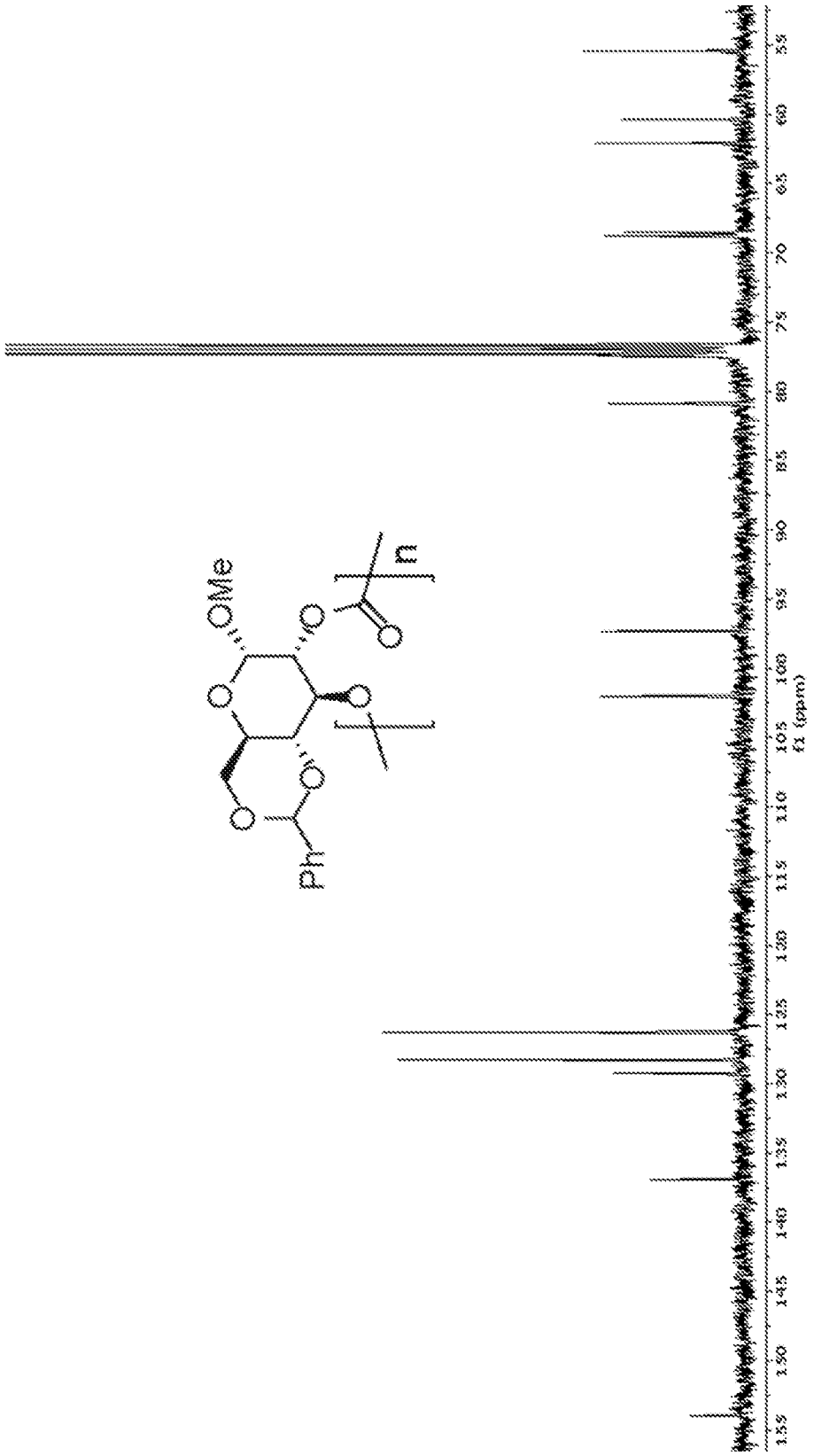


FIG 7B

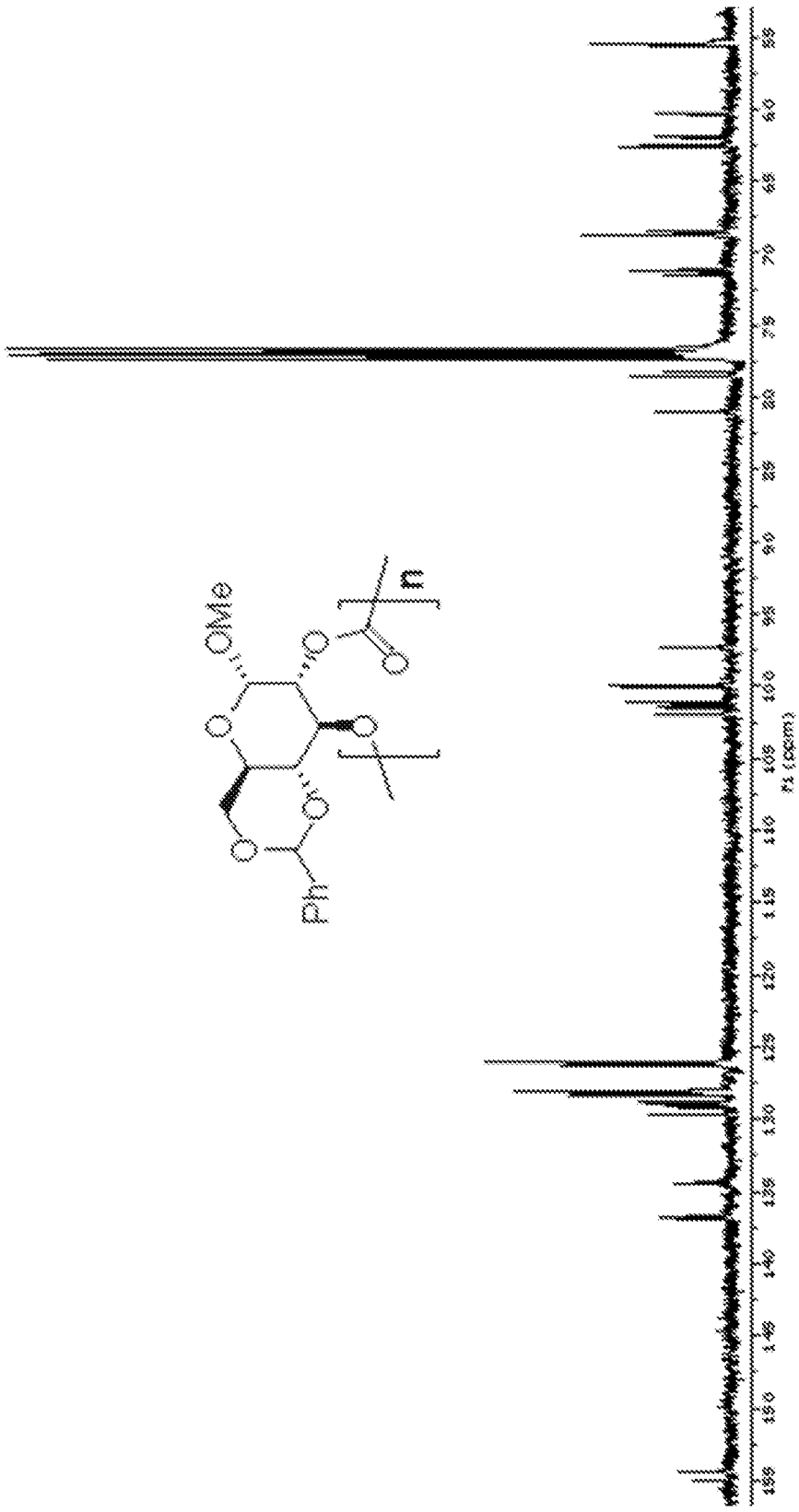


FIG 7C

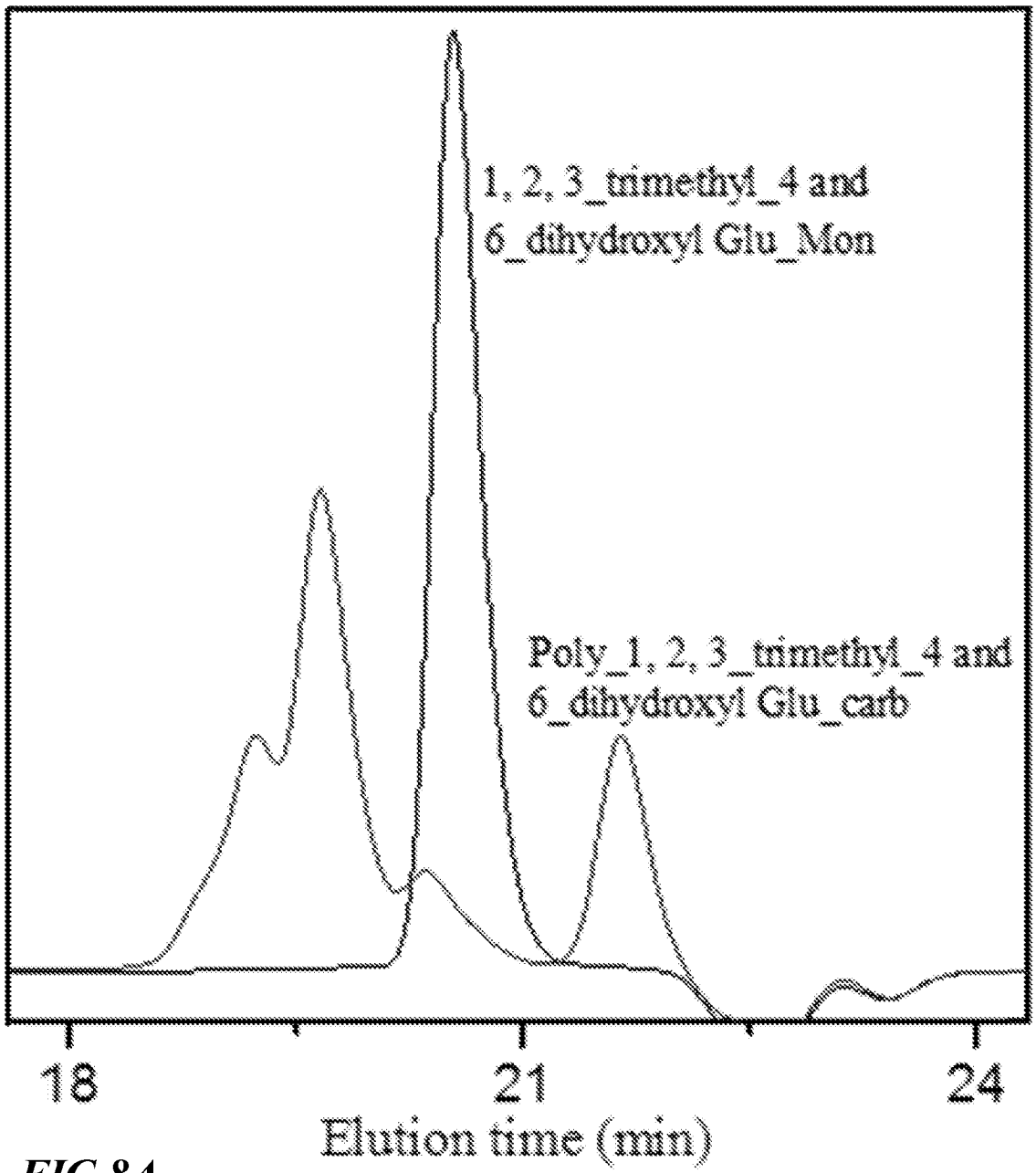

1, 2, 3_trimethyl_4 and
6_dihydroxyl Glu_Mon
Poly_1, 2, 3_trimethyl_4 and
6_dihydroxyl Glu_carb
18
21
24
Elution time (min)

FIG 8A

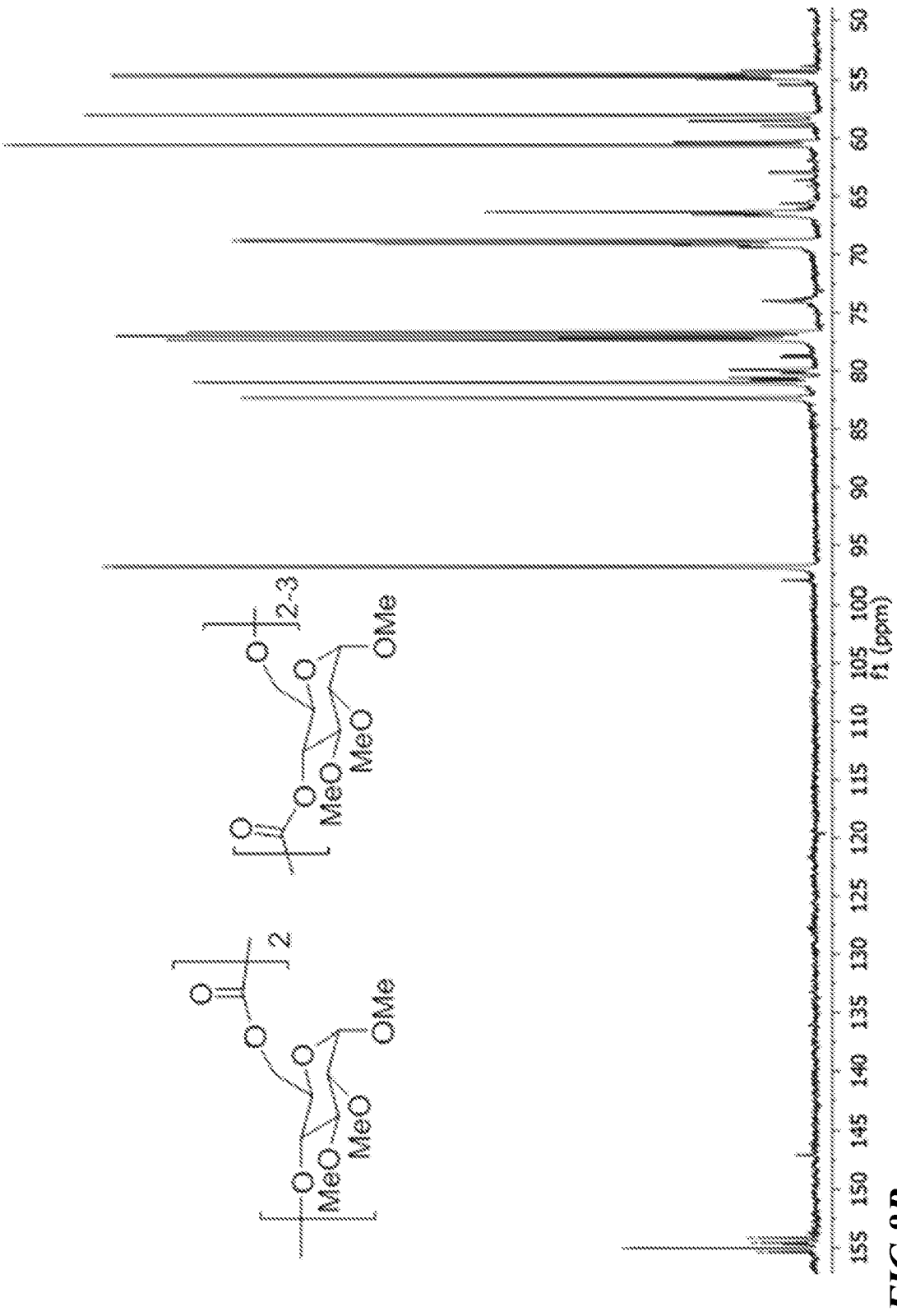

2
2-3
MeO
MeO
MeO
MeO
OMe
OMe
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50
f1 (ppm)

FIG 8B

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/052108

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07H1/00 C08G64/32
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
C07H C08G

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HANNES BLATTMANN ET AL: "Isocyanate- and Phosgene-Free Routes to Polyfunctional Cyclic Carbonates and Green Polyurethanes by Fixation of Carbon Dioxide", MACROMOLECULAR RAPID COMMUNICATIONS, vol. 35, no. 14, 30 July 2014 (2014-07-30) , pages 1238-1254, XP055180325, ISSN: 1022-1336, DOI: 10.1002/marc.201400209 abstract figures 1, 4, 18, 19, 25 ----- -/--	1-20

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 June 2016	11/07/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Gohlke, Pascale

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2016/052108

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2012/051448 A1 (TEXAS A & M UNIV SYS [US]; STREFF JENNIFER [US]; KRISTUFEK SAMANTHA [U) 19 April 2012 (2012-04-19) abstract page 11, line 1 - page 12, line 8 Scheme 9; page 19	1-20

X	WO 2013/036863 A2 (HYRAX ENERGY INC [US]; TEIXEIRA RODRIGO E [US]; KNAPP KURTIS G [US]; F) 14 March 2013 (2013-03-14) abstract claims 15, 16	1-14,19, 20

X	WO 2008/057263 A2 (CARGILL INC [US]; COCKREM MICHAEL CHARLES MILNER [US]) 15 May 2008 (2008-05-15) abstract examples page 4, lines 1-14	1-14,19, 20

A	HABA O ET AL: "SYNTHESIS OF POLYCARBONATE FROM DIMETHYL CARBONATE AND BISPHENOL-A THROUGH A NON-PHOSGENE PROCESS", JOURNAL OF POLYMER SCIENCE, POLYMER CHEMISTRY EDITION, INTERSCIENCE PUBLISHERS, NEW YORK, NY, US, vol. 37, no. 13, 1 July 1999 (1999-07-01), pages 2087-2093, XP000829807, ISSN: 0360-6376 abstract	1-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2016/052108

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2012051448 A1	19-04-2012	EP 2627691 A1	21-08-2013
		WO 2012051448 A1	19-04-2012
WO 2013036863 A2	14-03-2013	US 2014309416 A1	16-10-2014
		WO 2013036863 A2	14-03-2013
WO 2008057263 A2	15-05-2008	NONE	