Synthesis of carbohydrate esters and investigation reaction of Phosphoryl chloride from anomeric position of Per-Acetylated Carbohydrates

Hadi Jabbari

Department of Chemistry, Payame Noor University, P.O. Box 19395-4697 Tehran, Iran.

Abstract

Carbohydrates are a large class of organic compounds which can be found in the structure of living organisms. They are major energy source for both plants, and animals that play an important role in feeding the living organisms. Likewise, these compounds are quintessential reactions of ATP, RNA and DNA. The anomeric position of carbohydrates prepare them to chemical reactions.in this paper, Carbohydrate esters were prepared by acetic anhydride in the presence of sodium acetate and Lewis acid. Then selective anomeric position with MgO/MeOH was deacetylatd, then was reacted with phosphoryl chloride, In another method, the acetylated carbohydrates were reacted directly with phosphoryl chloride without deacetylation anomeric position. In two different situations, the same product was obtained. Phosphate ester carbohydrate was identified by ^{13}P-NMR technique.

Keywords: Carbohydrates, anomeric position, Phosphoryl chloride, carbohydrate esters

INTRODUCTION

Carbohydrates perform numerous roles in living organisms. Polysaccharides serve for the storage of energy and as structural components (e.g. cellulose in plants and chitin in arthropods). The 5-carbon monosaccharide ribose is an important component of coenzymes (e.g. ATP, FAD and NAD) and the backbone of the genetic molecule known as RNA. The related deoxyribose is a component of DNA. Saccharides and their derivatives include many other important biomolecules that play key roles in the immune system, fertilization, preventing pathogenesis, blood clotting, and development. [1-3]

They are found in a wide variety of natural and processed foods. Starch is a polysaccharide. Carbohydrates are of great importance in biology. The unique reaction, which makes life possible on the Earth, namely the assimilation of the green plants, produces sugar, from which originate, not only all carbohydrates but, directly or indirectly, all other components of living organisms. The carbohydrates are a major source of metabolic energy, both for plants and for animals that depend on plants for food. Aside from the sugars and starch that meet this vital nutritional role, carbohydrates also serve as a structural material (cellulose), a component of the energy transport compound ATP, recognition sites on cell surfaces, and one of three essential components of DNA and RNA. Importance can be considered under following headings [4, 5].

Protected carbohydrates bearing hemiacetal functionality serve as valuable intermediates in the synthesis of several classes of glycosyl donors used in oligosaccharide synthesis. Examples for these classes of compounds include the glycosyl , chloroacetimidates and the glycosyl halides such as he chlorides and the fluorides. They are also often useful in the synthesis of other naturally occurring complex molecules. There are several methods in the literature for the regioselective anomeric deacetylation of otherwise fully acetylated carbohydrates. These include methods utilizing bis (tributyltin) oxide [6], tributyltin methoxide [7], benzylamine [8], sodium methoxide [9], ammonium salts [10, 11], piperidine [12], Al2O3 [13], MgO, mercuric chloride/mercuric oxide [14], HClO –SiO [15], An alternative approach is the hydrolysis of glycosyl bromides using aqueous silver salts (example, AgNO) It can be easily seen that the former category of reactions often require use of either toxic or moisture/air

Address for correspondence: Hadi Jabbari, Department of Chemistry, Payame Noor University, P.O. Box 19395-4697 Tehran, Iran.
Email: hadijabbari@yahoo.com

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sensitive reagents as well as, frequently, long reaction time/harsh reaction conditions. Thus the need for milder and more effective methods in this context is clearly evident.

However, in this paper, a sample of carbohydrates consisting of glucose, galactose, xylose, fructose and lactose is acetylated using $Ac_2O/AcONa$under the 50-60 °C and anomeric configuration of acetylated carbohydrates using MgO/MeOH as a new catalyst has been released. Then, it is reacted with POCl3, from anomeric position reacted. All of these compounds are identified by FT-IR, ^{1}H, ^{13}C and ^{31}PNMR spectroscopy techniques.

Experiment

All materials were obtained from Merck Co.^{1}H,^{13}C and ^{31}P NMR spectra of in CDCl3 and/or DMSO-d6 were measured using Brucker 400 AC spectrometer as a solvent at room temperature (University of Tabriz, Tabriz, Iran and ShahidBeheshti University, Tehran, Iran).

Typical procedure for preparation of D-glucose pentaacetate (2a)

A mixture of D-glucose (15.0 g), acetic anhydride (70 mL), sodium acetate (15.0 g) and butyl acetate (150 mL) was refluxed with stirring for one-half hours. Then the reaction mixture was added to water (100 mL), the mixture was stirred and produced a neutral solution with a 3% sodium hydroxide After the concentration of the organic layer it give 62.0 g (yield 95%) of pentaacetyl-β-D-glucopyranose as crude crystals. The crude crystals contained 13% of pentaacetyl-α-D-glucopyranose, but recrystallization from ethanol gave 49.7 g of pure pentaacetyl-β-D-glucopyranose(M. p. 132°C, yield 77%).

δ (ppm)6.6 (d, 1H, J = 3.6 Hz), 5.80 (t, 1H, J = 9.8 Hz), 5.33 (t, 1H, J= 9.8 Hz,), 5.24 (dd, 1H, J = 10.5, 3.7 Hz), 4.29 (dd, J = 12.2, 4.3 Hz), 4.08-4.15 (m, 1H), 4.0 (dd, J = 12.3, 2.2 Hz), 1.50-1.70 (3s, $5CH_3$).

General procedure for selective anomericdeacetylation of D-glucose pentaacetate (3a)

MgO (1 mmol) was added to solution pentaacetyl-α-D-glucopyranose (1 mmol) in methanol (20 mL) .A drop of ammonium acetate solution was added to the reaction mixture. The reaction mixture was refluxed for 4-5 hours and controlled by TLC. then the solvent was separated, Solid matter is white . the compound was washed with hexane (3 times), and was crystallized by Ethyl acetate. and identified by NMR spectroscopy techniques.

^{1}H-NMR (CDCl3): δ (ppm)6.35 (d, 1H, ^{4}J= 3.8 Hz, H-1), 5.33 (dd, 1H, ^{3}J = 10.1 Hz, ^{3}J10.1= Hz), 4.98 (dd, 1H, ^{3}J = 10 Hz, ^{4}J =10 Hz), 4.98 (dd, 1H, ^{3}J=10.1 Hz, ^{4}J=4.0Hz), 4.38-5.1 (m, 2H), 4.77 (d, 1H,^{3}J = 10.8 Hz), 2.45 (s, 3H), 2.66 (s, 3H), 2.2 (s, 3H), 2.11 (s, 3H); ^{13}C-NMR ($CDCl_3$): δ (ppm)175.19, 170.5 , 166.35, 90.00, 72.51 , 72.29 , 69.31 , 66.20 , 59.01 .

The deacetylation of α-D-lactose octaacetate

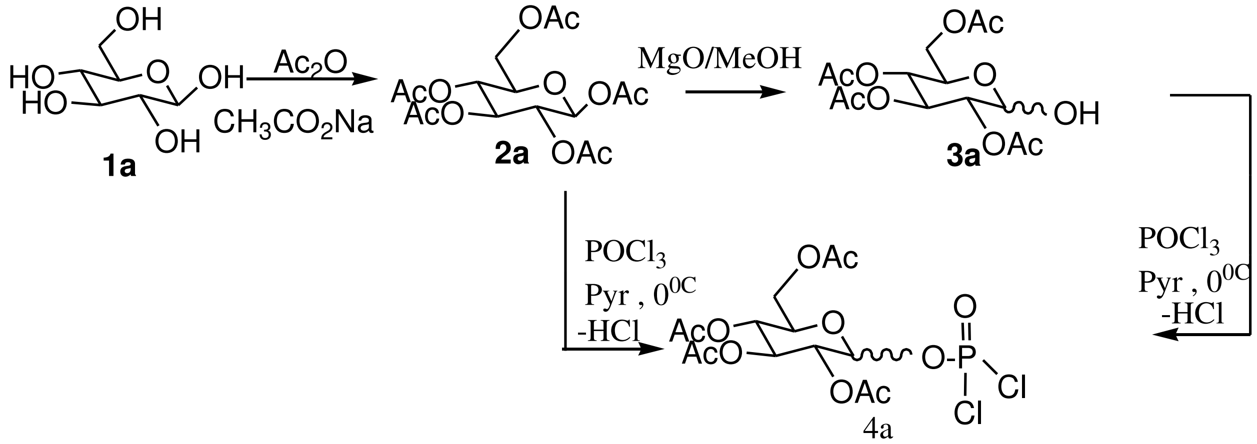
(^{i}pr)$_3$SnOEt (1mmol) was added by stirring to D-lactoseoctaacetate(1mmol) an appropriate solvent (20 ml). under reflux , stirring and boiling were continued for 4-5h (hexane/EtOAc=3:1).

^{1}HNNR ($CDCl_3$): δ(ppm)5.97 (d,1H, ^{4}J= 4.1 Hz), 5.52 (d, 1H,^{4}J = 3.0 Hz), 5.42 (dd, 1H, ^{3}J= 10.7 Hz, ^{4}J= 3.3 Hz), 5.25 (dd,1H, ^{3}J= 10.7 Hz, ^{4}J= 3.9 Hz), 4.52 (dd, 1H, J = 5,6 Hz), 4.17 (dd, 1H, ^{3}J= 11.4 Hz, ^{4}J=.4 Hz,), 4.11 (dd, 1H, ^{3}J= 11.4 Hz, ^{4}J= 6.7 Hz), 3.15 (s, 3H,), 2.11 (s, 3H,),2.06 (s, 3H,), 2.01 (s, 3H,); ^{13}C-NMR ($CDCl_3$): δ(ppm) 170.32, 170.12, 169.92, 1369.78, 91.17, 70.22 , 66.77 , 66.30 , 68.19 , 59.00 . general reaction to the preparation of phosphate esters of carbohydrates 1mmol of deacetylated carbohydrate or acetylated carbohydrate dissolved in 2 ml of pyridine. the solution to 0^{0c} was cooled.Under the nitrogen atmosphere Phosphoryl chloride drops added to the reaction mixture

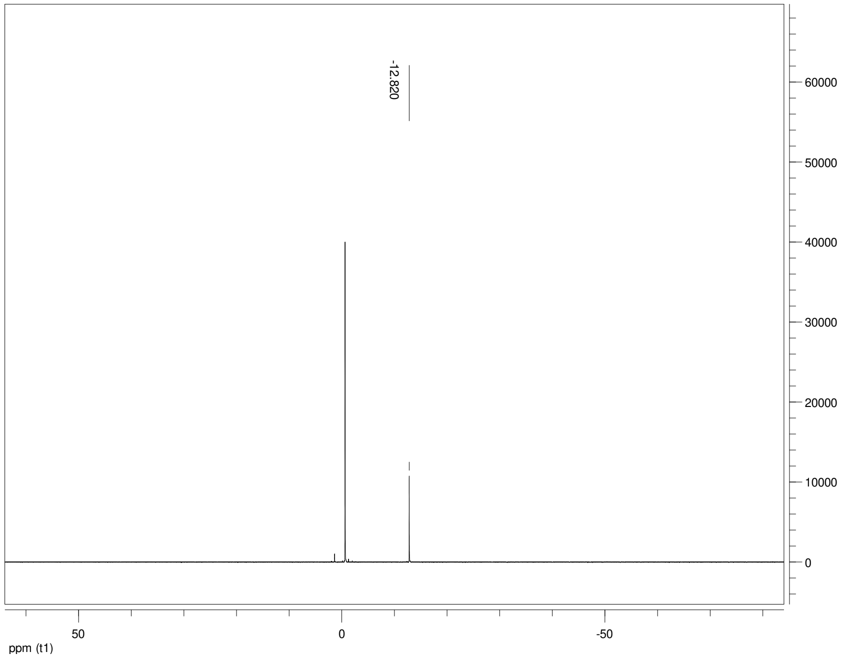
Heat is released by the addition of phosphoryl chloride.1mmol $POCl_3$ added within 1h. The reaction mixture was stirred for 1 h. Pale yellow product was obtained. the product was crystallized by a mixture of ethyl acetate, petroleum ether and ethanol in a ratio of 1: 1: 3. (yield 72%)

RESULTS AND DISCUSSION

This paper aimed to describe the full acetylation of some carbohydrates such as D-glucose , D-galactose ,), D-xylose , D-fructose and D-lactose in the presence of $Ac_2O/AcONa$ as well as selective deacetylation of anomeric position using MgO/MeOH as a heterogenous catalyst (Scheme 1, Tables 1 and 2).Anomeric configuration is deacetylated by MgO/MeOH as a catalyst, A convenient synthetic approach to regioselectivedeacetylation of full acetylated carbohydrates using heterogenous catalyst is described. In the next step, we reacted POCl3 with deacetylated anomeric position carbohydrate and acetylated carbohydrates. The same product was obtained. MgO/MeOH, efficiently catalyze the regioselective transesterification of anomeric acetates. This method offers an efficient solution for the otherwise difficult removal of methyl uronates anomeric acetates as well as a green alternative to published protocols since the MgO/MeOH catalysts are non-toxic and may be easily recycled and reused



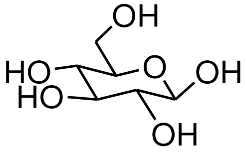
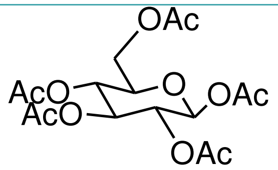
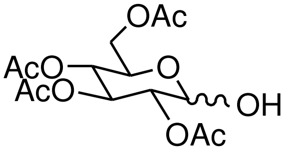
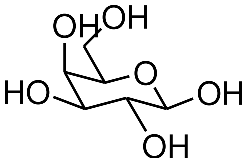
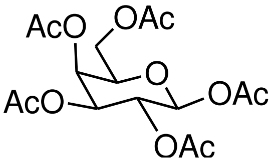
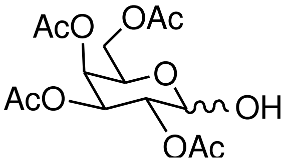
Scheme 1: acetylation of glucose and selective anomeric deacetylation and reaction with POCL3

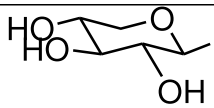
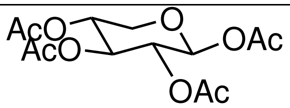
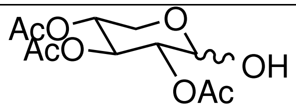
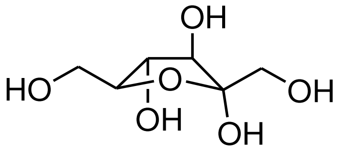
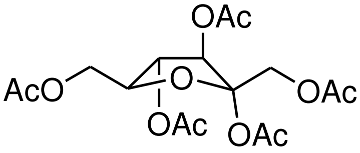
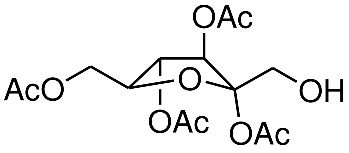
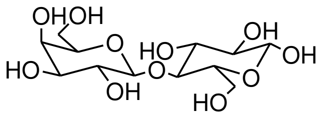
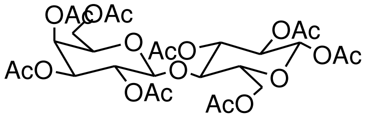
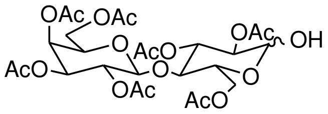


Scheme 2. Representatively, ^{31}P NMR spectrum of **4a**.

The ^{31}P NMR spectrum of **4a** is shown in Figure2. A singlet peak at δ -12.82 ppm corresponded to a unique phosphorous atom connected to oxygen, nitrogen and halogen atoms. (scheme 2)

Table 1: acetylation and selective anomeric deacetylation carbohydrates

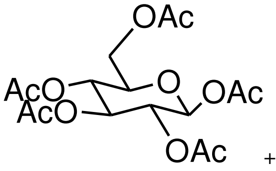
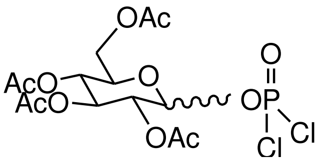
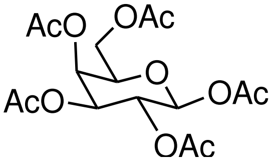
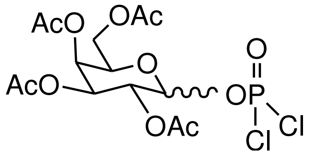
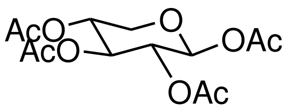
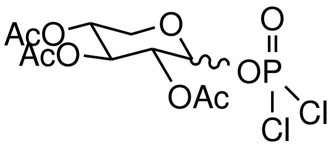
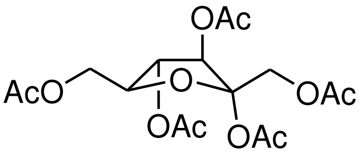
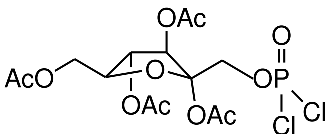
Entry	carbohydrate	Acetylated carbohydrate	Selective anomeric deacetylation	**yield (%)**
1				**72**
2				**70**

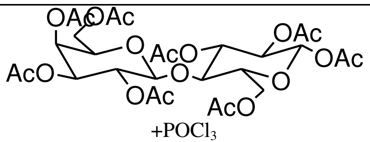
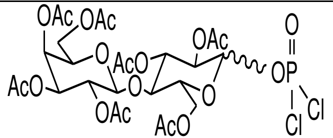
3				**66**
4				**62**
5				**70**

In this project, we acetylated various carbohydrates by anhydride acetic in the presence of sodium acetate. Then the anomeric position is deacetylated by the MgO/MeOH heterogeneous catalyst. Then we reacted with POCl3 and the carbohydrate phosphate ester was obtained from the anomeric position.

In this project, we reacted directly to the acetylated carbohydrates in the next step without deacetylation the anomeric position. The product of ester phosphate carbohydrate was obtained. The product is the same. In organic chemistry, the anomeric effect is a stereoelectronic effect that describes the tendency of heteroatomic substituents adjacent to a heteroatom within a cyclohexane ring to prefer the axial orientation instead of the less hindered equatorial orientation that would be expected from steric considerations.

Table 2: Reaction acetylated carbohydrates with $POCl_3$

Entry	Acetylated carbohydrate + $POCl_3$	Product	**Conversion (%)**
1	 $+POCl_3$		**82**
2	 $+POCl_3$		**79**
3	 $+POCl_3$		**69**
4	 $+POCl_3$		**75**

5	 +$POCl_3$		**65**

CONCLUSION

The present study investigated an productive manner for deacetylation of anomeric position. This method has several advantages such as the good-natured reaction conditions, experimental simplicity, good yield. then the basic reagents are unfavorable for anomeric deacetylation this approach can be very effective. In all cases, The yields were good to excellent. However, in this paper carbohydrates such as glucoss, xylose, fructose, galactose, lactose by acetic anhydride in the presence of sodium acetate were acetylated. Then the deacetylation of anomeric position by MgO/MeOH was reacted. After deacetylation anomeric position, we reacted with phosphoryl chloride and the product of carbohydrate phosphate ester from the anomeric position was obtained In the next step, we directly reacted the acetylated carbohydrates with phosphoryl chloride and the same product was obtained.

REFERENCES

1. Bhat SU, Naikoo RA, Ahmad Bhat R, Malla MA, Tomar R, Gatum NK, Tiwari KR. H-mordenite zeolite as an efficient, rapid and recyclable catalyst for chemoselective synthesis of 1, 1-diacetates under solvent-free conditions. Asian Journal of Green Chemistry. 2017 Jul 1;1(1):46-55.
2. Jabbari, H, Noroozi, J. synthesis of carbohydrate esters and selective anomeric deacetylation by MgO/MeOH. Chemical oggi chemistry today.2018,1,5-7.
3. Calvaresi EC, Hergenrother PJ. Glucose conjugation for the specific targeting and treatment of cancer. Chemical science. 2013;4(6):2319-33.
4. Park, J, Lee, H.Y, Cho, M.H, Park, S.B.Development of Cy-3 labeled glucose bioprobe and its application in bioimaging and screening for anticancer agents, AngewandteChemie International Edition. 2007, 46, 2018-2022.
5. T. Tanaka, M. Noguchi, A. Kobayashi and S.-I. Shoda, unprotected carbohydrates as starting material in chemical synthesis, Chem. Commun., 2008, 2016 —2018.
6. Noguchi M, Nakamura M, Ohno A, Tanaka T, Kobayashi A, Ishihara M, Fujita M, Tsuchida A, Mizuno M, Shoda SI. A dimethoxytriazine type glycosyl donor enables a facile chemo-enzymatic route toward α-linked N-acetylglucosaminyl-galactose disaccharide unit from gastric mucin. Chemical Communications. 2012;48(45):5560-2.
7. Novoa A, Barluenga S, Serba C, Winssinger N. Solid phase synthesis of glycopeptides using Shoda's activation of unprotected carbohydrates. Chemical Communications. 2013;49(69):7608-10.
8. Watanabe K, Itoh K, Araki Y, Ishido Y. A comparison of bis (tributyltin) oxide, potassium cyanide, and potassium hydroxide as reagents for the regioselective 1-O-deacetylation of fully acetylated sugars. Carbohydrate research. 1986 Oct 15;154(1):165-76.
9. a) Nudelman A, Herzig J, Gottlieb HE, Keinan E, Sterling J. Selective deacetylation of anomeric sugar acetates with tin alkoxides. Carbohydrate research. 1987 Apr 15;162(1):145-52.;
10. (b) Herzig J, Nudelman A, Gottlieb HE. Methanolysis of acetylated sugars and glycosides in the presence of tin oxides and alkoxides. Carbohydrate research. 1988 Jun 15;177:21-8.
11. Helferich B, Portz W. Über N-Glykoside. II. Mitteilung. Chemische Berichte. 1953 May;86(5):604-12.
12. Itoh T, Takamura H, Watanabe K, Araki Y, Ishido Y. A facile procedure for regioselective 1-O-deacylation of fully acylated sugars with sodium methoxide. Carbohydrate research. 1986 Nov 15;156:241-6.
13. Mikamo M. Facile 1-O-deacylation of per-O-acylaldoses. Carbohydrate research. 1989 Aug 1;191(1):150-3.
14. Rowell RM, Feather MS. Synthesis and properties of anomerically unsubstituted hepta-O-acetyl disaccharides. Carbohydrate Research. 1967 Aug 1;4(6):486-91.
15. Herzig J, Nudelman A. Regioselective heterogeneous O-deacylation of polyacylated sugars. Carbohydrate research. 1986 Sep 15;153(1):162-7.