Bachelor's thesis

NTNU
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Selective Functionalization of Glucose

Bachelor's thesis in Chemistry
Supervisor: Nebojsa Simic
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Content

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Abstract

In this text we will write and discuss about the subject of selectively functionalizing glucose. Including different methods to achieve selective functionalization and the effects it can have on the compound (Figure 1). Glucose is a molecule that is vastly spread in almost everything we eat and is found in many more places around the world and in different industries. Being able to selectively functionalize glucose can open the doors for new reactions, new glucose derivatives and the use in further synthesis in ways that have not been found yet.

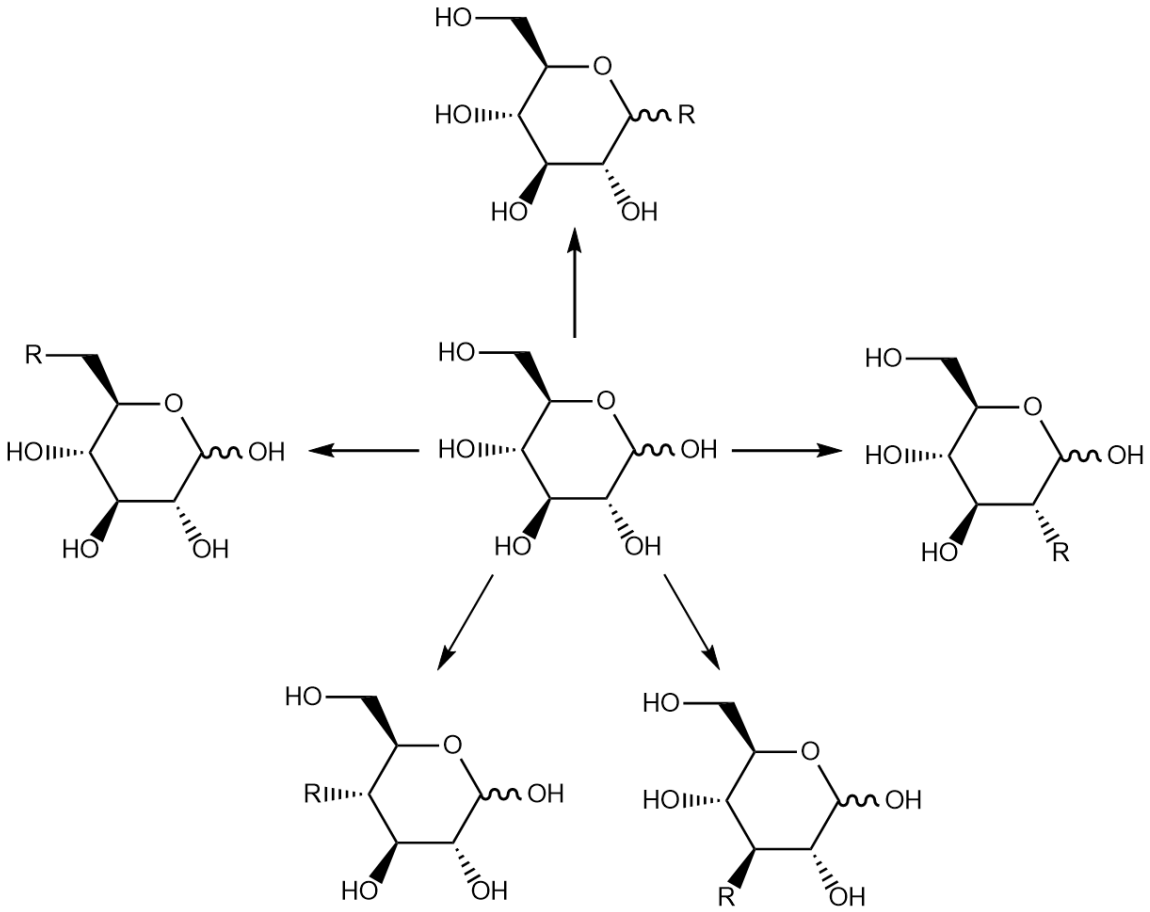

Figure 1: General idea of the selective functionalization of glucose

For the synthesis we will look at two different methods to achieve selective functionalization, protecting group chemistry and enzymatic reactions. After that examples and explanations on how different functional groups at different carbon positions in glucose can change the

chemical and physical properties of the molecule will be given. Once everything has been explained, the literature used, and its credibility will be discussed. Furthermore, the results from the literature and the potential of selectively functionalizing glucose for industrial use will also be discussed.

In this text the conclusion was drawn to protecting group chemistry and enzymatic reactions being able to selectively functionalize glucose. The efficiency and reliability of protecting group chemistry and enzymatic reactions compared to other methods may not be known. As there are numerous ways to synthesise selective glucose derivatives and there also being a just a great, if not bigger number of properties for the new derivatives. Many are already known and many more have yet to be found. As for the industrial use, the conclusion was drawn to the selective functionalization of glucose holding high potential for a potentially sustainable future with the possibility of new drugs and compounds to be created.

Introduction

General principles in synthesis of glucose derivatives

Carbon 1 and 6

In glucose, the carbons at position 1 and 6 (Figure 2) have distinct characteristics and are known for being easier to selectively functionalize. I will go more in depth as to why and how.

The easiest selective functionalization of glucose may be done at the anomeric carbon (C1). The C1 carbon is the only carbon in glucose which is bonded to two oxygens. This causes the electrons to be drawn away from it, due to the electron withdrawing effect, making it activated for nucleophilic attacks. (1)

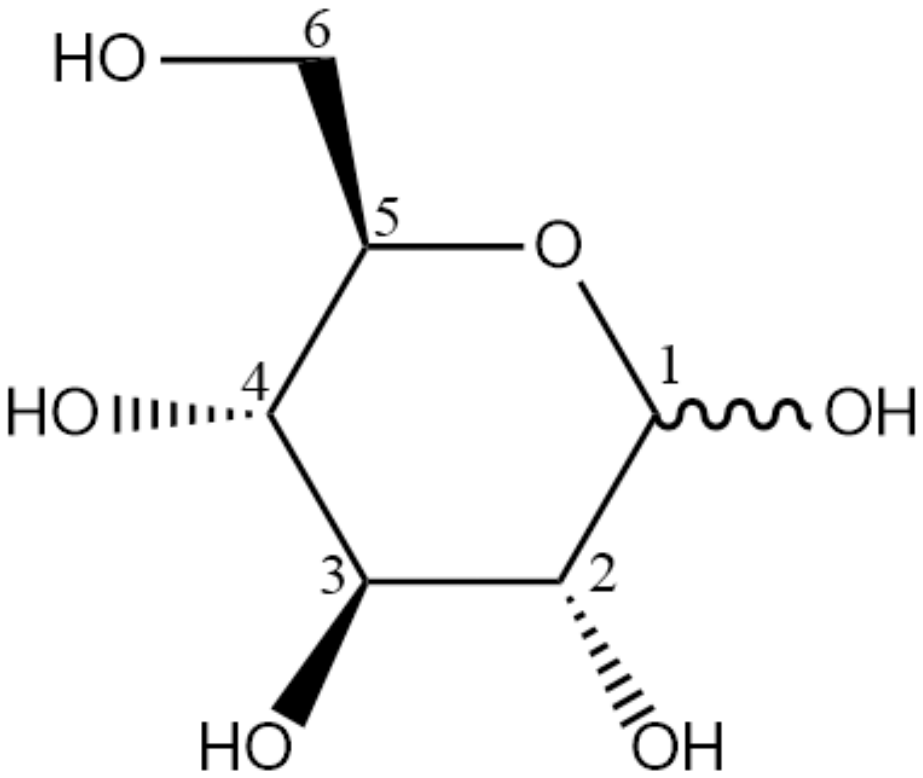

Figure 2: Structure of Glucose

When selectively functionalizing C1 in glucose it is important to note that one cannot simply add a strong base/reducing agent as this may react with all the hydroxyl groups in glucose. If one wants to selectively functionalize C1 only, different methods are used. Using protective groups to block the other hydroxyl groups is a common method that leaves only the C1 hydroxyl group accessible for further chemical synthesis. To start, one needs to protect all the hydroxyl groups with a suitable protecting group, such as acetyl. Acetyl can be inserted using

acetic anhydride and a catalyst such as pyridine, which will result in forming glucose pentaacetate (Figure 3) (2).

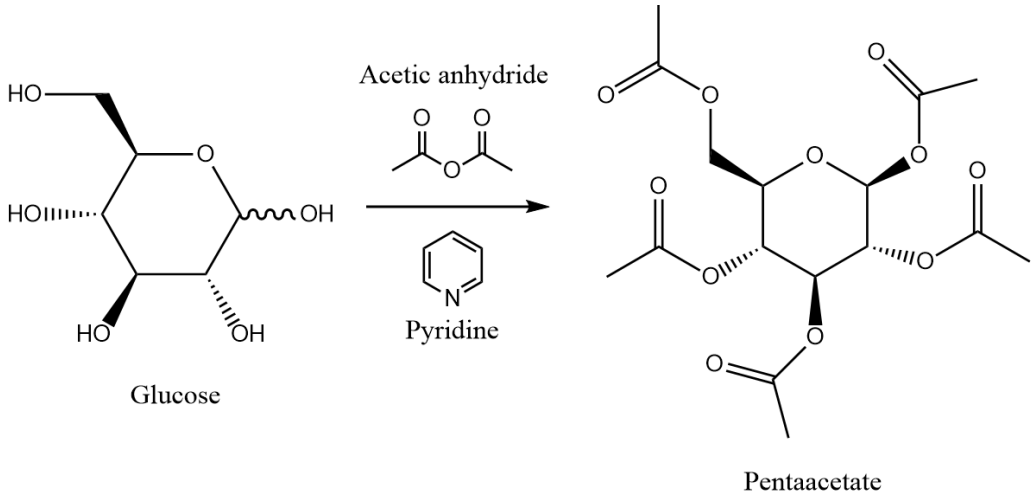

Figure 3: Synthesis of protecting all hydroxyl groups in glucose with acetic anhydride and pyridine.

The next step is to treat the protected glucose with a base such as sodium methoxide, which will selectively remove the acetyl group from C1. The corresponding product is now a glucose with a free hydroxyl group at C1 and acetyl groups on the other carbons (3). Selectively leaving the C1 hydroxyl group unprotected allows for the introduction of a variety of functional groups through oxidation, reduction, or substitution. Lastly, to remove the protecting groups a suitable base or acid is added. (4)

As for the carbon at position 6 (C6), its ability to be easily selectively functionalized is mostly due to two factors. The C6 carbon is outside the ring formation, making it less stereochemically hindered. The C6 carbons is also bonded to an electron-withdrawing group, and it is a primary carbon. This causes the positive charge at the C6 carbon to be less stabilized.

To selectively functionalize the C6 carbon the same method is used as for the functionalizing of C1, protection and selective deprotection. The only difference for the process of functionalizing C6 are the chemicals used. So, to begin with, one needs to protect the hydroxyl groups at position 1-4. This can be done by using a suitable protecting agent, such as tert-butyldimethylsylil (TBDMS). This reagent will not interact with the hydroxyl group at C6 due to steric hindrance. In addition to TBDMS, a mild Lewis-acid, such as 4-dimethylaminopyridine (DMAP) is added to catalyse the reaction. The use of a compound like DMAP is quite important in this reaction. DMAP will coordinate with the TBDMS

reagent and activate it towards nucleophilic attacks of the hydroxyl groups of glucose. Once both reagents have been added to a solution of glucose, the left-over hydroxyl group at C6 can easily be attacked by a number of reactions, as already explained previously (Figure 4).

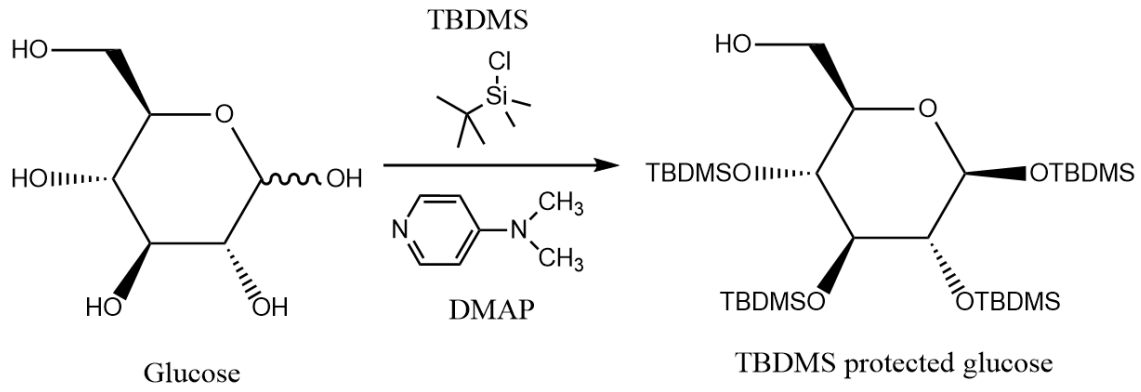

Figure 4: Synthesis of TBDMS protected glucose with DMAP

When the desired functional group is inserted to the C6 carbon, the protective groups need to be removed again. The removal of TBDMS requires an appropriate deprotection agent such as tetra-*n*-butylammonium fluoride (TBAF). TBAF is a mild fluoride-ion releasing agent, which can cleave the silicon-oxygen bonds of TBDMS, while sparing the other functional groups in the molecule. The reaction typically takes places in anhydrous conditions and the reaction mixture is buffered with an organic base to preserve a neutral pH and prevent the protonation of the fluoride ion, which could result in the creation of undesirable by-products. (5)

Carbon 2 to 4

The carbons at position 2 to 4 (C2 to C4) are adjacent to the carbon at position 1. These carbons are often referred to as the "glycosidic carbons" due to being involved in the formation of glycosidic bonds in carbohydrates. The selective functionalization of C2 to C4 can be challenging due to their similar reactivity. A chemical that targets the carbon at position 2 may, for instance, also react with the nearby carbons at positions 3 and 4. The destruction of the glucose molecule or the formation of undesirable by-products can result from this lack of selectivity. (6)

The similarity in their chemical reactivity is not the only reason as to why the selective functionalization is challenging. There are many other factors, but the second crucial factor is the regioselectivity of C2 to C4 in glucose. The carbons at positions 2, 3, and 4 have similar

steric and electronic environments, making regioselectivity an important consideration in the selective functionalization of glucose. It is difficult to achieve selective functionalization at one carbon while avoiding reaction with the others. There are several factors that can influence the regioselectivity of glucose reactions. The nature of the reagent, the catalyst, the reaction conditions, and the presence of functional groups or protecting groups are all examples of these. Because of differences in steric or electronic factors, certain reagents or catalysts may have a higher affinity for one carbon over another. Furthermore, reaction conditions such as temperature, solvent, and pH can influence a reaction regioselectivity. The presence of functional groups or protecting groups can also influence regioselectivity. Protecting groups can be used to shield specific functional groups from a reaction, enabling selective functionalization at a specific carbon. However, the introduction of protecting groups can complicate the synthesis and may necessitate additional steps to remove them. (7, 8)

To selectively functionalize C2, C3 and C4, it is possible to use protecting group chemistry, which is used for C1 and C6. However, due to the similarity in their chemical reactivity and regioselectivity, the process becomes much more complicated, necessitating several additional steps and chemicals required. One example of this is the C3 carbon. To selectively functionalize C3, one could start by selectively protecting the C1 and C6 carbon using suitable protecting agents. The resulting intermediate now has C2, C3 and C4 left unprotected (Figure 5). A method that could be used to selectively protect C2 and C4 without protecting C3 is by using orthogonal protecting groups.

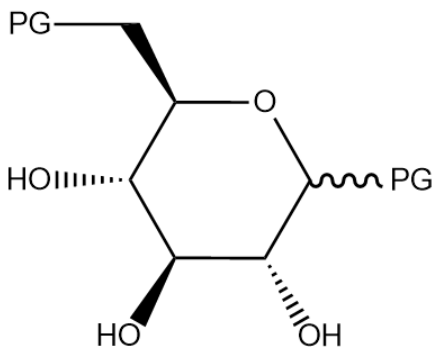

Figure 5: Glucose with C1 and C6 protected. PG here simply means protecting group.

Orthogonal protecting groups are a concept in synthetic organic chemistry that involves the selective protection and deprotection of functional groups during a multi-step synthesis. These groups are used to temporarily shield reactive functional groups from participating in reactions, allowing chemists to control the reactivity of a molecule during the synthesis of complex organic compounds (9). Orthogonal protecting groups are designed to be removed under different conditions than other protecting groups in the same molecule, enabling selective deprotection (10).

In theory, to use this method to now selectively leave C3 unprotected, one would need 2 protecting groups which can be removed under different conditions. One of the protecting groups would need to be used to protect the C2 and C4 carbon and the other protecting group to protect the C3 carbon (See first reactant in Figure 6). Once the orthogonal protecting groups have been added, a suitable deprotection agent needs to be added to selectively deprotect the C3 carbon (Figure 6).

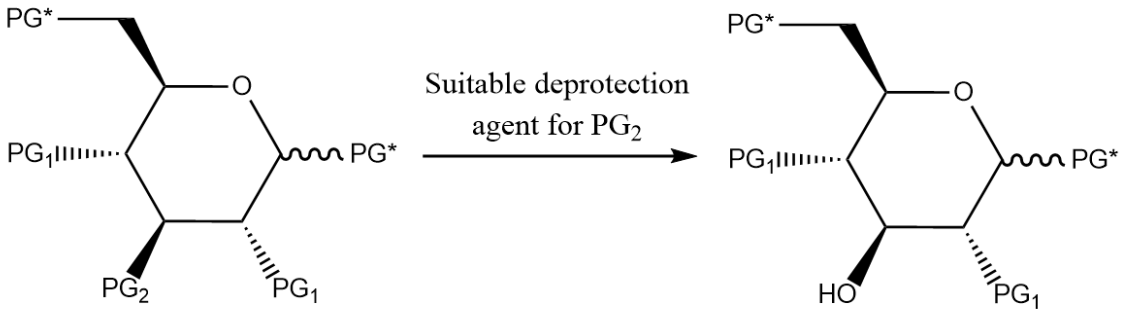

Figure 6: Theoretical example of selectively deprotecting the PG_2 group at C3. PG also means protecting group here.

Selective functionalizing through enzymatic reactions

The processes for selectively functionalizing C2 and C4 using protecting group chemistry are equally, if not more complicated. However, this opens the door to the use of alternative methods, such as enzymatic reactions. As research into enzymes and their applications has increased in recent years, the possibilities for their use in chemical synthesis have expanded (11).

One way to selectively functionalize glucose at the C2-C4 position could be to create 2-deoxyglucose, 3-deoxyglucose and 4-deoxyglucose as these will open the carbons for nucleophilic attacks (See figure 7). We will look at the use of the enzyme hexokinase, ribokinase and aldolase to give an example of how enzymes are able to selectively react with certain carbon positions (13, 14, 15). Hexokinase can be used to turn glucose into 2-deoxyglucose. The enzyme catalyses the

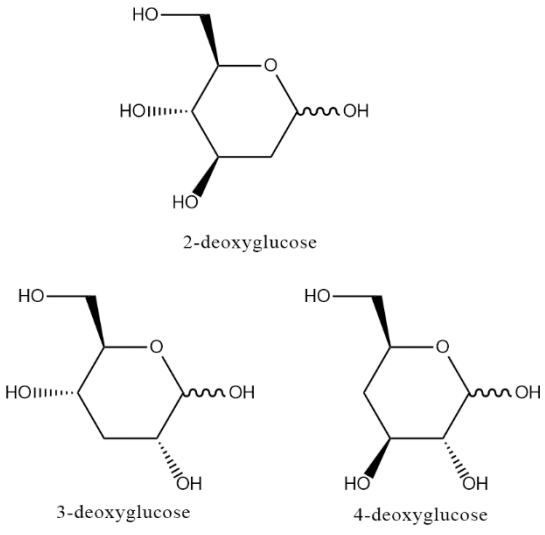

Figure 7: 2, 3 & 4-deoxyglucose

phosphorylation of glucose at the C6 carbon using Adenosine Triphosphate (ATP) as a phosphate donor, producing glucose-6-phosphate. To use this enzyme to selectively functionalize the C2 carbon one could add glucose to hexokinase and a non-hydrolysable ATP analog, such as adenosine 5'-O-(3-thiotriphosphate) (ATPγS), which can bind to the enzyme but cannot be hydrolysed. This will result in the formation of 2-deoxyglucose-6-phosphate (2DG6P), which has a phosphate group at the C6 position and a hydrogen atom at the C2 carbon (15). The 2DG6P can then be dephosphorylated using alkaline phosphatase, resulting in the formation of 2-deoxyglucose (2DG) with a free C2 hydroxyl group (Figure 8). (16)

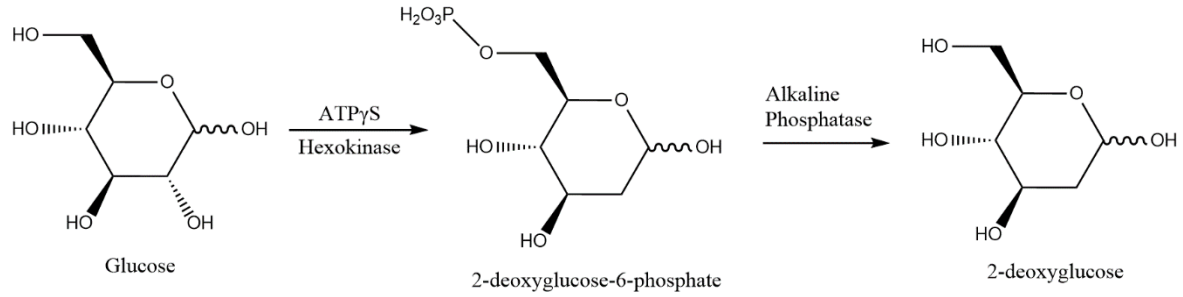

Figure 8: Synthesis of 2-deoxyglucose with hexokinase

To turn glucose into 3-deoxyglucose, the enzymes ribokinase and aldolase are commonly used. Ribokinase catalyses the phosphorylation of ribose at the C5 carbon to form ribose-5-phospholate, using ATP as a phosphate donor (Figure 9). The resulting ribose-5-phosphate can then be combined with glucose through an aldolase-catalysed reaction to form 3-deoxyglucose-6-phosphate. The resulting 3-deoxyglucose-6-phosphate can be further dephosphorylated at the C6 position by alkaline phosphatase to form 3-deoxyglucose (Figure 9). (13)

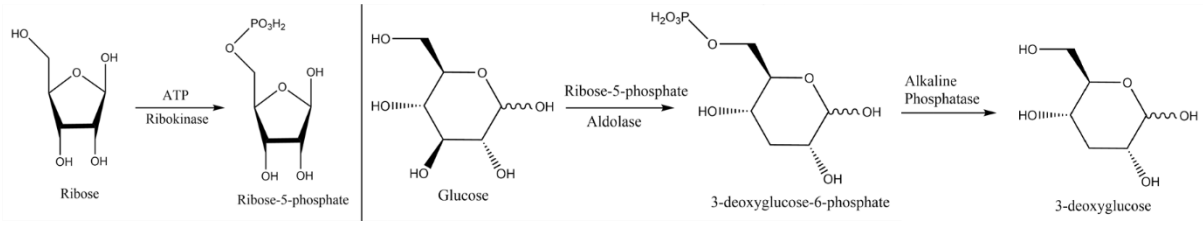

Figure 9: Synthesis of ribose-5-phosphate with ribokinase and synthesis of 3-deoxyglucose aldolase.

Lastly, to turn glucose into 4-deoxyglucose, aldolase is used in addition with 2-deoxyglucose-6-phosphate. In this reaction, the enzyme hexokinase may also be used, as it can be used to turn glucose into 2-deoxyglucose-6-phosphate as mentioned earlier. The reaction including

aldolase involves the condensation of dihydroxyacetone phosphate (DHAP) and 2-deoxyglucose-6-phosphate to form 4-deoxyglucose-6-phosphate and glyceraldehyde 3-phosphate (G3P). One advantage of using this process is that the reaction can be reversed by adding excess G3P, driving the equilibrium towards the formation of 4-deoxyglucose-6-phosphate (14). The resulting 4-deoxyglucose-6-phosphate can be further dephosphorylated by alkaline phosphatase to form 4-deoxyglucose (Figure 10). (17)

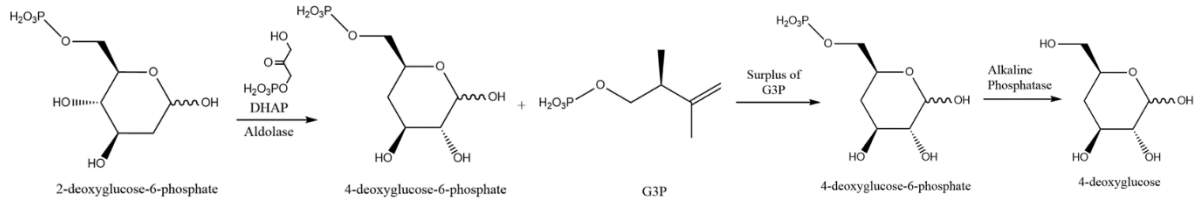

Figure 10: Synthesis of 4-deoxyglucose with aldolase

Selectivity of functional groups

In glucose derivatives, the position of the added functional group is important in determining their chemical and physical properties. Due to electronic and steric effects, when glucose is selectively functionalized at different positions, it can result in derivatives with varying reactivity profiles. When the glucose derivatives are involved in subsequent reactions, these differences in reactivity can have an even greater impact on reaction rates and outcomes. (18)

Another important factor influenced by the position of the functional group is stereochemistry. Because glucose has multiple chiral centres, adding a functional group at different positions can result in distinct stereoisomers with distinct properties (19). Furthermore, the position of the functional group can affect the solubility of glucose derivatives in different solvents. For example, adding a hydrophobic functional group to a specific position can reduce polar solvent solubility, while adding a hydrophilic group can increase it (20).

The functional groups position can also influence how glucose derivatives interact with other molecules such as enzymes, receptors, or other chemical compounds. In a broader context, these interactions may have implications for biological activity, pharmaceutical properties, or chemical reactivity (21). Furthermore, the presence of a functional group in a specific position can affect the stability of different conformations of the glucose derivative, potentially affecting its properties (22).

When selectively functionalizing glucose, a countless amount of varying functional groups can be used to replace the hydroxyl groups. We will look at some of them which are carboxylic acids (COOH), amino groups (NH2), and acetates (OCOCH3) (See figure 11).

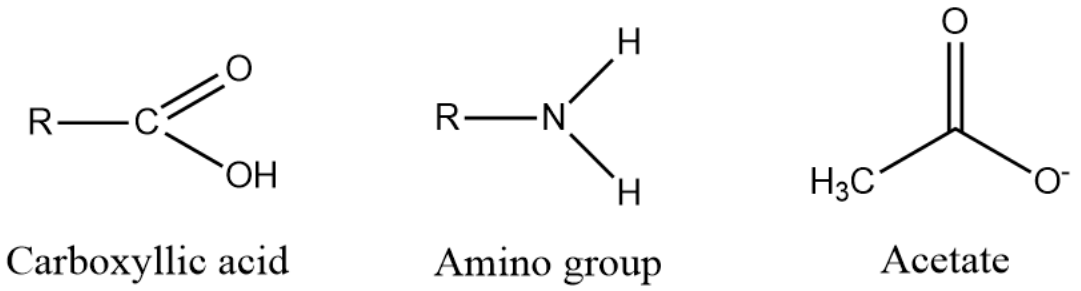

Figure 11: Visual representation of COOH, NH2 and OCOCH3

When a carboxylic acid group is introduced at different positions, it produces distinct derivatives such as gluconic acid (C1), 2-ketogluconic acid (C2), 3-ketogluconic acid (C3), 4-ketogluconic acid (C4), and glucuronic acid (C6). The position of the carboxylic acid group influences acidity, ionization, and hydrogen bonding capability, which can affect solubility, reactivity, and interactions with other molecules. To give an example of this, the pKa value of gluconic acid is around 3.86, whereas 2-ketogluconic acid has a pKa value of around 4.11 making it a weaker acid (See Figure 12 for an example of the molecules in question). (23)

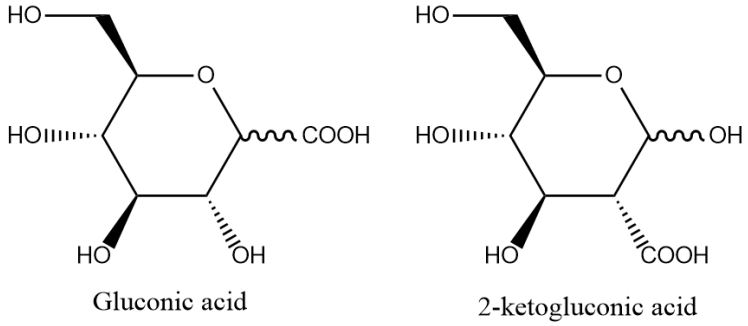

Figure 12: Visual representation of gluconic acid and 2-ketogluconic acid

When an amino group is introduced at different positions, different derivatives are formed, such as glucosamine (C1), 2-amino-2-deoxyglucose (C2), 3-amino-3-deoxyglucose (C3), 4-amino-4-deoxyglucose (C4), and 6-amino-6-deoxyglucose (C6). The position of the amino group affects nucleophilicity, hydrogen bonding capability, and basicity, all of which can affect reactivity and interactions with other molecules, such as enzymes or receptors (24). To give an example on how the chemical and physical properties of glucose can change with selective in positioning in mind, we will look at the basicity and hydrogen bonding

capabilities. An amino group at the C6 carbon (Figure 13) would be expected to be more basic due to its greater steric accessibility. The C3 position (Figure 13) may be less basic due to the increased steric hindrance compared to C6 and proximity to other hydroxyl groups. It should also be expected for the C6 positions to offer better hydrogen bonding capabilities due to same reasons as already mentioned. (25, 26)

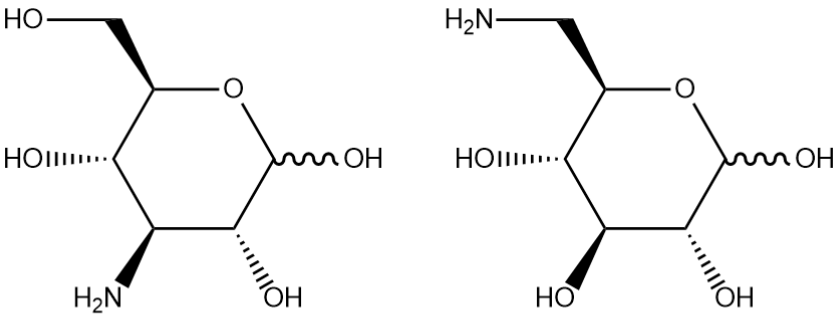

Figure 13: Visual representation of the glucose derivatives with an amino group at respectively the C3 and C6 position

Introducing an acetate group at different positions leads to distinct derivatives, such as 1-O-acetyl-α-D-glucopyranose (C1), 2-O-acetyl-α-D-glucopyranose (C2), 3-O-acetyl-α-D-glucopyranose (C3), 4-O-acetyl-α-D-glucopyranose (C4), and 6-O-acetyl-α-D-glucopyranose (C6) (Figure 14). The acetate groups position can influence the reactivity and stability of the glucose derivative during subsequent chemical transformations. Steric hindrance caused by an acetate group at a specific position in the molecule can affect the reactivity of other functional groups in the molecule, potentially affecting reaction rates and outcomes (27).

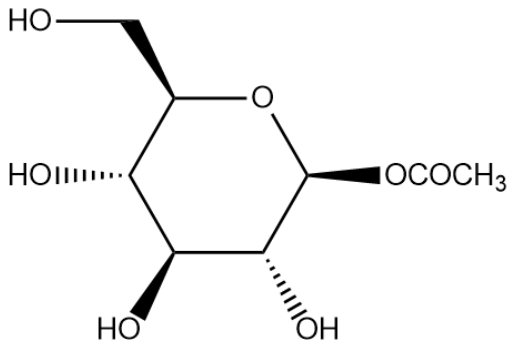

Figure 14: Visual representation of the glucose acetate derivative 1-O-acetyl-α-D-glucopyranose

Specific literature on how the chemical and physical properties of the glucose derivatives change with the selective position of acetates group is limited. However, it is possible to hypothesize based on known carbohydrate chemistry principles. For acetate functional groups it would be important to think about the steric hindrances and intramolecular interactions. There are also numerous other functional groups which could be selectively added to glucose and the same principles to hypothesize apply (known carbohydrate chemistry).

Discussion

Literature used and current status of knowledge

The process of selectively functionalizing glucose is an easy question with a very difficult answer. The functionalization at C1 and C6 have been widely researched for a long time and so have the C2, C3 and C4 positions as well, but the significant difference between them is the C2-C4 positions being much harder to research. The literature in this text has been used to give examples on the synthesis and to try and explain the effects of functionalization with selectivity in mind. According to the literature, the selective functionalization of C1 and C6 are much easier to carry out due to those two positions being much more reactive and less stable. There are also more factors that influence the selectivity. As for the synthesis of glucose derivatives at the C2 to C4 positions, the literature mentions many reasons as to why the process is more complicated and difficult to carry out. It is due to reasons such as stability and stereochemistry as they may influence the selectivity. The literature was also used to step into the territory of enzymatic reactions. As stated in the literature, enzymatic reactions have been researched more and more in recent years and they have proven to be able to selectively functionalize glucose. As for the effects of selectively functionalizing glucose, the literature mentions many aspects of the physical and chemical properties of glucose that can change depending on the reaction. The properties of the glucose derivatives can change depending on the functional group added and the position. There are numerous combinations of functional groups and position which can be utilized to change the properties of glucose to achieve different compounds. With the help of the literature, three different examples of functional groups were given with different positions in mind and the change in the properties of the derivative was explained.

The subject of selectively functionalizing glucose has been extensively researched for many years, but many of the answers to the questions have yet to be found. One literature used in the text can be dated all the way back to 1972, so even over 50 years ago there was research being made on reactions related to the selective functionalization of glucose. Judging by this, one could speculate that the research has been going on for even longer. But even though the subject has been researched for so long, there are many questions with answers yet to be found. The literature used to give an example on selectively functionalizing the C3 carbon in glucose using protecting group chemistry merely gives a general idea of the process. This fact might be used to further prove the point of the difficulty when it comes to selectively functionalizing glucose at the C2, C3 and C4 position.

Most of the literature used in this text originates from the 21st century, so one could argue that the credibility of the sources used is rather high. However, while certain literatures are not precisely about glucose because they employ specific glucose derivatives and other carbohydrates, the literature was merely used to provide theoretical examples, especially for the synthesis. As mentioned above, some of the literature dates back in time to the 20th century, so one might argue the credibility of those publications. Even though they are old, the literatures are from acknowledged publishers and are all peer-to-peer reviewed so one could say they have arguably high credibility, when it comes the to content of the literature itself.

Synthesis of glucose derivates and selectivity of functional groups

The problem in this text is about different ways one could selectively functionalize glucose to create glucose derivates and how the chemical and physical properties could change of the glucose derivates with selectivity in mind.

For the synthesis, we have looked at two different methods, protecting group chemistry and enzymatic reactions. When using protecting group chemistry there are multiple factors that come into play. The choice of protecting group is very important as the properties of the protecting group can influence the reactivity of the other carbon positions. The C2, C3 and C4 positions are the hardest to selectively functionalize in glucose. When using protecting groups to selectively functionalize those positions, the C1 and C6 positions should be protected first, and the protecting group used to do so, can further influence the reactivity of the remaining open positions. As for the of protecting groups used for the C2, C3 and C4 positions, multiple factors such as steric hindrance might affect the choice of reactants used. Overall, it points towards that the use of protecting groups for the C2, C3 and C4 positions may be a rather complicated process compared to the C1 and C6 position. In the introduction there were multiple mentions of "suitable" deprotecting agents, this is due to the choice of reactant used, may influence the result as well. The use of a wrong deprotecting agent may remove the functional group that was added through the process or may change other parts of the new glucose derivative. You can not fully predict which reactions, protecting agents and deprotecting agents work in the selective functionalization of glucose because every reagent affects the molecule differently. This is due to reasons such as steric hindrance and electronic effects. It also depends on the strength of the glycosidic bond created. The process of finding the best ways to selective functionalize glucose is a trial-and-error method and a lot of experimental checking. But to answer the question of how and if, the literature states that

protecting group chemistry is viable to selectively functionalize glucose. It may not be the most efficient method, but it is possible.

For the examples shown in the introduction of enzymatic reactions, it is important to note that they are merely examples of enzymes being able to selectively functionalize glucose. The reactants and reactions shown may not be the most effective way of doing so. With more research into enzymes the use of them could be steadily increased as they can be programmed to act like a key that perfectly fits the lock. What is meant by this, is that it is theoretically possible to create enzymes that could selectively change the functional group at a certain position in glucose to a chosen group. Enzymatic reactions may not have been researched as long and thoroughly as other chemical reactions, but this does not change the fact that enzymes have the possibility to play a significant role in the future of chemical synthesis. Even though there were no examples given of enzymes being able to selectively functionalize glucose at the C1 and C6 positions, it is important to note that they may be able to do so. The question is just about finding the correct enzyme and using a trial-and-error method for example, until it works. It may be assumed that such enzymes are already in existence, the literature does not mention those, but it is highly likely. However, to answer the question, the literature states that it is also possible to use enzymes for the selective functionalization of glucose through for example phosphorylation.

When comparing the results from the literature about using protecting group chemistry versus enzymatic reactions, certain points may be hypothesized. As mentioned, with more research into enzymes, they may be easier and more straightforward to use and can open the doors to the future in chemical synthesis. Protecting group chemistry is a widely known and thoroughly researched subject, so it would be wrong to say that this method is not as good. It is simply a question of time and research until the superior method is found, it may not even be one of the two methods discussed.

For the properties of the glucose derivates created from selective functionalization, we used carboxylic acid, amino groups, and acetate as examples. It is not easy to compare the different functional groups against each other as they are completely different compounds, but it is easier to compare the effects of selectivity. For carboxylic acids for example, the position of the acid changed the derivatives pKa values. This change in the properties is due to certain carbon positions being less reactive, for example. If the carboxylic acid group is added to the anomeric carbon C1, the pKa value is expected to be lower than if the acid is

added to the C3 position. The factors that influence this change are reactivity, resonance, bond strength, electronic properties and many more just to give an example. The literature states that the C1 carbon is more reactive than the C3 carbon, meaning a carboxylic acid group added to the C1 position will be more likely to deprotonate. The answer to how the properties of glucose derivatives change with selectivity in mind has already been partially answered in the introduction, by theoretical knowledge and practical examples. The knowledge of how certain factors can affect the properties of the derivatives can be utilized to create specific derivatives with certain properties, which can be further used in many fields and industries. A theoretical example of this could be to create a specific glucose derivative with bioactive properties which could be utilized to create new drugs to heal illnesses. There is an abundance of different functional groups with an even greater number of varying effects based on the selectivity. There are many already known functional groups and their effects on glucose with selectivity in mind, and many more have yet to be found. It has the ability to give chemical synthesis many more options than those who already exist, given enough time. It is not a question of if, but rather a question of when.

Assessment of what is reported

In the introduction, there were practical and theoretical examples given. For the most part of the introduction, the examples and literature written comes from studies where the experiments were done in a controlled environment. This means that what the literature states, should have been done under realistic conditions and are possible to repeat. As most of the literature comes from a not only theoretical standpoint, it is possible to assume that what is written in this text may be possible to reproduce as well. I should point out again that during the writing of the text, I was merely using and referencing the literature to answer the problem. The examples of the selective functionalization of the C1 and C6 positions were taken from practical examples where the results of those studies have shown it to be theoretically possible. This also applies to the effects of functional groups with selectivity in mind when it comes to the pKa values of gluconic acid versus 2-ketogluconic acid for example. The use of protecting group chemistry to selectively functionalize glucose at the C2, C3 and C4 position is purely theoretical in this text. There are also parts in the discussion such as the possibilities created by selective functionalization of glucose which are purely theoretical. For these parts it is important to understand that they may already be possible, but just not reported in this text.

When it comes to the discussion of which factors are more important than others in the selective functionalization of glucose, it may be hard to pick out certain factors. It is possible however, to say that factors such as stereochemistry, regioselectivity and reactivity may be more important factors as others due to them being mentioned repeatedly in the literatures. Common factors which are seen in multiple processes tend to be more important factors but are not proof for the statement and should not be interpreted as such.

Industrial use

The capability of certain chemical compounds and reactions to be used in the industry tend to be important factors for the investment in the research. Factors with a tendency to hold high importance are economic and environmental factors. This part will focus more on the use of enzymatic reactions as they may hold tremendous potential for the future of the selective functionalization of glucose.

When it comes to the question of price, creating new enzymes with the sought after properties may be highly expensive. Furthermore, the mass production of such enzymes also tends to hold a high economic burden. This opens the question of which industries could profit from the employment of enzymatic reactions. Some small-scale industries may not want to invest in the research and use of enzymatic reactions on an industrial scale due to the high potential price. However, pharmaceutical and research industries may differ. It is theoretically possible to create “wonder drugs” by selectively functionalizing glucose, and enzymes can hold a key part in the success of such studies. If by any chance, a new drug was found to treat terminally ill cancer patients, price would not be as high of an issue anymore. And for the research industry, price is also not that big of an issue due to them only needing lesser amounts of the reactants compared to large-scale mass production.

As for the environmental factors, the employment of enzymatic reactions could potentially decrease the environmental impact of creating certain glucose derivatives, compared to some other processes. As many industries start to focus on more sustainable ways, this has the potential to open new doors, while keeping the environmental impact lower. Not just the use of enzymes to selective functionalize glucose, but also creating new glucose derivates is important. If new glucose derivatives are found which can create already known drugs but with a lower environmental impact, it can increase the sustainability of the industry. It is not limited to drugs as the selective functionalization of glucose may increase the environmental and economic sustainability of many industries.

Conclusion

Protecting group chemistry as well as enzymatic reactions can be utilized to selectively functionalize glucose. Which reactants or enzymes are suitable depends on the factors such as reactivity, stereochemistry, electronic effects, regioselectivity and more. The difficulty of selectively functionalizing glucose at the C2, C3 and C4 positions compared to C1 and C6 are influenced by these factors. After the glucose molecule has been selectively functionalized, the chemical and physical properties of the new derivative may change. The properties may change depending on the functional group and position. This knowledge can be utilized to create a myriad of new glucose derivatives with many varying properties. In addition, the use of suitable reactants may also be very important in the synthesis of glucose derivatives. There are many ways to synthesise selective glucose derivatives and an even greater number of different properties where many have yet to be found. The use of selective functionalizing glucose may hold high potential for the industrial use. This is due to them potentially being able to create new drugs and decrease the economic and environmental impact of already existing industries.

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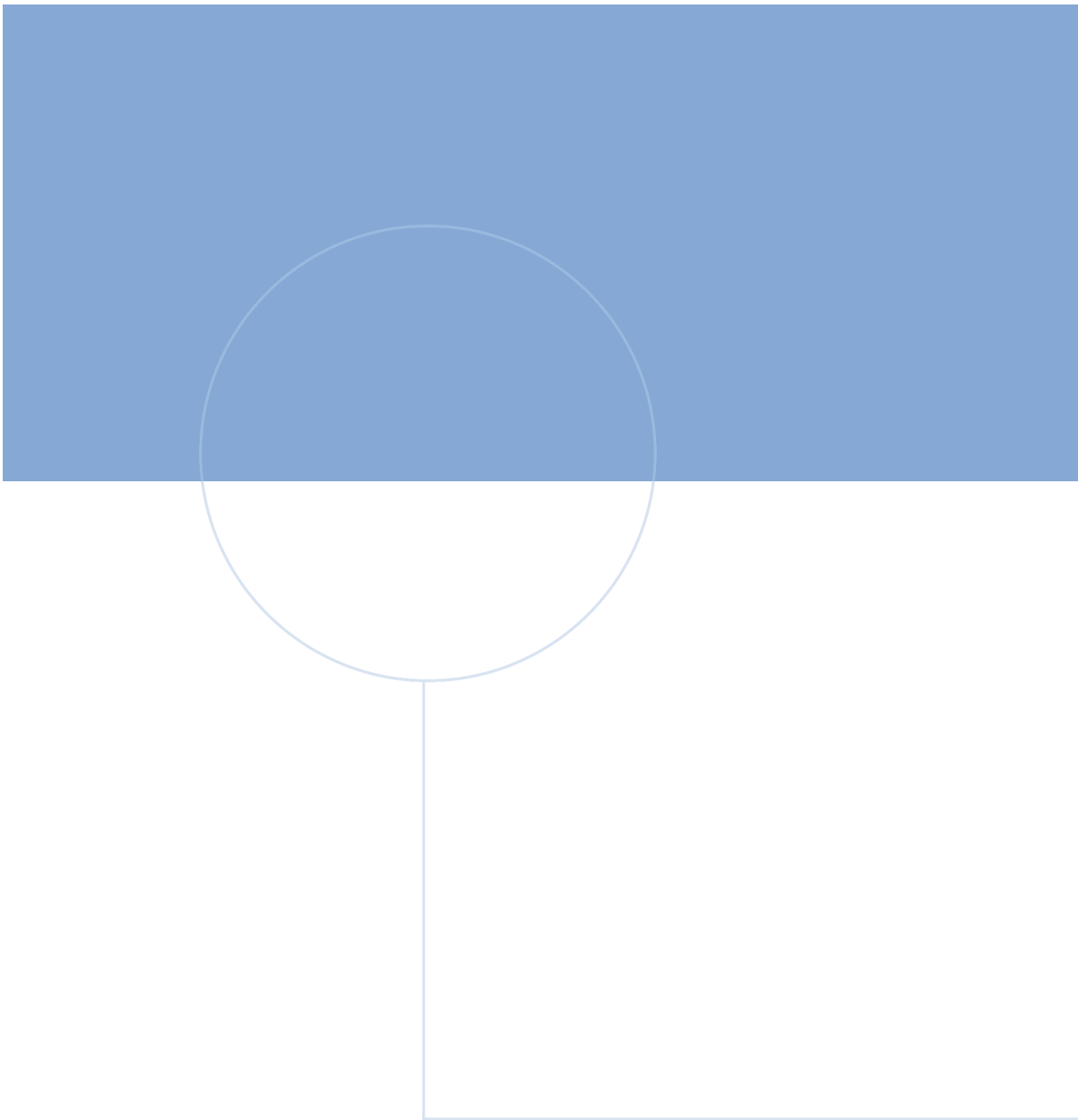

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