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Synthesis of a series of glucosyl triazole derivatives and their self-assembling properties

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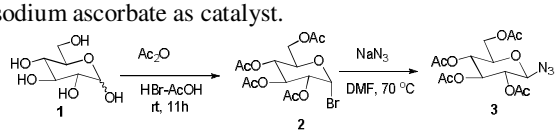
ABSTRACT

We report the synthesis and self-assembling properties of a new class of glucosyl triazole derivatives from glucose. The compounds are synthesized by a Cu (I) catalyzed azide/alkyne cycloaddition reaction, or the "click" reaction. Several efficient low molecular weight organogelators were obtained in this study. We found that triazole analogs containing long alkyl hydroxyl groups and phenyl groups typically are effective in forming supramolecular gels.

Low molecular weight gelators (LMWGs) have attracted considerable amount of attention over the last few decades. These small molecules can self-assemble in organic solvents or water and form typically fibrous supramolecular architectures that can immobilize the solvents.[1-3] The main driving forces for supramolecular gelation are non-covalent forces such as hydrogen bonding, hydrophobic interactions, π-π stacking, and van der Waals interactions, etc. The soft material formed by LMWGs have potential applications in biomedical sciences and as advanced materials.[3-6] Low molecular weight organogels and hydrogels have been studied for a variety of applications including drug delivery and tissue engineering and protein immobilization. [7-14]

Among the various classes of small molecular gelators, carbohydrate based gelators are of special interest to us since they can be synthesized from naturally abundant and readily available starting materials. We are working on the modification of readily available monosaccharides to obtain advanced functional materials. In our previous studies, various glucose and glucosamine derivatives have shown excellent gelation properties and a broad range of substituents can be present.[15-20] Here we would like to explore the effect of introducing a triazole functional group to the sugar ring. The triazole moiety may contribute to aromatic interactions and hydrogen bonding which may lead to effective LMWGs, also they can be synthesized by the "click" reaction conveniently.[21-22] The click chemistry has been widely used for the discovery of novel scaffolds for drugs or new materials and have a great impact in bioorganic chemistry and glycoscience.[23-25] There are many studies of synthesizing various glycoconjugates and glycomimetics using the click chemistry and efficient enzyme inhibitors have been obtained.[26] Though a few carbohydrate based triazole derivatives have been shown to be effective low molecular weight hydrogelators,[27-29] a systematic study of the structure and gelation properties of simple monosaccharide triazoles have not been reported. In this study, we prepared a library of peracetylated glucose triazoles and screened their gelation properties in a series of solvents. The sugar azide building block **3** can be synthesized in two steps from D-glucose **1** (Scheme 1). Terminal alkynes with different functional groups were selected for the click reaction using $CuSO_4$ and sodium ascorbate as catalyst.



Scheme 1. Synthesis of sugar azide **3** from D-glucose.

The glycosyl triazoles synthesized (**5-18**) are shown in Scheme 2, these include the carboxylic acids **5** and **6**, the alcohols (**7-12**) with different alkyl spacers to the triazole ring, the phenyl analogues **13** and **14**, long alkanes **15** and **16**, and the dimeric compounds **17** and **18**. Among this series, compounds **7** and **13** are known compounds reported in the literature and they are glucosidase inhibitors.[24-26] The gelation