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From Cationic Carbosilane Dendrimers and Glycodendrimers towards Multifunctional Dendritic Wedges

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Carbosilane dendrimers (CS-DDMs) with their excellent stability, inertness, and nonpolar structure have been successfully employed in biomedicine as drug delivery systems (DDS).¹ In our previous work, we synthesized a series of 1st – 3rd generation CS-DDMs bearing cationic (ammonium, phosphonium) moieties at the periphery. As the phosphonium CS-DDMs performed lowered *in vitro* cytotoxicity, high dendriplex stability and elevated transfection efficacy compared to the ammonium ones, but in general as well, they represent a promising alternative to current DDS (vectors) in gene therapy.² In a similar manner, we prepared CS glucose glycodendrimers to perform the first comparative study of the *in vitro* (MTT) and *in vivo* (modified FET) cytotoxicity with remarkable results.³

Interior of CS-DDMs is prepared by standard iterative reaction steps (catalytic hydrosilylation, ω -alkenylation, resp.). Therefore, a scope of possible modifications during the synthesis is limited. Recently, to extend the range of versatility, we developed a novel modular toolbar of multifunctional carbosilane dendritic wedges (CDWs) varying in several ways, such as generation, density of inner branching, or polarity.

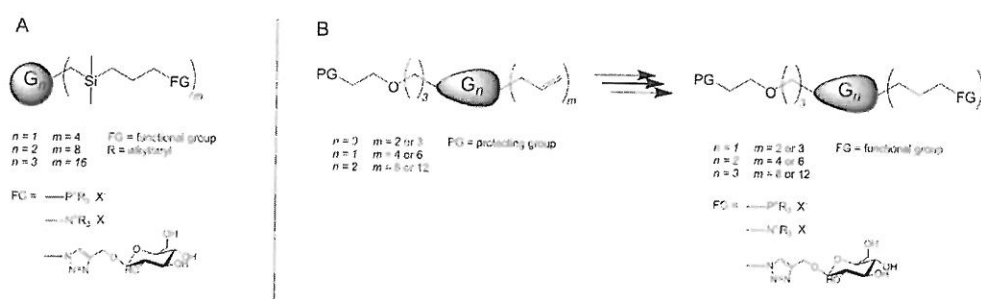


Fig. 1: A) published CS-DDMs with cationic peripheral units and CS glucose glycodendrimers, B) corresponding CDWs and suggested pathway towards their functionalization.

Here we present the CDWs of the 1st–2nd generation with allyl groups at the periphery and a hydroxy/amine terminated linker. The suggested synthesis requires highly selective reactions with excellent yields. Moreover, due to an employment of strong nucleophiles or basic/acidic conditions during the synthesis, it is essential to select convenient protecting groups, which will be briefly discussed.

Thus obtained CDWs can be modified following the same synthetic pathway used for the preparation of the cationic CS-DDMs and glycodendrimers. Moreover, the hydroxy/amine linker group enables an attachment of these CDWs to various substrates (hydrophobic/hydrophilic chains, multivalent cores, fluorescent molecules, *etc.*) to obtain *e.g.* amphiphilic segments of CDWs or Janus-type CDWs.⁴

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