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# Novel first-generation dendrimers on calix[4]resorcinol core equipped with multiple triazole units

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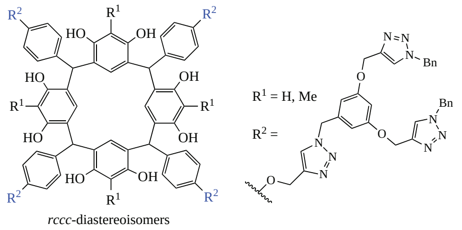
**Novel first-generation dendrimers on the calix[4]resorcinol core with four branches each containing multiple 1,2,3-triazole units have been synthesized in one-step by acid catalyzed condensation of resorcinols with a new aldehyde dendron, namely, 4-{3,5-bis[(1-benzyl-1*H*-1,2,3-triazol-4-yl)-methoxy]benzyloxy}benzaldehyde (obtained by alkyne–azide cycloaddition). The reaction proceeds stereoselectively to form *rccc*-diastereoisomers in high yields.**



*Keywords*: dendrimers, dendrons, calix[4]resorcinols, 1,2,3-triazoles, condensation, click reaction.

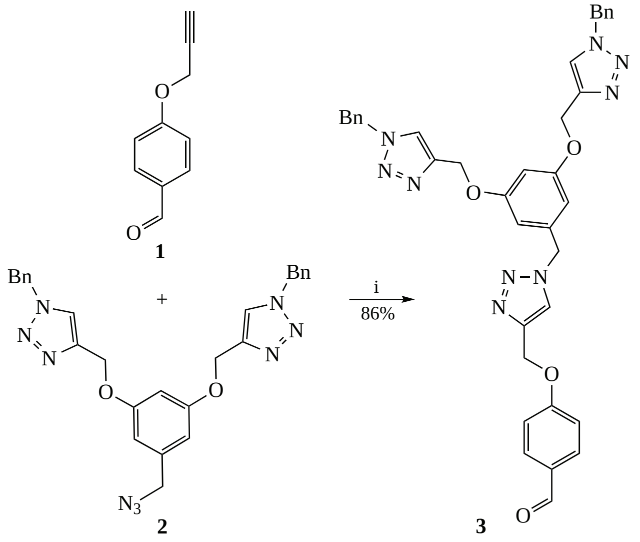
In recent decades, there has been a surge of interest towards dendrimers compounds. These macromolecules are of interest for both fundamental and applied research, in particular, for the design of drugs as well as effective catalytic systems. Their high chemical and thermal stability makes them attractive for applications in aggressive environment and at high temperatures.[1–8] However, less attention was devoted to calixarenes which are highly promising as dendrimer cores due to the possibility of their facile preparation and deep functionalization. To date, calixarene scaffold has been employed either as dendrimer core[9–15] or as a branching unit of growing dendrimer macromolecule,[16–20] or both.[21–24]

Calix[4]resorcinols as a dendrimer core offer a larger number of functional groups (8 to 12 phenyl hydroxyl groups) for the formation of dendrimer branches as compared to conventional calix[4]arenes. It should be noted that the core size does not change significantly and can be readily constructed in one stage by acid-catalyzed condensation of resorcinols with functionalized aldehydes. Dendrimers with resorcinol and stilbene fragments are interesting examples of using calix[4]resorcinols in the development of electrochromic windows (smart windows).[25,26] Nonlinear optical properties of high-molecular-weight dendrimers synthesized from calix[4]resorcinol and ferrocenyl dendrons with π-conjugated system were investigated.[27] Second- and third-generation poly(amido amino) dendrimers with terminal salicylidene groups were synthesized on a calixresorcinol scaffold.[28] Poly(aryl ether) dendrimers with peripheral *n*-propyl and allyl groups,[29] π-conjugated oligophenylene vinylene systems, and their supramolecular complexes with fullerene $C_{60}$ were also synthesized.[30]

In this work, we initially synthesized a new first-generation dendron **3** bearing three triazole fragments and aldehyde group with the aim to prepare new types of dendrimers on a calix[4]-resorcinol core. The click reaction of 4-(2-propyn-1-yloxy)-benzaldehyde **1** with 4,4′-[(5-azidomethyl-1,3-phenylene)bis-(oxymethylene)]bis(1-benzyl-1*H*-1,2,3-triazole) **2**[31] in the presence of $CuSO_4$/sodium ascorbate catalytic system in mixture of THF/$H_2O$ (5/3) at reflux over 17 h afforded the dendron **3** in 86% yield (Scheme 1).[†]

Subsequent condensation of equimolar amounts of dendron **3** with resorcinol or 2-methylresorcinol in refluxing $CHCl_3$ in the presence of trifluoroacetic acid gave new highly functionalized calix[4]resorcinols **4a**,**b** in 87–88% yields (Scheme 2). The macrocyclic products exist in *cone* conformation with *rccc*-configuration of substituents and represent first-generation dendrimers with calix[4]resorcinol core and three triazole fragments in each of four dendrimer branches.

Calix[4]resorcinols **4a**,**b** are beige powder-like substances soluble in chloroform, acetone, DMF, and DMSO, but insoluble in methanol or ethanol. Their structures were confirmed by NMR



**Scheme 1** *Reagents and conditions*: i, $CuSO_4 \cdot H_2O$ (10 mol%), Na ascorbate (10 mol%), THF, $H_2O$, reflux.

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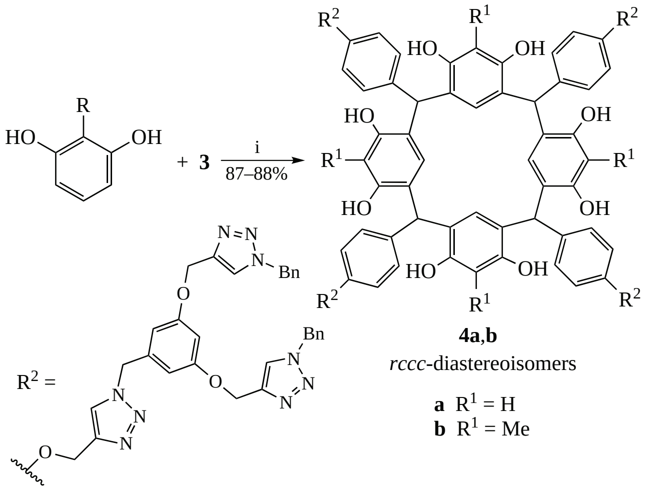
[†] For synthesis and characteristics of compound obtained, see Online Supplementary Materials.



**Scheme 2** *Reagents and conditions*: i, aldehyde **3** (4 equiv. per 4 equiv. resorcinol), $CHCl_3$, $CF_3CO_2H$, reflux.

($^1$H, $^{13}$C) and IR spectroscopy, mass spectrometry (MALDI-MS) and elemental analysis. The NMR signals were assigned on the basis of $^1$H, $^{13}$C, $^{15}$N, HSQC, and HMBC experiments. The configurational and conformational structural features are reflected in the NMR spectra of obtained macrocyclic compounds.

The existence of a high-symmetrical *cone* conformation with *rccc*-configuration of substituents in solution is characterized by one set of signals in the NMR spectra for each structural unit. We observed the effect of bulky substituents of the calixarene framework leading to the decrease in the rate of ‘boat–cone–boat’ interconversion: in case of **4b**, the H$^4$ peak was single and narrow while, but for compound **4a** this led to broadening of the H$^4$ peak on the verge of disappearance. The interconversion rate is most likely slow for the $^1$H NMR time scale, which results in multiplication (doubling) of the peaks of the lower rim substituents. As a result, several spatial forms can be observed, in which the substituents are oriented differently relative to each other. When the substituents contain anisotropic groups, noticeable changes in chemical shifts for some groups, in particular, methyl ones, may occur.

In conclusion, employing the click reaction we prepared a new benzaldehyde derivative, 4-{3,5-bis[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methoxy]benzyloxy}benzaldehyde, which represents the first-generation dendron containing three triazole units and aldehyde functionality. Involvement of this compound into condensation with resorcinols afforded low-generation dendrimers of new type with a calix[4]resorcinol core and three triazole fragments in each of four branches. The macrocyclic compounds prepared at this stage contain free hydroxy groups of calixresorcinol framework – the conventional growth points in the design of dendrimers on the calixarene nucleus. The compounds obtained can be promising for subsequent functionalization and target design of more complex and interesting macromolecules, including dendrimeric ones.

Interestingly, acid-catalyzed condensation of resorcinol and its derivatives with aldehydes, which is widely employed for the synthesis of functionalized calix[4]resorcinols including our research group,[32–35] appeared in this work as a prospective synthetic divergent strategy for preparation of novel dendrimeric compounds on calixarene core. In contrast to conventional approach for the construction of dendrimers starting from the ready dendrimer core, such core (calixresorcinol framework) is herein constructed at the late stage of dendrimer synthesis. This is the advantage of the suggested approach, because existing approaches to dendrimers involve several protection/deprotection steps of functional groups and multiple purification stages.

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*Online Supplementary Materials*

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.01.033.

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