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Bisfunctionalized Janus Molecules

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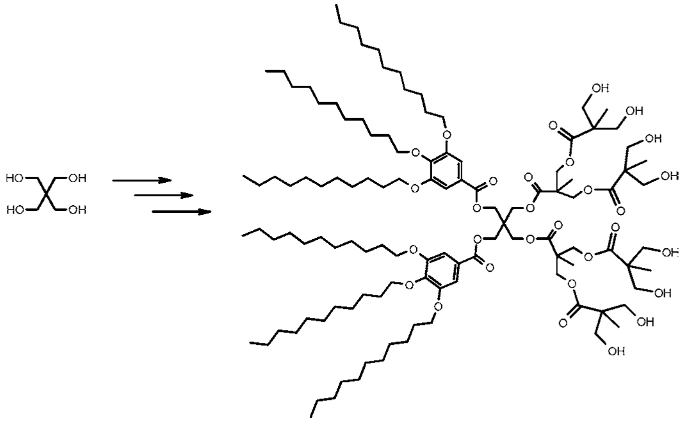
ABSTRACT



Bisfunctionalized dendritic multiester molecules were synthesized by combined protection–deprotection and divergent–convergent–divergent sequences in high yields leading to dendritic molecules that combine two functionally different surfaces, polar aliphatic arborol and nonpolar gallate ether moieties, resulting in a two-faced Janus molecule.

The growing demand for well-defined and functional materials in nanoscale supramolecular applications has led to a huge increase in the development of synthetic procedures that combine architectural control[1] and incorporation of functional groups.[2,3] As an answer to these demands, dendrimers and dendritic compounds offer an appealing solution due to their unique properties. As dendrimers are monodisperse, highly branched macromolecules with well-defined three-dimensional structures, they have many properties that differ significantly from those of corresponding linear polymers.[4] Due to the ability to control the synthesis, structure, and functionality of dendrimers, they have found use in applications such as catalysis,[5] light-harvesting systems,[6] molecular

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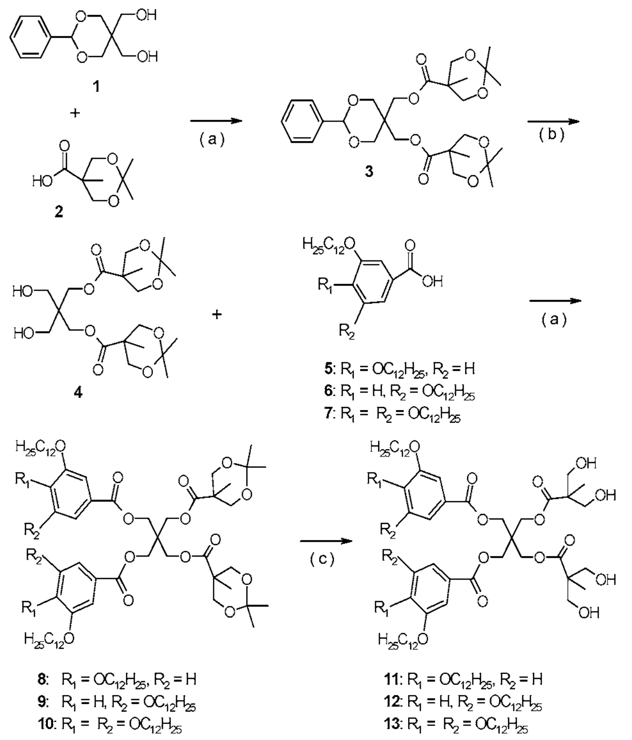
encapsulation,[7] and recently in biomedical applications.[8] Traditionally, dendritic compounds are prepared using two different synthesis concepts, i.e., divergent[9] or convergent[10] methods, and more recently, mixed methods, e.g., for self-assembling dendrimers, have emerged.[11]

The modular or mixed synthetic strategy enables combination of two totally different functionalities into one dendrimer molecule, e.g., highly polar and highly nonpolar regions are distributed onto the surface of the dendrimer. The preparation of low-molecular weight bisfunctionalized "bow-tie"[8a] or Janus[12] [*a Roman god of gates and doors, represented with a double-faced head*] dendrimers utilizes this approach and opens the door to tailoring of the overall properties of the dendrimers. The extreme functional differences, the two faces of Janus, at the outer perimeter of a molecule are especially needed when self-assembling systems are to be designed and prepared, as very elegantly demonstrated by Percec et al.[13] The synthetic strategy here combines a protection–deprotection sequence coupled with alternating divergent–convergent–divergent methods for formation of the dendrimer generations. Particular interest was focused on the use of gallate ether-type monodendrons due to their known self-assembling properties.[13] Coupling these nonpolar monodendrons with a polar aliphatic arborol part creates a family of bisfunctionalized multiester molecules with possible self-assembling or, when suitably modified, liquid crystalline properties.

The route to the first-generation bisfunctionalized multiester dendritic molecule is shown in Scheme 1.

Scheme 1. Synthesis of First-Generation Dendrimers[a]



[a] Reagents and conditions: (a) DCC, DPTS, CH_2Cl_2, rt, 20 h; (b) H_2, Pd/C, THF–EtOAc, 6 h; (c) THF–HCl (6 M), rt, 3 h.

The core molecule monobenzal-pentaerythritol **1** was prepared by the method of Issidorides and Gulen[14] from pentaerythritol in 76% yield.

The protected first-generation dendritic molecule **3** was esterified in dichloromethane by *N*,*N*-dicyclohexyl carbodiimide (DCC) coupling using 4-(dimethylamino)pyridinium *p*-toluenesulfonate (DPTS)[15] as a catalyst. After purification by column chromatography on silica, compound **3** was obtained in 97% yield. The benzylidene acetal protective group was removed by catalytic hydrogenolysis in quantitative yield to provide partially unprotected molecule **4**. The first-generation monodendron acids **5**–**7** were prepared from the corresponding hydroxybenzoic acid methyl esters with 1-bromododecane in DMF at 60 °C using K_2CO_3 as a base. Hydrolysis of the ester group with KOH in refluxing ethanol gave **5**–**7** in 95, 98, 95% yields, respectively.[16] The gallate ether monodendrons were then coupled with partly unprotected **4** in the presence of DCC and DPTS. The resulting acetonide-protected compounds **8**–**10** were easily separated from molecule **4** by column chromatography in 57, 86, and 81% yields, respectively. Removal of the acetonide groups in THF–HCl (6 M) mixture resulted in white solids, which, after separation by filtration and drying in vacuo, gave the fully unprotected first-generation compounds, **11**–**13** in 71, 83, and 92% yields, respectively.

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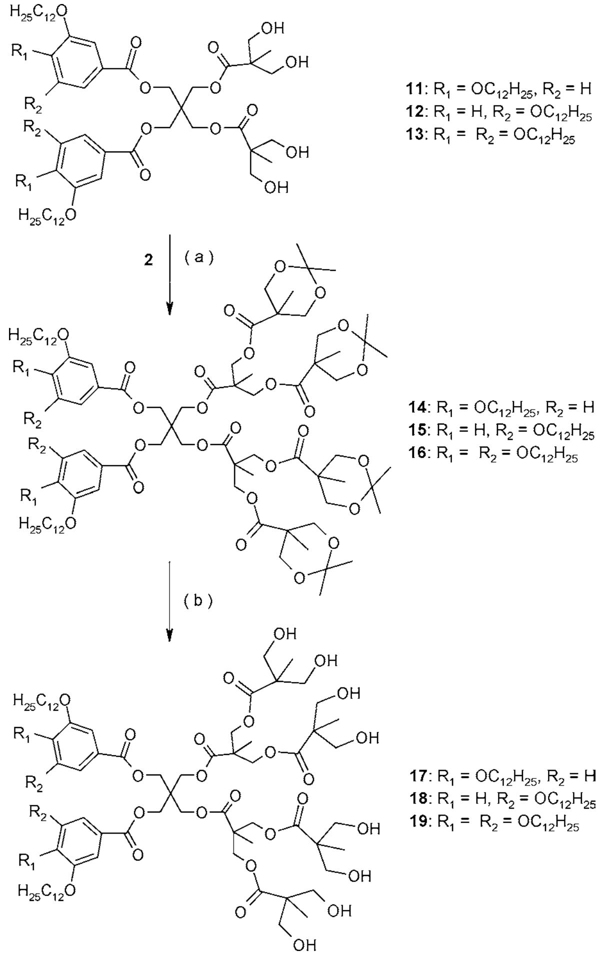
Scheme 2. Synthesis of Second-Generation Dendrimers[a]



[a] Reagents and conditions: (a) DCC, DPTS, CH_2Cl_2, rt, 20 h; (b) THF−HCl (6 M), rt, 3 h.

The second-generation bisfunctionalized dendritic molecules were synthesized using a divergent method (Scheme 2). Compound **11** was coupled with **2** in the presence of DCC and DPTS. Again, column chromatography was used to isolate **14** in 93% yield. Compounds **15** and **16** were prepared in a similar manner and after purification were obtained in 89 and 12% yields, respectively. The acetonide protection was removed with a THF−HCl (6 M) mixture. After the reaction was complete, the mixture was washed with CH_2Cl_2 and dried with $MgSO_4$. The evaporation and drying in vacuo afforded dendrimers **17**−**19** in 92, 95, and 82% yields, respectively. All compounds were fully characterized by ^{1}H and ^{13}C NMR, and ESI-TOF MS (see Supporting Information).

We have demonstrated that a protection−deprotection scheme in combination with a divergent−convergent−divergent method is a very efficient route to novel bisfunctionalized dendritic multiester molecules with two faces, viz. Janus. Using this facile modular synthetic method, we have combined nonpolar aromatic monodendrons with the aliphatic highly branched multiester molecules. Work toward higher generation bisfunctionalized Janus dendrimers and research on their thermal, self-assembling, and liquid crystalline properties are currently in progress in our laboratory.

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Supporting Information Available: Details of experimental procedures and characterization of compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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