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Supramolecular Diversity through Click Chemistry: Switching from Nanomicelles to 1D-Nanotubes and Tridimensional Hydrogels

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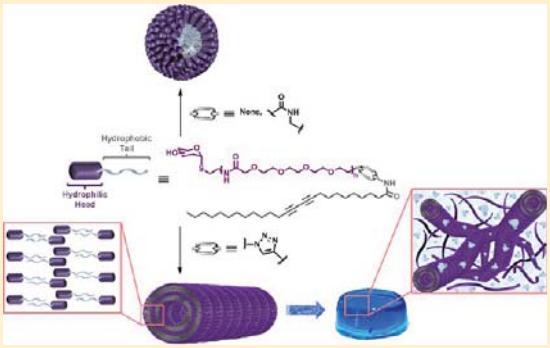
Supporting Information

ABSTRACT: The size and shape of nanoparticles are of prominent importance for their biological activities and for their application as smart drug delivery systems. Thus, synthetic designs allowing divergent synthesis of nanoscale materials with controlled size, morphology, and surface chemistry are currently highly desirable, but they remain a major challenge. Herein, we report a simple method for the creation of supramolecular diversity from structurally related diacetylenic-based glycolipids. We have found that neoglycolipids with an amide function between the hydrophilic and hydrophobic part of the amphiphile afford tridimensional micelles, while those having a triazole self-organize into 1D-nanotubes. Additionally, at higher concentrations, the clicked amphiphiles form hydrogels through three-dimensional networks of bundled nanotubes. Photopolymerization of the obtained nanomaterials leads to the formation of conjugated polydiacetylene backbone of alternating enyne groups, which rigidify glyconanomaterial structures enhancing their physical stability. The obtained nanostructures were extensively characterized using transmission electron microscopy (TEM), scanning electron microscopy (SEM), and atomic force microscopy (AFM) techniques, enabling the confirmation of the formation of tubular structures in water for all triazolo-substituted neoglycolipids and micellar structures for the glycolipid containing an amide group. This fact refutes the so-called isosteric character of 1,2,3-triazole and amide groups, at least, at the supramolecular level and point out to the possibility of using the CuAAC between azides and alkynes to create supramolecular diversity at the nanoscale. The functionality of the gel was, moreover, evaluated as a nanocontainer for the incarceration and controlled release of the antitumoral topotecan.



KEYWORDS: *click chemistry, supramolecular self-assembly, carbohydrate-coated robust nanomaterials, PDA-based hydrogels, PDA-based micelles, PDA-based lipid nanotubes*

INTRODUCTION

The advent of nanotechnology has increased the need for bottom-up approaches that can generate complex nanoscale systems from simple molecules or architectures.[1−6] In this sense, chemical self-assembly, the spontaneous association of molecules into well-defined structures held together by noncovalent interactions, is one of the most attractive approaches for constructing complex supramolecular nanostructures.[7−10] Hierarchical processes typical of chemical self-assembly, spontaneously produce ordered multivalent systems,[11−14] valuable tools in biology and nanotechnology, starting from prefunctionalized monomers.[15−20] As a result of the deep impact of nanoscale materials in the nascent field of nanomedicine, self-assembled nanostructures taking place in water are receiving special interest, as they can be directly applied in important biological processes.[21−24] Structure−activity relationship studies have shown that, beside the surface chemistry, the topology and size of nanoscale molecules are key factors for their biological activities, including their cellular uptake, circulation time, interaction with specific receptors, and their application as smart drug delivery systems.[25−27] In this sense, while spherical nanomaterials, preferentially with 50 nm size, are well suited for processes proceeding through a rapid cellular uptake, 1D-rodlike structure are more appropriate for those requiring improved circulation time. On the other hand, it has recently been reported that whereas spherical mannose-coated micelles are potent inhibitors of a globular lectin, concanavalin A, the mannose-coated 1D-cylindrical micelles are more suited for the inhibition of bacterial motility.[28,29] Thus, synthetic designs allowing the divergent synthesis of functionalized nanoscale materials with varied morphologies preferentially from a common intermediate, with no additional synthetic cost are highly desirable. Yet, designing molecular materials in which the self-assembled nanostructures are predetermined by molecular architecture remains a major challenge, especially if self-assembly is used to control the size, the morphology, and

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