Bengal Rose@dendritic box

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BENGAL ROSE@DENDRITIC BOX

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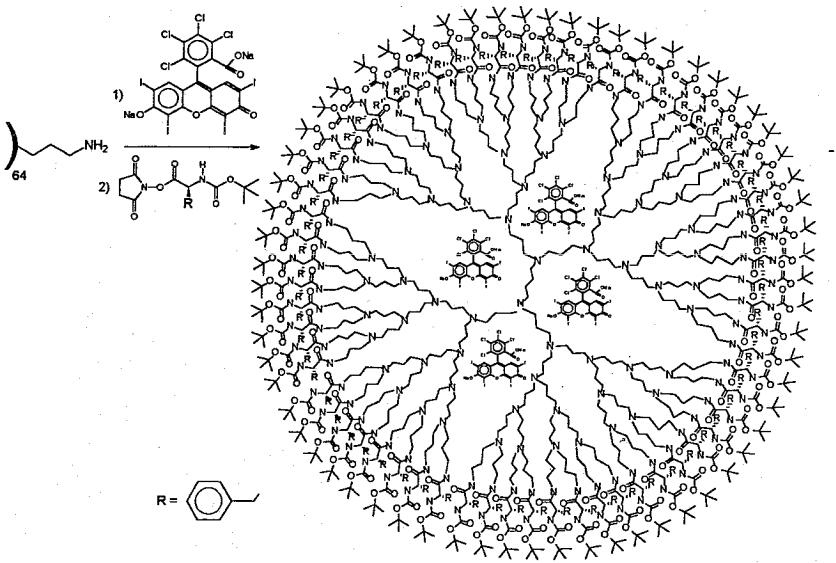
Abstract: Bengal Rose was succesfully encapsulated and liberated from a dendritic box. Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$ was investigated with several different techniques such as ultraviolet, circular dichroism and fluorescence spectroscopy.

INTRODUCTION

The possibilities opened by encapsulating guest molecules into dendritic hosts have been proposed by Maciejewski[1] in 1982 and discussed as main application of dendrimers ever since[2]. Despite the fact that dendrimers and hyperbranched polymers are subject of intensive research[3], examples of guest encapsulations are limited to dissolving an organic guest into the interior of a dendrimer. Fréchet et al. have been able to solubilize pyrene in water employing a water-soluble dendrimer[4], while Tomalia et al. have demonstrated by means of NMR-relaxation measurements that organic molecules, like aspirin can penetrate into the interior of a polyamidoamine (PAMAM) dendrimer[5]. However, both examples are based on dynamic processes and the guests can easily diffuse in or out of the dendrimer host depending on the equilibrium conditions.

Recently we have demonstrated, that it is possible to physically lock (imprison or encapsulate) guest molecules into a monomolecular dendritic container with a diameter of approximate 5 nm; the so-called dendritic box.[6]



Scheme 1: Synthesis of the dendritic box containing Bengal Rose

These dendritic boxes (scheme 1) are constructed from a flexible poly(propylene imine) dendrimer with 64 amine end groups[7] and a L-phenylalanine derivative. In solution this 64-L-Phe box possesses a highly-dense hydrogen-bonded shell with solid-state character, as has been demonstrated with ^{13}C NMR-relaxation data[6] and chiroptical studies[8]. Guest molecules are captured within the internal cavities of these boxes by constructing the dense shell in their presence[6].

RESULTS AND DISCUSSION

In this paper we like to illustrate some of the peculiar properties of these dendritic boxes by discussing the encapsulation of Bengal Rose as the guest as well as the properties of Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$[9]. After the construction of the dense shell in the presence of Bengal Rose, exhaustive dialysis with acetone/water (cellulose 24Å, 7 times, 5 % water in acetone) is employed in order to remove the adhered or excess Bengal Rose. Control experiments using different solvents, higher temperatures or sonification showed absolutely no release of any encapsulated Bengal Rose from Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$ indicative for an unmeasurably slow release. The number of encapsulated guest molecules is estimated by comparison of the ultraviolet (UV) spectra of guests that are in and out of the box. The relation between the number of encapsulated molecules of Bengal Rose as a function of the concentration of

Bengal Rose used in the shell-forming reaction is depicted in figure 1. This figure indicates that the maximum number of 4 guest molecules per dendritic box is directed by the architecture of the dendritic box, and obviously by the properties of the guest[10]. In cases below the maximum number a linear relationship is found, indicative for a solubility equilibrium between dye dissolved in DAB-*dendr*-$(NH_2)_{64}$ and dye dissolved in the bulk solvent.

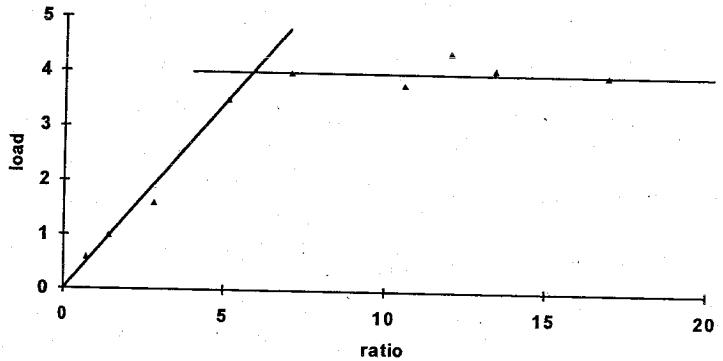


Figure 1: Number of Bengal Rose molecules trapped in the dendritic Box versus the initial mole ratio before the encapsulation reaction at 10^{-3} mol of box.

After encapsulation of 4 molecules of Bengal Rose we have investigated several of the optical properties of encapsulated guest. The ultraviolet-visible (UV-Vis) spectra of Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$ are identical to the spectra of Bengal Rose in organic solvents. However, there is large difference in fluorescence between Bengal Rose and Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$, both recorded in $CHCl_3$ (Figure 2).

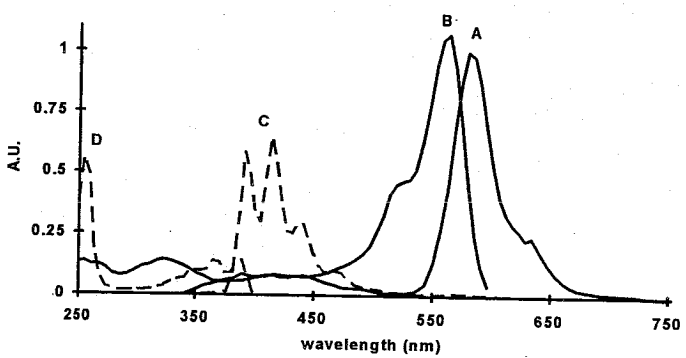


Figure 2: Fluorescence spectra in chloroform of Bengal Rose@DAB-dendr-(NH-t-BOC-L-Phe)$_{64}$ (A: emission; B: excitation) and of a saturated Bengal Rose solution (C: emission; D: excitation) with the intensities in arbitrary units (A.U.).

The strong fluorescence at λ = 600 nm for Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$, is completely absent in the case of the supramolecular isomer of Bengal Rose out of the box. In the latter the fluorescence is quenched effectively by the solvent. The emission of Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$ is relatively insensitive to solvent effects. Hence, we believe that we have prepared a fluorescent sphere with an environmental-independent emission profile.

Much to our surprise, we observed that the specific optical rotation of the *N*-tBOC-L-phenylalanine modified dendrimers decreased to almost zero going from dendrimers of the first generation (optical rotatory power $[\alpha]_D$ = -11, c=1, $CHCl_3$) with 4 end groups to dendrimers of the fifth generation ($[\alpha]_D$ = -0.1, c=1, $CHCl_3$) with 64 end groups. Furthermore, spectral evidence for this decrease in optical activity is gathered using circular dichroism (CD) and optical rotatory dispersion spectroscopy[8]. Stimulated by the observation of induced chirality of dyes dissolved into chiral bilayers and micelles[11], we have recorded circular dichroism spectra of Bengal Rose@DAB-*dendr*-(NH-*t*-BOC-L-Phe)$_{64}$ using chloroform as the solvent. Induced circular dichroism (induced CD) spectroscopy is based on the transfer of chirality from the environment to an achiral dye and is therefore applicable to these dendritic boxes, because the vanishing optical activity is caused by a compensation effect and local optical activity is thought to be still present.

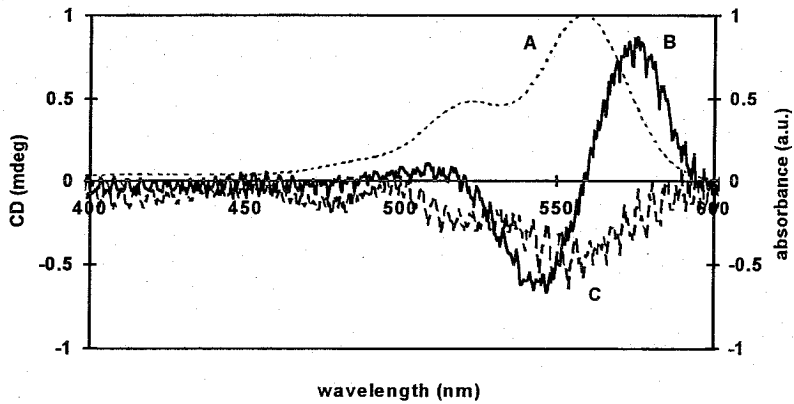


Figure 3: UV (A) and CD spectra of Bengal Rose@DAB-dendr-(NH-t-BOC-L-Phe)$_{64}$ containing 1 *(C) and* 4 *(B) molecules Bengal Rose*

In Figure 3 the CD spectra of dendritic boxes with 1 and 4 molecules of Bengal Rose per box are given. Although both samples show identical UV spectra, we observed a dramatic difference in the induced CD spectra of both samples. The dendritic box with 1 molecule of Bengal Rose encapsulated exhibits an induced CD spectrum related to the UV spectrum, in which all bands

possess a negative Cotton effect. However, an exciton-coupled spectrum is observed when 4 molecules of Bengal Rose are encapsulated into a single dendritic box. This exciton coupling indicates the close proximity of chromophores with a certain fixed orientation[12]. It is therefore additional evidence for the fact that at least two chromophores are encapsulated with some supramolecular ordering of the dyes in the box. All explanations for the induced CD observed are speculative[13]; however, it is reasonable to assume that some kind of chirality is present in the cavities of the dendritic box.

Finally, we like to report on the shape-selective liberation of guests from these dendritic boxes. Therefore, we have encapsulated 8-10 molecules of 4-nitrobenzoic acid together with 4 molecules of Bengal Rose. After exhaustive dialysis to remove the adhered and excess guest, a hydrolysis of the t-BOC groups with formic acid (95 % HCOOH, 16h) is performed. Subsequent dialysis (5 % water in acetone) of the reaction mixture yields a perforated dendritic box in which only the 4 molecules of Bengal Rose are entrapped, whereas all 4-nitrobenzoic acid is dissolved in the acetone/water mixture[14]. Bengal Rose cannot be liberated from the perforated box even not by the addition of hydrochloric acid (12 molar HCl). However, hydrolysis of the outer shell using 12 molar HCl under reflux for 2h liberates Bengal Rose after dialysis (100% water) and starting poly(propylene imine) dendrimer is recovered in 50-70% (Figure 4).

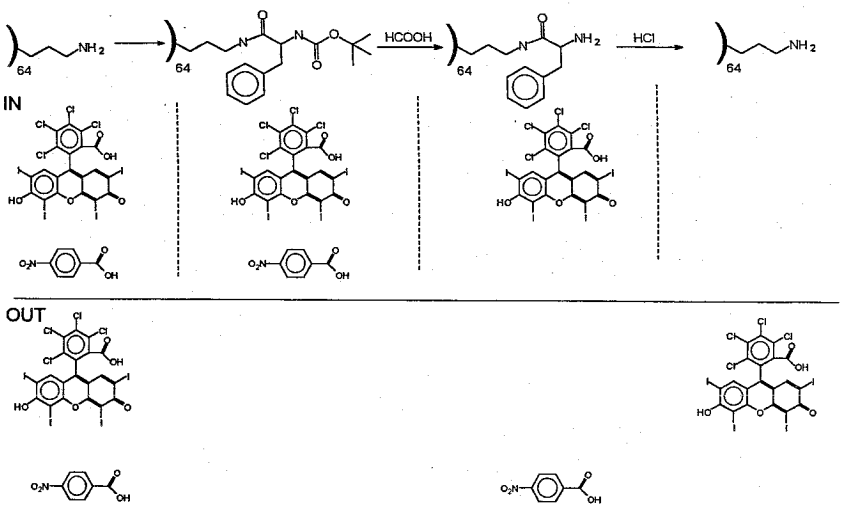


Figure 4: Shape-selective liberation of nitrobenzoic acid and Bengal Rose from nitrophenol@Bengal Rose@DAB-dendr-(NH-t-BOC-L-Phe)$_{64}$. Dialysis is performed at each step of the process.

The shape of guest as well as cavity determine the maximum number of guests entrapped into the dendritic box. More importantly a shape-selective liberation can be achieved by removing the shell in two steps. Apparently from the results presented here, the size of the guest, the size of the perforation made into the dense shell and the position of the guest[15] determine the possibility of removing the guests by dialysis. The absence of diffusion of the guests from the (perforated) box by solvent-induced conformational changes or protonation is proven by control experiments. Furthermore, the exhaustive dialysis employed ensures that the thermodynamically stable guest-host systems are obtained after hydrolysis and dialysis. Problems related to kinetic effects differentiating between guests that are liberated rapidly or more slowly are thus avoided.

CONCLUSIONS

In conclusion we have presented evidence that dendritic boxes can be made possessing a unimolecular compartmented structure in which guest molecules are physically locked. Evidence is presented that the encapsulation is dominated by the architecture of the dendrimer and that some kind of supramolecular ordering is present. Furthermore, a shape-selective liberation of guests encapsulated into a dendritic box can be accomplished by a two-step process. The results presented here for Bengal Rose as the guest are more generally applicable and show that a pathway for fine-tuning is available and further research with these new guest-host systems is in progress.

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