SOLVOPHOBICALLY DRIVEN SELF-ASSEMBLY OF CHIRAL SUPRAMOLECULAR DENDRIMERS

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Introduction

The influence of the dendritic architecture on chirality and vice versa is one of the least understood topics in the field of dendrimer chemistry. To date, chiral dendrimers have been synthesized into three general classes[1]: 1) dendrimers bearing stereogenic center(s) only at their core, 2) dendrimers with a surface of stereogenic centers, and 3) dendrimers containing stereogenic centers at every generation[2]. Intriguing questions regarding asymmetric induction, cryptochirality[3], optical rotation dependence on generation[4], secondary interactions and hydrogen bonding[5] easily arise by studying examples from each of these classes of chiral dendrimers, yet a definitive correlation and understanding of action/effect is still to be established.

We have previously developed in our laboratories dendritic units that self-assemble into cylindrical or spherical supramolecular dendrimers, that in turn self-organize into 2-D hexagonal columnar p6mm[6] or 3-D cubic Pm3m[7] liquid-crystalline (LC) lattices respectively (**Figure 1**). We aim to study further the effect of chirality on dendrimer architecture by focusing on the attachment of chiral motifs to the core of these dendritic units.

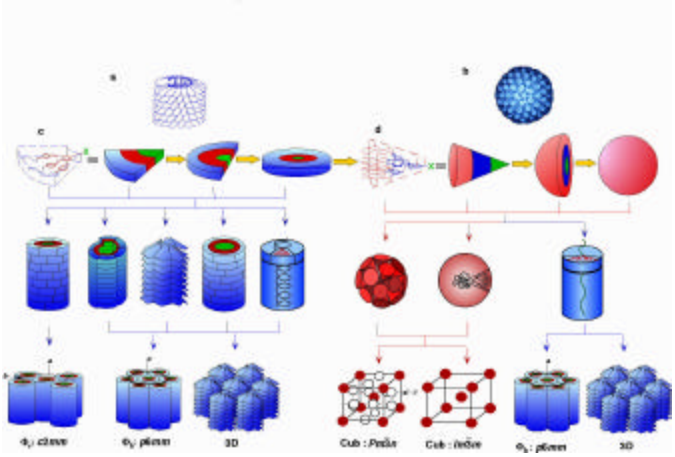


Figure 1. Rational design of libraries of quasi-equivalent building blocks.

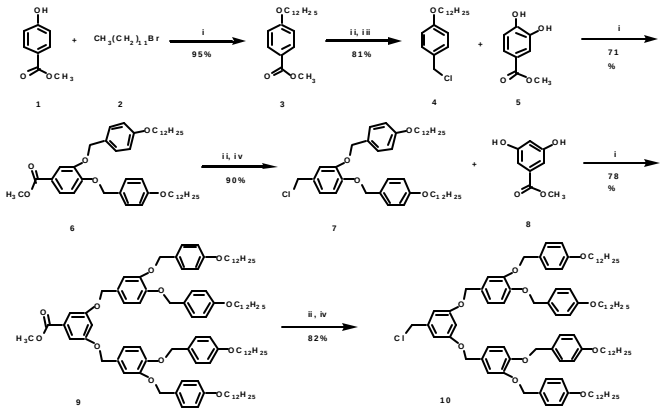
In particular we will discuss the first of two experiments – the effect on the hierarchical self-assembly in dilute solution in a solvophobic solvent and in bulk state of a monodendron functionalized with a DD, LL and DL Boc-N-Tyr-Ala-OMe dipeptide unit (**Scheme 2**), and how these experiments can serve as a powerful tool for helping to better understand the nature of the relation, interaction, and effect of chiral chores on dendritic building blocks.

Experimental

Materials. 1-Bromododecane (97%), methyl 4-hydrohybenzoate (99%), 3,4-dihydroxybenzoic acid (97%), 3,5-dihydroxybenzoic acid (97%), $SOCl_2$ (99%), $LiAlH_4$ (95%) (all from Aldrich), Boc-N-Tyr(Bzl)-OH (D, L, DL, 99%), H-Ala-OMe·HCl (D, L, DL, 99%) (Both from Bachem), Pd 10% on C (Lancaster), DMF, acetone, MeOH, EtOH, and anhydrous K_2CO_3 (from Fischer, ACS reagent) were used as received. CH_2Cl_2 (Fischer) was dried over CaH_2 and freshly distilled before use. THF (Fisher) was refluxed over sodium ketyl until the solution turned purple and distilled before use.

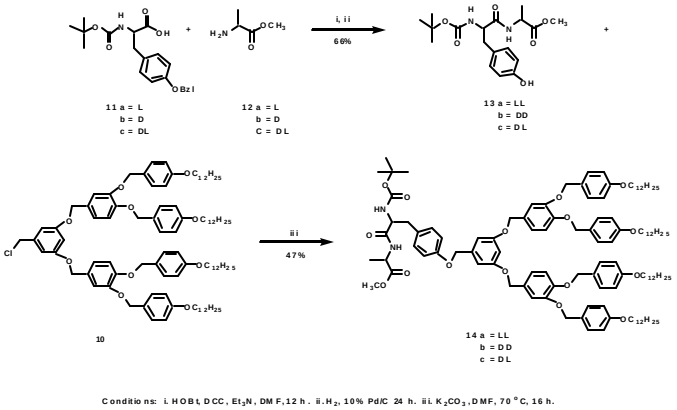
Techniques. ^1H NMR (500MHz) and ^{13}C NMR (125MHz) spectra recorded on a Bruker AMX 500 Spectrometer. CD spectra recorded on a Jasco J-720 spectropolarimeter in the range of 8-60 °C at 2 °C intervals. All CD experiments for the chiral dendrimer were carried out at a concentration of 1.6×10^{-4} M in Cyclohexane. Thermal transitions for samples that were freeze-dried from benzene were measured on a TA Instruments DSC 2920 Modulated DSC at 10 °C/min.

Synthesis. Experimental details of the synthesis (**Schemes 1 & 2**) will be reported elsewhere.



Conditions: i. K_2CO_3, DMF, 70 °C, 16 h. ii. LAH, THF, Reflux 2 h. iii. $SOCl_2$, DMF(Cat.), CH_2Cl_2, 5 min. iv. $SOCl_2$, DTBMP, CH_2Cl_2 5 min.

Scheme 1. Synthesis leading to **[4-3,4-3,5]12G$_2$CH$_2$Cl** dendron unit (**10**)



Conditions: i. HOBt, DCC, Et_3N, DMF, 12 h. ii. H_2, 10% Pd/C 24 h. iii. K_2CO_3, DMF, 70 °C, 16 h.

Scheme 2. Chiral self-assembling dendrimer **[4-3,4-3,5]12G$_2$CH$_2$-Tyr-Ala** (**14**)

Results and Discussion

Dendron **9** (**[4-3,4-3,5]12G$_2$CO$_2$CH$_3$**) was screened out of an extensive library for its ability to self-assemble in bulk into a racemic helical cylindrical object that self-organizes in a columnar hexagonal phase[6]. Alkylation of the desired dipeptide unit (**13 a**, **b**, and **c**) with **19** (**scheme 2**) provided the chiral dendrons **[4-3,4-3,5]12G$_2$CH$_2$-Tyr-Ala 14 a**, **b**, and **c**, which were analyzed by DSC, CD, UV and X-ray diffraction and compared. DSC traces for the **14a**, **b**, and **c** were virtually identical. The LL dipeptide dendrimer CD spectra as a function of temperature (**Figure 2**) was the mirror image of the DD dipeptide dendrimer (**Figure 3**), the DL dipeptide dendrimer showd no CD signal. UV spectra for all three dipeptide dendrimers as a function of temperature were identical and displayed an isosbestic point at low temperature (**Figure 4**), suggesting a dynamic equilibrium between the non-aggregated and the aggregated supramolecular form. Below a certain temperature the UV analysis shows a stiff supramolecular structure that is supported by NMR experiments. X-ray diffraction studies showed the supramolecular assembly to be helical, with the handedness of the helix being dictated by the stereogenic centers in the dipeptide unit. In addition, the helical assembly of all three dipeptide dendrimers was found to be tubular. The channel formed by the self-assembly of the dipeptide dendrimers had a diameter of about 70 Å in all three cases.

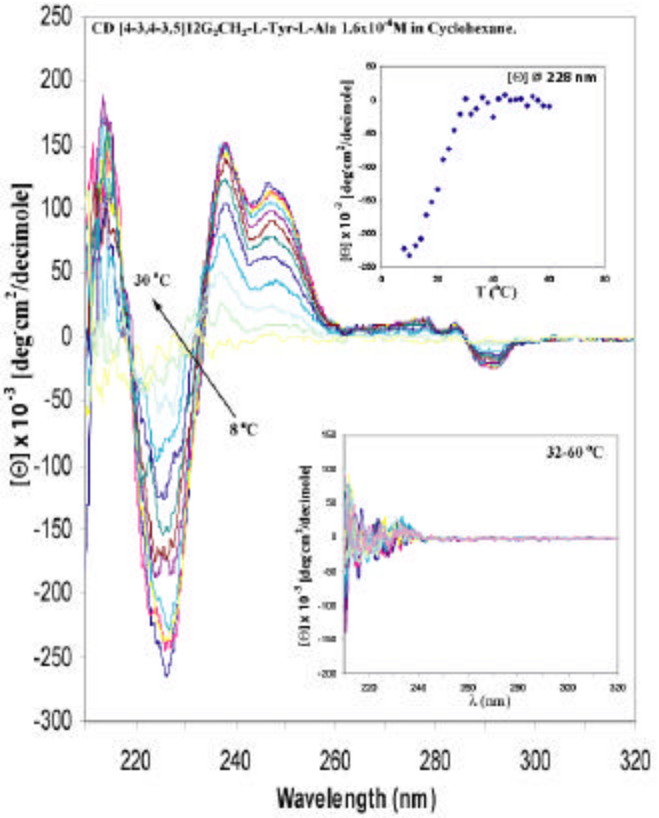


Figure 2. CD of **[4-3,4-3,5]12G$_2$CH$_2$-L-Tyr-L-Ala** as a function of Temp.

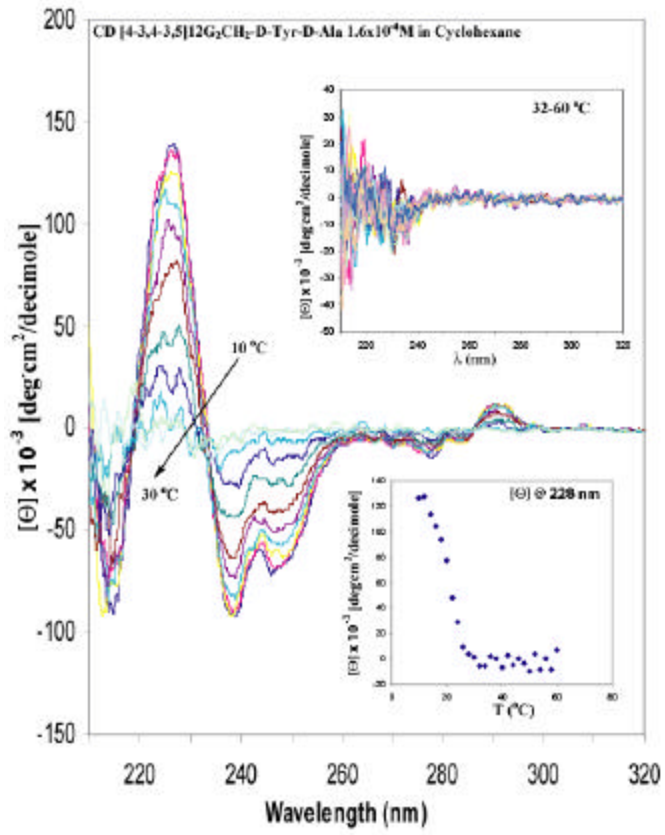


Figure 3. CD of **[4-3,4-3,5]12G$_2$CH$_2$-D-Tyr-D-Ala** as a function of Temp.

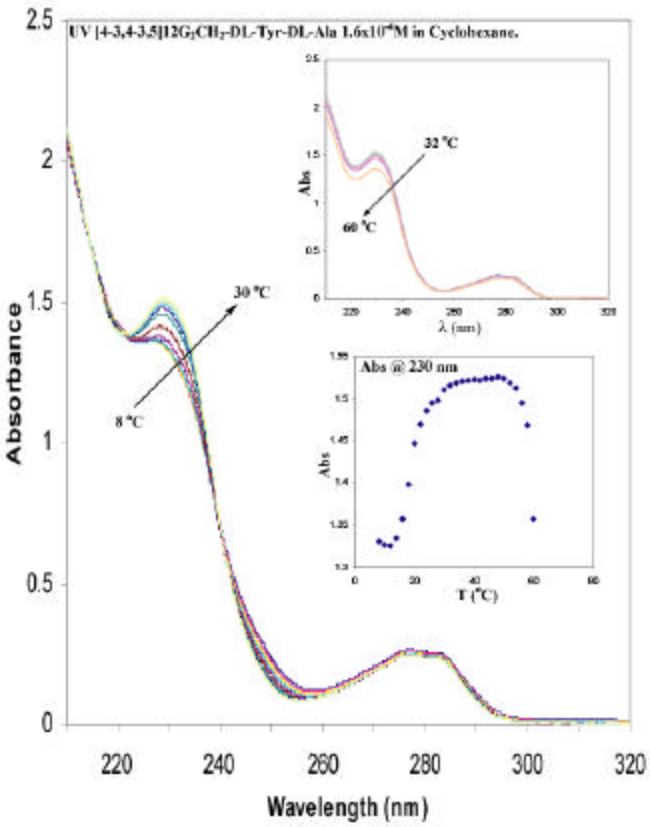


Figure 4. UV of **[4-3,4-3,5]12G$_2$CH$_2$-L-Tyr-L-Ala** as a function of Temp.

Conclusions

Solution and bulk experiments were compared (XRD, TEM, ED, CD, UV) and the structural analysis from bulk state allowed the elaboration of a hierarchical mechanism of internal structure formation into cylindrical chiral supramolecular dendrimers. This mechanism will be presented.

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References

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