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The Effects of Microenvironment Polarity and Dendritic Branching of Aliphatic Hydrocarbon Dendrons on the Self-Assembly of 2-Ureido-4-pyrimidinones

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Abstract: Two series of aliphatic hydrocarbon-based G1–G3 dendritic 2-ureido-4-pyrimidinones (UPy) (**S-G*n***)$_2$ and (**L-G*n***)$_2$, differing from one another by the distance between the branching juncture to the urea end, were prepared and characterized. These hydrocarbon dendrons were also appended to a *p*-aminonitrobenzene solvatochromic chromophore in order to probe their microenvironment polarity. While positive solvatochromism was observed which indicated the chromophore was solvent accessible, there was no significant difference between the microenvironment polarities on going from the G1 to the G3 dendrons. The self-assembling behavior and tautomeric preference of the dendritic UPy derviatives were examined by ^{1}H NMR spectroscopy. The dimerization constants (K_{dim*}) of the DDAA tautomers were unchanged at $10^7\,M^{-1}$ in $CDCl_3$ at both 25 and 50 °C, which were comparable to those of UPy compounds bearing other nonpolar substitutents. Furthermore, the lower limits on the K'_{dim*} of the DADA tautomeric forms of the (**S-G*n***)$_2$ and (**L-G*n***)$_2$ series were determined to be 10^6 and $10^5\,M^{-1}$ in $CDCl_3$, respectively. It was found that a closer proximity of the dendron branching juncture to the UPy unit could lead to a destabilization effect on the dimeric states. Hence, the (**L-G*n***)$_2$ dimers are more stable than those of (**S-G*n***)$_2$ in the DDAA form, but the latter are more stable than the former in the tautomeric DADA state. This study showed that both the highly nonpolar microenvironment and the proximity of the dendritic branching juncture to the UPy motif could alter the strength and profile of the hydrogen bond-mediated self-assembling process.

Keywords: dendrimers · dimerization · self-assembly · solvatochromism · tautomerism

Introduction

Molecular self-assembly provides a means to prepare materials with properties that are unattainable through traditional covalent chemical synthesis. In particular, self-assembly mediated by hydrogen bonding often furnishes materials with novel and tunable properties.[1] For example, Zimmerman reported the supramolecular heteromolecular hydrogen bonding interaction of ureidoguanosine and 2,7-diamido-1,8-naphthyridine[2] and its subsequent elaboration to supramolecular polymers.[3] The Meijer-Sijbesma 2-ureido-4-pyrimidinone (UPy) unit[4] has also been used extensively to prepare supramolecular polymers[5a] as well as self-assembled cyclic oligomers with tunable properties.[5b] One of the important issues in supramolecular chemistry is the ability to retain the binding mode and binding affinity of the key hydrogen bonding components with the introduction of new structural units in the binding motifs. However, it has been noted that minor structural variations on the various hetero-

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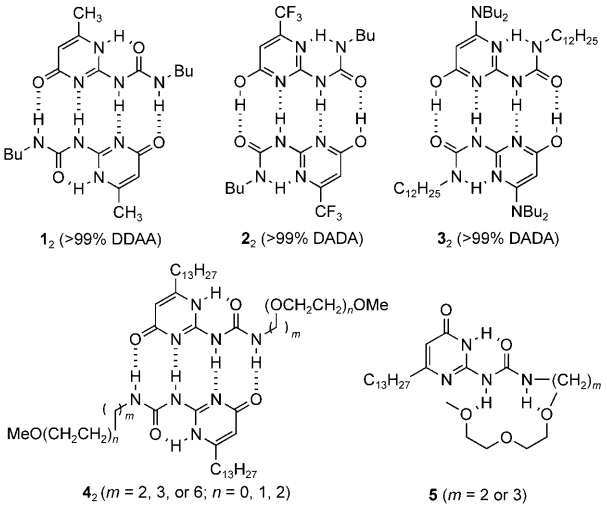
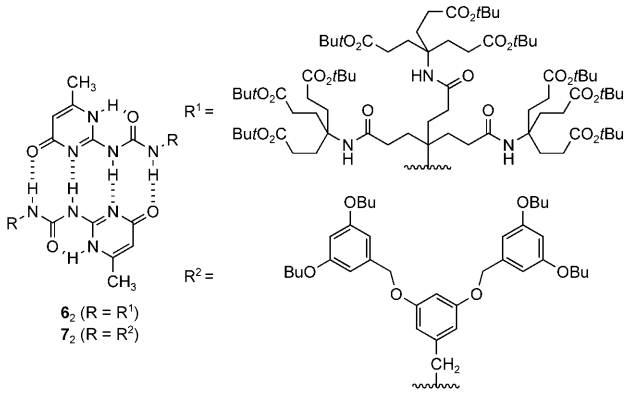
cyclic hydrogen bonding components can have substantial effects on the binding mode and binding affinity. For example, UPy **1** containing a methyl group at the C-6 position has a dimerization constant (K_{dim*}) of $6\times10^7\,M^{-1}$ in $CDCl_3$ at 25 °C.[4b] Replacing this methyl group with a trifluoromethyl $\mathbf{2}_2$[4a] or dibutylamino group $\mathbf{3}_2$[6] resulted in a shift of the binding mode of the UPy dimer from DDAA to DADA tautomeric form. In the case of the trifluoromethyl derivative, this change was accompanied by a reduction of the lower limit of K'_{dim*} to $5\times10^5\,M^{-1}$ owing to less favorable secondary interactions in the DADA binding mode. Recently, it was reported that substitution of the alkyl group on the urea end of the UPy with an oligo(ethylene oxide) (OEO) chain **4** could also modify the dimerization strength depending on the length of the spacer between the OEO and the UPy groups.[7] In particular, the K_{dim*} values of UPy **5** bearing an ethylene or trimethylene spacer ($m=2$ or 3) were 10^2–10^3 less than those bearing a hexamethylene spacer ($m=6$) or those without the OEO appendage. Based on ^{1}H NMR evidence, a backbiting model **5** in which the oxygen atoms of the OEO chain serve as intramolecular hydrogen bond acceptors was formulated.

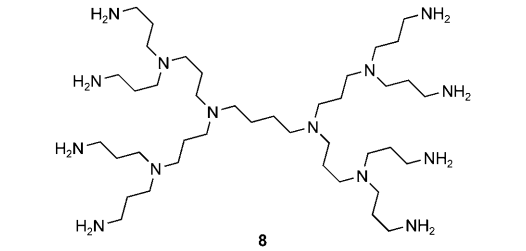


In addition to structural modifications described above, the strength of supramolecular binding can be modified by a change in solvent polarity. The binding constant can be reduced in the presence of a polar solvent, particularly a protic solvent owing to the presence of competitive hydrogen bonding. On the other hand, non-polar solvents, such as chloroform and toluene, are good solvents for promoting hydrogen bond mediated self-assembling owing to their non-polar and non-competing nature.[1a]

It is often desirable to maintain the strong assembling force in a polar solvent environment in order to enhance the utilities of the hydrogen bonding molecules. In fact, the strong binding of substrate molecules to enzyme active sites or bio-receptors in aqueous medium is a key factor in controlling the substrate selectivity in many biological recognition processes. In nature, biomolecules will wrap around themselves to form a binding pocket in which the microenvironment is significantly different from that of the aqueous surroundings. In biomimetic chemistry, a dendrimer is one of the ideal candidates to provide a tailor-made, local microenvironment around the hydrogen bonding module. For example, Kaifer reported one of the earliest examples of a series of G1–G3 dendritic UPys (e.g., **6**) encapsulated inside an **AB_3**-type oligoamide-oligoester dendron.[8] It was observed that the K_{dim*} values of the DDAA tautomers **6** remained constant at $10^7\,M^{-1}$ for the G1 and G2 analogues, but diminished abruptly to $3\,M^{-1}$ for the G3 compound. This was attributed to the steric bulkiness and the highly polar microenvironment of the G3 dendron by the authors, but could also arise from backbiting of the oligoamide-oligoester dendron in light of Meijer's recent findings.[7] We also disclosed a series of G1–G3 dendritic UPys (e.g., **7**) appended with Fréchet's oligoether dendron,[9] and yet all K_{dim*} values of the DDAA tautomers **7** remained unperturbed at $10^7\,M^{-1}$. In contrast to the oxygen atoms of the OEO chains, the relatively higher structural rigidity of Fréchet's dendrons and the relatively poor coordinating ability of the arylether oxygen atoms should disfavor the backbiting process. However, it had been shown that the interior polarity of Fréchet's dendrons increased gradually with increasing dendron generation according to a solvatochromic study.[10] Hence the invariance of the K_{dim*} values across the three generations of Fréchet type UPys **7** might alternatively suggest that the polarity of the microenvironment created by the dendron around the UPy unit may not have any significant effect on binding strength. This, together with other intriguing findings that oligopropyleneimine dendrimers **8**[11] and oligoamide-oligo(carboxylic acid) dendrons **9**,[12] despite having many polar amino and amido functionalities, showing decreasing polarity with increasing dendrimer generation, prompt us to further investigate the effect of the polarity of microenvironment on the strength of supramolecular binding



We decided to prepare two series of UPy dendrons (**S-G1**, **S-G2**, and **S-G3**) and (**L-G1**, **L-G2**, and **L-G3**) equipped with an aliphatic hydrocarbon dendron[13] and examine their binding properties under various conditions. Since the dendrons contain only sp^3 hybridized carbon atoms, and no lone pair or π electrons are available for backbiting and other



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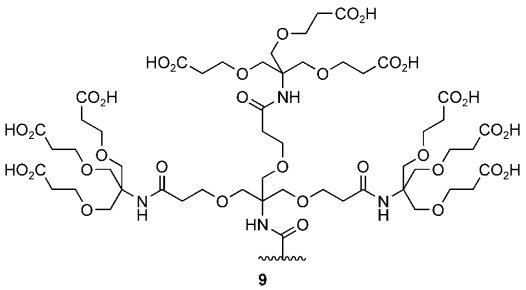

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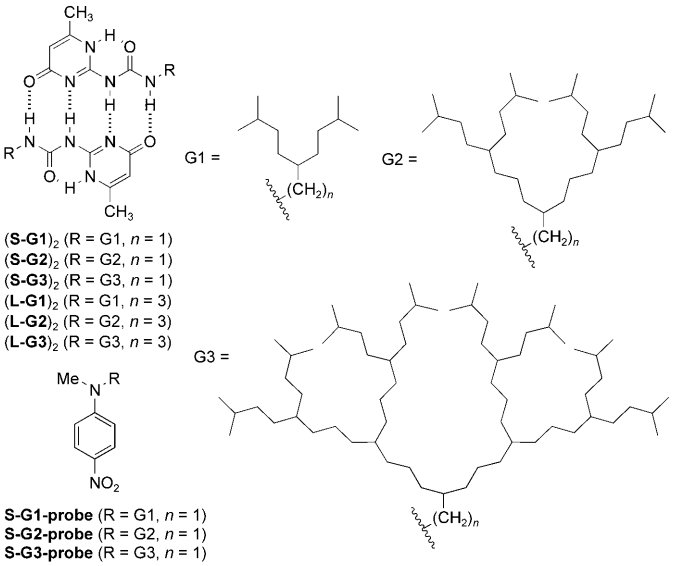


(**S-G1**)$_2$ (R = G1, *n* = 1)
(**S-G2**)$_2$ (R = G2, *n* = 1)
(**S-G3**)$_2$ (R = G3, *n* = 1)
(**L-G1**)$_2$ (R = G1, *n* = 3)
(**L-G2**)$_2$ (R = G2, *n* = 3)
(**L-G3**)$_2$ (R = G3, *n* = 3)

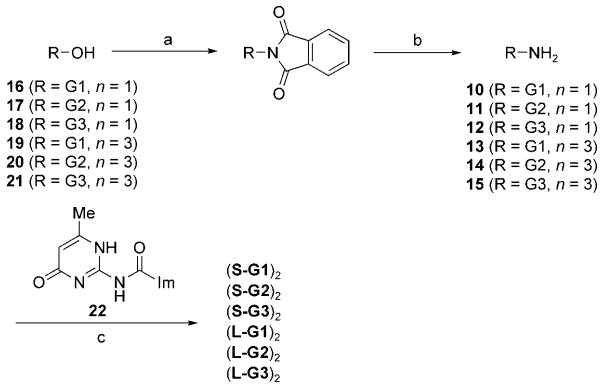
S-G1-probe (R = G1, *n* = 1)
S-G2-probe (R = G2, *n* = 1)
S-G3-probe (R = G3, *n* = 1)

complicating interferences, the variation of the binding strength across the different generation of UPys should arise solely from dendritic microenvironment and steric effects. These two series of compounds differ from one another in the proximity of the dendron to the central UPy unit. The first set of compounds **S-G*n*** contains a methylene spacer between the UPy and the first branching point of the dendron, while the second **L-G*n*** has a longer trimethylene spacer. Hence, the steric effect of the dendron should be less felt by the UPy unit in the latter series. We also examined the microenvironment of these hydrocarbon dendrons by carrying out solvatochromic studies on dendritic *p*-nitroaniline derivatives (**S-G*n*-probe**) of the shorter chain **S-G*n*** series. Based on these studies, we report that a) the polarity of the microenvironment of the three generation of hydrocarbon dendrons are nearly the same, b) all dendrons can preserve the dimerization strength ($K_{dim^*}=10^7\,M^{-1}$) of the DDAA UPy tautomers at 25 °C, and for the dendrons **L-G*n*** with a longer spacer, even at 50 °C, c) the % amount of DADA tautomer is different for these two series of compounds, and is also temperature dependent, d) the lower limits on K'_{dim^*} of the weaker DADA tautomers are found to be 10^5–$10^6\,M^{-1}$, and e) the proximity of the dendritic branching show that the UPy unit also exerts some effect on the binding strength. Hence the K_{dim^*} values of the (**L-G*n***)$_2$ are two times higher than those of the (**S-G*n***)$_2$ series in 10% [D$_6$]DMSO/CDCl$_3$ solution. Our experimental findings show that the microenvironment polarity and the dendritic branching can have significant influence on the binding strength and profile in supramolecular hydrogen bonding.

Results and Discussion

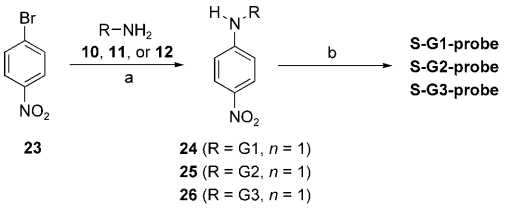
Synthesis

Synthesis of dendritic UPy dimers: Preparations of dendritic dimers (**S-G*n***)$_2$ and (**L-G*n***)$_2$ required the availability of dendritic amines (**10**–**15**), which in turn were synthesized from the corresponding known alcohols (**16**–**21**)[14] using Mitsunobu-type Gabriel amine synthesis. Reactions of these amines with the known imidazolide **22**[9,15] then afforded the desired dendritic dimers (**S-G*n***)$_2$ and (**L-G*n***)$_2$ in 35–90% overall yields from alcohols (**16**–**21**) (Scheme 1).



Scheme 1. Reagents and conditions: a) DIAD, Ph_3P, phthalimide, THF, 25 °C, 1 h, 77–99% yield; b) H_2NNH_2, THF, H_2O, reflux, 12 h, 74–100% yield; c) $CHCl_3$, 60 °C, 6 h, 47–95% yield.

Synthesis of dendritic solvatochromic probes: The widely studied *p*-(*N*,*N*-dialkylamino)nitrobenzene chromophore[16] was chosen to probe the polarity around the hydrocarbon dendrons. Our plan was to replace one of the alkyl groups with the shorter aliphatic hydrocarbon dendrons G1–G3 ($n=1$) to produce the dendritic **S-G*n*-probe**. However, owing to strong steric shielding of the hydrocarbon dendrons, direct *N*-alkylation of *p*-(*N*-methylamino)nitrobenzene using the corresponding dendritic bromide proved to be sluggish. In the end, a palladium catalyzed *N*-arylation of dendritic amines **10**–**12** with *p*-bromonitrobenzene **23** was employed (Scheme 2).[17] The reaction turned out to be very



Scheme 2. Reagents and conditions: a) $Pd(OAc)_2$, (oxydi-2,1-phenylene)-bis(diphenyl-phosphine), Cs_2CO_3, toluene, 110°C, 2 d, 31–83% yield; b) MeI, NaH, THF, 25°C, 24 h, 74–94% yield.

facile for G1 **10** and G2 **11** amino dendrons, producing the *N*-arylation products **24** and **25** in 67% and 83% yield, respectively. For the G3 **12** amino dendron, the yield of the product **26** dropped to 31%. Subsequent *N*-methylation of the *N*-arylation products **24**–**26** furnished the target solvatochromic probes **S-G*n*-probe** ($n=1$–3) in 74–94% yield.

Structural Characterizations

NMR spectroscopy: The structural identities and purities of all intermediates and target compounds were fully characterized by ^1H, ^{13}C NMR spectroscopy, high-resolution mass spectrometry (HRMS), and/or elemental analysis (see Supporting Information for details). The ^1H NMR signal assignments of the dendritic UPy dimers (**S-G*n***)$_2$ and (**L-G*n***)$_2$ were relatively straightforward. They all show three NH singlets ($\delta\sim13.1$, 11.9, and 10.1), one vinylic singlet ($\delta\sim5.8$), and one methyl singlet ($\delta\sim2.2$), indicating that the DDAA dimeric form is the dominant tautomer in $CDCl_3$. All other ^1H signals arising from the dendritic hydrocarbon moiety are located at the upfield region ($\delta=1.8$–0.8) except for the CH_2N signal ($\delta\sim3.2$). For the dendritic solvatochromic probes **S-G*n*-probe**, their ^1H NMR spectra revealed the characteristic AB system signals ($\delta\sim8.1$ and 6.6) originating from the *para*-substituted aromatic moiety.

Tautomeric behavior: ^1H NMR spectroscopy revealed one notable difference between the tautomeric properties of (**S-G*n***)$_2$ and (**L-G*n***)$_2$. For the (**S-G*n***)$_2$ series, another set of NH signals arising from the DADA tautomeric dimer was found at $\delta=13.4$, 11.2, and 9.8 (Figure 1). Based on the relative integration of the vinylic singlets at $\delta=6.1$ versus 5.8, the amount of DADA UPy dimer was found to be 4–6% (G1: 4%; G2: 4%; G3: 6%). However, the amount of DADA dimers was much less (~0.5%) for the (**L-G*n***)$_2$ series. It was also noted that the percentage of DADA tautomer was found to be, and theoretically should be (see Supporting Information for details), concentration independent in $CDCl_3$ solutions in the range of 2–50 mM. It is of interest to note that our previously reported oligoether-based dendritic UPy dimers $\mathbf{7}_2$ were shown to exist exclusively as DDAA tautomers in $CDCl_3$. The relative amount of DDAA was previously shown to be affected by the electronic property of the substituents on both the urea and pyrimidinone units.[4a] In our case, this must be as a result of steric or microenvironment factors as there is hardly any difference between the

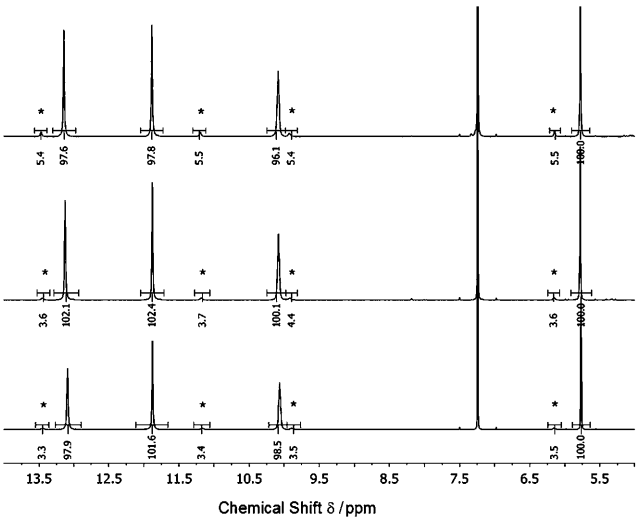


Figure 1. Partial ^1H NMR spectra (400 MHz, 50 mM in $CDCl_3$, 25°C) of dimers (**S-G*n***)$_2$ (top, G3; middle, G2; bottom, G1). Signals with an asterisk were as a result of the corresponding DADA tautomer.

electronic property of the shortened and the lengthened hydrocarbon dendrons. In fact, our observations are also in agreement with literature precedents; an *n*-butyl substituent at the urea position was found to give the DDAA dimer exclusively while a *tert*-butyl substituent at the same position was found to give rise to 3–3.5% DADA dimer when the substituent on the pyrimidinone end was an alkyl group.[4a]

Careful examination of the structures of the two tautomeric UPy dimers revealed that the substituent on the urea end in the DDAA form was located much closer to the pyrimindinone unit of its quadruple hydrogen bonding partner than in the DADA form (Figure 2a). As a result, the proximity of the dendritic branching indicates that the urea N should exert a stronger effect on the stability of the DDAA

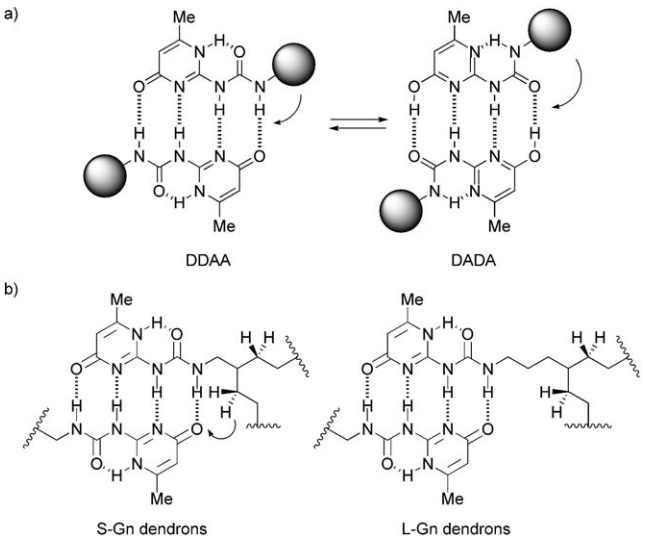


Figure 2. Proximity of the dendritic branching juncture at the urea end on the tautomeric behavior of DDAA and DADA UPy dimers.

than on the DADA dimers. For $(\mathbf{S\text{-}G}n)_2$, the branching juncture is just one carbon atom away from the urea N and this produces a stronger steric destabilization on the DDAA binding mode which then gives rise to a higher percentage of DADA tautomer as compared to the $(\mathbf{L\text{-}G}n)_2$ series (Figure 2b). This model can also be used to explain the presence of a substantial amount of DADA tautomeric dimer when the substituent at the urea end was a *tert*-butyl moiety as well as the finding that the amount of DADA tautomer increases with increasing size of the hydrocarbon dendrons. Furthermore, theoretical calculations indicated that the DADA tautomer had a smaller dipole moment than the DDAA monomer.[8] For the $(\mathbf{S\text{-}G}n)_2$ series, the DADA tautomers are relatively more stable than those of the $(\mathbf{L\text{-}G}n)_2$ compounds because the nonpolar hydrocarbon dendron is closer to the UPy unit. This effect was similar to the higher DADA ratio observed in nonpolar solvents such as toluene.[8]

Mass spectrometry: The formation of dendritic dimers was also supported by the observation of $[2M+H]^+$ or $[2M+Na]^+$ peaks in ESI-MS (Figure 3). The relative abundances of $[2M+H]^+$ to $[M+H]^+$ were not used to estimate the K_{dim*} values. In mass spectrometry, the solvation effect changes dramatically upon transition from solution phase to gas phase. Quantitative correlation of the relative abundances with the concentrations could lead to substantial errors in dimerization constants unless factors such as solvation for each ion are properly addressed.[18]

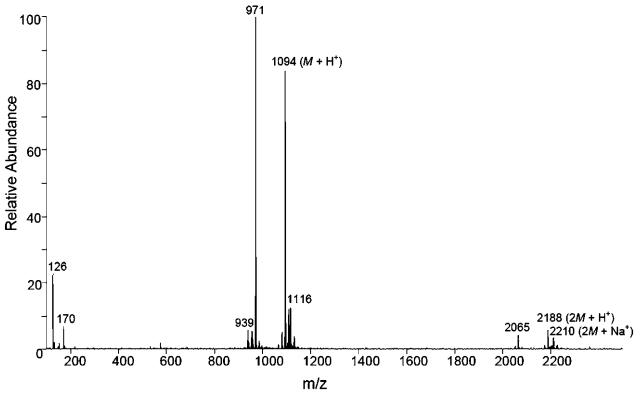


Figure 3. ESI-Mass spectrum of UPy dimer $(\mathbf{S\text{-}G3})_2$ showing monomeric and dimeric peaks.

Solvatochromic Study

Despite several reports on the microenvironment polarity of different types of dendrons, there is little information on the aliphatic hydrogen dendrons used in this study. Hence, solvatochromatic studies were carried out on the **S-G*n*-probe** in various solvents (Table 1). For all three dendritic probes, the UV absorption maximum (λ_{max}) underwent a bathochromic shift with increasing solvent polarity, suggesting the central chromophore was solvent accessible.[19] The λ_{max} values remained essentially unchanged for the different generation of hydrocarbon dendrons, revealing that the dendrons possessed a microenvironment of nearly the same polarity irrespective of the dendron size. This finding was in sharp contrast to the decreasing polarity with increasing generation observed for the oligopropyleneimine[11] and oligoamide-oligo(carboxylic acid) dendritic species,[12] and also different from the increasing polarity with increasing size for the Fréchet type oligoether dendrons.[10] Hence, in contrast to conventional polymers where they are always more polar than their small molecule analogues irrespective of polymer structure,[20] the polarity change of the microenvironment with increasing dendrimer size is structure dependent.

Table 1. λ_{max} values (nm) for dendritic hydrocarbon-based solvatochromic probes **S-G*n*-probe** (G1-G3) in various solvents.[a]

Solvent	π^*[b]	S-G1-probe	S-G2-probe	S-G3-probe
Diethyl ether	0.28	374	374	374
Toluene	0.54	386	385	384
Ethanol	0.54	395	394	393
Benzene	0.59	388	388	387
Acetone	0.71	394	396	395
CH_2Cl_2	0.82	399	399	398
DMF	0.88	406	405	404
DMSO	1.00	412	413	–[c]

[a] 0.1–0.01 mM at 25 °C. [b] Solvent polarizability parameter. [c] Insoluble.

Dimerization Strengths

Similar to previous studies,[4a] the lower limits on K_{dim*} of the two series of dendritic UPy dimers were estimated by ^{1}H NMR (600 MHz) studies in $CDCl_3$ at 25 °C. The ^{1}H signals of hydrogen bonded NHs owing to the DDAA tautomeric dimers were sharp and their chemical shift values remained unchanged in the concentration range from 10 mM to 10 μM (Figure 4). Furthermore, no signals attributable to the monomeric UPy species could be identified. Assuming DDAA dimer formation was above 95% at the lowest concentration (i.e., 10 μM) studied, the lower limit on K_{dim*} was calculated to be greater than $2\times10^7\,M^{-1}$ (Table 2). These values are comparable to those of Fréchet type oligoether dendritic UPy compounds and other UPy compounds bearing nonpolar substituents.[4,9]

The chemical shift values of the hydrogen bonded NHs owing to the DADA tautomeric pyrimidin-4-ol dimers in the $(\mathbf{S\text{-}G}n)_2$ series were also found to be concentration independent down to 100 μM. The lower limit on K'_{dim*} of the DADA tautomer could then be calculated using the relationship $K'_{dim*}=K_{dim*}\times[DADA_{dim}]/[DDAA_{dim}]$ (see Supporting Information for details). As the amount of DADA dimers only accounted for 3–6% of the total UPy concentration in the $(\mathbf{S\text{-}G}n)_2$ series, hence the lower limits on K'_{dim*} were around $10^6\,M^{-1}$. On the other hand, owing to the lower abundance (0.2–0.6%) of the DADA tautomers in the $(\mathbf{L\text{-}G}n)_2$ series, the lower limits on the respective K'_{dim*} values were lower ($10^5\,M^{-1}$). These values are also comparable to the K'_{dim*} lower limits ($4.5\times10^5\,M^{-1}$) observed for several

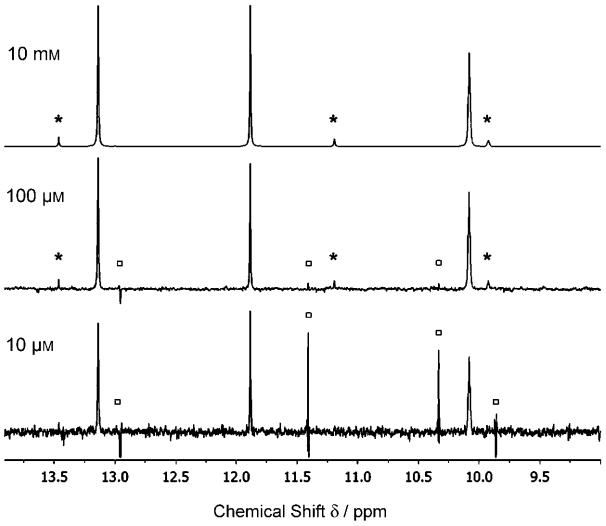


Figure 4. Partial ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C) spectra of (**S-G3**)$_2$ at different concentrations. Signals with an asterisk (*) and a square symbol (□) arose from the corresponding DADA tautomer and electronic artifact, respectively.

Table 2. K_{dim*} and K'_{dim*} values of various dendritic DDAA and DADA UPy compounds.

Compound	K_{dim*} of DDAA tautomer [M^{-1}]			K'_{dim*} of DADA tautomer [M^{-1}]
	$CDCl_3$ (25 °C)[a]	$CDCl_3$ (50 °C)[a]	10 % [D_6]DMSO in $CDCl_3$ (25 °C)[c]	$CDCl_3$ (25 °C)
S-G1	$>2\times10^7$	–[b]	110 ± 20	$>0.6\times10^6$
S-G2	$>2\times10^7$	–[b]	120 ± 20	$>0.8\times10^6$
S-G3	$>2\times10^7$	–[b]	120 ± 20	$>1.2\times10^6$
L-G1	$>2\times10^7$	$>2\times10^7$	290 ± 50	$>0.4\times10^5$
L-G2	$>2\times10^7$	$>2\times10^7$	320 ± 60	$>1\times10^5$
L-G3	$>2\times10^7$	$>2\times10^7$	320 ± 60	$>1.2\times10^5$

[a] Based on <5 % dissociation. [b] Not determined as a result of poor S/N ratio at 10 μM. [c] Based on 10 % integration error.

DADA pyrimidin-4-ol dimers in $CDCl_3$.[4a] It was also noted that slight structural variations of the dendritic appendage could significantly alter the relative stabilities of the two tautomeric forms.

We also examined the dimerization behavior of the dendrons in $CDCl_3$ at 50 °C. However, the ^{1}H NMR signal to noise ratios at 10 μM for the (**S-G*n***)$_2$ compounds were very poor to allow a reliable determination of the K_{dim*} values. For the (**L-G*n***)$_2$ series, no change in NH chemical shift values was observed down to 10 μM and no other NH signals arising from the 6[1*H*] monomer could be identified in the region of $\delta = 9.2$–6.0. In general, raising the temperature of the system should lead to a reduction of the dimerization constant, but in this case it was proven that the lower limits on K_{dim*} of the (**L-G*n***)$_2$ compounds at 50 °C were still in the order of $10^7\,M^{-1}$. The percentage of DADA tautomeric dimers in both series of compounds also increased (**S-G1**: 7 %; **S-G2**: 7 %; **S-G3**: 11 %; **L-G1**: 1 %; **L-G2**: 2 %; **L-G3**: 2 %), indicating that the DADA forms became relatively more stable as compared to the DDAA forms at higher temperature. Furthermore, the positions of the DADA NH signals of the (**S-G*n***)$_2$ series also remained unchanged down to 100 μM at 50 °C, while those of the (**L-G*n***)$_2$ series were difficult to assess owing to their lower abundance.

The difference between binding strengths of these two series of dendritic UPy compounds could not be addressed accurately as data obtained from the previous experiments were all lower limit values of K_{dim*} and K'_{dim*}. It was also difficult to extract information from competition experiments with these two structurally similar dendritic series. We therefore deliberately weakened the dimeric state by switching the measurements to a more polar solvent system. Previously it was shown that the 6[1*H*]-monomer was in equilibrium with the 4[1*H*] DDAA dimer in 10 % [D_6]DMSO/$CDCl_3$.[4a] We therefore conducted ^{1}H NMR experiments (20 mM, 25 °C) in this solvent system and also found two sets of signals for both the (**S-G*n***)$_2$ and (**L-G*n***)$_2$ series. The K_{dim*} values of both series of compounds were then calculated from the relative integration of the two methyl signals on the UPy unit (see Supporting Information for details). It was found that the **L-G*n*** possessed a K_{dim*} value ($3.0\pm0.6\times10^2\,M^{-1}$) that was three times that of the **S-G*n*** compounds ($1.0\pm0.2\times10^2\,M^{-1}$). Hence the proximity of the dendritic branching indicates that the UPy unit does have some influence on the dimerization constant, although this effect is less pronounced than expected.

Conclusions

We show here that the strength of hydrogen bonding interactions of dendritic UPy compounds can be affected by the polarity and the steric size of the dendron. By attaching a highly nonpolar hydrocarbon dendron to the quadruple hydrogen bonding UPy unit, the binding strength of the DDAA UPy tautomer was found to be constant at $10^7\,M^{-1}$ at 25 °C and even at 50 °C for the **L-G*n*** series. The weaker binding DADA UPy tautomers were found to possess a K'_{dim*} around 10^5–$10^6\,M^{-1}$, and the value was dependent on the branching pattern of the appended dendron. It was noted that **S-G*n*** dendrons, having a branching point closer to the UPy moieties, exerted a stronger destabilization effect on the dimeric state as compared to the **L-G*n*** series, and on the DDAA rather than the DADA tautomeric dimers. Solvatochromic studies of these nonpolar hydrocarbon dendrons revealed little differences in the polarity of the microenvironment from the smallest G1 to the biggest G3 dendron. Hence, rather surprisingly, increasing the size of the hydrocarbon dendron does not lead to a significant increase of the nonpolar microenvironment. Our study also revealed that the microenvironment polarity of a dendritic species can be higher, lower, or the same as its non-dendritic analog, and the direction of change is dependent on the chemical structure of the dendrimer itself. This finding is different from that of conventional polymers, where their polarity is generally higher than that of the monomeric unit.

Experimental Section

(S-G1)$_2$: A solution of **10** (379 mg, 2.05 mmol) and imidazolide **22** (539 mg, 2.46 mmol) in $CHCl_3$ (10 mL) was heated to 60 °C for 6 h. The solution was cooled to 25 °C and filtered, washed with 1 M HCl (2× 30 mL) and brine, dried ($MgSO_4$), filtered and concentrated in vacuo to afford the desired compound (651 mg, 95 %) as a white solid. M.p.: 174–175 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 13.10 (s, 1H, UPyN*H*), 11.89 (s, 1H, CH_2NHCON*H*), 10.08 (br s, 1H, CH_2N*H*), 5.78 (s, 1H, C=C*H*), 3.15 (t, 2H, ^3J(H,H) = 6.0 Hz, CH_2N), 2.21 (s, 3H, UPy-CH_3), 1.65–1.05 (m, 11H), 0.85 ppm (d, 12H, ^3J(H,H) = 6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 173.0, 156.8, 154.9, 148.2, 106.8, 43.9, 38.4, 35.7, 29.3, 28.5, 22.82, 22.76, 19.1 ppm; IR (KBr): $\tilde{\nu}$ = 3217, 2956, 2866, 2604, 1699, 1662, 1591, 1522, 1467, 1444, 1408, 1383, 1365, 1338, 1303, 1294, 1259, 1248, 1170, 1156, 1139, 1117 cm^{-1}; MS(ESI): *m*/*z* (%): 696 (70) [2*M*+Na]$^+$, 337 (100) [*M*+H]$^+$; HRMS(ESI) calcd for [2*M*+Na]$^+$: 695.4943; found: 695.4955; elemental analysis: calcd (%) for $C_{18}H_{32}N_4O_2$ (336.5): C 64.25, H 9.59, N 16.64; found: C 64.17, H 9.66, N 16.68.

(S-G2)$_2$: A solution of **11** (530 mg, 1.14 mmol) and imidazolide **22** (310 mg, 1.41 mmol) in $CHCl_3$ (10 mL) was heated to 60 °C for 6 h. The solution was cooled to 25 °C, filtered, then washed with 1 M HCl (2× 30 mL) and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc = 4:1) to afford the desired compound (529 mg, 79 %) as a pale yellow solid. R_f = 0.75 (hexane/EtOAc = 4:1); m.p.: 60–61 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 13.14 (s, 1H, UPyN*H*), 11.90 (s, 1H, CH_2NHCON*H*), 10.10 (br s, 1H, CH_2N*H*), 5.79 (s, 1H, C=C*H*), 3.16 (q, 2H, ^3J(H,H) = 6.0, CH_2N), 2.20 (s, 3H, UPy-CH_3), 1.80–1.60 (m, 1H), 1.55–1.05 (m, 34H), 0.85 ppm (d, 24H, ^3J(H,H) = 6.6, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 172.9, 156.8, 154.9, 148.0, 106.8, 44.1, 37.9, 37.8., 36.0, 34.2, 32.2, 31.35, 31.29, 28.5, 23.6, 22.9, 19.0 ppm; IR (KBr): $\tilde{\nu}$ = 3227, 3014, 2953, 2927, 2865, 2716, 2601, 1702, 1659, 1587, 1528, 1467, 1416, 1382, 1365, 1302, 1260, 1245, 1170, 1141 cm^{-1}; MS(ESI): *m*/*z* (%): 1178 (25) [2*M*+H]$^+$, 589 (100) [*M*+H]$^+$; HRMS(ESI) calcd for [2*M*+H]$^+$: 1178.0757; found: 1178.0762; elemental analysis: calcd (%) for $C_{36}H_{68}N_4O_2$ (589.0): C 73.42, H 11.64, N 9.51; found: C 73.90, H 12.00, N 9.28.

(S-G3)$_2$: A solution of **12** (86 mg, 0.091 mmol) and imidazolide **22** (40 mg, 0.18 mmol) in $CHCl_3$ (2 mL) was heated to 60 °C for 6 h. The solution was cooled to 25 °C and filtered. The resulting solution was concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc = 20:1 gradient to 5:1) to afford the desired compound (70 mg, 70 %) as a pale yellow liquid. R_f = 0.56 (hexane/EtOAc = 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 13.17 (s, 1H, UPyN*H*), 11.91 (s, 1H, CH_2NHCON*H*), 10.11 (br s, 1H, CH_2N*H*), 5.80 (s, 1H, C=C*H*), 3.17 (q, 2H, ^3J(H,H) = 5.4 Hz, CH_2N), 2.20 (s, 3H, UPy-CH_3), 1.75–1.05 (m, 83H), 0.86 ppm (d, 48H, ^3J(H,H) = 6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 173.0, 156.9, 154.9, 148.0, 106.9, 44.1, 38.2, 37.9, 37.6, 36.1, 34.6, 34.3, 34.2, 32.3, 31.4, 28.6, 28.3, 23.8, 22.9, 19.1 ppm; IR (KBr): $\tilde{\nu}$ = 3440, 3220, 2950, 2924, 2863, 2720, 2610, 1698, 1664, 1651, 1613, 1591, 1537, 1466, 1385, 1367, 1326, 1250, 1187, 1170, 1039, 1021 cm^{-1}; MS(ESI): *m*/*z* (%) 2188 (10) [2*M*+H]$^+$, 1094 (85) [*M*+H]$^+$; HRMS(ESI) calcd for [2*M*+H]$^+$: 2187.2025; found: 2187.2036; elemental analysis: calcd (%) for $C_{72}H_{140}N_4O_2$ (1093.9): C 79.05, H 12.90, N 5.12; found: C 79.39, H 13.13, N 4.76.

(L-G1)$_2$: A solution of **13** (510 mg, 2.39 mmol) and imidazolide **22** (630 mg, 2.87 mmol) in $CHCl_3$ (20 mL) was heated to 60 °C for 12 h. The solution was cooled to 25 °C and filtered, then washed with 1 M HCl (2× 30 mL) and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The solid was recrystallized in CH_2Cl_2/MeOH (1:1) solution and afforded the desired compound (408 mg, 47 %) as a white crystal. M.p.: 144–145 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 13.13 (s, 1H, UPyN*H*), 11.86 (s, 1H, CH_2NHCON*H*), 10.17 (br s, 1H, CH_2N*H*), 5.79 (s, 1H, C=C*H*), 3.21 (q, 2H, ^3J(H,H) = 5.7 Hz, CH_2N), 2.21 (s, 3H, UPy-CH_3), 1.75–1.40 (m, 3H), 1.35–1.05 (m, 12H), 0.84 ppm (d, 12H, ^3J(H,H) = 6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 173.1, 156.7, 154.9, 148.3, 106.8, 40.6, 37.8, 36.0, 31.3, 31.0, 28.5, 27.0, 22.8, 19.1 ppm; IR (KBr): $\tilde{\nu}$ = 3400, 3215, 2954, 2926, 2860, 1700, 1667, 1586, 1525, 1457, 1413, 1383, 1366, 1303, 1254, 1170, 1147, 1137, 1040, 1019 cm^{-1}; MS(ESI): *m*/*z* (%): 751 (35) [2*M*+Na]$^+$, 387 (100) [*M*+Na]$^+$; HRMS(ESI) calcd for [2*M*+Na]$^+$: 751.5569; found: 751.5568; elemental analysis: calcd (%) for $C_{20}H_{36}N_4O_2$ (364.53): C 65.90, H 9.95, N 15.36; found: C 66.28, H 10.22, N 15.18.

(L-G2)$_2$: A solution of **14** (555 mg, 1.19 mmol) and imidazolide **22** (340 mg, 1.55 mmol) in $CHCl_3$ (10 mL) was heated to 60 °C for 12 h then cooled to 25 °C and filtered. The solution was washed with 1 M HCl (2× 30 mL) and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc = 5:1) to afford the desired compound (670 mg, 91 %) as a white solid. R_f = 0.40 (hexane/EtOAc = 3:1); m.p. 41–42 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 13.15 (s, 1H), 11.83 (s, 1H), 10.19 (s, 1H, N*H*CH_2), 5.77 (s, 1H, C=C*H*), 3.19 (q, 2H, ^3J(H,H) = 6.6 Hz, CH_2NH), 2.19 (s, 3H, C=CCH_3), 1.65–1.35 (m, 6H), 1.35–1.00 (m, 33H), 0.84 ppm (d, 24H, ^3J(H,H) = 6.6 Hz, CH_3); ^{13}C NMR: δ = 173.1, 156.7, 154.8, 148.2, 106.7, 40.6, 37.9, 37.3, 36.01, 35.99, 34.2, 34.1, 31.3, 31.2, 28.5, 27.0, 23.8, 22.8, 19.0 ppm; IR (KBr): $\tilde{\nu}$ = 3215, 2954, 2926, 2868, 2718, 2606, 1701, 1668, 1589, 1526, 1467, 1413, 1383, 1366, 1304, 1255, 1170, 1139, 1041, 1016 cm^{-1}; MS(ESI): *m*/*z* (%) 1234 (39) [2*M*+H]$^+$, 617 (100) [*M*+H]$^+$; HRMS(ESI) calcd for [2*M*+H]$^+$: 1234.1383; found: 1234.1377; elemental analysis: calcd (%) for $C_{38}H_{72}N_4O_2$ (617.0): C 73.97, H 11.76, N 9.08; found: C 73.62, H 11.95, N 8.90.

(L-G3)$_2$: A solution of **15** (137 mg, 0.141 mmol) and imidazolide **22** (40 mg, 0.183 mmol) in $CHCl_3$ (5 mL) was heated to 60 °C for 12 h. The solution was cooled to 25 °C and filtered, then washed with 1 M HCl (2× 15 mL) and brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash chromatography (hexane/EtOAc = 10:1) to afford the desired compound (140 mg, 88 %) as a pale yellow liquid. R_f = 0.42 (hexane/EtOAc = 5:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 13.18 (s, 1H), 11.87 (s, 1H), 10.20 (s, 1H, N*H*CH_2), 5.81 (s, 1H, C=C*H*), 3.21 (q, 2H, ^3J(H,H) = 5.1 Hz, CH_2NH), 2.21 (s, 3H, C=CCH_3), 1.67–1.37 (m, 11H), 1.37–1.02 (m, 76H), 0.87 ppm (d, 48H, ^3J(H,H) = 6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 173.1, 156.7, 154.9, 148.2, 106.9, 40.8, 37.9, 37.7, 37.5, 36.1, 34.5, 34.3, 31.4, 31.3, 28.6, 27.2, 24.0, 23.8, 22.91, 22.90, 19.0 ppm; IR (KBr): $\tilde{\nu}$ = 3214, 2950, 2925, 2864, 2717, 2596, 1699, 1664, 1613, 1592, 1526, 1463, 1416, 1385, 1367, 1324, 1303, 1252, 1189, 1172, 1138, 1036 cm^{-1}; MS(ESI): *m*/*z* (%): 2244 (35) [2*M*+H]$^+$, 1122 (100) [*M*+H]$^+$; HRMS(ESI) calcd for [2*M*+H]$^+$ 2243.2651; found: 2243.2662.

Compound 24: A mixture of *p*-bromonitrobenzene (0.65 g, 3.22 mmol), $Pd(OAc)_2$ (0.072 g, 0.32 mmol), (oxydi-2,1-phenylene)bis(diphenylphosphine) (0.35 g, 0.65 mmol), and Cs_2CO_3 (0.68 g, 3.52 mmol) in toluene (10 mL) was degassed in a sealed tube using three freeze-pump-thaw cycles. After warming the mixture to room temperature, **10** (0.65 g, 3.51 mmol) was first dissolved in toluene (5 mL) and then added using a syringe. The mixture was then heated to 110 °C for 2 d with stirring. Et_2O was added to the reaction mixture after cooling to room temperature. The mixture was filtered through a pad of Celite and the filtrate was evaporated in vacuo to give a yellow oil which was purified by flash chromatography on silica gel (hexane/EtOAc = 15:1) to give the desired compound (0.66 g, 67 %) as a yellow oil. R_f = 0.17 (hexane/EtOAc = 15:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 8.13–8.02 (2H, m, Ar*H*), 6.57–6.45 (2H, m, Ar*H*), 4.46 (1H, br s, NH), 3.11 (2H, t, ^3J(H,H) = 6.0 Hz, NCH_2), 1.66–1.57 (1H, m, CH), 1.51 (2H, septet, ^3J(H,H) = 6.6 Hz, C*H*Me$_2$), 1.41–1.28 (4H, m, CH_2), 1.27–1.12 (4H, m, CH_2), 0.89 ppm (12H, d, ^3J(H,H) = 6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 154.1, 136.9, 126.4, 110.8, 46.8, 37.8, 35.7, 29.4, 28.3, 22.5 ppm; MS-(ESI): *m*/*z* (%): 307 (100) [*M*+H]$^+$; HRMS(ESI) calcd for [*M*+H]$^+$ 307.2385; found: 307.2395; elemental analysis: calcd (%) for $C_{18}H_{30}N_2O_2$ (306.4): C 70.55, H 9.87, N 9.14; found: C 70.32, H 9.89, N 9.12.

S-G1-probe: NaH (60 % in mineral oil) (0.15 g, 3.75 mmol) was added to a THF solution (10 mL) of **24** (0.63 g, 2.06 mmol) at 0 °C for 30 min. MeI (0.25 mL, 3.98 mmol) was added to the solution using a syringe. The mixture was then stirred at 25 °C for 24 h. H_2O was added to the reaction mixture and the aqueous layer was extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated in vacuo to give a yellow oil which was purified by flash chromatography (hexane/EtOAc = 10:1) to give the target com-

pound (0.62 g, 94%) as a yellow oil. R_f=0.54 (hexane/EtOAc=10:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=8.16–8.03 (2H, m, Ar*H*), 6.63–6.52 (2H, m, Ar*H*), 3.32 (2H, d, ^3J(H,H)=7.5 Hz, NCH_2), 3.08 (3H, s, NCH_3), 1.85–1.70 (1H, m, CH), 1.48 (2H, septet, ^3J(H,H)=6.6 Hz, C*H*Me$_2$), 1.34–1.23 (4H, m, CH_2), 1.22–1.09 (4H, m, CH_2), 0.86 ppm (12H, d, ^3J(H,H)=6.6 Hz, CH_3). ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ= 153.7, 136.3, 126.0, 110.1, 57.0, 39.8, 36.7, 35.4, 29.0, 28.3, 22.6, 22.4 ppm; MS(ESI): *m*/*z* (%): 321 (100) $[M+H]^+$; HRMS(ESI) calcd for $[M+H]^+$ 321.2542; found: 321.2535; elemental analysis: calcd (%) for $C_{19}H_{32}N_2O_2$ (320.1): C 71.21, H 10.06, N 8.74; found: C 71.66, H 10.24, N 8.79.

Compound 25: A mixture of *p*-bromonitrobenzene (0.14 g, 0.69 mmol), $Pd(OAc)_2$ (0.031 g, 0.14 mmol), (oxydi-2,1-phenylene)bis(diphenylphosphine) (0.15 g, 0.28 mmol), and Cs_2CO_3 (0.48 g, 2.49 mmol) in toluene (10 mL) was degassed in a sealed tube using three freeze-pump-thaw cycles. After warming the mixture to room temperature, **11** (0.34 g, 0.78 mmol) was first dissolved in toluene (10 mL) and was then added using a syringe. The mixture was then heated to 110°C for 2 d with stirring. Et_2O was added to the reaction mixture after cooling to room temperature. The mixture was filtered through a pad of Celite and the filtrate was evaporated in vacuo to give a yellow oil which was purified by flash chromatography on silica gel (hexane/CH_2Cl_2=2:1) to give the desired compound (0.32 g, 83%) as a yellow oil. R_f=0.4 (hexane/CH_2Cl_2=2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=8.08 (2H, d, ^3J(H,H)=9.0, Ar*H*), 6.52 (2H, d, ^3J(H,H)=9.0 Hz, Ar*H*), 4.46 (1H, brs, NH), 3.12 (2H, t, ^3J-(H,H)=5.4 Hz, NCH_2), 1.73–1.60 (1H, m, CH), 1.47 (4H, septet, ^3J-(H,H)=6.6 Hz, C*H*Me$_2$), 1.38–1.01 (30H, m), 0.86 ppm (24H, d, ^3J-(H,H)=6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ=153.9, 137.5, 126.5, 110.9, 47.1, 37.8, 37.6, 35.9, 34.0, 32.4, 31.2, 28.5, 23.8, 22.8 ppm; MS(ESI): *m*/*z* (%): 560 (65) $[M+H]^+$; HRMS(ESI) calcd for $[M+H]^+$ 559.5202; found: 559.5213; elemental analysis: calcd (%) for $C_{36}H_{66}N_2O_2$ (558.9): C 77.36, H 11.90, N 5.01; found: C 77.01, H 11.89, N 5.06.

S-G2-probe: NaH (60% in mineral oil) (0.077 g, 1.92 mmol) was added to a THF solution (10 mL) of **25** (0.30 g, 0.54 mmol) at 0°C for 30 min. MeI (0.2 mL, 3.18 mmol) was added to the solution using a syringe. The mixture was then stirred at 25°C for 24 h. H_2O was added to the reaction mixture and the aqueous layer was extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated in vacuo to give a yellow oil which was purified by flash chromatography (hexane/CH_2Cl_2=2:1) to give the target compound (0.23 g, 74%) as a yellow oil. R_f=0.48 (hexane/CH_2Cl_2=2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=8.11 (2H, d, ^3J(H,H)=9.3 Hz, Ar*H*), 6.59 (2H, d, ^3J(H,H)=9.3 Hz, Ar*H*), 3.24 (2H, d, ^3J(H,H)= 7.5 Hz, NCH_2), 3.08 (3H, s, NCH_3), 1.91–1.77 (1H, m, CH), 1.46 (4H, septet, ^3J(H,H)=6.6 Hz, C*H*Me$_2$), 1.37–1.03 (30H, m), 0.86 ppm (24H, d, ^3J(H,H)=6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ=153.9, 136.6, 126.3, 110.2, 57.4, 40.0, 37.8, 36.5, 36.0, 34.1, 32.1, 31.3, 28.5, 23.6, 22.8 ppm; MS(ESI): *m*/*z* (%): 574 (56) $[M+H]^+$; HRMS(ESI) calcd for $[M+H]^+$ 573.5359; found: 573.5355; elemental analysis: calcd (%) for $C_{37}H_{68}N_2O_2$ (573.0): C 77.56, H 11.96, N 4.89; found: C 77.48, H 11.95, N 4.64.

Compound 26: A mixture of *p*-bromonitrobenzene (0.084 g, 0.42 mmol), $Pd(OAc)_2$ (0.019 g, 0.085 mmol), (oxydi-2,1-phenylene)bis(diphenylphosphine) (0.089 g, 0.17 mmol), and Cs_2CO_3 (0.29 g, 1.50 mmol) in toluene (10 mL) was degassed in a sealed tube using three freeze-pump-thaw cycles. After warming the mixture to room temperature, **12** (0.46 g, 0.49 mmol) was first dissolved in toluene (10 mL) and was then added using a syringe. The mixture was then heated to 110°C for 2 d with stirring. Et_2O was added to the reaction mixture after cooling to room temperature. The mixture was filtered through a pad of Celite and the filtrate was evaporated in vacuo to give a yellow oil which was purified by flash chromatography on silica gel (hexane/CH_2Cl_2=2:1) to give the desired compound (0.16 g, 31%) as a yellow oil. R_f=0.5 (hexane/CH_2Cl_2=2:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=8.08 (2H, d, ^3J(H,H)=9.3 Hz, Ar*H*), 6.51 (2H, d, ^3J(H,H)=9.0 Hz, Ar*H*), 4.43 (1H, brs, NH), 3.12 (2H, d, ^3J(H,H)=5.7 Hz, NCH_2), 1.71–1.61 (1H, m, CH), 1.47 (8H, septet, ^3J(H,H)=6.6 Hz, C*H*Me$_2$), 1.39–1.03 (74H, m), 0.87 ppm (48H, d, ^3J(H,H)=6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ=153.7, 137.9, 126.6, 111.0, 47.1, 37.9, 37.4, 36.0, 34.3, 34.20, 34.16, 32.7, 31.4, 28.6, 24.0, 23.8, 22.92, 22.90, 22.8 ppm; MS(ESI): *m*/*z* (%): 1064 (13) $[M+H]^+$; HRMS (ESI) calcd for $[M+H]^+$: 1064.0836; found: 1064.0851; elemental analysis: calcd (%) for $C_{72}H_{138}N_2O_2$ (1063.9): C 81.29, H 13.07, N 2.63; found: C 81.22, H 13.67, N 2.69.

S-G3-probe: NaH (60% in mineral oil) (0.077 g, 1.92 mmol) was added to a THF solution (10 mL) of **26** (0.15 g, 0.14 mmol) at 0°C for 30 min. MeI (0.2 mL, 3.18 mmol) was added to the solution using a syringe. The mixture was then stirred at 25°C for 24 h. H_2O was added to the reaction mixture and the aqueous layer was extracted with CH_2Cl_2 (3×50 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), filtered, and evaporated in vacuo to give a yellow oil which was purified by flash chromatography (hexane/CH_2Cl_2=3:1) to give the target compound (0.14 g, 93%) as a yellow oil. R_f=0.33 (hexane/CH_2Cl_2=3:1). ^{1}H NMR (300 MHz, $CDCl_3$, 25°C): δ=8.11 (2H, d, ^3J(H,H)=9.6 Hz, Ar*H*), 6.59 (2H, d, ^3J(H,H)=9.3 Hz, Ar*H*), 3.33 (2H, d, ^3J(H,H)= 7.2 Hz, NCH_2), 3.08 (3H, s, NCH_3), 1.92–1.75 (1H, m, CH), 1.48 (8H, septet, ^3J(H,H)=6.6 Hz, C*H*Me$_2$), 1.37–1.01 (74H, m), 0.87 ppm (48H, d, ^3J(H,H)=6.6 Hz, CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25°C): δ=153.9, 136.8, 126.3, 110.3, 57.5, 40.1, 37.9, 37.4, 36.7, 36.0, 34.4, 34.2, 32.3, 31.4, 28.6, 23.8, 23.7, 22.92, 22.90, 22.8 ppm; MS(ESI): *m*/*z* (%): 1078 (5) $[M+H]^+$; HRMS(ESI) calcd for $[M+H]^+$: 1078.0993; found: 1078.1000; elemental analysis: calcd (%) for $C_{73}H_{140}N_2O_2$ (1077.9): C 81.34, H 13.09, N 2.60; found: C 80.99, H 12.86, N 2.28.

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