However, these systems are inferior to those involving the alkali metal and alkaline-earth metal peroxides.

In summary, the results of this study demonstrate the feasibility of efficiently generating singlet delta oxygen from gas–solid reactants without the problems associated with liquid-phase quenching. Furthermore, the required starting materials are commercially available, moderately priced, and safe to handle.

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[15] A 70 watt microwave discharge (2.45 GHz) of an oxygen–helium mixture at a total pressure of 5 Torr was used to record the $O_2$ $^1\Delta_g$ emission spectrum. At the typical flow conditions of the measurement $1 \times 10^{-5}$ moles of oxygen were delivered per second. A glass wool plug was placed in the discharge tube to aid in the recombination of oxygen atoms. If the discharge, gas flow, and vacuum pumping were simultaneously stopped, the emission signal decayed within one second.
[16] The BHP–chlorine sparger contained 100 mL of an aqueous mixture that was 1.1 M in NaOH and 7.5 M in $H_2O_2$. It was prepared by slowly adding the NaOH to cold 85% $H_2O_2$ over a 30-minute period while keeping the temperature of the mixture below 273 K. The sparger was immersed into a 258-K recirculating bath, and chlorine gas was introduced at a flow rate of 160 sccm. The sparger was connected to the inlet of a gas cell that was located in front of the spectrograph. The outlet of the cell was connected to a cold trap (−77 K) and a vacuum pump that maintained the pressure in the cell at 4 Torr. The addition of 6 Torr of either helium or nitrogen to the sparger effluent at the gas cell entrance resulted in comparable quenching of the $O_2$ $^1\Delta_g$ signal. Since the known quenching coefficients for He and $N_2$ with $O_2$ $^1\Delta_g$ differ by two orders of magnitude,[17] the increased quenching had to be due to a longer residence time in the liquid resulting from the increased backpressure of the added gas.
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## Controlled Release of a Dendritically Encapsulated Template Molecule**

Graham M. Dykes, David K. Smith,* and Gordon J. Seeley

Over the past few years there has been intense interest in the unique properties exhibited by molecules with branched superstructures (namely, dendrimers).[1] In particular, there has been a focus on the effect of dendritic encapsulation on a variety of physical and chemical properties—for example, the optical, redox, and catalytic behavior of core units have all been modified by dendritic functionalization.[2]

Chemists have increasingly begun to focus on the assembly of dendritic structures in which the core unit is held in place by noncovalent interactions rather than by covalent bonds.[3] Zimmerman et al. published reports of dendritically functionalized rosettes, assembled through hydrogen-bond formation,[4] as well as other hydrogen-bonded assemblies.[5] Hydrogen bonds have also been used by other research groups for dendritic assembly.[6] Kenda and Diederich reported well-defined "dendrophane" assemblies based on hydrophobic interactions,[7] whilst Percec et al. have used similar forces to assemble distinctive architectures from dendritic building blocks.[8] A wide range of dendrimers assembled around metal ions have also been reported.[9] Gibson and co-workers have used interactions between secondary amines and dibenzo[24]crown-8 to assemble dendrimers with rotaxane-like mechanical branching.[10] Recently, we used COOH···$NH_2$ hydrogen bonds at the focal point of individual dendritic branches to assemble them around hydrophilic dyes, thus modulating the solubility profiles and optical properties.[11]

Herein we report a novel series of dendritic branches based on L-lysine, in which the focal point has been functionalized with benzo[18]crown-6. We have characterized the strength and stoichiometry of binding with potassium and benzylammonium cations, and report the effect of dendritic branching on the host–guest binding process. In addition, we have assembled dendritic branches around a bis-ammonium cation, thus encapsulating it within a supramolecular dendritic shell. We were able to achieve controlled release of the encapsulated template molecule by the addition of potassium ions. In this way, we have achieved the controlled assembly and disassembly of a supramolecular dendrimer in solution for the first time.


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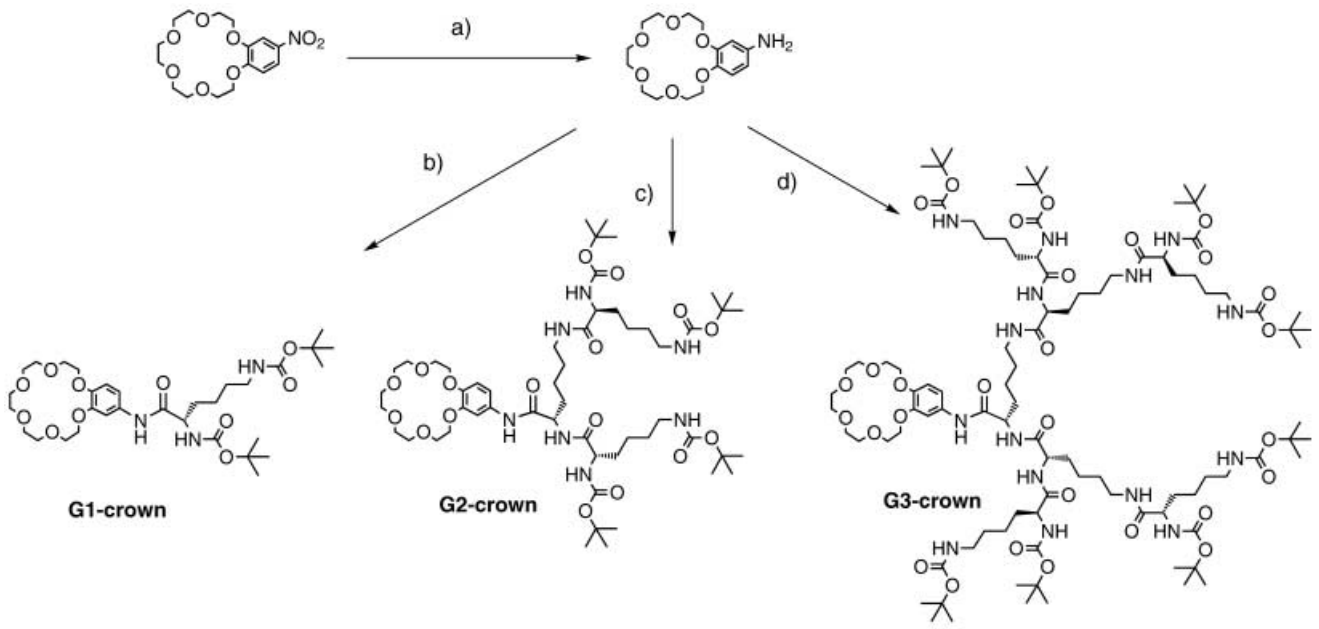


Scheme 1. Synthesis of the crown ether functionalized dendritic branches: a) Pd/C, EtOH, 99%; b) **G1-COOH**, DCC, HOBt, $Et_3N$, EtOAc, 87%; c) **G2-COOH**, HATU, $Et_3N$, EtOAc, 91%; d) **G3-COOH**, HATU, $Et_3N$, EtOAc, 63%.

The dendritic crowns **G1-crown**, **G2-crown**, and **G3-crown** were synthesized according to Scheme 1. Preformed dendritic branches based on L-lysine[12] which possess a carboxylic acid at the focal point were coupled to 4′-aminobenzo[18]crown-6.[13] As expected in convergent synthesis,[1c] the reaction became less favored with increasing dendritic generation, which necessitated a change in the coupling reagent from 1,3-dicyclohexylcarbodiimide/1-hydroxybenzotriazole (DCC/HOBt) to the more active *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium hexafluorophosphate (HATU) uronium salt for the synthesis of **G2-crown** and **G3-crown**.[14] Yields of 87, 91, and 63% were obtained for **G1-crown**, **G2-crown**, and **G3-crown**, respectively. The dendritic crowns were characterized by all standard methods, and data were in full agreement with the proposed structures.[15]

The ability of these receptors to bind $K^+$ ions was monitored by $^1H$ NMR titrations in MeOD solution. The chemical shift of the aromatic protons was followed during the addition of $K^+$ ions, and in all cases 1:1 complexes were formed (Figure 1). The binding for **G1-crown** and **G2-crown** was on the upper limits of determination by NMR methods, and log *K* values (Table 1) were estimated as $\geq 5$. By inspection of the data, it appeared that **G1-crown** binds $K^+$ ions more strongly than **G2-crown**. **G3-crown** binds $K^+$ ions slightly less strongly, with the log*K* value calculated as 4.1 (HypNMR).[16] The change in chemical shift of the aromatic protons induced by $K^+$ ions decreased as the dendritic generation of the receptor increased. Host–guest chemistry inside dendrimers is of considerable current interest,[2] and it has been previously observed that binding strengths (and induced shifts) decrease with increasing generation as a consequence of small amounts of nonselective binding within the dendritic branching.[17] In our case, the C=O groups within the branches may bind weakly to $K^+$ ions, thus competing with the crown ether at the focal point. Alternatively, the build-up of charge within the dendritic structure may be disfavored as a consequence of increasing amounts of branching shielding the charge from the polar solvent.

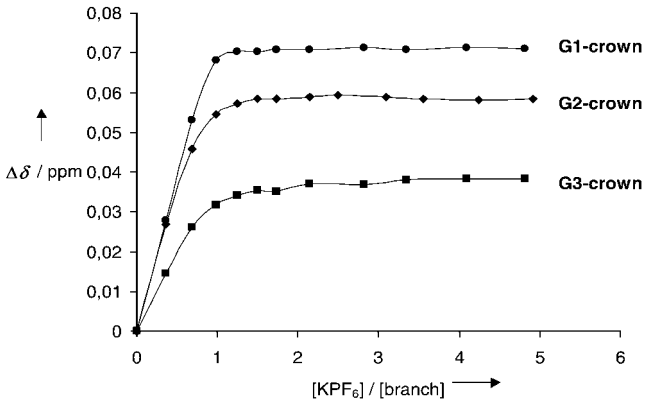


Figure 1. NMR titration curves for **G1-crown**, **G2-crown**, and **G3-crown** with $K^+$ ions in which the shift of the aromatic signal (at ca. $\delta = 6.9$ ppm) is monitored.

Table 1. Binding constants (log $K_a$, MeOD, $T = 300$ K) elucidated by $^1H$ NMR titration methods for 1:1 complexes of dendritic crown ethers with $K^+$ ions and **1**.

| Receptor | Guest cation | log $K_a$ | Standard deviation[a] | $\Delta\delta_{sat}$ [ppm] |
|---|---|---|---|---|
| **G1-crown** | $K^+$ | $\geq 5$ | excessive | 0.070[b] |
| **G2-crown** | $K^+$ | $\geq 5$ | excessive | 0.058[b] |
| **G3-crown** | $K^+$ | 4.10 | 0.14 | 0.038[b] |
| **G1-crown** | **1** | 3.58 | 0.14 | 0.115[c] |
| **G2-crown** | **1** | 3.28 | 0.23 | 0.104[c] |
| **G3-crown** | **1** | 2.31 | 0.12 | 0.108[c] |

[a] The standard deviation gives the +/− error for 67% confidence. [b] Saturation shift in the aromatic peak (at ca. $\delta = 6.9$ ppm) of the benzocrown ether induced by the addition of potassium cations. [c] Saturation shift in the $CH_2$ (benzyl) signal (at $\delta = 4.10$ ppm) of guest **1** induced by the addition of the dendritic crown ether.

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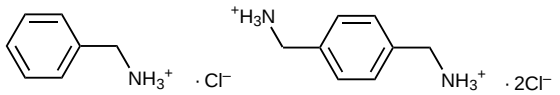
The ability of the receptors to bind the benzylammonium cation **1** was also investigated in MeOD. Binding constants




**1** **2**

(Table 1) were elucidated by NMR titrations in which the perturbation of the benzyl $CH_2$ protons of **1** on the addition of **Gn-crown** was monitored. The strength of binding decreased as the dendritic generation increased. As a control experiment, the dendritic branch functionalized with a methyl ester group, **G3-COOMe**,[18] was titrated with **1**. There was only a very small perturbation of the NMR signals of **1**, which is indicative of very weak, nonselective binding in the branches. As expected, therefore, the crown ether is the primary site for binding these cationic guests.

The ability of the more strongly binding potassium ion to trigger the release of the more weakly bound ammonium cation **1** from the complex was then investigated. A fivefold excess of **G1-crown** was mixed with **1** and the NMR signal of the benzyl $CH_2$ protons was monitored on the addition of $K^+$ ions. The addition of one equivalent of $K^+$ ions was sufficient to completely displace the benzylammonium guest (**1**) from the complex (Figure 2).[19]

The relatively strong crown···$NH_3^+$ interactions were then used to assemble a supramolecular dendrimer. The interaction between protonated 1,4-bis(aminomethyl)benzene (**2**) and **G2-crown** was monitored in MeOD by using NMR methods, and a Job plot analysis was performed to monitor the stoichiometry of the complex formed (Figure 3, ■). This plot was compared to the Job plot for the binding of **1** to **G2-crown** (Figure 3 ▲), and clearly illustrates the difference in stoichiometry between the two complexes. Hence, a 2:1 assembly was formed between **G2-crown** and compound **2** (Scheme 2), namely, formation of a supramolecular dendrimer takes place. The HypNMR program was used to elucidate the binding constants for the formation of 1:1 and 2:1 complexes, and values of $\log K_{11} = 2.06$ (0.37) and $\log K_{21} = 1.27$ (0.16) were obtained. The results indicate a noncooperative binding process in polar MeOH solution. Once again, this supramolecular dendrimer was smoothly disassembled by the addition of $K^+$ ions to the solution—releasing template **2** into solution—a process which was monitored by NMR methods. In a very recent paper,[10b] Gibson et al. reported the cooperative assembly of related dendritic structures in nonpolar solvents. In the future, the assembly process reported here will also be investigated in nonpolar solvents to determine whether there are any cooperative binding effects in this case.

In conclusion, we can assemble dendritic structures in competitive solvents such as methanol, and then disassemble them in a controlled manner. This approach is of general importance: it obviates the need for time-consuming covalent synthesis, and also has the advantage that compounds containing ammonium ions

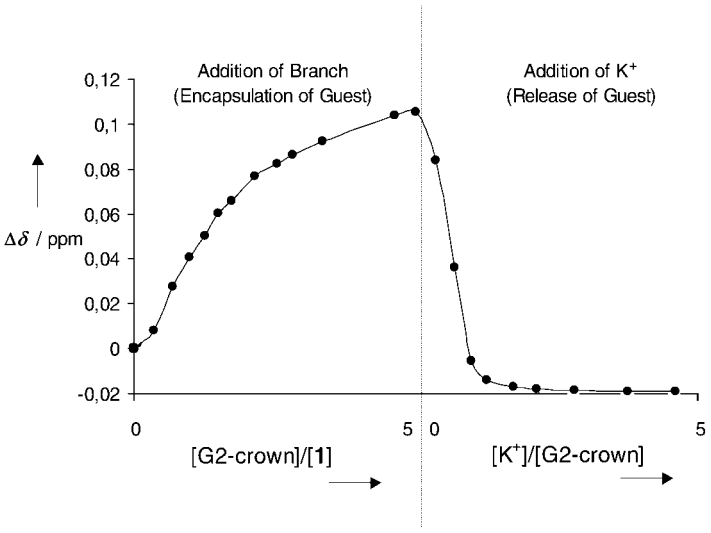



Figure 2. NMR shift of the $ArCH_2$ peak (at $\delta = 4.10$ ppm) of guest **1** on the addition of **G2-crown** followed by the addition of $KPF_6$.

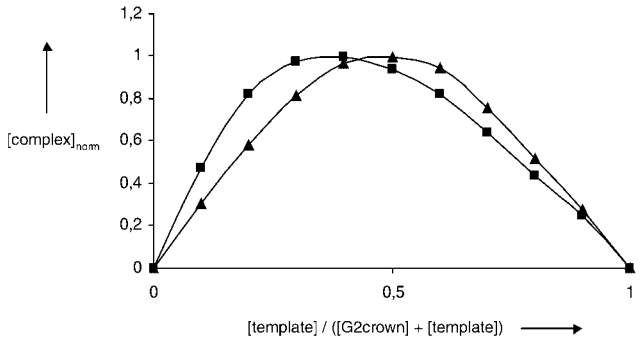
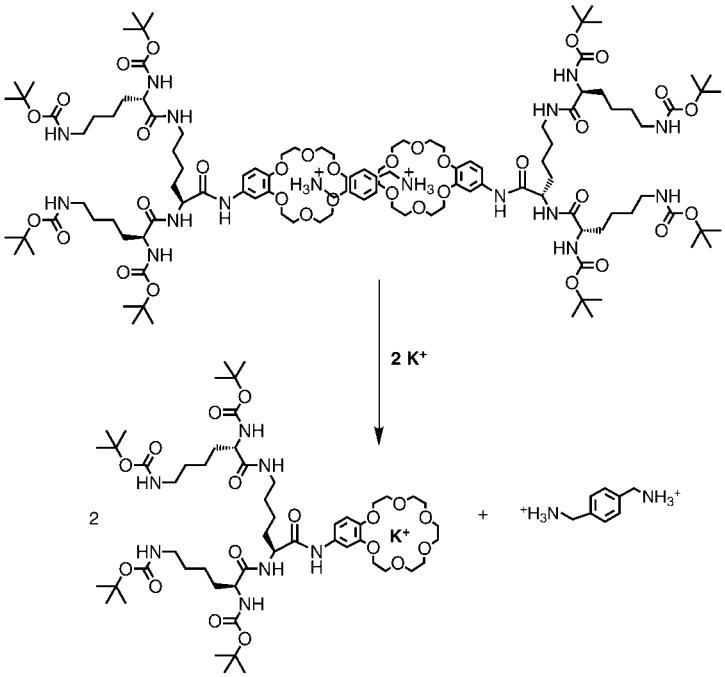



Figure 3. Job plot determined by $^1H$ NMR spectroscopy indicating the 2:1 stoichiometry of the complex formed between **G2-crown** and **2** (■), and the 1:1 stoichiometry of the complex formed between **G2-crown** and **1** (▲).




Scheme 2. Proposed structure of the supramolecular dendrimer generated by mixing **G2-crown** with compound **2**, and the disassembly process induced by the addition of $KPF_6$.

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which could act as potential templates are fairly common. This reversible dendritic encapsulation will be of particular use when the template is a functional molecule derivatized with $NH_3^+$ groups. The function will then be dendritically modified (or shielded) until such a point as $K^+$ ions are added, when controlled release of the functional template would be achieved. Investigations of the reversible encapsulation and controlled release of functional template molecules are currently in progress.

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[18] **G3COOMe** is the third-generation lysine-based dendritic branch in which the carboxylic acid at the focal point has been protected as a methyl ester. The full characterization of this compound has previously been published in reference [11b].

[19] The chemical shift of the benzyl peak after $K^+$-triggered release of the guest from the complex is not the same as at the start of the experiment because of the change in counter anion (from $Cl^-$ to $PF_6^-$) and the increase in ionic strength of the solution.


## Phosphite Dehydrogenase: A Versatile Cofactor-Regeneration Enzyme**

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The potential of enzyme-catalyzed transformations in organic synthesis is well recognized.[1] Oxidoreductases make up an important class of enzymes as they can perform highly stereoselective reductions of a variety of functional groups.[2] A drawback of the nicotinamide-dependent oxidoreductases is the prohibitively high expense of the cofactor for stoichiometric use. This impediment has been overcome by using a second enzyme system that can continuously replenish a catalytic amount of the active form of the cofactor.[3] Cofactor regeneration also simplifies product isolation and can influence the position of the equilibrium of the synthetic enzyme system, that is, the regeneration system may drive the reaction to completion when product formation would be unfavorable in its absence. The efficiency of a regeneration system is determined by the expense and stability of the regeneration enzyme and its substrate, the ease of product purification, the kinetic parameters of the regeneration enzyme ($k_{cat}$, $K_M$), and the thermodynamic driving force.

We recently described the unusual enzyme phosphite dehydrogenase (PtxD).[4,5] This protein catalyzes the oxidation of phosphite to phosphate with the concomitant reduction of $NAD^+$ to NADH. The enzyme can also use $NADP^+$ as the oxidant, albeit less effectively.[4] The equilibrium constant for the oxidation of phosphite by $NAD^+$ can be estimated as $10^{11}$ by using the reported redox potentials at pH 7.0 for

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