'Crowned' Arborols

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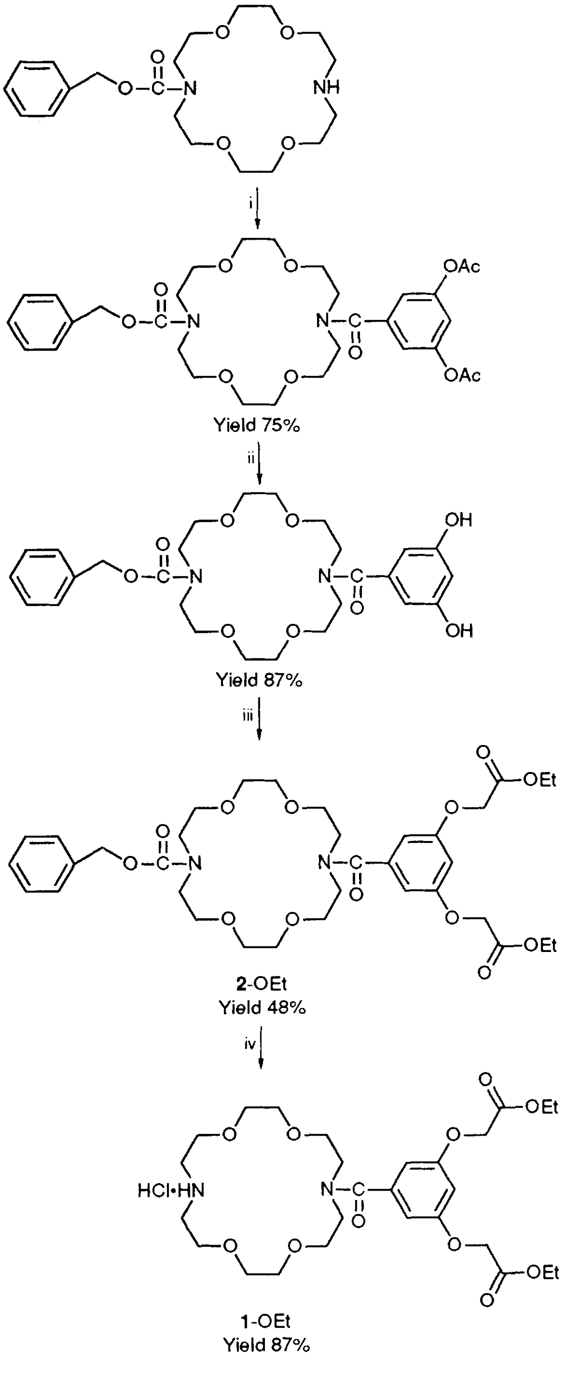
'Crowned' arborols are synthesized for the first time using a convergent method.

The novel class of cascade molecules, arborols, have recently been of much synthetic interest.[1–9] Tomalia *et al.*[4,5,9] have also reported a similar class of cascade molecules 'starburst-dendritic' polymers.

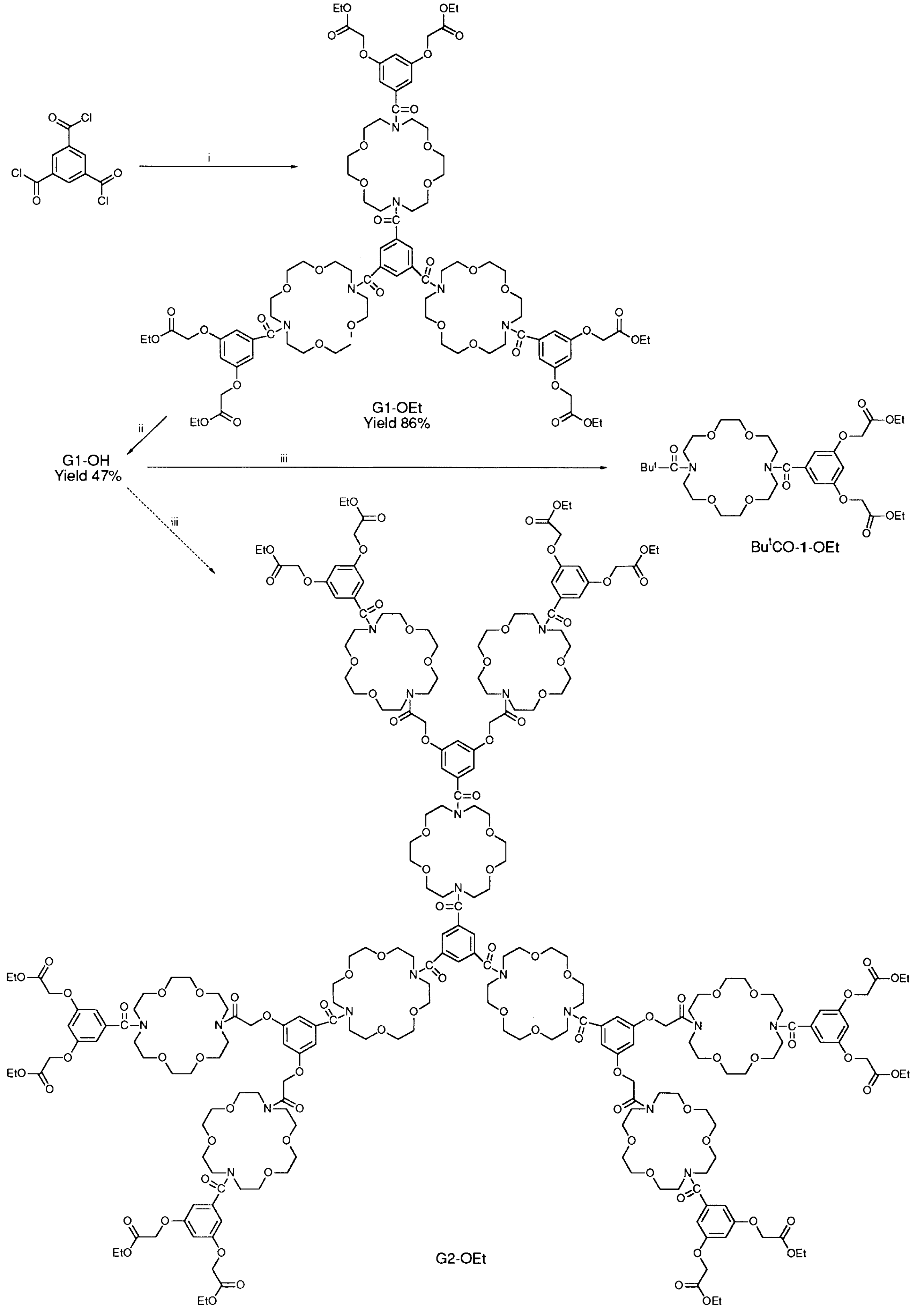
In order to increase the variety of functional groups that have been used in dendritic structures we have attempted to introduce crown ethers into arborols in the hope of producing novel properties. We expected that crown ethers would act as 'nests' in arborols and metal ions would 'perch on them like birds'. As a result, the metal binding event would induce some changes in the physical properties. We address here the first successful approach to the synthesis of 'crowned' arborols.

There are two different strategies for the synthesis of arborols, the divergent method going from a nucleus to branches[1–5] and the convergent method going from branches to a nucleus.[6–8] First we synthesized compound **1**-OEt, which serves as an arborol 'trunk' (Scheme 1). This compound was synthesized *via* four steps from *N*-benzyloxycarbonyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane in moderate yield. According to the divergent method we synthesized the first generation (G1-OEt) from trichloroformyl mesitylene (as a core) and **1**-OEt in THF in the presence of triethylamine (Scheme 2). G1-OEt (colourless oil) was identified on the basis of IR, NMR and mass spectral evidence and elemental analysis. After the hydrolysis of the ester groups, the product (G1-OH) was treated with **1**-OEt using pivaloyl chloride and triethylamine. We here met a few synthetic difficulties. The reaction of phenoxyacetic acid (reference compound for G1-OH) and **1**-OEt proceeded quantitatively to give an amide linkage whereas the reaction of G1-OH and **1**-OEt gave Bu^{t}CO-**1**-OEt but not the second generation (G2-OEt). The amide synthesis from carboxylic acids (RCO_2H) with the aid of pivaloyl chloride proceeds *via* a mixed acid anhydride, Bu^tCO_2COR and the two carbonyl groups can react competitively with nucleophiles. Without exception (to the best of our knowledge), however, the carbonyl group near R reacts preferentially because of steric hindrance of Bu^t. Furthermore, G1-OH was poorly soluble in most solvents. Finally, we abandoned the divergent method.

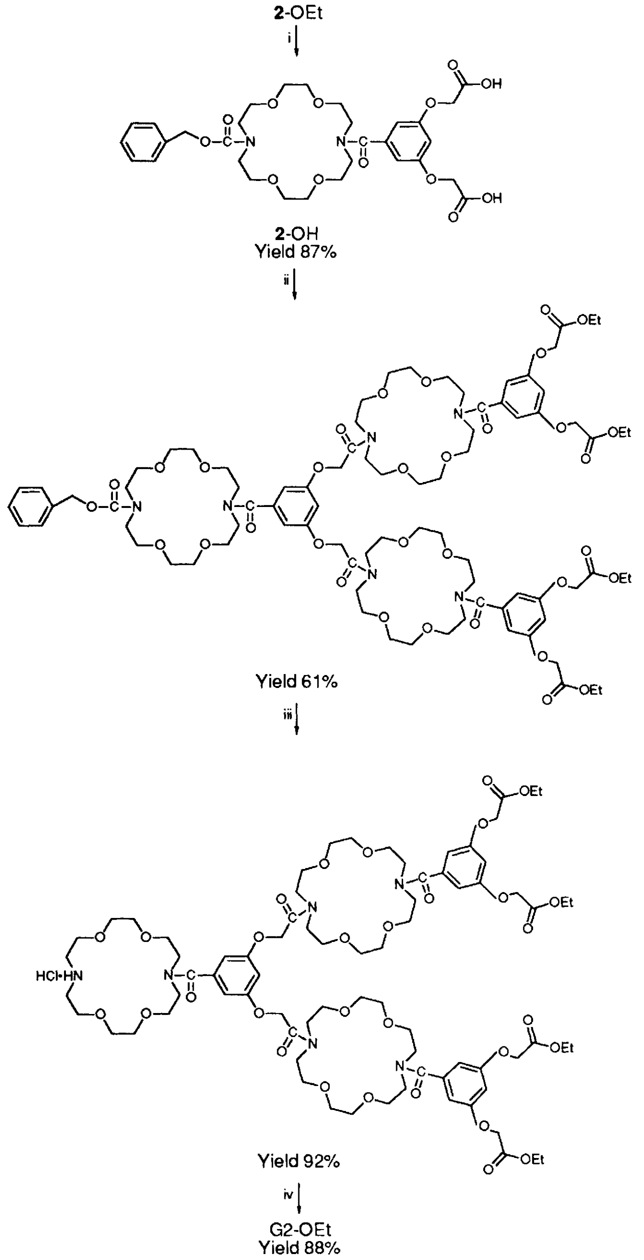
In order to use the convergent method we first synthesized branches (Scheme 3). Compound **2**-OEt was hydrolysed to **2**-OH, which was treated with **1**-OEt using pivaloyl chloride and triethylamine. As expected, the nucleophilic reaction with the carbonyl group near **2** occurred preferentially and Bu^{t}CO-**1**-OEt was not detected in the product mixture. The product was treated with trichloroformyl mesitylene (as a core) to give a 'crowned' arborol G2-OEt with two crowned



Scheme 1 *Reagents*: i, 3,5-diacetoxybenzoyl chloride, NEt_3 in benzene; ii, NaOH in aq. MeOH; iii, $BrCH_2CO_2Et$, K_2CO_3 in acetone; iv, H_2 and HCl·dioxane on Pd/C in EtOH



Scheme 2 *Reagents*: i, **1**-OEt, NEt$_3$ in THF; ii, NaOH in aq. MeOH; iii, **1**-OEt, Bu^{t}COCl, NEt$_3$ in THF



Scheme 3 *Reagents*: i, NaOH in aq. MeOH; ii, **1**-OEt, Bu^tCOCl, NEt_3 in THF; iii, H_2 and HCl·dioxane on Pd/C in EtOH; iv, trichloroformyl mesitylene, NEt_3 in THF

generations. G2-OEt (colourless oil) was identified on the basis of IR, NMR and mass spectral evidence and elemental analysis. The reactions illustrated in Scheme 3 occurred smoothly in moderate yields, with no solubility problem. The results indicate the superiority of the convergent method over the divergent method for the present purpose. We believe that by repeated use of the convergent method we can synthesize 'crowned' arborols of higher generation number.

The physical properties of G1-OEt and G2-OEt are now under intensive investigations. Of particular interest are (*i*) the selectivity towards alkali metal ions, (*ii*) the allosteric effect in the metal-binding process and (*iii*) the conformational change induced by the metal-binding event and the polyelectrolyte-like behaviour of the resultant metal complexes.

Received, 15th January 1992; Com. 2/00234E

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