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Preparation of novel polythioether dendrons on a solid support†

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A synthetic scheme for the solid-phase synthesis of unprecedented polythioether dendrons has been established, the dendrons prepared up to the fourth generation, and the applicability of the dendronized resins for supported catalysis has been demonstrated.

Of the various dendritic systems prepared during the past two decades,[1] many are based on heteroatom-containing functional groups (*i.e.* amines, amides, ethers) as connectors between the monomers. Although sulfur-based functional groups are abundantly represented in organic compounds, the only known example of a dendritic molecule with sulfur-derived connecting units is that of a poly(*m*-phenylene sulfide) dendron prepared by Gingras.[2] Molecules combining dendritic architecture and low-valent sulfur, motifs highly popular in nanochemistry, may be useful for various applications in this rapidly evolving field.[3]

While most of the dendritic systems are prepared in solution, solid-phase synthesis of a number of dendritic molecules has been reported, mainly over the last five years.[4] The number of types of supported dendrons is limited and includes polyphenylacetylenes, polyethers, polyureas and a number of polyamides (*e.g.* polylysine, polyamidoamine).[5–8] Recently, we developed a novel synthetic route to the solid phase synthesis of poly(aryl benzyl)ether dendrons.[9] Herein we report the efficient synthesis of their sulfur analogues, poly(aryl benzyl)thioether dendrons, **G*n*(X)**, on a solid support (Fig. 1).

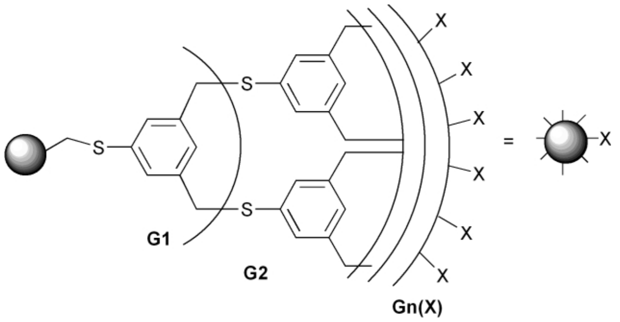
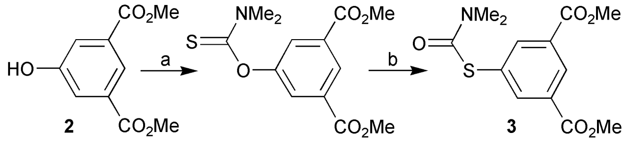
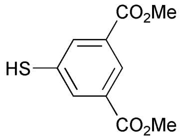


Fig. 1 Polythioether dendrons on a solid support.



Scheme 1 *Reagents and conditions:* a) DABCO, dimethylthiocarbamoyl chloride, DMA, 75 °C. b) 280 °C, 10 min.



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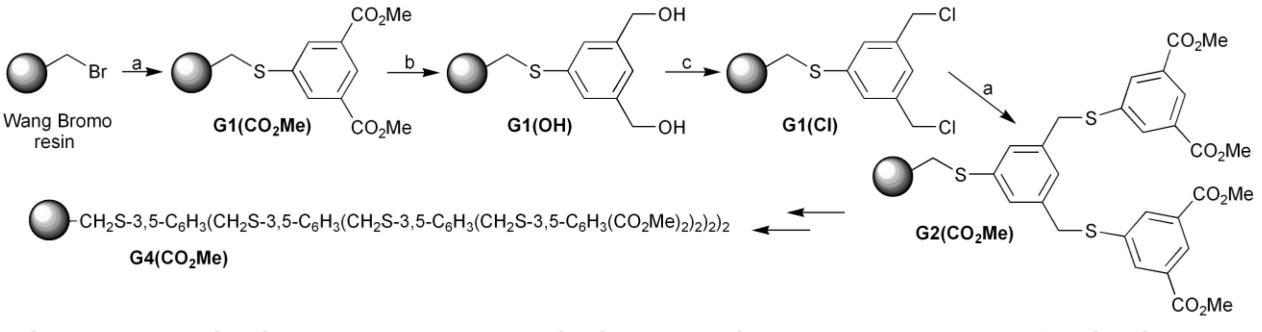
The relevant monomer **1** is not commercially available and its synthesis has never been reported. Thus, the synthetic procedure for the synthesis of **1** (or its synthone) had to be developed. Luckily, the commercially available 5-hydroxy isophthalate diester **2** (the monomer that we used for the preparation of the polyether dendrons) can easily be converted into **3**, the dimethylcarbamoyl derivate of **1**, *via* the Newman–Kwart rearrangement (Scheme 1).[10,11] The procedure is high-yielding and can be performed on a multigram scale. Compound **3** can be converted to **1** *via* methanolysis. However, the following purification is difficult due to the strong propensity of **1** to undergo oxidation. Fortunately, we discovered that **3** could be used in the relevant dendron-building procedures, forming **1** *in situ*.

The synthetic procedure is based on benzyl halide substitution by **1**, formed *in situ*, reduction of the esters and chlorodehydroxylation of the formed alcohols (Scheme 2). Thus, in three steps, the benzyl halide is reformed as the terminal function and the next generation of the dendron can be assembled. The synthesis, performed on Wang Bromo resin, yielded, in 10 steps, 42% of the fourth generation ester-terminated dendron. The synthesis was monitored, and the products characterized, using gel-phase ^{13}C NMR as well as acidolytic cleavage, followed by ^{1}H and ^{13}C NMR and mass spectrometry. Surprisingly, the cleavage always occurred between the resin and the Wang linker and not between the linker and the dendron (Scheme 3). Thus, a *p*-hydroxybenzyl-protected version of the dendron was always released from the resin. While the linker/protecting group is clearly visible in the



Scheme 2 *Reagents and conditions:* a) **3**, NaOMe 0.5 M in methanol, DMF, 70 °C. b) LiBH$_4$, B(OMe)$_3$, THF, 67 °C. c) C$_2$Cl$_6$, PPh$_3$, THF, r.t.

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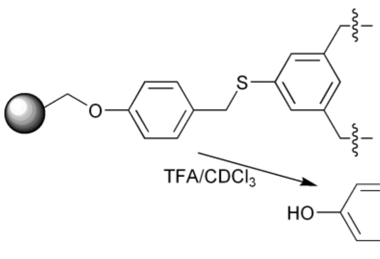
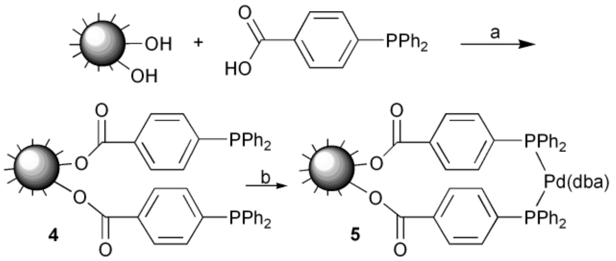
† Electronic supplementary information (ESI) available: procedures for the preparation of monomer **3**, resins **G1**–**G4**, **4**–**8**, and relevant characterisation data. See http://www.rsc.org/suppdata/cc/b3/b302324a/

DOI: 10.1039/b302324a



Scheme 3 Cleavage of the dendrons from the support.

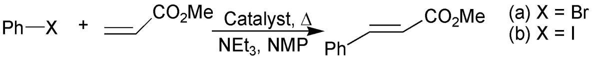


Scheme 4 *Reagents and conditions:* a) *N*,*N′*-diisopropylcarbodiimide, DMAP, DMF. b) Pd(dba)$_2$, THF, r.t.

^{1}H and ^{13}C NMR spectra, it is cleaved under the CI-MS conditions and disulfide-bridged dendron dimers are observed in the MS spectra.

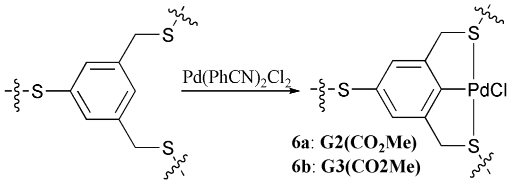
The aforementioned ^{1}H NMR measurements demonstrated excellent conversion and purity of each of the three repetitive steps as the following characteristic changes. Immobilization of **1** is accompanied by complete disappearance of the $–CH_2Cl$ signal (4.51 ppm) and appearance of the lowfield aromatic signals (8.46 and 8.14 ppm). Reduction results in complete disappearance of the signals of the isophthalate diester along with the appearance of $–CH_2OH/–CH_2OCOCF_3$ peaks (4.81 and 5.35 ppm respectively). The latter are cleanly replaced by the $–CH_2Cl$ signal upon chlorodehydroxylation.

Potential catalytic uses of the novel dendron constructs were demonstrated.[12] Thus, the third-generation OH-terminated dendron was esterified with 4-(diphenylphosphino)benzoic acid and the formed phosphine-terminated resin, **4**, was complexed with Pd(0) using a Pd(dba)$_2$ precursor (Scheme 4).[13,14] The polystyrene/polythioether dendron/Pd(0)–phosphine complex construct, **5**, was tested as a catalyst in the Heck reaction of bromobenzene and methyl acrylate (eqn. 1a). Although low-valent sulfur-containing molecules, are frequently reported as catalytic poisons, this was not the case with the thioether dendron-based catalyst and respectable activity was observed (89% yield after 14 h at 120 °C with 2.5% Pd).



(1)

Moreover, we discovered that, for iodobenzenes as substrates in the Heck reaction, there is no need for phosphines on the dendron. In fact, each isophthalate-derived unit in the interior of the dendron can serve as a precursor to the pincer complex of the SCS monoanionic tridentate ligand (Scheme 5).[3,15,16] Homogeneous catalysis with Pd complexes of such ligands has recently been reported.[16] Incubation of second- and third-generation dendritic resins, with Pd(PhCN)$_2$Cl$_2$ in THF at 70 °C, formed deep red resins **6**. Although severe broadening of signals, both in gel-phase ^{13}C NMR of the resins and ^{1}H NMR of the cleavage solutions, prevented characterization of the formed complexes, we have been able to characterize **8**, the pincer-type Pd complex of a supported non-dendritic model SCS ligand **7** (Scheme 6). Preliminary experiments demonstrated that resins **6** and **8** are efficient and recyclable catalysts for the Heck reaction of iodobenzene and methyl acrylate (eqn. 1b).[17]



Scheme 5 Metallation of the dendron units.

In conclusion, we developed a practical and efficient route to novel polythioether dendrons on solid support and demonstrated their potential use for supported catalysis. It is likely that, due to their unique structure, these compounds will be applied in other fields of material sciences as well.

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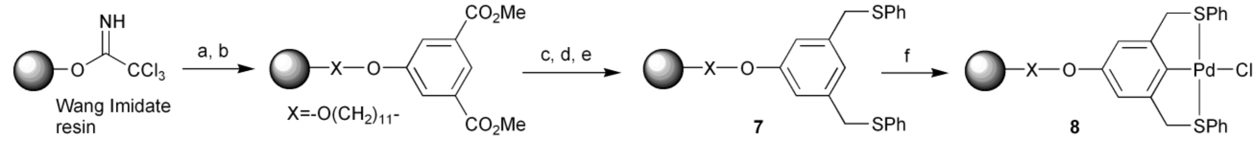
17 For instance, with **6a**, 2.5% Pd: 1st cycle 100% yield, 2nd cycle 98% yield.



Scheme 6 *Reagents and conditions:* a) 11-bromoundecan-1-ol, BF$_3$·OEt$_2$, DCM, cyclohexane, r.t. b) Dimethyl 5-hydroxyisophthalate, LiH, DMF, 60 °C. (c) LiBH$_4$, B(OMe)$_3$, THF, 67 °C. d) C$_2$Cl$_6$, PPh$_3$, THF, r.t. e) HSPh, Cs$_2$CO$_3$, DMF, 70 °C. f) Pd(PhCN)$_2$Cl$_2$, THF, 67 °C.

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