

Evaluation of routes to chiral core dendrimers

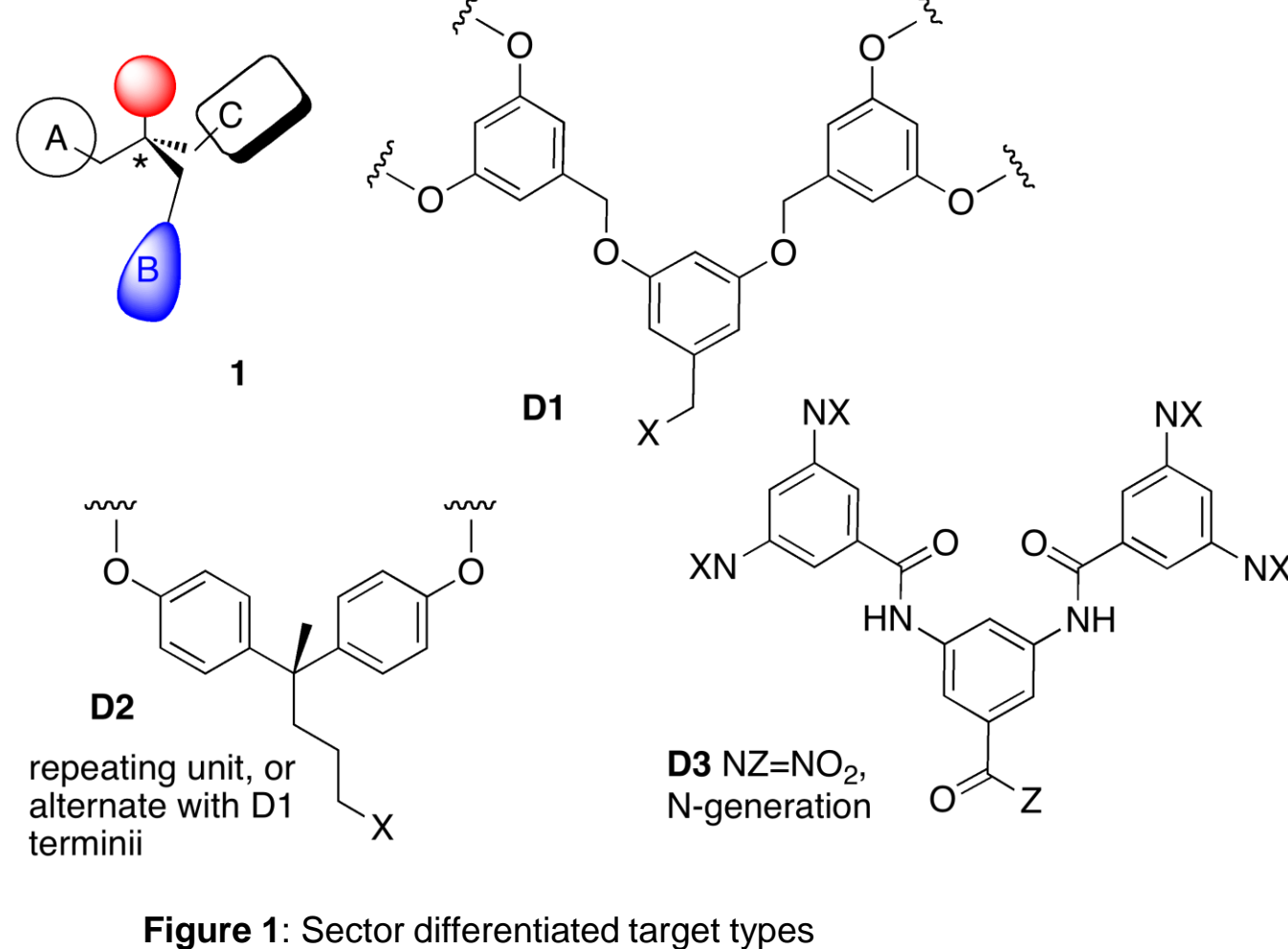
Rami Y. Morjan,² Adil A. Gobouri,¹ Stephen S. Barasa¹ and John. M. Gardiner¹

¹School of Chemistry and Manchester Interdisciplinary Biocentre, University of Manchester, Manchester, M1 7DN and ²Department of Chemistry, Islamic University of Gaza

1. Introduction and Aims

Dendrimers are macromolecules with a highly branched three-dimensional shape, produced in an iterative sequence of reaction steps, in which each reaction results in a new generation. Dendrimers have stimulated wide interest in the field of chemistry and biology, particularly with respect to applications to drug delivery and more recently imaging. They have also been of growing interest as macromolecular hosts, potential catalysts and have been attached to surfaces and polymeric materials, and have significant potential in new materials development. Dendrimers can have comparable molecular dimensions to some proteins and could potentially have internal microenvironments akin to the active site of an enzyme. Encapsulation within dendrimers has significant potential biomedical applications, whilst dendrimer surface behavior is of interest to evaluate interactions of dendrimer surface functionality (its most accessible region) with biological molecules. *Exploiting many of these areas are dependent on generating chirality in dendrimers.*

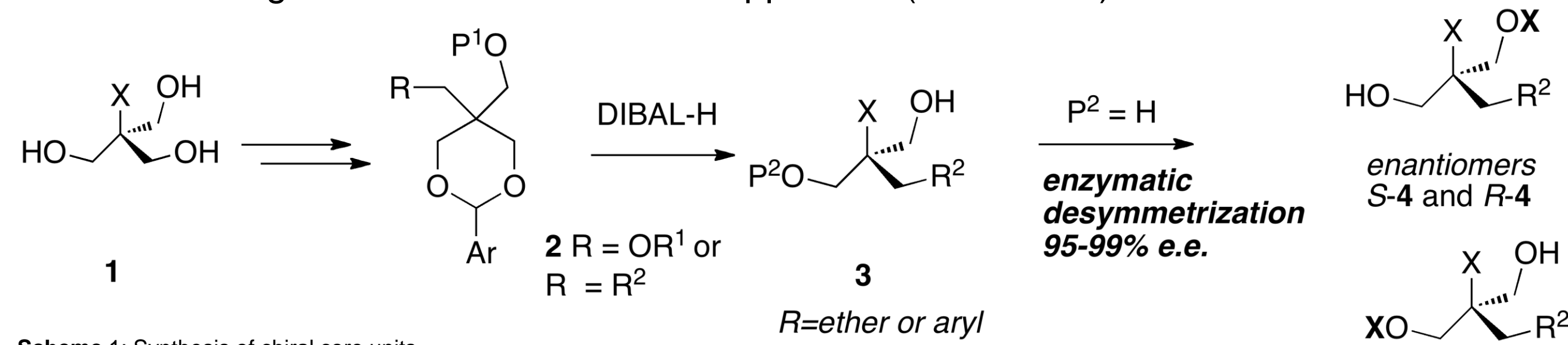
This poster describes work in two areas targeting chiral dendritic materials.¹ The first of these involves targeting new dendrimers with chirality resulting purely from differentiated dendrons represented by model 1 (Fig.1), aimed at developing new dendrimer surface/chiral nanotopology, and also bifunctional chiral materials. This involved preparing a set of dendrons D1-D3 (various generations, up to G3) suitable for a convergent assembly to core systems. The second area involved generating a matrix of new axially chiral dendrimers (section 3).



2. Chiral Dendron-differentiated targets

2.1 Synthesis of the core unit

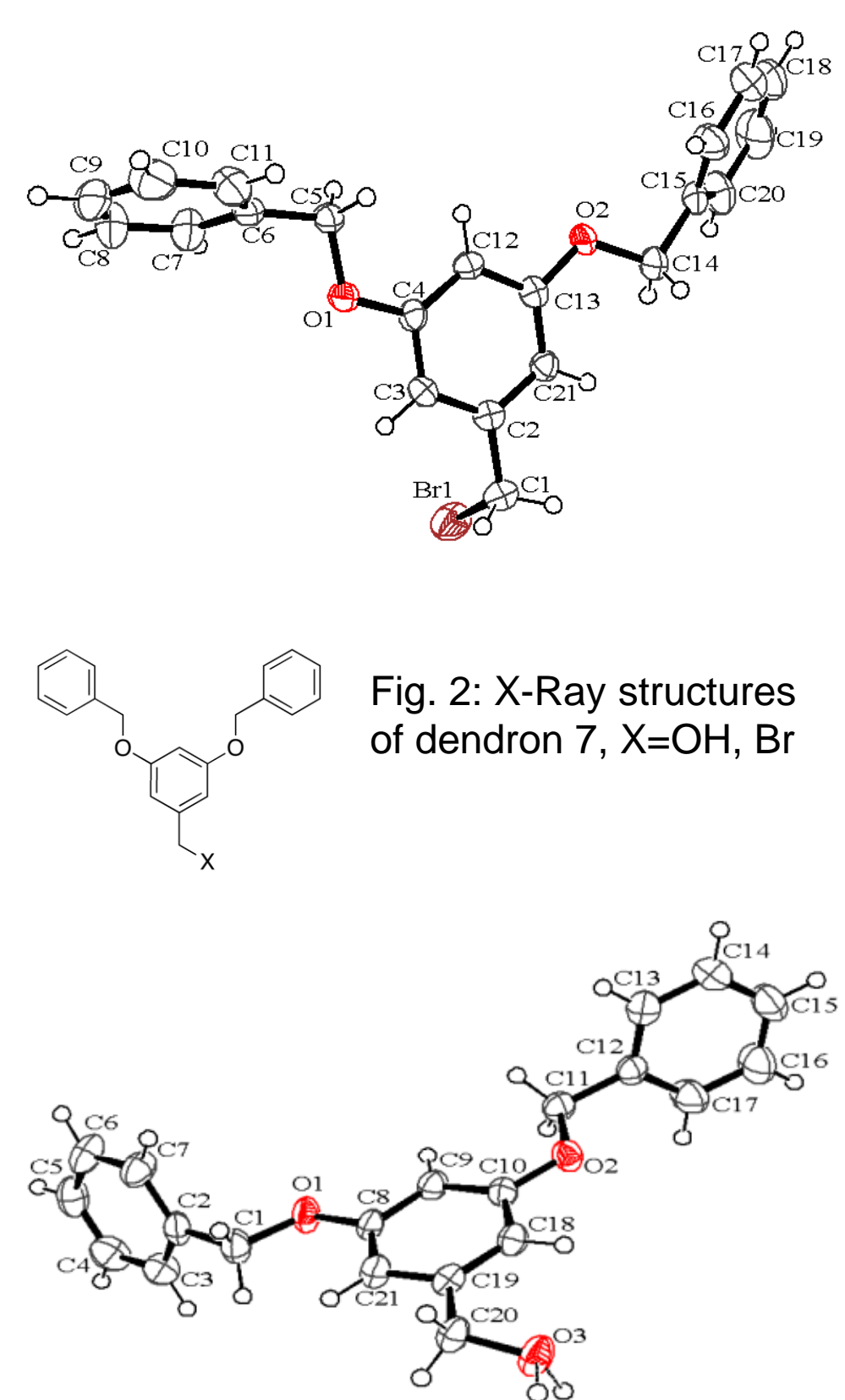
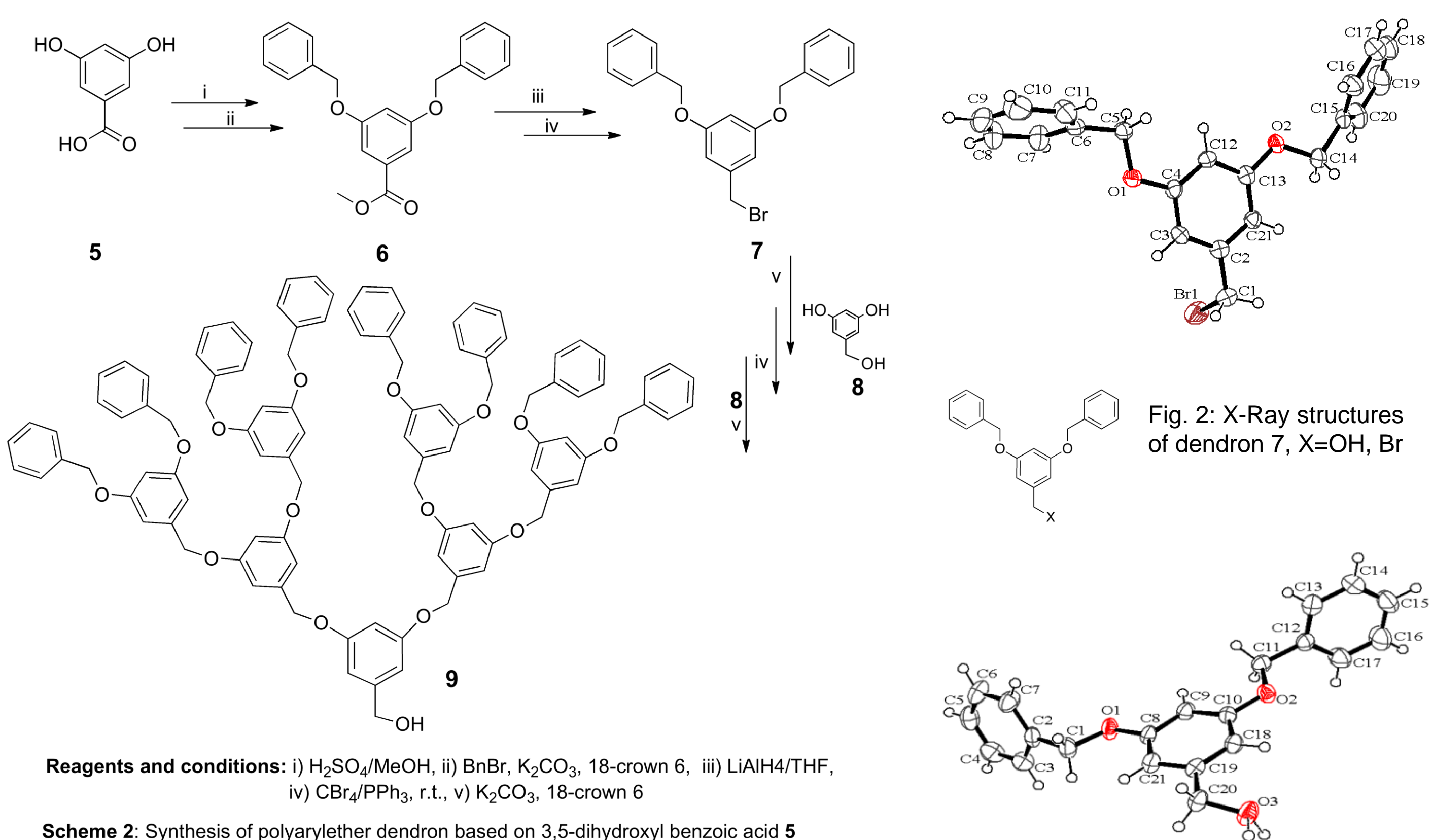
The main requirements of the synthesis of the first core are to build the differentiated scaffold in as few steps as possible. Simple starting materials and short synthesis will then make possible both the first synthesis of dendron-differentiated chiral dendrimers, and make it viable to prepare diversities of such structures. 1,1,1-Trihydroxymethylethane and 1,1,1-trihydroxynitroethane (R = Me or NO₂) were chosen as starting materials to illustrate the approach. (Scheme 1)



By proceeding via the acetals 2 a route to orthogonally protected cores was developed, with two noteworthy aspects. Firstly, we were able to diverge to both O- and C-linked branching in 2 from a common acetal derivative of 1 (ie through to the R group) and whilst illustrating dendron attachments via the racemate 3, we also identified a highly efficient enzymatic desymmetrization to generate the differentiated optically enriched cores 4. The notional symmetry of the diol/triol core is also differentiatable by attachment of different dendrons.

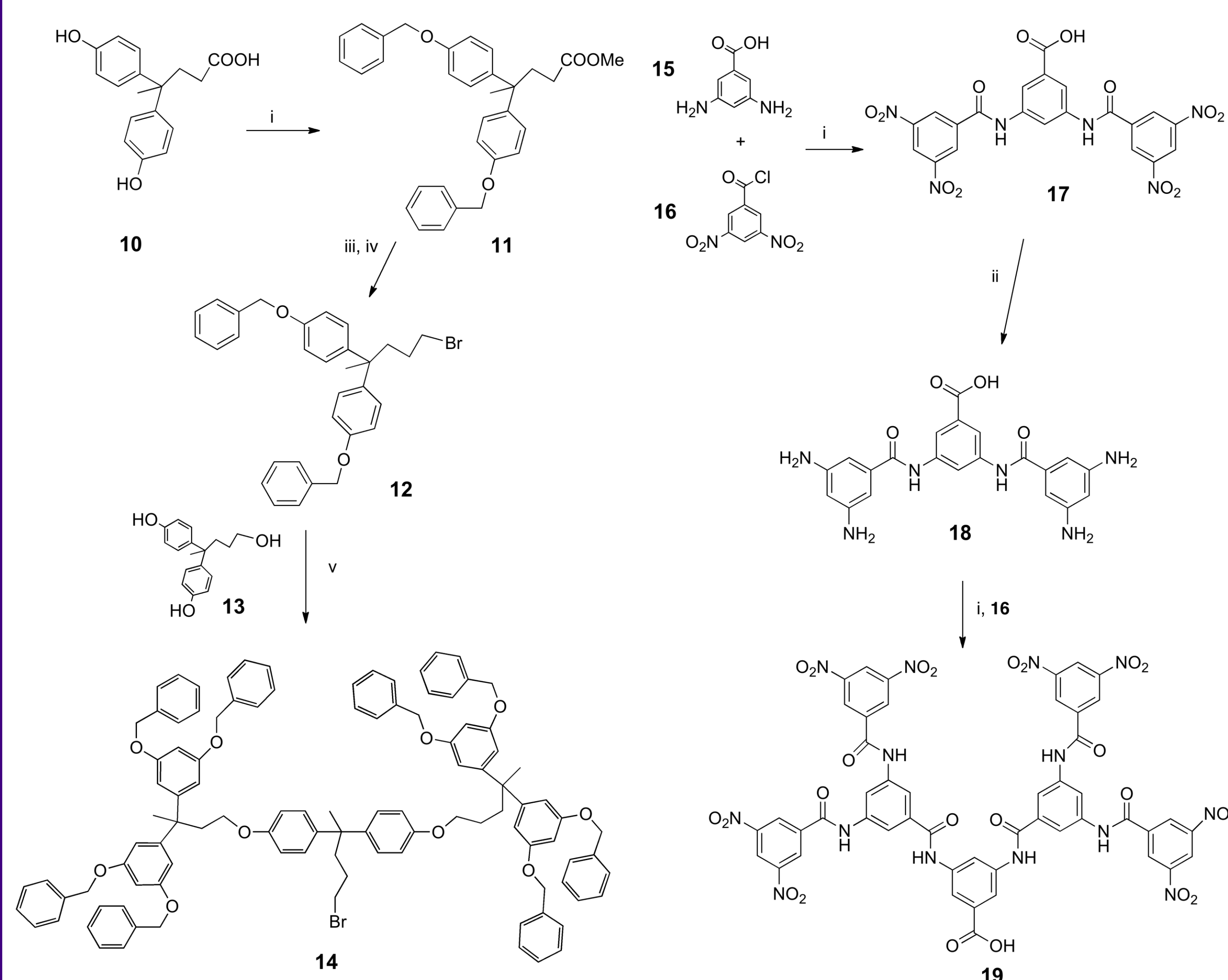
2.2 Synthesis of dendrimer fragments (dendrons)

The second stage of this project involved the synthesis of different dendrimer fragments to be attached to the core. As this work aimed to target a new example of chiral dendrimers of this type i.e. different types of dendrimer arms attached to core unit (previous researchers have used different generation numbers from the same dendron type, specifically Meijer's seminal work²), it was necessary to demonstrate synthesis of different dendrons with different generation numbers which then would be attached to the core. In order to achieve the target chiral dendrimer, up to three different dendrons were required. Two of them (Fréchet-type) with some modifications were synthesized via the convergent method (Schemes 2 and 3).



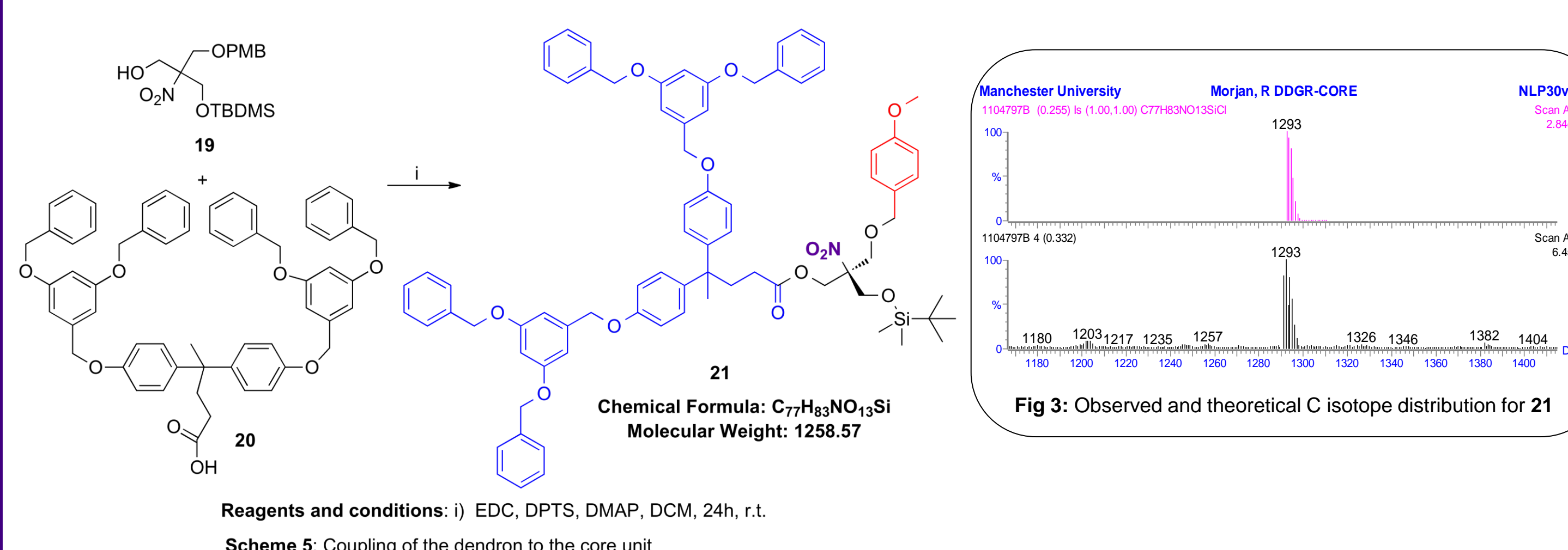
The hydroxyl-bearing dendron 9 (Scheme 2) was also iterated further to the relevant bromide. The dendron 14 was selected to offer a sufficiently differentiated backbone from the polyaryl ethers of Scheme 2.

Alongside these, we also wanted to have available at least one dendron with a non-aryl ether backbone. To this end a divergent method was utilized to prepare a third dendron type, eg 19 (Scheme 4) with a polyamido backbone.



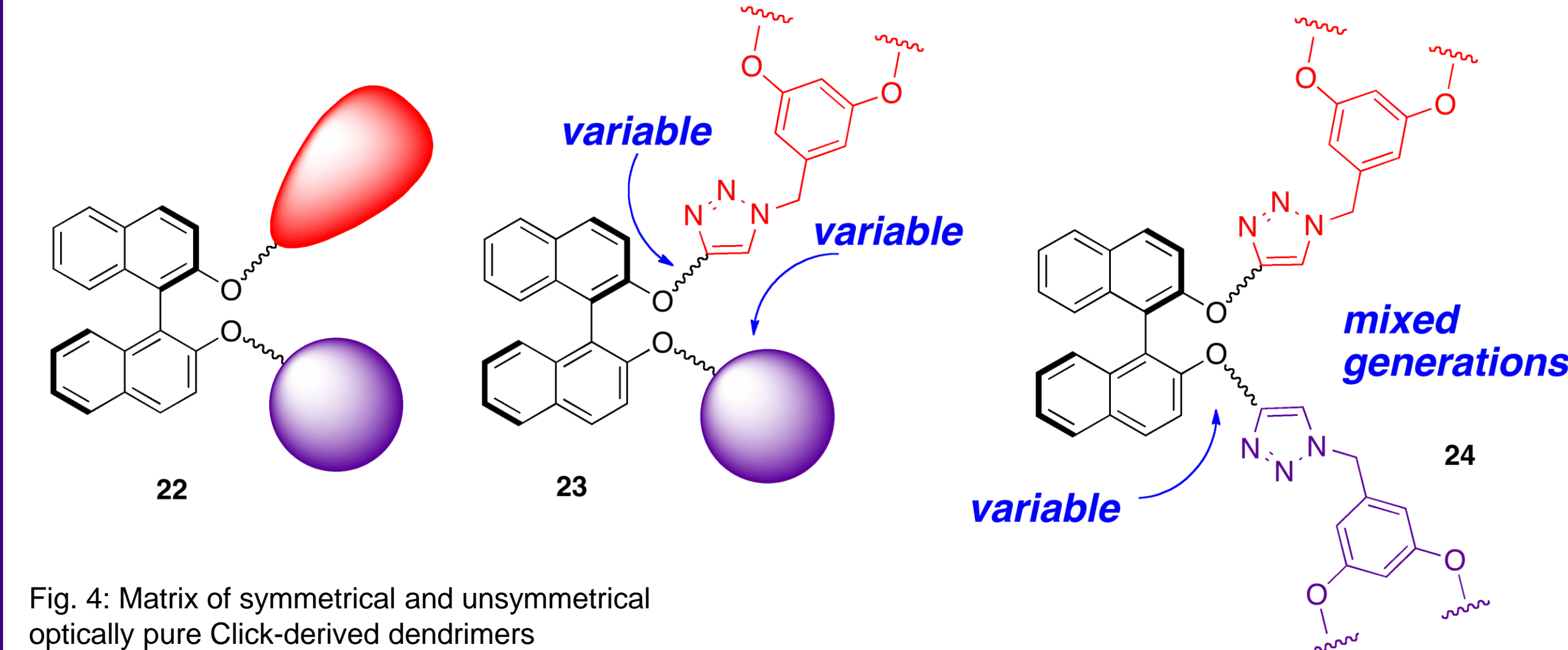
2.3 Attachment of dendrons to a core unit

The final stage of the first part of this project was to attach different dendrons to the core unit to generate the chiral dendrimer. A specific example is shown in (Scheme 5) and the MS data analysis for the coupled dendron-core are shown in Fig 3, for introduction of one



3. Axially chiral dendrimers via Click chemistry

Since the first example of Click chemistry applied to dendrimers,³ this is an area that has attracted growing interest. Additionally, from the original extensive studies of Meijer's lab, BINOL-cored dendrimers have shown great potential.^{4,5} We have used Click chemistry to prepare a matrix of different symmetrical and unsymmetrical chiral BINOL-based dendrimers 22. This matrix allows a definitive correlation of the effects of symmetry due to different types of dendrons (ie. 23) or generational variations (eg 24), and changes in linker chemistry to changes in specific and molar rotations, with molar rotations up to +750 (R) or -750 (S) for some dendrimers of type 23.



Acknowledgements

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