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Synthetic studies on tetraphenylmethane dendrimers

Saumitra Sengupta * and Subir K. Sadhukhan

Department of Chemistry, Jadavpur University, Calcutta 700 032, India

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Abstract

A convergent synthesis of a first generation centrally tetrahedral phenyl cinnamate dendrimer and related dendrons using a multifold Heck reaction strategy is described. © 1999 Published by Elsevier Science Ltd. All rights reserved.

There is a considerable current interest in the synthesis of centrally tetrahedral molecular architectures due to their potential applications in different spheres of material science.¹⁻⁵ Such molecules, for example, can be used as moleculer caltrops in scanning probe microscopy as shown with nanometric tripodaphyrins based on a tetraphenyl methane (TPM) core^{1a,b} or as new molecular electronic devices, as demonstrated with TPM based spiro-fused conjugated oligomers.² Tetraphenyl methane based cobalt clusters containing up to 40 cobalt atoms have recently been prepared in the search of new materials.³ It has also been shown that moleculer morphology can be precisely controlled with centrally tetrahedral conjugated hydrocarbons, especially with tetra-stilbenoid methane derivatives.⁴ On the other hand, a number of tetraphenylmethane derivatives, owing to their rigid tetrahedral framework which precludes intramoleculer interactions between their chromophores, have given rise to supramoleculer assemblies through intermoleculer non-covalent interactions.⁶ We envisaged that dendritic architectures comprised of centrally tetrahedral repeating units may also lead to interesting morphology and physicochemical properties and initiated a program on the synthesis of some centrally tetrahedral dendrimers 1a-c based on a tetraphenylmethane (TPM) core. Although, in recent years, great strides have been made towards synthesis of various types of dendrimers,⁷ there are no reports on genuine dendrimers that are based on a fully substituted centrally tetrahedral core. In this communication, we now report our preliminary results on the synthesis of a first generation TPM-based phenyl cinnamate dendrimer 1a.G₁ and in addition, present a facile synthetic approach towards TPM-based dendrons for utilization in higher generation dendrimer synthesis.

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^{*} Corresponding author. Fax: 91 33 4734266



The TPM-based cinnamate dendrimer $1a.G_1$ was synthesized in a convergent approach via a fourfold Heck reaction of tetra(*p*-iodophenyl)methane $(2a)^{5c}$ with the *p*-tritylphenyl acrylate wedge 3 (4.5 equiv.), the latter being readily prepared from *p*-trityl phenol and acryloyl chloride (Scheme 1). The best results were obtained under Jeffery's phase transfer conditions (Pd(OAc)₂, Bu₄NCl, NaHCO₃, DMF, 80°C)⁸ which gave $1a.G_1$ in 50% yield after column chromatography over silica gel (5–20% EtOAc in pet. ether)



Scheme 1. (i) **2a**, **3** (4.5 equiv.), 30% Pd(OAc)₂, Bu₄NCl, NaHCO₃, DMF, 80°C (50%); (ii) **2b**, **3** (4 equiv.), 20% Pd(OAc)₂, EtOH, 80°C (20%)



Scheme 2. (i) NaNO₂, H₂SO₄, 0°C then KI, H₂O, 80°C; (ii) conc. H₂SO₄, phenol; (iii) **3** (4 equiv.), 30% Pd(OAc)₂, Bu₄NCl, NaHCO₃, DMF, 80°C; (iv) CH₂=CHCOCl, Et₃N, CH₂Cl₂; (v) styrene (5 equiv.), 25% Pd(OAc)₂, Bu₄NCl, K₂CO₃, DMF, 80°C; (vi) RC=CH (5 equiv.), 25% PdCl₂(PPh₃)₂, Et₃N, CuI, DMF, rt; (vii) K₂CO₃, MeOH, rt

(R_f 0.4, 15% EtOAc in pet. ether).⁹ Poor conversions (<10%) were obtained under traditional Heck reaction conditions (Pd(OAc)₂, Et₃N with or without added P(o-Tol)₃) even after prolonged reactions. In view of the superior Heck-reactivity of arenediazonium salts over iodoarenes,¹⁰ the fourfold Heck reaction of the octazonium salt **2b**^{5d} with **3** (4.5 equiv.) was also studied (20% Pd(OAc)₂, EtOH, 80°C)^{5d} which, however, gave only poor yields of **1a.G**₁ (20%; 42% based on recovered **3**), presumably due to the limited solubilities of both the starting materials and the product in EtOH. Compound **1a.G**₁ was fully characterized by its ¹H and ¹³C NMR spectra. Further confirmation of its structure came from its FAB-MS data which showed the M⁺-1 ion at m/z 1871.⁹

We next turned our attention towards synthesis of phenyl cinnamate dendrons for use in the convergent assembly of higher generation cinnamate dendrimers 1a. For this, our primary goal was to synthesize an appropriate TPM-based AB₃ tecton. Towards this goal, New Fuchsin (4) was converted via conventional hexazotization and a threefold Sandmeyer reaction to the tri(iodoaryl)carbinol 5 in 40% overall yield (Scheme 2). Friedel–Crafts reaction of phenol with 5, under H₂SO₄ catalysis, then gave the *p*-(tri-iodotrityl)phenol derivative 6 (85%),⁹ our desired AB₃ tecton. A threefold Heck reaction of 6 with the acrylate wedge 3 (3.5 equiv.), again under Jeffery's phase transfer conditions, produced the key phenol 7 (42%)⁹ after silica gel chromatography (5–25% EtOAc in pet. ether) (R_f 0.3, 20% EtOAc in pet. Ether) and the latter upon acylation with acryloyl chloride then gave the second generation phenyl cinnamate dendron 8 in 80% yield.

The AB₃ tecton **6** also appeared to be ideally suited for the synthesis of other TPM-based dendrons that may be used towards convergent assembly of the conjugated dendrimers **1b**,**c**. Thus, it was envisaged

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that threefold Pd-catalyzed couplings of **6** with TPM-based styryl or acetylenic wedges, conversion of the resultant phenol to a triflate followed by fourfold coupling of the latter with tetra(*p*-styryl)methane⁵^c or tetra(*p*-ethynylphenyl) methane^{1b} would lead to the dendrimers **1b**, **c**. Moreover, such tripodal triflates appeared to be potentially useful in the synthesis of carbon-centered moleculer caltrops.^{1c} In view of such promises, we carried out some model studies on threefold Pd-catalyzed couplings of **6**. Thus, a threefold Heck reaction of **6** with styrene gave rise to the tristilbenoid dendron **9** in 75% yield whereas Sonogashira-couplings of **6** with phenylacetylene and trimethylsilyl-acetylene led to the linear conjugated TPM dendrons **10a**,**b** in somewhat moderate yields (Scheme 2). The tris-trimethysilylethynyl adduct **10b** was subsequently desilylated with K₂CO₃ in MeOH to give the highly useful AB₃ tecton **10c** in 54% yield.

In summary, we have synthesized the first generation of a centrally tetrahedral phenyl cinnamate dendrimer using a fourfold Heck reaction strategy. A short synthetic sequence leading to higher generation TPM-based cinnamate, stilbene and tolan dendrons have also been developed starting from a cheap dyestuff material. Convergent assembly of these dendrons with appropriate central cores towards synthesis of higher generation TPM dendrimers 1a-c is currently under investigation.

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- 9. Compound **1a.G**₁: FAB-MS: *m/z* 1871 (M⁺-1); ¹H NMR (300 MHz, CDCl₃): 6.59 (d, 4H, J=16 Hz), 7.06 (d, 8H, J=8.8 Hz), 7.16–7.31 (76H, m), 7.48–7.53 (8H, m), 7.82 (d, 4H, J=16 Hz); ¹³C NMR (75 MHz, CDCl₃): 64.7, 68.2, 117.9, 120.3, 126.0, 127.5, 127.9, 131.1, 131.3, 132.1, 132.6, 144.3, 145.5, 146.6, 148.1, 148.8, 165.1. Compound **6**: ¹H NMR (300 MHz, CDCl₃): 2.33 (s, 9H), 6.65 (dd, 3H, J=8.4, 2.4 Hz), 6.70 (d, 2H, J=6.6 Hz), 6.99 (d, 2H, J=6.6 Hz), 7.02 (d, 3H, J=2.1 Hz), 7.65 (d, 3H, J=8.4 Hz); ¹³C NMR (75 MHz, CDCl₃): 28.2, 63.3, 98.7, 114.5, 130.1, 131.9, 137.8, 138.0, 140.5, 146.5, 153.6. Compound **7**: ¹H NMR (500 MHz, CDCl₃): 2.44 (s, 9H), 6.58 (d, 3H, J=15.8 Hz), 6.81 (d, 2H, J=8.7 Hz), 7.11–7.33 (65H, m), 7.59 (d, 3H, J=8.5 Hz), 8.16 (d, 3H, J=15.8 Hz); ¹³C NMR (75 MHz, CDCl₃): 20.2, 64.1, 64.6,

114.6, 118.1, 120.3, 126.0, 127.5, 129.1, 131.1, 132.1, 133.0, 137.3, 143.6, 144.2, 146.6, 148.7, 153.9, 165.4. Compound **9**: ¹H NMR (300 MHz, CDCl₃): 2.35 (s, 9H), 6.73 (d, 2H, J=8.7 Hz), 7.00 (d, 3H, J=16.2 Hz), 7.05–7.11 (m, 6H), 7.14 (d, 2H, J=8.7 Hz), 7.20–7.31 (m, 6H), 7.34 (d, 3H, J=5.4 Hz), 7.35 (d, 3H, J=15 Hz), 7.45–7.54 (m, 9H); ¹³C NMR (75 MHz, CDCl₃): 20.2, 63.7, 114.3, 124.4, 126.1, 126.5, 127.4, 128.6, 129.1, 129.7, 132.2, 132.7, 133.7, 134.7, 137.8, 139.2, 146.3, 153.4. Compound **10**c: ¹H NMR (300 MHz, CDCl₃): 2.35 (s, 9H), 3.26 (s, 3H), 6.70 (d, 2H, J=8.7 Hz), 6.93 (d, 3H, J=8.0 Hz), 7.00 (d, 2H, J=8.5 Hz), 7.01 (s, 3H), 7.33 (d, 3H, J=8.1 Hz); ¹³C NMR (75 MHz, CDCl₃): 20.9, 64.0, 80.9, 82.3, 114.5, 119.6, 128.3, 131.7, 132.1, 138.0, 139.9, 147.0, 153.7.

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