



## Short communication

# Synthesis and antioxidant properties of enone core based dendrimers with carbazole as surface group

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## ABSTRACT

Synthesis of enone core based dendrimers with carbazole as surface group has been achieved. All the synthesized dendrimers showed excellent antioxidant behavior with commercially available 1,1-diphenyl-2-picryl hydrazyl (DPPH).

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## 1. Introduction

Dendrimers are monodisperse macromolecules possessing well-defined branched structure that can be precisely tailored into discrete and designated functionality to create multifunctional materials. Dendrimers are also often referred to as artificial proteins [1]. The size, shape, branching length and density and their surface functionality of dendrimers make them as ideal carriers in biomedical applications such as drug delivery [2], gene transfection [3], and imaging [4] and as catalyst in homogeneous as well as heterogeneous medium [5]. Some of the surface modified dendrimers themselves may act as nano-drugs [6,7] against cancer, tumors, bacteria and viruses. Recent successes in simplifying and optimizing the synthesis of dendrimers such as 'lego' [8] and 'click' [9] techniques, provide a large variety of structural variation while at the same time reducing the cost of their production. The surface of dendrimers provides as excellent platform for drug delivery. Very recently, PAMAM dendrimers have been successfully used as carriers of boron isotopes in boron neutron-capture treatment of cancer tumors [10] and in nonsteroidal anti-inflammatory drugs [11]. Hybrid dendrimers such as glycodendrimers exhibits potential

application in medicinal field [12,13]. Synthesis of permanent fluorescence sensing hyper branched dendritic architecture [14] as well as bactericidal efficacy of novel dendrimers [15] and axially chiral enantiopure dendrimers [16] has been reported from our laboratory recently. Very recently the bio and pharmaceutical application of the dendrimers are well-defined in the literature [17–19]. The enone nucleus is present in various natural products [20] and known to be a very important organic residue in many potentially bioactive compounds [21]. However the synthesis and biological activity of hexanone core based bioactive carbazole [22] hyper branched dendritic architecture are yet to be investigated. To the best of our knowledge the antioxidant study of the carbazole based dendrimer is still a rare observation. Therefore, we report herein for the first time the synthesis of hexanone core based dendritic architecture **1a**, **1b**, **1c** and **1d** with carbazole as surface group and their antioxidant activity tested with commercially available DPPH.

## 2. Chemistry

Synthesis of bioactive enone based dendrimers (**1a–d**) up to third generation was achieved by simple *O*-alkylation method using convergent synthetic route which include LAH reduction, benzylic chlorination and NBS bromination starting from a bioactive carbazole moiety scheme (**1–4**). 2.1 Equiv. of dendritic bromide **3**,

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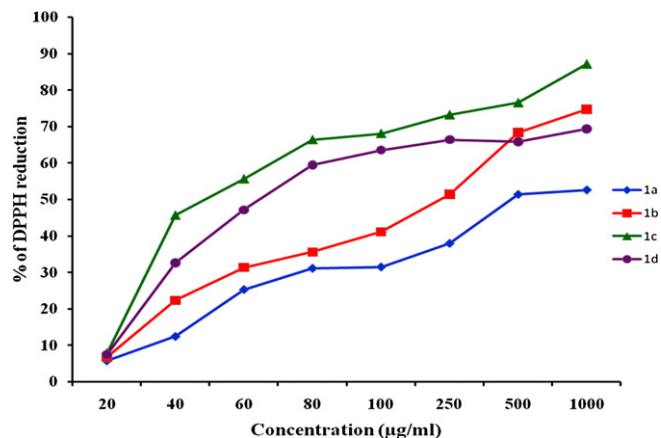


Fig. 1. DPPH scavenging activity spectrophotometric assay of various concentrations of the dendrimers **1a**, **1b**, **1c** and **1d**.

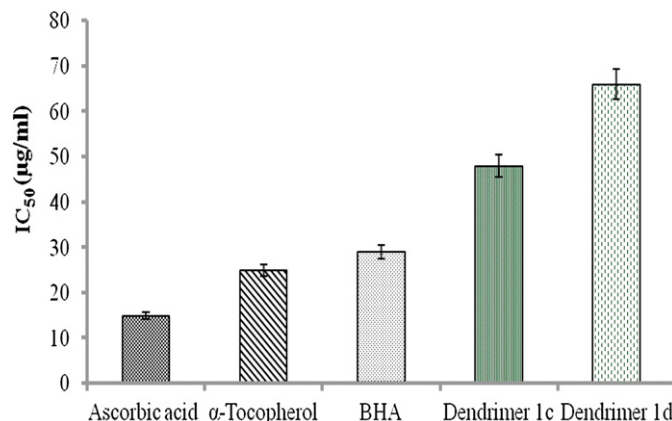


Fig. 2. DPPH scavenging capacities (IC<sub>50</sub>) of dendrimer **1c** and **1d** with standard drugs.

chlorides **7**, **10**, and **13** react with 1 equiv. of 2,6-bis(4-hydroxy benzylidene)cyclohexanone **4** in the presence of K<sub>2</sub>CO<sub>3</sub> to give the dendrimers **1a–d** in 65–80% yield and the rest of the yield contained mono alkylated product. All the new compounds gave satisfactory IR, <sup>1</sup>H and <sup>13</sup>C NMR, mass spectral and elemental analysis.

### 3. Biology

Antioxidant activity of all the dendrimers was tested by DPPH free radical scavenging activity by spectrometric assay method [23]. Samples at different concentration were prepared and tested for DPPH scavenging activity. The percentage of inhibition was calculated and the antioxidant activity of the dendrimers and standard antioxidants like Ascorbic acid, α-Tocopherol and Butylated Hydroxyanisole (BHA) were recorded and compared. The antioxidant activity and IC<sub>50</sub> value of the dendrimers with standard drugs are shown in the Figs. 1 and 2 respectively.

### 4. Results and discussion

Synthesis of dendrimers **1a–d** was achieved by simple *O*-alkylation method using convergent synthetic route starting from a bioactive carbazole moiety. Alkylation of 2,6-bis(4-hydroxy benzylidene)cyclohexanone **4** with carbazole dendritic bromide **3** in the presence of K<sub>2</sub>CO<sub>3</sub> and 18-crown-6 in DMF afforded the zeroth generation dendrimer **1a** in 80% yield. Dendritic bromide **3** was obtained in 84% yield by the radical bromination of 9-*p*-tolyl carbazole **2** which in turn was obtained by the known procedure [24] (Scheme 1).

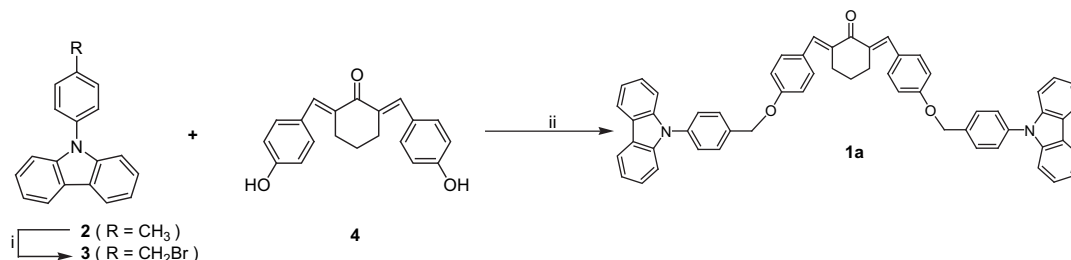
In the <sup>1</sup>H NMR spectrum, **1a** displayed a quintet at δ 1.80 and a triplet at δ 2.95 for two type of methylene protons of hexanone moiety and a sharp singlet appeared at δ 5.21 integrating for four

methylene protons in addition to the olefinic and aromatic protons and in <sup>13</sup>C NMR spectrum the two type of hexanone methylene, *O*-methylene carbons and the carbonyl carbon appeared at δ 23.1, δ 28.6, δ 69.6, and δ 190.2 respectively in addition to the olefinic and aromatic carbons. The structure of the dendrimer **1a** was further confirmed from mass spectrum and elemental analysis.

Similarly first generation dendrimer **1b** was obtained from the first generation dendritic chloride **7** [G1]-Cl. Reaction of methyl-3,5-dihydroxy benzoate with 2.1 equiv. of dendritic bromide **3** afforded methyl-carboxylate **5** in 72% yield. Reduction of **5** with lithium aluminum hydride in dry THF afforded the dendritic alcohol **6** [G1]-OH, which on further treatment with SOCl<sub>2</sub> in dry DCM at 0 °C, gave the dendritic chloride **7** [G1]-Cl in 83% yield. Reaction of 1.0 equiv. of hexanone **4** with 2.1 equiv. of the dendritic chloride **7** [G1]-Cl in dry DMF afforded the first generation dendrimer **1b** in 76% yield (Scheme 2).

In the <sup>1</sup>H NMR spectrum, dendrimer **1b** displayed two broad singlet each integrating for two and four proton at δ 1.72 and δ 2.84 for two types of methylene protons of hexanone unit and two sharp singlet at δ 5.09 and δ 5.17 each integrating for four and eight protons respectively for *O*-methylene protons in addition to the olefinic and the aromatic protons, and in <sup>13</sup>C NMR spectrum the two type of methylene carbon of hexanone and two type of *O*-methylene carbon and the carbonyl carbon appeared at δ 22.9, δ 28.5, δ 69.8, δ 70.0 and at δ 190.1 respectively in addition to the olefinic and the aromatic carbons. In the FAB – mass spectrum, the molecular ion peak appeared at *m/z* 1572 (M<sup>+</sup>) and the structure of the dendrimer **1b** was further confirmed from satisfactory elemental analysis. Application of similar sequence afforded the second generation dendrimer **1c** in 65% yield from the second generation dendritic chloride **10** [G2]-Cl (Scheme 3).

In the <sup>1</sup>H NMR spectrum of dendrimer **1c** displayed two broad singlet at δ 1.68 and δ 2.79 integrating for two and four protons for methylene protons of hexanone moiety and three sharp singlet at



Scheme 1. Reagents and Conditions: (i) NBS, BZ<sub>2</sub>O<sub>2</sub>, CCl<sub>4</sub>, reflux, 6 h, **3** (84%); (ii) K<sub>2</sub>CO<sub>3</sub>, 18-crown-6, DMF, 60 °C, 48 h, **1a** (80%).

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