

# Trisubstituted Triptycenes: Toward the Preparation of Three-Dimensional Dendrimers

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**Abstract** A synthesis of benzyl trisubstituted triptycenes is described. These triptycenes are precursors for producing a first generation ( $G_1$ ) poly(triptycylether) dendrimer, a derivative of known poly(arylether) dendrimers. The molecule necessary for the further elaboration into the eventual dendrimer is a carboxylic acid ester triptycene terminated with two ether substituents on another ring; the zero generation ( $G_0$ ). The synthesis begins with formation of the Diels-Alder adduct of benzoquinone and methyl 2-anthroate. This adduct is aromatized under basic conditions and the resulting anion trapped with a benzyl halide as an electrophile to form the trisubstituted triptycene. Access to the trisubstituted system is obtained through a highly improved, efficient and chromatography free preparation of anthracene derivatives, mainly methyl 2-anthroate.

**Keywords:** triptycenes, dendrimers, monodendrons

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## 1. Introduction

Triptycene was first synthesized in six steps by P. D. Bartlett in 1942. [1] One motive for preparation of this compound was comparison of the reactivity of the bridgehead carbons and hydrogens to those of the triphenylmethyl system. [2,3,4] Triptycene has also been used to study barriers to rotation and as molecular motors. [4] Various modifications of triptycenes have been used for explosives detection, [5,6] as anticancer drugs, [7] in the synthesis of modified porphyrins, [8] and for studying electron transfer reactions. [8,9] Formation of triptycenes has also been used as evidence for the existence of benzyne as a reactive intermediate. [10] Therefore synthesis of the triptycene monomer system (generation 0,  $G_0$ ) as described in this report can then lead to preparation of triptycyl ether monodendrons and finally dendrimers. Polymers using triptycene as the repeating unit can lead to microporous materials for various applications, such as gas absorption and cation traps. [11,12,13] To our knowledge this particular  $G_0$  system has not been synthesized in prior work. The only triptycene system related to ours is reported in a paper published in 1973 [14] that contains the triptycene quinone adduct (**5**) (discussed below). However, the published system from (**5**) did not meet the required structure necessary to generate the envisaged dendrimer. A dendrimer made of poly(ether triptycenes) will be different than the traditional poly(aryl ethers) synthesized in previous work [15,16] as the triptycene system will be more bulky and rigid, deter back

folding, and contain cavities for various chemical interactions.

## 2. Experimental

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. All  $^1\text{H}$  NMR spectra were recorded on a Varian 200 MHz NMR or a Varian 500 MHz NMR. NMR resonances are given in  $\delta$  units based on an internal tetramethylsilane (TMS) standard. IR spectra were obtained on a Midac FT-IR or a Mattson FT-IR as KBr pellets except where noted. All IR signals are reported in reciprocal centimeters vs. % transmittance. EI mass spectra were obtained from the Mass Spectrometry Center in Amherst MA. The spectra were recorded on a JEOL MStation with a source temp of 200°C, voltage 10kV, resolution of 5000 and scan range of 475-575. Analytical TLC was performed using coated polyester and aluminum silica gel plates (200-400 mesh, 60 Å). Silica gel for flash chromatography was 200-400 mesh, 60 Å.

All solvents and materials were purchased from commercial suppliers and used as received with the following exceptions. THF was distilled as needed from sodium/benzophenone and methylene chloride was distilled as needed from calcium hydride. All reactions were conducted under ambient atmosphere unless an inert atmosphere of nitrogen or argon was specified.

**Anthraquinone-2-carboxylic acid (2):** A 1 L 3-neck round bottom flask was charged with 42g (184 mmol) of  $\text{HIO}_4$  in 400 mL of acetonitrile. The resulting suspension was stirred vigorously for approximately 20 min. Then

35g (350 mmol) of  $\text{CrO}_3$  were added immediately followed by 10g (45 mmol) of 2-methylanthraquinone **1**. A deep orange solution appeared followed by an exothermic reaction. At this point a precipitate formed making the solution viscous and hard to stir. An additional portion of acetonitrile (100 mL) was added to facilitate stirring and the solution was stirred for 4 hours at room temperature. The reaction was monitored using TLC (ethyl acetate: hexanes: acetic acid). Upon completion the entire mixture was poured into 5 L of water. The precipitate was then filtered and washed with distilled water to remove all of the chromium salts by washing until the filtrate was colorless. The precipitate was dried overnight on the funnel under vacuum. The product yield was 11.1g (98%) of **2** as a yellow powder used directly in the next step. Melting point and spectral analysis agreed with the literature. [18]

**Anthracene-2-carboxylic acid (3):** A 2L, 3-neck, round bottom flask was charged with 10g (40 mmol) of (**2**), 45g (688 mmol) Zn dust, and 5g (31 mmol) of  $\text{CuSO}_4$ . To this mixture of solids was added 500mL of concentrated  $\text{NH}_4\text{OH}$  and the mixture was stirred vigorously and refluxed for 4 hours. Once the reaction was complete (TLC ethyl acetate: hexanes: acetic acid), the entire mixture was filtered and then thoroughly washed with hot concentrated ammonium hydroxide solution followed by hot distilled water. The remaining Zn was dissolved in concentrated HCl. The basic filtrates were combined, cooled with ice, and acidified producing a precipitate. The acidic solution from the zinc dissolution was filtered, and the resulting solid was dissolved in a minimum amount of hot acetic acid. This acetic acid solution was filtered to remove residual zinc metal. The acetic acid filtrate was poured into distilled water to produce a precipitate. All the precipitates were then filtered and dried under vacuum. The product yield was 8.6g (98%) of **3** as a yellow powder which was used without purification. Melting point and spectral analysis agreed with the literature. [18]

**Methyl-2-anthroate (4):** To a 3-neck 2 L round bottom flask were added 8g (36 mmol) of (**3**), 400 mL of  $\text{CH}_3\text{OH}$ , 500 mL of  $\text{C}_6\text{H}_6$  and finally 7 mL of  $\text{H}_2\text{SO}_4$ . Then a condenser with a Dean-Stark trap was fitted to the flask. The solution was refluxed for 24 hours. TLC of the reaction (ethyl acetate: hexanes) showed no starting material remaining. The Dean-Stark trap was then replaced with a simple downward distillation. The distillate was collected until crystals began to form on the walls of the reaction flask. At this point the heat was removed and the flask cooled to room temperature resulting in the formation of a precipitate. The precipitate was filtered and washed with 200 mL of water, followed by 100 mL of cold methanol. The filtrate was put on ice and neutralized with saturated aqueous sodium carbonate. The neutralized filtrate was extracted with ethyl acetate. The combined organics were extracted with brine and dried over sodium sulfate. The organic solution was filtered and the solvent removed *in vacuo*. The solid was recrystallized from ethanol and filtered. The combined yield 8.0g (95%) of (**4**) as a yellow powder with a MP of 192-193°C. [18]

**8-methoxycarbonyltriptycene-2,5-dione (5a/5b)** A dry 200 mL round bottom flask was purged with nitrogen and covered in aluminum foil. The flask was charged with 7.0g (30 mmol) of (**4**) and 30 mL of freshly distilled

dioxane, then heated to 70°C until the solid dissolved. The mixture was then treated with 7.0g (65 mmol) of twice recrystallized 1,4-benzoquinone and 10 additional mL of freshly distilled dioxane. The mixture was refluxed for 24 hrs with monitoring by TLC (hexanes: ethyl acetate 80:20). The reaction was cooled to room temperature and dioxane evaporated *in vacuo*. Excess benzoquinone was removed by steam distillation by adding 500 mL of water and treating with steam from an external source. When the distillate ran clear (no benzoquinone), the heat was removed and the distillation pot cooled. The black/brown residue in the water layer was extracted with toluene (3x75 mL). The toluene solution was treated with Norit and sodium sulfate, then filtered through a thin layer of Celite. The filtered solution was concentrated *in vacuo*, then recrystallized from methanol to give 5.1g (15 mmol, 50% yield) of pale yellow crystals of a mixture of diastereomers **5a** and **5b**, mp 133-135°C.  $^1\text{H}$  NMR: ( $\text{CDCl}_3$ ):  $\delta$  3.13-3.19 (d, bridge, 2H), 3.89-3.93 (s,  $\text{CO}_2\text{CH}_3$ , 3H), 4.98 (s, bridgehead, 2H), 6.37 (s, olefin, 2H), 7.19-9.1 (m, Ar-H, 7H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  48-49 (bridgehead, bridge), 52 ( $\text{CH}_3$ ), 124-127 (Ar), 128 (olefin), 167 (ester C=O), 197 (quinone C=O). Some peaks in  $^1\text{H}$  and  $^{13}\text{C}$  NMR exist as sets of two due to existence of diastereomers. FTIR (neat): 3064-2949 (C-H stretch), 1721 (ester C=O), 1673 (quinone C=O), 1614 (olefin C=C).

**2,5-Bis(benzyloxy)-8-methoxycarbonyl triptycene (6):** A 250 mL three neck round bottom flask was dried under vacuum with a heat gun, purged with nitrogen, and kept under this inert atmosphere. The flask was then charged with 100 mL of dry methanol and 0.67g (29 mmol) of sodium metal. The mixture was stirred until all the sodium metal dissolved completely. Then 2g (5.8 mmol) of the Diels-Alder adduct (**5**) was added and the mixture was stirred for 1.5 hours. At this time, 5.5mL (46.2 mmol) of benzyl bromide was added in one portion and the mixture heated to reflux for 10 hrs and monitored by TLC (ethyl acetate: hexanes). After 10 hours the mixture was cooled to room temperature and the precipitate was collected by filtration and washed copiously with water to remove any sodium methoxide, methanol, or benzyl bromide. The filtrate was extracted three times with an equal volume of ether. The combined organics were extracted with brine, dried with sodium sulfate, filtered, and concentrated. The filtrate residue was flash chromatographed using a gradient mixture of hexane with increasing ethyl acetate. The combined yield of (**6**) was 2.6g (86%) with a mp of 138-140°C.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  8.1-7.0 (m, ArH, 17H) 6.6 (s, hydroquinone, 2H), 6.0 (s, bridgehead, 2H), 5.1 (s,  $\text{BnCOPh}$ , 4H) 3.93 (s,  $\text{CO}_2\text{CH}_3$ , 3H). FTIR (KBr pellet): 3064-2946  $\text{cm}^{-1}$  (CH stretch), 1720  $\text{cm}^{-1}$  (C=O ester stretch), 1271 and 1054  $\text{cm}^{-1}$  (C-O ether/ester). MS EI+ m/z (524.20) and composition  $\text{C}_{36}\text{H}_{28}\text{O}_4$ .

**2,5-Bis(benzyloxy)-8-hydroxymethyl triptycene (7):** A 3-neck, 100 mL round bottom flask was dried under vacuum with a heat gun. After cooling, the system was flushed with  $\text{N}_2$  and kept under the same atmosphere throughout the reaction. Then 2.3g (4.4 mmol) of (**6**) was dissolved in THF and transferred into the round bottom. A 1M LAH/THF solution (13mL) was added slowly. The solution was then stirred for 3 hrs at room temperature and monitored using TLC (ethyl acetate: hexanes). The flask was cooled with ice and the reaction was slowly quenched

with saturated  $\text{Na}_2\text{SO}_4$ . The solution was then filtered to remove any precipitate, and the precipitate was washed with ether. The filtrate was collected and diluted with an equal volume of water and extracted with ether 3 times. The organics were extracted with brine and dried over sodium sulfate. The solution was filtered, concentrated, and dried under vacuum. A white foamy solid was obtained. The yield of (7) was quantitative (2.2g), with a mp of 70–72°C.

$^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.6–6.9 (m, ArH, 17H), 6.5 (s, hydroquinone, 2H), 5.9 (s, bridgehead, 2H), 5.1 (s,  $\text{BzCH}_2\text{OPh}$ , 4H), 4.5 (s,  $\text{BnCH}_2\text{-OH}$ , 2H), IR (KBr pellet): 3100–2900  $\text{cm}^{-1}$  (CH stretch), 3600–3200  $\text{cm}^{-1}$  (OH stretch), 1210  $\text{cm}^{-1}$  (C–O ether). MS EI+ m/z 496.1 and composition  $\text{C}_{35}\text{H}_{28}\text{O}_3$ .

**2,5-Bis(benzyloxy)-8-bromomethyl triptycene (8):** A 3-neck, 50 mL round bottom flask was dried under vacuum with a heat gun and purged with  $\text{N}_2$  and kept under this atmosphere throughout the reaction. A suspension of 60 mg (0.34 mmol) of NBS in 10 mL of anhydrous methylene chloride was added to the flask and then treated at 0°C with 0.03 mL (0.025 g, 0.41 mmol) of dimethylsulfide. The reaction temperature was then cooled to -20°C and 0.120 g (0.24 mmol) of (7) was added. The reaction was then allowed to warm to 0° and stirred at this temperature for 4 hrs. The reaction was monitored using TLC (ethyl acetate: hexanes). After 4 hrs, the reaction mixture was poured into 30 mL of ether and washed 3 times with water and then brine. The ethereal solution was dried with sodium sulfate, filtered and concentrated. The residue was chromatographed using ethyl acetate/hexanes. The yield of (8) was 0.098 g (73%) of an off white solid after drying under vacuum.

$^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  7.5–7.0 (m, ArH, 17H), 6.8 (s, hydroquinone, 2H), 5.85 (s, bridgehead, 2H), 5.1

(s,  $\text{BnCH}_2\text{OPh}$ , 4H), 4.4 (s,  $\text{BnCH}_2\text{-Br}$ , 2H). MS EI+ m/z (558, 560), (479.1 loss of Br $^-$ ), (297.1 loss of Br $^-$  and two tolyl cations) and composition  $\text{C}_{35}\text{H}_{27}\text{O}_2\text{Br}$ .

### 3. Results and Discussion

The retrosynthesis of the trisubstituted triptycene, bis(benzyloxy) triptycene methyl ester (6) **G**<sub>0</sub>, is shown in Figure 1. This precursor is required for further elaboration to the bromomethyl triptycene (discussed below), that is the active form for coupling. Bis(benzyloxy) triptycene ester (7) forms through enolate O-alkylation [17] and concomitant aromatization of the base generated dienolate produced from triptycene quinone adduct (5). This differs from the highly acidic media used by Bartlett<sup>1</sup> to produce the air sensitive triptycene-hydroquinone that must be isolated and then deprotonated/benzyloxy to produce (6). Our method uses a one pot approach to generate the hydroquinone anionic synthon *in situ* which is then trapped using benzyl bromide to generate (6). The quinone adduct (5) is formed by Diels-Alder reaction of methyl 2-anthroate (4) with benzoquinone. Methyl 2-anthroate was synthesized from commercially available 2-methylanthraquinone (1). We further report a substantial improvement in the synthesis of this methyl 2-anthroate system (4) with an overall yield of 91% relative to the previously reported yield of 48%. [18] The improvement in the synthesis of this anthracene derivative stems from the need for large amounts of starting materials or polymer precursors required to synthesize dendrimers convergently, which is the final overall goal of our preparation. With this higher yielding, efficient and chromatography free route, starting materials can be readily synthesized in sufficient quantities.

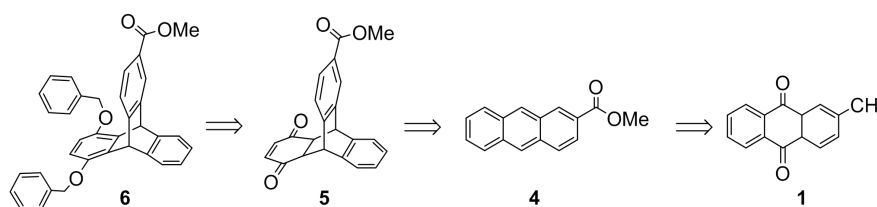


Figure 1. Retrosynthetic analysis for trisubstituted triptycenes

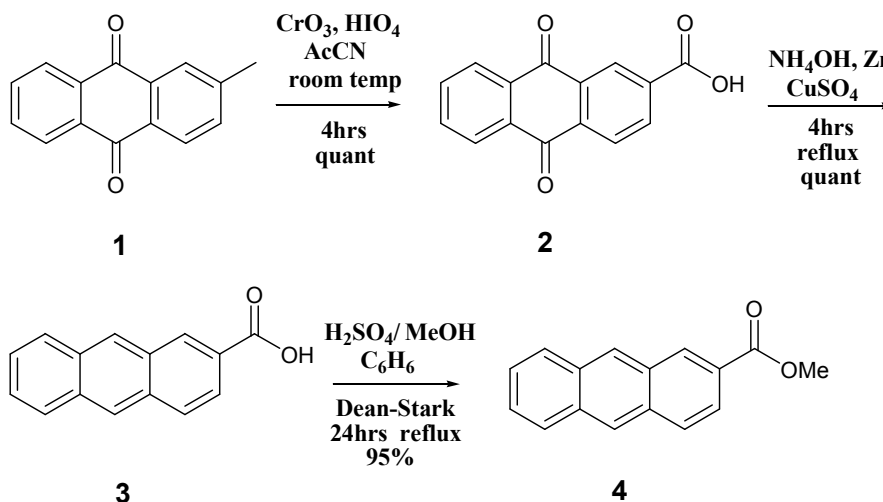


Figure 2. Preparation of 2-methyl anthroate

In Figure 2, our synthetic route began with the oxidation of 2-methylanthraquinone (**1**) to anthraquinone-2-carboxylic (**2**) acid, using chromium trioxide and periodic acid in acetonitrile at room temperature. [19] The quinone acid (**2**) was used directly in the next step: reduction to anthracene-2-carboxylic acid (**3**) using zinc and cupric sulfate in refluxing ammonia [20]. The crude anthracene-2-carboxylic acid was then esterified to methyl 2-anthroate (**4**) using a methanol/benzene cosolvent, concentrated sulfuric acid, and a Dean-Stark trap [21]. The above route produced the desired anthracene Diels-Alder precursor in high overall yield (91%). Spectral and physical analysis of compounds **1-4** are identical with spectral and physical data previously reported in the literature for these compounds. [18,22]

Methyl 2-anthroate (**4**) was then reacted with 1,4-benzoquinone (**5**) via a Diels-Alder reaction in dioxane to furnish the triptycene-quinone adduct as previously reported in the literature [14]. This product was obtained in a 65% yield. This adduct forms as a mixture of endo and exo isomers: these are also chiral but the racemic mixtures were not resolved. The triptycene-quinone adduct was then refluxed in methanol in the presence of methoxide and benzyl bromide to furnish 2,5-bis(benzyloxy)-8-methoxycarbonyl triptycene (**6**) ( $G_0$  ester) [17].  $^1\text{H}$  NMR indicated the success of the aromatization by the

disappearance of the bridge hydrogens at 3.13 ppm, the olefin hydrogens shifting from 6.37 ppm to 6.6 ppm, and the bridgehead from 4.98 ppm to 6.0 ppm. Mass spectral data agreed with the calculated MW of 524.20 m/z.

Having these results in hand we further functionalized 2,5-bis(benzyloxy)-8-methoxycarbonyl triptycene (**6**) to its corresponding 2,5-bis(benzyloxy)-8-bromomethyl triptycene (**8**) via direct halogenation of 2,5-bis(benzyloxy)-8-hydroxymethyl triptycene (**7**) using a method developed by Corey et al. in a 73% yield. [23] The triptycene alcohol (**7**) was synthesized by quantitative reduction of (**6**) with LAH in THF at room temperature. These transformations are shown in Figure 4.

The structures above were corroborated by both  $^1\text{H}$  NMR and MS analysis. NMR for the triptycene alcohol showed the disappearance of the methyl ester hydrogen peak at 3.93 ppm and the appearance of the benzyl methylene hydrogen peak at 4.5 ppm. MS data corresponded to the calculated mass of 496.1 m/z for (**7**). The NMR spectrum of triptycene bromide showed no significant change except for a slight upfield shift of the benzyl methylene hydrogens that appeared at 4.4 ppm owing to the lower electronegativity of bromine relative to oxygen. The MS data showed the bromine compound as an isotopic pair at 558/560 m/z.

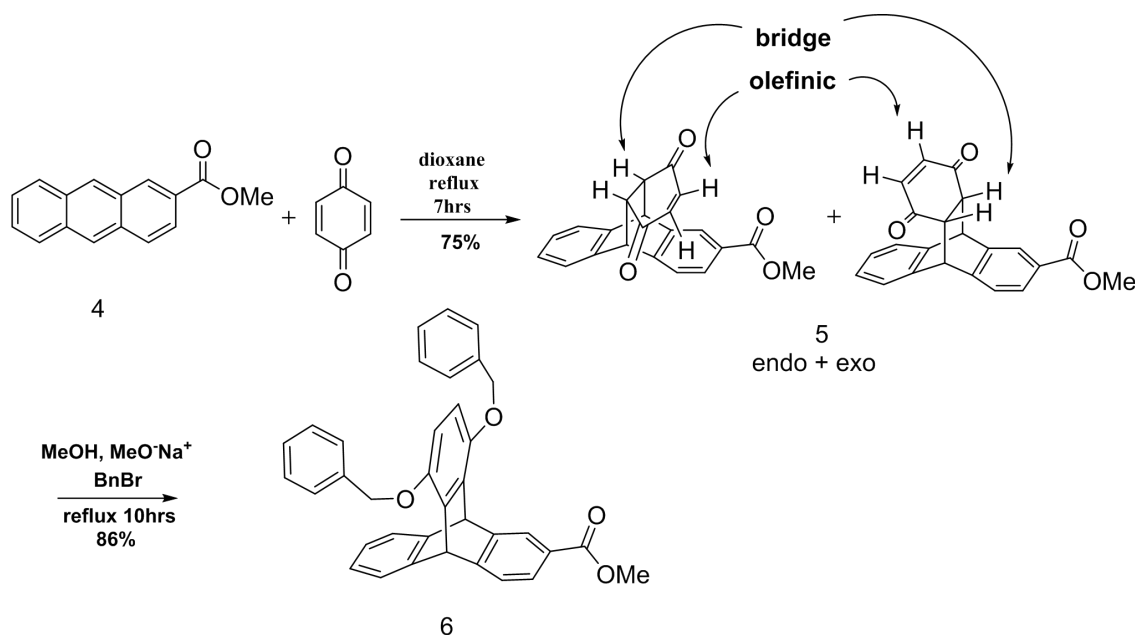


Figure 3. Preparation of trisubstituted triptycene **6**

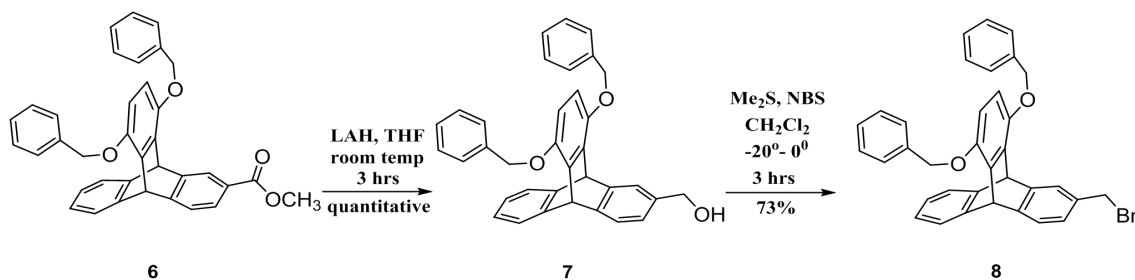


Figure 4. Preparation of triptycene alcohol **7** and triptycene bromide **8**



## 4. Summary

In summary, we have reported an efficient and relatively high yielding synthesis of tri-substituted triptycenes that provide several options for different transformations leaving the triptycene skeleton intact and thereby allowing us to attach this bulky system to a variety of nucleophilic dendrimers or other nucleophiles allowing the studies described in the introduction. These structures provide an entrance into the incorporation of the bulky and three dimensionally rigid triptycene framework into dendritic structures.

## Acknowledgements

EI mass spectra were obtained from the Mass Spectrometry Center in Amherst MA.

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