

## Isolation and Characterization of Silyl Enol Ether Intermediates in the Synthesis of 5,6,9,10-Tetrahydro-7,8-benzocyclooctenedione

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**Abstract:** The 5,6,9,10-tetrahydro-7,8-benzocyclooctenedione **4** has been synthesized through fragmentation of a bicyclo[4.2.0]octane system using an acyloin reaction on the *trans*-2,3-dicarboethoxy-1,2,3,4-tetrahydronaphthalene **1** in the presence of trimethylchlorosilane (TMCS). The two intermediates of this reaction, bis(trimethylsiloxy) derivatives **2** and **3**, have been isolated and characterized.

**Keywords:** 7,8-benzocyclooctenedione, acyloin reaction, conrotatory electrocyclic ring opening, fragmentation of bicyclo[4.2.0]octane systems, eight-membered rings.

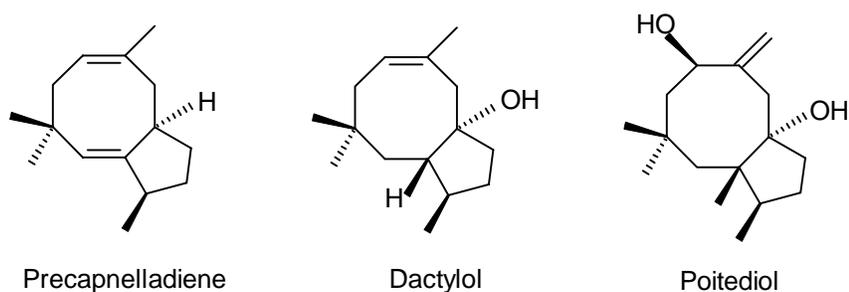
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### Introduction

Among medium-sized cyclic compounds, the eight-membered ones are the most difficult to assemble due to their high degree of ring strain and the transannular interactions present in these molecules [1]. In recent years we have been interested in these ring structures, that occur widely in nature, particularly in higher plants and marine organisms, and many cyclooctanoid natural products have been found to exhibit interesting biological activities. Precapnelladiene [**2b**], dactylol [**2c**], and

poitediol [**2d**] (Figure 1) are examples of sesquiterpenes isolated from marine sources that contain this ring in their skeletons, and they have been the target of several synthetic projects [2]. To synthesize these structures, special strategies have been developed [**2a**].  $\alpha$ -Diketones, on the other hand, are useful precursors in syntheses of acyclic and cyclic alkynes. They also react with *o*-phenylenediamines to form quinazolines. Another major application is in ring cleavage and conversion into dicarboxylic acids [3]. Bichromophoric molecules containing cyclic  $\alpha$ -diketones incorporating a benzene ring are also excellent substrates for intramolecular energy transfer studies [4].

Figure 1



Some examples of fragmentation of bicyclo[4.2.0]octane systems for synthesis of compounds involving eight-membered rings have been reviewed in literature [**2a**]. We planned the construction of an eight-membered ring by a fragmentation process using an acyloin reaction on *trans*-2,3-dicarboethoxy-1,2,3,4-tetrahydronaphthalene (**1**) in the presence of trimethylchlorosilane (TMCS), and then electrocyclic ring opening to the bis(trimethylsiloxy)cyclooctatriene derivative **3**, followed by hydrolysis of this silyl enol ether derivative to the target molecule. In order to illustrate the reaction pathway we have found it necessary and useful to characterize the silyl enol ether intermediates of the main reaction.

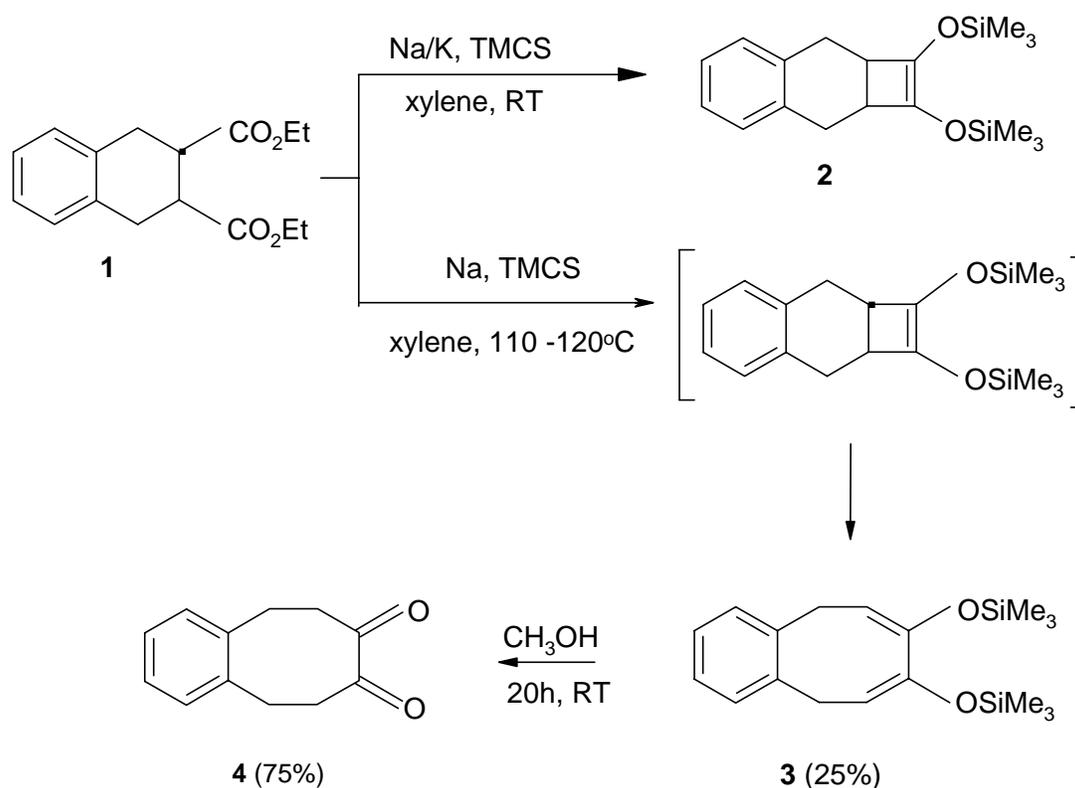
## Results and Discussion

Preparation of the title benzocyclooctenedione has been reported [5], but the authors did not publish any experimental details. Our synthetic scheme began with the known diester **1**, which was prepared by a literature procedure [6] from the Diels-Alder reaction between diethyl fumarate and an *o*-xylylene intermediate [7], which has been obtained in turn by 1,4-dehalogenation of  $\alpha,\alpha'$ -dibromo-*o*-xylylene in the presence of highly reactive metallic nickel.

The modified acyloin cyclization [8] of diester **1** afforded the corresponding enediol bis-trimethylsilylether **2**, which is relatively unstable because this 1,2-bis(trimethylsilyloxy)cyclobutene system readily rearranges into the bis(trimethylsilyloxy)cyclooctatriene derivative **3**. For isolation of **2** the reaction must be carried out at lower (i.e. room) temperatures. In practice the acyloin reaction was carried out in xylene with sodium - potassium alloy which is liquid at room temperature. The yield of the reaction after bulb-to-bulb distillation of the crude product was 55% (Scheme 1).

For preparation of **3** in one step, the acyloin reaction was performed with sodium in xylene at 110-120°C during 6h. In order to ensure the ring-opening of the intermediary cyclobutene derivative **2** the reaction mixture was further heated to reflux for an additional 3h. Compound **2** is analogous to a *trans*-bicyclo[4.2.0]oct-7-ene derivative [9] which must readily be converted, via a conrotatory electrocyclic ring opening, into a 1,3-cyclooctadiene derivative. Compound **3** is however relatively unstable, and we could only purify it by bulb-to-bulb distillation *in vacuo*. The <sup>1</sup>H-NMR spectrum of the product shows clearly that **3** is produced in 25% yield. Methanolysis of freshly distilled silyl enol ether derivative **3** in anhydrous methanol under argon furnished the desired  $\alpha$ -diketone **4** which was purified by column chromatography on silicagel. The yield was 75% (Scheme 1).

**Scheme 1.** Preparation of diketone **4** from diester **1**.



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## Experimental

### General

All reactions were carried out under pure, dry argon. Xylene was distilled from sodium and trimethylchlorosilane was distilled from CaH<sub>2</sub> under an argon atmosphere. <sup>1</sup>H- and <sup>13</sup>C-NMR spectra were determined in deuteriochloroform solutions on a Bruker AM-400 or a Bruker AC-200 spectrometer. IR spectra were recorded on a Bruker IFS 25. Mass spectra were obtained on a Varian MAT 311A instrument using an ionizing current of 70 eV.

### *Preparation of 1,2-bis(trimethylsilyloxy)-2a,3,8,8a-tetrahydro-cyclobuta[b]naphthalene (2).*

Sodium-potassium alloy was prepared by heating sodium (90 mg, 4 mmol) and potassium (780 mg, 20 mmol) under xylene (30 mL) until melted and then carefully mixing the molten metals with a magnetic stirrer. On cooling, the alloy remains liquid. Then, a solution of diester **1** (552 mg, 2 mmol) and trimethylchlorosilane (3 mL, 24 mmol) in xylene (5 mL) was added through an addition funnel over 3h and the reaction mixture was then left stirring overnight under argon. The solution was filtered under a blanket of argon (the alloy is pyrophoric!) and concentrated in a rotary evaporator under vacuum to give the crude product. Purification of the crude product by bulb-to-bulb distillation gave the title compound **2** as a colorless oil (364 mg, 55%, b.p. 135-150°C, 0.3 mmHg); IR (neat):  $\nu_{\max}$ . 3060, 3015, 2962-2870, 1560, 1387, 1250, 840, 750 cm<sup>-1</sup>; <sup>1</sup>H-NMR (400MHz, CDCl<sub>3</sub>):  $\delta$  = 0.1 (s, 18H), 2.35 (dt,  $J_1$  = 8.5 Hz,  $J_2$  = 2.00 Hz, 2H), 2.8 (d,  $J$  = 8.5 Hz, 4H), 6.97 (m, 4H, ArH) ppm; <sup>13</sup>C-NMR (100MHz, CDCl<sub>3</sub>):  $\delta$  = 0.34 (6×CH<sub>3</sub>), 34.14 (2×CH<sub>2</sub>), 45.20 (2×CH), 106.22 (2×C=), 126.2 (2×CH), 130.7 (2×CH), 138.7 (2×C) ppm; MS (70 eV):  $m/z$  (%) = 332 (5) [M<sup>+</sup>], 147 (39), 130 (21), 86 (26), 73 (100).

### *Preparation of 7,8-bis(trimethylsilyloxy)-5,10-dihydro-benzocyclooctatriene (3) and 7,8-benzocyclo-octenedione (4).*

A mixture of diester **1** (2.58 g, 9.34 mmol) and trimethylchlorosilane (5.9 mL, 46.68 mmol) in xylene (50 mL) was added dropwise over 3h to metallic sodium (1.07 g, 46.68 mmol) dispersed in xylene (50 mL) with vigorous stirring at 110-120°C under an argon atmosphere. Stirring was continued at 110-120°C for an additional 6h, and then at reflux temperature for 3h. After cooling and filtration of inorganic substances, the filtrate was concentrated in a rotary evaporator under vacuum to give the crude product, which was purified by bulb-to-bulb distillation at 130-150°C/0.3 mmHg to afford product **3** as a colorless oil (770 mg, 25%); IR (neat):  $\nu_{\max}$ . 3060, 3015, 2960 - 2900, 1636, 1387, 1295, 1251, 845, 748 cm<sup>-1</sup>; <sup>1</sup>H-NMR (400MHz, CDCl<sub>3</sub>):  $\delta$  = 0.12 (s, 18H), 3.3 (d,  $J$  = 8.2 Hz, 4H), 5.00 (t,  $J$  = 8.2 Hz, 2H), 7.05 (m, 4H, ArH) ppm; <sup>13</sup>C-NMR (100MHz, CDCl<sub>3</sub>):  $\delta$  = 0.8 (6×CH<sub>3</sub>), 33.9 (2×CH<sub>2</sub>), 106.24 (2×=CH), 117.95 (2×C=), 126.66 (2×CH), 130.65 (2×CH), 136.48 (2×C) ppm.

Methanolysis of freshly distilled silyl enol ether **3** in anhydrous methanol (25 mL) under argon at room temperature for 20h and then evaporation of solvent and volatile compounds, gave a golden yellow oil which was purified by column chromatography on silica gel eluted with dichloromethane. Compound **4** was thus obtained as a golden yellow oil (330 mg, 75%); IR (neat):  $\nu_{\max}$ . 3016, 1705 (C = O), 759  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.8 (t,  $J$  = 6.5 Hz, 4H), 2.95 (t,  $J$  = 6.5 Hz, 4H), 7.2 (m, 4H, ArH) ppm;  $^{13}\text{C-NMR}$  (100MHz,  $\text{CDCl}_3$ ):  $\delta$  = 28.6 ( $2\times\text{CH}_2$ ), 41.4 ( $2\times\text{CH}_2$ ), 128.05 ( $2\times\text{CH}$ ), 130.21 ( $2\times\text{CH}$ ), 137.71 ( $2\times\text{C}$ ), 207.15 ( $2\times\text{C}=\text{O}$ ) ppm; MS (70 eV):  $m/z$  (%) = 188 (77)[ $\text{M}^+$ ], 145 (7), 118 (100), 104 (23).

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*Sample Availability:* Available from the authors.