

# Ultrasonic synthesis and crystal structure analysis of two trimethylsilyloxy-substituted bicyclo[2.2.2]octene derivatives

H T SRINIVASA<sup>a</sup>, H NAGARAJAIAH<sup>a</sup>, B S PALAKSHAMURTHY<sup>b</sup>,  
S HARIPRASAD<sup>a</sup> and NOOR SHAHINA BEGUM<sup>a,\*</sup>

<sup>a</sup>Department of Studies in Chemistry, Central College Campus, Bangalore University,  
Dr. B R Ambedkar Street, Bangalore 560 001, India

<sup>b</sup>Department of Post Graduate Studies and Research in Physics, Tumkur University, Tumkur 572 103, India  
e-mail: noorsb@rediffmail.com; noorsb05@gmail.com

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**Abstract.** The compounds: 11-trimethylsilyloxy-1,2,3,4,4a,9a-hexahydro-1,4-etheno-anthraquinone and 4-benzyl-8-trimethylsilyloxy-4-aza-tricyclo[5.2.2.0]undec-8-ene-3,5-dione were synthesized by the Diels–Alder [ $4\pi_s + 2\pi_s$ ] cycloaddition reaction of 2-(trimethylsilyloxy)-1,3-cyclohexadiene with naphthaquinone and *N*-benzylmaleimide under ultrasonic conditions. The crystal structure analysis was done using single crystal X-ray diffraction method. In both the compounds, the trimethylsilyloxy- and naphthaquinone/*N*-benzylmaleimide moieties are *endo*- to the bicyclic ring.

**Keywords.** Ultrasonication; trimethylsilyloxy-derivatives; bicyclo[2.2.2]octene; Diels–Alder reaction; crystal structure; C–H...O and  $\pi\cdots\pi$  interactions.

## 1. Introduction

The atomic radius of silicon is larger than carbon, whereas the electronegativity of silicon is lower in comparison to carbon.<sup>1</sup> However, when elemental silicon is converted into organosilyl- based reagents, the silyl- groups behave as weak electron donating groups, becoming prone to attack by nucleophiles.<sup>2</sup> This renders the organosilyl- moiety to behave as anionic synthons. The synthons have wide applications in synthetic organic chemistry.

Cyclohexa-1,3-dienes and silyl- substituted 1,3-cyclohexadienes have been used for construction of the bicyclo[2.2.2]octene derivatives employing the Diels–Alder [ $4\pi_s + 2\pi_s$ ] reaction.<sup>3</sup> Recent work has shown that the *endo*- product is invariably predominant in the reaction of dienes with dienophiles.<sup>4</sup> The formation of the *endo*- isomer plays an important role in the design of drugs,<sup>5</sup> natural products<sup>6</sup> and other organosilicon based reagents.<sup>7</sup> Recently, the quantitative relationship between structural studies and reactivity properties of silyl- derivatives were studied.<sup>8</sup> The structural studies indicated a self-assembly facilitated *via* the rare co-existence of dimeric and catemeric patterns of bicyclo[2.2.2]octadiene, bicyclo[2.2.2]octane

and bis(trimethylsilyl)-5-norbornene skeletons, respectively.<sup>9,10</sup> All these parameters were attributed to the influence of the trimethylsilyl- group.

These findings prompted us to synthesize compounds 11-trimethylsilyloxy-1,2,3,4,4a,9a-hexahydro-1,4-etheno-anthraquinone (**3a**) and 4-benzyl-8-trimethylsilyloxy-4-aza-tricyclo[5.2.2.0<sup>2,6</sup>]undec-8-ene-3,5-dione (**3b**). The single crystal X-ray diffraction studies revealed that the product with *endo*- stereospecific geometry is preferred over the *exo*- product in the Diels–Alder cycloaddition reactions.

## 2. Experimental

### 2.1 Materials and characterization

All the chemicals were reagent grade and used as such without purification. Ultrasonic reactions were performed using OSCAR ultrasonic cleaner-109 (9.5 litres, 34 KHz power and 250 watts ultrasonic power). The reactions were monitored using TLC and the products purified by column chromatography on silica gel (60–120) mesh using 5% ethyl acetate in hexane as an eluent. The compounds were crystallized with ethyl acetate to get good crystals for crystallographic studies. IR spectra were recorded on Shimadzu FTIR-8400 spectrophotometer. The structures were confirmed

\*For correspondence

using  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR (Bruker 400 spectrometer). Elemental analyses were obtained using Carlo-Erba 1106 analyser.

## 2.2 Experimental procedure for the preparation of 11-trimethylsilyloxy-1,2,3,4,4a,9a-hexahydro-1,4-etheno-anthraquinone (**3a**) and 4-benzyl-8-trimethylsilyloxy-4-aza-tricyclo[5.2.2.0<sup>2,6</sup>]undec-8-ene-3,5-dione (**3b**)

Cyclohexenone (**1**) was treated with chlorotrimethylsilane and triethylamine in dimethylformamide as a solvent to obtain compound 2-(trimethylsilyloxy)-1,3-cyclohexadiene (**2**) under classical thermal conditions.<sup>11</sup> A mixture of naphthaquinone (1.58 g, 10 mmol); or *N*-benzylmaleimide (1.87 g, 10 mmol) and 2-(trimethylsilyloxy)-1,3-cyclohexadiene (**2**) (3.36 g, 20 mmol) in 10 mL toluene were irradiated in a water bath under ultrasonication for 2 h at room temperature (scheme 1).<sup>12</sup> After completion of the reaction the solvent was removed under reduced pressure, extracted with ethyl acetate (10 ml), washed with water and dried over anhydrous sodium sulphate. Single crystals of 11-trimethylsilyloxy-1,2,3,4,4a,9a-hexahydro-1,4-etheno-anthraquinone (**3a**) and 4-benzyl-8-trimethylsilyloxy-4-aza-tricyclo[5.2.2.0<sup>2,6</sup>]undec-8-ene-3,5-dione (**3b**) were obtained individually by re-crystallization using ethyl acetate at room temperature.

## 2.3 Physical measurements

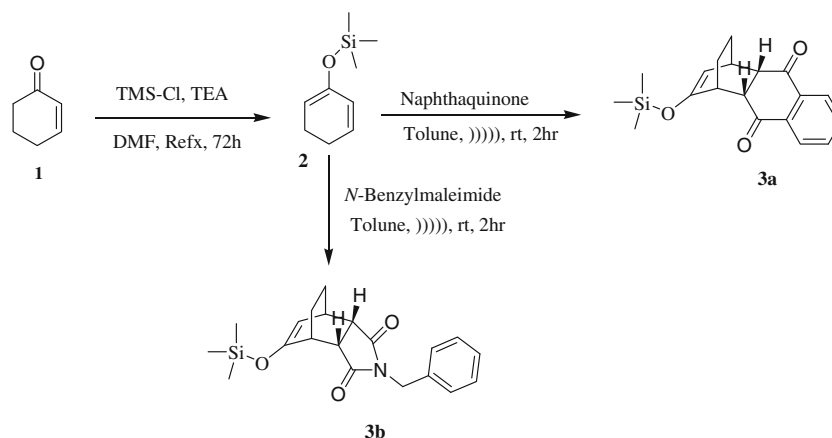
**2.3a 11-Trimethylsilyloxy-1,2,3,4,4a,9a-hexahydro-1,4-etheno-anthraquinone (3a):** Yield: 92%. M. p.: 112–113°C. IR: 2922, 2852 (alkyl CH<sub>2</sub>), 1680 (C = O), 1631 (Ar-CH = CH-), 1234 (-OSiMe<sub>3</sub>) cm<sup>-1</sup>;  $^1\text{H}$ -NMR:  $\delta$  8.14 (m, 2H, Ar-H), 7.80 (m, 2H, Ar-H), 4.95 (d, 1H,  $J$  = 2.5, C = CH), 3.43–3.15 (m, 4H, 4  $\times$  CH),

2.93–1.51 (m, 4H, 2  $\times$  CH<sub>2</sub>), 0.12 (s, 9H, -SiMe<sub>3</sub>) ppm;  $^{13}\text{C}$ -NMR:  $\delta$  198.6 (C = O), 197.6 (C = O), 155.9 (C = C-O-Si), 136.4 (-C = C-, Ar), 132.3 (CH = CH, Ar), 127.1 (CH = CH, Ar), 102.5 (C = C-O), 51.6 (CH), 37.3 (CH<sub>2</sub>), 26.5 (CH), 0.0 (-SiMe<sub>3</sub>) ppm; GC-MS: 326.3[M+1], 318, 292, 276, 271, 254 [base peak], 73; Anal. Calcd for C<sub>19</sub>H<sub>22</sub>O<sub>3</sub>Si: C, 69.90%; H, 6.79%. Found: C, 69.81%; H 6.74%.

**2.3b 4-Benzyl-8-trimethylsilyloxy-4-aza-tricyclo[5.2.2.0<sup>2,6</sup>]undec-8-ene-3,5-dione (3b):** Yield: 70%. M. p.: 114–115°C. IR: 2955, 2856 (CH<sub>2</sub>), 1770 (C = O), 1633 (Ar-CH = CH-), 1251 (-SiMe<sub>3</sub>) cm<sup>-1</sup>;  $^1\text{H}$ -NMR:  $\delta$  7.32 (m, 5H, Ar-H), 4.86 (m, 1H, -C = CH), 4.84 (s, 2H, Ar-CH<sub>2</sub>-N), 3.13–2.74 (m, 4H, 4  $\times$  CH), 1.58 (m, 4H, 4  $\times$  CH<sub>2</sub>), 0.12 (s, 9H, -SiMe<sub>3</sub>) ppm;  $^{13}\text{C}$ -NMR:  $\delta$  178.6 (C = O), 177.8 (C = O), 154.3 (C = C-O-Si), 135.9 (C = C, Ar), 132.3 (CH = CH, Ar), 127.6 (CH = CH, Ar), 101.3 (C = C-O), 45.1 (Ar-CH<sub>2</sub>-N), 44.5 (CH), 32.2 (CH<sub>2</sub>), 25.2 (CH), 0.02 (-SiMe<sub>3</sub>) ppm; GC-MS: 355 [M + 1], 189, 168, 151, 91[base peak], 73; Anal. Calcd for C<sub>20</sub>H<sub>25</sub>NO<sub>3</sub>Si: C, 67.57%; H, 7.09%; N 3.94%. Found: C, 67.74%; H 6.80%; N, 3.57%.

## 2.4 X-Ray diffraction analysis

Good quality single crystals were obtained upon re-crystallization of compounds **3a** and **3b** by slow evaporation of their solutions in ethyl acetate solvent. The X-ray diffraction data, for the compounds **3a** and **3b** were collected on a Bruker Smart CCD Area Detector System using MoK $\alpha$  (0.71073 Å) radiation. The data were reduced using SAINT-Plus.<sup>13</sup> The structures were solved by direct method using SHELXS97<sup>14</sup> and refined by difference Fourier syntheses using SHELXL97.<sup>14</sup> The positions and anisotropic



**Scheme 1.** Ultrasonic synthesis of compounds **3a** and **3b**.

displacement parameters of all non-hydrogen atoms were included in the full-matrix least-square refinement using SHELXL97<sup>14</sup> and the procedures were carried until convergence was reached. Then the hydrogen atoms were fixed geometrically and were refined isotropically. Molecular diagrams were generated using ORTEP.<sup>15</sup> The mean plane calculations were done using the program PARST.<sup>16</sup>

**2.4a Compound (3a):** Intensity data were collected at 296 K in the  $\omega$ - $\Phi$  scan mode. A total of 38323 reflections were collected, resulting in 7653 [R(int) = 0.0561] independent reflections, of which the number of reflections satisfying  $I > 2\sigma(I)$  criteria were 4598. The R factor on convergence R = 0.0676.

**2.4b Compound (3b):** Intensity data were collected at 296 K in the  $\omega$ - $\Phi$  scan mode. A total of 22289

reflections were collected, resulting in 4189 [R(int) = 0.0428] independent reflections, of which the number of reflections satisfying  $I > 2\sigma(I)$  criteria were 3155. The R factor on convergence R = 0.0451.

### 3. Results and discussion

#### 3.1 Chemistry

The infrared spectrum of compounds **3a** and **3b** shows a sharp band at  $1251\text{ cm}^{-1}$  characteristic to the presence of trimethylsilyl- group. The IR spectrum also showed a strong band at  $1770\text{ cm}^{-1}$  confirming the presence of C=O group. In the  $^1\text{H-NMR}$  spectra of compound **3a** a doublet at  $\delta$  4.95 ppm indicated the vinylic proton and multiplet signal at  $\delta$  8.14–7.80 ppm confirmed the aromatic protons. In compound **3b** benzylic protons resonate at  $\delta$  4.84 ppm in addition to vinylic and aromatic

**Table 1.** Crystal data and structure refinement of compounds **3a** and **3b**.

Compound	<b>3a</b>	<b>3b</b>
Empirical formula	$\text{C}_{19}\text{H}_{22}\text{O}_3\text{Si}$	$\text{C}_{20}\text{H}_{25}\text{NO}_3\text{Si}$
Formula weight	326.46	355.50
Temperature	296(2)K	296(2)K
Wavelength	0.71073 Å	0.71073 Å
Crystal system, space group	Monoclinic, $P2_1/c$	Triclinic, $P\bar{1}$
Unit cell dimensions		
a	16.070(7) Å	9.0565(11)
b	17.935(7) Å	9.9342(12)
c	13.160(5) Å	11.7672(15)
$\alpha$ (°)	90	84.659(4)
$\beta$ (°)	112.360(7)	69.482(4)
$\gamma$ (°)	90	77.424(4)
Volume Å <sup>3</sup>	3508(2)	967.6(2)
z	8	2
Calculated density (Mg/m <sup>3</sup> )	1.236	1.220
Absorption coefficient (mm <sup>-1</sup> )	0.146	0.139
F(000)	1392	380
Crystal size (mm)	0.18 × 0.16 × 0.16	0.18 × 0.16 × 0.16
Theta range for data collection	1.78 to 27.00 deg.	1.85 to 27.00
Limiting indices	−20 ≤ h ≤ 20, −22 ≤ k ≤ 22, −16 ≤ l ≤ 16	−11 ≤ h ≤ 11 −12 ≤ k ≤ 12 −15 ≤ l ≤ 15
Reflections collected/unique	38323/7653 [R(int) = 0.0561]	22289/4189 [R(int) = 0.0428]
Completeness to theta	27.00 100.0%	27.00 98.9%
Max. and min. transmission	0.9770 and 0.9742	0.9781 and 0.9754
Refinement method	Full-matrix least-squares on F <sup>2</sup>	Full-matrix least-squares on F <sup>2</sup>
Data/restraints/parameters	7653/0/431	4189/0/229
Goodness-of-fit on F <sup>2</sup>	0.968	0.962
Final R indices [ $I > 2\sigma(I)$ ]	R1 = 0.0676, wR2 = 0.1334	R1 = 0.0451, wR2 = 0.1044
R indices (all data)	R1 = 0.1190, wR2 = 0.1508	R1 = 0.0645, wR2 = 0.1122
Largest diff. peak and hole (e.Å <sup>-3</sup> )	0.273 and −0.217	0.213 and −0.267

protons. All this information attributed to the formation of compounds **3a** and **3b**. All other analytical data were in good agreement with the reported chemical structure.<sup>17</sup>

### 3.2 Crystallography

Summary of crystallographic data and other structure refinement parameters of the compound **3a** are as shown in table 1. Tables 2 and 3 show the respective hydrogen bond interactions in compounds **3a** and **3b**, respectively. The ORTEP diagram of the two independent molecules present in the asymmetric unit of compound **3a**, showing 50% probability ellipsoids and the atom numbering scheme is shown in figure 1. The ORTEP view of the molecule **3b** with atom labelling (thermal ellipsoids drawn at 50% probability)

is shown in figure 2. Figures 3 and 5 show the C–H...O intermolecular interaction in compounds **3a** and **3b**, respectively. Figure 4 shows the  $\pi$ – $\pi$  interaction in compound **3a**.

In compound **3a** there are two independent molecules in the asymmetric unit. One of the oxygen atom of one molecule is disordered over two sites with an occupancy ratio of 0.754 (2):0.246 (1), resulting in a major and a minor conformer. The bicyclic eight-membered rings are substituted with naphthaquinone at the one side and the silyloxy- group at the other side. Both the substituents are *endo*- to the bicyclic rings with dihedral angles of 108° and 115°, respectively. In the molecule, cyclohexene rings A(C6B/C9B/C8B/C5B/C10B/C7B) and B(C7B/C8B/C9B/C10B/C11B/C12B), and the cyclohexane ring C(C5B/C6B/C10B/C11B/C12B/C7B) of the bicyclo[2.2.2]octene unit adopt distorted boat

**Table 2.** Non-bonded interactions and possible hydrogen bonds (Å, °) for compound **3a** (D-donor; A-acceptor; H-hydrogen).

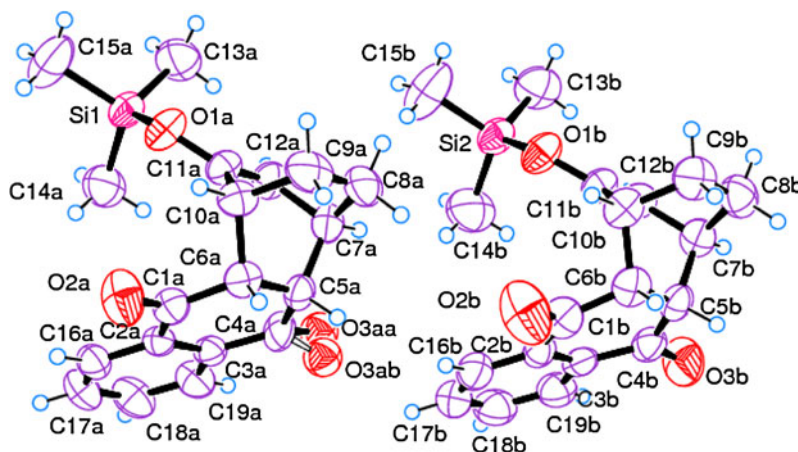
D–H...A	D–H	H...A	D...A	D–H...A
C17A–H17A...O2B <sup>i</sup>	0.930	2.494	3.182(5)	130
C18A–H18A...O2A <sup>ii</sup>	0.930	2.668	3.493(4)	148

Symmetry code: (i)  $-x, +y + 1/2, -z + 1/2$ , (ii)  $x, -y + 1/2 + 1, +z - 1/2$

**Table 3.** Non-bonded interactions and possible hydrogen bonds (Å, °) for compound **3b** (D-donor; A-acceptor; H-hydrogen).

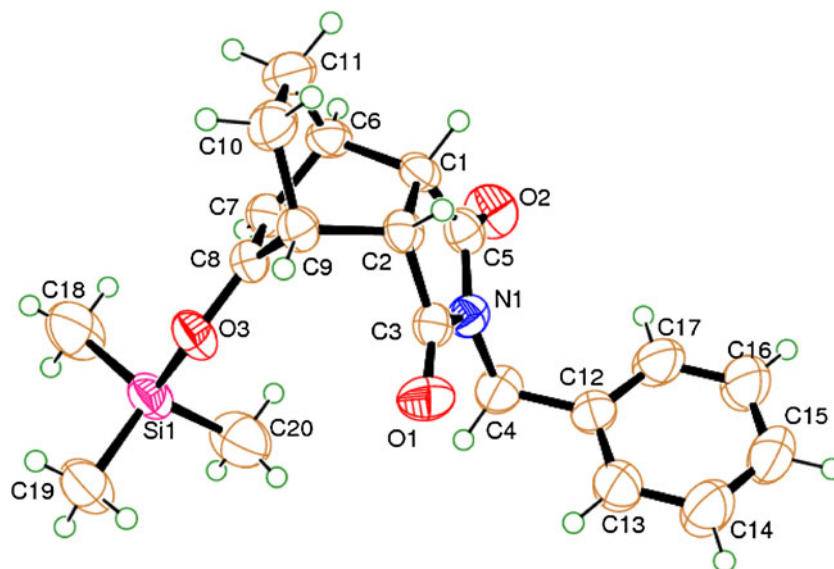
D–H...A	D–H	H...A	D...A	D–H...A
C2–H2...O1 <sup>i</sup>	0.980	2.485	3.359 (2)	148
C4–H4A...O2 <sup>ii</sup>	0.970	2.490	3.343(2)	146

Symmetry code: (i)  $-x + 1, -y + 2, -z + 1$ , (ii)  $-x, -y + 2, -z + 2$

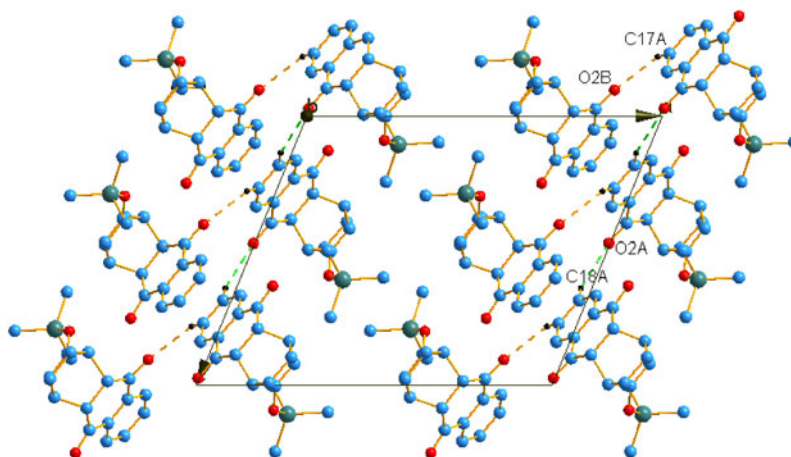


**Figure 1.** ORTEP diagram of the two independent molecules present in the asymmetric unit of compound **3a**, showing 50% probability ellipsoids and the atom numbering scheme.





**Figure 2.** ORTEP view of compound **3b**, showing 50% probability ellipsoids and the atom-numbering scheme.



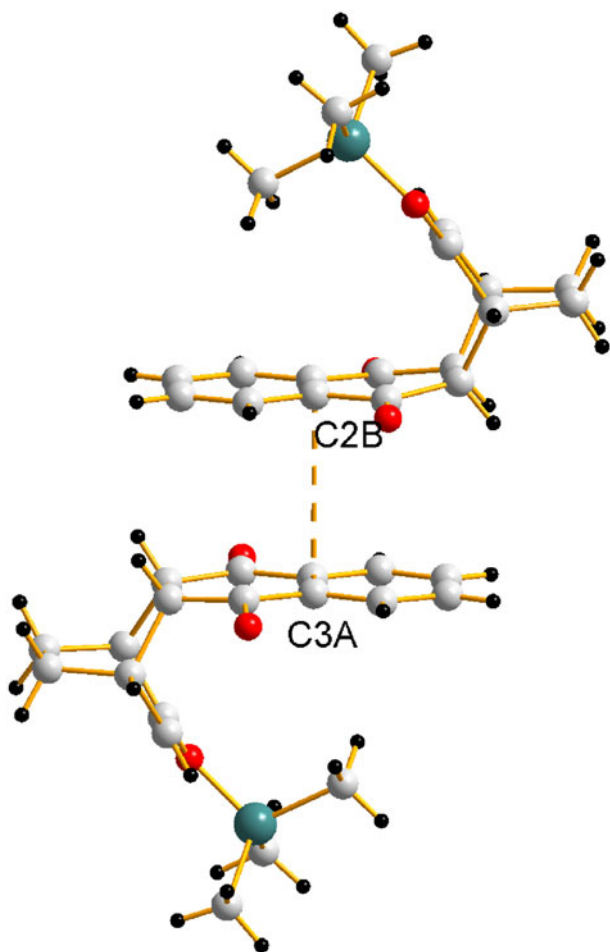
**Figure 3.** Crystal structure of **3a** viewed along 'c' axis. Dotted lines indicate intermolecular C–H...O interactions.

like conformations as reported earlier.<sup>18</sup> The ring puckering parameters  $Q$ ,  $\theta$  and  $\phi$  are 0.875 (2) Å,  $-60.15$  (2)° and  $90.4$  (1)°, respectively for ring A, 0.786 (2) Å,  $-179.85$  (2)° and  $90.41$  (2)°, respectively for ring B, and 0.816 (2) Å,  $119.93$  (2)° and  $90.14$  (2)°, respectively for ring C.<sup>19</sup>

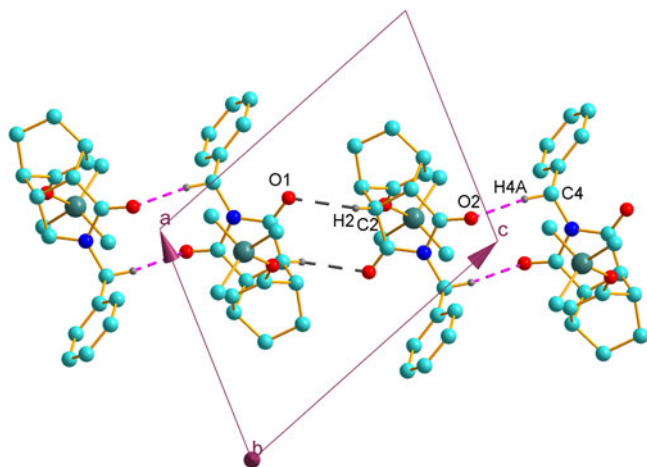
The crystal structure of the compound **3a** is stabilized by two types of C–H...O intermolecular interactions. These interactions result in the formation of chains along 'c' axis (figure 3). The molecular packing is further stabilized by  $\pi$ – $\pi$  stacking interactions between naphthaquinone rings with the shortest centroid–centroid distance being 3.636 Å for C3A–C2B carbons (figure 4).

Compound **3b** crystallizes in triclinic crystal system with space group  $P\bar{1}$  (figure 5). The bicyclo[2.2.2]octene

ring is substituted with *N*-benzylmaleimide at one end and the trimethylsilyloxy-group at the other end. Due to steric-hindrance in the ring both the substituents adopt *endo*-conformation, this is in good agreement with the theoretical predictions.<sup>20,21</sup> The phenyl ring of *N*-benzylmaleimide group is positioned axially to the methyl-pyrrolidine-2,5-dione ring with a dihedral angle of  $67.36$  (5)°. In the molecule, cyclohexene rings A(C6/C7/C8/C9/C10/C11) and B(C6/C7/C8/C9/C1/C2), and the cyclohexane ring C(C6/C1/C2/C9/C10/C11) of the bicyclo[2.2.2]octene unit, all the three rings adopt distorted boat conformations as seen in compound **3a**. The ring puckering parameters  $Q$ ,  $\theta$  and  $\phi$  are 0.787 (2) Å,  $89.29$  (1)° and  $0.787$  (2)°, respectively for ring A, 0.81 (2) Å,  $94.31$  (2)° and  $176.46$  (2)°, respectively for ring B, and 0.889 (2) Å,  $90.7$  (1)°



**Figure 4.** Compound **3a**, showing  $\pi$ - $\pi$  stacking interactions between naphthaquinone rings.



**Figure 5.** Molecular packing of compound **3b** viewed along 'a-c' diagonal plane. Dotted lines indicate intermolecular C-H...O interactions.

and  $-176.25(1)^\circ$ , respectively for ring C.<sup>19</sup> Both the oxygen atoms of the pyrrolidine-2,5-dione ring are taking part in the hydrogen bond.

The crystal structure is stabilized by two types of C-H...O intermolecular interactions, both the interactions result in the formation of centrosymmetric head-to-head dimers generating one-dimensional chain along 'a-c' diagonal plane with graph set motif  $R_2^2(8)$  and  $R_2^2(10)$ , respectively.

The overall conformation in compounds **3a** and **3b** are very similar. For example, the dihedral angle between the three rings of bicyclo[2.2.2]oct-5-ene unit of compound **3a** is  $108^\circ/108^\circ$ ,  $109^\circ/108^\circ$ ,  $108^\circ/108^\circ$ , and the compound **3b** is  $108^\circ$ ,  $107^\circ$  and  $106^\circ$ . The substituents in both the compounds are *endo*- to each other.

#### 4. Conclusion

We report the synthesis of two trimethylsilyloxy-substituted bicyclo[2.2.2]octene derivatives by Diels-Alder  $[4\pi_s+2\pi_s]$  cycloaddition reactions using ultrasound conditions. Single crystal X-ray diffraction studies showed both the products to have *endo*- stereochemistry. The molecular structures reveal that there is presence of C-H...O and  $\pi$ - $\pi$  interactions that stabilize the structure.

#### Supplementary material

The CIF files are deposited at the Cambridge Crystallographic Data Centre, The deposition number of compound **3a** is CCDC-892079 and **3b** is CCDC-892080.

#### Acknowledgements

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