

# Synthesis, isolation and spectroscopic characterisation of 3-chloro-[6](2,4)-troponophane: the first 2,4-polymethylene-bridged troponoid

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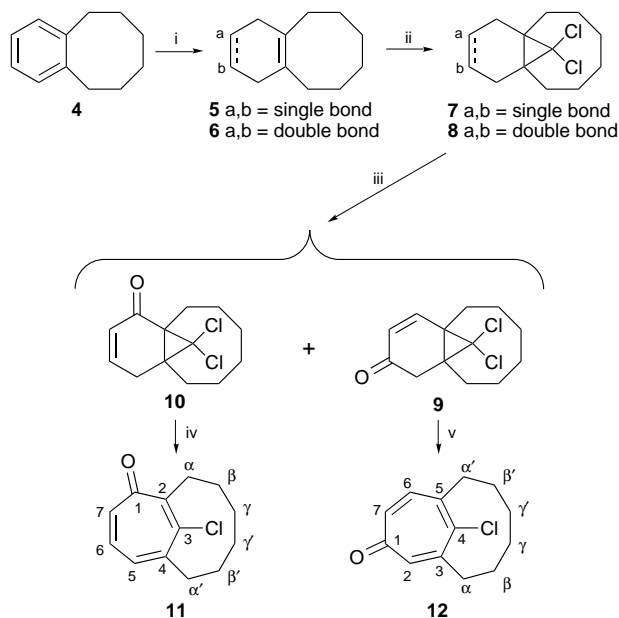
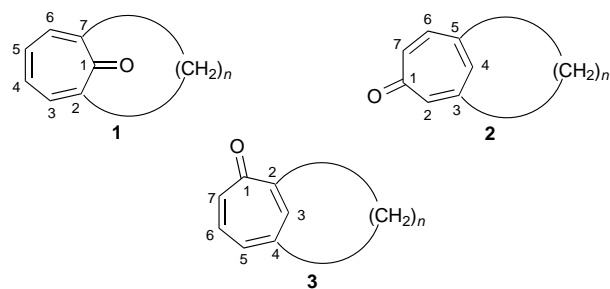
## Treatment of the tricyclic enone **10** with perchloric acid results in formation of the title troponophane **11**, the first example of a (2,4)-polymethylene bridged troponoid.

The delocalisation energies per electron within non-benzenoid rings are usually substantially smaller than those associated with comparable benzenoid rings. Consequently, short-bridged non-benzenoid cyclophanes have attracted considerable attention because of the expectation that there is likely to be greater deformation (relative to benzenoid counterparts) of the conjugated carbocyclic ring in accommodating any strain created by the introduction of bridges between non-adjacent ring carbons.<sup>1</sup> There is a further expectation that such deformations will be manifested in unusual reactivity patterns.<sup>1</sup> Studies of troponophanes have been especially interesting in this regard and numerous  $[n](2,7)$ -troponophanes **1** have been described including trimethylene-bridged systems ( $n = 3$ ).<sup>1,2</sup> Their  $[n](3,5)$  counterparts **2** are much less common<sup>3</sup> but include a system where  $n = 6$ .<sup>4</sup> In contrast,  $[n](2,4)$ -troponophanes **3** remain virtually unknown.<sup>5</sup> Calculations<sup>†</sup> suggest that for a given value of  $n$  (where  $n \leq 6$ ) the order of stability amongst the 'meta'-troponophanes is **1** > **2** > **3** meaning that the last system is probably the most strained of the three and, therefore, likely to be the most interesting. Consequently, we now report on the synthesis, isolation, spectroscopic properties and some aspects of the chemistry of the title compound **11**, the first example of a 2,4-polymethylene-bridged troponoid.

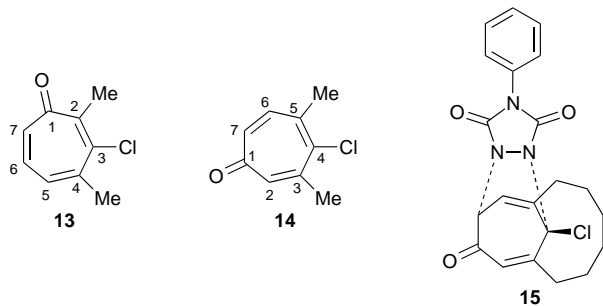
The synthesis of compound **11** is outlined in Scheme 1 and follows very much the same strategy as used in the preparation of the isomeric  $[6](3,5)$ -troponophane **12**.<sup>4</sup> Thus, Birch reduction of cyclooctene **4**<sup>7</sup> with lithium in liquid ammonia afforded a ca. 15 : 1 : 100 mixture of compounds **4**, **5**<sup>8</sup> and **6**<sup>9</sup> which was subjected to reaction with chloroform-potassium *tert*-butoxide in diethyl ether between  $-30$  and  $20$  °C. In this manner dichlorocarbene adducts **7**<sup>4</sup> (<1%) and **8** (75% from **4**) (mp  $86-88$  °C; lit.,<sup>4</sup> mp  $87-88$  °C) were obtained and these could be separated from one another by fractional crystallisation. Allylic oxidation of alkene **8** was accomplished using the chromium trioxide-3,5-dimethylpyrazole (3,5-DMP) complex,<sup>10</sup> and the enones **9**<sup>4</sup> (44%) and **10**<sup>‡</sup> (20%) (mp  $97-100$  °C) thereby obtained were separated from one another by chromatography on silica.<sup>11</sup> Treatment of a ca. 0.3 M chloroform solution of compound **10** with ca. 12 equiv. of 70% aq. perchloric acid resulted in its slow (20 h at  $20$  °C) conversion into the target troponophane **11**<sup>§</sup> (71%) which could be isolated by flash

chromatography<sup>11</sup> on silica gel ( $R_f$  0.5 in  $\text{CH}_2\text{Cl}_2$ ) and which was obtained as a light green oil. Enone **9** was subjected to similar conditions in order to provide a sample of the isomeric troponophane **12** which was identical with material obtained previously.<sup>4</sup>

The  $^1\text{H}$  NMR spectrum of compound **11** possessed features strongly suggestive of the presence of a phane system. Thus, the one-proton multiplet at  $\delta$  0.43 is assigned to one of the protons associated with  $\text{C}_\gamma$  of the hexamethylene bridge which is forced to project into the shielding zone of the troponoid ring. In addition, the chemical shifts ( $\delta$  3.14–2.93) and the multiplicities of the signals due to three of the four protons attached to  $\text{C}_\alpha$  and  $\text{C}_{\alpha'}$  are reminiscent of those reported for the analogous protons in 13-bromo[7]-metacyclophane<sup>12</sup> and  $[7](3,7)$ -troponophane.<sup>13</sup> The fourth such proton (attached to  $\text{C}_\alpha$ ) resonates upfield, at  $\delta$  1.87, by virtue of its projecting into the shielding zone of the adjacent carbonyl group. Spectral comparisons were made with the model compound **13** (mp  $52-55$  °C)<sup>§</sup> (readily prepared by established methods<sup>14</sup> from *o*-xylene). The low field regions in the  $^{13}\text{C}$  NMR spectra of these two compounds were similar although the resonance due to C-1 in troponophane **11** was deshielded by 1.7 ppm relative to its counterpart in tropone **13**, an observation consistent with the expectation that the troponoid ring within the former compound is buckled. In the  $^1\text{H}$  NMR spectra of compounds **11** and **13**, signal multiplicities and coupling constants for the troponoid ring protons were essentially identical but the chemical shifts of the



**Scheme 1** Reagents and conditions: i, Li (19 mol),  $\text{NH}_3$ ,  $-78$  °C then **4** in THF,  $\text{Bu}^t\text{O}^-$ ,  $-78$  to  $-30$  °C, 5.5 h then MeOH; ii,  $\text{Bu}^t\text{O}^- \text{K}^+$  (1.6 equiv.),  $\text{CHCl}_3$  (1.5 equiv.),  $\text{Et}_2\text{O}$ ,  $-30$  to  $20$  °C, 16.5 h; iii,  $\text{CrO}_3$  (30 equiv.), 3,5-DMP (30 equiv.),  $\text{CH}_2\text{Cl}_2$ ,  $-20$  to  $-10$  °C, 3.5 h; iv, 70% aq.  $\text{HClO}_4$  (ca. 12 equiv.),  $\text{CHCl}_3$ ,  $20$  °C, 20 h; v, 70% aq.  $\text{HClO}_4$  (ca. 12 equiv.),  $\text{CHCl}_3$ ,  $20$  °C, 1 h



**Table 1** Comparison of selected  $^1\text{H}$  NMR spectral parameters for compounds **11–14** (acquired in  $\text{C}_6\text{D}_6$  solution at  $21.2^\circ\text{C}$ )

|                | $\delta$ |       |       |       | Coupling constants/Hz |                   |                   |
|----------------|----------|-------|-------|-------|-----------------------|-------------------|-------------------|
|                | H-2      | H-5   | H-6   | H-7   | $J_{2,7}/J_{7,2}$     | $J_{5,6}/J_{6,5}$ | $J_{6,7}/J_{7,6}$ |
| <b>11</b>      |          | 5.58  | 6.03  | 6.44  |                       | 6.0               | 11.9              |
| <b>13</b>      |          | 5.90  | 6.03  | 6.65  |                       | 8.6               | 11.8              |
| $\Delta\delta$ |          | -0.32 | 0.00  | -0.21 |                       |                   |                   |
| <b>12</b>      | 6.13     |       | 5.97  | 6.41  | 2.7                   |                   | 12.0              |
| <b>14</b>      | 6.85     |       | 6.03  | 6.63  | 2.7                   |                   | 12.2              |
| $\Delta\delta$ | -0.72    |       | -0.06 | -0.22 |                       |                   |                   |

signals due to two of the troponoid ring protons in **11** were shielded relative to their counterparts in model **13**, a situation similar to that observed previously in comparing troponophane **12** with model compound **14**<sup>4</sup> (Table 1).

The behaviour of troponophane **11** towards cycloaddition processes has been examined but we have yet to obtain convincing evidence of the participation of this compound in any such reaction. In contrast, the isomeric troponophane **12** reacts almost instantaneously with 4-phenyl-3,5-dihydro-1,2,4-triazole-3,5-dione (in  $\text{CH}_2\text{Cl}_2$  at  $20^\circ\text{C}$ ) to give adduct **15**<sup>§</sup> (mp  $210\text{--}212^\circ\text{C}$ ) in 95% yield. These observations are consistent with semi-empirical calculations<sup>†</sup> which suggest that troponophane **12** has a higher lying HOMO than isomer **11** ( $\Delta E = 0.23$  eV) and should, therefore, be more reactive towards electron-deficient dienophiles in normal electron demand Diels–Alder cycloaddition processes.

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### Footnotes

<sup>†</sup> AM1 semi-empirical calculations (ref. 6) were carried out using the SPARTAN ver. 4.1.1 software package (as provided by Wavefunction Inc., Irvine, CA. 92715) on a Silicon Graphics workstation.

<sup>‡</sup> All new compounds had spectroscopic data [IR, UV (where appropriate), NMR and mass spectrum] consistent with the assigned structure. Satisfactory combustion and/or high resolution mass spectral analytical data were obtained for all new compounds. Reported yields refer to isolated materials.

<sup>§</sup> Selected spectral data for **11**:  $^{13}\text{C}$  NMR (75 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta$  186.4 (C), 151.7 (C), 148.7 (C), 144.4 (C), 136.6 (CH), 132.9 (CH), 121.4 (CH), 34.5 ( $\text{CH}_2$ ), 34.3 ( $\text{CH}_2$ ), 29.9 ( $\text{CH}_2$ ), 28.7 ( $\text{CH}_2$ ), 26.8 ( $\text{CH}_2$ ) and 26.4 ( $\text{CH}_2$ );  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta$  6.44 (d,  $J$  11.9 Hz, 1 H, H 7), 6.03 (dd,  $J$  11.9 and 6.0 Hz, 1 H, H 6), 5.58 (d,  $J$  6.0 Hz, 1 H, H 5), 3.14–2.93 (complex m, 3 H), 1.87 (ddd,  $J$  13.7, 8.3 and 3.3 Hz, 1 H), 1.76–1.56 (complex m, 2 H), 1.48–1.22 (complex m, 3 H), 1.18–1.02 (complex m, 2 H), 0.43 (m, 1 H); MS  $m/z$  (EI, 30 eV) 225 (3%) 223 (9) [(M + H)<sup>+</sup>], 224 (16) 222 (50) [M<sup>+</sup>], 188 (54) [(M + H - Cl)<sup>+</sup>], 187 (100) [(M - Cl)<sup>+</sup>] and 159 (45) [(M - CO - Cl)<sup>+</sup>];  $\nu_{\text{max}}(\text{NaCl})/\text{cm}^{-1}$  1626 and 1597;  $\lambda_{\text{max}}(\text{CHCl}_3)/\text{nm}$  266 (log  $\epsilon$  3.99) and 354 (3.54) (HRMS: M<sup>+</sup>, 222.0815.  $\text{C}_{13}\text{H}_{15}^{35}\text{ClO}$  requires M<sup>+</sup>, 222.0811). For **13**:  $^{13}\text{C}$  NMR (75 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta$  184.7 (C), 148.4 (C), 145.7 (C), 142.9 (C), 136.3 (CH), 132.5 (CH), 129.4 (CH), 28.0 ( $\text{CH}_3$ ) and 21.6 ( $\text{CH}_3$ );  $^1\text{H}$  NMR (300 MHz,  $\text{C}_6\text{D}_6$ ):  $\delta$  6.65 (br d,  $J$  11.8 Hz, 1 H, H 7), 6.03 (dd,  $J$  11.8 and 8.6 Hz, 1 H, H 6), 5.90 (br d,  $J$  8.6 Hz, 1 H, H 5), 2.46 (s, 3 H,  $\text{CH}_3$ ) and 1.89 (s, 3 H,  $\text{CH}_3$ );  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$  1628 and 1576;  $\lambda_{\text{max}}(\text{CHCl}_3)/\text{nm}$  250 (log  $\epsilon$  4.06) and 318 (3.77). For **15**:  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  186.2 (C), 168.9 (C), 150.6 (C), 130.6 (C), 129.2 (CH), 128.7 (CH), 125.5 (CH), 125.0 (CH), 118.7 (CH), 84.8 (C), 63.0 (CH), 37.4 ( $\text{CH}_2$ ), 31.6 ( $\text{CH}_2$ ), 29.7 ( $\text{CH}_2$ ), 26.5 ( $\text{CH}_2$ ), 24.8 (CH) and 23.1 ( $\text{CH}_2$ ) (two signals obscured or overlapping);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.45–7.35 (complex m, 5 H), 6.26 (d,  $J$  7.7 Hz, 1 H, H 6), 5.83 (d,  $J$  1.1 Hz, 1 H, H 2), 5.25 (dd,  $J$  7.7 and 1.1 Hz, 1 H, H 7), 3.09 (m, 2 H), 2.46 (m, 2 H), 2.28 (m, 1 H), 1.91 (m, 1 H), 1.55 (m, 5 H), 1.23 (m, 1 H);  $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$  1727, 1672 and 1403 (HRMS: M<sup>+</sup>, 397.1195.  $\text{C}_{21}\text{H}_{20}^{35}\text{ClN}_3\text{O}_3$  requires M<sup>+</sup>, 397.1193).

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