4

Experimental

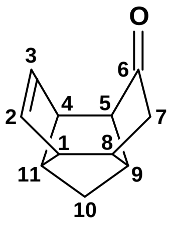
4.1. Analytical apparatus

Analysis	Apparatus
Melting point*	B-540 Büchi
Infrared	Bruker Tensor 27 spectrophotometer
GC-MS	Agilent 6890N GC equipped with an Agilent 7683 autosampler, ZB-1 capillary column and an Agilent 5973 MSD
NMR	Bruker Avance III Ultra Shield 600 MHz spectrophotometer
XRD	Bruker Smart X2S benchtop crystallographic system

*** Melting points are uncorrected.**

4.2. Synthesis of tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-one and derivatives

4.2.1. Tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-one[51]



1

Exo-11-bromopentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione[51] (**117**, 12.000 g, 50.2 mmol), acetic acid (140 cm^3) and zinc powder (19.700 g, 0.301 mol) was stirred and refluxed for 8 hours. The reaction mixture was filtered after it was allowed to cool to room temperature. The filter cake was washed with small amounts of dichloromethane and the combined filtrate partitioned between water and dichloromethane. The organic layer was separated and washed with a 10% Na_2CO_3 solution and water and dried over anhydrous sodium sulphate. Removal of the solvent yielded the ketoalkene **1** (6.135 g, 76%, melting point: 192.3^{o}C, literature[51]). A pure sample was obtained by recrystallisation from pentane.

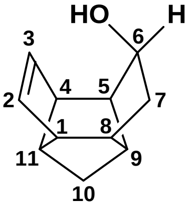
IR spectrum: ν_{max} 2949, 1733, 1138, 717 cm^{-1}.

^{13}C-NMR [CDCl$_3$]: δ_C 221.2 (C-6, C=O), 137.8 (C-2, 1 × CH), 136.4 (C-3, 1 × CH), 59.8 (C-11, 1 × CH), 56.1 (C-8, 1 × CH), 52.0 (C-9, 1 × CH), 50.1 (C-1, 1 × CH), 46.4 (C-4, 1 × CH), 42.6 (C-7, 1 × CH$_2$), 38.5 (C-5, 1 × CH), 33.9 (C-10, 1 × CH$_2$).

^{1}H-NMR [CDCl$_3$]: δ_H 6.04 (H-3, 1 × CH), 5.95 (H-2, 1 × CH), 3.05 (H-11, 1 × CH), 2.84 (H-9, 1 × CH), 2.77 (H-1, 1 × CH), 2.61 (H-4, 1 × CH), 2.45 (H-5, 1 × CH), 2.36 (H-8, 1 × CH), 2.15 (H-7$_s$, 1 × ½CH$_2$, 18.43 Hz, 5.88 Hz), 2.00 (H-7$_a$, 1 × ½CH$_2$, 18.43 Hz), 1.81 (H-10$_s$, 1 × ½ CH$_2$, 11.07 Hz), 1.75 (H-10$_a$, CH$_2$, 11.07 Hz).

MS spectrum: EI, *m/z* 160 (M^+).

4.2.2. *Endo*-tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-ol[51]



118

A solution of ketoalkene **1** (1.000 g, 6.25 mmol) in 20 cm^3 of ethanol was placed in an ice bath. Small portions of NaBH$_4$ (0.474 g, 12.5 mmol) were added over a period of 5 minutes. The reaction mixture was stirred for 4 hours during which time the temperature returned to room temperature. The reaction mixture was returned to an ice bath and unreacted NaBH$_4$ was destroyed by the slow addition of an excess amount of 3% hydrochloric acid solution. Extraction with dichloromethane yielded the alcohol **118** (0.853 g, 85%; melting point: 167.1 – 169.5°C, literature[51]). A pure sample was obtained by recrystallisation from pentane.

IR spectrum: ν_{max} 3342, 2933, 2863, 1737, 1109, 1084, 1044, 1001, 723 cm^{-1}.

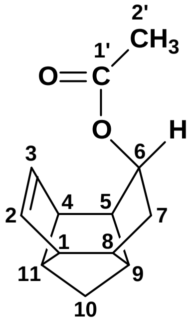
^{13}C-NMR [CDCl$_3$]: δ_C 139.9 (C-2, 1 × CH), 139.4 (C-3, 1 × CH), 77.5 (C-6, 1 × CH), 59.4 (C-11, 1 × CH), 52.4 (C-5, 1 × CH), 51.6 (C-4, 1 × CH), 47.7 (C-1, 1 × CH), 46.7 (C-9, 1 × CH), 42.4 (C-8, 1 × CH), 39.0 (C-7, 1 × CH$_2$), 32.3 (C-10, 1 × CH$_2$).

^{1}H-NMR [CDCl$_3$]: δ_H 6.39 (H-3, 1 × CH), 6.03 (H-2, 1 × CH), 4.45 (H-6, 1 × CH), 2.91 (H-11, 1 ×-CH), 2.55 (H-1, 1 × CH), 2.47 (H-4, H-9, 2 × CH), 2.27 (H-7$_s$, 1 × ½CH$_2$, H-5, 1 × CH), 2.13 (H-8, 1 × CH), 1.80 (1 × OH), 1.57 (H-10$_s$, 1 × ½CH$_2$, 10.86 Hz), 1.54 (H-10$_a$, 1 × ½CH$_2$, 10.86 Hz) 1.49 and 1.46 (H-7$_a$, 1 × ½CH$_2$, 14.22 Hz, 4.56 Hz).

MS spectrum: EI, *m/z* 162 (M^+).

4.2.3. *Endo*-tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-yl acetate

Endo-tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-yl acetate (**121**) was prepared according to the methods described below.



121

Method 1

A mixture of the alcohol **118** (0.200 g, 1.23 mmol) and a catalytic amount of PTS (0.166 g, 2.10 mmol) in dry THF (10 cm^3) was refluxed for 30 minutes. Analysis of the reaction mixture with GC showed that a mixture of isomeric products had formed. The products were not isolated and the method was subsequently abandoned.

Method 2[168]

A catalytic amount of iodine (0.160 g, 0.620 mmol) was added to a stirred solution of alcohol **118** (1.000 g, 6.20 mmol) and dry pyridine (0.500g, 6.30 mmol) in 5 cm^3 of dry THF at room temperature. Analysis of the reaction mixture with GC showed that only 50% conversion to products had occurred in three days. The product was not isolated from the reaction mixture and the method was abandoned.

Method 3

The alcohol **118** (1.000 g, 6.20 mmol) and dry pyridine (0.500g, 6.30 mmol) were dissolved in 5 cm^3 of dry THF and placed in an ice bath. Acetic anhydride (0.643 g, 6.30 mmol) was added drop wise to the THF solution. The reaction mixture was stirred in the ice bath for 3 hours. The progress of the reaction was monitored with GC and fresh aliquots of the reagents were added until full conversion to product was achieved. The reaction mixture was slowly diluted with cold water. The mixture was extracted twice with dichloromethane and the combined organic layers washed with saturated Na_2CO_3 solution. Removal of the solvent under reduced pressure yielded the ester **121** as colourless oil (0.732 g, 73%).

Method 4

The alcohol **118** (0.334 g, 2.06 mmol) and dry pyridine (0.166 g, 2.10 mmol) were dissolved in 5 cm^3 of dry THF and placed in an ice bath. Acetyl chloride (0.165 g, 2.10 mmol) was added drop wise to the THF solution. The reaction mixture was stirred in the ice bath for 2 hours and then diluted with cold water. The mixture was extracted twice with dichloromethane and the combined organic layers washed with saturated Na_2CO_3 solution. Removal of the solvent under reduced pressure yielded the ester **121** as colourless oil (0.327 g, 78%).

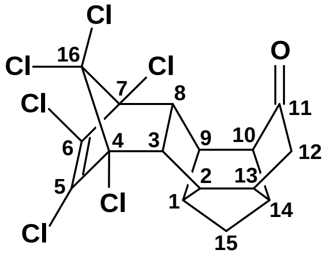
IR spectrum: ν_{max} 2939, 2866, 1727, 1361, 1237, 1195, 1080, 1039, 849, 726 cm^{-1}.

^{13}C-NMR [CDCl$_3$]: δ_C 171.1 (C-1', C=O), 140.6 (C-3, 1 × CH), 136.0 (C-2, 1 × CH), 78.5 (C-6, 1 × CH), 58.5 (C-11, 1 × CH), 51.1 (C-9, 1 × CH), 49.5 (C-5, 1 × CH), 47.5 (C-1, 1 × CH), 46.6 (C-4, 1 × CH), 41.9 (C-8, 1 × CH), 35.4 (C-7, 1 × CH_2), 32.1 (C-10, 1 × CH_2), 21.3 (C-2', 1 × CH_3).

^{1}H-NMR [CDCl$_3$]: δ_H 6.15 (H-3, 1 × CH), 5.81 (H-2, 1 × CH), 5.12 (H-6, 1 × CH), 2.84 (H-11, 1 × CH), 2.47 (H-9, H-1, 2 × CH), 2.40 (H-4, 1 × CH), 2.33 (H-5, 1 × CH), 2.20 (H-7_a, 1 × ½ CH_2), 2.09 (H-8, 1 × CH), 2.01 (H-2', 1 × CH_3), 1.63 (H-7_s, 1 × ½ CH_2), 1.55 (H-10_s, 1 × ½CH_2, 10.86 Hz), 1.52 (H-10_a, 1 × ½CH_2, 10.86 Hz).

MS spectrum: EI, *m/z* 204 (M^+).

4.2.4. 4,5,6,7,16,16-Hexachlorohexacyclo[7.6.1.0^{3,8}.0^{2,13}.0^{10,14}]hexadec-5-en-11-one



126b

The ketoalkene **1** (1.723 g, 11.0 mol) and 1,2,3,4,5,5-hexachloro-1,3-cyclopentadiene (2.934 g, 11.0 mmol) were added to toluene and refluxed for two days. Upon cooling the adduct **126b** (1.978 g, 43%; melting point: 124.3°C, decomposition) was isolated from the mixture by filtration.

IR spectrum: ν_{max} 2916, 2848, 1724, 1463, 719 cm^{-1}.

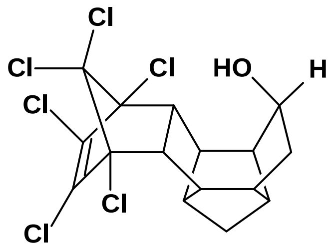
^{13}C-NMR [CDCl$_3$]: δ_C 220.1 (C-11, C=O), 131.01 (C-5/ C-6, 1 × CH), 130.99 (C-5/ C-6, 1 × CH), 104.2 (C-16, 1 × C), 80.9 (C-4/ C-7, 1 × C), 80.8 (C-4/ C-7, 1 × C), 56.5 (C-10, 1 × CH), 56.1 (C-8, 1 × CH), 55.6 (C-3, 1 × CH), 47.9 (C-1, 1 × CH), 46.3 (C-14, 1 × CH), 46.2 (C-9, 1 × CH), 41.0 (C-13, 1 × CH), 41.0 (C-12, 1 × CH_2), 40.7 (C-2, 1 × CH), 33.6 (C-15, 1 × CH_2).

^{1}H-NMR [CDCl$_3$]: δ_H 3.06 (H-3, H-8, 2 × CH), 2.66 (H-13, 1 × CH), 2.62 (H-14, 1 × CH), 2.50 (H-10, 1 × CH), 2.48 (H-9, 1 × CH), 2.45 (H-1, 1 × CH), 2.35 (H-12_s, 1 × ½ CH_2), 2.34 (H-2, 1 × CH), 2.21 (H-12_a, 1 × ½ CH_2), 1.76 (H-15_s, 1 ×½ CH_2, 11.28 Hz), 1.68 (H-15_a, 1 × ½ CH_2, 11.28 Hz).

MS spectrum: EI, *m/z* 432 (M^+).

XRD data: Please Refer to **Chapter 6**, p. 175.

4.2.5. *Exo*-11-hydroxy-4,5,6,7,16,16-hexachlorohexacyclo[7.6.1.0^{3,8}.0^{2,13}.0^{10,14}]hexadec-5-ene



125

Method 1

The hydroxyalkene **118** (0.240 g, 1.50 mmol) and 1,2,3,4,5,5-hexachloro-1,3-cyclopentadiene (0.404 g, 1.50 mmol) were added to toluene and refluxed for two days. Hydroxyalkene **118** (0.207 g, 86%) was recovered from the reaction mixture.

Method 2

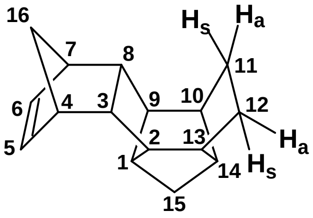
The ketone **134b** (1.082 g, 2.50 mmol) was dissolved in 20 cm^3 of THF and 10 cm^3 of ethanol in an ice bath. Small portions of $NaBH_4$ (0.189 g, 3.20 mmol) was added over a period of 5 minutes. The reaction mixture was stirred overnight during which time the temperature returned to room temperature. The reaction mixture was returned to an ice bath and unreacted $NaBH_4$ was destroyed by the slow addition of an excess amount of 3% hydrochloric acid solution. The reaction mixture was extracted with dichloromethane and analysed with GC-MS. Only starting material was detected.

Method 3[12]

The ketone **134b** (1.500 g, 3.46 mmol) was dissolved in a 0.4 M solution of $CeCl_3{\cdot}7H_2O$ in 25 cm^3 of THF and 15 cm^3 of methanol and cooled to 0^{o}C in an ice bath. Small portions of $NaBH_4$ (0.262 g, 6.93 mmol) was added at such a rate that the temperature of the reaction mixture remained at approximately 0^{o}C. After addition of the $NaBH_4$, the reaction mixture was stirred at room temperature for 4 hours and then refluxed for 8 hours. The reaction mixture was extracted with dichloromethane and analysed with GC-MS. Only starting material was detected.

4.2.6. Hexacyclo[7.6.1.0^{3,8}.0^{2,13}.0^{10,14}]hexadec-5-ene

A mixture of **126a/126b** (1.237 g, 2.80 mmol), hydrazine hydrate (32 cm^3), potassium hydroxide (4.332 g, 9.60 mmol) and diethylene glycol (30 cm^3) was refluxed for two hours. The refluxed condenser was removed and heating continued until the temperature of the mixture reached



127

195°C. The mixture was heated at this temperature for 4 hours. The mixture was allowed cool to room temperature and poured into an excess amount of 10% hydrochloric acid. The mixture was extracted twice with dichloromethane. Removal of the solvent under reduced pressure yielded a residue (1.006 g) that contained a mixture of partially dehalogenated hydrocarbons. The residue was dissolved in THF (20 cm^3). To the solution was added *t*-butanol (0.172 g, 2.30 mmol) and sodium (1.569 g, 68.3 mmol) chopped into small cubes. The reaction mixture was refluxed for 36 hours. The excess sodium in the cooled reaction mixture was destroyed with ethanol. The reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was separated and dried over anhydrous sodium sulphate. Removal of the solvent yielded the cage alkene **127** (0.319 g, 53%).

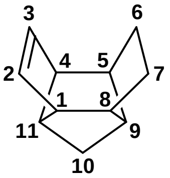
IR spectrum: ν_{max} 2930, 2863, 1455, 725 cm^{-1}.

^{13}C-NMR [CDCl$_3$]: δ_C 135.8 (C-5, C-6, 2 × CH), 53.6 (C-16, 1 × CH$_2$), 48.7 (C-14, 1 × CH), 47.4 (C-4, C-7, 2 × CH), 47.3 (C-3, C-8, 2 × CH), 46.5 (C-1, 1 × CH), 45.0 (C-10, C-13, 2 ×CH), 43.8 (C-2, C-9, 2 × CH), 30.8 (C-15, 1 × CH$_2$), 25.4 (C-12, 1 × CH$_2$).

^{1}H-NMR [CDCl$_3$]: δ_H 6.03 (H-5, H-6, 2 × CH), 2.69 (H-4, H-7, 2 × CH), 2.58 (H-1, 1 × CH), 2.57 (H-3, H-8, 2 × CH), 1.99 (H-10, H-13, H-14, 3 × CH), 1.78 (H-11$_a$, H-12$_a$, 2 × ½CH$_2$), 1.66 (H-2, H-9, 2 × CH), 1.49 (H-11$_s$, H-12$_s$, 2 × ½CH$_2$), 1.36 (H-16, 1 × CH$_2$), 1.29 (H-15, 1 × CH$_2$).

MS spectrum: EI, *m/z* 212 (M$^+$).

4.2.7. Tetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-ene



159

A mixture of the cage compound **1** (1.600 g, 10.9 mmol), hydrazine hydrate (1.4 cm^3), potassium hydroxide (1.892 g, 33.8 mmol) and diethylene glycol (14 cm^3) was refluxed for two hours. The refluxed condenser was removed and heating continued until the temperature of the mixture reached 195°C. The mixture was heated at this temperature for 4 hours. During this time a white solid collected at the bottom of the cooler. The reaction mixture was allowed to cool to room temperature and the crude product (1.418 g) collected from the cooler. The solid was taken up in dichloromethane and washed with water. The organic layer was separated and dried over anhydrous sodium sulphate. Removal of the solvent yielded the cage alkene **159** (0.844 g, 58%).

IR spectrum: ν_{max} 3055, 2933, 2861, 848, 749, 706 cm^{-1}

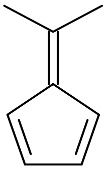
^{13}C-NMR [$CDCl_3$]: δ_C 138.8 (C-2, C-3, 2 × CH), 57.8 (C-11, 1 × CH), 47.6 (C-1, C-4, 2 × CH), 46.2 (C-5, C-8, 2 × CH), 31.2 (C-10, 1 × CH), 28.3 (C-6, C-7, 2 × CH_2).

^{1}H-NMR [$CDCl_3$]: δ_H 6.06 (H-2, H-3, 2 × CH), 2.38 (H-1, H-4, 2 × CH), 2.38 (H-9, 1 × CH), 2.17 (H-5, H-8, 2 × CH), 1.52 (H-10, 1 × CH_2), 1.48 (H-6_a, H-7_a, 2 × ½CH_2), 2.75 (H-11, 1 × CH), 1.60 (H-6_s, H-7_s, 2 × ½CH_2)

MS spectrum: *m/z* 146 (M^+).

4.3. Synthesis of 10-isopropylidenetetracyclo[6.3.0.0^{4,11}.0^{5,9}]undec-2-en-6-one

4.3.1. 6,6-Dimethylfulvene[233]

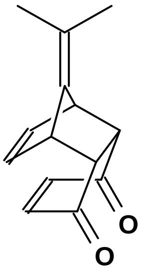


21

Pyrrolidine (21.336 g, 0.300 mol) was added to a stirred solution of acetone (11.615 g, 0.200 mol) and cyclopentadiene (33.053 g, 0.500 mol) in methanol (200 cm^3) in an ice bath. Acetic acid (19.216 g, 0.230 mol) was added to the reaction mixture after 15 minutes. The reaction mixture was poured into a large excess of water and extracted with diethyl ether. The organic layer was dried over anhydrous sodium sulphate. The solvent and unreacted cyclopentadiene were removed under reduced pressure using a room temperature water bath. Diethyl ether could be omitted during the extraction step when larger amounts (~10g) of 6,6-dimethylfulvene were prepared. The reaction mixture was poured into water in a separatory funnel and the organic layer was separated and dried over anhydrous sodium sulphate. Removal of the unreacted cyclopentadiene under reduced pressure yielded 6,6-dimethylfulvene (**21**, 19.080 g, 90%) of purity > 90% (GC) in all runs. The spectral data was identical to that of an authentic sample.

4.3.2. *Exo*-11-(propan-2-ylidene)tricyclo[6.2.1.0^{2,7}]undeca-4,9-diene-3,6-dione

The adduct (**22b**) was prepared according to the methods described below. The spectral data was identical to that of an authentic sample.



22b

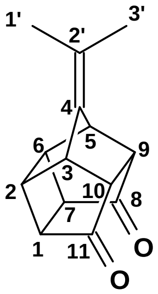
Method 1[183]**: Water as solvent**

6,6-dimethylfulvene **21** (21.200 g, 0.200 mol) was added drop wise to a mechanically stirred mixture of 1,4-benzoquinone **11** (21.600 g, 0.200 mol) in 100 cm^3 of water. (Mechanical stirring is essential becomes the reaction mixture is highly viscous.) The mixture was stirred for 12 hours during which time the product solidified. The solid product was crushed with a mortar and pestle. To the fine powder was added a small amount of ethanol to produce a slurry. The slurry was filtered and the filter cake washed numerous times with small amounts of ethanol until the filtrate became clear and almost colourless. The yield of adduct **22b** was 25.731 g (60%). A pure sample was obtained by recrystallisation from ethanol. The spectral data was identical to that of an authentic sample.

Method 2: No solvent

6,6-dimethylfulvene **21** (10.600 g, 0.100 mol) was added to 1,4-benzoquinone **11** (10.800 g, 0.100 mol) in a small beaker. The mixture was stirred mechanically for 12 hours during which time the mixture solidified. The solid product was crushed with a mortar and pestle. To the fine powder was added a small amount of ethanol to produce a slurry. The slurry was filtered and the filter cake washed numerous times with small amounts of ethanol until the filtrate became clear and colourless. The yield of adduct **22b** was 16.504 g (77%). A pure sample was obtained by recrystallisation from ethanol. The spectral data was identical to that of an authentic sample.

4.3.3. 4-Isopropylidenepentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione[183]



23

Solutions of the adduct **22b** in acetone (0.500 g/50 cm^3) was placed in Pyrex tubes. The content of each tube was purged with dry N_2 for 2 minutes. The tubes were sealed and then irradiated with a 1000 W medium pressure mercury vapour lamp at room temperature for 2 hours. During this time, crystals of the cage compound formed inside the tubes. Filtration of the crystals yielded the cage dione **23** (melting point: 245.0^{o}C, literature[183]). A second crop was obtained by careful evaporation of the solvent until a powdered product settled out. The powder was filtered and washed with small amounts of ethanol. The total yield of the cage dione was 0.200 g (40%). A pure sample was obtained by recrystallisation from acetone.

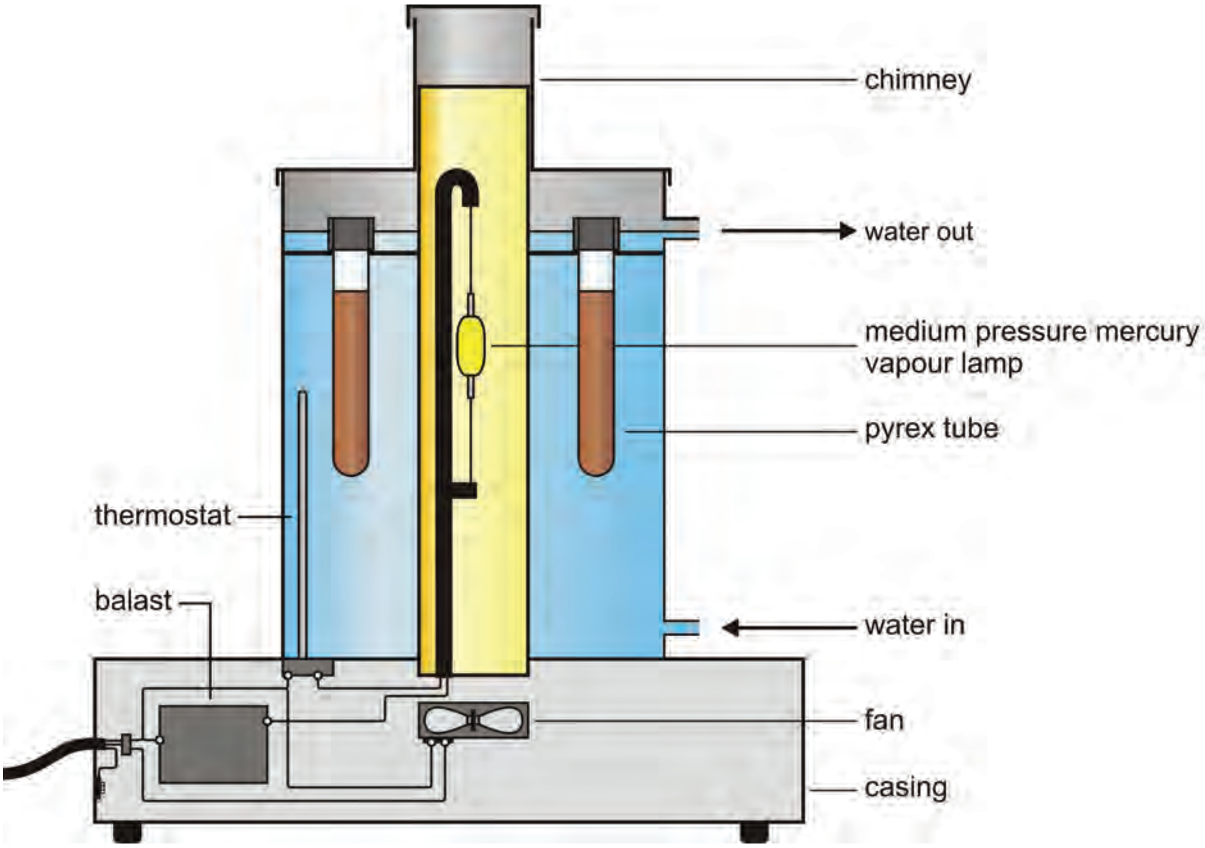


Figure 4.1: Irradiation apparatus with safety temperature cut-off developed during this study.

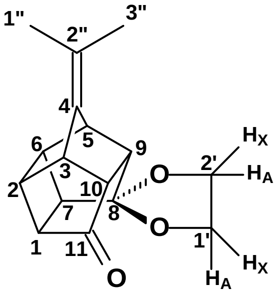
IR spectrum: ν_{max} 3002, 1728, 1041 cm^{-1}.

^{13}C-NMR [CDCl$_3$]: 212.1 (C-8, C-11, 2 × C=O), 140.2 (C-4, 1 × C), 121.9 (C-2', 1 × C), 53.5 (C-3, C-5, 2 × CH), 44.4 (C-9, C-10, 2 × CH), 43.2 (C-2, C-6, 2 × CH), 38.1 (C-1, C-7, 2 × CH), 21.3 (C-1', C-3', 2 × CH$_3$).

^{1}H-NMR [CDCl$_3$]: 3.25 (H-2, H-6, 2 × CH) 3.16 (H-1, H-7, 2 × CH), 2.81 (H-9, H-10, 2 × CH), 2.69 (H-3, H-5, 2 × CH), 1.73 (H-1', H-3', 2 × CH$_3$).

MS spectrum: 214 (M$^+$).

4.3.4. 8-(Ethylene ketal)-4-isopropylidenepentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-11-one



132

A mixture of dione **23** (10.000 g, 0.470 mol), ethylene glycol (2.900 g, 0.470 mol), PTS (0.125 g) and toluene (50 cm^3) was refluxed (Dean-Stark apparatus) for 12 hours. The reaction mixture was allowed to cool to room temperature, poured into 50 cm^3 of 10% Na$_2$CO$_3$ solution and extracted with dichloromethane. The organic layer was washed with two portions of saturated sodium chloride solution and once with water. Evaporation of the solvent under reduced pressure yielded the ketal **132** (10.400 g, 86% melting point: 175.8^{o}C). A pure sample was obtained by recrystallisation from acetone.

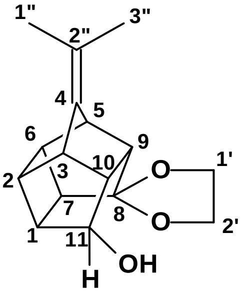
IR spectrum: ν_{max} 2980, 1734, 1104 cm^{-1}.

^{13}C-NMR [CDCl$_3$]: δ_C 215.1 (C-11, 1 × C=O), 140.4 (C-4, 1 × C), 119.7 (C-2", 1 × C), 113.9 (C-8, 1 × C), 65.7 (C-2', 1 × CH$_2$), 64.6 (C-1', 1 × CH$_2$), 52.1 (C-7, 1 × CH), 49.9 (C-9, 1 × CH), 44.8 (C-1, 1 × CH), 43.2 (C-3, 1 × CH), 41.7 (C-10, 1 × CH), 41.4 (C-5, 1 × CH), 40.8 (C-2, 1 × CH), 35.6 (C-6, 1 × CH), 21.02 (C-3", 1 × CH$_3$), 20.99 (C-1", 1 × CH$_3$).

^{1}H-NMR [CDCl$_3$]: δ_H 3.92 (H-2'$_A$, 1 × ½CH$_2$), 3.92 (H-2'$_X$, 1 × ½CH$_2$), 3.85 (H-1'$_A$, 1 × ½ CH$_2$), 3.92 (H-1'$_X$, 1 × ½ CH$_2$), 3.16 (H-1, 1 × CH), 2.98 (H-2, 1 × CH), 2.95 (H-10, 1 × CH), 2.83 (H-6, 1 × CH), 2.67 (H-3, 1 × CH), 2.58 (H-5, 1 × CH), 2.49 (H-7, 1 × CH), 2.46 (H-9, 1 × CH), 1.69 (H-1", 1 × CH$_3$), 1.67 (H-3", 1 × CH$_3$).

MS spectrum: *m/z* 258 (M$^+$).

4.3.5. *Endo*-8-(ethylene ketal)-11-hydroxy-4-isopropylidenepentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]-undecane-8-one



133

Ketal **132** (4.000 g, 16.0 mmol) was dissolved in 100 cm^3 of THF and 30 cm^3 of ethanol in an ice bath. Small portions of NaBH$_4$ (1.200 g, 3.20 mmol) was added over a period of 5 minutes. The reaction mixture was stirred for 4 hours during which the temperature returned to room temperature. The alcohol was precipitated by the addition of an excess amount of water and isolated by filtration. Recrystallisation from acetone yielded the pure alcohol **133** (3.100 g, 74%, melting point: 169.4 – 173.7^{o}C).

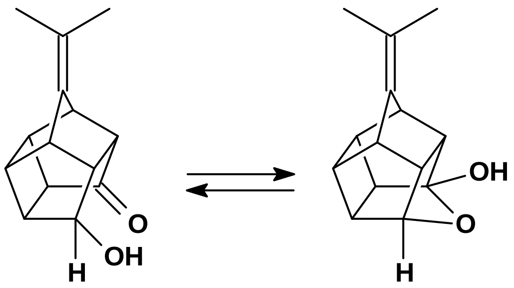
IR spectrum: ν_{max} 3428, 2958, 1455, 1076, 572 cm^{-1}.

^{13}C-NMR [CDCl$_3$]: δ_C 139.1 (C-4, 1 × C), 117.4 (C-2", 1 × C), 115.7 (C-8, 1 × C), 72.7 (C-11, 1 × CH), 65.6 (C-1'/ C-2', 1 × CH$_2$), 63.0 (C-2'/ C-1', 1 × CH$_2$), 46.8 (C-7, 1 × CH), 46.4 (C-9, 1 × CH), 43.6 (C-5, 1 × CH), 42.7 (C-3, 1 × CH), 39.3 (C-10, 1 × CH), 39.2 (C-6, 1 × CH), 39.0 (C-1, 1 × CH), 38.4 (C-2, 1 × CH), 20.8 (C-1"/ C-3", 1 × CH$_3$), 20.7 (C-3"/ C-1", 1 × CH$_3$).

^{1}H-NMR [CDCl$_3$]: δ_H 5.34 (OH), 4.00 (H-1'/ H-2', 1 × CH$_2$), 3.93 (H-2'/ H-1', 1 × ½CH$_2$, 43.29), 3.86 (H-2'/ H-1', 1 × ½CH$_2$, 43.29), 3.65 (H-11, 1 × ½ CH), 3.63 (H-11, 1 × ½ CH), 2.89 (H-5, 1 × CH), 2.72 (H-1, 1 × CH), 2.67 (H-6, 1 × CH), 2.57 (H-2, 1 × CH), 2.48 (H-7, 1 × CH), 2.48 (H-10, 1 × CH), 2.24 (H-9, 1 × CH), 1.65 (H-1"/ H-3", 1 × CH$_3$), 1.63 (H-3"/ H-1", 1 × CH$_3$).

MS spectrum: *m/z* 260 (M$^+$).

4.3.6. *Endo*-11-hydroxy-4-isopropylidenepentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]-undecane-8-one



134

To a solution of hydroxyketal **133** (2.600 g, 10.0 mmol) in 25 cm^3 of THF was added 25 cm^3 of 10% hydrochloric acid solution. The mixture was refluxed for 3 hours. After cooling the mixture was extracted twice with 25 cm^3 portions of dichloromethane. The combined extracts was washed with 10% Na_2CO_3 solution, dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The crude product was recrystallised from acetonitrile to yield a mixture of **134a** and **134b** (1.858 g, 86%, melting point: 160.0 – 165.6°C).

IR spectrum: ν_{max} 3559, 2975, 1717, 1344, 989 cm^{-1}.

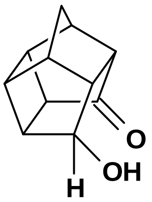
^{13}C-NMR [$CDCl_3$]: δ_C. 219.1 (C=O), 145.9 (C), 140.4 (C), 119.3 (C), 118.9 (C), 115.8 (C), 81.8 (CH), 72.5 (CH), 54.6 (CH), 53.4 (CH), 53.3 (CH), 49.1 (CH), 46.4 (CH), 45.3 (CH), 44.8 (CH), 44.2 (CH), 43.9 (CH), 42.5 (CH), 41.10 (CH), 41.05 (CH), 40.7 (CH), 40.6 (CH), 40.5 (CH), 36.0 (CH), 21.0 (CH_3), 20.9 (CH_3), 20.8 (CH_3), 20.7 (CH_3).

^{1}H-NMR [$CDCl_3$]: δ_H 4.63 (1 × CH), 4.60 (OH), 4.07 (1 × CH), 3.06 – 2.98 (2 × CH), 2.98 – 2.95 (1 × CH), 2.93 – 2.88 (2 × CH), 2.87 – 2.79 (4 × CH), 2.76 (1 × CH), 2.59 (1 × CH), 2.54 (1 × CH), 2.50 – 2.43 (3 × CH), 1.85 (OH), 1.65 (2 × CH_3), 1.59 (1 × CH_3), 1.57 (1 × CH_3).

MS spectrum: *m/z* 216 (M^+).

4.3.7. Halogenation of cage alcohols

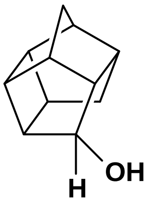
4.3.7.1. 11-Hydroxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-one



139

Hydroxyketone **139** was synthesised from the dione **44**[68] according to the procedure reported by Dekker and Oliver[200]. The spectral data was identical to that of an authentic sample.

4.3.7.2. *Endo*-pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-ol



140

Decarbonylation of **139** was achieved with a standard literature procedure[171]. The spectral data was identical to that reported by Dekker and Oliver[200].

Halogenation method 1: PPh_3 and CCl_4[234]

To a solution of the alcohol (0.100 mol) in THF (45 cm^3) and CCl_4 (45 cm^3) was added triphenylphosphine (0.130 mol). The reaction mixture was refluxed for 1 – 24 hours depending on the results of continual GC analysis.

Halogenation method 2: TMSCl and SeO_2[210]

Chlorotrimethylsilane (20.0 mmol) and selenium dioxide (0.20 mmol) was added to 10 cm^3 of THF. The mixture was stirred for 10 minutes at room temperature. Cage alcohol (10.3 mmol) was added and the reaction mixture was refluxed for 5 hours. Analysis of the reaction mixture with GC-MS revealed the success of the reaction.

Halogenation method 3: $POCl_3$ and pyridine[51]

Phosphorus oxychloride (6.50 mmol) was slowly added to a solution of the alcohol (1.30 mmol) in 5 cm^3 pyridine. The reaction mixture was refluxed for 5 hours and then poured into ice water. This mixture was extracted with dichloromethane, washed with 10% hydrochloric acid, and analysed with GC-MS.

Halogenation method 4: $SOCl_2$

The alcohol (9.00 mmol) was added to an excess amount of thionyl chloride and cooled in an ice bath. The mixture was stirred at room temperature and poured into an excess amount of water. The water mixture was extracted with dichloromethane. The solution was analysed with GC-MS. The reaction was repeated at reflux temperature.

Halogenation method 5: $SOCl_2$ and pyridine[213]

The alcohol (9.00 mmol) was dissolved in dry THF and cooled in an ice bath. To the solution was added dropwise pyridine (0.8 cm^3, 10 mmol) and then thionyl chloride (1.0 cm^3, 14 mmol). The mixture was refluxed overnight, allowed to cool and poured into an excess amount of water. The water mixture was extracted with dichloromethane. The solution was analysed with GC-MS.

Halogenation method 6: MsCl and LiCl[211]

To a stirred solution of alcohol (0.100 mol) and pyridine (0.110 mol) was added lithium chloride (0.100 mol) dissolved in a minimum amount of dry dimethylformamide. The mixture was cooled in an ice bath and then treated dropwise with methanesulphonyl chloride (0.110 mol). Stirring was continued for 1.5 hours after which the reaction mixture was poured into ice water. The reaction mixture was extracted with dichloromethane and analysed with GC-MS.

Halogenation method 7: $CeCl_3{\cdot}7H_2O$, NaI and SiO_2 with microwave radiation[216]

Sodium iodide (1.00 mmol), $CeCl_3{\cdot}7H_2O$ (1.00 mmol), SiO_2 (1 g) and alcohol (1.00 mmol) were intimately mixed in a mortar and irradiated with microwaves for 30 seconds using high level (900 W). The reaction mixture was cooled to room temperature and irradiated for a further 30 seconds. The reaction mixture was extracted with dichloromethane and analysed with GC-MS.

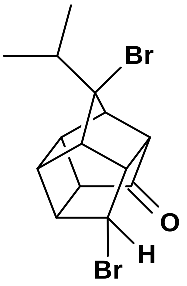
Halogenation method 8: PPh_3 and I_2 with microwave radiation[217]

In a mortar a mixture of alcohol (1.00 mmol), I_2 (1.00 mmol) and triphenylphosphine (1.00 mmol) was ground to a homogeneous mixture. The mixture was sealed in a plastic container and irradiated in a microwave oven for 1 minute. The reaction mixture was extracted with dichloromethane and analysed with GC-MS.

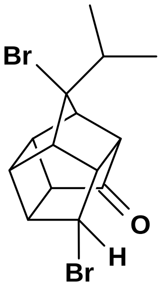
Halogenation method 9: CH_3SO_3H and NaI[218]

To a vigorously stirred solution of NaI (2.00 mmol) and alcohol (1.00 mmol) in acetonitrile (10 cm^3) under nitrogen was added methanesulphonic acid (2.00 mmol) in 2 cm^3 of acetonitrile at room temperature. The reaction mixture was stirred for 15 minutes and was then quenched with water. The reaction mixture was extracted with dichloromethane and analysed with GC-MS.

4.3.8. *Exo*-4,11-dibromo-4-isopropylpentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8-one



151a



151b

The mixture **134a/134b** (1.800 g, 8.00 mmol) was heated in an excess amount of 48% HBr for 3 hours. The content of the reaction flask was poured into water. The residue remaining in the flask was dissolved in dichloromethane and added to the water mixture. The water mixture was extracted with dichloromethane. The organic layer was washed with 10% sodium carbonate solution and then with saturated sodium chloride solution. Removal of the solvent under reduced pressure yielded **151a/151b** as thick oil (0.050 g, 2%) that sometimes solidified to a white solid (melting point: 96.7 – 100.7^{o}C) on standing for a few weeks.

IR spectrum: ν_{max} 2997, 2970, 2935, 2875, 1736, 1466, 1296, 1261, 1101, 856, 787, 771, 730, 667 cm^{-1}.

^{13}C-NMR [CDCl$_3$]: δ_C 213.39 (C-8, C=O), 213.36 (C-8, C=O), 88.4 (C-4, C), 87.0 (C-4, C), 57.62 (CH), 57.61 (CH), 57.3 (CH), 54.7 (CH), 53.6 (CH), 53.5 (C-11, CH), 52.84 (CH), 52.76 (CH), 52.4 (C-11, CH), 51.6 (CH), 47.6 (CH), 45.43 (CH), 45.36(CH), 45.3 (CH), 44.3 (CH), 41.2 (CH), 37.4 (CH), 34.4 (C-2', CH), 34.2 (CH), 31.7 (C-2', CH), 19.95 (C-1'/C-3', CH$_3$), 19.90 (C-1'/C-3', CH$_3$), 19.8 (C-1'/C-3', CH$_3$), 19.6 (C-1'/C-3', CH$_3$).

^{1}H-NMR [CDCl$_3$]: δ_H 4.40 (1 × CH), 4.28 (1 × CH), 3.54 (1 × CH), 3.48 (3 × CH), 3.30 (2 × CH), 3.19 (2 × CH), 3.09 (1 × CH), 2.93 (4 × CH), 2.73 (2 × CH), 2.59 (1 × CH), 1.54 (2 × CH), 1.14 (1 × CH$_3$), 1.10 (1 × CH$_3$), 1.07 (1 × CH$_3$), 1.02 (1 × CH$_3$).

MS spectrum: *m/z* 360 (M$^+$).

4.3.9. Reductive dehalogenation of the dibromoketone 151

Method 1: Zinc and acetic acid

The dibromoketone mixture **151a/151b**, (1.200 g, 3.00 mmol), acetic acid (15 cm^3) and zinc powder (1.526 g, 23.0 mmol) was refluxed for 10 minutes to 12 hours. The reaction mixture was filtered and the filtrate poured into water. A precipitate formed that was filtered and washed consecutively with 10% sodium carbonate solution and water. The precipitate was poorly soluble in conventional solvents and could not be analysed satisfactorily.

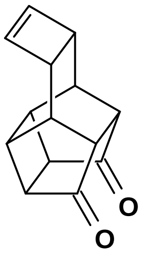
Method 2: Zinc and methanol

The dibromoketone mixture **151a/151b**, (1.200 g, 3.00 mmol) and zinc powder (1.526 g, 2.30 mmol) was refluxed in methanol (15 cm^3) for 12 hours. The reaction mixture was filtered to separate the unreacted zinc. Analysis of the filtrate with GC-MS indicated only the presence of starting material.

Method 3: Zinc and ammonium chloride[215]

The dibromoketone mixture **151a/151b**, (1.200 g, 2.00 mmol) and zinc powder (1.526 g, 4.00 mmol) was refluxed in a mixture of saturated aqueous ammonium chloride (4 cm^3) and THF (2 cm^3) for 5 hours. Unreacted zinc was separated and washed with water. The reaction mixture was diluted with water and extracted with dichloromethane. Analysis of the organic layer with GC-MS indicated only the presence of starting material.

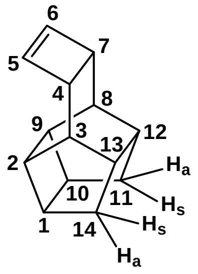
4.4. Synthesis of Hexacyclo[8.4.0.$0^{2,9}$.$0^{3,13}$.$0^{4,7}$.$0^{4,12}$]tetradec-5-en-11,14-dione



3

Compound **3** was synthesised according to the procedure reported by Barborak *et. al*[147]. The spectral data was identical to that of an authentic sample. Spectra for **3** are reported in the spectral data section (➡ p. 167).

4.4.1. Hexacyclo[8.4.0.$0^{2,9}$.$0^{3,13}$.$0^{4,7}$.$0^{4,12}$]tetradec-5-ene



175

A mixture of the cage compound **3** (1.000 g, 4.70 mmol), hydrazine hydrate (2 cm^3), potassium hydroxide (1.785 g, 3.20 mmol) and diethylene glycol (10 cm^3) was refluxed for two hours. The refluxed condenser was removed and heating continued until the temperature of the mixture reached 195°C. The mixture was heated at this temperature for 4 hours. The mixture was allowed to cool to room temperature and poured into an excess amount of 10% hydrochloric acid. The mixture was extracted twice with dichloromethane. The organic layer was separated and dried over anhydrous sodium sulphate. Removal of the solvent yielded the cage alkene **175** (0.608 g, 70%).

IR spectrum: ν_{max} 3030, 2931, 2893, 752 cm^{-1}

^{13}C-NMR [CDCl$_3$]: δ_C 140.5 (C-5, C-6, 2 × CH), 41.1 (C-3, C-8, 2 × CH), 41.0 (C-4, C-7, 2 × CH), 37.3 (C-12, C-13, 2 × CH), 36.7 (C-1, C-10, 2 × CH), 36.1 (C-2, C-9, 2 × CH), 27.1 (C-11, C-14, 2 × CH$_2$)

^{1}H-NMR [CDCl$_3$]: δ_H 6.16 (H-5, H-6, 2 × CH), 2.94 (H-4, H-7, 2 × CH), 2.63 (H-1, H-10, 2 × CH), 2.50 (H-2, H-9, 2 × CH), 2.18 (H-12, H-13, 2 × CH), 1.78 (H-11$_s$, H-14$_s$, 2 × ½CH$_2$, 11.70 Hz), 1.51 (H-3, H-8, 2 × CH), 0.86 (H-11$_a$, H-14$_a$, 2 × ½CH$_2$, 11.70 Hz)
MS spectrum: *m/z* 184 (M$^+$).

4.5. ROMP reactions

4.5.1. General method for ROMP

The cage monomer was dissolved in dry THF or CHCl$_3$ in a mini reactor (glass vial) or conventional reflux setup (**Figure 4.2**). Grubbs catalyst was added to the solution. The amounts of monomer, catalyst and solvent as well as the reaction conditions used in the various runs are indicated in **Table 4.1**. After the specified reaction time had elapsed, the reaction mixtures were poured into vigorously stirred methanol. Precipitates were filtered off and dried at 100°C to constant mass.

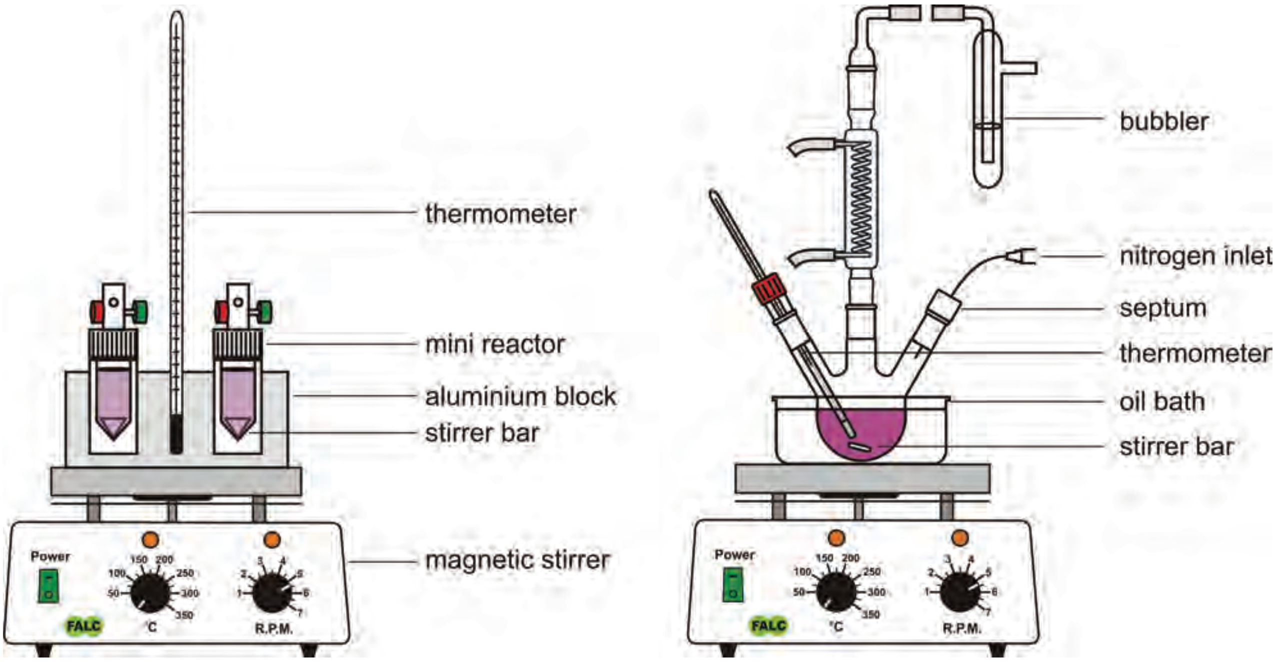
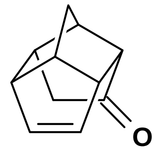
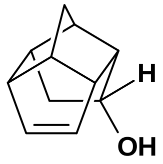
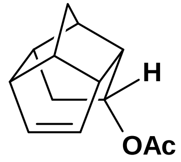
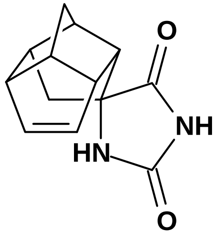


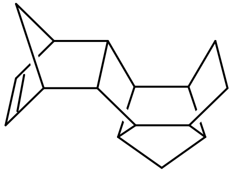
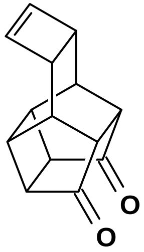
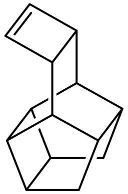
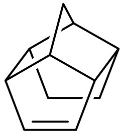
Figure 4.2: Apparatus used for polymerisation reactions.

Table 4.1: ROMP of cage monomers with Grubbs-I and Grubbs-II

Monomer	m (mg)	catalyst	m (mg)	ratio	Solvent	V (cm^3)	t (^oC)	t (h)	yield
 **1**	160.3	Grubbs-I	16.5	50: 1	THF	1.0	25	24	–
	159.6	Grubbs-II	16.9	50: 1	THF	1.0	25	24	–
	160.4	Grubbs-II	17.1	50: 1	THF	1.0	66	24	–
	327.0	Grubbs-II	34.7	50: 1	THF	1.0	25	24	–
	30.0	Grubbs-II	3.2	50: 1	$CHCl_3$	0.4	40	3	–
 **118**	112.0	Grubbs-I	11.4	50: 1	THF	1.0	25	24	–
	125.0	Grubbs-II	14.1	46:1	THF	1.0	25	24	–
	162	Grubbs-II	17.0	50: 1	THF	1.0	25	20	–
 **121**	212.0	Grubbs-I	19.1	45: 1	THF	1.0	25	24	–
	250.0	Grubbs-II	21.4	49: 1	THF	1.0	25	24	–
 **156**	57.5	Grubbs-I	5.0	42: 1	$CHCl_3$	2.0	25	24	–
	50.2	Grubbs-II	5.2	36:1	$CHCl_3$	2.0	25	24	–
	230.0	Grubbs-II	17.0	50: 1	$CHCl_3$	3.0	61	5	–

[#] Solubility poor in $CHCl_3$ and THF at 25°C.

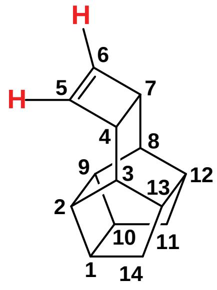
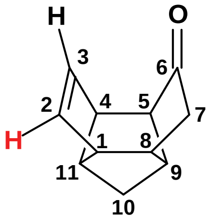
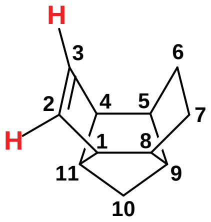
Table 4.1: ROMP of cage monomers with Grubbs-I and Grubbs-II (continued)

Monomer	m (mg)	Catalyst	m (mg)	Ratio	Solvent	V (cm^3)	t (^oC)	t (h)	yield
 **127**	103.0	Grubbs-I	8.0	50: 1	THF	1.0	25	24	7%
	90.0	Grubbs-II	8.5	42: 1	THF	1.0	25	24	15%
 **3**	60.0	Grubbs-I	2.5	50: 1	THF	1.0	45	20	21%
	40.0	Grubbs-II	3.2	50: 1	THF	4.5	25	20	45%
	40.0	Grubbs-II	3.2	50: 1	THF	2.0	61	20	52%
	30.0	Grubbs-II	2.4	50: 1	$CDCl_3$	0.4	45	3	48%
 **175**	114.0	Grubbs-I	10.7	48:1	THF	1.0	25	12	73%
	158.0	Grubbs-II	15.2	48: 1	THF	1.0	25	12	83%
 **159**	124.0	Grubbs-I	14.0	50: 1	THF	1.0	25	15	No data
	130.0	Grubbs-II	15.0	51: 1	THF	1.0	25	15	19%[a]

4.5.2. General method for ROMP NMR experiments

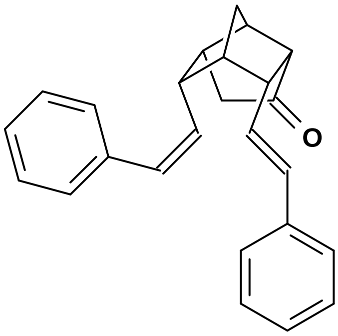
An NMR tube was charged with a solution of cage monomer and Grubbs-II catalyst in dry deuterated solvent. The solution was equilibrated at 40°C in the NMR machine after which spectra were collected at 10-minute intervals for 3 hours. The amounts of monomer, catalyst and solvent used in the various runs are indicated in **Table 4.2**. The conversion of monomer to polymer was determined from the ratio of the integrals of appropriate olefinic proton(s) in the cage monomer and the TMS signal at δ_H 0.00.

Table 4.2: NMR experiments with selected cage monomers and Grubbs-II

Monomer	Solvent	Mon :cat	Data collection range	t (°C)	Sample information
 **3**	$CDCl_3$	50: 1	0 – 21 ppm	40°C	30 mg **3** 2.4 mg Gr^{II} 0.4 ml $CHCl_3$
 **1**	$CDCl_3$	50: 1	0 – 21 ppm	40°C	30 mg **1** 3.2 mg Gr^{II} 0.4 ml $CHCl_3$
	C_6D_6	50: 1	0 – 31 ppm	40°C	30 mg **1** 3.2 mg Gr^{II} 0.4 ml $CHCl_3$
	$CDCl_3$	50: 1	0 – 31 ppm	40°C	30 mg **1** 3.2 mg Gr^{II} 0.4 ml $CHCl_3$
 **159**	$CDCl_3$	50: 1	0 – 21 ppm	40°C	30 mg **159** 3.5 mg Gr^{II} 0.4 ml $CHCl_3$

4.5.3. GC-MS analysis of the 1/Grubbs-II reaction mixture

An additional experiment was performed to verify that no coordination took place between the **1** and Grubbs-II. An equimolar mixture of **1** and Grubbs-II was stirred in chloroform at 40^{o}C for 12 hours. After this time an excess amount of styrene (capping reagent) was added. Analysis of the reaction mixture did not yield the expected (**157**) at m/z 340.



157

4.6. Molecular modelling

4.6.1. Hardware specifications

4.6.1.1. Desktop computer

HPPro3010 computer with the following specifications: Intel® Core™ 2 Quad CPU; Q8400 @ 2.66 GHz; 3.46 GB of RAM (2.66 GHz).

4.6.1.2. High performance computing cluster

The high performance computing cluster has the following specifications: 336 CPUs; 1 × Master Node: HP BL460C G6 - 2 Quad Core 2.93 GHz, 16 GB RAM, 2 146 GB HDD; 40 × Compute Nodes: HP BL460C G6 - 2 Quad Core 2.93 GHz, 16GB RAM, 2 146 GB HDD, ProLiant BL2x220c G5, HP BL460C G1; 1 × HP EVA 4400 SAN 3TB; 1 × Storage Server :HP BL460C G6; Operating system on compute nodes: Scientific Linux SL release 5.3; Cluster operating system : Rocks 5.2 - Scientific Linux SL release 5.3.

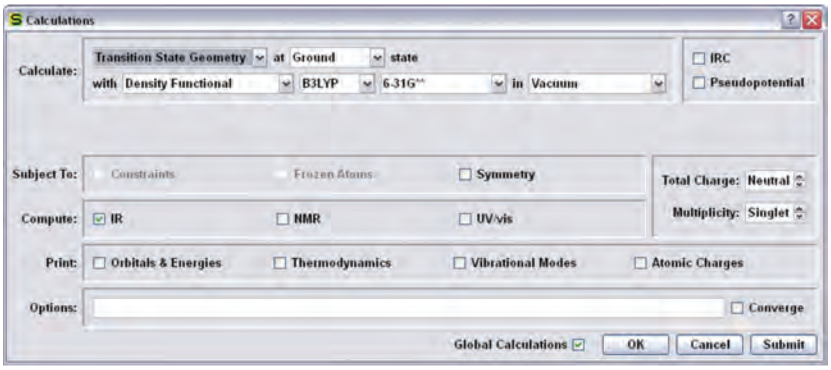
4.6.2. Software specifications

Molecular modelling were performed with Spartan '08 (revision 1.2.0) and the DMol^3 application in Accelrys Materials Studio® 5.0.

4.6.3. Molecular modelling techniques

Geometry optimisations, determination of electronic properties, conformational searches, and transition state searches were performed with the above-mentioned software applications. The energy values obtained in this study are the electronic energies at 0 K.

4.6.3.1. Geometry optimisation



Calculations

Calculate: Transition State Geometry at Ground state

with Density Functional B3LYP 6-31G** in Vacuum

☐ IRC

☐ Pseudopotential

Subject To: Constraints Frozen Atoms ☐ Symmetry

Total Charge: Neutral

Multiplicity: Singlet

Compute: ☑ IR ☐ NMR ☐ UV/vis

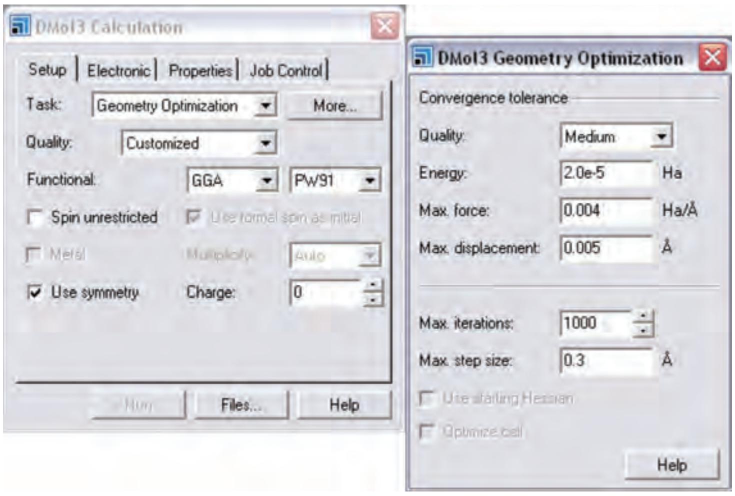
Print: ☐ Orbitals & Energies ☐ Thermodynamics ☐ Vibrational Modes ☐ Atomic Charges

Options: ☐ Converge

Global Calculations ☑

Figure 4.3: General setup used for geometry optimisation calculations in Spartan®.

Geometry optimisations in systems involving organic compounds only were performed with Spartan® '08 at the B3LYP/6-31G** level of theory (**Figure 4.3**). Calculations for systems involving ruthenium complexes were performed with the DMol^3 application in Accelrys Materials Studio® 5.0 at the GGA-PW91/DNP level of theory. **Figure 4.4** shows the setup used for geometry optimisation with DMol^3. The criteria applied for convergence of geometric optimisations were threshold values for energy (2×10^{-5} Ha), gradient (0.004 Ha·Å^{-1}), and displacement convergence (0.005 Å).



DMol3 Calculation

Task: Geometry Optimization

Quality: Customized

Functional: GGA PW91

☐ Spin unrestricted ☑ Use formal spin as initial

☐ Metal Multiplicity: Auto

☑ Use symmetry Charge: 0

DMol3 Geometry Optimization

Convergence tolerance

Quality: Medium

Energy: 2.0e-5 Ha

Max. force: 0.004 Ha/Å

Max. displacement: 0.005 Å

Max. iterations: 1000

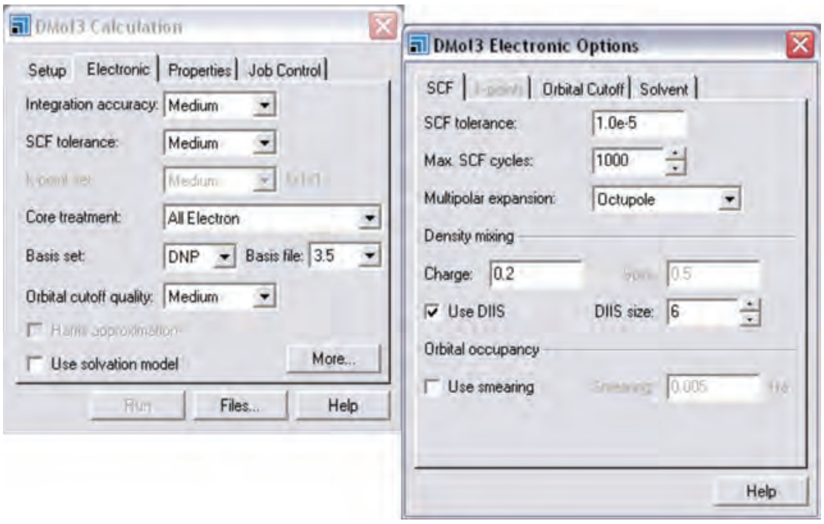
Max. step size: 0.3 Å

☐ Use starting Hessian

☐ Optimize cell

Figure 4.4: Setup for geometry optimisation with DMol^3.

The maximum number of iterations, multiplicity, and charge were set to 1000, automatic and zero, respectively (**Figure 4.5**). A maximum step size of 0.3 Å was used and a self consisted field (SCF) density convergence threshold value of 1 × 10^{-5} Ha was specified. The maximum number of SCF cycles was set to 1000.



DMol3 Calculation

Integration accuracy: Medium

SCF tolerance: Medium

Core treatment: All Electron

Basis set: DNP

Basis file: 3.5

Orbital cutoff quality: Medium

☐ Use solvation model

DMol3 Electronic Options

SCF tolerance: 1.0e-5

Max. SCF cycles: 1000

Multipolar expansion: Octupole

Density mixing

Charge: 0.2

☑ Use DIIS

DIIS size: 6

Orbital occupancy

☐ Use smearing

Figure 4.5: Electronic setup for geometry optimisation with $DMol^3$.

The electronic energy, total electron density, HOMOs and LUMOs of structures were obtained for structures optimised with Spartan'08 and $DMol^3$.

4.6.3.2. Conformation search

Conformation searches were performed on Spartan®'08. A torsion angle (dihedral angle) was defined by selecting four adjacent atoms (**a**, **b**, **c** and **d**) in a structure (**Figure 4.6**). The dihedral angle was varied by rotation of atoms **a** and **d** relative to the bond formed between atoms **b** and **c**.

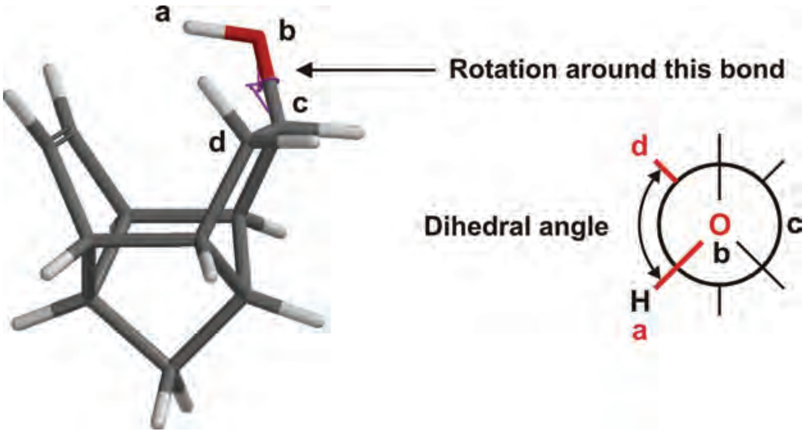
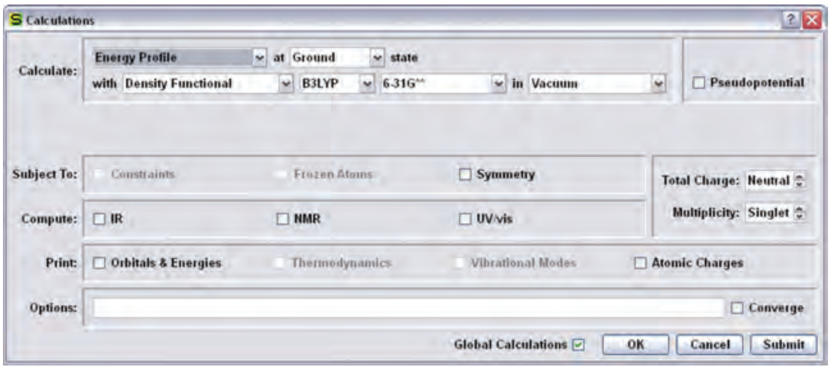


Figure 4.6: Determination of the dihedral angle.

To run a conformational search in Spartan®'08, an energy profile must be calculated (**Figure 4.7**). The rotation was executed in 36 steps starting at -179° and continuing through to +180°. A wealth of information was obtained from conformation searches. Plotting the energy against the dihedral angle provided information about the most stable conformer and the energy required for rotation about the specified bond. Calculation of orbital properties gave access to information about the changes in the shapes, sizes, and energies of different orbitals with changes in dihedral angle.

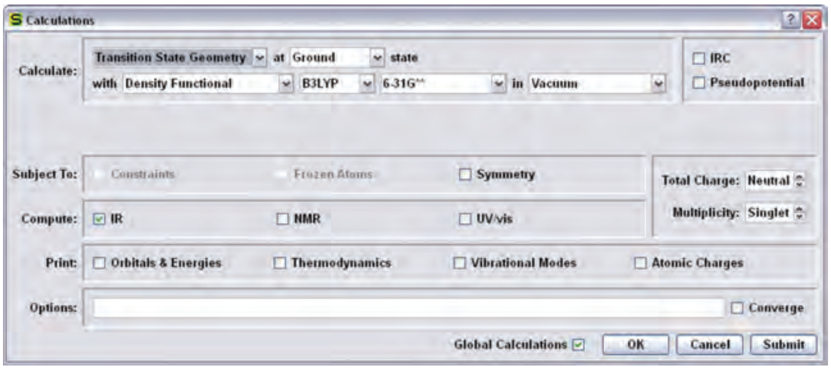


Calculate: Energy Profile at Ground state
with Density Functional B3LYP 6-31G** in Vacuum
☐ Pseudopotential
Subject To: Constraints Frozen Atoms ☐ Symmetry
Total Charge: Neutral
Multiplicity: Singlet
Compute: ☐ IR ☐ NMR ☐ UV/vis
Print: ☐ Orbitals & Energies Thermodynamics Vibrational Modes ☐ Atomic Charges
Options: ☐ Converge
Global Calculations ☑

Figure 4.7: Setup for a conformational search in Spartan®'08.

4.6.3.3. Transition state calculations

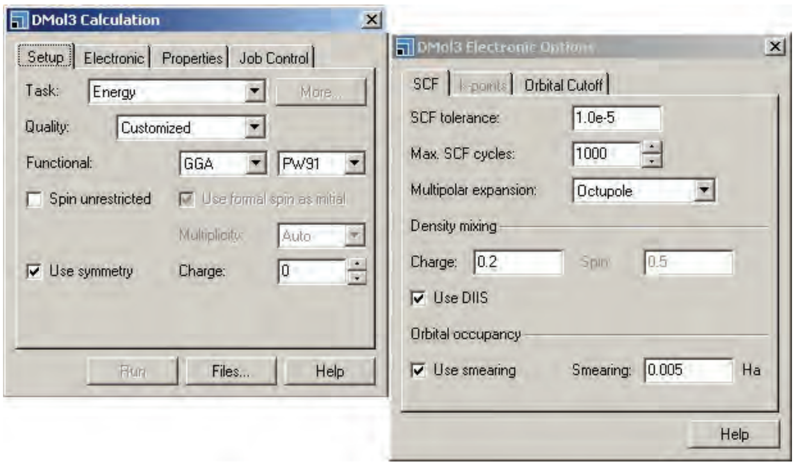
Transition state geometries can be calculated with Spartan®'08 (**Figure 4.8**). A sensible initial structure was constructed followed by preliminary testing with a low cost semi-empirical calculation. To determine the success of the calculation, the IR spectrum of the transition state was calculated. The structure associated with the first-order saddle point will exhibit one imaginary frequency and the normal mode of vibration associated with this frequency should emulate the motion of the atoms along the reaction coordinate. Successful calculations were recalculated at the B3LYP/6-31G** level of theory



Calculate: Transition State Geometry at Ground state
with Density Functional B3LYP 6-31G** in Vacuum
☐ IRC
☐ Pseudopotential
Subject To: Constraints Frozen Atoms ☐ Symmetry
Total Charge: Neutral
Multiplicity: Singlet
Compute: ☑ IR ☐ NMR ☐ UV/vis
Print: ☐ Orbitals & Energies ☐ Thermodynamics ☐ Vibrational Modes ☐ Atomic Charges
Options: ☐ Converge
Global Calculations ☑

Figure 4.8: Properties determined for geometry-optimised structures.

The principles of calculating a transition state in DMol^3 are the same as those previously described for Spartan$^{®}$'08. Preliminary transition state structures were optimised and vibrational analysis performed to evaluate the success of the calculation. These calculations were performed at the GGA-PW91/DNP level of theory. The setup used in DMol^3 is shown in **Figure 4.9**.



Task: Energy

Quality: Customized

Functional: GGA PW91

☐ Spin unrestricted ☑ Use formal spin as initial

Multiplicity: Auto

☑ Use symmetry Charge: 0

SCF tolerance: 1.0e-5

Max. SCF cycles: 1000

Multipolar expansion: Octupole

Density mixing

Charge: 0.2 Spin: 0.5

☑ Use DIIS

Orbital occupancy

☑ Use smearing Smearing: 0.005 Ha

Figure 4.9: Setup for determination of a transition state in DMol^3.

The task was set to "Energy" and a minimum SFC tolerance of 1 $\times 10^{-5}$ Ha was specified. The maximum number of SCF cycles was set to 1000. In the orbital occupancy section, the "smearing" option was selected and set to 0.005 Ha.