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# Decagram Synthesis of Dimethyl 1,4-Cubanedicarboxylate Using Continuous–Flow Photochemistry

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# Contents

# 1 General Experimental

Methanol, benzene, 1,4–dioxane and all other solvents and reagents were used as received from standard chemical suppliers unless otherwise stated.

TLC was performed on aluminium–precoated plates coated with silica gel 60 with an F254 indicator; visualised under UV light (254 nm) and/or by staining with cerium ammonium molybdate (CAM). Flash column chromatography was performed with Sigma Aldrich 60 silica gel (40–63 micron).

Fourier–transform infrared (FT–IR) spectra are reported in wavenumbers ($cm^{-1}$) and were recorded using a diamond ATR accessory, as solids or neat liquids.

$^{1}H$ NMR and $^{13}C$ NMR spectra were recorded in $CDCl_3$, DMSO–$d_6$ and $CD_3OD$ solutions at 298 K at 400 MHz. Chemical shifts are reported in δ units using $CHCl_3$ (δ 7.27 ppm $^{1}H$, δ 77.00 ppm $^{13}C$), DMSO–d6 (δ 2.51 ppm $^{1}H$, δ 77.00 ppm $^{13}C$) $CD_3OD$ (δ 3.31 ppm $^{1}H$, δ 77.00 ppm $^{13}C$) as an internal standard. Coupling constants (*J*) were recorded in Hz and are corrected. The following abbreviations for the multiplicity of the peaks are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sxt (sextet), spt (septet), oct (octet) br (broad), and m (multiplet). Melting points were obtained in an open capillary and are uncorrected. Electrospray low resolution mass spectra were recorded on a H2Os ZMD quadrupole spectrometer. High resolution mass spectra were recorded on a Bruker Daltonics MaXis mass spectrometer equipped with a time of flight analyzer.

## 2 Continuous–Flow experiments

The microfluidic devices were constructed with Adtech Polymer Engineering® FEP tubing (0.8 mm ID x 1.6 mm OD). The connections were made with Upchurch Scientific® Super Flangeless™ nuts (natural PEEK, ¼–28 Flat-Bottom for 1/16 OD tubing) and Upchurch Scientific® Super Flangeless™ ferrules (yellow ETFE, ¼–28 Flat–Bottom for 1/16 OD tubing). Upchurch Scientific® Luer Adapters (PEEK, 1/4–28 Female to Female) were used to connect syringes to the tubing. The feed solutions were conveyed to the microreactors using an Aladdin Single–Syringe Pump or an Ismatec® REGLO Digital Ms–2/6 peristaltic pump for large–scale reactions. Osram® (UVC 9W G23), Phillips® UVB–Broadand (PL–S 9W/12/2P) and Phillips® UVB–Narrowband (PL–L 36W/01/4P) lamps were used for the different experiments reported.

### 2.1 Continuous–Flow Reactors (Figures S1-S4)

The reactor was build according our previously reported procedure.[1]


**Figure S1.** 9 W UVB-broadband and 36 W UVB–broadband and narrowband used for the [2+2] photocycloaddition.

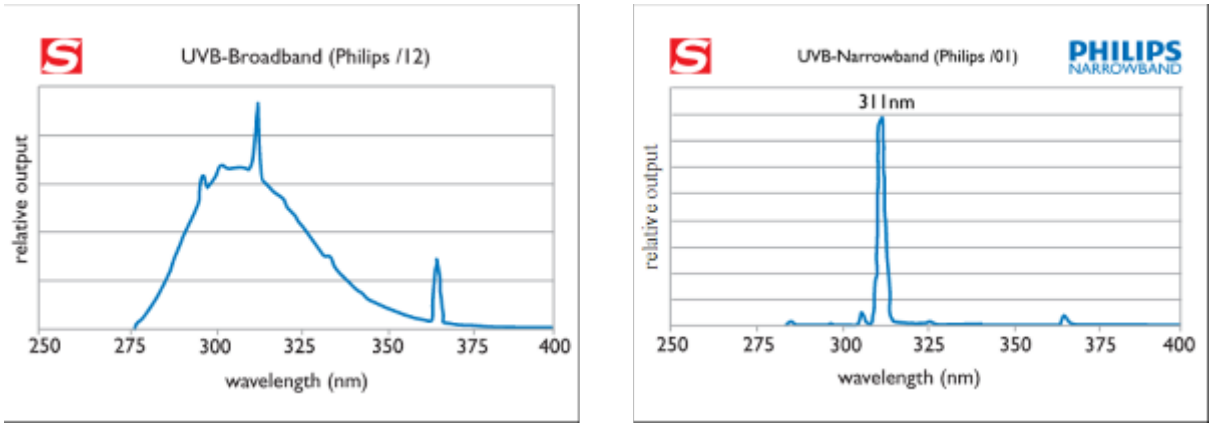



**Figure S2.** UV–spectra of UVB broadband and narrowband lamps.

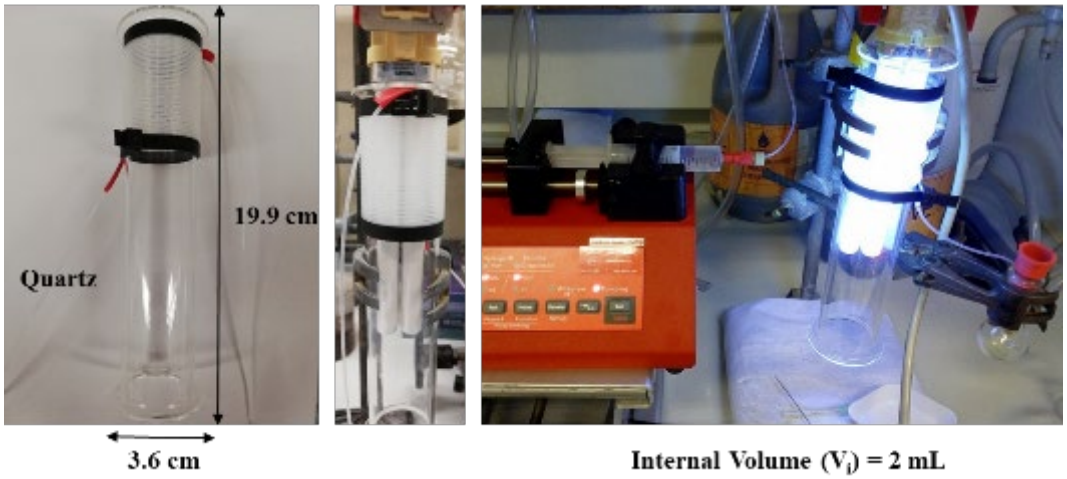



**Figure S3.** Pictures and size of the setup used with 9 W UVB–broadband lamp.

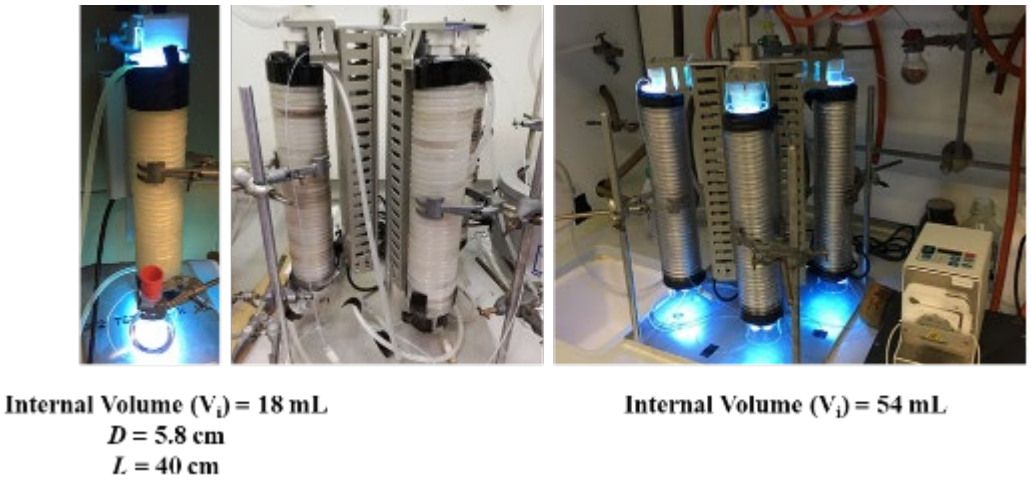
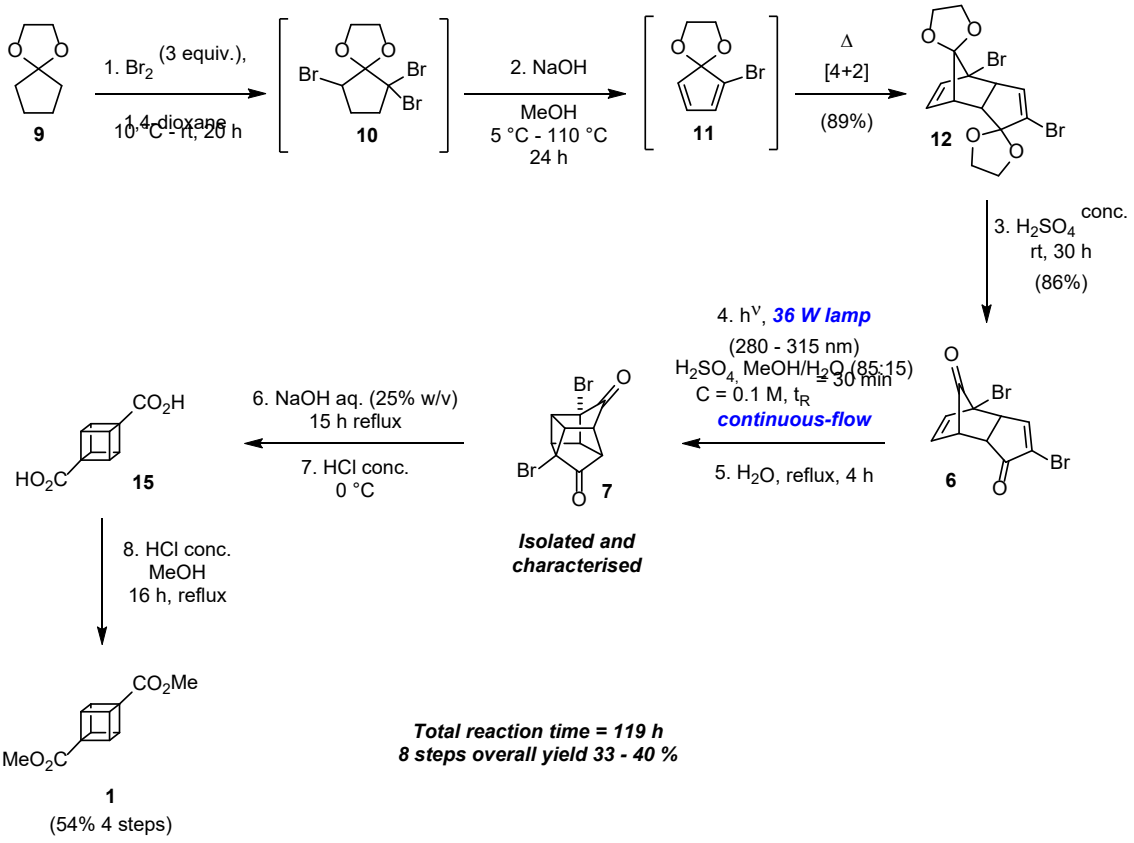



**Figure S4.** Pictures and size of the setup used with 36 W UVB–Narrowband lamp.

# 3 Overall Synthetic Route to Dimethyl 1,4–Cubanedicarboxylate



## 4 Selection of the irradiation source (Figures S5, S6)

The UV–absorption spectrum of **6** shows two main peaks. A strong UV absorbance at 247 nm due to $\pi \rightarrow \pi^*$ transition and a weaker, difficult to observe, band between 300 and 350 nm corresponding to the $n \rightarrow \pi^*$ transition, previously mentioned by Tsanaktsidis *et al.* to be responsible for the desired transformations.[2] Consequently, it was decided to investigate the use of UV–C ($\lambda$ = 200 – 280 nm, $\lambda_{max}$ = 254 nm), UV–B broadband ($\lambda$ = 280 – 370 nm) and UV–B narrowband ($\lambda$ = 280 – 315 nm) lamps as described above.

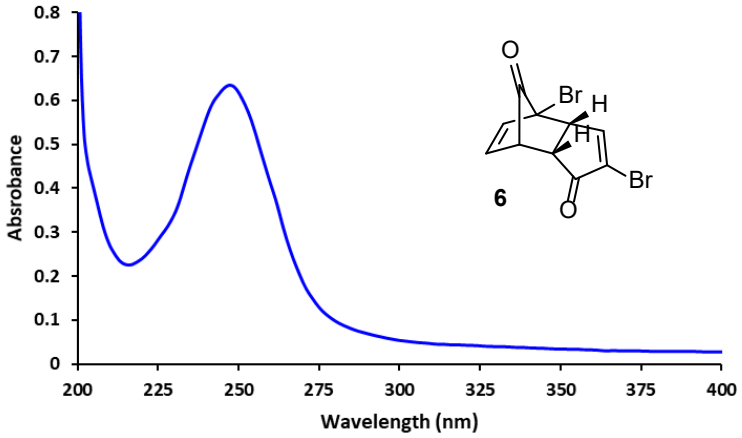



**Figure S5**. UV–spectrum of dione **6** in acidic ($H_2SO_4$) methanol/water (85:15).

Although, 1,4–cubanedicarboxylic acid **15** could be obtained using the 9 W UV–C lamp, fouling of the tubing was observed over time (Figure S6).

**Figure S6.** Irreversibly damaged FEP flow reactor after UV–C irradiation.

## 5 $^{1}$H NMR of the aliquot obtained after the [2+2]cycloaddition (Figure S7)

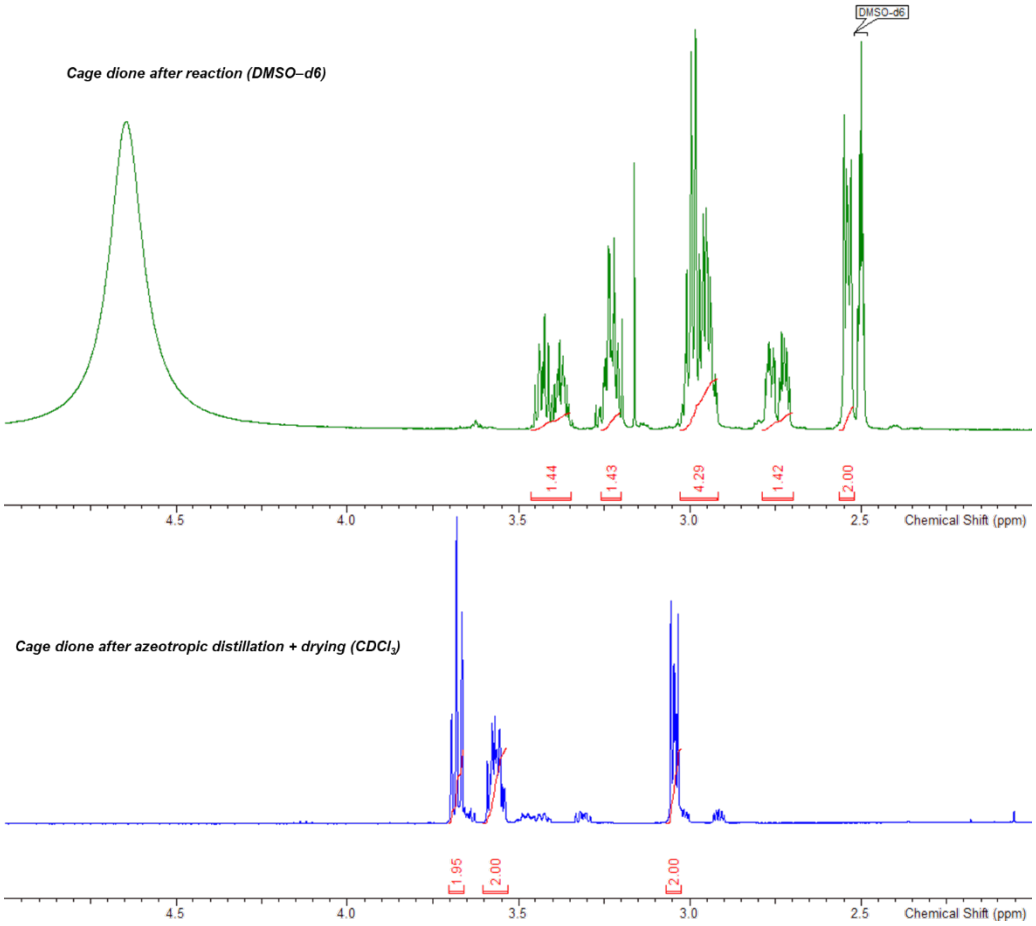
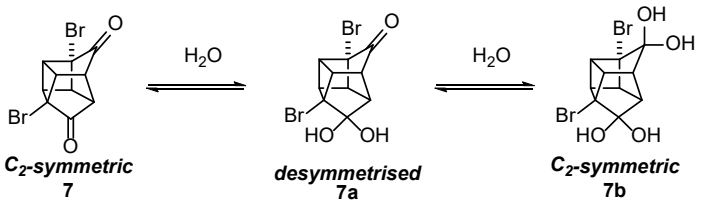



**Figure S7.** (*Green*) Photocycloadduct obtained after reaction (mixture of hydrates, DMSO–$d_6$) (*Blue*) Photocycloadduct **7** after azeotropic distillation and drying ($CDCl_3$).

# 6 Characterisation of the hydrates (Table S1)

The paper by K. Fodor-Csorba *et al*. and the associated characterisation of the dione **7** on Scifinder actually corresponds to the dihydrate form, according the $^{1}$H and $^{13}$C NMR described herein. The Fodor-Csorba $^{1}$H NMR data includes a doublet ($J$ = 21.9 Hz) at $\delta_H$ 5.99 integrating for 4 protons which we did not observe.[3]




**Scheme 4.** Dione **7** and its hydrate(s).

**Table S1.** $^{1}$H and $^{13}$C NMR chemical shifts of **7a** and **7b** (DMSO–$d_6$, 400 MHz).

| Authors | Compounds | $^{1}$H (ppm) | $^{13}$C (ppm) |
|---|---|---|---|
| **K. Fodor-Csorba *et al.*** | Characterised as dione **7** but is a better fit for dihydrate **7b** | 5.99 (d, 4H, $J$ = 21.9); 3.04 – 2.90 (m, 4H), 2.58 – 2.51 (m, 2H) | 105.9, 67.2, 50.7, 49.1, 43.8 |
| **This work** | **7a** | 3.41 – 3.46 (m, 1H), 3.35 – 3.40 (m, 1H), 3.20 – 3.26 (m, 2H), 2.77 (m, 1H), 2.72 (m, 1H) | 205.9 (CO), 107.5 ($C(OH)_2$), 66.5 (C–Br), 56.1 (C–Br), 48.4 (CH), 48.0 (CH), 47.4 (CH), 46.9 (CH), 43.8 (CH), 39.5 (CH) |
| **This work** | **7b** | 2.93 – 3.03 (m, 4H), 2.52 – 2.57 (m, 2H) | 106.1 (2 x $C(OH)_2$), 67.4 (2 x C–Br), 50.9 (CH), 49.2 (CH), 44.0 (CH) |

## 6.1 $^{1}$H COSY NMR (400 MHz, DMSO–$d_6$) (Figure S8)

The $^{1}$H COSY NMR recorded on the product mixture obtained following the [2+2] photochemical step shows six chemically non–equivalent protons for the desymmetrised monohydrate **7a** and the three chemically distinct proton environments of the $C_2$–symmetric dihydrate **7b**. This allowed us to differentiate the protons environment of both molecules and calculate the conversion in continuous–flow.

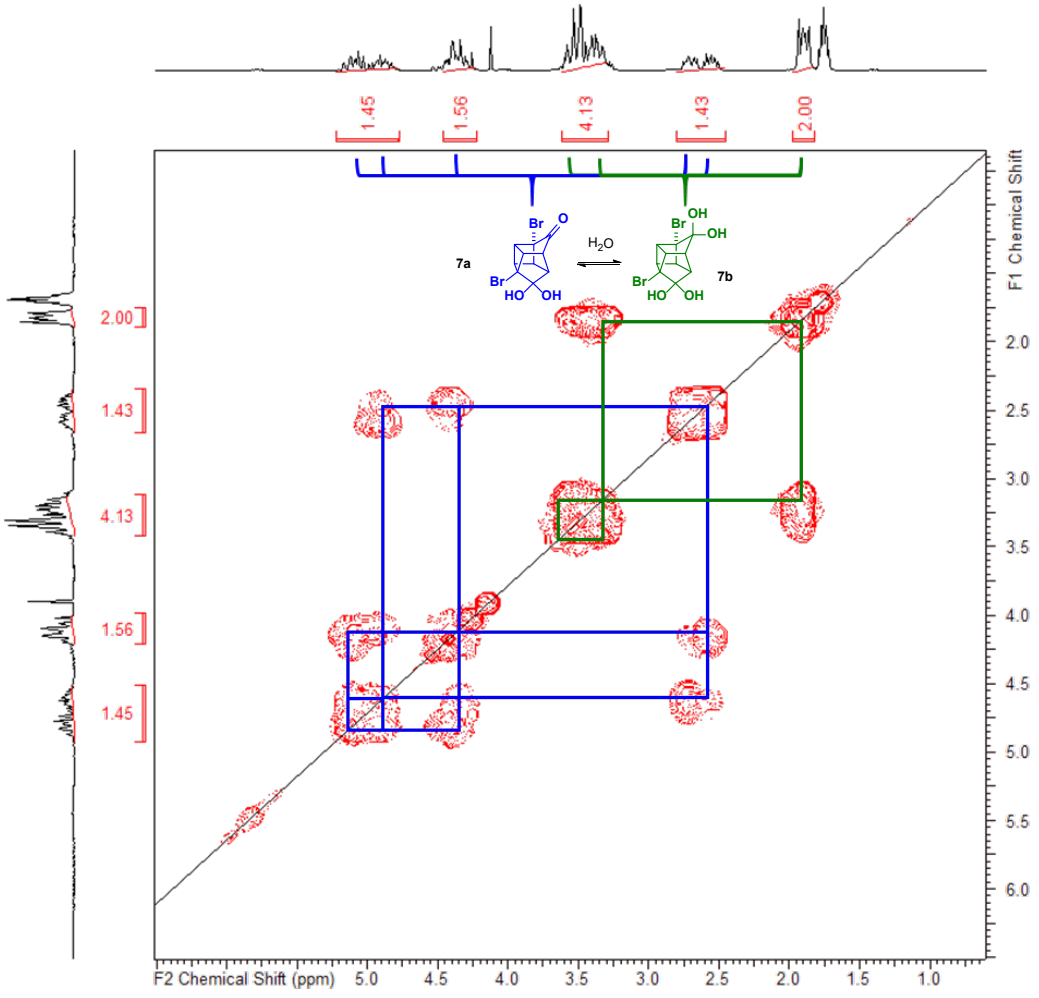
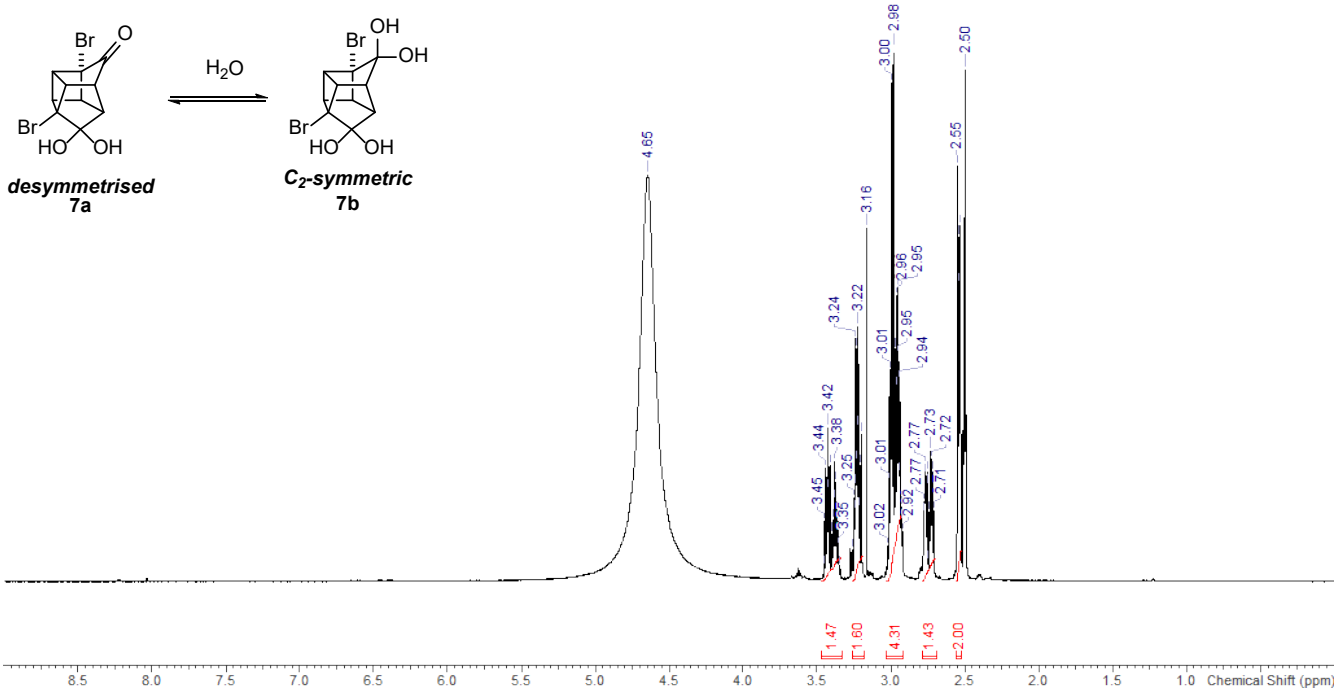
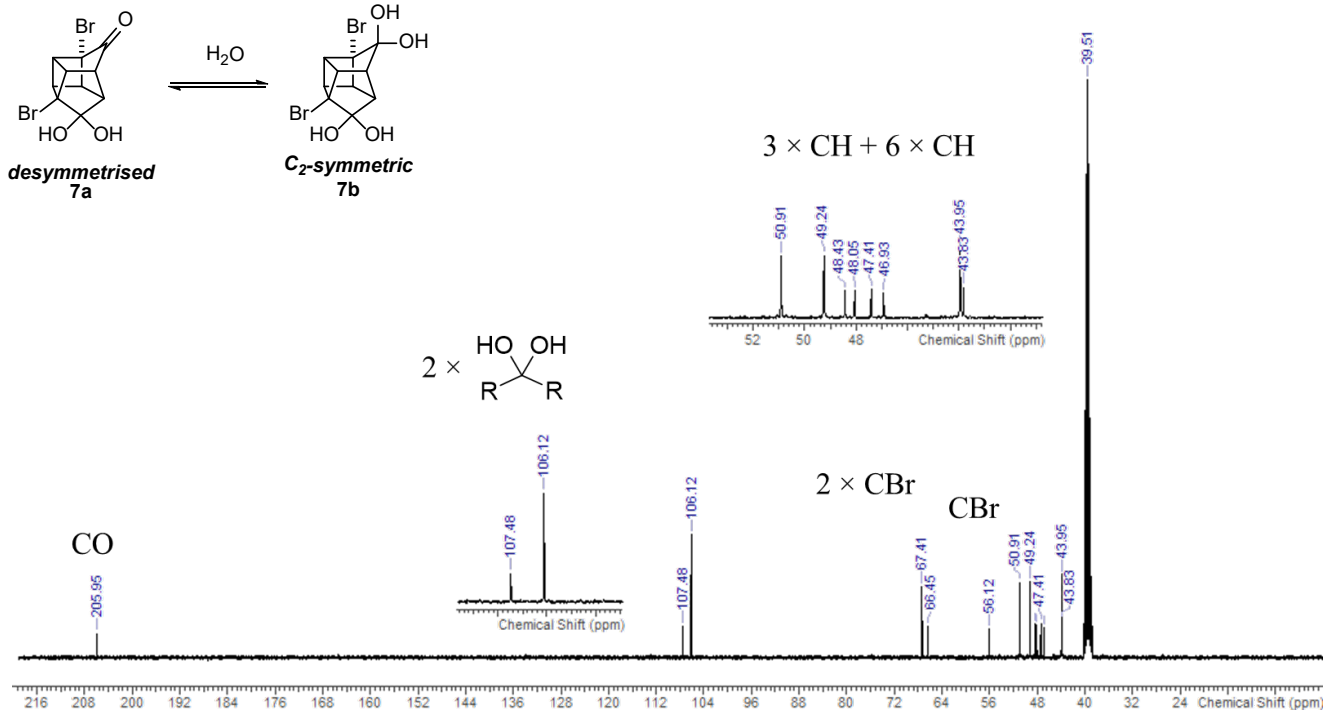



**Figure S8.** $^{1}$H COSY NMR spectrum of the mixture of hydrates **7a** and **7b** (DMSO–$d_6$, 400 MHz).

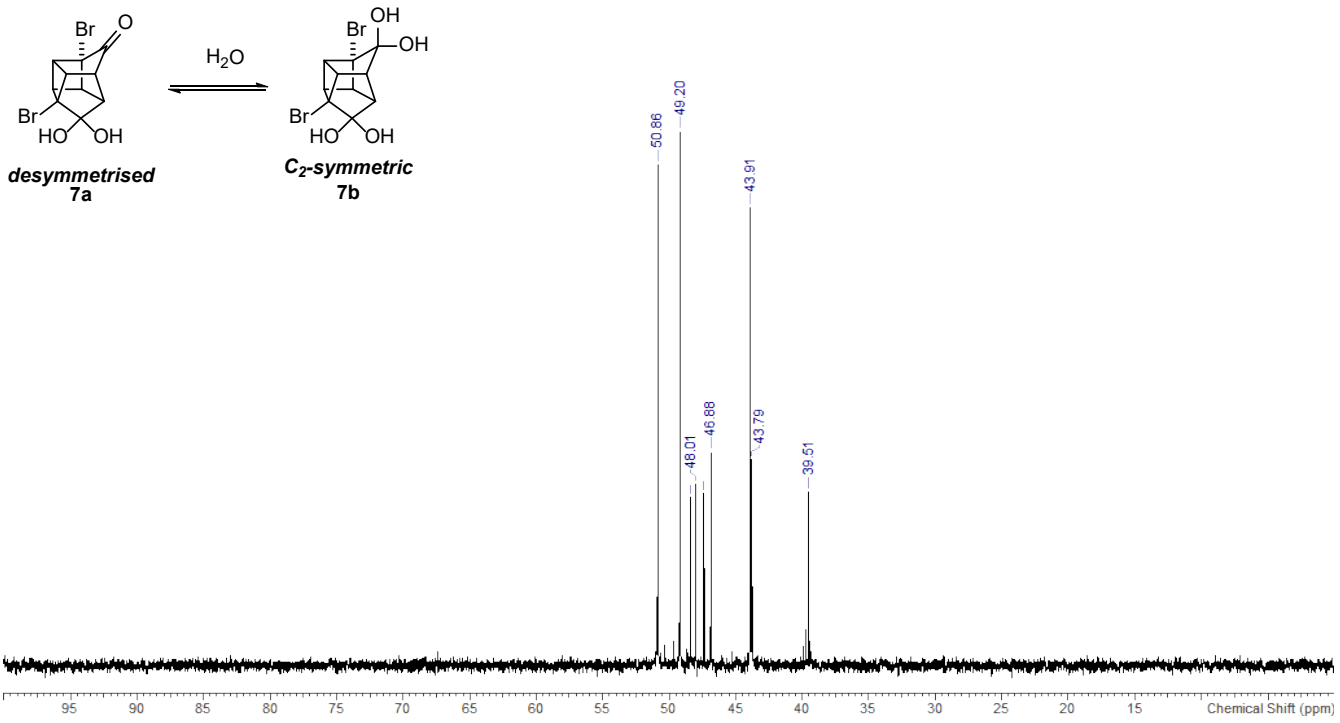
## 6.2 $^{1}$H NMR (400 MHz, DMSO–$d_6$)




## 6.3 $^{13}$C NMR (101 MHz, DMSO–$d_6$)



## 6.4 $^{13}$C NMR DEPT 45 (101 MHz, DMSO–$d_6$)




*desymmetrised*
**7a**

*$C_2$-symmetric*
**7b**

# 7 Characterisation of the dione 7

As depicted in S9, **7** possesses a $C_2$–rotational axis going through the middle of the two bonds coloured in yellow on the molecular model. Therefore, three chemically distinct proton environments are expected by $^1$H NMR analysis, with H–3 and H–1 anticipated to appear as doublets and H–2 as a doublet of doublets.

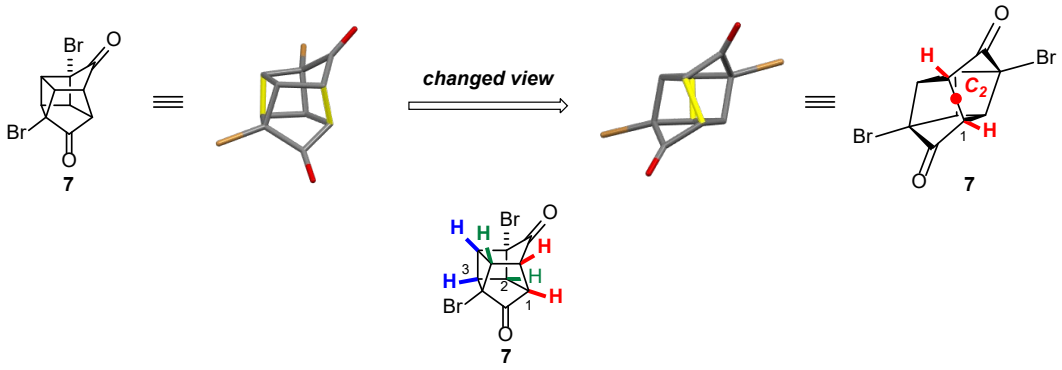



**Figure S9.** Presence of a $C_2$ axis in **7**.

With the $^1$H NMR spectrum of the dione **7** in hand, we observed three proton environments compared to the two reported previously. This can be explained by our use of a higher field NMR instrument (400 MHz) compared to that used by Eaton and Chapman (100 MHz).[4,5] However, as the dihydrate **7b** and dione **7** are $C_2$–symmetric molecules only $^{13}$C NMR analysis allowed them to be differentiated. While the assignment of $H_2$ was given by $^1$H COSY NMR (see below), the HMBC NMR did not reveal the correlations needed to enable the unambiguous assignment of $H_1$ and $H_3$. Work on similar caged molecules (Figure S10) by Dunn *et al.*, and Stedman and Davis has shown that protons α–to the carbonyl are located in its shielding zone.[6],[7] Thus, our assignments of H– and H–3 are based on these observations.[5]

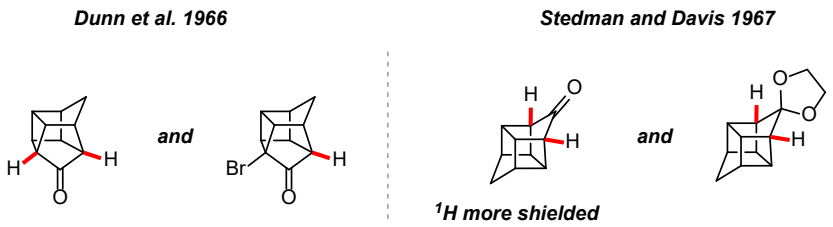
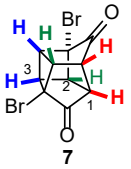



**Figure S10.** Studied structures by Dunn et al., and Stedman and Davis to determine the shielding of α–protons.[6,7]

Eaton and Chapman reported chemical shifts according the tau (τ) scale. Their values have been transformed to the delta (δ) scale with the following relationship: $\delta = 10 - \tau$.




**7**

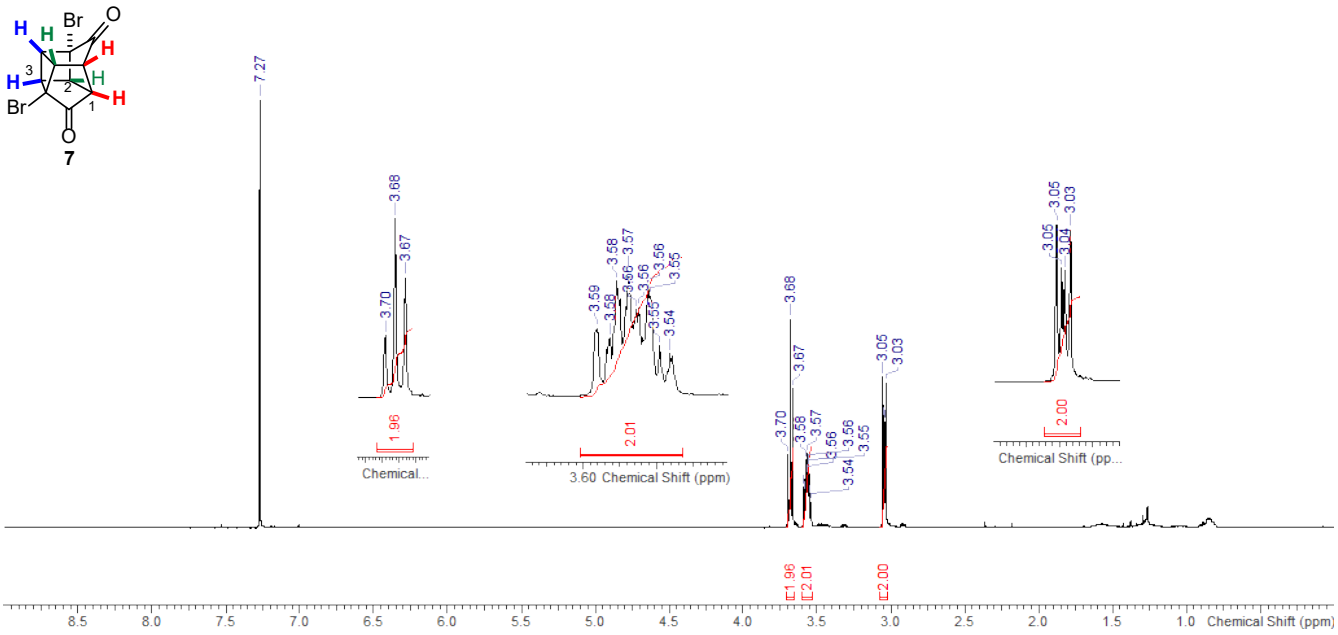
**Table S2.** $^{1}$H NMR characterisation data of **7** reported by Eaton and Chapman in $CDCl_3$ (100 and 400 MHz).

| Authors | $^{1}$H NMR τ (ppm) (originally reported) | $^{1}$H NMR δ (ppm) | $^{13}$C NMR δ (ppm) |
|---|---|---|---|
| **Eaton *et al.*** | 6.37 (m, 4H),<br>6.95 (m, 2H) | 3.63 (m, 4H)<br>3.05 (m, 2H) | - |
| **Chapman *et al.*** | 6.28 – 6.44 (m, 4H)<br>6.86 – 7.02 (m, 2H) | 3.56 – 3.72 (m, 4H)<br>2.98 – 3.14 (m, 2H) | - |
| **This work** | - | 3.04 (dd, $J$ = 5.1, 3.2 Hz, 2$H_1$) | 41.0 ($CH_1$) |
| | | 3.53 – 3.60 (m, 2$H_2$) | 43.6 ($CH_2$) |
| | | 3.66 – 3.70 (m, 2$H_3$) | 45.1 ($CH_3$) |
| | | - | 53.1 (C–Br) |
| | | - | 203.2 (CO) |

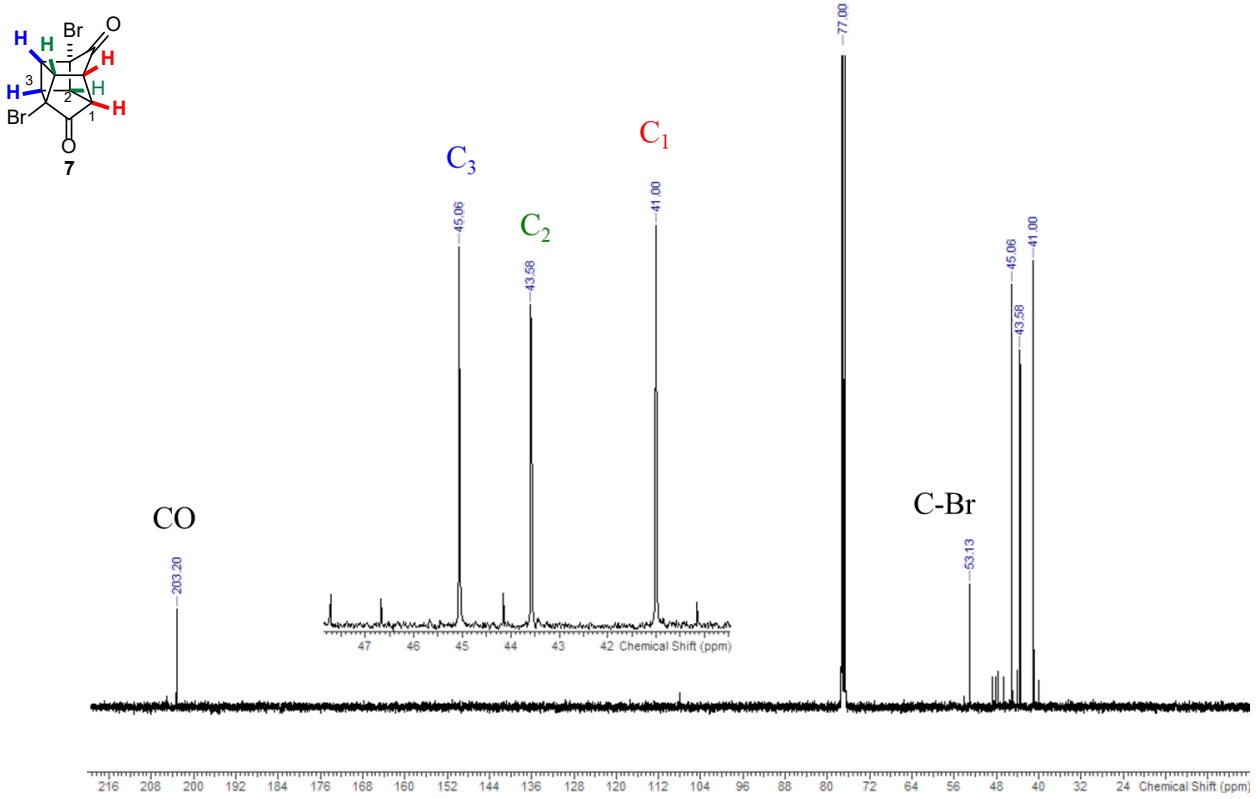
**Note:** The dione **7** is hygroscopic and readily reverts to a the mixture of hydrates on standing at room temperature. Repeated azeotropic distillation with toluene on the rotavap allows the isolation of dione **7**. Chapman *et al.* reported using dessication to obtain this dione from its hydrates.[5]

**Procedure:** Add toluene in a mixture of hydrates and heat slowly under vacuum at 60 °C. Repeat this procedure several times. Afterwards, chloroform is added (most of the solid should dissolved as the dione **7** is soluble in chloroform, and evaporate). This last sequence is repeated 2–3 times and the sample is left under high–vacuum for 1 h.

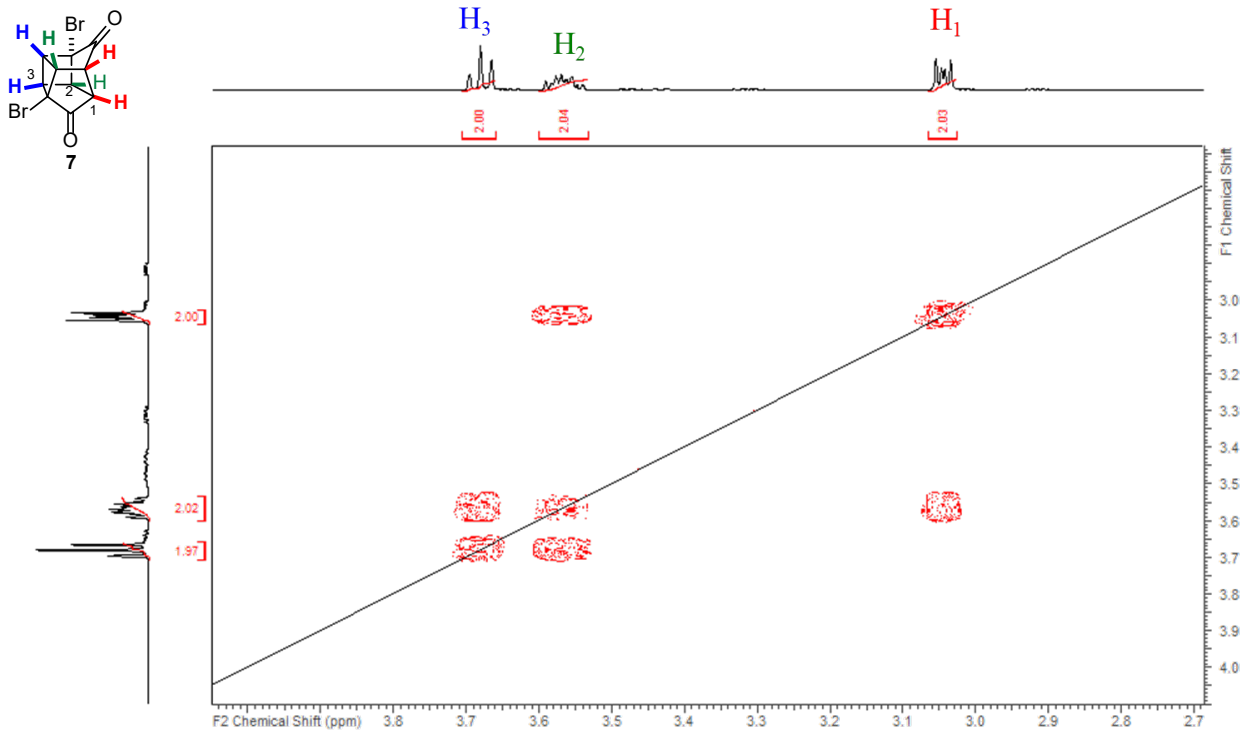
## 7.1 $^{1}$H NMR (400 MHz, $CDCl_3$)




## 7.2 $^{13}$C NMR (101 MHz, $CDCl_3$)



## 7.3 $^{1}$H COSY NMR (400 MHz, $CDCl_3$)




**Note: 7** is contaminated with traces of hydrates.

## 8 Conversion calculated for the formation of the [2+2]cycloadduct according the residence time

As noted above, the [2+2]cycloadduct **7** is given as a mixture with its hydrates **7a** and **7b**. The conversion was calculated by using the sum of the integral values of both "observed" products, compared to the respective integral value of the characteristic olefinic proton of the dione **6.**

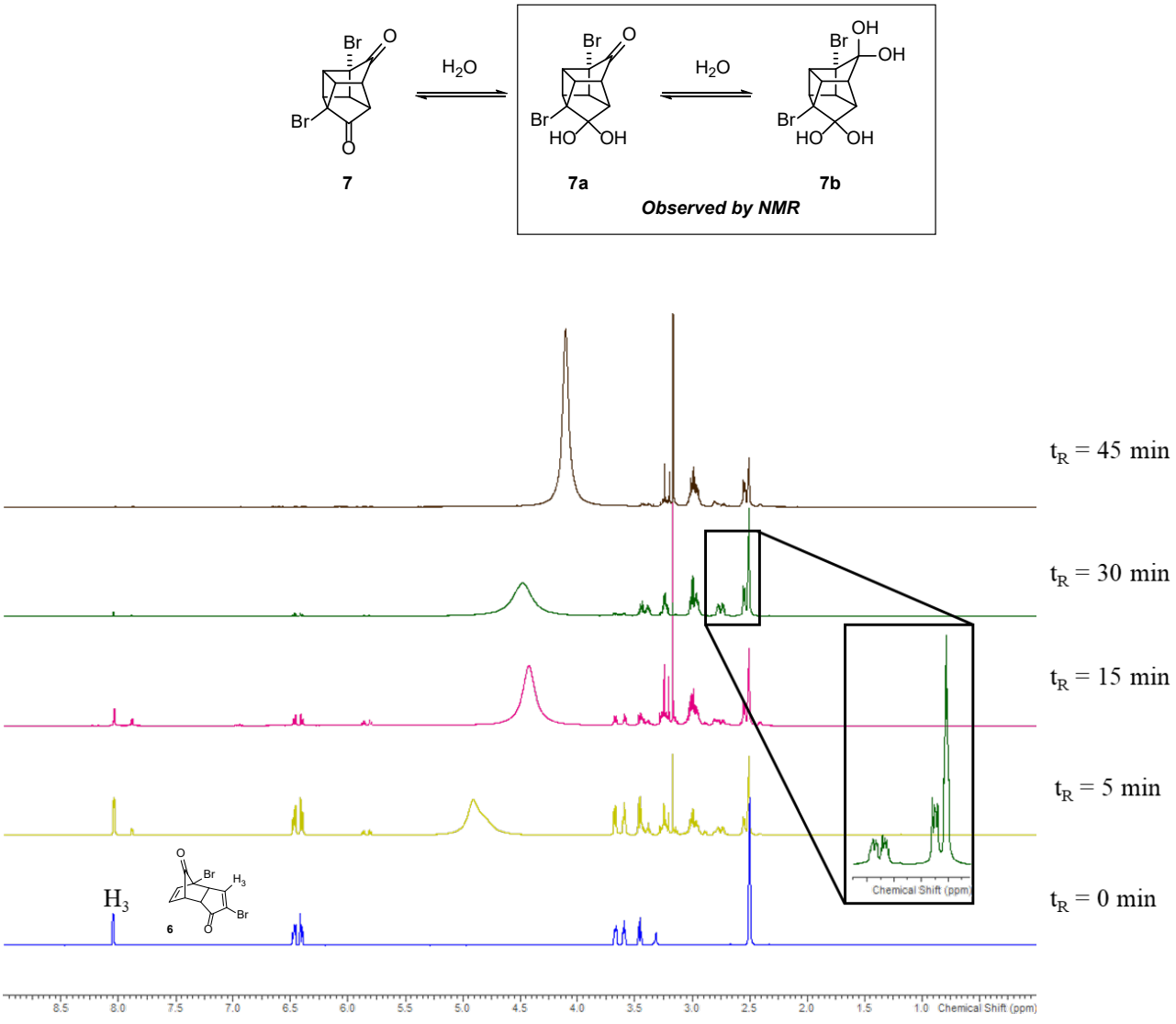



**Figure S11.** [1]H NMR collected according the residence time using 9 W UV–B broadband lamp**.**

**Formula :**

$$Conversion\ \% = \frac{I\left(\frac{2.54\ ppm}{2}\right) + I\left(\frac{2.75\ ppm}{2}\right)}{I\left(\frac{8.03\ ppm}{1}\right) + I\left(\frac{2.54\ ppm}{2}\right) + I\left(\frac{2.75\ ppm}{2}\right)} * 100$$

**Theoretical productivity calculations for the photochemical reactors:**

$$P_{theo} = \left(\frac{Flow\ rate\ \times\ Concentration}{1000}\right) \times MW\ \times 60 \times Conversion$$

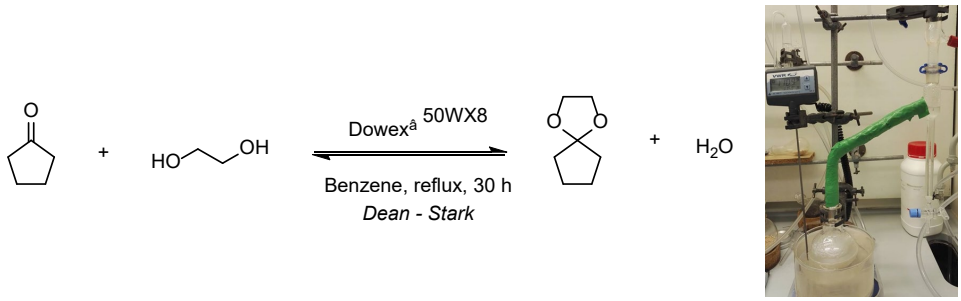
**Concentration** = 0.1 M

**Molecular Weight** = 317.96 $g.mol^{-1}$

**Conversion** = 99%

# 9 Synthetic Procedures

## 9.1 Synthesis of 1,4–dioxaspiro[4.4]nonane (9)




A solution cyclopentanone **8** (100 mL, 1.13 mol, 1.0 equiv.) and ethylene glycol (80 mL, 1.44 mol, 1.3 equiv.) in anhydrous benzene (200 mL) containing Dowex® 50WX8 50–100 (H) cation exchange resin (1.20 g, prewashed with anhydrous MeOH, followed by drying under vacuum) was heated at reflux under a Dean and Stark apparatus for 30 h. After cooling to room temperature, the resulting yellow mixture was washed with NaOH (4%) (2 × 100 mL) and brine (2 × 200 mL), dried over $MgSO_4$ and distilled to afford 1,4–dioxaspiro[4.4]nonane **9** (112.6 g, 0.88 mol, 78%) as a colourless oil.

**Formula** $C_7H_{12}O_2$

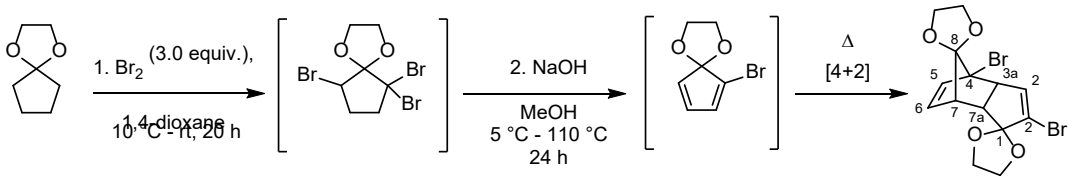
**MW** 128.17 g.mol$^{-1}$

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 3.90 (s, 4H), 1.81 – 1.74 (m, 4H), 1.71 – 1.65 (m, 4H) ppm;

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 118.5, 64.2, 35.9 (2C, $CH_2$), 23.5 (2C, $CH_2$) ppm.

Data consistent with the literature.[8]

## 9.2 Synthesis of *Endo*–2,4–dibromodicyclopentadiene–1,8–dione bisethylene ketal (12)




A solution of 1,4–dioxaspiro[4.4]nonane **9** (50.0 g, 390.0 mmol, 1.0 equiv.) in anhydrous 1,4–dioxane (310 mL) at 5 – 10 °C was purged with argon over 15 minutes. Molecular bromine (70 mL, 1.37 mol, 3.5 equiv.) was added dropwise (2 h), ensuring that the temperature was maintained between 10 – 15 °C, before being stirred at room temperature for 20 h. A NaOH (4%) trap was linked to the reaction flask to ensure the trapping of formed HBr. A solution of NaOH (121.4 g, 3.04 mol, 7.8 equiv.) in MeOH (610 mL) was added dropwise via a dropping funnel over 2 h then the resulting brown mixture was heated at reflux for 24 h, before being cooled to room

temperature and poured into a stirred ice–water bath (1.5 L). After filtration, the beige precipitate was washed with ice–cold $H_2O$ (200 mL) and dried under high–vacuum for 6 h, to afford *endo*–2,4–dibromodicyclopentadiene–1,8–dione bisethylene ketal **12** (69.78 g, 171.8 mmol, 88%) as a pale beige solid.

**Formula** $C_{14}H_{14}O_4Br_2$

**MW** 406.07 g $mol^{-1}$

**mp** 180 – 181 °C (hexane/EtOAc)

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 6.4, 3.7 Hz, 1H, $H_6$), 6.08 (d, *J* = 2.3 Hz, 1H, $H_3$), 5.84 (dd, *J* = 6.5, 0.7 Hz, 1H, $H_5$), 4.28 – 4.11 (4H, m, acetal), 4.04 – 3.87 (4H, m, acetal), 3.51 (dd, *J* = 7.4, 2.4 Hz, 1H, $H_{3a}$), 3.08 (1H, dd, J 7.4, 4.7 Hz, $H_{7a}$), 2.73 (1H, td, *J* = 4.7, 0.7 Hz, $H_7$) ppm;

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 134.5 ($C_3H$), 133.1 ($C_5H$), 132.6 ($C_6H$), 128.1 ($C_1O$), 126.1 ($C_8O$), 115.9 ($C_2Br$), 67.8 ($C_4Br$), 66.4 (acetal), 66.3 (acetal), 65.3 (acetal), 65.2 (acetal), 55.7 ($C_{3a}H$), 49.6 ($C_{7a}H$), 47.3 ($C_7H$) ppm;

**IR** 2986 (w), 2890 (w), 1616 (w), 1471 (w), 1266 (m), 1142 (m), 1008 (s), 954 (s) 743 (s) $cm^{-1}$.

Data consistent with the literature.[9]

**Figure S12.** Picture of cyclopentanone ethylene ketal after the addition of bromine.

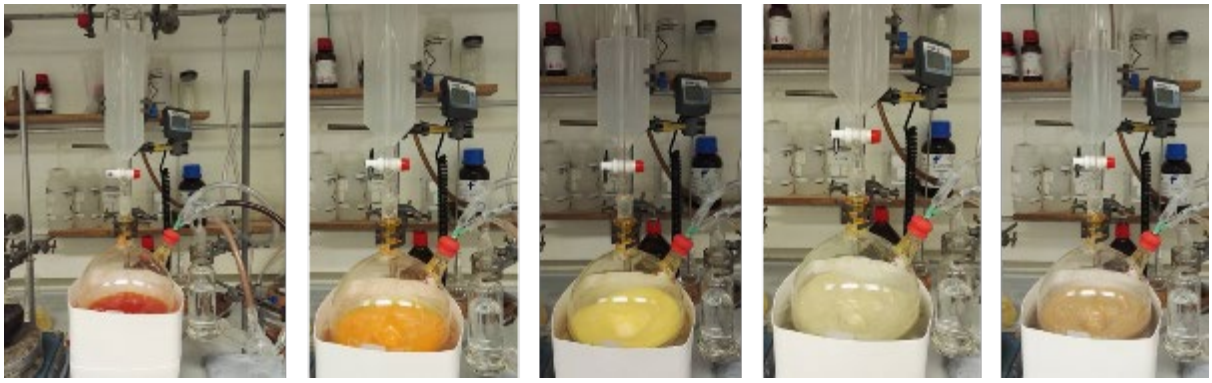
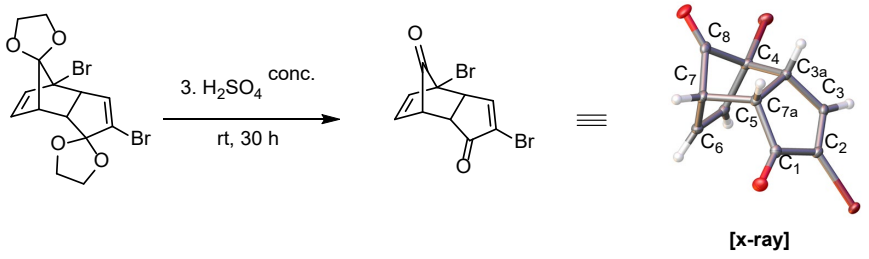


**Figure S13.** (*From left to right*) Change of colour with the addition of NaOH in methanol in the brominated cyclopentanone ethylene ketal.

**Figure S14.** (*Left*) Refluxed solution poured in an ice–water bath (*Right*) obtained *endo*–2,4–dibromodicylopentandien–1,8–one **12** after drying under high–vacuum.

## 9.3 Synthesis of *Endo*–2,4–dibromocyclopentadiene–1,8–dione (6)




To a 500 mL flask, *endo*–2,4–dibromodicyclopentadiene–1,8–dione bisethylene ketal **12** (58.5 g, 0.14 mol, 1.0 equiv.) was dissolved portionwise in concentrated $H_2SO_4$ (>95%) (180 mL) at room temperature. After 30 h stirring at room temperature, the solution was slowly poured into a vigorously stirred ice–water bath (1 L), forming a beige precipitate. The resulting slurry was filtered under vacuum, washed with cold $H_2O$ and dried under high–vacuum. The crude solid (47.2 g) was dissolved in EtOAc (472 mL) in a 2 L beaker with heating and

stirring, then hexane (236 mL) was added. The pale beige precipitate formed was isolated by vacuum filtration, washed with ice–cold hexane/EtOAc (75 mL, 1:1), dried under vacuum and recrystallised from EtOAc/hexane to yield the title compound (28.15 g, 0.089 mol) as colourless crystals. Further evaporation of the filtrate gave a second crop (10.49 g, 0.033 mol) of colourless crystals to afford, overall, *endo*–2,4–dibromocyclopentadiene–1,8–dione **6** (38.64 g, 121.0 mmol, 84%).

**Formula** $C_{10}H_6O_2Br_2$

**MW** 317.96 g $mol^{-1}$

**mp** 164 – 165 °C as crystals

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 2.9 Hz, 1H, $H_3$), 6.36 (dd, *J* = 7.0, 3.9 Hz, 1H, $H_6$), 6.26 (dt, *J* = 6.8, 0.9 Hz, 1H, $H_5$), 3.59 (ddd, *J* = 4.8, 3.9, 0.9 Hz, 1H, $H_7$), 3.53 (1H, dd, *J* = 6.5, 2.9 Hz, $H_{3a}$), 3.21 (1H, dd, *J* = 6.4, 5.1 Hz, $H_{7a}$) ppm;

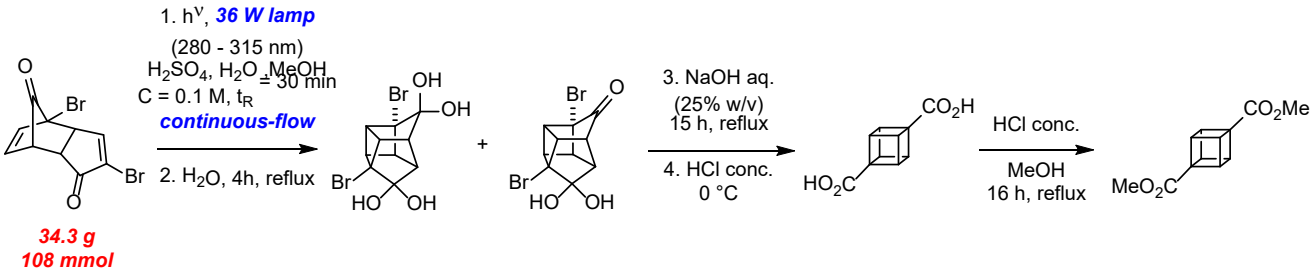
**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 197.0 ($C_1O$), 192.4 ($C_8O$), 156.4 ($C_3H$), 134.1 ($C_5H$), 133.9 ($C_6H$), 129.8 ($C_2Br$), 60.3 ($C_4Br$), 49.0 ($C_{3a}H$), 47.3 ($C_7H$), 44.1 ($C_{7a}H$) ppm;

**IR** 1789 (s), 1717 (s), 1580 (w), 1554 (w), 985 (m), 886 (m), 722 (s), 684 (s) $cm^{-1}$.

Data consistent with the literature.[9]


**Figure S15.** Recrystallisation of *endo*–2,4–dibromocyclopentadiene–1,8–dione **6**.

## 9.4 Synthesis of Dimethyl 1,4–cubanedicarboxylate (1)




In a 2 L flask, *endo*–2,4–dibromocyclopentadiene–1,8–one **1.5** (34.31 g, 108.0 mmol, 1.0 equiv.) was dissolved in MeOH (907 mL), $H_2O$ (163 mL) and $H_2SO_4$ (1.36 mL) then degassed with bubbling argon for 15 minutes. The resulting colourless solution was pumped (flow rate of 1.8 $mL.min^{-1}$) through the photoflow microreactor ($V_i$ = 54 mL) using a peristaltic pump and a 36 W UV–B narrowband lamp. After reaching the steady–state (≈ 50 min), the product stream was collected until the solution had passed through the photoreactor. Pure methanol was then pumped through for 50 minutes. The resulting yellow solution was concentrated under vacuum then the obtained solid was heated at reflux in $H_2O$ (312 mL) for 3.5 h to ensure full hydrolysis of any remaining dimethyl ketal. On cooling to room temperature, aq. NaOH (81.12 g, 26% w/v, 312 mL) was added portionwise to the mixture, and the dark brown solution stirred for 15 h at reflux. The solution was cooled to 0 °C, and concentrated HCl (~ 160 mL) was added dropwise until a pH ≈ 1 – 2 was reached. The brown precipitate was filtrated, and washed successively with ice–cold $H_2O$ (200 mL) and ice–cold MeOH (15 mL). The crude solid was concentrated under high–vacuum for 6 h, then transferred to a 250 mL flask and heated under reduced pressure for several hours (60 °C) to afford 1,4–cubanedicarboxylic acid **15** (≈ 17.93 g) as a brown crude solid.

Afterwards, to 1,4–cubanedicarboxylic acid **15** (7.00 g) in anhydrous MeOH (200 mL) under argon in a 500 mL flask, was added concentrated HCl (2.0 mL, 66.0 mmol, 1.8 equiv.) dropwise. After 16 h at reflux under argon, the solvent was concentrated under vacuum and the obtained solid dissolved in $CH_2Cl_2$ (150 mL). The organic phase was washed with $H_2O$ (7 × 100 mL), then the aqueous phases were combined and extracted with $CH_2Cl_2$ (4 × 150 mL). The organic phases were combined, dried over $MgSO_4$, and concentrated under vacuum. The obtained black solid was dry–loaded and purified by flash column chromatography (8:2 hexane/EtOAc) to afford dimethyl 1,4–cubanedicarboxylate **1** (5.67 g, 25.7 mmol) as a white solid. This was subsequently repeated with 1,4–cubanedicarboxylic acid **15** (8.56 g) in anhydrous MeOH (245 mL) and concentrated HCl (2.45 mL, 0.081 mol, 1.8 equiv.), as above, to afford dimethyl 1,4–cubanedicarboxylate **1** (7.12 g, 32.3 mmol). Dimethyl 1,4–cubanedicarboxylate **1** (12.79 g, 58.1 mmol) was thus obtained in 54% overall yield from *endo*–2,4–dibromocyclopentadiene–1,8–one **6**.

**1,4–Cubanedicarboxylic acid**

**Formula** $C_{10}H_8O_4$;

**MW** 192.17 g $mol^{-1}$;

**$^1$H NMR** (400 MHz, $CD_3OD$) δ 4.19 (s, 6H) ppm;

**$^{13}$C NMR** (101 MHz, $CD_3OD$) δ 175.5 (2C, CO), 57.8 (2C, C cubyl), 48.3 (6C, CH cubyl) ppm.

Data consistent with the literature.[9]

**Dimethyl 1,4–cubanedicarboxylate**

**Formula** $C_{12}H_{12}O_4$;

**MW** 220.22 g $mol^{-1}$;

**$R_f$** 0.51 (8:2 hexane/EtOAc);

**mp** 163 – 164 °C;

**$^1$H NMR** (400 MHz, $CDCl_3$) δ 4.25 (s, 6H), 3.72 (s, 6H) ppm;

**$^{13}$C NMR** (101 MHz, $CDCl_3$) δ 172.0 (2C, CO), 55.8 (2C, C cubyl), 51.6 (2C, $CO_2CH_3$), 47.1 (6C, CH cubyl) ppm;

**IR** 3000 (s), 2955 (w), 1717 (s), 1440 (s), 1323 (s), 1206 (s), 1089 (s) $cm^{-1}$.

Data consistent with the literature.[9]

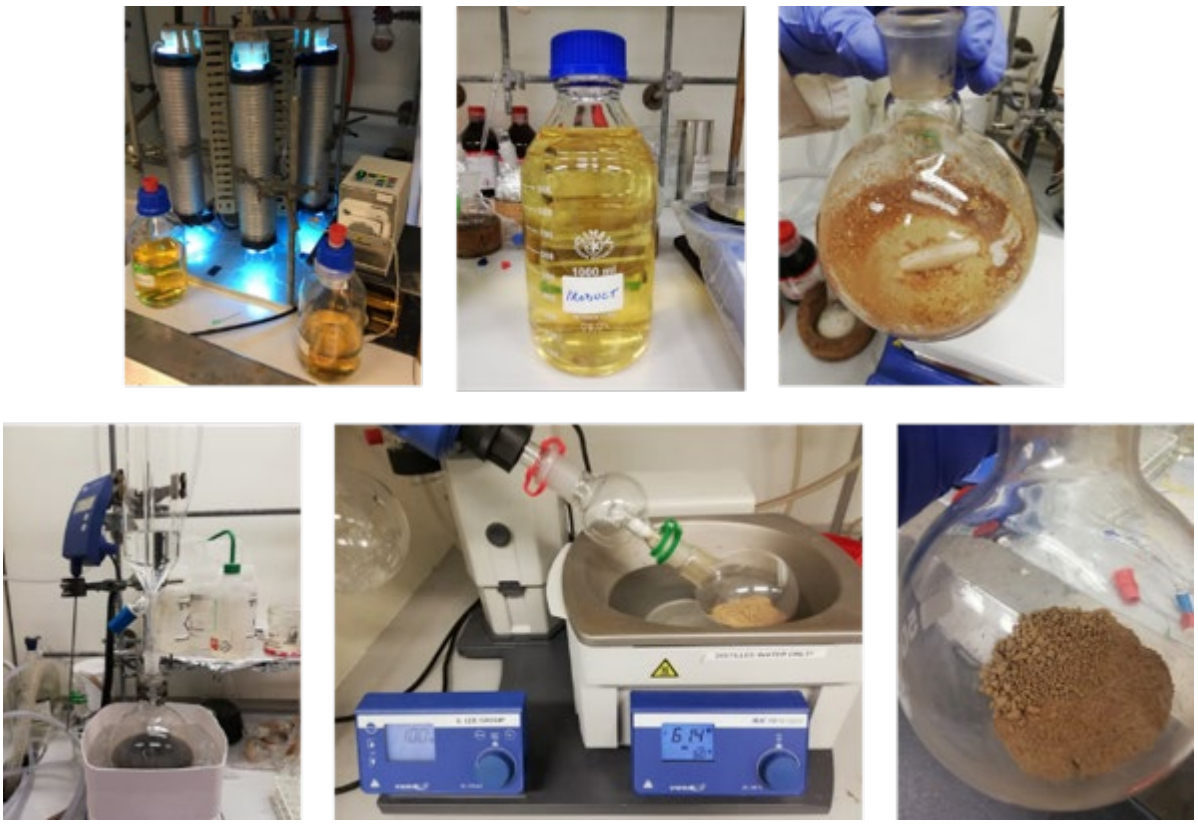


**Figure S16.** From collected [2+2] cycloadduct to 1,4–cubanedicarboxylic **15** : (*middle top*) obtained solution after the photoreaction (*Top left*) [2+2]photocycloadduct **7a** and **7b** and after evaporation (*bottom right*) Addition of HCl (*middle bottom*) Drying of 1,4–cubanedicarboxylic acid (*Bottom right*) 1,4–cubanedicarboxylic acid **15**.

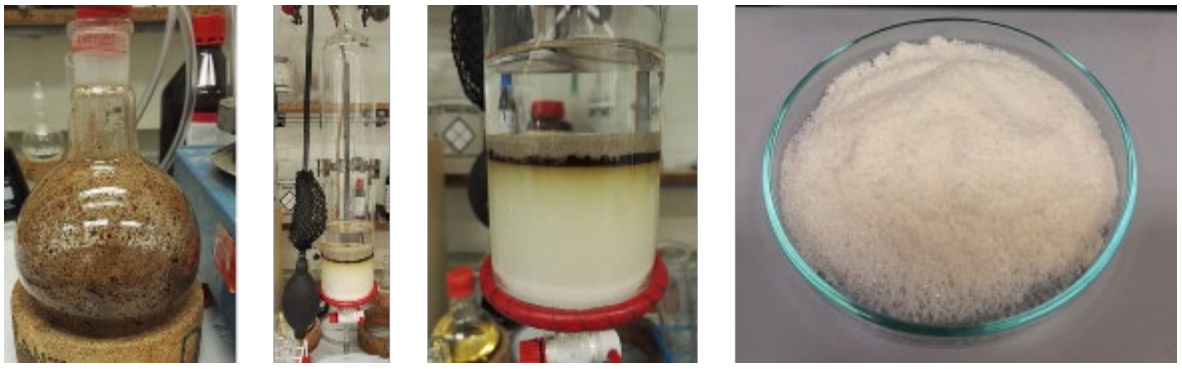
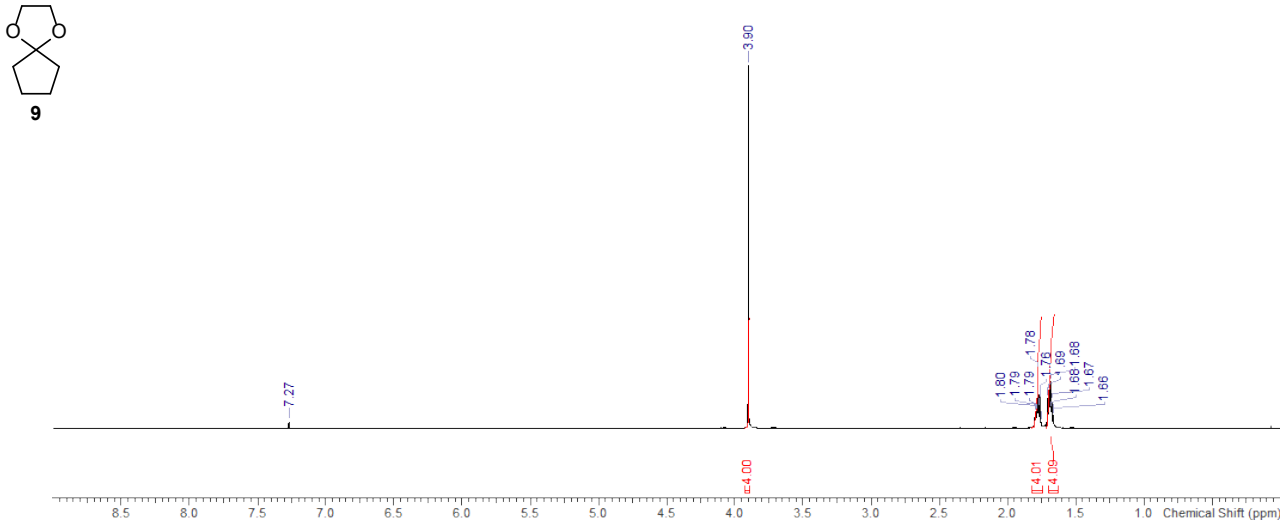


**Figure S17.** (*From left to right*) Obtained dimethyl 1,4–cubanedicarboxylate **1** after reaction + workup and dry–loaded compound on chromatography column and sample after purification.

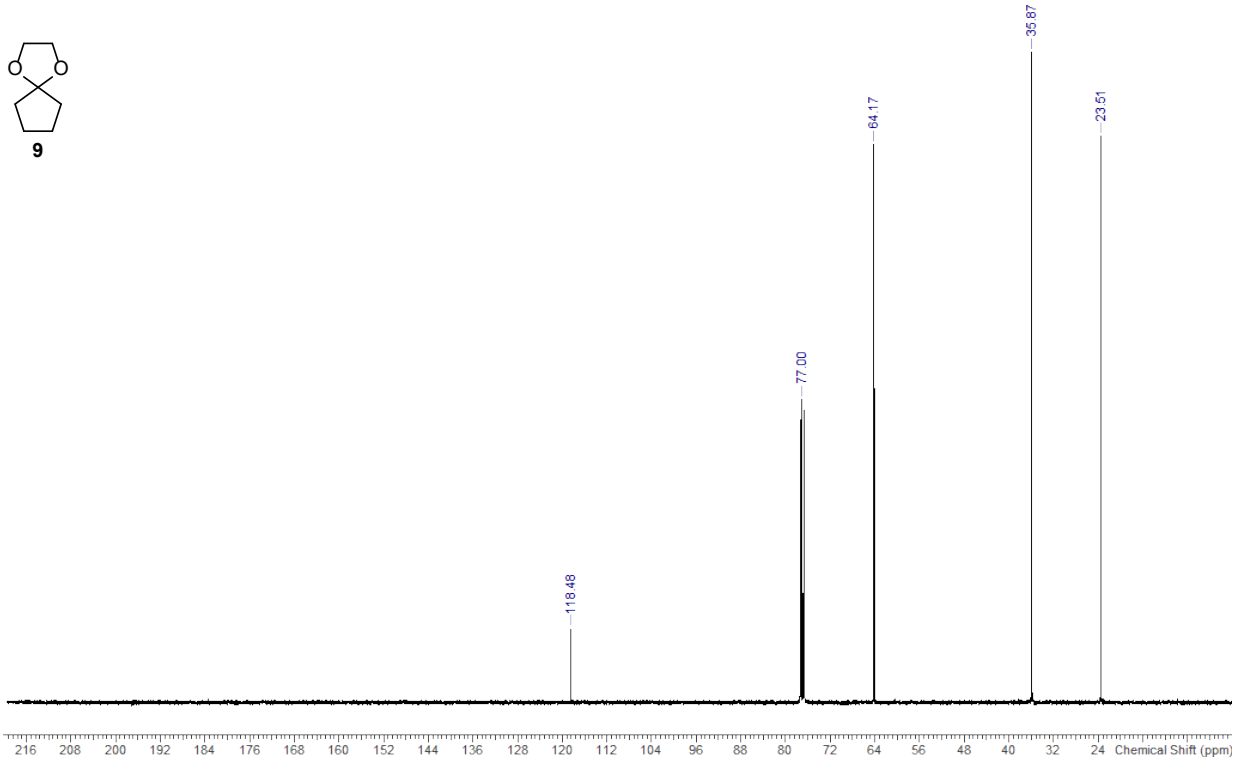
# 10 NMR Spectra

## 10.1 1,4–dioxaspiro[4.4]nonane (9)

### 10.1.1 $^{1}$H NMR (400 MHz, $CDCl_3$)

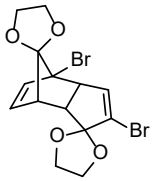



### 10.1.2 $^{13}$C NMR (101 MHz, $CDCl_3$)

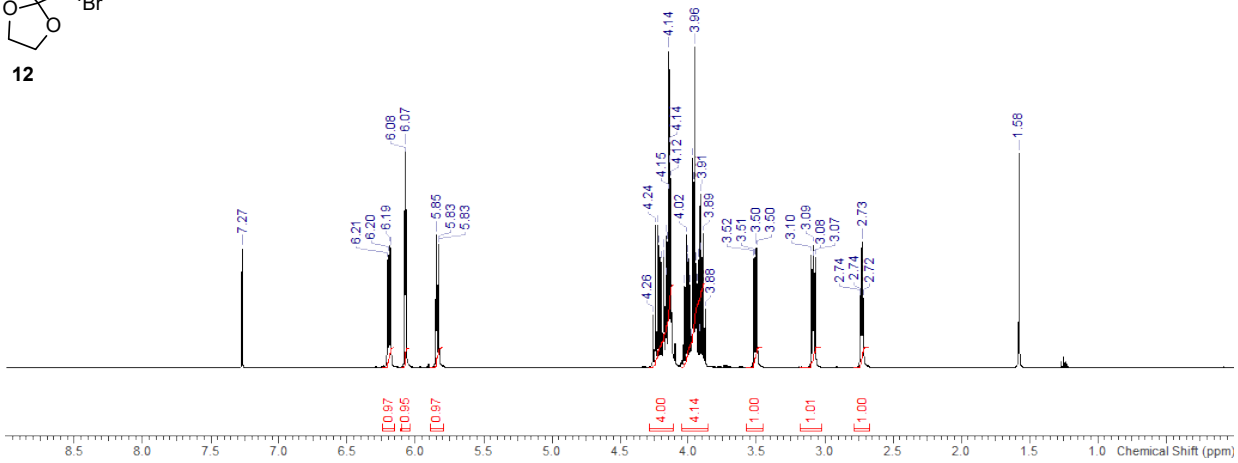


## 10.2 *Endo*–2,4–dibromodicyclopentadiene–1,8–dione bisethylene ketal (12)

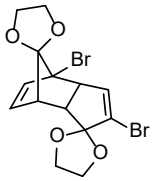
### 10.2.1 $^{1}$H NMR (400 MHz, $CDCl_3$)




12



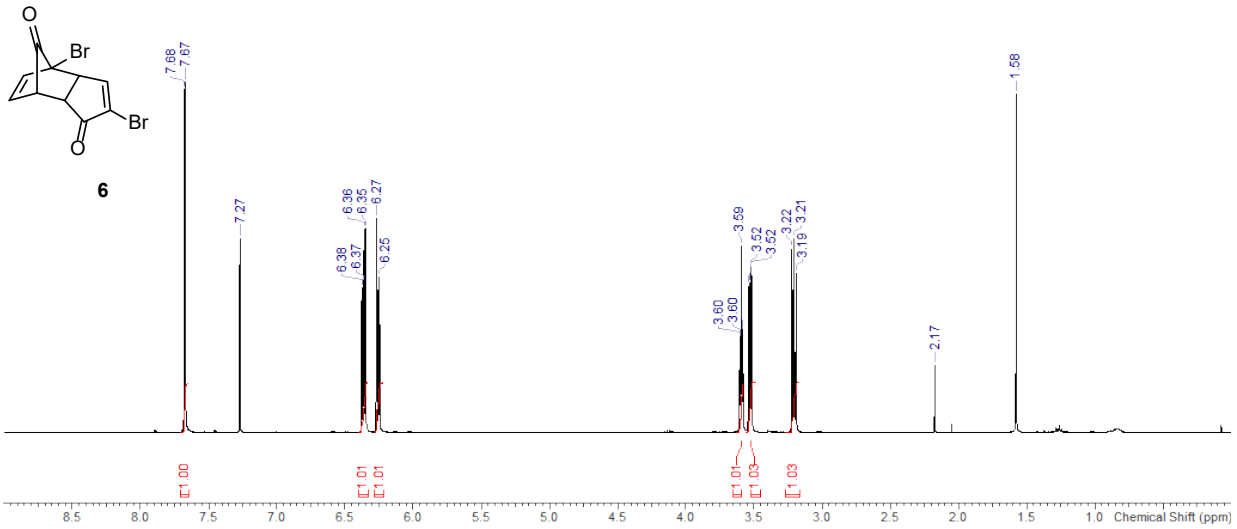

### 10.2.2 $^{13}$C NMR (101 MHz, $CDCl_3$)



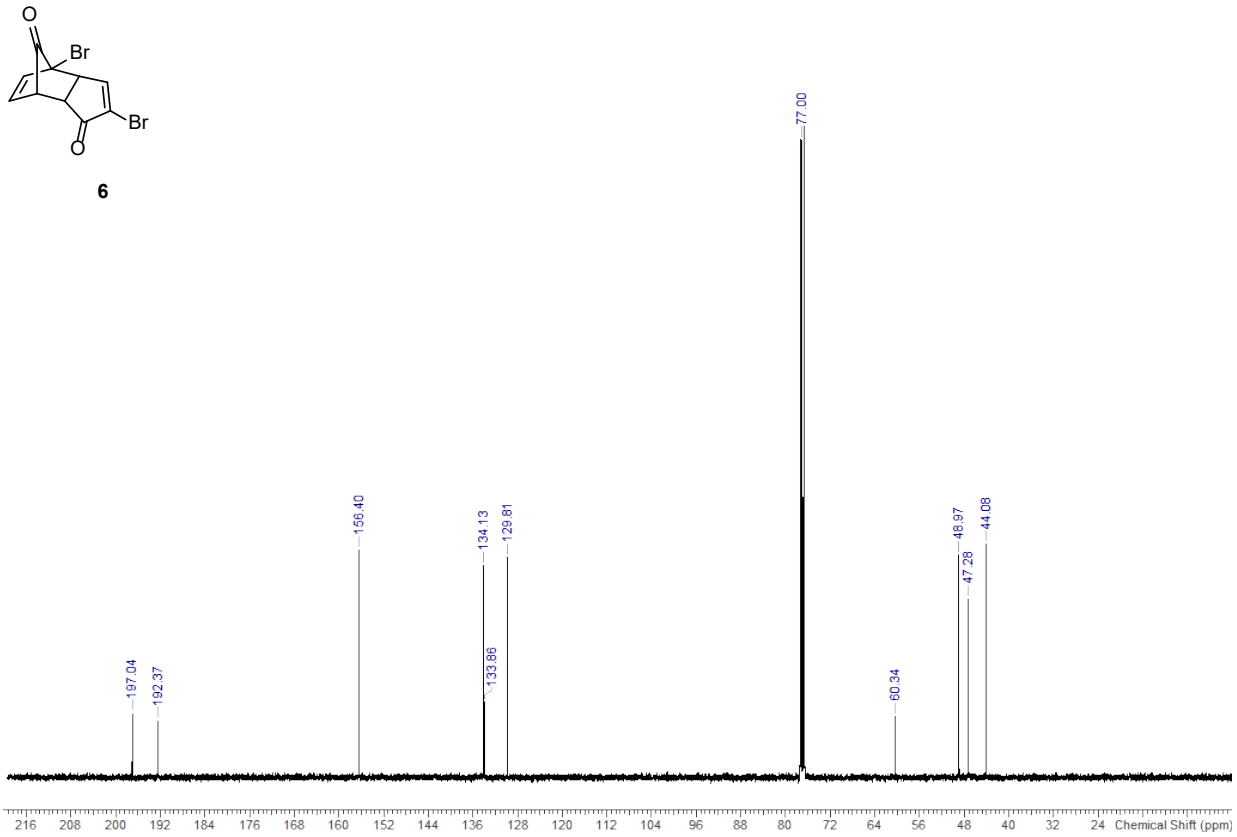

12

## 10.3 *Endo*–2,4–dibromocyclopentadiene–1,8–dione (6)

### 10.3.1 $^{1}$H NMR (400 MHz, $CDCl_3$)

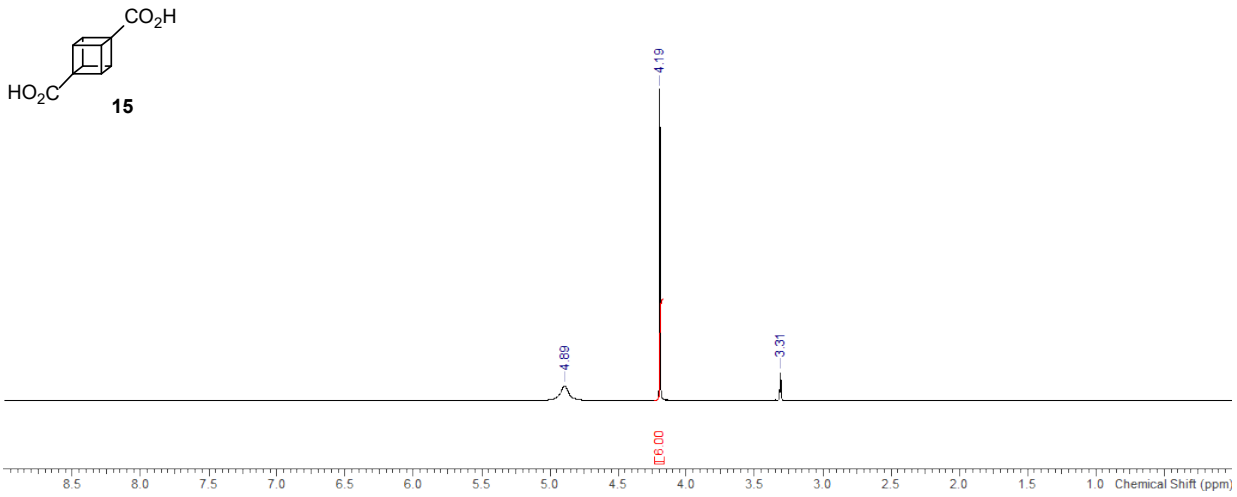



### 10.3.2 $^{13}$C NMR (101 MHz, $CDCl_3$)

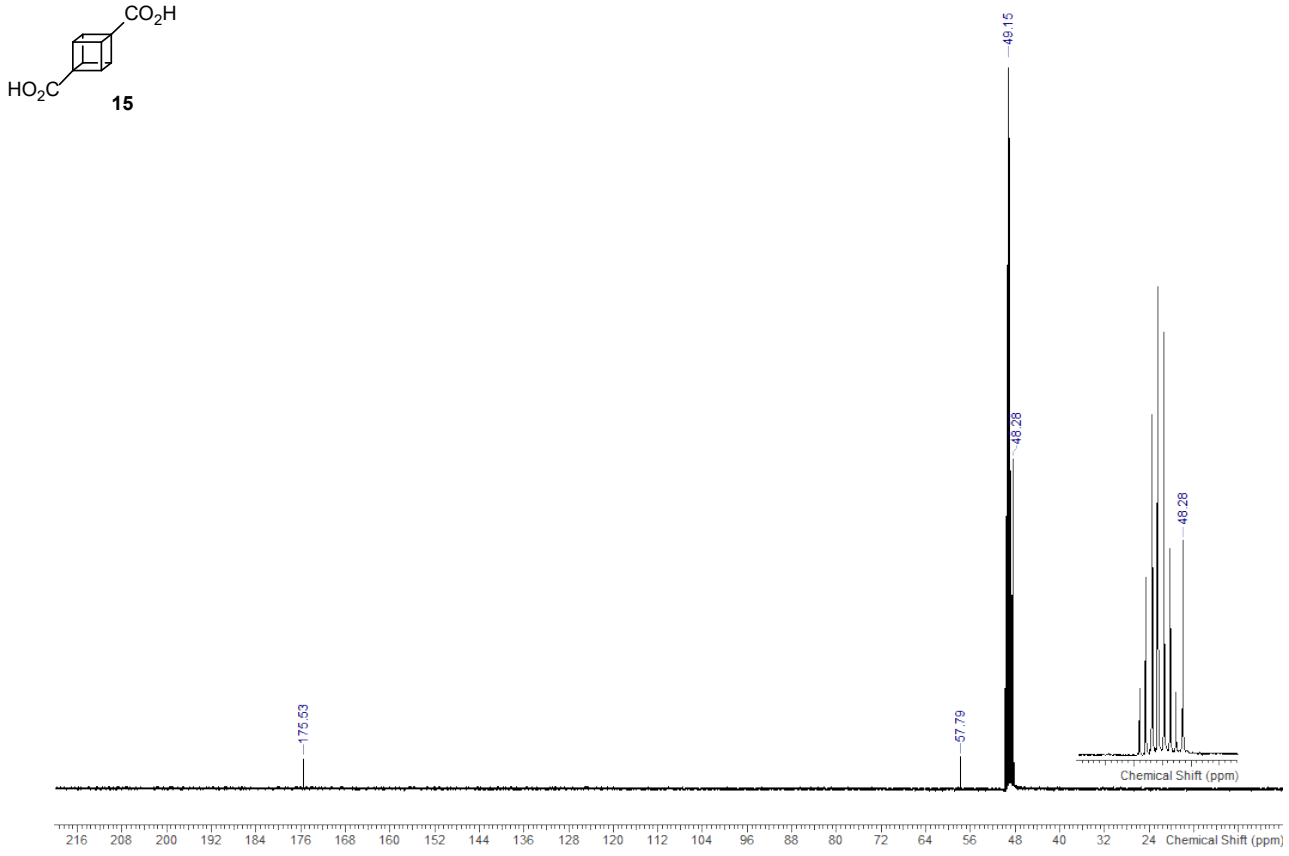


## 10.4 1,4–Cubanedicarboxylic acid (15)

### 10.4.1 $^{1}$H NMR (400 MHz, $CD_3OD$)

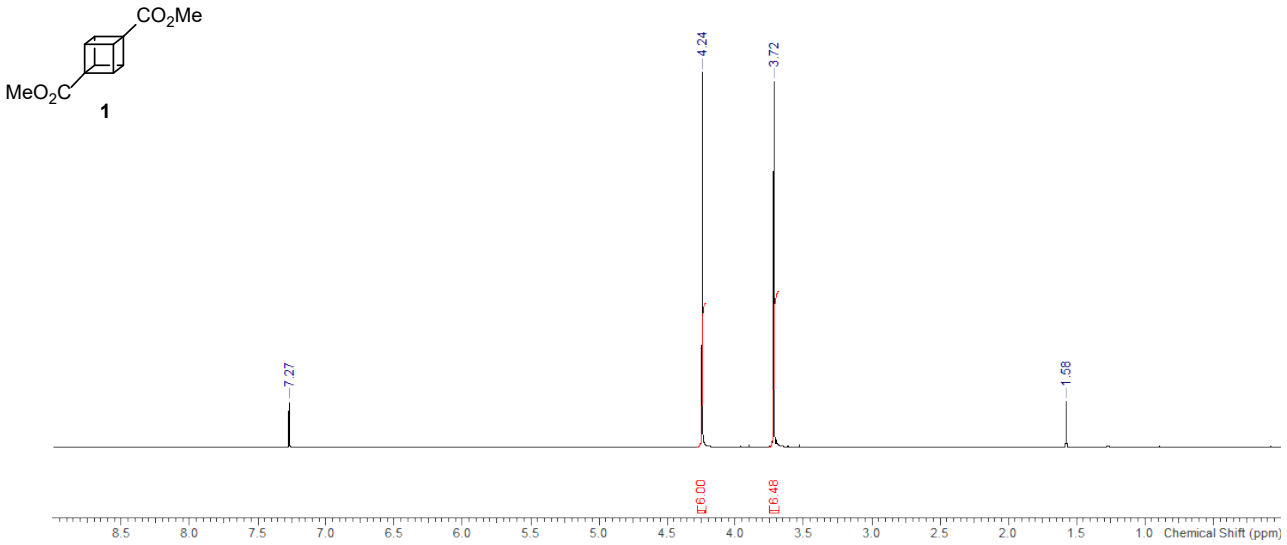



### 10.4.2 $^{13}$C NMR (101 MHz, $CD_3OD$)

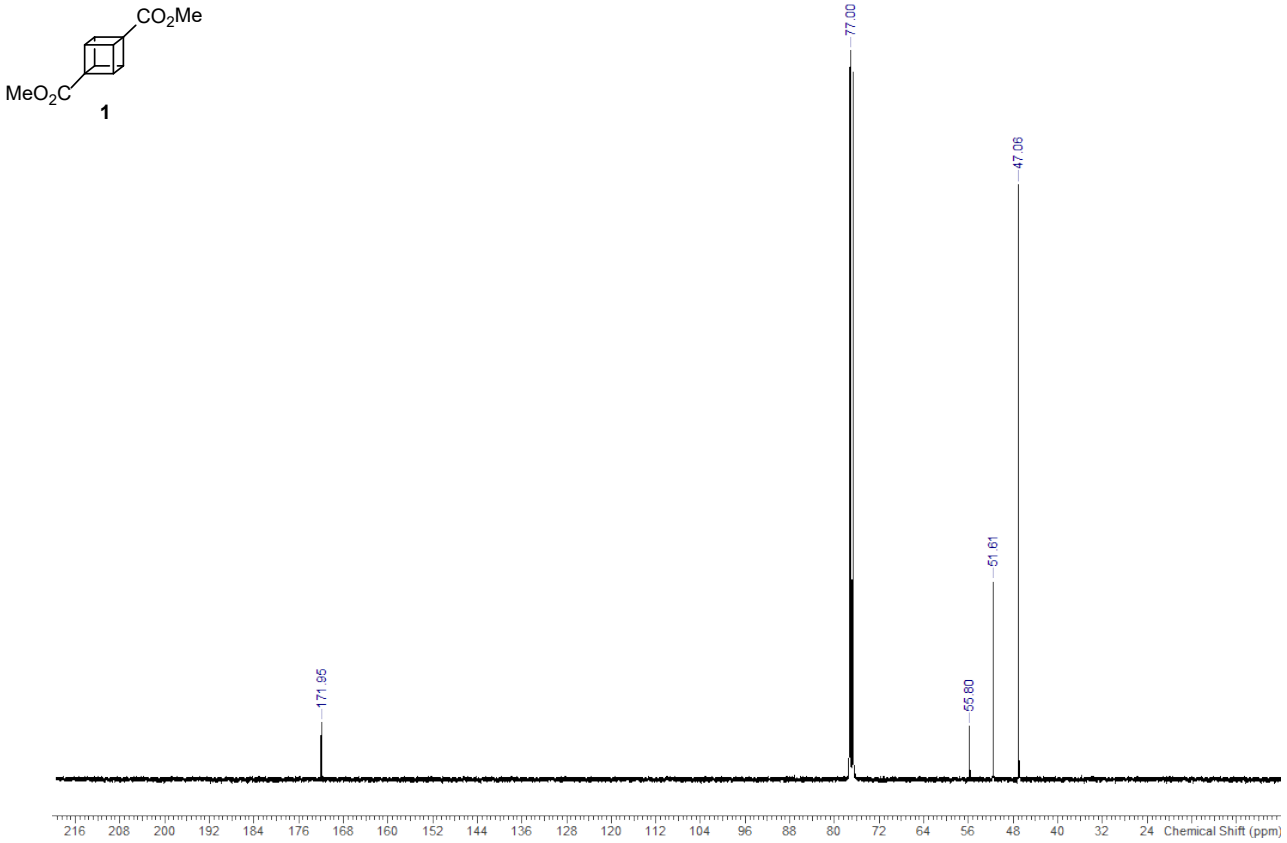


# 11 Dimethyl 1,4–cubanedicarboxylate (1)

## 11.1.1 $^{1}$H NMR (400 MHz, $CDCl_3$)




## 11.1.2 $^{13}$C NMR (101 MHz, $CDCl_3$)



# 12 X-Ray Crystallographic Data

## 12.1 *Endo*–2,4–dibromocyclopentadiene–1,8–dione (6) [1894382]

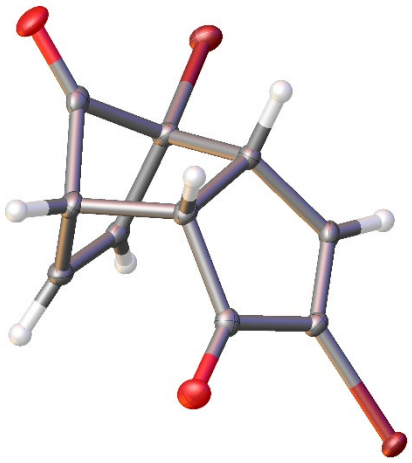


**Figure S18.** Structure of **6** with thermal ellipsoids drawn at the 50% probability level.

**Experimental.** Single clear colourless fragment-shaped crystals of **DC_8346_009** were recrystallised from a mixture of hexane and EtOAc by slow evaporation. A suitable crystal 0.47×0.20×0.05 $mm^3$ was selected and mounted on a MITIGEN holder silicon oil on a Rigaku AFC12 FRE-HF diffractometer. The crystal was kept at a steady $T$ = 100(2) K during data collection. The structure was solved with the **ShelXT** (Sheldrick, 2015) structure solution program using the Intrinsic Phasing solution method and by using **Olex2** (Dolomanov et al., 2009) as the graphical interface. The model was refined with version 2016/6 of **ShelXL** (Sheldrick, 2015) using Least Squares minimisation.

**Table S3.** Crystal data of **6**.

| | |
|---|---|
| Formula | $C_{10}H_6Br_2O_2$ |
| $D_{calc.}$/ g cm$^{-3}$ | 2.207 |
| $\mu$/mm$^{-1}$ | 8.436 |
| Formula Weight | 317.97 |
| Colour | clear colourless |
| Shape | fragment |
| Size/mm$^3$ | 0.47×0.20×0.05 |
| $T$/K | 100(2) |
| Crystal System | monoclinic |
| Space Group | $P2_1/c$ |
| $a$/Å | 7.7120(2) |
| $b$/Å | 6.4673(2) |
| $c$/Å | 19.3311(6) |
| $\alpha$/° | 90 |
| $\beta$/° | 96.995(3) |
| $\mu$/° | 90 |
| V/Å$^3$ | 956.98(5) |
| $Z$ | 4 |
| $Z'$ | 1 |
| Wavelength/Å | 0.71073 |
| Radiation type | Mo$K_\alpha$ |
| $\Theta_{min}$/° | 3.196 |
| $\Theta_{max}$/° | 28.495 |
| Measured Refl. | 23163 |
| Independent Refl. | 2429 |
| Reflections with I > 2(I) | 2289 |
| $R_{int}$ | 0.0632 |
| Parameters | 127 |
| Restraints | 0 |
| Largest Peak | 0.588 |
| Deepest Hole | -0.585 |
| GooF | 1.116 |
| $wR_2$ (all data) | 0.0545 |
| $wR_2$ | 0.0534 |
| $R_1$ (all data) | 0.0281 |
| $R_1$ | 0.0256 |

# 13 References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