Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Benzophenone as a Cheap and Effective Photosensitizer for the Photocatalytic Synthesis of Dimethyl Cubane-1,4-dicarboxylate

Callum Prentice,[a,b] Alice E. Martin,[a] James Morrison,[c] Andrew D. Smith[b] and Eli Zysman-Colman*[a]*

[a]*Organic Semiconductor Centre, EaStCHEM, School of Chemistry, University of St Andrews, St Andrews, Fife, KY16 9ST, UK.*

[b]*EaStCHEM, School of Chemistry, University of St Andrews, St Andrews, Fife, KY16 9ST, UK.*

[c]*Pharmaceutical Sciences, IMED Biotech Unit, Astra Zeneca, Macclesfield, SK10 2NA, UK.*

E-mail: eli.zysman-colman@st-andrews.ac.uk, ads10@st-andrews.ac.uk

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Experimental Section

General Synthetic Procedures. The following starting materials were synthesised according to literature materials, **2**.[1] All other reagents and solvents were obtained from commercial sources and used as received. Air-sensitive reactions were performed under a nitrogen atmosphere using Schlenk techniques, no special precautions were taken to exclude air or moisture during work-up and crystallisation. Flash column chromatography was carried out using silica gel (Silia-P from Silicycle, 60 Å, 40-63 μm). Analytical thin-layer-chromatography (TLC) was performed with silica plates with aluminum backings (250 μm with F-254 indicator). ^{1}H, and ^{13}C and NMR spectra were recorded on a Bruker Advance spectrometer (500 MHz for ^{1}H, 125 MHz for ^{13}C). The following abbreviations have been used for multiplicity assignments: “s” for singlet, “d” for doublet, “dd” for doublet of doublets, “t” for triplet, “dt” for doublet of triplets, “ddd” for doublet of doublet of doublets and “m” for multiplets. ^{1}H and ^{13}C NMR spectra were referenced residual solvent peaks with respect to TMS (δ = 0 ppm). Melting points were measured using open-ended capillaries on an Electrothermal 1101D Mel-Temp apparatus and are uncorrected.

Photocatalysis Set-up

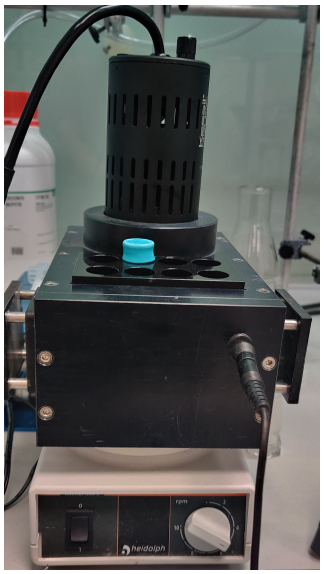


Figure **S1**. Experimental set-up for photocatalysis reactions in a photoreactor using PR160L – Kessil LED lights (λ_{exc} = 390 nm).

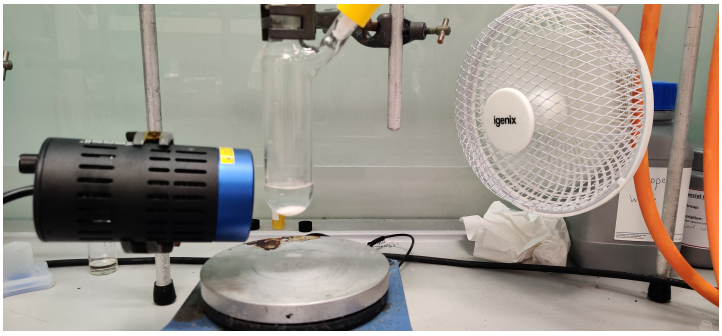


Figure **S2**. Experimental set-up for photocatalysis reactions outside of a photoreactor using PR160L – Kessil LED lights (λ_{exc} = 390 nm).

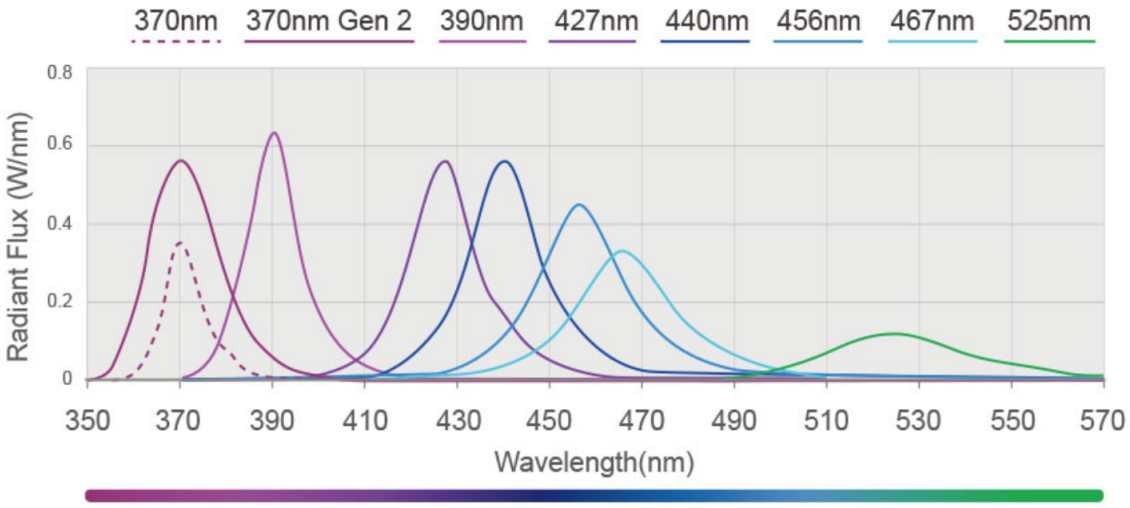


Figure **S3**. Emission spectra of PR160L lamps. The 390 nm lamp was used in this work.

Method for BCl_3 catalysed [2+2] cycloaddition

An oven dried 7 mL vial with magnetic stirrer was charged with *endo*-2,4-dibromodicyclopentadiene-8-oxane-1-one (31.8 mg, 0.1 mmol, 1.0 equiv.). The vial was sealed with a suba-seal and air was exchanged with nitrogen three times. Dry DCM (1.9 mL) and BCl_3 (0.1 mL, 1 M, 1.0 equiv.) were added, and the reaction mixture was sparged with nitrogen for 10 minutes. The vial was placed in a photoreactor box as shown in Figure S1 and irradiated with a 370 nm Kessil LED light for 24 hours. The reaction mixture was quenched with distilled water (5 mL) then extracted with DCM (3 x 5 mL). The organic phases were combined, dried with $MgSO_4$, filtered, and concentrated under vacuum to afford crude product.

General Method for Benzophenone Catalysed [2+2] Cycloaddition.

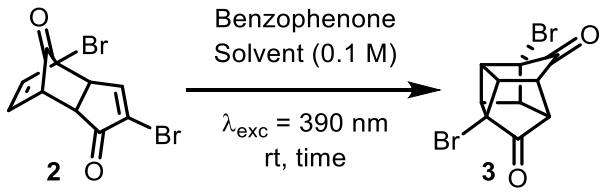
A Schlenk flask or vial with magnetic stirrer was charged with **3** (1.0 equiv.) and benzophenone. The flask or vial was sealed with a suba-seal and MeCN was added, and the solution was sparged with nitrogen for 15 minutes. The flask or vial was then irradiated by a 390 nm Kessil LED for 24 hours either inside a photoreactor or outside (Figures S1-S2). The progress of the reaction was monitored by taking an aliquot and submitting it to ^{1}H NMR analysis and conversions were calculated using the same methods as Collin and Linclau.[1]

Theoretical Calculations

Calculations were performed with Gaussian16, Revision C.01,[2] employing either pure or hybrid levels of DFT using the 6-31G(d,p)[3] basis set with a variety of functionals; B3LYP, PBE0 and BLYP.[4–7] An ultrafine integration grid (99 radial shells with 590 angular points per shell) was used. Implicit solvation was used at both the optimisation and single point steps using the Polarizable Continuum Model (PCM),[8,9] employing parameters for DCM ($\varepsilon = 8.93$).[10–12] Corrections for dispersion were also included for optimisation and single point calculations using the Grimme DFT-D3 correction with Becke Johnson dampening.[13,14] Calculations were submitted and processed using an in-house developed software, *Silico*, which incorporates a number of publicly available software libraries, including: cclib[15] for parsing of result files and Open Babel[16]/Pybel[17] for file interconversion.

Solvent Optimization

Table S1. Optimization of the photocatalyzed intramolecular [2+2] cycloaddition.[a]

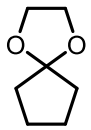


Entry	Catalyst Loading / mol%	time / h	Solvent	Conversion / %[b]
1	100	72	CH_2Cl_2	97
2	100	72	MeCN	100
3	50	24	MeCN	100
4	100	24	DMF	N.D.
5	100	24	MeOH	N.D.

[a]Conditions: **2**, benzophenone, solvent (0.1 M), N_2, LED (λ_{exc} = 390 nm), rt, outside photoreactor (see Figure **S2**). [b]From crude ^{1}H NMR, N.D. = **3** not detected.

Compound Characterization

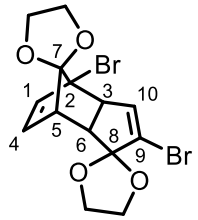
1,4–dioxaspiro[4.4]nonane, 7:



Colourless oil, **Yield:** 52%. **^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm):** 3.90 (s, 4H, OC*H*$_2$C*H*$_2$O), 1.80 – 1.75 (m, 4H, C*H*$_2$CH$_2$CH$_2$C*H*$_2$), 1.71 – 1.65 (m, 4H, CH$_2$C*H*$_2$C*H*$_2$CH$_2$). **^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ_C (ppm):** 118.5 (O*C*O), 64.2 (O*C*H$_2$*C*H$_2$O), 35.9 (*C*H$_2$CH$_2$CH$_2$*C*H$_2$), 23.6 (CH$_2$*C*H$_2$*C*H$_2$CH$_2$).

Data matches that previously reported.[1]

***endo*–2,4–dibromodicyclopentadiene–1,8–dione bisethylene ketal, 8:**

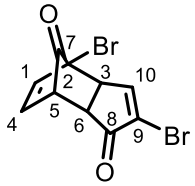


Beige solid, **Yield:** 59%. **Mp**: 164-165 °C {Lit:[18] 174-176 °C). **^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm):** 6.19 (1H, dd, *J* = 6.4, 3.6 Hz, C(4)*H*), 6.07 (1H, d, *J* = 2.5 Hz, C(10)*H*), 5.84 (1H, dd, *J* = 6.4, 1.3 Hz, C(1)*H*), 4.26 – 4.11 (4H, m, OCH_2CH_2O), 4.04 – 3.87 (4H, m, OCH_2CH_2O), 3.50 (1H, dd, *J* = 7.4, 2.5 Hz, C(3)*H*), 3.08 (1H, dd, *J* = 7.4, 4.7 Hz, C(6)*H*), 2.72 (1H, td, *J* = 4.7, 0.7 Hz, C(6)*H*), **^{13}C NMR (101 MHz, $CDCl_3$) δ_C (ppm):** 134.6 (*C*(10)), 133.1 (*C*(1)), 132.6 (*C*(4)), 128.1 (*C*(8)), 126.1 (*C*(7)), 115.7(*C*(2)), 67.8 (*C*(2)), 66.5 (O*C*H_2CH_2O), 66.3 (O*C*H_2CH_2O), 65.4 (OCH_2*C*H_2O), 65.3 (OCH_2*C*H_2O), 55.8 (*C*(3)), 49.6 (*C*(6)), 47.3 (*C*(5)).

GCMS $C_{14}H_{14}Br_2O_4$ $[M]^+$ found: 406.0, theoretical: 406.1, retention time = 8.9 min.

Data matches that previously reported.[1]

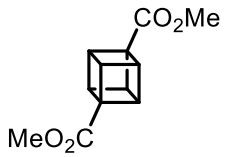
***endo*-2,4-dibromodicyclo-pentadiene-1,8-dione, 2:**



Colourless solid, **Yield:** 51%. **Mp:** 154-155 °C {Lit.[19] 154-155 °C}. **^{1}H NMR (400 MHz, $CDCl_3$) δ_H (ppm):** 7.67 (1H, d, *J* = 3.1 Hz, C(10)*H*), 6.36 (1H, dd, *J* = 6.9, 3.9 Hz, C(4)*H*), 6.25 (1H, dt, J= 6.9, 0.8 Hz, C(1)*H*), 3.59 (1H, ddd, *J* = 5.2, 3.9, 0.6 Hz, C(5)*H*), 3.52 (1H, dd, J = 6.9, 3.0 Hz, C(3)*H*), 3.20 (1H, dd, *J* = 6.4, 5.0 Hz, C(6)*H*). **^{13}C NMR (101 MHz, $CDCl_3$) δ_C (ppm):** 197.1 (*C*(8)), 192.5 (*C*(7)), 156.5 (*C*(10)), 134.2 (*C*(1)), 133.9 (*C*(4)), 129.9 (*C*(9)), 60.4 (*C*(9)), 49.0 (*C*(3)), 47.3 (*C*(5)), 44.1 (*C*(6)).

Data matches that previously reported.[1]

Dimethyl 1,4-cubanedicarboxylate, 1:



A Schlenk flask with magnetic stirrer was charged with **3** (328 mg, 1.0 mmol, 1 equiv.) and benzophenone (91.0 mg, 0.5 mmol, 0.5 equiv.). The flask was sealed with a suba-seal and MeCN (10 mL) was added, and the solution was sparged with nitrogen for 15 minutes. The vial was placed in front of a 390 nm Kessil LED light and stirred for 24 hours. Solvent was removed from the reaction mixture under reduced pressure, and the crude product was used without further purification.

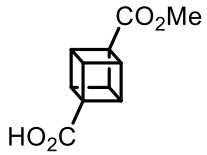
The crude materials of six runs were combined and suspended in water (10 mL). NaOH solution (10 mL, 26% w/v solution) was added to the brown suspension and the reaction was refluxed vigorously for 16 h. The solution was removed from heat and left to cool to room temperature, then HCl was added dropwise to reach a pH of 1-2. The solution was filtered and washed with ice-cold water. In our hands, the 1,4-cubanedicarboxylic acid did not precipitate out and filtration simply removed excess benzophenone. The filtrate was then concentrated *in vacuo* to yield a dark brown solid. This material was then suspended in methanol and filtered to remove some of the salts. This filtrate was then concentrated *in vacuo* and thoroughly dried to yield a brown solid which was used without further purification.

Crude 1,4-cubanedicarboxylic acid (ca. 6.0 mmol) was dissolved in methanol (30 mL) and concentrated HCl (0.89 mL, 10.8 mmol, 1.8 equiv.) was added to the reaction mixture. The reaction was then refluxed for 16 h under a nitrogen atmosphere. The solvent was removed under reduced pressure to obtain a brown solid, which was then dissolved in CH_2Cl_2 (30 mL). Water (30 mL) was added, and the aqueous phase was extracted with DCM (3 × 30 mL). The organic phases were combined, washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford the crude product. Purification via silica gel chromatography using EtOAc:Hexane (80:20) afforded 0.27 g (20%) of dimethyl 1,4-cubanedicarboxylate, **1**. **Mp**: 160-164 °C {Lit:[1] 164-165 °C}. **^{1}H NMR (400 MHz, $CDCl_3$)**

δ_H (ppm): 4.23 (s, 6H, C*H*), 3.71 (s, 6H, OCH_3). **$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ (ppm):** 172.0 (*C*=O), 55.8 (*C*COOCH$_3$), 51.7 (O*C*H$_3$), 47.1 (*C*H).

Data matches that previously reported.[1]

4-(methoxycarbonyl)cubane-1-carboxylic acid, 5:

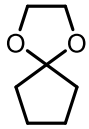


A round bottom flask with magnetic stirrer was charged with **1** (0.25 g, 1.14 mmol, 1.0 equiv.) and dissolved in THF (10 mL). NaOH (2.3 M, 0.5 mL, 1.0 equiv.) in MeOH was added dropwise and the reaction was stirred at room temperature for 24 h. The reaction was concentrated *in vacuo* and suspended in water. Extraction with CH_2Cl_2 (3 × 10 mL) yielded unreacted **1** (0.11 g, 44%). The aqueous phase was acidified with 2M HCl to a pH of 1 and extracted with CH_2Cl_2 (3 × 10 mL). The organic phases were combined, washed with brine (1 × 10 mL), dried (Na_2SO_4) and concentrated *in vacuo* to yield 0.12 g of 4-(methoxycarbonyl)cubane-1-carboxylic acid, **5**, as a colourless solid in 50% yield.

Mp: 180-182 °C {Lit:[20] 182-183 °C}. **^{1}H NMR (400 MHz, DMSO) δ_H (ppm):** 12.41 (s, 1H, COO*H*) 4.16 – 4.12 (m, 6H, C*H*), 3.62 (s, 3H, OCH_3). **^{13}C{^{1}H} NMR (126 MHz, DMSO) δ (ppm):** 172.7 (*C*=O), 172.2 (*C*=O), 56.0 (*C*COO), 55.5 (*C*COO), 51.8 (O*C*H_3), 46.58 (*C*H), 46.55 (*C*H).

Data matches that previously reported.[20]

NMR Spectra:



7, ^{1}H, $CDCl_3$, 400 MHz

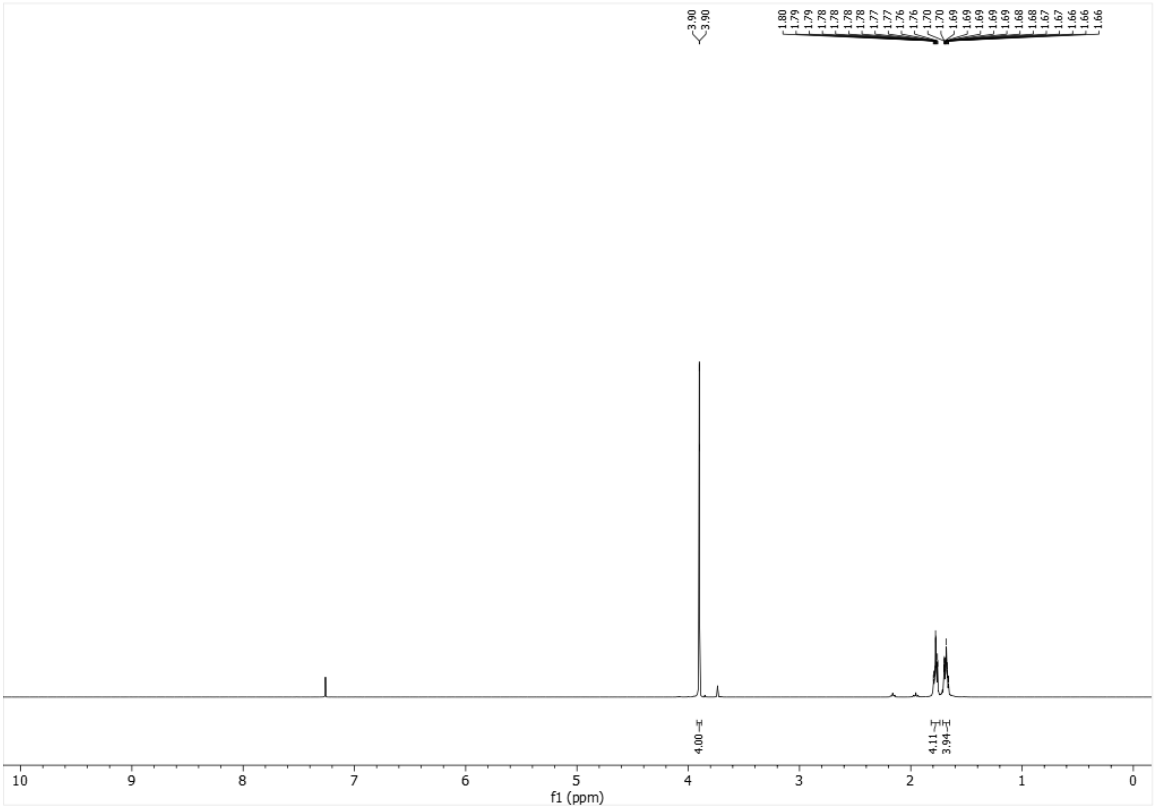


Figure **S4**. ^{1}H NMR spectrum of 1,4-dioxaspiro[4.4]nonane in $CDCl_3$ with ethylene glycol and cyclopentanone impurities.

7, ^{13}C, $CDCl_3$, 101 MHz

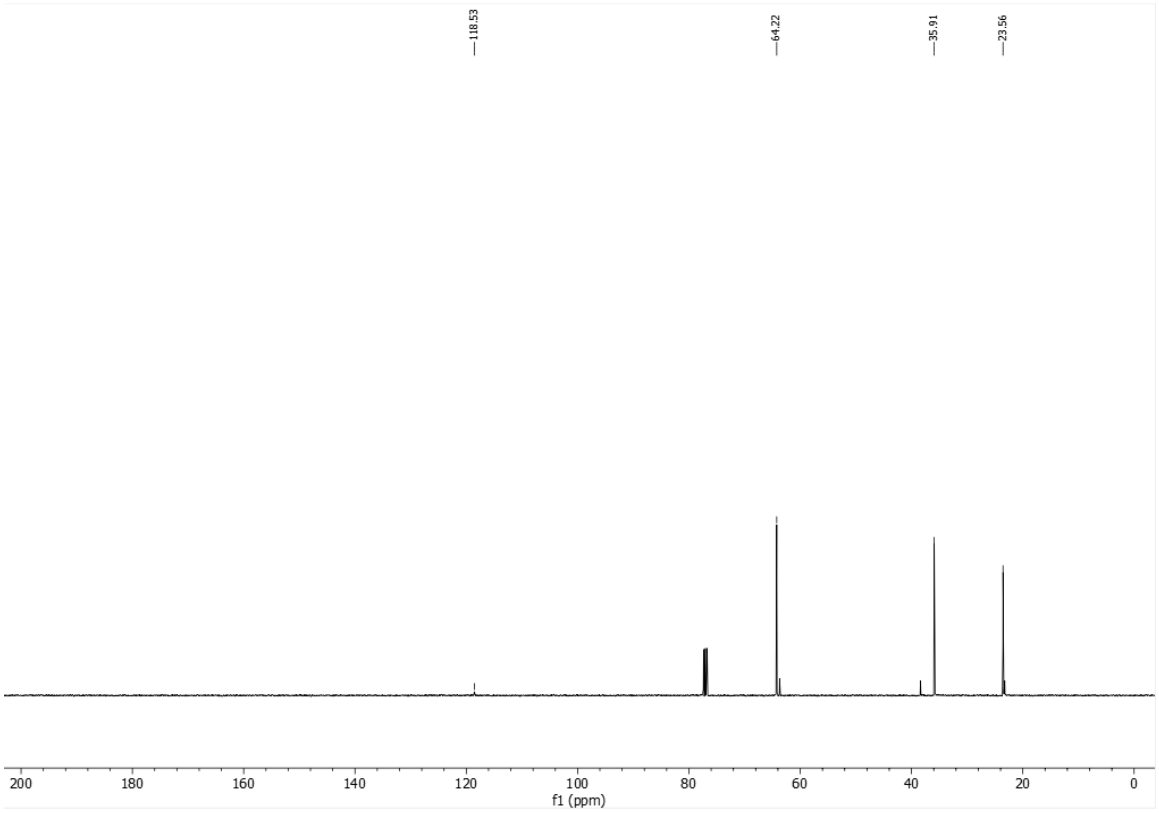
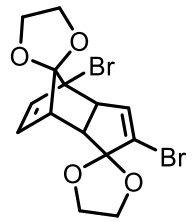


Figure **S5**. ^{13}C NMR spectrum of 1,4-dioxaspiro[4.4]nonane in $CDCl_3$ with ethylene glycol and cyclopentanone impurities.



8, ^{1}H, $CDCl_3$, 400 MHz

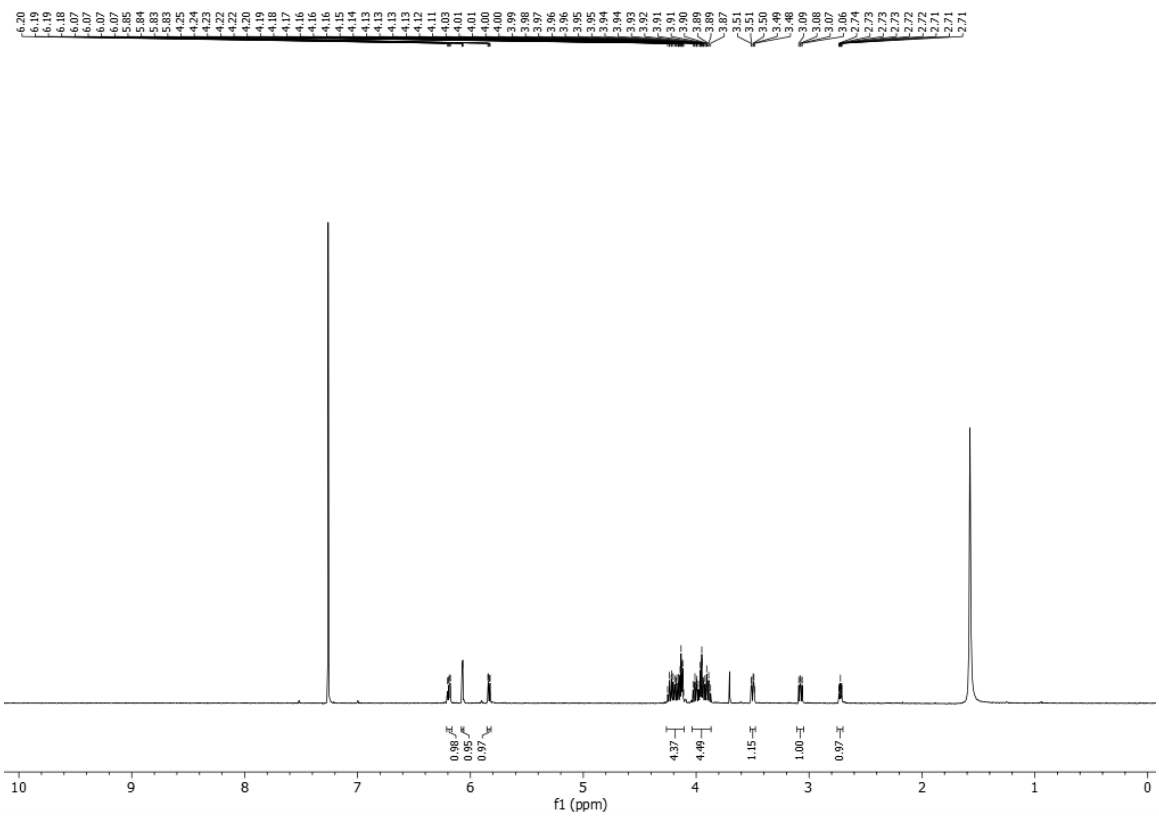


Figure **S6**. ^{1}H NMR spectrum of endo-2,4-dibromodicyclopentadiene-1,8-dione bisethylene ketal in $CDCl_3$.

8, ^{13}C, $CDCl_3$, 101 MHz

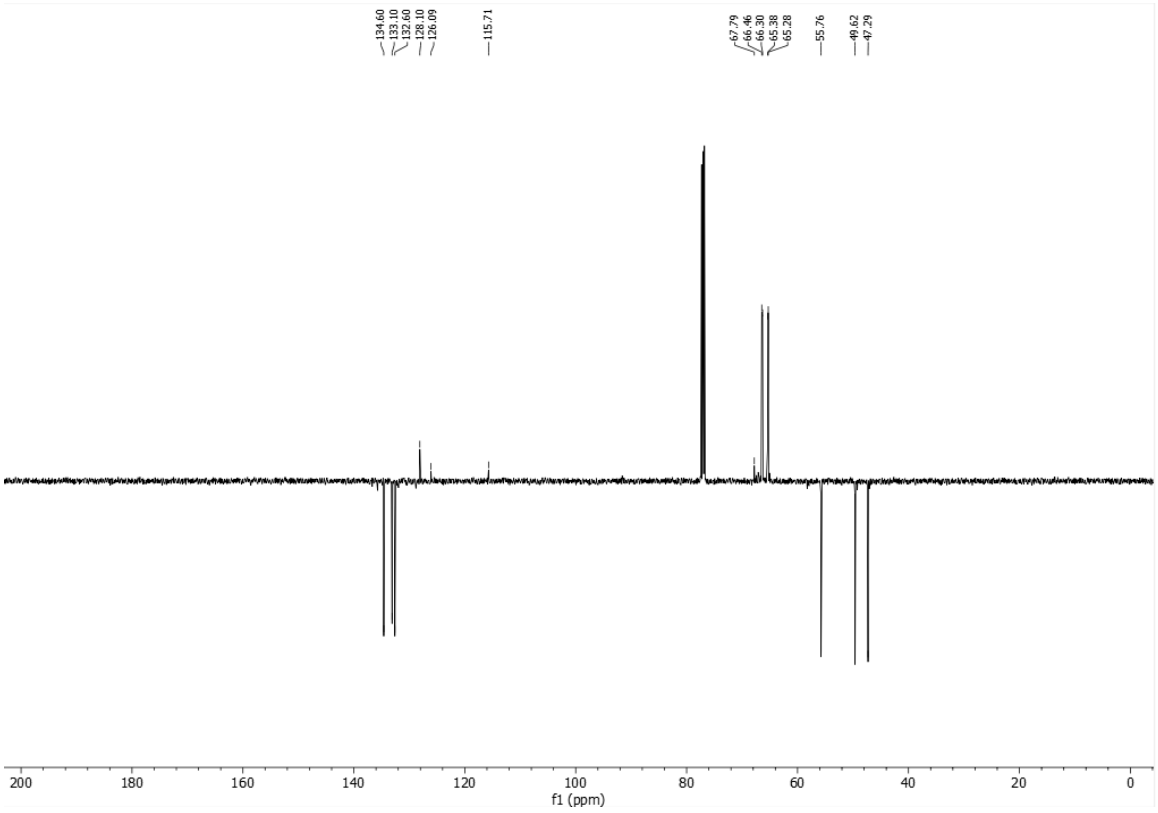
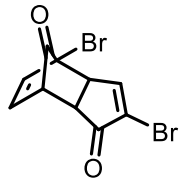


Figure **S7**. ^{13}C NMR spectrum of endo-2,4-dibromodicyclopentadiene-1,8-dione bisethylene ketal in $CDCl_3$.



2, ^{1}H, $CDCl_3$, 400 MHz

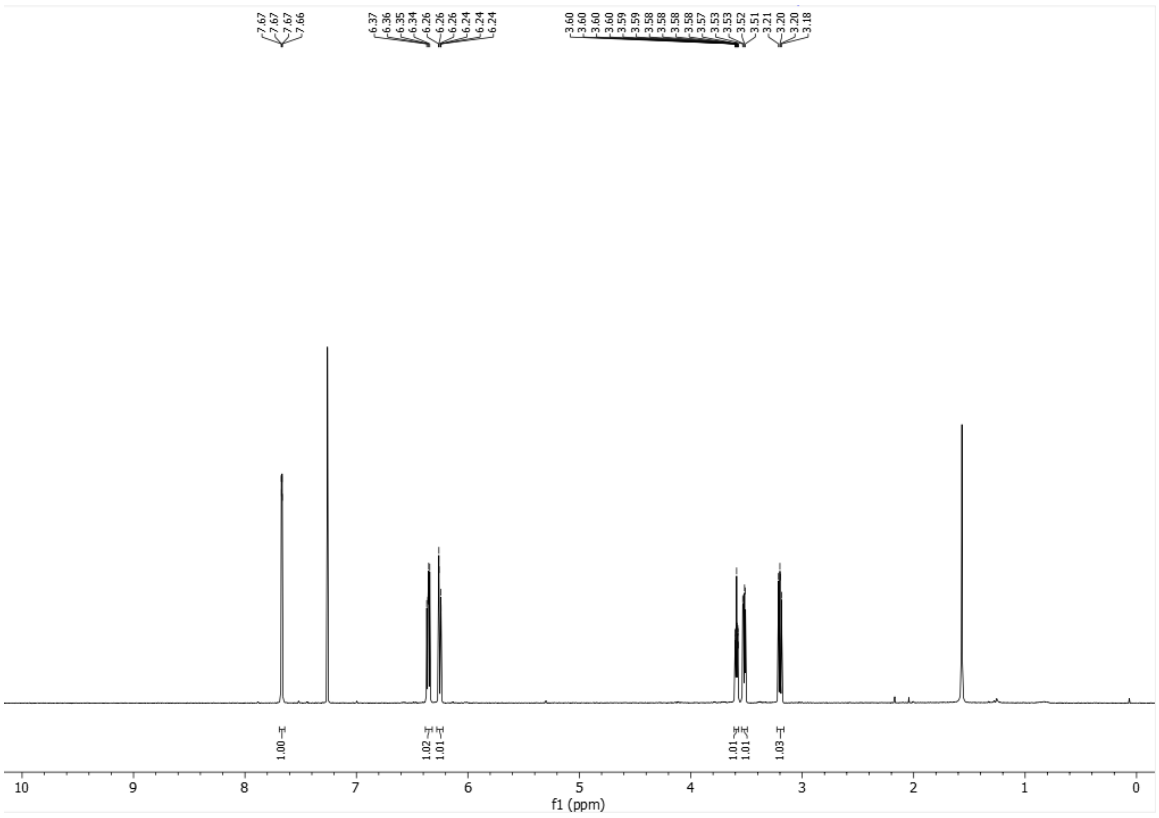


Figure **S8**. ^{1}H NMR spectrum of endo-2,4-bibromodicyclopentadiene-1,8-dione in $CDCl_3$.

2, ^{13}C, $CDCl_3$, 101 MHz

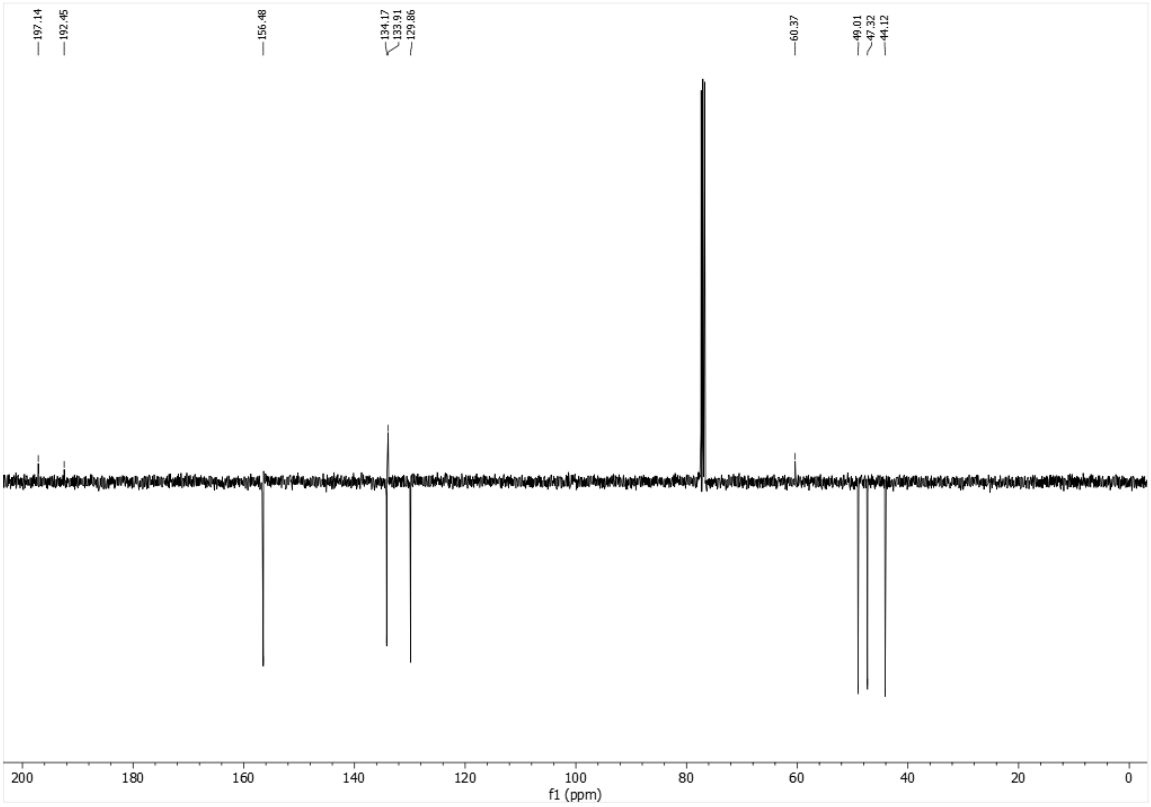
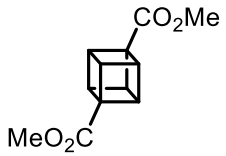


Figure **S9**. ^{13}C NMR spectrum of endo-2,4-bibromodicyclopentadiene-1,8-dione in $CDCl_3$.

Dimethyl cubane-1,4-dicarboxylate, 1:



1, ^{1}H, $CDCl_3$, 400 MHz

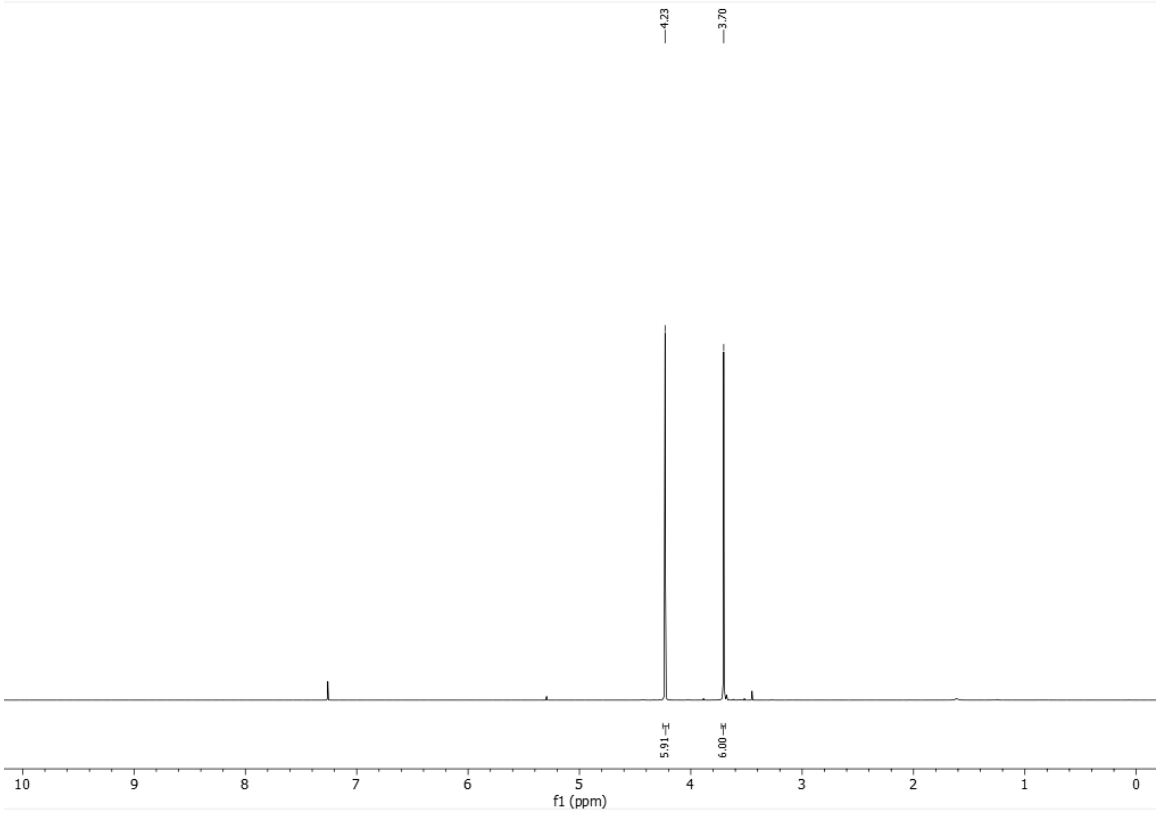


Figure **S10**. ^{1}H NMR spectrum of dimethyl cubane-1,4-dicarboxylate in $CDCl_3$.

1, ^{13}C, $CDCl_3$, 126 MHz

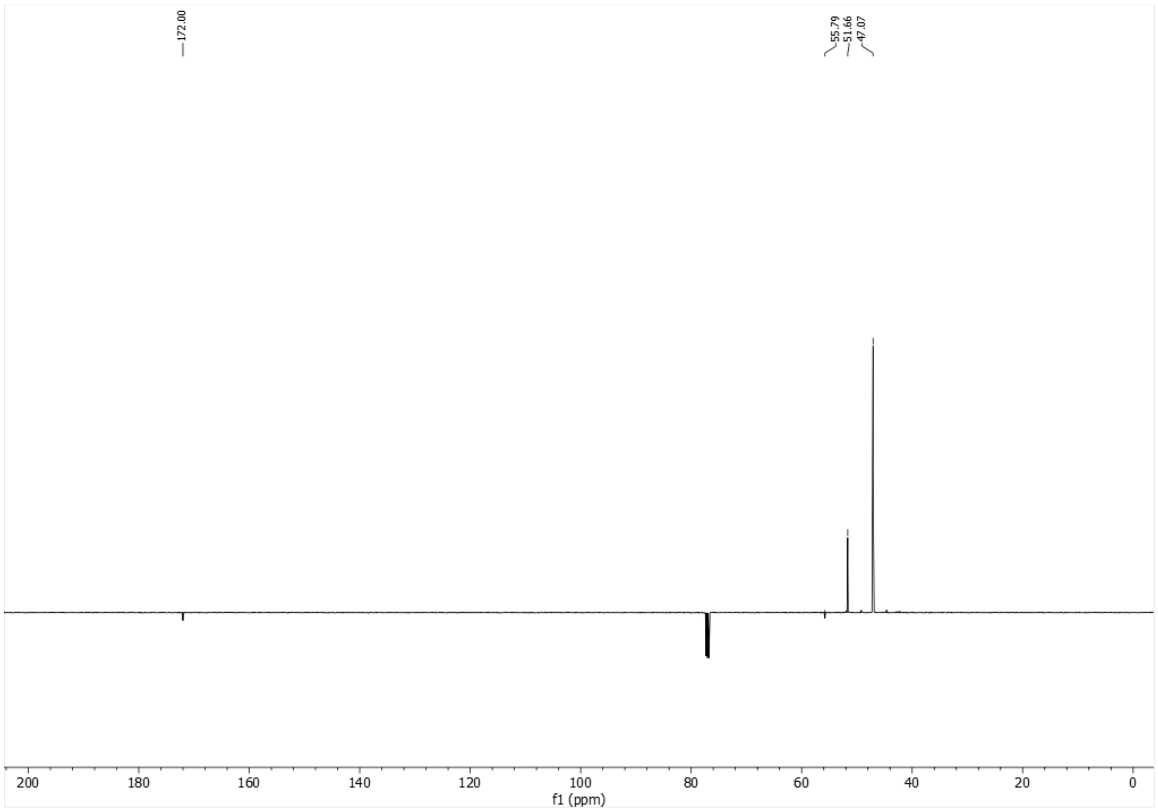
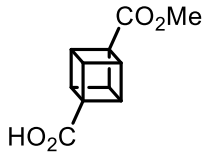


Figure **S11**. ^{13}C NMR spectrum of dimethyl cubane-1,4-dicarboxylate in $CDCl_3$.

4-(methoxycarbonyl)cubane-1-carboxylic acid, 5:



5, ^{1}H, DMSO, 400 MHz

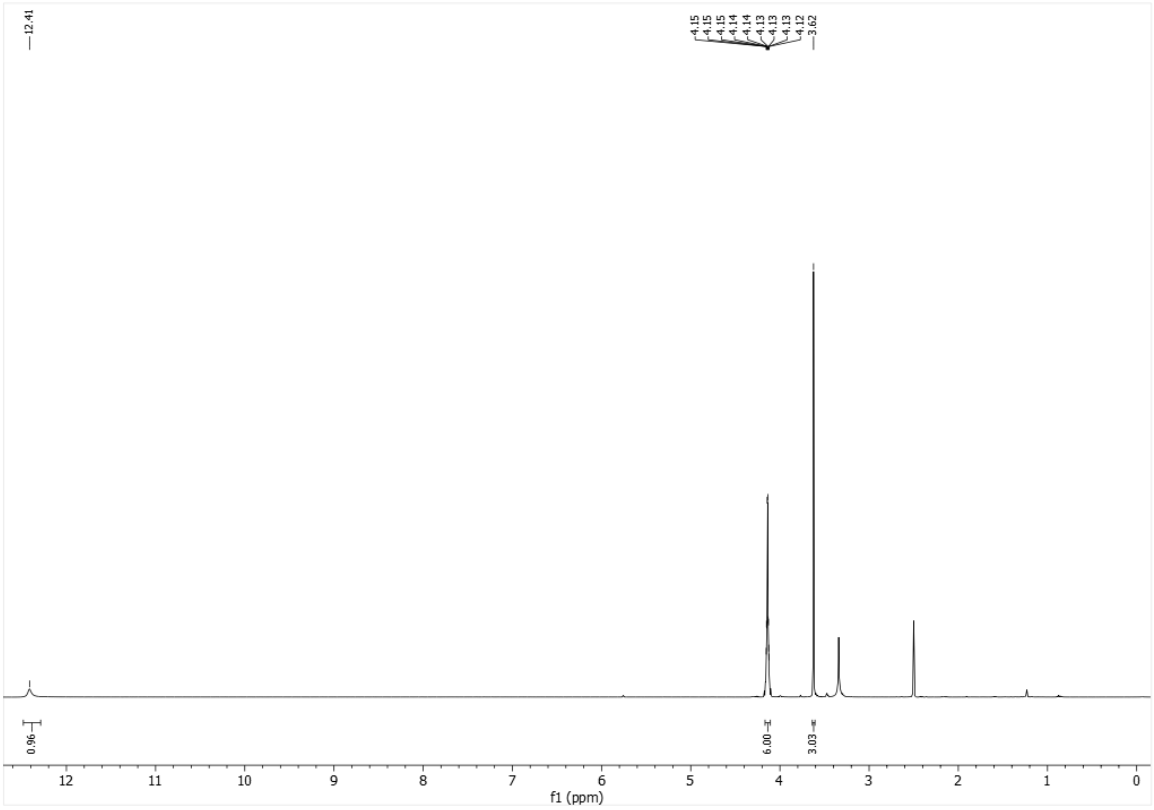


Figure **S12**. ^{1}H NMR spectrum of 4-(methoxycarbonyl)cubane-1-carboxylic acid in DMSO.

5, ^{13}C, DMSO, 126 MHz

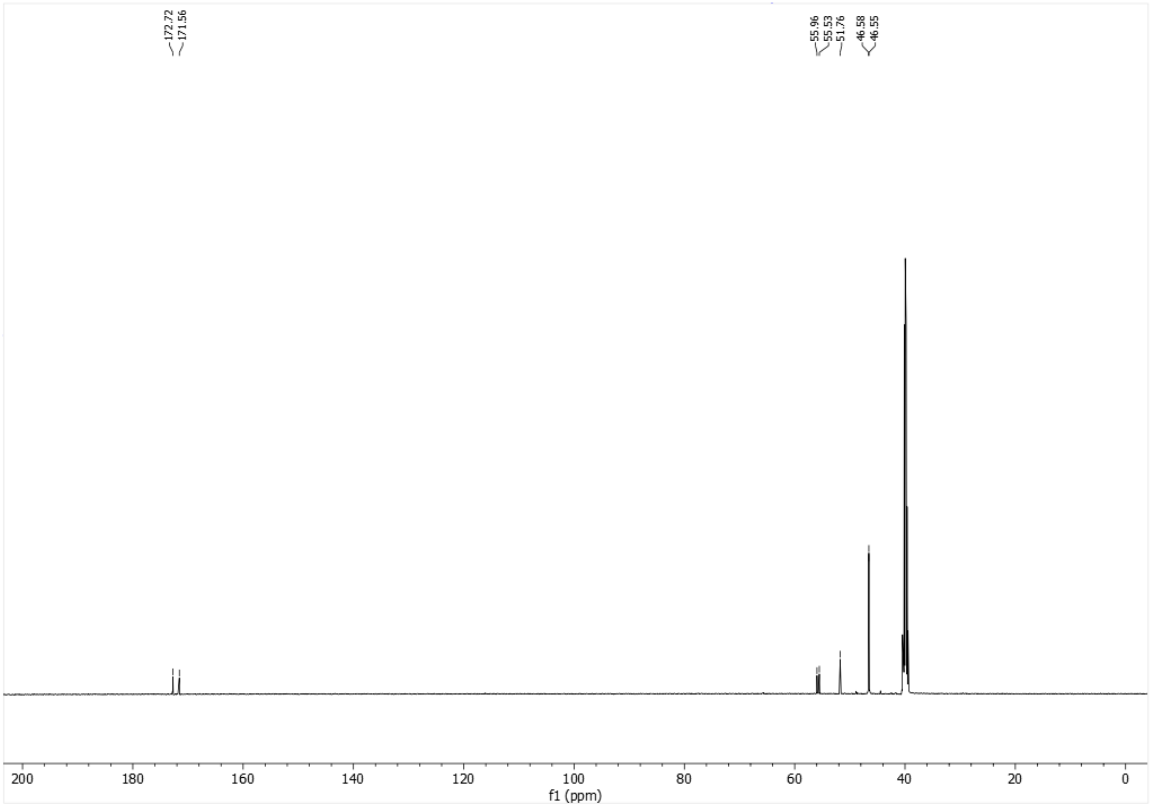
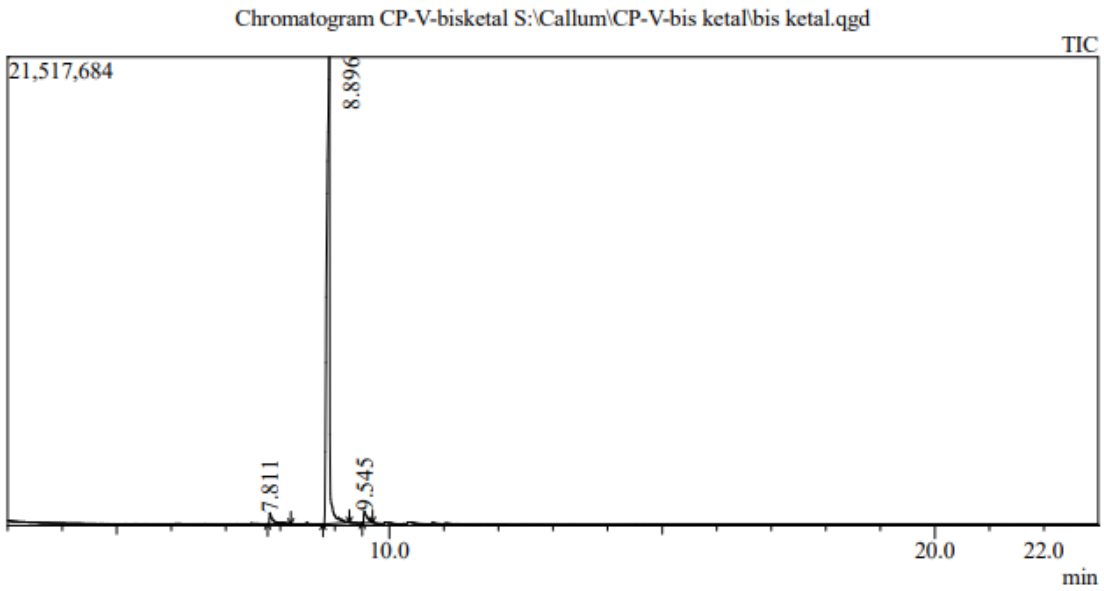


Figure **S13**. ^{13}C NMR spectrum of 4-(methoxycarbonyl)cubane-1-carboxylic acid in DMSO.

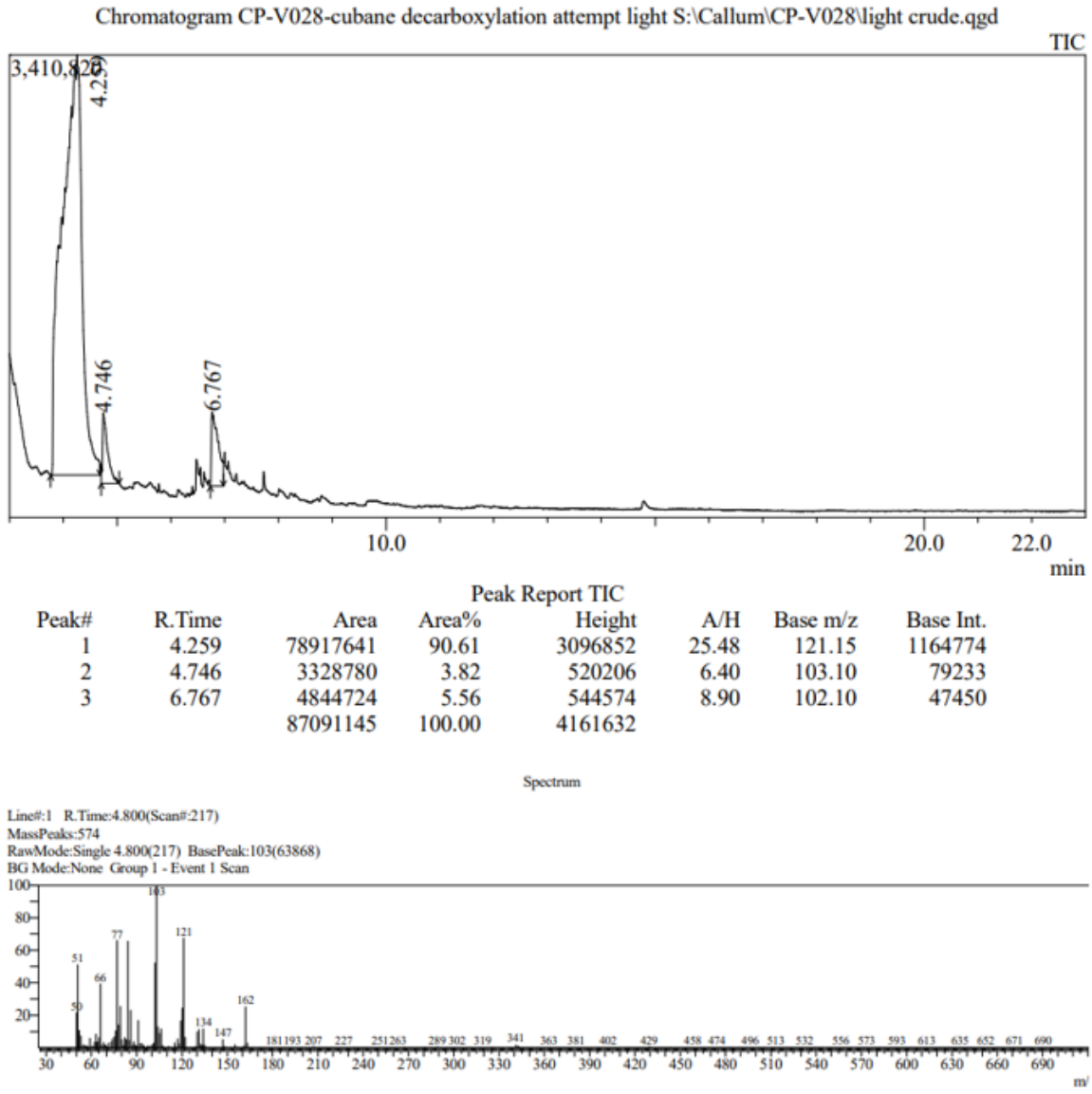
GCMS Trace



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	A/H	Base m/z	Base Int.
1	7.811	2282218	2.67	498609	4.58	131.10	49495
2	8.896	80967649	94.73	21435649	3.78	360.95	1617201
3	9.545	2221919	2.60	537561	4.13	405.00	44622
		85471786	100.00	22471819			

Figure **S14**. GCMS trace of endo-2,4-dibromodicyclopentadiene-1,8-dione bisethylene ketal.



Peak Report TIC

Peak#	R.Time	Area	Area%	Height	A/H	Base m/z	Base Int.
1	4.259	78917641	90.61	3096852	25.48	121.15	1164774
2	4.746	3328780	3.82	520206	6.40	103.10	79233
3	6.767	4844724	5.56	544574	8.90	102.10	47450
		87091145	100.00	4161632			

Figure **S15**. GCMS trace of the crude reaction mixture for the decarboxylation of **5**. Peak at 4.75 minutes proposed to be **6** as it has the correct mass of 162.

Absorption Measurements

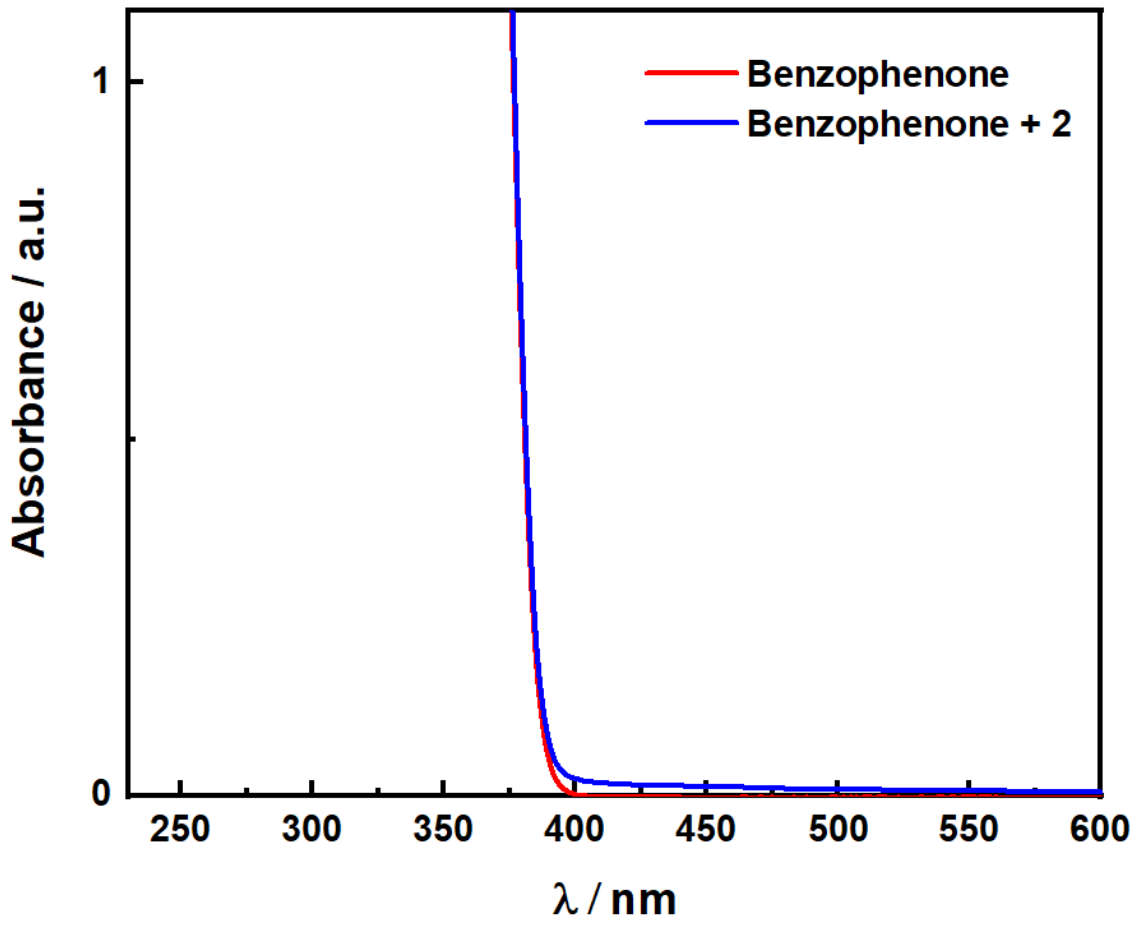


Figure **S16**. Absorption spectrum of benzophenone with and without **2** in MeCN at 0.1 M concentration.

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