# Supporting Information

# Sensitized [2+2] intramolecular photocycloaddition of unsaturated enones using UV LEDs in a continuous flow reactor: kinetic and preparative aspects

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## Table of contents

## Materials and methods

### Flow System

Mikroglas Dwell Device® microreactor (Invenios Europe, Langen, Germany) made of Foturan® glass of dimensions (1.15 m × 2000 µm × 500 µm). The 1.15 m long channel of this dwell device offers extended reaction time. Moreover, the reactor includes a channel for the flow of heat exchange fluid thus providing temperature control. The Foturan® glass is resistant to aggressive liquids (strong acids, bases) allowing the usage of a wide range of solvents in addition to its transparency up to 300 nm making it favorable for UV/Vis photochemical reactions (Figure S1).

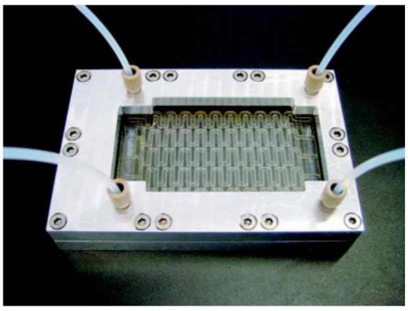


**Figure S1.** Mikroglas Dwell Device®.

### Syringe pump

The different flow rates of the reactions performed were regulated using a Harvard Apparatus (Holliston, MA, USA) PHD ULTRA CP syringe pump fitted with 8 mL stainless steel syringes.

### LED Systems

1- A lab assembled UV LEDs composed of 18 identical LEDs from Roithner Lasertechnik (Vienna, Austria), 365 ± 15 nm ), placed at equal distances to provide homogeneous illumination (LEDs A). The wavelength of the emitted irradiation is 365 nm. The average emitted photon flux of this UV LEDs assembly is around 90 $mW.cm^{-2}$ (Figure S2).

**Figure S2.** Mikroglas Dwell device irradiated by LEDs A.

2- UV LEDs (365 nm, irradiance up to 250 $mW.cm^{-2}$) Omnicure® AC475 model from Lumen Dynamics (Excelitas Technologies, Waltham, MA, USA) (LEDs B). The power of these UV LEDs can be changed but only 100 % power (irradiance 230 $mW.cm^{-2}$) was assessed (Figure S3). Note that the irradiance was measured at the surface of the reactor using a radiometer.

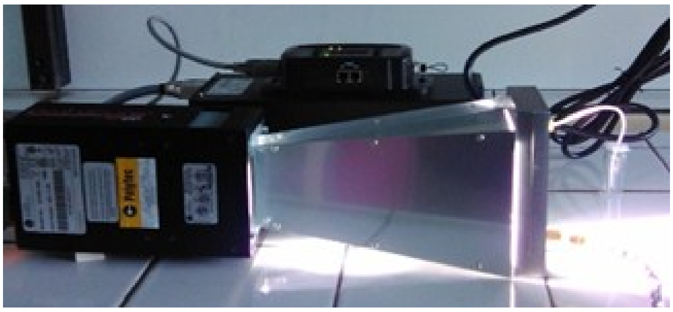


**Figure S3.** Mikroglas Dwell device irradiated by LEDs B.

**Radiometer**

The $X9_2$ meter in combination RCH-008-4 light detector (Gigahertz-Optiks, Türkenfeld, Germany) was used to measure the irradiance of the light that reaches to the surface of the used microfluidic device (Figure S4).


**Figure S4.** The $X9_2$ radiometer used for measuring light emitted.

## Kinetics Studies

To determine the order of the cycloaddition reaction, the kinetic curves for the reaction of 3-(2-ketenyloxy)-2-cyclohexen-1-one with 4,4-dimethoxybenzophenone were plotted. These curves were then used to extrapolate the rate constants $k_x$. For a given 3-(2-ketenyloxy)-2-cyclohexen-1-one derivative, a series of five reactions with different UV irradiation times were performed under continuous conditions. The percentage of conversion was determined by $^1H$ NMR with an internal standard. The time of irradiation was regulated by adjusting the flow rate of the syringe pump and the flow system used is the Mikroglass Dwell Device ($V_{int}$ = 1.15 mL).

**Table S1** Results of sensitized [2+2] cycloaddition in flow where [**1d**]$_0$ = 37 mM and [DMBP **3b**]$_0$ = 4.63 mM (data for Table 3, entry 1)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 750 | 1.53 | 7.0 | 0.1 |
| 500 | 2.30 | 16.5 | 0.6 |
| 375 | 3.06 | 20.8 | 1.5 |
| 250 | 4.60 | 25.0 | 3.2 |
| 125 | 9.20 | 46.2 | 12.0 |
| 62.5 | 18.4 | 67.7 | 25.0 |

**Table S2** Results of sensitized [2+2] cycloaddition in flow where [**1d**]$_0$ = 37.0 mM and [B]$_0$ = 9.25 mM (data for Table 3, entry 2)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 1000 | 1.15 | 6.0 | 0.1 |
| 750 | 1.53 | 16.3 | 0.6 |
| 500 | 2.30 | 27.4 | 1.9 |
| 375 | 3.06 | 36.1 | 2.9 |
| 250 | 4.60 | 51.6 | 6.4 |
| 125 | 9.20 | 74.6 | 16.0 |

**Table S3** Results of sensitized [2+2] cycloaddition in flow where [**1d**]$_0$ = 37.0 mM and [DMBP **3b**]$_0$ = 18.5 mM (data for Table 3, entry 3)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 1500 | 0.77 | 14.6 | 0.6 |
| 1000 | 1.15 | 22.4 | 1.0 |
| 750 | 1.53 | 31.0 | 1.6 |
| 500 | 2.30 | 48.9 | 3.1 |
| 375 | 3.06 | 61.6 | 4.4 |
| 250 | 4.60 | 74.7 | 6.5 |

**Table S4** Results of sensitized [2+2] cycloaddition in flow where [**1d**]$_0$ = 37.0 mM and [DMPP **3b**]$_0$ = 37.0 mM (data for Table 3, entry 4)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 2000 | 0.58 | 22.0 | 0.5 |
| 1500 | 0.77 | 31.4 | 0.9 |
| 1000 | 1.15 | 42.8 | 1.4 |
| 750 | 1.53 | 55.5 | 2.2 |
| 500 | 2.30 | 72.7 | 3.7 |
| 375 | 3.06 | 81.4 | 4.9 |

**Table S5** Results of sensitized [2+2] cycloaddition in flow where [**1d**]$_0$ = 37.0 mM and [DMBP **3b**]$_0$ = 74.0 mM (data for Table 3, entry 5)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % pinacol |
|---|---|---|---|
| 2500 | 0.46 | 32.4 | 0.0 |
| 2000 | 0.58 | 37.7 | 0.5 |
| 1500 | 0.77 | 49.5 | 1.0 |
| 1000 | 1.15 | 68.0 | 1.6 |
| 750 | 1.53 | 76.4 | 2.3 |
| 500 | 2.30 | 87.6 | 3.6 |

**Table S6** Results of sensitized [2+2] cycloaddition in flow where [**1a**]$_0$ = 37.0 mM and [DMPP **3b**]$_0$ = 74.0 mM (data for Table 3, entry 6)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 100 | 11.5 | 46.0 | 3.0 |
| 75 | 15.3 | 66.0 | 6.9 |
| 50 | 23.0 | 74.0 | 9.9 |
| 25 | 46.0 | 90.0 | 15.9 |
| 20 | 57.5 | 92.7 | 19.2 |
| 10 | 115.0 | 99.5 | 31.0 |

**Table S7** Results of sensitized [2+2] cycloaddition in flow where [**1b**]$_0$ = 37.0 mM and [DMPP **3b**]$_0$ = 74.0 mM (data for Table 3, entry 7)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 460 | 2.5 | 29.0 | 3.6 |
| 230 | 5.0 | 50.0 | 5.5 |
| 115 | 10.0 | 65.0 | 8.5 |
| 46 | 25.0 | 85.0 | 19.2 |
| 23 | 50.0 | 96.5 | 31.0 |
| 15 | 76.7 | 99.5 | 37.0 |

**Table S8** Results of sensitized [2+2] cycloaddition in flow where [**1c**]$_0$ = 37.0 mM and [DMPP **3b**]$_0$ = 74.0 mM (data for Table 3, entry 8)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 460 | 0.56 | 67.0 | 4.8 |
| 230 | 0.77 | 79.0 | 7.7 |
| 115 | 1.15 | 91.0 | 13.8 |
| 90 | 1.53 | 96.0 | 17.1 |
| 60 | 2.30 | 99.5 | 23.1 |

**Table S9** Results of sensitized [2+2] cycloaddition in flow where [**1d**]$_0$ = 37.0 mM and [DMPP **3b**]$_0$ = 74.0 mM (data for Table 3, entry 9)

| Flow (µl.min$^{-1}$) | Irradiation time (min) | % [2+2] Cycloadduct | % Pinacol |
|---|---|---|---|
| 2500 | 0.5 | 44.0 | 1.0 |
| 1500 | 0.8 | 65.0 | 1.4 |
| 920 | 1.3 | 72.0 | 2.6 |
| 460 | 2.5 | 91.0 | 5.4 |
| 230 | 5.0 | 98.8 | 9.9 |

**Table S10** Results of the pinacolization reaction in flow for [DMBP **3b**]$_0$ = 37.0 mM (data for Table 3, entry 10)

| Flow rate (µl/min) | Irradiation time (min) | % Pinacol |
|---|---|---|
| 20 | 57.5 | 5.0 |
| 15 | 76.7 | 6.5 |
| 10 | 115.0 | 7.5 |
| 7 | 164.3 | 10.5 |
| 5 | 230.0 | 15.5 |

**Table S11** Results of the pinacolization reaction in flow for [DMBP **3b**]$_0$ = 74.0 mM (data for Table 3, entry 11)

| Flow rate (µl/min) | Irradiation time (min) | % Pinacol |
|---|---|---|
| 200 | 6.0 | 1.3 |
| 150 | 7.5 | 1.7 |
| 100 | 11.5 | 2.4 |
| 75 | 15.0 | 2.8 |
| 30 | 38.0 | 5.0 |
| 20 | 57.0 | 8.0 |
| 10 | 115.0 | 14.8 |

In order to obtain the initial assumptions for the numerical fits for the DMBP **3b,** the concentration factor was simplified by assuming that DMBP **3b** is constant and equal to the initial DMBP **3b** concentration $[DMBP]_0$ in equations S1 and S2 (that correspond to equations 12 and 13 in the main text):

$$\frac{d\ Pinacol}{dt} = 2 \times k_{Pinacol}^{Exper.} \times DMBP \quad \text{(S1)}$$

$$\frac{d\ Product}{dt} = k_{[2+2]}^{Exper.} \times DMBP \times Substrate = k_{[2+2]}^{Exper.} \times [DMBP]_0 \times Substrate \quad \text{(S2)}$$

A straightforward integration gives:

$$Ln(DMBP) = Ln([DMBP]_0) - k_{Pinacol}^{Exper.} \times t \quad \text{(S3)}$$

$$Ln(Substrate) = Ln([Substrate]_0) - k_{[2+2]}^{Exper.} \times [DMBP]_0 \times t \quad \text{(S4)}$$

**Table S12** Initial assumptions for the numerical fits using simplified equations S3 and S4. The entries correspond to those of Table 3.[a]

| Entry | Substrate[b] | DMBP **3b** mmol.L$^{-1}$ | $k_{[2+2]}^{Exper.}$ (mol$^{-1}$.L.s$^{-1}$) | $R^{2c}$ | $k_{Pinacol}^{Exper.} \times 10^3$ (s$^{-1}$) | $R^{2c}$ |
|---|---|---|---|---|---|---|
| 1 | **1d** | 4.6 | 17.2 | 0.995 | 16.0 | 0.977 |
| 2 | **1d** | 9.3 | 18.1 | 0.992 | 17.5 | 0.902 |
| 3 | **1d** | 18.5 | 17.0 | 0.991 | 15.0 | 0.986 |
| 4 | **1d** | 37.0 | 15.4 | 0.997 | 16.5 | 0.988 |
| 5 | **1d** | 74.0 | 12.6 | 0.996 | 17.5 | 0.967 |
| 6 | **1a** | 74.0 | 0.80 | 0.993 | 4.5 | 0.996 |
| 7 | **2b** | 74.0 | 1.4 | 0.994 | 9.5 | 0.996 |
| 8 | **1c** | 74.0 | 4.75 | 0.98 | 17.5 | 0.999 |
| 9 | **1d** | 74.0 | 14.0 | 0.997 | 24.0 | 0.995 |
| 10 | - | 37.0 | - | - | 0.8 | 0.972 |
| 11 | - | 74.0 | - | - | 1.5 | 0.996 |

[a] Mikroglas Dwell Device® microreactor made of Foturan® glass with a rectangular shape of dimensions 115 mm × 2 mm × 0.5 mm was used as photo-microreactor illuminated by UV LEDs B (λ = 365 ± 15 nm, 230 mW.cm$^{-2}$). [b] Substrate concentration 37 mM. [c] $R^2$: correlation coefficient of the plotted graph

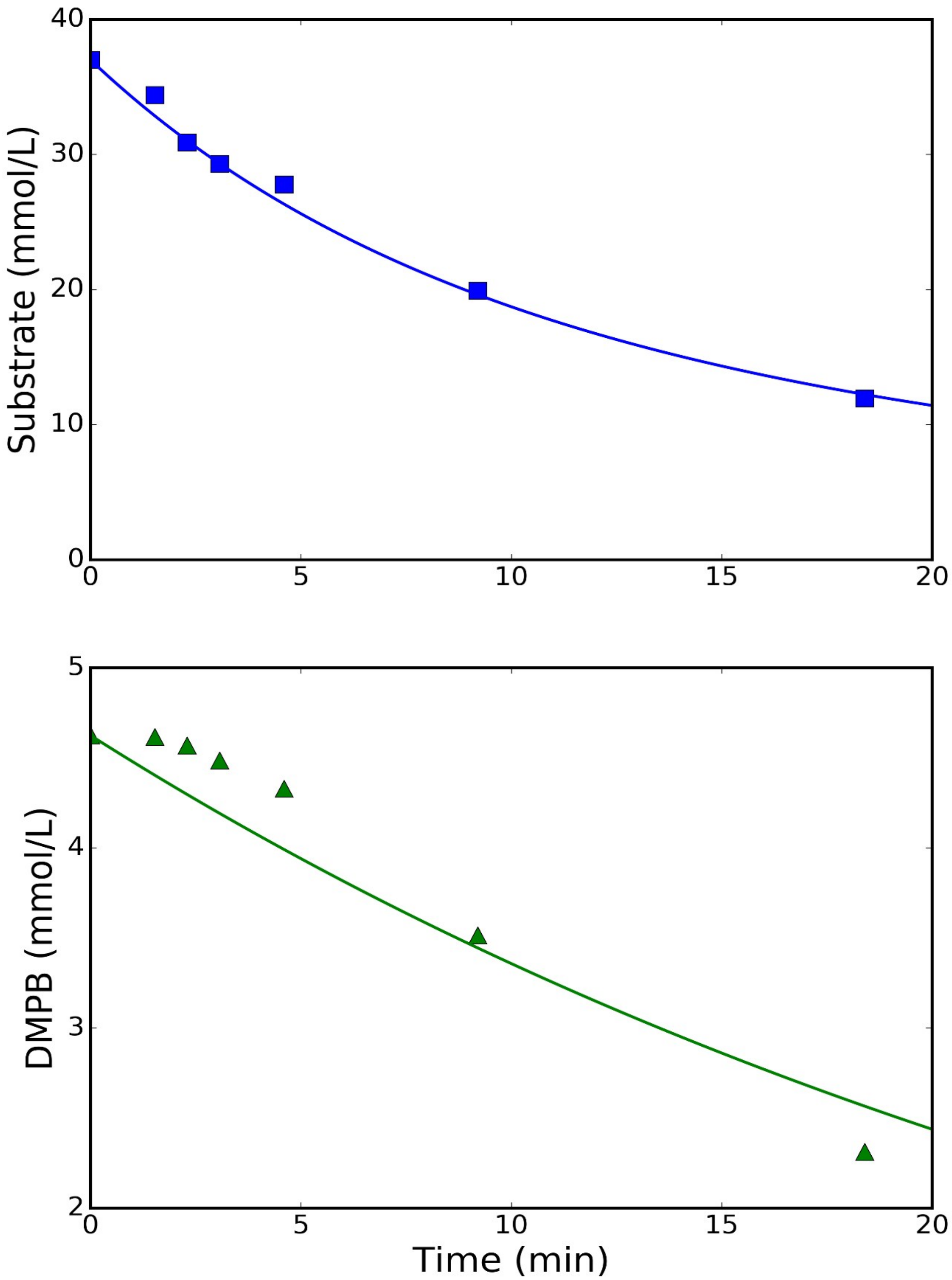



**Fig. S5** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 1 (**1d**: 37 mM, DMBP **3a** 4.6 mM) obtained using data of Table S1.

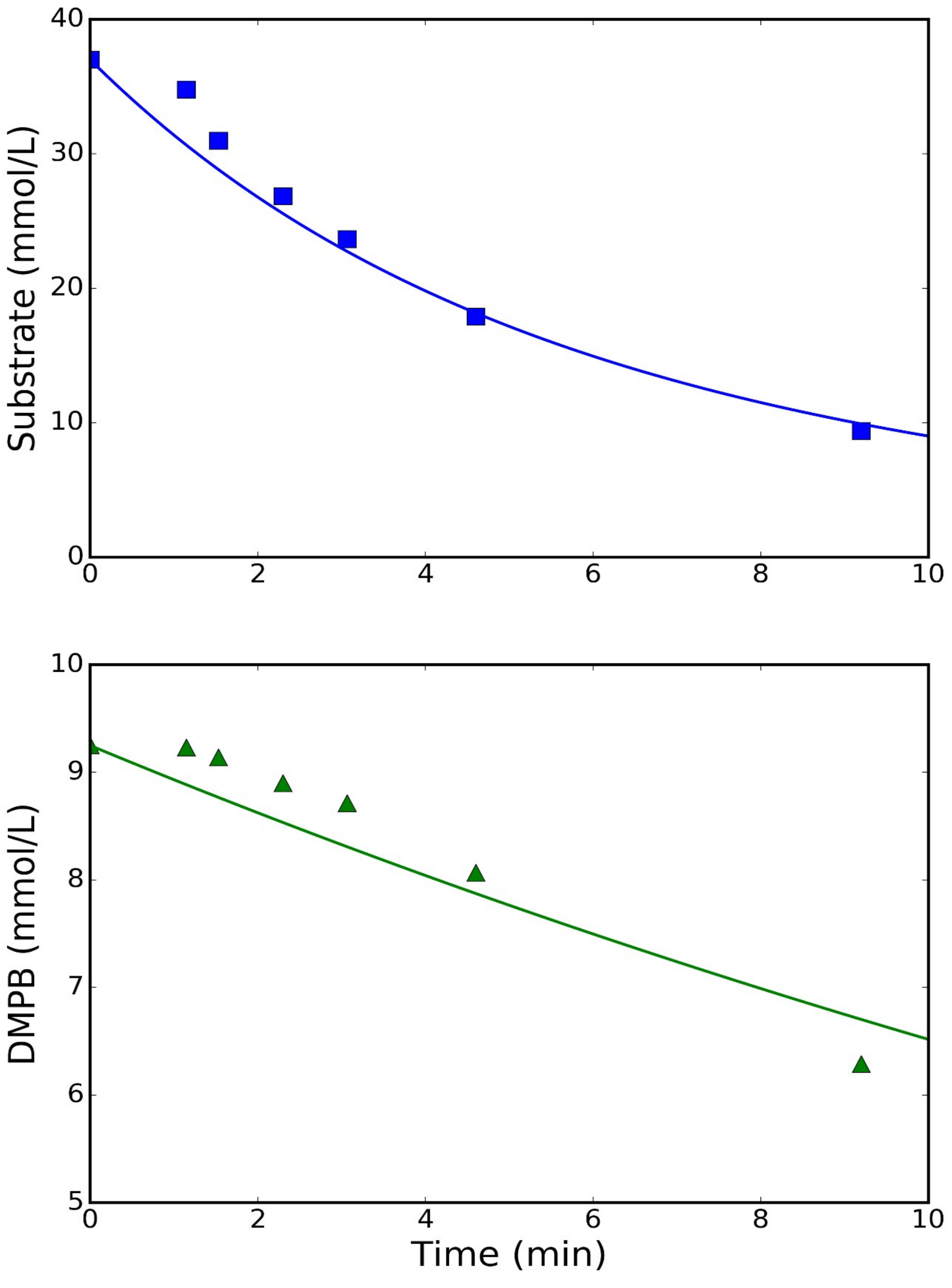



**Fig. S6** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 2 (**1d**: 37 mM, DMBP **3a** 9.2 mM) obtained using data of Table S2.

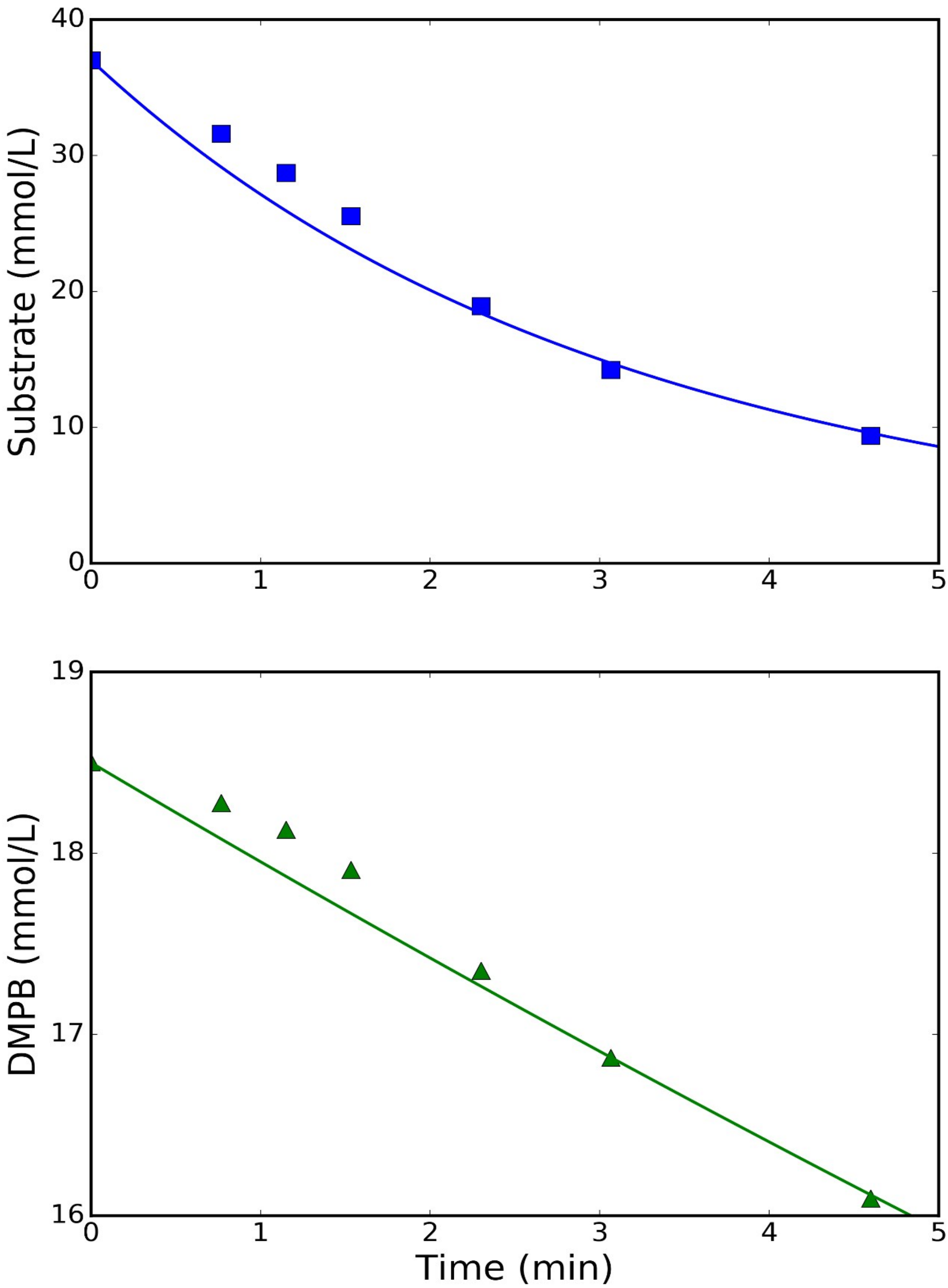



**Fig. S7** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 3 (**1d**: 37 mM, DMBP **3a** 18.5 mM) obtained using data of Table S3.

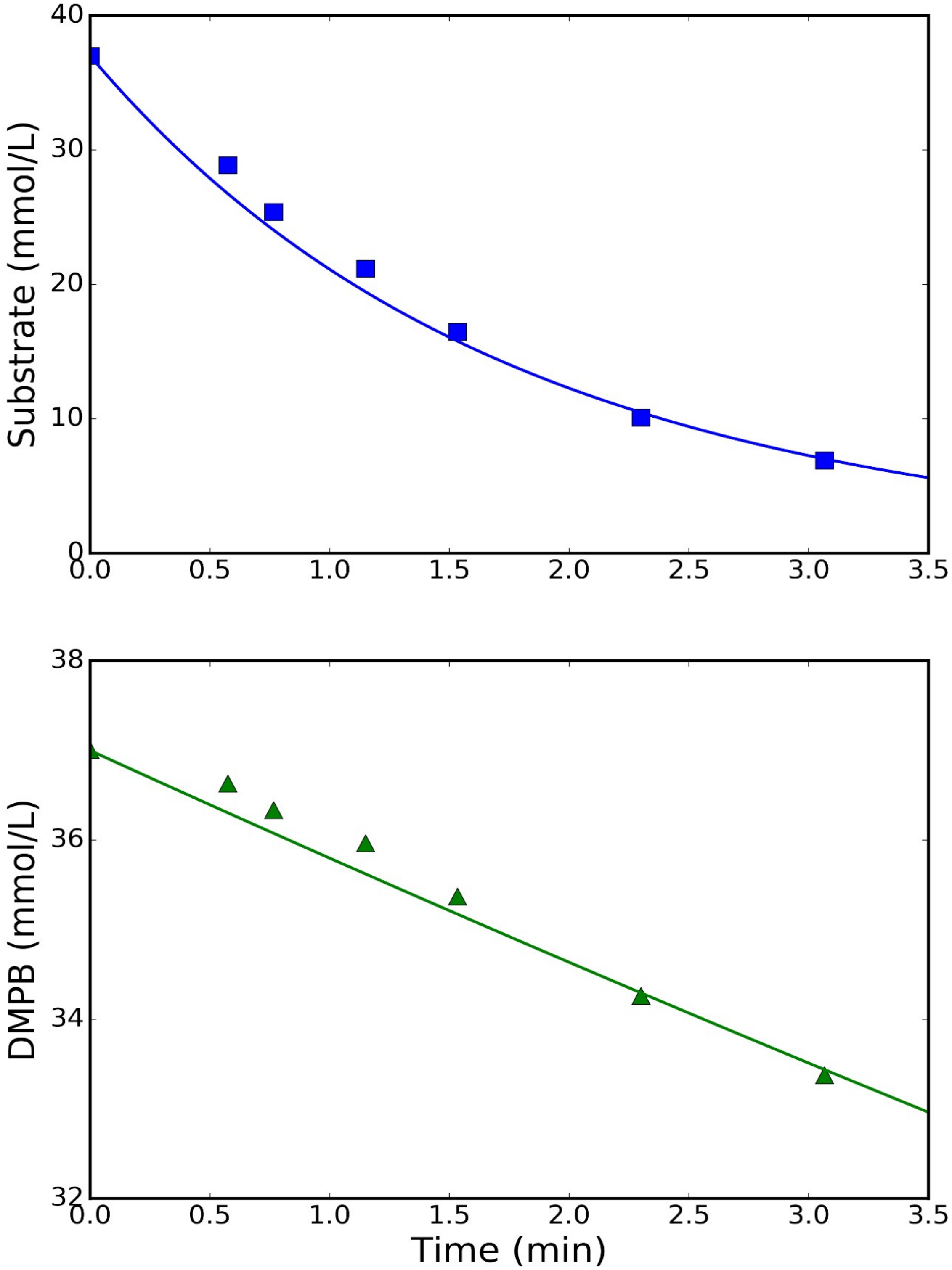



**Fig. S8** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 4 (**1d**: 37 mM, DMBP **3a** 37.0 mM) obtained using data of Table S4.

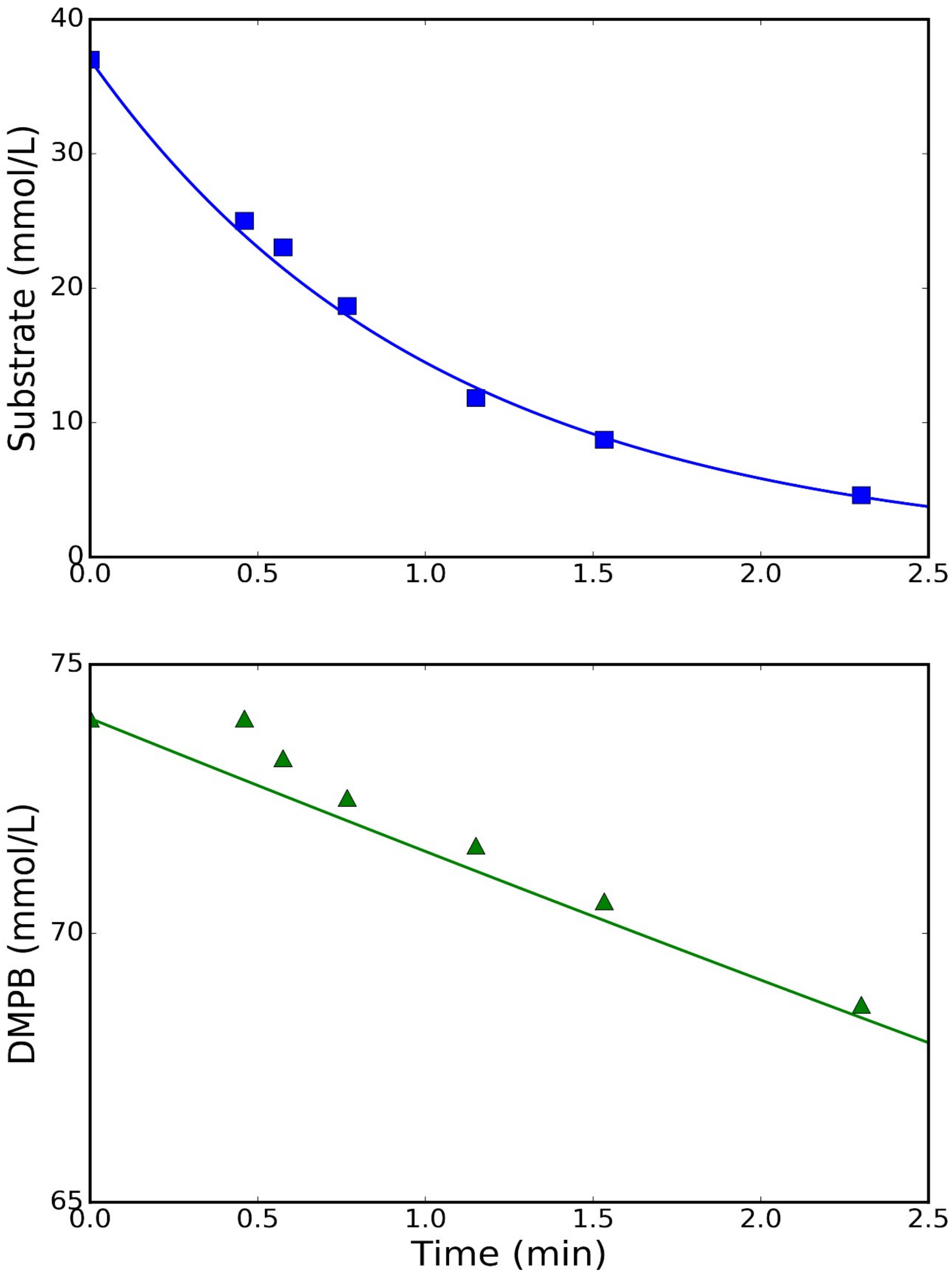



**Fig. S9** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 5 (**1d**: 37 mM, DMBP **3a** 74.0 mM) obtained using data of Table S5.

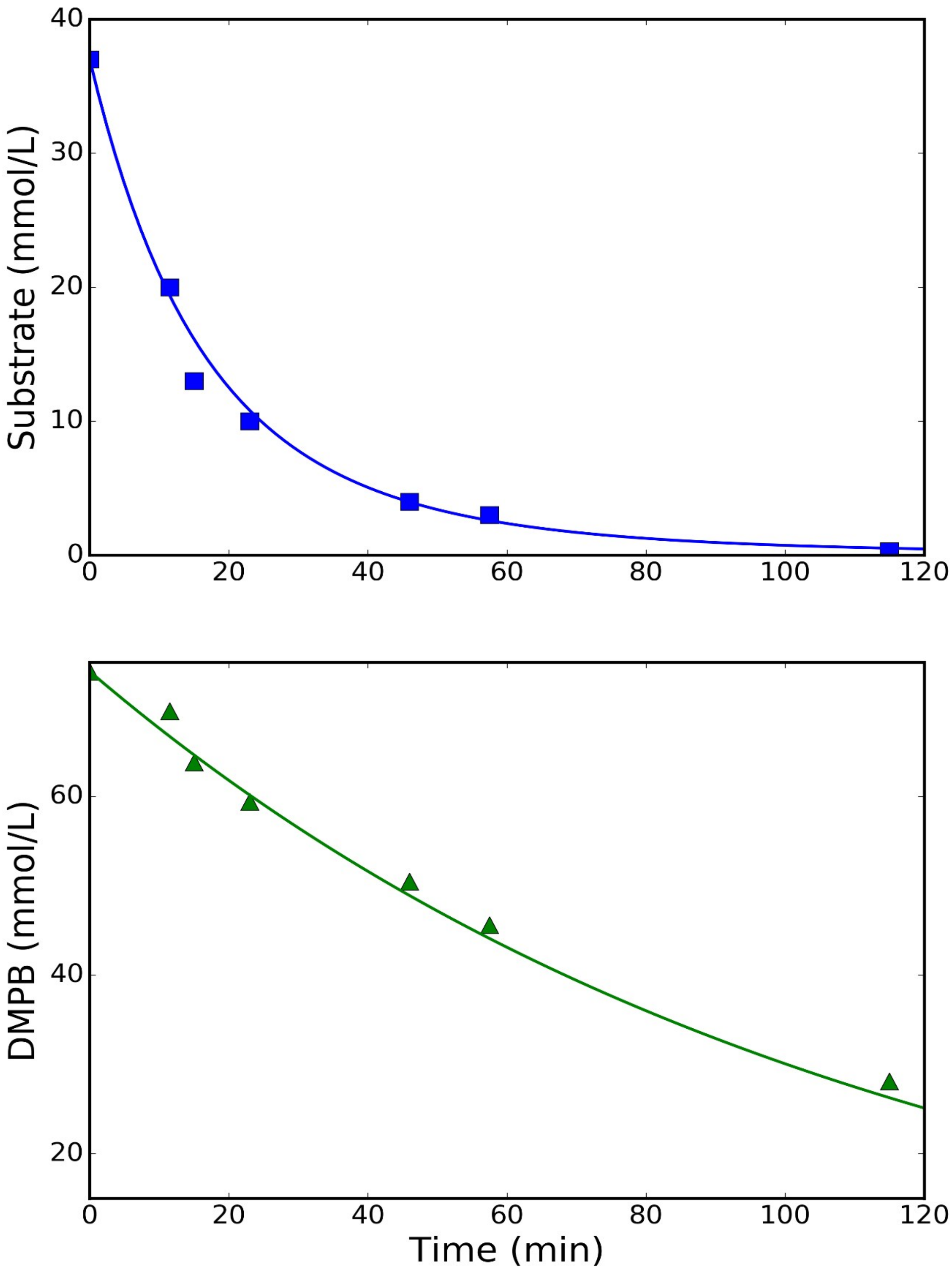



**Fig. S10** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 6 (**1a**: 37 mM, DMBP **3a** 74.0 mM) obtained using data of Table S6.

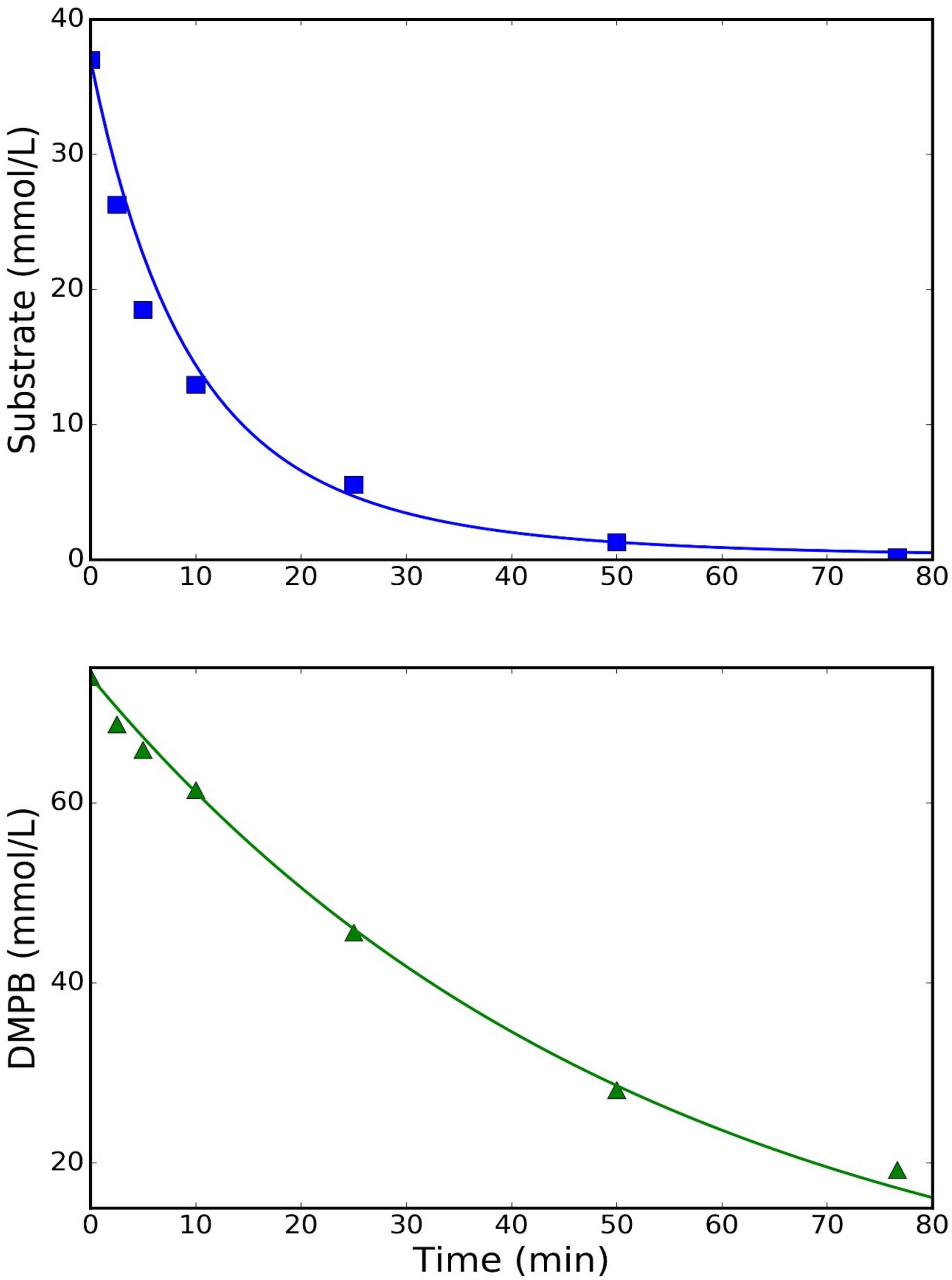



**Fig. S11** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 7 (**1b**: 37 mM, DMBP **3a** 74 mM) obtained using data of Table S7.

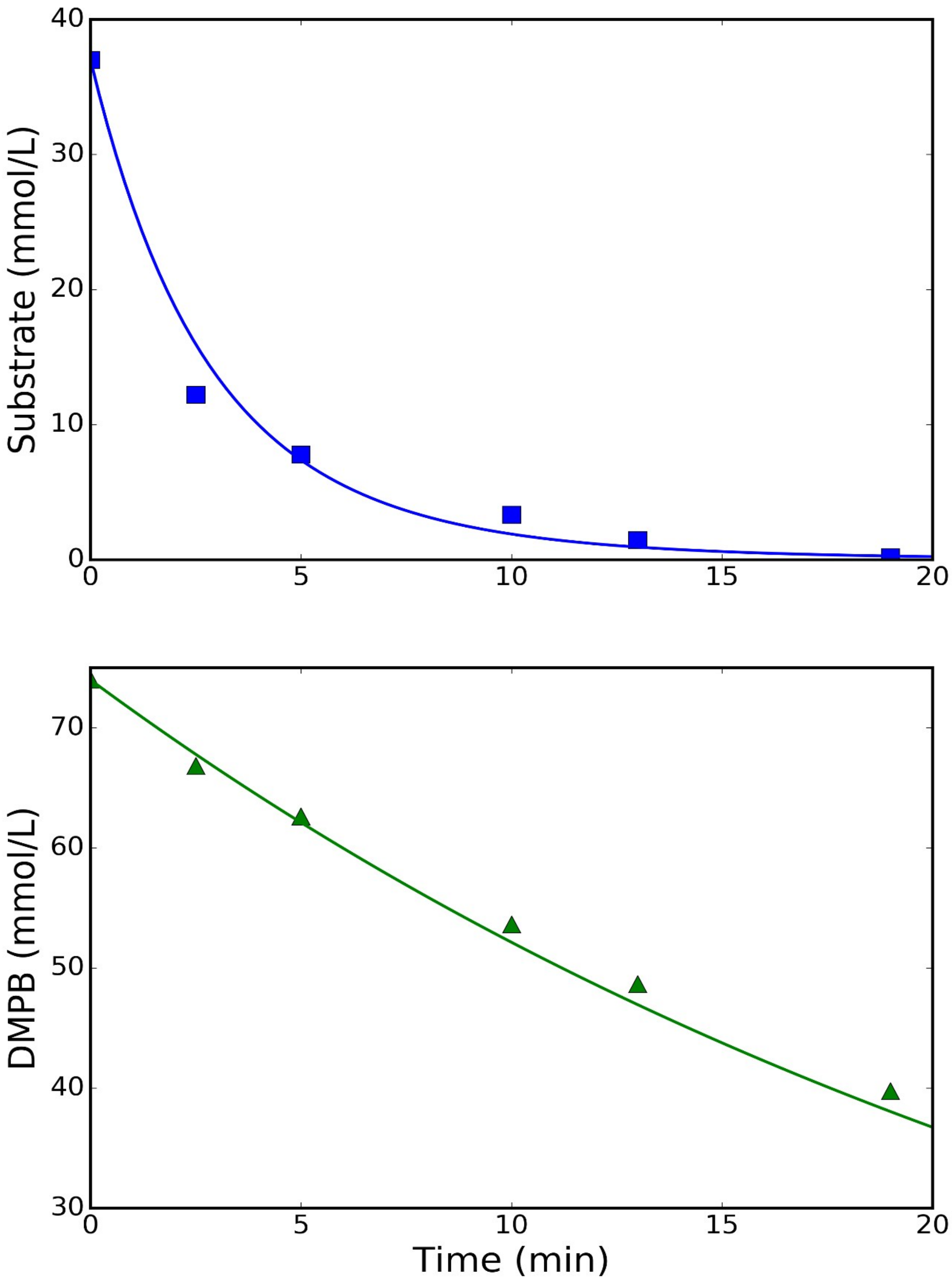



**Fig. S12** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 8 (**1c**: 37 mM, DMBP **3a** 74 mM) obtained using data of Table S8.

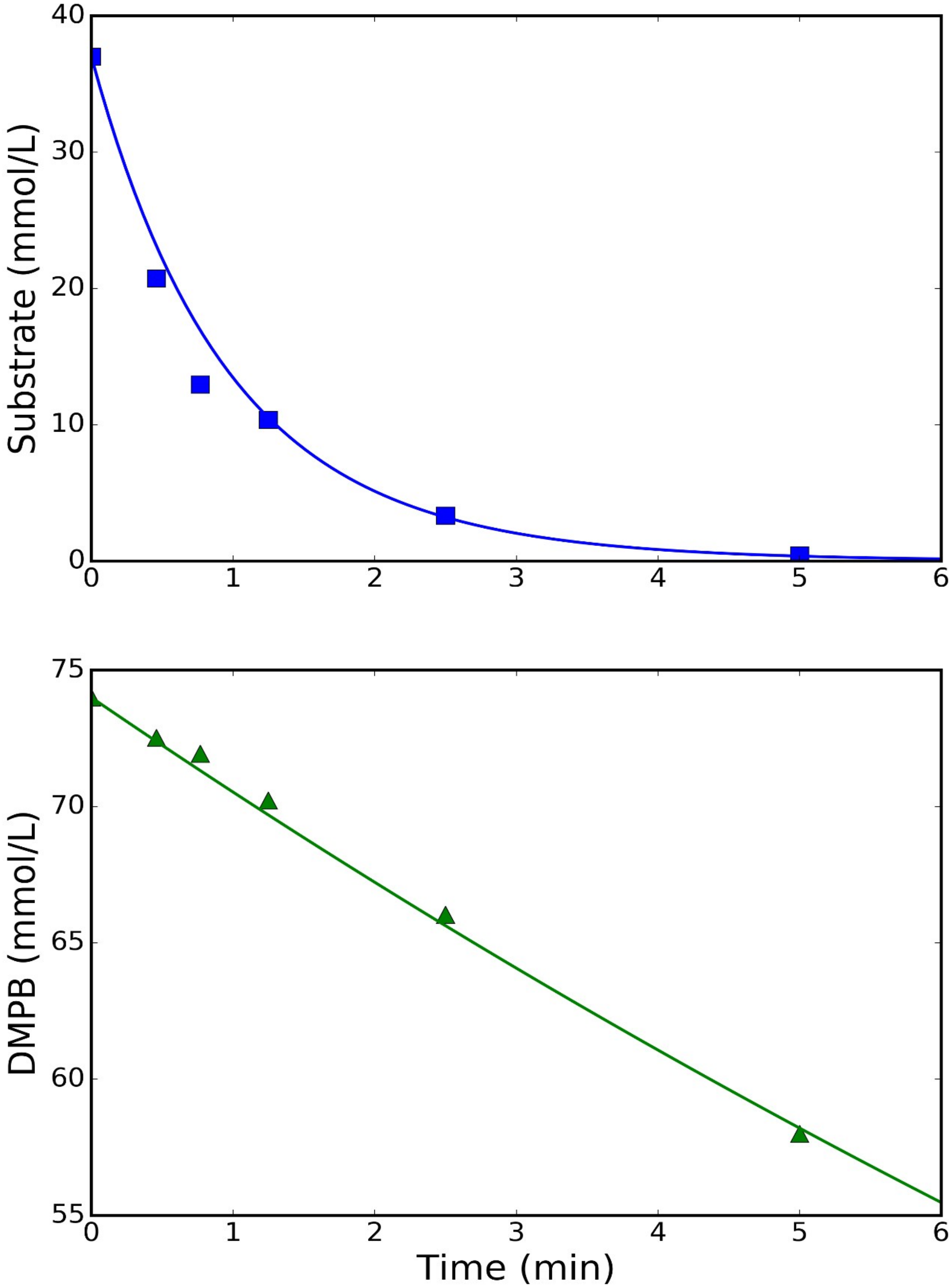



**Fig. S13** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 9 (**1d**: 37 mM, DMBP **3a** 74.0 mM) obtained using data of Table S9.

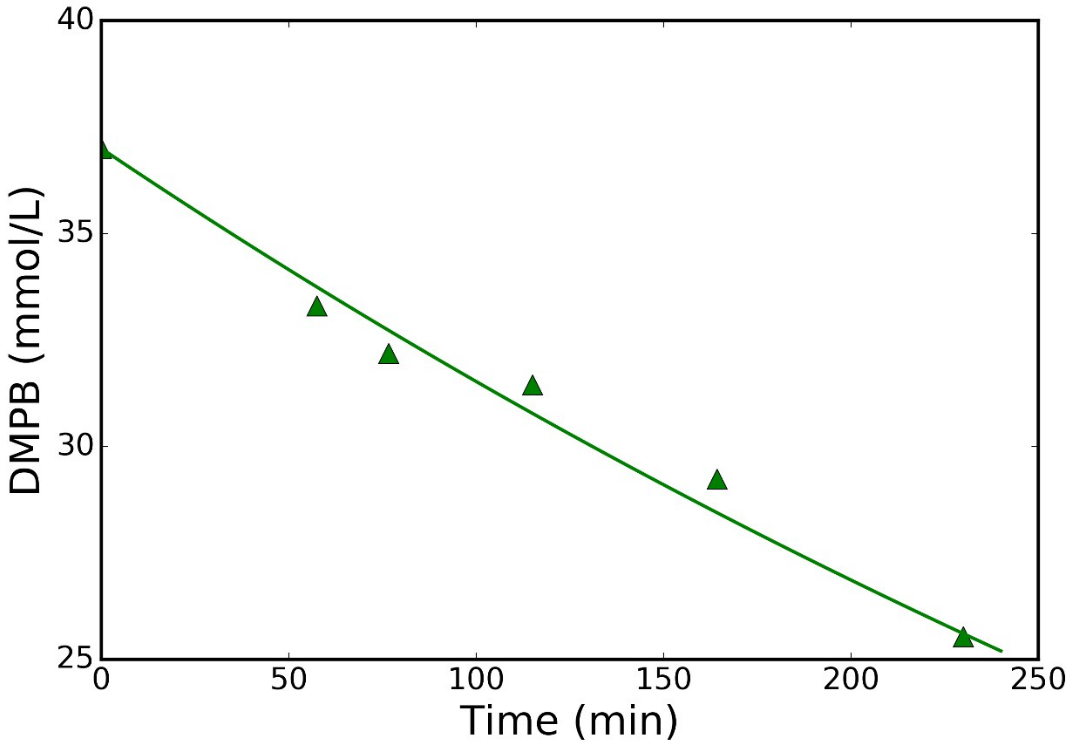



**Fig. S14** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 10 (no substrate, DMBP **3a** 37.0 mM) obtained using data of Table S10.

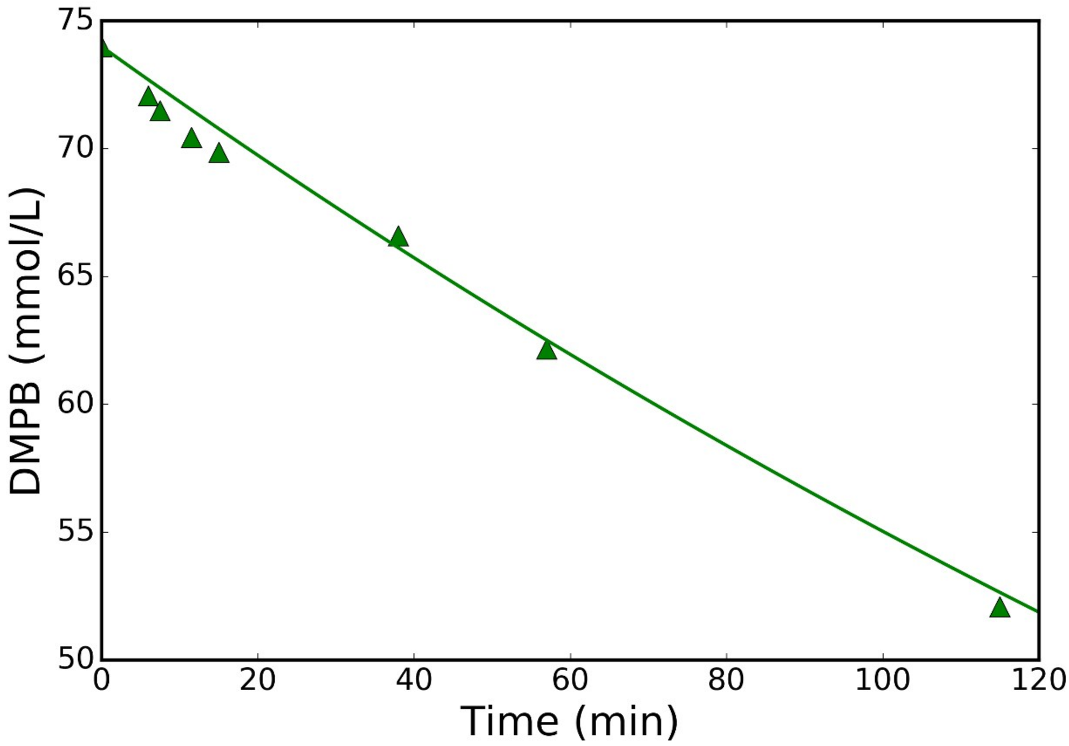
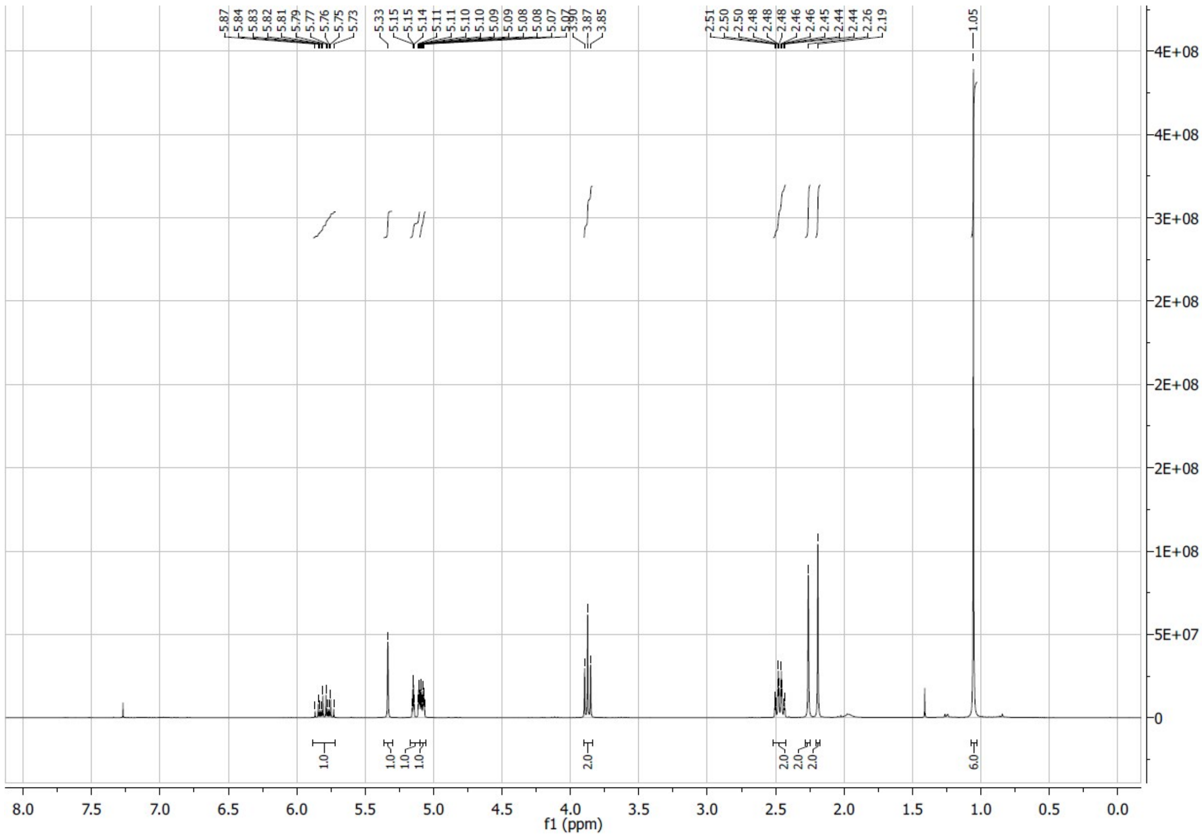
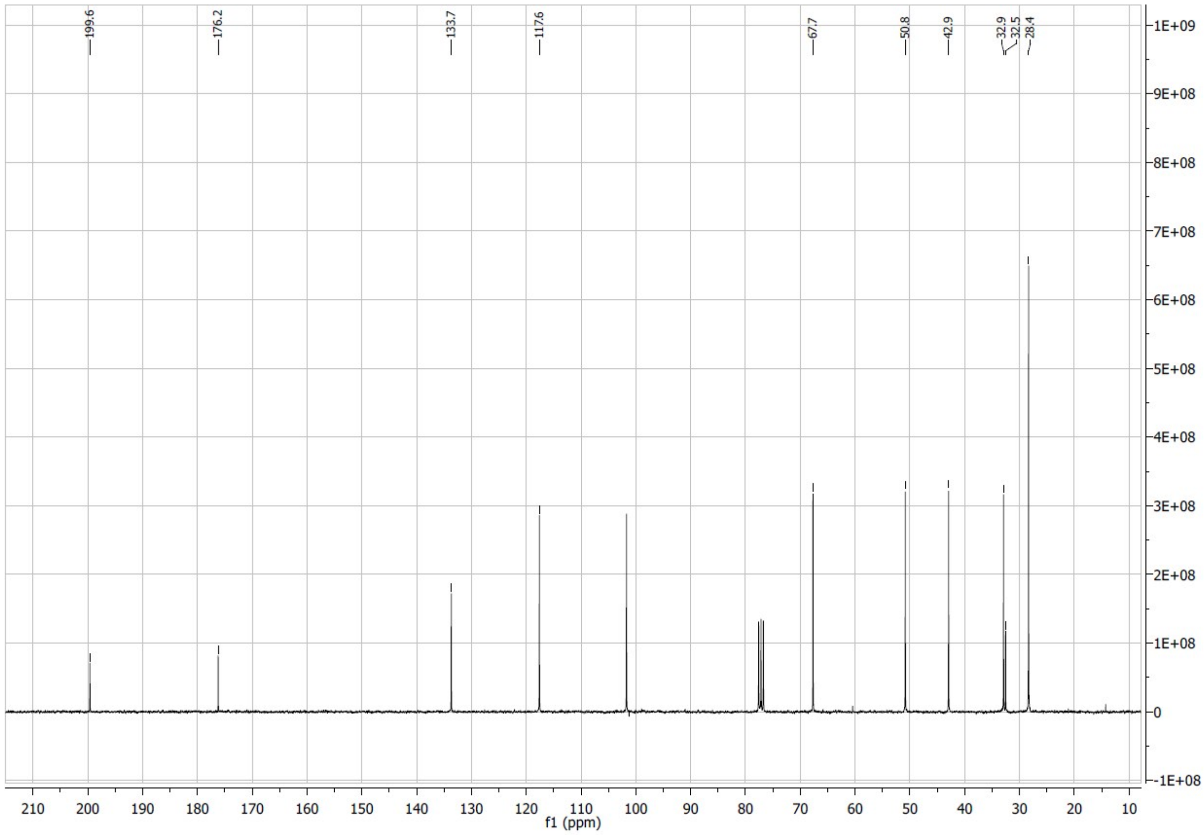



**Fig. S15** Numerical integrations according to equations S1 and S2 (that correspond to equations 12 and 13 in the main text) for photocyclization in Table 3, entry 1 (no substrate, DMBP **3a** 74.0 mM) obtained using data of Table S11

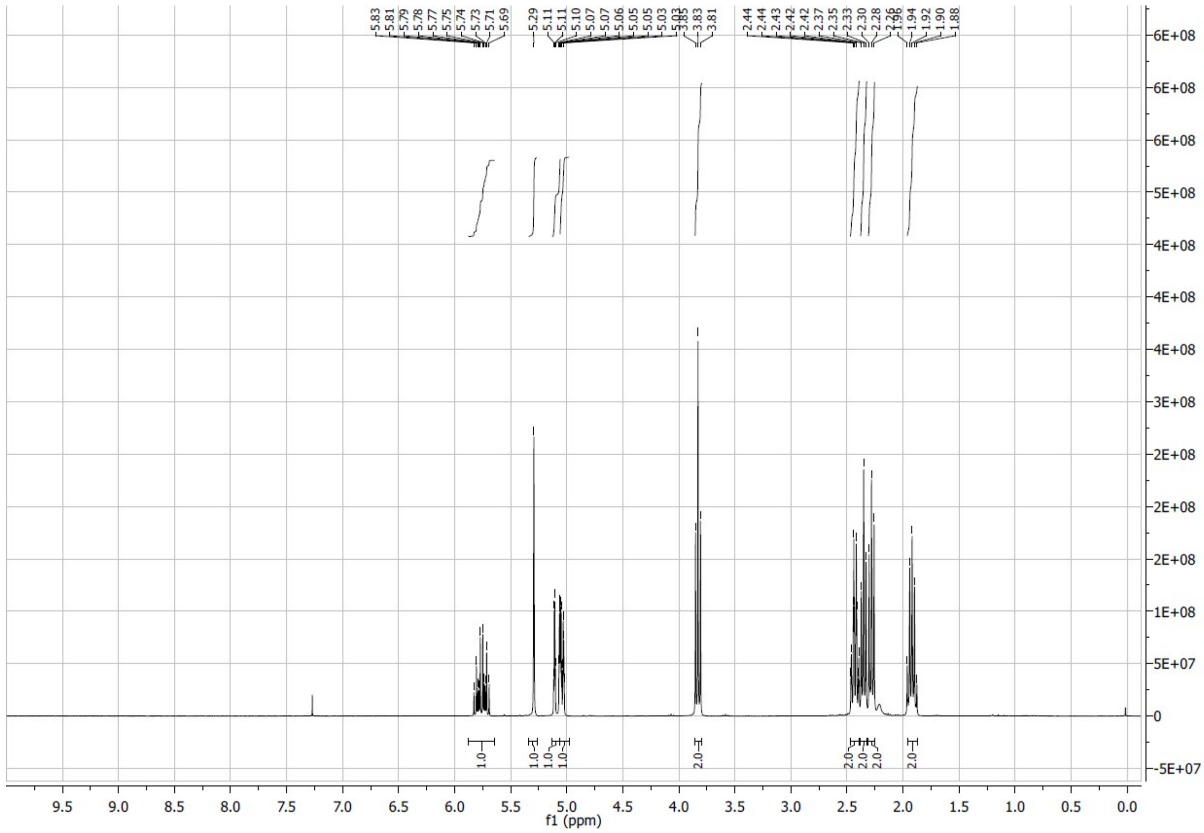
## Copies of NMR spectra

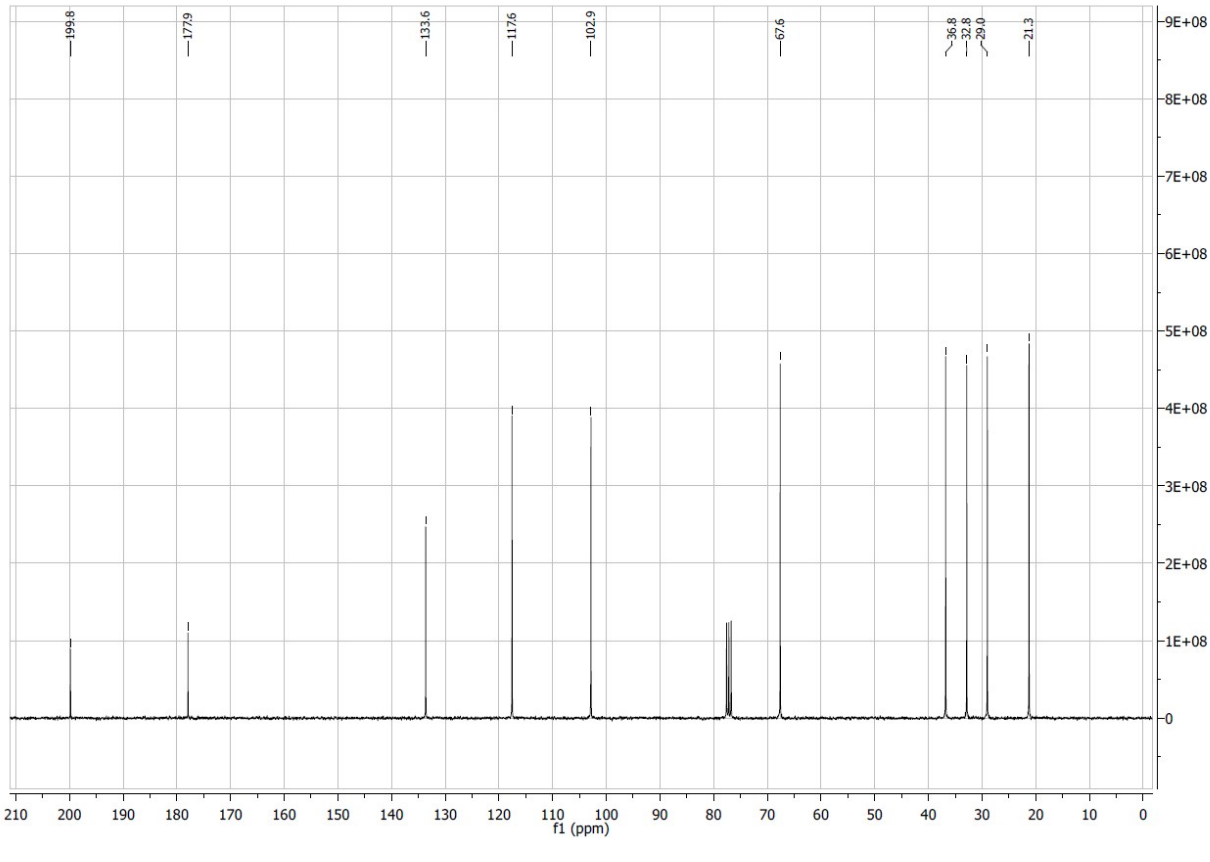
### 3-(but-3-en-1-yloxy)-5,5-dimethylcyclohex-2-en-1-one 1d



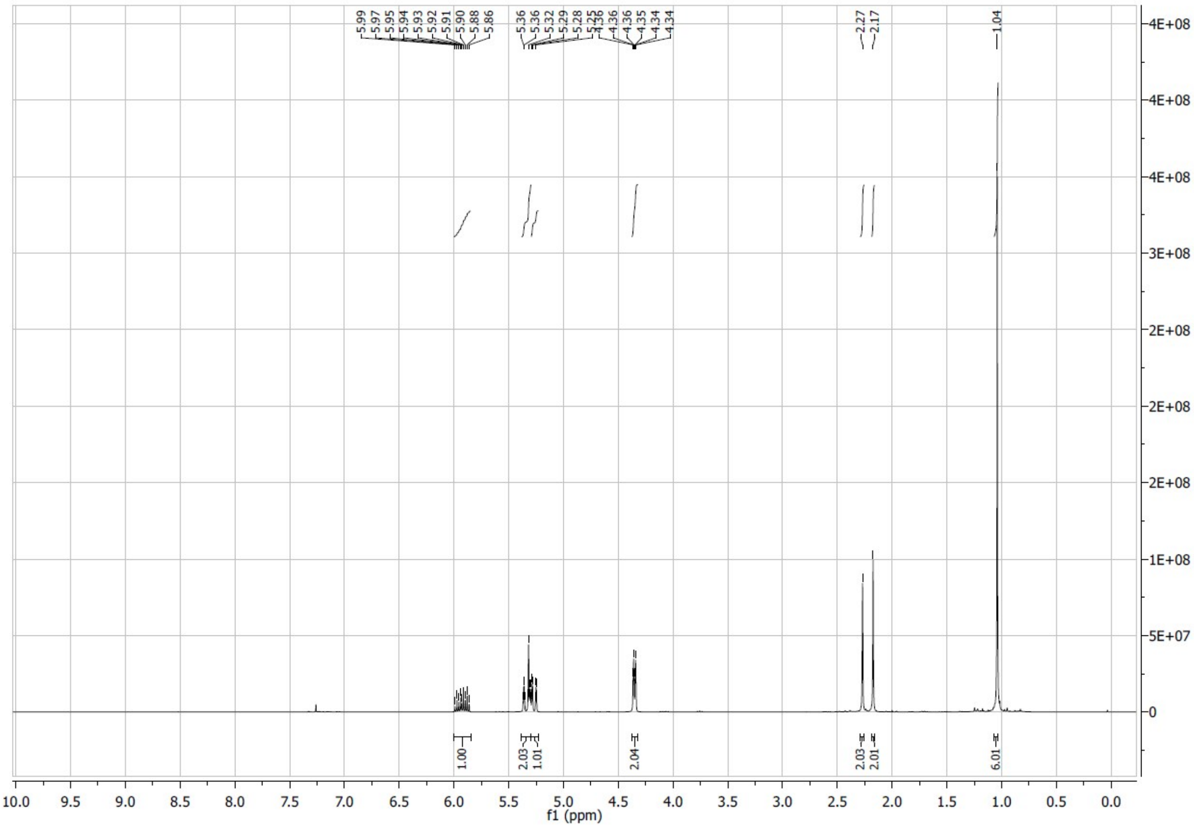


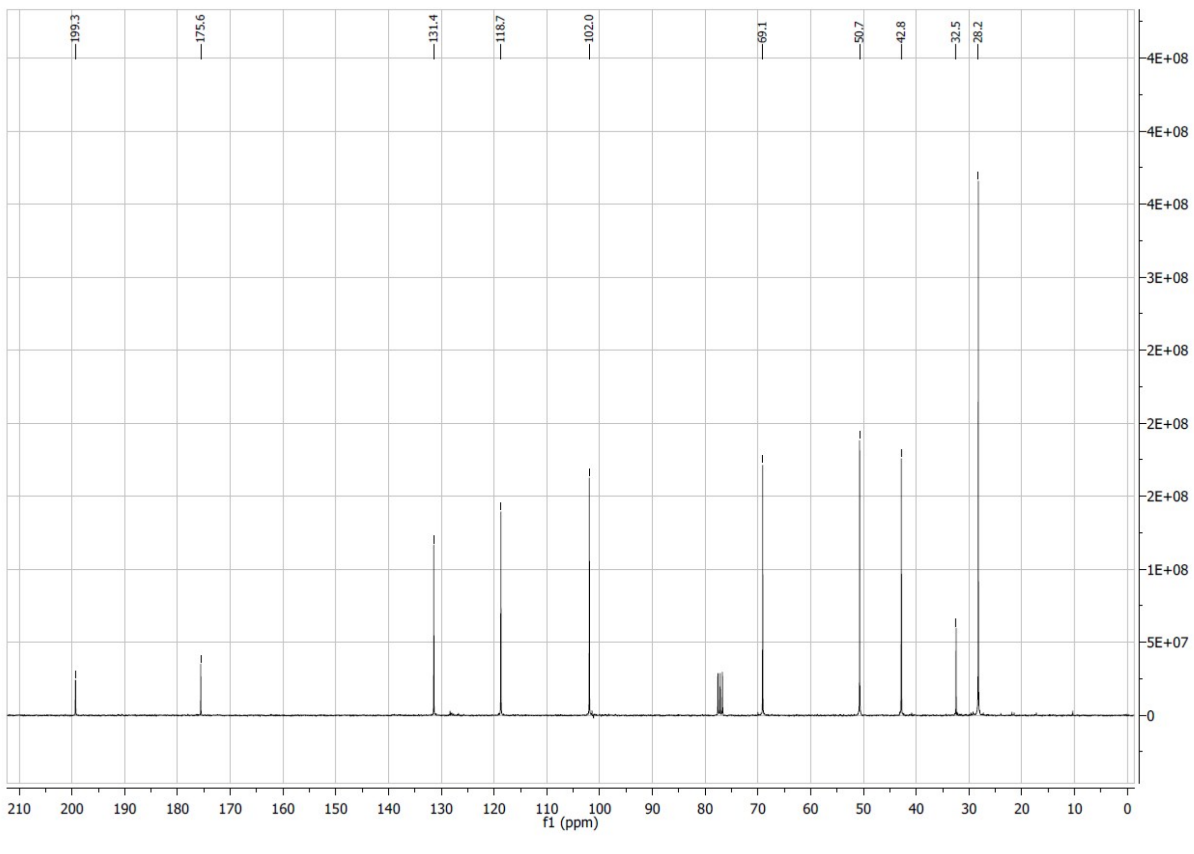
**3-(but-3-en-1-yloxy)cyclohex-2-en-1-one 1c**



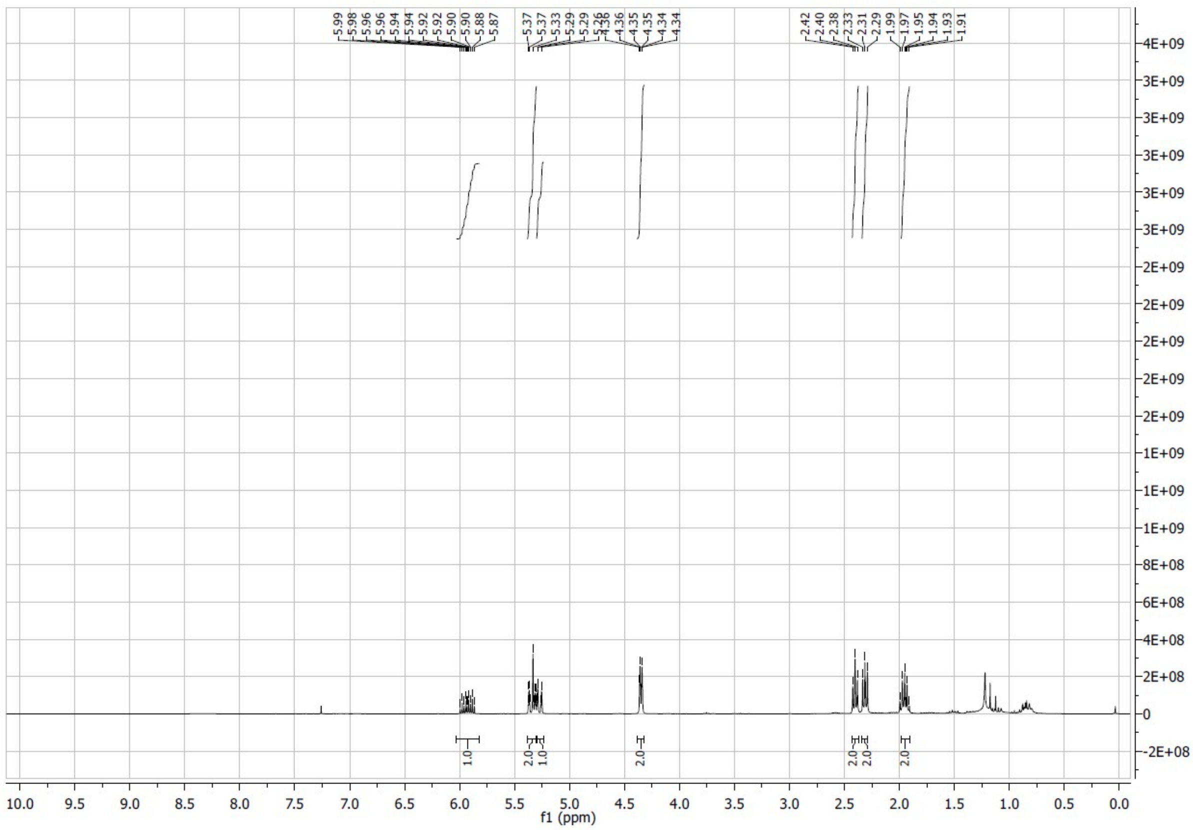


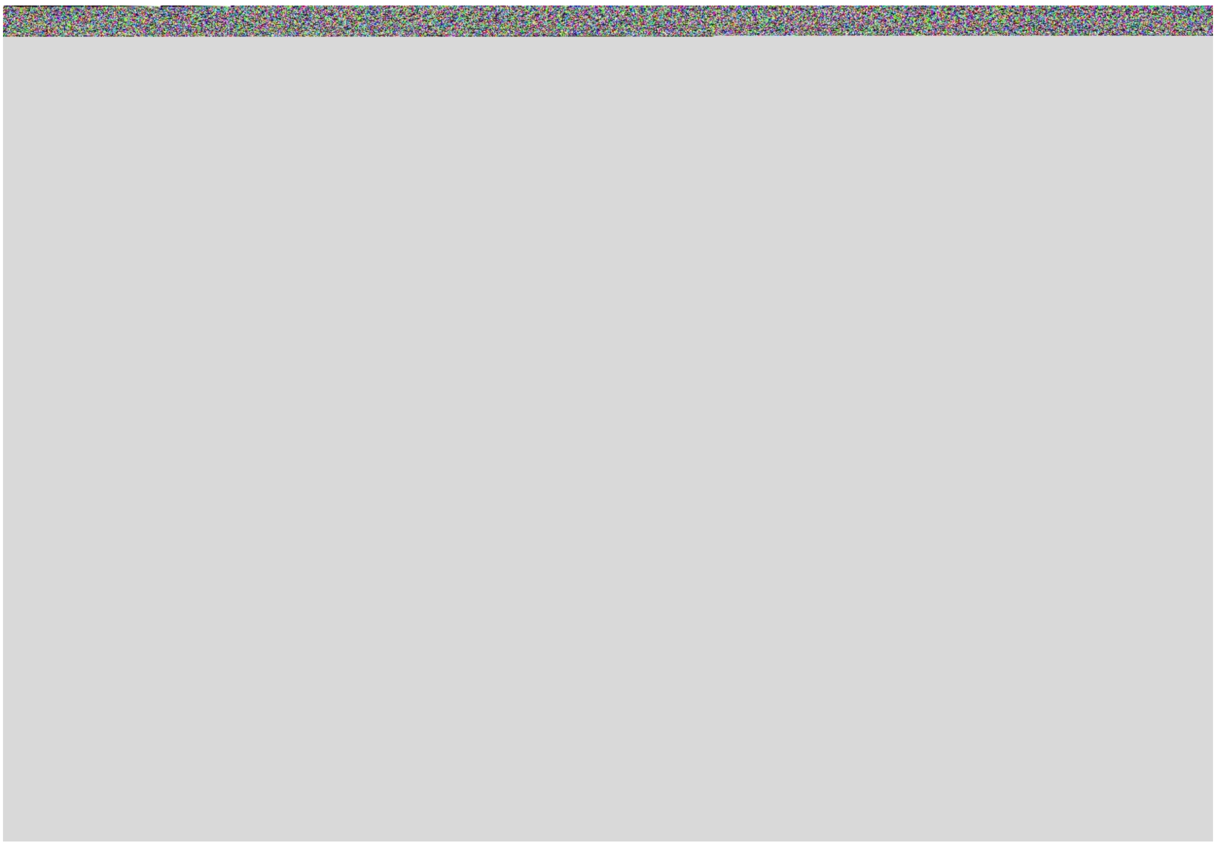
**3-(allyloxy)-5,5-dimethylcyclohex-2-en-1-one 1b**



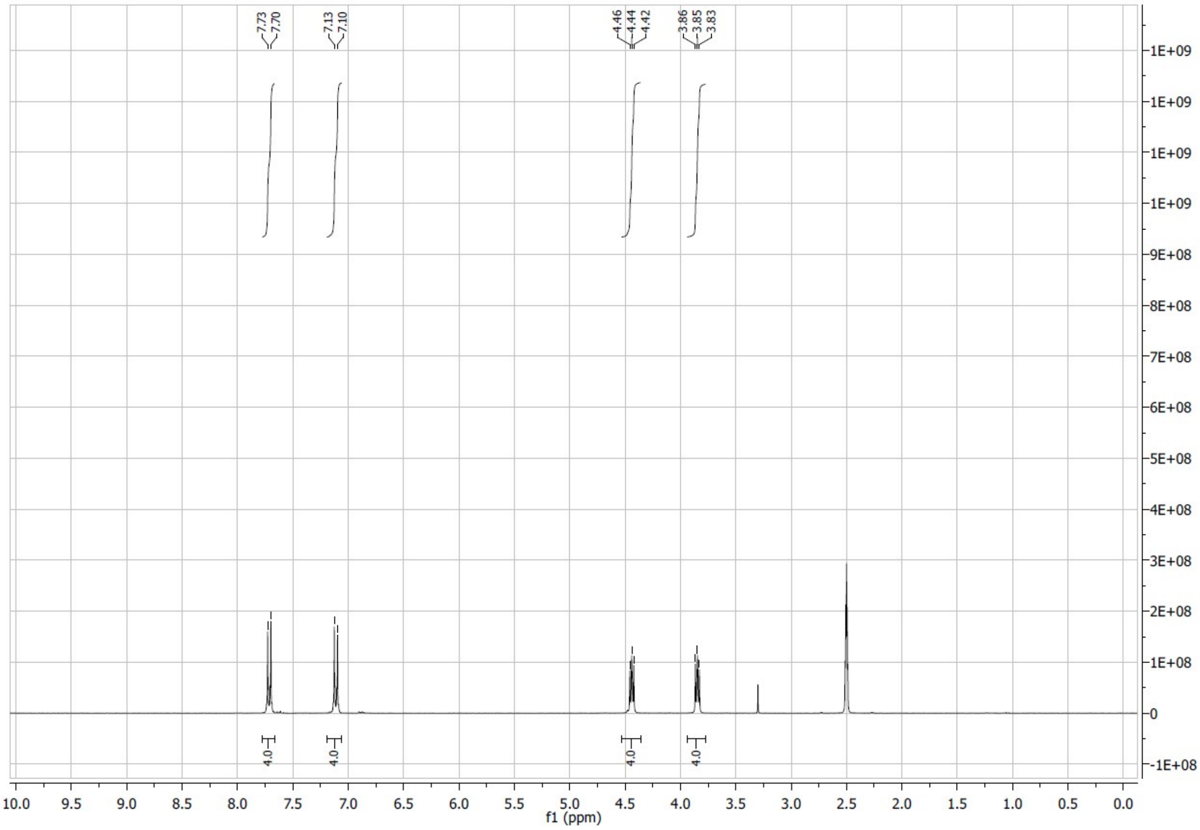



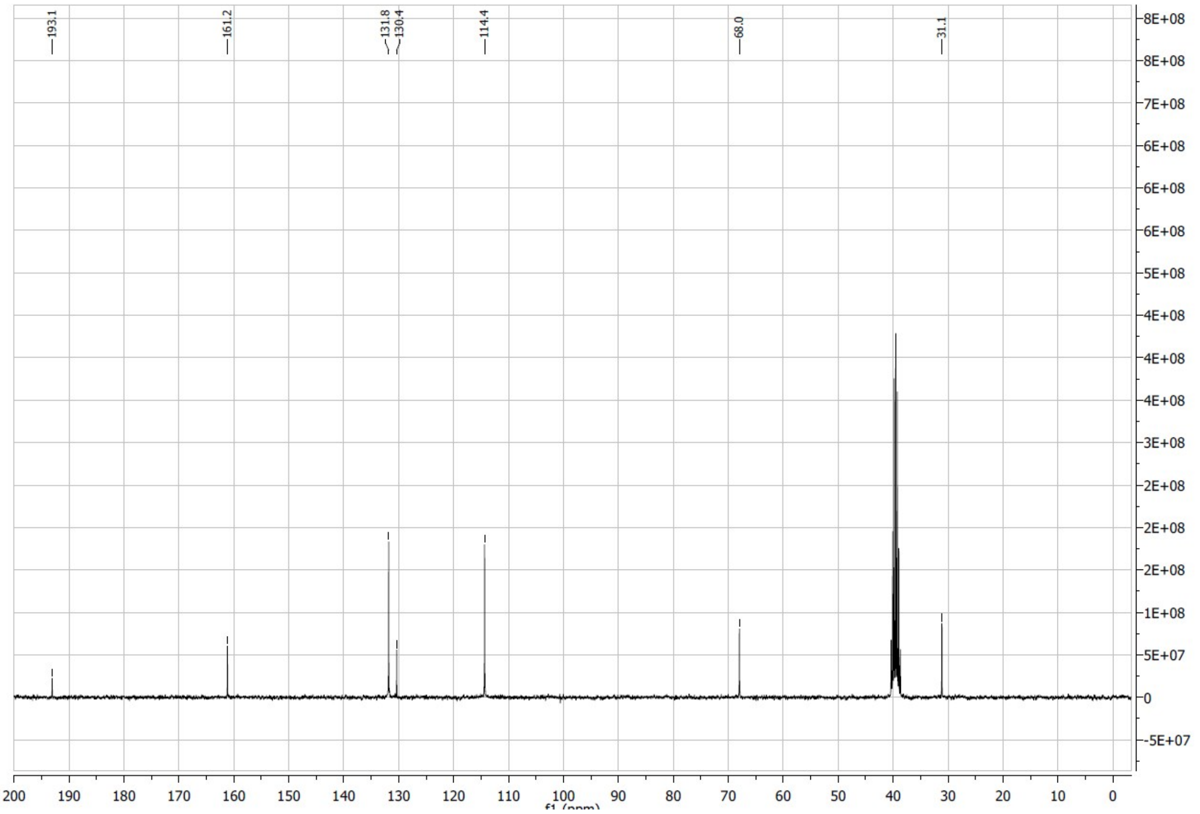
**3-(allyloxy)cyclohex-2-en-1-one 1a**



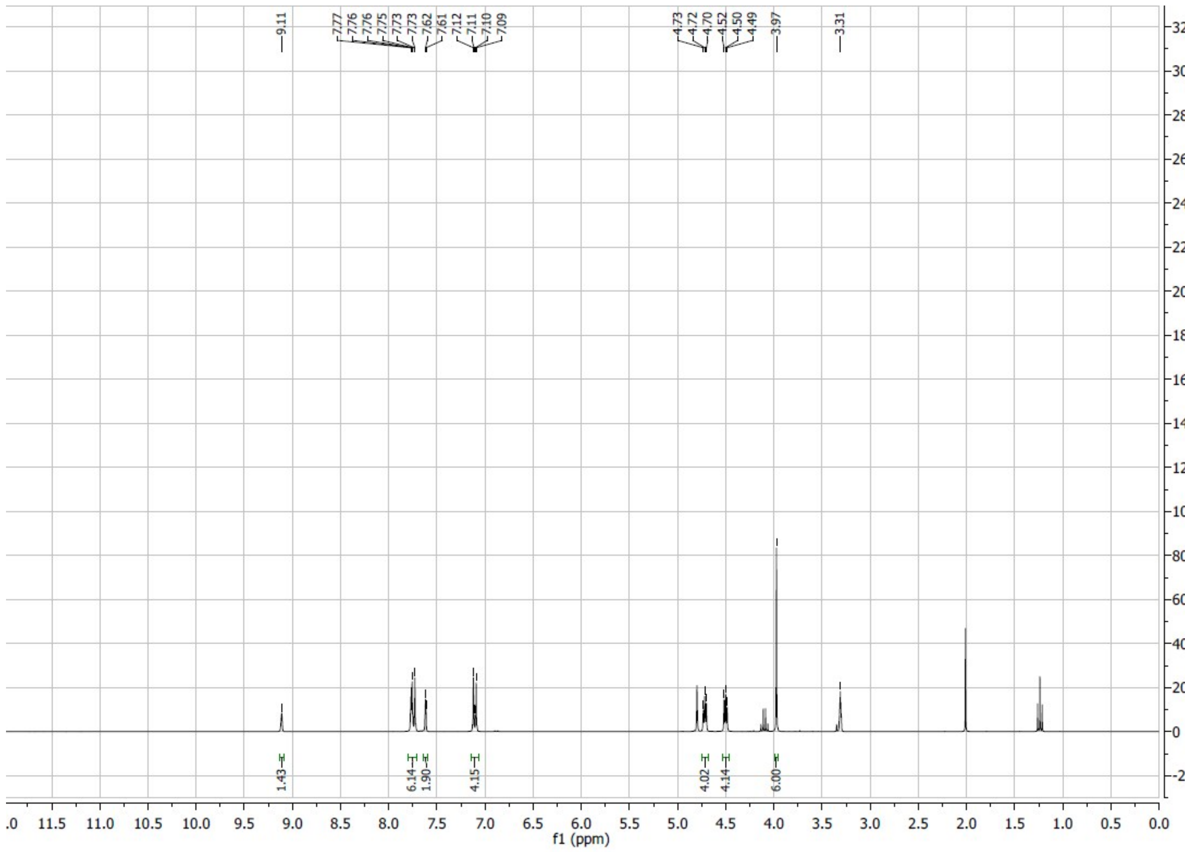



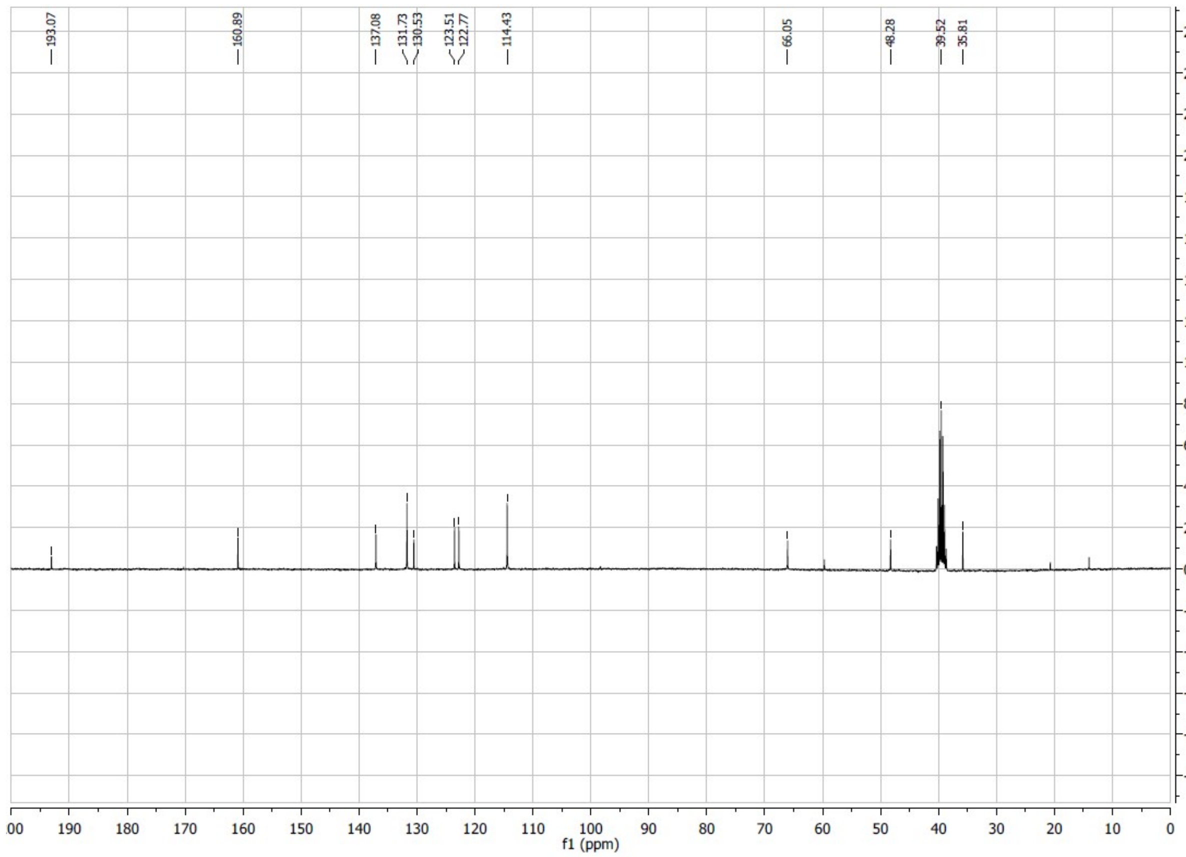
**4-4'-(2-bromoethoxy)benzophenone**



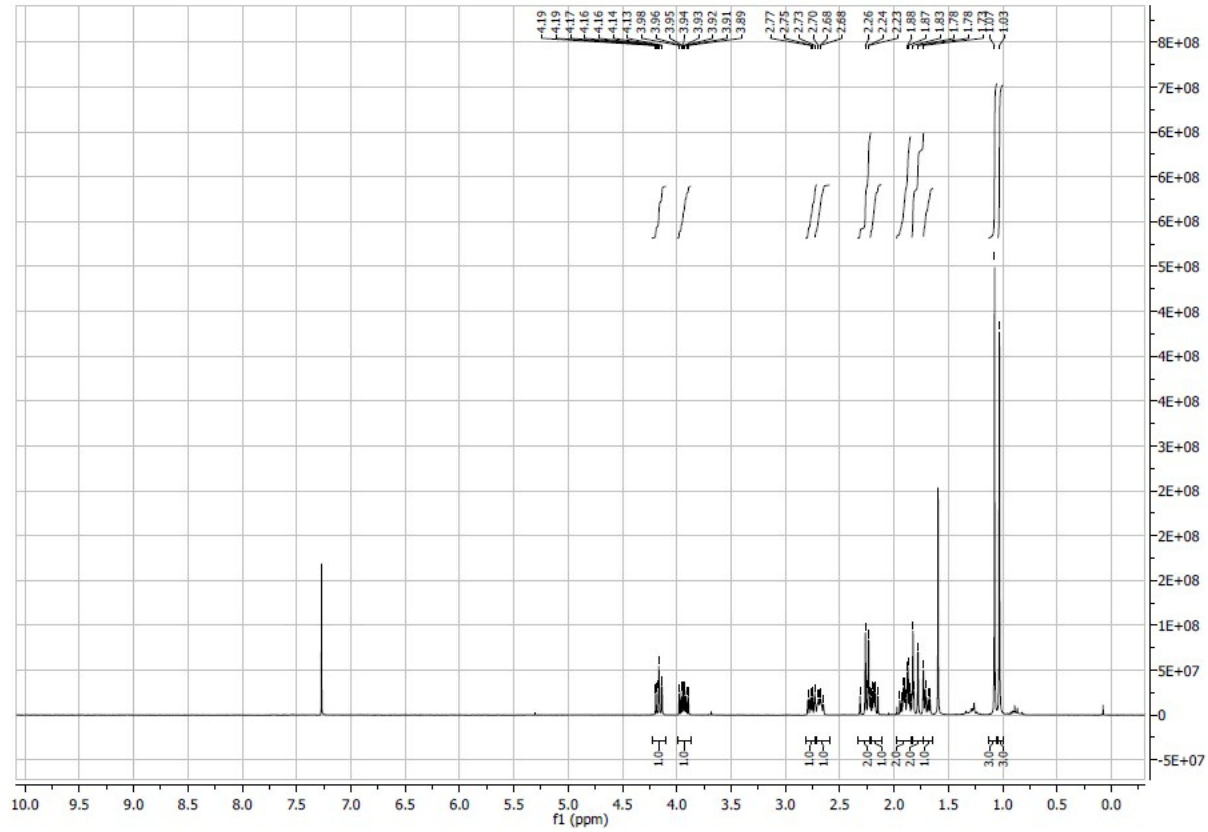



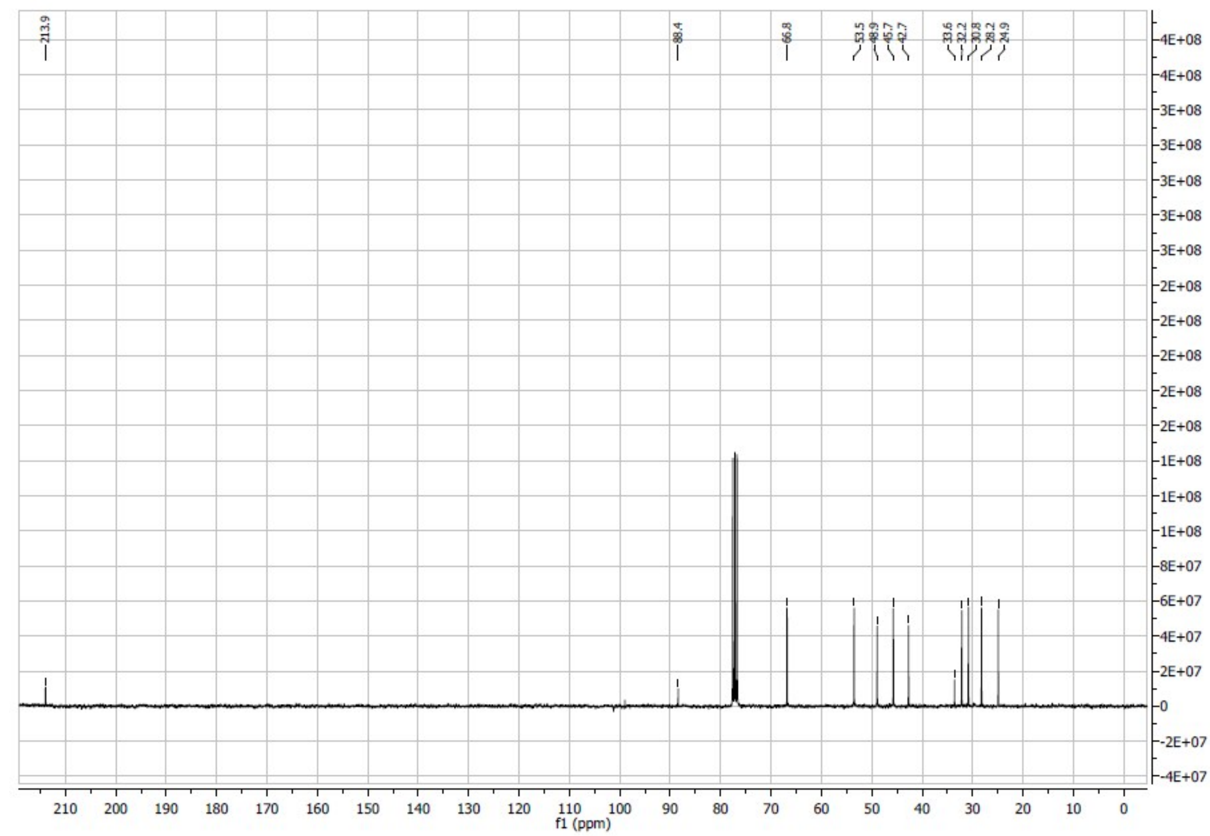
**4, 4'-(2-(1methylimidazolium)ethoxy)benzophenone dibromide**



**7,7-dimethylhexahydro-2H-benzo[1,4]cyclobuta[1,2-b]furan-5(6H)-one 2d**



**Hexahydro-2H-benzo[1,4]cyclobuta[1,2-b]furan-5(6H)-one 2c**