## Electronic Supplementary Information

# Radical-Mediated Dehydrogenation of Bile Acids by Means of Hydrogen Atom Transfer to Triplet Carbonyls

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## 1. Experimental procedures

**Chemicals.** BSs (NaCA, NaCDCA and NaDCA), BAs (LA and UDCA), benzophenone (BP), *S*-ketoprofen (*S*-KP), sodium chloride, sodium hydroxide and acetonitrile ($CH_3CN$) were purchased by Sigma-Aldrich. NaLA and NaUDCA were prepared by basification of the free acids with the stoichiometric amount of NaOH.

**Irradiation and Absorption Measurements**

UV spectra were recorded on a Cary 300 (Varian) spectrophotometer. Irradiations of NaCA at the concentration of 10 mM with 1 x $10^{-5}$ M of KPMe was performed in a Luzchem photoreactor (model LZC-4V) with lamps emitting at $\lambda_{max}$ = 350 nm in quartz cuvettes purged with $O_2$ or $N_2$ using Milli-Q water as solvent ([NaCl] = 0.2 M).

**Laser Flash Photolysis**

A pulsed Nd: YAG L52137 V LOTIS TII at the excitation wavelength of 266 nm was used. It contained a pulsed laser, a 77250 Oriel monochromator and an oscilloscope DP04054 Tektronix. The output signal from the oscilloscope was transferred to a personal computer. The single pulses were *ca*. 10 ns duration, and the energy was 15 mJ/pulse. Transient spectra were recorded at room temperature using quartz cells of 1 cm path length containing $N_2$-purged solutions of 1 x $10^{-5}$ M of KPMe in aqueous solution ([NaCl] = 0.2 M) and different concentrations of BSs.

**Nuclear Magnetic Resonance (NMR).** A Brucker 300 MHz spectrometer was used for the NMR experiments except of the NOEDIFF experiments that were performed in a Brucker 400 MHz spectrometer. The signal of the solvent chloroform was used as a reference for the determination of the chemical shifts (δ) in ppm.

**UPLC-MS.** Chromatography was performed on an ACQUITY UPLC system (Waters Corp.) containing a conditioned autosampler at 4 °C. The separation was carried out on an ACQUITY UPLC BEH C18 column (50 mm × 2.1 mm i.d., 1.7 μm) at the temperature of 40 °C. The analysis was performed with isocratic elution of 60% ACN and 40% water (containing 0.01% formic acid) as the mobile phase during 12 minutes followed by a gradient to reach 100% of

MeOH. The injection volume was 1μL. The Waters ACQUITY™ XevoQToF Spectrometer (Waters Corp.) was connected to the UPLC system via an electrospray ionization (ESI) interface. The ESI source was operated in negative ionization mode depending on the experiment with the capillary voltage at 3.0 kV. The temperature of the source and desolvation was set at 120 °C and 500 °C, respectively. All data collected in Centroid mode were acquired using Masslynx™ software (Waters Corp.).

**Synthetic procedures**

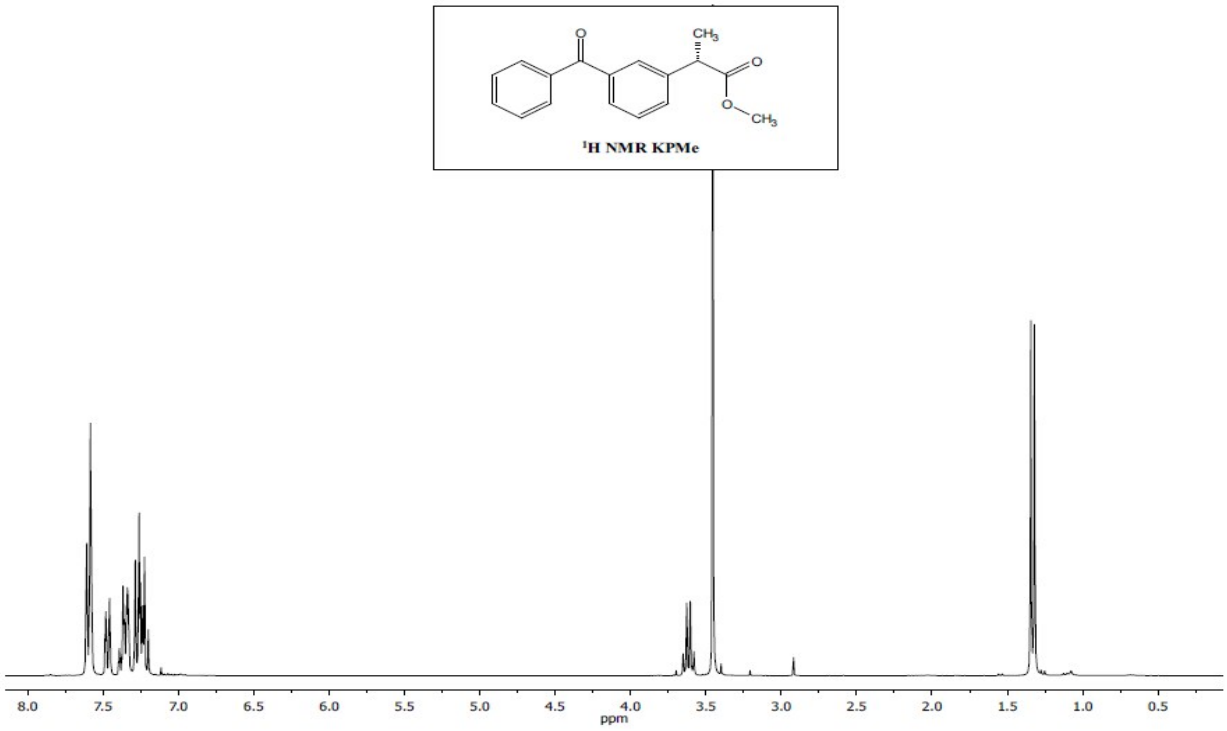
KPMe and CAMe were prepared following standard procedures:

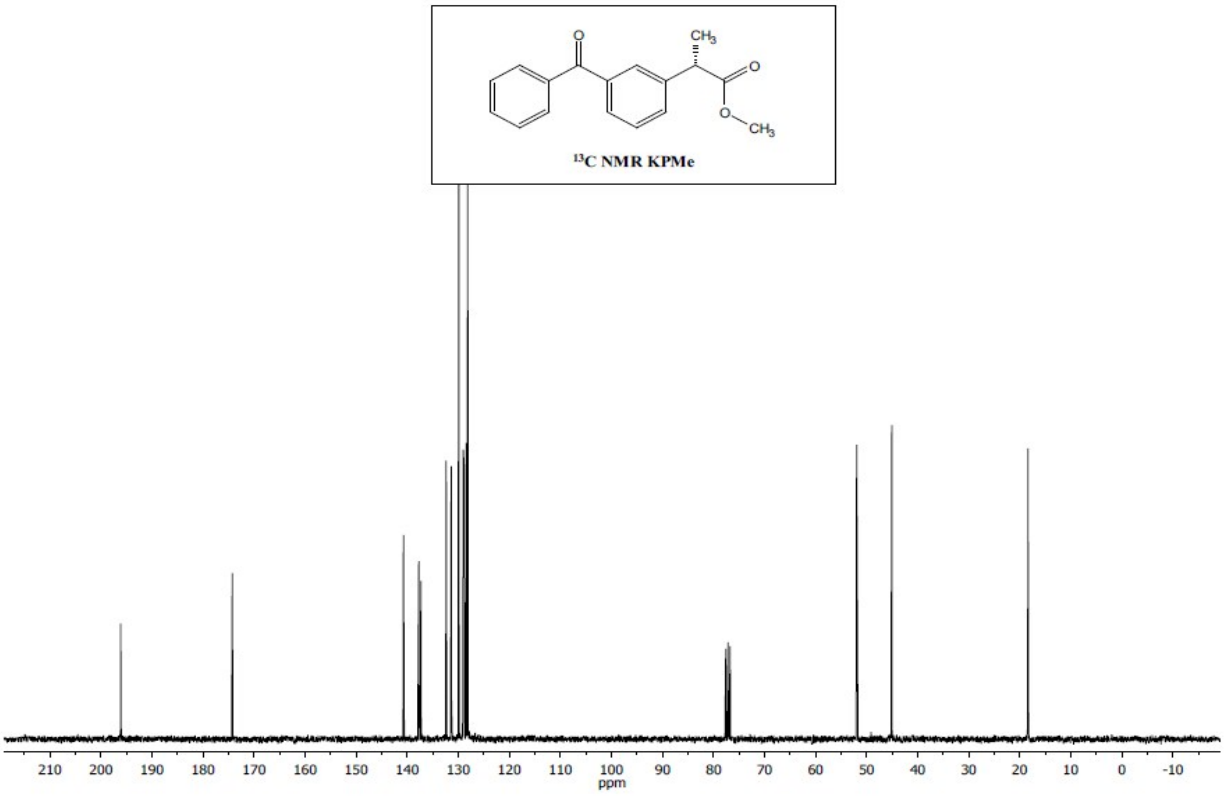
**Synthesis of KPMe.** Briefly, to a stirred solution of *S*-KP (0.500 g, 1.97 mmol) in 4 mL of MeOH, a catalytic amount of $H_2SO_4$ was added. The reaction was refluxed overnight, re-dissolved in AcOEt, washed with $NaHCO_3$, dried over $MgSO_4$ and concentrated under vacuum. The crude was purified by column chromatography ($SiO_2$, AcOEt:Hex, 50:50) to give KPMe (0.516 g, 98%). $^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) 1.33 (d, $J$ = 7.2 Hz, 3H, $CH_3$); 3.45 (s, 1H, $OCH_3$); 3.61 (q, $J$ = 7.2 Hz, 1H, CH); 7.17-7.65 (m, 9H, arom). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) 196.1 (C), 174.3 (C), 140.7 (C), 137.7 (C), 137.3 (C), 132.4 (CH), 131.4 (CH), 129.9 (2xCH), 129.0 (CH), 128.9 (CH), 128.4 (CH), 128.2 (2xCH), 52.0 ($CH_3$), 45.1 (CH), 18.4 ($CH_3$). m/z found 291.0995, calculated for $C_{17}H_{16}O_3Na$ ($MH^+$) 291.0995.

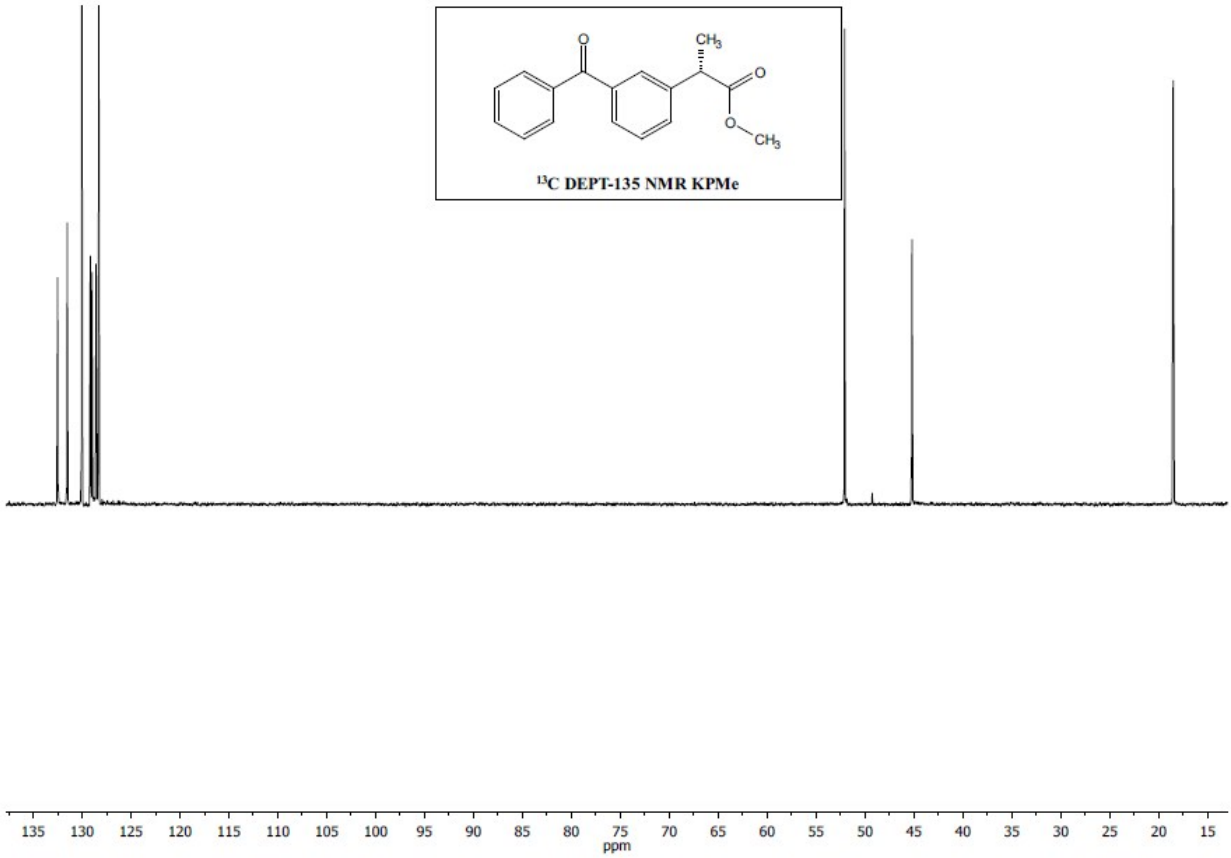
**Synthesis of CAMe.** Briefly, to a stirred solution of CA (2 g, 4.9 mmol) in 10 mL of MeOH, 0.3 mL of HCl and 5 mL of dimetoxypropanone were added. The reaction was stirred overnight and then re-dissolved in AcOEt, washed with $NaHCO_3$ and brine and dried over $MgSO_4$. Concentration under vacuum gave CAMe (1.95 g, 94%). $^1$H NMR (300 MHz, $CDCl_3$): δ (ppm) 0.69 (s, 3H, $CH_3$); 0.90 (s, 3H, $CH_3$); 0.98 (d, $J$ = 6.3 Hz, 3H, 21-$CH_3$); 3.46 (m, 1H, 3β-H); 3.66 (s, 3H, $CH_3$); 3.86 (*br* s, 1H, 7β-H); 3.98 (*br* s, 1H, 12β-H). $^{13}$C NMR (75 MHz, $CDCl_3$): δ (ppm) 174.9 (C), 73.2 (CH), 72.0 (CH), 68.6 (CH), 51.6 ($CH_3$), 47.1 (CH), 46.5 (C), 41.7 (CH), 41.6 (CH), 39.6 (CH+$CH_2$), 35.4 ($CH_2$+CH), 34.9 (C), 34.8 ($CH_2$), 31.2 ($CH_2$), 31.0 ($CH_2$), 30.4 ($CH_2$), 28.3 ($CH_2$), 27.6 ($CH_2$), 26.5 (CH), 23.4 ($CH_2$), 22.6 ($CH_3$), 17.4 ($CH_3$), 12.6 ($CH_3$). m/z found 423.3122, calculated for $C_{25}H_{43}O_5$ ($MH^+$) 423.3110.

## 2. Characterization of the synthesized compounds

### 2.1. $^{1}H$,$^{13}C$ and $^{13}C$ DEPT-135 NMR of KPMe

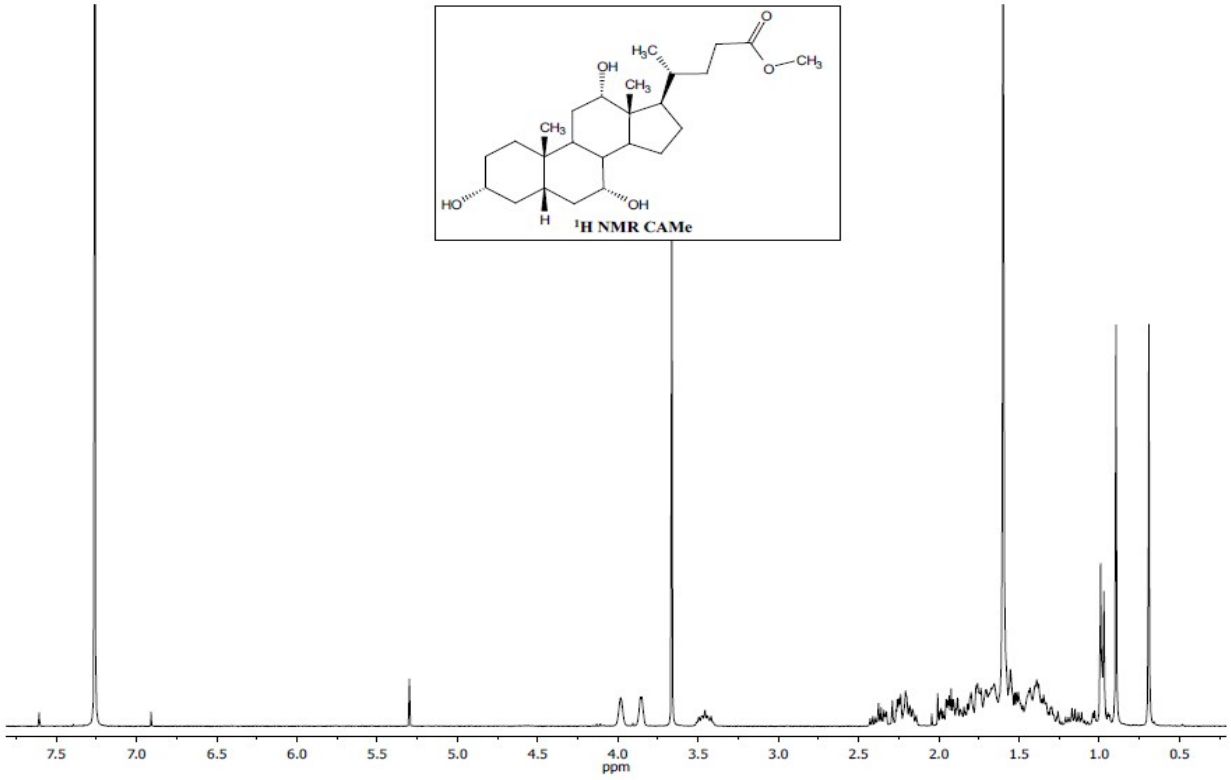


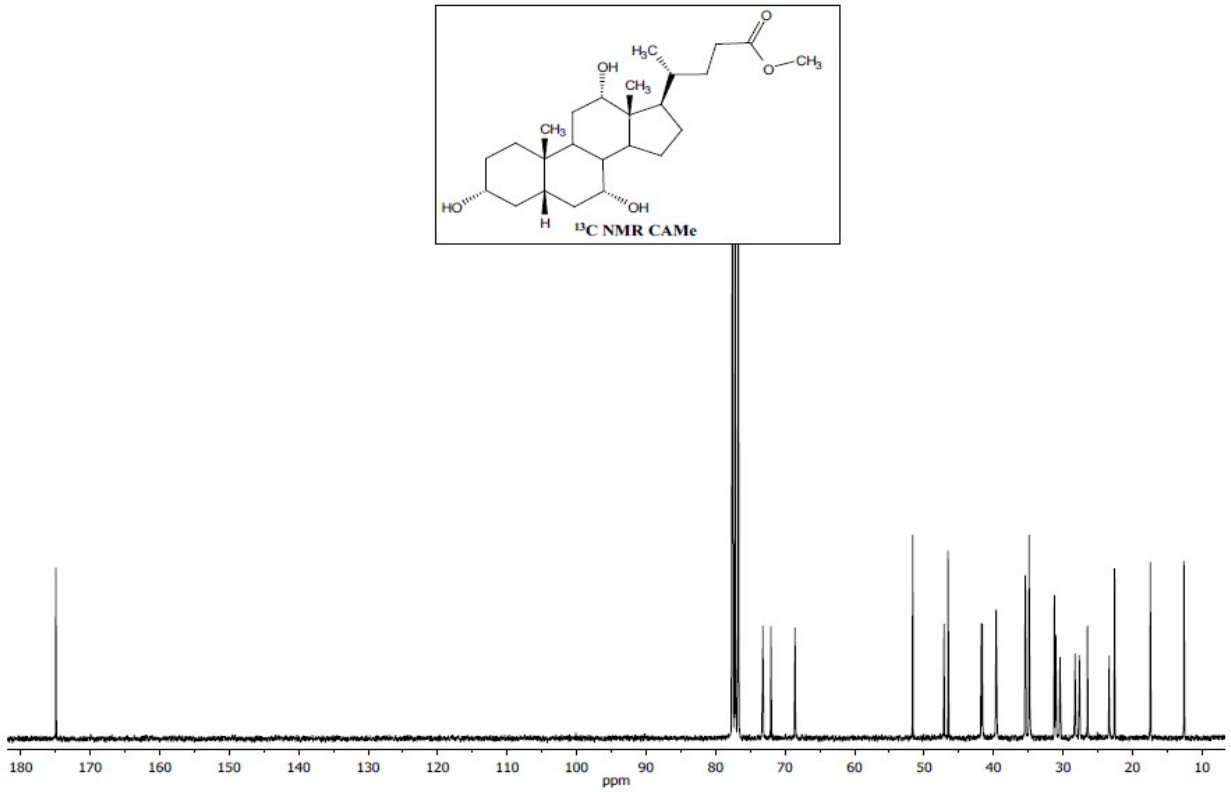



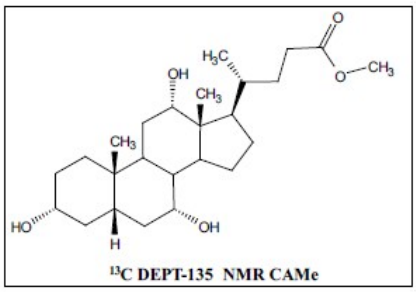



**$^{13}$C DEPT-135 NMR KPMe**

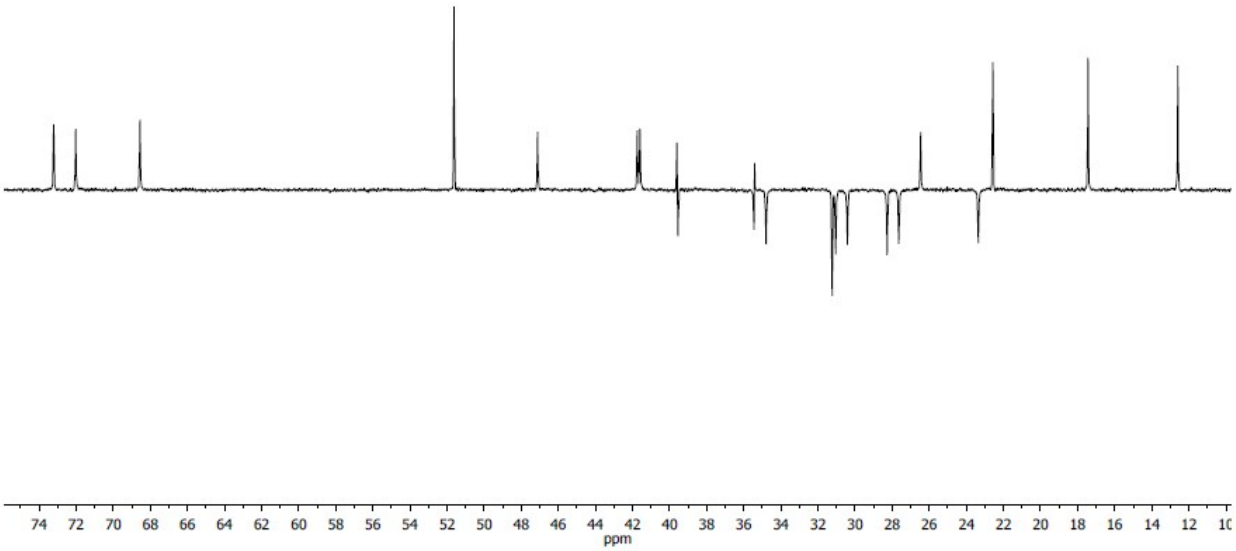
## 2.2. $^{1}H$,$^{13}C$ and $^{13}C$ DEPT-135 NMR of CAMe



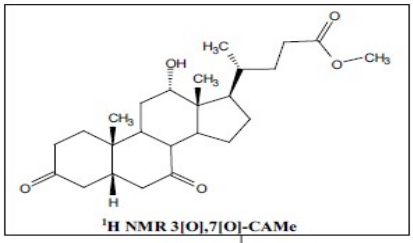



$^{13}$C DEPT-135 NMR CAMe

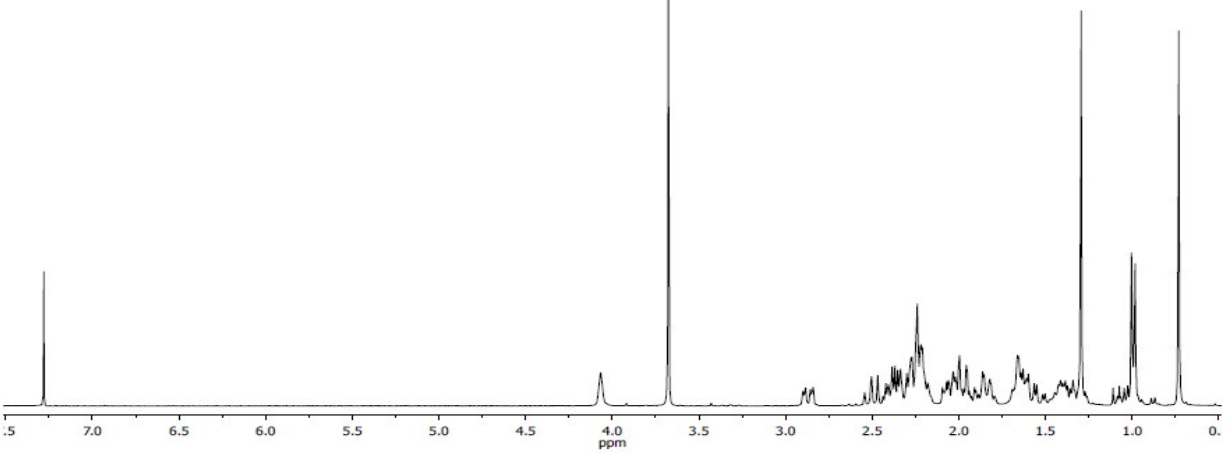


## 3. Characterization of the photoproducts

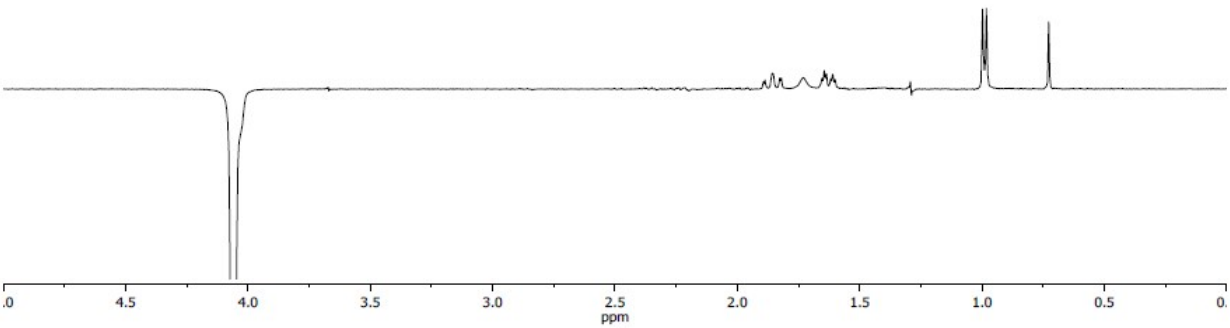
### 3.1. $^{1}$H, NOEDIFF, $^{13}$C, $^{13}$C DEPT-135 and $^{1}$H-$^{13}$C HSQC NMR of 3[O],7[O]-CAMe

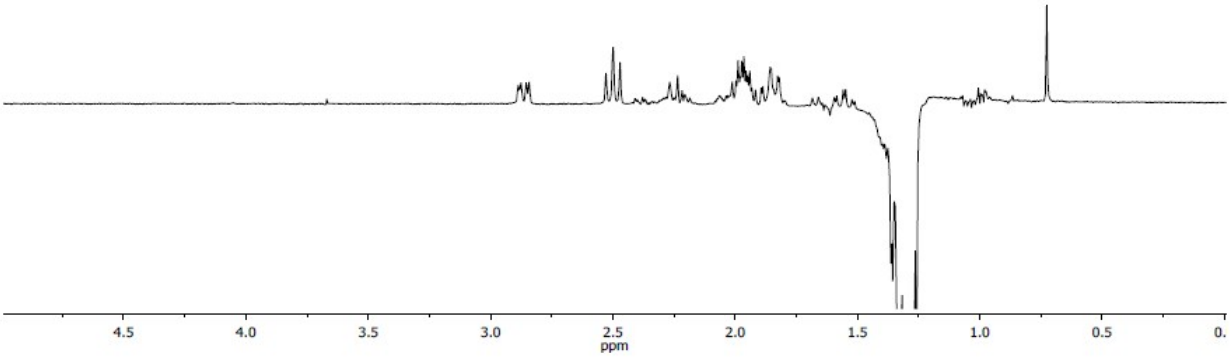


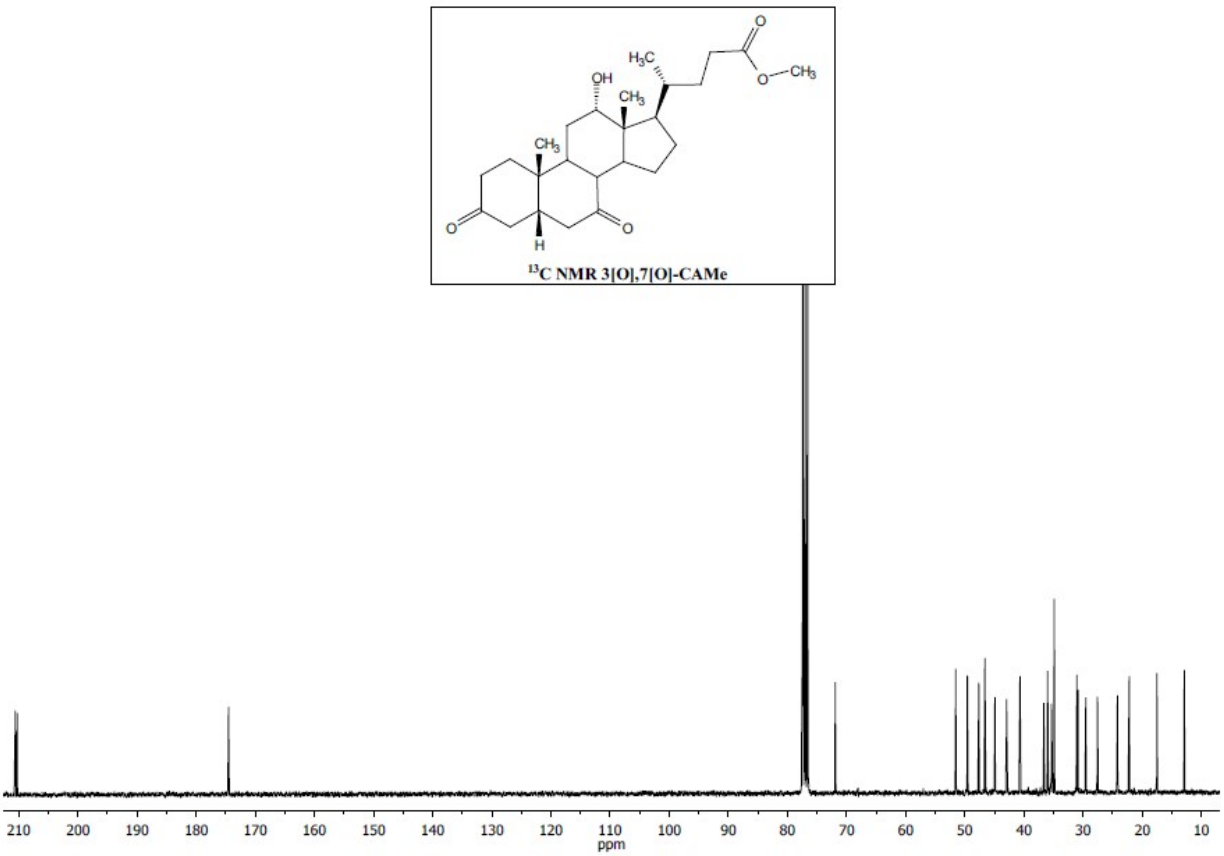

$^{1}$H NMR 3[O],7[O]-CAMe




$^{1}$H NOE NMR 3[O],7[O]-CAMe




$^{13}$C NMR 3[O],7[O]-CAMe
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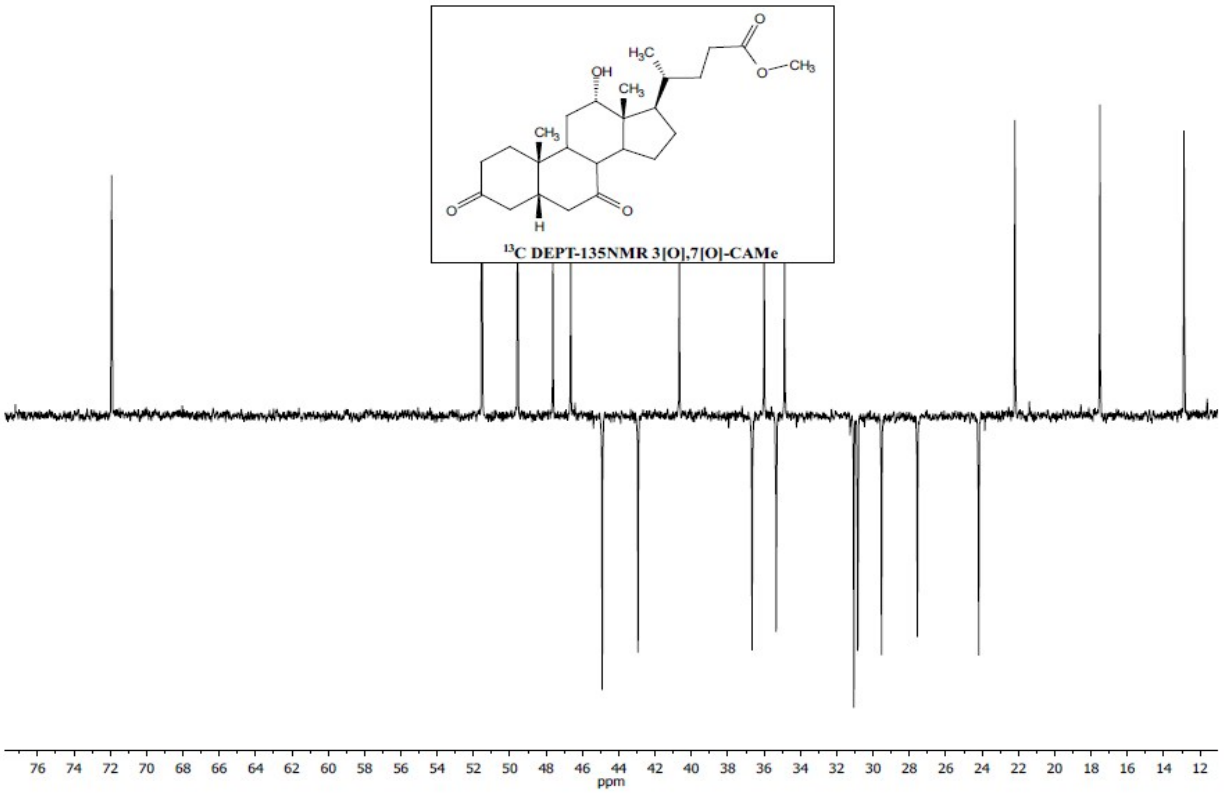
ppm


$^{13}$C DEPT-135NMR 3[O],7[O]-CAMe
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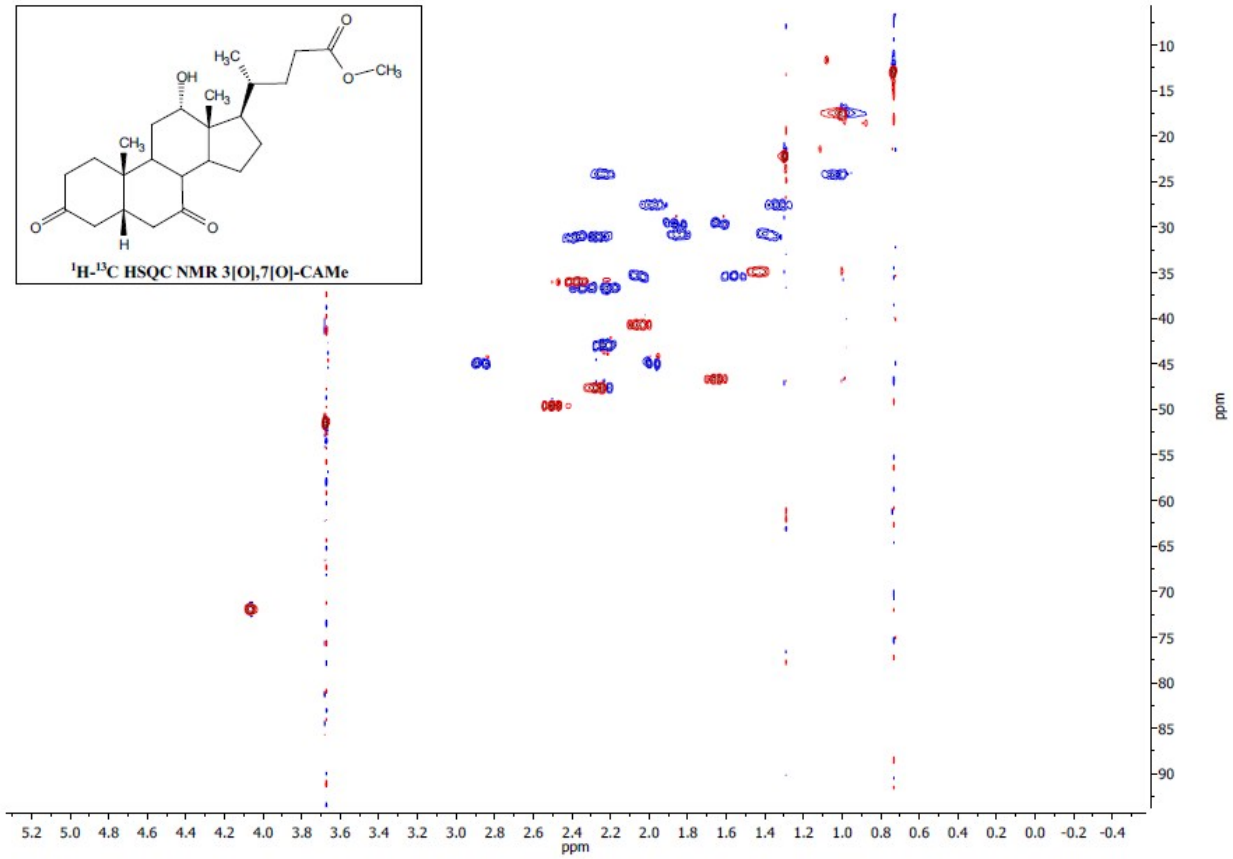
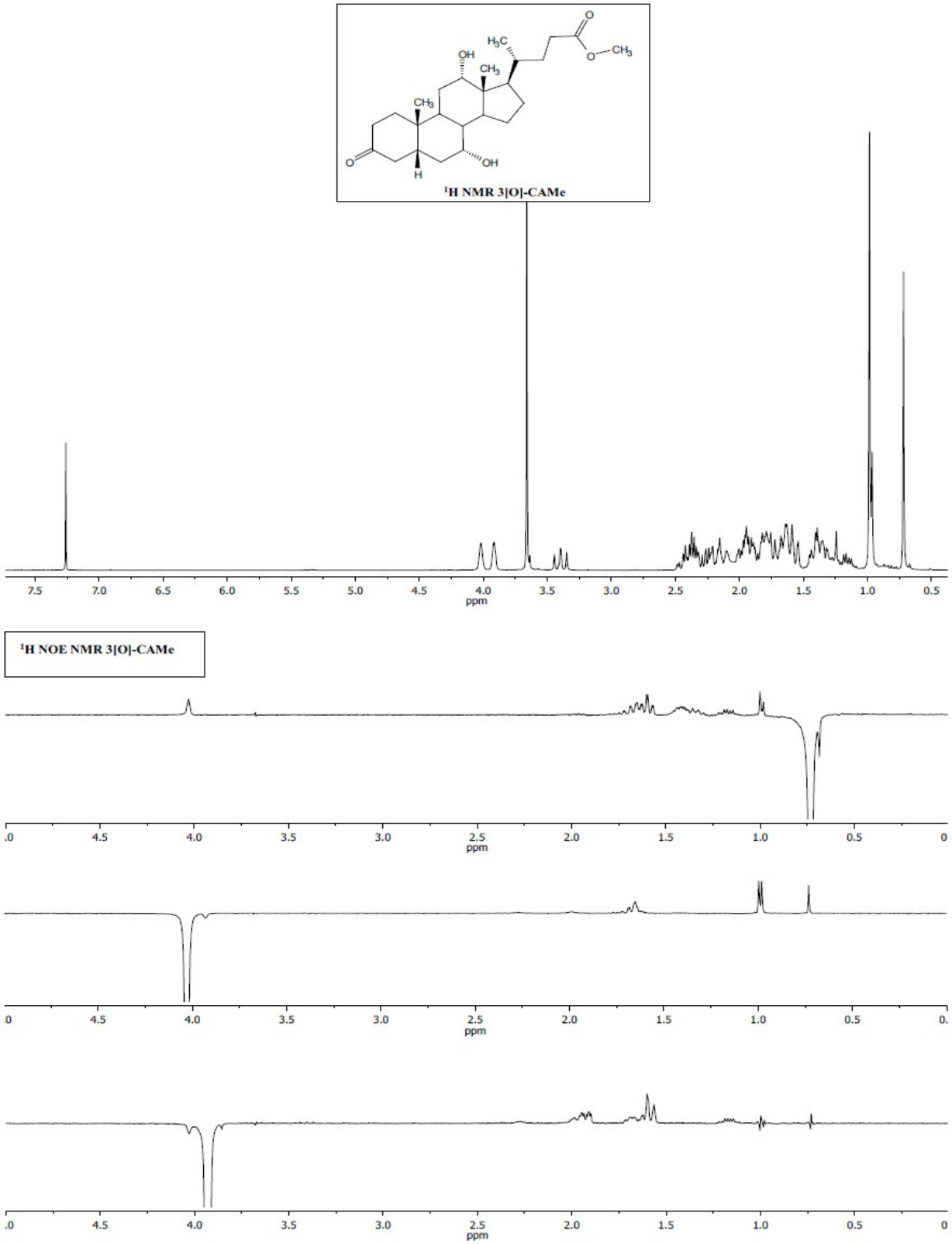
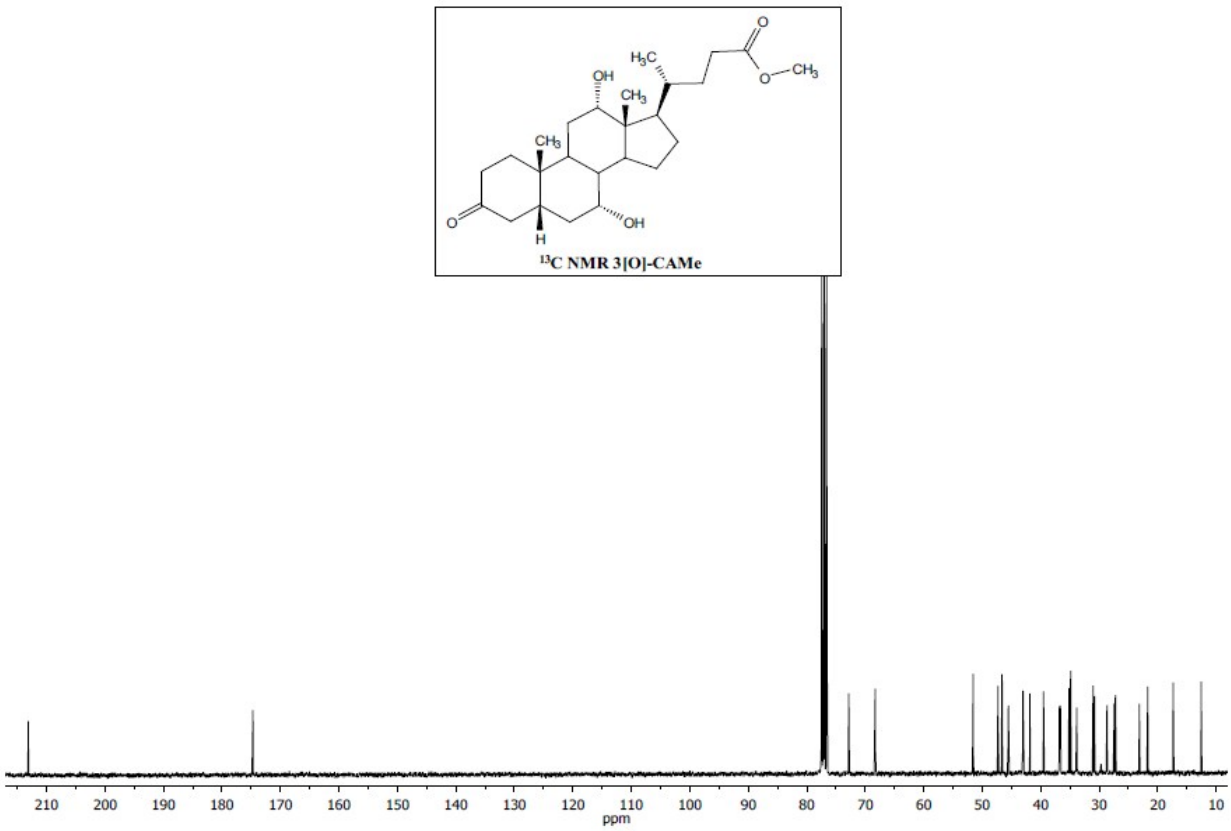
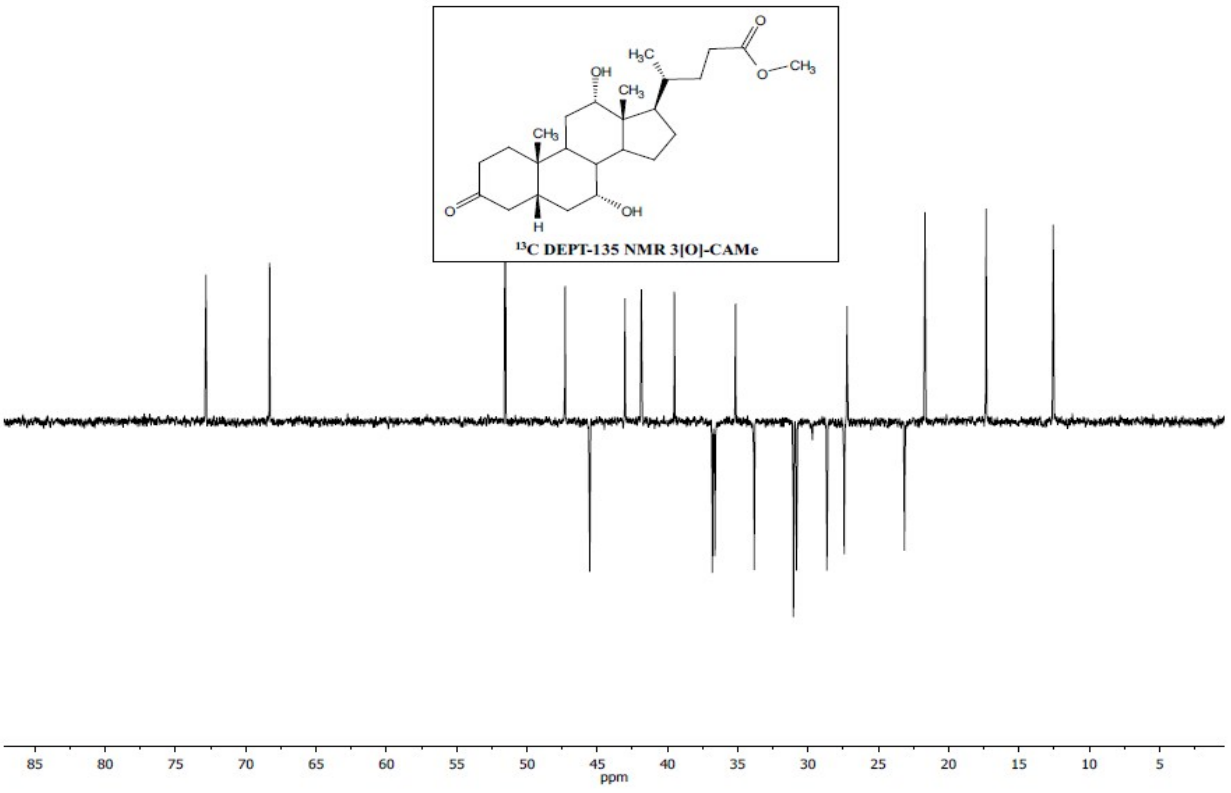
ppm

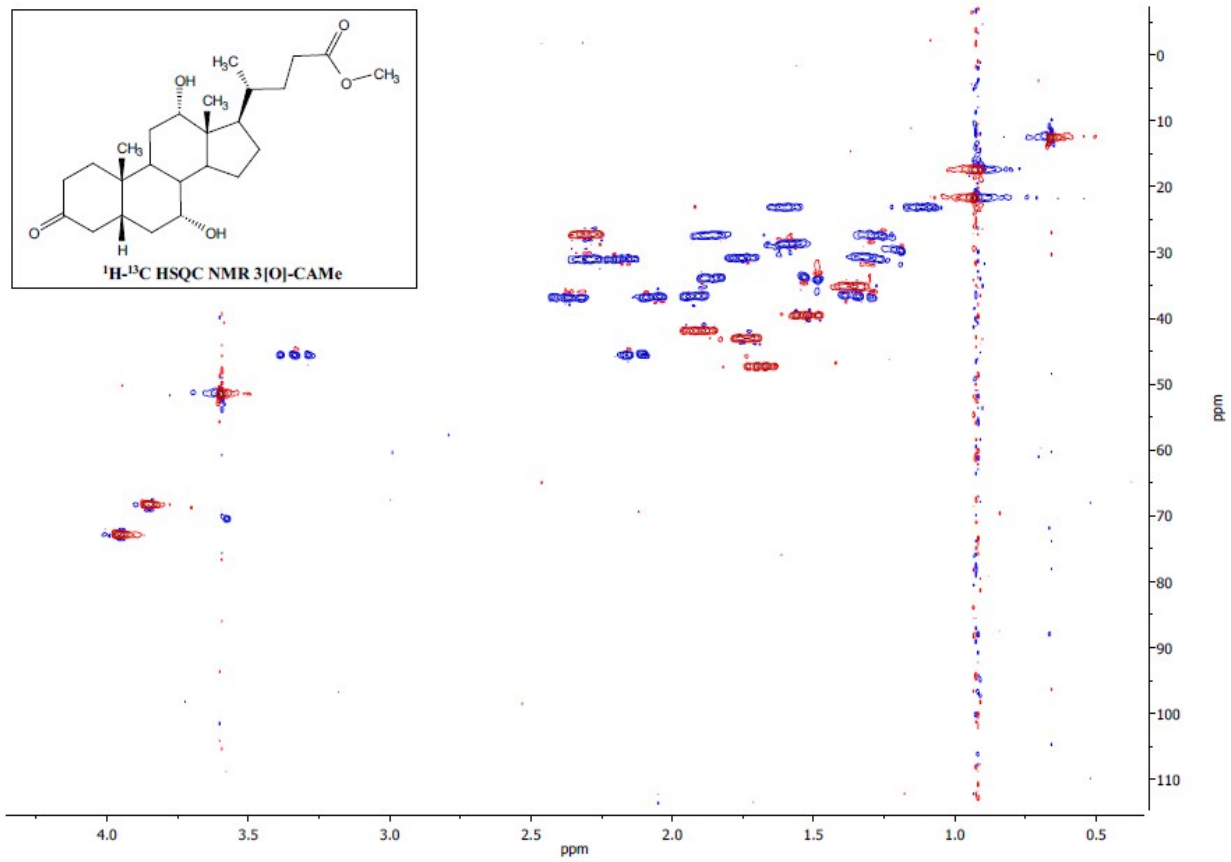

$^{1}$H-$^{13}$C HSQC NMR 3[O],7[O]-CAMe
ppm
ppm

### 3.2. $^{1}H$, NOEDIFF, $^{13}C$, $^{13}C$ DEPT-135 and $^{1}H$-$^{13}C$ HSQC NMR of 3[O]-CAMe

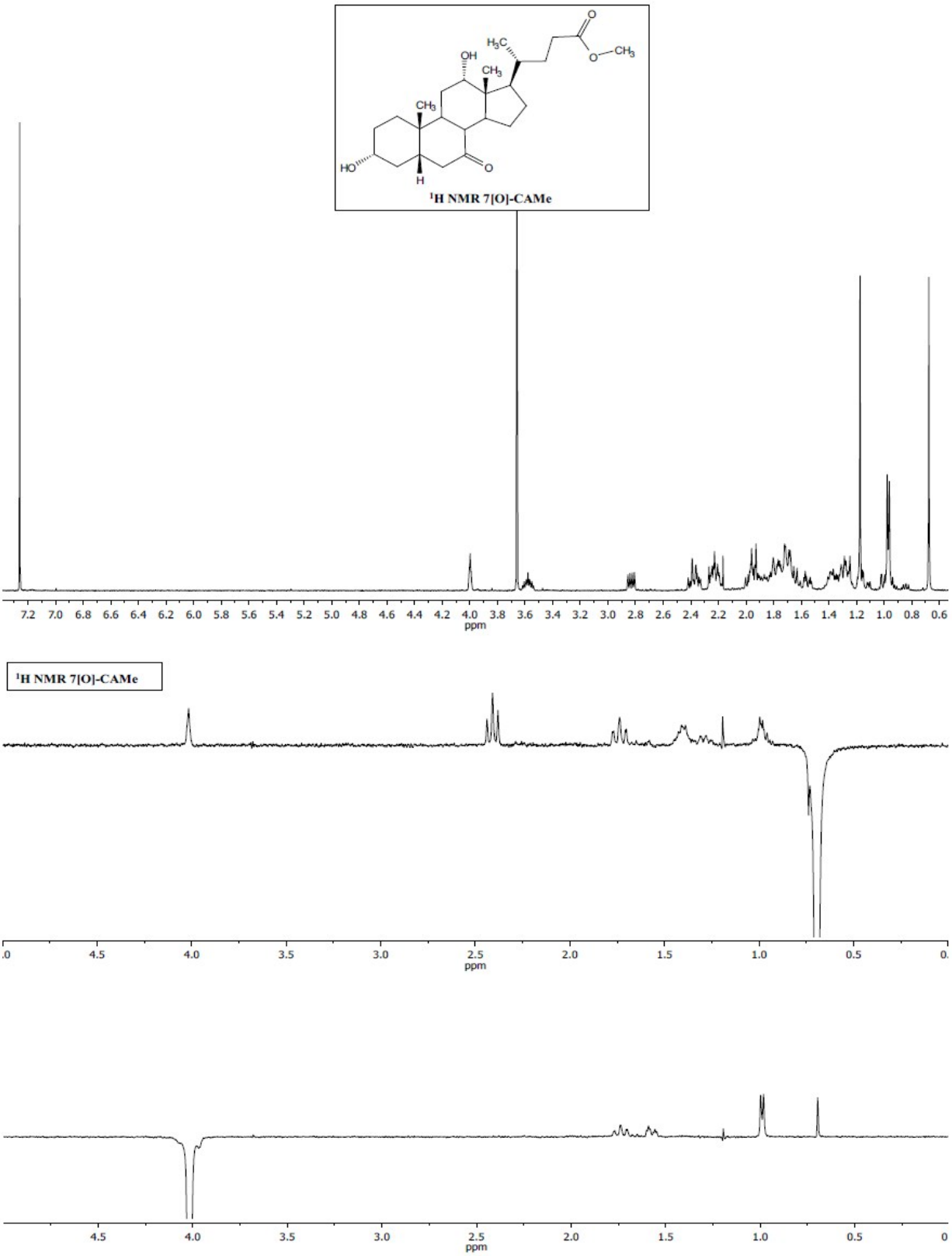


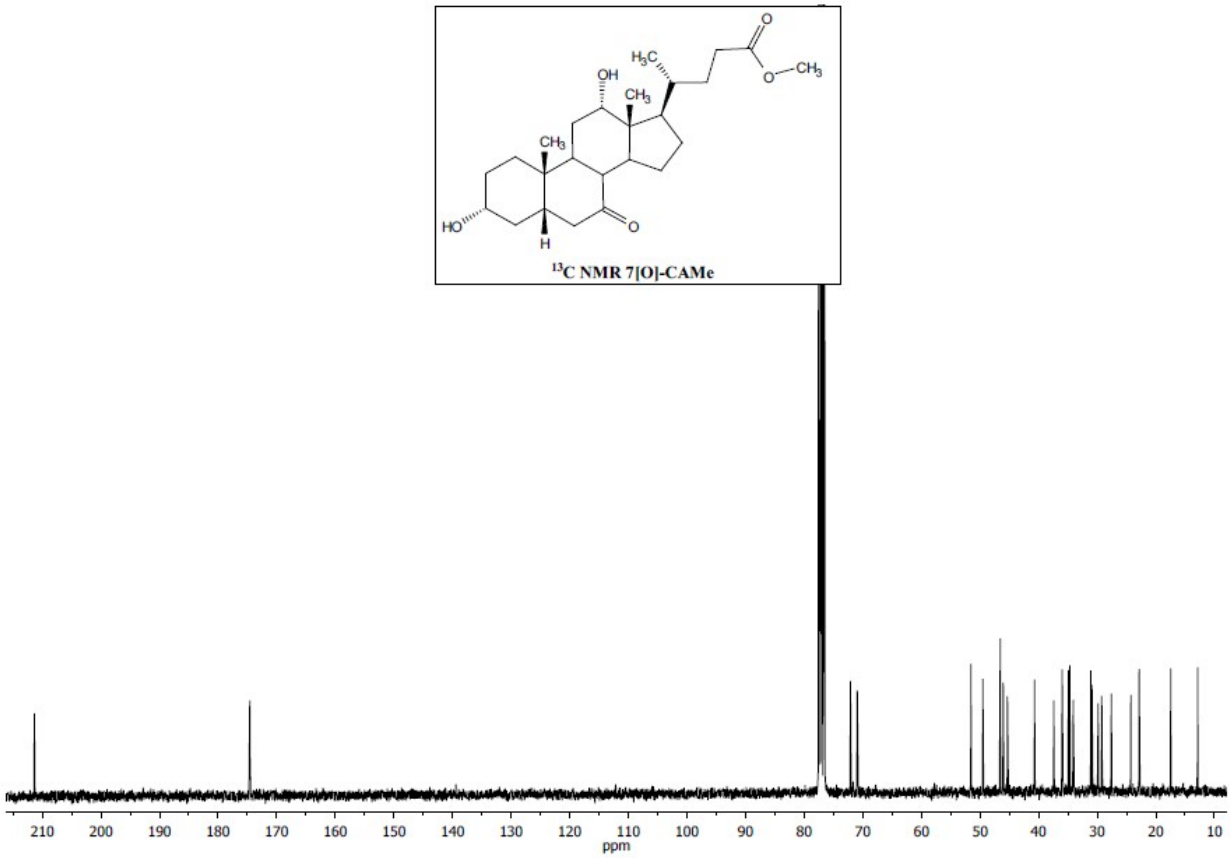

$^{13}$C NMR 3[O]-CAMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm


$^{13}$C DEPT-135 NMR 3[O]-CAMe
85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5
ppm


$^1$H-$^{13}$C HSQC NMR 3[O]-CAMe
ppm
ppm

### 3.3. $^{1}H$, NOEDIFF, $^{13}C$, $^{13}C$ DEPT-135 and $^{1}H$-$^{13}C$ HSQC NMR of 7[O]-CAMe




$^{13}$C NMR 7[O]-CAMe
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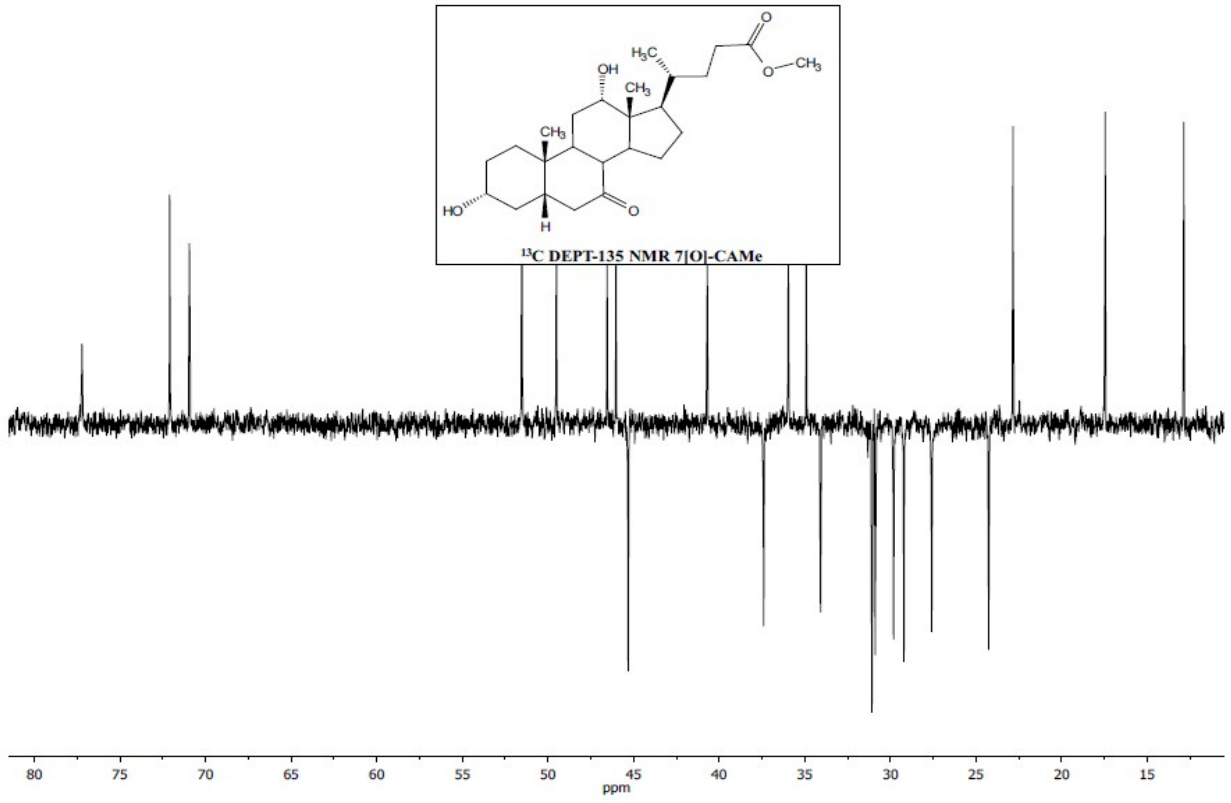
$^{13}$C DEPT-135 NMR 7[O]-CAMe
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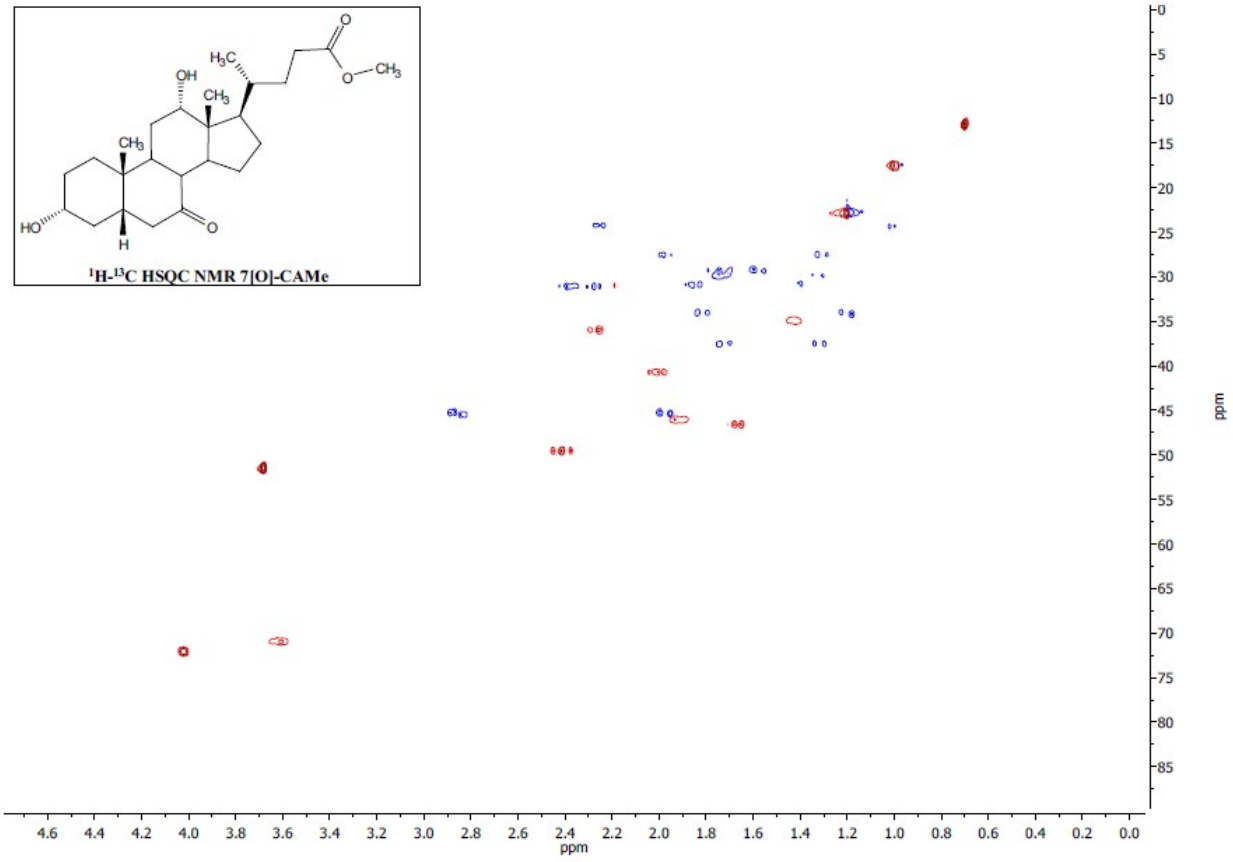
OH
CH3
H3C
O
O
CH3
CH3
HO
O
H
¹H-¹³C HSQC NMR 7[O]-CAMe
ppm
ppm

**4. UPLC-MS analysis**

Irradiation of NaCA in aqueous NaCl (0.2 M) in the presence of KPMe with lamps emiting at $\lambda_{max}$ = 350 nm was monitored by UPLC-MS. Relative photoproduct concentrations at different irradiation times have been determined by standard procedures from three independent irradiations.

Table S1. Photoproduct evolution during the irradiation of NaCA with KPMe ($\lambda_{max}$=350 nm). Experiment 1.

| Time (h) | CA | 3[O]-CA | 7[O]-CA | 3[O],7[O]-CA |
|---|---|---|---|---|
| 0 | 100 | 0.0 | 0.0 | - |
| 1 | 77 | 15.3 | 7.7 | - |
| 2 | 75 | 16.7 | 8.3 | - |
| 3 | 71 | 19.3 | 9.7 | - |
| 4 | 67 | 22.0 | 11.0 | - |
| 5 | 63 | 24.7 | 12.3 | - |
| 6 | 32 | 45.3 | 22.7 | 2 |
| 7 | 38 | 41.3 | 20.7 | 5 |
| 8 | 23 | 46.0 | 23.0 | 7 |
| 9 | 35 | 38.7 | 19.3 | 8 |

Table S2. Photoproduct evolution during the irradiation of NaCA with KPMe ($\lambda_{max}$=350 nm). Experiment 2.

| Time (h) | CA | 3[O]-CA | 7[O]-CA | 3[O],7[O]-CA |
|---|---|---|---|---|
| 0 | 100 | 0.0 | 0.0 | - |
| 1 | 78 | 14.7 | 7.3 | - |
| 2 | 75 | 16.7 | 8.3 | - |
| 3 | 71 | 19.3 | 9.7 | - |
| 4 | 69 | 20.7 | 10.3 | - |
| 5 | 69 | 20.7 | 10.3 | - |
| 6 | 67 | 22.0 | 11.0 | 2 |
| 7 | 58 | 28.0 | 14.0 | 6 |
| 8 | 50 | 28.0 | 14.0 | 8 |
| 9 | 50 | 28.0 | 14.0 | 8 |

Table S3. Photoproduct evolution during the irradiation of NaCA with KPMe ($\lambda_{max}$=350 nm). Experiment 3.

| Time (h) | CA | 3[O]-CA | 7[O]-CA | 3[O],7[O]-CA |
|---|---|---|---|---|
| 0 | 100 | 0.0 | 0.0 | - |
| 1 | 98 | 1.3 | 0.7 | - |
| 2 | 77 | 15.3 | 7.7 | - |
| 3 | 71 | 19.3 | 9.7 | - |
| 4 | 65 | 23.3 | 11.7 | - |
| 5 | 75 | 16.7 | 8.3 | - |
| 6 | 65 | 23.3 | 11.7 | 3 |
| 7 | 59 | 27.3 | 13.7 | 6 |
| 8 | 44 | 32.0 | 16.0 | 8 |
| 9 | 44 | 32.0 | 16.0 | 8 |

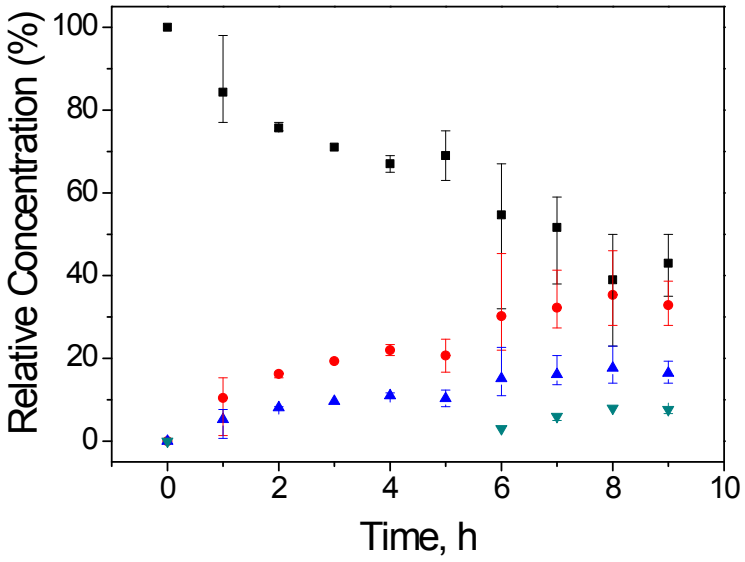


Figure S1. CA (■), 3[O]-CA(●),7[O]-CA(▲) and 3[O],7[O]-CA(▼) evolution during the irradiation of NaCA with KPMe ($\lambda_{max}$=350 nm).

Table S4. Kinetic constants for the degradation of CA and the formation of 3[O]-CA, 7[O]-CA and 3[O],7[O]-CA.

| Compound | $k$ ($h^{-1}$) |
|---|---|
| CA | 9.6 |
| 3[O]-CA | 6.4 |
| 7[O]-CA | 3.2 |
| 3[O],7[O]-CA | 0.9 |