A Laboratory-scale Annular Continuous Flow Reactor for UV Photochemistry using Excimer Lamps for Discrete Wavelength Excitation and its use in a Wavelength Study of a Photodecarboxlyative Cyclisation

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1. General Method and Materials

All solvents and reagents were used without further purification from the bottle. All reagents were used NMR spectra (^1H, ^{13}C) were recorded with Bruker AV400, DPX300, AV(III)400 spectrometers at ambient temperatures unless otherwise specified. Chemical shift values are reported in ppm, and solvent resonances were used as internal standards ($CHCl_3$: δ = 7.26 ppm for ^1H, δ = 77.16 ppm for ^{13}C; DMSO-d_6: δ = 2.50 ppm for ^1H, δ = 39.52 ppm for ^{13}C. 1,3,5-Trimethoxybenzene was used an internal standard for determining the yield of **2** unless otherwise specified. Coupling constants (*J*) are quoted in Hertz. Proton NMR multiplicities and connectivities were assigned by using COSY experiments. Carbon NMR multiplicities and connectivities were assigned by using DEPT, HMQC and HMBC experiments. IR spectra were recorded as a thin film with a Bruker Alpha FTIR spectrometer. HRMS were recorded with a Bruker Apex IV FT-ICRMS instrument (ESI). **1** was prepared *in situ* from 4-phthalimidobutyric acid and 0.5 equiv. K_2CO_3, the mixture was stirred for 15 min in acetone:H_2O (1:1) at the desired concentration. 4-phthalimidobutyric acid was prepared from phthalic anhydride and 4-aminobutanoic acid as reported in the literature.[1]

2. Continuous flow UV reactor details

2.1. Rig design:

The rig consists of an open ended ¼” stainless steel tube inside of a closed end 12 mm stainless steel tube. Each of these two tubes is connected to a stainless steel T-piece. The side arm of the ¼” T-piece is connected to the in-flow of a Julabo F250 circulating bath filled with a 50-50 mix of ethylene glycol and water. The side-arm of the 12 mm T-piece is connected to the out-flow of the cooling bath. A 1/16” stainless steel tube runs down the length of the ¼” tube and is welded into the bottom of the 12 mm tube with an excess of approximately 1 cm. This is connected to a Jasco PU-980 HPLC pump and serves as the organic in-flow. This is placed into of a 15.6 mm OD grade 214 quartz tube that has been modified in house such that one is sealed. The quartz tube is connected to a Bola GL 32 PTFE T-piece using a Bola GL 32 16 mm PTFE gasket.

The reactor is then inserted into one of the lamps.

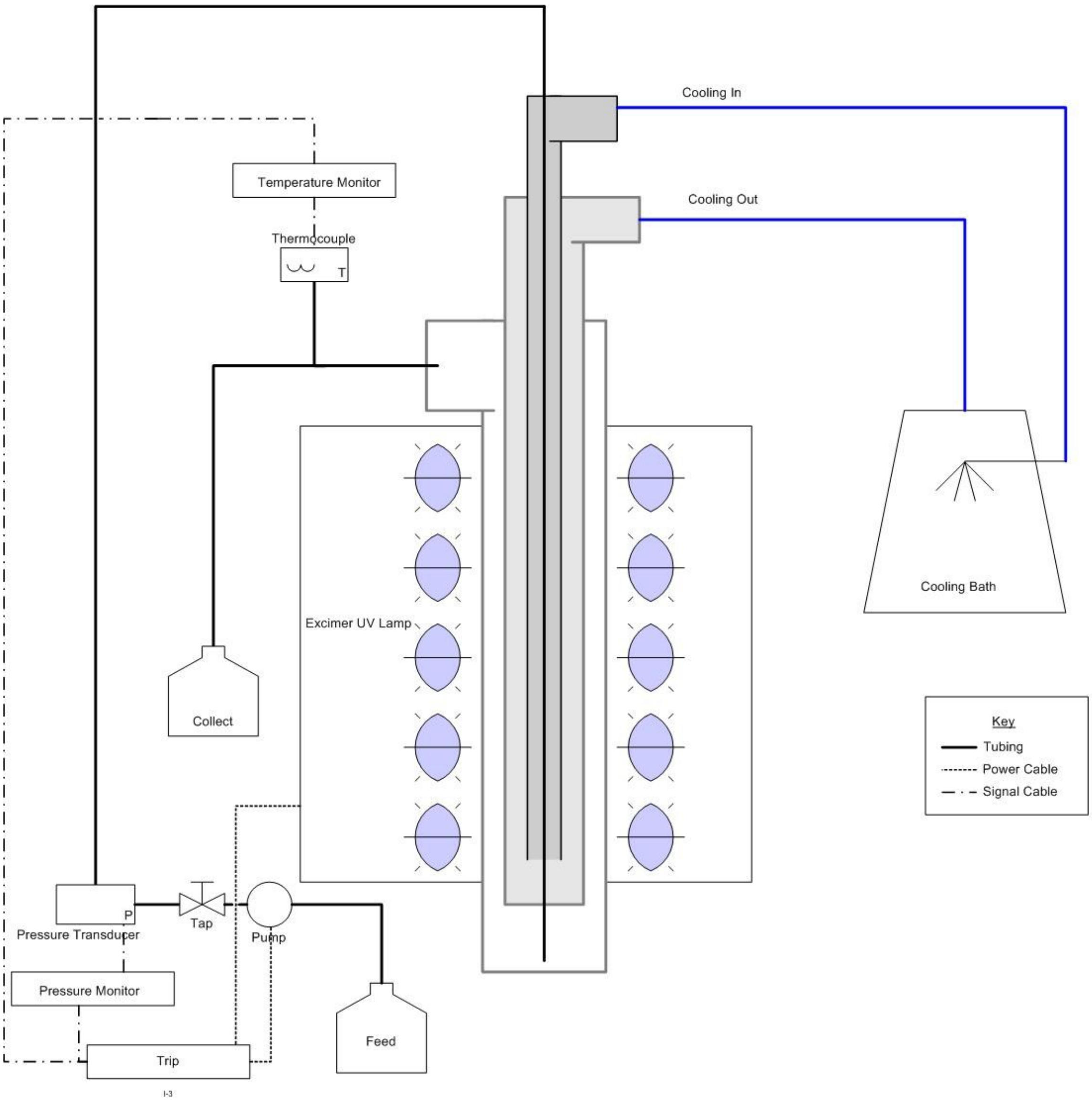


Figure S3: Nottingham UV photochemistry rig diagram as a bird’s eye perspective.

The inner dimensions of the quartz tube and outer dimensions of the metal cooling stick, result in a flow path length of 120 microns, minimising the inner filter effects. The reactor volume is 1.37 mL and the overall system volume is 10.0 mL.

3. Experimental details

3.1. General Procedure for the preparation and irradiation of **1**:

The reactor was flushed with 50 mL of a mixture of degassed acetone-water (1:1 by volume). The circulating bath was set to 30 °C and allowed to reach temperature. 4-Phthalimidobutyric acid (7.0 g, 30.0 mmol) was suspended in deionised water (75 mL). K_2CO_3 (2.08 g, 15.0 mmol) was added and the resulting mixture was stirred until completely dissolved. Acetone (75 mL) was added and stirred for 10 minutes, giving a 0.2 M solution with respect to **1**. The solution was degassed with argon for 10 minutes and pumped through the reactor at 0.2 mL min^{-1} under irradiation by the corresponding lamp (222, 282, 308 nm). Samples were taken for one flow rate before changing to the next, allowing for equilibration of the system before taking the next samples. Two system volumes were allowed to flow through the rig at each flow rate before collection.

Samples were taken once the system had been equilibrated for a particular flow rate. A 0.5 mL sample was collected in triplicate for each flow rate. The solvent was evaporated before a known mass of 1,3,5-trimethoxybenzene was added and the sample contents were re-dissolved in D_6-DMSO. The product yield was determined by comparison of ^1H NMR integrations of the internal standard and signals corresponding to **2** (^1H signal at 1.43 ppm). The yields reported in table 1 of the manuscript are averaged values from the triplicate samples taken for each flow rate, wavelength and concentration. This process was repeated for concentrations of 0.2 M and 0.1 M with each of the three lamps, XeCl, XeBr, and KrCl (308 nm, 282 nm, and 222 nm irradiation respectively).

***NB. 2** could be isolated from the bulk via the removal of acetone by rotary evaporation, followed by extraction with $CHCl_3$. The organic layer was dried over $MgSO_4$ and the solvent was removed to give **2** as a white solid.

3.2. Product degradation at 222 nm

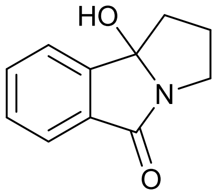
The degradation of **2** by high energy UV (222 nm) was studied by calculating the change in concentration of **2** before and after irradiation. The reactor was flushed with 50 mL of a mixture of degassed acetone-water (1:1 by volume). The circulating bath was set to 30 °C and allowed to reach temperature. Tricyclic alcohol **2** (0.96 g, 5.05 mmol) was dissolved in 50 mL of acetone-water (1:1 by volume). The reagent solution was stirred for 30 min and then degassed with argon for 10 min. Three 0.5 mL samples of the starting solution of **2** before irradiation were taken and prepared for ^1H NMR as described previously. The reagent solution was pumped through the reactor using the 222 nm lamp at a flow rate of 0.2 mL min^{-1}. Two system volumes were allowed to flow through the rig before collection. Three 0.5 mL samples were collected and prepared for ^1H NMR as previously described.

^1H NMR was used to measure the change in concentration after running through the rig under high-energy (222 nm) irradiation. No further products were detected in the ^1H NMR spectra and the change in concentration was calculated (7.25% ± 4.37%).

3.3 Daisy chained reaction with solid supported acid.

The UV reactor outlet was connected to a stainless steel reactor containing Amberlyst 15 (wet form) (5 g). This reactor was then connected to a further reactor packed with $NbOPO_4$ (1 g) and glass beads to aid mixing and prevent excess pressure build up. **1** was flowed at the optimal conditions for conversion to **2** (manuscript table 1, entry 17 – 308 nm, 0.1 M, 0.2 mL min^{-1}).

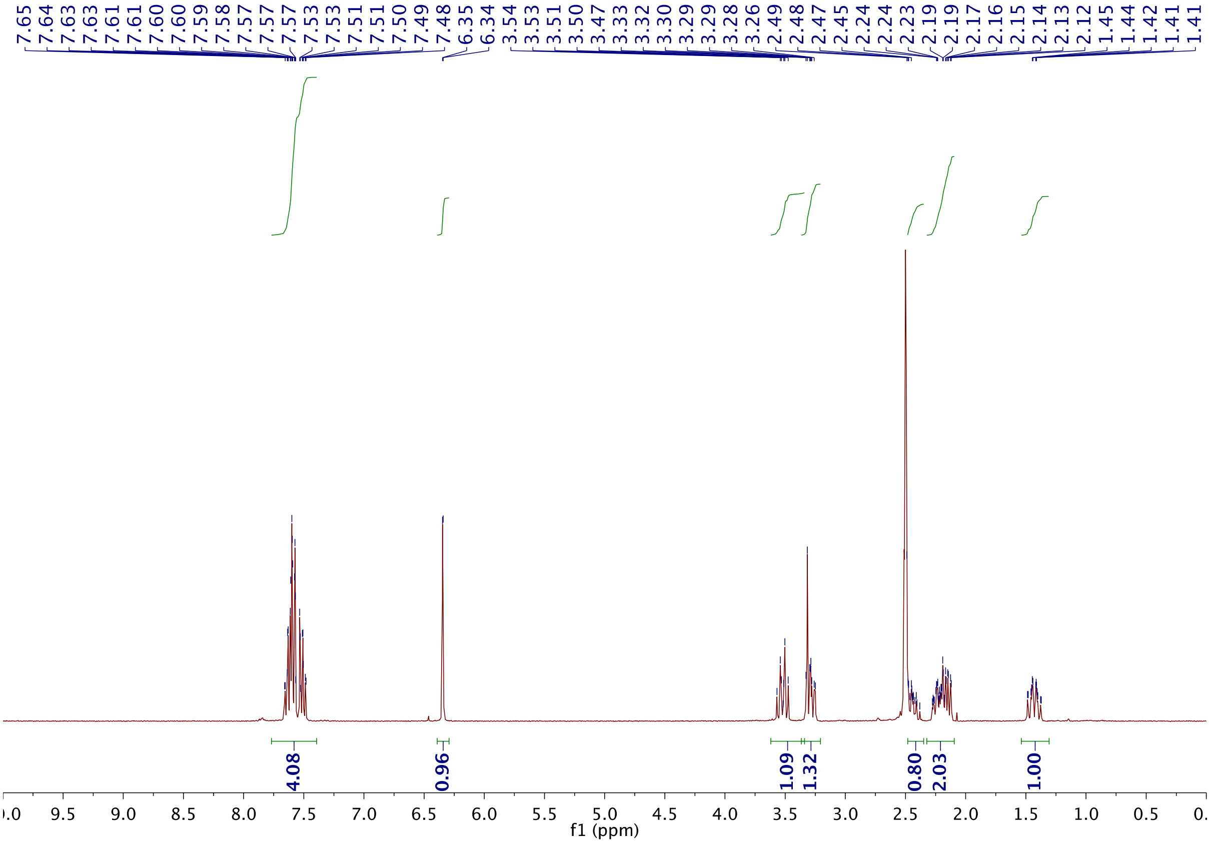
4. Characterisation data and spectra



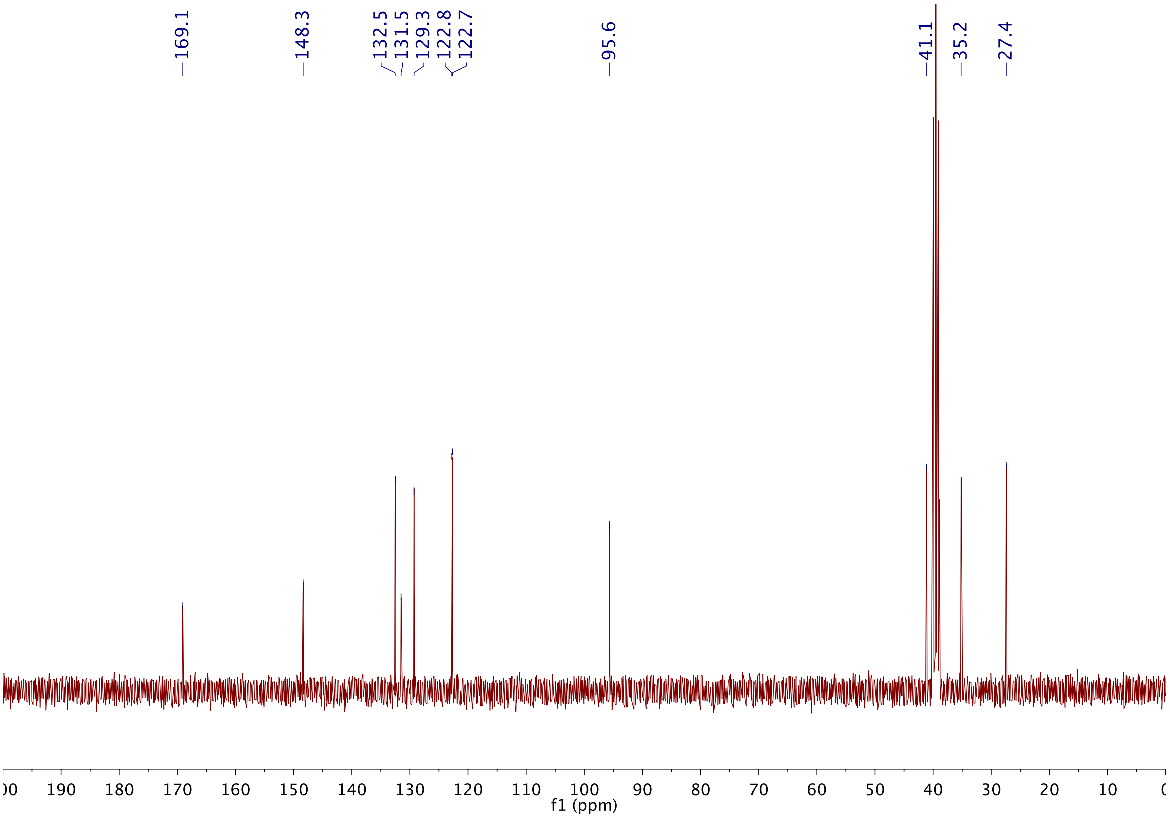
9b-hydroxy-1,2,3,9b-tetrahydro-5H-pyrrolo[2,1-a]isoindol-5-one (**2**)[2]

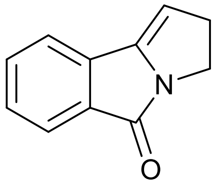
^{1}H NMR (300 MHz, DMSO-*d*$_6$) δ = 7.75 – 7.44 (4H, m), 6.35 (OH, s), 3.52 (1H, dt, *J* = 11.2, 8.4 Hz), 3.38 – 3.19 (1H, m), 2.64 – 2.35 (1H, m), 2.30 – 2.09 (2H, m), 1.43 (1H, tdd, *J* = 12.5, 8.5, 1.7 Hz), OH not apparent. **^{13}C NMR** (300 MHz, DMSO) δ = 169.1, 148.3, 132.5, 131.5, 129.3, 122.8, 122.7, 95.6, 41.1, 35.2, 27.4. **HRMS** (ESI) m/z calc. for $C_{11}H_{11}NO_2Na$ requires 212.0682 [M+Na]$^+$ found 212.0688.

Representative ^{1}H NMR spectra of 2:



Representative ^{13}C NMR spectra of 2:

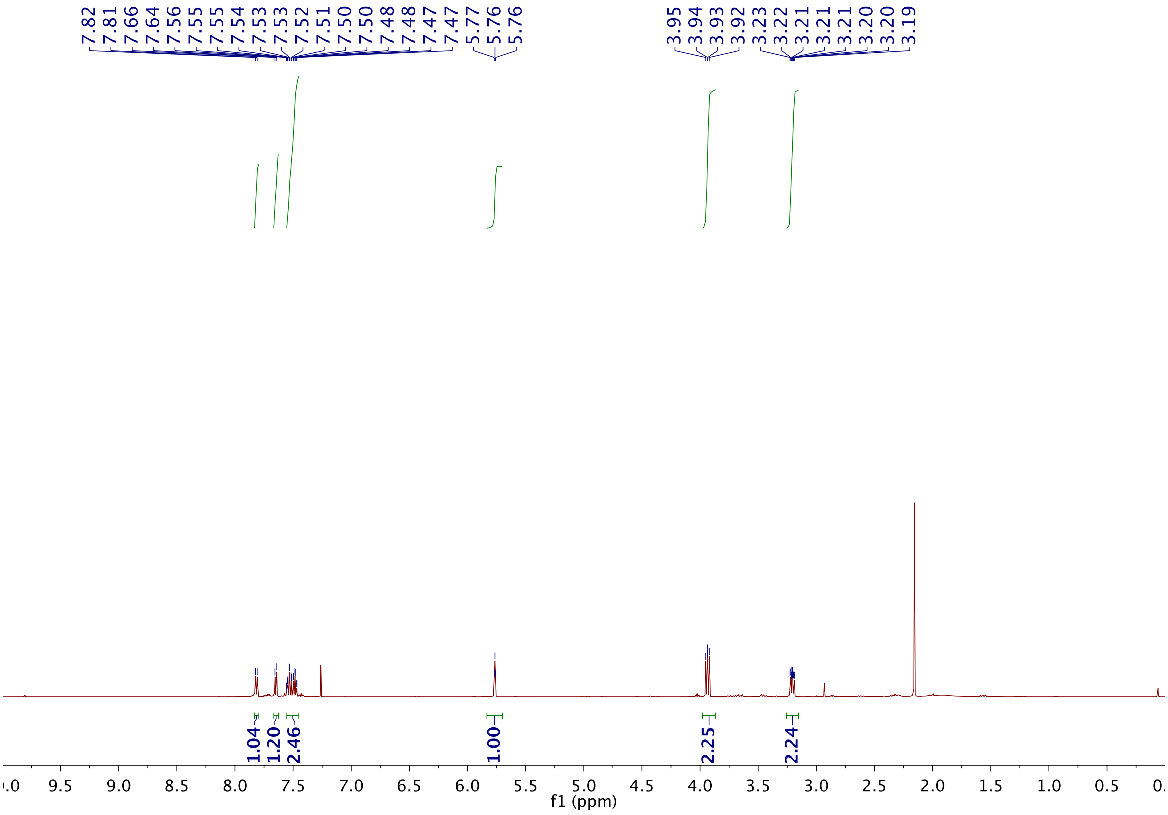




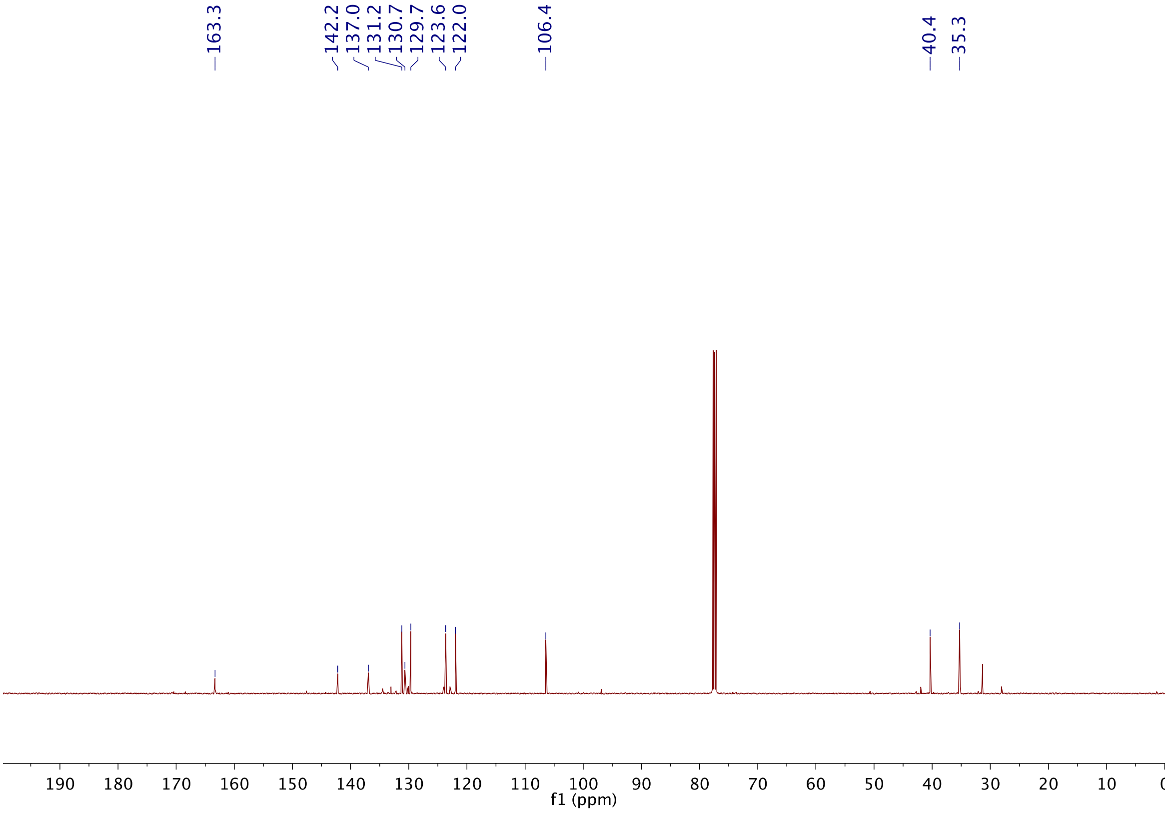
2,3-dihydro-5H-pyrrolo[2,1-a]isoindol-5-one (3)[3]

Product isolated as a yellow oil. **^{1}H NMR** (400 MHz, CDCl$_3$) δ = 7.82 (1H, d, *J* = 7.5 Hz), 7.65 (1H, d, *J* = 7.5 Hz), 7.54 – 7.48 (2H, m), 5.76 (1H, t, *J* = 3.1 Hz), 3.94 (2H, dd, *J* = 8.3, 7.2 Hz), 3.21 (2H, ddd, *J* = 8.3, 7.2, 3.1 Hz). **^{13}C NMR** (400 MHz, CDCl$_3$) δ = 163.3, 142.2, 137.0, 131.2, 130.7, 129.7, 123.6, 122.0, 106.4, 40.4, 35.3. **FTIR** (Film) ν 3341, 2957, 2898, 1771, 1703, 1613, 1467, 1397, 1365, 1331, 1191, 1114, 1072, 1019, 949, 872, 801, 763, 722, 695, 596, 531, 429 cm^{-1}. **HRMS** (ESI) m/z calc. for $C_{11}H_9NONa$ requires 194.0576 [M+Na]$^+$ found 194.0575.

Representative ^{1}H NMR spectra of 3:



Representative ^{13}C NMR spectra of 3:



5. References

1. E. Guénin, M. Monteil, N. Bouchemal, T. Prangé, M. Lecouvey, *Eur. J. Org. Chem.* 2007, **20**, 3380-3391.

2. O. Shvydkiv, K. Nolan, M. Oelgemöller, *Beilstein J. Org. Chem.* 2011, **7**, 1055-1063.

3. D. Ha, C. Yun, E. Yu, *Tetrahedron Lett.* 1996, **37**, 2577-2580.