Electronic Supplementary Information

Direct Fixation of [^{11}C]-CO_2 by Amines: Formation of [^{11}C-*carbonyl*]-Methylcarbamates

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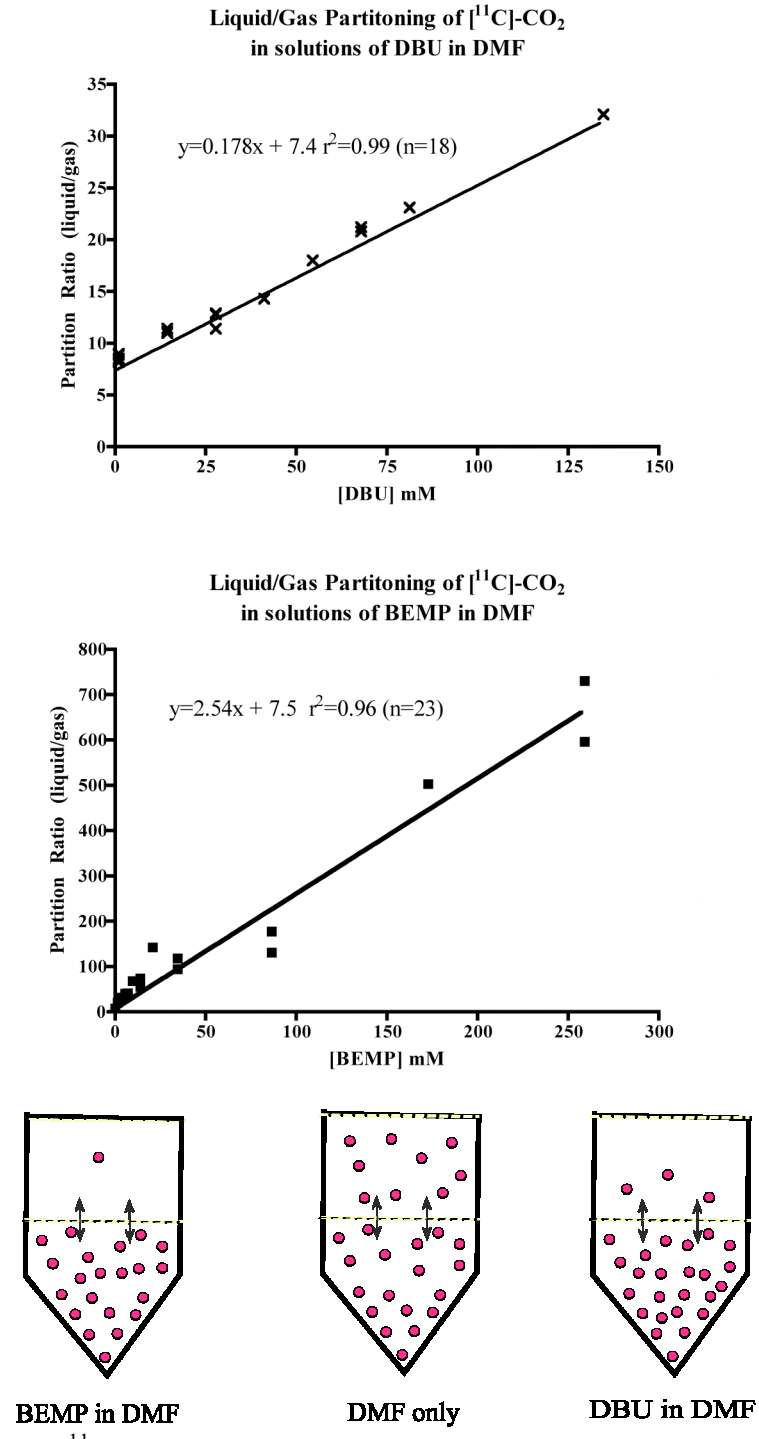

Figure S1. Partition of [^{11}C]-CO_2 between solution and gas phase: effect of DBU and BEMP.

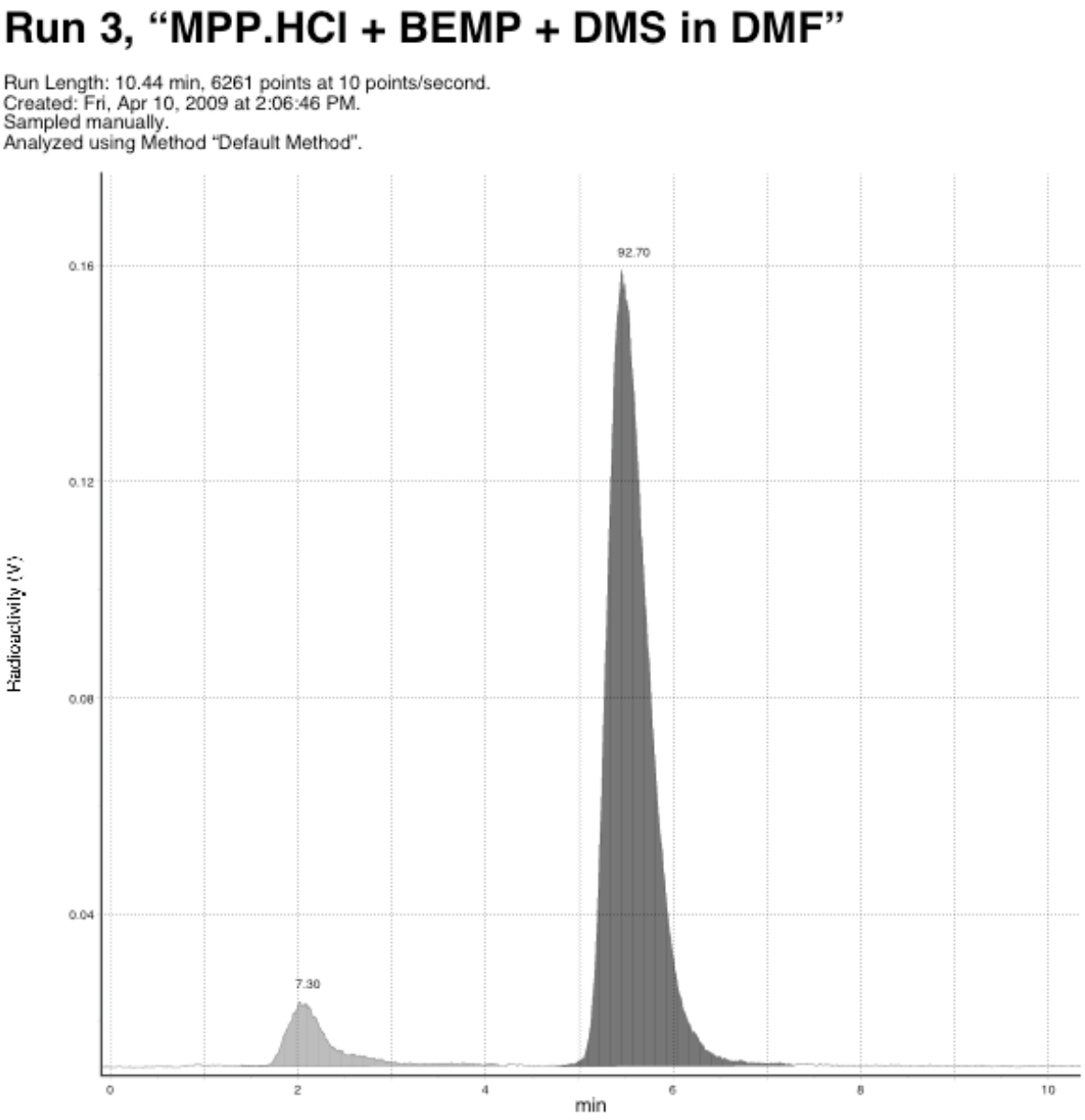

Figure S2. Sample HPLC chromatogram of model [^{11}C-*carbonyl*]-carboxymethylation reactions. HPLC conditions: Phenomenex Synergi Max 5µ, 150x4.6 mm, 48% MeOH/52% H_2O + 1% formic acid, 2 ml/min (taken from Table 2 entry #2). The peak with Rt of 5.5 min corresponds to [^{11}C-*carbonyl*]- 4-(2-methoxyphenyl)-1-piperazinecarboxylic acid, methyl ester.

Characterisation of 4-(2-methoxyphenyl)-1-piperazinecarboxylic acid, methyl ester.

Proton and carbon-13 NMR spectra were recorded at 25 °C on a Varian Mercury 400 MHz spectrometer. Electrospray ionization mass spectrometry was conducted with MDS Sciex QStar mass spectrometer to obtain the HRMS. Elemental Analysis was performed by the Analytical Laboratory for Environmental Science, University of Toronto, using a PerkinElmer Model 2400II CHN analyzer with Perkin-Elmer AD-6 autobalance. Samples were calibrated against thermal standard acetanilide (C: 71.09, H: 6.71, N: 10.36) before and after analysis.

HRMS (ESI, positive mode; m/z, %) Calculated for mass $C_{13}H_{18}N_2O_3$ H+: 251.1395 amu. Found 251.1347.

Anal. Calcd. For $C_{13}H_{18}N_2O_3$: C; 62.38, H; 7.25, N; 11.19. Found: C: 62.48, H; 7.15, N;11.30.

^{1}H NMR and ^{13}C NMR follow.:

Acquisition Time (sec)	2.5559	***Date***	Aug 7 2009	***Date Stamp***	Aug 7 2009		
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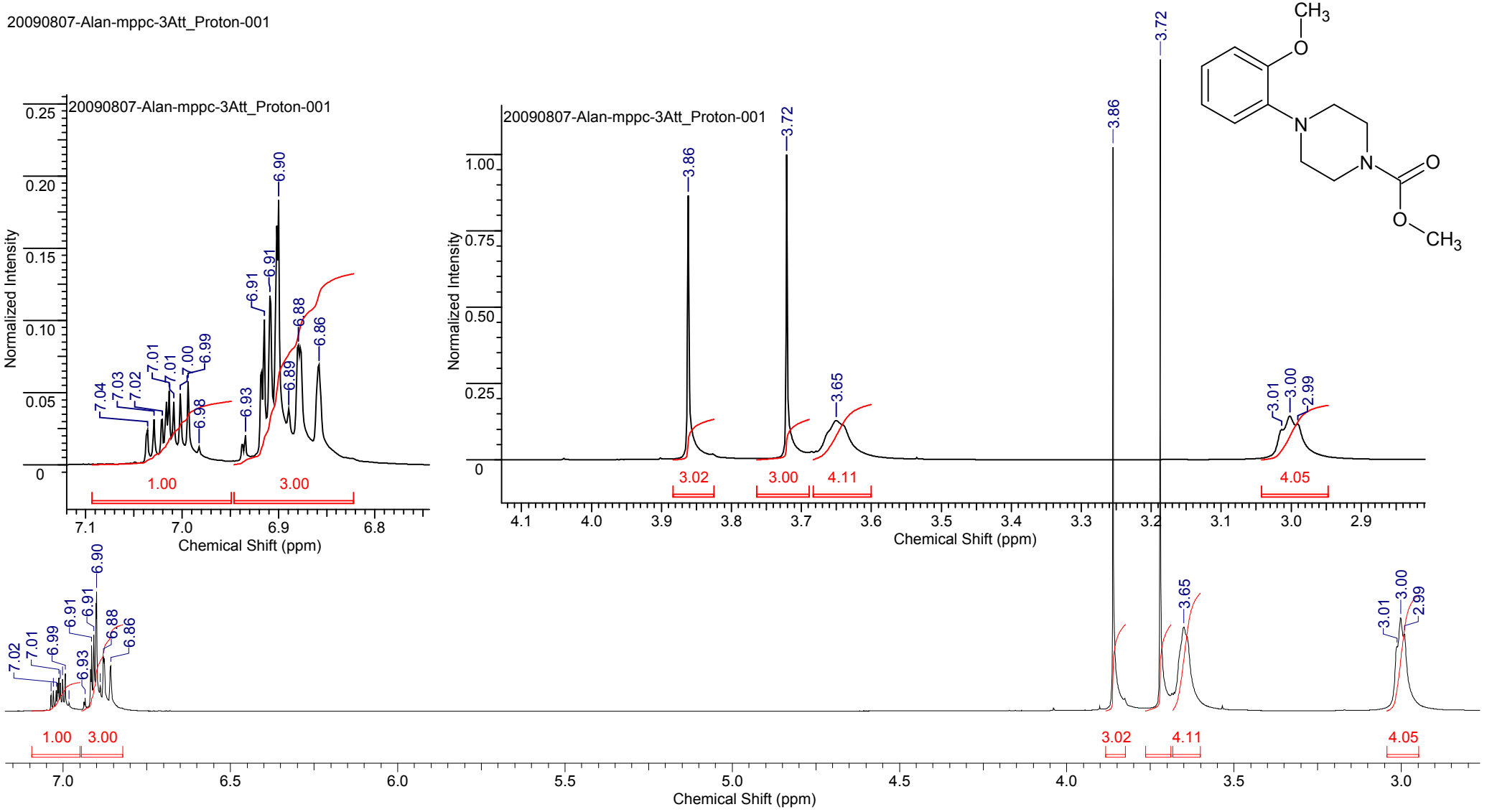
Points Count	16384	***Pulse Sequence***	s2pul	***Receiver Gain***	18.00	***Solvent***	CHLOROFORM-d
Spectrum Offset (Hz)	2409.4858	***Sweep Width (Hz)***	6410.26	***Temperature (degree C)***	25.000		

1H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 2.95 - 3.04 (m, 4 H) 3.65 (br. s., 4 H) 3.72 (s, 3 H) 3.86 (s, 3 H) 6.82 - 6.95 (m, 3 H) 6.95 - 7.09 (m, 1 H)



Formula $C_{13}H_{18}N_2O_3$	***FW***	250.2936					
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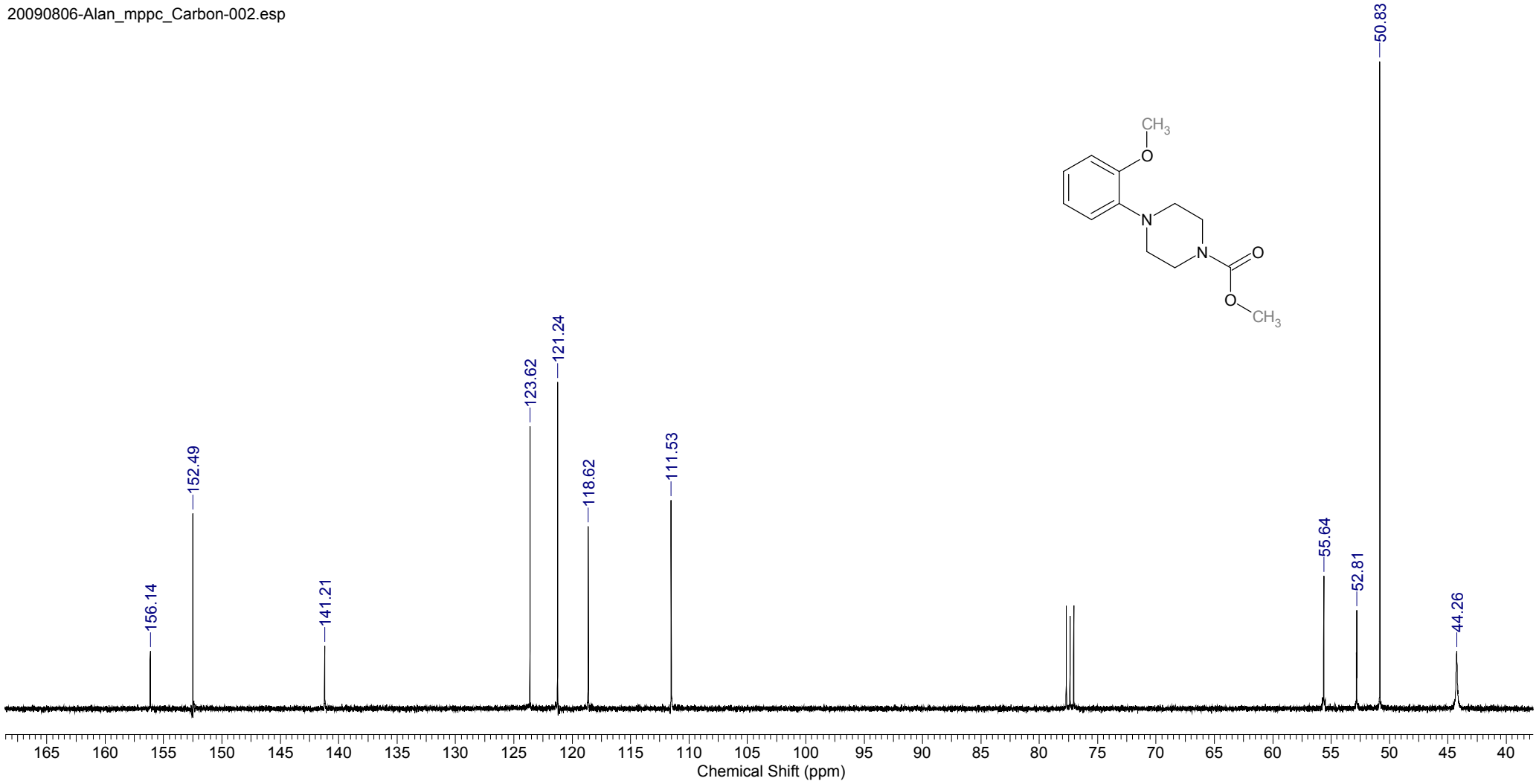
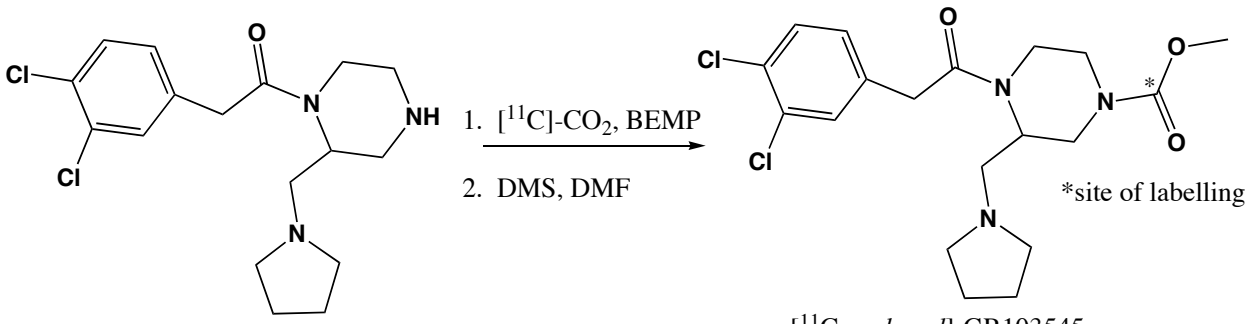
Frequency (MHz)	100.47	***Nucleus***	13C	***Number of Transients***	512	***Original Points Count***	31337
Points Count	32768	***Pulse Sequence***	s2pul	***Solvent***	CHLOROFORM-d	***Spectrum Offset (Hz)***	10548.6270
Sweep Width (Hz)	24096.38	***Temperature (degree C)***	25.000				

13C NMR (100 MHz, CHLOROFORM-*d*) δ ppm 44.3, 50.8, 52.8, 55.6, 111.5, 118.6, 121.2, 123.6, 141.2, 152.5, 156.1





norcarbomethoxy GR103545 [^{11}C-*carbonyl*]-GR103545

Scheme S1: Radiosynthesis of [^{11}C-*carbonyl*]-GR103545.

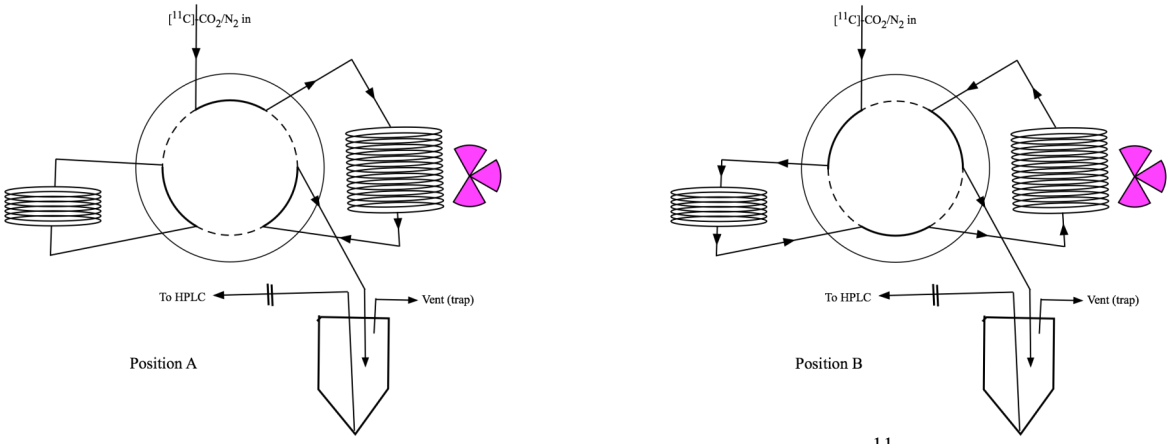


Figure S3. Two valve configurations used in the radiosynthesis of [^{11}C-*carbonyl*]-GR103545.

Radiosynthesis of [^{11}C-*carbonyl*]-GR103545.

While the procedure can be carried out in a conventional sealed vial it is most convenient to use a steel HPLC sample loop/6-port-2-positon valve for the radiosynthesis as this provides the advantages of ease of automation (valve control) and increased surface area for [^{11}C]-CO_2 trapping.

Prior to end-of-bombardment (EOB) a de-gassed solution of dimethylsulphate (4 μL) in DMF (400 μL) is loaded into a 0.4 mL PTFE tubing coil (1/32" ID) with the valve in position A (Fig. S3). A solution of norcarbomethoxy GR103545 (0.1 mg) in DMF (40 μL) is then loaded onto the steel loop using a standard commercial injection port (Valco #VISF-1). [^{11}C]-CO_2 is passed through the coated steel loop in a stream of N_2 (10 mL/min) until trapped radioactivity peaks as measured by a proximal small radiation detector. One min later the valve is switched to position B (Fig.S3) and the same N_2 stream pushes the methylating solution through the steel loop into a 5 mL V-vial. The reaction mixture is then immediately diluted with 10% MeOH in water (1.5 mL) and injected onto an HPLC column for purification. HPLC purification conditions: Phenomenex C18 Luna(2) 10μ, 250x10 mm eluted with 60% MeOH/40% H_2O containing 0.1N NH_4HCO_2 at 7 ml/min. The product, eluting at 7-8 min, is collected and evaporated to dryness at 70 °C under vacuum in a rotary evaporator and reconstituted in saline (10mL) and ethanol (1 mL). Sterile filtration into a vial containing 1N $NaHCO_3$ (1 mL) yields the final formulated product, sterile and pyrogen-free, suitable for PET imaging studies. Product identity was established by co-injections with authentic GR103545 using analytical HPLC under a variety of

conditions (columns, eluents, pH). Chiral HPLC, using literature conditions (Ravert et al. Nucl. Med. Biol., 2002, 29, 47-53) showed that the product was greater than 99% ee.