Figure S1. Partition of $^{[11]}$C-CO$_2$ between solution and gas phase: effect of DBU and BEMP.
Run 3, “MPP.HCl + BEMP + DMS in DMF”

Run Length: 10.44 min, 6261 points at 10 points/second.
Created: Fri, Apr 10, 2009 at 2:06:46 PM.
Sampled manually.
Analyzed using Method “Default Method”.

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$_2$O + 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 acetonilide (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_{2}O_{3} H+: 251.1395 amu. Found 251.1347.

 Anal. Calcd. For C_{13}H_{18}N_{2}O_{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.
1H NMR (400 MHz, CHLOROFORM-\textit{d}) \( \delta \) 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)
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

[11C]-CO2, BEMP

DMS, DMF

Scheme S1: Radiosynthesis of [11C-carbonyl]-GR103545.

Radiosynthesis of [11C-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 [11C]-CO2 trapping.

Prior to end-of-bombardment (EOB) a degassed 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). [11C]-CO2 is passed through the coated steel loop in a stream of N2 (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 N2 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% H2O containing 0.1N NH4HCO3 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 NaHCO3 (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.
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.