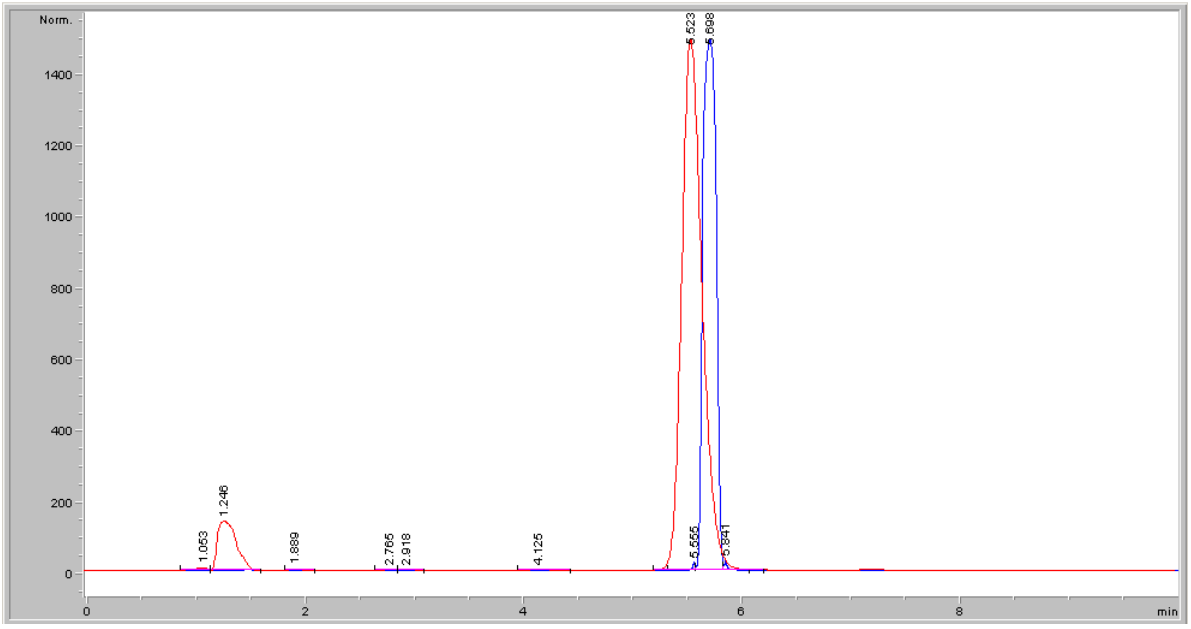
Supplementary Information for manuscript:

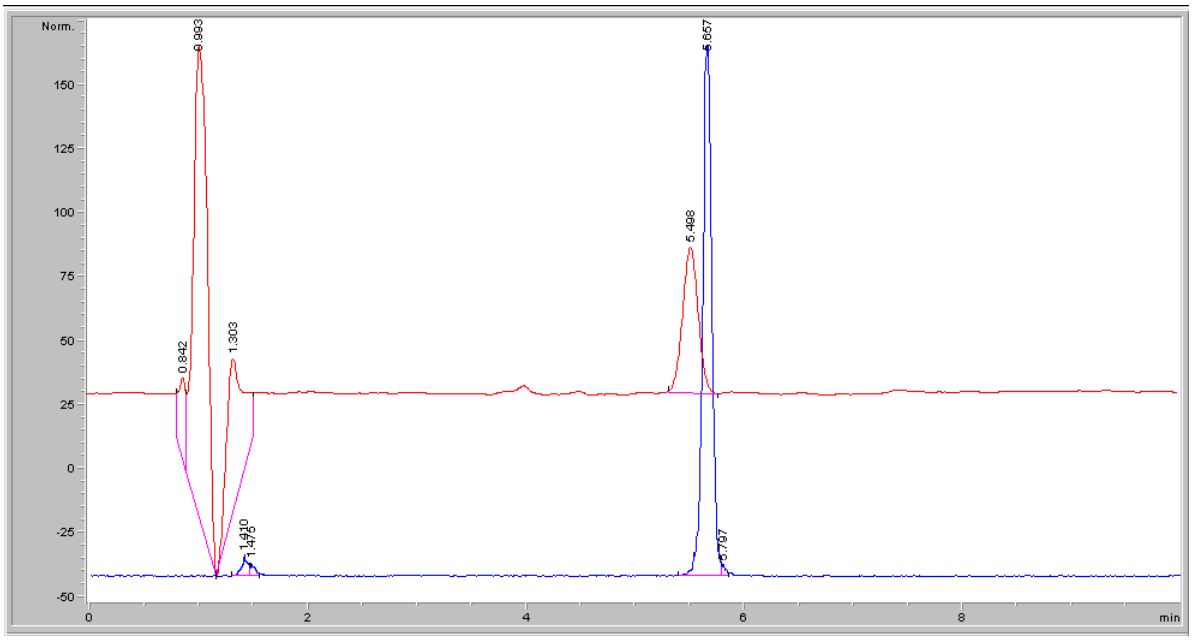
Microfluidic reactions using [^{11}C]carbon monoxide solutions for the synthesis of a Positron Emission Tomography radiotracer

Steven Kealey, Christophe Plisson, T. Lee Collier, Nicholas J. Long, Stephen M. Husbands, Laurent Martarello, Antony D. Gee

Example of analytical HPLC chromatogram of [^{11}C]MK-0233 after semi-prep-HPLC and formulated in ethanol-saline solution. Coinjected with an unlabelled reference sample of MK-0233. Red line shows UV trace (354 nm), blue line shows radioactivity trace.



Example of analytical HPLC chromatogram of [^{11}C]MK-0233 after semi-prep-HPLC and formulated in ethanol-saline solution. Red line shows UV trace (354 nm), blue line shows radioactivity trace.



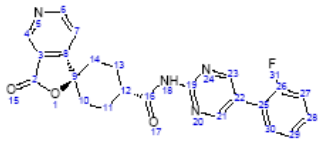
^{1}H NMR spectrum of MK-0233

07 11 2007

z4847 N2065-97-1 id11930

File Name	\\wersfux050.corpnet2.com\specdata\MIRROR\a400\archive_NMR_Lab\z4847_01			Date	Oct 31 2007
Nucleus	1H	Solvent	DMSO-d6	Temperature (degree C) 25.000	Number of Transients 128
Frequency (MHz)	399.73	Sweep Width (Hz)	6395.40		

Formula	$C_{23}H_{18}FN_3O_3$
FW	418.4204
Stereochemistry	CO(16) O(1) trans
Other Info	from "Peakdale"



Chemist: V. Rampazzo
Spectroscopist: E. Moro
AC eLNB: N3630-27
Project: 16031
NMR Spectra: z4847 (1H), qc7529 (ghsqcad), qc7528 (gcosy), qc7527 (noesy1d), qc7526 (noesy1d), qc7525 (1H)
IR Spectra:

Comment: ***CO(16) O(1) trans, from "Peakdale"***
Stereochemistry confirmed by dipolar correlations between
-CH(12) and CH_2(11,13) and CH_2(10,14) 1.84 ppm
-CH(7) CH_2(11,13) and CH2(10, 14) at 2.17
The spectrum is concordant with the spectrum of the N2065-46-1 id11260.
Traces of aliphatic impurities.

Atom1	Shift1 (ppm)	(ppm)	Type	X's
10, 14	1.88	[1.77 .. 1.94]	m	2
13, 11	2.03	[1.96 .. 2.10]	m	4
10, 14	2.16	[2.10 .. 2.22]	m	2
12	3.01	[2.94 .. 3.09]	m	1
30, 28	7.37	[7.32 .. 7.43]	m	2
29	7.51	[7.46 .. 7.56]	m	1
27	7.69	[7.65 .. 7.72]	t	1
7	7.78	[7.75 .. 7.81]	dd	1
23, 21	8.89	[8.87 .. 8.91]	m	2
6	8.92	[8.90 .. 8.94]	d	1
4	9.09	[9.08 .. 9.10]	m	1
18	10.84	[10.78 .. 10.90]	m	1

Signature ..... Reviewed by .....

Mass spectrum (ES +) of MK-0233

Openlynx Report - V.Rampazzp — Page 1

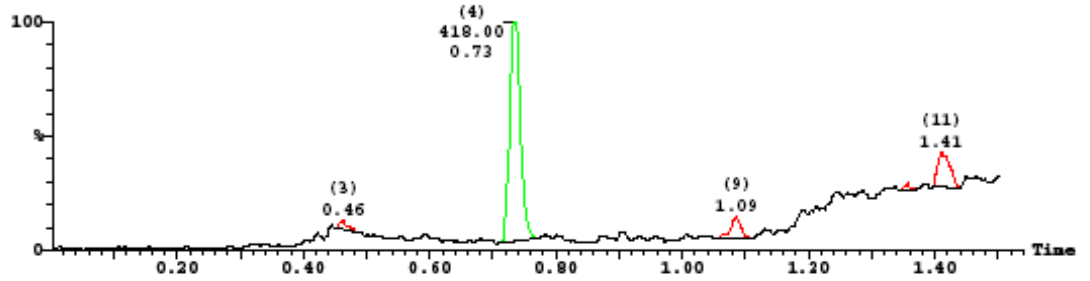
Sample: 1 — Vial:1:A,2 — ID:ID 11930
File:ID 11930 — Date:31-Oct-2007 — Time:10:13:24
Description:N2065-97-1

Printed: Fri Nov 09 09:20:45 2007

Sample Report:

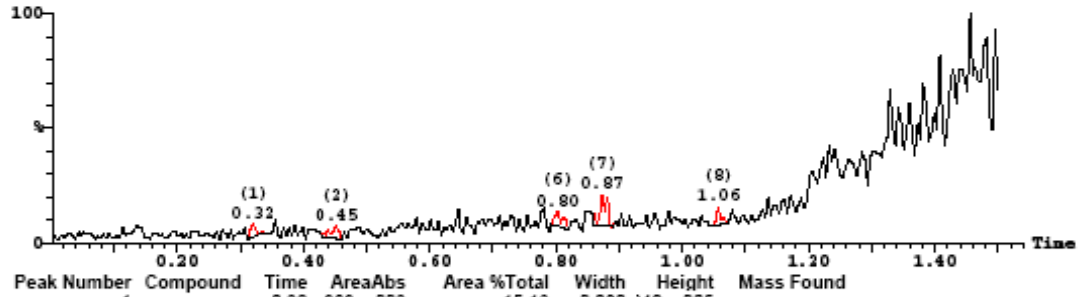
Sample 1 Vial 1:A,2 ID ID_11930 File ID_11930 Date 31-Oct-2007 Time 10:13:24 Description N2065-97-1

MS ES+ :TIC Smooth (Mn, 1x1) — 1.3e+007



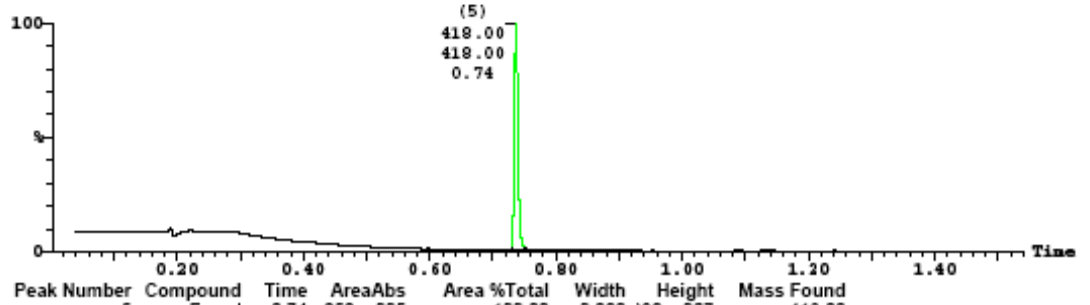
Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
3		0.46	.003e+003	2.18	0.040	144e+005	
4	Found	0.73	.459e+005	76.49	0.060	224e+007	418.00
9		1.09	.228e+004	6.93	0.050	242e+006	
10		1.36	.853e+003	0.89	0.020	490e+005	
11		1.41	.344e+004	13.51	0.040	955e+006	

MS ES- :119_899 — 3.4e+006



Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
1		0.32	.383e+003	15.16	0.030	942e+005	
2		0.45	.477e+003	15.75	0.030	394e+005	
6		0.80	.103e+003	19.73	0.030	206e+005	
7		0.87	.401e+003	34.35	0.030	856e+005	
8		1.06	.360e+003	15.01	0.020	763e+005	

DAD: TIC — 3.4e+007



Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
5	Found	0.74	.252e+005	100.00	0.020	892e+007	418.00

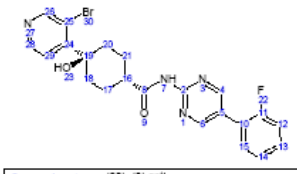
^{1}H NMR of radiolabelling precursor, trans-4-(3-bromopyridin-4-yl)-4-hydroxy-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-cyclohexanecarboxamide

20 03 2007

qc6362 N1082-80-1 ID9997

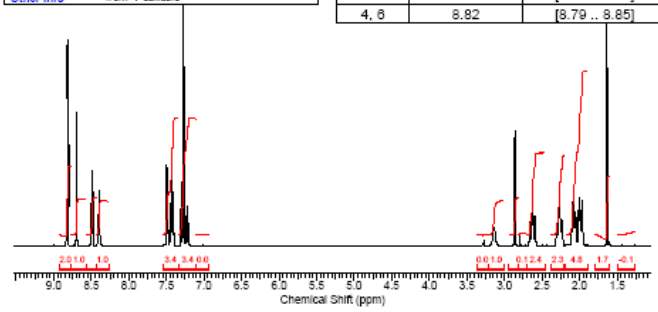
	\\versfux050.corpnet2.com\specdata\au400\qc400\qc6362.fid\versfux050.corpnet2.com\specdata\au400\qc400\qc6362			Date	Mar 16
Nucleus	1H	Solvent	CHLOROFORM-d	Temperature (degree C)	25.000	Number of Transients	128
Frequency (MHz)	399.87	Sweep Width (Hz)	6410.26		

Formula $C_{23}H_{19}BrFN_4O_2$
FW 471.3222



Stereochemistry (23), (8) anti
Other Info from "Peakdale"

Atom1	Shift1 (ppm)	(ppm)	Type	X's
20, 18	1.99	[1.92 .. 2.06]	d	2
17, 21	2.08	[2.04 .. 2.12]	d	2
21, 17	2.27	[2.21 .. 2.34]	t	2
20, 18	2.63	[2.56 .. 2.70]	t	2
23	2.86	[2.83 .. 2.89]	s	1
16	3.13	[3.08 .. 3.19]	m	1
12, 14	7.25	[7.17 .. 7.32]	m	2
13, 15	7.42	[7.39 .. 7.46]	m	2
29	7.50	[7.46 .. 7.53]	d	1
7	8.39	[8.36 .. 8.43]	m	1
28	8.49	[8.46 .. 8.53]	d	1
26	8.70	[8.68 .. 8.71]	s	1
4, 6	8.82	[8.79 .. 8.85]	m	2



Signature .....

Reviewed by .....

Chemist: V. Rampazzo
Spectroscopist: E. Moro
CASS eLNB: N1017-46
Project:16031
NMR Spectra: DMSO: z4384 (1H, cosy, roesy), qc6343 (1H), qc6344 (NOESY1D), qc6345 (NOESY1D), qc6346 (HSQCAD), qc6347(NOESY_zq), qc6358 (1H), qc6359 (1H+ 10 ul D2O), qc6360 (1H+10ul D2O+ 10ul DCl (1:100)), qc6361(1H+10ul D2O+ 10ul DCl (1:100)+2ul DCl (1:10)), i2487 (1H, 90C), s4845 (1H)

CDCl3: qc6362 (1H), qc6363(gcosy), qc6364(noesyzq), qc6365(roesy)
IR Spectra:

Comment: from "Peakdale" (23), (8) *anti*
The relative stereochemistry anti was confirmed on the sample acquired in CDCl3 by dipolar correlation between:
-CH(29) and CH_2(18, 20) ax, CH_2(18, 20) eq
-NH(7) and CH_2(18, 20) ax, CH_2(17, 21) eq
-OH(23) and CH_2(18, 20)eq, CH_2(17, 21) ax
The ROESY spectra showed several unexpected correlations. Some of them can be explained by transfer via TOCSY contacts, others however remained dubious. Changed spin lock and/or mixing times did not clarify the findings. The possibility of inter- or intramolecular hydrogen bonds as origine of the unexpected ROE's was investigated by changing the concentration, the solvent and by adding D2O. The stereochemistry assignment was finally carried out using a NOESY_zq recorded in CDCl3. The spectrum only showed reasonable correlations.
The spectrum in DMSO showed very sharp OH (23) and NH(7) signals.
Traces of aliphatic impurities and residual solvents.

MS (ES +) of radiolabelling precursor, trans-4-(3-bromopyridin-4-yl)-4-hydroxy-N-[5-(2-fluorophenyl)-2-pyrimidinyl]-cyclohexanecarboxamide

Openlynx Report - Valeria Rampazzo Page 1

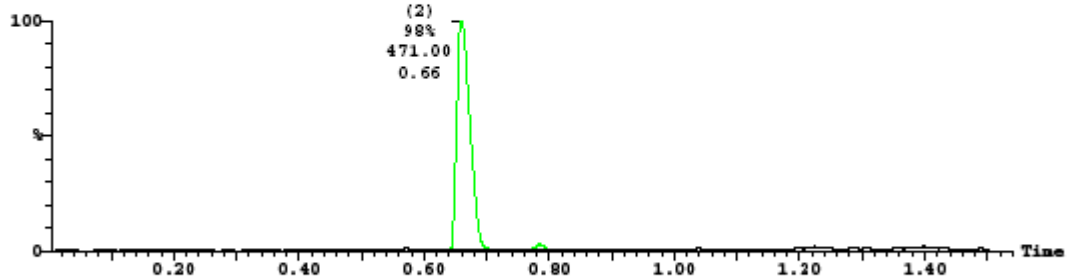
Sample: 1 Vial:3:7 ID:ID 9997
File:ID 9997 Date:12-Mar-2007 Time:17:03:45
Description:N1082-80-1

Printed: Wed Mar 21 15:28:00 2007

Sample Report:

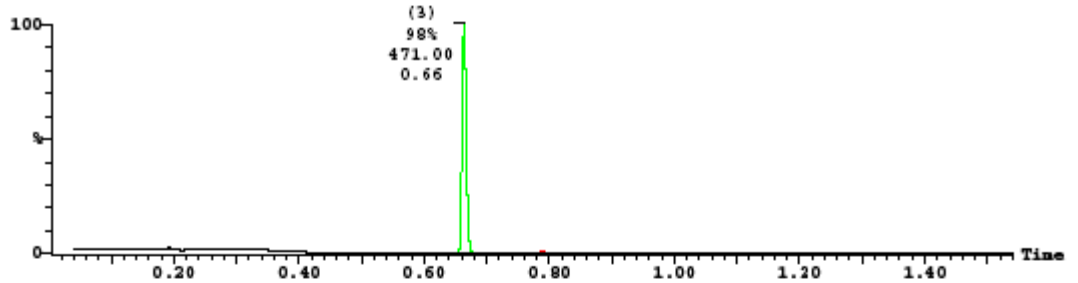
Sample 1 Vial 3:7 ID ID_9997 File ID_9997 Date 12-Mar-2007 Time 17:03:45 Description N1082-80-1

MS ES+ :BPI Smooth (Mn, 1x1) 2.0e+006



Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
2	Found	0.66	.756e+004	98.35	0.080	)50e+006	471.00
4	Found	0.78	.970e+002	1.65	0.050	)35e+004	471.00

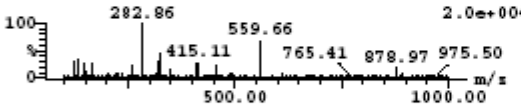
DAD: TIC 1.7e+008



Peak Number	Compound	Time	AreaAbs	Area %Total	Width	Height	Mass Found
1		0.57	.408e+003	0.25	0.040	39e+005	
3	Found	0.66	.329e+006	97.99	0.030	714e+008	471.00
5		0.79	.407e+004	1.04	0.020	790e+006	
6		0.81	.793e+003	0.72	0.030	143e+006	

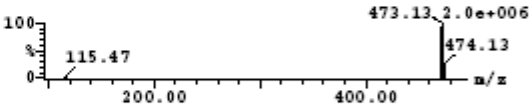
Peak ID	Compound	Time	Mass Found	TIC
1		0.57		257.0

Combine (149:150-(143:144+156:157)) 1:MS ES+ 2.0e+004



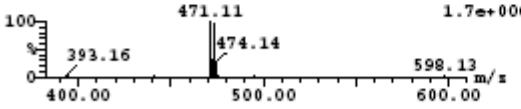
Peak ID	Compound	Time	Mass Found	TIC
2	Found	0.66	471.0000	306.0

Combine (171:173-(162:163+185:186)) 1:MS ES+



Peak ID	Compound	Time	Mass Found	TIC
3	Found	0.66	471.0000	009.0

Combine (172:174-(168:169+178:179)) 1:MS ES+ 1.7e+006



Peak ID	Compound	Time	Mass Found	TIC
4	Found	0.78	471.0000	382.0

Combine (203:205-(195:196+212:213)) 1:MS ES+ 5.5e+004