

## Supporting information

### Synthesis and *in vitro/in vivo* pharmacological evaluation of [<sup>11</sup>C]-ThioABP, a novel radiotracer for imaging mGluR5 with PET

Selena Milicevic Sephton,<sup>a</sup> Linjing Mu,<sup>\*b</sup> Andrienne Müller,<sup>a</sup> Cindy A. Wanger-Baumann,<sup>a</sup> Roger Schibli,<sup>a</sup> Stefanie D. Krämer<sup>a</sup> and Simon M. Ametamey<sup>\*a</sup>

|                                                |       |
|------------------------------------------------|-------|
| <b><sup>1</sup>H NMR Spectra and HPLC data</b> | S2-S4 |
| <b>IC<sub>50</sub> curves</b>                  | S5    |
| <b>Metabolite studies</b>                      | S6    |

<sup>1</sup>H NMR spectra were recorded in Fourier transform mode at the field strength specified using standard 5 mm diameter tubes. Chemical shifts in ppm is quoted relative to residual solvent signals calibrated as follows: CDCl<sub>3</sub> δ<sub>H</sub> (CHCl<sub>3</sub>) = 7.26 ppm; d<sub>6</sub>-DMSO δ<sub>H</sub> (CD<sub>3</sub>SOCHD<sub>2</sub>) = 2.50 ppm. Unless otherwise stated spectra were collected at ambient temperature.

|                                                               |      |
|---------------------------------------------------------------|------|
| <sup>1</sup> H/ <sup>13</sup> C NMR of <b>5</b> (400/100 MHz) | S2/3 |
|---------------------------------------------------------------|------|

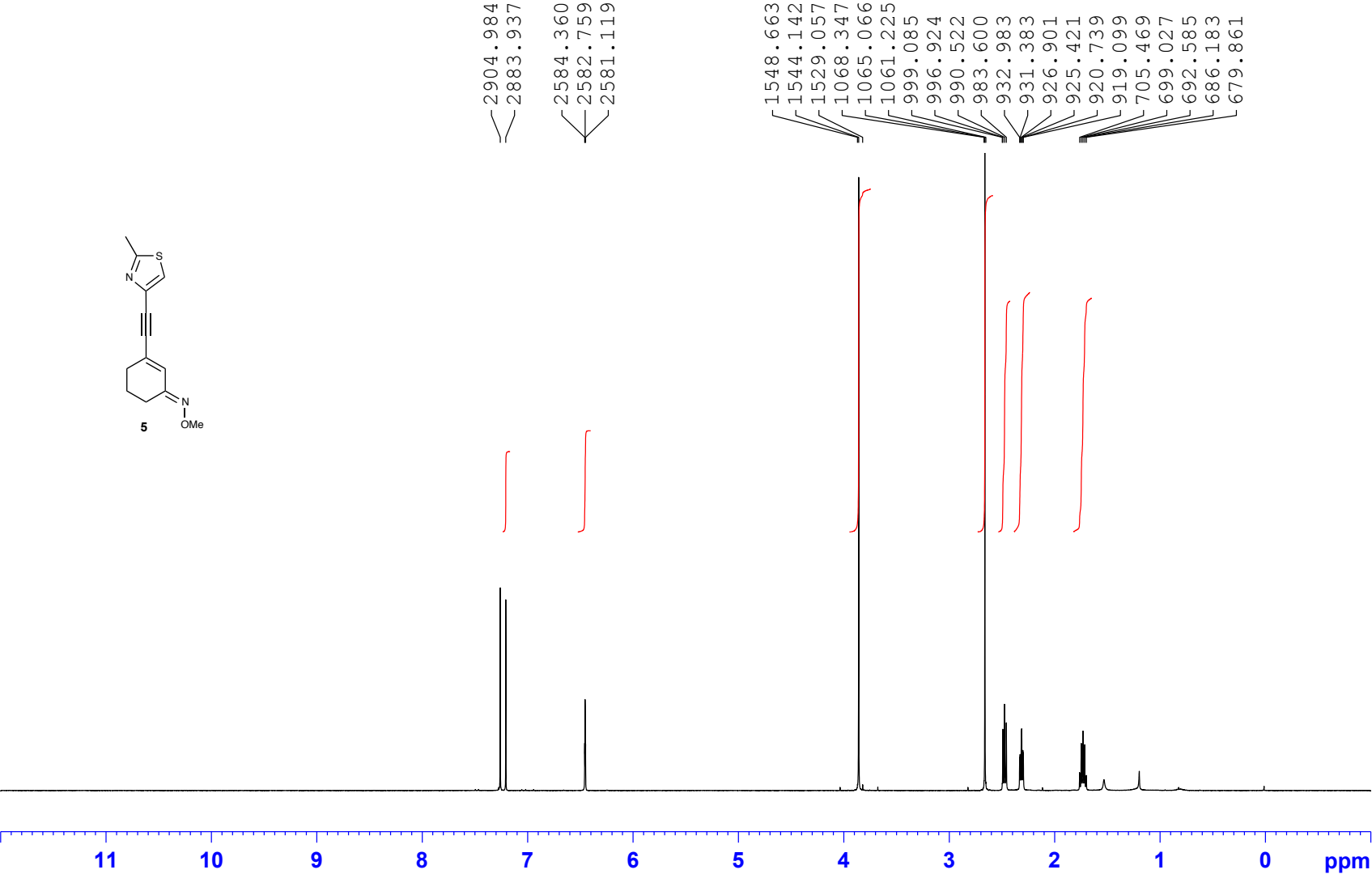
HPLC analysis was performed on Waters ACE column (C18, 3 µm, 4.6x50 mm) at 1 mL/min 45% aq. MeCN.

|                                                                       |    |
|-----------------------------------------------------------------------|----|
| HPLC of [ <sup>11</sup> C]-ThioABP and co-elution with cold reference | S4 |
| IC <sub>50</sub> curves of ThioABP                                    | S5 |

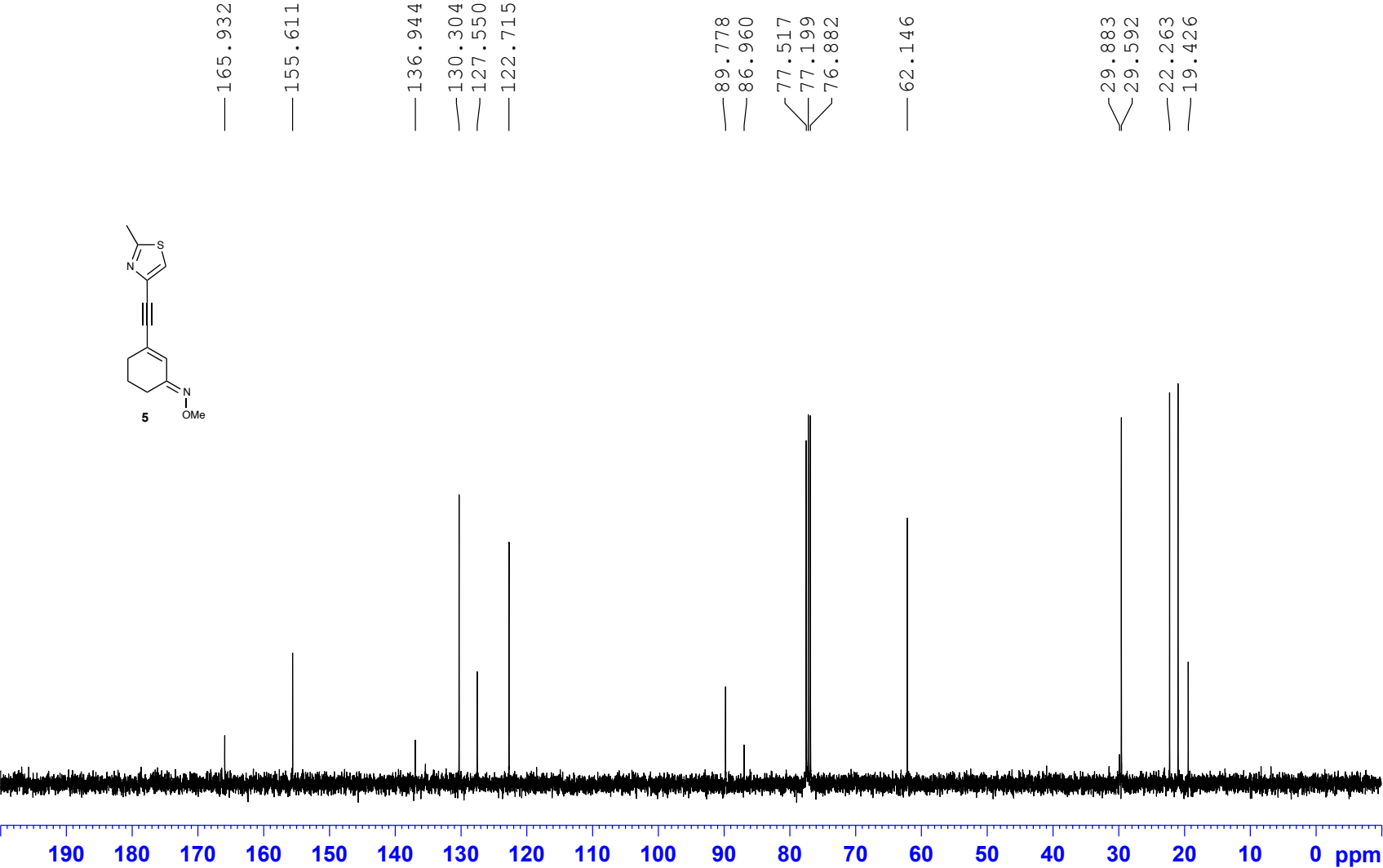
Metabolite studies were performed on male Wistar rats and animals were sacrificed 10 min p.i. Analysis of blood and brain samples was done using radio-TLC analysis eluting with EtOAc:pentane 2:1.

|                                 |    |
|---------------------------------|----|
| Radio-TLC of metabolite studies | S6 |
|---------------------------------|----|

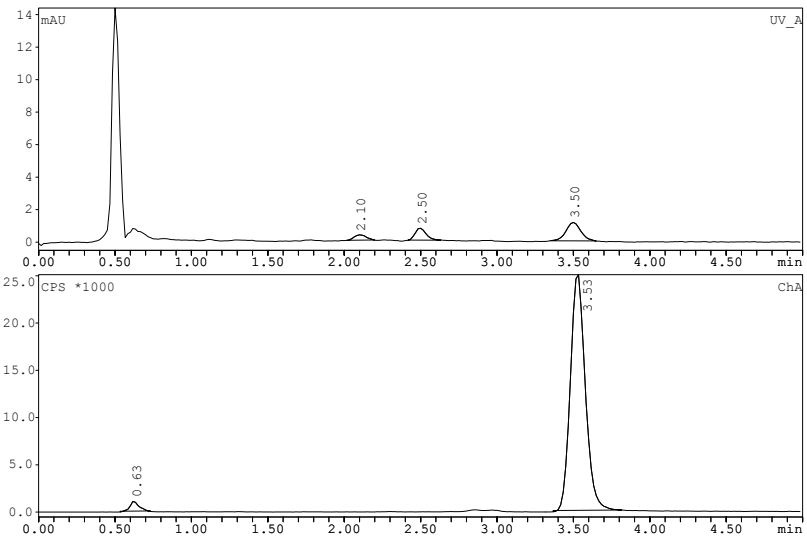
SDM-III-109CHA, CDCl3, 400MHz, 01.12.2011.



SDM-III-109CHA, CDCl3, 100MHz, 01.12.2011.



Measurement ThioABP171012 ETH Zuerich Page 1/1  
D:\GINA\_NT\MGLUR5\ISO45\_ACN IN 5MIN\THIOABP171012 Print date: 17.10.2012



Sample description

Study: MGLUR5  
Measurement: ThioABP171012, injection : 17.10.2012 10:32  
Method: ISO45\_ACN IN 5MIN from: 01.04.2011 05:30 Position: 1  
Station number: 2  
Inj. volume (µl): 5.0  
Radio detector: raytest Gabi Star Serial Nr.: #30168 raytest GINA star 20.04.09 V4.8

Integration ChA

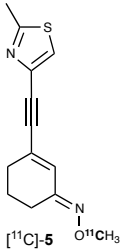
| Substance  | R/T min | Type | Area Counts | %Area % |
|------------|---------|------|-------------|---------|
| Reg #1     | 0.63    | BB(  | 4001.6      | 2.31    |
| Reg #2     | 3.53    | BB(  | 169333.0    | 97.69   |
| Sum in ROI |         |      | 173334.5    |         |
| Area       |         |      | 194517.4    |         |
| Ext. BKG   |         |      | 0.00 CPS    |         |

Integration UV\_A

| Substance  | R/T min | Type | Area mAU*min | %Area % |
|------------|---------|------|--------------|---------|
| Reg #1     | 2.10    | BB(  | 1.791318     | 13.79   |
| Reg #2     | 2.50    | BB(  | 3.599373     | 27.71   |
| Reg #3     | 3.50    | BB(  | 7.600594     | 58.51   |
| Sum in ROI |         |      | 12.991285    |         |

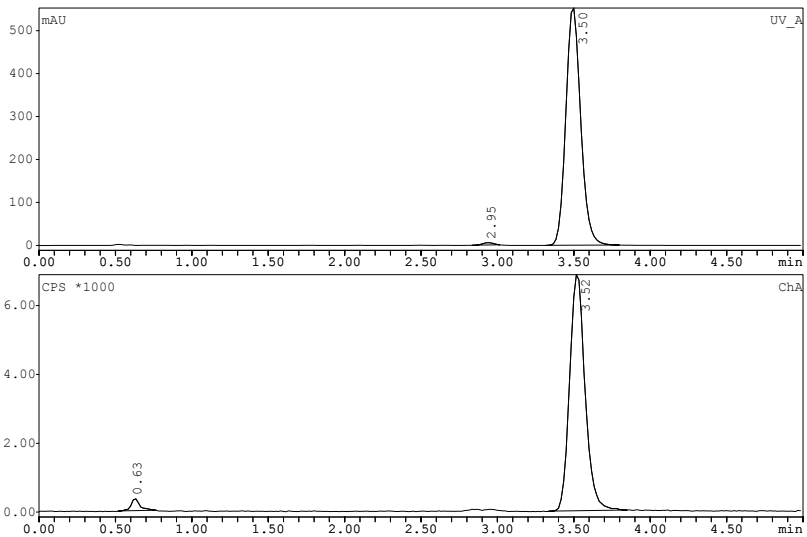
Integration Grad

| Substance  | R/T min | Type | Area %B*min | %Area % |
|------------|---------|------|-------------|---------|
| Reg #1     | 3.03    | BB(  | 0.000000    | 0.00    |
| Sum in ROI |         |      | 0.000000    |         |



formulated  
tracer

Measurement ThioABP171012-co ETH Zuerich Page 1/1  
D:\GINA\_NT\MGLUR5\ISO45\_ACN IN 5MIN\THIOABP171012-CO Print date: 17.10.2012



Sample description

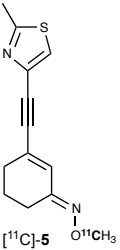
Study: MGLUR5  
Measurement: ThioABP171012-co, injection : 17.10.2012 10:52  
Method: ISO45\_ACN IN 5MIN from: 01.04.2011 05:30 Position: 1  
Station number: 2  
Inj. volume (µl): 5.0  
Radio detector: raytest Gabi Star Serial Nr.: #30168 raytest GINA star 20.04.09 V4.8

Integration ChA

| Substance  | R/T min | Type | Area Counts | %Area % |
|------------|---------|------|-------------|---------|
| Reg #1     | 0.63    | BB(  | 1385.92     | 2.79    |
| Reg #2     | 3.52    | BB(  | 48281.39    | 97.21   |
| Sum in ROI |         |      | 49667.31    |         |
| Area       |         |      | 59605.76    |         |
| Ext. BKG   |         |      | 0.00 CPS    |         |

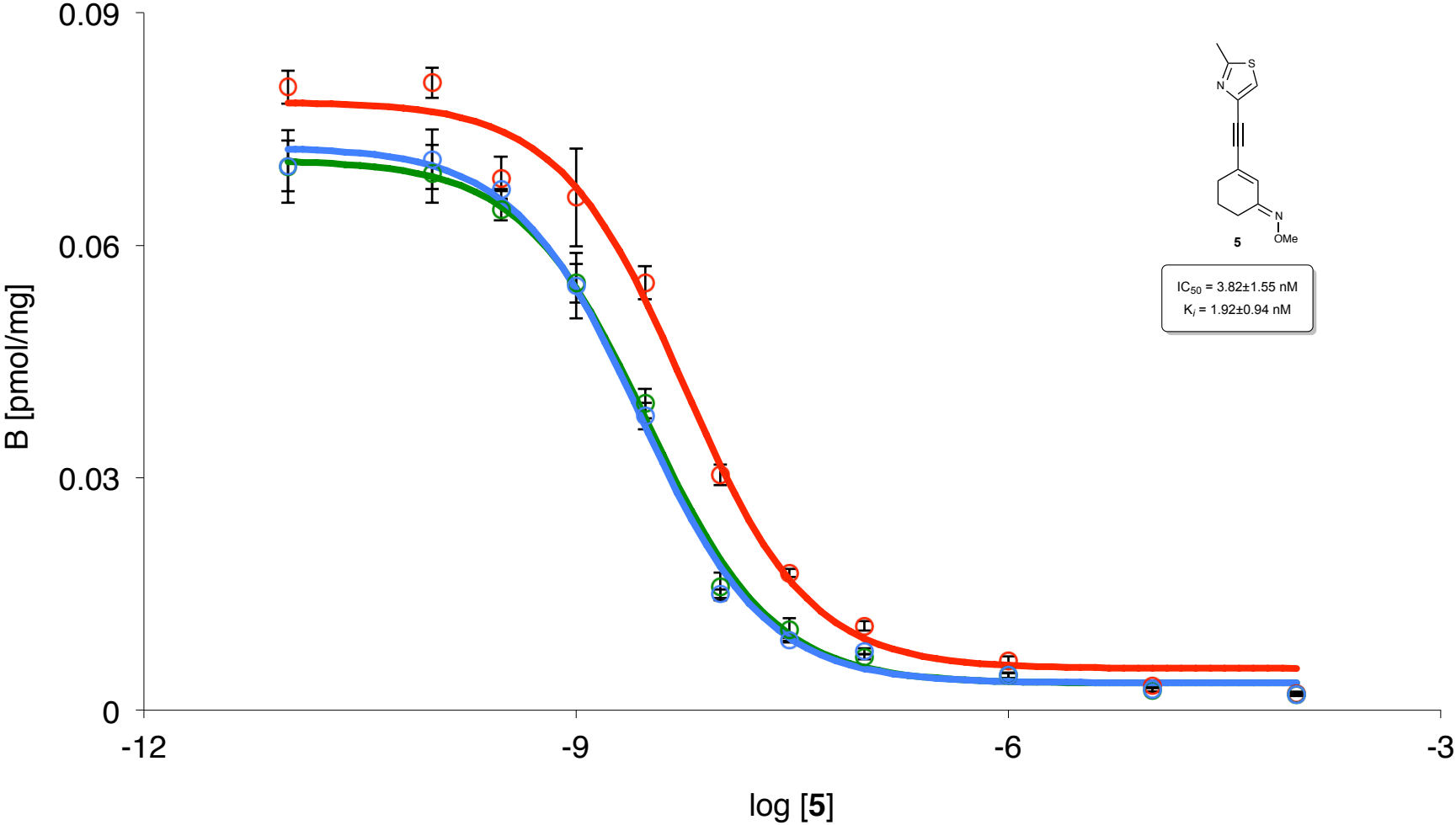
Integration UV\_A

| Substance  | R/T min | Type | Area mAU*min | %Area % |
|------------|---------|------|--------------|---------|
| Reg #1     | 2.95    | BB(  | 26.034       | 0.69    |
| Reg #2     | 3.50    | BB(  | 3754.588     | 99.31   |
| Sum in ROI |         |      | 3780.621     |         |



coinjection  
with cold reference

IC<sub>50</sub> binding curve for **5**



## Metabolite studies for [ $^{11}\text{C}$ ]-ThioABP

