Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Preparation, *in vitro* and *in vivo* evaluation, and molecular dynamics (MD) simulation studies of novel F-18 labeled tumor imaging agents targeting focal adhesion kinase (FAK)

Yu Fang[a,b], Dawei Wang[a], Xingyu Xu[a], Gila Dava[a], Jianping Liu[a], Xiang Li[a], Qianqian Xue[a], Huan Wang[a], Jiangshan Zhang[b], Huabei Zhang[a,*]

[a] Key Laboratory of Radiopharmaceuticals, Ministry of Education, College of Chemistry, Beijing Normal University, Beijing 100875, P. R. China.

[b] College of Chemistry and Chemical Engineering, Anyang Normal University, No. 436 Xian’ge Avenue, Anyang 455000, P. R. China

Corresponding Author:

For H. Zhang: phone +86-10-58802012, E-mail hbzhang@bnu.edu.cn.

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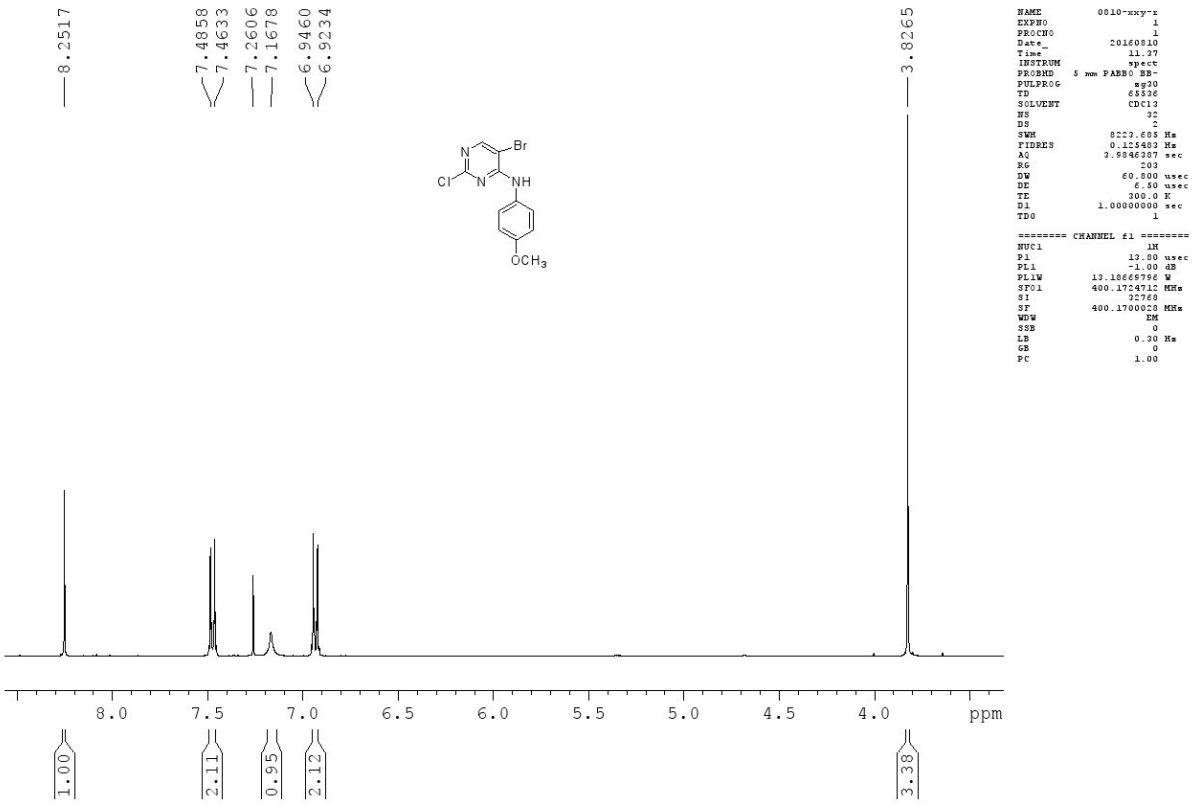
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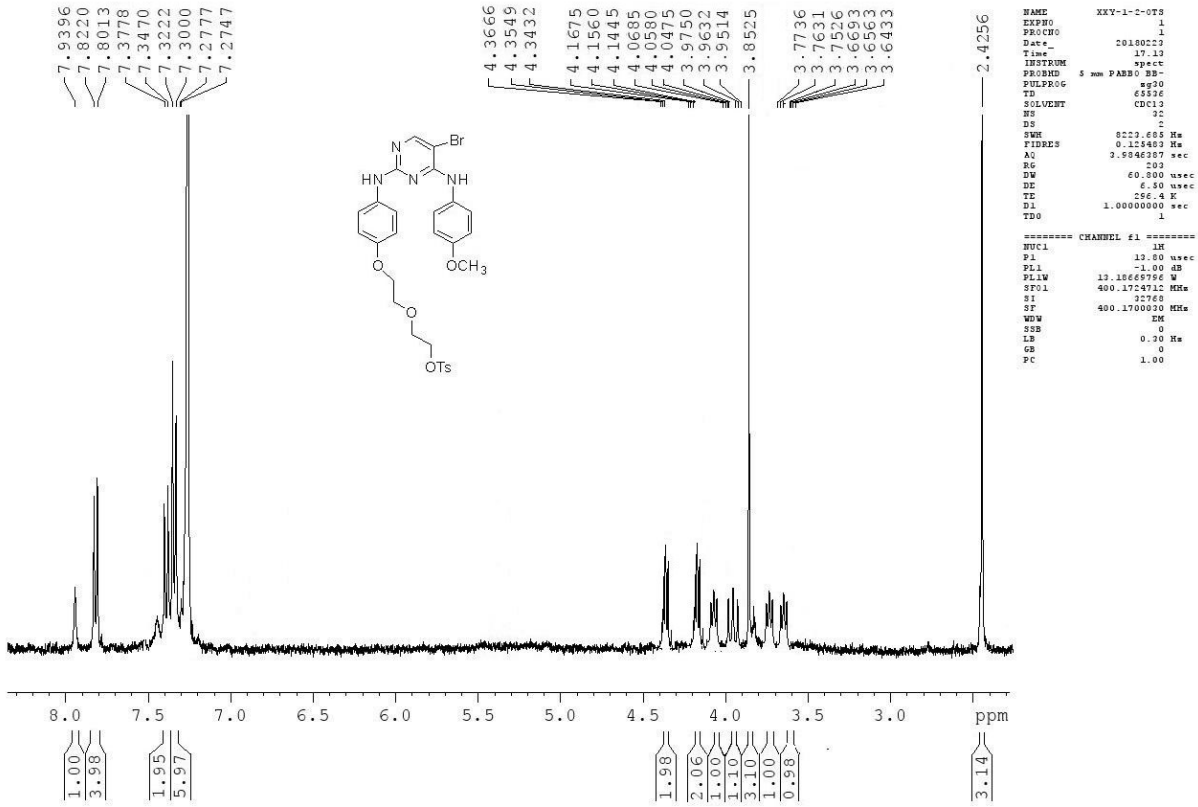
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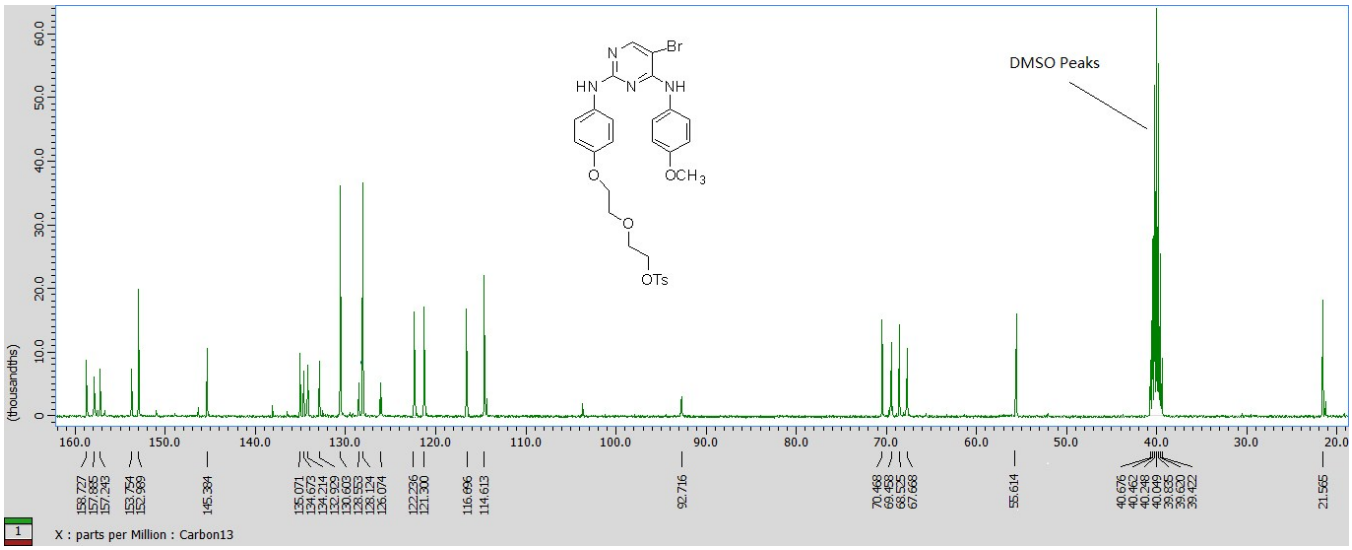
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OCH3
O
OTs
(thousandths)
X : parts per Million : Carbon13

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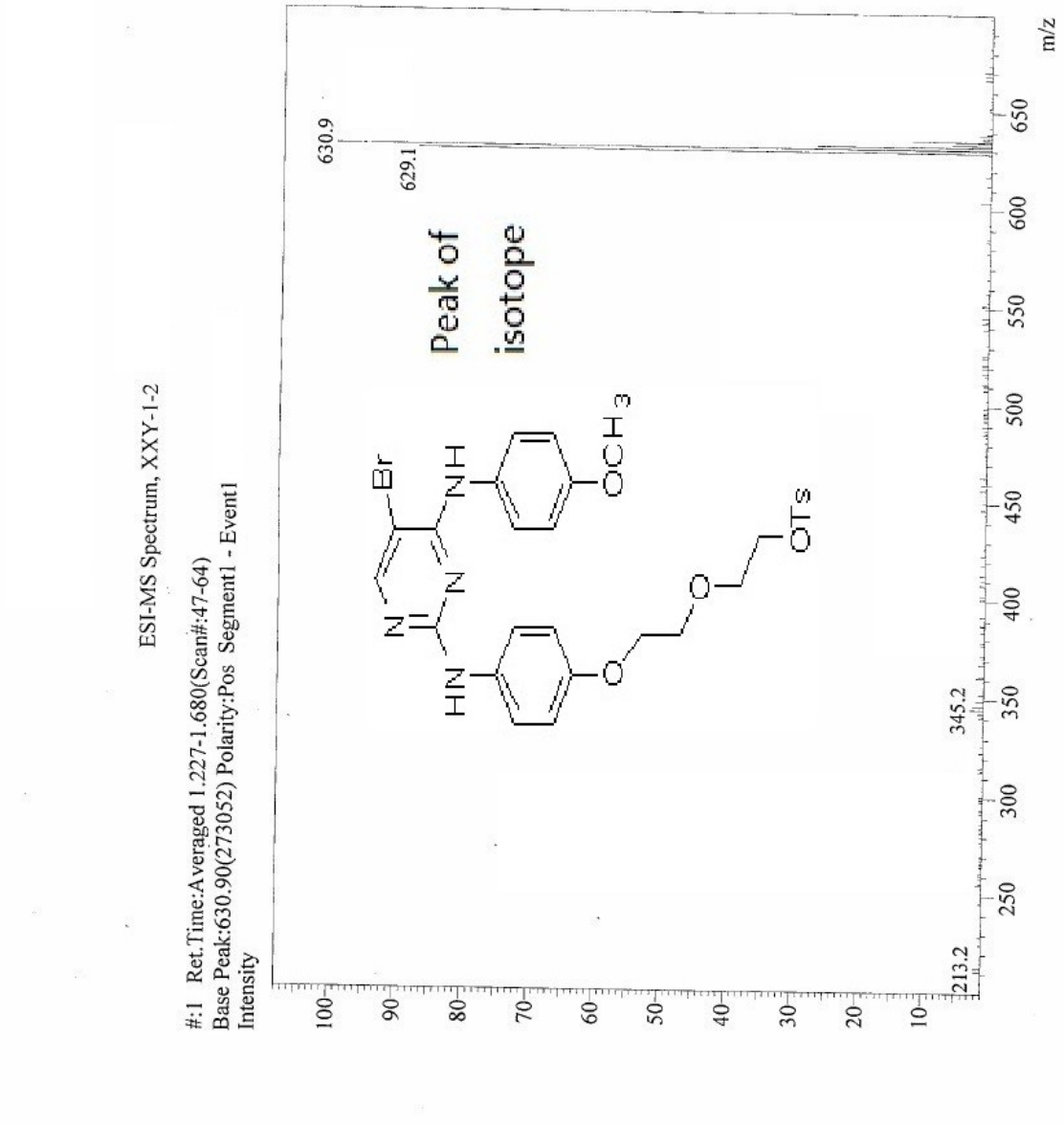
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HN
O
O
OTs
m/z

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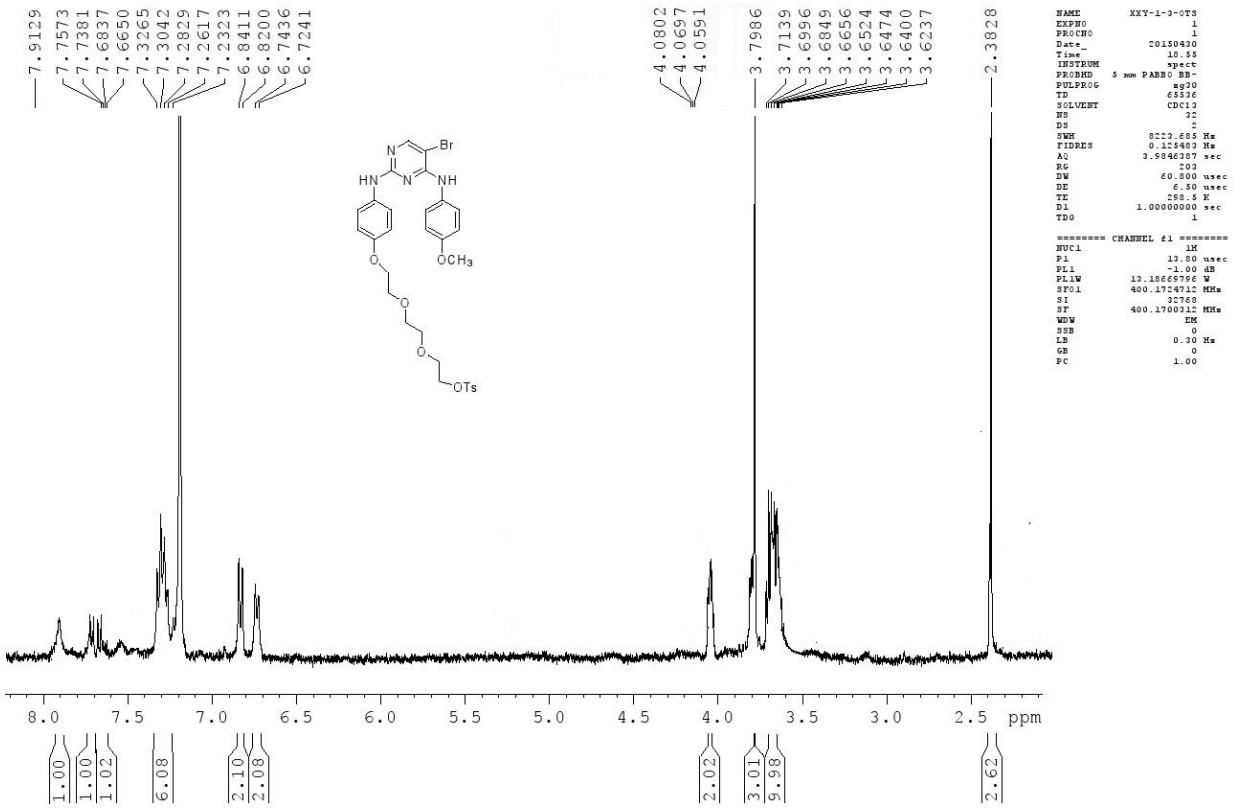
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SI 32768
SF 400.1700312 MHz
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LB 0.30 Hz
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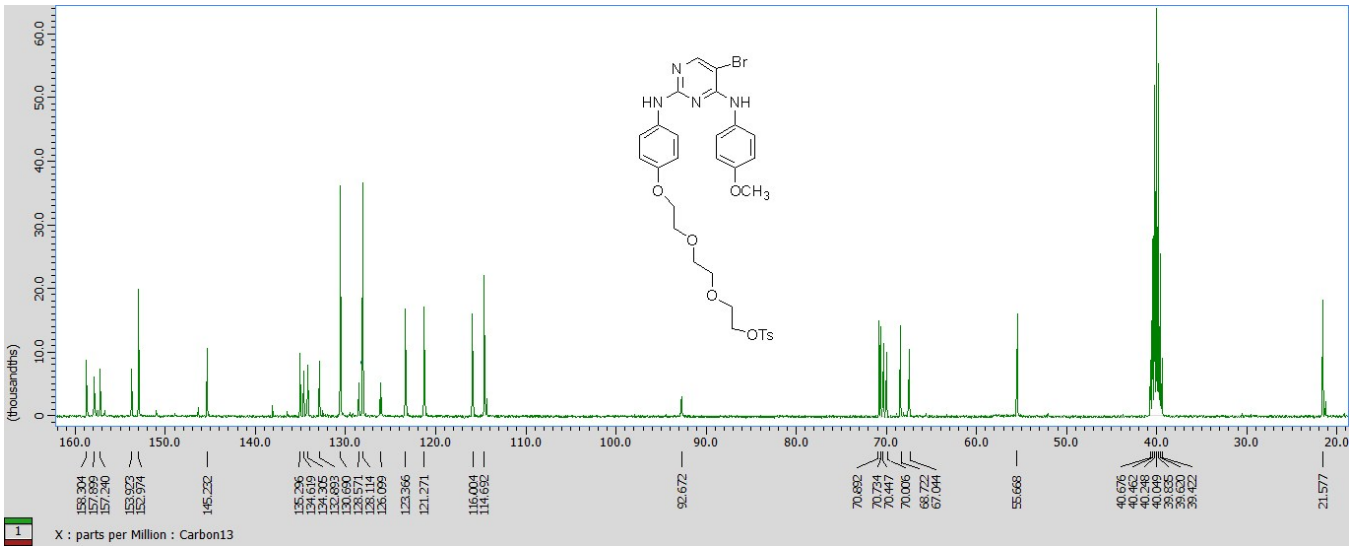
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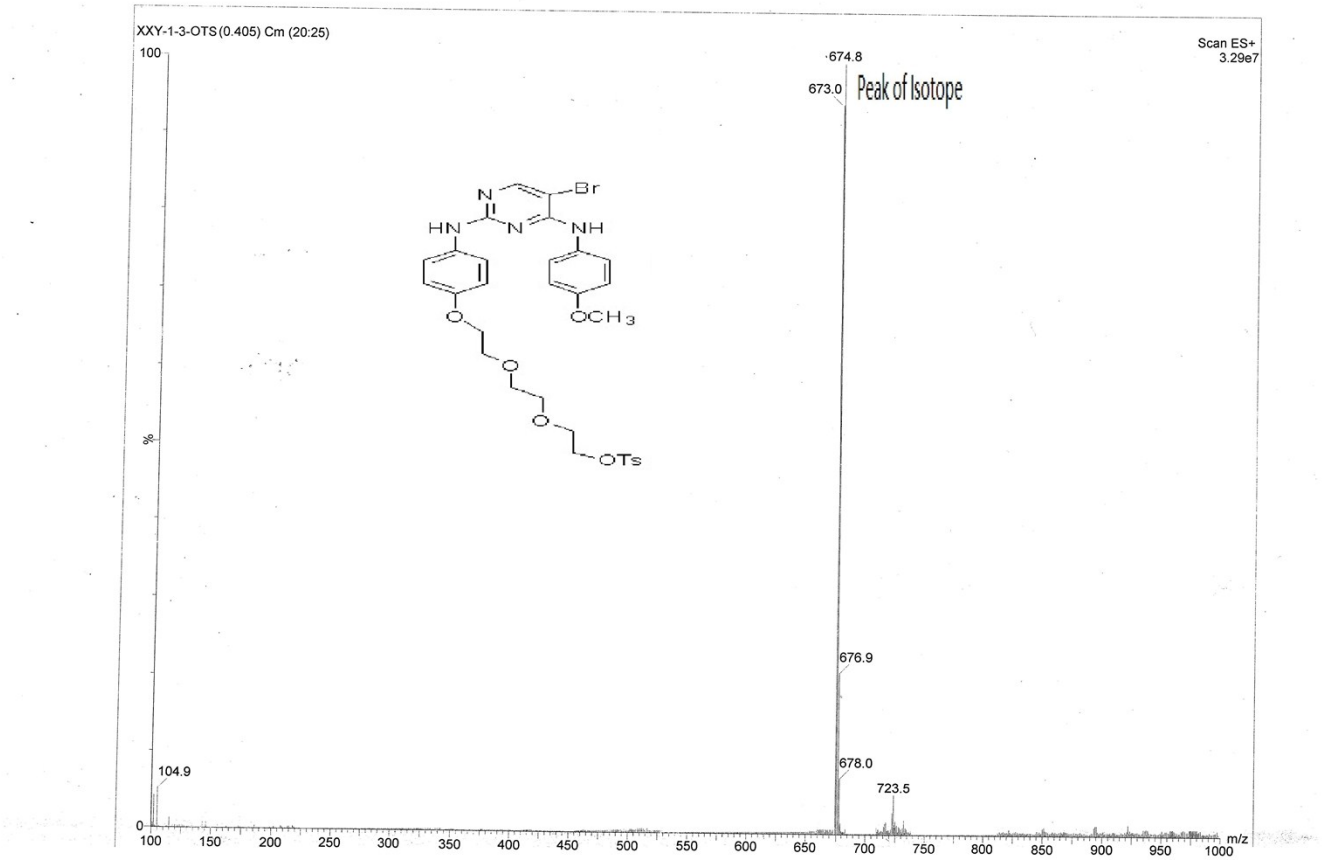
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m/z

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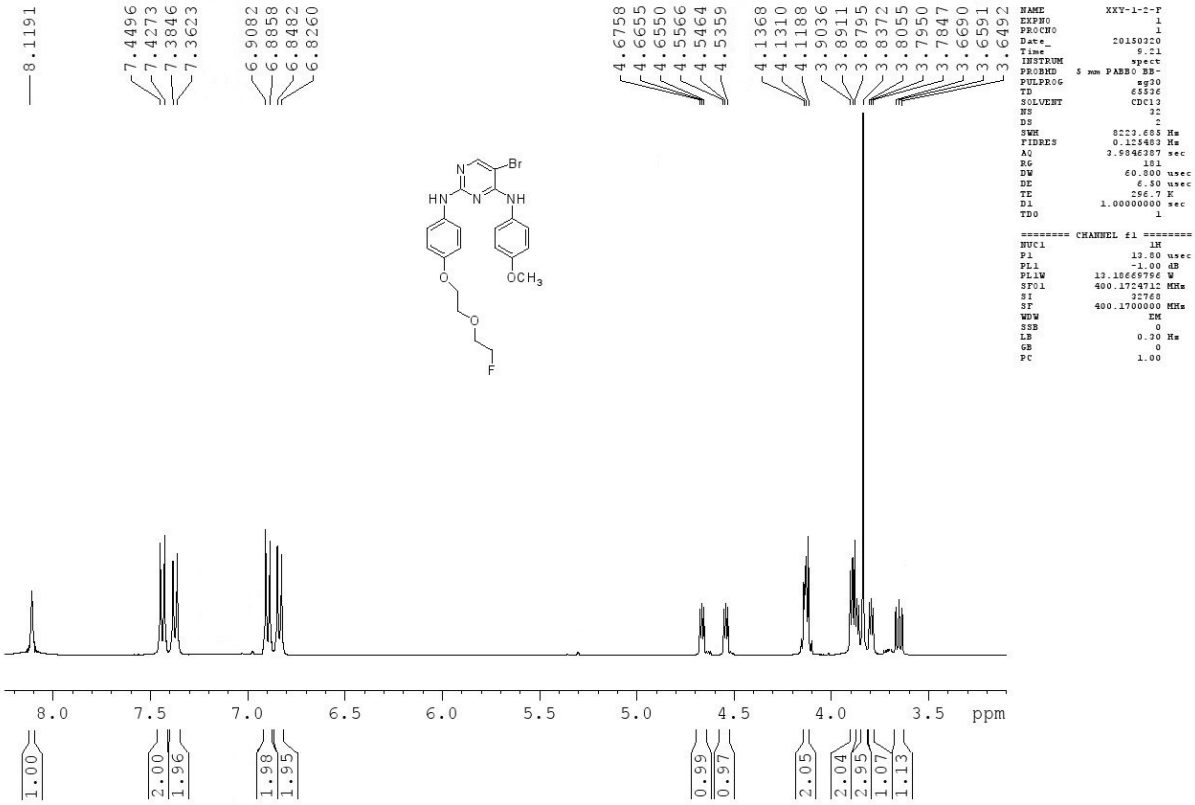


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FIDRES             0.125483 Hz
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TE                   296.7 K
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SI                      32768
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GB                          0
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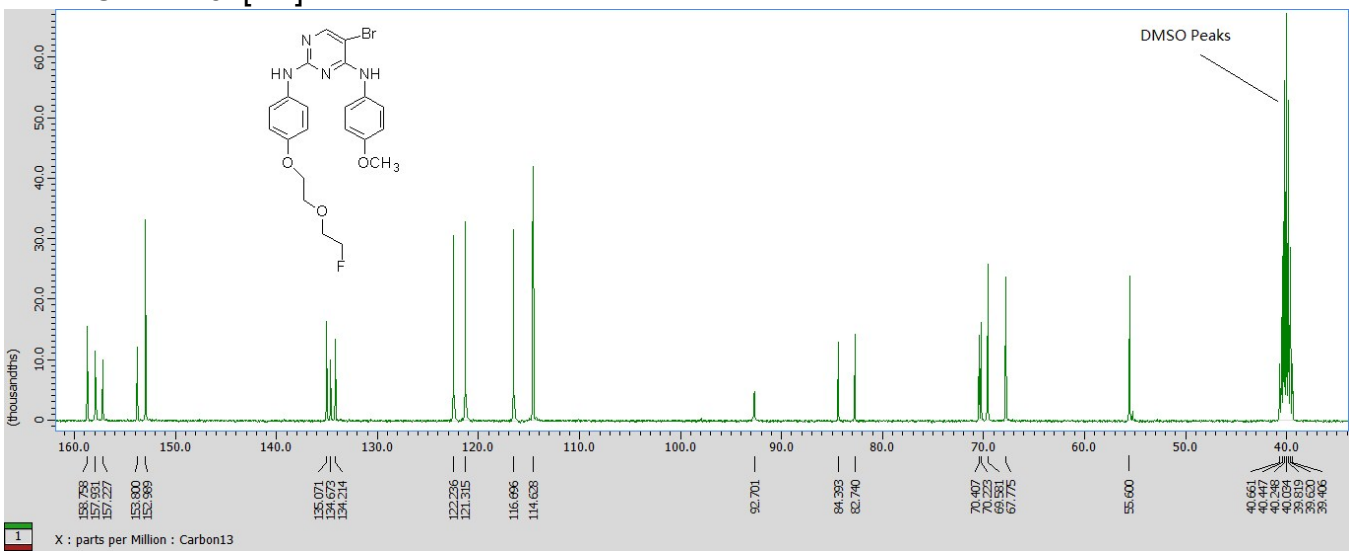

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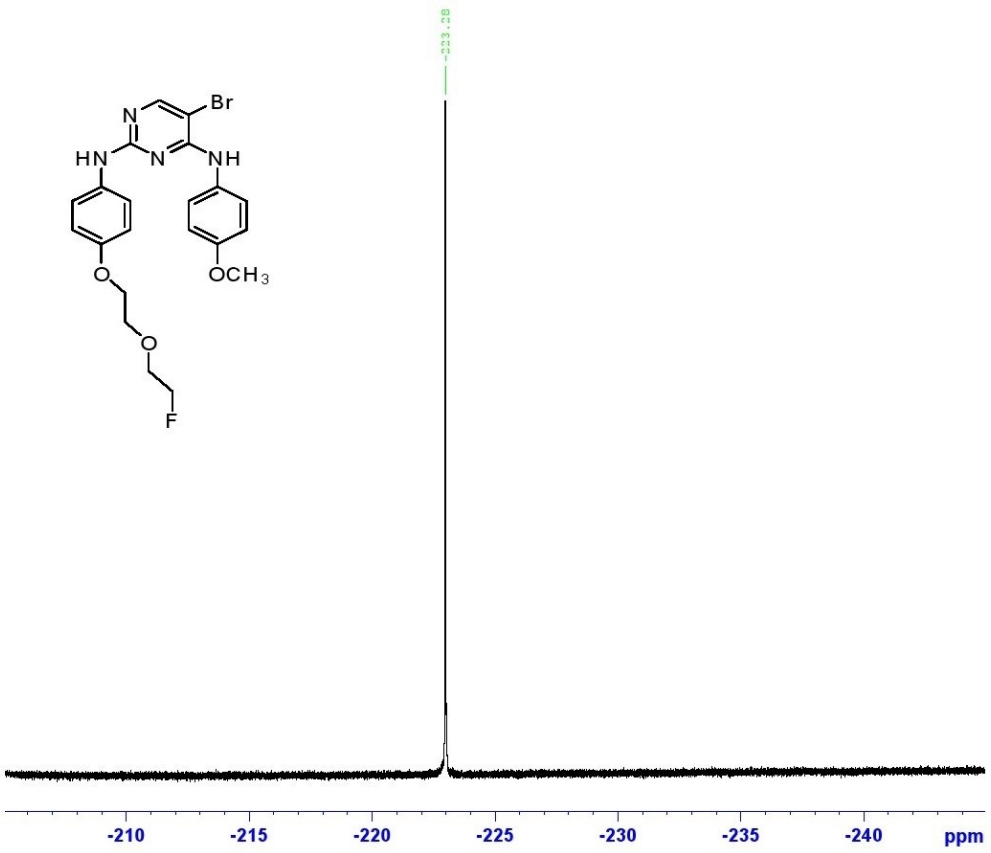


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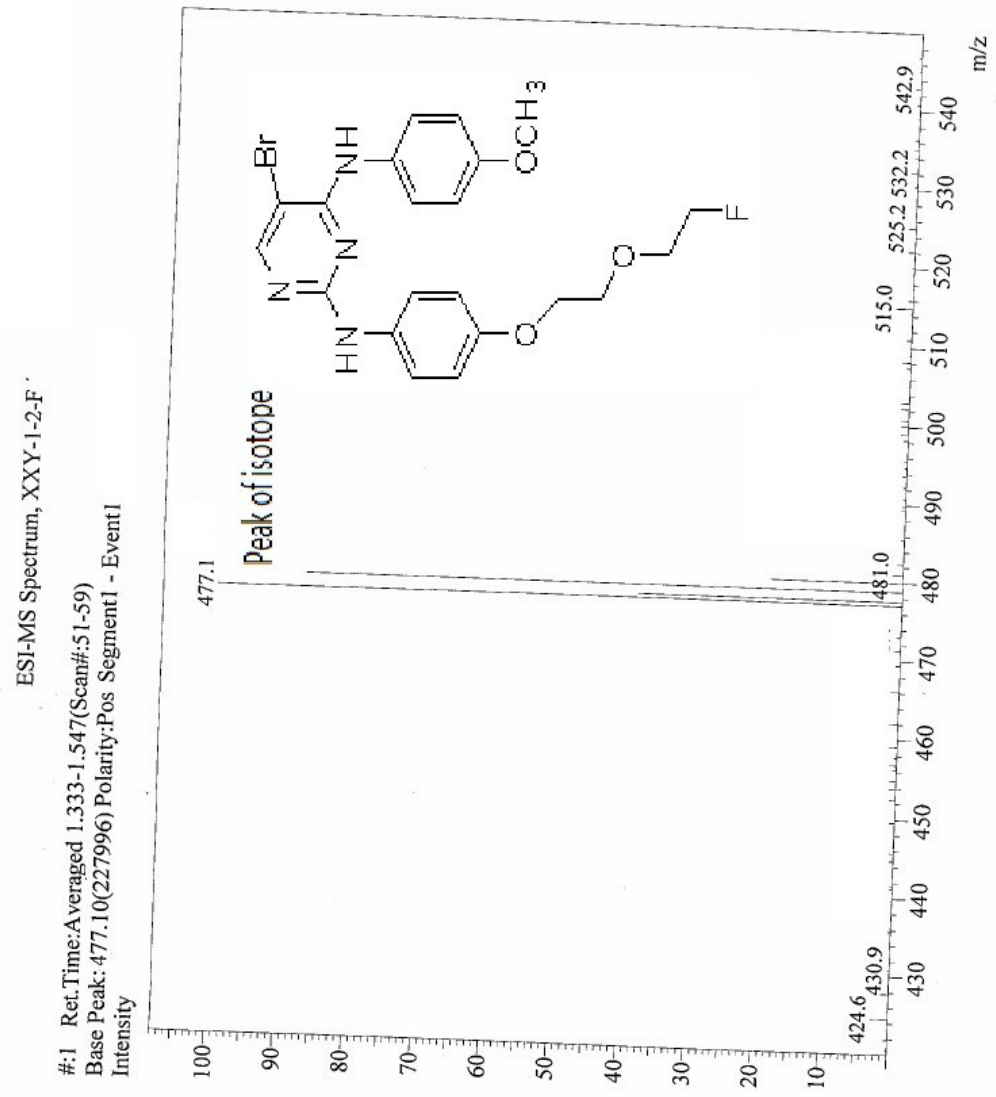

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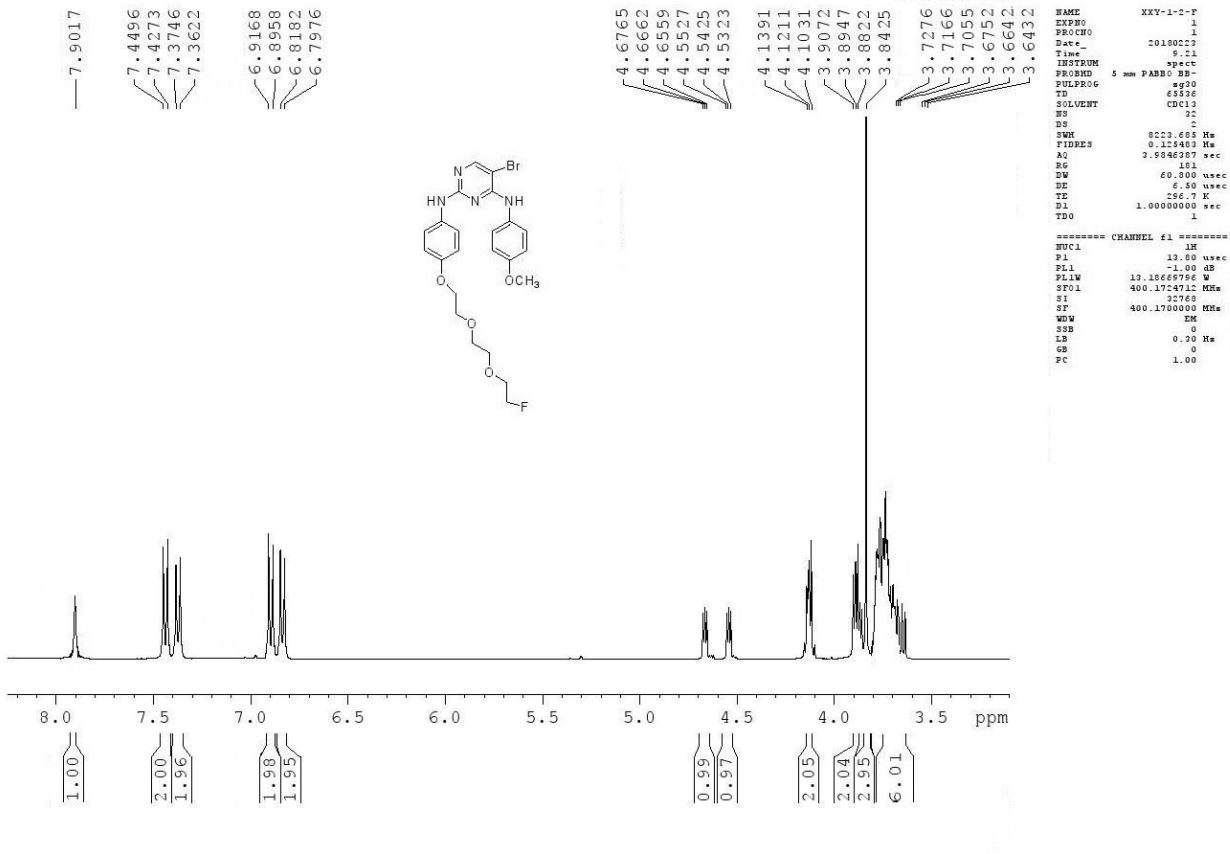

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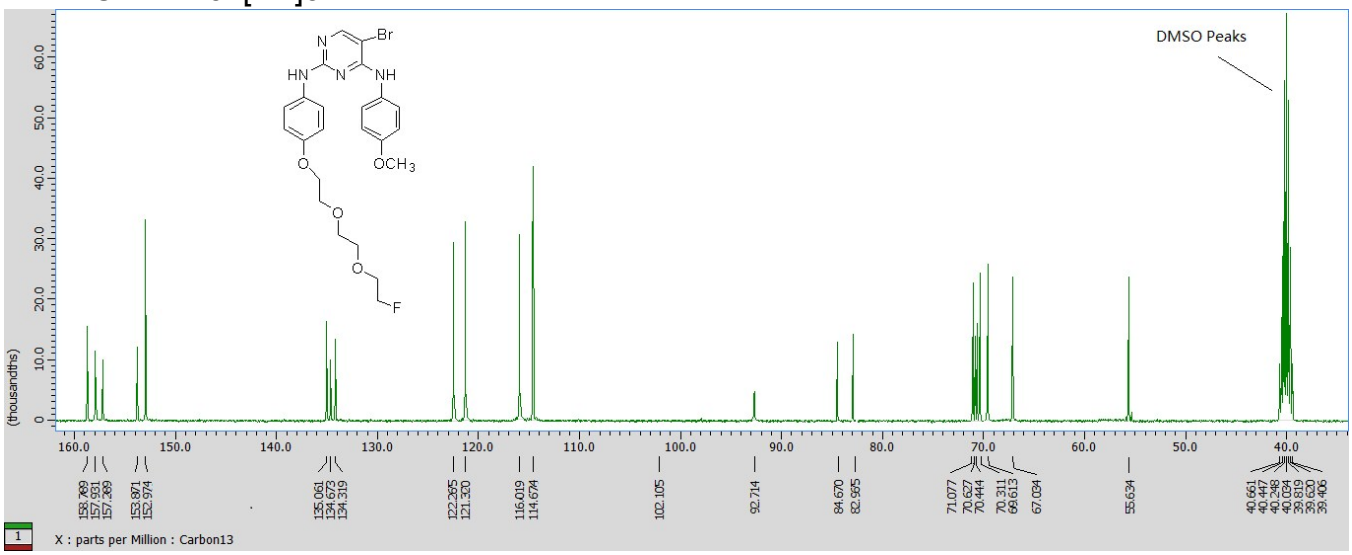

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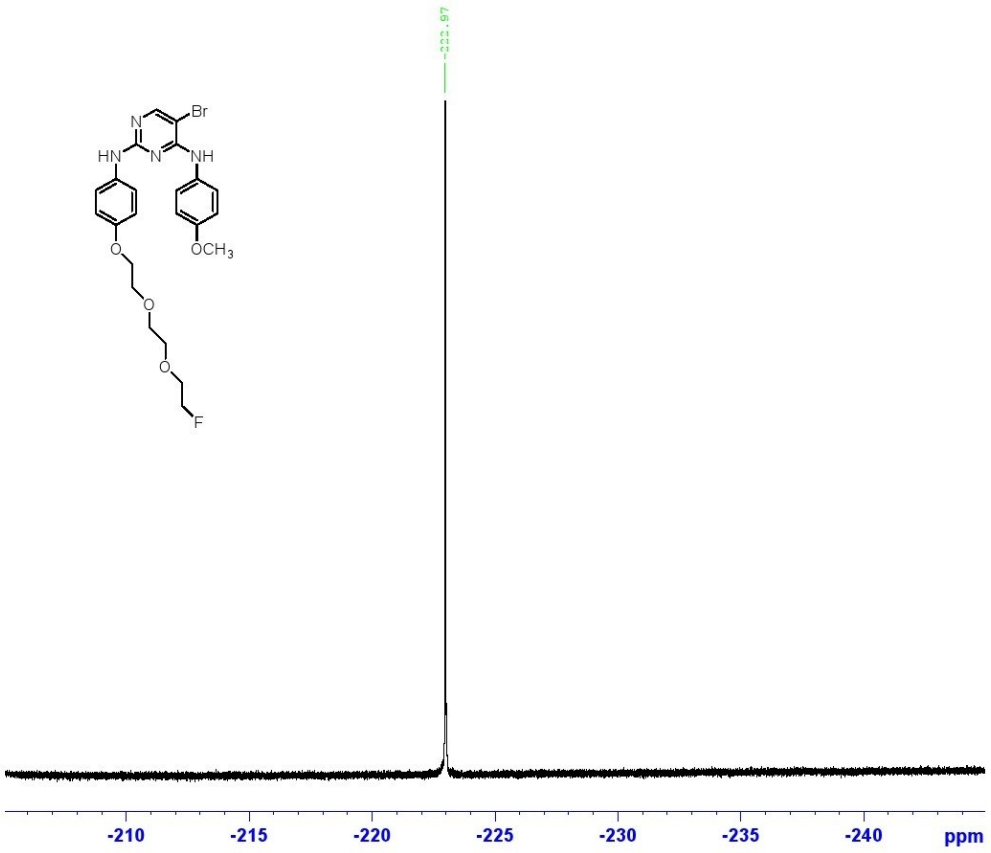


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SOLVENT              CDCl3
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SWH            15000.000 Hz
FIDRES             0.114441 Hz
AQ             4.3691168 sec
RG                 201.95
DW                33.333 usec
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TD0                     1

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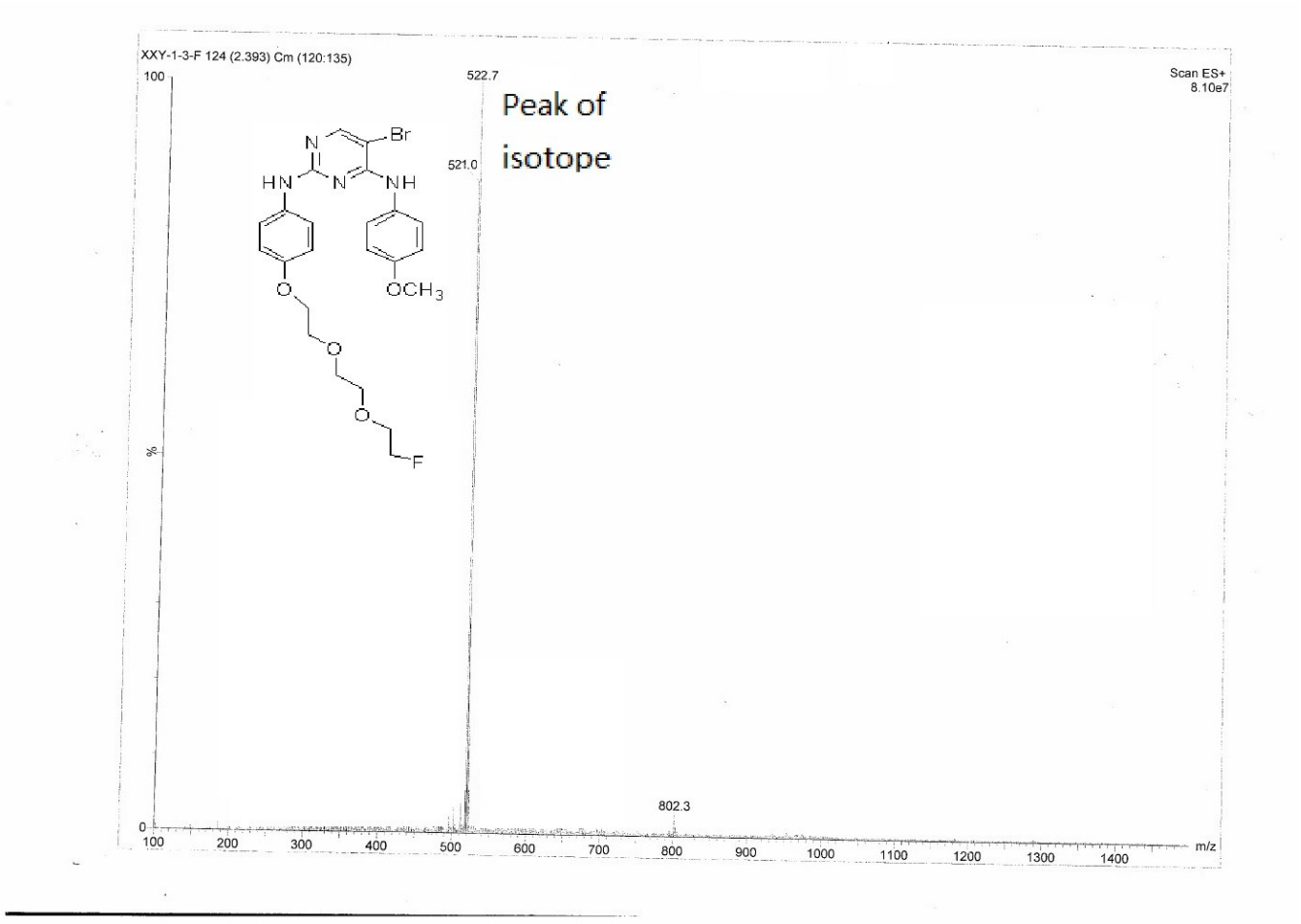
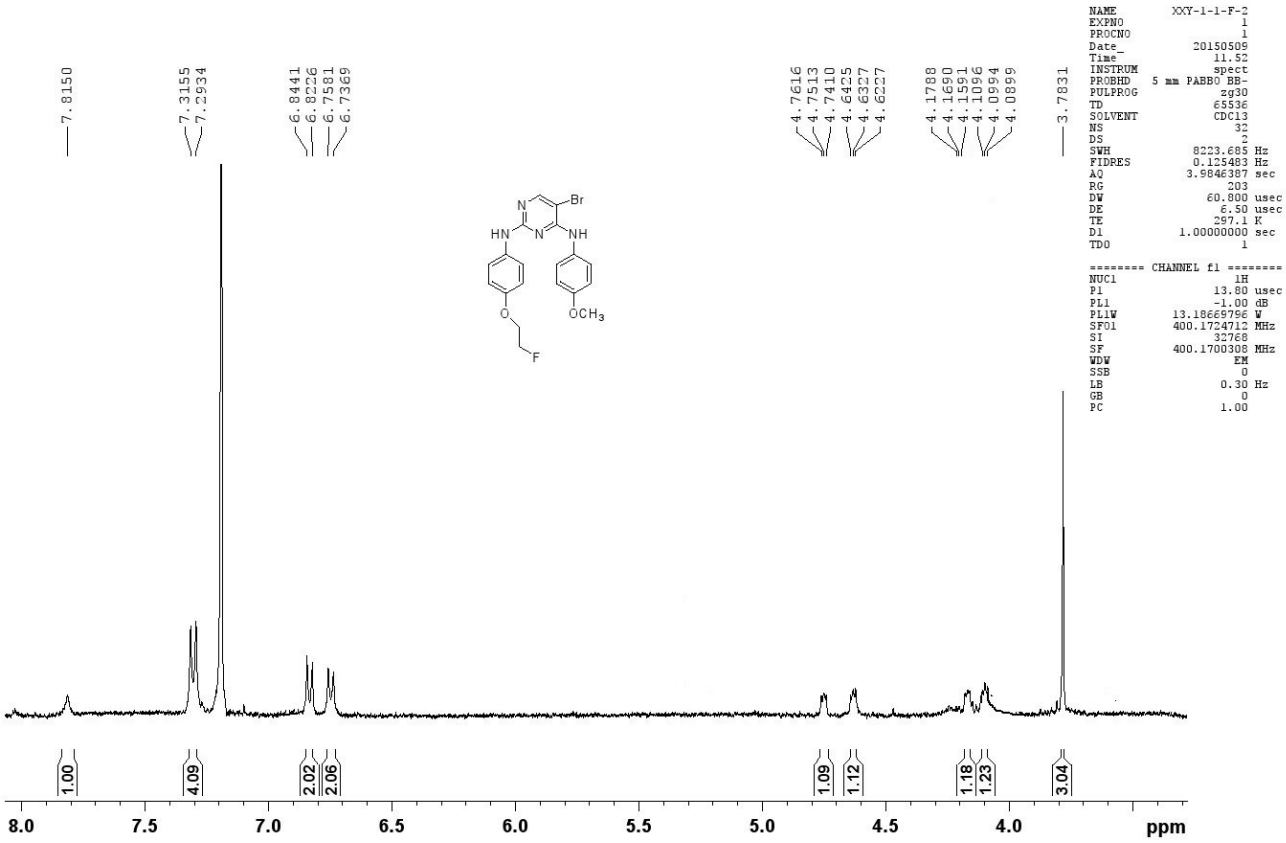
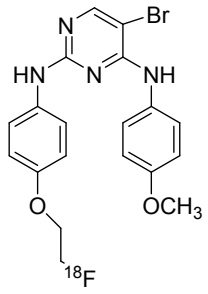


^{1}H-NMR of [^{19}F]**0 (including the chemical structure of** [^{19}F]**1)** [a]



the chemical structure of [^{18}F]**1**



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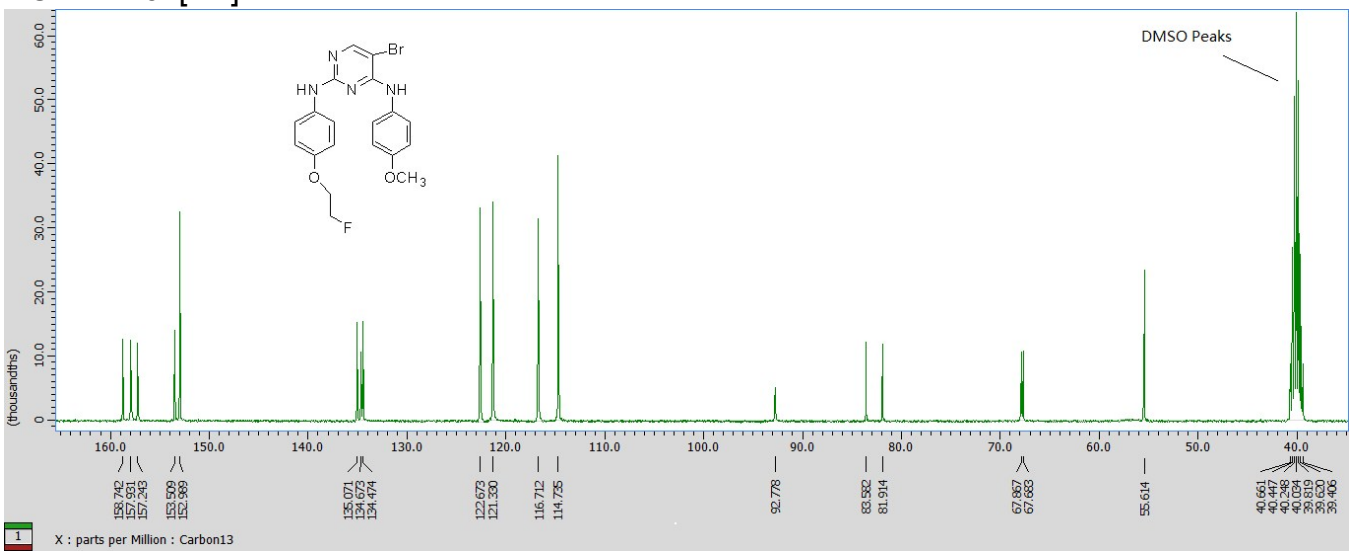

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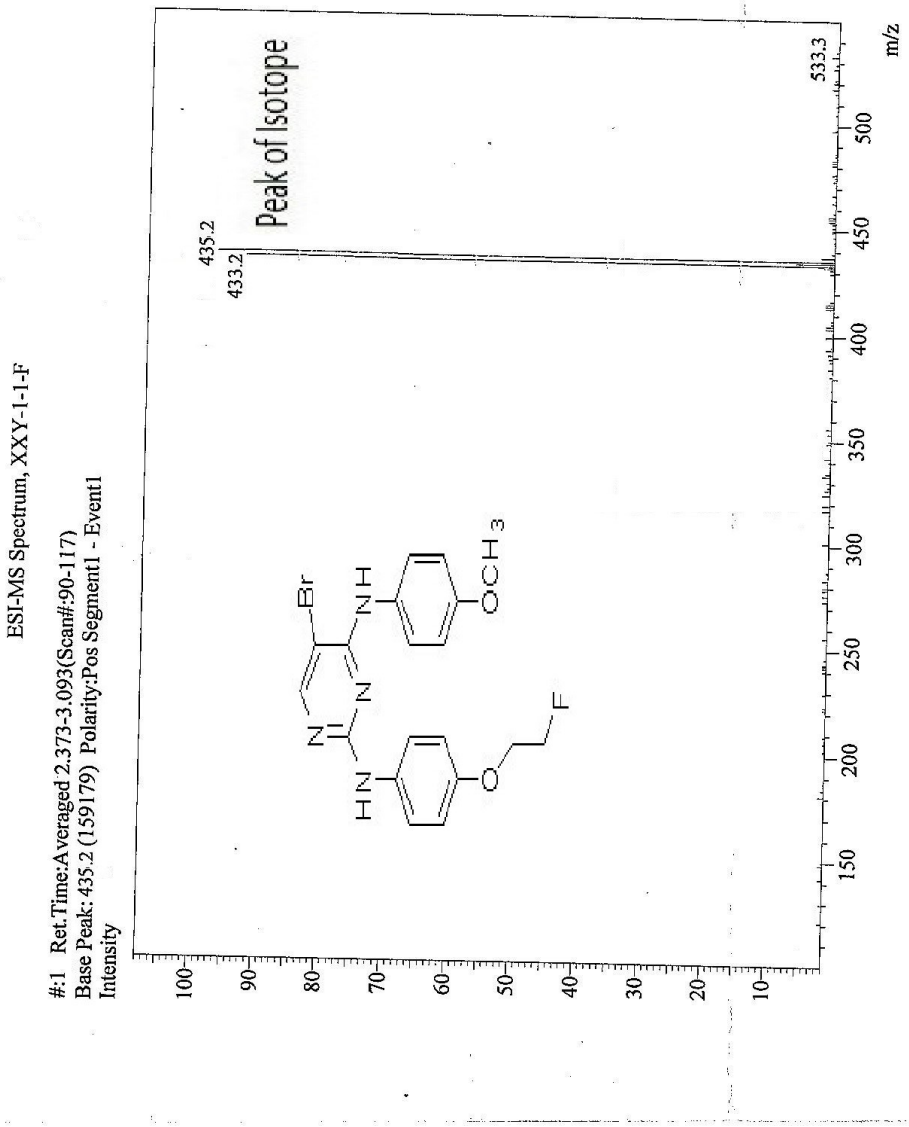


[a] The chemical structure and the related spectrum of [^{19}F]**1**, and the chemical structure of its corresponding F-18 labeled radiotracer [^{18}F]**1**, were cited from our published work:

D. Wang, Y. Fang, H. Wang, X. Xu, J. Liu and H. Zhang, RSC Advance, 2017, 7, 22388-22399.

(Note: The [^{19}F]**1** in this work was named **8a** in the above published work, and its corresponding F-18 labeled radiotracer [^{18}F]**1** was named [^{18}F]-**8a** in the above published work.)

Table S1

Biodistribution in S180-tumor-bearing mice after intravenous injection of [^{18}F]**1** [a,b] (logP = 3.32±0.04)

Organs	Time (min)				
	5	15	30	60	120
Blood	6.62±0.25	4.73±0.82	2.19±0.01	1.93±0.10	0.81±0.01
Brain	1.20±0.12	0.89±0.18	1.19±0.18	1.51±0.12	0.83±0.14
Heart	1.23±0.15	2.44±0.22	2.45±0.46	1.97±0.29	1.61±0.20
Liver	3.29±0.02	1.99±0.23	1.75±0.32	1.57±0.30	0.50±0.06
Spleen	1.98±0.03	1.65±0.11	2.28±0.12	1.74±0.19	0.92±0.34
Lung	8.73±1.26	8.96±1.35	7.39±1.29	4.23±0.57	3.81±0.44
Kidney	0.70±0.09	1.62±0.23	4.58±0.44	6.39±0.79	7.37±0.64
Muscle	1.38±0.21	1.47±0.19	1.73±0.20	1.97±0.25	1.59±0.27
Bone	1.88±0.13	1.95±0.25	3.79±0.42	4.16±0.46	4.71±0.53
Intestine [b]	0.06±0.02	0.43±0.07	0.28±0.06	0.11±0.02	0.34±0.08
Stomach [b]	0.05±0.01	0.23±0.03	0.42±0.03	0.37±0.09	1.35±0.05
Tumor	3.39±0.25	3.69±0.51	3.71±0.43	3.23±0.14	3.11±0.22
Tumor/Muscle	2.46	2.51	2.14	1.64	1.96
Tumor/Bone	1.80	1.89	0.98	0.78	0.66
Tumor/Blood	0.55	0.78	1.69	1.67	3.84

[a] The preparation and the related biological evaluation results of [^{19}F]**1** and its corresponding F-18 labeled radiotracer [^{18}F]**1**, were cited from our published work: D. Wang, Y. Fang, H. Wang, X. Xu, J. Liu and H. Zhang, RSC Advance, 2017, 7, 22388-22399.

(Note: The [^{19}F]**1** in this work was named **8a** in the above published work, and its corresponding F-18 labeled radiotracer [^{18}F]**1** was named [^{18}F]-**8a** in the above published work. The chemical structures of [^{19}F]**1** and [^{18}F]**1** were shown in the *Supplementary Materials*.)

The *in vivo* biodistribution studies of [^{18}F]**1** in S180-tumor-bearing mice, were performed in the same batch with the F-18 radiotracers in this work, and were cited from the above published work. What's more, we have checked some errors in the calucation of the logP and a few of biodistribution data of the [^{18}F]**1** from our original experimental data. Therefore, we have made corrections in theses tables and adjusted some discussions in the corresponding positions in the manuscript.

[b] Expressed as % injected dose per gram (%ID/g) unless otherwise indicated. Data are the average for five mice ± standard deviation.

Table S2

Biodistribution in S180-tumor-bearing mice after intravenous injection of [^{18}F]**2** [a,b,c] (logP = 2.97±0.10)

Organs	Time (min)					
	5	15	30	60	120	30 (blockade) [c]
Blood	6.17±0.36	4.36±0.62	3.08±0.26	3.24±0.25	2.31±0.18	2.86±0.31
Brain	2.52±0.44	1.70±0.13	2.32±0.31	2.05±0.32	1.83±0.32	1.96±0.20
Heart	2.37±0.15	2.81±0.09	2.93±0.14	2.88±0.23	2.61±0.25	2.48±0.08
Liver	3.52±0.49	3.36±0.56	2.59±0.20	2.36±0.46	1.73±0.25	2.89±0.52
Spleen	2.94±0.01	2.34±0.14	2.68±0.28	1.93±0.04	1.61±0.21	2.53±0.14
Lung	10.45±0.52	6.13±0.48	2.84±0.34	2.61±0.20	1.94±0.32	2.35±0.23
Kidney	5.67±0.12	5.62±0.27	5.95±0.11	6.12±0.12	6.73±0.11	5.83±0.68
Muscle	1.87±0.28	2.25±0.20	2.39±0.41	2.37±0.14	2.47±0.18	2.64±0.13

Bone	2.52±0.20	3.30±0.52	3.84±0.63	4.08±0.53	4.51±0.71	3.39±0.24
Intestine [b]	1.20±0.07	2.66±0.09	3.30±0.09	4.33±0.09	5.18±0.02	3.33±0.07
Stomach [b]	0.47±0.08	0.51±0.04	0.51±0.01	0.45±0.03	0.27±0.03	0.57±0.09
Tumor	3.59±0.36	4.11±0.62	5.96±0.09	4.07±0.50	3.86±0.14	0.72±0.05
Tumor/Muscle	2.86	2.40	2.49	1.72	1.56	/
Tumor/Bone	2.12	1.64	1.55	1.00	0.86	/
Tumor/Blood	0.58	0.94	1.94	1.26	1.67	/

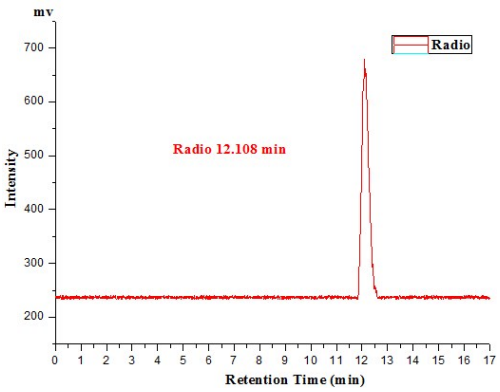
[a]Expressed as % injected dose per gram (%ID/g) unless otherwise indicated. Data are the average for five mice ± standard deviation. [b]Expressed as % injected dose per organ (%ID) . [c] Each animal received PF-562,271 (a dose of 33 mg/kg, p.o.) at one hour before the intravenous radiotracer injection (blocking study).

Table S3

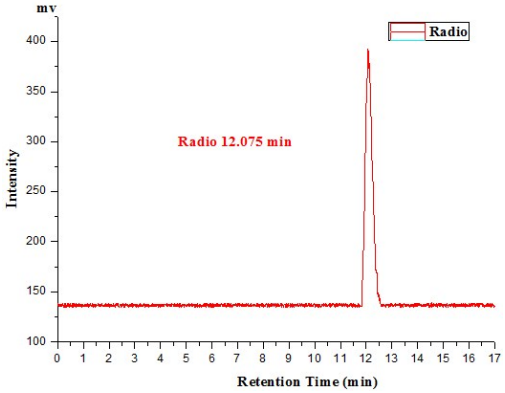
Biodistribution in S180-tumor-bearing mice after intravenous injection of [^{18}F]**3** [a] (logP = 2.86±0.06)

Organs	**Time (min)**				
	5	**15**	**30**	**60**	**120**
Blood	6.48±0.92	4.19±0.33	2.41±0.15	2.35±0.22	2.13±0.14
Brain	2.54±0.11	2.43±0.07	1.91±0.10	2.50±0.12	2.57±0.07
Heart	2.48±0.18	1.61±0.24	1.26±0.09	1.63±0.09	1.86±0.13
Liver	4.14±0.12	4.65±0.28	3.74±0.11	2.24±0.16	1.85±0.04
Spleen	2.87±0.24	2.11±0.19	1.47±0.13	1.25±0.11	0.98±0.07
Lung	10.63±0.61	6.44±0.73	4.86±0.30	4.09±0.63	3.53±0.32
Kidney	2.07±0.16	3.49±0.12	4.39±0.07	5.89±0.48	6.50±0.91
Muscle	3.10±0.05	2.55±0.23	2.07±0.10	2.58±0.29	2.65±0.20
Bone	3.16±0.16	2.57±0.03	3.07±0.10	3.90±0.17	3.50±0.34
Intestine [b]	0.90±0.06	2.24±0.12	4.62±0.04	4.78±0.02	5.72±0.13
Stomach [b]	1.54±0.08	1.44±0.06	1.54±0.10	1.56±0.16	1.52±0.19
Tumor	3.08±0.20	2.80±0.33	3.24±0.07	2.97±0.47	2.88±0.44
Tumor/Muscle	0.99	1.10	1.57	1.54	1.46
Tumor/Bone	0.98	1.09	1.06	1.02	1.11
Tumor/Blood	0.47	0.67	1.34	1.26	1.35

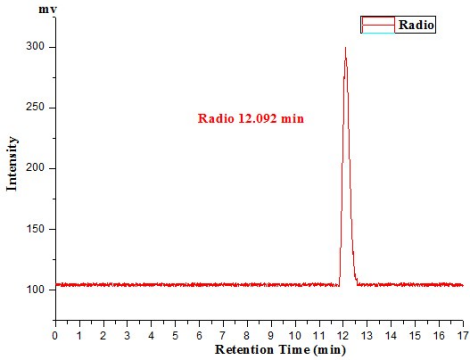
[a] Expressed as % injected dose per gram (%ID/g) unless otherwise indicated. Data are the average for five mice ± standard deviation. [b]Expressed as % injected dose per organ (%ID) .



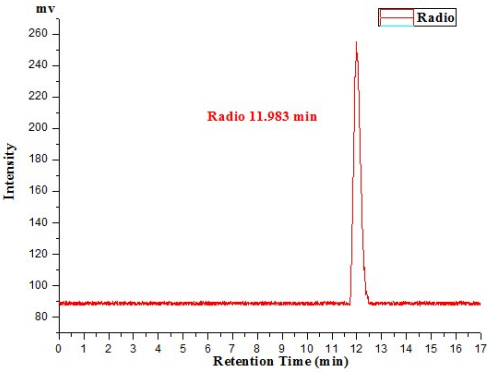
[^{18}F]**2**--normal saline, 37 °C, 1 h



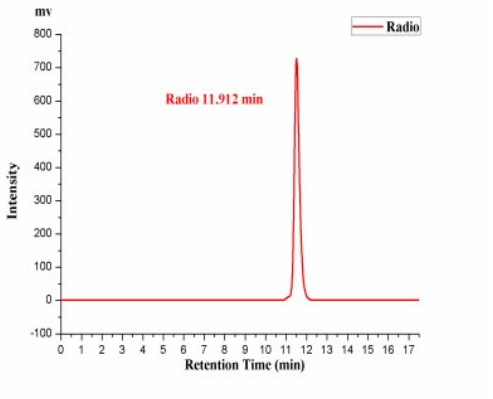
[^{18}F]**2**--normal saline, 37 °C, 2 h



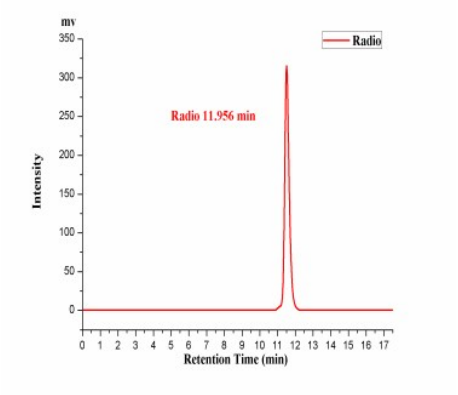
[^{18}F]**2**--murine plasma, 37 °C, 1 h



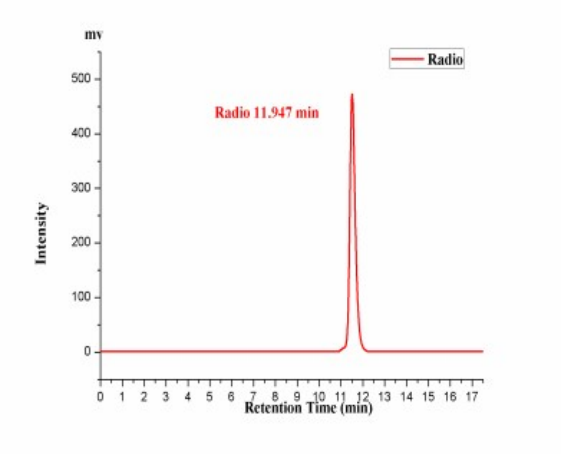
[^{18}F]**2**--murine plasma, 37 °C, 2 h



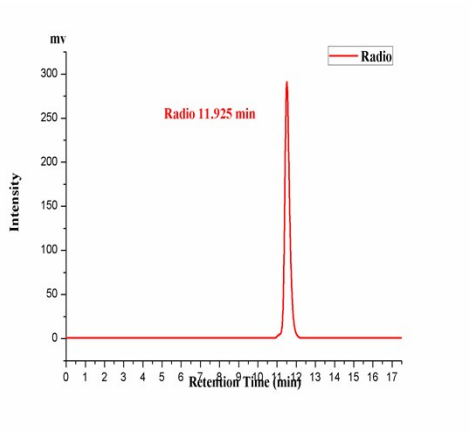
[^{18}F]**3**--normal saline, 37 °C, 1 h



[^{18}F]**3**--normal saline, 37 °C, 2 h



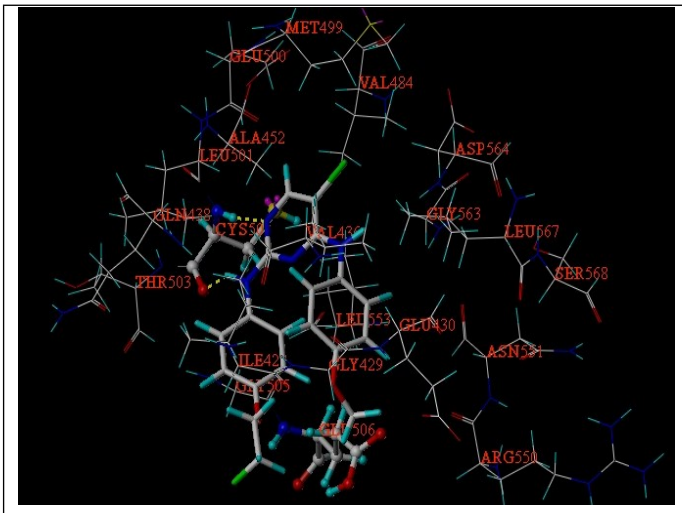
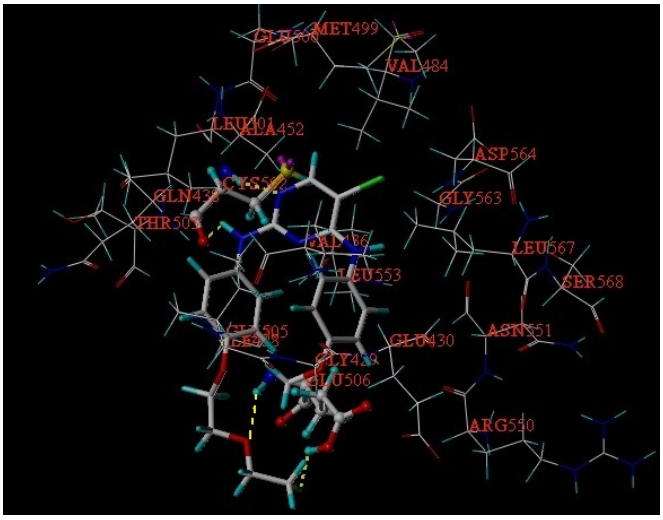
[^{18}F]**3**--murine plasma, 37 °C, 1 h

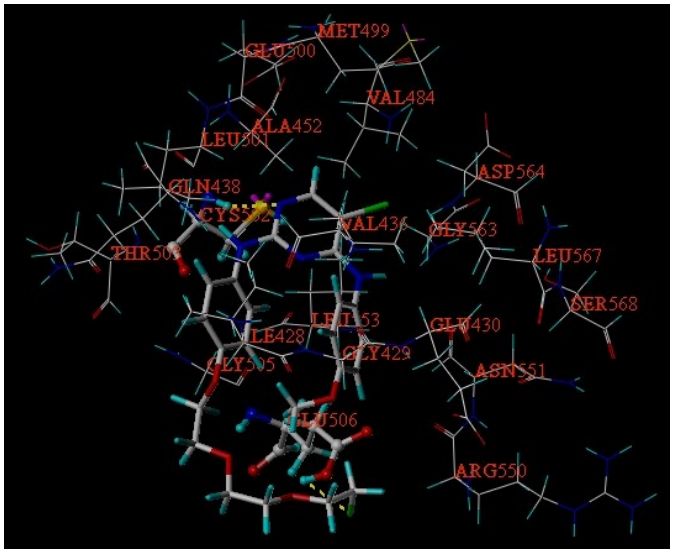


[^{18}F]**3**--murine plasma, 37 °C, 2 h

Fig. S1. The HPLC chromatogram of F-18 labeled radiotracers in normal saline and murine plasma at 37 °C after 1 h and 2 h, respectively. The HPLC profile data were exported from the *.lcd files by Shimadzu LCSolution Software, and were graphically interpreted and coordinate translated by Origin 8.0.

The in vitro stability of [^{18}F]**1 was shown in** our published work: D. Wang, Y. Fang, H. Wang, X. Xu, J. Liu and H. Zhang, RSC Advance, 2017, 7, 22388-22399.

	
[^{19}F]**1** in the FAK binding pocket	[^{19}F]**2** in the FAK binding pocket



[^{19}F]**3** in the FAK binding pocket

Fig. S2. The docking studies on the interaction of [^{19}F]**1** [^{19}F]**2 and** [^{19}F]**3** with the FAK**.** (Most of the residues in the binding pocket of the FAK were shown as ‘‘Lines’’ , while the key residue which have hydrogen-bonding interactions with the F-19 standards were shown as ‘‘Ball and Stick’’, the F-19 standards were shown as ‘‘Capped Sticks’’, and the hydrogen bonds were shown as ‘‘Yellow Dotted Line’’).