Supporting Information

Synthesis of [^{18}F]PS13 and Evaluation as a PET Radioligand for Cyclooxygenase-1 in Monkey

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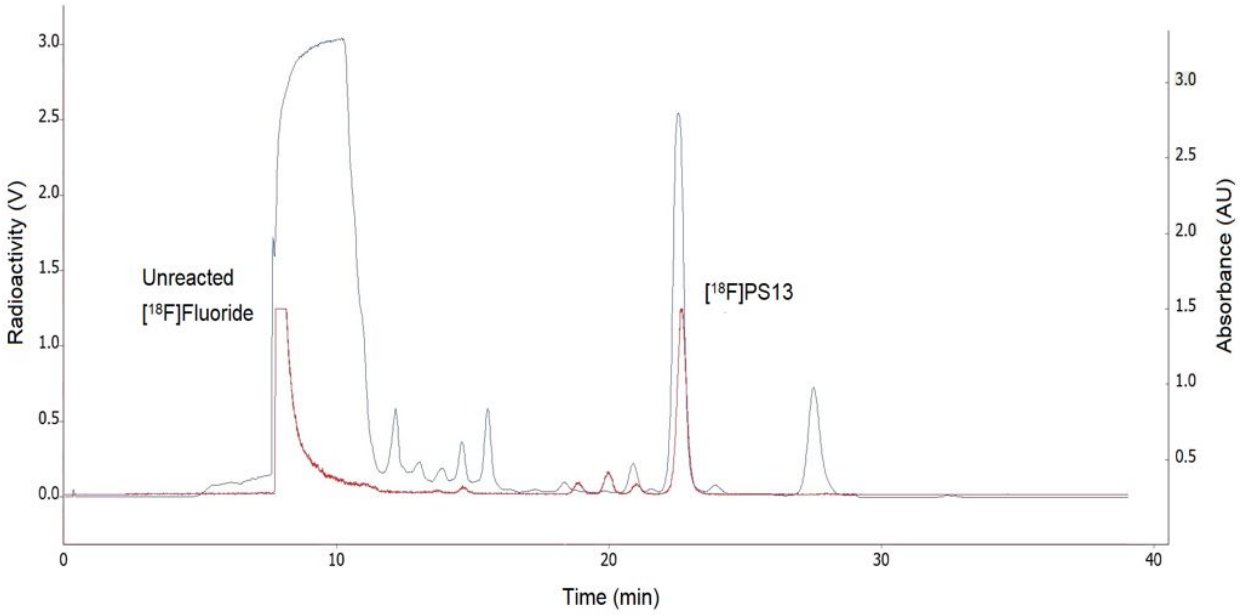

Figure S1. Representative reversed phase HPLC radiochromatogram for the separation of [^{18}F]PS13. See 'Methods' in main text for separation conditions.

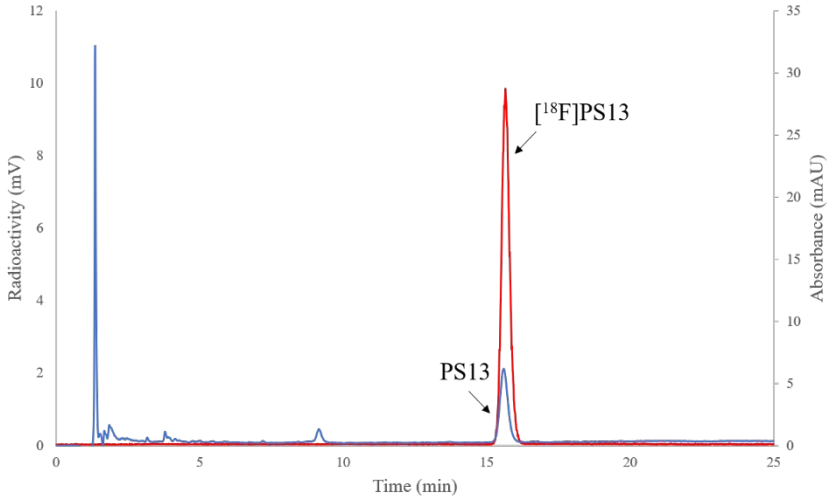

Figure S2. Representative reversed phase analytical HPLC radiochromatogram for [^{18}F]PS13. See 'Methods' in main text for analytical conditions.

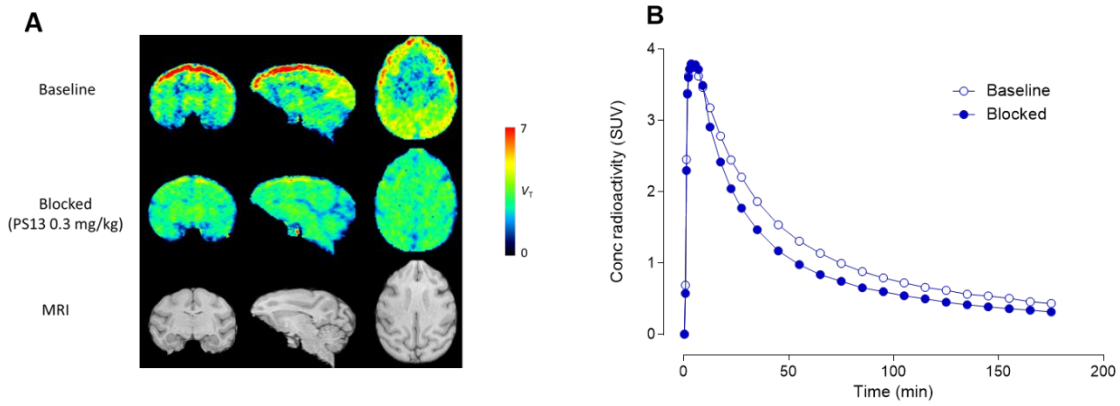

Figure S3. PET data obtained in monkey B with [^{18}F]PS13. Panel A: images of brain V_T at baseline (top row) and under pre-blocked conditions (middle row), and corresponding MRI images (bottom row); (left column: coronal image; middle column: sagittal images; right column; transaxial images). Panel B: whole brain-time activity curves at baseline and under pre-blocked conditions.

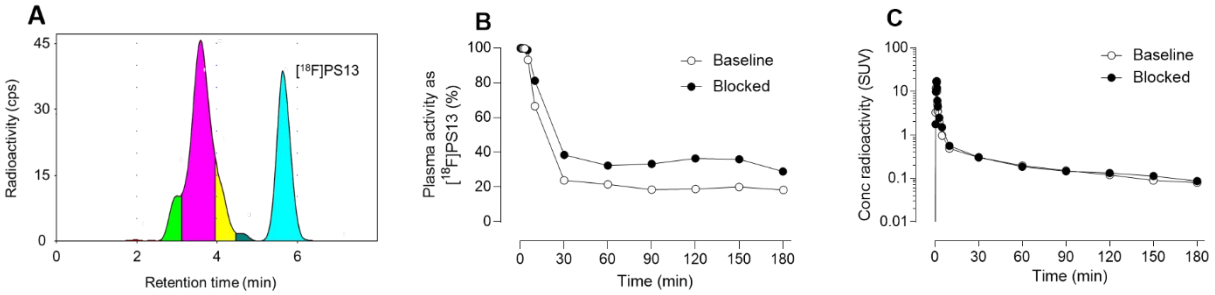

Figure S4. Analysis of plasma in monkey B after intravenous injection of [^{18}F]PS13. Panel A: reversed phase radio-HPLC of plasma at 180 minutes after intravenous injection of [^{18}F]PS13 at baseline. Panel B: time-course of percentage of radioactivity in plasma represented by unchanged [^{18}F]PS13 at baseline and under pre-blocked conditions. Panel C: time-course of unchanged [^{18}F]PS13 concentration in plasma at baseline and under pre-blocked conditions.

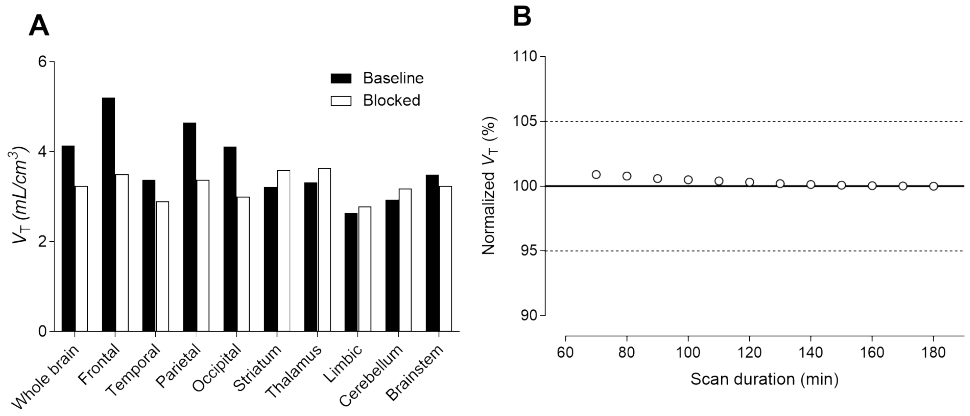

Figure S5. Analysis of PET data from experiment in monkey B with [^{18}F]PS13. Panel A: regional V_T values at baseline and under pre-blocked conditions. Panel B: dependence of whole brain V_T on duration of PET data from time if radiotracer injection used for calculation with values normalized to the terminal value.

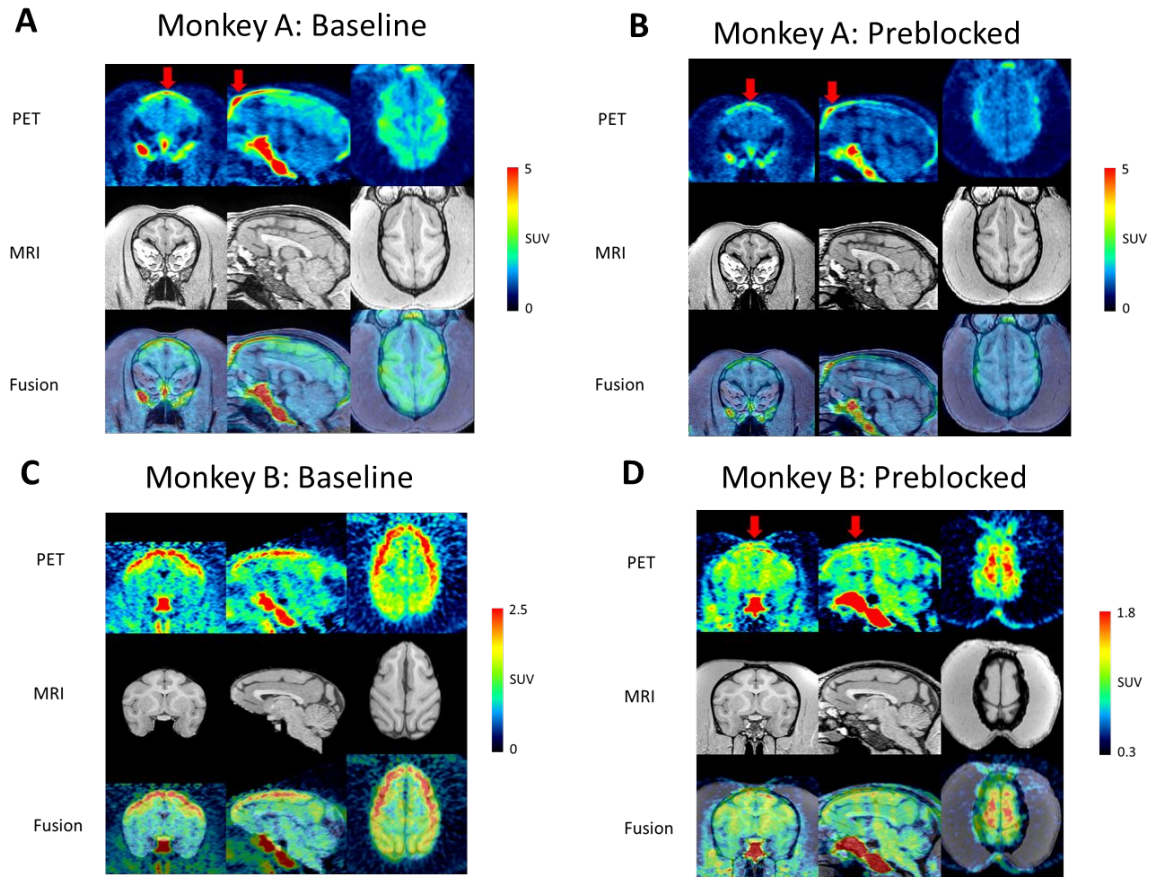

Figure S6. Uptake of radioactivity (SUV) in monkey skull regions after intravenous administration of [^{18}F]PS13. Panel A: monkey A at baseline. Panel B: monkey A under pre-blocked conditions. Panel C: monkey B at baseline. Panel D: monkey B under pre-blocked conditions. Top rows: PET images. Middle rows: corresponding MRI images. Bottom row: PET/MRI Fusion images. Left columns: coronal images. Middle columns: sagittal images. Right columns: transaxial images. Red arrows indicate skull regions with noticeable radioactivity uptake (Panels A, B, and D).

Table S1. Plasma free fraction (f_P) values for [^{18}F]PS13 in PET experiments.

Monkey	Study type	f_P (%)[a]	Normalized f_P (%)[b]
A	Baseline	1.14	1.35
B	Baseline	2.79	1.66
A	Pre-block	1.57	1.36
B	Pre-block	1.42	4.52

[a] Values before normalization against a stored reference sample.
[b] Values normalized against that measured on the same day for a single reference sample to account for factors, such as operator variation.

Table S2. V_T values in monkey B under baseline and pre-blocked conditions when studied with [^{11}C]PS13 and [^{18}F]PS13.[a]

Region	[^{18}F]PS13			[^{11}C]PS13		
	Baseline V_T	**Blocked V_T**	**Blocking (%)**	**Baseline V_T**	**Blocked V_T**	**Blocking (%)**
Whole brain	4.14	3.24	22	7.47	4.18	44
Frontal cortex	5.21	3.51	33	9.44	4.39	53
Temporal cortex	3.38	2.90	14	6.36	3.67	42
Parietal cortex	4.65	3.38	27	8.65	4.23	51
Occipital cortex	4.12	3.00	27	7.79	4.11	47
Striatum	3.22	3.60	–12	6.35	4.52	29
Thalamus	3.32	3.64	–9	6.51	4.67	28
Limbic region	2.64	2.79	–5	5.38	3.86	28
Cerebellum	2.94	3.18	–8	5.07	4.35	14
Brainstem	3.49	3.24	7	5.08	4.26	16

[a] V_T values were calculated from Logan graphical analysis. See main text for detailed description of experiment with [^{18}F]PS13. The molar activity of the radioligand at baseline was 3.11 GBq/μmol and the amount of carrier PS13 injected was 3.0 nmol/kg. The experiment with [^{11}C]PS13 was performed and analyzed identically, except that the molar activity of the radioligand at baseline was 221 GBq/μmol and the dose of carrier was far less at 0.10 nmol/kg. The pre-blocking dose or PS13 in each case was 0.3 mg//kg i.v., administered over 15–5 min before the radioligand.

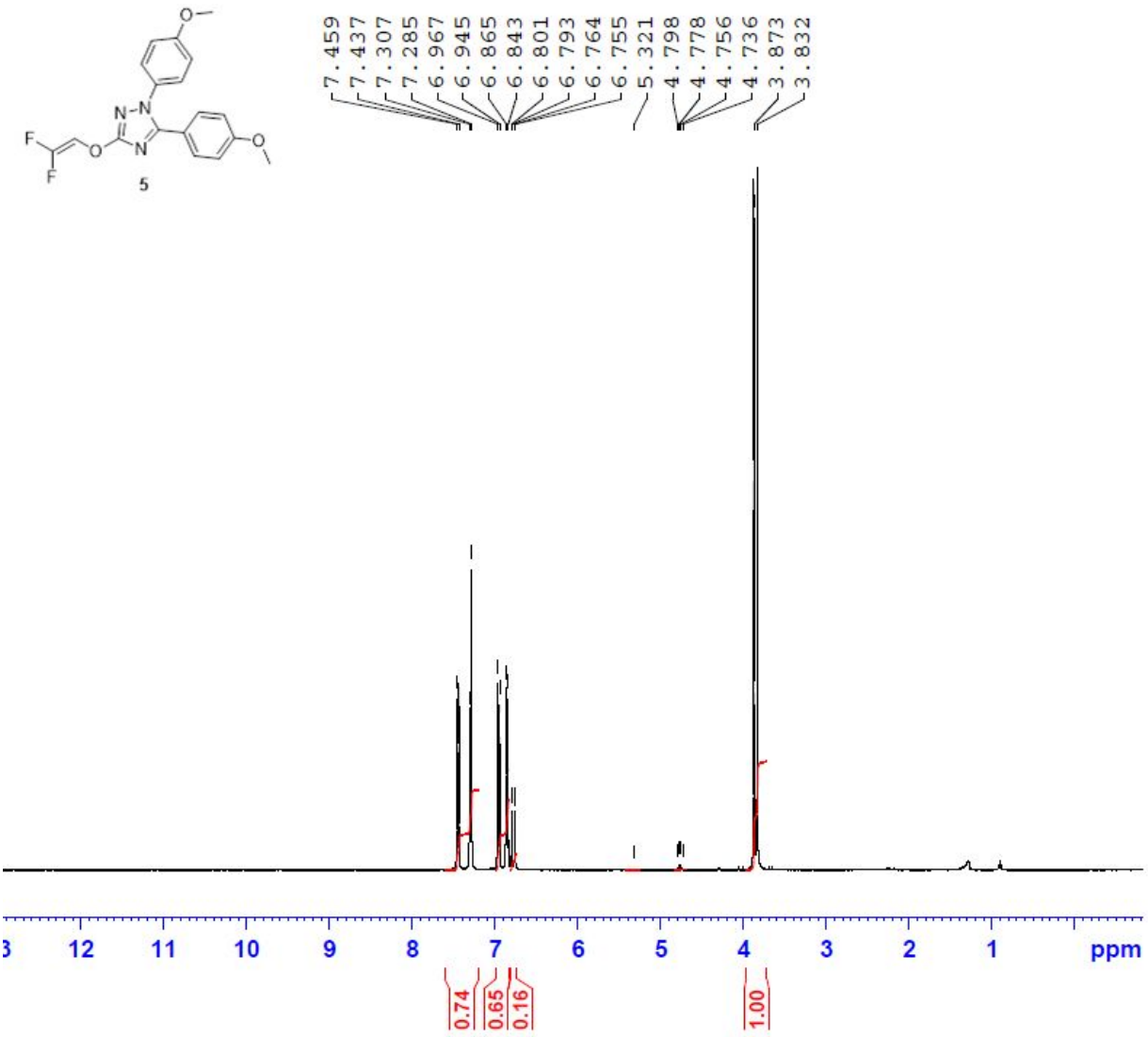

Figure S7. ^{1}H NMR ($CDCl_3$) of *gem*-difluoroalkene, **5**.

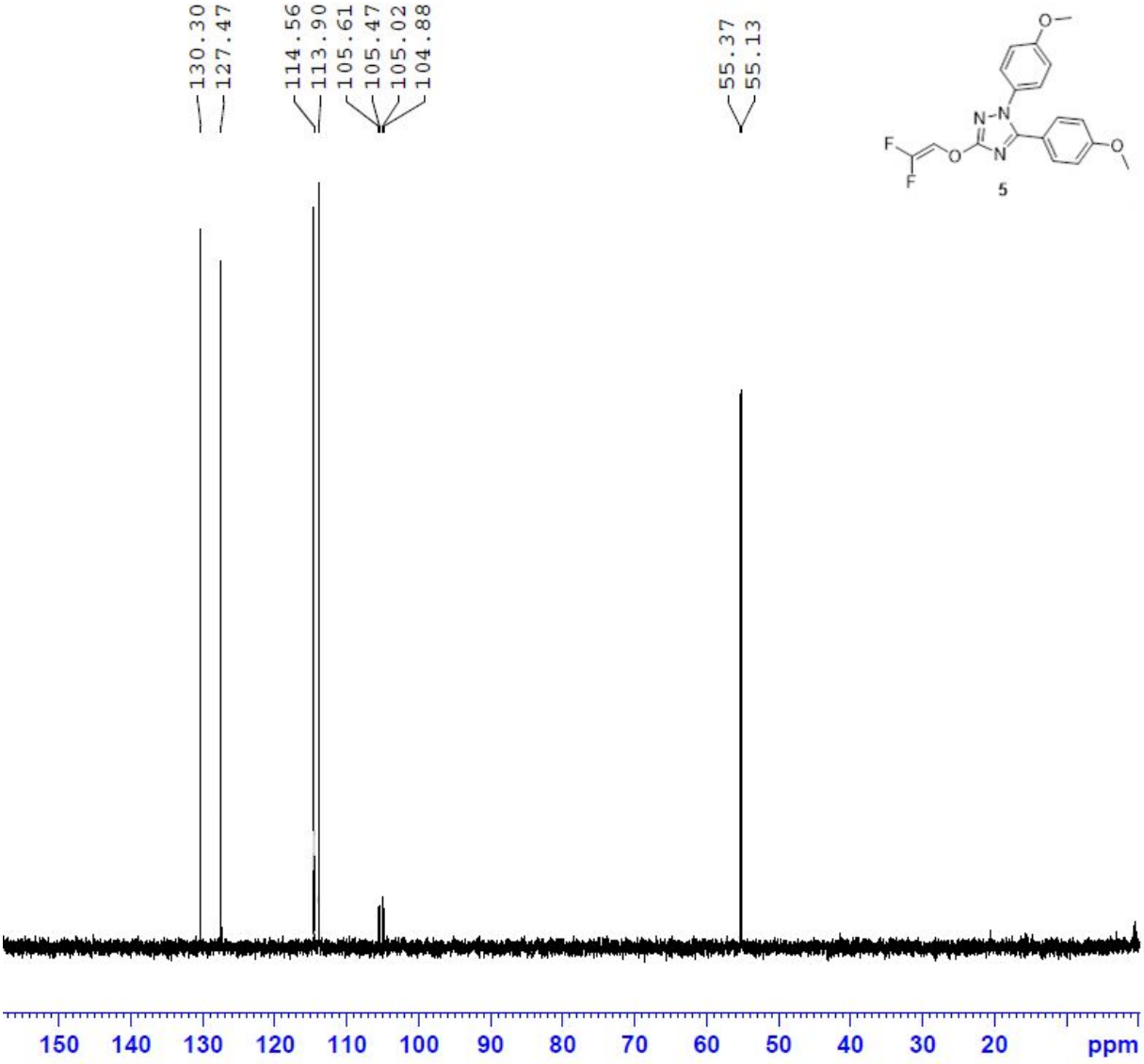

Figure S8. ^{13}C NMR (dept 135, $CDCl_3$) of *gem*-difluoroalkene, **5**.

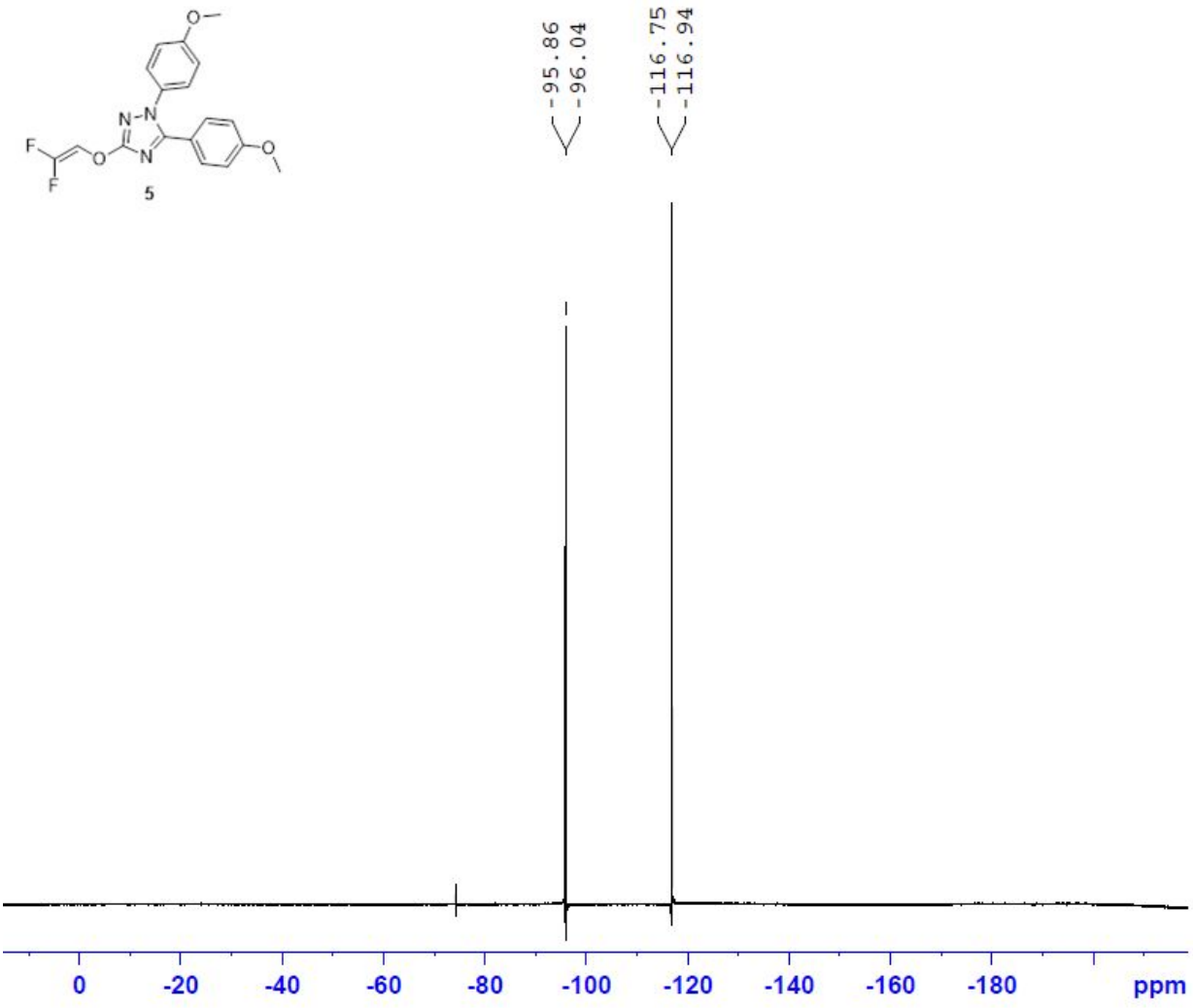

Figure S9. ^{19}F NMR ($CDCl_3$) of *gem*-difluoroalkene, **5**.