

Supporting Information

for

Synthesis, dynamic NMR characterization and XRD studies of novel *N,N'*-substituted piperazines for bioorthogonal labeling

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Email: Constantin Mamat - c.mamat@hzdr.de

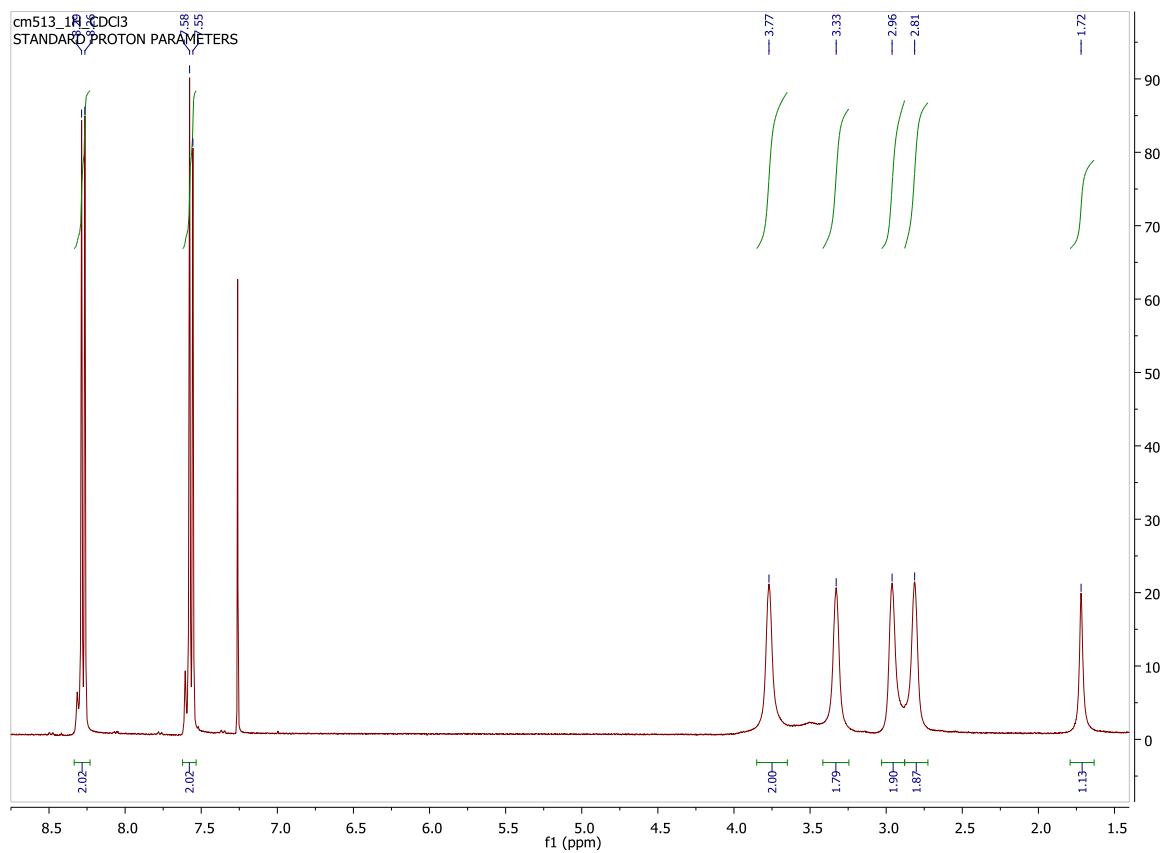
* Corresponding author

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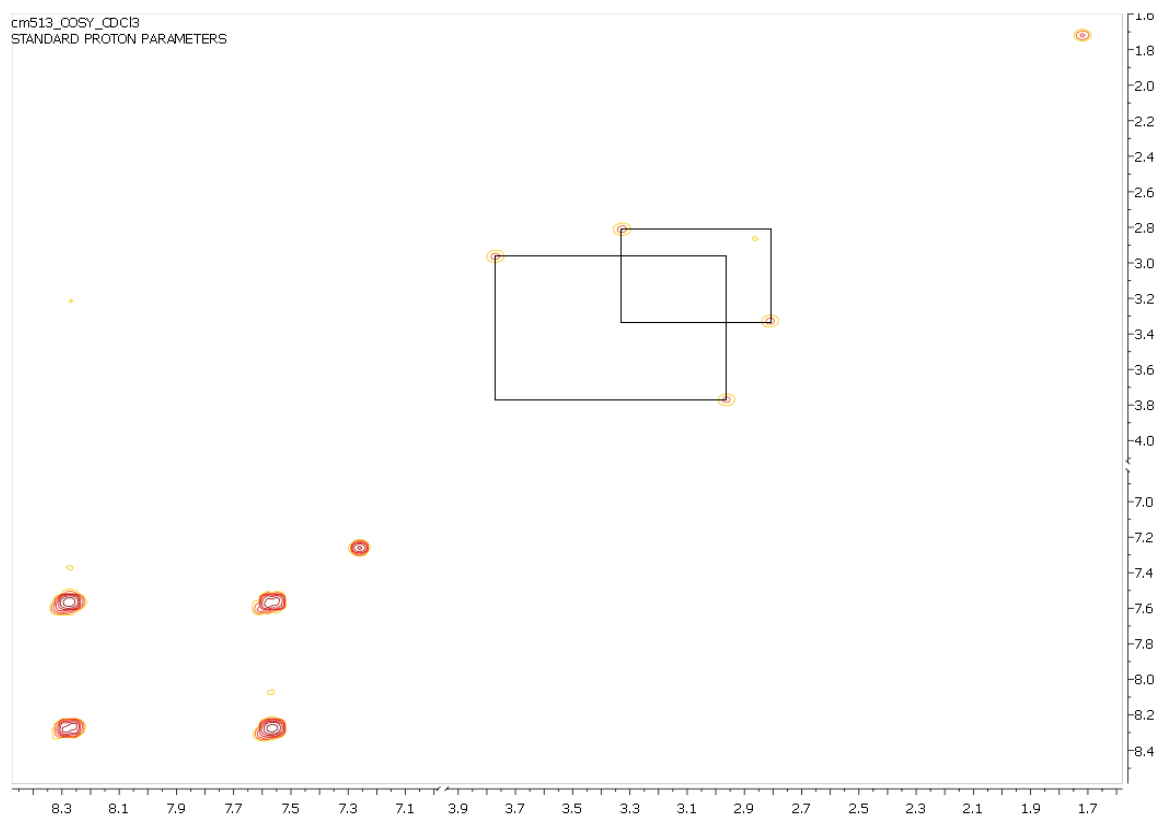
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NMR Spectra of compounds

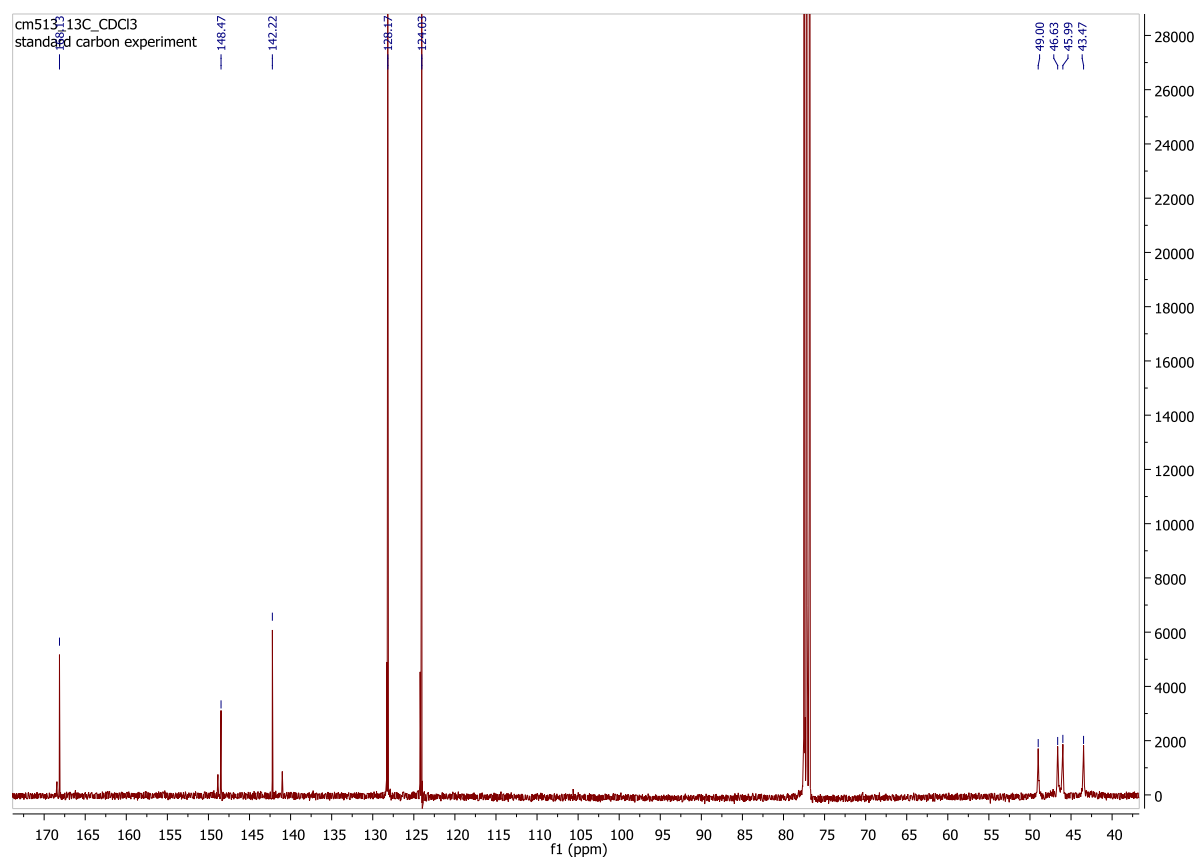
^1H NMR of compound **3a**



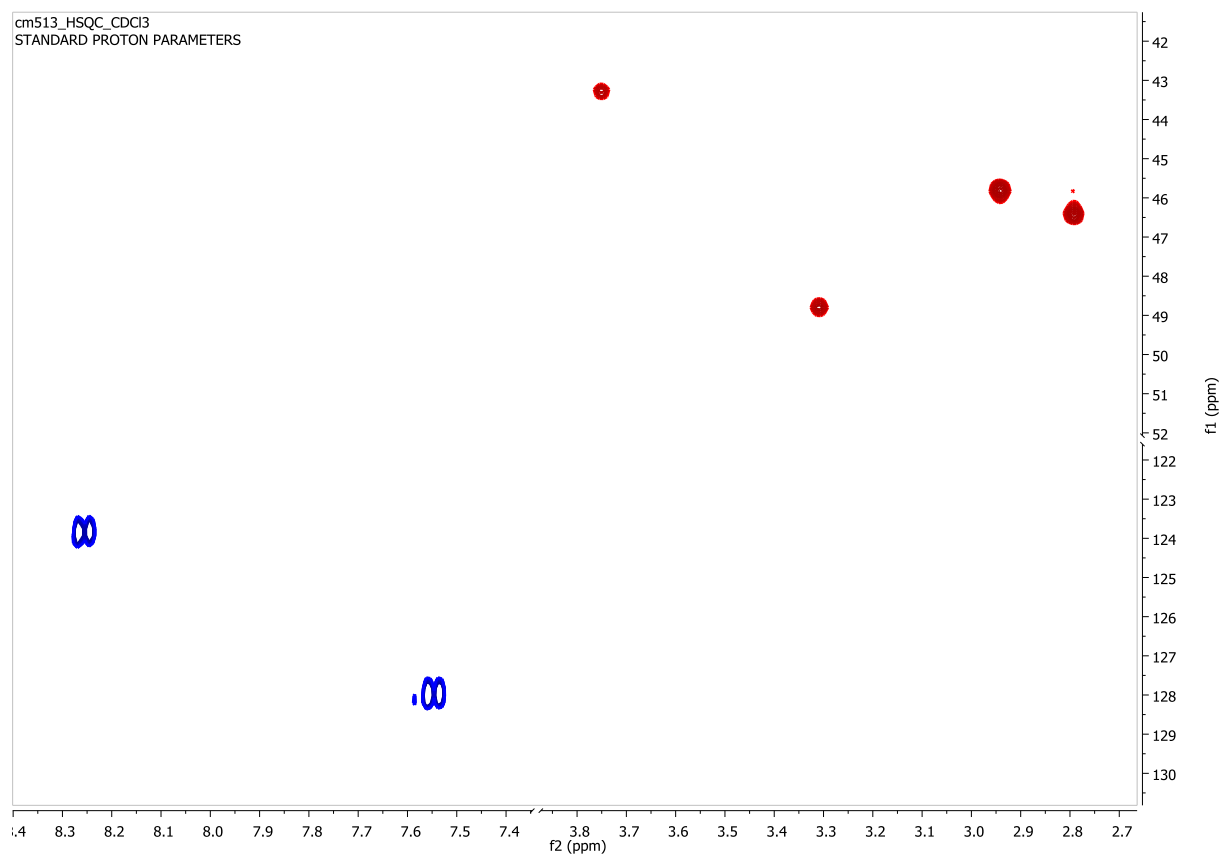
H,H-COSY of compound **3a**



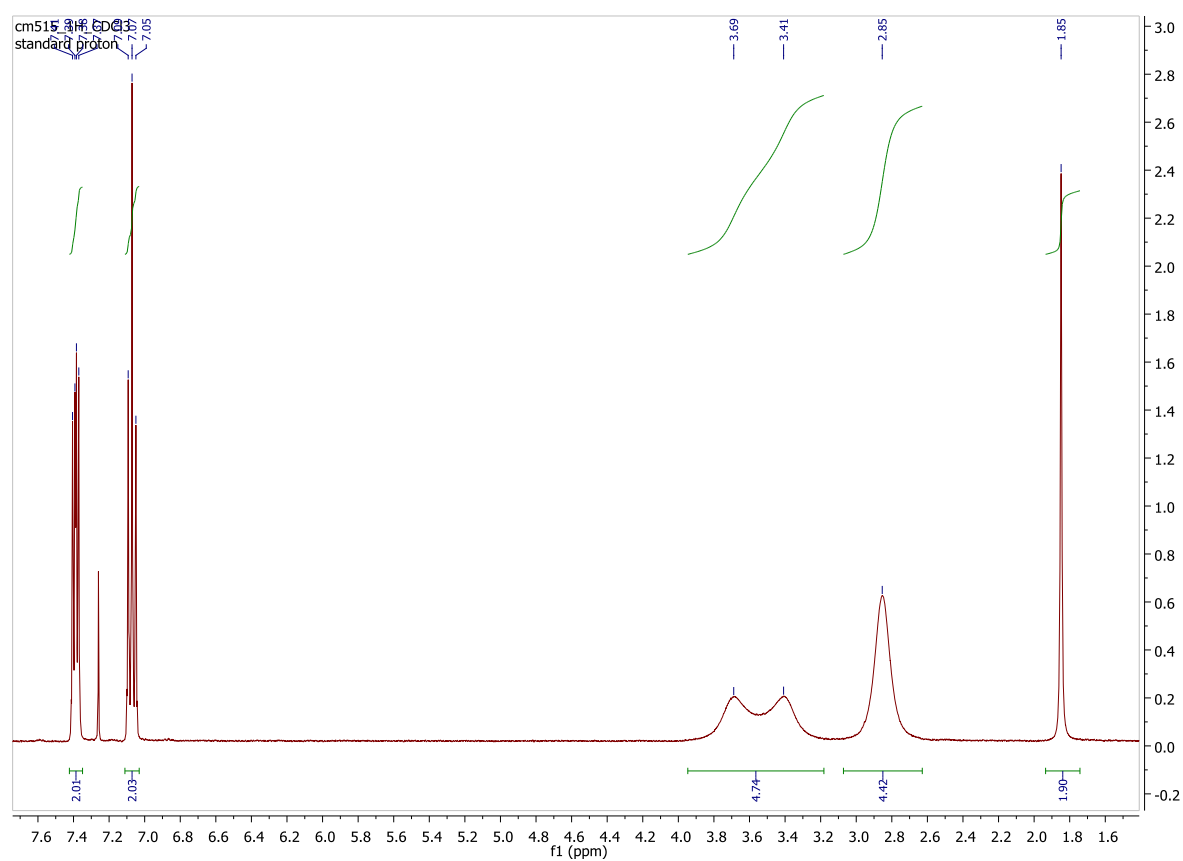
^{13}C NMR of compound **3a**



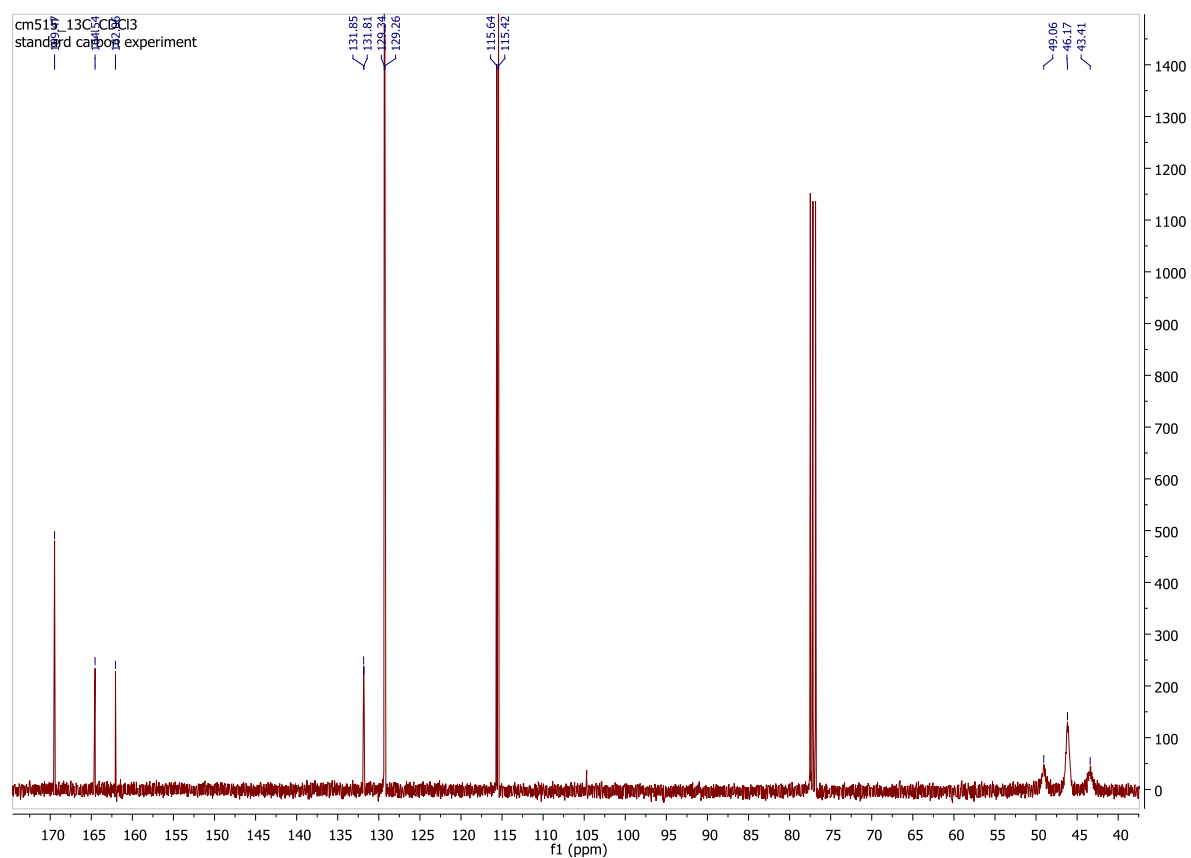
HSQC of compound **3a**



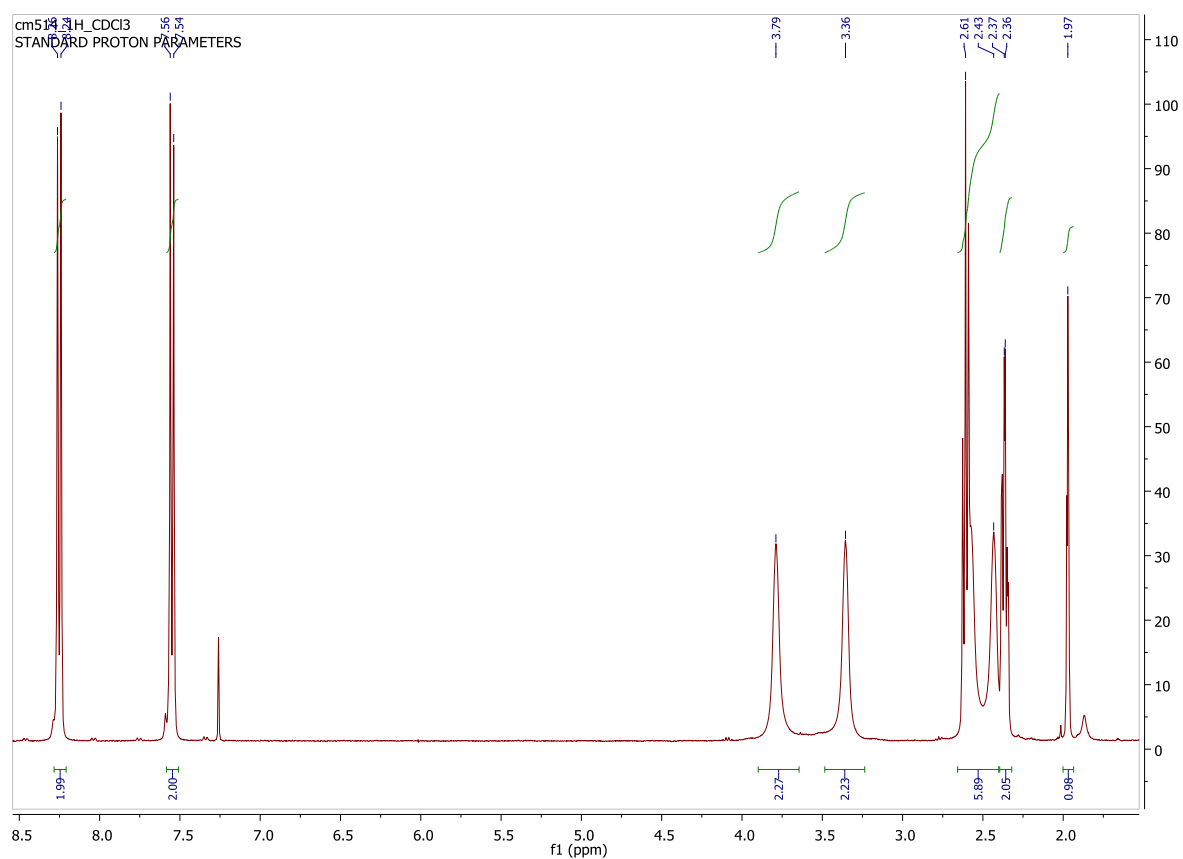
^1H NMR of compound **3b**



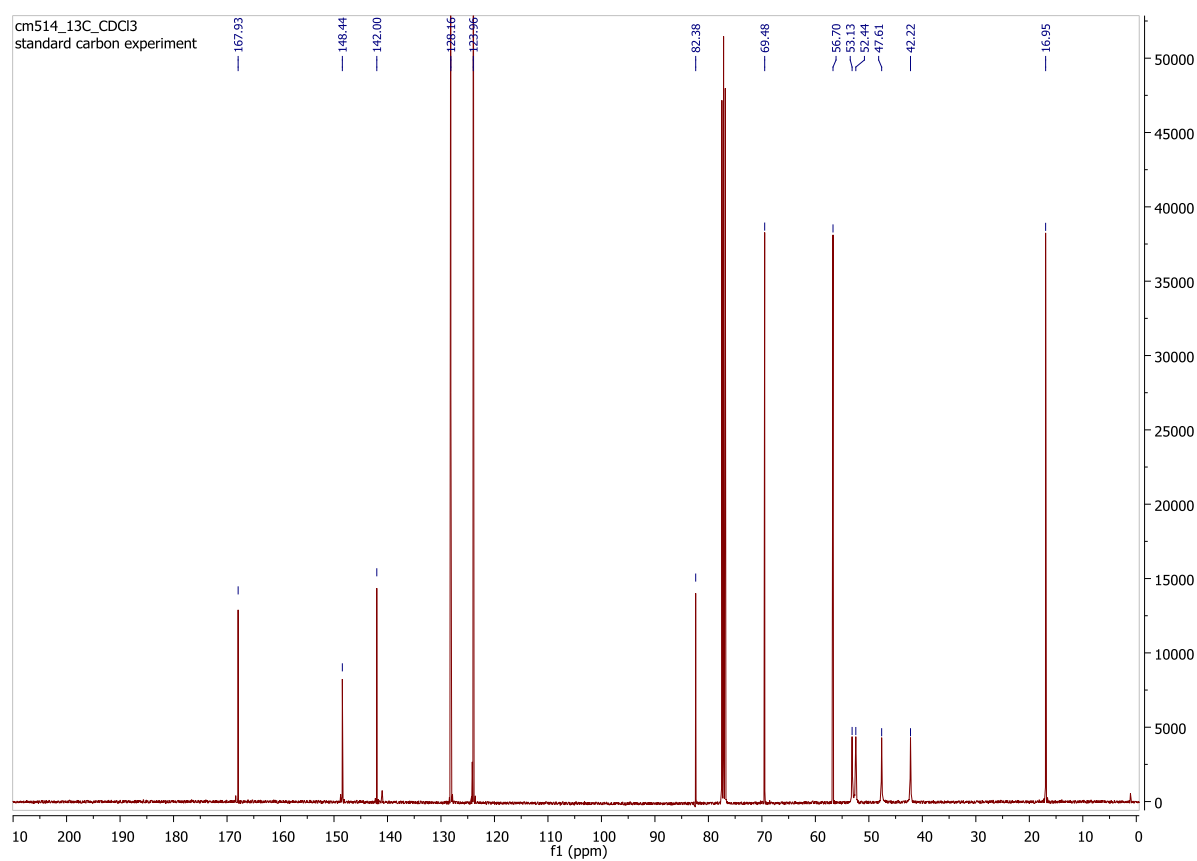
^{13}C NMR of compound **3b**



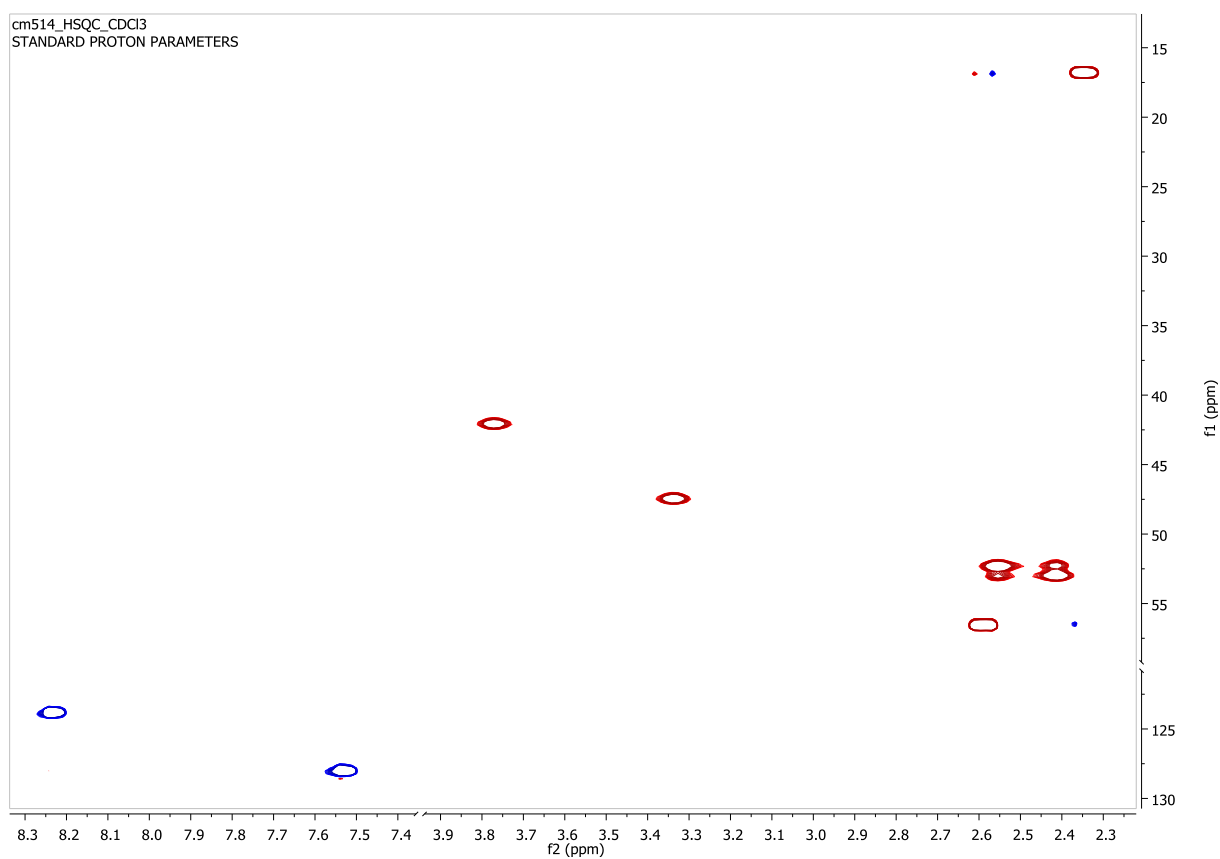
¹H NMR of compound **4a**



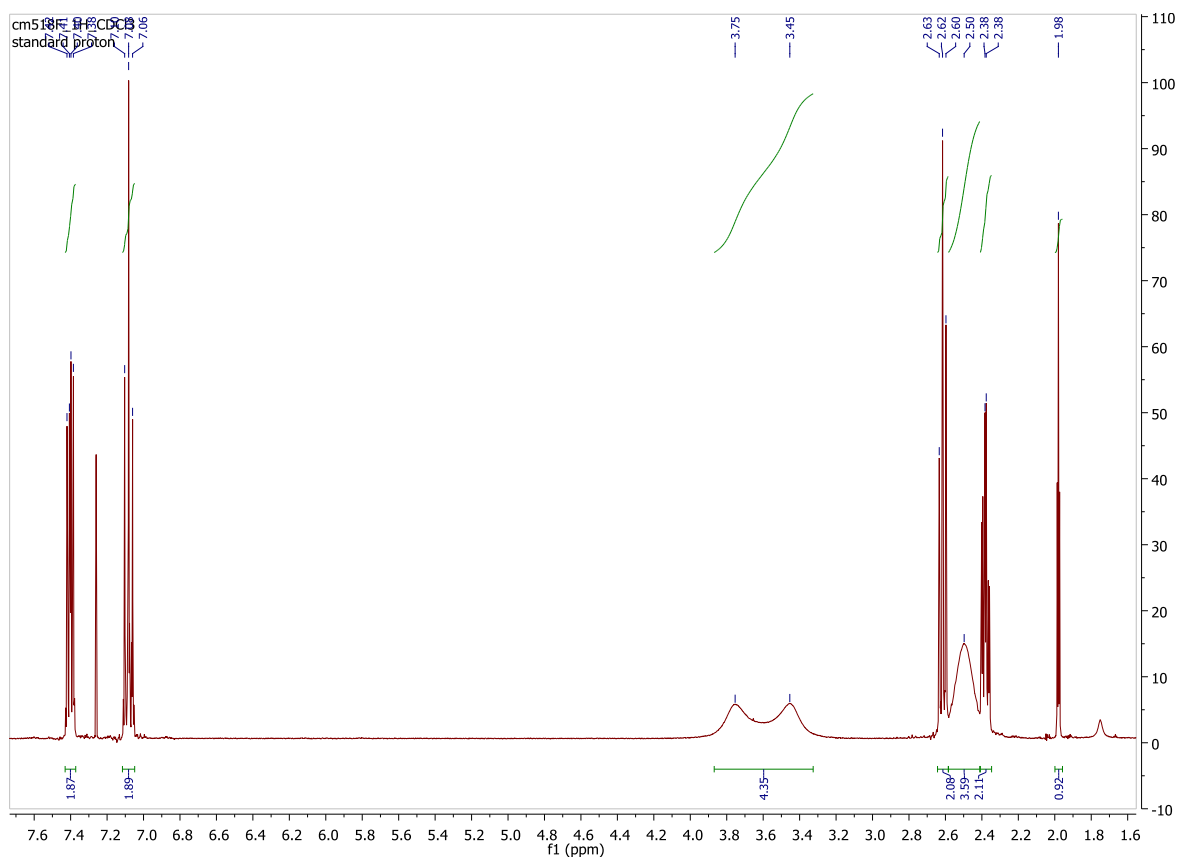
¹³C NMR of compound **4a**



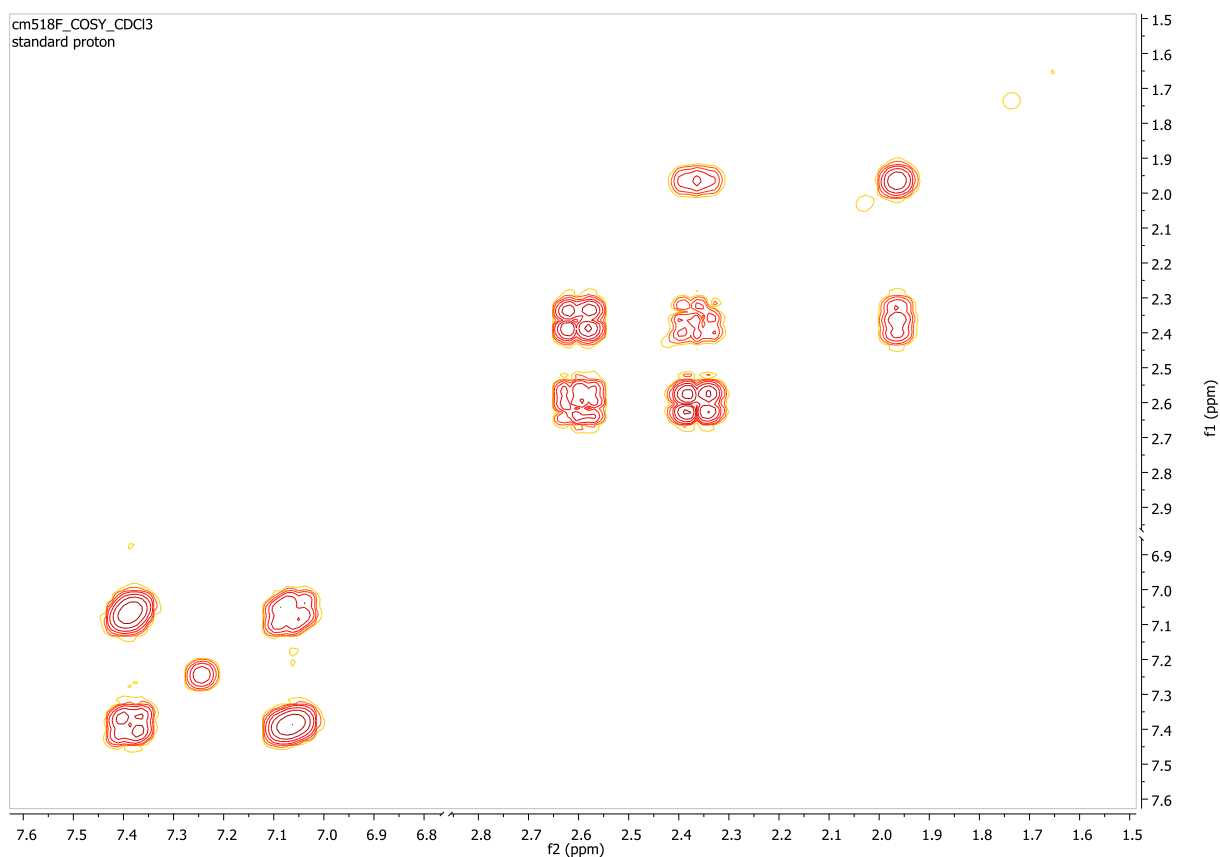
HSQC of compound **4a**



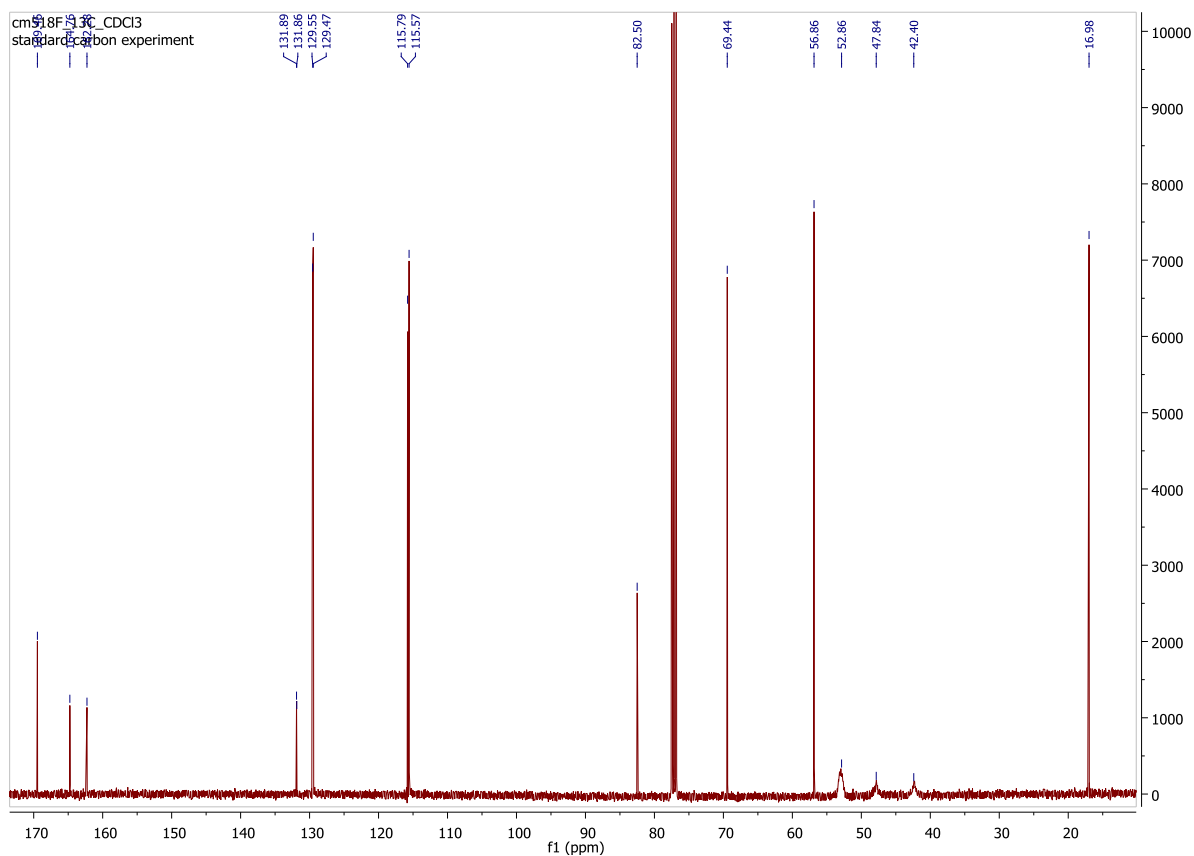
^1H NMR of compound **4b**



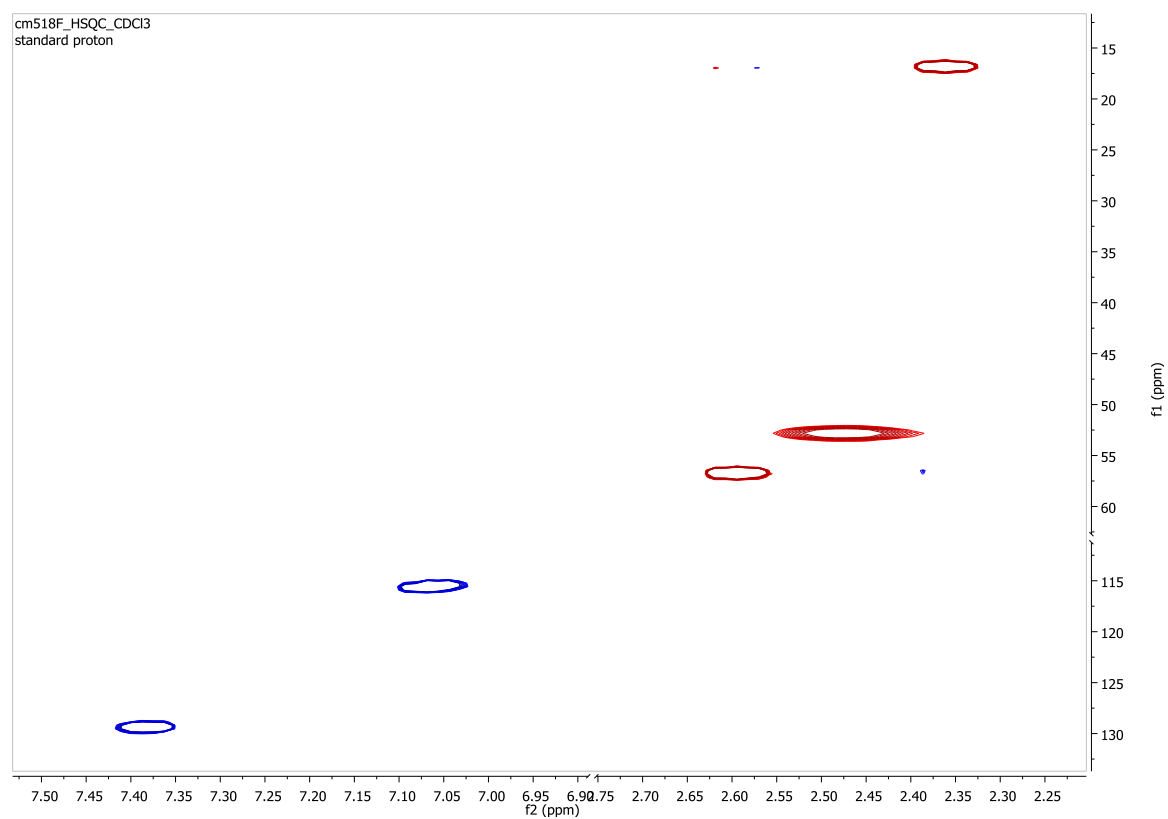
H,H-COSY of compound **4b**



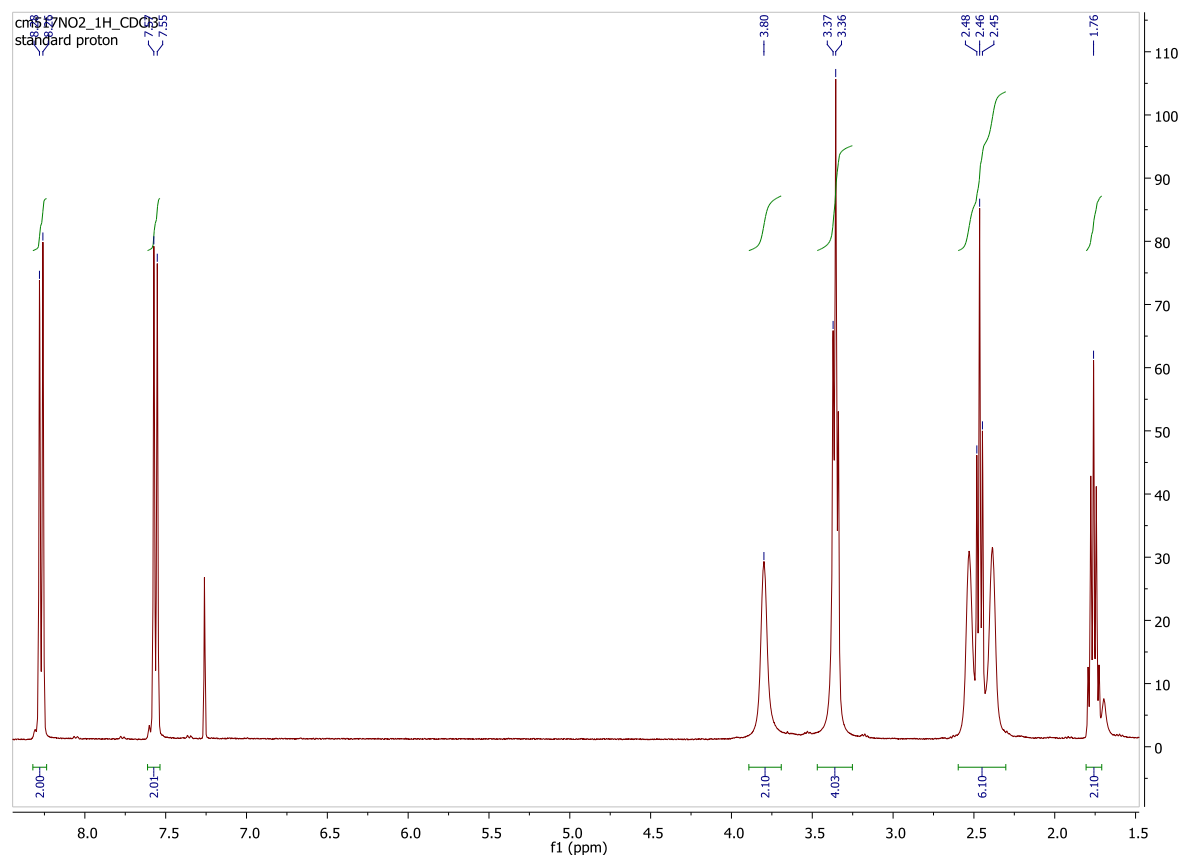
^{13}C NMR of compound **4b**



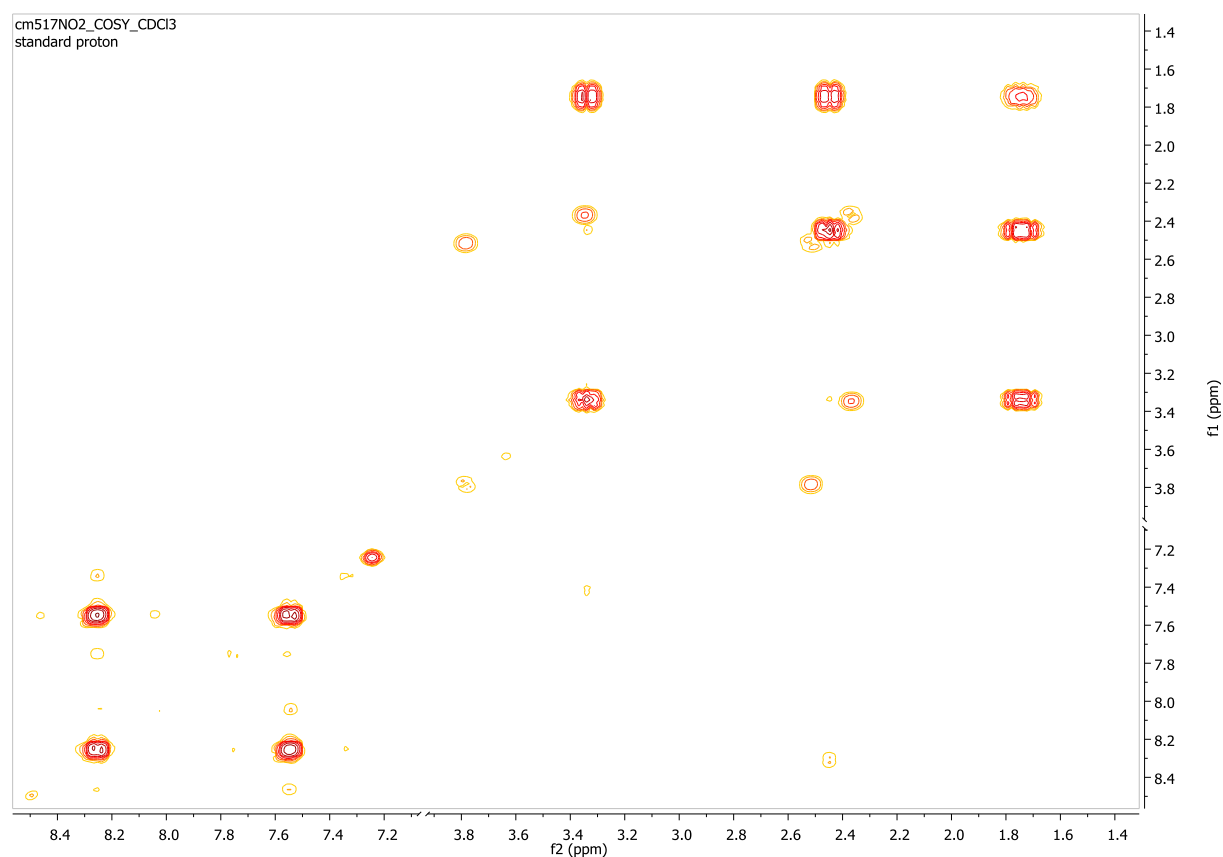
HSQC of compound **4b**



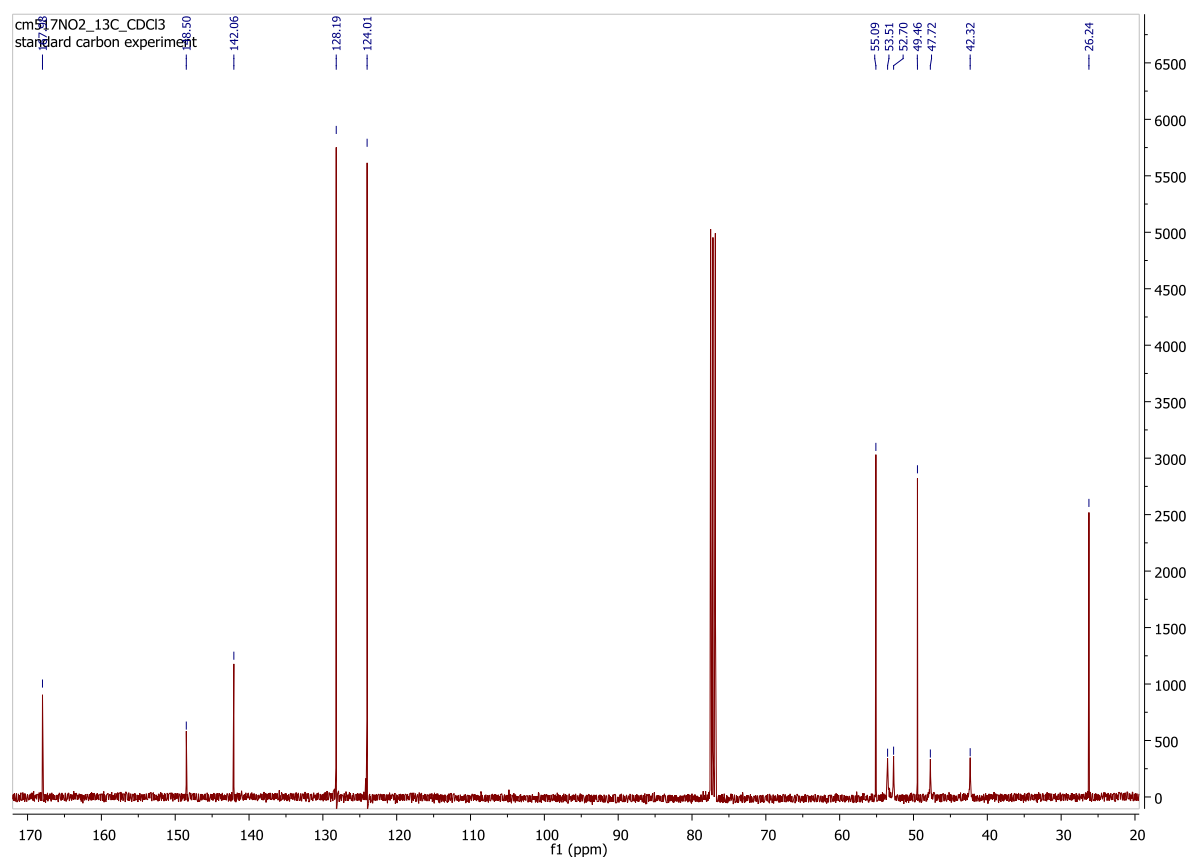
^1H NMR of compound **5a**



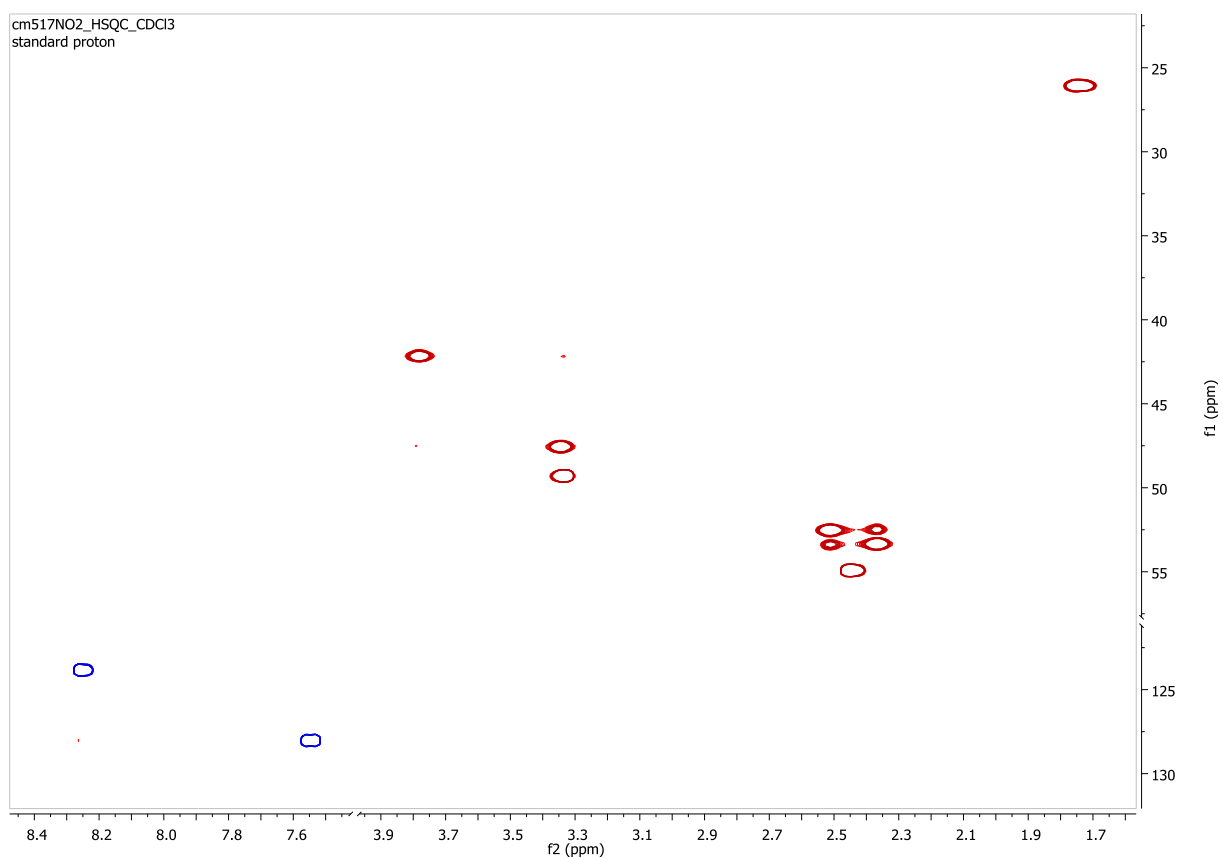
H,H-COSY of compound **5a**



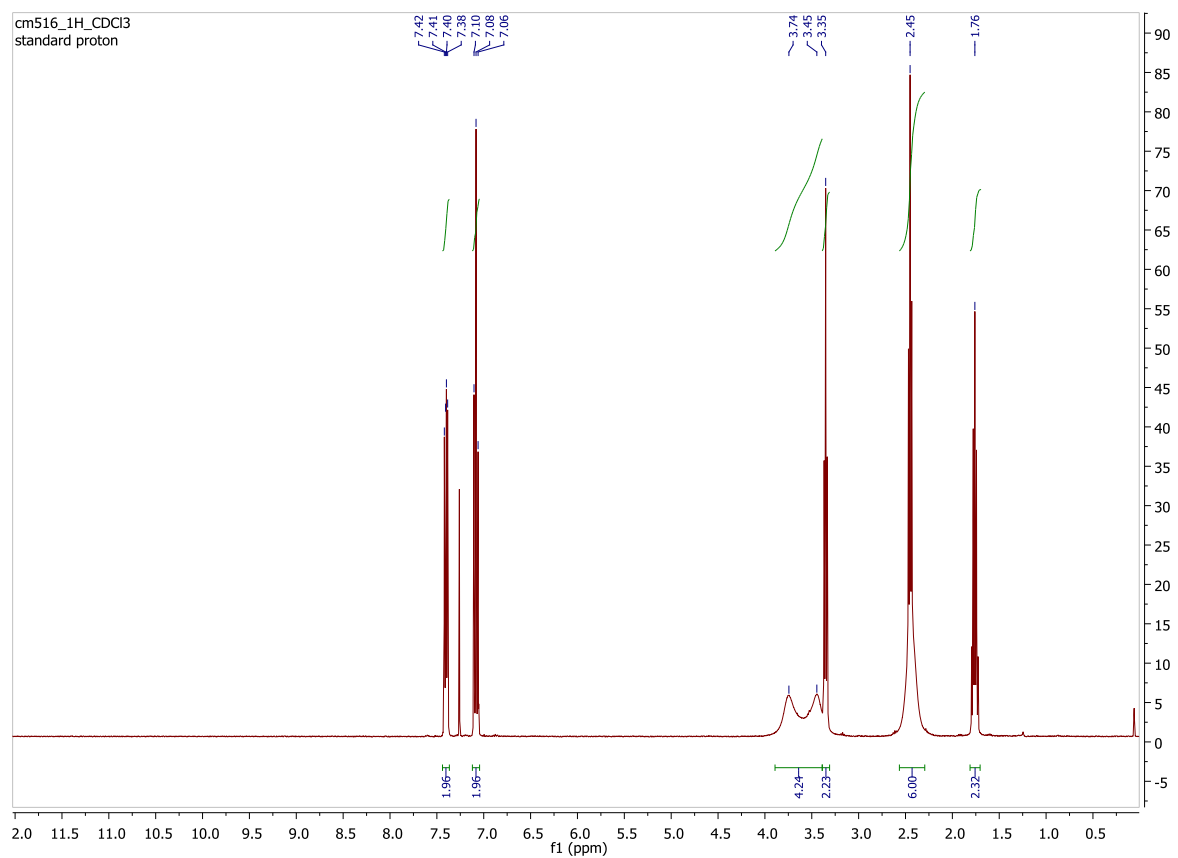
^{13}C NMR of compound **5a**



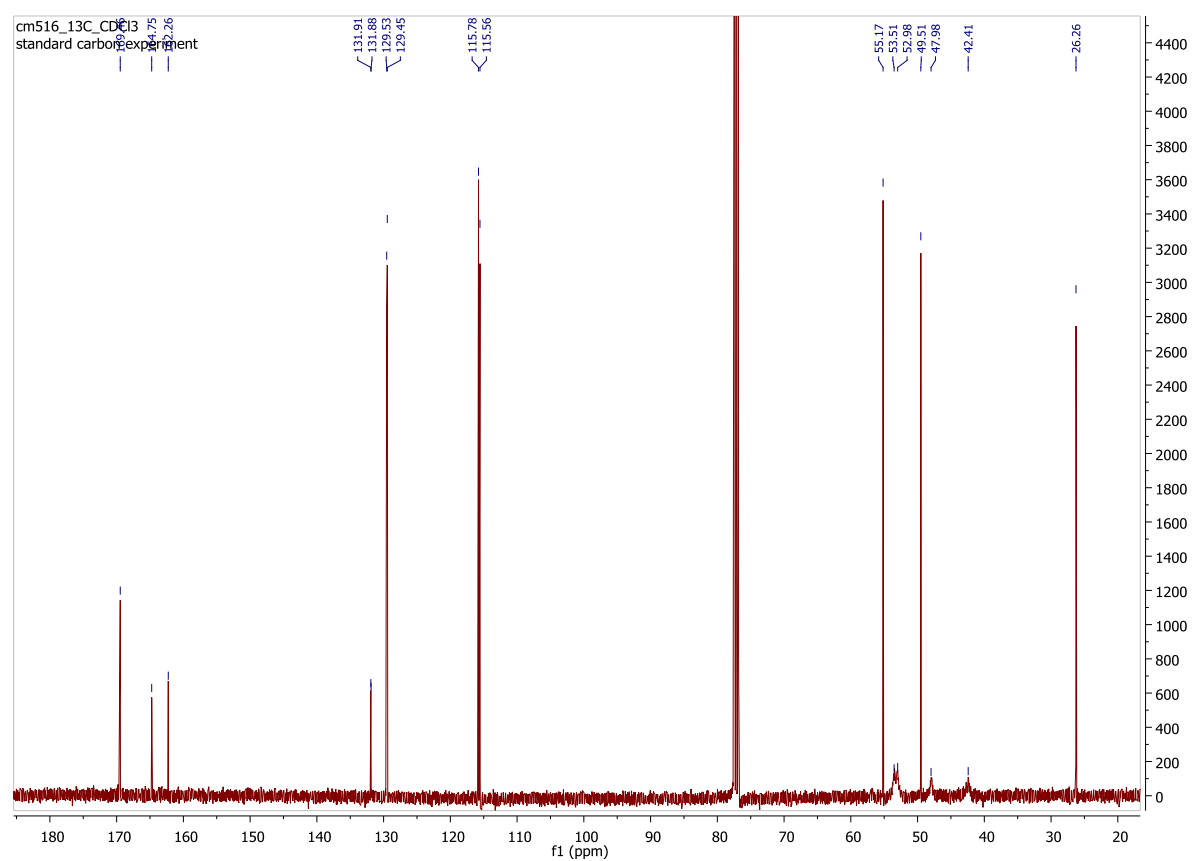
HSQC of compound **5a**



^1H NMR of compound **5b**

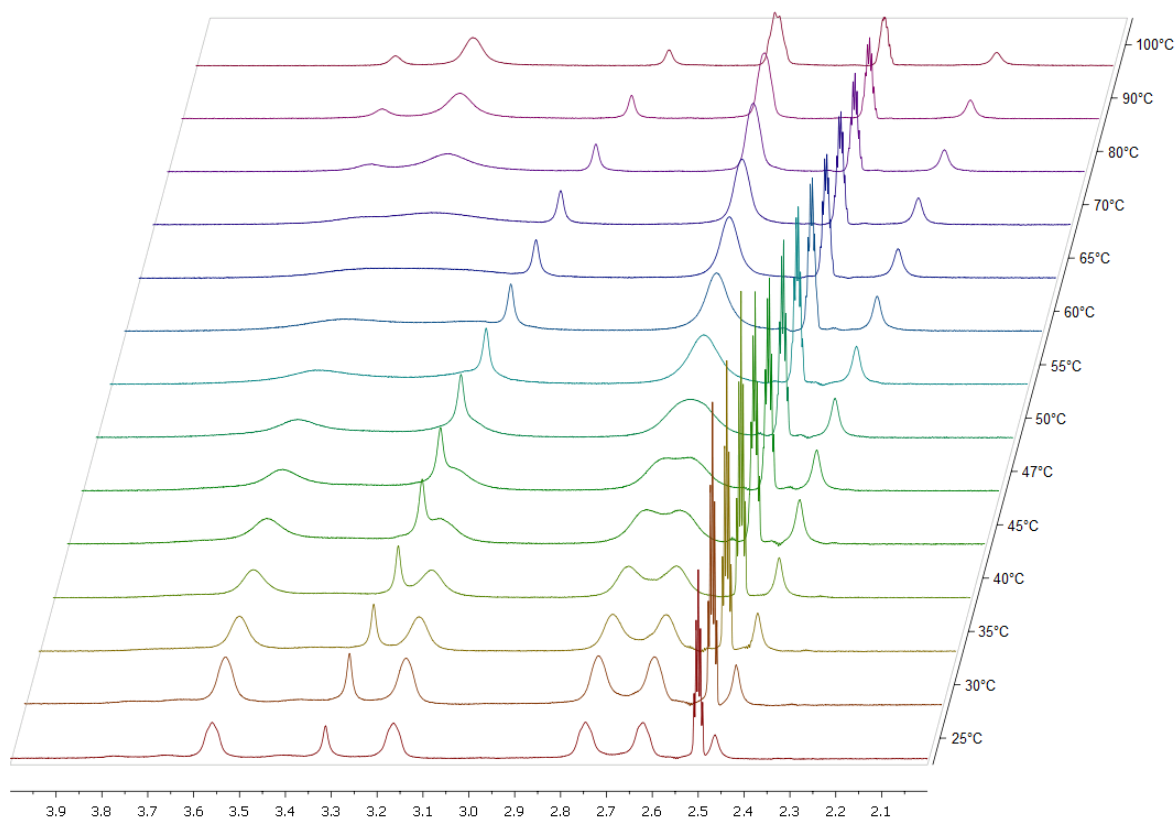


^{13}C NMR of compound **5b**

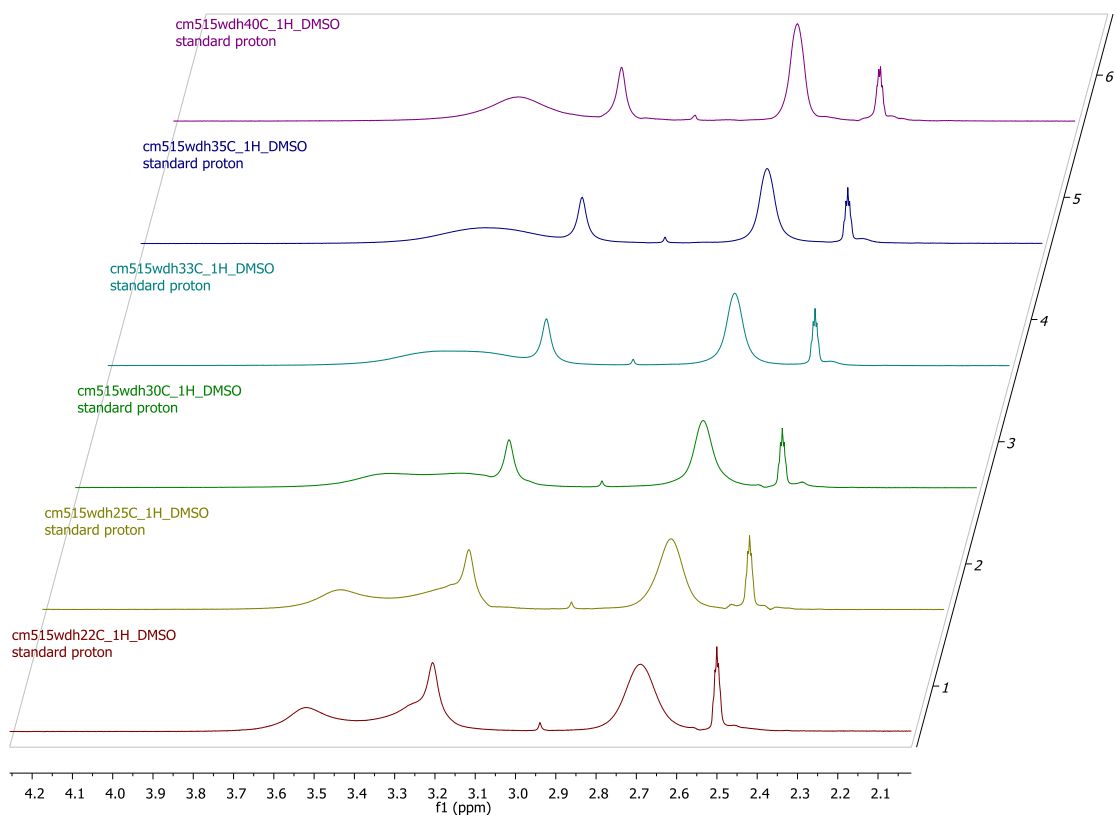


Dynamic NMR spectra

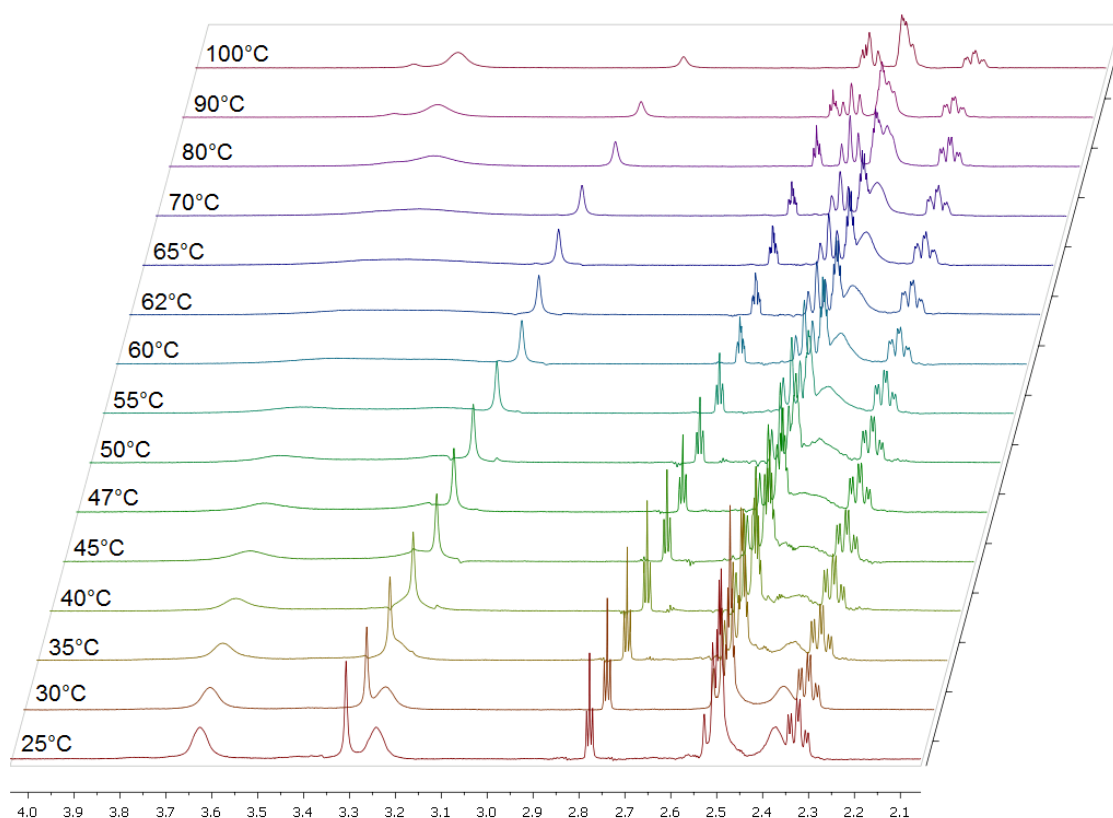
^1H NMR of **3a** measured at various temperatures (25–100 °C) in DMSO- d_6



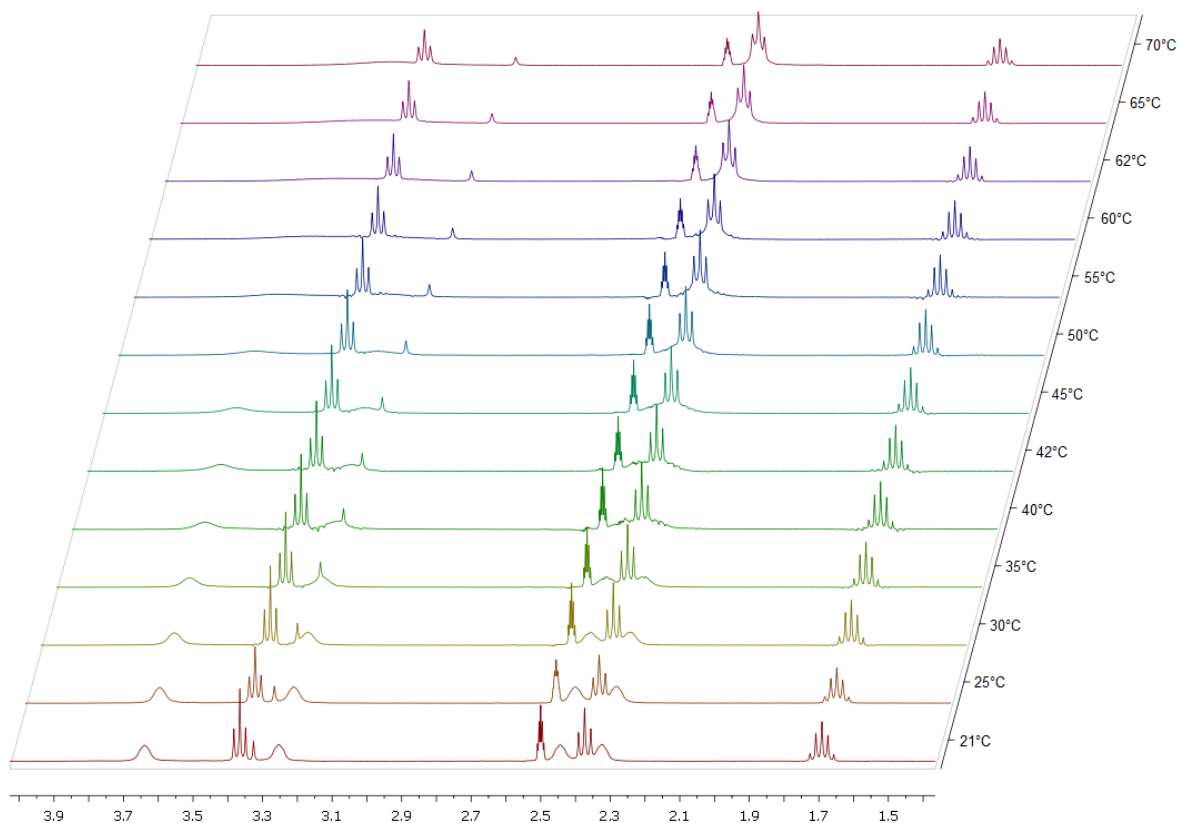
^1H NMR of **3b** measured at various temperatures (21–70 °C) in DMSO- d_6



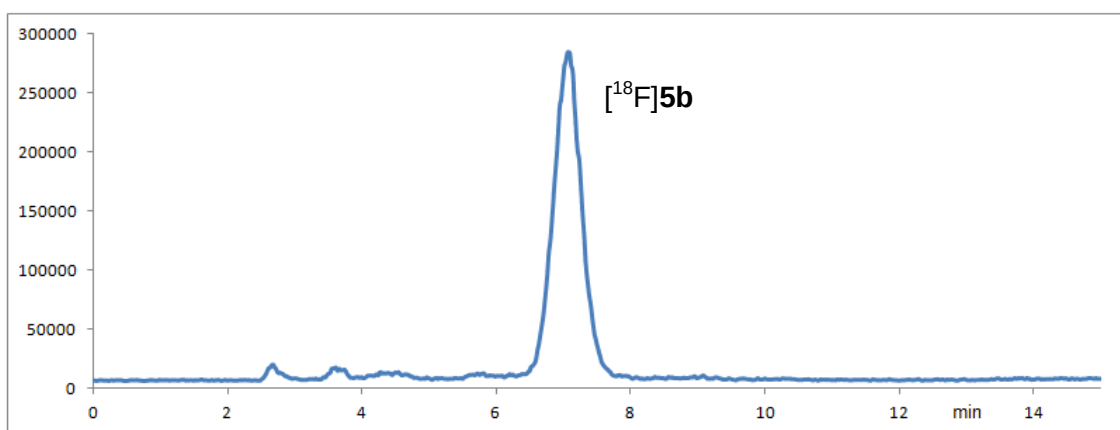
^1H NMR of **4a** measured at various temperatures (25–100 °C) in $\text{DMSO}-d_6$



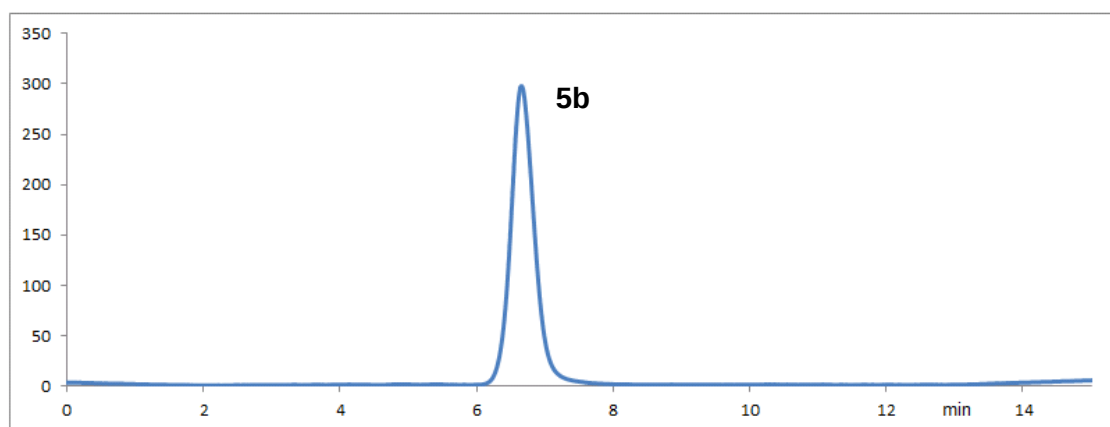
^1H NMR of **5a** measured at various temperatures (21–70 °C) in $\text{DMSO}-d_6$



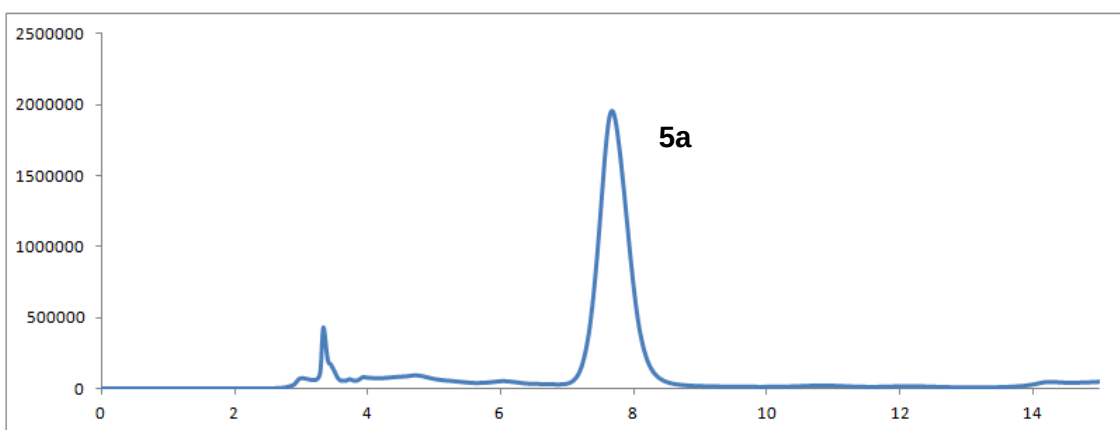
Radiochemical HPLC/TLC analyses



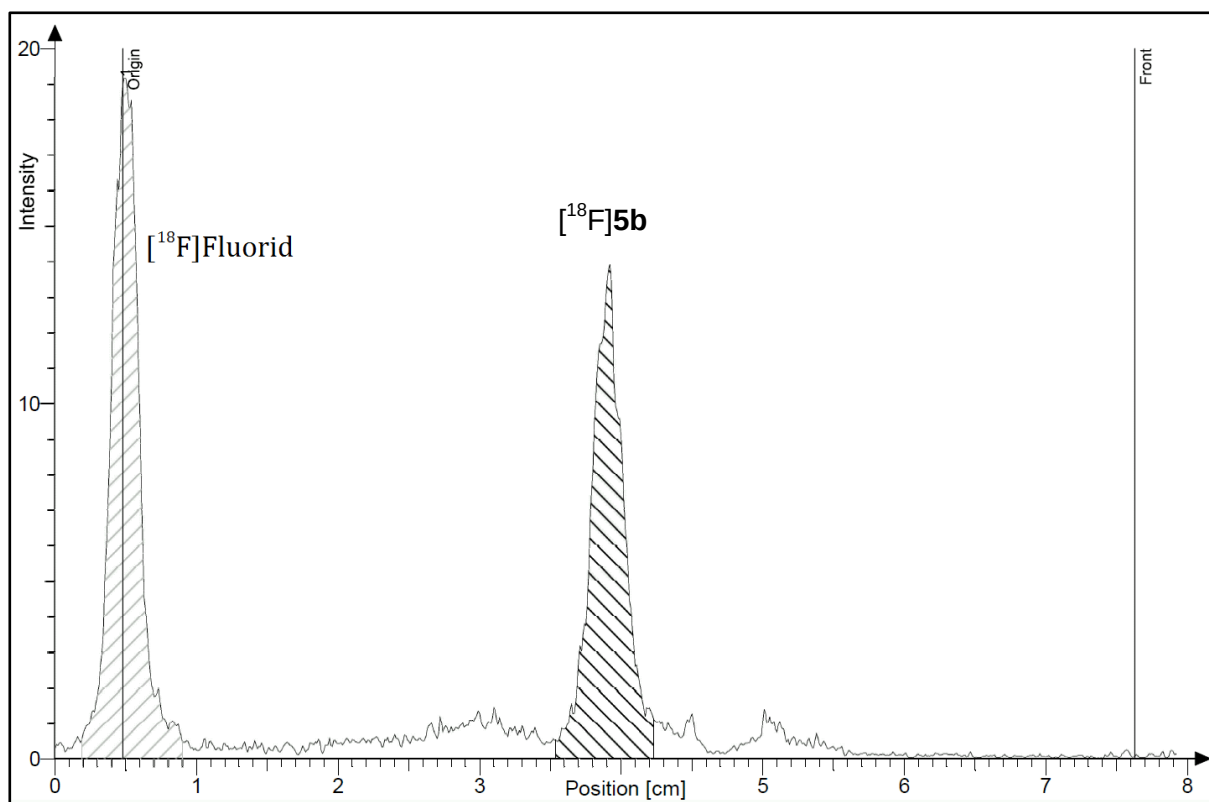
Radio-HPLC-chromatogram (γ -trace) of $[^{18}\text{F}]\mathbf{5b}$ ($t_R = 7.1$ min).



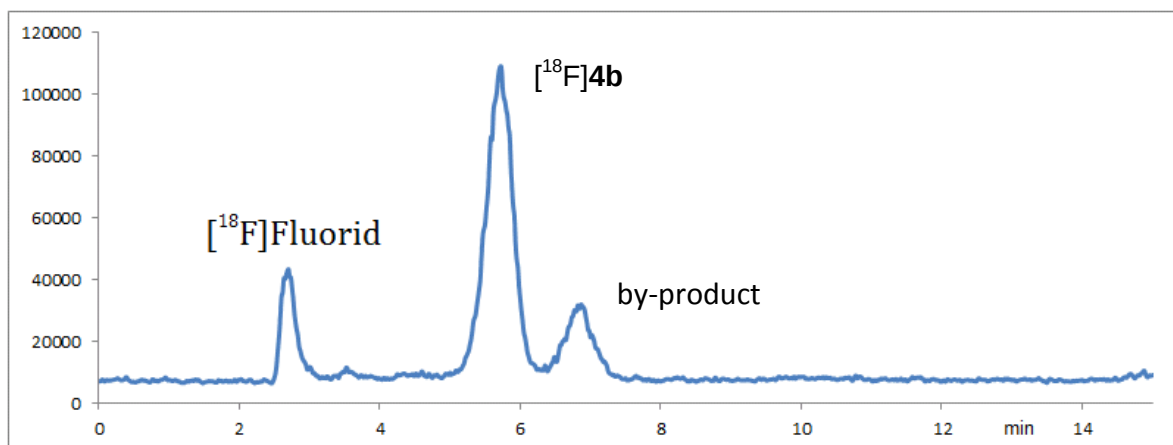
HPLC-chromatogram (UV-trace) of $\mathbf{5b}$ ($t_R = 6.7$ min).



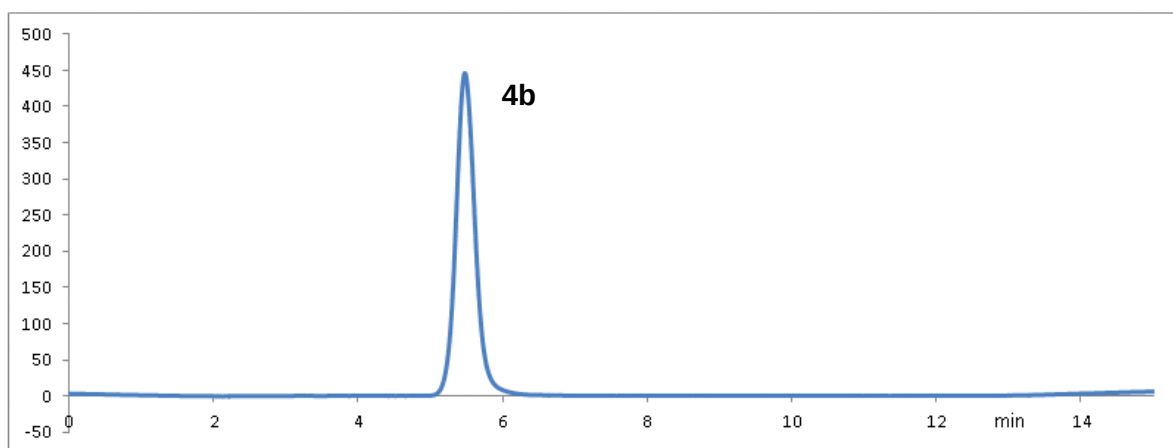
HPLC-chromatogram (UV-trace) of $\mathbf{5a}$ ($t_R = 7.7$ min).



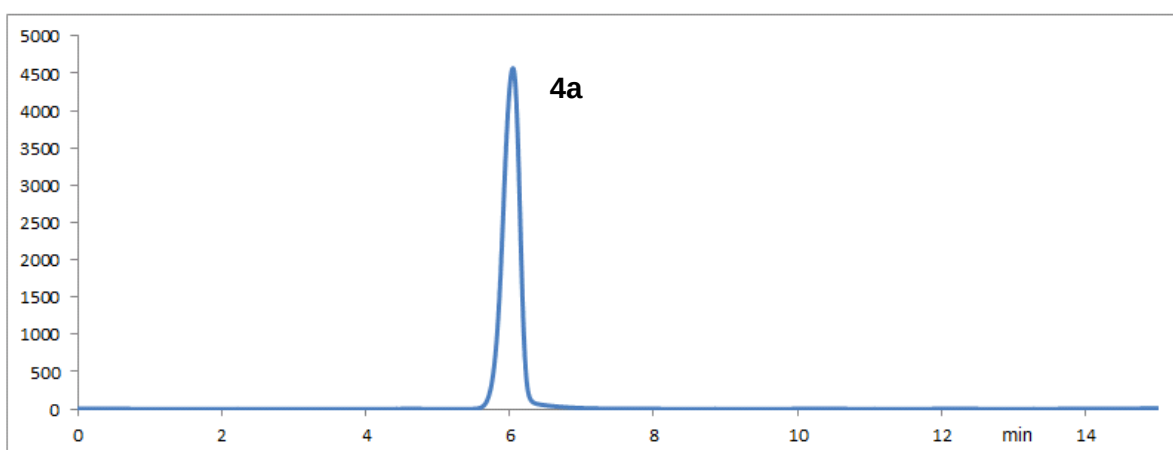
Radio-TLC (reaction mixture) of labeling of [¹⁸F]**5b** $R_f = 0.49$ (ethanol).



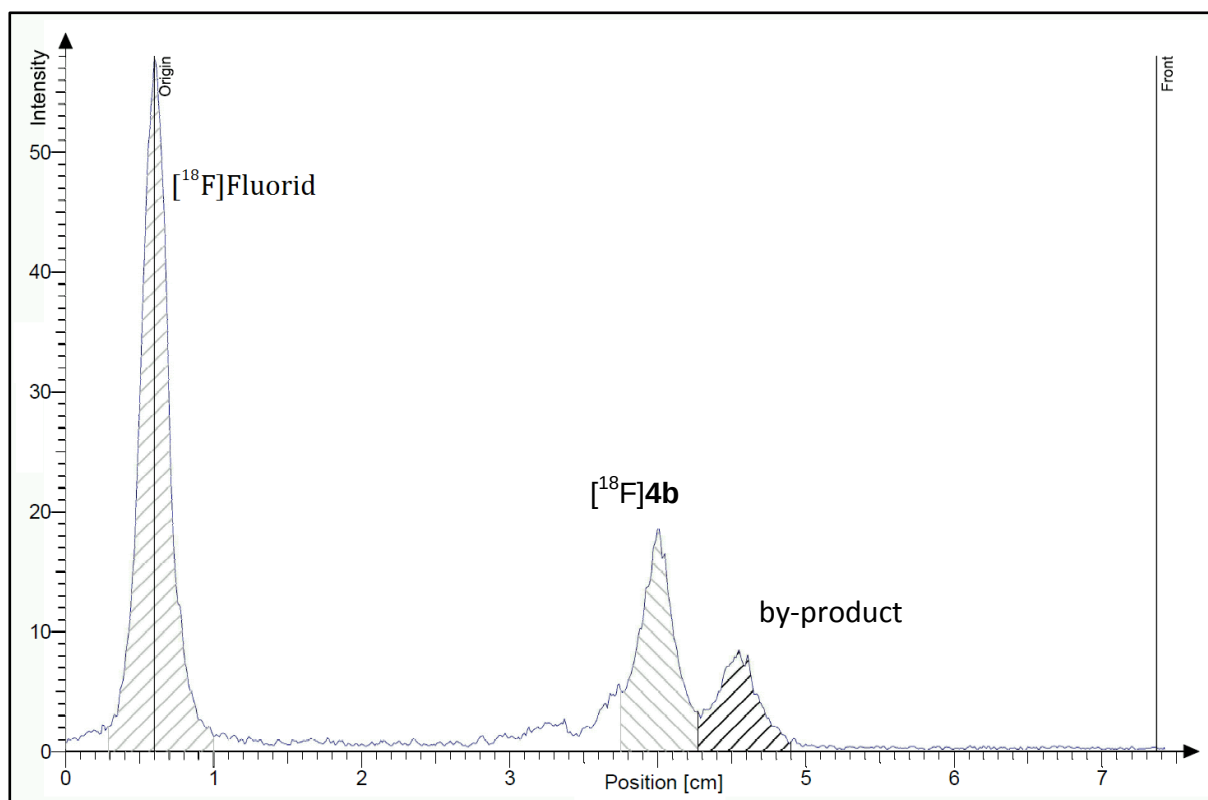
Radio-HPLC-chromatogram (γ -trace) of $[^{18}\text{F}]\mathbf{4b}$ ($t_R = 5.7$ min), the unknown byproduct ($t_R = 6.9$ min) and remaining $[^{18}\text{F}]\text{fluoride}$ ($t_R = 2.7$ min).



HPLC-chromatogram (UV-trace) of reference compound **4b** ($t_R = 5.5$ min).



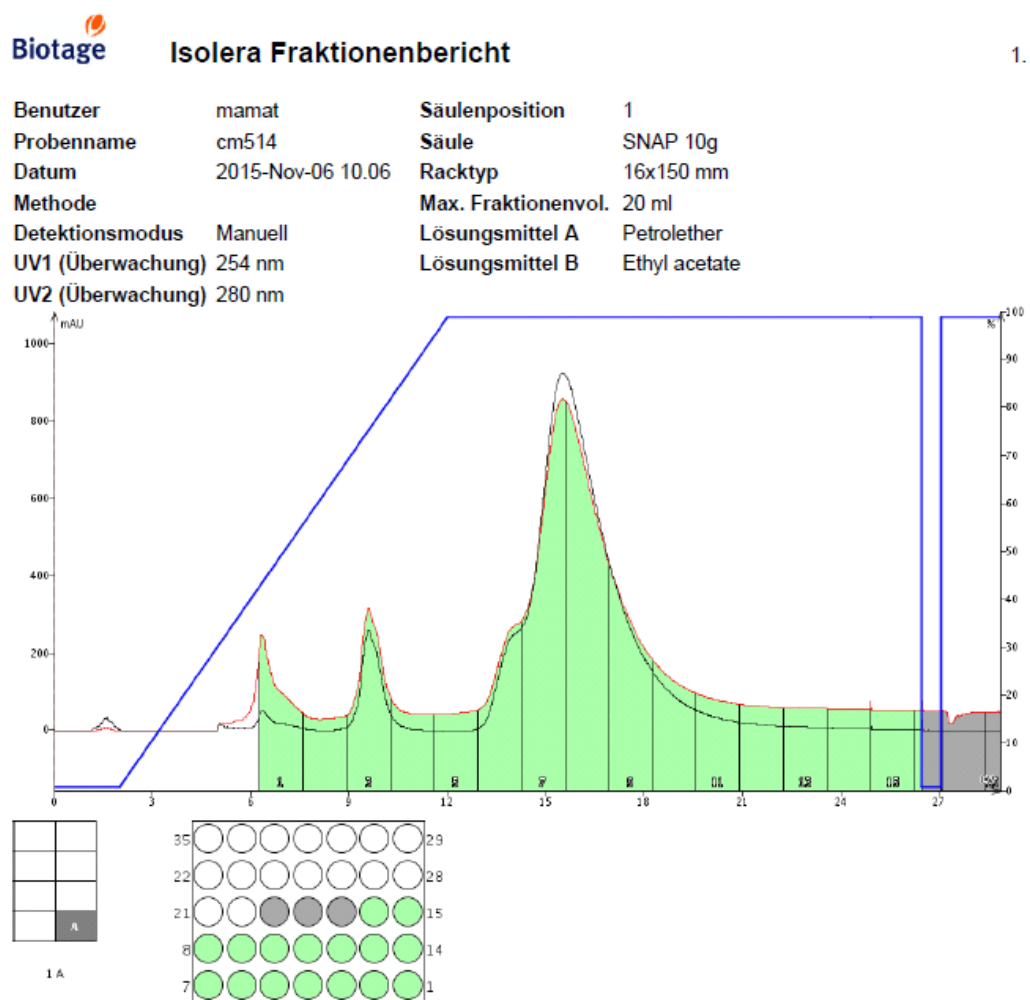
HPLC-chromatogram (UV-trace) of precursor **4a** ($t_R = 6.0$ min).*



Radio-TLC (reaction mixture) of labeling of [¹⁸F]**4b** ($R_f = 0.50$ in ethanol).

Chromatographic purifications of compounds 4a, 4b, 5a and 5b using Biotage

Biotage-chromatogram of compound 4a



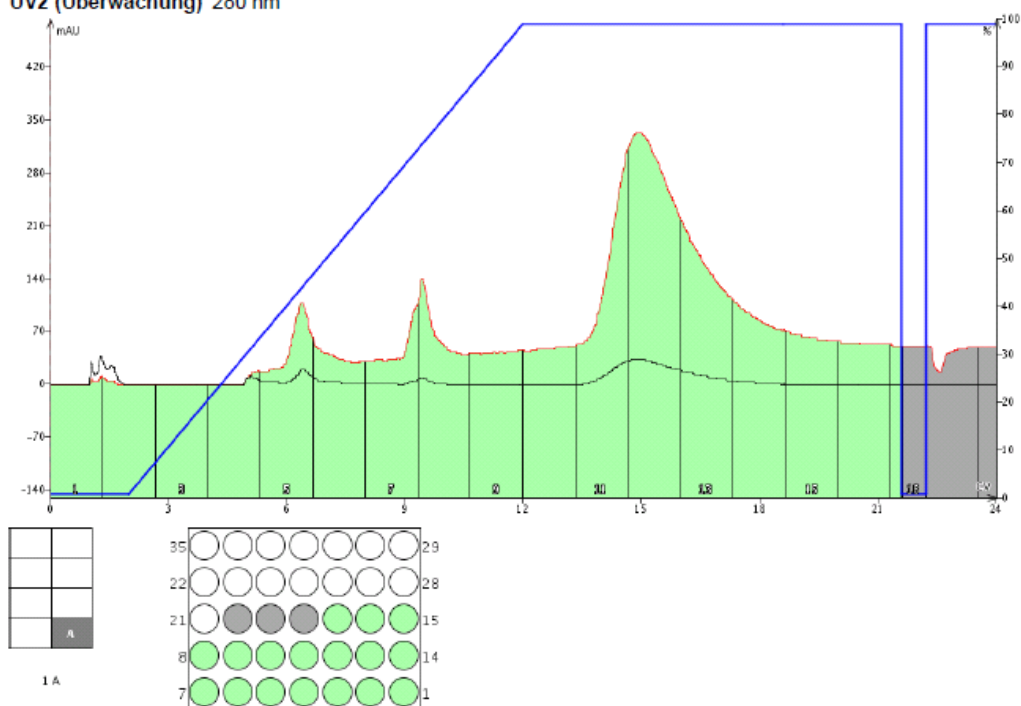
Biotage-chromatogram of 4b



Isolera Fraktionenbericht

1.

Benutzer	mamat	Säulenposition	1
Probenname	cm518 F	Säule	SNAP 10g
Datum	2015-Nov-19 11.09	Racktyp	16x150 mm
Methode	cm515	Max. Fraktionenvol.	20 ml
Detektionsmodus	Manuell	Lösungsmittel A	Petrolether
UV1 (Überwachung)	254 nm	Lösungsmittel B	Ethyl acetate
UV2 (Überwachung)	280 nm		



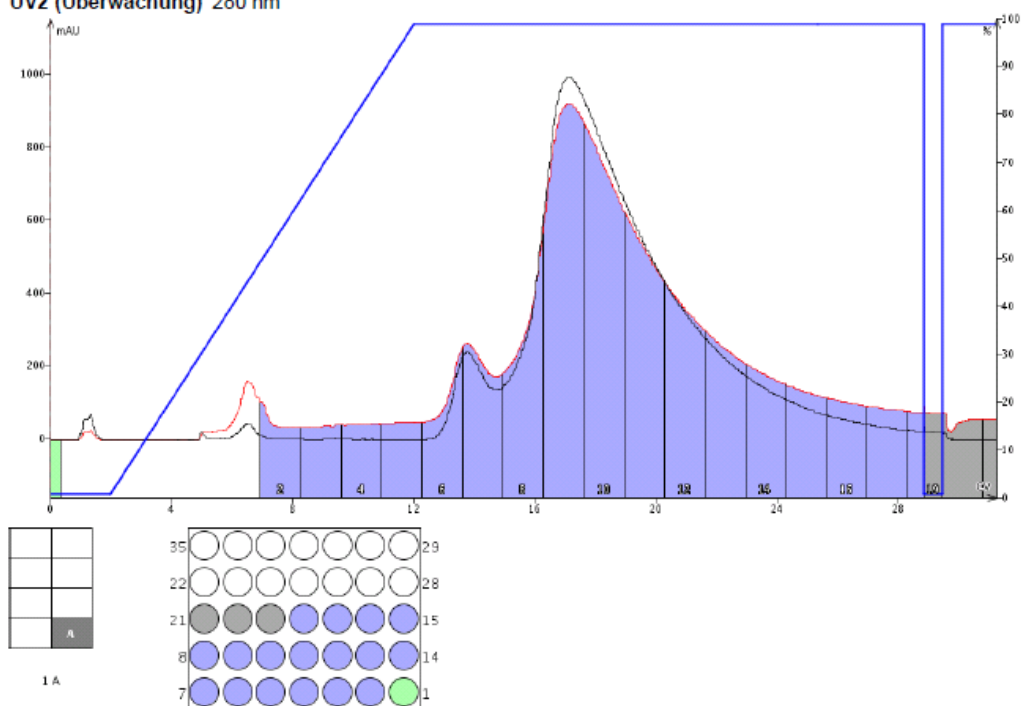
Biotage-chromatogram of 5a



Isolera Fraktionenbericht

1.

Benutzer	mamat	Säulenposition	1
Probenname	cm517 NO2	Säule	SNAP 10g
Datum	2015-Nov-19 09.24	Racktyp	16x150 mm
Methode	cm515	Max. Fraktionenvol.	20 ml
Detektionsmodus	Manuell	Lösungsmittel A	Petrolether
UV1 (Überwachung)	254 nm	Lösungsmittel B	Ethyl acetate
UV2 (Überwachung)	280 nm		



Biotage-chromatogram of **5b**



Isolera Fraktionenbericht

1.

Benutzer	mamat	Säulenposition	1
Probenname	cm515	Säule	SNAP 10g
Datum	2015-Nov-12 10.18	Racktyp	16x150 mm
Methode	cm515	Max. Fraktionenvol.	20 ml
Detektiionsmodus	Manuell	Lösungsmittel A	Petrolether
UV1 (Überwachung)	254 nm	Lösungsmittel B	Ethyl acetate
UV2 (Überwachung)	280 nm		

