

# SUPPORTING INFORMATION

## MCR scaffolds get hotter with <sup>18</sup>F- Labeling

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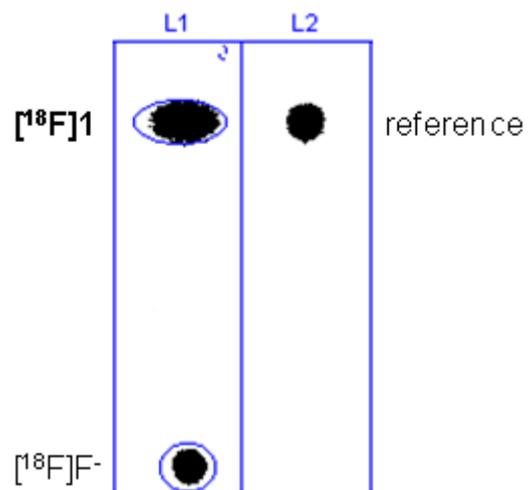
<sup>2</sup> Department of Nuclear Medicine and Molecular Imaging, University Medical Center Groningen, University of Groningen, The Netherlands

\* Correspondence: p.h.elsinga@umcg.nl (P.H.E); a.s.s.domling@rug.nl.com (A.D.)

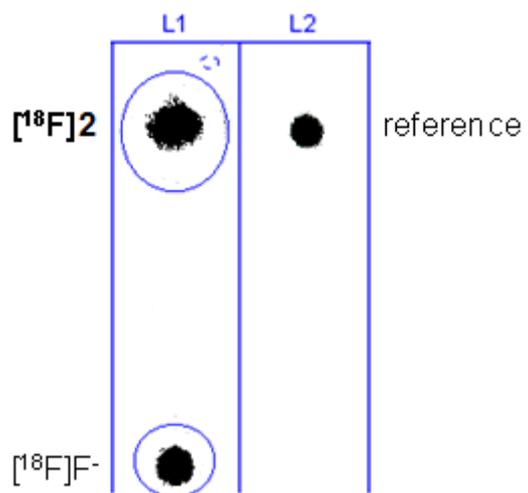
† These authors contributed equally to this paper.

### Table of contents

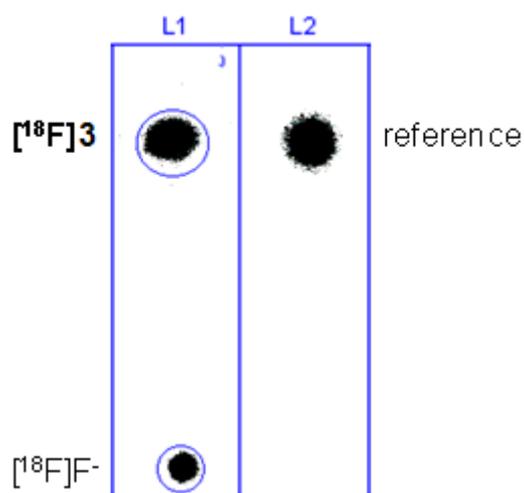
Figure S1 to Figure S13: Examples of the radio-TLCs	2
Table S1. TLC-SG retention factor (R <sub>f</sub> ) profiles for the tested compounds	8
Figure S14: Effect of temperature in RCC of [ <sup>18</sup> F]1	9
Scheme S1: Recent late-stage strategies for the <sup>18</sup> F-fluorination of (hetero)arenes	10
Scheme S2: Proposed mechanism for copper-mediated oxidative <sup>18</sup> F-fluorination of aryl boronic esters	11
Spectra of compounds	12



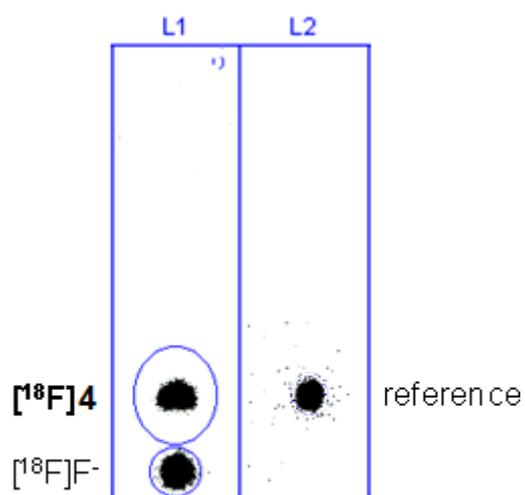
**Figure S1.** Example of the radio-TLC profile of 4- $[^{18}\text{F}]$ fluorobenzaldehyde  $[^{18}\text{F}]1$ .



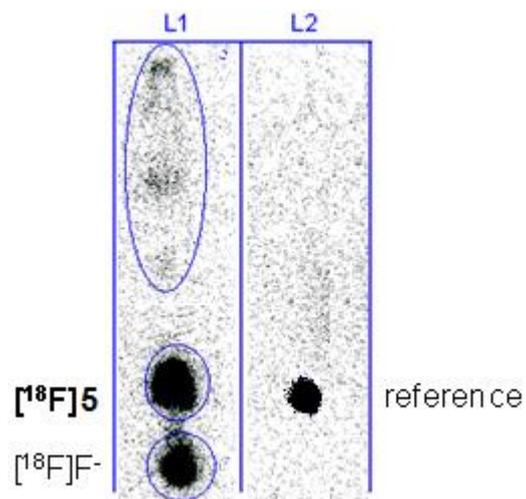
**Figure S2.** Example of the radio-TLC profile of 4- $[^{18}\text{F}]$ fluorobenzonitrile  $[^{18}\text{F}]2$ .



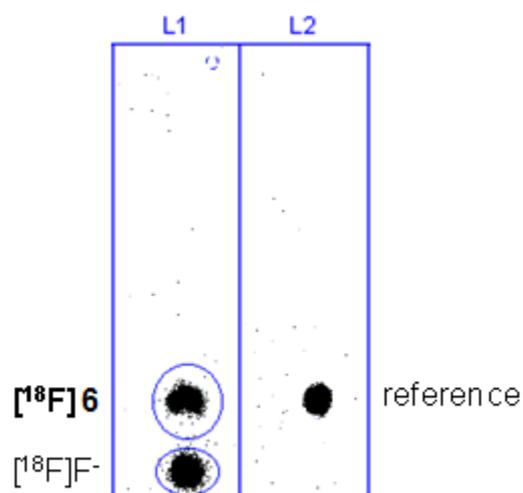
**Figure S3.** Example of the radio-TLC profile of 4- $^{18}\text{F}$ fluoro-1,2-dimethoxybenzene  $^{18}\text{F}$ 3.



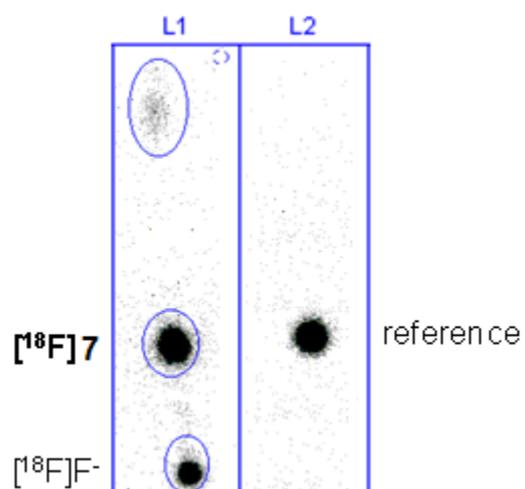
**Figure S4.** Example of the radio-TLC profile of *N*-(tert-butyl)-2-(4- $^{18}\text{F}$ fluorophenyl)-2-(2-oxoazetidin-1-yl)acetamide  $^{18}\text{F}$ 4.



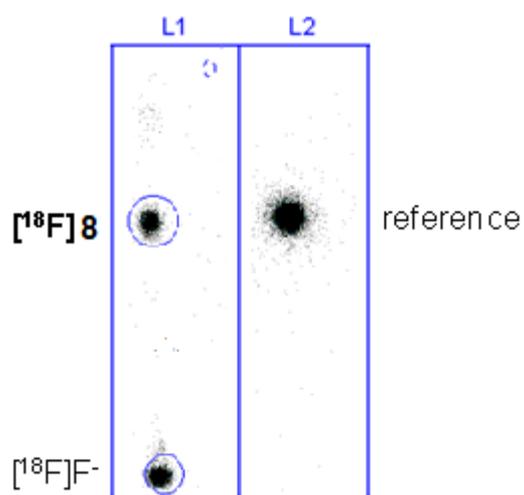
**Figure S5.** Example of the radio-TLC profile of *N*-(4-bromobenzyl)-2-(4-[ $^{18}\text{F}$ ]fluorophenyl)-2-(2-oxoazetidin-1-yl) [ $^{18}\text{F}$ ]5.



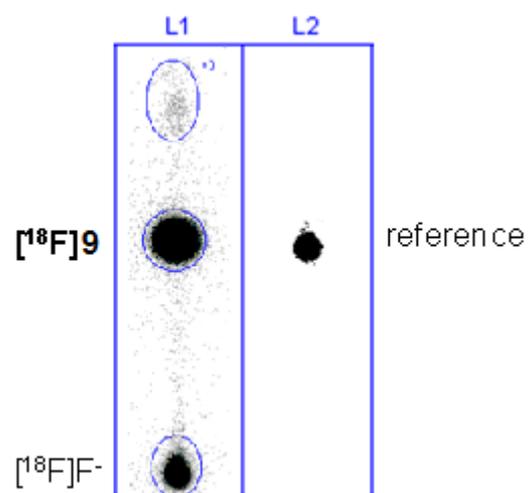
**Figure S6.** Example of the radio-TLC profile of 4-((1-(benzo[d][1,3]dioxol-5-ylmethyl)-1H-tetrazol-5-yl)(4-[ $^{18}\text{F}$ ]fluorophenyl)methyl)morpholine [ $^{18}\text{F}$ ]6.



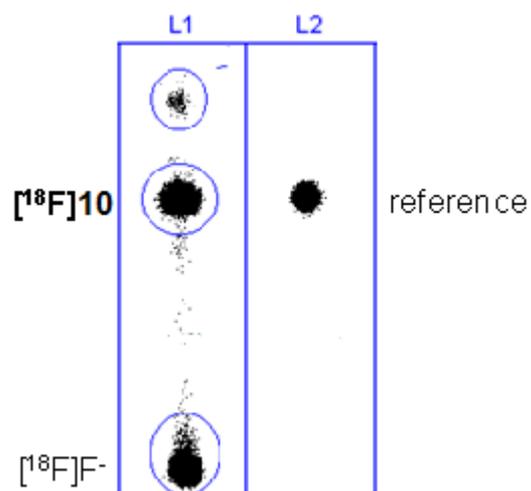
**Figure S7.** Example of the radio-TLC profile of 4-((1-(2,6-dimethylphenyl)-1H-tetrazol-5-yl)(4-[<sup>18</sup>F]fluorophenyl)methyl)morpholine [<sup>18</sup>F]7.



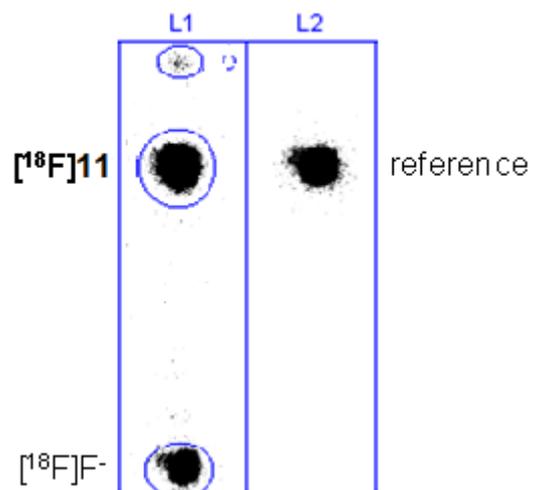
**Figure S8.** Example of the radio-TLC profile of 1-(1-benzyl-1H-tetrazol-5-yl)-N-(4-chlorobenzyl)-1-(4-[<sup>18</sup>F]fluorophenyl)methanamine [<sup>18</sup>F]8.



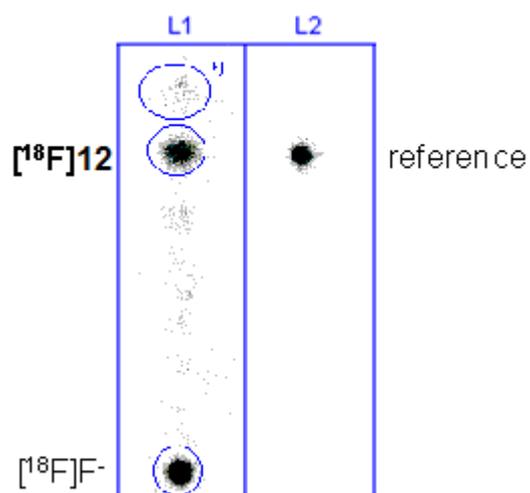
**Figure S9.** Example of the radio-TLC profile of 5-(4-[ $^{18}\text{F}$ ]fluorophenyl)oxazole [ $^{18}\text{F}$ ]9.



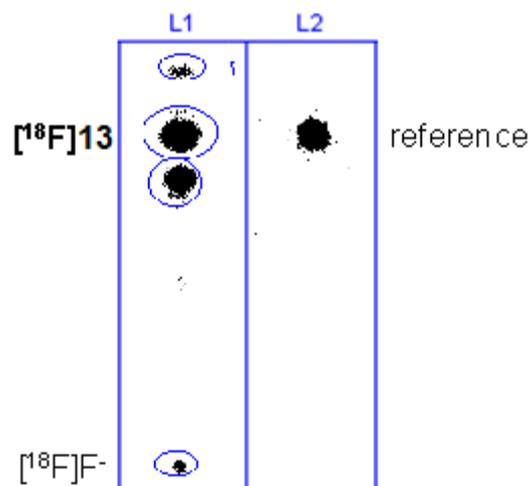
**Figure S10.** Example of the radio-TLC profile of 5-(3-[ $^{18}\text{F}$ ]fluorophenyl)oxazole [ $^{18}\text{F}$ ]10.



**Figure S11.** Example of the radio-TLC profile of 1-(4-[<sup>18</sup>F]fluorophenyl)-2-oxo-2-((3,4,5-trimethoxybenzyl)amino)ethyl 3-bromo-2-methylbenzoate [<sup>18</sup>F]11.



**Figure S12.** Example of the radio-TLC profile of 2-((benzo[d][1,3]dioxol-5-ylmethyl)amino)-1-(4-[<sup>18</sup>F]fluorophenyl)-2-oxoethyl 2,4-dimethylbenzoate [<sup>18</sup>F]12



**Figure S13.** Example of the radio-TLC profile of 2-(benzylamino)-1-(4-[<sup>18</sup>F]fluorophenyl)-2-oxoethyl cyclohexanecarboxylate [<sup>18</sup>F]13.

**Table S1.** TLC-SG retention factor ( $R_f$ ) profiles for the tested compounds

Compound	$R_f$	Hexane:ethyl acetate ratio
[ <sup>18/19</sup> F]1	0.85	2:1
[ <sup>18/19</sup> F]2	0.85	2:1
[ <sup>18/19</sup> F]3	0.80	2:1
[ <sup>18/19</sup> F]4	0.40	1:1
[ <sup>18/19</sup> F]5	0.30	1:1
[ <sup>18/19</sup> F]6	0.35	2:1
[ <sup>18/19</sup> F]7	0.40	2:1
[ <sup>18/19</sup> F]8	0.60	2:1
[ <sup>18/19</sup> F]9	0.50	2:1
[ <sup>18/19</sup> F]10	0.65	2:1
[ <sup>18/19</sup> F]11	0.75	2:1
[ <sup>18/19</sup> F]12	0.8	2:1
[ <sup>19</sup> F]13	0.85	2:1
[ <sup>18</sup> F]F <sup>-</sup>	0.0	1:1; 2:1
copper-[ <sup>18</sup> F]fluoride complex	1.0	1:1; 2:1

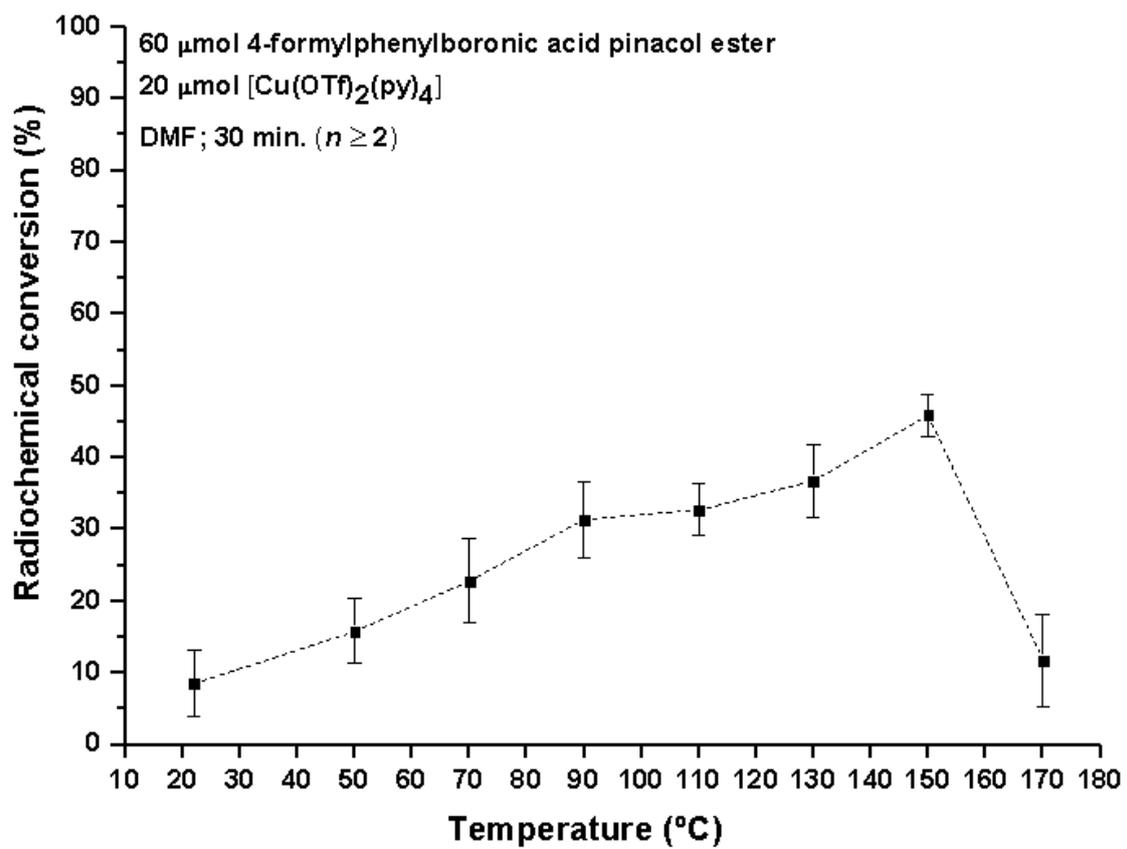
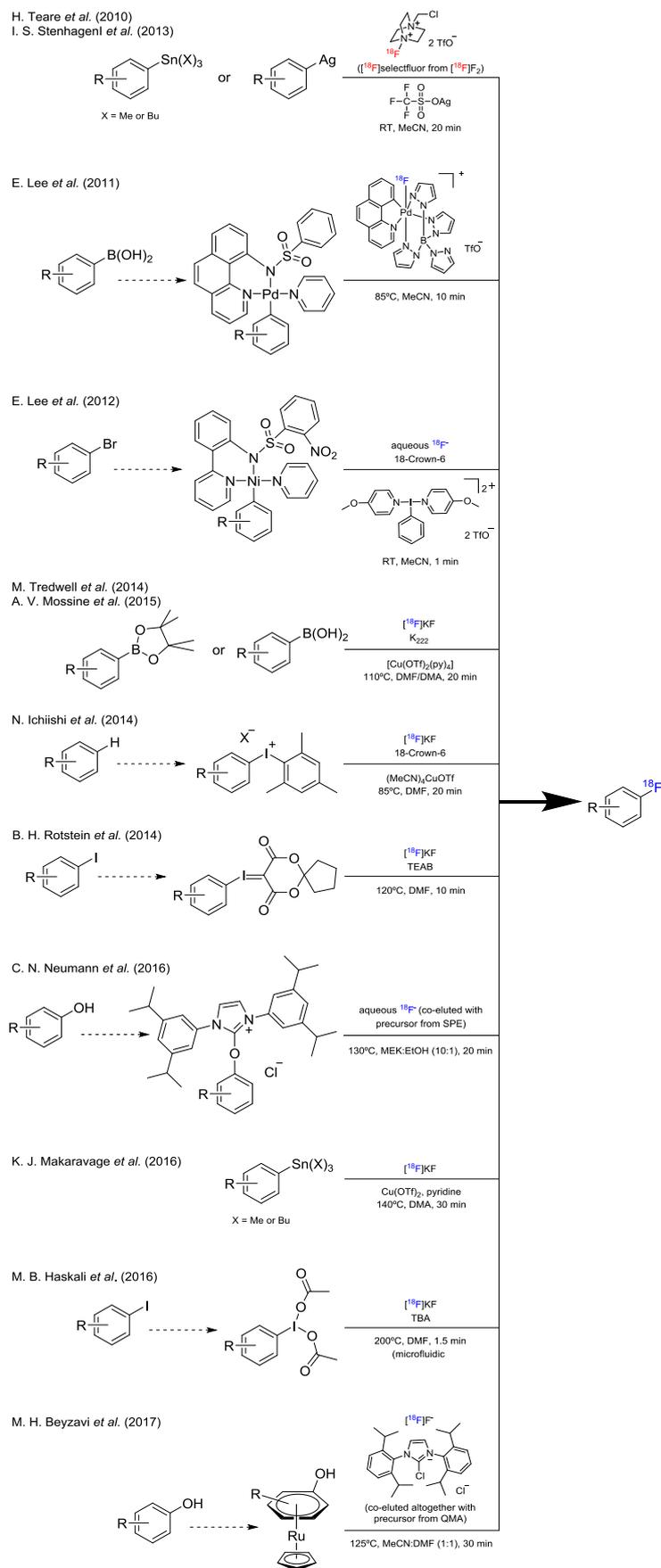
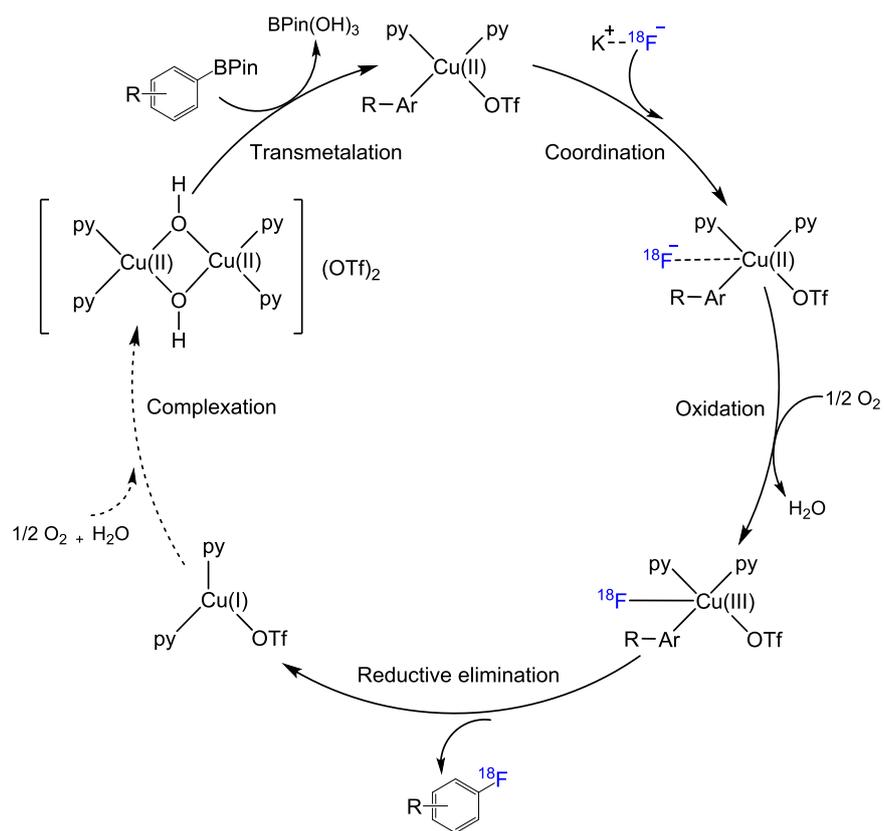


Figure S14. Effect of temperature in RCC of  $[\text{}^{18}\text{F}]\mathbf{1}$ .



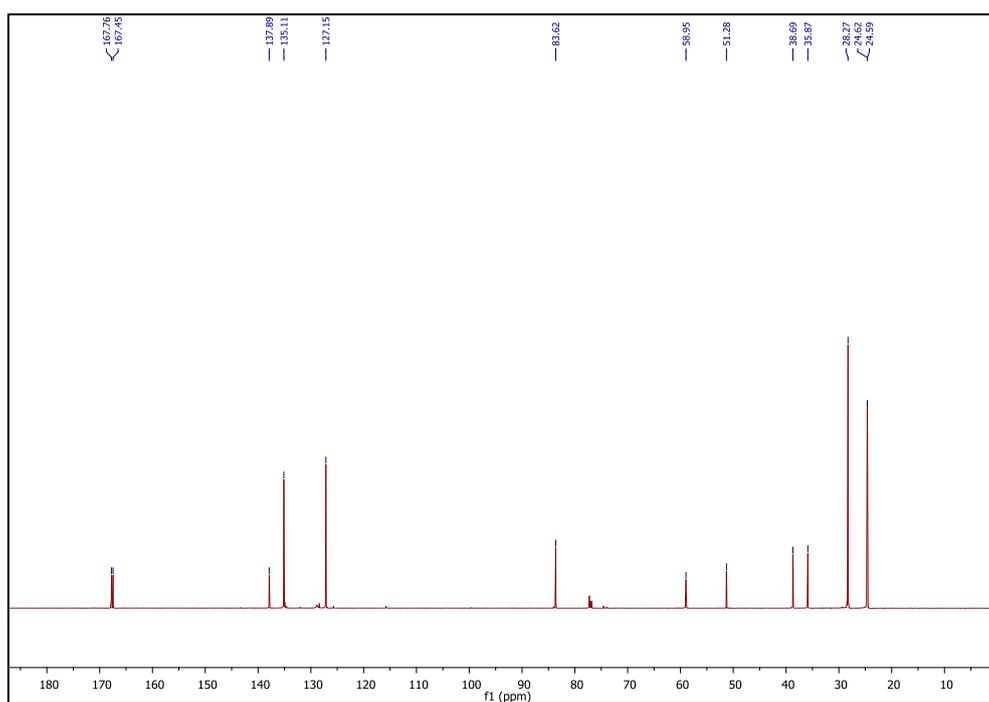
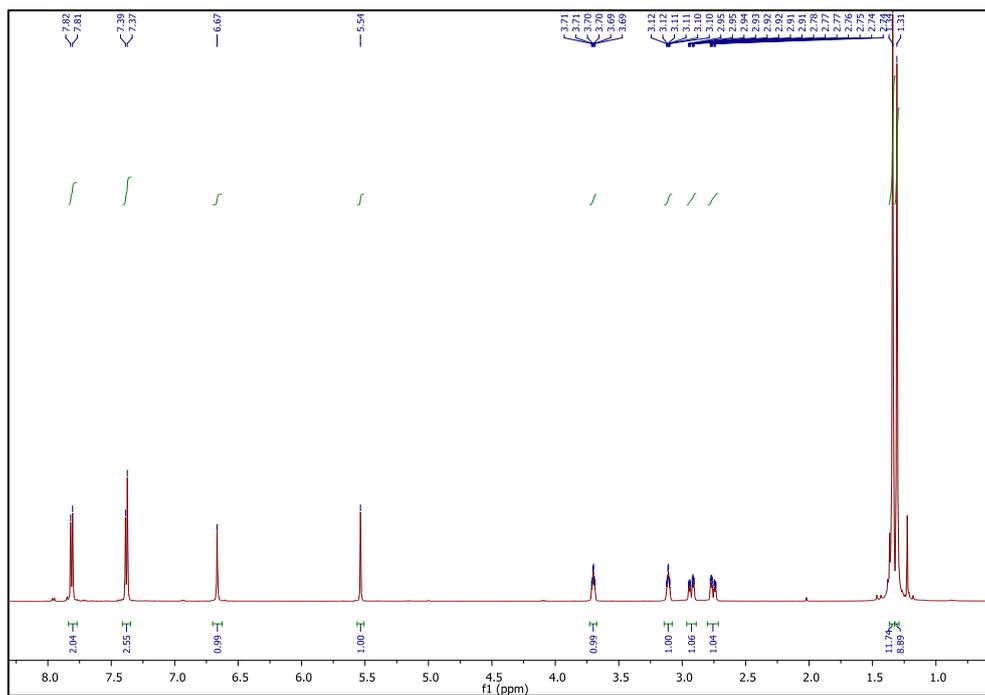
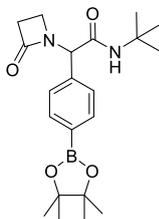
**Scheme S1.** Recent late-stage strategies for the  $^{18}F$ -fluorination of (hetero)arenes.



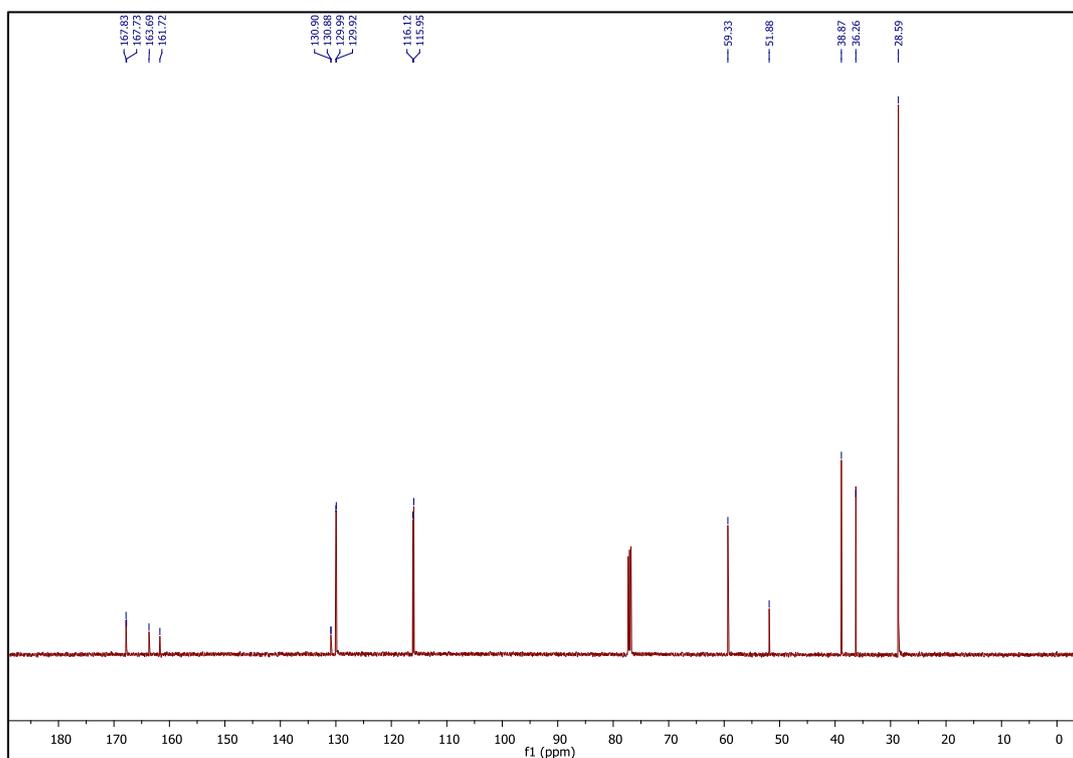
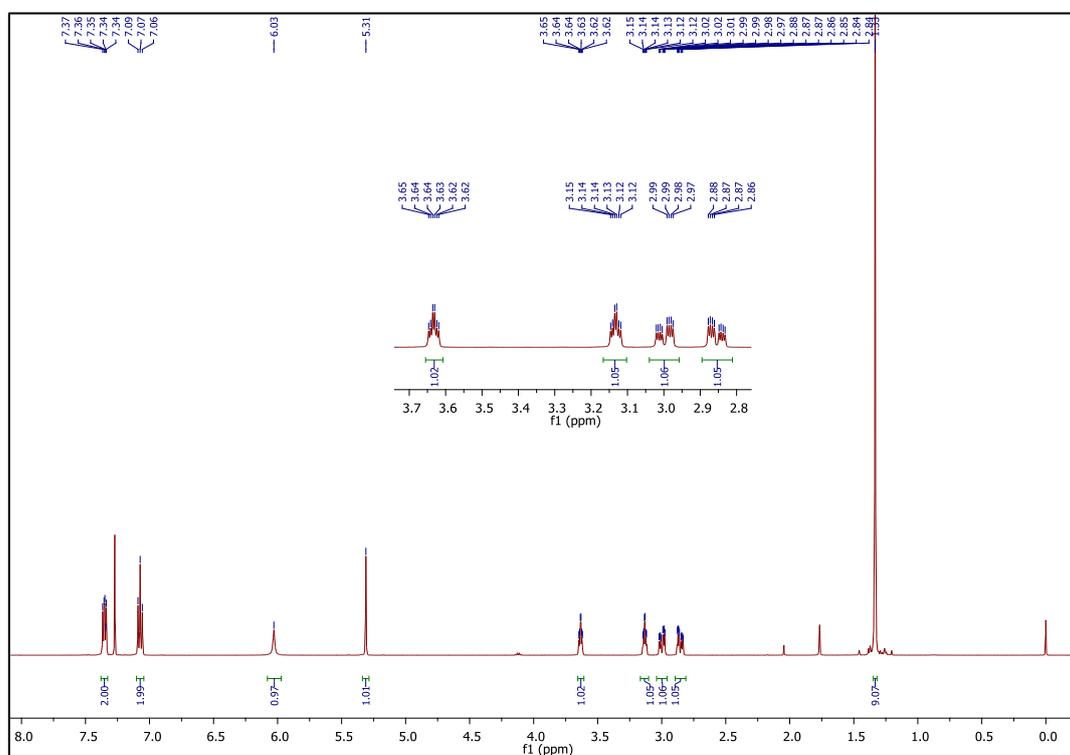
**Scheme S2.** Proposed mechanism for copper-mediated oxidative  $^{18}\text{F}$ -fluorination of aryl boronic esters.

## Spectra of compounds

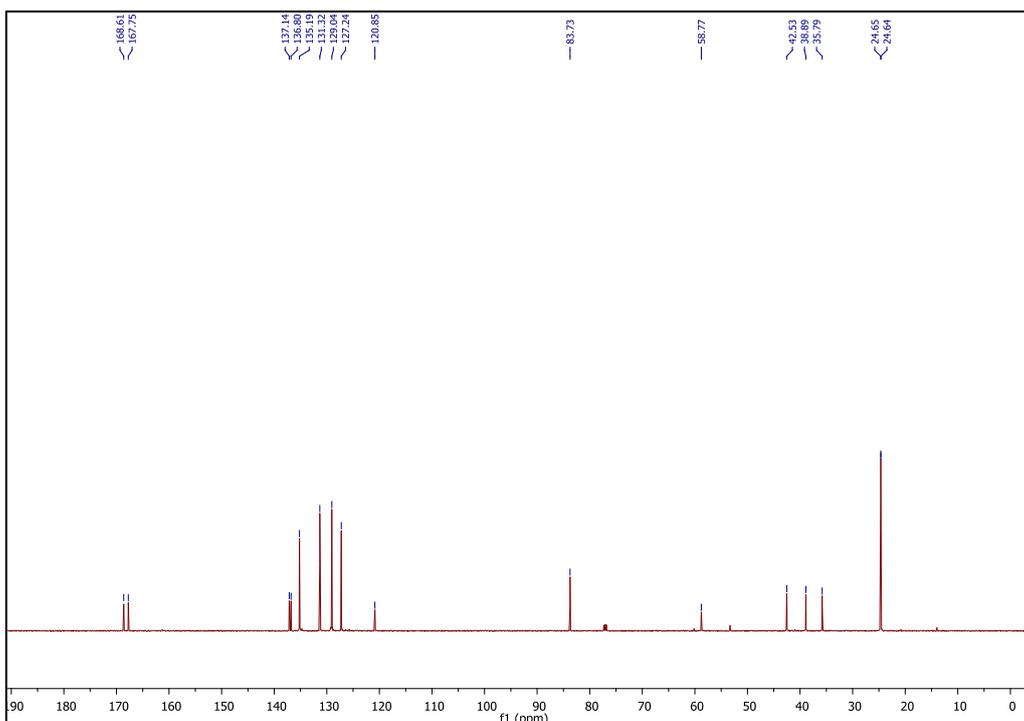
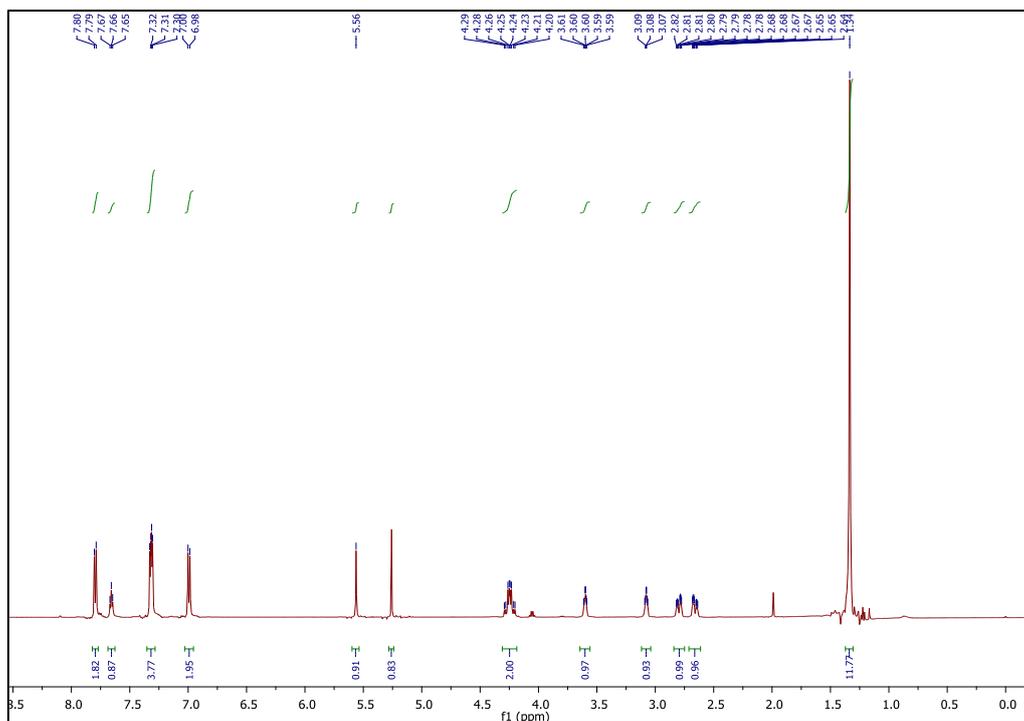
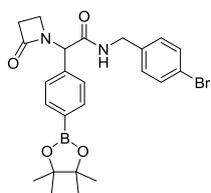
*N*-(tert-butyl)-2-(2-oxoazetidin-1-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide (4):



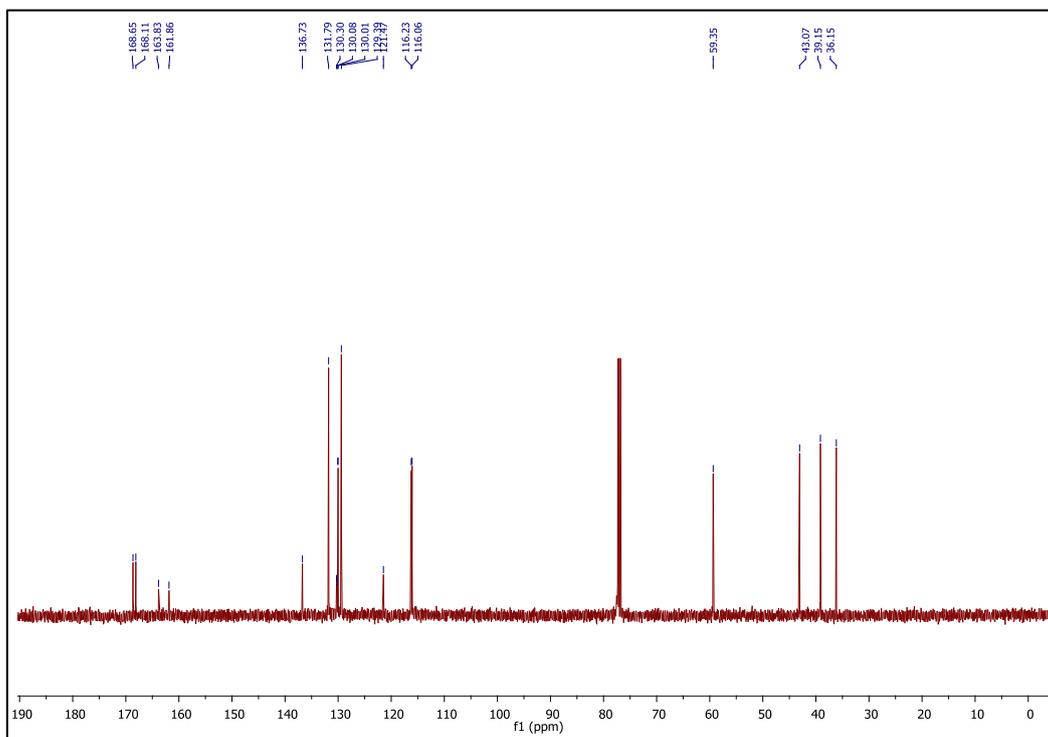
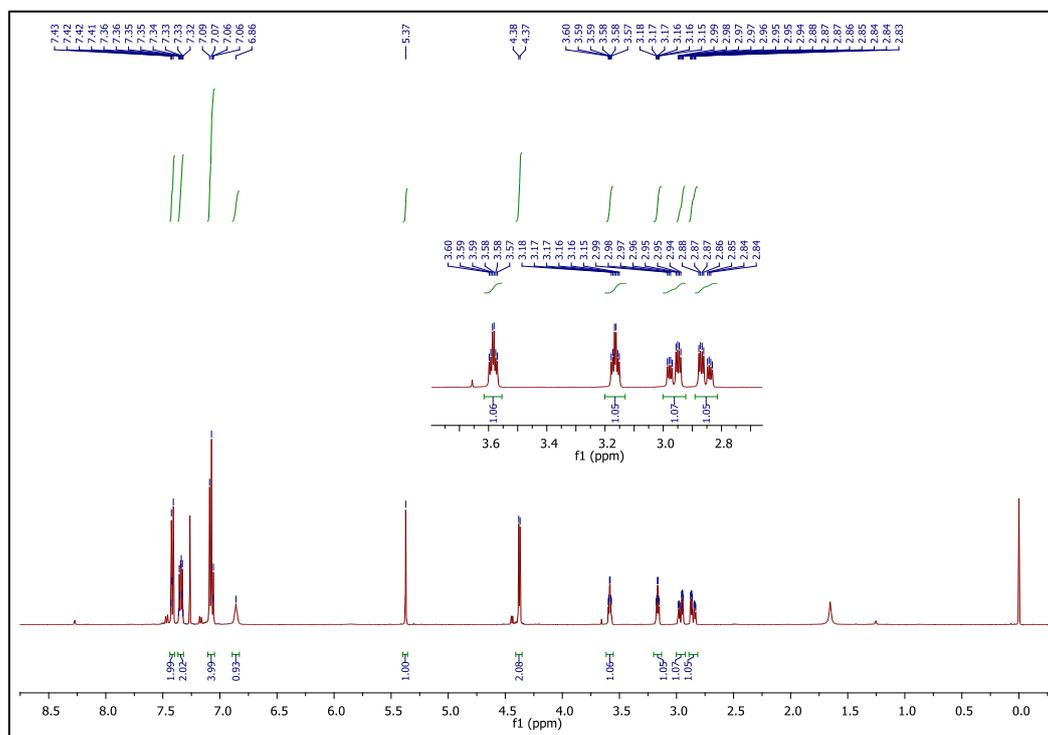
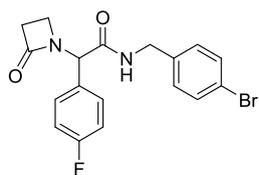
**N-(tert-butyl)-2-(4-fluorophenyl)-2-(2-oxoazetidin-1-yl)acetamide ([<sup>19</sup>F]4):**



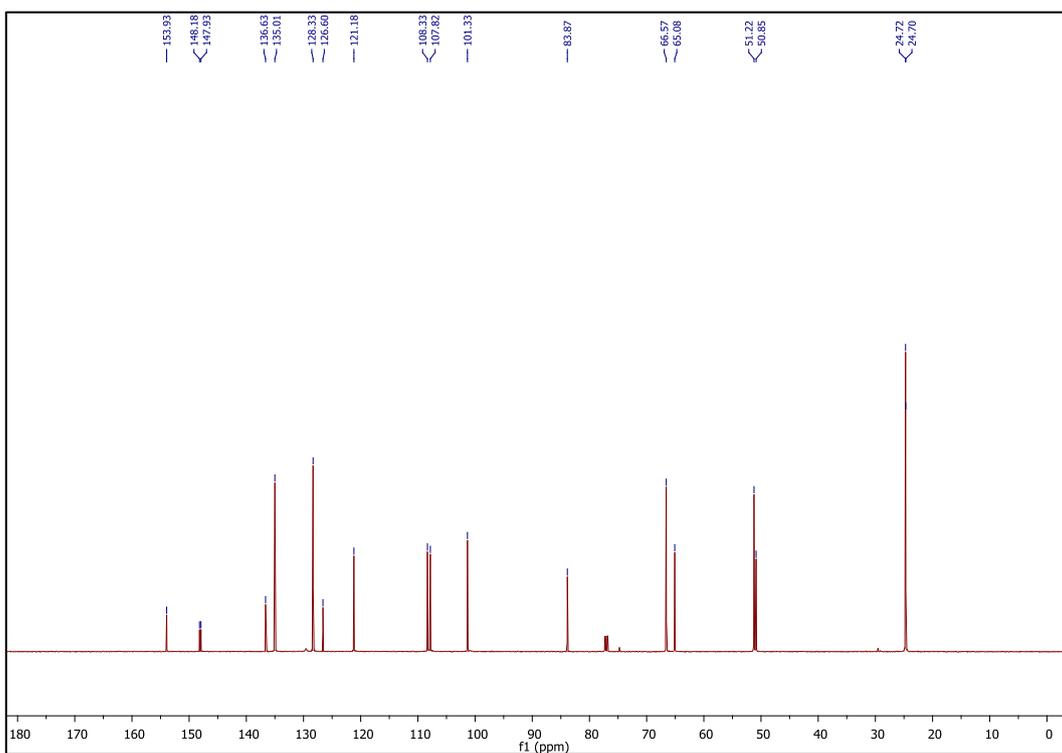
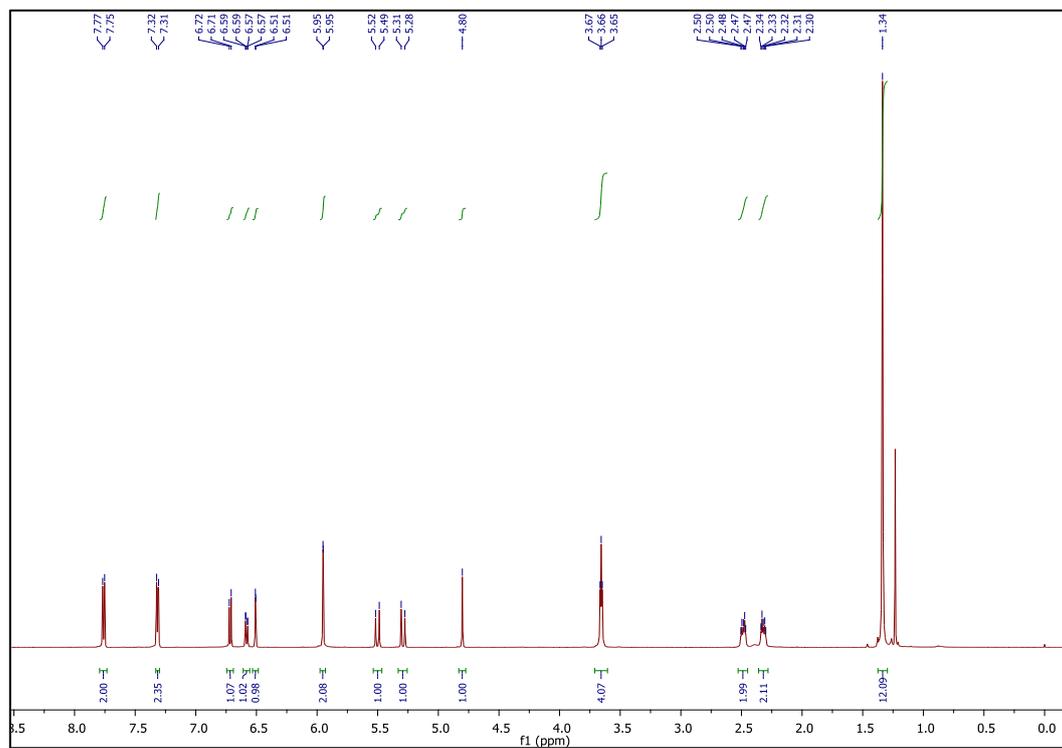
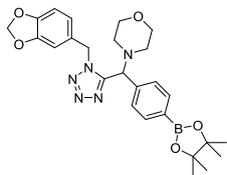
**N-(4-bromobenzyl)-2-(2-oxoazetidin-1-yl)-2-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetamide**  
**(5):**



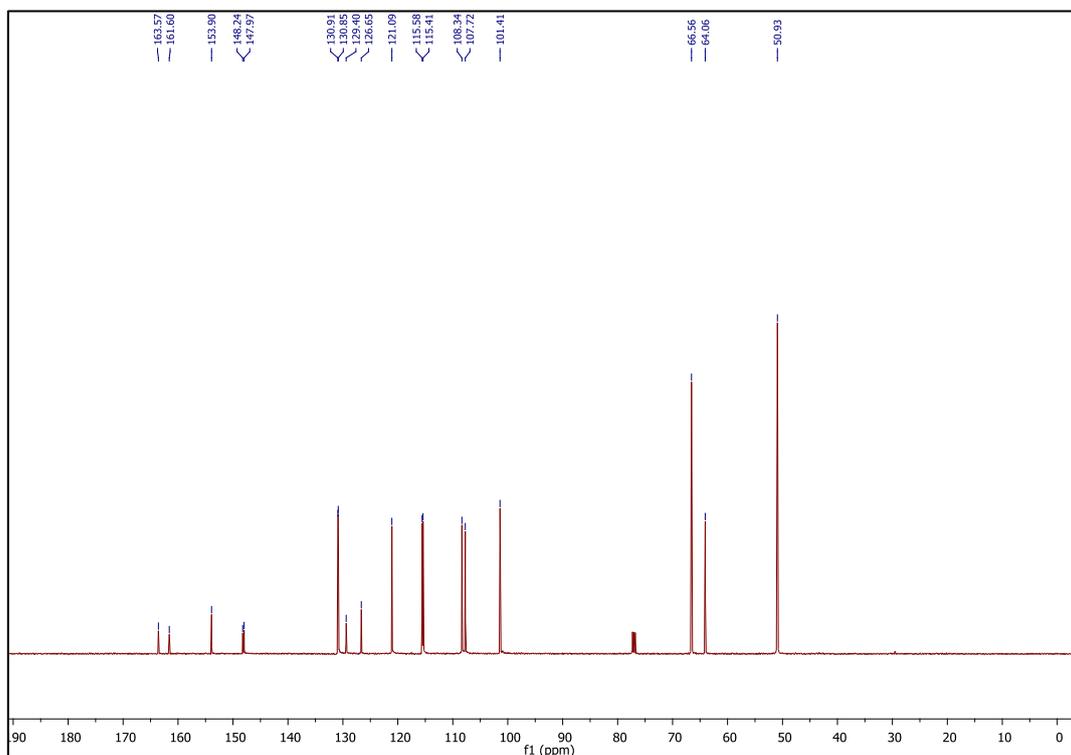
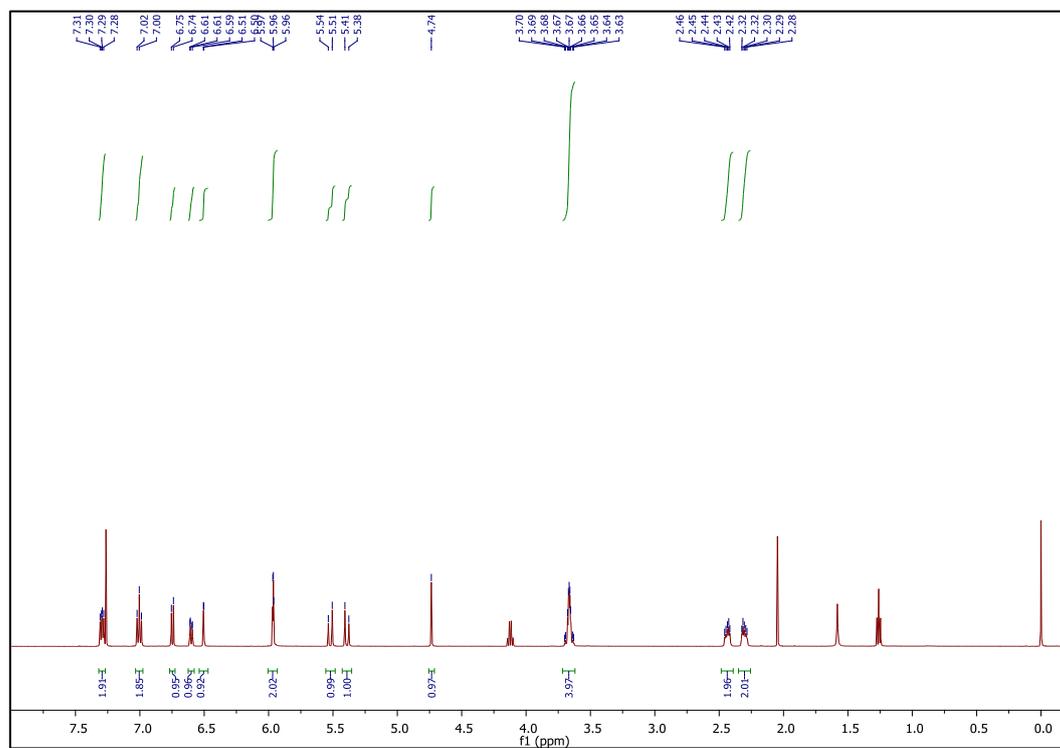
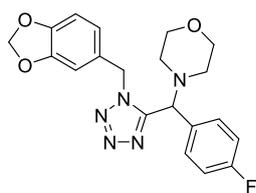
**N-(4-bromobenzyl)-2-(4-fluorophenyl)-2-(2-oxazetidin-1-yl) ([<sup>19</sup>F]5):**



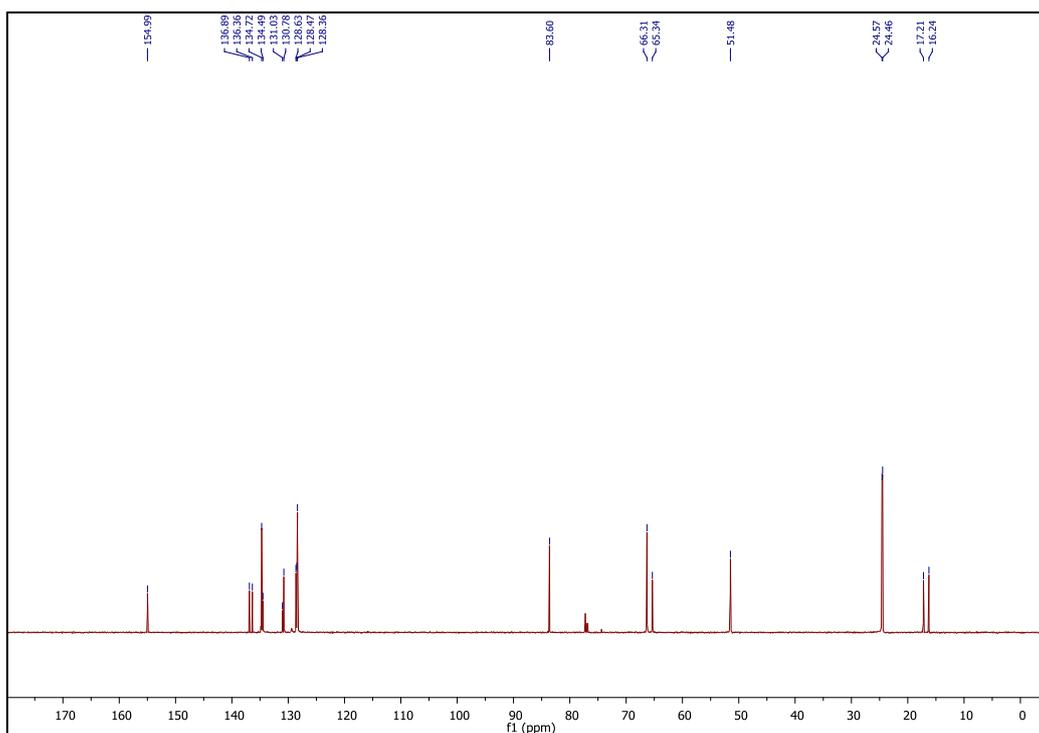
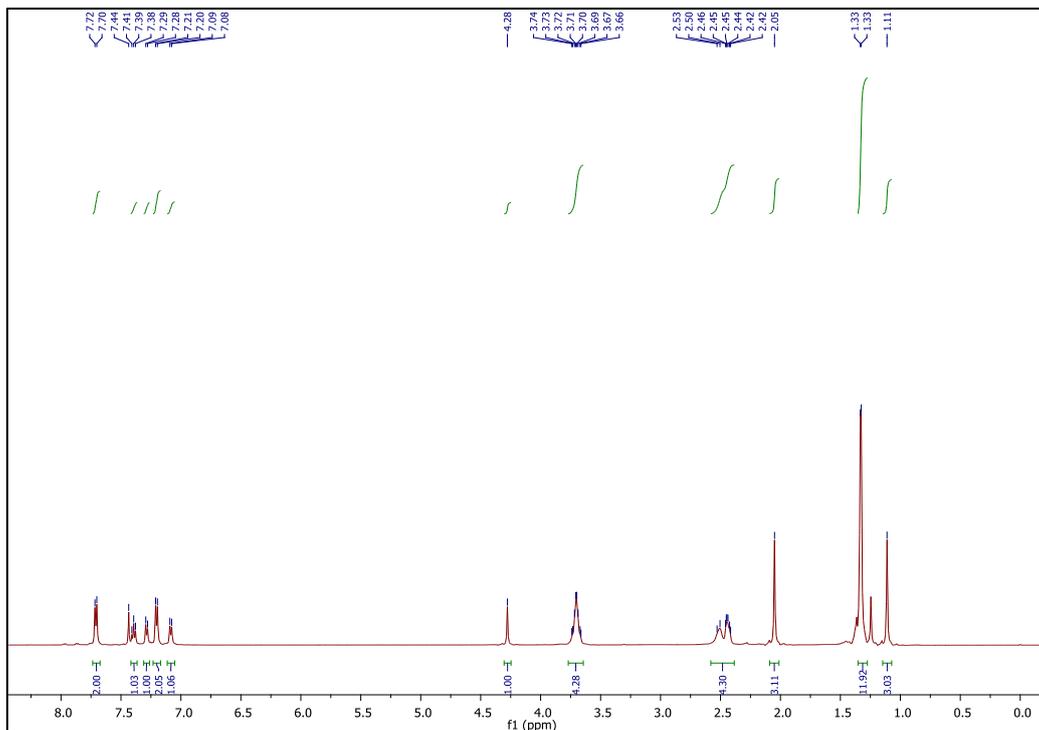
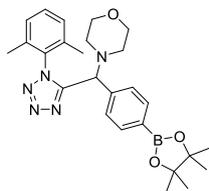
4-((1-(benzo[d][1,3]dioxol-5-ylmethyl)-1H-tetrazol-5-yl)(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methyl)morpholine (6):



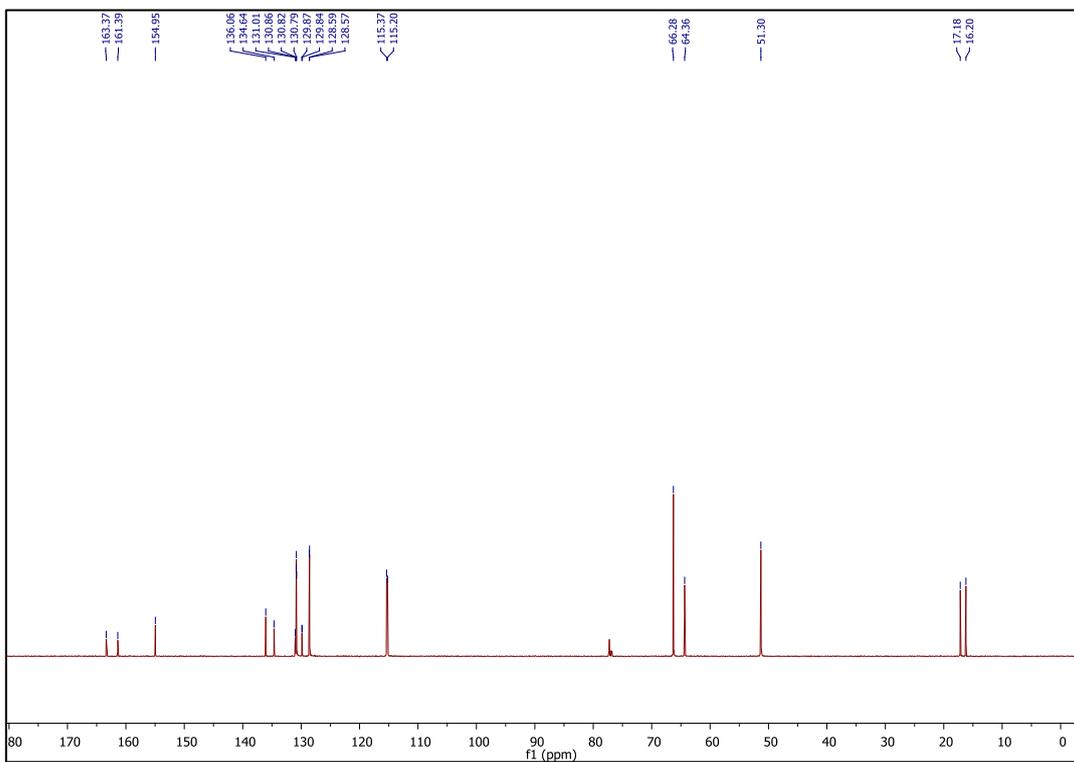
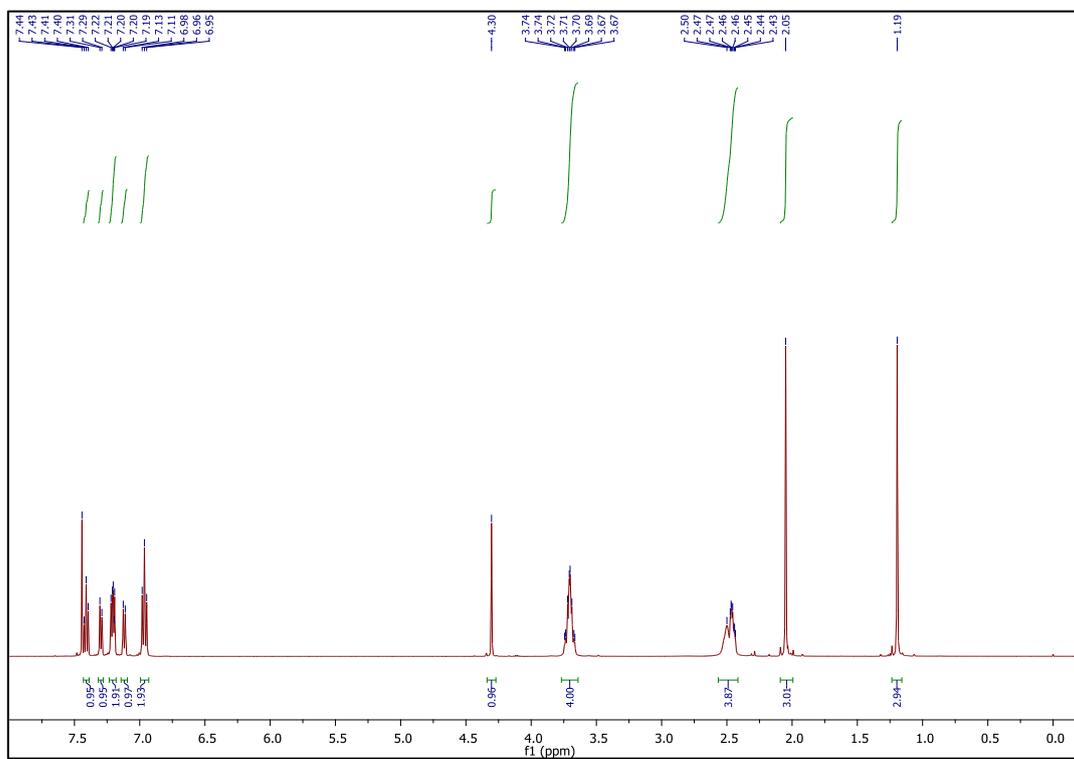
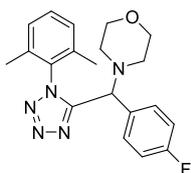
4-((1-(benzo[d][1,3]dioxol-5-ylmethyl)-1H-tetrazol-5-yl)(4-fluorophenyl)methyl)morpholine ( $^{19}\text{F}$ 6):



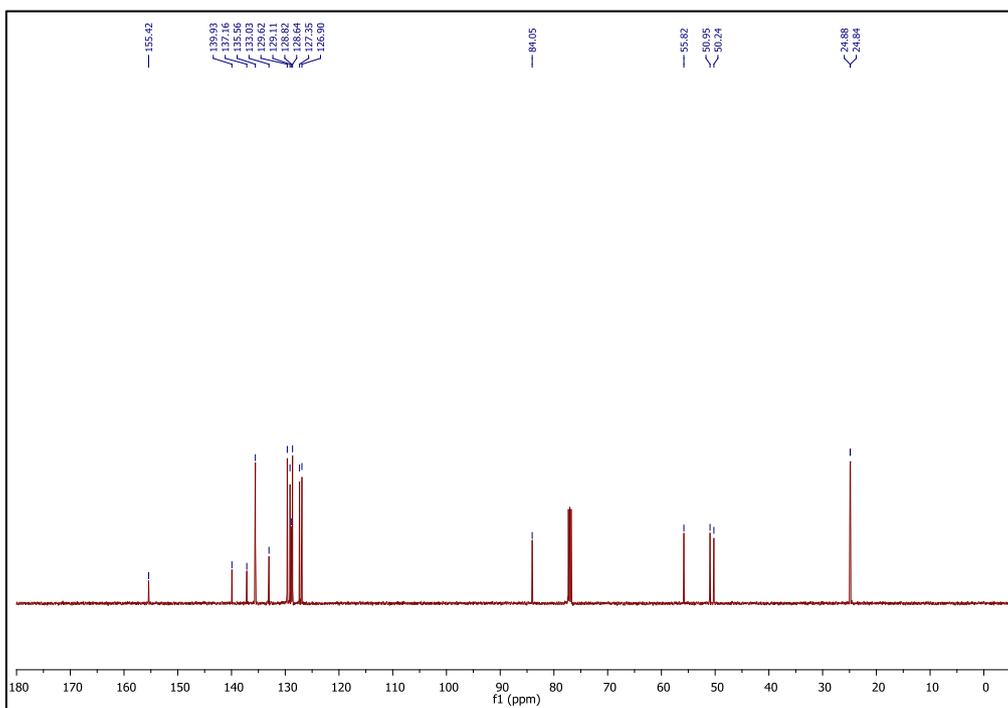
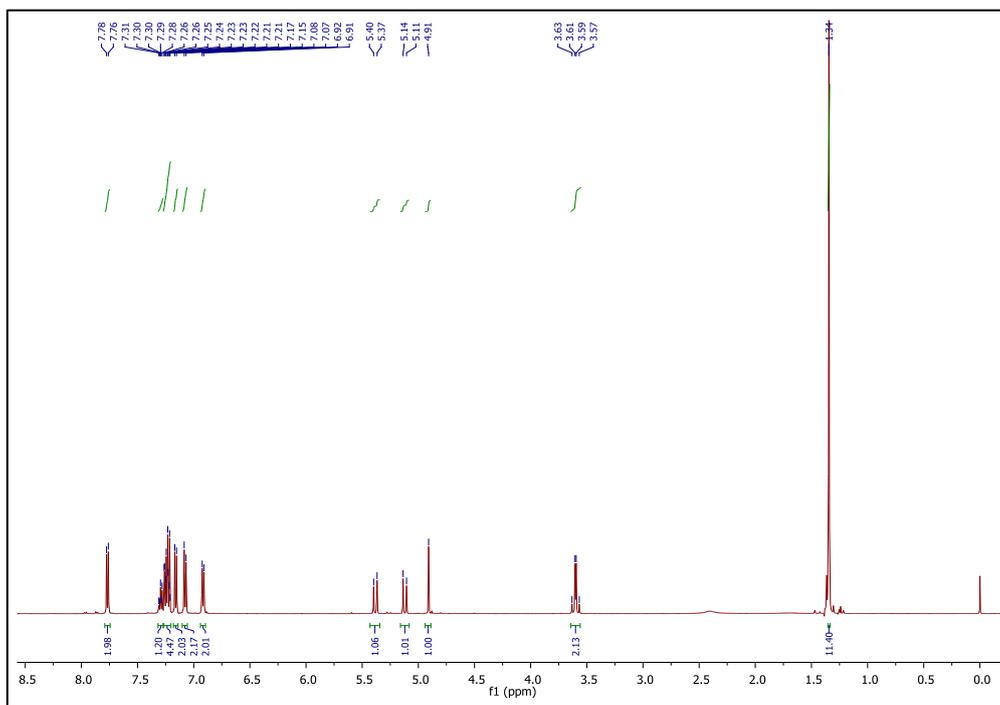
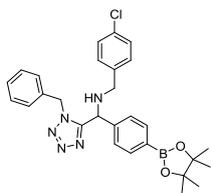
4-((1-(2,6-dimethylphenyl)-1H-tetrazol-5-yl)(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methyl)morpholine (7):



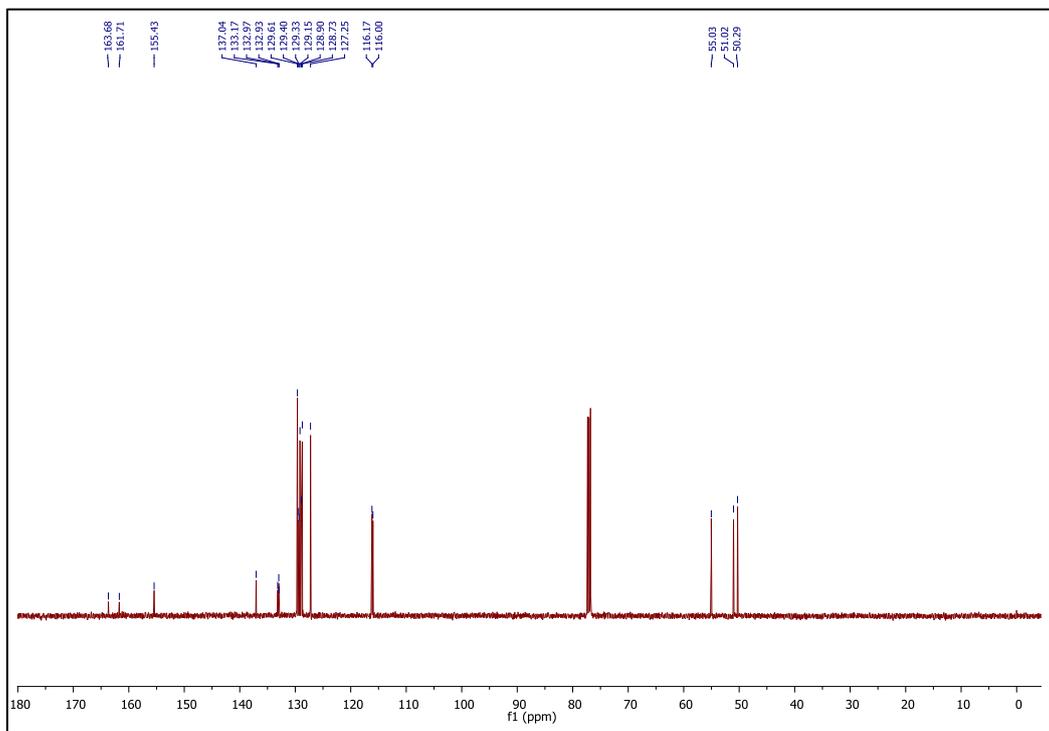
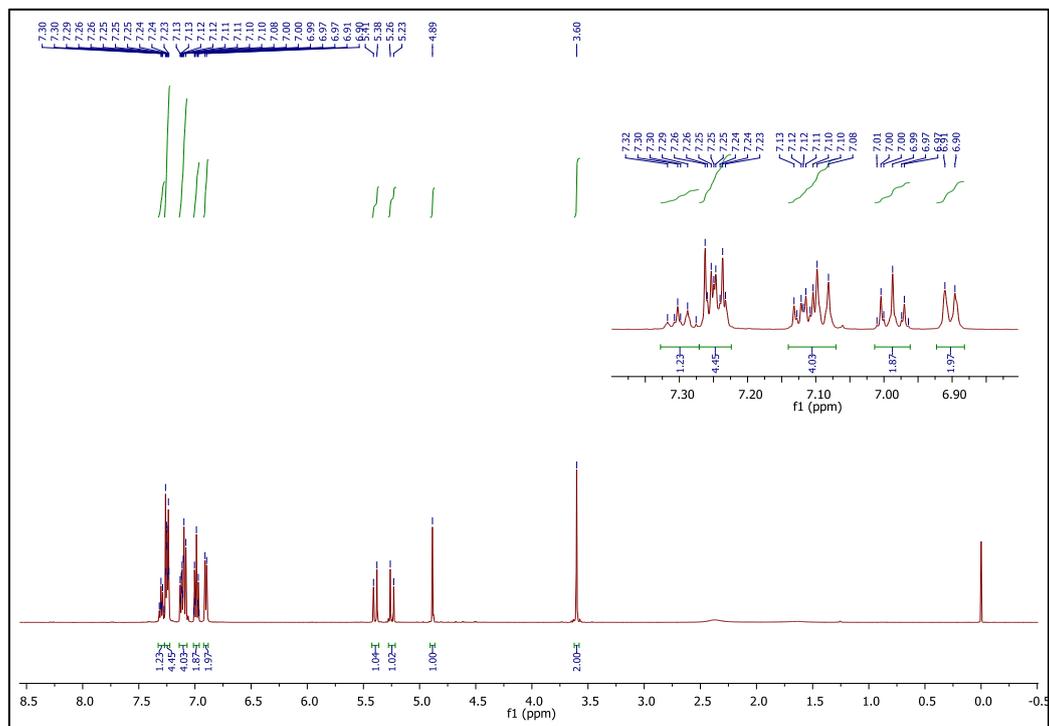
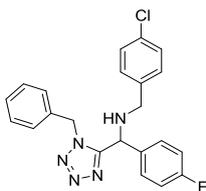
4-((1-(2,6-dimethylphenyl)-1H-tetrazol-5-yl)(4-fluorophenyl)methyl)morpholine ( $[^{19}\text{F}]7$ ):



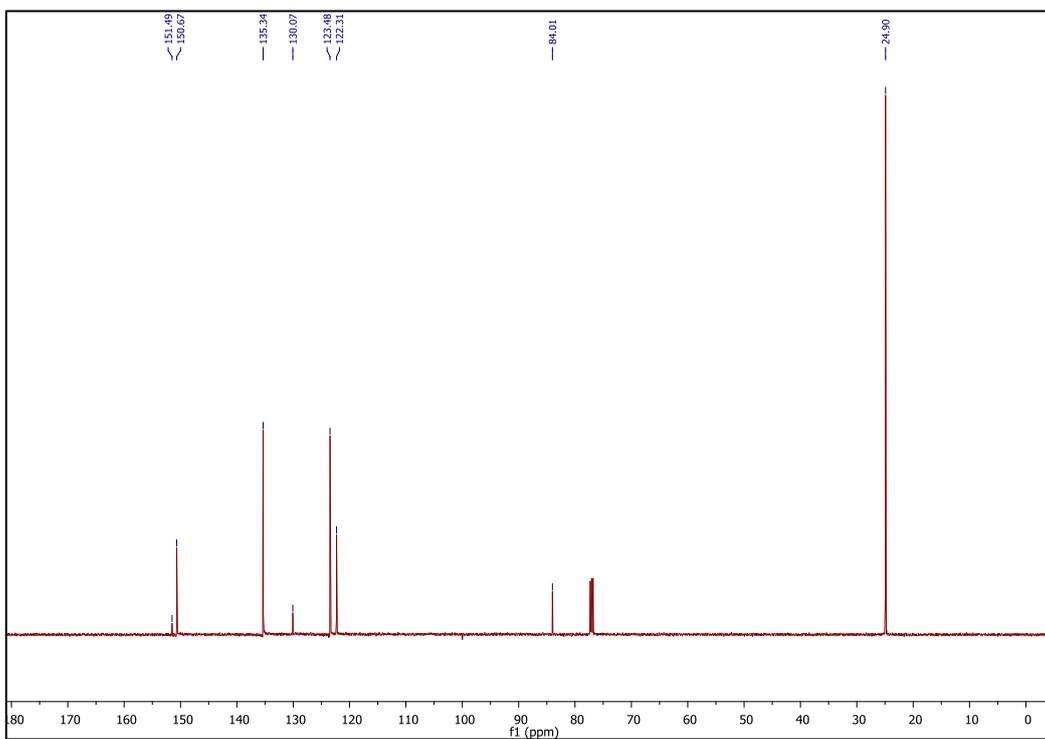
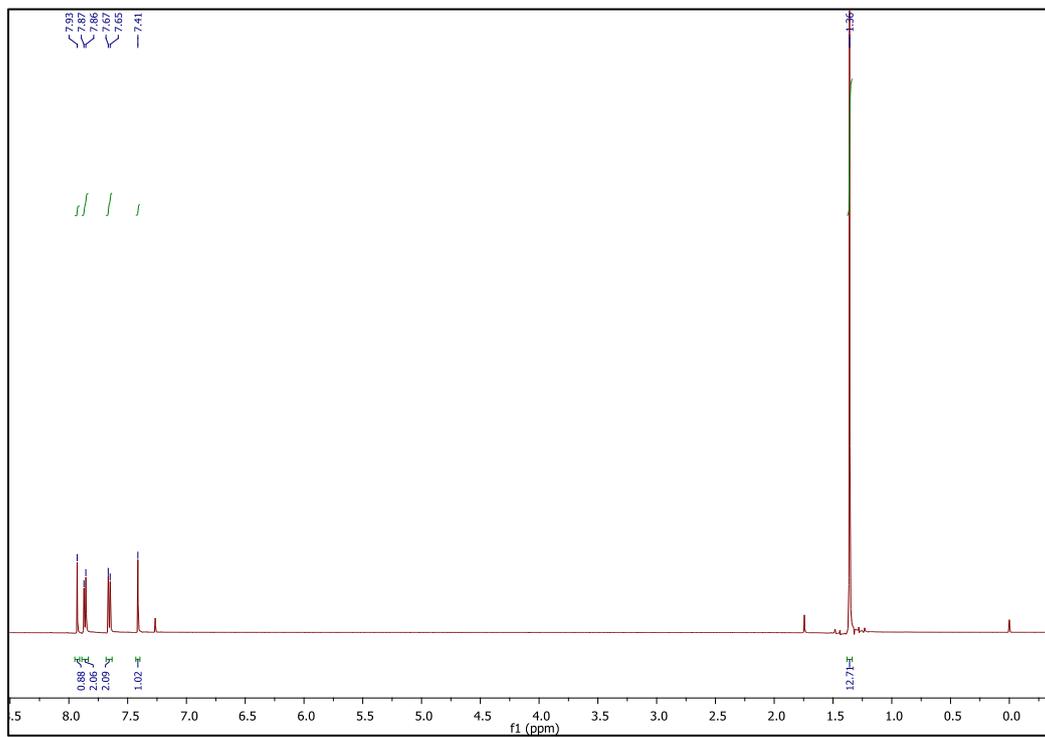
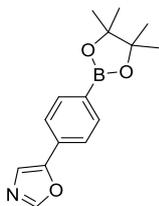
**1-(1-benzyl-1H-tetrazol-5-yl)-N-(4-chlorobenzyl)-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)methanamine (8):**



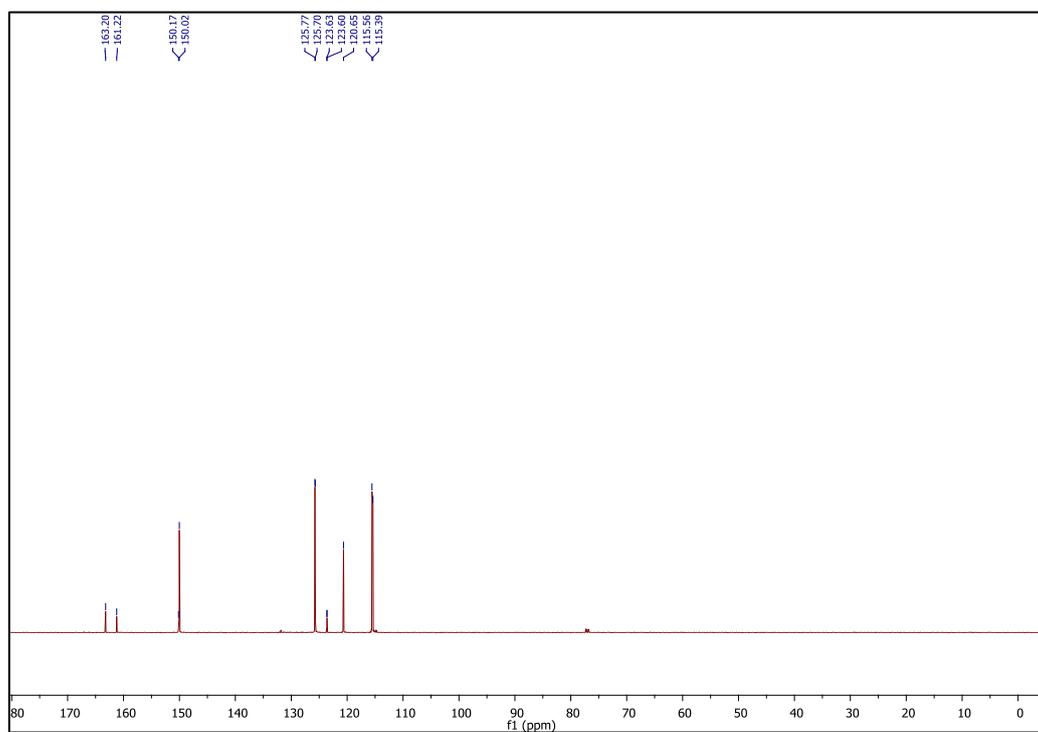
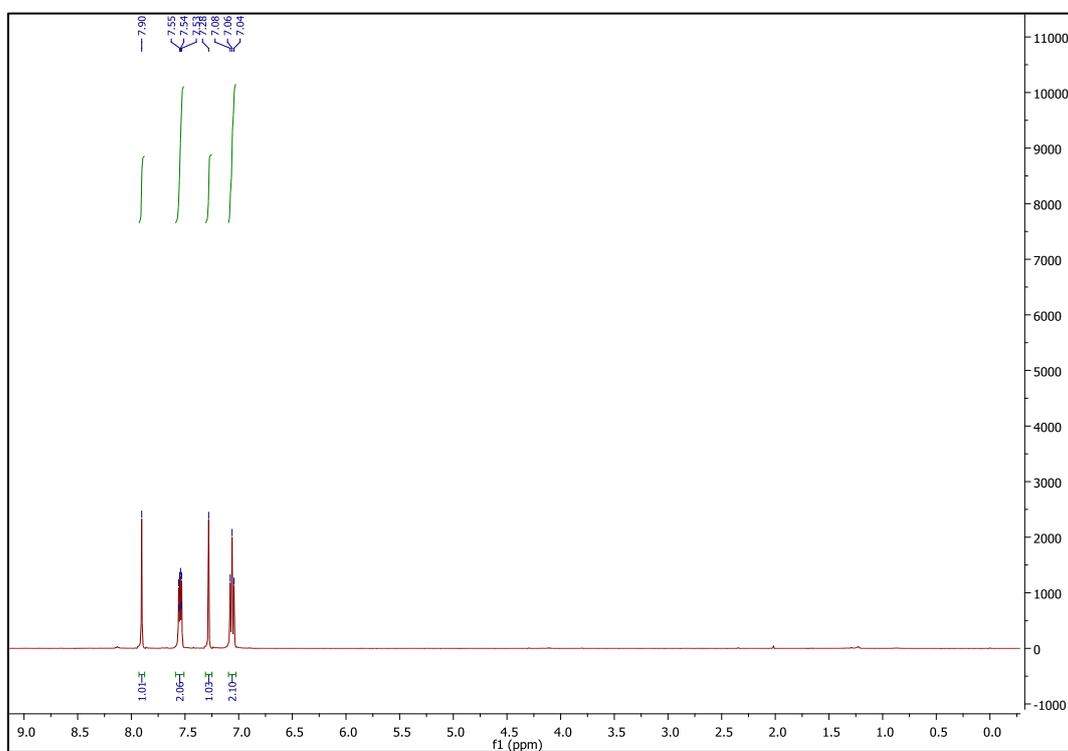
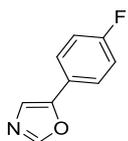
1-(1-benzyl-1H-tetrazol-5-yl)-N-(4-chlorobenzyl)-1-(4-fluorophenyl)methanamine (<sup>19</sup>F]8):



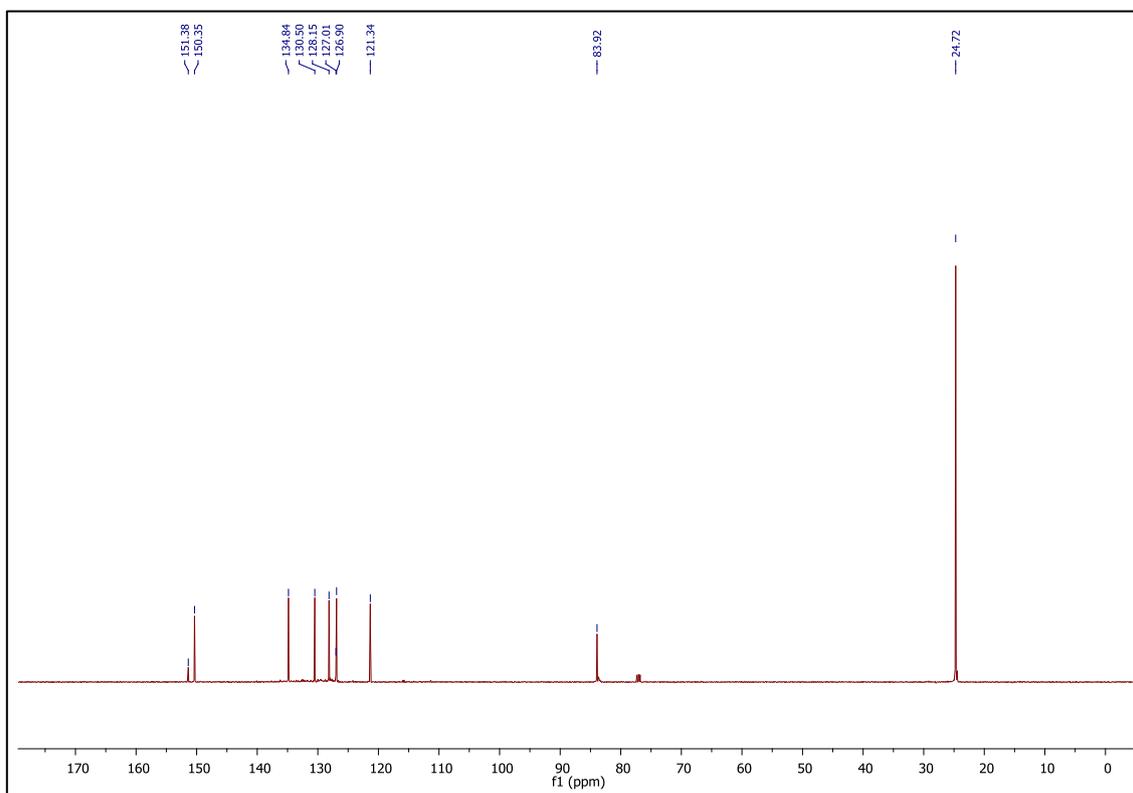
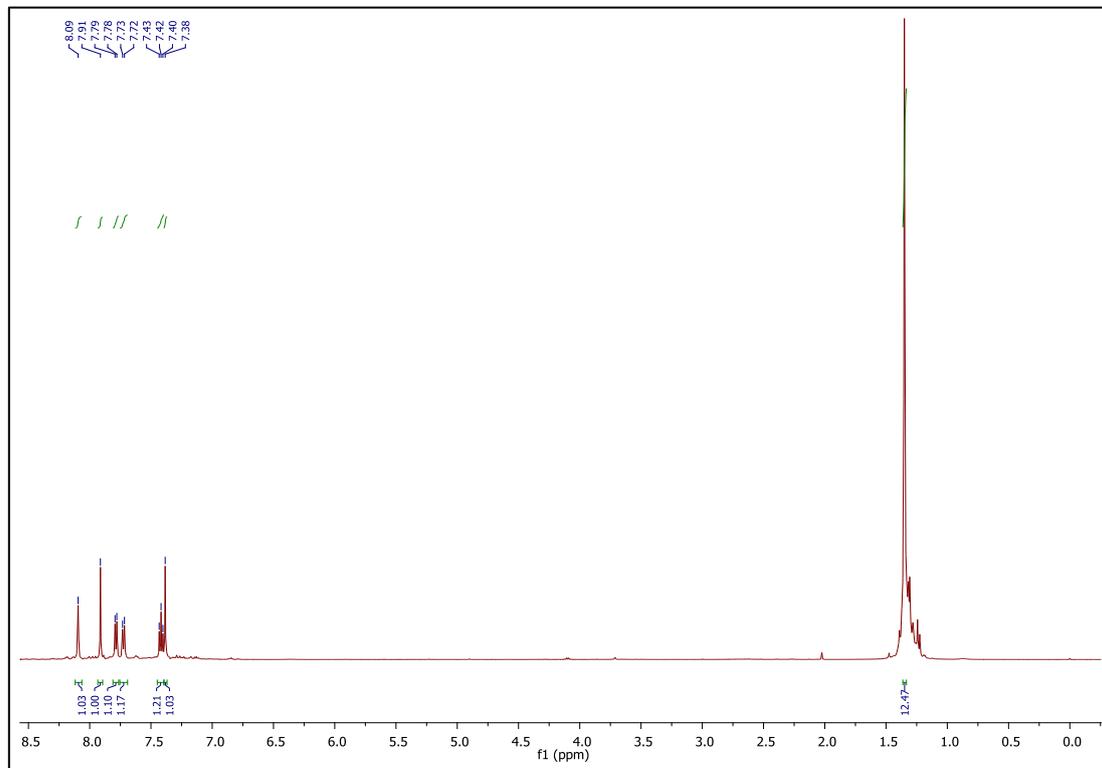
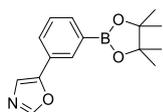
5-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)oxazole (9):



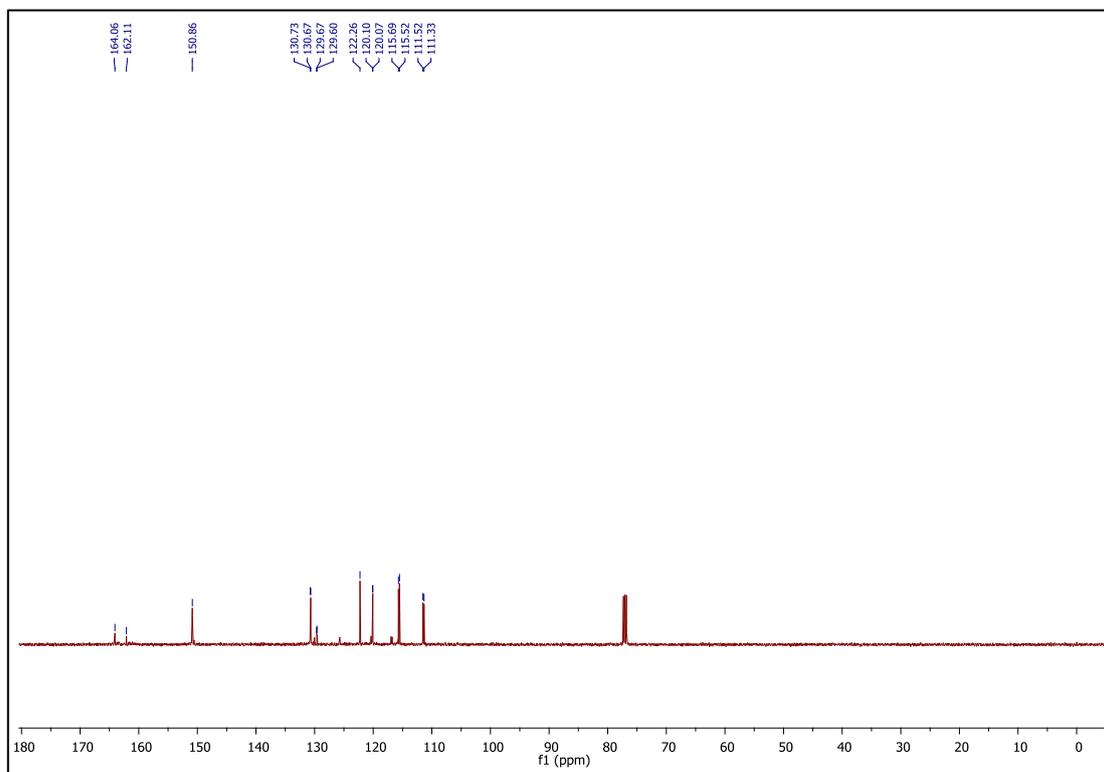
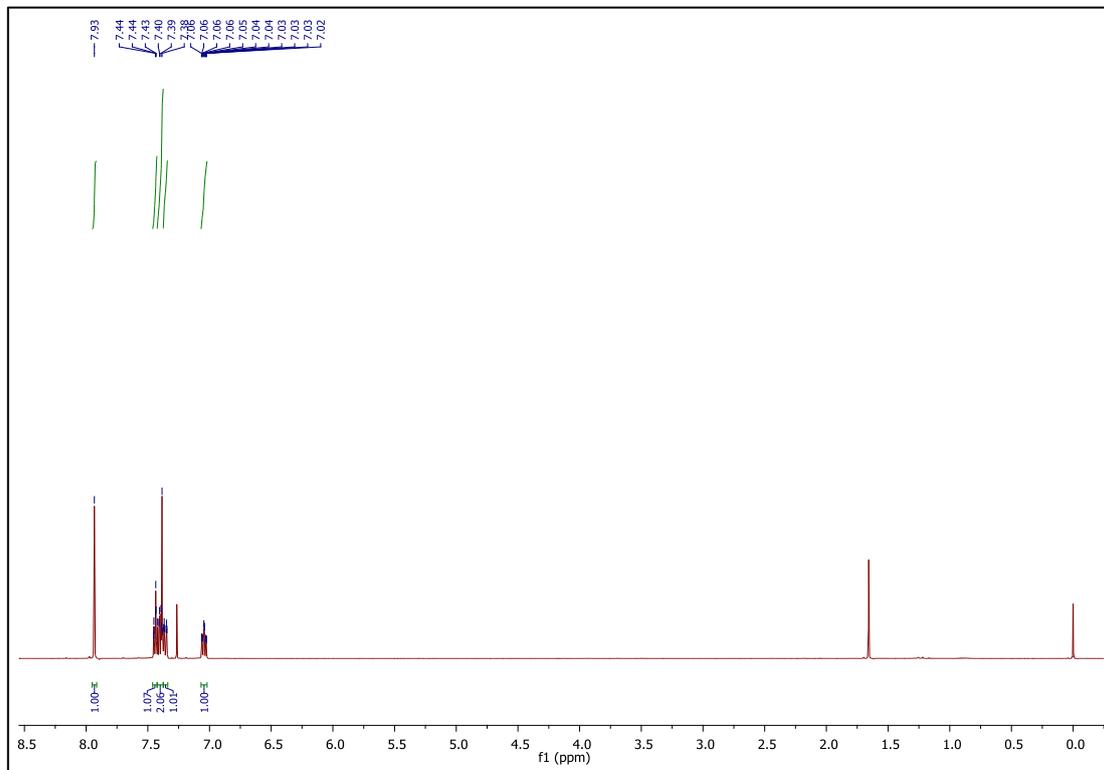
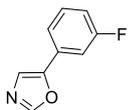
5-(4-fluorophenyl)oxazole (<sup>19</sup>F):



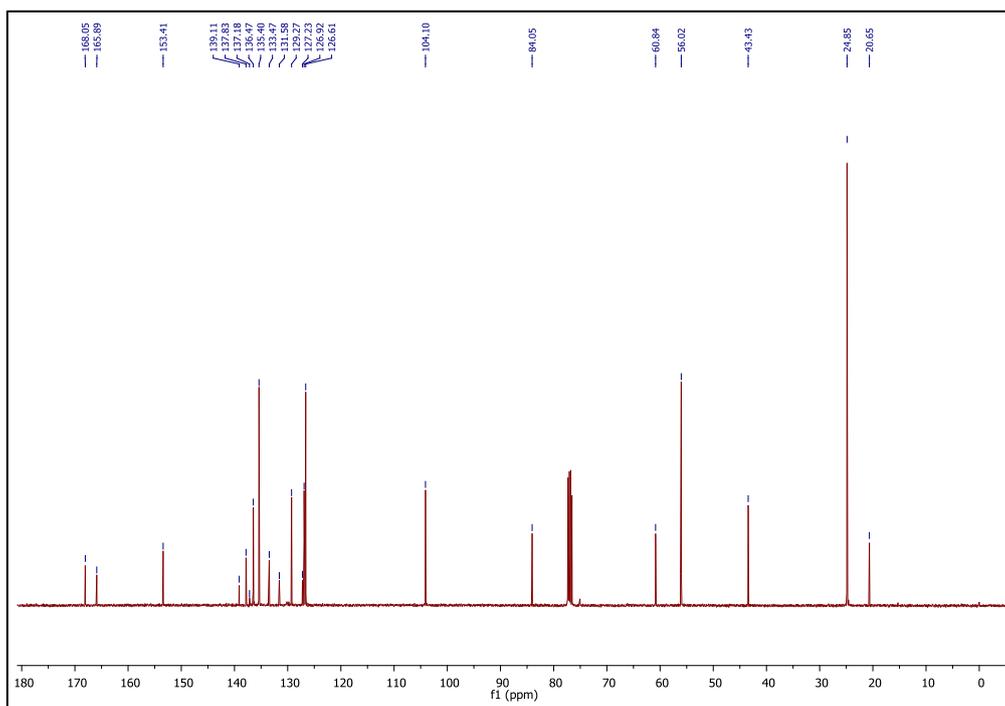
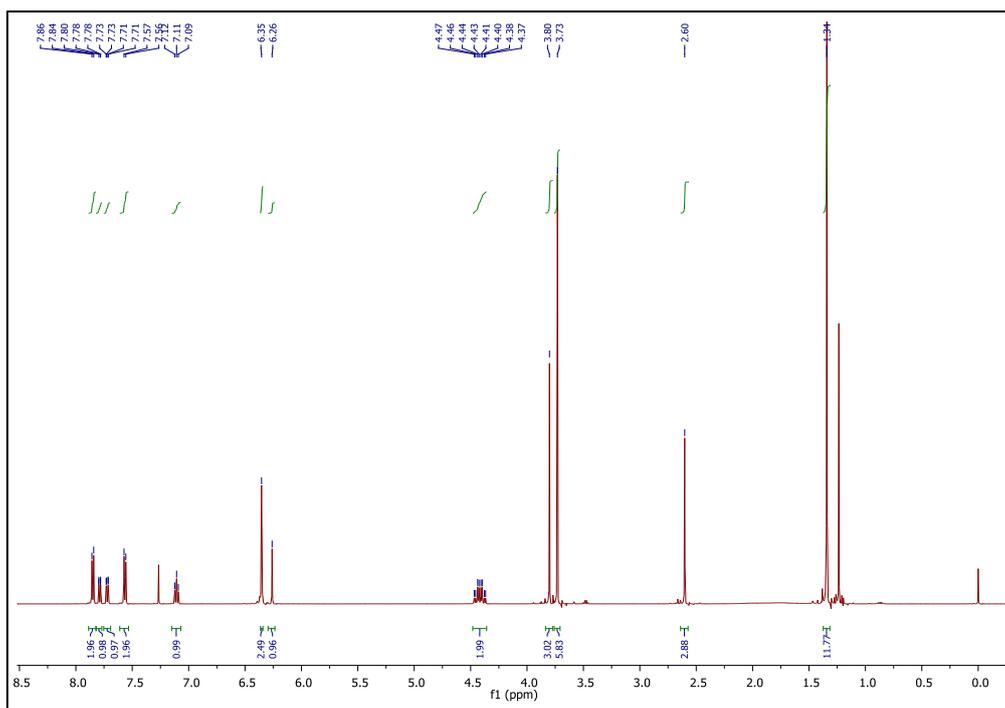
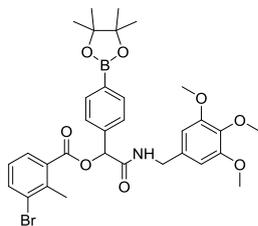
5-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)oxazole (10):



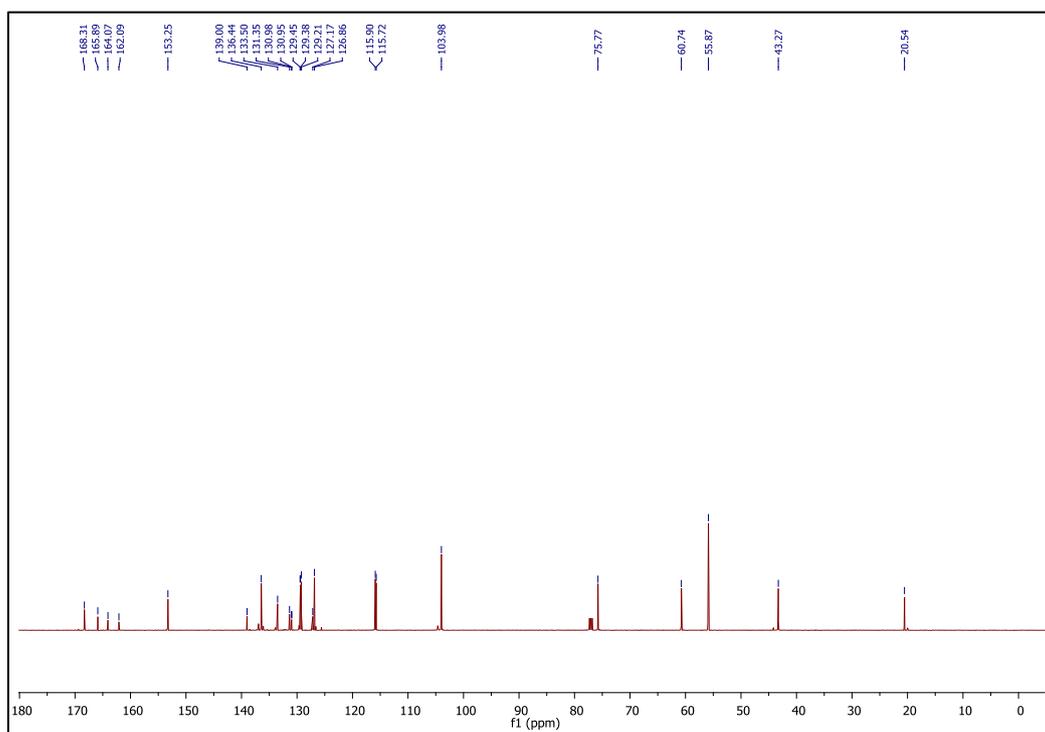
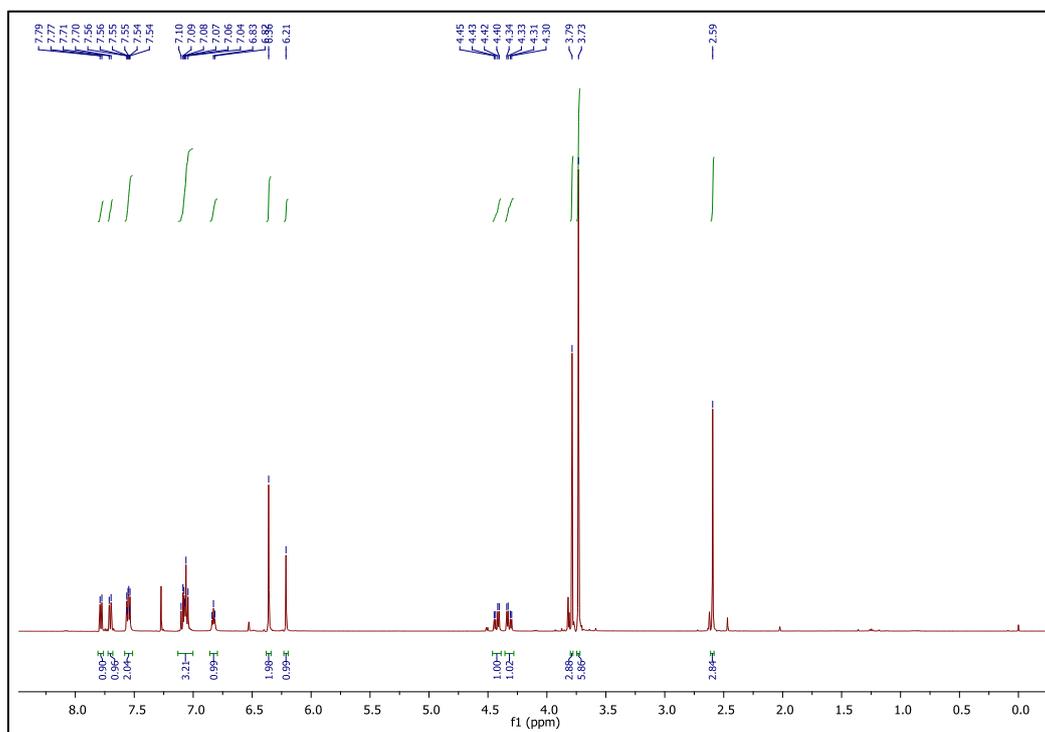
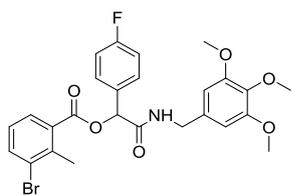
5-(3-fluorophenyl)oxazole ( $[^{19}\text{F}]10$ ):



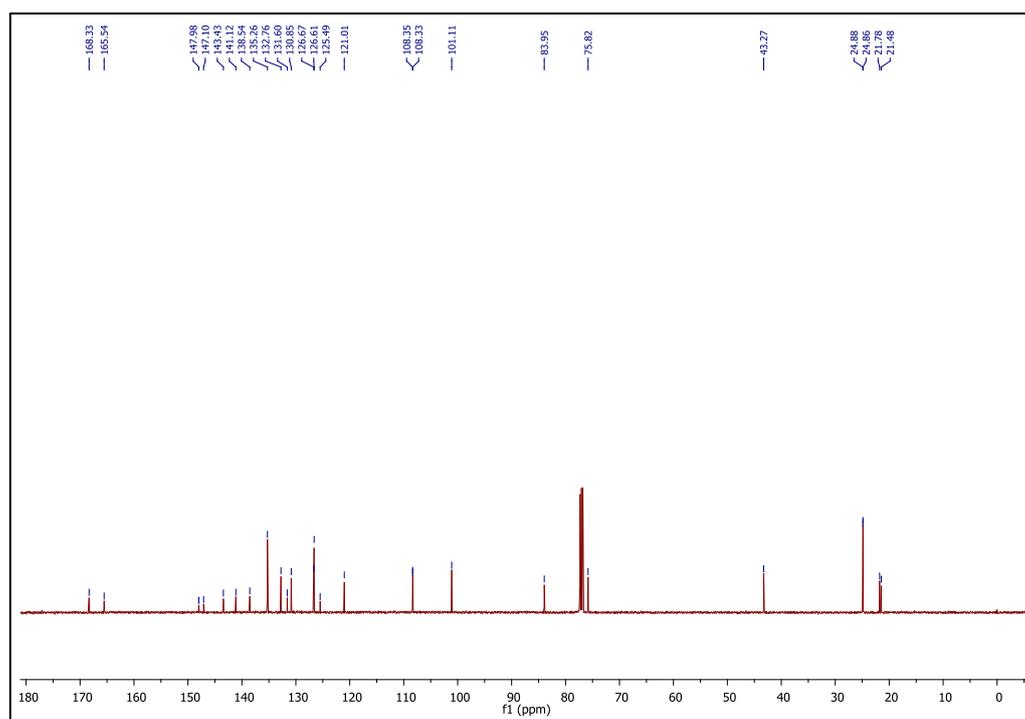
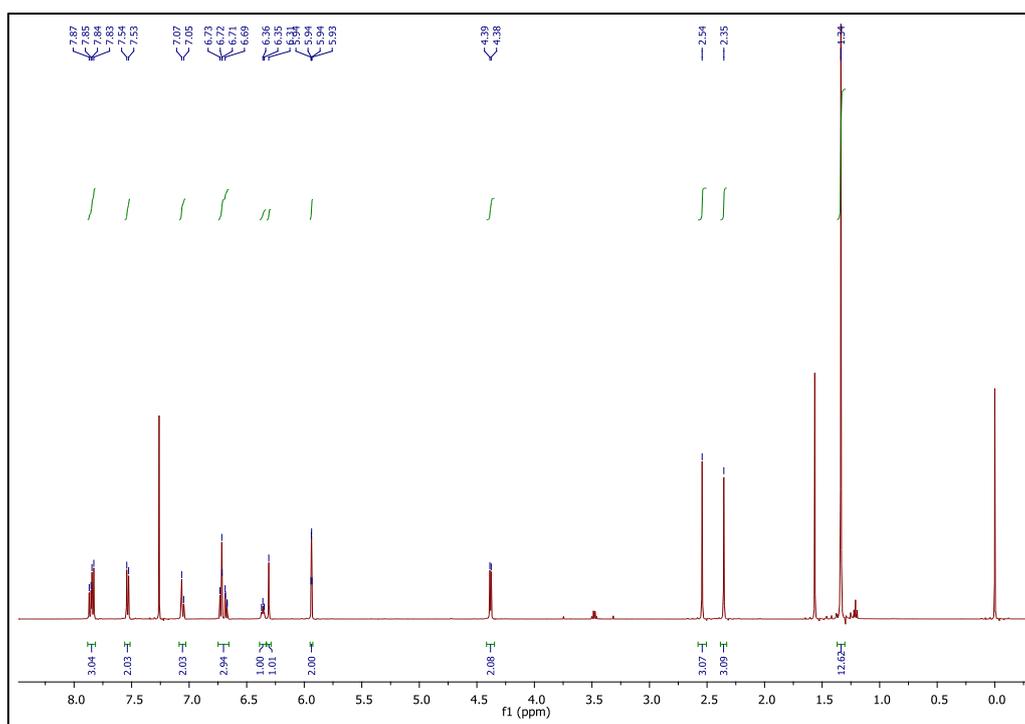
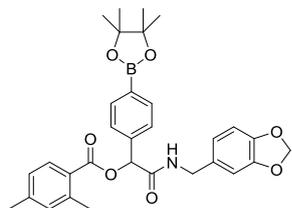
2-oxo-1-(4-(4,4,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-2-((3,4,5-trimethoxybenzyl)amino)ethyl 3-bromo-2-methylbenzoate (11):



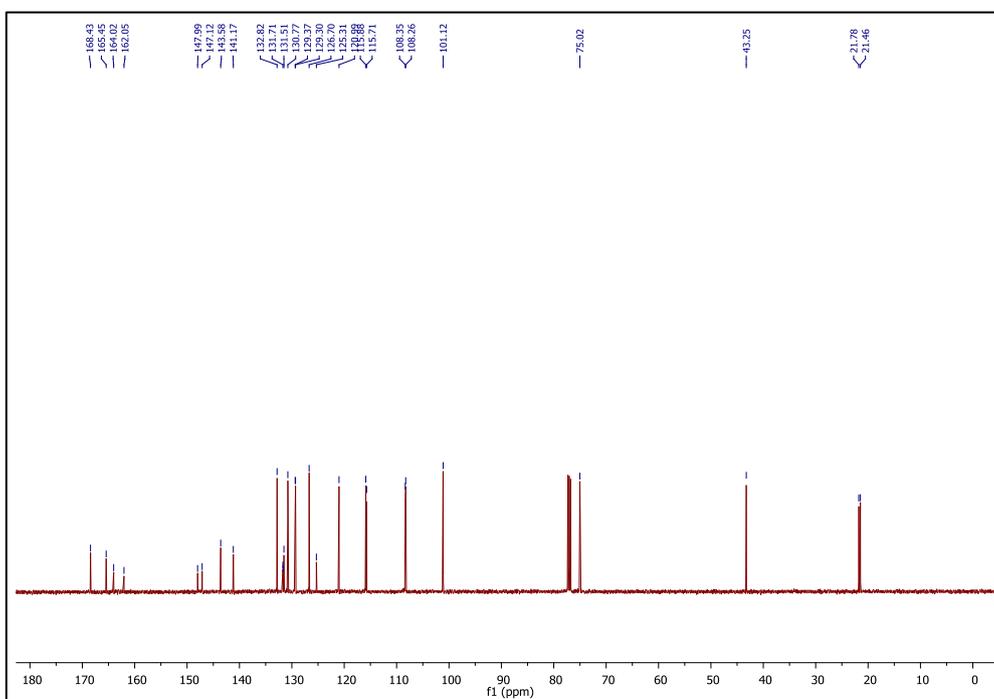
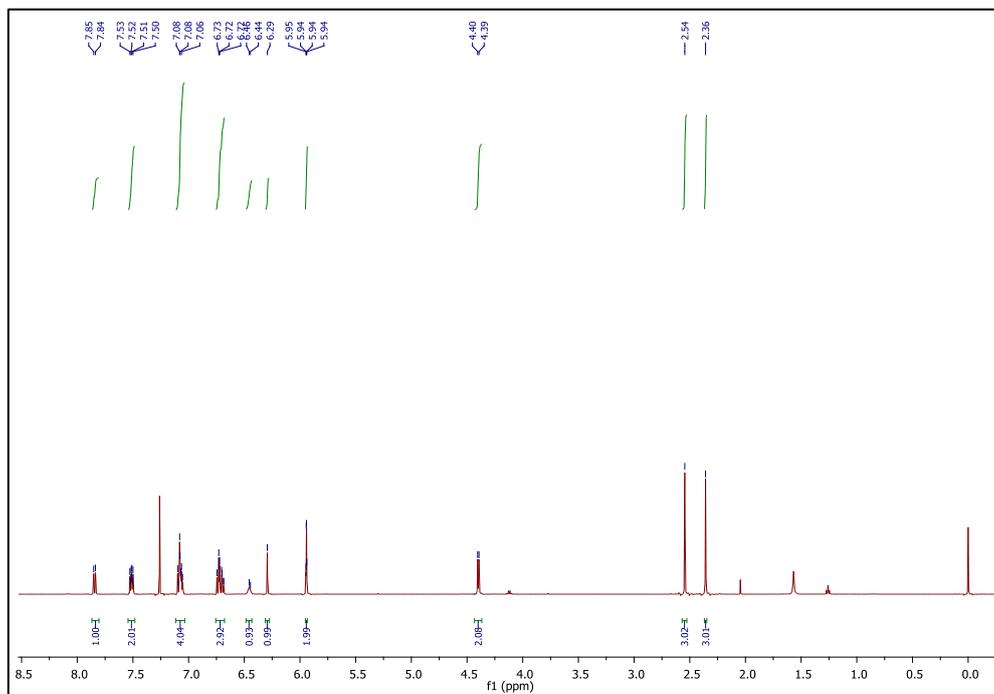
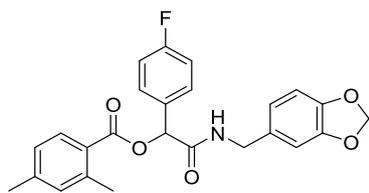
1-(4-fluorophenyl)-2-oxo-2-((3,4,5-trimethoxybenzyl)amino)ethyl 3-bromo-2-methylbenzoate ( $[^{19}\text{F}]11$ ):



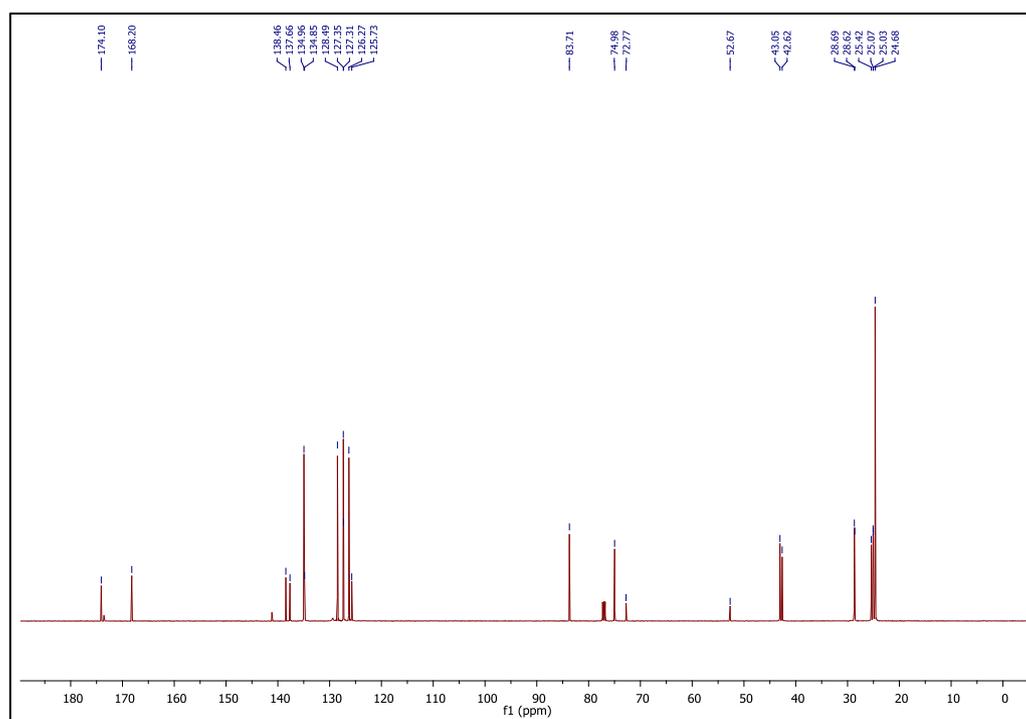
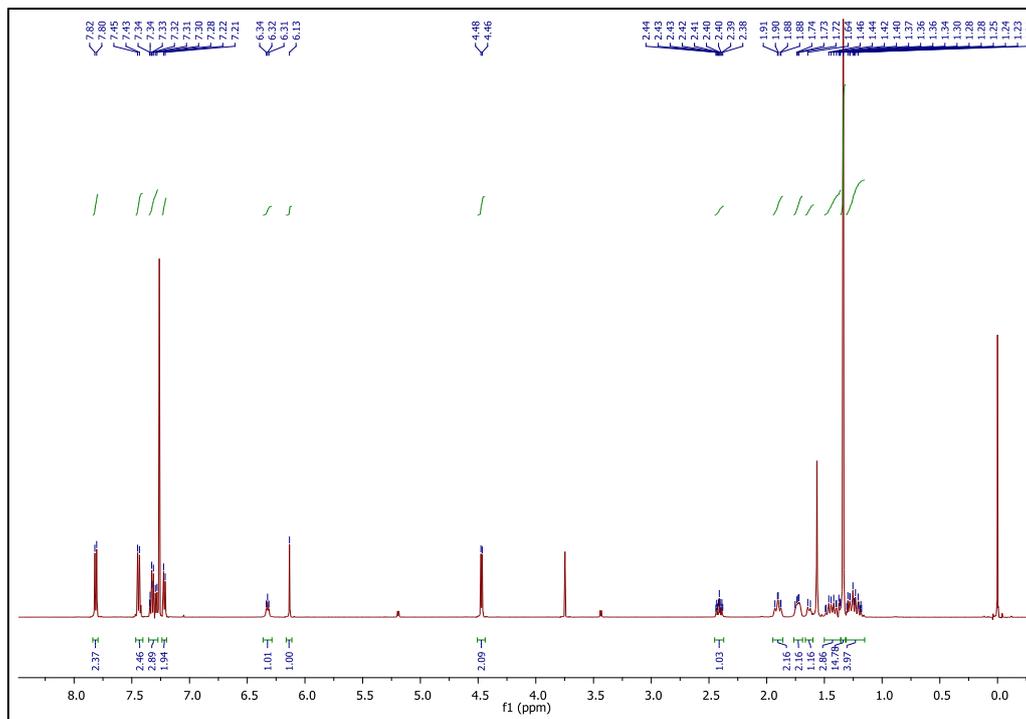
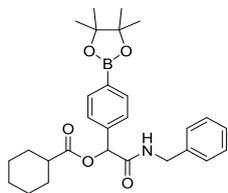
2-((benzo[d][1,3]dioxol-5-ylmethyl)amino)-2-oxo-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl 2,4-dimethylbenzoate (12):



2-((benzo[d][1,3]dioxol-5-ylmethyl)amino)-1-(4-fluorophenyl)-2-oxoethyl 2,4-dimethylbenzoate ( $[^{19}\text{F}]12$ ):



2-(benzylamino)-2-oxo-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)ethyl cyclohexanecarboxylate  
(13):



2-(benzylamino)-1-(4-fluorophenyl)-2-oxoethyl cyclohexanecarboxylate ( $[^{19}\text{F}]13$ ):

