

# **Supporting Information File 2**

for

## **Continuous gas/liquid–liquid/liquid flow synthesis of 4-fluoropyrazole derivatives by selective direct fluorination**

Jessica R. Breen<sup>1</sup>, Graham Sandford<sup>1\*</sup>, Dmitrii S. Yufit<sup>2</sup>, Judith A. K. Howard<sup>2</sup>, Jonathan Fray<sup>3</sup> and Bhairavi Patel<sup>3</sup>

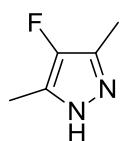
Address: <sup>1</sup>Department of Chemistry, Durham University, South Road, Durham, DH1 3LE, UK; <sup>2</sup>Chemical Crystallography Group, Department of Chemistry, Durham University, South Road, Durham, DH1 3LE, UK and <sup>3</sup>Pfizer Global Research & Development, Ramsgate Road, Sandwich, Kent, CT13 9NJ, UK

Email: Graham Sandford\* - [Graham.Sandford@durham.ac.uk](mailto:Graham.Sandford@durham.ac.uk)

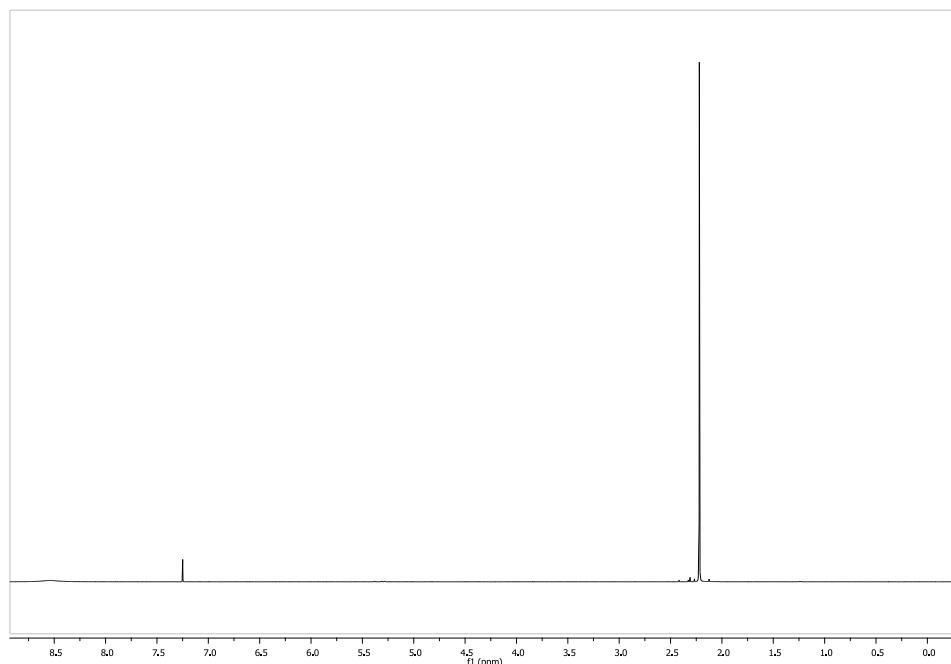
\*Corresponding author

## **NMR spectra**

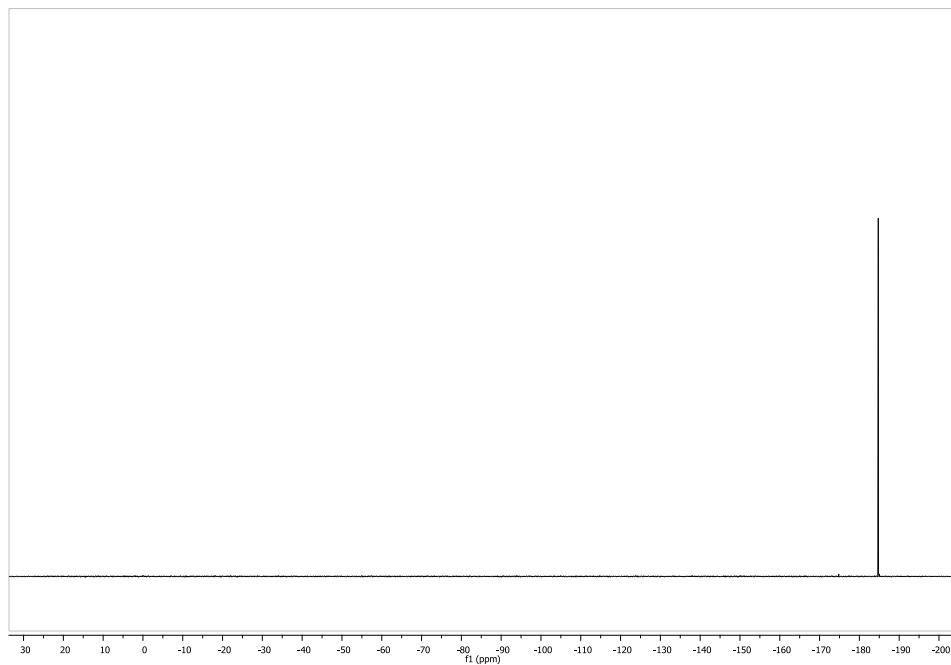
**4-Fluoro-3,5-dimethyl-1*H*-pyrazole (4a)**



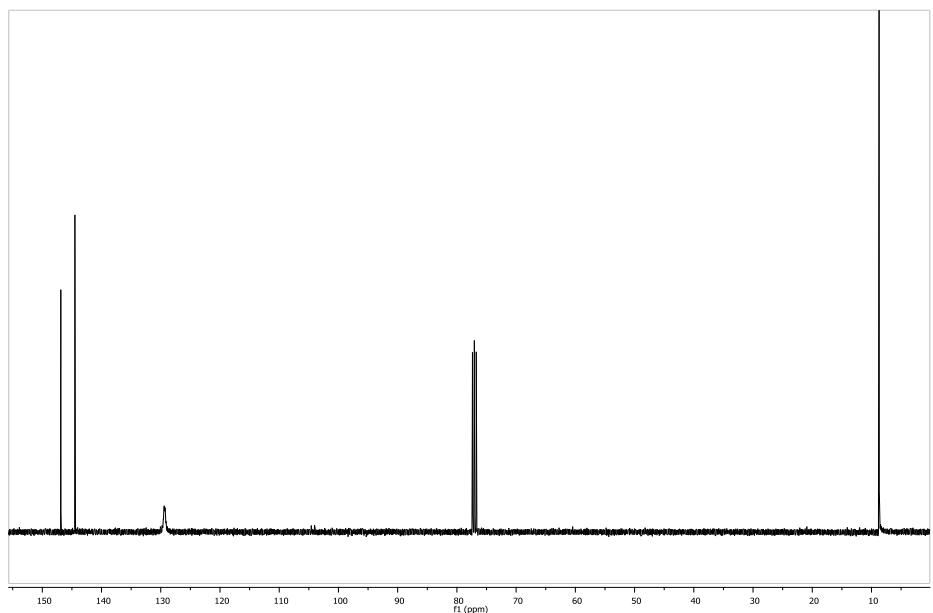
$^1\text{H}$  NMR (700 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



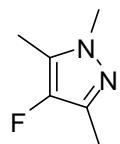
$^{19}\text{F}$  NMR (658 MHz,  $\text{CDCl}_3$ )



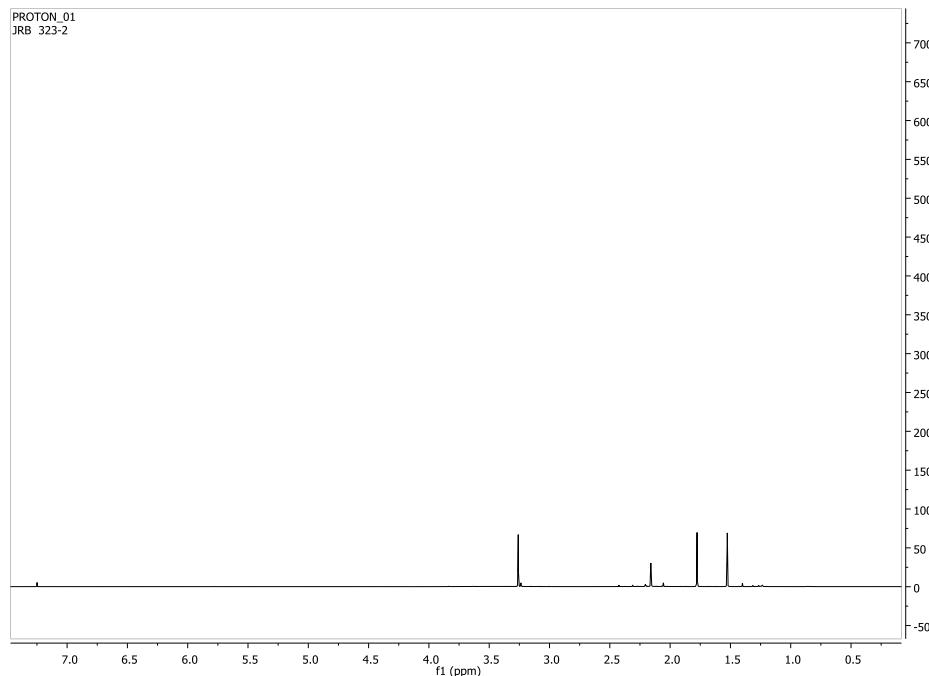
$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



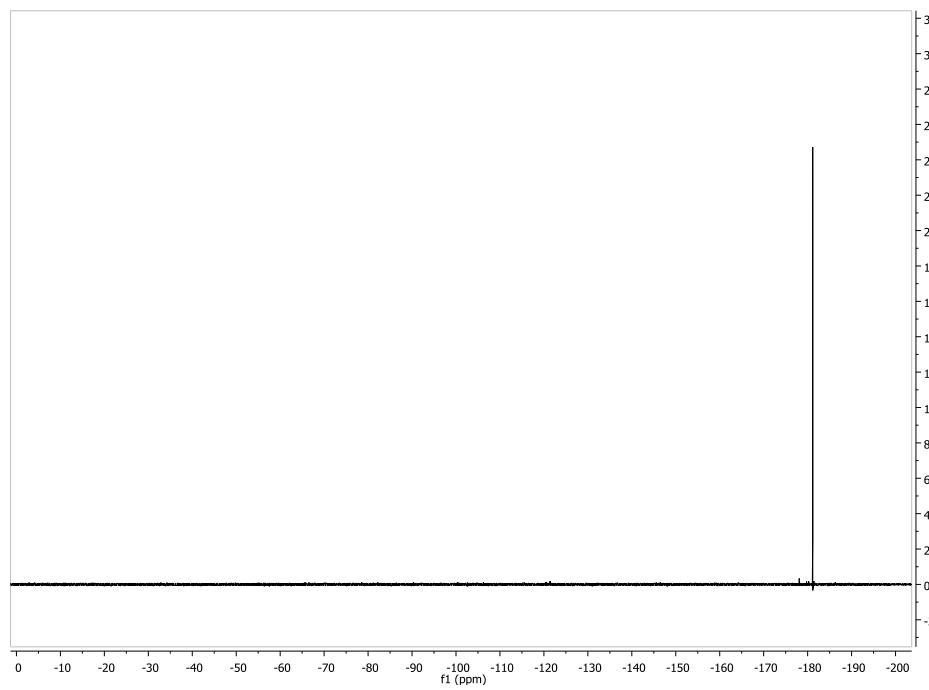
**4-Fluoro-1,3,5-trimethyl-1*H*-pyrazole (4b)**



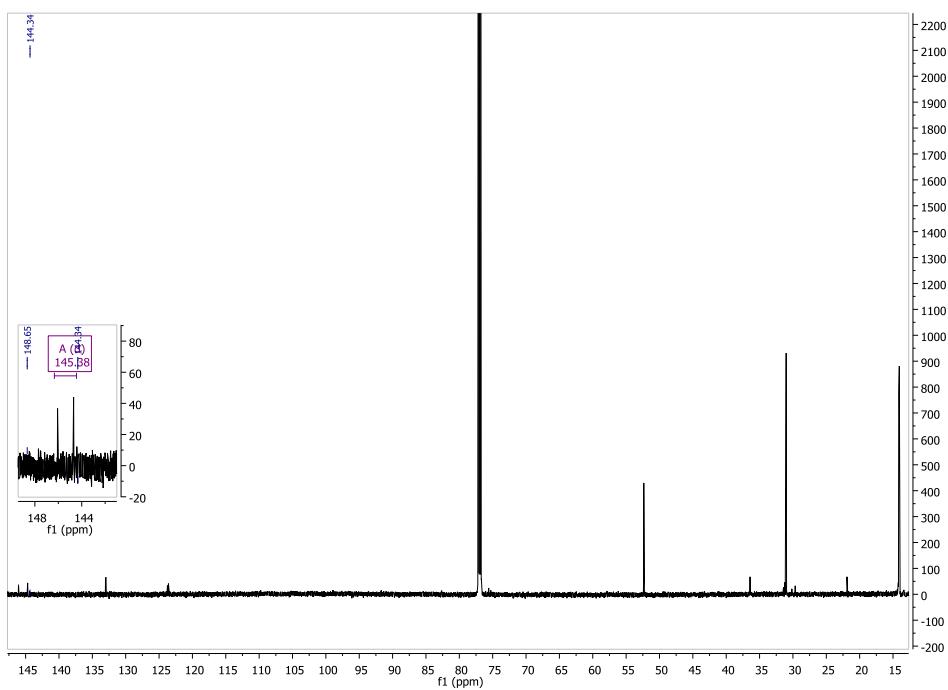
$^1\text{H}$  NMR (700 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



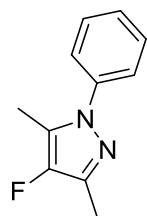
$^{19}\text{F}$  NMR (658 MHz,  $\text{CDCl}_3$ ,  $\text{CFCl}_3$ )



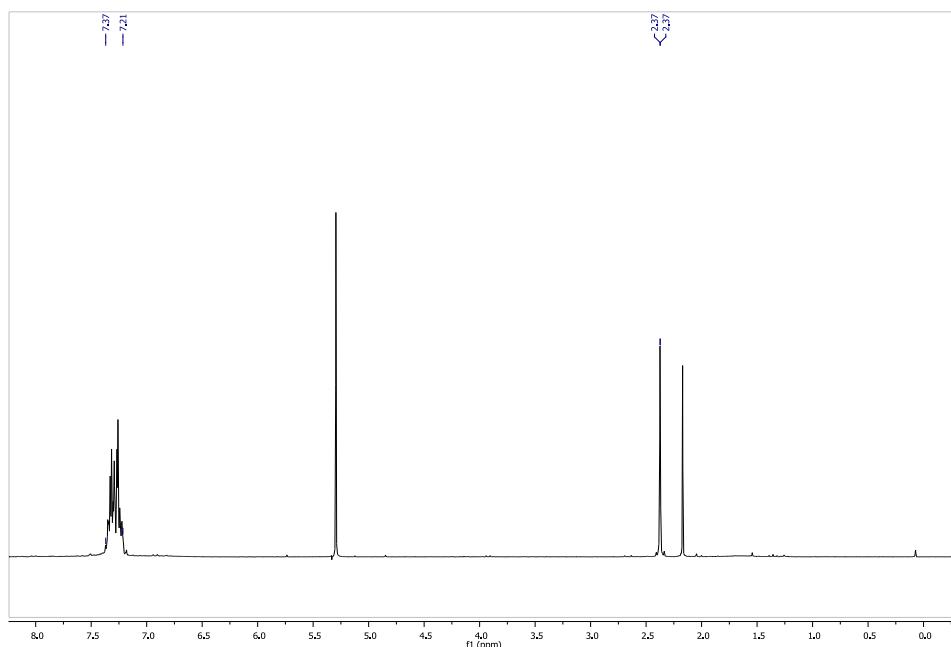
$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



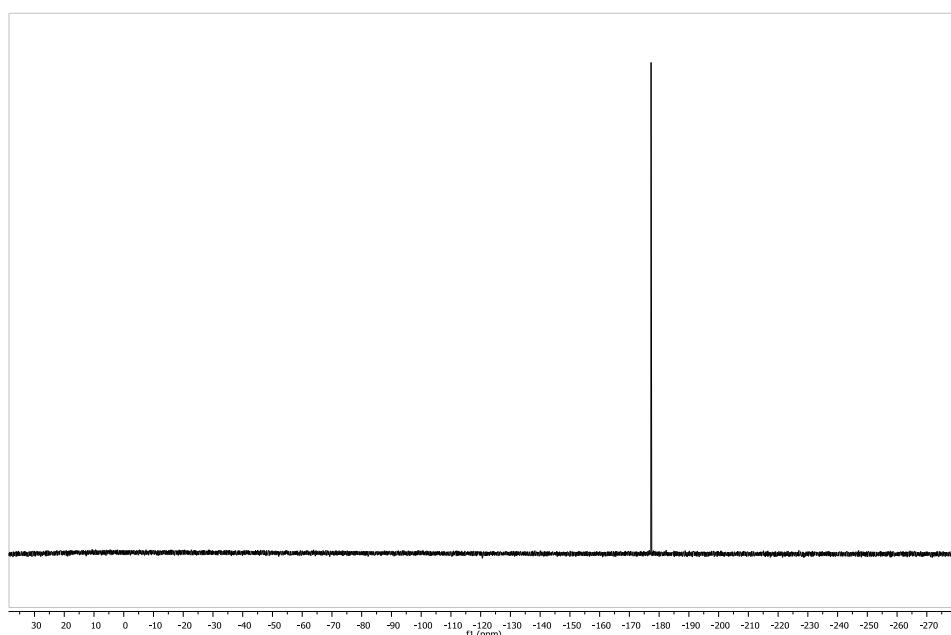
**4-Fluoro-3,5-dimethyl-1-phenyl-1*H*-pyrazole (4c)**



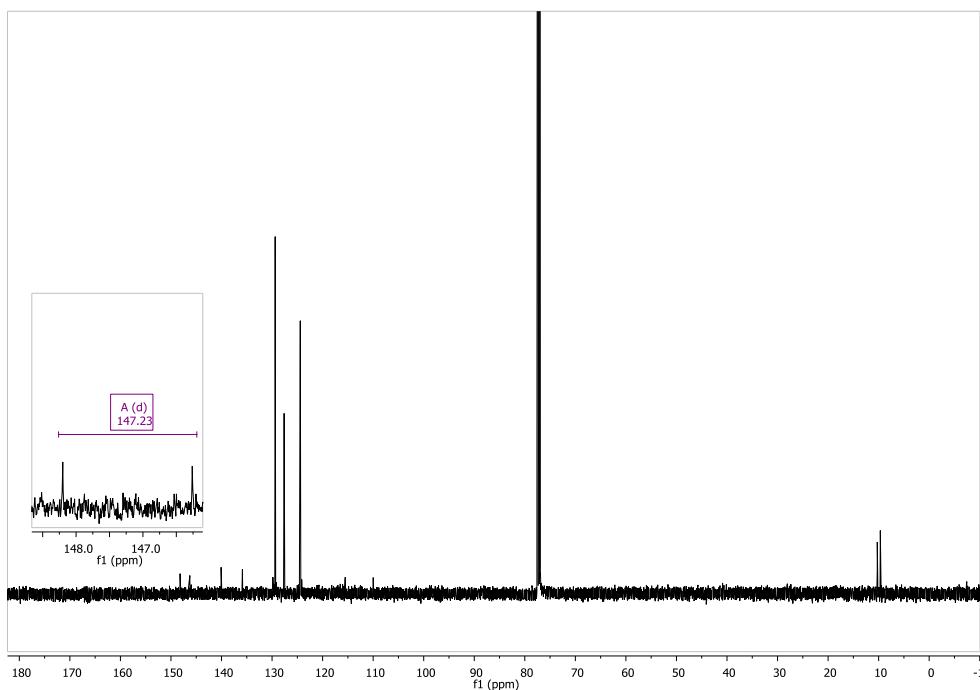
$^1\text{H}$  NMR (700 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



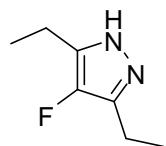
$^{19}\text{F}$  NMR (658 MHz,  $\text{CDCl}_3$ ,  $\text{CFCl}_3$ )



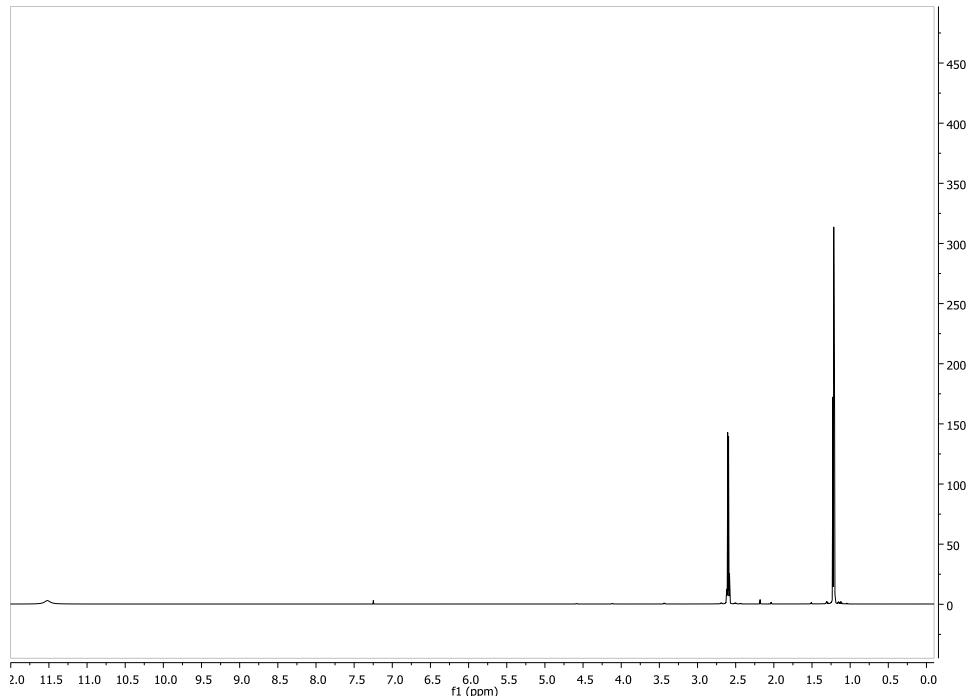
$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



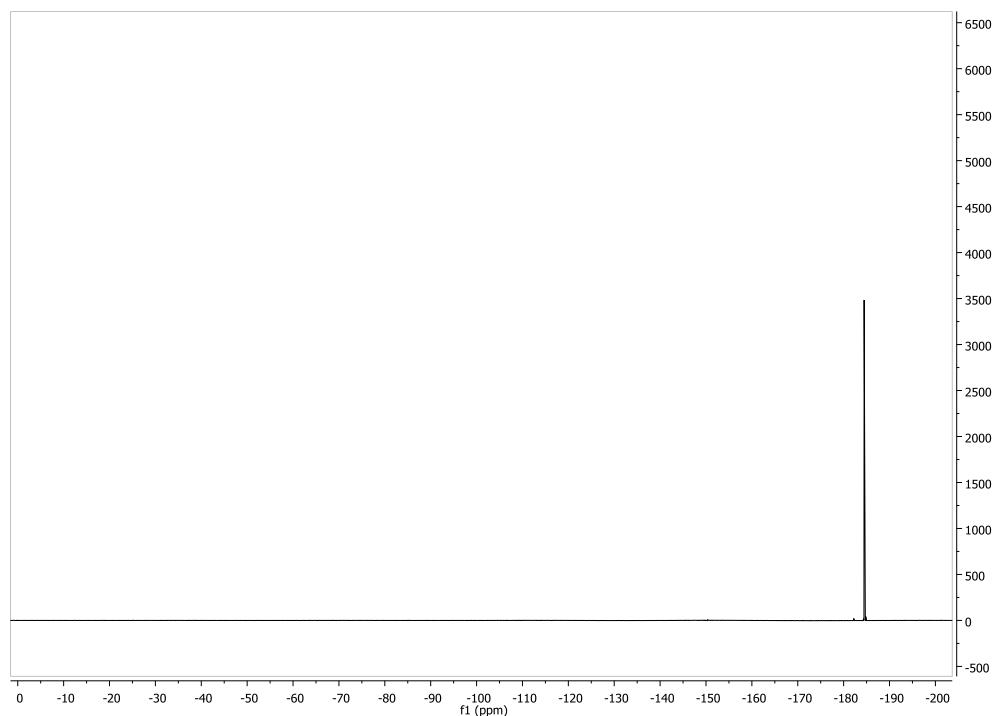
**3,5-Diethyl-4-fluoro-1*H*-pyrazole (4d)**



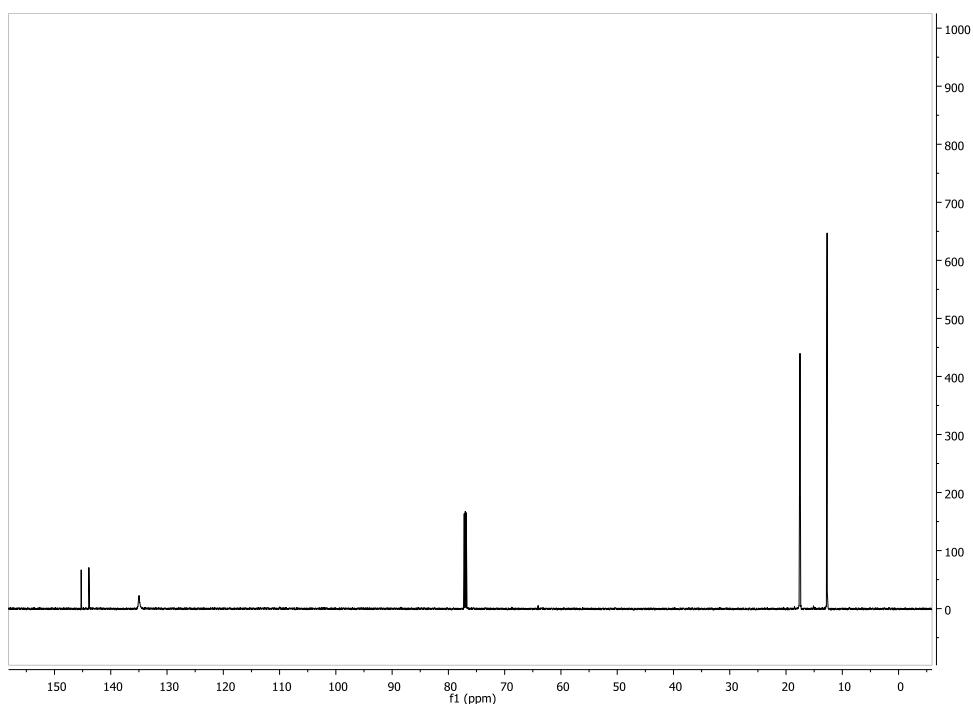
<sup>1</sup>H NMR (700 MHz, CDCl<sub>3</sub>, Me<sub>4</sub>Si)



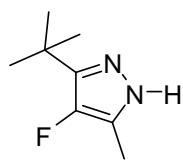
<sup>19</sup>F NMR (658 MHz, CDCl<sub>3</sub>, CFCl<sub>3</sub>)



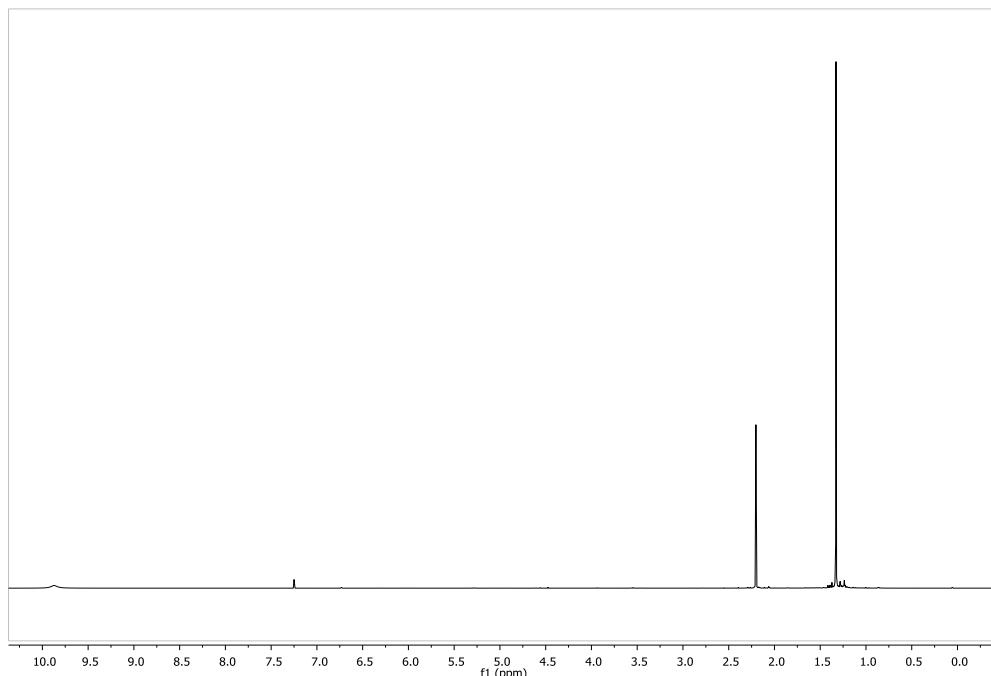
$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



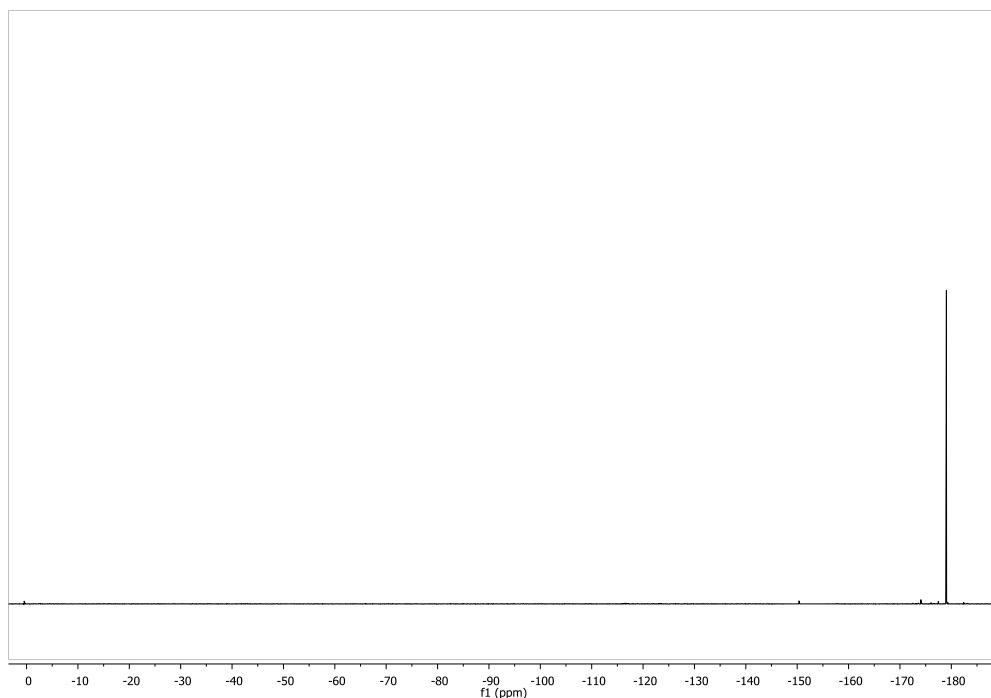
**3-*tert*-Butyl-4-fluoro-5-methyl-1*H*-pyrazole (4e)**



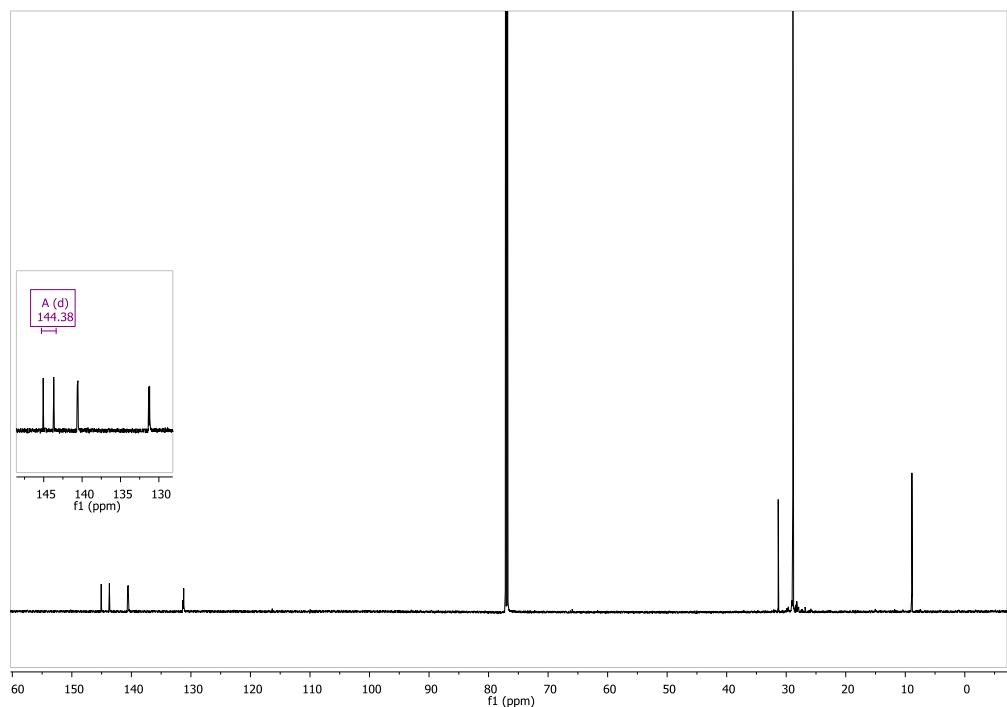
$^1\text{H}$  NMR (700 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



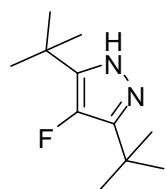
$^{19}\text{F}$  NMR (658 MHz,  $\text{CDCl}_3$ ,  $\text{CFCl}_3$ )



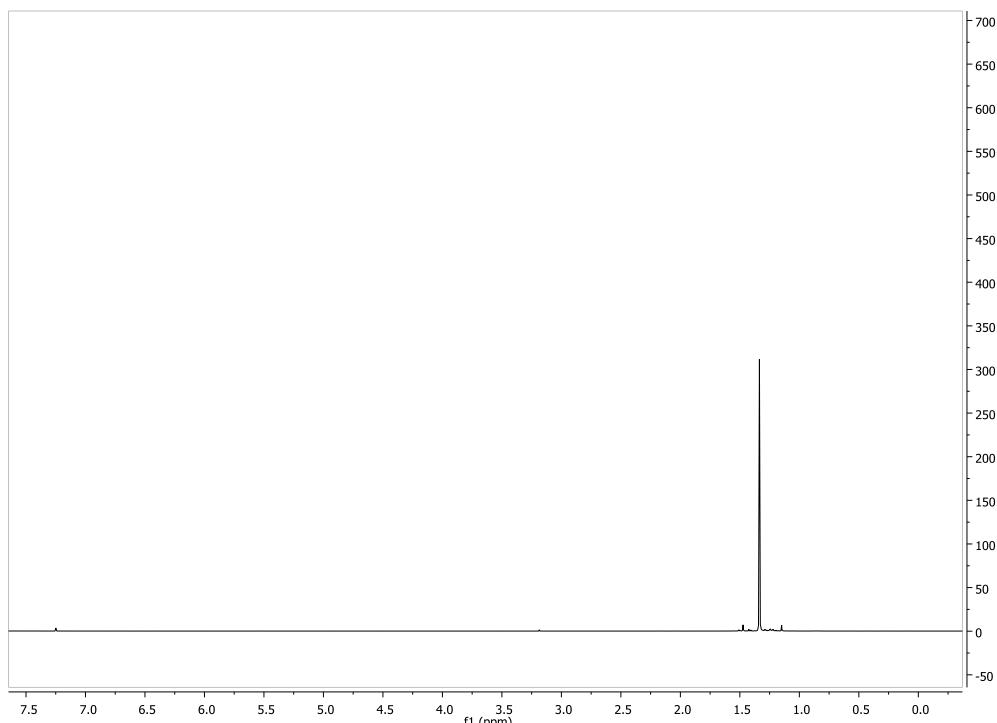
$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



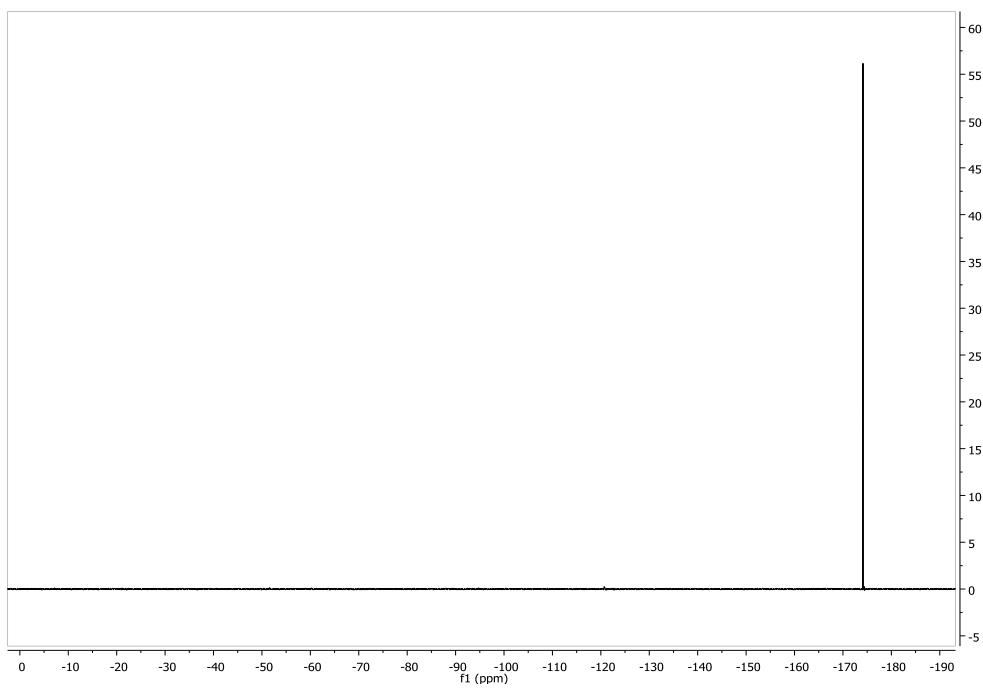
**3,5-Di-*tert*-butyl-4-fluoro-1*H*-pyrazole (4f)**



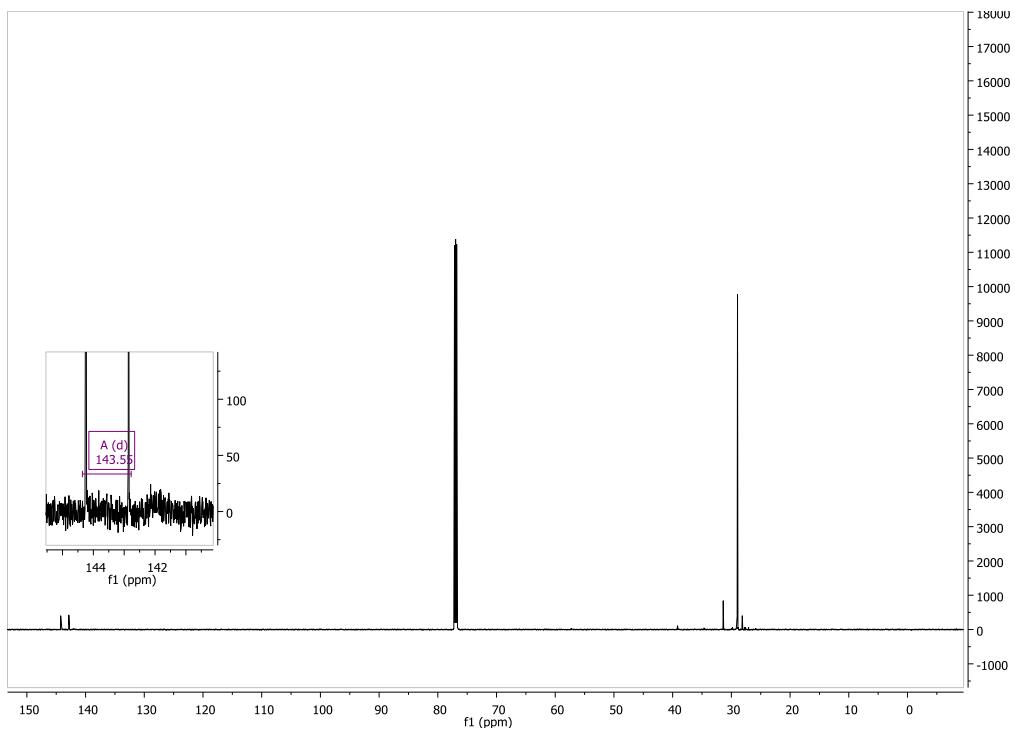
$^1\text{H}$  NMR (700 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



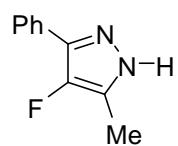
$^{19}\text{F}$  NMR (658 MHz,  $\text{CDCl}_3$ ,  $\text{CFCl}_3$ )



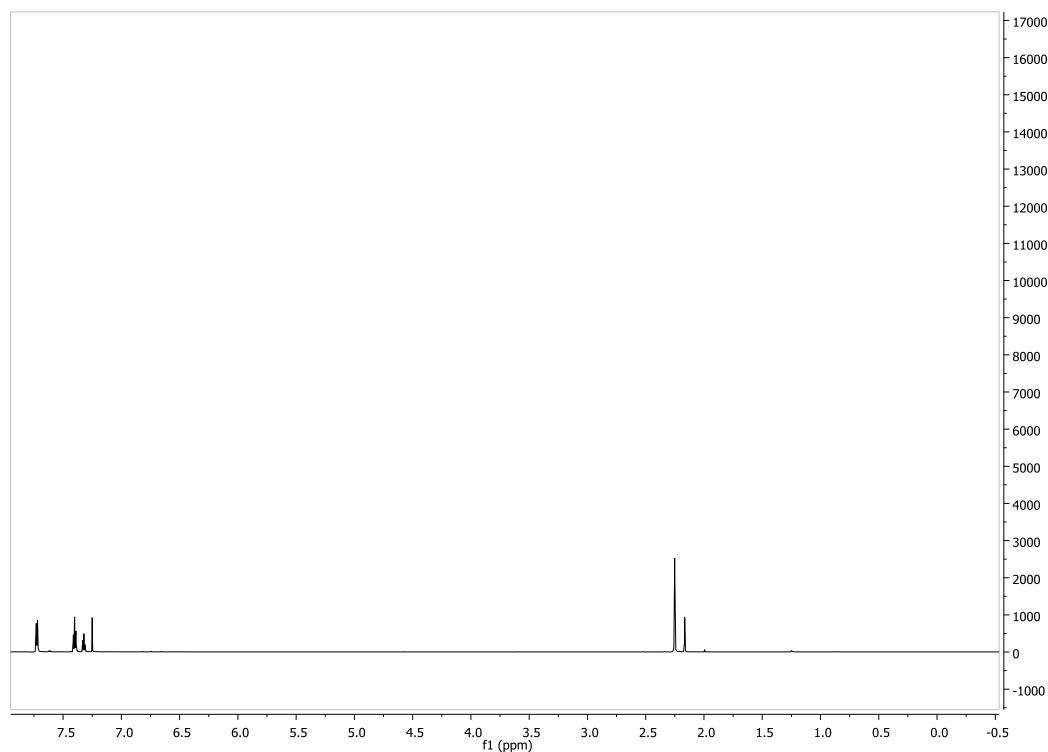
$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



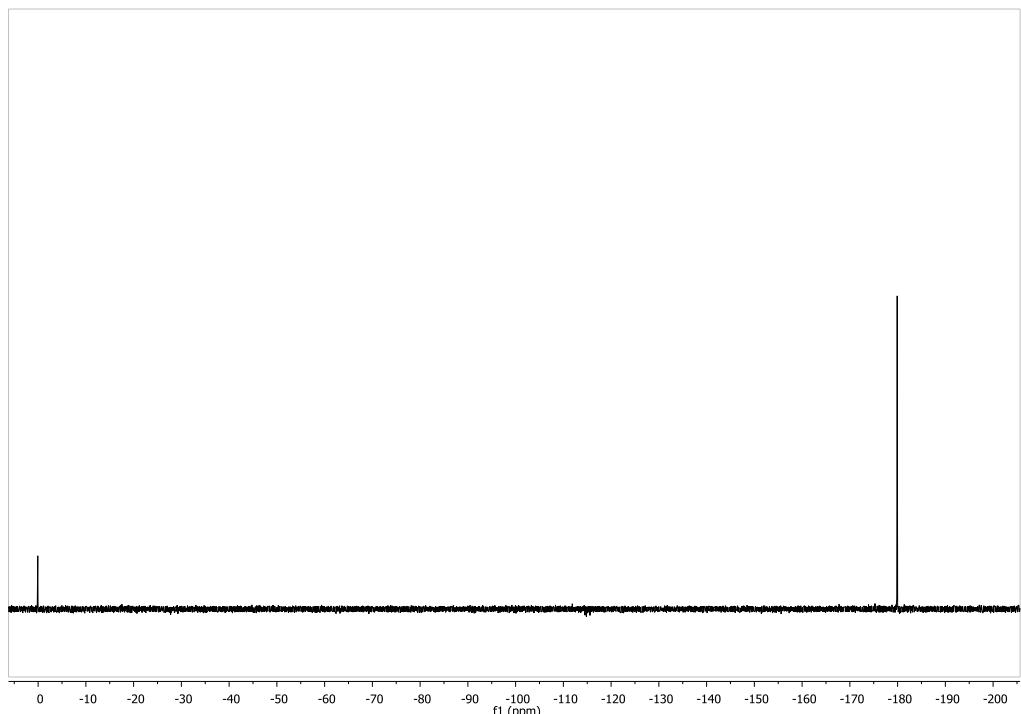
**4-Fluoro-5-methyl-3-phenyl-1*H*-pyrazole (4g)**



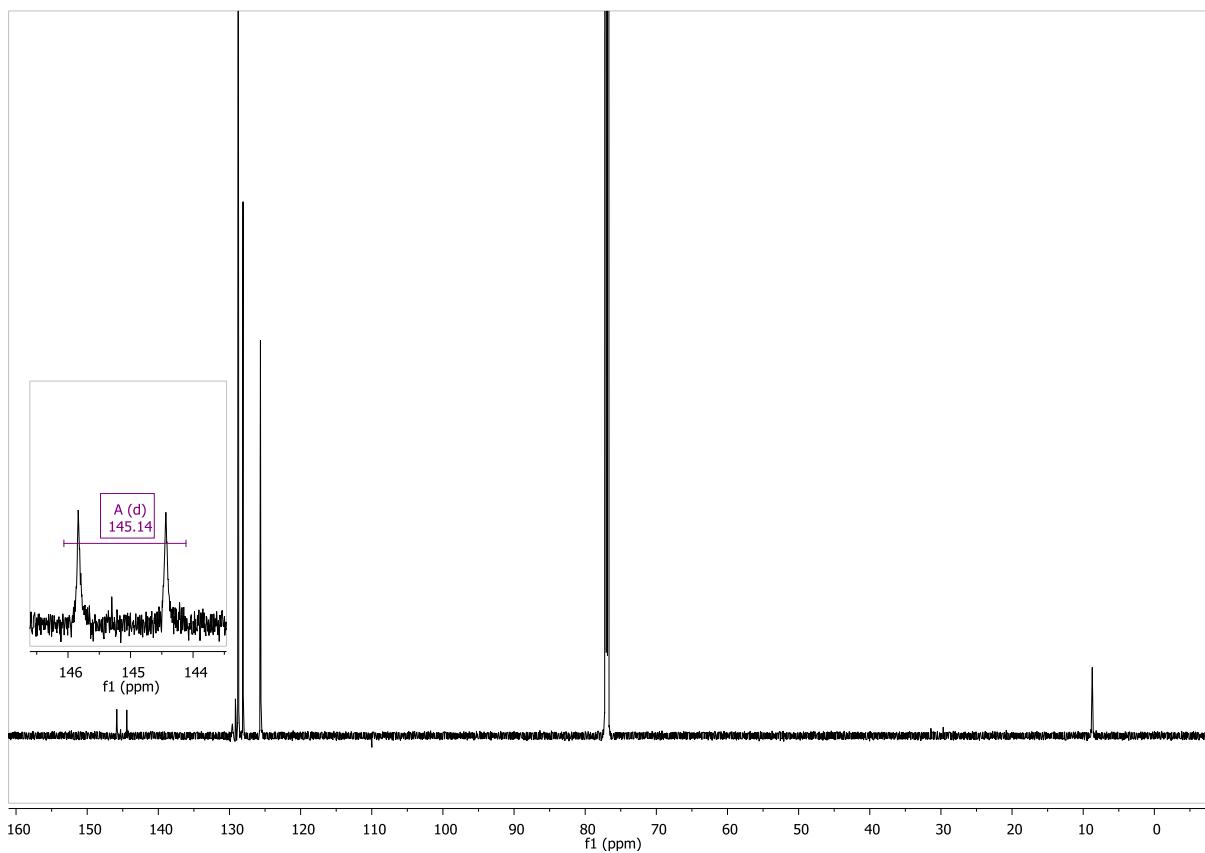
$^1\text{H}$  NMR (700 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



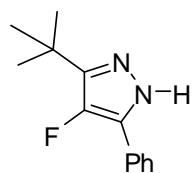
$^{19}\text{F}$  NMR (658 MHz,  $\text{CDCl}_3$ ,  $\text{CFCl}_3$ )



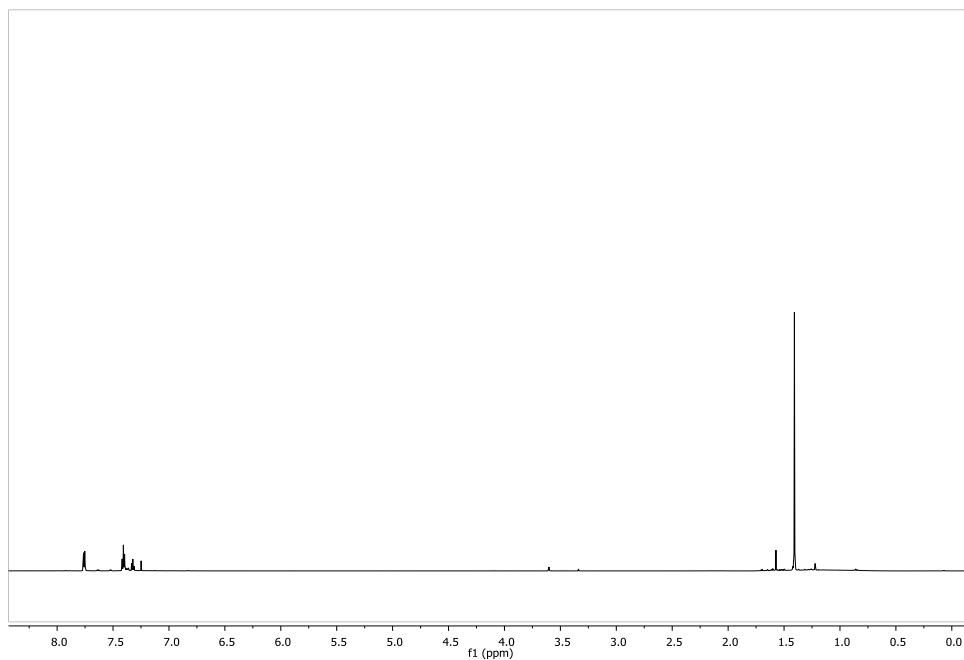
$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )



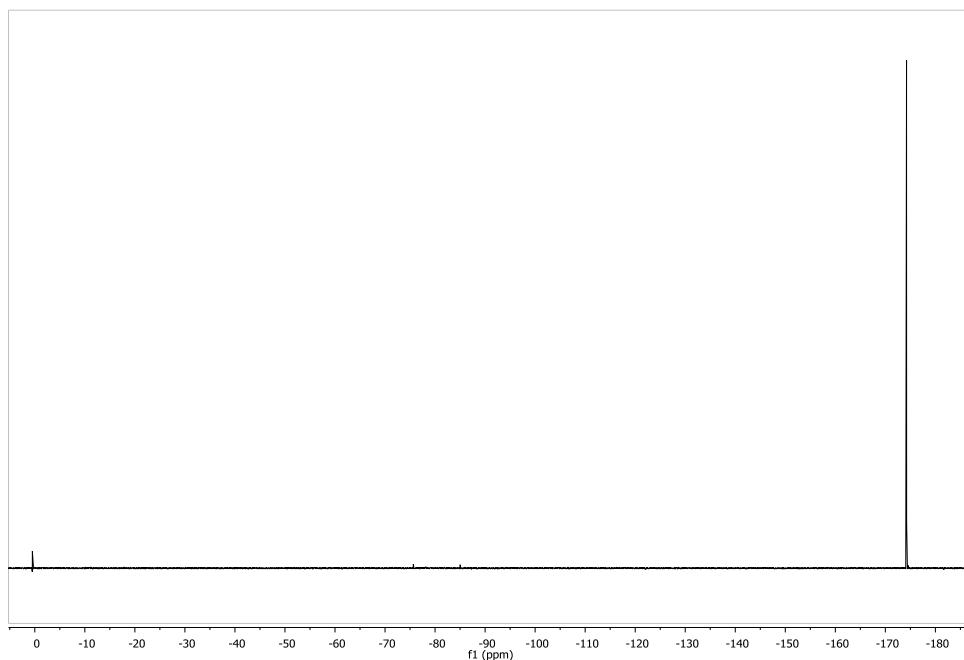
**3-*tert*-Butyl-4-fluoro-5-phenyl-1*H*-pyrazole (4h)**



<sup>1</sup>H NMR (700 MHz, CDCl<sub>3</sub>, Me<sub>4</sub>Si)



<sup>19</sup>F NMR (658 MHz, CDCl<sub>3</sub>, CFCl<sub>3</sub>)



$^{13}\text{C}$  NMR (176 MHz,  $\text{CDCl}_3$ ,  $\text{Me}_4\text{Si}$ )

