

Supplementary Information

Strategies for the Efficient Synthesis of Biheterocyclic 5-[2-(Trifluoromethylheteroaryl)-ethyl]-1,3,4-oxadiazoles from Levulinic Acid

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¹H/¹³C NMR spectra for the series of the 5(2)-[2-(trifluoromethyl heteroaryl)ethyl]-1,3,4-oxadiazoles are shown. The ¹H and ¹³C (1D and 2D) spectra were recorded at 298 K on a Bruker DPX 400 spectrometer (¹H at 400.13 MHz, ¹³C at 100.63 MHz) with digital resolution of ± 0.01 ppm. 0.1 M CDCl₃ or 0.1 M in DMSO-*d*₆ solutions were used, all the chemical shifts are expressed in ppm, with respect to internal TMS.

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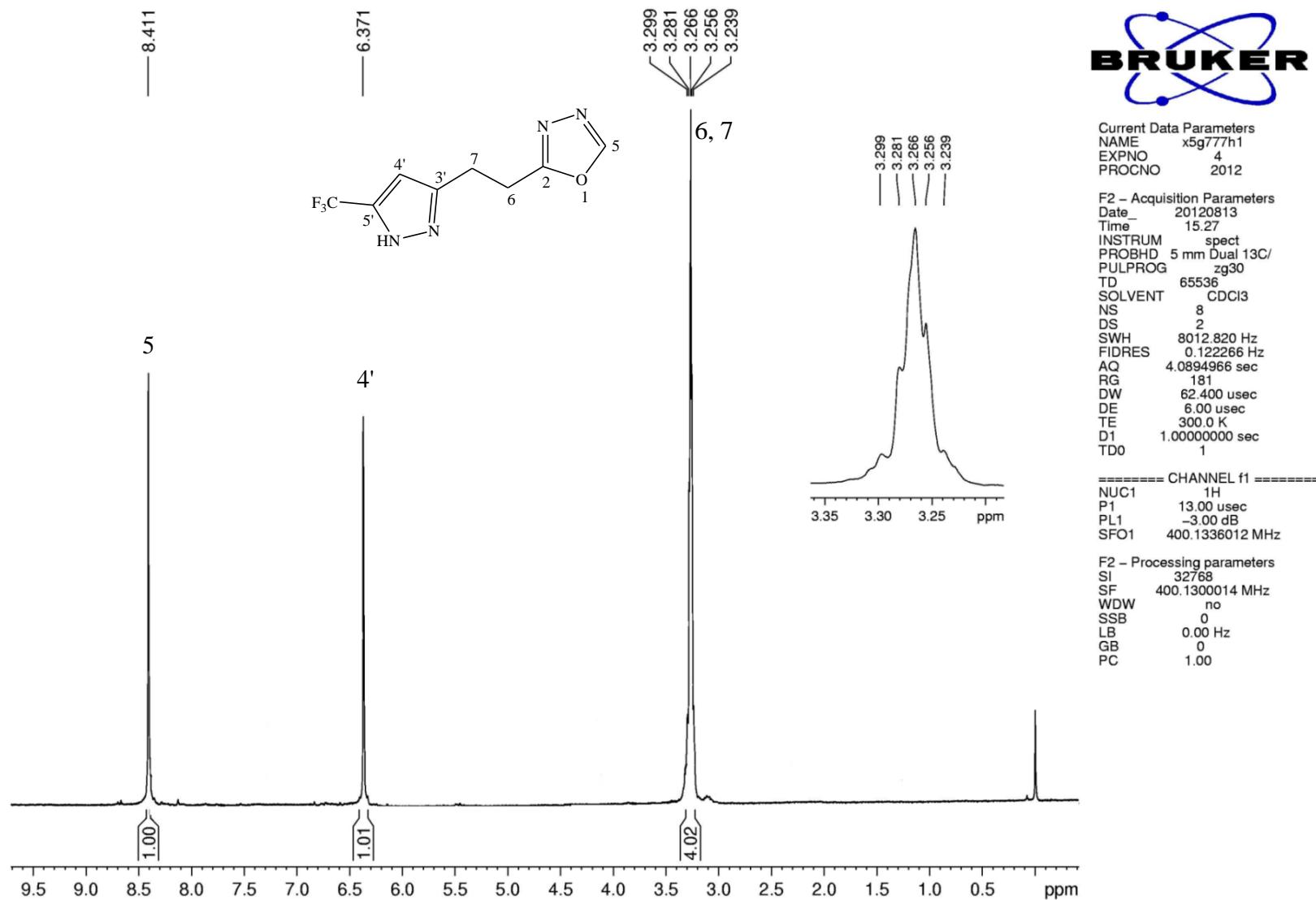


Figure S1. ¹H NMR spectrum (400 MHz, CDCl₃) of 2-[2-(5-trifluoromethyl-1H-pyrazol-3-yl)ethyl]-1,3,4-oxadiazole (**4a**).

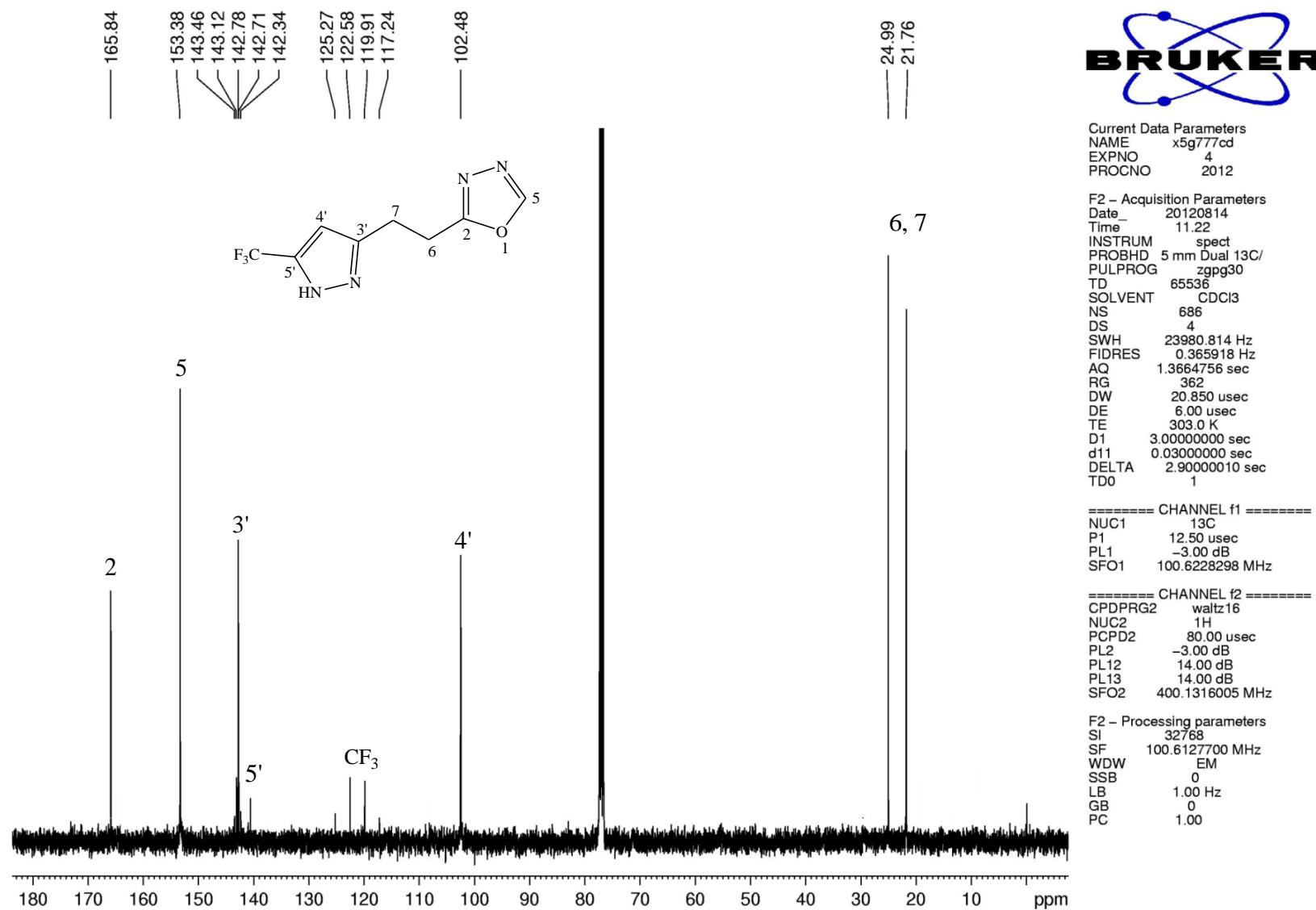


Figure S2. ¹³C NMR spectrum (100 MHz, CDCl₃) of 2-[2-(5-trifluoromethyl-1H-pyrazol-3-yl)ethyl]-1,3,4-oxadiazole (**4a**).

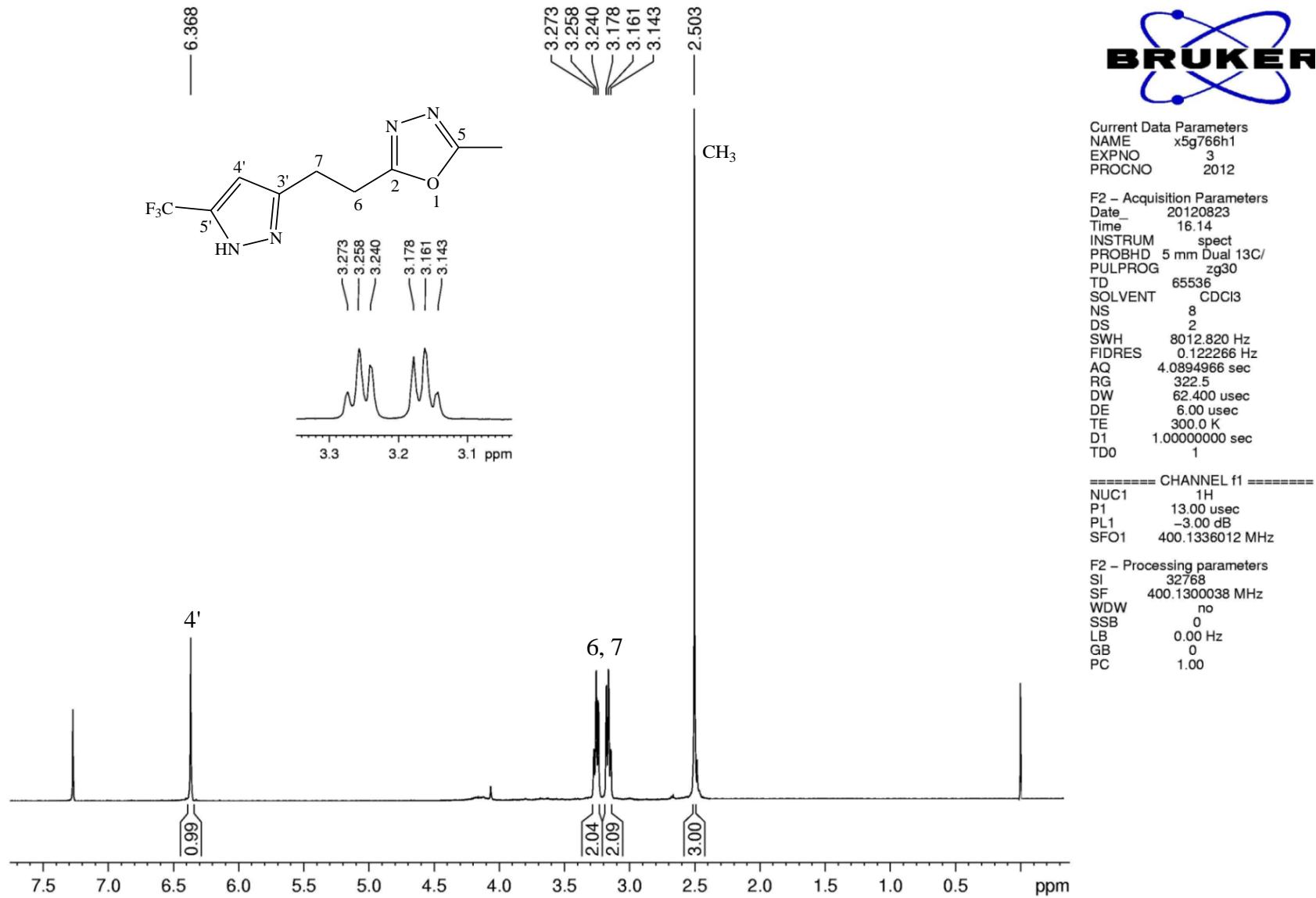
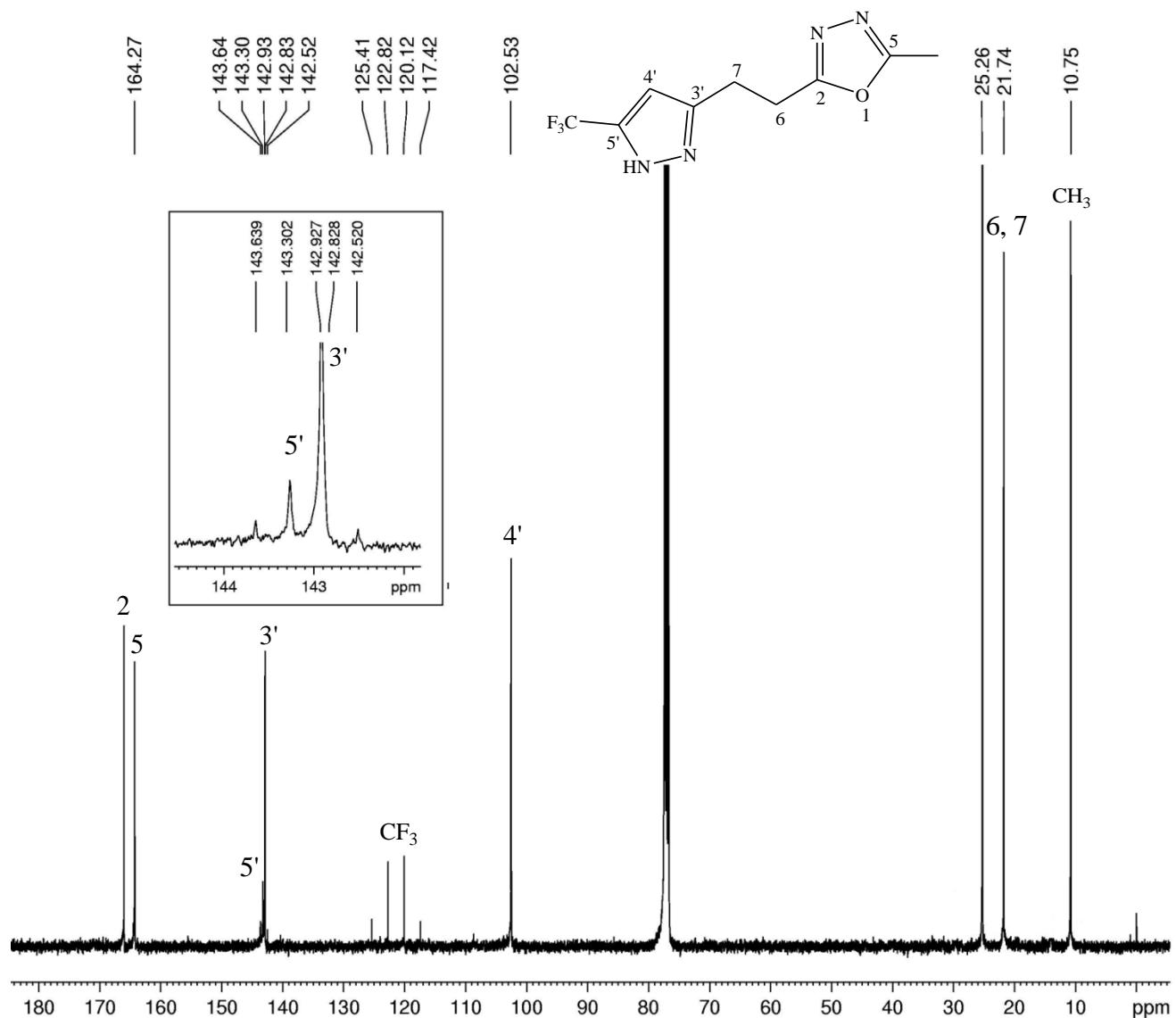


Figure S3. ¹H NMR spectrum (400 MHz, CDCl₃) of 5-methyl-2-[2-(5-trifluoromethyl-1H-pyrazol-3-yl)ethyl]-1,3,4-oxadiazole (**5a**).



Current Data Parameters

NAME x5g766cd
EXPNO 3
PROCNO 2012

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PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 17165
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 362
DW 20.850 usec
DE 6.00 usec
TE 318.0 K
D1 3.0000000 sec
d11 0.0300000 sec
DELTA 2.90000010 sec
TDO 1

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PL1 -3.00 dB
SFO1 100.6228298 MHz

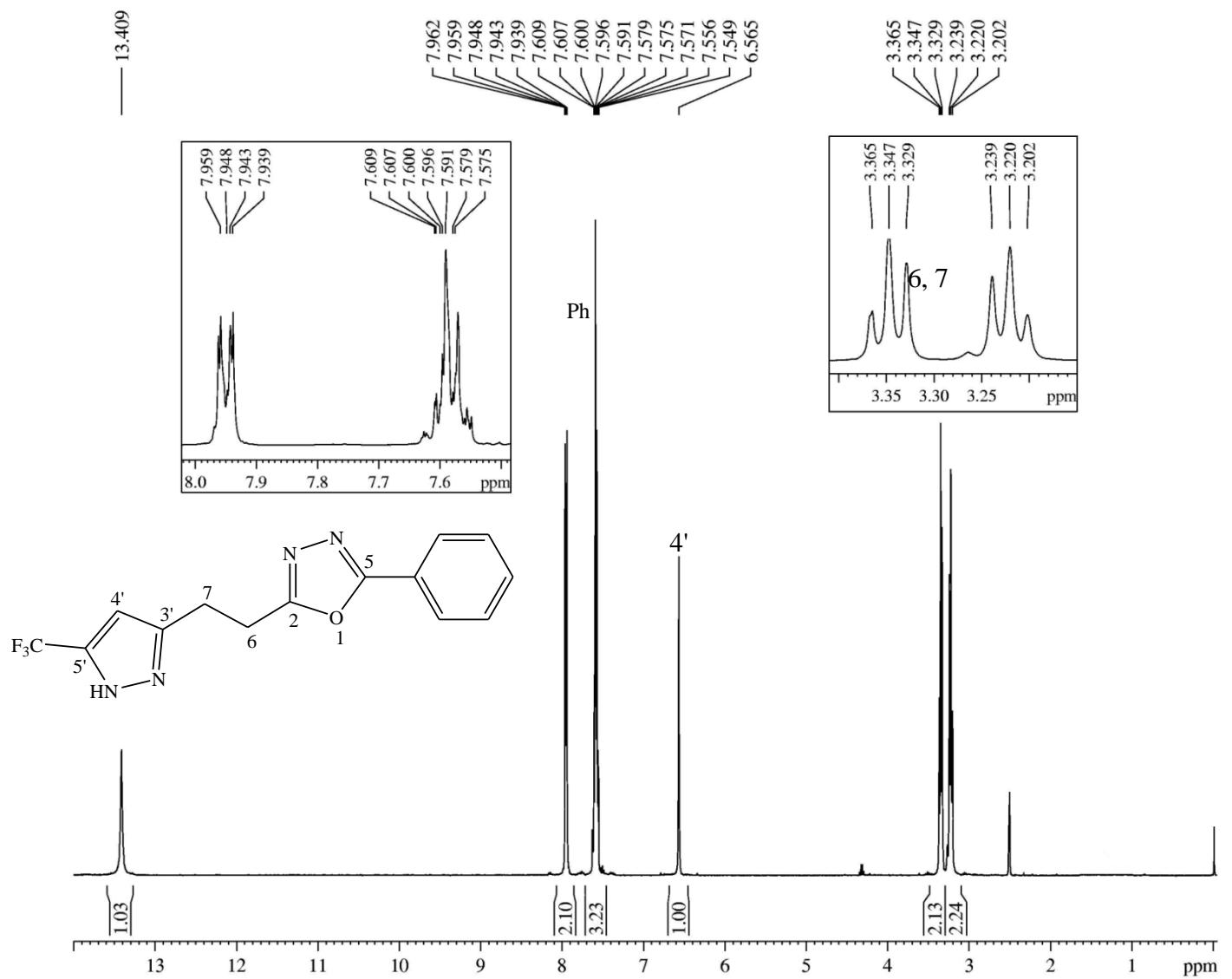
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PL2 -3.00 dB
PL12 14.00 dB
PL13 14.00 dB
SFO2 400.1316005 MHz

F2 – Processing parameters

SI 32768
SF 100.6127622 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

Figure S4. ^{13}C NMR spectrum (400 MHz, CDCl_3) of 5-methyl-2-[2-(5-trifluoromethyl-1*H*-pyrazol-3-yl)ethyl]-1,3,4-oxadiazole (**5a**).



Current Data Parameters
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 EXPNO 1
 PROCNO 2012

F2 – Acquisition Parameters
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 Time 12.06
 INSTRUM spect
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 PULPROG zg30
 TD 65536
 SOLVENT DMSO
 NS 8
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.122266 Hz
 AQ 4.0894966 sec
 RG 128
 DW 62.400 usec
 DE 6.00 usec
 TE 318.0 K
 DI 1.0000000 sec
 TD0 1

===== CHANNEL f1 =====
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 P1 13.00 usec
 PL1 -3.00 dB
 SFO1 400.1336012 MHz

F2 – Processing parameters
 SI 32768
 SF 400.1300000 MHz
 WDW no
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.00

Figure S5. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of 5-phenyl-2-[2-(5-trifluoromethyl-1*H*-pyrazol-3-yl)ethyl]-1,3,4-oxadiazole (**6a**).

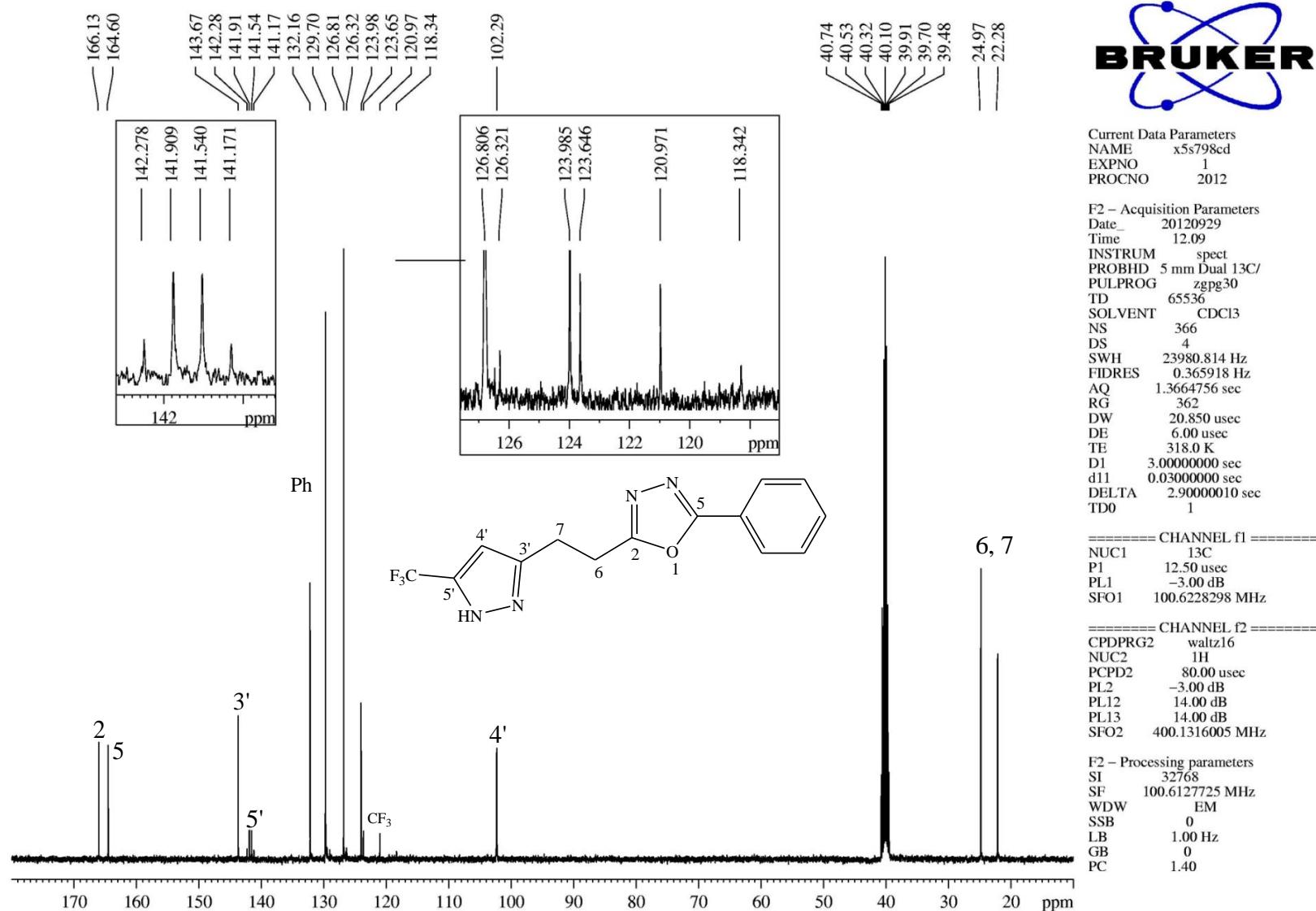
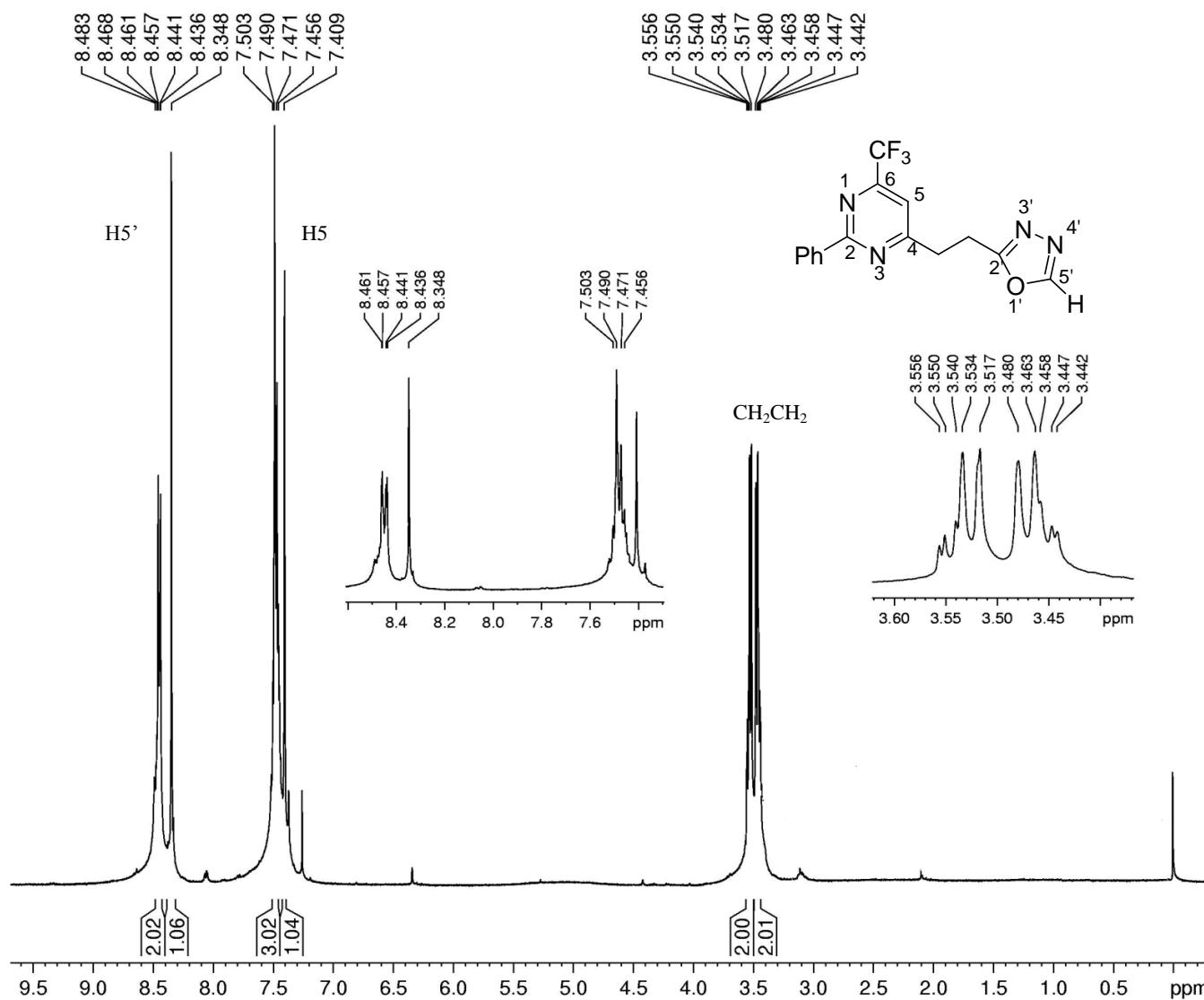


Figure S6. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of 5-phenyl-2-[2-(5-trifluoromethyl-1*H*-pyrazol-3-yl)ethyl]-1,3,4-oxadiazole (**6a**).



Current Data Parameters
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 EXPNO 2
 PROCNO 2012

F2 – Acquisition Parameters
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 Time 16.19
 INSTRUM spect
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 PULPROG zg30
 TD 65536
 SOLVENT CDCl₃
 NS 8
 DS 2
 SWH 8012.820 Hz
 FIDRES 0.122266 Hz
 AQ 4.0894966 sec
 RG 50.8
 DW 62.400 usec
 DE 6.00 usec
 TE 303.0 K
 D1 1.0000000 sec
 TD0 1

===== CHANNEL f1 ======
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 P1 13.00 usec
 PL1 -3.00 dB
 SFO1 400.1336012 MHz

F2 – Processing parameters
 SI 32768
 SF 400.1300066 MHz
 WDW no
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.40

Figure S7. ¹H NMR spectrum (400 MHz, CDCl₃) of 2-[2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl]-1,3,4-oxadiazole (**4b**).

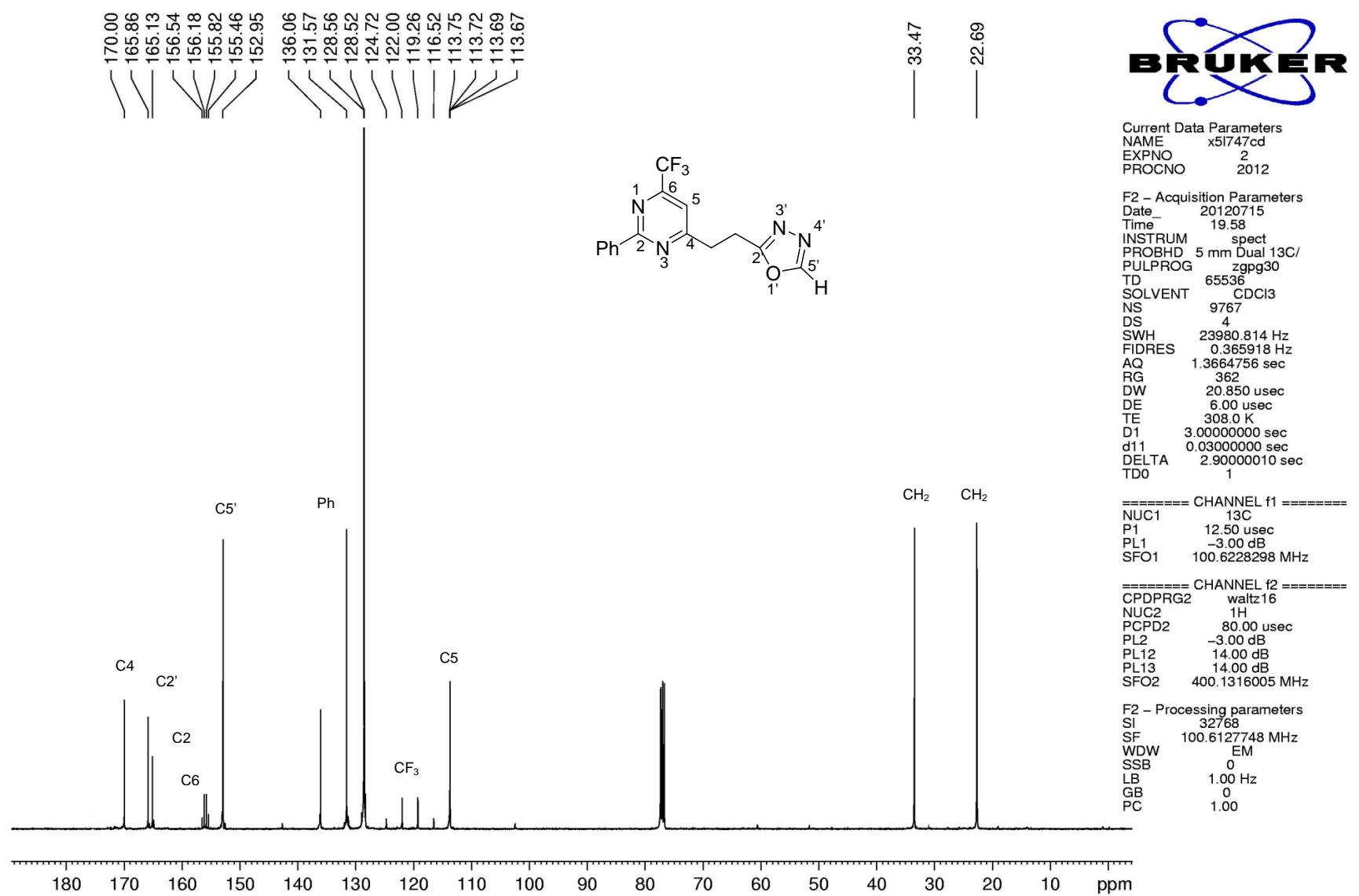


Figure S8. ¹³C NMR spectrum (100 MHz, CDCl₃) of 2-[2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl]-1,3,4-oxadiazol-2-yl (**4b**).

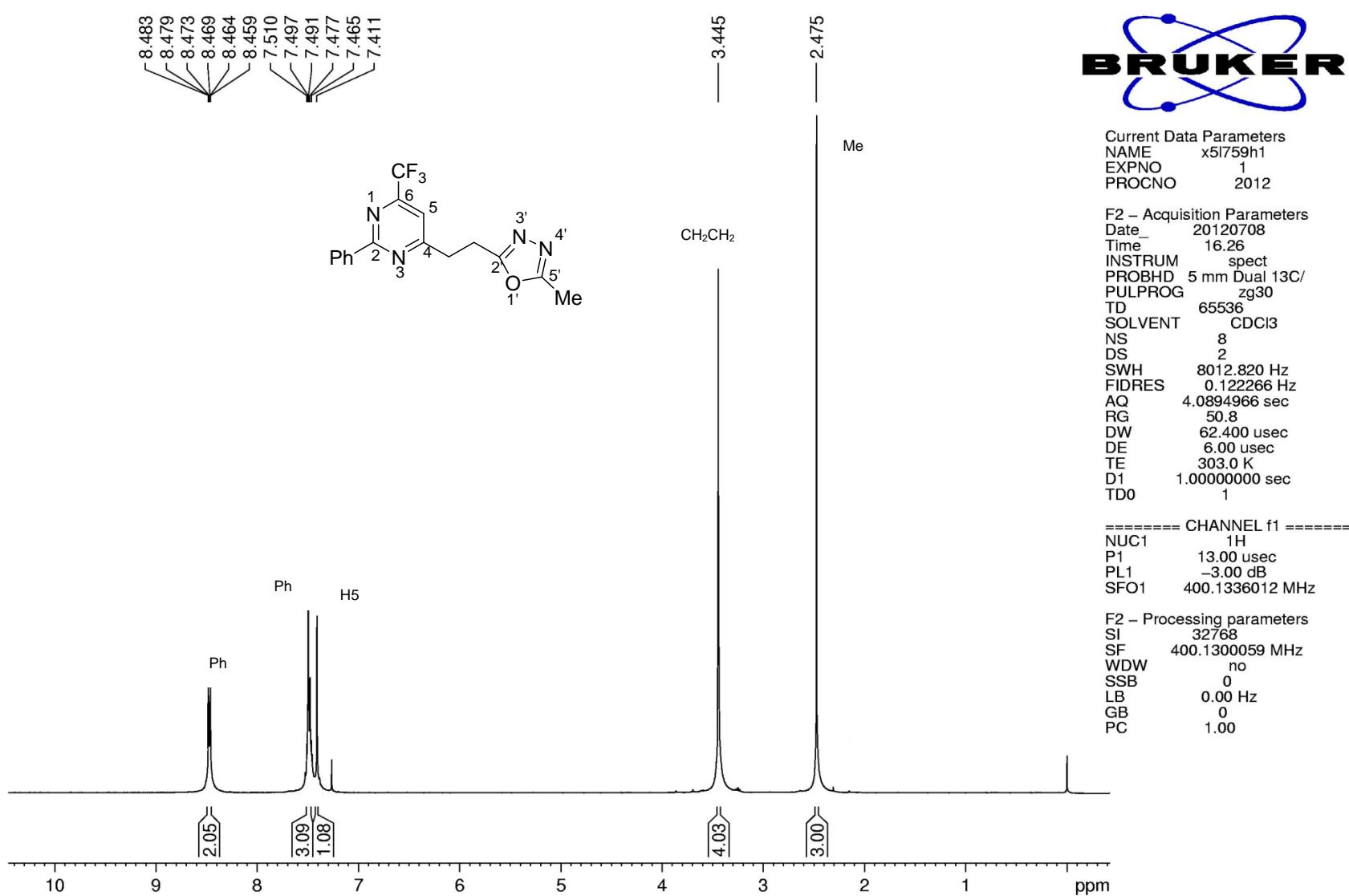


Figure S9. ¹H NMR spectrum (400 MHz, CDCl₃) of 5-methyl-2-[2-(2-phenyl-6-trifluoromethylpyrimidin4-yl)ethyl]-1,3,4-oxadiazole (**5b**).

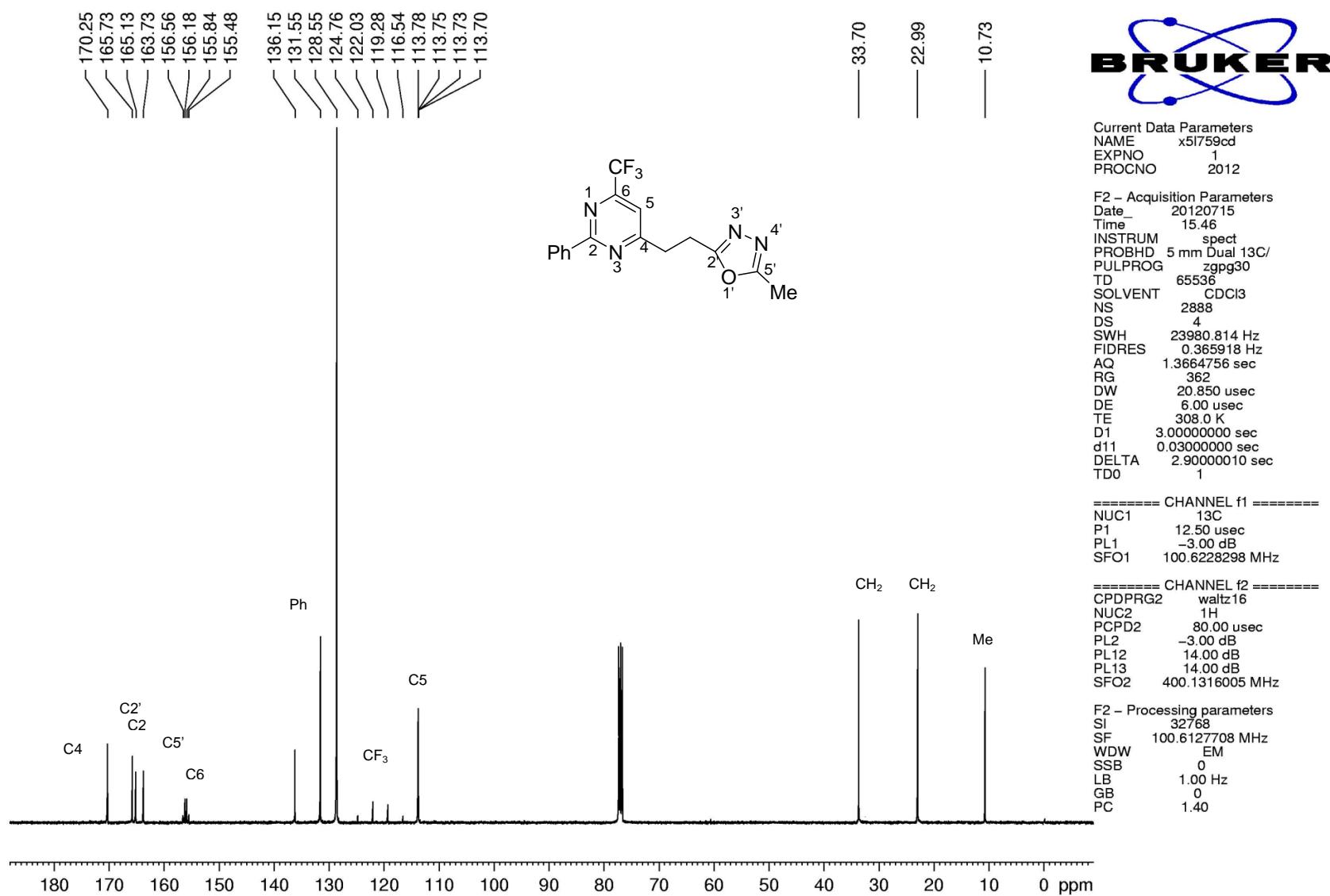


Figure S10. ^{13}C NMR spectrum (100 MHz, CDCl₃) of 5-methyl-2-[2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl]-1,3,4-oxadiazole (**4b**).

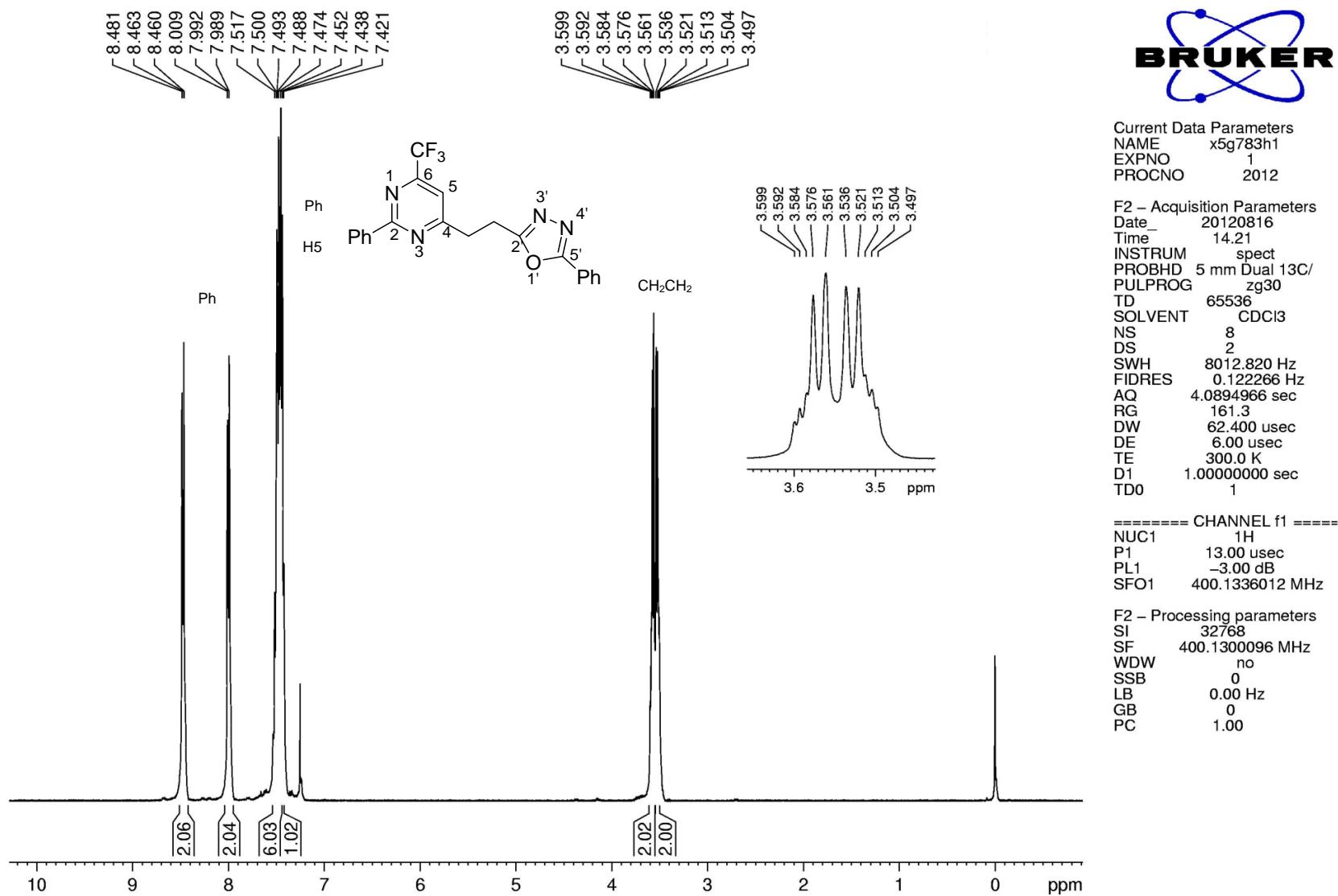
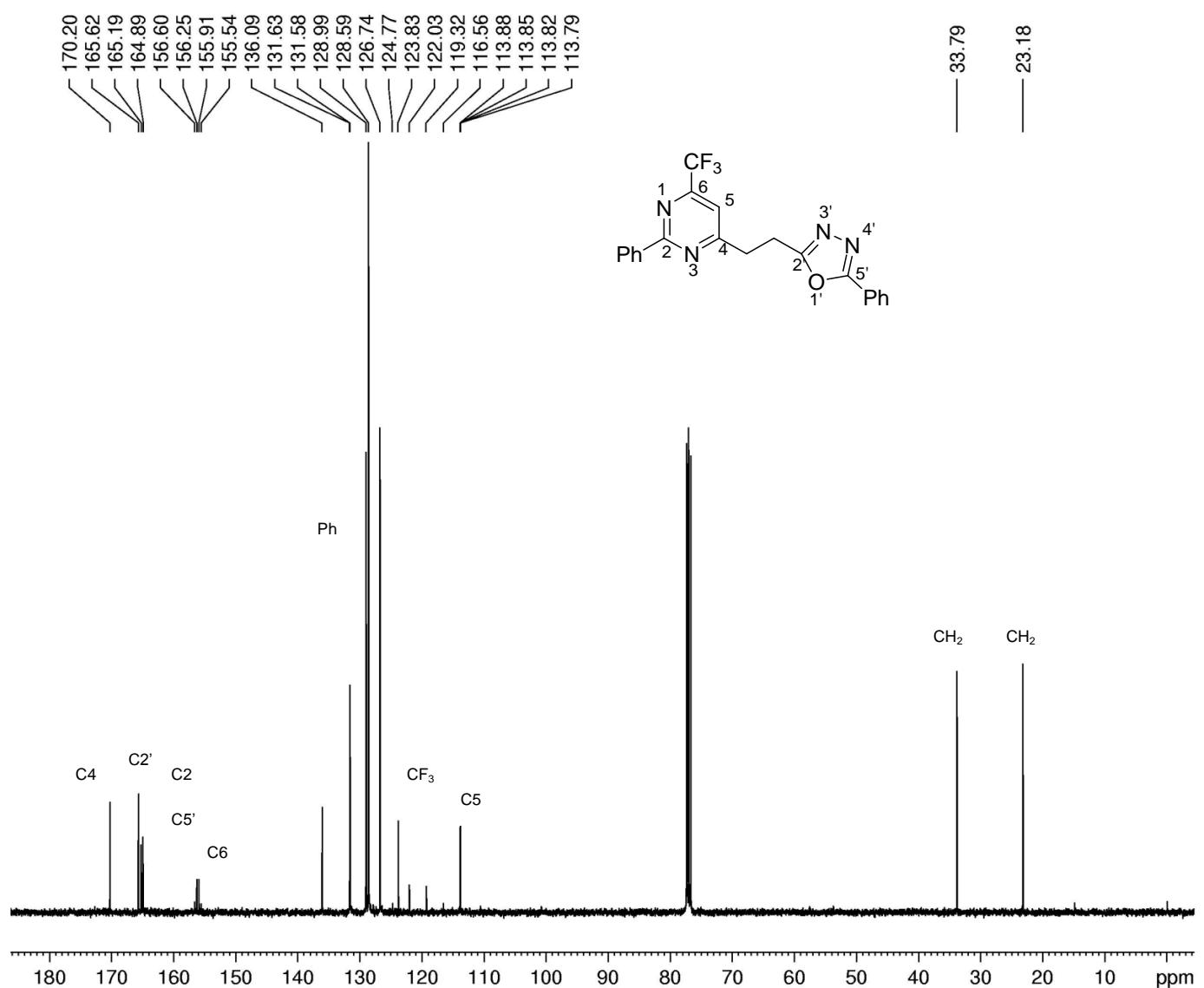


Figure S11. ¹H NMR spectrum (400 MHz, CDCl₃) of 2-phenyl-5-(2-(5-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazole (**6b**).



Current Data Parameters
NAME x5g783cd
EXPNO 1
PROCNO 2012

F2 - Acquisition Parameters
Date 20120816
Time 16.56
INSTRUM spect
PROBHD 5 mm Dual 13C/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 363
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 101.6
DW 20.850 usec
DE 6.00 usec
TE 300.0 K
D1 3.0000000 sec
d11 0.0300000 sec
DELTA 2.90000010 sec
TD0 1

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P1 12.50 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 14.00 dB
PL13 14.00 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127729 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Figure S12. ^{13}C NMR spectrum (100 MHz, CDCl_3) of 5-phenyl-2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)-ethyl)-1,3,4-oxadiazole (**6b**).

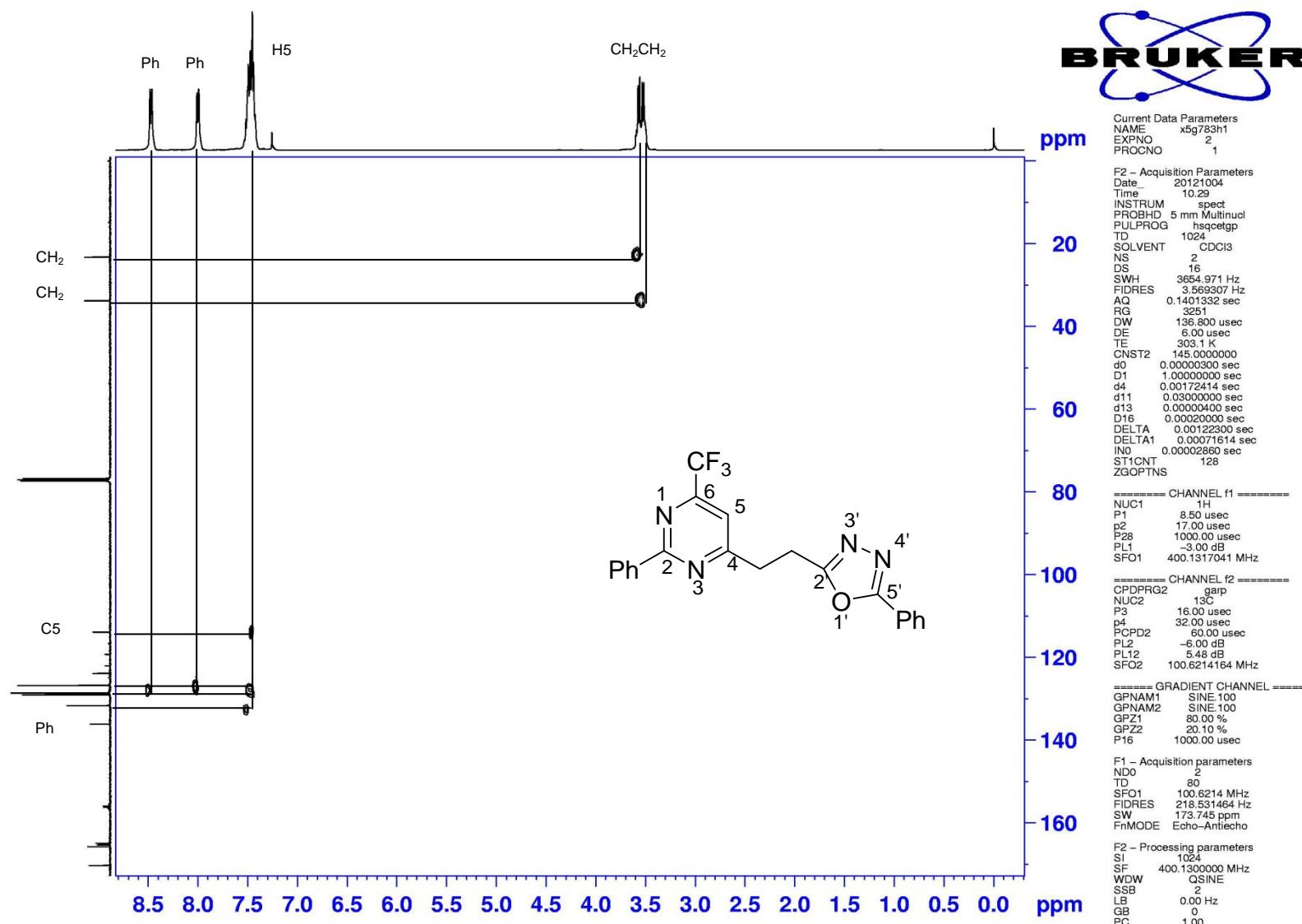


Figure S13. HMQC NMR spectrum (CDCl₃) of 5-phenyl-2-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)-ethyl)-1,3,4-oxadiazole (**6b**).

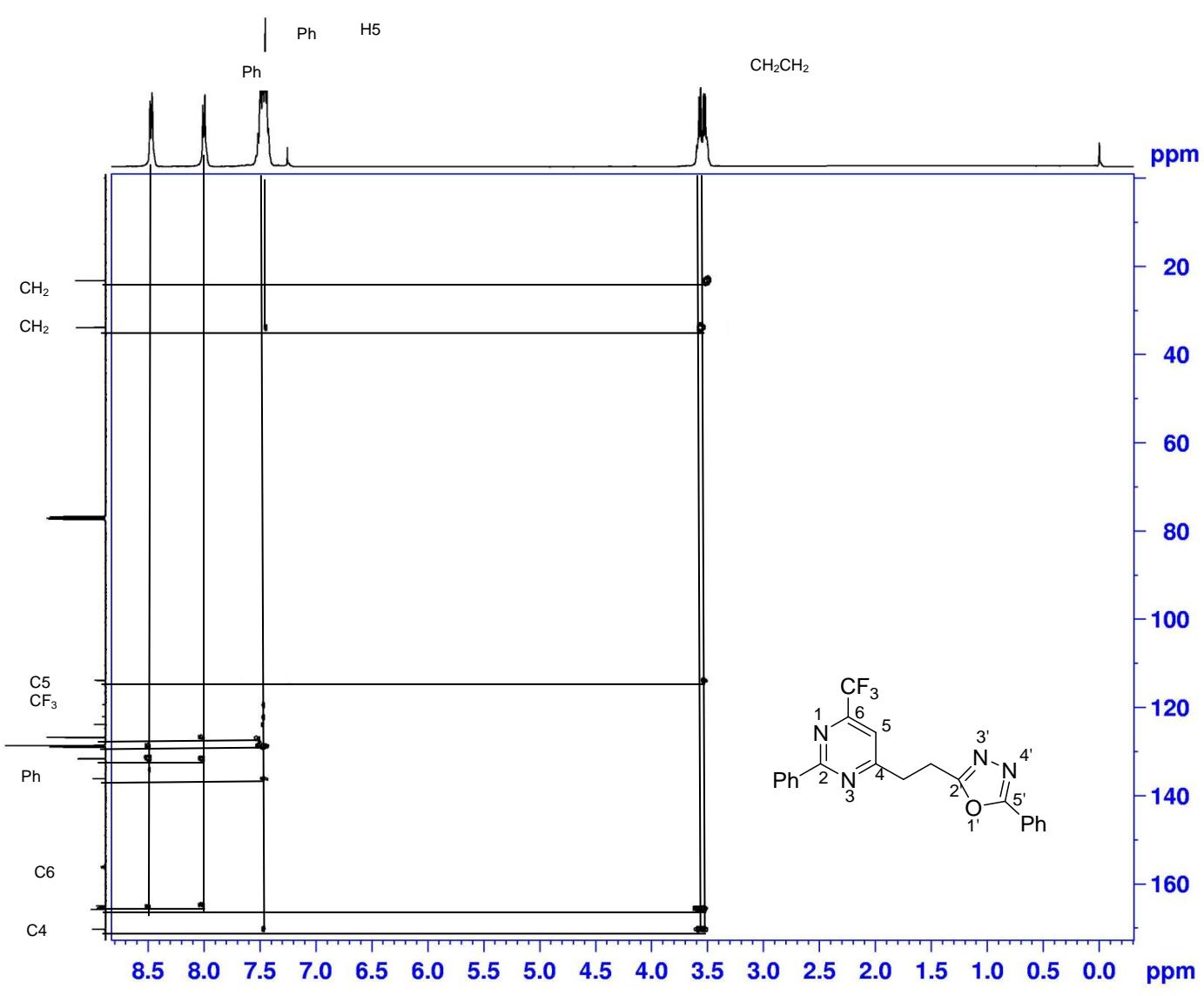


Figure S14. HMBC NMR spectrum (CDCl₃) of 5-phenyl-2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)-ethyl)-1,3,4-oxadiazole (**6b**).

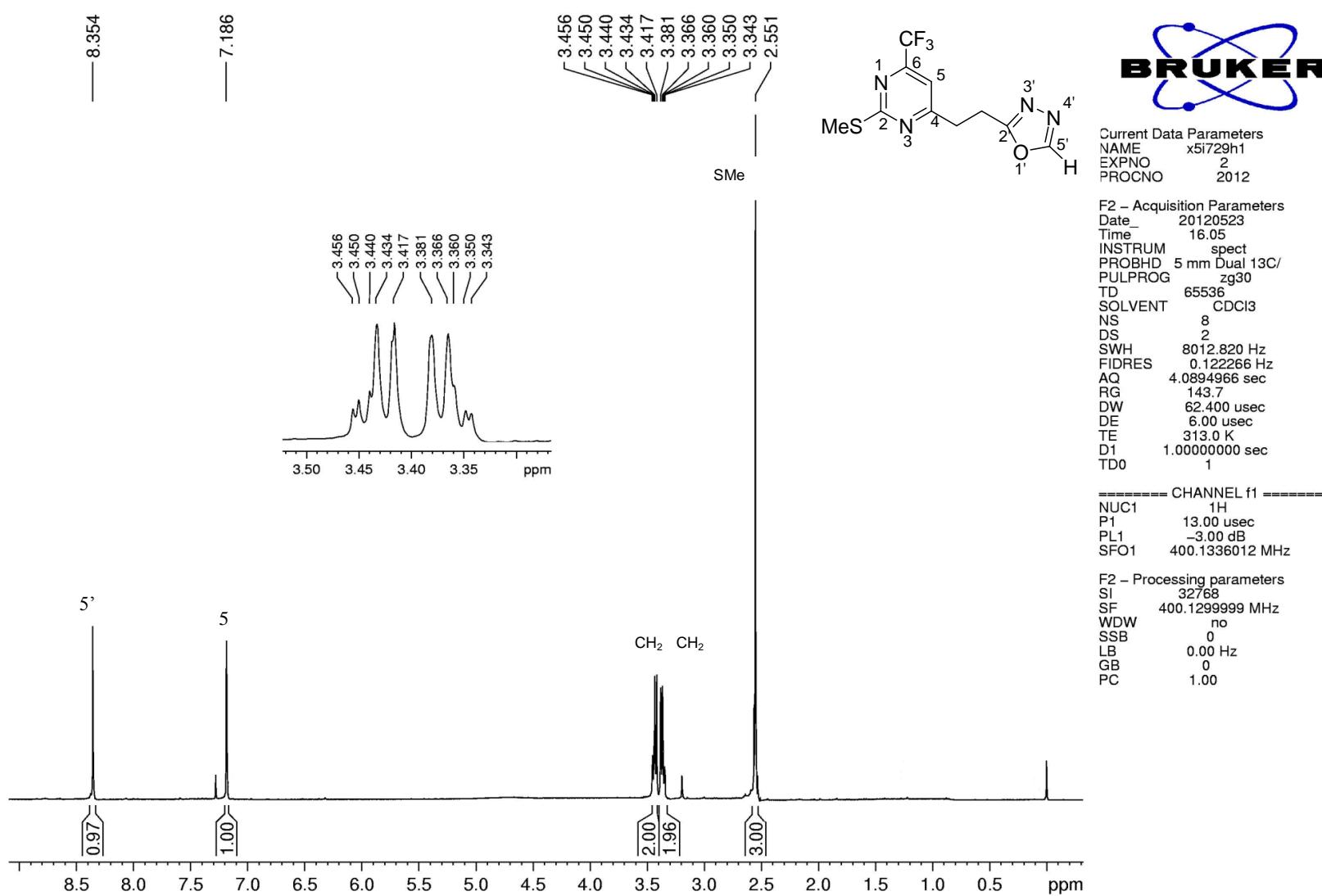
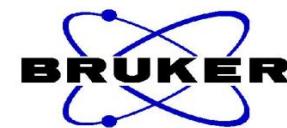
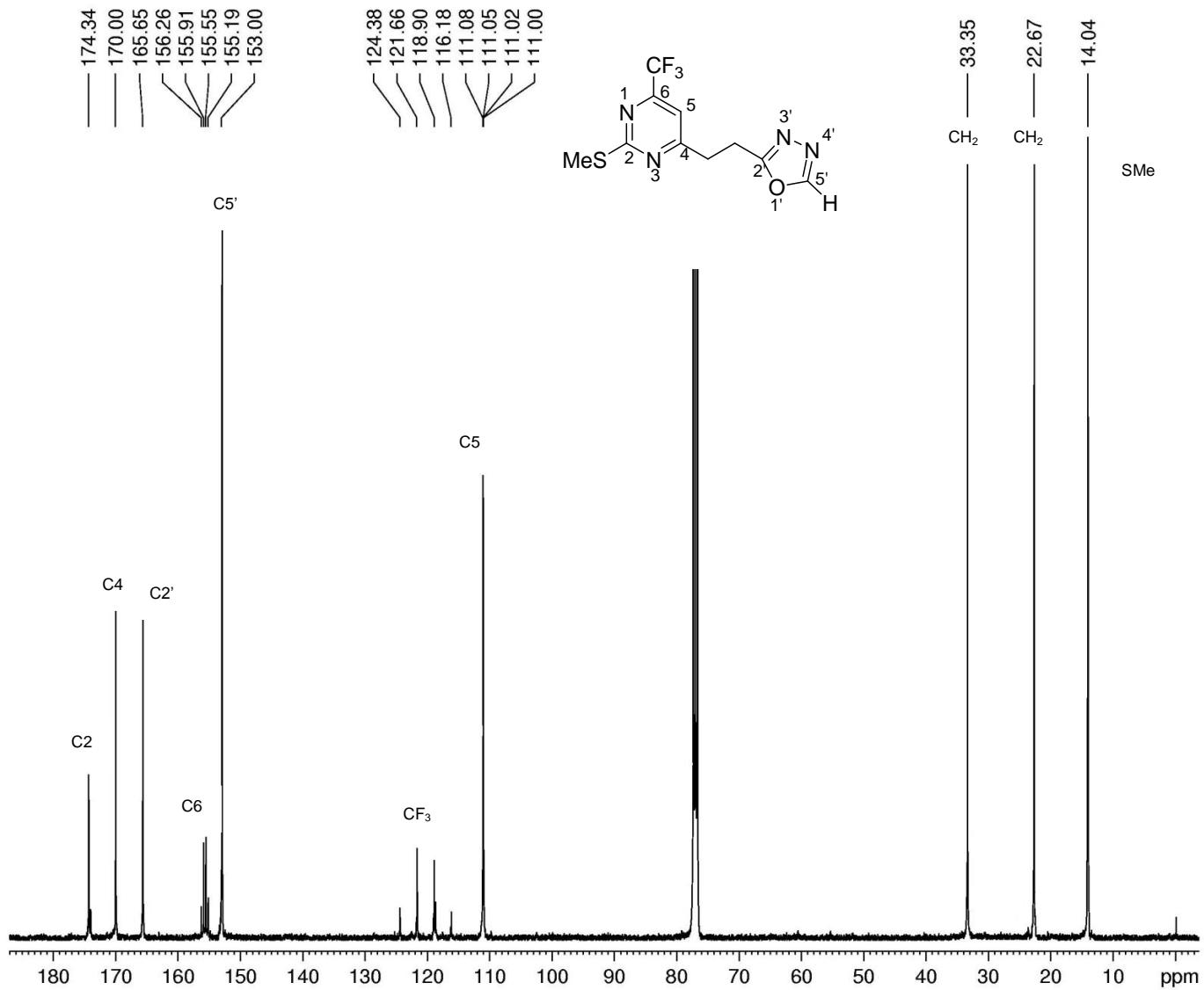


Figure S15. ¹H NMR spectrum (400 MHz, CDCl₃) of 2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]-1,3,4-oxadiazole (**4c**).



Current Data Parameters
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EXPNO 2
PROCNO 2012

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PULPROG zgpg30
TD 65536
SOLVENT CDCl₃
NS 16871
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 40.3
DW 20.850 usec
DE 6.00 usec
TE 308.0 K
D1 3.0000000 sec
d11 0.03000000 sec
DELTA 2.90000010 sec
TD0 1

===== CHANNEL f1 =====
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P1 12.50 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 14.00 dB
PL13 14.00 dB
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127700 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Figure S16. ¹³C NMR spectrum (100 MHz, CDCl₃) of 2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]-1,3,4-oxadiazole (**4c**).

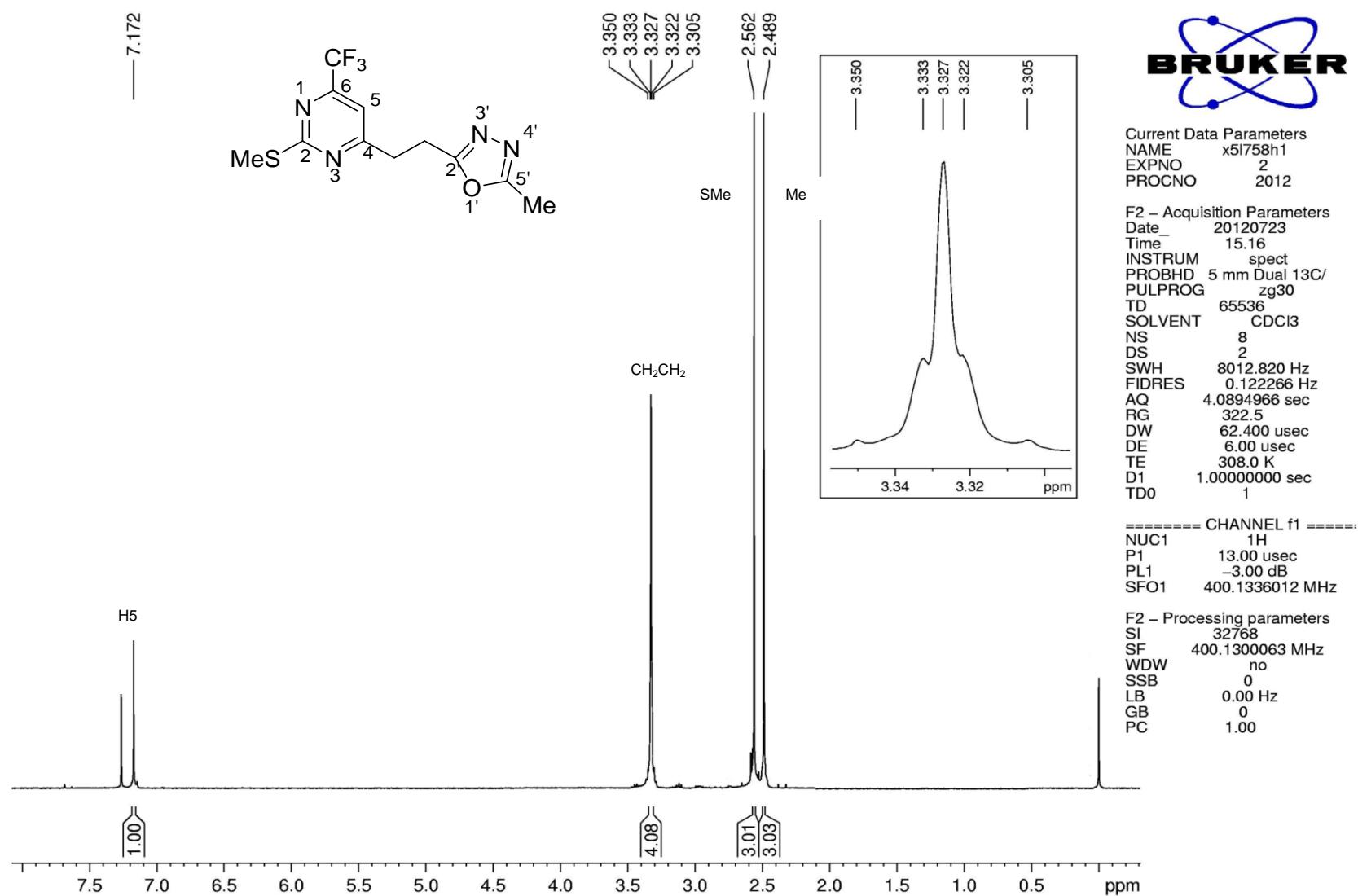


Figure S17. ^1H NMR spectrum (400 MHz, CDCl_3) of 5-methyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**5c**).

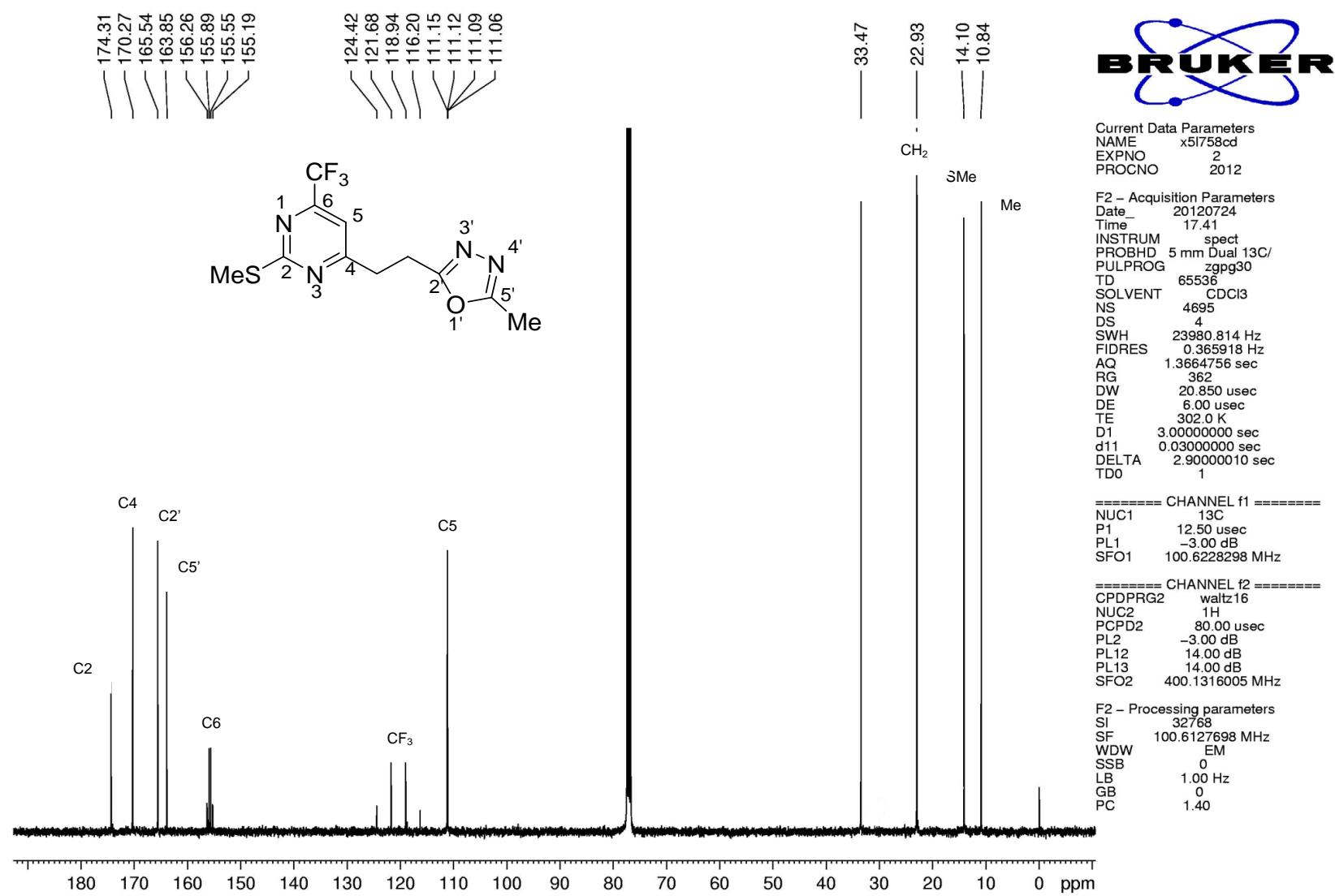


Figure S18. ¹³C NMR spectrum (400 MHz, CDCl₃) of 5-methyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**4c**).

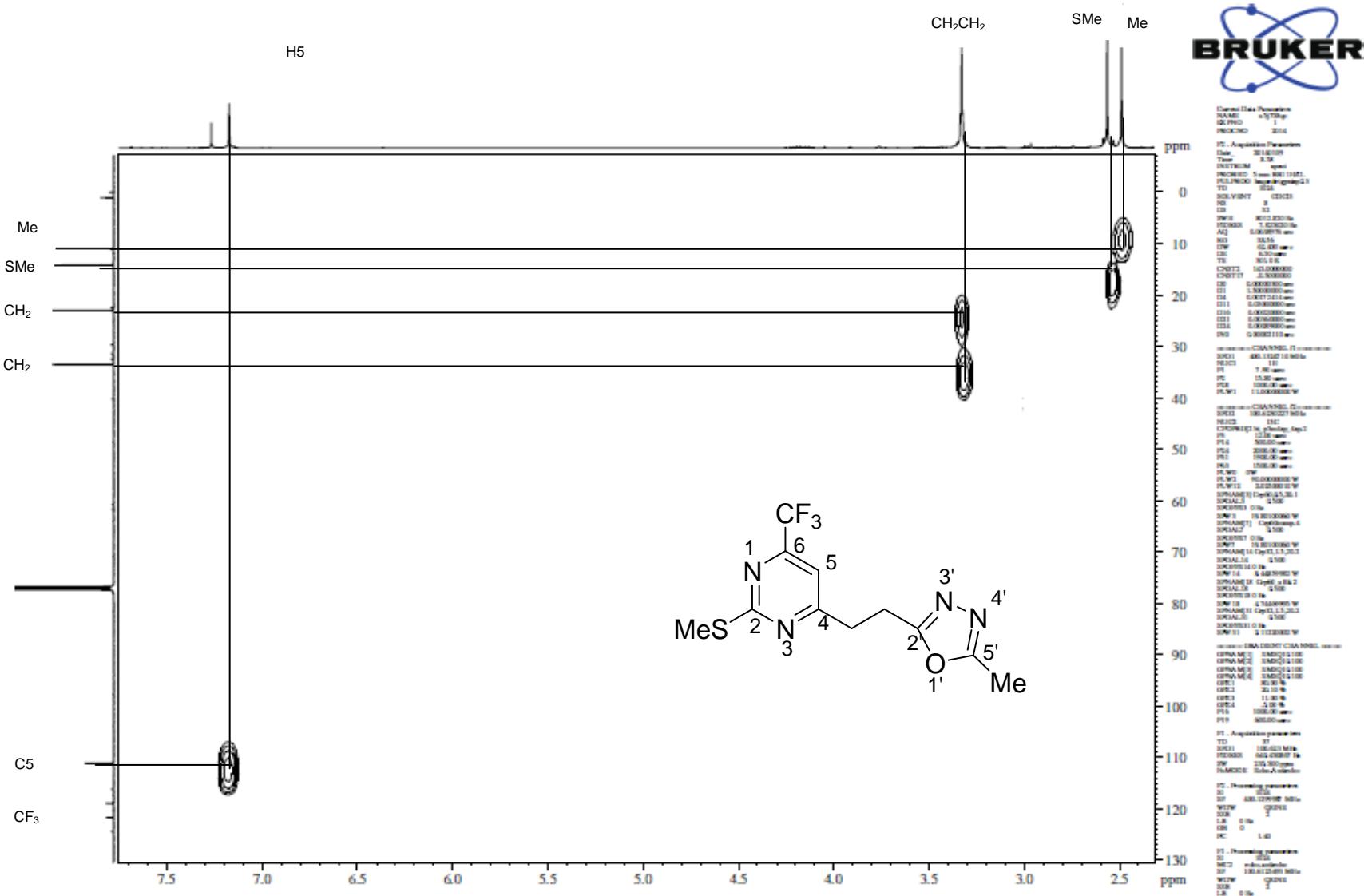


Figure S19. 2D-HMQC spectrum of 5-methyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**5c**).

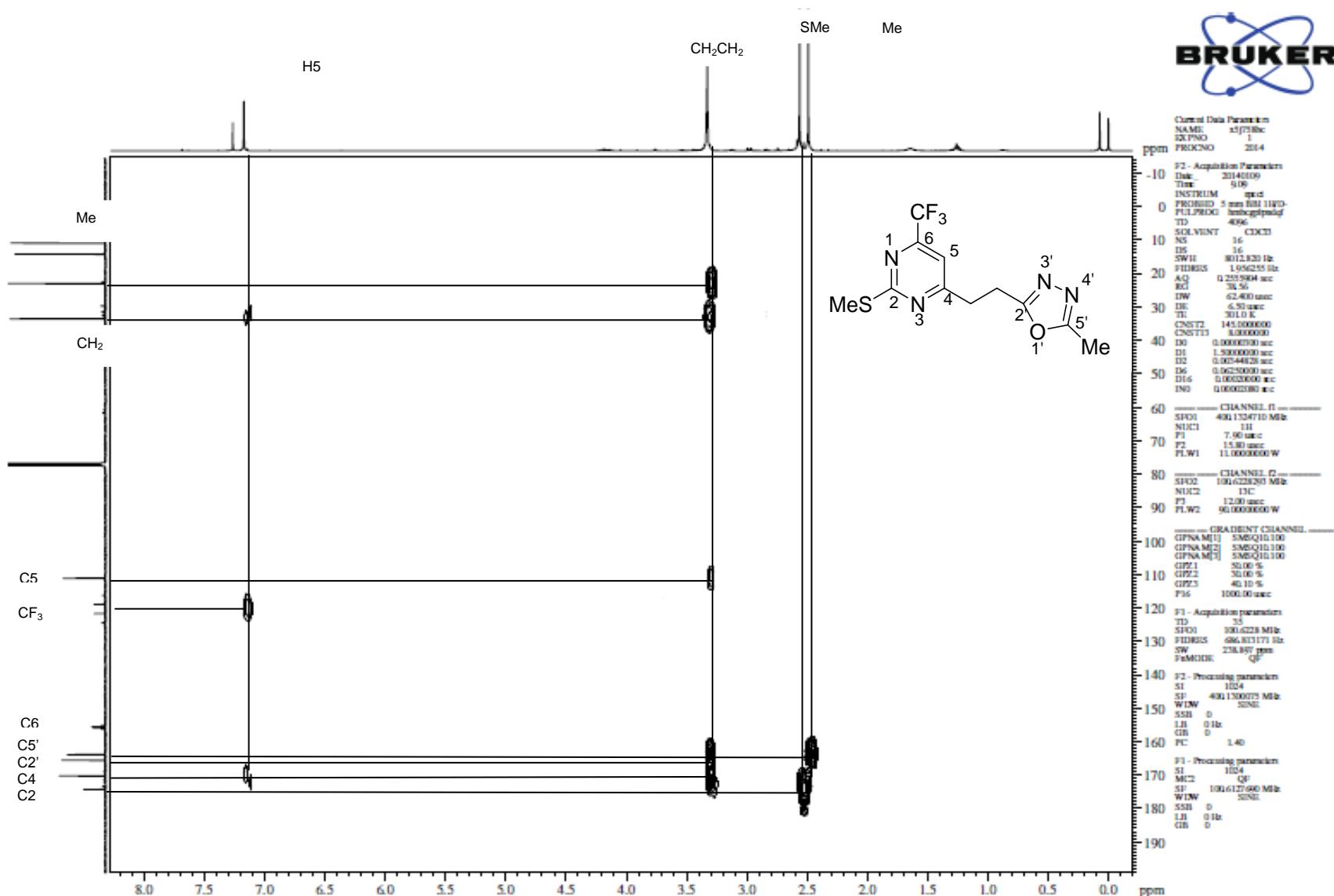


Figure S20. 2D-HMBC spectrum of 5-methyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**5c**).

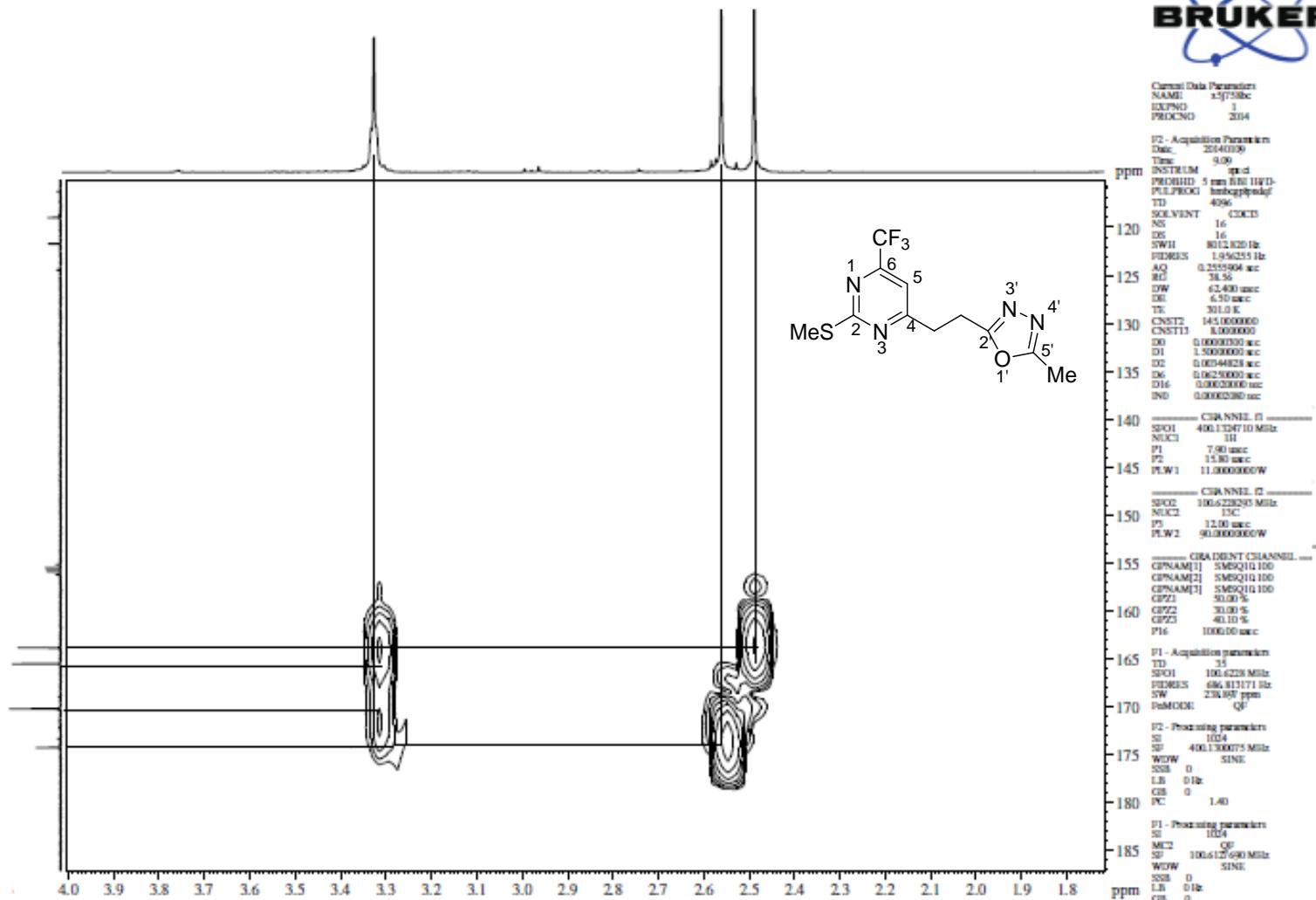


Figure S21. Expanded 2D-HMBC spectrum of 5-methyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**5c**).

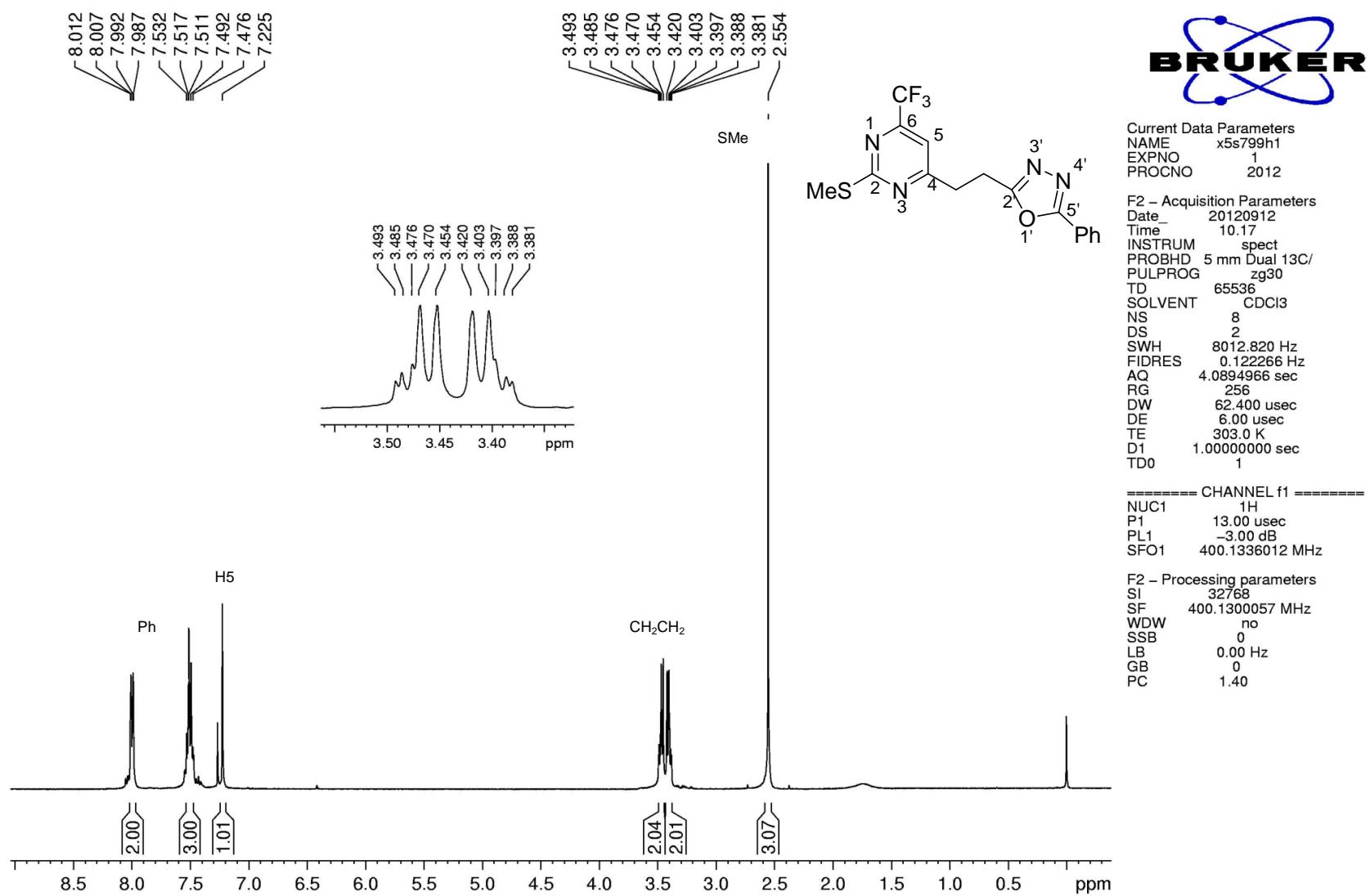
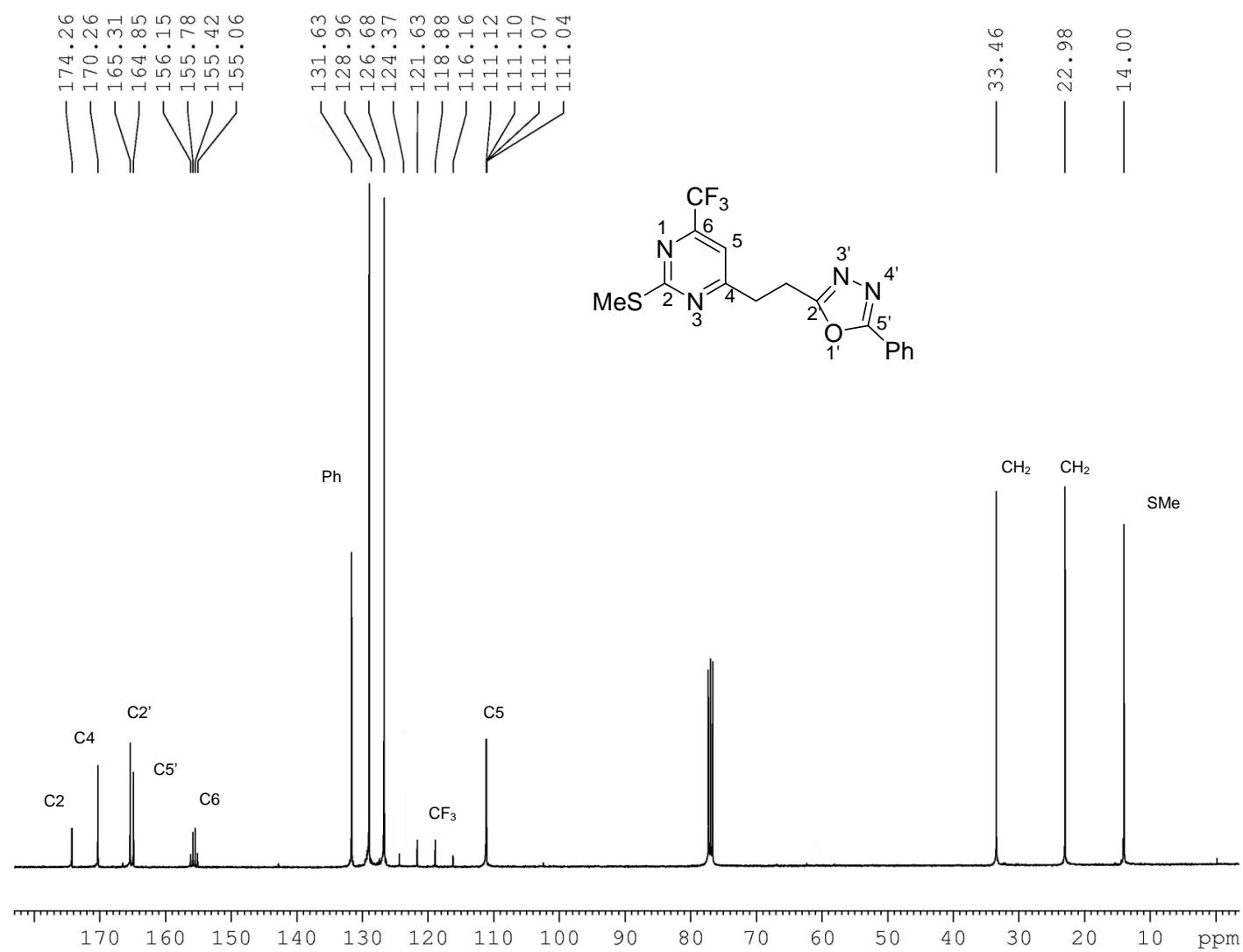


Figure S22. ¹H NMR spectrum (400 MHz, CDCl₃) of 5-phenyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**6c**).



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EXPNO 1
PROCNO 2012

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FIDRES 0.365918 Hz
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TE 303.0 K
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d1l 0.0300000 sec
DELTA 0.8999998 sec
TDO 1

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SF01 100.6228298 MHz

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PLL2 14.00 dB
PLL3 14.00 dB
SF02 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.612774 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

Figure S23. ^{13}C NMR spectrum (100 MHz, CDCl_3) 5-phenyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**5c**).

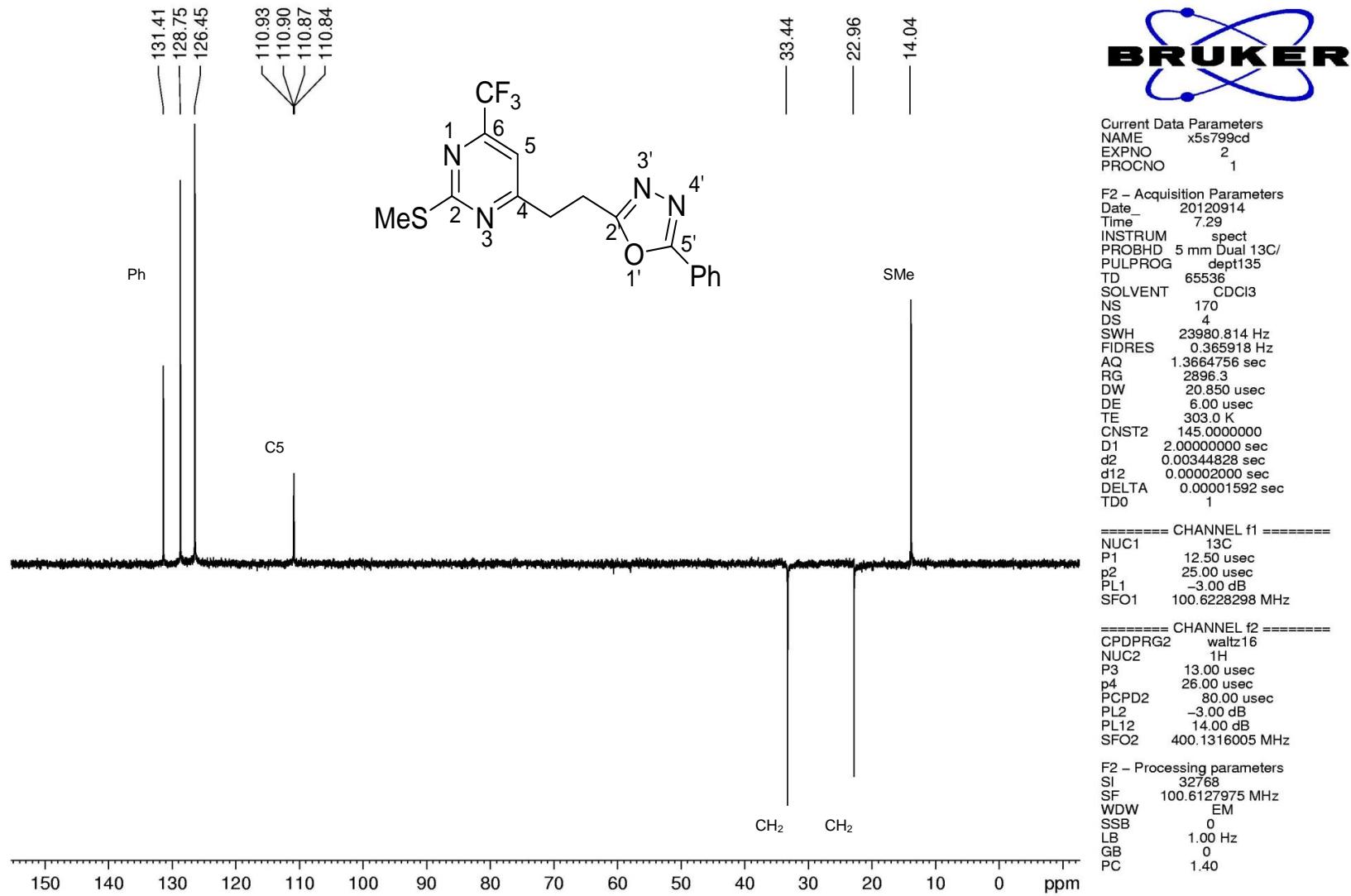


Figure S24. ¹³C DEPT135 NMR spectrum (100 MHz, CDCl₃) of 5-methyl-2-[2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl]1,3,4-oxadiazole (**6c**).

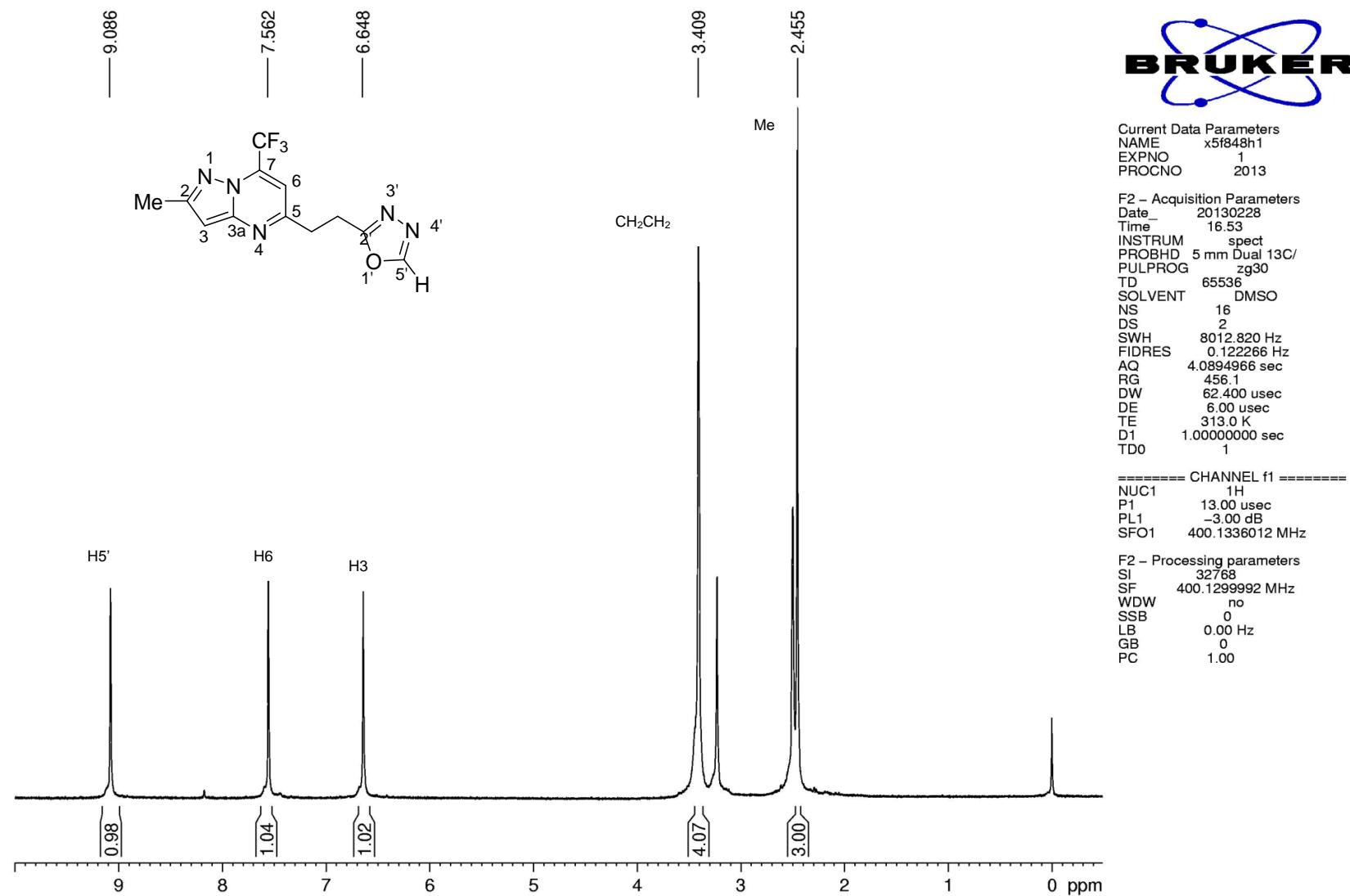


Figure S25. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of 2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**4d**).

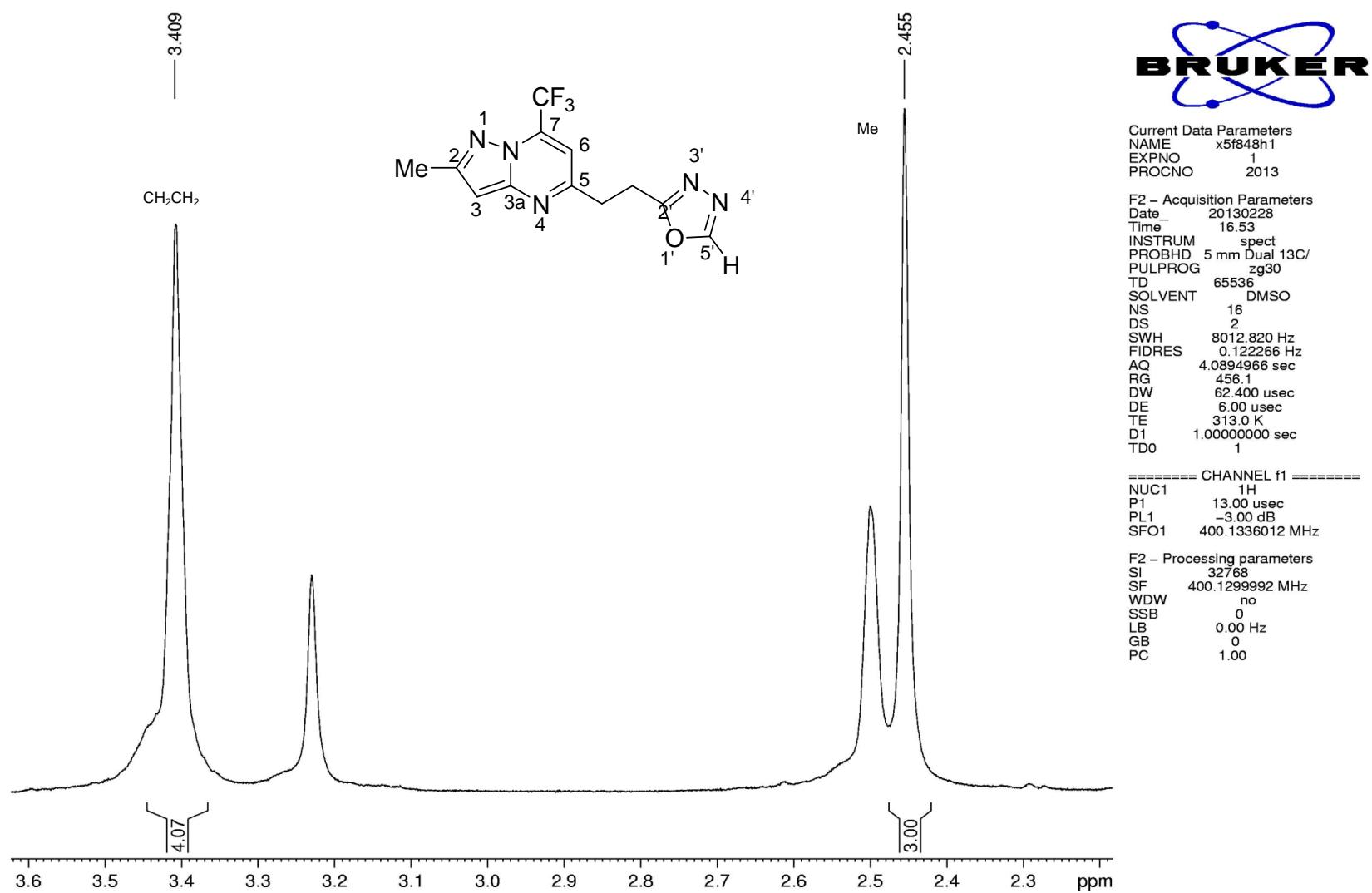


Figure S26. Expanded ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of 2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**4d**).

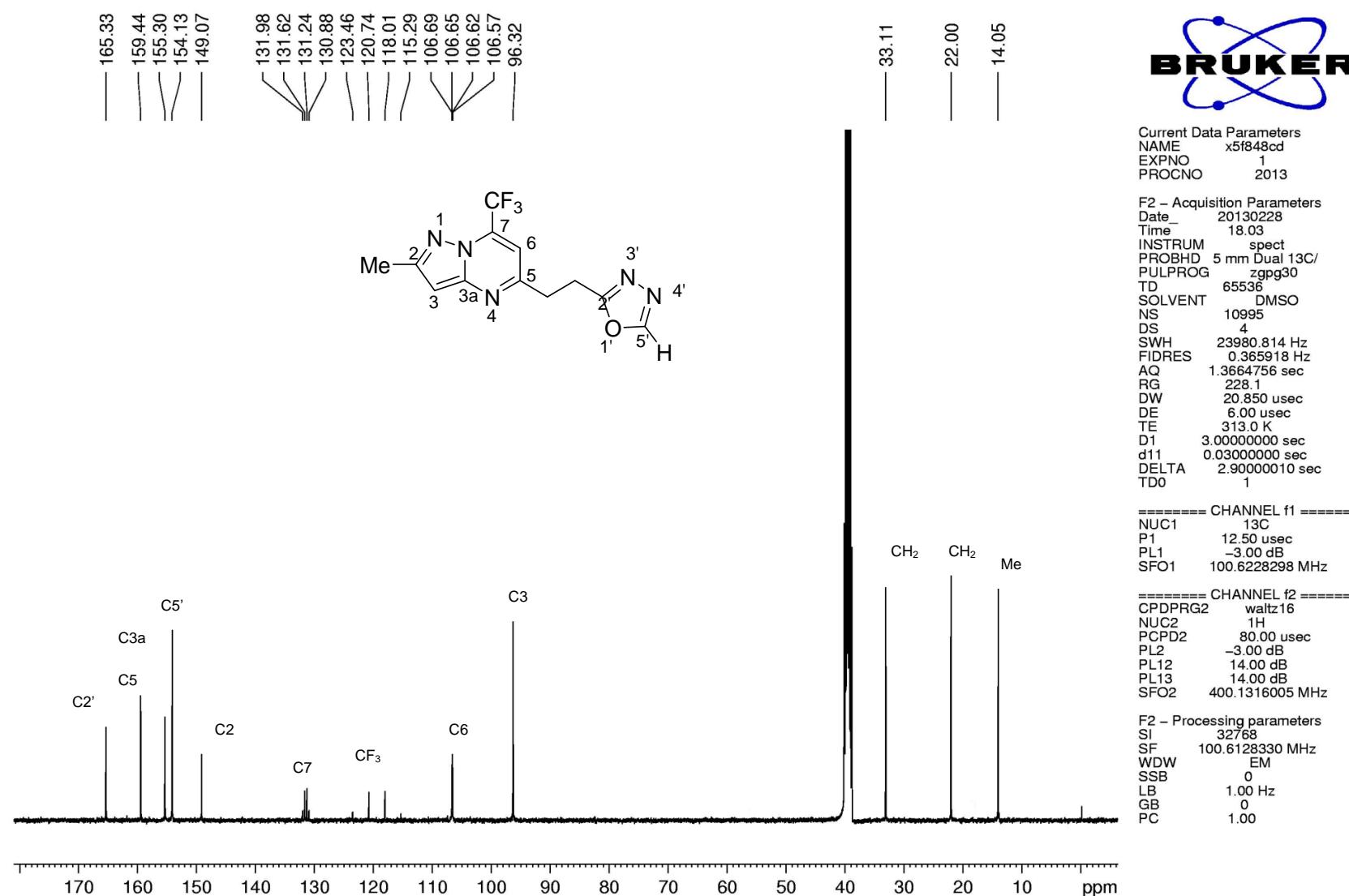


Figure S27. ^{13}C NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of 5-(2-(1,3,4-oxadiazol-2-yl)ethyl)-2-methyl-7-(trifluoromethyl)pyrazolo[1,5-*a*]pyrimidine (**3d**).

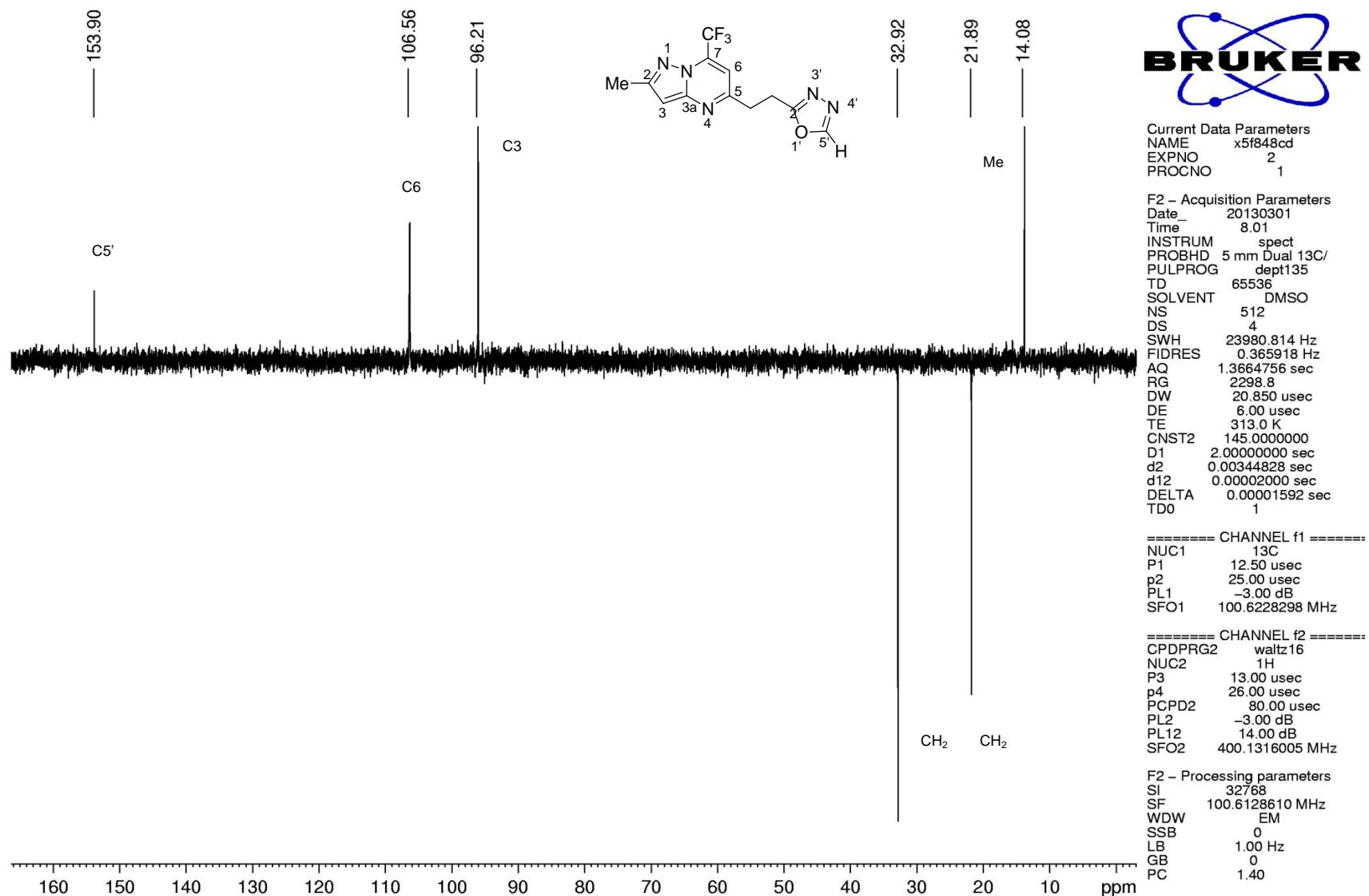
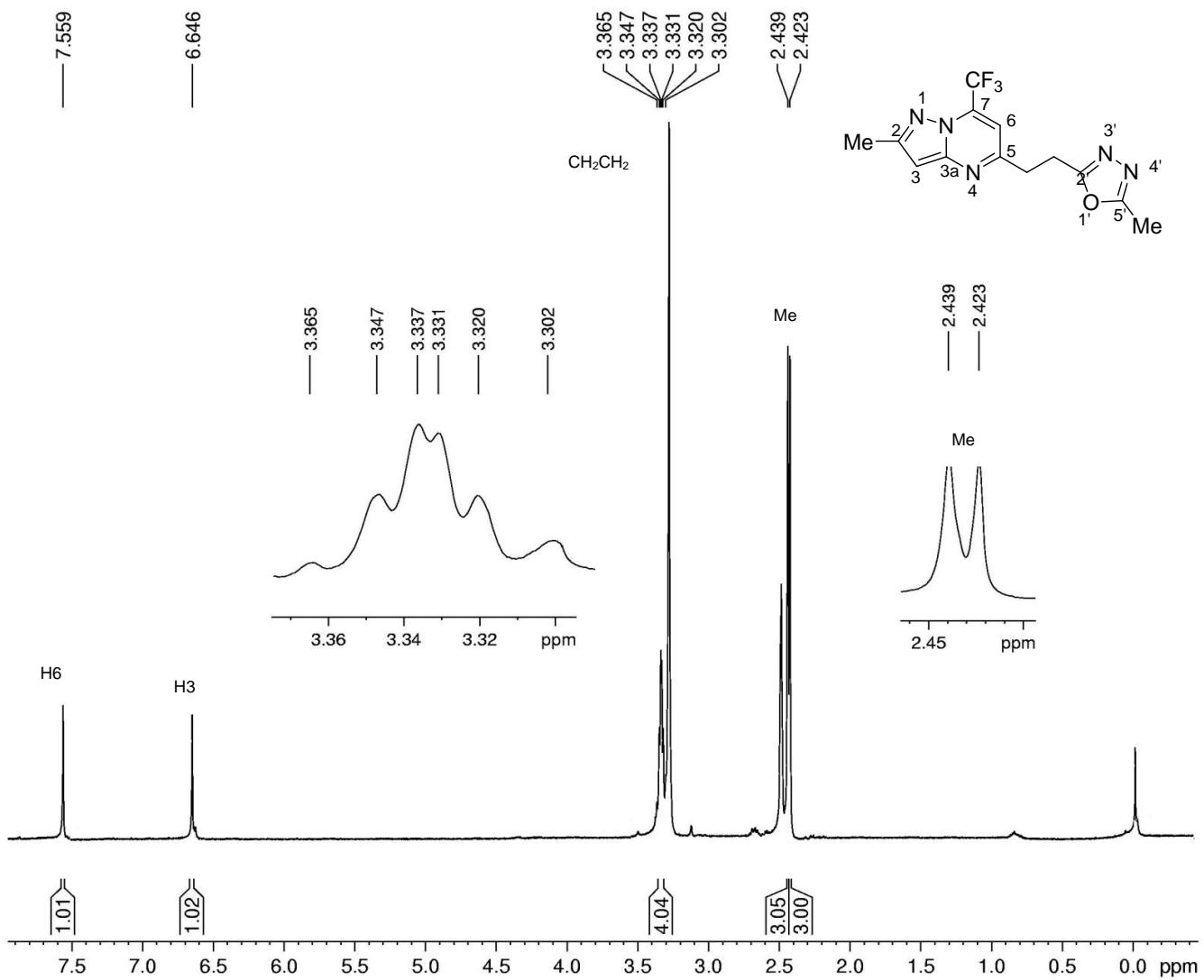


Figure S28. ¹³C DEPT 135 NMR spectrum (DMSO-*d*₆) of 2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**4d**).



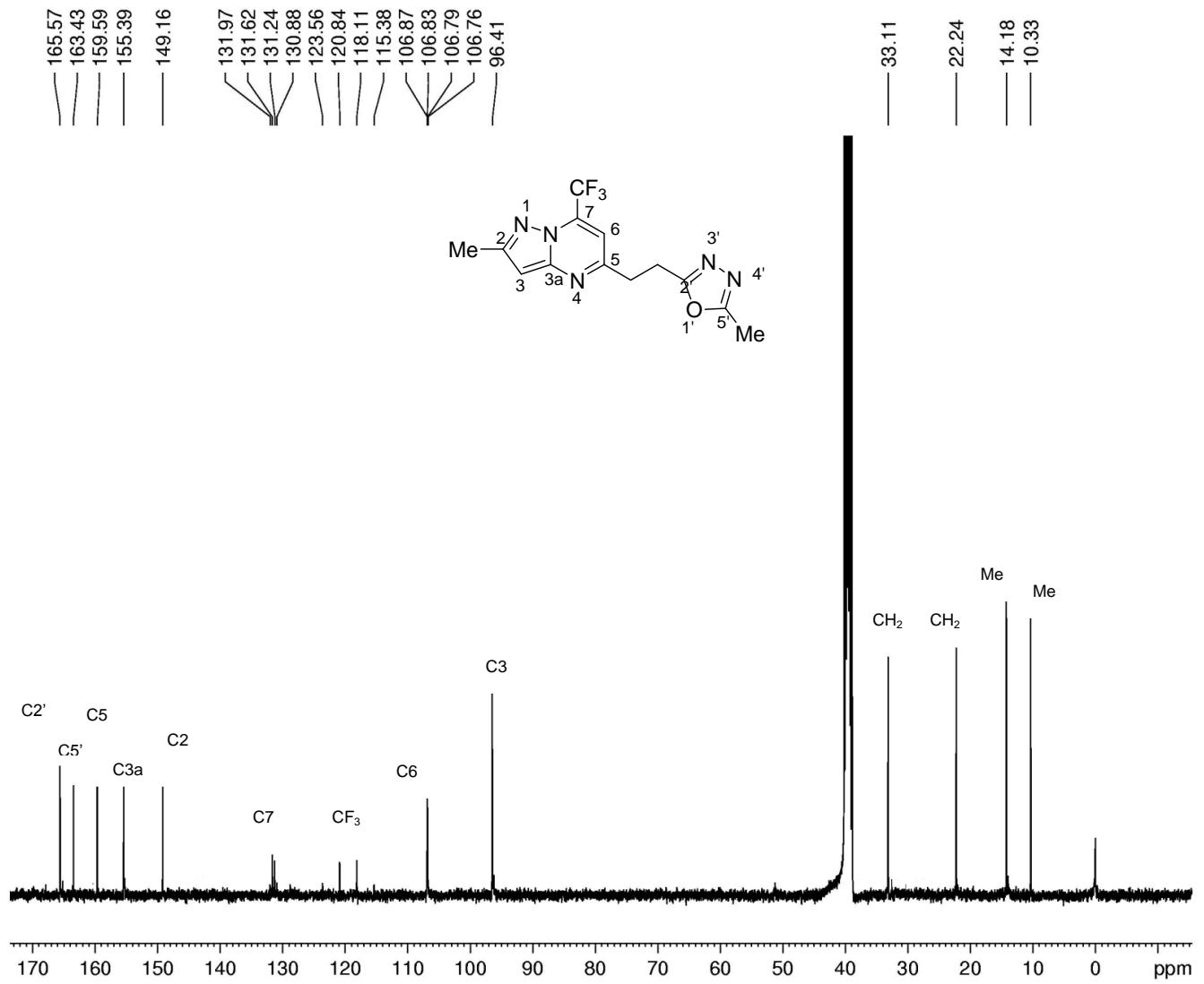
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EXPNO 1
PROCNO 2013

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TD 65536
SOLVENT CDCl3
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DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 322.5
DW 62.400 usec
DE 6.00 usec
TE 303.0 K
D1 1.0000000 sec
TD0 1

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PL1 -3.00 dB
SFO1 400.1336012 MHz

F2 – Processing parameters
SI 32768
SF 400.1319053 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40

Figure S29. ^1H NMR spectrum (400 MHz, DMSO- d_6) of 5-methyl-52-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**5d**).



Current Data Parameters
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 EXPNO 1
 PROCNO 2013

F2 – Acquisition Parameters
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 PULPROG zgpg30
 TD 65536
 SOLVENT CDCl₃
 NS 9517
 DS 4
 SWH 23980.814 Hz
 FIDRES 0.365918 Hz
 AQ 1.3664756 sec
 RG 362
 DW 20.850 usec
 DE 6.00 usec
 TE 303.0 K
 D1 3.0000000 sec
 d11 0.03000000 sec
 DELTA 2.90000010 sec
 TD0 1

===== CHANNEL f1 =====:
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 P1 12.50 usec
 PL1 -3.00 dB
 SFO1 100.6228298 MHz

===== CHANNEL f2 =====:
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 PL2 -3.00 dB
 PL12 14.00 dB
 PL13 14.00 dB
 SFO2 400.1316005 MHz

F2 – Processing parameters
 SI 32768
 SF 100.6133010 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Figure S30. ¹³C NMR spectrum (400 MHz, DMSO-*d*₆) of 5-methyl-2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**4d**).

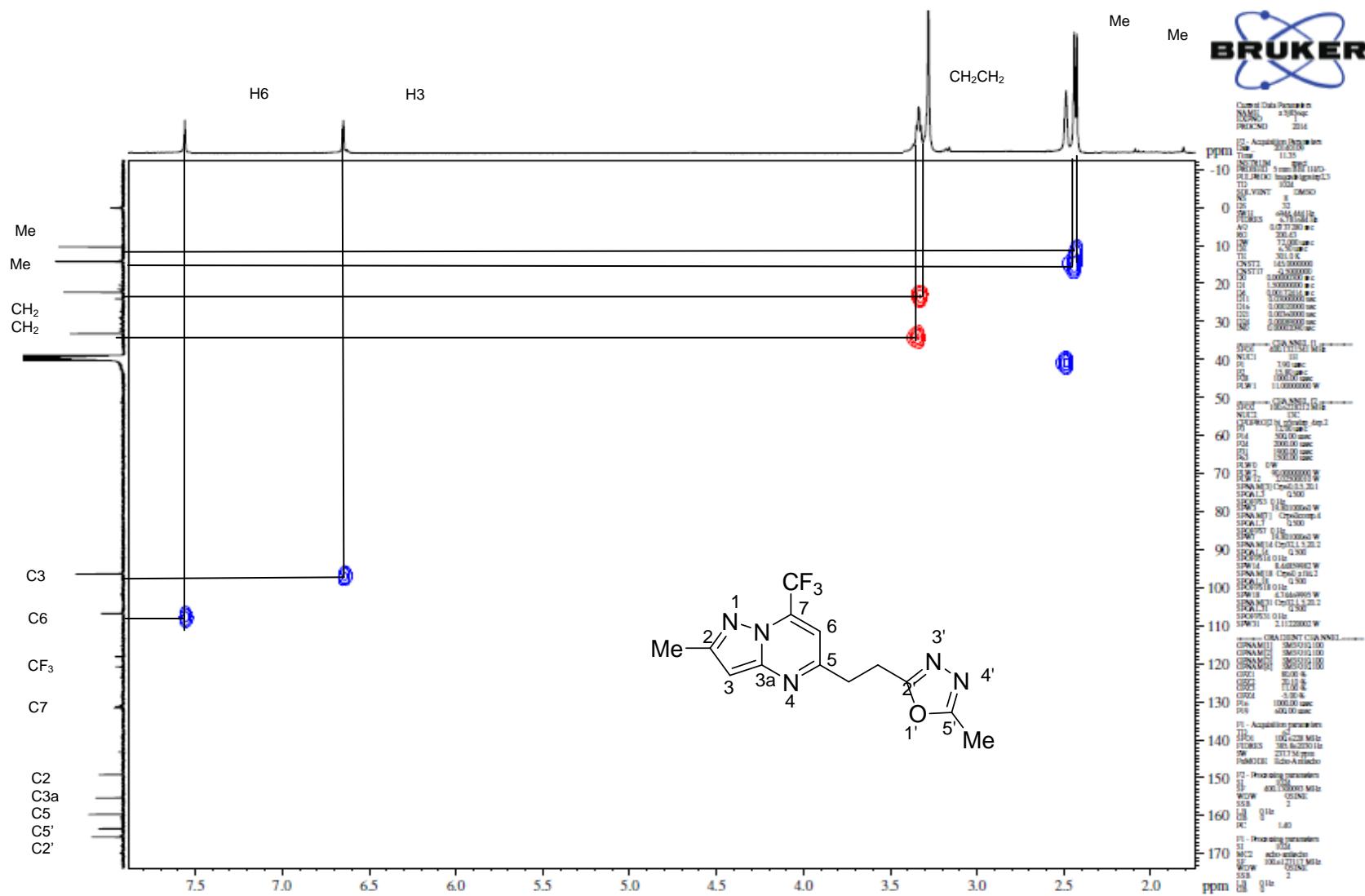


Figure S31. 2D-HMDS NMR spectrum (DMSO-*d*₆) of 5-methyl-2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**5d**).

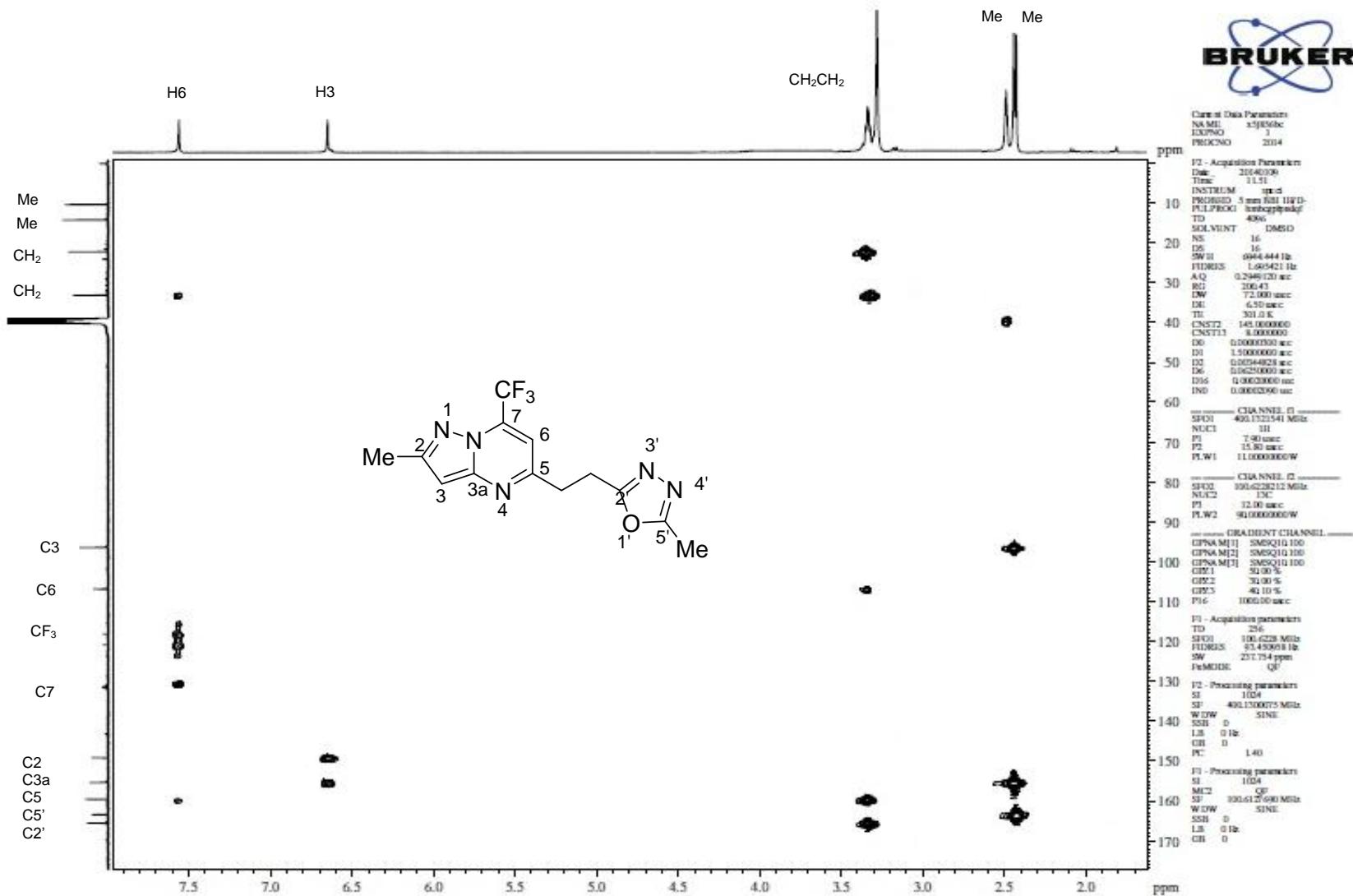


Figure S32. 2D-HMBC NMR spectrum ($\text{DMSO}-d_6$) of 5-methyl-2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**5d**).

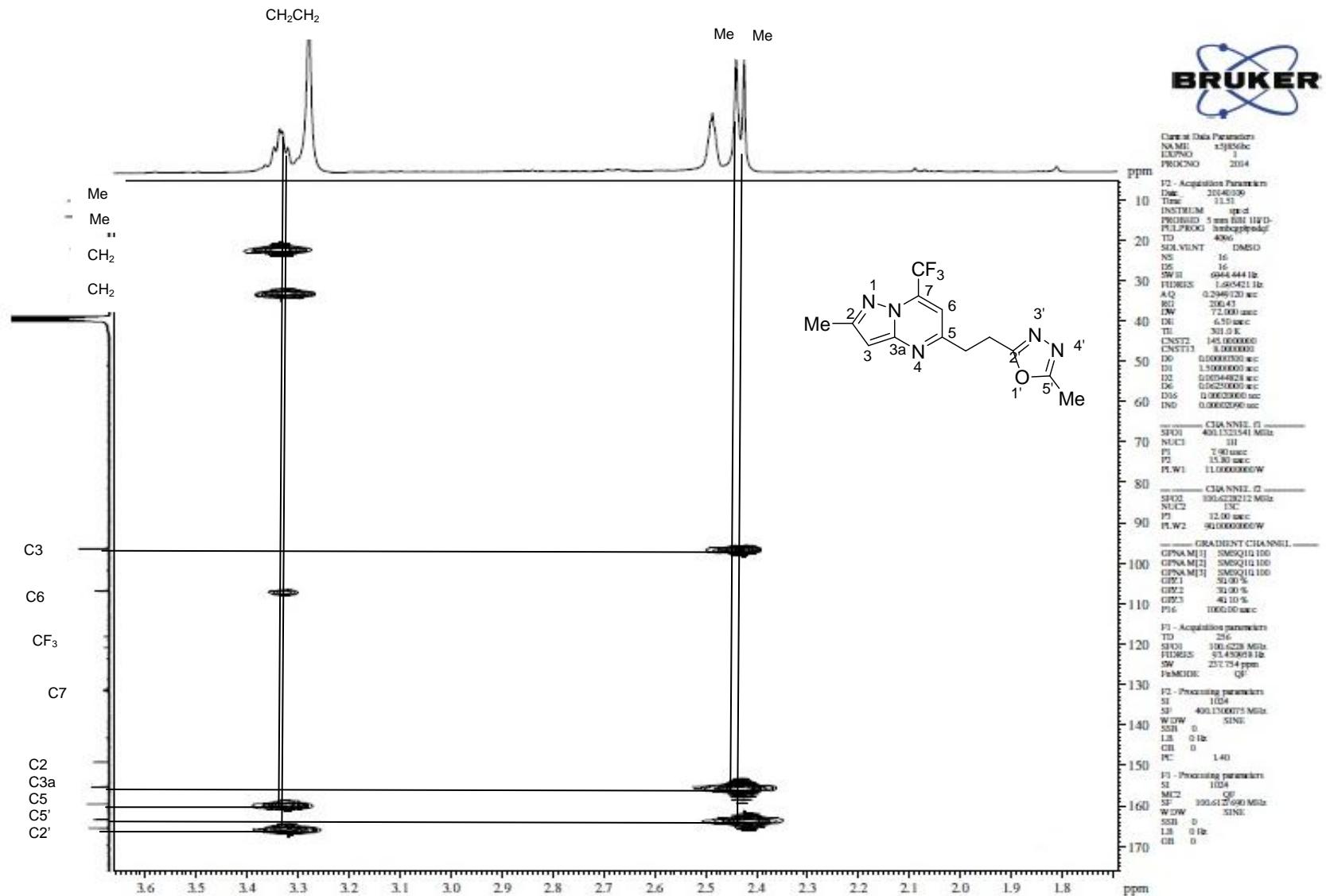


Figure S33. Expanded HMBC NMR spectrum ($\text{DMSO}-d_6$) of 5-methyl-2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**5d**).

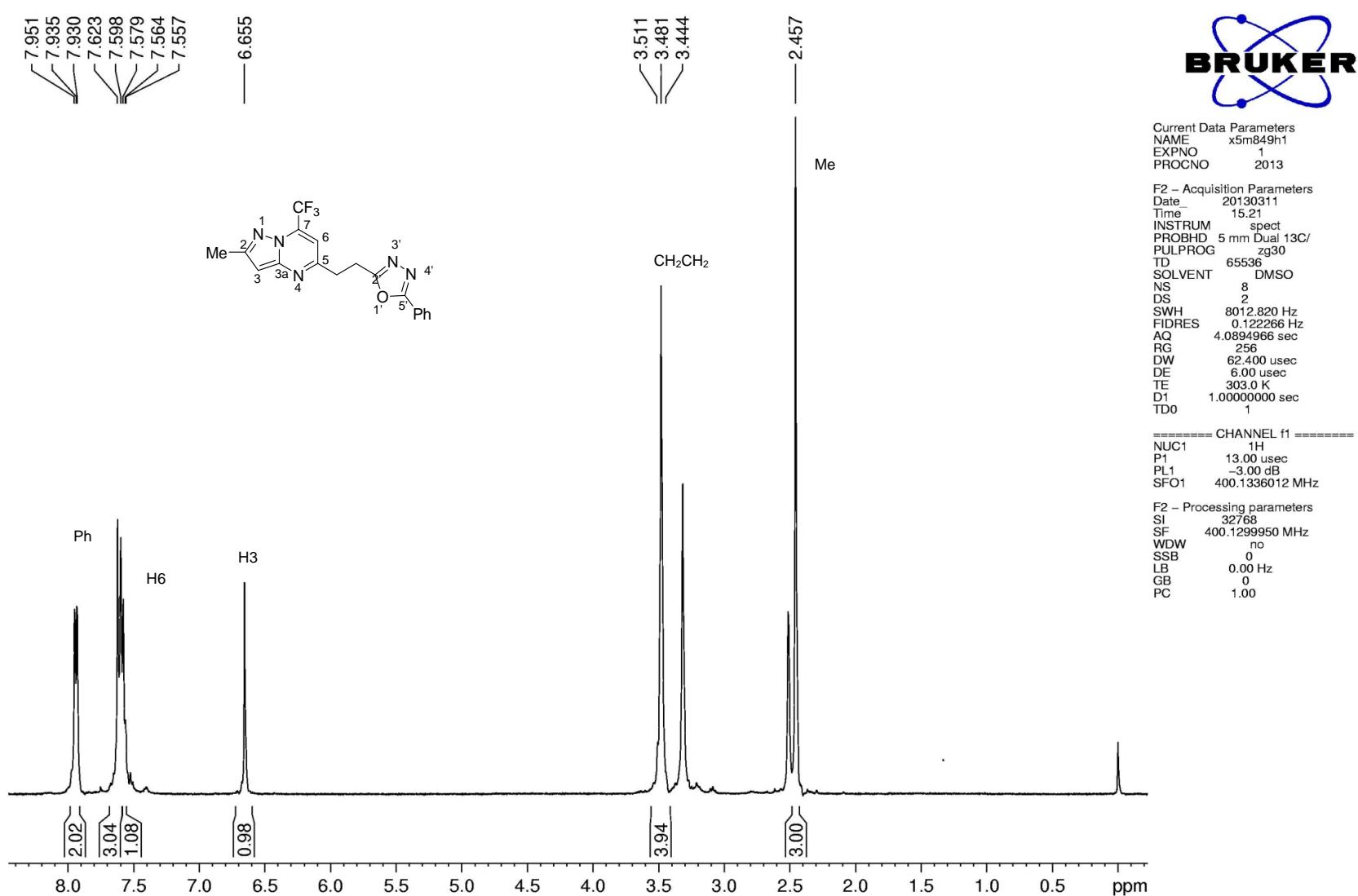


Figure S34. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of 5-phenyl-2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-a]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**6d**).

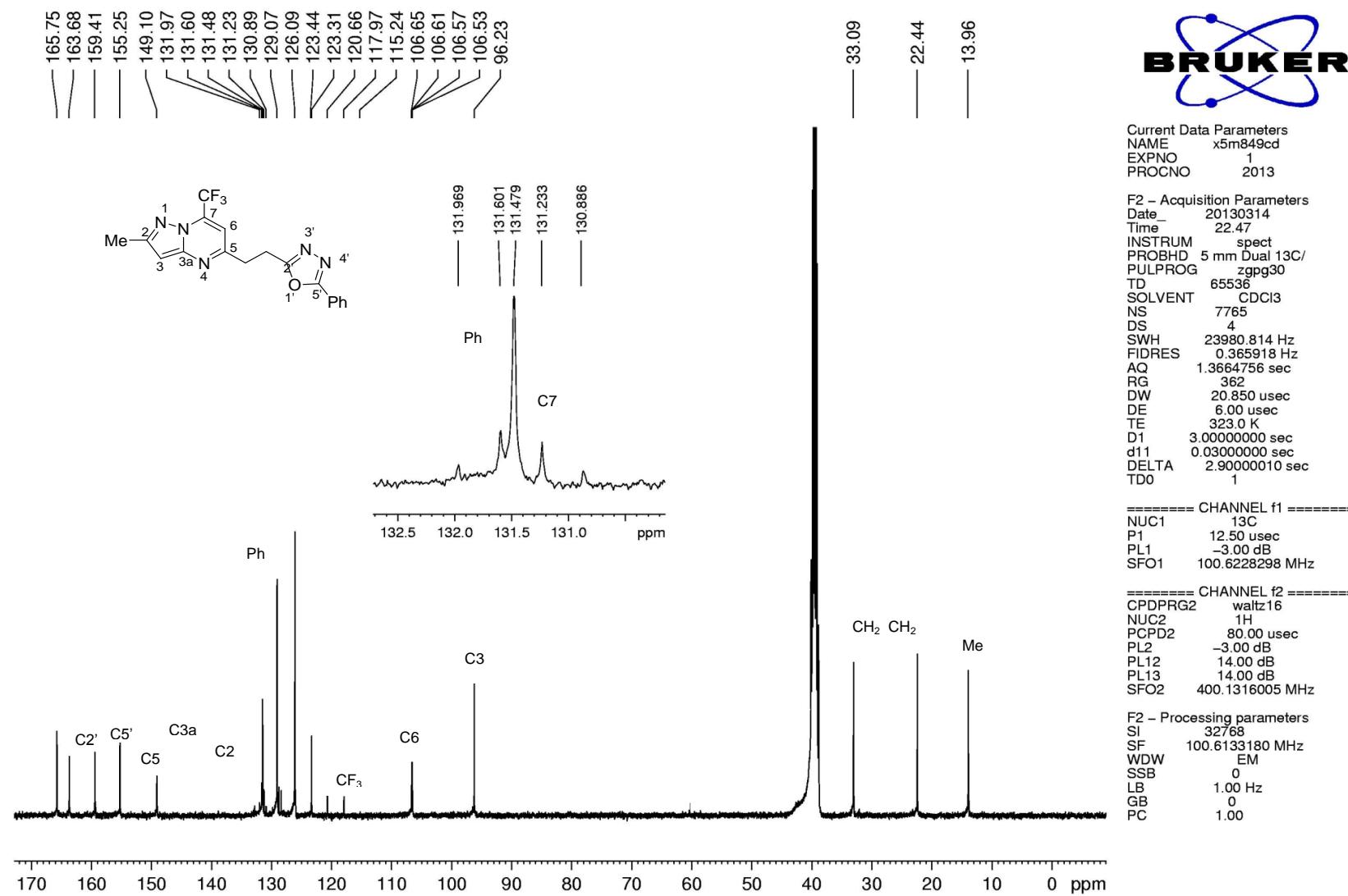


Figure S35. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of 5-phenyl-2-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazole (**6d**).

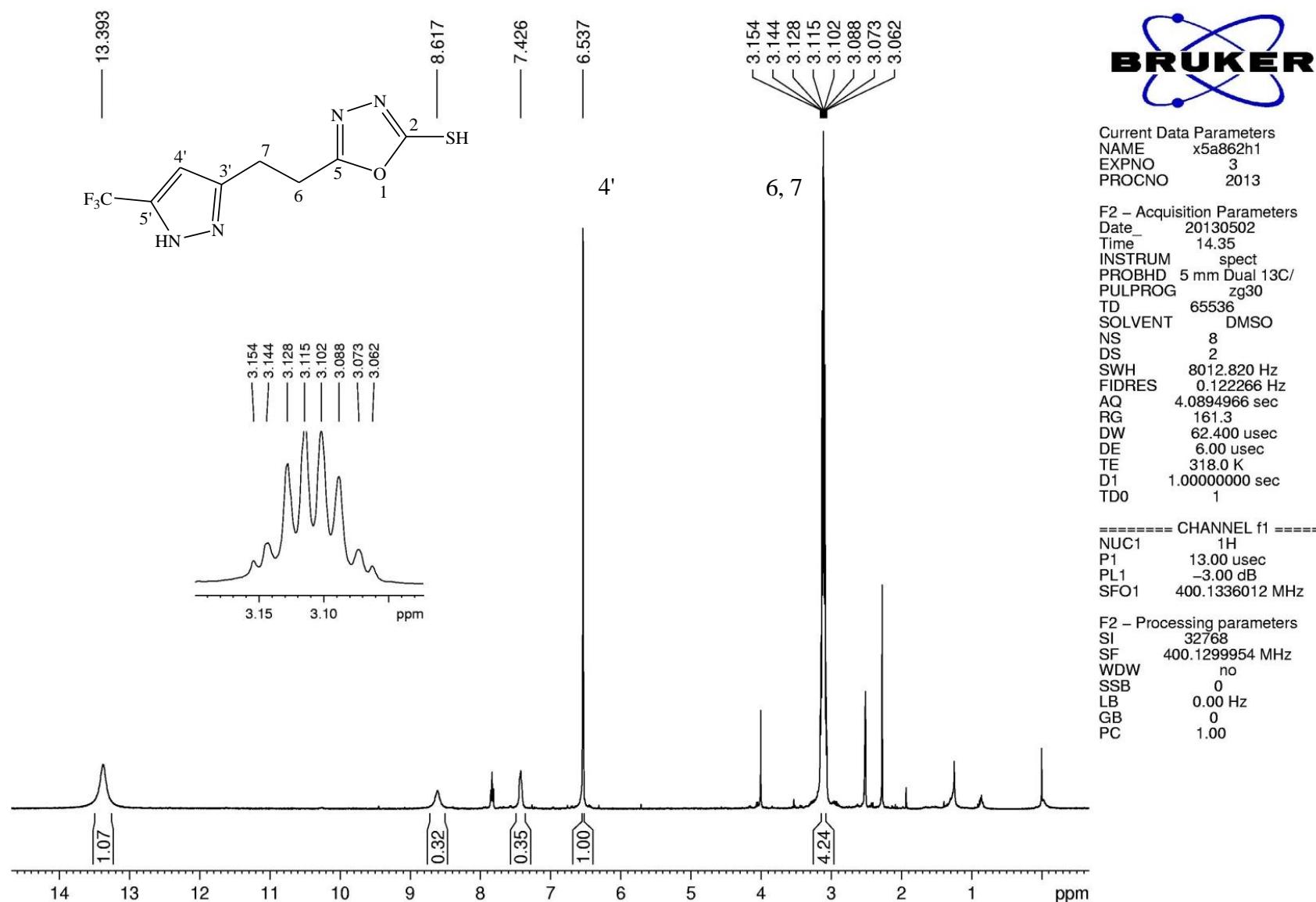
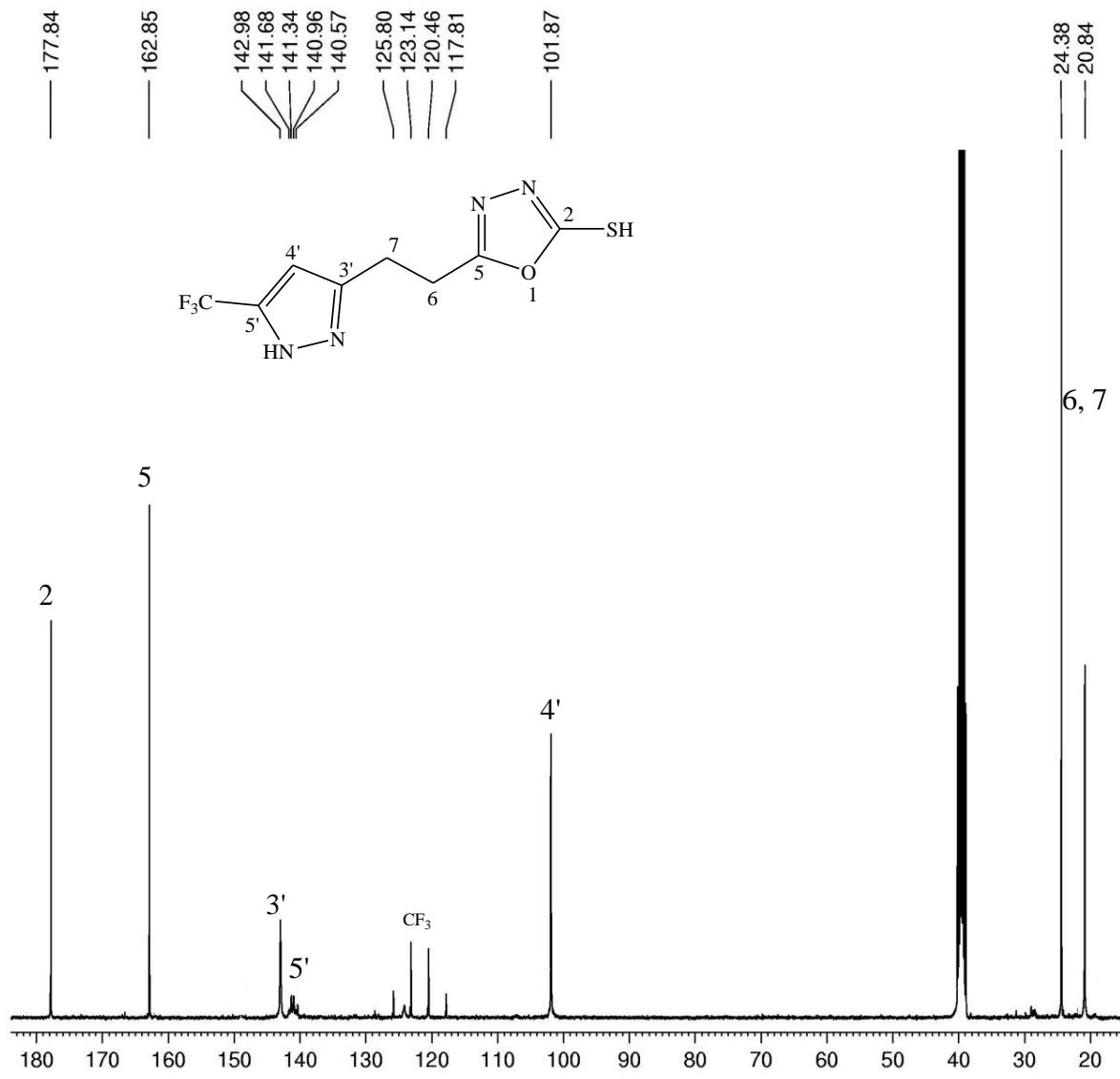


Figure S36. ^1H NMR spectrum (400 MHz, $\text{DMSO}-d_6$) of 5-(2-(5-trifluoromethyl-1*H*-pyrazol-3-yl)ethyl)-1,3,4-oxadiazol-2-thiol (**7a**).



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 PROCNO 2013

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 FIDRES 0.365918 Hz
 AQ 1.3664756 sec
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 TE 303.0 K
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 d11 0.03000000 sec
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 SFO1 100.6228298 MHz

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F2 - Processing parameters
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 SF 100.6128158 MHz
 WDW EM
 SSB 0
 LB 1.00 Hz
 GB 0
 PC 1.40

Figure S37. ^{13}C NMR spectrum (100 MHz, $\text{DMSO}-d_6$) of 5-(2-(5-trifluoromethyl-1*H*-pyrazol-3-yl)ethyl)-1,3,4-oxadiazol-2-thiol (**6a**).

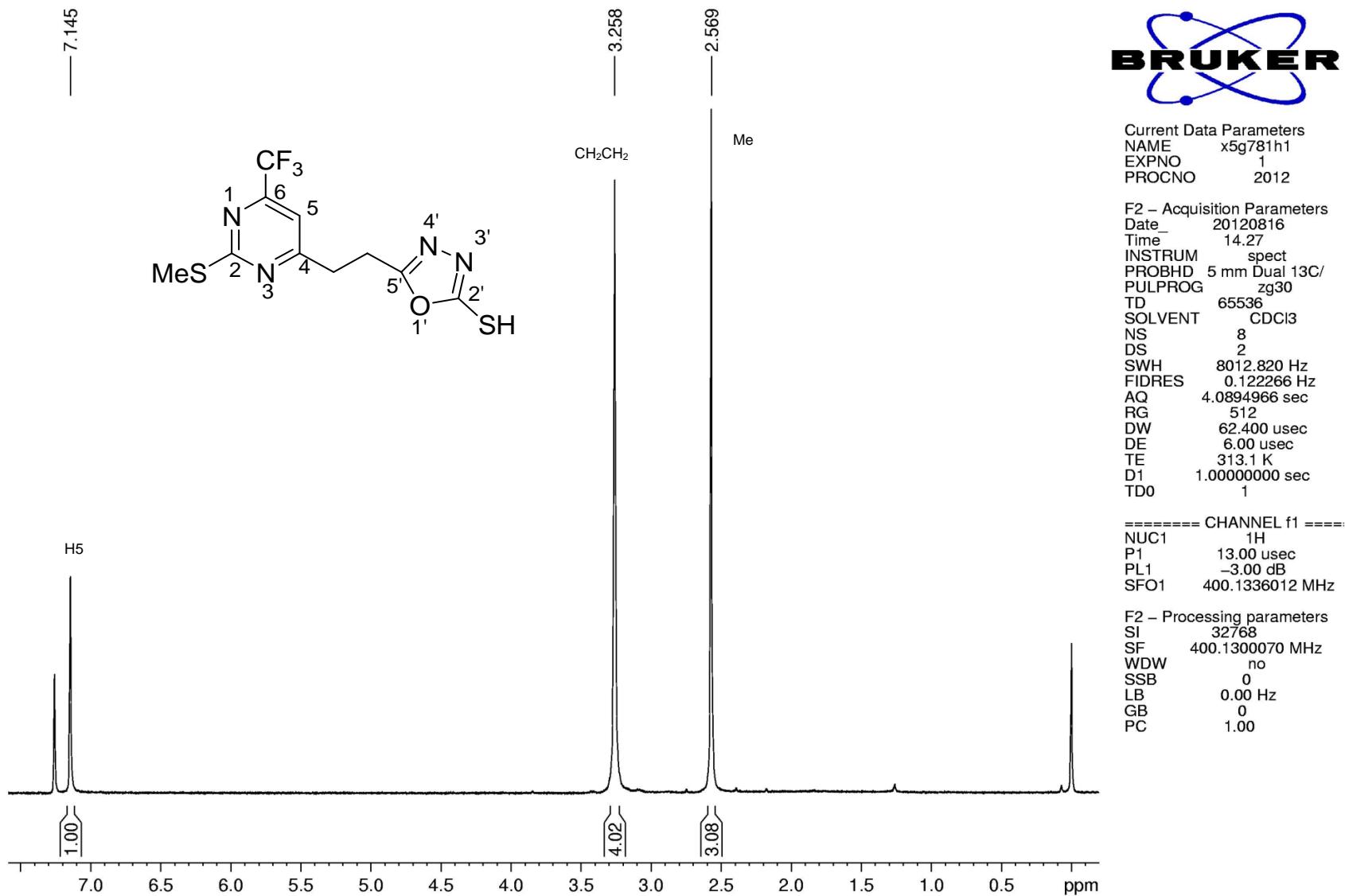
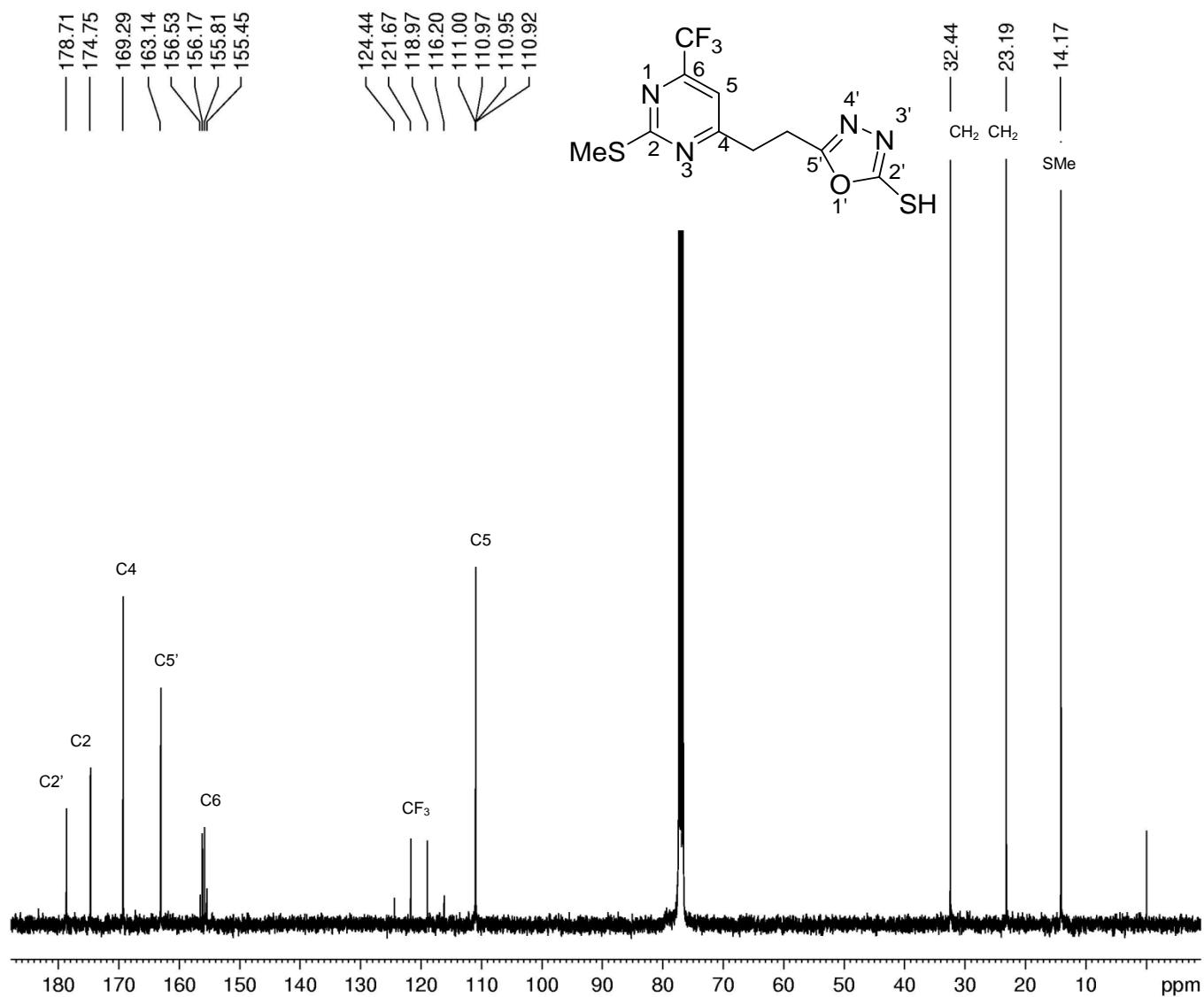


Figure S38. ¹H NMR spectrum (400 MHz, CDCl₃) of 5-[2-(thiomethyl)-6-trifluormethylpyrimidin-4-yl]ethyl]-1,3,4-oxadiazol-2-thiol (**7c**).



Current Data Parameters
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 EXPNO 1
 PROCNO 2012

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===== CHANNEL f2 =====
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 PCPD2 80.00 usec
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 PL13 14.00 dB
 SFO2 400.1316005 MHz

F2 – Processing parameters
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 SF 100.6127635 MHz
 WDW EM
 SSB 0
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 PC 1.40

Figure S39. ^{13}C NMR spectrum (100 MHz, CDCl_3) of 5-(2-(thiomethyl-6-trifluormethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thiol (**7c**).

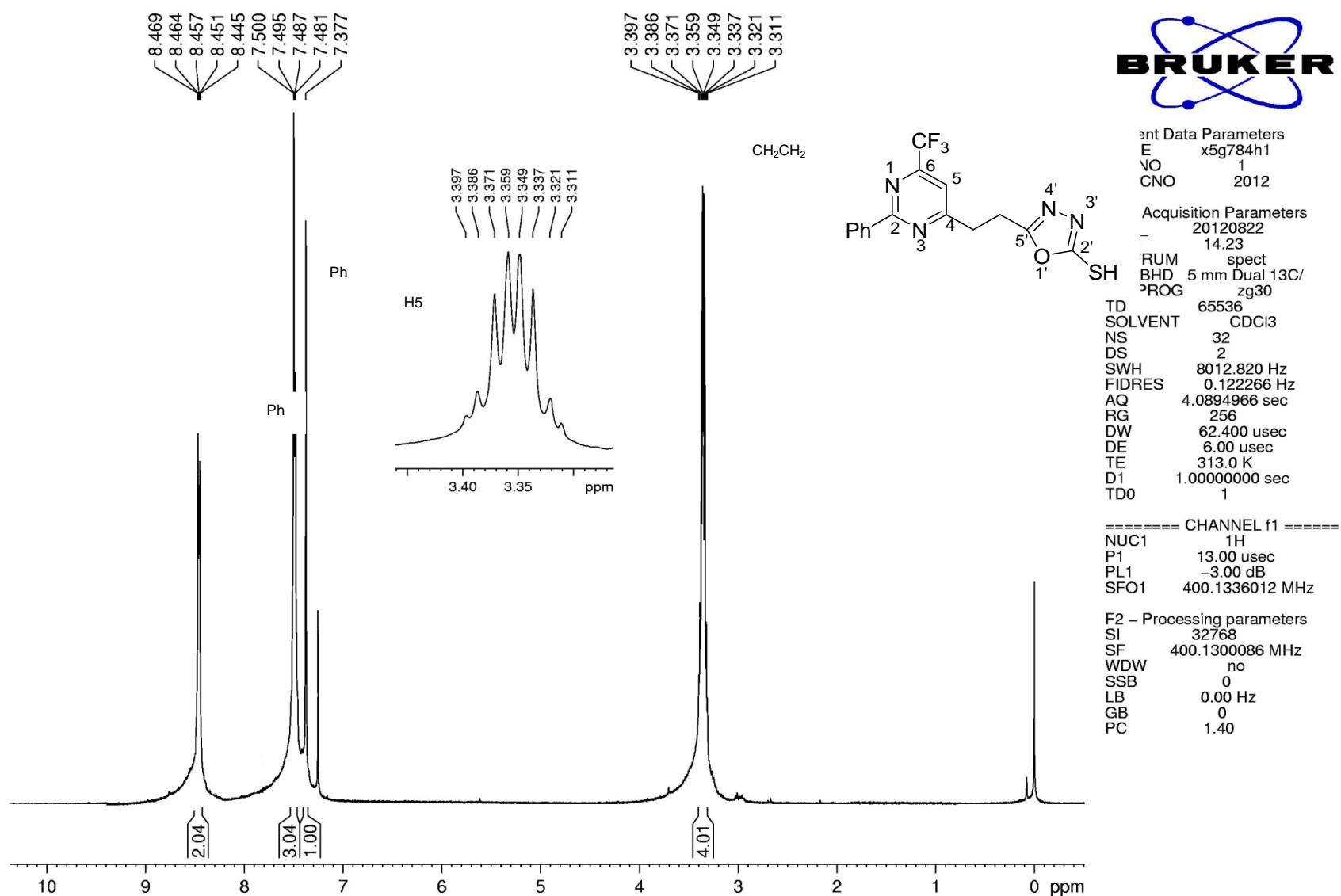


Figure S40. ¹H NMR spectrum (400 MHz, CDCl₃) of 5-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thiol (**7b**).

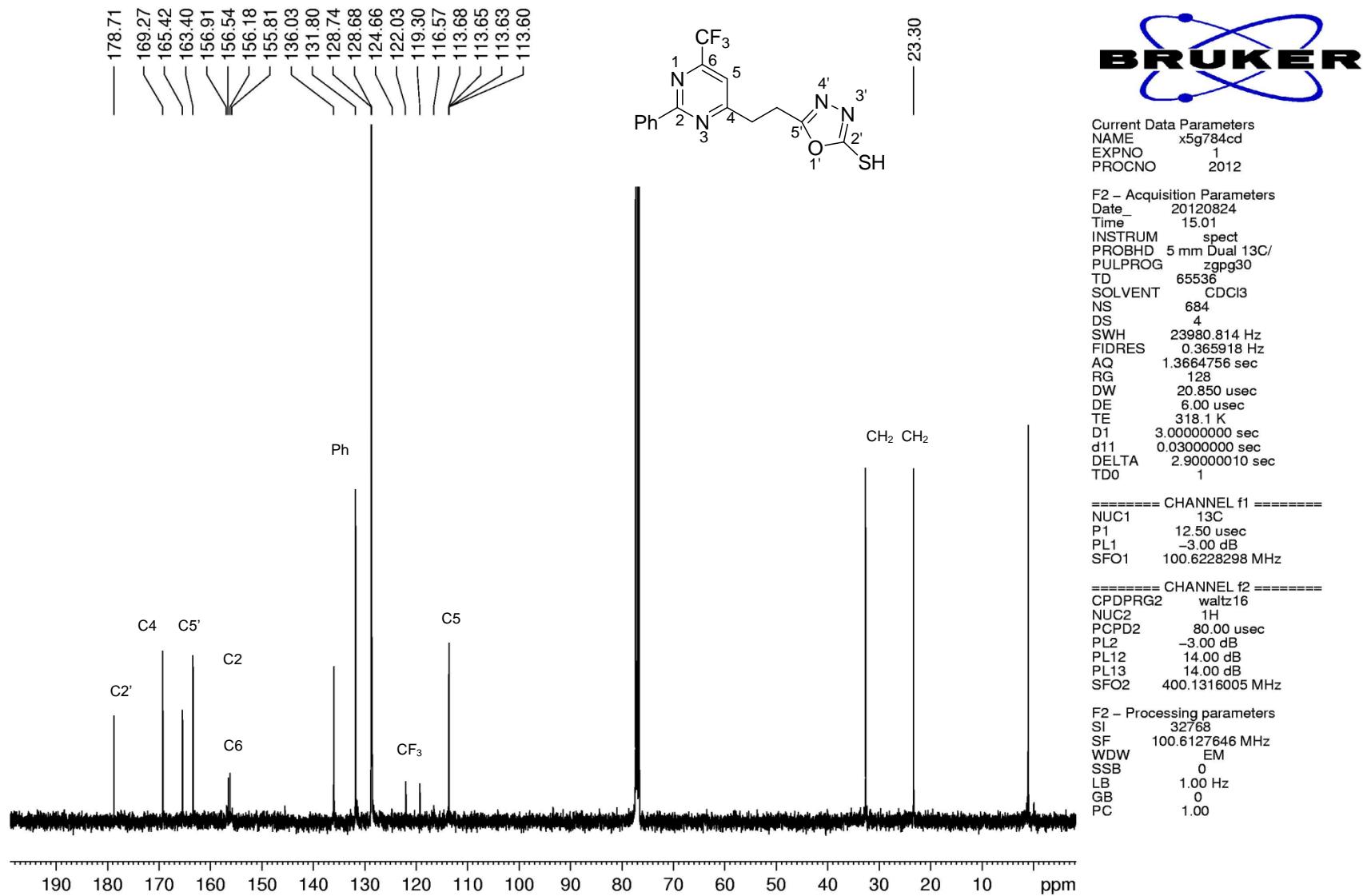


Figure S41. ^{13}C NMR spectrum (100 MHz, CDCl₃) of 5-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thiol (**7b**).

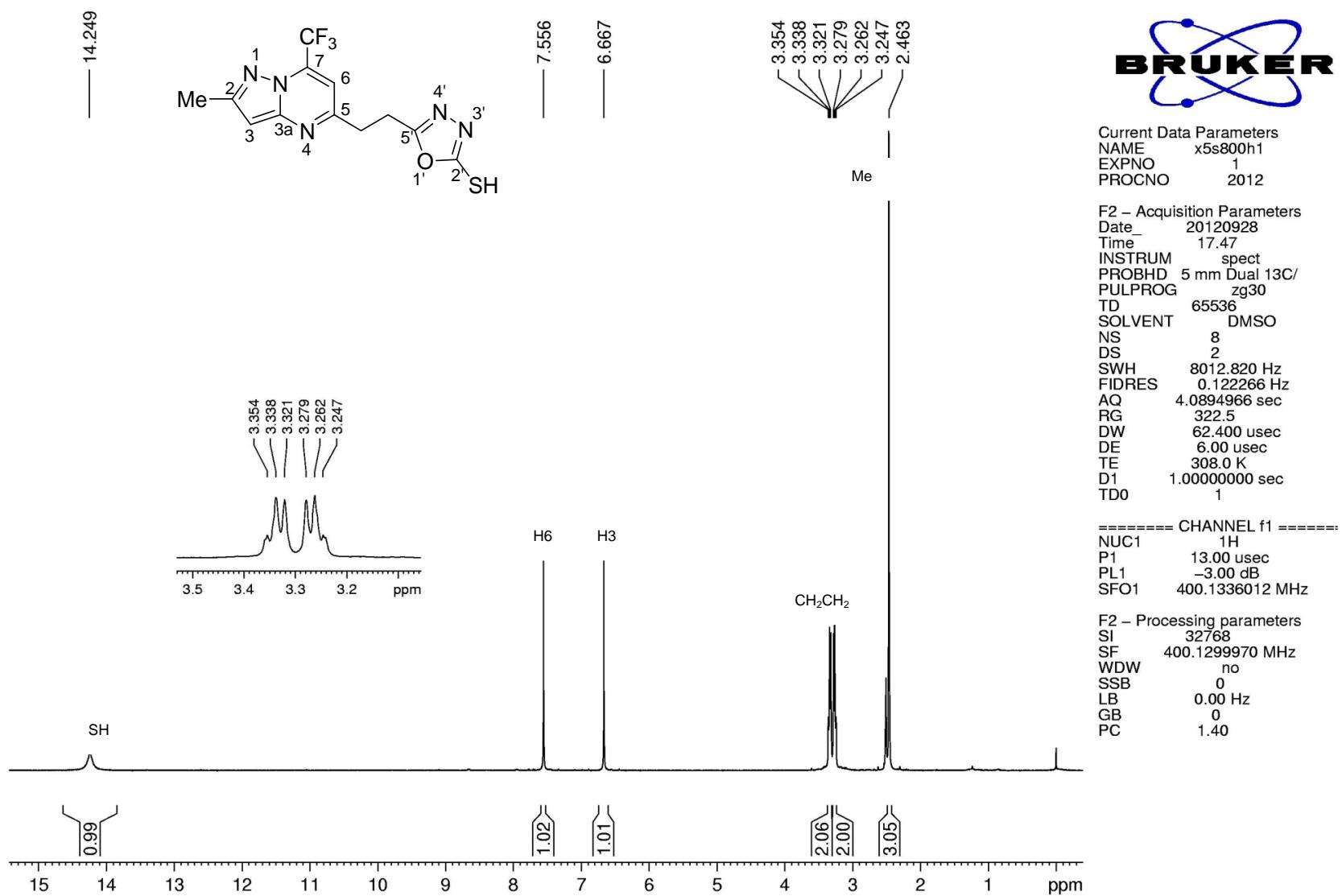


Figure S42. ¹H NMR spectrum (400 MHz, DMSO-*d*₆) of 5(2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl)-1,3,4-oxadiazol-2-thiol (**7d**).

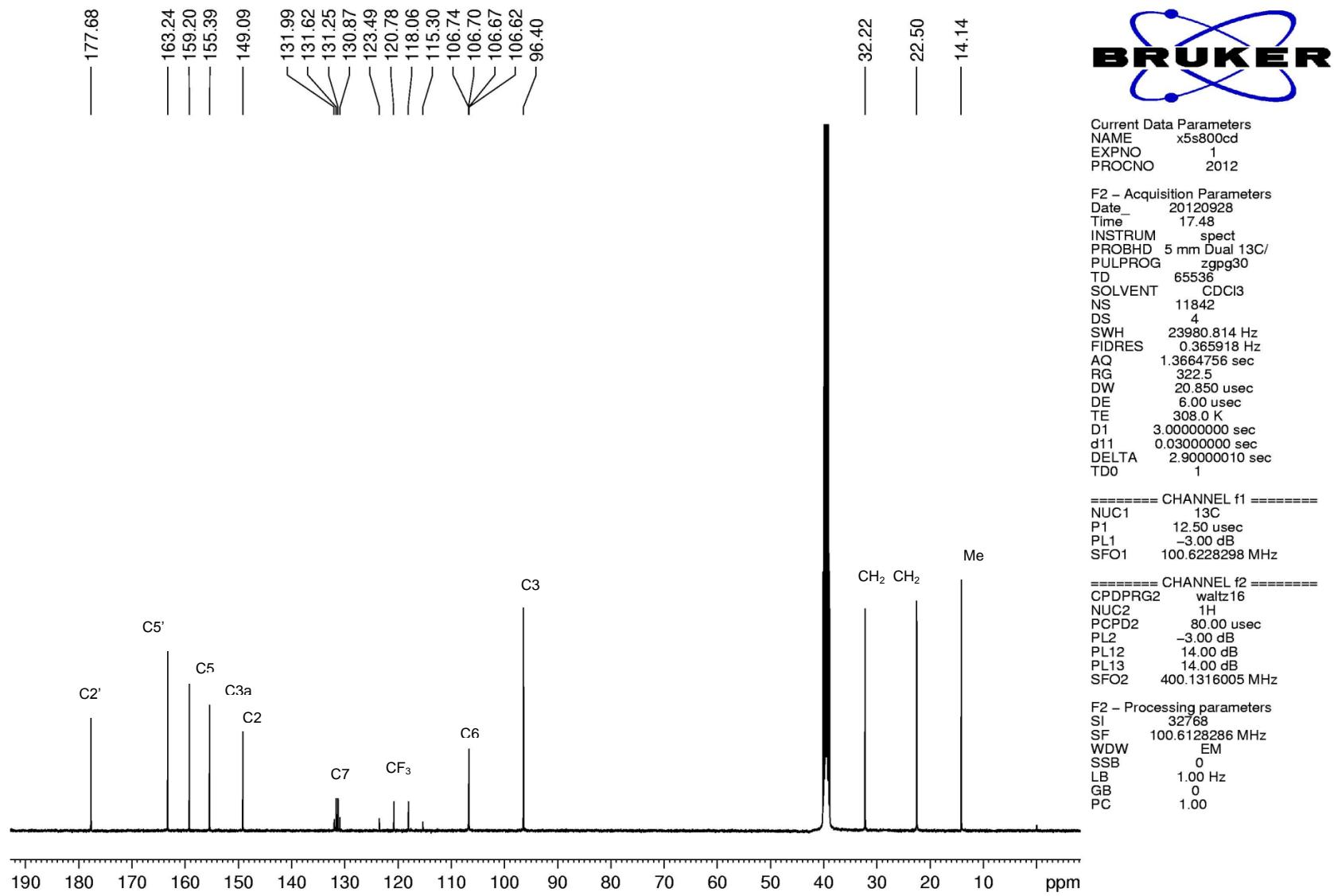


Figure S43. ¹³C NMR spectrum (100 MHz, DMSO-*d*₆) of 5-[2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl]-1,3,4-oxadiazol-2-thiol (**7d**).

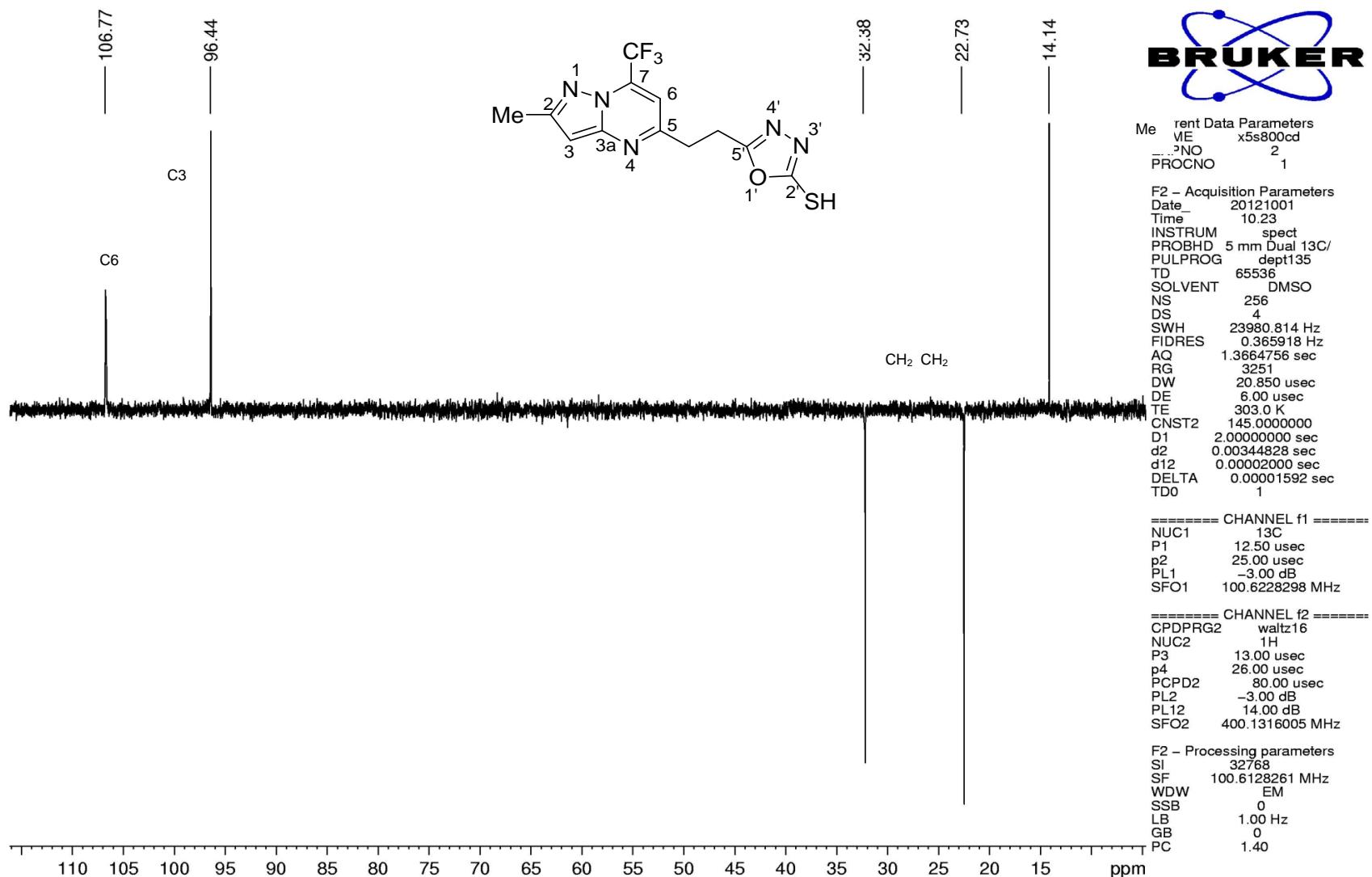


Figure S44. ^{13}C DEPT 135 NMR spectrum (DMSO-*d*₆) of 5-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl)-1,3,4-oxadiazol-2-thiol (**7d**).

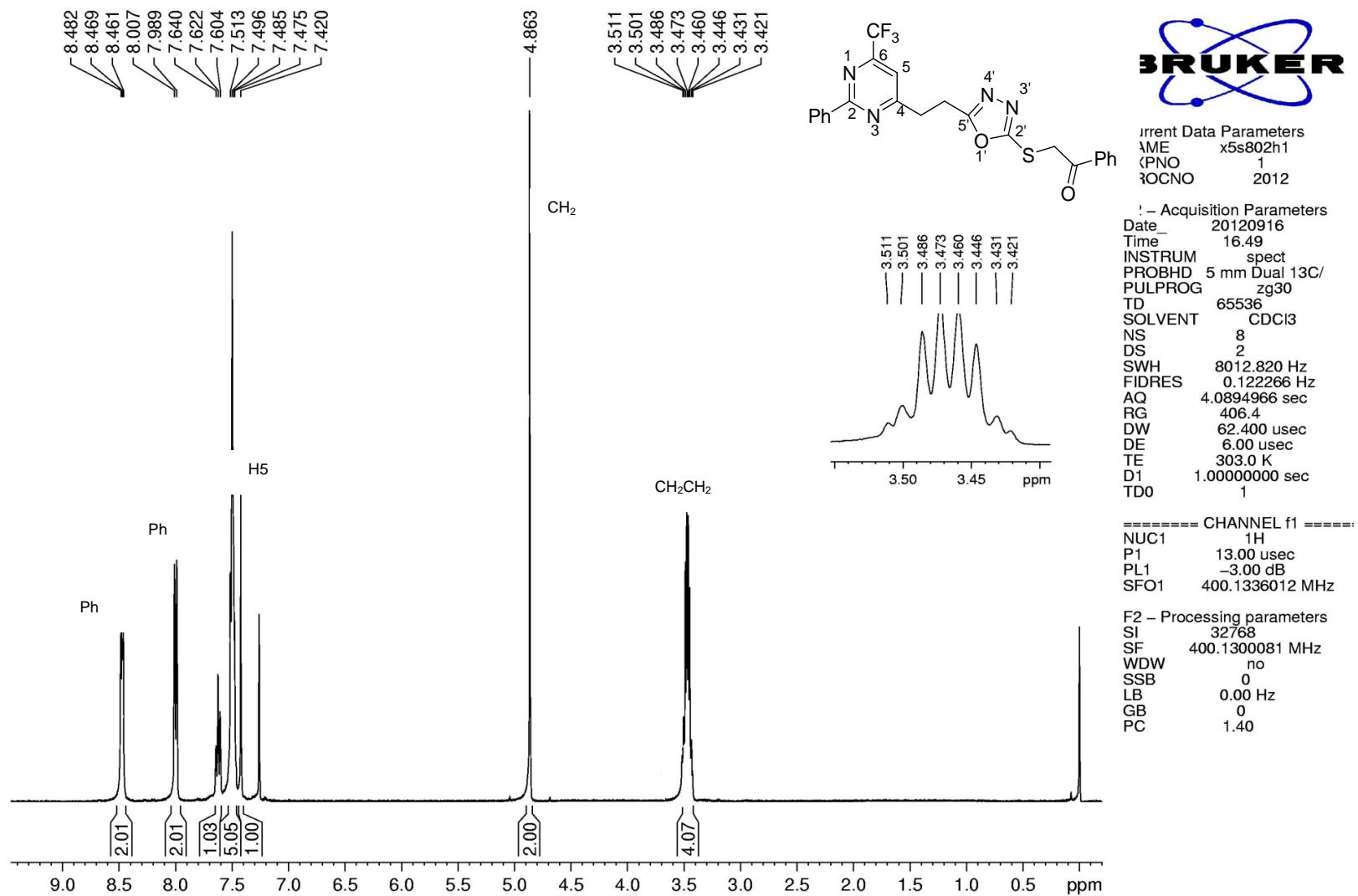
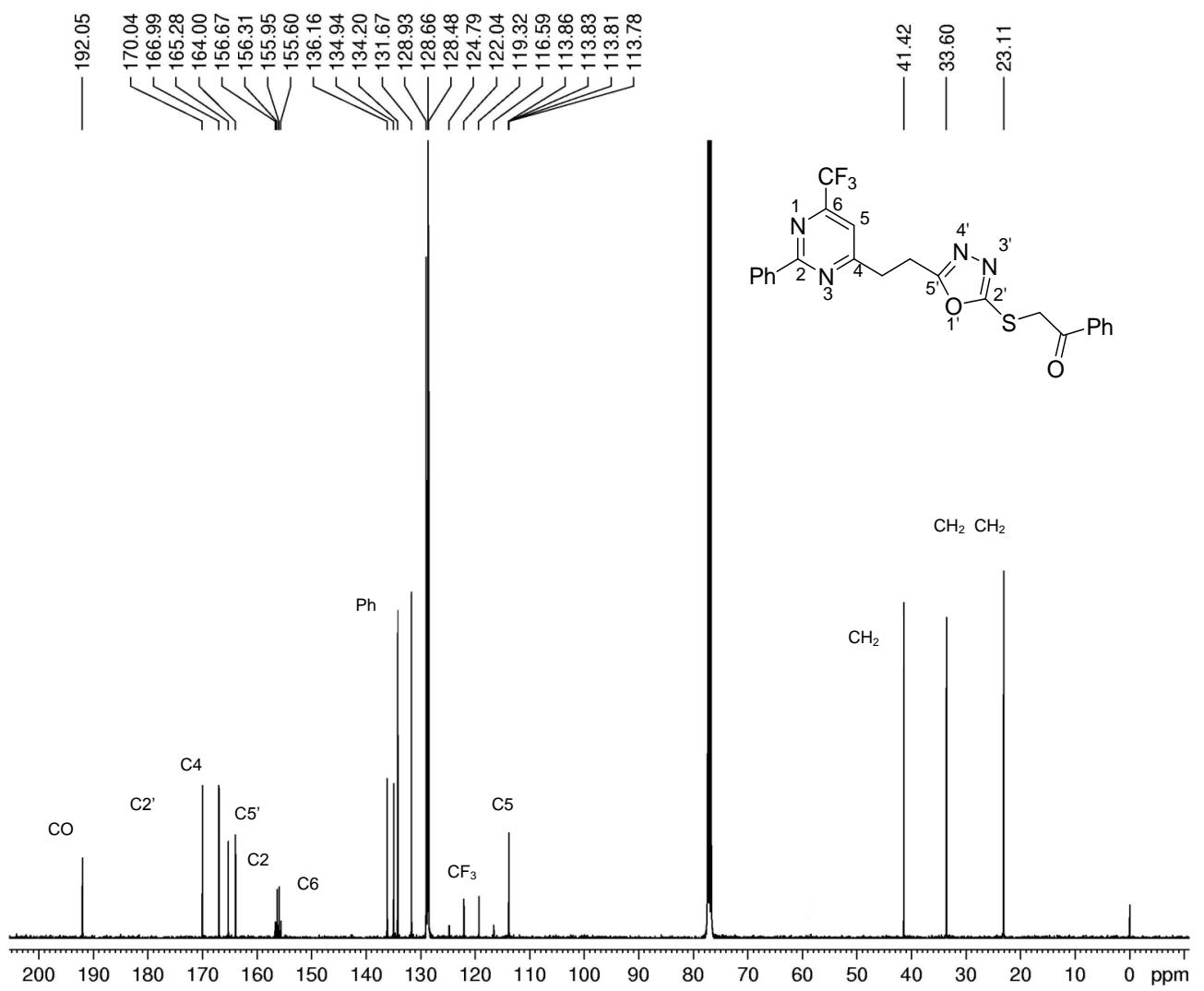


Figure S45. ¹H NMR spectrum (400 MHz, CDCl₃) of 1-phenyl-2-[(5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-yl)thio]ethanone or 2-[5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl]acetophenone (**8b**).



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PROCNO 2012

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DE 6.00 usec
TE 303.0 K
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d11 0.03000000 sec
DELTA 2.90000010 sec
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SFO1 100.6228298 MHz

===== CHANNEL f2 =====:
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PCPD2 80.00 usec
PL2 -3.00 dB
PL12 14.00 dB
PL13 14.00 dB
SFO2 400.1316005 MHz

F2 – Processing parameters
SI 32768
SF 100.6127681 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

Figure S46. ^{13}C NMR spectrum (100 MHz, CDCl_3) of 1-phenyl-2-[{5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-yl}thio]ethanone or 2-[5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl]acetophenone (**8b**).

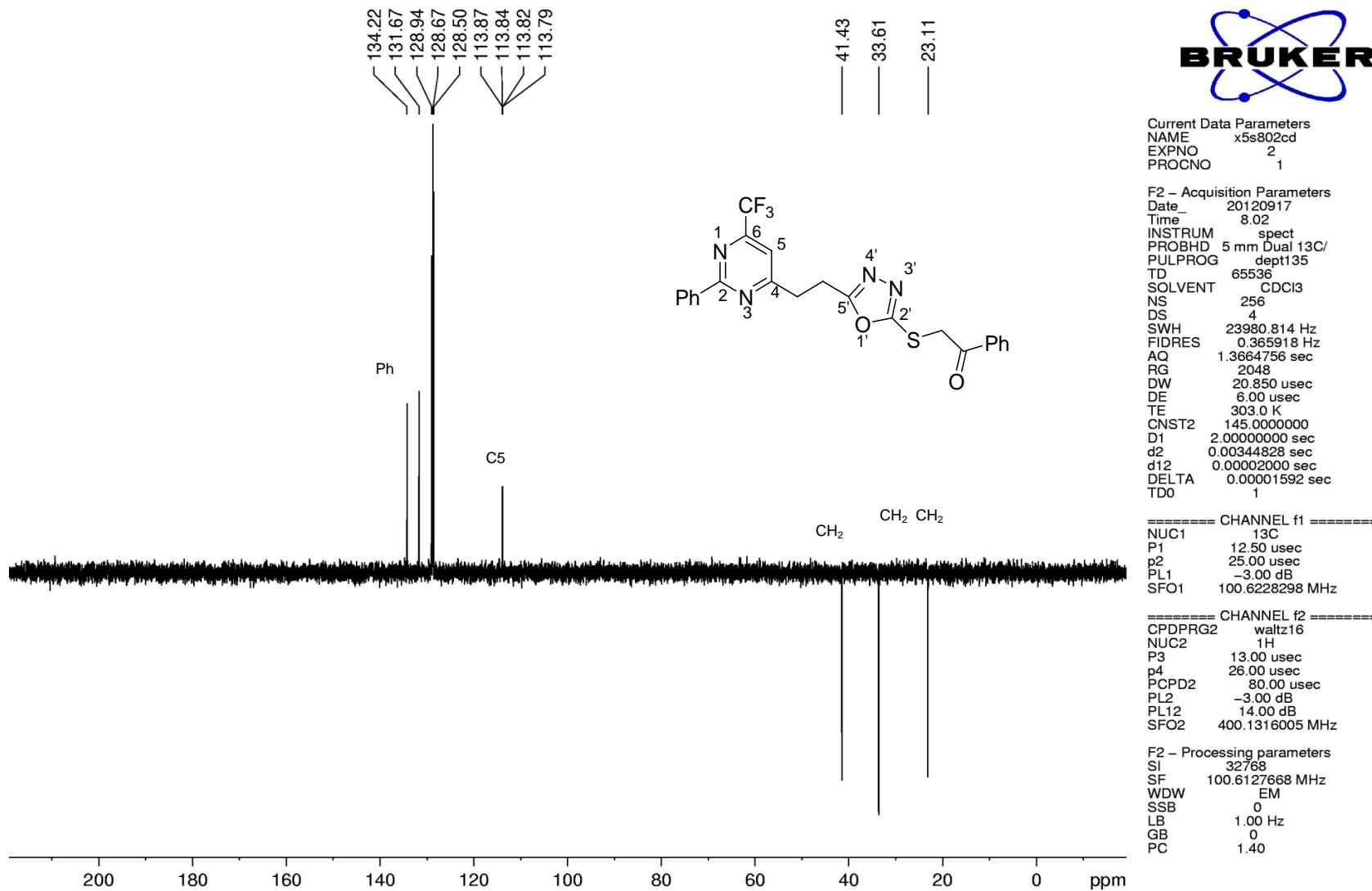


Figure S47. ^{13}C DEPT135 NMR spectrum (100 MHz, CDCl_3) of 1-phenyl-2-[5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-yl]thio]ethanone or 2-[5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl]acetophenone (**8b**).

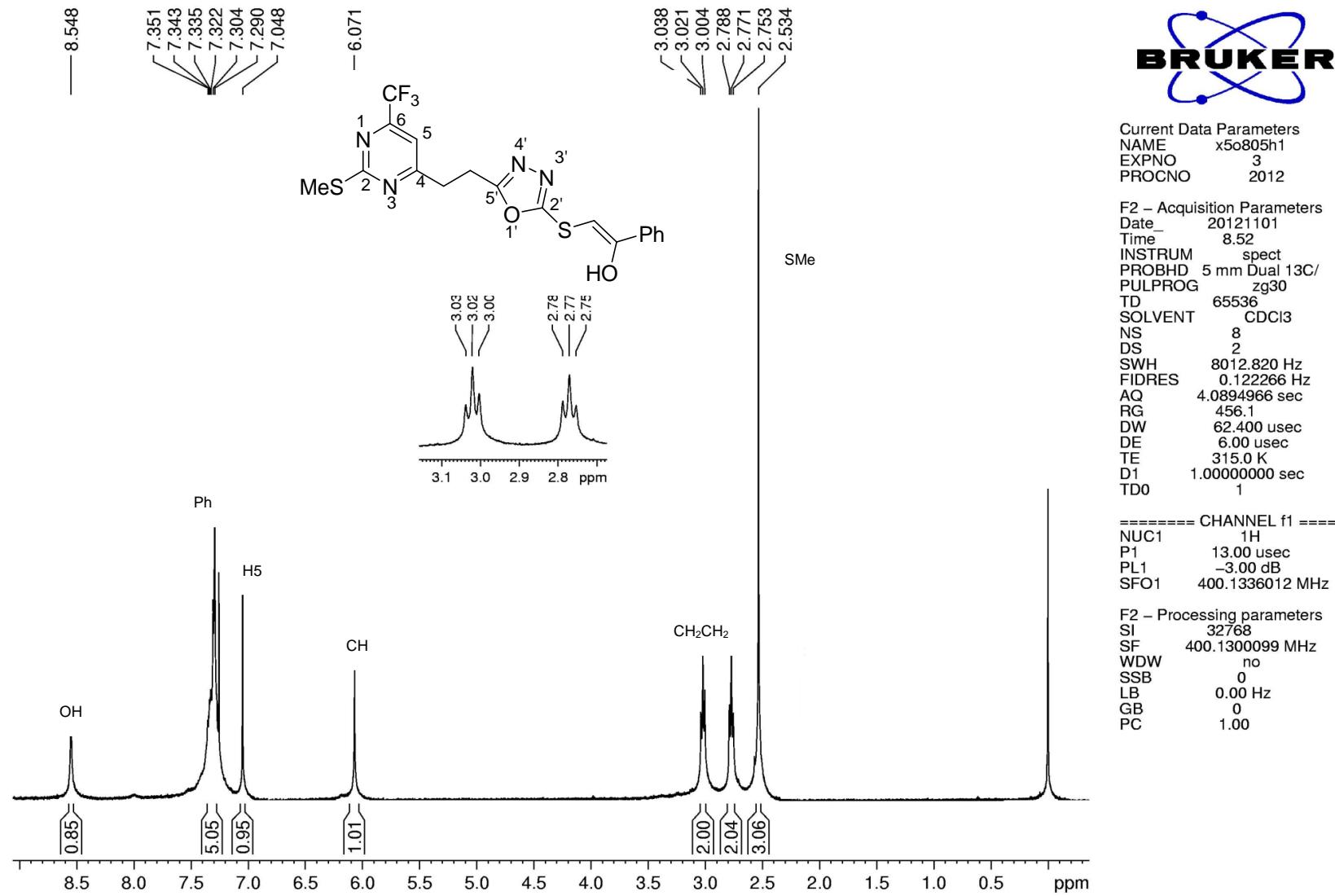


Figure S48. ^1H NMR spectrum (400 MHz, CDCl_3) of 2-(5-(2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl) acetophenone (enol form, **8c**).

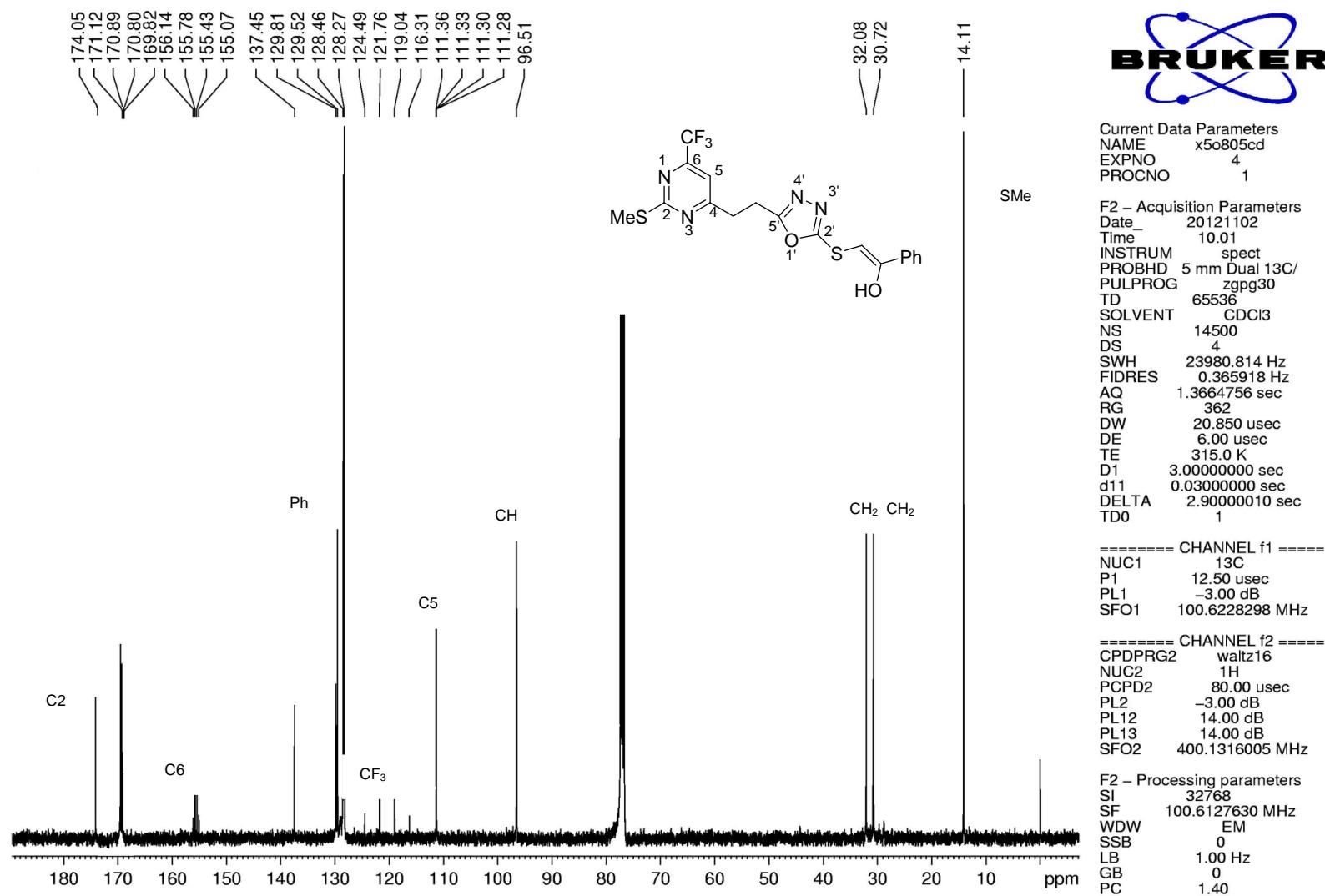


Figure S49. ^{13}C NMR spectrum (100 MHz, CDCl₃) of 2-[5-(2-(2-methylthio-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-yl]thio]-1-phenylethanone or 2-(5-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl) acetophenone (**8c**).

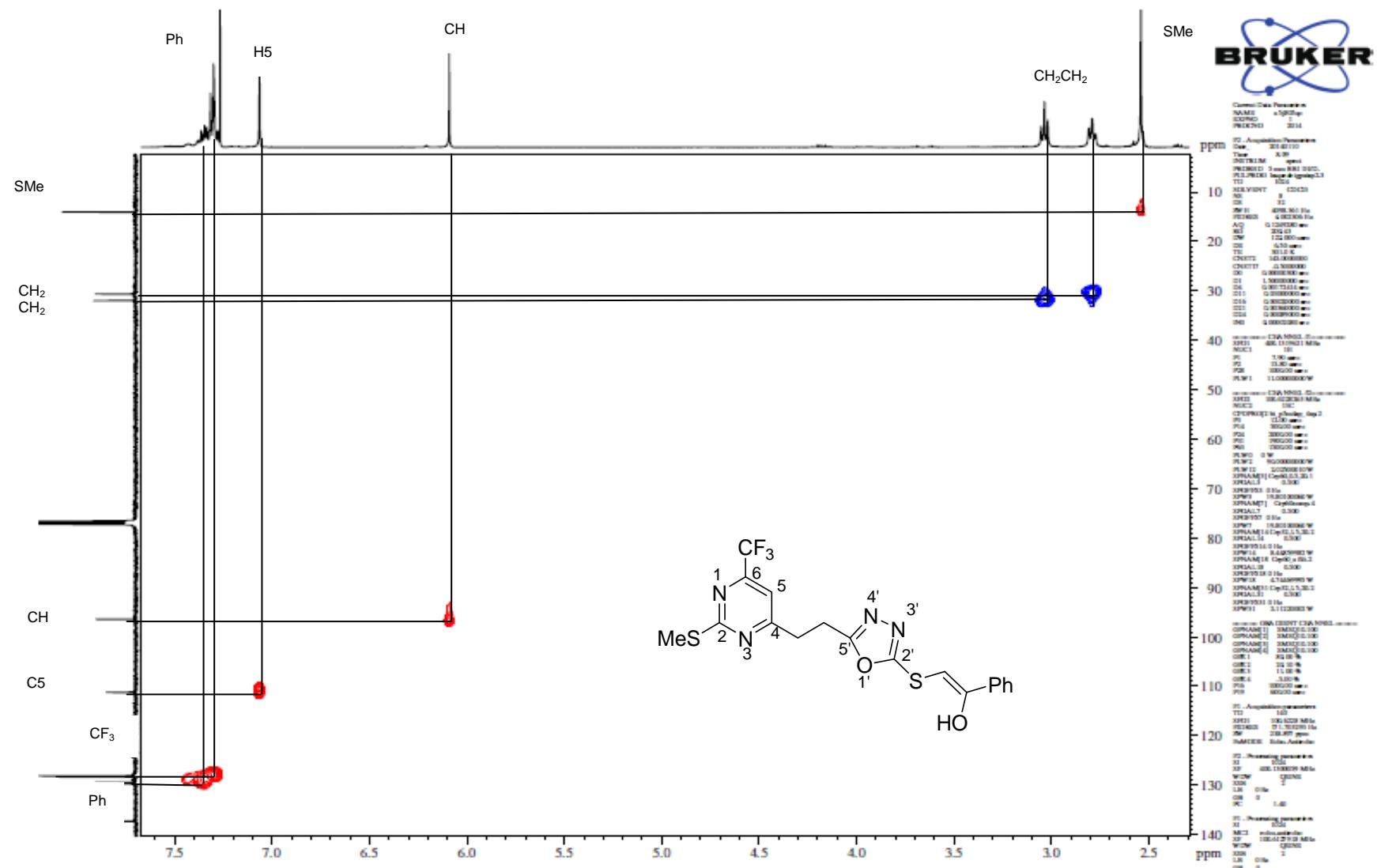


Figure S50. 2D-HMQC NMR spectrum (CDCl_3) of 2-[5-(2-(2-methylthio-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-yl]thio]-1-phenylethanone or 2-(5(2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl) acetophenone (**8c**).

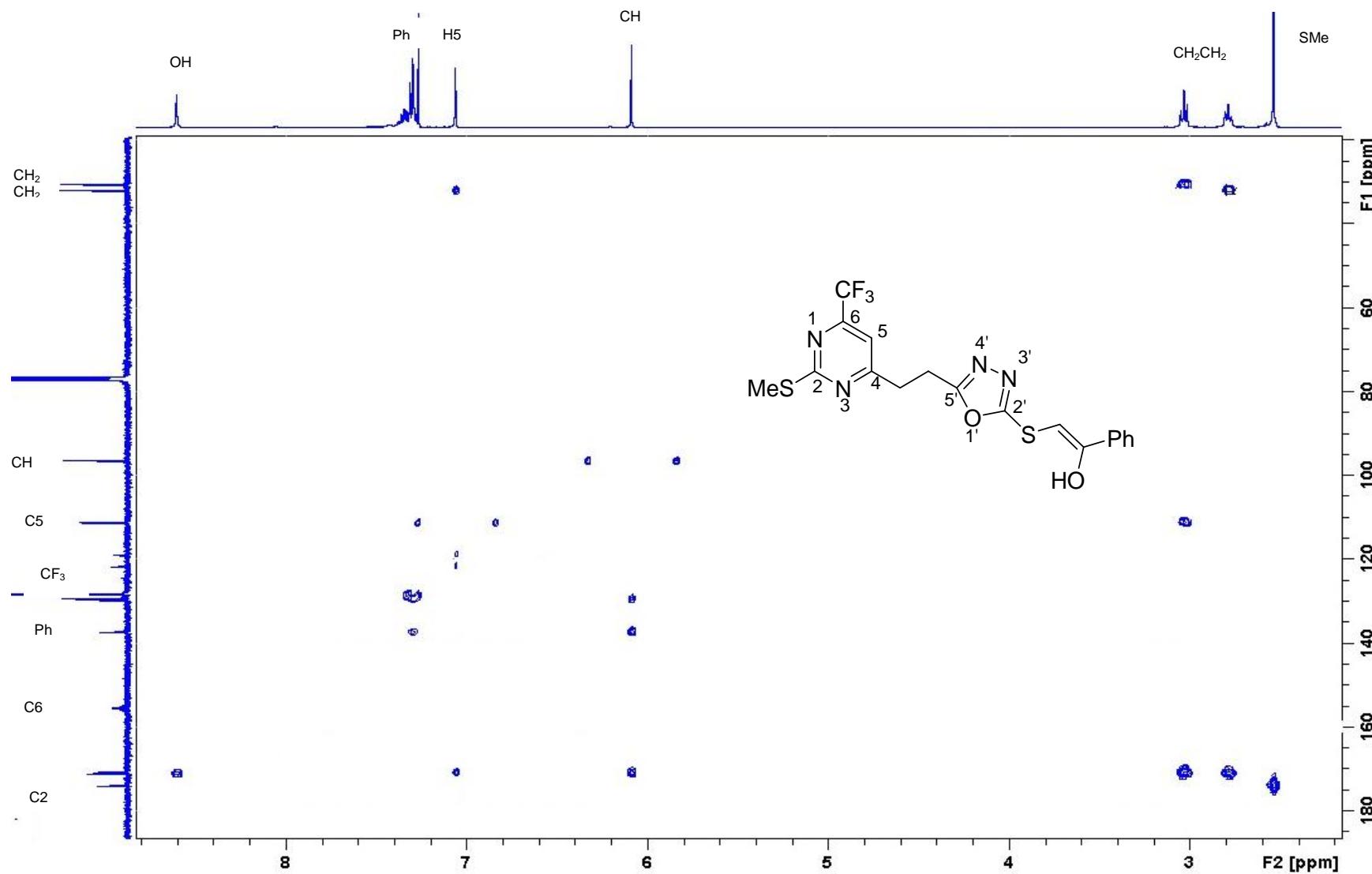


Figure S51. HMBC NMR spectrum of 2-[(5-(2-(2-methylthio-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-yl)thio]-1-phenylethanone or 2-(5-(2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl) acetophenone (**8c**).

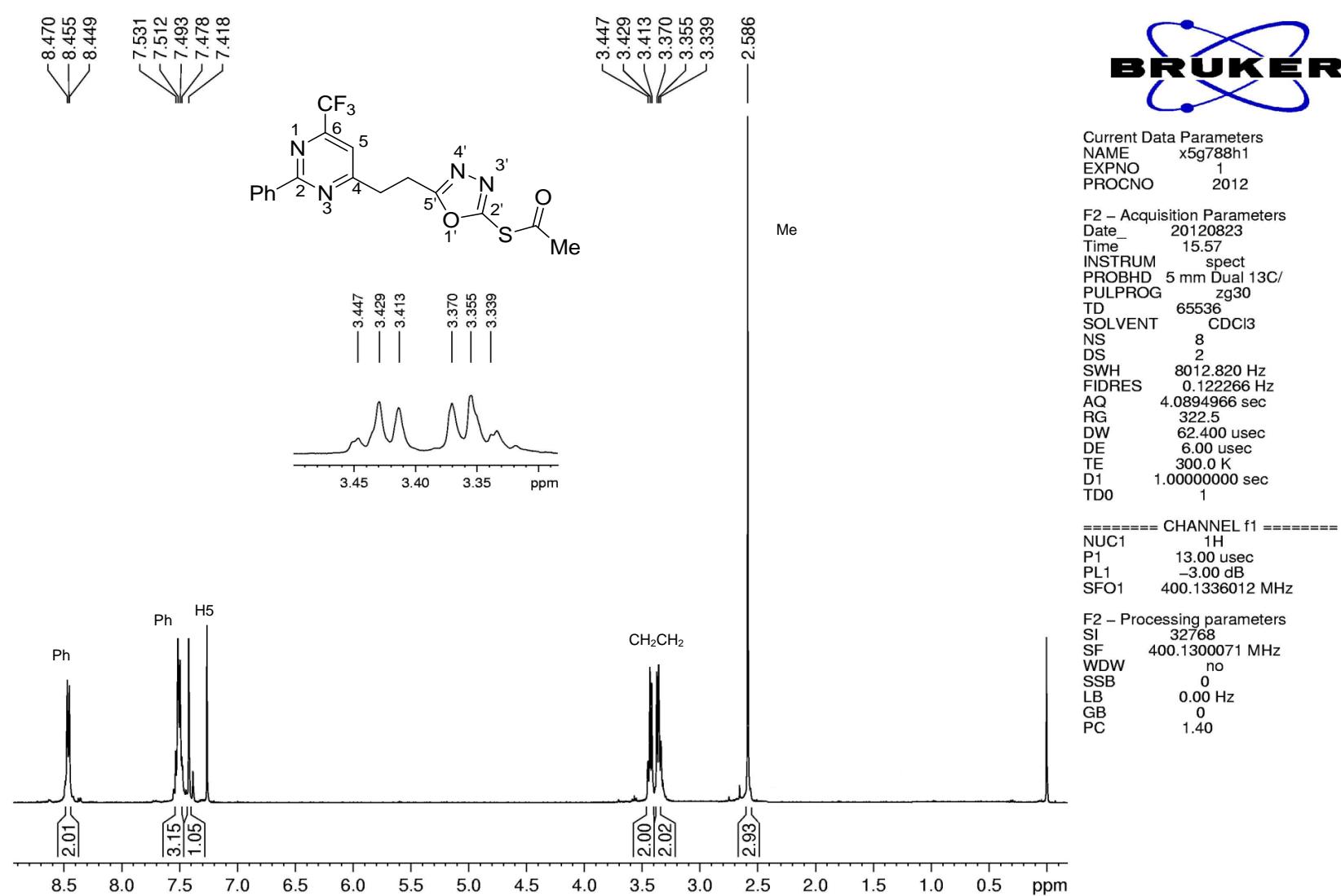


Figure S52. ¹H NMR spectrum (400 MHz, CDCl₃) of 5-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl-1,3,4-oxadiazol-2-yl ethanethioate (**9b**).

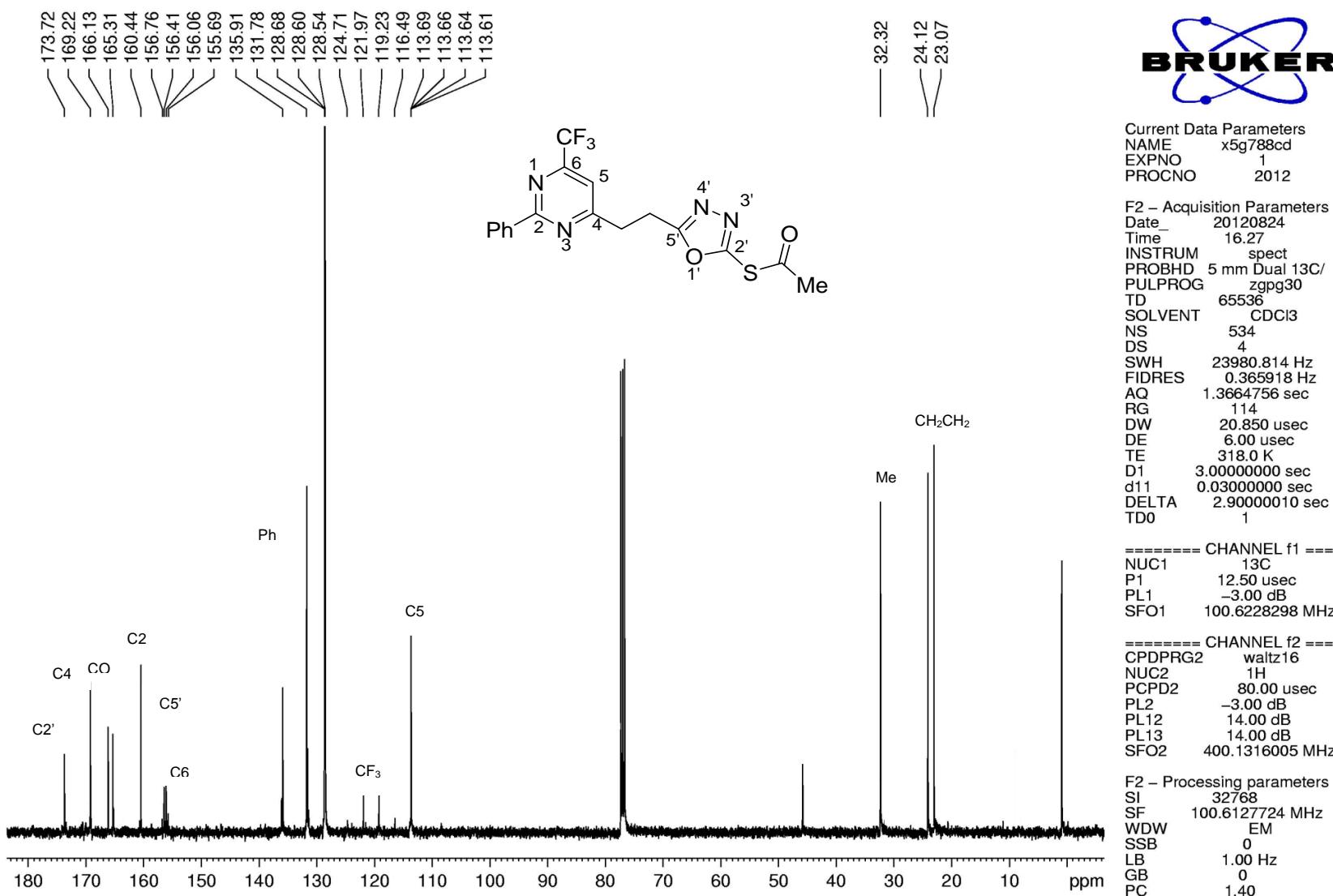


Figure S53. ¹³C NMR spectrum (100 MHz, CDCl₃) of 5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl ethanethioate (**9b**).

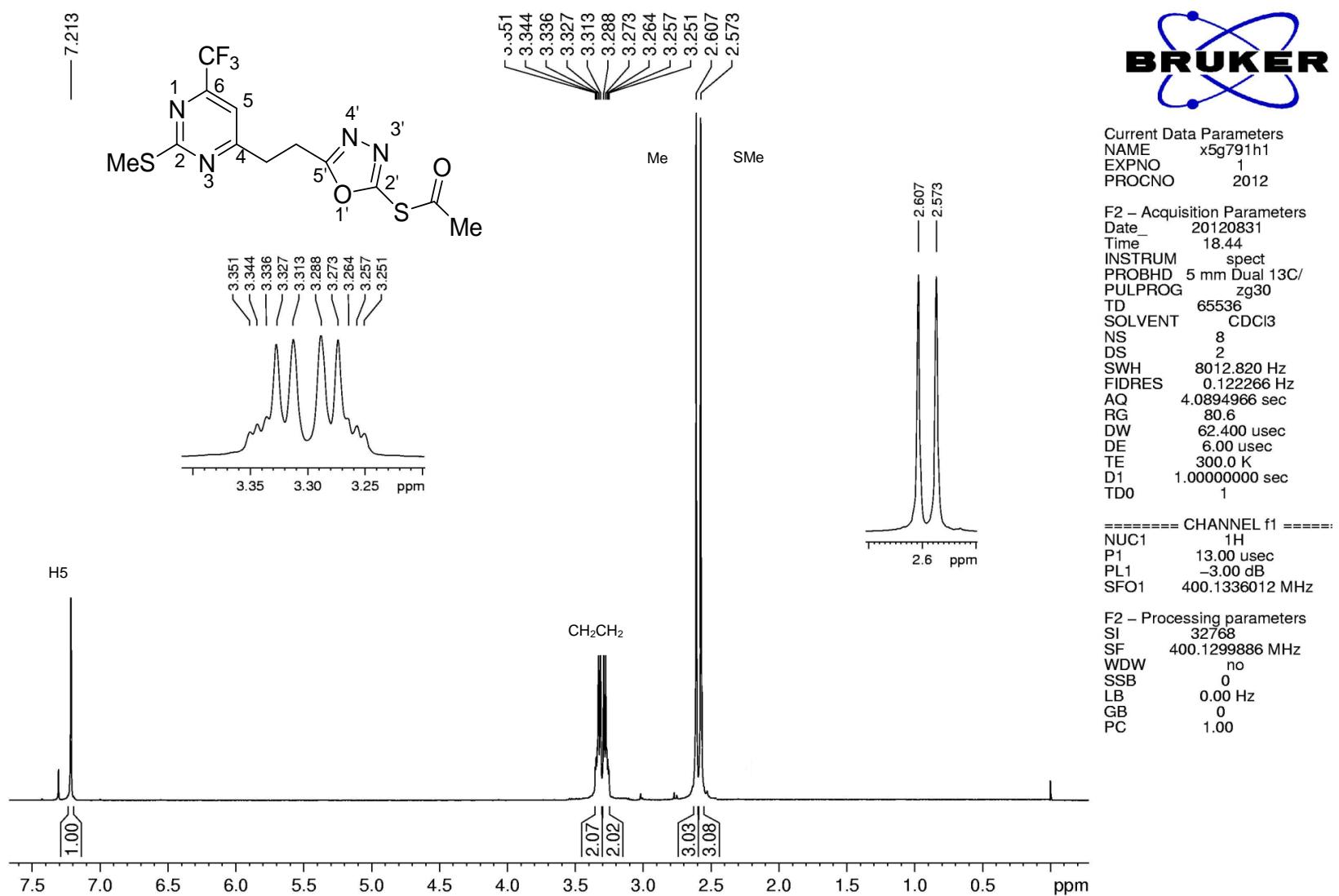


Figure S54. ^1H NMR spectrum (400 MHz, CDCl_3) of 5-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioate (**9c**).

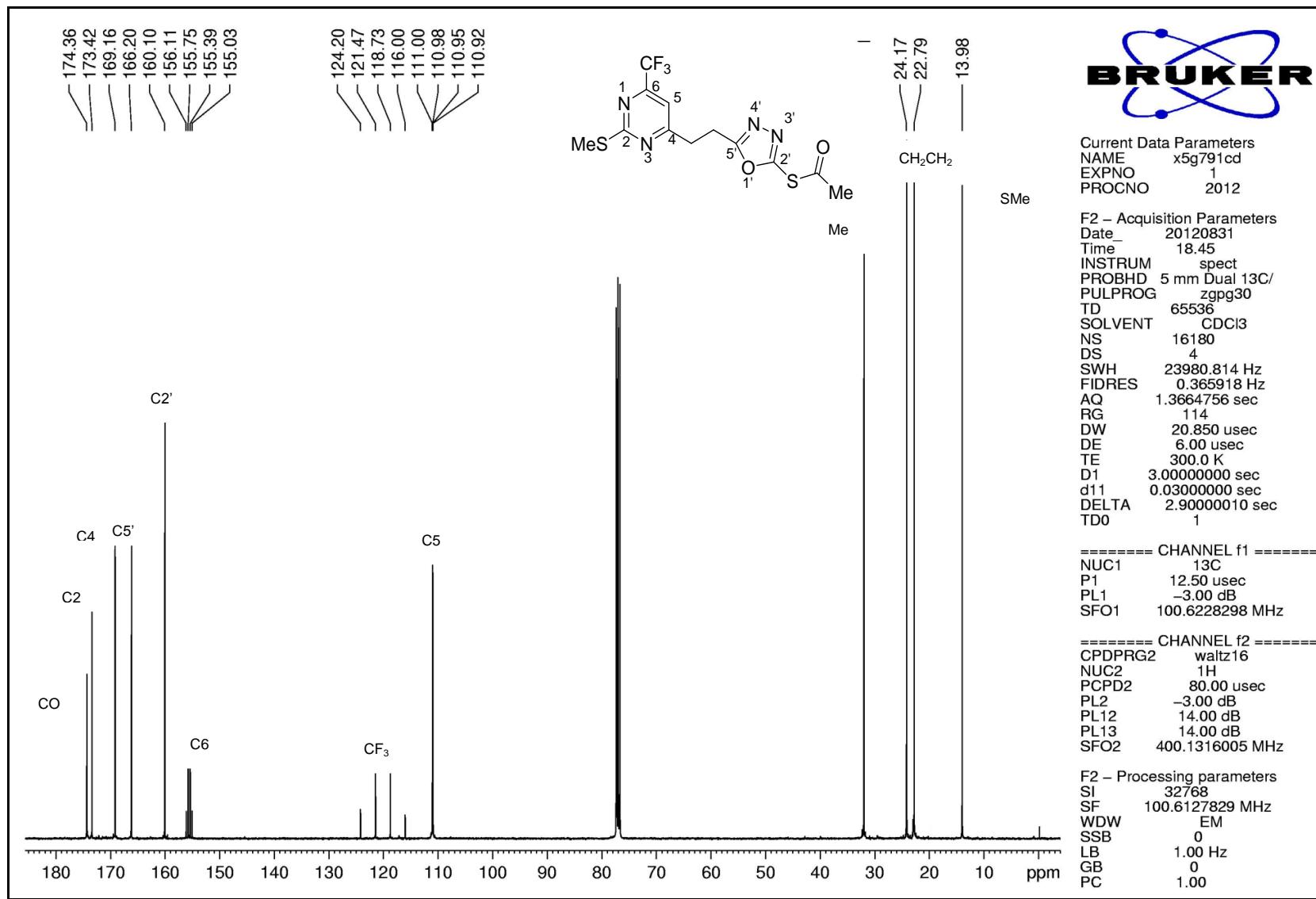


Figure S55. ^{13}C NMR spectrum (100 MHz, CDCl₃) of 5-(2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl ethanethioate (**9c**).

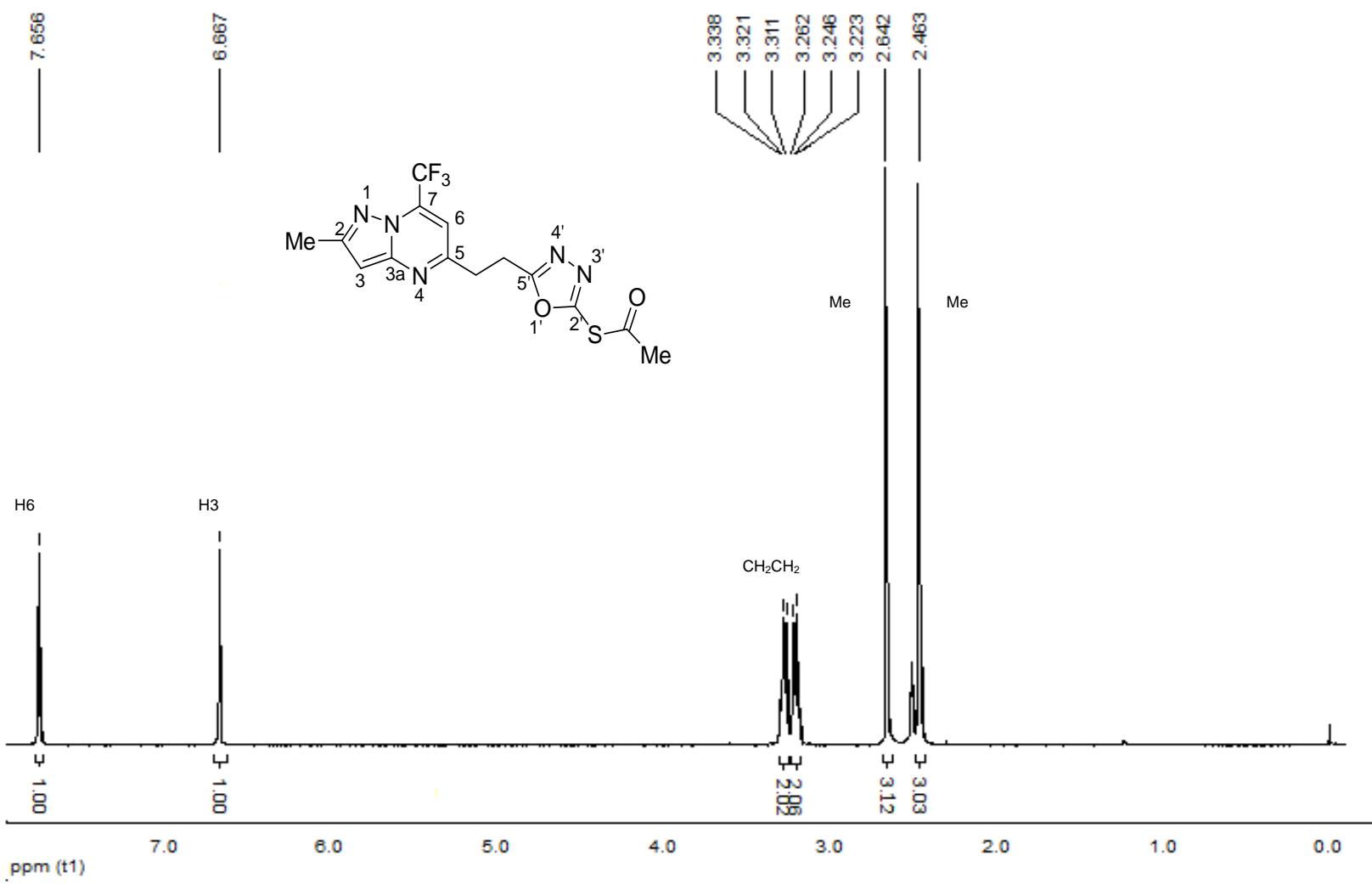


Figure S56. ^1H NMR spectrum (400 MHz, DMSO- d_6) of 5-(2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl)-1,3,4-oxadiazol-2-thioyl ethanethioate (**9d**).

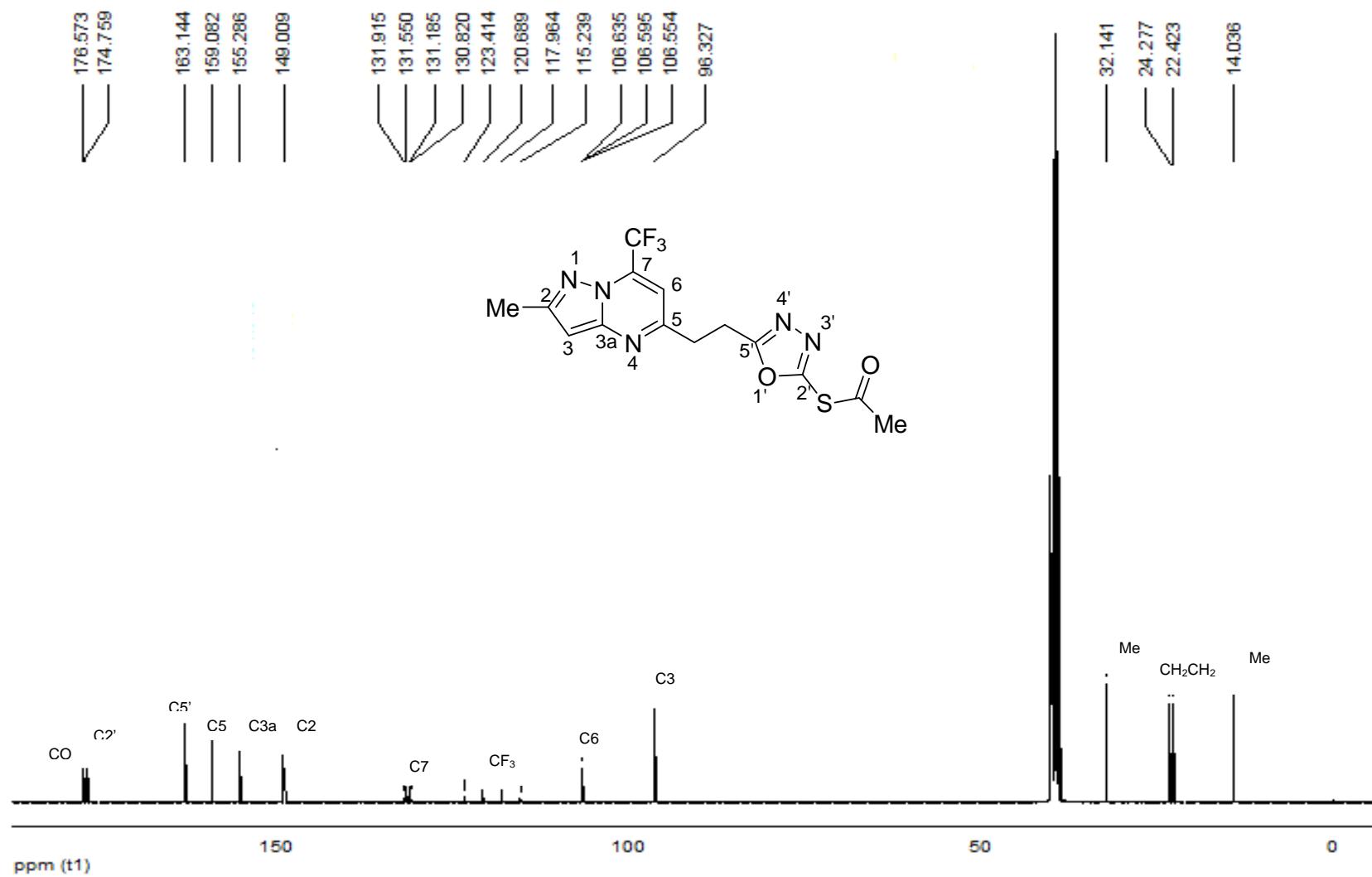
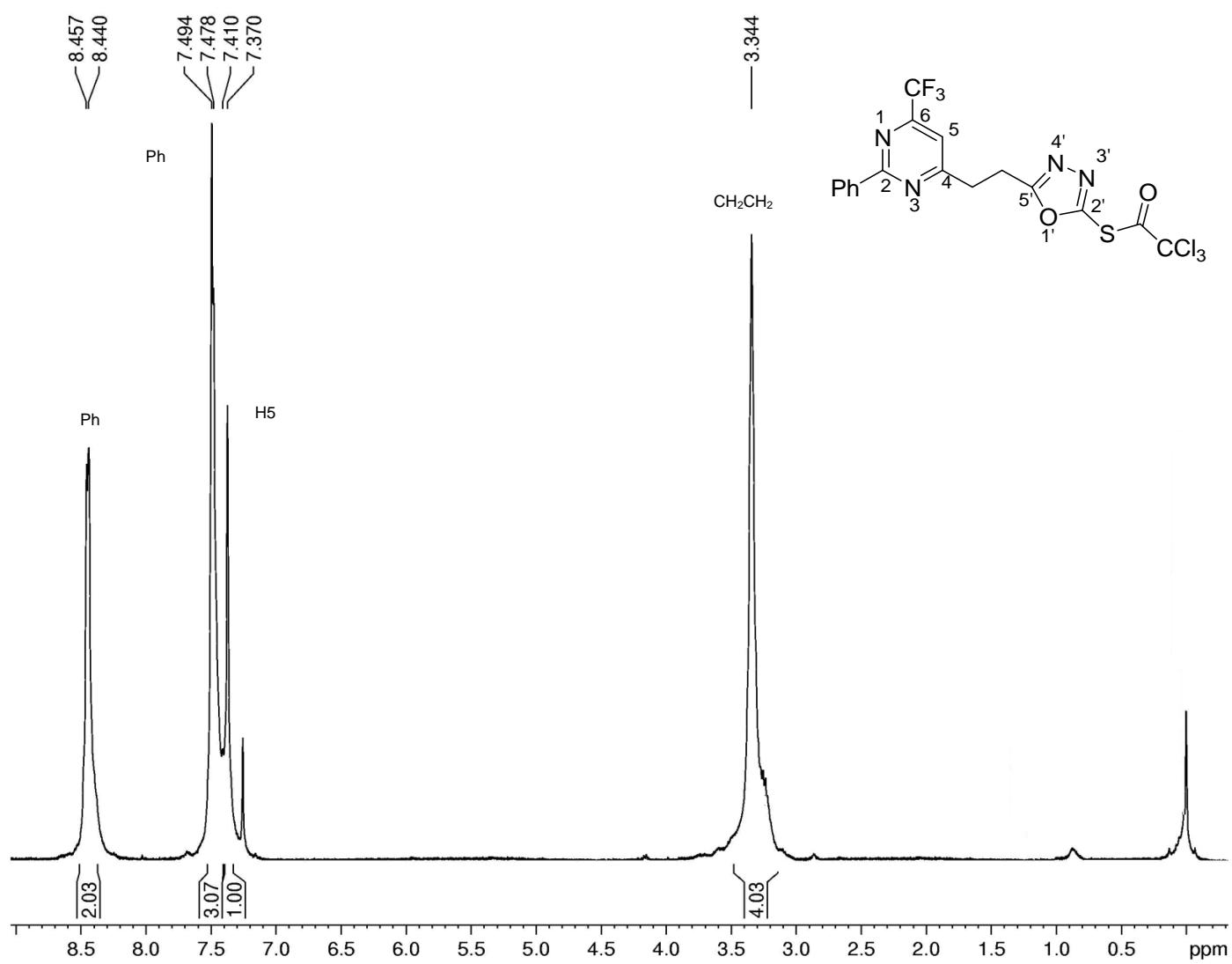


Figure S57. ^{13}C NMR spectrum (100 MHz, DMSO-*d*₆) of 5-(2-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)ethyl)-1,3,4-oxadiazol-2-thioyl ethanethioate (**9d**).



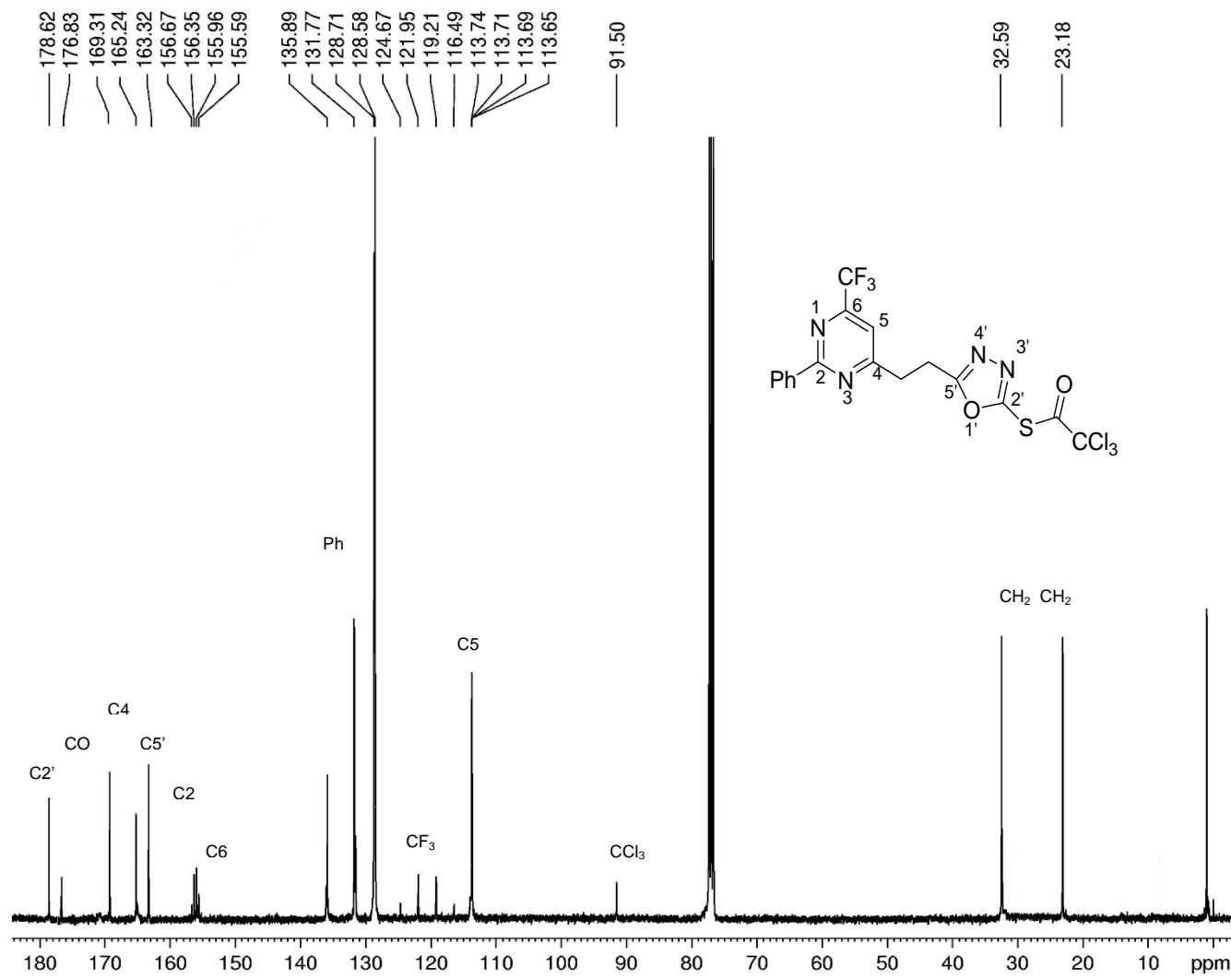
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WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

Figure S58. ¹H NMR spectrum (400 MHz, CDCl₃) of 5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl 2,2,2-trichloroethanethioate (**10b**).



Current Data Parameters
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PROCNO 2013

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DELTA 1.8999999 sec
TD0 1

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PL1 -3.00 dB
SFO1 100.6228298 MHz

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PCPD2 80.00 usec
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PL12 14.00 dB
PL13 14.00 dB
SFO2 400.1316005 MHz

F2 – Processing parameters
SI 32768
SF 100.6127716 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Figure S59. ^{13}C NMR spectrum (100 MHz, CDCl₃) of 5-(2-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl 2,2,2-trichloroethanethioate (**10b**).

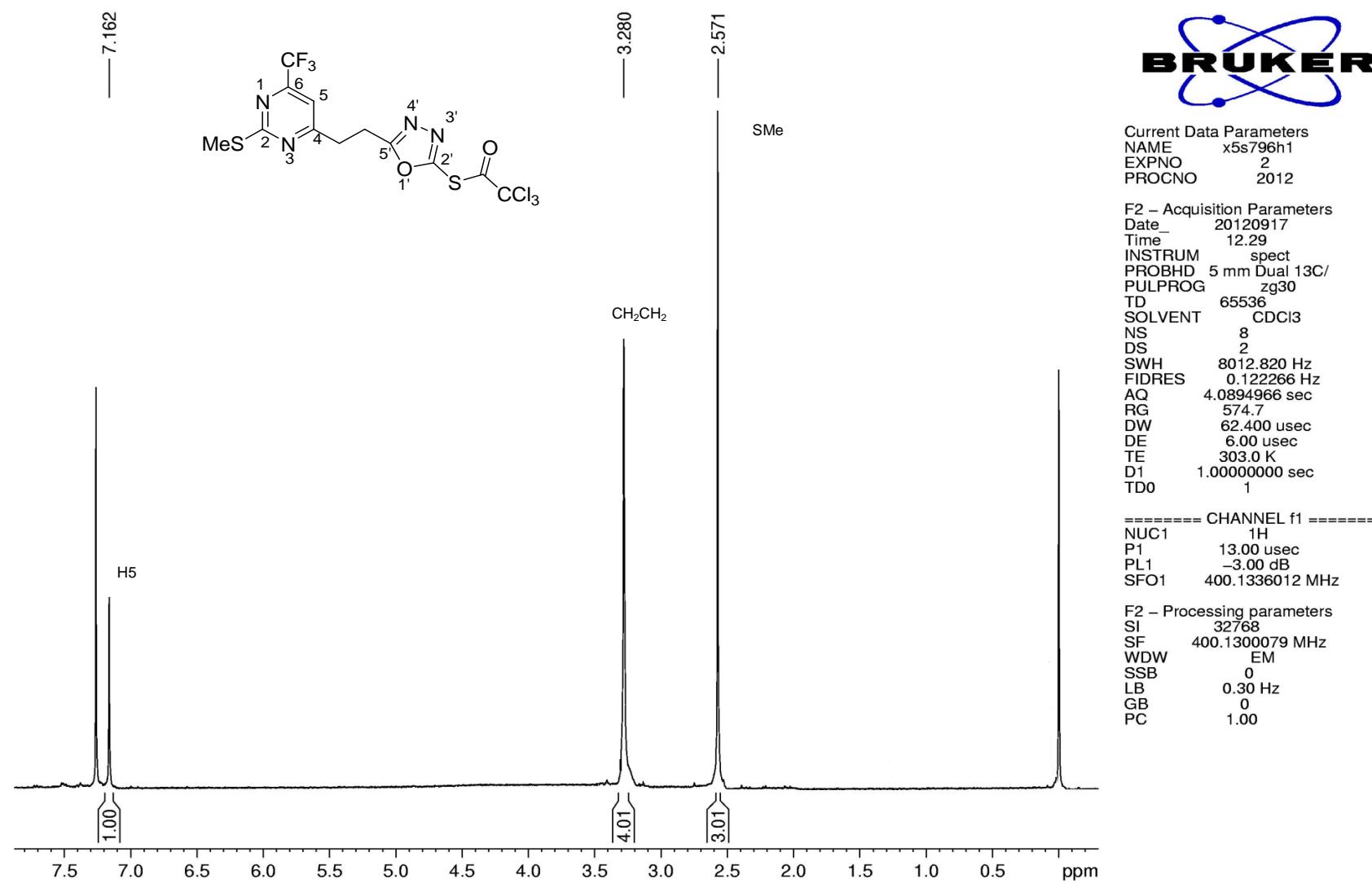


Figure S60. ^1H NMR spectrum (400 MHz, CDCl_3) of 5-(2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl 2,2,2-trichloroethanethioate (**10c**).

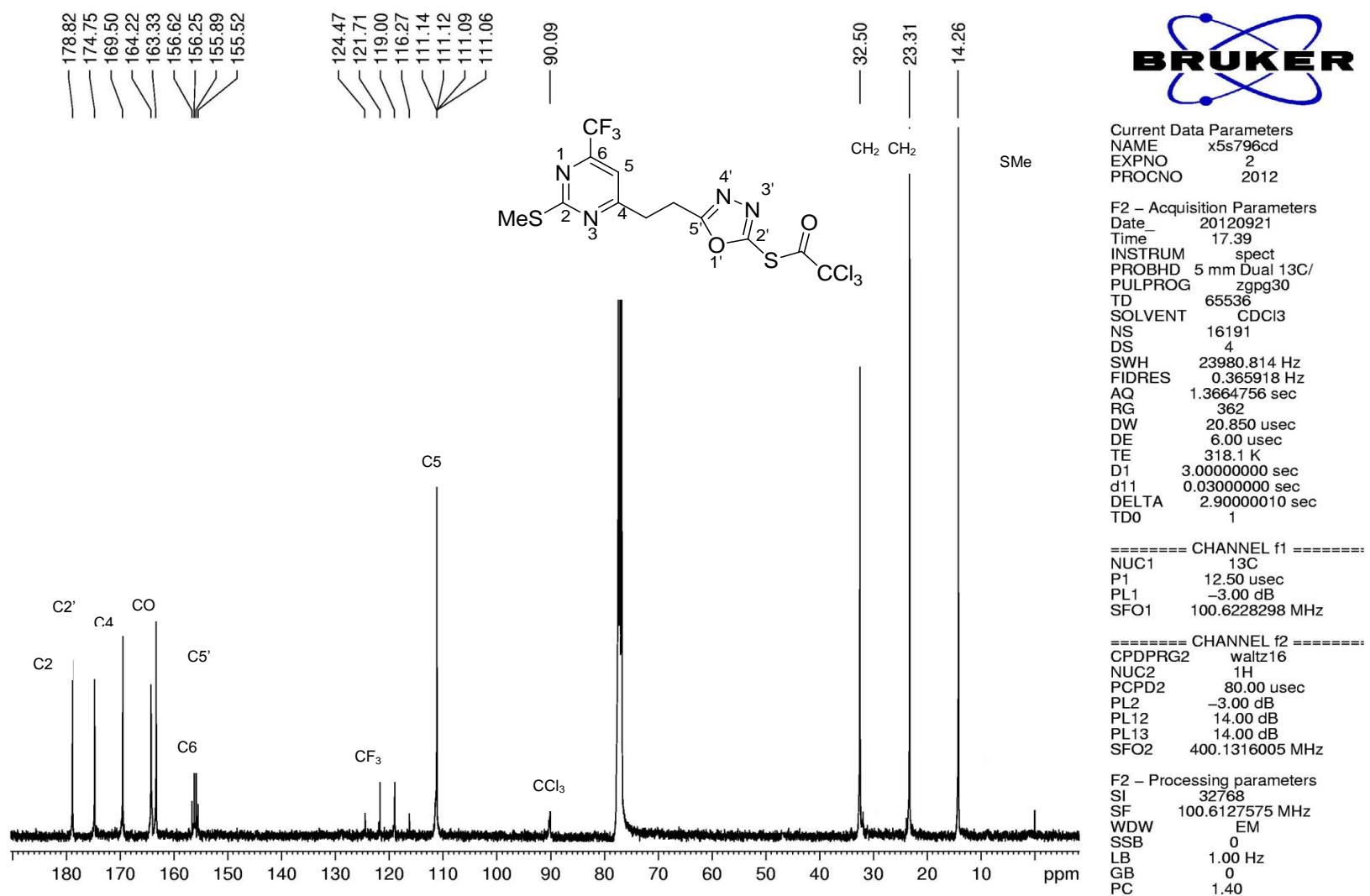


Figure S61. ^{13}C NMR spectrum (100 MHz, CDCl₃) of 5-(2-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)ethyl)-1,3,4-oxadiazol-2-thioyl 2,2,2-trichloroethanethioate (**10c**).

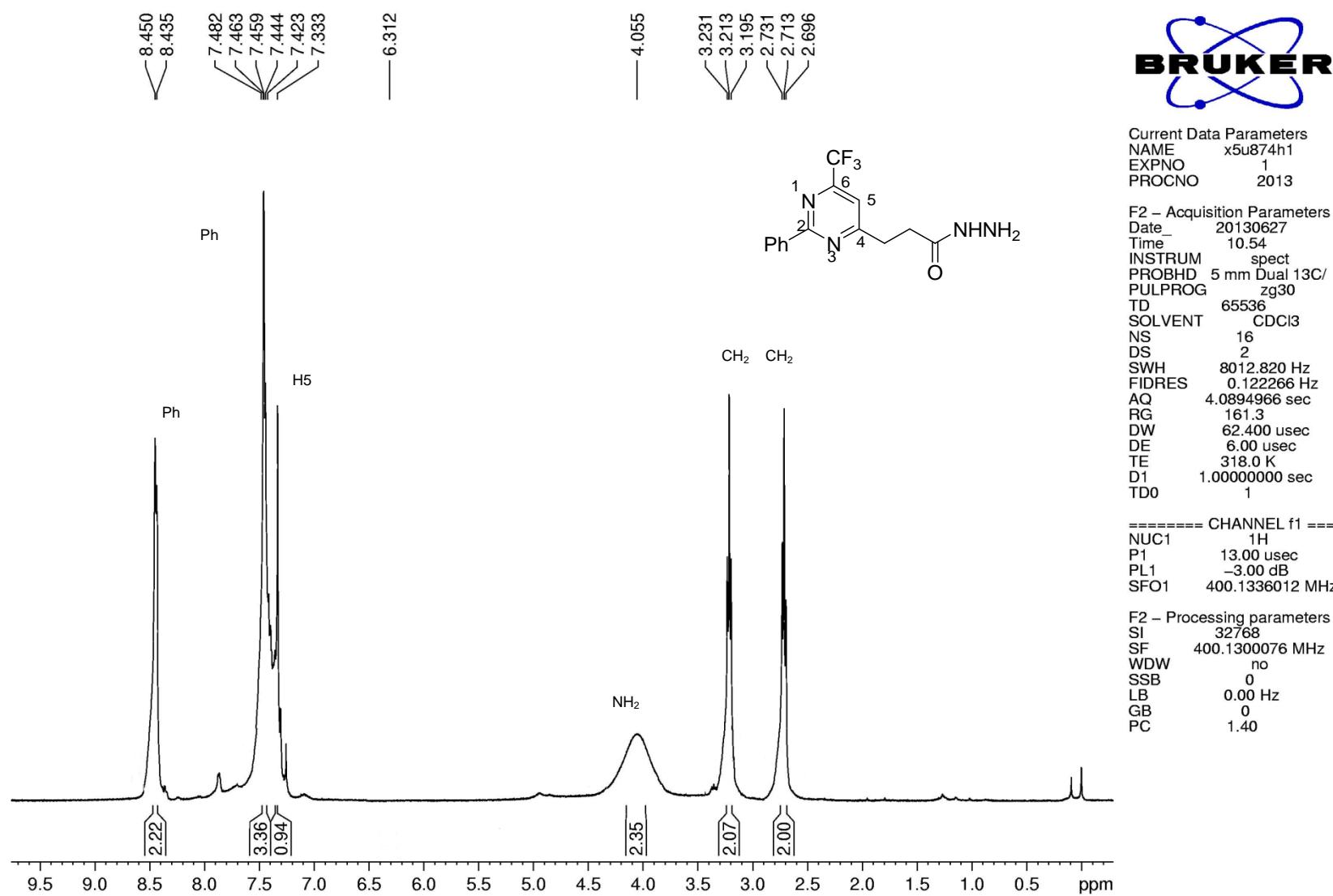


Figure S62. ¹H NMR spectrum (400 MHz, CDCl₃) of 3-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)-propanoylhydrazide **3b**.

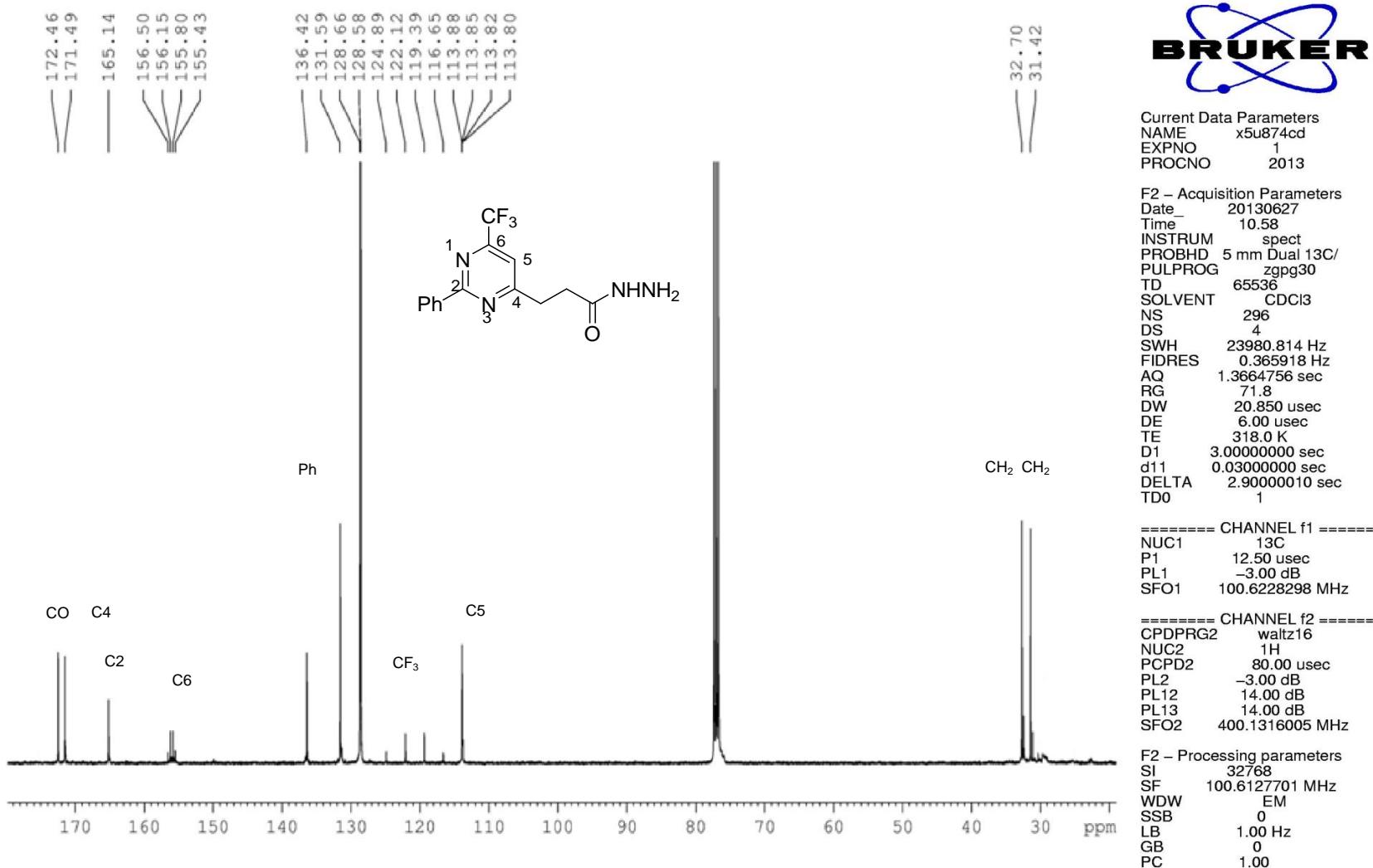


Figure S63. ¹³C NMR spectrum (100 MHz, CDCl₃) of 3-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)-propanoylhydrazide **3b**.

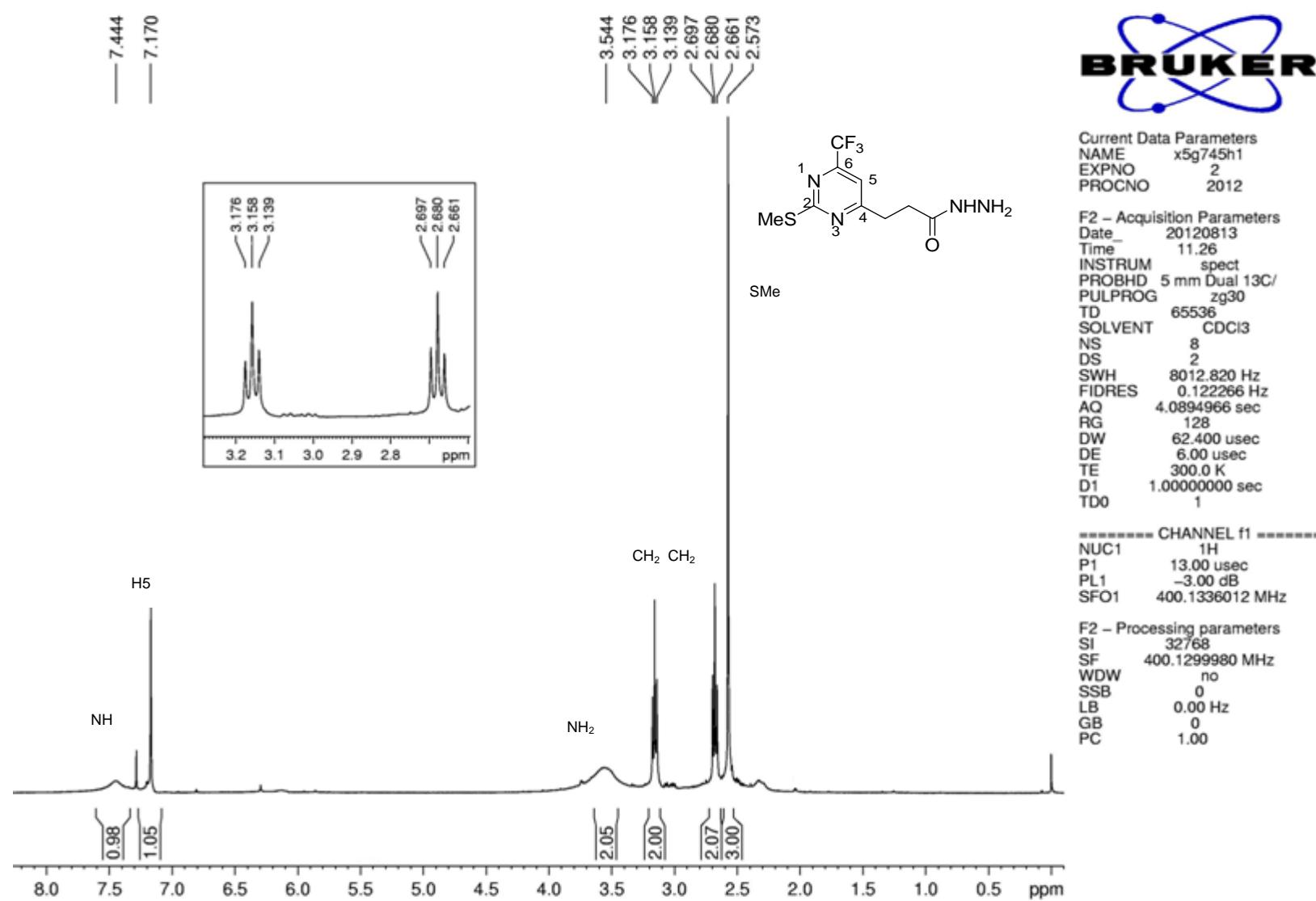


Figure S64. ¹H NMR spectrum (400 MHz, CDCl₃) of 3-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)-propanoylhydrazide **3c**.

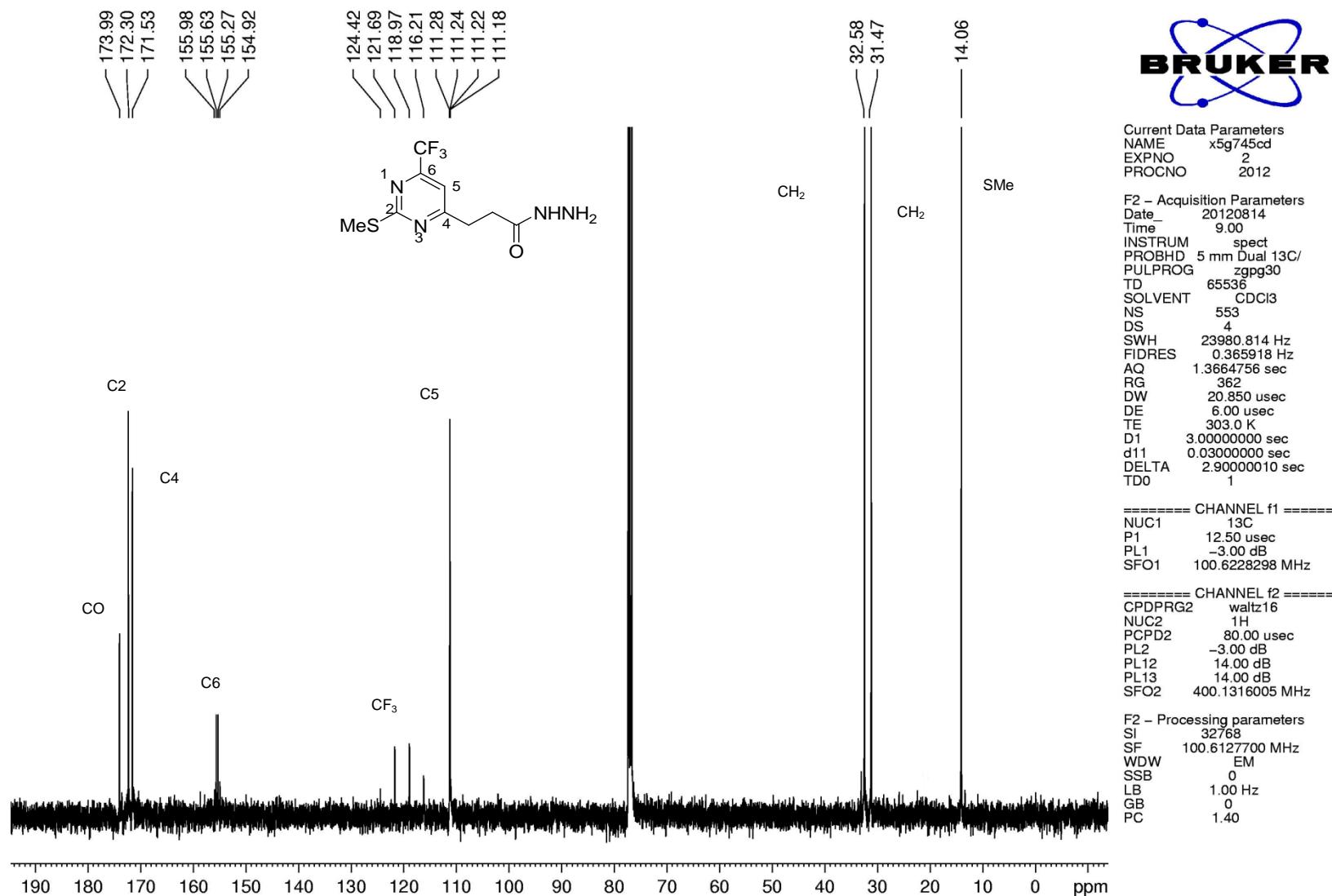


Figure S65. ¹³C NMR spectrum (100 MHz, CDCl₃) of 3-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)-propanoylhydrazide **3c**.

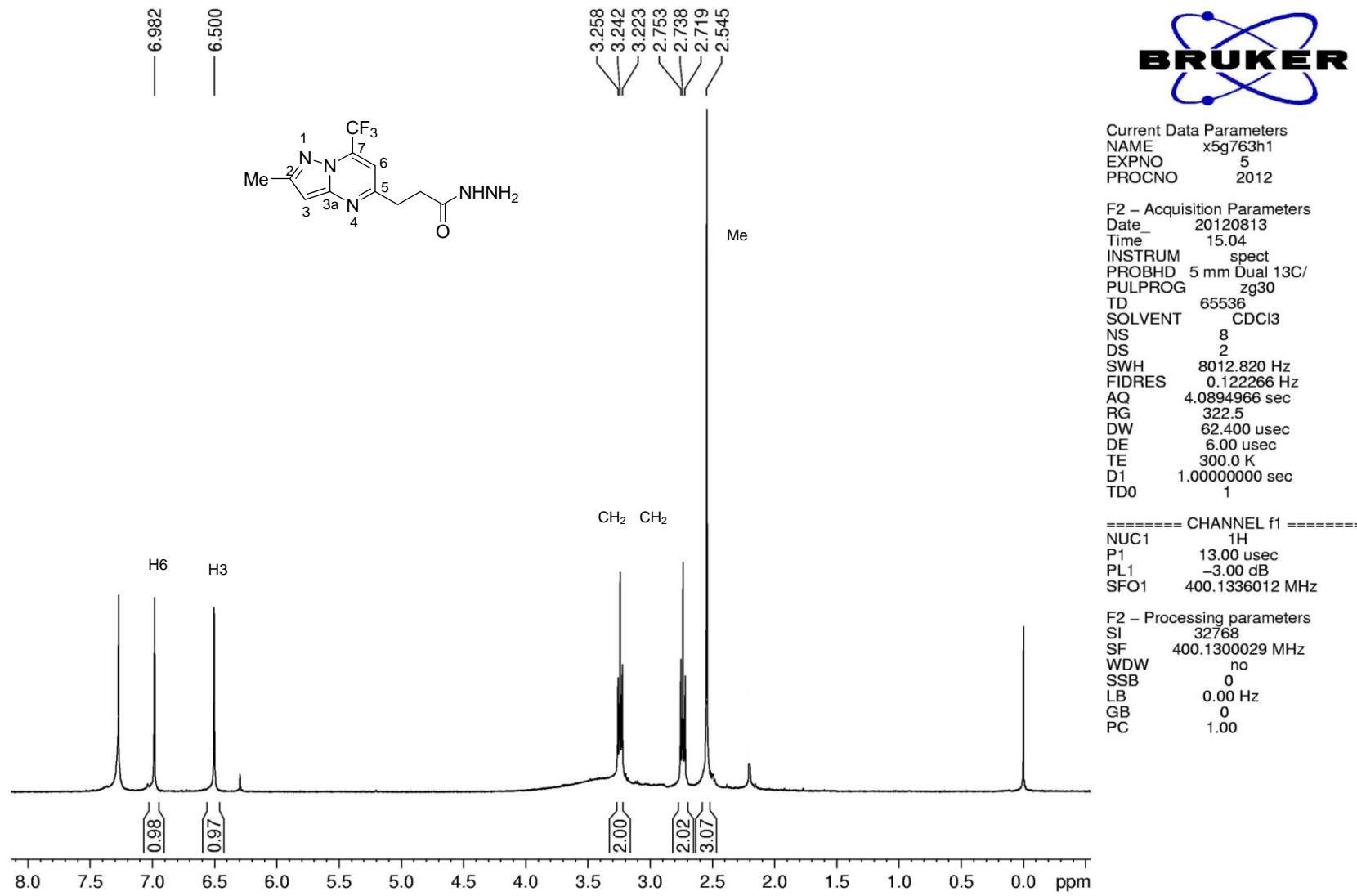
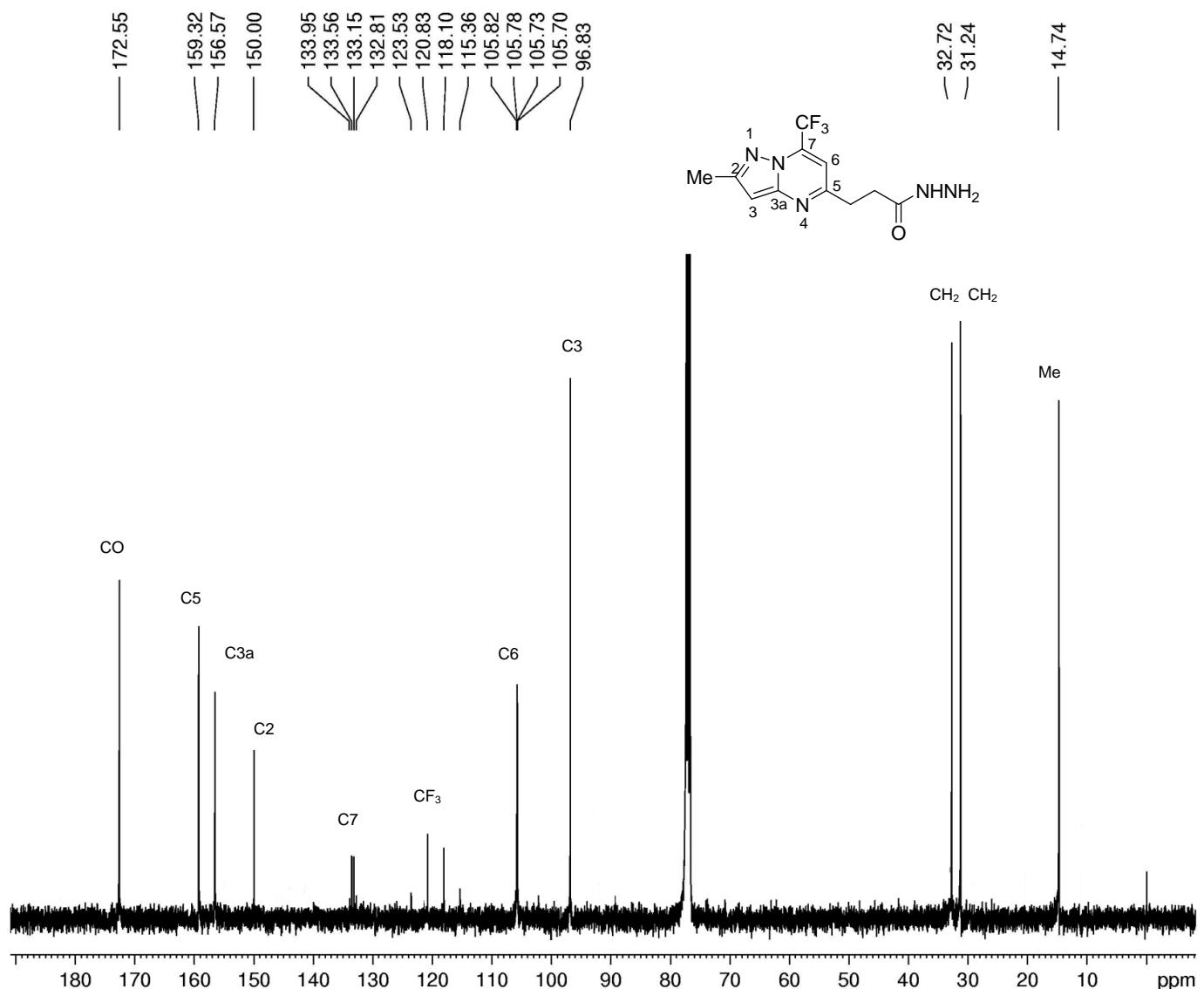


Figure S66. ^1H NMR spectrum (400 MHz, CDCl_3) 3-(2-methyl-7-trifluoromethylpirazolo[1,5-*a*]pirimidin-5-yl)propanoylhydrazide **3d**.



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PROCNO 2012

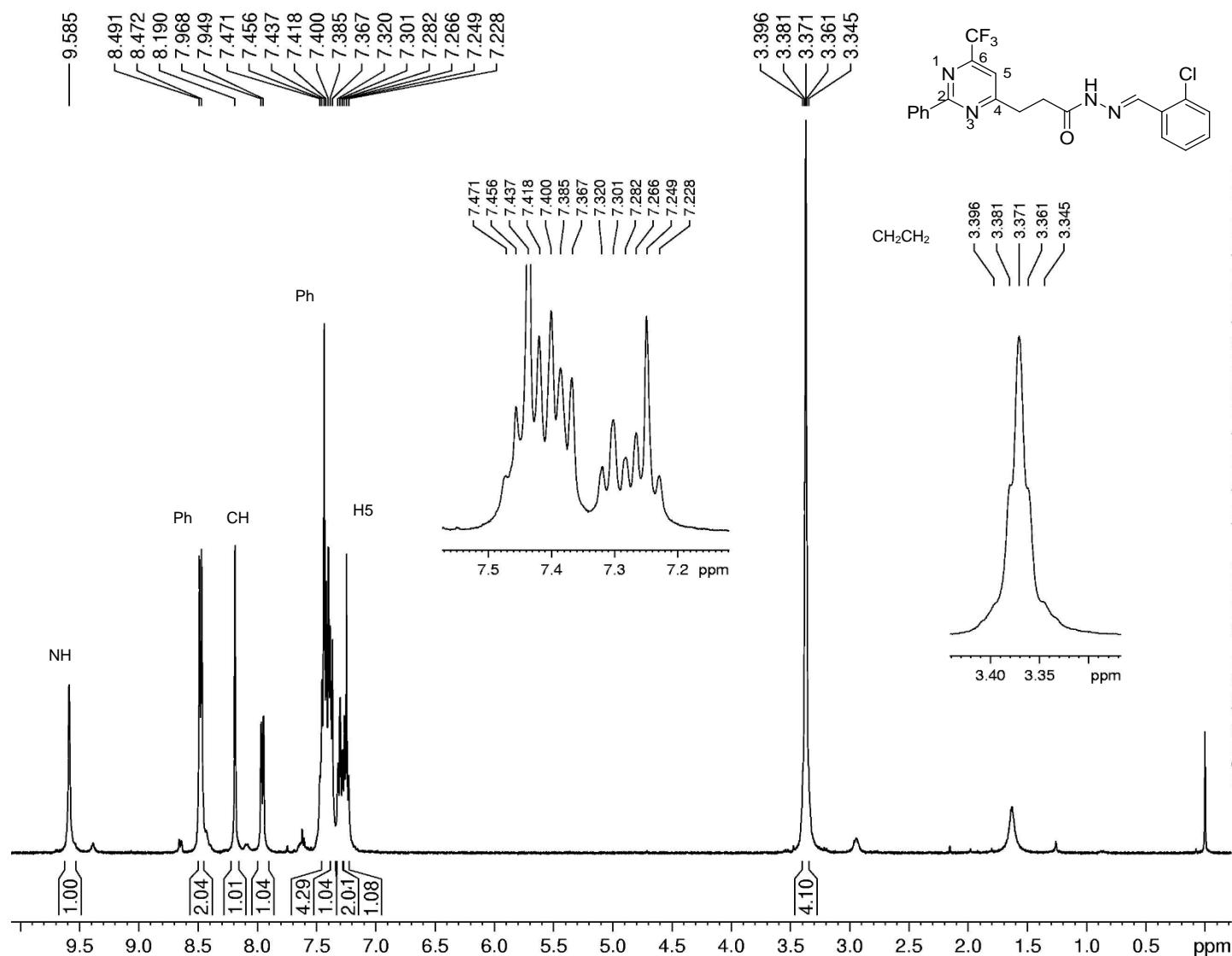
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SFO1 100.6228298 MHz

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PL13 14.00 dB
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F2 – Processing parameters
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SSB 0
LB 1.00 Hz
GB 0
PC 1.00

Figure S67. ¹³C NMR spectrum (400 MHz, CDCl₃) of 3-(2-methyl-7-trifluoromethylpyrazolo[1,5-a]pirimidin-5-yl)propanoylhydrazide 3d.



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PROCNO 2013

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DE 6.00 usec
TE 308.0 K
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TD0 1

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SFO1 400.1336012 MHz

F2 – Processing parameters
SI 32768
SF 400.1300122 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

Figure S68. ^1H NMR spectrum (400 MHz, CDCl_3) of *N*'-(2-chlorobenzylidene)-3-(2-phenyl-6-(trifluoromethyl)pyrimidin-4-yl)propanehydrazide **12b**.

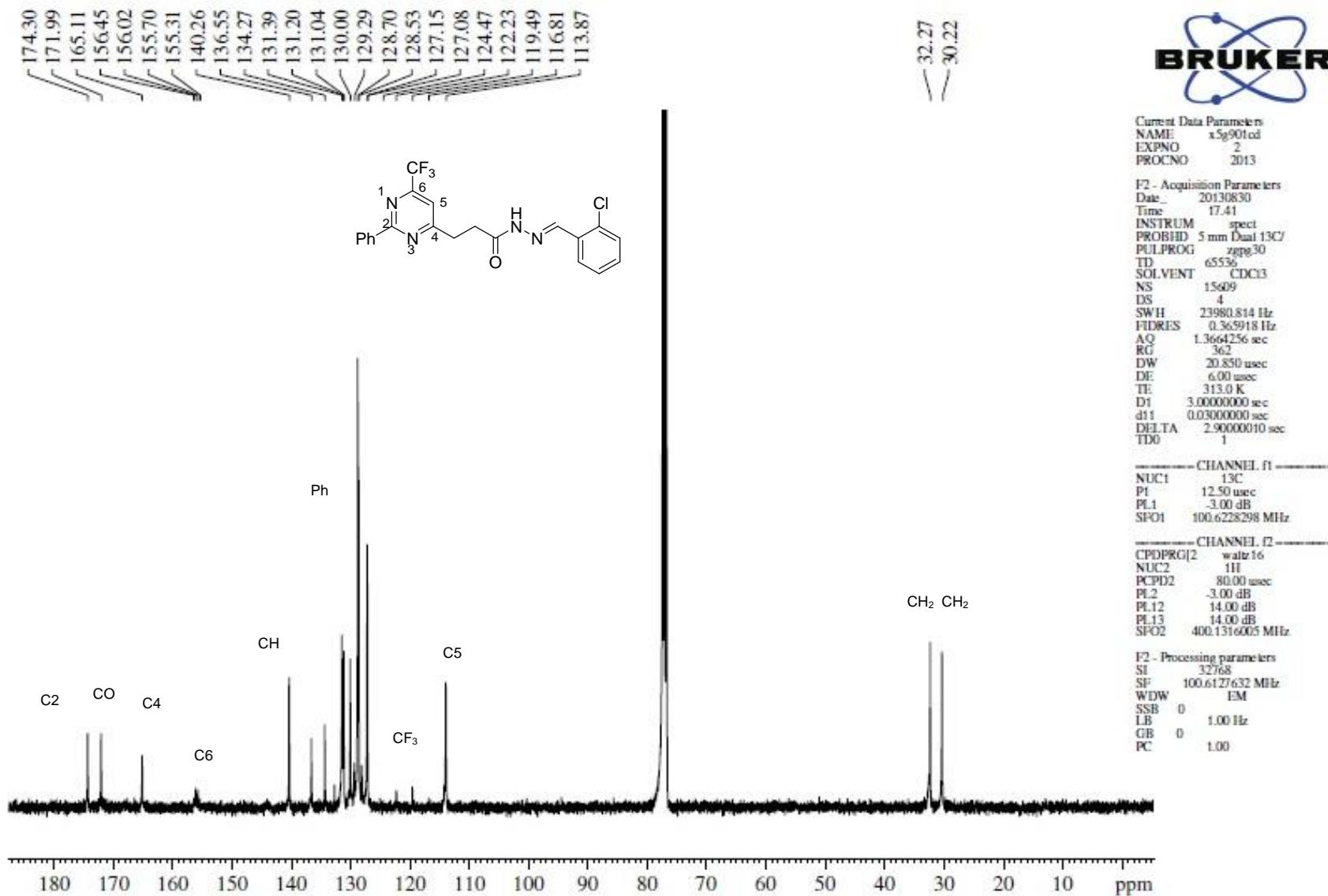


Figure S69. ^{13}C NMR spectrum (400 MHz, CDCl_3) of N' -(2-chlorobenzylidene)-3-(2-phenyl-6-(trifluoromethyl)pyrimidin-4-yl)propanehydrazide **12b**.

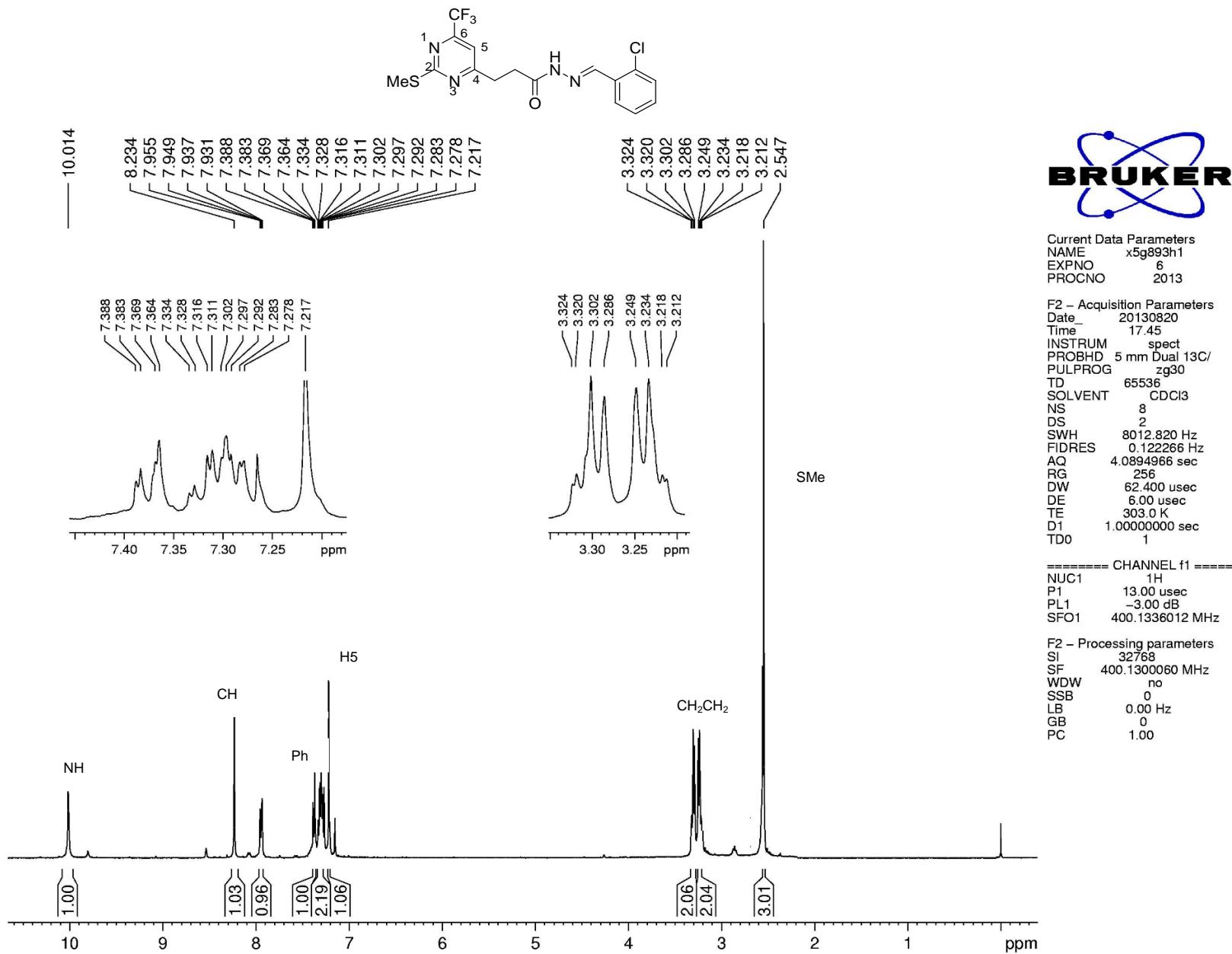
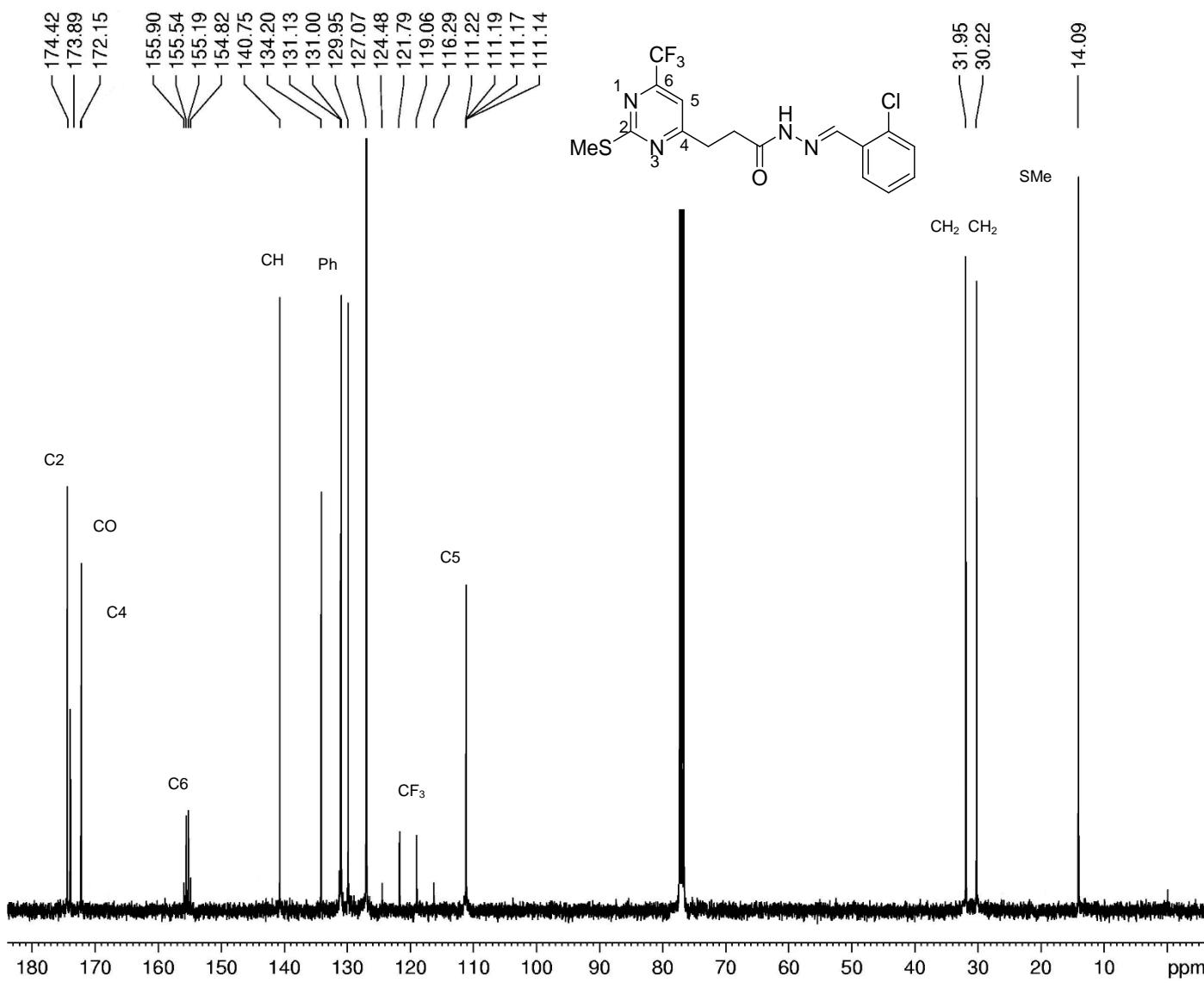


Figure S70. ¹H NMR spectrum (400 MHz, CDCl₃) of N'-(2-chlorobenzylidene)-3-(2-thiomethyl-6-(trifluoromethyl)pyrimidin-4-yl)propanehydrazide **12b**.



Current Data Parameters
NAME x5g893cd
EXPNO 6
PROCNO 2013

F2 – Acquisition Parameters
Date_ 20130820
Time 17.47
INSTRUM spect
PROBHD 5 mm Dual 13C/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1175
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 362
DW 20.850 usec
DE 6.00 usec
TE 303.0 K
D1 3.0000000 sec
d11 0.03000000 sec
DELTA 2.90000010 sec
TD0 1

===== CHANNEL f1 =====
NUC1 13C
P1 12.50 usec
PL1 -3.00 dB
SFO1 100.6228298 MHz

===== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 14.00 dB
PL13 14.00 dB
SFO2 400.1316005 MHz

F2 – Processing parameters
SI 32768
SF 100.6127728 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00

Figure S71. ^{13}C NMR spectrum (400 MHz, CDCl_3) of N' -(2-chlorobenzylidene)-3-(2-thiomethyl-6-(trifluoromethyl)pyrimidin-4-yl)propanehydrazide **12b**.

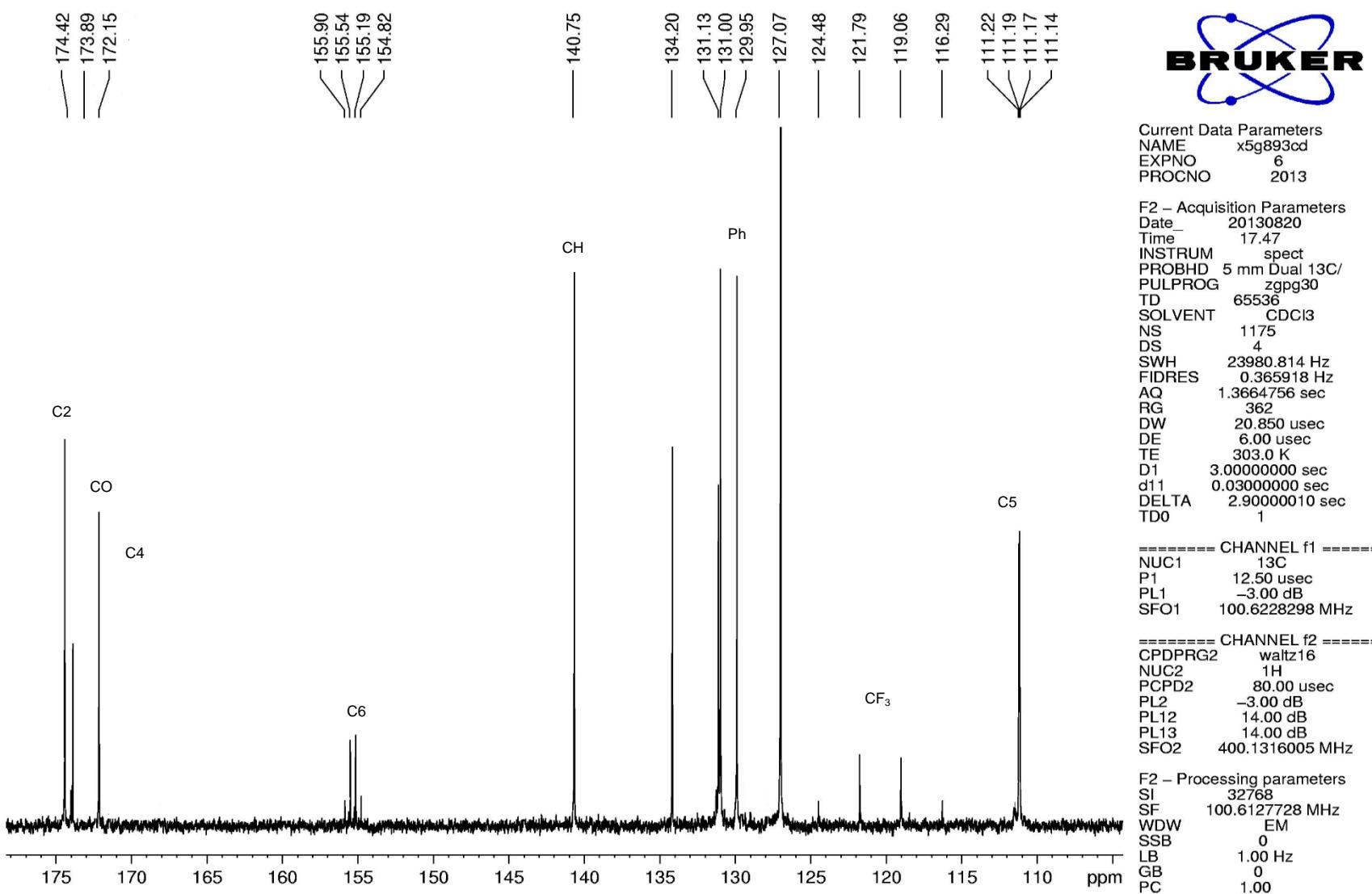


Figure S72. ¹³C NMR spectrum (400 MHz, CDCl₃) of *N'*-(2-chlorobenzylidene)-3-(2-thiomethyl-6-(trifluoromethyl)pyrimidin-4-yl)propanehydrazide **12b**, expanded between 105–180 ppm.

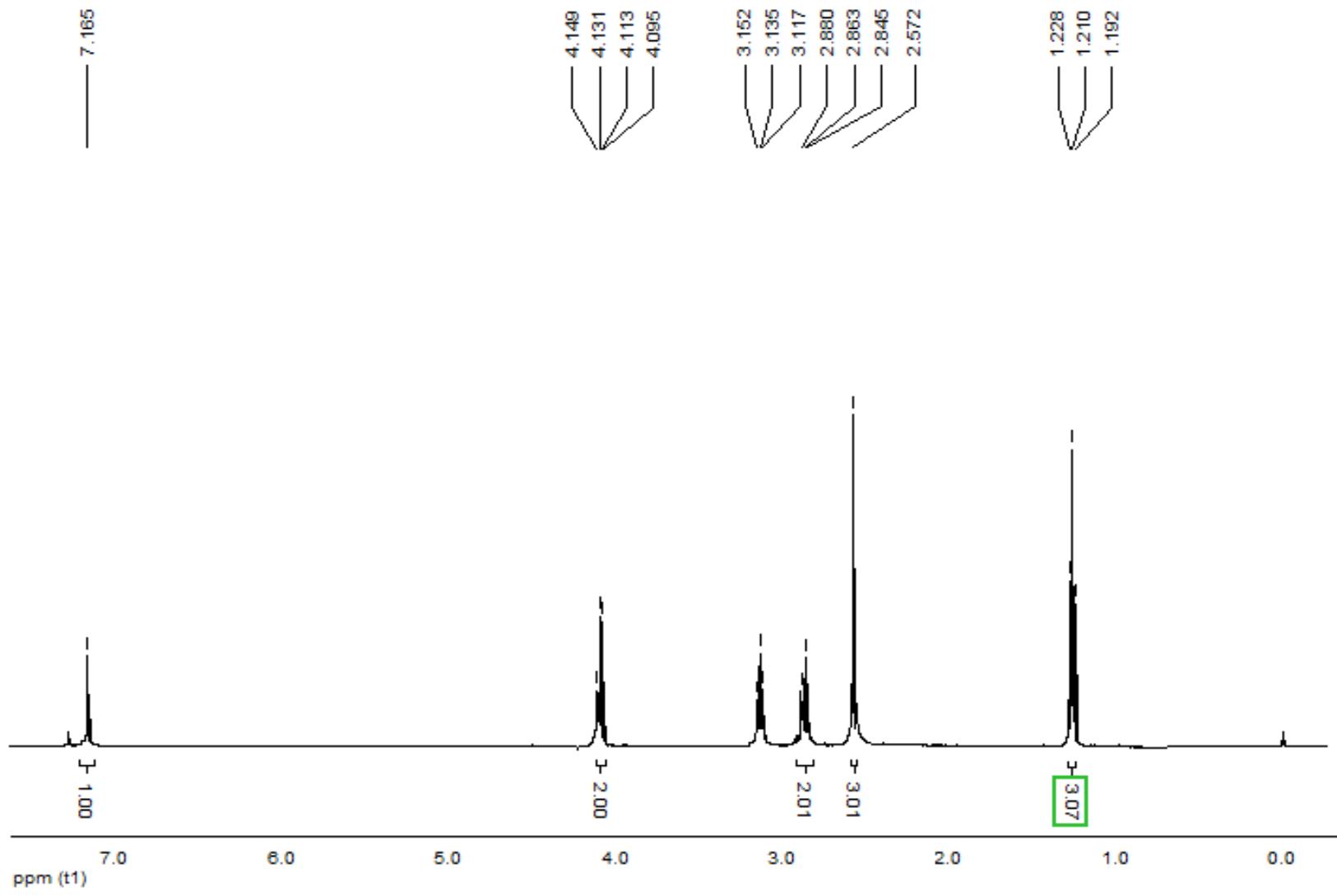


Figure S73. ^1H NMR spectrum (400 MHz, CDCl_3) of ethyl 3-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)propanoate **13c**.

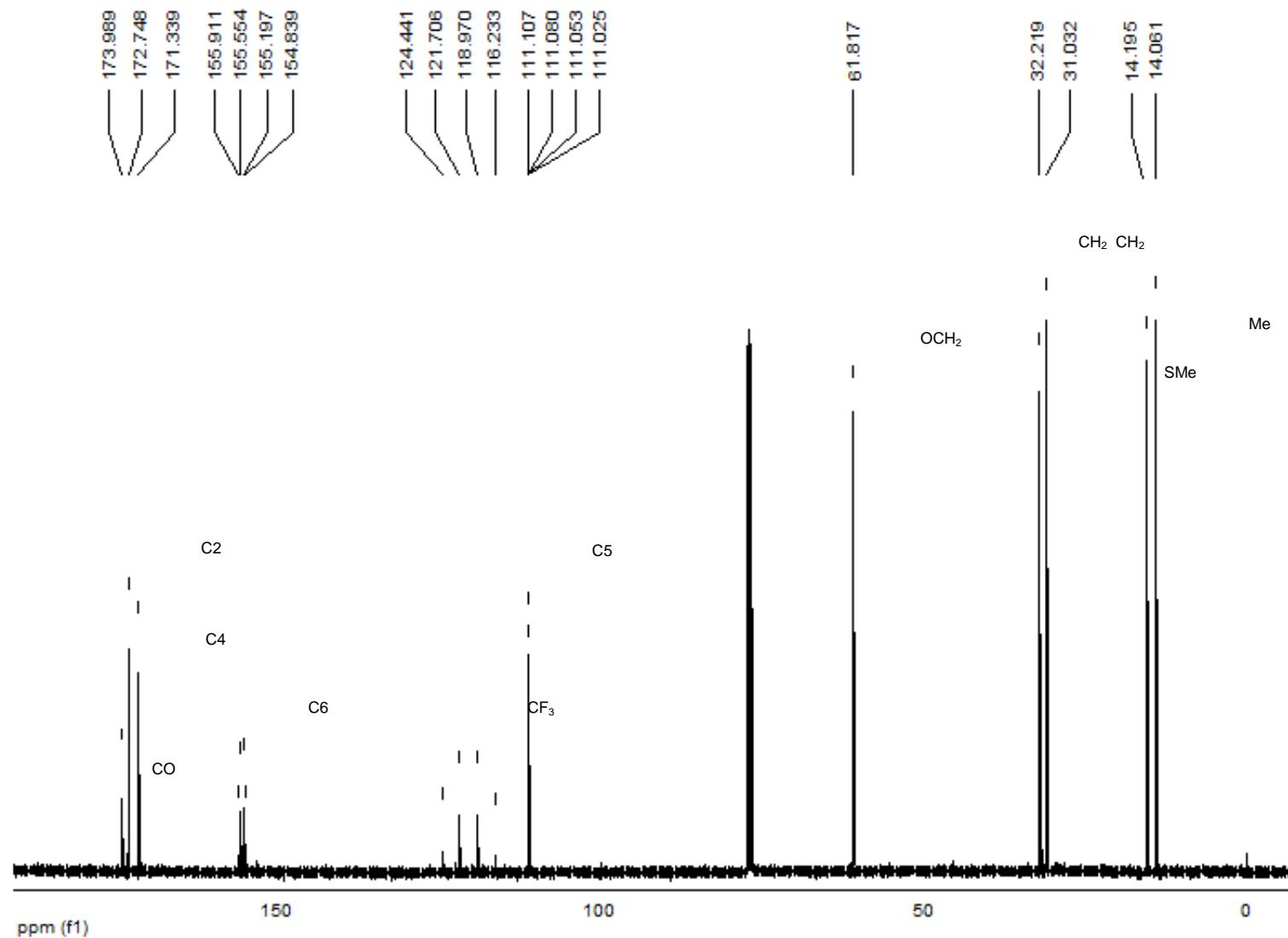


Figure S74. ¹³C NMR spectrum (400 MHz, CDCl₃) of ethyl 3-(2-thiomethyl-6-trifluoromethylpyrimidin-4-yl)propanoate **13c**.

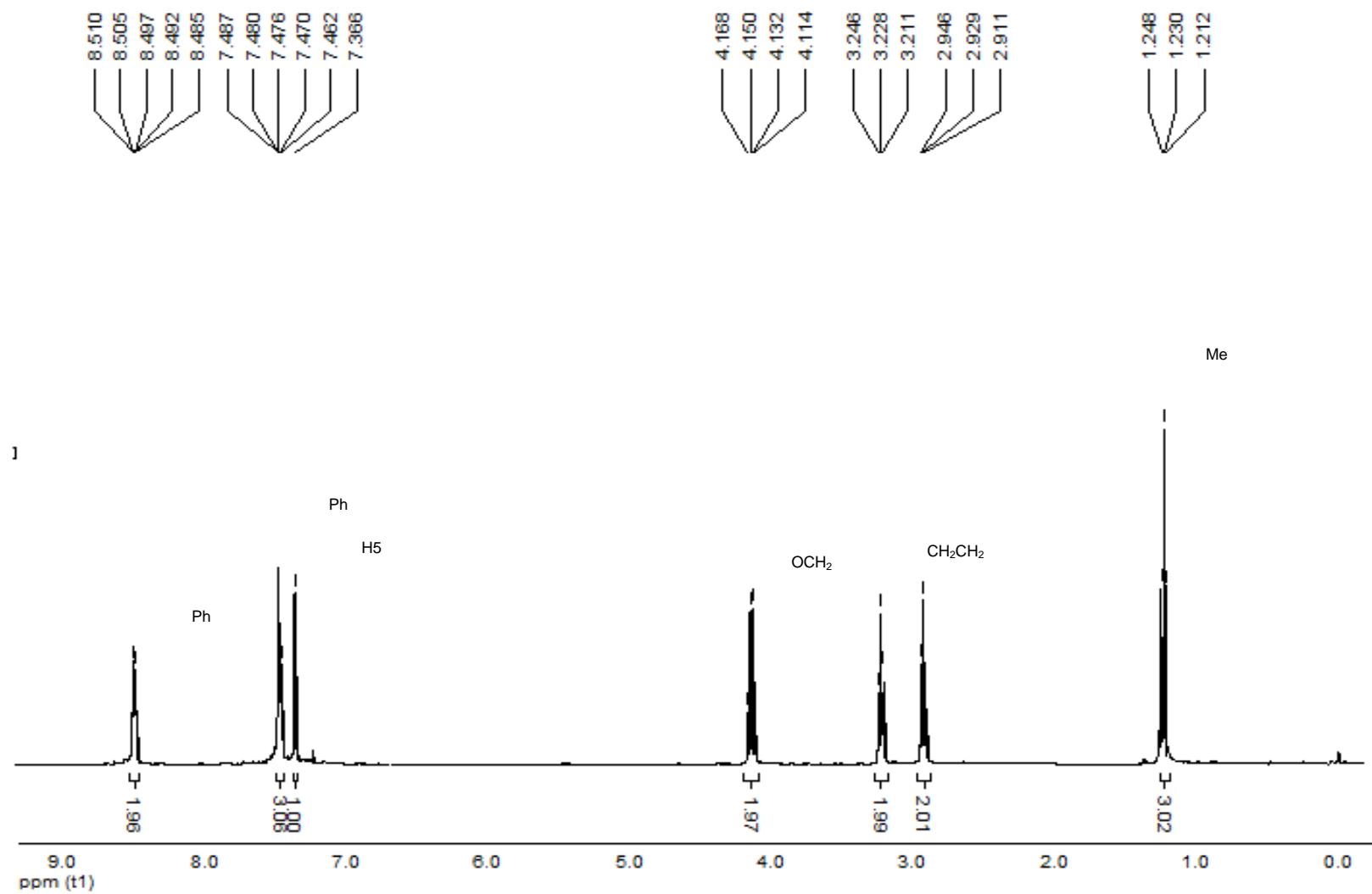


Figure S75. ^1H NMR spectrum (400 MHz, CDCl_3) of ethyl 3-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)propanoate **13b**.

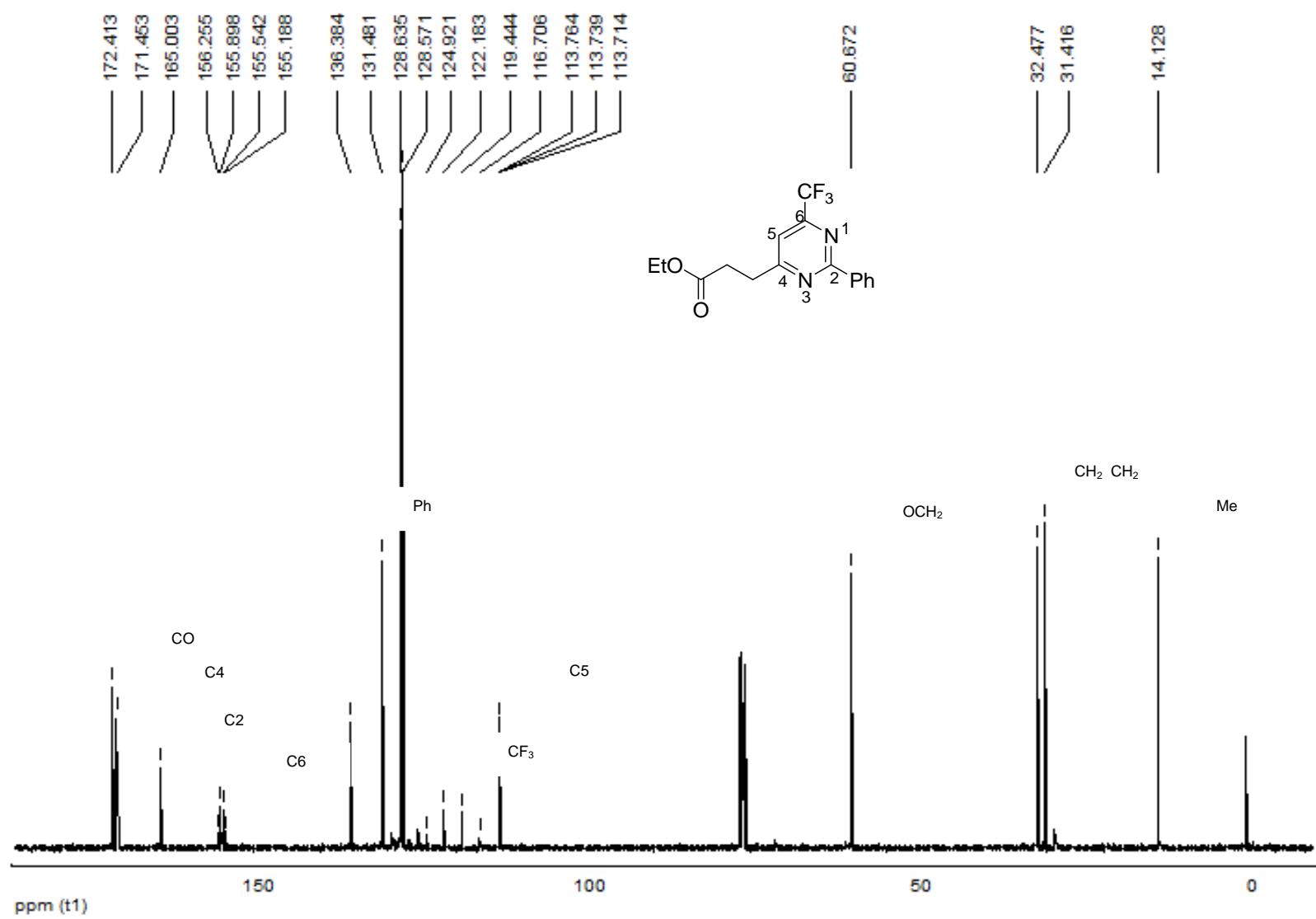


Figure S76. ^{13}C NMR spectrum (400 MHz, CDCl_3) of ethyl 3-(2-phenyl-6-trifluoromethylpyrimidin-4-yl)propanoate **13b**.

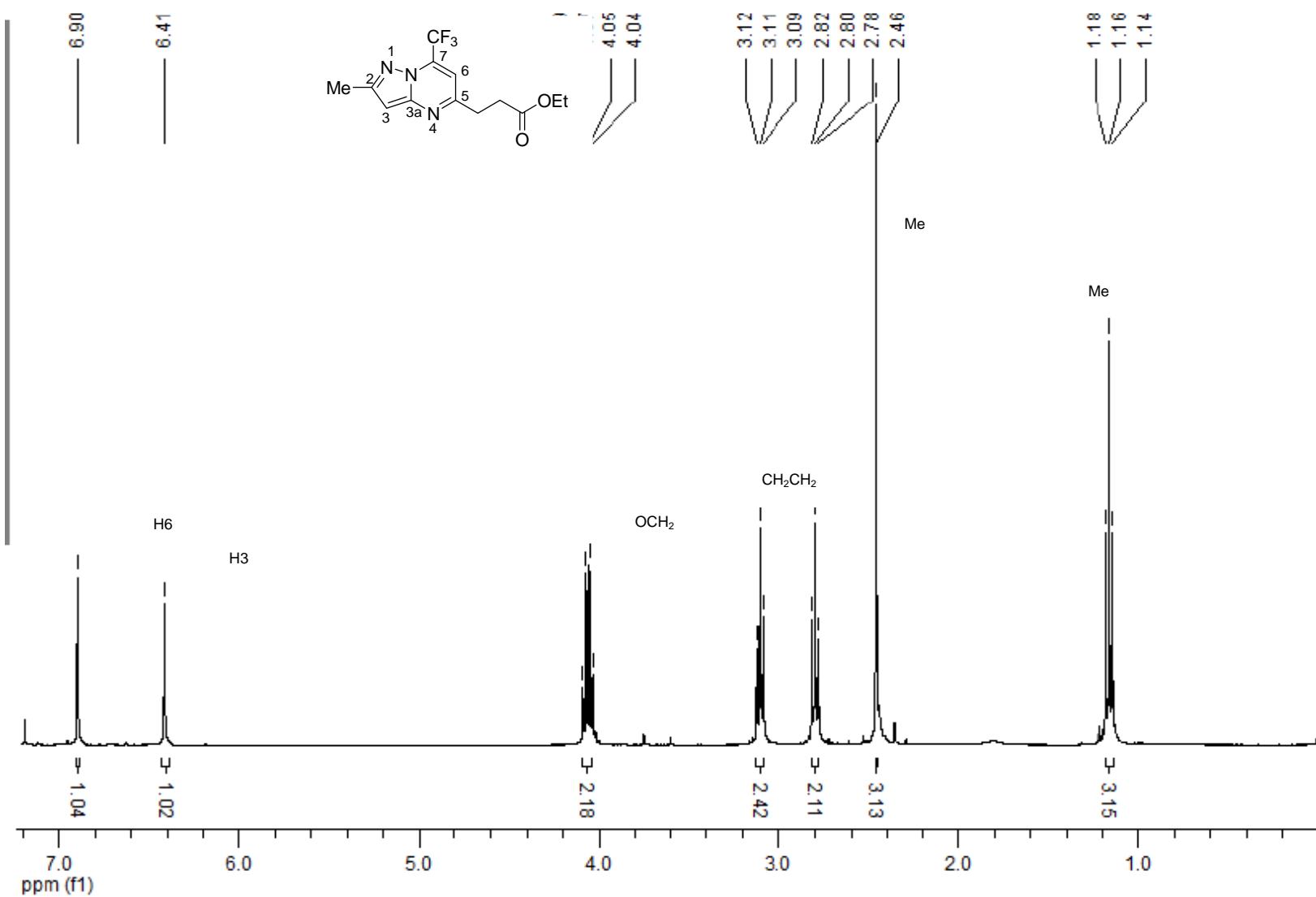


Figure S77. ¹H NMR spectrum (400 MHz, CDCl₃) of ethyl 3-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)-propanoate **13d**.

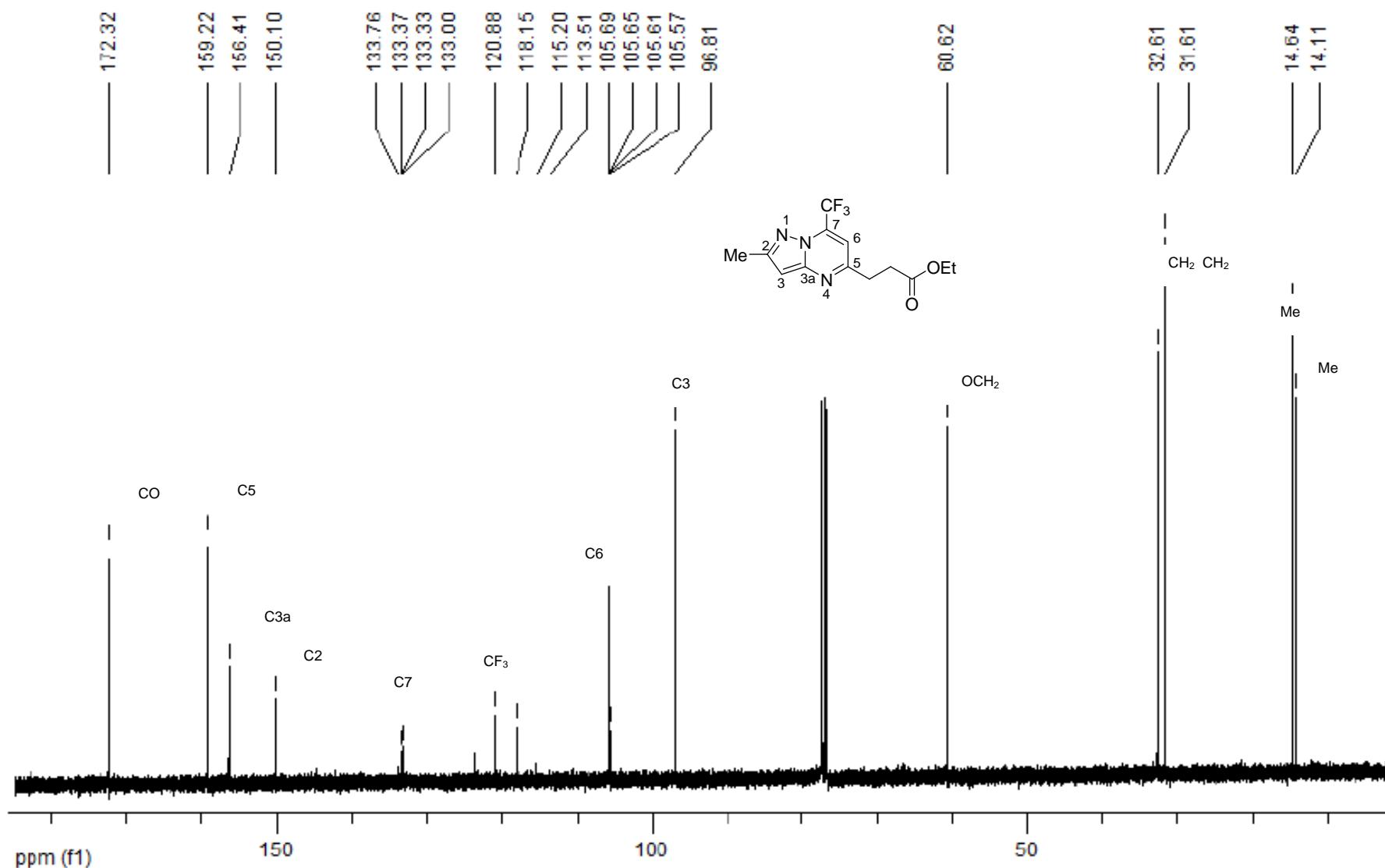


Figure S78. ^{13}C NMR spectrum (400 MHz, CDCl_3) of ethyl 3-(2-methyl-7-trifluoromethylpyrazolo[1,5-*a*]pyrimidin-5-yl)-propanoate **13d**.