

Leveraging the 3-Chloro-4-fluorophenyl Motif to Identify Inhibitors of Tyrosinase from *Agaricus bisporus*

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Figures S1-S38: ¹H-NMR and ¹³C-NMR spectra of synthesized compounds.....S2

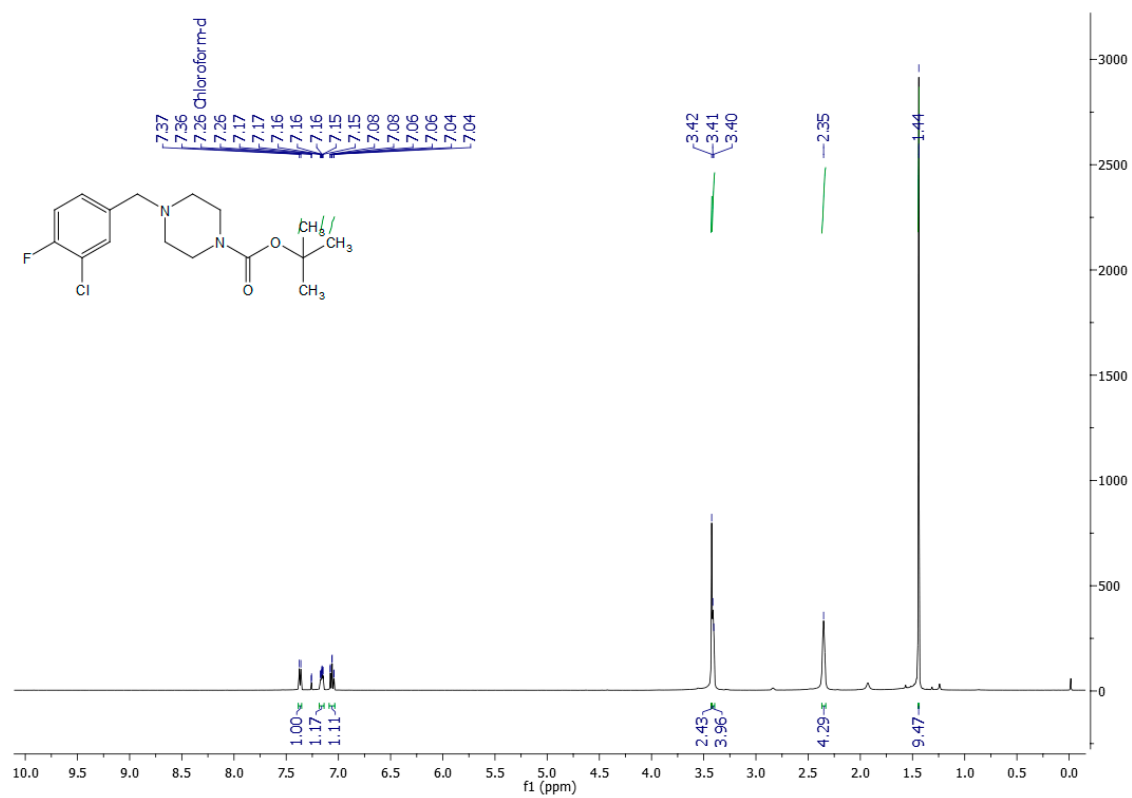


Figure S1: ¹H-NMR (CDCl₃) spectrum of *tert*-Butyl 4-[(3-chloro-4-fluorophenyl)methyl]piperazine-1-carboxylate

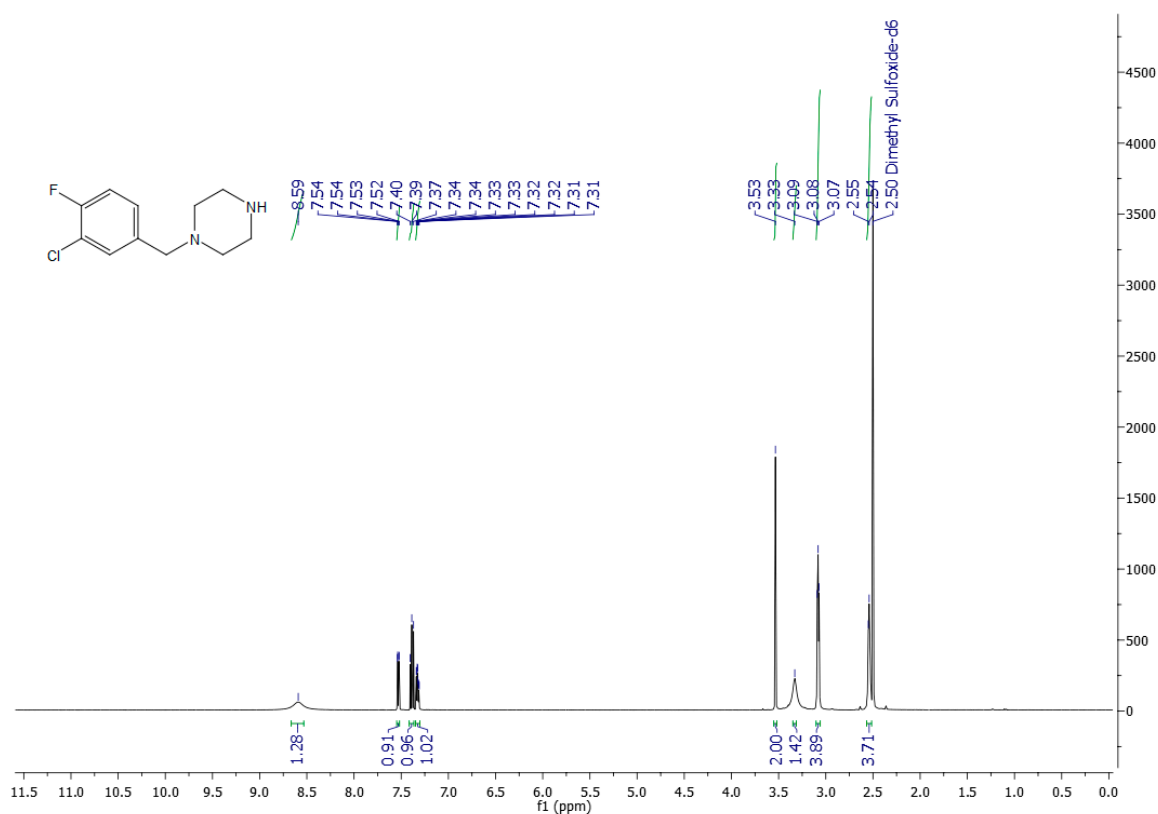


Figure S2: ¹H-NMR (DMSO-d₆) spectrum of 1-[(3-chloro-4-fluorophenyl)methyl]piperazine (**6**)

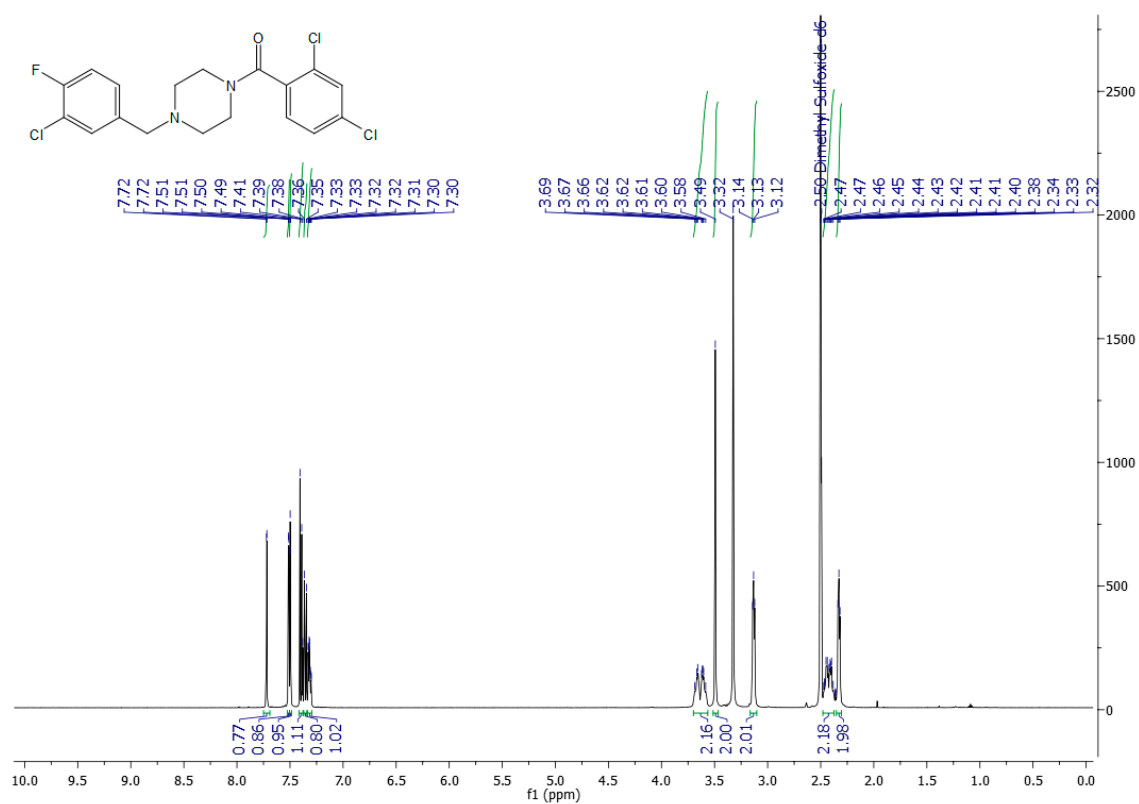


Figure S3: ¹H-NMR (DMSO-d₆) spectrum of (4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)(2,4-dichlorophenyl)methanone (**1d**)

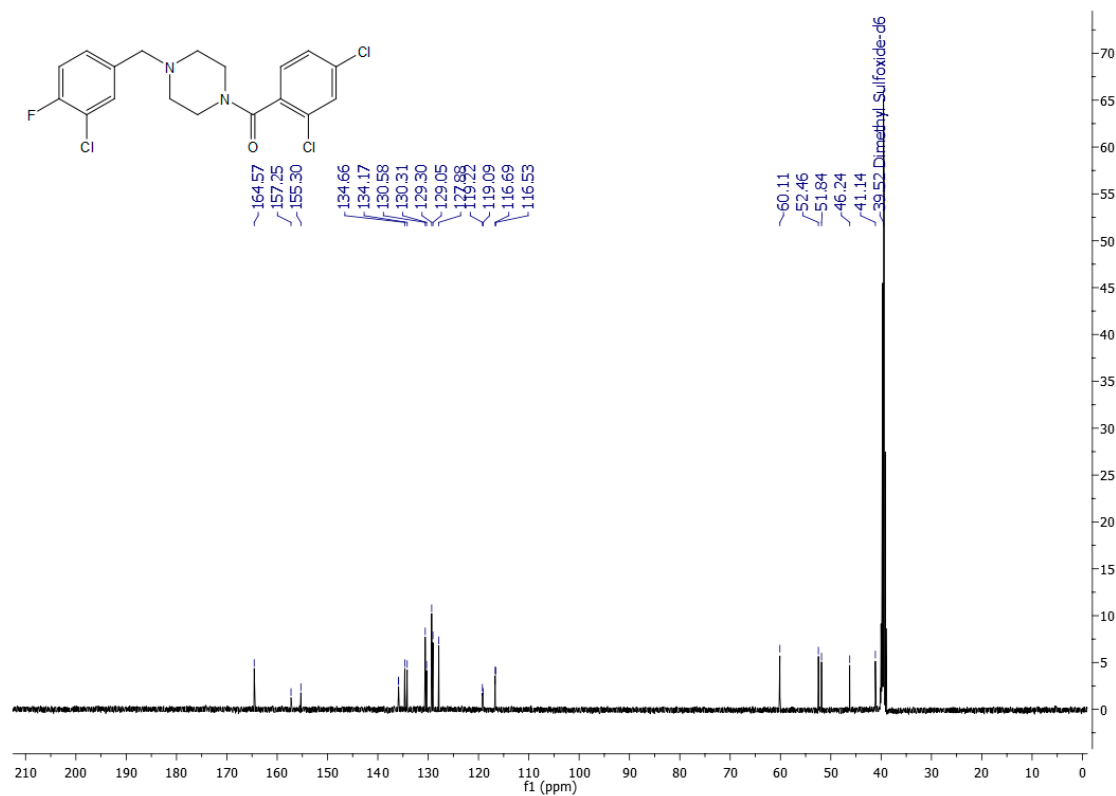


Figure S4: ¹³C-NMR (DMSO-d₆) spectrum of (4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)(2,4-dichlorophenyl)methanone (**1d**)

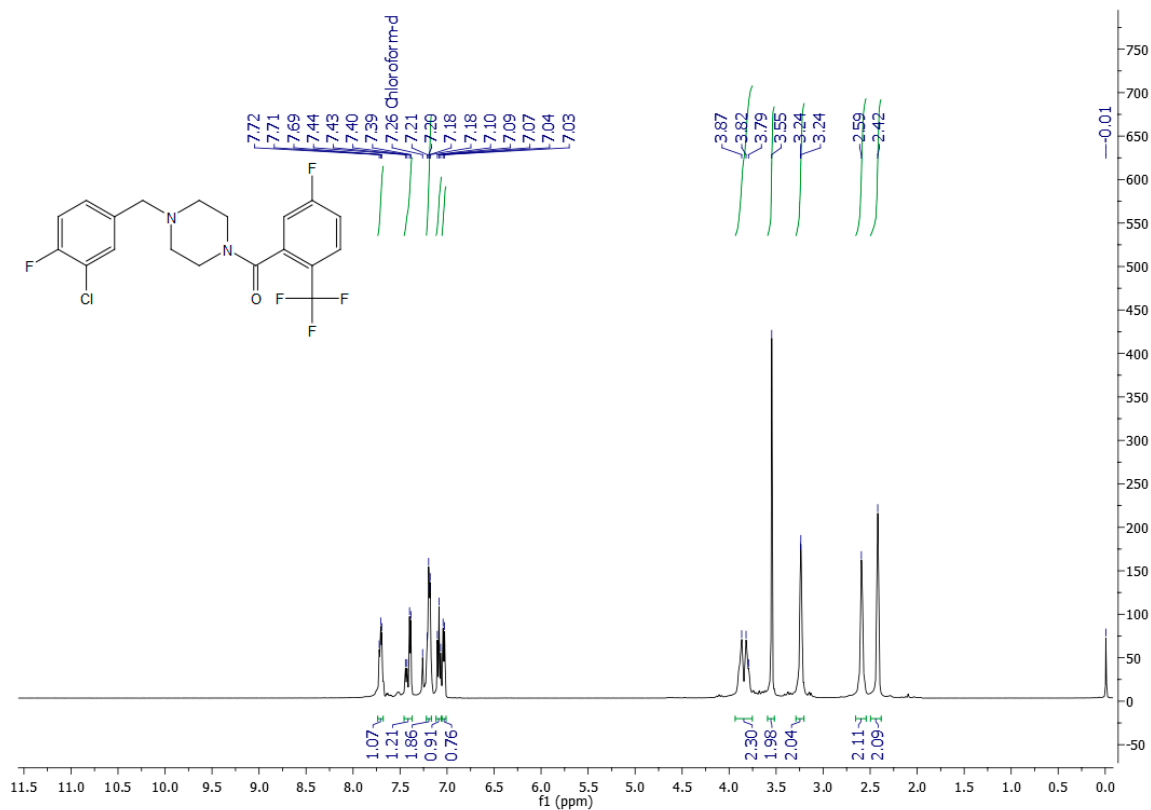


Figure S5: ¹H-NMR (CDCl₃) spectrum of (4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)(5-fluoro-2-(trifluoromethyl)phenyl)methanone (**1e**)

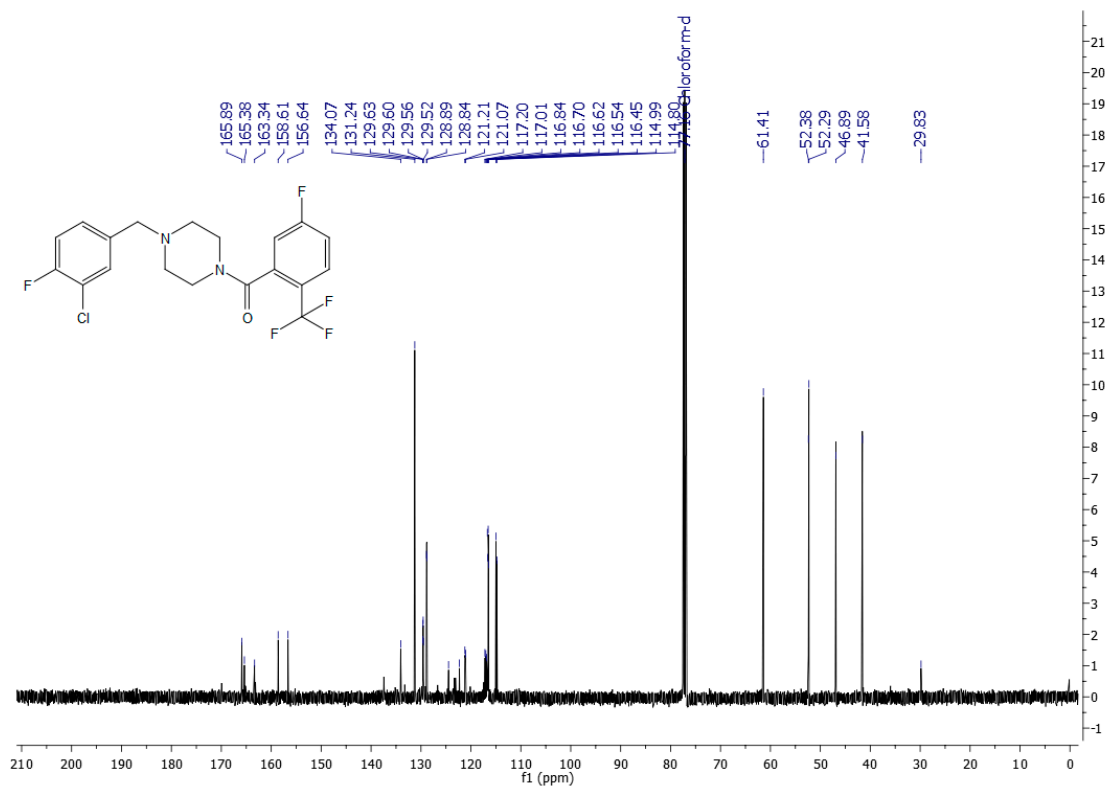


Figure S6: ^{13}C -NMR (CDCl_3) spectrum of (4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)(5-fluoro-2-(trifluoromethyl)phenyl)methanone (**1e**)

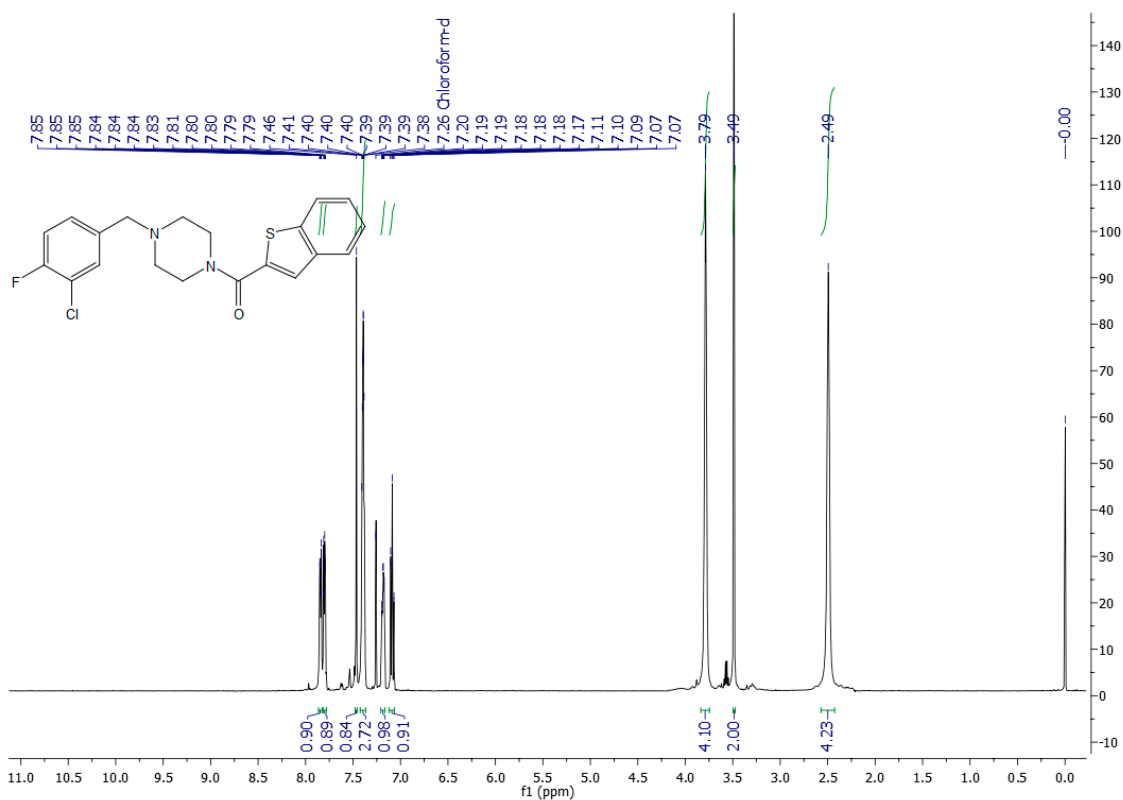


Figure S7: ^1H -NMR (CDCl_3) spectrum of Benzo[*b*]thiophen-2-yl(4-(3-chloro-4-fluorobenzyl)piperazin-1-yl)methanone (**1f**)

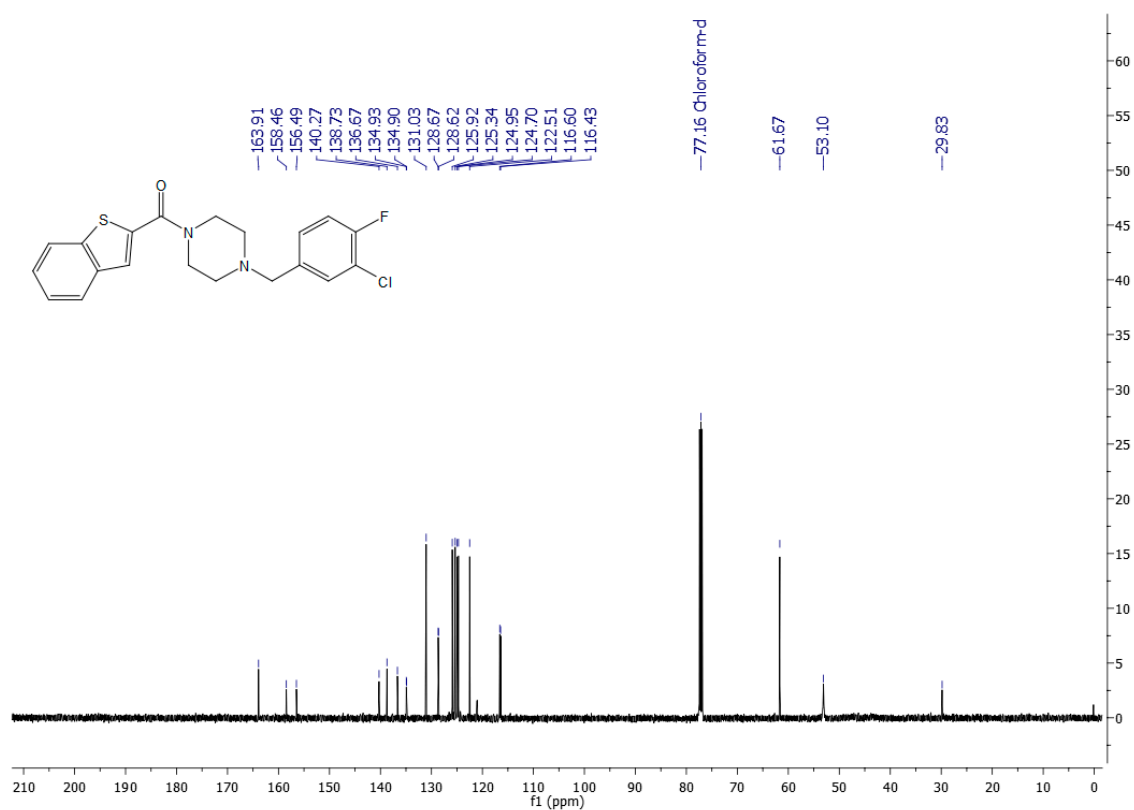


Figure S8: ¹³C-NMR (CDCl₃) spectrum of Benzo[b]thiophen-2-yl(4-(3-chloro-4-fluorobenzyl)piperazin-1-yl)methanone (1f)

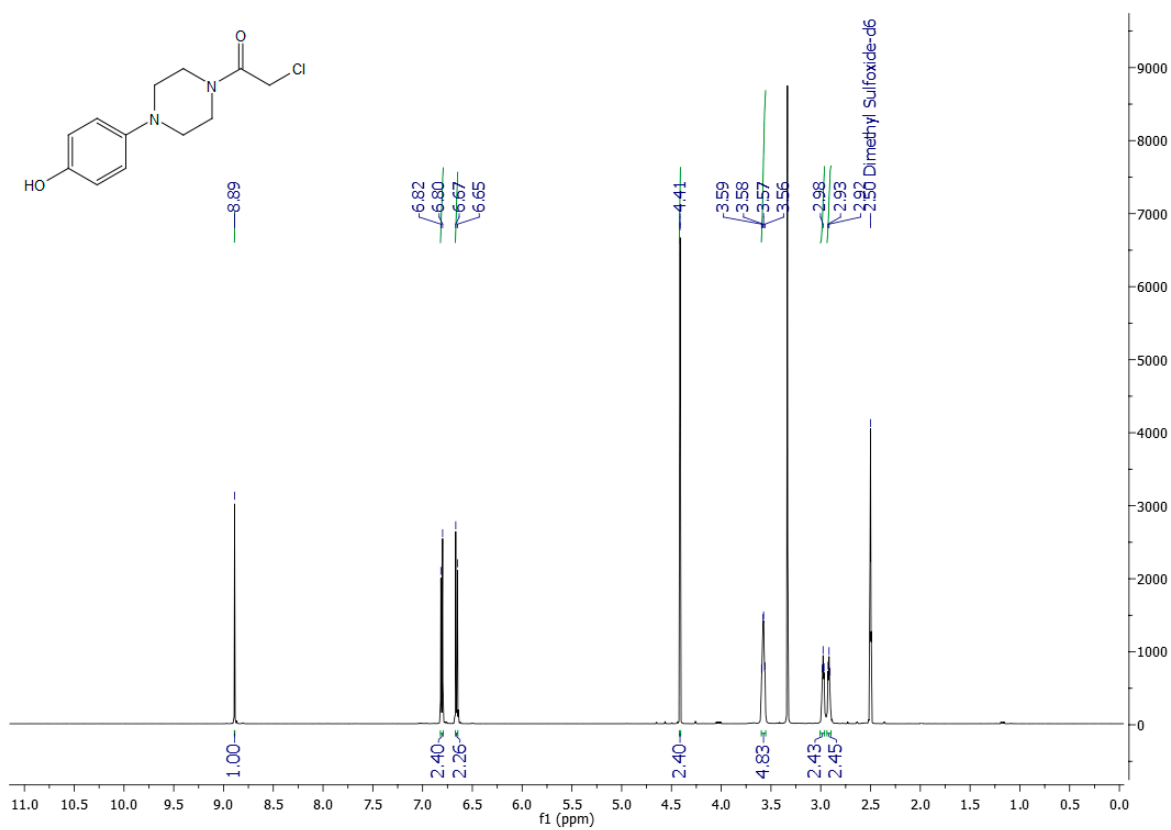


Figure S9: ^1H -NMR ($\text{DMSO-}d_6$) spectrum of 2-Chloro-1-[4-(4-hydroxyphenyl)piperazin-1-yl]ethanone (**8a**)

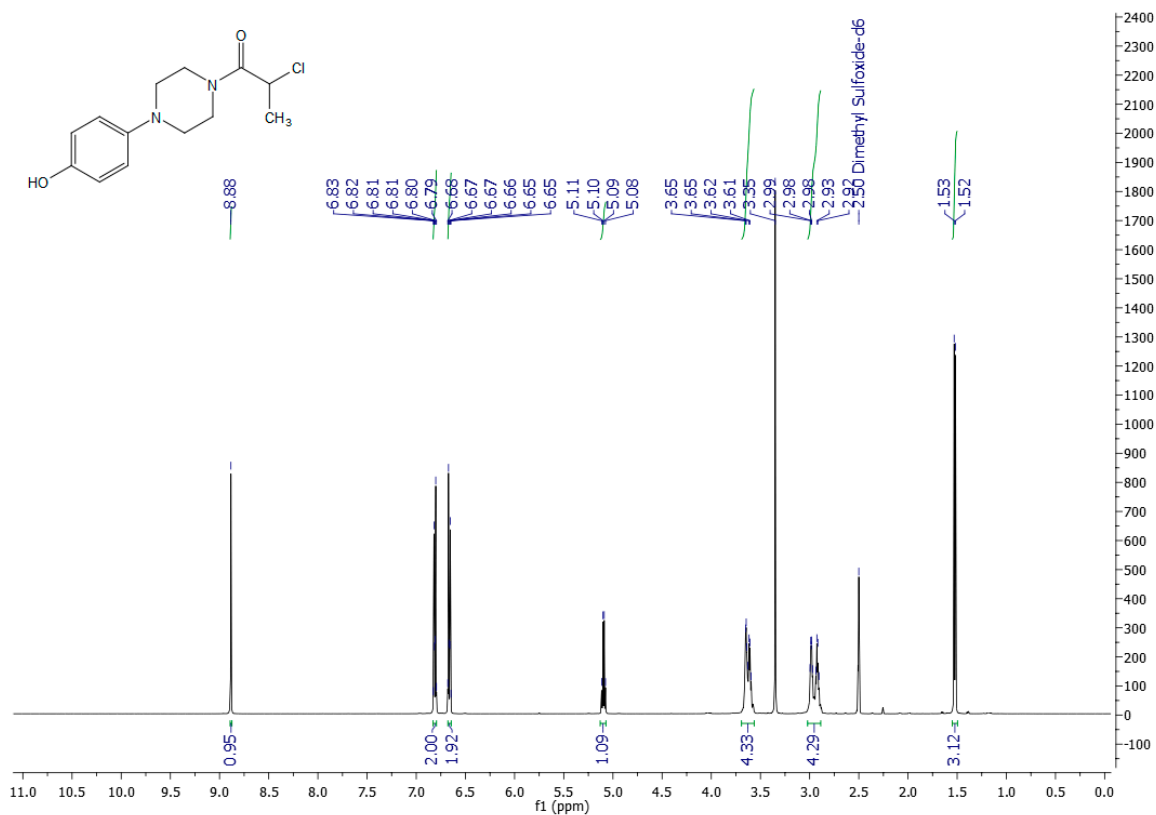


Figure S10: ^1H -NMR ($\text{DMSO-}d_6$) spectrum of 2-Chloro-1-(4-(4-hydroxyphenyl)piperazin-1-yl)propan-1-one (**8b**)

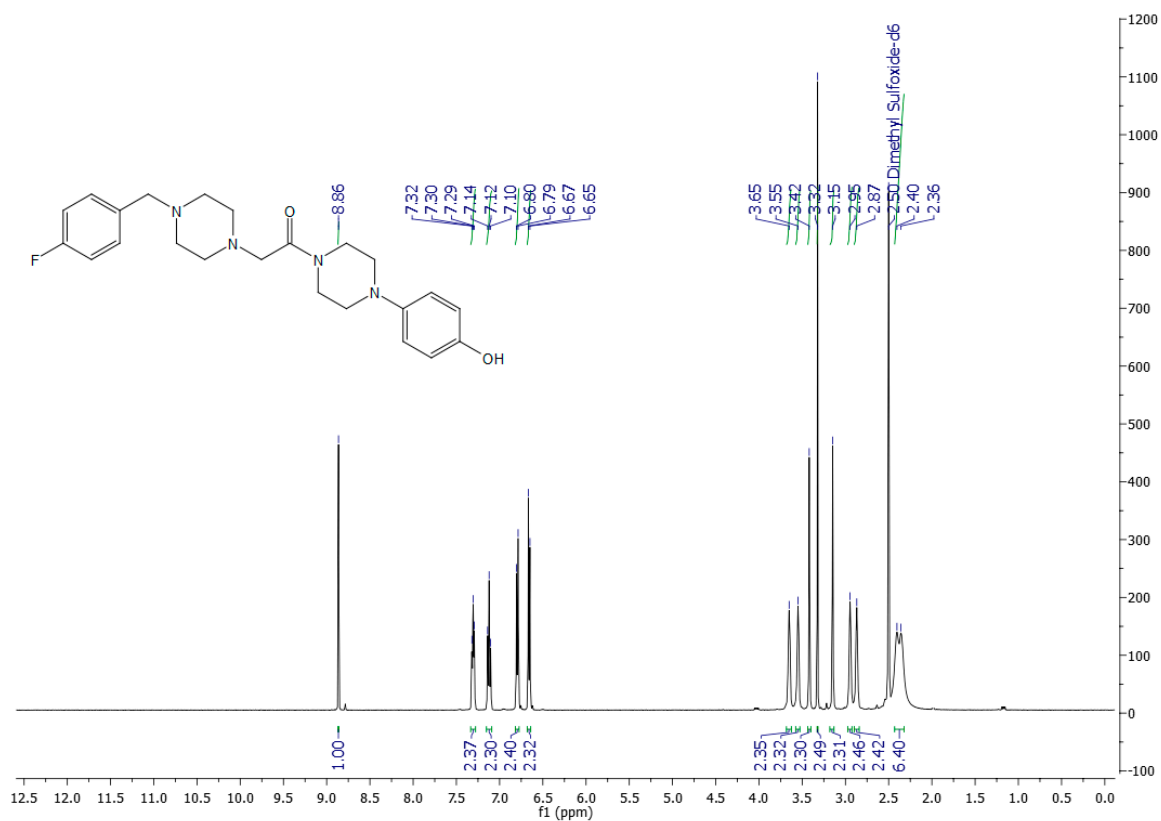


Figure S11: ^1H -NMR (DMSO- d_6) spectrum of 2-(4-(4-Fluorobenzyl)piperazin-1-yl)-1-(4-(4-hydroxyphenyl)piperazin-1-yl)ethanone (**2b**)

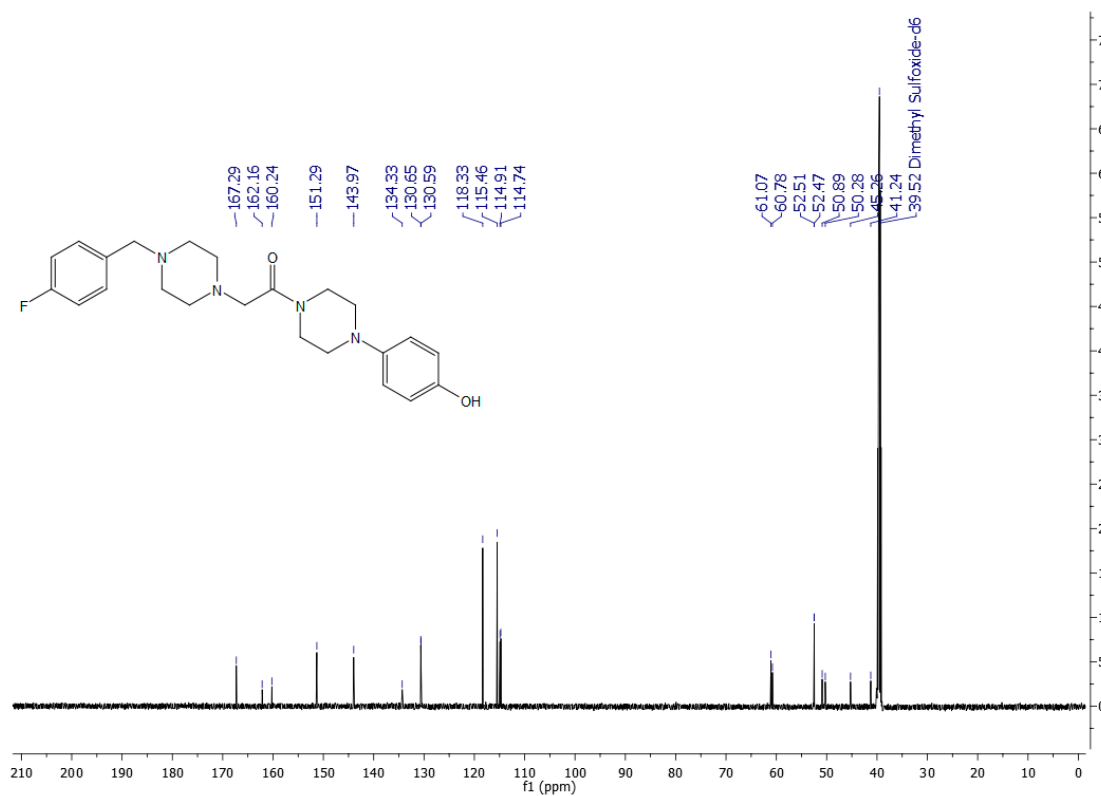


Figure S12: ^{13}C -NMR ($\text{DMSO-}d_6$) spectrum of 2-(4-(4-Fluorobenzyl)piperazin-1-yl)-1-(4-(4-hydroxyphenyl)piperazin-1-yl)ethanone (**2b**)

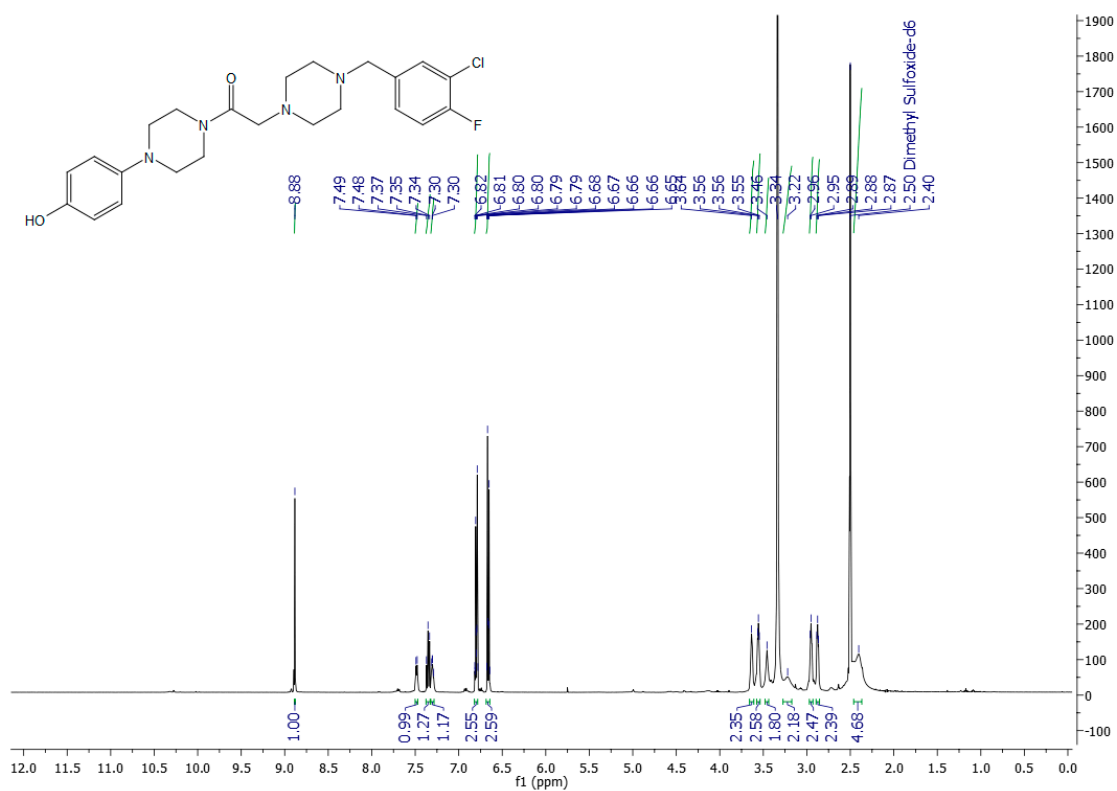


Figure S13: ^1H -NMR ($\text{DMSO-}d_6$) spectrum of 2-(4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)-1-(4-(4-hydroxyphenyl)piperazin-1-yl)ethanone (**2c**)

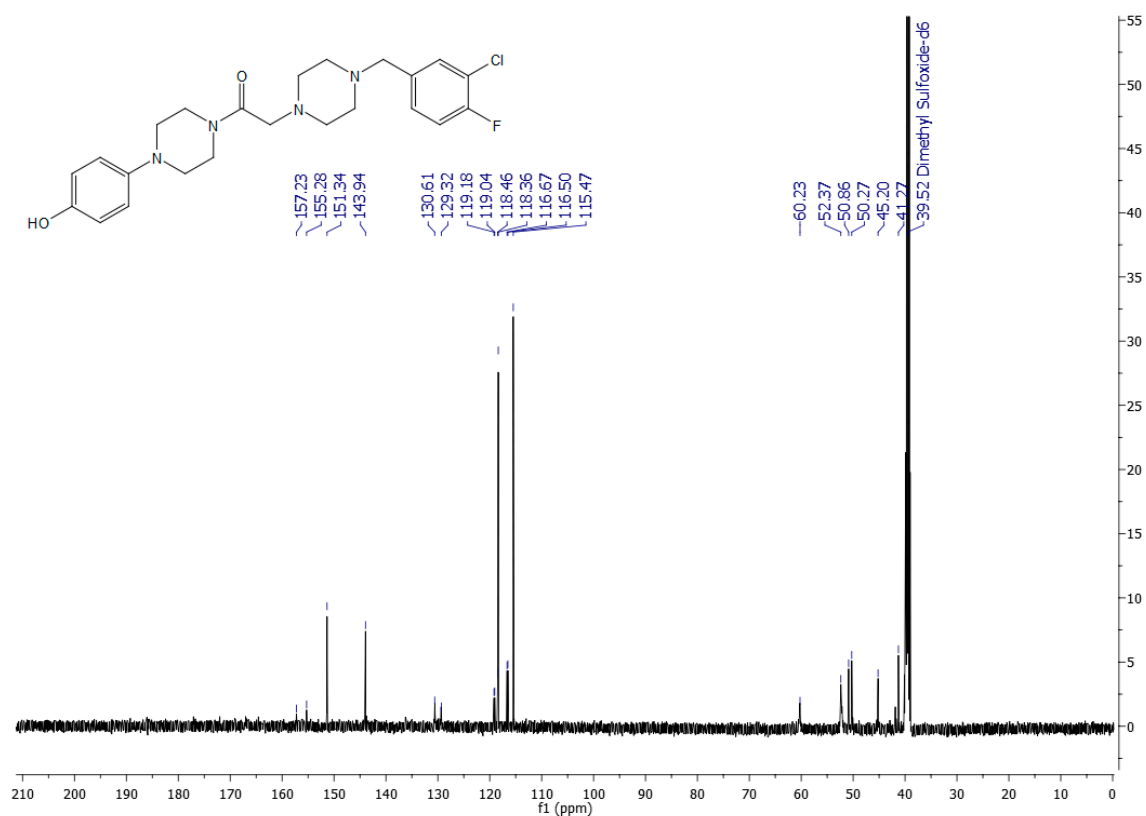


Figure S14: ^{13}C -NMR (DMSO- d_6) spectrum of 2-(4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)-1-(4-(4-hydroxyphenyl)piperazin-1-yl)ethanone (2c)

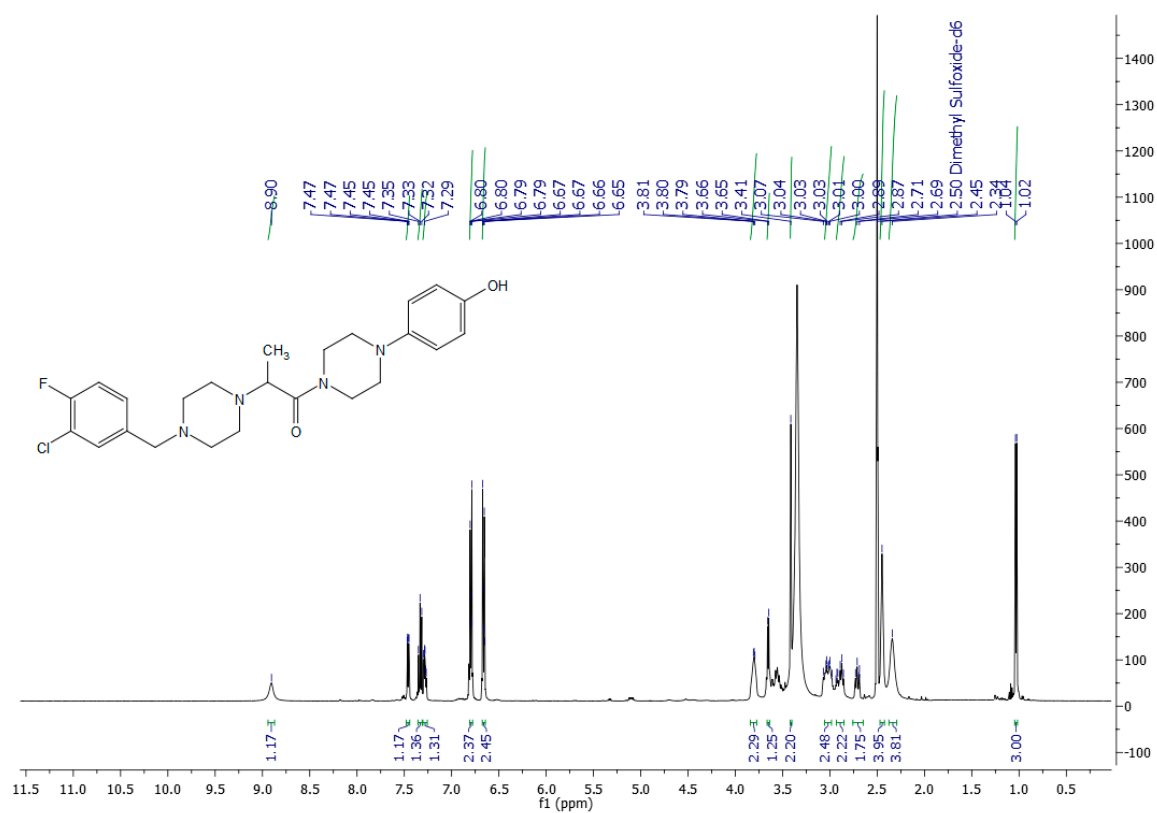


Figure S15: ^1H -NMR ($\text{DMSO-}d_6$) spectrum of 2-(4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)-1-(4-(4-hydroxyphenyl)piperazin-1-yl)propan-1-one (**2d**)

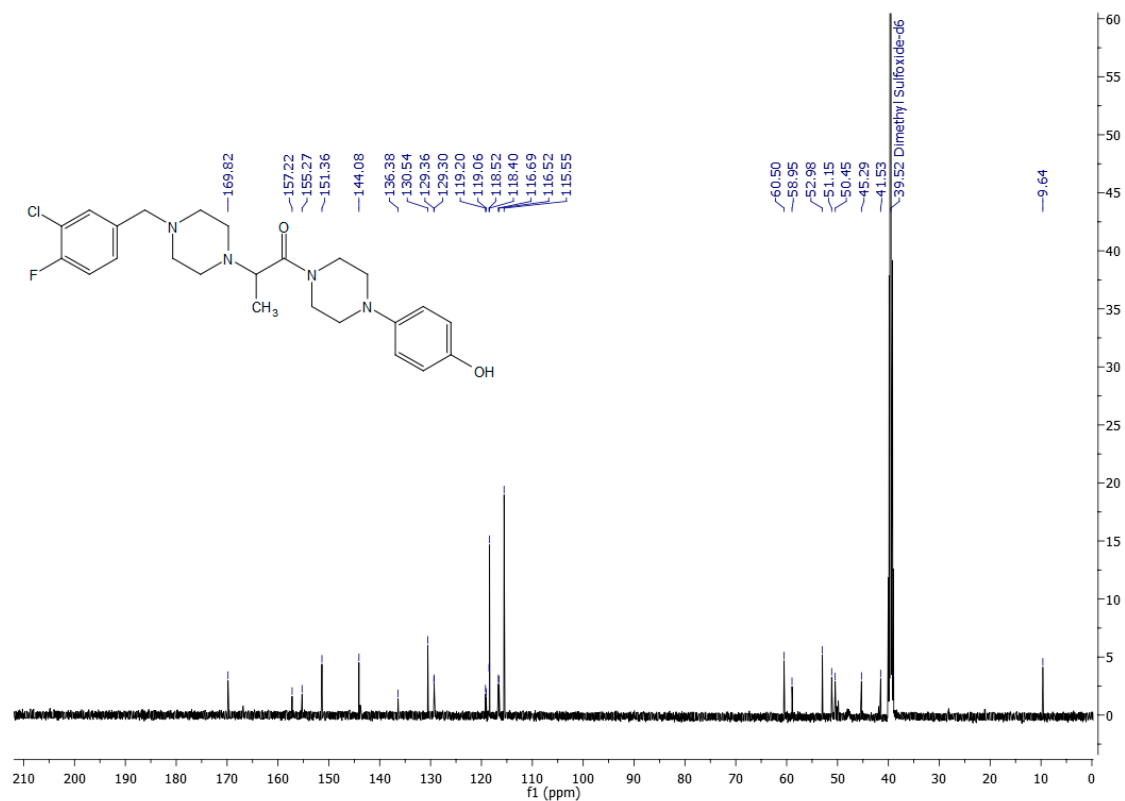


Figure S16: ^{13}C -NMR ($\text{DMSO-}d_6$) spectrum of 2-(4-(3-Chloro-4-fluorobenzyl)piperazin-1-yl)-1-(4-(4-hydroxyphenyl)piperazin-1-yl)propan-1-one (**2d**)

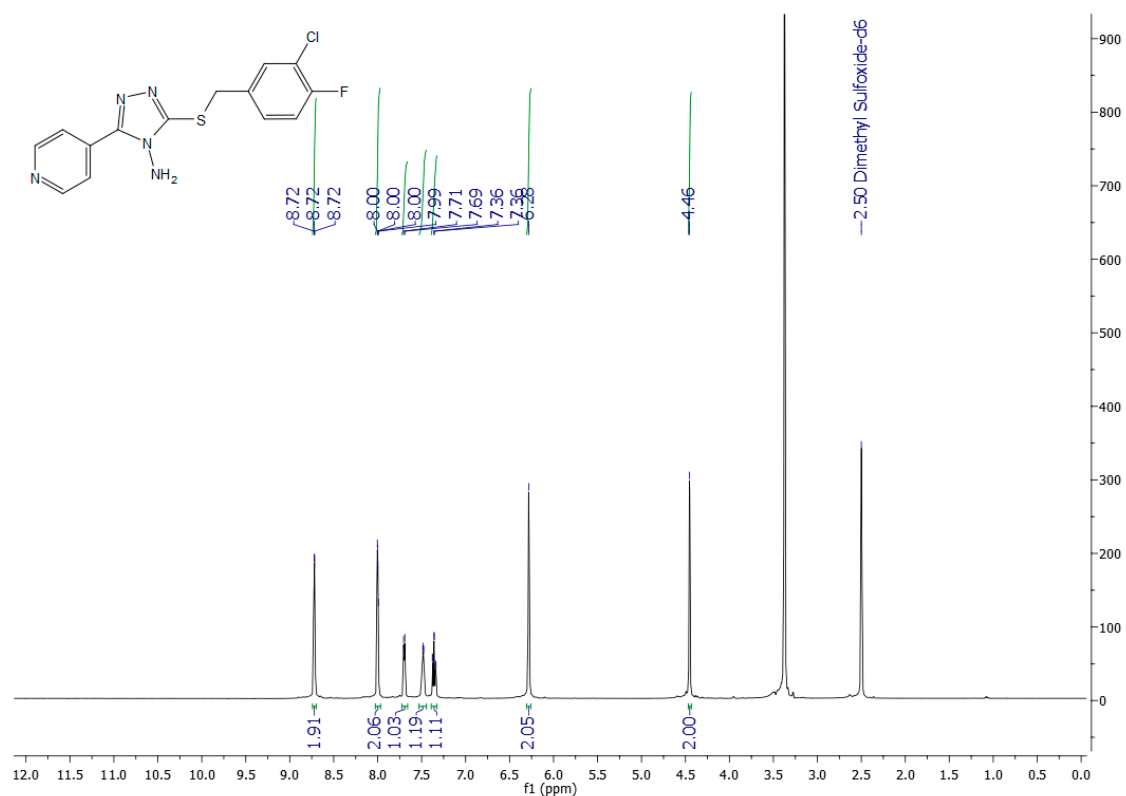


Figure S17: ¹H-NMR (DMSO-*d*₆) spectrum of 3-(3-Chloro-4-fluorobenzylthio)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (**3b**)

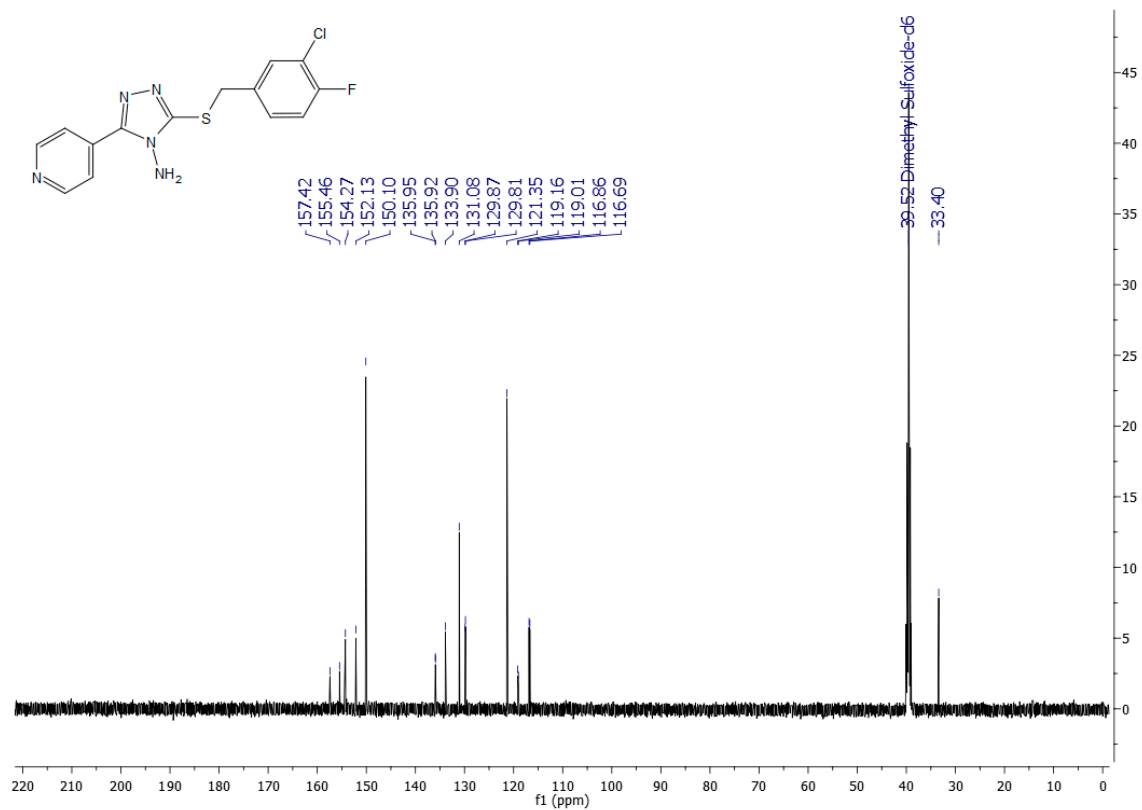


Figure S18: ^{13}C -NMR ($\text{DMSO-}d_6$) spectrum of 3-(3-Chloro-4-fluorobenzylthio)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (**3b**)

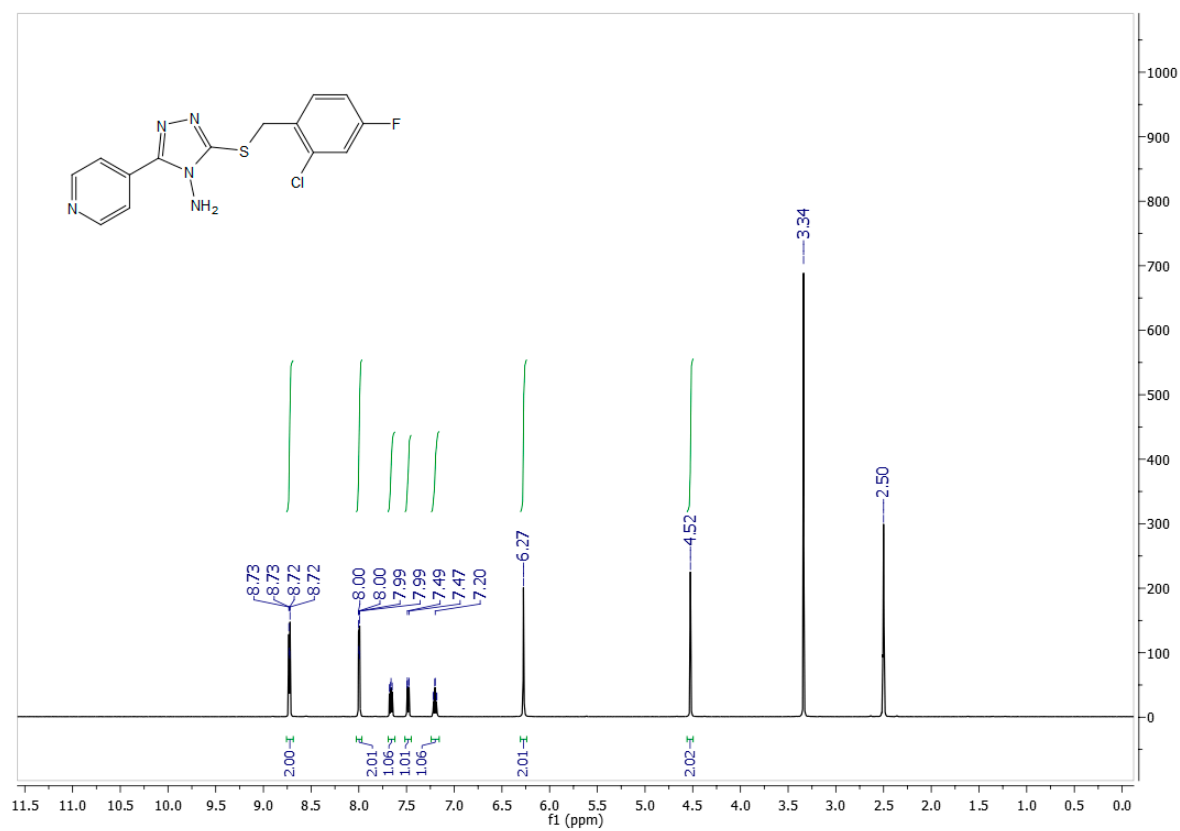


Figure S19: ^1H -NMR ($\text{DMSO-}d_6$) spectrum of 3-((2-Chloro-4-fluorobenzyl)thio)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (**3c**)

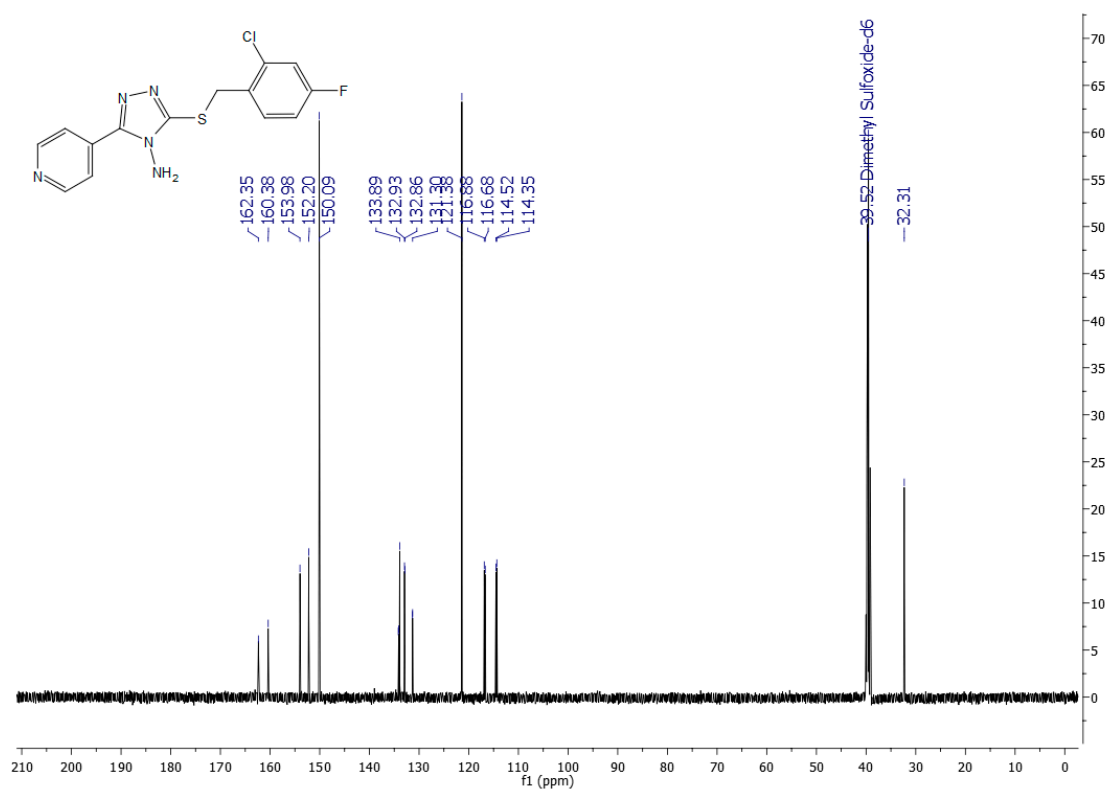


Figure S20: ¹³C-NMR (DMSO-*d*₆) spectrum of 3-((2-Chloro-4-fluorobenzyl)thio)-5-(pyridin-4-yl)-4H-1,2,4-triazol-4-amine (3c)

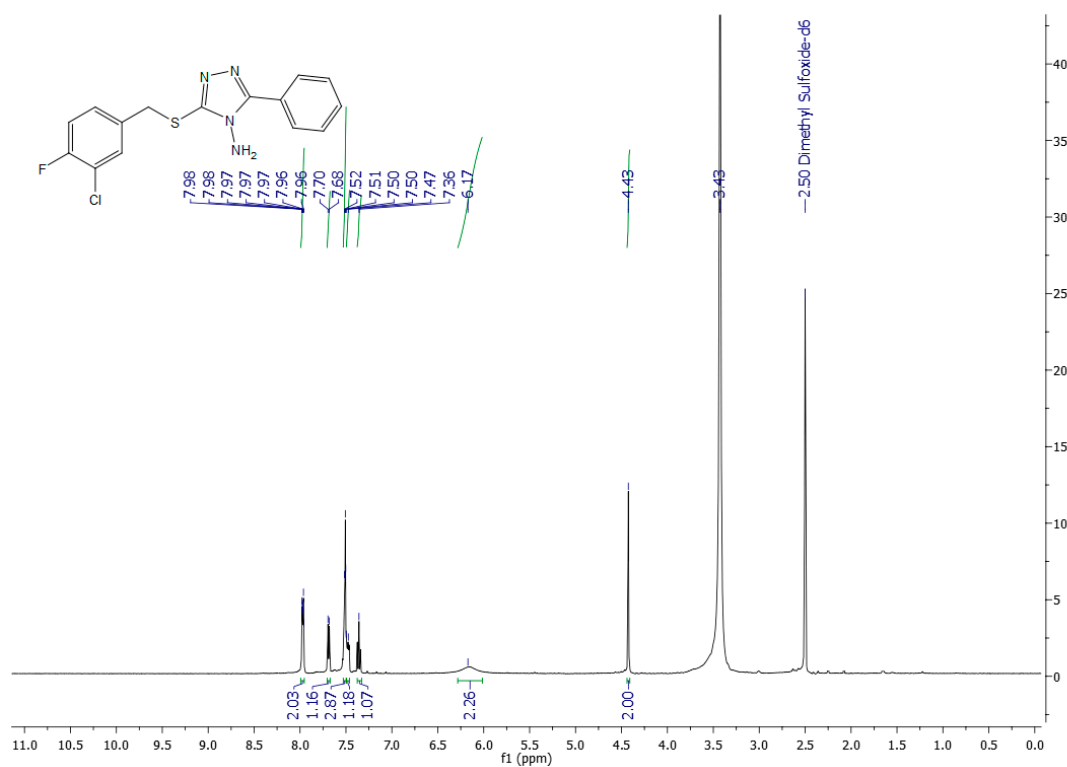


Figure S21: ¹H-NMR (DMSO-*d*₆) spectrum of 3-(3-Chloro-4-fluorobenzylthio)-5-phenyl-4H-1,2,4-triazol-4-amine (3d)

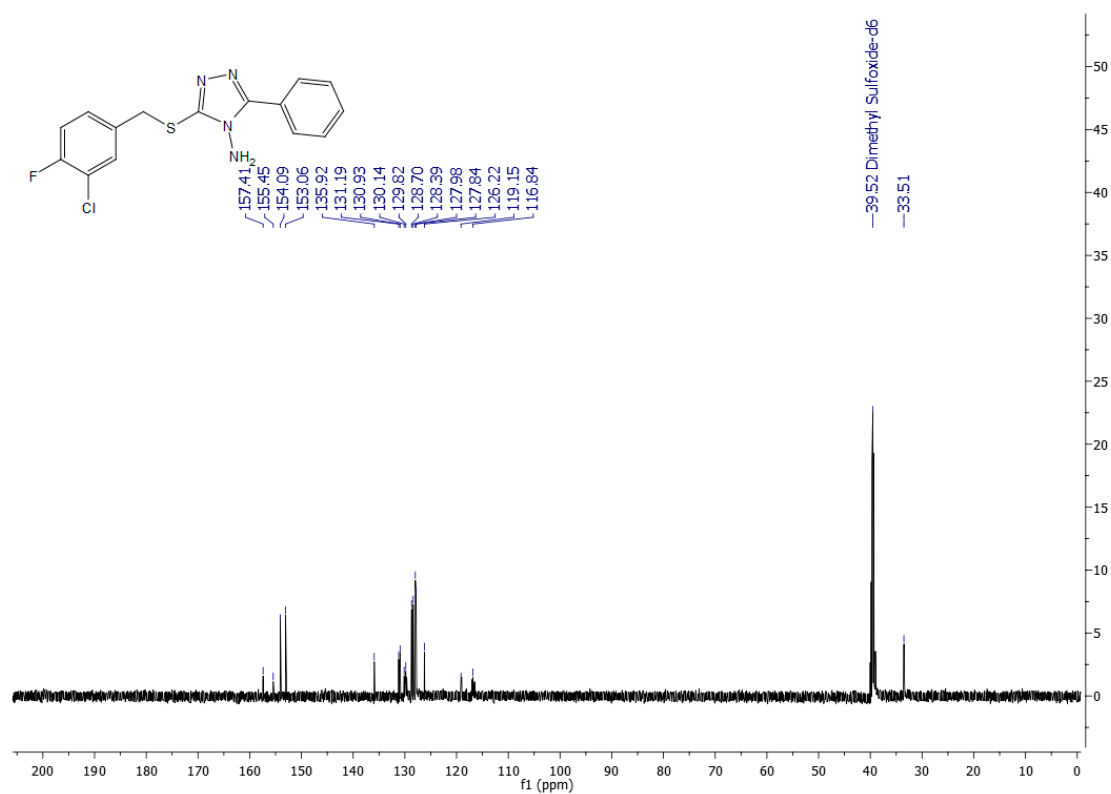


Figure S22: ¹³C-NMR (DMSO-*d*₆) spectrum of 3-(3-Chloro-4-fluorobenzylthio)-5-phenyl-4H-1,2,4-triazol-4-amine (3d)

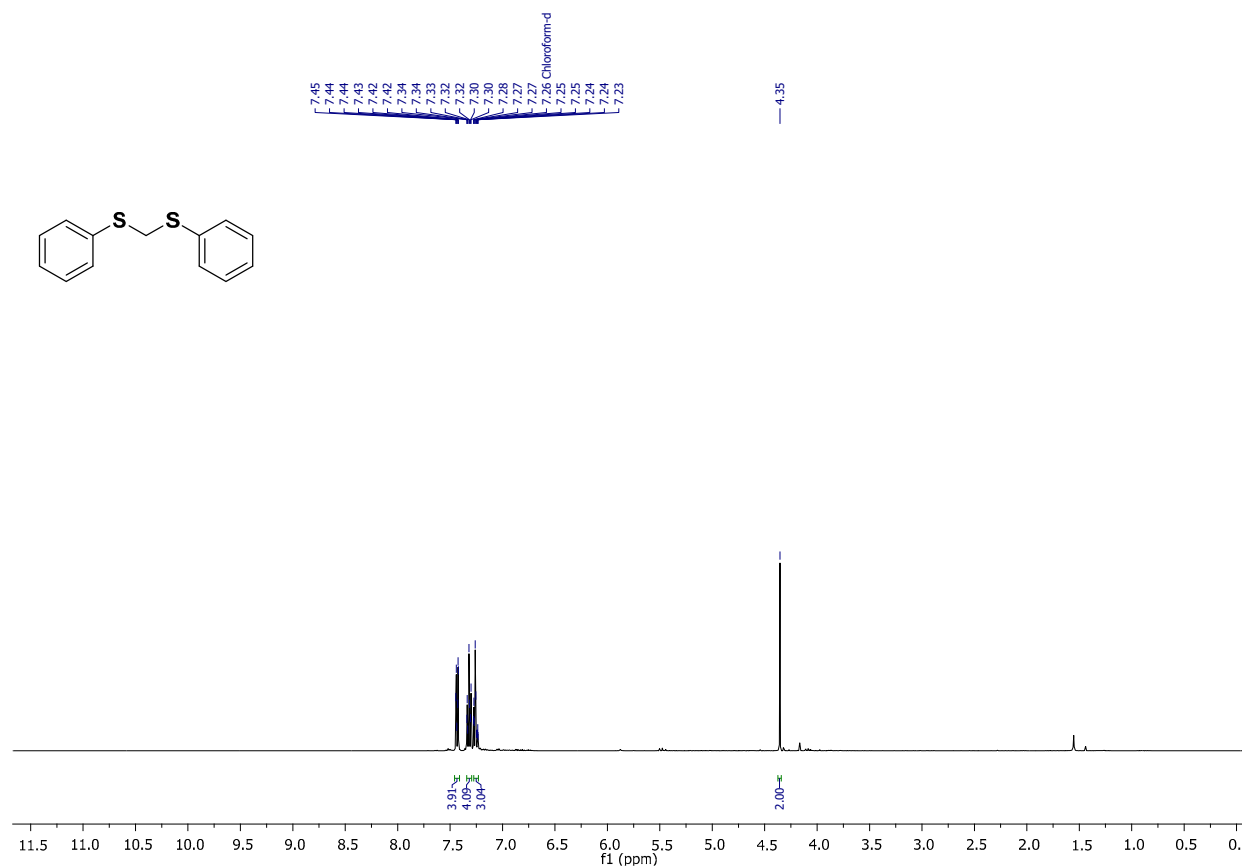


Figure S23: ^1H -NMR (CDCl_3) spectrum of phenylsulfanylmethylsulfanylbenzene (**4b**)

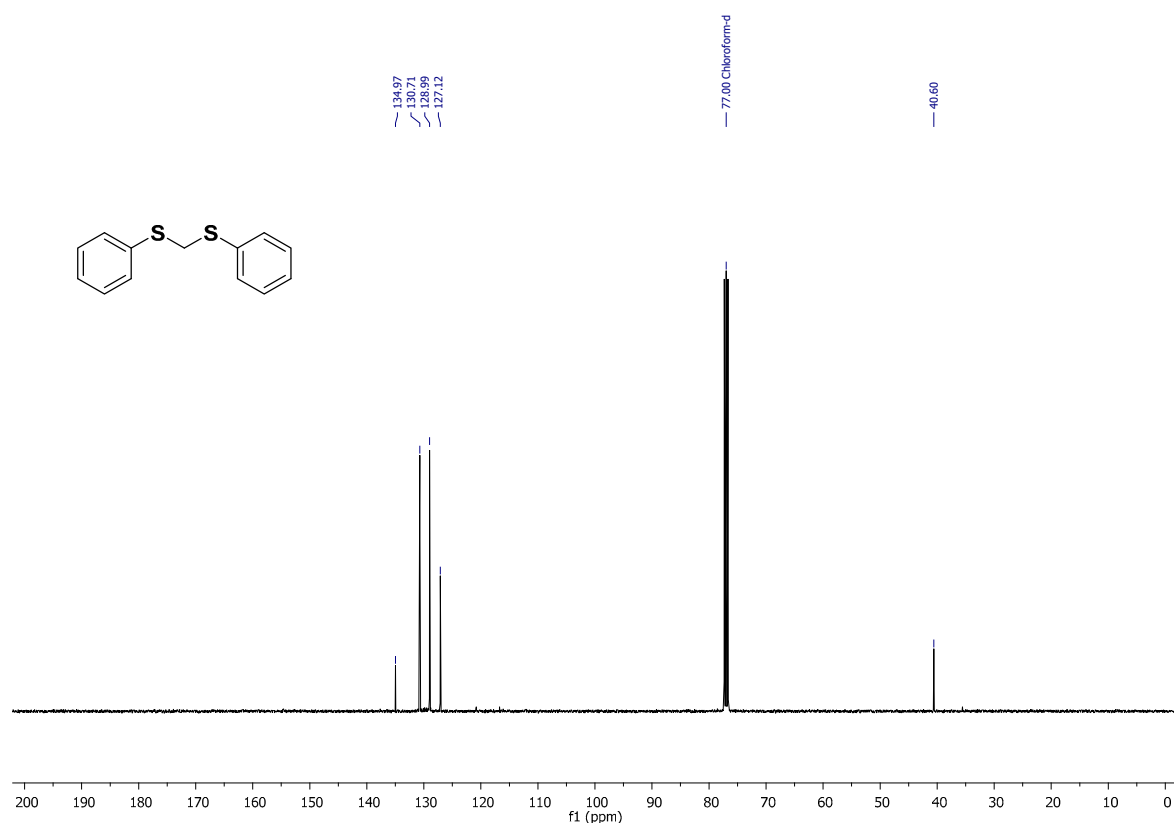


Figure S24: ^{13}C -NMR (CDCl_3) spectrum of phenylsulfanylmethylsulfanylbenzene (**4b**)

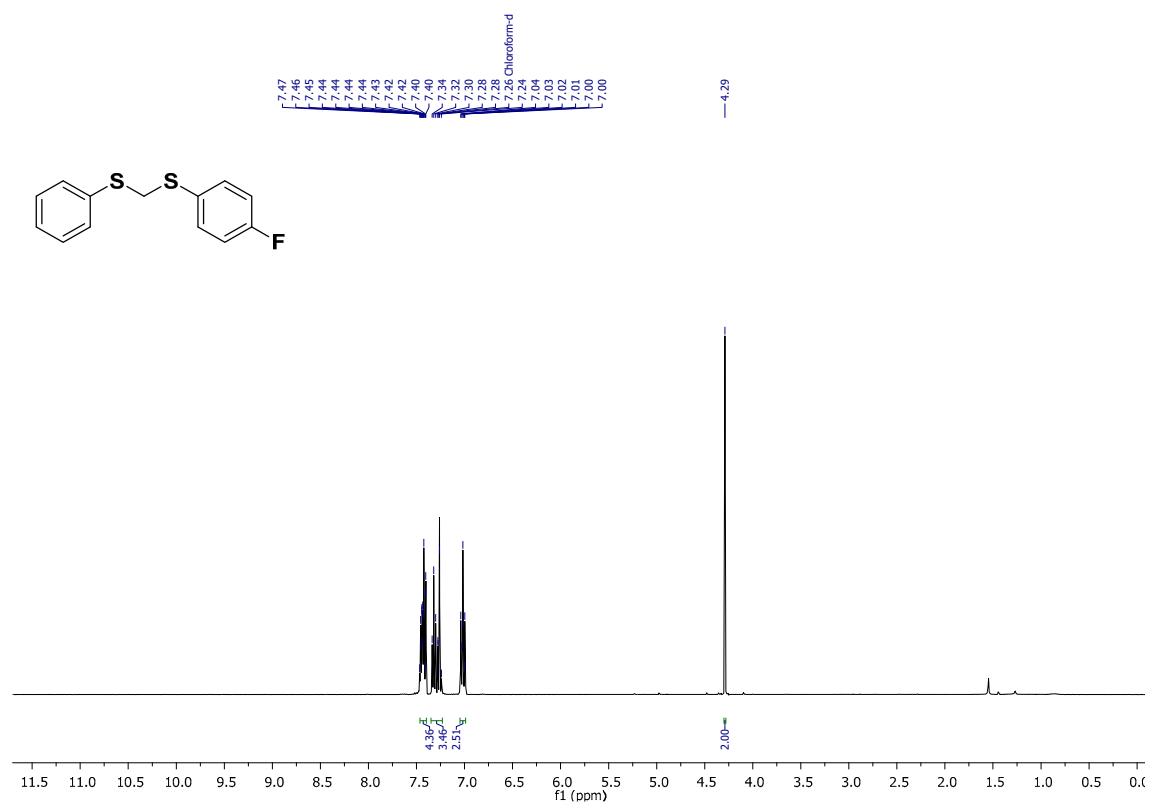


Figure S25: ^1H -NMR (CDCl_3) spectrum of 1-fluoro-4-[(phenylsulfanyl)methyl]sulfanylbenzene (4c)

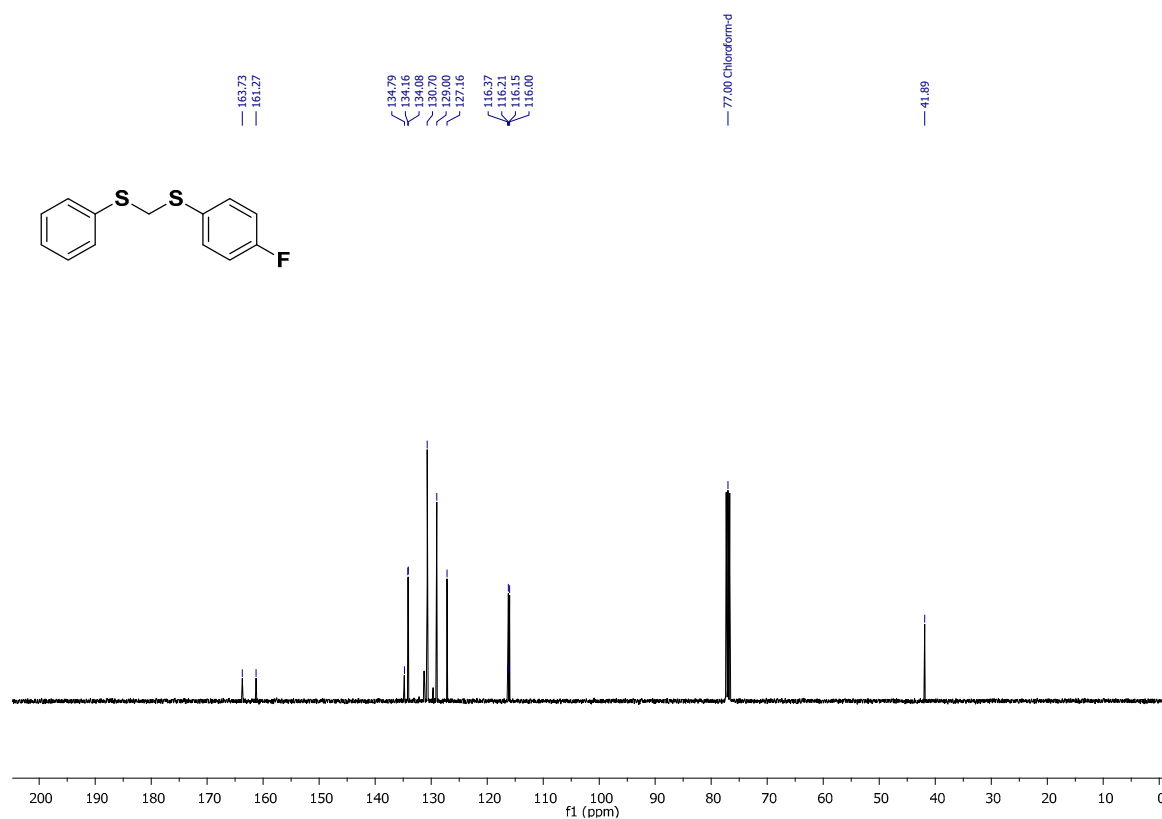
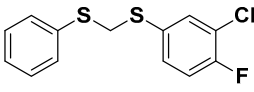


Figure S26: ^{13}C -NMR (CDCl_3) spectrum of 1-Fluoro-4-[(phenylsulfanyl)methyl]sulfanylbenzene (4c)

c1ccccc1SSc2ccc(F)c(Cl)c2

¹³C NMR spectrum (CDCl₃) of 4-(chloromethyl)thiobenzene derivative. The spectrum shows peaks corresponding to the chemical structure, with the following chemical shifts (ppm) labeled:

- 158.52
- 156.86
- 134.33
- 133.73
- 131.73
- 131.68
- 131.08
- 131.01
- 129.06
- 127.43
- 121.51
- 117.95
- 117.09
- 116.95
- 77.00 (CDCl₃)
- 41.69

Figure S28: ^{13}C -NMR (CDCl_3) spectrum of 2-chloro-1-fluoro-4-[[[(phenylsulfanyl)methyl]sulfanyl]benzene (**4d**)

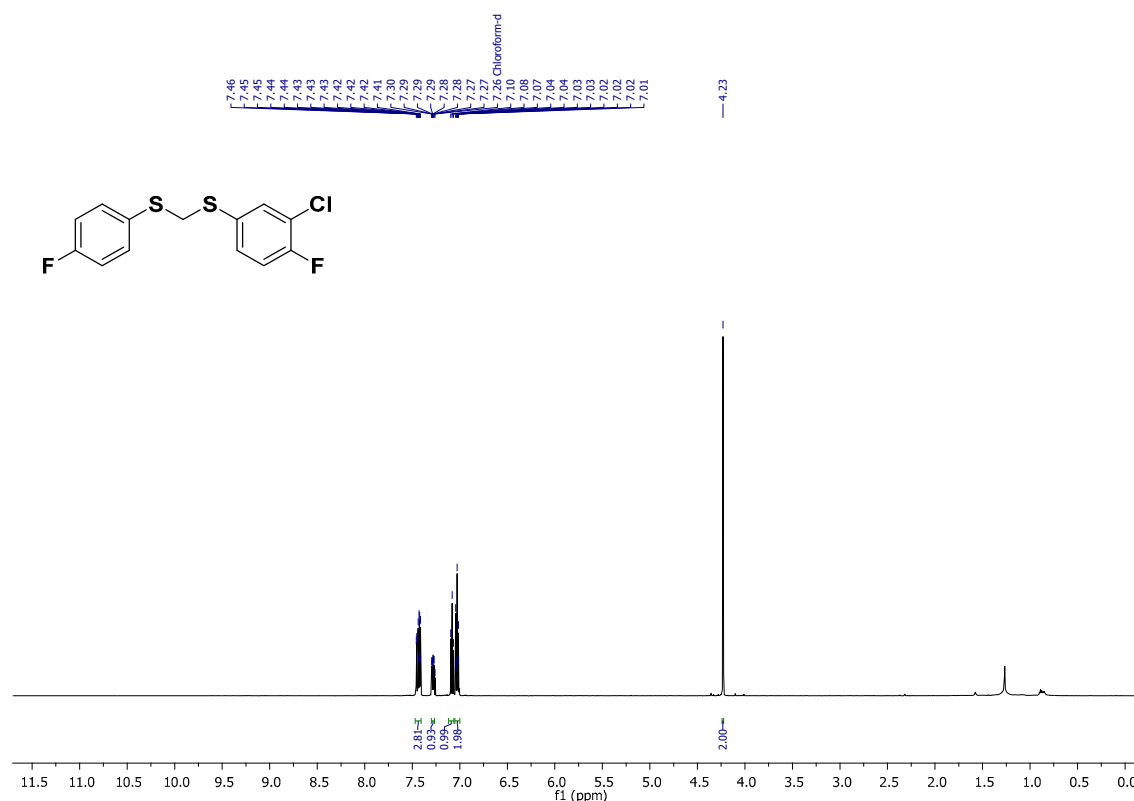


Figure S29: ^1H -NMR (CDCl_3) spectrum of 2-chloro-1-fluoro-4-(([(4-fluorophenyl)sulfanyl)methyl]sulfanyl) benzene (**4e**)

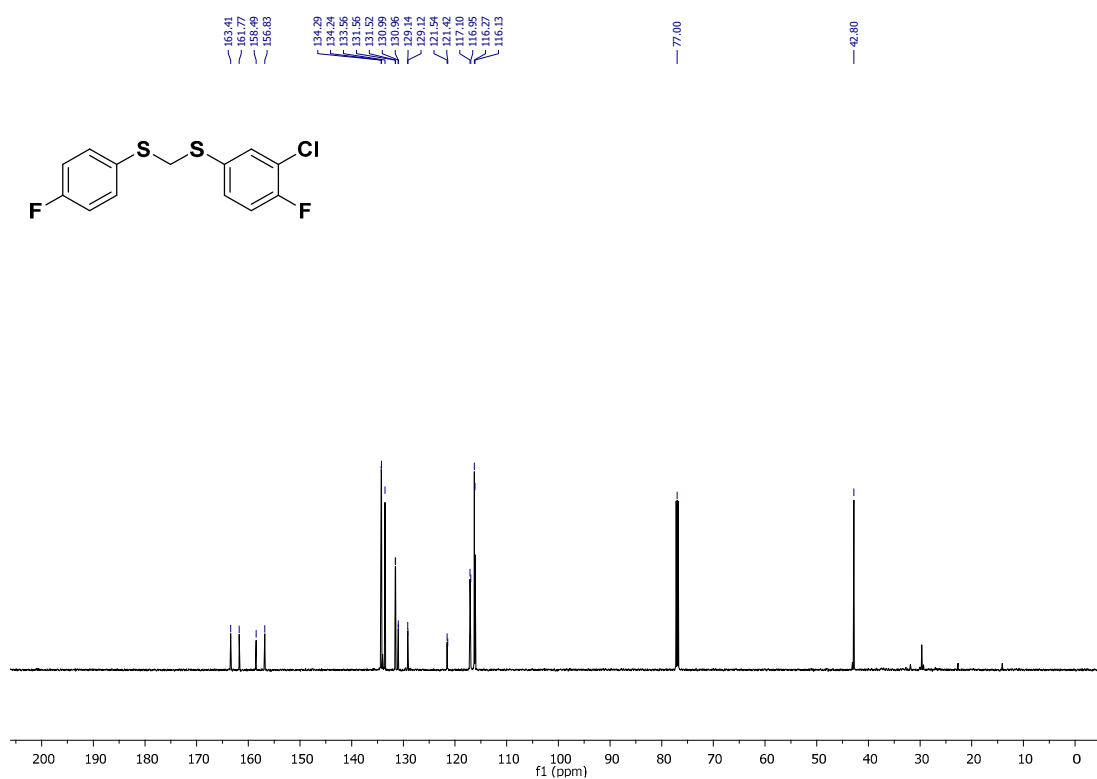


Figure S30: ¹³C-NMR (CDCl₃) spectrum of 2-chloro-1-fluoro-4-(((4-fluorophenyl)sulfanyl)methyl)sulfanyl) benzene (**4e**)

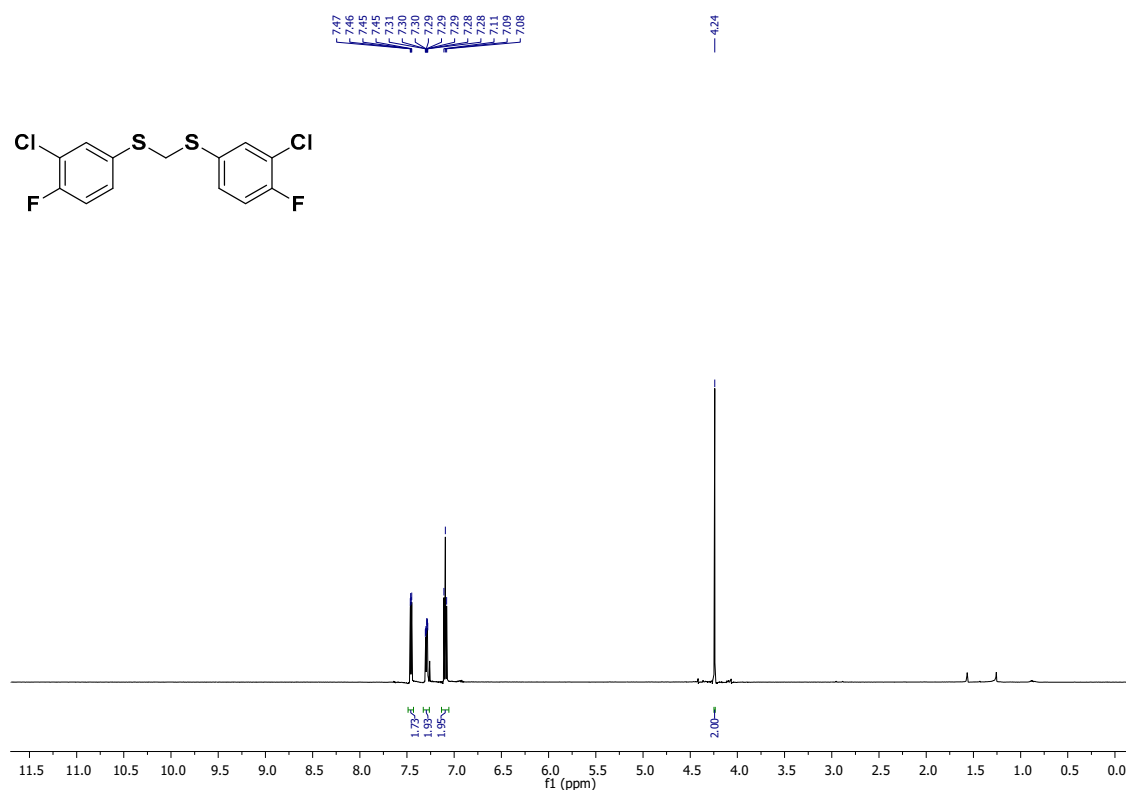


Figure S31: ¹H-NMR (CDCl₃) spectrum of 2-chloro-4-[(3-chloro-4-fluorophenyl)sulfanylmethylsulfanyl]-1-fluorobenzene (**4f**)

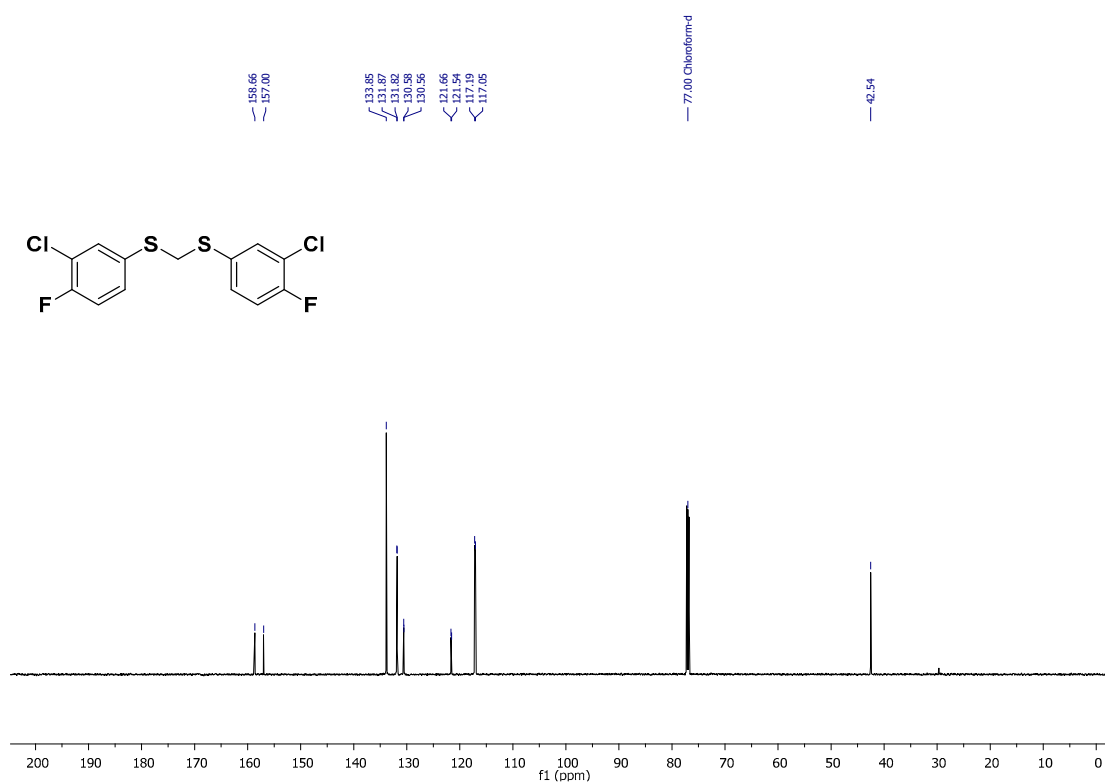


Figure S32: ¹³C-NMR (CDCl₃) spectrum of 2-chloro-4-[(3-chloro-4-fluorophenyl)sulfanylmethylsulfanyl]-1-fluorobenzene (**4f**)

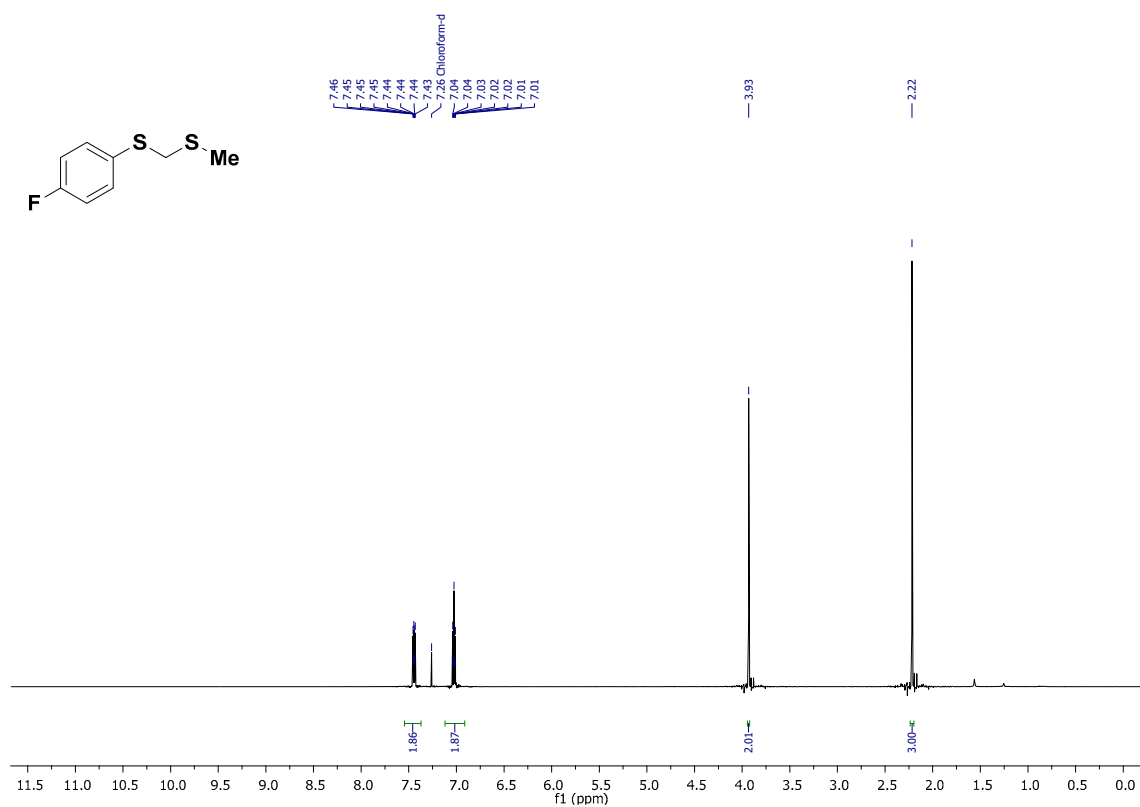


Figure S33: ^1H -NMR (CDCl_3) spectrum of 1-fluoro-4-[[[(methylsulfanyl)methyl]sulfanyl]benzene (4g)

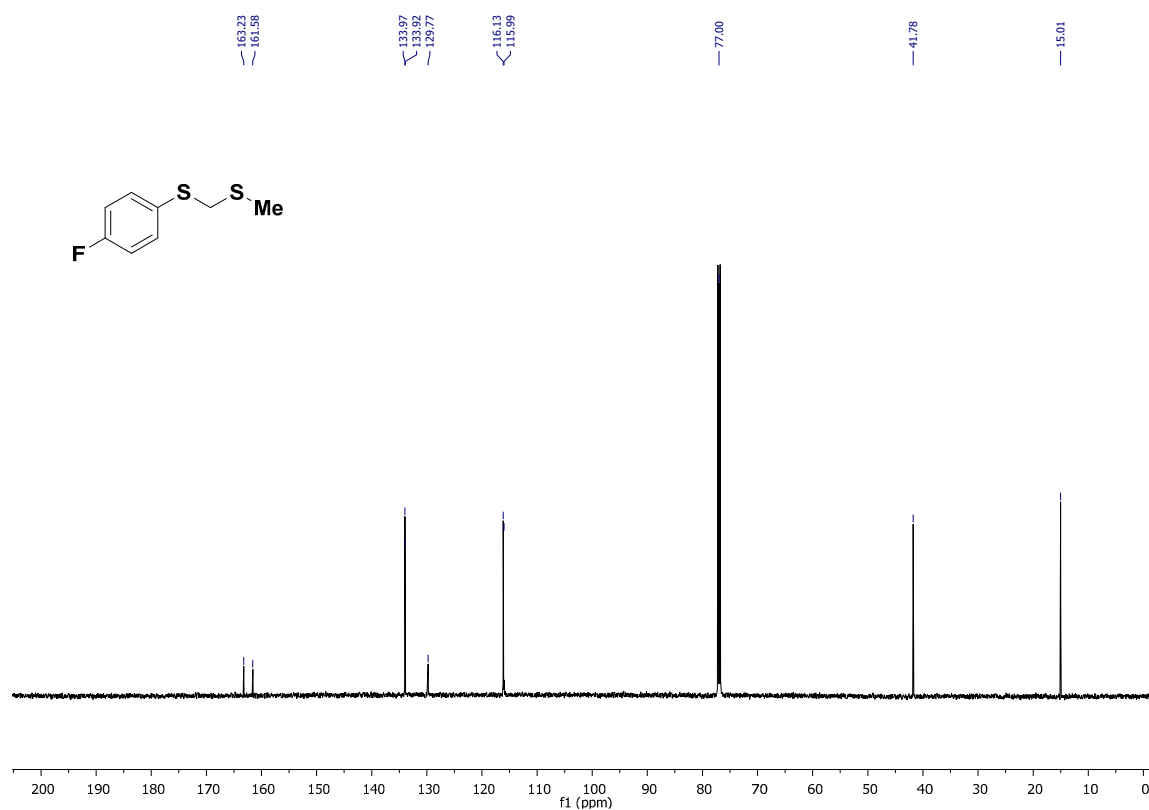


Figure S34: ^{13}C -NMR (CDCl_3) spectrum of 1-fluoro-4-[[[(methylsulfanyl)methyl]sulfanyl]benzene (4g)

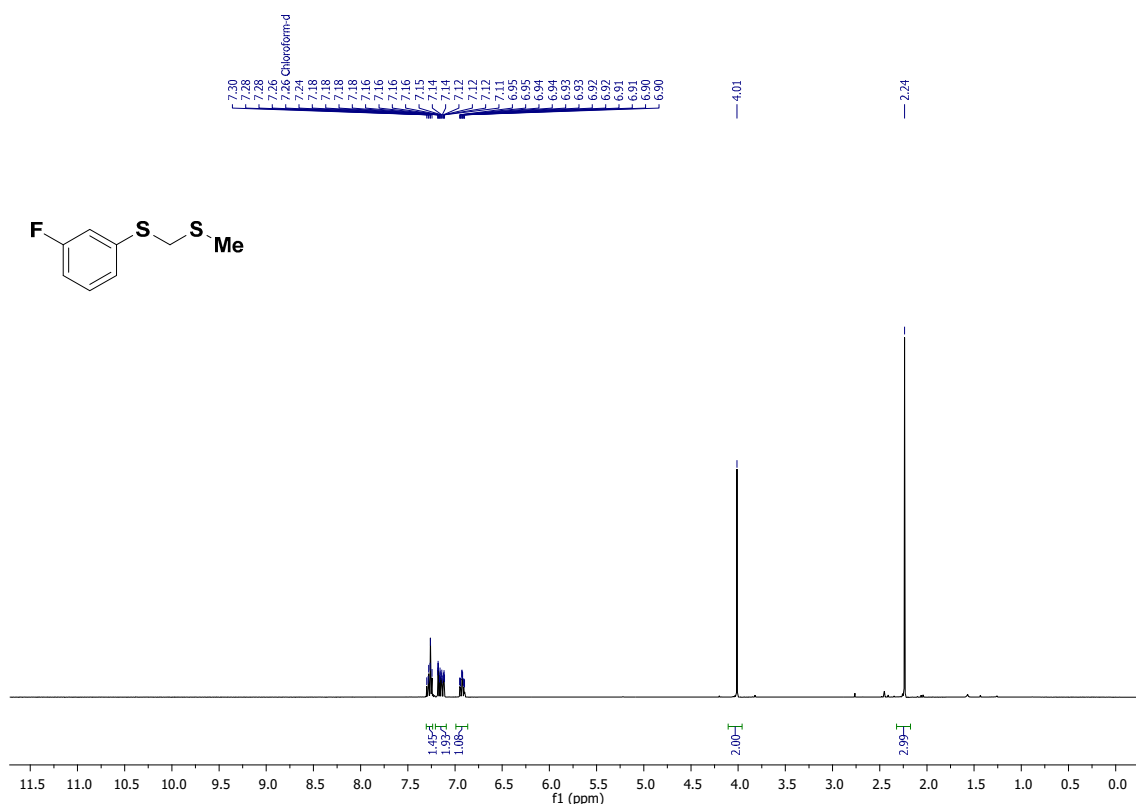


Figure S35: ¹H-NMR (CDCl₃) spectrum of 1-fluoro-3-[(methylsulfanyl)methyl]sulfany]benzene (4h)

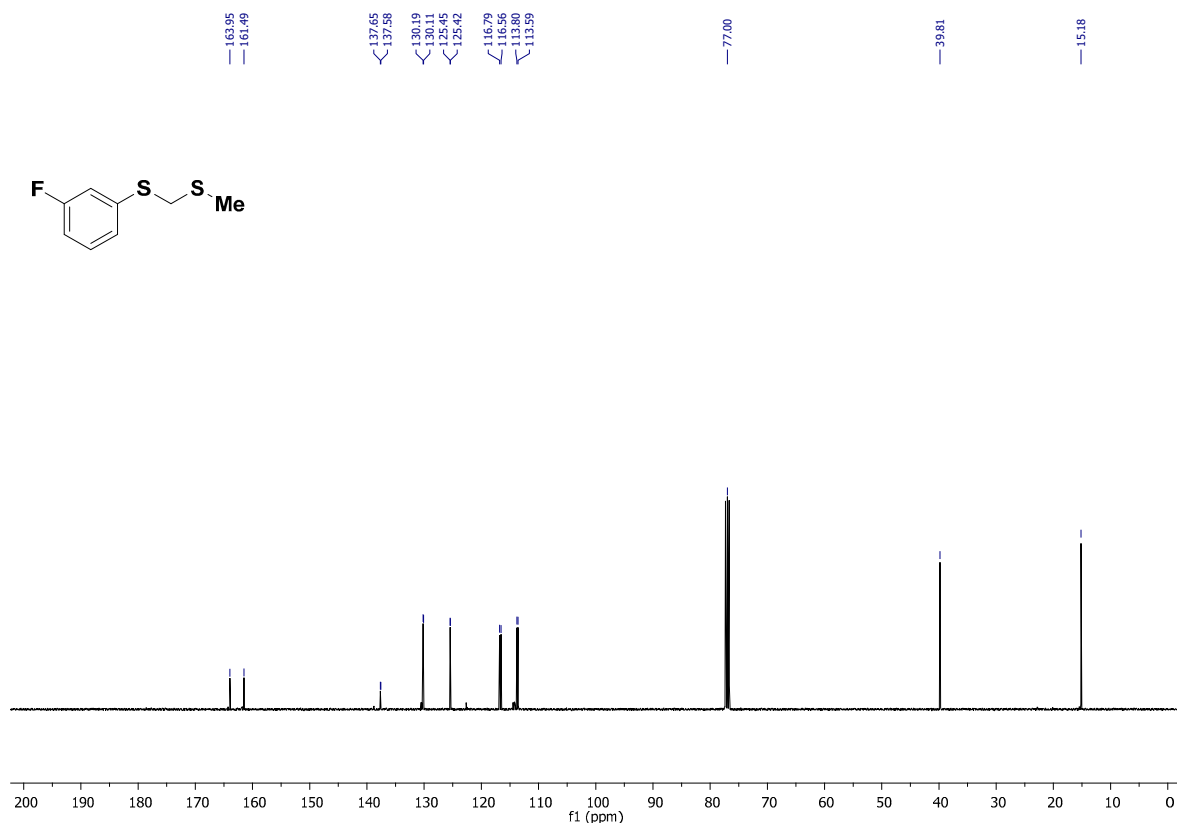


Figure S36: ^{13}C -NMR (CDCl_3) spectrum of 1-fluoro-3-[[[(methylsulfonyl)methyl]sulfonyl]benzene (4h)

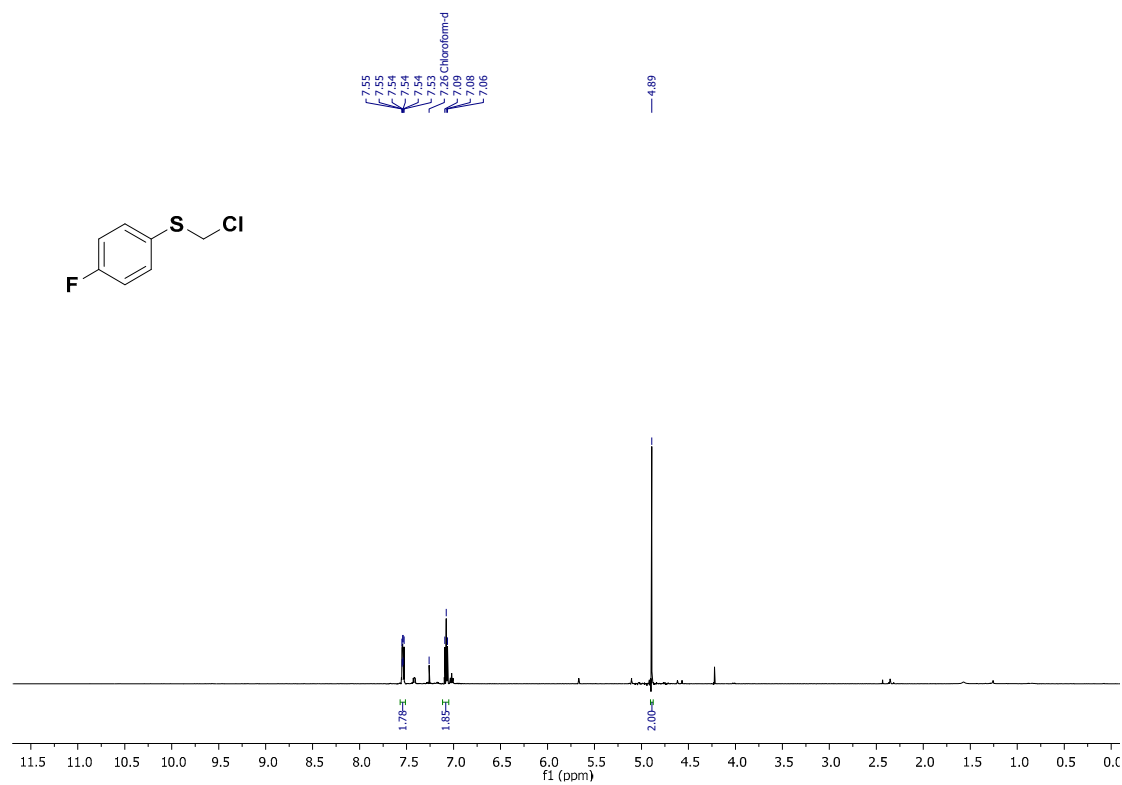


Figure S37: ^1H -NMR (CDCl_3) spectrum of 1-[(chloromethyl)sulfonyl]-4-fluorobenzene (14c)

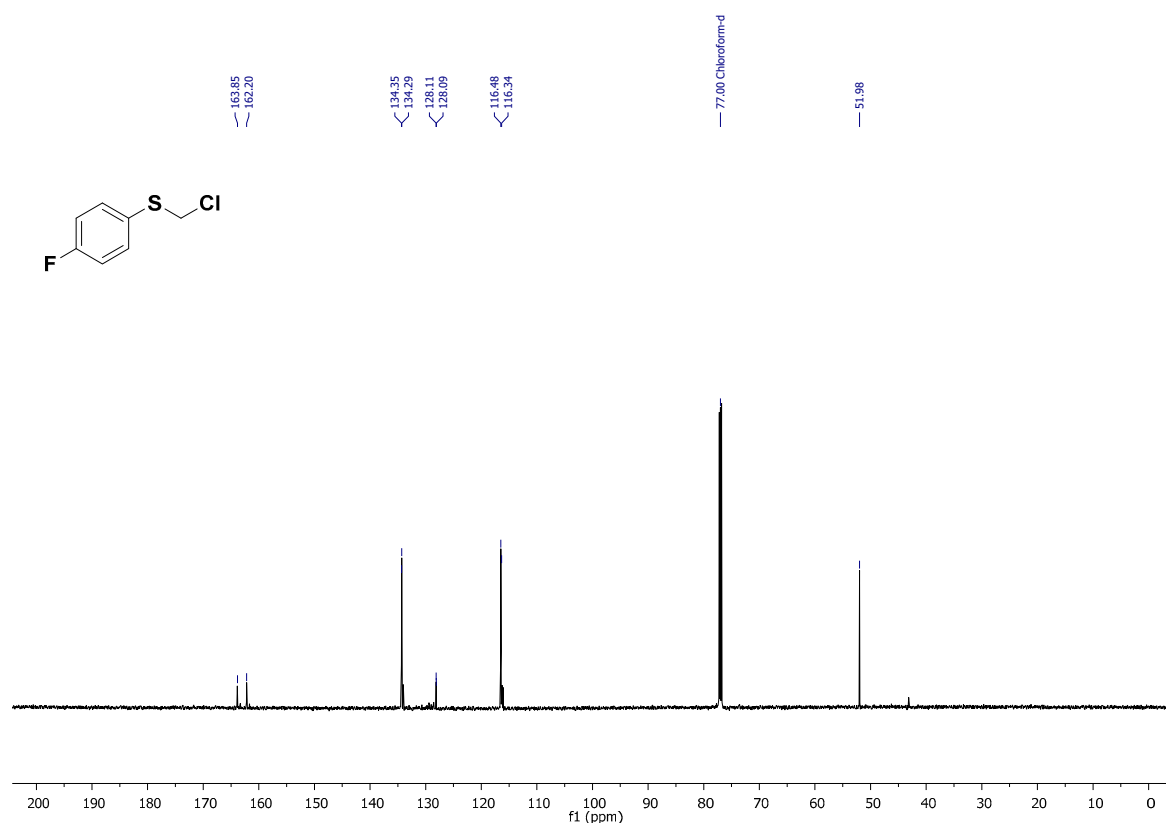


Figure S38: ^{13}C -NMR (CDCl₃) spectrum of 1-[(chloromethyl)sulfanyl]-4-fluorobenzene (**14c**)