

Supplementary Material

Synthesis of Novel Methyl 7- [(Hetero)Arylamino]Thieno[2,3-*b*]Pyrazine-6- Carboxylates and Antitumor Activity Evaluation: Effects in Human Tumor Cells growth, Cell Cycle Analysis, Apoptosis and Toxicity in Non-tumor Cells

Juliana M. Rodrigues¹, Ricardo C. Calhella², António Nogueira², Isabel C.F.R. Ferreira², Lillian Barros², and Maria-João R. P. Queiroz^{1,*}

¹ Centro de Química- Universidade do Minho (CQUM), Campus de Gualtar 4710-057 Braga Portugal; id7018@alunos.uminho.pt (J.M.R.); mjrpq@quimica.uminho.pt (M.-J.R.P.Q.)

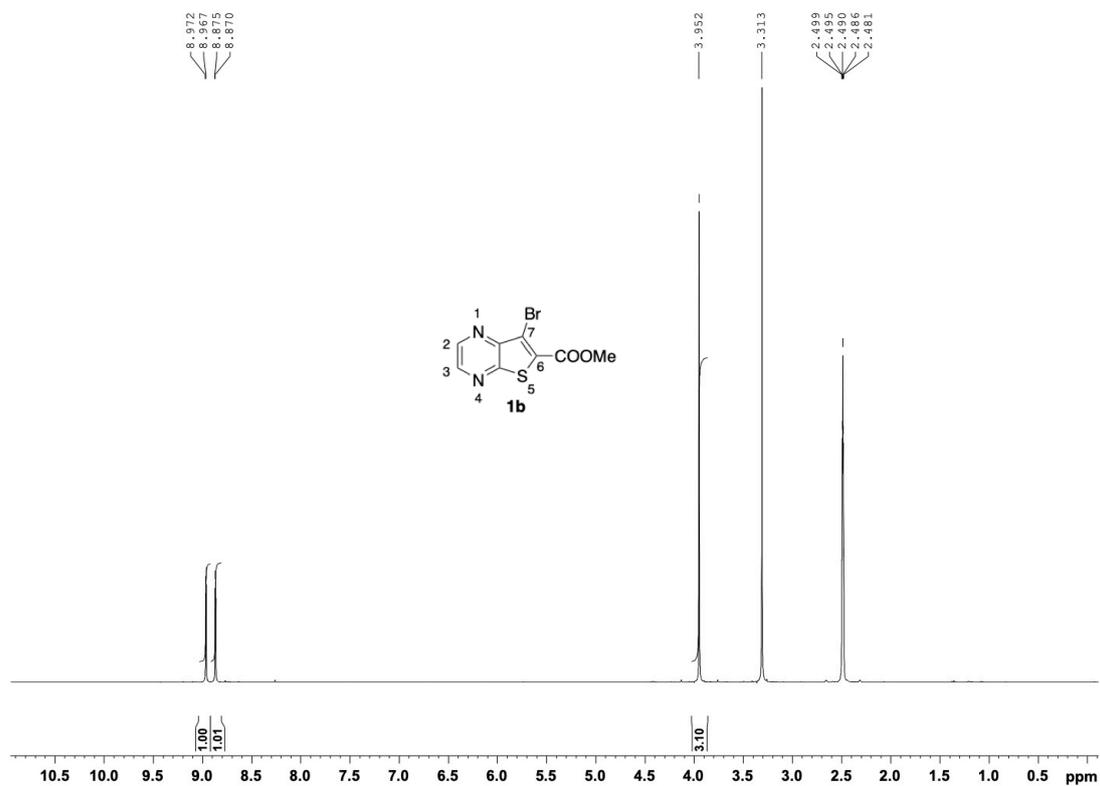
² Centro de Investigação de Montanha (CIMO) - Instituto Politécnico de Bragança, Campus de Santa Apolónia 5300-253 Bragança, Portugal; calhella@ipb.pt (R.C.C.); ajmnogueira@ipb.pt (A.N.); iferreira@ipb.pt (I.C.F.R.F.); lillian@ipb.pt (L.B.)

*Correspondence: mjrpq@quimica.uminho.pt (M.-J.R.P.Q.)

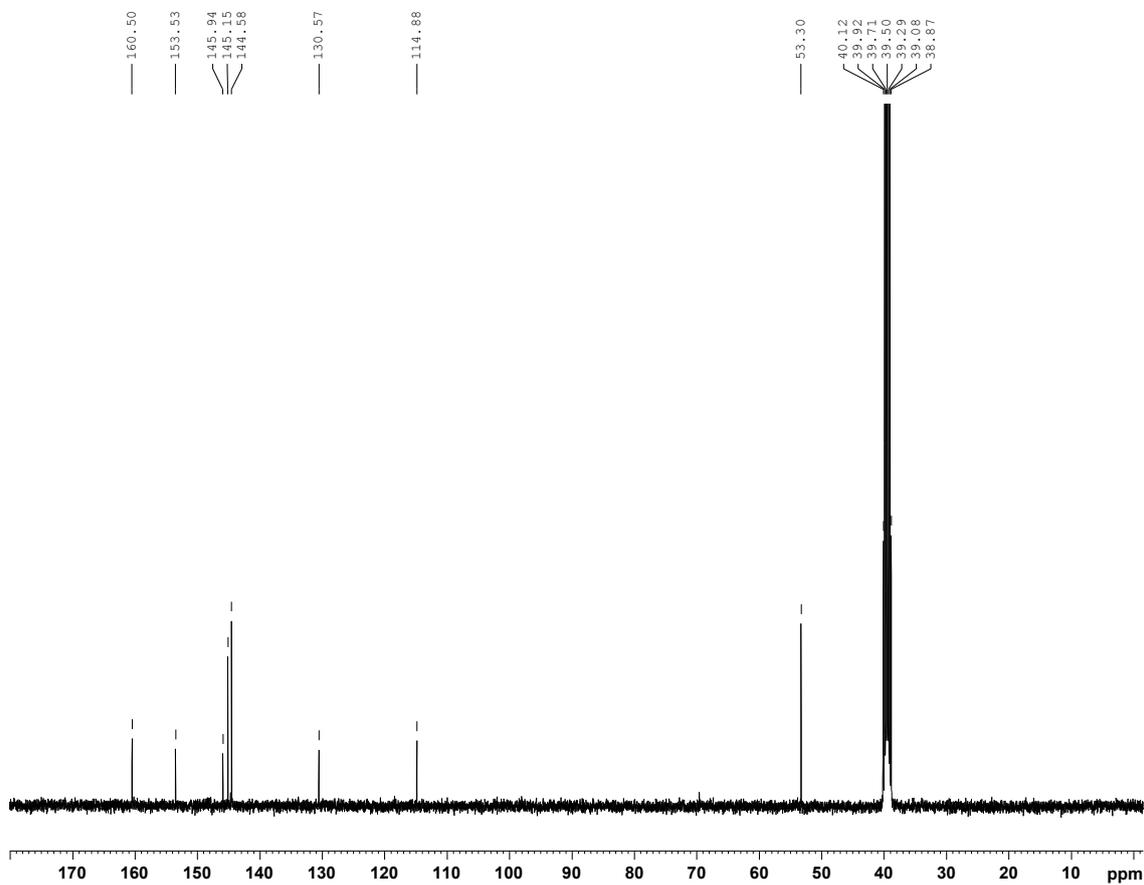
¹ H and ¹³ C spectra of compound 1b	2
¹ H and ¹³ C spectra of compound 2a	3
¹ H and ¹³ C spectra of compound 2b	4
¹ H and ¹³ C spectra of compound 2c	5
¹ H and ¹³ C spectra of compound 2d	6
¹ H and ¹³ C spectra of compound 2e	7
¹ H and ¹³ C spectra of compound 2f	8
¹ H and ¹³ C spectra of compound 2g	9
¹ H and ¹³ C spectra of compound 2h	10
¹ H, ¹³ C and ¹⁹ F spectra of compound 2i	11
¹ H, ¹³ C and ¹⁹ F spectra of compound 2j	13
¹ H, ¹³ C and ¹⁹ F spectra of compound 2k	15
¹ H and ¹³ C spectra of compound 2l	17
¹ H and ¹³ C spectra of compound 2m	18
¹ H and ¹³ C spectra of compound 2n	19
¹ H and ¹³ C spectra of compound 2o	20

Methyl 7-bromothieno[2,3-*b*]pyrazine-6-carboxylate **1b**

^1H NMR (DMSO- d_6 , 400 MHz) of compound **1b**

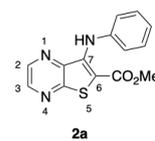
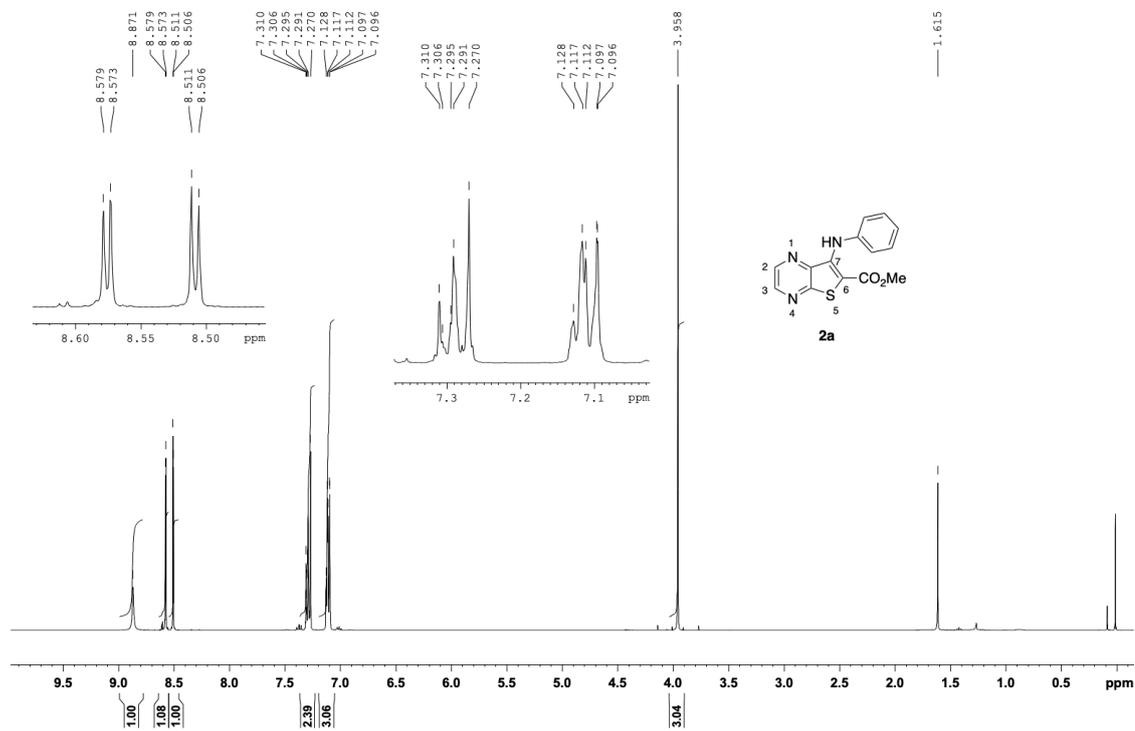


^{13}C NMR (DMSO- d_6 , 100.6 MHz) of compound **1b**

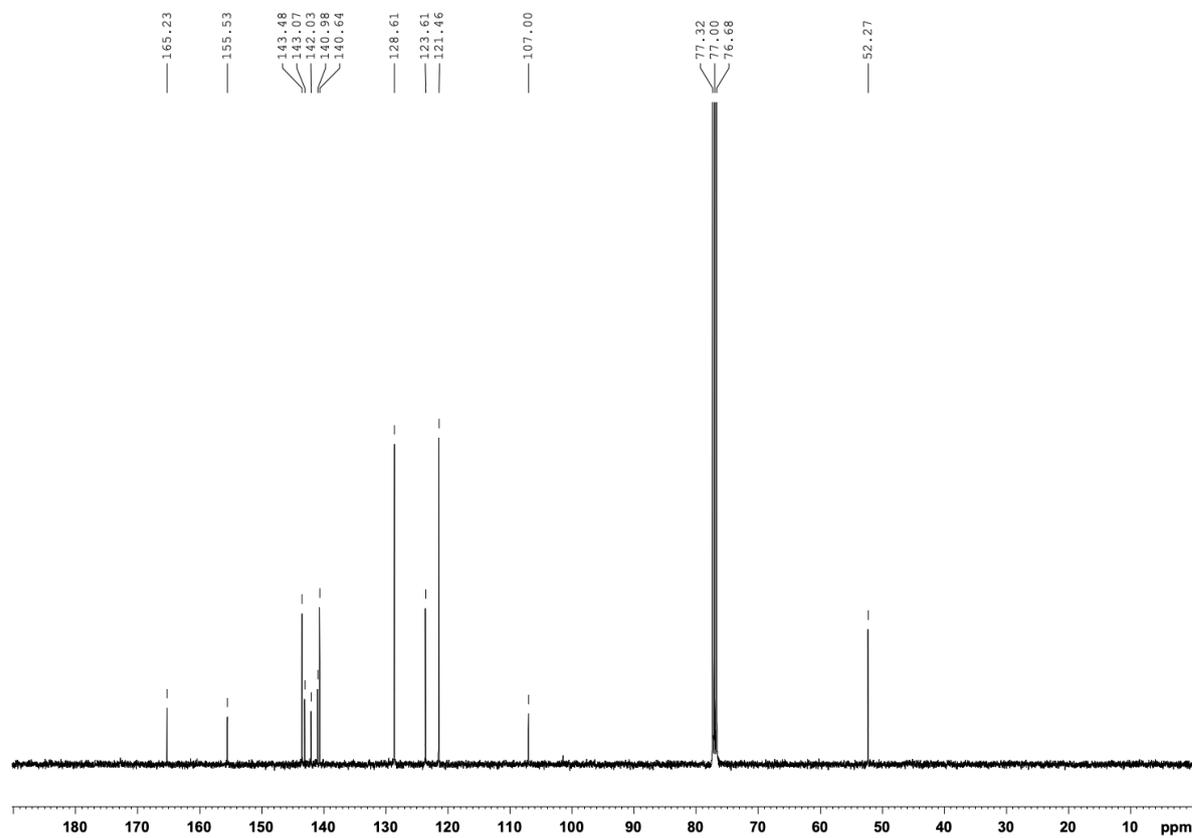


Methyl 7-(phenylamino)thieno[2,3-*b*]pyrazine-6-carboxylate **2a**

^1H NMR (CDCl_3 , 400 MHz) of compound **2a**

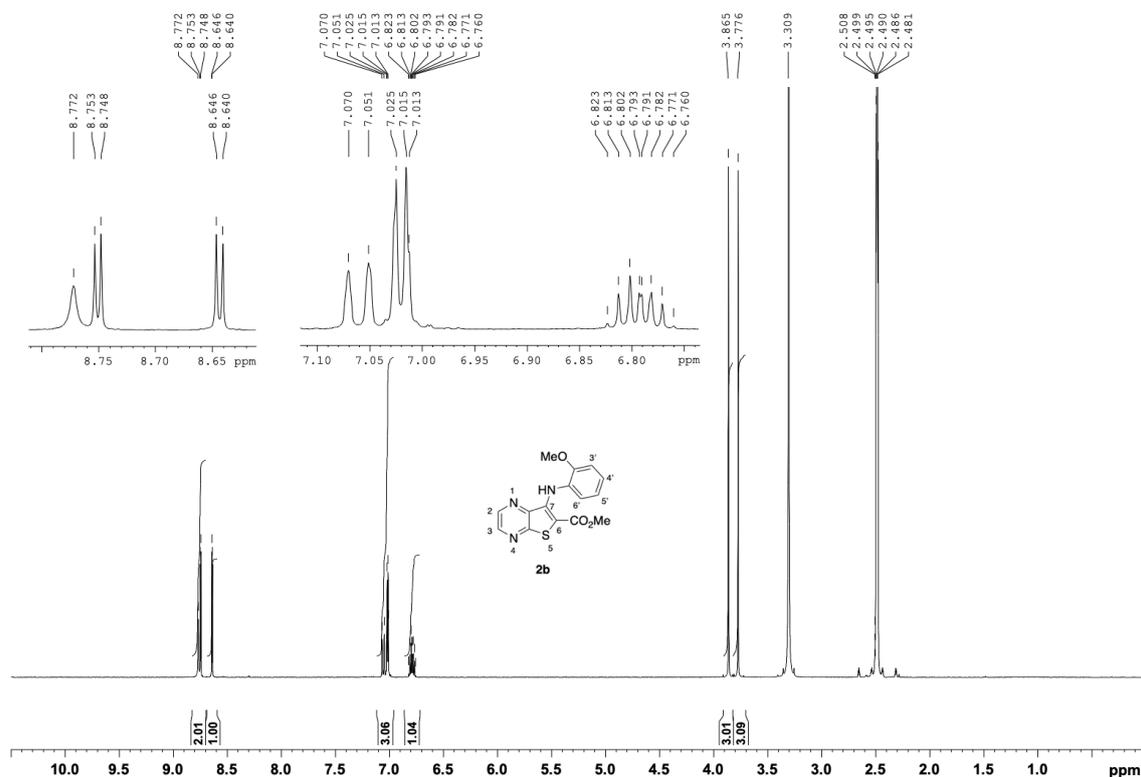


^{13}C NMR (CDCl_3 , 100.6 MHz) of compound **2a**

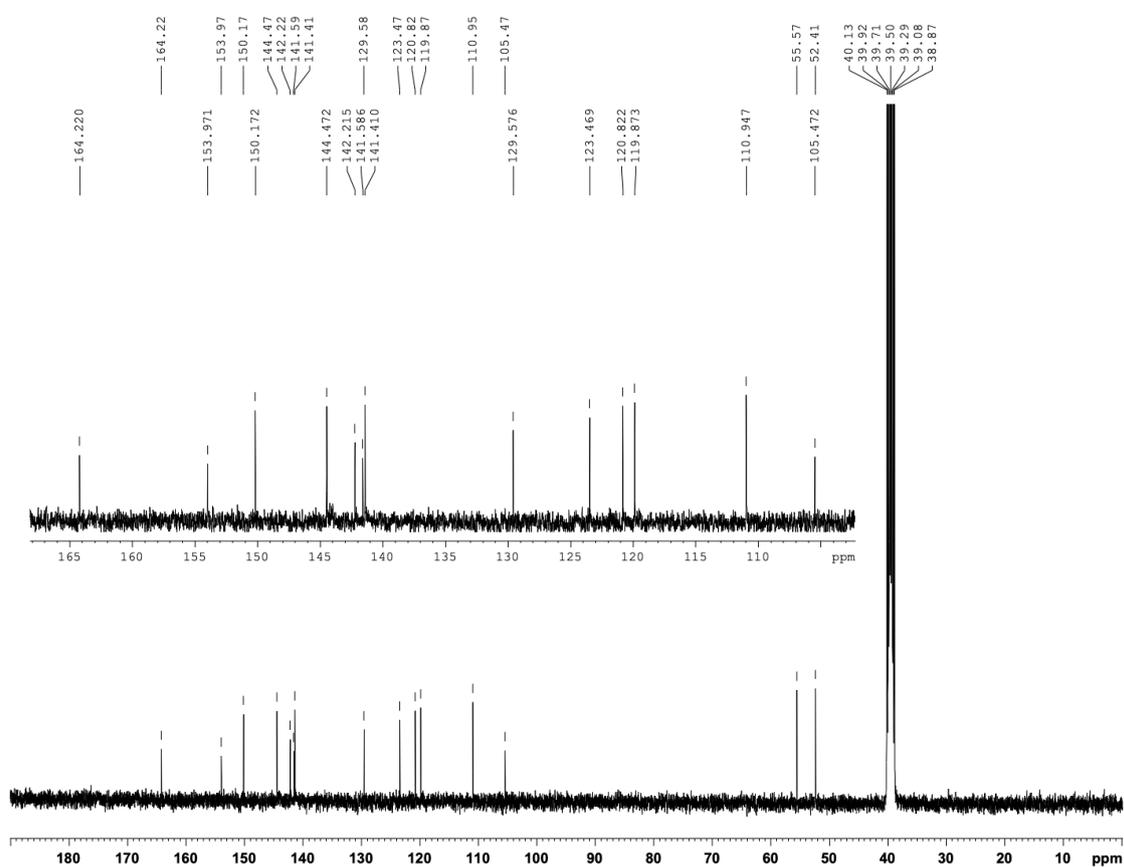


Methyl 7-[(2-methoxyphenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate **2b**

^1H NMR (DMSO- d_6 , 400 MHz) of compound **2b**

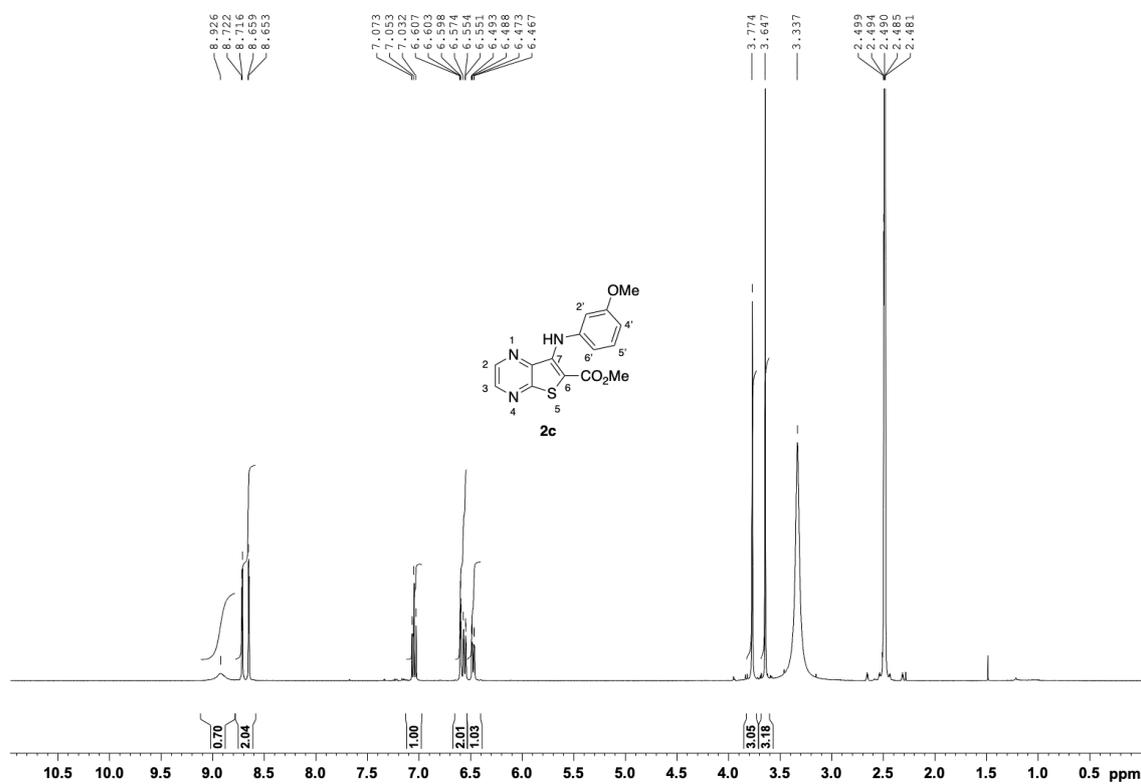


^{13}C NMR (DMSO- d_6 , 100.6 MHz) of compound **2b**

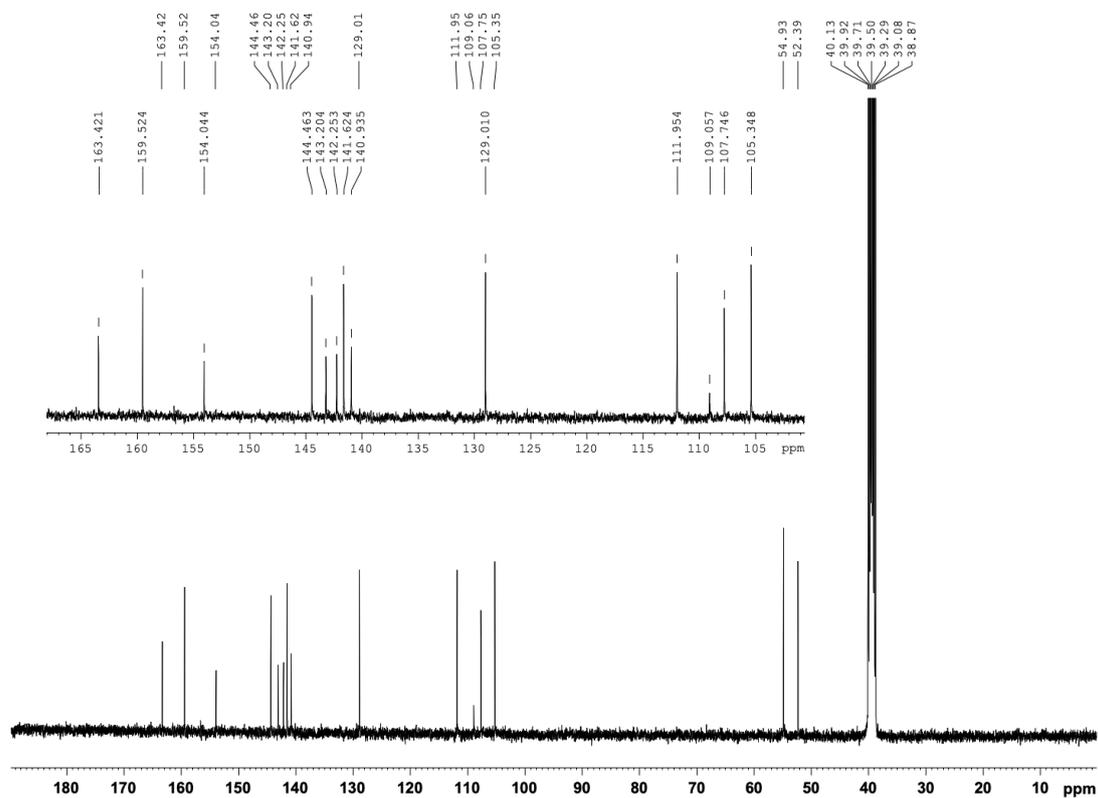


Methyl 7-[(3-methoxyphenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate **2c**

^1H NMR (DMSO- d_6 , 400 MHz) of compound **2c**

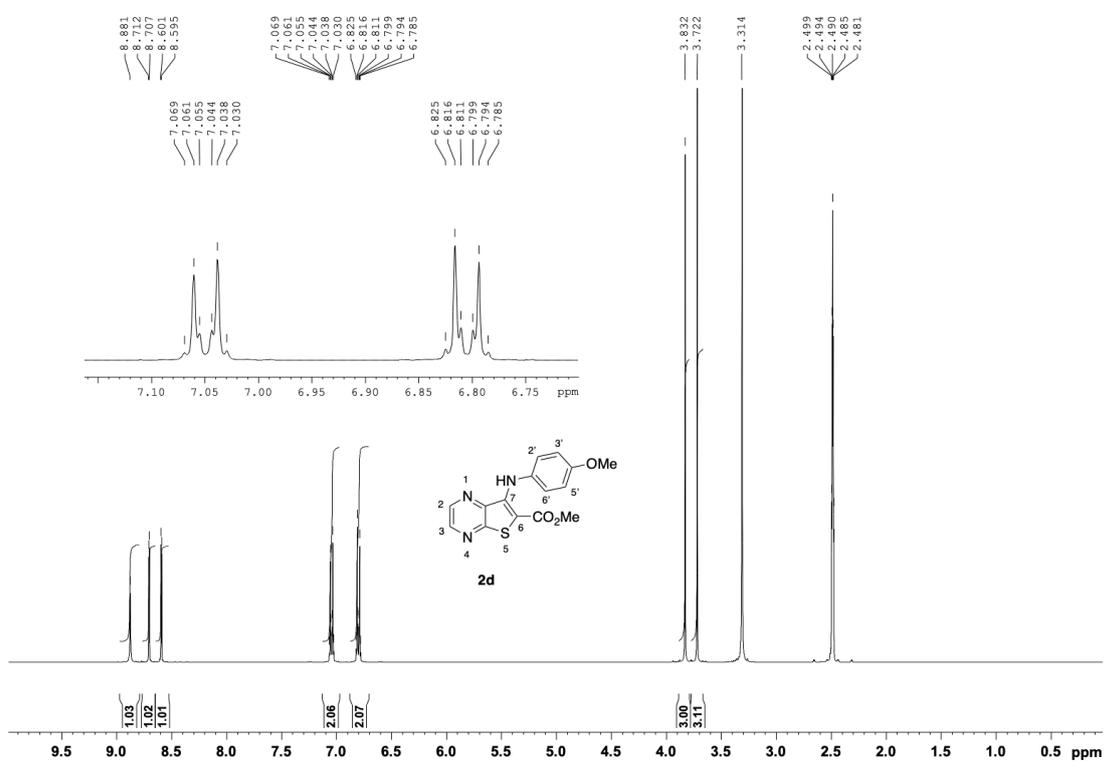


^{13}C NMR (DMSO- d_6 , 100.6 MHz) of compound **2c**

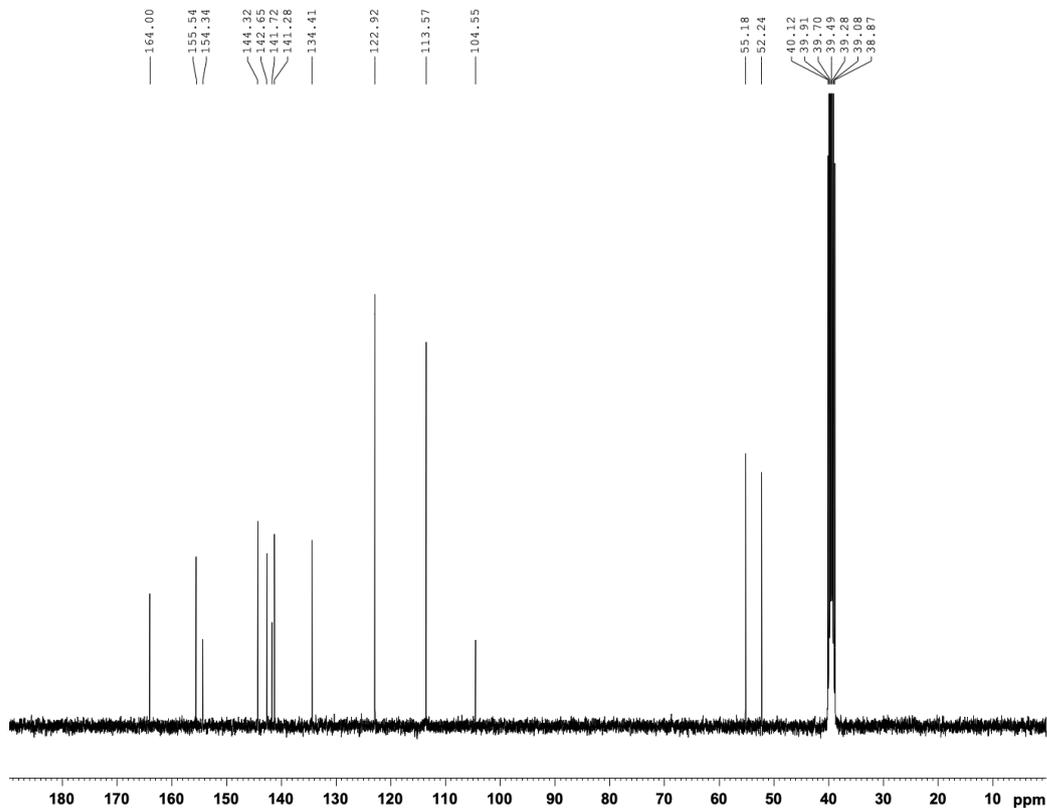


Methyl 7-[(4-methoxyphenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate **2d**

^1H NMR (DMSO- d_6 , 400 MHz) of compound **2d**

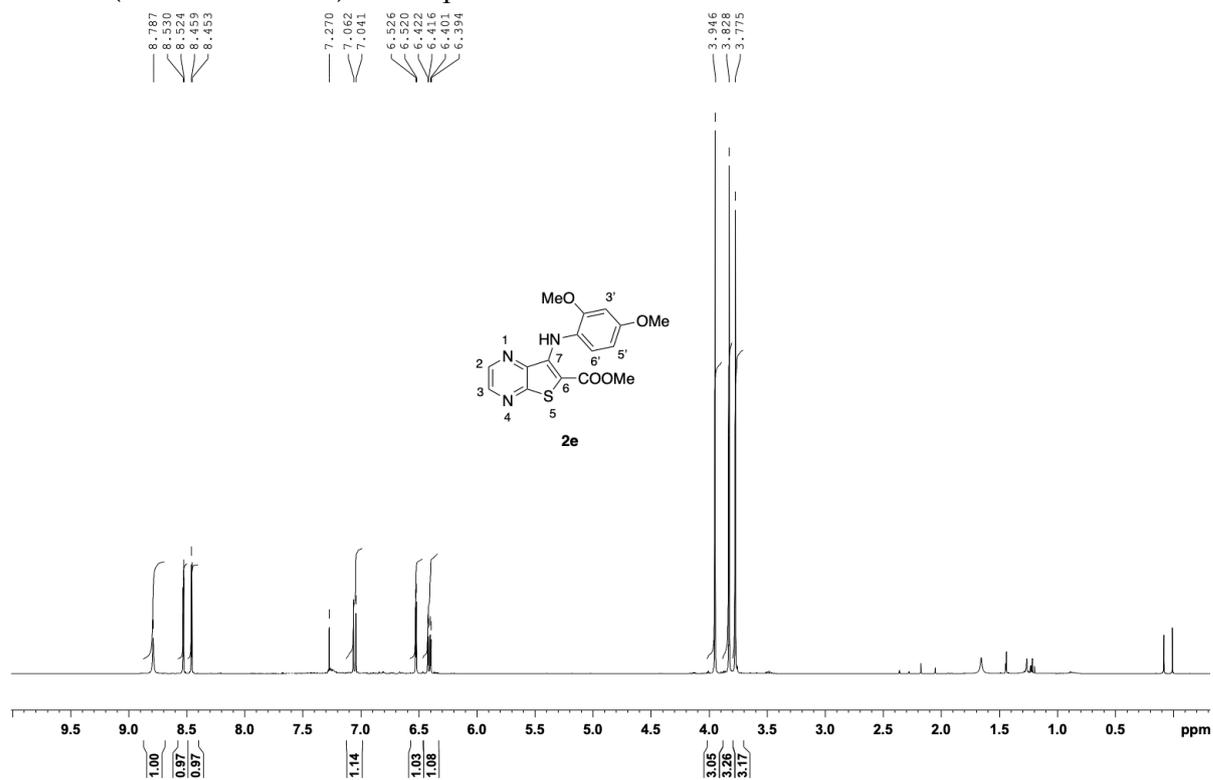


^{13}C NMR (DMSO- d_6 , 100.6 MHz) of compound **2d**

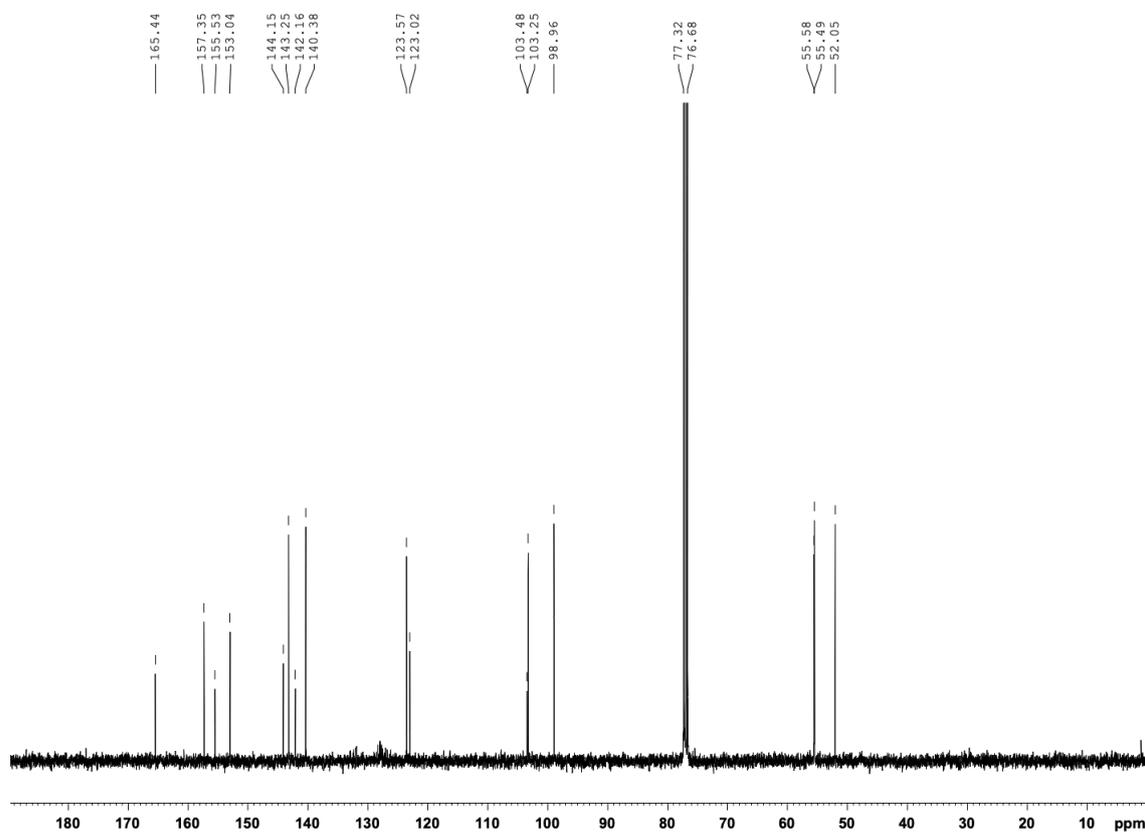


Methyl 7-[(2,4-dimethoxyphenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate **2e**

^1H NMR (CDCl_3 , 400 MHz) of compound **2e**

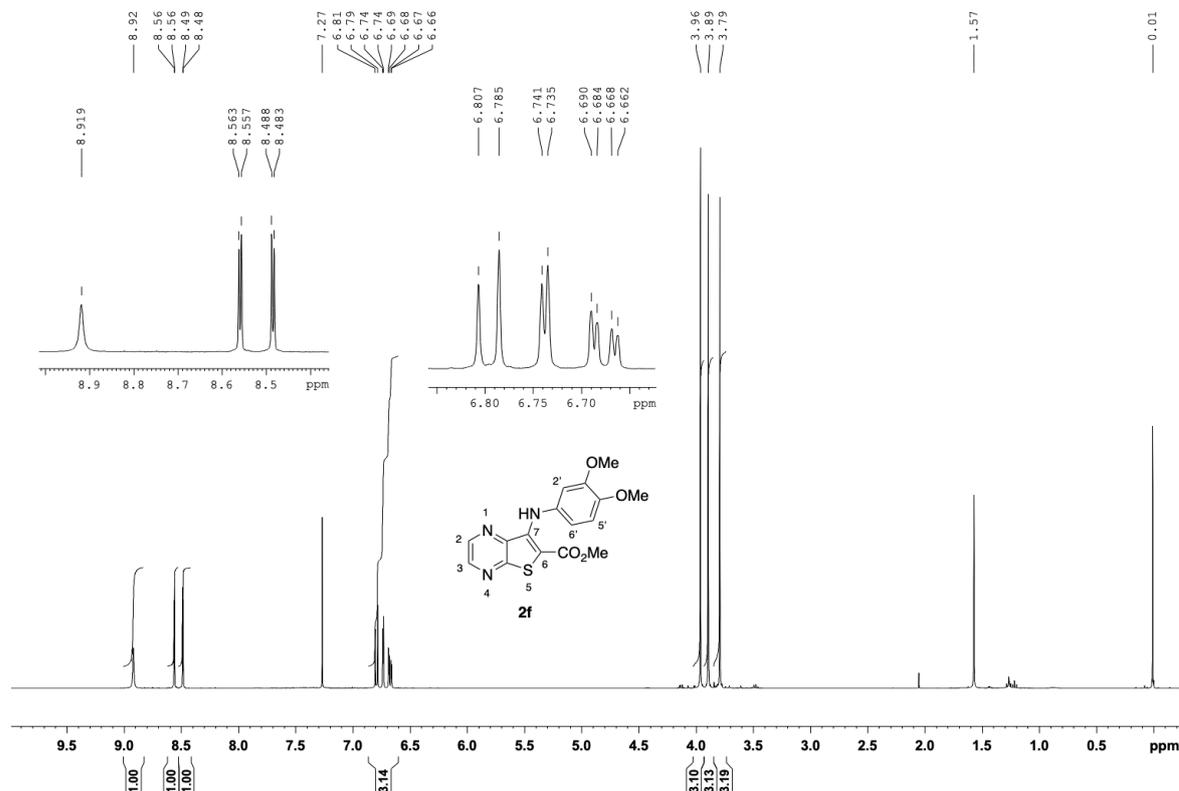


^{13}C NMR (CDCl_3 , 100.6 MHz) of compound **2e**

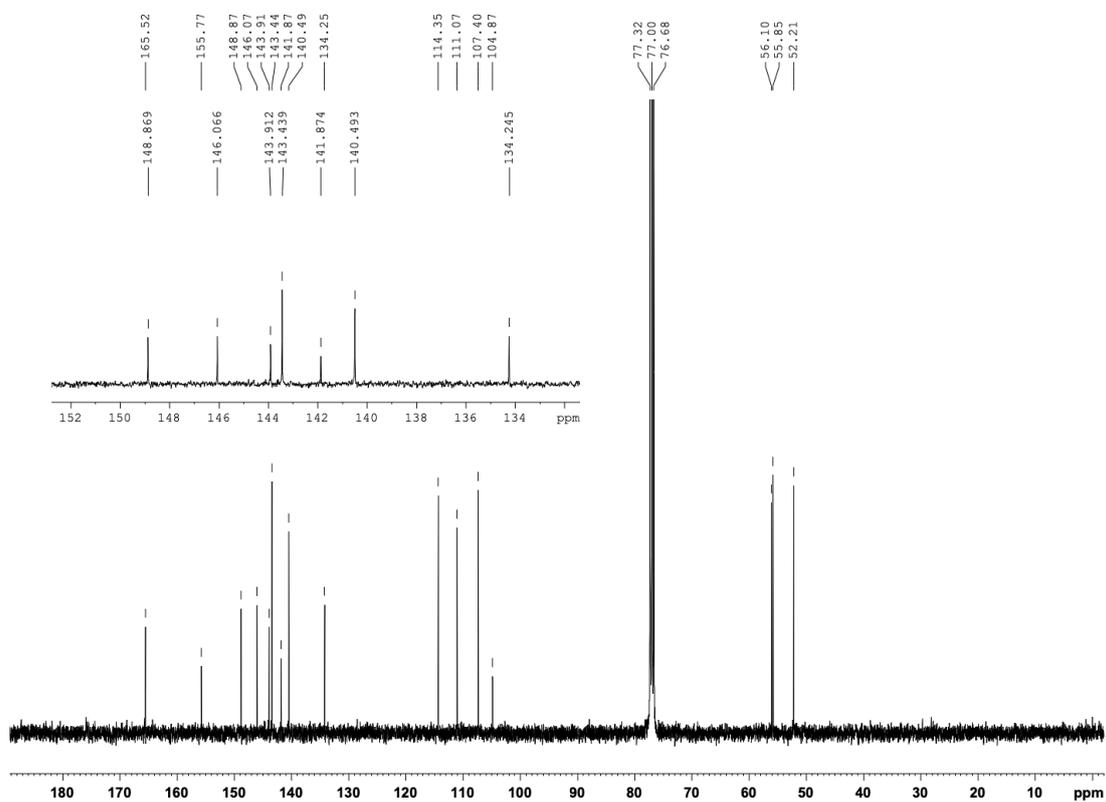


Methyl 7-[(3,4-dimethoxyphenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate **2f**

^1H NMR (CDCl_3 , 400 MHz) of compound **2f**

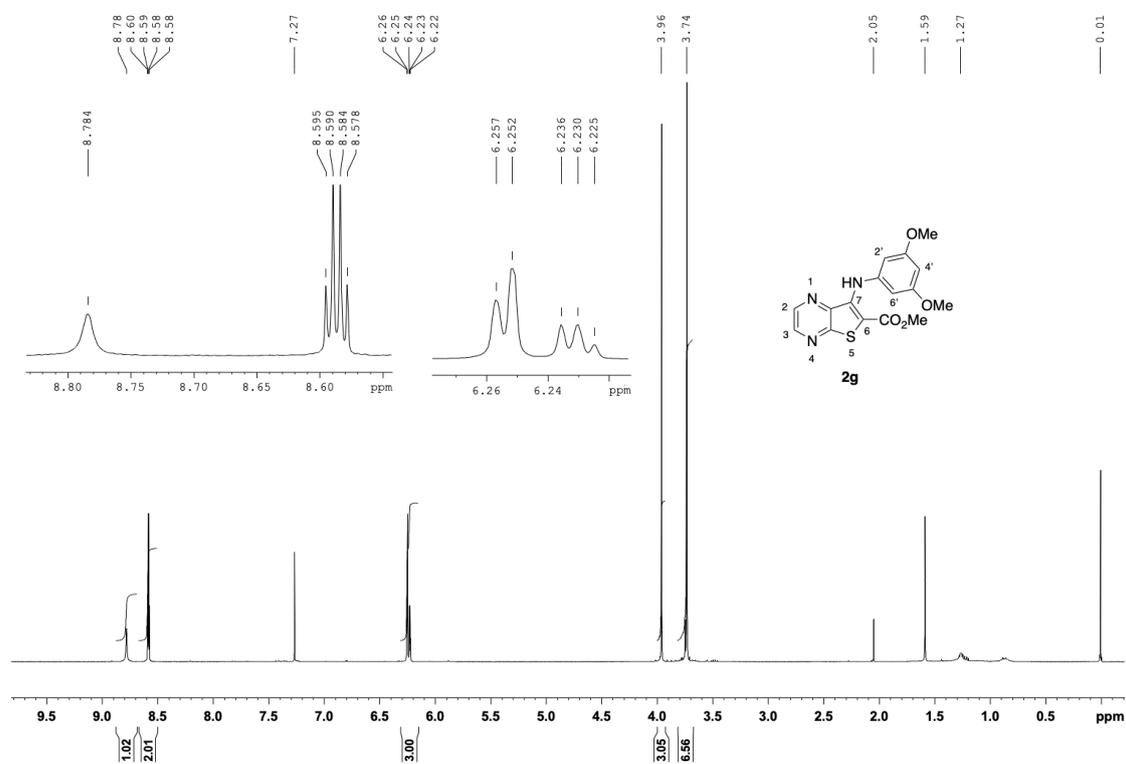


^{13}C NMR (CDCl_3 , 100.6 MHz) of compound **2f**

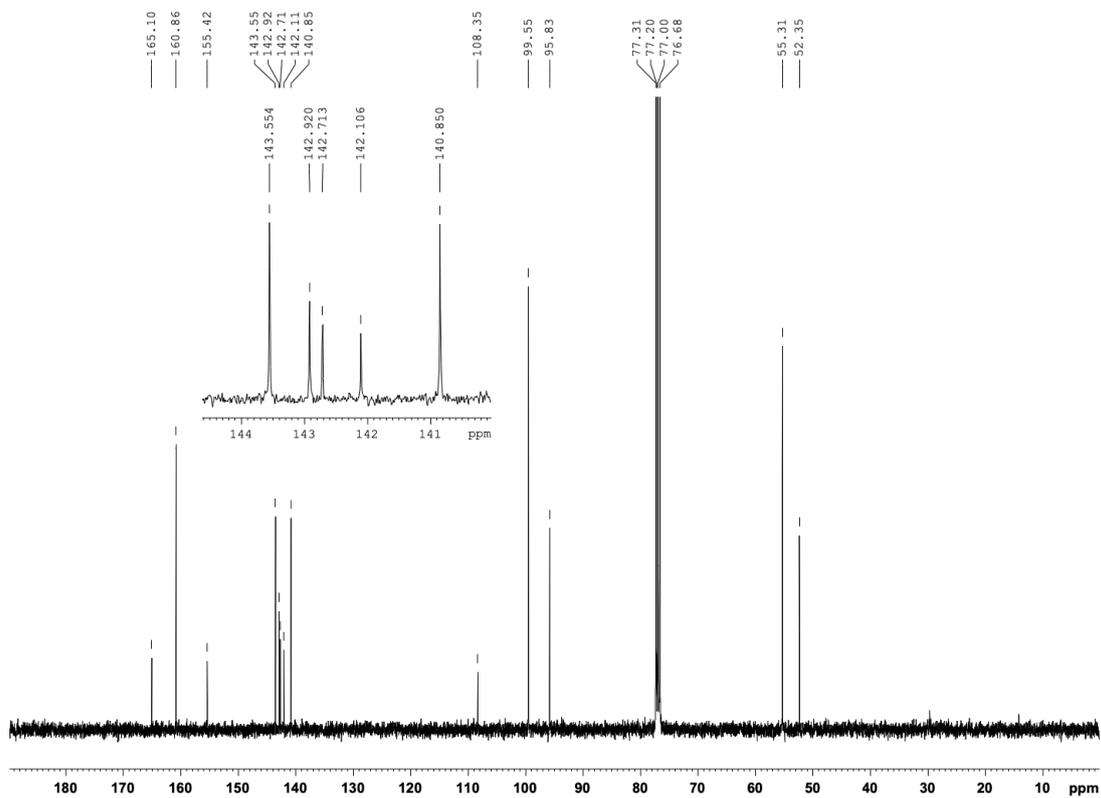


Methyl 7-[(3,5-dimethoxyphenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate **2g**

^1H NMR (CDCl_3 , 400 MHz) of compound **2g**

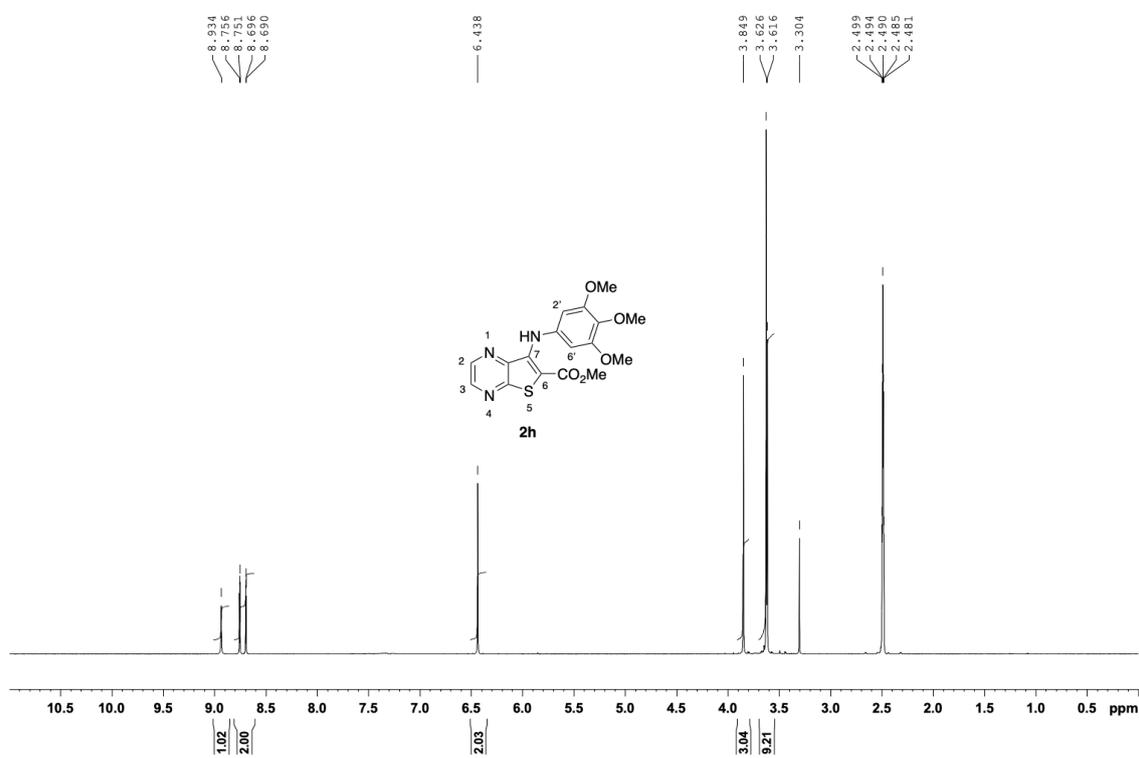


^{13}C NMR (CDCl_3 , 100.6 MHz) of compound **2g**

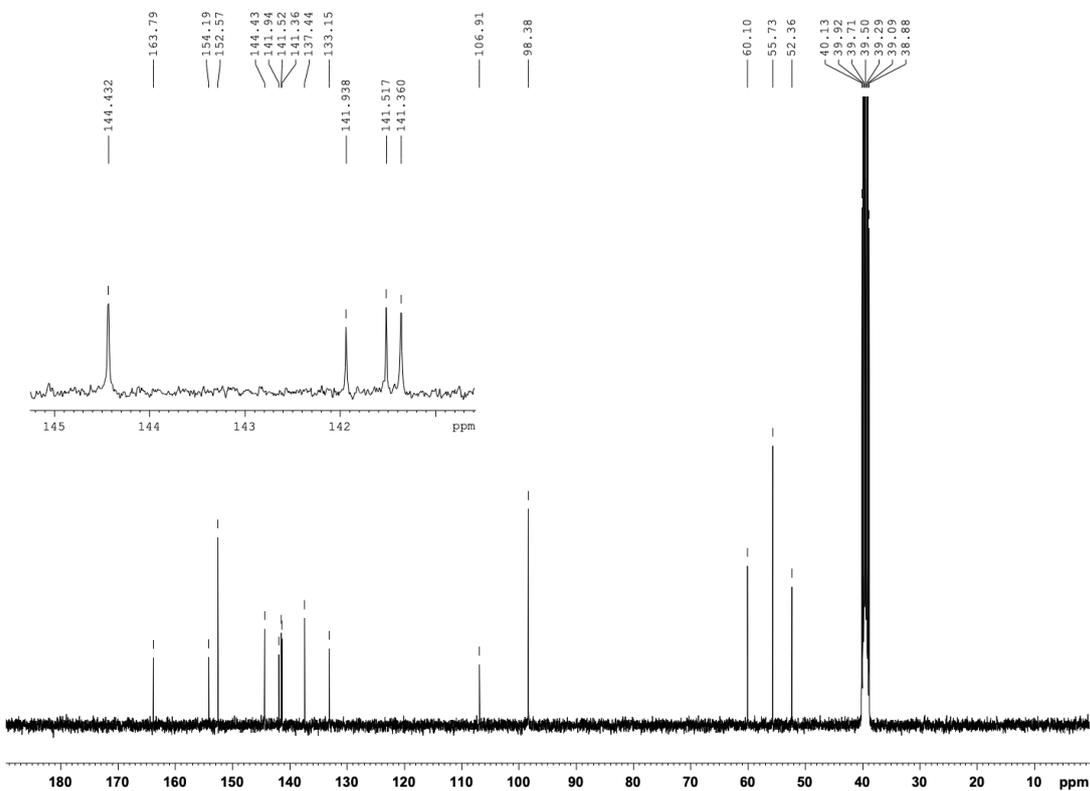


Methyl 7-[(3,4,5-trimethoxyphenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate 2h

¹H NMR (DMSO-*d*₆, 400 MHz) of compound 2h

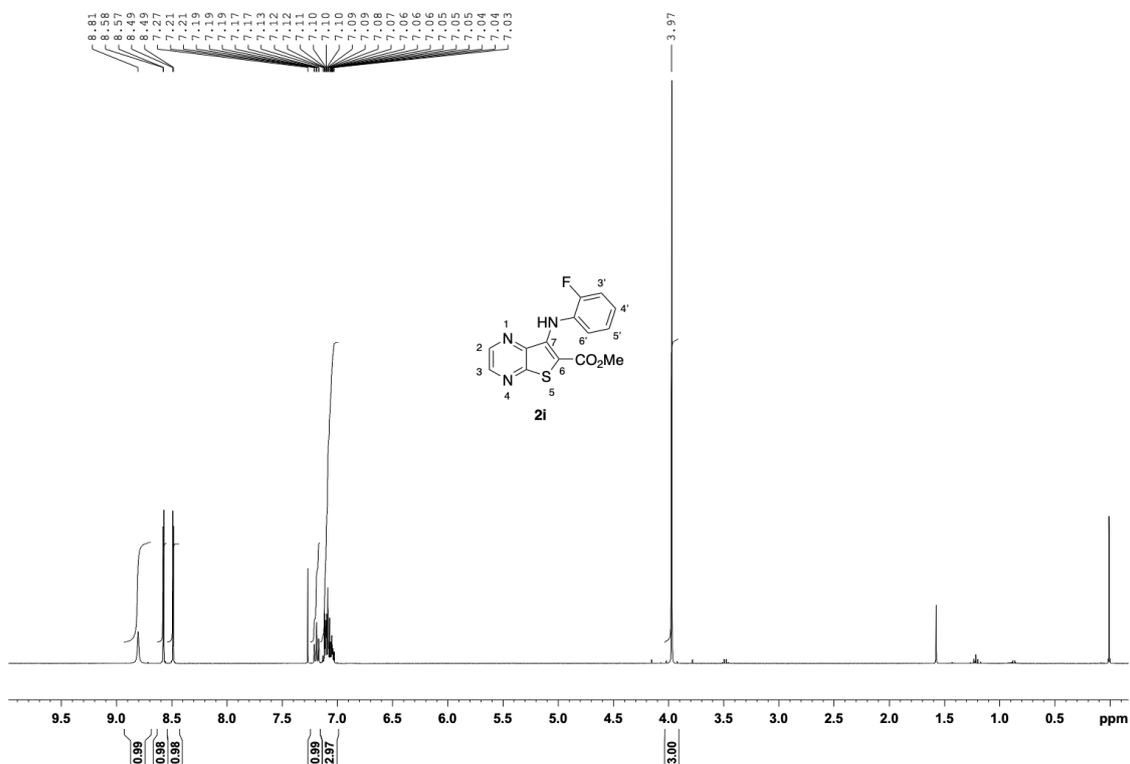


¹³C NMR (DMSO-*d*₆, 100.6 MHz) of compound 2h

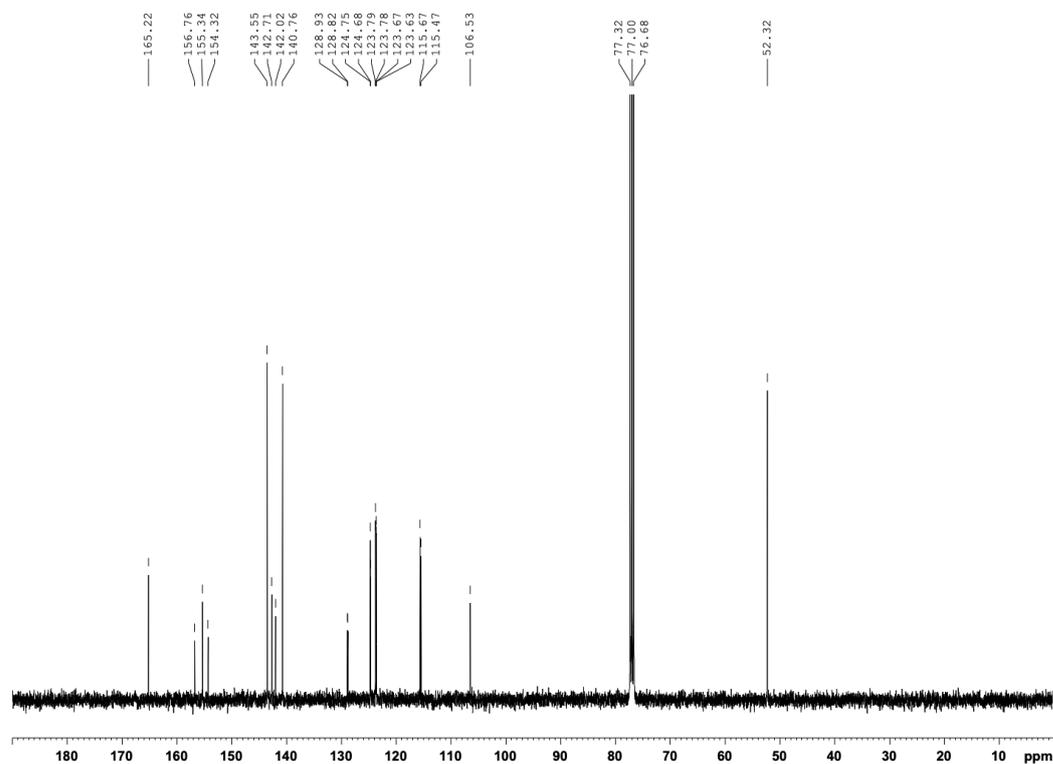


Methyl 7-[(2-fluorophenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate **2i**

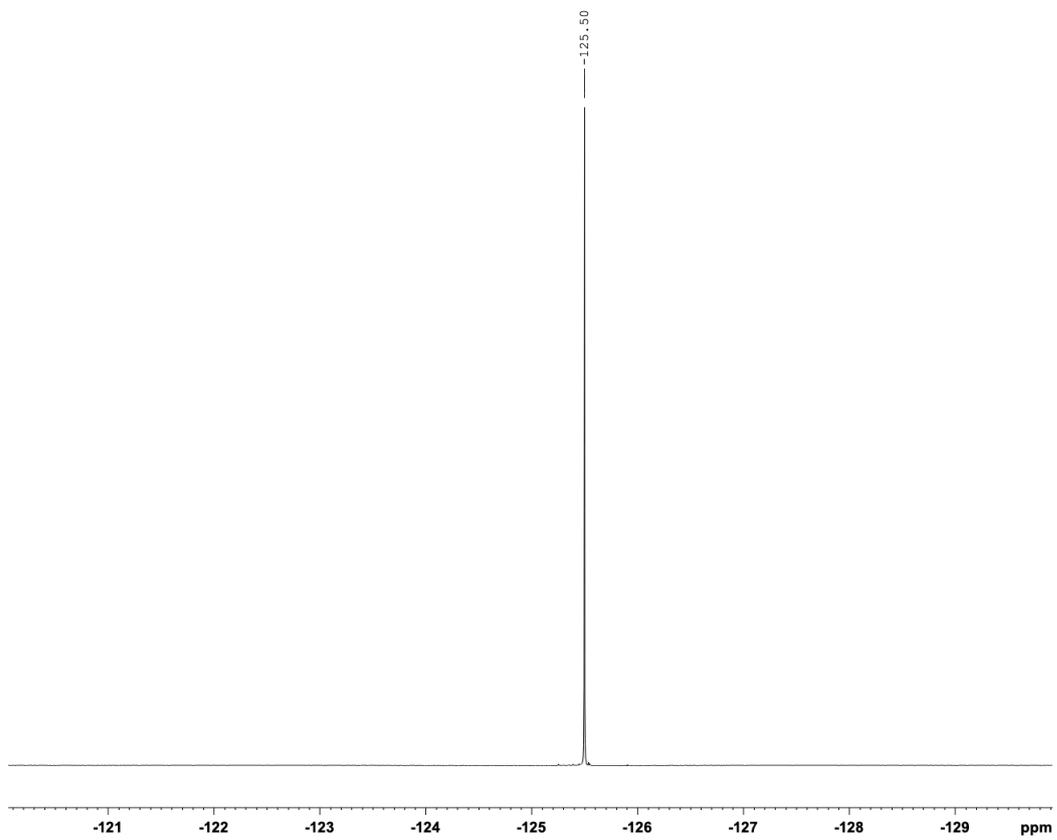
^1H NMR (CDCl_3 , 400 MHz) of compound **2i**



^{13}C NMR (CDCl_3 , 100.6 MHz) of compound **2i**

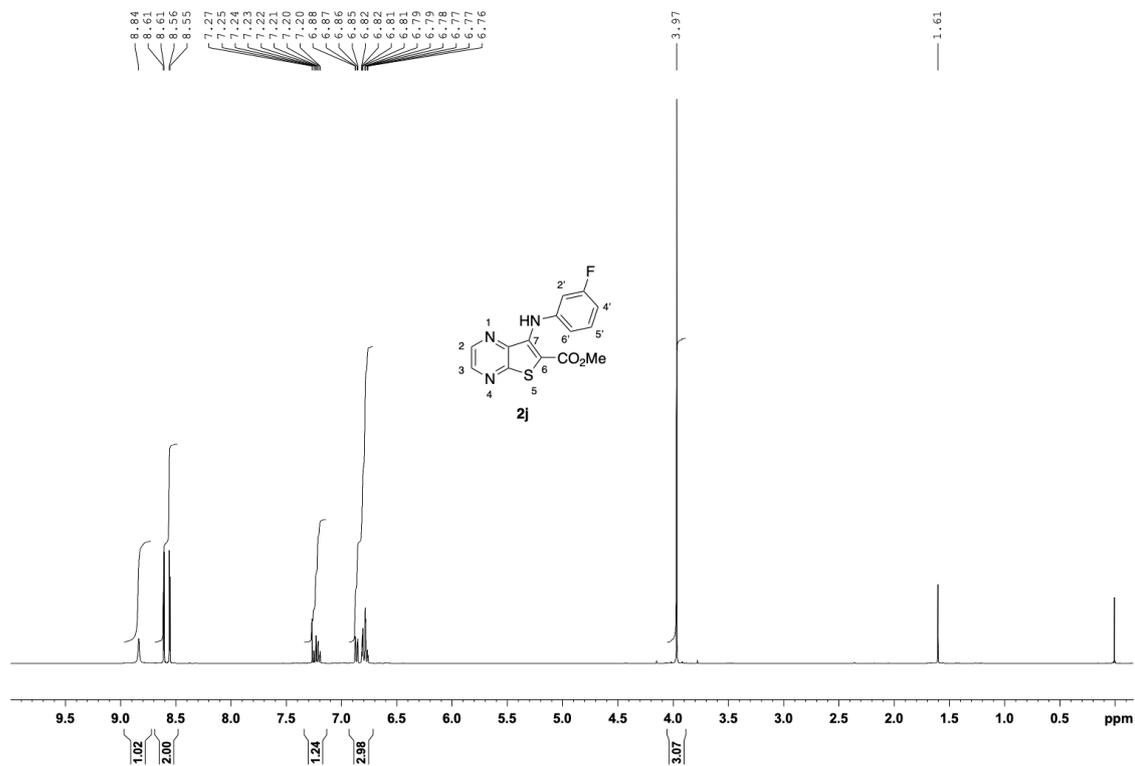


^{19}F NMR (CDCl_3 , 376.48 MHz) of compound **2i**

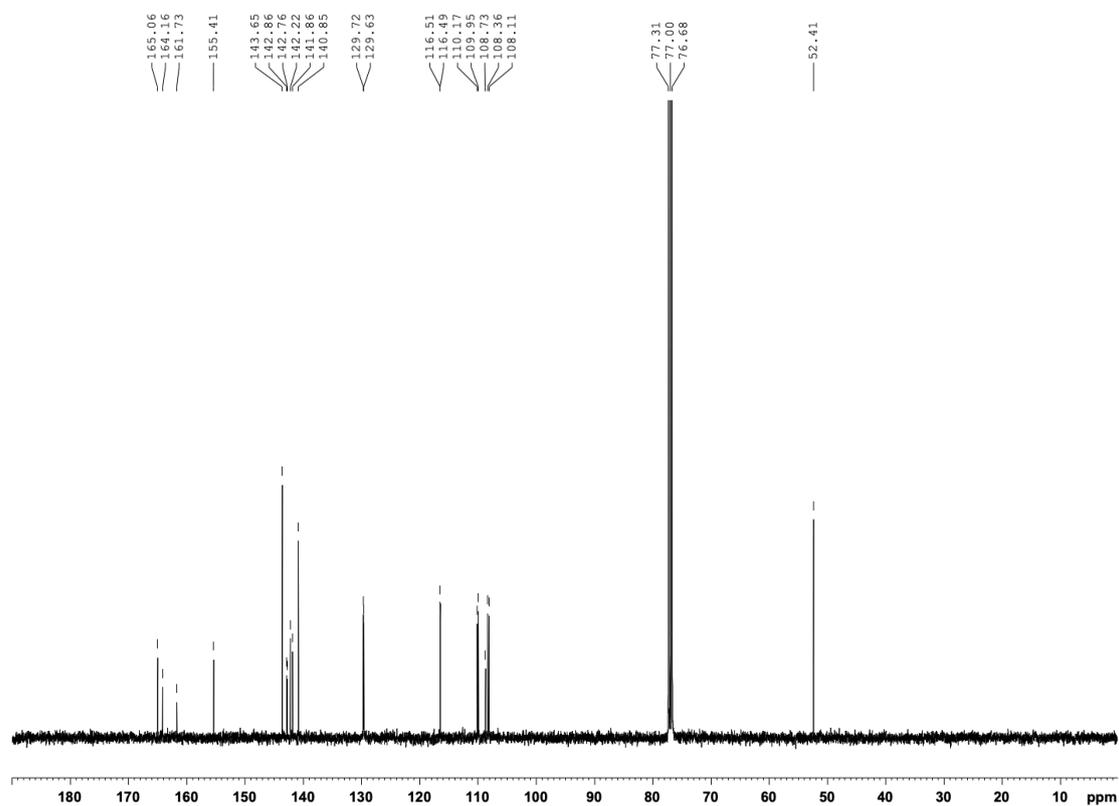


Methyl 7-[(3-fluorophenyl)amino]thieno[2,3-b]pyrazine-6-carboxylate 2j

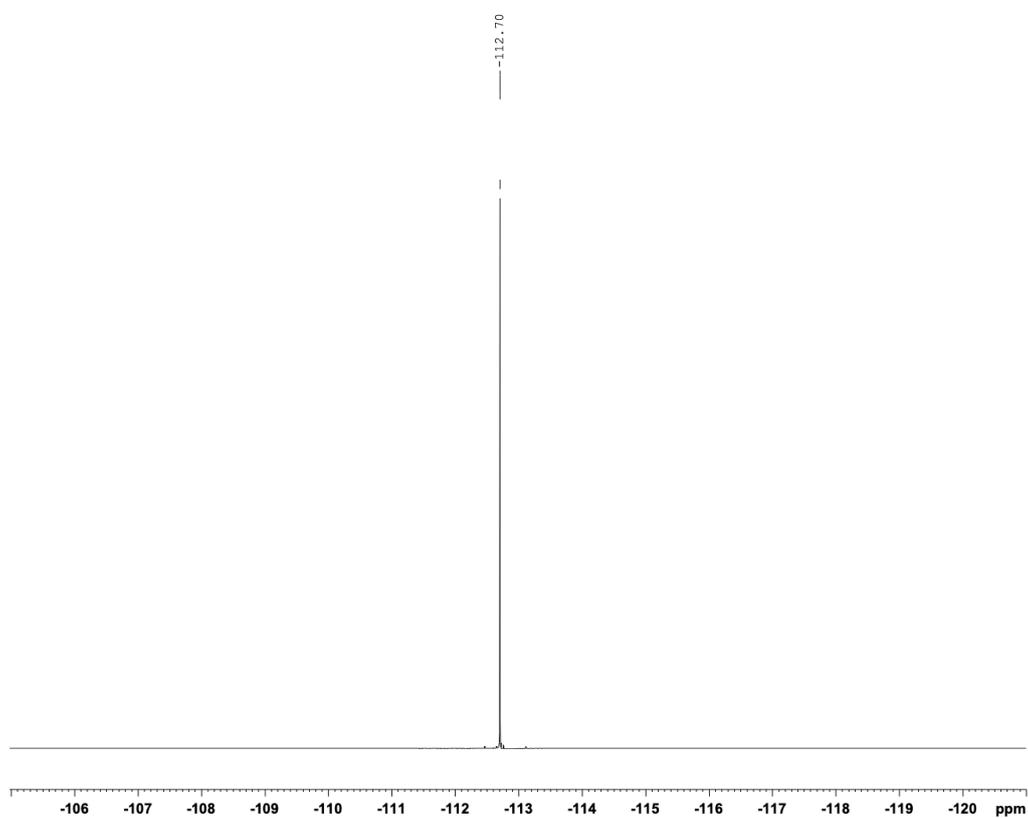
^1H NMR (CDCl_3 , 400 MHz) of compound 2j



^{13}C NMR (CDCl_3 , 100.6 MHz) of compound 2j

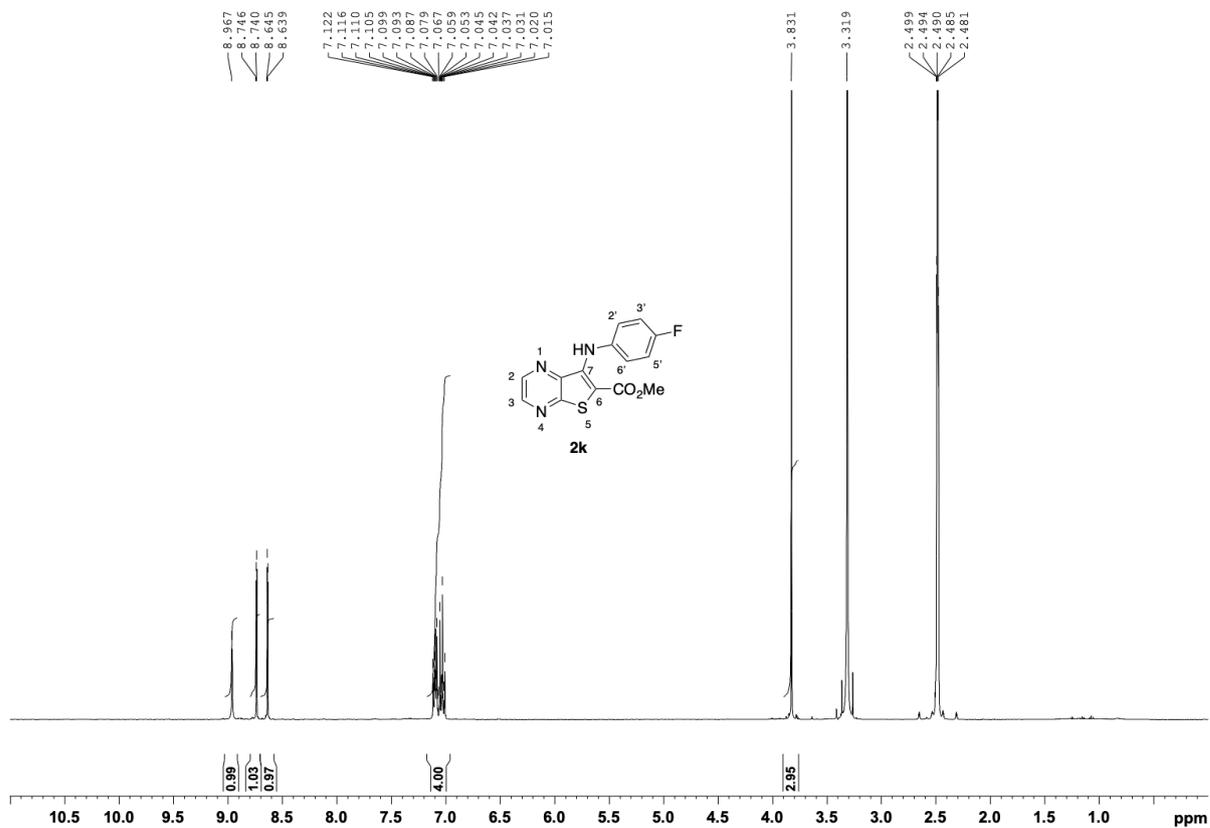


^{19}F NMR (CDCl_3 , 376.48 MHz) of compound **2j**

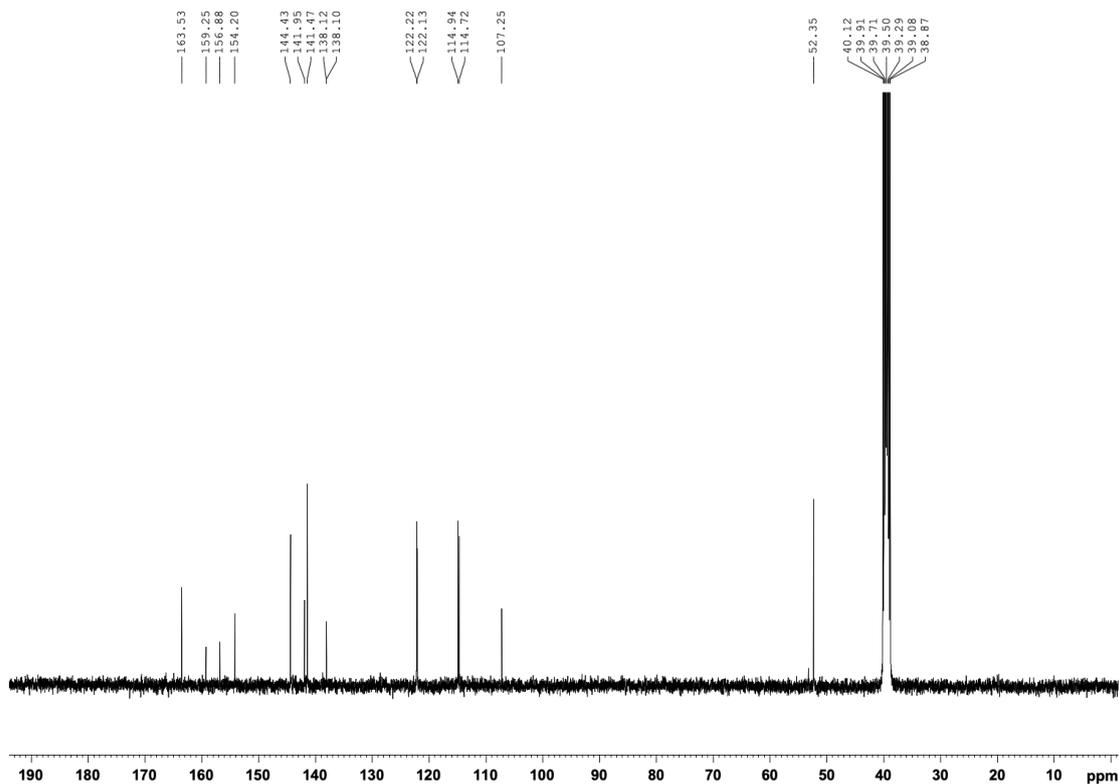


Methyl 7-[(4-fluorophenyl)amino]thieno[2,3-b]pyrazine-6-carboxylate **2k**

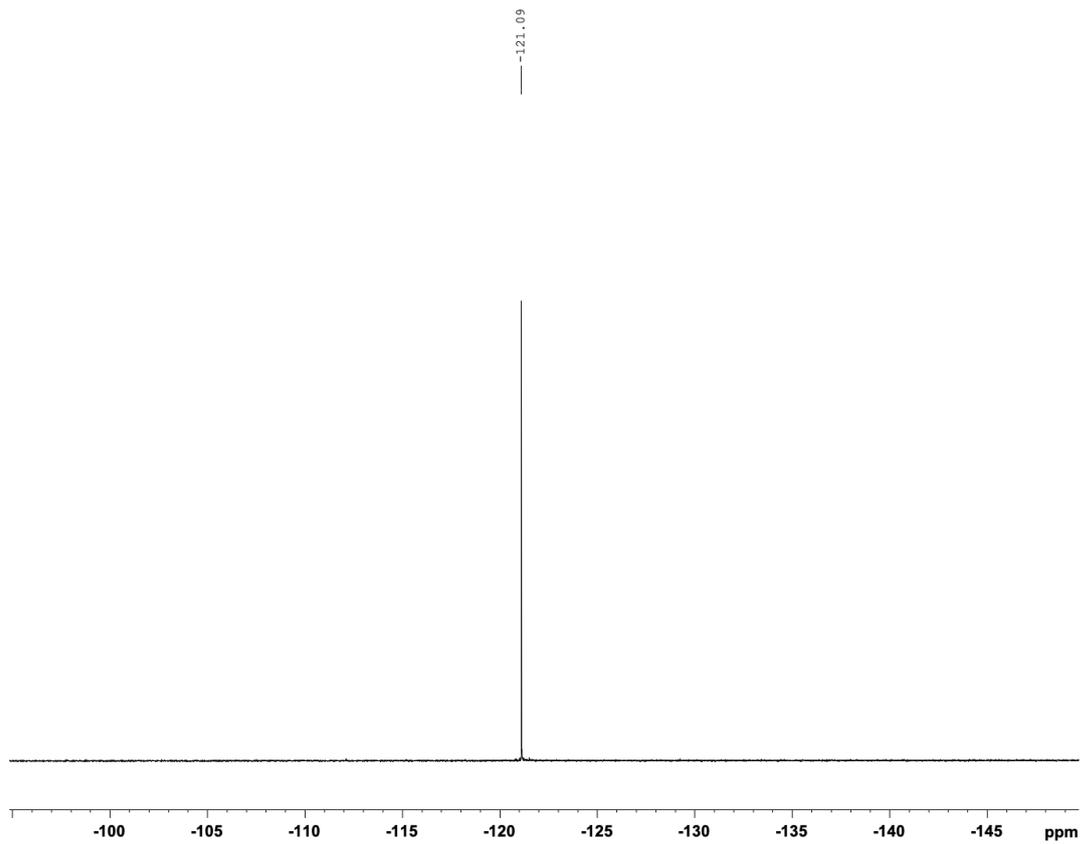
^1H NMR (DMSO- d_6 , 400 MHz) of compound **2k**



^{13}C NMR (DMSO- d_6 , 100.6 MHz) of compound **2k**

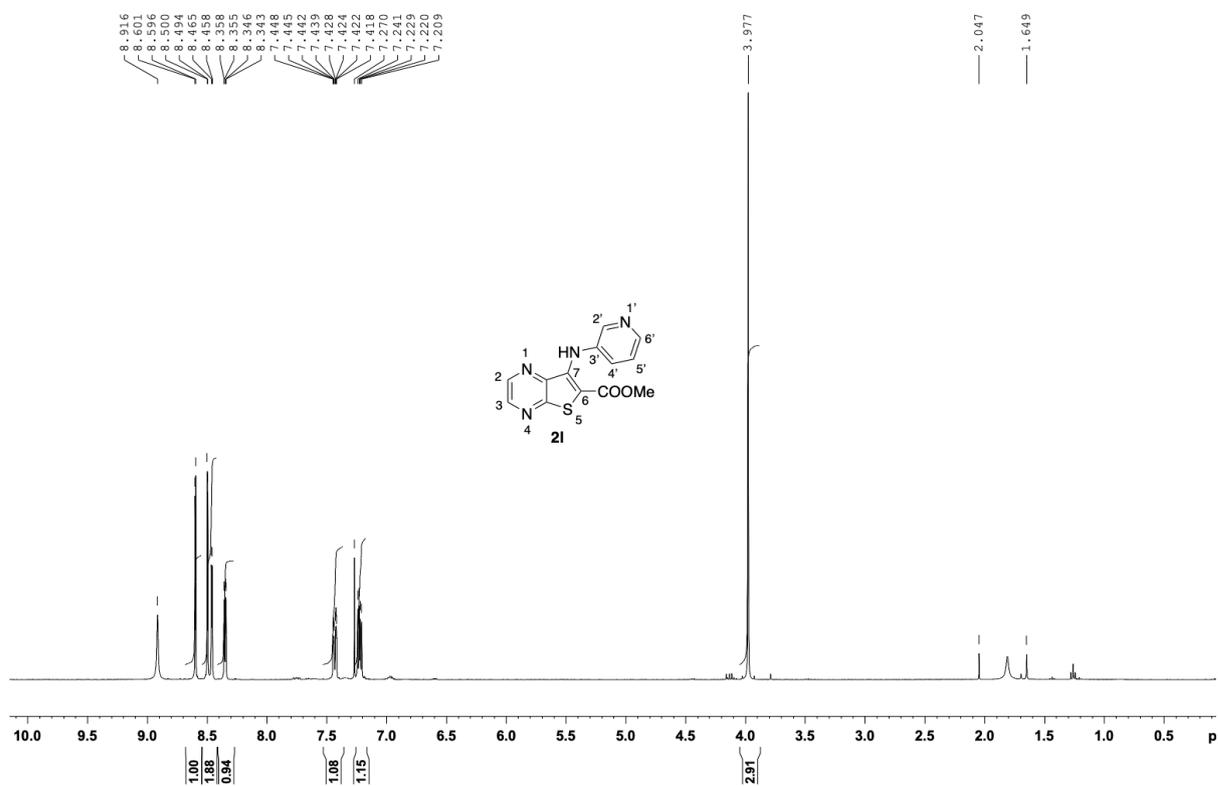


^{19}F NMR (DMSO- d_6 , 376.48 MHz) of compound **2k**

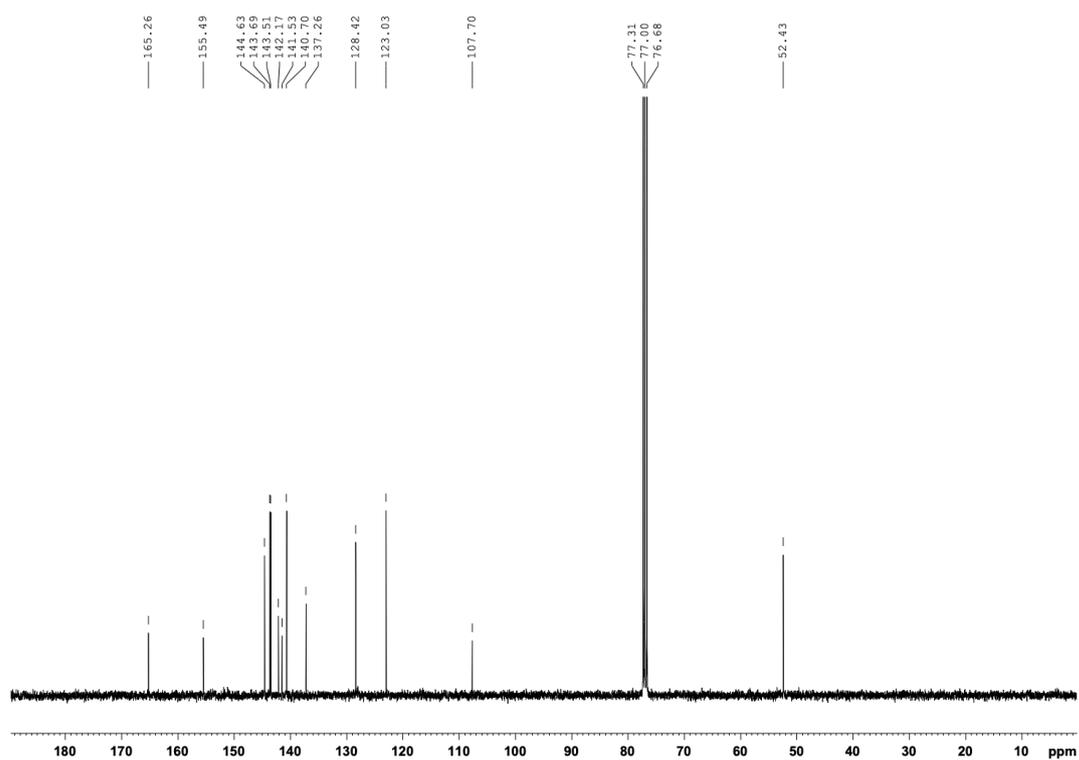


Methyl 7-(pyridin-3-ylamino)thieno[2,3-*b*]pyrazine-6-carboxylate 21

^1H NMR (CDCl_3 , 400 MHz) of compound 21

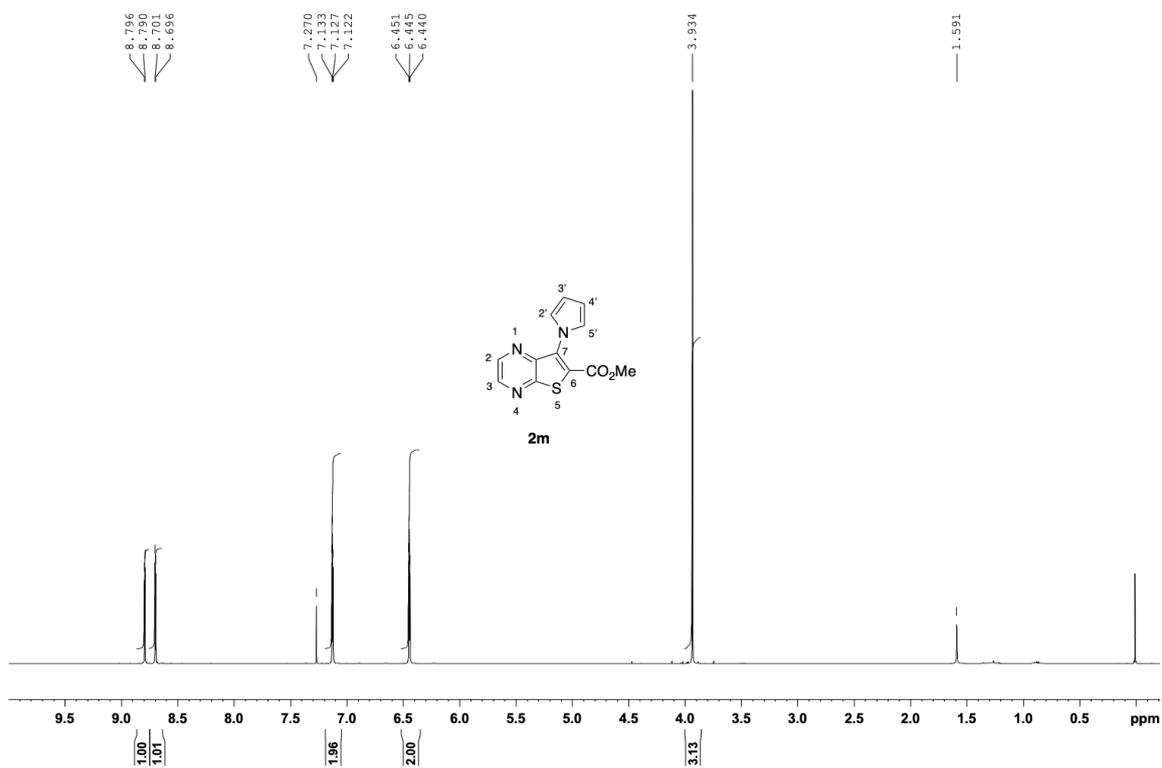


^{13}C NMR (CDCl_3 , 100.6 MHz) of compound 21

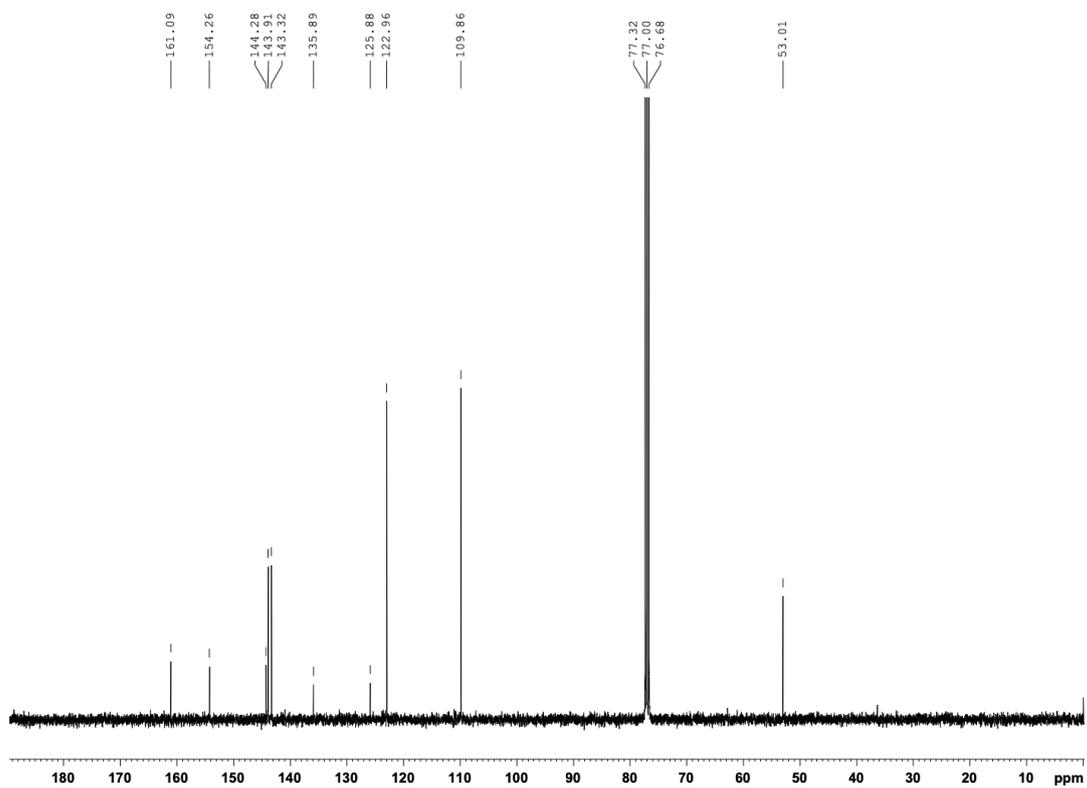


Methyl 7-(1*H*-pyrrol-1-yl)thieno[2,3-*b*]pyrazine-6-carboxylate **2m**

¹H NMR (CDCl₃, 400 MHz) of compound **2m**

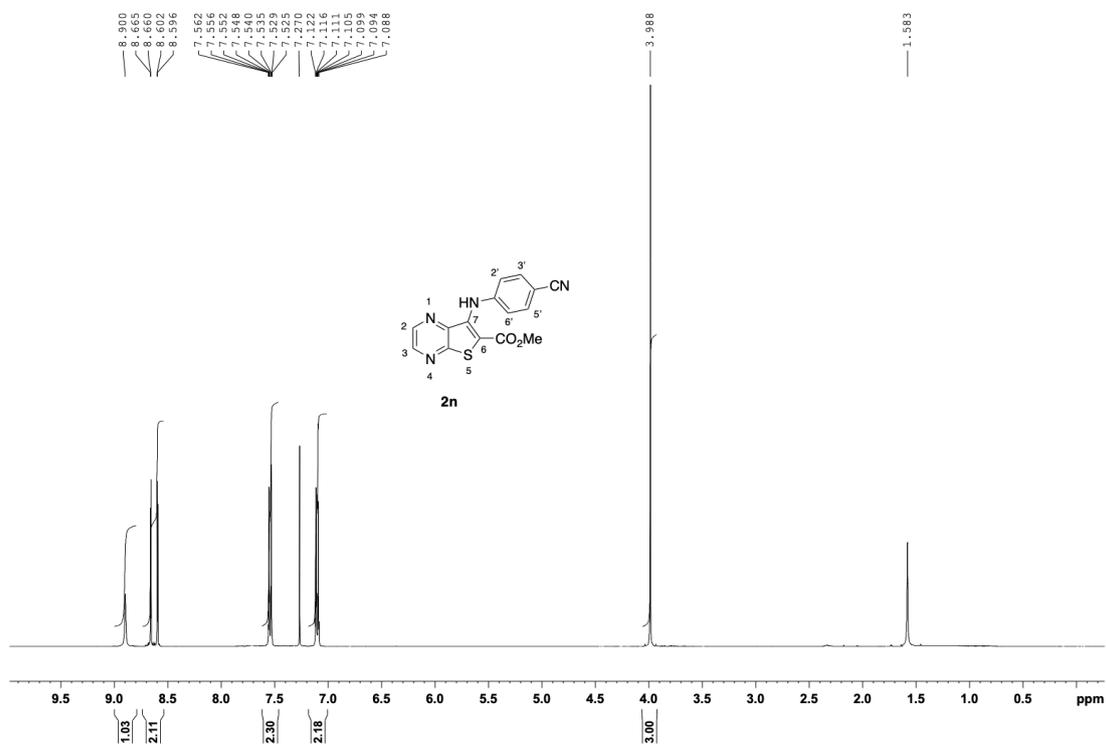


¹³C NMR (CDCl₃, 100.6 MHz) of compound **2m**

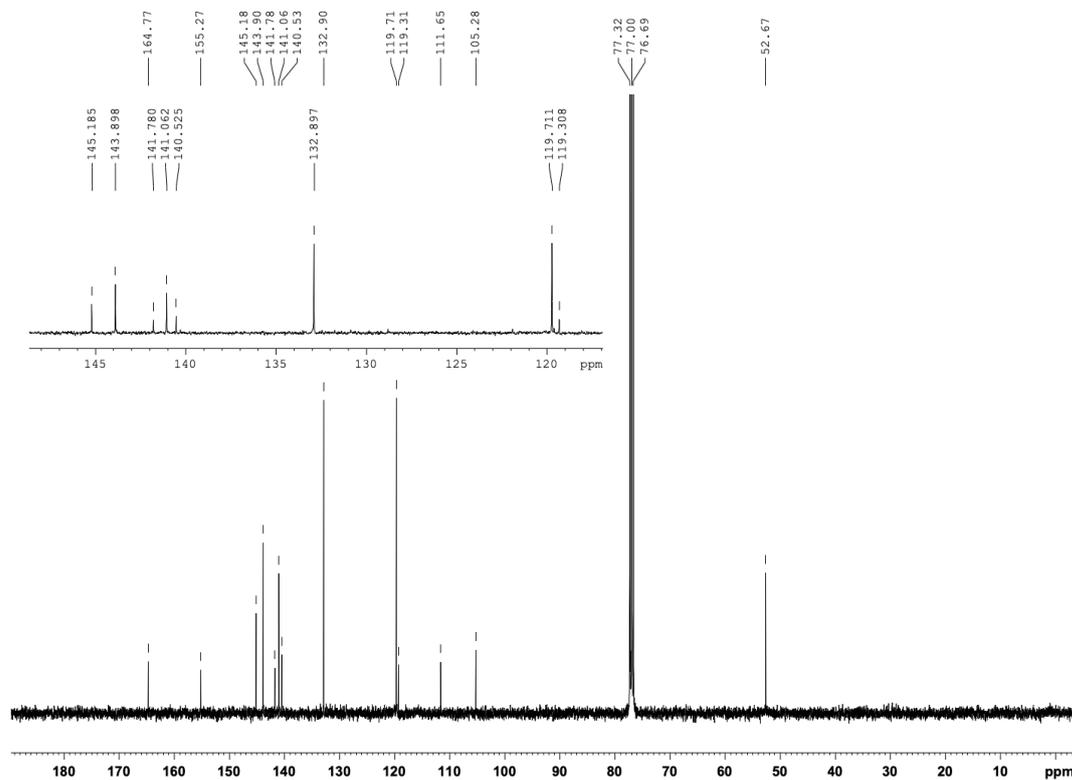


Methyl 7-[(4-cyanophenyl)amino]thieno[2,3-*b*]pyrazine-6-carboxylate 2n

^1H NMR (CDCl_3 , 400 MHz) of compound 2n

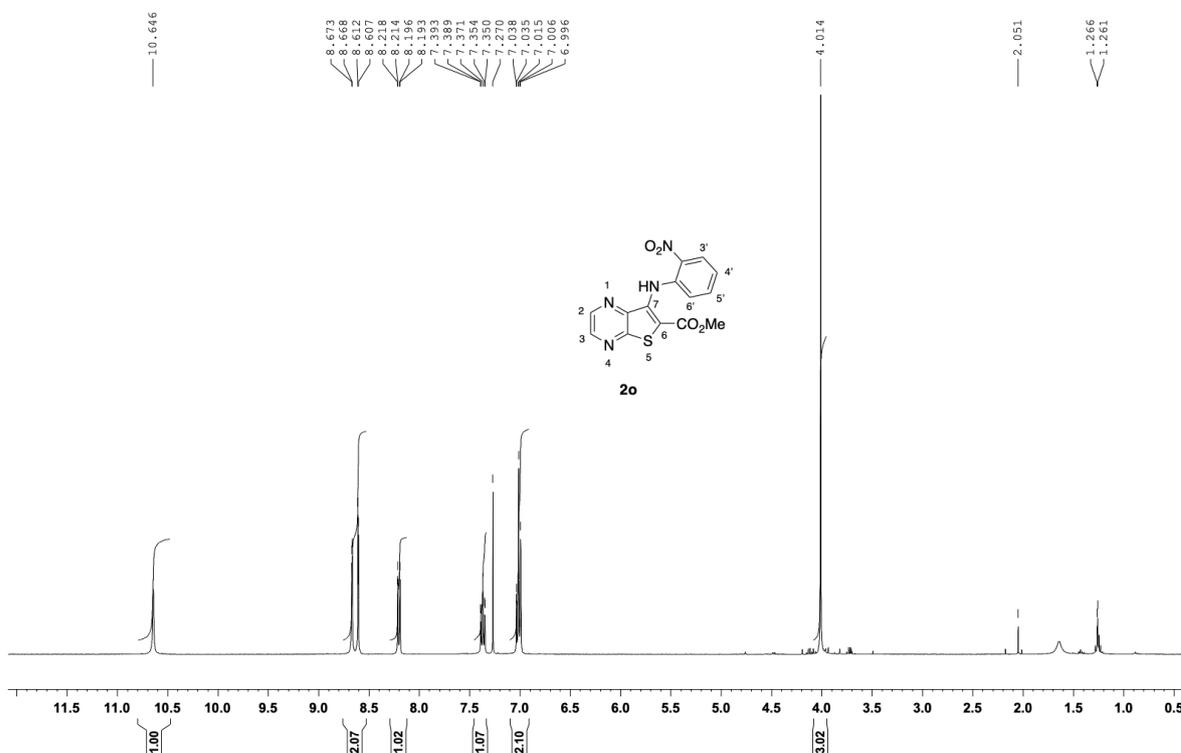


^{13}C NMR (CDCl_3 , 100.6 MHz) of compound 2n



Methyl 7-[(2-nitrophenyl)amino]thieno[2,3-b]pyrazine-6-carboxylate 2o

^1H NMR (CDCl_3 , 400 MHz) of compound 2o



^{13}C NMR (CDCl_3 , 100.6 MHz) of compound 2o

