Supplementary Information

Metal-Free Regioselective Direct Thiolation of 2-Pyridones

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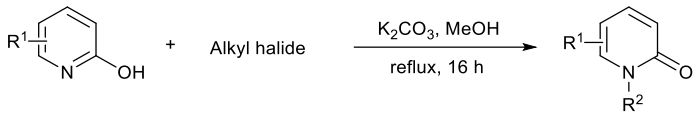
I. Substrate Preparation

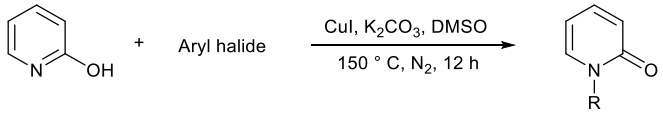
General Procedure for the Preparation of *N*-Alkylated Pyridone Substrates:



To a suspension of 2-hydroxypyridine (5 mmol, 1 equiv.) in MeOH (20 mL), K_2CO_3 (7.5 mmol, 1.5 equiv.) and alkyl halide (7.5 mmol, 1.5 equiv.) were added. The reaction mixture was heated to reflux for 16 h. Upon completion, the solvent was evaporated, distilled deionized H_2O (20 mL) was added, and the mixture was extracted with ethyl acetate (EtOAc) (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting organic residue was purified by flash chromatography column over silica gel (SiO_2) to afford the *N*-alkylated pyridones.

The *N*-alkylated pyridone substrates employed in this work are known compounds and their ^{1}H NMR data agreed with the literature.

General Procedure for the Preparation of *N*-Arylated Pyridone Substrates:

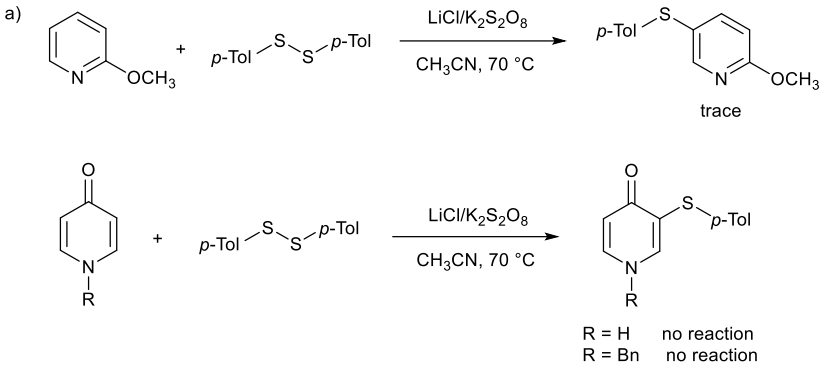


The mixture of 2-hydroxypyridine (5 mmol, 1 equiv.), Aryl halides (10 mmol, 2 equiv.), CuI (0.5 mmol, 0.1 equiv.) and K_2CO_3 (5 mmol, 1 equiv.) in DMSO (10 ml) was heated and stirred at 150 °C for 12 h under a nitrogen atmosphere. Upon completion, distilled deionized H_2O (5 mL) was added, and the mixture was extracted with ethyl acetate (EtOAc) (2 × 20 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting organic residue was purified by flash chromatography column over silica gel (SiO_2) to afford the *N*-arylated pyridones.

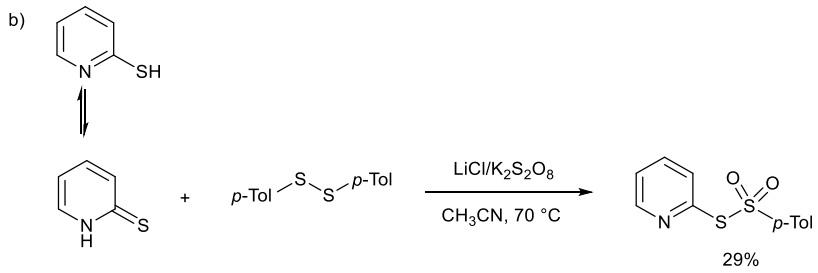
The *N*-arylated pyridone substrates employed in this work are known compounds and their ^{1}H NMR data agreed with the literature.

(Reference: A. Modak, S. Rana and D. Maiti, *J. Org. Chem.*, 2015, **80**, 296.

II. Additional Control Experiments



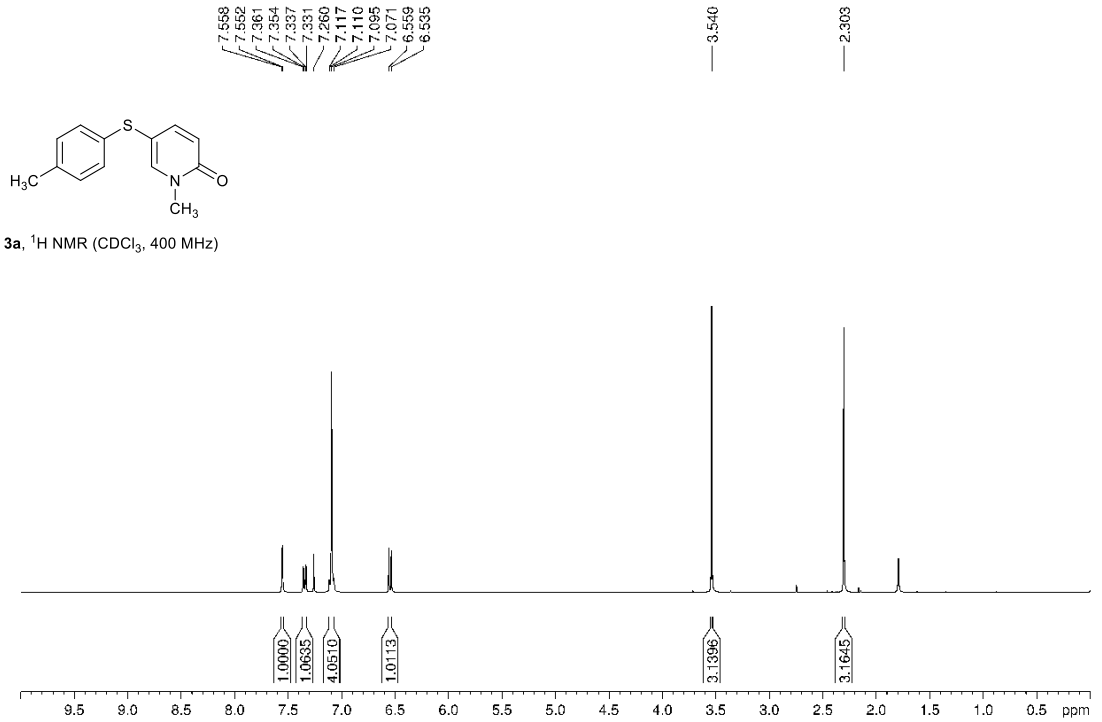
According to the results from the above control experiments (a), 2-methoxypyridine as well as 4-pyridones were not suitable substrates for this transformation. Thus, the lactam tautomeric form is essential for the reaction to take place.



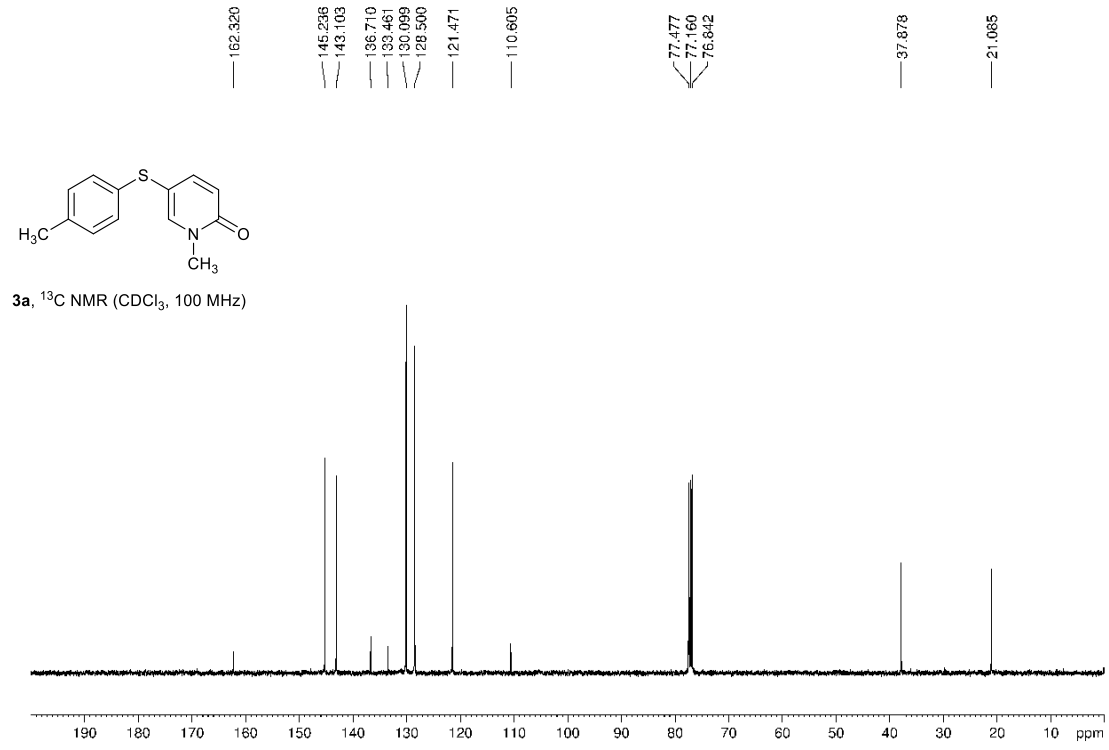
Furthermore, 2-mercaptopyridine (or 2-pyridinethione) was not capable of reacting as a nucleophile with disulfide in this reaction. Instead, a small amount of *S*-(pyridin-2-yl) 4-methylbenzenesulfonothioate was formed (confirmed by LCMS and NMR).

III. ^{1}H and ^{13}C Spectra of Products

1-Methyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3a)

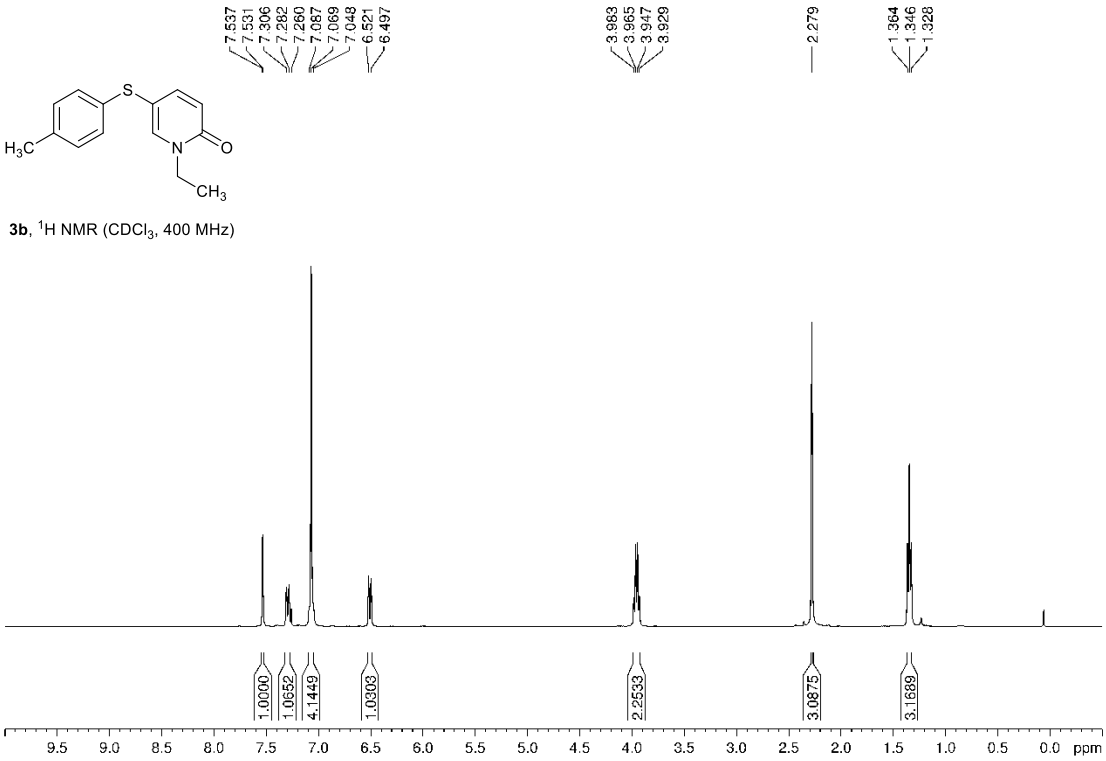


3a, ^{1}H NMR ($CDCl_3$, 400 MHz)

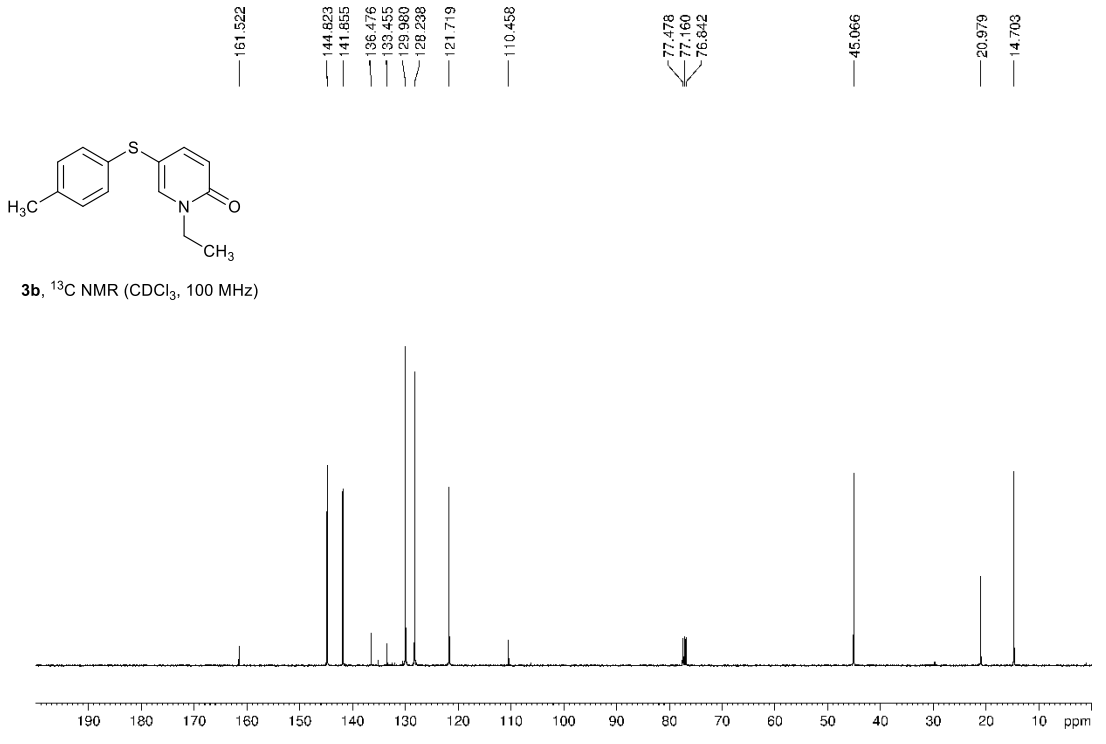


3a, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3b)

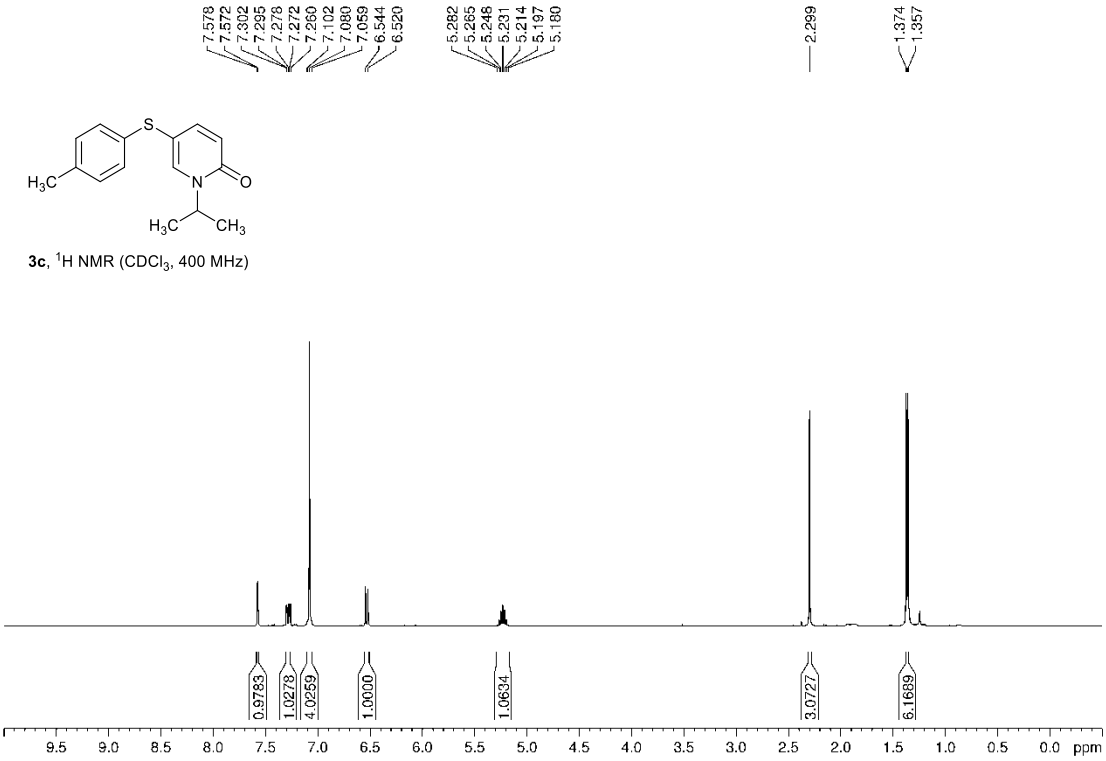


3b, ^{1}H NMR ($CDCl_3$, 400 MHz)

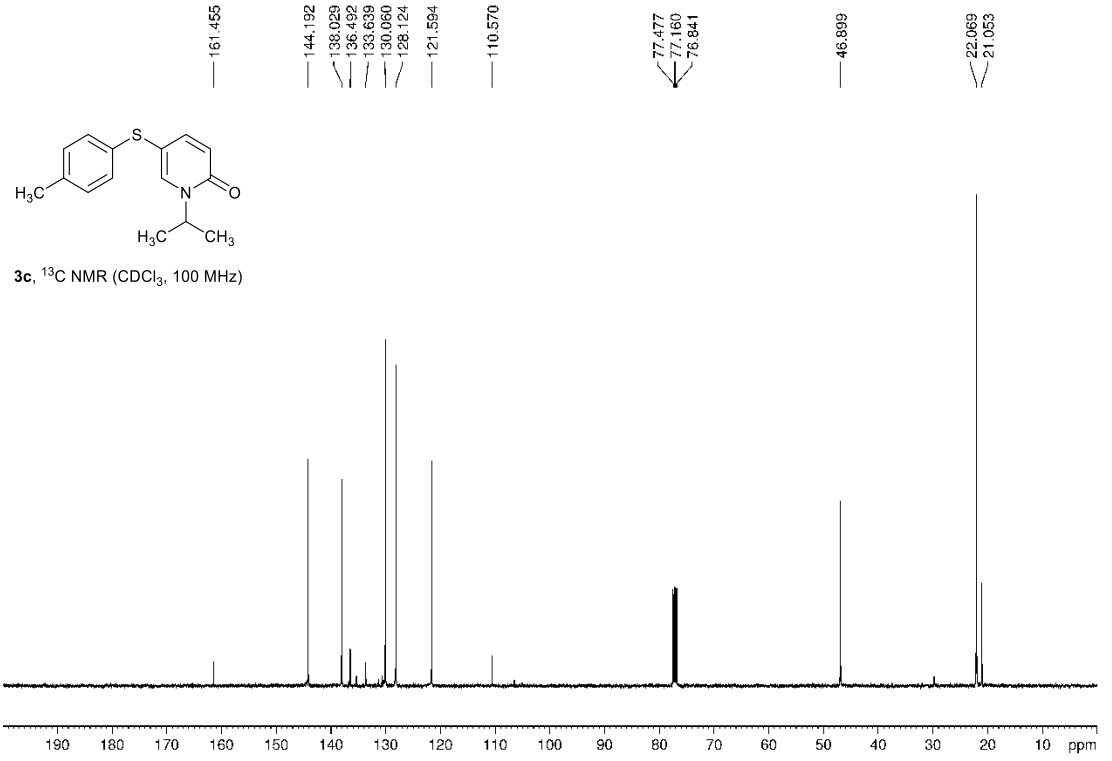


3b, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Isopropyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3c)

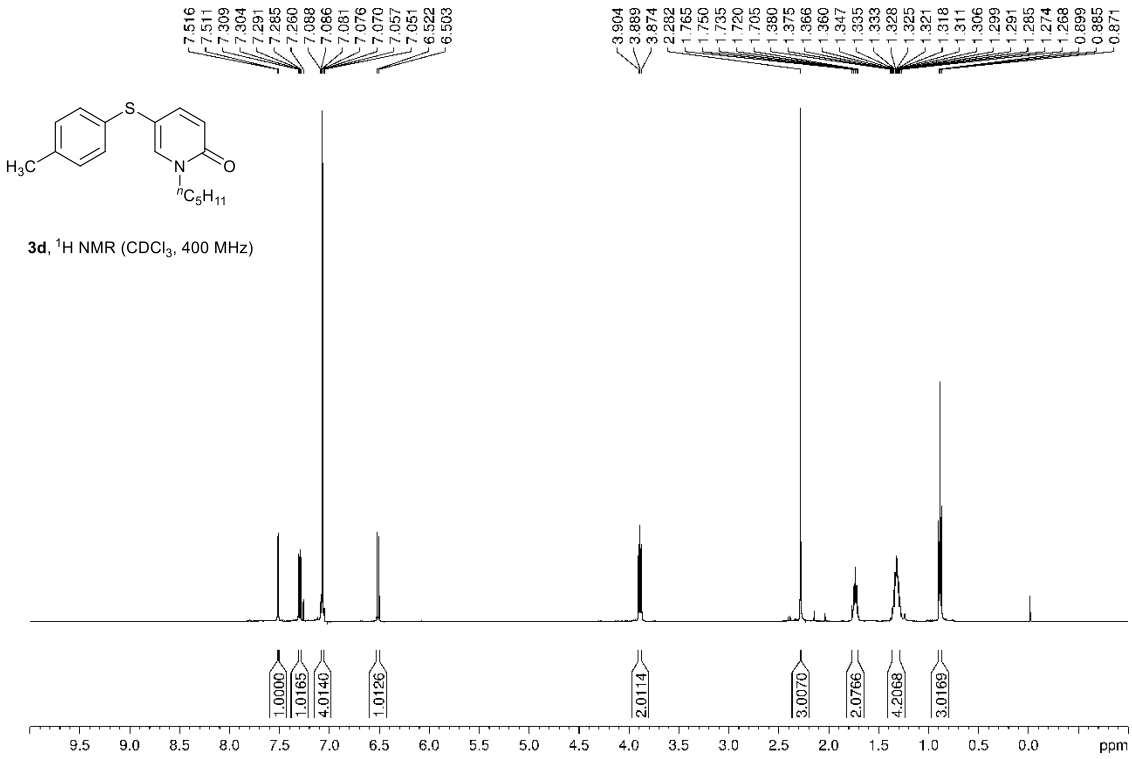


3c, ^{1}H NMR ($CDCl_3$, 400 MHz)

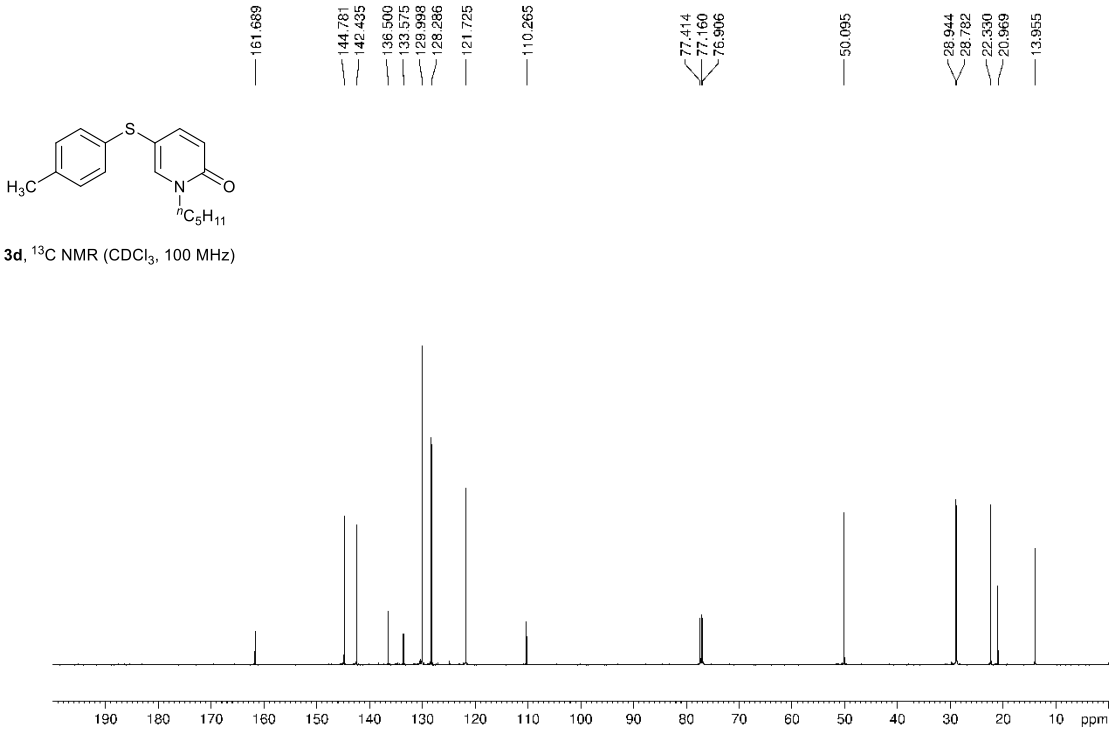


3c, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Pentyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3d)

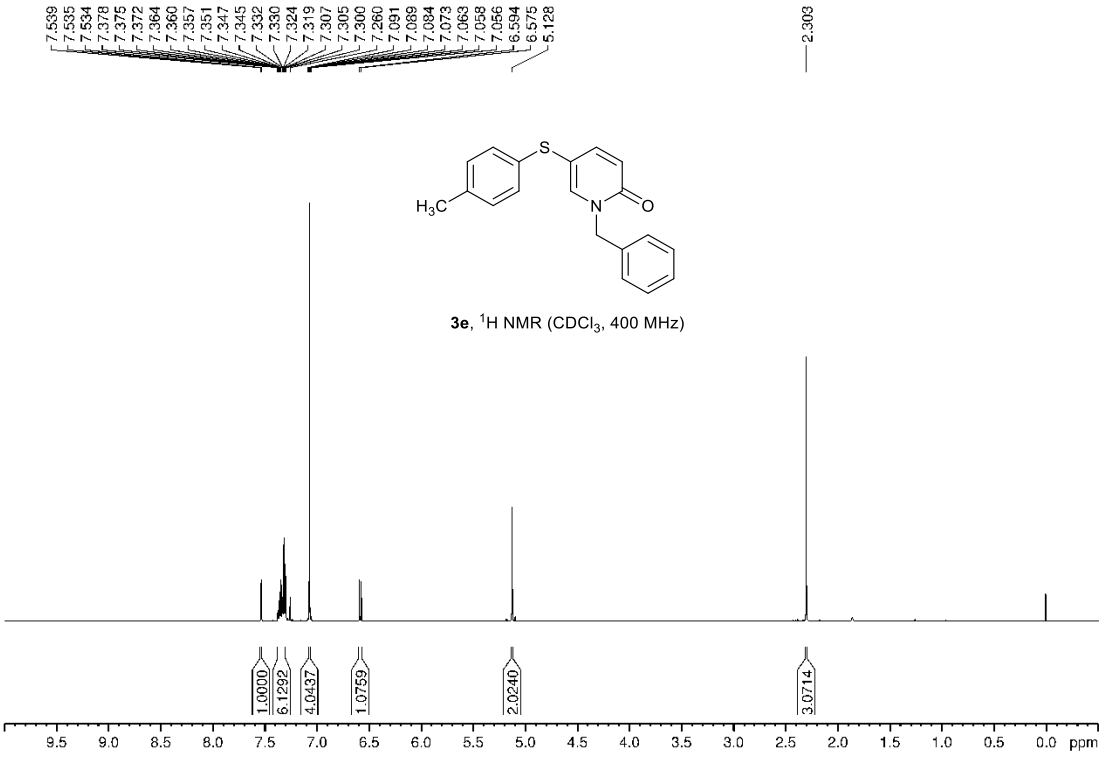


3d, ^{1}H NMR ($CDCl_3$, 400 MHz)

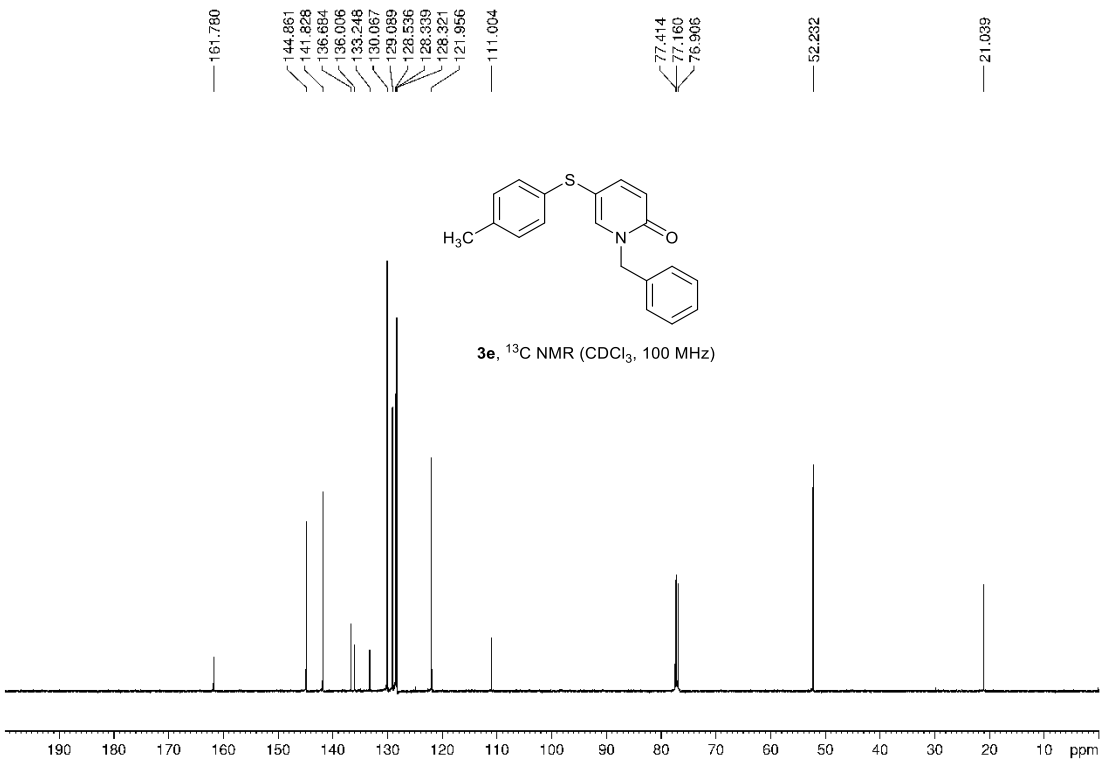


3d, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Benzyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3e)

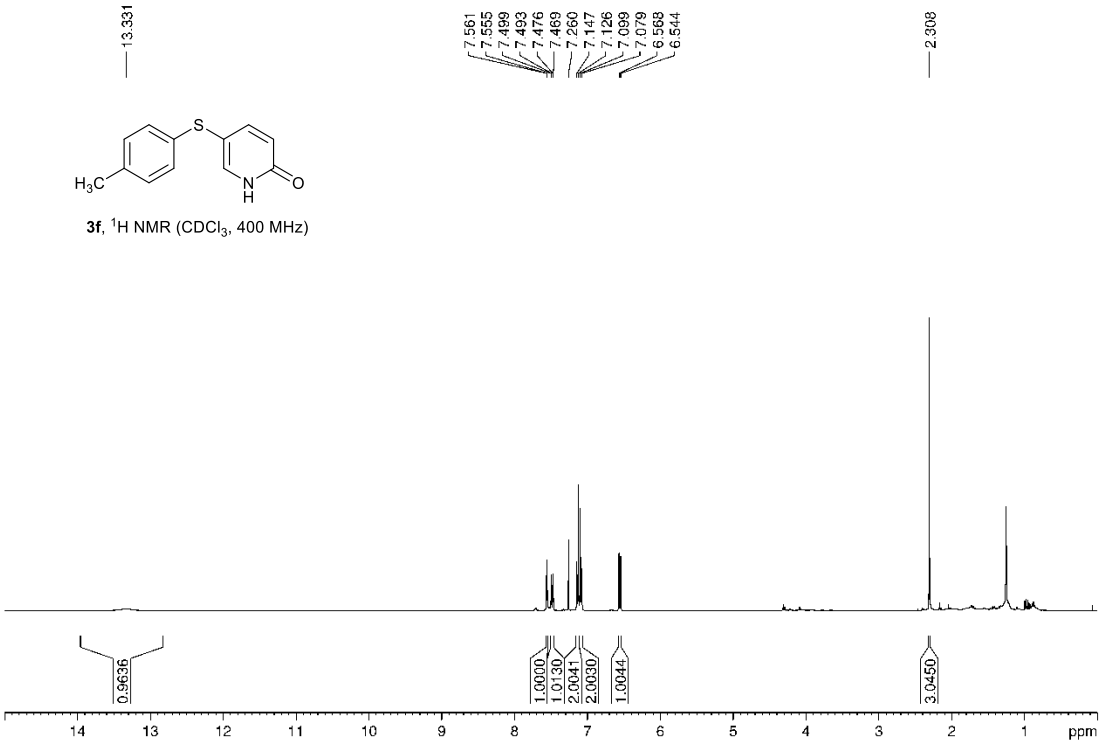


3e, ^{1}H NMR ($CDCl_3$, 400 MHz)

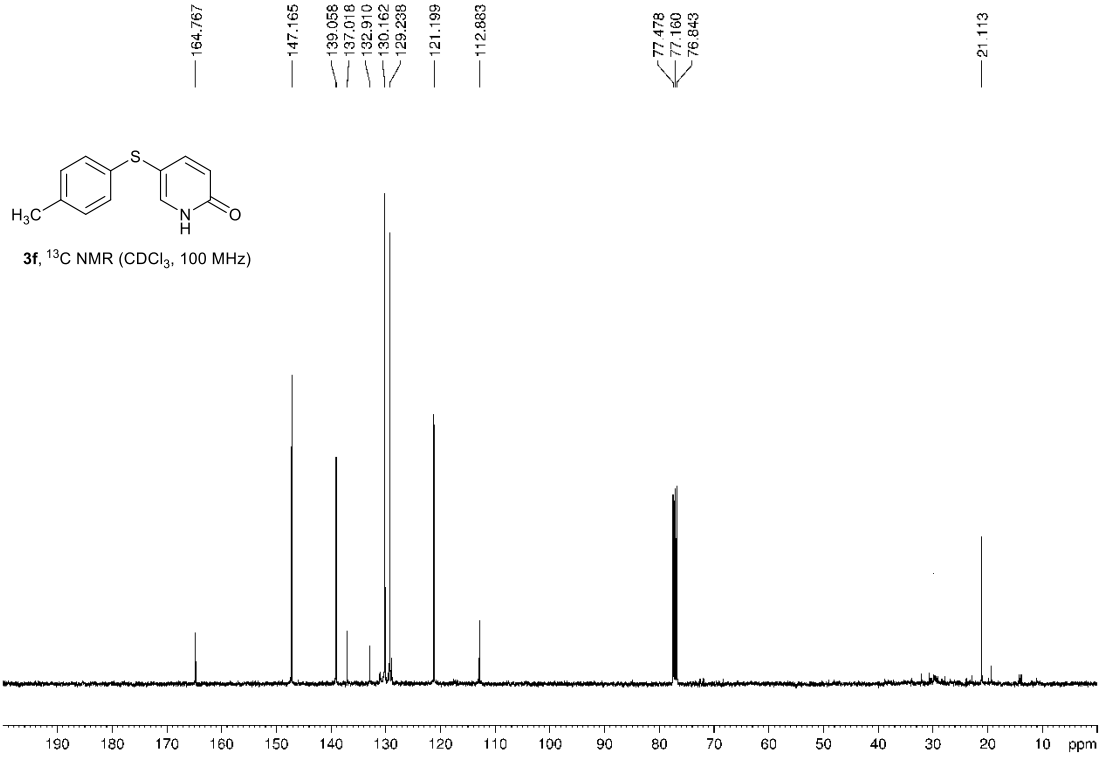


3e, ^{13}C NMR ($CDCl_3$, 100 MHz)

5-(*p*-Tolylthio)pyridin-2(1*H*)-one (3f)

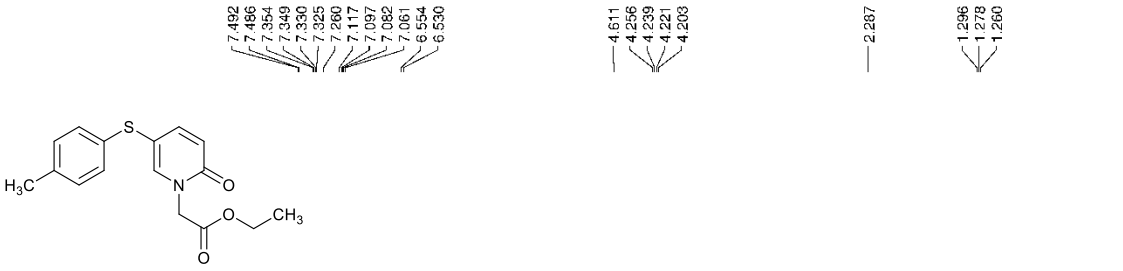


3f, ^{1}H NMR ($CDCl_3$, 400 MHz)

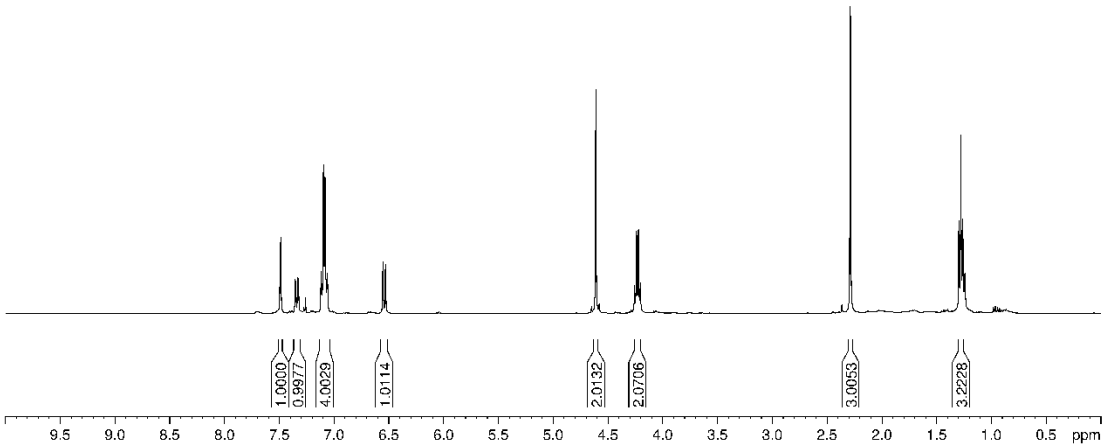


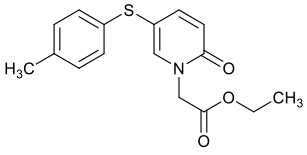
3f, ^{13}C NMR ($CDCl_3$, 100 MHz)

Ethyl 2-(2-oxo-5-(*p*-tolylthio)pyridin-1(2*H*)-yl)acetate (3g)

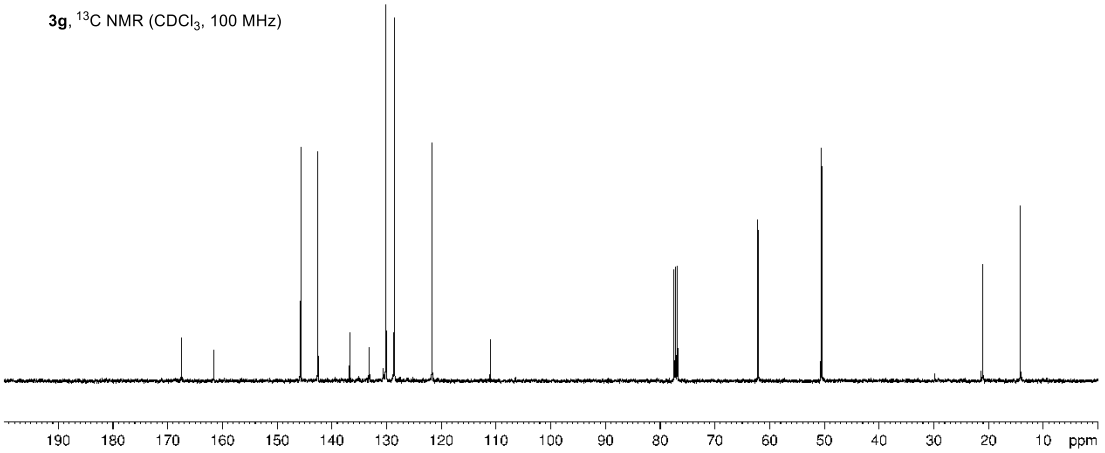


3g, ^{1}H NMR ($CDCl_3$, 400 MHz)

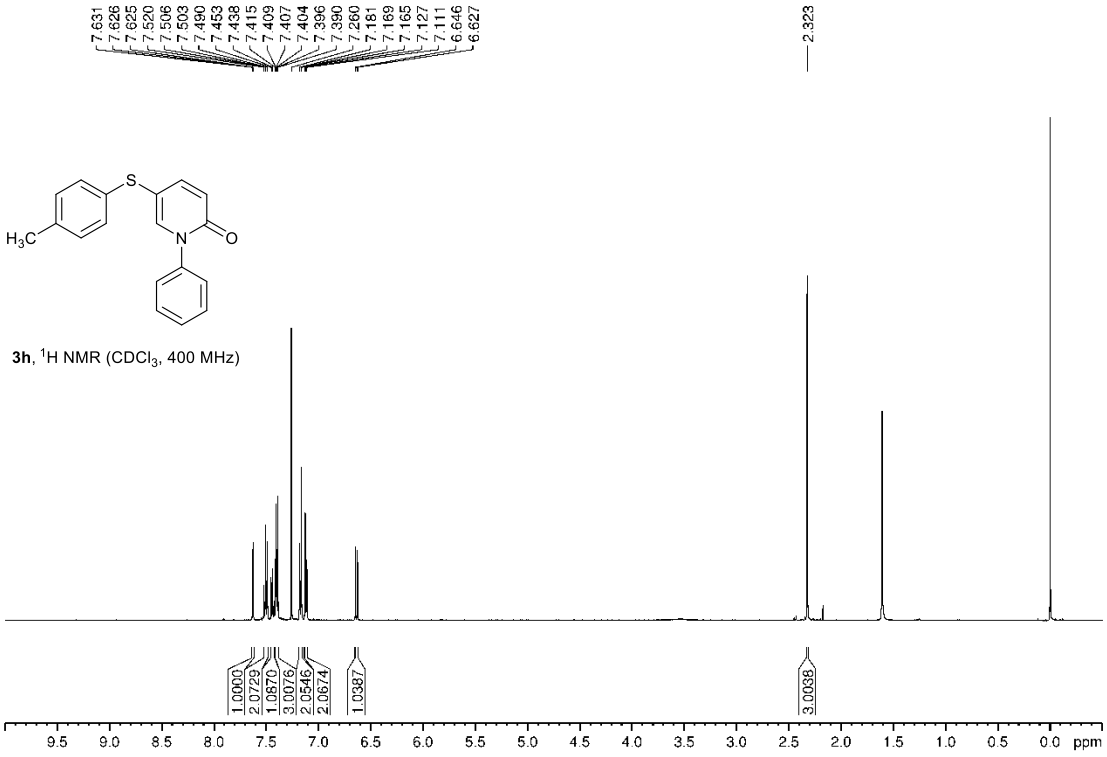


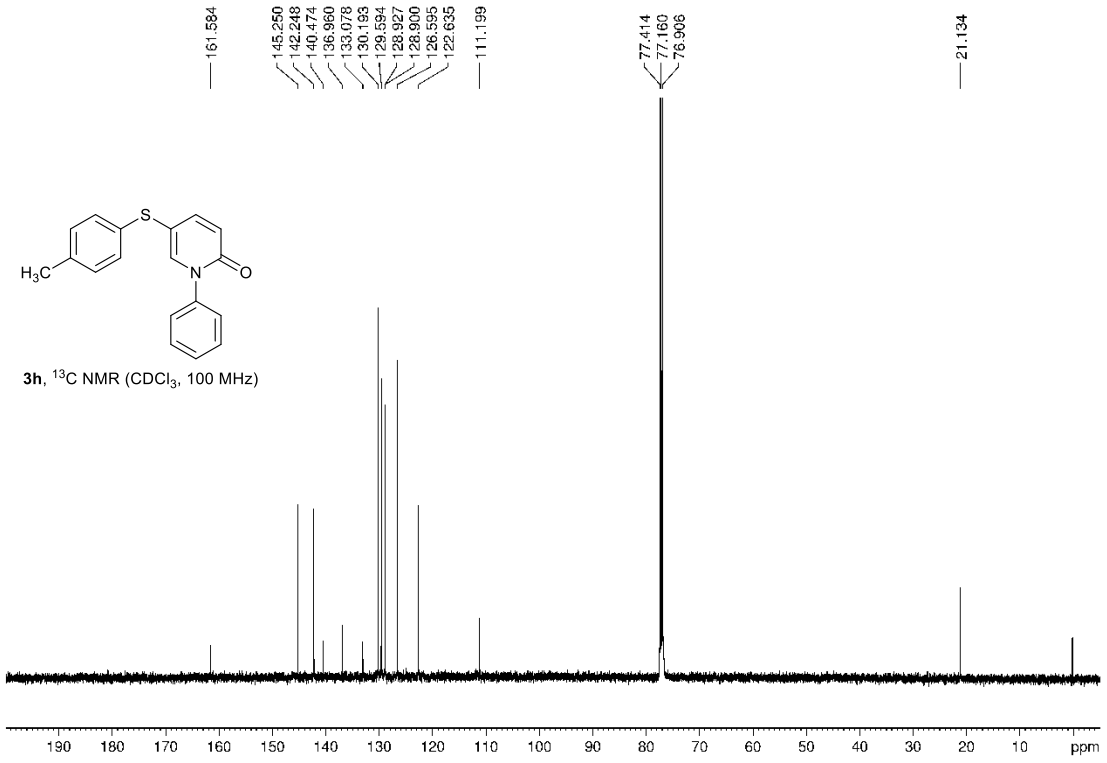


3g, ^{13}C NMR ($CDCl_3$, 100 MHz)

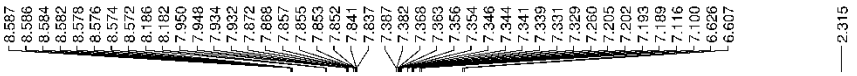


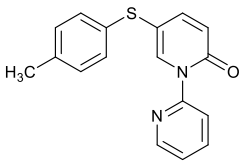
1-Phenyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3h)



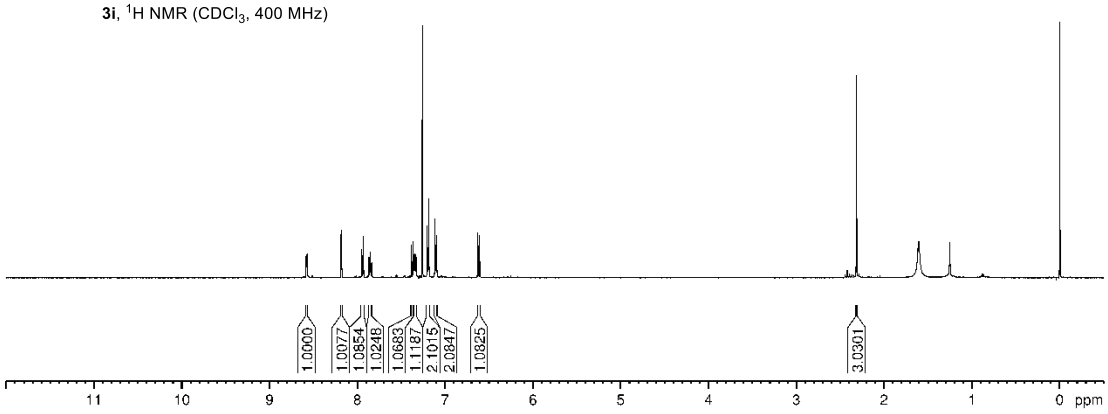


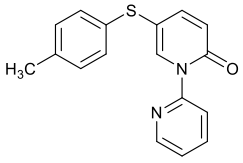
5-(*p*-Tolylthio)-2*H*-[1,2'-bipyridin]-2-one (3i)



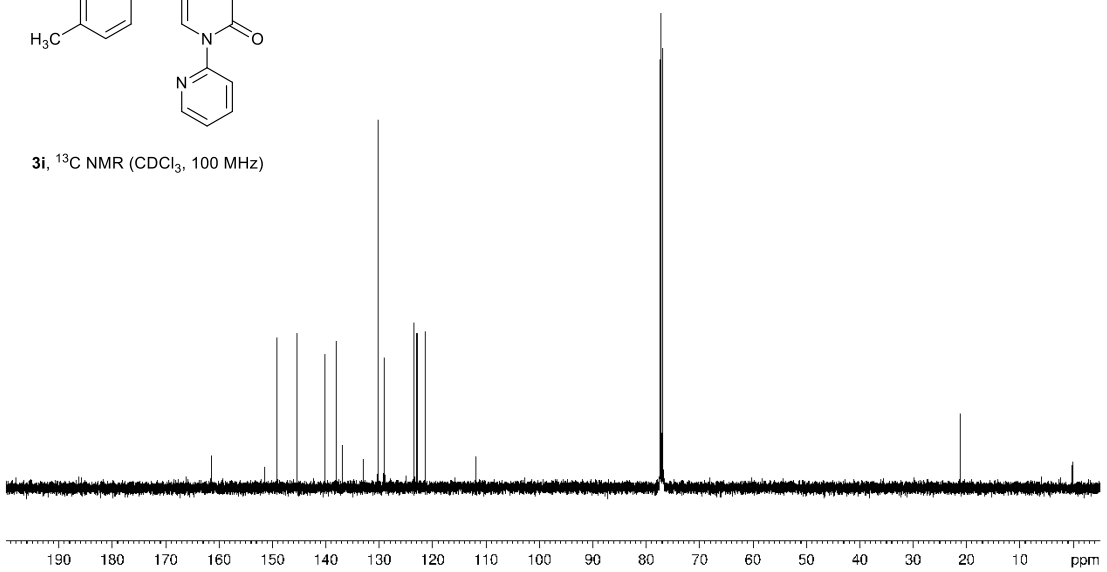


3i, ^{1}H NMR ($CDCl_3$, 400 MHz)



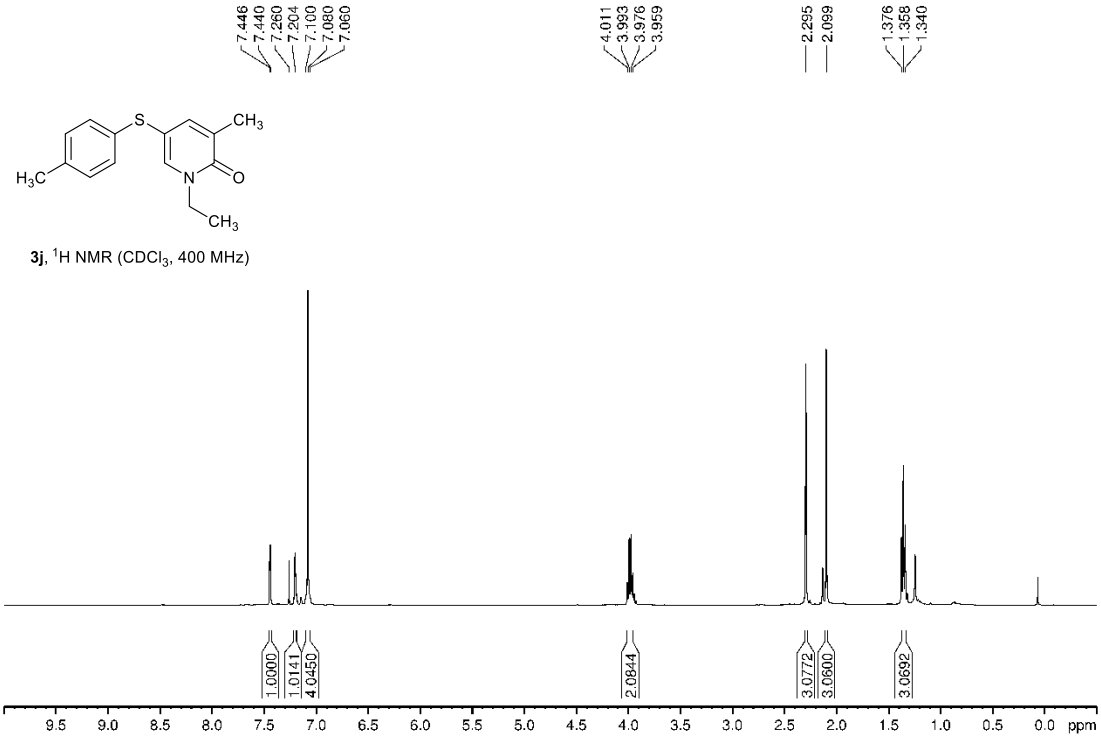


3i, ^{13}C NMR ($CDCl_3$, 100 MHz)

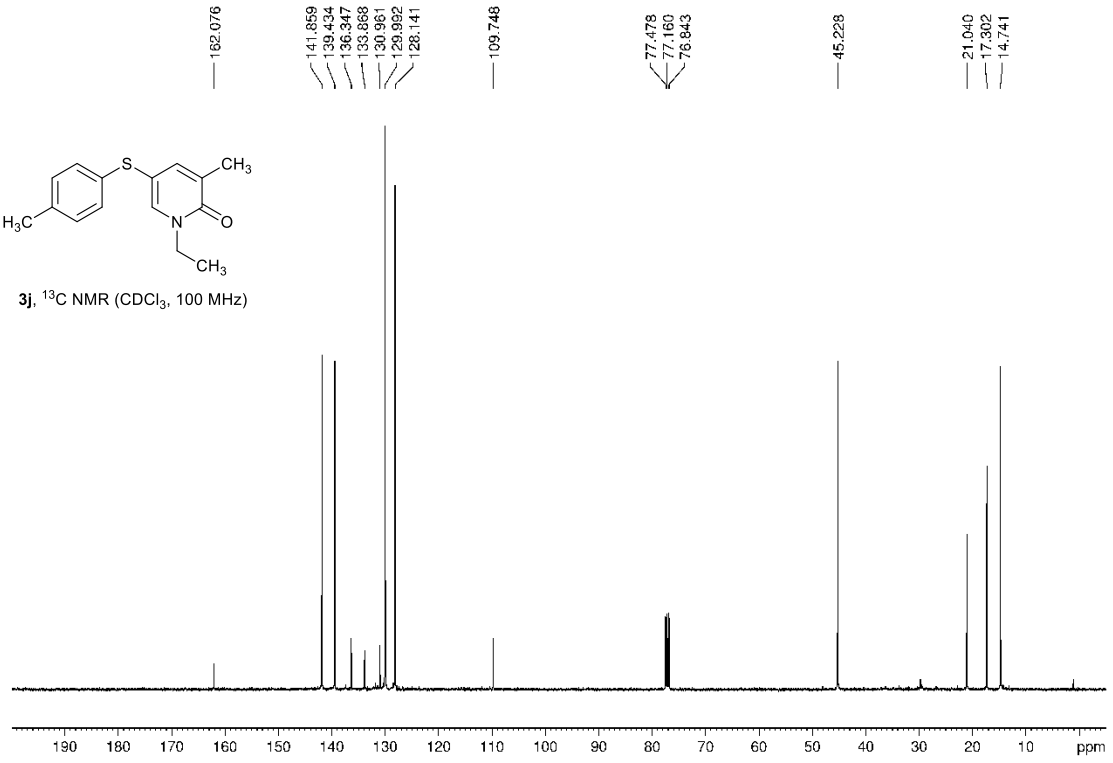


1-Ethyl-3-methyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3j)

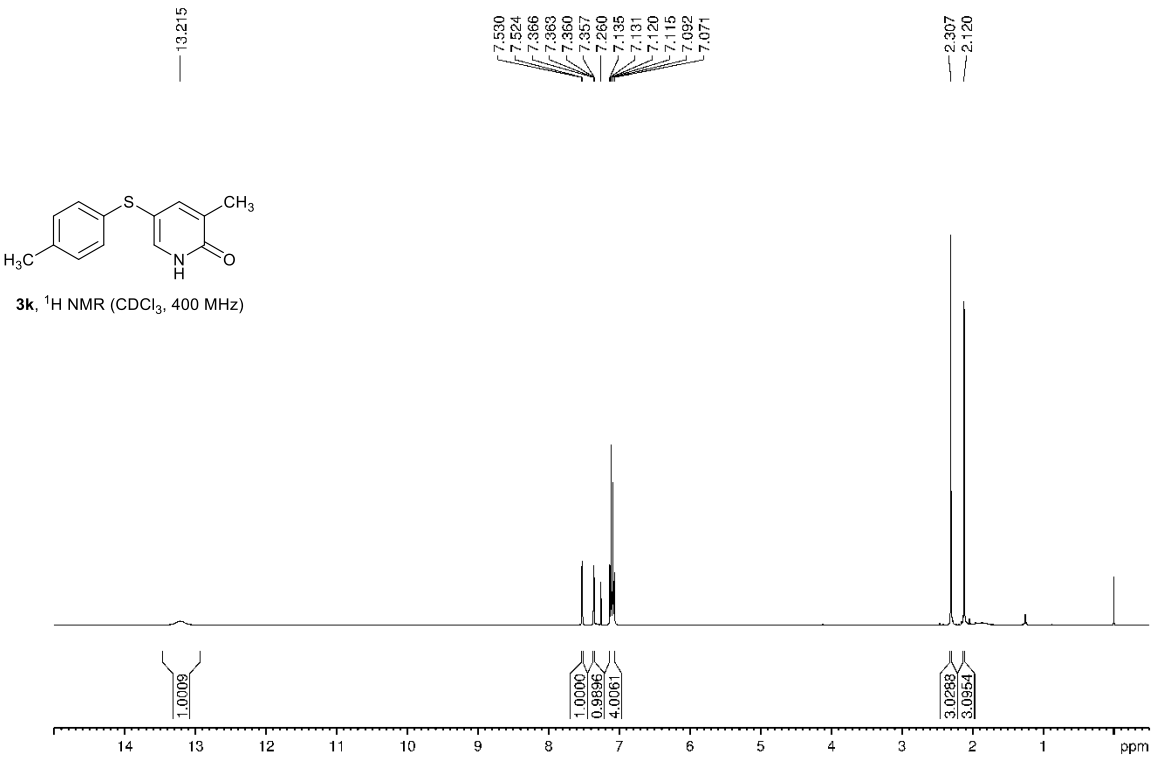
3j, ^{1}H NMR ($CDCl_3$, 400 MHz)



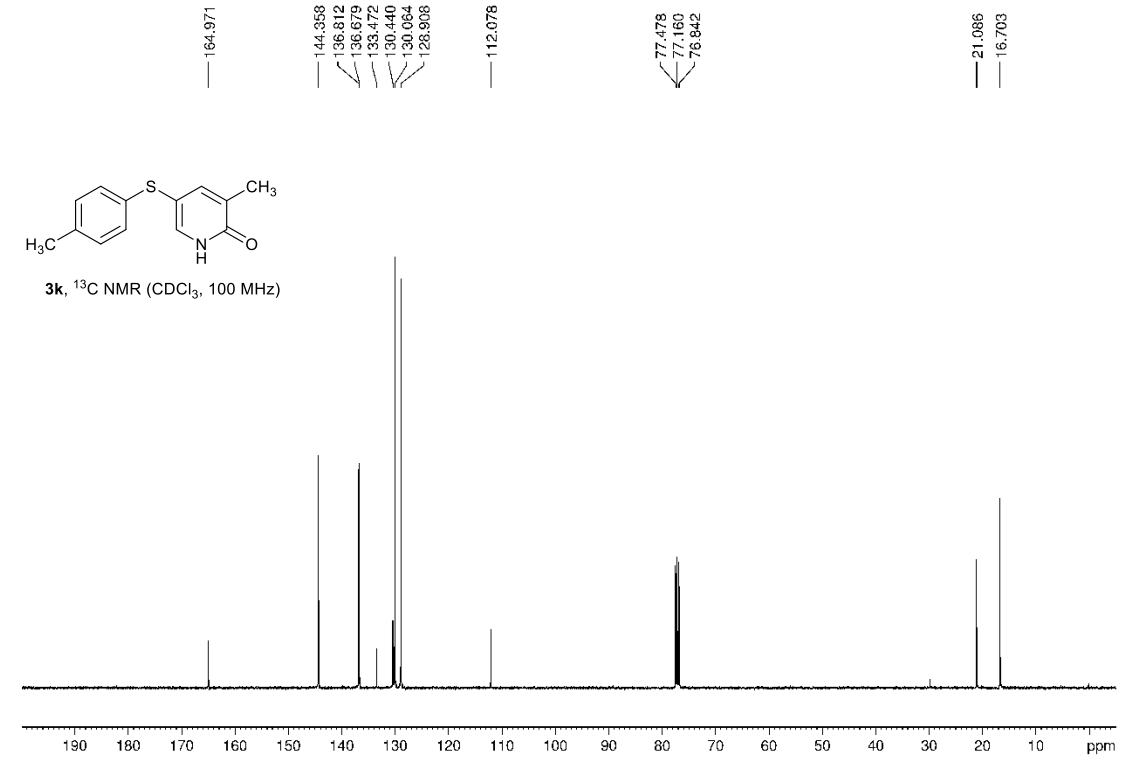
3j, ^{13}C NMR ($CDCl_3$, 100 MHz)



3-Methyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3k)

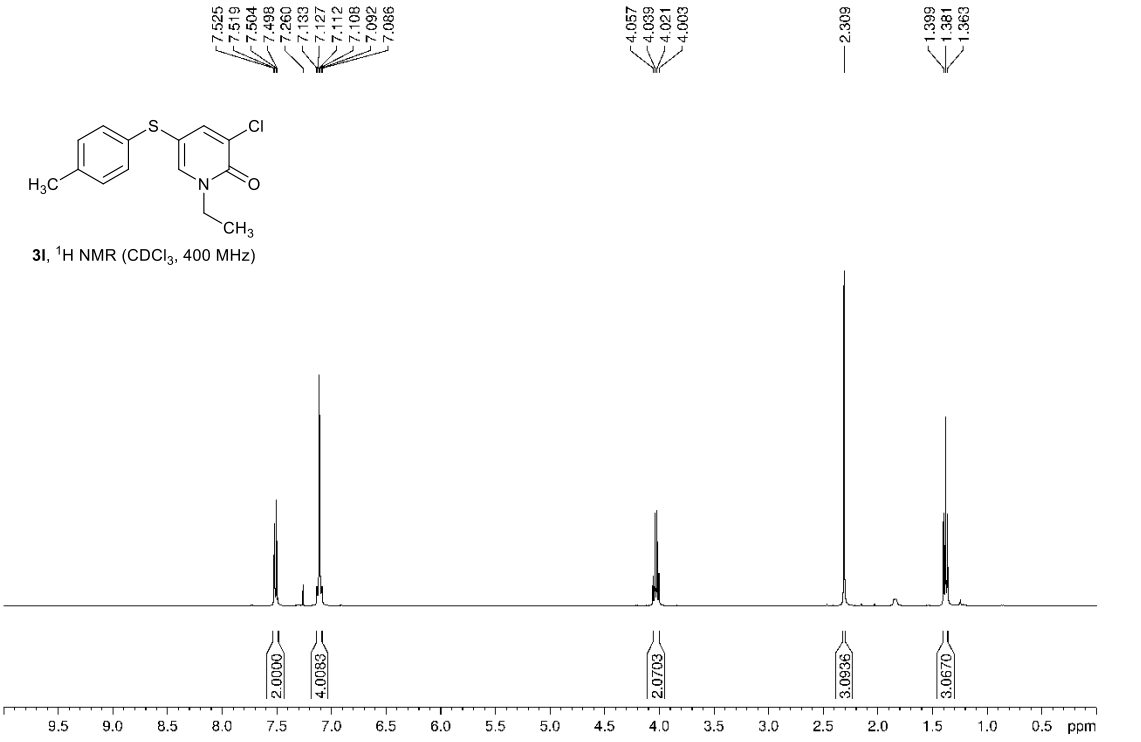


3k, ^{1}H NMR ($CDCl_3$, 400 MHz)

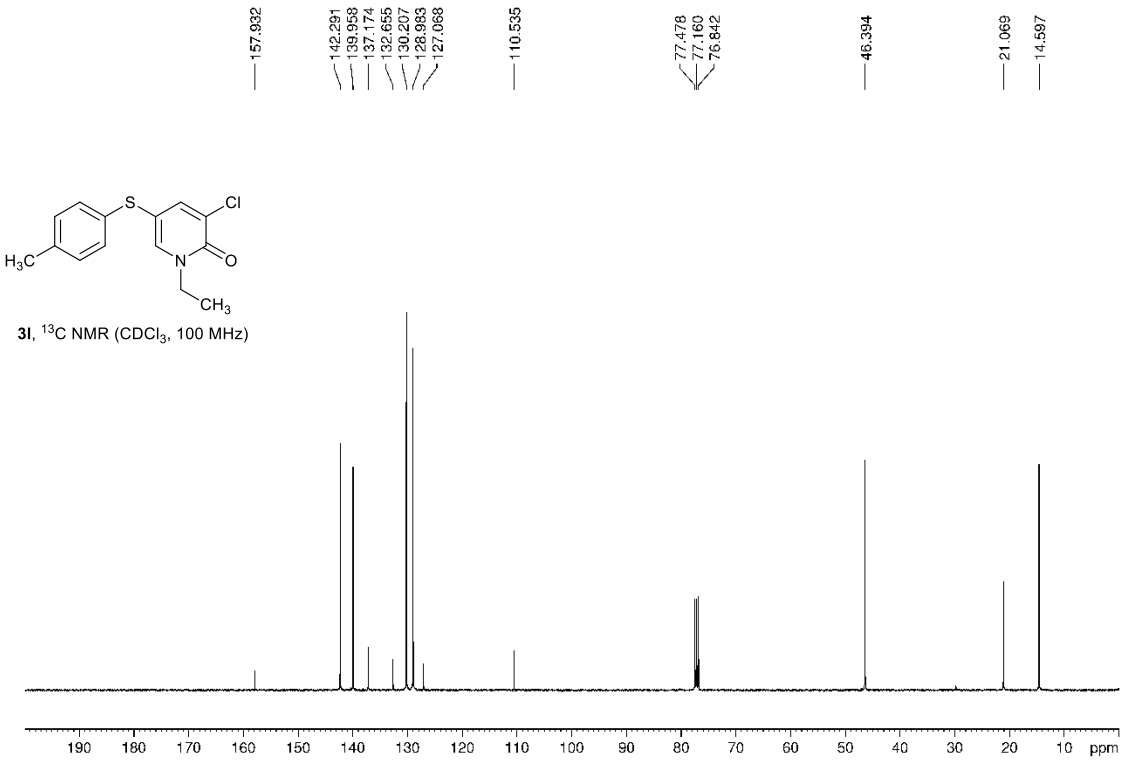


3k, ^{13}C NMR ($CDCl_3$, 100 MHz)

3-Chloro-1-ethyl-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3l)

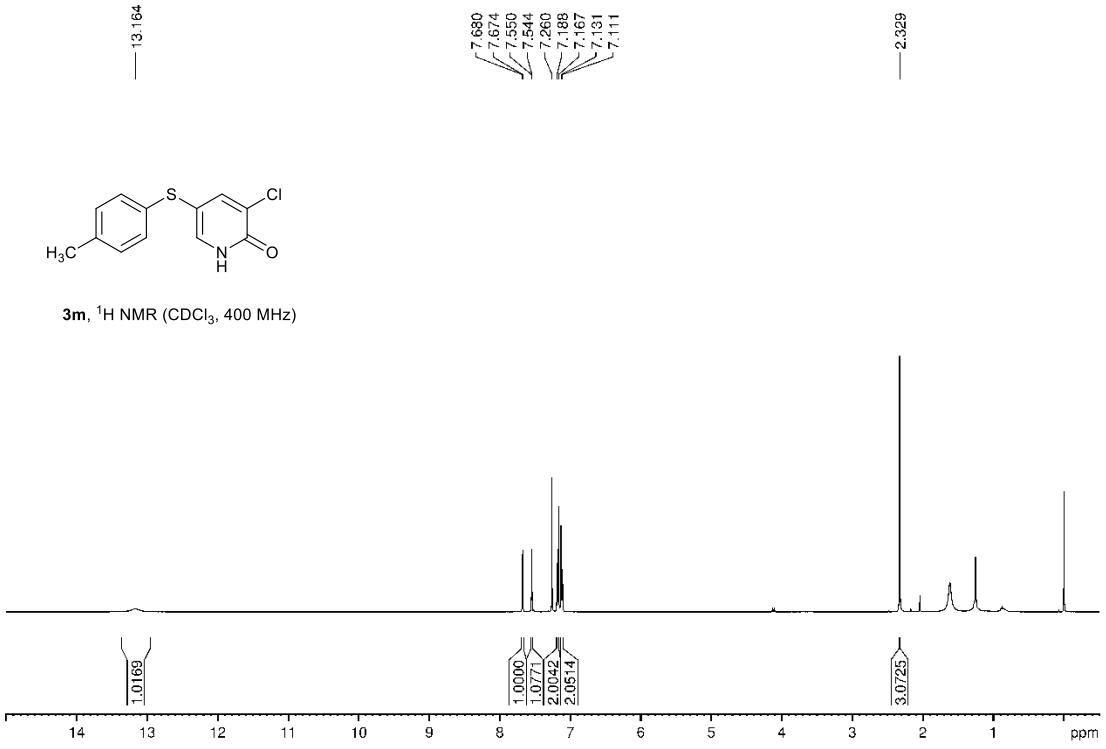


3l, ^{1}H NMR ($CDCl_3$, 400 MHz)

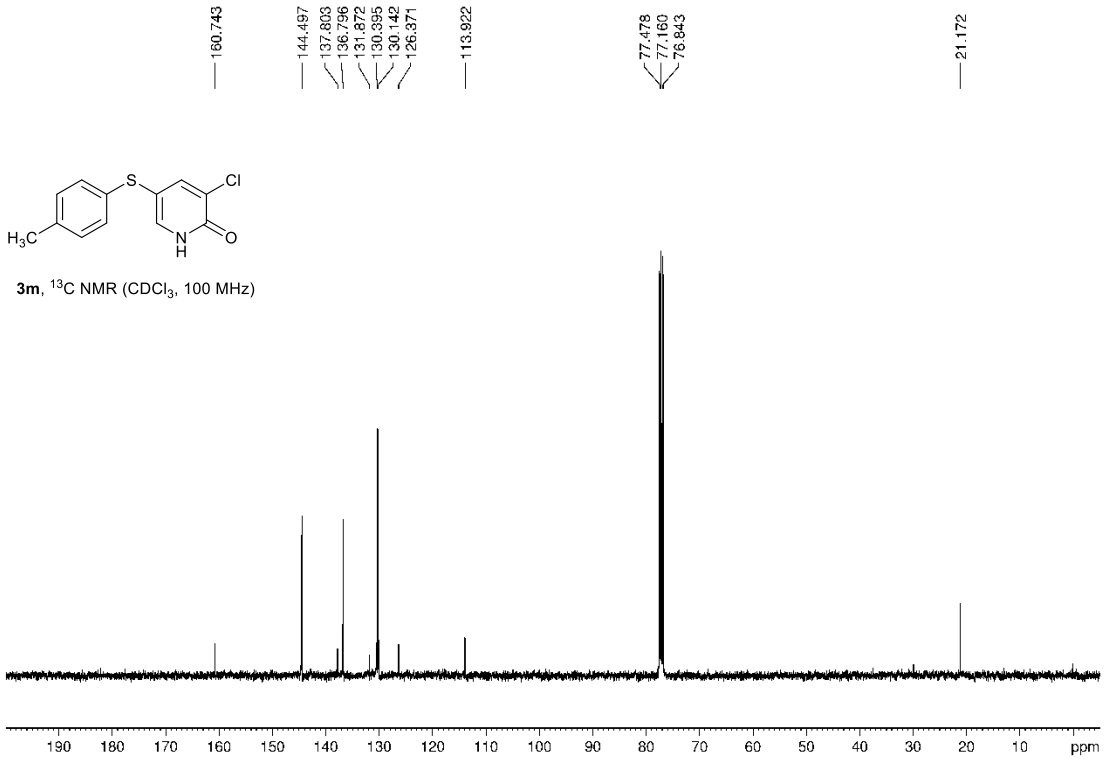


3l, ^{13}C NMR ($CDCl_3$, 100 MHz)

3-Chloro-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3m)

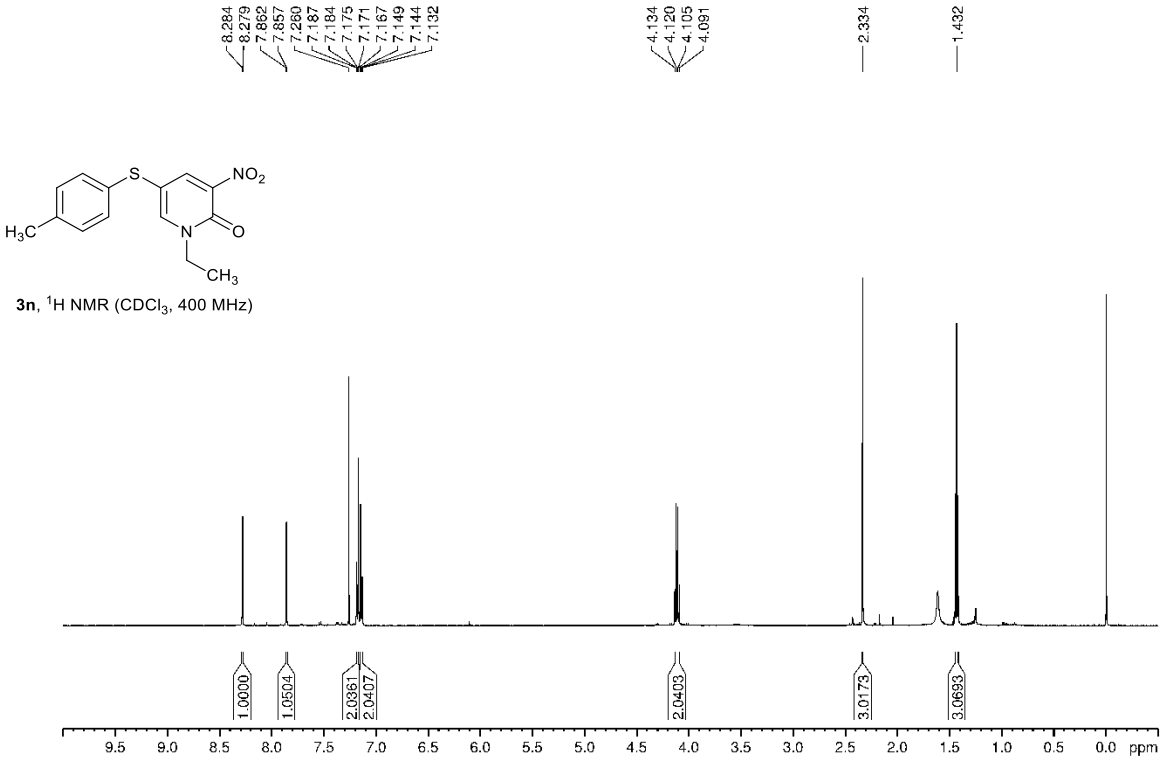


3m, ^{1}H NMR ($CDCl_3$, 400 MHz)

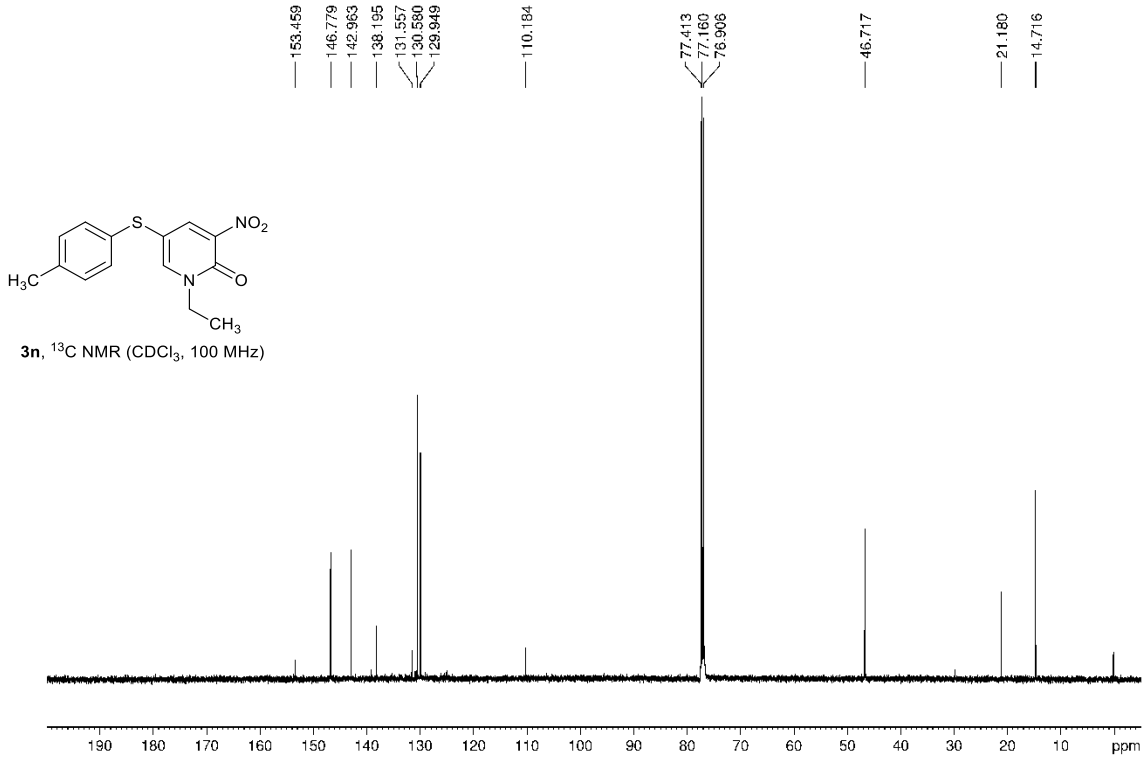


3m, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-3-nitro-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3n)

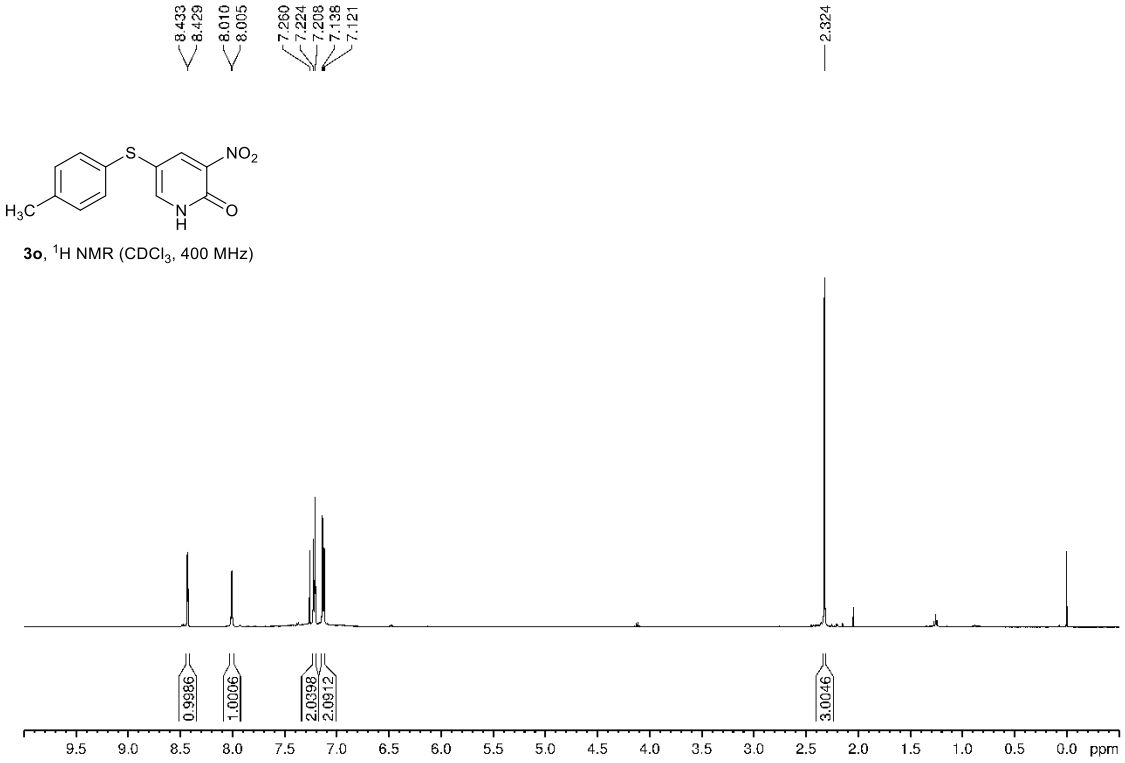


3n, ^{1}H NMR ($CDCl_3$, 400 MHz)

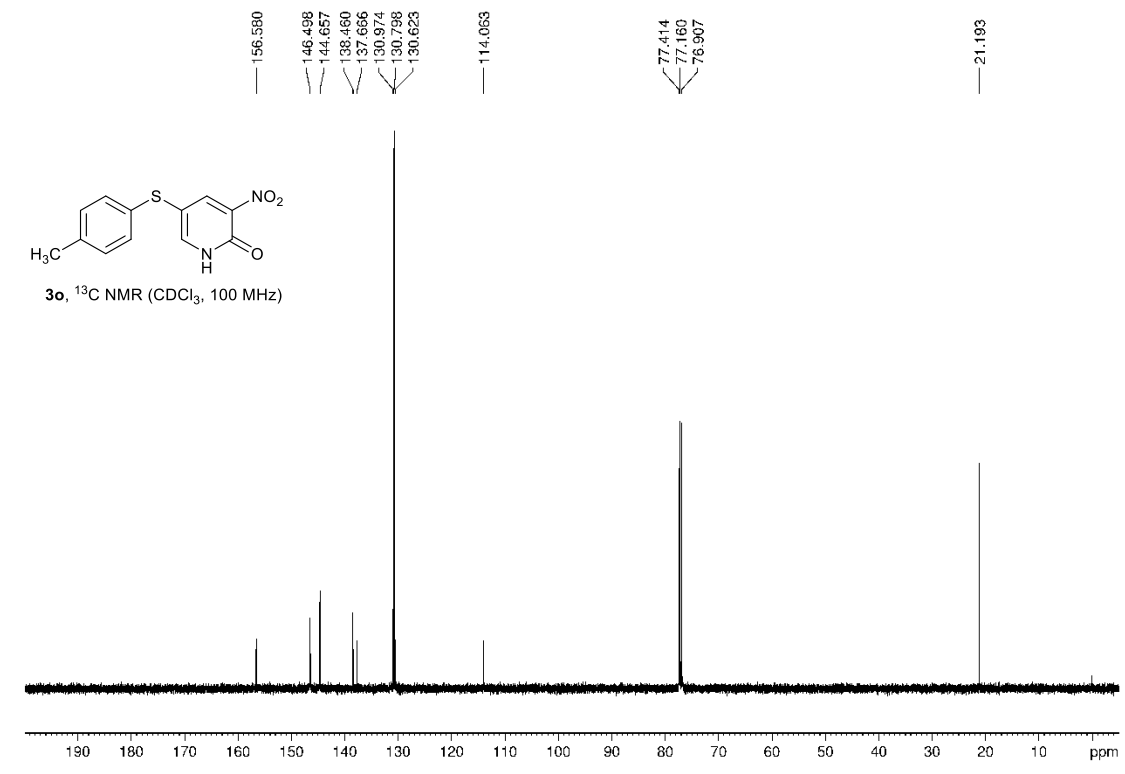


3n, ^{13}C NMR ($CDCl_3$, 100 MHz)

3-nitro-5-(*p*-tolylthio)pyridin-2(1*H*)-one (3o)

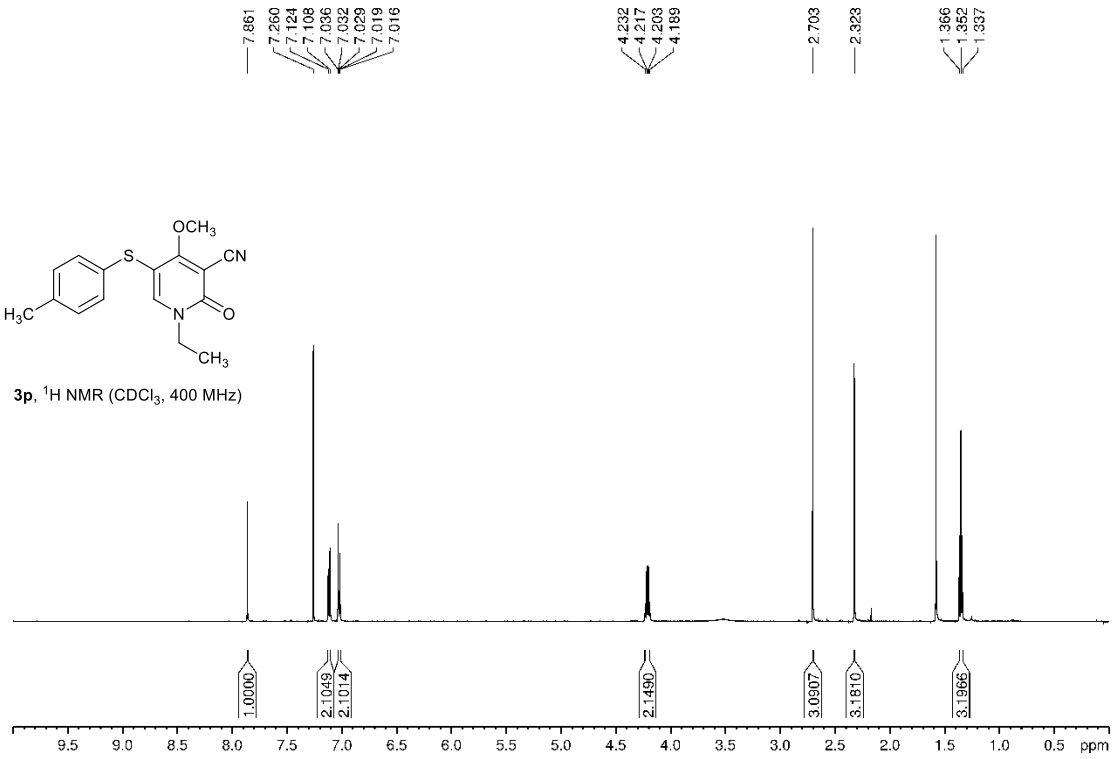


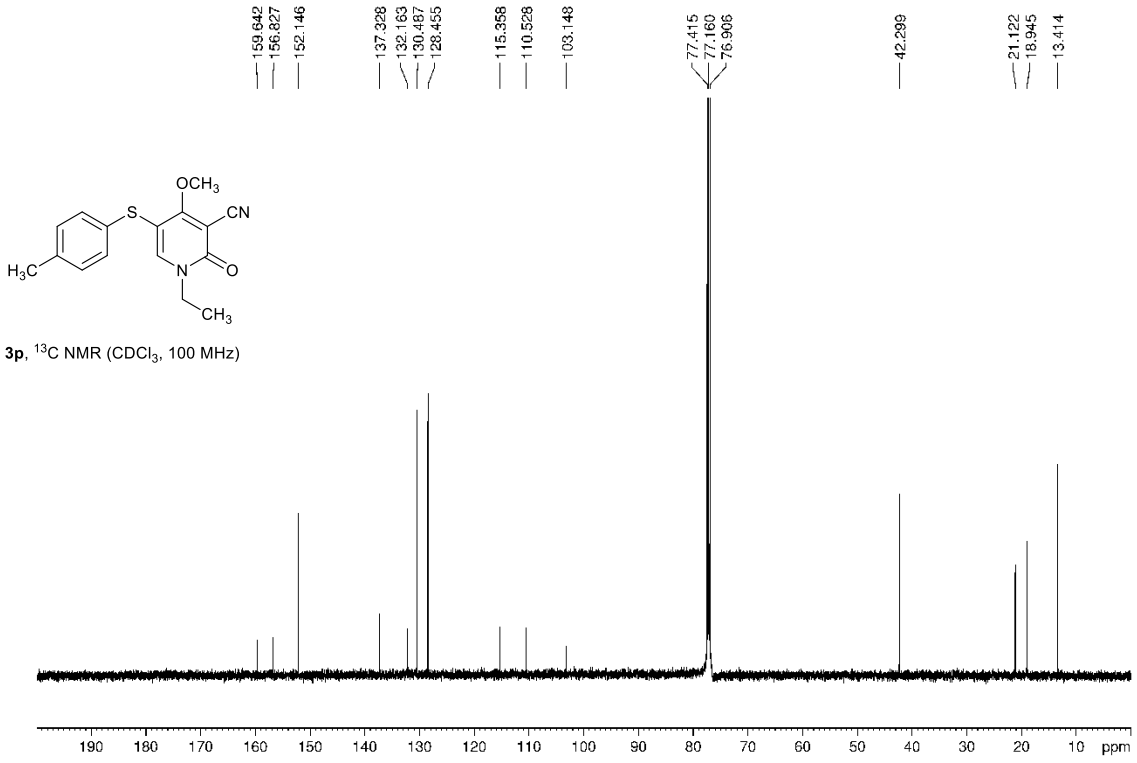
3o, ^{1}H NMR ($CDCl_3$, 400 MHz)



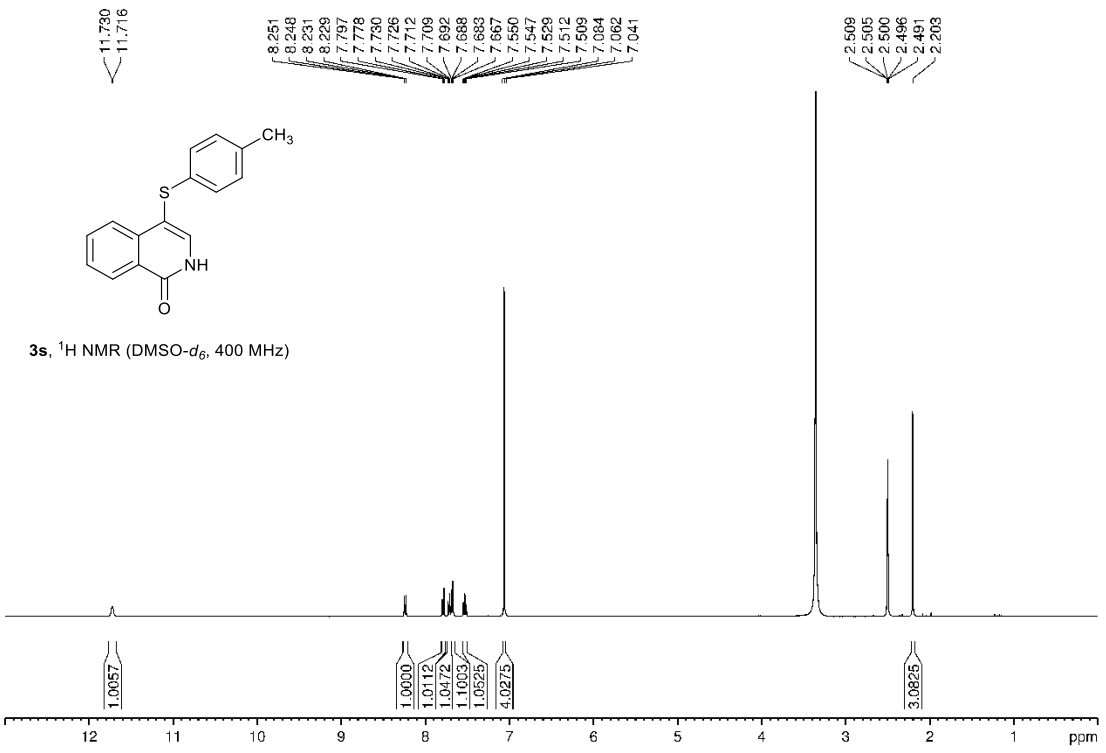
3o, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-4-methoxy-2-oxo-5-(*p*-tolylthio)-1,2-dihydropyridine-3-carbonitrile (3p)

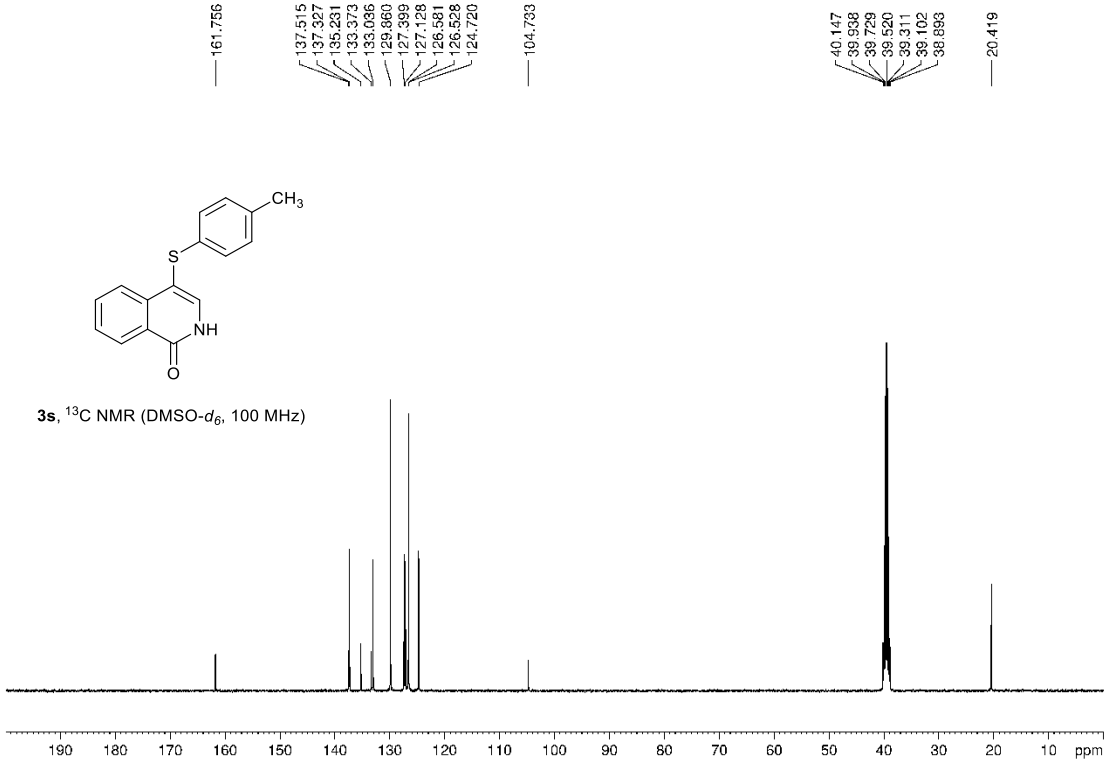




4-(*p*-Tolylthio)isoquinolin-1(2*H*)-one (3s)

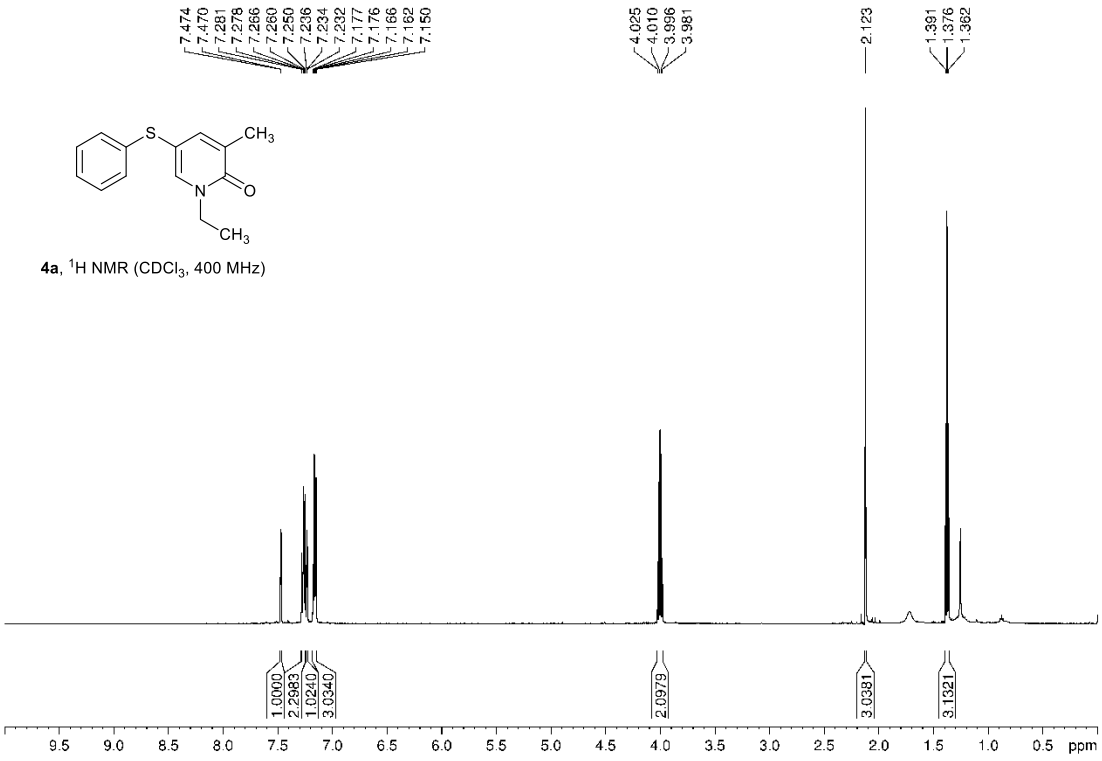


3s, ^{1}H NMR (DMSO-d_6, 400 MHz)

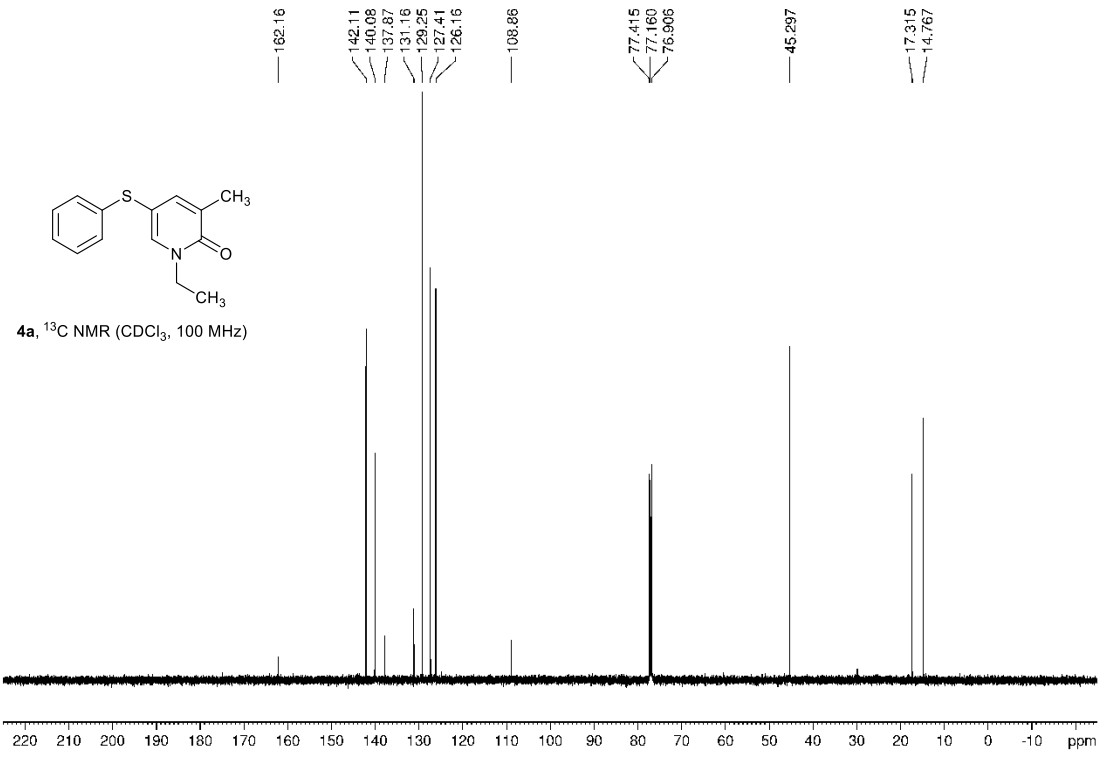


3s, ^{13}C NMR (DMSO-d_6, 100 MHz)

1-Ethyl-3-methyl-5-(phenylthio)pyridin-2(1*H*)-one (4a)

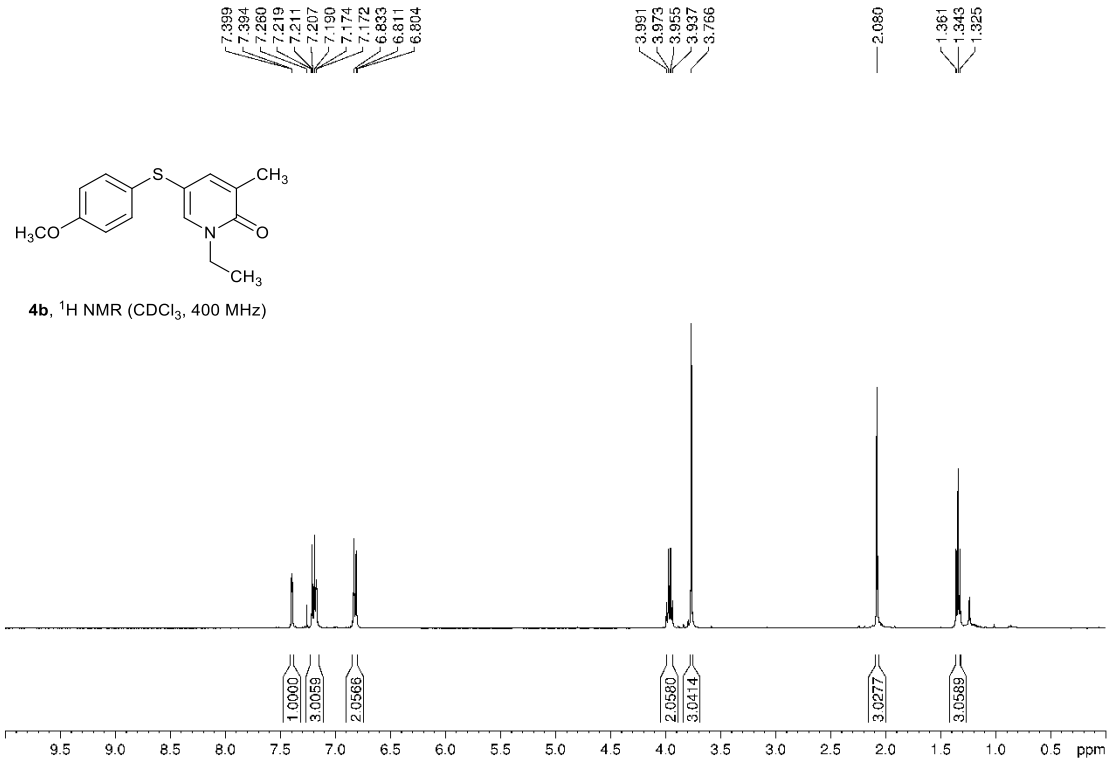


4a, ^{1}H NMR ($CDCl_3$, 400 MHz)

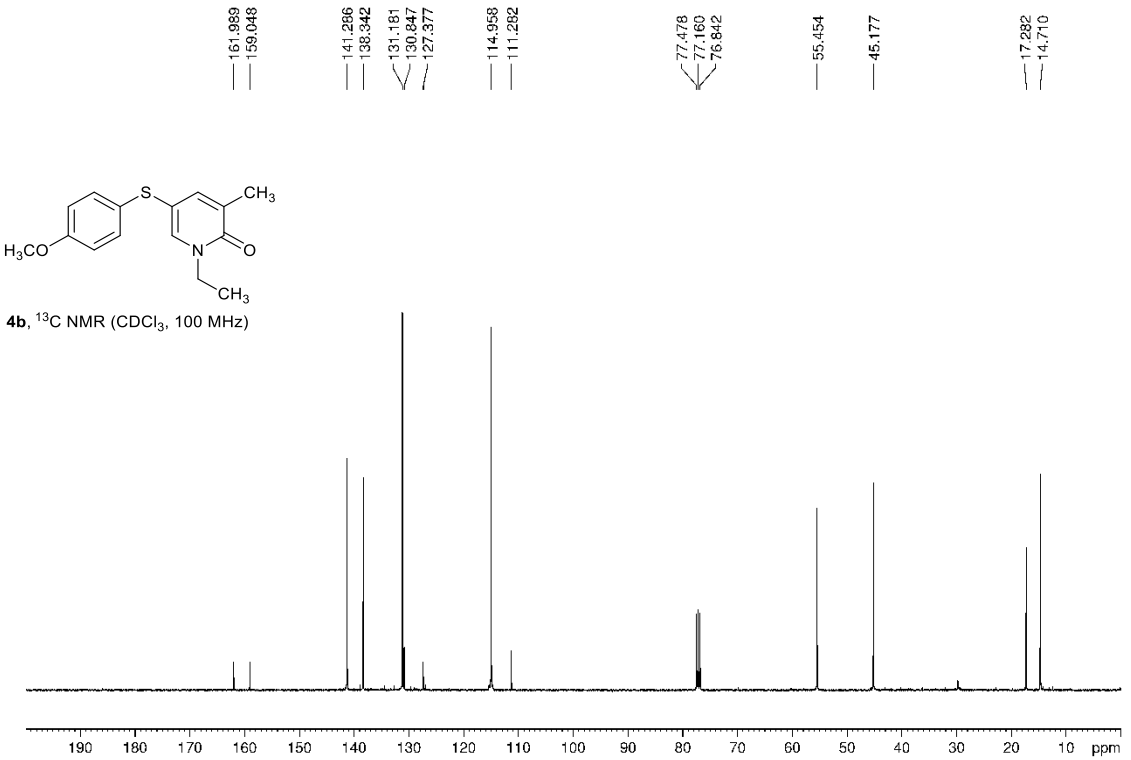


4a, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-5-((4-methoxyphenyl)thio)-3-methylpyridin-2(1*H*)-one (4b)

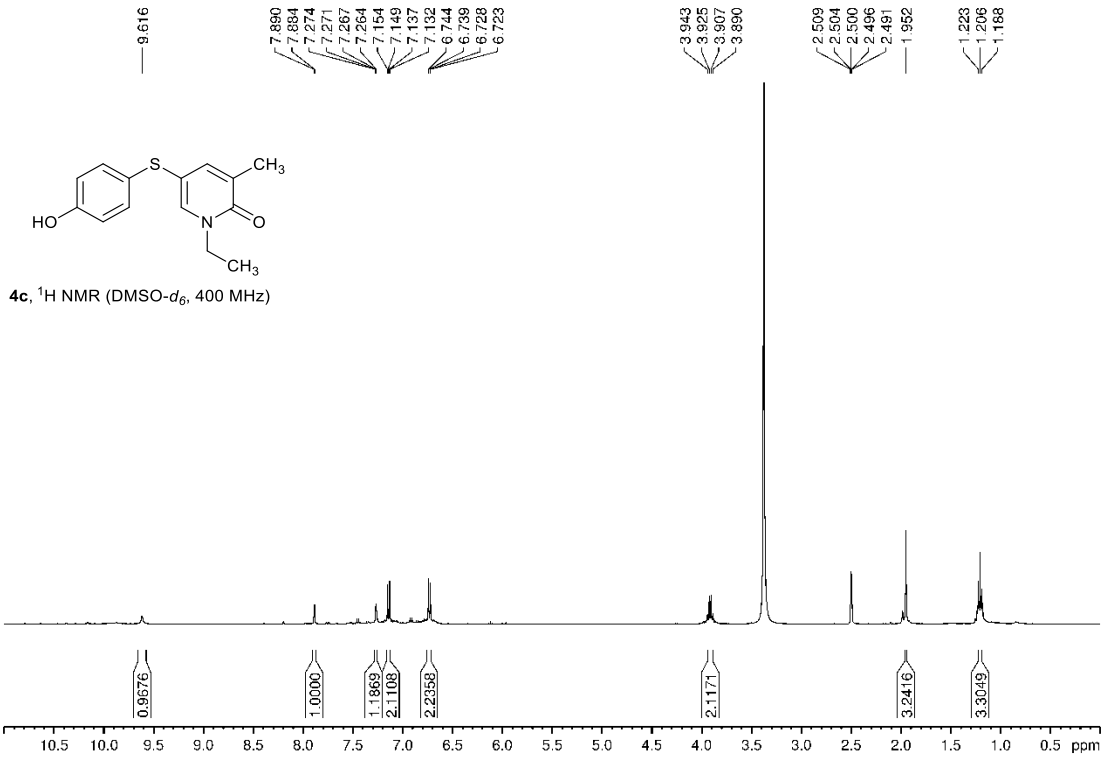


4b, ^{1}H NMR ($CDCl_3$, 400 MHz)

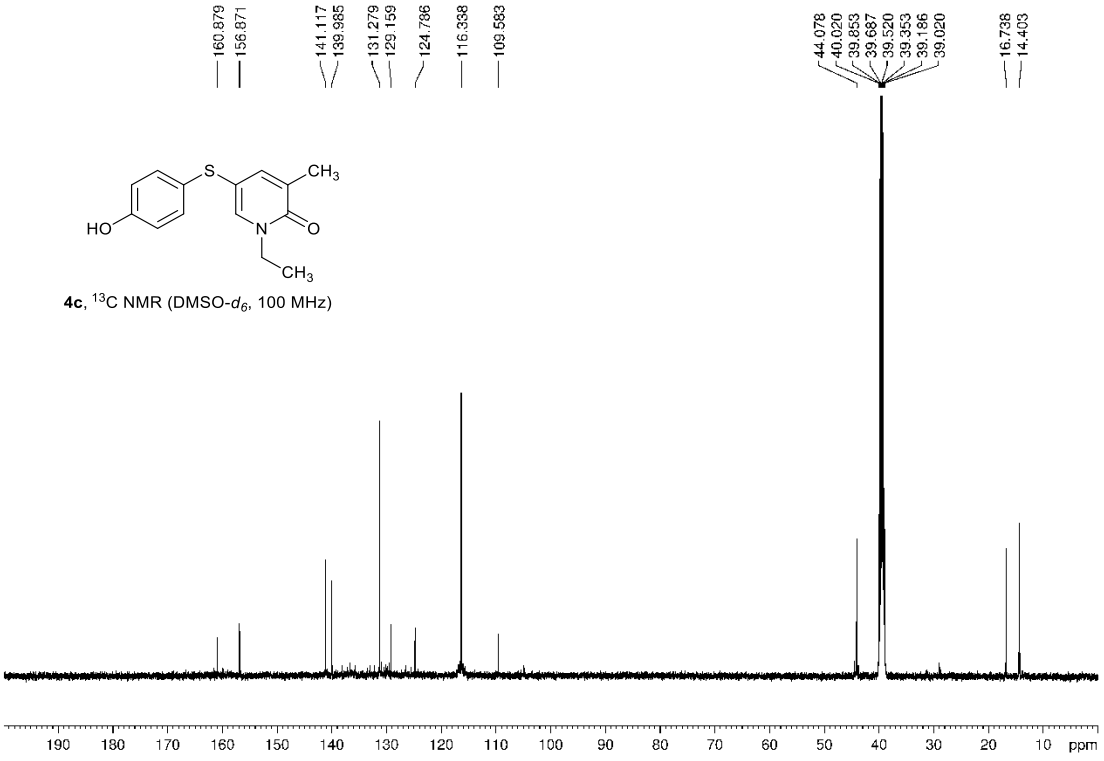


4b, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-5-((4-hydroxyphenyl)thio)-3-methylpyridin-2(1*H*)-one (4c)

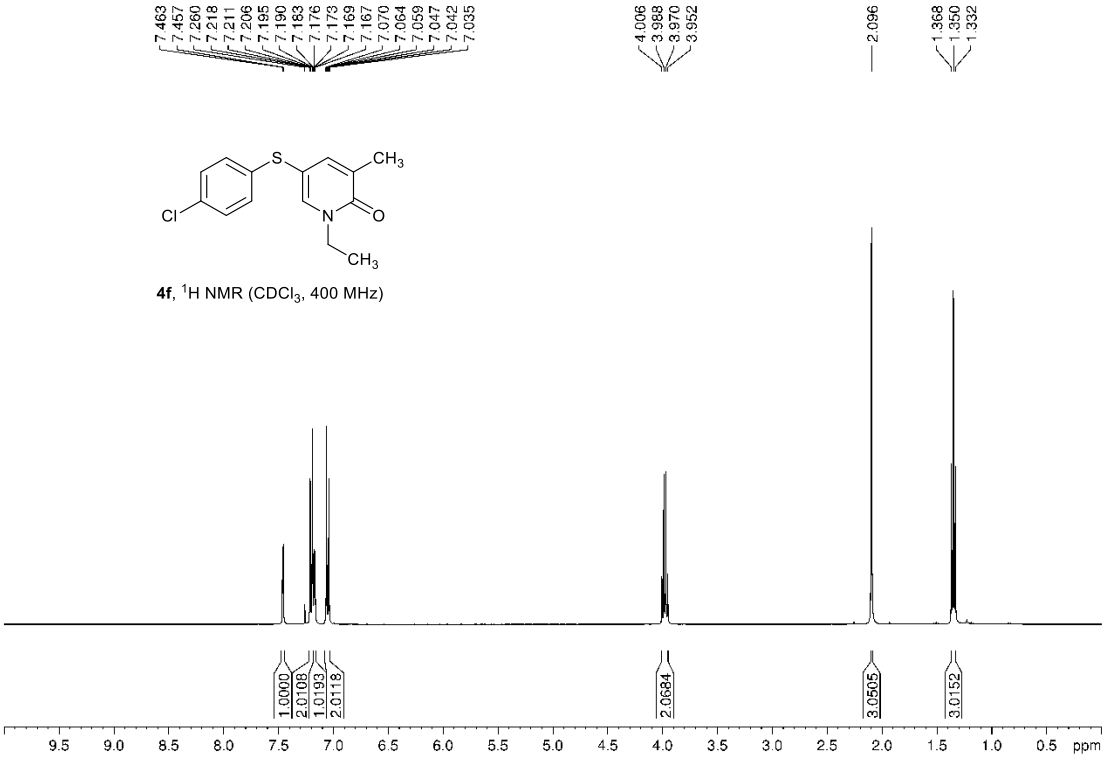


4c, ^{1}H NMR (DMSO-d_6, 400 MHz)

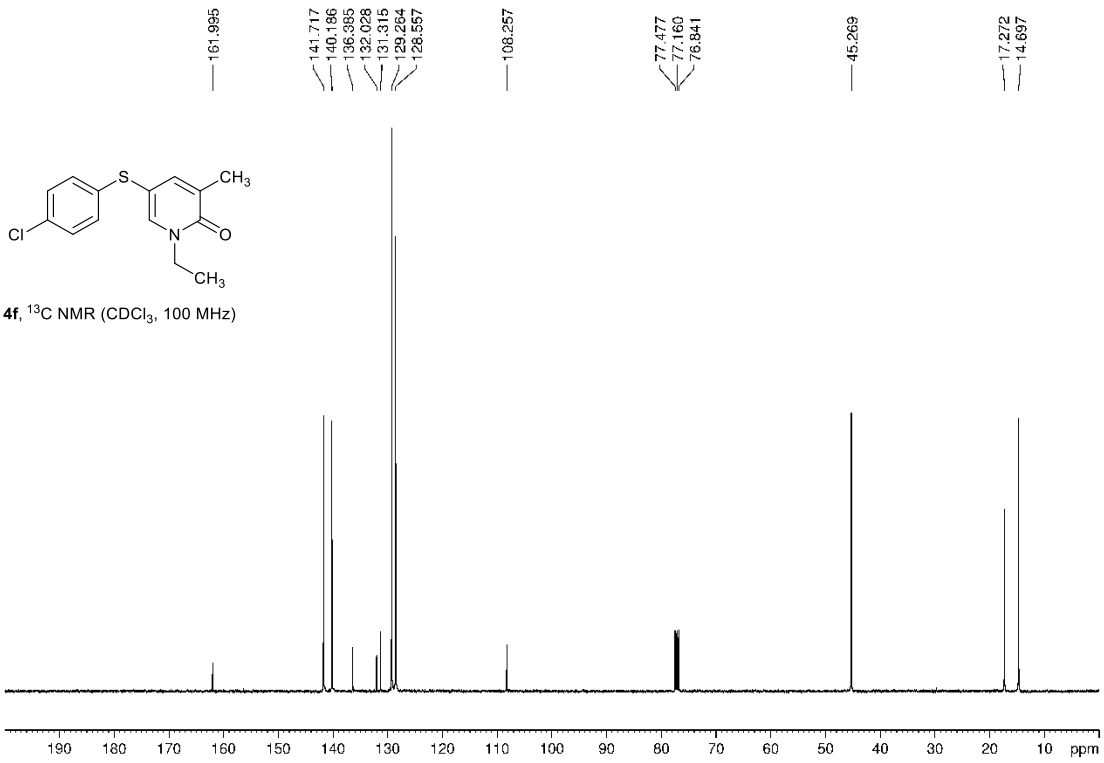


4c, ^{13}C NMR (DMSO-d_6, 100 MHz)

5-((4-Chlorophenyl)thio)-1-ethyl-3-methylpyridin-2(1*H*)-one (4f)

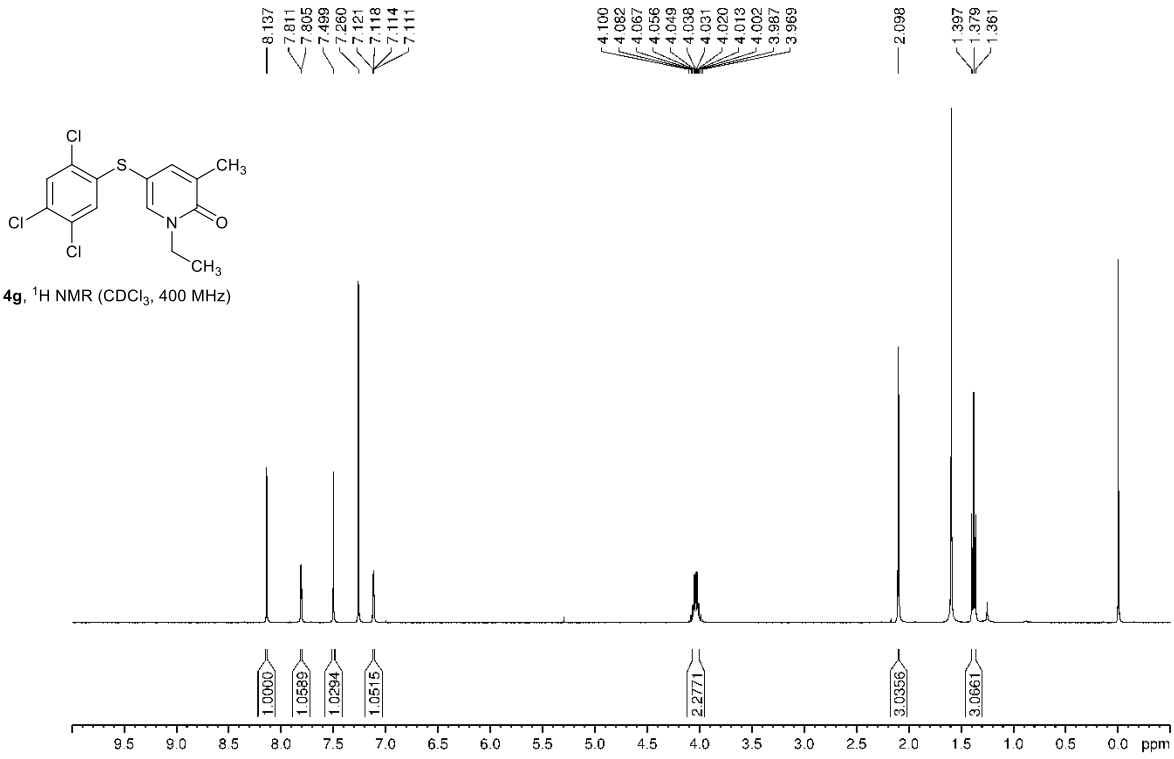


4f, ^{1}H NMR ($CDCl_3$, 400 MHz)

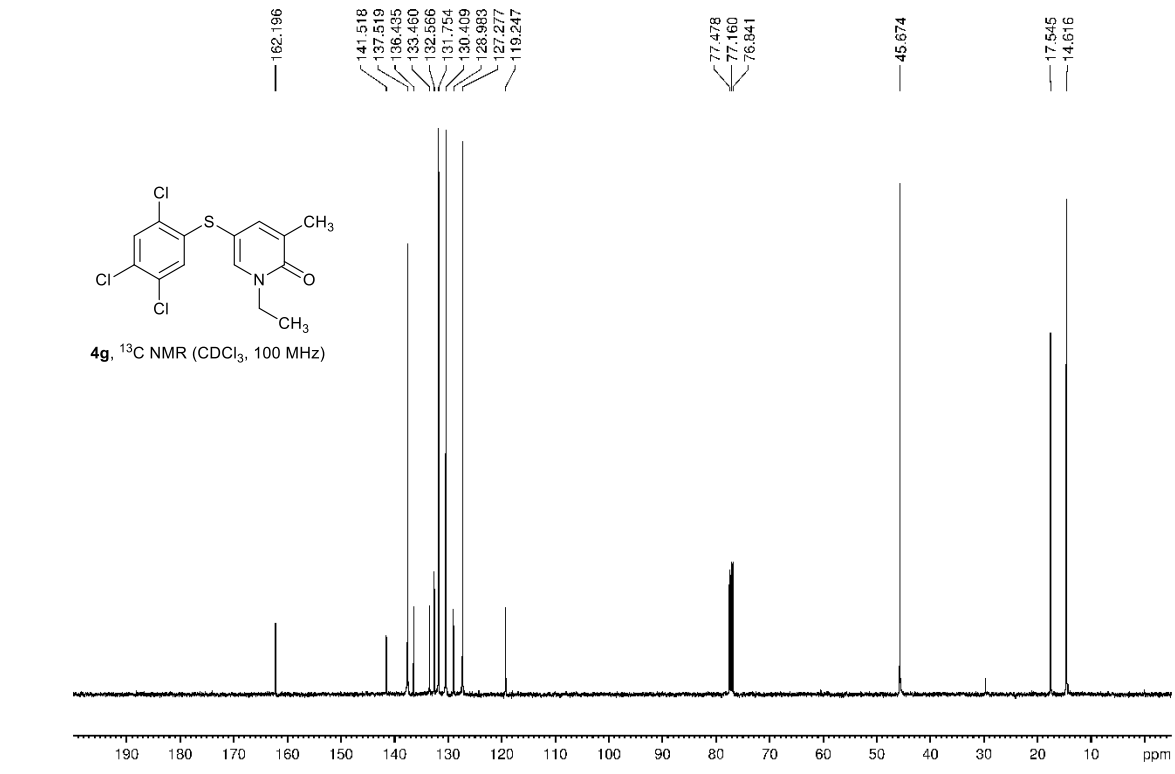


4f, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-3-methyl-5-((2,4,5-trichlorophenyl)thio)pyridin-2(1*H*)-one (4g)

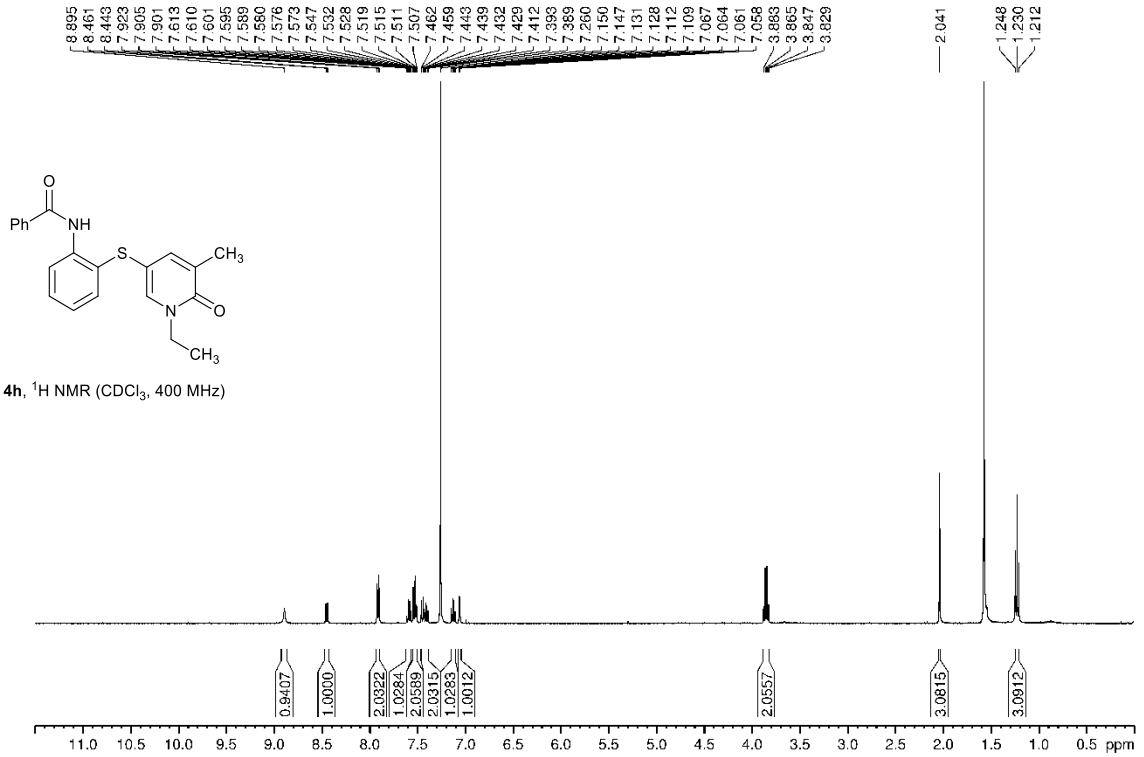


4g, ^{1}H NMR ($CDCl_3$, 400 MHz)

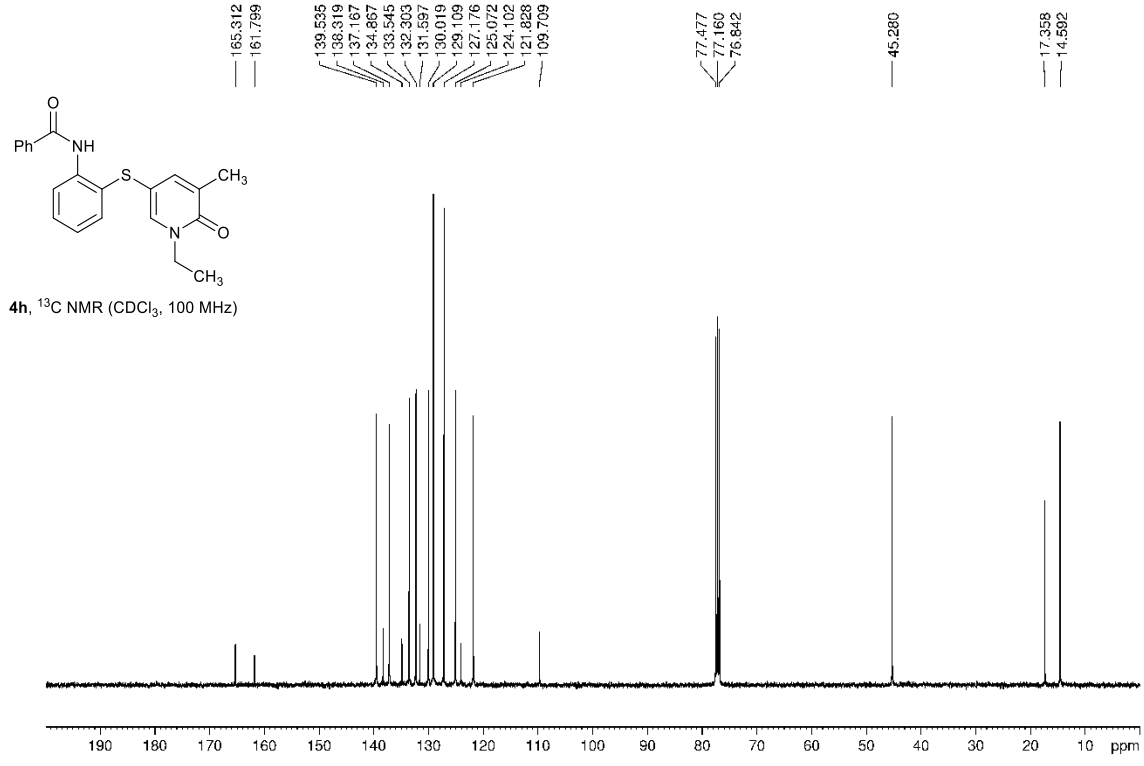


4g, ^{13}C NMR ($CDCl_3$, 100 MHz)

N-(2-((1-Ethyl-5-methyl-6-oxo-1,6-dihydropyridin-3-yl)thio)phenyl)benzamide (4h)

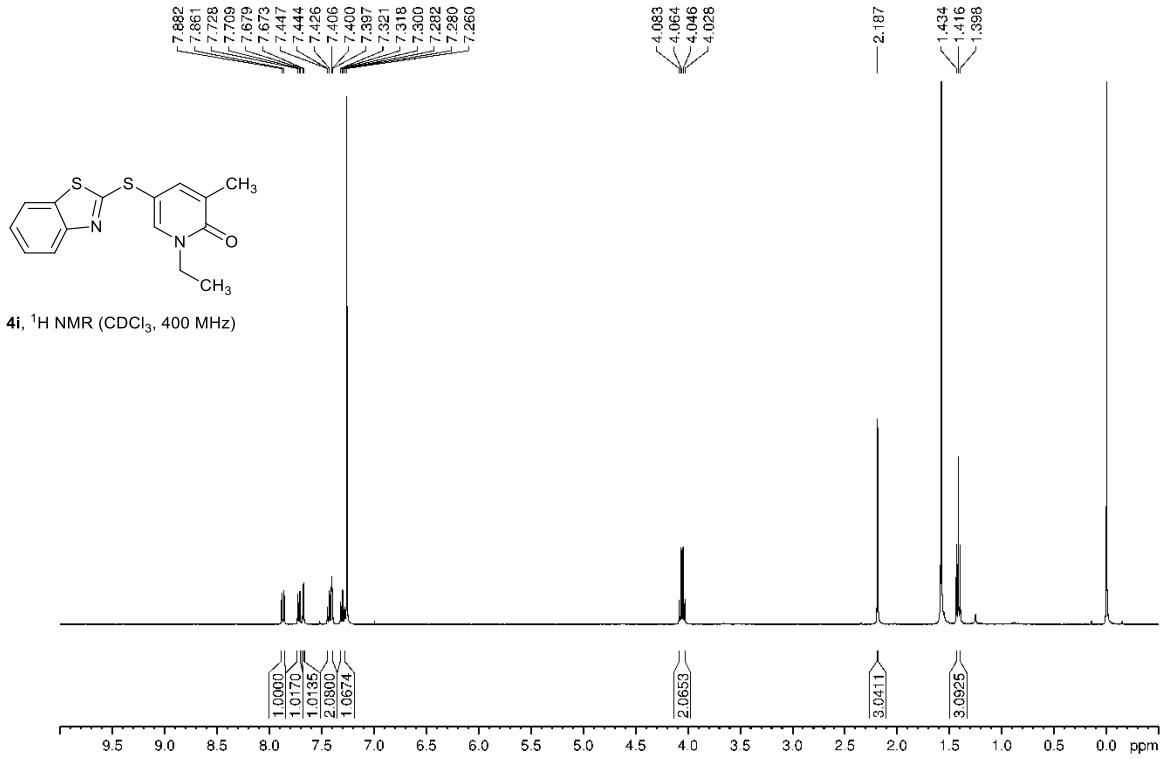


4h, ^{1}H NMR ($CDCl_3$, 400 MHz)

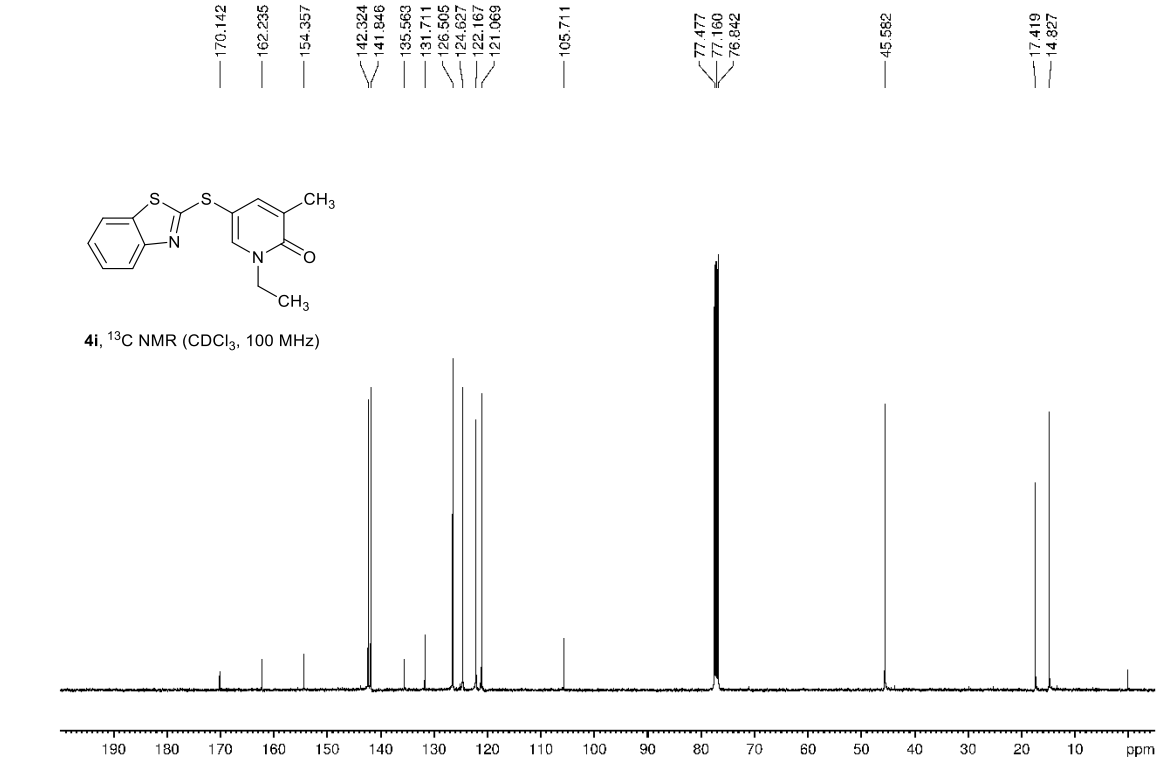


4h, ^{13}C NMR ($CDCl_3$, 100 MHz)

5-(Benzo[d]thiazol-2-ylthio)-1-ethyl-3-methylpyridin-2(1*H*)-one (4i)

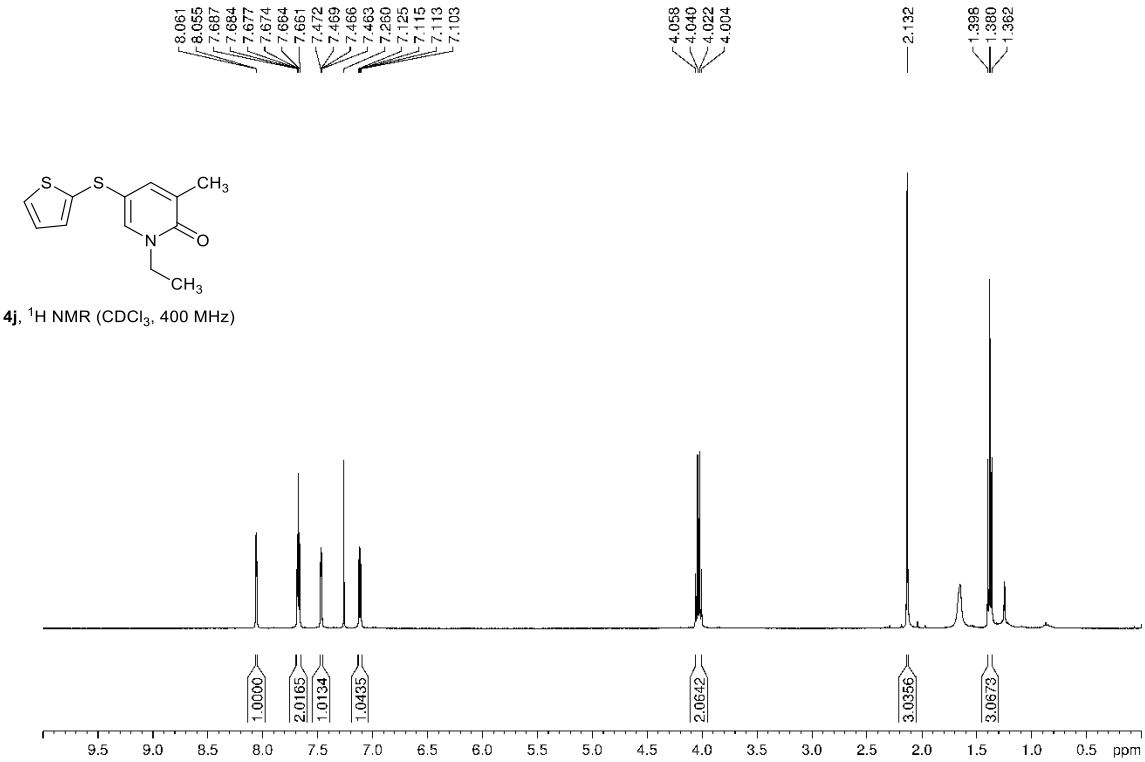


4i, ^{1}H NMR ($CDCl_3$, 400 MHz)

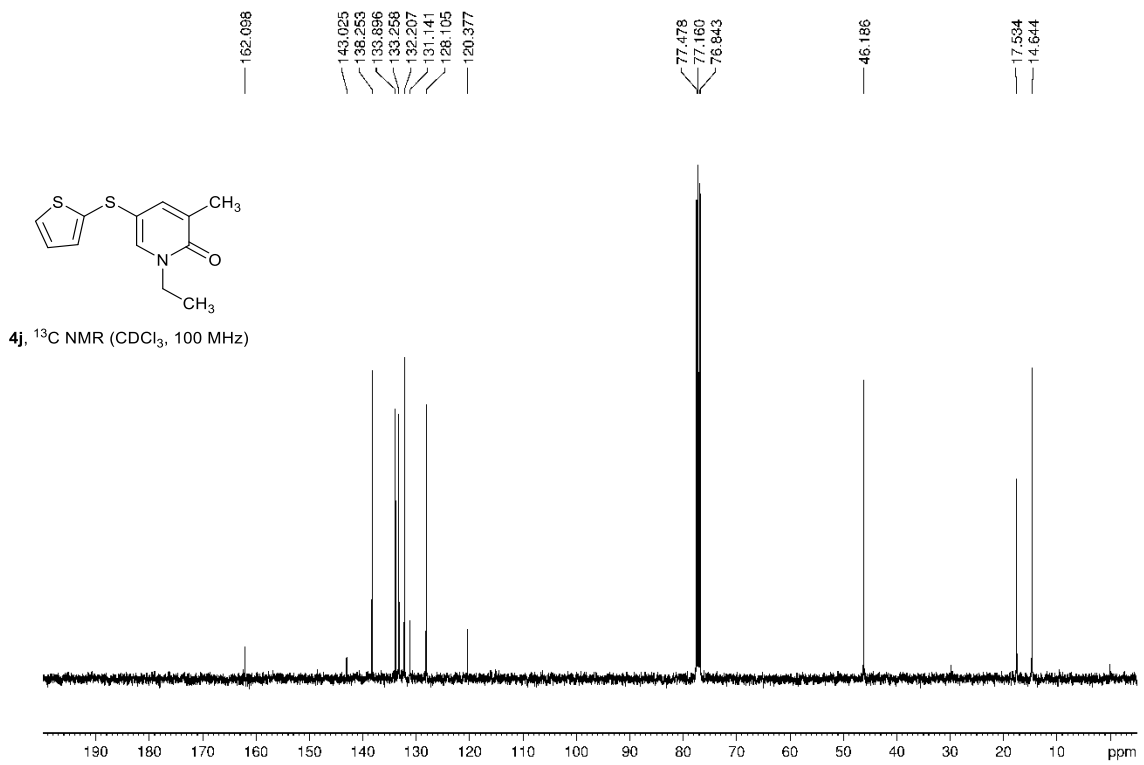


4i, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-3-methyl-5-(thiophen-2-ylthio)pyridin-2(1*H*)-one (4j)

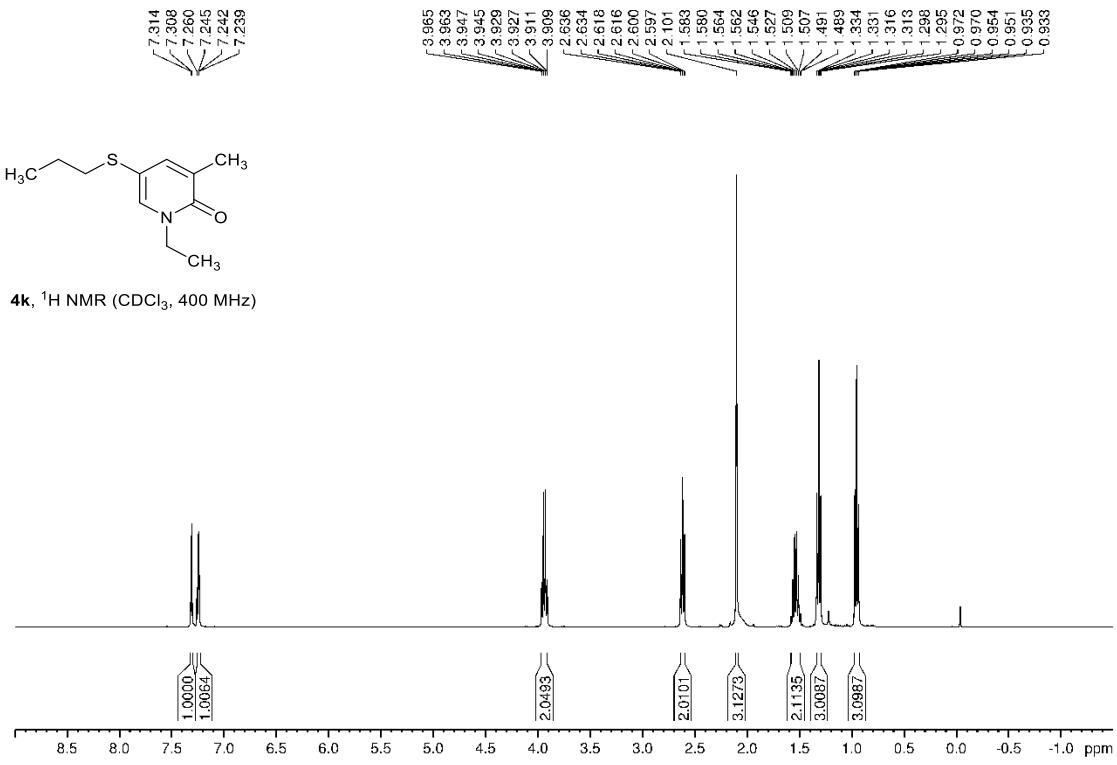


4j, ^{1}H NMR ($CDCl_3$, 400 MHz)

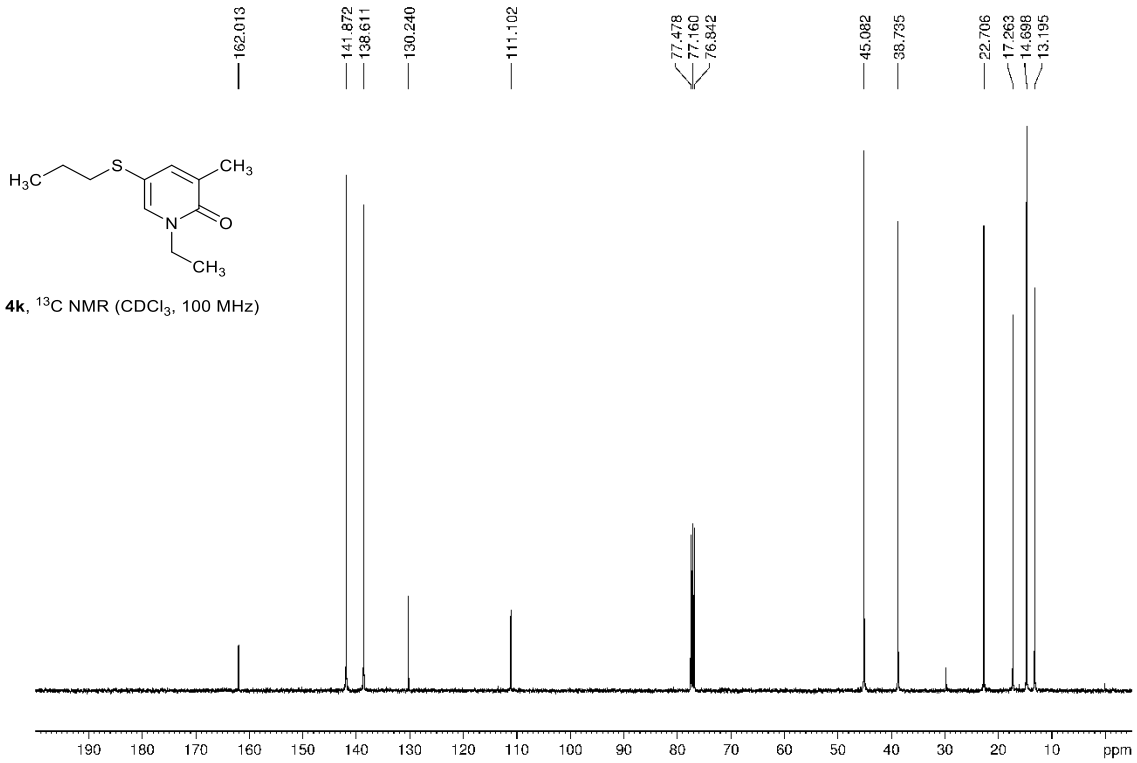


4j, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-3-methyl-5-(propylthio)pyridin-2(1*H*)-one (4k)

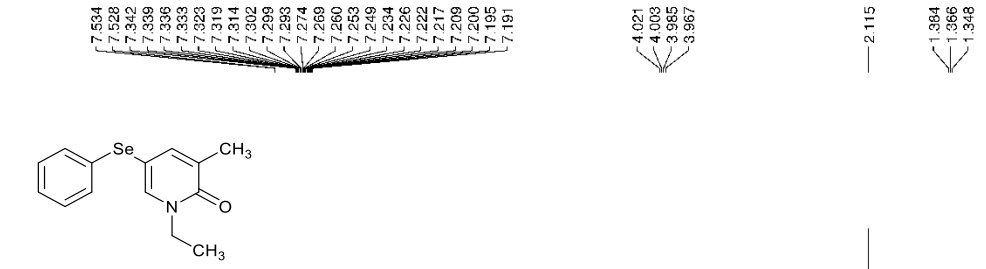


4k, ^{1}H NMR ($CDCl_3$, 400 MHz)

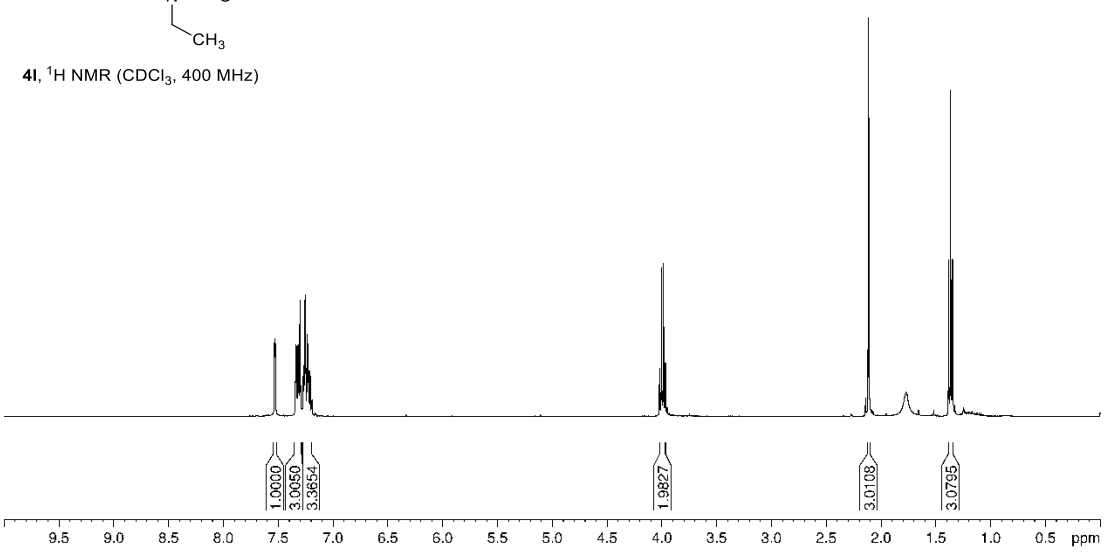


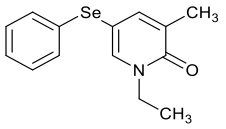
4k, ^{13}C NMR ($CDCl_3$, 100 MHz)

1-Ethyl-3-methyl-5-(phenylselanyl)pyridin-2(1*H*)-one (4l)

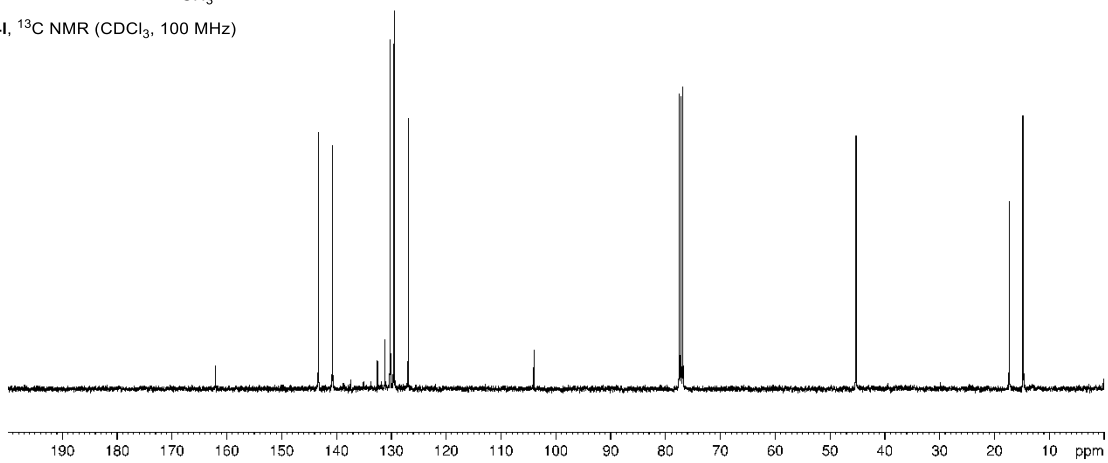


4l, ^{1}H NMR ($CDCl_3$, 400 MHz)

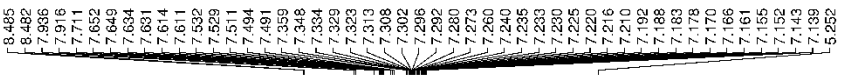


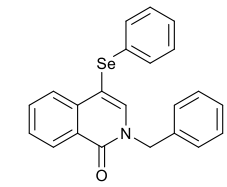


4l, ^{13}C NMR ($CDCl_3$, 100 MHz)

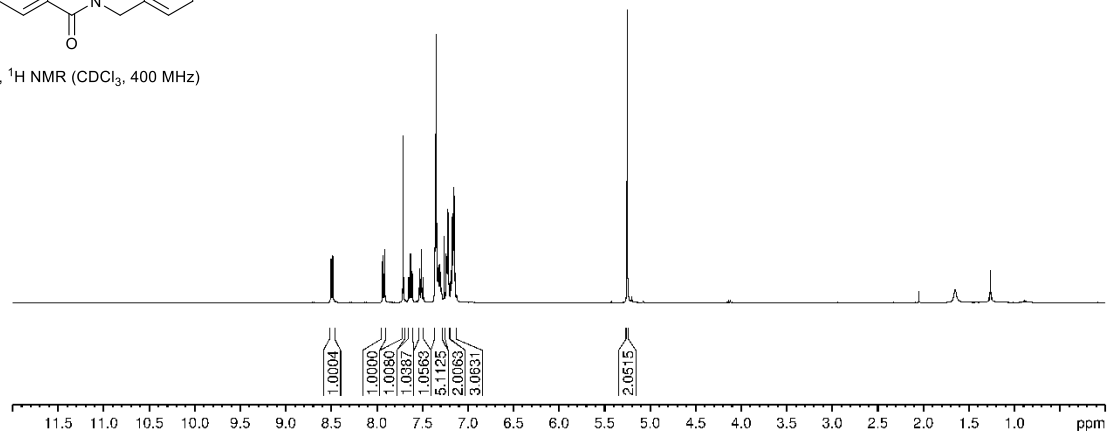


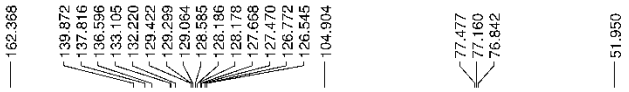
2-Benzyl-4-(phenylselanyl)isoquinolin-1(2*H*)-one (4m)

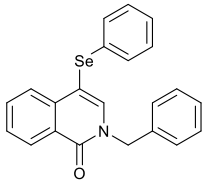




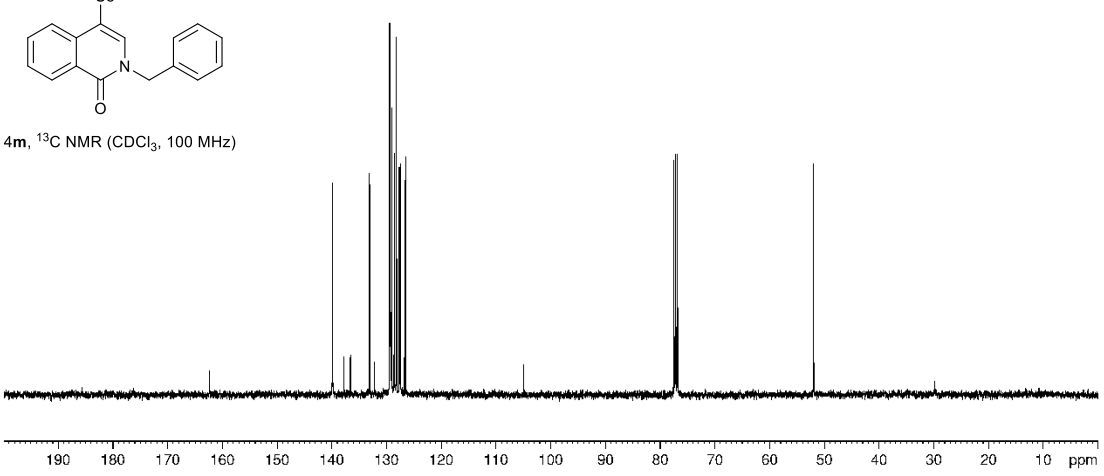
4**m**, ^{1}H NMR ($CDCl_3$, 400 MHz)



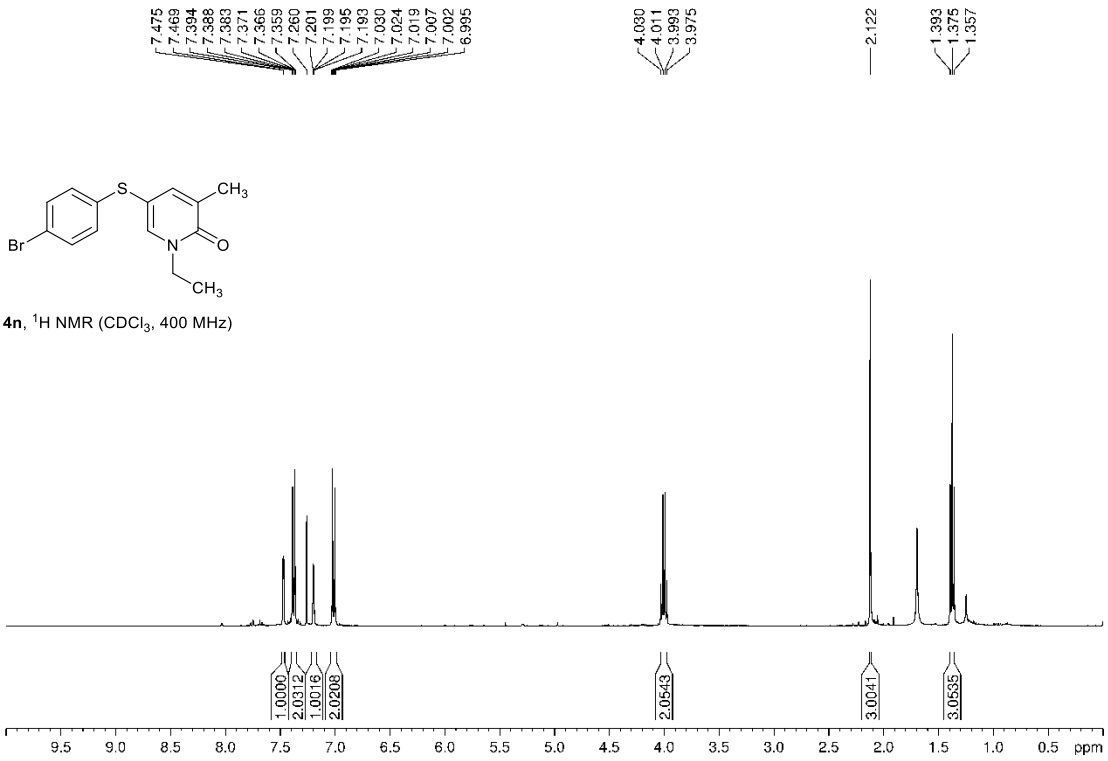




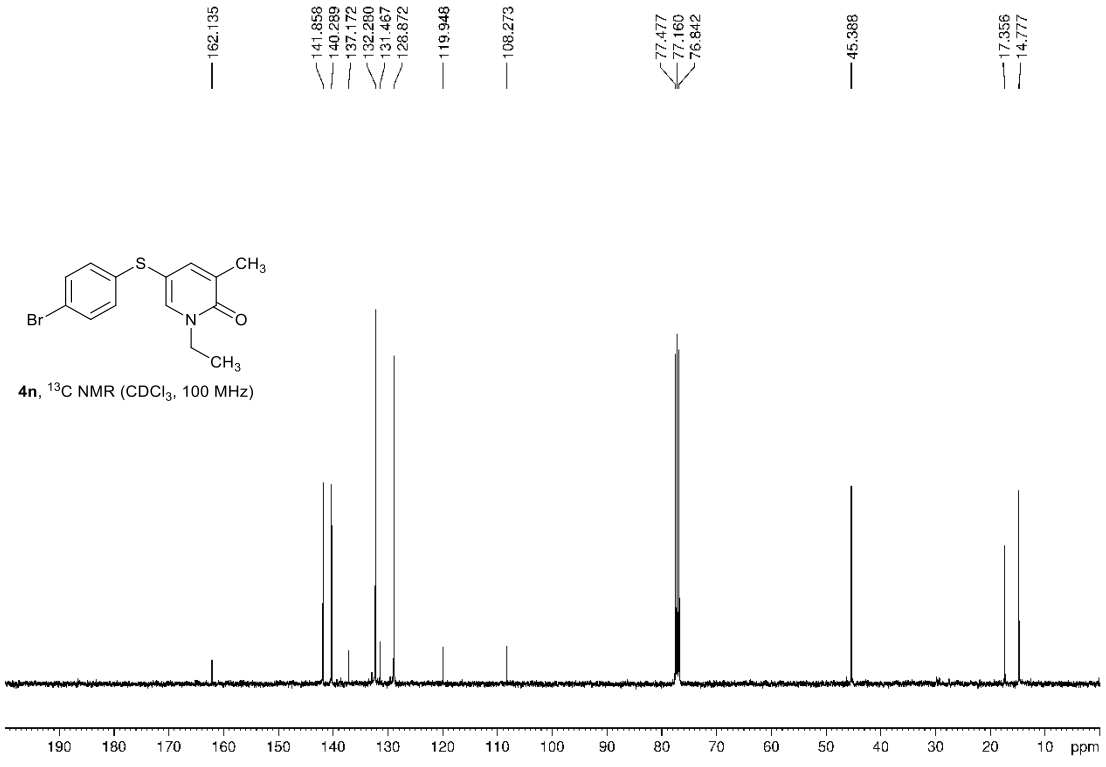
4**m**, ^{13}C NMR ($CDCl_3$, 100 MHz)



5-((4-Bromophenyl)thio)-1-ethyl-3-methylpyridin-2(1*H*)-one (4n)



4n, ^{1}H NMR ($CDCl_3$, 400 MHz)



4n, ^{13}C NMR ($CDCl_3$, 100 MHz)