

University of Dundee

A Continuous Flow Strategy for the Facile Synthesis and Elaboration of Semi-Saturated Heterobicyclic Fragments

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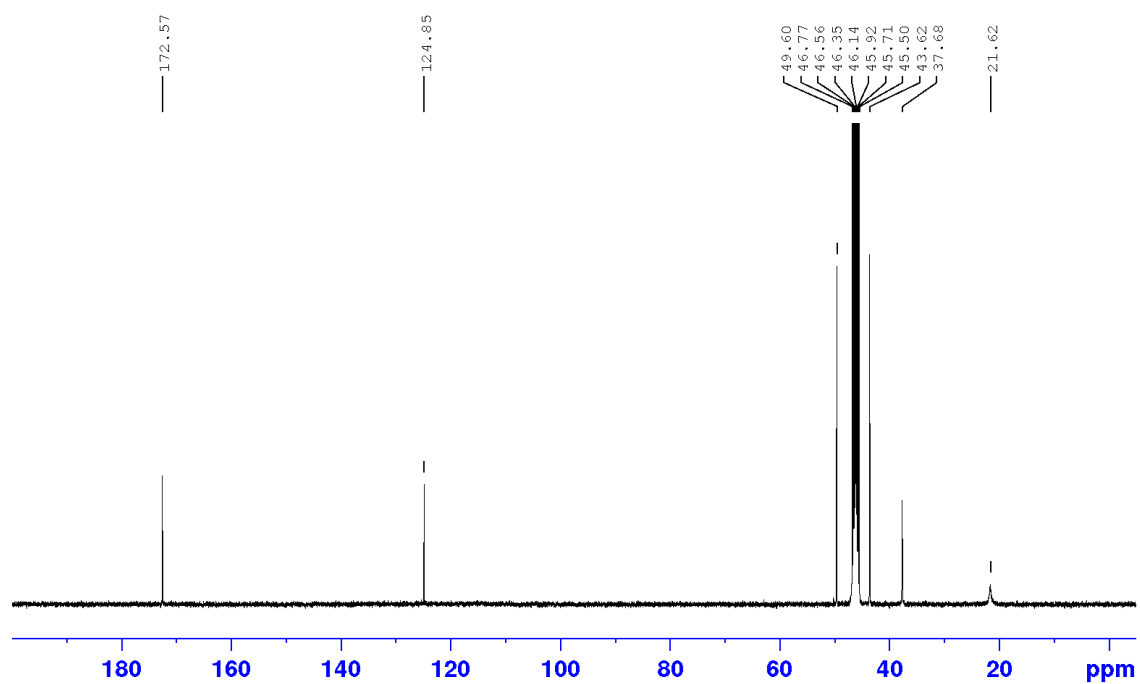
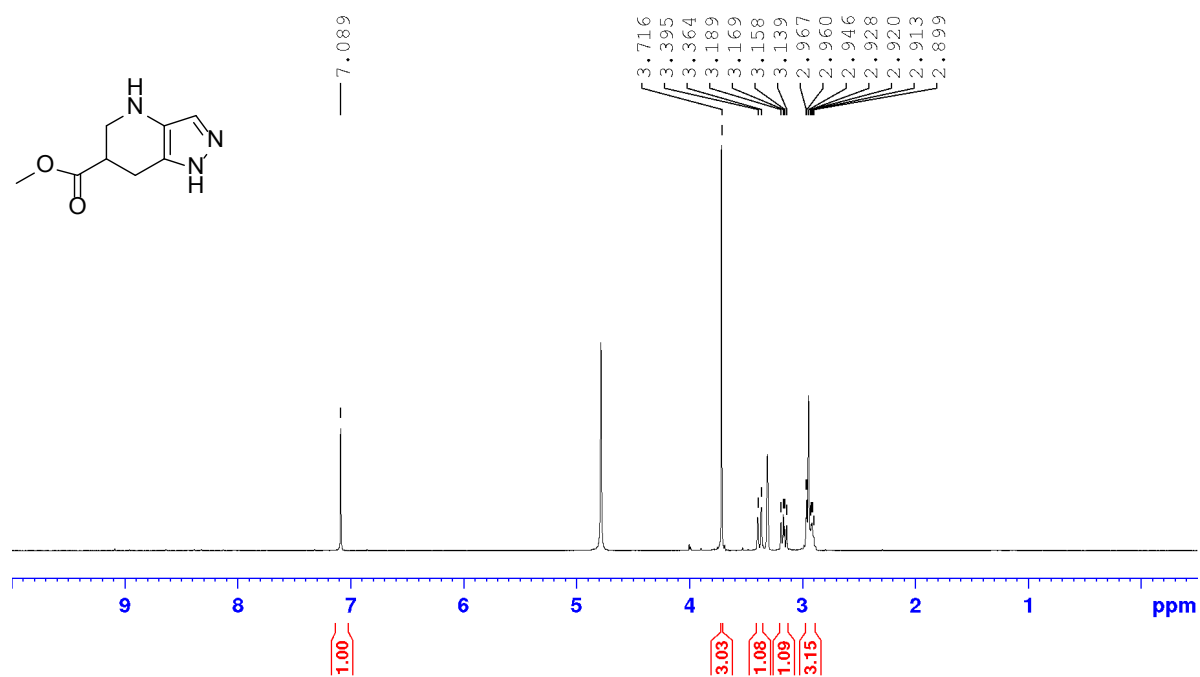
1. Fragment criteria of the Drug Discovery Unit (DDU)'s fragment library

Fragment criteria ^a	DDU range
LogP	-2 to 2
LogD	-2 to 2
Heavy atom count	5 to 18
Hydrogen bond acceptor	≤ 6
Hydrogen bond donor	≤ 3
Total polar surface area	≤ 90
Rotable bonds	≤ 3
Solubility	Sample concentration > 1 mM based on comparison to residual DMSO-d ₆ peak.
Stability	< 1% increase in impurities after 48 hours
Aggregation	No evidence in the waterLOGSY of aggregation of the compound in buffer.
Purity	≥ 95%

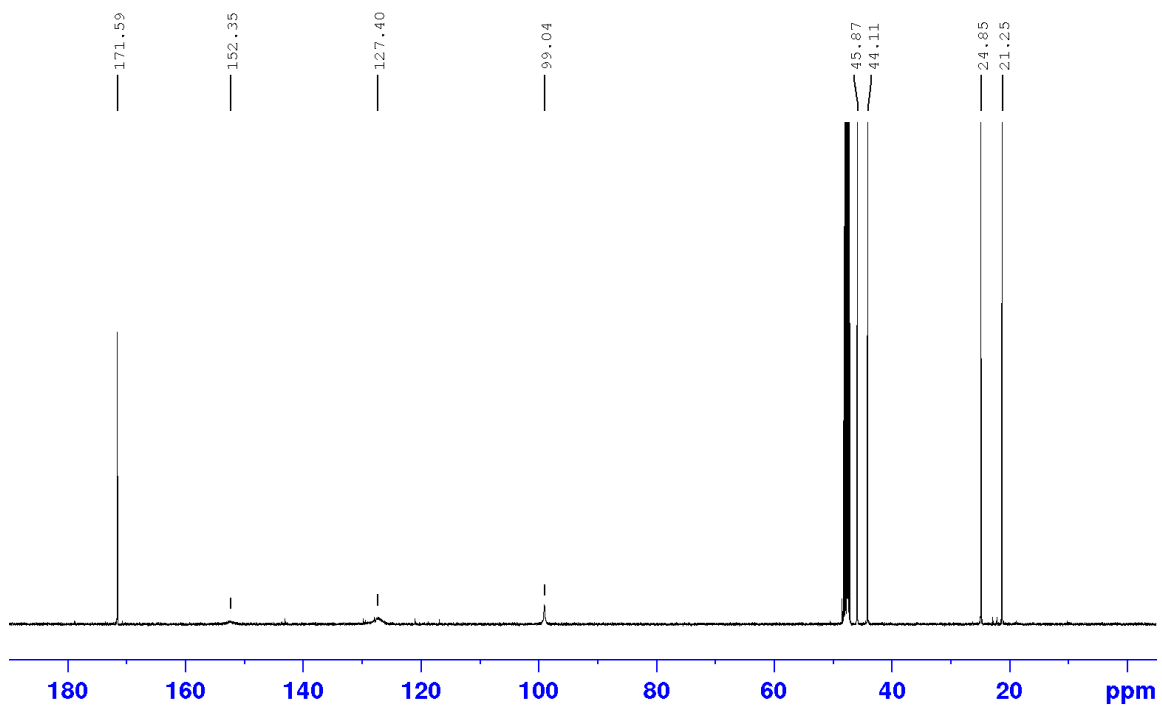
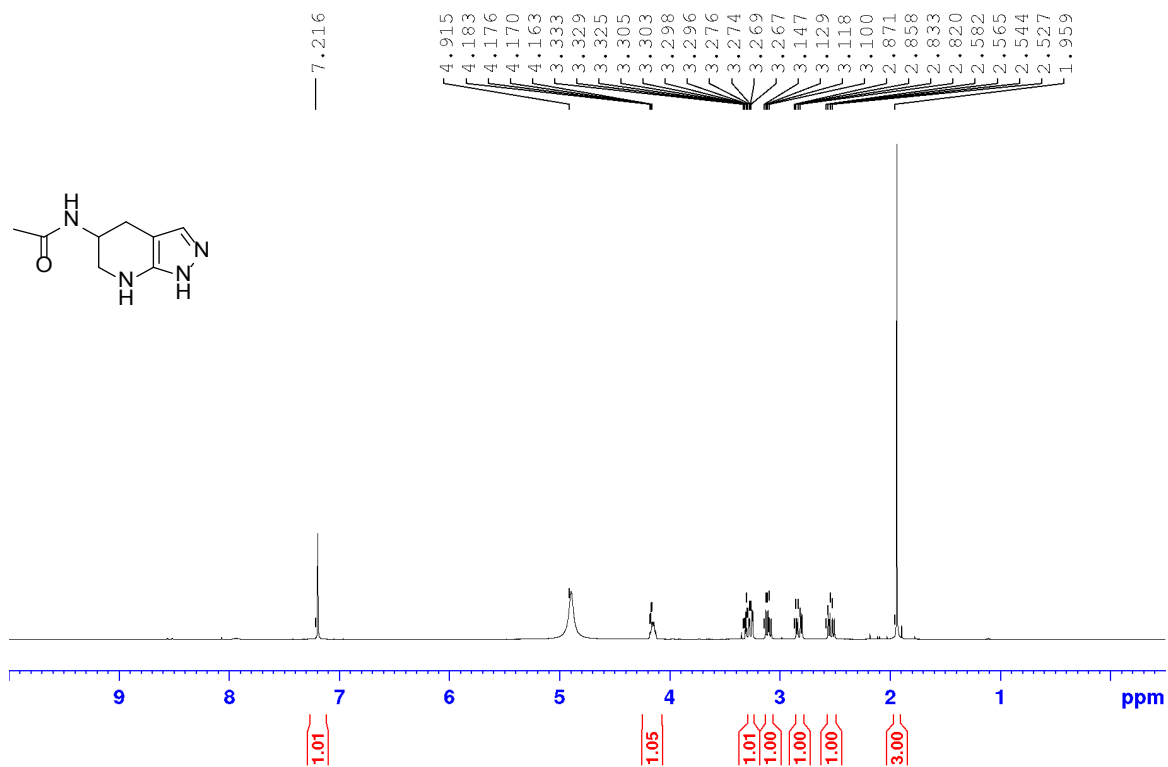
[a] Physicochemical and quality control parameters employed by the DDU.

2. NMR spectra

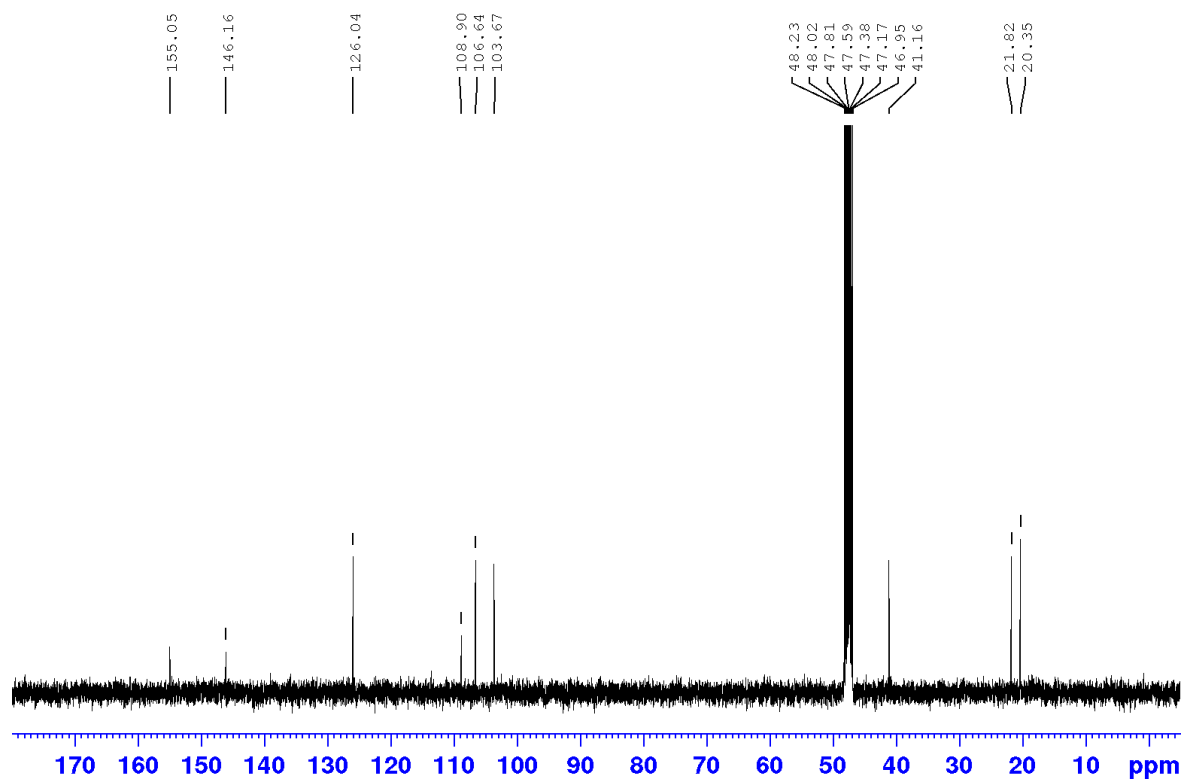
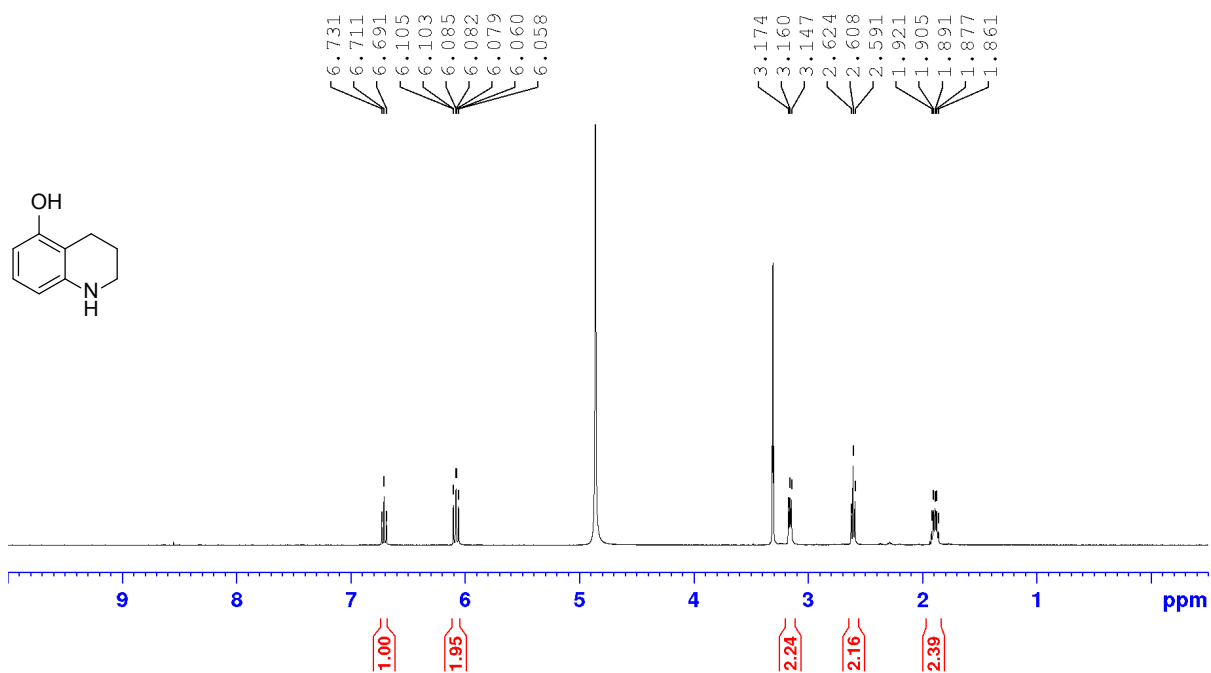
methyl 4,5,6,7-tetrahydro-1H-pyrazolo[4,3-b]pyridine-6-carboxylate (**18**)



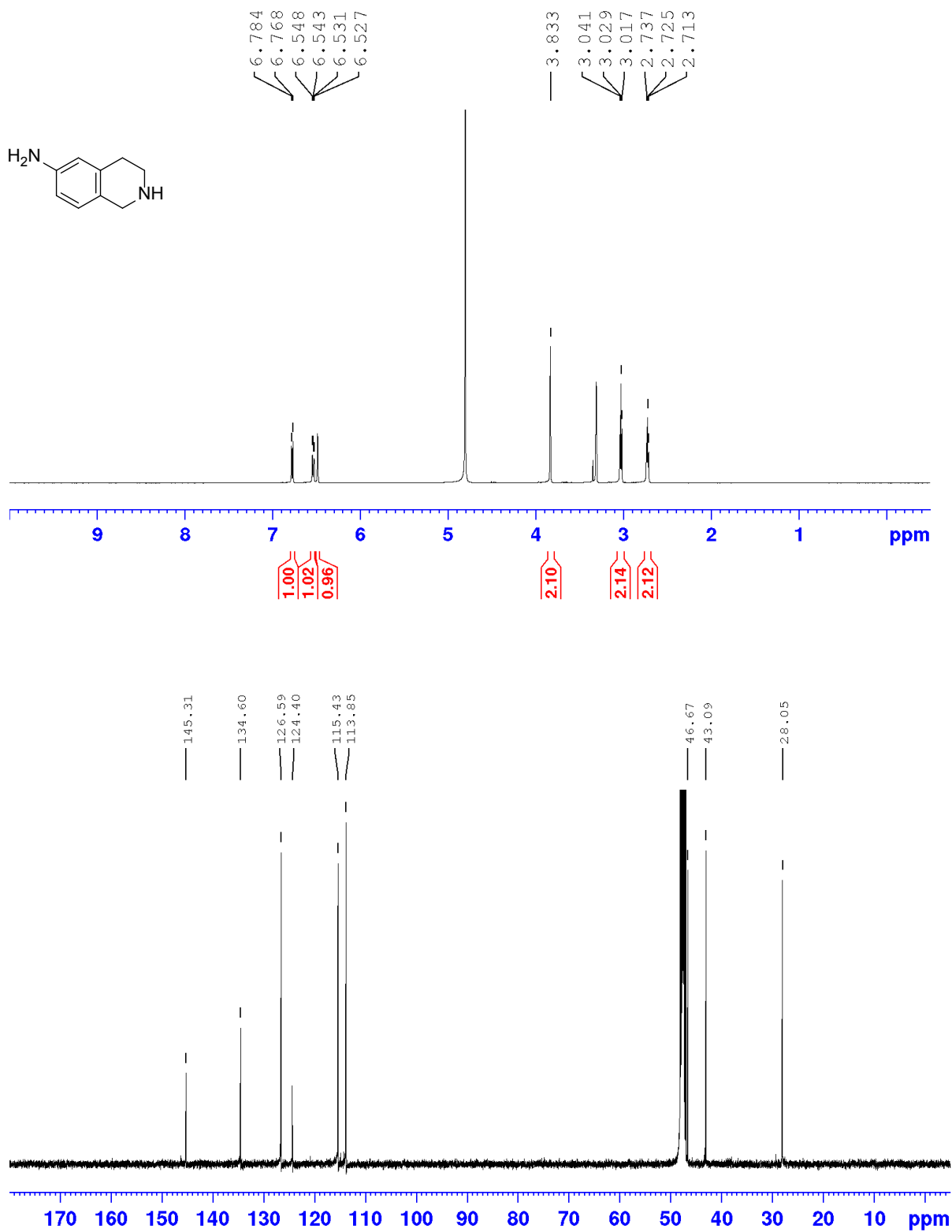
N-(4,5,6,7-tetrahydro-1H-pyrazolo[3,4-b]pyridin-5-yl)acetamide (**19**)



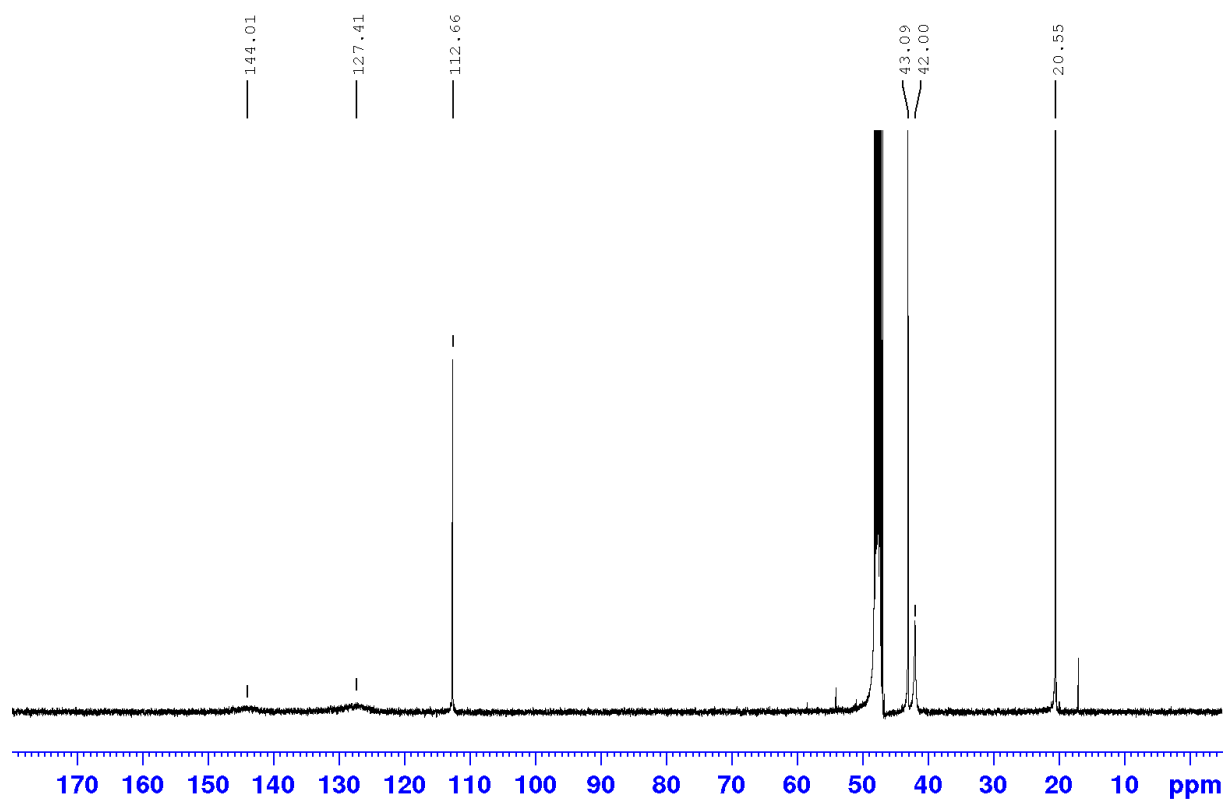
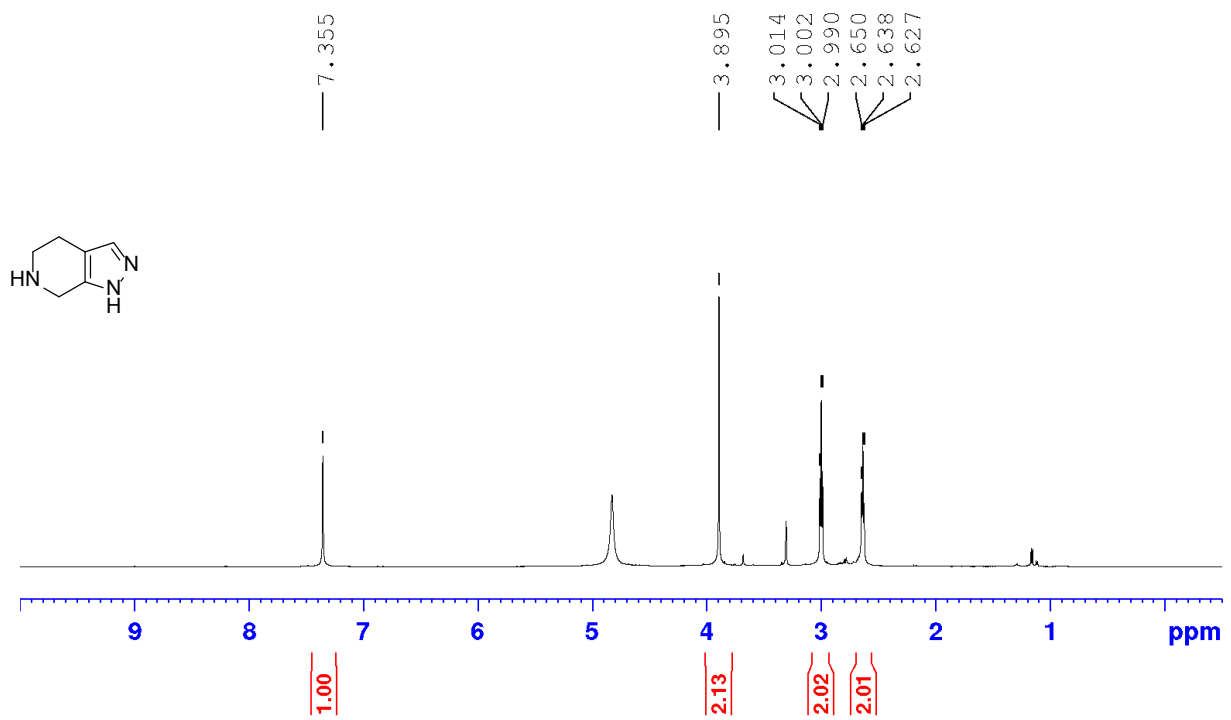
1,2,3,4-tetrahydroquinolin-5-ol (**20**)¹



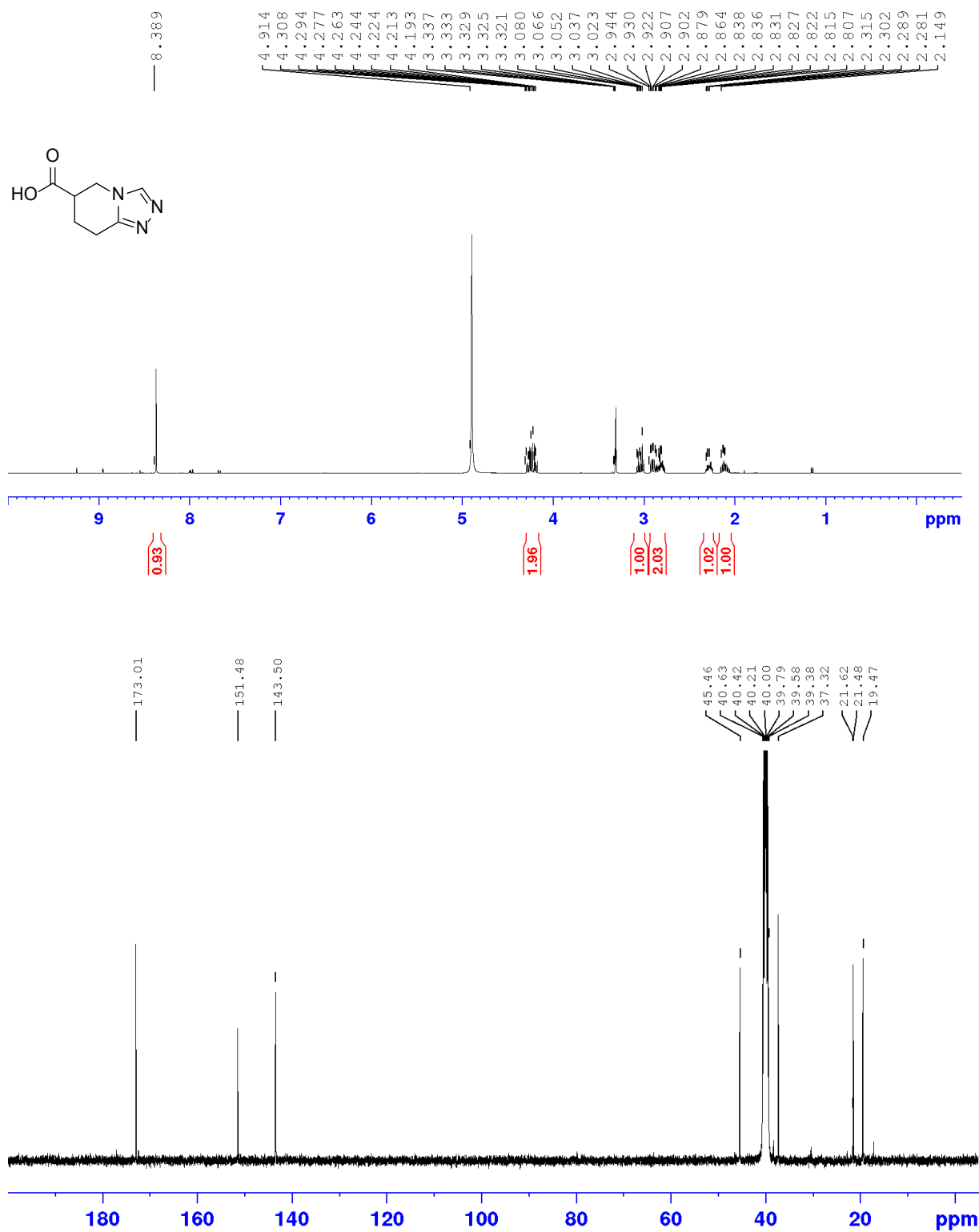
1,2,3,4-tetrahydroisoquinolin-6-amine (**21**)²



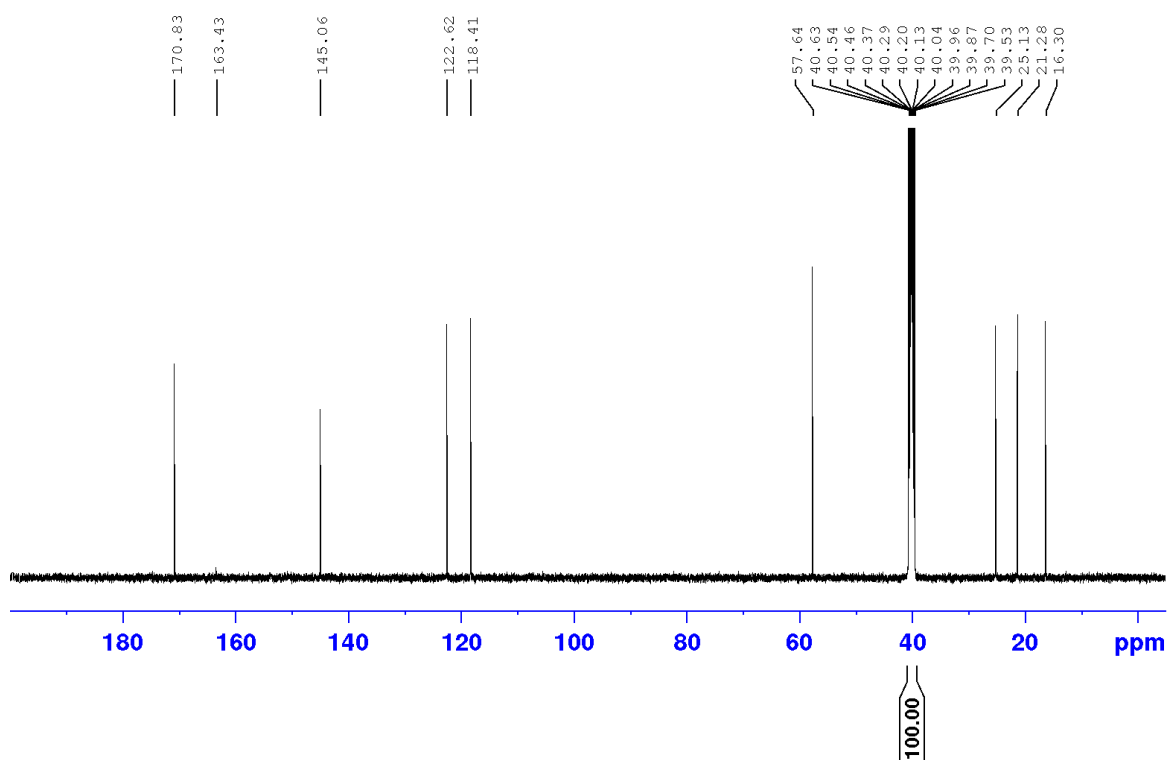
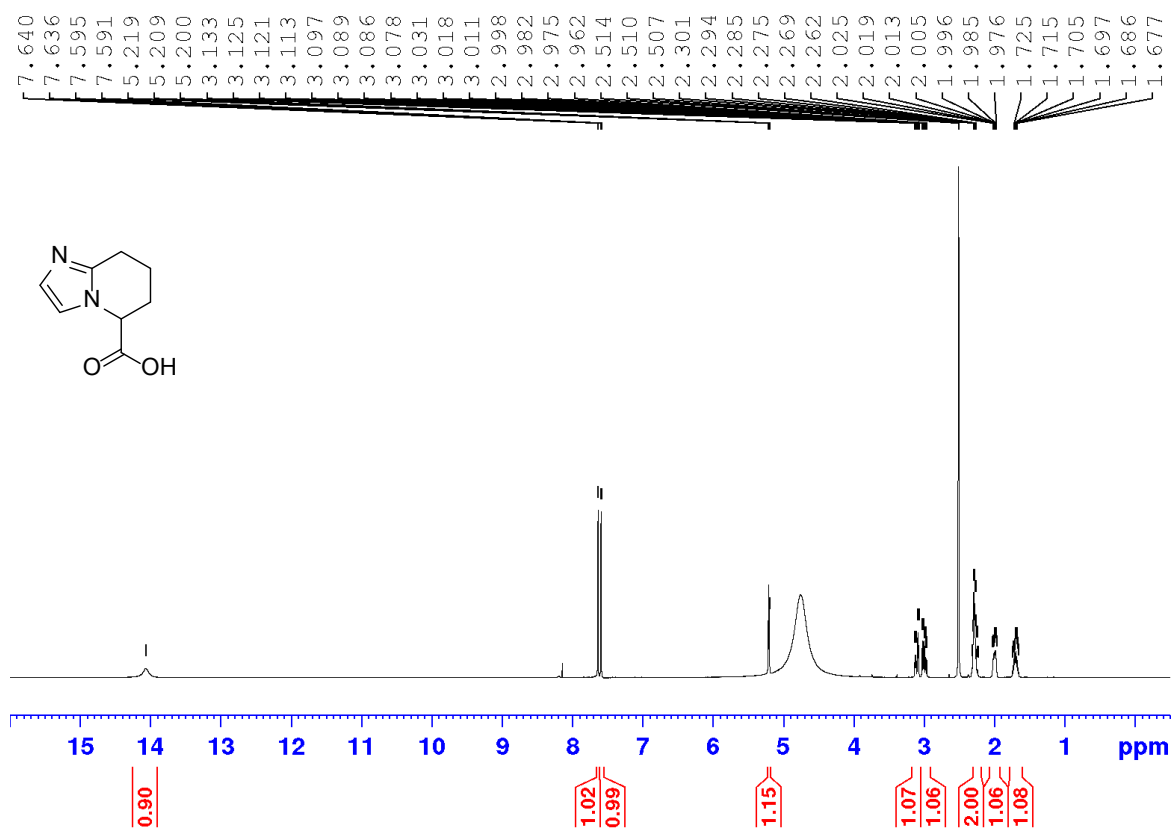
4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (**22**)³



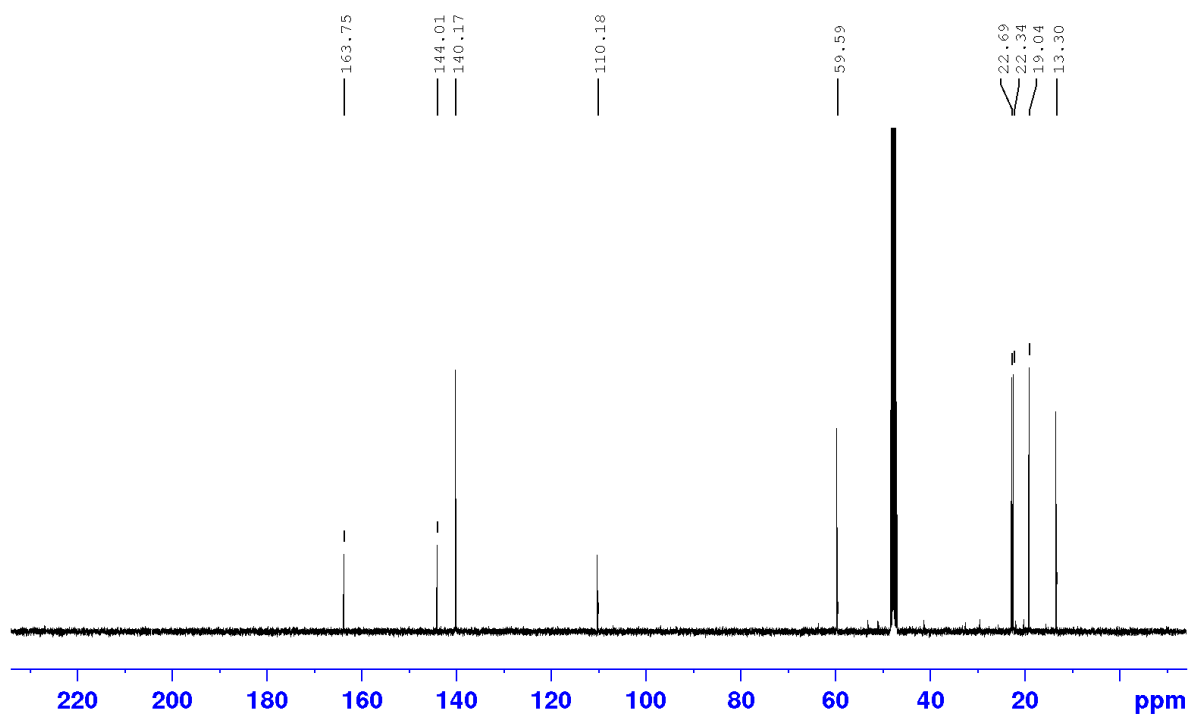
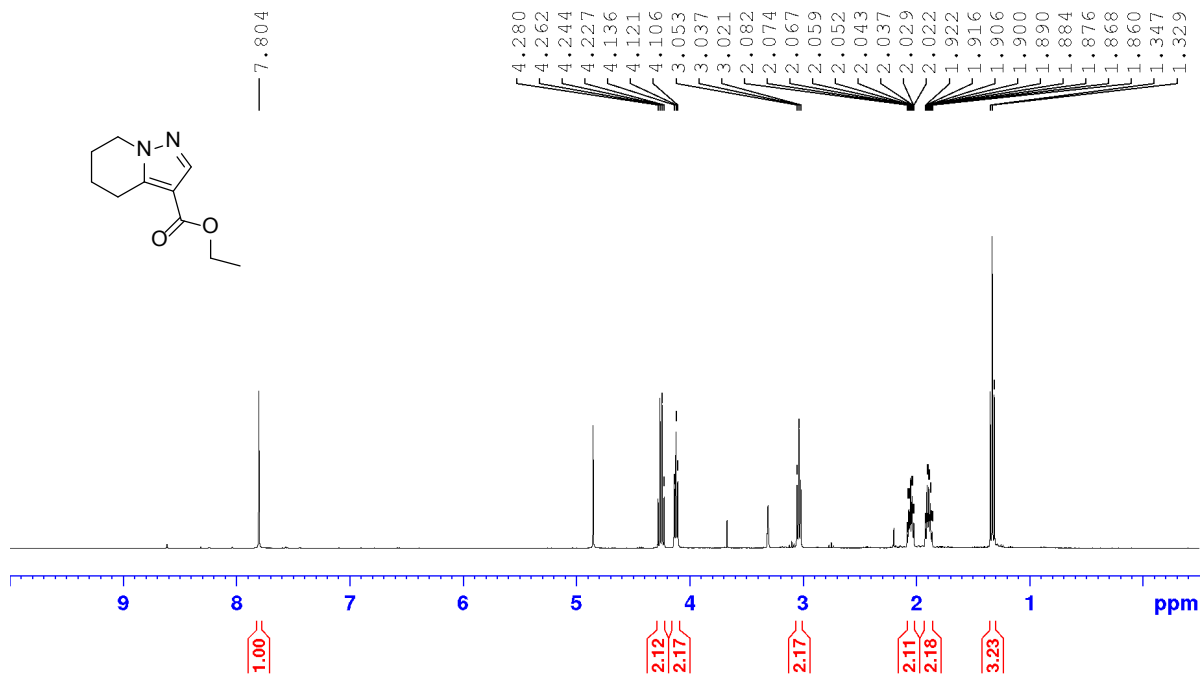
5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine-6-carboxylic acid (**23**)⁴



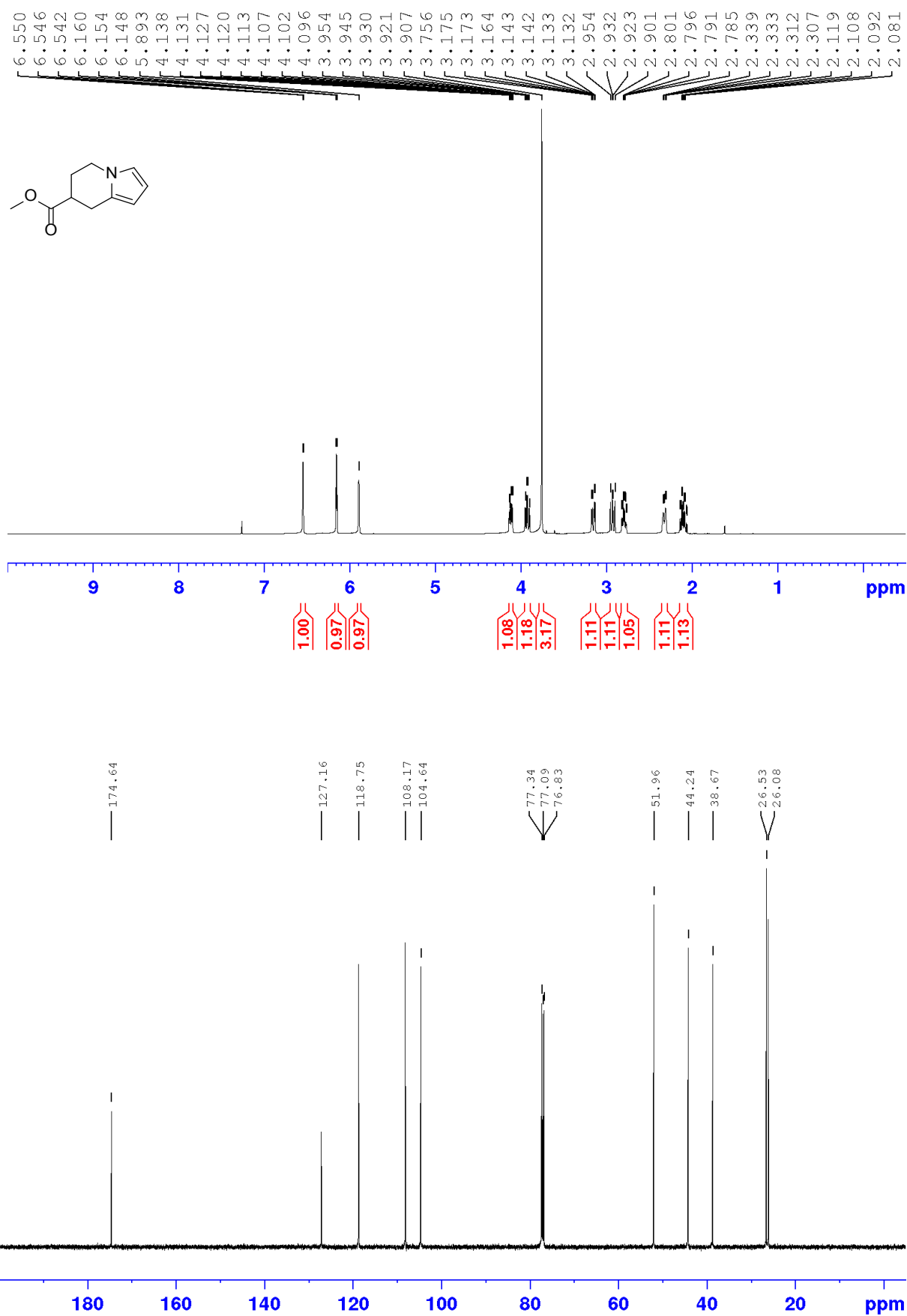
5,6,7,8-tetrahydroimidazo[1,2-a]pyridine-5-carboxylic acid (**24**)⁵



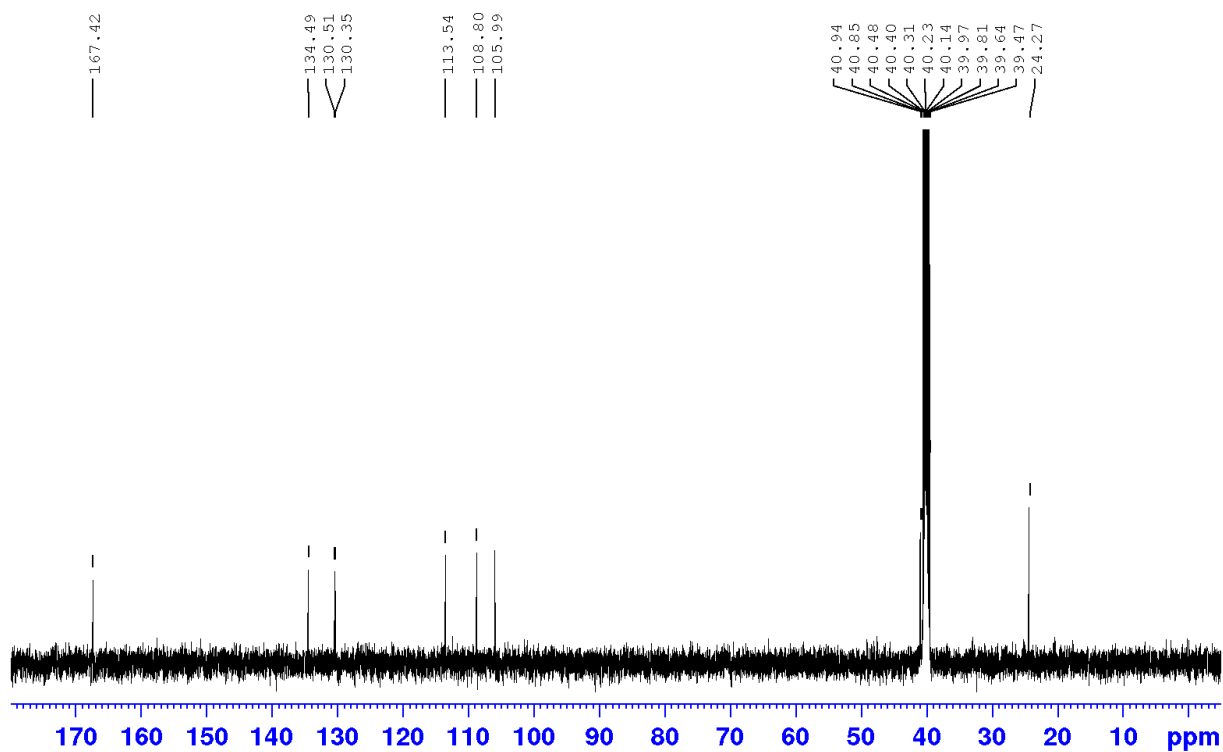
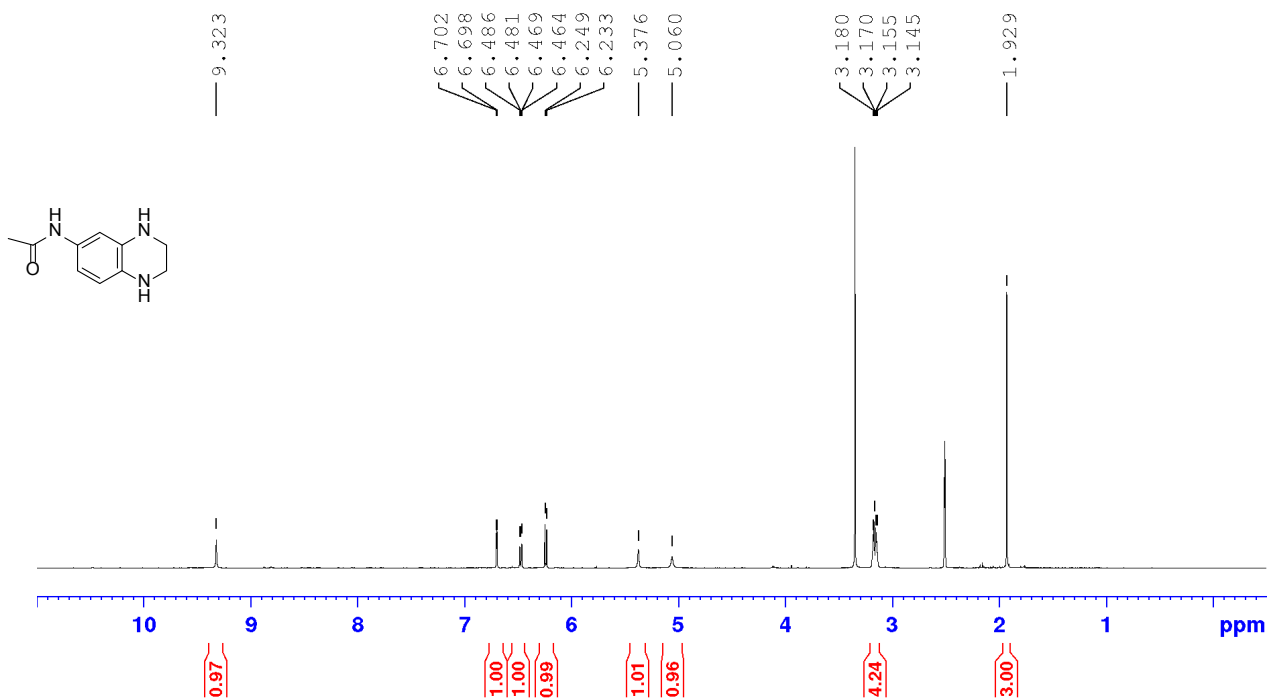
ethyl 4,5,6,7-tetrahydropyrazolo[1,5-a]pyridine-3-carboxylate (**25**)⁶



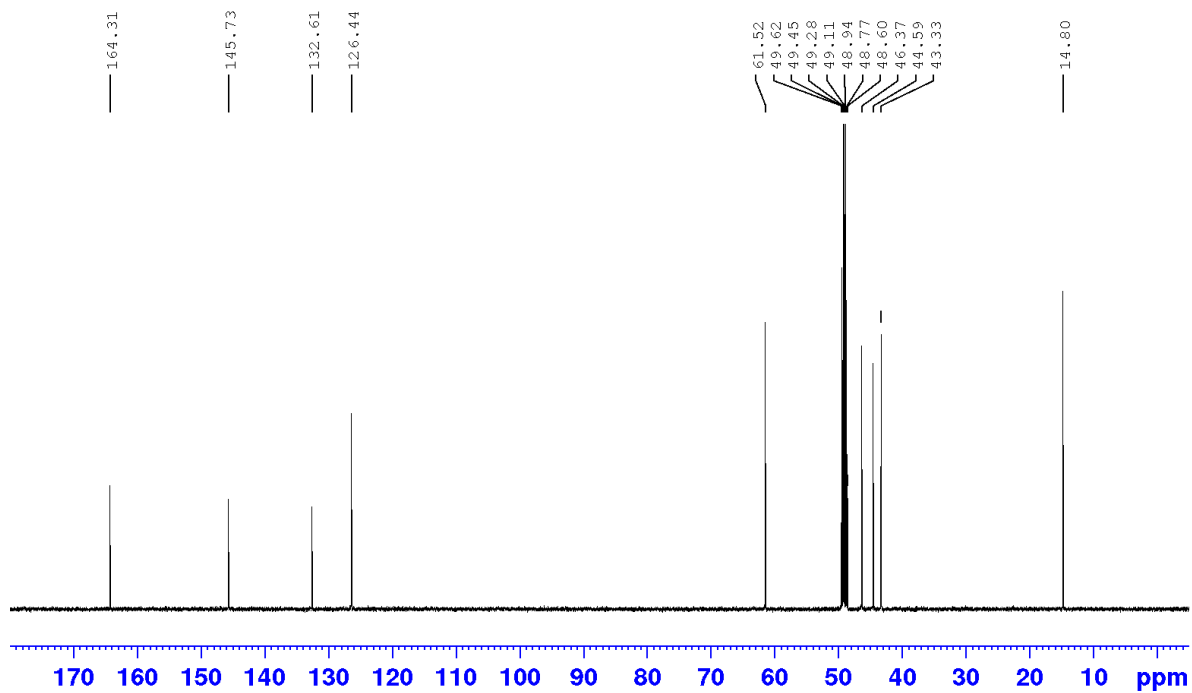
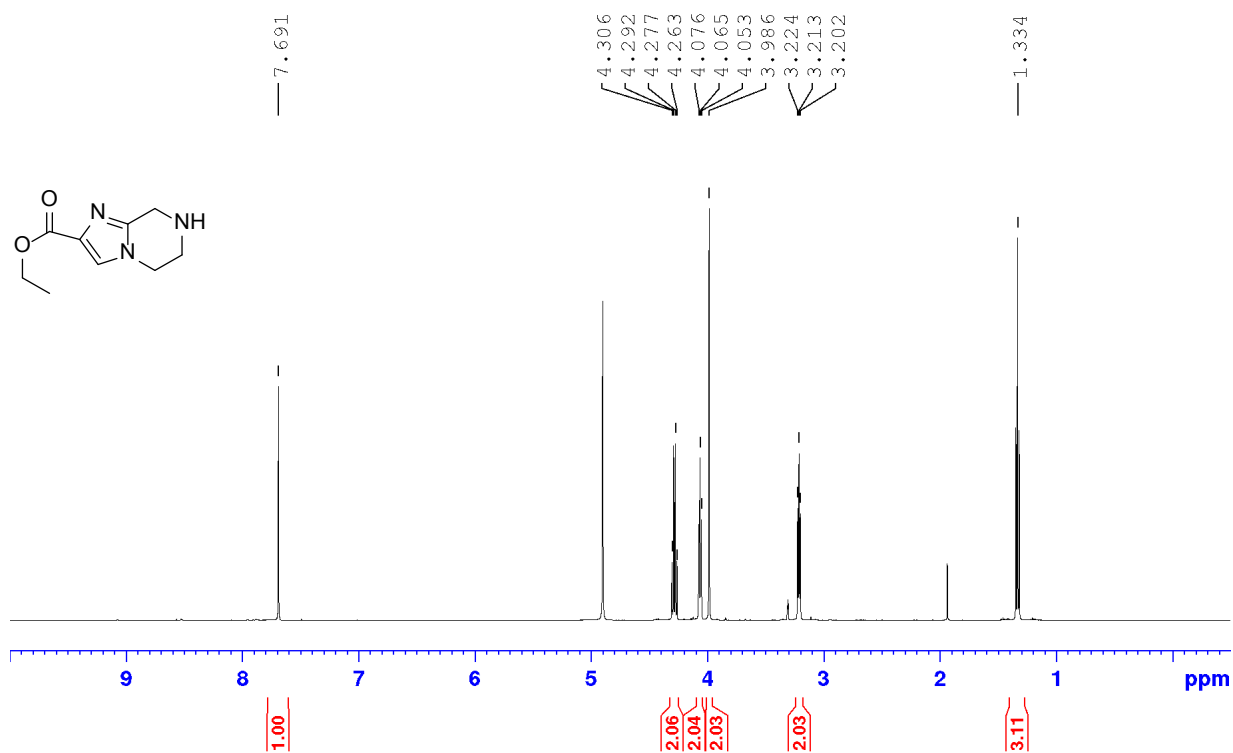
methyl 5,6,7,8-tetrahydroindolizine-7-carboxylate (**26**)



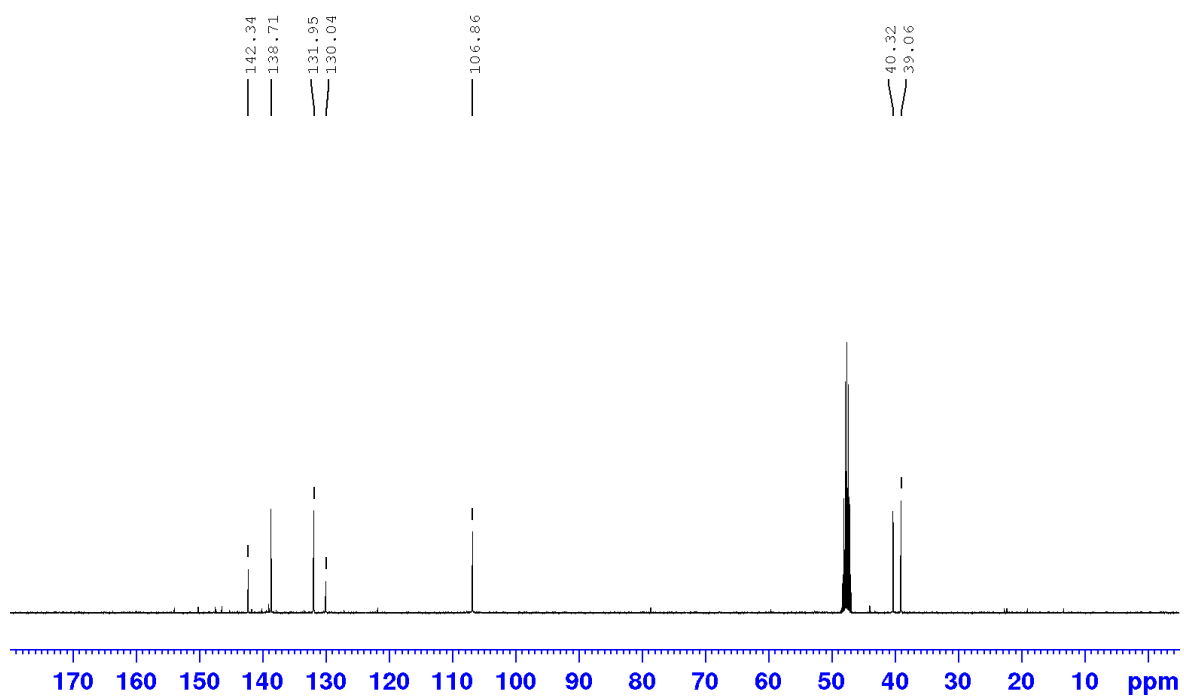
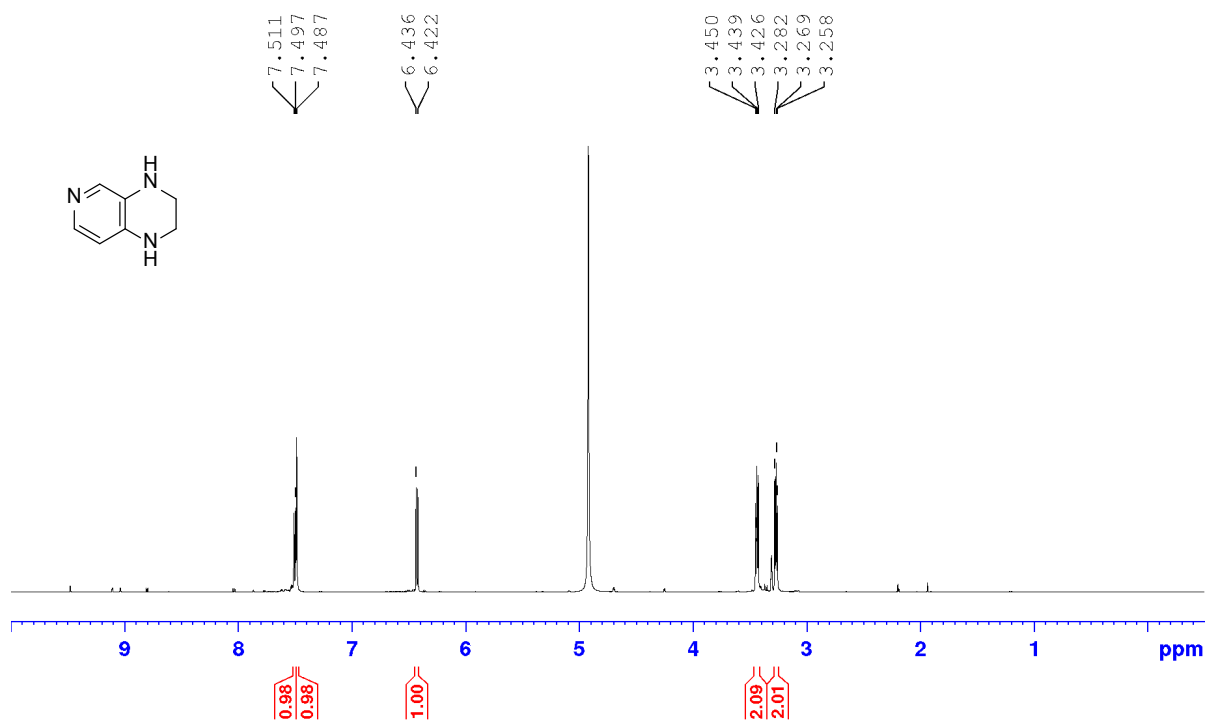
N-(1,2,3,4-tetrahydroquinoxalin-6-yl)acetamide (**27**)



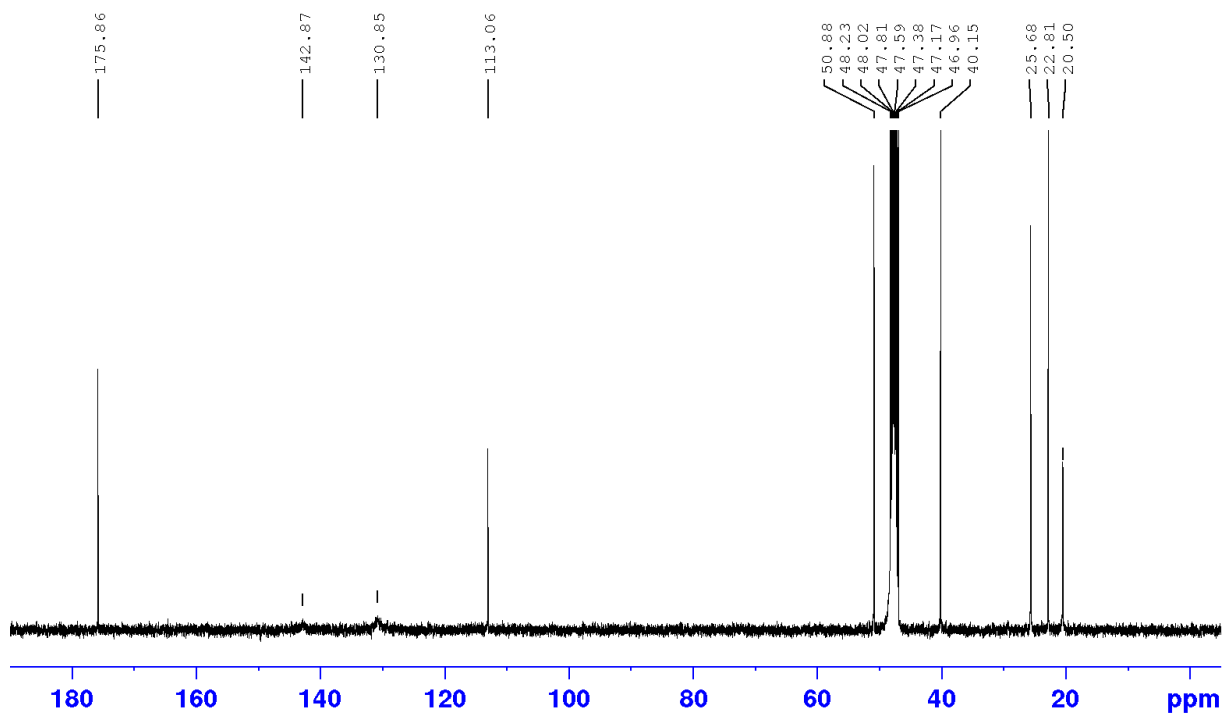
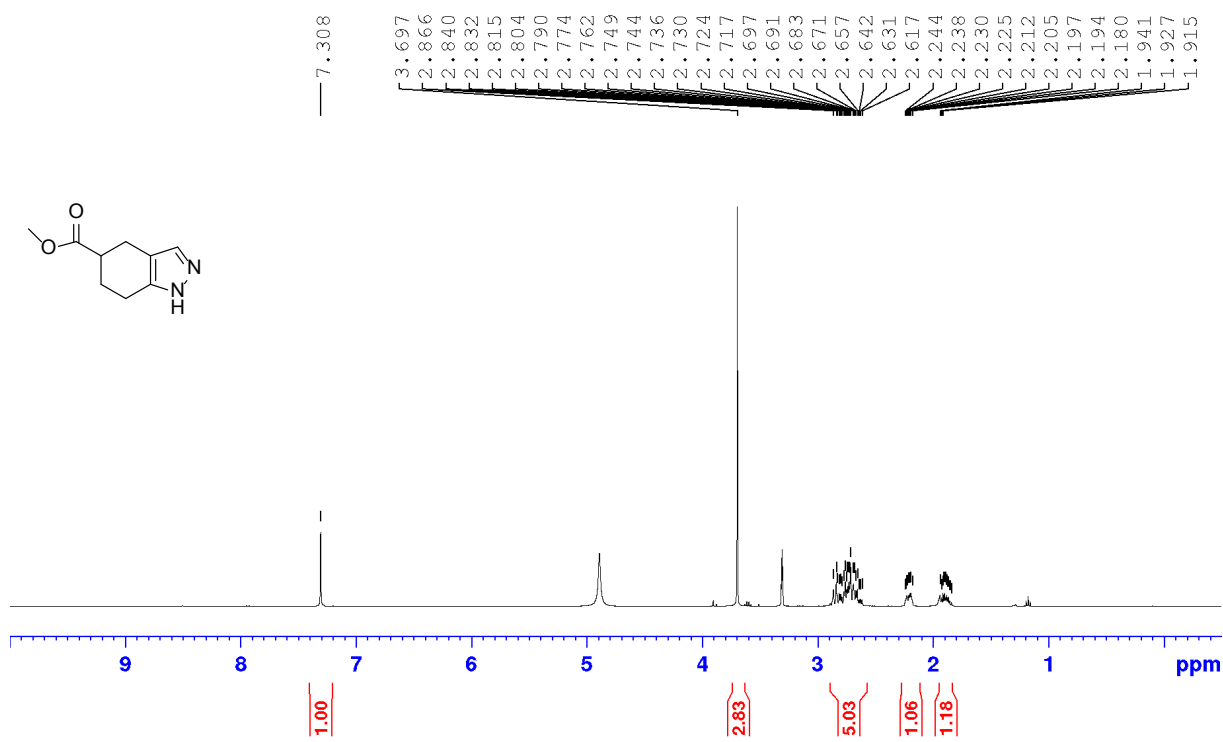
ethyl 5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxylate (**28**)⁷



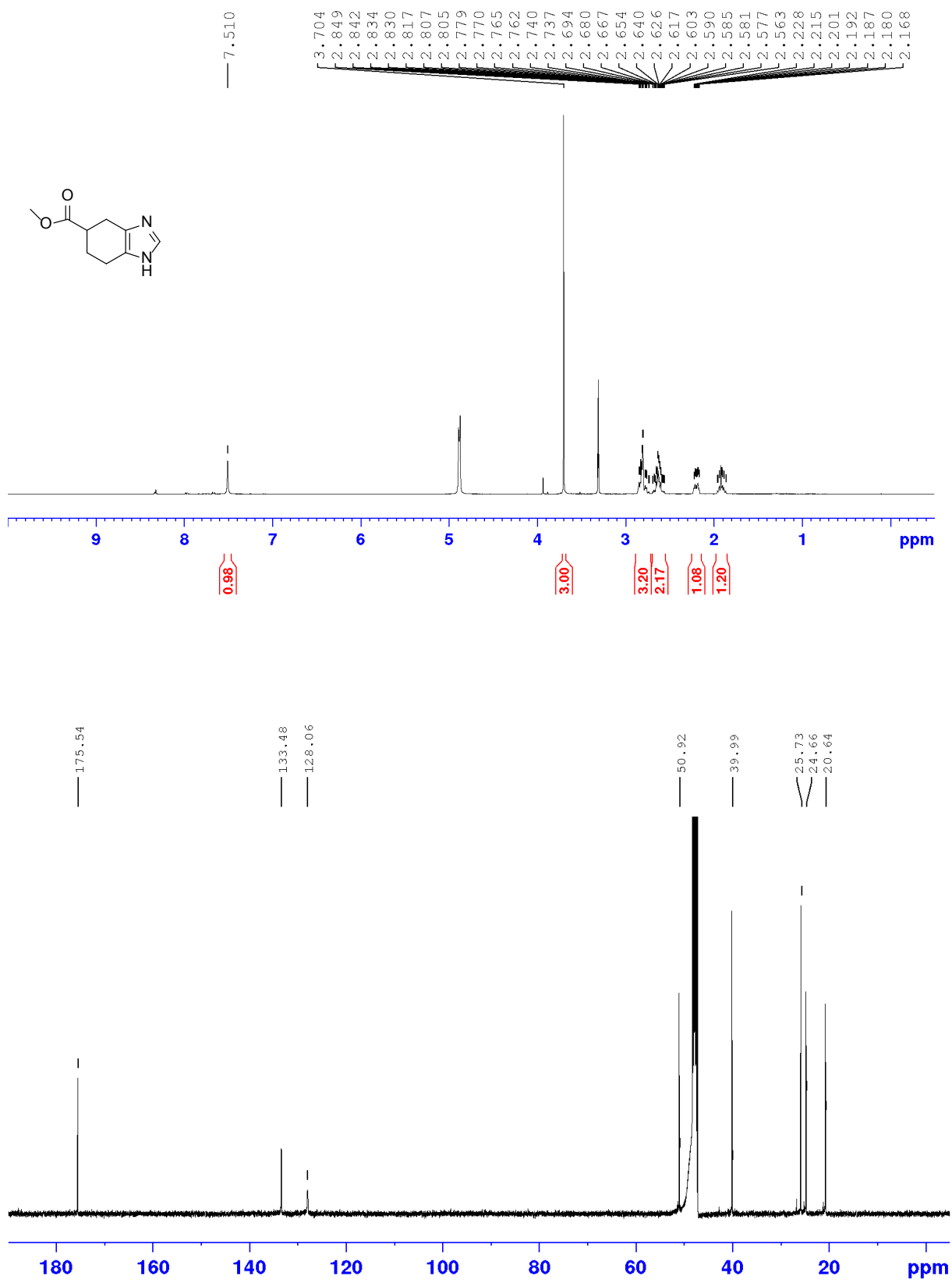
1,2,3,4-tetrahydropyrido[3,4-b]pyrazine (**29**)⁸



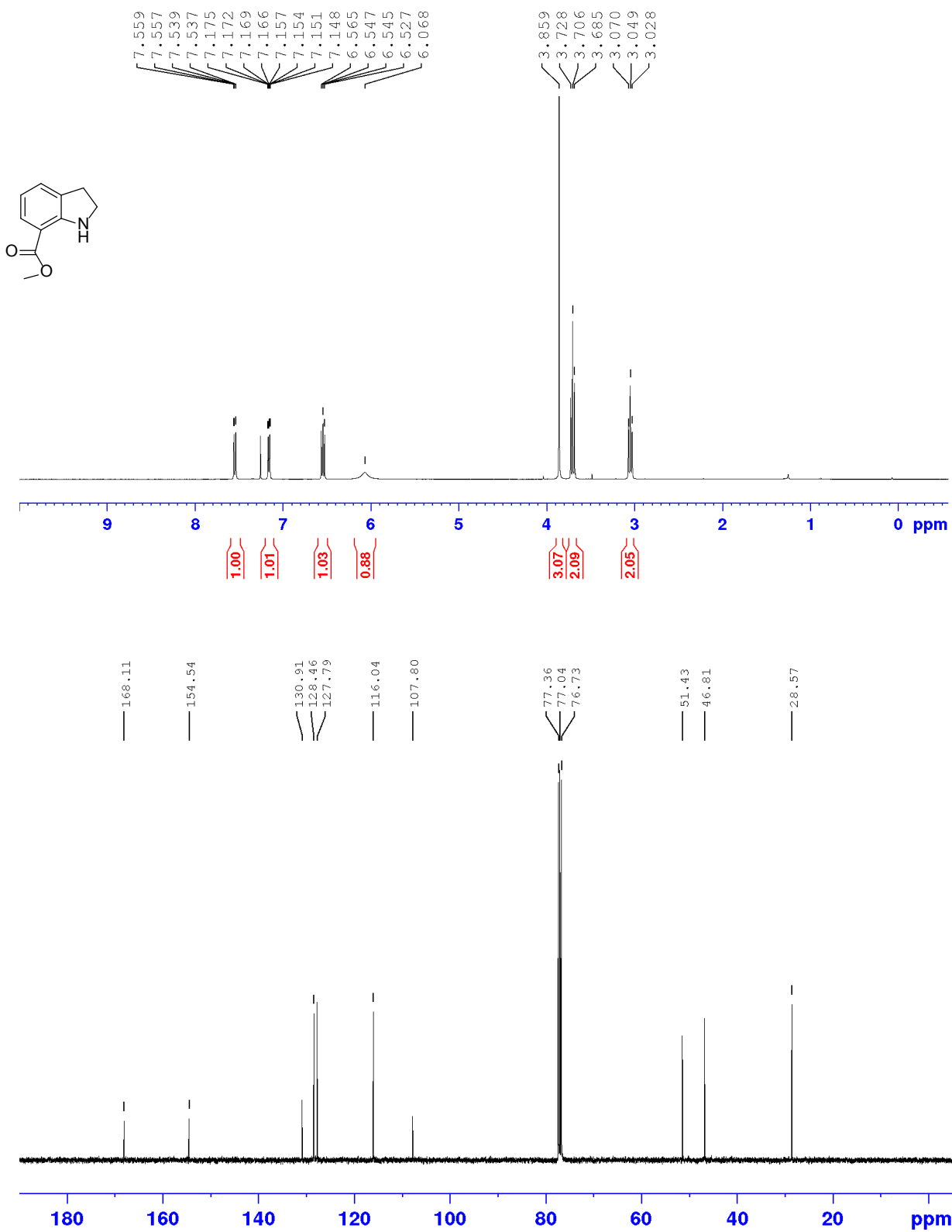
methyl 4,5,6,7-tetrahydro-1H-indazole-5-carboxylate (**30**)⁹



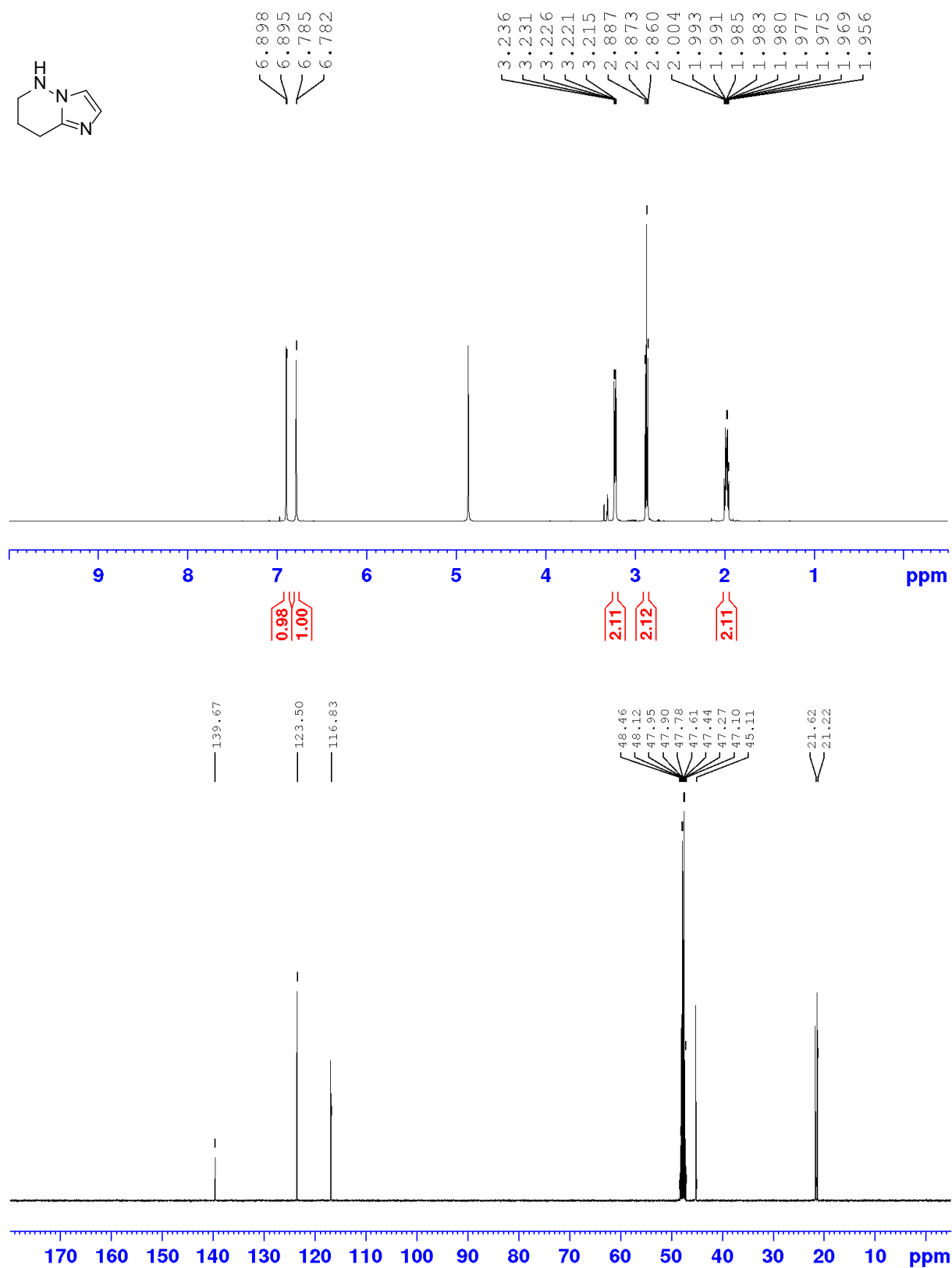
methyl 4,5,6,7-tetrahydro-1H-benzo[d]imidazole-5-carboxylate (**31**)¹⁰



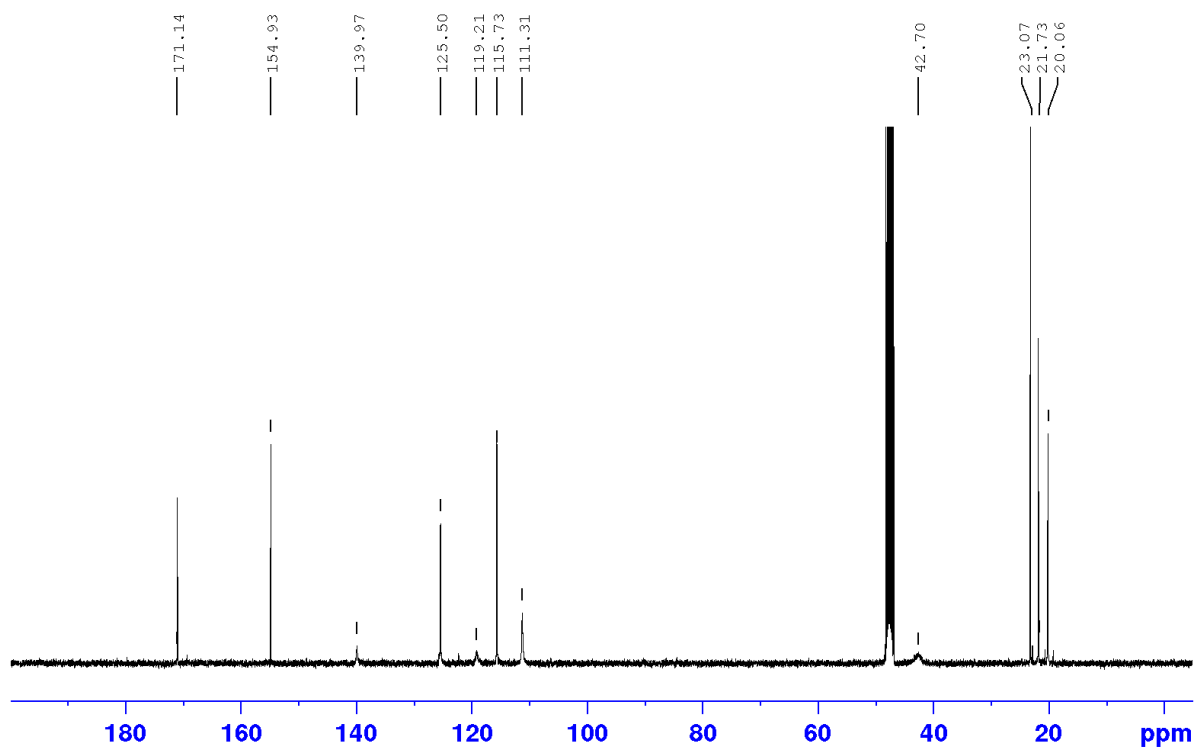
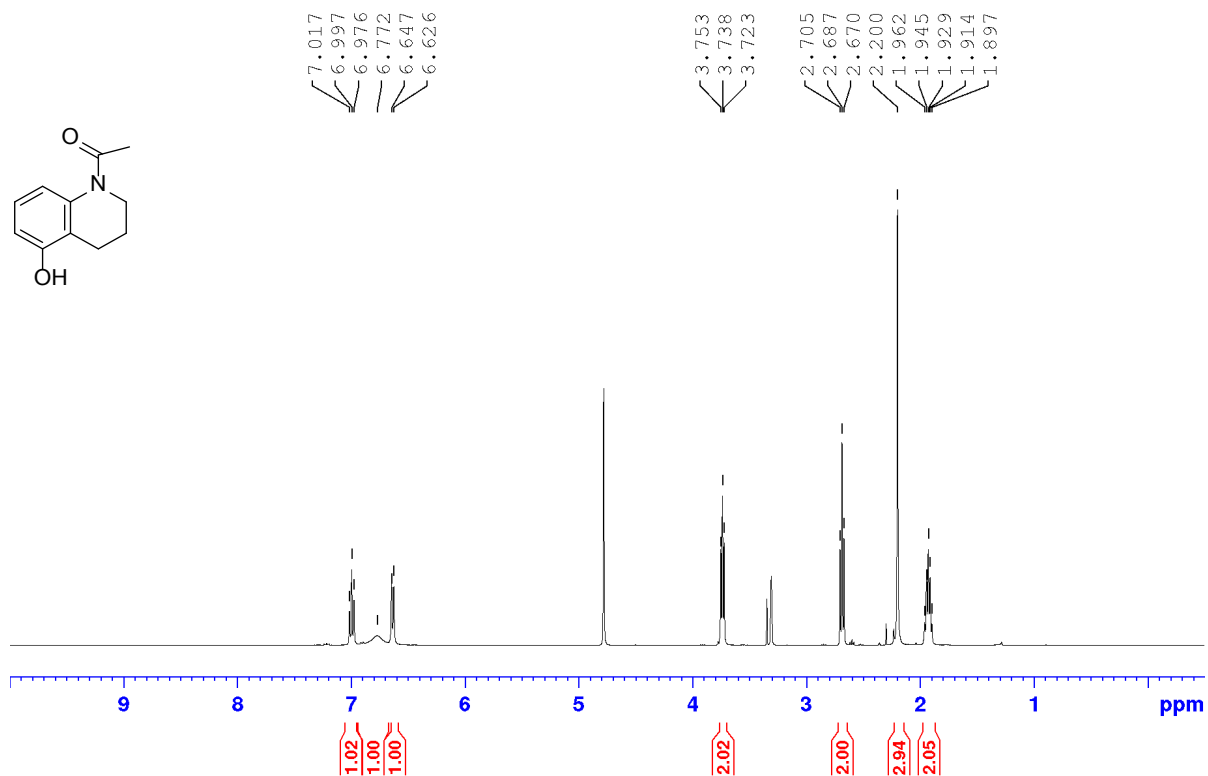
methyl indoline-7-carboxylate (**32**)¹¹



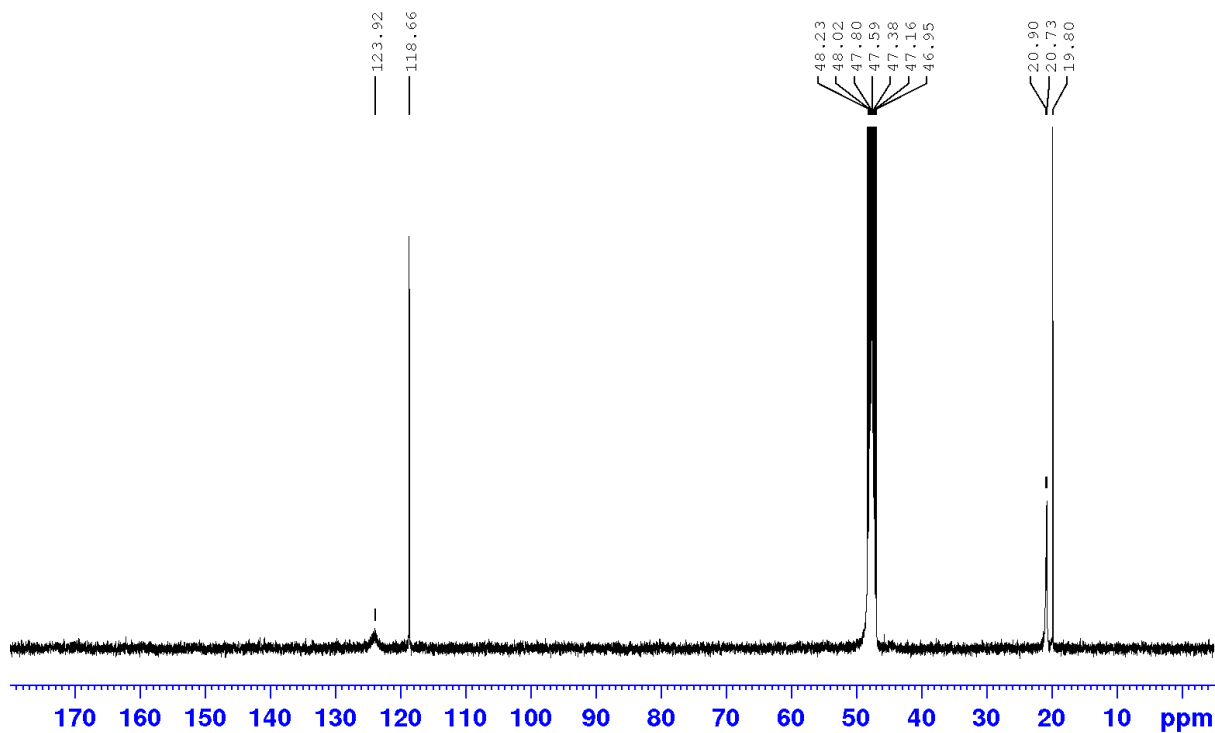
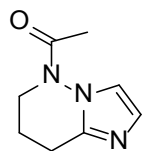
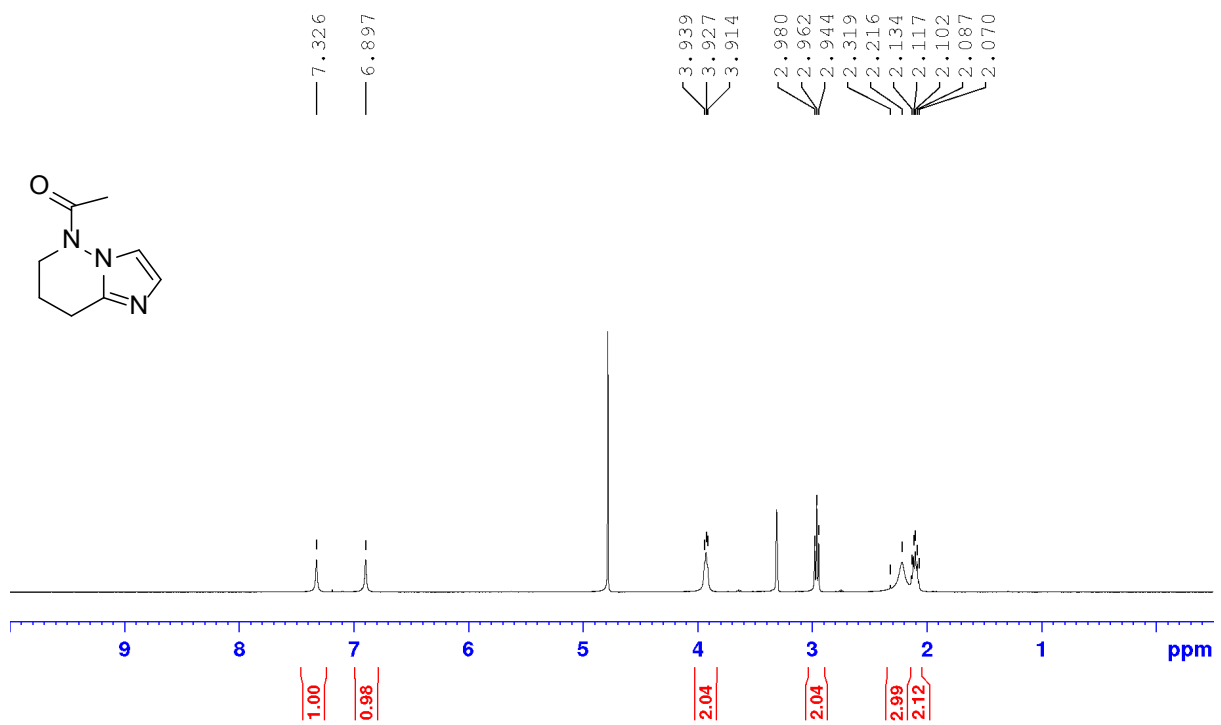
5,6,7,8-tetrahydroimidazo[1,2-b]pyridazine (**33**)¹²



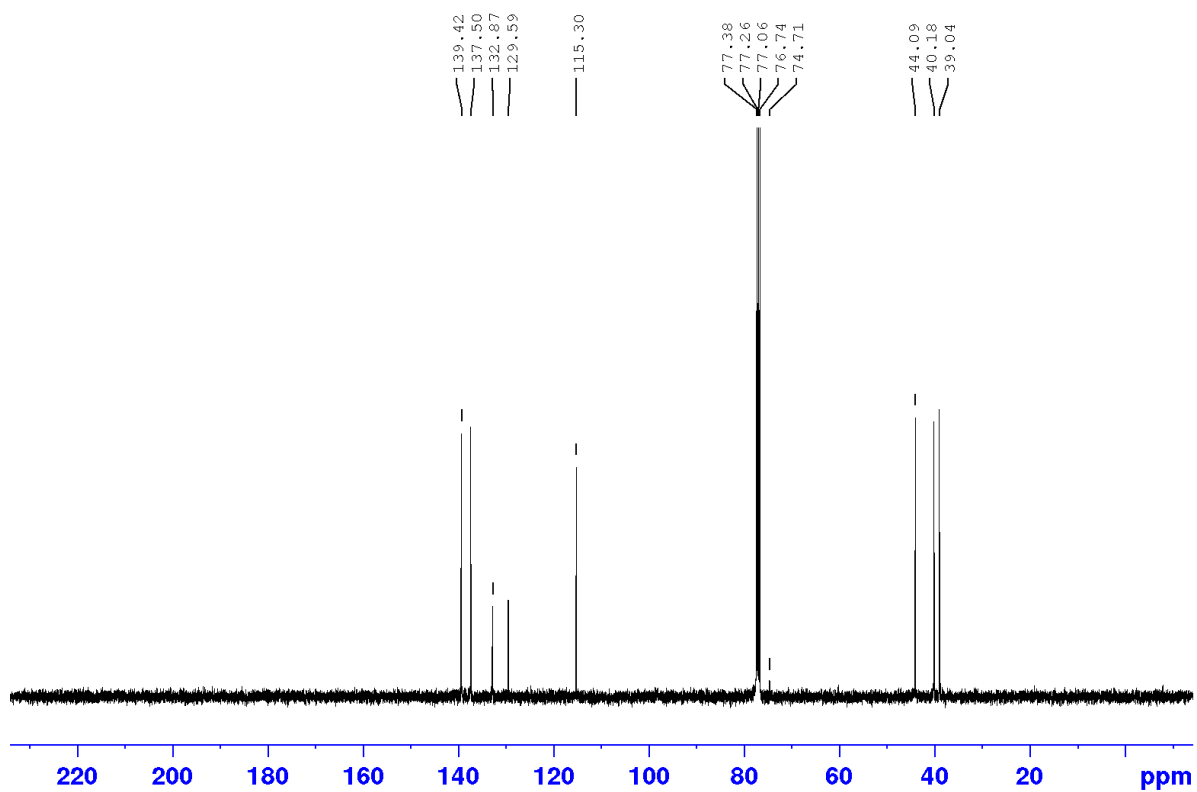
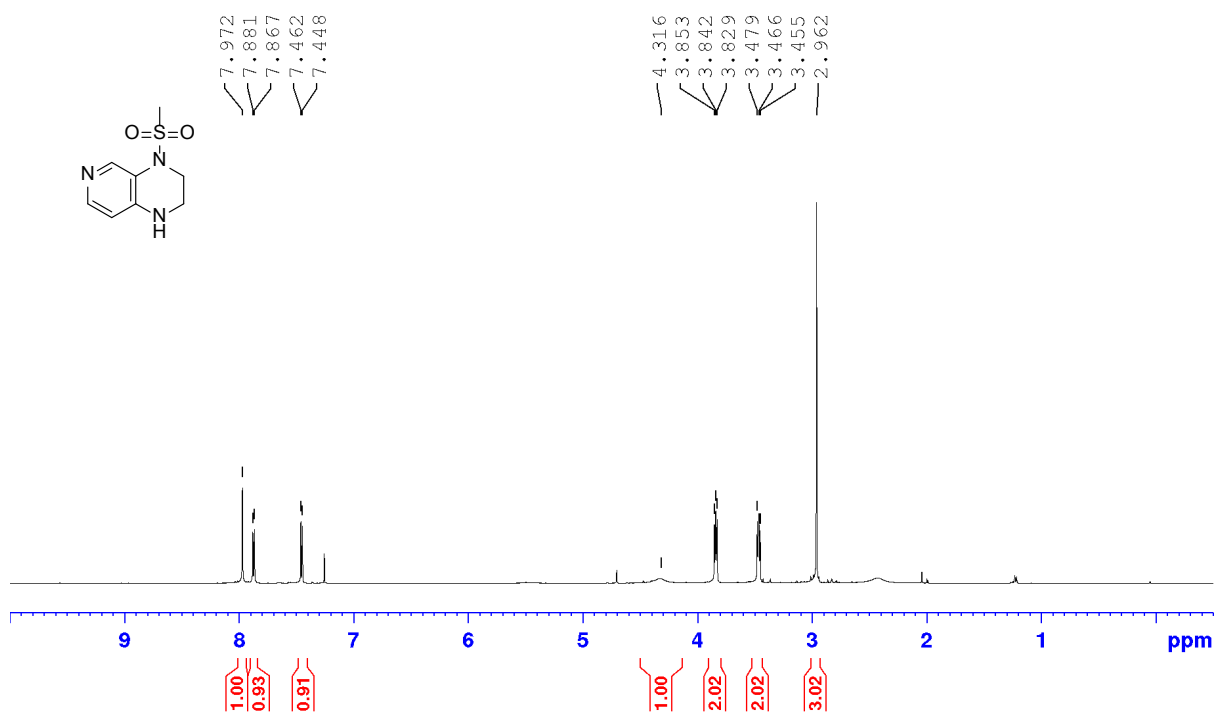
1-(5-hydroxy-3,4-dihydroquinolin-1(2H)-yl)ethan-1-one (35)



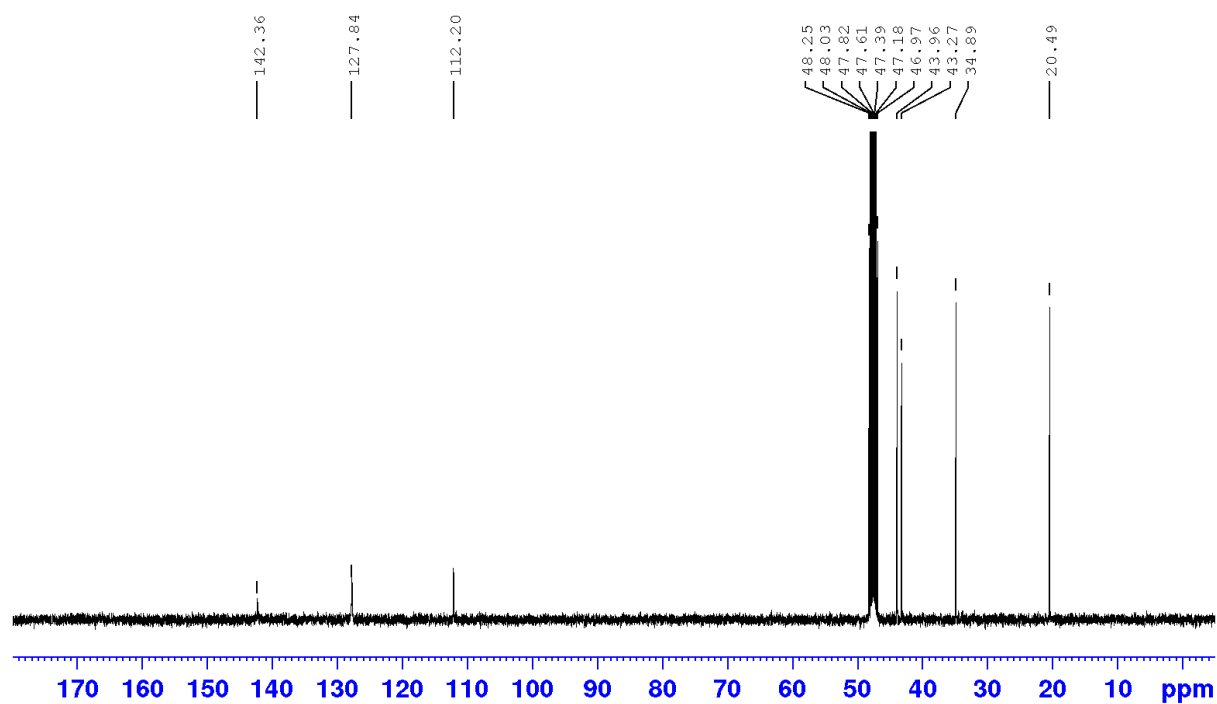
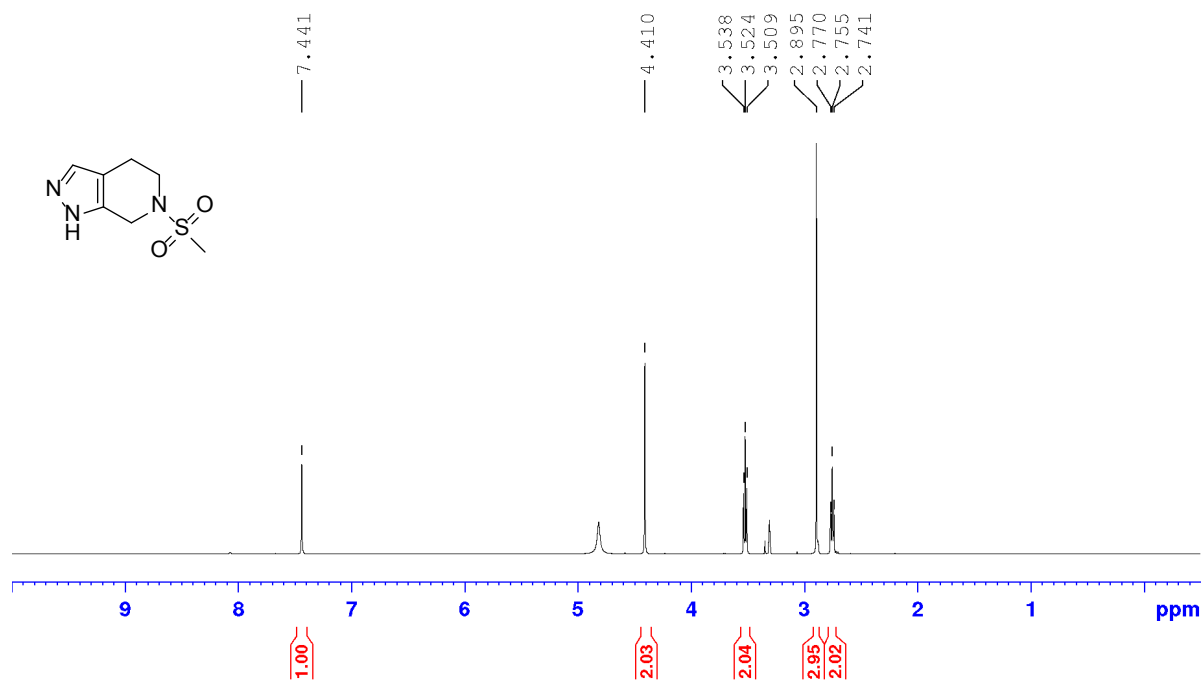
1-(7,8-dihydroimidazo[1,2-b]pyridazin-5(6H-yl)ethan-1-one (36)



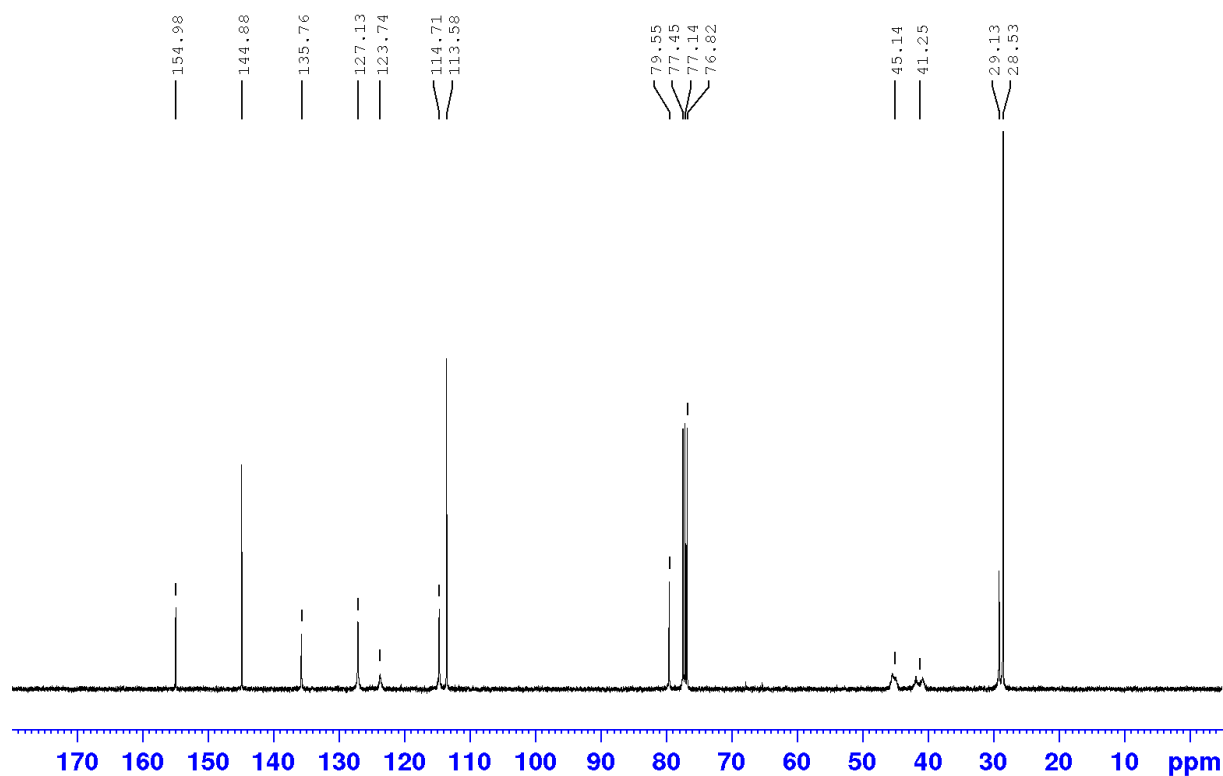
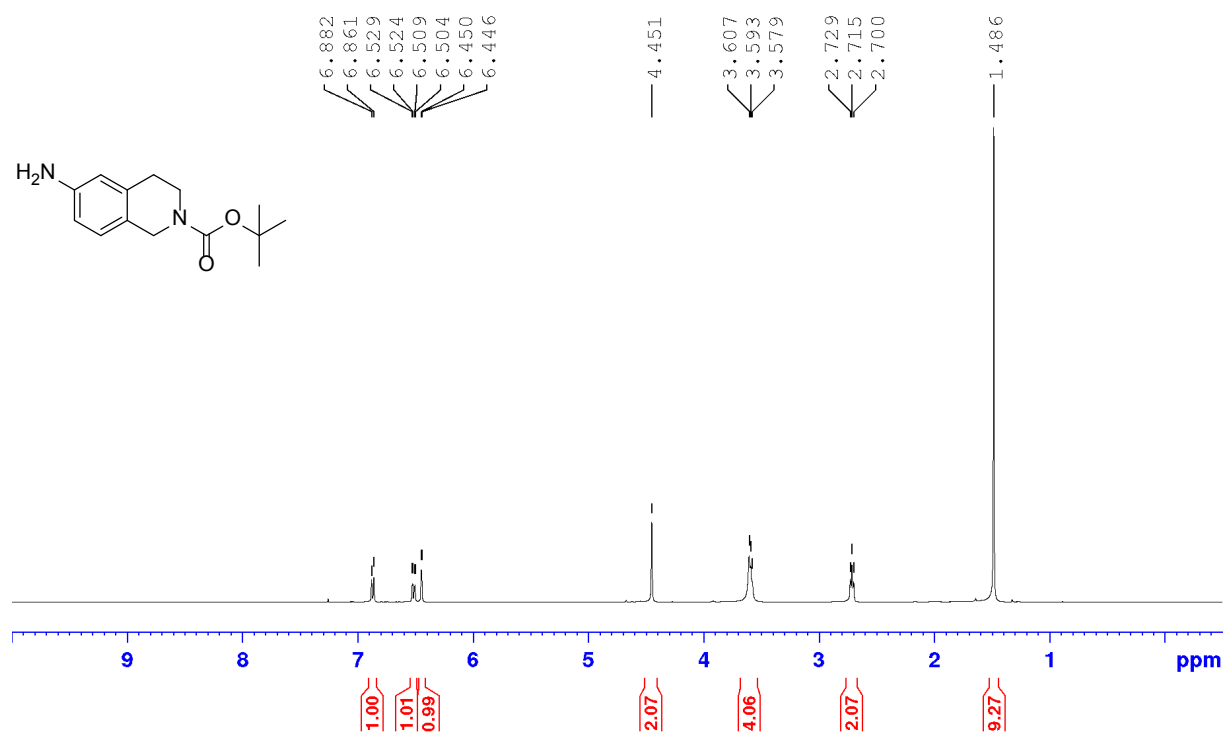
1-(methylsulfonyl)-1,2,3,4-tetrahydropyrido[3,4-b]pyrazine (**37**)



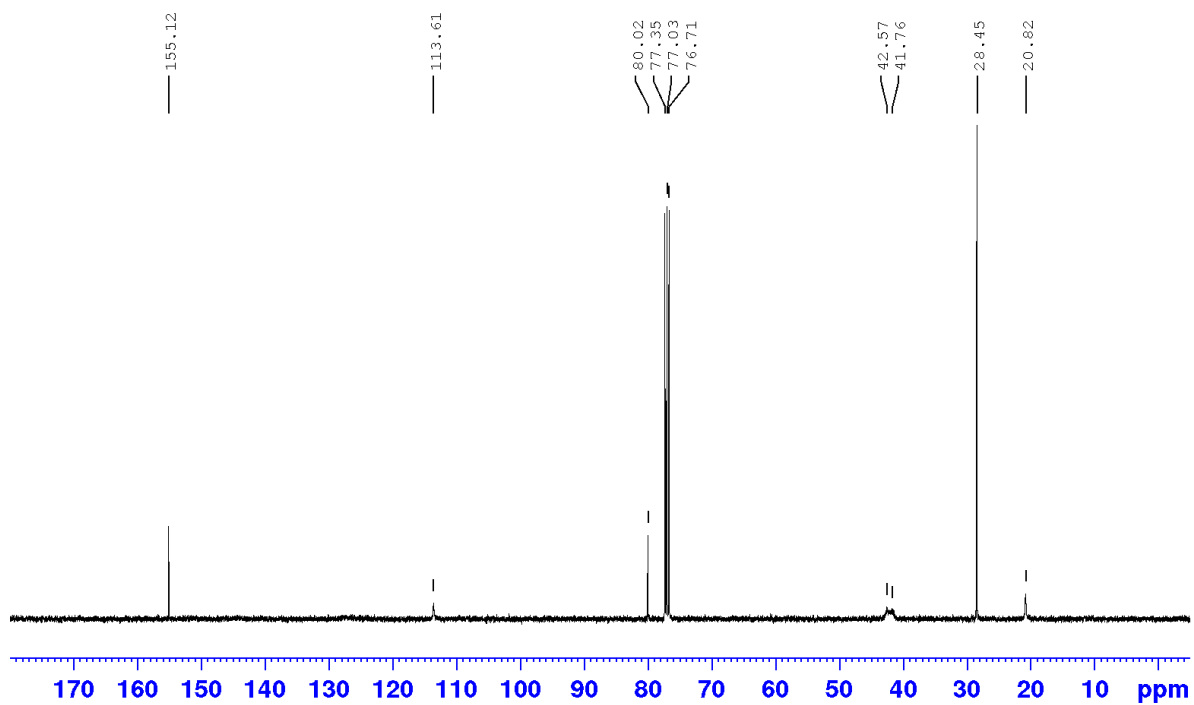
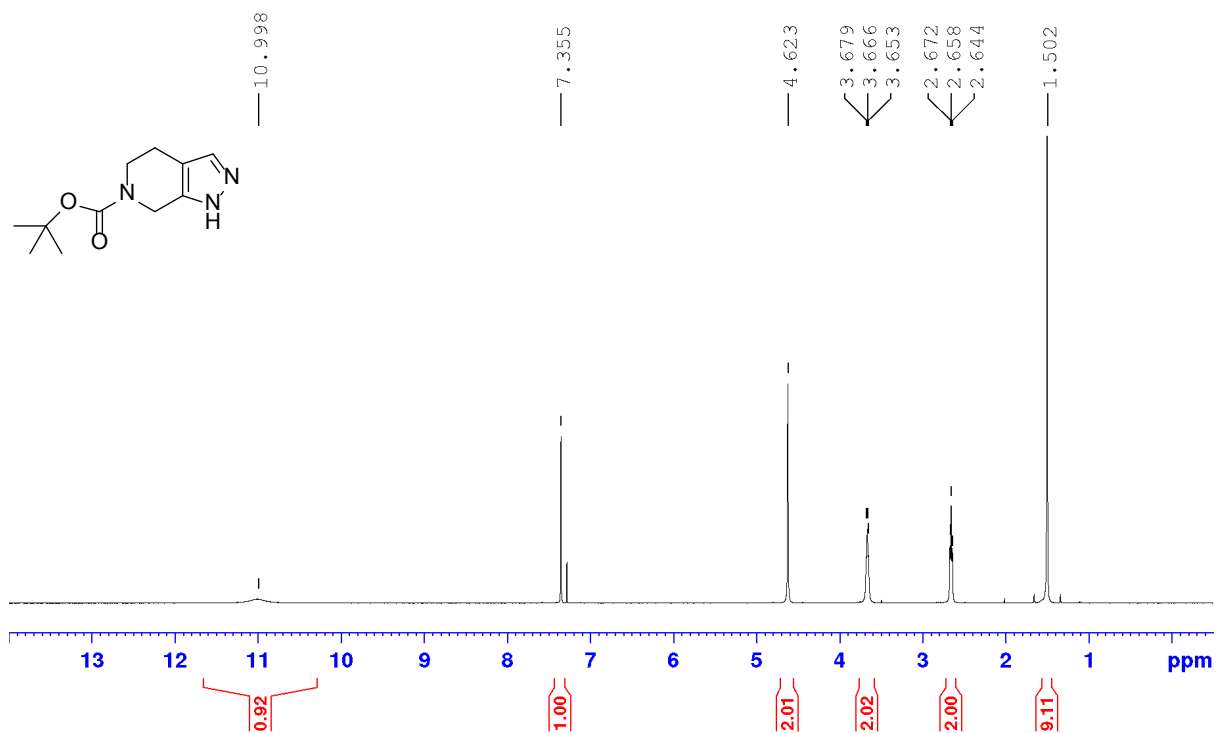
6-(methylsulfonyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine (**38**)



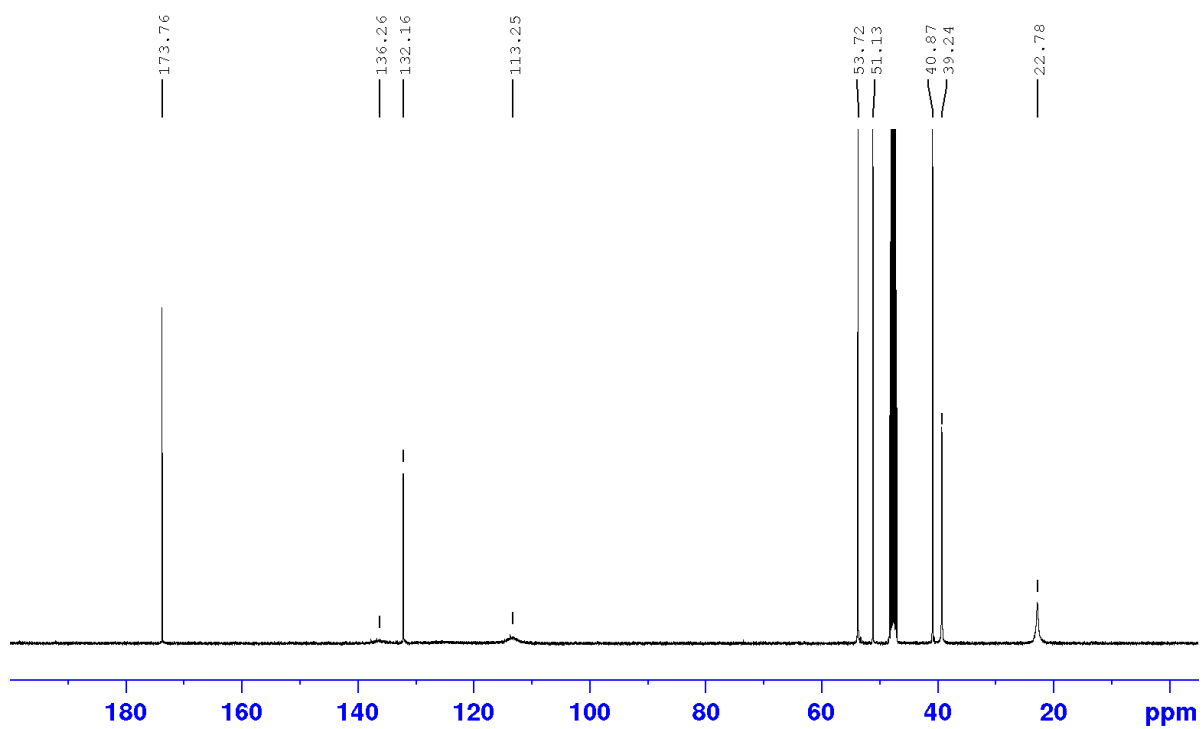
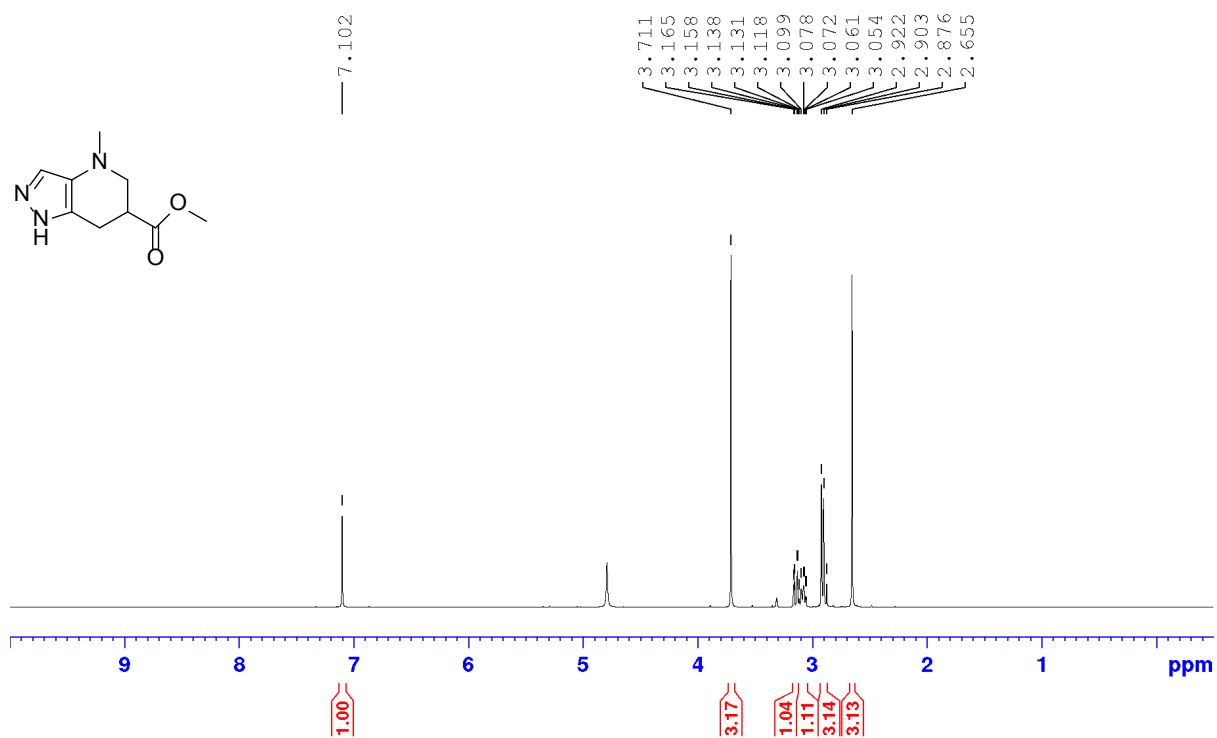
tert-butyl 6-amino-3,4-dihydroisoquinoline-2(1H)-carboxylate (**39**)¹³



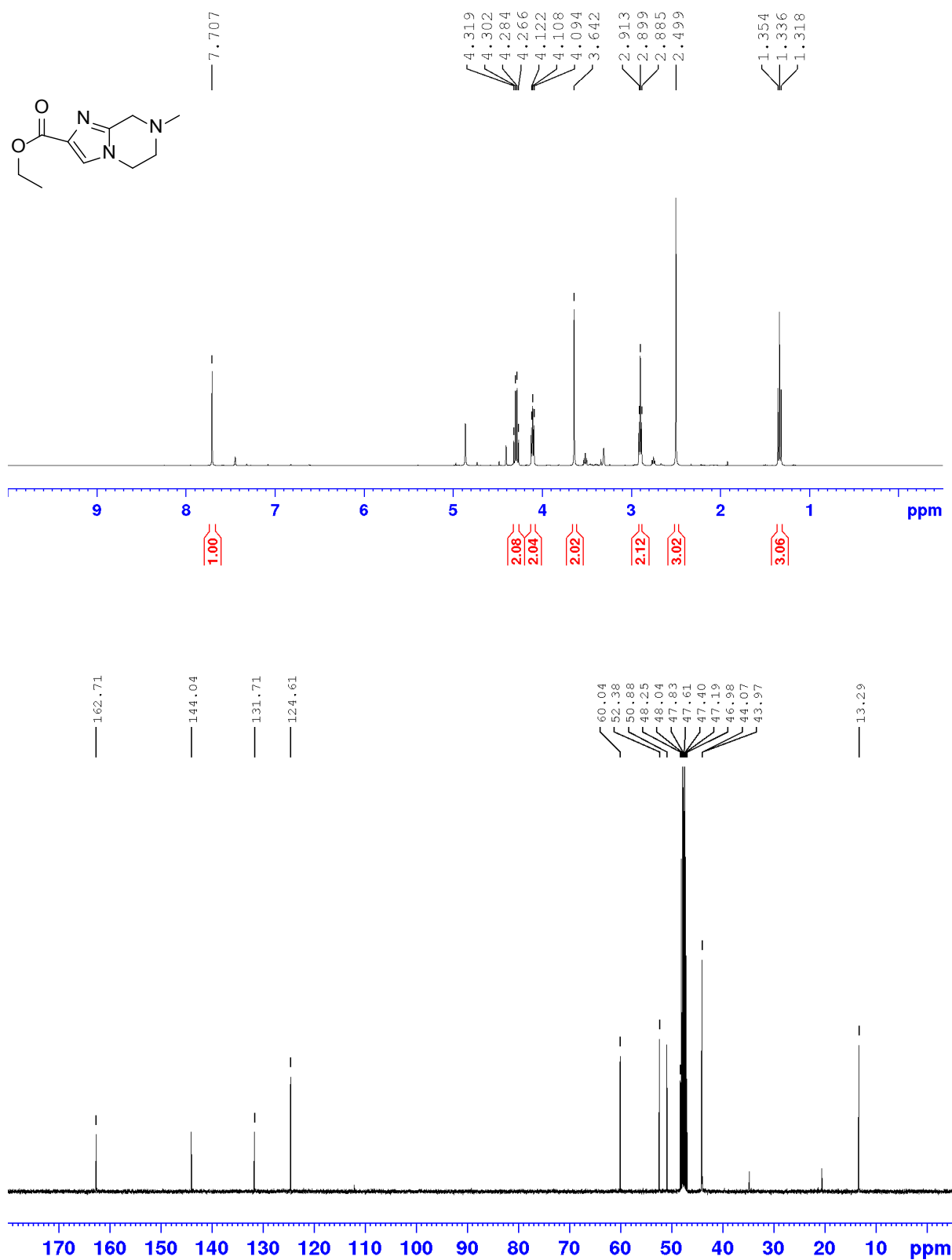
tert-butyl 1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridine-6-carboxylate (**40**)¹⁴



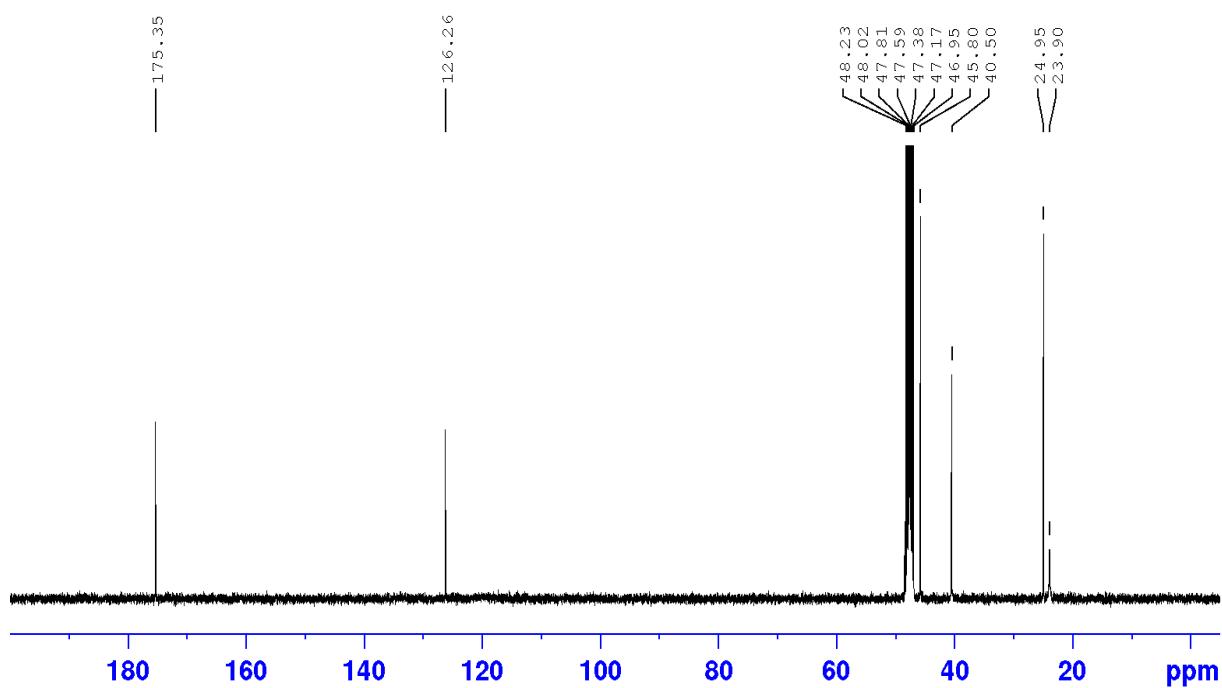
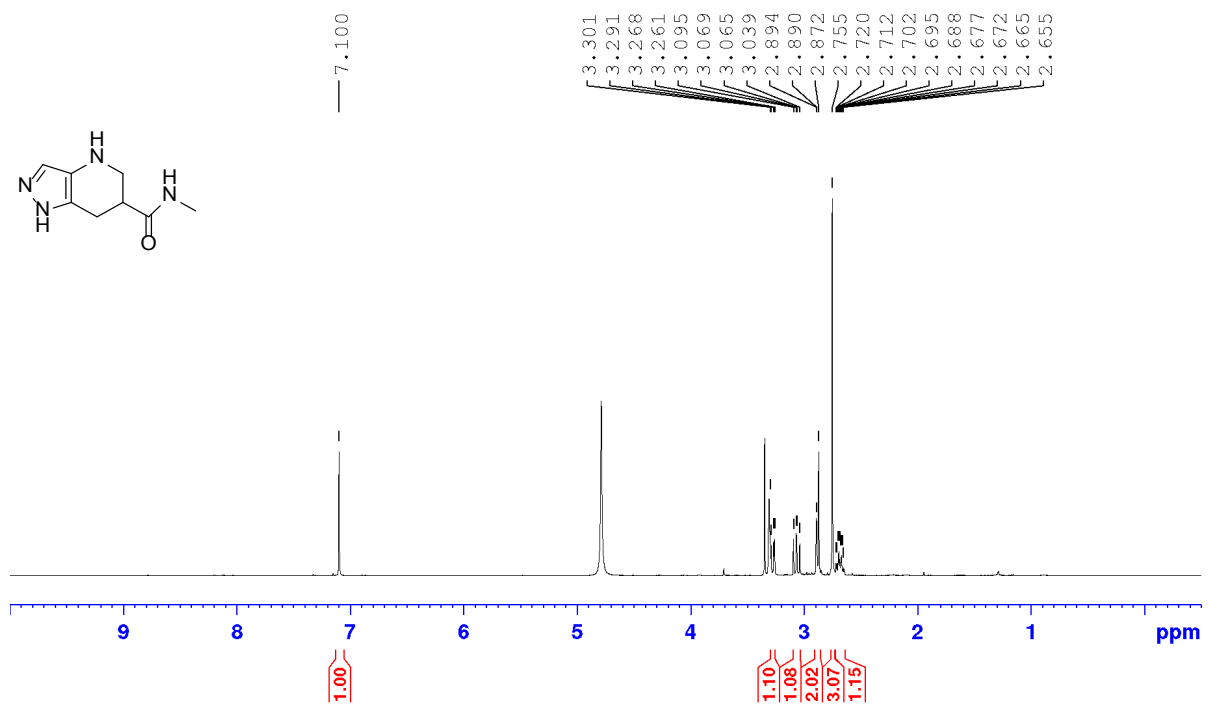
methyl 4-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-b]pyridine-6-carboxylate (**41**)



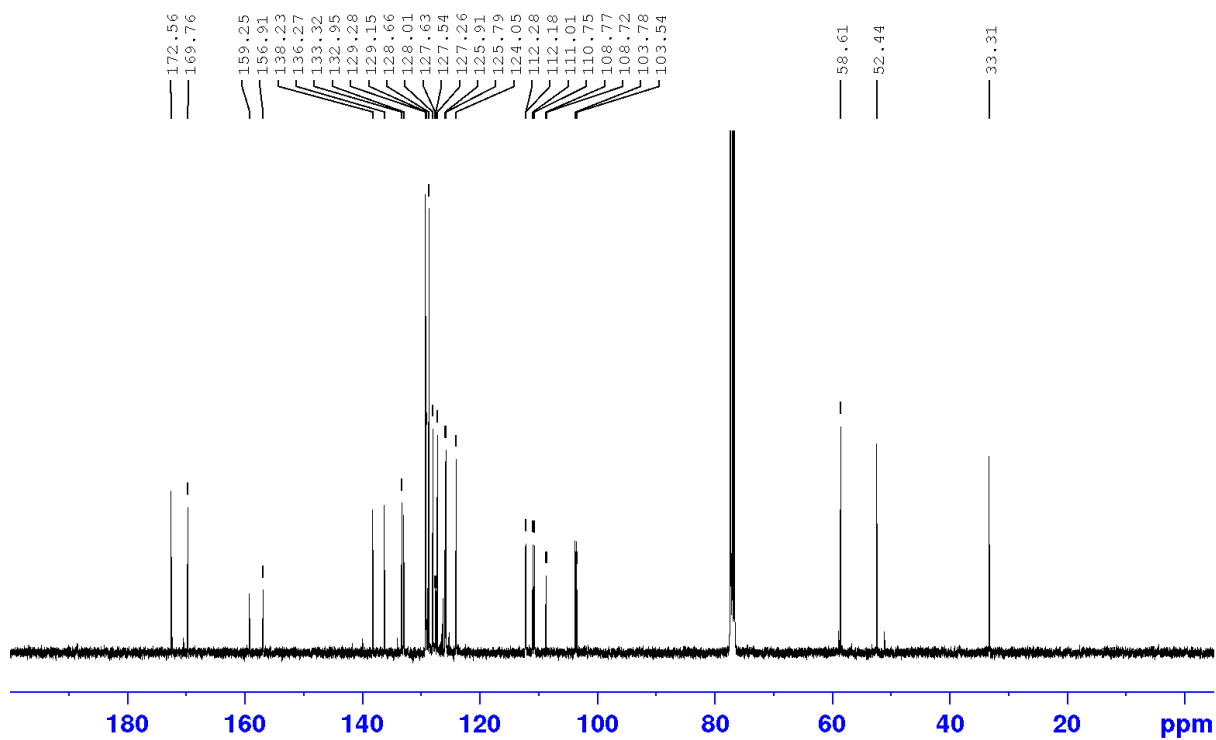
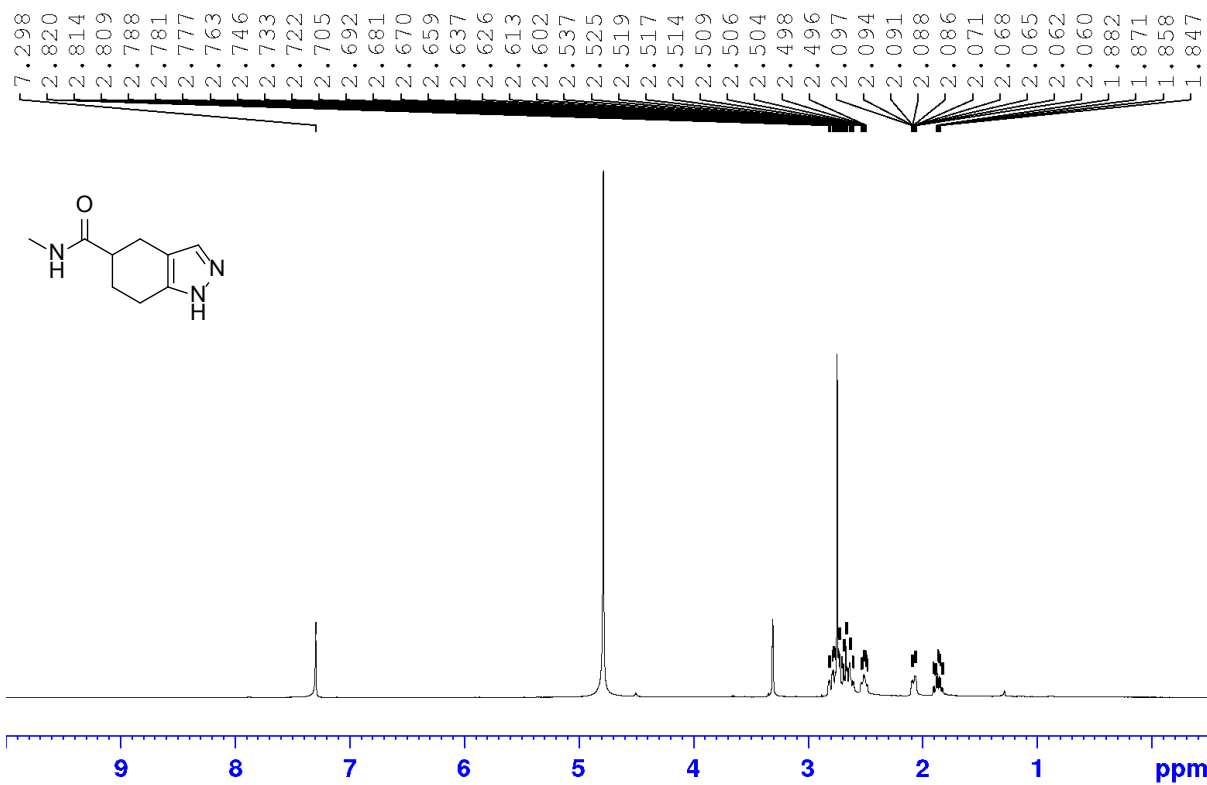
ethyl 7-methyl-5,6,7,8-tetrahydroimidazo[1,2-a]pyrazine-2-carboxylate (**42**)¹⁵



N-methyl-4,5,6,7-tetrahydro-1H-pyrazolo[4,3-b]pyridine-6-carboxamide (**43**)



N-methyl-4,5,6,7-tetrahydro-1H-indazole-5-carboxamide (**44**)



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