Electronic Supplementary Material (ESI) for RSC Advances.

Supporting Information

Metal free direct formation of various substituted pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amines and their further functionalization

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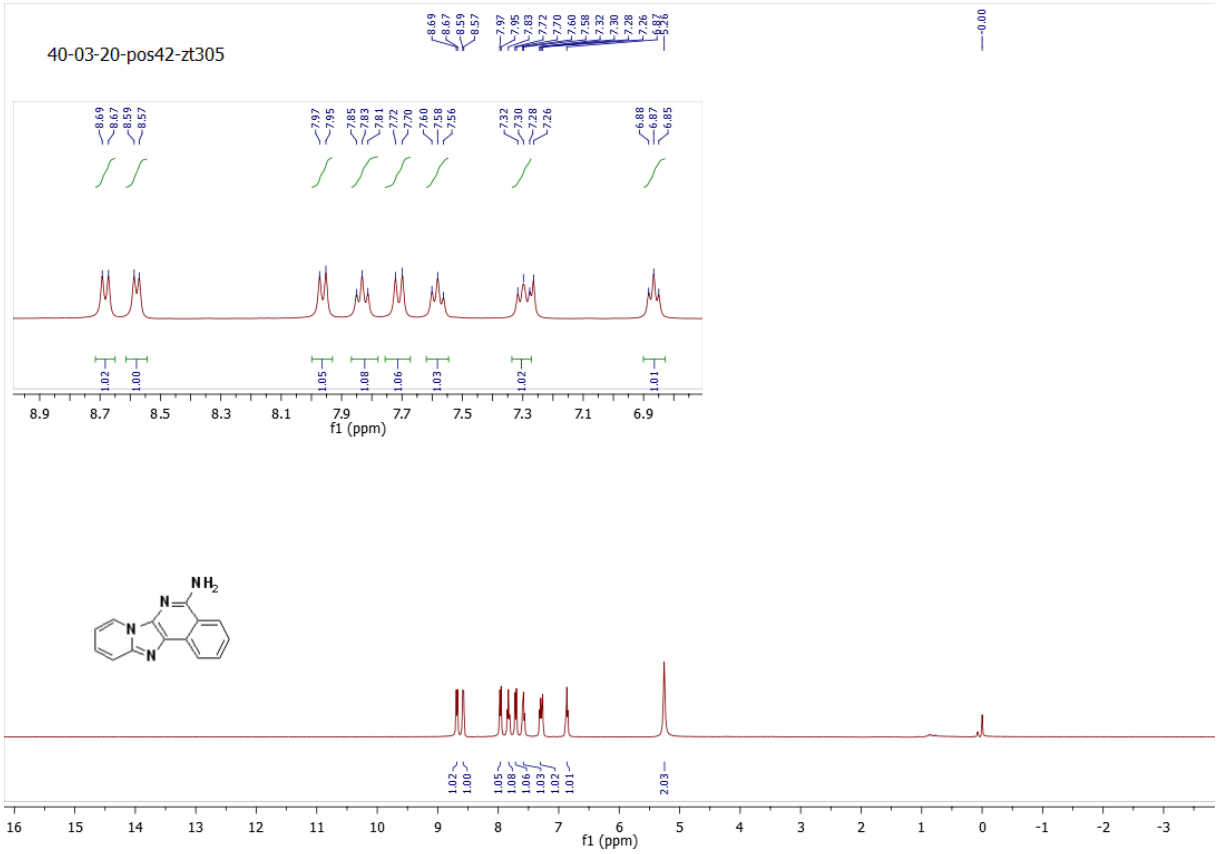
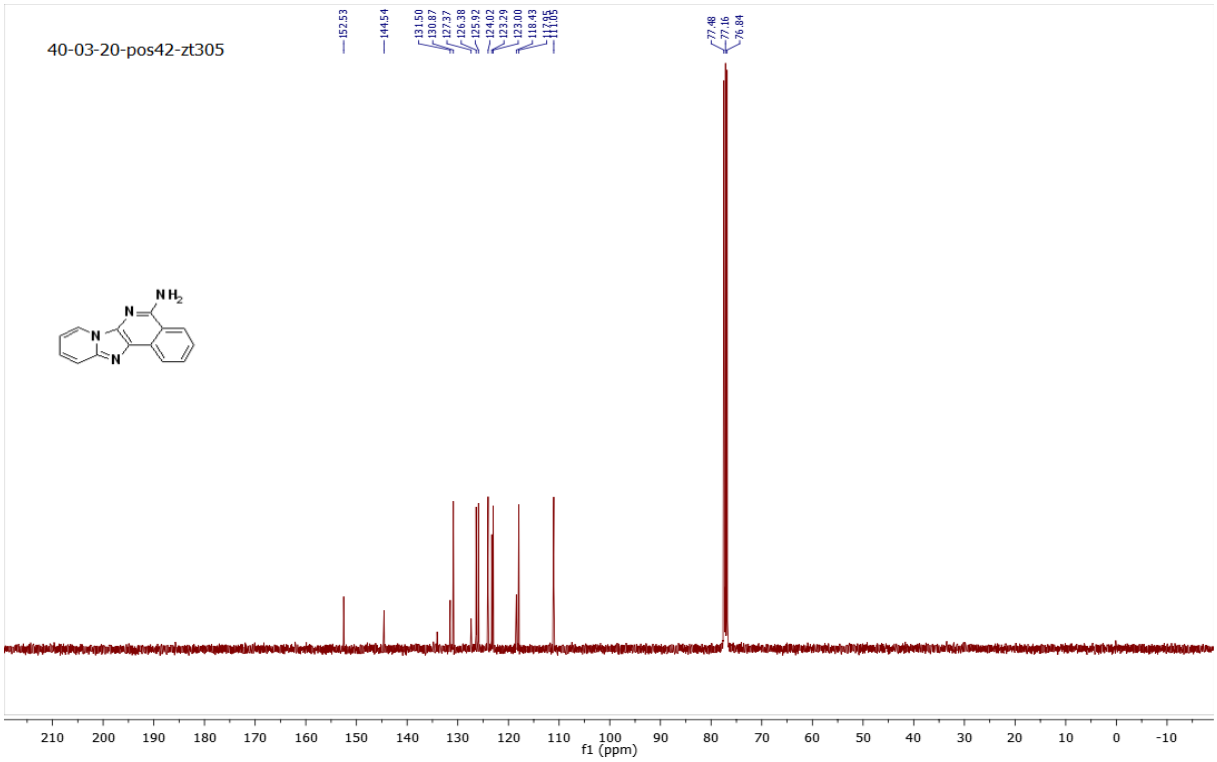
Pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (1a)

^{1}H NMR (400.13 MHz, $CDCl_3$)

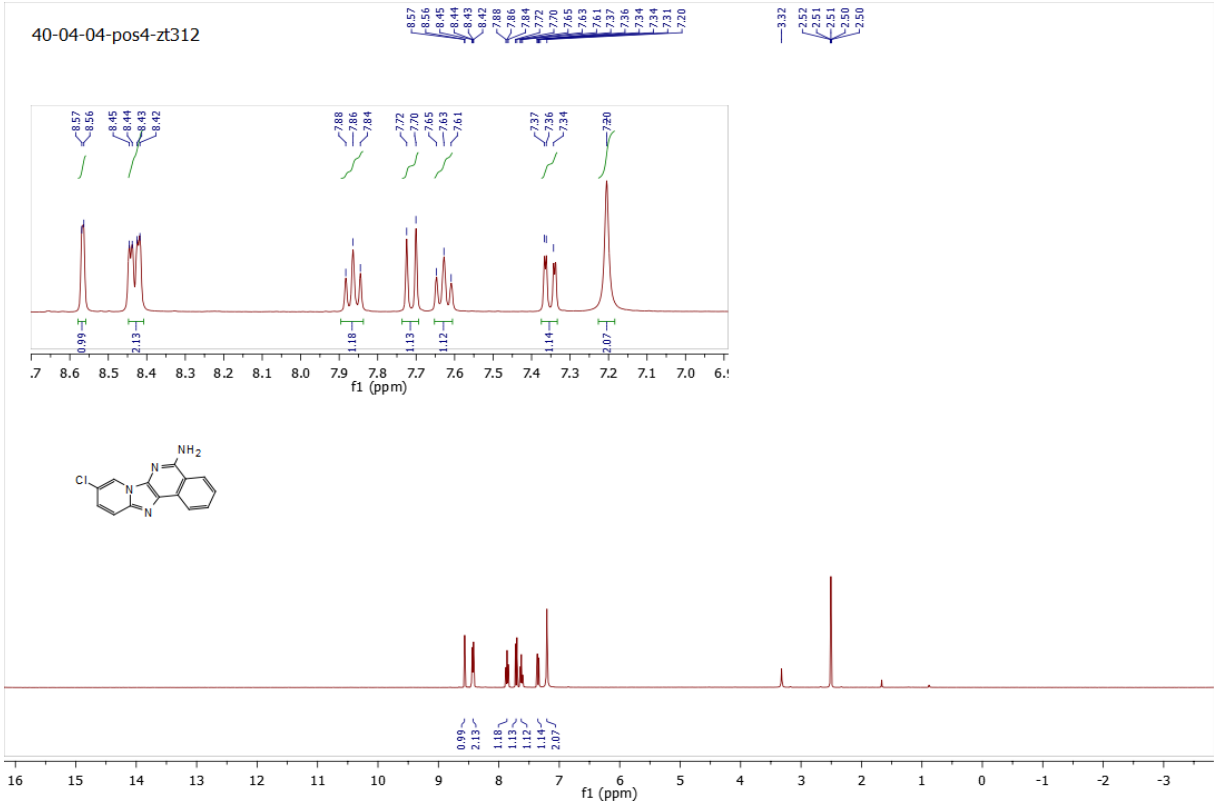


^{13}C NMR (101 MHz, $CDCl_3$)

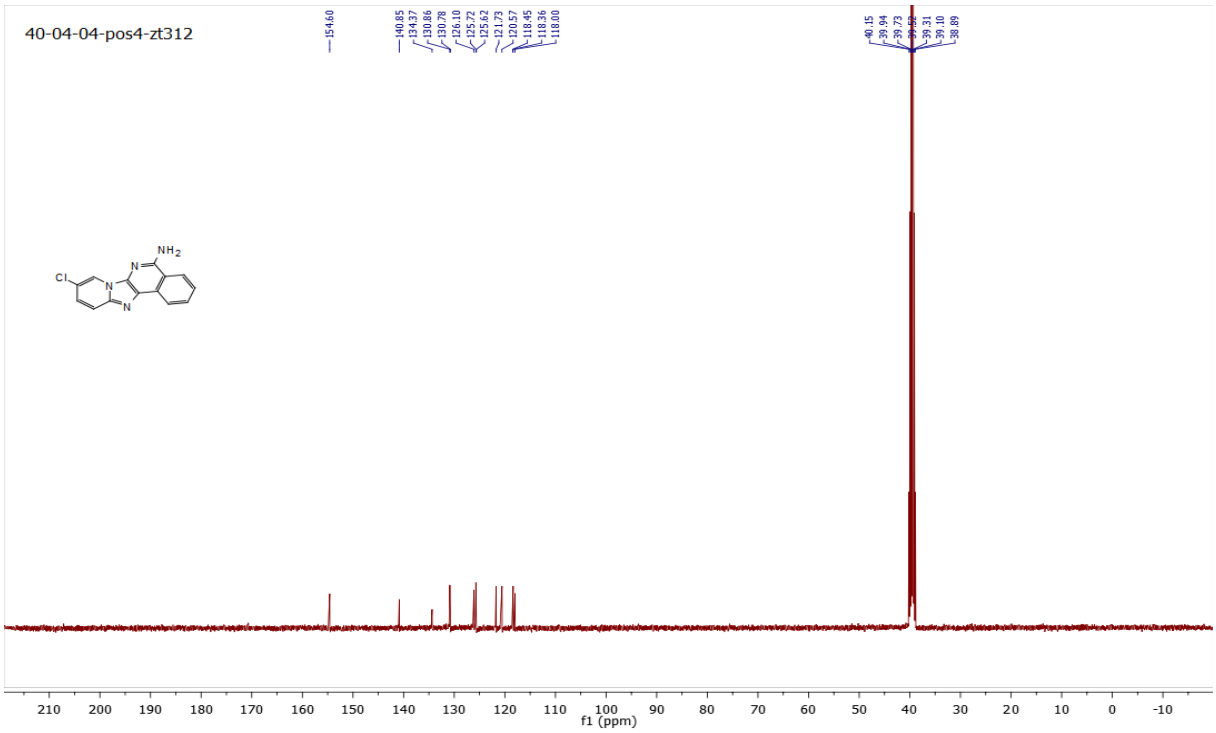


9-Chloropyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (1b)

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

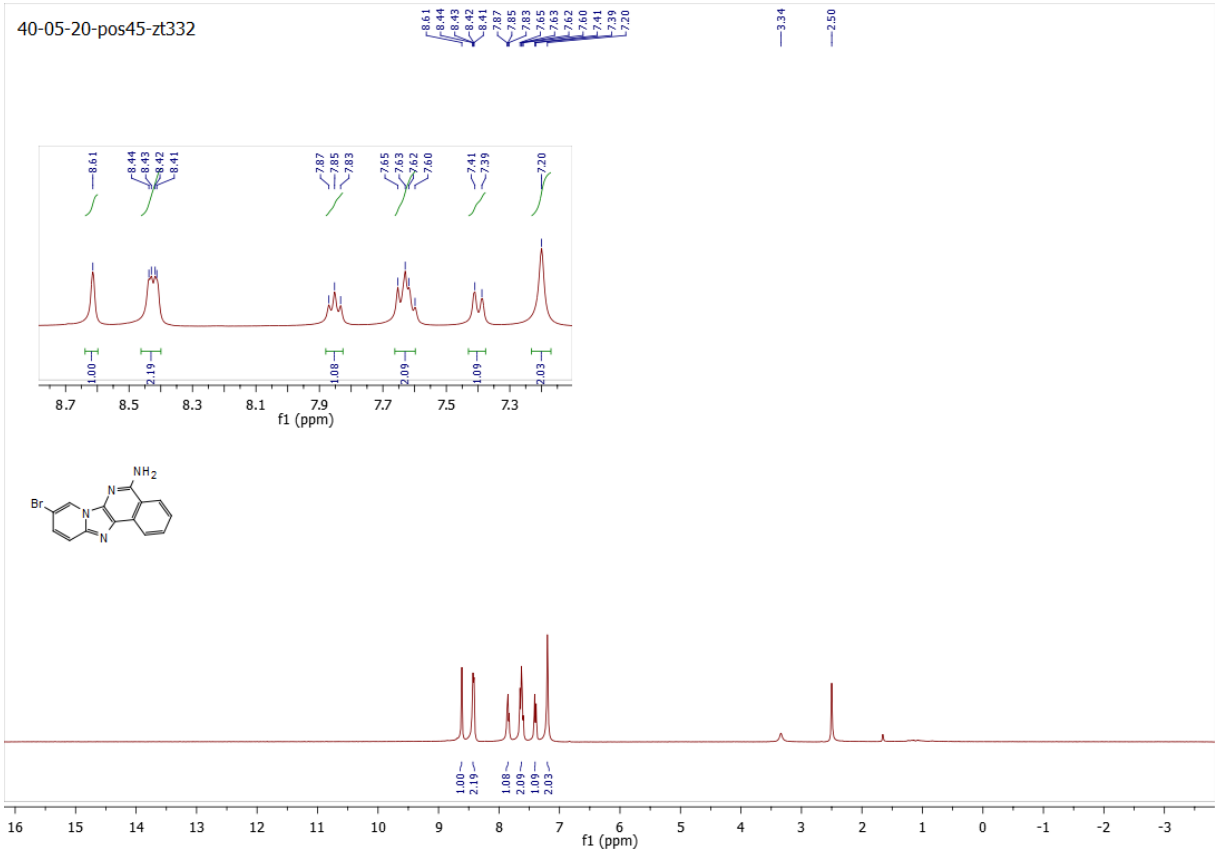


^{13}C NMR (101 MHz, DMSO-d_6)

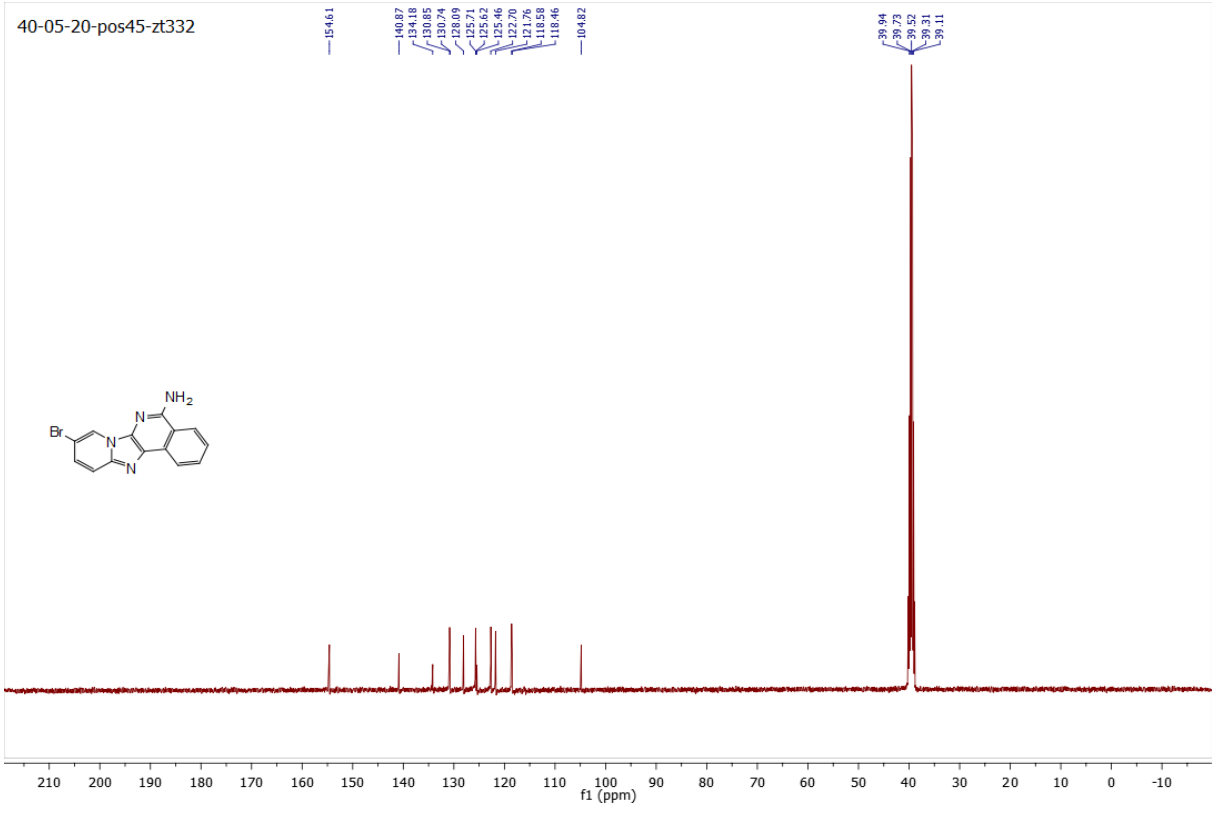


9-Bromopyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (1c)

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

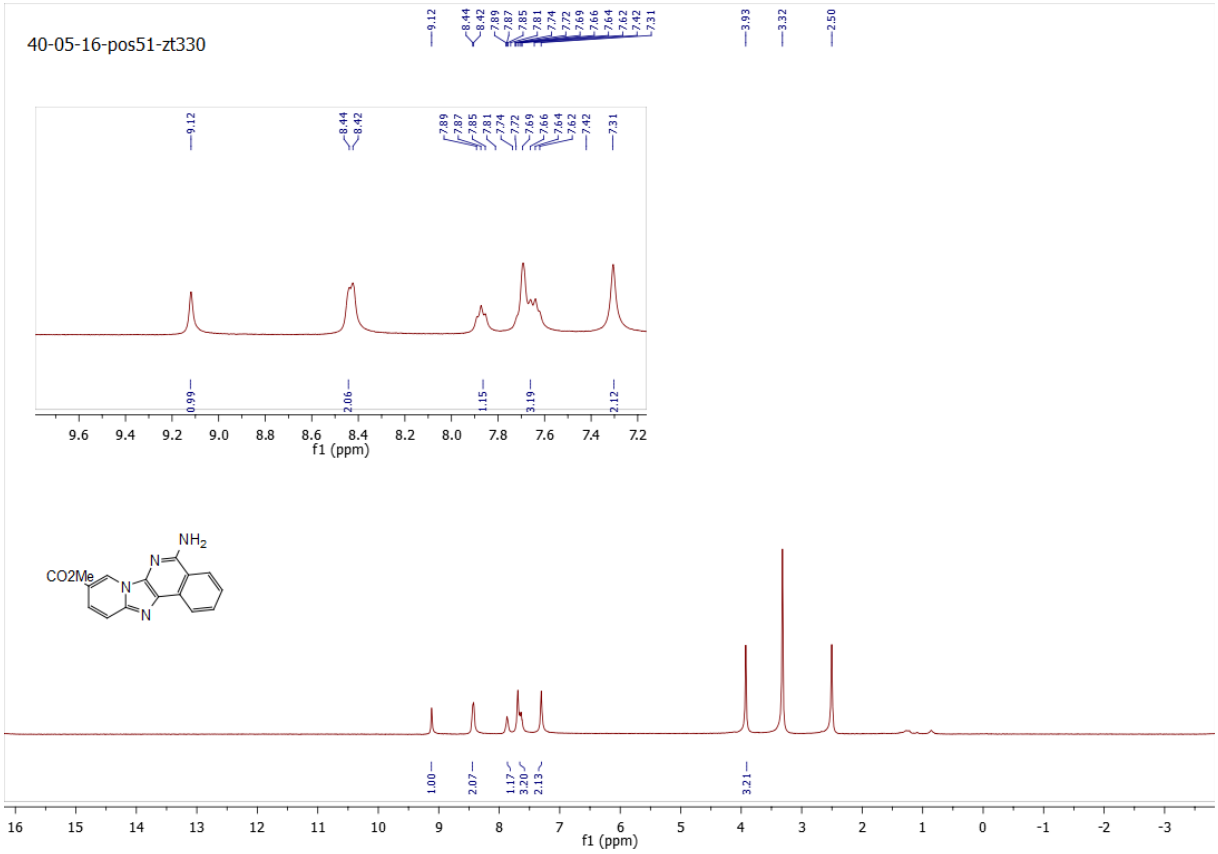


^{13}C NMR (101 MHz, DMSO-d_6)

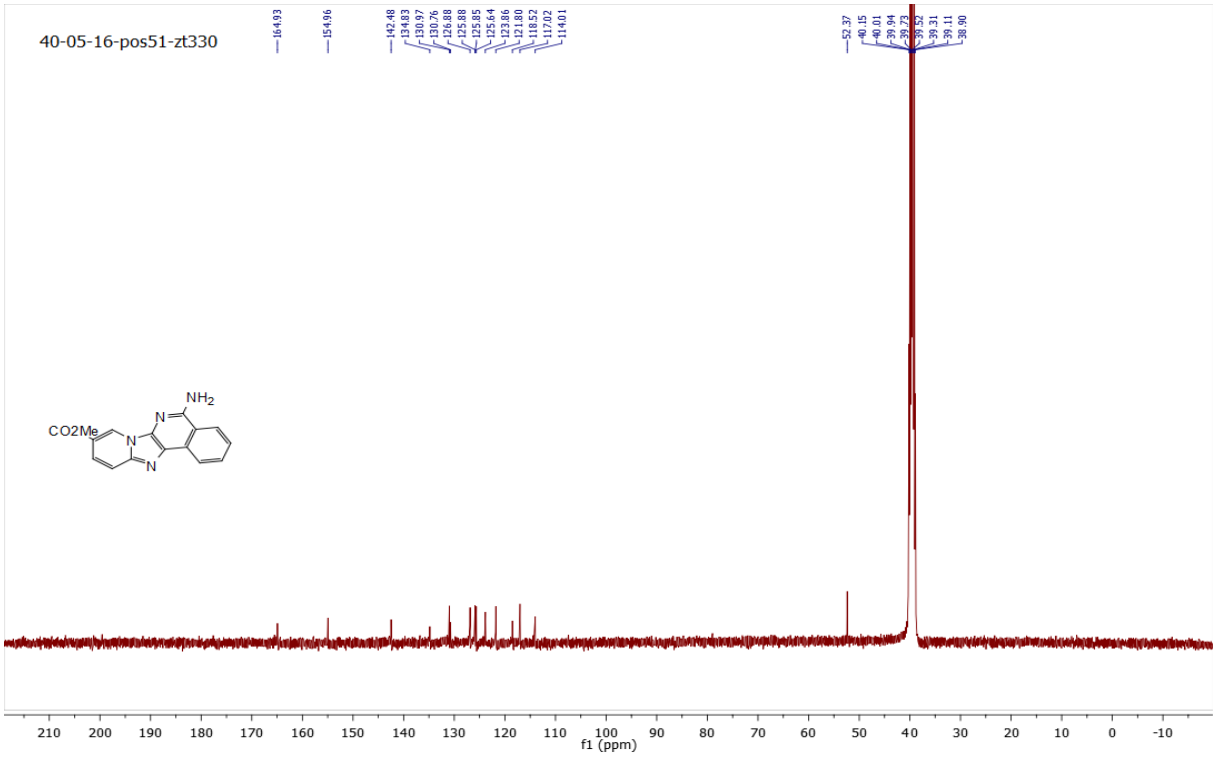


Methyl 5-aminopyrido[2',1':2,3]imidazo[4,5-*c*]isoquinoline-9-carboxylate (1d)

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

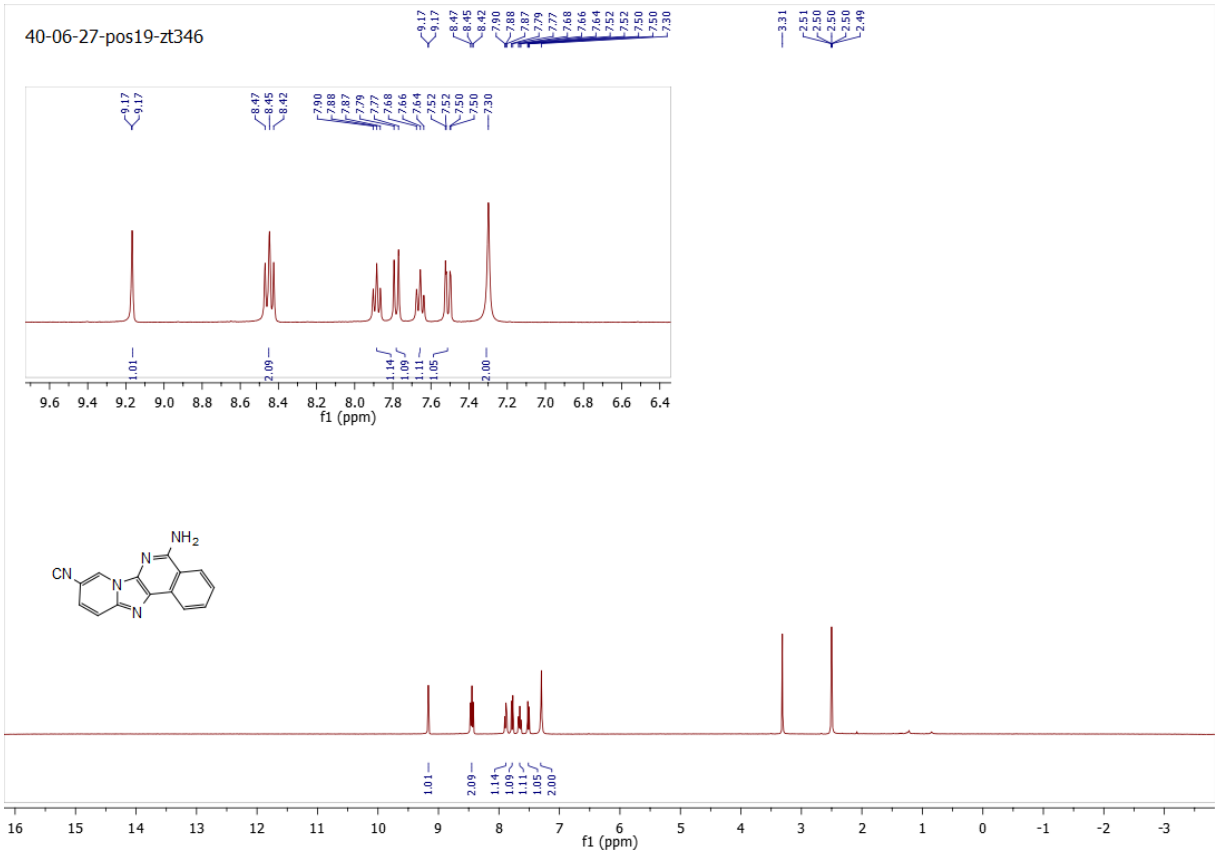


^{13}C NMR (101 MHz, DMSO-d_6)

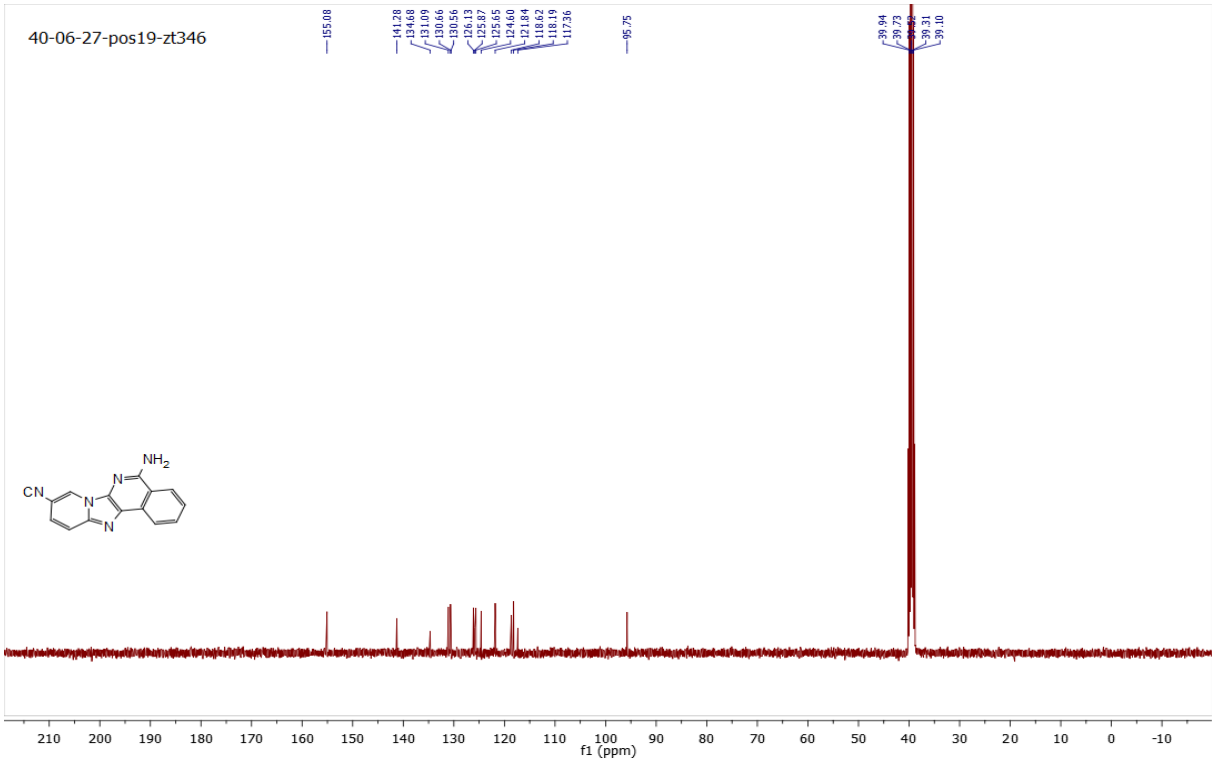


5-Aminopyrido[2',1':2,3]imidazo[4,5-*c*]isoquinoline-9-carbonitrile (1e)

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

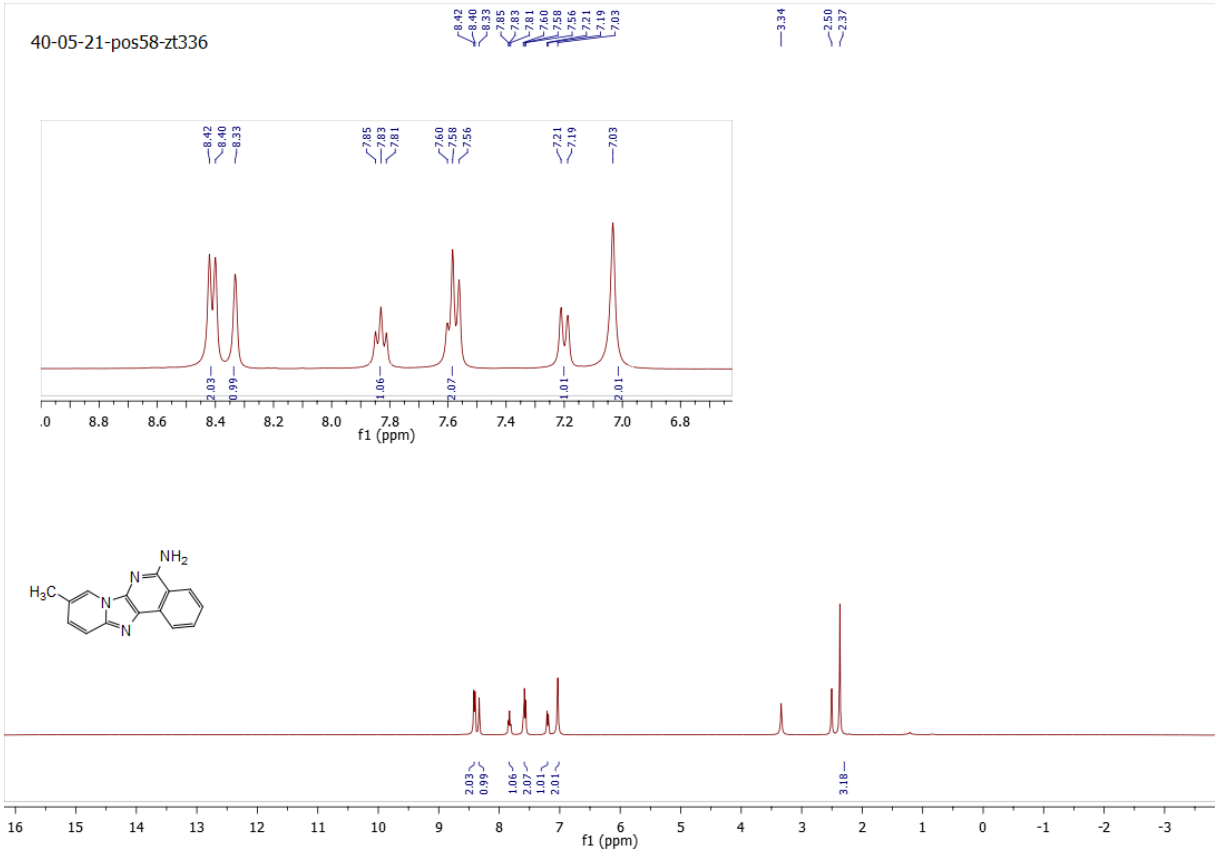


^{13}C NMR (101 MHz, DMSO-d_6)

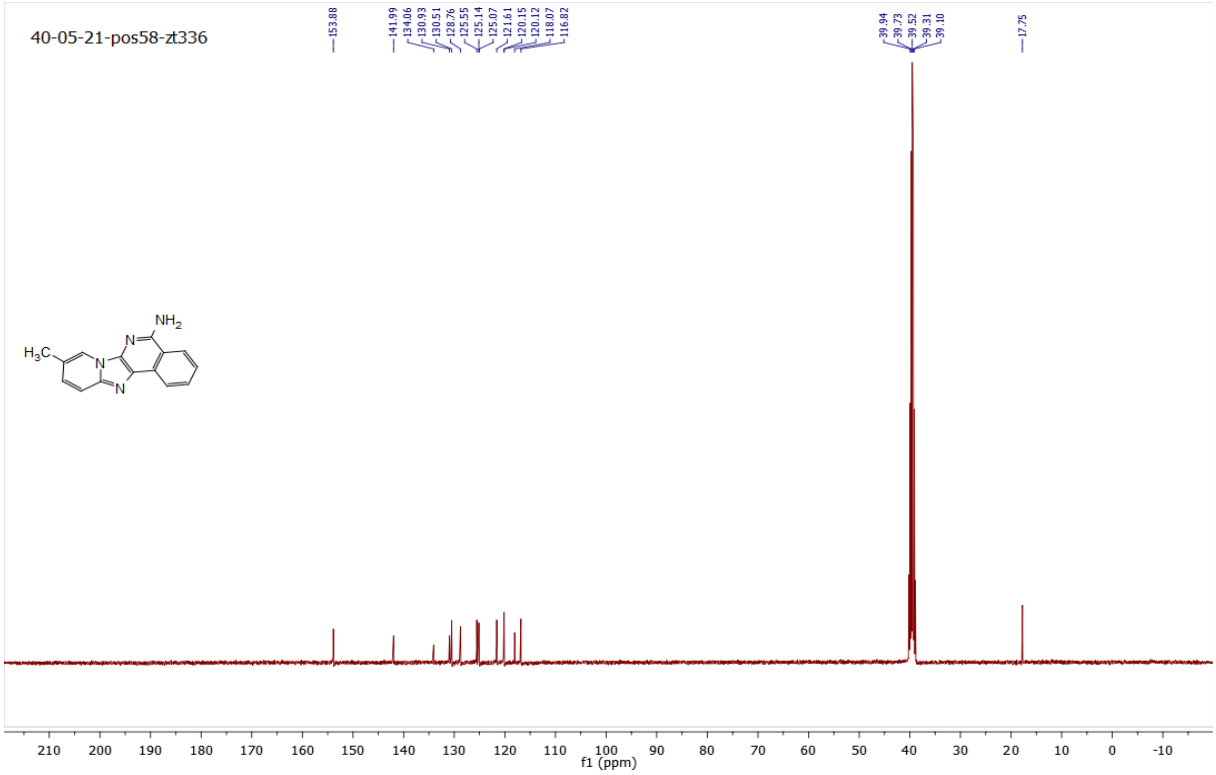


9-Methylpyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (1f)

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

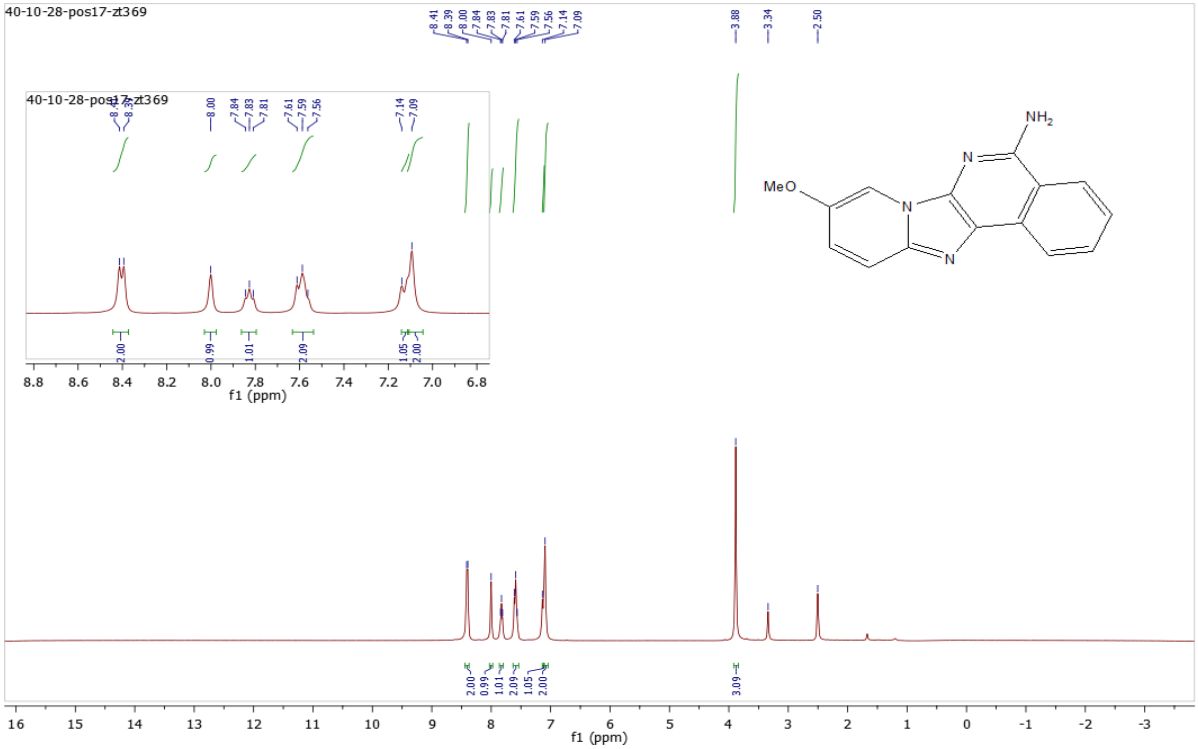


^{13}C NMR (101 MHz, DMSO-d_6)

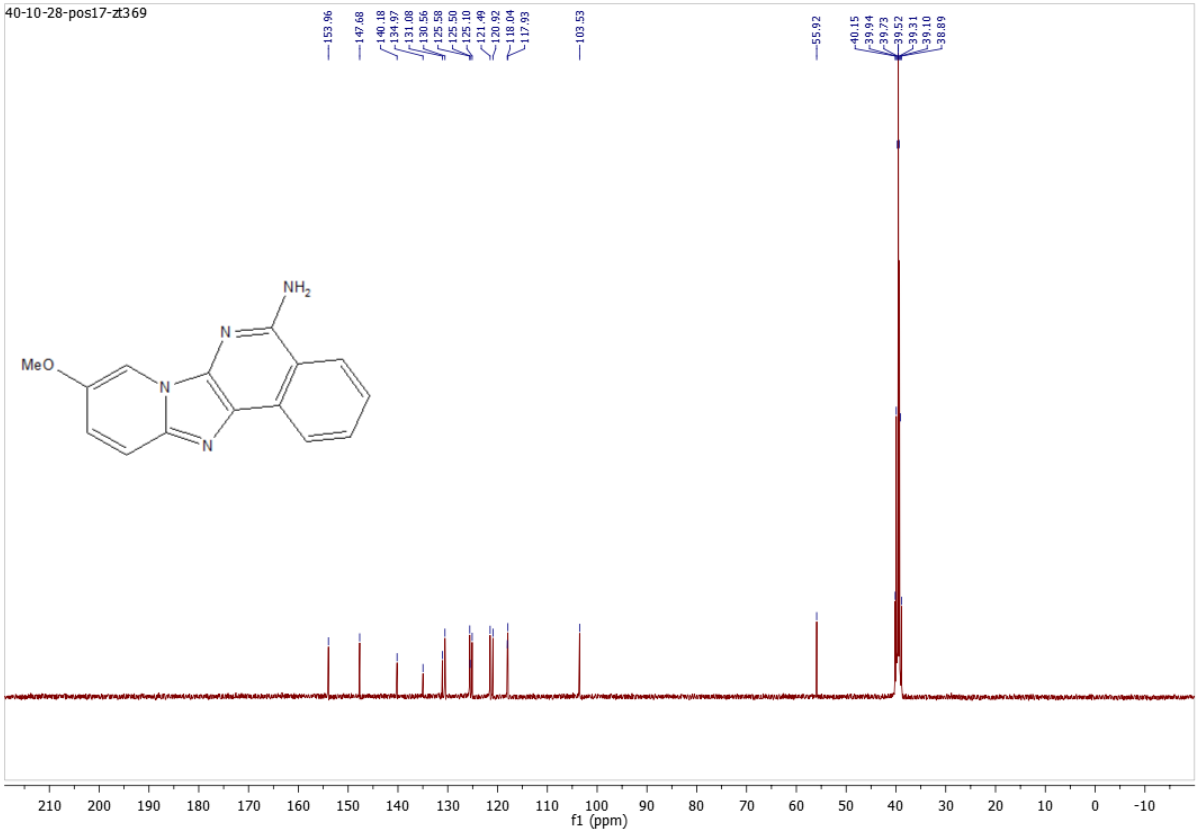


9-Methoxypyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (1g)

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

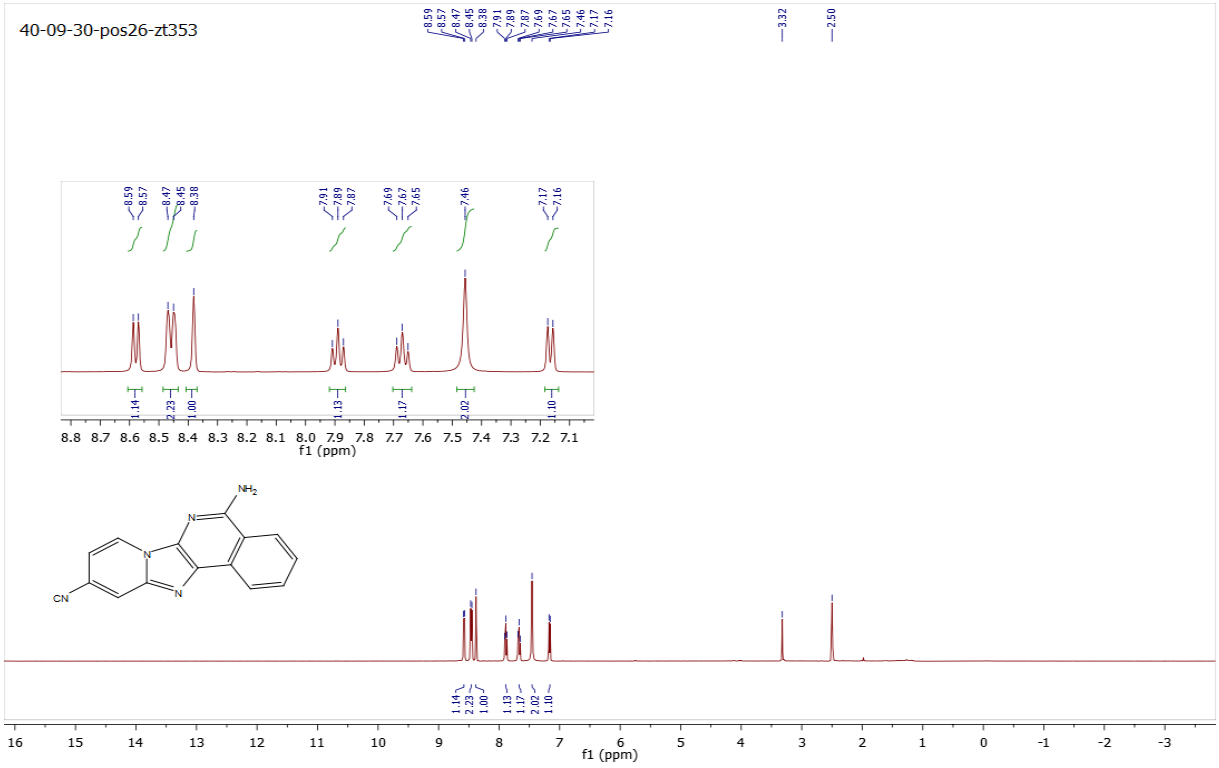


^{13}C NMR (101 MHz, DMSO-d_6)

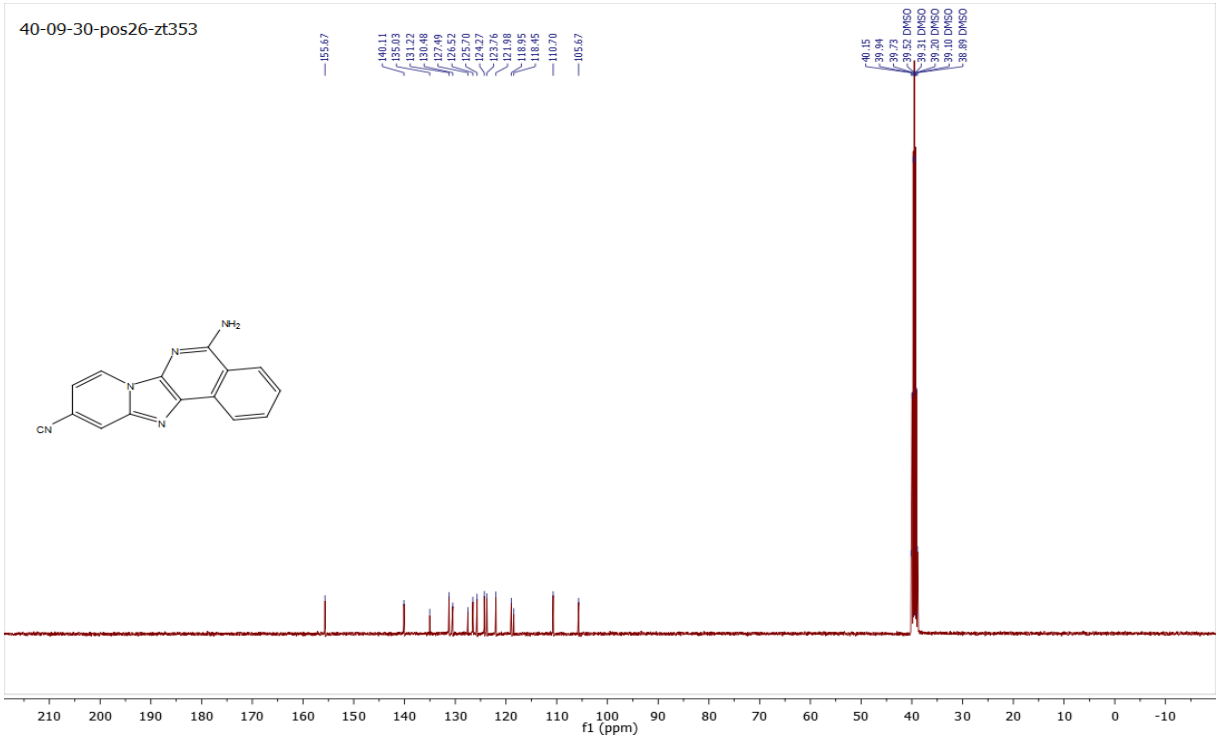


5-Aminopyrido[2',1':2,3]imidazo[4,5-*c*]isoquinoline-10-carbonitrile (1h)

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

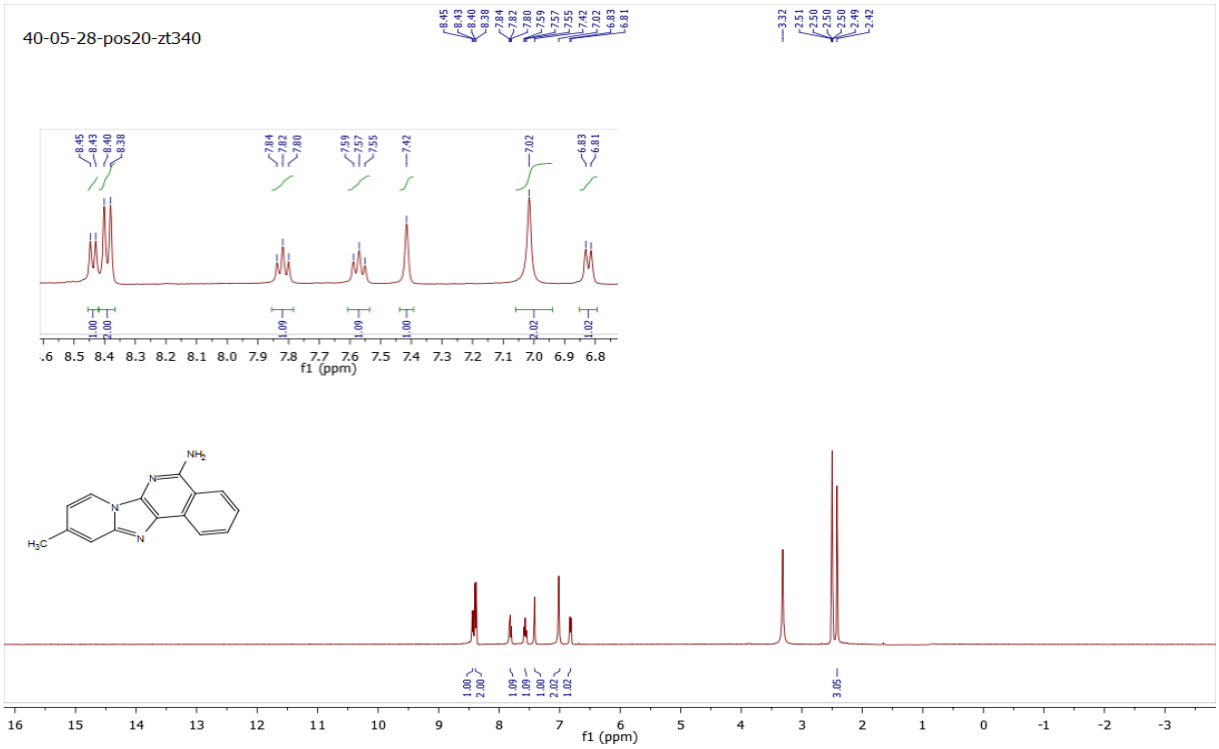


^{13}C NMR (101 MHz, DMSO-d_6)

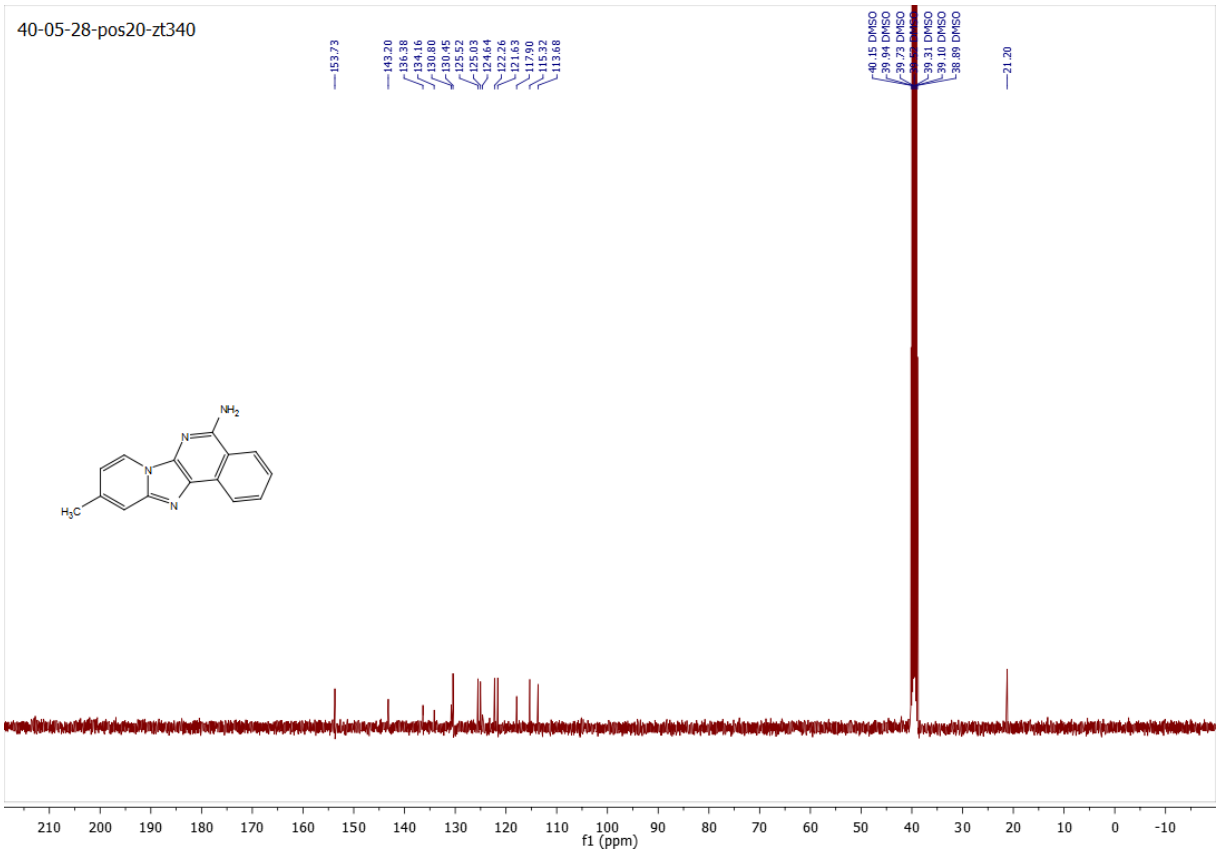


10-Methylpyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (1i)

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

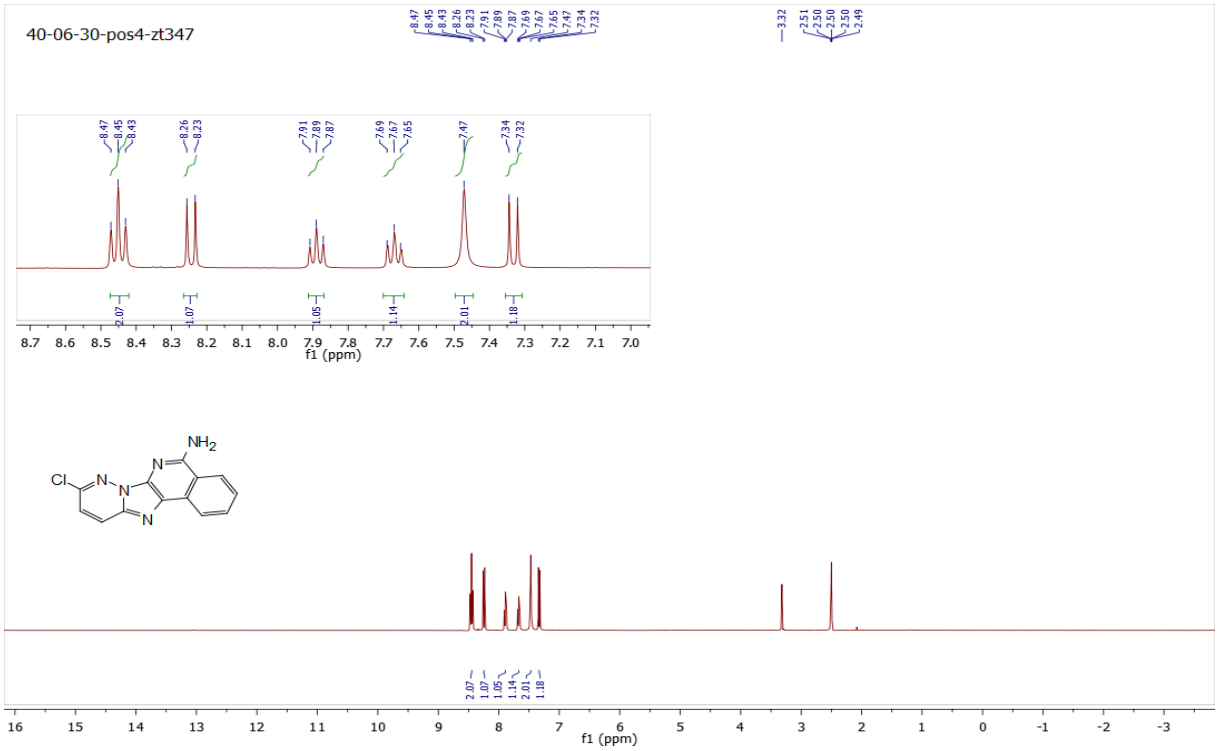


^{13}C NMR (101 MHz, DMSO-d_6)

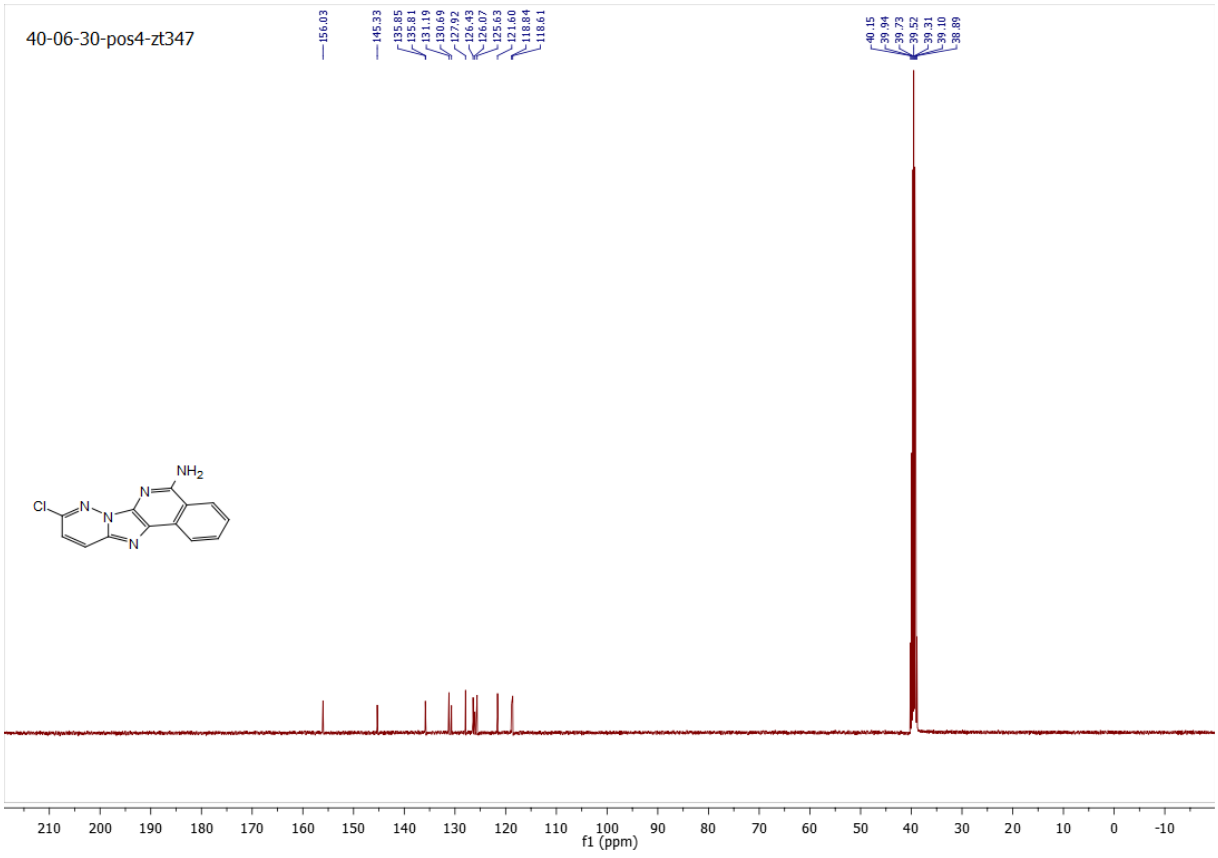


9-Chloropyridazino[6',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (1j)

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

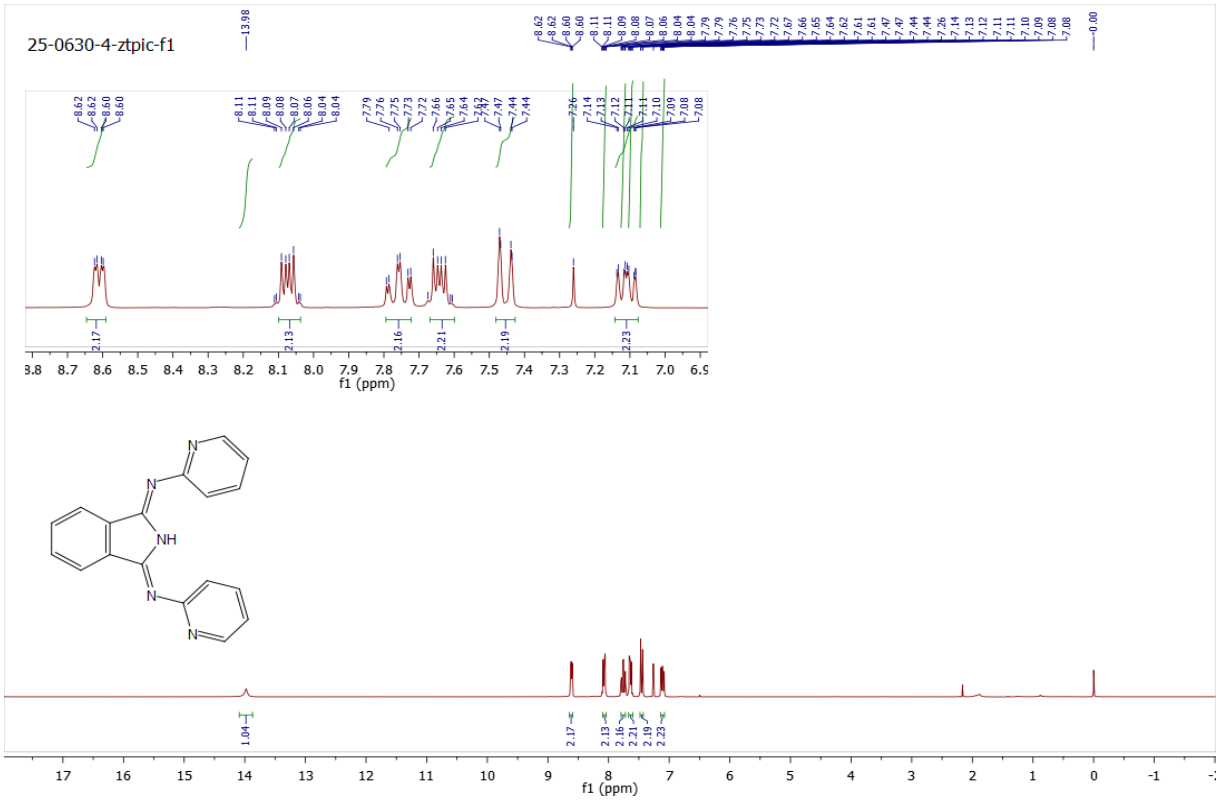


^{13}C NMR (101 MHz, DMSO-d_6)

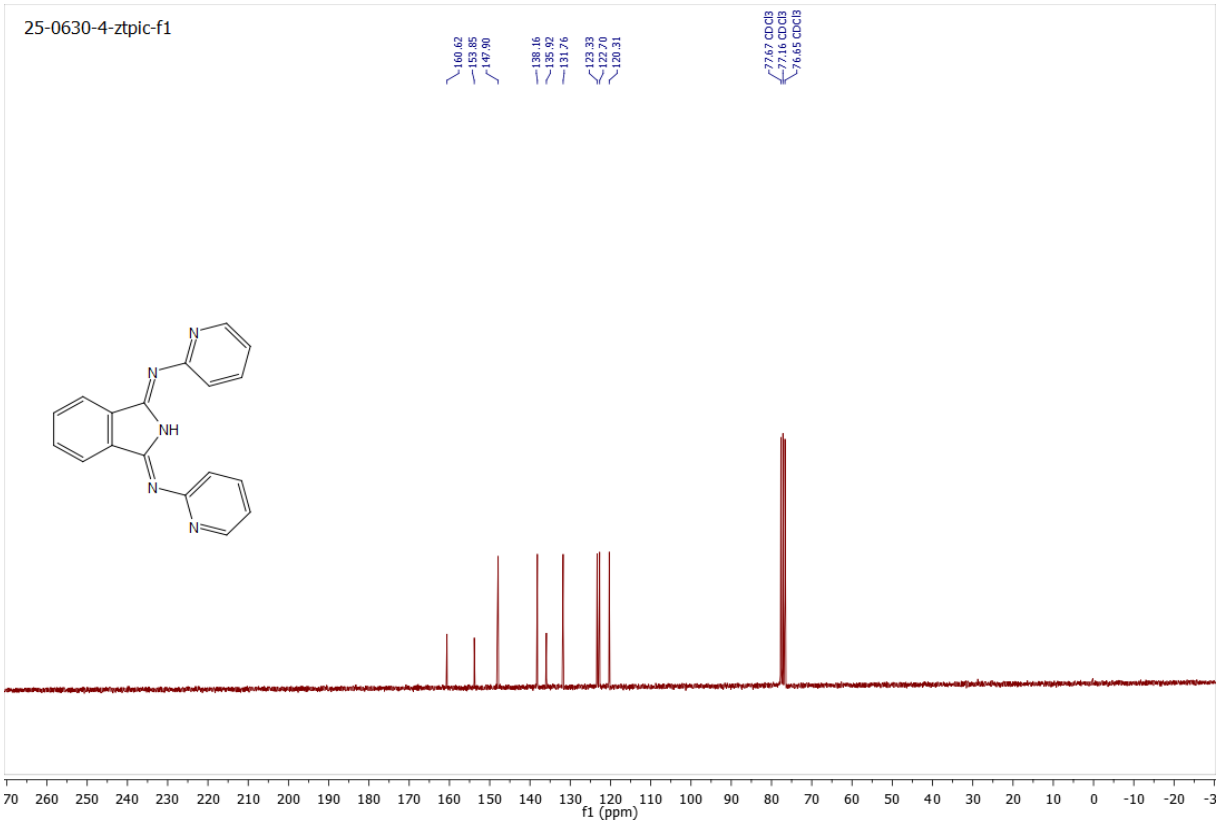


1,3-Bis (2-pyridylimino)isoindole (BPI)* (2a)

^{1}H NMR (250.13 MHz, $CDCl_3$)

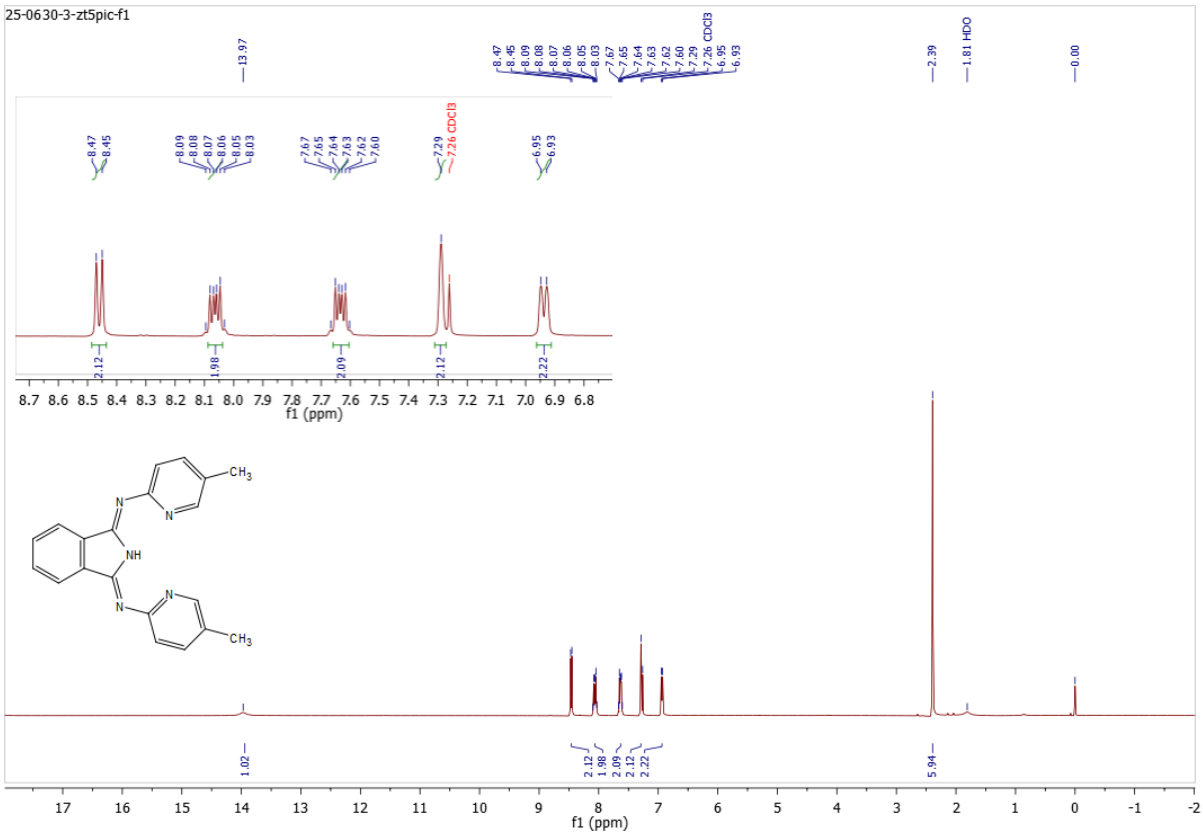


^{13}C NMR (101 MHz, $CDCl_3$)

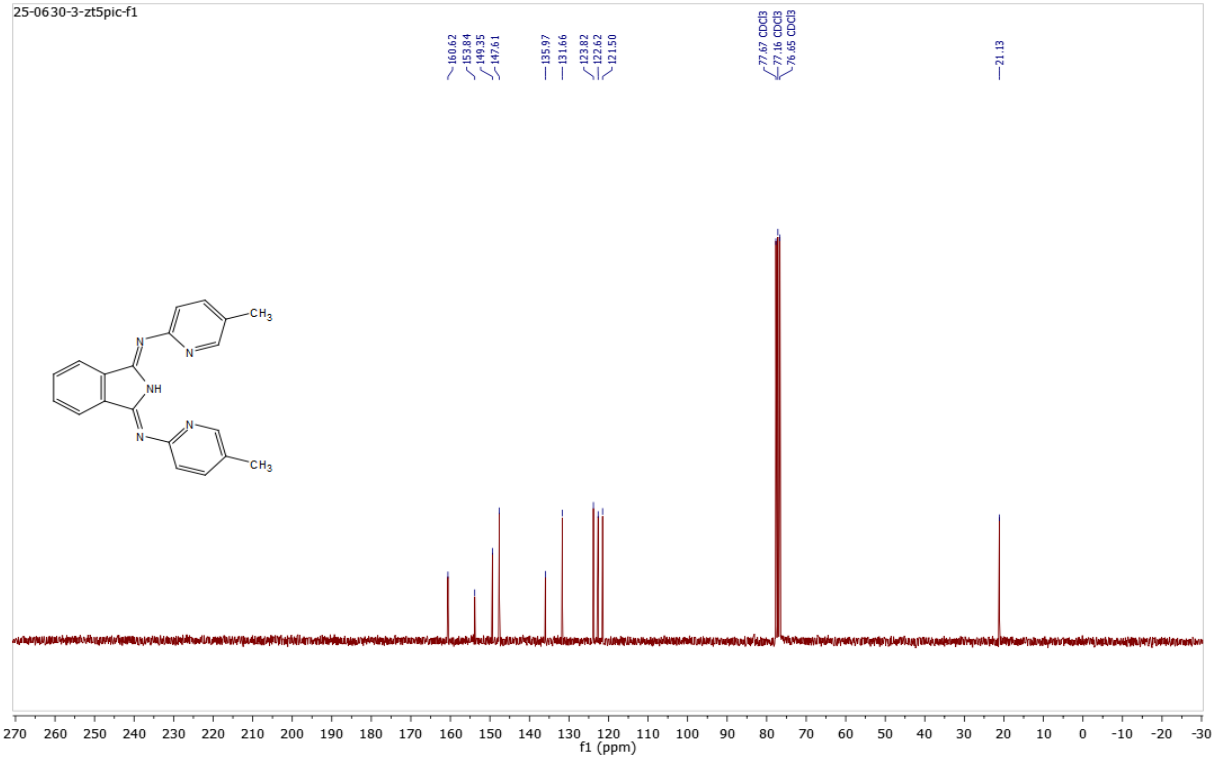


1,3-Bis (5-methyl-2-pyridylimino)isoindole (2f)*

^{1}H NMR (250.13 MHz, $CDCl_3$)

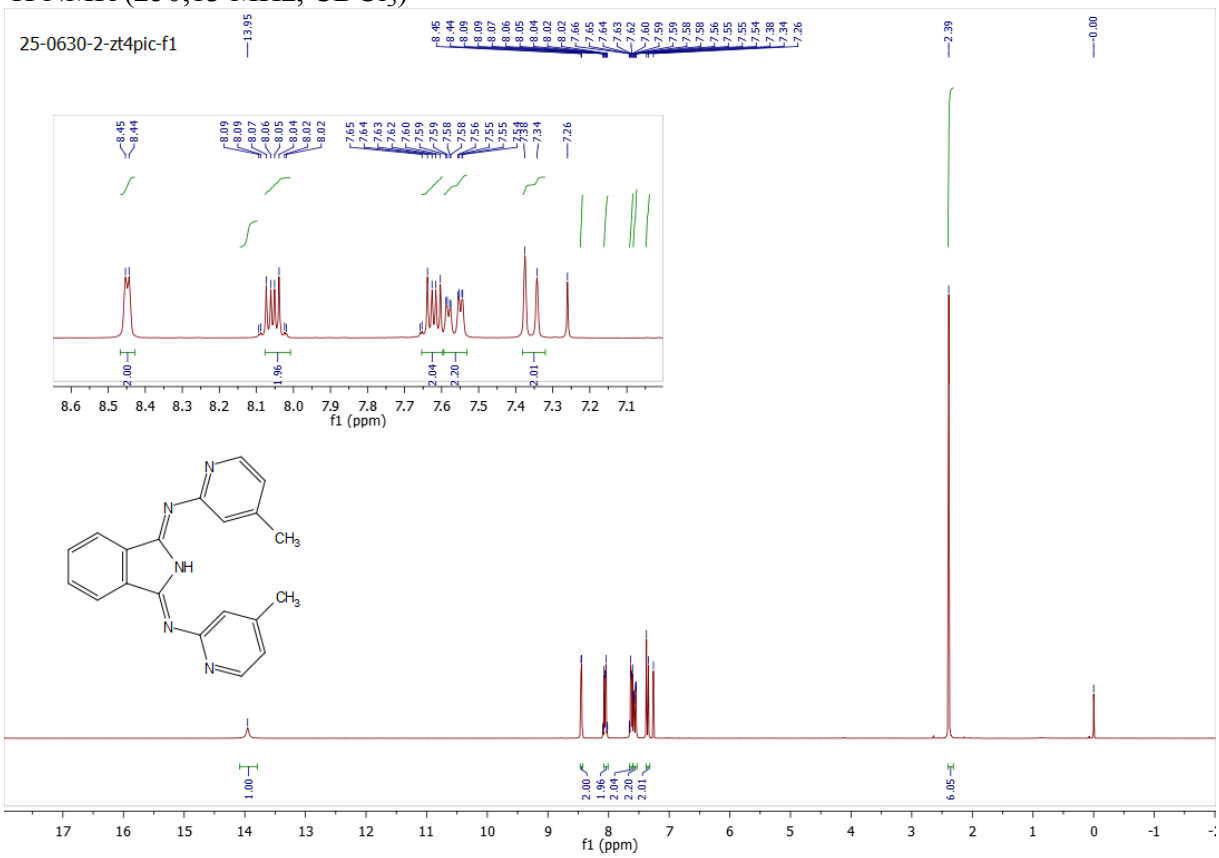


^{13}C NMR (63 MHz, $CDCl_3$):

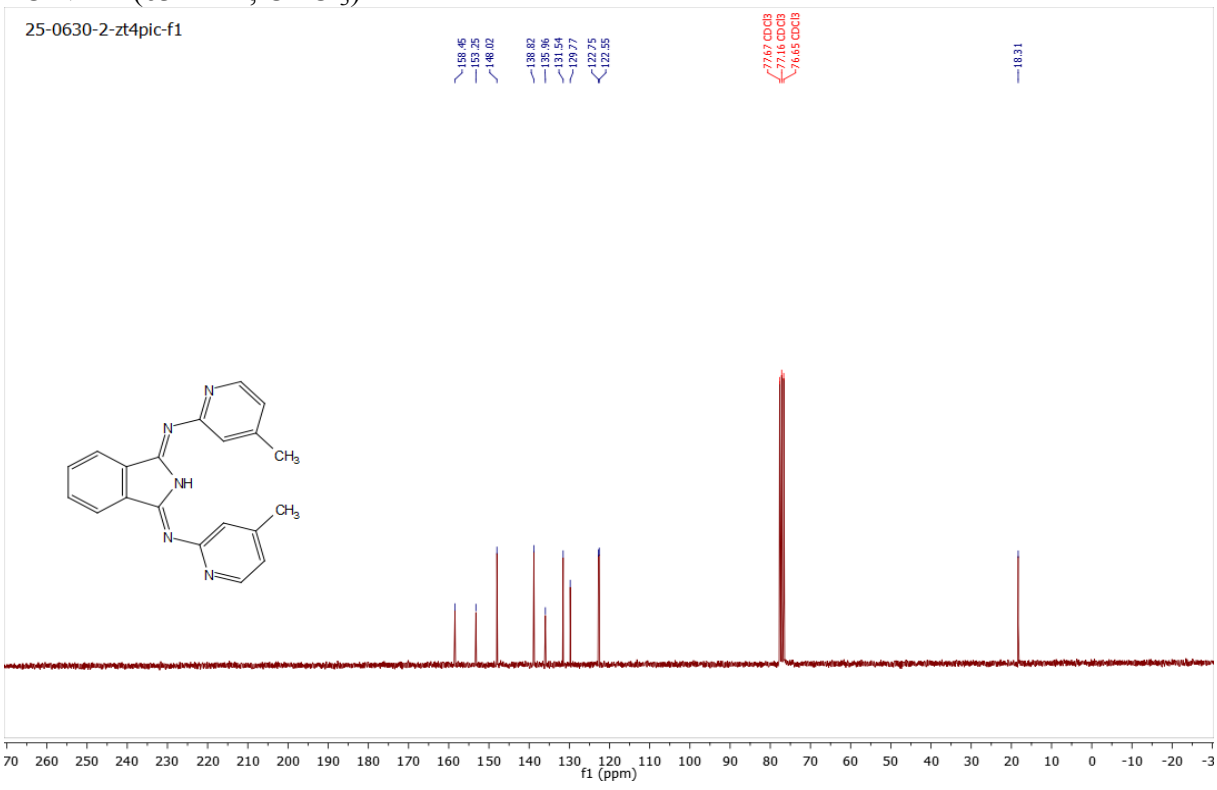


1,3-Bis (4-methyl-2-pyridylimino)isoindole (2i)*

^{1}H NMR (250,13 MHz, $CDCl_3$)

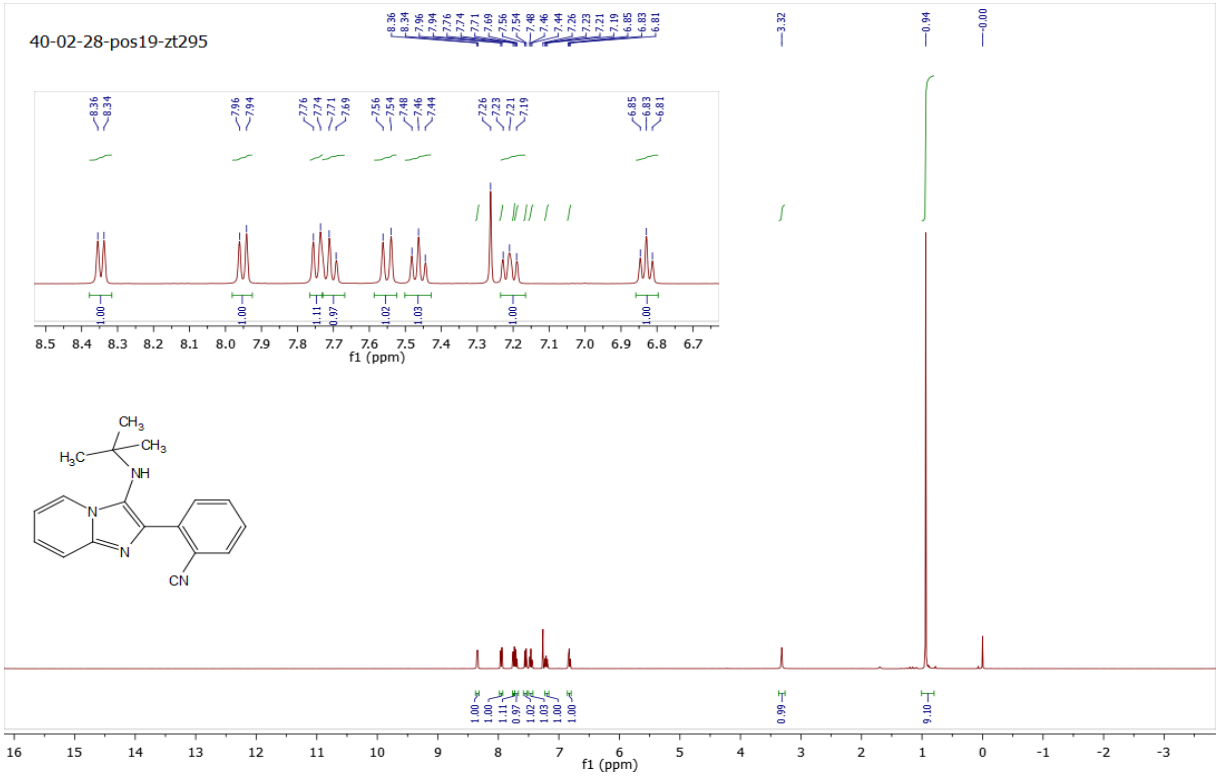


^{13}C NMR (63 MHz, $CDCl_3$)

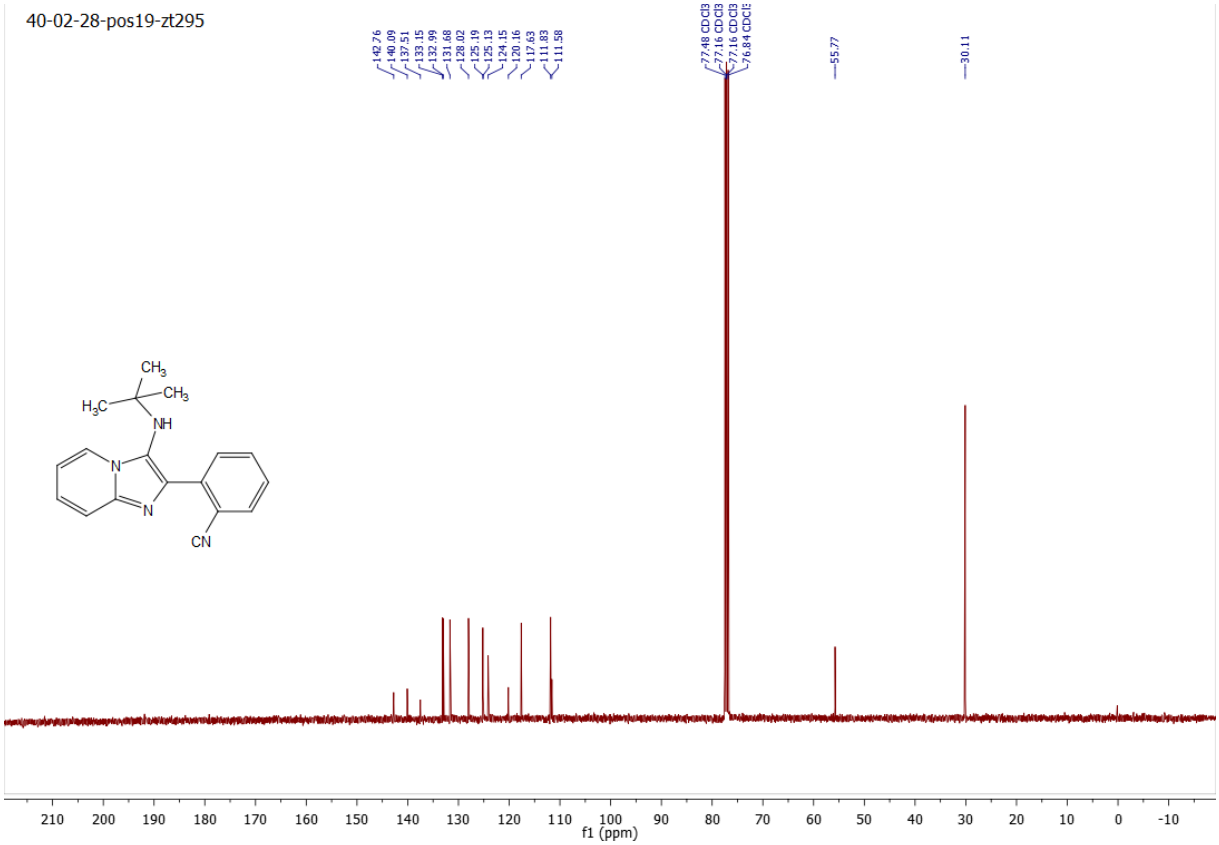


2-(3-*tert*-Butylamino-imidazo[1,2-*a*]pyridin-2-yl)-benzonitrile (3a)

^{1}H NMR (400.13 MHz, $CDCl_3$)

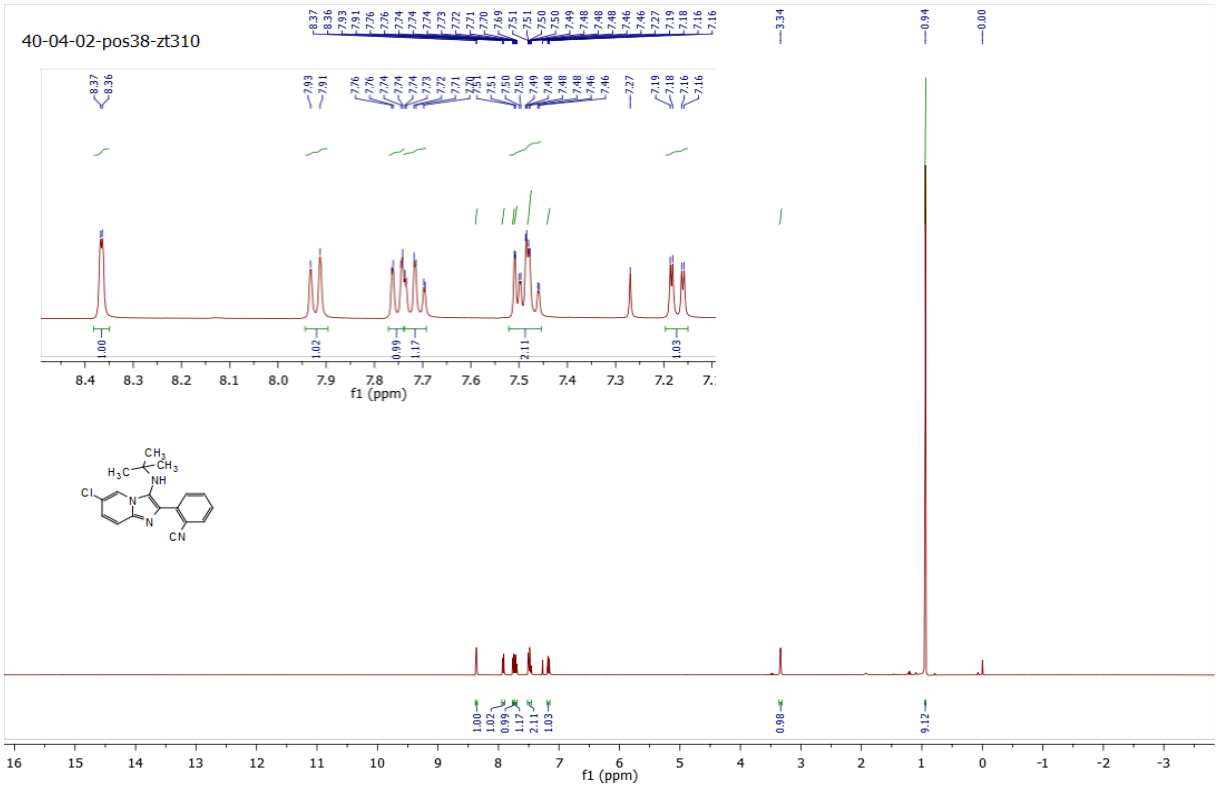


^{13}C NMR (101 MHz, $CDCl_3$)

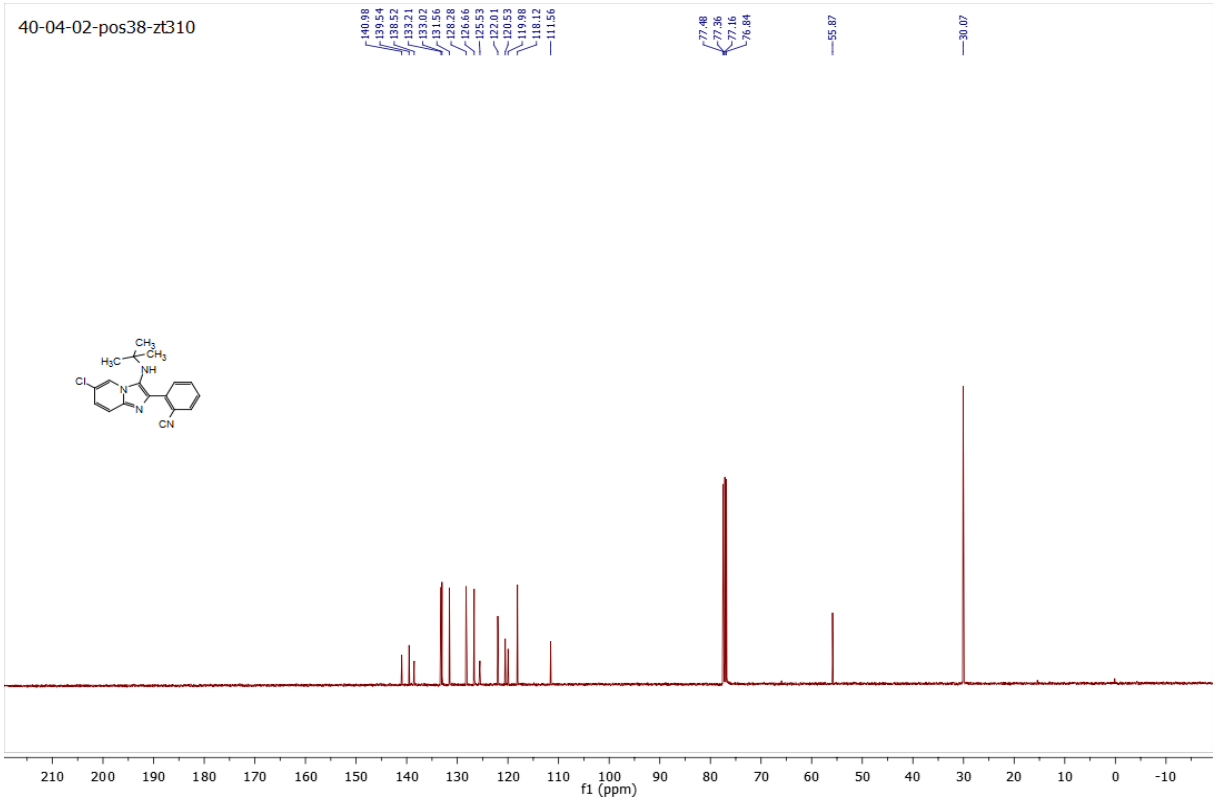


2-[3-(*tert*-Butylamino)-6-chloro-imidazo [1, 2-*a*] pyridin-2-yl] benzonitrile (3b)

^{1}H NMR (400.13 MHz, $CDCl_3$)

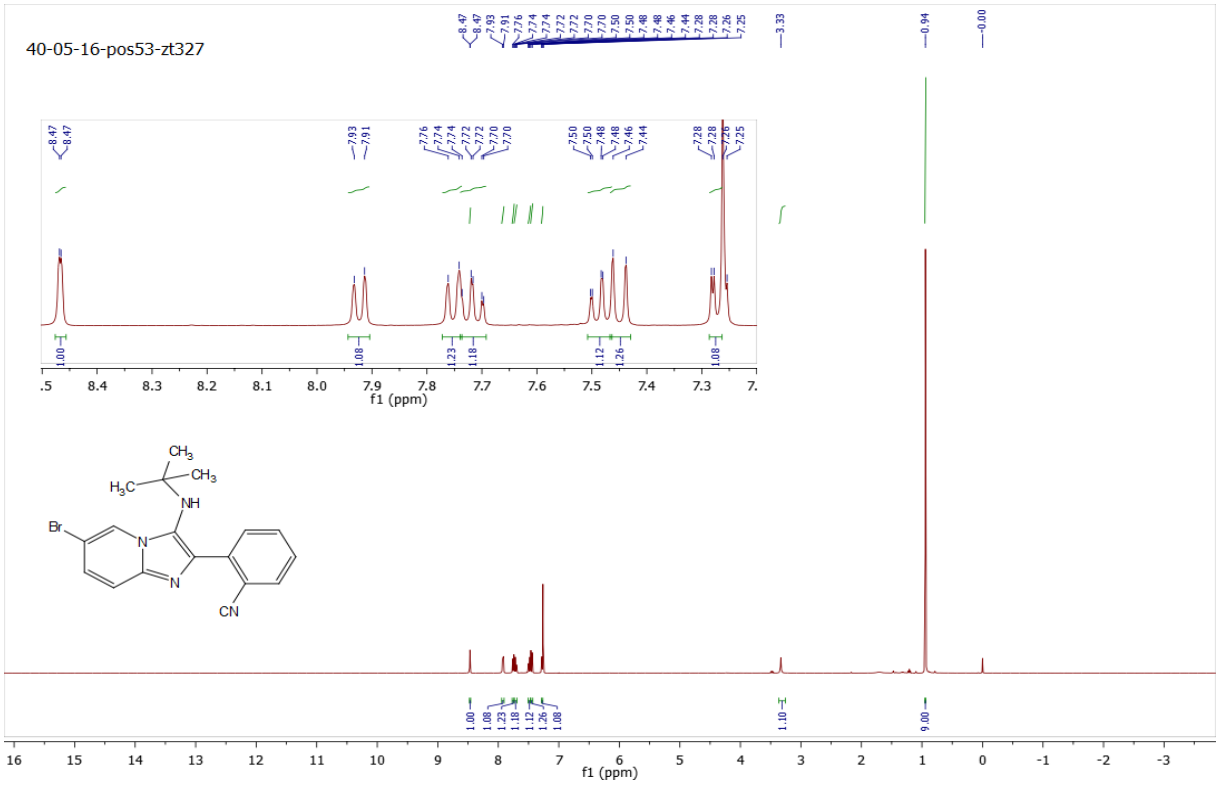


^{13}C NMR (101 MHz, $CDCl_3$)

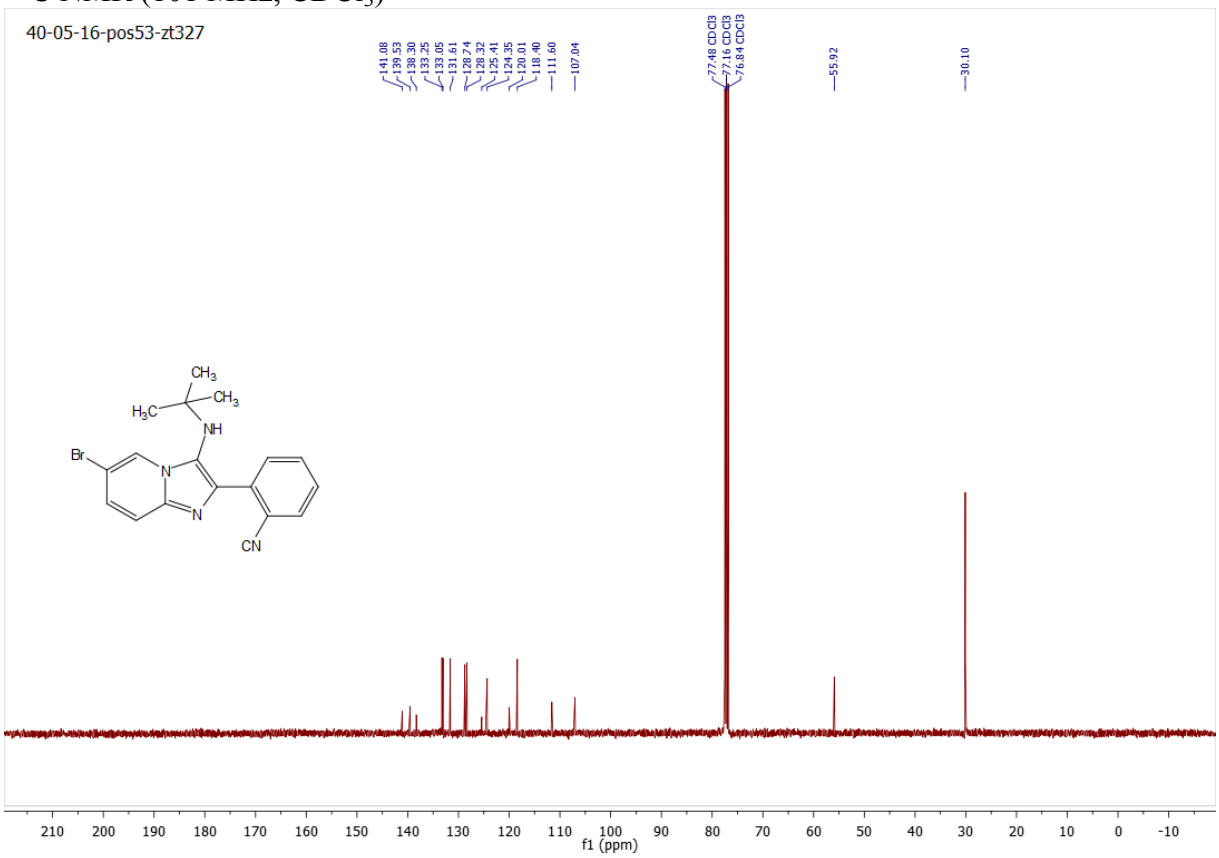


2-(6-Bromo-3-(*tert*-butylamino)imidazo[1,2-*a*]pyridin-2-yl)benzonitrile (3c)

^{1}H NMR (400.13 MHz, $CDCl_3$)

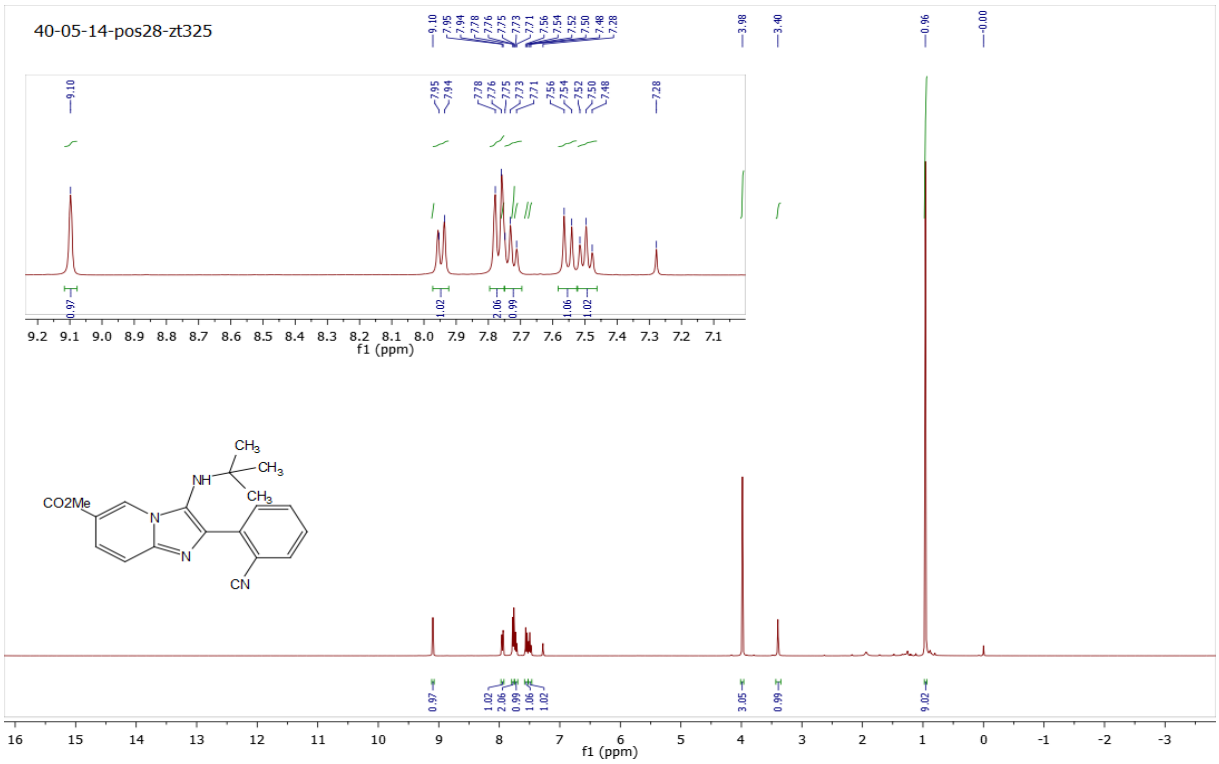


^{13}C NMR (101 MHz, $CDCl_3$)

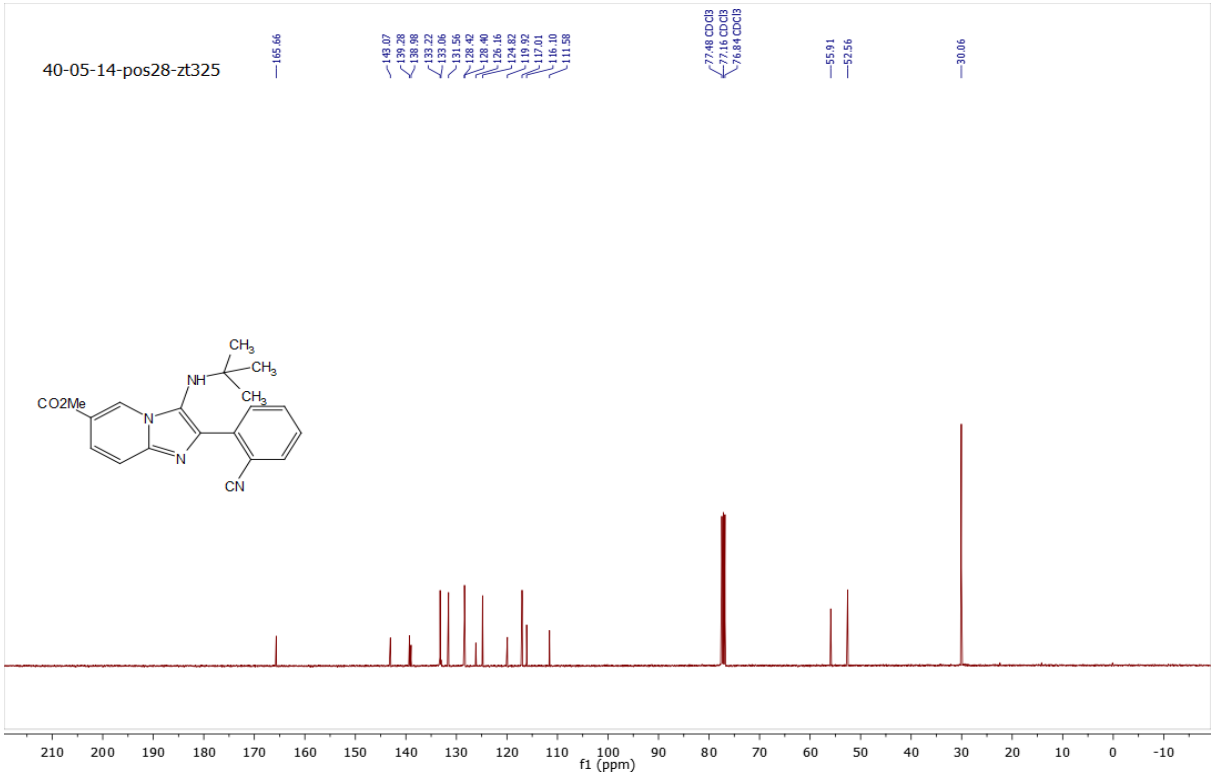


Methyl 3-(*tert*-butylamino)-2-(2-cyanophenyl)imidazo[1,2-a]pyridine-6-carboxylate (3d)

^{1}H NMR (400.13 MHz, $CDCl_3$)

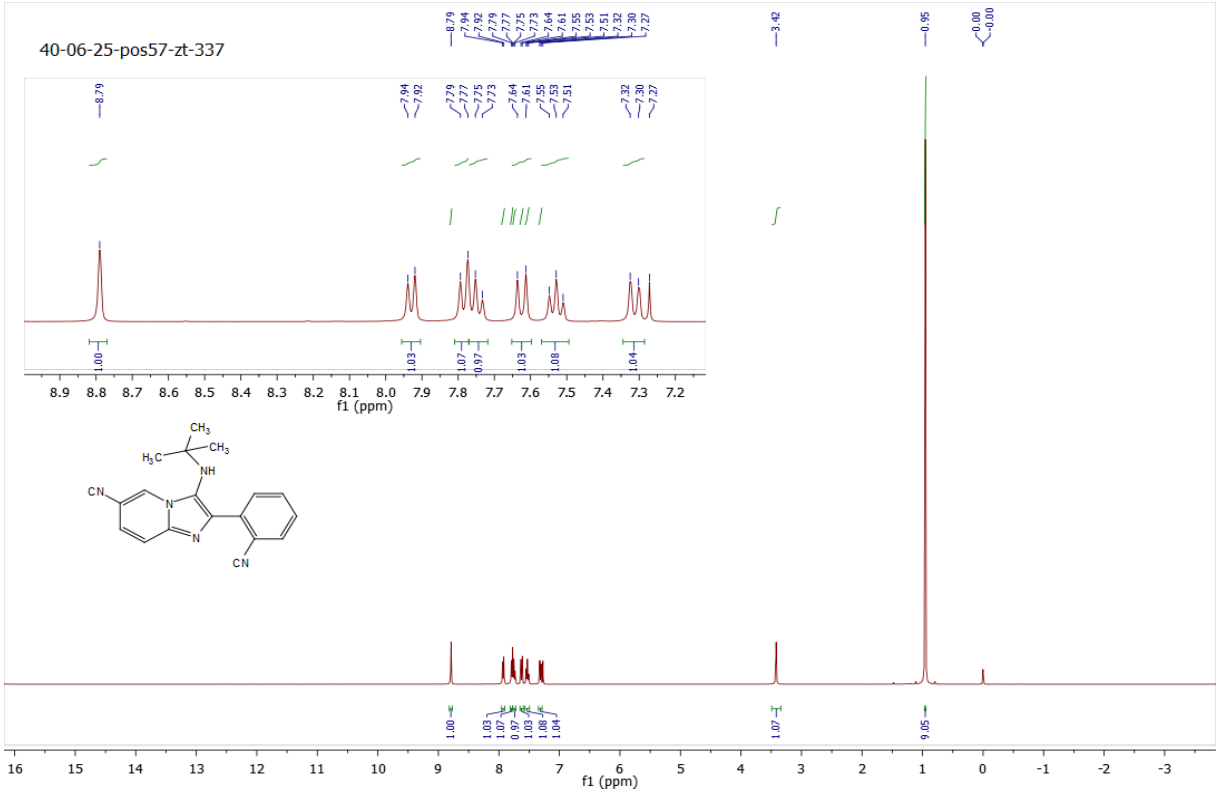


^{13}C NMR (101 MHz, $CDCl_3$)

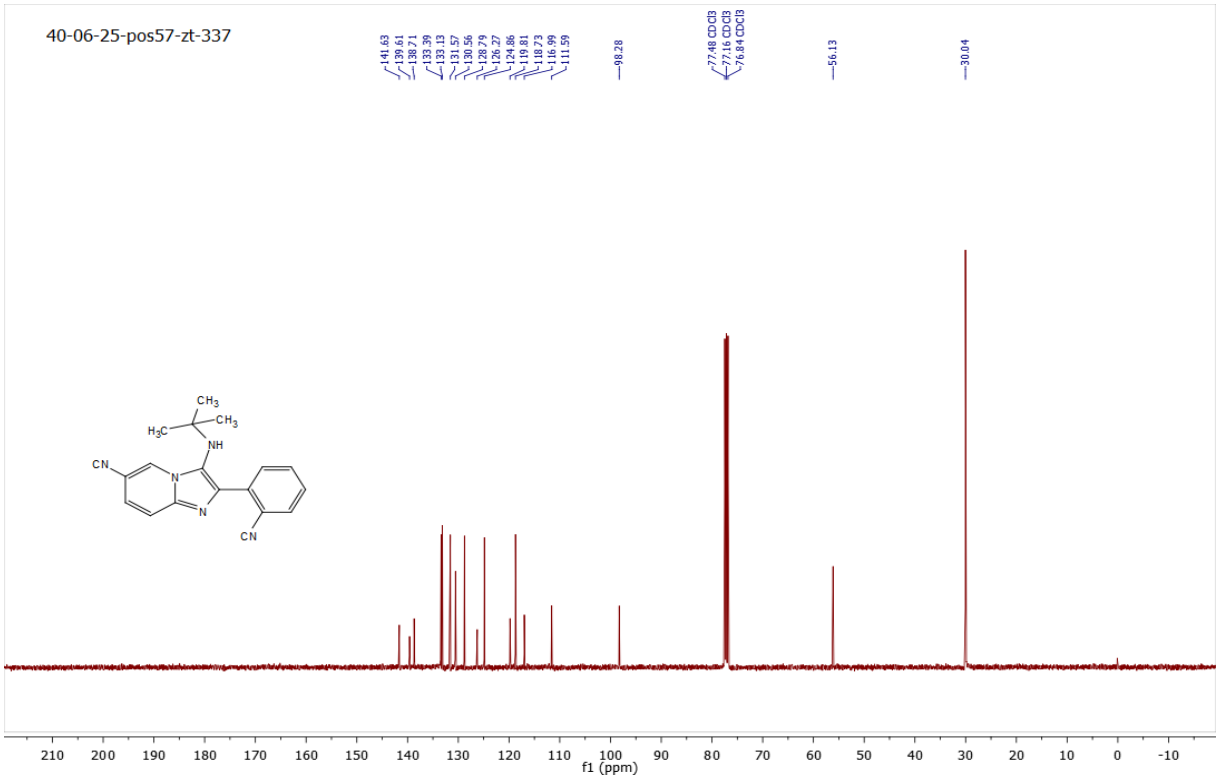


3-(*tert*-Butylamino)-2-(2-cyanophenyl)imidazo[1,2-a]pyridine-6-carbonitrile (3e)

^{1}H NMR (400.13 MHz, $CDCl_3$)

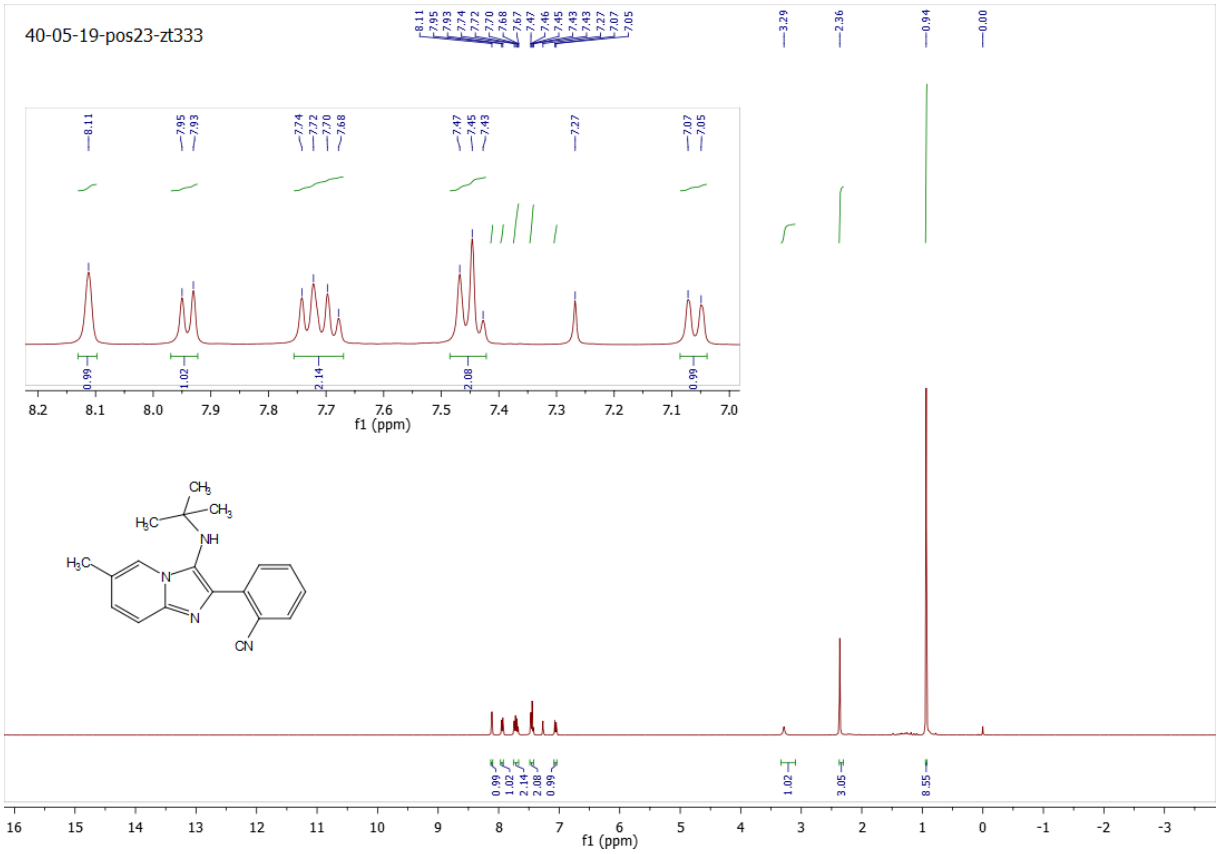


^{13}C NMR (101 MHz, $CDCl_3$)

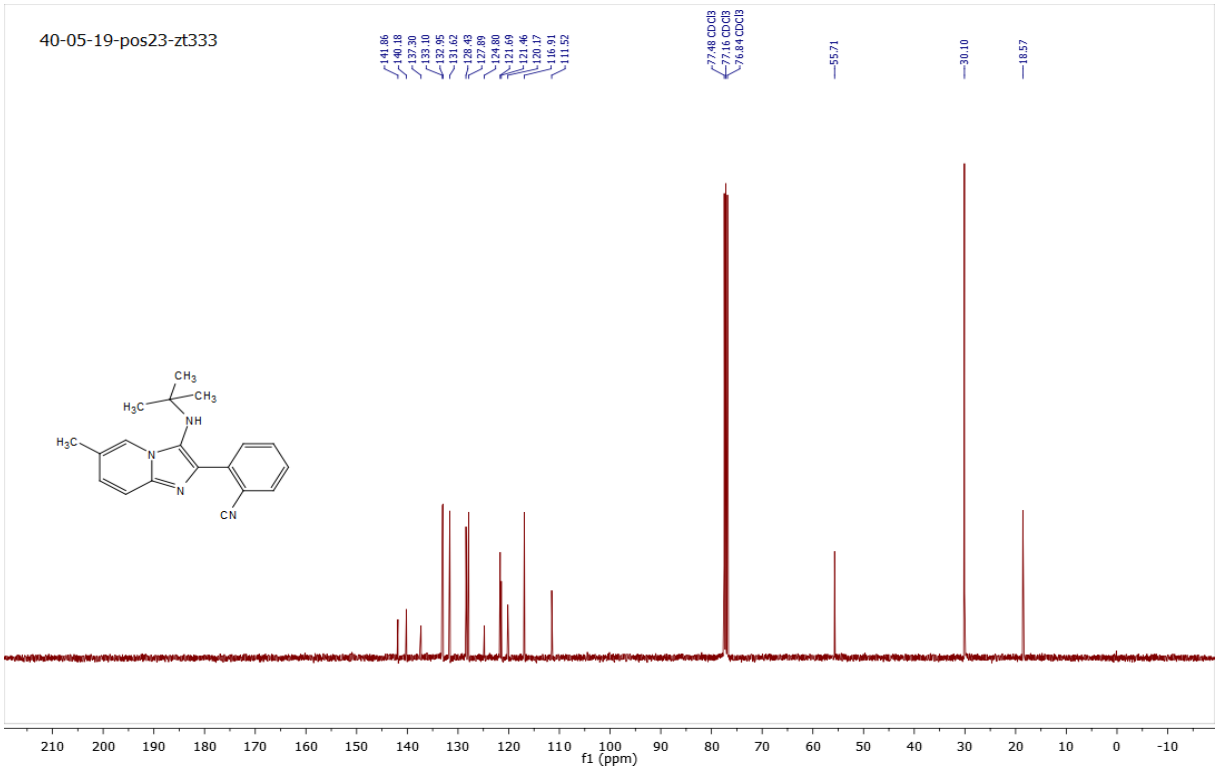


2-(3-(*tert*-Butylamino)-6-methylimidazo[1,2-a]pyridin-2-yl)benzonitrile (3f)

^{1}H NMR (400.13 MHz, $CDCl_3$)

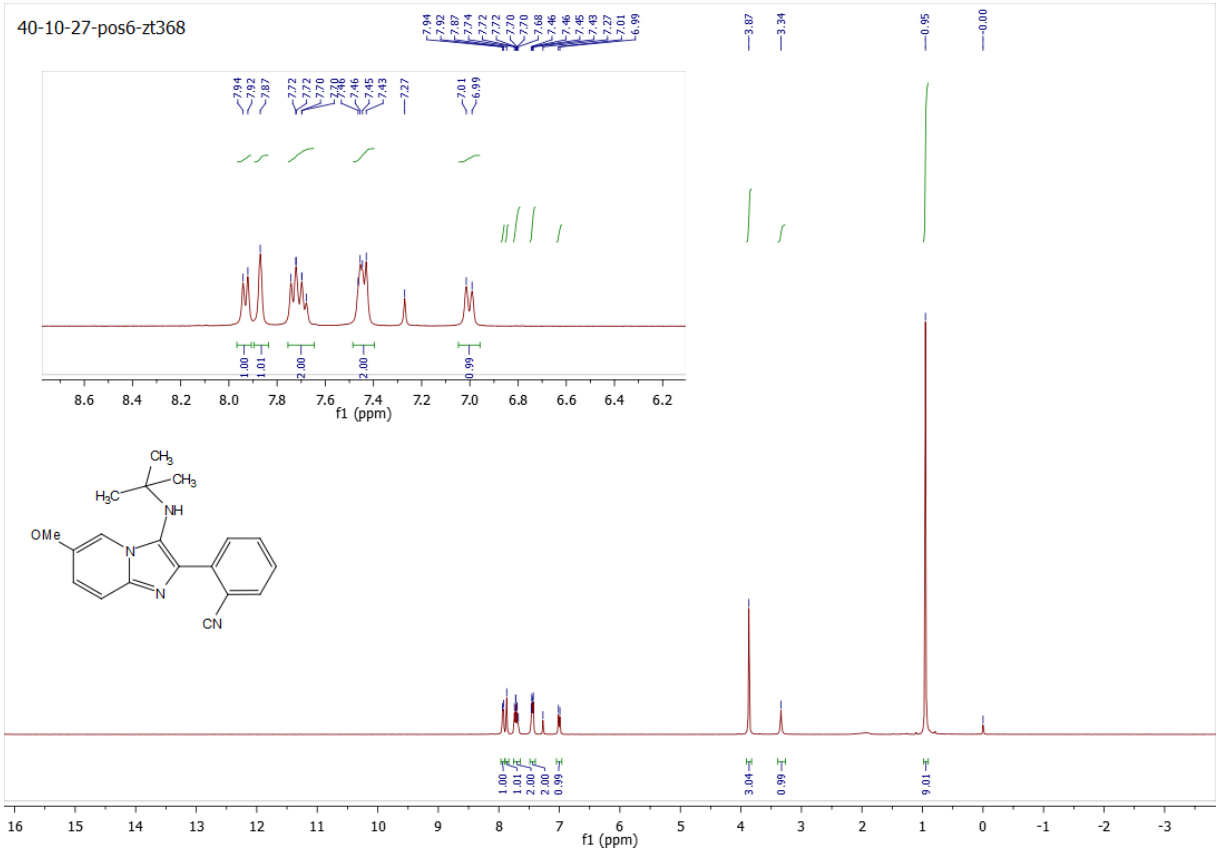


^{13}C NMR (101 MHz, $CDCl_3$)

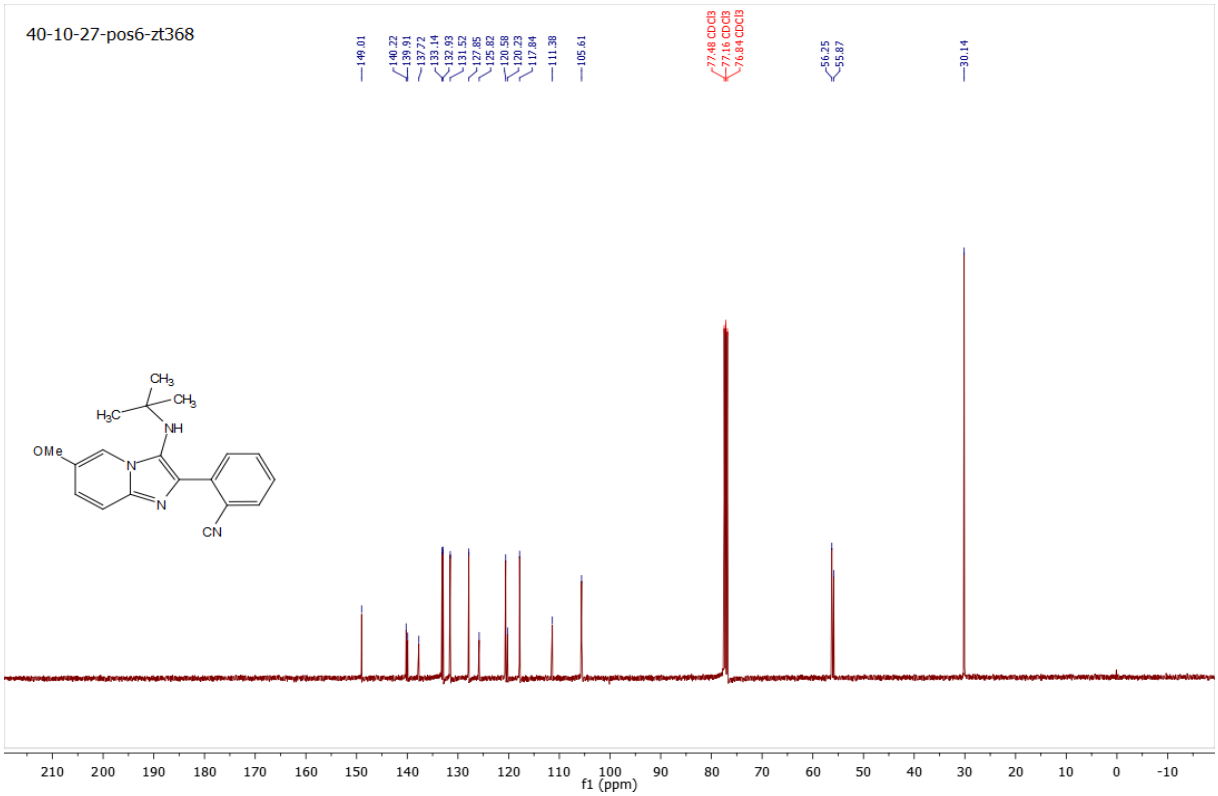


2-(3-(*tert*-Butylamino)-6-methoxyimidazo[1,2-*a*]pyridin-2-yl)benzonitrile (3g)

^{1}H NMR (400.13 MHz, $CDCl_3$)

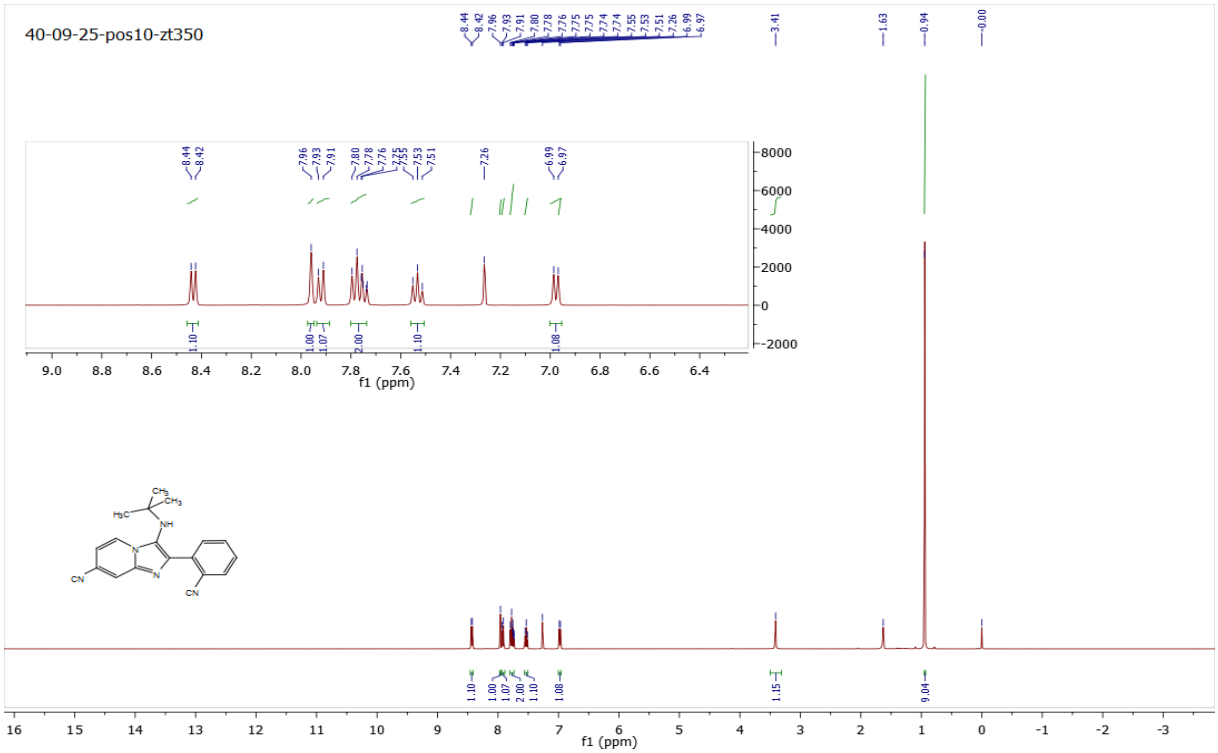


^{13}C NMR (101 MHz, $CDCl_3$)

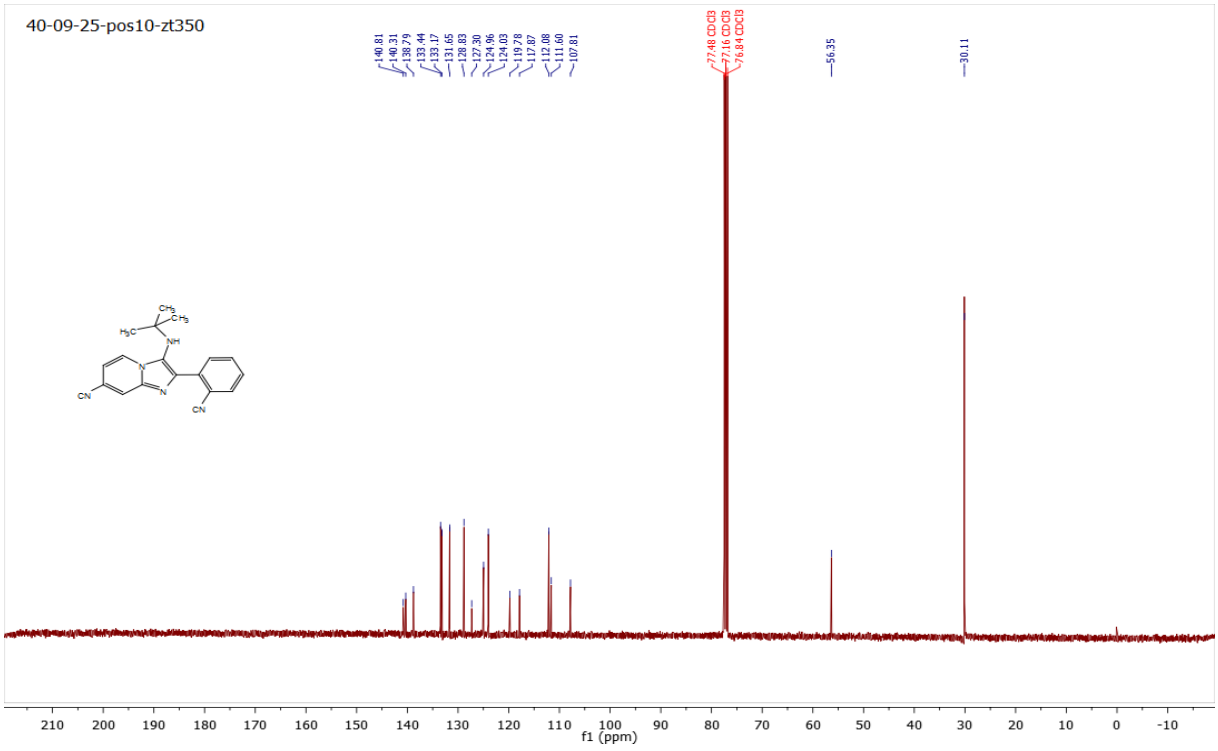


2-(3-(*tert*-Butylamino)-7-isocyanoimidazo[1,2-*a*]pyridin-2-yl)benzonitrile (3h)

^{1}H NMR (400.13 MHz, $CDCl_3$)

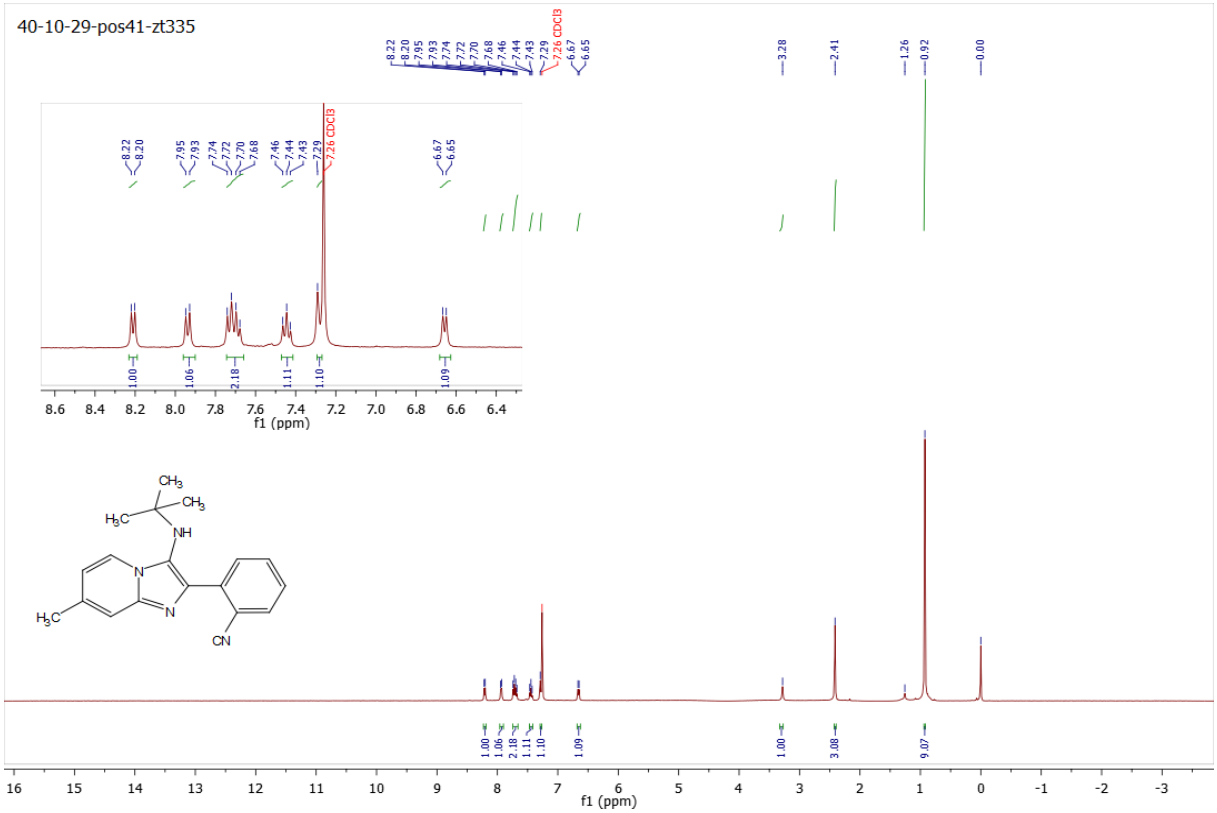


^{13}C NMR (101 MHz, $CDCl_3$)

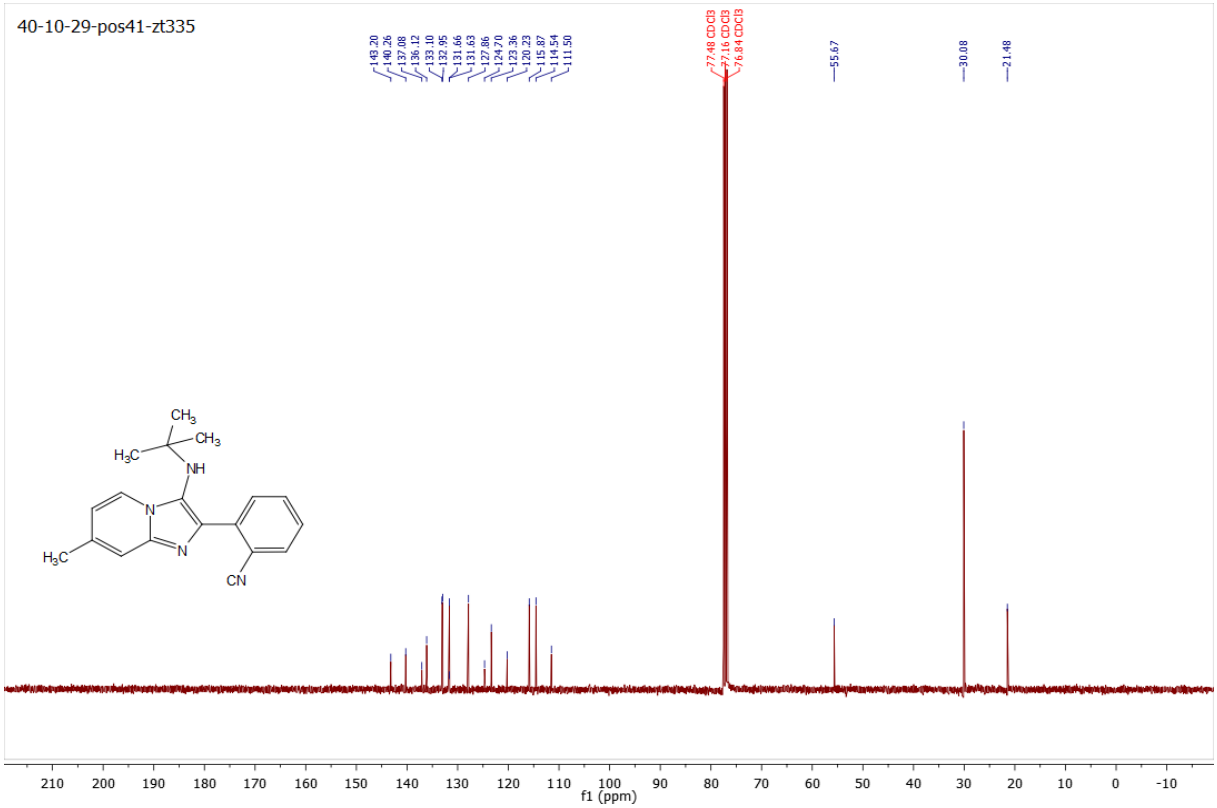


2-(3-(*tert*-Butylamino)-7-methylimidazo[1,2-*a*]pyridin-2-yl)benzonitrile (3i)

^{1}H NMR (400.13 MHz, $CDCl_3$)

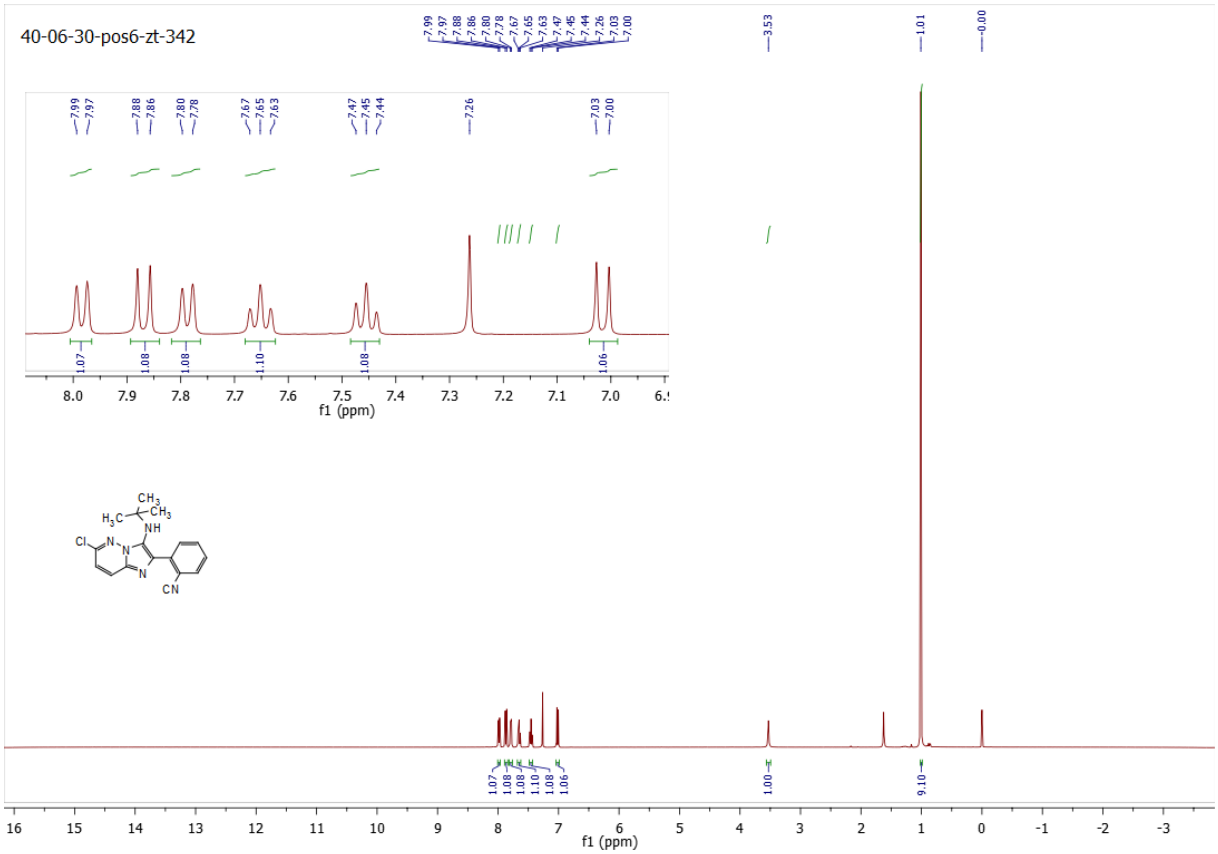


^{13}C NMR (101 MHz, $CDCl_3$)

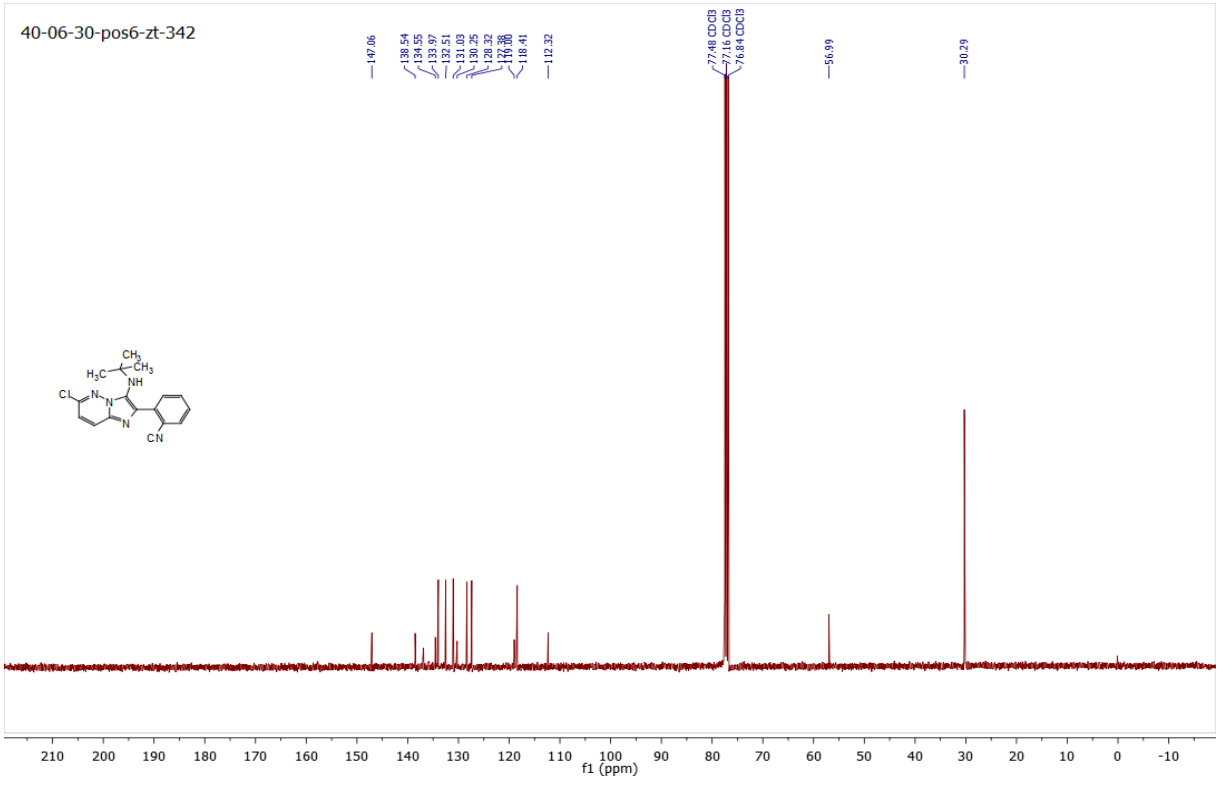


2-(3-(*tert*-Butylamino)-6-chloroimidazo[1,2-*b*]pyridazin-2-yl)benzonitrile (3j)

^{1}H NMR (400.13 MHz, $CDCl_3$)

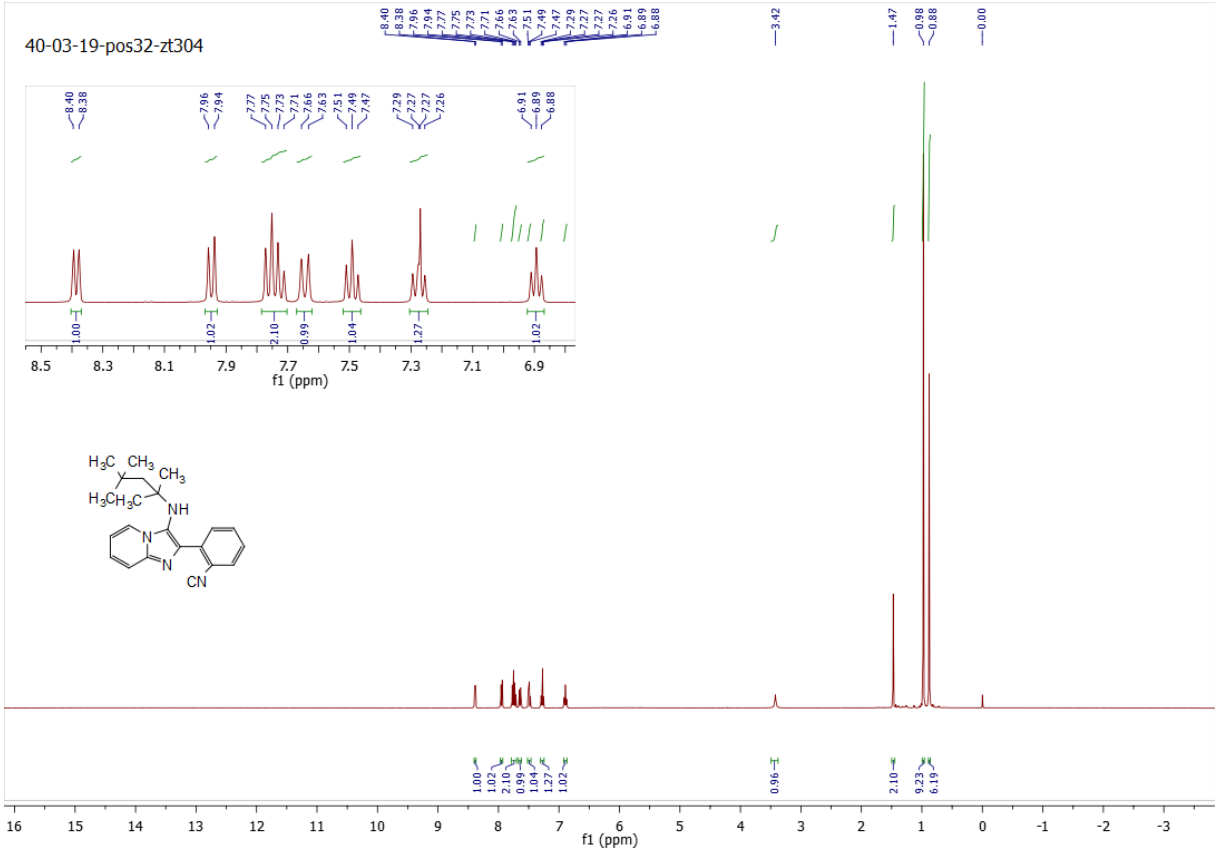


^{13}C NMR (101 MHz, $CDCl_3$)

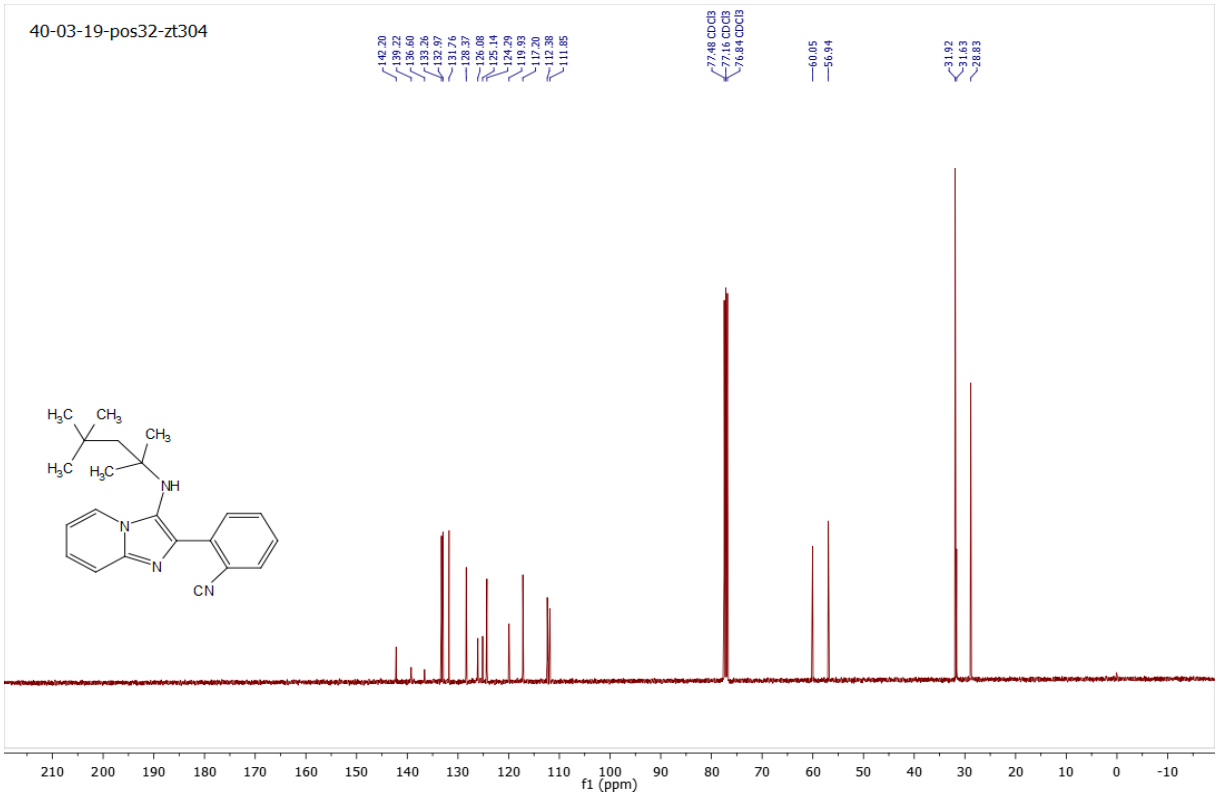


2-[3-(1,1,3,3-Tetramethylbutylamino)imidazo[1,2-*a*]pyridin-2-yl]benzonitrile (4a)

^{1}H NMR (400.13 MHz, $CDCl_3$)

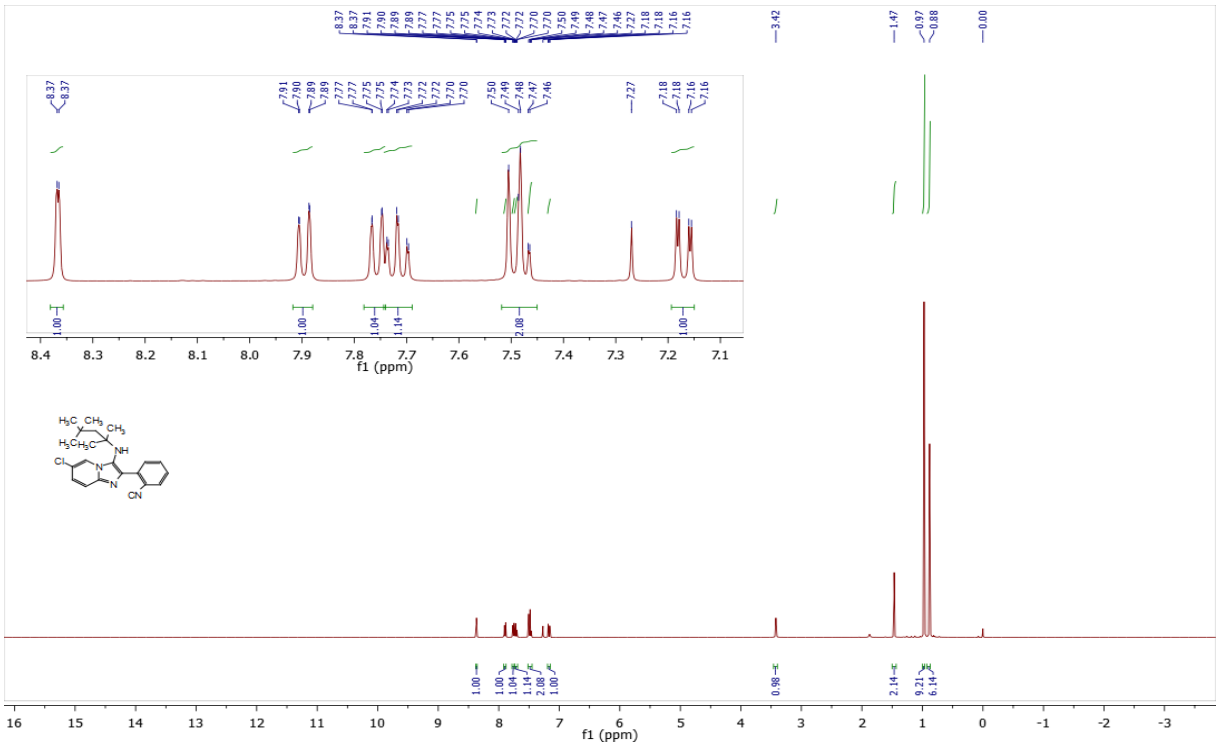


^{13}C NMR (101 MHz, $CDCl_3$)

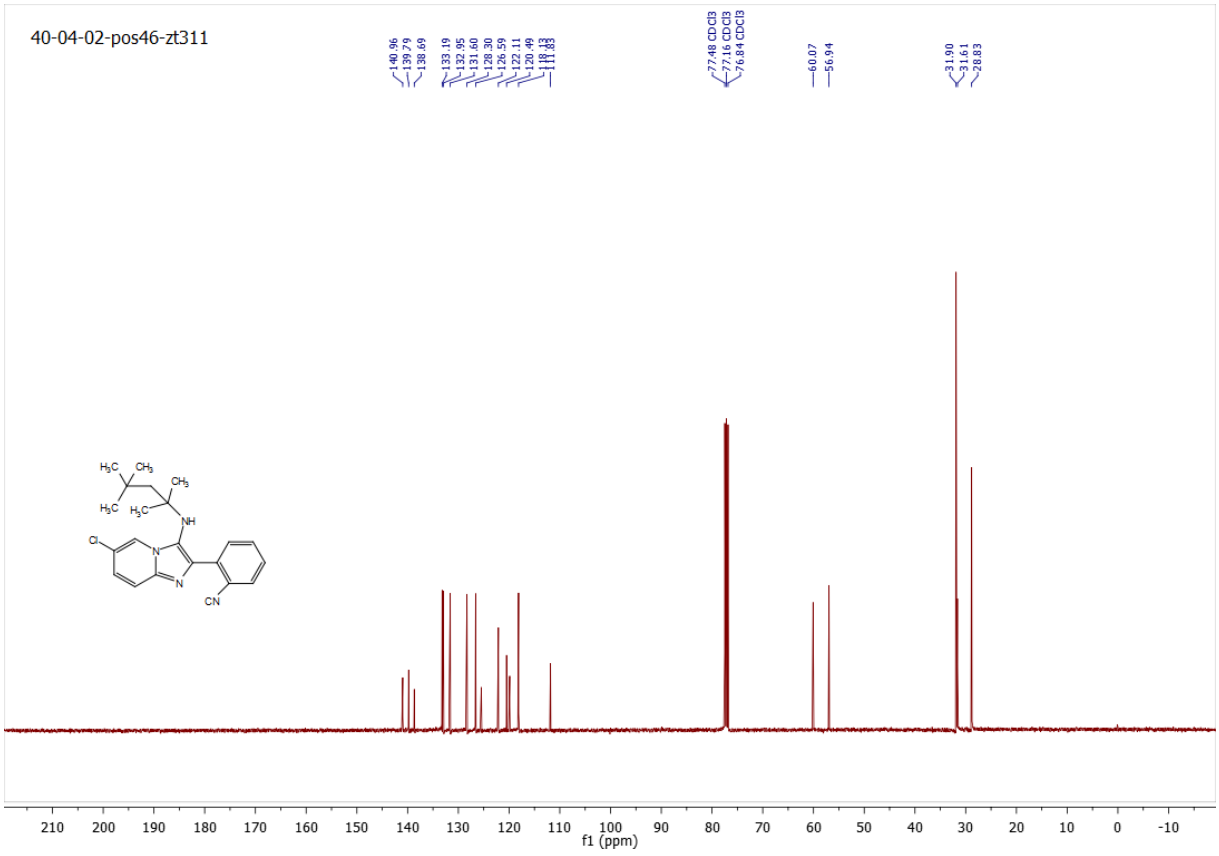


2-[6-chloro-3-(1,1,3,3-Tetramethylbutylamino)imidazo[1,2-a]pyridin-2-yl]benzonitrile(4b)

^{1}H NMR (400.13 MHz, $CDCl_3$)

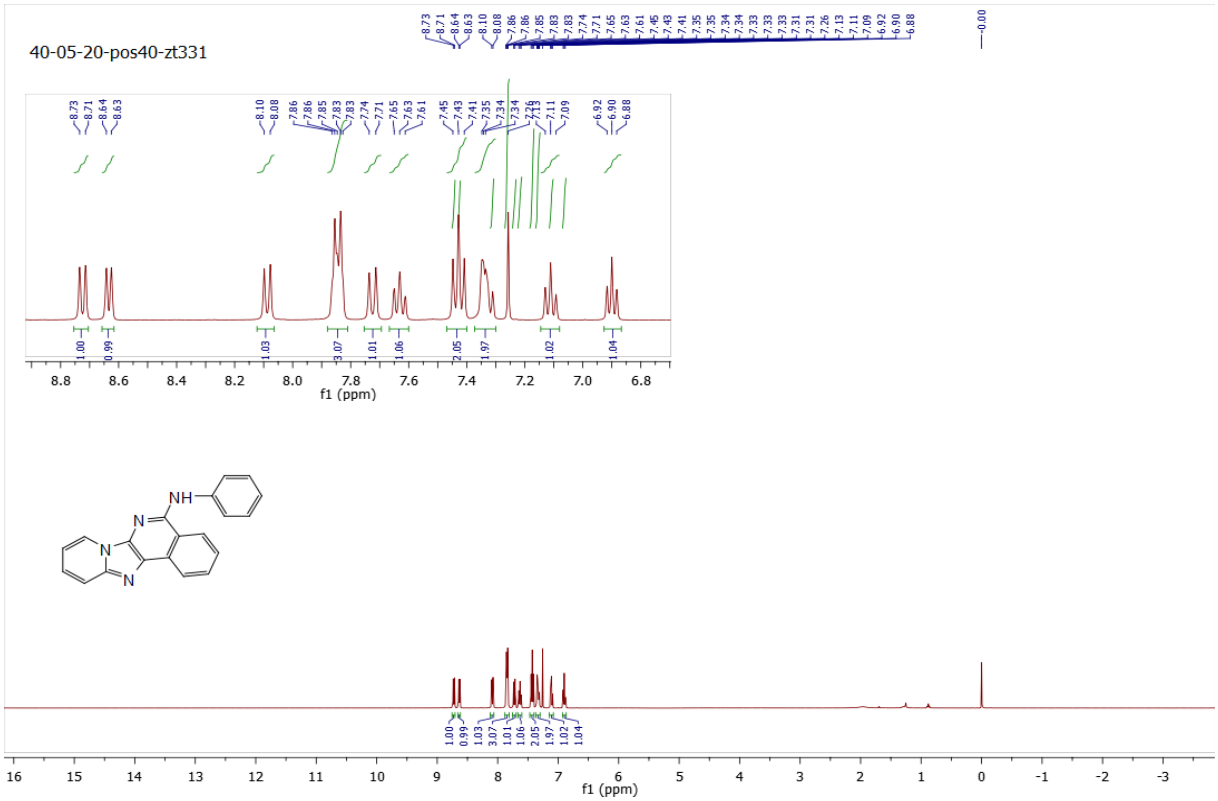


^{13}C NMR (101 MHz, $CDCl_3$)

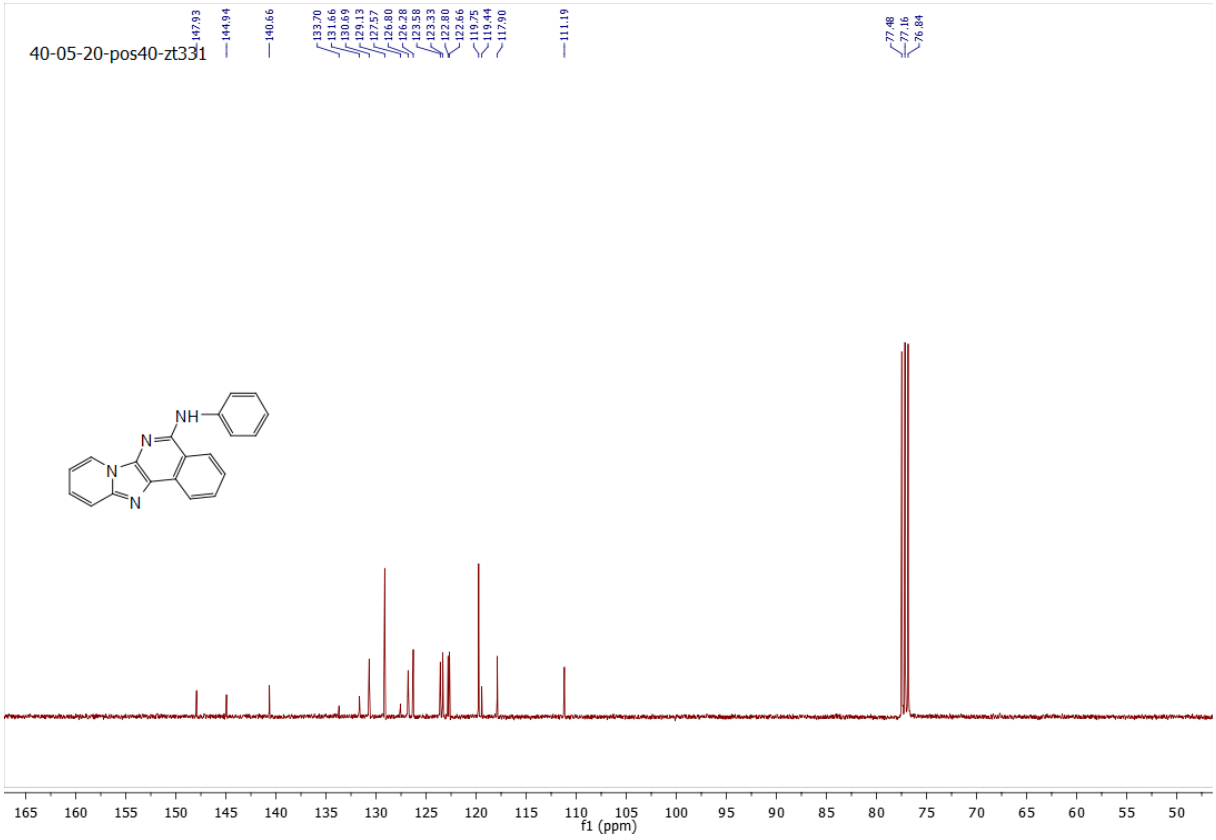


***N*-Phenylpyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (5a)**

^{1}H NMR (400.15 MHz, $CDCl_3$)

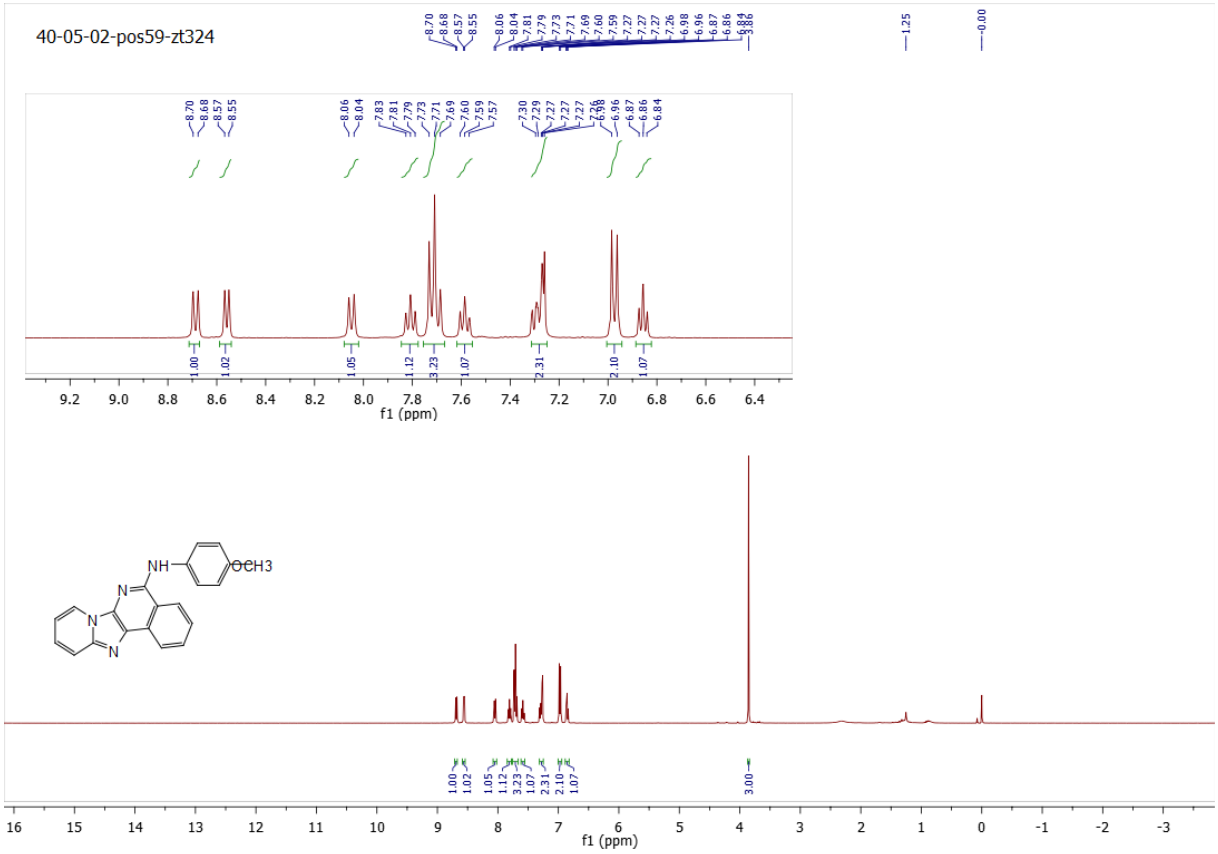


^{13}C NMR (101MHz, $CDCl_3$)

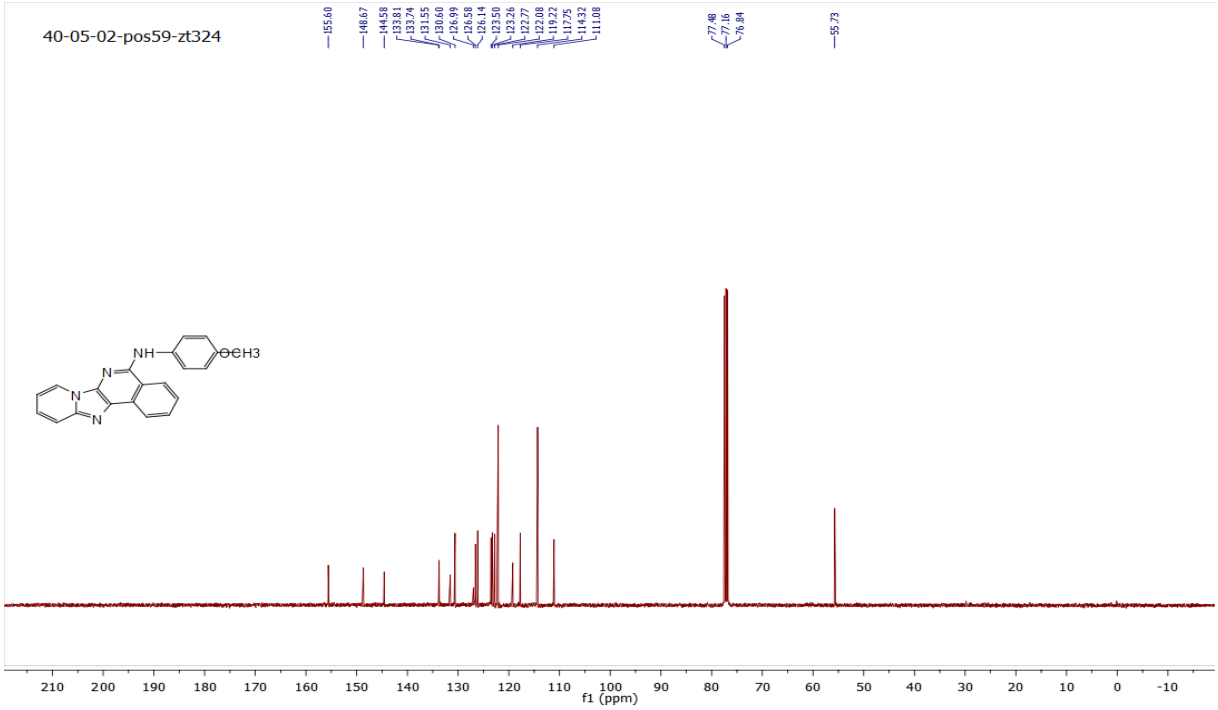


***N*-(4-Methoxyphenyl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (5b)**

^{1}H NMR (400.13 MHz, $CDCl_3$)

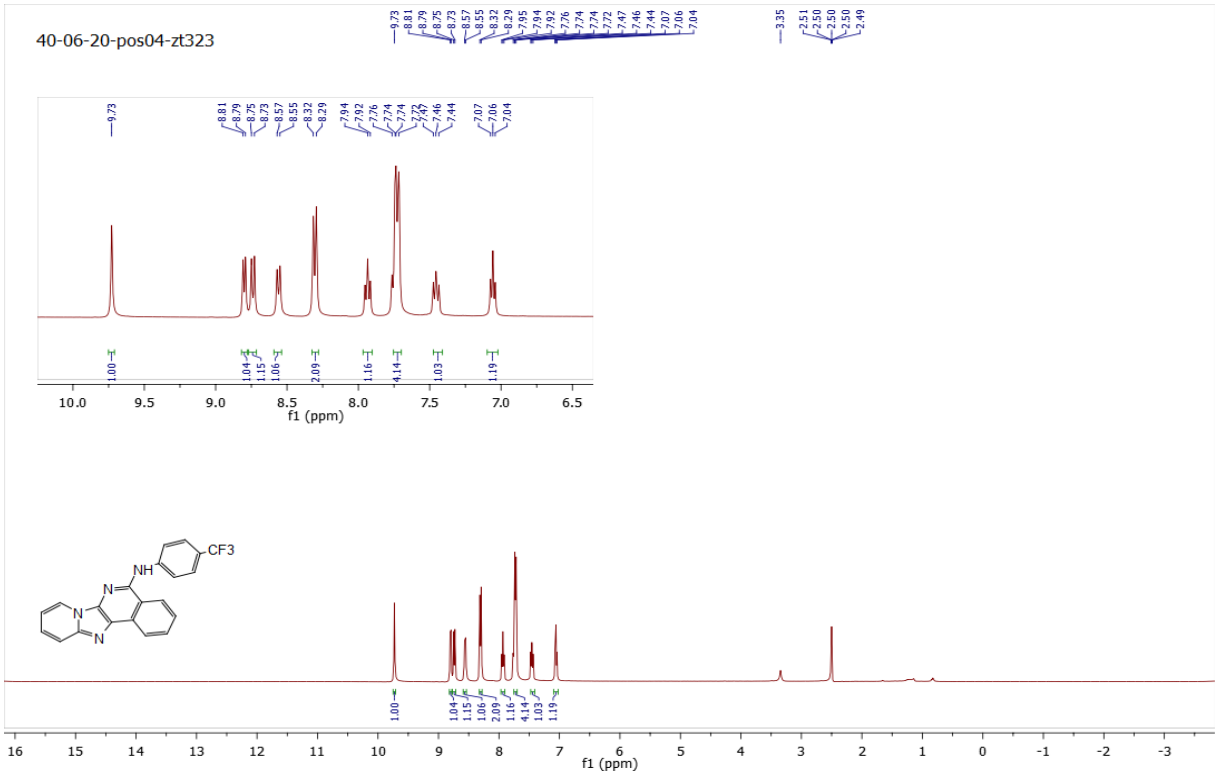


^{13}C NMR (101MHz, $CDCl_3$)

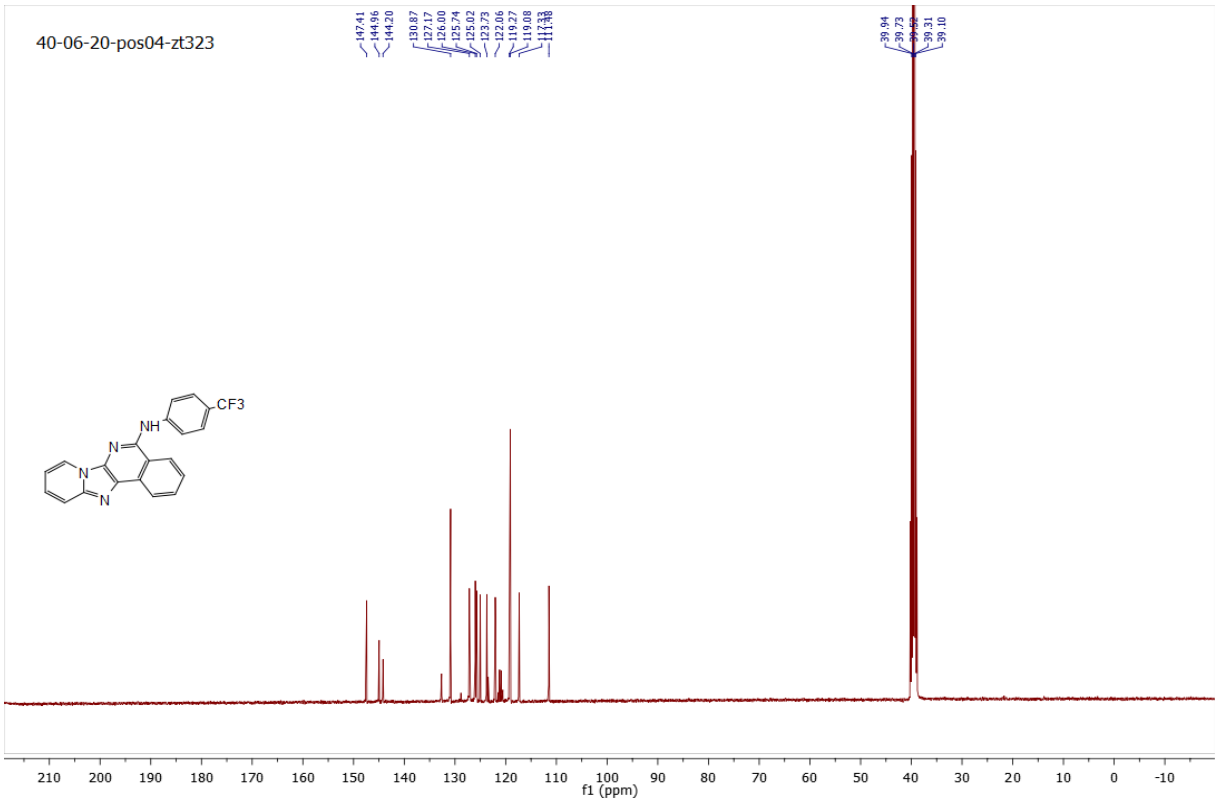


N-(4-(Trifluoromethyl)phenyl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinoline-5-amine (5c)

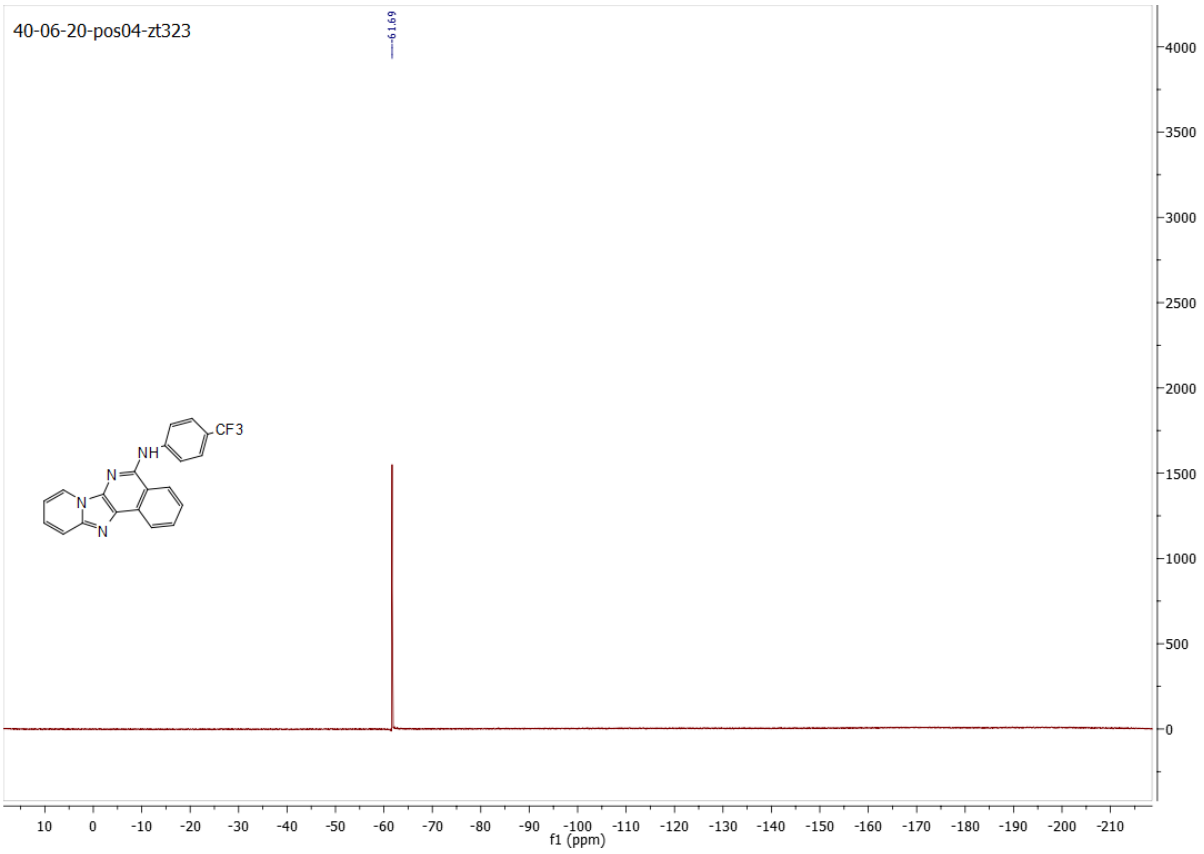
^{1}H NMR (400.13 MHz, DMSO-*d6*)



^{13}C NMR (101 MHz, DMSO-*d6*)

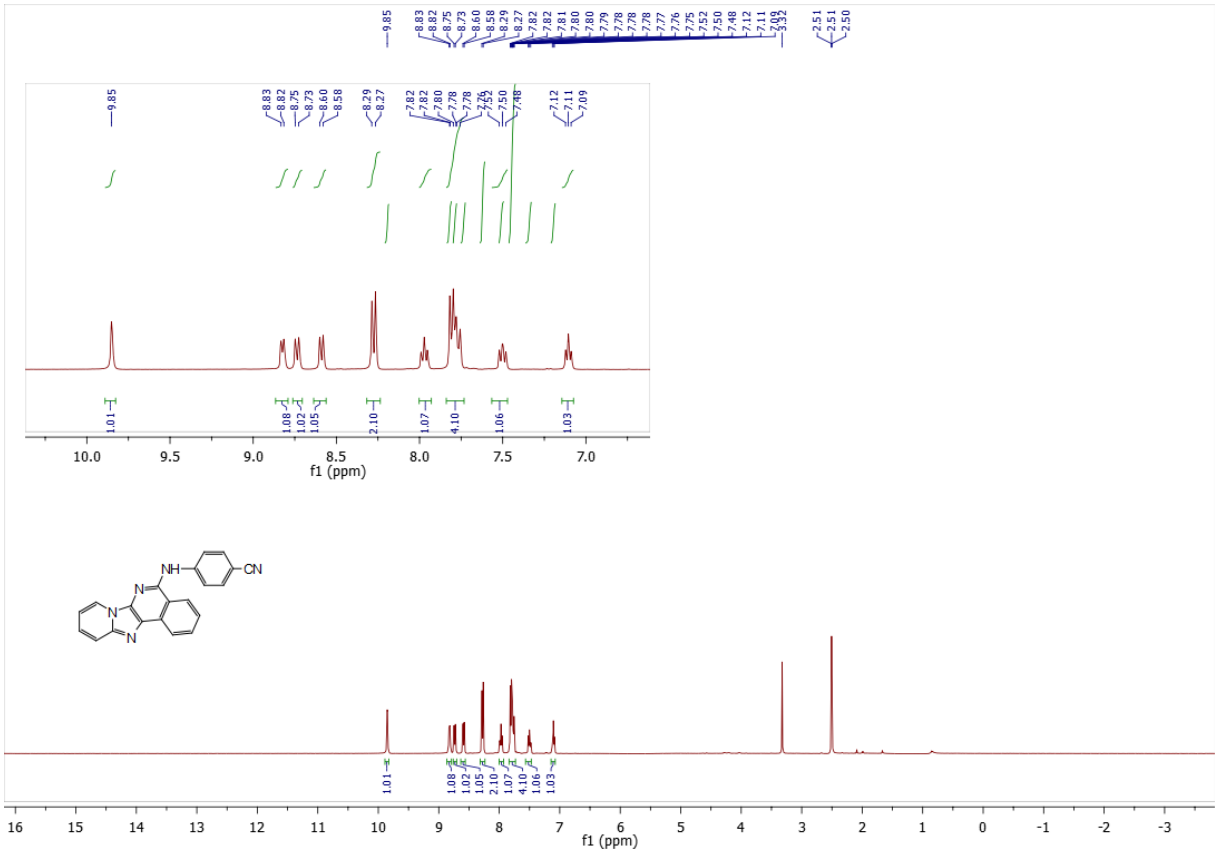


^{19} F NMR (376 MHz, DMSO-*d6*)

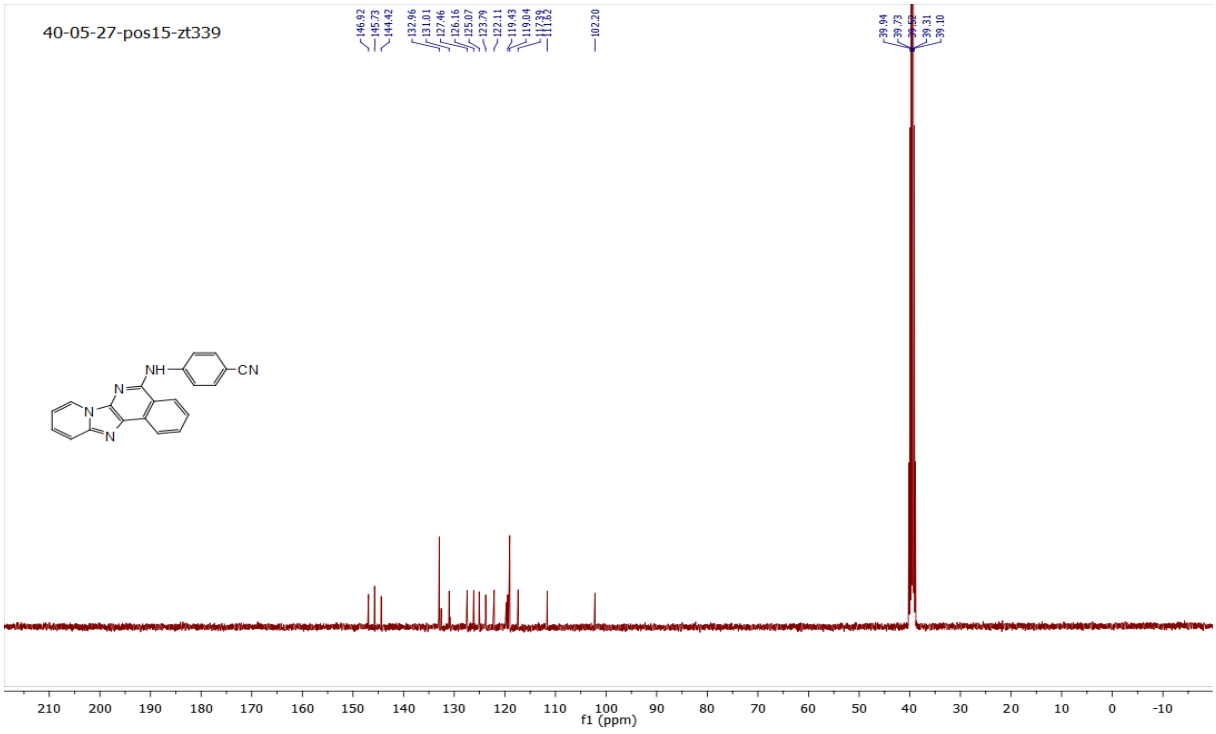


4-(Pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-ylamino)benzonitrile (5d)

^{1}H NMR (400.13 MHz, DMSO-d_6)

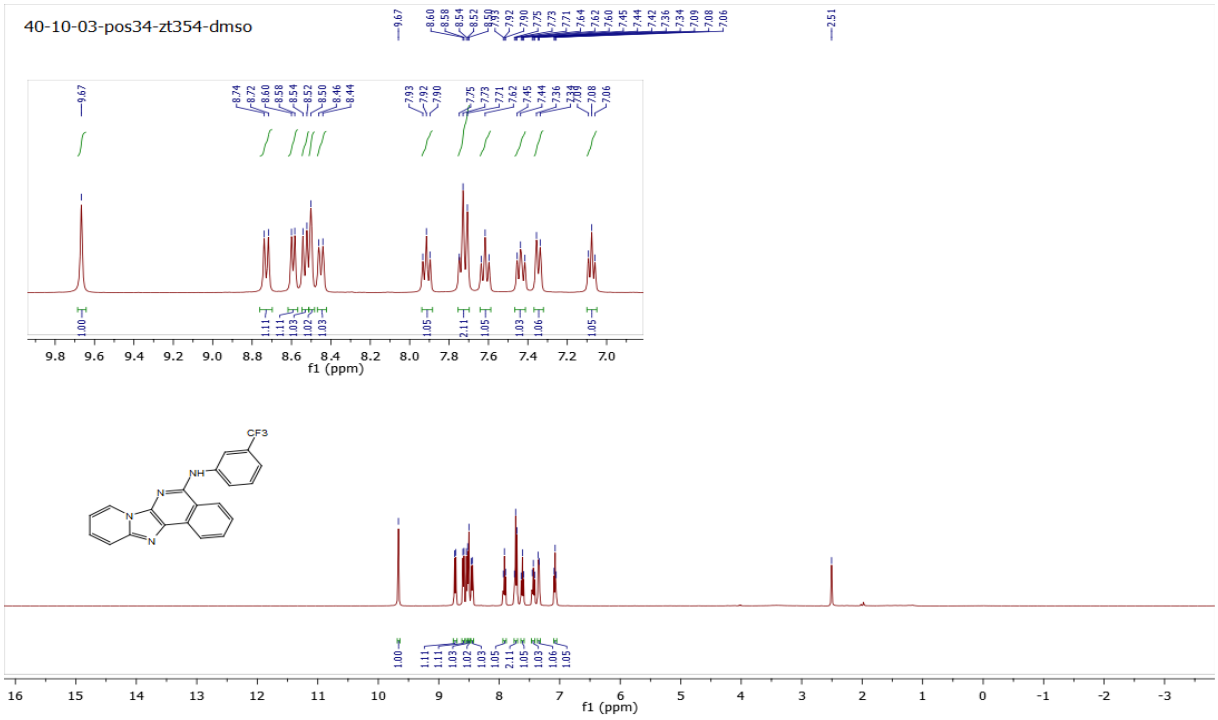


^{13} C NMR (101 MHz, DMSO-d_6)

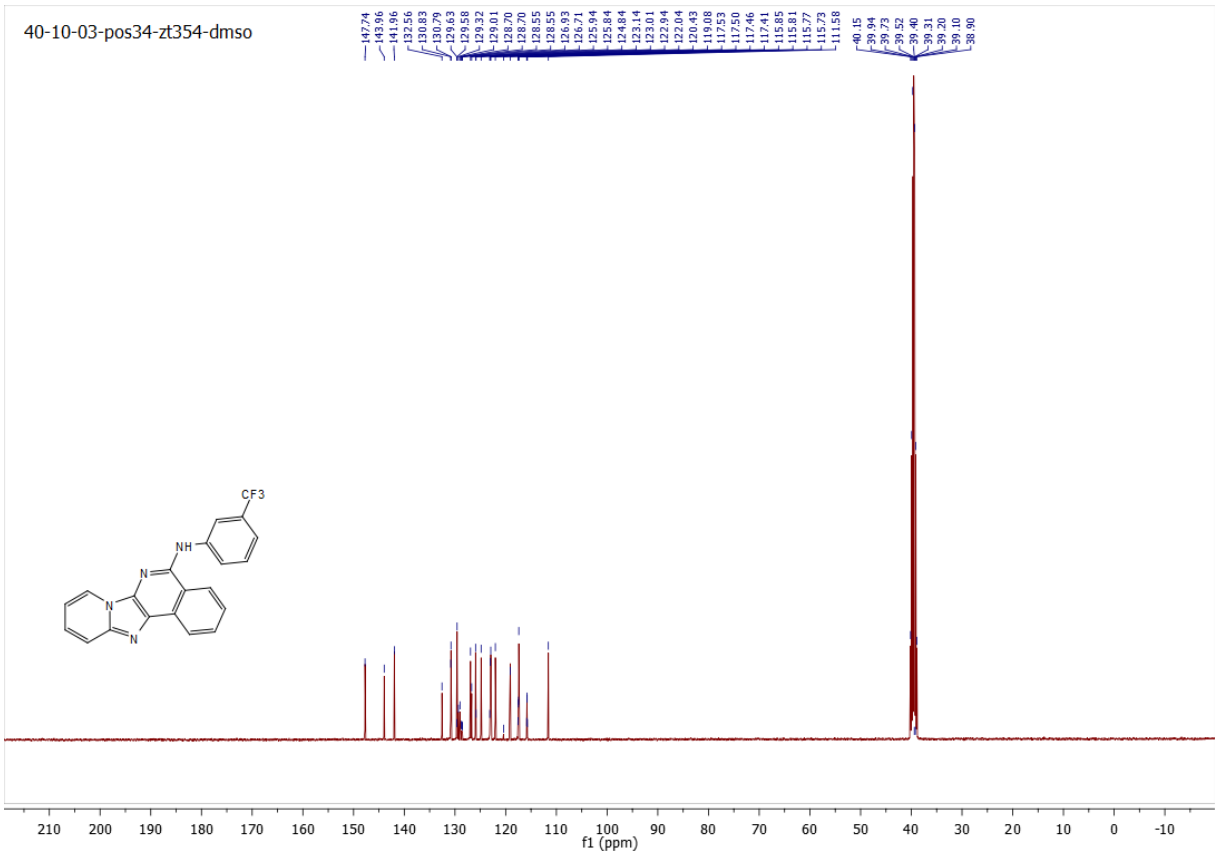


***N*-(3-(Trifluoromethyl)phenyl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinoline-5-amine (5e)**

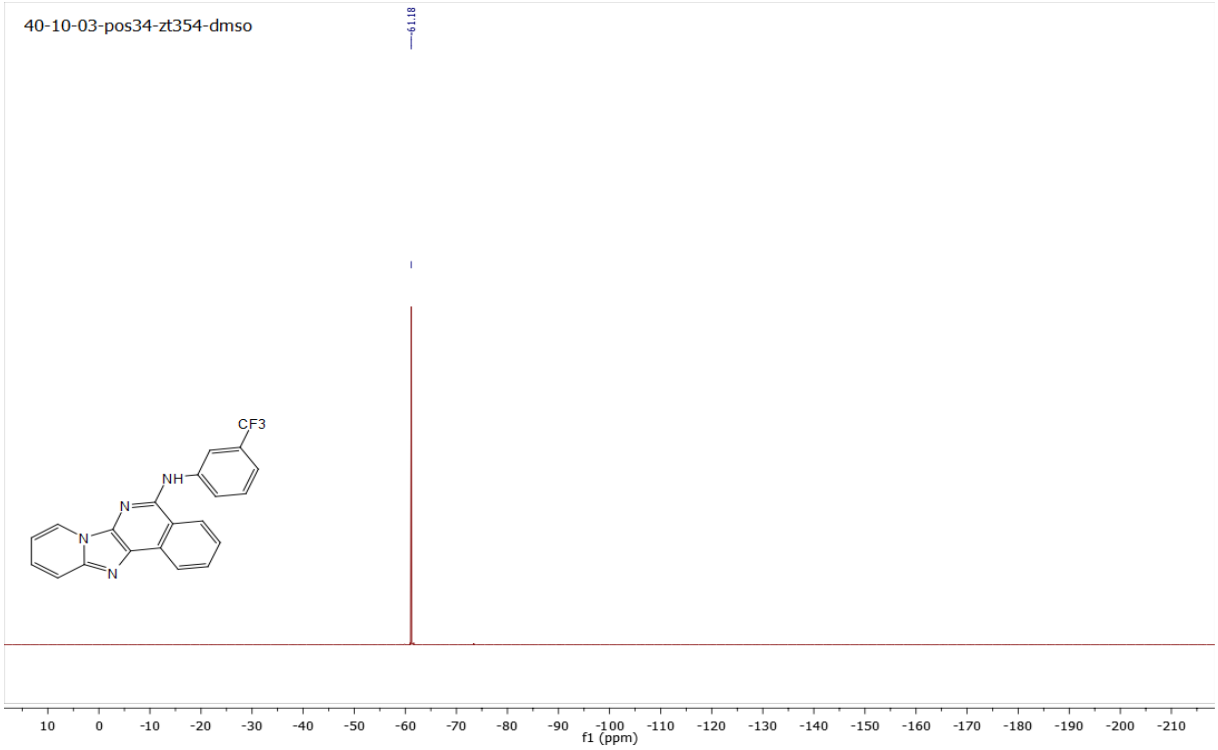
^{1}H NMR (400.13 MHz, DMSO-*d6*)



^{13}C NMR (101MHz, DMSO-*d6*)

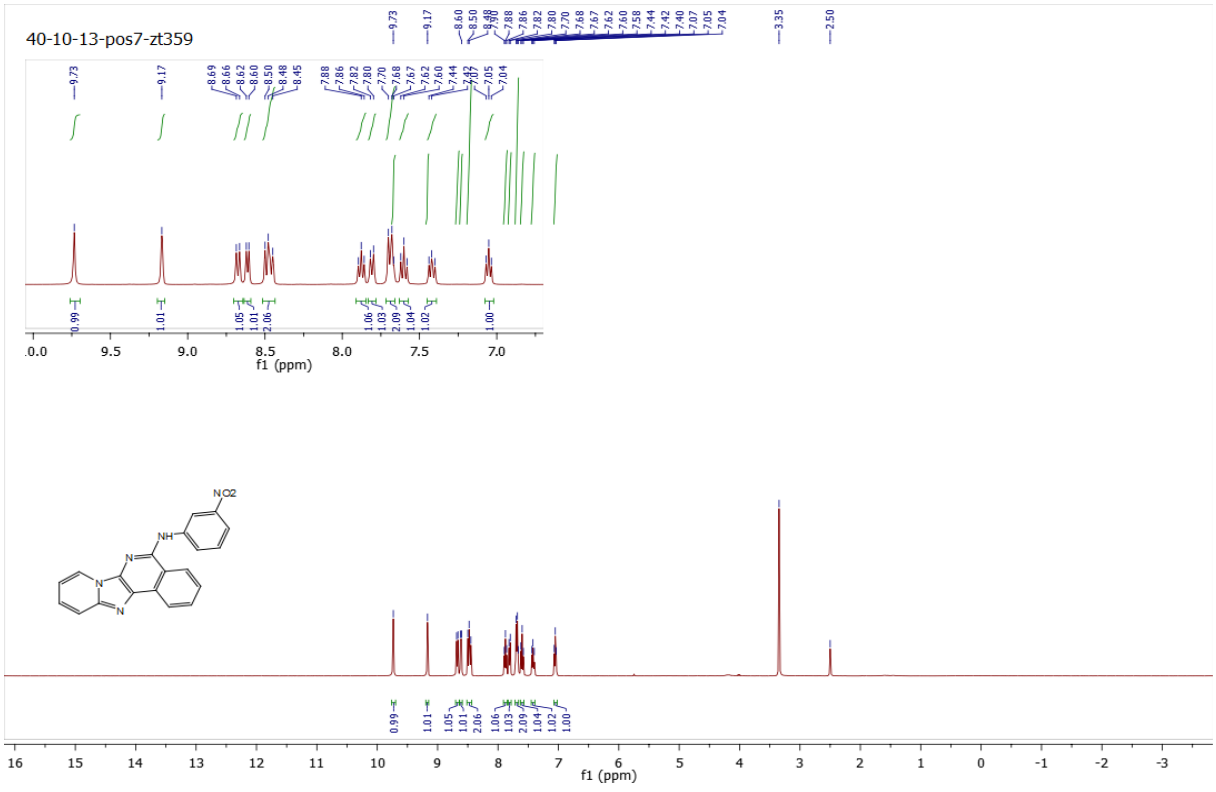


^{19} F NMR (376 MHz, DMSO-*d6*)

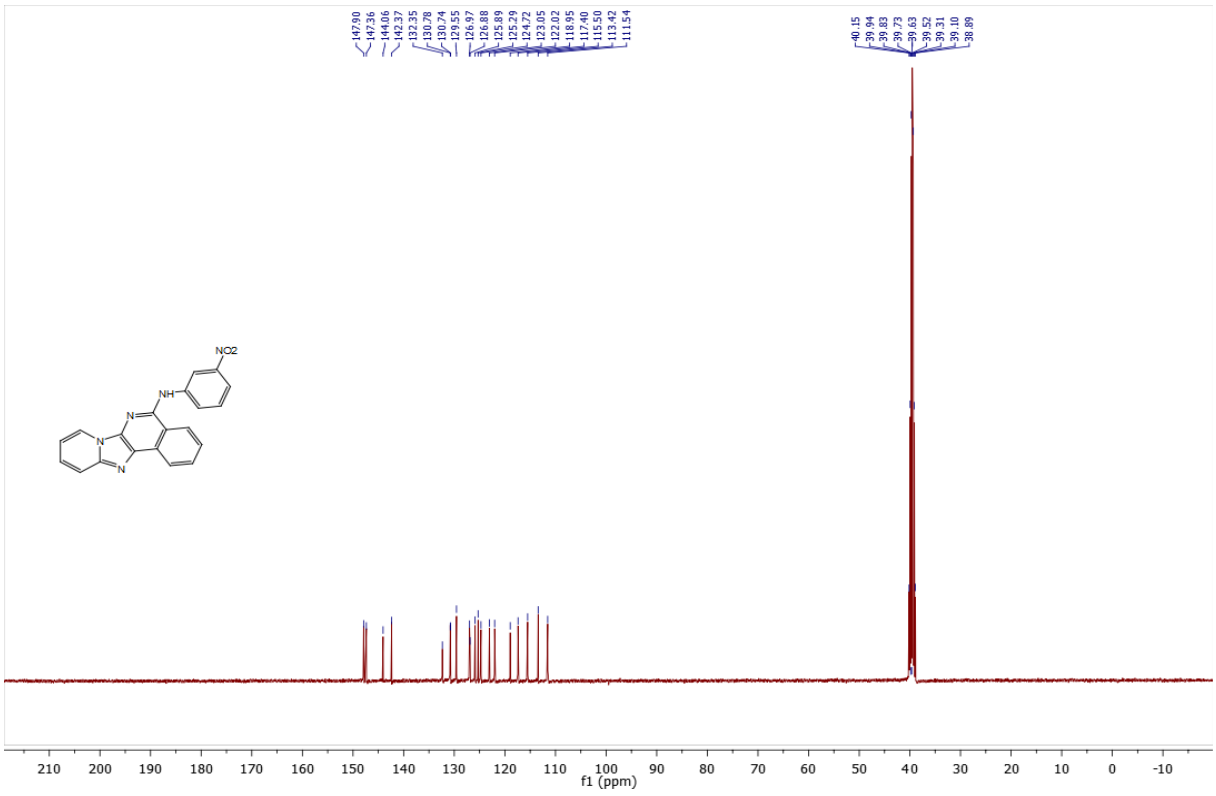


***N*-(3-Nitrophenyl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (5f)**

^{1}H NMR (400.13 MHz, DMSO-*d6*)

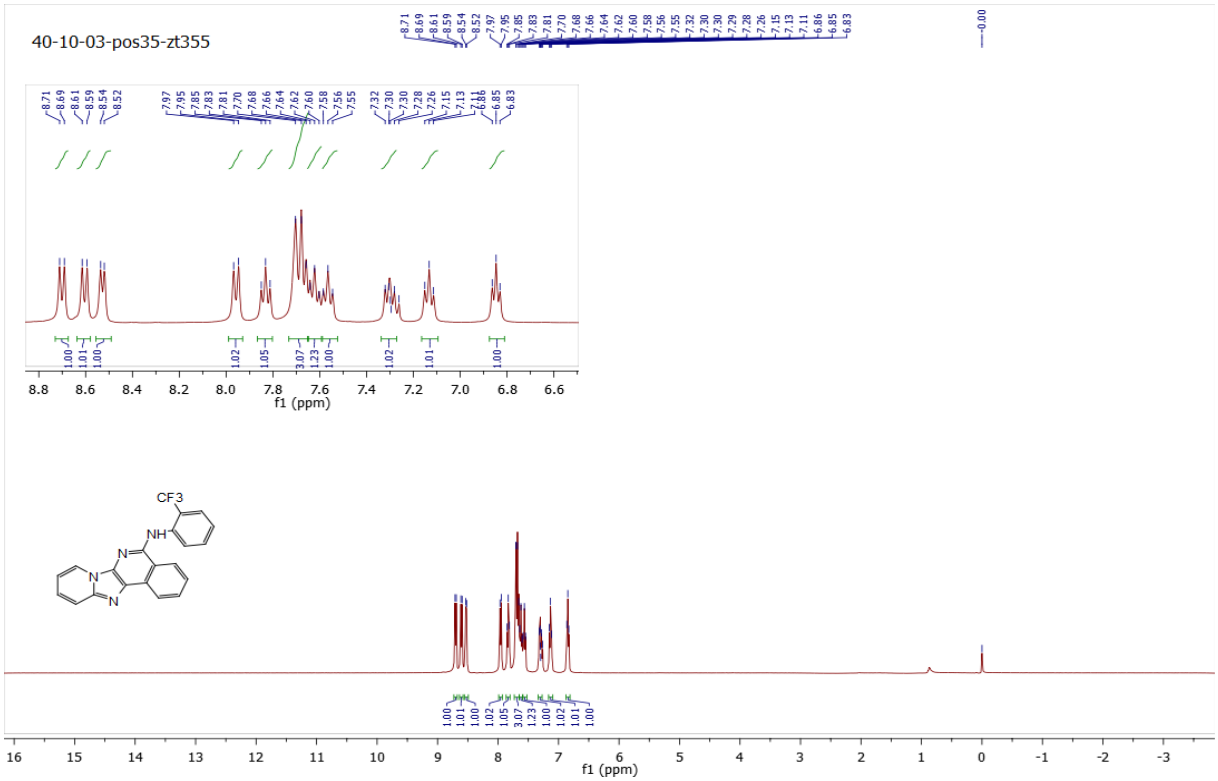


^{13}C NMR (101 MHz, DMSO-*d6*)

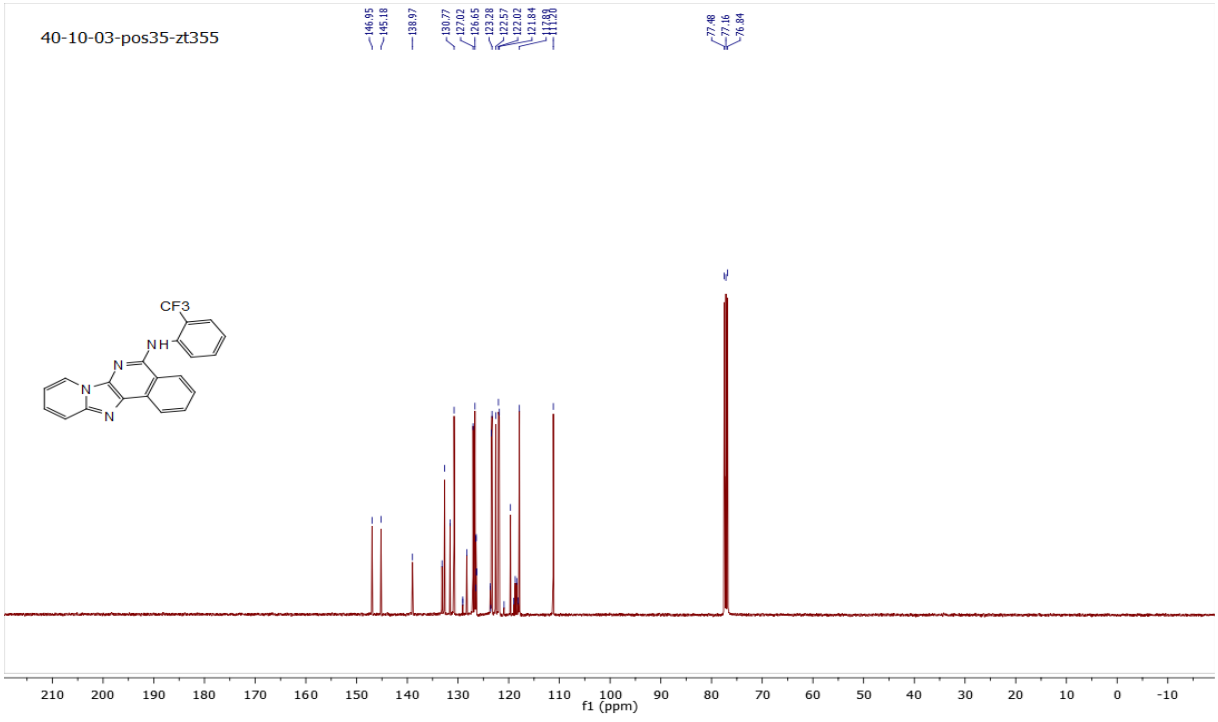


***N*-(2-(Trifluoromethyl)phenyl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinoline-5-amine (5g)**

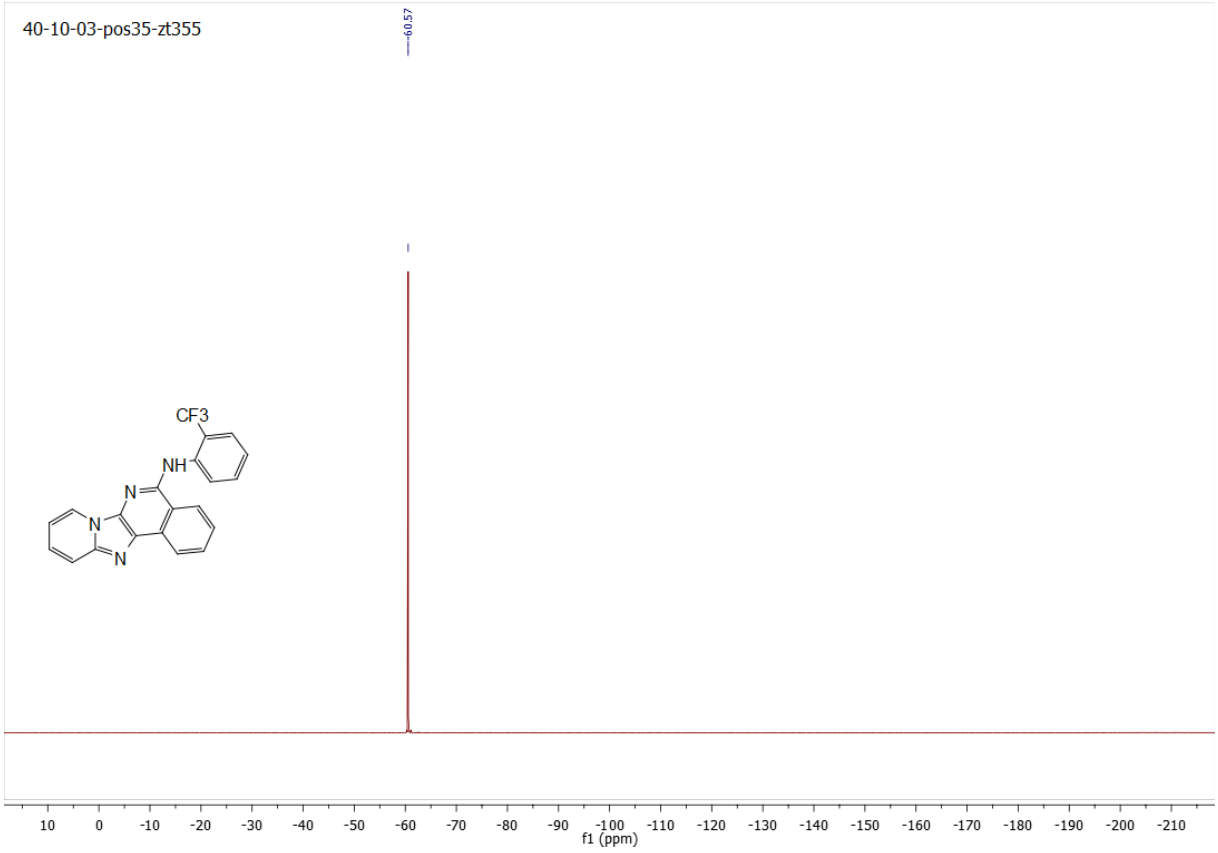
^{1}H NMR (400.13 MHz, $CDCl_3$)



^{13}C NMR (101MHz, $CDCl_3$)

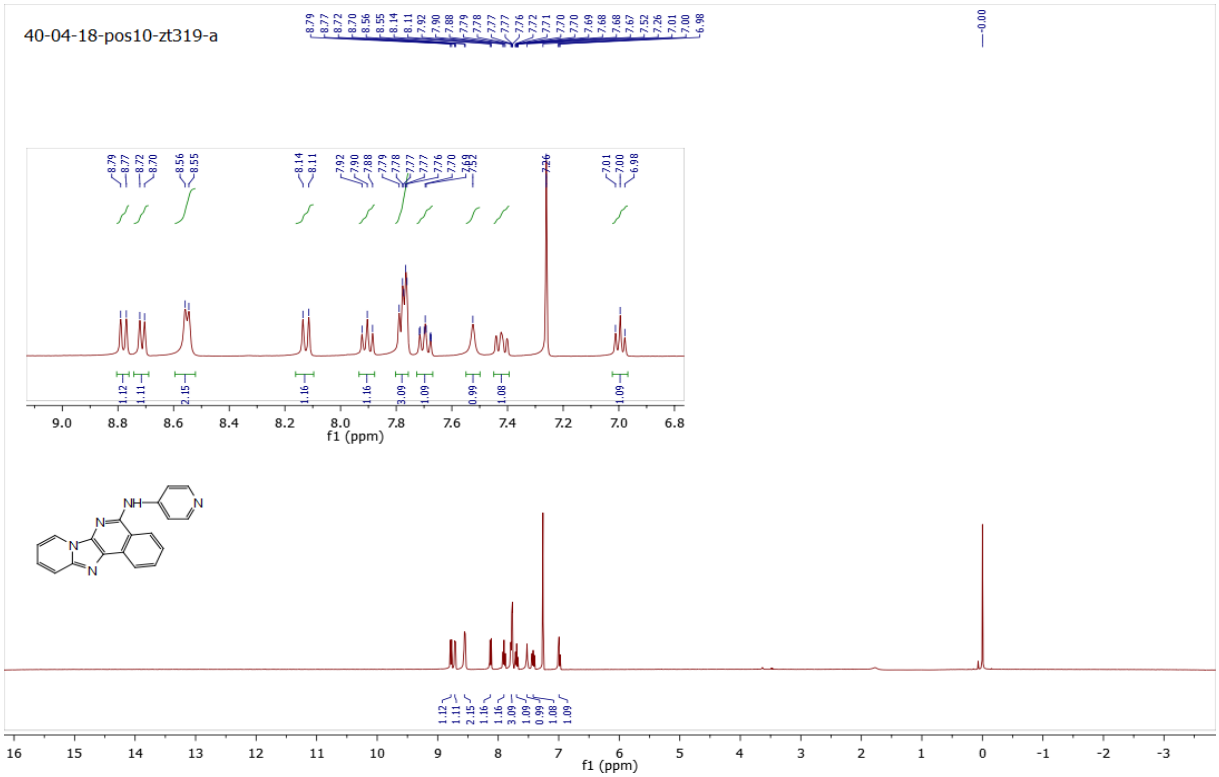


^{19} F NMR (376 MHz, $CDCl_3$)

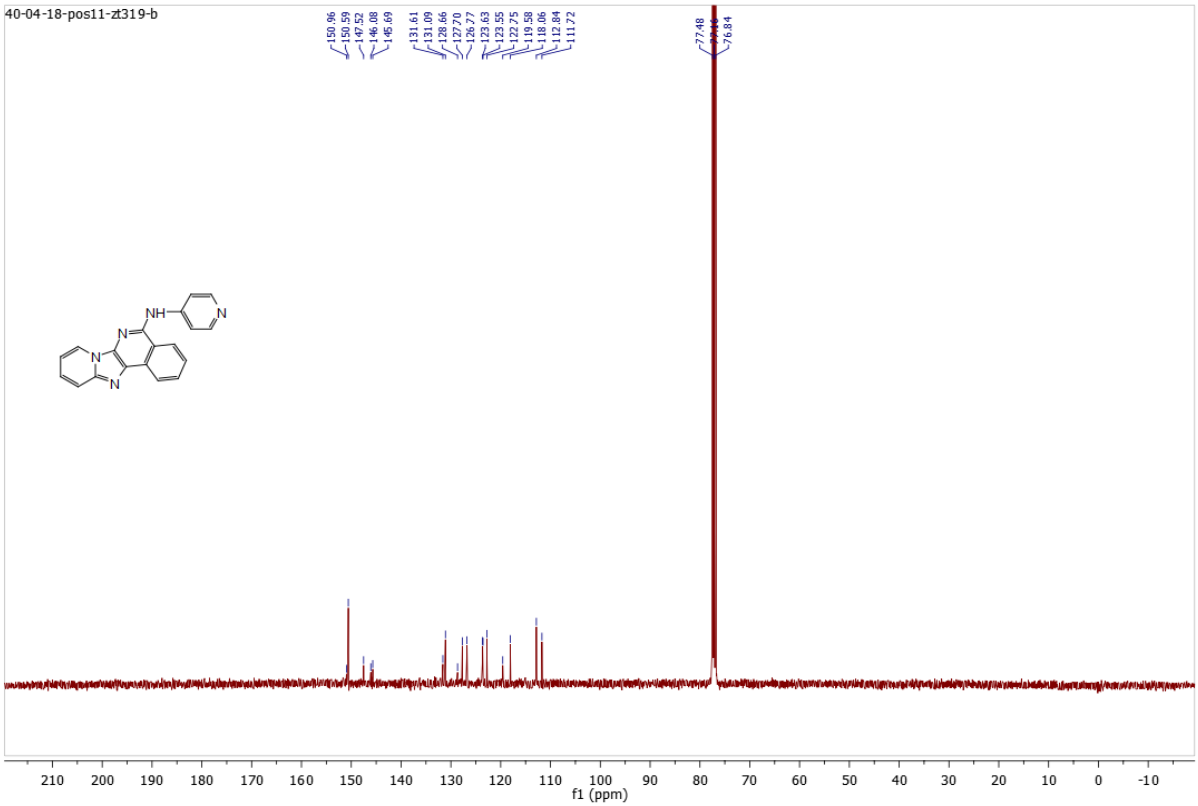


***N*-(Pyridin-4-yl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (5h)**

^{1}H NMR (400.13 MHz, $CDCl_3$)

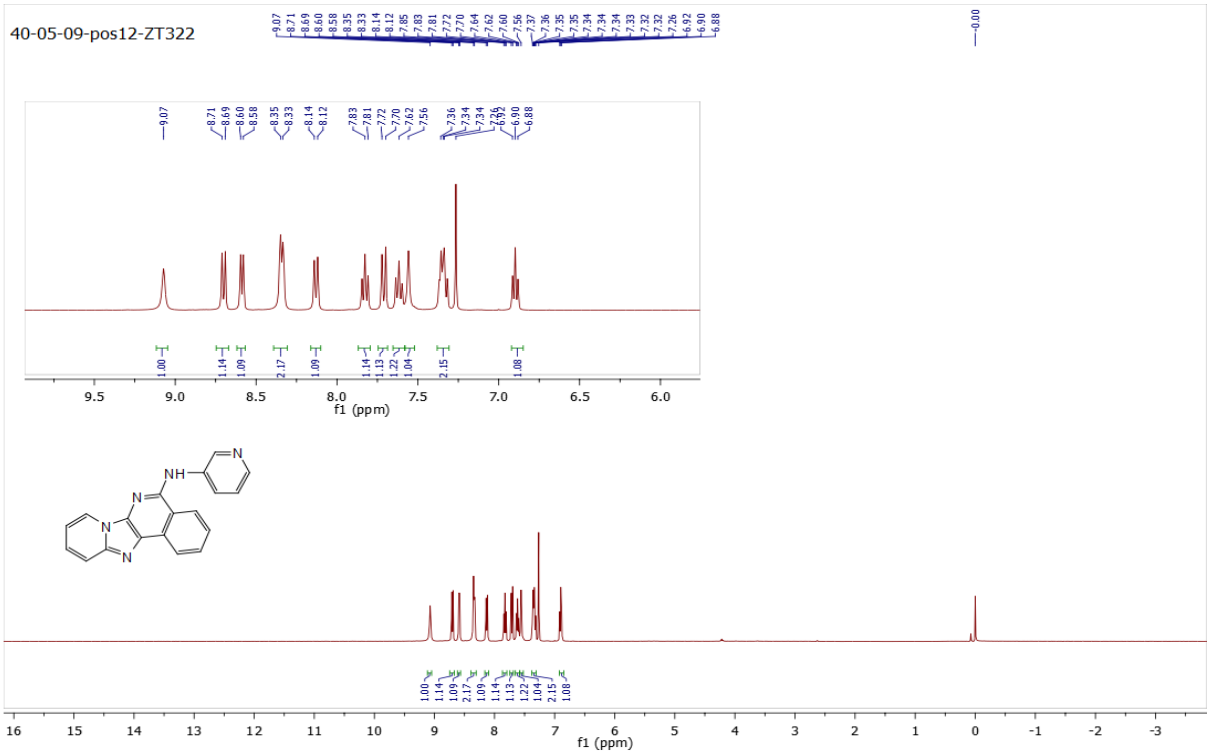


^{13}C NMR (101 MHz, $CDCl_3$)

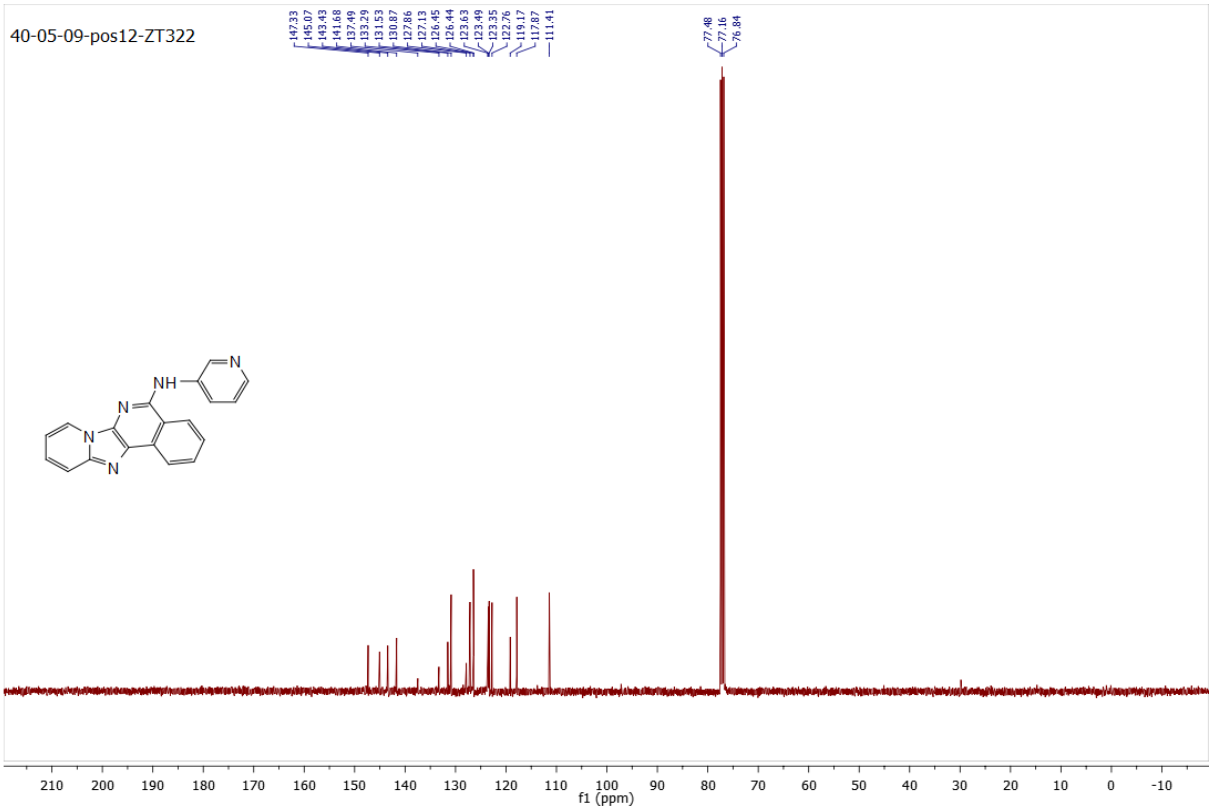


***N*-(Pyridin-3-yl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (5i)**

^{1}H NMR (400.13 MHz, $CDCl_3$)

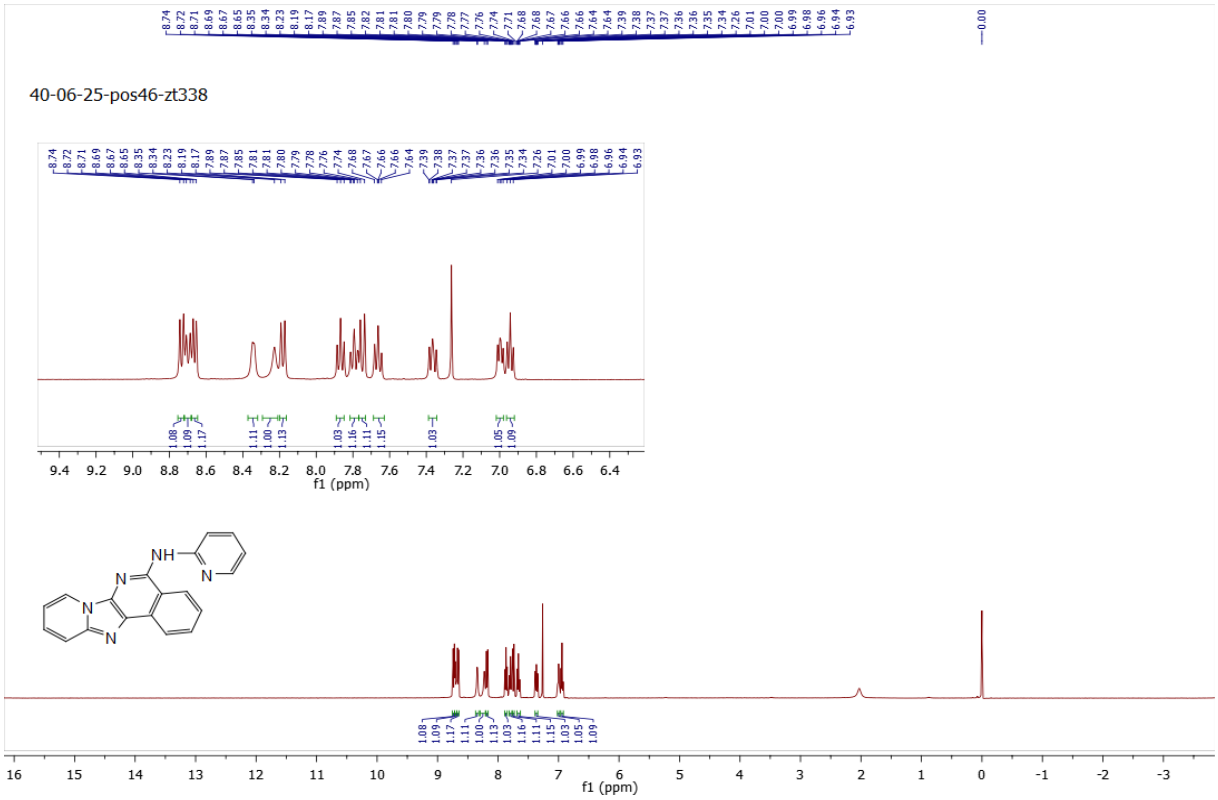


^{13}C NMR (101 MHz, $CDCl_3$)

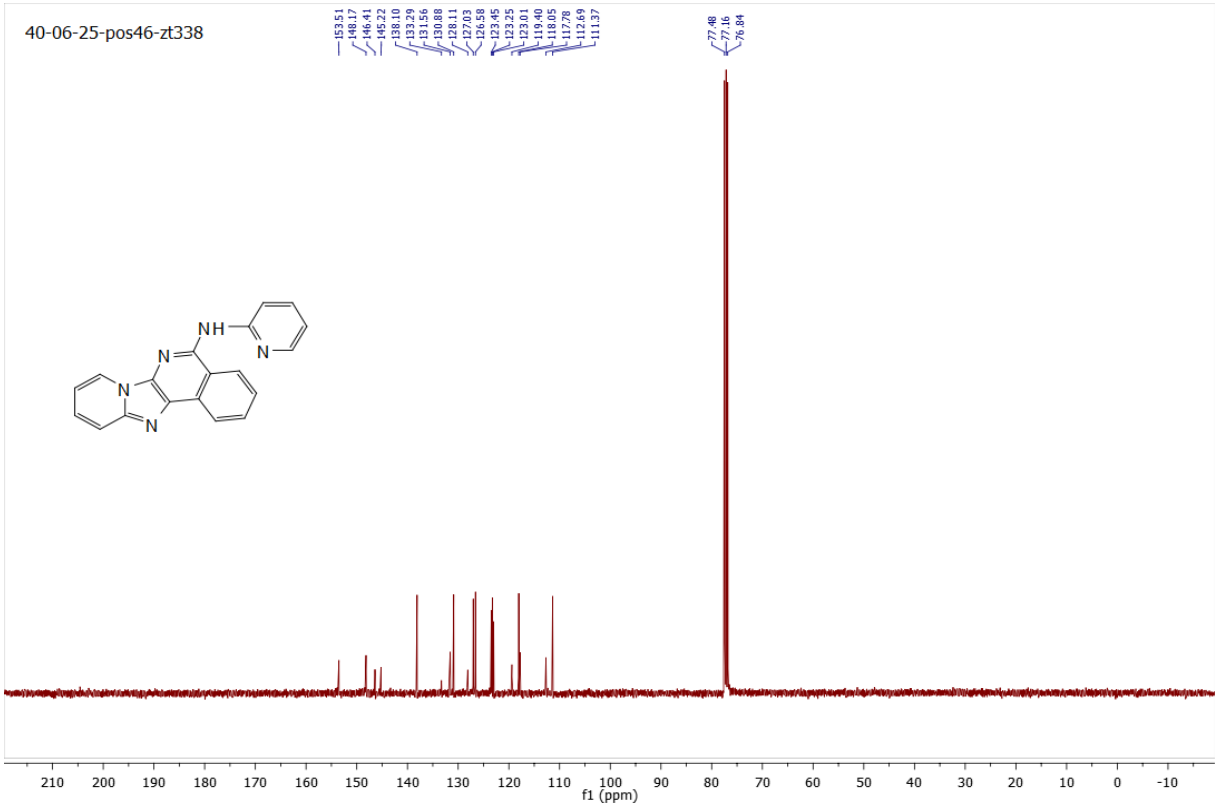


***N*-(Pyridin-2-yl)pyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-amine (5j)**

^{1}H NMR (400.13 MHz, $CDCl_3$)

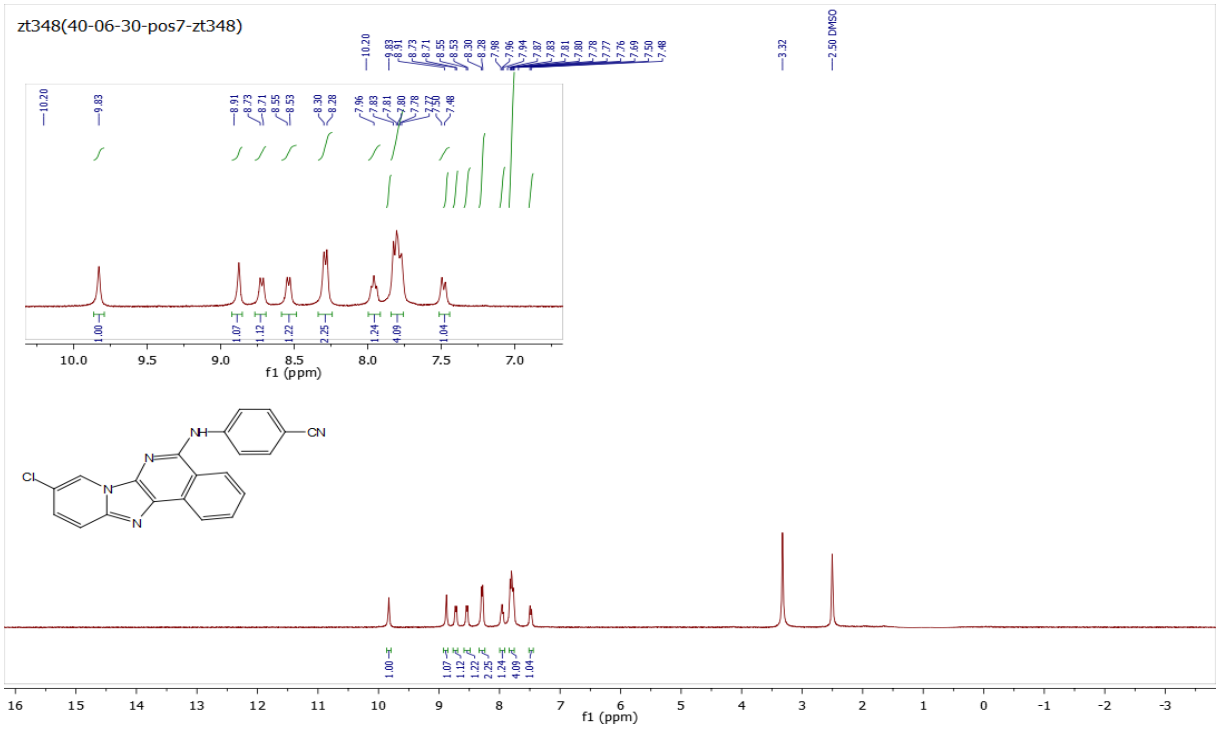


^{13}C NMR (101 MHz, $CDCl_3$)

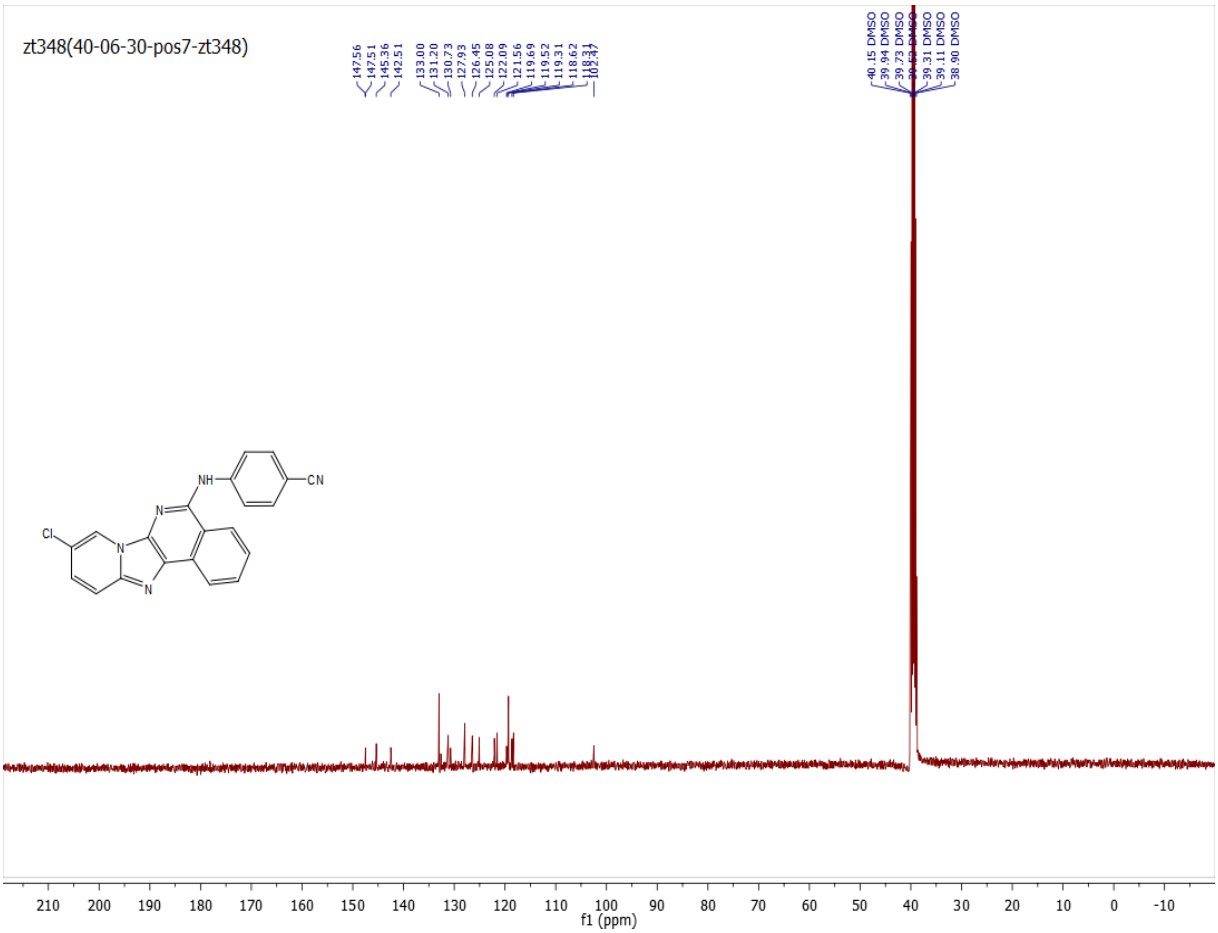


4-((9-Chloropyrido[2',1':2,3]imidazo[4,5-*c*]isoquinolin-5-yl)amino)benzonitrile (5m)

^{1}H NMR (400.13 MHz, DMSO-d_6)

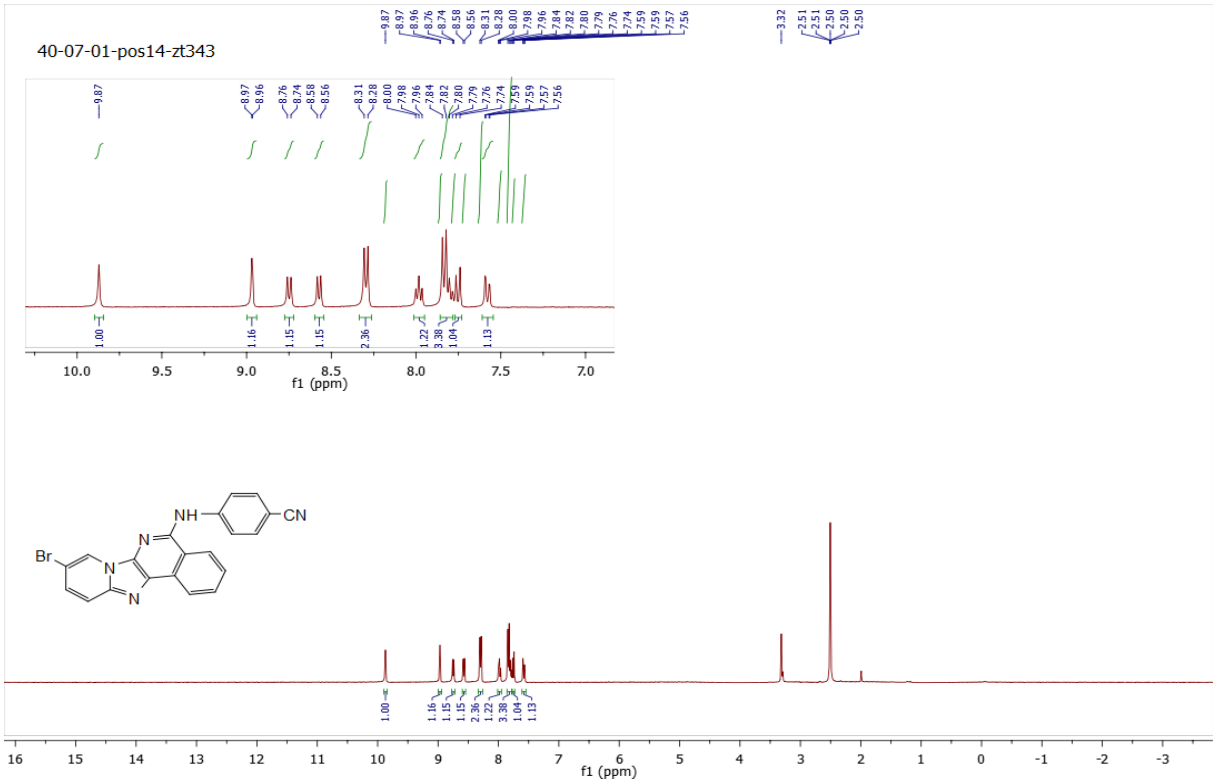


^{13}C NMR (101 MHz, DMSO-d_6)

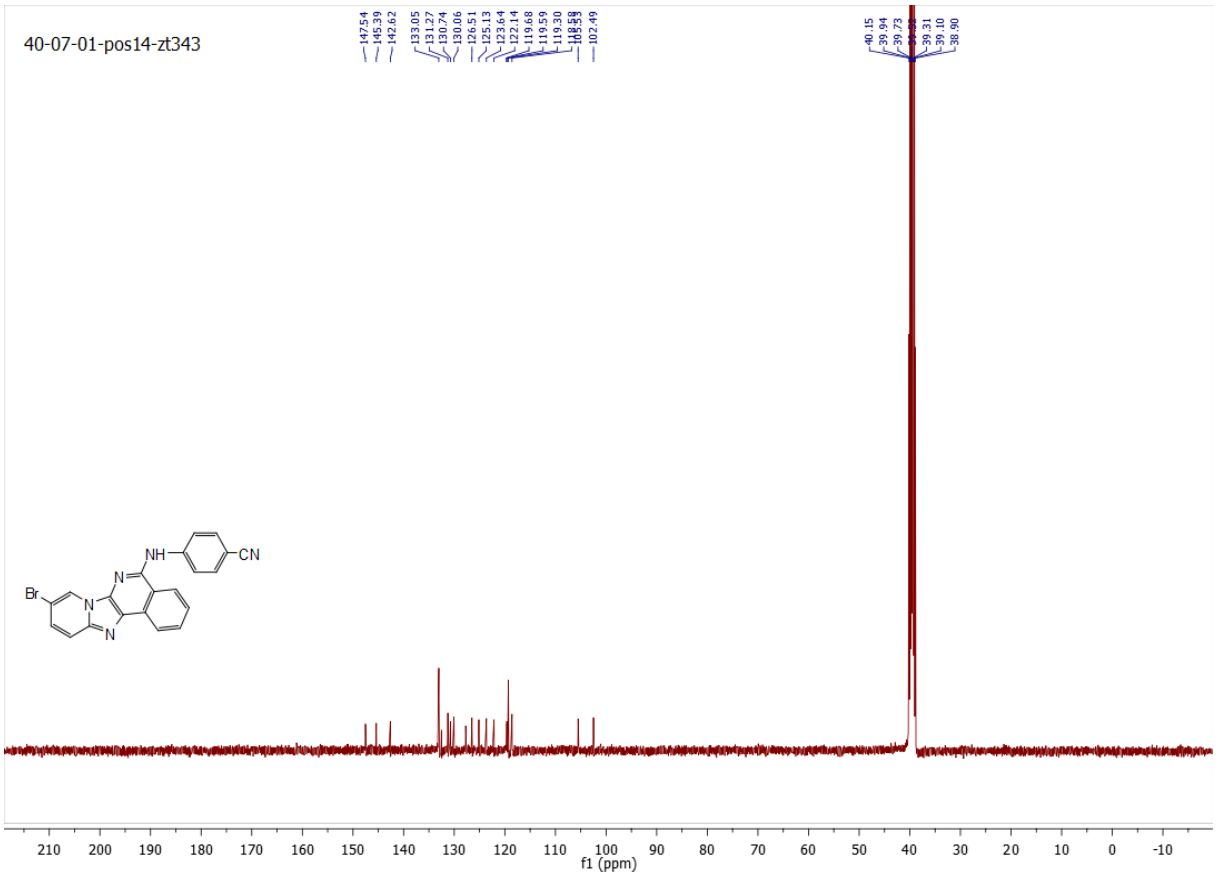


4-((9-Bromopyrido[2',1':2,3]imidazo[4,5-c]isoquinolin-5-yl)amino)benzonitrile (5n)

^{1}H NMR (400.13 MHz, DMSO-d_6)

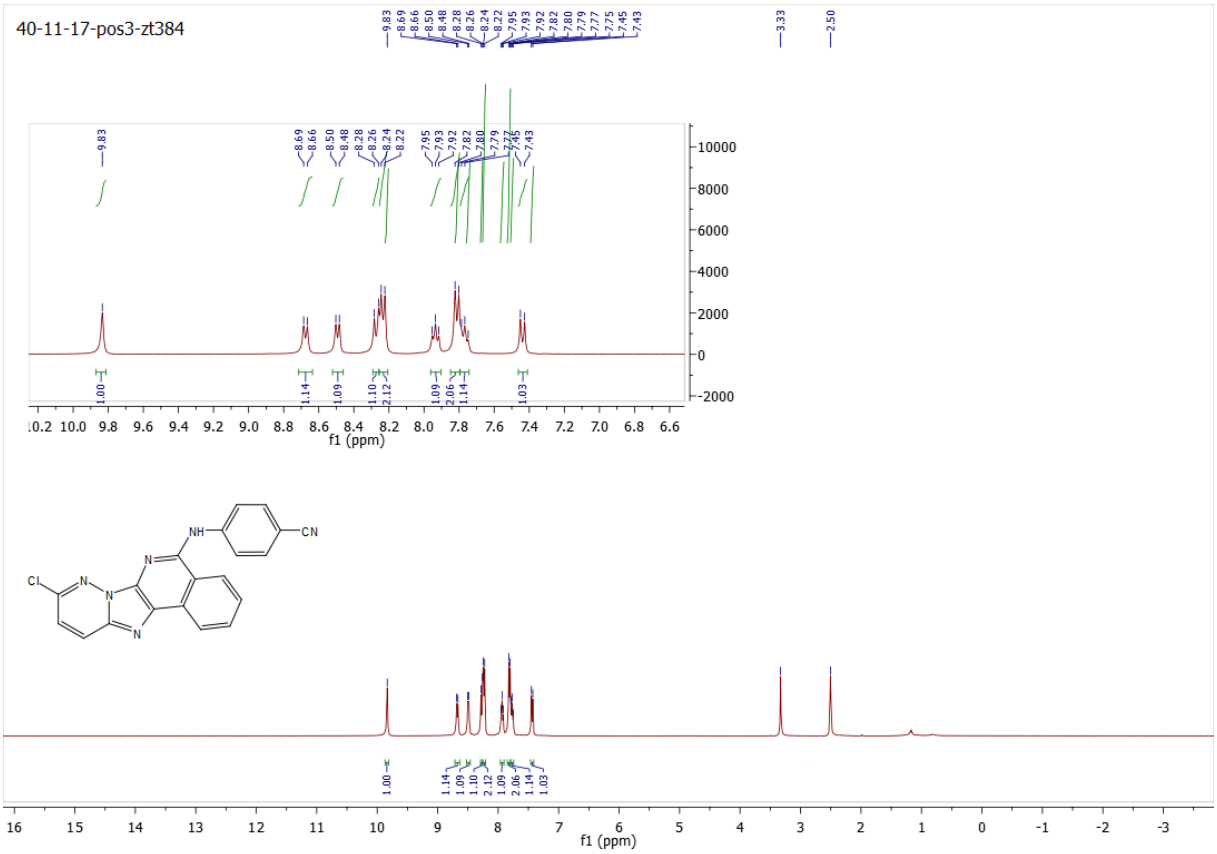


^{13}C NMR (101MHz, DMSO-d_6)

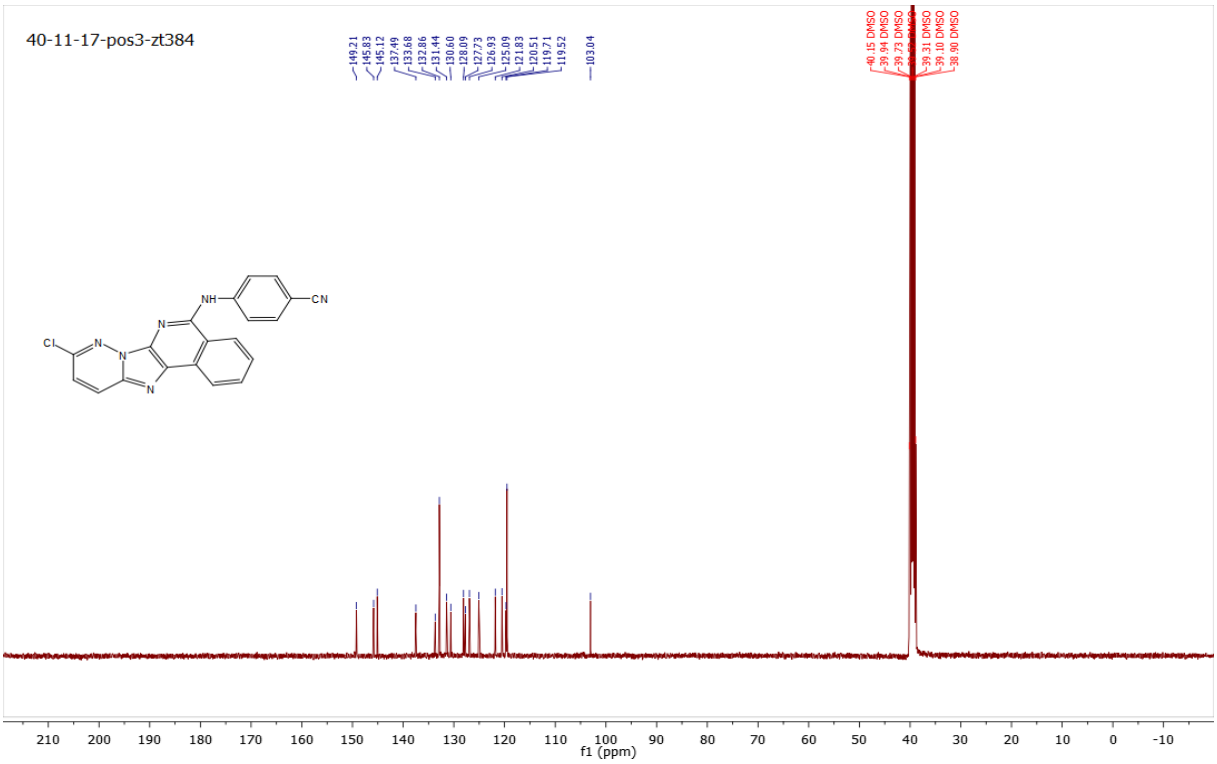


4-((9-Chloropyridazino[6',1':2,3]imidazo[4,5-*c*]isoquinolin-5-yl)amino)benzonitrile (5o).

^{1}H NMR (400.13 MHz, DMSO-d_6)



^{13}C NMR (101 MHz, DMSO-d_6)



Crystallographic data collections and structural determinations.

Crystallographic studies of compound **1e** and **5c** were performed at room temperature (296 K) on a Bruker-Nonius Kappa-CCD diffractometer with Mo Kα radiation (0.71073 Å). Only small, twinned and poor quality crystals were obtained, so that no significant reflection could be detected over θ = 19°. Unit-cell determination and refinement as well as data collection were carried out usinge Collect[1] and Dirax[2] programs. The data reduction data was performed using EvalCCD program[3].

The structure determination, found by direct methods, and the refinement of atomic parameters, based on full-matrix least-squares on F^2, were performed using the SHELX-2014 programs[1] within the WINGX package[3].

Supplementary crystallographic data can be found in the CCDC deposit (CCDC 1046891-1046892), and obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif/.

- *COLLECT*, Bruker AXS BV, 1997-2004.
- Dirax/lsq, Duisenberg & Schreurs, 1989-2000.
- Sheldrick, G. M. *Programs for Crystal Structure Analysis*; University of Göttingen: Göttingen, Germany, 2014
- WinGX, Farrugia, J. Appl. Cryst. 45, 849-854, 2012.

Table 1. Crystal data and structure refinement for table1.

Identification code	**Compound 1e**	**Compound 5c**
Empirical formula	C_{15} H_{11} N_5 O_2	C_{23} H_{14} F_3 N_4 O
Formula weight /g.mol^{-1}	293.29	419.38
Temperature / K	296(2)	296(2)
Wavelength / Å	0.71073	0.71073
Crystal system	Triclinic	Monoclinic
Space group	P -1	C 2/c
Unit cell dimensions	a = 6.8520(10) Å; α= 102.68(4)° b = 9.607(5) Å; β= 93.21(3)° c = 10.857(7) Å; γ = 92.50(3)°	a = 43.065(3) Å; α= 90° b = 5.4072(11) Å; β= 91.73(2)° c = 17.347(8) Å; γ = 90°
Volume / Å^3	695.0(6)	4038(2)
Z	2	8
Density (calculated)/ Mg/m^3	1.401	1.380
Absorption coefficient / mm^{-1}	0.099	0.107
F(000)	304	1720
Crystal size / mm	0.25 x 0.15 x 0.10	0.20 x 0.15 x 0.03
Theta range for data collection	2.982 to 26.690°.	2.349 to 26.370°.
Index ranges	-8<=h<=8, -12<=k<=11, -13<=l<=11	-53<=h<=53, -6<=k<=6, 0<=l<=21
Independent reflections	1872 [R(int) = 0.071]	4120 [R(int) = 0.1316]
Data / restraints / parameters	1872 / 6 / 212	4120 / 15 / 246

Goodness-of-fit on F^2	1.067	1.221
Final R indices [I>2sigma(I)]	R1 = 0.1313, wR2 = 0.3112	R1 = 0.1407, wR2 = 0.3764
R indices (all data)	R1 = 0.2353, wR2 = 0.3824	R1 = 0.3147, wR2 = 0.4492
Largest diff. peak and hole / e.$Å^{-3}$	0.430 / -0.314	0.921 / -0.746
CCDC	1046891	1046892