Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Para-Selective Radical Alkylation of Pyridines with Diacyl Peroxides and Peresters

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Table of Contents

1. General information

All air- or moisture-sensitive reactions and manipulations were carried out using standard Schlenk techniques under an argon atmosphere and magnetic induced stirring. Solvents were removed by rotary evaporation at 20–40 °C at an appropriate pressure.

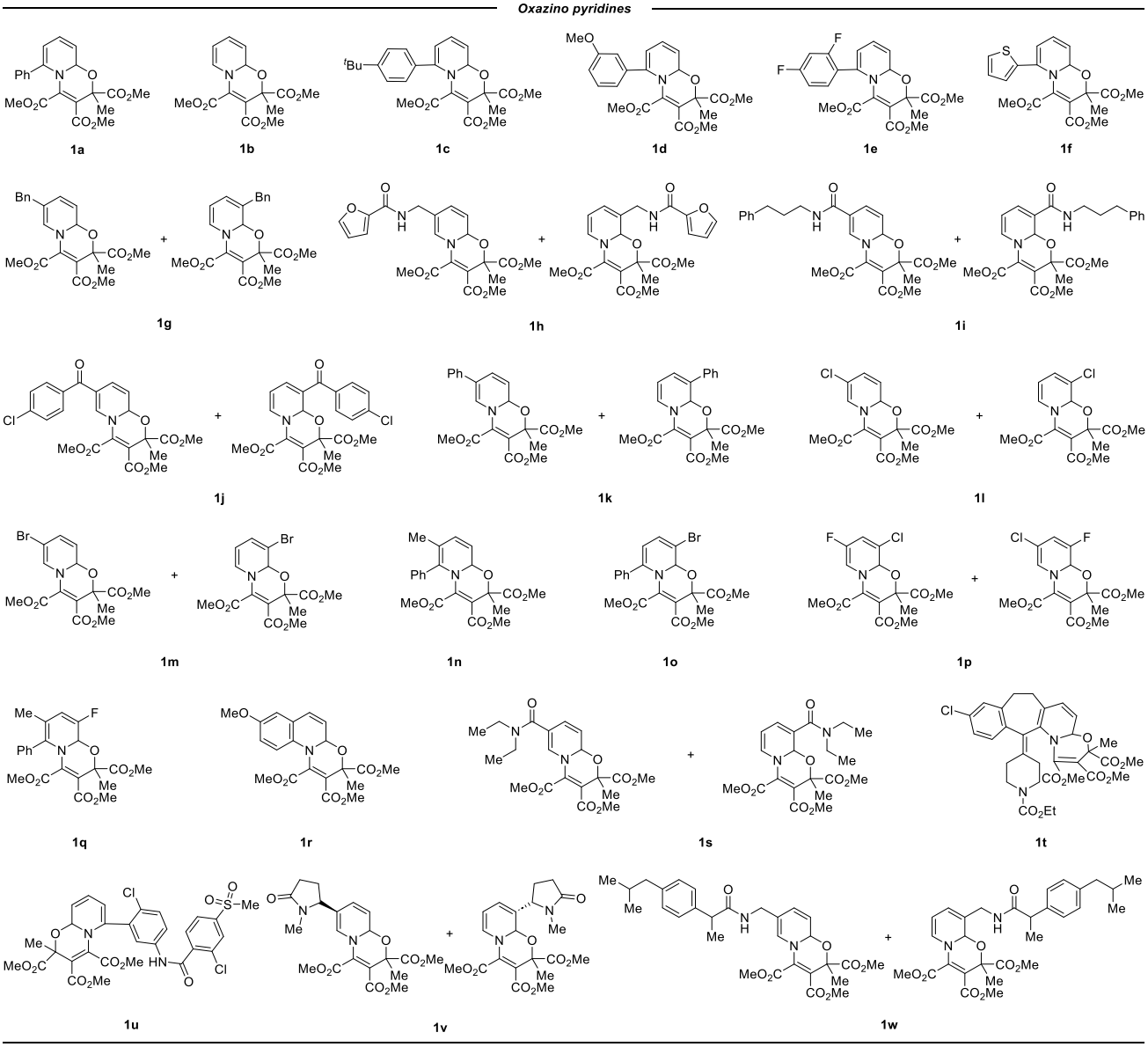
Regents and solvents: Reagents were purchased at the highest commercial grade from *ABCR*, *BLD Pharm*, *Sigma-Aldrich* or *TCI* and were used as received. Commercial solvents were used without further purification. All deuterated solvents were purchased from *Sigma-Aldrich* or *Euriso-Top*.

Chromatography: All reactions were monitored by thin layer chromatography (**TLC**) using *silica gel 60 F_{254}* plates (*Merck*). The spots were visualized using UV light (254 nm). Column chromatography was performed on silica gel (40-63 µm) (*Merck* or *VWR*) using pressurized air. Reversed phase medium pressure liquid chromatography (**RP-MPLC**) was performed on a *C-850 FlashPrep device* (*Büchi*) using *FlashPure EcoFlex* C18 50 µm flash cartridges (spherical, 4 g) (*Büchi*) as the stationary phase. Water (Milli-Q grade) and acetonitrile (HPLC grade) were used as the mobile phase in gradient elution modes. Detection was carried out using UV absorption (λ = 210 nm, 230 nm, 254 nm, 320 nm).

Spectroscopy and instruments: NMR spectra of **^{1}H** (300 MHz, 400 MHz and 600 MHz), **^{13}C** (75 MHz, 100 MHz and 150 MHz) and **^{19}F** (282 MHz, 376 MHz and 564 MHz) spectrum were measured on a *DPX 300 (Bruker), DD2 500 (Agilent) or DD2 600 (Agilent)* spectrometer. Chemical shifts are reported in parts per million (ppm) and the spectra were referenced using the residual $CDCl_3$ signals (δ_H = 7.26 ppm, δ_C = 77.16 ppm). Peak multiplicities are defined as s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). High-resolution mass spectroscopic measurements (**HRMS**) were conducted on a *Bruker MicroTof* device with electrospray ionization. Melting points (**Mp**) were determined using a *M-560* melting point apparatus (*Büchi*) and are uncorrected. **IR** spectra were measured on a *FTIR-4600LE FTIR* spectrometer (*Jasco*). IR signals are categorized as strong (s), medium (m) and weak (w). Absorption maxima are reported in cm^{-1}. Optical rotary powers ($[\alpha]_D^{X\,°C}$) were measured on a *Perkin Elmer 341* polarimeter in chloroform at 20–23 °C.

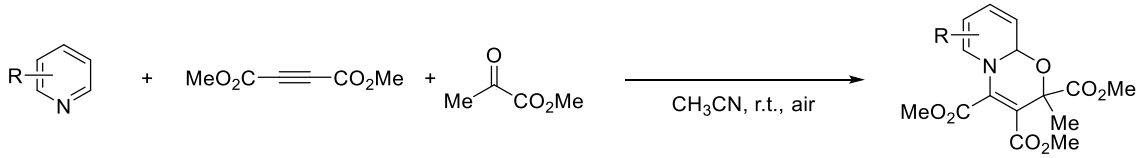
2. Preparation of starting materials

➢ Synthesis of oxazino pyridines



Oxazino pyridines **1a-1w** were prepared according to literature procedures.[1,2] Analytical data are in agreement with those reported in the literature.[1,2]

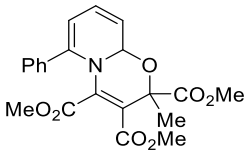
General procedure A:



The corresponding pyridine (3.0 mmol, 1.0 equiv.) and methyl pyruvate (0.54 mL, 6.0 mmol, 2.0 equiv.) were dissolved in acetonitrile (6.0 mL, 0.5 M) in a 25 mL round-bottom flask with a magnetic stirring bar under air atmosphere. Then, dimethyl acetylenedicarboxylate (0.74 mL, 6.0 mmol, 2.0 equiv.) was added dropwise to the

stirred reaction mixture. The reaction mixture was stirred at room temperature and monitored by TLC. When completion, the solvent was removed with a rotary evaporator under reduced pressure and the residue was subjected to flash column chromatography over silica gel to give the corresponding oxazino pyridines.

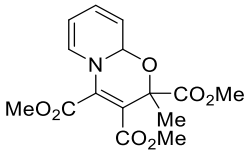
Trimethyl 2-methyl-6-phenyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1a)



1a was prepared according to the general procedure A with 2-phenylpyridine (0.86 ml, 6.0 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1a** was obtained as a yellow solid (1.96 g, 82% yield, containing diastereomers, dr = 1/1).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 7.50-7.15 (m, 5H, Dia. 1 and Dia. 2), 6.56-6.35 (m, 1H, Dia. 1 and Dia. 2), 5.79-5.63 (m, 1H, Dia. 1 and Dia. 2), 5.57-5.18 (m, 2H, Dia. 1 and Dia. 2), 3.86 and 3.76 (s, 3H, Dia. 1 and Dia. 2), 3.67 and 3.65 (s, 3H, Dia. 1 and Dia. 2), 3.13 (s, 3H, Dia. 1 and Dia. 2), 1.92 and 1.64 (s, 3H, Dia. 1 and Dia. 2).

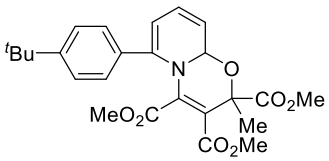
Trimethyl 2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1b)



1b was prepared according to the general procedure A with pyridine (0.49 ml, 6.0 mmol, reaction time = 2 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1b** was obtained as a yellow solid (1.76 g, 91% yield, containing diastereomers, dr = 3/1).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), 3:1 mixture of diastereomers) δ 6.35-6.18 (m, 2H, major and minor), 5.94-5.50 (m, 2H, major and minor), 5.35-5.24 (m, 1H. major and minor), 3.93 (s, 3H, major and minor), 3.77 (major) and 3.72 (minor) (s, 3H), 3.73 (s, 3H, major and minor), 1.77 (major) and 1.75 (minor) (s, 3H).

Trimethyl 6-(4-(*tert*-butyl)phenyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1c)



1c was prepared according to the general procedure A with 2-(4-(*tert*-butyl)phenyl)pyridine (634 mg, 3.00 mmol reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 4/1), the desired compound **1c** was obtained as a yellow solid (915 mg, 67% yield, containing diastereomers, dr = 1/1).

Rf = 0.50 (*n*-pentane/EtOAc = 5/2).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 7.40-7.31 (m, 3H, Dia. 1 and Dia. 2), 7.20-7.15 (m, 1H, Dia. 1 and Dia. 2), 6.52-6.39 (m, 1H, Dia. 1 and Dia. 2), 5.55-5.31 (m, 1H, Dia. 1 and Dia. 2), 5.55-5.31 (m, 1H, Dia. 1 and Dia. 2), 5.30-5.24 (m, 1H, Dia. 1 and Dia. 2), 3.86 and 3.76 (s, 3H, Dia. 1 and Dia. 2), 3.67 and 3.65 (s, 3H, Dia. 1 and Dia. 2), 3.10 (s, 3H, Dia. 1 and Dia. 2), 1.92 and 1.64 (s, 3H, Dia. 1 and Dia. 2), 1.31 (s, 9H, Dia. 1 and Dia. 2).

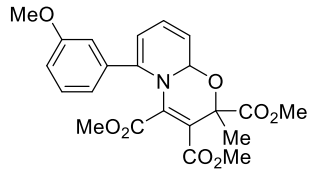
^{13}C NMR (101 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 170.9, 170.3, 165.8, 165.3, 163.2, 162.8, 151.8, 151.6, 142.1, 141.0, 139.5, 138.8, 133.3, 132.9, 128.2, 127.3, 126.7, 125.2, 124.1, 123.1, 114.1, 113.3, 103.64, 103.58, 81.6, 80.7, 78.6, 78.0, 53.2, 52.7, 52.3, 52.14, 52.13, 52.07, 34.70, 34.69, 31.3, 31.2, 24.6, 22.8.

HRMS (ESI): m/z $[M + Na]^+$ Calcd for $C_{25}H_{29}NO_7Na$: 478.18362, found: 478.18344.

IR (neat): 2952 (w), 1739 (m), 1717 (m), 1569 (m), 1423 (m), 1269 (m), 1229 (s), 1202 (m), 1120 (m).

Mp: 69-71 °C.

Trimethyl 6-(3-methoxyphenyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1d)



1d was prepared according to the general procedure A with 2-(3-methoxyphenyl)pyridine (555 mg, 3.00 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 4/1), the desired compound **1d** was obtained as a yellow solid (1.11 g, 86% yield, containing diastereomers, dr = 1/1).

Rf = 0.33 (*n*-pentane/EtOAc = 5/2)

^{1}H NMR (500 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 7.22 (m, 1H, Dia. 1 and Dia. 2), 7.11-6.97 (m, 1H, Dia. 1 and Dia. 2), 6.87-6.72 (m, 2H, Dia. 1 and Dia. 2), 6.51-6.38 (m, 1H, Dia. 1 and Dia. 2), 5.76-5.64 (m, 1H, Dia. 1 and Dia. 2), 5.57-5.19 (m, 2H, Dia. 1 and Dia. 2), 3.83 and 3.76 (s, 3H, Dia. 1 and Dia. 2), 3.80 and 3.78 (s, 3H, Dia. 1 and Dia. 2), 3.67 and 3.65 (s, 3H, Dia. 1 and Dia. 2), 3.19 and 3.18 (s, 3H, Dia. 1 and Dia. 2), 1.91 and 1.64 (s, 3H, Dia. 1 and Dia. 2).

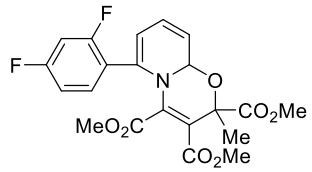
^{13}C NMR (126 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 171.0, 170.3, 165.9, 165.5, 163.0, 162.6, 159.5, 141.8, 140.7, 139.5, 138.7, 137.5, 137.2, 129.5, 127.3, 126.7, 124.6, 123.6, 120.7, 114.9, 114.7, 114.5, 113.7, 103.8, 103.7, 81.6, 80.7, 78.8, 78.2, 55.5, 55.4, 53.2, 52.9, 52.5, 52.3, 52.2, 24.7, 22.9.

HRMS (ESI): m/z $[M + Na]^+$ Calcd for $C_{22}H_{23}NO_8Na$: 452.13159, found: 452.13115.

IR (neat): 2952 (w), 1739 (m), 1734 (m), 1560 (m), 1433 (m), 1261 (m), 1225 (s), 1120 (m), 1077 (m), 765 (m), 752 (s).

Mp: 47-50 °C.

Trimethyl 6-(2,4-difluorophenyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1e)

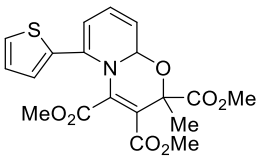


1e was prepared according to the general procedure A with 2-(2,4-difluorophenyl)pyridine (1.15 g, 6.00 mmol, reaction time = 2 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1e** was obtained as a yellow solid (2.35 g, 90% yield, containing diastereomers, dr = 1/1).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) 7.59-7.20 (m, 1H, Dia. 1 and Dia. 2), 6.92-6.73 (m, 2H, Dia. 1 and Dia. 2), 6.52-6.36 (m, 1H, Dia. 1 and Dia. 2), 5.80-5.69 (m, 1H, Dia. 1 and Dia. 2), 5.57-5.21 (m,

2H, Dia. 1 and Dia. 2), 3.83 and 3.66 (s, 3H, Dia. 1 and Dia. 2), 3.75 and 3.65 (s, 3H, Dia. 1 and Dia. 2), 3.30 and 3.25 (s, 3H, Dia. 1 and Dia. 2), 1.84 and 1.63 (s, 3H, Dia. 1 and Dia. 2).

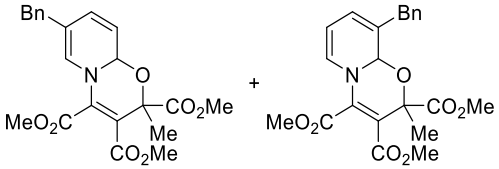
Trimethyl 2-methyl-6-(thiophen-2-yl)-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1f)



1f was prepared according to the general procedure A with 2-(thiophen-2-yl)pyridine (484 mg, 3.00 mmol, reaction time = 96 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1f** was obtained as a yellow solid (1.15 g, 95% yield, containing diastereomers, dr = 1/1).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 7.47-6.88 (m, 3H, Dia. 1 and Dia. 2), 6.50-6.36 (m, 1H, Dia. 1 and Dia. 2), 5.79-5.65 (m, 1H, Dia. 1 and Dia. 2), 5.55-5.14 (m, 2H, Dia. 1 and Dia. 2), 3.82 and 3.76 (s, 3H, Dia. 1 and Dia. 2), 3.71 and 3.69 (s, 3H, Dia. 1 and Dia. 2), 3.34 (s, 3H, Dia. 1 and Dia. 2), 1.90 and 1.62 (s, 3H, Dia. 1 and Dia. 2).

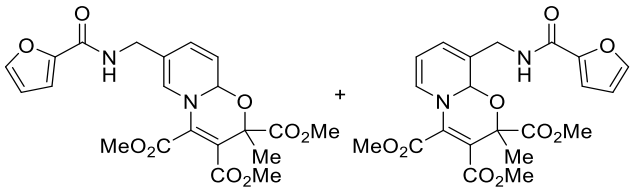
Trimethyl 7-benzyl-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-benzyl-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate 1g



1g was prepared according to the general procedure A with 3-benzylpyridine (508 mg, 3.00 mmol, reaction time = 24 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1g** was obtained as a yellow solid (1.12 g, 90% yield, containing regioisomers and diastereomers, ratio = 32/6/7/5).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 7.33-7.26 (m, 2H), 7.24-7.13 (m, 3H), 6.22-5.96 (m, 2H), 5.81-5.50 (m, 1H), 5.28-5.18 (m, 1H), (3.90, 3.89 and 3.87 (s, 3H, Reg. and Dia.)), 3.77-3.50 (m, 8H), (1.75, 1.73, 1.55 and 1.53 (s, 3H, Reg. and Dia.)).

Trimethyl 7-((furan-2-carboxamido)methyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-((furan-2-carboxamido)methyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1h)

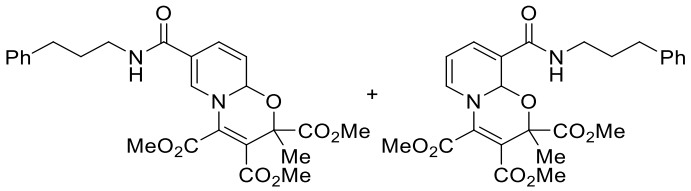


1h was prepared according to the general procedure A with *N*-(pyridin-3-ylmethyl)furan-2-carboxamide (606 mg, 3.00 mmol, reaction time = 24 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1h** was obtained as a yellow solid (1.23 g, 92% yield, containing regioisomers and diastereomers, ratio = 16/10/7/7).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 7.43-7.37 (m, 1H), 7.09-7.03

(m, 1H), 7.02-6.91 (m, 1H), 6.48-6.42 (m, 1H), 6.33-6.13 (m, 2H), 5.76-5.08 (m, 2H), 4.43-3.98 (m, 2H), 3.88-3.59 (m, 9H), (1.75, 1.70 and 1.68 (s, 3H, Reg. and Dia.)).

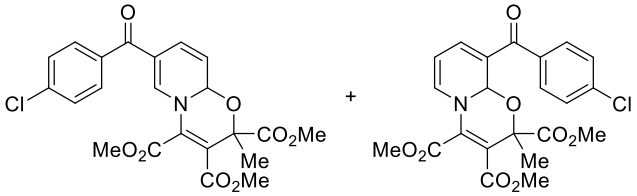
Trimethyl 2-methyl-7-((3-phenylpropyl)carbamoyl)-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 2-methyl-9-((3-phenylpropyl)carbamoyl)-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1i)



1i was prepared according to the general procedure A with *N*-(3-phenylpropyl)nicotinamide (721 mg, 3.00 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1i** was obtained as a yellow solid (1.24 g, 85% yield, containing regioisomers and diastereomers, ratio = 3/3/2/2).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 7.86 (t, *J* = 5.3 Hz, 1H), 7.49-7.10 (m, 6H), 6.49-6.28 (m, 1H), 5.86-5.41 (m, 2H), 3.98-3.67 (m, 9H), 3.50-3.30 (m, 2H), 2.76-2.62 (m, 2H), 1.99-1.58 (m, 5H).

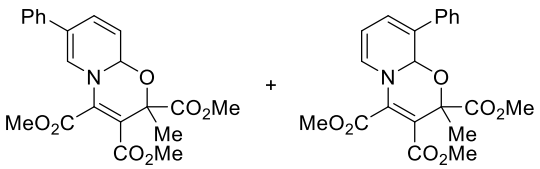
Trimethyl 7-(4-chlorobenzoyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-(4-chlorobenzoyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1j)



1j was prepared according to the general procedure A with (4-chlorophenyl)(pyridin-3-yl)methanone (652 mg, 3.00 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 5/2), the desired compound **1j** was obtained as a yellow solid (1.25 g, 90% yield, containing regioisomers and diastereomers, ratio = 3/3/2/2).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) 7.63-7.37 (m, 4H), 7.11-5.37 (m, 4H), 3.93-3.69 (m, 9H), (1.77, 1.75 and 1.74 (s, 3H, Reg. and Dia.)).

Trimethyl 2-methyl-7-phenyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 2-methyl-9-phenyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1k)

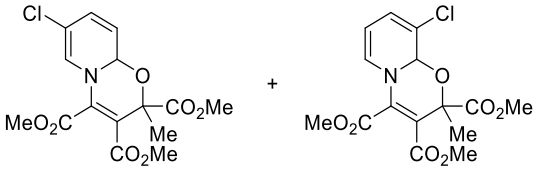


1k was prepared according to the general procedure A with 3-phenylpyridine (466 mg, 3.00 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1k** was obtained as a yellow solid (1.08 g, 90% yield, containing regioisomers and diastereomers, ratio = 17/12/7/4).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 7.55-7.17 (m, 5H), 6.75-6.31

(m, 2H), 6.30-5.40 (m, 2H), 3.95 and 3.94 (s, 3H, Reg. and Dia.), 3.81-3.63 (m, 6H), (1.80, 1.78, 1,77 and 1.73 (s, 3H, Reg. and Dia.)).

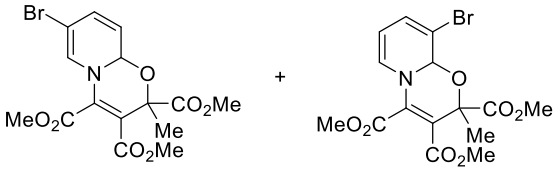
Trimethyl 7-chloro-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-chloro-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1l)



1l was prepared according to the general procedure A with 3-chloropyridine (339 mg, 3.00 mmol, reaction time = 24 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1l** was obtained as a yellow gum (964 mg, 90% yield, containing regioisomers and diastereomers, ratio = 4/4/1/1).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 6.44-6.36 (m, 1H), 6.32-6.21 (m, 1H), 5.78-5.17 (m, 2H), 3.93 and 3.91 (s, 3H, Reg. and Dia.), 3.80-3.67 (m, 6H), (1.77, 1.75, and 1.74 (s, 3H, Reg. and Dia.)).

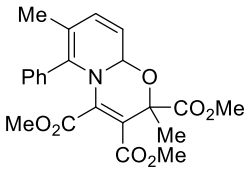
Trimethyl 7-bromo-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-bromo-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1m)



1m was prepared according to the general procedure A with 3-bromopyridine (471 mg, 3.00 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 10/3), the desired compound **1m** was obtained as a yellow gum (1.15 g, 95% yield, containing regioisomers and diastereomers, ratio = 4/4/1/1).

^{1}H NMR (300 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 6.72-6.46 (m, 1H), 6.42-6.21 (m, 1H), 5.91-5.04 (m, 2H), 3.93 and 3.91 (s, 3H, Reg. and Dia.), 3.84-3.65 (m, 6H), (1.77, 1.75, and 1.74 (s, 3H, Reg. and Dia.)).

Trimethyl 2,7-dimethyl-6-phenyl-2H,9aH-pyrido[2,1-b][1,3]oxazine-2,3,4-tricarboxylate (1n)

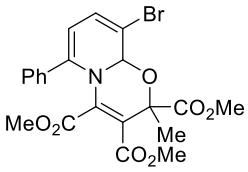


1n was prepared according to the general procedure A with 3-methyl-2-phenylpyridine (508 mg, 3.00 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 2/1), the desired compound **1n** was obtained as a yellow solid (1.02 g, 82% yield, containing diastereomers, dr = 1/1).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 7.50-6.98 (m, 5H, Dia. 1 and Dia. 2), 6.54-6.22 (m, 1H, Dia. 1 and Dia. 2), 5.92-5.64 (m, 1H, Dia. 1 and Dia. 2), 5.52-5.36 (m, 1H, Dia. 1 and Dia. 2), 3.74 (s, 3H, Dia. 1 and Dia. 2), 3.60 (s, 3H, Dia. 1 and Dia. 2), 3.17 (s, 3H, Dia. 1 and Dia. 2), 1.87 (s, 3H, Dia. 1 and Dia.

2), 1.61 (s, 3H, Dia. 1 and Dia. 2).

Trimethyl 9-bromo-2-methyl-6-phenyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1o)



1o was prepared according to the general procedure A with 5-bromo-2-phenylpyridine (700 mg, 3.00 mmol, reaction time = 7 d). After purification by flash chromatography (*n*-pentane/EtOAc = 4/1), the desired compound **1o** was obtained as a yellow gum (615 mg, 43% yield, containing diastereomers, dr = 1/1).

Rf = 0.50 (*n*-pentane/EtOAc = 5/2)

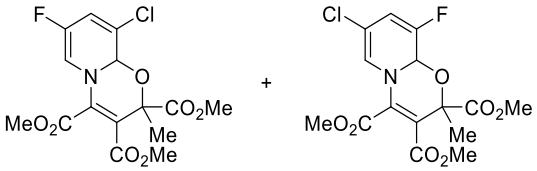
^{1}H NMR (500 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 7.54-7.18 (m, 5H, Dia. 1 and Dia. 2), 6.84-6.69 (m, 1H, Dia. 1 and Dia. 2), 5.71-5.09 (m, 2H, Dia. 1 and Dia. 2), 3.87 and 3.80 (s, 3H, Dia. 1 and Dia. 2), 3.69 and 3.67 (s, 3H, Dia. 1 and Dia. 2), 3.15 (s, 3H, Dia. 1 and Dia. 2), 1.96 and 1.69 (s, 3H, Dia. 1 and Dia. 2).

^{13}C NMR (126 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 170.5, 169.8, 165.6, 165.2, 162.8, 162.4, 140.7, 139.0, 138.3, 135.4, 135.0, 129.6, 129.10, 129.08, 129.0, 128.5, 125.1, 107.8, 107.0, 103.34, 103.33, 85.3, 84.8, 79.5, 79.1, 53.4, 52.9, 52.6, 52.44, 52.39, 52.3, 24.4, 22.1.

HRMS (ESI): m/z $[M + Na]^+$ Calcd for $C_{21}H_{20}NO_7BrNa$: 500.03154, found: 500.03143.

IR (neat): 2952 (w), 1739 (s), 1267 (s), 1231 (s), 1123 (m), 762 (m), 732 (m), 701 (m).

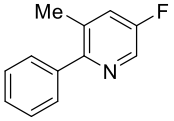
Trimethyl 9-chloro-7-fluoro-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 7-chloro-9-fluoro-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1p)



1p was prepared according to the general procedure A with 3-chloro-5-fluoropyridine (393 mg, 3.00 mmol, 1.00 equiv.), methyl pyruvate (1.1 mL, 12 mmol, 4.0 equiv.) and dimethyl acetylenedicarboxylate (1.5 mL, 12 mmol, 4.0 equiv.) (reaction time = 7 d). After purification by flash chromatography (*n*-pentane/EtOAc = 5/1), the desired compound **1p** was obtained as a yellow gum (923 mg, 82% yield, containing regioisomers and diastereomers, ratio = 14/14/3/1).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 6.57-5.18 (m, 3H), 3.90 and 3.89 (s, 3H, Reg. and Dia.), 3.79-3.68 (m, 6H), (1.74, 1.71 and 1.70 (s, 3H, Reg. and Dia.).

5-Fluoro-3-methyl-2-phenylpyridine (S1) and Trimethyl 9-fluoro-2,7-dimethyl-6-phenyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1q)



The synthesis of 5-fluoro-3-methyl-2-phenylpyridine **S1** was conducted following a modified literature procedure[3]:

under argon, 2-bromo-5-fluoro-3-picoline (0.60 mL, 5.0 mmol, 1.0 equiv.), phenylboronic acid (854 mg, 7.00 mmol, 1.40 equiv.), tetrakis(triphenylphosphine)palladium (116 mg, 0.100 mmol, 2.00 mol%) and sodium carbonate (1.06 g, 10.0 mmol, 2.00 equiv) were dissolved in THF and water (4:1, 30 mL). The reaction mixture was bubbled by argon for 5 minutes and then heated at 100 °C for 24 h. THF was evaporated in vacuuo. Water (20 mL) was added and the reaction mixture was extracted with ethyl acetate (3×20 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, concentrated under reduced pressure and purified by column chromatography (silica, *n*-pentane/Et_2O = 10/1) to give the desired pyridine as a colourless oil (748 mg, 80% yield).

Rf = 3.50 (*n*-pentane/Et_2O = 10/1)

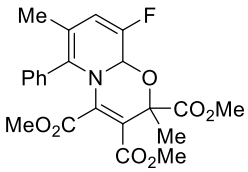
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 2.8, 0.7 Hz, 1H), 7.51-7.38 (m, 5H), 7.36-7.29 (m, 1H), 2.37 (s, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 158.6 (d, *J* = 256.1 Hz), 155.1 (d, *J* = 3.7 Hz), 139.8, 135.1 (d, *J* = 22.8 Hz), 132.8 (d, *J* = 3.9 Hz), 129.1, 128.4, 128.2, 125.0 (d, *J* = 17.6 Hz), 20.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ -130.6.

HRMS (ESI): m/z $[M + Na]^+$ Calcd for $C_{12}H_{10}NFNa$: 210.06895, found: 210.06890.

IR (neat): 1462 (s), 1446 (s), 1428 (s), 1269 (s), 1192 (s), 742 (m), 712 (m), 700 (m).



1q was synthesized according to the general procedure A with 5-fluoro-3-methyl-2-phenylpyridine **S1** (468 mg, 2.50 mmol, reaction time = 48 h). After purification by flash chromatography (pentane/EtOAc = 4/1), the desired compound **1q** was obtained as a yellow gum (992 mg, 92% yield, containing diastereomers, dr = 1/1).

Rf = 0.55 (pentane/EtOAc = 5/2)

^{1}H NMR (500 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 7.47-7.04 (m, 5H, Dia. 1 and Dia. 2), 6.11-5.96 (m, 1H, Dia. 1 and Dia. 2), 5.64-5.12 (m, 1H, Dia. 1 and Dia. 2), 3.86 and 3.76 (s, 3H, Dia. 1 and Dia. 2), 3.62-3.61 (s, 3H, Dia. 1 and Dia. 2), 3.16 and 3.15 (s, 3H, Dia. 1 and Dia. 2), 1.95-1.54 (m, 6H).

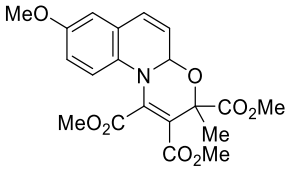
^{13}C NMR (126 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 170.7, 170.0, 165.7, 165.2, 163.4, 163.0, 150.4, 149.7, 148.3, 147.6, 142.2, 141.1, 133.6, 133.5, 132.6, 132.5, 131.02, 130.98, 130.32, 130.28, 129.7, 128.9, 128.7, 128.6, 128.2, 127.9, 123.8, 123.1, 110.1, 110.0, 109.5, 109.4, 106.61, 106.58, 106.39, 106.36, 79.6, 79.3, 78.9, 78.7, 78.6, 78.1, 53.3, 52.9, 52.5, 52.43, 52.40, 52.3, 24.4, 22.6, 17.81, 17.79, 17.77.

^{19}F NMR (470 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ -125.9, -126.8.

HRMS (ESI): m/z $[M + Na]^+$ Calcd for $C_{22}H_{22}NO_7FNa$: 454.12725, found: 454.12723.

IR (neat): 2953 (w), 1720 (s), 1585 (m), 1433 (m), 1241 (m), 1204 (s), 1145 (s), 1123 (s), 702 (m).

Trimethyl 8-methoxy-3-methyl-3*H*,4a*H*-[1,3]oxazino[3,2-*a*]quinoline-1,2,3-tricarboxylate (1r)



1r was prepared according to the general procedure A with 6-methoxyquinoline (398 mg, 2.50 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 3/1), the desired compound **1r** was obtained as a yellow solid (605 mg, 60% yield, containing diastereomers, dr = 1/1).

Rf = 0.40 (*n*-pentane/EtOAc = 5/2)

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 6.83-6.73 (m, 3H, Dia. 1 and Dia. 2), 6.71-6.64 (m, 1H, Dia. 1 and Dia. 2), 6.00-5.89 (m, 1H, Dia. 1 and Dia. 2), 5.49-5.09 (m, 1H, Dia. 1 and Dia. 2), 3.86 and 3.85 (s, 3H, Dia. 1 and Dia. 2), 3.80-3.56 (m, 9H), 1.75 and 1.64 (s, 3H, Dia. 1 and Dia. 2).

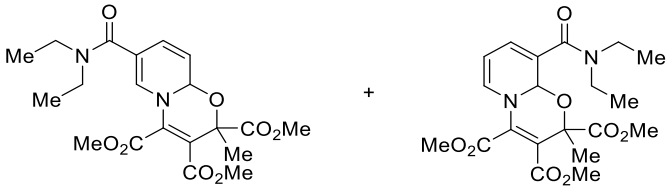
^{13}C NMR (101 MHz, $CDCl_3$, δ (ppm), 1:1 mixture of diastereomers) δ 171.2, 169.8, 165.8, 165.5, 164.6, 164.1, 155.0, 154.9, 140.5, 139.6, 130.3, 129.9, 129.7, 129.3, 126.3, 125.7, 122.32, 122.29, 119.3, 119.0, 115.9, 115.5, 115.3, 115.2, 113.6, 113.3, 79.3, 78.9, 78.6, 78.3, 55.8, 53.4, 53.30, 53.26, 52.9, 52.6, 52.5, 25.0, 22.7.

HRMS (ESI): m/z $[M + Na]^+$ Calcd for $C_{20}H_{21}NO_8Na$: 426.11594, found: 426.11587.

IR (neat): 2952 (w), 1735 (m), 1707 (m), 1499 (m), 1270 (m), 1242 (m), 1271 (m), 1174 (m), 1126 (m), 1057 (m), 854 (m), 813 (m).

Mp: 120-122 °C.

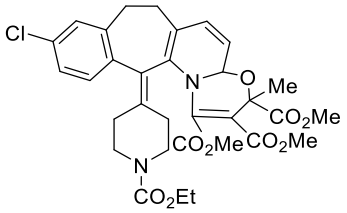
Trimethyl 7-(diethylcarbamoyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-(diethylcarbamoyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1s)



1s was prepared according to the general procedure A with *N*,*N*-diethylnicotinamide (535 mg, 3.00 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 1/1), the desired compound **1s** was obtained as a yellow gum (1.19 g, 94% yield, containing regioisomers and diastereomers, ratio = 16/7/4/3).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 6.75-5.17 (m, 4H), 3.92 and 3.91 (s, 3H, Reg. and Dia.), 3.82-3.66 (m, 6H), 3.56-3.18 (m, 4H), 1.80-1.57 (m, 3H), 1.25-1.10 (m, 6H).

Trimethyl 10-chloro-13-(1-(ethoxycarbonyl)piperidin-4-ylidene)-3-methyl-4a,7,8,13-tetrahydro-3*H*-benzo[4',5']cyclohepta[1',2':5,6]pyrido[2,1-*b*][1,3]oxazine-1,2,3-tricarboxylate (1t)

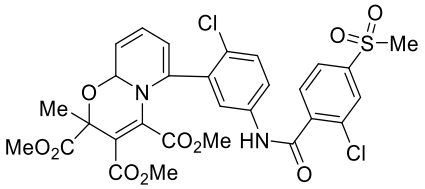


1t was prepared according to the general procedure A with loratadine (2.29 g, 6.00 mmol, reaction time = 12 h). After purification by flash chromatography (*n*-pentane/EtOAc = 1/1), the desired compound **1t** was obtained as a yellow solid (3.61 g, 96% yield, containing diastereomers, dr = 2/1).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), 2:1 mixture of diastereomers) δ 7.20-7.11 (m, 2H), 7.01-6.92 (m, 1H), 6.22-6.12 (m, 1H), 5.72-5.53 (m, 1H), 5.45-5.25 (m, 1H), 4.19-4.09 (m, 2H), 4.04-3.63 (m, 11H), 3.14-2.92 (m, 2H), 2.88-

2.61 (m, 3H), 2.43-2.26 (m, 3H), 2.24-2.13 (m, 1H), 2.07-1.96 (m, 1H), 1.85 and 1.64 (s, 3H, Dia. 1 and Dia. 2), 1.31-1.18 (m, 3H).

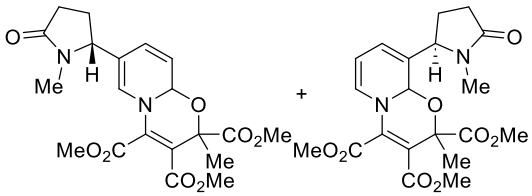
Trimethyl 6-(2-chloro-5-(2-chloro-4-(methylsulfonyl)benzamido)phenyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1u)



1u was prepared according to the general procedure A with vismodegib (1.26 g, 3.00 mmol, reaction time = 12 h). After purification by flash chromatography (*n*-pentane/EtOAc = 1/1), the desired compound **1u** was obtained as a yellow solid (1.72 g, 86% yield, containing diastereomers and atropisomers, ratio = 8/4/2/1).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing diastereomers and atropisomers): 8.67-8.39 (m, 1H), 8.11-7.31 (m, 6H), 6.56-6.36 (m, 1H), 5.79-5.22 (m, 3H), 3.84-3.57 (m, 6H), (3.41, 2.32, 2.31 and 2.38 (s, 3H, Dia. and atropisomers)), (3.08, 3.07, 3.06 and 3.05 (s, 3H, Dia. and atropisomers)), 1.92-1.59 (m, 3H).

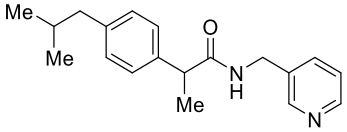
Trimethyl 2-methyl-7-((*R*)-1-methyl-5-oxopyrrolidin-2-yl)-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 2-methyl-9-((*R*)-1-methyl-5-oxopyrrolidin-2-yl)-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1v)



1v was prepared according to the general procedure A with (-)cotinine (528 mg, 3.00 mmol, reaction time = 12 h). After purification by flash chromatography (*n*-pentane/EtOAc = 1/1), the desired compound **1v** was obtained as a yellow solid (1.17 g, 93% yield, containing regioisomers and diastereomers, ratio = 1/1/1/1).

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 6.34-6.04 (m, 2H), 5.84-5.25 (m, 2H), 3.98-3.61 (m, 10H), (2.76, 2.73, 2.66 and 2.64 (s, 3H, Reg. and Dia.)), 2.52-2.19 (m, 3H), 2.09-1.96 (m, 1H), (1.75, 1.74, 1.72 and 1.71 (s, 3H, Reg. and Dia.)).

2-(4-Isobutylphenyl)-*N*-(pyridin-3-ylmethyl)propenamide (S2), Trimethyl 7-((2-(4-isobutylphenyl)propanamido)methyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-((2-(4-isobutylphenyl)propanamido)methyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1w)



The synthesis of 2-(4-isobutylphenyl)-*N*-(pyridin-3-ylmethyl)propanamide **S2** was conducted following a modified literature procedure[2]: to a solution of 2-(4-isobutylphenyl)propanoic acid (1.03 g, 5.00 mmol, 1.00 equiv.) in dry CH_2Cl_2 (30 mL), pyridin-3-ylmethanamine (541 mg, 5.00 mmol, 1.00 equiv.), *N*-(3-dimethylaminopropyl)-*N*′-

ethylcarbodiimide hydrochloride (1.06 g, 5.50 mmol, 1.10 equiv.), 4-dimethylaminopyridine (61 mg, 0.50 mmol, 0.10 equiv.) and triethylamine (0.76 mL, 5.5 mmol, 1.1 equiv.) were added. The resulting mixture was stirred at room temperature until the reaction was complete as monitored by TLC. The reaction was worked up by dilution with water and extraction with EtOAc (3×20 mL). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography (silica, DCM/MeOH = 30/1) to give the desired pyridine **S2** as a colorless solid (1.21 g, 81% yield).

Rf = 0.45 (DCM/MeOH = 10/1)

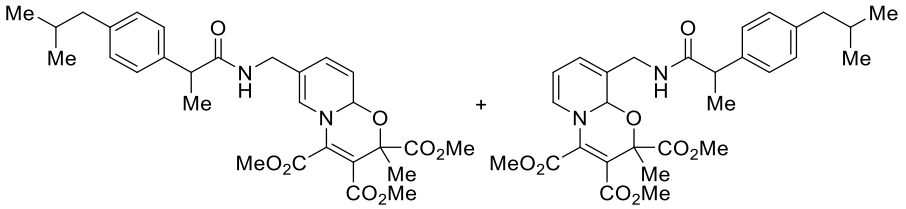
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.42 (d, *J* = 2.3 Hz, 1H), 7.49 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.23-7.16 (m, 3H), 7.14-7.07 (m, 2H), 5.83 (s, 1H), 4.39 (d, *J* = 6.0 Hz, 2H), 3.58 (q, *J* = 7.2 Hz, 1H), 2.44 (d, *J* = 7.2 Hz, 2H), 1.92-1.71 (m, 1H), 1.53 (d, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 174.8, 148.7, 148.5, 141.1, 138.4, 135.7, 134.5, 129.9, 127.5, 123.7, 46.9, 45.1, 41.1, 30.3, 22.5, 18.5.

HRMS: m/z $[M + H]^+$ calcd $C_{19}H_{24}N_2OH$: 297.1954, found: 297.1961.

IR (neat): 3285 (w), 2954 (m), 1651 (s), 1540 (m), 1511 (m), 1464 (m), 712 (m).

Mp: 98-100 °C



1w was prepared according to the general procedure A with 2-(4-isobutylphenyl)-*N*-(pyridin-3-ylmethyl)propanamide **S2** (741 mg, 2.50 mmol, reaction time = 48 h). After purification by flash chromatography (*n*-pentane/EtOAc = 2/1), the desired compound **1w** was obtained as a yellow solid (946 mg, 70% yield, containing regioisomers and diastereomers, ratio = 3/3/1/1).

Rf = 0.45 (*n*-pentane/EtOAc = 5/2)

^{1}H NMR (500 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 7.22-7.14 (m, 2H), 7.13-7.07 (m, 2H), 6.24-5.97 (m, 2H), 5.74-5.16 (m, 2H), 4.26-3.49 (m, 13H), 2.48-2.40 (m, 2H), 1.88-1.78 (m, 1H), (1.73, 1.72, 1.71 and 1.68 (s, 3H, Reg. and Dia.)), 1.58-1.46 (m, 3H), 0.92-0.86 (m, 6H).

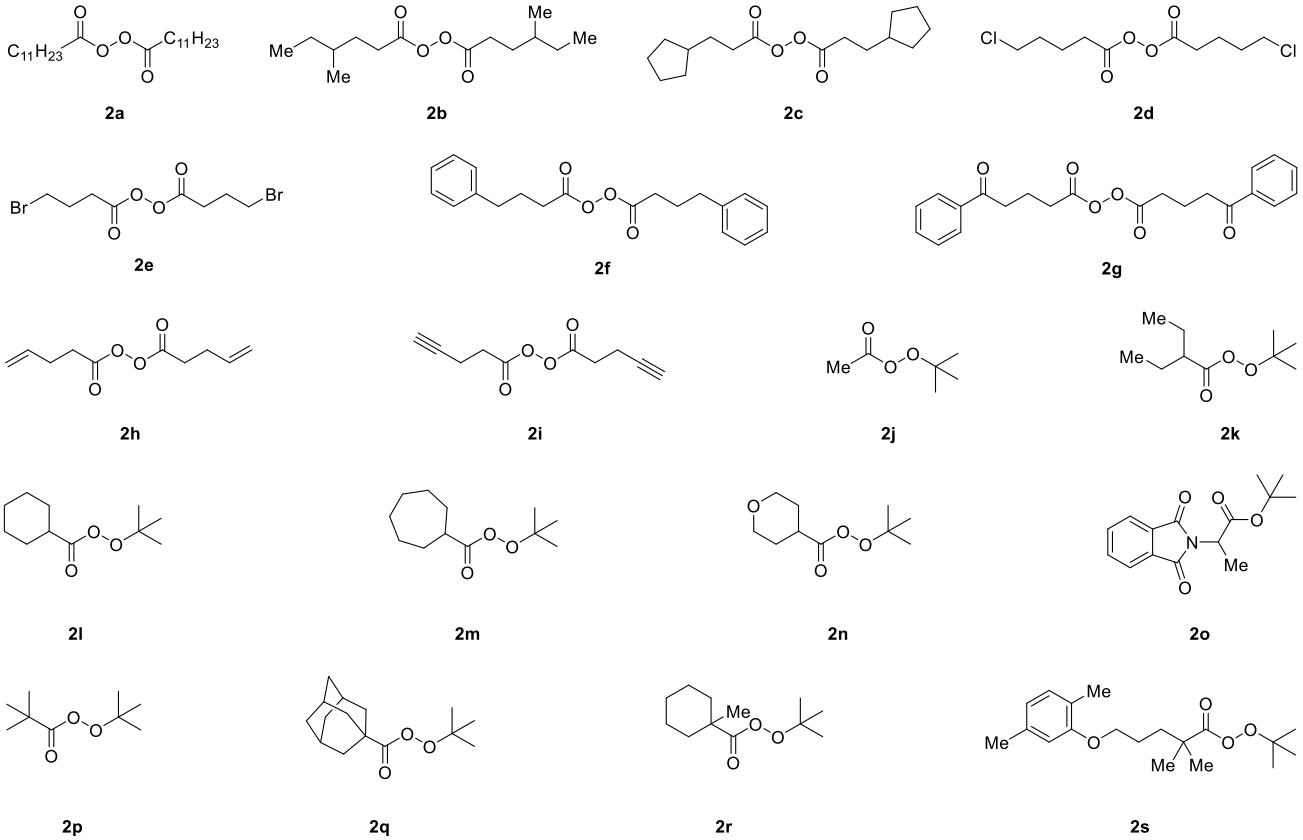
^{13}C NMR (126 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers) δ 174.31, 174.26, 172.0, 171.9, 165.0, 164.6, 163.7, 163.4, 163.4, 141.3, 141.1, 141.0, 140.71, 140.70, 138.81, 138.80, 129.9, 129.8, 129.7, 127.5, 127.45, 127.43, 127.41, 126.6, 125.1, 124.9, 124.13, 124.05, 123.34, 123.30, 123.2, 122.9, 117.0, 115.0, 114.7, 100.7, 100.6, 81.42, 81.37, 80.0, 78.97, 78.95, 77.4, 77.29, 77.25, 77.0, 53.5, 53.40, 53.39, 53.2, 53.0, 52.9, 52.8, 52.21, 52.20, 52.16, 52.1, 47.0, 46.92, 46.87, 45.2, 45.14, 45.12, 41.9, 40.9, 30.3, 24.01, 23.99, 23.9, 23.6, 22.52, 22.51, 18.7, 18.6.

HRMS (ESI): m/z $[M + Na]^+$ calcd $C_{29}H_{36}N_2O_8Na$: 563.2358, found: 563.2364.

IR (neat): 2953 (w), 1738 (s), 1578 (s), 1433 (m), 1258 (s), 1236 (s), 1205 (s), 752 (s).

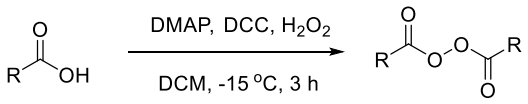
➢ Synthesis of peroxides and peresters

Peroxides and Peresters



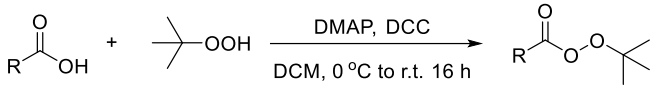
Peroxide **2a** and perester **2j** (50 wt.% in odorless mineral spirits) were purchased and used as received. **2b-2i** were prepared according to the general procedure B. **2k-2s** were prepared according to the general procedure C. Analytical data are in agreement with those reported in the literature.[4–6]

General procedure B: preparation of diacyl peroxides



Diacyl peroxides were prepared according to a literature procedure[4–6]: a solution of an aliphatic carboxylic acid (3.0 mmol, 1.0 equiv.), DMAP (36.6 mg, 0.300 mmol, 0.100 equiv.) and 30 wt% solution of hydrogen peroxide in H_2O (0.43 ml, 3.8 mmol, 1.3 equiv.) in DCM (4.0 mL) was cooled to -15 °C. After stirring for 15 min, DCC (680 mg, 3.30 mmol, 1.10 equiv.) was added. The mixture was stirred for 3 h at -15 °C. Then, the reaction solution was dried with anhydrous Na_2SO_4, filtered through a short pad of silica gel and washed by additional 50 mL of DCM. The combined solution was concentrated in a rotary evaporator under vacuum at 20 °C, and then purified by flash column chromatography on silica gel (*n*-pentane/EtOAc) to give the desired diacyl peroxide.

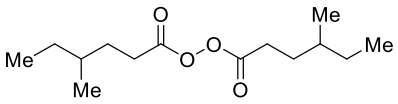
General procedure B: preparation of peresters



2k-2s

Peresters were prepared according to a literature procedure[4–6]: a solution of an aliphatic carboxylic acid (2.5 mmol, 1.0 equiv.) and 70 wt% solution of *tert*-butylhydroperoxide in H_2O (0.33 ml, 2.5 mmol, 1.0 equiv.) in DCM (5.0 mL) was cooled to 0 °C. After stirring vigorously for 10 min, a solution of DMAP (31 mg, 0.25 mmol, 0.10 equiv.) and DCC (565 mg, 2.75 mmol, 1.10 equiv.) in DCM (2.5 mL) was added in one portion. Then, the reaction mixture was allowed to warm to room temperature and stirring was continued for 16 h. Then, the reaction solution was dried with anhydrous Na_2SO_4, filtered through a short pad of silica gel and washed by additional 50 mL of DCM. The combined solution was concentrated in a rotary evaporator under vacuum at 20 °C, and then purified by flash column chromatography on silica gel (*n*-pentane/EtOAc) to give the desired perester.

4-Methylhexanoic peroxyanhydride (2b)



2b was prepared according to the general procedure B with 4-methylhexanoic acid (391 mg, 3.00 mmol, reaction time = 3 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2b** was obtained as a colorless oil (248 mg, 66% yield).

Rf = 0.69 (*n*-pentane/EtOAc = 100/1)

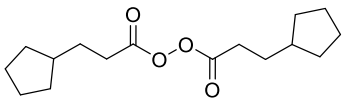
^{1}H NMR (300 MHz, $CDCl_3$) δ 2.53-2.33 (m, 4H), 1.83-1.68 (m, 2H), 1.61-1.27 (m, 6H), 1.26-1.06 (m, 2H), 0.93-0.82 (m, 12H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 169.6, 33.9, 31.3, 29.0, 27.9, 18.7, 11.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd $C_{14}H_{26}O_4Na$: 281.17233, found: 281.17230.

IR (neat): 2961 (w), 2931 (w), 2876 (w), 1810 (m), 1780 (m), 1061 (s).

3-Cyclopentylpropanoic peroxyanhydride (2c)

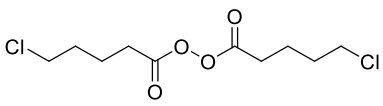


2c was prepared according to the general procedure B with 3-cyclopentylpropanoic acid (0.43 mL, 3.0 mmol, reaction time = 3 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2c** was obtained as a colorless oil (313 mg, 74% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.49-2.39 (m, 4H), 1.87-1.67 (m, 10H), 1.66-1.44 (m, 8H), 1.18-0.99 (m, 4H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 169.5, 39.6, 32.4, 31.1, 29.5, 25.2.

6-Chlorohexanoic 5-chloropentanoic peroxyanhydride (2d)



2d was prepared according to the general procedure B with 5-chloropentanoic acid (410 mg, 3.00 mmol, reaction time = 3 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2d** was obtained as a colorless oil (186 mg, 46% yield).

Rf = 0.13 (*n*-pentane/EtOAc = 100/1)

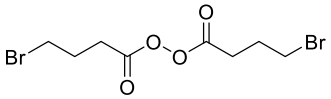
^{1}H NMR (300 MHz, $CDCl_3$) δ 3.64-3.50 (m, 4H), 2.54-2.43 (m, 4H), 1.94-1.84 (m, 8H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 168.8, 44.3, 31.5, 29.3, 22.2.

HRMS (ESI): m/z $[M + Na]^+$ $C_{10}H_{16}O_4Cl_2Na$: 293.03179, found: 293.03181.

IR (neat): 2960 (w), 1807 (w), 1777 (s), 1046 (m), 651 (w), 422 (w).

4-Bromobutanoic peroxyanhydride (2e)

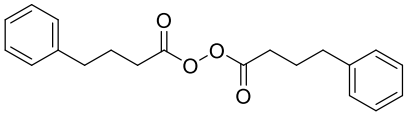


2e was prepared according to the general procedure B with 4-bromobutanoic acid (498 mg, 3.00 mmol, reaction time = 3 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2e** was obtained as a colorless oil (385 mg, 78% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.50 (t, *J* = 6.3 Hz, 4H), 2.66 (t, *J* = 7.1 Hz, 4H), 2.35-2.18 (m, 4H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 168.4, 31.8, 28.5, 27.7.

5-Phenylpentanoic peroxyanhydride (2f)

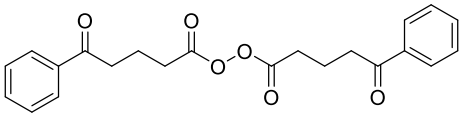


2f was prepared according to the general procedure B with 4-phenylbutanoic acid (493 mg, 3.00 mmol, reaction time = 12 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2f** was obtained as a colorless oil (326 mg, 67% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.08 (m, 10H), 2.79-2.66 (m, 4H), 2.51-2.36 (m, 4H), 2.14-1.94 (m, 4H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 169.2, 140.8, 128.7, 128.6, 126.3, 34.9, 29.4, 26.5.

5-Oxo-5-phenylpentanoic peroxyanhydride (2g)

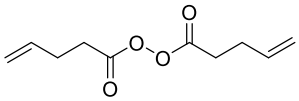


2g was prepared according to the general procedure B with 5-oxo-5-phenylpentanoic acid (576 mg, 3.00 mmol, reaction time = 3 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2g** was obtained as a colorless solid (454 mg, 80% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01-7.92 (m, 4H), 7.60-7.52 (m, 2H), 7.51-7.41 (m, 4H), 3.14 (t, *J* = 7.0 Hz, 4H), 2.60 (t, *J* = 7.0 Hz, 4H), 2.24-2.09 (m, 4H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 199.0, 169.1, 136.8, 133.4, 128.8, 128.2, 37.0, 29.4, 19.3.

Pent-4-enoic peroxyanhydride (2h)

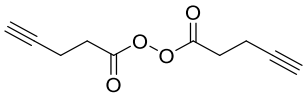


2h was prepared according to the general procedure B with pent-4-enoic acid (300 mg, 3.00 mmol, reaction time = 3 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2h** was obtained as a colorless oil (184 mg, 62% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86-5.67 (m, 2H), 5.11-4.94 (m, 4H), 2.52-2.31 (m, 8H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 168.7, 135.5, 116.6, 29.5, 28.7.

Pent-4-ynoic peroxyanhydride (2i)

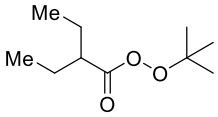


2i was prepared according to the general procedure B with pent-4-ynoic acid (294 mg, 3.00 mmol, reaction time = 3 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2i** was obtained as a colorless oil (160 mg, 55% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.67-2.58 (m, 4H), 2.57-2.49 (m, 4H), 2.01-1.95 (m, 2H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 167.5, 81.2, 70.1, 29.5, 14.5.

***tert*-Butyl 2-ethylbutaneperoxoate (2k)**

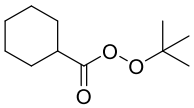


2k was prepared according to the general procedure C with 2-ethylbutanoic acid (580 mg, 5.00 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2k** was obtained as a colorless oil (856 mg, 91% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.26-2.13 (m, 1H), 1.74-1.46 (m, 4H), 1.32 (s, 9H), 0.92 (t, J = 7.4 Hz, 6H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 173.6, 83.1, 46.8, 26.3, 25.4, 12.0.

***tert*-Butyl cyclohexanecarboperoxoate (2l)**

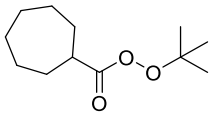


2l was prepared according to the general procedure C with cyclohexanecarboxylic acid (580 mg, 5.00 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2l** was obtained as a colorless oil (861 mg, 86% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45-2.32 (m, 1H), 1.96-1.87 (m, 2H), 1.84-1.75 (m, 2H), 1.71-1.64 (m, 1H), 1.59-1.46 (m, 2H), 1.34 (s, 9H), 1.31-1.20 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 173.3, 83.4, 41.3, 29.2, 26.3, 25.7, 25.5.

***tert*-Butyl cycloheptanecarboperoxoate (2m)**

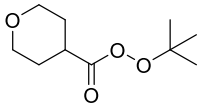


2m was prepared according to the general procedure C with cycloheptanecarboxylic acid (356 mg, 2.50 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2m** was obtained as a colorless oil (520 mg, 97% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.58-2.44 (m, 1H), 2.00-1.85 (m, 2H), 1.81-1.64 (m, 4H), 1.58-1.39 (m, 6H), 1.32 (s, 9H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 174.3, 83.4, 43.0, 31.2, 28.3, 26.4, 26.3.

***tert*-Butyl tetrahydro-2H-pyran-4-carboperoxoate (2n)**

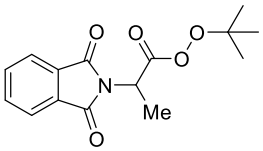


2n was prepared according to the general procedure C with tetrahydro-2H-pyran-4-carboxylic acid (325 mg, 2.50 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 100/1), the desired compound **2n** was obtained as a colorless oil (370 mg, 74% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 4.01 (dt, J = 11.8, 3.6 Hz, 2H), 3.54-3.40 (m, 2H), 2.74-2.58 (m, 1H), 2.00-1.80 (m, 4H), 1.35 (s, 9H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 171.6, 83.6, 66.9, 38.3, 28.6, 26.1.

***tert*-Butyl 2-(1,3-dioxoisoindolin-2-yl)propanoate (2o)**



2o was prepared according to the general procedure C with 2-(1,3-dioxoisoindolin-2-yl)propanoic acid (548 mg, 2.50 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), the desired compound **2o** was obtained as a colorless solid (328 mg, 45% yield).

Rf = 2.5 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.84 (m, 2H), 7.80-7.71 (m, 2H), 5.07 (q, J = 7.3 Hz, 1H), 1.75 (d, J = 7.4 Hz, 3H), 1.28 (s, 9H).

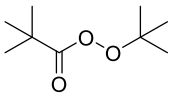
^{13}C NMR (76 MHz, $CDCl_3$) δ 167.2, 167.1, 134.5, 131.9, 123.7, 84.7, 46.5, 26.2, 15.4.

HRMS (ESI): m/z $[M + Na]^+$ $C_{15}H_{17}NO_5Na$: 314.09989, found: 314.09973.

IR (neat): 1778 (s), 1712 (s), 1385 (s), 1368 (m), 1176 (m), 1063 (m), 720 (s).

Mp: 53-54 °C.

***tert*-Butyl 2,2-dimethylpropaneperoxoate (2p)**

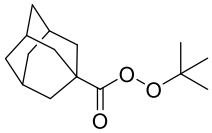


2p was prepared according to the general procedure C with pivalic acid (256 mg, 2.50 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 50/1), the desired compound **2p** was obtained as a colorless oil (139 mg, 38% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 9H), 1.26 (s, 9H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 175.3, 83.5, 39.0, 27.4, 26.3.

***tert*-Butyl adamantane-1-carboperoxoate (2q)**

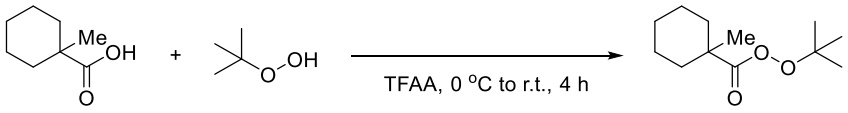


2q was prepared according to the general procedure C with adamantane-1-carboxylic acid (451 mg, 2.50 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 50/1), the desired compound **2q** was obtained as a colorless oil (365 mg, 58% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.09-2.01 (m, 3H), 2.00-1.93 (m, 6H), 1.78-1.71 (m, 6H), 1.34 (s, 9H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 174.5, 83.6, 41.4, 39.1, 36.6, 28.1, 26.4.

***tert*-Butyl 1-methylcyclohexane-1-carboperoxoate (2r)**



2r

2r was prepared according to a literature[6]: 1-methylcyclohexane-1-carboxylic acid (356 mg, 2.50 mmol, 1.00 equiv.) was dissolved in trifluoroacetic anhydride (TFAA, 0.47 mL, 3.3 mmol, 1.4 equiv.). 5 M solution of *tert*-butylhydroperoxide in decane (0.50 ml, 2.5 mmol, 1.0 equiv.) was added at 0 °C and then the reaction mixture was stirred at r.t. for 4 h. When completion, the reaction mixture was concentrated on a rotary evaporator under vacuum at 20 °C, and then purified by flash column chromatography on silica gel (*n*-pentane/EtOAc = 20/1) to give the perester **2r** as a colorless oil (345 mg, 65% yield).

Rf = 0.45 (*n*-pentane/EtOAc = 20/1)

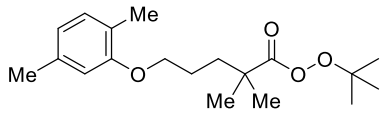
^{1}H NMR (300 MHz, $CDCl_3$) δ 2.14-1.94 (m, 2H), 1.66-1.49 (m, 4H), 1.49-1.38 (m, 2H), 1.37-1.20 (m, 14H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 174.6, 83.4, 43.7, 43.1, 35.7, 35.4, 26.4, 25.8, 25.7, 23.2.

HRMS (ESI): m/z $[M + Na]^+$ $C_{12}H_{22}O_3Na$: 237.14612, found: 237.14608.

IR (neat): 2932 (s), 1764 (s), 1451 (m), 1365 (m), 1189 (s), 1082 (s), 1004 (m).

***tert*-Butyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentaneperoxoate (2s)**



2s was prepared according to the general procedure C with 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoic acid (626 mg, 2.50 mmol, reaction time = 16 h). After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), the desired compound **2s** was obtained as a colorless oil (540 mg, 68% yield).

Rf = 0.45 (*n*-pentane/EtOAc = 20/1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (dd, *J* = 7.6, 3.8 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.62-6.57 (m, 1H), 3.93 (t, *J* = 5.6 Hz, 2H), 2.31-2.28 (m, 3H), 2.18-2.15 (m, 3H), 1.85-1.72 (m, 4H), 1.35-1.26 (m, 15H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.5, 157.1, 136.6, 130.5, 123.8, 120.9, 112.1, 83.5, 68.0, 42.5, 37.5, 26.4, 25.4, 25.3, 21.5, 15.9.

HRMS (ESI): m/z $[M + Na]^+$ calcd $C_{19}H_{30}O_4Na$: 345.20363, found: 345.20361.

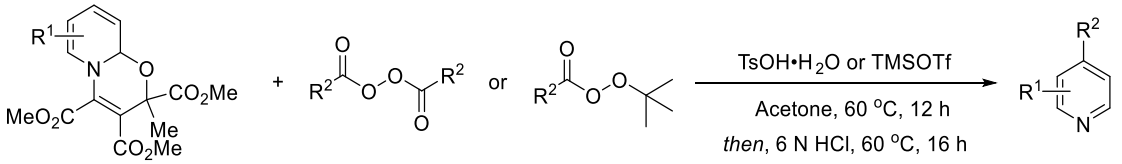
IR (neat): 2977 (w), 1765 (m), 1509 (m), 1389 (w), 1269 (w), 1265 (w), 1157 (m), 1095 (m), 1021 (m), 801 (m).

3. General procedures

3.1 General procedure D: Optimization of reaction conditions

To an oven-dried 10 mL Schlenk tube equipped with a stir bar, oxazino pyridine **1a** (20.0 mg, 0.500 mmol, 1.0 equiv.), lauroyl peroxide **2a** (40.0 mg, 0.100 mmol, 2.0 equiv.), and an acid were added under argon. Solvent (0.5 mL) was added via a syringe and the reaction mixture was heated at 60 °C for 12 h (When 10 mol% iron(II) trifluoromethanesulfonate were used, the reaction runs at room temperature for 24 h). After cooling down to room temperature, 6 N HCl (1.0 mL) was added to the reaction mixture and the tube was heated at 60 °C for 16 h. The reaction mixture was basified with saturated Na_2CO_3 aqueous solution and extracted with EtOAc (3×5 mL). The combined organic phase was washed sat. Na_2CO_3 aqueous solution (5 mL), brine (5 mL) and dried over anhydrous Na_2SO_4. Then the solvent was removed under reduced pressure. 1,3,5-Trimethoxybenzene (8.4 mg, 0.050 mmol, 1.0 equiv.) was added as an internal standard, the mixture was dissolved in $CDCl_3$, and a ^1H NMR spectrum was recorded. The yield of **3a** was determined by ^1H NMR integration relative to the internal standard (standard: δ = 6.09 ppm; typical peak of **3a**: δ = 7.06 ppm (dd, *J* = 5.0, 1.6 Hz, 1H)).

3.2 General procedure E: *para*-Selective alkylation of pyridines enabled by peroxides and peresters

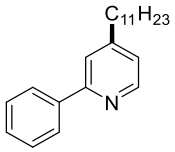


1 **2** **3-5**

Under argon, oxazino pyridine **1** (0.2 mmol, 1.0 equiv.), *p*-toluenesulfonic acid monohydrate TsOH • H_2O or trimethylsilyl trifluoromethanesulfonate TMSOTf (0.3 mmol, 1.5 equiv.) were dissolved in acetone (2.0 mL, when TMSOTf as the acid, 99.9% extra-dry acetone over molecular sieves was used) in an oven-dried 10 mL Schlenk tube equipped with a stir bar. A diacyl peroxides or a perester **2** (0.4-0.5 mmol, 2.0-2.5 equiv.) was added and the reaction mixture was heated at 60 °C for 12-24 h. After cooling down to room temperature, 6 N HCl (4.0 mL) was added to the reaction mixture and the tube was heated at 60 °C for 16 h. The reaction mixture was basified with saturated Na_2CO_3 aqueous solution and extracted with EtOAc (3×10 mL). The combined organic phase was washed with saturated Na_2CO_3 aqueous solution (10 mL), brine (10 mL) and dried over anhydrous Na_2SO_4. Then the solvent was removed under reduced pressure. The residue was purified by column chromatography (SiO_2; *n*-pentane/EtOAc) to give pyridine **3-5**. If necessary, further purification was accomplished by MPLC.

4. Spectral data of products

2-Phenyl-4-undecylpyridine (3a)



Pyridine **3a** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), lauroyl peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3a** was obtained as a yellow oil (45.9 mg, 75%).

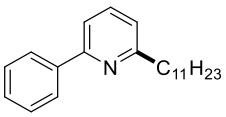
TLC: Rf = 0.50 (*n*-pentane/EtOAc = 10/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.01-7.94 (m, 2H), 7.54 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.51-7.35 (m, 3H), 7.06 (dd, *J* = 5.1, 1.6 Hz, 1H), 2.70-2.61 (m, 2H), 1.73-1.59 (m, 2H), 1.39-1.23 (m, 16H), 0.88 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.5, 152.7, 149.6, 139.8, 128.9, 128.8, 127.1, 122.6, 121.0, 35.7, 32.0, 30.6, 29.78, 29.75, 29.7, 29.6, 29.5, 29.4, 22.8, 14.3.

Analytical data are in agreement with those reported in the literature.[7]

2-Phenyl-6-undecylpyridine (3a') was prepared from direct alkylation of 2-phenylpyridine.



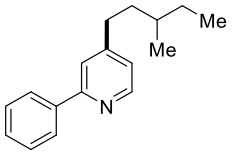
Pyridine **3a'** was prepared according to general procedure E using 2-phenylpyridine (28.6 μL, 0.200 mmol, 1.0 equiv.), lauroyl peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. Purification by flash chromatography (*n*-pentane/EtOAc = 50/1) over silica gel to give the product **3a** in 16% yield and **3a'**. **3a'** was further purified by MPLC (MeCN/H_2O, v/v ratio was 20:80 to 60:40 over 5 min, then kept at 60:40 for 5 min, then increased from 60:40 to 90:10 over 5 min and finally kept at 90:10 for 30 min) to afford pyridine **3a'** as a colourless oil (14.1 mg, 23% yield).

TLC: Rf = 0.50 (*n*-pentane/Et_2O = 100/1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-7.96 (m, 2H), 7.68-7.61 (m, 1H), 7.52 (dd, *J* = 7.87, 1.00 Hz, 1H), 7.50-7.43 (m, 2H), 7.42-7.35 (m, 1H), 7.08 (dd, *J* = 7.61, 0.95 Hz, 1H), 2.89-2.81 (m, 2H), 1.87-1.74 (m, 2H), 1.46-1.20 (m, 16H), 0.94-0.83 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 156.8, 139.9, 136.8, 128.65, 128.64, 127.0, 121.0, 117.7, 38.6, 31.9, 29.8, 29.69, 29.66, 29.63, 29.57, 29.5, 29.4, 22.7, 14.1.

4-(3-Methylpentyl)-2-phenylpyridine (3b)



Pyridine **3b** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2b** (103 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3b** was obtained as a yellow oil (34.5 mg, 73%).

TLC: Rf = 0.64 (*n*-pentane/EtOAc = 20/3)

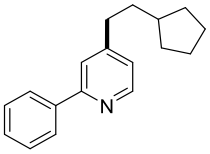
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 5.1, 0.7 Hz, 1H), 8.04-7.95 (m, 2H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.54-7.39 (m, 3H), 7.09 (dd, *J* = 5.1, 1.6 Hz, 1H), 2.81-2.52 (m, 2H), 1.81-1.64 (m, 1H), 1.58-1.35 (m, 3H), 1.32-1.17 (m, 1H), 0.98 (d, *J* = 6.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.6, 152.9, 149.6, 139.8, 128.9, 128.8, 127.1, 122.5, 120.9, 37.5, 34.2, 33.2, 29.4, 19.2, 11.4.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{21}NH$: 240.17450, found: 240.17468.

IR (neat): 2958 (w), 1599 (s), 1555 (m), 1445 (m), 1404 (m), 774 (s), 693 (s).

4-(2-Cyclopentylethyl)-2-phenylpyridine (3c)



Pyridine **3c** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2c** (113 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3c** was obtained as a yellow oil (32.2 mg, 65%).

TLC: Rf = 0.45 (*n*-pentane/EtOAc = 10/1)

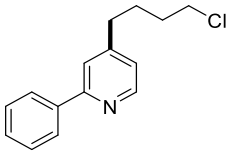
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.02-7.91 (m, 2H), 7.57-7.53 (m, 1H), 7.52-7.36 (m, 3H), 7.06 (dd, *J* = 5.1, 1.6 Hz, 1H), 2.73-2.63 (m, 2H), 1.88-1.75 (m, 3H), 1.73-1.47 (m, 6H), 1.22-1.06 (m, 2H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.5, 152.8, 149.6, 139.8, 128.9, 128.8, 127.1, 122.5, 120.9, 39.7, 37.1, 34.9, 32.7, 25.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{18}H_{21}NNa$: 274.15678, found: 274.15662.

IR (neat): 2942 (w), 1599 (s), 1555 (m), 1445 (m), 1404 (m), 774 (s), 693 (s).

4-(4-Chlorobutyl)-2-phenylpyridine (3d)



Pyridine **3d** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2d** (108 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3d** was obtained as a yellow oil (35.5 mg, 73%).

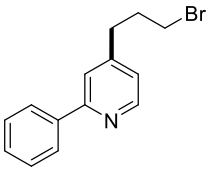
TLC: Rf = 0.37 (*n*-pentane/EtOAc = 20/3)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.02-7.93 (m, 2H), 7.55 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.51-7.36 (m, 3H), 7.06 (dd, *J* = 5.0, 1.6 Hz, 1H), 3.61-3.51 (m, 2H), 2.76-2.66 (m, 2H), 1.90-1.77 (m, 4H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.7, 151.6, 149.8, 139.6, 129.0, 128.8, 127.1, 122.4, 120.8, 44.8, 34.7, 32.0, 27.6.

Analytical data are in agreement with those reported in the literature.[1]

4-(3-bromopropyl)-2-phenylpyridine (3e)



Pyridine **3e** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2e** (129 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **3e** was obtained as a colorless oil (30.8 mg, 56%).

TLC: Rf = 0.13 (*n*-pentane/EtOAc = 10/1)

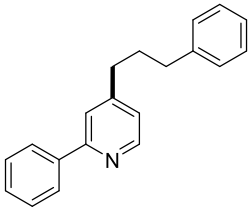
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 5.1, 0.8 Hz, 1H), 8.01-7.91 (m, 2H), 7.57 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.54-7.35 (m, 3H), 7.09 (dd, *J* = 5.1, 1.6 Hz, 1H), 3.57 (t, *J* = 6.3 Hz, 2H), 2.86 (t, *J* = 7.9 Hz, 2H), 2.22-2.07 (m, 2H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.9, 150.5, 149.9, 139.5, 129.1, 128.9, 127.1, 122.5, 121.0, 44.0, 33.1, 32.4.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{14}H_{14}NBrNa$: 298.02018, found: 298.02020.

IR (neat): 1600 (s), 1555 (m), 1474 (m), 1444 (s), 1405 (m), 776 (s), 694 (s).

2-Phenyl-4-(3-phenylpropyl)pyridine (3f)



Pyridine **3f** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2f** (127 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3f** was obtained as a colorless oil (35.6 mg, 65%).

TLC: Rf = 0.40 (*n*-pentane/EtOAc = 10/1)

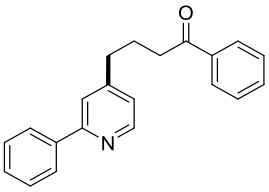
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 5.1, 0.8 Hz, 1H), 8.00-7.93 (m, 2H), 7.54 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.51-7.37 (m, 3H), 7.35-7.27 (m, 2H), 7.24-7.16 (m, 3H), 7.07 (dd, *J* = 5.0, 1.6 Hz, 1H), 2.75-2.65 (m, 4H), 2.09-1.97 (m, 2H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.7, 152.1, 149.7, 141.8, 139.7, 129.0, 128.8, 128.6, 127.1, 126.1, 122.5, 121.0, 35.5, 35.0, 32.0. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{20}H_{19}NNa$: 296.14094, found: 296.14097.

IR (neat): 1600 (s), 1555 (m), 1474 (m), 1444 (s), 1405 (m), 776 (s), 694 (s).

1-Phenyl-4-(2-phenylpyridin-4-yl)butan-1-one (3g)



Pyridine **3g** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2g** (153 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 5/1), pyridine **3g** was obtained as a colorless oil (45.8 mg, 76%).

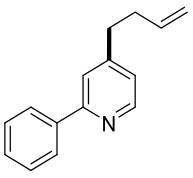
TLC: Rf = 0.35 (*n*-pentane/EtOAc = 10/3)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.01-7.88 (m, 4H), 7.59-7.51 (m, 2H), 7.50-7.37 (m, 5H), 7.09 (dd, *J* = 5.0, 1.6 Hz, 1H), 3.02 (t, *J* = 7.1 Hz, 2H), 2.82-2.72 (m, 2H), 2.21-2.07 (m, 2H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 199.7, 157.7, 151.5, 149.8, 139.5, 136.9, 133.2, 129.0, 128.8, 128.7, 128.1, 127.1, 122.5, 121.0, 37.5, 34.7, 24.6.

Analytical data are in agreement with those reported in the literature.[8]

4-(But-3-en-1-yl)-2-phenylpyridine (3h)



Pyridine **3h** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2h** (79 mg, 0.40 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification

by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3h** was obtained as a colorless oil (24.3 mg, 58%).

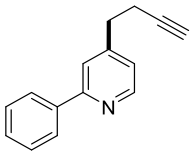
TLC: Rf = 0.44 (*n*-pentane/EtOAc = 10/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.00-7.94 (m, 2H), 7.57-7.52 (m, 1H), 7.52-7.36 (m, 3H), 7.07 (dd, *J* = 5.1, 1.6 Hz, 1H), 5.94-5.75 (m, 1H), 5.12-4.97 (m, 2H), 2.82-2.72 (m, 2H), 2.49-2.38 (m, 2H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.6, 151.6, 149.7, 139.7, 137.2, 129.0, 128.8, 127.1, 122.6, 121.0, 115.9, 35.0, 34.5.

Analytical data are in agreement with those reported in the literature.[9]

4-(But-3-yn-1-yl)-2-phenylpyridine (3i)



Pyridine **3i** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2i** (77.7 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **3i** was obtained as a colorless oil (20.0 mg, 49%).

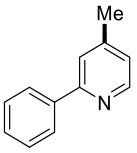
TLC: Rf = 0.23 (*n*-pentane/EtOAc = 10/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (dd, *J* = 5.1, 0.8 Hz, 1H), 8.01-7.94 (m, 2H), 7.61 (dd, *J* = 1.6, 0.8 Hz, 1H), 7.52-7.36 (m, 3H), 7.12 (dd, *J* = 5.0, 1.6 Hz, 1H), 2.90 (t, *J* = 7.3 Hz, 2H), 2.56 (td, *J* = 7.3, 2.6 Hz, 2H), 2.02 (t, *J* = 2.6 Hz, 1H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.7, 149.9, 149.8, 139.6, 129.0, 128.8, 127.1, 122.4, 120.9, 82.9, 69.8, 34.3, 19.6.

Analytical data are in agreement with those reported in the literature.[7]

4-Methyl-2-phenylpyridine (3j)



Pyridine **3j** was prepared according to the modified general procedure E: under argon, oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), DL-10-camphorsulfonic acid (69.7 mg, 0.300 mmol, 1.5 equiv.) were dissolved in acetonitrile (2.0 mL) in an oven-dried 10 mL Schlenk tube equipped with a stir bar. Commercial 50 wt% solution of *tert*-butyl peracetate in odorless mineral spirits **2j** (0.13 mL, 0.40 mmol, 2.0 equiv.) were added and the reaction mixture was heated at 100 °C for 5 h. After cooling down to room temperature, **2j** (0.13 mL, 0.40 mmol, 2.0 equiv.) was added again under argon and the reaction mixture was heated at 100 °C for another 12 h. After completion, 6 N HCl (4.0 mL) was added to the reaction mixture and the tube was heated at 60 °C for 16 h. The reaction mixture was basified with saturated Na_2CO_3 aqueous solution and extracted with EtOAc (10 mL x 3). Then, the organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was purified by column chromatography (SiO_2; *n*-pentane/EtOAc = 10/1) to give pyridine **3j** as colorless oil (11.2 mg, 33% yield).

In situ formed acetyl peroxide as the methyl radical precursor: under argon, acetic anhydride (0.38 mL, 4.0 mmol,

20 equiv.) was slowly added to a suspension of urea•H_2O_2 (135.5 mg, 1.440 mmol, 7.2 equiv.) in dry acetone (1.0 mL) in a 10 mL Schlenk tube equipped with a magnetic stirring bar at room temperature and the mixture was stirred for 5 h. Another 10 mL oven-dried Schlenk tube equipped with a magnetic stirring bar was charged with oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), DL-10-camphorsulfonic acid (DL-10-CSA, 69.7 mg, 0.300 mmol, 1.5 equiv.) and subjected to three cycles of vacuum/argon backfill. Then dry acetone (1.0 mL) was added. Afterwards, the former reaction mixture was transferred to the later tube using a glass pipette under the argon flow. The reaction mixture was stirred at 60 °C for 12 h. When completion, 6 N HCl (4 mL) was added to the reaction mixture and the tube was heated at 60 °C for 16 h. The mixture was basified with saturated Na_2CO_3 aqueous solution and extracted with EtOAc (10 mL, 3 times). The organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent was removed with a rotary evaporator under reduced pressure. The residue was subjected to flash column chromatography (SiO_2; *n*-pentane/EtOAc = 10/1) to give pyridine **3j** as colorless oil (14.8 mg, 44% yield).

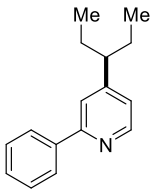
TLC: Rf = 0.60 (*n*-pentane/EtOAc = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.02-7.93 (m, 2H), 7.57-7.53 (m, 1H), 7.51-7.36 (m, 3H), 7.08-7.02 (m, 1H), 2.42 (s, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.5, 149.6, 147.9, 139.7, 128.9, 128.8, 127.1, 123.3, 121.7, 21.4.

Analytical data are in agreement with those reported in the literature.[1]

4-(Pentan-3-yl)-2-phenylpyridine (3k)



Pyridine **3k** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2k** (94.1 mg, 0.500 mmol, 2.5 equiv.), and trimethylsilyl trifluoromethanesulfonate (54.3 μL, 0.300 mmol, 1.5 equiv.) in dry acetone (2.0 mL). The reaction mixture was heated at 60 °C for 24 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3k** was obtained as a colorless oil (37.0 mg, 83%).

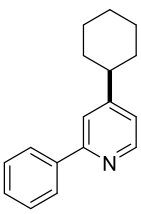
TLC: Rf = 0.73 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.1 Hz, 1H), 8.04-7.95 (m, 2H), 7.52-7.37 (m, 4H), 7.03 (dd, *J* = 5.0, 1.6 Hz, 1H), 2.40 (tt, *J* = 9.4, 5.3 Hz, 1H), 1.81-1.68 (m, 2H), 1.67-1.52 (m, 2H), 0.81 (t, *J* = 7.4 Hz, 6H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.5, 155.8, 149.6, 139.9, 128.9, 128.8, 127.1, 122.0, 120.6, 49.6, 28.8, 12.2.

Analytical data are in agreement with those reported in the literature.[6]

4-Cyclohexyl-2-phenylpyridine (3l)



Pyridine **3l** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2l** (100 mg, 0.500 mmol, 2.5 equiv.), and trimethylsilyl trifluoromethanesulfonate (54.3 μL, 0.300 mmol, 1.5 equiv.) in dry acetone (2.0 mL). The reaction mixture was heated at 60 °C for 24 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3l** was obtained as a yellow oil (36.6 mg, 77%).

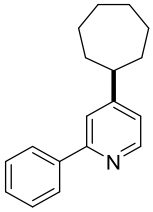
TLC: Rf = 0.70 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (d, *J* = 5.1 Hz, 1H), 8.04-7.93 (m, 2H), 7.56 (d, *J* = 1.6 Hz, 1H), 7.52-7.35 (m, 3H), 7.08 (dd, *J* = 5.1, 1.7 Hz, 1H), 2.57 (tt, *J* = 11.5, 3.5 Hz, 1H), 1.97-1.84 (m, 4H), 1.83-1.73 (m, 1H), 1.55-1.38 (m, 4H), 1.36-1.22 (m, 1H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.6, 157.5, 149.7, 139.9, 128.9, 128.8, 127.1, 121.0, 119.5, 44.3, 33.7, 26.7, 26.1.

Analytical data are in agreement with those reported in the literature.[7]

4-Cycloheptyl-2-phenylpyridine (3m)



Pyridine **3m** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2m** (107 mg, 0.500 mmol, 2.5 equiv.), and trimethylsilyl trifluoromethanesulfonate (54.3 μL, 0.300 mmol, 1.5 equiv.) in dry acetone (2.0 mL). The reaction mixture was heated at 60 °C for 24 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **3m** was obtained as a yellow oil (39.2 mg, 78%).

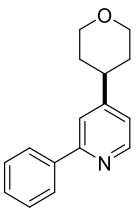
TLC: Rf = 0.75 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (d, *J* = 5.1 Hz, 1H), 8.03-7.94 (m, 2H), 7.54 (d, *J* = 1.6 Hz, 1H), 7.51-7.36 (m, 3H), 7.06 (dd, *J* = 5.1, 1.6 Hz, 1H), 2.72 (tt, *J* = 10.3, 3.6 Hz, 1H), 2.00-1.90 (m, 2H), 1.88-1.78 (m, 2H), 1.76-1.52 (m, 8H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 159.3, 157.6, 149.7, 139.9, 128.84, 128.78, 127.1, 120.9, 119.4, 46.7, 36.1, 28.0, 27.3.

Analytical data are in agreement with those reported in the literature.[7]

2-Phenyl-4-(tetrahydro-2*H*-pyran-4-yl)pyridine (3n)



Pyridine **3n** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2n** (101 mg, 0.500 mmol, 2.5 equiv.), and trimethylsilyl trifluoromethanesulfonate (54.3 μL, 0.300 mmol, 1.5 equiv.) in dry acetone (2.0 mL). The reaction mixture was heated at 60 °C for 24 h. After purification

by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **3n** was obtained as a yellow oil (33.8 mg, 71%).

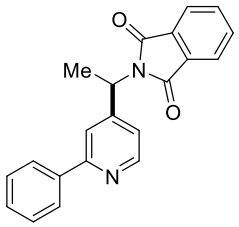
TLC: Rf = 0.33 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, *J* = 5.1 Hz, 1H), 8.01-7.94 (m, 2H), 7.59-7.55 (m, 1H), 7.52-7.37 (m, 3H), 7.10 (dd, *J* = 5.1, 1.6 Hz, 1H), 4.18-4.07 (m, 2H), 3.63-3.47 (m, 2H), 2.83 (tt, *J* = 10.8, 5.2 Hz, 1H), 1.97-1.75 (m, 4H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.9, 155.2, 150.0, 139.6, 129.0, 128.8, 127.1, 120.7, 119.3, 68.1, 41.2, 33.1.

Analytical data are in agreement with those reported in the literature.[7]

2-(1-(2-Phenylpyridin-4-yl)ethyl)isoindoline-1,3-dione (3o)



Pyridine **3o** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2o** (233 mg, 0.800 mmol, 4.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 24 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **3o** was obtained as a yellow oil (21.0 mg, 33%).

TLC: Rf = 0.20 (*n*-pentane/EtOAc = 5/1)

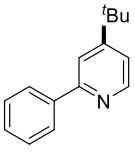
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.99-7.91 (m, 2H), 7.88-7.81 (m, 2H), 7.80-7.77 (m, 1H), 7.75-7.69 (m, 2H), 7.49-7.38 (m, 3H), 7.35-7.31 (m, 1H), 5.59 (q, *J* = 7.3 Hz, 1H), 1.96 (d, *J* = 7.3 Hz, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 168.1, 158.2, 150.1, 149.7, 139.4, 134.3, 131.9, 129.2, 128.8, 127.2, 123.6, 120.8, 119.4, 48.8, 17.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{21}H_{16}N_2O_2Na$: 351.11040, found: 351.11031.

IR (neat): 1774 (w), 1707 (s), 1383 (s), 1354 (m), 1145 (w), 1046 (w), 879 (w), 721 (m), 695 (m).

4-(*tert*-Butyl)-2-phenylpyridine (3p)



Pyridine **3p** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2p** (69.7 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **3p** was obtained as a colorless oil (30.2 mg, 72%).

TLC: Rf = 0.39 (*n*-pentane/EtOAc = 20/3)

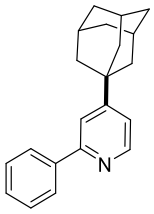
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, *J* = 5.3 Hz, 1H), 8.01-7.94 (m, 2H), 7.73-7.69 (m, 1H), 7.52-7.37 (m, 3H),

7.24 (dd, J = 5.3, 1.8 Hz, 1H), 1.37 (s, 9H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 160.9, 157.8, 149.8, 140.3, 128.94, 128.90, 127.3, 119.6, 118.0, 35.1, 30.8.

Analytical data are in agreement with those reported in the literature.[1]

4-(Adamantan-1-yl)-2-phenylpyridine (3q)



Pyridine **3q** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2q** (101 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 25/2), pyridine **3q** was obtained as a colorless oil (42.1 mg, 73%).

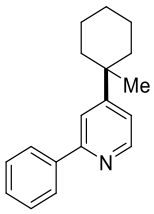
TLC: Rf = 0.70 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, J = 5.3 Hz, 1H), 8.02-7.93 (m, 2H), 7.71-7.64 (m, 1H), 7.52-7.35 (m, 3H), 7.21 (dd, J = 5.3, 1.8 Hz, 1H), 2.18-2.11 (m, 3H), 1.97-1.94 (m, 6H), 1.87-1.73 (m, 6H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 160.7, 157.6, 149.6, 140.2, 128.7, 127.1, 119.0, 117.5, 42.5, 36.6, 36.5, 28.7. (One carbon signal is missing due to overlap.)

Analytical data are in agreement with those reported in the literature.[7]

4-(1-Methylcyclohexyl)-2-phenylpyridine (3r)



Pyridine **3r** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2r** (85.7 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **3r** was obtained as a colourless oil (37.4 mg, 75%).

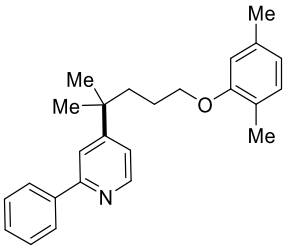
TLC: Rf = 0.78 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (dd, J = 5.3, 0.8 Hz, 1H), 8.03-7.88 (m, 2H), 7.70 (dd, J = 2.0, 0.8 Hz, 1H), 7.52-7.37 (m, 3H), 7.23 (dd, J = 5.3, 1.9 Hz, 1H), 2.11-1.99 (m, 2H), 1.68-1.56 (m, 4H), 1.49-1.40 (m, 4H), 1.23 (s, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 159.8, 157.7, 149.7, 140.1, 128.7, 127.1, 120.1, 118.5, 38.3, 37.3, 30.2, 26.2, 22.6. (One carbon signal is missing due to overlap.)

Analytical data are in agreement with those reported in the literature.[7]

4-(5-(2,5-Dimethylphenoxy)-2-methylpentan-2-yl)-2-phenylpyridine (3s)



Pyridine **3s** was prepared according to general procedure E using oxazino pyridine **1a** (79.9 mg, 0.200 mmol, 1.0 equiv.), perester **2s** (129 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **3s** was obtained as a colorless oil (41.0 mg, 58%).

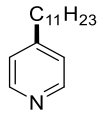
TLC: Rf = 0.36 (*n*-pentane/EtOAc = 10/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (d, *J* = 5.2 Hz, 1H), 8.04-7.95 (m, 2H), 7.74-7.68 (m, 1H), 7.53-7.38 (m, 3H), 7.24 (dd, *J* = 5.4, 1.8 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 6.57 (s, 1H), 3.88 (t, *J* = 6.1 Hz, 2H), 2.29 (s, 3H), 2.17 (s, 3H), 1.94-1.85 (m, 2H), 1.68-1.53 (m, 2H), 1.41 (s, 6H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 159.2, 157.7, 157.0, 149.7, 140.1, 136.6, 130.4, 128.9, 128.8, 127.2, 123.6, 120.8, 120.0, 118.4, 112.0, 68.0, 40.2, 37.9, 28.5, 25.1, 21.5, 15.9.

Analytical data are in agreement with those reported in the literature.[7]

4-Undecylpyridine (4a)



Pyridine **4a** was prepared according to general procedure E using oxazino pyridine **1b** (64.7 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **4a** was obtained as a yellow oil (26.3 mg, 57%).

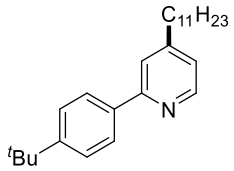
TLC: Rf = 0.28 (*n*-pentane/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50-8.40 (m, 2H), 7.13-7.06 (m, 2H), 2.58 (t, *J* = 6.8 Hz, 3H), 1.67-1.51 (m, 2H), 1.33-1.17 (m, 16H), 0.87 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 152.0, 149.6, 124.1, 35.4, 32.0, 30.4, 29.8, 29.7, 29.6, 29.53, 29.46, 29.3, 22.8, 14.2.

Analytical data are in agreement with those reported in the literature.[10]

2-(4-(*tert*-Butyl)phenyl)-4-undecylpyridine (4b)



Pyridine **4b** was prepared according to general procedure E using oxazino pyridine **1c** (91.1 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 25/2), pyridine **4b** was obtained as a yellow oil (47.5 mg, 66%).

TLC: Rf = 0.77 (*n*-pentane/EtOAc = 5/1)

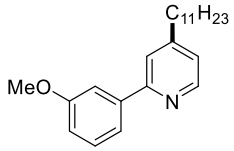
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.55 (dd, *J* = 5.0, 0.8 Hz, 1H), 7.97-7.88 (m, 2H), 7.54-7.52 (m, 1H), 7.51-7.47 (m, 2H), 7.03 (dd, *J* = 5.0, 1.6 Hz, 1H), 2.71-2.60 (m, 2H), 1.74-1.59 (m, 2H), 1.37 (s, 9H), 1.35-1.22 (m, 16H), 0.92-0.84 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 157.5, 152.5, 152.0, 149.5, 137.0, 126.7, 125.7, 122.3, 120.7, 35.6, 34.8, 32.0, 31.4, 30.6, 29.8, 29.74, 29.66, 29.6, 29.5, 29.3, 22.8, 14.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{26}H_{39}NNa$: 388.29747, found: 388.29771.

IR (neat): 2955 (m), 2923 (s), 2853 (m), 1601 (s), 1467 (s), 1270 (w), 1114 (w), 824 (s).

2-(3-Methoxyphenyl)-4-undecylpyridine (4c)



Pyridine **4c** was prepared according to general procedure E using oxazino pyridine **1d** (85.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **4c** was obtained as a yellow oil (37.9 mg, 56%).

TLC: Rf = 0.55 (*n*-pentane/EtOAc = 5/1)

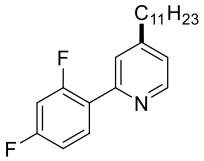
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.57 (dd, *J* = 2.6, 1.6 Hz, 1H), 7.56-7.51 (m, 2H), 7.41-7.33 (m, 1H), 7.06 (dd, *J* = 5.1, 1.6 Hz, 1H), 7.00-6.92 (m, 1H), 3.90 (s, 3H), 2.71-2.61 (m, 2H), 1.73-1.55 (m, 2H), 1.39-0.97 (m, 16H), 0.92-0.75 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 160.1, 157.3, 152.7, 149.5, 141.3, 129.8, 122.7, 121.1, 119.5, 115.0, 112.2, 55.5, 35.6, 32.0, 30.6, 29.8, 29.74, 29.66, 29.6, 29.5, 29.4, 22.8, 14.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{23}H_{33}NONa$: 362.24544, found: 362.24535.

IR (neat): 2923 (s), 2852 (s), 1598 (s), 1556 (m), 1462 (s), 1433 (m), 1225 (s), 1044 (s), 784 (s), 693 (s).

2-(2,4-Difluorophenyl)-4-undecylpyridine (4d)



Pyridine **4d** was prepared according to general procedure E using oxazino pyridine **1e** (87.1 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **4d** was obtained as a yellow oil (52.0 mg, 72%).

TLC: Rf = 0.60 (*n*-pentane/EtOAc = 10/1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 5.0, 0.8 Hz, 1H), 8.01-7.92 (m, 1H), 7.58-7.53 (m, 1H), 7.07 (dd, *J* = 5.1, 1.6 Hz, 1H), 7.02-6.95 (m, 1H), 6.93-6.85 (m, 1H), 2.65 (t, 2H), 1.71-1.60 (m, 2H), 1.34-1.21 (m, 16H), 0.87 (t, *J* = 6.7 Hz, 3H).

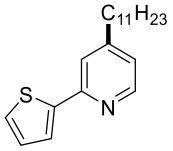
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2 (dd, *J* = 250.3, 11.9 Hz), 160.6 (dd, *J* = 253.2, 11.9 Hz), 152.6 (d, *J* = 2.6 Hz), 152.5, 149.7, 132.3 (dd, *J* = 9.7, 4.6 Hz), 124.6 (d, *J* = 8.7 Hz), 122.9, 111.9 (dd, *J* = 21.0, 3.7 Hz), 104.5 (d, *J* = 25.4 Hz), 104.3 (d, *J* = 25.3 Hz), 35.6, 32.0, 30.5, 29.8, 29.74, 29.66, 29.54, 29.46, 29.3, 22.8, 14.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -109.7 (d, *J* = 8.4 Hz), -112.8 (d, *J* = 8.4 Hz).

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{22}H_{29}NF_2H$: 346.23395, found: 346.23408.

IR (neat): 2924 (s), 2853 (m), 1063 (s), 1557 (m), 1504 (m), 1469 (m), 1431 (m), 1399 (m), 1262 (m), 1138 (m), 1104 (m), 968 (s), 848 (s), 817 (m).

2-(Thiophen-2-yl)-4-undecylpyridine (4e)



Pyridine **4e** was prepared according to general procedure E using oxazino pyridine **1f** (81.1 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **4e** was obtained as a yellow oil (36.5 mg, 58%).

TLC: Rf = 0.75 (*n*-pentane/EtOAc = 20/3)

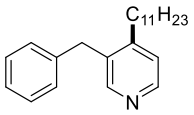
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.57 (dd, *J* = 3.7, 1.2 Hz, 1H), 7.50-7.43 (m, 1H), 7.37 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.10 (dd, *J* = 5.1, 3.6 Hz, 1H), 6.97 (dd, *J* = 5.1, 1.6 Hz, 1H), 2.67-2.55 (m, 2H), 1.71-1.53 (m, 2H), 1.37-1.18 (m, 16H), 0.93-0.81 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 152.6, 152.5, 149.5, 145.2, 128.1, 127.4, 124.3, 122.5, 119.0, 35.5, 32.0, 30.5, 29.8, 29.73, 29.65, 29.55, 29.46, 29.3, 22.8, 14.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{20}H_{29}NSNa$: 338.19129, found: 338.19112.

IR (neat): 2922 (s), 2851 (m), 1599 (s), 1553 (m), 1468 (m), 1438 (m), 1401 (m), 822 (w), 700 (s).

3-Benzyl-4-undecylpyridine (4f)



Pyridine **4f** was prepared according to general procedure E using oxazino pyridine **1g** (82.7 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **4f** was obtained as a yellow oil (32.0 mg, 50%).

TLC: Rf = 0.15 (*n*-pentane/EtOAc = 5/1)

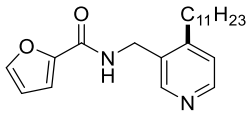
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, *J* = 5.0 Hz, 1H), 8.36 (s, 1H), 7.31-7.23 (m, 2H), 7.22-7.14 (m, 1H), 7.13-7.04 (m, 3H), 4.01 (s, 2H), 2.59-2.44 (m, 2H), 1.44 (dd, *J* = 9.8, 5.6 Hz, 2H), 1.24 (d, *J* = 6.6 Hz, 16H), 0.93-0.80 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 151.3, 150.4, 148.2, 139.9, 134.2, 128.7, 128.6, 126.4, 124.2, 36.4, 32.3, 32.0, 29.8, 29.73, 29.72, 29.64, 29.61, 29.51, 29.46, 22.8, 14.3.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{33}NH$: 324.26827, found: 324.26858.

IR (neat): 2922 (s), 2852 (m), 1593 (m), 1494 (m), 1453 (m), 1410 (m), 1197 (w), 727 (s), 697 (s).

***N*-((4-undecylpyridin-3-yl)methyl)furan-2-carboxamide (4g)**



Pyridine **4g** was prepared according to general procedure E using oxazino pyridine **1h** (89.3 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (EtOAc), pyridine **4g** was obtained as a yellow oil (32.1 mg, 45%).

TLC: Rf = 0.46 (EtOAc)

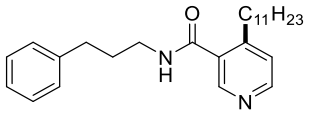
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (s, 1H), 8.45 (d, *J* = 5.0 Hz, 1H), 7.41 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.18-7.05 (m, 2H), 6.56-6.44 (m, 2H), 4.65 (d, *J* = 5.6 Hz, 2H), 2.73-2.58 (m, 2H), 1.67-1.49 (m, 2H), 1.38-1.03 (m, 16H), 0.97-0.75 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 158.1, 150.8, 150.4, 149.5, 147.7, 144.2, 131.3, 124.4, 114.8, 112.4, 38.5, 32.03, 31.99, 30.5, 29.73, 29.69, 29.62, 29.60, 29.5, 22.8, 14.3. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{22}H_{32}N_2O_2Na$: 379.23560, found: 379.23630.

IR (neat): 2923 (s), 2852 (m), 1655 (s), 1594 (s), 1527 (m), 1469 (m), 1300 (m), 1182 (w), 1101 (w), 754 (m).

***N*-(3-phenylpropyl)-4-undecylnicotinamide (4h)**



Pyridine **4h** was prepared according to general procedure E using oxazino pyridine **1i** (96.9 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 1/1), pyridine **4h** was obtained as a brown solid (48.8 mg, 62%).

TLC: Rf = 0.45 (EtOAc)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50-8.34 (m, 2H), 7.35-7.24 (m, 2H), 7.22-7.16 (m, 3H), 7.13 (d, *J* = 5.1 Hz, 1H), 6.23 (t, *J* = 5.9 Hz, 1H), 3.47 (td, *J* = 7.0, 5.8 Hz, 2H), 2.82-2.59 (m, 4H), 2.04-1.87 (m, 2H), 1.64-1.49 (m, 2H), 1.35-1.16 (m, 16H), 0.92-0.76 (m, 3H).

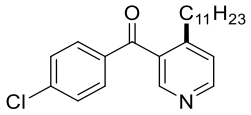
^{13}C NMR (76 MHz, $CDCl_3$) δ 167.7, 150.8, 150.6, 147.3, 141.3, 132.6, 128.7, 128.4, 126.2, 124.9, 39.8, 33.5, 32.7, 32.0, 31.3, 30.7, 29.73, 29.72, 29.68, 29.6, 29.5, 29.4, 22.8, 14.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{26}H_{38}N_2ONa$: 417.28764, found: 417.28769.

IR (neat): 2923 (s), 2852 (m), 1638 (s), 1561 (m), 1538 (m), 1454 (m), 698 (s).

Mp: 50-51 °C.

(4-Chlorophenyl)(4-undecylpyridin-3-yl)methanone (4i)



Pyridine **4i** was prepared according to general procedure E using oxazino pyridine **1j** (80.2 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (DCM/EtOAc = 10/1), pyridine **4i** was obtained as a yellow solid (32.0 mg, 43%).

TLC: Rf = 0.34 (DCM/EtOAc = 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, *J* = 5.2 Hz, 1H), 8.48 (s, 1H), 7.84-7.69 (m, 2H), 7.51-7.40 (m, 2H), 7.27 (d, *J* = 5.0 Hz, 1H), 2.69-2.61 (m, 2H), 1.59-1.44 (m, 2H), 1.30-1.17 (m, 16H), 0.86 (t, *J* = 6.7 Hz, 3H).

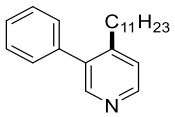
^{13}C NMR (76 MHz, $CDCl_3$) δ 195.3, 151.5, 151.3, 149.0, 140.5, 135.8, 134.2, 131.6, 129.2, 125.1, 32.8, 32.0, 30.8, 29.70, 29.69, 29.5, 29.4, 29.3, 22.8, 14.3. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{23}H_{30}NOClNa$: 394.19081, found: 394.19086.

IR (neat): 2923 (s), 2852 (m), 1666 (s), 1585 (s), 1275 (s), 1092 (s), 923 (s), 848 (s).

Mp: 48-50 °C.

3-Phenyl-4-undecylpyridine (4j)



Pyridine **4j** was prepared according to general procedure E using oxazino pyridine **1k** (79.8 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **4j** was obtained as a yellow oil (32.8 mg, 53%).

TLC: Rf = 0.46 (*n*-pentane/EtOAc = 20/3)

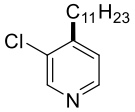
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 5.1 Hz, 1H), 8.41 (s, 1H), 7.48-7.35 (m, 3H), 7.32-7.27 (m, 2H), 7.20 (d, *J* = 5.1 Hz, 1H), 2.64-2.51 (m, 2H), 1.55-1.41 (m, 2H), 1.30-1.13 (m, 16H), 0.87 (t, *J* = 6.7 Hz, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 150.3, 149.3, 148.6, 138.1, 137.7, 129.5, 128.5, 127.6, 124.0, 32.4, 32.0, 30.4, 29.7, 29.52, 29.45, 29.4, 29.3, 22.8, 14.3. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{22}H_{31}NNa$: 332.23487, found: 332.23481.

IR (neat): 2924 (s), 2853 (m), 1589 (w), 1465 (w), 1444 (w), 1440 (w), 761 (w), 702 (m).

3-Chloro-4-undecylpyridine (4k)



Pyridine **4k** was prepared according to general procedure E using oxazino pyridine **1l** (71.5 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **4k** was obtained as a yellow oil (28.5 mg, 40%).

TLC: Rf = 0.72 (*n*-pentane/EtOAc = 5/1).

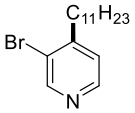
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.35 (d, *J* = 5.0 Hz, 1H), 7.13 (d, *J* = 4.9 Hz, 1H), 2.76-2.65 (m, 2H), 1.67-1.53 (m, 2H), 1.39-1.22 (m, 16H), 0.90-0.83 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 149.4, 149.3, 147.7, 132.2, 124.9, 32.9, 32.0, 29.7, 29.6, 29.5, 29.5, 29.4, 28.9, 22.8, 14.3. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{26}NClH$: 268.18265, found: 268.18263.

IR (neat): 2923 (s), 2852 (m), 1584 (w), 1465 (w), 1399 (w), 1094 (w), 1031 (w), 722 (w).

3-Bromo-4-undecylpyridine (4l)



Pyridine **4l** was prepared according to general procedure E using oxazino pyridine **1m** (80.2 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 20/1), pyridine **4l** was obtained as a yellow oil (36.0 mg, 45%).

TLC: Rf = 0.72 (*n*-pentane/EtOAc = 5/1)

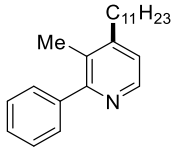
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.41 (d, *J* = 4.9 Hz, 1H), 7.16 (d, *J* = 4.9 Hz, 1H), 2.79-2.67 (m, 2H), 1.70-1.53 (m, 2H), 1.37-1.22 (m, 16H), 0.93-0.86 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 151.9, 151.0, 148.2, 125.2, 123.3, 35.5, 32.0, 29.7, 29.6, 29.5, 29.4, 29.0, 22.8, 14.3. (Two carbon signals are missing due to overlap.)

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{26}NBrH$: 312.13214, found: 312.13211.

IR (neat): 2923 (s), 2852 (m), 1582 (w), 1466 (w), 1398 (w), 1085 (w), 1018 (w), 722 (w).

3-Methyl-2-phenyl-4-undecylpyridine (4m)



Pyridine **4m** was prepared according to general procedure E using oxazino pyridine **1n** (82.7 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc = 10/1), pyridine **4m** was obtained as a yellow oil (31.0 mg, 48%).

TLC: Rf = 0.18 (*n*-pentane/EtOAc = 10/1)

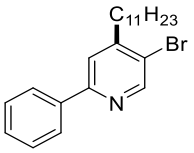
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (d, *J* = 4.9 Hz, 1H), 7.50-7.32 (m, 5H), 7.06 (d, *J* = 4.9 Hz, 1H), 2.65 (t, *J* = 8.0 Hz, 2H), 2.25 (s, 3H), 1.69-1.54 (m, 2H), 1.45-1.18 (m, 16H), 0.92-0.82 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 159.3, 151.1, 146.5, 141.5, 129.2, 128.2, 127.7, 122.7, 33.4, 32.0, 29.80, 29.79, 29.76, 29.7, 29.6, 29.53, 29.48, 22.8, 16.0, 14.3. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{23}H_{33}NH$: 324.26827, found: 324.26858.

IR (neat): 2922 (s), 2852 (m), 1583 (w), 1464 (w), 1402 (w), 1007 (w), 755 (w), 700 (s).

5-Bromo-2-phenyl-4-undecylpyridine (4n)



Pyridine **4n** was prepared according to general procedure E using oxazino pyridine **1o** (95.5 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/Et_2O = 20/1), pyridine **4n** was obtained as a colourless oil (42.5 mg, 55%).

TLC: Rf = 0.75 (*n*-pentane/Et_2O = 10/1).

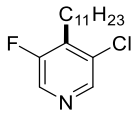
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (s, 1H), 8.03-7.92 (m, 2H), 7.56 (s, 1H), 7.52-7.39 (m, 3H), 2.82-2.69 (m, 2H), 1.75-1.59 (m, 2H), 1.45-1.24 (m, 16H), 0.95-0.84 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 156.4, 151.7, 151.5, 138.6, 129.3, 128.9, 126.9, 122.1, 121.8, 35.8, 32.0, 29.78, 29.76, 29.7, 29.52, 29.48, 29.2, 22.8, 14.3. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{22}H_{30}NBrNa$: 410.14528, found: 410.14528.

IR (neat): 2923 (s), 2852 (m), 1589 (w), 1577 (w), 1463 (m), 1442 (m), 1367 (w), 776 (m), 692 (m).

3-Chloro-5-fluoro-4-undecylpyridine (4o)



Pyridine **4o** was prepared according to general procedure E using oxazino pyridine **1p** (75.1 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/Et_2O = 30/1), pyridine **4o** was obtained as a colorless oil (24.0 mg, 42%).

TLC: Rf = 0.87 (*n*-pentane/Et_2O = 10/1)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.29 (s, 1H), 2.83-2.67 (m, 2H), 1.63-1.54 (m, 2H), 1.39-1.24 (m, 16H), 0.92-0.84 (m, 3H).

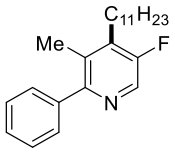
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3 (d, *J* = 257.9 Hz), 145.3 (d, *J* = 4.4 Hz), 137.3 (d, *J* = 16.4 Hz), 135.9 (d, *J* = 25.4 Hz), 132.5 (d, *J* = 1.9 Hz), 32.1, 29.7, 29.6, 29.53, 29.47, 29.4, 28.34, 28.33, 26.2 (d, *J* = 1.8 Hz), 22.8, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -129.9.

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{16}H_{25}NFClH$: 286.17323, found: 286.17310.

IR (neat): 2925 (s), 2854 (m), 1554 (w), 1465 (w), 881 (w), 771 (w).

5-Fluoro-3-methyl-2-phenyl-4-undecylpyridine (4p)



Pyridine **4p** was prepared according to general procedure E using oxazino pyridine **1q** (86.3 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/Et_2O = 30/1), pyridine **4p** was obtained as a colourless oil (36.5 mg, 54%).

TLC: Rf = 0.62 (*n*-pentane/Et_2O = 20/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.45-7.36 (m, 5H), 2.77-2.66 (m, 2H), 2.28 (s, 3H), 1.63-1.50 (m, 2H), 1.45-1.21 (m, 16H), 0.92-0.83 (m, 3H).

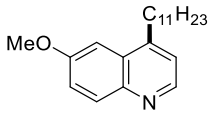
^{13}C NMR (76 MHz, $CDCl_3$) δ 157.6 (d, *J* = 252.6 Hz), 155.5 (d, *J* = 4.4 Hz), 140.9, 137.9 (d, *J* = 13.1 Hz), 134.3 (d, *J* = 25.5 Hz), 131.0 (d, *J* = 1.9 Hz), 129.2, 128.3, 127.9, 32.0, 29.9, 29.8, 29.75, 29.67, 29.52, 29.47, 29.0, 26.0 (d, *J* = 3.1 Hz), 22.8, 16.3 (d, *J* = 1.7 Hz), 14.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ -135.1.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{23}H_{32}NFNa$: 364.24110, found: 364.24124.

IR (neat): 2923 (s), 2853 (m), 1462 (m), 1395 (m), 1260 (m), 755 (m), 716 (m), 699 (s).

2-Methyl-5-undecyl-1,8-naphthyridine (4q)



Pyridine **4q** was prepared according to general procedure E using oxazino pyridine **1r** (80.7 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc= 10/1), pyridine **4q** was obtained as a white solid (22.2 mg, 36%).

TLC: Rf = 0.28 (*n*-pentane/EtOAc= 5/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.4 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.35 (dd, *J* = 9.2, 2.8 Hz, 1H), 7.24 (d, *J* = 2.8 Hz, 1H), 7.18 (d, *J* = 4.4 Hz, 1H), 3.95 (s, 3H), 3.05-2.88 (m, 2H), 1.83-1.67 (m, 2H), 1.46-1.18 (m, 16H), 0.92-0.83 (m, 3H).

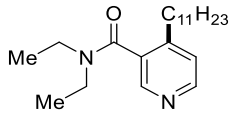
^{13}C NMR (76 MHz, $CDCl_3$) δ 157.6, 147.9, 147.3, 144.5, 131.8, 128.6, 121.3, 121.1, 101.9, 55.6, 32.4, 32.0, 29.80, 29.78, 29.75, 29.70, 29.6, 29.5, 22.8, 14.3. (One carbon signal is missing due to overlap.)

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{21}H_{31}NONa$: 336.22979, found: 336.22979.

IR (neat): 2923 (s), 2852 (m), 1620 (m), 1508 (m), 1470 (m), 1240 (m), 1227 (s), 1034 (s), 844 (m).

Mp: 54-55 °C.

***N,N*-Diethyl-4-undecylnicotinamide (5a)**



Pyridine **5a** was prepared according to general procedure E using oxazino pyridine **1s** (84.5 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (*n*-pentane/EtOAc= 1/1), pyridine **5a** was obtained as a yellow oil (37.2 mg, 56%).

TLC: Rf = 0.46 (EtOAc)

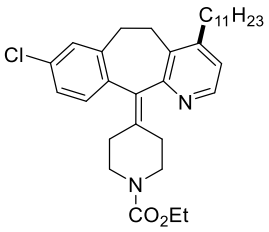
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, *J* = 5.1 Hz, 1H), 8.37 (s, 1H), 7.16 (d, *J* = 5.1 Hz, 1H), 3.90-3.24 (m, 2H), 3.11 (q, *J* = 7.1 Hz, 2H), 2.56 (t, *J* = 8.0 Hz, 2H), 1.66-1.51 (m, 2H), 1.35-1.16 (m, 19H), 1.06 (t, *J* = 7.1 Hz, 3H), 0.88-0.80 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 168.2, 149.8, 148.6, 146.3, 133.0, 124.3, 43.0, 39.0, 32.6, 32.0, 29.9, 29.7, 29.6, 29.5, 29.4, 22.8, 14.22, 14.18, 12.8.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{21}H_{36}N_2ONa$: 355.27199, found: 355.27213.

IR (neat): 2923 (s), 2853 (m), 1632 (s), 1456 (w), 1428 (w), 1286 (m), 1100 (m).

Ethyl 4-(8-chloro-4-undecyl-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (5b)



Pyridine **5b** was prepared according to general procedure E using oxazino pyridine **1t** (125 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. Purification by flash chromatography (*n*-pentane/EtOAc= 1/2) afforded crude **5b**, which was further purified by MPLC (MeCN/H_2O, v/v ratio was 20:80 to 60:40 over 10 min, then kept at 60:40 for 10 min, then increased from 60:40 to 90:10 over 5 min and finally kept at 90:10 for 10 min) to afford pyridine **5b** as a brown gum (75.1 mg, 70%).

TLC: Rf = 0.67 (EtOAc)

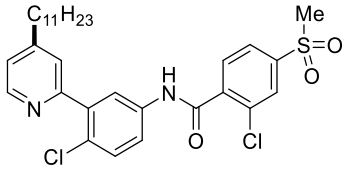
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, *J* = 5.0 Hz, 1H), 7.17-7.06 (m, 3H), 6.96 (d, *J* = 5.0 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.86-3.71 (m, 2H), 3.45-3.30 (m, 1H), 3.27-3.04 (m, 3H), 3.00-2.73 (m, 2H), 2.64-2.53 (m, 2H), 2.43-2.34 (m, 3H), 2.26-2.14 (m, 1H), 1.61-1.49 (m, 2H), 1.34-1.14 (m, 19H), 0.92-0.78 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 158.5, 155.6, 150.1, 146.6, 139.3, 136.8, 136.6, 134.9, 132.9, 131.6, 131.1, 129.5, 126.1, 123.1, 61.4, 44.9, 44.8, 32.7, 32.1, 32.0, 30.7, 30.1, 29.8, 29.74, 29.66, 29.6, 29.5, 26.6, 22.8, 14.8, 14.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{33}H_{45}N_2O_2ClNa$: 559.30618, found: 559.30573.

IR (neat): 2925 (w), 2854 (w), 1689 (m), 1432 (m), 1222 (m), 1116 (w), 747 (s), 664 (m).

2-Chloro-*N*-(4-chloro-3-(4-undecylpyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (5c)



Pyridine **5c** was prepared according to general procedure E using oxazino pyridine **1u** (133 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 °C for 12 h. After purification by flash chromatography (DCM/EtOAc= 10/3), pyridine **5c** was obtained as a brown oil (49.5 mg, 44%).

TLC: Rf = 0.30 (DCM/EtOAc= 10/3)

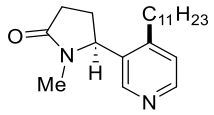
^{1}H NMR (300 MHz, $CDCl_3$) δ 10.20 (s, 1H), 8.13 (d, *J* = 5.1 Hz, 1H), 8.04 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.84 (d, *J* = 1.7 Hz, 1H), 7.69-7.60 (m, 2H), 7.52-7.42 (m, 3H), 6.96 (dd, *J* = 5.2, 1.7 Hz, 1H), 2.97 (s, 3H), 2.68-2.55 (m, 2H), 1.66-1.51 (m, 2H), 1.35-1.15 (m, 16H), 0.91-0.79 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 164.1, 155.6, 152.8, 148.5, 142.6, 140.9, 138.8, 137.2, 132.3, 131.0, 130.0, 128.9, 127.3, 125.8, 125.7, 123.2, 123.0, 121.8, 44.5, 35.4, 32.0, 30.3, 29.8, 29.7, 29.6, 29.49, 29.46, 29.4, 22.8, 14.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{30}H_{36}N_2O_3SCl_2Na$: 597.17159, found: 597.17134.

IR (neat): 2924 (m), 2853 (w), 1683 (m), 1603 (m), 1543 (m), 1463 (m), 1377 (m), 1316 (s), 1154 (s), 753 (w).

***(S)*-1-Methyl-5-(4-undecylpyridin-3-yl)pyrrolidin-2-one (5d)**



Pyridine **5d** was prepared according to general procedure E using oxazino pyridine **1v** (84.1 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.) and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 ºC for 12 h. After purification by flash chromatography (EtOAc), pyridine **5d** was obtained as a brown oil (25.4 mg, 39%).

TLC: Rf = 0.25 (EtOAc)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, *J* = 5.1 Hz, 1H), 8.28 (s, 1H), 7.12 (d, *J* = 5.0 Hz, 1H), 4.87-4.78 (m, 1H), 2.71 (s, 3H), 2.66-2.57 (m, 2H), 2.55-2.42 (m, 3H), 1.89-1.78 (m, 1H), 1.65-1.52 (m, 2H), 1.39-1.21 (m, 16H), 0.90-0.76 (m, 3H).

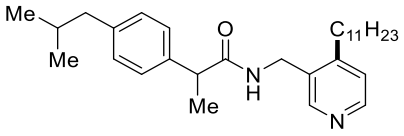
^{13}C NMR (76 MHz, $CDCl_3$) δ 175.6, 149.4, 149.0, 147.3, 134.2, 124.5, 58.8, 32.0, 31.8, 30.6, 29.9, 29.7, 29.64, 29.61, 29.53, 29.46, 29.4, 28.6, 27.9, 22.8, 14.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{21}H_{34}N_2ONa$: 353.25633, found: 353.25609.

IR (neat): 2924 (m), 2853 (w), 1696 (s), 1595 (w), 1465 (w), 1395 (w), 770 (w).

Spec.Rot.: -47.29 (c = 0.50, $CHCl_3$).

2-(4-Isobutylphenyl)-*N*-((4-undecylpyridin-3-yl)methyl)propanamide (5e)



Pyridine **5e** was prepared according to general procedure E using oxazino pyridine **1w** (108 mg, 0.200 mmol, 1.0 equiv.), peroxide **2a** (160 mg, 0.400 mmol, 2.0 equiv.), and *p*-toluenesulfonic acid monohydrate (57.1 mg, 0.300 mmol, 1.5 equiv.) in acetone (2.0 mL). The reaction mixture was heated at 60 ºC for 12 h. After purification by flash chromatography (EtOAc), pyridine **5e** was obtained as a brown oil (28.8 mg, 32%).

TLC: Rf = 0.40 (EtOAc).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (s, 1H), 8.25 (s, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.09 (d, *J* = 8.1 Hz, 2H), 7.05-6.99 (m, 1H), 5.70 (t, *J* = 5.6 Hz, 1H), 4.49-4.30 (m, 2H), 3.55 (q, *J* = 7.2 Hz, 1H), 2.51-2.45 (m, 2H), 2.43 (d, *J* = 7.2 Hz, 2H), 1.92-1.72 (m, 1H), 1.52 (d, *J* = 7.2 Hz, 3H), 1.49-1.42 (m, 2H), 1.32-1.20 (m, 16H), 0.90-0.83 (m, 9H).

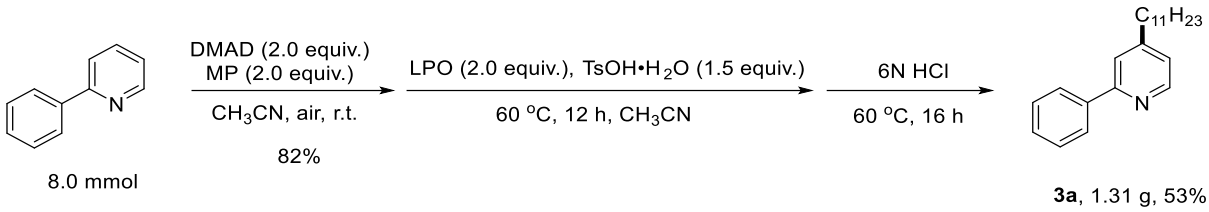
^{13}C NMR (76 MHz, $CDCl_3$) δ 174.3, 150.4, 149.6, 149.1, 141.0, 138.3, 131.6, 129.8, 127.4, 124.0, 46.8, 45.1, 39.0, 32.0, 31.7, 30.3, 30.0, 29.8, 29.74, 29.67, 29.64, 29.58, 29.5, 22.8, 22.5, 18.5, 14.2.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{30}H_{46}NONa$: 473.35024, found: 473.35023.

IR (neat): 2923 (s), 2853 (m), 1649 (m), 1539 (w), 1464 (w), 1226 (w), 1190 (w), 849 (w), 721 (w).

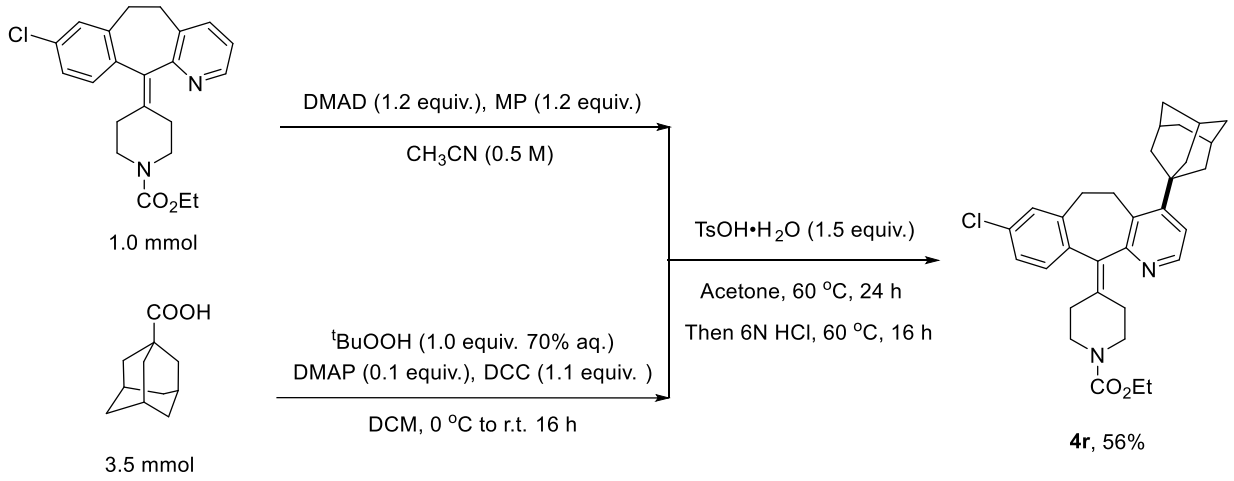
5. Synthetic utility

5.1 One-pot gram-scale synthesis from 2-phenyl pyridine



Under argon, 2-phenylpyridine (1.2 mL, 8.0 mmol, 1.0 equiv.) and methyl pyruvate (1.5 mL, 16 mmol, 2.0 equiv.) were dissolved in dry acetonitrile (16 mL) in an oven-dried 100 mL Schlenk tube equipped with a stir bar. Dimethyl acetylenedicarboxylate (2.0 mL, 16 mmol, 2.0 equiv.) was added dropwise. Then the reaction mixture was stirred at room temperature for 48 h. After completion, *p*-toluenesulfonic acid monohydrate (2.3 g, 12 mmol, 1.5 equiv.), LPO (6.4 g, 16 mmol, 2.0 equiv.) and dry acetonitrile (34 ml) were added under argon. The reaction mixture was heated at 60 °C for 24 h. After cooling down to room temperature, the reaction mixture was transferred to a 1 L round-bottom flask and 6 N HCl (160 mL) was added. Continually, the mixture was heated at 60 °C for 24 h. The reaction mixture was basified with $NaHCO_3$ and saturated Na_2CO_3 aqueous solution slowly under stirring. Afterwards, the mixture was extracted with EtOAc (3×100 mL) and the combined organic extracts were washed with saturated Na_2CO_3 aqueous solution (50 mL) and water (50 mL). The organic phase was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The residue was purified by column chromatography (SiO_2; *n*-pentane/EtOAc = 20/1) to give pyridine **3a** (1.31 g, 53 %). The characterization data match the one from the two-pot experiment.

5.2 Reaction of loratadine with 1-adamantyl carboxylic acid



Ioratadine (383 mg, 1.00 mmol, 1.0 equiv.) and methyl pyruvate (0.14 mL, 1.2 mmol, 1.2 equiv.) were dissolved in acetonitrile (2.0 mL) in a 25 mL round-bottom flask equipped with a stir bar. Dimethyl acetylenedicarboxylate (0.15 mL, 1.2 mmol, 1.2 equiv.) was added dropwise. Then the reaction mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure to give the crude oxazino pyridine **1t**.

A solution of adamantane-1-carboxylic acid (630 mg, 3.50 mmol, 3.5 equiv.) and 70 wt% solution of *tert*-butylhydroperoxide in H_2O (0.48 ml, 3.5 mmol, 3.5 equiv.) in DCM (5.0 mL) was cooled to 0 °C. After stirring vigorously for 10 min, a solution of DMAP (42.8 mg, 0.350 mmol, 0.35 equiv.) and DCC (795 mg, 3.85 mmol,

3.85 equiv.) in DCM (2.5 mL) was added in one portion. Then, the reaction mixture was allowed to warm to room temperature and stirred for 16 h. Then, the reaction solution was dried with anhydrous Na_2SO_4, filtered through a short pad of silica gel and washed by additional 50 mL of DCM. The combined solution was concentrated in a rotary evaporator under vacuum at 20 °C to give the crude perester **2q**.

Under argon, to a solution of crude oxazino pyridine **1t** in acetone (6 mL) in an oven-dried 50 ml Schlenk tube equipped with a stir bar, *p*-toluenesulfonic acid monohydrate (2.3 g, 12 mmol, 1.5 equiv.) and crude perester **2q** in 4 mL acetone were added. Afterwards, the reaction mixture was heated at 60 °C for 24 h. Then, 6 N HCl (20 mL) was added to the reaction mixture and the tube was heated at 60 °C for 24 h. The reaction mixture was basified with saturated Na_2CO_3 and extracted by EtOAc (3×50 mL). Then, the organic phase was dried with anhydrous Na_2SO_4, filtered and the solvent was removed with a rotary evaporator under reduced pressure. The residue was subjected to flash column chromatography (EtOAc/*n*-pentane = 2/1) over silica gel to give the corresponding product **4r**, which was further purified by MPLC (MeCN/H_2O, v/v ratio was 20:80 to 60:40 over 10 min, then kept at 60:40 for 10 min, then increased from 60:40 to 90:10 over 5 min and finally kept at 90:10 for 10 min) to afford pyridine **4r** as a brown gum (284.6 mg, 56% yield).

TLC: Rf = 0.45 (EtOAc)

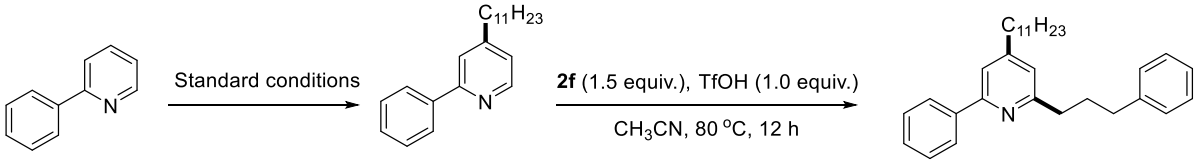
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 5.5 Hz, 1H), 7.15-7.06 (m, 3H), 7.04 (d, *J* = 2.1 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.85-3.69 (m, 2H), 3.62-3.54 (m, 1H), 3.48-3.30 (m, 2H), 3.28-3.19 (m, 1H), 3.16-3.07 (m, 1H), 3.02-2.89 (m, 1H), 2.52-2.45 (m, 2H), 2.31-2.21 (m, 1H), 2.18-2.13 (m, 3H), 2.12-1.99 (m, 6H), 1.99-1.93 (m, 1H), 1.86-1.74 (m, 6H), 1.24 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.5, 156.3, 155.7, 147.3, 138.5, 135.5, 135.2, 134.6, 132.9, 132.3, 131.9, 130.4, 125.9, 120.3, 61.4, 45.0, 44.6, 41.8, 38.2, 36.8, 33.2, 30.8, 30.4, 29.0, 26.8, 14.8.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{32}H_{37}N_2O_2ClNa$: 539.24358, found: 539.24390.

IR (neat): 2906 (m), 2850 (w), 1696 (s), 1433 (m), 1223 (s), 1115 (m), 752 (s).

5.3 Consecutive *para*,*ortho*-difunctionalization of 2-phenyl pyridine



3a, 75%

6a, 43% based on **3a**

Pyridine **3a** was prepared according to general procedure E. Pyridine **6a** was synthesized according to a literature[11]: to an oven-dried Schlenk tube, pyridine **3a** (155 mg, 0.500 mmol, 1.0 equiv.) and peroxide **2f** (245 mg, 0.750 mmol, 1.5 equiv.) were added, followed by the addition of CH_3CN (2.0 mL) was added sequentially. The reaction mixture was heated at 80 °C for 12 h, and then cooled to r.t. The solvent was removed by rotary evaporation, and then diluted with EtOAc, washed with 10% aq. NaOH (3×15 mL). The aqueous phase was extracted with EtOAc (3×15 mL) and the organic phase was dried with anhydrous Na_2SO_4. After filtration and removal of the solvent, the residue was purified on silica gel (*n*-pentane/Et_2O = 30/1) to afford **6a** as a colorless oil (90.9 mg, 43% yield).

TLC: Rf = 0.55 (*n*-pentane/Et_2O = 10/1)

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02-7.95 (m, 2H), 7.49-7.37 (m, 3H), 7.35 (d, *J* = 1.4 Hz, 1H), 7.33-7.26 (m, 2H), 7.25-7.15 (m, 3H), 6.90 (d, *J* = 1.4 Hz, 1H), 2.92-2.82 (m, 2H), 2.73 (t, *J* = 7.8 Hz, 2H), 2.65-2.52 (m, 2H), 2.22-2.06

(m, 2H), 1.71-1.60 (m, 2H), 1.37-1.19 (m, 16H), 0.95-0.83 (m, 3H).

^{13}C NMR (76 MHz, $CDCl_3$) δ 161.8, 157.0, 152.7, 142.6, 140.2, 128.74, 128.68, 128.65, 128.4, 127.2, 125.8, 121.5, 118.4, 38.1, 35.8, 35.6, 32.1, 31.6, 30.7, 29.80, 29.76, 29.7, 29.6, 29.5, 29.4, 22.8, 14.3.

HRMS (ESI): m/z $[M + Na]^+$ calcd for $C_{31}H_{41}NNa$: 450.31312, found: 450.31324.

IR (neat): 2923 (s), 2852 (m), 1603 (m), 1558 (m), 1454 (m), 1424 (m), 775 (m), 695 (s).

6. References

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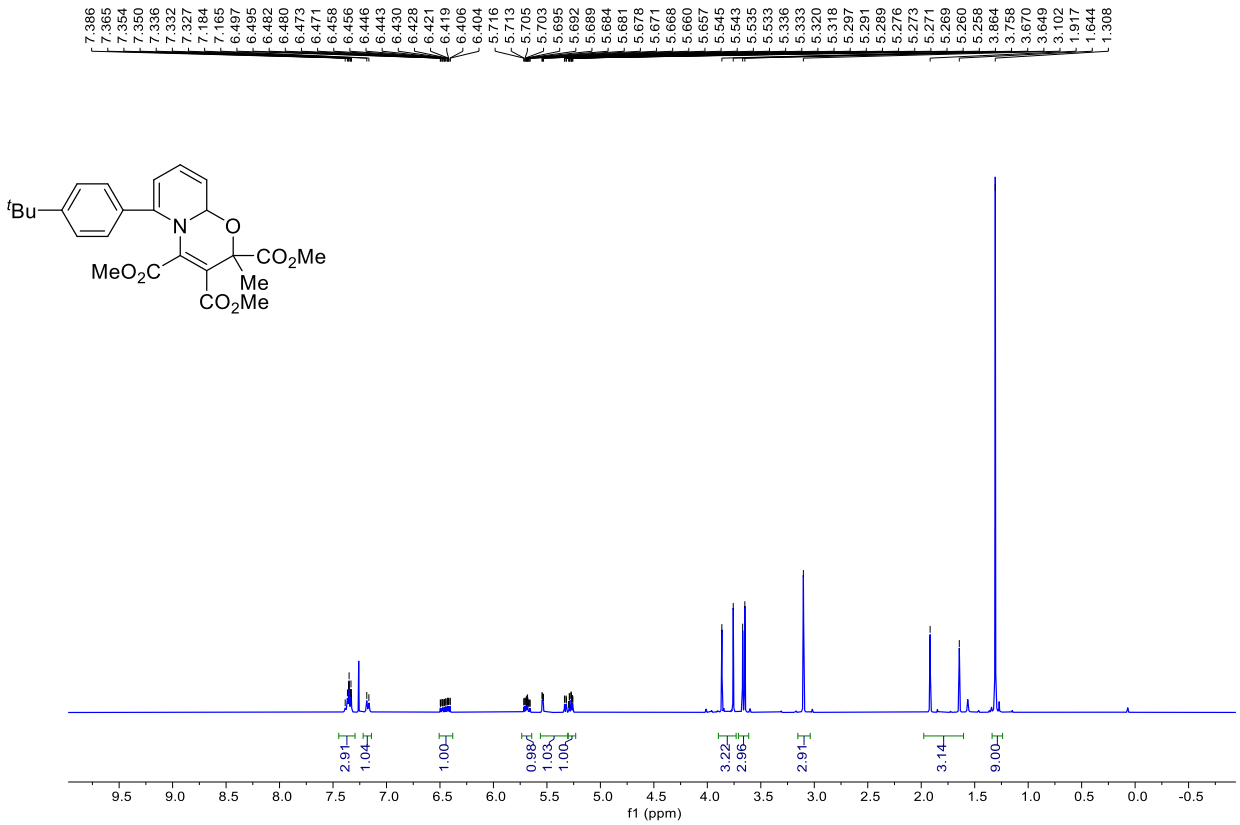
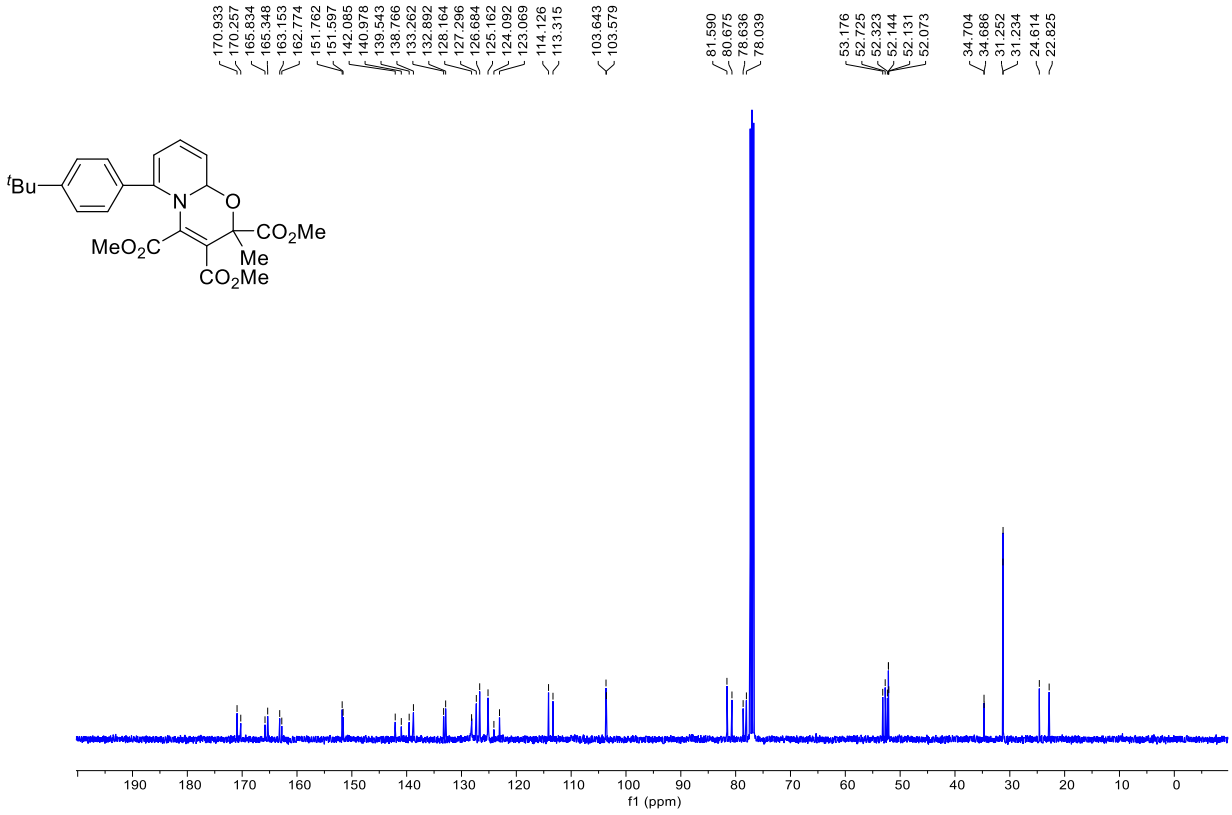
7. NMR spectra of products

Trimethyl 6-(4-(*tert*-butyl)phenyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1c)

^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

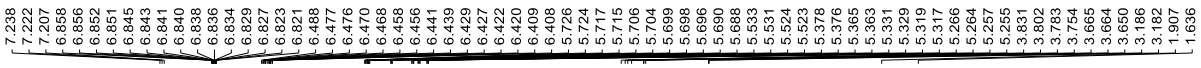


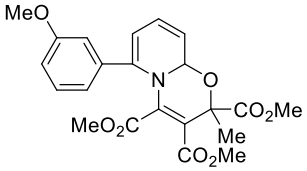
^{13}C NMR (101 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

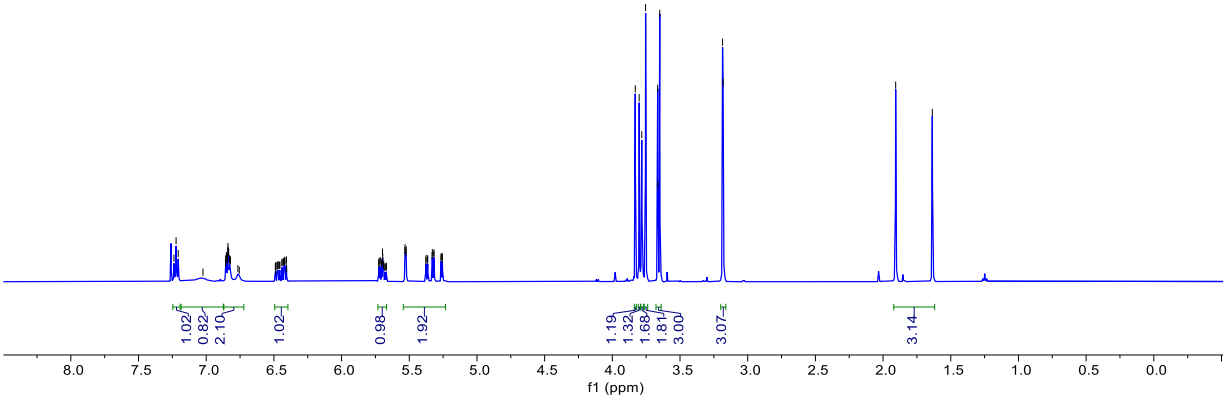


Trimethyl 6-(3-methoxyphenyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1d)

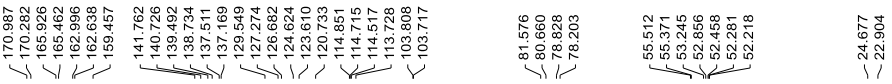
^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

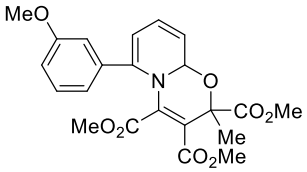


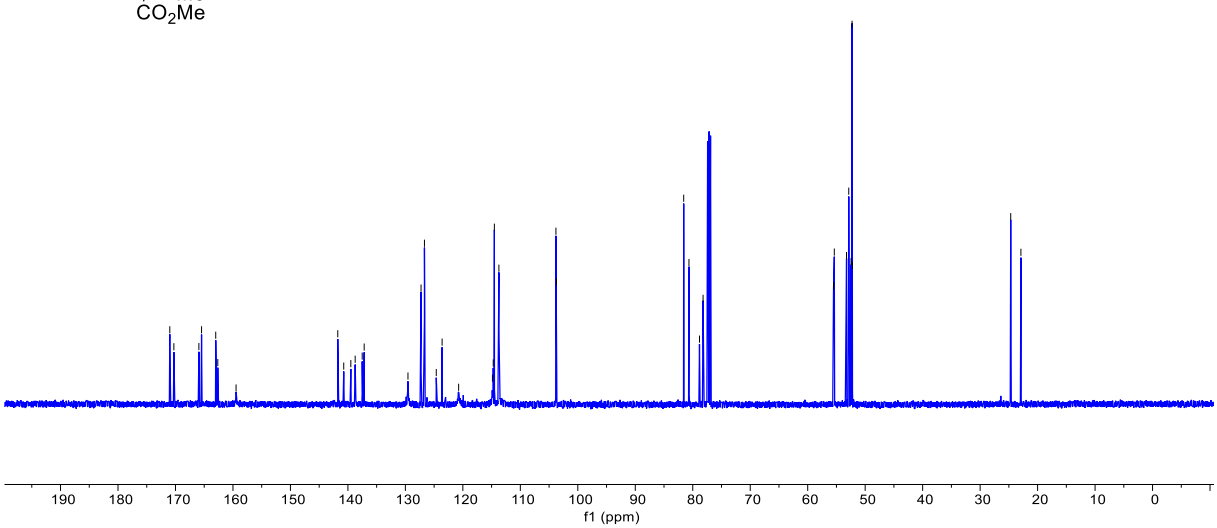




^{13}C NMR (101 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

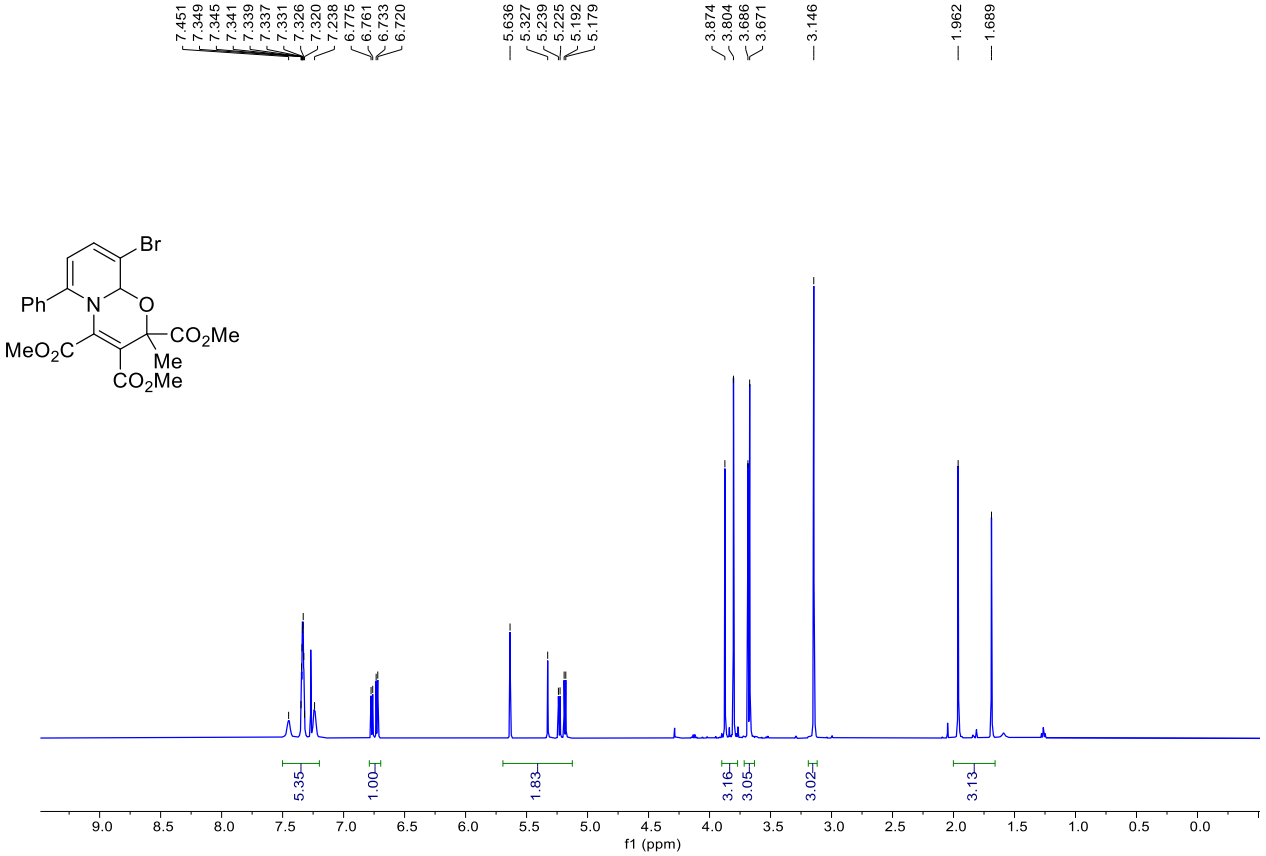




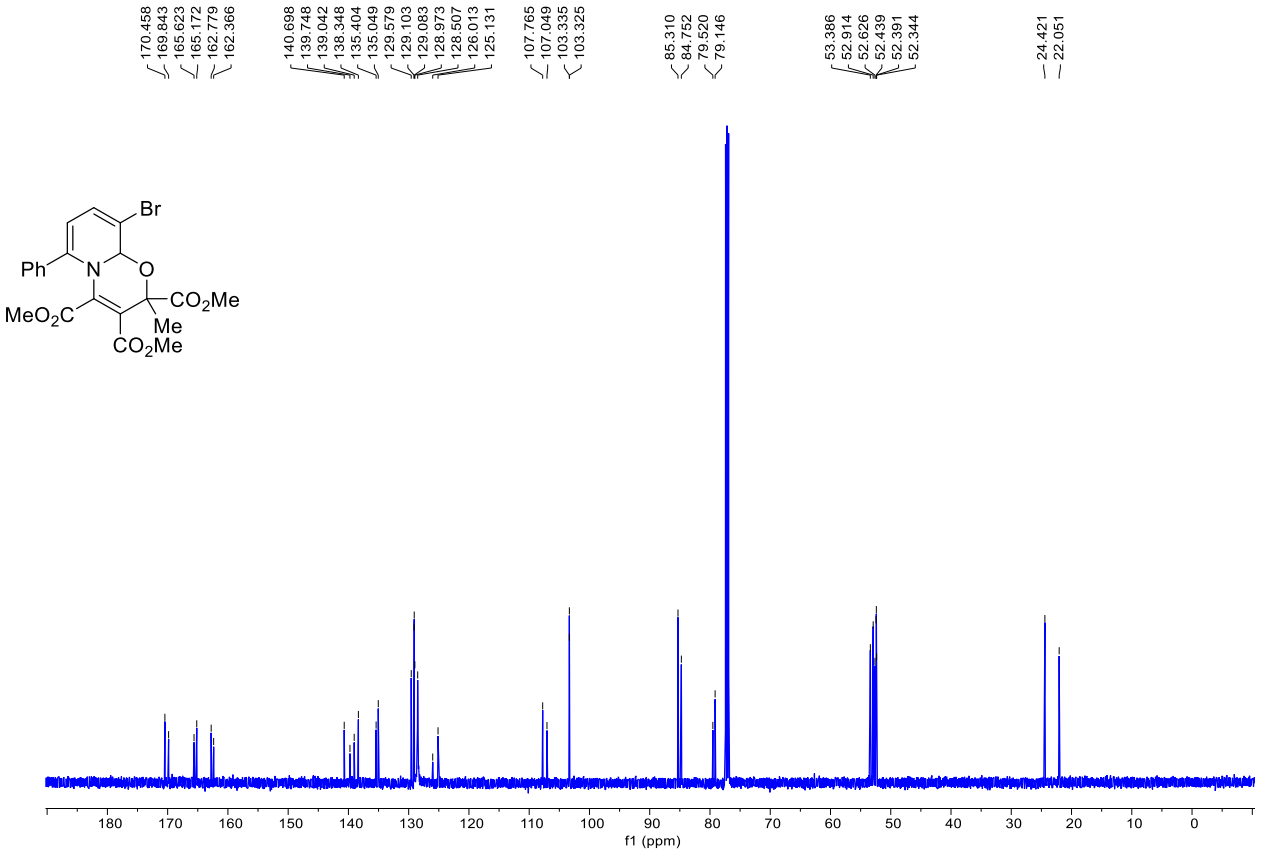


Trimethyl 9-bromo-2-methyl-6-phenyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1o)

^{1}H NMR (500 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

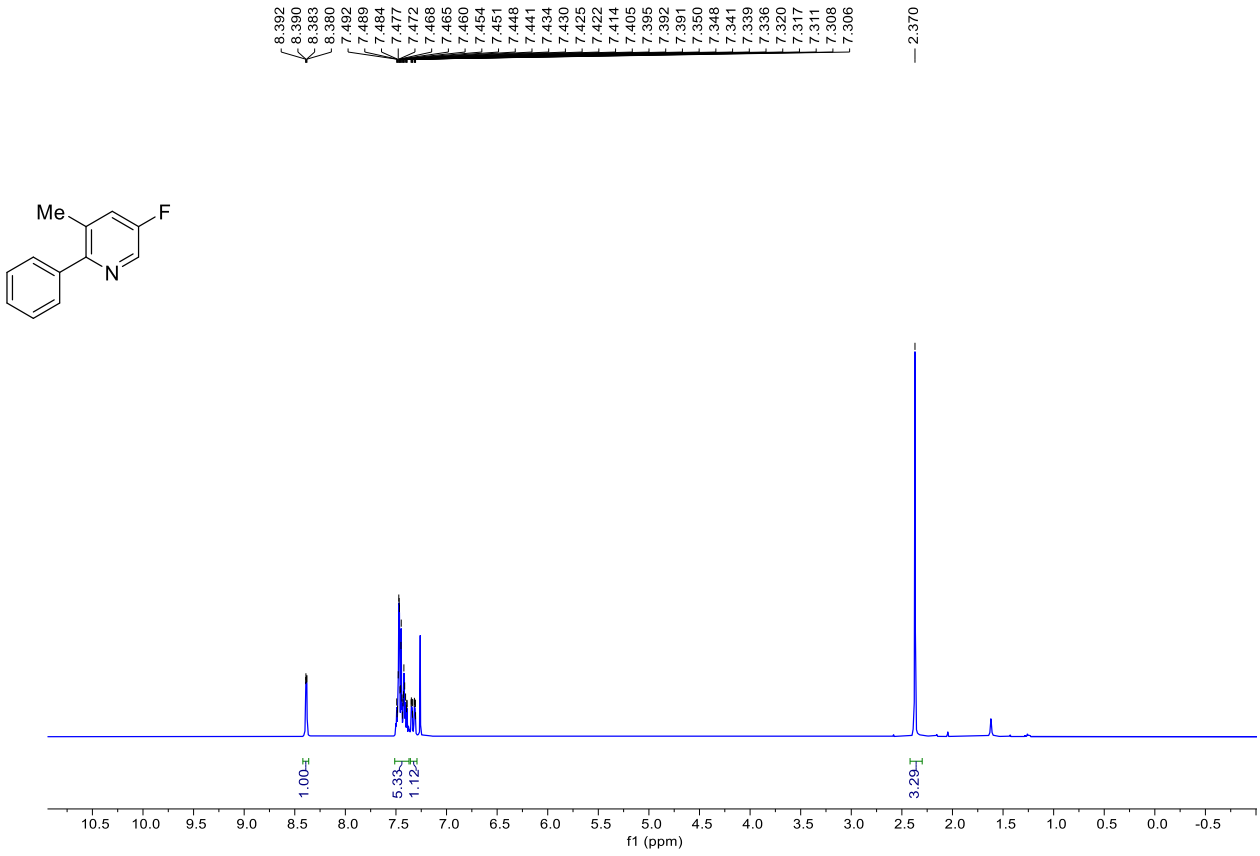


^{13}C NMR (126 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

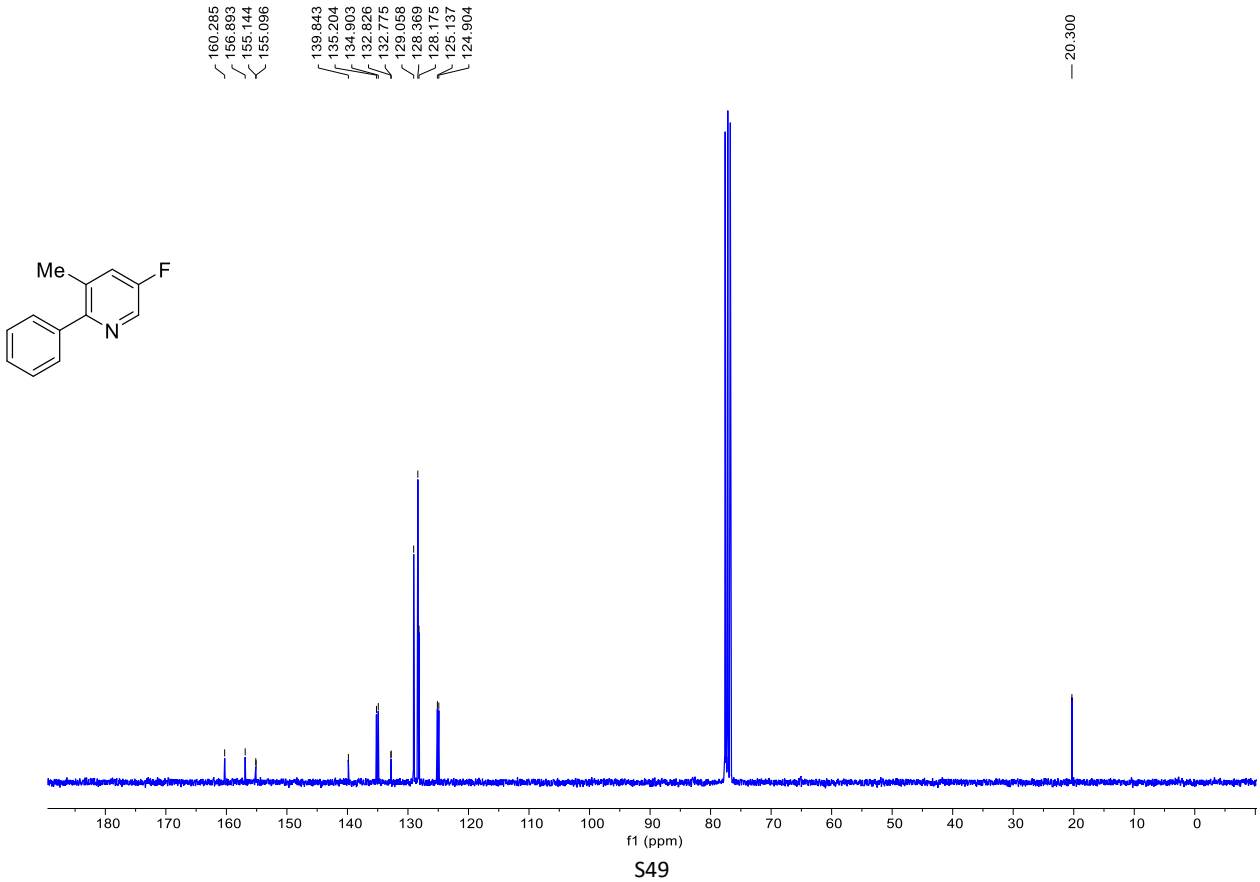


5-Fluoro-3-methyl-2-phenylpyridine (S1)

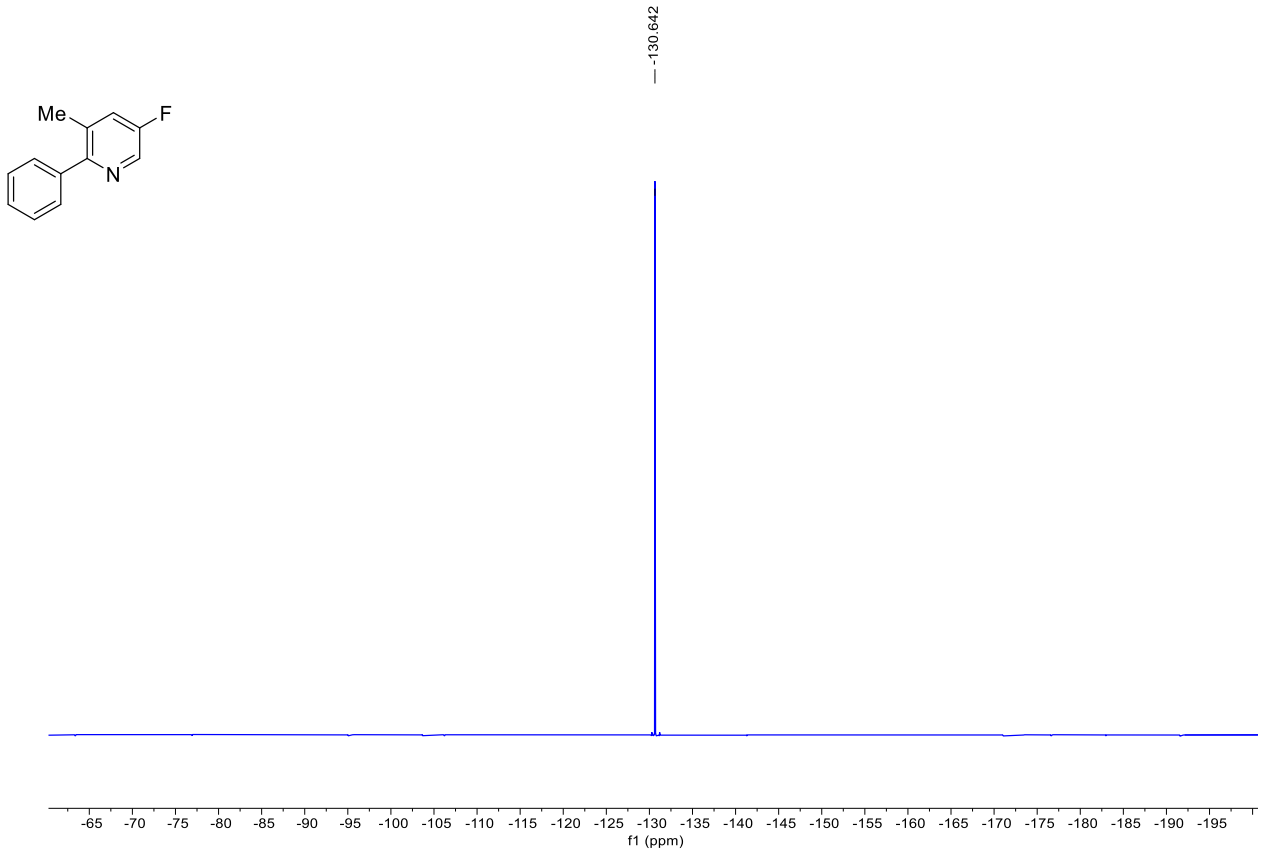
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (76 MHz, $CDCl_3$)

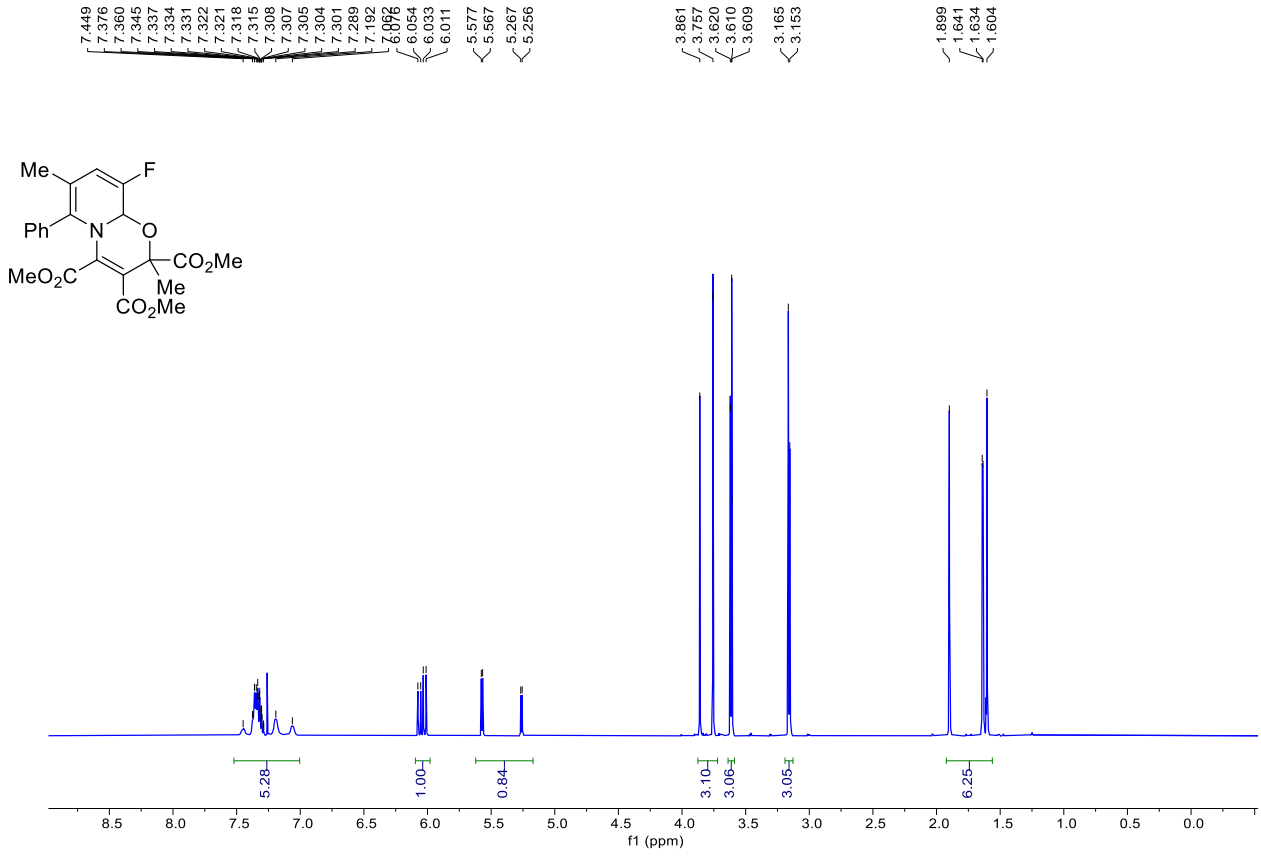


^{19}F NMR (282 MHz, $CDCl_3$)

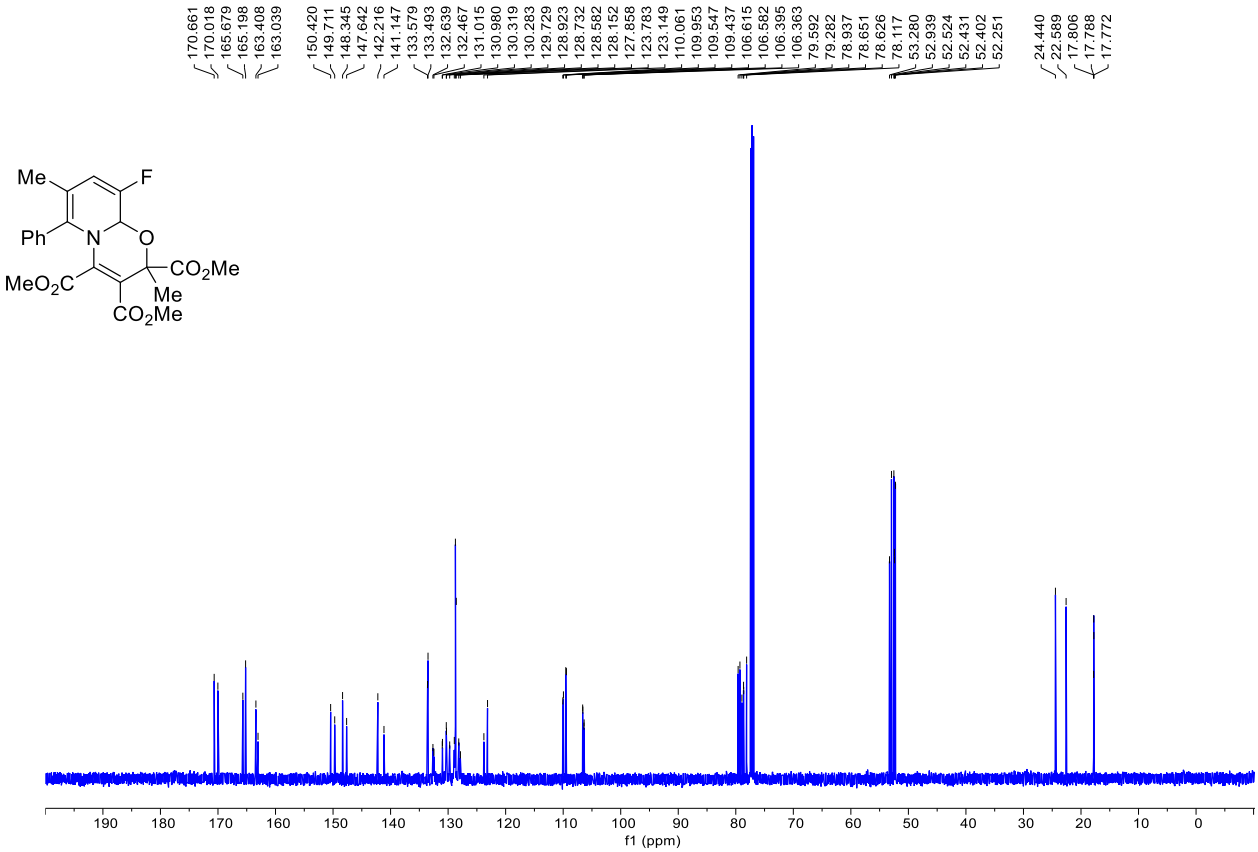


Trimethyl 9-fluoro-2,7-dimethyl-6-phenyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1q)

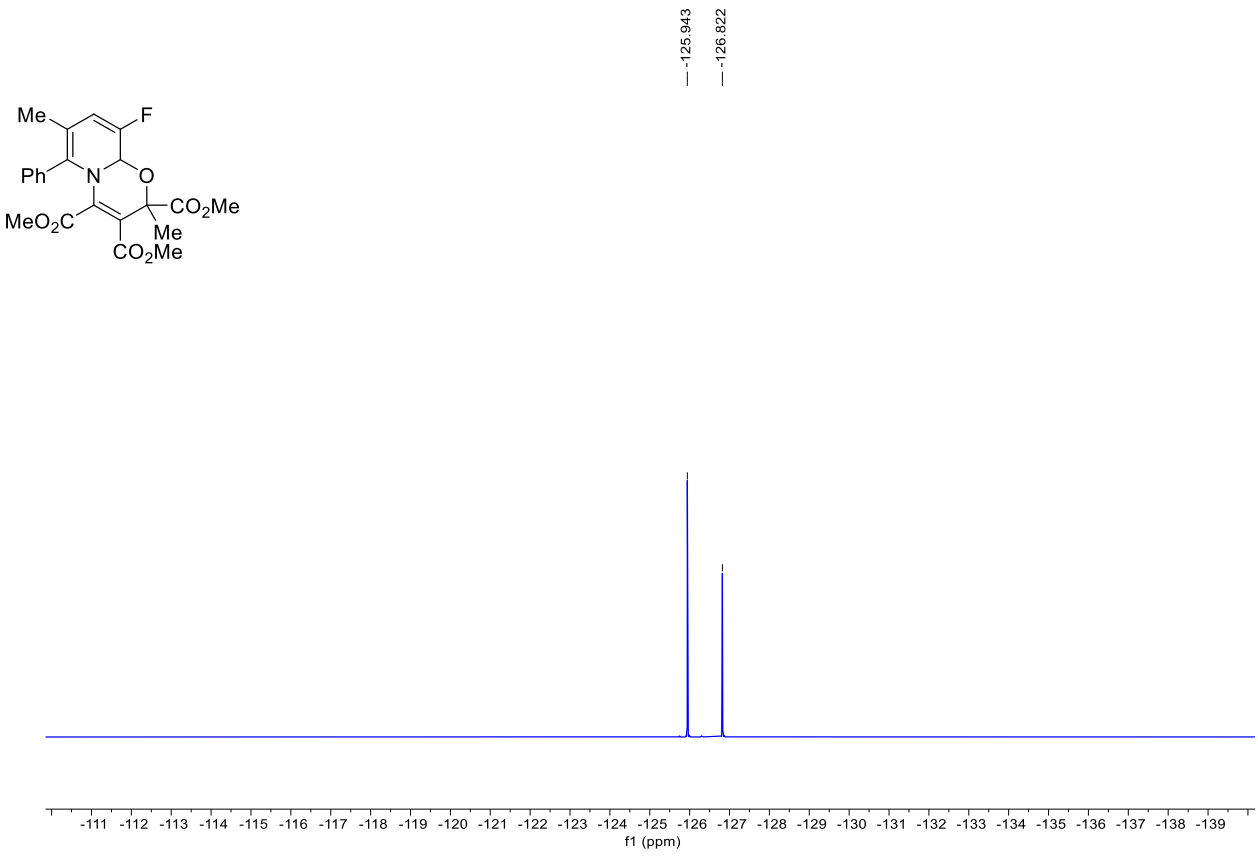
^{1}H NMR (500 MHz, $CDCl_3$, δ (ppm), containing diastereomers)



^{13}C NMR (126 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

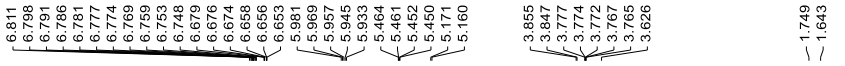


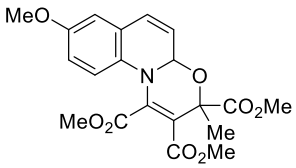
^{19}F NMR (470 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

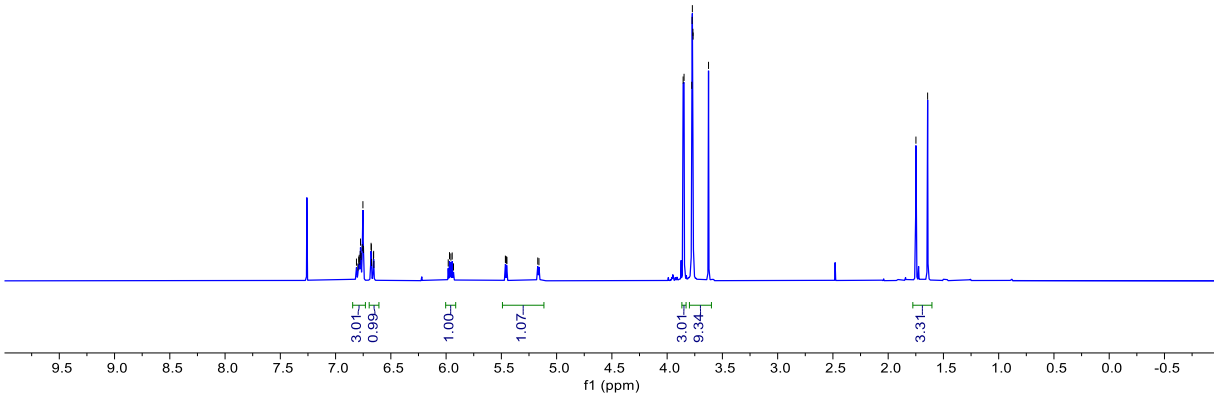


Trimethyl 8-methoxy-3-methyl-3*H*,4a*H*-[1,3]oxazino[3,2-*a*]quinoline-1,2,3-tricarboxylate (1r)

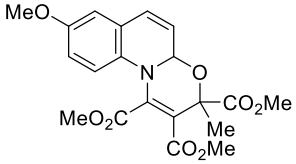
^{1}H NMR (400 MHz, $CDCl_3$, δ (ppm), containing diastereomers)





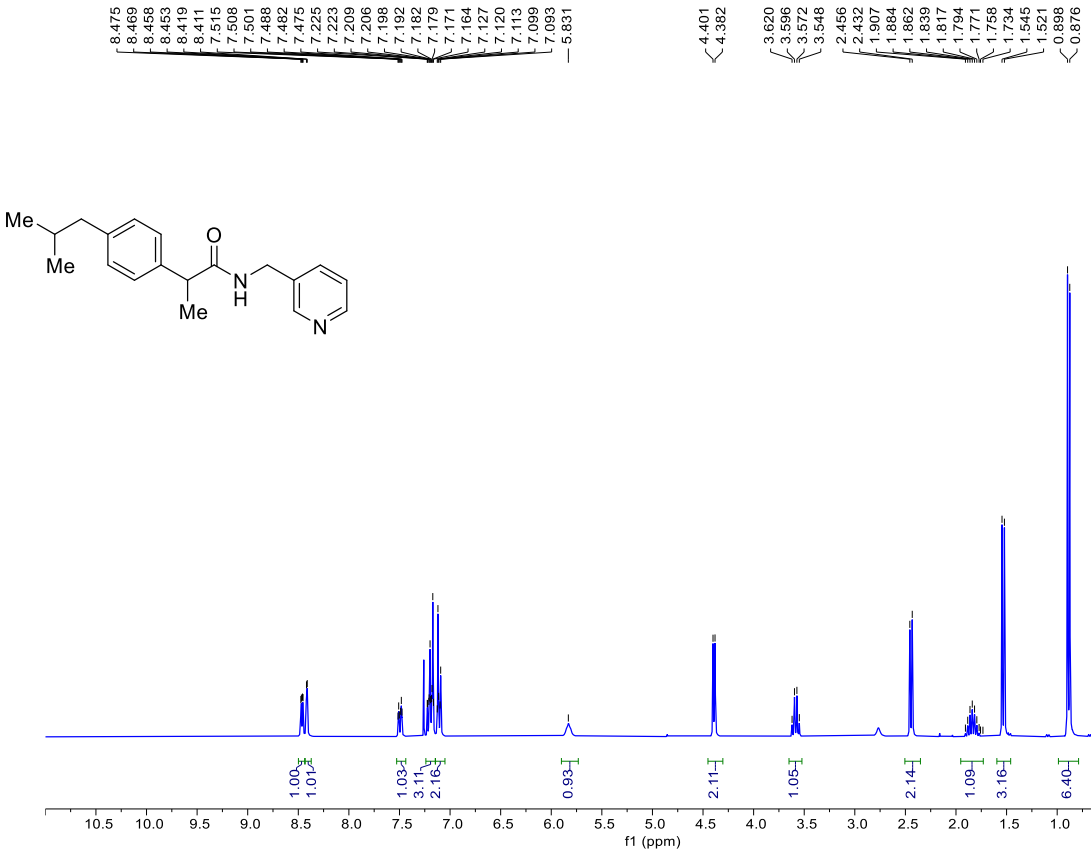


^{13}C NMR (101 MHz, $CDCl_3$, δ (ppm), containing diastereomers)

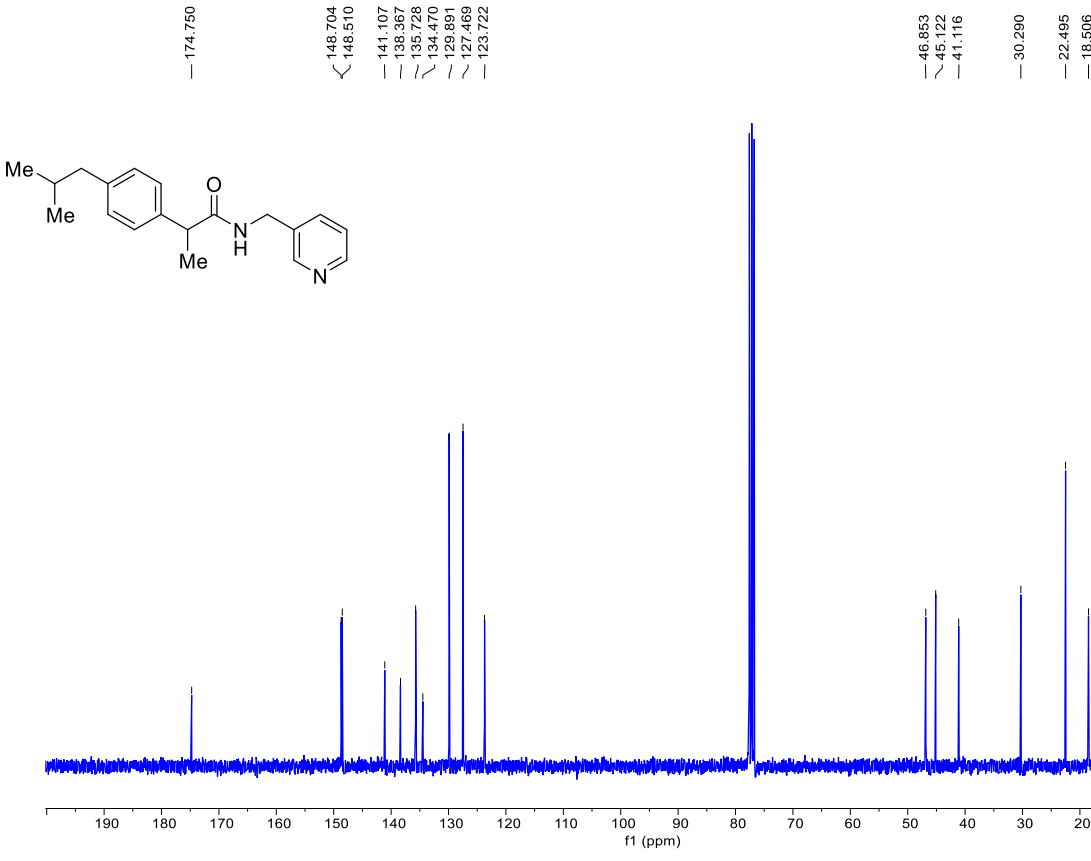


2-(4-isobutylphenyl)-*N*-(pyridin-3-ylmethyl)propenamide (S2)

^{1}H NMR (300 MHz, $CDCl_3$)

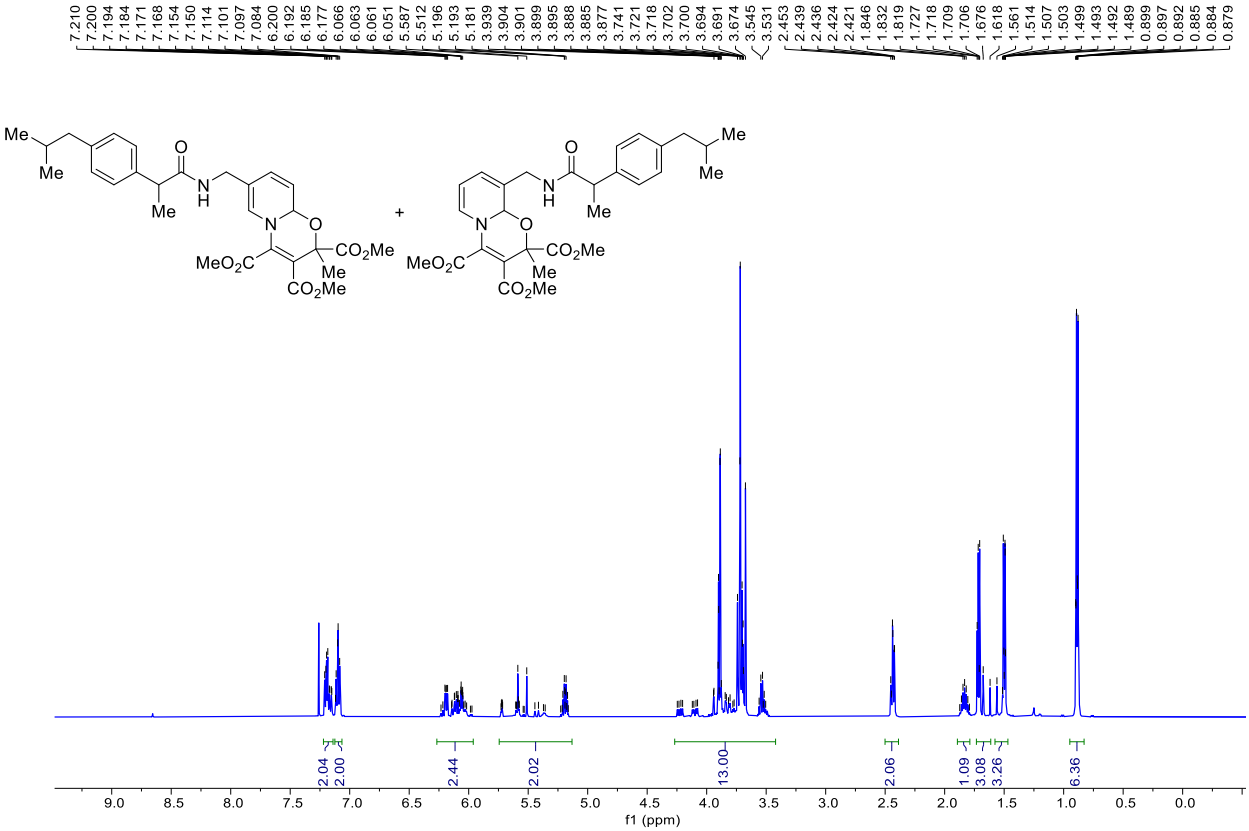


^{13}C NMR (76 MHz, $CDCl_3$)

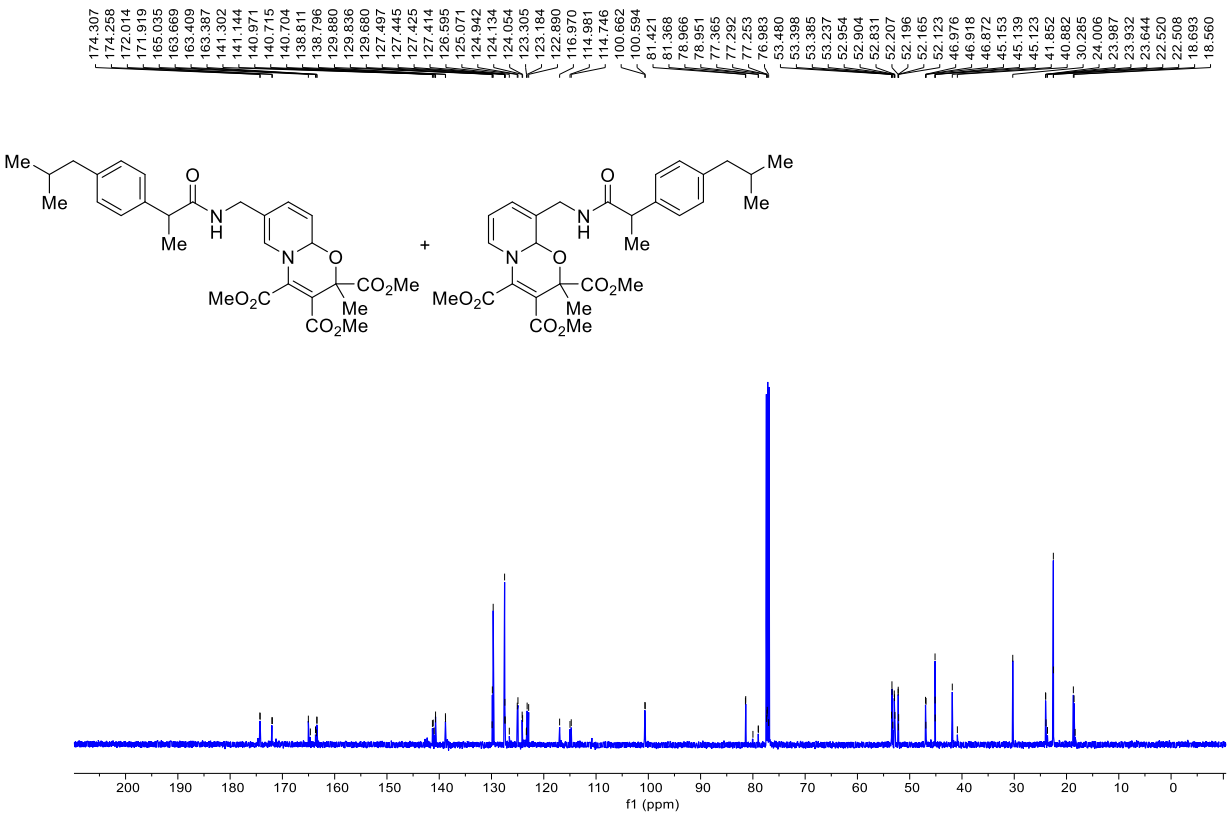


Trimethyl 7-((2-(4-isobutylphenyl)propanamido)methyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate and Trimethyl 9-((2-(4-isobutylphenyl)propanamido)methyl)-2-methyl-2*H*,9a*H*-pyrido[2,1-*b*][1,3]oxazine-2,3,4-tricarboxylate (1w)

^{1}H NMR (500 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers)

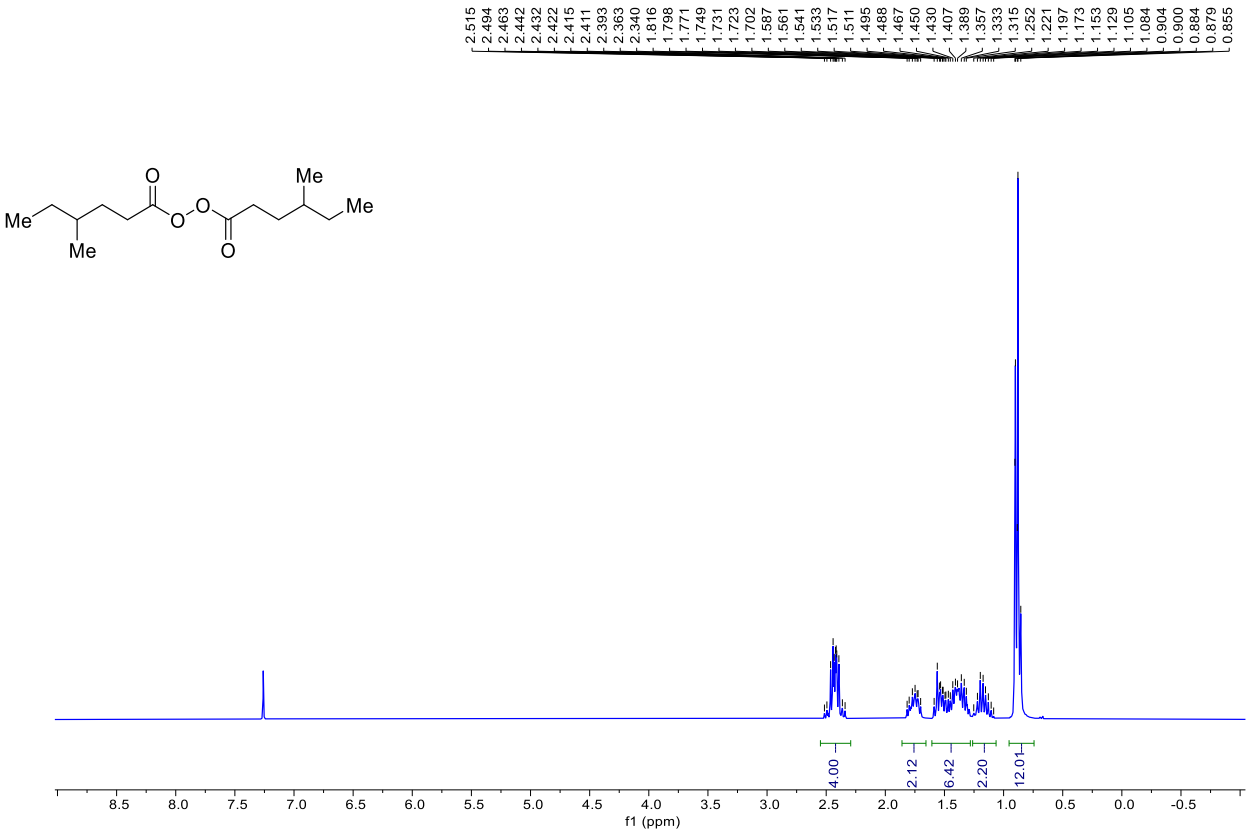


^{13}C NMR (126 MHz, $CDCl_3$, δ (ppm), containing regioisomers and diastereomers)

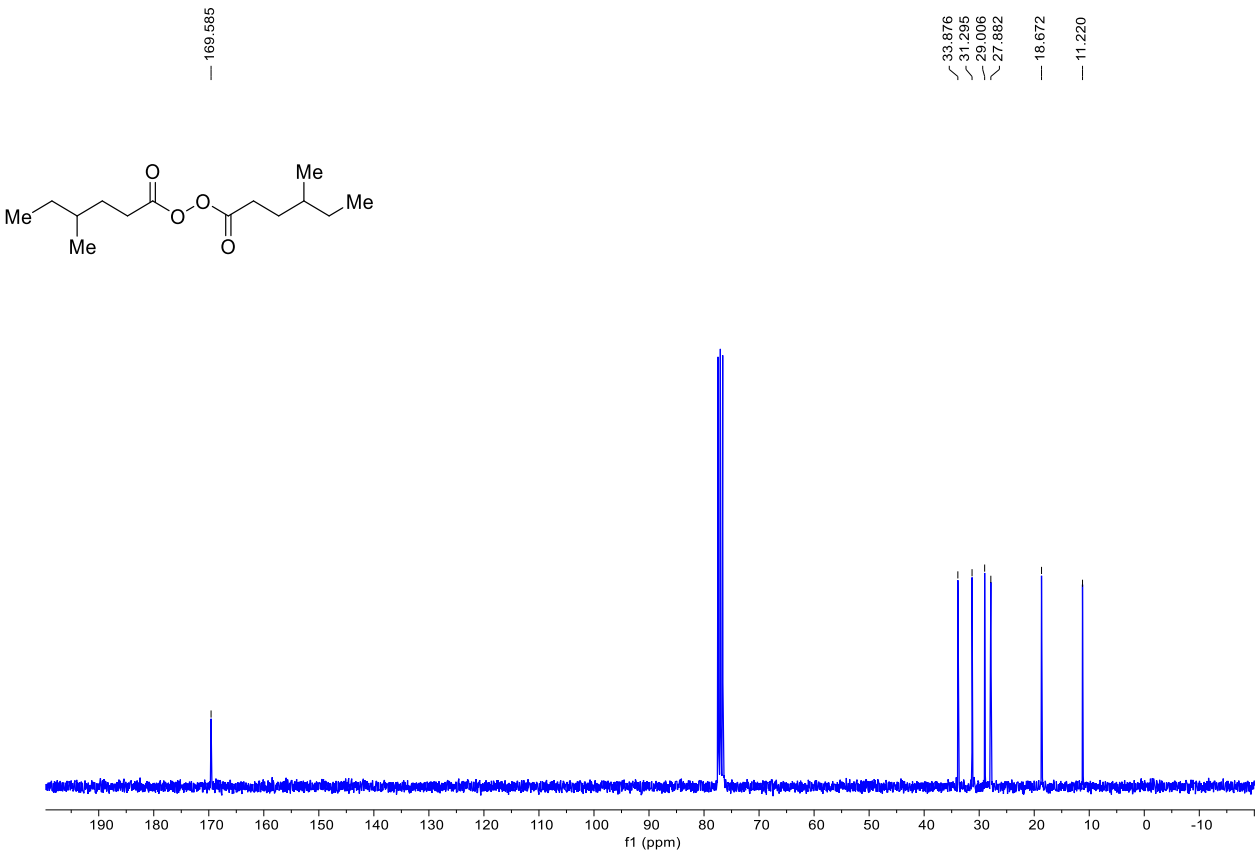


4-Methylhexanoic peroxyanhydride (2b)

^{1}H NMR (300 MHz, $CDCl_3$)

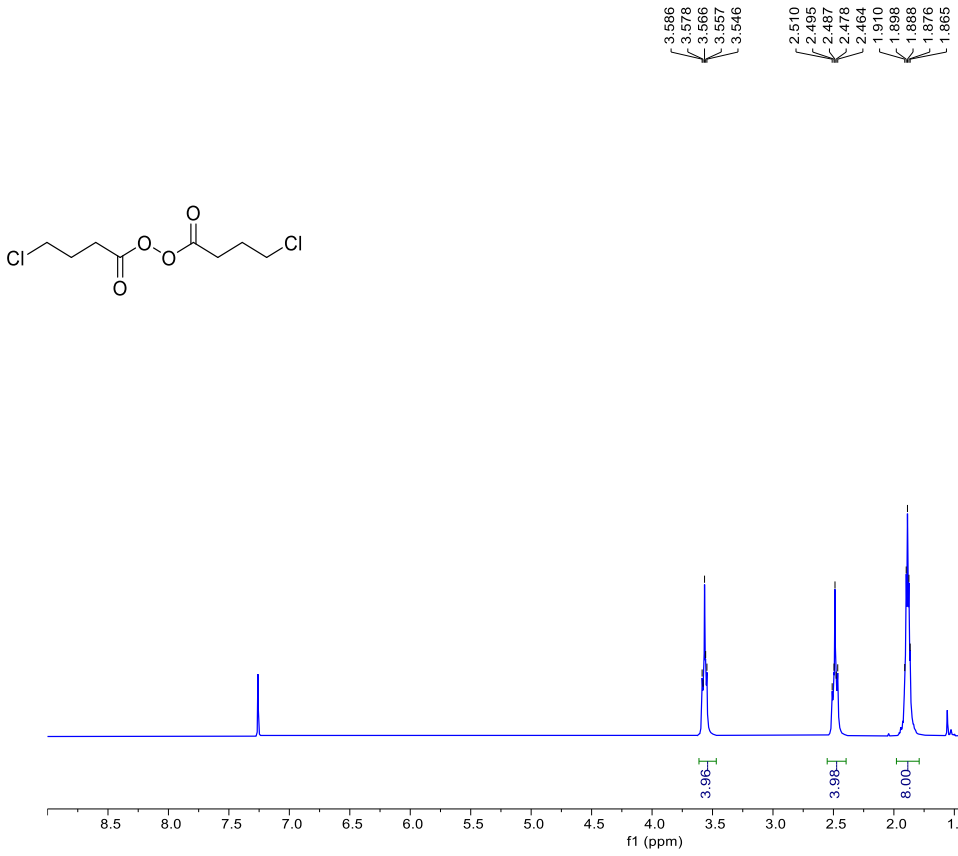


^{13}C NMR (76 MHz, $CDCl_3$)

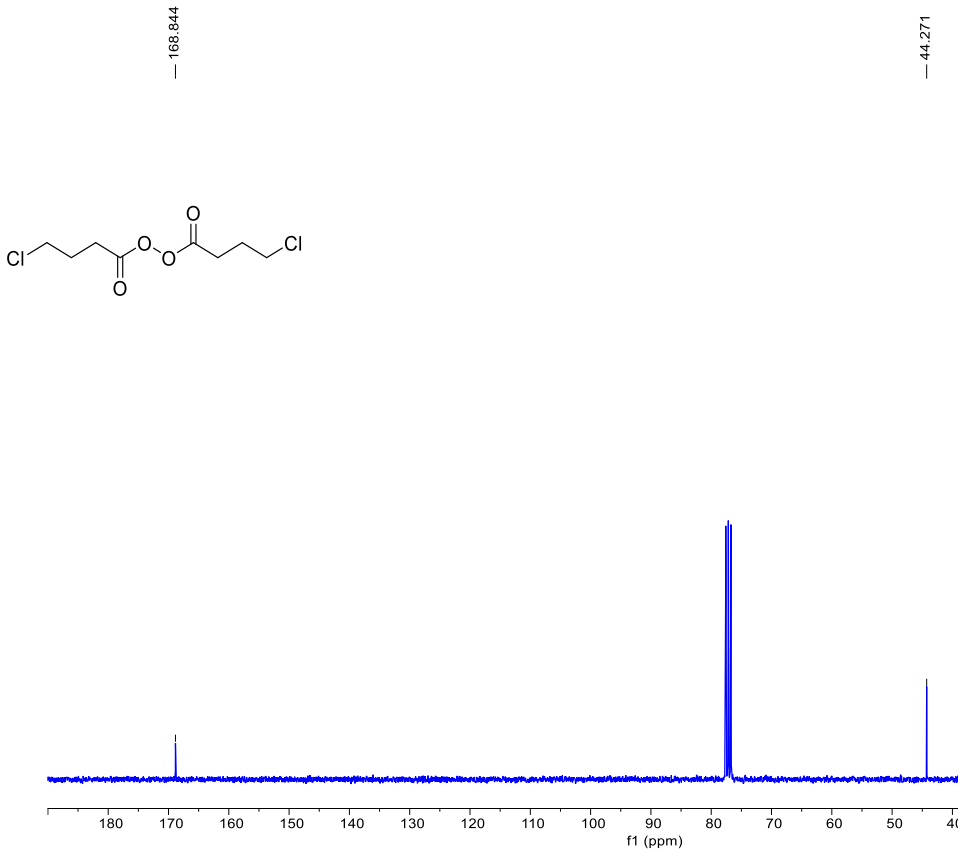


6-Chlorohexanoic 5-chloropentanoic peroxyanhydride (2d)

^{1}H NMR (300 MHz, $CDCl_3$)

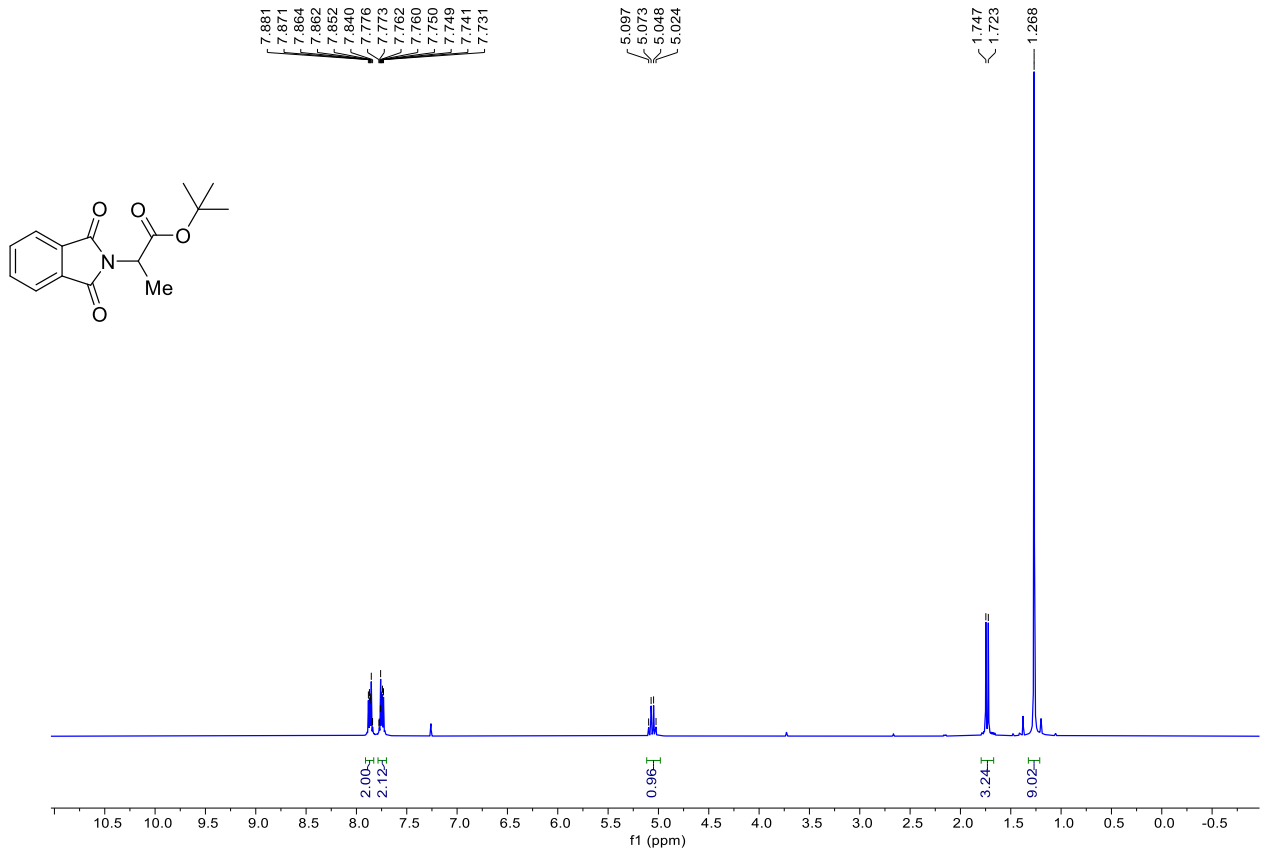


^{13}C NMR (76 MHz, $CDCl_3$)

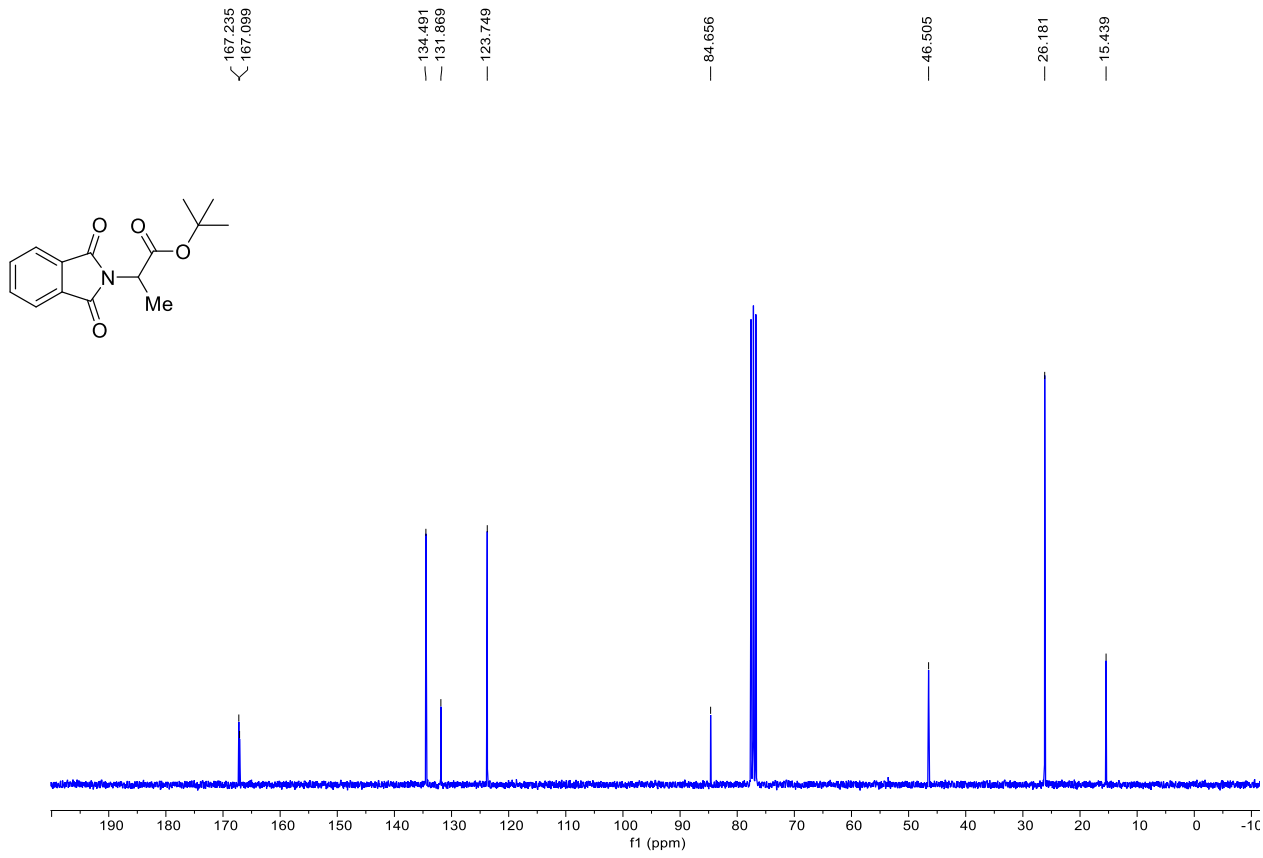


***tert*-Butyl 2-(1,3-dioxoisoindolin-2-yl)propanoate (2o)**

^{1}H NMR (300 MHz, $CDCl_3$)

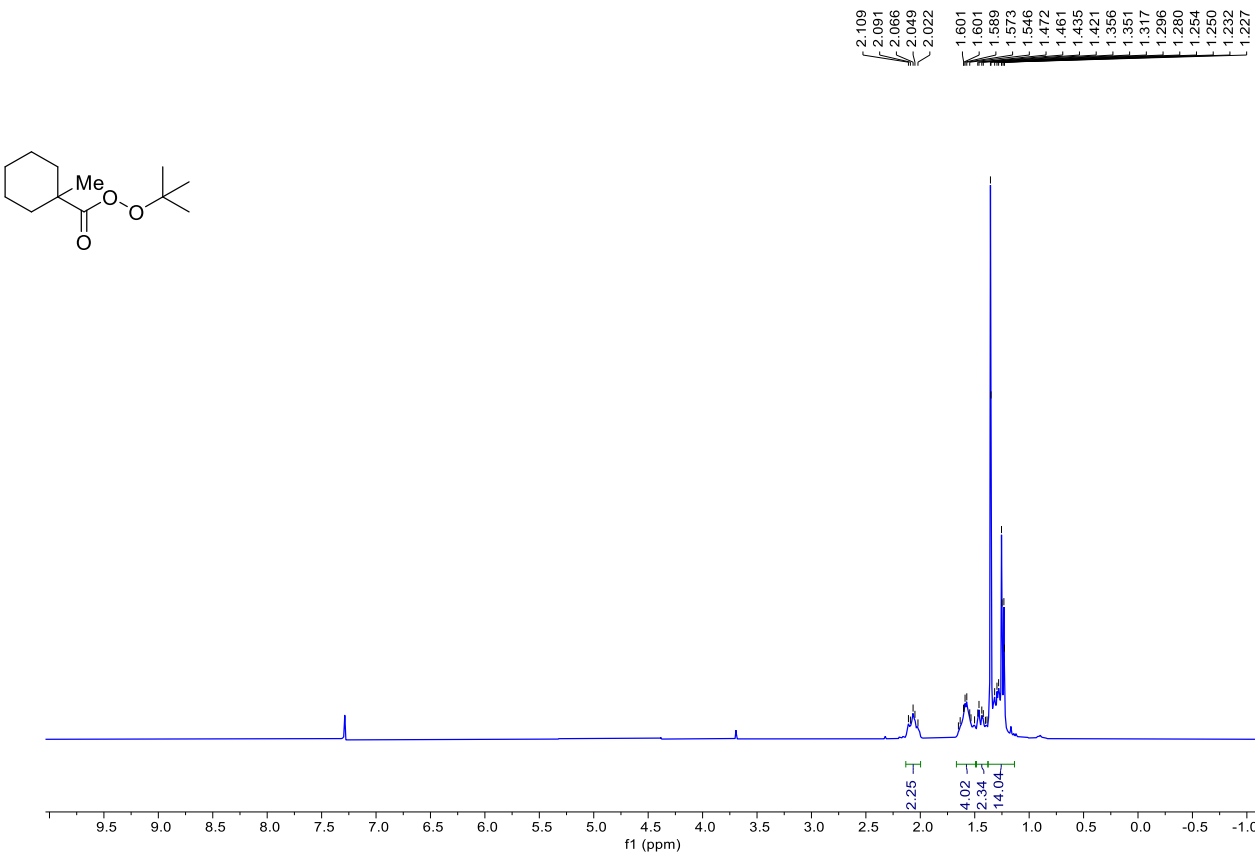


^{13}C NMR (76 MHz, $CDCl_3$)

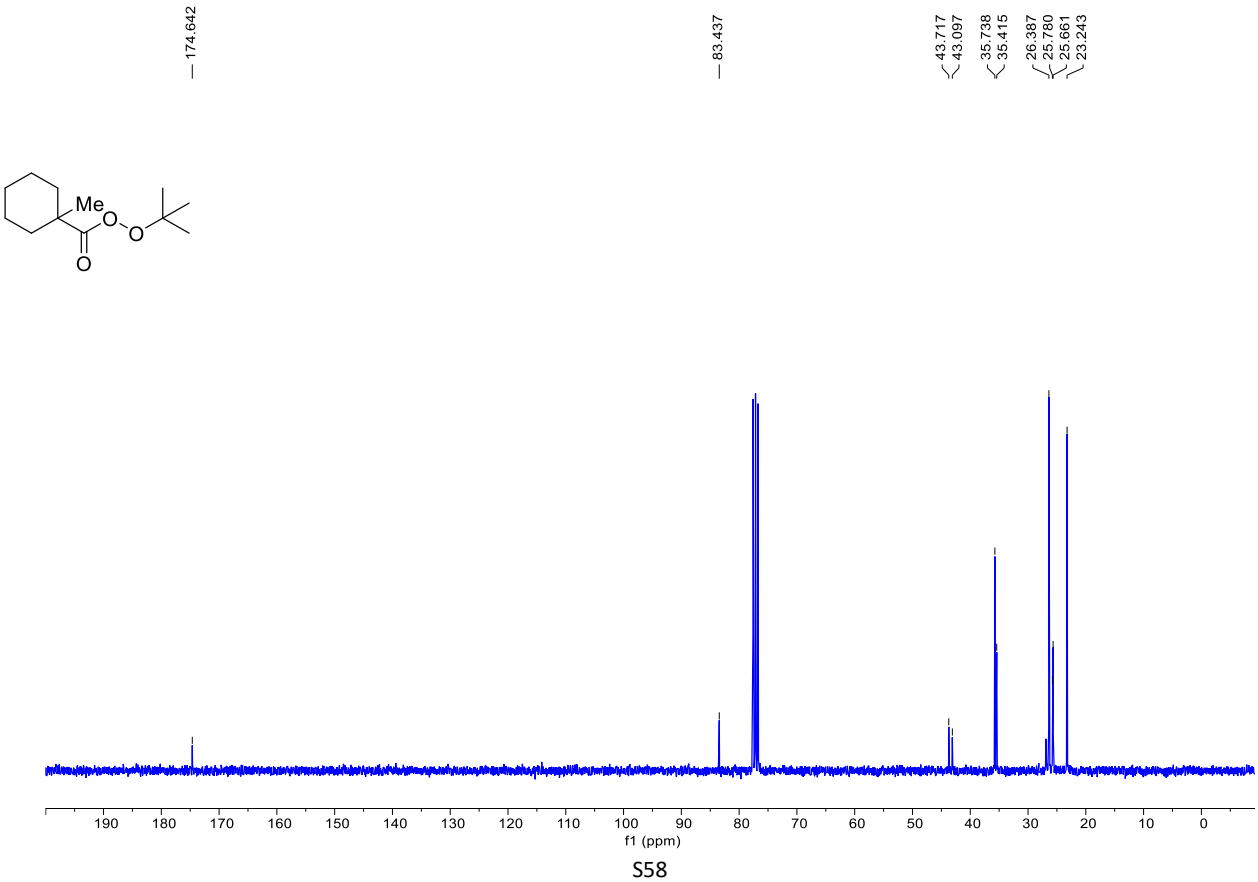


***tert*-Butyl 1-methylcyclohexane-1-carboperoxoate (2r)**

^{1}H NMR (300 MHz, $CDCl_3$)

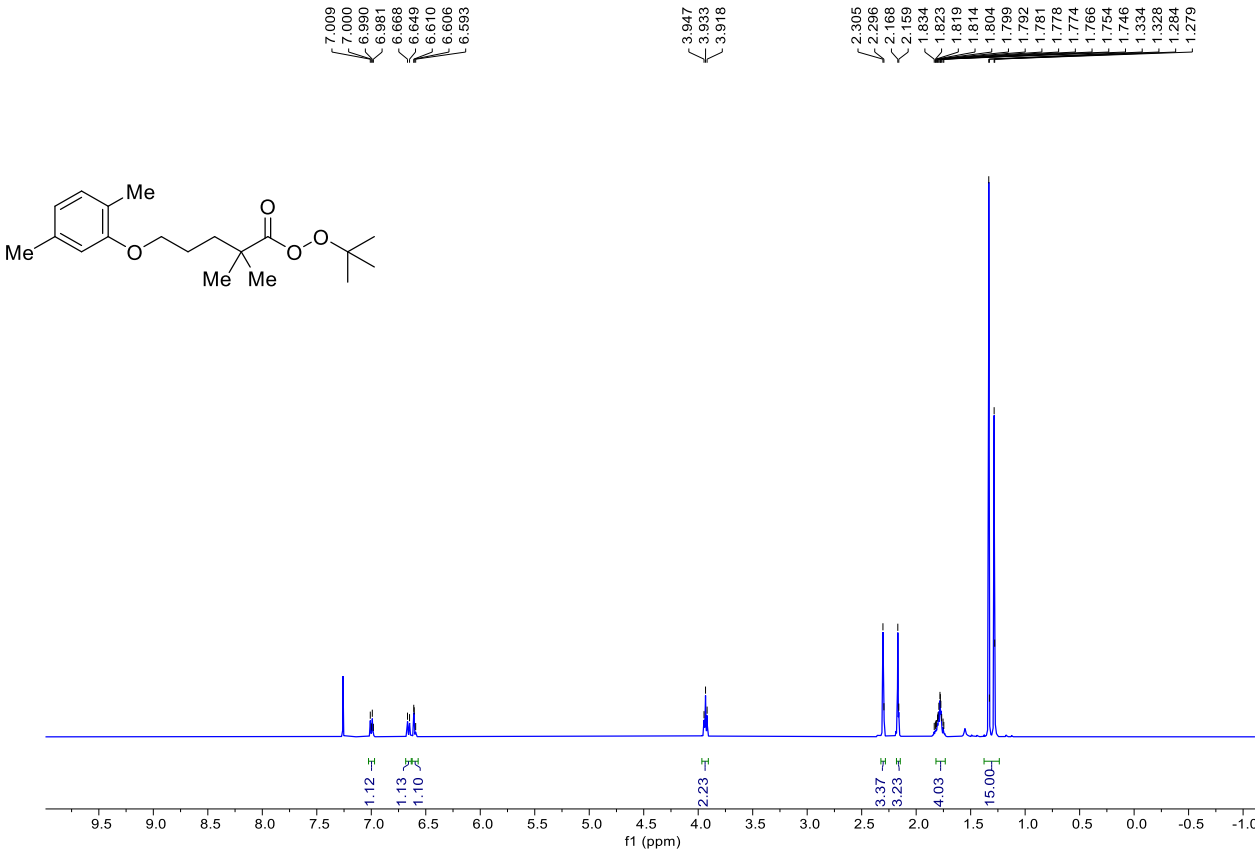


^{13}C NMR (76 MHz, $CDCl_3$)

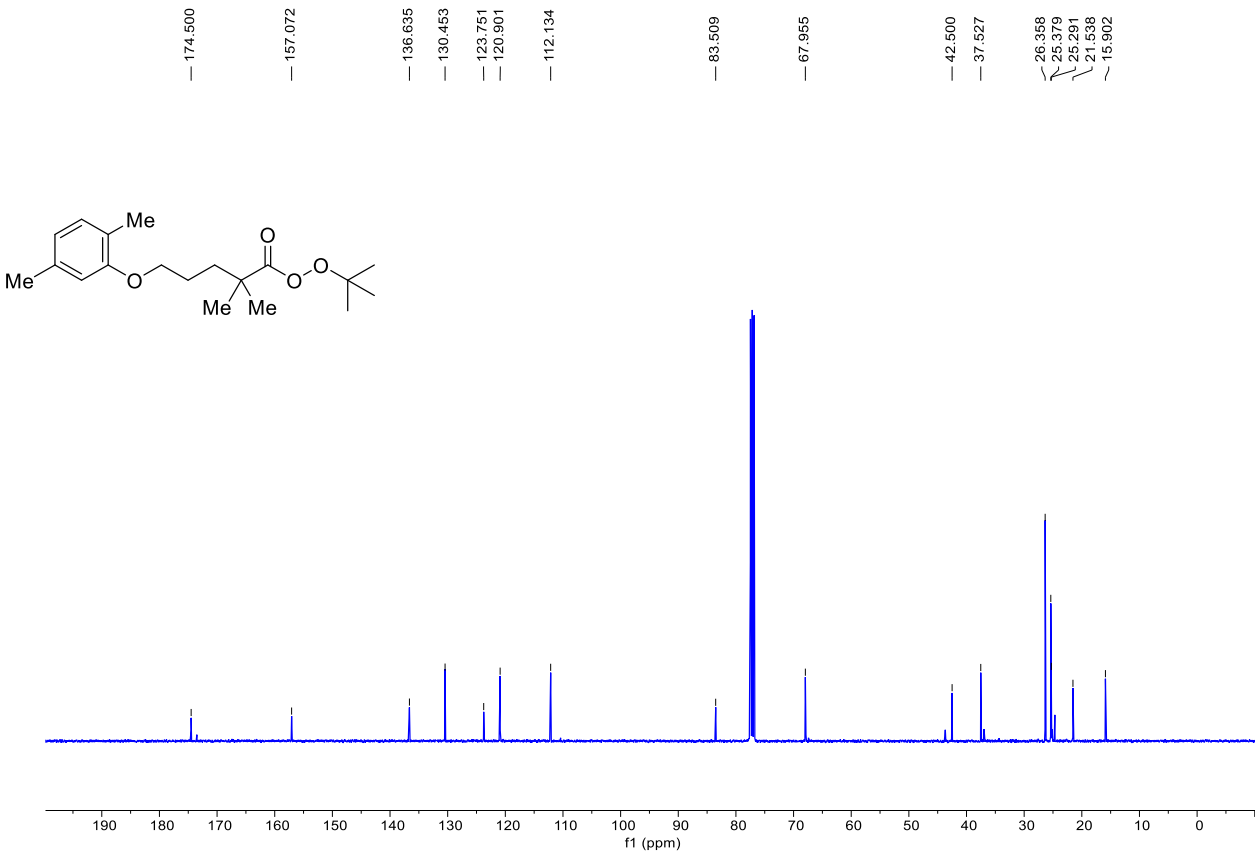


***tert*-Butyl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentaneperoxoate (2s)**

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

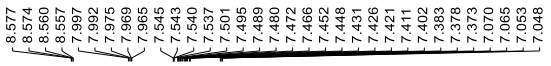


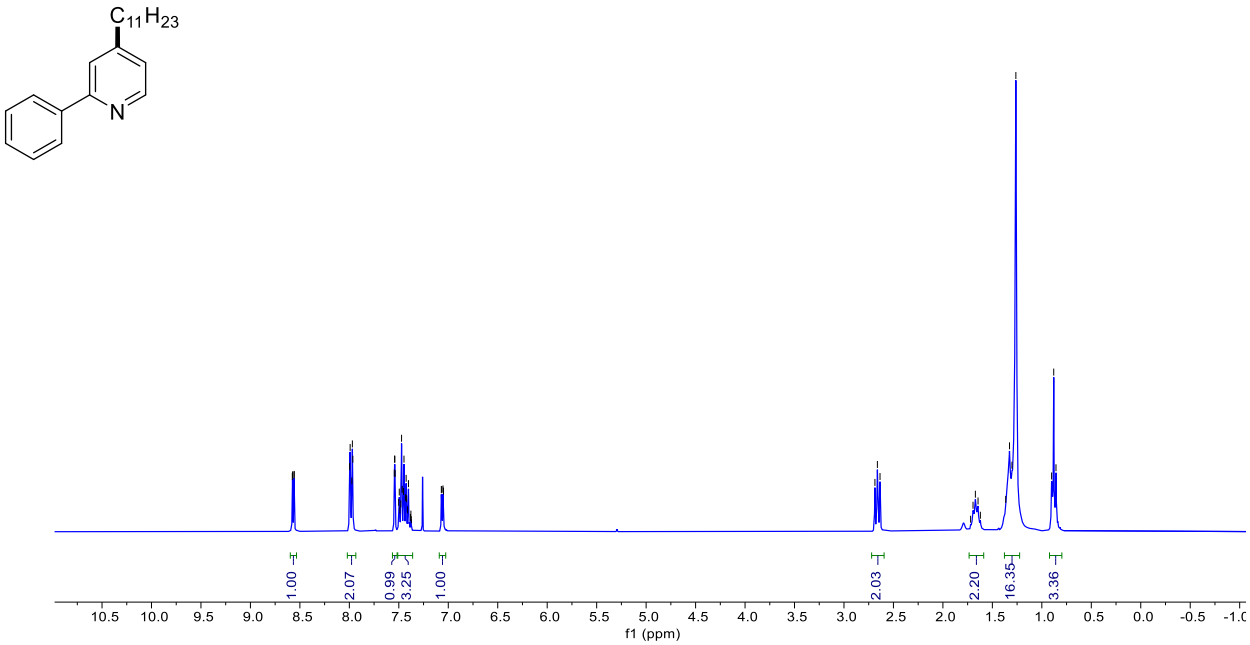
^{13}C NMR (101 MHz, $CDCl_3$)



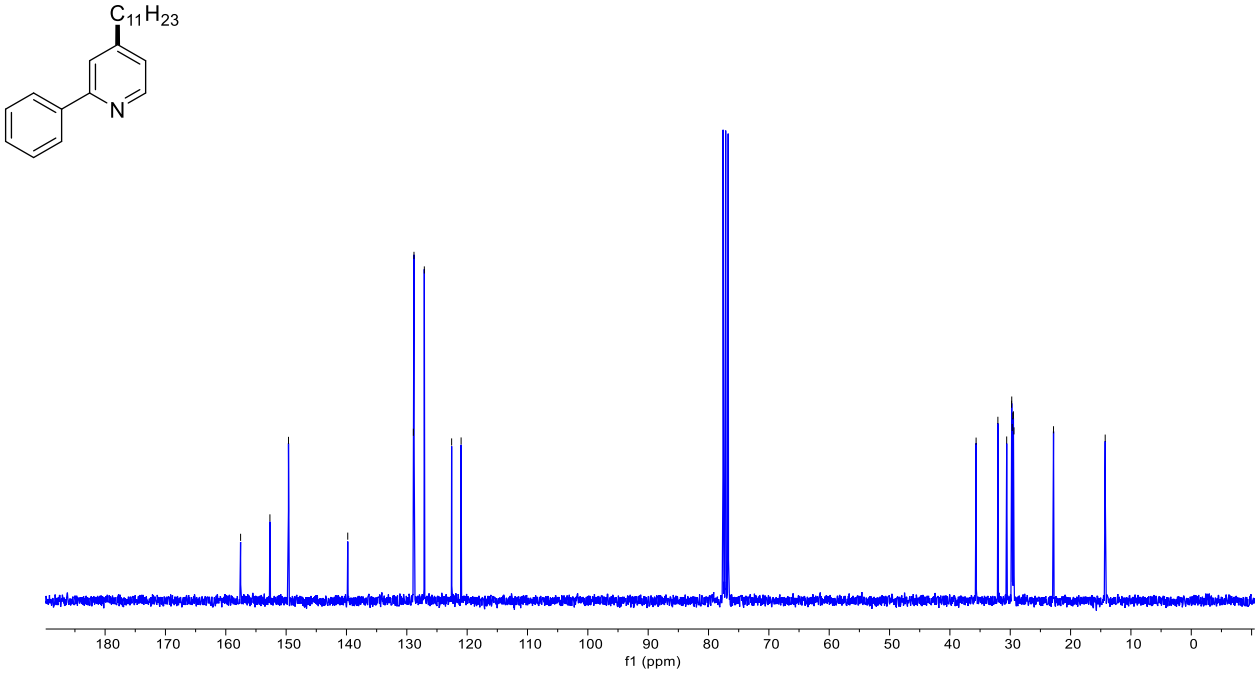
2-Phenyl-4-undecylpyridine (3a)

^{1}H NMR (300 MHz, $CDCl_3$)



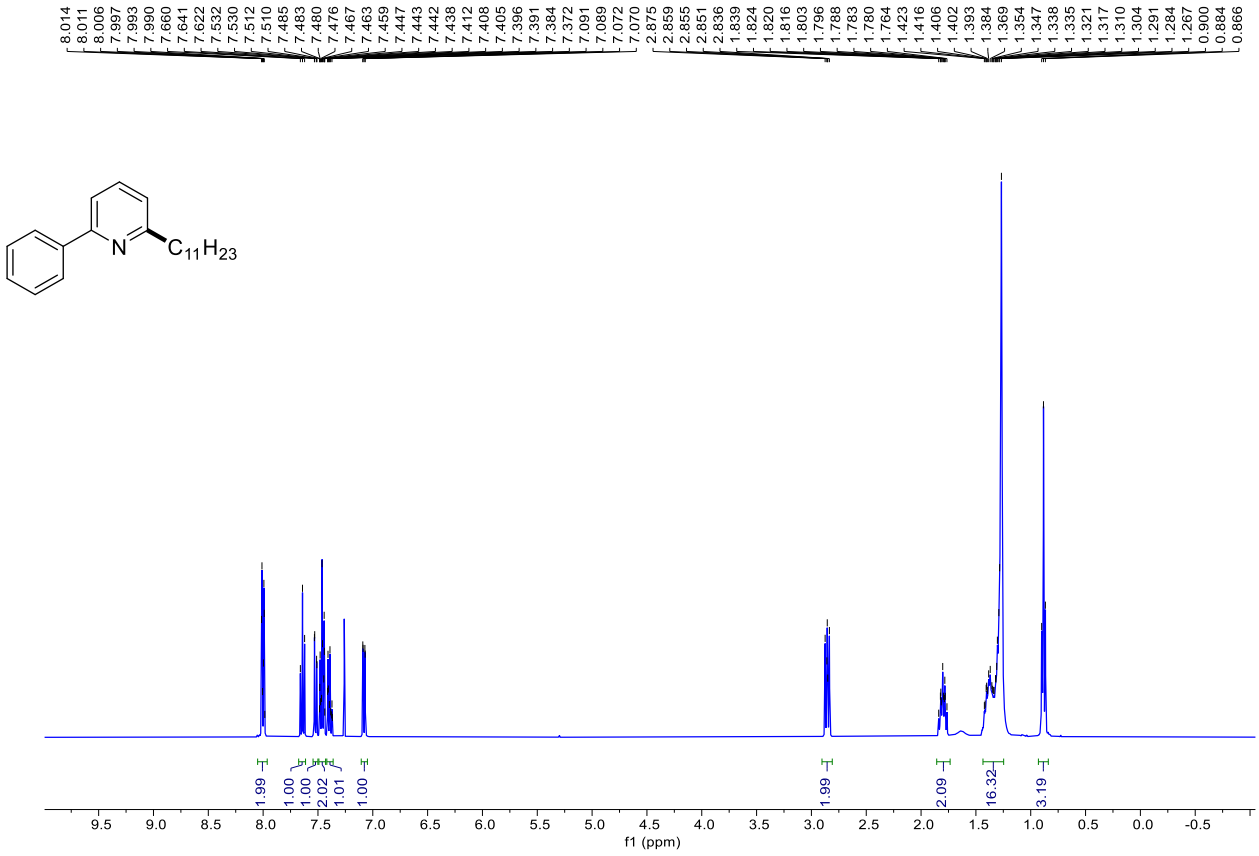


^{13}C NMR (76 MHz, $CDCl_3$)

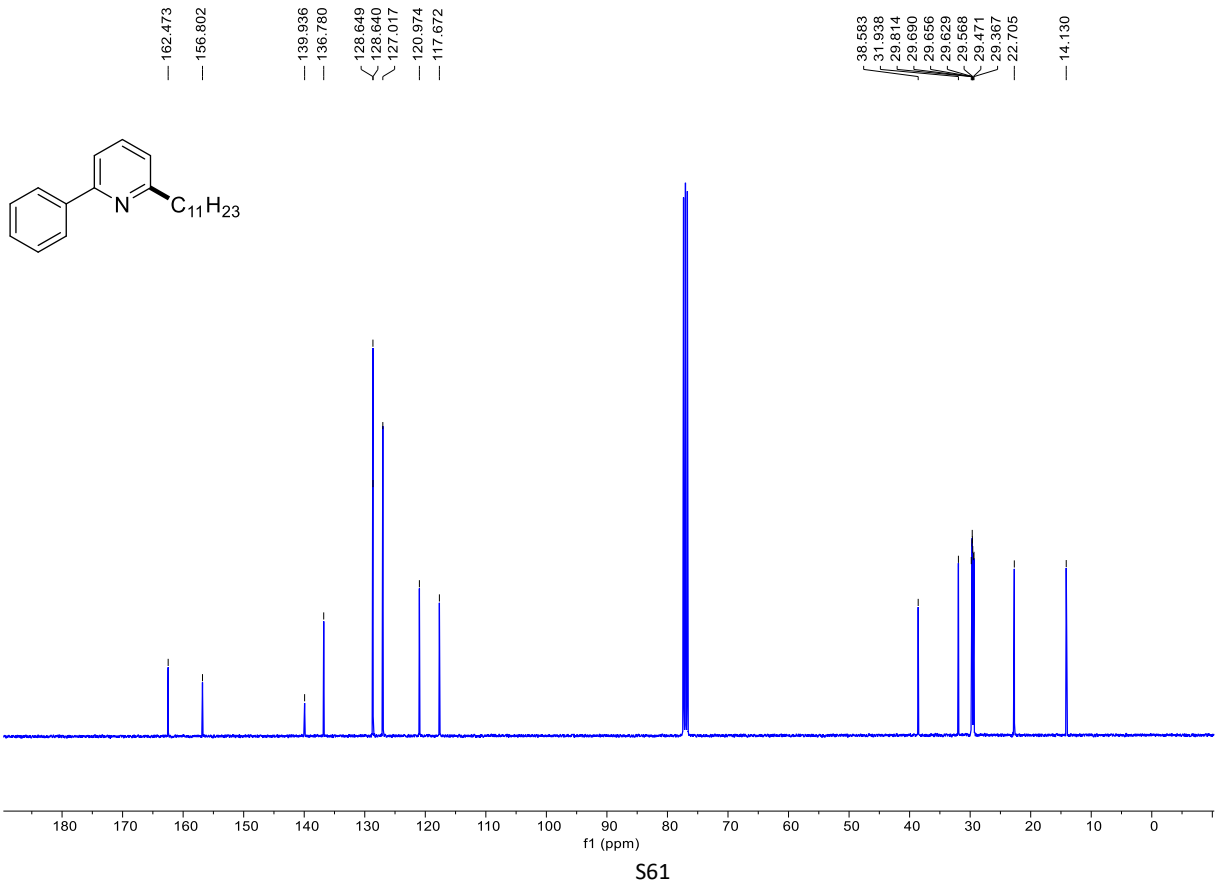


2-Phenyl-6-undecylpyridine (3a')

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

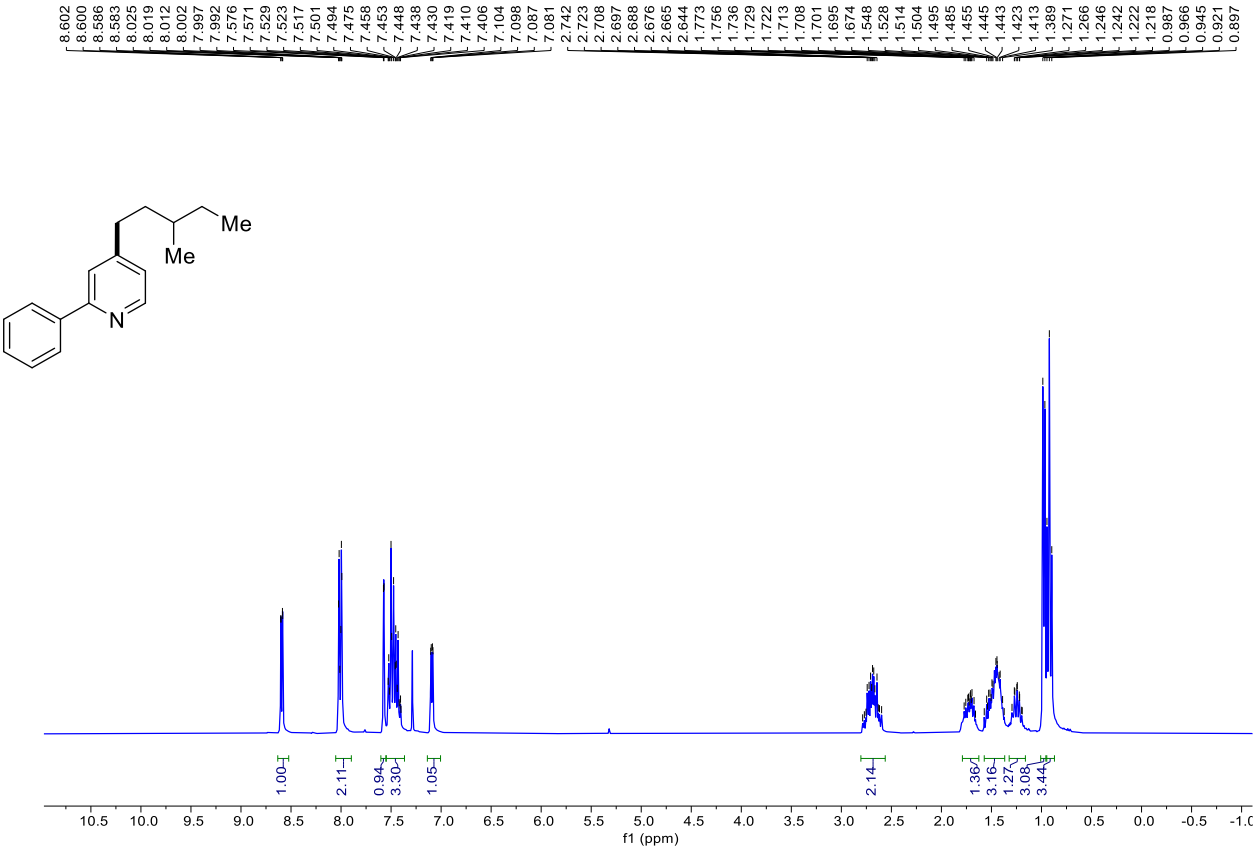


^{13}C NMR (101 MHz, $CDCl_3$)

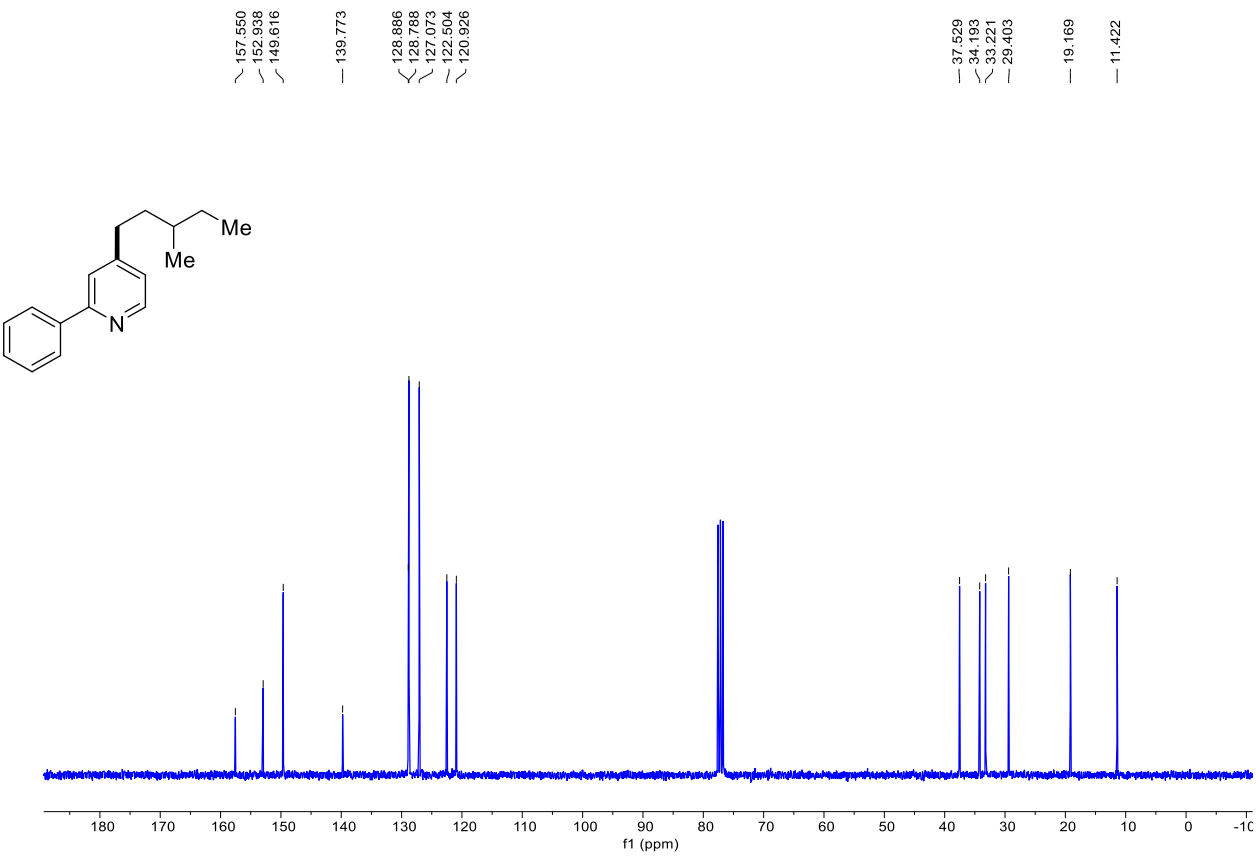


4-(3-Methylpentyl)-2-phenylpyridine (3b)

^{1}H NMR (300 MHz, $CDCl_3$)

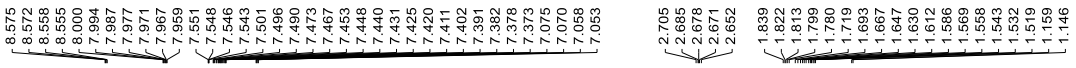


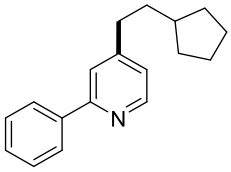
^{13}C NMR (76 MHz, $CDCl_3$)

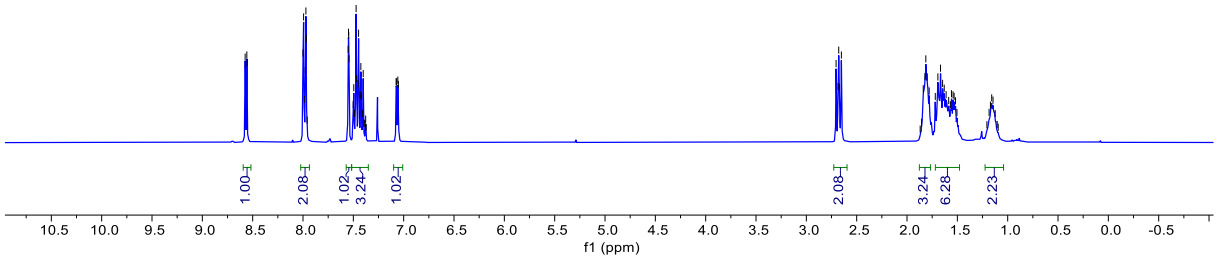


4-(2-Cyclopentylethyl)-2-phenylpyridine (3c)

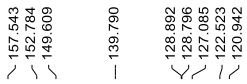
^{1}H NMR (300 MHz, $CDCl_3$)

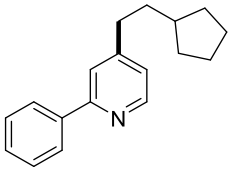


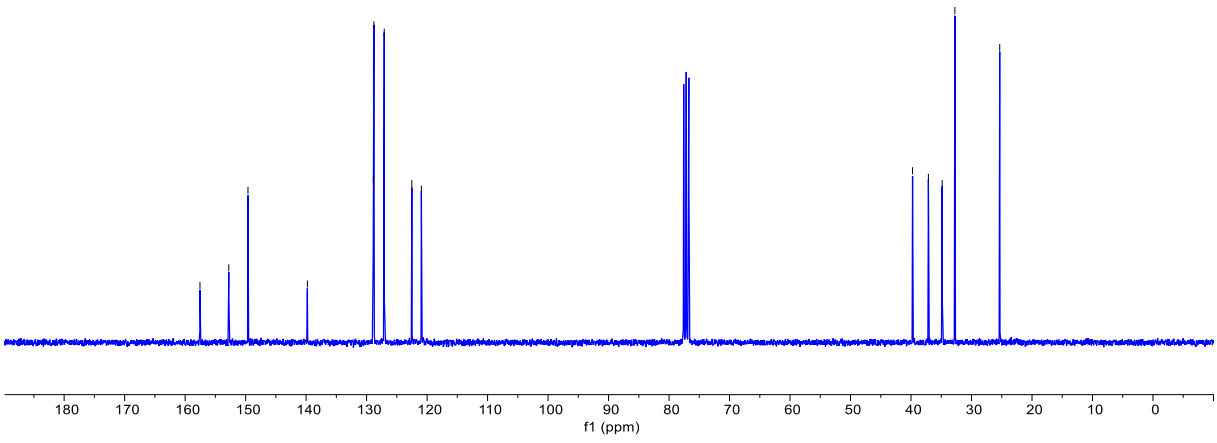




^{13}C NMR (76 MHz, $CDCl_3$)

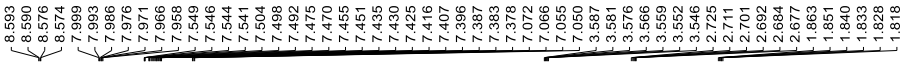


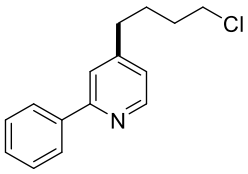


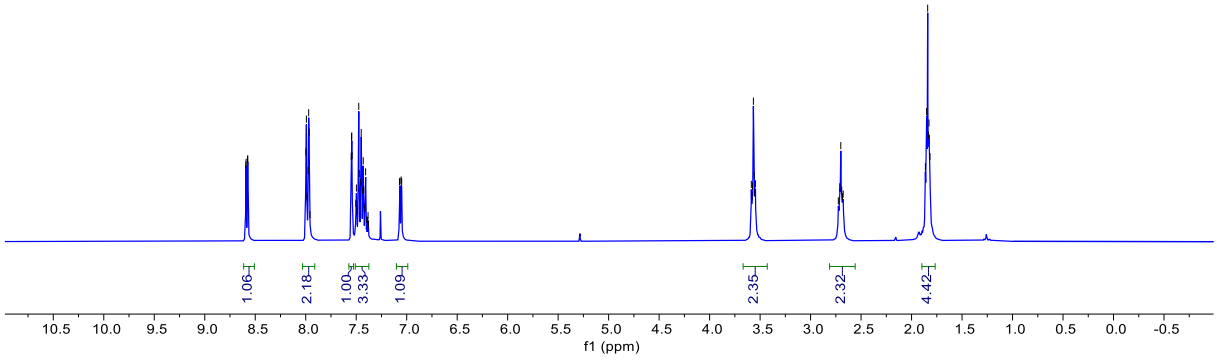


4-(4-Chlorobutyl)-2-phenylpyridine (3d)

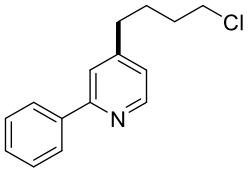
^{1}H NMR (300 MHz, $CDCl_3$)





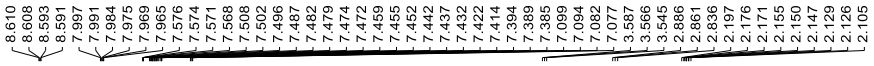


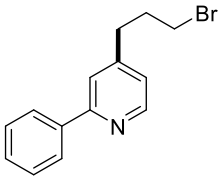
^{13}C NMR (76 MHz, $CDCl_3$)

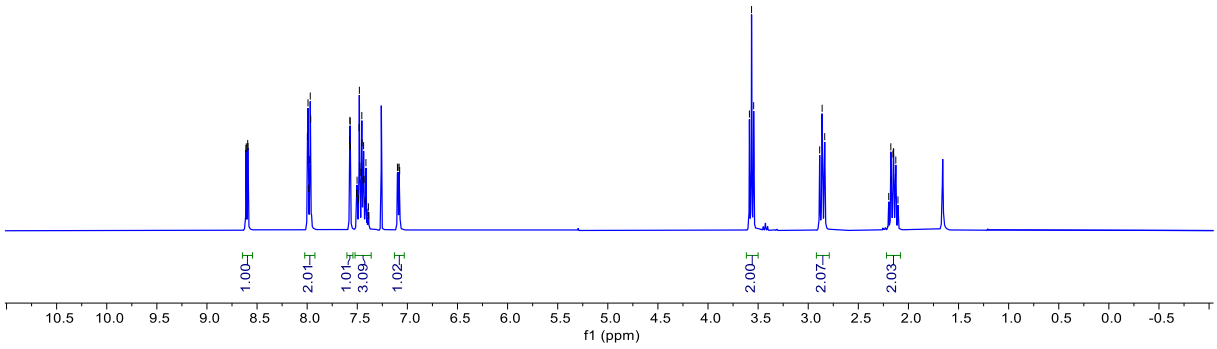


4-(3-bromopropyl)-2-phenylpyridine (3e)

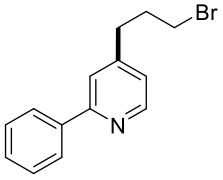
^{1}H NMR (300 MHz, $CDCl_3$)





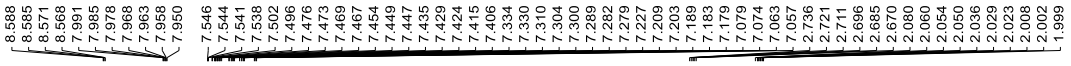


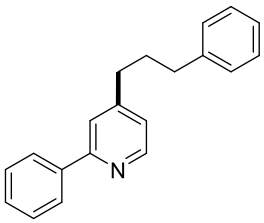
^{13}C NMR (76 MHz, $CDCl_3$)

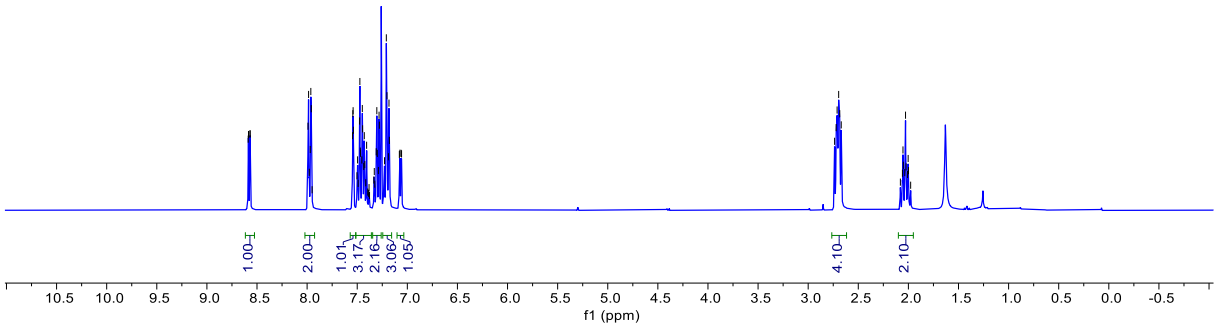


2-Phenyl-4-(3-phenylpropyl)pyridine (3f)

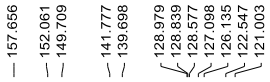
^{1}H NMR (300 MHz, $CDCl_3$)

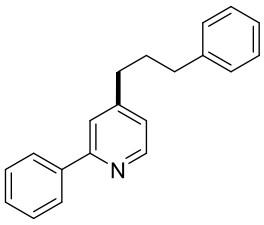






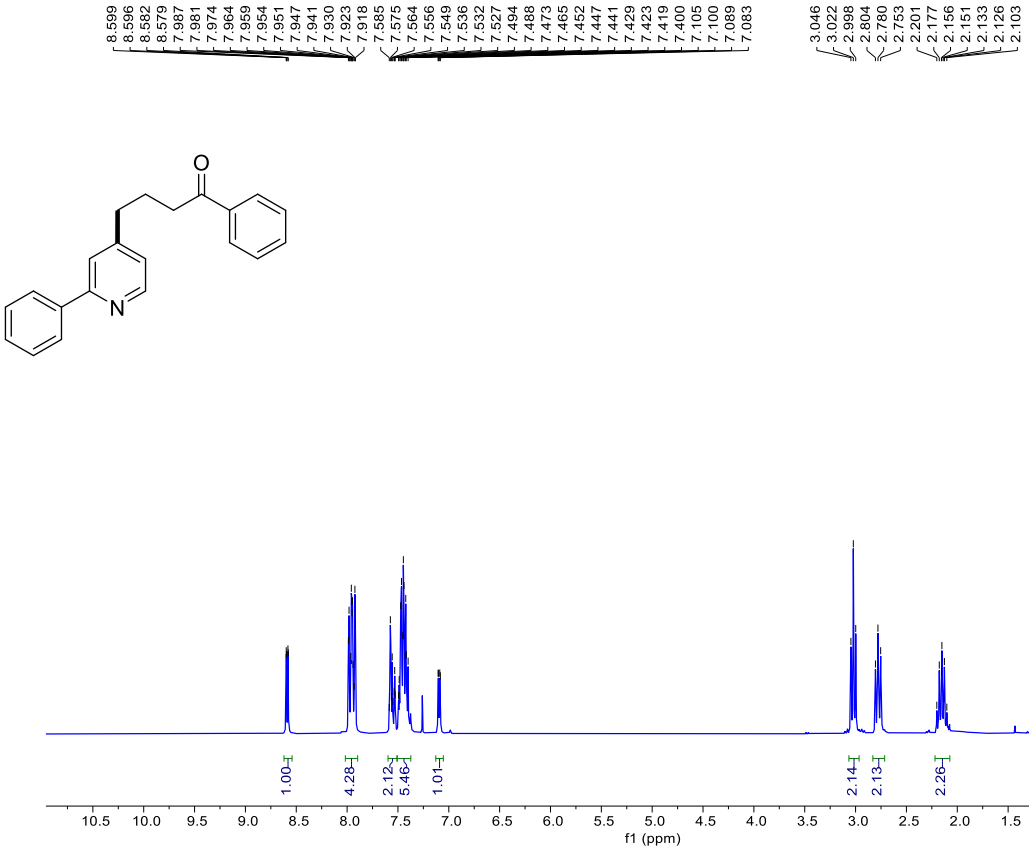
^{13}C NMR (76 MHz, $CDCl_3$)



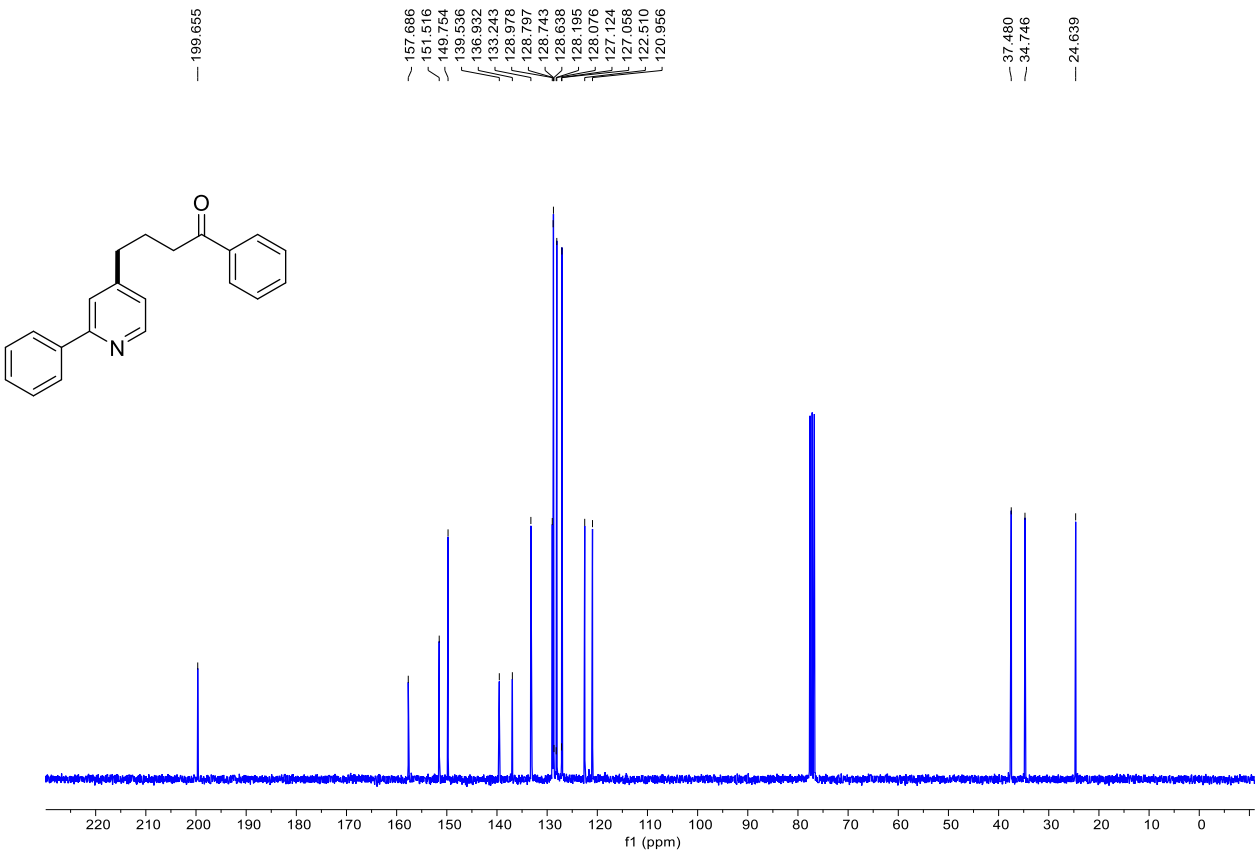


1-Phenyl-4-(2-phenylpyridin-4-yl)butan-1-one (3g)

^{1}H NMR (300 MHz, $CDCl_3$)

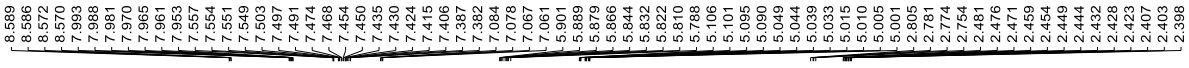


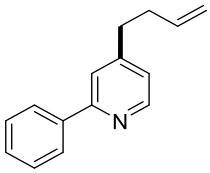
^{13}C NMR (76 MHz, $CDCl_3$)

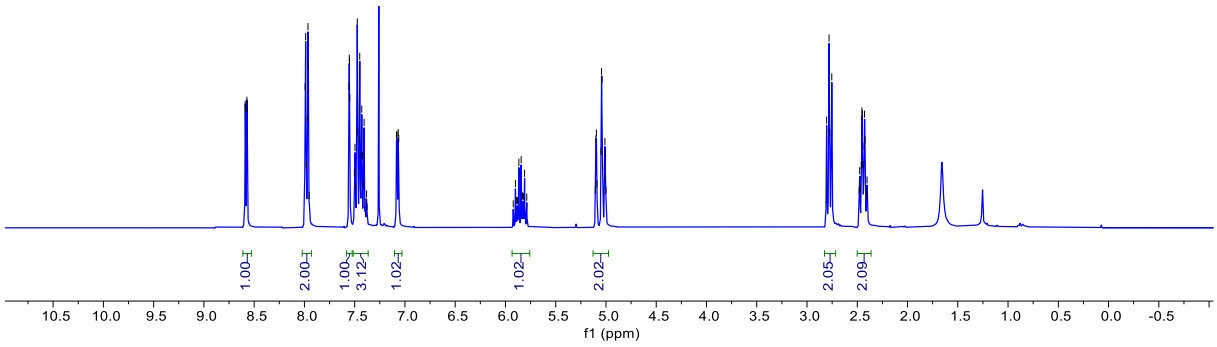


4-(But-3-en-1-yl)-2-phenylpyridine (3h)

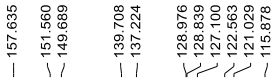
^{1}H NMR (300 MHz, $CDCl_3$)

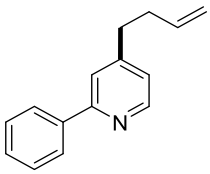






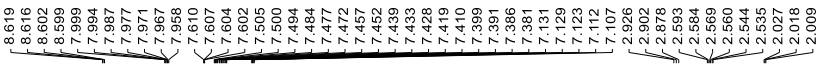
^{13}C NMR (76 MHz, $CDCl_3$)

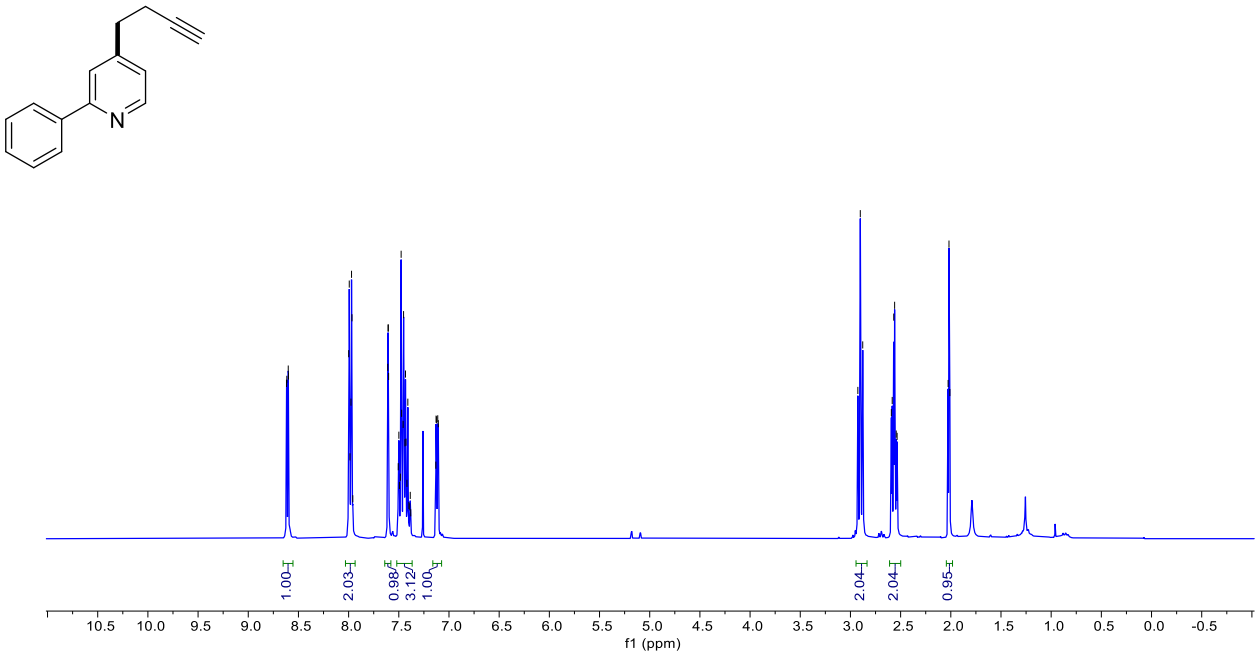




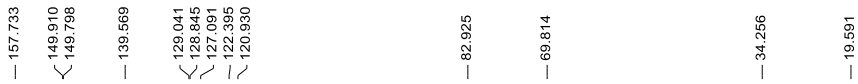
4-(But-3-yn-1-yl)-2-phenylpyridine (3i)

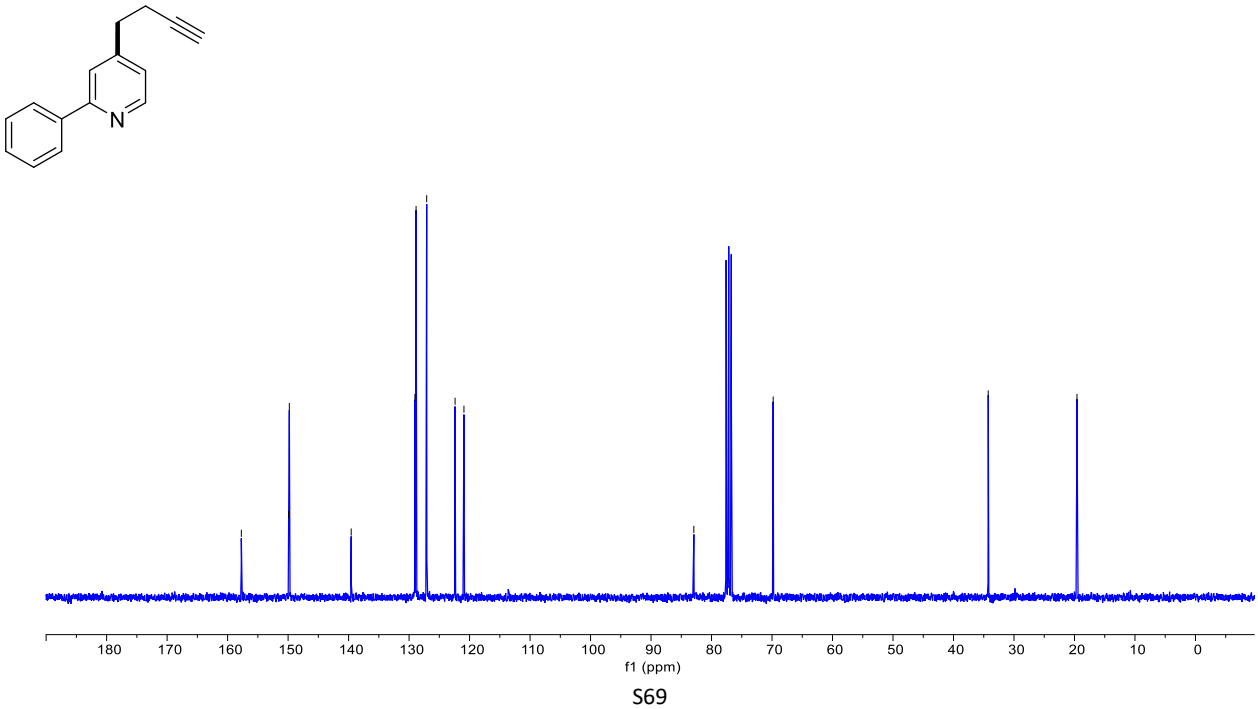
^{1}H NMR (300 MHz, $CDCl_3$)





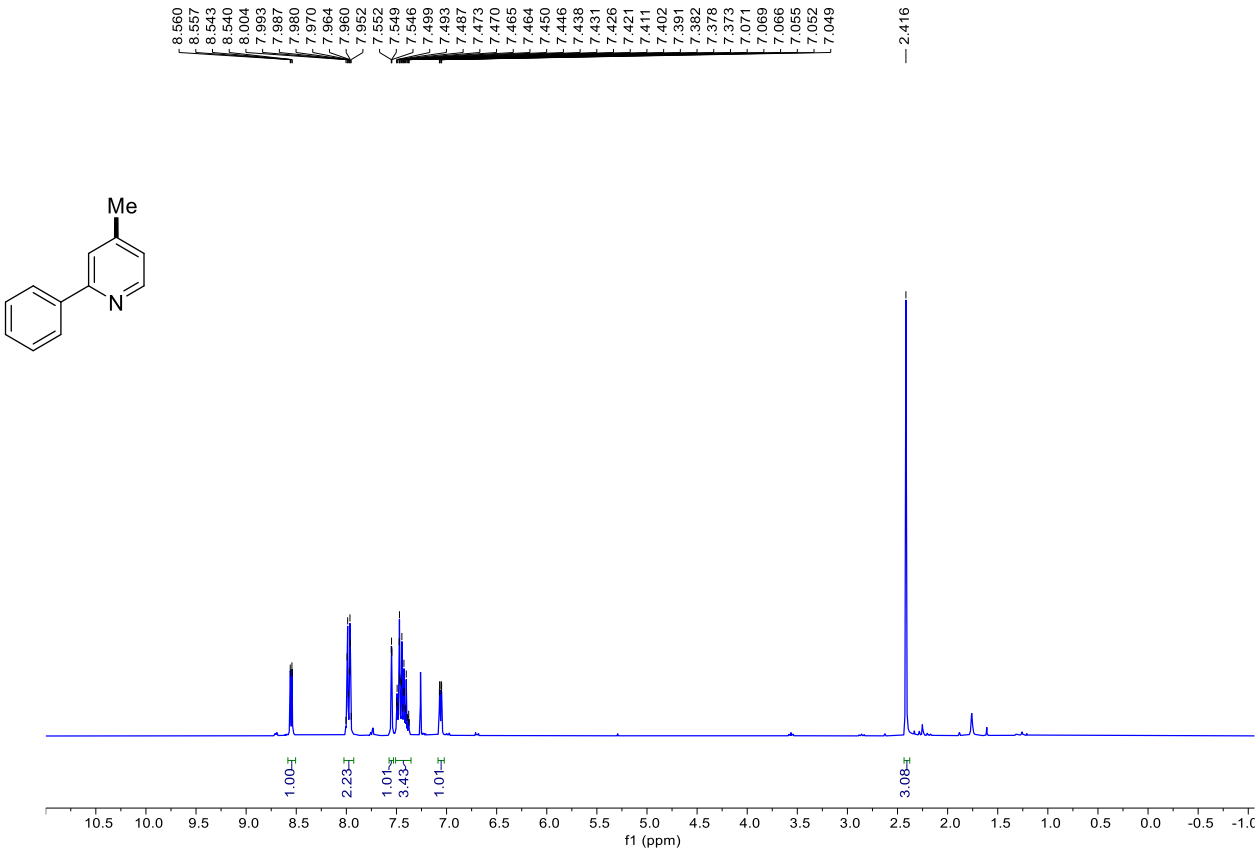
^{13}C NMR (76 MHz, $CDCl_3$)



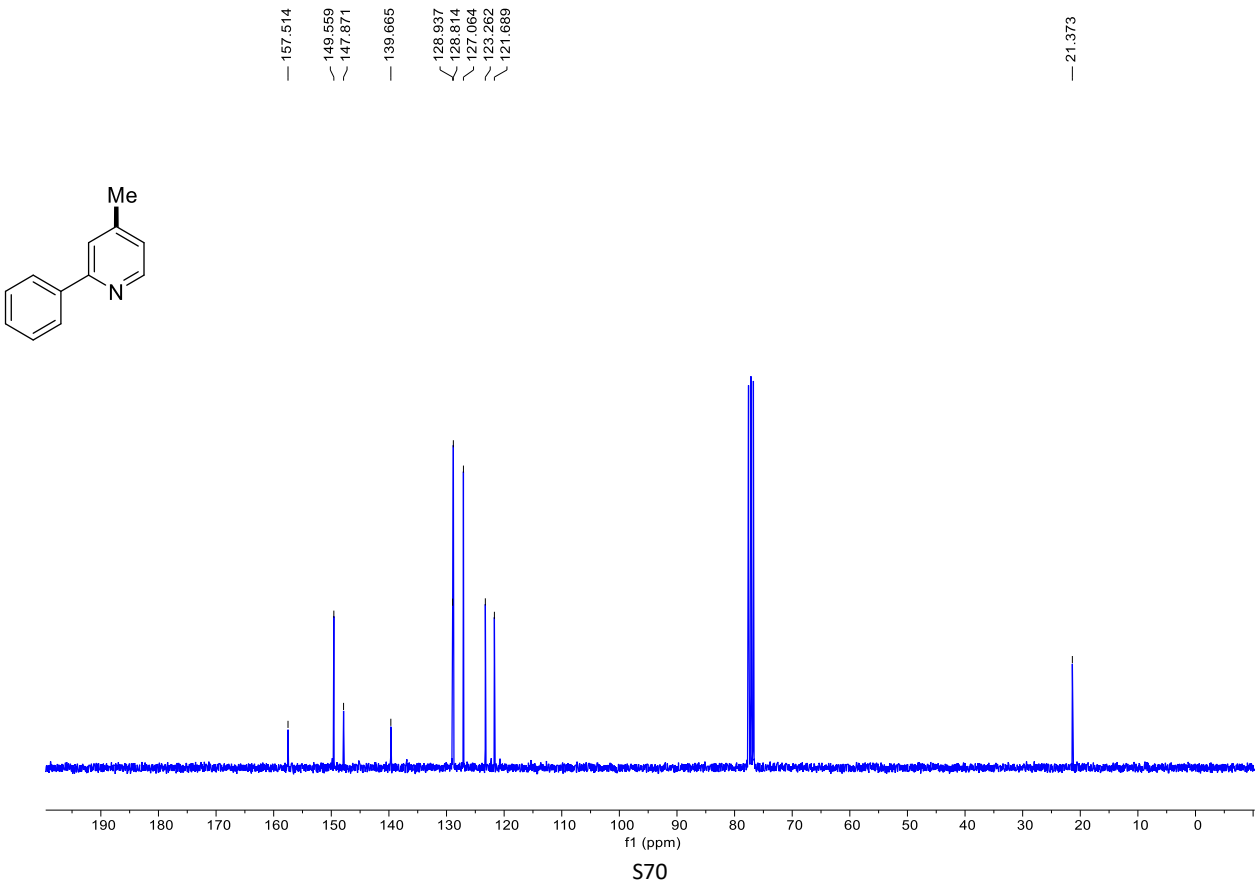


4-Methyl-2-phenylpyridine (3j)

^{1}H NMR (300 MHz, $CDCl_3$)

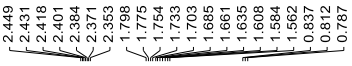


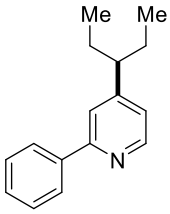
^{13}C NMR (76 MHz, $CDCl_3$)

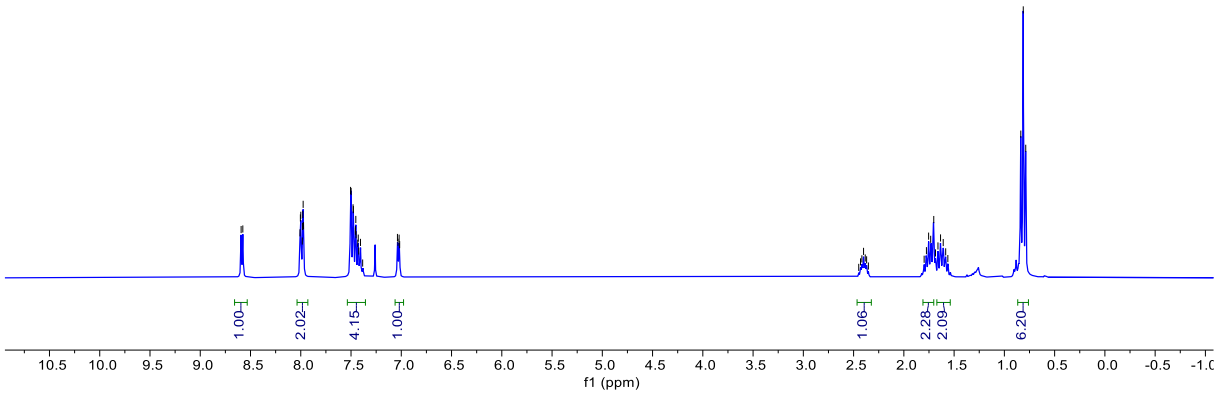


4-(Pentan-3-yl)-2-phenylpyridine (3k)

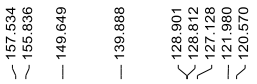
^{1}H NMR (300 MHz, $CDCl_3$)

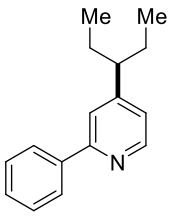


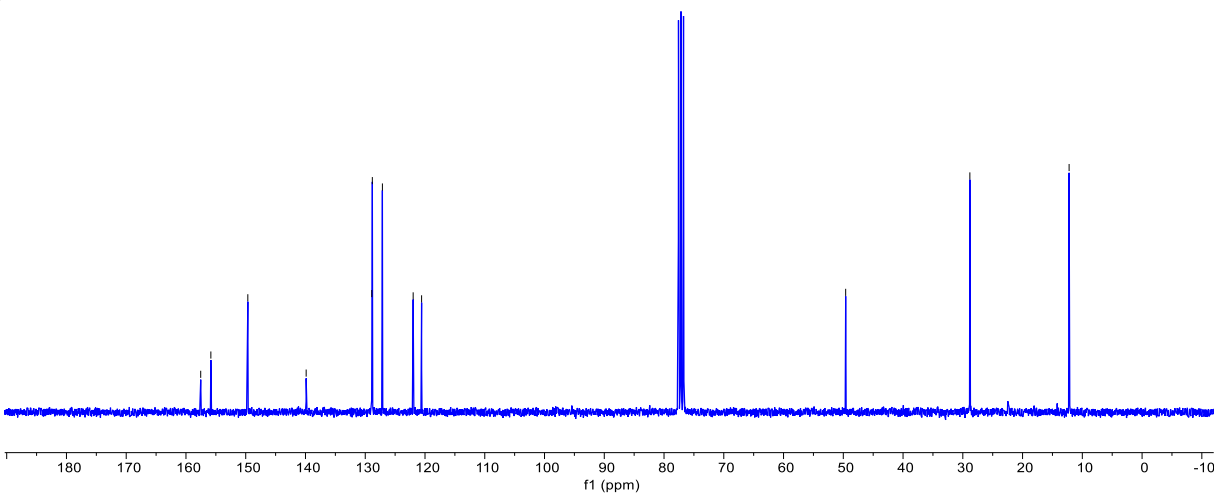




^{13}C NMR (76 MHz, $CDCl_3$)

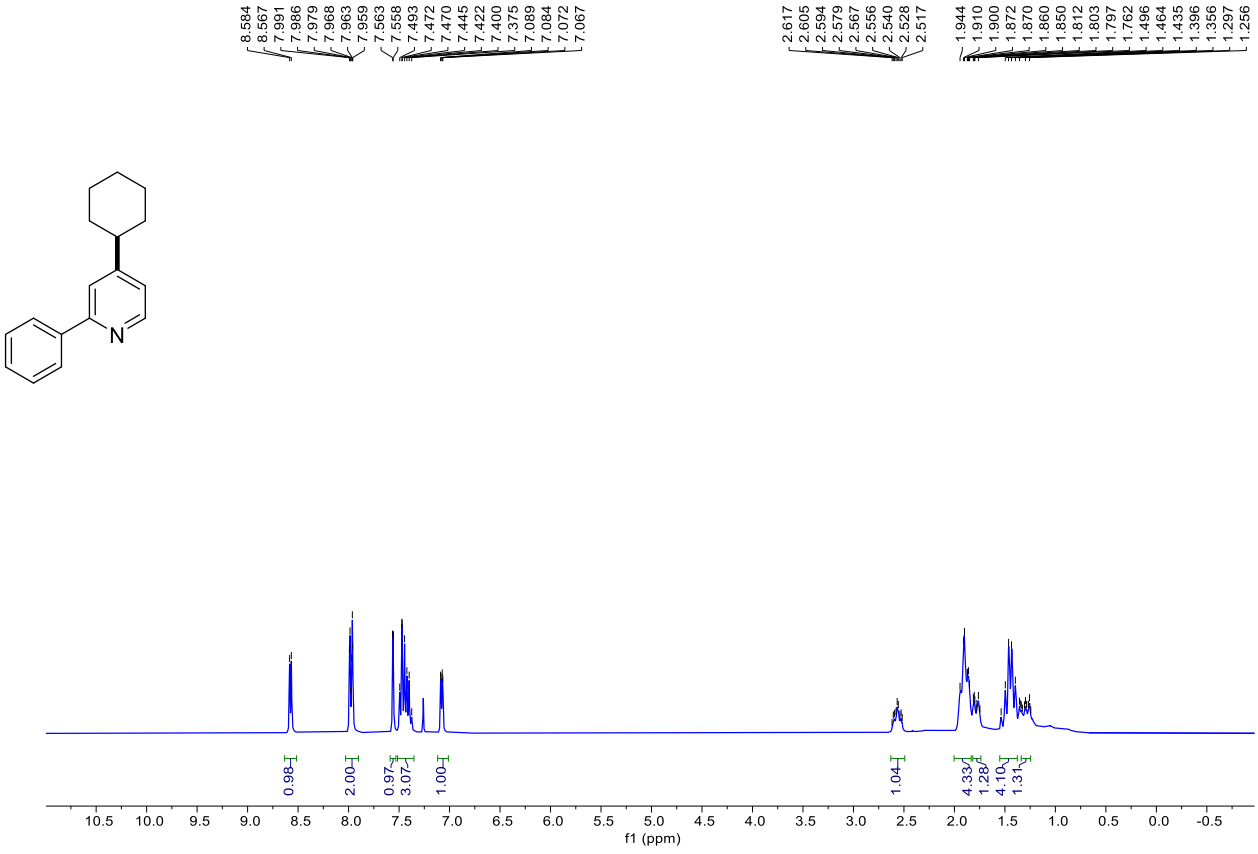




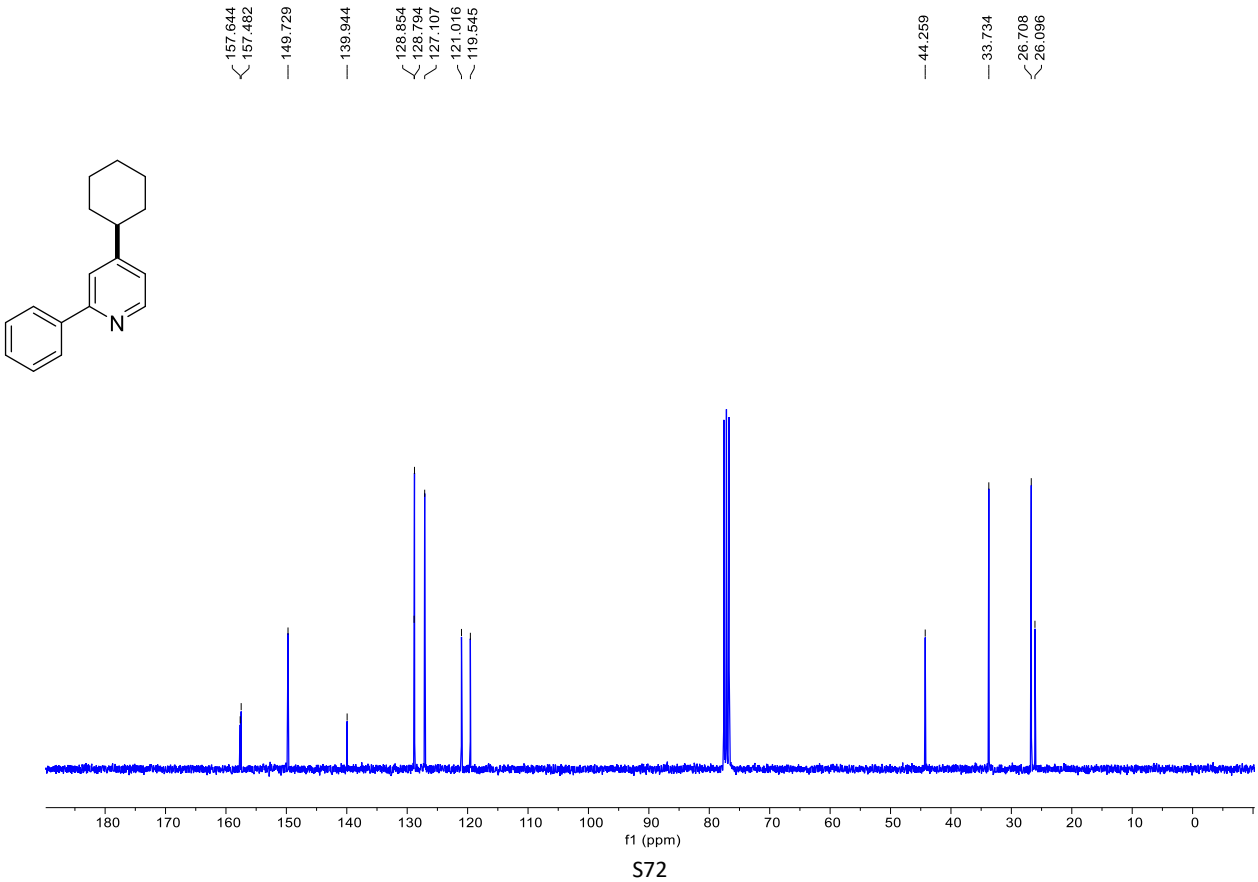


4-Cyclohexyl-2-phenylpyridine (3l)

^{1}H NMR (300 MHz, $CDCl_3$)

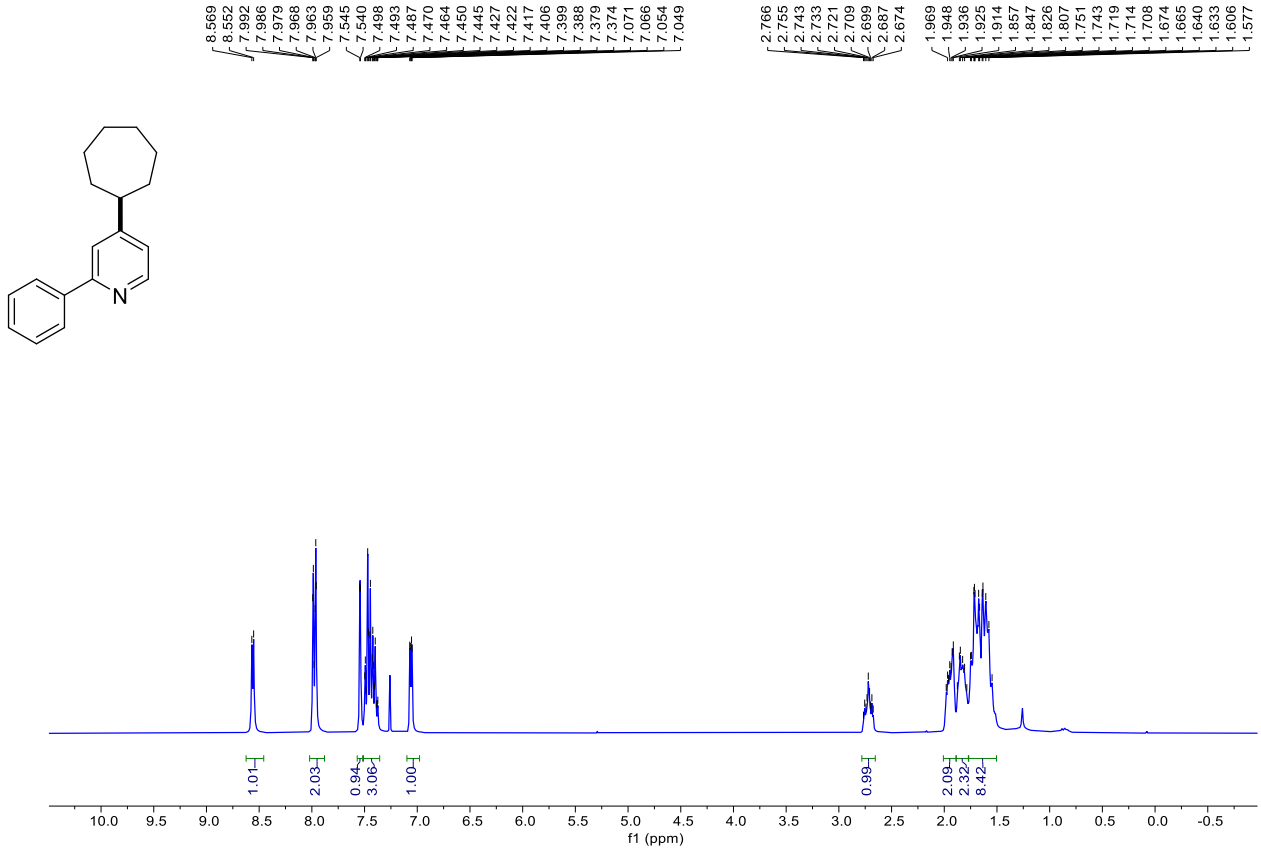


^{13}C NMR (76 MHz, $CDCl_3$)

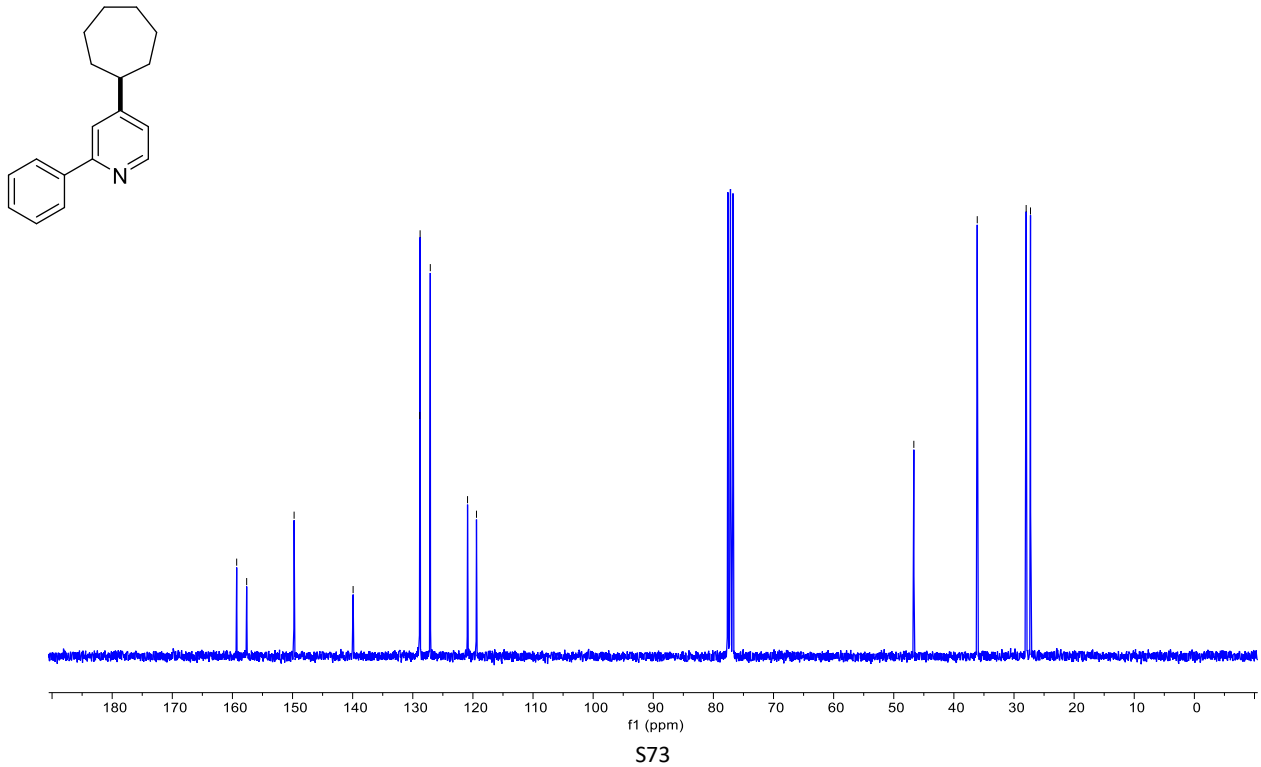


4-Cycloheptyl-2-phenylpyridine (3m)

^{1}H NMR (300 MHz, $CDCl_3$)

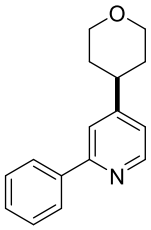


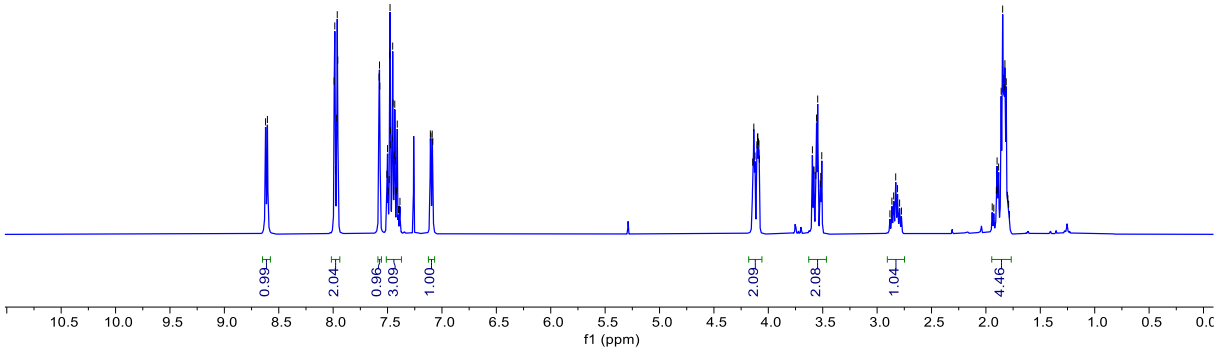
^{13}C NMR (76 MHz, $CDCl_3$)



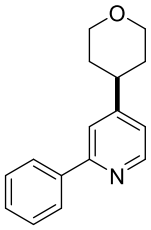
2-Phenyl-4-(tetrahydro-2H-pyran-4-yl)pyridine (3n)

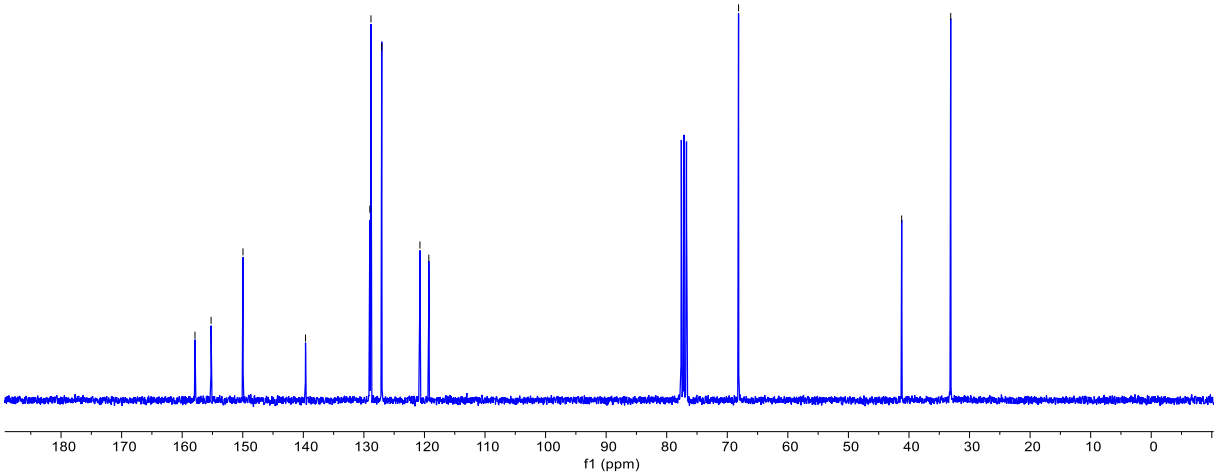
^{1}H NMR (300 MHz, $CDCl_3$)





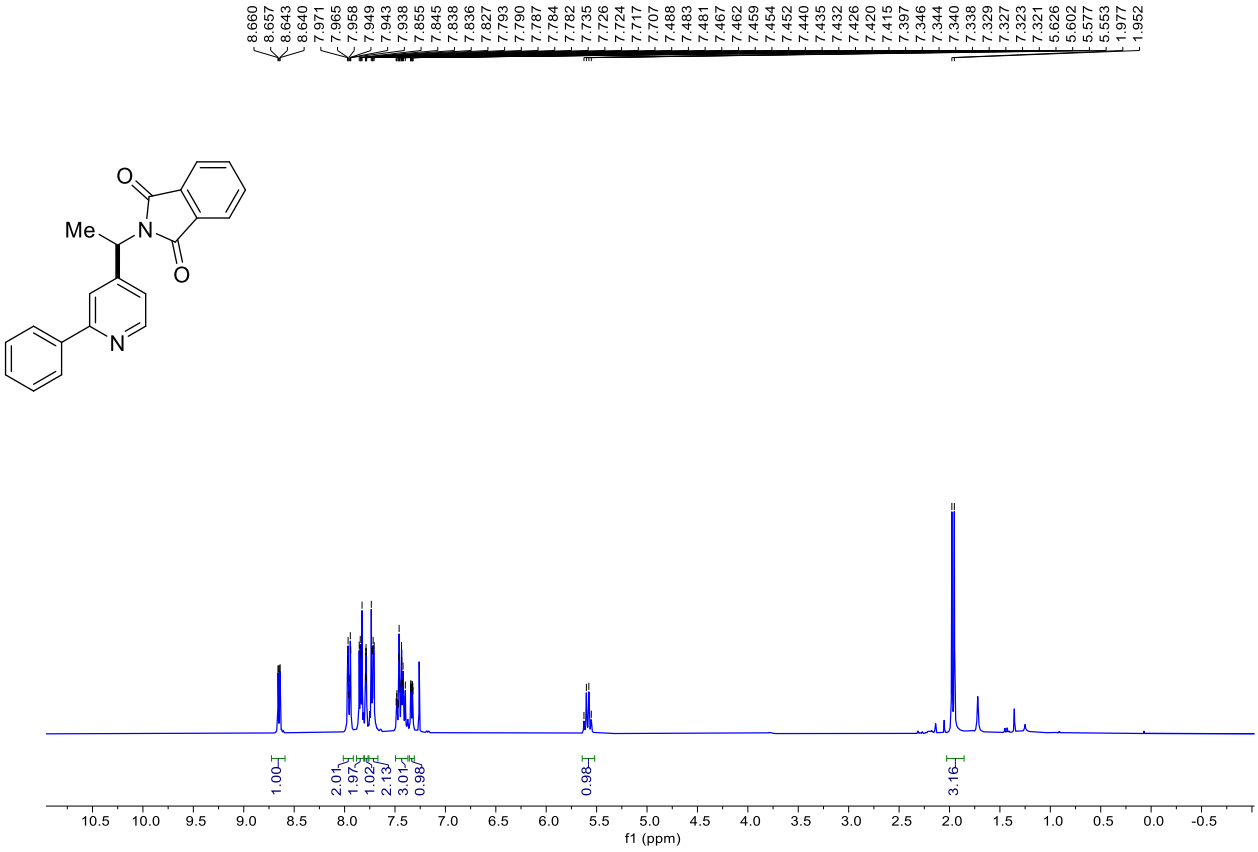
^{13}C NMR (76 MHz, $CDCl_3$)



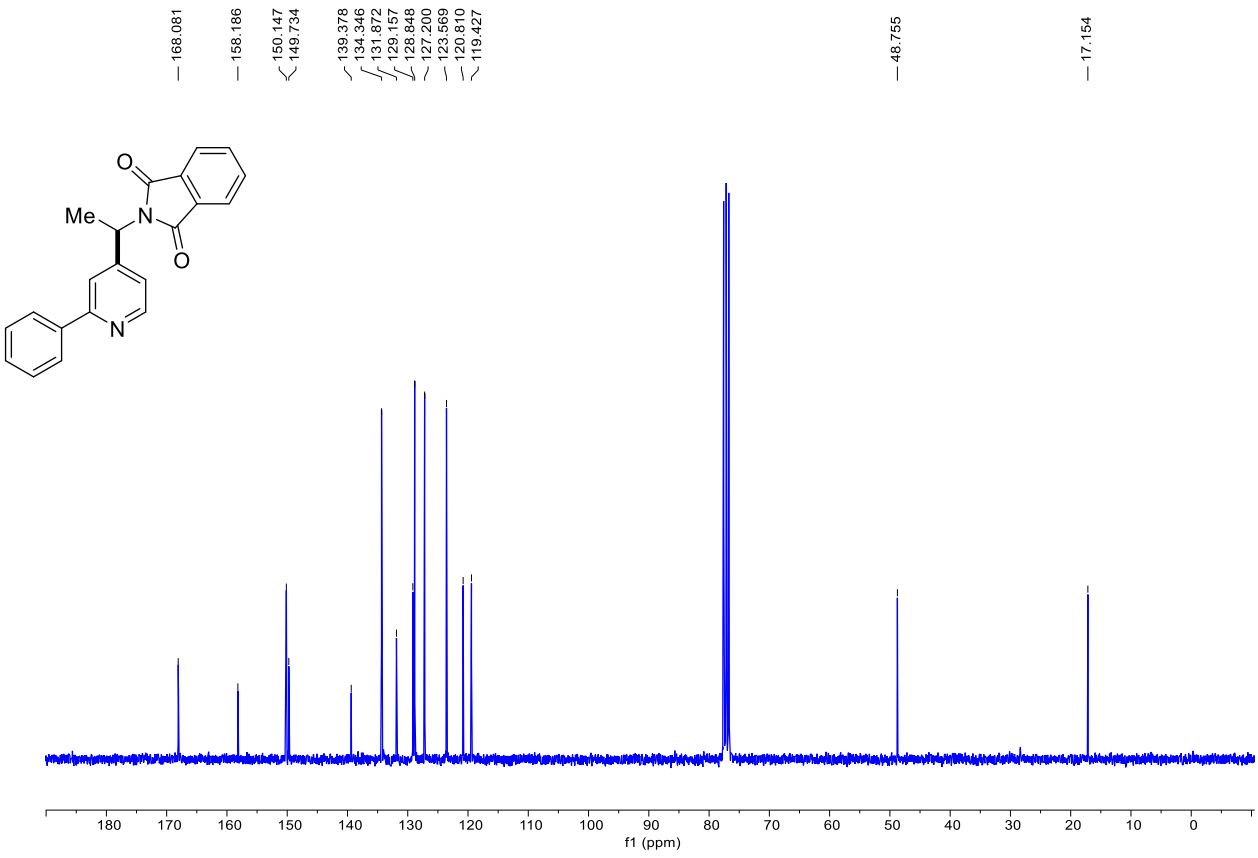


2-(1-(2-Phenylpyridin-4-yl)ethyl)isoindoline-1,3-dione (3o)

^{1}H NMR (300 MHz, $CDCl_3$)

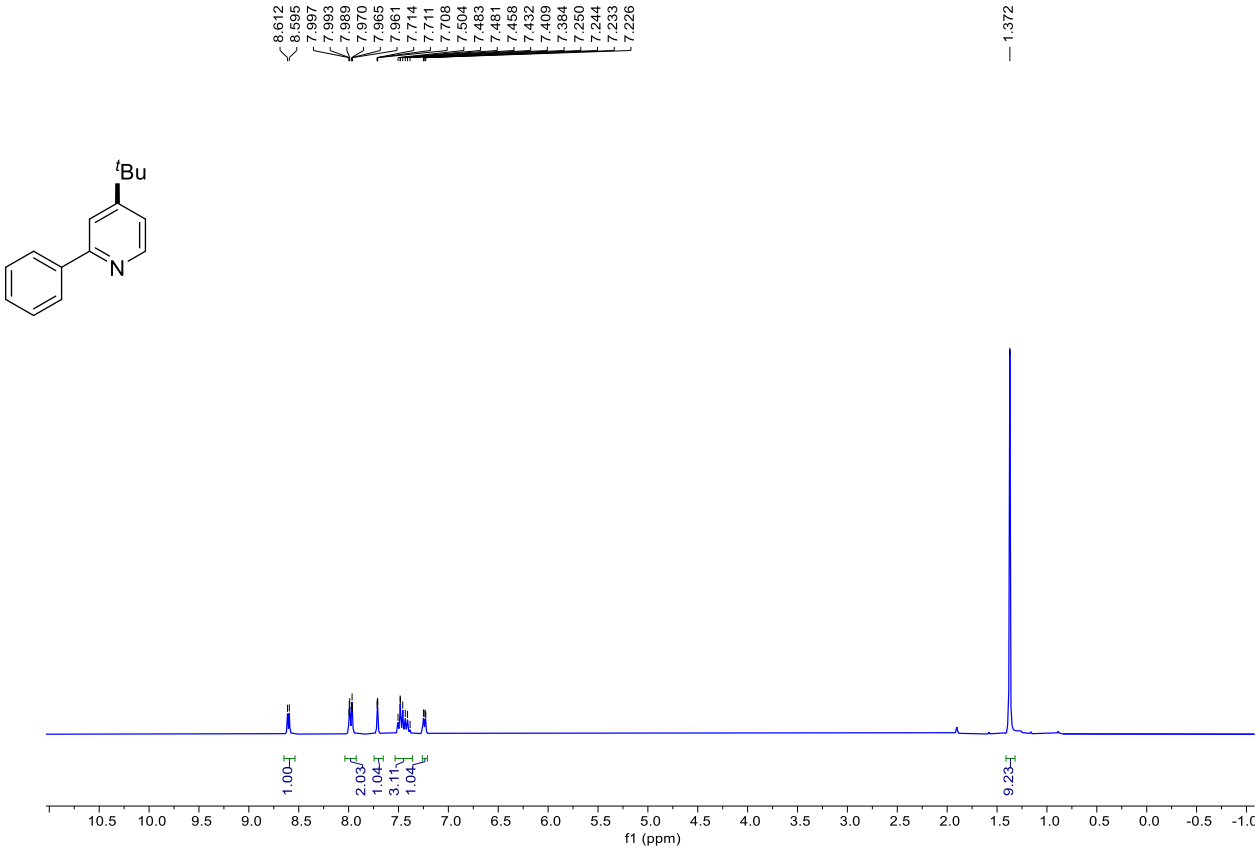


^{13}C NMR (76 MHz, $CDCl_3$)

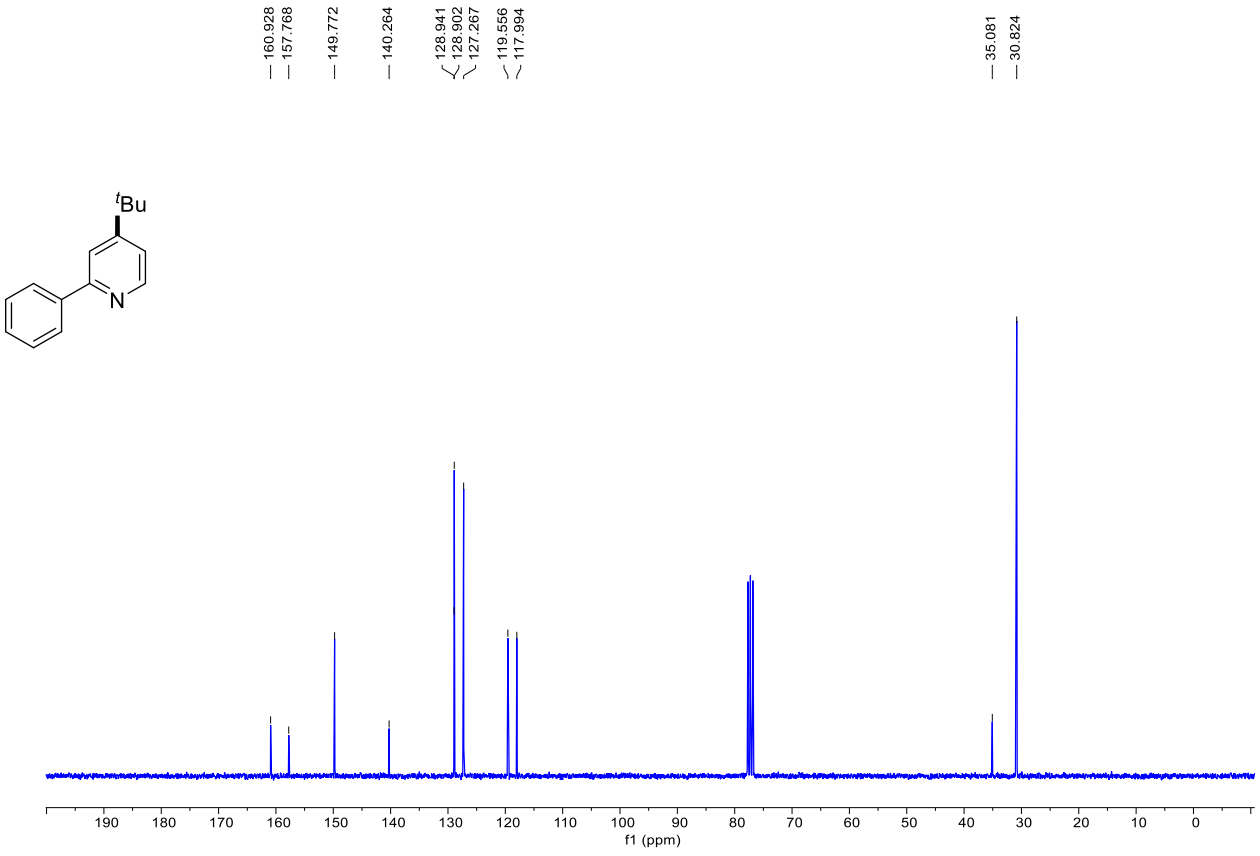


4-(*tert*-Butyl)-2-phenylpyridine (3p)

^{1}H NMR (300 MHz, $CDCl_3$)

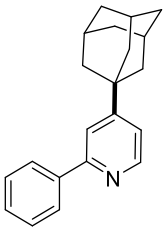


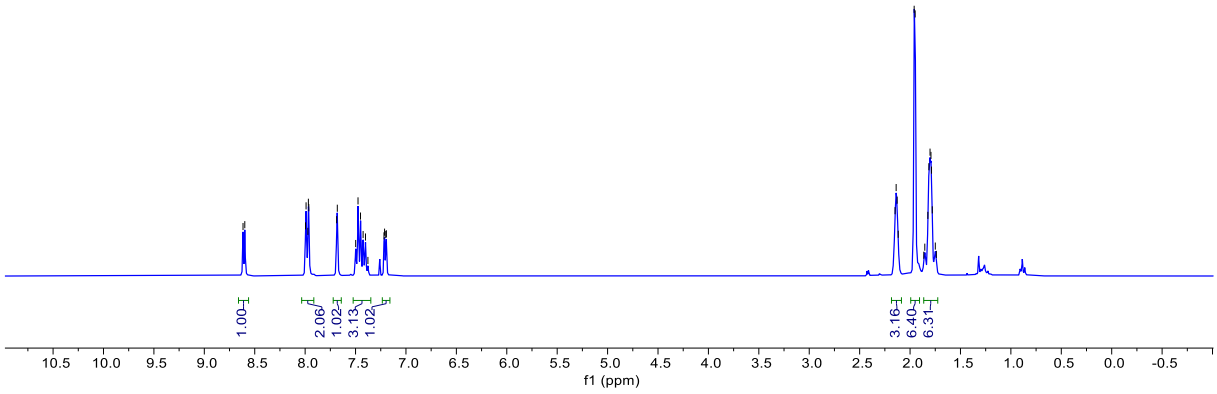
^{13}C NMR (76 MHz, $CDCl_3$)



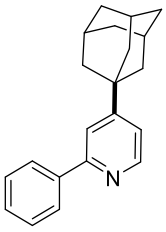
4-(Adamantan-1-yl)-2-phenylpyridine (3q)

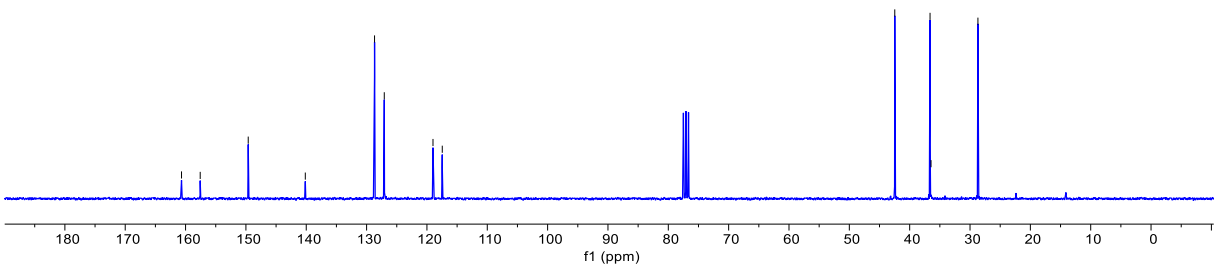
^{1}H NMR (300 MHz, $CDCl_3$)





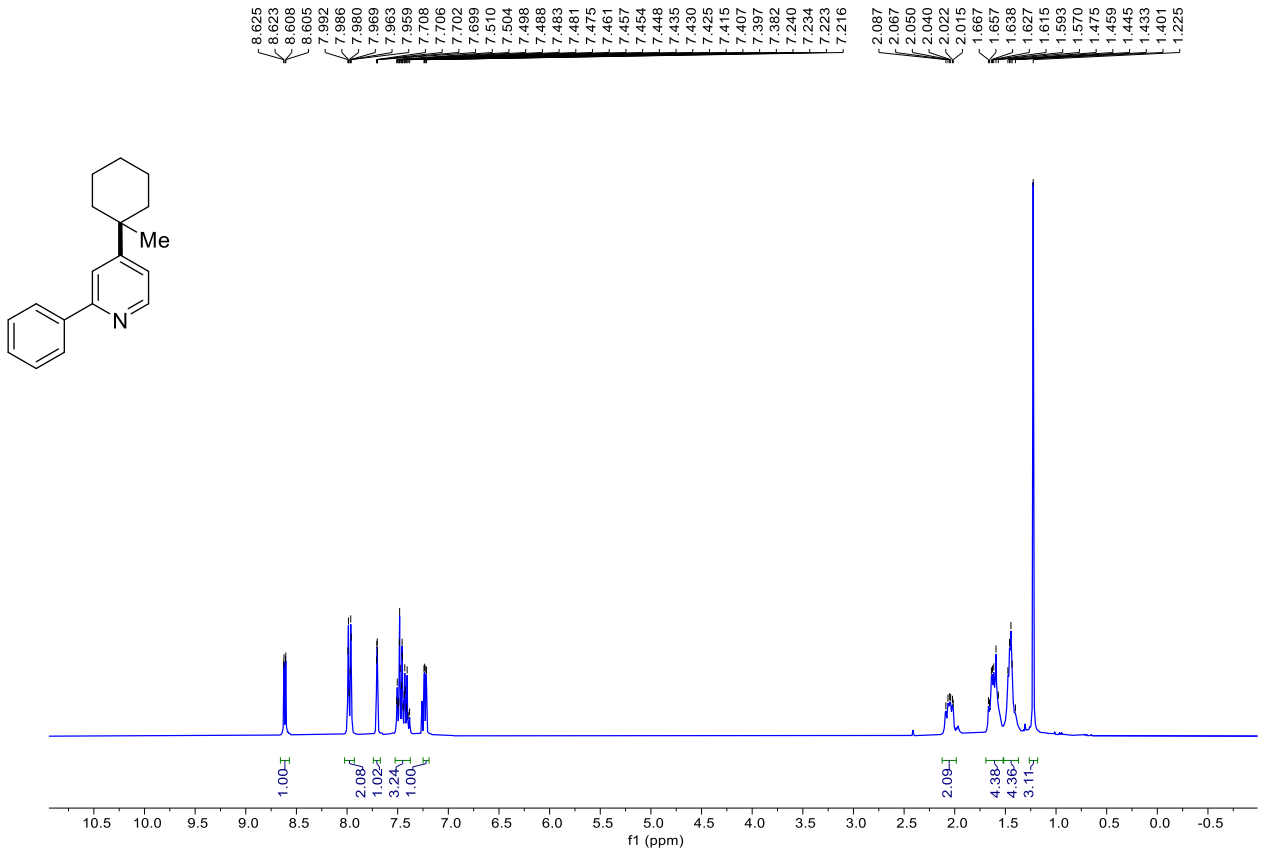
^{13}C NMR (76 MHz, $CDCl_3$)



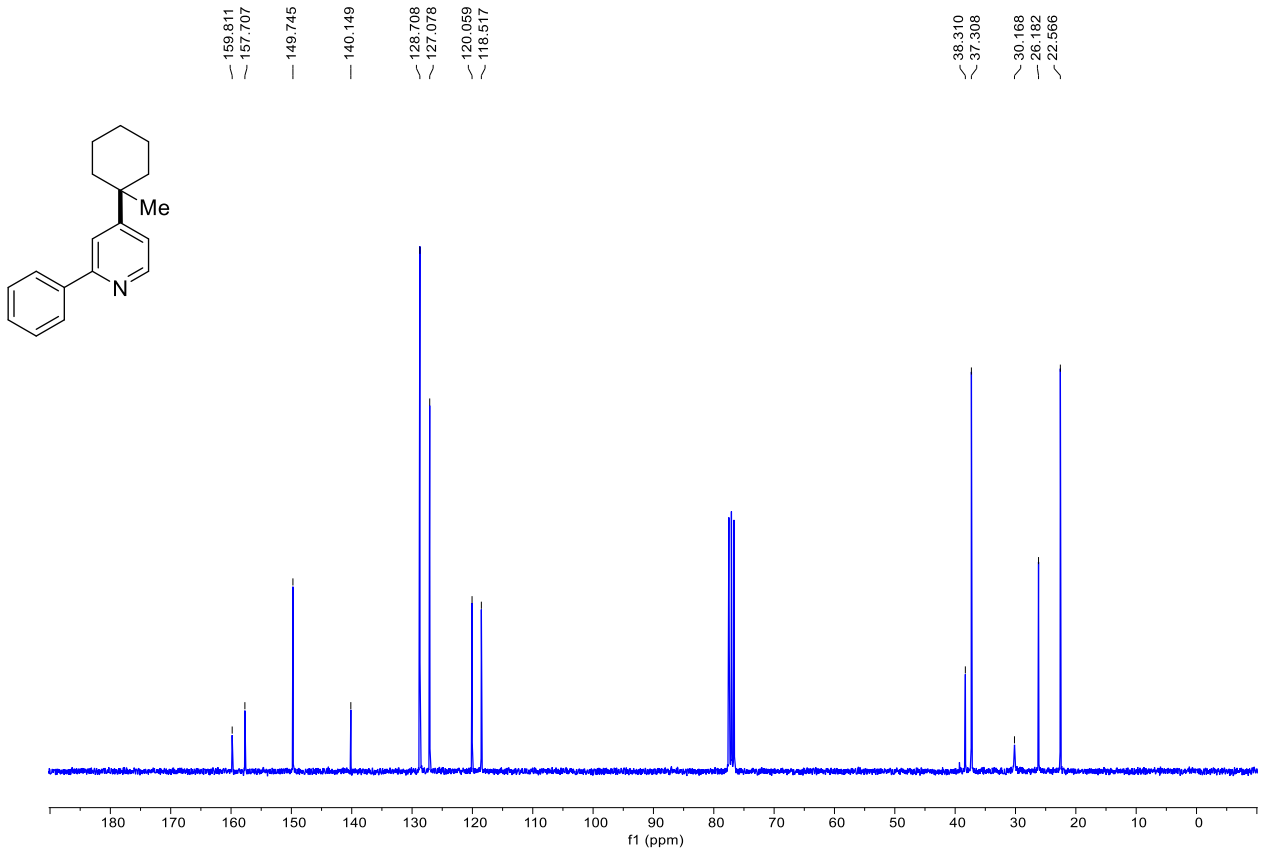


4-(1-methylcyclohexyl)-2-phenylpyridine (3r)

^{1}H NMR (300 MHz, $CDCl_3$)

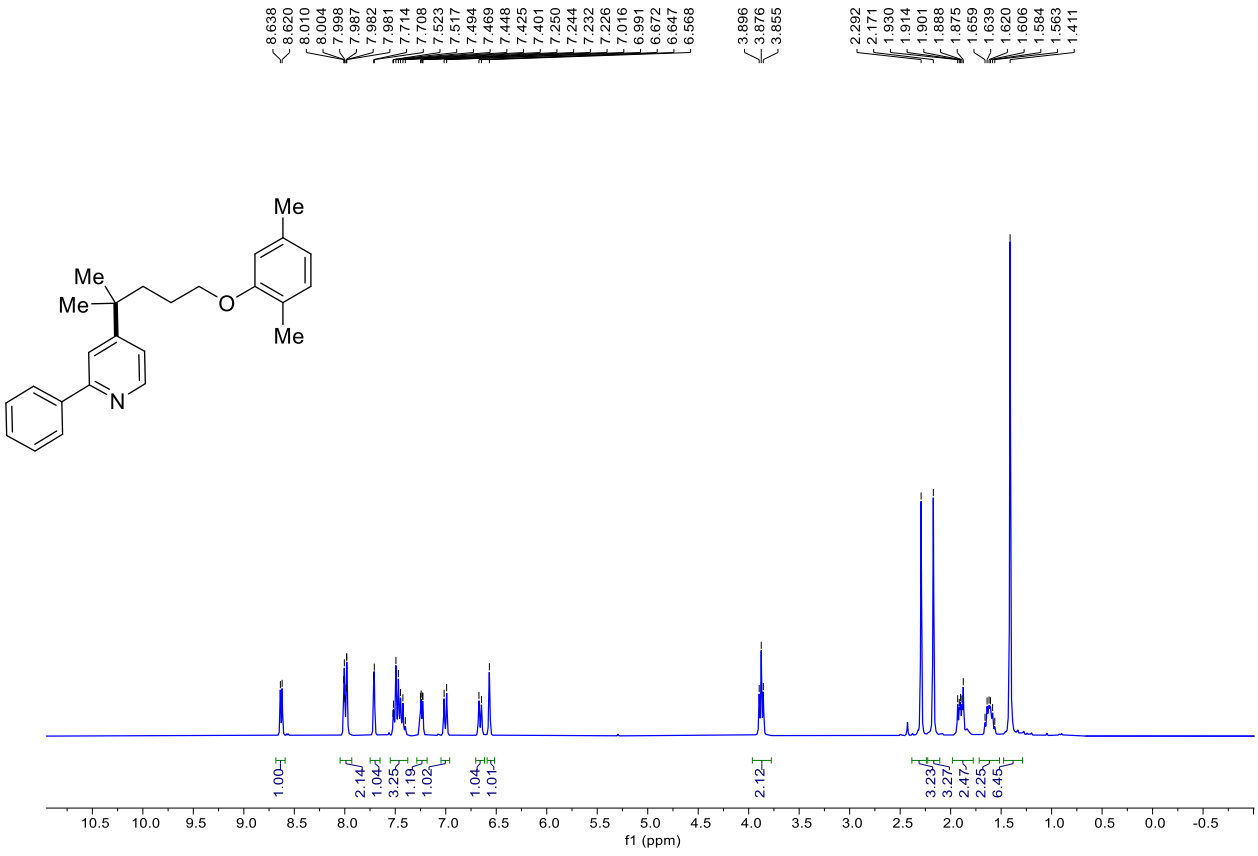


^{13}C NMR (76 MHz, $CDCl_3$)

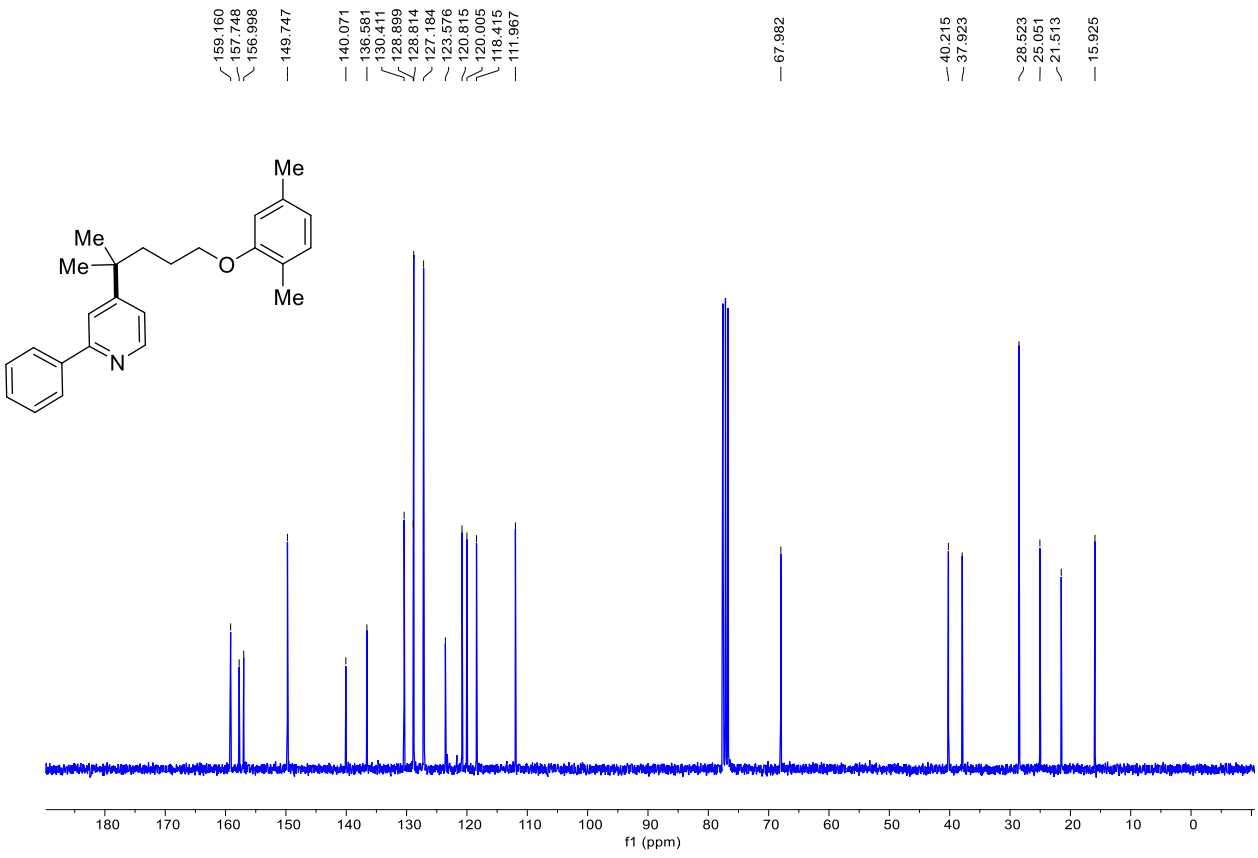


4-(5-(2,5-dimethylphenoxy)-2-methylpentan-2-yl)-2-phenylpyridine (3s)

^{1}H NMR (300 MHz, $CDCl_3$)

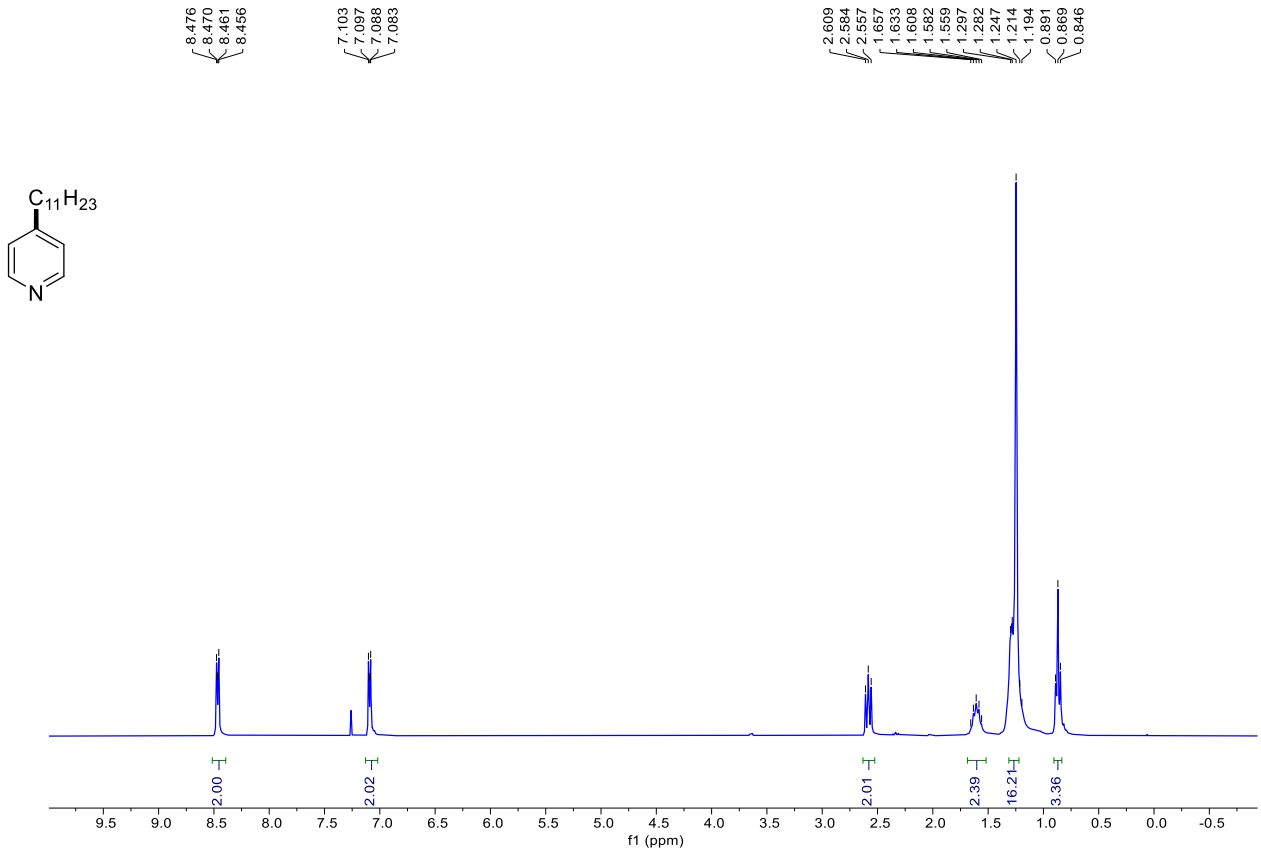


^{13}C NMR (76 MHz, $CDCl_3$)

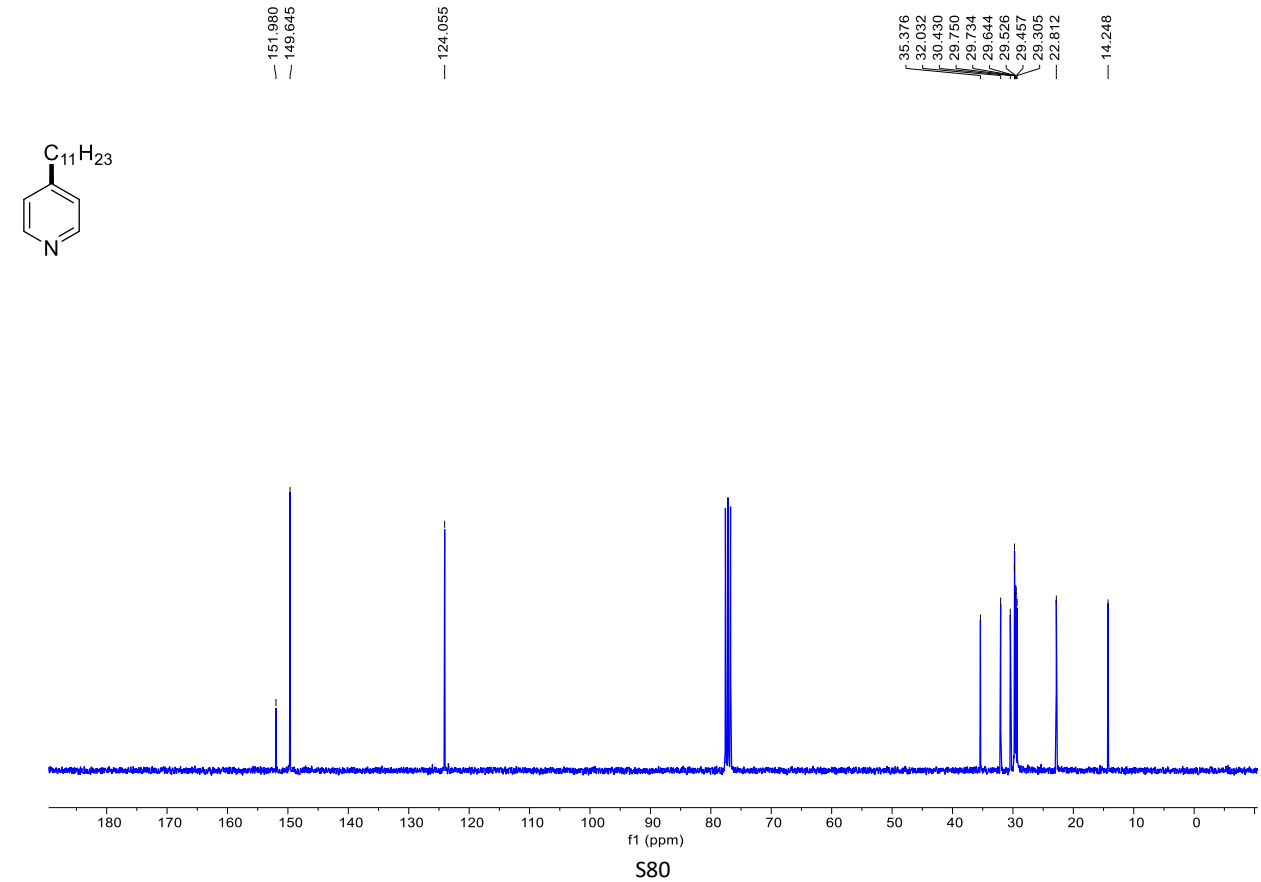


4-Undecylpyridine (4a)

^{1}H NMR (300 MHz, $CDCl_3$)

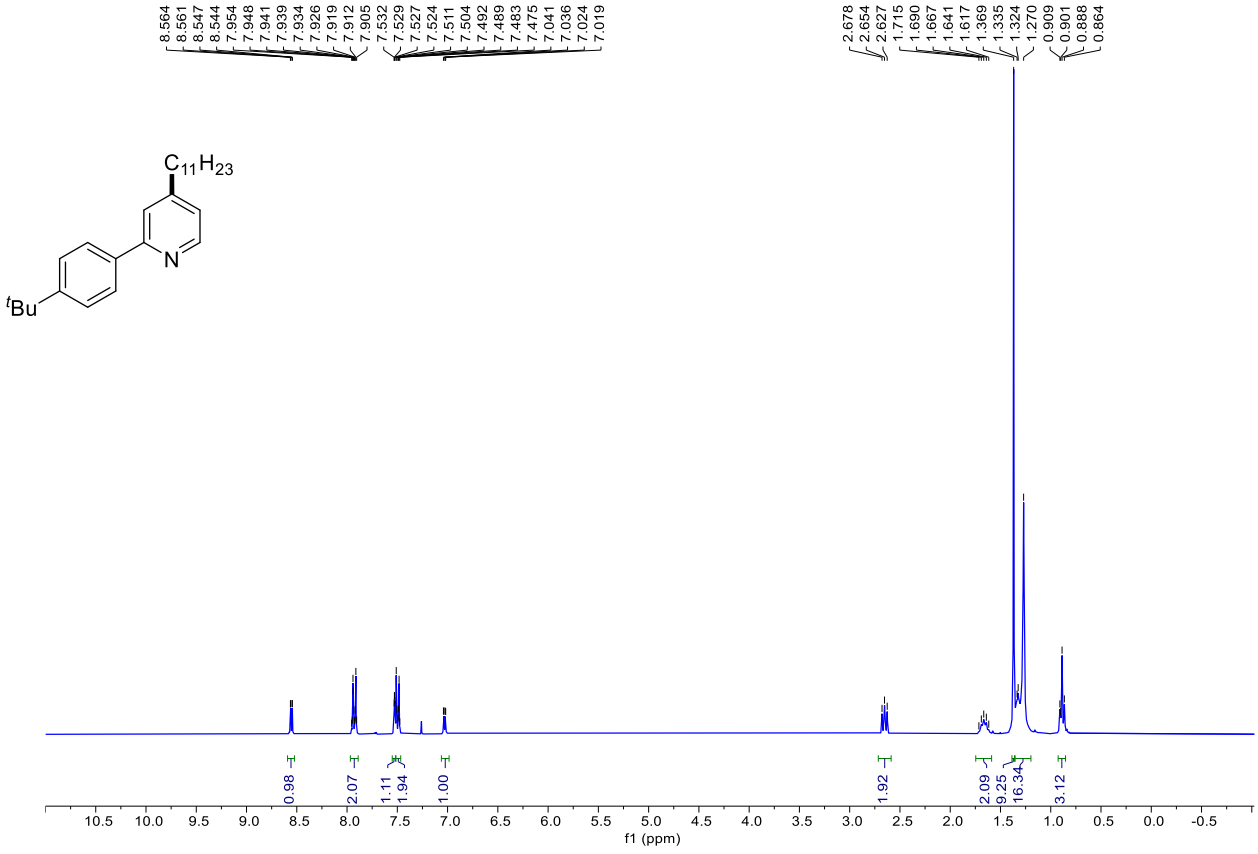


^{13}C NMR (76 MHz, $CDCl_3$)

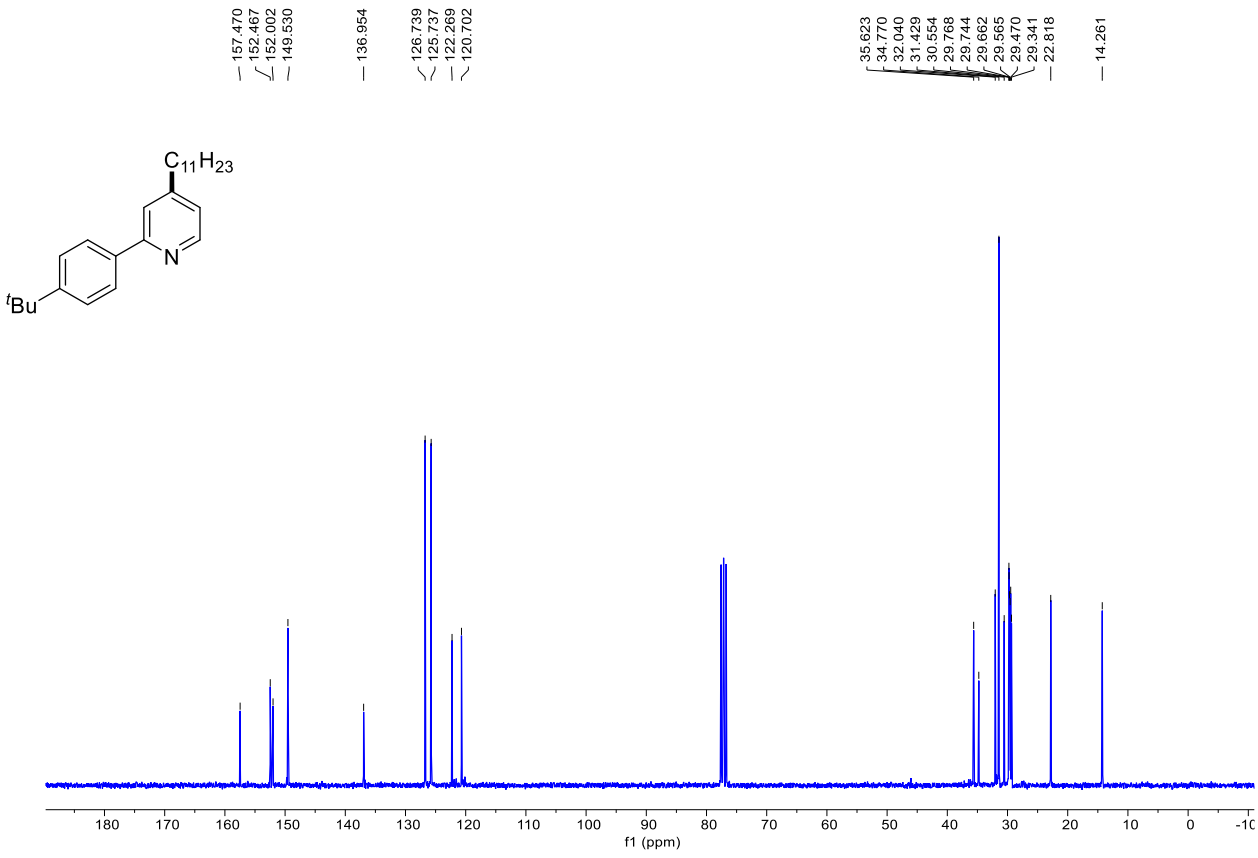


2-(4-(*tert*-Butyl)phenyl)-4-undecylpyridine (4b)

^{1}H NMR (300 MHz, $CDCl_3$)

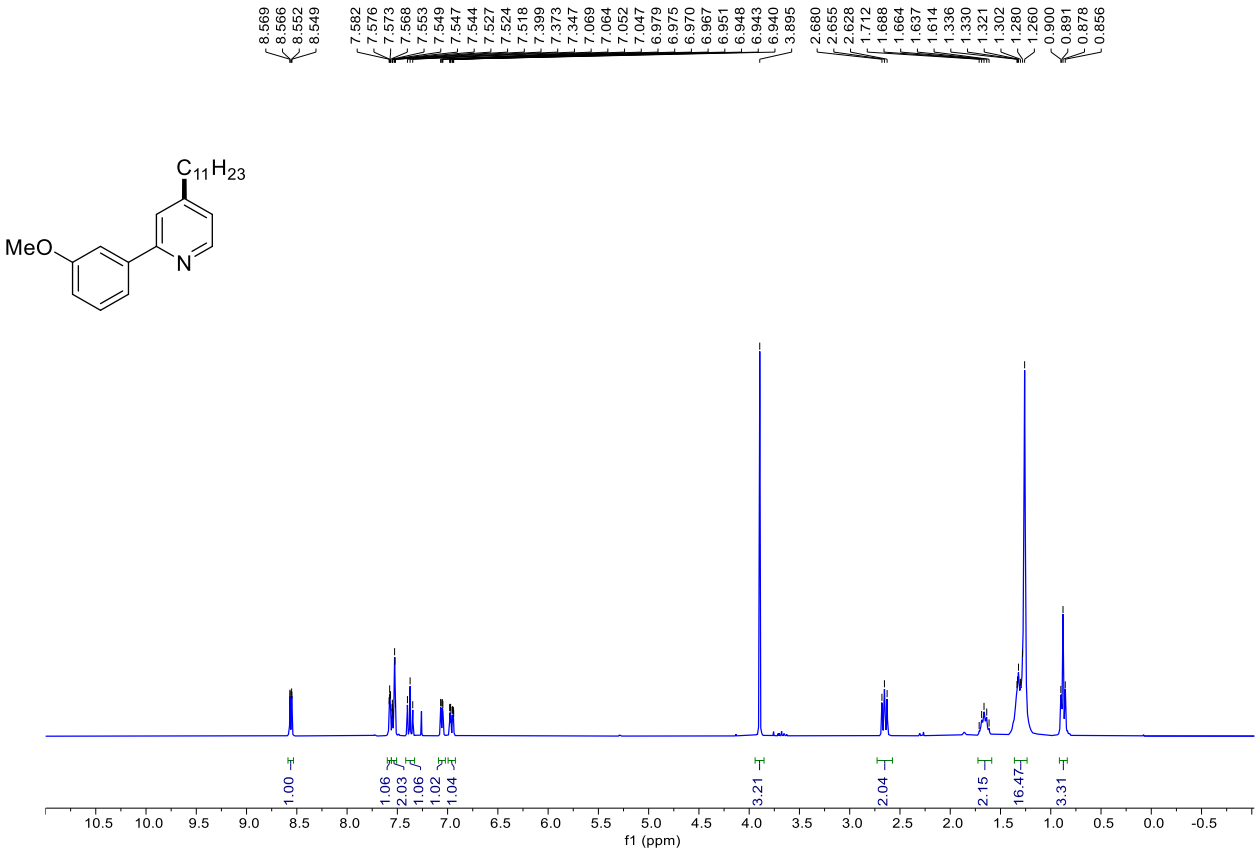


^{13}C NMR (76 MHz, $CDCl_3$)

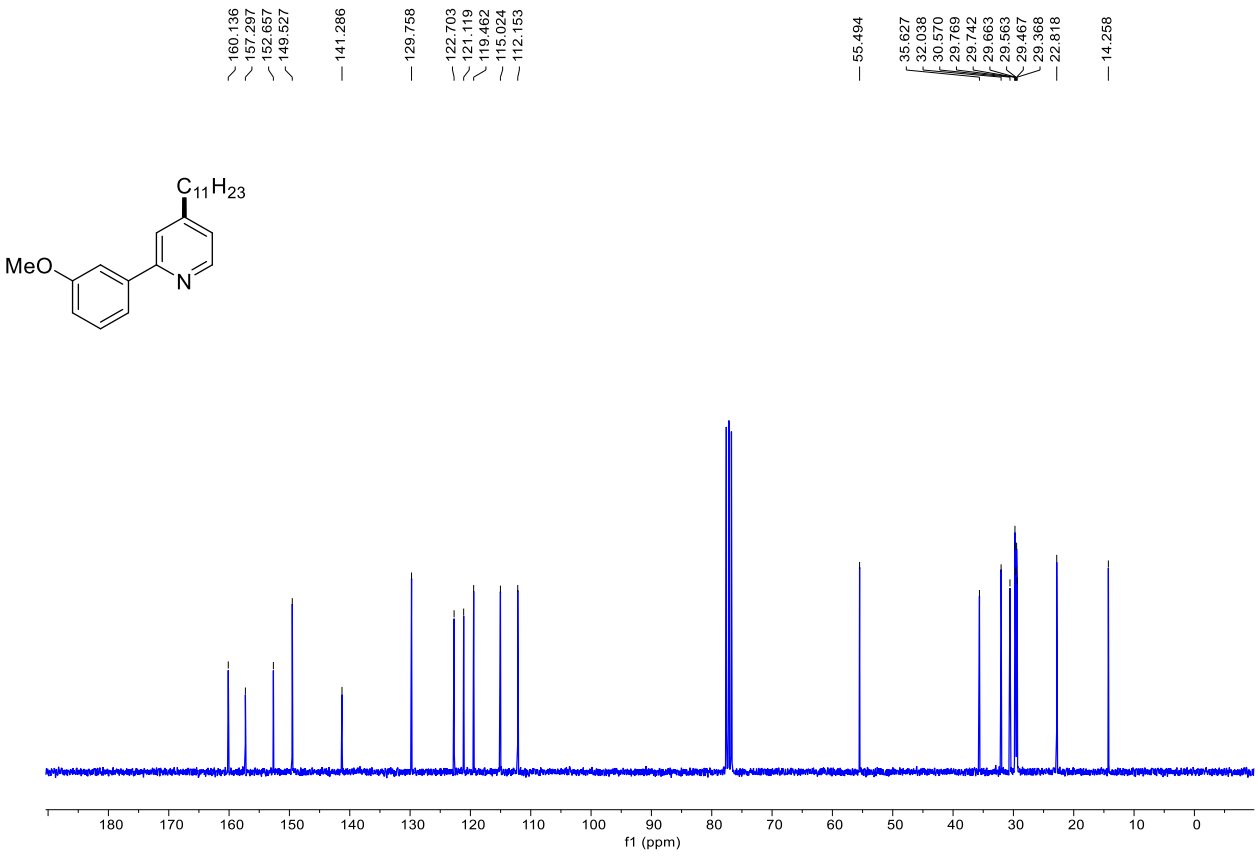


2-(3-Methoxyphenyl)-4-undecylpyridine (4c)

^{1}H NMR (300 MHz, $CDCl_3$)

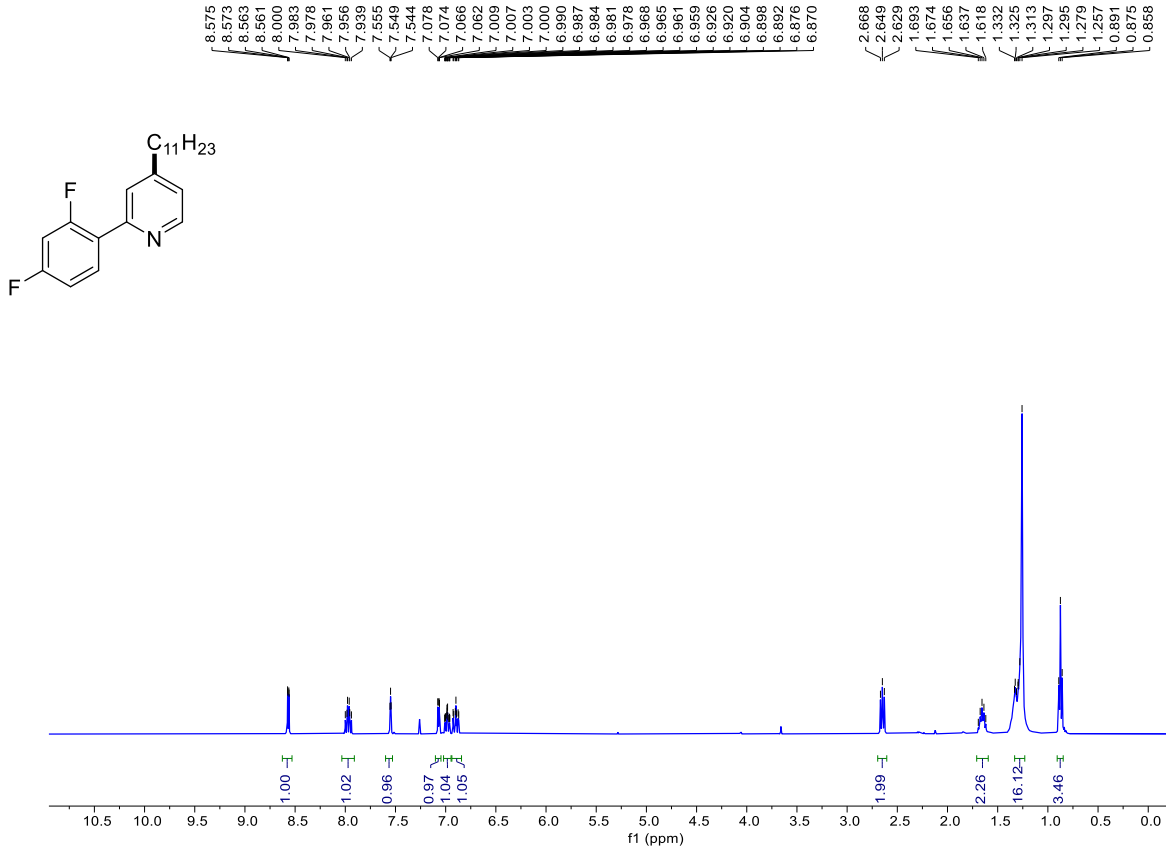


^{13}C NMR (76 MHz, $CDCl_3$)

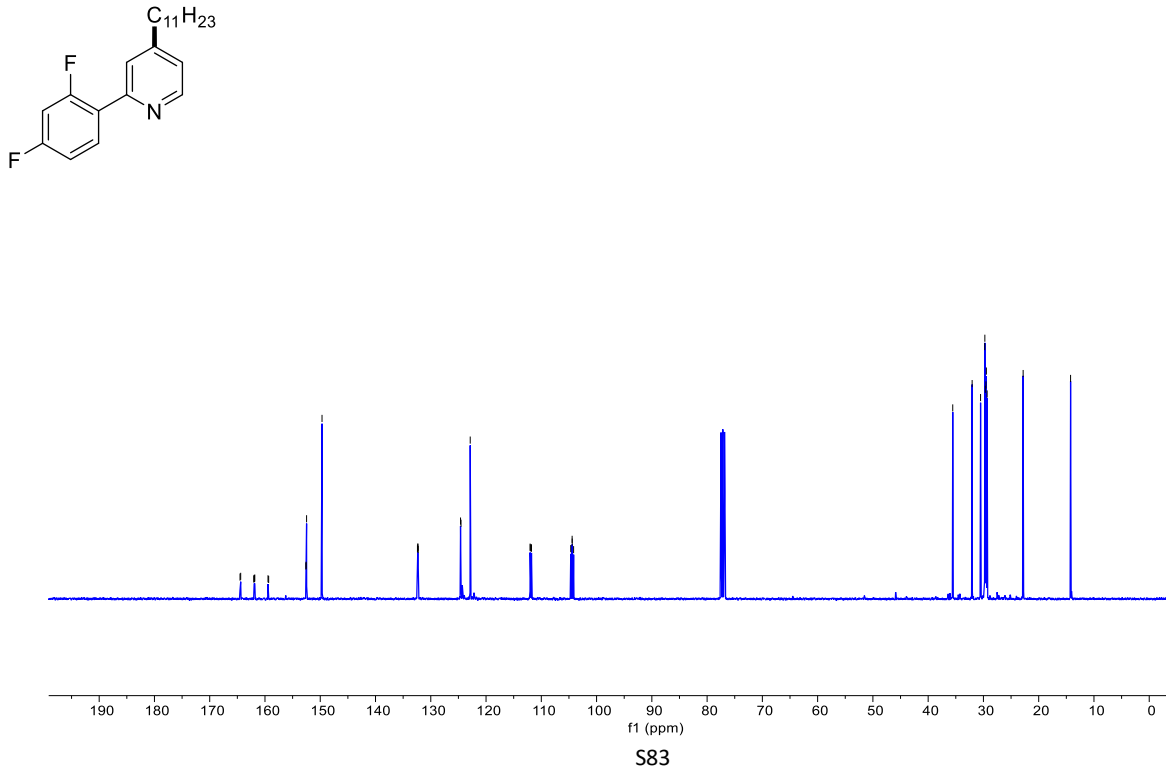


2-(2,4-Difluorophenyl)-4-undecylpyridine (4d)

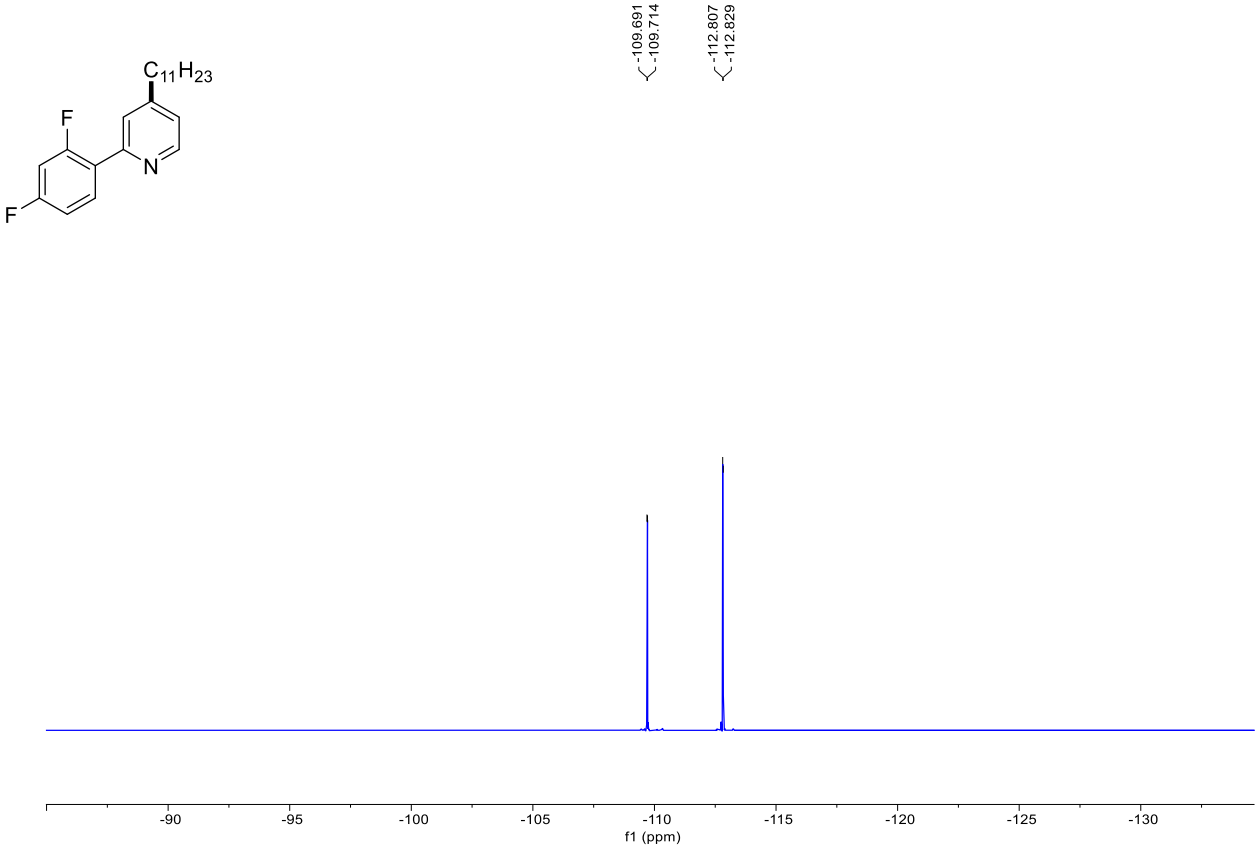
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (76 MHz, $CDCl_3$)

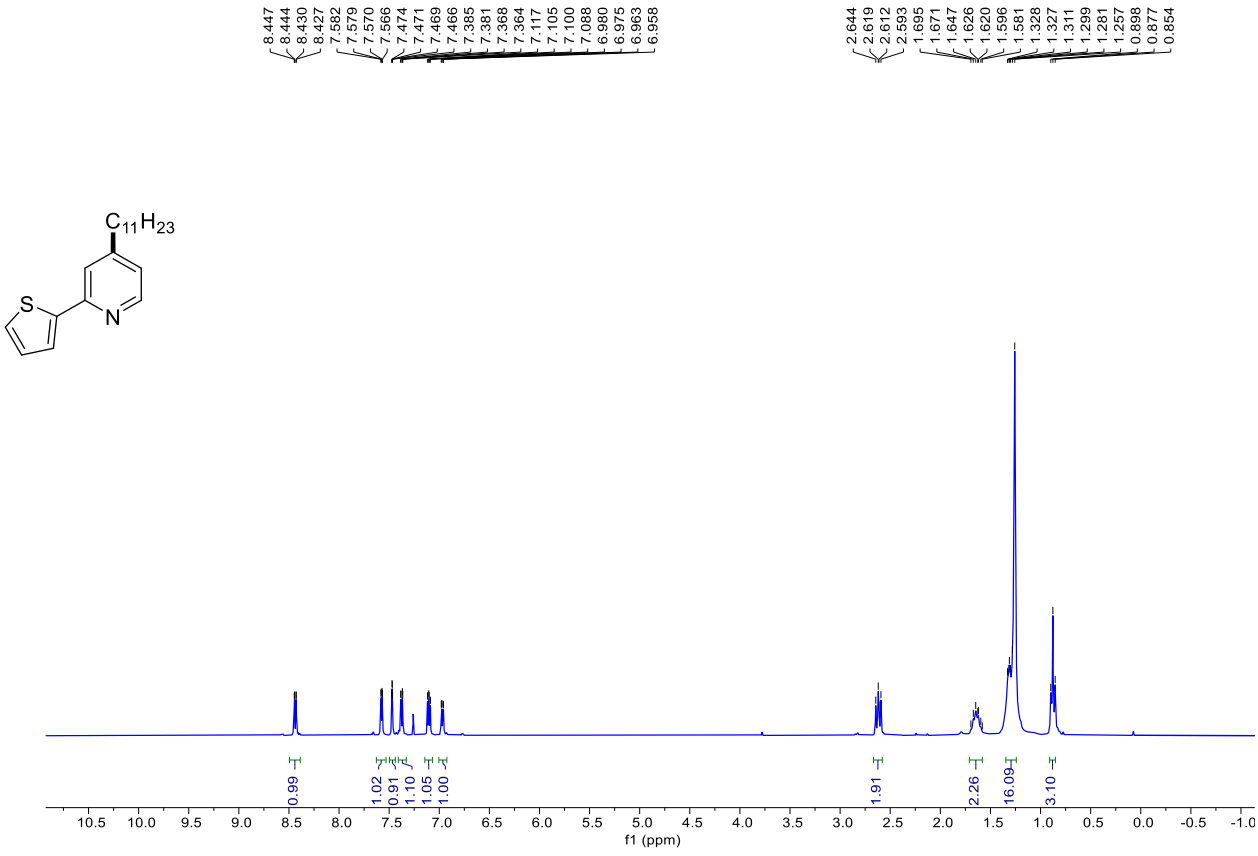


^{19}F NMR (376 MHz, $CDCl_3$)

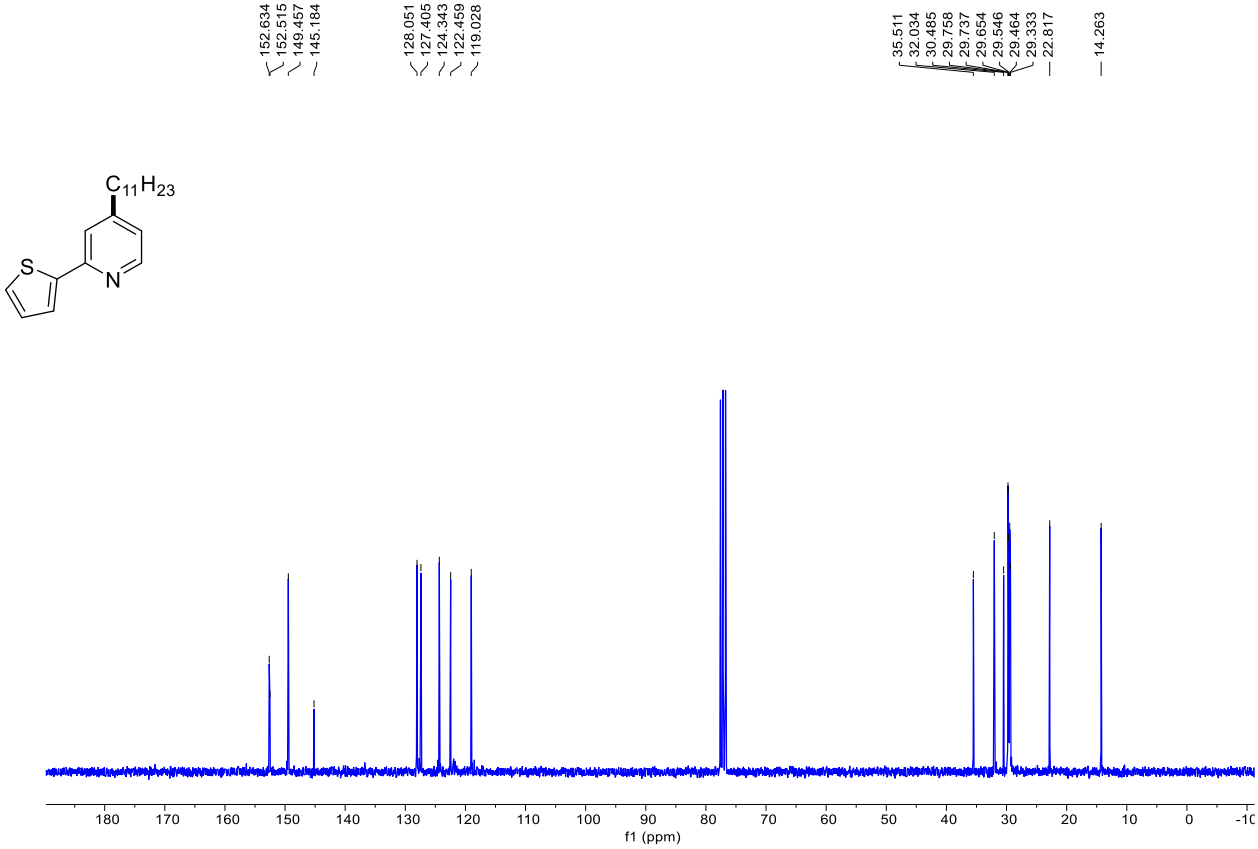


2-(Thiophen-2-yl)-4-undecylpyridine (4e)

^{1}H NMR (300 MHz, $CDCl_3$)

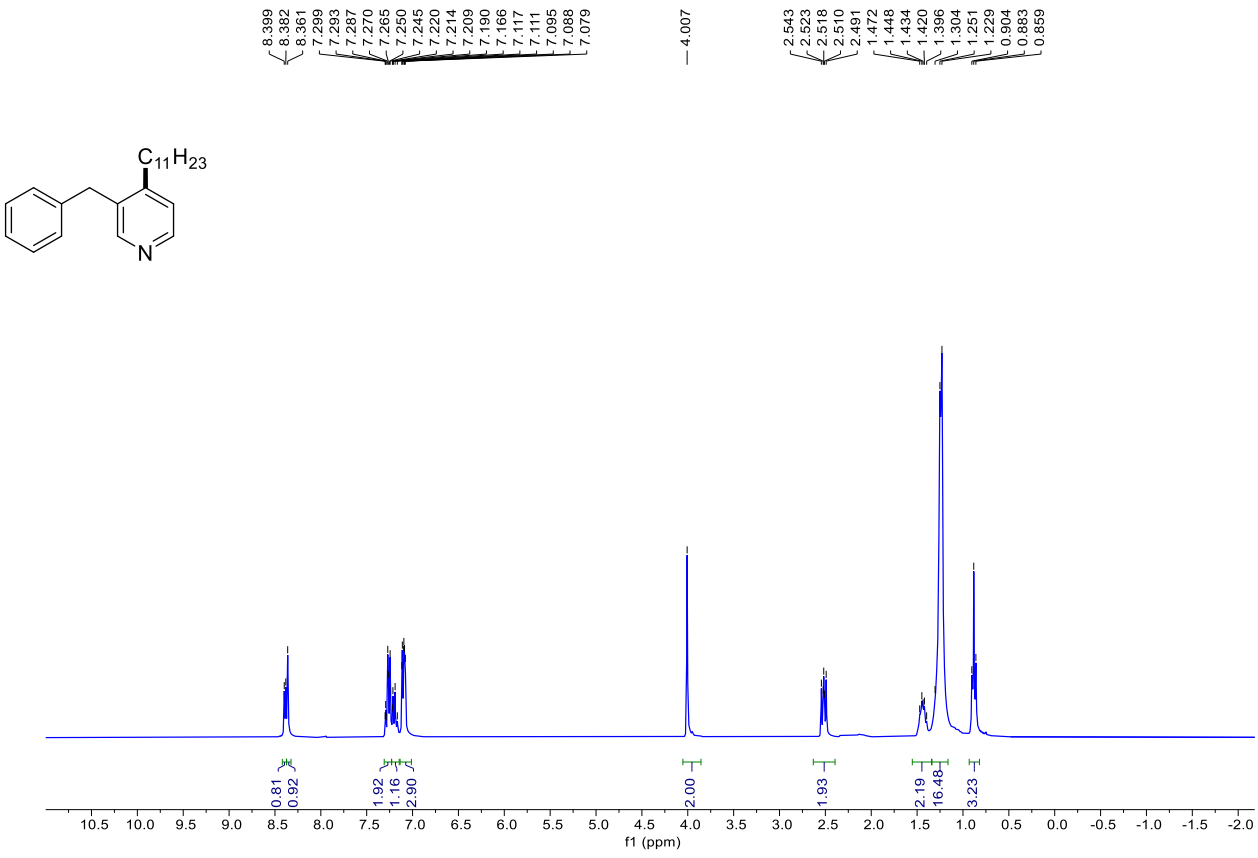


^{13}C NMR (76 MHz, $CDCl_3$)

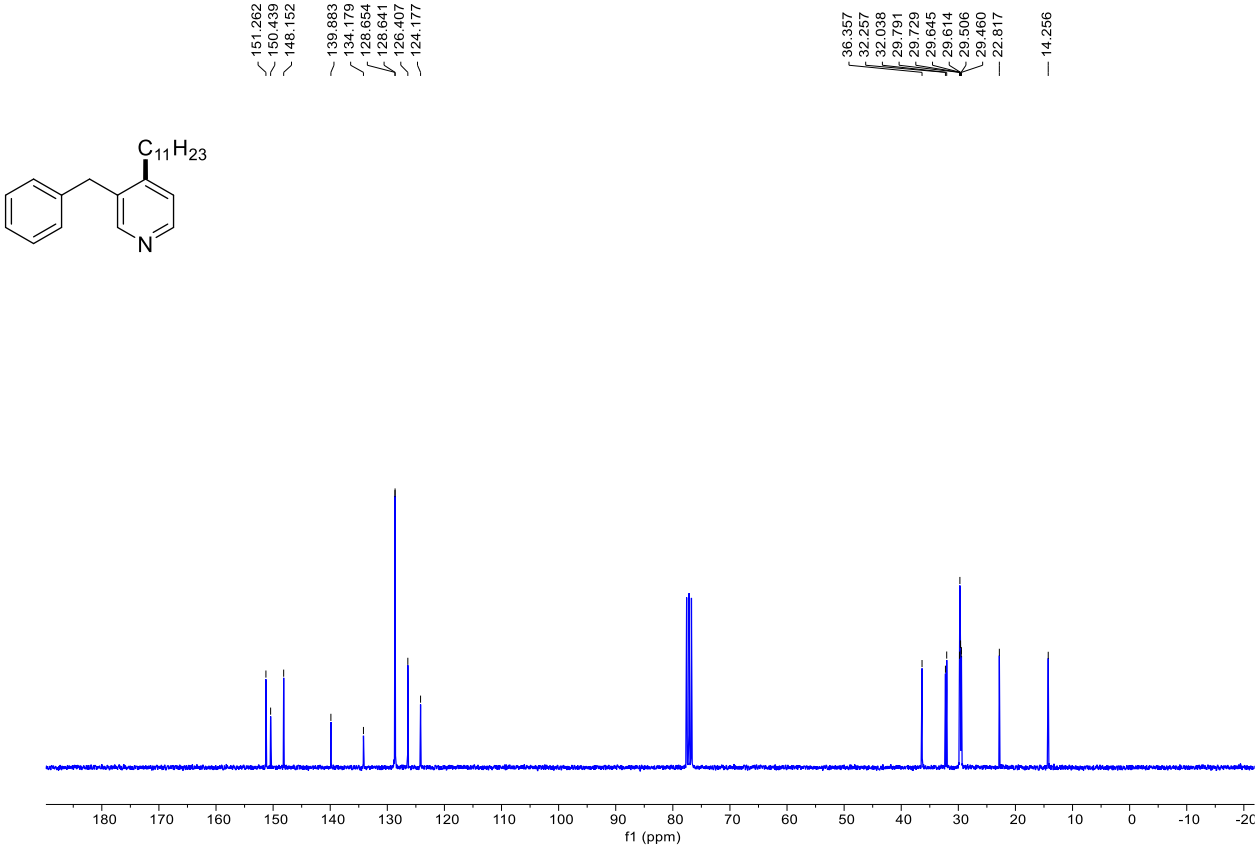


3-Benzyl-4-undecylpyridine (4f)

^{1}H NMR (300 MHz, $CDCl_3$)

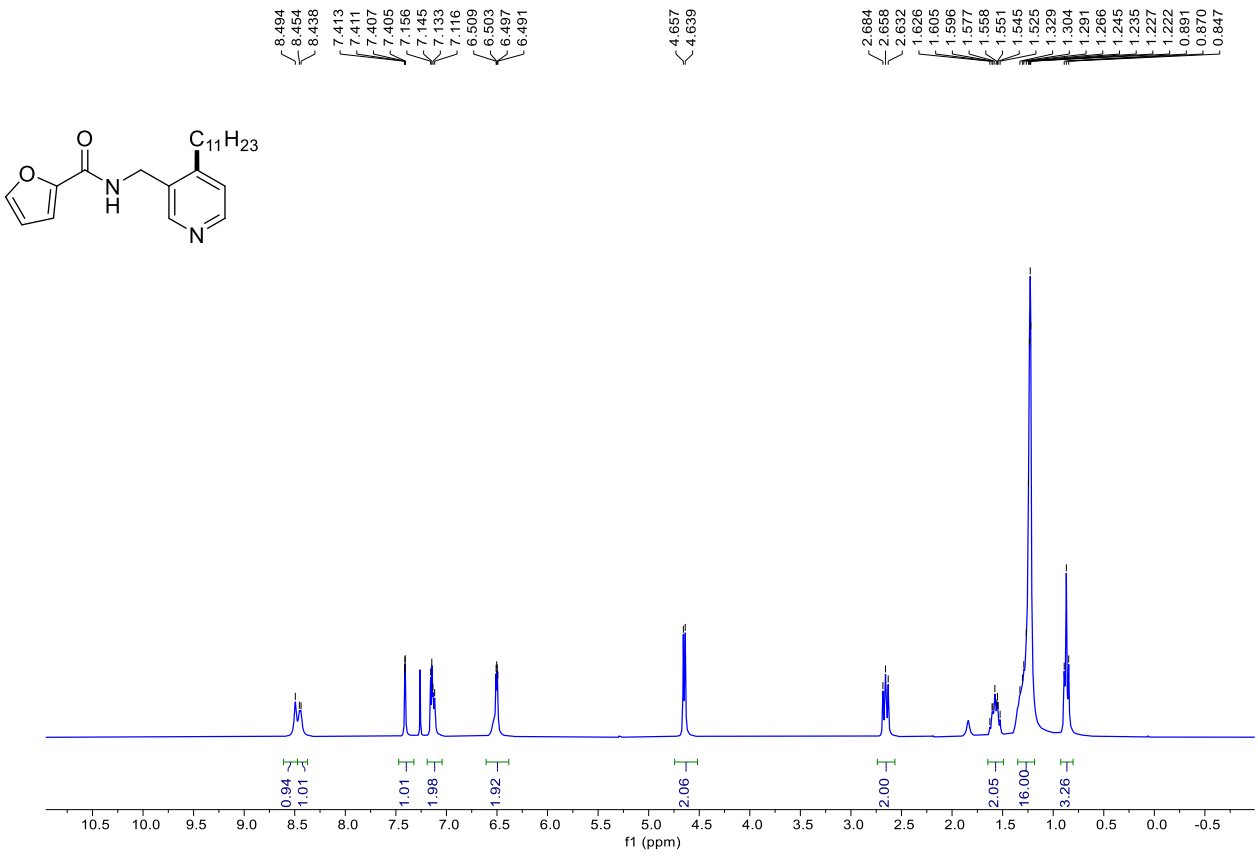


^{13}C NMR (76 MHz, $CDCl_3$)

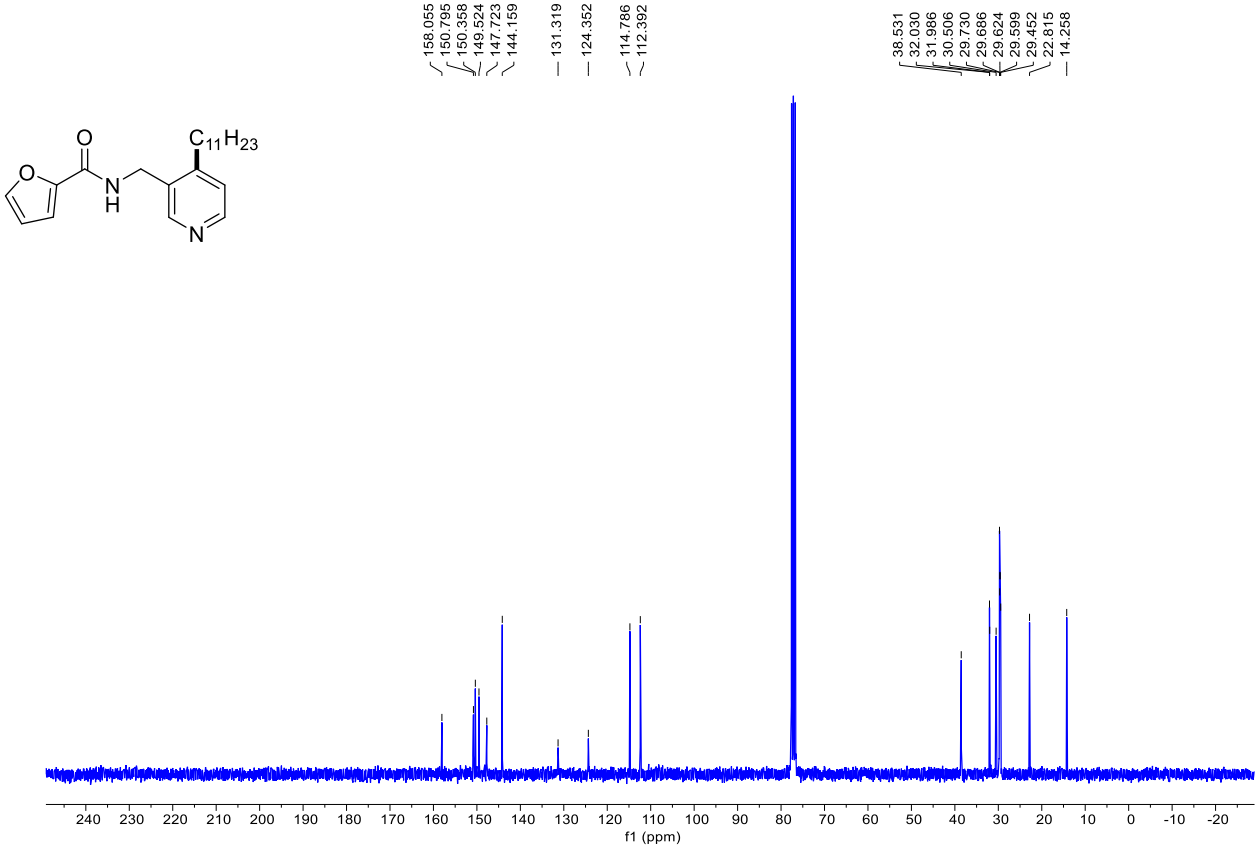


***N*-((4-Undecylpyridin-3-yl)methyl)furan-2-carboxamide (4g)**

^{1}H NMR (300 MHz, $CDCl_3$)

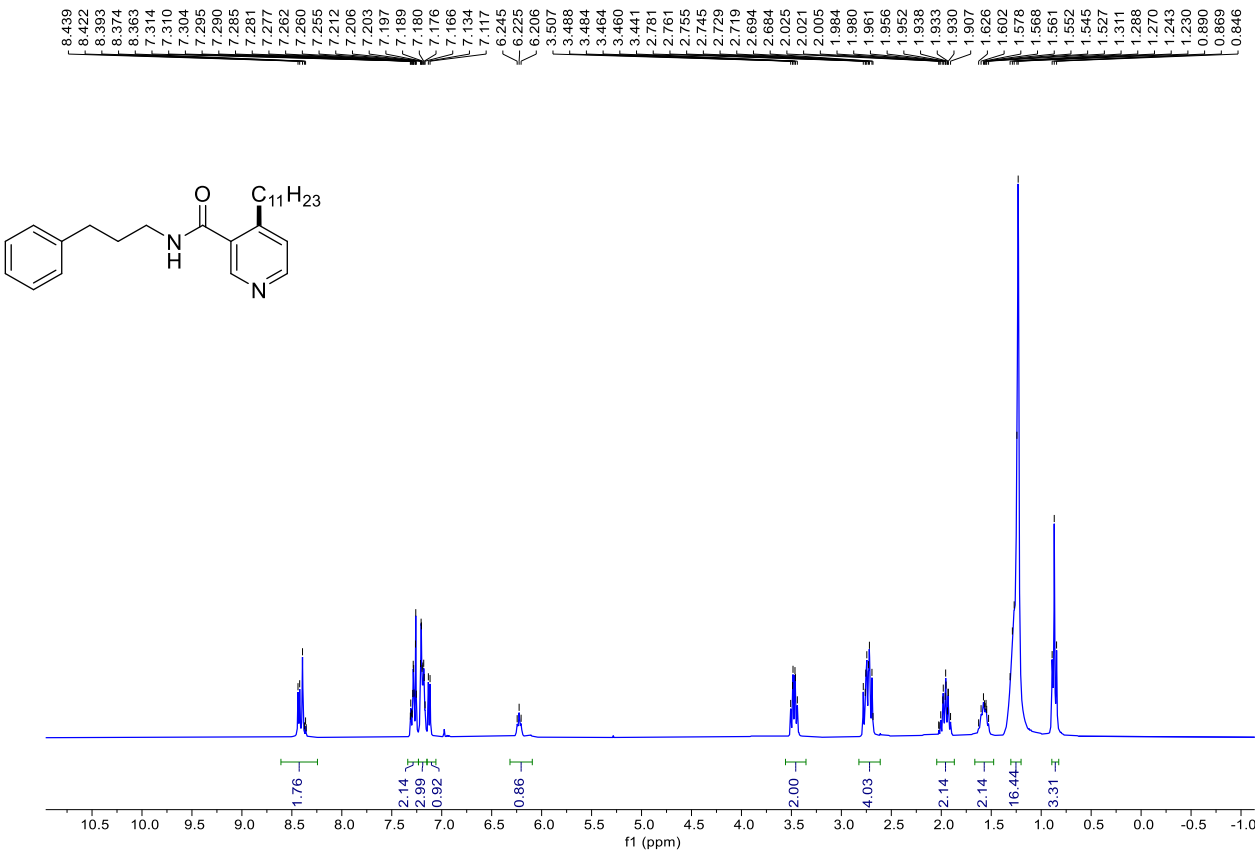


^{13}C NMR (76 MHz, $CDCl_3$)

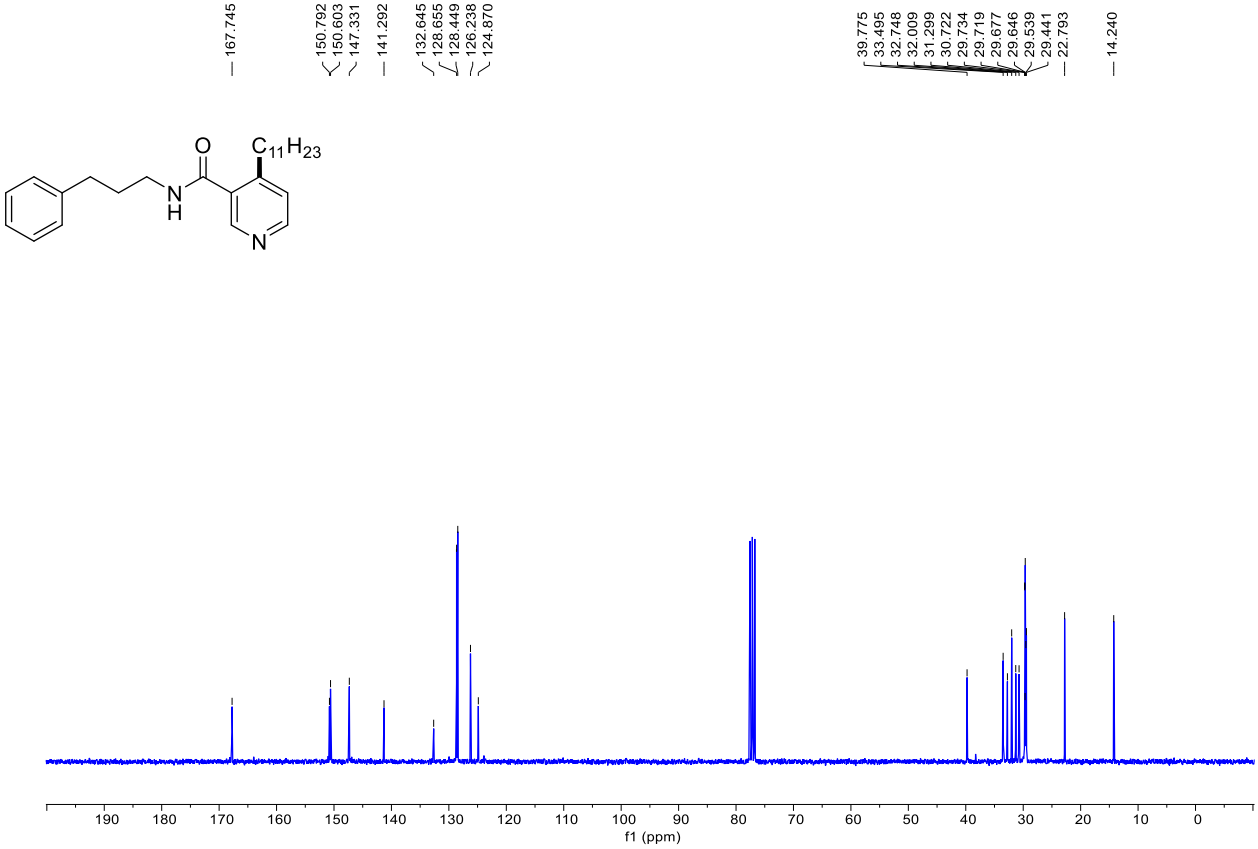


***N*-(3-Phenylpropyl)-4-undecylnicotinamide (4h)**

^{1}H NMR (300 MHz, $CDCl_3$)

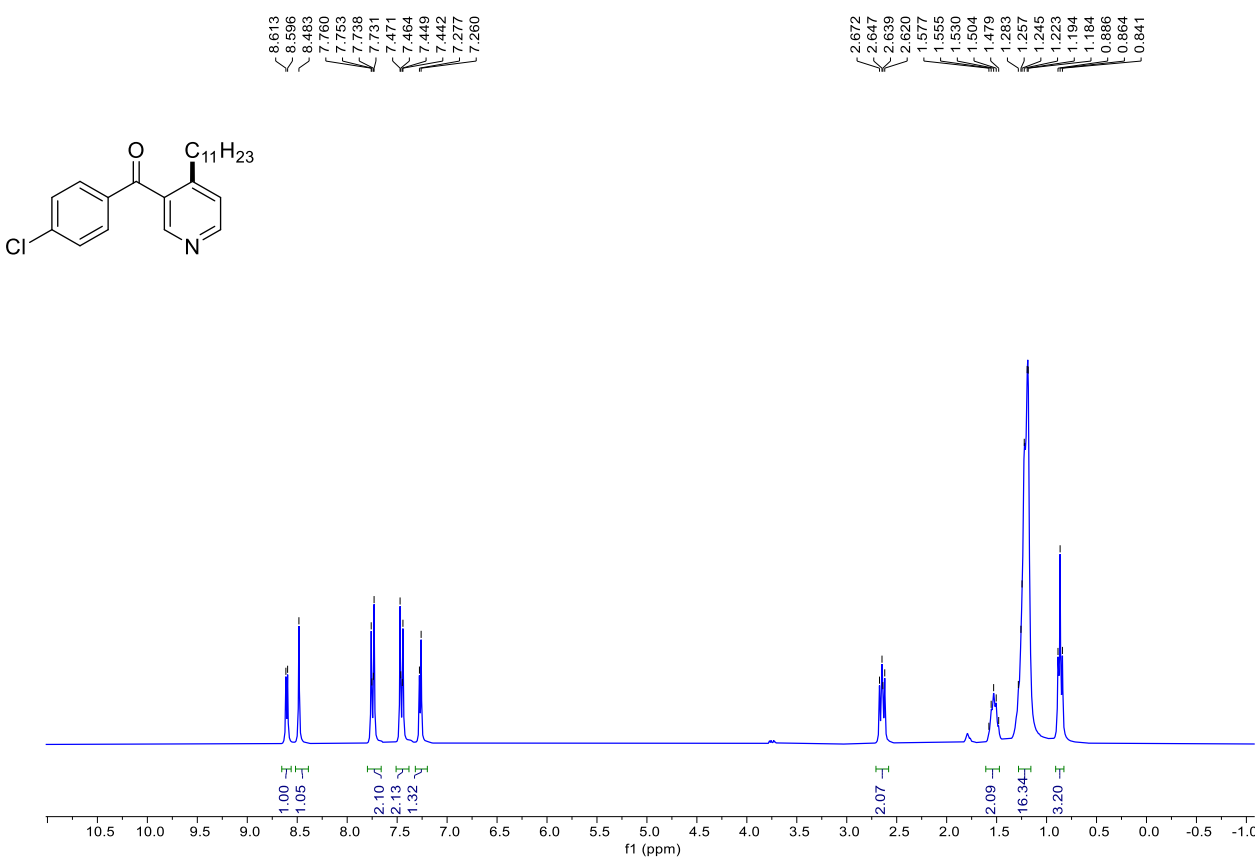


^{13}C NMR (76 MHz, $CDCl_3$)

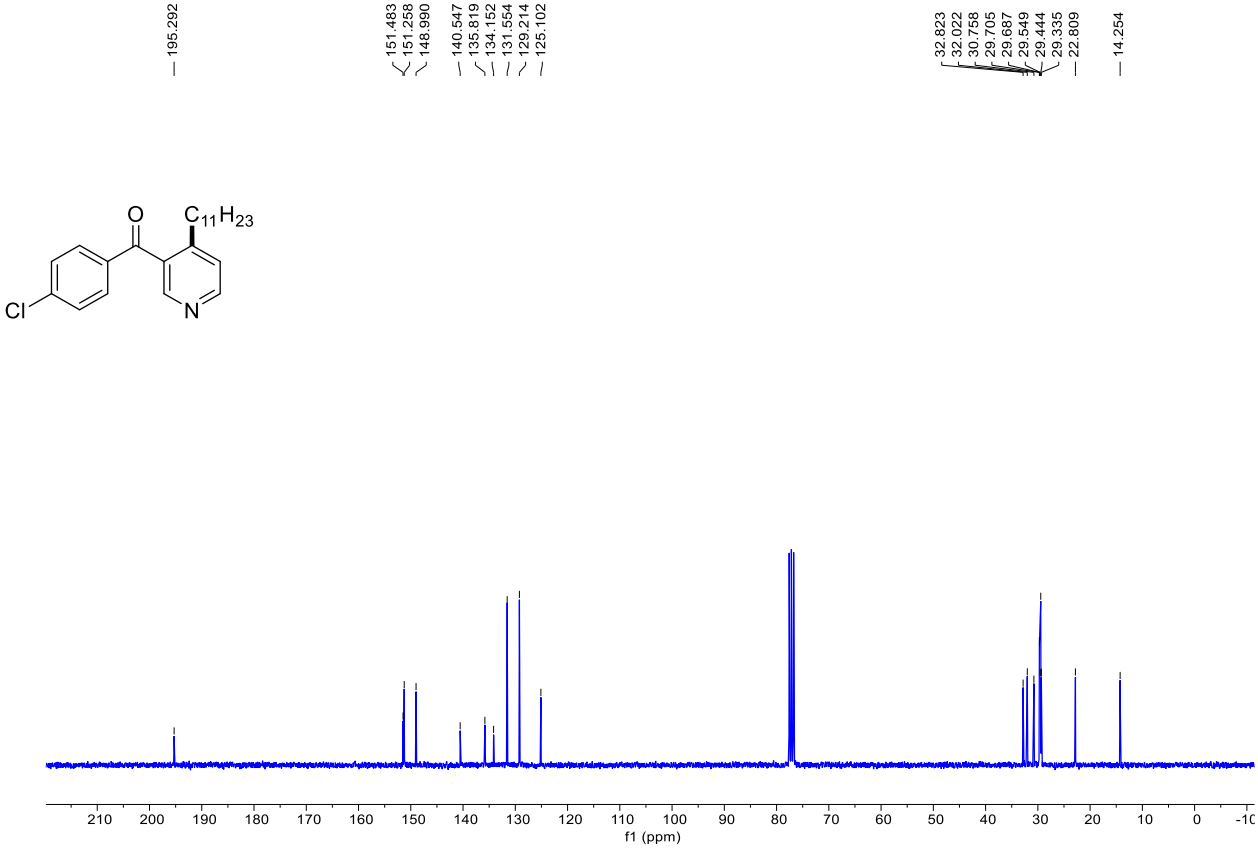


(4-Chlorophenyl)(4-undecylpyridin-3-yl)methanone (4i)

^{1}H NMR (300 MHz, $CDCl_3$)

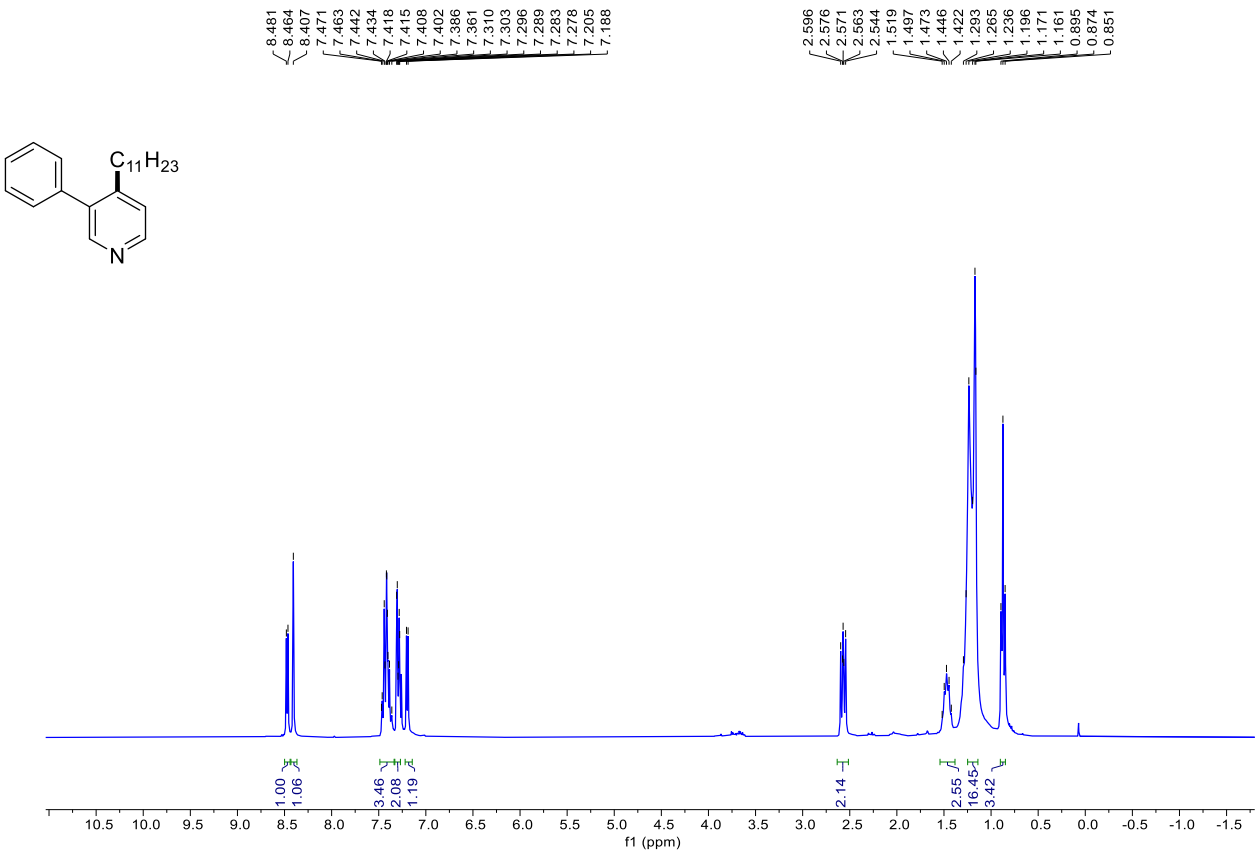


^{13}C NMR (76 MHz, $CDCl_3$)

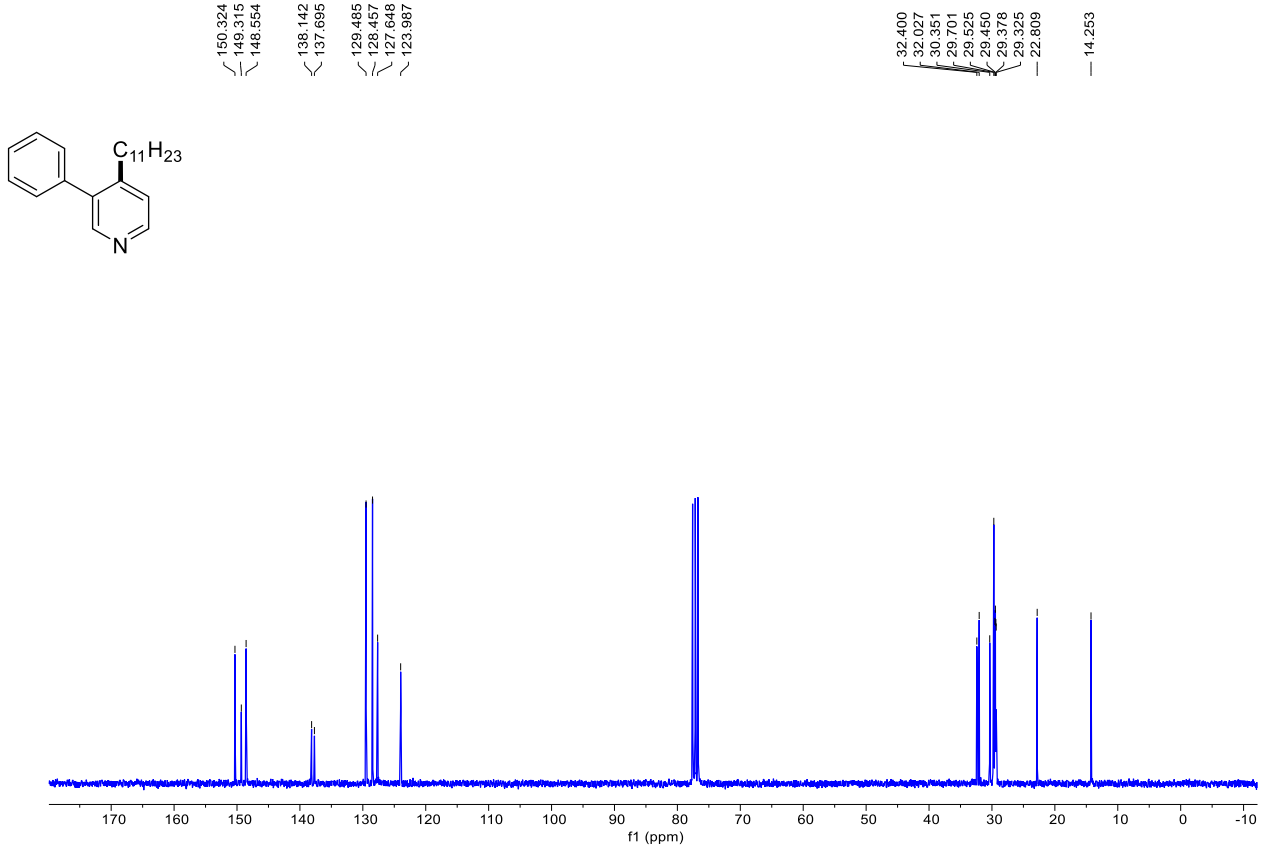


3-Phenyl-4-undecylpyridine (4j)

^{1}H NMR (300 MHz, $CDCl_3$)

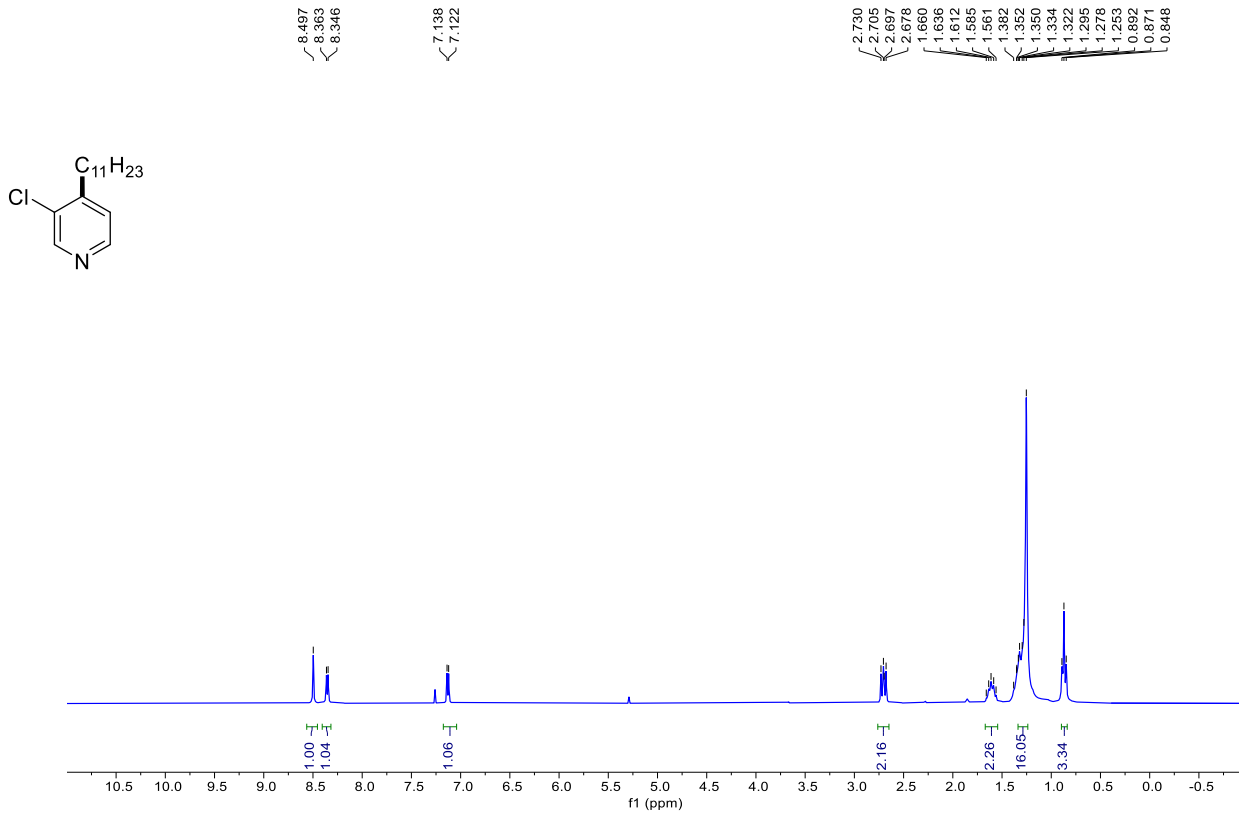


^{13}C NMR (76 MHz, $CDCl_3$)

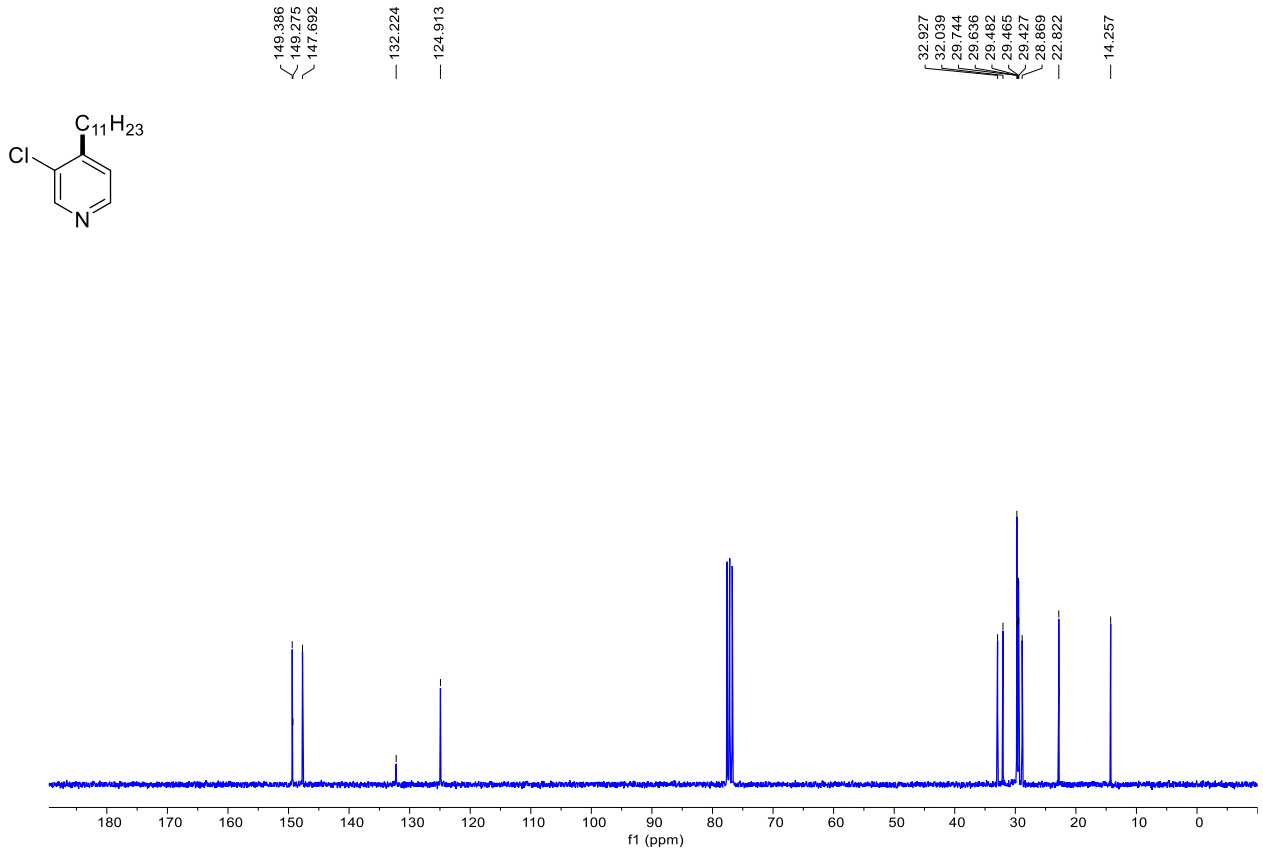


3-Chloro-4-undecylpyridine (4k)

^{1}H NMR (300 MHz, $CDCl_3$)

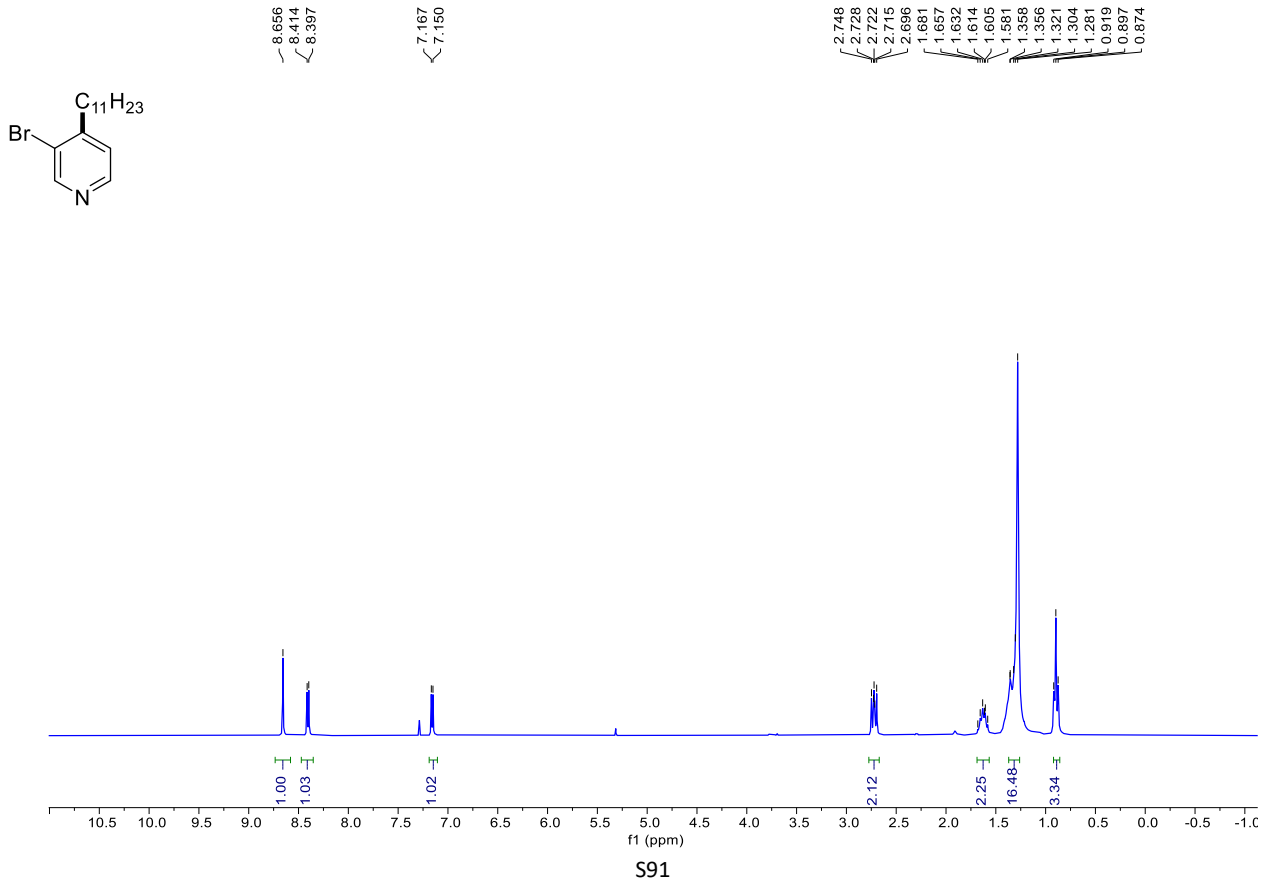


^{13}C NMR (76 MHz, $CDCl_3$)

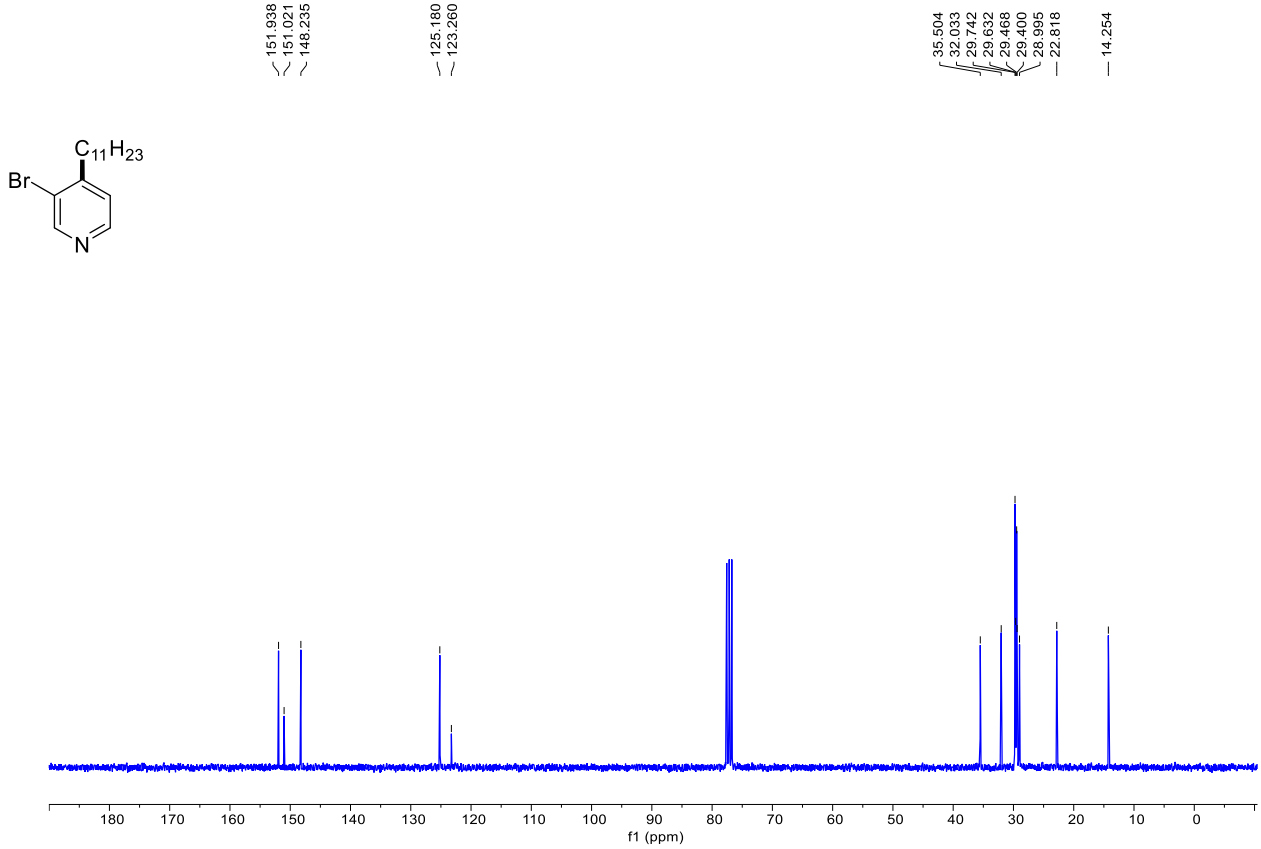


3-Bromo-4-undecylpyridine (4l)

^{1}H NMR (300 MHz, $CDCl_3$)

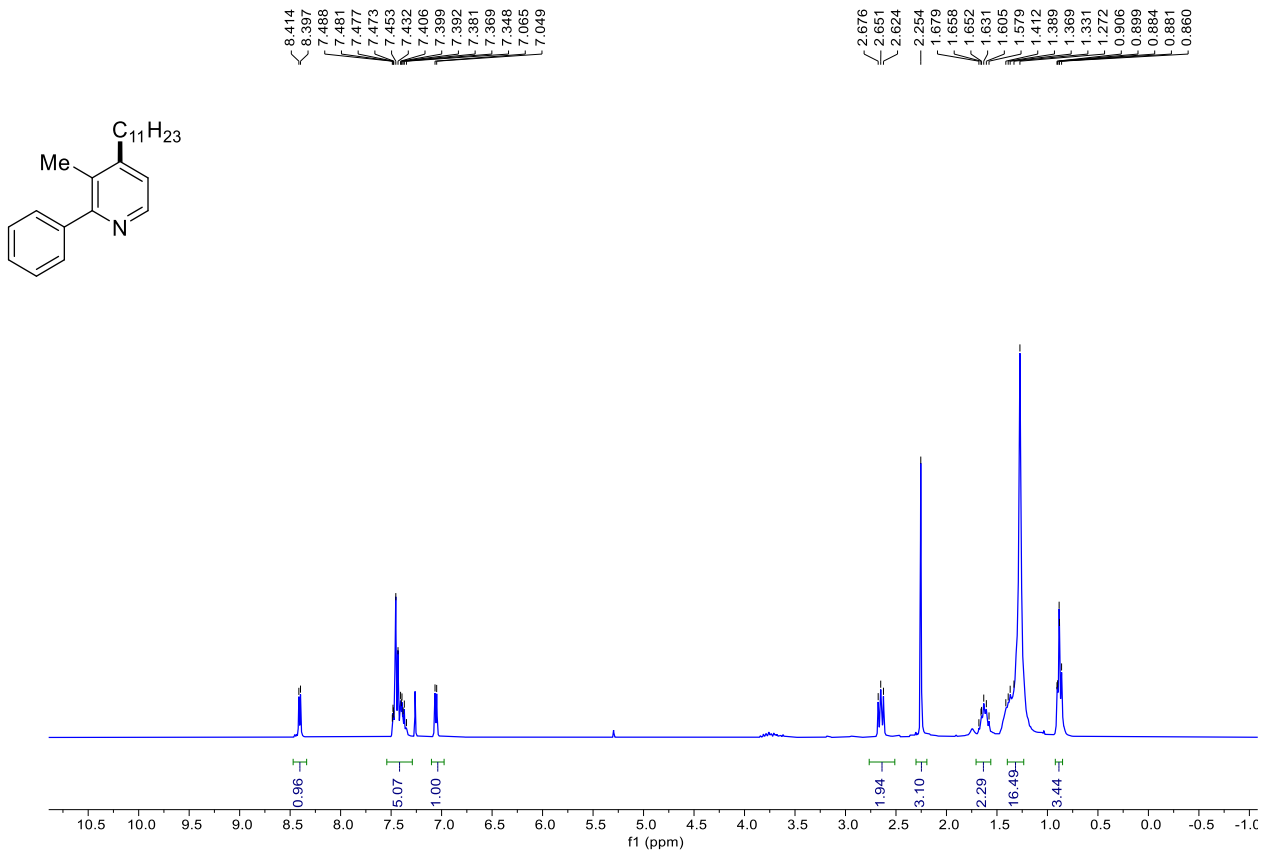


^{13}C NMR (76 MHz, $CDCl_3$)

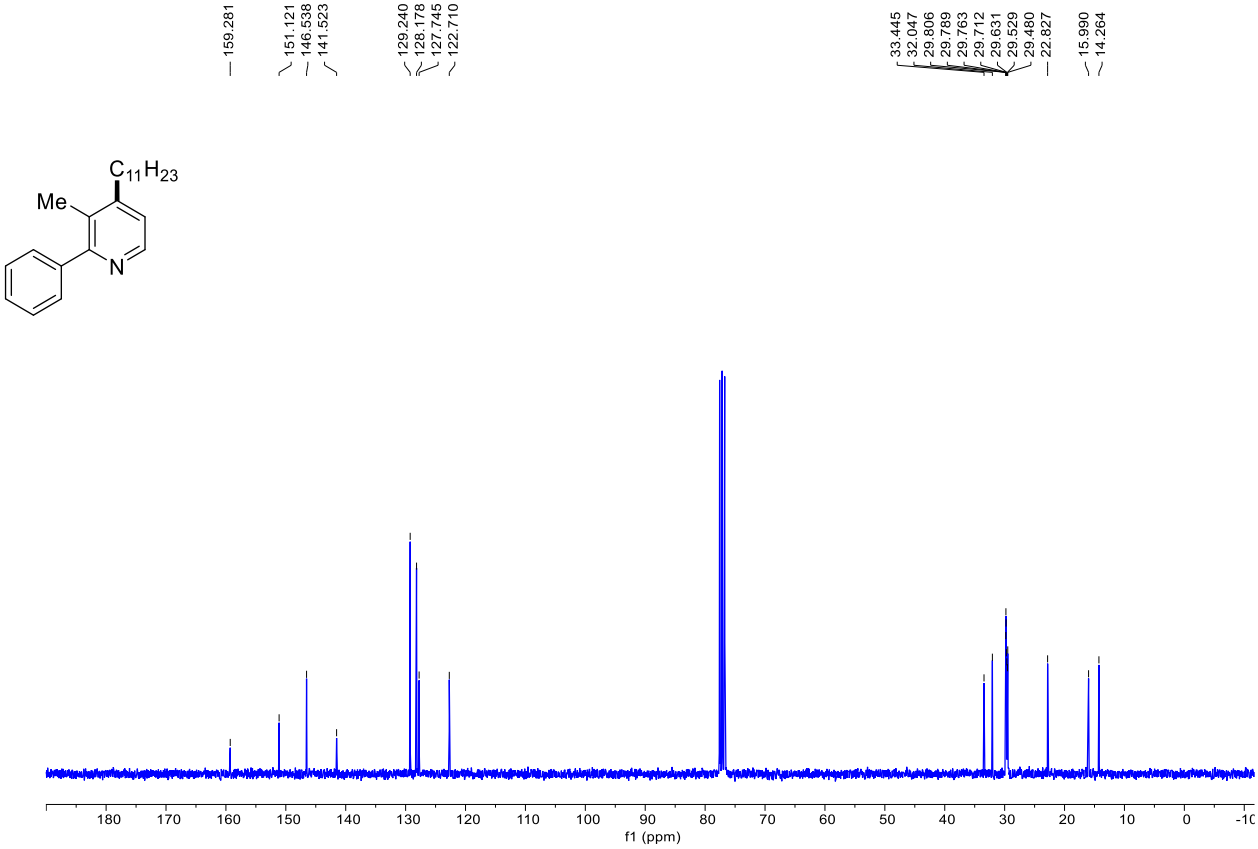


3-Methyl-2-phenyl-4-undecylpyridine (4m)

^{1}H NMR (300 MHz, $CDCl_3$)

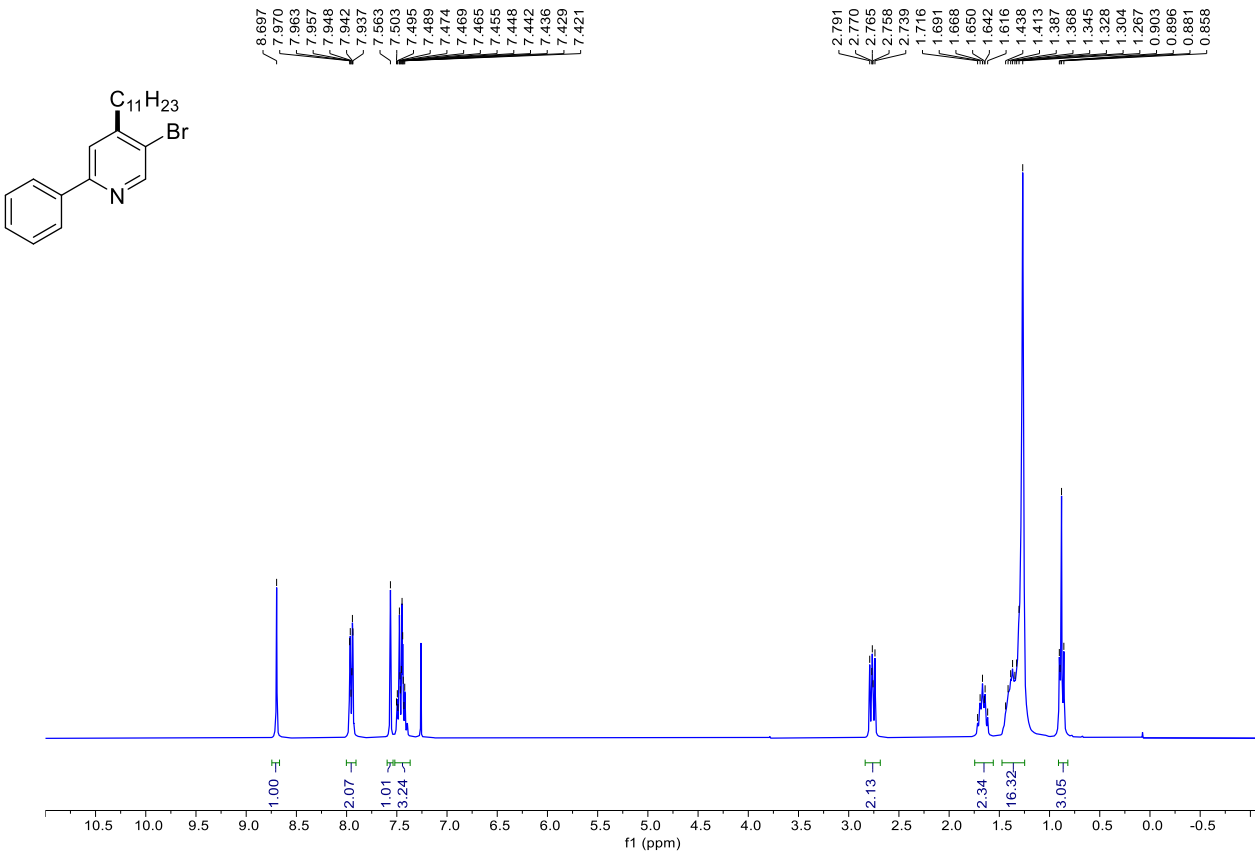


^{13}C NMR (76 MHz, $CDCl_3$)

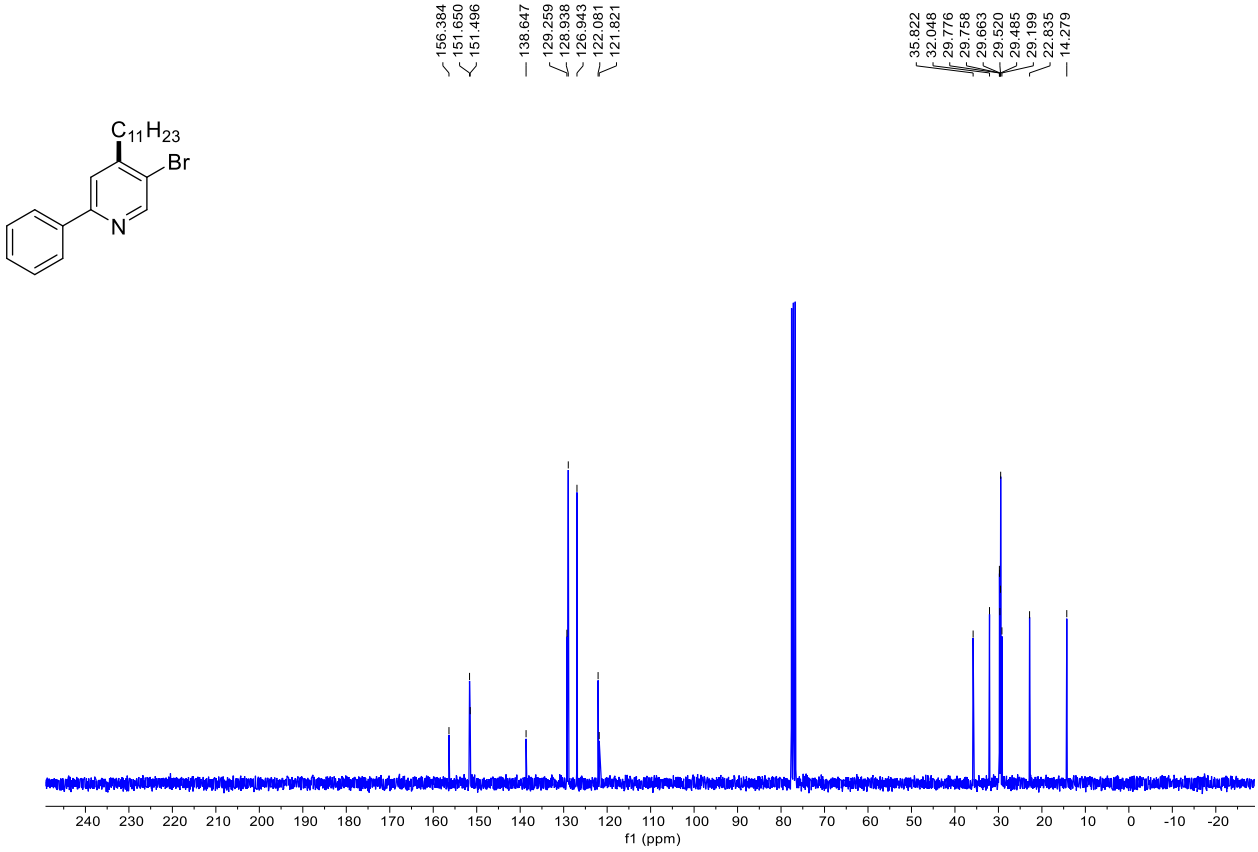


5-Bromo-2-phenyl-4-undecylpyridine (4n)

^{1}H NMR (300 MHz, $CDCl_3$)

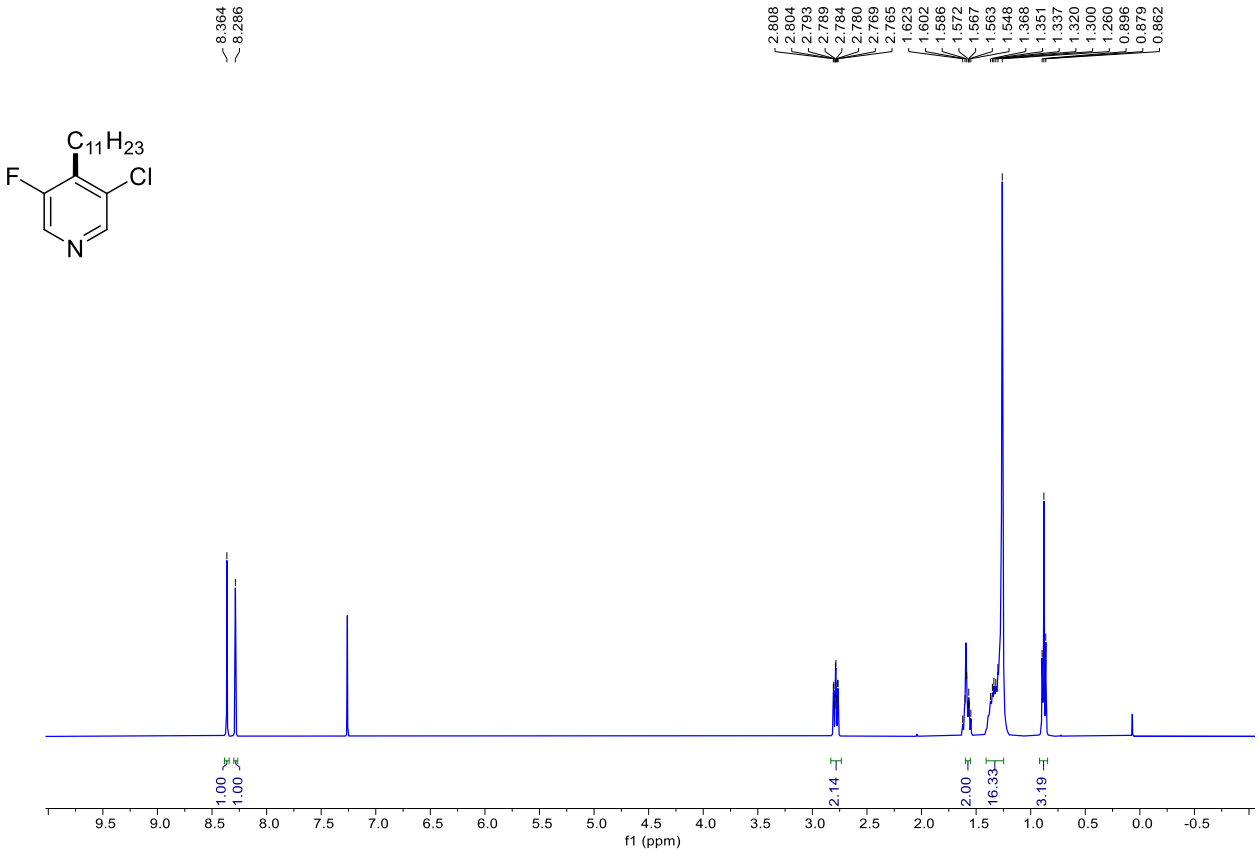


^{13}C NMR (76 MHz, $CDCl_3$)

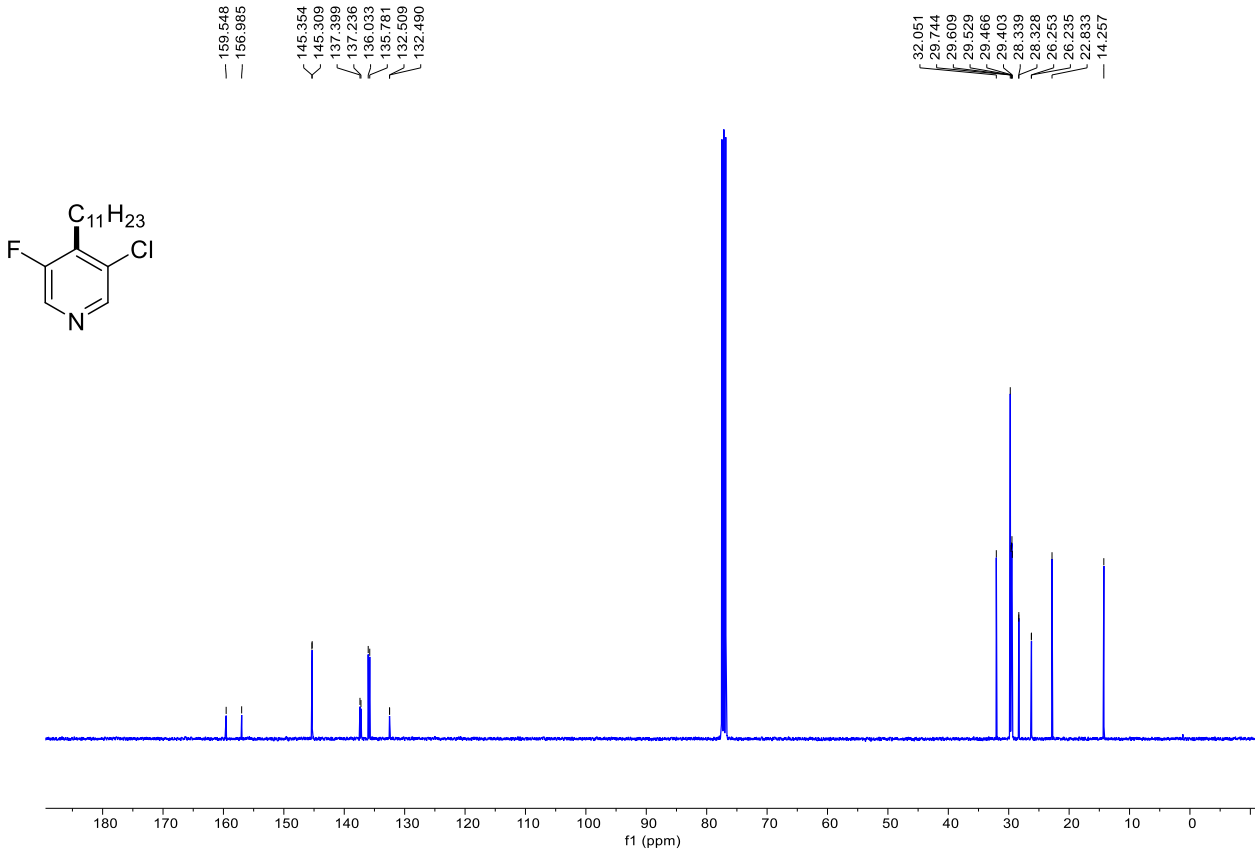


3-Chloro-5-fluoro-4-undecylpyridine (4o)

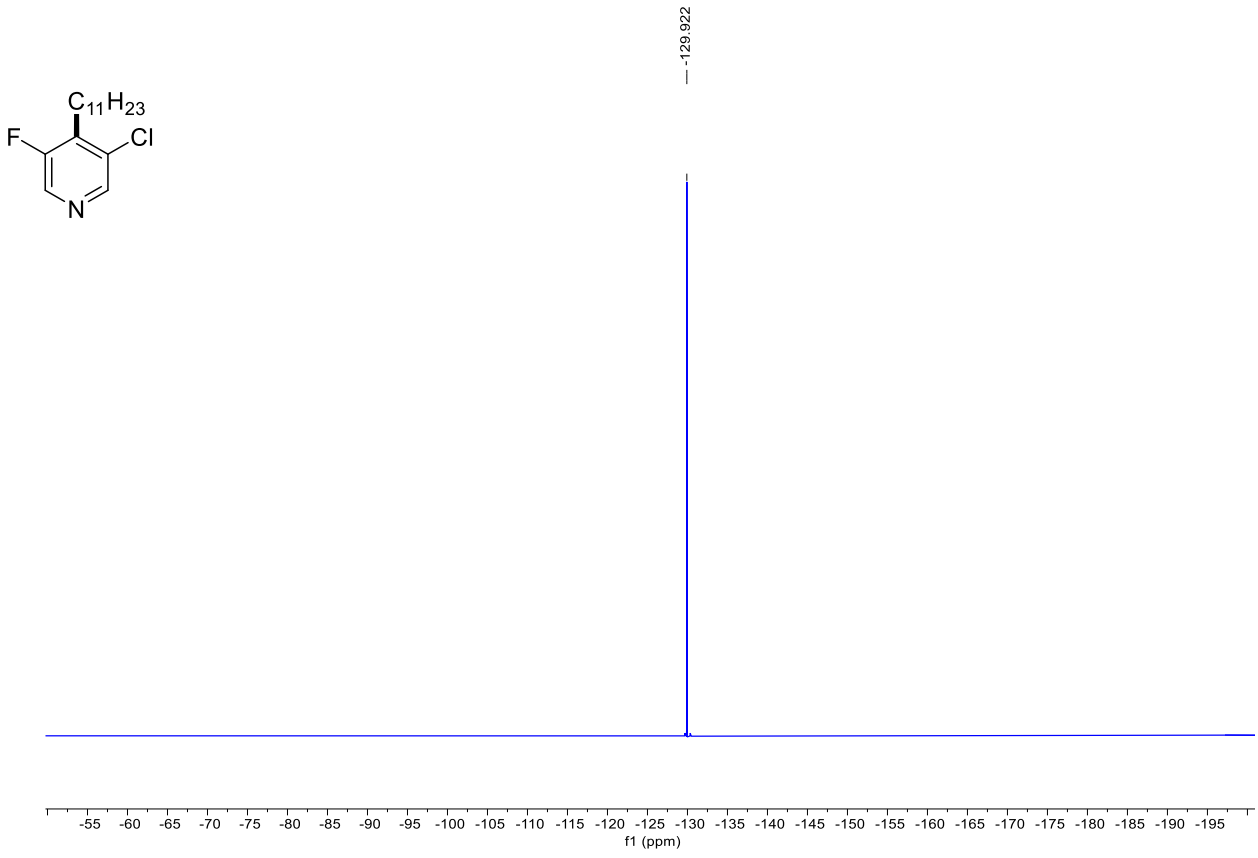
^{1}H NMR (400 MHz, $CDCl_3$)



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

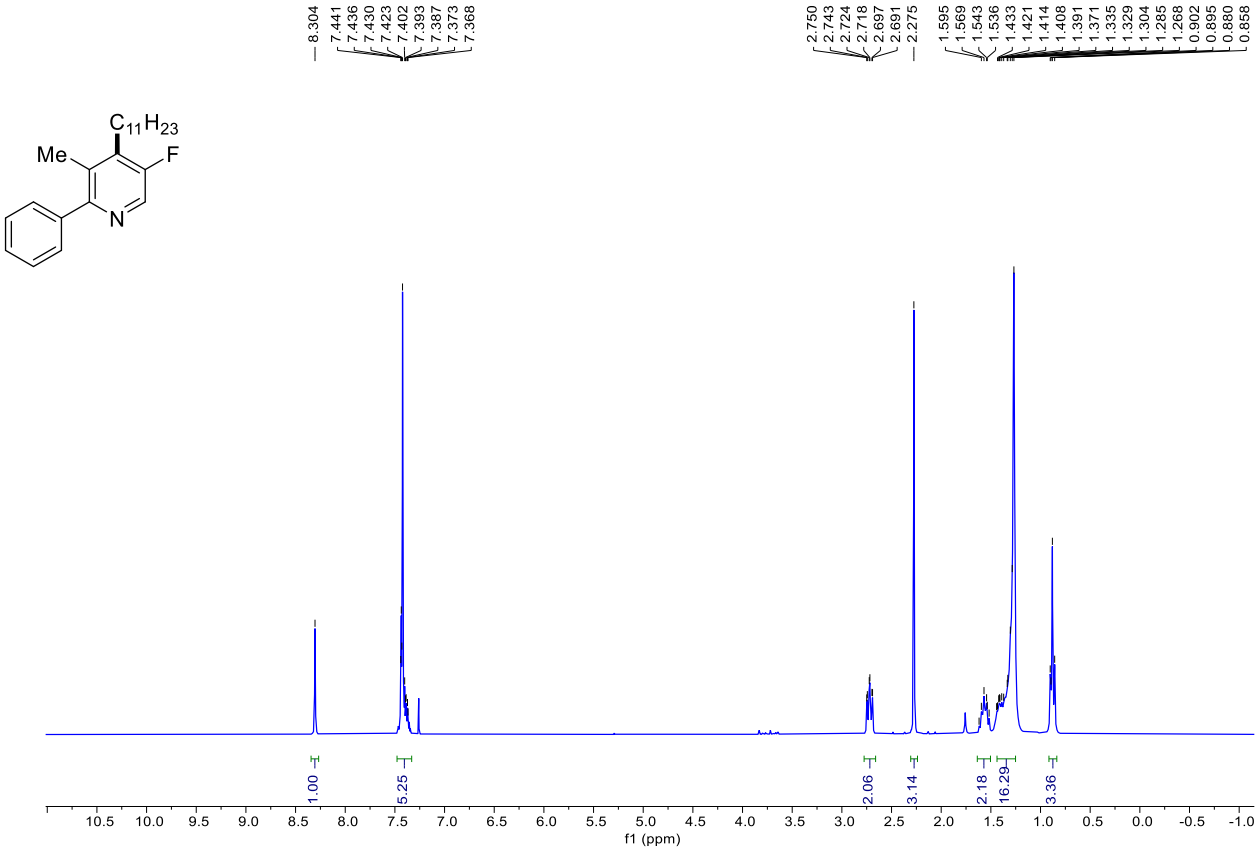


^{19}F NMR (376 MHz, $CDCl_3$)

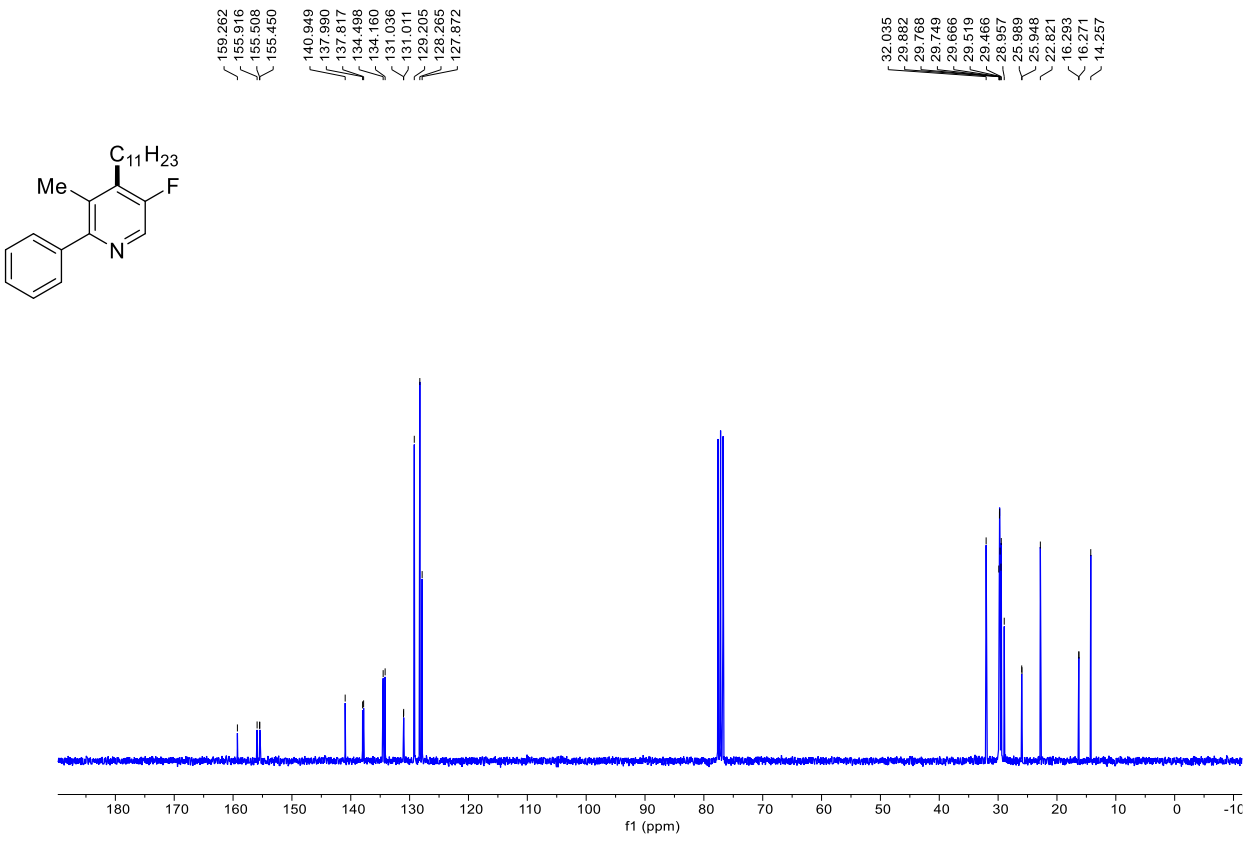


5-Fluoro-3-methyl-2-phenyl-4-undecylpyridine (4p)

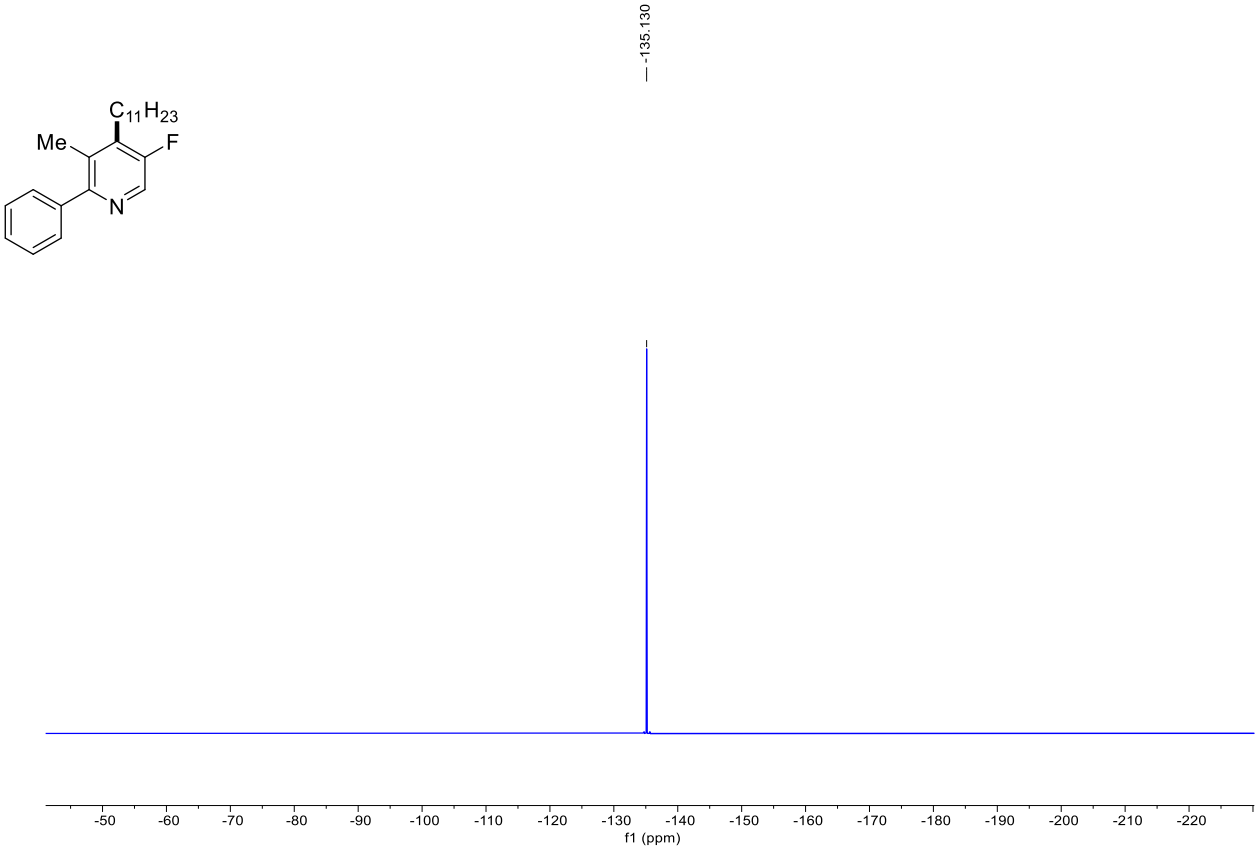
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (76 MHz, $CDCl_3$)

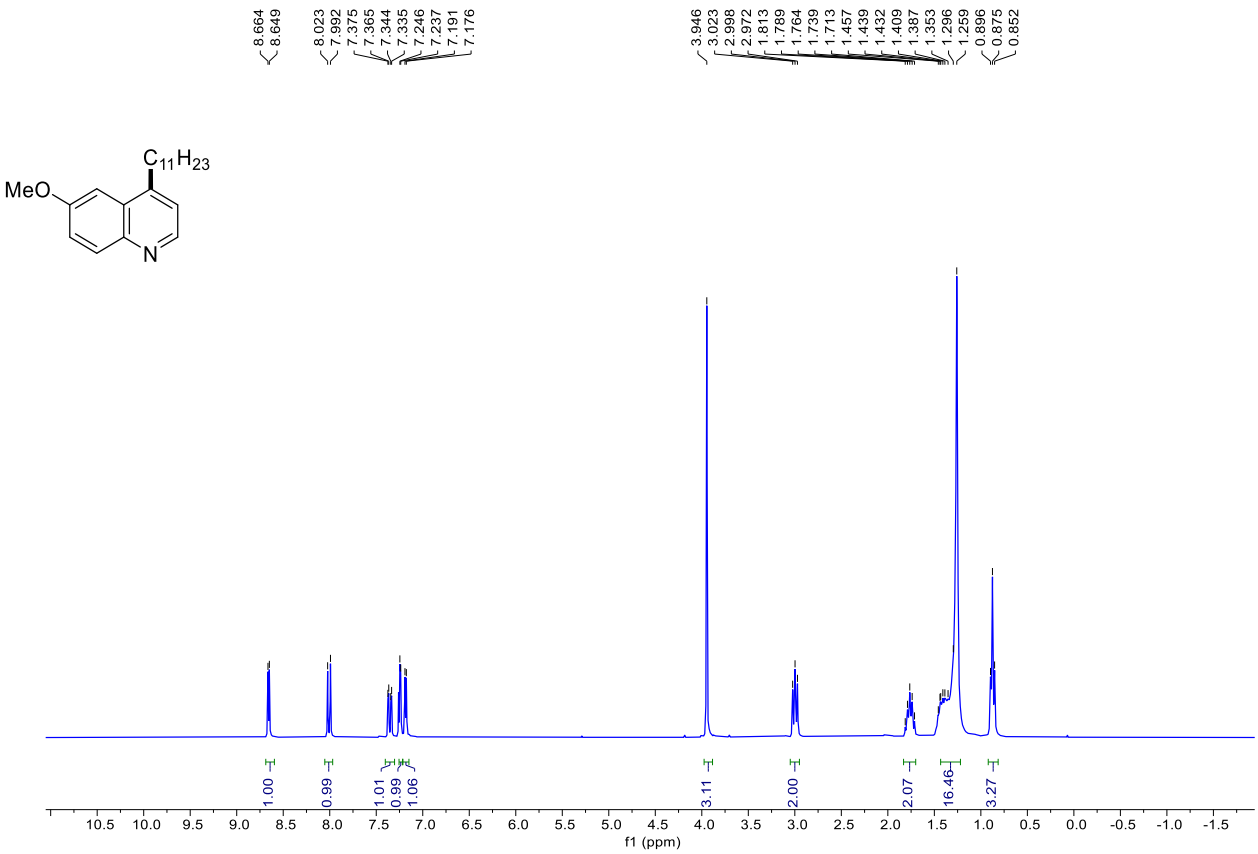


^{19}F NMR (282 MHz, $CDCl_3$)

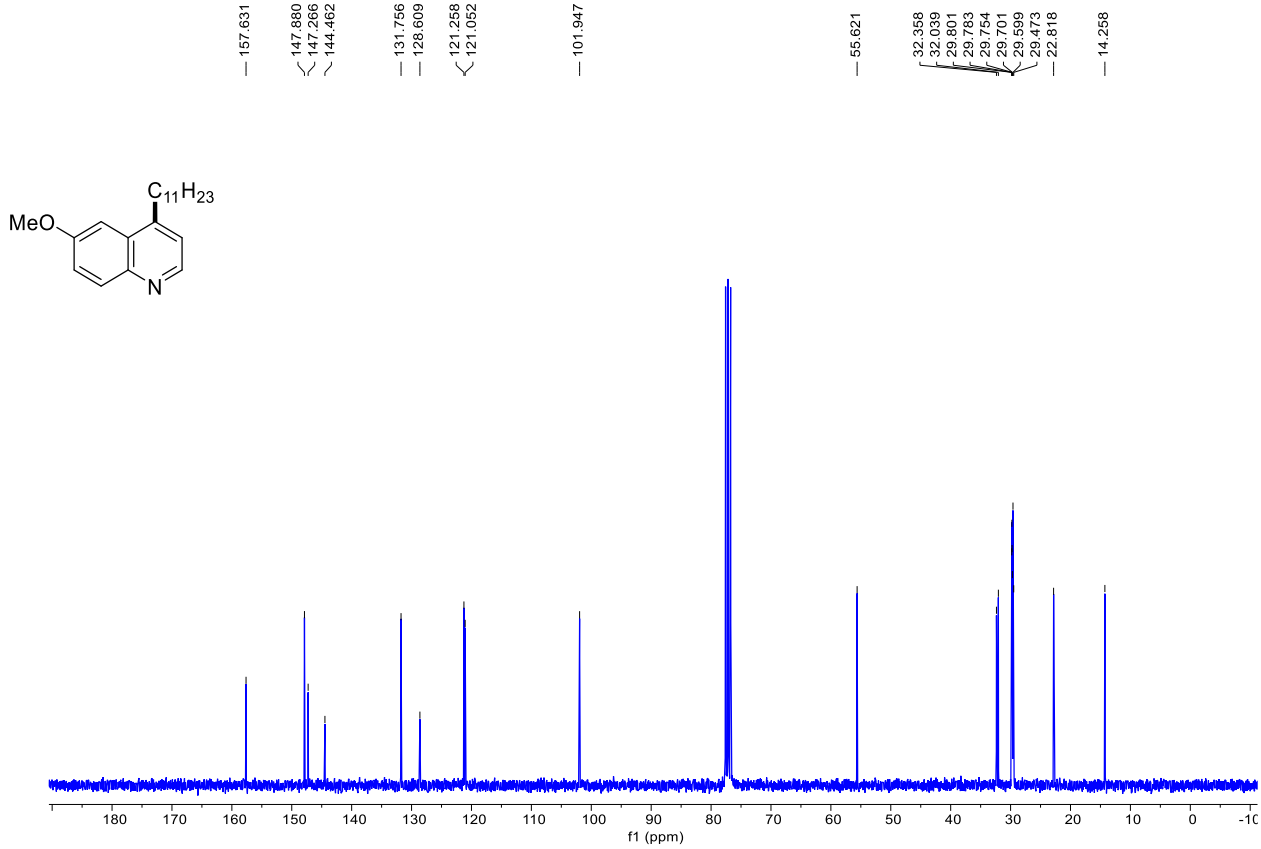


2-Methyl-5-undecyl-1,8-naphthyridine (4q)

^{1}H NMR (300 MHz, $CDCl_3$)

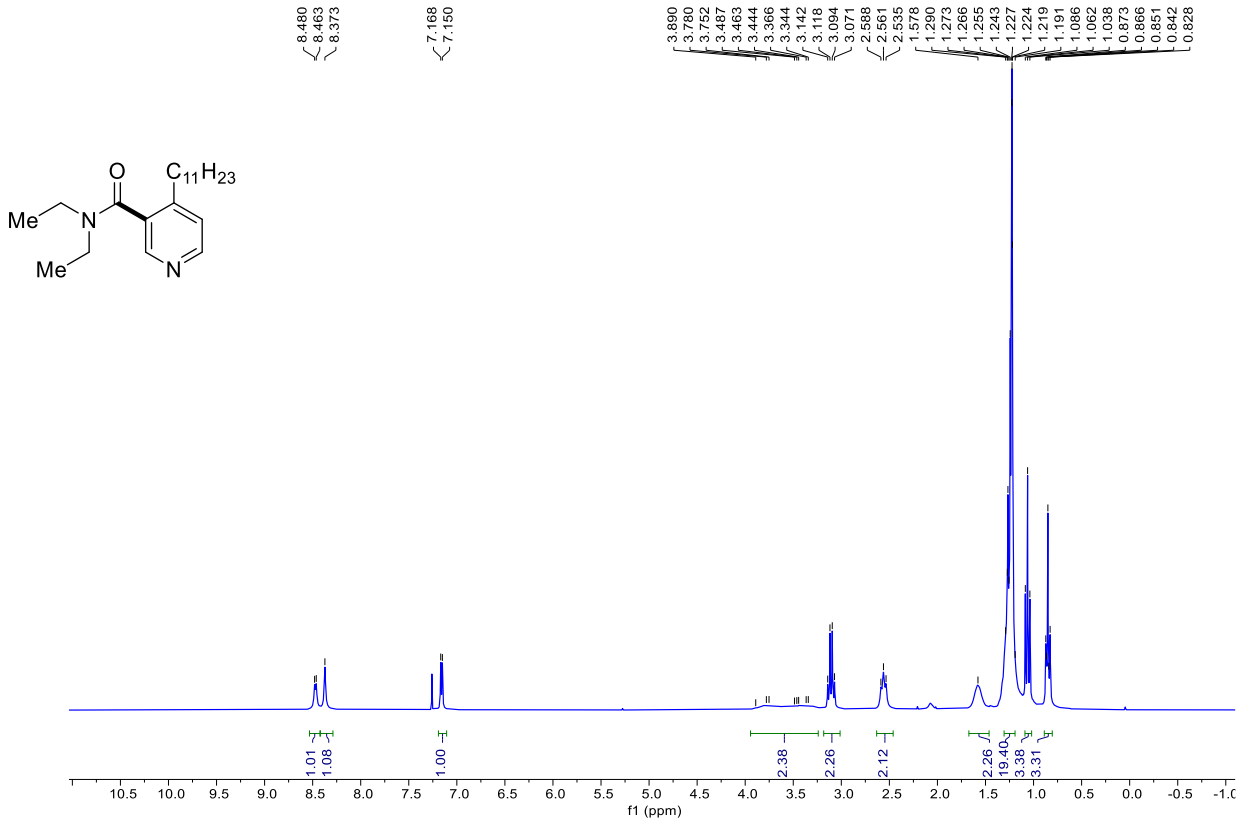


^{13}C NMR (76 MHz, $CDCl_3$)

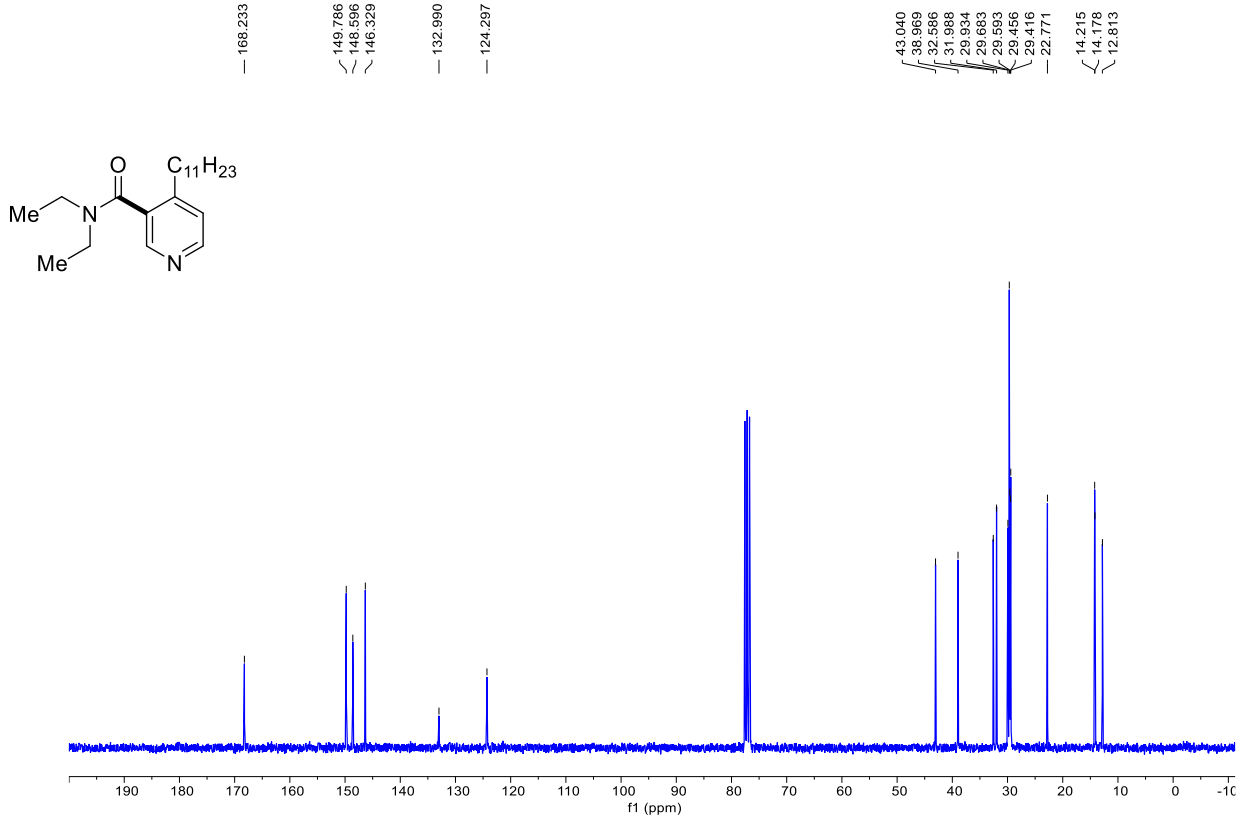


***N,N*-Diethyl-4-undecylnicotinamide (5a)**

^{1}H NMR (300 MHz, $CDCl_3$)

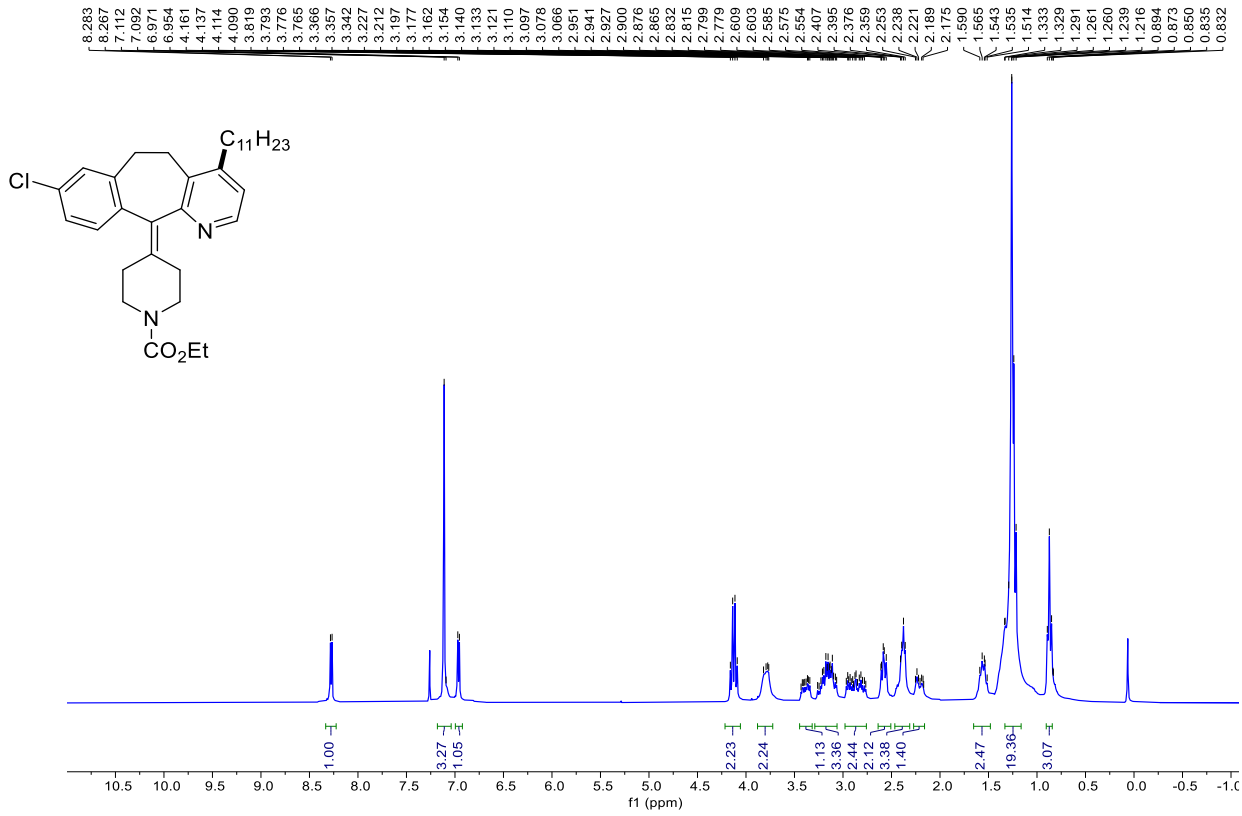


^{13}C NMR (76 MHz, $CDCl_3$)

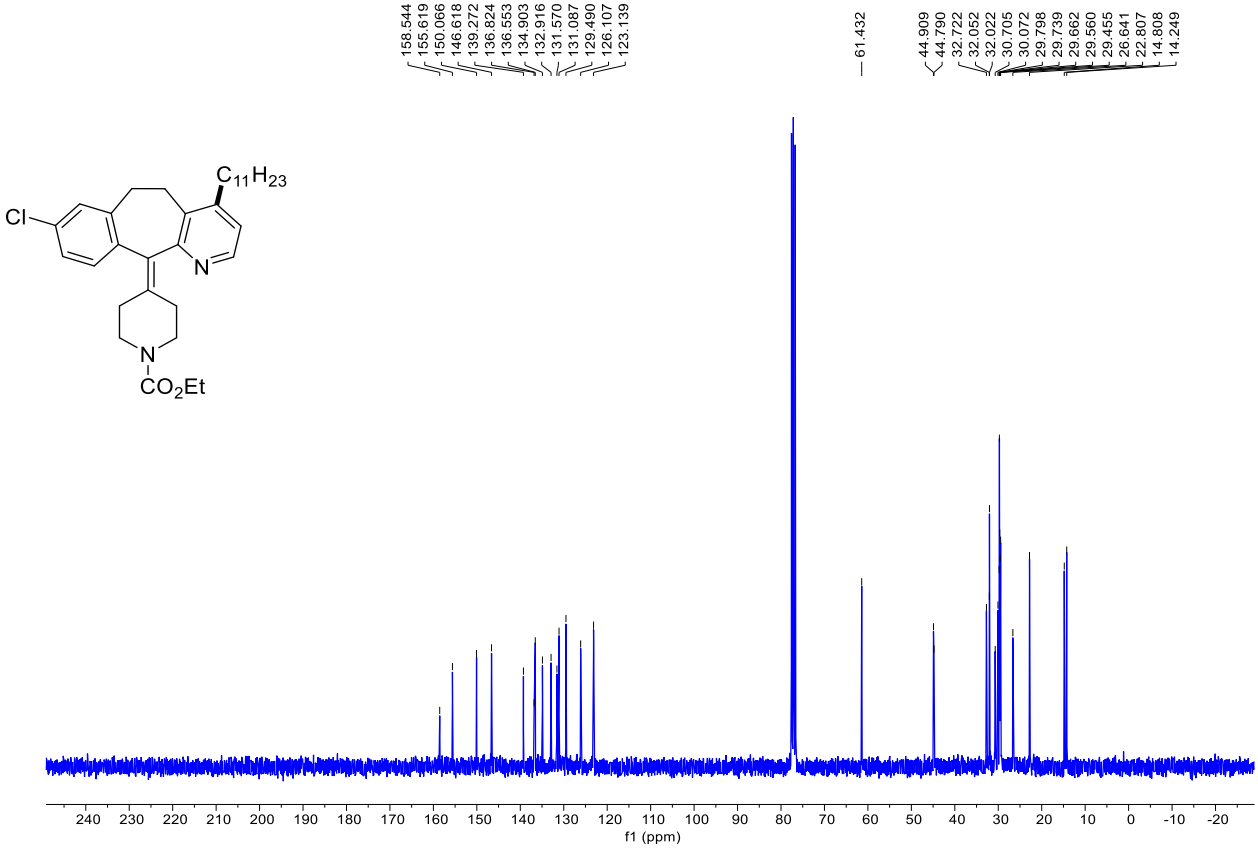


Ethyl 4-(8-chloro-4-undecyl-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (5b)

^{1}H NMR (300 MHz, $CDCl_3$)

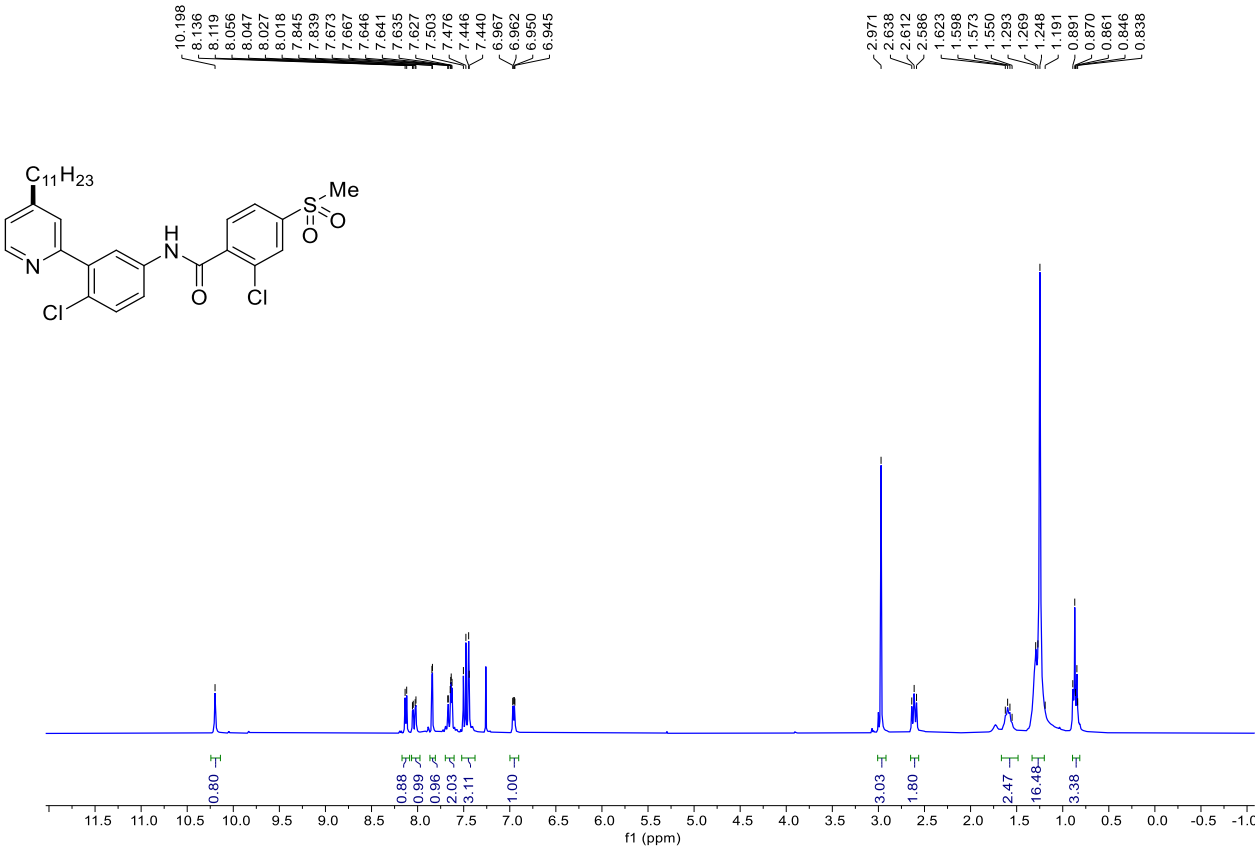


^{13}C NMR (76 MHz, $CDCl_3$)

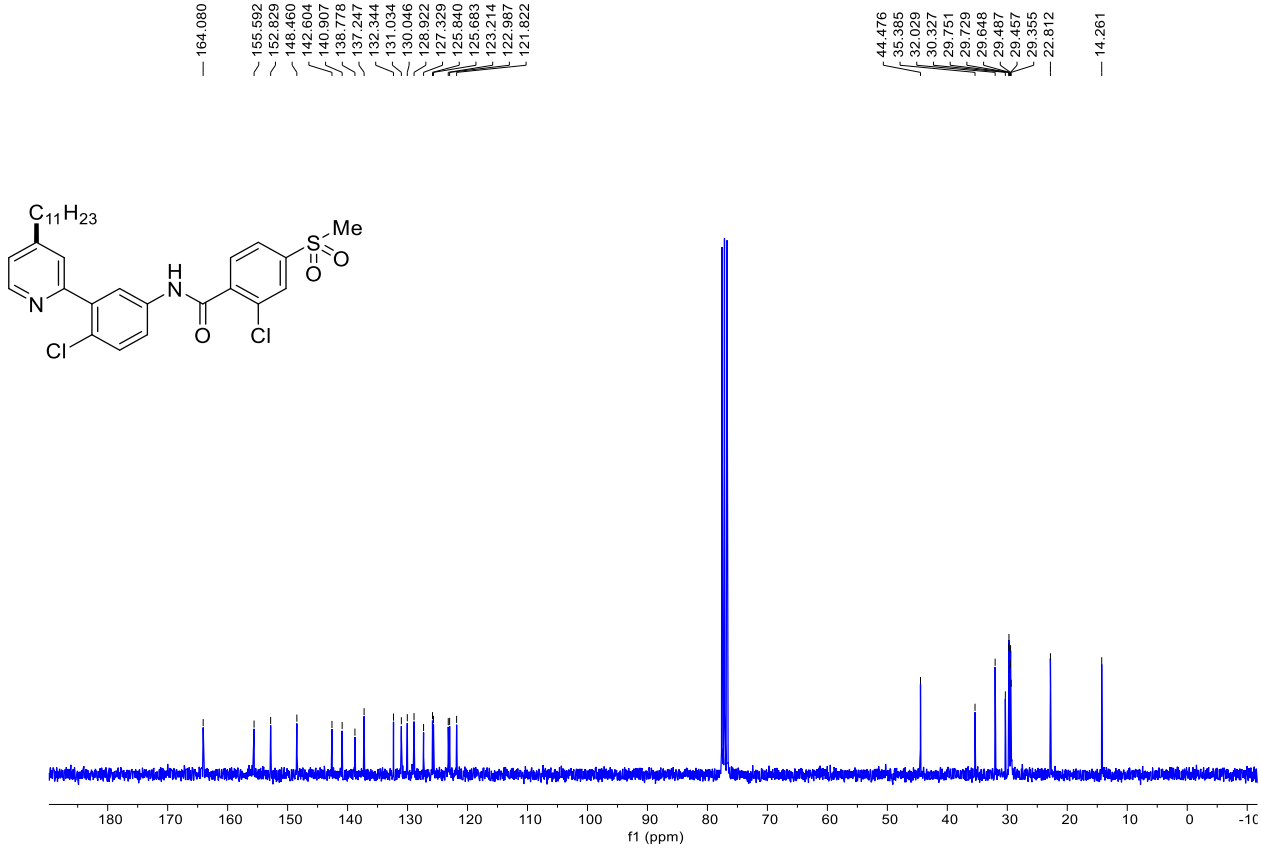


2-Chloro-*N*-(4-chloro-3-(4-undecylpyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (5c)

^{1}H NMR (300 MHz, $CDCl_3$)

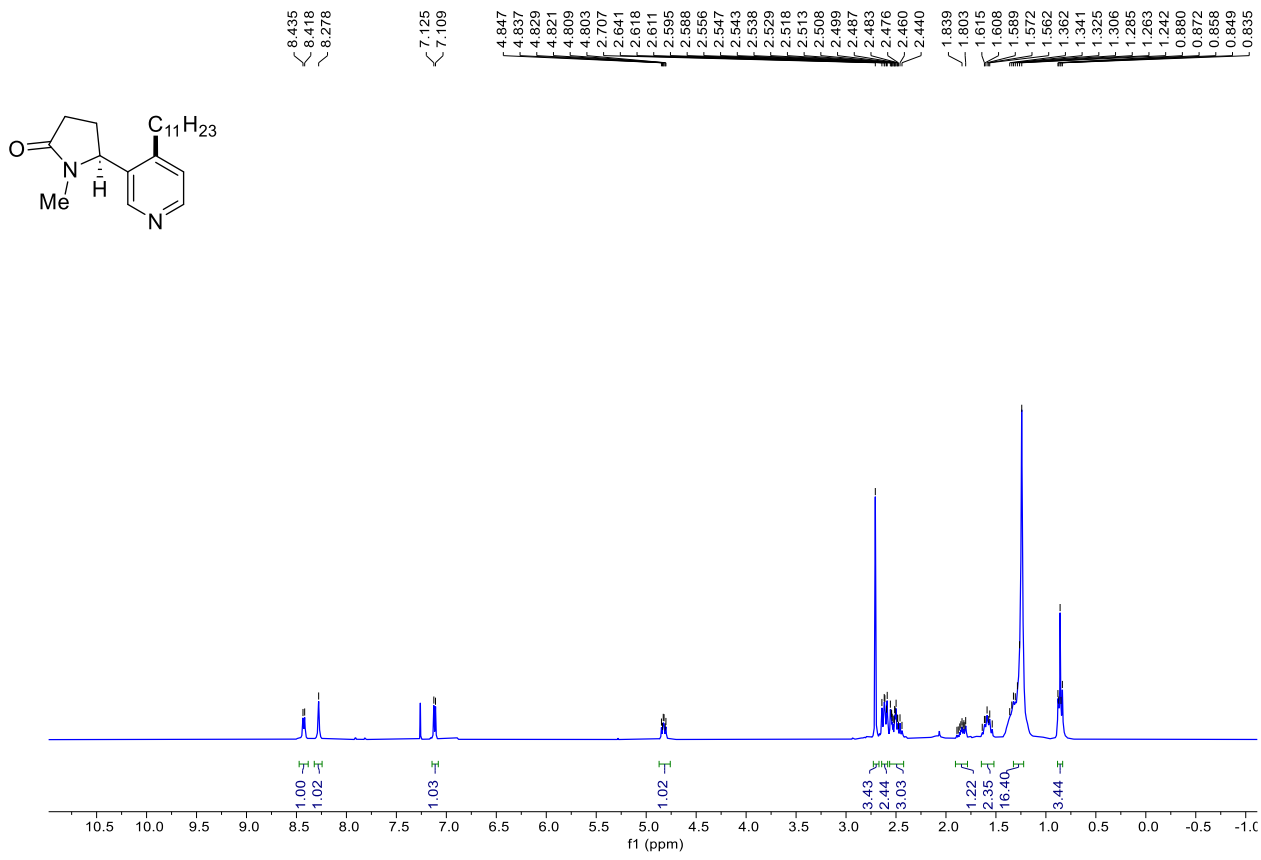


^{13}C NMR (76 MHz, $CDCl_3$)

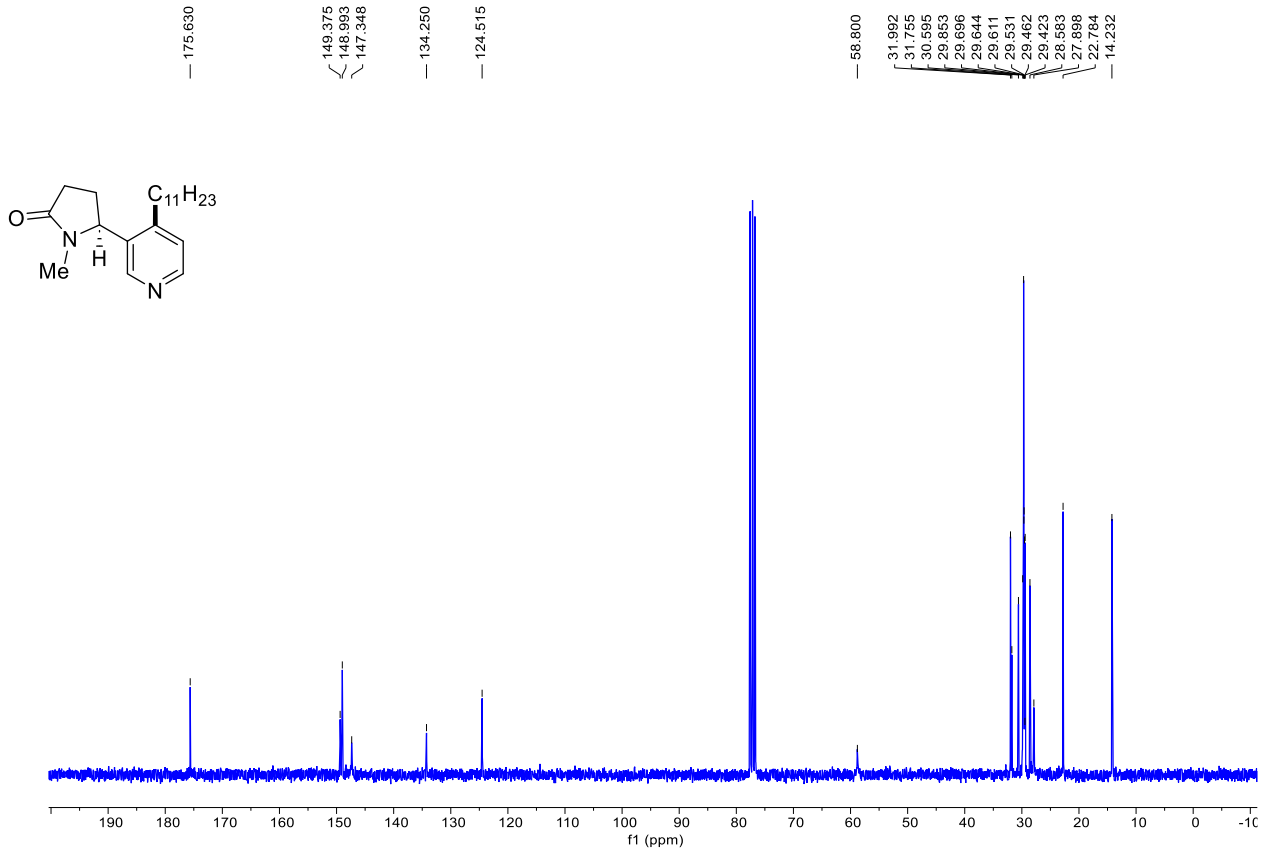


***(S)*-1-Methyl-5-(4-undecylpyridin-3-yl)pyrrolidin-2-one (5d)**

^{1}H NMR (300 MHz, $CDCl_3$)

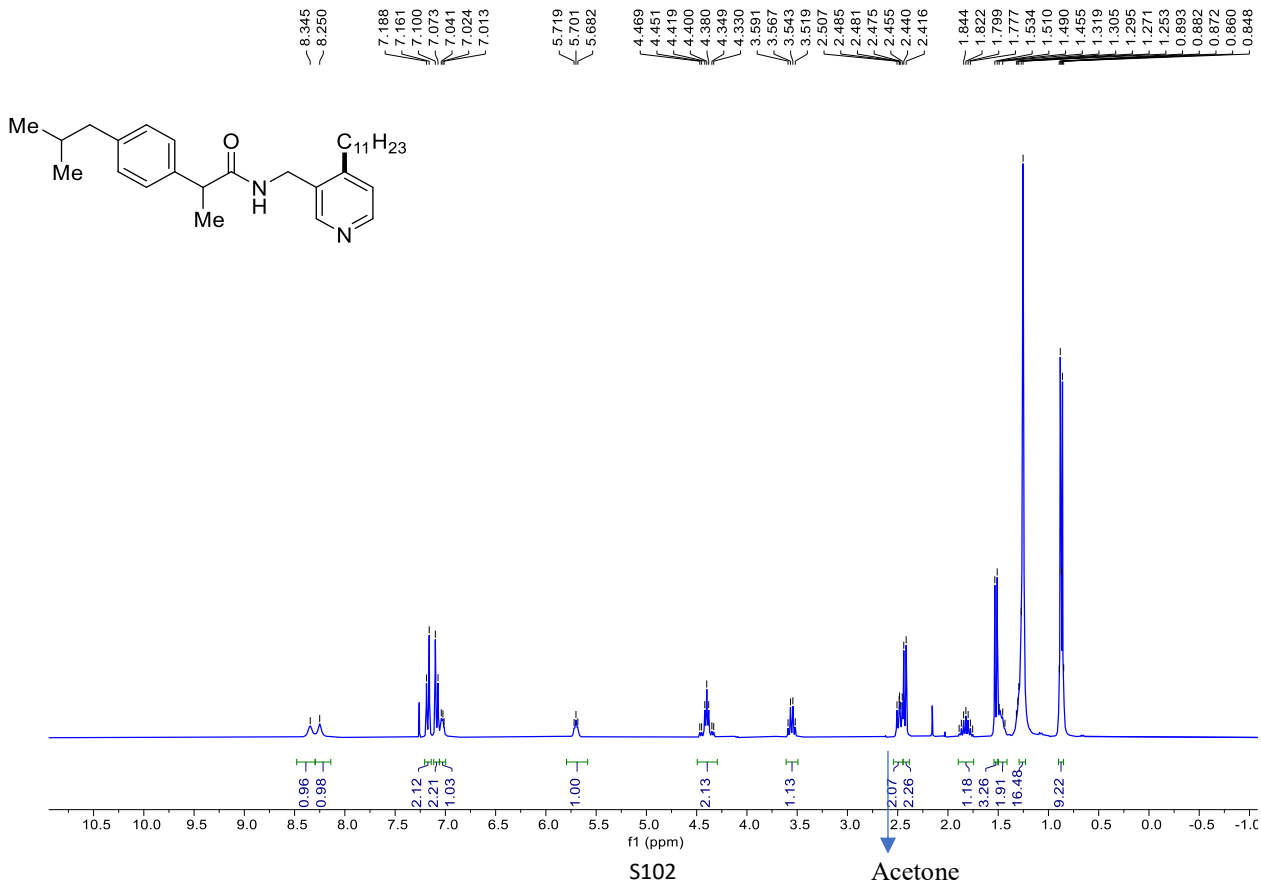


^{13}C NMR (76 MHz, $CDCl_3$)

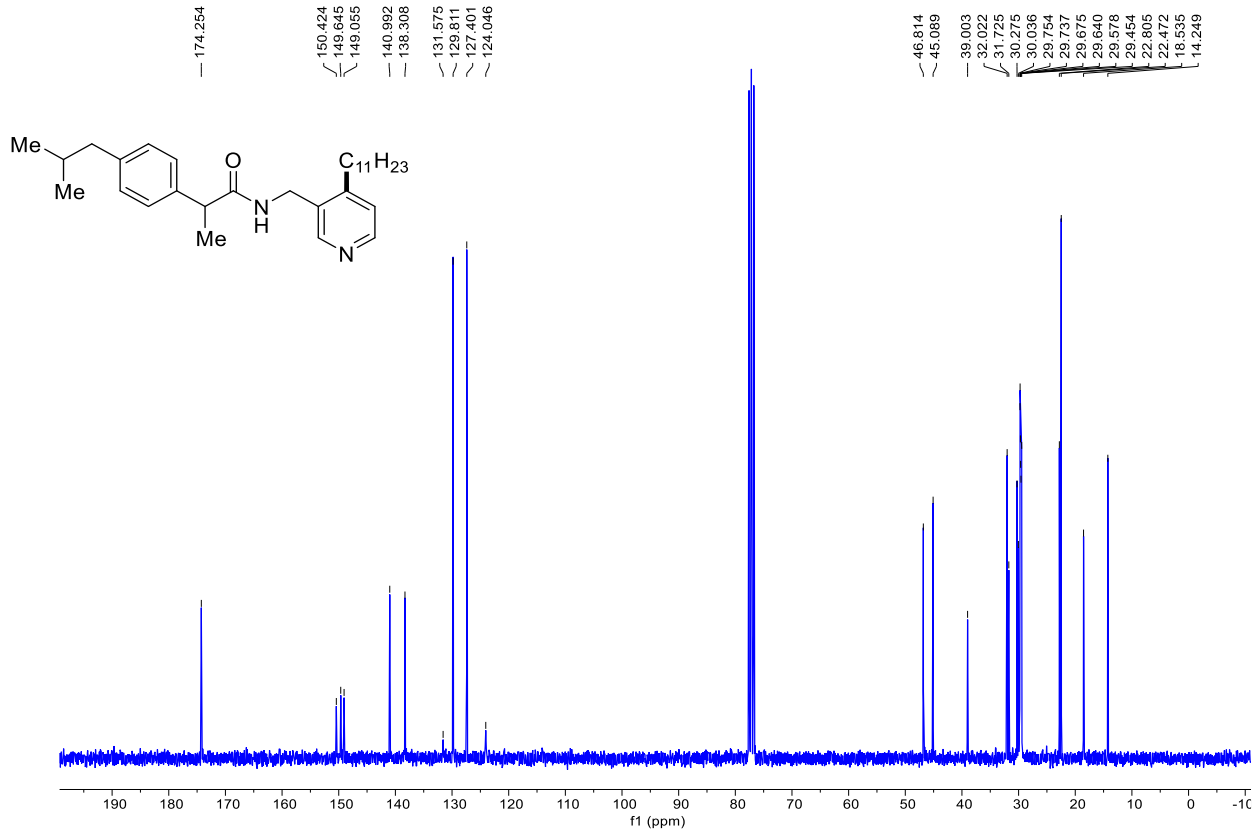


2-(4-isobutylphenyl)-*N*-((4-undecylpyridin-3-yl)methyl)propenamide (5e)

^{1}H NMR (300 MHz, $CDCl_3$)

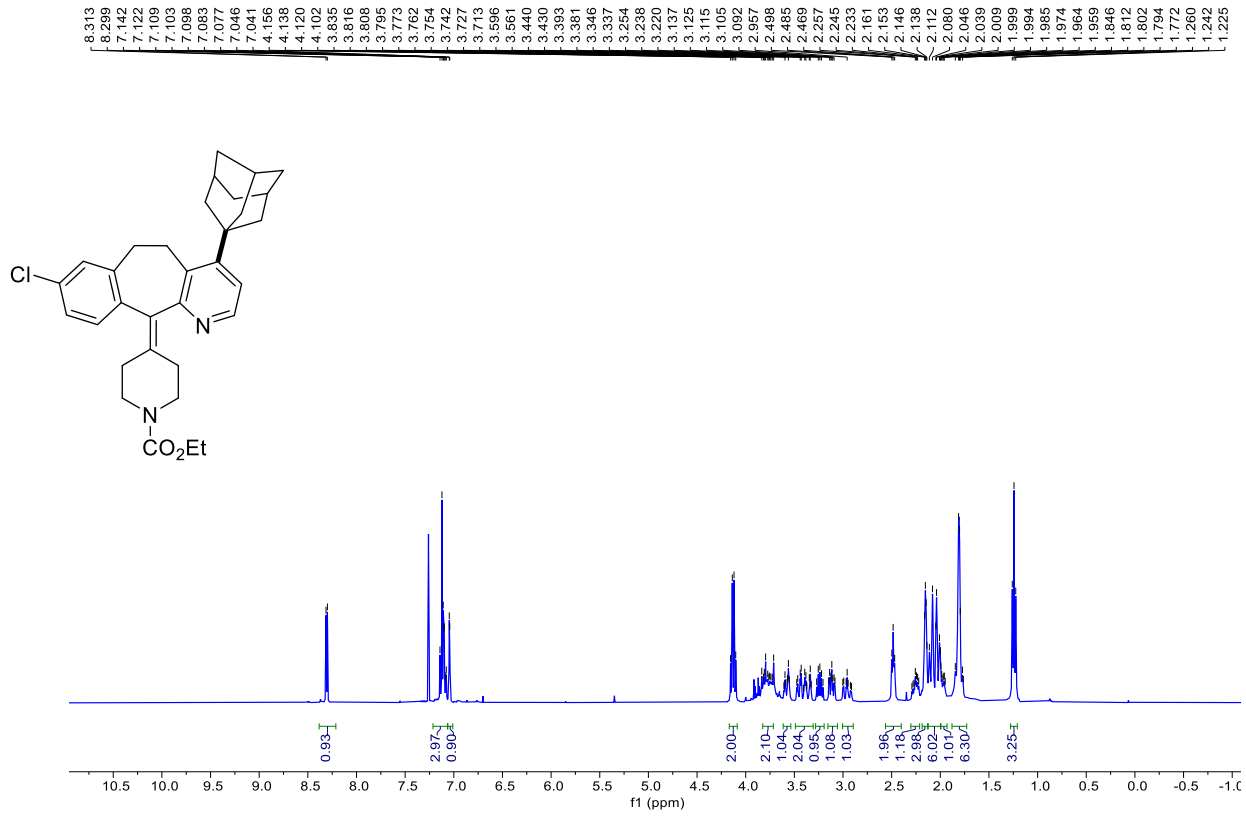


^{13}C NMR (76 MHz, $CDCl_3$)

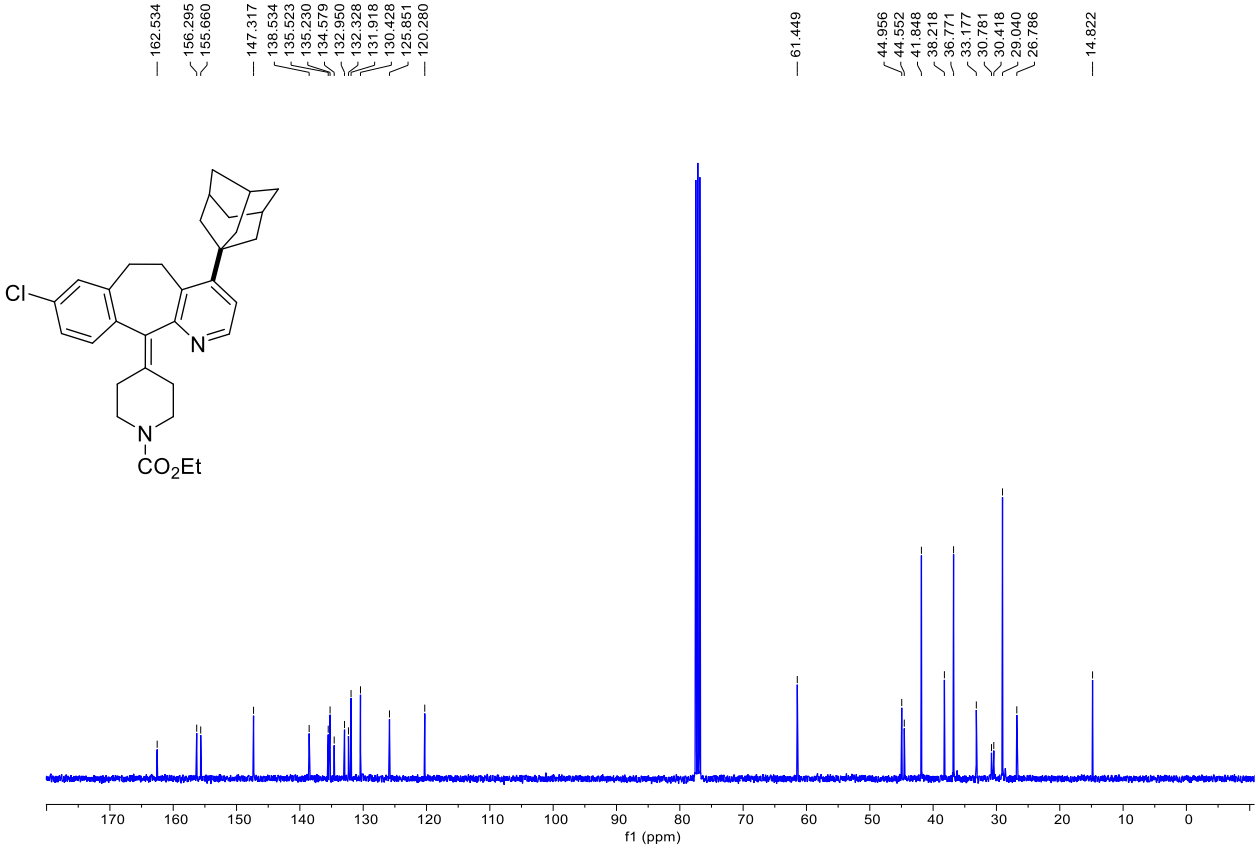


Ethyl 4-(4-(adamantan-1-yl)-8-chloro-5,6-dihydro-11*H*-benzo[5,6]cyclohepta[1,2-*b*]pyridin-11-ylidene)piperidine-1-carboxylate (4r)

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

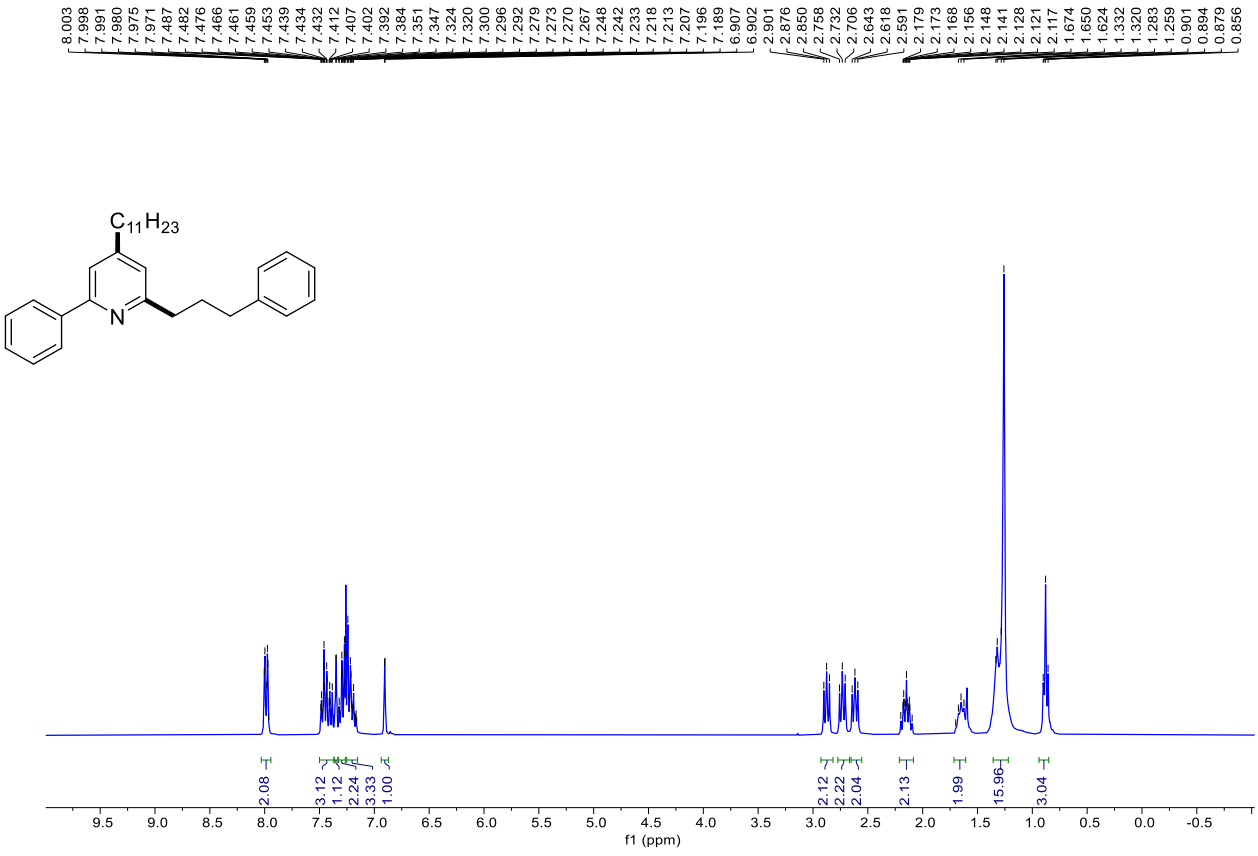


^{13}C NMR (101 MHz, $CDCl_3$)



2-Phenyl-6-(3-phenylpropyl)-4-undecylpyridine (6a)

^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (76 MHz, $CDCl_3$)