Light-Induced Alkylation of (Hetero)aromatic Nitriles in a Transition-Metal-Free C–C-Bond Metathesis

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Supporting Information

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I. General Information

Solvents and reagents

Unless stated otherwise, all solvents and reagents were obtained from commercial suppliers and used without prior purification. Phenanthrene (97%) was purchased from Acros Organics. *fac*-Ir(ppy)$_3$ was prepared according to a procedure by Konno and coworkers.[1] Reaction solvents for irradiations were degassed in an ultrasonic bath by argon sparging for 20 minutes. Anhydrous tetrahydrofuran, diethyl ether as well as benzene were distilled from potassium or sodium and benzophenone.

Reaction conditions

Reactions requiring anhydrous conditions were performed in dried glassware under an atmosphere of argon.

Chromatography

Chromatographic purification of products was performed as flash column chromatography on silica gel (35–70 µm, Acros Organics) according to the procedure of Still.[2] Thin-layer chromatography (TLC) was carried out on silica plates (TLC Silica 60 F254 by Merck). Visualization of the compounds was accomplished by projecting UV-light onto the developed plates and by Ninhydrin or Dragendorff stain.

NMR spectra

NMR spectra were recorded on a Bruker Avance-III HD (^{1}H-NMR: 300 MHz, ^{13}C-NMR: 75.5 MHz), a Bruker Avance-II (^{1}H-NMR: 400 MHz, ^{13}C-NMR: 100.6 MHz, ^{19}F-NMR: 376.5 MHz) or a Bruker Avance-III (^{1}H-NMR: 600 MHz, ^{13}C-NMR: 151.1 MHz) spectrometer. Chemical shifts are referenced to residual solvent signals ($CDCl_3$: 7.26 ppm and 77.16 ppm, DMSO-d_6: 2.50 ppm and 39.52 ppm for ^{1}H-NMR and ^{13}C-NMR respectively) and reported in parts per million (ppm) relative to tetramethylsilane (TMS). Multiplicities of NMR signals are abbreviated as follows: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and combinations thereof, app = apparent. For ^{19}F-NMR spectra, chemical shifts are reported in ppm relative to C(^{35}Cl)$_2$(^{37}Cl)F. The spectrometer was calibrated using α,α,α-trifluorotoluene in $CDCl_3$ (–63.9 ppm).

Infrared spectra

Infrared (IR-) spectra were recorded on a FTIR-spectrometer (Bruker Tensor 27) equipped with a diamond ATR unit and are reported in terms of frequency of absorption $\bar{\nu}$ [cm^{-1}].

UV-Vis spectra

UV-Vis spectra were recorded on an Evolution 201 UV-Visible Spectrophotometer by Thermo Scientific.

Mass spectra

Electron spray ionization (ESI) mass spectra were recorded on a 1200-series HPLC-system (Agilent-Technologies) with binary pump and integrated diode array detector coupled to a LC/MSD-Trap-XTC-mass spectrometer (Agilent-Technologies) or on a Micromass-Q-TOF-Ultima-3-mass spectrometer (Waters). High resolution mass spectra were recorded on a Micromass-Q-TOF-Ultima-3-mass spectrometer (Waters) with LockSpray-interface and a suitable external calibrant. The reported high resolution masses refer to the neutral molecules since the mass of the single electron (which is removed to form the cationic species) was considered during calibration. LIFDI mass spectra were recorded on a double focusing LIFDI sector field mass spectrometer (Thermo Fischer DFS).

Melting points

Melting points were determined in open capillary tubes using a Krüss-Optronic KSP 1 N thermoelectric melting point meter.

Microwave assisted reactions

Microwave-assisted reactions were performed using a *Discover SP* microwave apparatus from CEM.

II. Light Sources, Glassware and Setup for Irradiations

Light sources:

25 W energy-saving UV/vis CFL bulb: Reptile UVB200 from Exo-Terra. (http://www.exo-terra.com/en/products/reptile_uvb200.php).

25 W energy-saving UV-A lamp: UV-A spotlight from Eurolite with an UV-A lamp from Omnilux with λ_{max} = 368 nm (http://eshop.steinigke.de/de/mpn51100700-eurolite-uv-strahler-mit-uv-es-lampe-25w.html).

23 W energy-saving vis CFL bulb: Tornado (cool daylight, 6500 K) from Philips (http://www.philips.de/c-p/8727900926002/tornado-spiralfoermige-energiesparlampe/ubersicht).

Glassware:

All reactions on a preparative scale (Scheme 3) were performed in round-bottom flasks made of DURAN® and all screening reactions in Tables S1–S11 as well as in Scheme S1 were performed in 10 mL vials made of AR-GLAS®. According to the manufacturer, these glasses exhibit no significant transmission of light with wavelengths of less than about 290 nm.

For detailed technical information, the reader is directed to the homepage of Schott: http://www.schott.com/tubing/english/product_selector/#!/region--all/lang--english/filter--list.

Setup for irradiations:

The energy-saving lamps were placed in a distance of approximately 2 cm from the reaction vessel. As described in the general procedure, alkylations on a preparative scale were performed in 100 mL round-bottom flasks. In these cases, the back sides of the flasks were wrapped with aluminum foil to increase the efficiency of irradiation. A typical reaction setup is shown in Figure S1.

Figure S1: Setup for irradiations on a preparative scale under irradiation with a 25 W energy-saving UV/vis CFL bulb.

Irradiations with sunlight were performed by placing the reaction vessel outside (September 2016, Mainz, Germany, 49°59'27.9"N) from morning to evening. The samples were kept in a fridge at –28 °C overnight. This procedure was repeated until full consumption of the respective radical precursor was achieved as judged by TLC.

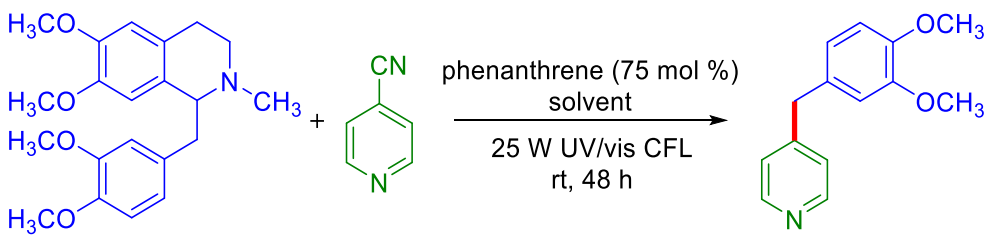
III. Optimization Studies

III.1 Alkylations using phenanthrene as photoredox catalyst

General procedure for screening reactions with phenanthrene:

A 10 mL glass vial (see section II) equipped with a mechanic stir bar and a septum was charged with 4-cyanopyridine (**1a**), (±)-laudanosine (**3a**) as well as phenanthrene and flushed with argon. Degassed solvent (8 mL, unless stated otherwise) was added, followed by argon sparging for 1 min. If indicated, TMSCN was added via syringe. The solution was irradiated with a 25 W UV/vis CFL bulb (see section II) from a distance of approximately 2 cm for the indicated time. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added, followed by extraction with EtOAc (3 x 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Yields were determined by ^{1}H-NMR spectroscopy using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S1: Solvent screening for the alkylation of (hetero)aromatic nitriles in a transition metal-free C–C-bond metathesis.

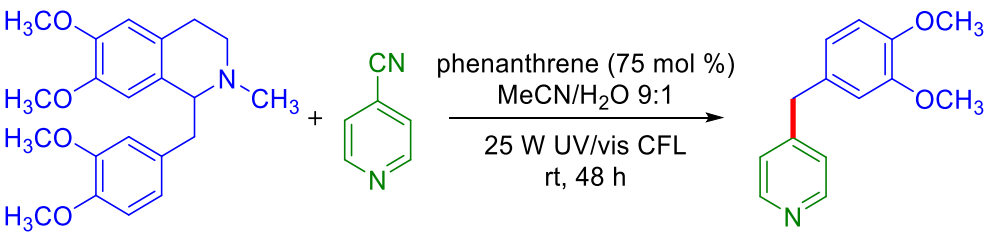


3a (3.0 equiv) **1a** (1.0 equiv) **8a**

Entry	Solvent	8a (%)
1	MeCN/H_2O 9:1	17
2	MeCN	15
3	DMI	15
4	DMSO	15
5	DMF	11

Procedure: The reactions were performed according to the general procedure using (±)-laudanosine (**3a**, 172 mg, 480 µmol), 4-cyanopyridine (**1a**, 16.7 mg, 160 µmol) and phenanthrene (21.4 mg, 120 µmol). Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S2: Influence of the reactant ratios on the alkylation of (hetero)aromatic nitriles in a transition metal-free C–C-bond metathesis.

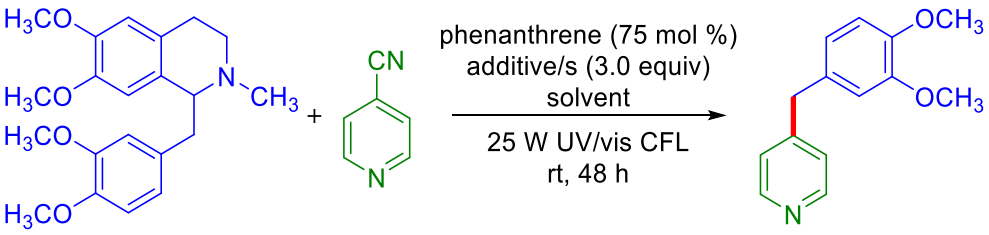


3a **1a** **8a**

Entry	3a (equiv.)	1a (equiv.)	8a (%)
1	1.0	5.0	37
2	**1.0**	**3.0**	**36**
3	1.0	1.0	27
4	3.0	1.0	17
5	5.0	1.0	16

Procedure: The reactions were performed according to the general procedure using varying reactant ratios. One equivalent corresponds to 160 µmol. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S3: Additive screening for the alkylation of (hetero)aromatic nitriles in a transition metal-free C–C-bond metathesis.

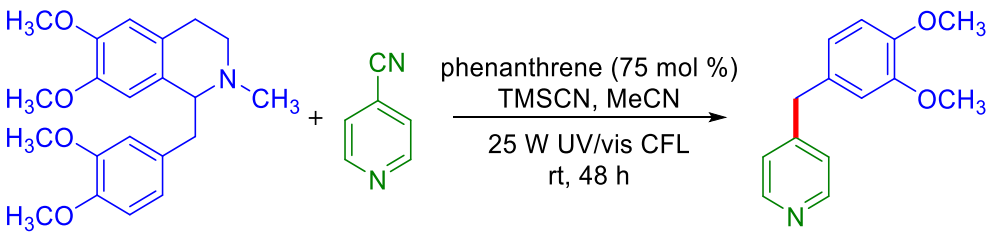


3a (1.0 equiv) **1a** (3.0 equiv) **8a**

Entry	Additive/s	Solvent	8a (%)
1	**TMSCN**	**MeCN**	**63**
2	TMSCl	MeCN	24
3	CsF	MeCN/H_2O 9:1	17
4	KCN	MeCN/H_2O 9:1	traces
5	TMSCN, CsF	MeCN	traces
6	KCN, CsF	MeCN/H_2O 9:1	traces

Procedure: The reactions were performed according to the general procedure using an additional cyanide source and/or CsF (3.0 equiv. each). One equivalent corresponds to 160 µmol. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard. **Please note:** Although a mixture of MeCN and H_2O was originally chosen as solvent (Table S1), pure MeCN was used from this point on as TMSCN is not stable in aqueous solutions.

Table S4: Influence of the TMSCN loading on the alkylation of (hetero)aromatic nitriles in a transition metal-free C–C-bond metathesis.

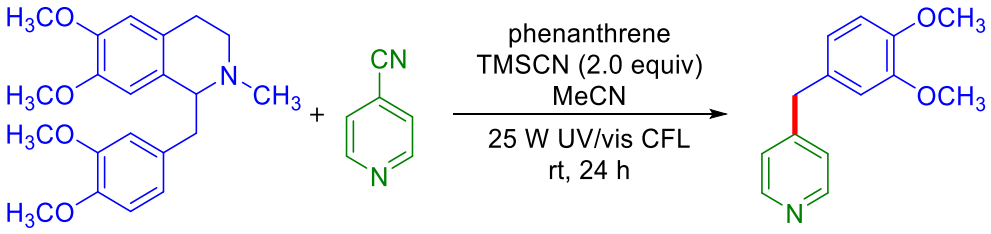


3a (1.0 equiv) **1a** (3.0 equiv) **8a**

Entry	TMSCN (equiv.)	8a (%)
1	0.50	40
2	0.75	44
3	1.00	49
4	**2.00**	**61**
5	3.00	63
6	4.00	61
7	5.00	60

Procedure: The reactions were performed according to the general procedure using varying amounts of TMSCN. One equivalent corresponds to 160 µmol. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S5: Influence of the phenanthrene loading on the alkylation of (hetero)aromatic nitriles in a transition metal-free C–C-bond metathesis.

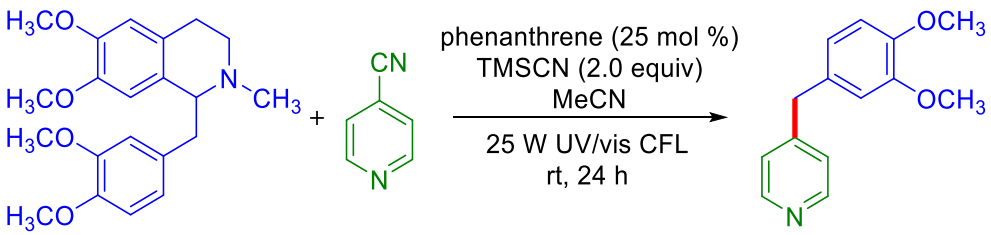


3a (1.0 equiv) **1a** (3.0 equiv) **8a**

Entry	Phenanthrene (mol%)	8a (%)
1	0	50
2	5	54
3	15	60
4	**25**	**64**
5	50	61
6	75	61
7	100	60
8	125	61
9	150	59

Procedure: The reactions were performed according to the general procedure using varying amounts of phenanthrene. One equivalent corresponds to 160 µmol. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S6: Concentration screening for the alkylation of (hetero)aromatic nitriles in a transition metal-free C–C-bond metathesis.



3a (1.0 equiv) **1a** (3.0 equiv) **8a**

Entry	[3a] (mmol/L)	8a (%)
1	10	55
2	**20**	**64**
3	80	43
4	160	30

Procedure: The reactions were performed according to the general procedure. One equivalent corresponds to 160 µmol. Different reactant concentrations were obtained by altering the volume of MeCN. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

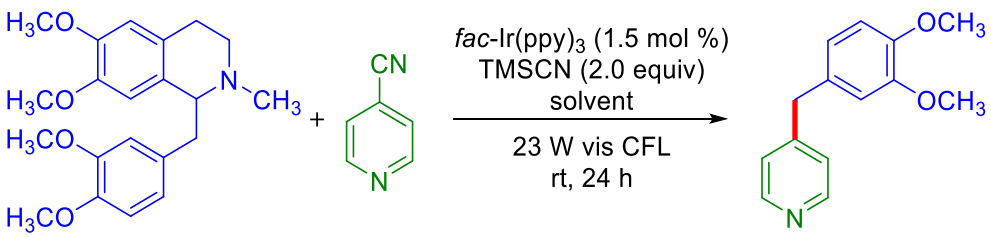
III.2 Alkylations using *fac*-Ir(ppy)$_3$ as photoredox catalyst

fac-Ir(ppy)$_3$ has been demonstrated to reduce aromatic nitriles upon excitation by visible light [$E_{1/2}(Ir^{IV}/^3[Ir^{III}]^*)$ = –1.73 V vs SCE][3].[4] The resulting Ir^{IV}-species is a strong electron acceptor [$E_{1/2}(Ir^{IV}/Ir^{III})$ = +0.77 V vs SCE][3]. Thus, it seemed possible that this transition metal complex could promote the C–C-bond metathesis reported herein [$E_{1/2}$(**1a**/**2a**) = –1.66 V vs SCE,[5] typically: $E_{1/2}(R_3N^{\cdot+}/R_3N) \leq 1.1$ V vs SCE[6]]. Optimization studies were undertaken and the results are listed below (Tables S7–S9). To account for the much lower catalyst loading, the concentration was increased by reducing the total volume to 2 mL instead of 8 mL (used for phenanthrene-catalyzed reactions), which is more promising according to the literature.[4b] Literature reports also suggest that the nonappearance of the nitrile´s own UV-mediated redox processes upon irradiation with visible light will cause these reactions to afford better yields when an excess of the radical source is utilized.[4]

General procedure for screening reactions with *fac*-Ir(ppy)$_3$:

A 10 mL glass vial (see section II) equipped with a mechanic stir bar and a septum was charged with 4-cyanopyridine (**1a**), (±)-laudanosine (**3a**) as well as *fac*-Ir(ppy)$_3$ and flushed with argon. Degassed solvent (2 mL) was added, followed by argon sparging for 1 min. After addition of TMSCN via syringe, the solution was irradiated with a 23 W vis CFL bulb (see section II) from a distance of approximately 2 cm for the indicated time. A saturated aqueous solution of $NaHCO_3$ (20 mL) was added, followed by extraction with EtOAc (3 x 30 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. Yields were determined by ^{1}H-NMR spectroscopy using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S7: Solvent screening for the alkylation of (hetero)aromatic nitriles in a visible light-induced C–C-bond metathesis in the presence and absence of TMSCN.

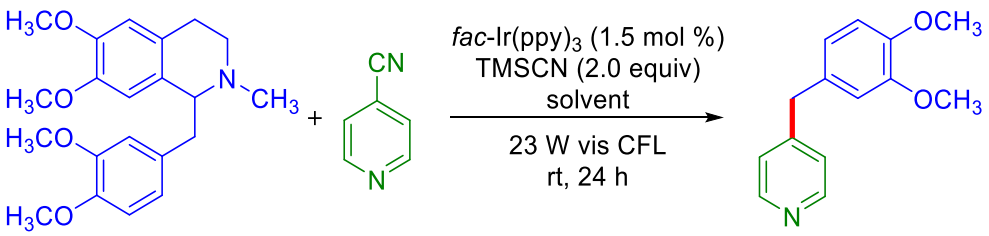


3a (2.0 equiv) **1a** (1.0 equiv) **8a**

Entry	Solvent	TMSCN added?	8a (%)
1	MeCN	No	42
2	**MeCN**	**Yes**	**51**
3	DMSO	No	37
4	DMSO	Yes	41
5	DMI	No	47
6	DMI	Yes	53

Procedure: The reactions were performed according to the general procedure using (±)-laudanosine (**3a**, 114 mg, 320 µmol), 4-cyanopyridine (**1a**, 16.7 mg, 160 µmol) and *fac*-Ir(ppy)$_3$ (1.57 mg, 2.40 µmol) and, where indicated, TMSCN (40 µL, 320 µmol). Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S8: Influence of the reactant ratios on the alkylation of (hetero)aromatic nitriles in a visible light-induced C–C-bond metathesis.

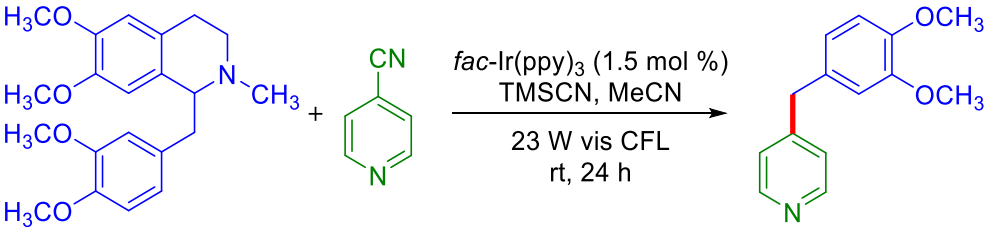


3a **1a** **8a**

Entry	3a (equiv.)	1a (equiv.)	8a (%)
1	1.0	2.0	15
2	1.0	1.0	26
3	**2.0**	**1.0**	**51**
4	3.0	1.0	37
5	4.0	1.0	40

Procedure: The reactions were performed according to the general procedure using varying reactant ratios. One equivalent corresponds to 160 µmol. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

Table S9: Influence of the TMSCN loading on the alkylation of (hetero)aromatic nitriles in a visible light-induced C–C-bond metathesis.



3a (2.0 equiv) **1a** (1.0 equiv) **8a**

Entry	TMSCN (equiv.)	8a (%)
1	0	42
2	**2.0**	**51**
3	3.0	35
4	4.0	29

Procedure: The reactions were performed according to the general procedure using varying amounts of TMSCN. One equivalent corresponds to 160 µmol. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

IV. Mechanistic Considerations

IV.1 Absorption Spectra

Absorption spectra of phenanthrene as well as 4-cyanopyridine (4-CP) in the presence and absence of TMSCN are depicted in Figure S2.

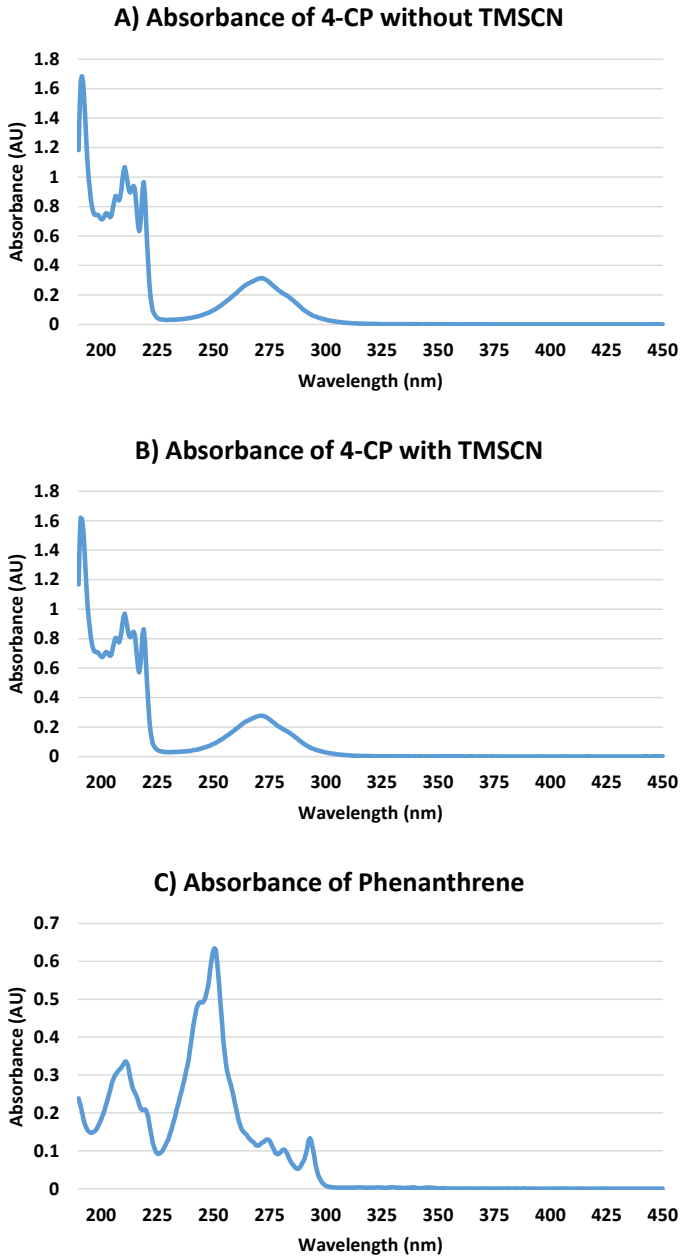


Figure S2: Absorption spectra at 190–450 nm measured for: A) 4-cyanopyridine (1.0×10^{-4} mmol/mL), B) 4-cyanopyridine (1.0×10^{-4} mmol/mL) with TMSCN (0.67×10^{-4} mmol/mL, 0.67 equiv.), C) phenanthrene (1.0×10^{-5} mmol/mL).

The obtained spectroscopic data show that the absorption maxima of 4-cyanopyridine are not shifted upon addition of TMSCN (potential Lewis acid/base interaction) and no new absorption maxima are observed. It is noteworthy that the ratio of 4-cyanopyridine relative to TMSCN was the same as given in the general procedure (see section V.2). This indicates that the beneficial impact of TMSCN as additive does probably not originate from a coordination of the pyridine's nitrogen to the TMS-group. Since the used glassware shows no significant transmission of light with wavelengths of less than about 290 nm (see section II), the absorption of phenanthrene and 4-cyanopyridine was compared at 290–400 nm and 315–400 nm (UV-A region) respectively (Figure S3). All spectra were recorded at concentrations (0.01–0.001 mmol/mL) which are approximately equal to those used in the general procedure (laudanosine: 0.02 mmol/mL, TMSCN: 0.04 mmol/mL, 4-cyanopyridine: 0.06 mmol/mL, phenanthrene: 0.005 mmol/mL, see section V.2). While phenanthrene absorbs significantly at wavelengths below approximately 350 nm, 4-cyanopyridine displays no significant absorption within the UV-A region. This finding is of particular interest for the interpretation of selected control experiments outlined in section IV.

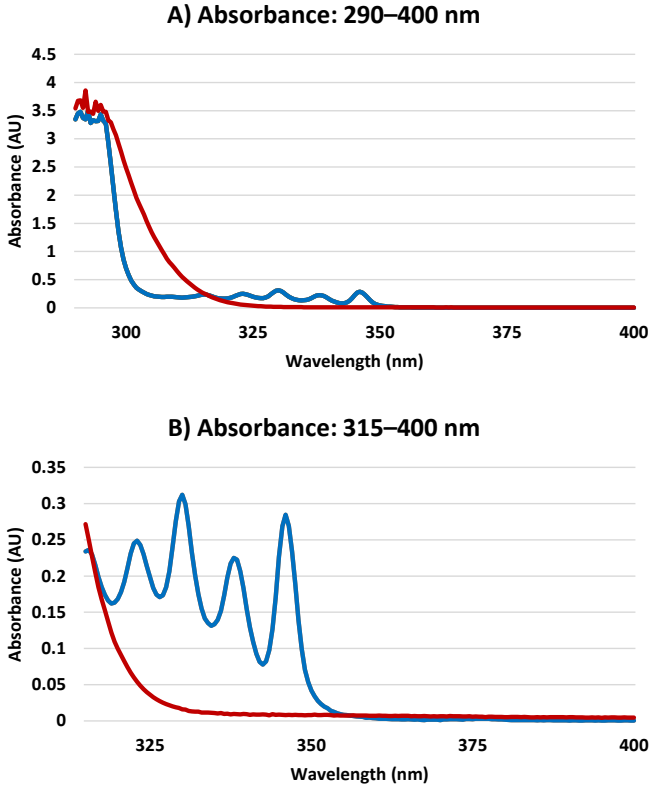


Figure S3: Absorption spectra of 4-cyanopyridine (red, 1.0×10^{-2} mmol/mL) and phenanthrene (blue, 1.0×10^{-3} mmol/mL) measured at: A) 290–400 nm, B) 315–400 nm.

Furthermore, the occurrence of potential charge-transfer-complexes (which may also be active photocatalysts) between 4-cyanopyridine, laudanosine and phenanthrene was investigated by comparing the absorption spectra of mixtures of these reactants with the absorption spectra of the pure compounds (Figure S4).

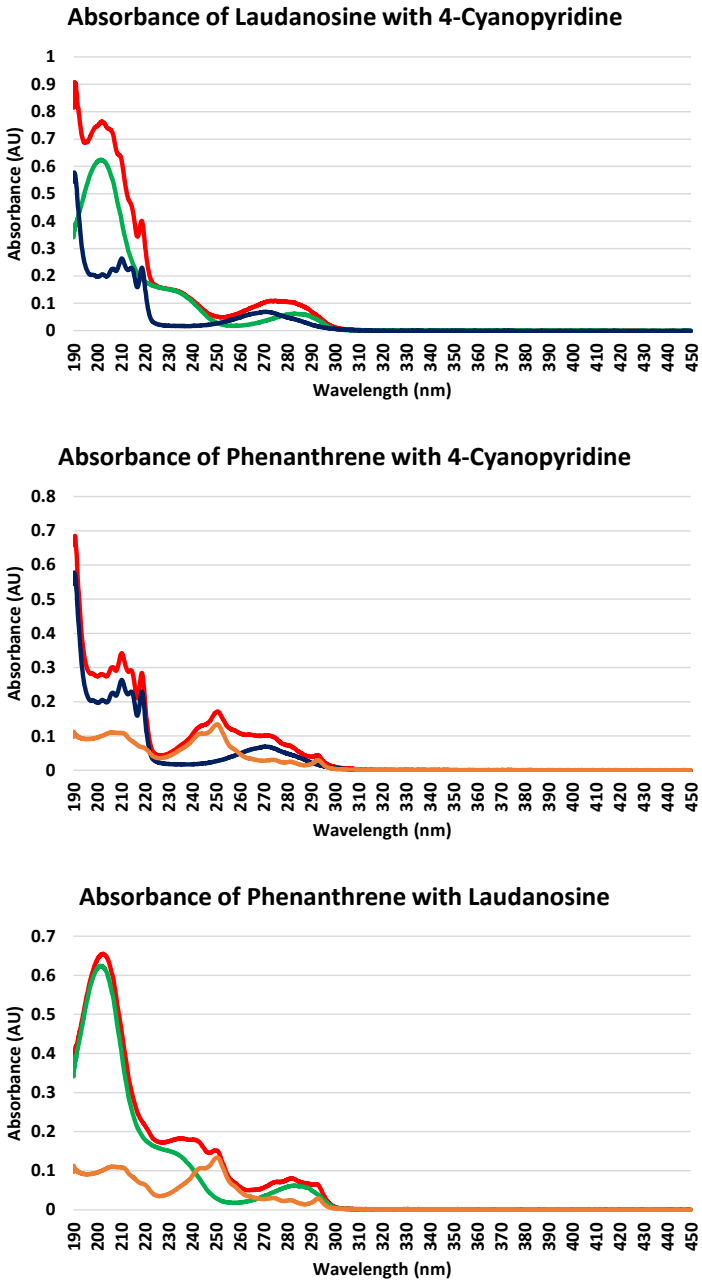


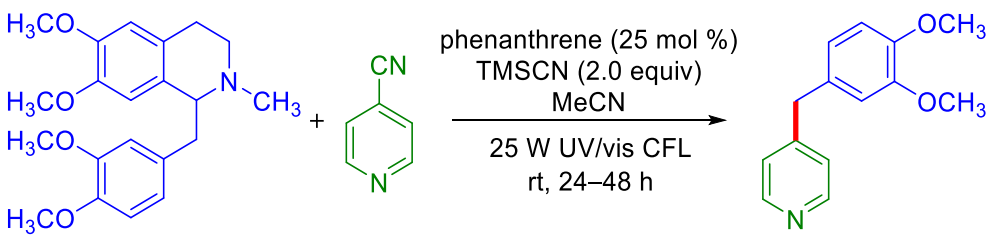
Figure S4: Exclusion of a charge-transfer-complex as potential photocatalyst based on absorption spectra measured for laudanosine (green, 1.0 equiv, 1.0×10^{-5} mol/L), 4-cyanopyridine (blue, 3.0 equiv, 3.0×10^{-5} mol/L), phenanthrene (orange, 0.25 equiv, 0.25×10^{-5} mol/L) and mixtures thereof (red).

In every case, the absorption spectrum obtained for the mixture of two components (red) proved to have no new maxima in comparison to the absorption spectra measured for the single components (green, blue, orange). This is in line with theoretical expectations, as the absorption spectrum of a mixture of chromophores is supposed to be a combination of the absorption of its components if no further interactions (e.g. formation of charge-transfer complexes) occur. In all cases, the absorption of single compounds and mixtures was measured using the same stoichiometric ratios as applied in the general procedure (section V.2).

IV.2 Control Experiments

The control experiments summarized in Table S10 give insight into the designed transition metal-free C–C-bond metathesis.

Table S10: Control experiments for the alkylation of (hetero)aromatic nitriles in a transition metal-free C–C-bond metathesis using different UV-lamps.



3a (1.0 equiv) **1a** (3.0 equiv) **8a**

Entry	Conditions	Light source	Irradiation time (h)	8a (%)
1	standard	UV/vis CFL	24	64
2	no phenanthrene	UV/vis CFL	24	50
3	standard	UV/vis CFL	48	63
4	no phenanthrene	UV/vis CFL	48	49
5	standard	UV-A lamp	24	54
6	no phenanthrene	UV-A lamp	24	10
7	no TMSCN	UV/vis CFL	24	45
8	no phenanthrene and no TMSCN	UV/vis CFL	24	36
9	exclusion of light	none	24	0

Procedure: The reactions were performed according to the general procedure for screening reactions with phenanthrene (see section III.1) using different light sources. One equivalent corresponds to 160 µmol. Where indicated, the reactions were performed in the absence of phenanthrene and/or TMSCN or under exclusion of light. A specification of the light sources is provided in section II. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

As expected, the unchanged starting materials were recovered after stirring the reaction mixture for 24 h in the dark (entry 9). Thus, the reaction is entirely light-induced.

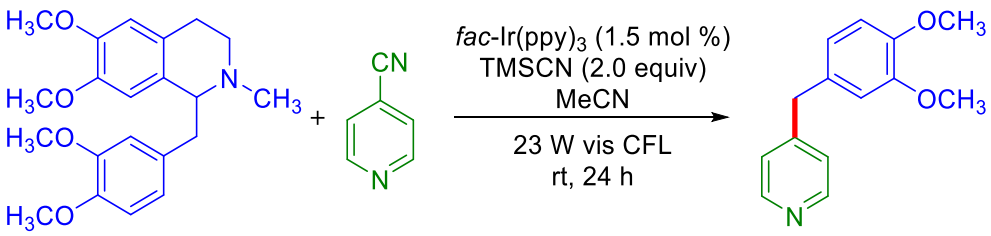
Furthermore, the control experiments highlight that the addition of phenanthrene results in improved yields (entries 1–6). Similar findings have previously been reported for light-induced *ipso*-substitutions.[7] It is noteworthy that phenanthrene does not simply accelerate the reaction but rather improves the overall yield, regardless of the reaction time (entries 1–4). To prove that the beneficial effect of phenanthrene is indeed attributed to light-induced SET processes mediated by this arene, the model reaction of 4-cyanopyridine (**1a**) with (±)-laudanosine (**3a**) was performed under irradiation with a 25 W energy-saving UV-A lamp (λ_{max} = 368 nm, see section II). Given the absorption spectra of 4-cyanopyridine (**1a**) and phenanthrene (see Figures S2 and S3), UV-A light should easily excite phenanthrene while leaving the aromatic nitrile largely unaffected. Thus, if excited phenanthrene was to increase the yield of this *ipso*-substitution reaction by means of light-induced SET processes, its beneficial effect should be much more pronounced under irradiation with UV-A light. Indeed, the addition of phenanthrene led to a tremendously increased yield using the UV-A spotlight (entries 5 and 6) while this effect was much smaller when the usual 25 W UV/vis CFL bulb (high UV-B output, see section II) was utilized (entries 1–4). As stated above, this indicates that phenanthrene-mediated SET processes do indeed merge with the nitrile's own redox reactions.

The control experiments also show the beneficial effect of TMSCN on the reaction outcome (entries 1 and 7 as well as Table S4). If this effect was attributed to the coordination of the pyridine's nitrogen to the Lewis-acidic TMS group, the addition of TMSCN should lead to a shift of the aromatic nitrile's absorption maxima, which was not observed (see section IV.1). Therefore, we speculate that the favorable impact of TMSCN is solely based on its role as a source of cyanide anions which help to trap the intermediate iminium ion **5a** and to stabilize the kinetically labile aminonitrile **9a** in solution.[8] This compound decomposes on silica and cannot be isolated from the irradiated reaction mixture. However, its yield can be determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction. Using 1,4-bis(trimethylsilyl)benzene as internal standard, the yield of *α*-aminonitrile **9a** was calculated to be 65% in the presence of TMSCN (conditions as in entry 1 in Table S10) and only 39% in the absence of an additional cyanide source (conditions as in entry 7 in Table S10). This indicates that the beneficial effect of TMSCN on the double C–C-bond cleavage presented

herein is indeed attributed to the additional cyanide trapping and stabilizing the intermediate iminium ion **5a**.

Table S11 summarizes control experiments performed concerning the visible light-induced C–C-bond metathesis using *fac*-Ir(ppy)$_3$ as photoredox catalyst.

Table S11: Control experiments for the alkylation of (hetero)aromatic nitriles in a visible light-induced C–C-bond metathesis.



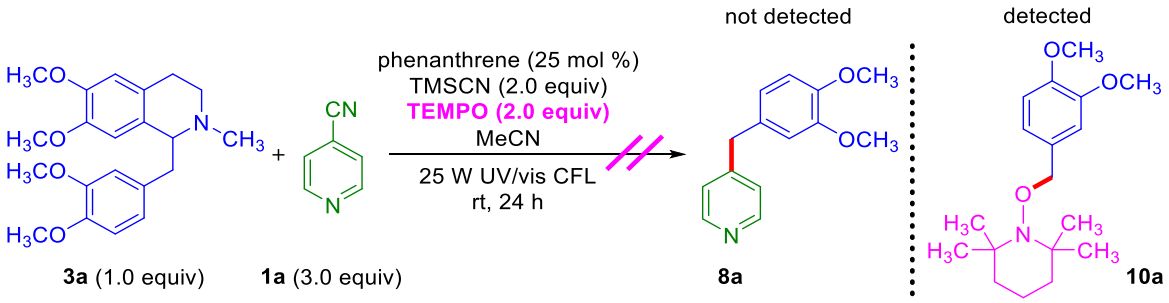
3a (2.0 equiv) **1a** (1.0 equiv) **8a**

Entry	Conditions	8a (%)
1	standard	51
2	no *fac*-Ir(ppy)$_3$	traces
3	exclusion of light	0

Procedure: The reactions were performed according to the general procedure for screening reactions with *fac*-Ir(ppy)$_3$ (see section III.2). One equivalent corresponds to 160 µmol. If indicated, the reactions were performed in the absence of *fac*-Ir(ppy)$_3$ or under exclusion of light. Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard.

The formation of traces of **8a** upon irradiation of the starting materials in the absence of *fac*-Ir(ppy)$_3$ is probably attributed to some minor UV-output of the household CFL bulb (entry 2). Again, no product was detected after stirring the reaction mixture in the dark (entry 3). Thus, as stated above, the C–C-bond metathesis reported herein is indeed light-induced.

To provide evidence for a homolytic C–C-bond cleavage, 4-cyanopyridine (**1a**) was reacted with (±)-laudanosine (**3a**) under optimized conditions, but in the presence of 2.0 equivalents of TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) as a radical scavenger (Scheme S1). In this case, no *ipso*-substitution product **8a** could be detected and adduct **10a** was identified instead (HPLC-MS).

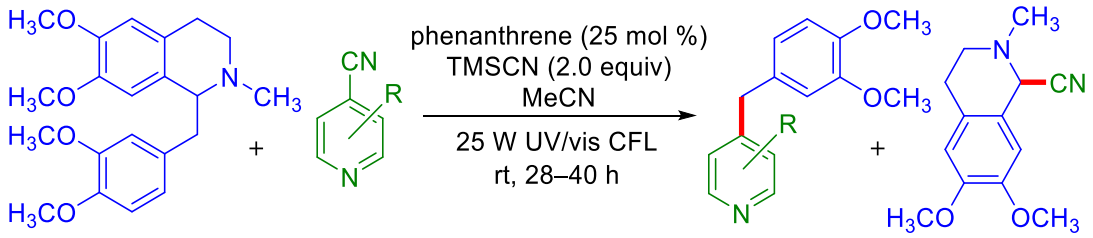


Scheme S1: Quenching of the presented *ipso*-substitution by TEMPO. The reaction was performed as described for entry 1 in Table S10, but in the presence of TEMPO (320 µmol, 2.0 equiv).

IV.3 Fate of the Iminium Ion – Formation of α-Aminonitrile 9a

After fragmentation of the formed amine radical cation **4a** via homolytic cleavage of a C(sp^3)–C(sp^3)-σ-bond, iminium ion **5a** is formed which is trapped by cyanide anions to form the corresponding α-aminonitrile **9a** (see main manuscript, Scheme 2).[8] To complete this mechanistic discussion, Table S12 summarizes the yields of α-aminonitrile **9a** determined for exemplary irradiations on a preparative scale (see main paper, Scheme 3).

Table S12: Yields of α-aminonitrile **9a** calculated for exemplary irradiations on a preparative scale (see main manuscript, Scheme 3).



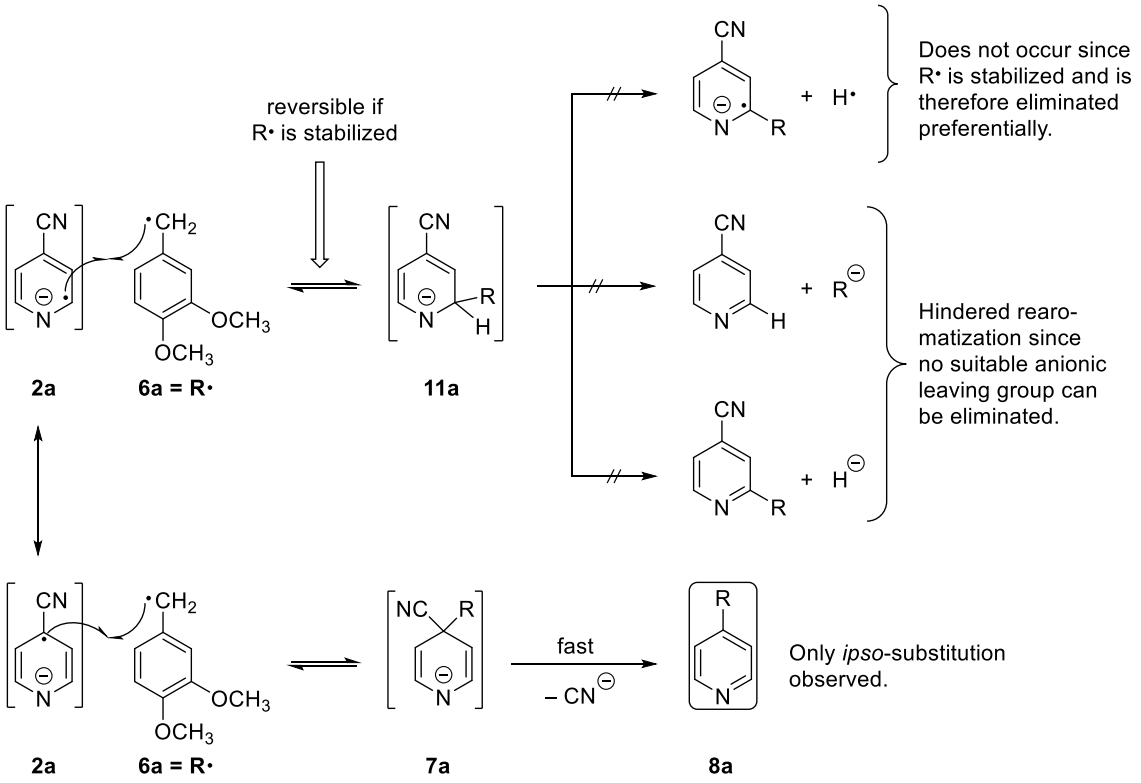
Compound	8 (%)[a]	9a (%)[b]
8a	64	79
8a[c]	66	84
8k	71	54
8l	63	72
8n	62	57
8o	43	63
8p	28	68
8q	27	59
8r	34	48
8s	40	39

Procedure: The reactions were performed according to the general procedure for irradiations on a preparative scale (see section VI.2). [a]Isolated yields. [b]Yields were determined by ^{1}H-NMR spectroscopy of the reaction mixture after extraction using 1,4-bis(trimethylsilyl)benzene as internal standard. [c]Irradiation with sunlight.

IV.4 Regioselectivity and formation of by-products

The C–C-bond metathesis presented herein relies on the selective combination of the aromatic nitriles' persistent radical anions **2** with transient benzylic radicals **6**. The predominant cross coupling of these radicals may be explained by the so called persistent radical effect which has been reviewed in detail.[9]

Given that the unpaired electron density is delocalized in the radical anions **2**, the attack by radicals **6** might occur at multiple sites. Nonetheless, only coupling adjacent to the cyano-substituent proceeding through an *ipso*-substitution pathway is observed. It is known that the radical addition to (hetero)aromatics can be reversible if well-stabilized radicals are used and if the subsequent rearomatization to form the alkylated products is hindered or slow.[10] This probably indicates that the attack of stabilized benzylic radicals such as **6a** onto cyanoarene-derived radical anions such as **2a** occurs in a reversible fashion, and therefore, **6a** is eliminated from intermediate **11a** in case of a hindered subsequent rearomatization (Scheme S2, top). However, if elimination of the cyanide leaving group enables rapid rearomatization of intermediate **7a**, radical combination will ultimately lead to alkylated aromatics such as **8a** (Scheme S2, bottom).



Scheme 2: Putative mechanistic explanation for the observed regioselectivity of the initial radical combination between the persistent radical anion **2a** and the transient radical **6a**.

Since regioisomers were not observed, their potential occurrence cannot be held responsible for the moderate yields obtained for some coupling products **8** (see main manuscript, Scheme 3). Furthermore, all reactions showed full consumption of 1-alkyl-2-methyl-1,2,3,4-tetrahydroisoquinolines **3** indicating that incomplete conversion was not an issue.

Although by-products have generally not been isolated, it might be speculated that in cases where the radical **6** which would be liberated in the course of a C–C-σ-bond-cleavage in radical cation **4** is not thoroughly stabilized, the common scission of the α-C–H-bond leading to the corresponding iminium ion is favored. The latter can subsequently either be trapped by cyanide to form the respective α-quaternary aminonitrile or be deprotonated to the corresponding enamine. Indeed, both of these by-products could be detected (HPLC-MS) in the course of the failed syntheses of compounds **8v** and **8w** (see main manuscript, Scheme 3). Dimerization of benzylic radicals **6** via recombination represents another potential side-reaction which has been observed to some minor extent.

IV.5 Conclusion

The reduction potentials of all substrates and of the excited states of 4-cyanopyridine (**1a**) and phenanthrene are given in the main paper. As stated there, these reduction potentials strongly indicate that all SET processes depicted in our mechanistic proposal (see main manuscript, Scheme 2) are feasible. This is further supported by fluorescence quenching studies clearly showing that the fluorescence of excited phenanthrene is quenched by both, aromatic nitriles[7b] and tertiary amines[11]. Thus, the reported C–C-bond metathesis is most likely operating through an oxidative as well as a reductive quenching cycle. As outlined in the main paper, aromatic nitriles become strong electron acceptors upon excitation with UV-light [$E_{1/2}(^3$[**1a**]*/**2a**) ≈ +1.65 V, calculated for the triplet state according to the literature].[6, 12] Therefore, it must be assumed that an auto-catalyzed reaction sequence based on the direct oxidation of the employed tetrahydroisoquinolines by the excited state of the aromatic nitrile is also involved. This assumption is strongly supported by control experiments (Table S10). The desired *ipso*-substitution product is also obtained in the absence of a photoredox catalyst, albeit with a somewhat lower yield.

Based on UV-VIS-absorption spectra (see section IV.1), no proof could be found for any possible charge-transfer-complexes as potential redox-active photocatalysts. Apart from this,

it was shown that the beneficial effect of TMSCN does not result from its Lewis-acidity (a possible coordination of the pyridine's nitrogen to the TMS group would significantly lower the pyridine's LUMO). Instead, control experiments indicate that TMSCN serves as an additional source of cyanide anions which help trapping the intermediate iminium ions **5a** and to stabilize it in solution (see section IV.2). Our experimental evidence for the formation of α-aminonitrile **9a** (Table S12) is supported by previous work stating the capacity of cyanide anions to easily trap the iminium ions **5a** to form α-aminonitrile **9a**.[8]

The control experiments outlaid above (see section IV.2) provide additional evidence for the reaction to proceed through light-induced SET processes with benzylic radicals **6a** as key intermediates. Using TEMPO as radical scavenger completely prevented the formation of product **8a** and the expected recombination product **10a** was detected instead (Scheme S1).

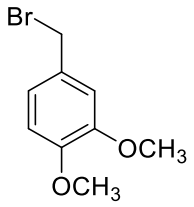
Taking all these experimental details into consideration, the putative mechanism can be envisioned as outlined in Scheme 2 of the main manuscript: Excited phenanthrene readily reduces 4-cyanopyridine (**1a**) to the corresponding radical anion **2a** and is thereby oxidized to the phenanthrene radical cation. The latter easily abstracts an electron from tetrahydroisoquinoline **3a** which leads to the regeneration of phenanthrene and to the formation of amine radical cation **4a**. Alternatively excited phenanthrene oxidizes tetrahydroisoquinoline **3a** providing amine radical cation **4a** and the phenanthrene radical anion. Subsequent reduction of 4-cyanopyridine (**1a**) then furnishes radical anion **2a** and phenanthrene. Furthermore, amine radical cation **4a** can be formed via direct oxidation by excited 4-cyanopyridine (**1a**) with concomitant generation of radical anion **2a**.

In each case, the formed amine radical cation **4a** undergoes homolytic cleavage of a C(sp^3)–C(sp^3)-σ-bond liberating iminium ion **5a** and benzylic radical **6a**. This represents an unprecedented reaction mode, because normally tertiary amine radical cations such as **4a** tend to be rapidly transformed to the corresponding iminium ions via α-H-abstraction or via α-H-deprotonation with subsequent one-electron oxidation.[13] The remaining steps comprising the combination of the transient benzylic radical **6a** with the nitrile's persistent radical anion **2a** to form the anionic intermediate **7a** as well as the subsequent elimination of cyanide to afford the final product **8a**, are widely accepted based on previous research on SET-induced *ipso*-substitutions of (hetero)aromatic nitriles.[4a, 7b, 7c, 9, 14]

V. Experimental Procedures & Compound Characterization

V.1 Preparation of 1-alkyl-2-methyl-1,2,3,4-tetrahydroisoquinolines

1-Cyano-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**9a**), which was used as building block for the preparation of all tetrahydroisoquinolines, was prepared in three steps (without chromatographic workup) from homoveratrylamine according to a procedure previously reported by our group.[15] 3,4-Dihydroisoquinoline was prepared as previously described[16] and subsequently transformed to the 2-methyl-3,4-dihydroisoquinolin-2-ium iodide following a literature procedure.[17] 2-Methyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (**9b**) was synthesized by adopting a procedure published by our group.[15] Unless stated otherwise, all alkyl bromides employed for the synthesis of 1-alkyl-tetrahydroisoquinolines were obtained from commercial suppliers and used without prior purification. Exceptions are listed below, followed by the general alkylation protocol.



4-(Bromomethyl)-1,2-dimethoxybenzene. This compound was prepared using a modified procedure by Oeveren et al.[18] Under an argon atmosphere, phosphorus tribromide (2.23 mL, 6.44 g, 23.8 mmol, 0.40 equiv.) was added slowly to an ice-cold solution of (3,4-dimethoxyphenyl)methanol (10.0 g, 59.5 mmol, 1.00 equiv.) in dry diethyl ether (100 mL). After stirring for 1 h at 0 °C and for 4 h at room temperature, the reaction mixture was poured onto crushed ice (100 g). The phases were separated and the aqueous layer was extracted with diethyl ether (2 x 100 mL). The combined organic phases were washed with ice-cold water (150 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure to afford the title compound (13.05 g, 56.5 mmol, 95%) as a colorless solid.

Mp.: 52–54 °C (Lit.[19]: 52–53 °C).

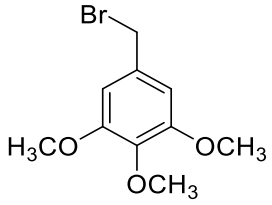
R_f: 0.35 (SiO_2, ^{c}Hex/EtOAc 7:1).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 6.94 (dd, *J* = 8.2, 2.1 Hz, 1H, H-5), 6.91 (d, *J* = 2.1 Hz, 1H, H-3), 6.80 (d, *J* = 8.2 Hz, 1H, H-6), 4.49 (s, 2H, CH_2Br), 3.89 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 149.3 & 149.2 (C-1, C-2), 130.3 (C-4), 121.6 (C-5), 112.1 (C-3), 111.1 (C-6), 56.0 (2C, 2 × OCH_3), 34.5 (CH_2Br).

IR: $\tilde{\nu}$ [cm^{-1}] = 2958, 2936, 2835, 1515, 1463, 1262, 1245, 1212, 1159, 1142.

The analytical data are consistent with those reported in the literature.[19]



5-(Bromomethyl)-1,2,3-trimethoxybenzene. This compound was prepared as described for 4-(brommethyl)-1,2-dimethoxybenzene using phosphorus tribromide (2.71 g, 10.0 mmol, 0.40 equiv.) as well as (3,4,5-trimethoxyphenyl)methanol (4.96 g, 25.0 mmol, 1.00 equiv.) and the respective amounts of solvents. The title compound (6.15 g, 23.7 mmol, 95%) was obtained as a colorless solid.

Mp.: 71.0–72.5 °C, Lit.[20]: 72.3–73.4 °C.

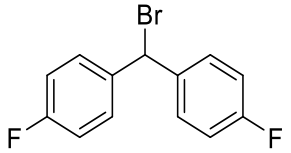
R_f: 0.51 (SiO_2, ^{c}Hex/EtOAc 3:1).

^{1}H-NMR (400 MHz, $CDCl_3$): δ/ppm = 6.61 (s, 2H, H-4, H-6), 4.45 (s, 2H, CH_2Br), 3.86 (s, 6H, C^1-OCH_3, C^3-OCH_3), 3.83 (s, 3H, C^2-OCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 153.4 (2C, C-1, C-3), 138.2 (C-2), 133.3 (C-5), 106.2 (2C, C-4, C-6), 60.9 (C^2-O*C*H_3), 56.2 (2C, C^1-O*C*H_3, C^3-O*C*H_3), 34.4 (CH_2Br).

IR: $\tilde{\nu}$ [cm^{-1}] = 2962, 2939, 2838, 1591, 1506, 1460, 1421, 1335, 1242, 1153.

The analytical data are consistent with those reported in the literature.[20]



4,4'-(Bromomethylene)bis(fluorobenzene). This compound was prepared using a modified procedure by Brown et al.[21] Under an argon atmosphere, acetyl bromide (3.73 mL, 6.15 g, 5.00 mmol, 5.00 equiv.) was added slowly to a solution of bis(4-fluorophenyl)methanol (2.20 g, 10.0 mmol, 1.00 equiv.) in dry benzene (40 mL). After stirring for 18 h at room temperature, diethyl ether (150 mL) and an ice-cold, saturated, aqueous solution of $NaHCO_3$ (75 mL) were added. The phases were separated and the organic layer was washed with a

cold, saturated, aqueous solution of $NaHCO_3$ (2 x 75 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure to afford the title compound (2.73 g, 9.64 mmol, 96%) as a pale yellow oil.

R_f: 0.73 (SiO_2, ^{c}Hex/EtOAc 6:1).

^{1}H-NMR (300 MHz, $CDCl_3$): δ/ppm = 7.48–7.37 (m, 4H, H-3, H-5, H-3', H-5'), 7.09–6.98 (m, 4H, H-2, H-6, H-2', H-6'), 6.27 (s, 1H, C*H*BrPh_2).

^{19}F-NMR (376.5 MHz, $CDCl_3$): δ/ppm = –114.57 (tt, *J* = 8.3, 5.2 Hz, 2F, C^1-F, $C^{1'}$-F).

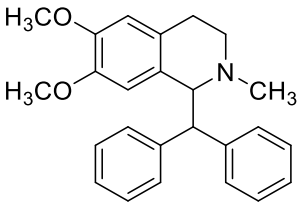
^{13}C-NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): δ/ppm = 162.4 (d, *J* = 248.2 Hz, 2C, C-1, C-1'), 137.0 (d, *J* = 3.3 Hz, 2C, C-4, C-4'), 130.3 (d, *J* = 8.3 Hz, 4C, C-3, C-5, C-3', C-5'), 115.7 (d, *J* = 21.5 Hz, 4C, C-2, C-6, C-2', C-6'), 53.6 (*C*HBrPh_2).

IR: $\tilde{\nu}$ [cm^{-1}] = 1603, 1505, 1411, 1229, 1157, 1099, 1015, 855, 786, 727.

The analytical data are consistent with those reported in the literature.[22]

General Procedure for the synthesis of 1-alkyl-2-methyl-1,2,3,4-tetrahydroisoquinolines:

Under an argon atmosphere, a solution of KHMDS (1.197 g, 6.00 mmol, 1.50 equiv.) in dry THF (20 mL) was added dropwise to a stirred solution of 1-cyano-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**9a**, 929 mg, 4.00 mmol, 1.00 equiv) in dry THF (45 mL) at 0 °C. After 10 min, a solution of the required bromide (4.40 mmol, 1.10 equiv.) in dry THF (15 mL) was added dropwise and the reaction mixture was stirred for 1 h at 0 °C and for 4 h at room temperature. Ethanol (21 mL), $NaCNBH_3$ (880 mg, 14.0 mmol, 3.50 eq) as well as acetic acid (1.26 mL, 22.0 mmol, 5.50 equiv.) were added and the mixture was stirred at ambient temperature for 15 h. After careful addition of a saturated, aqueous solution of $NaHCO_3$ (150 mL), the mixture was extracted with dichloromethane (3 x 200 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure. Flash column chromatography on silica using eluent mixtures composed of ^{c}Hex, EtOAc and Et_2NH (columns were packed with pure cyclohexane) afforded the desired product. **Please note:** The quality of KHMDS is essential for the outcome of the reaction. The KHMDS employed must be fully soluble in dry THF.



1-Benzhydryl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (3b). This compound was prepared according to the general procedure using bromodiphenylmethane (1.09 g, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:2) afforded the title compound (1.33 g, 3.55 mmol, 89%) as a pale yellow solid. The product is obtained as a mixture of two rotamers (ratio ≈ 1:1) which can be distinguished in the ^{13}C-NMR spectrum. Due to overlapping signals in the ^{1}H-NMR spectrum, a separate assignment for each rotamer is not feasible.

Mp.: 149.0–151.0 °C, Lit.[23]: 153.0–154.0 °C.

R_f: 0.32 (^{c}Hex/EtOAc/Et_2NH 20:1:1).

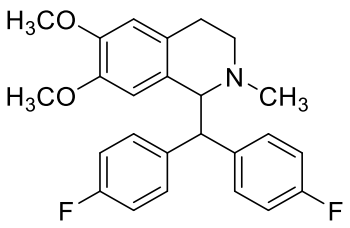
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.40–7.29 (m, 4H, 4 × H_{Ph}), 7.23–7.09 (m, 4H, 4 × H_{Ph}), 7.08–7.04 (m, 2H, 2 × H_{Ph}), 6.55 (s, 1H, H-5), 5.54 (s, 1H, H-8), 4.24–4.13 (m, 2H, H-1, $CHPh_2$), 3.84 (s, 3H, C^6-OCH_3), 3.26 (s, 3H, C^7-OCH_3), 3.30–3.19 (m, 1H, H_a-3), 2.94–2.82 (m, 1H, H_a-4), 2.74–2.66 (m, 1H, H_b-3), 2.47 (s, 3H, NCH_3), 2.46–2.39 (m, 1H, H_b-4).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 147.3 (C-6), 145.4 (C-7), 143.5 (2C, C-1', C-1'', one rotamer), 143.4 (2C, C-1', C-1'', other rotamer), 129.8 (4C, C-2', C-6', C-2'', C-6'', one rotamer), 128.5 (4C, C-2', C-6', C-2'', C-6'', other rotamer), 128.32 (4C, C-3', C-5', C-3'', C-5'', one rotamer), 128.30 (4C, C-3', C-5', C-3'', C-5'', other rotamer), 127.2 (C-8a), 126.3 (2C, C-4', C-4'', one rotamer), 126.13 (2C, C-4', C-4'', other rotamer), 126.11 (C-4a), 112.7 (C-8), 111.0 (C-5), 66.0 (C-1), 58.5 ($CHPh_2$), 55.7 (C^6-O*C*H_3), 55.2 (C^7-O*C*H_3), 44.0 (C-3), 41.9 (NCH_3), 22.4 (C-4).

IR: $\bar{\nu}$ [cm^{-1}] = 2935, 2910, 2834, 1514, 1465, 1451, 1256, 1228, 1122, 1102.

ESI-MS: m/z = 374.3 (100%, $[M+H]^+$, calc. 374.2).

The analytical data are consistent with those reported in the literature.[23]



1-(Bis(4-fluorophenyl)methyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (3c). This compound was prepared according to the general procedure using 4,4'-

(bromomethylene)bis(fluorobenzene) (1.25 g, 4.42 mmol, 1.11 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:2) afforded the title compound (1.37 g, 3.35 mmol, 84%) as a pale yellow solid. The product is obtained as a mixture of rotamers (ratio ≈ 1:1) which differ only in selected signals in the ^{1}H-NMR and ^{13}C-NMR spectrum.

Mp.: 146.0–147.0 °C.

R_f: 0.27 (^{c}Hex/EtOAc/Et_2NH 4:0.2:0.2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.31–7.24 (m, 4H, H-2', H-6', H-2'', H-6'', one rotamer), 7.05–6.93 (m, 8H, H-2', H-6', H-2'', H-6'', other rotamer & H-3', H-5', H-3'', H-5'', one rotamer), 6.92–6.84 (m, 4H, H-3', H-5', H-3'', H-5'', other rotamer), 6.54 (s, 2H, H-5, both rotamers), 5.53 (s, 2H, H-8, both rotamers), 4.19 (d, *J* = 9.8 Hz, 2H, $CHAr_2$, both rotamers), 4.04 (d, *J* = 9.8 Hz, 2H, H-1, both rotamers), 3.84 (s, 6H, C^6-OCH_3, both rotamers), 3.34 (s, 6H, C^7-OCH_3, both rotamers), 3.17 (ddd, *J* = 13.8, 11.1, 5.8 Hz, 2H, H_a-3, both rotamers), 2.85 (ddd, *J* = 17.3, 11.1. 6.7 Hz, 2H, H_a-4, both rotamers), 2.73–2.64 (m, 2H, H_b-3, both rotamers), 2.44 (s, 6H, NCH_3, both rotamers), 2.46–2.36 (m, 2H, H_b-4, both rotamers).

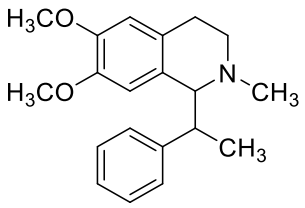
^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 161.6 (d, *J* = 245.2 Hz, 2C, C-4', C-4'', one rotamer), 161.4 (d, *J* = 244.4 Hz, 2C, C-4', C-4'', other rotamer), 147.5 (2C, C-6, both rotamers), 145.7 (2C, C-7, both rotamers), 139.1 (d, *J* = 3.1 Hz, 2C, C-1', C-1'', one rotamer), 138.8 (d, *J* = 3.2 Hz, 2C, C-1', C-1'', other rotamer), 131.1 (d, *J* = 7.9 Hz, 4C, C-2', C-6', C-2'', C-6'', one rotamer), 129.8 (d, *J* = 7.5 Hz, 4C, C-2', C-6', C-2'', C-6'', other rotamer), 126.6 (2C, C-8a, both rotamers), 126.3 (2C, C-5a, both rotamers), 115.2 (d, *J* = 21.2 Hz, 4C, C-3', C-5', C-3'', C-5'', one rotamer), 115.1 (d, *J* = 20.9 Hz, 4C, C-3', C-5', C-3'', C-5'', other rotamer), 112.6 (2C, C-8, both rotamers), 111.2 (2C, C-5, both rotamers), 66.4 (2C, C-1, both rotamers), 56.8 (2C, *C*HAr_2, both rotamers), 55.8 (2C, C^6-O*C*H_3, both rotamers), 55.3 (2C, C^7-O*C*H_3, both rotamers), 44.2 (2C, C-3, both rotamers), 42.0 (2C, NCH_3, both rotamers), 22.4 (2C, C-4, both rotamers).

^{19}F-NMR (376.5 MHz, $CDCl_3$): δ/ppm = –117.96 (tt, *J* = 8.4, 5.4 Hz, 2F, $C^{4'}$-F, $C^{4''}$-F, one rotamer), –118.26 (tt, *J* = 8.8, 5.3 Hz, 2F, $C^{4'}$-F, $C^{4''}$-F, other rotamer).

IR: $\tilde{\nu}$ [cm^{-1}] = 2936, 2910, 1603, 1507, 1465, 1255, 1223, 1158, 1121, 1101.

ESI-MS: m/z = 410.3 (100%, $[M+H]^+$, calc. 410.2).

ESI-HRMS: calc. for $[C_{25}H_{26}NO_2F_2]$: m/z = 410.1932, found: m/z = 410.1938.



6,7-Dimethoxy-2-methyl-1-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (3d). This compound was prepared according to the general procedure using (1-bromomethyl)benzene (814

mg, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:2) afforded the title compound (1.14 g, 3.65 mmol, 91%) as a yellow oil. The title compound is obtained as a mixture of diastereomers (ratio **A**:**B** ≈ 1.13:1.00).

R_f: 0.26 (^{c}Hex/EtOAc/Et_2NH 60:1:2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): major diastereomer **A**, δ/ppm = 7.34–7.28 (m, 2H, H-3', H-5'), 7.27–7.14 (m, 3H, H-2', H-4', H-6'), 6.55 (s, 1H, H-5), 5.84 (s, 1H, H-8), 3.84 (s, 3H, C^6-OCH_3), 3.70 (d, *J* = 3.8 Hz, 1H, H-1), 3.48 (s, 3H, C^7-OCH_3), 3.33–3.25 (m, 1H, PhC*H*CH_3), 3.03 (dt, *J* = 11.2, 4.6 Hz, 1H, H_a-3), 2.94–2.70 (m, 1H, H_a-4), 2.61 (s, 3H, NCH_3), 2.60–2.41 (m, 2H, H_b-3, H_b-4), 1.09 (d, *J* = 7.0 Hz, 3H, PhCHC*H*$_3$); minor diastereomer **B**, δ/ppm = 7.27–7.14 (m, 3H, H-3', H-4', H-5'), 7.07–7.03 (m, 2H, H-2', H-6'), 6.51 (s, 1H, H-5), 5.53 (s, 1H, H-8), 3.81 (s, 3H, C^6-OCH_3), 3.40 (d, *J* = 9.1 Hz, 1H, H-1), 3.31 (s, 3H, C^7-OCH_3), 3.33–3.25 (m, 1H, H_a-3), 2.94–2.70 (m, 3H, PhC*H*CH_3, H_b-3, H_a-4), 2.60–2.41 (m, 1H, H_b-4), 2.40 (s, 3H, NC*H*$_3$), 1.41 (d, *J* = 7.0 Hz, 3H, PhCHC*H*$_3$).

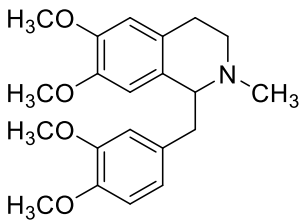
^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): major diastereomer **A**, δ/ppm = 147.0 (C-6), 146.0 (C-7), 145.1 (C-1'), 128.7 (C-4a), 128.5 (2C, C-2', C-6'), 128.2 (2C, C-3', C-5'), 127.3 (C-8a), 126.0 (C-4'), 110.9 (C-8), 110.7 (C-5), 70.9 (C-1), 55.8 (C^6-O*C*H_3), 55.3 (C^7-O*C*H_3), 50.7 (C-3), 44.8 (NCH_3), 43.8 (Ph*C*HCH_3), 28.4 (C-4), 14.4 (PhCH*C*H_3); minor diastereomer **B**, δ/ppm = 147.0 (C-6), 145.9 (C-1'), 145.6 (C-7), 128.9 (2C, C-2', C-6'), 128.2 (2C, C-3', C-5'), 128.1 (C-8a), 126.2 (C-4'), 125.8 (C-4a), 112.4 (C-8), 110.8 (C-5), 69.3 (C-1), 55.7 (C^6-O*C*H_3), 55.2 (C^7-O*C*H_3), 46.8 (Ph*C*HCH_3), 45.3 (C-3), 42.7 (NCH_3), 23.0 (C-4), 18.8 (PhCH*C*H_3).

IR: $\tilde{\nu}$ [cm^{-1}] = 2934, 2904, 2833, 2792, 1514, 1451, 1259, 1226, 1195, 1125.

ESI-MS: m/z = 312.2 (100%, $[M+H]^+$, calc. 312.2).

ESI-HRMS: calc. for [$C_{20}H_{26}NO_2$]: m/z = 312.1964, found: m/z = 312.1963.

The title compound has previously been described in literature, but has not yet been characterized by NMR spectroscopy or mass spectrometry.[24]



1-(3,4-Dimethoxybenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline, (±)-laudanosine (3a). Under an argon atmosphere, a solution of KHMDS (3.59 g, 18.0 mmol, 1.20 equiv.) in dry THF (40 mL) was added to a solution of 1-cyano-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**9a**, 3.48 g, 15.0 mmol, 1.00 Äquiv.) in dry THF (80 mL) at 0 °C.

After 15 min, a solution of 4-(bromomethyl)-1,2-dimethoxybenzene (4.16 g, 18.0 mmol, 1.20 equiv.) in dry THF (60 mL) was added and the reaction mixture was stirred for 1 h at 0 °C and for 5 h at room temperature. Ethanol (40 mL), $NaCNBH_3$ (3.30 g, 52.5 mmol, 3.50 equiv.) and acetic acid (4.71 mL, 4.95 g, 82.5 mmol, 5.50 equiv.) were added and the mixture was stirred at room temperature for 16 h. After careful addition of an ice-cold, saturated, aqueous solution of $NaHCO_3$ (200 mL), the mixture was extracted with dichloromethane (3 x 300 mL) and the combined organic layers were dried over Na_2SO_4. The solvent was removed under reduced pressure and the crude product was purified via flash chromatography on silica (column packed with pure ^{c}Hex, eluent: ^{c}Hex/EtOAc/Et_2NH 60:10:2 → 60:15:2) furnishing the title compound (4.72 g, 13.2 mmol, 88%) as a colorless solid.

Mp.: 113.0–115.0 °C (Lit.[15]: 114–116 °C).

R_f: 0.25 (SiO_2, ^{c}Hex/EtOAc/Et_2NH 30:10:2).

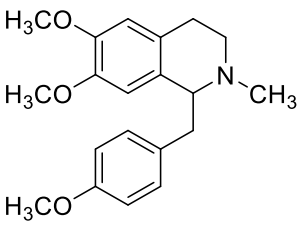
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 6.75 (d, *J* = 8.1 Hz, 1H, H-5'), 6.63 (dd, *J* = 8.1, 2.0 Hz, 1H, H-6'), 6.59 (d, *J* = 2.0 Hz, 1H, H-2'), 6.54 (s, 1H, H-5), 6.05 (s, 1H, H-8), 3.83 & 3.82 & 3.77 (3s, 3 × 3H, C^6-OCH_3, $C^{3'}$-OCH_3, $C^{4'}$-OCH_3), 3.67 (dd, *J* = 7.7, 4.9 Hz, 1H, H-1), 3.56 (s, 3H, C^7-OCH_3), 3.20–3.08 (m, 2H, H_a-3, C*H*$_a$H$_b$Ar), 2.86–2.70 (m, 3H, H_b-3, H_a-4, CH$_a$*H*$_b$Ar), 2.61–2.50 (m, 1H, H_b-4), 2.53 (s, 3H, NCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 148.6 (C-3'), 147.4 & 147.3 (C-6, C-4'), 146.4 (C-7), 132.6 (C-1'), 129.4 (C-8a), 126.2 (C-4a), 121.9 (C-6'), 113.1 (C-2'), 111.3 (C-5), 111.2 (C-8), 111.1 (C-5'), 65.0 (C-1), 56.0 & 55.91 & 55.86 (C^6-O*C*H$_3$, $C^{3'}$-O*C*H$_3$, $C^{4'}$-O*C*H$_3$), 55.7 (C^7-O*C*H$_3$), 47.1 (C-3), 42.8 (NCH_3), 41.0 (CH_2Ar), 25.7 (C-4).

IR: $\tilde{\nu}$ [cm^{-1}] = 2958, 2936, 2835, 1514, 1463, 1262, 1211, 1159, 1142, 1025.

ESI-MS: m/z = 358.2 (100%, $[M+H]^+$, calc. 358.2), 380.2 (5%, $[M+Na]^+$, calc. 380.2).

The analytical data are consistent with those reported in the literature.[15]



6,7-Dimethoxy-1-(4-methoxybenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (3e). This compound was prepared according to the general procedure using 1-(bromomethyl)-4-methoxybenzene (885 mg, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2,

^{c}Hex/EtOAc/Et_2NH 40:2:2) afforded the title compound (1.18 g, 3.60 mmol, 90%) as a yellow oil.

R_f: 0.19 (^{c}Hex/EtOAc/Et_2NH 4:0.2:0.2).

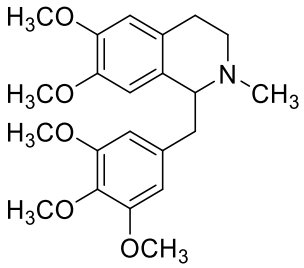
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.04–6.98 (m, 2H, H-2', H-6'), 6.83–6.77 (m, 2H, H-3', H-5'), 6.55 (s, 1H, H-5), 6.00 (s, 1H, H-8), 3.83 (s, 3H, C^6-OCH_3), 3.77 (s, 3H $C^{4'}$-OCH_3), 3.66 (dd, *J* = 7.9, 5.1 Hz, 1H, H-1), 3.55 (s, 3H, C^7-OCH_3), 3.23–3.08 (m, 2H, H_a-3, C*H*$_a$H$_b$Ar), 2.90–2.70 (m, 3H, H_b-3, H_a-4, CH$_a$*H*$_b$Ar), 2.64–2.49 (m, 1H, H_b-4), 2.53 (s, 3H, NCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 158.0 (C-4'), 147.3 (C-6), 146.3 (C-7), 132.1 (C-1'), 130.8 (2C, C-2', C-6'), 129.4 (C-8a), 126.0 (C-4a), 113.6 (2C, C-3', C-5'), 111.2 (C-5), 111.1 (C-8), 65.0 (C-1), 46.9 (C-3), 42.8 (NCH_3), 40.5 (CH_2Ar), 25.6 (C-4).

IR: $\tilde{\nu}$ [cm^{-1}] = 2935, 2834, 2795, 1611, 1511, 1464, 1247, 1227, 1101, 1035.

ESI-MS: m/z = 328.2 (100%, $[M+H]^+$, calc. 328.2).

The analytical data are consistent with those reported in the literature.[25]



6,7-Dimethoxy-2-methyl-1-(3,4,5-trimethoxybenzyl)-1,2,3,4-tetrahydroisoquinoline (3f).

This compound was prepared according to the general procedure using 5-(bromomethyl)-1,2,3-trimethoxybenzene (1.15 g, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:10:2 → 30:10.2) afforded the title compound (1.23 g, 3.16 mmol, 79%) as a yellow oil.

R_f: 0.24 (^{c}Hex/EtOAc/Et_2NH 30:10:2).

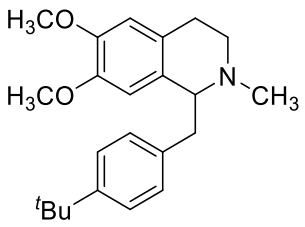
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 6.56 (s, 1H, H-5), 6.30 (s, 2H, H-2', H-6'), 6.03 (s, 1H, H-8), 3.82 (s, 3H, C^6-OCH_3), 3.80 (s, 3H, $C^{4'}$-OCH_3), 3.77 (s, 6H, $C^{3'}$-OCH_3, $C^{5'}$-OCH_3), 3.72–3.67 (m, 1H, H-1), 3.57 (s, 3H, C^7-OCH_3), 3.20–3.10 (m, 2H, H_a-3, C*H*$_a$H$_b$Ar), 2.89–2.69 (m, 3H, H_b-3, H_a-4, CH$_a$*H*$_b$Ar), 2.59 (dt, *J* = 15.8, 4.7 Hz, 1H, H_b-4), 2.54 (s, 3H, NCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 153.0 (2C, C-3', C-5'), 147.4 (C-6), 146.4 (C-7), 136.3 (C-4'), 135.8 (C-1'), 129.2 (C-8a), 126.1 (C-4a), 111.3 (C-5), 111.2 (C-8), 106.8 (2C, C-3', C-5'), 64.9 (C-1), 60.9 ($C^{4'}$-O*C*H$_3$), 56.2 (2C, $C^{3'}$-O*C*H$_3$, $C^{5'}$-O*C*H$_3$), 55.9 (C^6-O*C*H$_3$), 55.6 (C^7-O*C*H$_3$), 47.0 (C-3), 42.8 (NCH_3), 41.8 (*C*H$_a$H$_b$Ar), 25.6 (C-4).

IR: $\tilde{\nu}$ [cm^{-1}] = 2937, 2835, 1589, 1509, 1462, 1421, 1337, 1238, 1229, 1125, 1103, 1013.

ESI-MS: m/z = 388.3 (100%, $[M+H]^+$, calc. 348.2), 410.2 (8%, $[M+Na]^+$, calc. 410.2).

The analytical data are consistent with those reported in the literature.[26]



1-(4-(*tert*-Butyl)benzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (3g).

This compound was prepared according to the general procedure using 1-(bromomethyl)-4-(*tert*-butyl)benzene (1.00 g, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:2) afforded the title compound (1.24 g, 3.51 mmol, 88%) as a yellow oil.

R_f: 0.33 (^{c}Hex/EtOAc/Et_2NH 4:0.2:0.2).

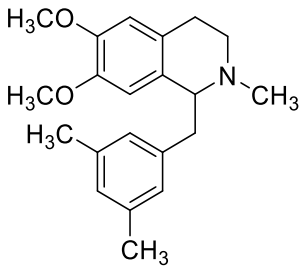
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.32–7.27 (m, 2H, H-3', H-5'), 7.06–7.01 (m, 2H, H-2', H-6'), 6.56 (s, 1H, H-5), 5.84 (s, 1H, H-8), 3.83 (s, 3H, C^6-OCH_3), 3.72 (dd, *J* = 8.8, 4.8 Hz, 1H, H-1), 3.43 (s, 3H, C^7-OCH_3), 3.27–3.17 (m, 2H, H_a-3, C*H*$_a$H$_b$Ar), 2.94–2.76 (m, 2H, H_b-3, H_a-4), 2.73 (dd, *J* = 13.4, 8.8 Hz, 1H, CH_a*H*$_b$Ar), 2.67–2.58 (m, 1H, H_b-4), 2.56 (s, 9H, $C(CH_3)_3$).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 148.8 (C-4'), 147.2 (C-6), 146.0 (C-7), 137.1 (C-1'), 129.6 (2C, C-2', C-6'), 129.3 (C-8a), 125.6 (C-4a), 125.2 (2C, C-3', C-5'), 111.2 (C-8), 111.1 (C-5), 64.9 (C-1), 55.8 (C^6-O*C*H$_3$), 55.3 (C^7-O*C*H$_3$), 46.6 (C-3), 42.7 (NCH_3), 40.6 (CH_2Ar), 34.5 (*C*$(CH_3)_3$), 31.5 (3C, C(*C*H$_3$)$_3$), 25.5 (C-4).

IR: $\tilde{\nu}$ [cm^{-1}] = 2952, 2906, 2866, 2833, 1514, 1464, 1256, 1227, 1140, 1103.

ESI-MS: m/z = 354.3 (100%, $[M+H]^+$, calc. 354.2).

ESI-HRMS: calc. for $[C_{23}H_{32}NO_2]$: m/z = 354.2433, found: m/z = 354.2433.



1-(3,5-Dimethylbenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (3h).

This compound was prepared according to the general procedure using 1-(bromomethyl)-3,5-

dimethylbenzene (876 mg, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 40:2:2) afforded the title compound (1.20 g, 3.68 mmol, 92%) as a yellow oil.

R_f: 0.22 (^{c}Hex/EtOAc/Et_2NH 40:1:1).

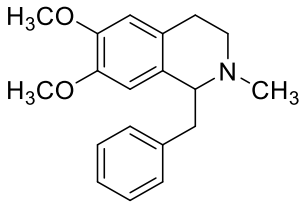
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 6.84 (s, 1H, H-4'), 6.75 (s, 2H, H-2', H-6'), 6.57 (s, 1H, H-5), 5.98 (s, 1H, H-8), 3.84 (s, 3H, C^6-OCH_3), 3.71 (dd, *J* = 8.3, 5.0 Hz, 1H, H-1), 3.52 (s, 3H, C^7-OCH_3), 3.24–3.11 (m, 2H, H_a-3, C*H*$_a$H$_b$Ar), 2.92–2.82 (m, 1H, H_a-4), 2.81–2.73 (m, 1H, H_b-3), 2.73–2.58 (m, 2H, H_b-4, CH$_a$*H*$_b$Ar), 2.55 (s, 3H, NCH_3), 2.27 (s, 6H, $C^{3'}$-C*H*$_3$, $C^{5'}$-C*H*$_3$).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 147.3 (C-6), 146.3 (C-7), 140.2 (C-1'), 137.7 (2C, C-3', C-5'), 129.7 (C-8a), 127.7 (3C, C-2', C-4', C-6'), 125.7 (C-5a), 111.2 (2C, C-5, C-8), 65.0 (C-1), 55.8 (C^6-O*C*H$_3$), 55.4 (C^7-O*C*H$_3$), 46.8 (C-3), 42.8 (NCH_3), 41.3 (*C*H$_2$Ph), 25.6 (C-4), 21.4 (2C, 2 × *C*H$_3$).

IR: $\bar{\nu}$ [cm^{-1}] = 2934, 2833, 2796, 1606, 1514, 1464, 1255, 1227, 1139, 1103.

ESI-MS: m/z = 326.3 (100%, $[M+H]^+$, calc. 326.2).

ESI-HRMS: calc. for [$C_{21}H_{28}NO_2$]: m/z = 326.2120, found: m/z = 326.2114.



1-Benzyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (3i). This compound was prepared according to the general procedure using benzyl bromide (753 mg, 523 µL, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:2) afforded the title compound (1.09 g, 3.67 mmol, 92%) as a yellow oil.

R_f: 0.16 (^{c}Hex/EtOAc/Et_2NH 60:1:2).

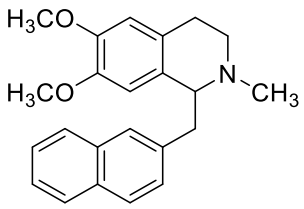
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.29–7.23 (m, 2H, H-3', H-5'), 7.22–7.16 (m, 1H, H-4'), 7.13–7.08 (m, 2H, H-2', H-6'), 6.56 (s, 1H, H-5), 5.94 (s, 1H, H-8), 3.83 (s, 3H, C^6-OCH_3), 3.73 (dd, *J* = 8.1, 5.0 Hz, 1H, H-1), 3.50 (s, 3H, C^7-OCH_3), 3.25–3.15 (m, 2H, H_a-3, C*H*$_a$H$_b$Ph), 2.90–2.73 (m, 3H, H_b-3, H_a-4, CH$_a$*H*$_b$Ph), 2.60 (dt, *J* = 15.9, 4.4 Hz, 1H, H_b-4), 2.54 (s, 3H, NCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 147.3 (C-6), 146.3 (C-7), 140.2 (C-1'), 130.0 (2C, C-2', C-6'), 129.4 (C-8a), 128.3 (2C, C-3', C-5'), 126.0 (C-4'), 125.9 (C-4a), 111.2 (C-5), 111.1 (C-8), 65.0 (C-1), 55.8 (C^6-O*C*H$_3$), 55.5 (C^7-O*C*H$_3$), 46.9 (C-3), 42.8 (NCH_3), 41.3 (CH_2Ph), 25.6 (C-4).

IR: $\bar{\nu}$ [cm^{-1}] = 2934, 2833, 2796, 1514, 1464, 1452, 1256, 1227, 1139, 1103.

ESI-MS: m/z = 298.2 (100%, $[M+H]^+$, calc. 298.2).

The analytical data are consistent with those reported in the literature.[27]



6,7-Dimethoxy-2-methyl-1-(naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (3j).

This compound was prepared according to the general procedure using 2-(bromomethyl)naphthalene (983 mg, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:1 → 60:2:2) afforded the title compound (705 mg, 2.03 mmol, 51%) as a yellow oil.

R_f: 0.14 (^{c}Hex/EtOAc/Et_2NH 60:1:2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.83–7.70 (m, 3H, 3 × $H_{Naphthyl}$), 7.52 (s, 1H, $H_{Naphthyl}$), 7.47–7.38 (m, 2H, 2 × $H_{Naphthyl}$), 7.30 (dd, *J* = 8.4, 1.3 Hz, 1H, $H_{Naphthyl}$), 6.57 (s, 1H, H-5), 5.94 (s, 1H, H-8), 3.86–3.79 (m, 1H, H-1), 3.84 (s, 3H, C^6-OCH_3), 3.37 (dd, *J* = 13.4, 5.1 Hz, 1H, C*H*$_a$H$_b$-Ar), 3.29 (s, 3H, C^7-OCH_3), 3.28–3.19 (m, 1H, H_a-3), 2.98 (dd, *J* = 13.4, 7.9 Hz, 1H, CH$_a$*H*$_b$-Ar), 2.93–2.75 (m, 2H, H_b-3, H_a-4), 2.68–2.54 (m, 1H, H_b-4), 2.57 (s, 3H, NCH_3).

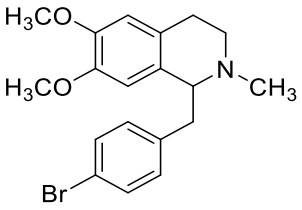
^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 147.3 (C-6), 146.3 (C-7), 137.7 (C-2'), 133.6 ($C_{Naphthyl}$), 132.1 ($C_{Naphthyl}$), 129.4 (C-8a), 128.4 ($CH_{Naphthyl}$), 128.3 ($CH_{Naphthyl}$), 127.7 ($CH_{Naphthyl}$), 127.6 (2C, 2 × $CH_{Naphthyl}$), 126.0 (2C, C-4a, $CH_{Naphthyl}$), 125.3 ($CH_{Naphthyl}$), 111.3 (C-5), 111.1 (C-8), 64.9 (C-1), 55.8 (C^6-O*C*H$_3$), 55.3 (C^7-O*C*H$_3$), 46.9 (C-3), 42.9 (NCH_3), 41.5 (CH_2-Ar), 25.6 (C-4).

IR: $\tilde{\nu}$ [cm^{-1}] = 2934, 2833, 2795, 1510, 1464, 1451, 1256, 1227, 1138, 1102, 1017.

ESI-MS: m/z = 348.3 (100%, $[M+H]^+$, calc. 348.2).

ESI-HRMS: calc. for [$C_{23}H_{26}NO_2$]: m/z = 348.1964, found: m/z = 348.1969.

The analytical data are consistent with those reported in the literature.[23]



1-(4-Bromobenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (3u). This compound was prepared according to the general procedure using 1-bromo-4-(bromomethyl)benzene (1.10 g, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 40:1:1) afforded the title compound (1.49 g, 3.96 mmol, 99%) as a yellow oil.

R_f: 0.15 (^{c}Hex/EtOAc/Et_2NH 40:1:1).

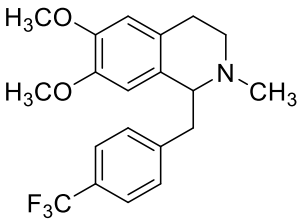
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.38–7.32 (m, 2H, H-3', H-5'), 6.98–6.93 (m, 2H, H-2', H-6'), 6.54 (s, 1H, H-5), 6.06 (s, 1H, H-8), 3.86 (s, 3H, C^6-OCH_3), 3.68 (t, *J* = 6.4 Hz, 1H, H-1), 3.61 (s, 3H, C^7-OCH_3), 3.20–3.05 (m, 2H, H_a-3, C*H*$_a$H$_b$Ar), 2.86–2.69 (m, 3H, H_b-3, H_a-4, CH$_a$*H*$_b$Ar), 2.58–2.47 (m, 1H, H_b-4), 2.50 (s, 3H, NCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 147.4 (C-6), 146.5 (C-7), 139.1 (C-1'), 131.7 (2C, C-3', C-5'), 131.2 (2C, C-2', C-6'), 128.9 (C-8a), 126.4 (C-4a), 119.9 (C-4'), 111.3 (C-5), 110.9 (C-8), 64.7 (C-1), 55.9 (C^6-O*C*H$_3$), 55.7 (C^7-O*C*H$_3$), 47.0 (C-3), 42.8 (NCH_3), 40.7 (CH_2Ar), 25.6 (C-4).

IR: $\tilde{\nu}$ [cm^{-1}] = 2934, 2832, 2793, 1514, 1464, 1256, 1227, 1138, 1103, 1012.

ESI-MS: m/z = 376.3 (100%, $[M+H]^+$, calc. 376.1).

The analytical data are consistent with those reported in the literature.[28]



6,7-Dimethoxy-2-methyl-1-(4-(trifluoromethyl)benzyl)-1,2,3,4-tetrahydroisoquinoline (3v). This compound was prepared according to the general procedure using 1-(bromomethyl)-4-(trifluoromethyl)benzene (1.05 g, 4.40 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 40:1:2 → 40:2:2) afforded the title compound (1.29 g, 3.54 mmol, 89%) as a yellow oil.

R_f: 0.24 (^{c}Hex/EtOAc/Et_2NH 40:2:2).

^{1}H-NMR, COSY (600 MHz, $CDCl_3$): δ/ppm = 7.51–7.48 (m, 2H, H-3', H-5'), 7.21–7.18 (m, 2H, H-2', H-6'), 6.55 (s, 1H, H-5), 6.01 (s, 1H, H-8), 3.84 (s, 3H, C^6-OCH_3), 3.74 (t, *J* = 6.5 Hz, 1H, H-1), 3.56 (s, 3H, C^7-OCH_3), 3.23–3.14 (m, 2H, H_a-3, C*H*$_a$H$_b$Ar), 2.91 (dd, *J* = 13.6, 7.3 Hz, 1H, CH$_a$*H*$_b$Ar), 2.85–2.74 (m, 2H, H_b-3, H_a-4), 2.57–2.50 (m, 1H, H_b-4), 2.52 (s, 3H, NCH_3).

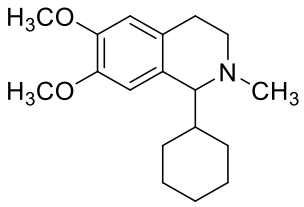
^{13}C-NMR, HSQC, HMBC (151 MHz, $CDCl_3$): δ/ppm = 147.5 (C-6), 146.5 (C-7), 144.3 (C-1'), 130.2 (2C, C-2', C-6'), 128.7 (C-8a), 128.3 (q, *J* = 32.2 Hz, C-4'), 126.3 (C-4a), 125.0 (q, *J* = 3.8 Hz, 2C, C-3', C-5'), 124.5 (q, *J* = 272 Hz, CF_3), 111.3 (C-5), 110.7 (C-8), 64.6 (C-1'), 55.9 (C^6-O*C*H$_3$), 55.6 (C^7-O*C*H$_3$), 46.9 (C-3), 42.8 (NCH_3), 41.0 (CH_2Ar), 25.5 (C-4).

^{19}F-NMR (376.5 MHz, $CDCl_3$): δ/ppm = –63.47 (s, 3F, CF_3).

IR: $\tilde{\nu}$ [cm^{-1}] = 2937, 2835, 1515, 1324, 1257, 1228, 1161, 1119, 1067, 1018.

ESI-MS: m/z = 366.2 (100%, $[M+H]^+$, calc. 366.2).

ESI-HRMS: calc. for [$C_{20}H_{23}F_3NO_2$]: m/z = 366.1681, found: m/z = 366.1667.



1-Cyclohexyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (3w). This compound was prepared according to the general procedure using bromocyclohexane (718 mg, 4.40 mmol, 1.10 equiv.). After addition of the bromide, the mixture was allowed to reach room temperature and was subsequently heated to 55–60 °C for 4 h before proceeding with the standard reduction procedure. Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:2) afforded the title compound (716 mg, 2.47 mmol, 62%) as a yellow oil.

R_f: 0.46 (^{c}Hex/EtOAc/Et_2NH 40:2:2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 6.57 (s, 1H, H-5), 6.51 (s, 1H, H-8), 3.84 (s, 6H, 2 × OCH_3), 3.22–3.13 (m, 1H, H_a-4), 3.11 (d, *J* = 6.0 Hz, 1H, H-1), 2.77–2.54 (m, 3H, H_b-3, H-4), 2.42 (s, 3H, NCH_3), 1.91–1.57 (m, 5H, 5 × $H_{c\text{-}Hex}$), 1.55–1.45 (m, 1H, H-1'), 1.27–0.84 (m, 5H, 5 × $H_{c\text{-}Hex}$).

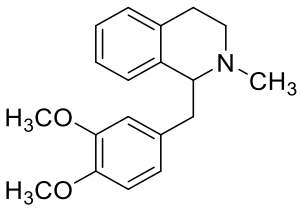
^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 147.2 (C-6), 146.5 (C-7), 128.8 (C-8a), 127.4 (C-4a), 112.3 (C-8), 111.2 (C-5), 69.0 (C-1), 56.1 & 55.9 (2C, 2 × OCH_3), 48.0 (C-3), 44.7 (C-1'), 44.1 (NCH_3), 30.9 (2C, C-2', C-6'), 27.0 (CH_2), 26.9 (CH_2), 26.7 (CH_2), 25.3 (C-3).

IR: $\tilde{\nu}$ [cm^{-1}] = 2924, 2849, 2792, 1513, 1464, 1449, 1254, 1226, 1076.

ESI-MS: m/z = 290.2 (100%, $[M+H]^+$, calc. 290.2).

ESI-HRMS: calc. for [$C_{18}H_{28}NO_2$]: m/z = 290.2120, found: m/z = 290.2126.

The analytical data are consistent with those reported in the literature.[29]



1-(3,4-dimethoxybenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (3x). This compound was prepared according to the general procedure using 2-methyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (1.033 g, 6.00 mmol, 1.00 eqiv.) and 4-(bromomethyl)-1,2-dimethoxybenzene (1.525 g, 6.60 mmol, 1.10 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc/Et_2NH 60:1:2) afforded the title compound (1.085 g, 3.65 mmol, 61%) as a yellow oil.

R_f: 0.26 (^{c}Hex/EtOAc/Et_2NH 40:2:2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 7.14–7.01 (m, 3H, H-5, H-6, H-7), 6.79 (br d, *J* = 7.5 Hz, 1H, H-8), 6.76 (d, *J* = 8.2 Hz, 1H, H-5'), 6.67 (dd, *J* = 8.2, 2.0 Hz, 1H, H-6'), 6.51 (d, *J* = 2.0 Hz, 1H, H-2'), 3.85 (s, 3H, $C^{4'}$-OCH_3), 3.79 (t, *J* = 5.9 Hz, 1H, H-1), 3.73 (s, 3H, $C^{3'}$-OCH_3), 3.20–3.13 (m, 1H, H_a-3), 3.11 (dd, *J* = 13.8, 5.3 Hz, 1H, C*H*$_a$H$_b$Ar), 2.91–2.80 (m, 2H, H_a-4, CH$_a$*H*$_b$Ar), 2.77–2.69 (m, 1H, H_b-3), 2.64 (dt, *J* = 16.1, 5.1 Hz, 1H, H_b-4), 2.52 (s, 3H, NCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 148.4 (C-3'), 147.3 (C-4'), 137.8 (C-8a), 134.7 (C-4a), 132.4 (C-1'), 128.8 (C-5), 128.1 (C-8), 126.0 (C-6), 125.3 (C-7), 121.7 (C-6'), 112.9 (C-2'), 110.9 (C-5'), 65.2 (C-1), 55.9 ($C^{4'}$-O*C*H_3), 55.7 ($C^{3'}$-O*C*H_3), 47.6 (C-3), 43.0 (NCH_3), 41.0 (CH_2Ar), 26.4 (C-4).

IR: $\tilde{\nu}$ [cm^{-1}] =2934, 2834, 1515, 1464, 1452, 1263, 1238, 1155, 1141, 1030.

ESI-MS: m/z = 298.3 (100%, $[M+H]^+$, calc. 298.2).

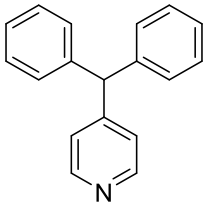
ESI-HRMS: calc. for [$C_{19}H_{24}NO_2$]: m/z = 298.1807, found: m/z = 298.1818.

V.2 Alkylation of (hetero)aromatic nitriles in a C–C-bond metathesis

General Procedure for irradiations on a preparative scale:

A 100 mL round-bottom flask equipped with a magnetic stir bar and a septum was charged with the 1-alkyl-2-methyl-1,2,3,4-tetrahydroisoquinoline (1.00 mmol, 1.00 equiv.), the aromatic nitrile (3.00 mmol, 3.00 equiv.) as well as phenanthrene (44.6 mg, 250 µmol, 0.25 equiv.). The flask was flushed with argon, followed by the addition of degassed acetonitrile (50 mL). After argon sparging for 1 min, TMSCN (250 µL, 198 mg, 2.00 mmol,

2.00 equiv.) was added via syringe and the resulting solution was irradiated for 28–40 h with a 25 W energy-saving UV/vis CFL-bulb (distance bulb–sample approximately 2 cm). Once the 1-alkyl-2-methyl-1,2,3,4-tetrahydroisoquinoline was consumed (judged by TLC), saturated, aqueous $NaHCO_3$ solution (30 mL) was added, followed by extraction with EtOAc (3 x 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Flash column chromatography afforded the respective *ipso*-substitution products.



4-Benzhydrylpyridine (8b). This compound was prepared according to the general procedure (36 h irradiation time) using 1-benzhydryl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3b**, 374 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 4:1) afforded the title compound (185 mg, 753 µmol, 75%) as a pale yellow solid.

Mp.: 123.5–125.0 °C, Lit.[30]: 124.3–125.6 °C.

R_f: 0.58 (^{c}Hex/EtOAc 1:2).

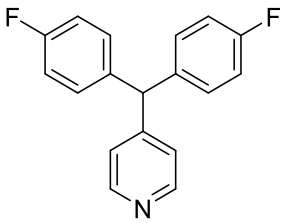
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.54–8.50 (m, 2H, H-2, H-6), 7.35–7.29 (m, 4H, H-3', H-3'', H-5', H-5''), 7.28–7.22 (m, 2H, H-4', H-4''), 7.13–7.08 (m, 4H, H-2', H-2'', H-6', H-6''), 7.06–7.03 (m, 2H, H-3, H-5), 5.51 (s, 1H, $CHPh_2$).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 152.8 (C-4), 150.0 (2C, C-2, C-6), 142.2 (2C, C-1', C-1''), 129.4 (4C, C-2', C-2'', C-6', C-6''), 128.7 (4C, C-3', C-3'', C-5', C-5''), 127.0 (2C, C-4', H-4''), 124.7 (2C, C-3, C-5), 56.3 ($CHPh_2$).

IR: $\tilde{\nu}$ [cm^{-1}] = 3061, 3027, 1592, 1558, 1494, 1450, 1414, 757, 700, 605.

ESI-MS: m/z = 246.2 (100%, $[M+H]^+$, calc. 246.2).

The analytical data are consistent with those reported in the literature.[30]



4-(Bis(4-fluorophenyl)methyl)pyridine (8c). This compound was prepared according to the general procedure (28 h irradiation time) using 1-(bis(4-fluorophenyl)methyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3c**, 409 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 4:1) afforded a mixture of the title compound (74% based on ^{1}H-NMR spectrum) and some remaining 4-cyanopyridine. Further purification by preparative HPLC furnished the pure title compound (175 mg, 622 µmol, 62%) as a pale yellow oil.

R_f: 0.53 (^{c}Hex/EtOAc 1:2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.53 (br s, 2H, H-2, H-6), 7.07–6.96 (m, 10H, H-3, H-5, 8 × H-Ar), 5.47 (s, 1H, $CHAr_2$).

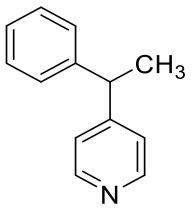
^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 161.9 (d, *J* = 246.2 Hz, 2C, C-4', C-4''), 152.4 (C-4), 150.1 (2C, C-2, C-6), 137.8 (d, *J* = 3.4 Hz, 2C, C-1', C-1''), 130.8 (d, *J* = 7.9 Hz, 4C, C-2', C6', C-2'', C-6''), 124.5 (2C, C-3, C-5), 115.7 (d, *J* = 21.3 Hz, 4C, C-3', C5', C-3'', C-5''), 54.8 ($CHAr_2$).

^{19}F-NMR (376.5 MHz, $CDCl_3$): δ/ppm = –116.67 (tt, *J* = 5.0, 2.6 Hz, 2F, $C^{4'}$-F, $C^{4''}$-F).

IR: $\tilde{\nu}$ [cm^{-1}] = 3070, 3040, 1597, 1506, 1413, 1225, 1159, 1099, 824.

ESI-MS: m/z = 282.1 (100%, $[M+H]^+$, calc. 282.1).

ESI-HRMS: calc. for $[C_{18}H_{14}NF_2]$: m/z = 282.1094, found: m/z = 282.1099.



4-(1-Phenylethyl)pyridine (8d). This compound was prepared according to the general procedure (36 h irradiation time) using 6,7-dimethoxy-2-methyl-1-(1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (**3d**, 311 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 3:1) afforded the title compound (129 mg, 704 µmol, 70%) as a yellow oil.

R_f: 0.47 (^{c}Hex/EtOAc 1:2).

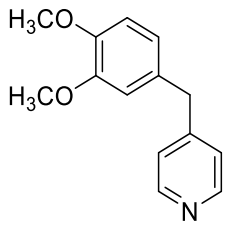
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.52–8.46 (m, 2H, H-2, H-6), 7.34–7.28 (m, 2H, H-3', H-5'), 7.25–7.17 (m, 3H, H-2', H-4', H-6'), 7.15–7.10 (m, 2H, H-3, H-5), 4.11 (q, *J* = 7.2 Hz, 1H, C*H*CH_3), 1.64 (d, *J* = 7.2 Hz, 3H, CHC*H*$_3$).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 155.1 (C-4), 149.9 (2C, C-2, C-6), 144.5 (C-1'), 128.7 (2C, C-3', C-5'), 127.7 (2C, C-2', C-6'), 126.7 (C-4'), 123.1 (2C, C-3, C-5), 44.3 (*C*HCH_3), 21.2 (CH*C*H_3).

IR: $\tilde{\nu}$ [cm^{-1}] = 3027, 2971, 2933, 1595, 1557, 1494, 1452, 1413, 830, 700.

ESI-MS: m/z = 184.0 (100%, $[M+H]^+$, calc. 184.1).

The analytical data are consistent with those reported in the literature.[31]



4-(3,4-Dimethoxybenzyl)pyridine (8a). This compound was prepared according to the general procedure (28 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 1:2) afforded the title compound (147 mg, 641 µmol, 64%) as a yellow oil. This reaction was also performed using sunlight as sole energy source (28 h of discontinuous irradiation). This afforded the title compound (152 mg, 663 µmol, 66%) as a yellow oil.

R_f: 0.21 (^{c}Hex/EtOAc 1:2).

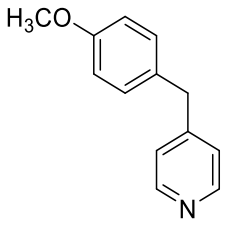
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.49 (br s, 2H, H-2, H-6), 7.09 (m, *J* = 4.7 Hz, 2H, H-3, H-5), 6.81 (d, *J* = 8.1 Hz, 1H, H-5´), 6.71 (dd, *J* = 8.1, 2.0 Hz, 1H, H-6´), 6.66 (d, *J* = 2.0 Hz, 1H, H-2´), 3.90 (s, 2H, CH_2), 3.86/3.82 (2 x s, 2 x 3H, 2 x OCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 150.4 (C-4), 149.9 (C-2,6), 149.2 (C-3´), 147.9 (C-4´), 131.4 (C-1´), 124.2 (2C, C-3,5), 121.2 (C-6´), 112.3 (C-2´), 111.4 (C-5´), 56.0 & 55.9 (2C, OCH_3), 40.9 (CH_2).

IR: $\tilde{\nu}$ [cm^{-1}] = 2999, 2936, 2835, 1599, 1514, 1464, 1416, 1261, 1238, 1140.

ESI-MS: m/z = 230.1 (100%, $[M+H]^+$, calc. 230.1).

The analytical data are consistent with those reported in the literature.[7c]



4-(4-Methoxybenzyl)pyridine (8e). This compound was prepared according to the general procedure (28 h irradiation time) using 6,7-dimethoxy-1-(4-methoxybenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3e**, 327 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 3:1 → 2:1) afforded the title compound (122 mg, 612 µmol, 61%) as a pale yellow oil.

R_f: 0.40 (^{c}Hex/EtOAc 1:2).

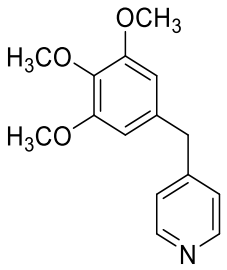
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.50–8.45 (m, 2H, H-2, H-6), 7.11–7.03 (m, 4H, H-3, H-5, H-2', H-6'), 6.88–6.81 (m, 2H, H-3', H-5'), 3.90 (s, 2H, CH_2), 3.78 (s, 3H, OCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 158.5 (C-4'), 150.6 (C-4), 149.9 (2C, C-2, C-6), 131.0 (C-1'), 130.0 (2C, C-2', C-6'), 124.2 (2C, C-3, C-5), 114.2 (2C, C-3', C-5'), 55.4 (CH_2), 40.4 (OCH_3).

IR: $\bar{\nu}$ [cm^{-1}] = 3030, 2956, 2934, 2836, 1601, 1512, 1415, 1249, 1179, 1034.

ESI-MS: m/z = 200.1 (100%, $[M+H]^+$, calc. 200.1).

The analytical data are consistent with those reported in the literature.[32]



4-(3,4,5-Trimethoxybenzyl)pyridine (8f). This compound was prepared according to the general procedure (36 h irradiation time) using 6,7-dimethoxy-1-(4-methoxybenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3f**, 388 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 1:2) afforded the title compound (114 mg, 439 µmol, 44%) as a pale yellow oil.

R_f: 0.18 (^{c}Hex/EtOAc 1:2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.52–8.48 (m, 2H, H-2, H-6), 7.12–7.08 (m, 2H, H-3, H-5), 6.36 (s, 2H, H-2', H-6'), 3.89 (s, 2H, CH_2Ar), 3.82 (s, 3H, $C^{4'}$-OCH_3), 3.80 (s, 6H, $C^{3'}$-OCH_3, $C^{5'}$-OCH_3).

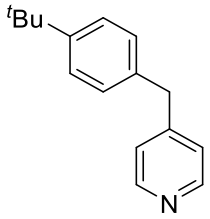
^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 153.5 (2C, C-3', C-5'), 150.0 (2C, C-2, C-6), 149.9 (C-4), 136.8 (C-4'), 134.5 (C-1'), 124.2 (2C, C-3, C-5), 106.2 (2C, C-2', C-6'), 61.0 ($C^{4'}$-O*C*H_3), 56.2 (2C, $C^{3'}$-O*C*H_3, $C^{5'}$-O*C*H_3), 41.6 (CH_2Ar).

IR: $\bar{\nu}$ [cm^{-1}] = 2939, 2838, 1592, 1507, 1460, 1417, 1331, 1239, 1126, 1007.

ESI-MS: m/z = 260.1 (100%, $[M+H]^+$, calc. 260.1).

ESI-HRMS: calc. for [$C_{15}H_{18}NO_3$]: m/z = 260.1287, found: m/z = 260.1288.

The analytical data are consistent with those reported in the literature.[33] However, ^{13}C-NMR, high resolution mass spectrometry and IR data have not yet been reported for this compound.



4-(4-*tert*-Butylbenzyl)pyridine (8g). This compound was prepared according to the general procedure (36 h irradiation time) using 1-(4-(*tert*-butyl)benzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3g**, 354 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 3:1) afforded the title compound (109 mg, 481 µmol, 48%) as a pale yellow oil.

R_f: 0.49 (^{c}Hex/EtOAc 1:2).

^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.51–8.47 (m, 2H, H-2, H-6), 7.36–7.31 (m, 2H, H-3', H-5'), 7.13–7.08 (m, 4H, H-3, H-5, H-2', H-6'), 3.93 (s, 2H, CH_2Ar), 1.31 (s, 9H, $C(CH_3)_3$).

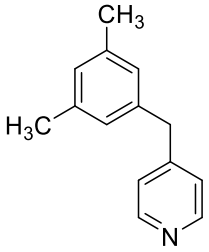
^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 150.3 (C-4), 149.9 (2C, C-2, C-6), 149.6 (C-4'), 135.9 (C-1'), 128.8 (2C, C-2', C-6'), 125.7 (2C, C-3', C-5'), 124.3 (2C, C-3, C-5), 40.8 (*C*H_2), 34.5 (*C*$(CH_3)_3$), 31.5 (3C, C(*C*$H_3)_3$).

IR: $\bar{\nu}$ [cm^{-1}] = 3026, 2962, 2868, 1600, 1514, 1413, 1364, 1269, 828, 813.

ESI-MS: m/z = 226.1 (100%, $[M+H]^+$, calc. 226.2).

ESI-HRMS: calc. for [$C_{16}H_{20}N$]: m/z = 226.1596, found: m/z = 226.1592.

The analytical data are consistent with those reported in the literature.[34]



4-(3,5-Dimethylbenzyl)pyridine (8h). This compound was prepared according to the general procedure (28 h irradiation time) using 1-(3,5-dimethylbenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3h**, 326 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 3:1) afforded the title compound (84.8 mg, 430 µmol, 43%) as a pale yellow oil.

R_f: 0.50 (^{c}Hex/EtOAc 1:2).

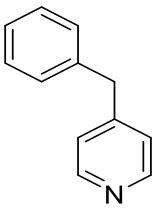
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.49 (d, *J* = 5.1 Hz, 2H, H-2, H-6), 7.13–7.08 (m, 2H, H-3, H-5), 6.89 (s, 1H, H-4'), 6.79 (s, 2H, H-3',H-5'), 3.88 (s, 2H, CH_2), 2.29 (s, 6H, 2 × CH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 150.3 (C-4), 149.9 (2C, C-2, C-6), 138.9 (C-1'), 138.4 (2C, C-3', C-5'), 128.4 (C-4'), 127.0 (2C, C-2', C-6'), 124.3 (2C, C-3, C-5), 41.2 (CH_2), 21.4 (2C, 2 × CH_3).

IR: $\tilde{\nu}$ [cm^{-1}] = 3019, 2917, 2860, 1597, 1560, 1465, 1415, 856, 798.

ESI-MS: m/z = 198.1 (100%, $[M+H]^+$, calc. 198.1).

ESI-HRMS: calc. for [$C_{14}H_{16}N$]: m/z = 198.1283, found: m/z = 198.1287.



4-Benzylpyridine (8i). This compound was prepared according to the general procedure (28 h irradiation time) using 1-benzyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroiso-quinoline (**3i**, 297 mg, 1.00 mmol, 1.00 equiv.) and 4-cyanopyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 3:1) afforded the title compound (47.6 mg, 281 µmol, 28%) as a pale yellow oil.

R_f: 0.43 (^{c}Hex/EtOAc 1:2).

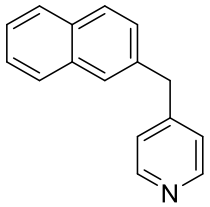
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.52–8.46 (m, 2H, H-2, H-6), 7.35–7.29 (m, 2H, H-3', H-5'), 7.27–7.22 (m, 1H, H-4'), 7.20–7.15 (m, 2H, H-2', H-6'), 7.12–7.08 (m, 2H, H-3, H-5), 3.96 (s, 2H, C*H*$_2$Ph).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 150.1 (C-4), 149.9 (2C, C-2, C-6), 139.0 (C-1'), 129.1 (2C, C-2', C-6'), 128.8 (2C, C-3', C-5'), 126.8 (C-4'), 124.3 (2C, C-3, C-5), 41.3 (CH_2Ph).

IR: $\tilde{\nu}$ [cm^{-1}] = 3065, 3028, 1597, 1559, 1495, 1453, 1415, 786, 740, 700.

ESI-MS: m/z = 170.0 (100%, $[M+H]^+$, calc. 170.1).

The analytical data are consistent with those reported in the literature.[7c]



4-(Naphthalen-2-ylmethyl)pyridine (8j). This compound was prepared according to the general procedure (40 h irradiation time) using 6,7-dimethoxy-2-methyl-1-(naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (**3j**, 347 mg, 1.00 mmol, 1.00 equiv.) and 4-cyano-pyridine (**1a**, 312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex → ^{c}Hex/EtOAc 4:1 → 3:1) afforded the title compound (86.0 mg, 392 µmol, 39%) as a colorless solid.

Mp.: 45.0–46.5 °C.

R_f: 0.36 (^{c}Hex/EtOAc 1:2).

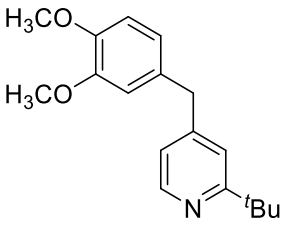
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.56–8.48 (m, 2H, H-2, H-6), 7.86–7.76 (m, 3H, 3 × $H_{Naphthyl}$), 7.64 (s, 1H, $H_{Naphthyl}$), 7.52–7.43 (m, 2H, 2 × $H_{Naphthyl}$), 7.30–7.26 (m, 1H, $H_{Naphthyl}$), 7.16–7.12 (m, 2H, H-3, H-5), 4.12 (s, 2H, CH_2).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 150.0 (2C, C-2, C-6), 149.9 (C-4), 136.4 (C-2'), 133.6 ($C_{Naphthyl}$), 132.3 ($C_{Naphthyl}$), 128.5 ($C_{Naphthyl}$), 127.8 ($C_{Naphthyl}$), 127.7 ($C_{Naphthyl}$), 127.6 ($C_{Naphthyl}$), 127.4 ($C_{Naphthyl}$), 126.4 ($C_{Naphthyl}$), 125.9 ($C_{Naphthyl}$), 124.4 (2C, C-3, C-5), 41.5 (CH_2).

IR: $\tilde{\nu}$ [cm^{-1}] = 3052, 3024, 2990, 1599, 1559, 1508, 1415, 812, 755.

ESI-MS: m/z = 220.1 (100%, $[M+H]^+$, calc. 220.1).

The analytical data are consistent with those reported in the literature.[35]



2-(*tert*-Butyl)-4-(3,4-dimethoxybenzyl)pyridine (8k). This compound was prepared according to the general procedure (28 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 4-cyano-2-(*tert*-butyl)pyridine (481 mg, 3.00 mmol, 3.00 equiv.), which had been prepared according to a procedure by Minisci et al.[36] Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 4:1) afforded the title compound (203 mg, 711 µmol, 71%) as a colorless oil.

R_f = 0.16 (SiO_2, ^{c}Hex/EtOAc 4:1).

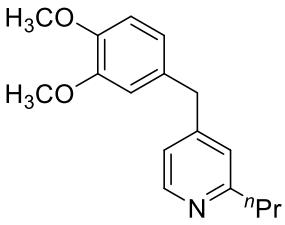
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.44 (dd, *J* = 5.0, 0.6 Hz, 1H, H-6), 7.16 (dd, *J* = 1.5, 0.6 Hz, 1H, H-3), 6.88–6.86 (m, 1H, H-5), 6.81 (*pseudo*-d, *J* = 8.1 Hz, 1H, H-5'), 6.71 (dd, *J* = 8.1, 2.0 Hz, 1H, H-6'), 6.68 (*pseudo*-d, *J* = 2.0 Hz, 1H, H-2'), 3.90 (s, 2H, CH_2), 3.86 (s, 3H, $C^{4'}$-OCH_3), 3.83 (s, 3H, $C^{3'}$-OCH_3), 1.34 (s, 9H, $C(CH_3)_3$).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 169.5 (C-2), 150.3 (C-4), 149.1 (C-3'), 148.7 (C-6), 147.8 (C-4'), 131.8 (C-1'), 121.2 (2C, C-5, C-6'), 119.6 (C-3), 112.3 (C-2'), 111.4 (C-5'), 56.0 (2C, 2 × OCH_3), 41.2 (CH_2), 37.4 ($C(CH_3)_3$), 30.3 ($C(CH_3)_3$).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957, 2904, 2834, 1597, 1514, 1464, 1261, 1237, 1140, 1029.

ESI-MS (pos.): *m/z* = 286.2 (100%, $[M+H]^+$, calc. 286.2).

ESI-HRMS (pos.): calc. for [$C_{18}H_{24}NO_2$]: m/z = 286.1807, found: 286.1802.



4-(3,4-Dimethoxybenzyl)-2-propylpyridine (8l). This compound was prepared according to the general procedure (28 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 4-cyano-2-propylpyridine (439 mg, 3.00 mmol, 3.00 equiv.), which had been prepared according to a procedure by Minisci et al.[36] Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 2:1) afforded the title compound (172 mg, 634 µmol, 63%) as a pale yellow oil.

R_f = 0.13 (SiO_2, ^{c}Hex/EtOAc 2:1).

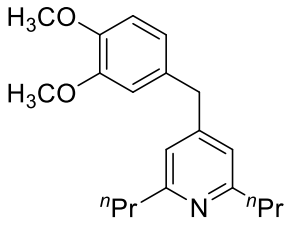
^{1}H-NMR, COSY (300 MHz, $CDCl_3$): 8.39 (d, *J* = 5.1 Hz, 1H, H-6), 6.94 (br s, 1H, H-3), 6.90 (dd, *J* = 5.1, 1.4 Hz, 1H, H-5), 6.81 (d, *J* = 8.1 Hz, H-6'), 6.71 (dd, *J* = 8.1, 2.0 Hz, 1H, H-5'), 6.65 (d, *J* = 1.9 Hz, 1H, H-2'), 3.87 (s, 2H, Aryl-CH_2), 3.86 (s, 3H, C$^{4'}$-OCH_3), 3.82 (s, 3H, C$^{3'}$-OCH_3), 2.74–2.66 (m, 2H, C$H_2CH_2CH_3$), 1.78–1.65 (m, 2H, $CH_2CH_2CH_3$), 0.94 (t, *J* = 7.4 Hz, 3H, CH_3).

^{13}C-NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): δ/ppm = 162.4 (C-2), 150.5 (C-4), 149.3 (C-6), 149.1 (C-3'), 147.8 (C-4'), 131.7 (C-1´), 123.2 (C-3), 121.5 (C-5), 121.2 (C-5'), 112.3 (C-2'), 111.4 (C-6'), 56.0 & 55.9 (2C, 2 × OCH_3), 40.9 (Aryl-CH_2), 40.4 (C$H_2CH_2CH_3$), 23.2 ($CH_2CH_2CH_3$), 14.0 (CH_3).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2959, 2934, 2871, 2835, 1601, 1515, 1464, 1261, 1237, 1140.

ESI-MS (pos.): *m/z* = 272.2 (100%, $[M+H]^+$, calc. 272.2).

ESI-HRMS (pos.): calc. for [$C_{17}H_{22}NO_2$]: m/z = 272.1651, found: 272.1647.



4-(3,4-Dimethoxybenzyl)-2,6-dipropylpyridine (8m). This compound was prepared according to the general procedure (28 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 4-cyano-2,6-dipropylpyridine (565 mg, 3.00 mmol, 3.00 equiv.), which had been prepared according to a procedure by Minisci et al.[36] Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 6:1) afforded the title compound (214 mg, 684 µmol, 68%) as a pale yellow oil.

R_f = 0.12 (SiO_2, ^{c}Hex/EtOAc 6:1).

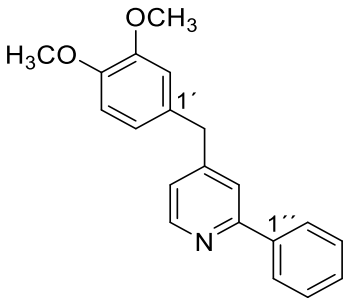
^{1}H-NMR, COSY, HSQC, HMBC (400 MHz, $CDCl_3$): δ/ppm = 6.80 (d, *J* = 8.1 Hz, 1H, H-5'), 6.75 (br s, 2H, H-3,5), 6.70 (dd, *J* = 8.1, 2.0 Hz, 1H, H-6'), 6.66 (d, *J* = 2.0 Hz, 1H, H-2'), 3.86 (s, 3H, C$^{4'}$-OCH_3), 3.84 (s, 2H, Aryl-CH_2), 3.82 (s, 3H, C$^{3'}$-OCH_3), 2.70–2.65 (m, 4H, 2 × C$H_2CH_2CH_3$), 1.74–1.63 (m, 4H, 2 × $CH_2CH_2CH_3$), 0.93 (t, *J* = 7.4 Hz, 3H, CH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 161.9 (2C, C-2,6), 150.5 (C-4), 149.0 (C-3'), 147.7 (C-4'), 132.0 (C-1'), 121.1 (C-6'), 120.3 (2C, C-3, C-5), 112.2 (C-2'), 111.3 (C-5'), 56.0 & 55.9 (2C, 2 x OCH_3), 40.9 (Aryl-CH_2), 40.6 (2C, 2 × C$H_2CH_2CH_3$), 23.6 (2C, 2 × $CH_2CH_2CH_3$), 14.0 (2C, 2 x CH_3).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2958, 2933, 2871, 1601, 1565, 1514, 1464, 1261, 1237, 1030.

ESI-MS (pos.): *m/z* = 314.3 (100%, $[M+H]^+$, calc. 314.2).

ESI-HRMS (pos.): calc. for [$C_{20}H_{28}NO_2$]: m/z = 314.2120, found: 314.2126.



4-(3,4-Dimethoxybenzyl)-2-phenylpyridine (8n). This compound was prepared according to the general procedure (28 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 4-cyano-2,6-dipropylpyridine (541 mg, 3.00 mmol, 3.00 equiv.), which had been prepared according to a procedure by Yu et al.[37] Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 4:1) afforded the title compound (190 mg, 622 µmol, 62%) as a pale yellow oil.

R_f = 0.16 (SiO_2, ^{c}Hex/EtOAc 4:1).

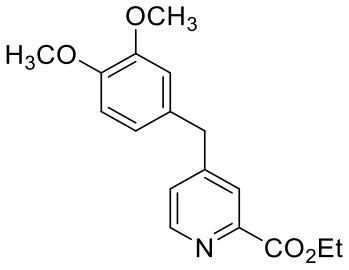
^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ/ppm = 8.58 (d, *J* = 5.0 Hz, 1H, H-6), 7.99–7.92 (m, 2H, H-2'', C-6''), 7.56–7.52 (m, 1H, H-3), 7.49–7.36 (m, 3H, H-3'', H-4'', H-5''), 7.05 (dd, *J* = 5.0, 1.5 Hz, 1H, H-5), 6.83 (d, *J* = 8.1 Hz, 1H, H-5'), 6.76 (dd, *J* = 8.1, 1.9 Hz, 1H, H-6'), 6.71 (d, *J* = 1.9 Hz, 1H, H-2'), 3.98 (s, 2H, CH_2), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3).

^{13}C-NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): δ/ppm = 157.7 (C-2), 151.1 (C-4), 149.8 (C-6), 149.2 (C-3'), 147.9 (C-4'), 139.5 (C-1''), 131.5 (C-1'), 129.0 (C-4''), 128.8 (2C, C-2'', C-6''), 127.0 (2C, C-3'', C-5''), 122.7 (C-5), 121.3 (C-6'), 121.1 (C-3), 112.3 (C-2'), 111.4 (C-5'), 56.0 & 56.0 (2C, 2 × OCH_3), 41.1 (CH_2).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3057, 3000, 2935, 2834, 1597, 1514, 1446, 1261, 1237, 1028.

ESI-MS (pos.): *m/z* = 306.2 (100%, $[M+H]^+$, calc. 306.1).

ESI-HRMS (pos.): calc. for [$C_{20}H_{20}NO_2$]: m/z = 306.1494, found: 306.1487.



Ethyl 4-(3,4-dimethoxybenzyl)picolinate (8o). This compound was prepared according to the general procedure (28 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and ethyl 4-cyanopicolinate (529 mg, 3.00 mmol, 3.00 equiv.), which had been

prepared according to a procedure by Heinisch et al.[38] Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 1:1) afforded the title compound (130 mg, 431 µmol, 43%) as a yellow oil.

R_f = 0.13 (SiO_2, ^{c}Hex/EtOAc 1:1).

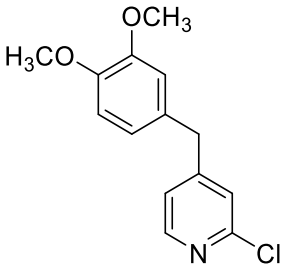
^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ/ppm = 8.57 (d, *J* = 4.9 Hz, 1H, H-6), 7.92 (s, 1H, H-3), 7.21 (dd, *J* = 5.0, 1.7 Hz, 1H, H-5), 6.77 (d, *J* = 8.1 Hz, 1H, H-5'), 6.66 (dd, *J* = 8.1, 2.0 Hz, 1H, H-6'), 6.61 (d, *J* = 2.0 Hz, 1H, H-2'), 4.40 (q, *J* = 7.1 Hz, 2H, C*H*$_2$CH$_3$), 3.92 (s, 2H, Aryl-CH$_2$), 3.80 (s, 3H, C$^{4'}$-O*C*H$_3$), 3.77 (s, 3H, C$^{3'}$-O*C*H$_3$), 1.37 (t, *J* = 7.1 Hz, 3H, CH$_2$C*H*$_3$).

^{13}C-NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): δ/ppm = 165.3 (*C*O$_2$Et), 151.8 (C-4), 149.8 (C-6), 149.1 (C-3'), 148.3 (C-2), 147.9 (C-4'), 130.7 (C-1'), 127.0 (C-5), 125.4 (C-3), 121.1 (C-6'), 112.1 (C-2'), 111.4 (C-5'), 61.9 (*C*H$_2$CH$_3$), 55.9 & 55.8 (2C, 2 × OCH$_3$), 40.7 (Aryl-CH$_2$), 14.3 (CH$_2$*C*H$_3$).

IR (ATR): $\bar{\nu}$ [cm^{-1}] = 2981, 2937, 2836, 1715, 1596, 1514, 1297, 1261, 1201, 1026.

ESI-MS (pos.): *m/z* = 324.2 (6%, [M+Na]$^+$, calc. 324.1), 302.3 (100%, [M+H]$^+$, calc. 302.1).

ESI-HRMS (pos.): calc. for [$C_{17}H_{19}NO_4Na$]: m/z = 324.1212, found: 324.1216.



2-Chloro-4-(3,4-dimethoxybenzyl)pyridine (**8p**)**.** This compound was prepared according to the general procedure (28 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 2-chloro-4-cyanopyridine (416 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 4:1) afforded the title compound (74.2 mg, 281 µmol, 28%) as a colorless oil.

R_f = 0.11 (SiO_2, ^{c}Hex/EtOAc 4:1).

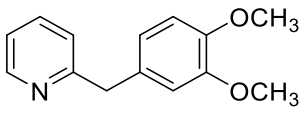
^{1}H-NMR, COSY (300 MHz, $CDCl_3$): δ/ppm = 8.24 (d, *J* = 5.1 Hz, 1H, H-6), 7.11–7.09 (m, 1H, H-3), 7.03–6.99 (m, 1H, H-5), 6.81 (d, *J* = 8.1 Hz, 1H, H-5'), 6.69 (dd, *J* = 8.1, 2.0 Hz, 1H, H-6´), 6.63 (d, *J* = 2.0 Hz, 1H, H-2´), 3.88 (br s, 2H, CH$_2$), 3.85 (s, 3H, C$^{4'}$-OCH$_3$), 3.82 (s, 3H, C$^{3'}$-OCH$_3$).

^{13}C-NMR, HSQC, HMBC (75.5 MHz, $CDCl_3$): δ/ppm = 153.9 (C-4), 151.8 (C-2), 149.6 (C-6), 149.2 (C-3'), 148.1 (C-4'), 130.4 (C-1'), 124.4 (C-3), 122.9 (C-5), 121.3 (C-6'), 112.2 (C-2'), 111.5 (C-5'), 56.0 & 55.9 (2C, 2 × OCH$_3$), 40.5 (CH$_2$).

IR (ATR): $\bar{\nu}$ [cm^{-1}] = 3000, 2935, 2909, 2835, 1591, 1515, 1464, 1384, 1261, 1028.

ESI-MS (pos.): *m/z* = 264.4 (100%, [M+H]$^+$, calc. 264.1).

ESI-HRMS (pos.): calc. for [$C_{14}H_{15}NO_2Cl$]: m/z = 264.0791, found: 264.0795.



2-(3,4-Dimethoxybenzyl)pyridine (**8q**). This compound was prepared according to the general procedure (30 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 2-cyanopyridine (312 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 3:2) afforded the title compound (62.2 mg, 271 µmol, 27%) as a pale yellow oil.

R_f = 0.25 (SiO_2, ^{c}Hex/EtOAc 1:1).

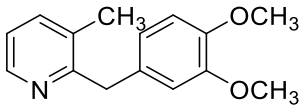
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.54–8.50 (m, 1H, H-6), 7.55 (app td, *J* = 7.7, 1.8 Hz, 1H, H-4), 7.10–7.06 (m, 2H, H-3, H-5), 6.78 (br s, 3H, H-2', H-5', H-6'), 4.07 (s, 2H, CH_2), 3.82 & 3.81 (2 × s, 2 × 3H, 2 × OCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 161.3 (C-2), 149.3 (C-6), 149.0 & 147.6 (2C, C-3', C-4'), 136.6 (C-4), 132.1 (C-1'), 123.0 & 121.2 (2C, C-3, C-5), 121.1 & 112.3 & 111.3 (3C, C-2', C-5', C-6'), 55.9 (2C, 2 × OCH_3), 44.3 (CH_2).

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3065, 3004, 2955, 2835, 1591, 1515, 1465, 1260, 1237, 1140.

ESI-MS (pos.): *m/z* = 230.1 (100%, $[M+H]^+$, calc. 230.1).

The analytical data are consistent with those reported in the literature.[7c]



2-(3,4-Dimethoxybenzyl)-3-methylpyridine (8r). This compound was prepared according to the general procedure (30 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 2-cyano-3-methylpyridine (354 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 2:1) afforded the title compound (83.0 mg, 341 µmol, 34%) as a pale yellow oil.

R_f = 0.12 (SiO_2, ^{c}Hex/EtOAc 2:1).

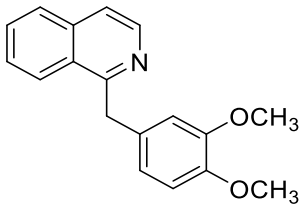
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.37–8.34 (m, 1H, H-6), 7.34–7.31 (m, 1H, H-4), 6.99 (dd, *J* = 7.6, 4.9 Hz, 1H, H-5), 6.72 (d, *J* = 1.9 Hz, 1H, H-2´), 6.69 (d, *J* = 8.2 Hz, 1H, H-5´), 6.64 (dd, *J* = 8.2, 1.9 Hz, 1H, H-6´), 4.06 (s, 2H, CH_2), 3.75 & 3.74 (2 × s, 2 × 3H, 2 × OCH_3), 2.23 (s, 3H, CH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 158.8 (C-2), 148.7 & 147.3 (2C, C-3',C-4'), 146.6 (C-6), 137.9 (C-4), 131.6 & 131.4 (2C, C-3, C-1'), 121.6 (C-5), 120.5 (CH_{Aryl}), 111.9 & 111.0 (2C, 2 × CH_{Aryl}), 55.7 & 55.6 (2C, 2 × OCH_3), 41.7 (CH_2), 18.8 (CH_3).

IR (ATR): $\bar{\nu}$ [cm^{-1}] = 2998, 2934, 2834, 1589, 1512, 1447, 1259, 1236, 1140, 1027.

ESI-MS (pos.): *m/z* = 244.1 (100%, $[M+H]^+$, calc. 244.1).

The analytical data are consistent with those reported in the literature.[7c]



1-(3,4-Dimethoxybenzyl)isoquinoline (8s). This compound was prepared according to the general procedure (30 h irradiation time) using (±)-laudanosine (**3a**, 357 mg, 1.00 mmol, 1.00 equiv.) and 1-cyanoisoquinoline (436 mg, 3.00 mmol, 3.00 equiv.). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 2:1) afforded the title compound (112 mg, 401 µmol, 40%) as a brown foam.

R_f = 0.11 (SiO_2, ^{c}Hex/EtOAc 2:1).

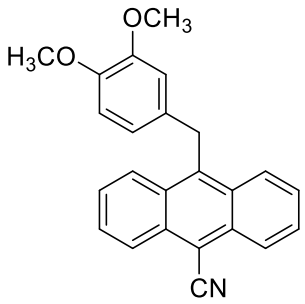
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.45 (d, *J* = 5.8 Hz, 1H, H-3), 8.13–8.09 (m, 1H, H-8), 7.70 (d, *J* = 8.2 Hz, H-5), 7.52 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H, H-6), 7.47–7.41 (m, 2H, H-4, H-7), 6.82 (d, *J* = 2.0 Hz, 1H, H-2'), 6.76 (dd, *J* = 8.2, 2.0 Hz, 1H, H-6'), 6.68 (d, *J* = 8.2 Hz, 1H, H-5'), 4.56 (s, 2H, CH_2), 3.73 & 3.72 (2 × s, 2 × 3H, 2 × OCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 160.1 (C-1), 148.7 (C-4'), 147.3 (C-3'), 141.8 (C-3), 136.3 (2C, C-4a, C-8a), 131.9 (C-1'), 129.6 (C-6), 127.2 (C-5), 127.0 (C-7), 125.5 (C-8), 120.5 (C-6'), 119.6 (C-4), 111.8 (C-2'), 111.0 (C-5'), 55.6 (2C, 2 × OCH_3), 41.5 (CH_2).

IR (ATR): $\bar{\nu}$ [cm^{-1}] = 3052, 2999, 3935, 2834, 1588, 1514, 1463, 1259, 1141, 1028.

ESI-MS (pos.): *m/z* = 280.2 (100%, $[M+H]^+$, calc. 280.1).

The analytical data are consistent with those reported in the literature.[7c]



9-Cyano-10-(3,4-dimethoxybenzyl)anthracene (8t). This compound was prepared by modifying the general procedure using (±)-laudanosine (**3a**, 286 mg, 800 µmol, 1.00 equiv.) and 9,10-dicyanoanthracene (548 mg, 2.40 mmol, 3.00 equiv.). Due to the low solubility of the aromatic nitrile, 80 mL acetonitrile were used and the reaction mixture was irradiated simultaneously with two 25 W energy-saving UV/vis CFL bulbs from opposite directions (no aluminum foil was used). Flash column chromatography (SiO_2, ^{c}Hex/EtOAc 6:1) afforded the title compound (76.7 mg, 217 µmol, 27%) as a yellow solid.

Mp.: 193.2–194.0 °C, Lit.[39]: 195 °C.

R_f: 0.14 (SiO_2, ^{c}Hex/EtOAc 6:1).

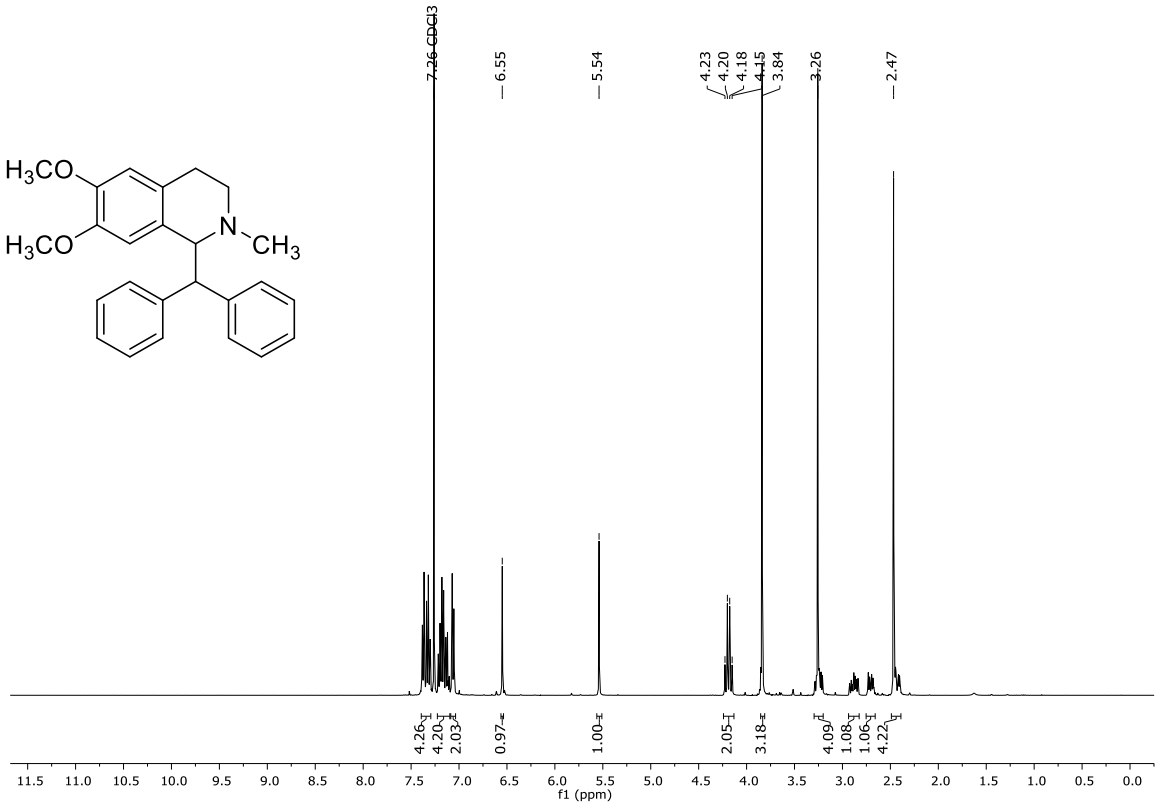
^{1}H-NMR, COSY (400 MHz, $CDCl_3$): δ/ppm = 8.51–8.48 (m, 2H, H-1,8), 8.32 (d, *J* = 8.9 Hz, 2H, H-4,5), 7.73–7.69 (m, 2H, C-2,7), 7.60–7.55 (m, 2H, H-3,6), 6.75 (d, *J* = 2.0 Hz, 1H, H-2´), 6.66 (d, *J* = 8.3 Hz, 1H, H-5´), 6.45–6.42 (m, 1H, H-6´), 5.00 (s, 2H, CH_2), 3.79 (s, 3H, $C^{4´}$-OCH_3), 3.74 (s, 3H, $C^{3´}$-OCH_3).

^{13}C-NMR, HSQC, HMBC (100.6 MHz, $CDCl_3$): δ/ppm = 149.2 (C-3´), 147.8 (C-4´), 139.8 (C-10), 133.3 (2C, C-8a,9a), 132.3 (C-1´), 130.0 (2C, C-4a,10a), 128.6 (2C, C-2,7), 127.0 (2C, C-3,6), 126.4 (2C, C-1,8), 125.8 (2C, C-4,5), 120.1 (C-6´), 117.7 (CN), 111.5/111.4 (2C, C-2´,5´), 105.7 (C-9), 56.0 (2C, 2 × OCH_3), 33.8 (CH_2).

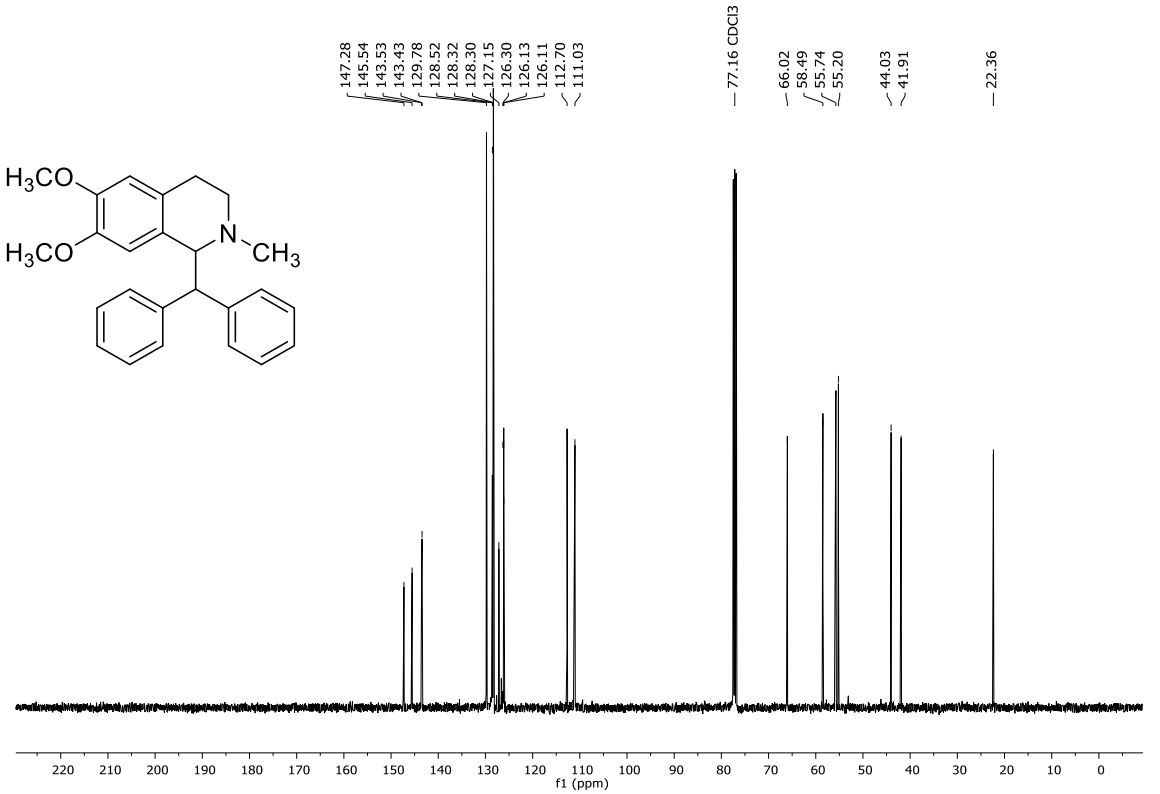
IR: $\tilde{\nu}$ [cm^{-1}] = 3000, 2956, 2934, 2835, 2212, 1514, 1445, 1272, 1186, 1028.

LIFDI-FD: calc. for $[C_{24}H_{19}NO_2]^{\bullet+}$: m/z = 353.1, found: 353.3.

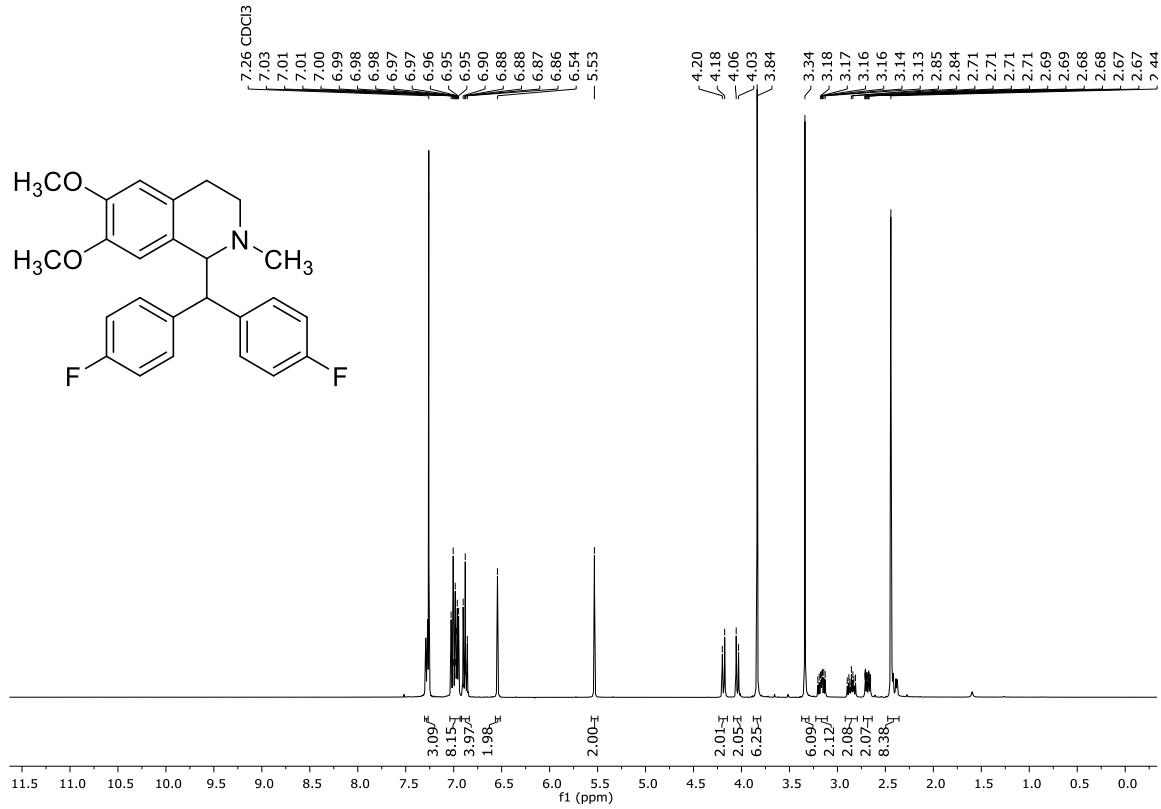
VI. NMR Spectra



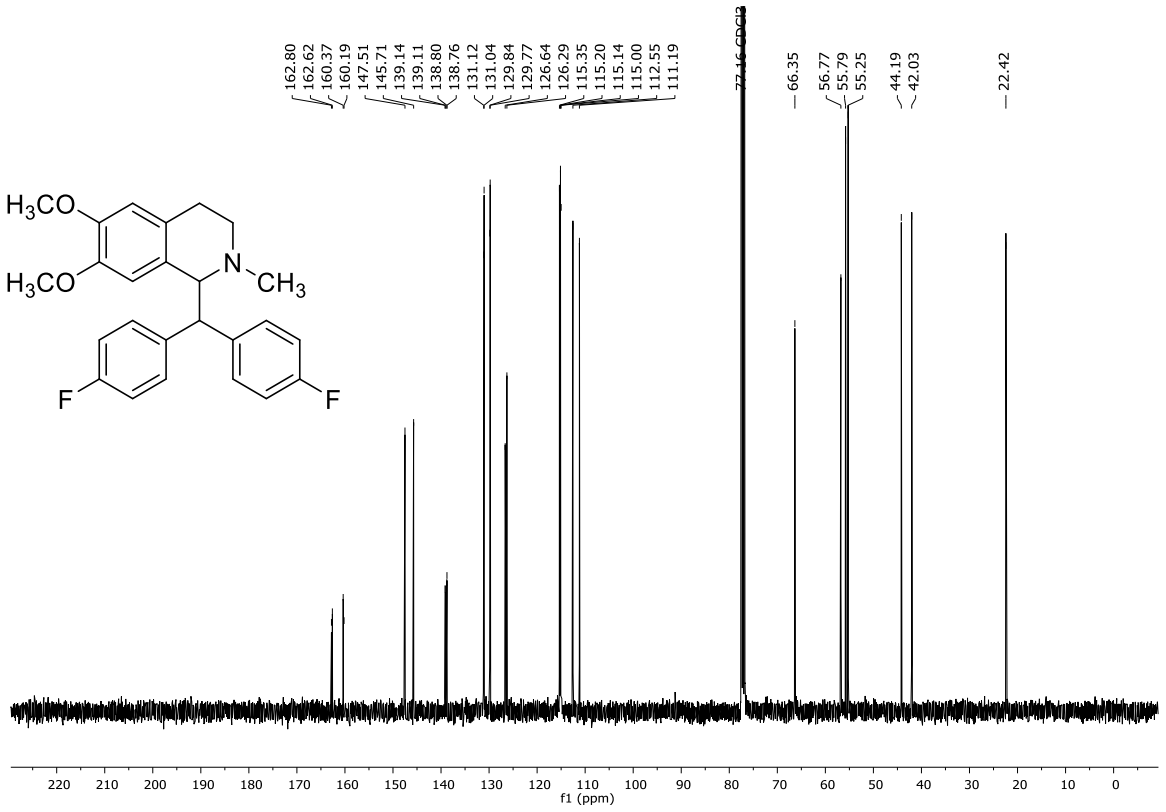
^{1}H-NMR (400 MHz, $CDCl_3$): 1-benzhydryl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-isoquinoline (**3b**, rotamers).



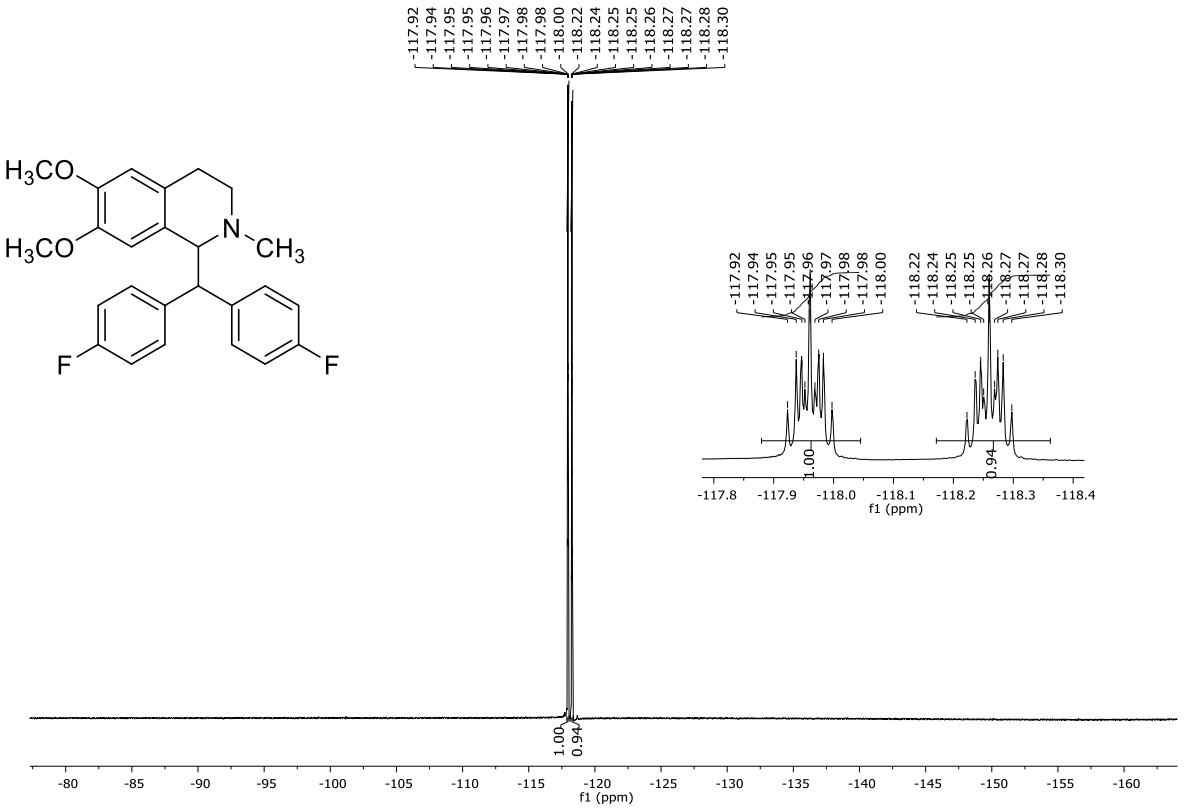
^{13}C-NMR (100.6 MHz, $CDCl_3$): 1-benzhydryl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-isoquinoline (**3b**, rotamers).



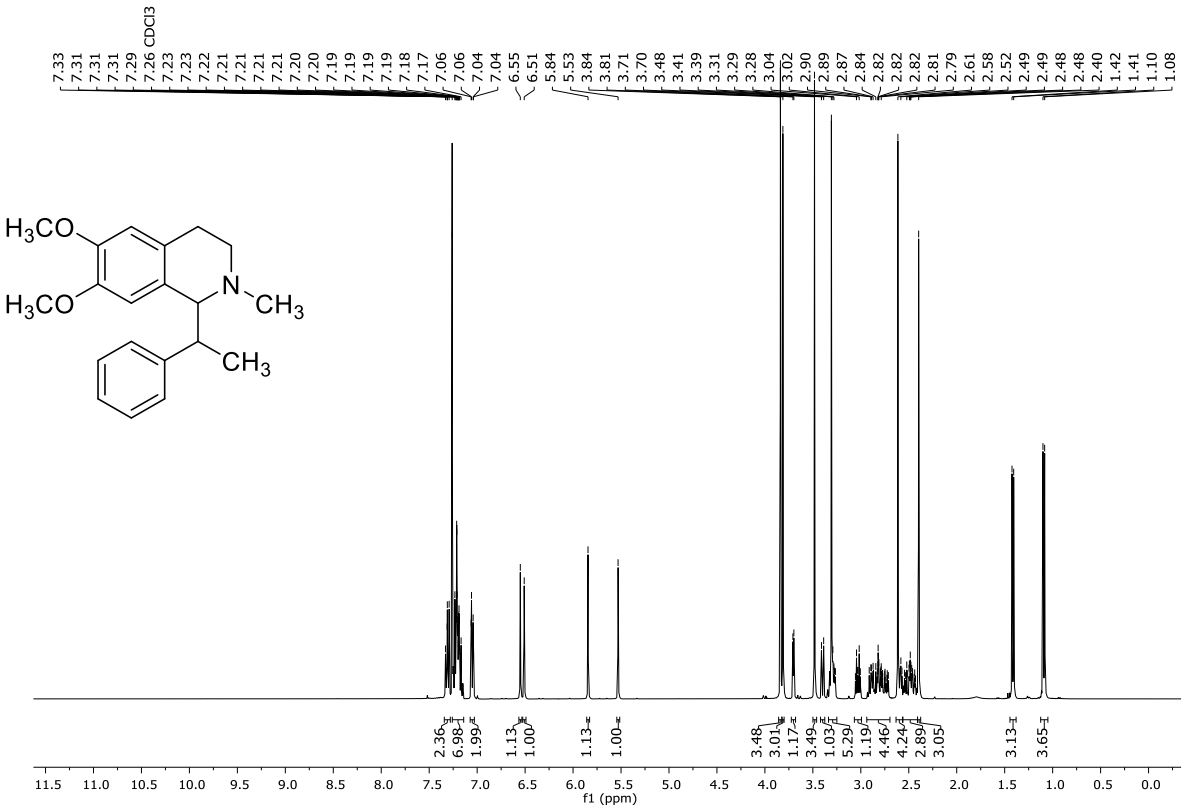
^{1}H-NMR (400 MHz, $CDCl_3$): 1-(bis(4-fluorophenyl)methyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3c**, rotamers).



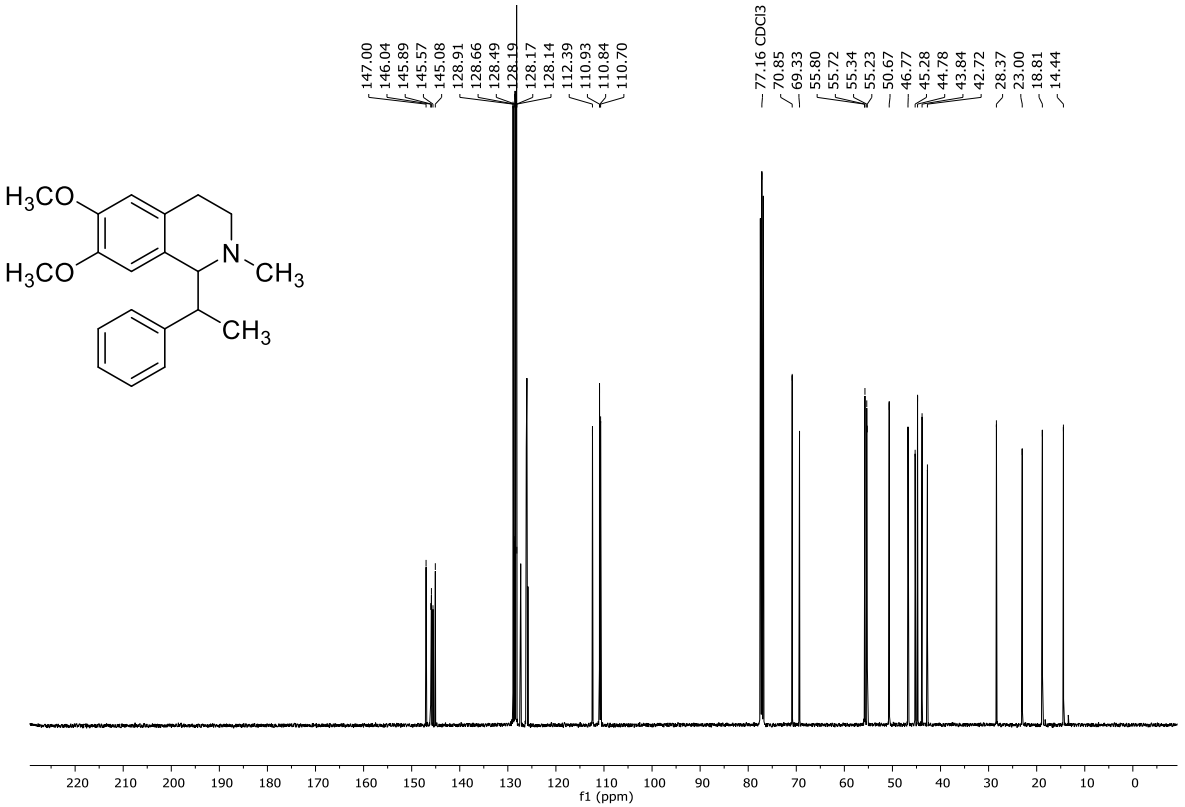
^{13}C-NMR (100.6 MHz, $CDCl_3$): 1-(bis(4-fluorophenyl)methyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3c**, rotamers).



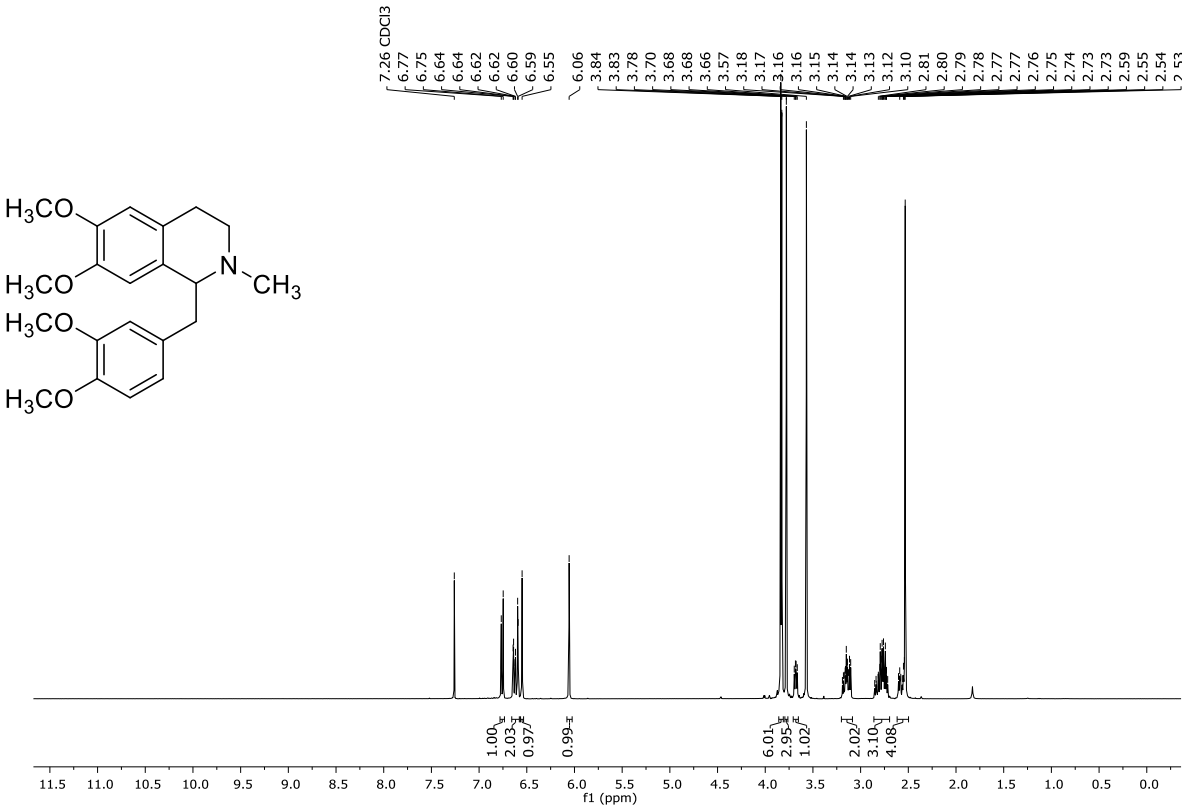
^{19}F-NMR (376.5 MHz, $CDCl_3$): 1-(bis(4-fluorophenyl)methyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3c**, rotamers).



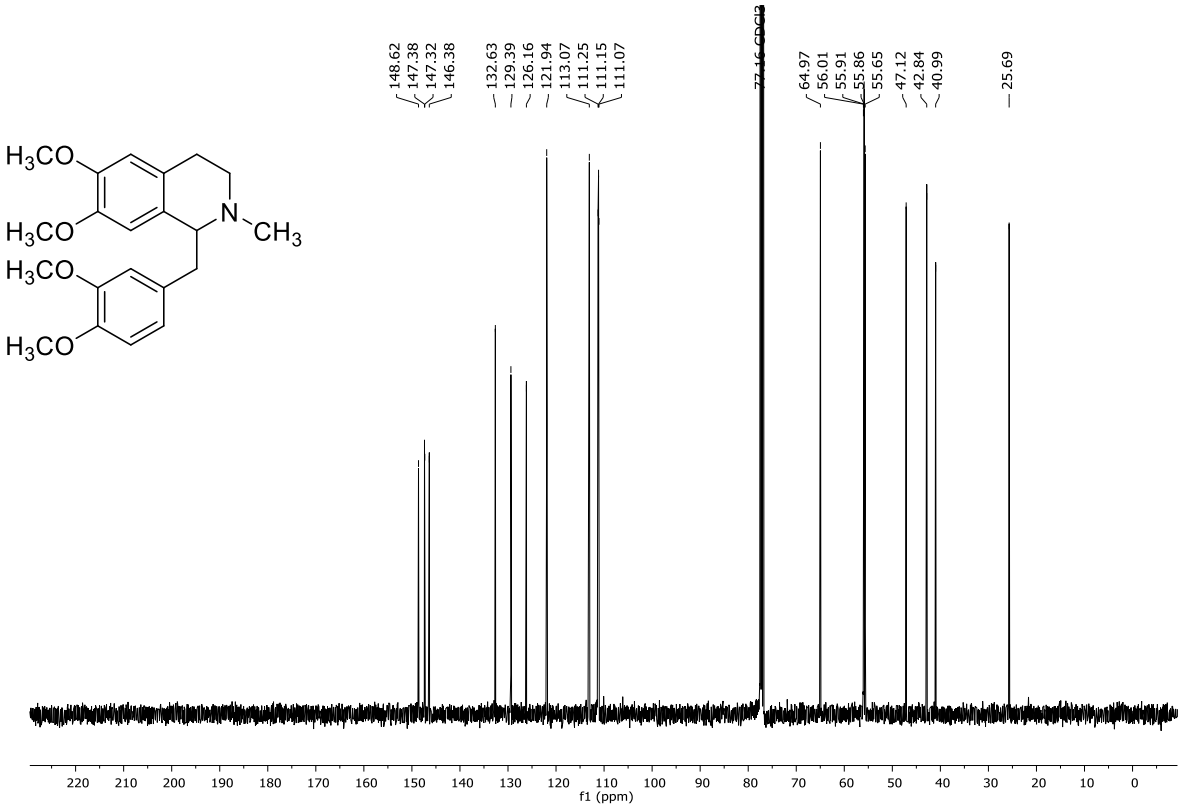
^{1}H-NMR (400 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(1-phenylethyl)-1,2,3,4-tetrahydro-isoquinoline (**3d**, two diastereomers).



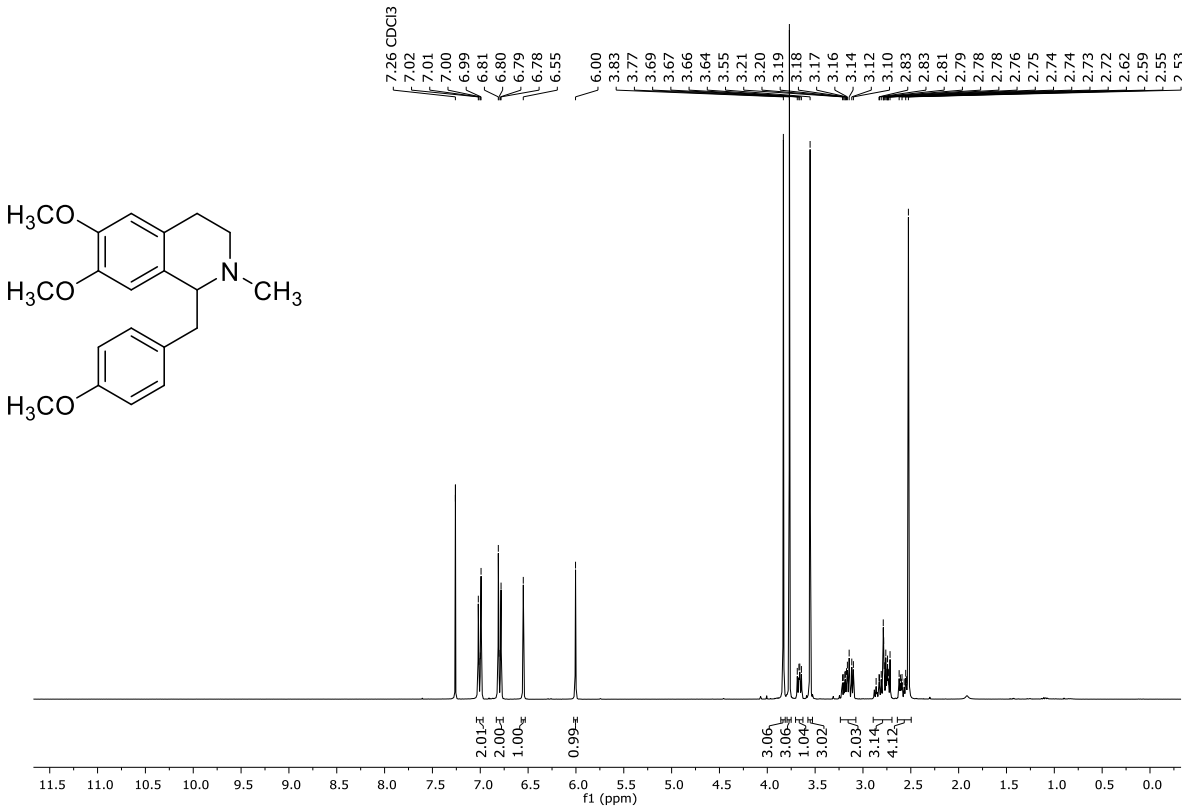
^{13}C-NMR (100.6 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(1-phenylethyl)-1,2,3,4-tetrahydro-isoquinoline (**3d,** two diastereomers).



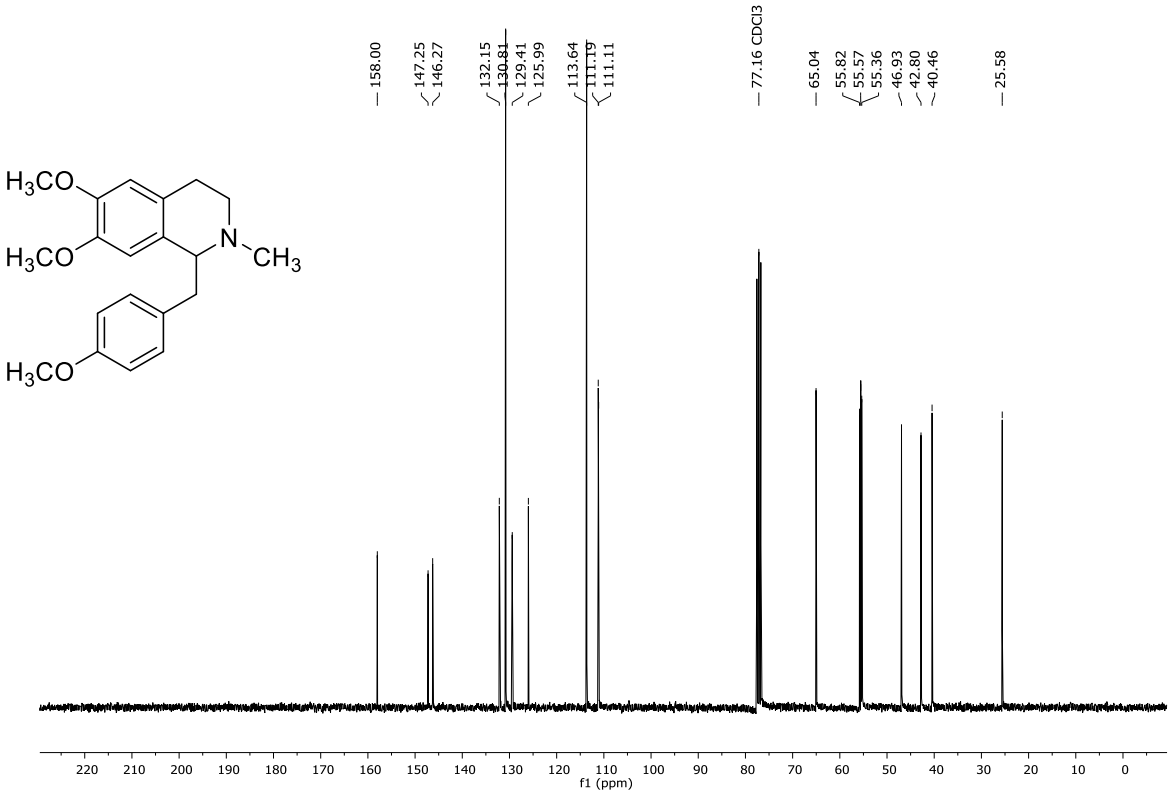
^{1}H-NMR (400 MHz, $CDCl_3$): (±)-laudanosine (**3a**).



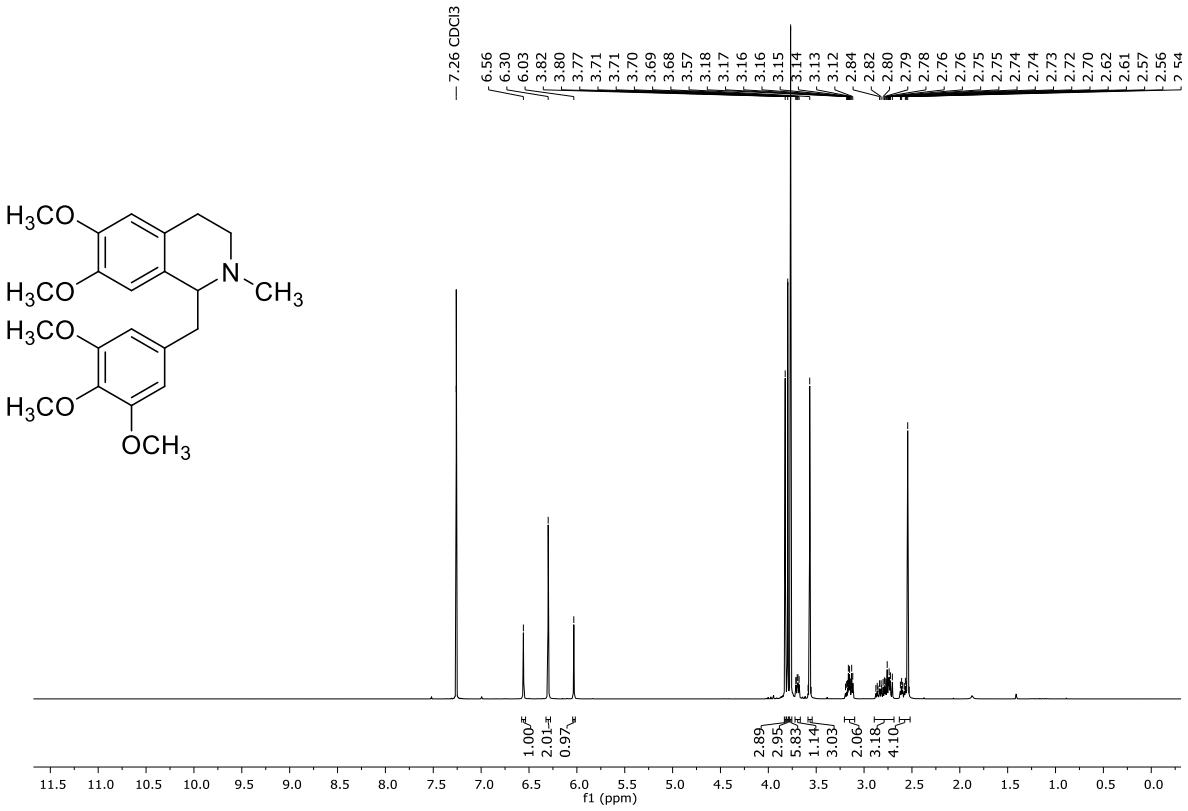
^{13}C-NMR (100.6 MHz, $CDCl_3$): (±)-laudanosine (**3a**).



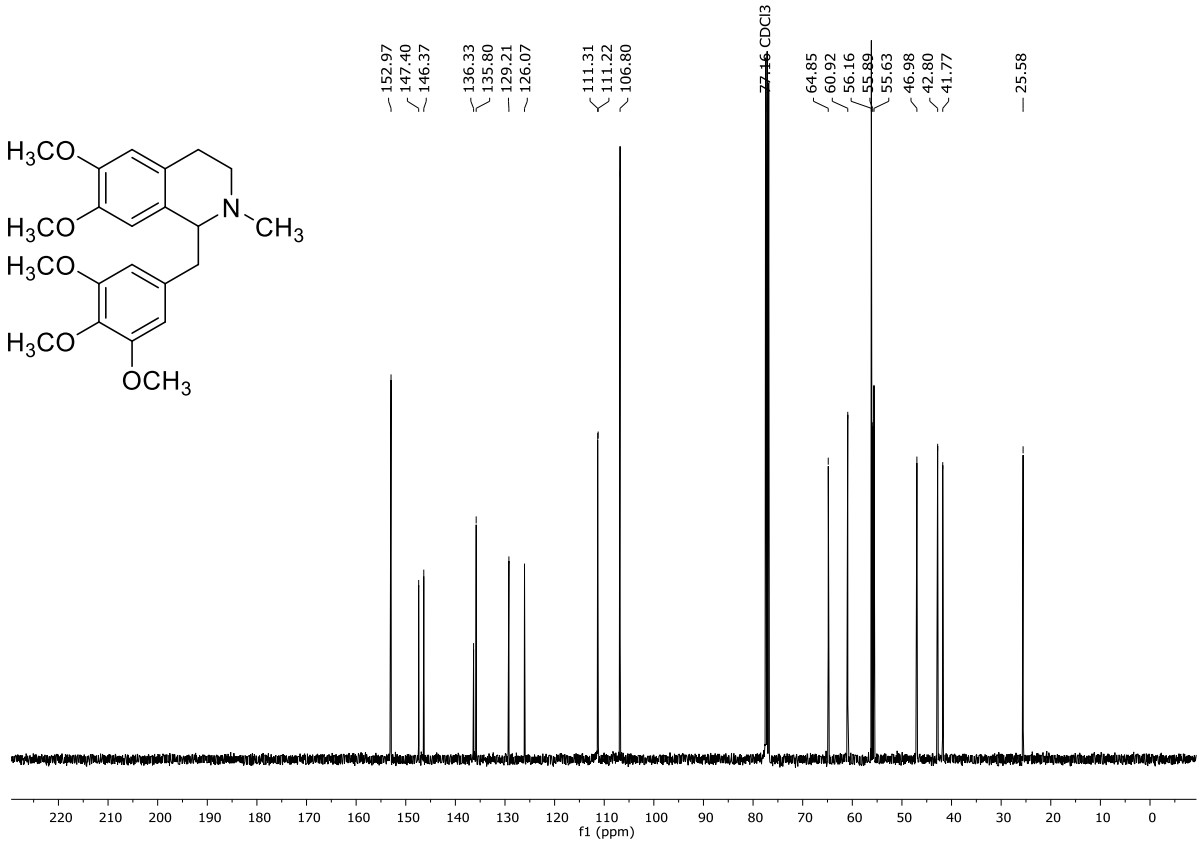
^{1}H-NMR (300 MHz, $CDCl_3$): 6,7-dimethoxy-1-(4-methoxybenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3e**).



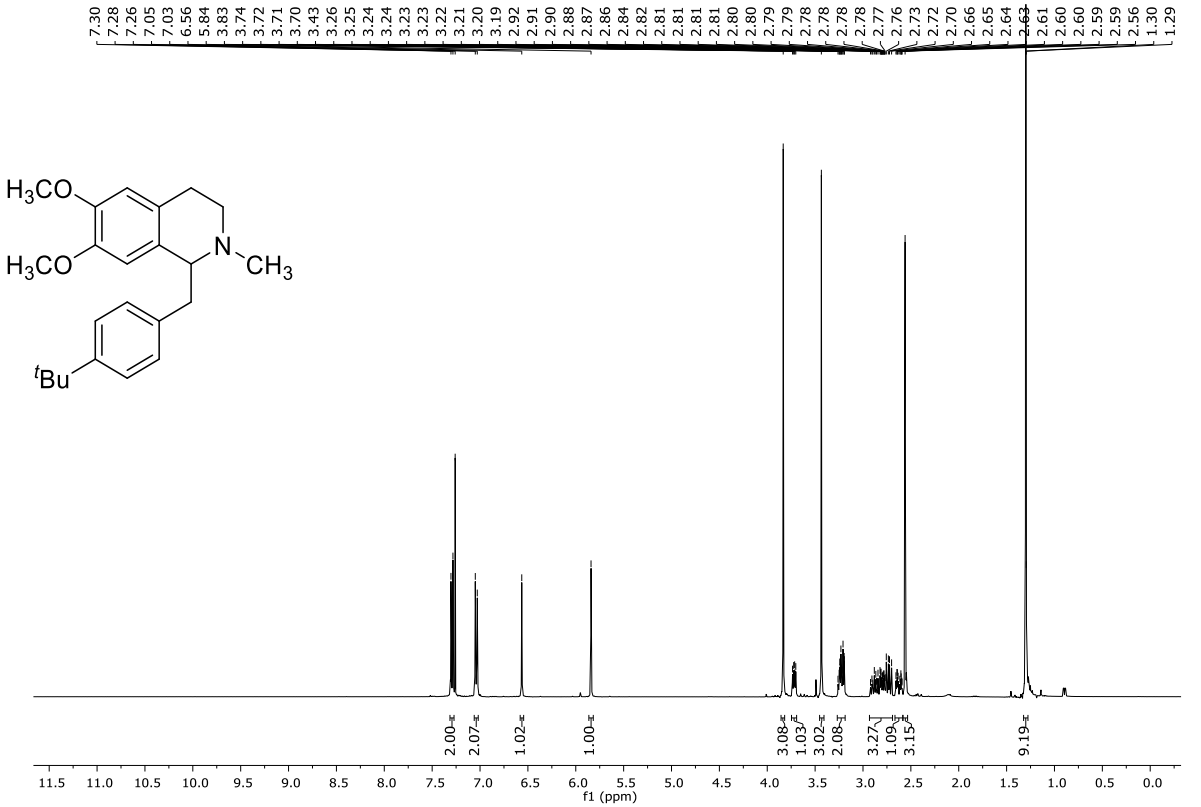
^{13}C-NMR (75.5 MHz, $CDCl_3$): 6,7-dimethoxy-1-(4-methoxybenzyl)-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3e**).



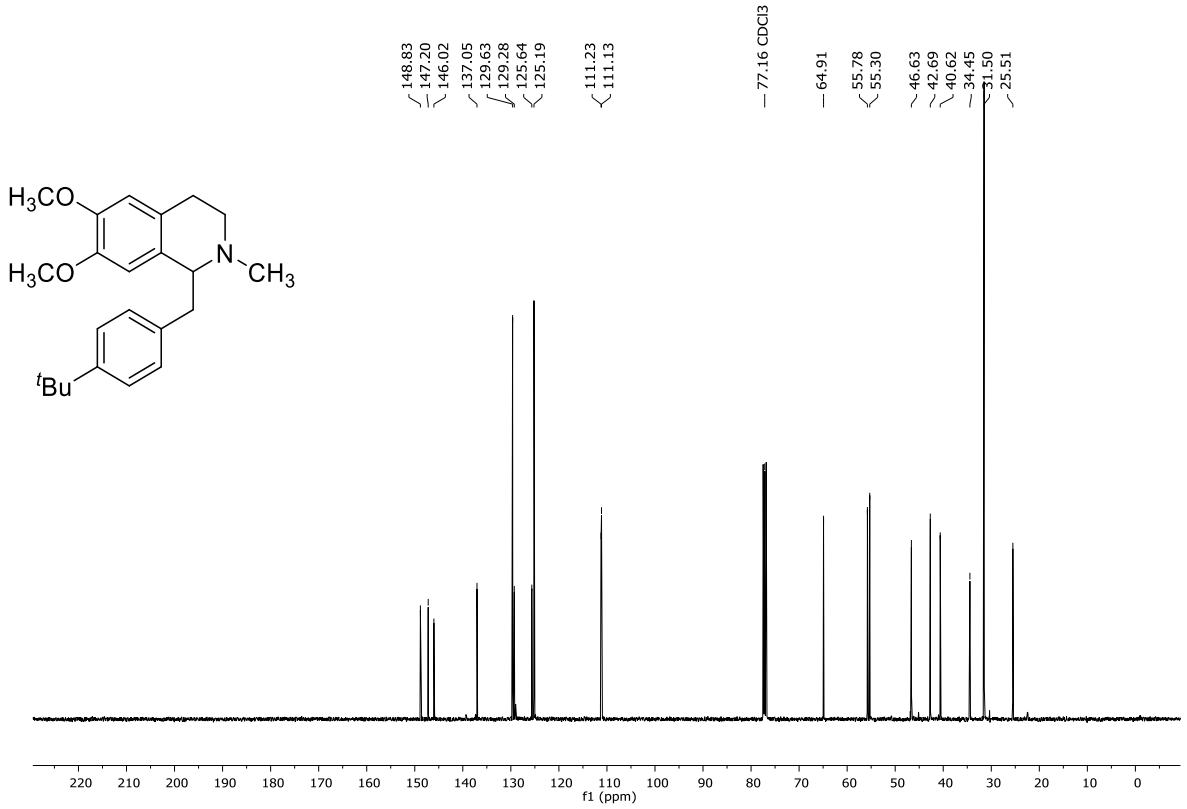
^{1}H-NMR (400 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(3,4,5-trimethoxybenzyl)-1,2,3,4-tetrahydroisoquinoline (**3f**).



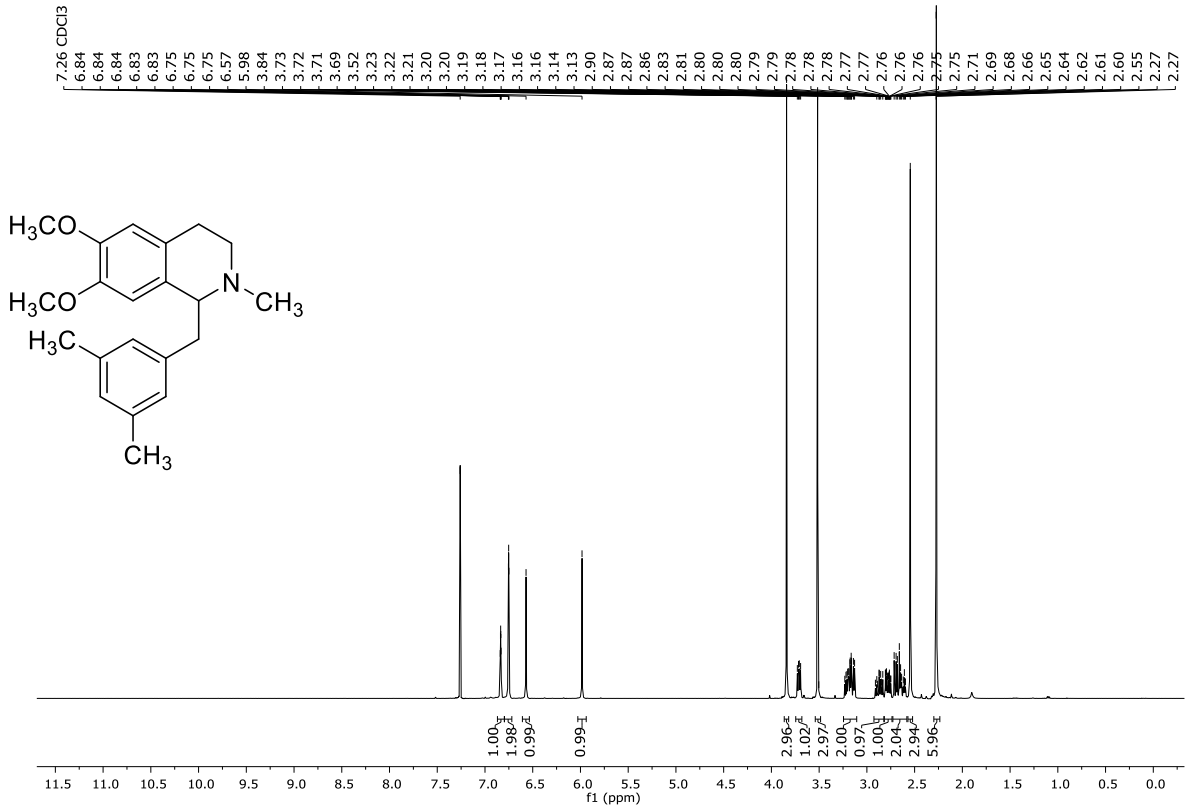
^{13}C-NMR (100.6 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(3,4,5-trimethoxybenzyl)-1,2,3,4-tetrahydroisoquinoline (**3f**).



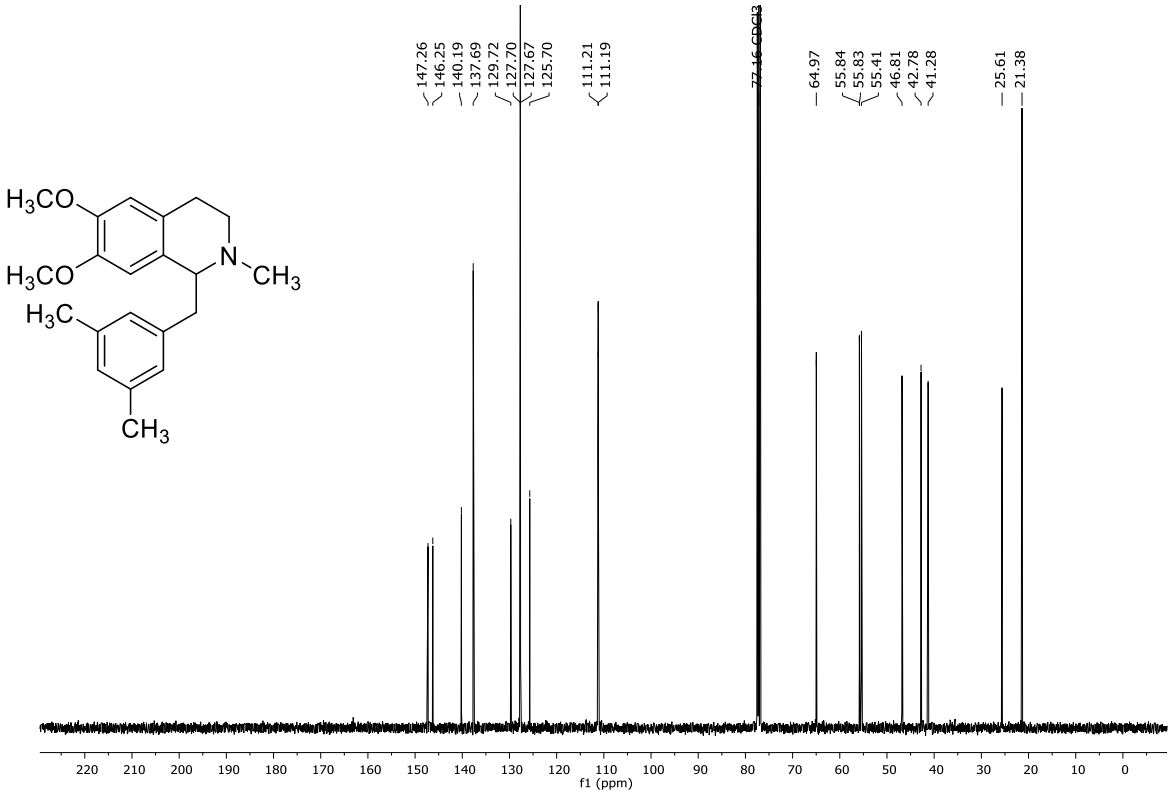
^{1}H-NMR (400 MHz, $CDCl_3$): 1-(4-(*tert*-butyl)benzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3g**).



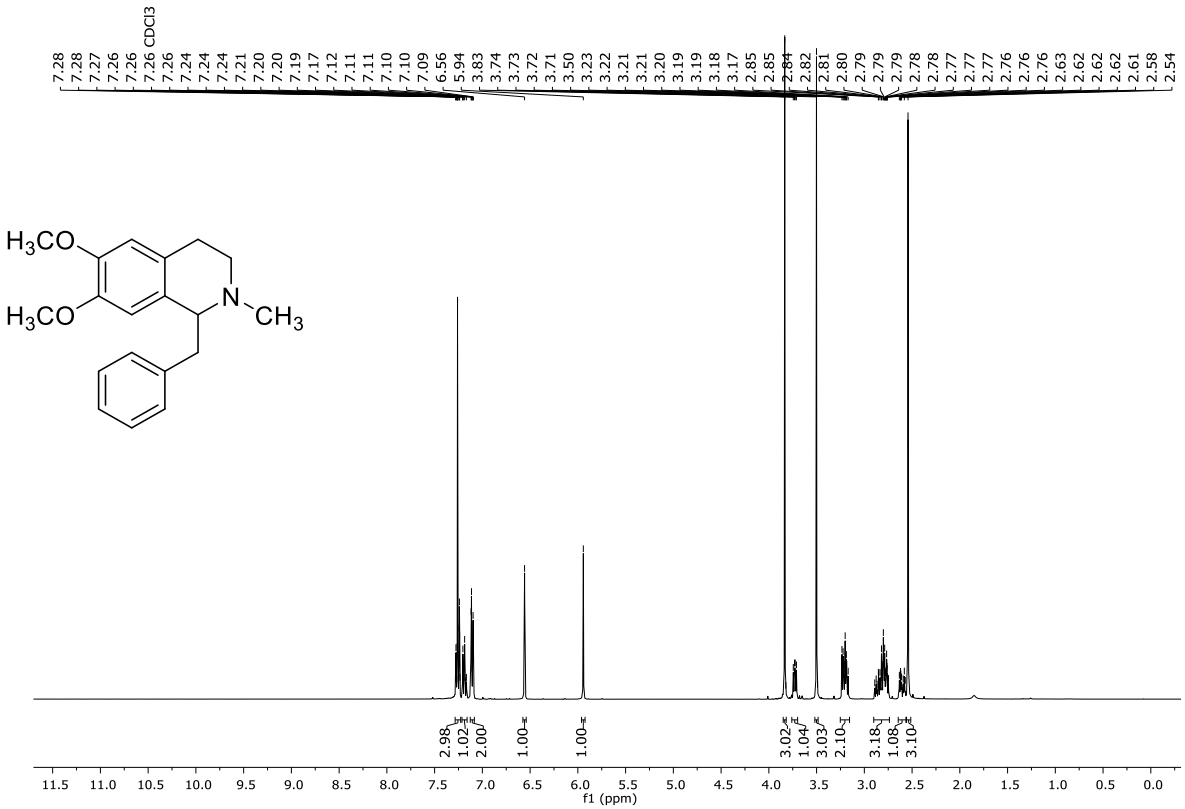
^{13}C-NMR (100.6 MHz, $CDCl_3$): 1-(4-(*tert*-butyl)benzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3g**).



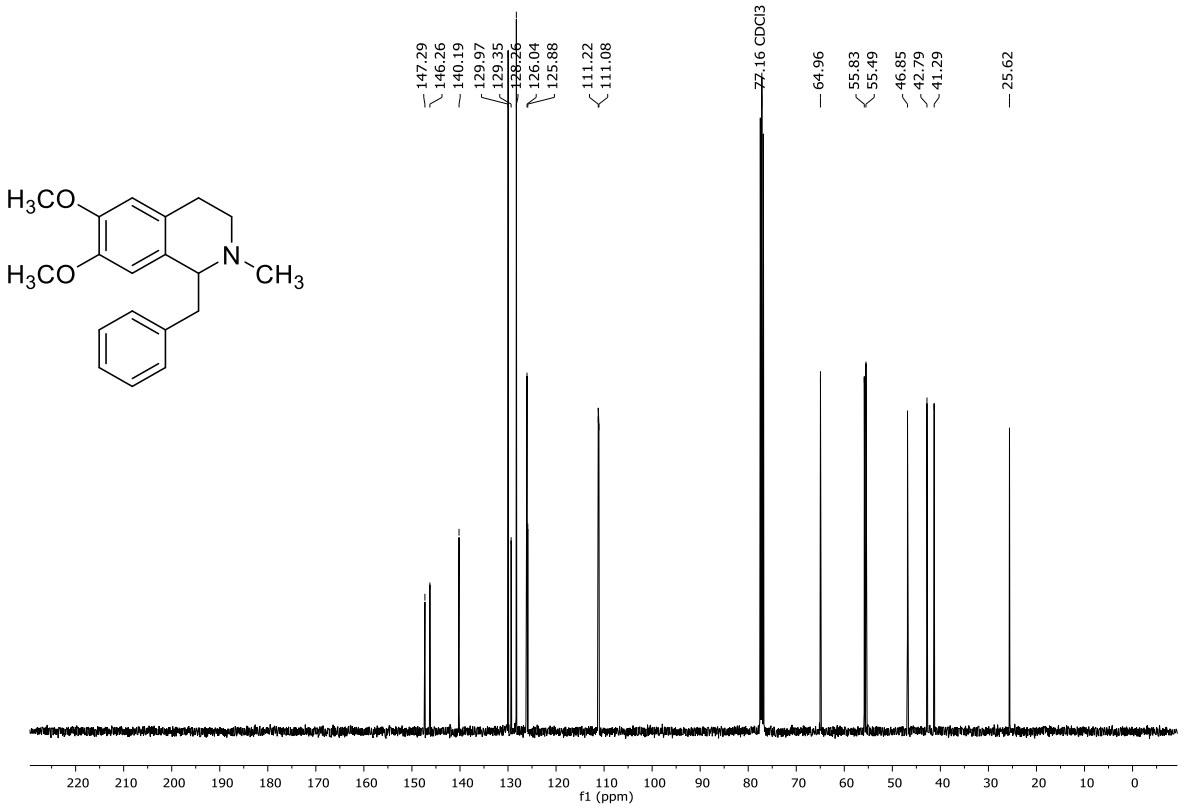
^{1}H-NMR (400 MHz, $CDCl_3$): 1-(3,5-dimethylbenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**3h**).



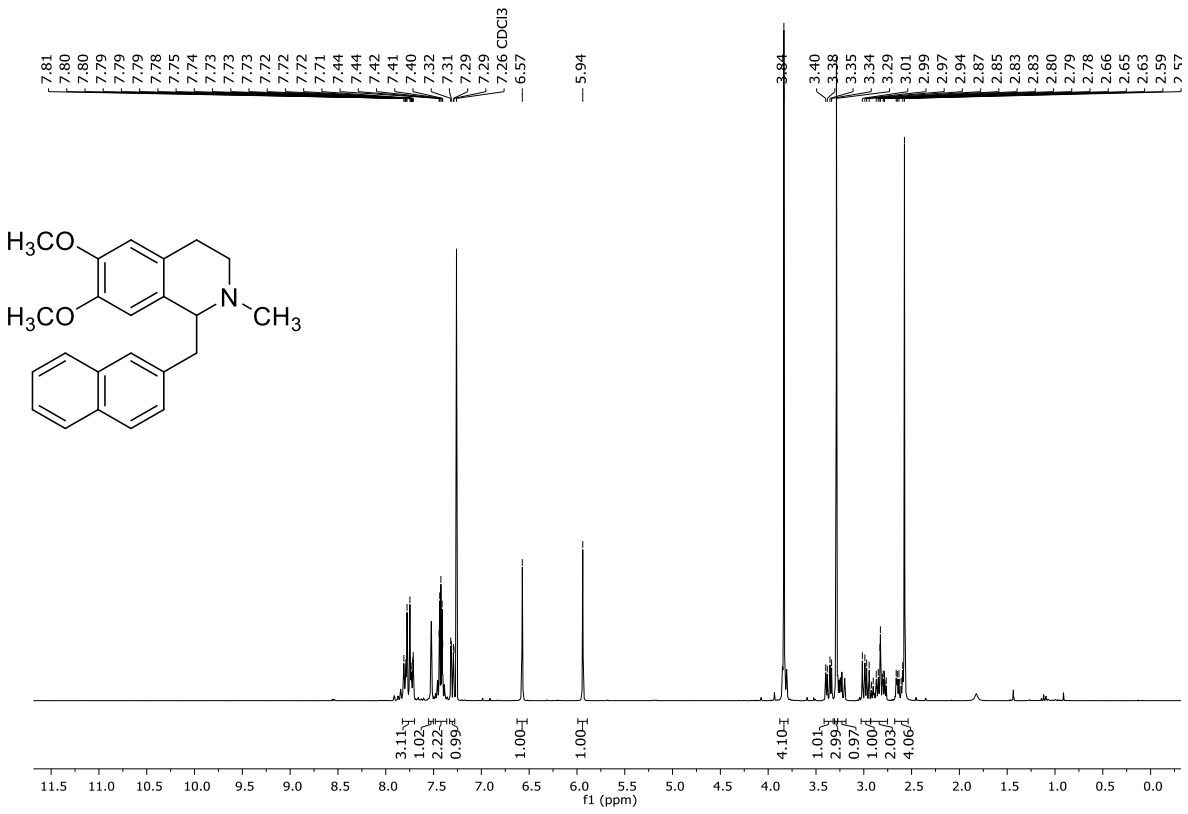
^{13}C-NMR (100.6 MHz, $CDCl_3$): 1-(3,5-dimethylbenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetra-hydroisoquinoline (**3h**).



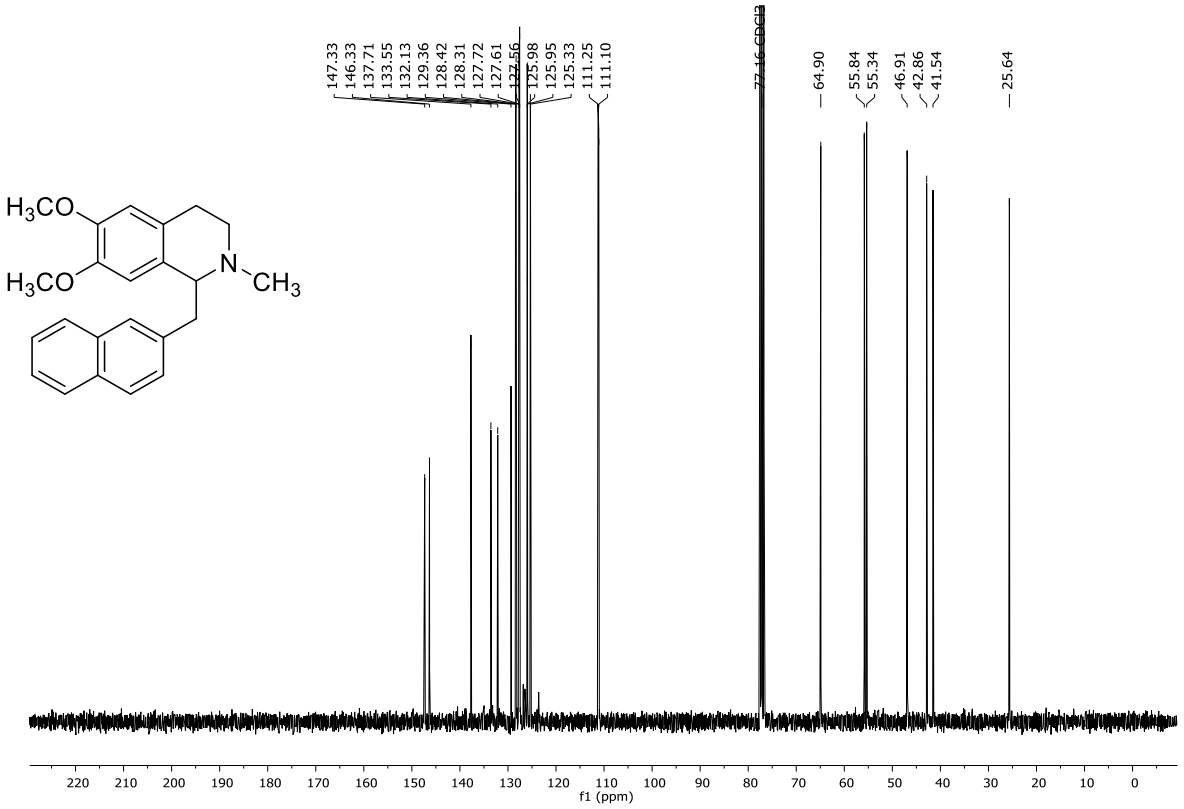
^{1}H-NMR (400 MHz, $CDCl_3$): 1-benzyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroiso-quinoline (**3i**).



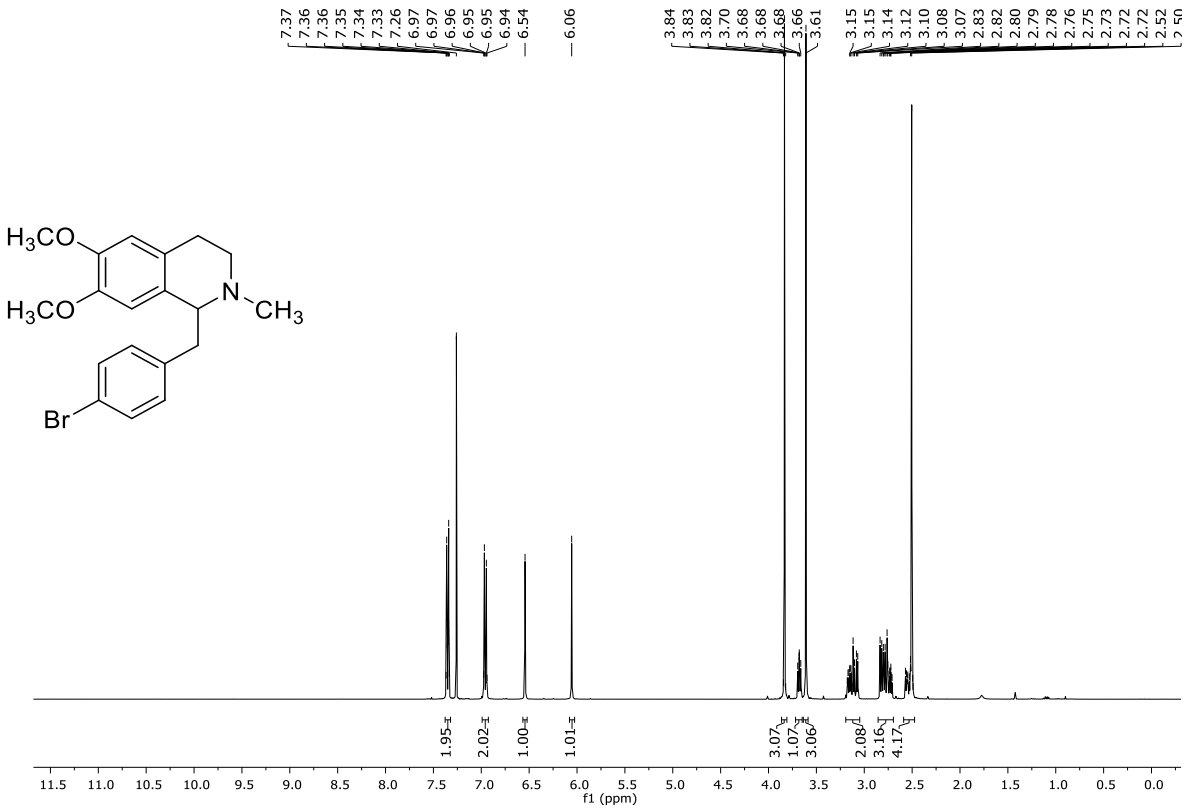
^{13}C-NMR (100.6 MHz, $CDCl_3$): 1-benzyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-isoquinoline (**3i**).



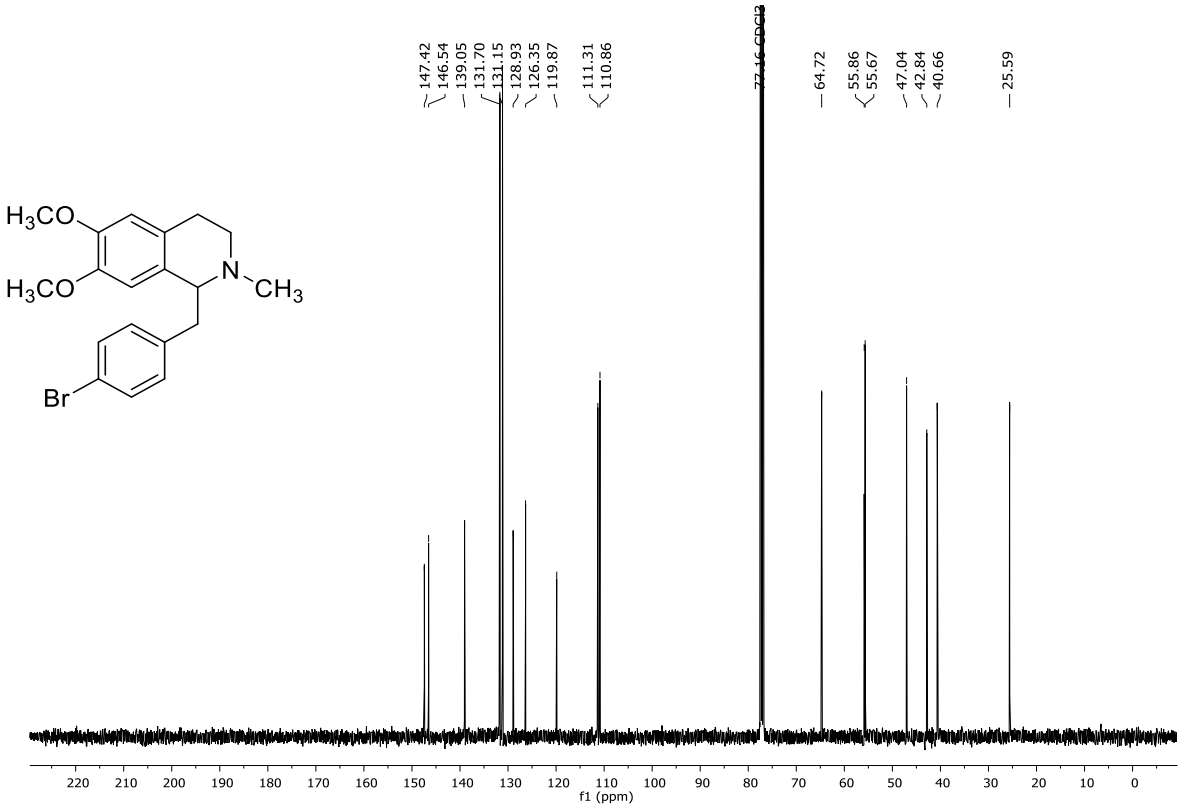
^{1}H-NMR (300 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (**3j**).



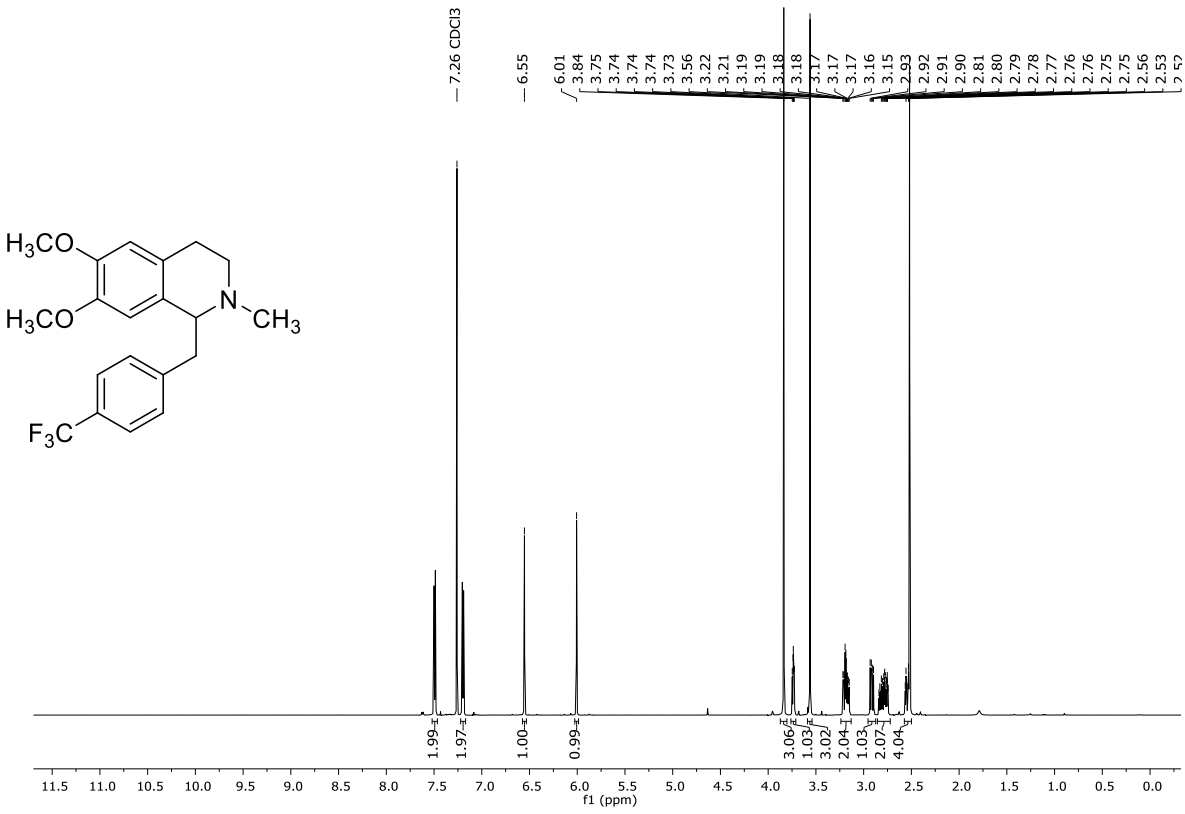
^{13}C-NMR (75.5 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(naphthalen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline (**3j**).



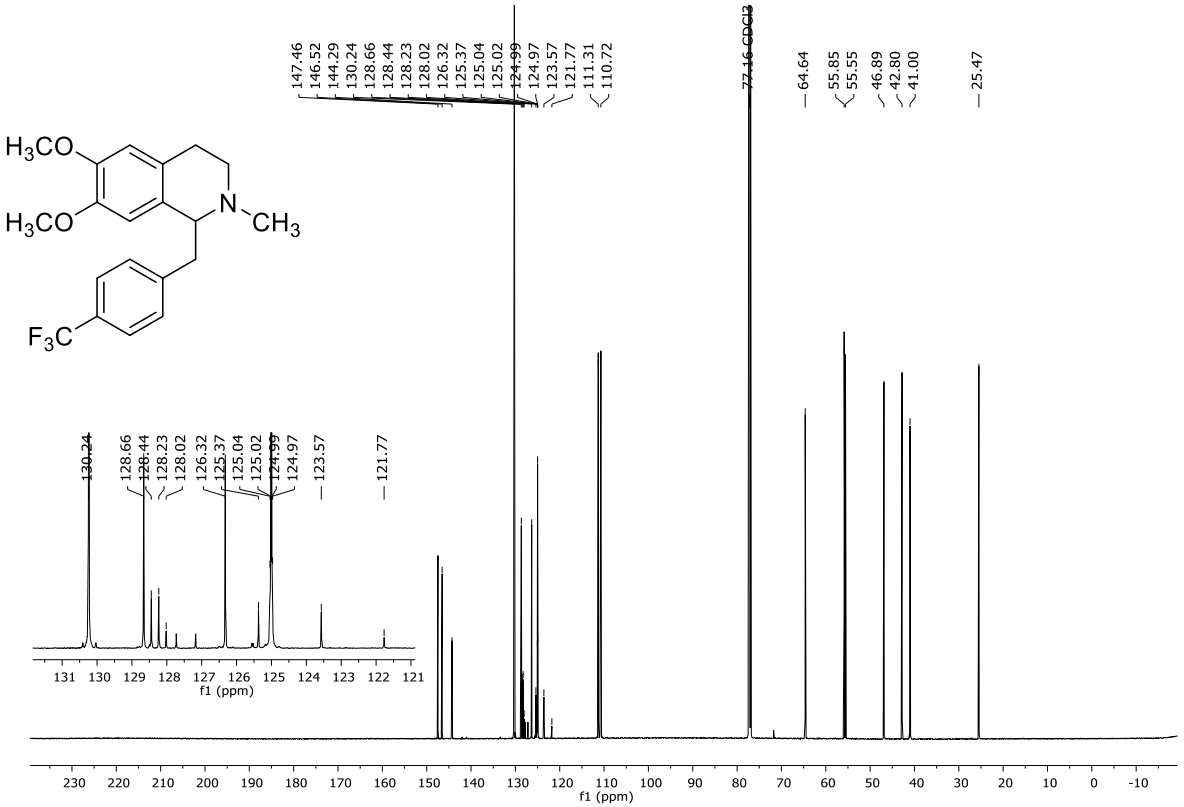
^{1}H-NMR (400 MHz, $CDCl_3$): 1-(4-bromobenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-isoquinoline (**3u**).



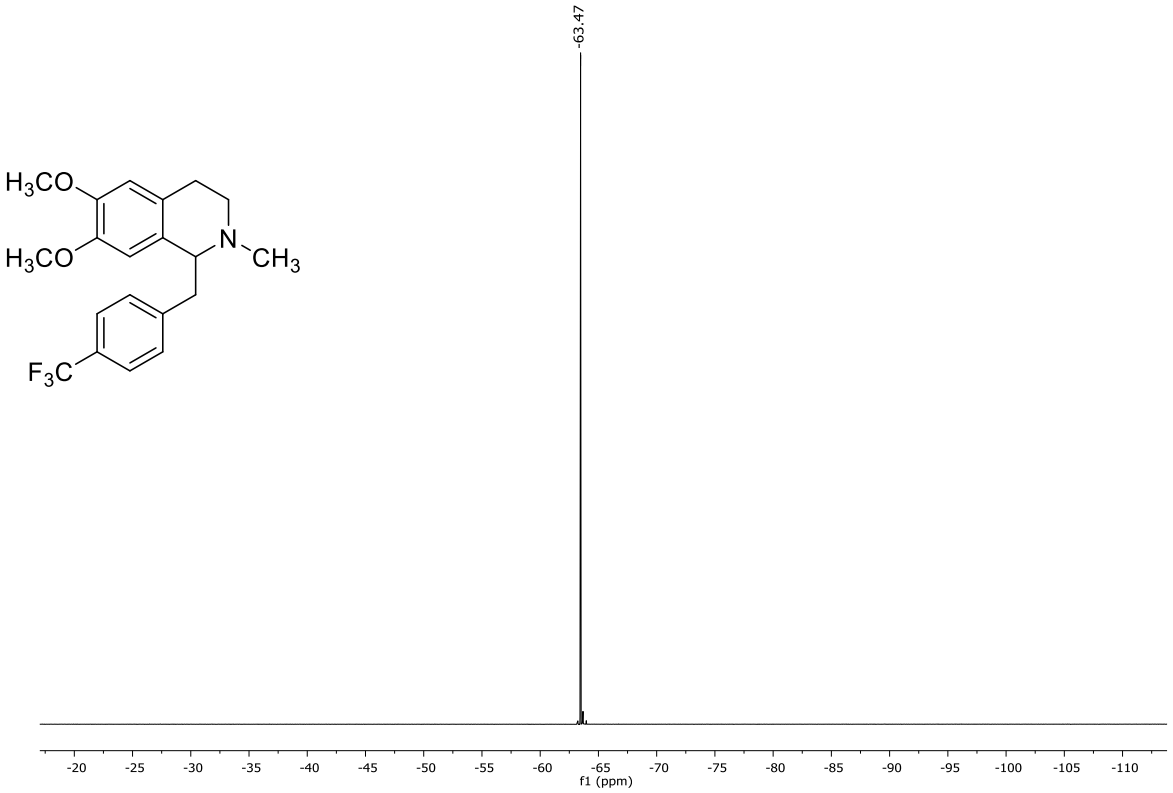
^{13}C-NMR (75.5 MHz, $CDCl_3$): 1-(4-bromobenzyl)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-isoquinoline (**3u**).



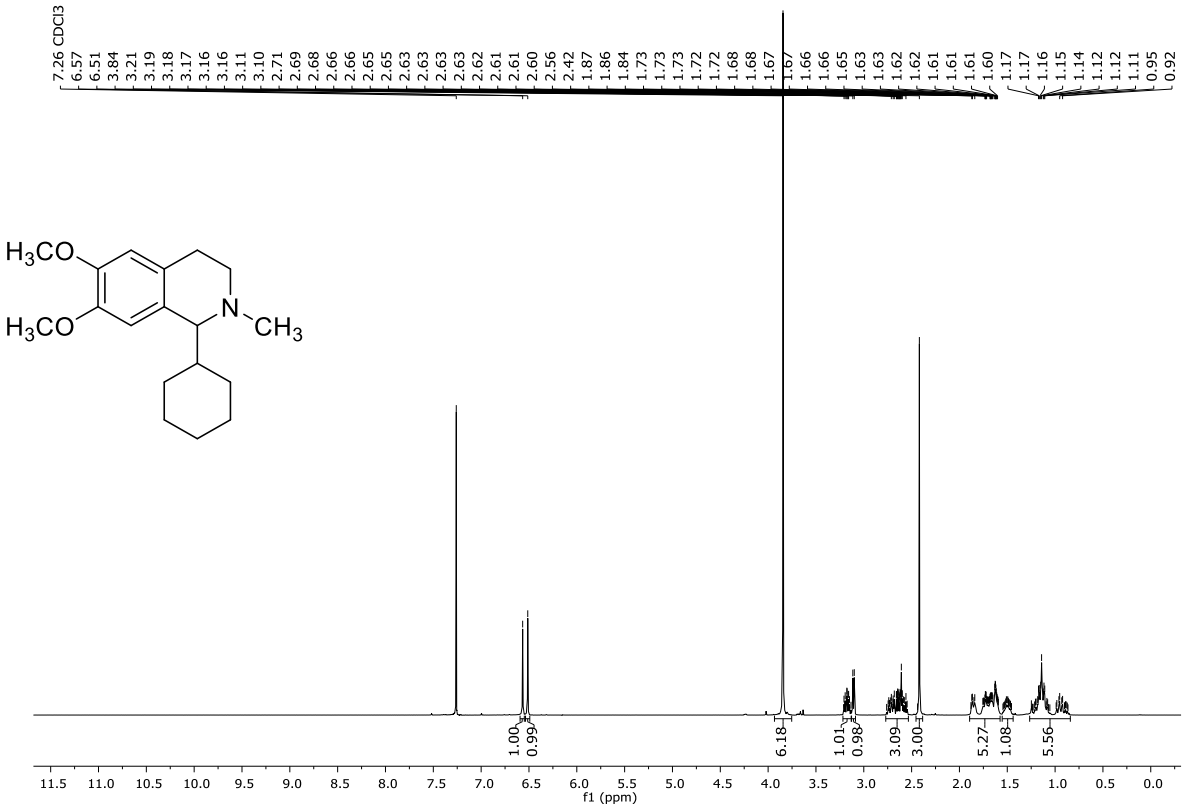
^{1}H-NMR (600 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(4-(trifluoromethyl)benzyl)-1,2,3,4-tetrahydroisoquinoline (**3v**).



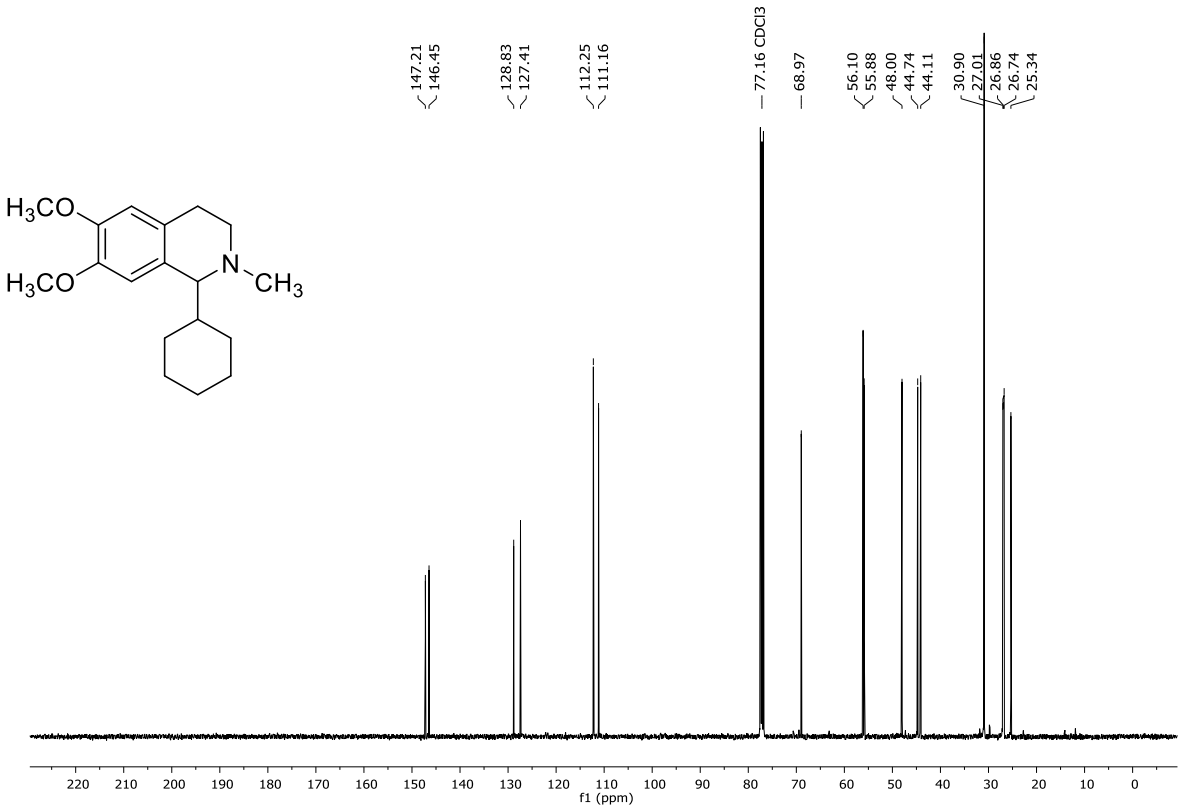
^{13}C-NMR (151 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(4-(trifluoromethyl)benzyl)-1,2,3,4-tetrahydroisoquinoline with zoom to show ^{19}F-^{13}C coupling (**3v**).



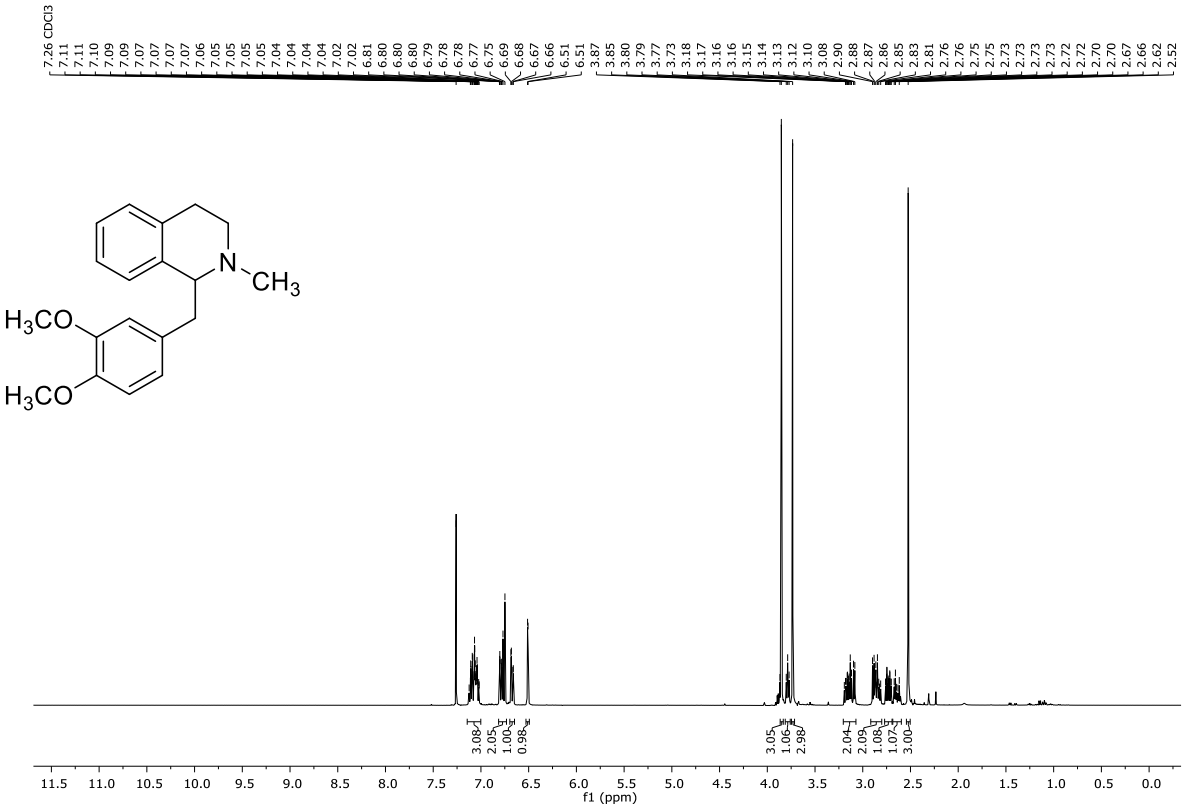
^{19}F-NMR (376.5 MHz, $CDCl_3$): 6,7-dimethoxy-2-methyl-1-(4-(trifluoromethyl)benzyl)-1,2,3,4-tetrahydroisoquinoline (**3v**).



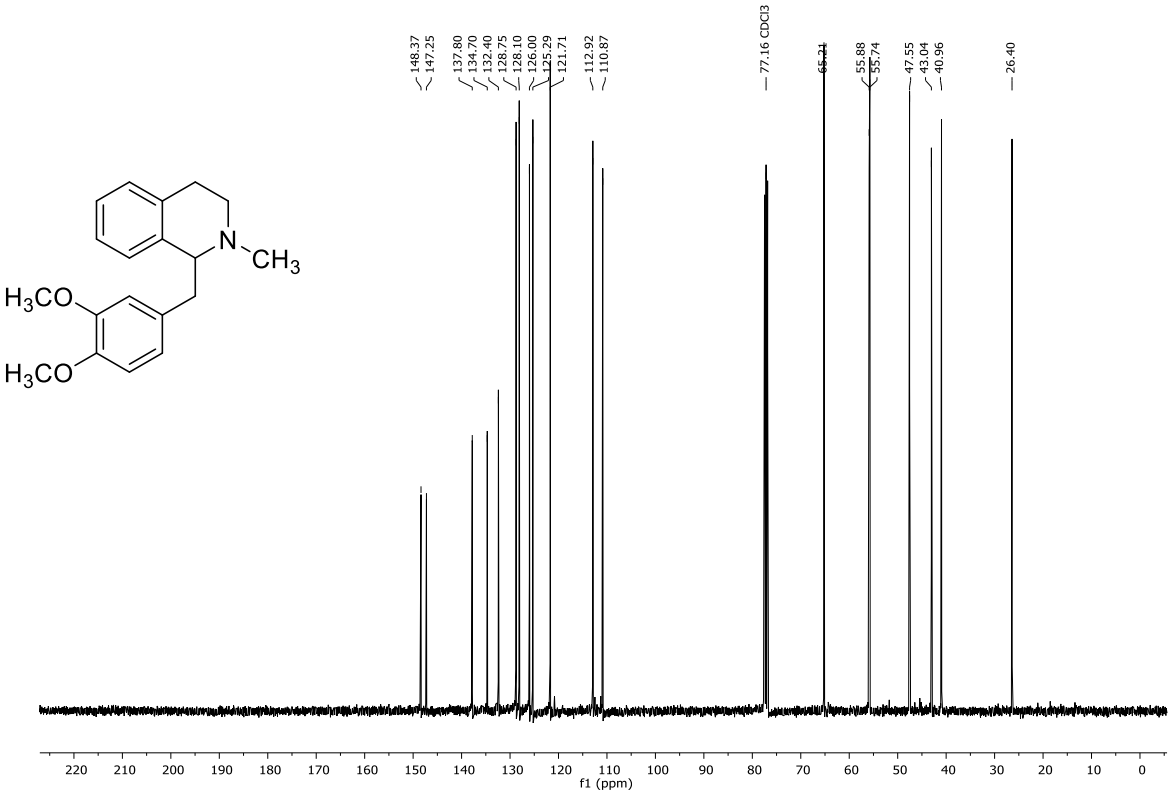
^{1}H-NMR (400 MHz, $CDCl_3$): 1-cyclohexyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-isoquinoline (**3w**).



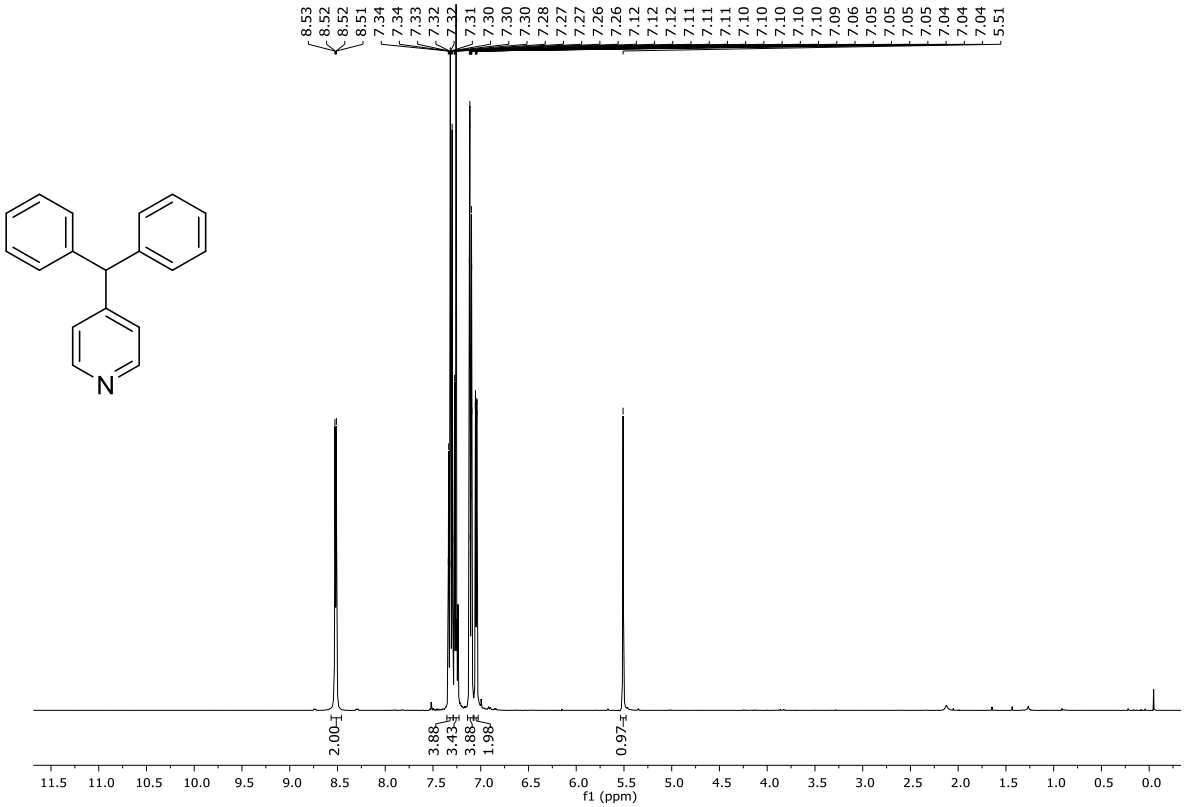
^{13}C-NMR (100.6 MHz, $CDCl_3$): 1-cyclohexyl-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-isoquinoline (**3w**).



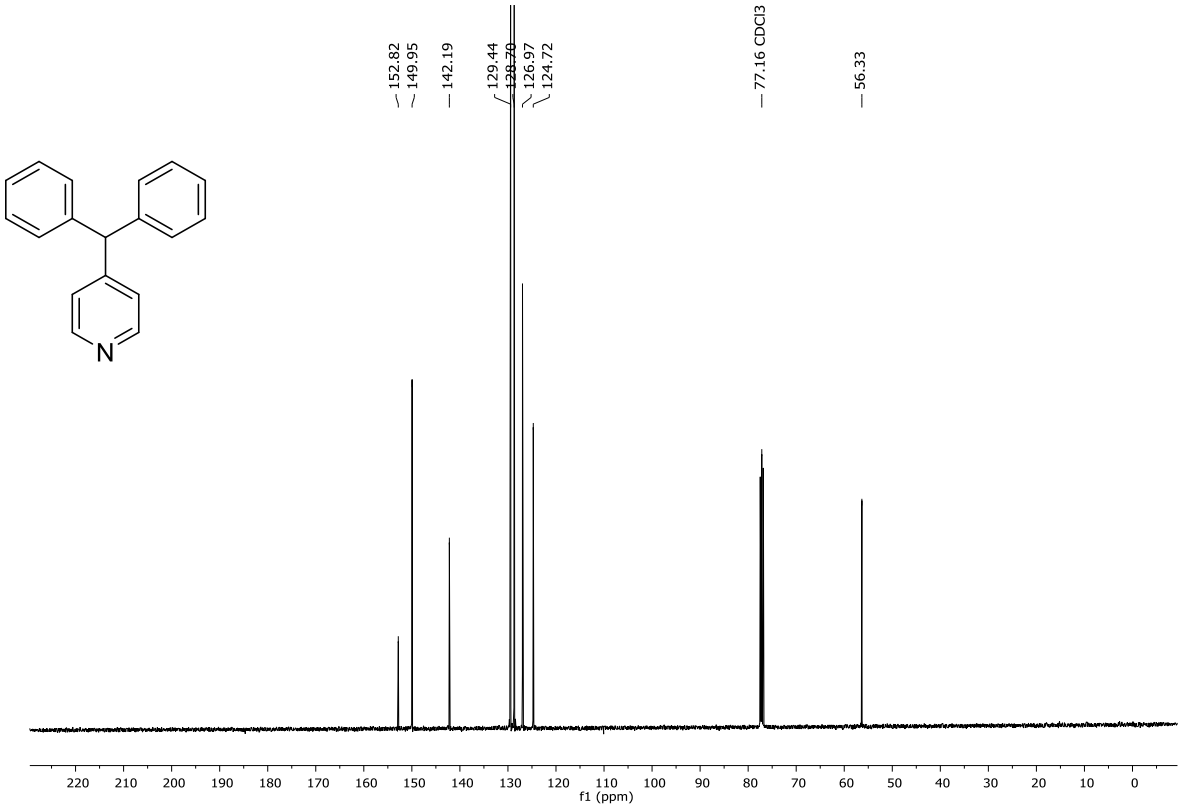
^{1}H-NMR (400 MHz, $CDCl_3$): 1-(3,4-dimethoxybenzyl)-2-methyl-1,2,3,4-tetrahydroiso-quinoline (**3x**).



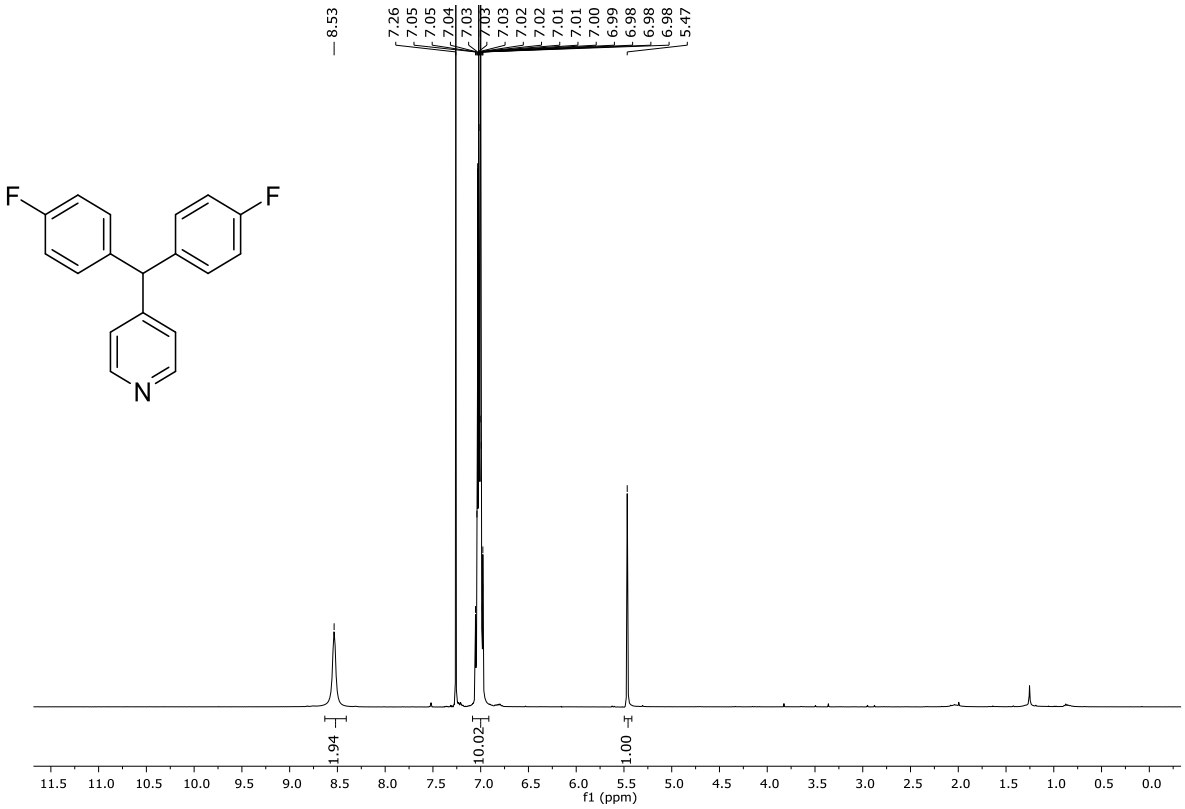
^{13}C-NMR (100.6 MHz, $CDCl_3$): 1-(3,4-dimethoxybenzyl)-2-methyl-1,2,3,4-tetrahydroiso-quinoline (**3x**).



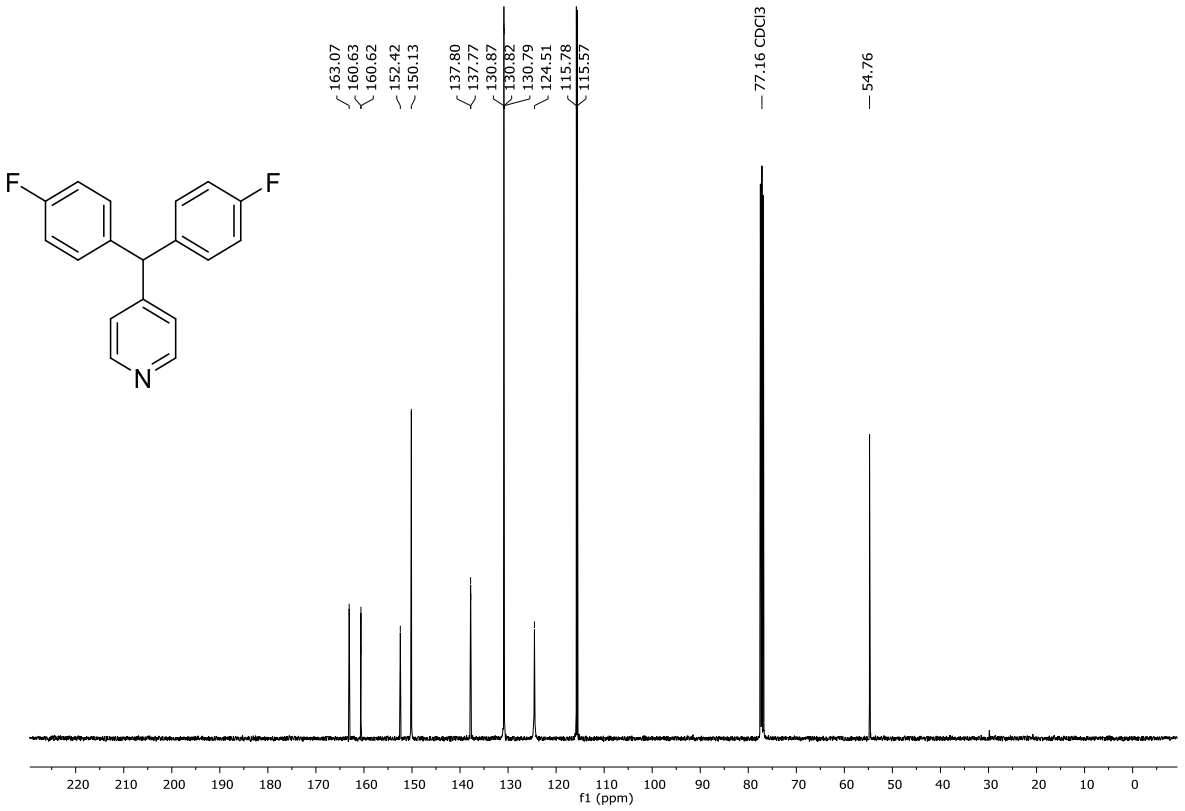
^{1}H-NMR (400 MHz, $CDCl_3$): 4-benzhydrylpyridine (**8b**).



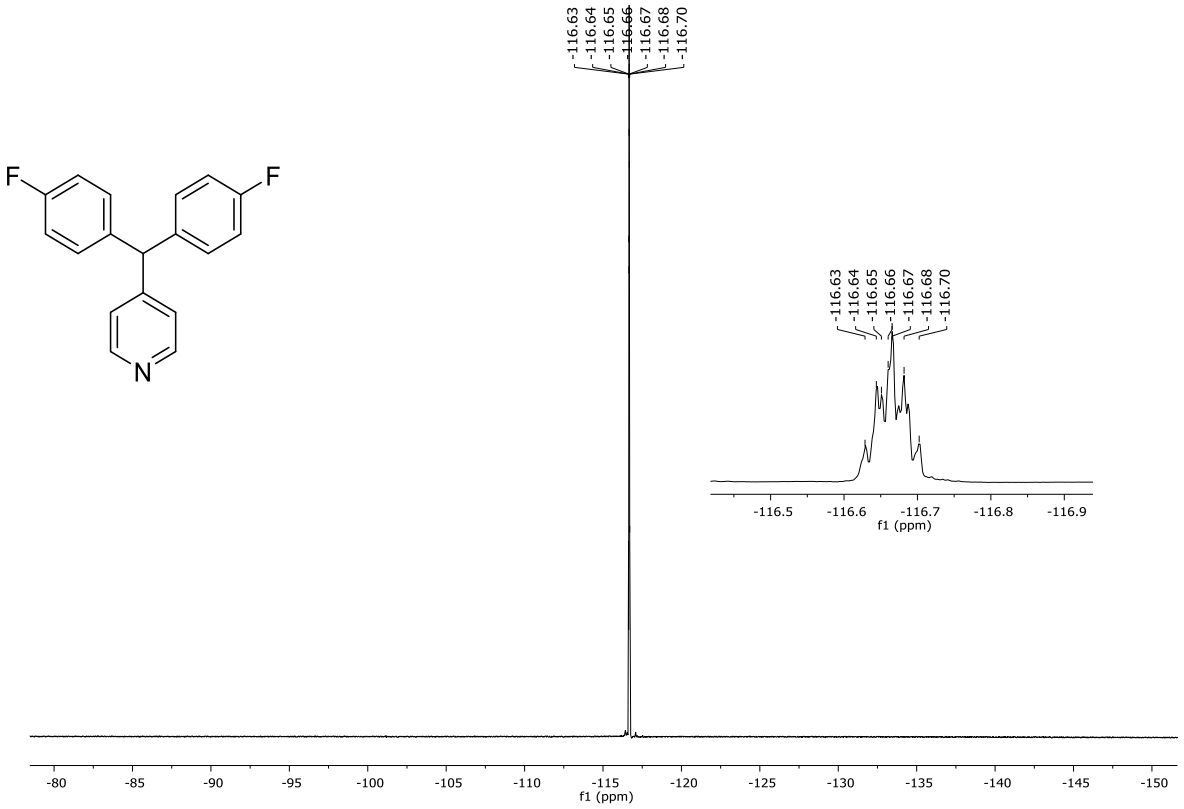
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-benzhydrylpyridine (**8b**).



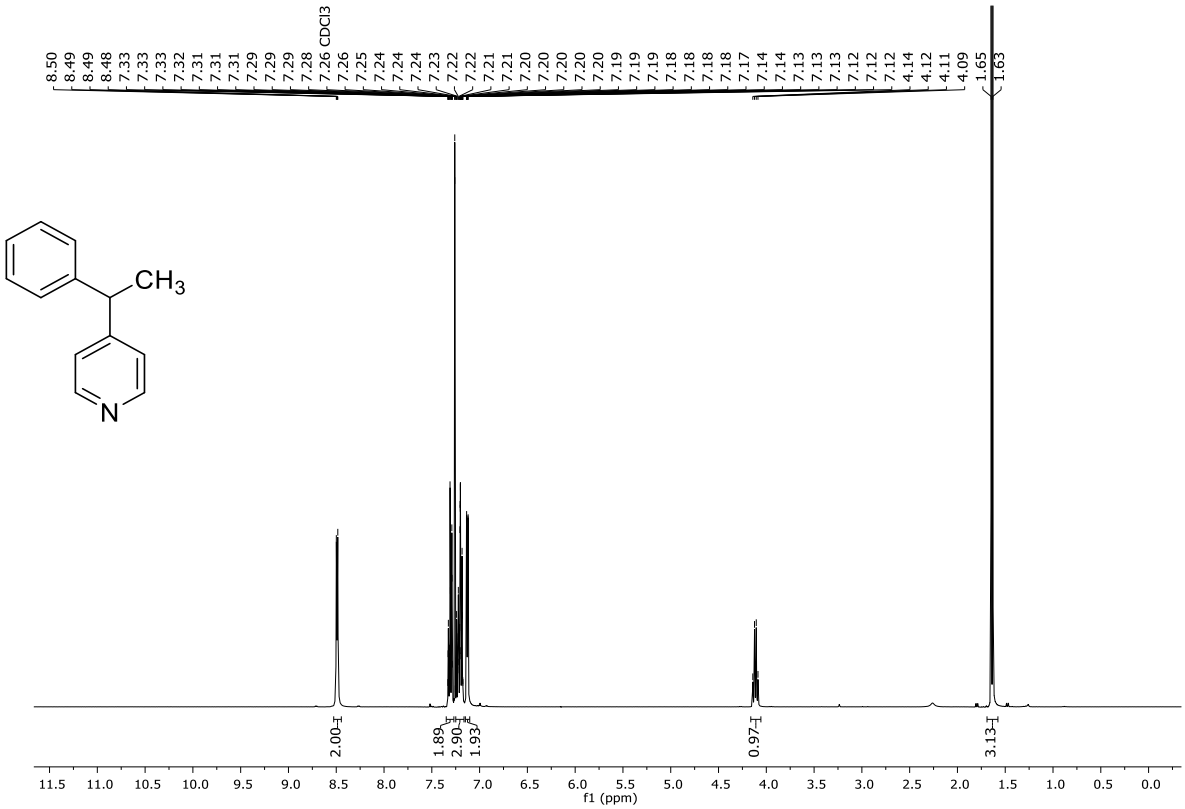
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(bis(4-fluorophenyl)methyl)pyridine (**8c**).



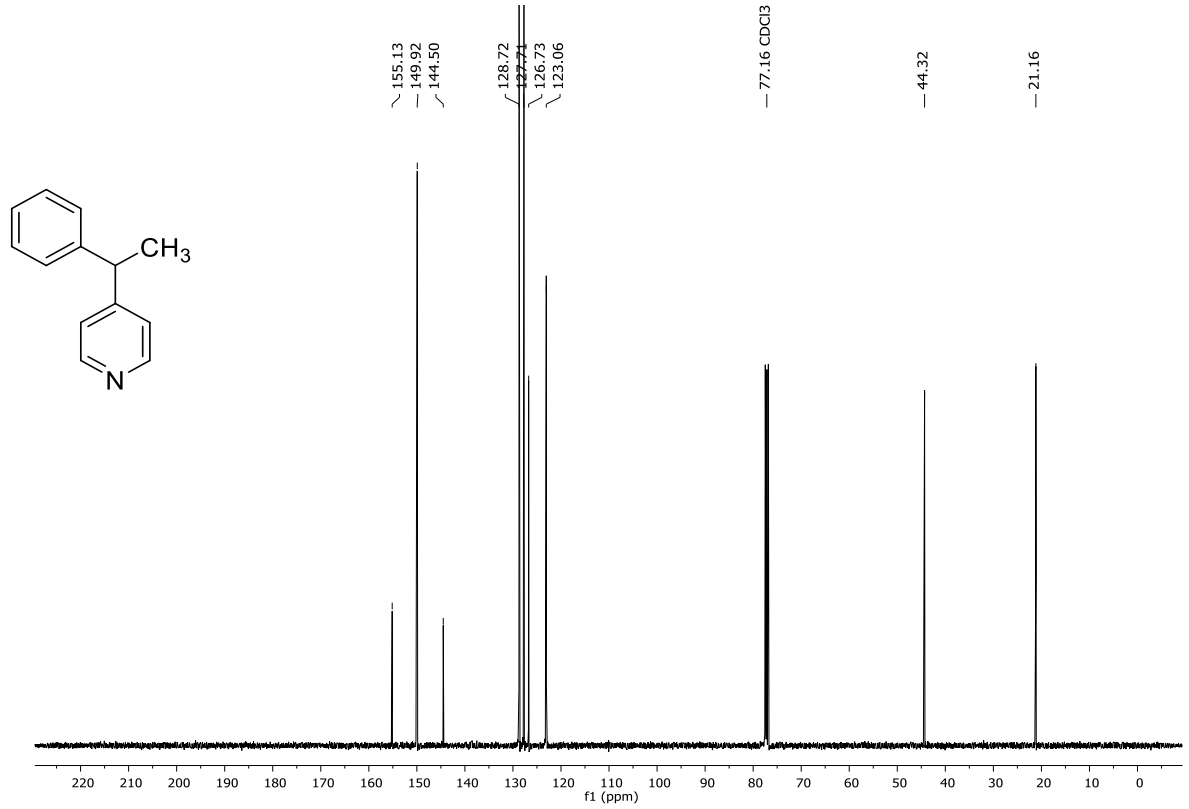
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(bis(4-fluorophenyl)methyl)pyridine (**8c**).



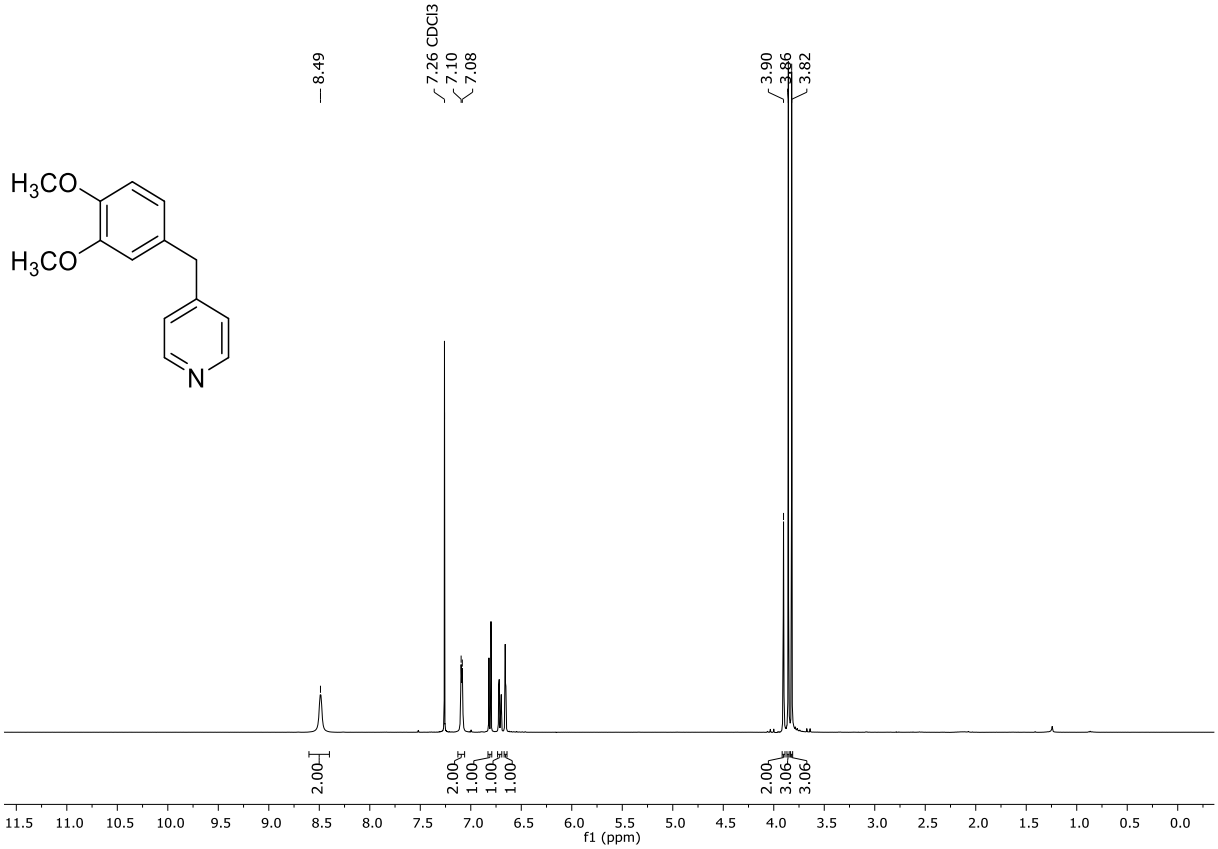
^{19}F-NMR (376.5 MHz, $CDCl_3$): 4-(bis(4-fluorophenyl)methyl)pyridine (**8c**).



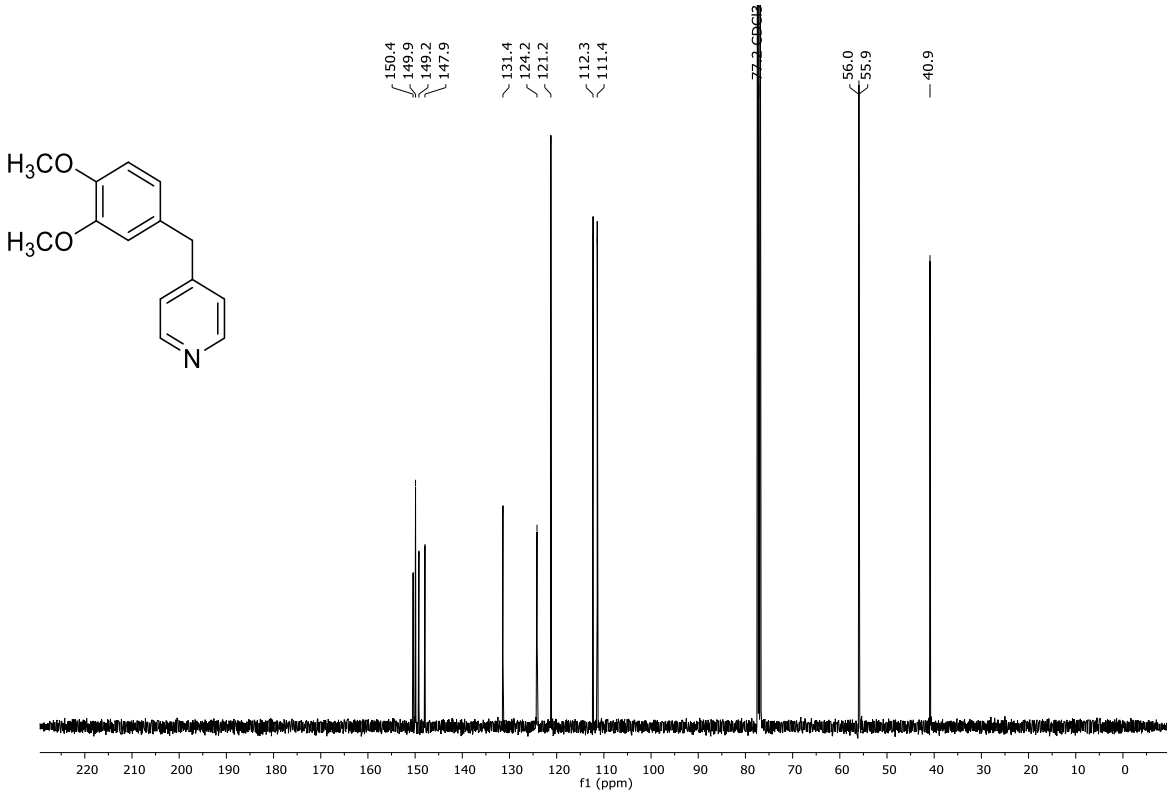
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(1-phenylethyl)pyridine (**8d**).



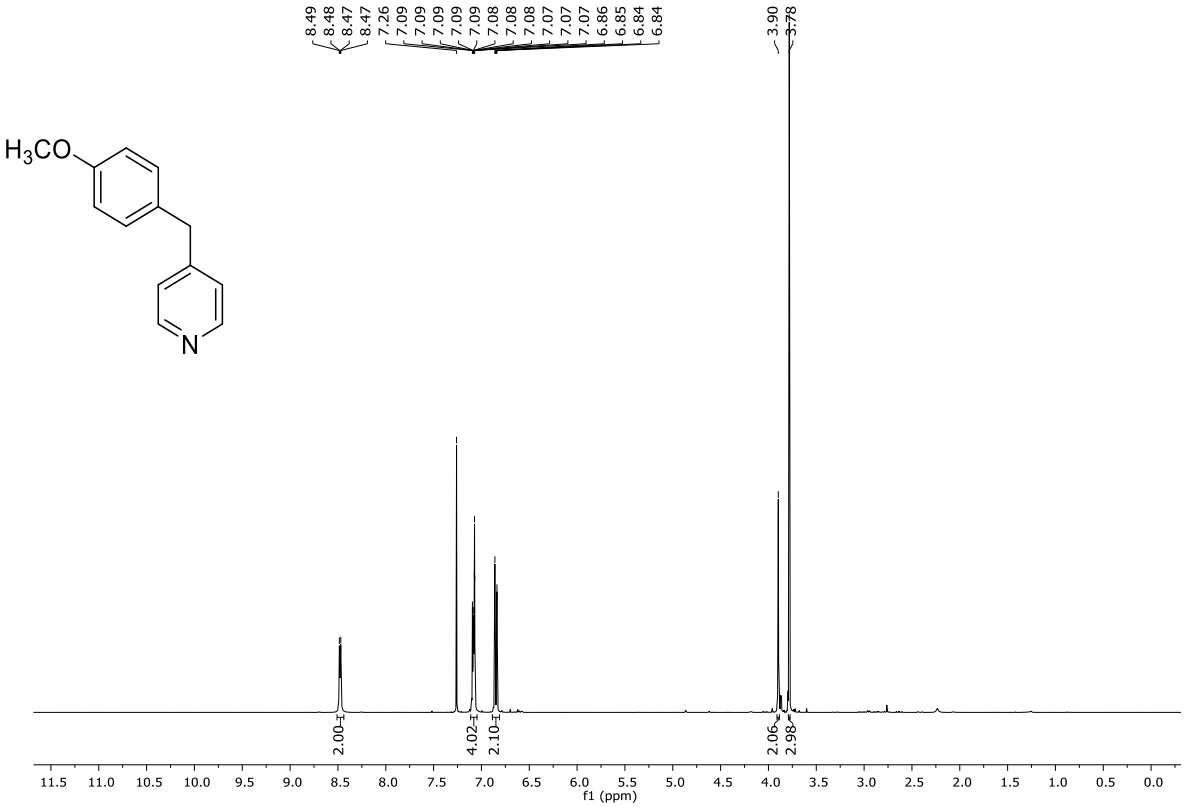
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(1-phenylethyl)pyridine (**8d**).



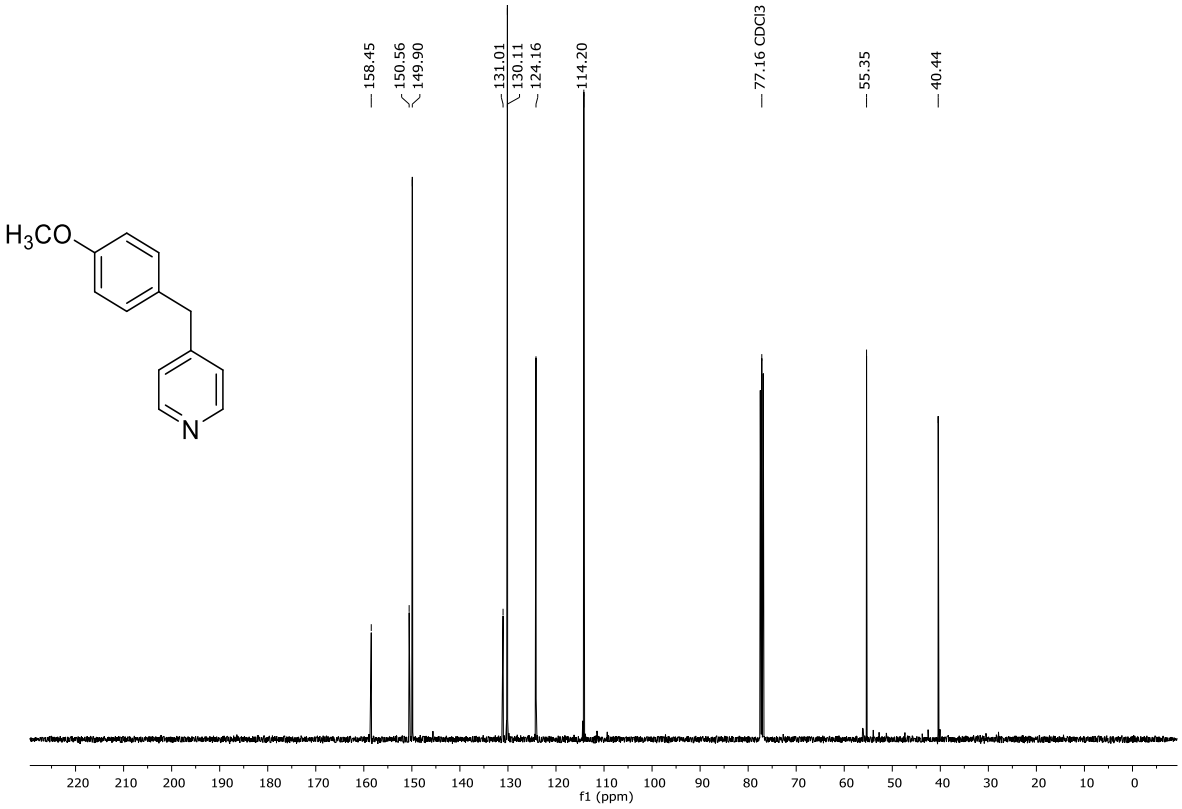
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(3,4-dimethoxybenzyl)pyridine (**8a**).



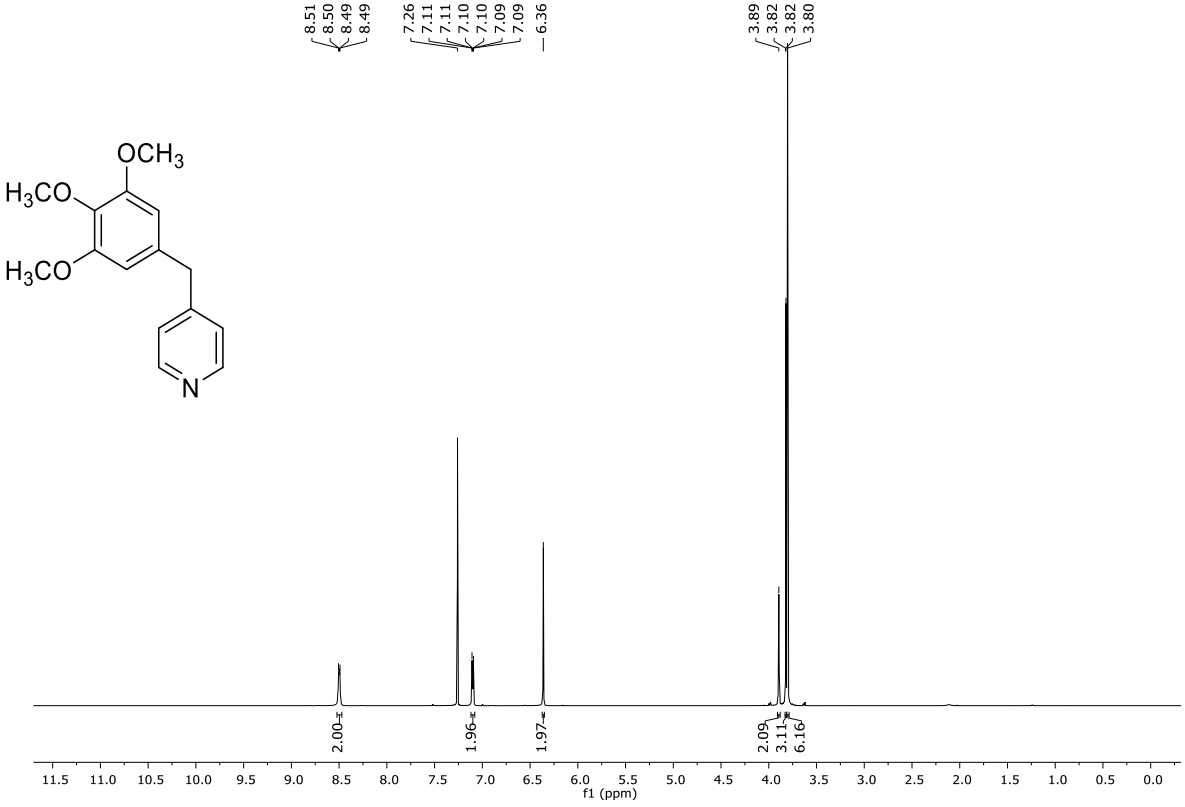
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(3,4-dimethoxybenzyl)pyridine (**8a**).



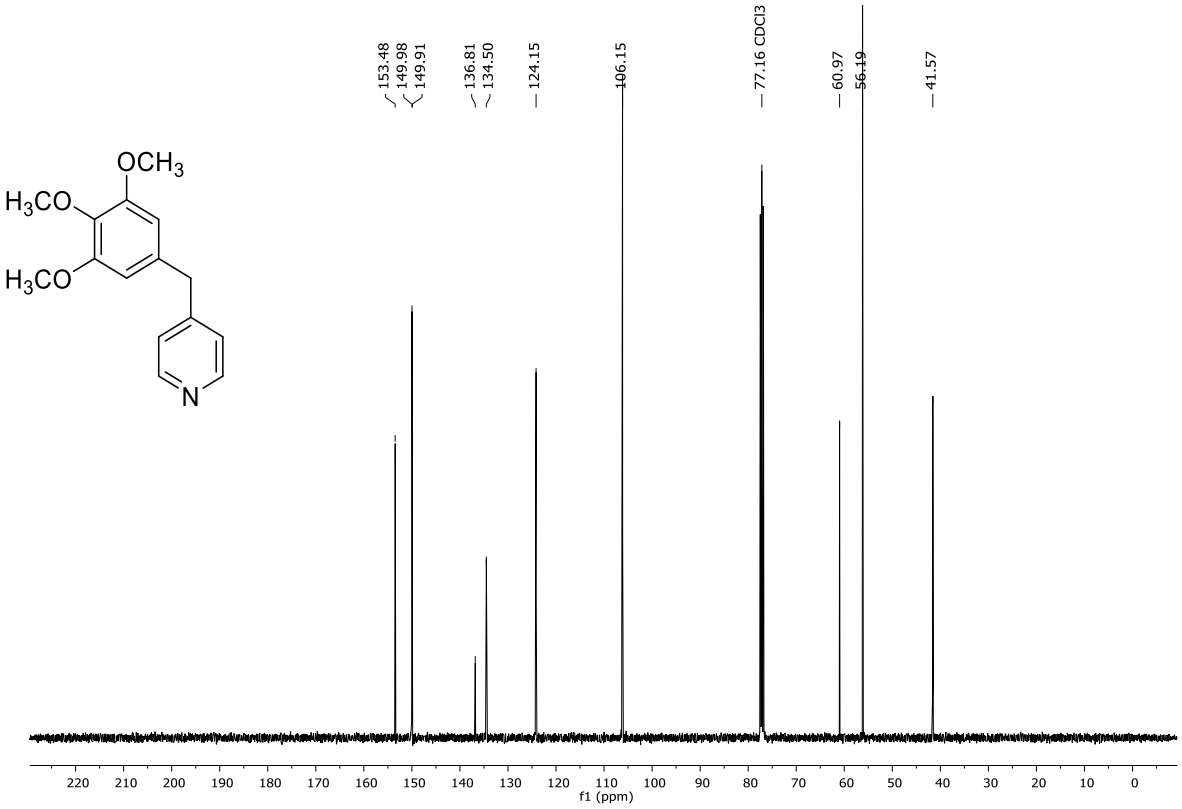
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(4-methoxybenzyl)pyridine (**8e**).



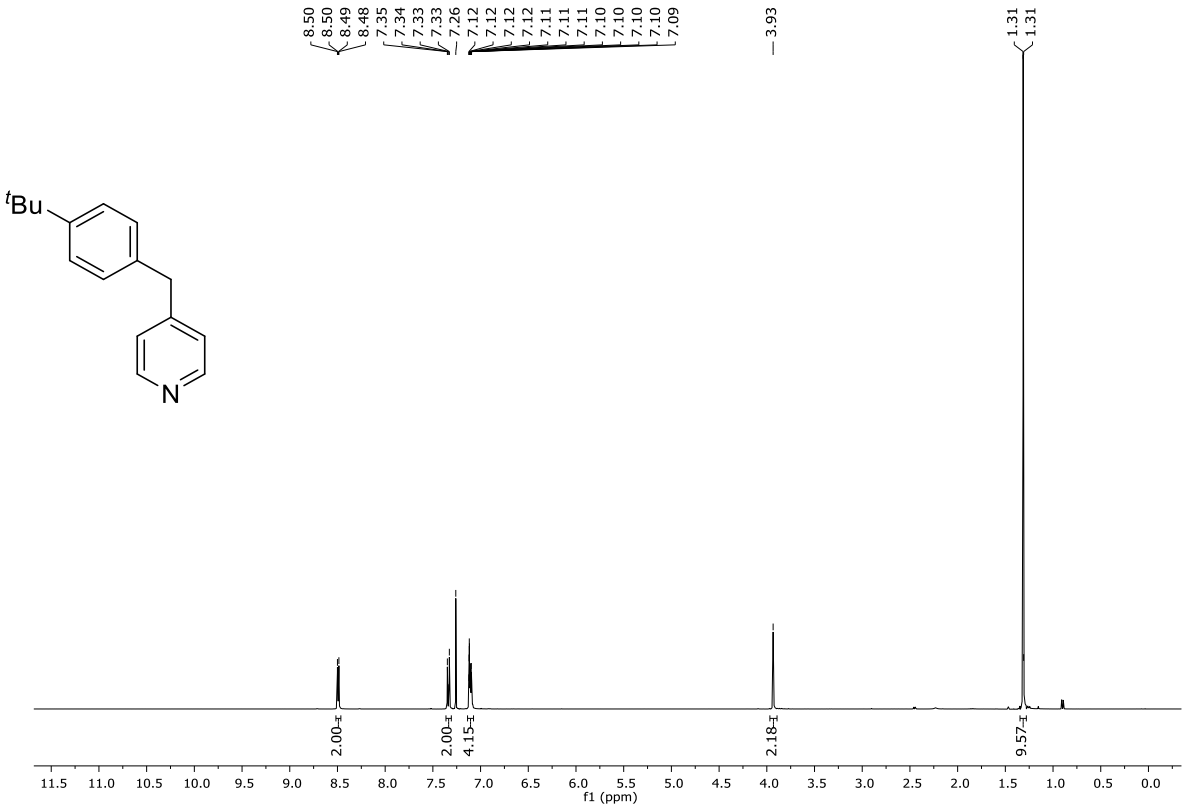
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(4-methoxybenzyl)pyridine (**8e**).



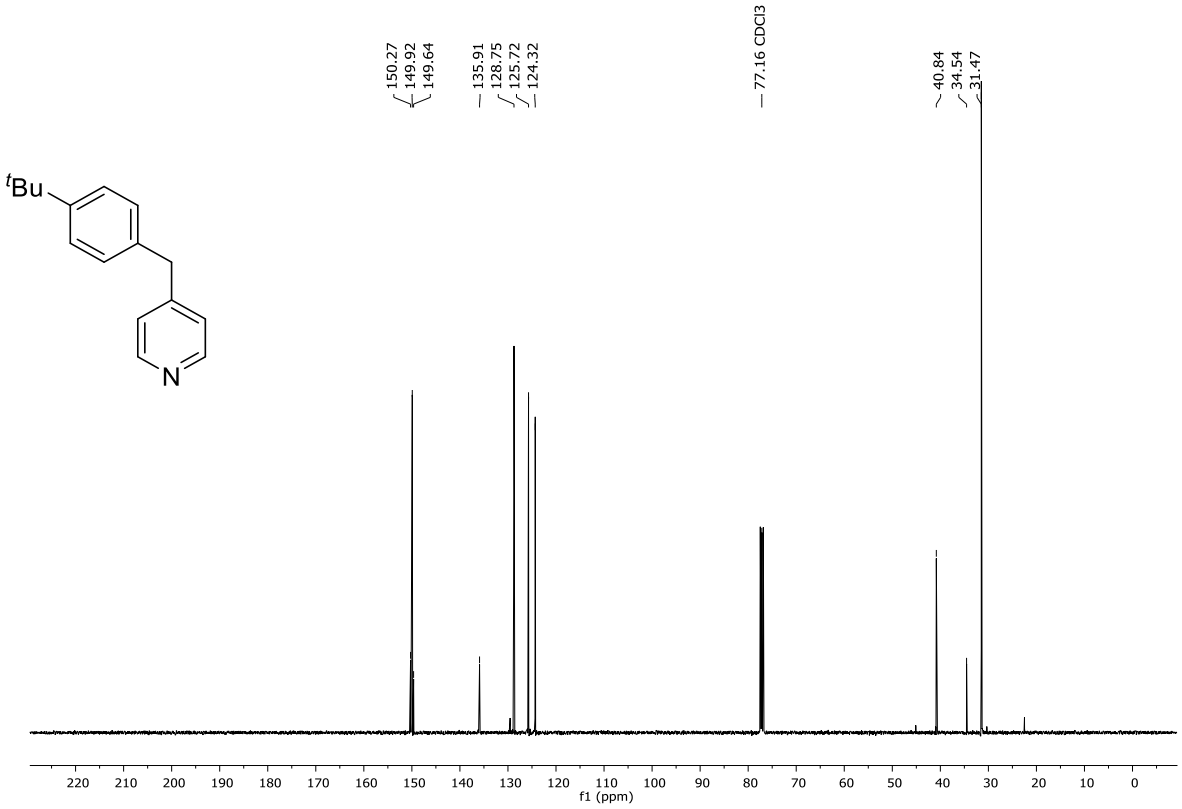
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(3,4,5-trimethoxybenzyl)pyridine (**8f**).



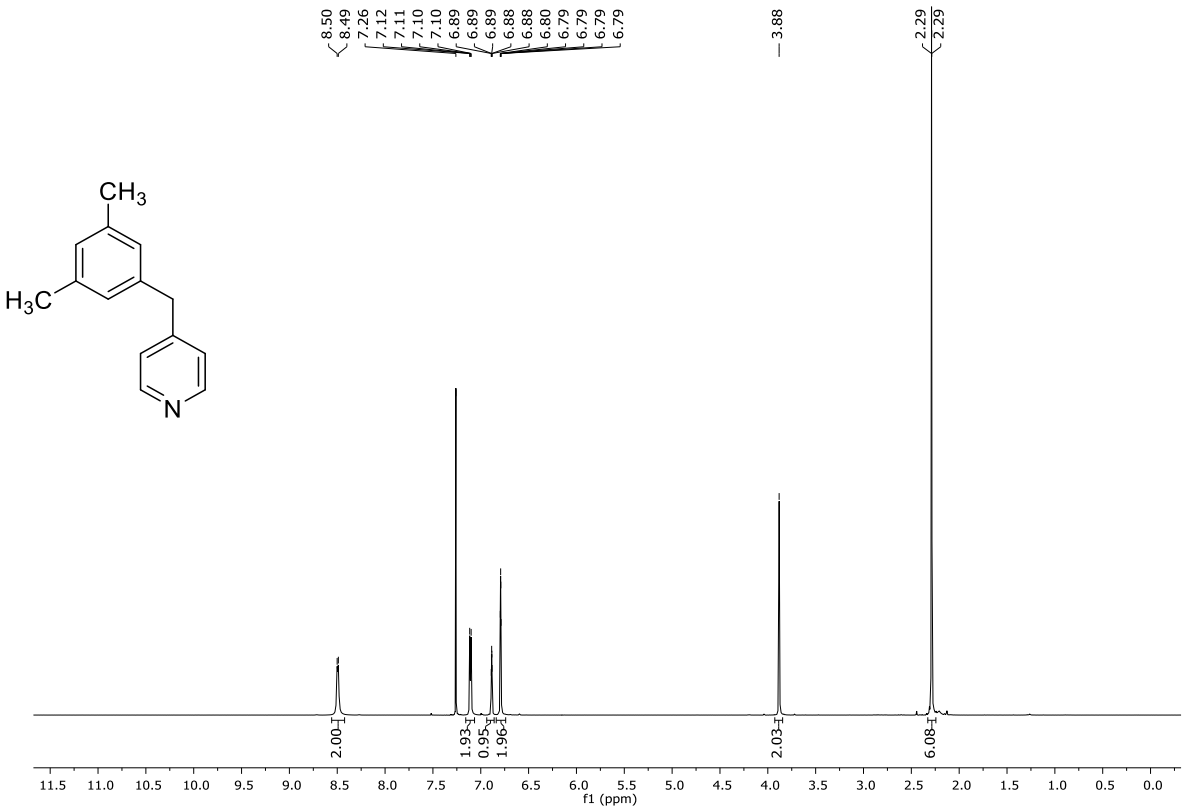
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(3,4,5-trimethoxybenzyl)pyridine (**8f**).



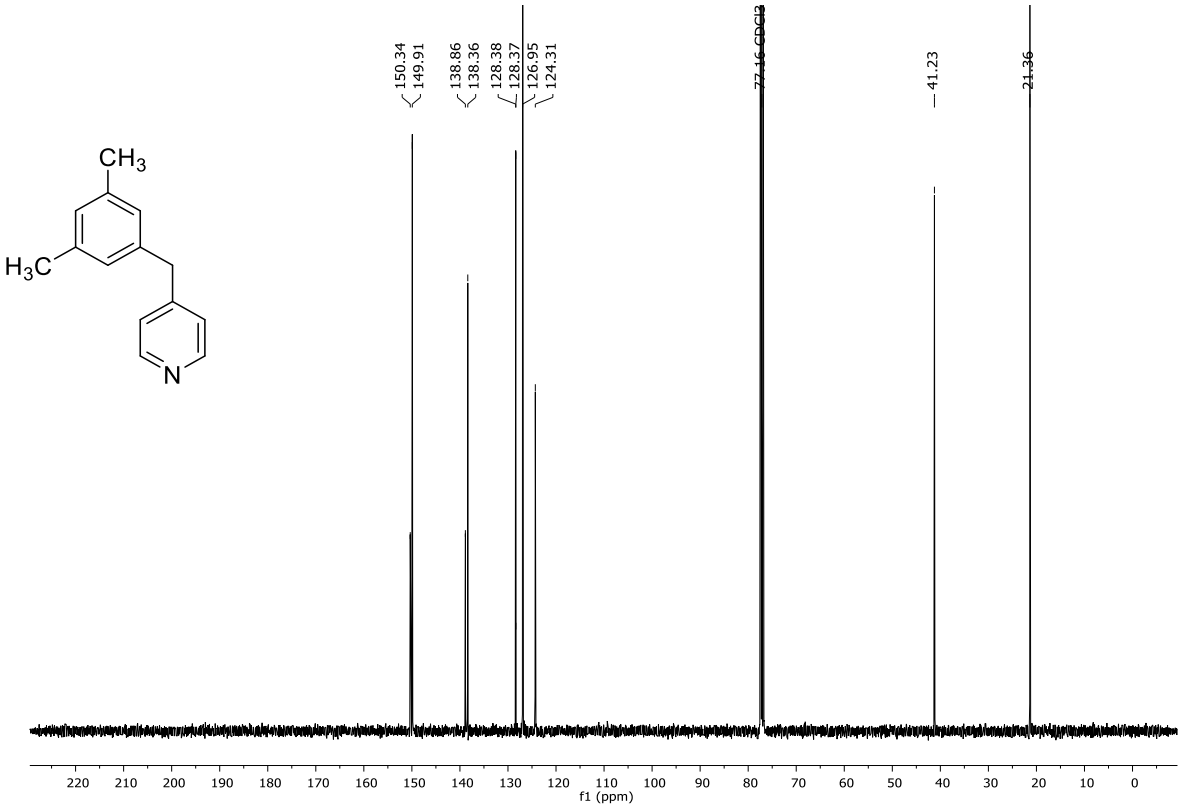
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(4-*tert*-butylbenzyl)pyridine (**8g**).



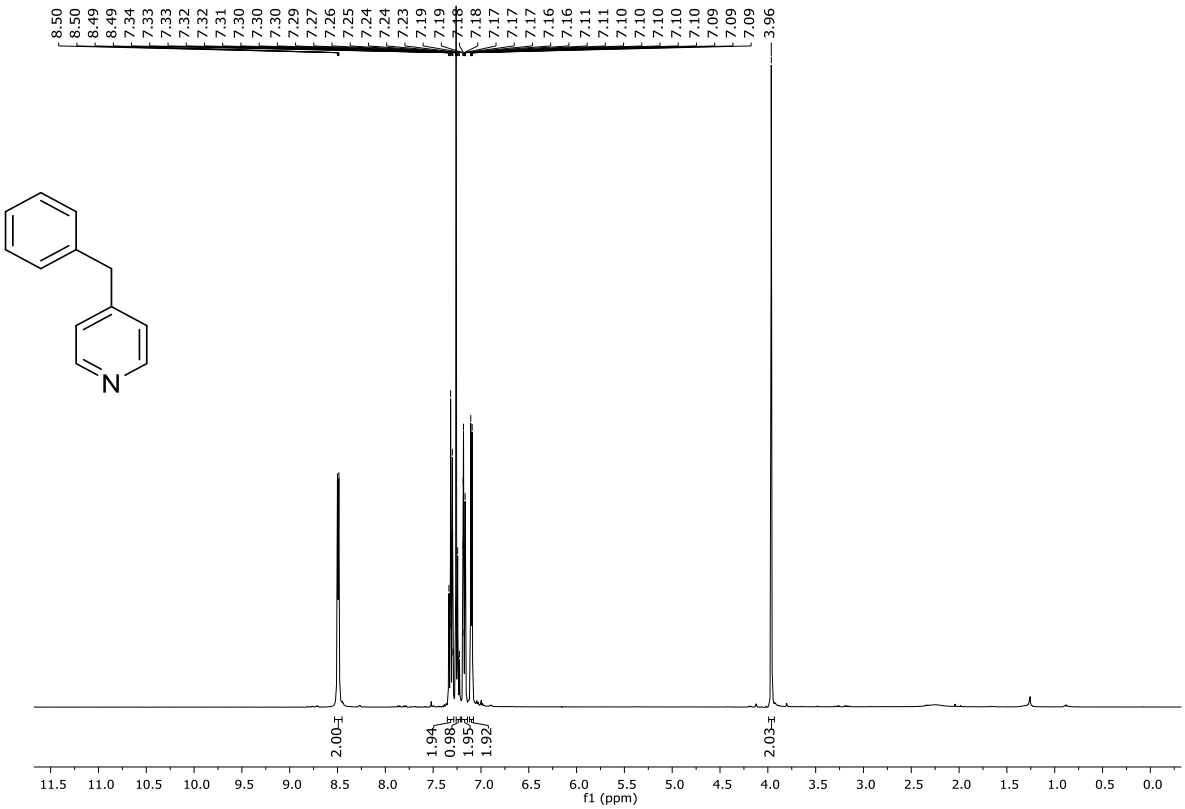
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(4-*tert*-butylbenzyl)pyridine (**8g**).



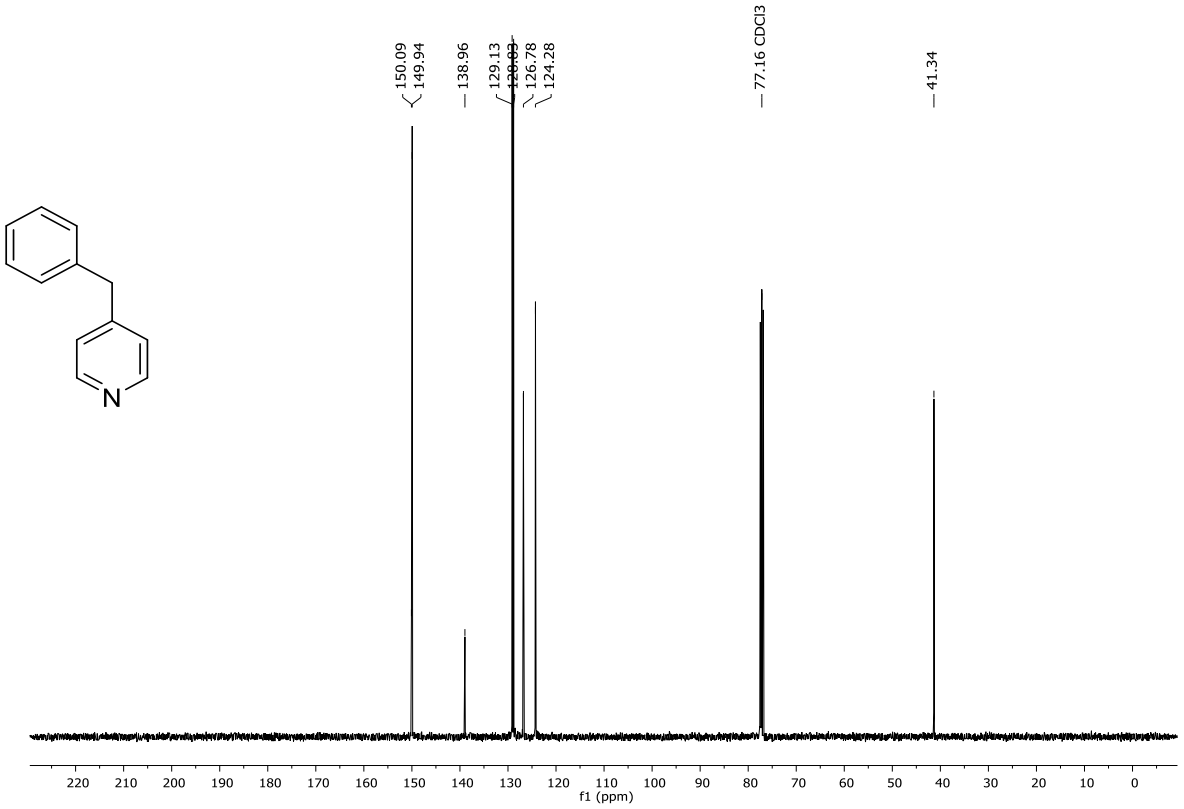
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(3,5-dimethylbenzyl)pyridine (**8h**).



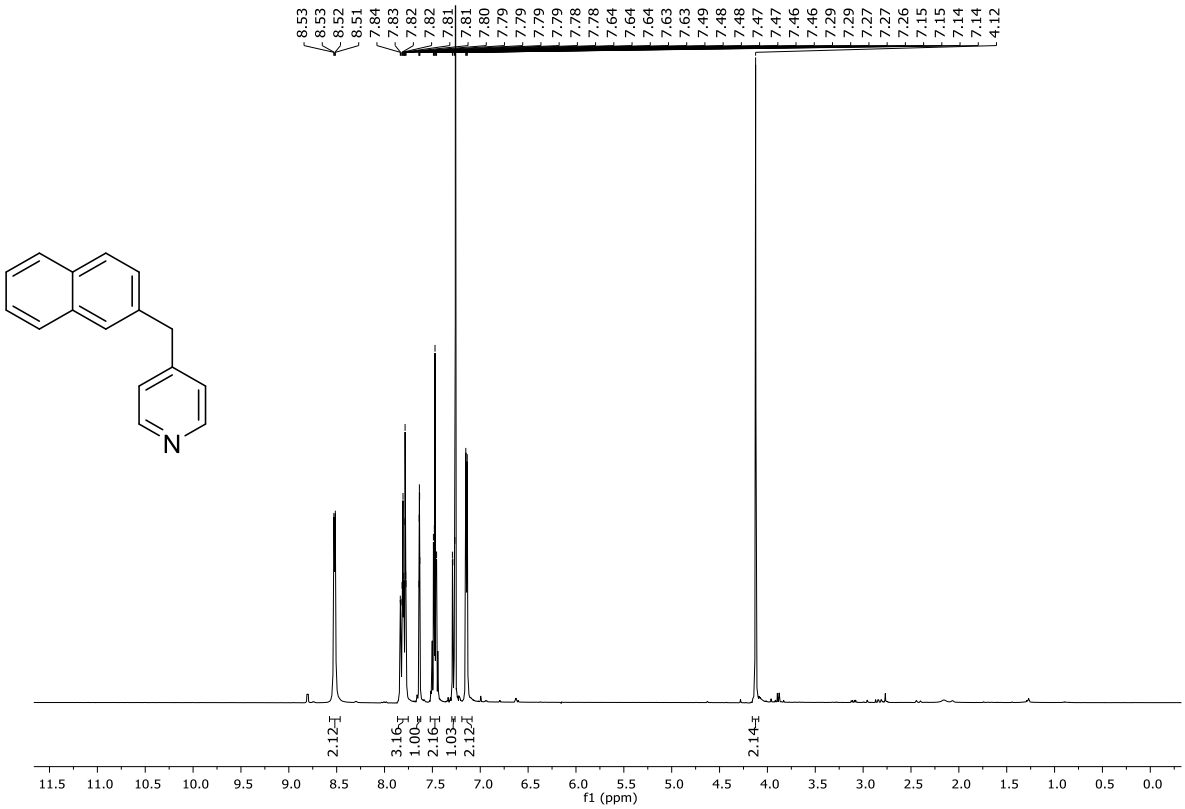
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(3,5-dimethylbenzyl)pyridine (**8h**).



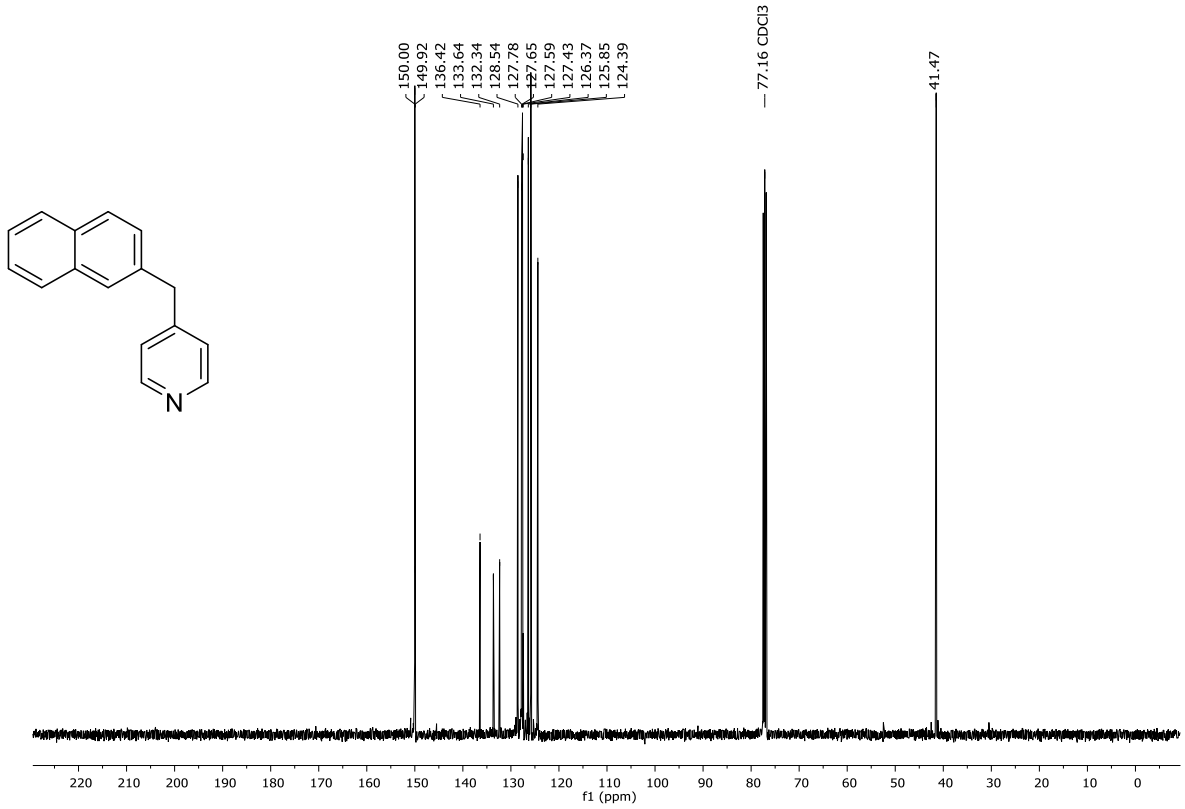
^{1}H-NMR (400 MHz, $CDCl_3$): 4-Benzylpyridine (**8i**).



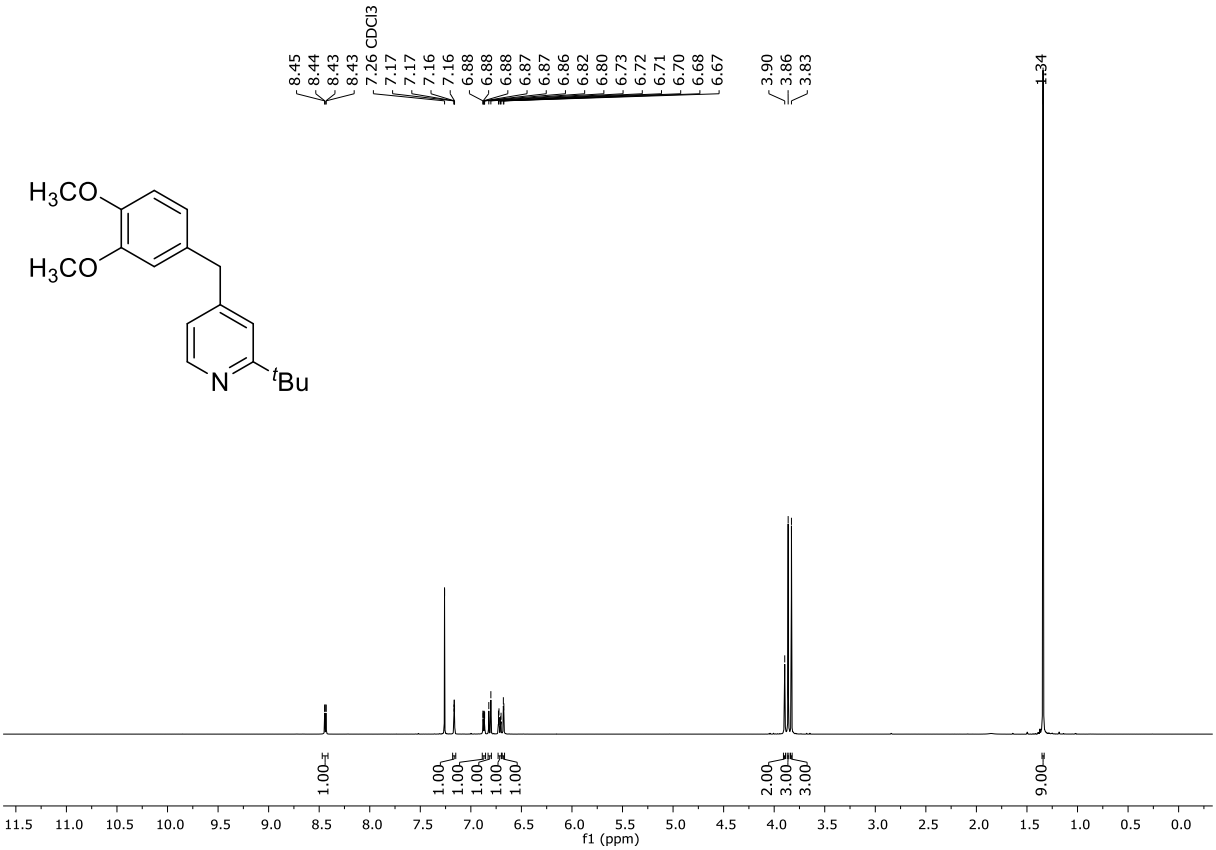
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-Benzylpyridine (**8i**).



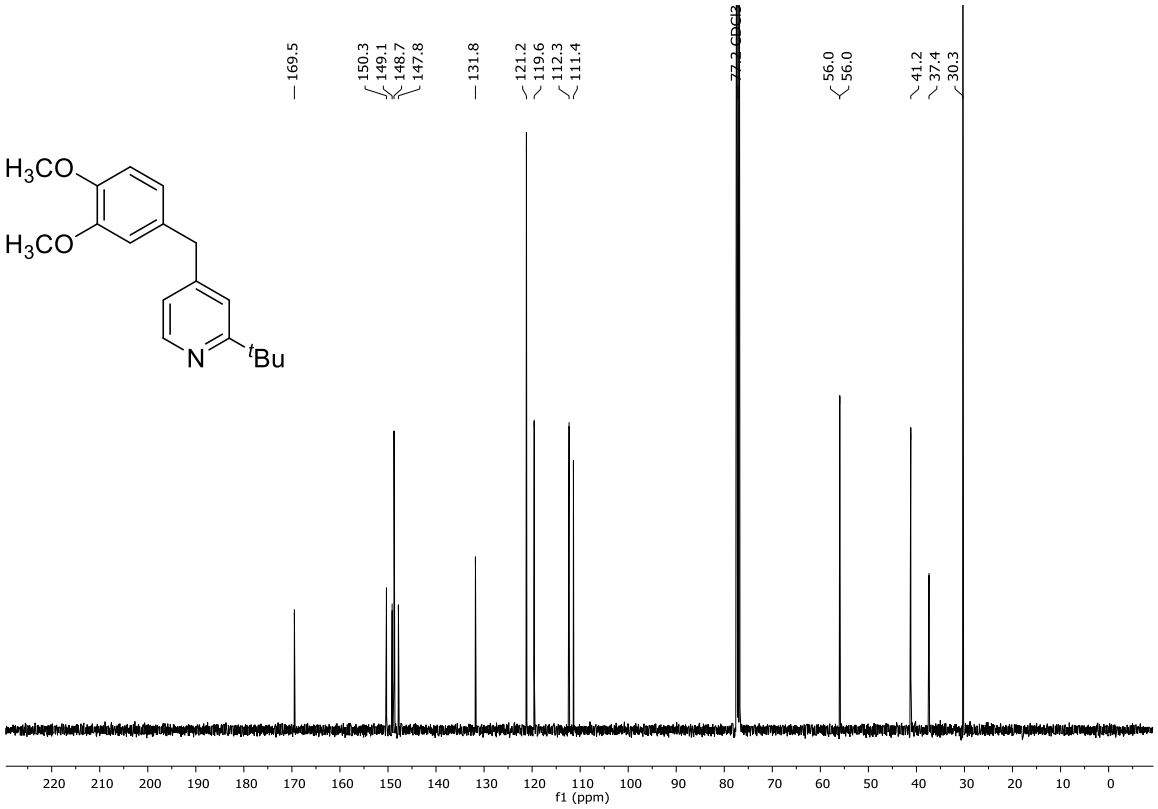
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(naphthalen-2-ylmethyl)pyridine (**8j**).



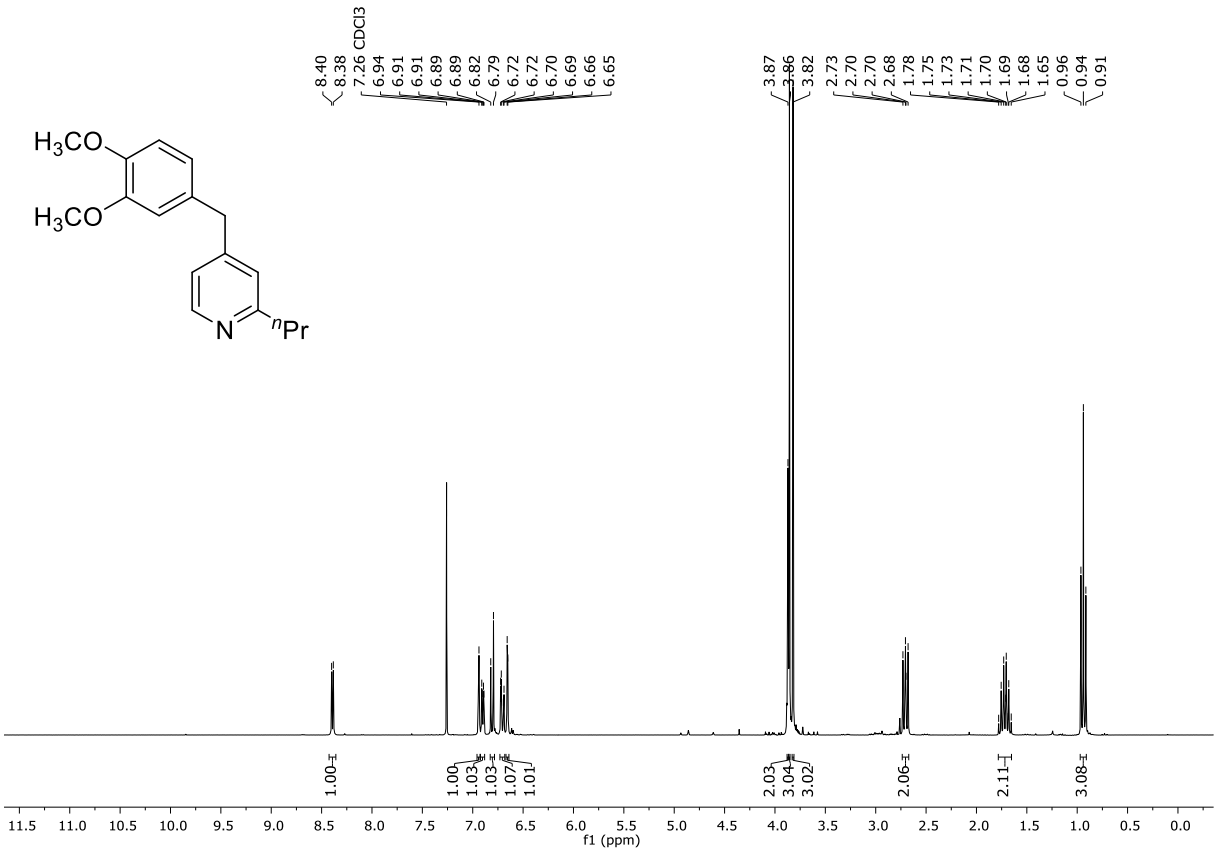
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(naphthalen-2-ylmethyl)pyridine (**8j**).



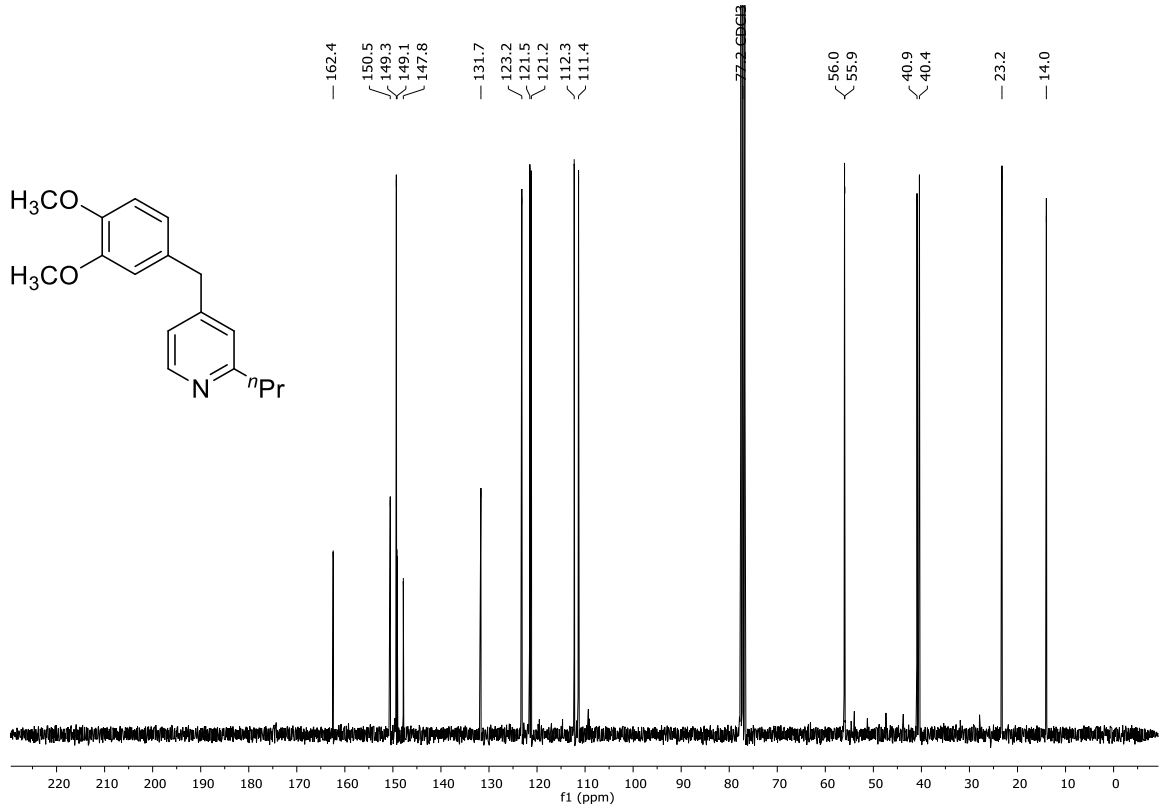
^{1}H-NMR (400 MHz, $CDCl_3$): 2-(*tert*-Butyl)-4-(3,4-dimethoxybenzyl)pyridine (**8k**).



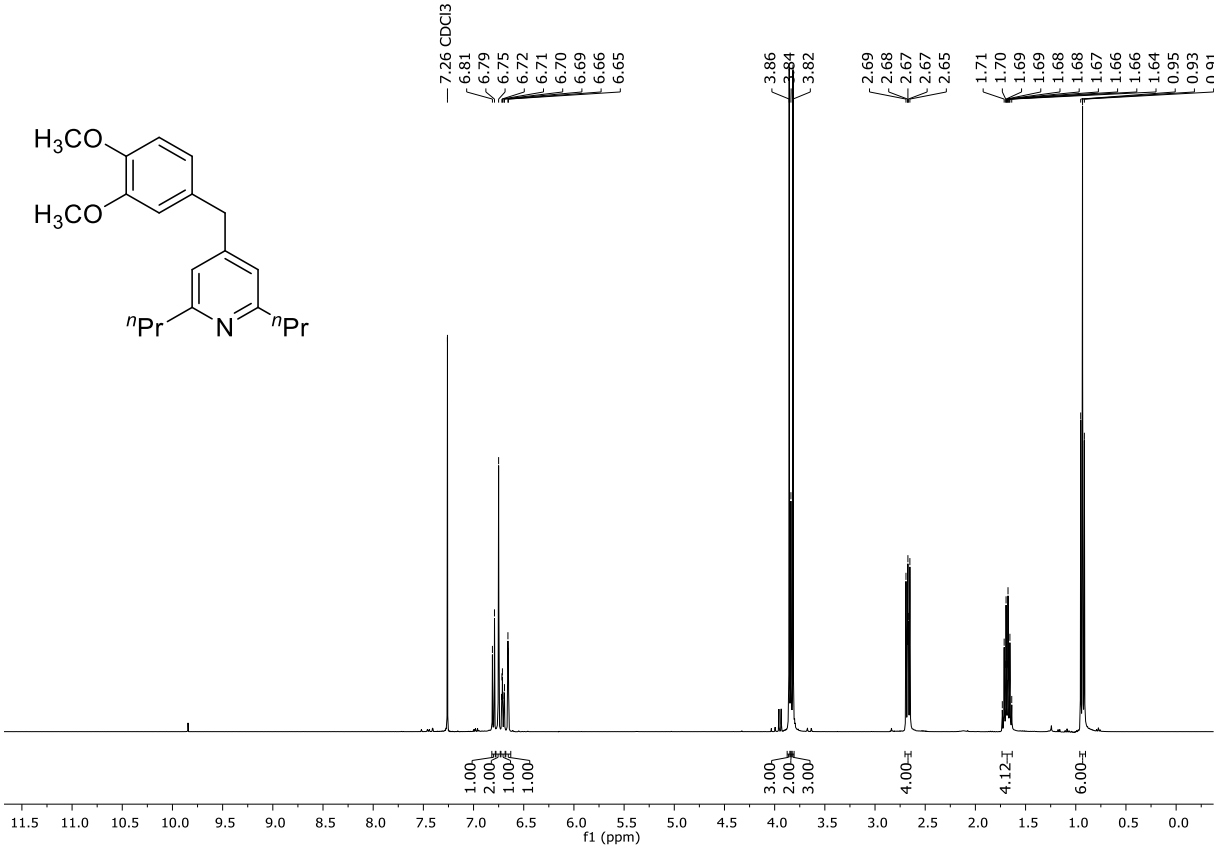
^{13}C-NMR (100.6 MHz, $CDCl_3$): 2-(*tert*-Butyl)-4-(3,4-dimethoxybenzyl)pyridine (**8k**).



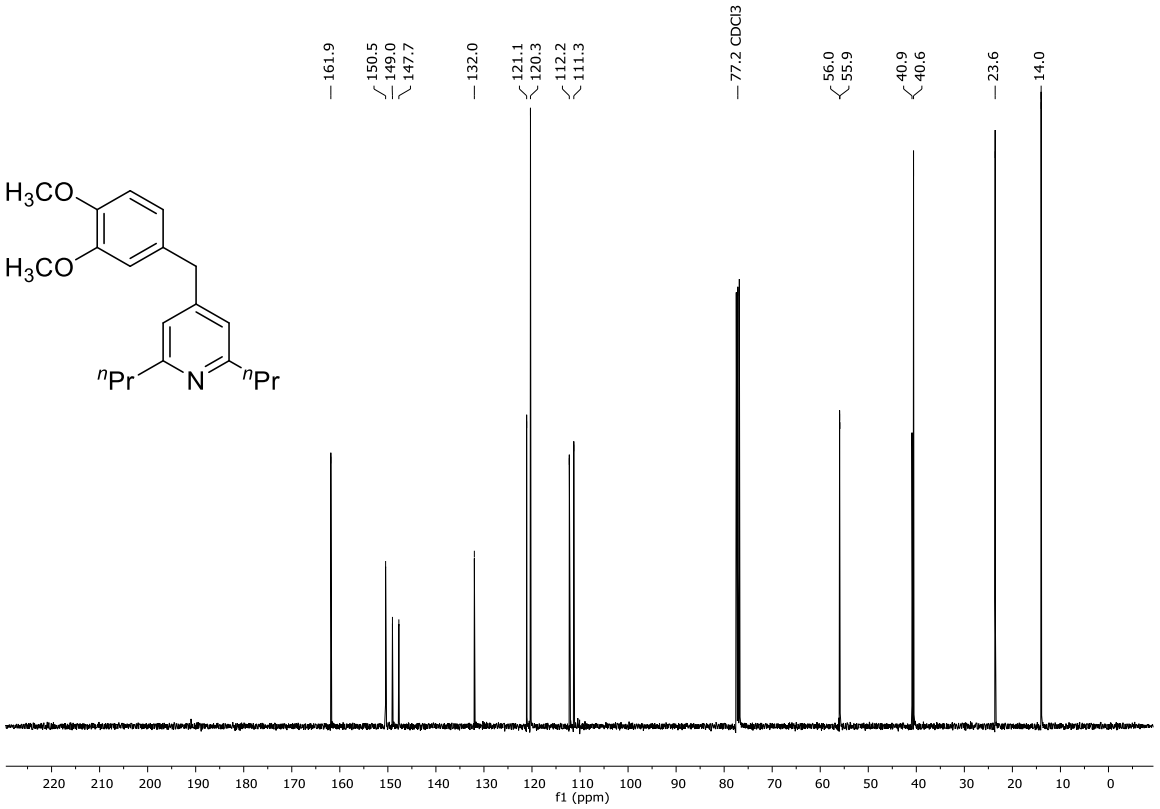
^{1}H-NMR (300 MHz, $CDCl_3$): 4-(3,4-Dimethoxybenzyl)-2-propylpyridine (**8l**).



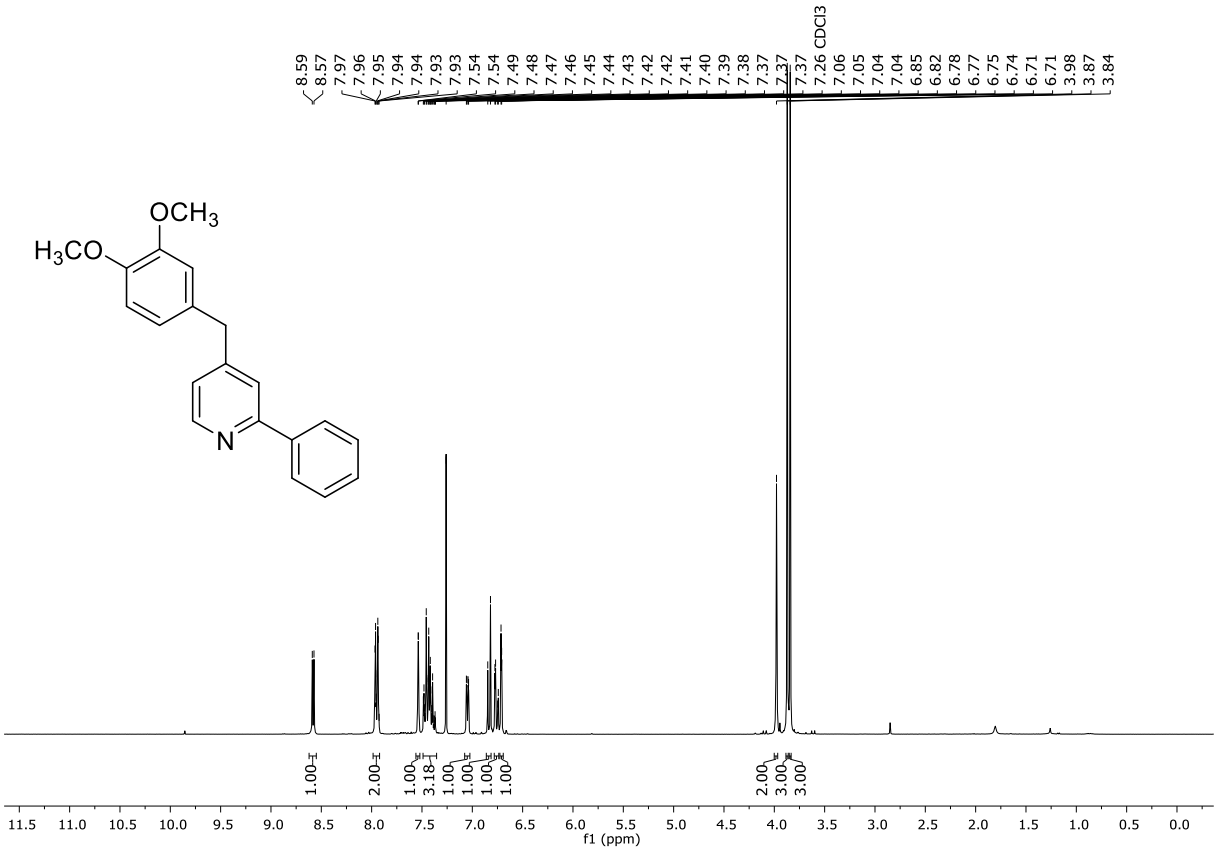
^{13}C-NMR (75.5 MHz, $CDCl_3$): 4-(3,4-Dimethoxybenzyl)-2-propylpyridine (**8l**).



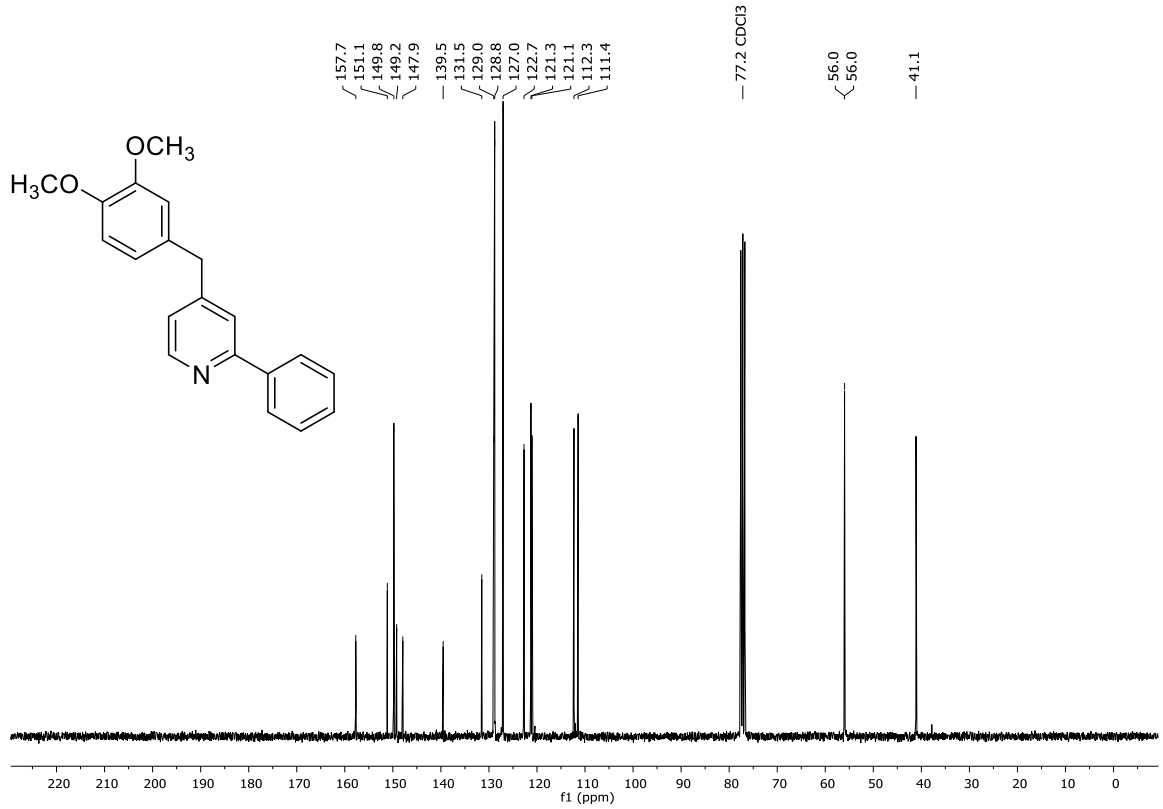
^{1}H-NMR (400 MHz, $CDCl_3$): 4-(3,4-Dimethoxybenzyl)-2,6-dipropylpyridine (**8m**).



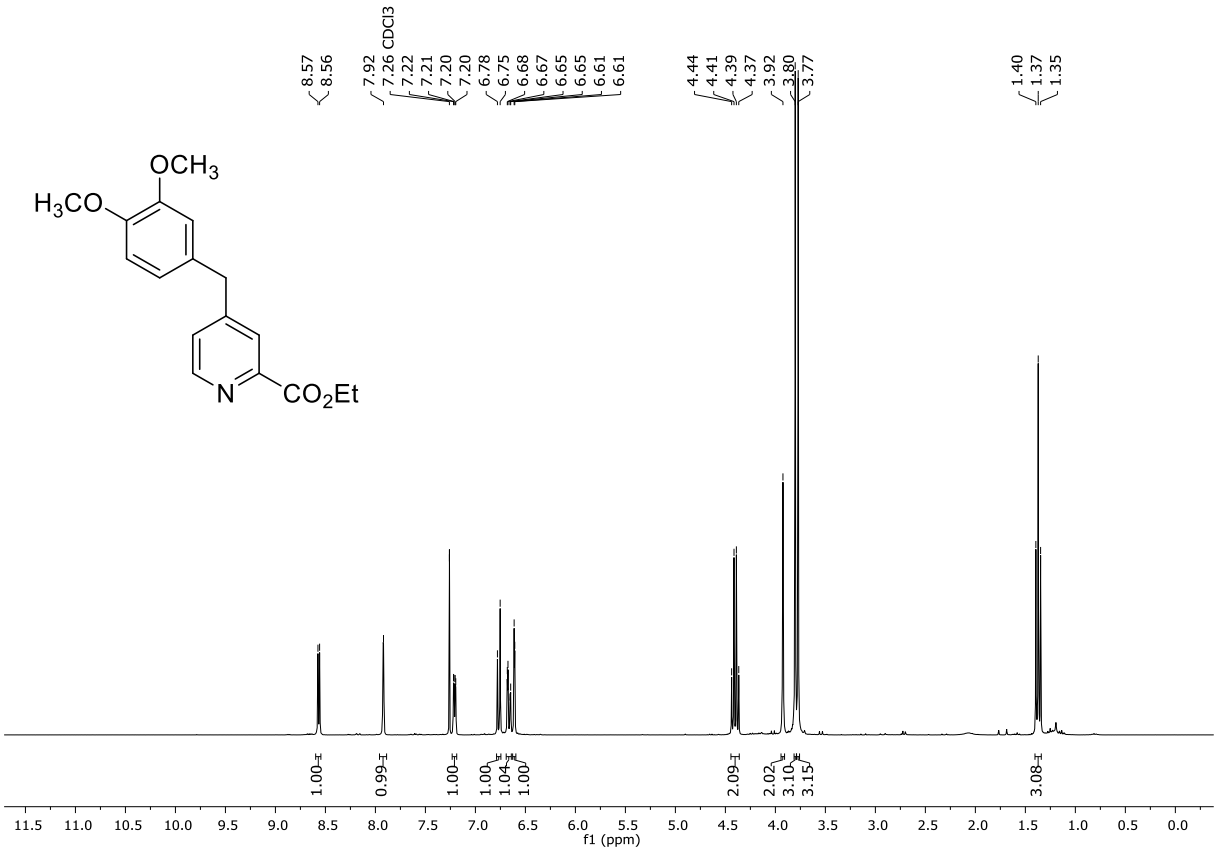
^{13}C-NMR (100.6 MHz, $CDCl_3$): 4-(3,4-Dimethoxybenzyl)-2,6-dipropylpyridine (**8m**).



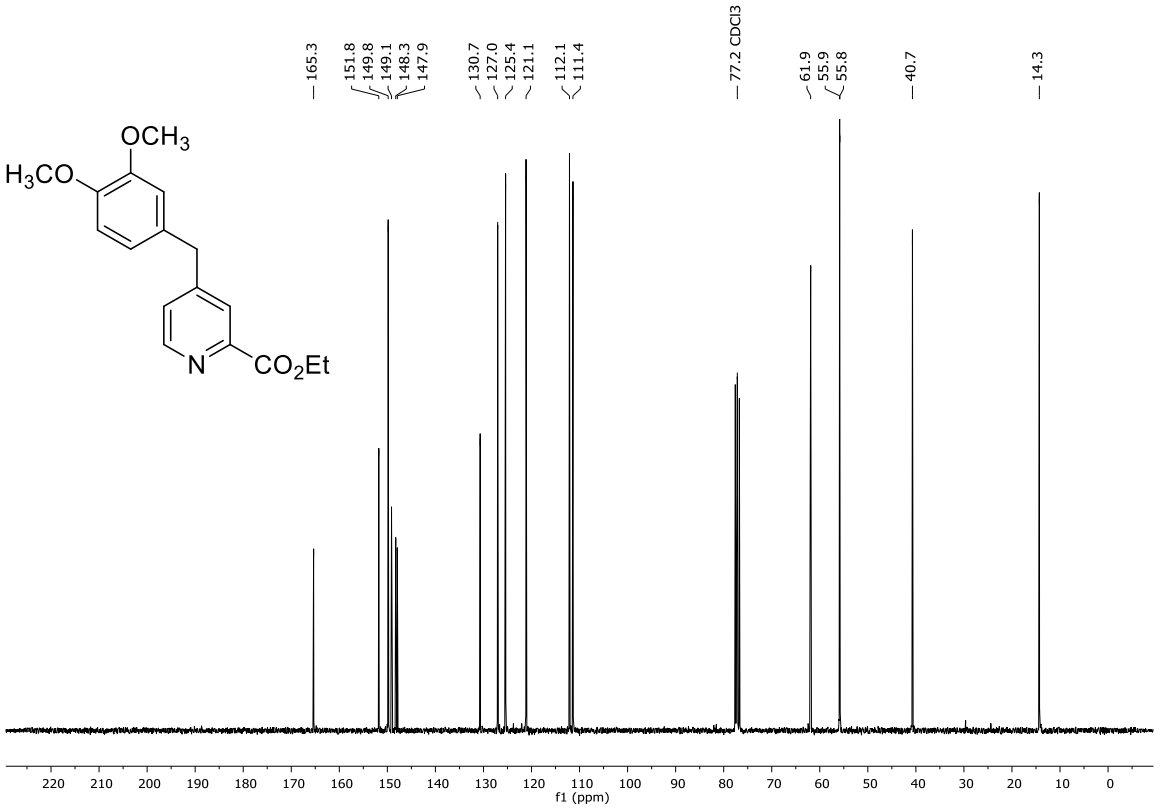
^{1}H-NMR (300 MHz, $CDCl_3$): 4-(3,4-Dimethoxybenzyl)-2-phenylpyridine (**8n**).



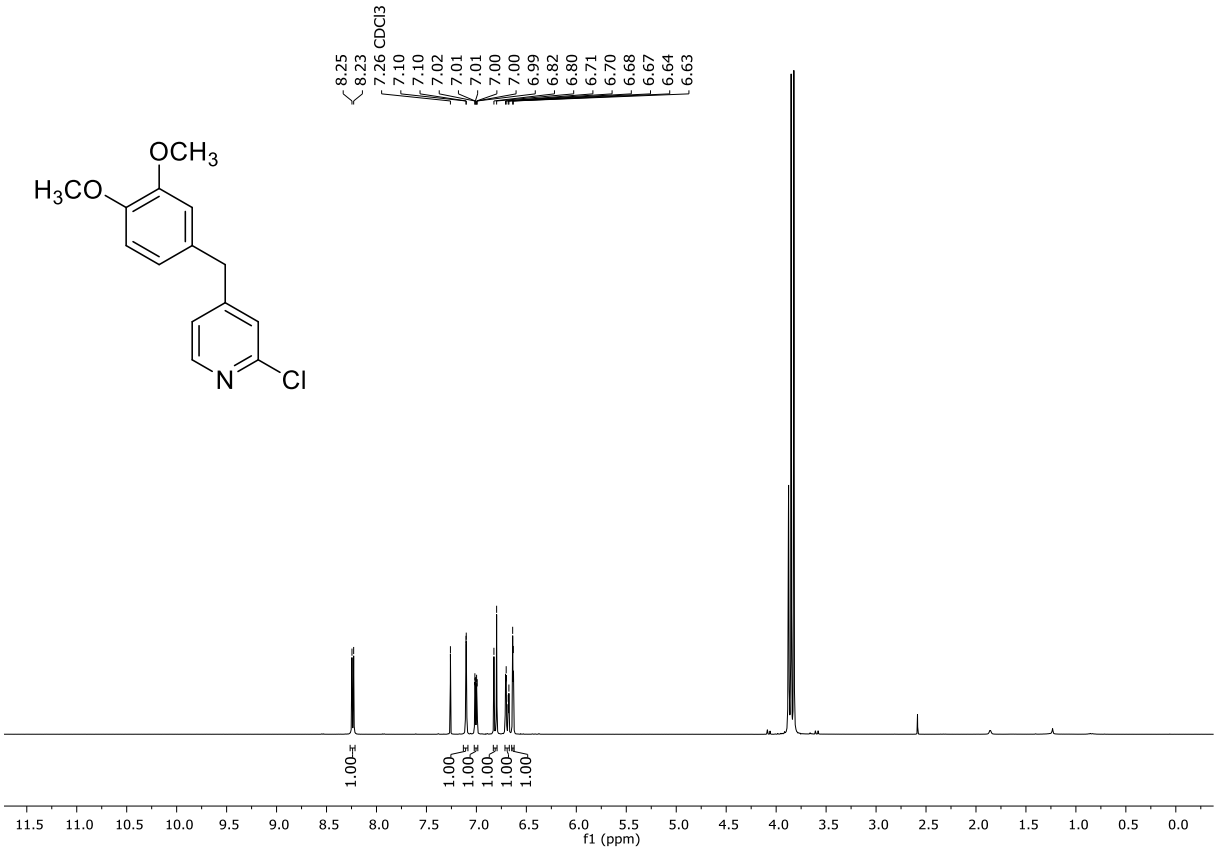
^{13}C-NMR (75.5 MHz, $CDCl_3$): 4-(3,4-Dimethoxybenzyl)-2-phenylpyridine (**8n**).



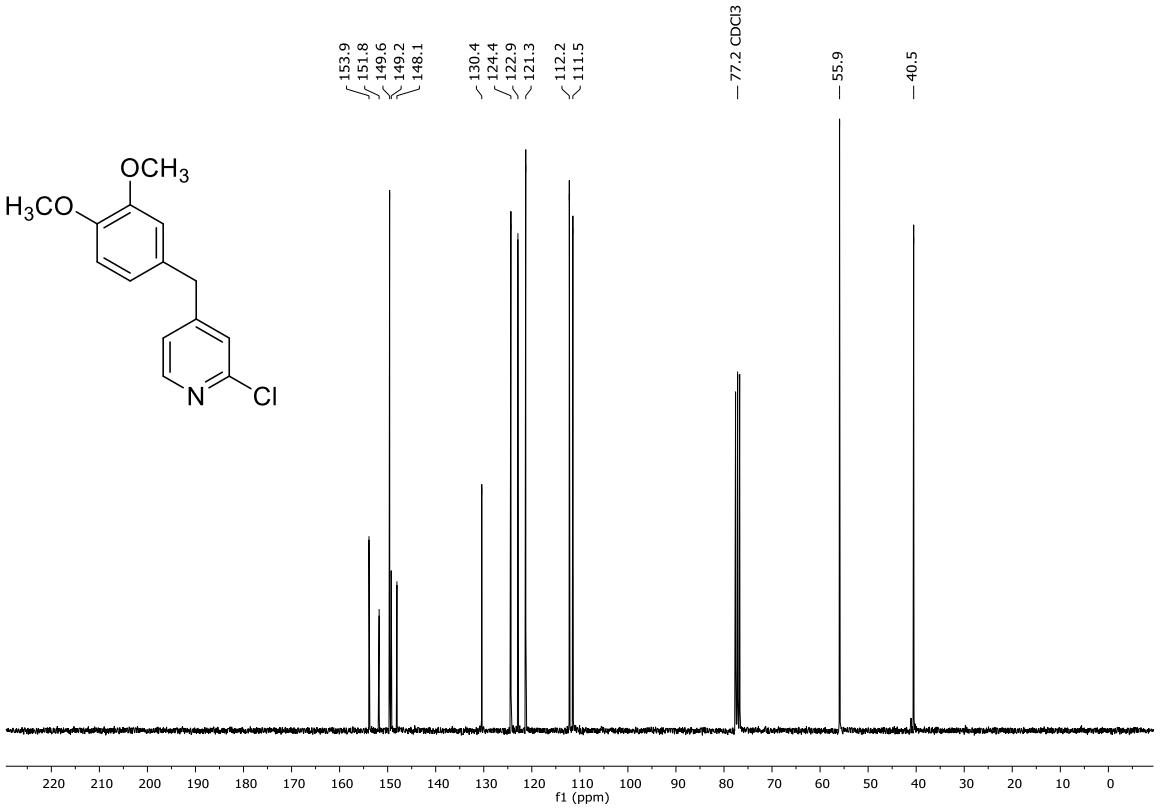
^{1}H-NMR (300 MHz, $CDCl_3$): Ethyl 4-(3,4-dimethoxybenzyl)picolinate (**8o**).



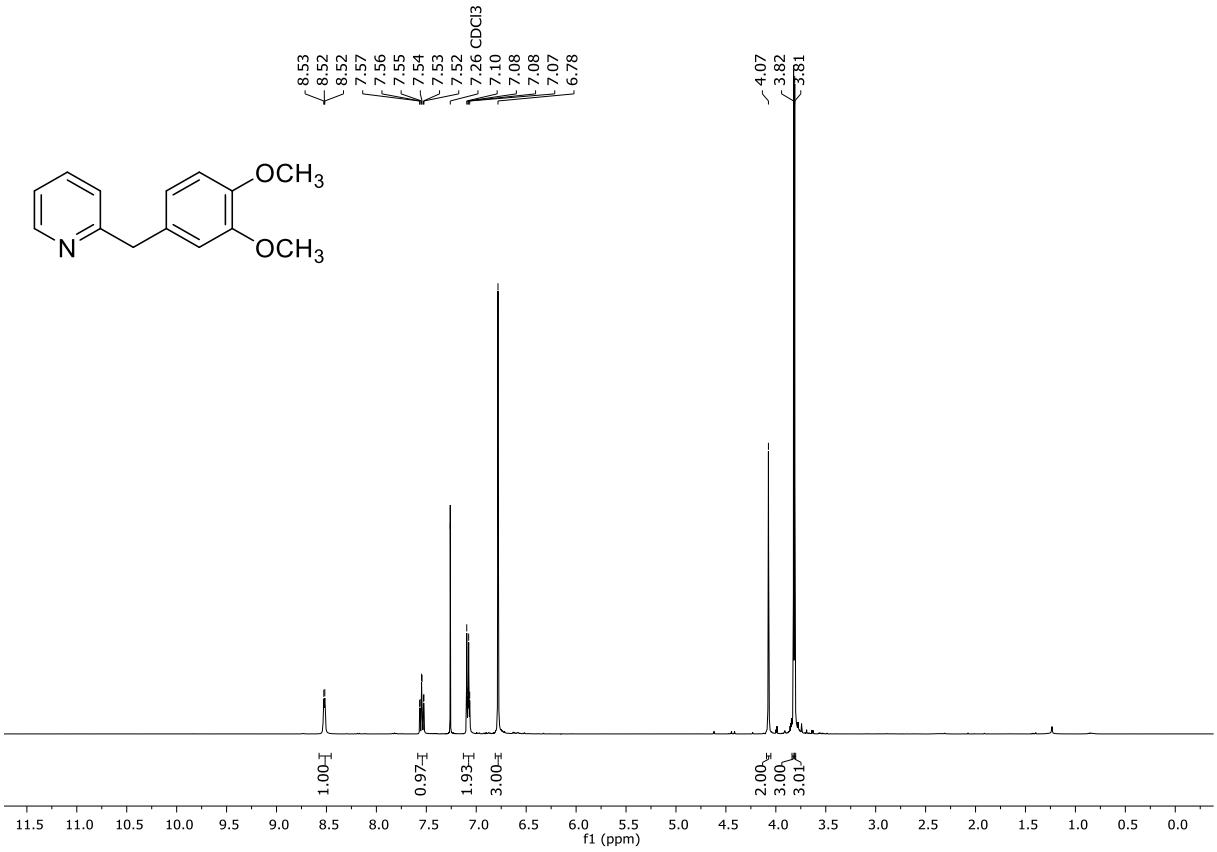
^{13}C-NMR (75.5 MHz, $CDCl_3$): Ethyl 4-(3,4-dimethoxybenzyl)picolinate (**8o**).



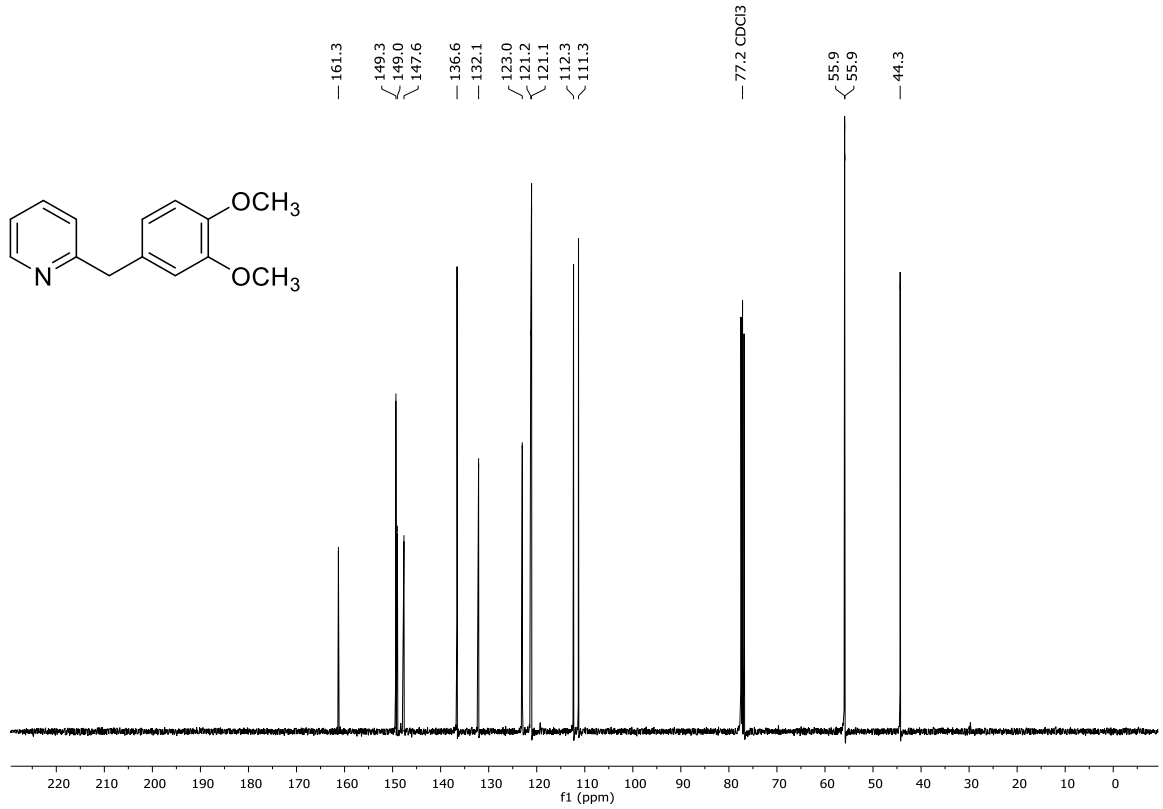
^{1}H-NMR (300 MHz, $CDCl_3$): 2-Chloro-4-(3,4-dimethoxybenzyl)pyridine (**8p**).



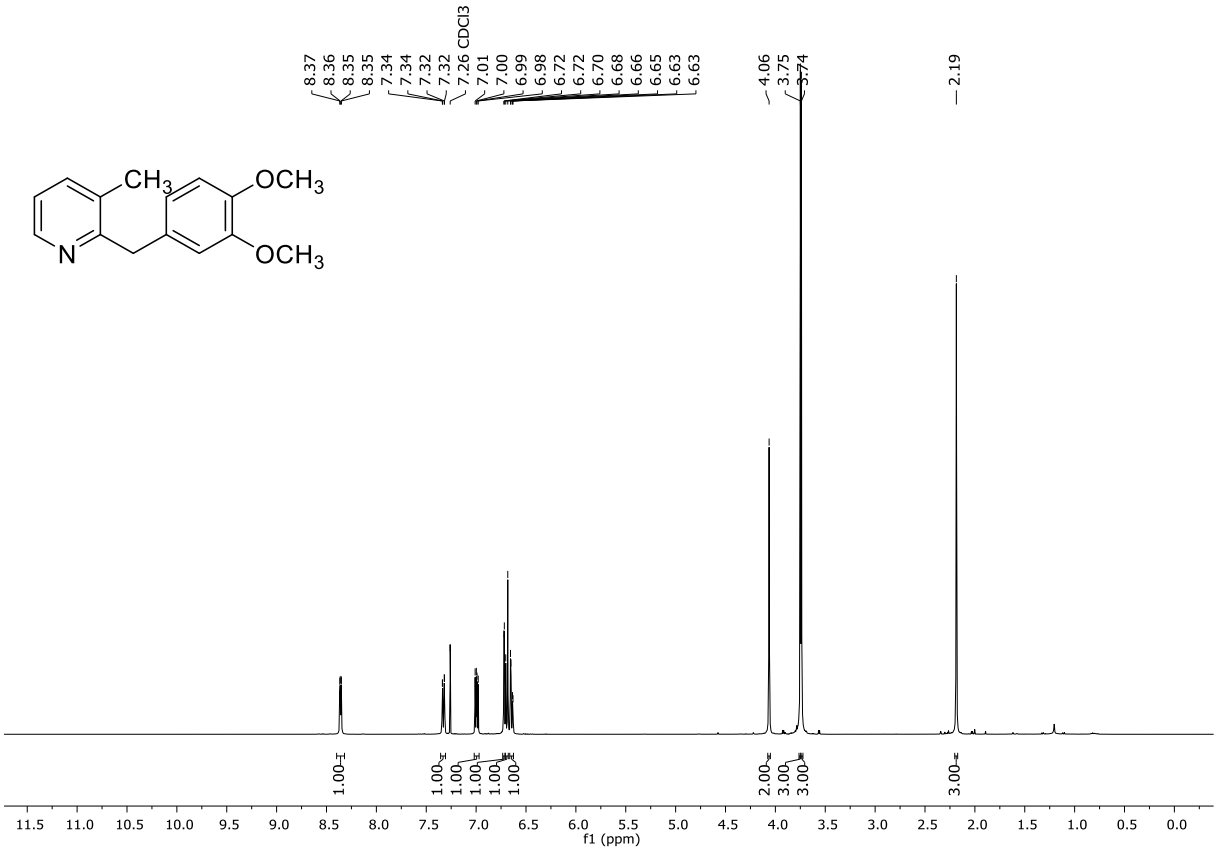
^{13}C-NMR (75.5 MHz, $CDCl_3$): 2-Chloro-4-(3,4-dimethoxybenzyl)pyridine (**8p**).



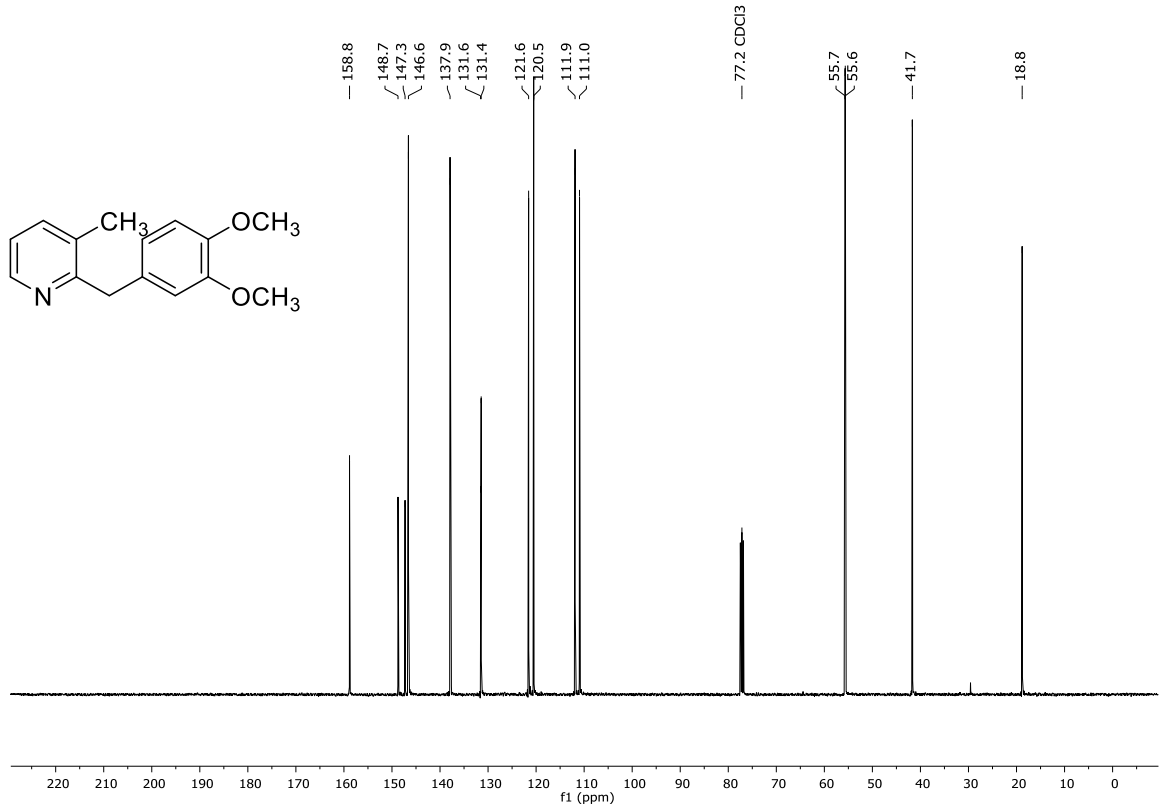
^{1}H-NMR (400 MHz, $CDCl_3$): 2-(3,4-Dimethoxybenzyl)pyridine (**8q**).



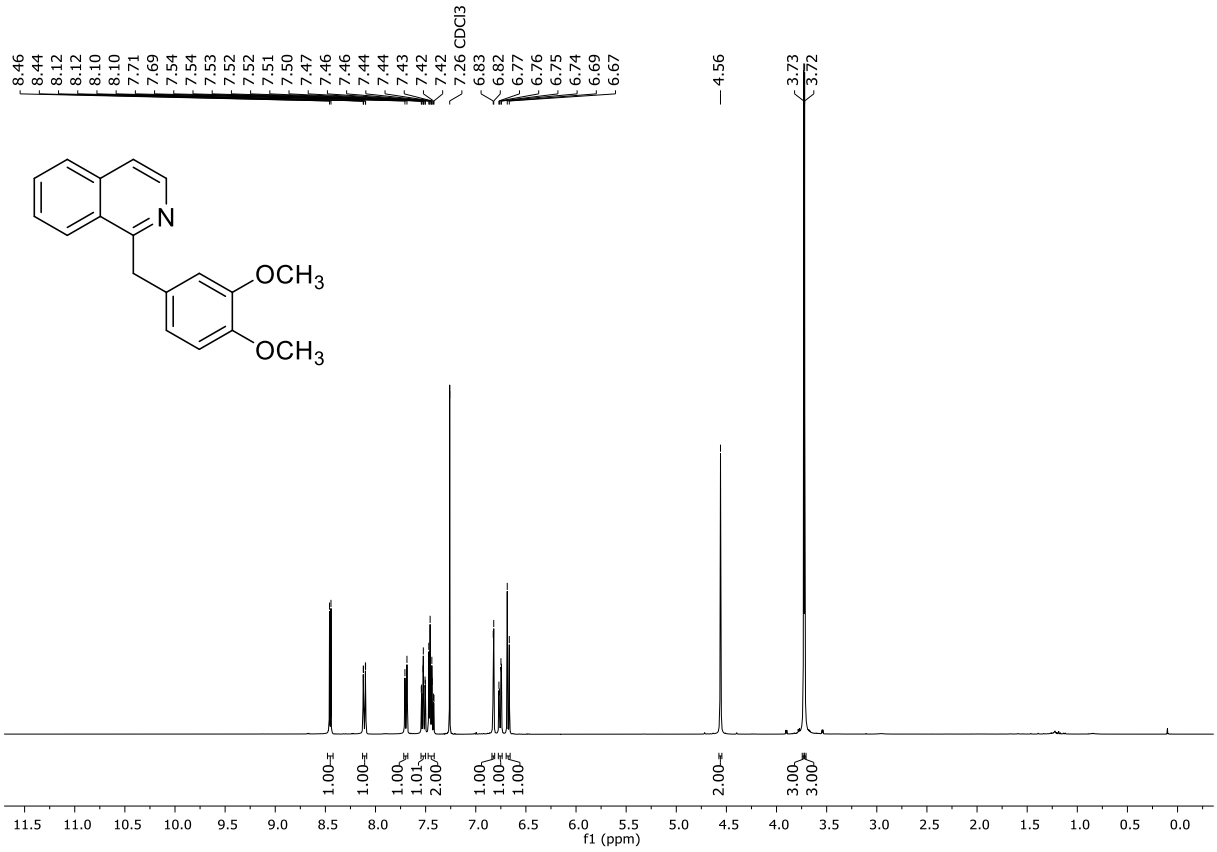
^{13}C-NMR (100.6 MHz, $CDCl_3$): 2-(3,4-Dimethoxybenzyl)pyridine (**8q**).



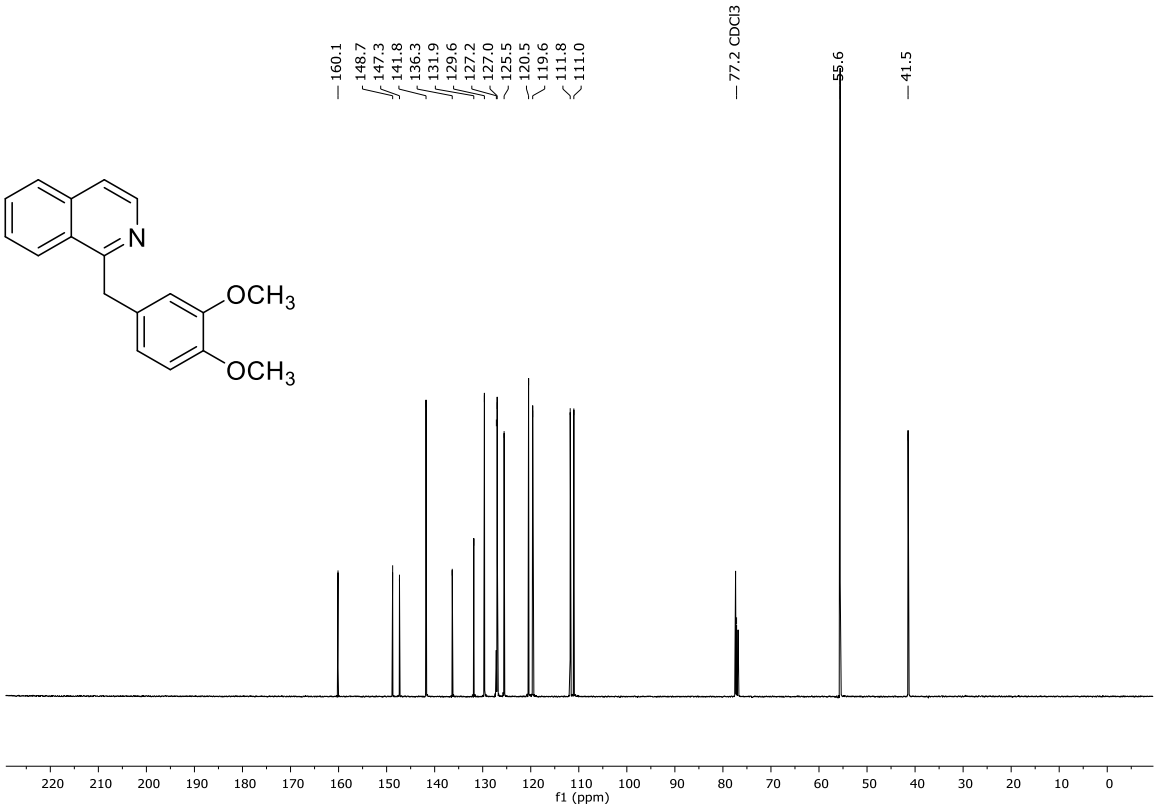
^{1}H-NMR (300 MHz, $CDCl_3$): 2-(3,4-Dimethoxybenzyl)-3-methylpyridine (**8r**).



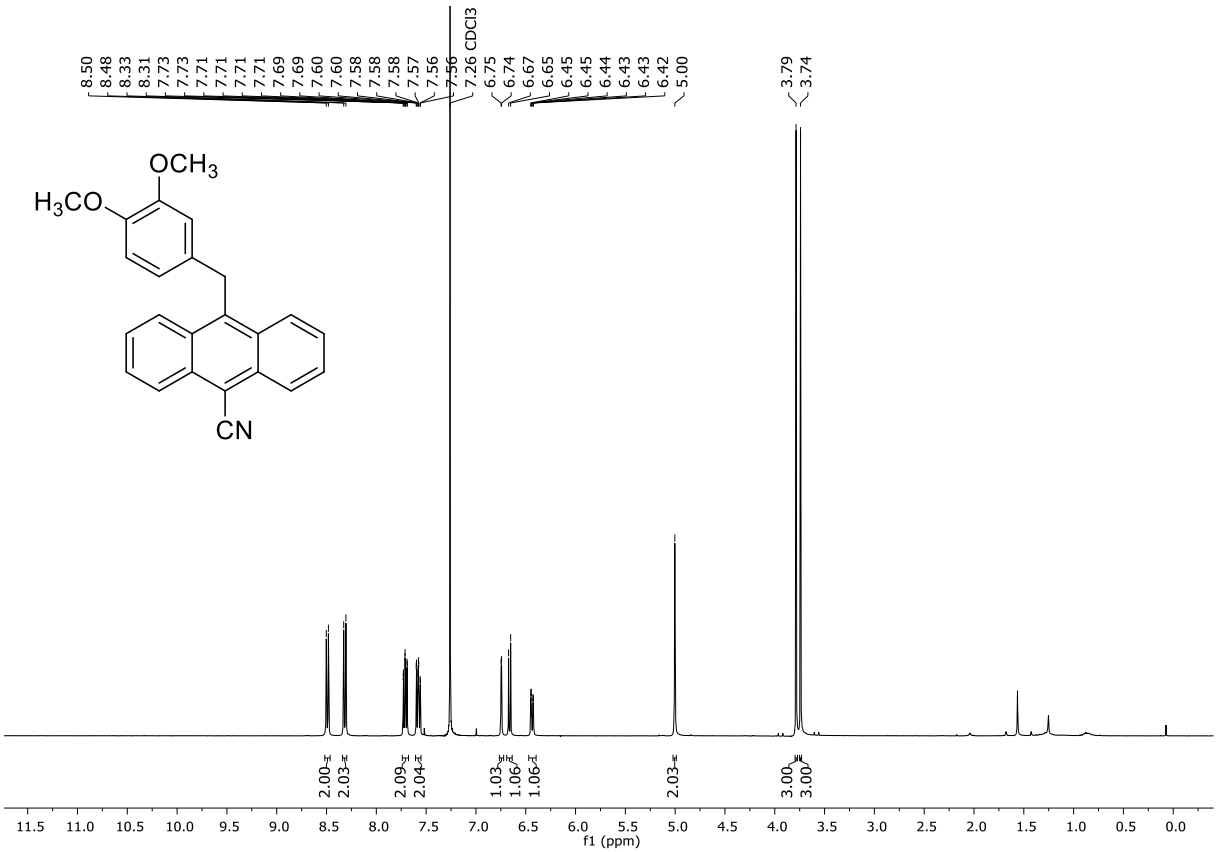
^{13}C-NMR (75.5 MHz, $CDCl_3$): 2-(3,4-Dimethoxybenzyl)-3-methylpyridine (**8r**).



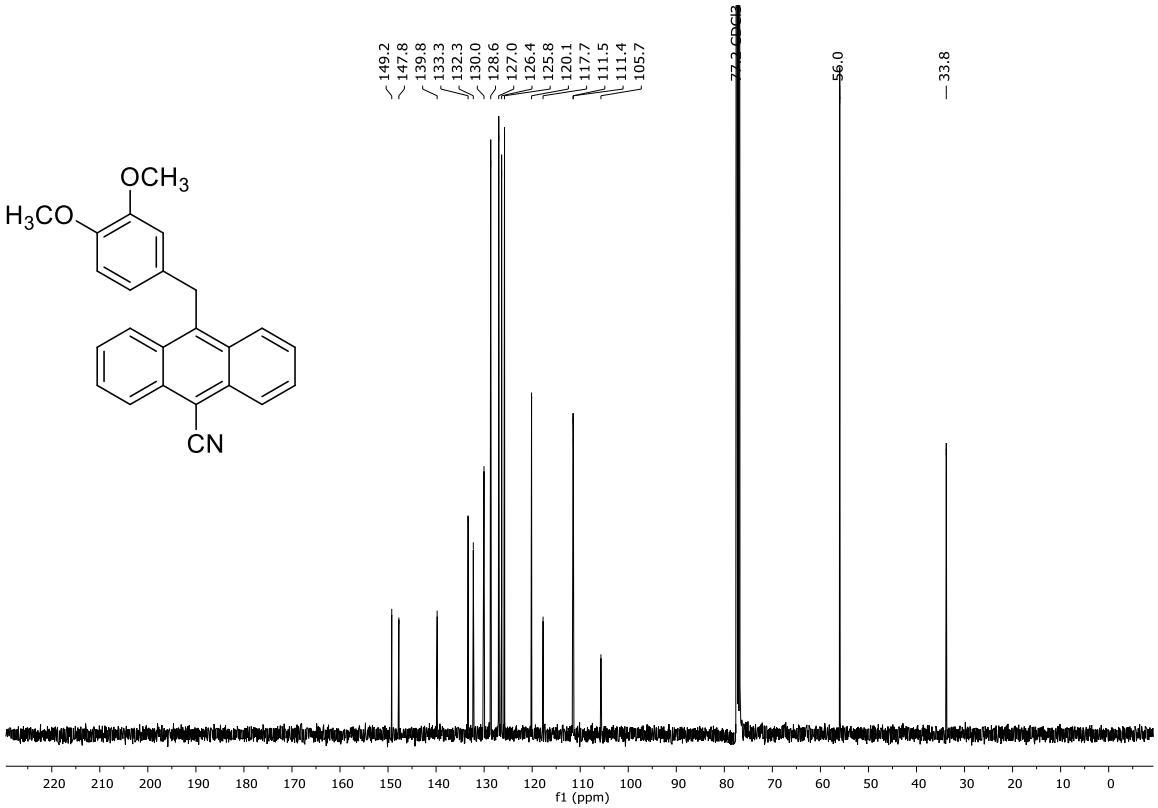
^{1}H-NMR (300 MHz, $CDCl_3$): 1-(3,4-dimethoxybenzyl)isoquinoline (**8s**).



^{13}C-NMR (75.5 MHz, $CDCl_3$): 1-(3,4-dimethoxybenzyl)isoquinoline (**8s**).



^{1}H-NMR (400 MHz, $CDCl_3$): 9-Cyano-10-(3,4-Dimethoxybenzyl)anthracene (**8t**).



^{13}C-NMR (100.6 MHz, $CDCl_3$): 9-Cyano-10-(3,4-Dimethoxybenzyl)anthracene (**8t**).

VII. References

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