Turning Light into Carbinols: A Metal-free Radical Strategy for Pyridine Based Triaryl Scaffolds

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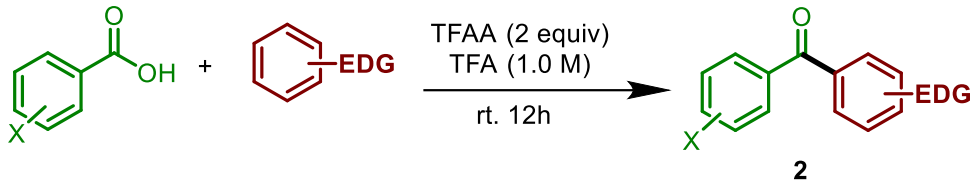
1. General information

All the solvent and reagents are commercially available and used as received (unless otherwise noted). Analytical thin layer chromatography (TLC) plates (silica gel 60 F254) were visualized either with a UV lamp (254 nm), or by submersion in the chosen stain for TLC. Flash column chromatography was carried out by using an automatic LC system. NMR experiments were carried out in the deuterated solvent of choice. Proton ^{1}H NMR spectra were recorded on a Bruker Avance Neo 400 MHz and proton-decoupled carbon $^{13}C\{1H\}$ NMR spectra were recorded at 75 MHz. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent as the internal reference. The following abbreviations are used for the multiplicity: s: singlet; d: doublet; t: triplet; q: quadruplet; p: pentuplet; h: heptaplet; m: multiplet or overlap of non-equivalent resonances; br s: broad singlet. Coupling constants (*J*) are reported in Hertz (Hz). High resolution mass spectra were determined on an AEI MS-9 using electrospray ionization (ESI) and a time-of-flight (TOF). Photochemical reactions have been carried out in a homemade photobox, equipped with a 3D-printed vial holder, a 390 nm Kessil lamp as the light source and a fan as the cooling system and placed on a stirrer plate. (for more details see Figures S1, S2).

2. Preparation of Substrates

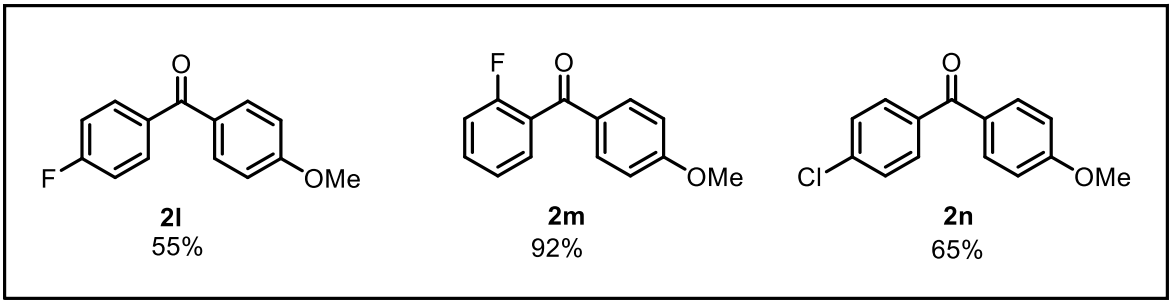
2.1. General procedure for the preparation of Benzophenones

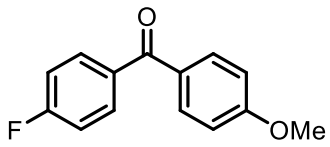
Benzophenones were prepared from a benzoic acid and an electron-rich aromatic according to the following reported procedure:[1]



Benzoic acid (0.75 mmol, 1.0 equiv), electron-rich aromatic (1.125 mmol, 1.5 equiv), TFAA (2 equiv), and TFA (0.8 mL) were added to a 10 mL screw-cap glass vial. The mixture was stirred at room temperature for 12 hours and monitored by TLC or GC-MS. After completion, the solvent was evaporated under reduced pressure, and the crude residue was purified by flash column chromatography on silica gel (Hex/EtOAc) to afford the corresponding ketone.

The following benzophenones (**2l-2n**) were prepared according to the general procedure.

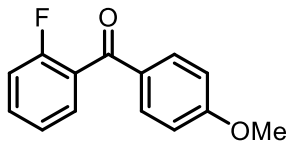




(4-Fluorophenyl)(4-methoxyphenyl)methanone (2l)[1]

Eluent: C.Hex/EtOAc (9:1); White solid (55%). Mp: 122°C. The data are in accordance with previously reported data.[1]

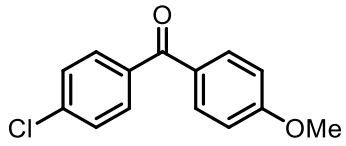
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (dt, *J* = 8.6, 2.4 Hz, 4H), 7.15 (t, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.7 Hz, 2H), 3.89 (s, 3H).



(2-Fluorophenyl)(4-methoxyphenyl)methanone (2m)[2]

Eluent: C.Hex/EtOAc (9:1); white solid (92%). Mp: 73°C. The data are in accordance with previously reported data.[2]

^{1}H NMR (400 MHz, CDCl3): δ 7.81 (d, *J* = 8.5 Hz, 2H), 7.55-7.47 (m, 2H), 7.24 (t, *J* = 7.7 Hz, 1H), 7.13 (t, *J* = 8.5 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 3.88 (s, 3H).

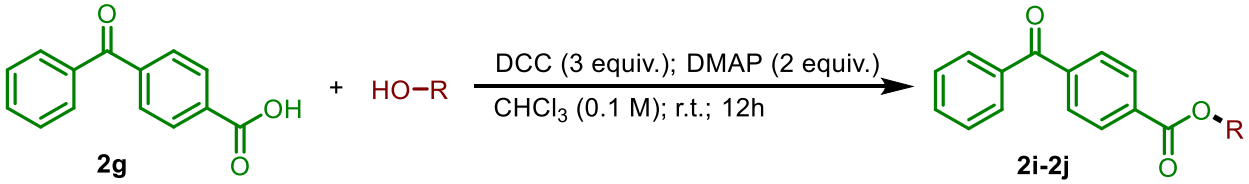


(4-chlorophenyl)(4-methoxyphenyl)methanone (2n)[1]

Eluent: C.Hex/EtOAc (9:1); white solid (65%). Mp: 123°C. The data are in accordance with previously reported data.[1]

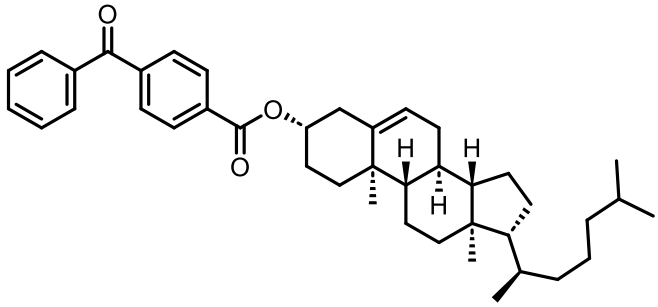
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 2H), 3.84 (s, 3H).

2.2. General procedure A for the esterification of benzophenone 2g



A flame-dried round-bottom flask was equipped with a magnetic stir bar and charged with compound **2g** (4.0 mmol, 4 equiv.), the corresponding alcohol (1.0 mmol, 1 equiv.), and DMAP (2.0 mmol, 2 equiv.). The flask was sealed with a rubber septum, purged with nitrogen, and anhydrous $CHCl_3$ (5 mL, 0.2 M) was added. A solution of DCC (3.0 mmol, 3 equiv.) in anhydrous $CHCl_3$ (5 mL) was then added dropwise via syringe. The reaction progress was monitored by TLC.

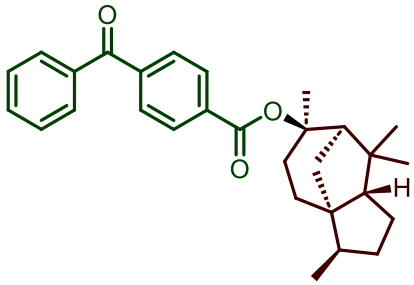
Upon completion, n-hexane was added to the mixture, and the resulting precipitate was filtered and washed with n-hexane (3 × 5 mL). The combined filtrates were successively washed with 0.2 M HCl (1 ×), saturated aqueous $NaHCO_3$ (1 ×), and distilled water (1 ×). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by crystallization from EtOAc.



(3S,8S,9S,10R,13R,14S,17R)-10,13-Dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-benzoylbenzoate (2i)

White solid (76%). Mp: 129-131 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.5 Hz, 2H), 7.91–7.76 (m, 4H), 7.66 – 7.57 (m, 1H), 7.54–7.45 (m, 2H), 5.47–5.41 (m, 1H), 4.96–4.83 (m, 1H), 2.49 (d, *J* = 7.9 Hz, 2H), 2.08–1.90 (m, 4H), 1.89–1.71 (m, 2H), 1.64-1.45 (m, 6H), 1.42–0.96 (m, 17H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.87 (dd, *J* = 6.6, 1.8 Hz, 6H), 0.70 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 196.2, 165.4, 141.3, 139.6, 137.2, 134.1, 133.0, 130.3, 129.9, 129.6, 128.6, 123.1, 75.3, 56.9, 56.3, 50.2, 42.5, 39.9, 39.7, 38.3, 37.2, 36.8, 36.3, 36.0, 32.1, 32.0, 28.4, 28.2, 28.0, 24.5, 24.0, 23.0, 22.7, 21.2, 19.5, 18.9, 12.0. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{41}H_{55}O_3^+$ 595.4146; Found 595.4143.

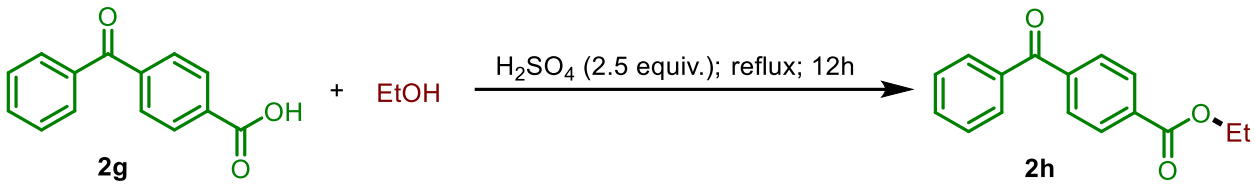


(3R,3aS,6R,7R,8aS)-3,6,8,8-tetramethyloctahydro-1H-3a,7-methanoazulen-6-yl 4-benzoylbenzoate (2j)

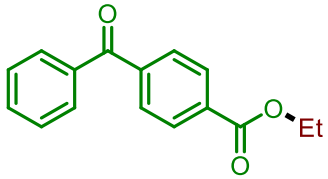
White solid (34%). Mp: 125-127 °C

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27–8.19 (m, 2H), 7.95–7.85 (m, 2H), 7.85–7.80 (m, 2H), 7.68–7.58 (m, 1H), 7.55–7.47 (m, 2H), 1.94–1.35 (m, 13H), 1.33 (s, 3H), 1.27 (d, *J* = 1.0 Hz, 3H), 1.00 (s, 3H), 0.84 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 196.1, 170.4, 142.2, 137.0, 133.2, 132.6, 130.3, 130.2, 130.0, 128.7, 75.6, 61.2, 56.7, 54.3, 43.6, 42.1, 41.6, 37.2, 35.5, 31.7, 30.3, 29.1, 27.8, 25.5, 15.7. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{29}H_{35}O_3^+$ 431.2581; Found 431.2584.

2.3. General procedure B for the esterification of benzophenone 2h



A flame-dried round-bottom flask was equipped with a magnetic stir bar and charged with compound **2g** (3.0 mmol, 1 equiv.), ethanol as solvent (0.4 M) and concentrated H_2SO_4 (7.5 mmol, 2.5 equiv.). The reaction was refluxed overnight. Upon completion, the mixture was cooled to room temperature and neutralized with saturated aqueous solution of $NaHCO_3$. The mixture was extracted with EtOAc (3×20 mL) and the combined organic phase was washed with distilled H_2O (3×20 mL). The crude residue was purified by flash column chromatography on silica gel (Hex/EtOAc) to afford the corresponding benzophenone **2h** in 92% yield. (Hex/EtOAc 30:1).



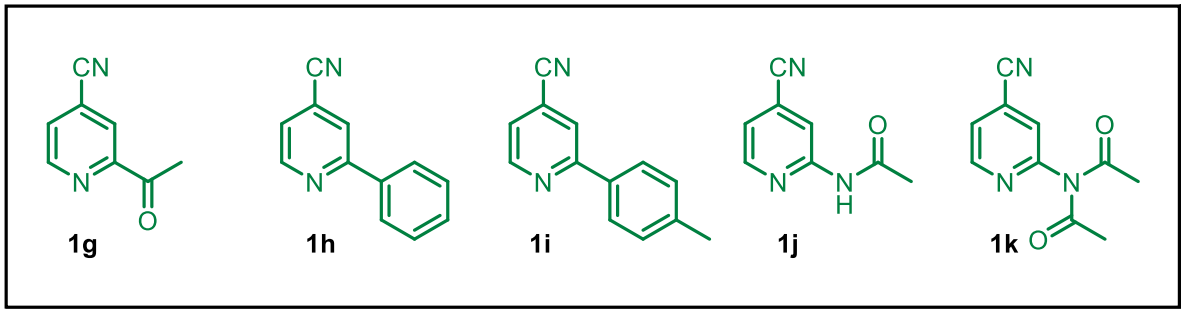
Ethyl 4-benzoylbenzoate (2h)

Eluent: C.Hex/EtOAc (9:1); white solid (65%). Mp: 123°C. The data are in accordance with previously reported data.[1]

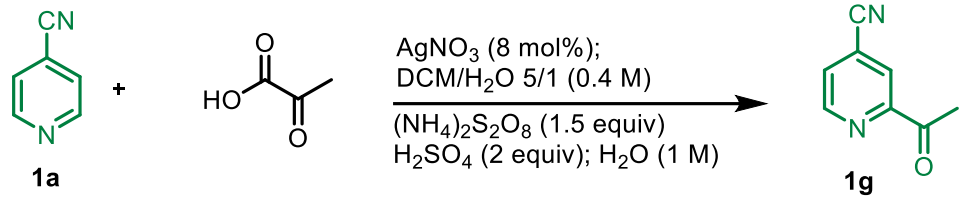
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0 Hz, 2H), 7.60 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 3.84 (s, 3H).

2.4. Preparation of cyanopyridines 1g-1k

Cyanopyridines **1g-1k** were prepared following reported procedures:



Synthesis of 2-acetylisonicotinonitrile (1g):

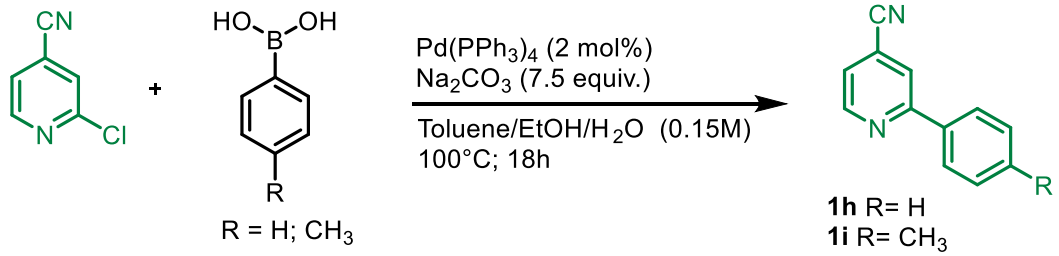


Compound **1g** was prepared according to the following reported procedure:[3]

In a flame-dried round-bottom flask to a solution of **1a** (1.0 equiv., 2.0 mmol), $AgNO_3$ (8 mol%) and pyruvic acid (2.50 equiv.) in DCM/H_2O (5/1 v/v 0.4 M) was added a solution of $(NH_4)_2S_2O_8$ (1.5 equiv.) and concentrated sulfuric acid (2.0 equiv.) in H_2O (1 M) dropwise at 0°C for 1 h. The mixture was warmed to 25°C and let it stir for another 1 h. The mixture was then adjusted to pH 8 with 1 M NaOH (aq.) and then filtered through a celite pad. The filtrate was extracted with DCM (2×). Combined extracts were washed with H_2O (2×) and brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography to afford **1g** in 78% yield (1.56 mmol; 228 mg) as a white solid. The reported data are in accordance with the previously reported data.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, J = 4.9, 0.9 Hz, 1H), 8.25 (p, J = 0.7 Hz, 1H), 7.69 (dd, J = 4.9, 1.6 Hz, 1H), 2.74 (d, J = 0.6 Hz, 3H).

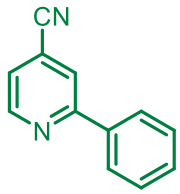
Synthesis of 1h and 1i:



Compounds **1h** and **1i** were prepared according to the following reported procedure:[4]

A flame-dried round bottom flask was charged with 2-chloroisonicotinonitrile (1.0 equiv), phenylboronic acid (1.2 equiv), $Pd(PPh_3)_4$ (2 mol%), and Na_2CO_3 (7.5 equiv). The flask was sealed with a rubber septum and N_2 was fluxed in the flask for 2 min. Degassed toluene (0.33 M), EtOH (1.33 M) and H_2O (0.33M) were added *via* syringe. The reaction mixture was additionally fluxed with N_2 for 5 minutes and then stirred vigorously at 100 °C for 18 h. Upon completion, the solution was cooled to room temperature and poured into a separatory funnel containing brine and extracted with

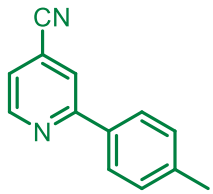
Et_2O (3×). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated under reduced pressure and the crude residue purified with column chromatography (C.Hex/EtOAc 9/1).



2-Phenylisonicotinonitrile (1h)

The reaction was run on a 2.0 mmol scale to afford **1h** as a white solid (1.54 mmol; 277.3 mg) in 77% yield. The reported data are in accordance with the previously reported data.[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, *J* = 5.0, 1.0 Hz, 1H), 8.05–7.97 (m, 2H), 7.94 (t, *J* = 1.2 Hz, 1H), 7.56–7.46 (m, 3H), 7.44 (dd, *J* = 5.0, 1.4 Hz, 1H).

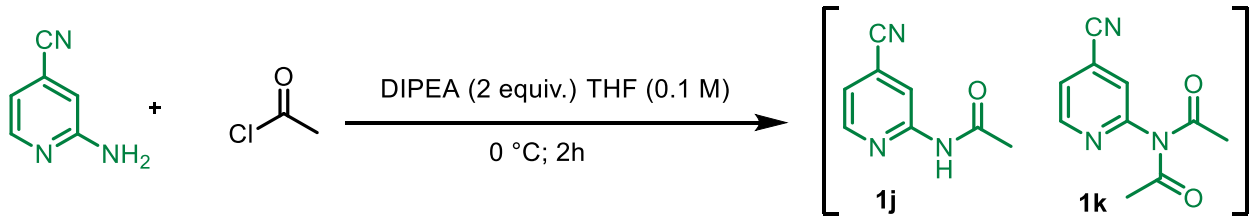


2-(p-Tolyl)isonicotinonitrile (1i)

The reaction was run on a 2.0 mmol scale to afford **1i** as a white solid (1.66 mmol; 322.2 mg) in 83% yield. The reported data are in accordance with the previously reported data.[4]

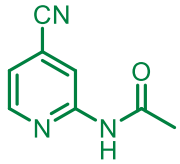
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.93–7.86 (m, 3H), 7.40 (dd, *J* = 4.9, 1.4 Hz, 1H), 7.35–7.26 (m, 2H), 2.42 (s, 3H).

Synthesis of 1j and 1k:



Compounds **1h** and **1i** were prepared according to the following reported procedure:[5]

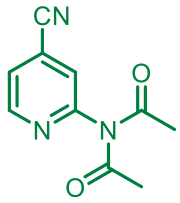
A flame-dried round bottom flask was charged with 2-aminoisonicotinonitrile (1.0 equiv.), DIPEA (2 equiv.) and dissolved in THF (0.1 M). The flask was sealed with a rubber septum and N_2 was bubbled in the solution for 2 min. The reaction mixture was cooled to 0° C and a solution of acetyl chloride (1.0 equiv. for **1j** and 2.0 equiv. for **1k**) in THF (0.1 M) was added dropwise and the reaction was stirred for 2 h. The corresponding products were isolated by extraction from EtOAc/water. No silica gel chromatography is needed.



***N*-(4-cyanopyridin-2-yl)acetamide (1j)**

The reaction was run on a 2.0 mmol scale to afford **1j** as a white solid (1.80 mmol; 289.9 mg) in 90% yield. The reported data are in accordance with the previously reported data.[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54–8.49 (m, 1H), 8.41 (dd, *J* = 5.1, 0.9 Hz, 1H), 8.29 (s, 1H), 7.24 (dd, *J* = 5.1, 1.4 Hz, 1H), 2.24 (s, 3H).



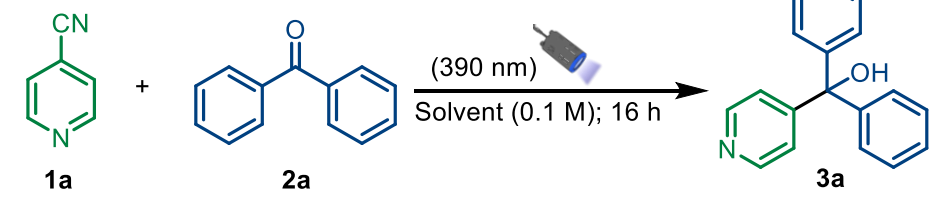
***N*-acetyl-*N*-(4-cyanopyridin-2-yl)acetamide (1k)**

The reaction was run on a 2.0 mmol scale to afford **1j** as a white solid (1.84 mmol; 373.6 mg) in 92% yield. The reported data are in accordance with the previously reported data.[5]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (dd, *J* = 5.1, 0.9 Hz, 1H), 7.59 (dd, *J* = 5.1, 1.4 Hz, 1H), 7.51 (t, *J* = 1.1 Hz, 1H), 2.29 (s, 6H).

3. Optimization for the light-mediated coupling of benzophenone 2a onto 4-cyanopyridine 1a

Optimization of reaction conditions in batch

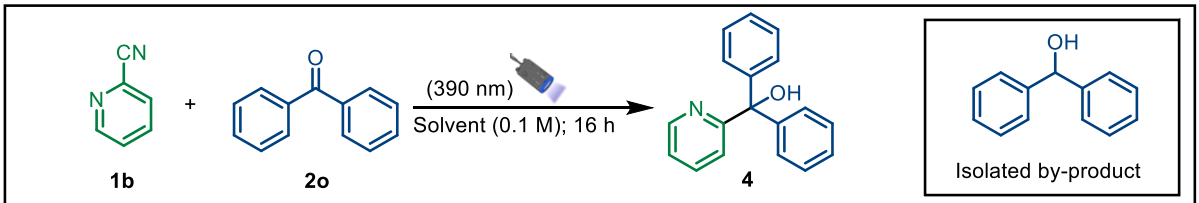


Entry	1a (equiv.)	2a (equiv.)	H-Donor (equiv.)	Solvent (0.1 M)	Yield[a]
1	3	1	Me_3N-BH_3 (2)	EtOAc	40%
2	3	1	γ-terpinene (10)	EtOAc	16%
3	3	1	2-propanol (5)	EtOAc	45%
4	1	1.2	2-propanol (5)	EtOAc	70%
5	1	1.2	2-propanol (10)	EtOAc	92%(90%)[b]
6	1	1.2	-	EtOAc/2-propanol 1/1	88%
7[c]	1	1.2	2-propanol (10)	EtOAc	82%
8[d]	1	1.2	2-propanol (10)	EtOAc	80%
9	1	1.2	2-propanol (10)	MeCN	85%
10	1	1.2	2-propanol (10)	MeCN/H_2O 9/1	72%
11	1	1.2	2-propanol (10)	Acetone	61%
12	1	1.2	2-propanol (10)	2-MeTHF	10%
13[e]	1	1.2	2-propanol (10)	EtOAc	0%
14	1	1.2	-	EtOAc	0%

Scheme S1. Reaction conditions: reaction run on 0.2 mmol scale in 0.2mL of solvent under N_2. Reactions were irradiated with a 40 W Kessil lamp (390 nm) for 16 h. a) Yield determined by GC-FID with the addition of byphenyl as internal standard. b) Isolated yield c) K_3PO_4 (0.4 mmol; 2 equiv.) as additive d) reaction performed under air e) No light

4. Optimization for the light-mediated coupling of benzophenone 2o onto 2-cyanopyridine 1b

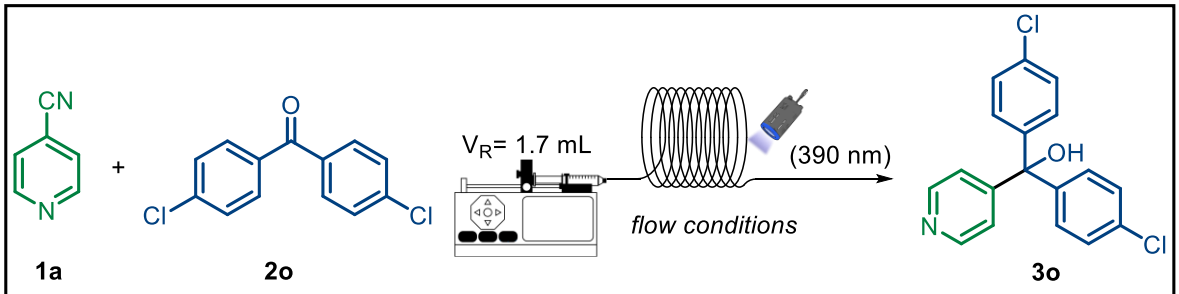
Optimization of reaction conditions in batch



Entry	1b (equiv.)	2o (equiv.)	H-Donor (equiv.)	Solvent (0.1 M)	Additives	Yield[a]
1	1	1.2	2-propanol (10)	EtOAc		7%
2	1	2	2-propanol (10)	EtOAc		10%
3	1	2	2-propanol (10)	EtOAc	TFA (3 equiv.)	11%
4	1	3	2-propanol (10)	EtOAc	$NaHCO_3$ (1.5 equiv.)	10%
5	1	3	2-propanol (10)	EtOAc/HFIP 1/1		13%
6	3	1	2-propanol (10)	EtOAc		16%
7	3	1	2-propanol (10)	EtOAc/HFIP 1/1		24%
8	3	1	2-propanol (5)	EtOAc/HFIP 1/1		35%
9	3	1	2-propanol (5)	EtOAc/HFIP/H_2O 4/2/1		(45%)[b]
10	3	1	2-propanol (5)	DCM/HFIP 1/1		15%

Scheme S2. Reaction conditions: reaction run on 0.2 mmol scale in 0.2mL of solvent under N_2. Reactions were irradiated with a 40 W Kessil lamp (390 nm) for 16 h. a) Yield determined by GC-FID with the addition of byphenyl as internal standard. b) Isolated yield.

5. Optimization for the conditions in flow

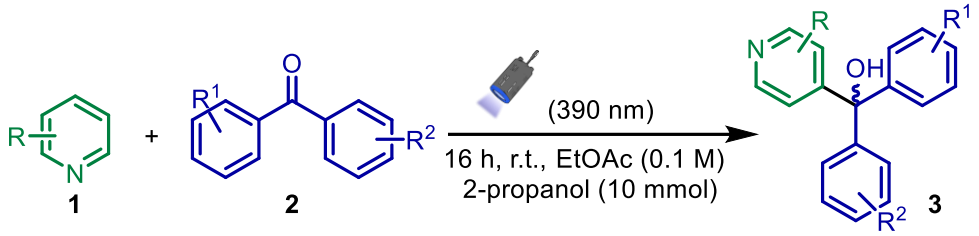


Entry	flow rate	solvent	RTD (min)[a]	yield[b]	Productivity (mmol/d)
1	2 mL/h	EtOAc (0.1 M)	51	80%	3.8
2	1.8 mL/h	EtOAc (0.1 M)	56	95%	4.1
3	1.5 mL/h	EtOAc (0.2 M)	68	90%	6.5
4	1.2 mL/h	EtOAc (0.2 M)	85	99%(98%)[c]	5.8

Scheme S3. Reaction conditions: **1a** (0.2 mmol 1.0 equiv.), **2o** (0.24 mmol, 1.2 equiv.), 2-propanol (2 mmol, 10 equiv.), EtOAc as solvent. Reactions were irradiated with two 40 W Kessil lamp (390nm). a) Ritention Time Distribution b) Yield determined by GC-FID with the addition of byphenyl as internal standard c) Isolated yield

6. General procedure for the light-mediated coupling of benzophenone 2 onto cyanopyridine 1

General procedure C/C' for reactions in batch



A dried 10 mL (Pyrex® Boro 3.3) tube was charged with a magnetic stirring bar, **1** (0.2 mmol), **2** (0.24 mmol) [for procedure **C' 2** (0.4 mmol)], 2-propanol (2.0 mmol) and EtOAc (2 mL 0.1 M). The tube was sealed with a rubber septum and N_2 was bubbled in the solution for 2 min. The tube was placed in a 3D printed reactor, stirred inside a photobox, equipped with a cooling fan, (see Figure S1) and irradiated with a 390 nm 40W Kessil LED lamp. The lamp was placed at distance of 6 cm from the reactor. After completion the crude mixture was purified by column chromatography to afford the pure compound **3**.

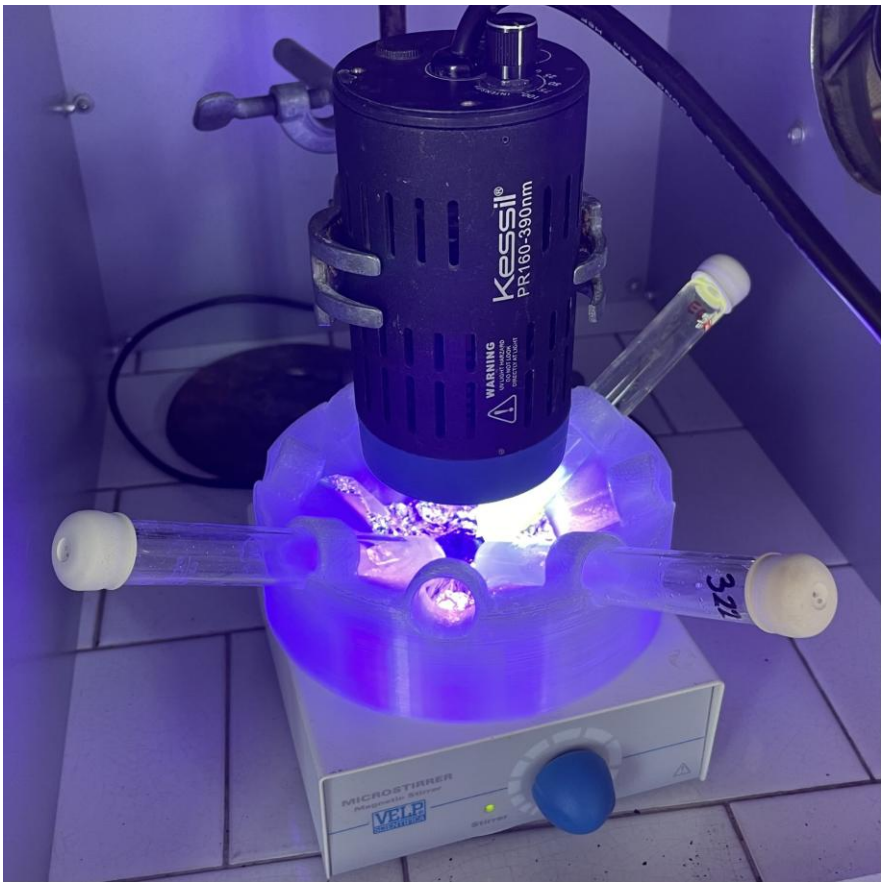
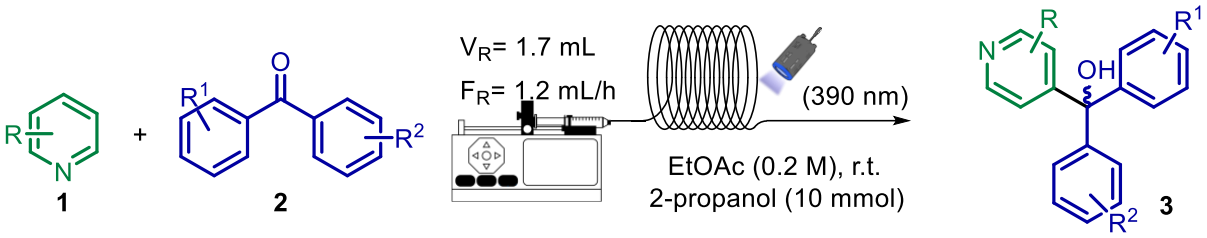


Figure S1. Photochemical set-up for the scope in batch

General procedure D for reactions in flow



A dried 10 mL (Pyrex® Boro 3.3) tube was charged with **1** (0.2 mmol), **2** (0.24 mmol), 2-propanol (2.0 mmol) and EtOAc (1 mL 0.2 M). The tube was sealed with a rubber septum and N_2 was bubbled in the solution for 2 min. The solution was taken up with a 3 mL syringe, mounted on a syringe pump and pushed into a MR-LAB-V microreactor (Little Things Factory GmbH) (volume 1.7 mL, Figure S2). For all the additional information visit (https://ltf-gmbh.com/product/mr-lab-v/). The system was equipped with a BPR (back pressure resistance) of 20 Psi and the optimal flow rate is 1.2 mL/h. Two 390 nm 40W Kessil LED lamp were placed at 5 cm distance from the reactor as shown in Figure S2 and placed inside a photobox, equipped with a cooling fan. After completion the crude mixture was purified by column chromatography to afford the pure compound **3**.

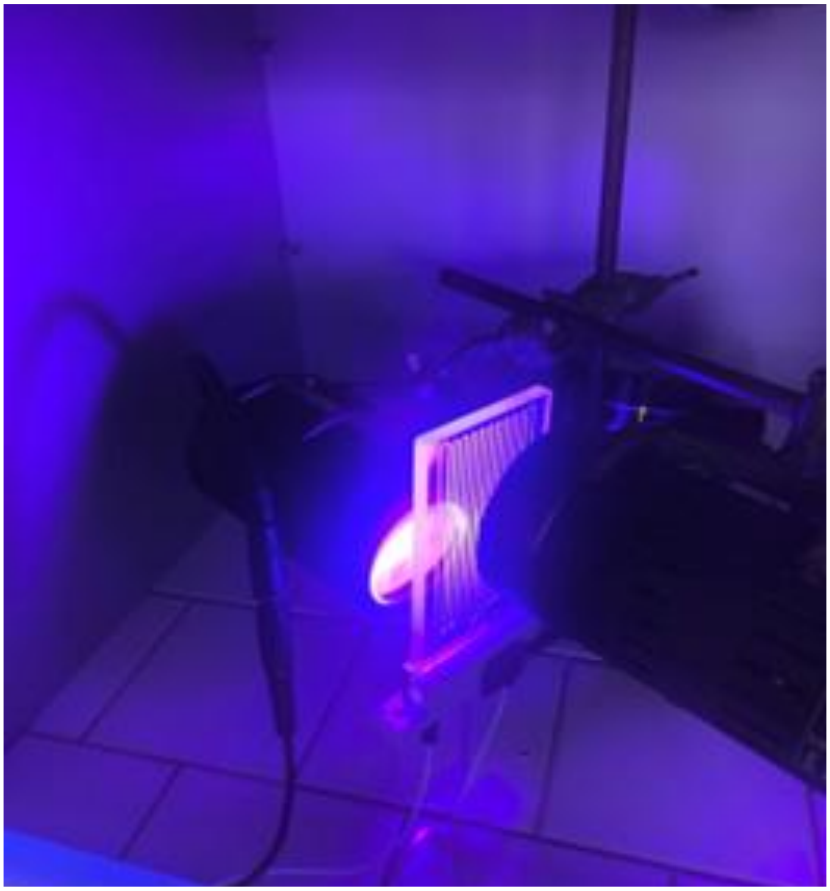
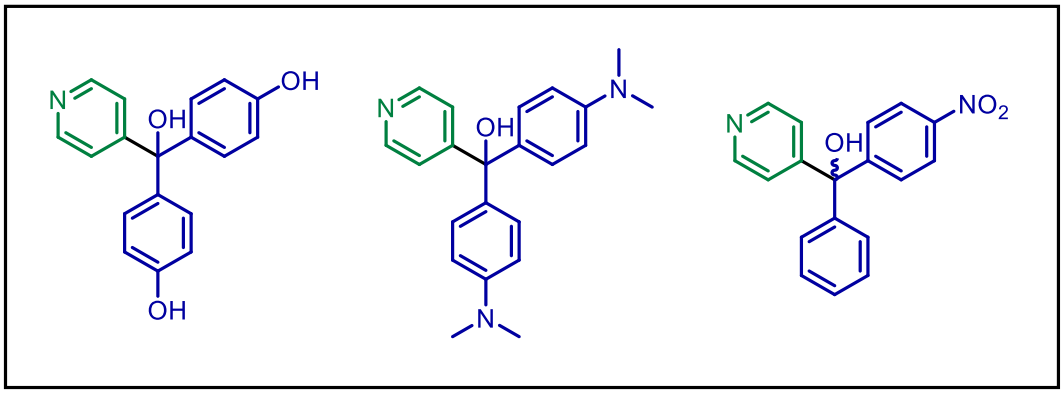
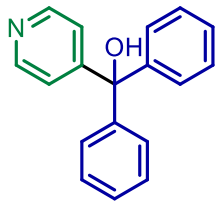


Figure S2. Photochemical set-up for the scope in flow

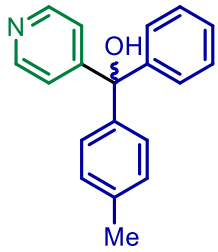
Limitation of the scope





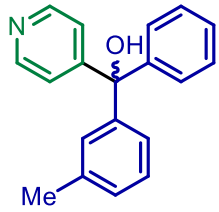
Diphenyl(pyridin-4-yl)methanol (3a)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid following procedure **C** (0.18 mmol; 47.0 mg) in 90% yield. Mp: 234-236 °C. The data are in accordance with previously reported data.[6]
^{1}H NMR (400 MHz, DMSO-d$_6$) δ 8.54–8.48 (m, 2H), 7.37–7.17 (m, 12H), 6.71 (s, 1H). **^{13}C NMR (101 MHz, DMSO-d$_6$)** δ 156.0, 149.2, 146.4, 127.8, 127.6, 127.1, 122.6, 79.9.



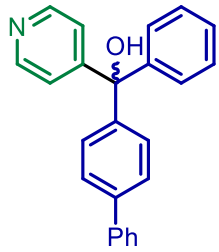
Phenyl(pyridin-4-yl)(p-tolyl)methanol (3b)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.198 mmol; 54.5 mg) in 99% yield. Following general procedure **D** (0.192 mmol; 52.8 mg) in 96% yield. Mp: 190-193 °C.
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.47–8.40 (m, 2H), 7.38–7.22 (m, 7H), 7.14 (s, 4H), 3.94 (s, 1H), 2.36 (s, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 155.9, 149.3, 145.9, 143.0, 137.6, 129.0, 128.3, 128.0, 127.9, 127.8, 122.8, 81.2, 21.1. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{18}NO^+$ 276.1383; Found 276.1385.



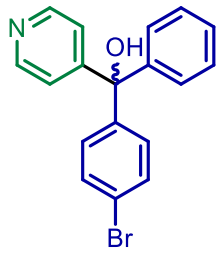
Phenyl(pyridin-4-yl)(m-tolyl)methanol (3c)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.198 mmol; 54.6 mg) in 99% yield. Mp: 180-182 °C.
^{1}H NMR (400 MHz, Acetone-d$_6$) δ 8.54–8.46 (m, 2H), 7.37–7.25 (m, 7H), 7.24–7.16 (m, 2H), 7.14–7.01 (m, 2H), 2.81 (s, 1H), 2.27 (s, 3H). **^{13}C NMR (101 MHz, Acetone-d$_6$)** δ 157.1, 150.3, 147.6, 147.5, 138.3, 129.5, 128.9, 128.9, 128.8, 128.7, 128.2, 81.6, 21.7. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{18}NO^+$ 276.1383; Found 276.1386.



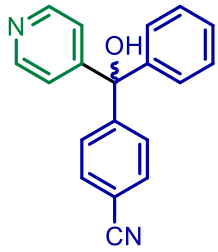
[1,1'-Biphenyl]-4-yl(phenyl)(pyridin-4-yl)methanol (3d)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.172 mmol; 58.0 mg) in 86% yield. Mp: 178-181 °C.
1H NMR (400 MHz, CDCl$_3$) δ 8.54 (d, *J* = 5.3 Hz, 2H), 7.62–7.48 (m, 4H), 7.48–7.40 (m, 2H), 7.39-7.30 (m, 10H), 3.32 (s, 1H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 155.5, 150.9, 149.6, 145.7, 144.7, 140.8, 140.5, 129.0, 128.4, 128.4, 128.0, 128.0, 127.7, 127.2, 127.1, 125.4, 122.8, 81.3. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{20}NO^+$ 338.1539; Found 338.1535.



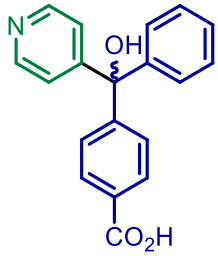
(4-Bromophenyl)(phenyl)(pyridin-4-yl)methanol (3e)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.156 mmol; 52.8 mg) in 78% yield. Mp: 200-201 °C.
^{1}H NMR (400 MHz, DMSO) δ 8.56–8.48 (m, 2H), 7.57–7.49 (m, 2H), 7.38–7.28 (m, 3H), 7.25–7.18 (m, 4H), 7.17 (s, 2H), 6.82 (s, 1H). **^{13}C NMR (101 MHz, DMSO)** δ 155.4, 149.3, 145.9, 145.8, 130.7, 129.9, 127.9, 127.6, 127.3, 122.5, 120.5, 79.6. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{18}H_{15}BrNO^+$ 340.0332; Found 340.0337.



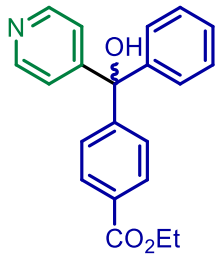
4-(Hydroxy(phenyl)(pyridin-4-yl)methyl)benzonitrile (3f)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C'** (0.142 mmol; 40.6 mg) in 71% yield. Mp: 100-101 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45–8.37 (m, 2H), 7.66–7.56 (m, 2H), 7.50–7.41 (m, 2H), 7.40–7.28 (m, 3H), 7.24–7.22 (m, 2H), 7.20–7.16 (m, 2H), 4.30 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 154.7, 150.8, 149.6, 144.7, 132.1, 128.7, 128.6, 128.5, 127.9, 122.7, 118.6, 111.7, 81.0. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{15}N_2O^+$ 287.1179; Found 287.1183.



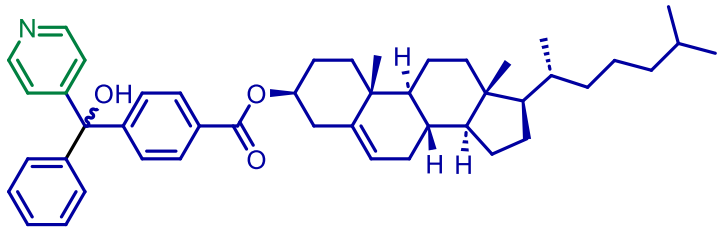
4-(Hydroxy(phenyl)(pyridin-4-yl)methyl)benzoic acid (3g)

Eluent: DCM/MeOH (95:5); Obtained as a pale red solid. Following general procedure **C** (0.196 mmol; 59.8 mg) in 98% yield. Following general procedure **D** (0.154 mmol; 47.0 mg) in 77% yield. Mp: 258-261 °C.
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.55 – 8.49 (m, 2H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.38 – 7.28 (m, 5H), 7.26 – 7.17 (m, 4H), 6.87 (s, 1H). **^{13}C NMR (101 MHz, DMSO-d_6)** δ 167.2, 155.4, 150.8, 149.3, 145.9, 130.0, 128.9, 127.9, 127.8, 127.6, 127.3, 122.6, 79.9. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{16}NO_3^+$ 306.1125; Found 306.1122.



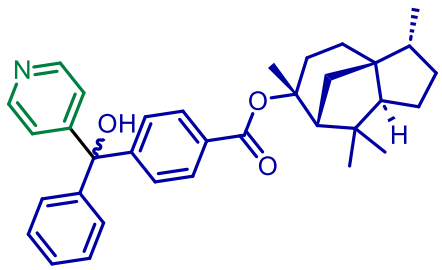
Ethyl 4-(hydroxy(phenyl)(pyridin-4-yl)methyl)benzoate (3h)

Eluent: DCM/MeOH (98:2); Obtained as a white solid. Following general procedure **C** (0.194 mmol; 64.6 mg) in 97% yield. Mp: 161-162 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35–8.28 (m, 2H), 8.00–7.92 (m, 2H), 7.41–7.34 (m, 2H), 7.29 (dd, *J* = 5.3, 2.0 Hz, 3H), 7.25–7.19 (m, 4H), 5.05 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 166.4, 155.6, 150.6, 149.2, 145.3, 129.8, 129.4, 128.4, 128.0, 128.0, 127.9, 122.9, 81.0, 61.2, 14.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{20}NO_3^+$ 334.1438; Found 334.1441.



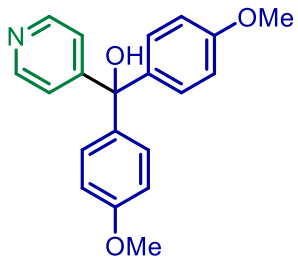
(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl 4-(hydroxy(phenyl)(pyridin-4-yl)methyl)benzoate (3i)

Eluent: DCM/MeOH (98:2); Obtained as a white solid as a mixture of diastereoisomers (dr 1:1.1). Following general procedure **C** with the addition of DCM (0.5 M) (0.13 mmol; 87.5 mg) in 65% yield. Mp: 131-132 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57–8.40 (m, 2H), 8.04–7.91 (m, 2H), 7.56–7.42 (m, 2H), 7.39–7.27 (m, 5H), 7.22–7.06 (m, 2H), 5.88 (dr_1, d, *J* = 3.9 Hz, 0.6H), 5.38 (dr_2, dd, *J* = 5.3, 1.8 Hz, 0.4H), 4.89 (dtd, *J* = 42.5, 11.0, 5.3 Hz, 1H), 3.14 (dtd, *J* = 85.1, 5.4, 2.5 Hz, 1H), 2.52–2.31 (m, 2H), 2.10–1.76 (m, 6H), 1.73–1.60 (m, 3H), 1.59–1.45 (m, 3H), 1.30–1.18 (m, 9H), 1.14–1.01 (m, 6H), 0.92 (dd, *J* = 17.9, 7.7 Hz, 3H), 0.88–0.82 (m, 8H), 0.68 (dr_1, s, 1.6H) 0.63 (dr_2, s, 1.4H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.9, 165.9, 149.7, 149.2, 148.9, 148.8, 143.5, 141.0, 139.8, 129.92, 129.90, 128.8, 128.6, 128.1, 126.8, 126.6, 126.4, 126.1, 125.5, 76.0, 74.5, 74.2, 57.4, 55.5, 55.1, 51.2, 50.2, 50.0, 44.9, 43.2, 43.0, 42.8, 39.7, 39.62, 39.59, 38.7, 38.3, 38.0, 37.9, 37.5, 37.4, 37.1, 36.8, 36.3, 36.2, 35.8, 35.7, 28.4, 28.15, 28.13, 28.0, 27.9, 26.8, 24.9, 23.9, 23.9, 23.0, 22.9, 22.7, 21.4, 20.8, 19.8, 19.4, 18.9, 12.1, 12.1. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{46}H_{60}NO_3^+$ 674.4568; Found 674.4572.



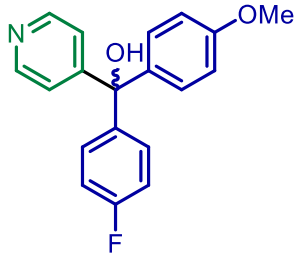
(3R,3aS,6R,7R,8aS)-3,6,8,8-tetramethyloctahydro-1H-3a,7-methanoazulen-6-yl 4-(hydroxy(phenyl)(pyridin-4-yl)methyl)benzoate (3j)

Eluent: DCM/MeOH (98:2); Obtained as a white solid. Following general procedure **C** with the addition of DCM (0.5 M). (0.140 mmol; 71.3 mg) in 70% yield. Mp: 106-108 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45–8.30 (m, 2H), 7.90 (d, *J* = 8.6 Hz, 2H), 7.38–7.27 (m, 5H), 7.25–7.16 (m, 4H), 4.46 (s, 1H), 2.65–2.52 (m, 1H), 2.19–2.06 (m, 2H), 1.92–1.77 (m, 2H), 1.66 (ddd, *J* = 10.0, 5.5, 2.4 Hz, 2H), 1.62 (s, 3H), 1.56–1.32 (m, 5H), 1.27 (dtd, *J* = 11.9, 7.6, 6.0 Hz, 1H), 1.12 (s, 3H), 0.95 (s, 3H), 0.83 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.3, 155.5, 150.0, 149.3, 145.4, 145.4, 131.5, 129.4, 128.4, 128.1, 128.0, 127.8, 122.9, 87.6, 81.1, 57.0, 57.0, 56.9, 54.1, 43.6, 41.4, 41.2, 37.1, 33.5, 31.4, 28.6, 27.5, 26.22, 26.21, 25.4, 15.7. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{34}H_{40}NO_3^+$ 510.3003; Found 510.3002.



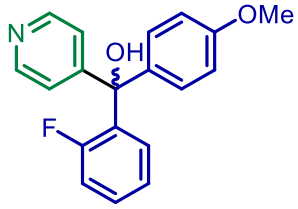
Bis(4-methoxyphenyl)(pyridin-4-yl)methanol (3k)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.102 mmol; 32.8 mg) in 51% yield. Following general procedure **D** (0.110 mmol; 35.3 mg) in 55% yield. Mp: 157-161 °C. The data are in accordance with previously reported data.[7]
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.47–8.40 (m, 2H), 7.30–7.24 (m, 2H), 7.20–7.11 (m, 4H), 6.88–6.80 (m, 4H), 3.80 (s, 6H), 3.74 (brs, 1H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 159.1, 156.3, 149.3, 138.3, 129.2, 122.7, 113.6, 80.7, 55.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{20}NO_3^+$ 322.1438; Found 322.1435.



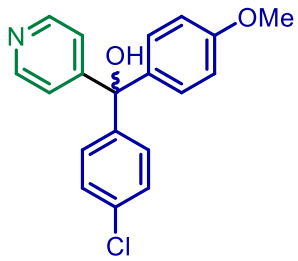
(4-Fluorophenyl)(4-methoxyphenyl)(pyridin-4-yl)methanol (3l)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.184 mmol; 56.9 mg) in 92% yield. Mp: 158-159 °C.
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.43–8.37 (m, 2H), 7.29–7.20 (m, 4H), 7.17–7.09 (m, 2H), 7.05–6.94 (m, 2H), 6.89–6.80 (m, 2H), 4.22 (s, 1H), 3.80 (s, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 162.2 (d, *J*= 247.1 Hz), 159.2, 156.0, 149.3, 141.9 (d, *J* = 3.3 Hz), 137.9, 129.7 (d, *J* = 8.1 Hz), 129.2, 122.7, 115.0 (d, *J* = 21.4 Hz), 113.7, 80.6, 55.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{17}FNO_2^+$ 310.1238; Found 310.1242.



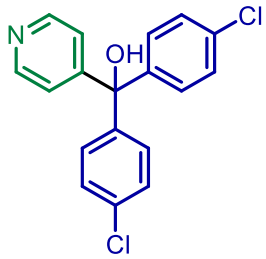
(2-Fluorophenyl)(4-methoxyphenyl)(pyridin-4-yl)methanol (3m)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** with the addition of DCM (0.5 mL - 0.4 M) (0.114 mmol; 35.2 mg) in 57% yield. Mp: 207-208 °C.
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.57–8.51 (m, 2H), 7.38–7.28 (m, 1H), 7.25–7.22 (m, 2H), 7.19–7.13 (m, 2H), 7.10–7.04 (m, 2H), 6.92–6.81 (m, 3H), 3.81 (s, 3H), 3.48 (s, 1H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 160.9 (d, *J* = 245.8 Hz), 159.4, 154.7, 149.7, 136.3, 133.2 (d, *J* = 10.2 Hz), 130.3 (d, *J* = 8.9 Hz), 130.0 (d, *J* = 3.2 Hz), 128.8, 124.1 (d, *J* = 3.4 Hz), 122.5, 116.5 (d, *J* = 22.7 Hz), 113.7, 79.9, 55.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{17}FNO_2^+$ 310.1238; Found 310.1237.



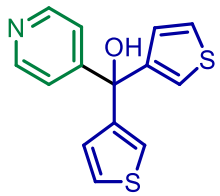
(4-Chlorophenyl)(4-methoxyphenyl)(pyridin-4-yl)methanol (3n)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.148 mmol; 48.1 mg) in 74% yield. Mp: 160-161 °C.
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.51–8.44 (m, 2H), 7.38–7.23 (m, 6H), 7.22–7.12 (m, 2H), 6.93–6.85 (m, 2H), 4.08 (s, 1H), 3.85 (s, 3H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 159.3, 155.7, 144.5, 137.7, 133.7, 129.3, 129.3, 128.4, 122.7, 113.8, 80.6, 55.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{17}ClNO_2^+$ 326.0942; Found 326.0940.



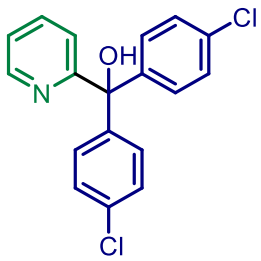
bis(4-Chlorophenyl)(pyridin-4-yl)methanol (3o)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C** (0.180 mmol; 52.9 mg) in 90% yield. Following general procedure **D** (0.196 mmol; 64.5 mg) in 98% yield. Mp: 182-185 °C. The data are in accordance with previously reported data.[8]
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.49–8.43 (m, 2H), 7.34–7.26 (m, 4H), 7.25–7.21 (m, 2H), 7.21–7.15 (m, 4H), 3.75 (s, 1H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 154.9, 149.7, 143.8, 134.2, 129.3, 128.7, 122.6, 80.6.



Pyridin-4-yldi(thiophen-3-yl)methanol (3p)

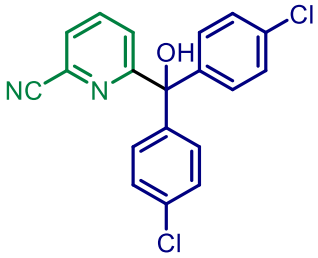
Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C'**. (0.164 mmol; 44.8 mg) in 82% yield. Mp: 155-156 °C.
^{1}H NMR (400 MHz, CDCl$_3$) δ 8.56–8.50 (m, 2H), 7.47–7.41 (m, 2H), 7.31 (dd, J = 5.1, 1.3 Hz, 2H), 6.96 (dd, J = 5.1, 3.6 Hz, 2H), 6.89 (dd, J = 3.6, 1.3 Hz, 2H), 3.96 (s, 1H). **^{13}C NMR (101 MHz, CDCl$_3$)** δ 154.6, 150.5, 149.7, 127.1, 126.8, 126.5, 121.5, 77.1. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{14}H_{12}NOS_2^+$ 274.0355; Found 274.0355.



Bis(4-chlorophenyl)(pyridin-2-yl)methanol (4)

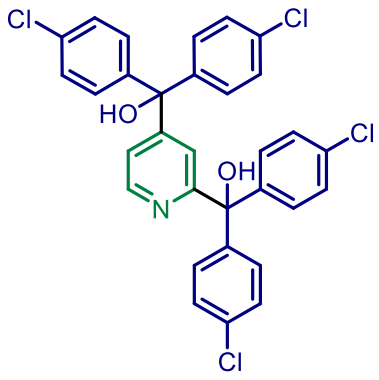
Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following a modified procedure. A dried 10 mL (Pyrex® Boro 3.3) tube was charged with a magnetic stirring bar, **1b** (0.6 mmol), **2o** (0.2 mmol), 2-propanol (1.0 mmol) and EtOAc/HFIP/H_2O [(4/2/1 v/v) (2 mL 0.1 M)]. The tube was sealed with a rubber septum and N_2 was bubbled in the solution for 2 min. The tube was placed in a 3D printed reactor, stirred inside a photobox, equipped with a cooling fan, (see Figure S1) and irradiated with a 390 nm 40W Kessil LED lamp. The lamp was placed at distance of 6 cm from the reactor. After completion the crude mixture was purified by column chromatography to afford the pure compound **4**. (0.090 mmol; 29.6 mg) in 45% yield. Mp: 85-86 °C. The data are in accordance with previous reported data.[9]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.66 (td, *J* = 7.7, 1.8 Hz, 1H), 7.32–7.16 (m, 9H), 7.05 (dt, *J* = 7.9, 1.1 Hz, 1H), 6.25 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.4, 148.1, 144.4, 136.9, 133.7, 129.6, 128.3, 122.9, 122.8, 80.2.



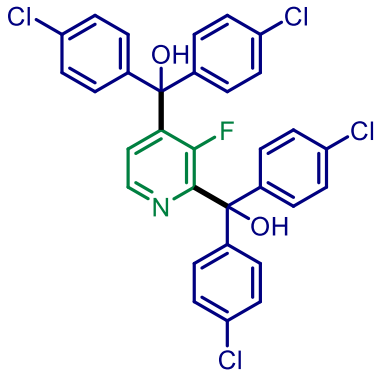
6-(Bis(4-chlorophenyl)(hydroxy)methyl)picolinonitrile (5)

Eluent: C.Hex/EtOAc (6:4); Obtained as a amorphous solid. Following general procedure **C'**. (0.104 mmol; 36.8 mg) in 52% yield.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (t, *J* = 7.9 Hz, 1H), 7.68 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.35 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.32–7.28 (m, 4H), 7.22–7.12 (m, 4H), 5.36 (s, 1H) **^{13}C NMR (101 MHz, $CDCl_3$)** δ 165.1, 143.2, 137.9, 134.2, 132.5, 129.5, 128.6, 127.6, 126.0, 116.7, 80.6. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{13}Cl_2N_2O^+$ 355.0399; Found 355.0401.



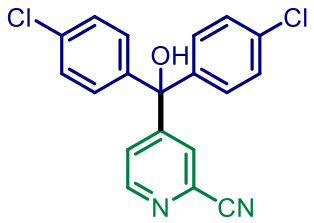
Pyridine-2,4-diylbis(bis(4-chlorophenyl)methanol) (6)

Eluent: C.Hex/EtOAc (5:5); Obtained as a white solid. Following general procedure **C'**. (0.150 mmol; 86.8 mg) in 75% yield. Mp: 197-198 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (dt, *J* = 5.2, 0.8 Hz, 1H), 7.26–7.17 (m, 5H), 7.15 (dt, *J* = 6.9, 2.3 Hz, 5H), 7.06–6.93 (m, 8H), 6.89 (dd, *J* = 1.7, 0.8 Hz, 1H), 6.04 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 162.7, 155.5, 148.0, 144.1, 143.3, 134.5, 133.8, 129.4, 129.1, 128.7, 128.3, 121.7, 121.4, 80.7, 80.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{31}H_{22}Cl_4NO_2^+$ 580.0399; Found 580.0396.



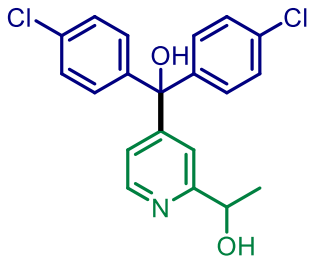
(3-Fluoropyridine-2,4-diyl)bis(bis(4-chlorophenyl)methanol) (7)

Eluent: C.Hex/EtOAc (5:5); Obtained as a white solid. Following general procedure **C'**. (0.140 mmol; 83.6 mg) in 70% yield. Mp: 183-184 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 5.0, 0.8 Hz, 1H), 7.34–7.27 (m, 4H), 7.26–7.22 (m, 4H), 7.17–7.13 (m, 4H), 7.11–7.08 (m, 4H), 7.04 (t, *J* = 5.2 Hz, 1H), 6.68 (s, 1H), 3.18 (d, *J* = 6.2 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 154.2 (d, *J* = 259.1 Hz), 150.8 (d, *J* = 15.7 Hz), 144.1 (d, *J* = 9.8 Hz), 143.6 (d, *J* = 6.2 Hz), 142.4, 141.9, 134.7, 133.9, 129.2 (d, *J* = 2.5 Hz), 128.8, 128.7, 128.6, 128.5, 128.3, 124.7, 79.60, 78.6 (d, *J* = 5.2 Hz). **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{31}H_{21}Cl_4FNO_2^+$ 598.0305; Found 598.0306.



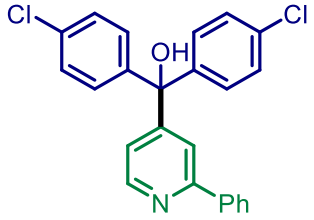
4-(Bis(4-chlorophenyl)(hydroxy)methyl)picolinonitrile (8)

Eluent: C.Hex/EtOAc (5:5); Obtained as a white solid. Following general procedure **C'**. (0.126 mmol; 44.6 mg) in 63% yield. Mp: 151-153 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.39 (dt, *J* = 1.7, 0.8 Hz, 1H), 7.35–7.31 (m, 4H), 7.22 (ddd, *J* = 5.1, 1.8, 0.8 Hz, 1H), 7.02–6.95 (m, 4H), 5.48 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 153.8, 151.4, 138.9, 134.5, 133.9, 130.5, 129.4, 129.1, 127.5, 117.2, 54.7. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{19}H_{13}Cl_2N_2O^+$ 355.0399; Found 355.0401.



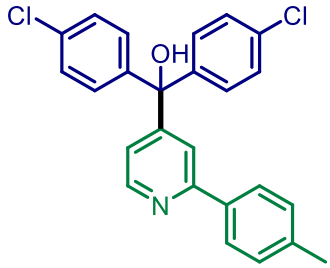
1-(4-(Bis(4-chlorophenyl)(hydroxy)methyl)pyridin-2-yl)ethan-1-ol (9)

Eluent: C.Hex/EtOAc (4:6); Obtained as a white gel. Following general procedure **C'**. (0.120 mmol; 44.8 mg) in 60% yield.
^{1}H NMR (400 MHz, CD_3OD) δ 8.39 (dd, *J* = 5.3, 0.8 Hz, 1H), 7.56 (q, *J* = 0.8 Hz, 1H), 7.37–7.29 (m, 4H), 7.29–7.19 (m, 5H), 4.84 (s, 1H), 3.35 (s, 1H), 3.31 (p, *J* = 1.7 Hz, 1H), 1.42 (d, *J* = 6.6 Hz, 3H). **^{13}C NMR (101 MHz, CD_3OD)** δ 166.2, 158.7, 148.9, 146.0 (d, *J* = 1.7 Hz), 134.6, 130.7, 130.7, 129.2, 122.7, 119.9, 81.3, 71.3, 24.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{18}Cl_2NO_2^+$ 374.0709; Found 374.0712.



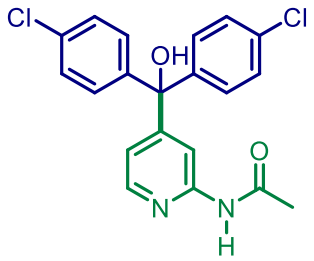
Bis(4-chlorophenyl)(2-phenylpyridin-4-yl)methanol (10)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C'**. (0.160 mmol; 64.8 mg) in 80% yield. Mp: 200 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (dd, *J* = 5.2, 0.8 Hz, 1H), 7.92–7.84 (m, 2H), 7.70 (dd, *J* = 1.8, 0.9 Hz, 1H), 7.48–7.35 (m, 3H), 7.34–7.29 (m, 4H), 7.24–7.17 (m, 4H), 7.11 (dd, *J* = 5.2, 1.8 Hz, 1H), 3.16 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.9, 155.4, 149.7, 143.8, 139.2, 134.2, 129.3, 129.3, 128.9, 128.7, 127.2, 121.1, 119.3, 80.8. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{24}H_{18}Cl_2NO^+$ 406.0760; Found 406.0756.



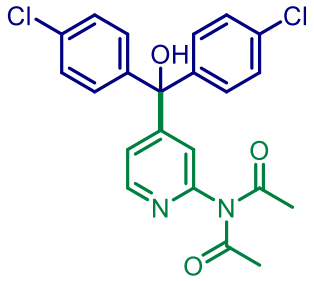
Bis(4-chlorophenyl)(2-(p-tolyl)pyridin-4-yl)methanol (11)

Eluent: C.Hex/EtOAc (6:4); Obtained as a white solid. Following general procedure **C'**. (0.162 mmol; 67.9 mg) in 81% yield. Mp: 208-209 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63–8.55 (m, 1H), 7.84–7.76 (m, 2H), 7.67 (dt, *J* = 1.6, 0.7 Hz, 1H), 7.36–7.26 (m, 4H), 7.28–7.20 (m, 6H), 7.08 (dt, *J* = 5.2, 1.7 Hz, 1H), 2.95 (d, *J* = 21.9 Hz, 1H), 2.39 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 157.9, 155.2, 149.7, 143.8, 139.4, 136.5, 134.2, 129.6, 129.3, 128.7, 127.0, 120.7, 118.9, 80.9, 21.4. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{25}H_{20}Cl_2NO^+$ 420.0916; Found 420.0920.



***N*-(4-(Bis(4-chlorophenyl)(hydroxy)methyl)pyridin-2-yl)acetamide (12)**

Eluent: C.Hex/EtOAc (1:1); Obtained as a white solid. Following general procedure **C'**. (0.154 mmol; 59.4 mg) in 77% yield. Mp: 157-161 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.24 (s, 1H), 8.11 (d, *J* = 5.4 Hz, 1H), 7.30–7.25 (m, 4H), 7.25–7.14 (m, 4H), 6.93 (dd, *J* = 5.4, 1.7 Hz, 1H), 4.05 (s, 1H), 2.10 (s, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 169.2, 157.6, 151.8, 147.4, 143.8, 134.1, 129.3, 128.5, 119.0, 113.0, 80.7, 24.7. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{17}Cl_2N_2O_2^+$ 387.0662; Found 387.0665.

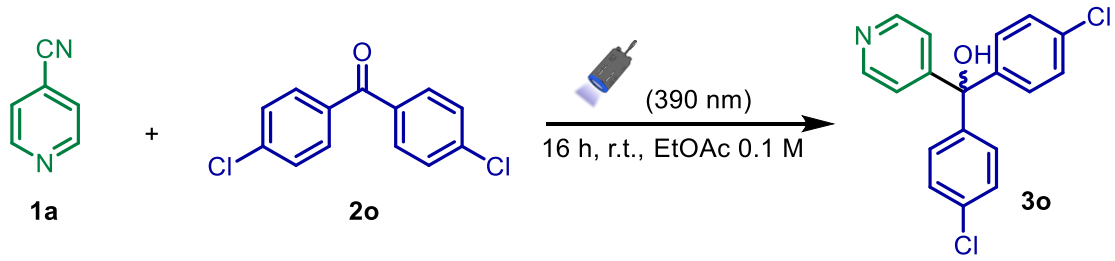


***N*-Acetyl-*N*-(4-(bis(4-chlorophenyl)(hydroxy)methyl)pyridin-2-yl)acetamide (13)**

Eluent: C.Hex/EtOAc (1:1); Obtained as a white solid. Following general procedure **C'**. (0.170 mmol; 72.8 mg) in 85% yield. Mp: 153-155 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (dd, *J* = 5.2, 0.7 Hz, 1H), 7.34–7.29 (m, 4H), 7.28–7.25 (m, 1H), 7.20–7.14 (m, 5H), 3.54 (s, 1H), 2.22 (s, 6H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 172.7, 158.2, 152.9, 149.7, 143.3, 134.5, 129.2, 128.8, 123.0, 122.9, 80.5, 26.8. **HRMS** (EI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{18}Cl_2N_2O_3^+$ 429.0767; Found 429.0763.

7. Scale up reactions

7.1. Reaction in batch



A dried 200 mL (Pyrex®) vessel was charged with a magnetic stirring bar, **1a** (1.0 g; 9.6 mmol), **2o** (2.9 g; 11.5 mmol), 2-propanol (7.5 mL; 96.0 mmol) and EtOAc (96 mL 0.1M). The vessel was sealed with a rubber septum and N_2 was bubbled in the solution for 5 min. The vessel was placed in a photo-box, equipped with a cooling fan (see Figure S3) and irradiated with a 390 nm 40W Kessil LED lamp.

The lamp was placed at 1 cm distance from the upper part of the vessel. After completion the crude mixture was purified by column chromatography to afford pure **3o** (2.53 g 7.68 mmol, 80% yield).

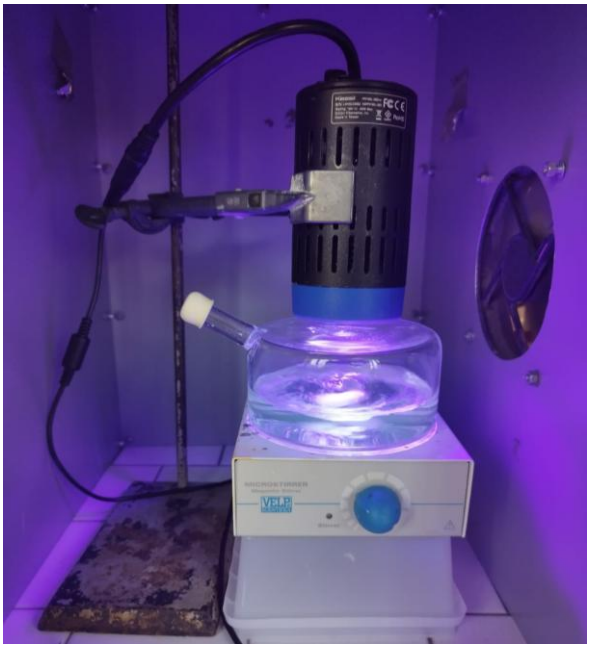
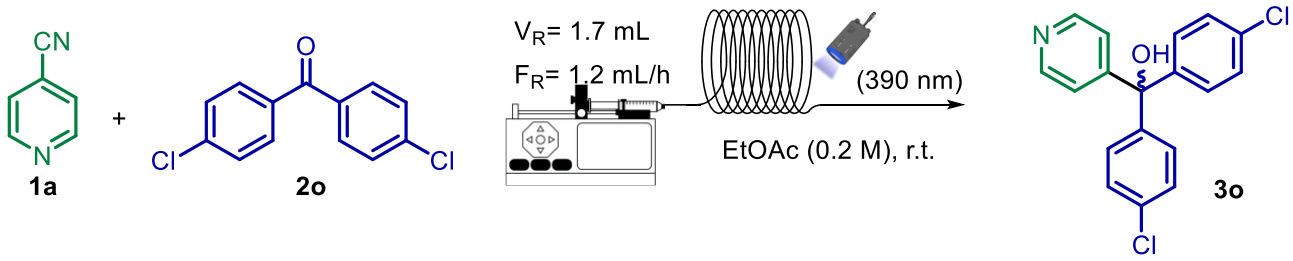


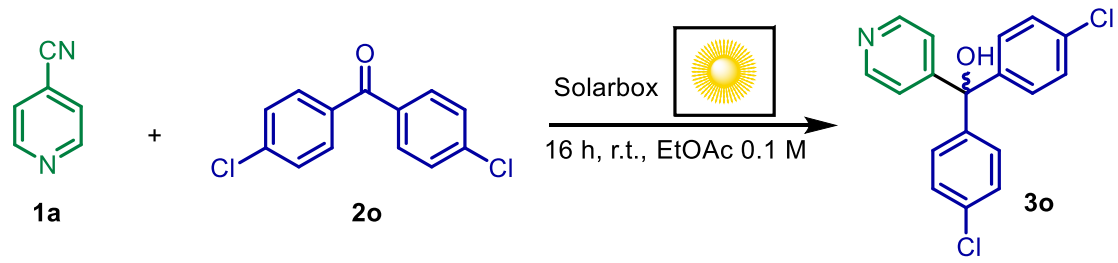
Figure S3. Set-up for the scale-up reaction in batch

7.2. Reaction in flow



In an oven dried 250 mL Schlenk flask, equipped with a magnetic stirring bar, was charged with **1a** (1.0 g; 9.6 mmol), **2o** (2.9 g; 11.5 mmol), 2-propanol (7.5 mL; 96.0 mmol) and EtOAc (48 mL 0.2 M). The flask was sealed with a rubber septum and N_2 was bubbled in the solution for 5 min. The solution was stirred until the mixture was completely homogeneous. The solution was taken up with a 50 mL syringe, mounted on a syringe pump and pushed into a MR-LAB-V microreactor (**Little Things Factory GmbH)** (volume 1.7 mL, Figure S2). For all the additional information visit (https://ltf-gmbh.com/product/mr-lab-v/). The system was equipped with a BPR (back pressure resistance) of 20 Psi and the optimal flow rate is 1.2 mL/h. Two 390 nm 40W Kessil LED lamp were placed at 5 cm distance from the reactor as shown in Figure S2 and placed inside a photobox, equipped with a cooling fan. Once the first 50 mL of solution were injected in the reactor, additional solution was taken up with the 50 mL siringue. After completion the crude mixture was purified by column chromatography to afford the pure compound **3o** (2.68 g 8.16 mmol, 85% yield).

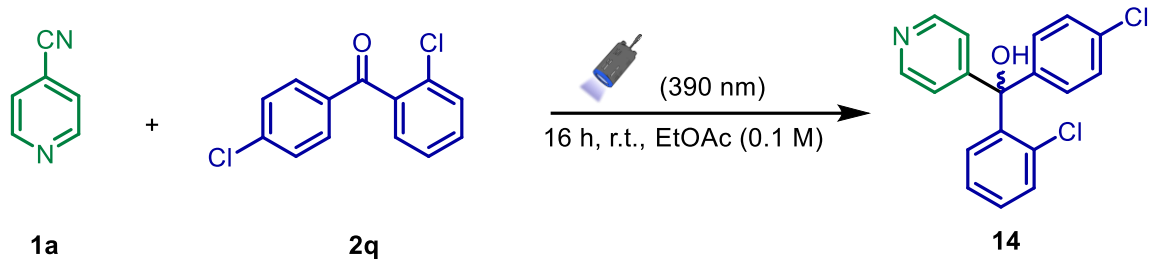
7.3. Reaction in Solarbox



A dried 200 mL (Pyrex®) vessel was charged with a magnetic stirring bar, **1a** (1.0 g; 9.6 mmol), **2o** (2.9 g; 11.5 mmol), 2-propanol (7.5 mL; 96.0 mmol) and EtOAc (96 mL 0.1 M). The vessel was sealed with a rubber septum and N_2 was bubbled in the solution for 5 min. The vessel was placed in a Solarbox (Solarbox 1500e; Co.Fo.Me.Gra., Italy, Milan), equipped with a cooling fan, , a magnetic stirrer placed below (see Figure S4) and irradiated with a 1.5 kW Xenon lamp, with light intensity: 500 $W \cdot m^{-2}$ (the emission spectrum of the employed lamp is available online at: https://cofomegra.it/). After completion the crude mixture was purified by column chromatography to afford the pure **3o** (2.56 g, 7.77 mmol, 81% yield).

Figure S4. Set-up for the scale-up reaction in Solarbox

8. Synthesis of Fenarimol's analogue

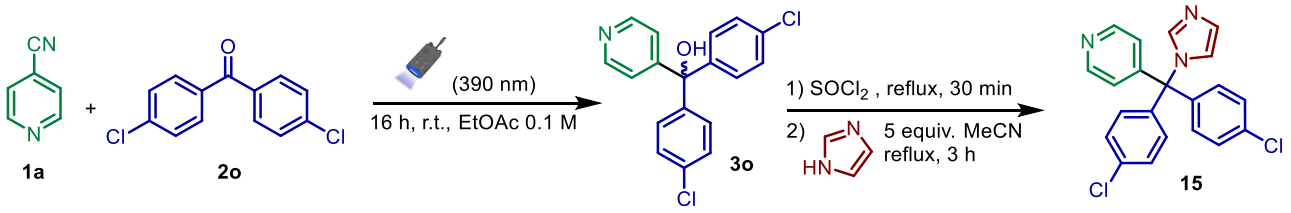


1a **2q** **14**

The following procedure was followed for both the reaction on a (0.2 mmol) and (1.0 mmol) scale.

A dried (Pyrex®) vessel was charged with a magnetic stirring bar, **1a** (1.0 equiv.), **2q** (1.2 equiv.), 2-propanol (10 equiv.) and EtOAc (0.1 M). The vessel was sealed with a rubber septum and N_2 was bubbled in the solution for 2 min. The vessel was placed in a photo-box, equipped with a cooling fan (see Figure S2 for 0.2 mmol scale and Figure S3 for 1.0 mmol scale) and irradiated with a 390 nm 40W Kessil LED lamp. After completion the crude mixture was purified by column chromatography to afford pure **14**. Obtained as a white solid. Yield on a 0.2 mmol scale (57.3 mg 0.174 mmol, 87% yield). Yield on a 1.0 mmol scale (279.7 mg 0.85 mmol, 85% yield). Mp: 210-211 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60–8.50 (m, 2H), 7.42 (dd, J = 7.9, 1.4 Hz, 1H), 7.34–7.28 (m, 3H), 7.21–7.13 (m, 5H), 6.70 (dd, J = 7.9, 1.6 Hz, 1H), 4.58 (s, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 154.1, 149.9, 142.8, 141.9, 134.0, 133.1, 131.8, 131.2, 130.0, 129.3, 129.1, 128.6, 126.9, 122.6, 81.5.
HRMS (EI) m/z: $[M+H]^+$ Calculated for $C_{18}H_{14}Cl_2NO^+$ 330.0447; Found 330.0446.

9. Synthesis of Clotrimazole's analogue



1a **2o** **3o** **15**

The following procedure was followed for both the reaction on a (0.2 mmol) and (1.0 mmol) scale. For the 1st step was followed the general procedure **C**. (**3o** was isolated by column chromatography). For the 2nd step was followed a slightly modified reported procedure.[8]
A dried (Pyrex®) vessel was charged with **3o** (1.0 equiv.) and thionyl chloride (1.2 M) and the mixture was refluxed for 30 minutes. Then the crude was concentrated under reduced pressure. The residue was then dissolved in MeCN (0.1 M) and imidazole was added (5.0 equiv.). The mixture was refluxed for 3h. Upon completion, the mixture was cooled to room temperature and quenched with $NaHCO_3$ (sat.) solution. The crude was extracted with EtOAc (3x). The organic layers were collected and dried with Na_2SO_4, filtrated and concentrated under reduced pressure. The crude mixture was subjected to column chromatography (DCM/MeOH 95/5) to afford pure **15** as a white solid. Yield on a 0.2 mmol

scale (66.7 mg 0.176 mmol, 88% yield) over 2 steps. Yield on a 1.0 mmol scale (322.2 mg 0.85 mmol, 85% yield). Mp: 142-144 °C. The data is in accordance with the previously reported data.[8]
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68–8.61 (m, 2H), 7.41 (t, *J* = 1.2 Hz, 1H), 7.38–7.32 (m, 4H), 7.12 (t, *J* = 1.1 Hz, 1H), 7.08–6.99 (m, 6H), 6.76 (t, *J* = 1.4 Hz, 1H). **^{13}C NMR (101 MHz, $CDCl_3$)** δ 150.7, 150.4, 139.3, 138.7, 135.3, 131.0, 129.6, 129.0, 124.0, 121.3, 73.8.

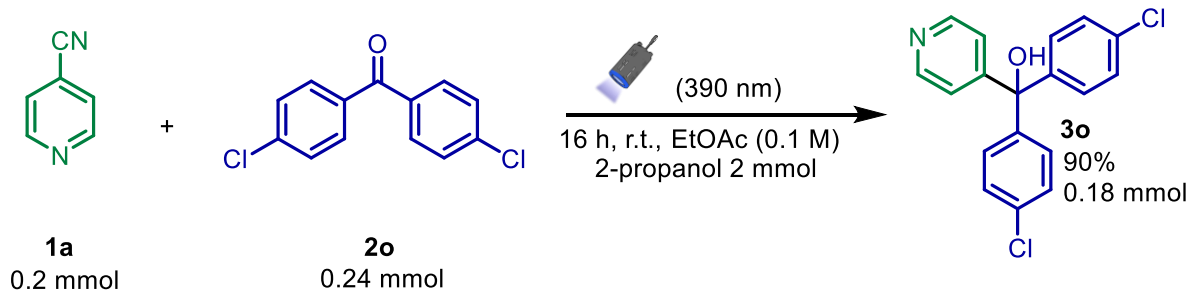
10. Green metrics

The Process Mass Intensity (PMI), E-factor, Atom Economy (AE) and EcoScale were calculated for selected reactions herein reported:

An Eco Scale of above 75 is considered an excellent green method, above 50 is acceptable, while scores below 50 indicate inadequate eco-friendliness. Eco Scale can be calculated as: Eco Scale = 100 - sum of the individual penalties.[10]

Synthesis of 3o on 0.2 mmol scale in batch:

3o was prepared according to general procedure **C**.



$$AE = \frac{MM_{3o}}{MM_{\mathbf{1a}} + MM_{\mathbf{2o}}} \times 100 = \frac{329.04\ {}^{g}/_{mol}}{354.03\ {}^{g}/_{mol}} \times 100 = 92.9\%$$

$$PMI = \frac{Mass_{\mathbf{1a}} + Mass_{\mathbf{2o}} + Mass_{2-propanol} + Mass_{EtOAc}}{Mass_{\mathbf{3}}} = \frac{380.8\ mg}{59.2\ mg} = 6.43\ {}^{Kg}/_{Kg}$$

$$E_{factor} = PMI - 1 = 5.43\ {}^{Kg}/_{Kg}$$

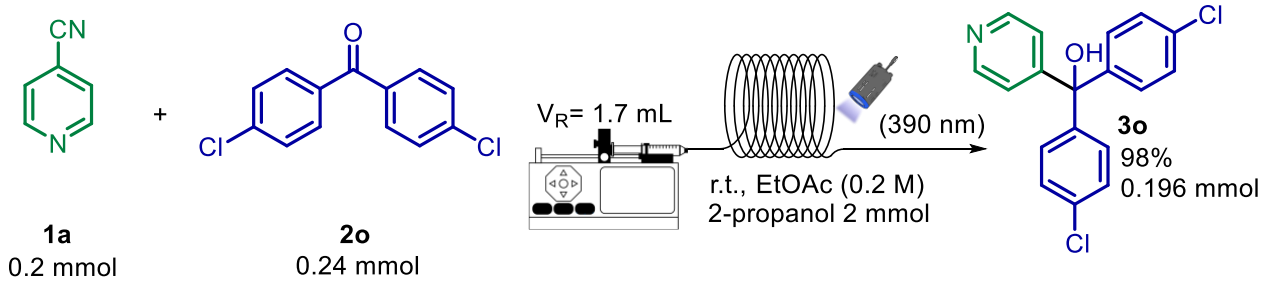
Entry	Parameter	Value	Penalty Points
1	Yield	(100-90)/2	5
2	Price of substrates	< €10	0
3	Safety[a]	Not dangerous	0
4	Technical Setup	Photochemical apparatus	2
5	Temperature/Time	r.t. ; < 24 h	1
6	Workup and purification	column chromatography	10
[a] Based on the hazard warning symbols		**Total Penalty Points**	**18**

Scheme S4. Penalty points to calculate the EcoScale value

$$EcoScale = 100 - Penalty\ Points\ = 82$$

Synthesis of 3o on 0.2 mmol scale in flow:

3o was prepared according to general procedure **D**.



$$AE = \frac{MM_{3o}}{MM_{\mathbf{1a}} + MM_{\mathbf{2o}}} \times 100 = \frac{329.04\ {}^{g}/_{mol}}{354.03\ {}^{g}/_{mol}} \times 100 = 92.9\%$$

$$PMI = \frac{Mass_{\mathbf{1a}} + Mass_{\mathbf{2o}} + Mass_{2-propanol} + Mass_{EtOAc}}{Mass_{\mathbf{3}}} = \frac{290.8\ mg}{64.5\ mg} = 4.5\ {}^{Kg}/_{Kg}$$

$$E_{factor} = PMI - 1\ = 3.5\ {}^{Kg}/_{Kg}$$

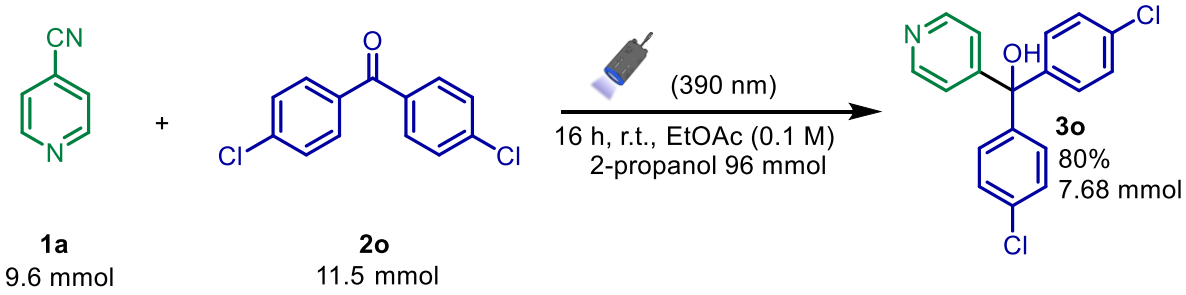
Entry	Parameter	Value	Penalty Points
1	Yield	(100-98)/2	1
2	Price of substrates	< €10	0
3	Safety[a]	Not dangerous	0
4	Technical Setup	Photochemical apparatus	2
5	Temperature/Time	r.t. ; < 24 h	1
6	Workup and purification	column chromatography	10
[a] Based on the hazard warning symbols		**Total Penalty Points**	**14**

Scheme S5. Penalty points to calculate the EcoScale value

$$EcoScale = 100 - Penalty\ Points\ = 86$$

Synthesis of 3o on 9.6 mmol scale in batch:

3o was prepared according to gram scale procedure described in section **7.1**.



1a
9.6 mmol

2o
11.5 mmol

3o
80%
7.68 mmol

$$AE = \frac{MM_{3o}}{MM_{\mathbf{1a}} + MM_{\mathbf{2o}}} \times 100 = \frac{329.04\ {}^{g}/_{mol}}{354.03\ {}^{g}/_{mol}} \times 100 = 92.9\%$$

$$PMI = \frac{Mass_{\mathbf{1a}} + Mass_{\mathbf{2o}} + Mass_{2-propanol} + Mass_{EtOAc}}{Mass_{\mathbf{3}}} = \frac{90.75\ g}{2.53\ g} = 35.9\ {}^{Kg}/_{Kg}$$

$$E_{factor} = PMI - 1\ = 34.9\ {}^{Kg}/_{Kg}$$

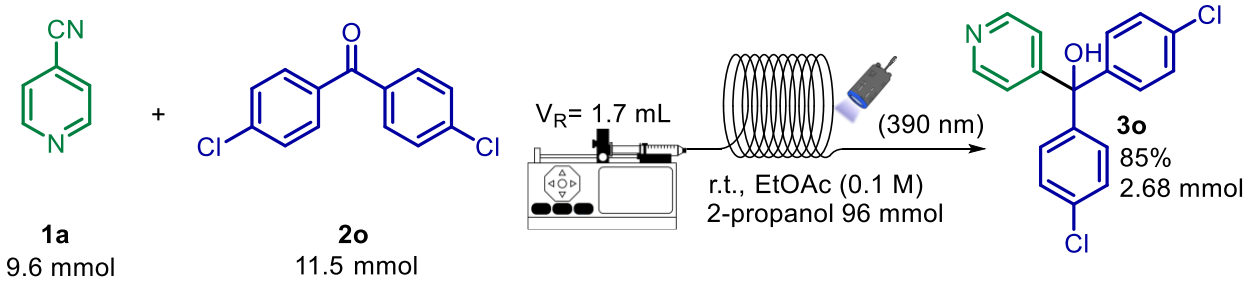
Entry	Parameter	Value	Penalty Points
1	Yield	(100-80)/2	10
2	Price of substrates	< €10	0
3	Safety[a]	Not dangerous	0
4	Technical Setup	Photochemical apparatus	2
5	Temperature/Time	r.t. ; < 24 h	1
6	Workup and purification	column chromatography	10
[a] Based on the hazard warning symbols		**Total Penalty Points**	**23**

Scheme S6. Penalty points to calculate the EcoScale value

$$EcoScale = 100 - Penalty\ Points\ = 77$$

Synthesis of 3o on 9.6 mmol scale in flow:

3o was prepared according to gram scale procedure described in section **7.2**.



$$AE = \frac{MM_{3o}}{MM_{\mathbf{1a}} + MM_{\mathbf{2o}}} \times 100 = \frac{329.04\ {}^{g}/_{mol}}{354.03\ {}^{g}/_{mol}} \times 100 = 92.9\%$$

$$PMI = \frac{Mass_{\mathbf{1a}} + Mass_{\mathbf{2o}} + Mass_{2-propanol} + Mass_{EtOAc}}{Mass_{\mathbf{3}}} = \frac{47.5\ g}{2.68\ g} = 17.7\ {}^{Kg}/_{Kg}$$

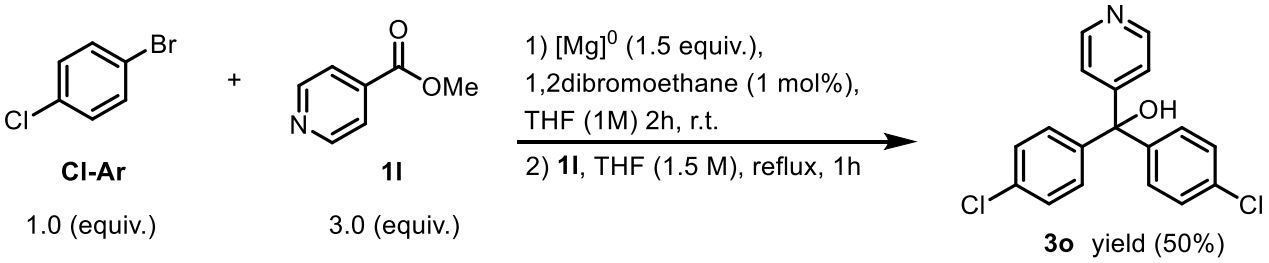
$$E_{factor} = PMI - 1\ = 16.7\ {}^{Kg}/_{Kg}$$

Entry	Parameter	Value	Penalty Points
1	Yield	(100-85)/2	7.5
2	Price of substrates	< €10	0
3	Safety[a]	Not dangerous	0
4	Technical Setup	Photochemical apparatus	2
5	Temperature/Time	r.t. ; > 24 h	2
6	Workup and purification	column chromatography	10
[a] Based on the hazard warning symbols		**Total Penalty Points**	**21.5**

Scheme S7. Penalty points to calculate the EcoScale value

$$EcoScale = 100 - Penalty\ Points\ = 78.5$$

Synthesis of 3o reported in literature:[8]



$$AE = \frac{MM_{3o}}{MM_{\boldsymbol{Cl-Ar}} + 2x\ (MM_{\boldsymbol{1l}}) + MM_{Mg}} \times\ 100 = \frac{329.04\ {}^{g}/_{mol}}{488.01\ {}^{g}/_{mol}} \times 100 = 67.4\%$$

$$PMI = \frac{Mass_{\boldsymbol{Cl-Ar}} + Mass_{\boldsymbol{1l}} + Mass_{Mg} + Mass_{THF}}{Mass_{\boldsymbol{3}}} = \frac{275.0\ g}{21.38\ g} = 12.9\ {}^{Kg}/_{Kg}$$

$$E_{factor} = PMI - 1\ = 11.9\ {}^{Kg}/_{Kg}$$

Entry	Parameter	Value	Penalty Points
1	Yield	(100-50)/2	25
2	Price of substrates	< €10	0
3	Safety[a]	Flammable	5
4	Technical Setup	Common setup	0
5	Temperature/Time	heating 1h	2
6	Workup and purification	liquid-liquid extraction + column chromatography	13
[a] Based on the hazard warning symbols		**Total Penalty Points**	**45.0**

Scheme S8. Penalty points to calculate the EcoScale value

$$EcoScale = 100 - Penalty\ Points\ = 55.0$$

11. Mechanistic Studies

11.1. Kinetic study for the formation of 9

Following general procedure **C'** 4 different dried (Pyrex®) tubes were charged with **1g** (1.0 equiv.), **2o** (2.0 equiv.), 2-propanol (10 equiv.) and EtOAc (0.1 M). The reactions were irradiated with a 40W 390 Kessil lamp. After 2h one tube was concentrated under reduced pressure and subjected to ^{1}H-NMR. Next, after 4h a second tube was equally concentrated under reduced pressure and subjected to ^{1}H NMR. Equally the remaining tubes were checked respectively after 8h and 16h. After 2 h, the consumption of the starting material **1g** is evident (characteristic signals at δ 8.87 (d) and 2.74 (s)), along with the concomitant formation of product **9**. The spectra clearly indicate the direct formation of the coupled product accompanied by the reduction of acetophenone to the corresponding benzylic alcohol (characteristic signals at δ 8.40 (d) and 2.03 (d)).

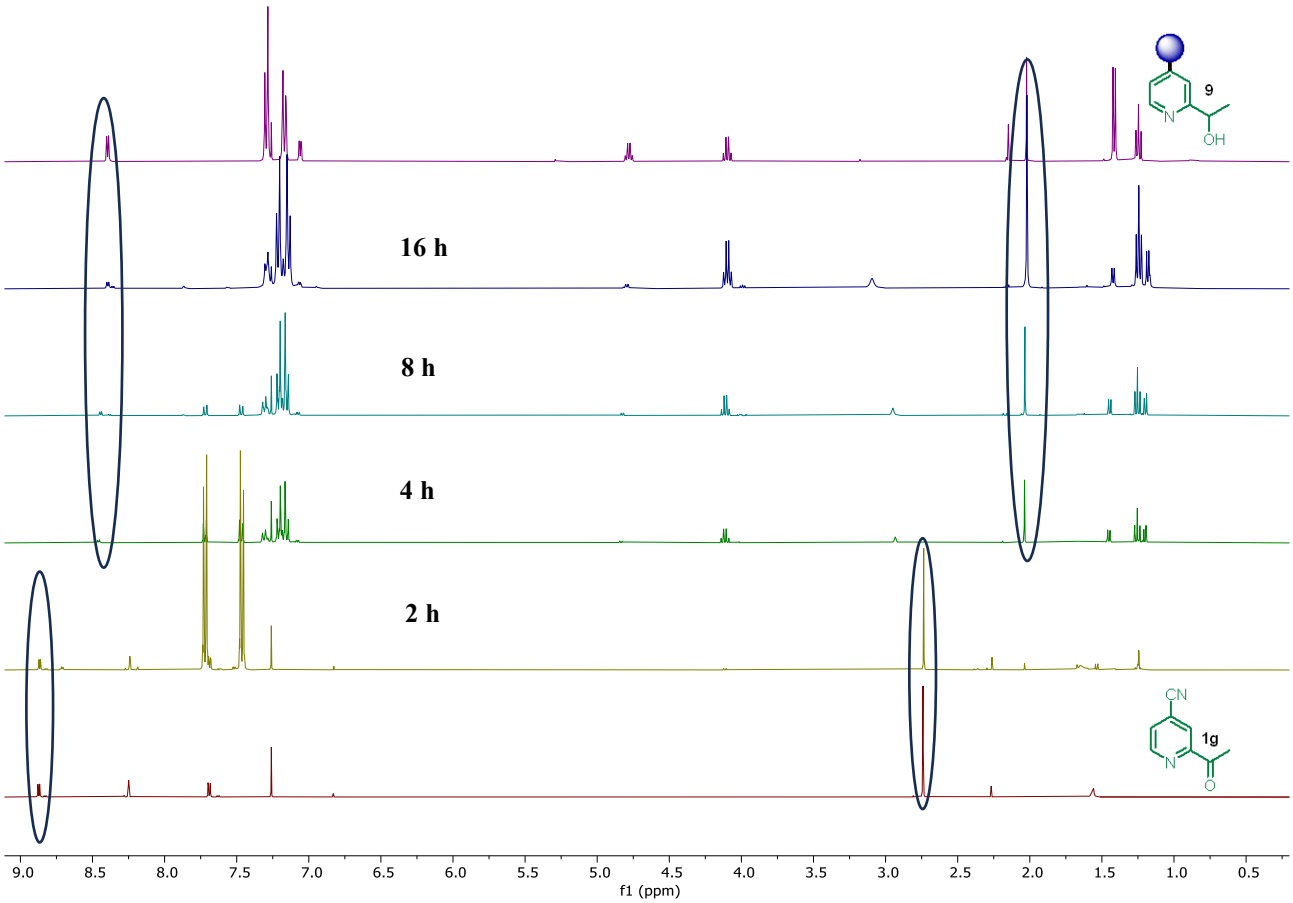
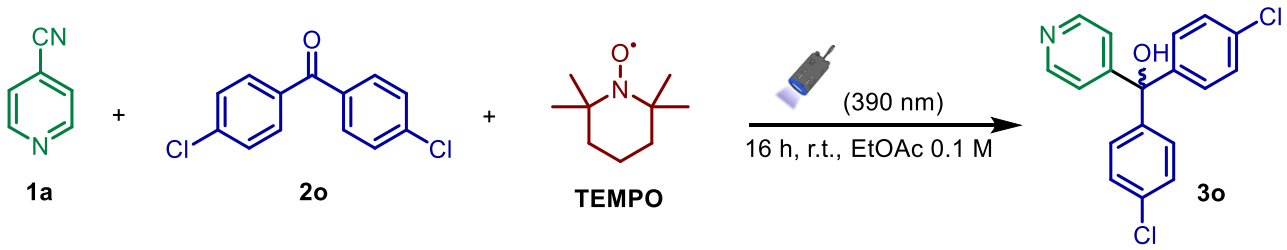


Figure S5. Kinetic analysis in time by ^{1}H-NMR for the consumption of **1g** and the formation of **9**

11.2. Reaction with TEMPO



The get more insights on the reaction mechanism we performed a reaction in presence of TEMPO as a radical scavenger. Following the general procedure **C** and with the addition of TEMPO (93.8 mg, 6 mmol, 3.0 equiv.) the reactivity was completely suppressed. After 16h the reaction was stopped and there is no evidence of the formation of the final product. We performed a LC-MS analysis on the crude mixture and it was possible to detect the 2-propanol/TEMPO adduct as shown in Figure 6.

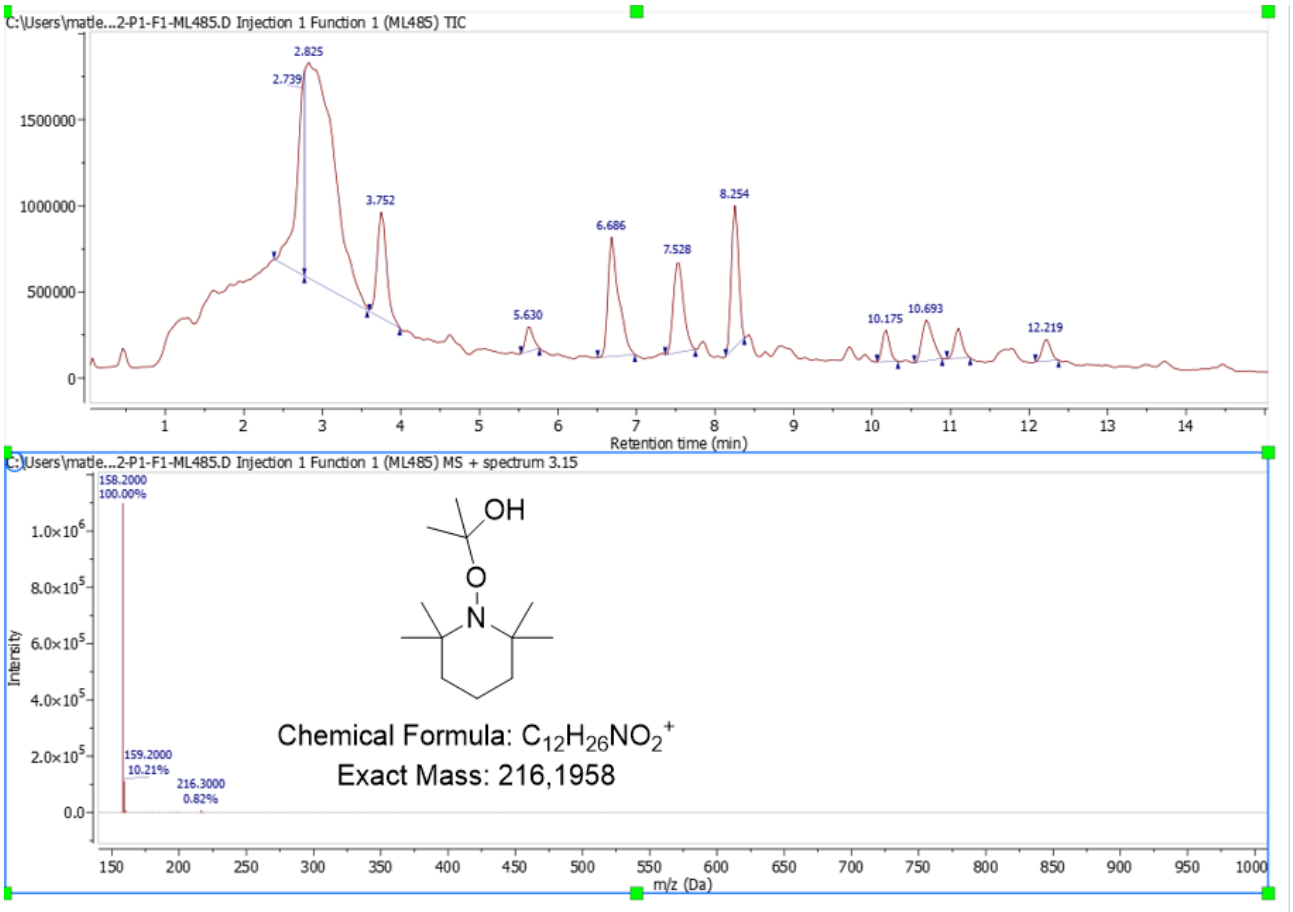
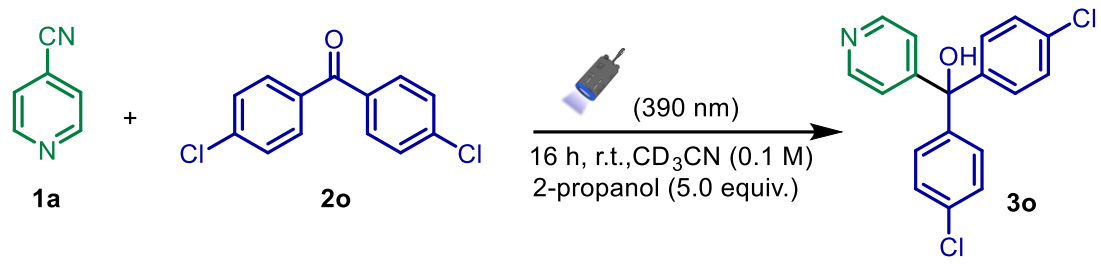


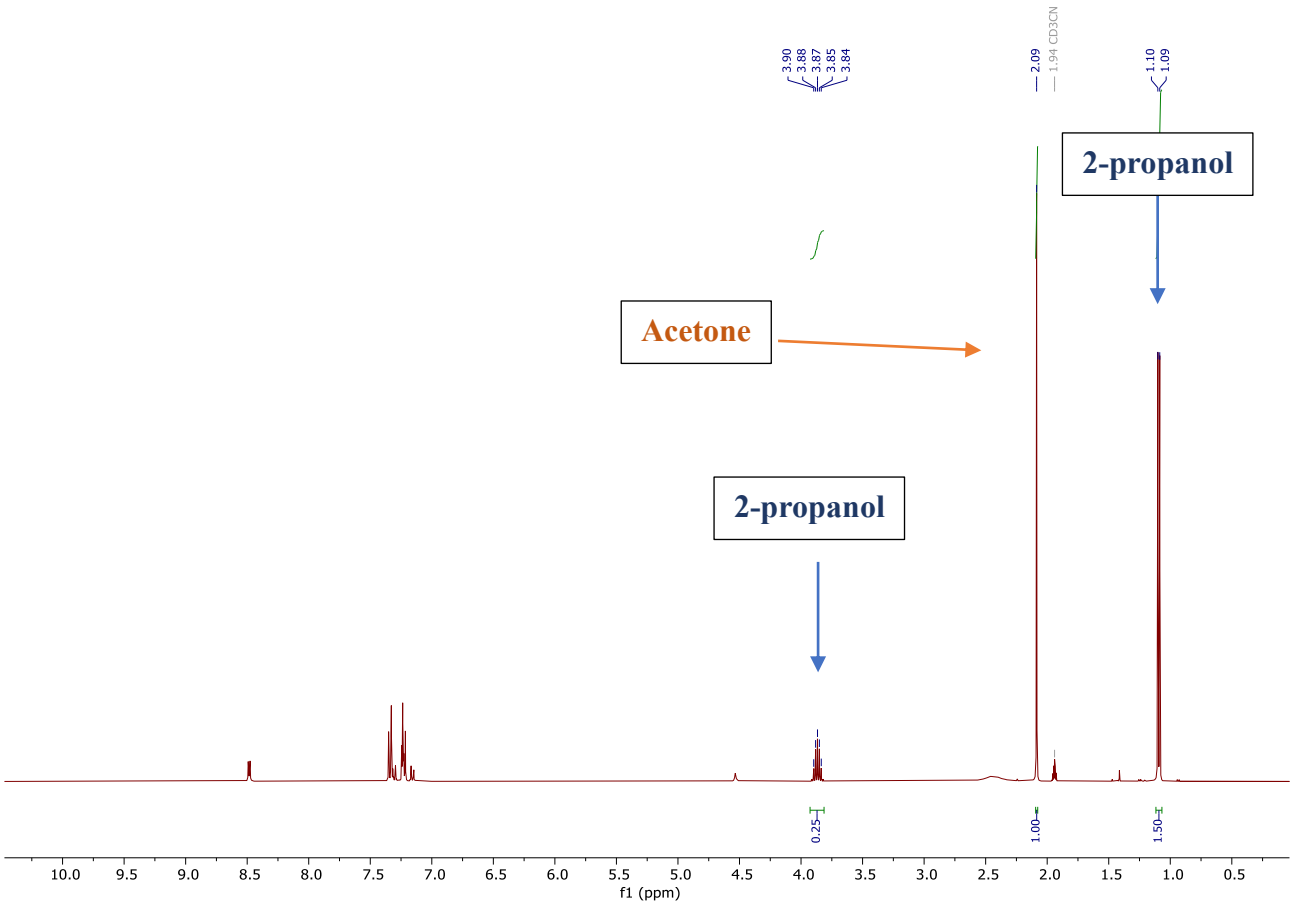
Figure S6. Detection of 2-propanol/TEMPO (RT= 2.741 min) adduct in the reaction between **1a** and **2o**.

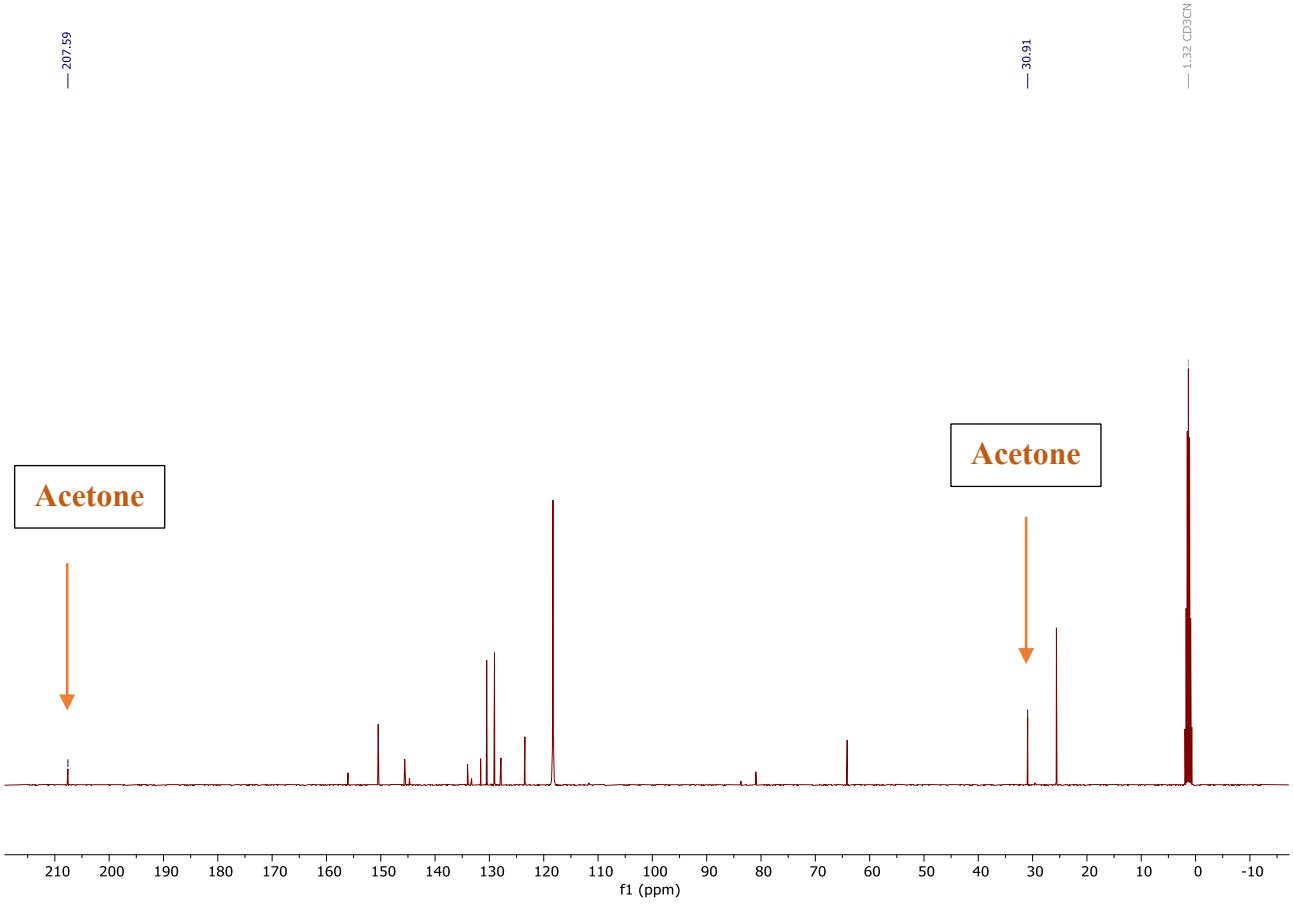
11.3. NMR detection of the formation of Acetone

To get more insight on the faith of the corresponding ketyl radical deriving from 2-propanol we performed the reaction between **1a** and **2o** in deuterated solvent (CD_3CN) to detect the possible formation of acetone by ^{1}H-NMR and ^{13}C-NMR analysis.

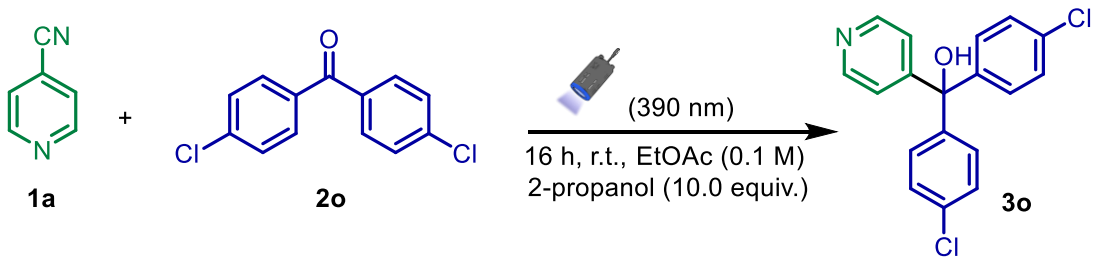


A dried (Pyrex®) vessel was charged with a magnetic stirring bar, **1a** (5.2 mg; 0.05 mmol; 1.0 equiv.), **2o** (15mg; 0.06 mmol; 1.2 equiv.), 2-propanol (20 µL; 0.25 mmol; 5.0 equiv.) and CD_3CN (0.5 mL 0.1 M). The vessel was sealed with a rubber septum and N_2 was bubbled in the solution for 1 min. The vessel was placed in a photo-box, equipped with a cooling fan (see Figure S2) and irradiated with a 390 nm 40W Kessil LED lamp. After completion, the crude mixture was directly analyzed by ^{1}H and ^{13}C NMR. In both spectra, characteristic signals of acetone were detected, present in a 1:1.5 ratio with respect to 2-propanol.


3.90
3.88
3.87
3.85
3.84
2.09
1.94 CD3CN
1.10
1.09
2-propanol
Acetone
2-propanol
0.25
1.00
1.50
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


207.59
30.91
1.32 CD3CN
Acetone
Acetone
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

11.4. Quantum yield evaluation



The quantum yield (Φ_{-1}) was determined based on the consumption of **1a** by performing three independent reactions on a 0.3 mmol scale, following procedure **C**. The reactions were quenched after 7, 15, and 30 minutes, respectively.

Experimental setup (see Figure S7): For each experiment, 3 mL of the reaction mixture were transferred into a quartz cuvette (optical path length: 10 mm) and irradiated with a 40 W Kessil lamp (390 nm) positioned at a distance of 5 cm. The cuvette was mounted on an optical bench equipped with a photon counter placed behind the vial holder. Conversion values were quantified by GC-FID, using biphenyl as an external standard. Each experiment was repeated three times, and the final quantum yield was reported as the average value. Prior to each irradiation, the photon flux was measured in the absence of the reaction solution.

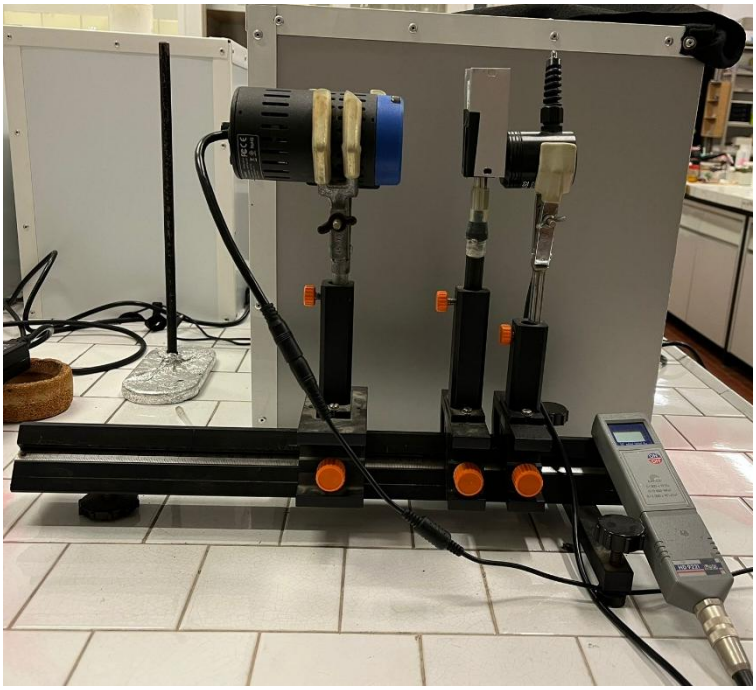


Figure S7. Experimental setup for the quantum yield determination.

Calculations: quantum yield of consumption Φ_{-1} was defined as follows:

$$\Phi_{-1} = \frac{mol\ of\ consumed\ starting\ material}{mol\ of\ photons\ absorbed}$$

It was so calculated in accordance with the following equation:

$$\Phi_{-1} = \frac{V * C_0 * conversion}{Einstein_{Abs} * t}$$

where V is the volume of the irradiated solution, C_0 the initial concentration and t the irradiation time.

$Einstein_{Abs}$ value was calculated as follows:

$$Einstein_{Abs} = \frac{P_{Abs}}{Energy\ at\ 370\ nm * N_A}$$

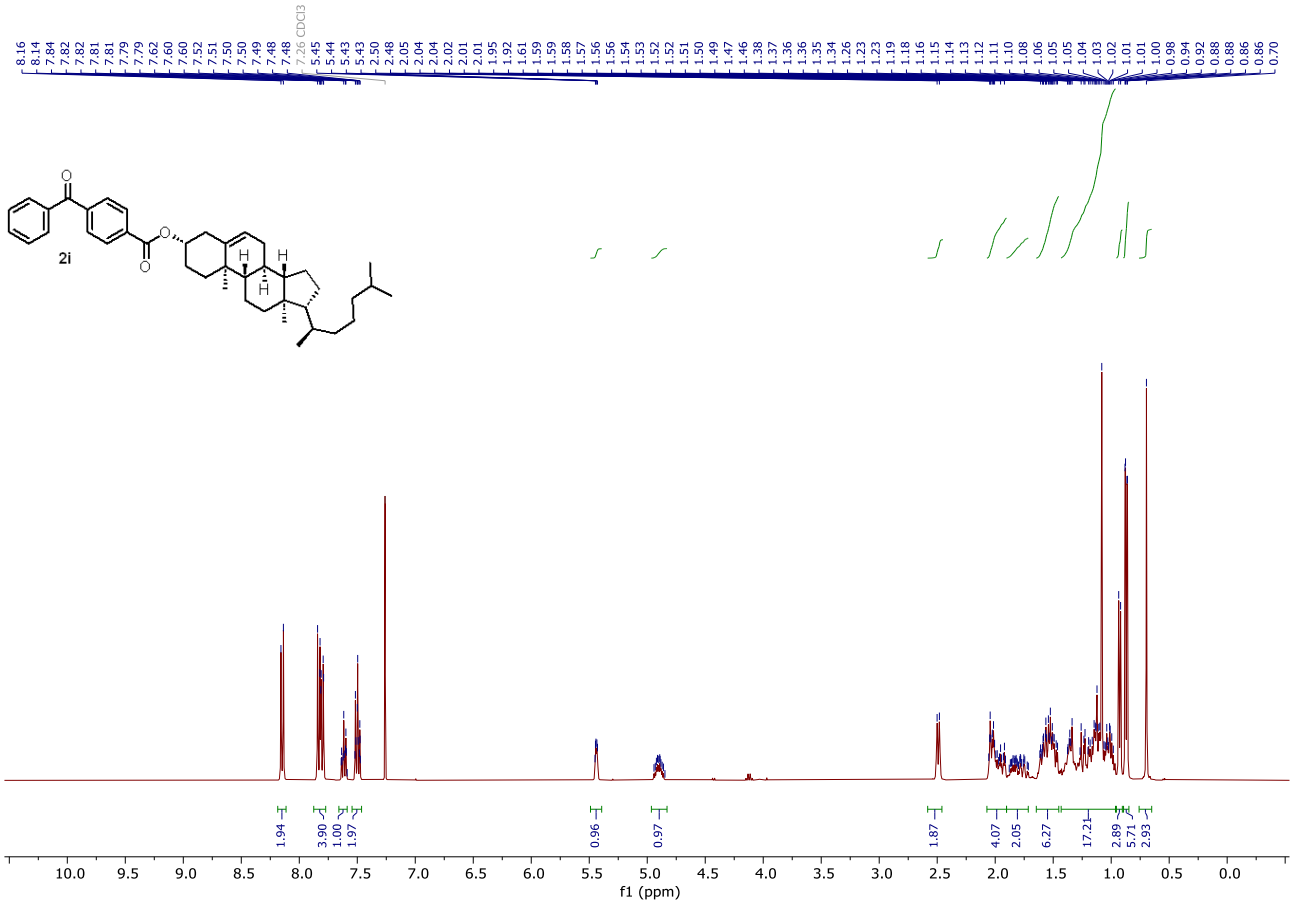
where P_{Abs} (power of absorbed light) was calculated as:

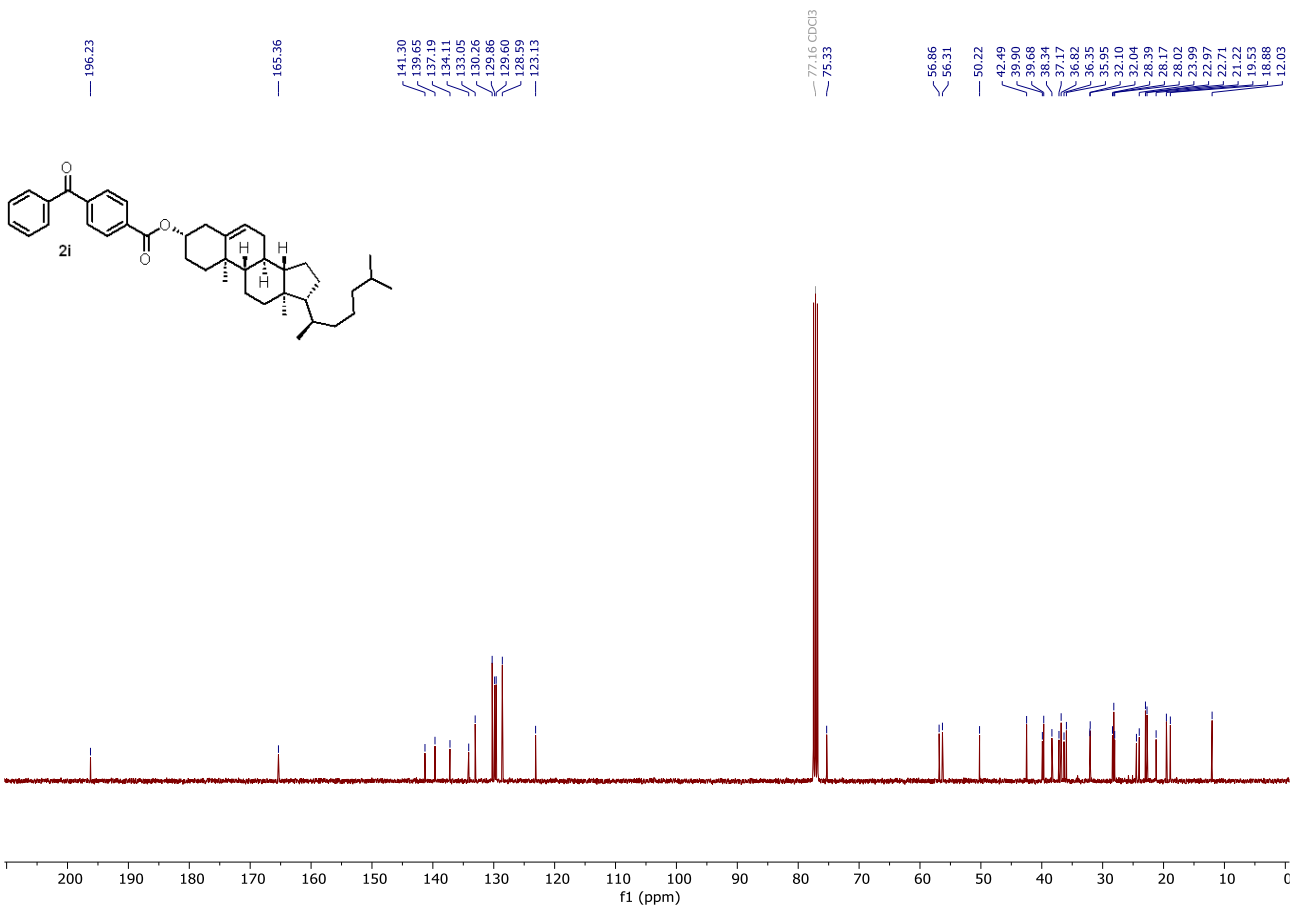
$$P_{Abs} = A * (irradiance\ with\ the\ sample - irradiance\ without\ the\ sample)$$

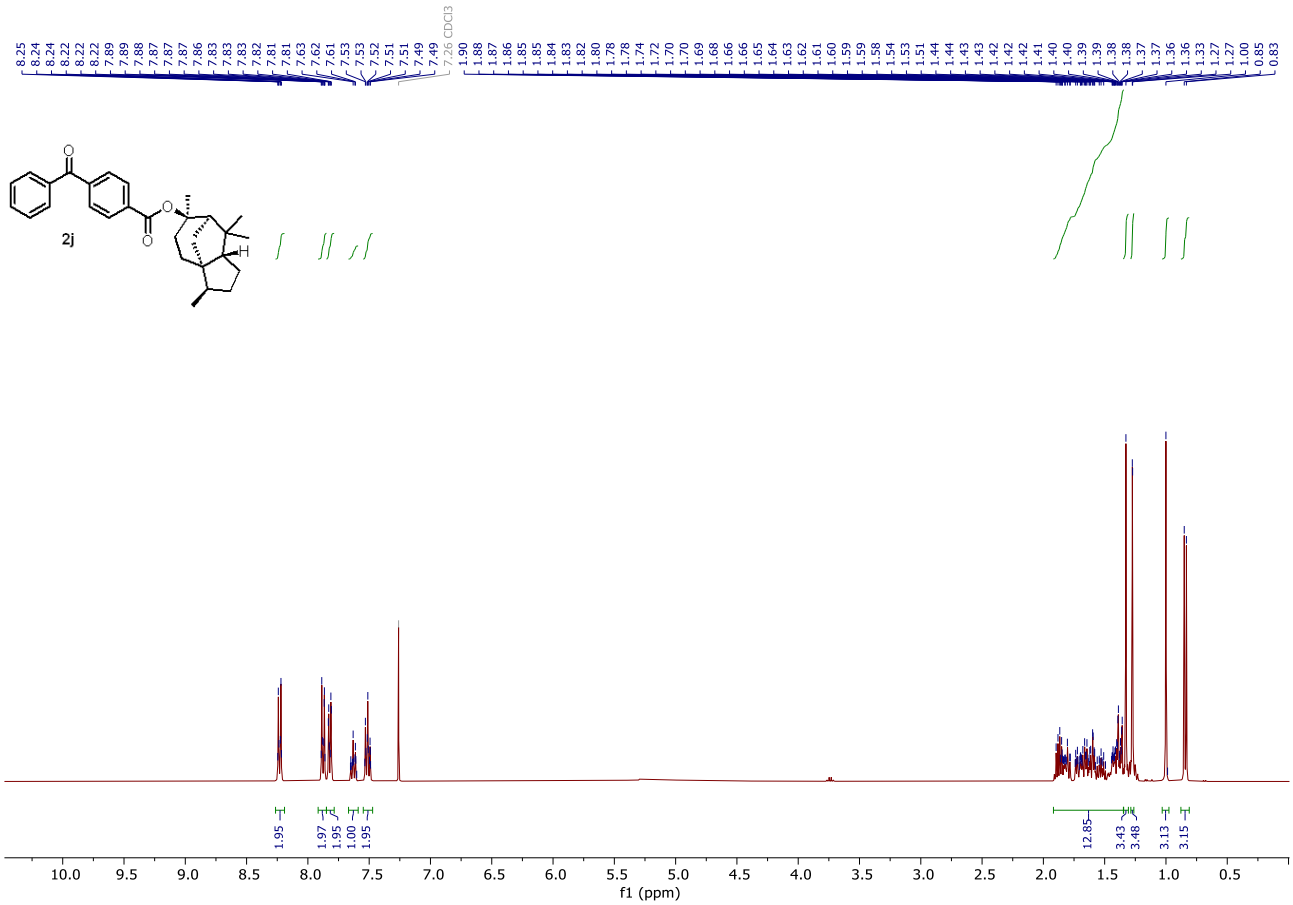
where A is the irradiated area.

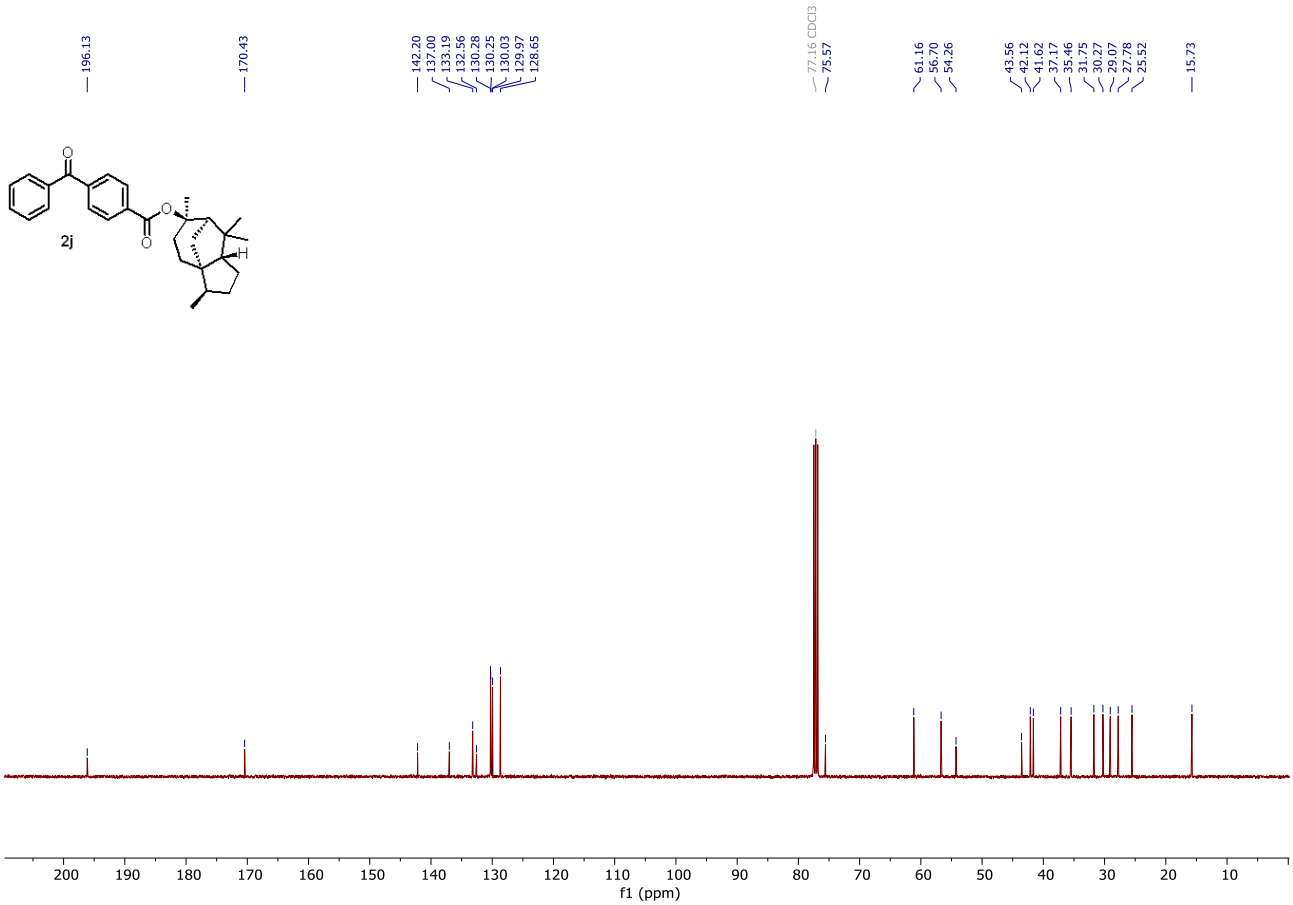
An average quantum yield value of $\mathbf{\Phi_{-1} = 1.71}$ was obtained from this evaluation.

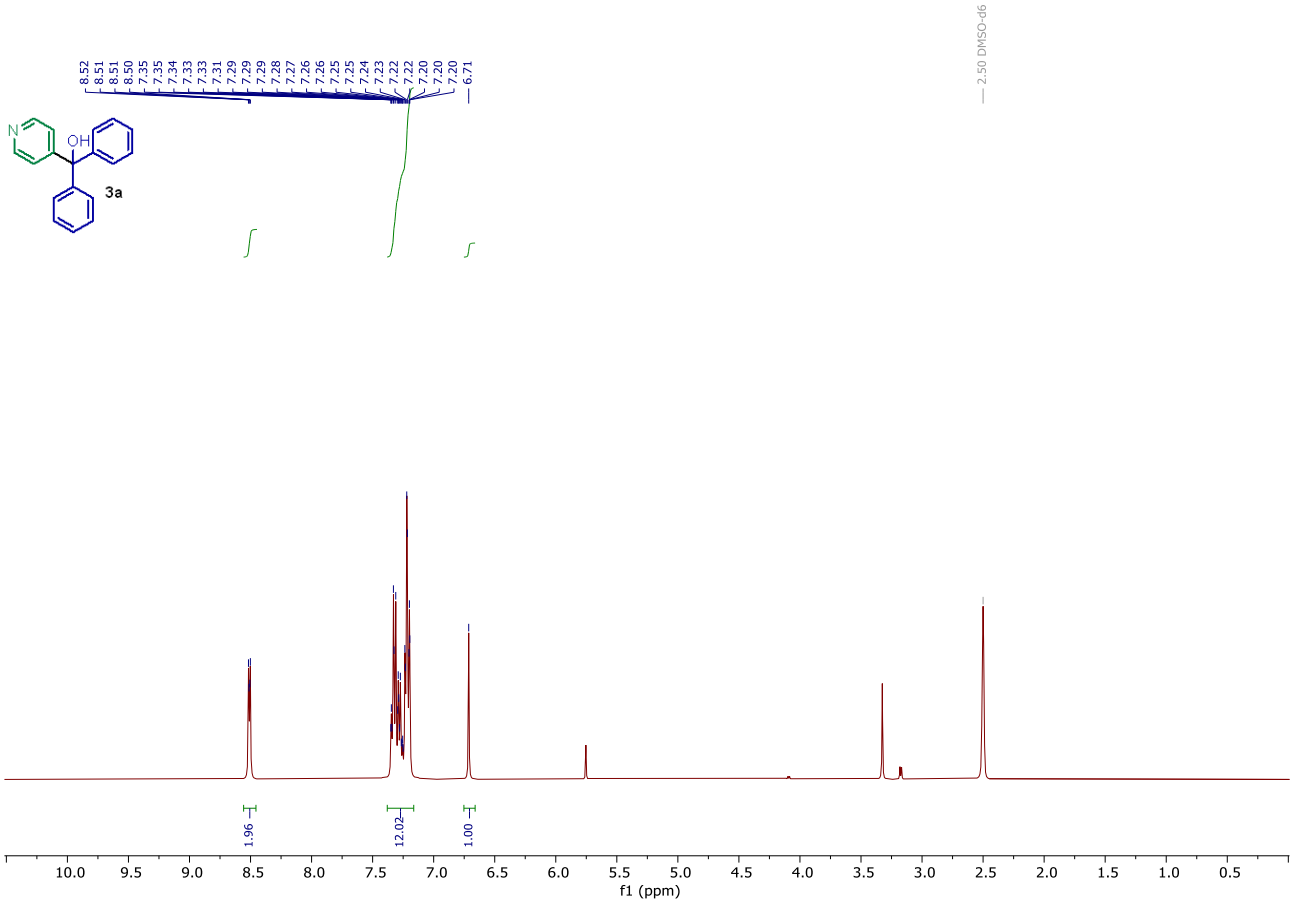
12. Copy of ^{1}H and ^{13}C NMR Spectra

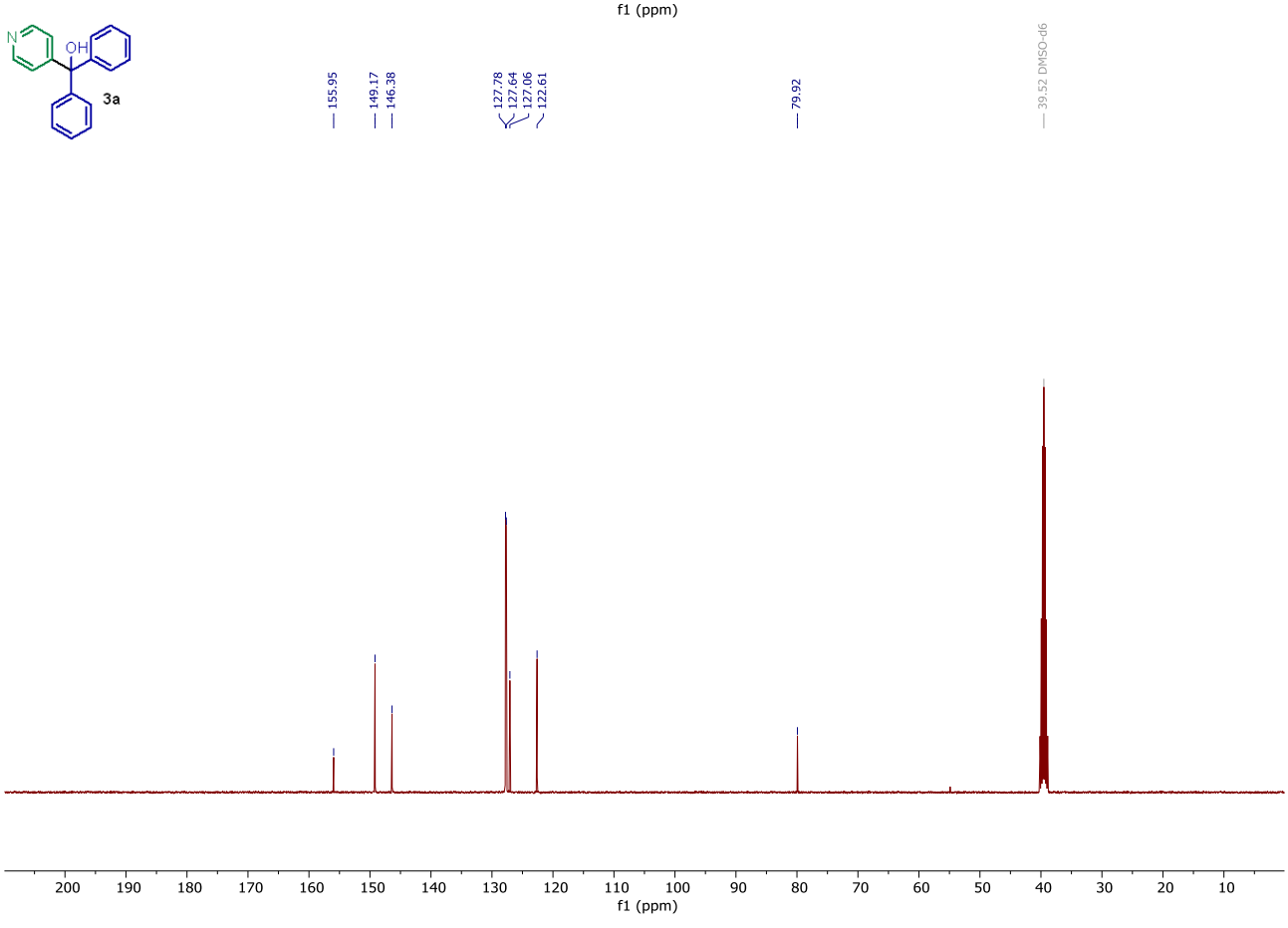


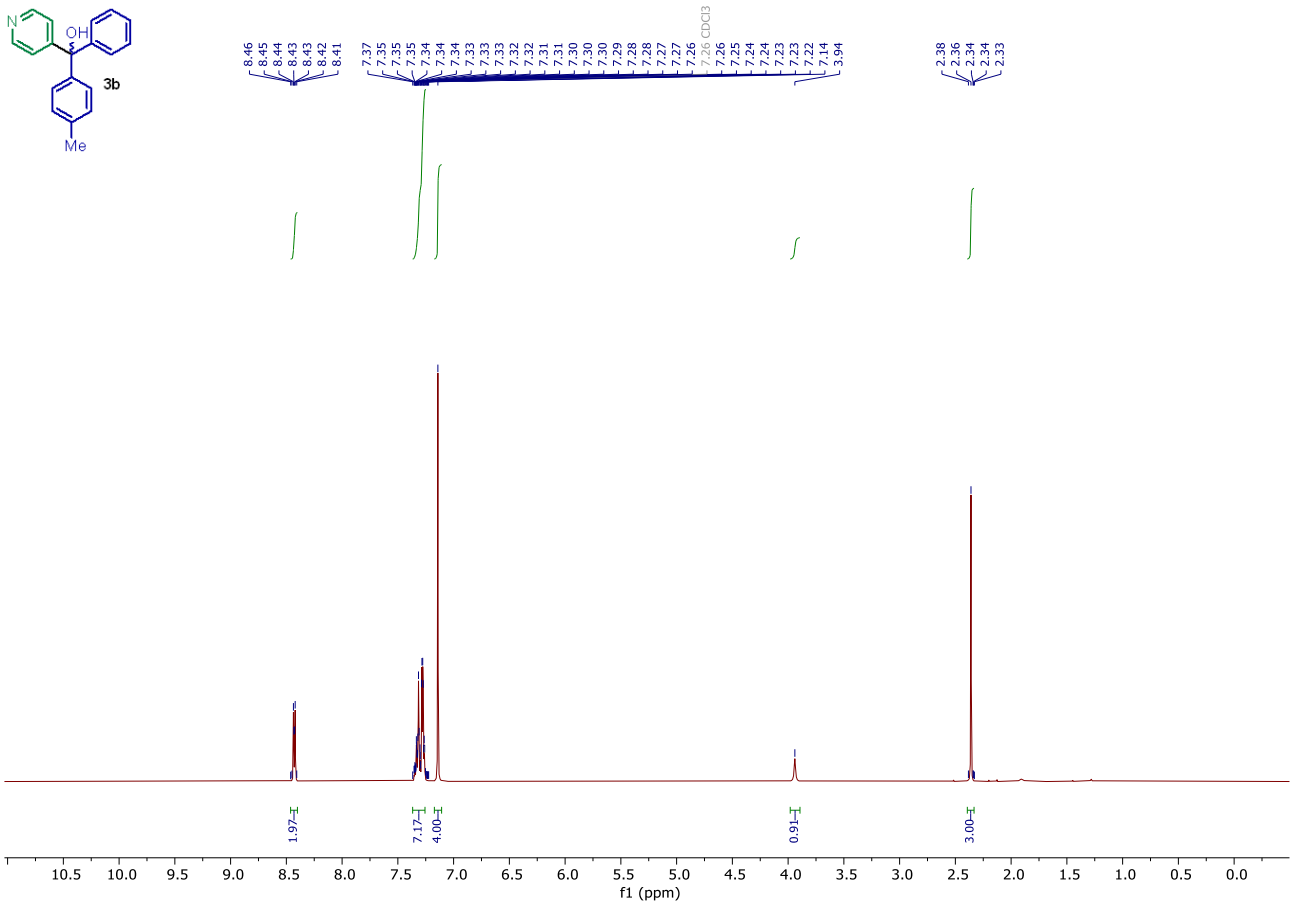


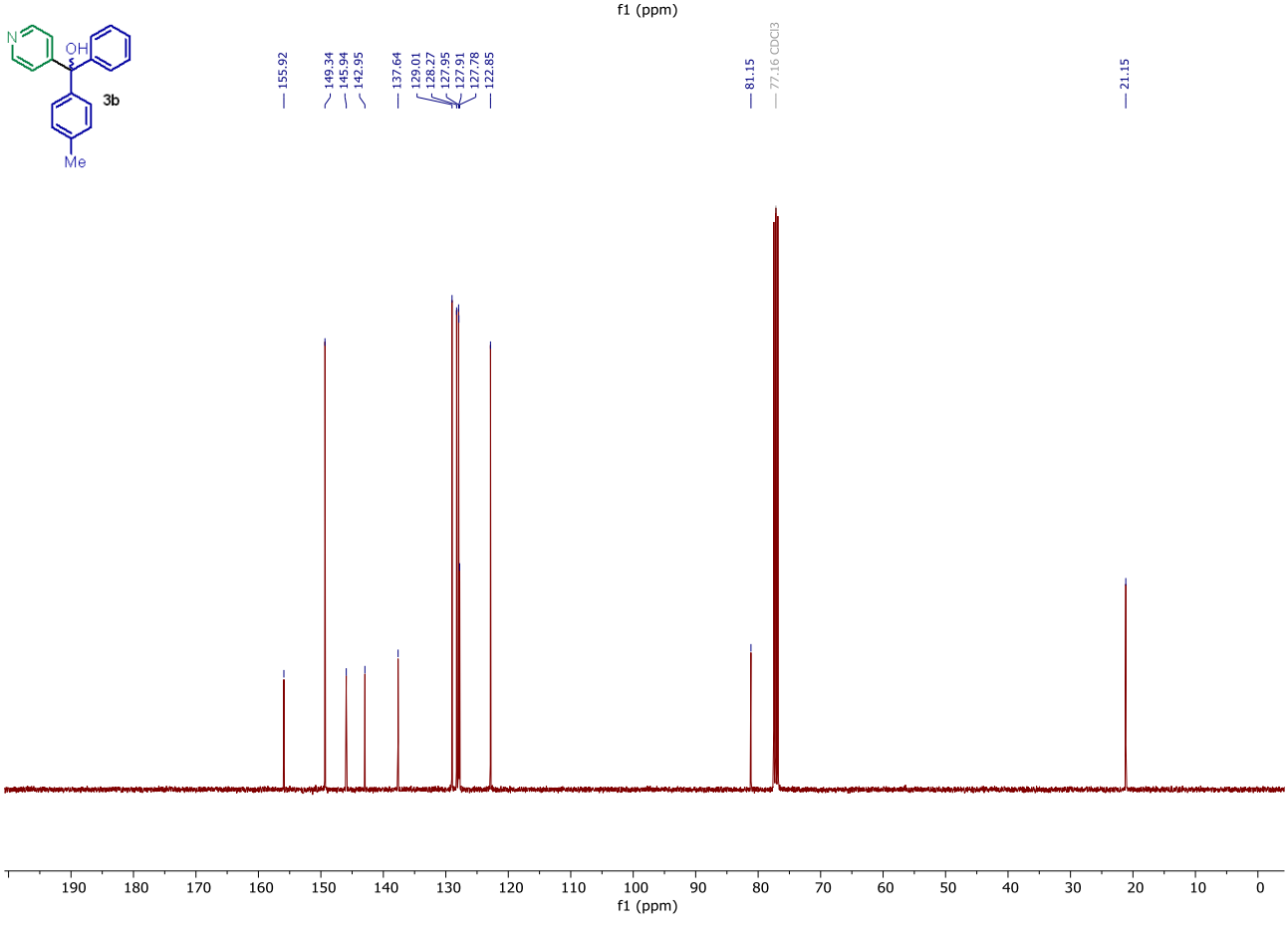

8.25 8.24 8.24 8.22 8.22 8.22 7.89 7.89 7.88 7.87 7.87 7.87 7.86 7.83 7.83 7.83 7.82 7.81 7.81 7.63 7.62 7.61 7.53 7.53 7.52 7.51 7.51 7.49 7.49 7.26 CDCl3
1.90 1.88 1.87 1.86 1.85 1.85 1.84 1.83 1.82 1.80 1.78 1.78 1.74 1.72 1.70 1.70 1.69 1.68 1.66 1.66 1.65 1.64 1.63 1.62 1.61 1.60 1.59 1.59 1.58 1.54 1.53 1.51 1.44 1.43 1.43 1.42 1.42 1.42 1.41 1.40 1.40 1.39 1.39 1.38 1.38 1.37 1.37 1.36 1.36 1.33 1.27 1.27 1.00 0.85 0.83
2j
1.95 1.97 1.95 1.00 1.95 12.85 3.43 3.48 3.13 3.15
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

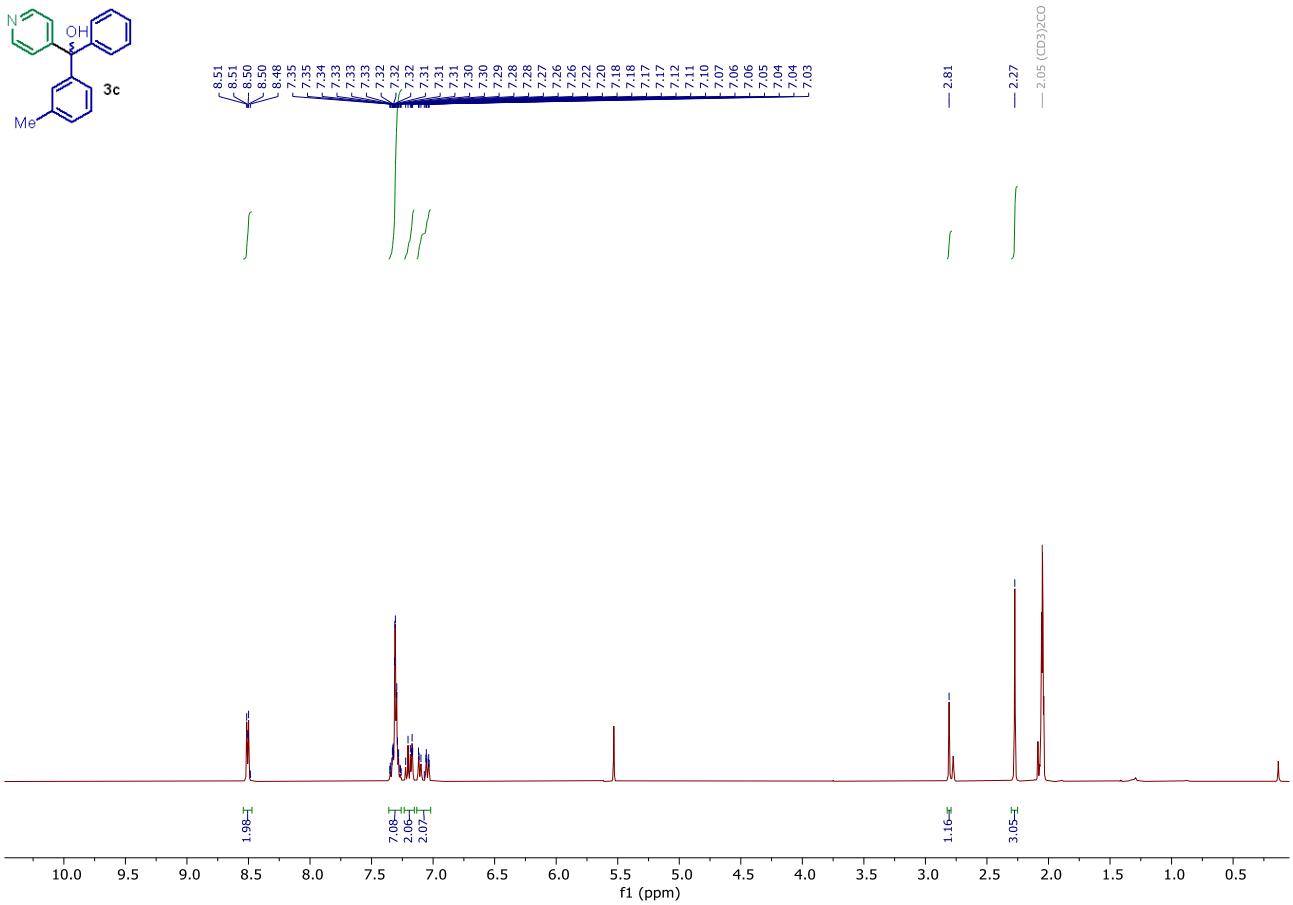

196.13 170.43 142.20 137.00 133.19 132.56 130.28 130.25 130.03 129.97 128.65 77.16 CDCl3 75.57 61.16 56.70 54.26 43.56 42.12 41.62 37.17 35.46 31.75 30.27 29.07 27.78 25.52 15.73
2j
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

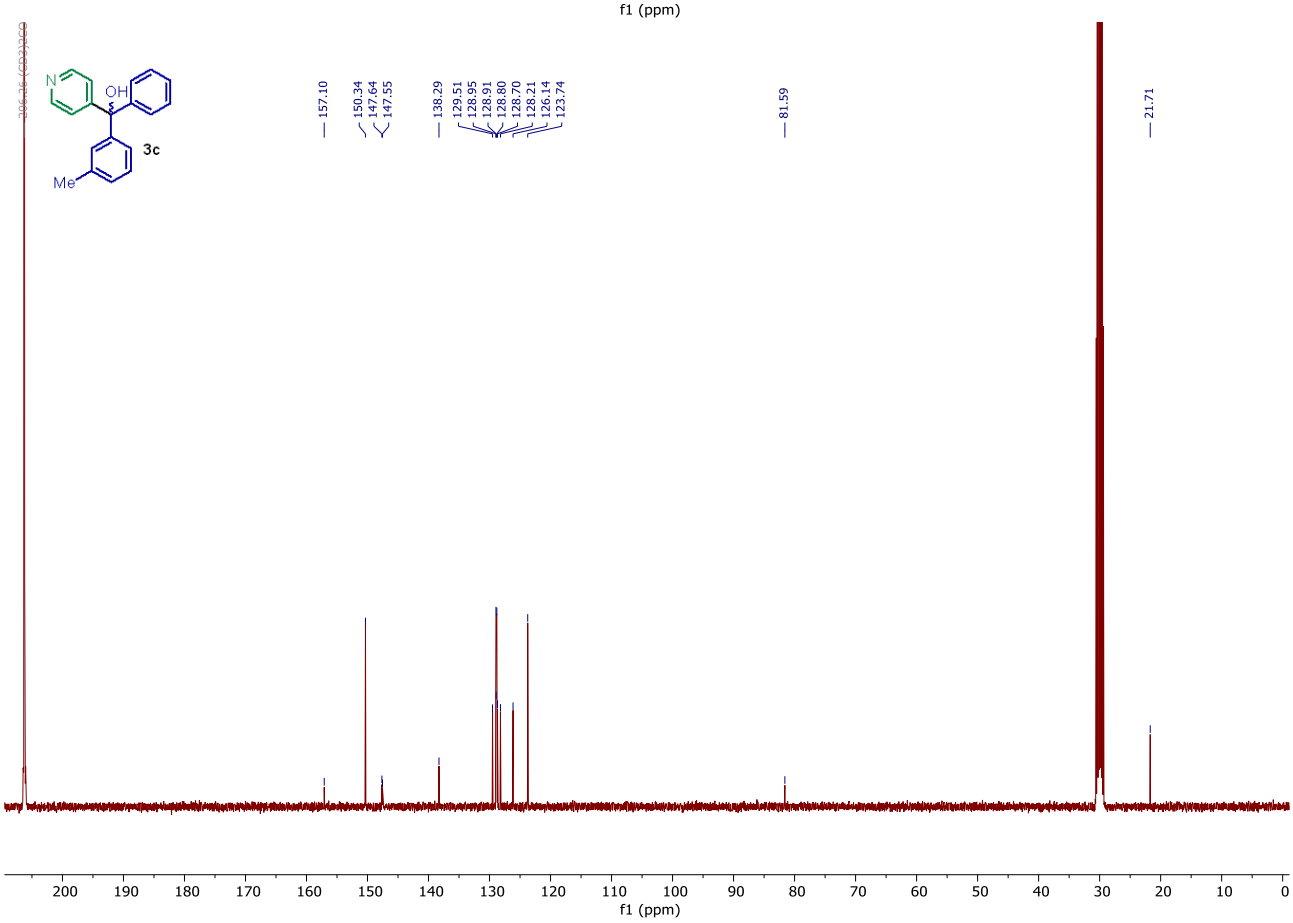

8.52
8.51
8.51
8.50
7.35
7.35
7.34
7.33
7.33
7.31
7.29
7.29
7.29
7.28
7.27
7.26
7.26
7.25
7.25
7.24
7.23
7.22
7.22
7.20
7.20
7.20
6.71
2.50 DMSO-d6
N
OH
3a
1.96
12.02
1.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

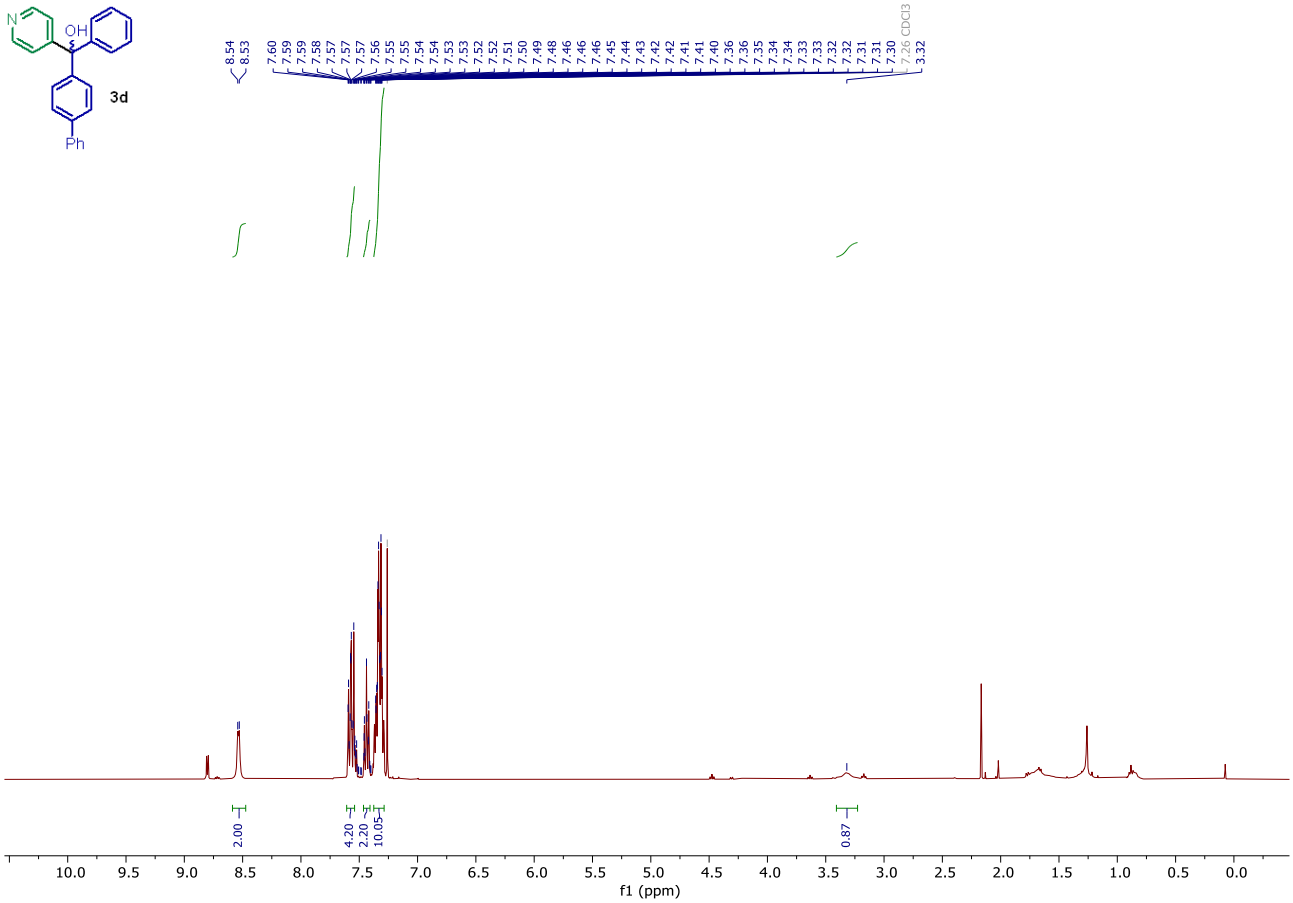

N
OH
3a
155.95
149.17
146.38
127.78
127.64
127.06
122.61
79.92
39.52 DMSO-d6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


N
OH
3b
Me
8.46
8.45
8.44
8.43
8.43
8.42
8.41
7.37
7.35
7.35
7.35
7.34
7.34
7.34
7.33
7.33
7.33
7.32
7.32
7.31
7.31
7.30
7.30
7.30
7.29
7.28
7.28
7.27
7.27
7.26
7.26 CDCl3
7.26
7.25
7.24
7.24
7.23
7.23
7.22
7.14
3.94
2.38
2.36
2.34
2.34
2.33
1.97
7.17
4.00
0.91
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


N
OH
3b
Me
155.92
149.34
145.94
142.95
137.64
129.01
128.27
127.95
127.91
127.78
122.85
81.15
77.16 CDCl3
21.15
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


3c
8.51
8.51
8.50
8.50
8.48
7.35
7.34
7.33
7.33
7.32
7.32
7.32
7.31
7.31
7.31
7.30
7.30
7.29
7.28
7.27
7.26
7.26
7.22
7.20
7.18
7.18
7.17
7.17
7.12
7.11
7.10
7.07
7.06
7.06
7.05
7.04
7.04
7.03
2.81
2.27
2.05 (CD3)2CO
1.98
7.08
2.06
2.07
1.16
3.05
f1 (ppm)


3c
206.26 (CD3)2CO
157.10
150.34
147.64
147.55
138.29
129.51
128.95
128.91
128.80
128.70
128.21
126.14
123.74
81.59
21.71
f1 (ppm)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7.57
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7.57
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7.55
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7.53
7.52
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7.51
7.50
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7.46
7.45
7.44
7.43
7.42
7.42
7.41
7.41
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7.35
7.34
7.34
7.33
7.33
7.32
7.32
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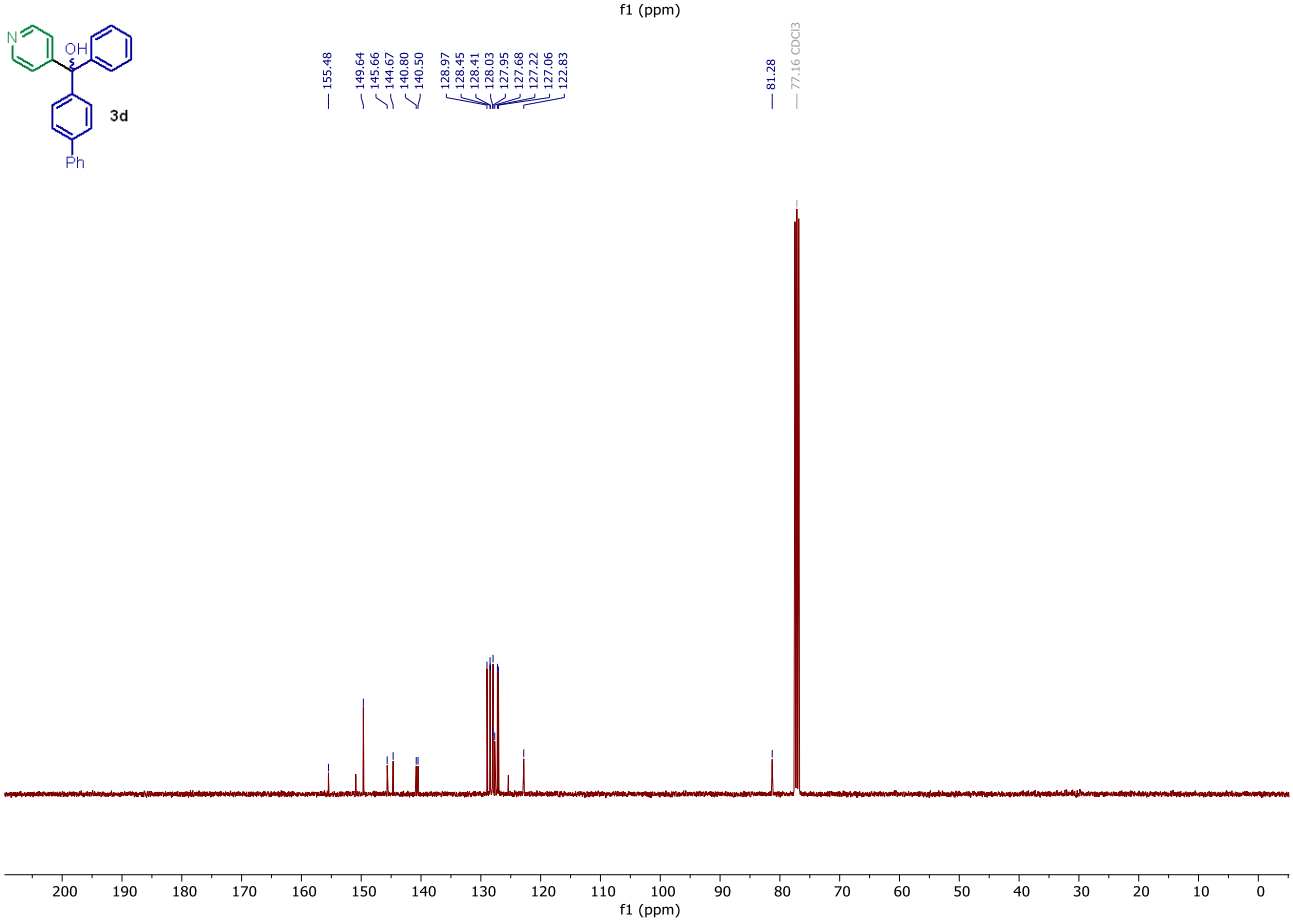
7.30
7.26 CDCl3
3.32
2.00
4.20
2.20
10.05
0.87
f1 (ppm)


3d
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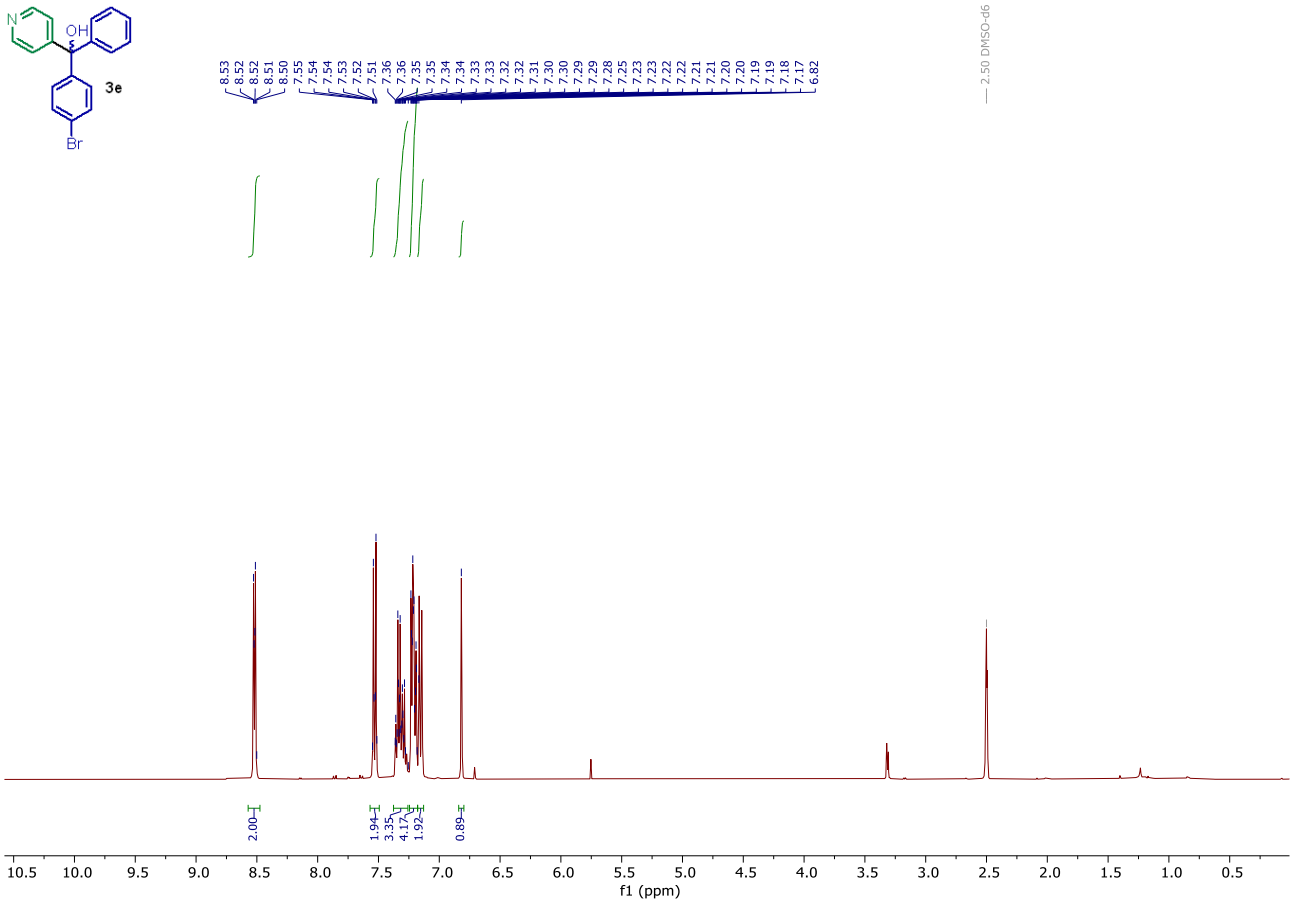
145.66
144.67
140.80
140.50
128.97
128.45
128.41
128.03
127.95
127.68
127.22
127.06
122.83
81.28
77.16 CDCl3
f1 (ppm)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8.50
7.55
7.54
7.54
7.53
7.52
7.51
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7.36
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7.34
7.34
7.33
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7.30
7.29
7.29
7.28
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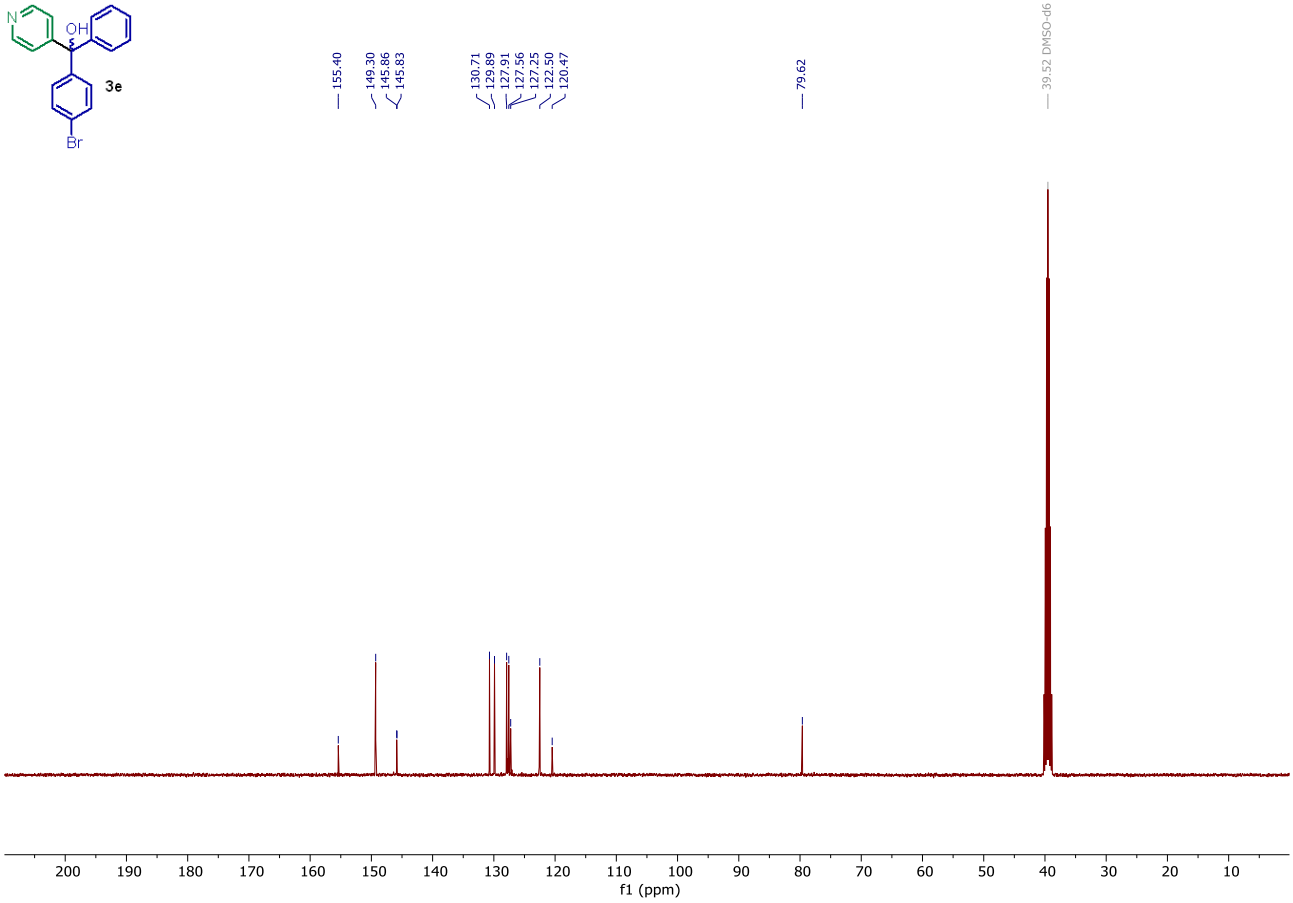
7.23
7.23
7.22
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.18
7.17
6.82
2.50 DMSO-d6
2.00
1.94
3.35
4.17
1.92
0.89
f1 (ppm)


3e
155.40
149.30
145.86
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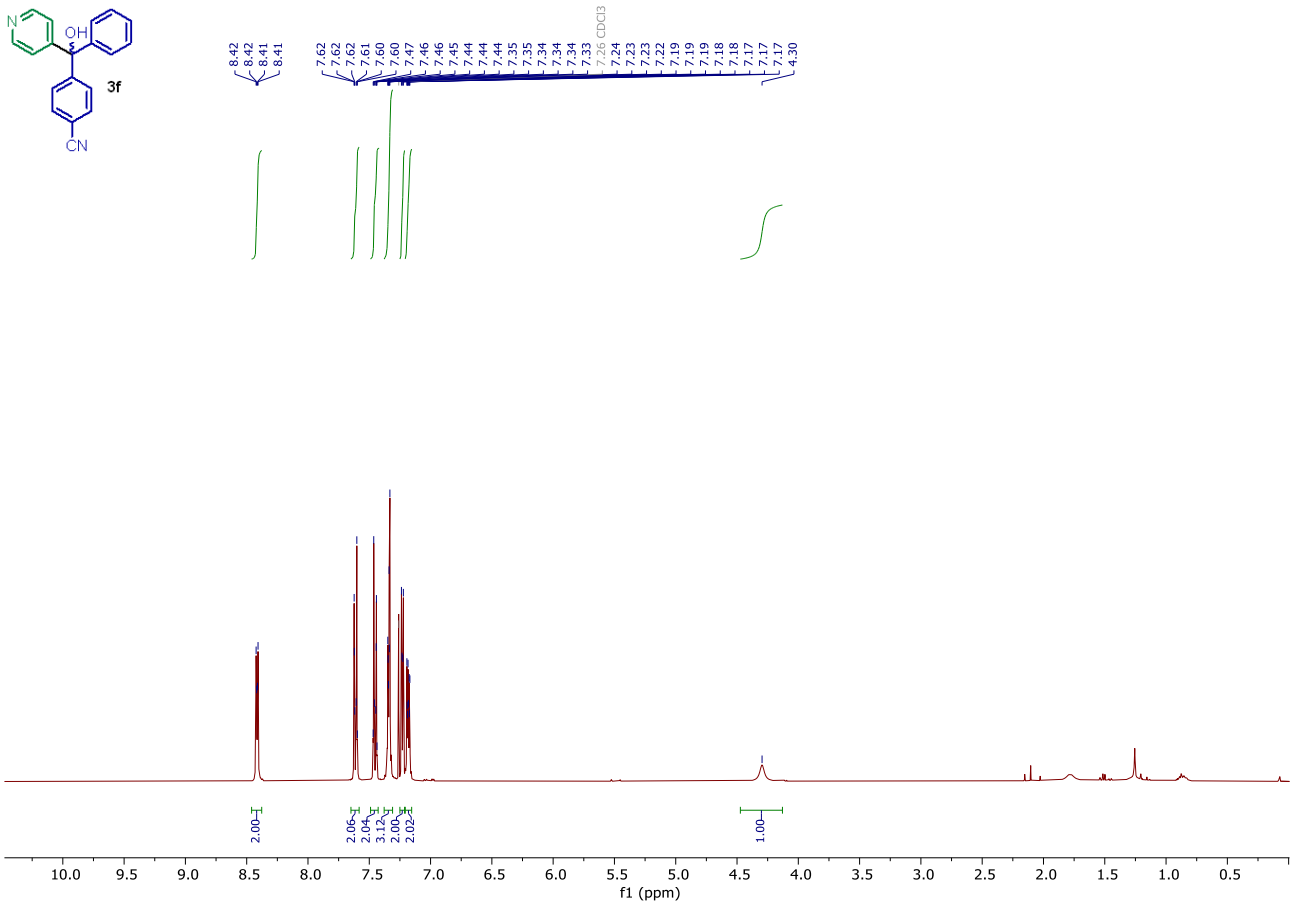
127.91
127.56
127.25
122.50
120.47
79.62
39.52 DMSO-d6
f1 (ppm)


3f
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8.42
8.41
8.41
7.62
7.62
7.62
7.61
7.60
7.60
7.47
7.46
7.46
7.45
7.44
7.44
7.44
7.35
7.35
7.34
7.34
7.34
7.33
7.26 CDCl3
7.24
7.23
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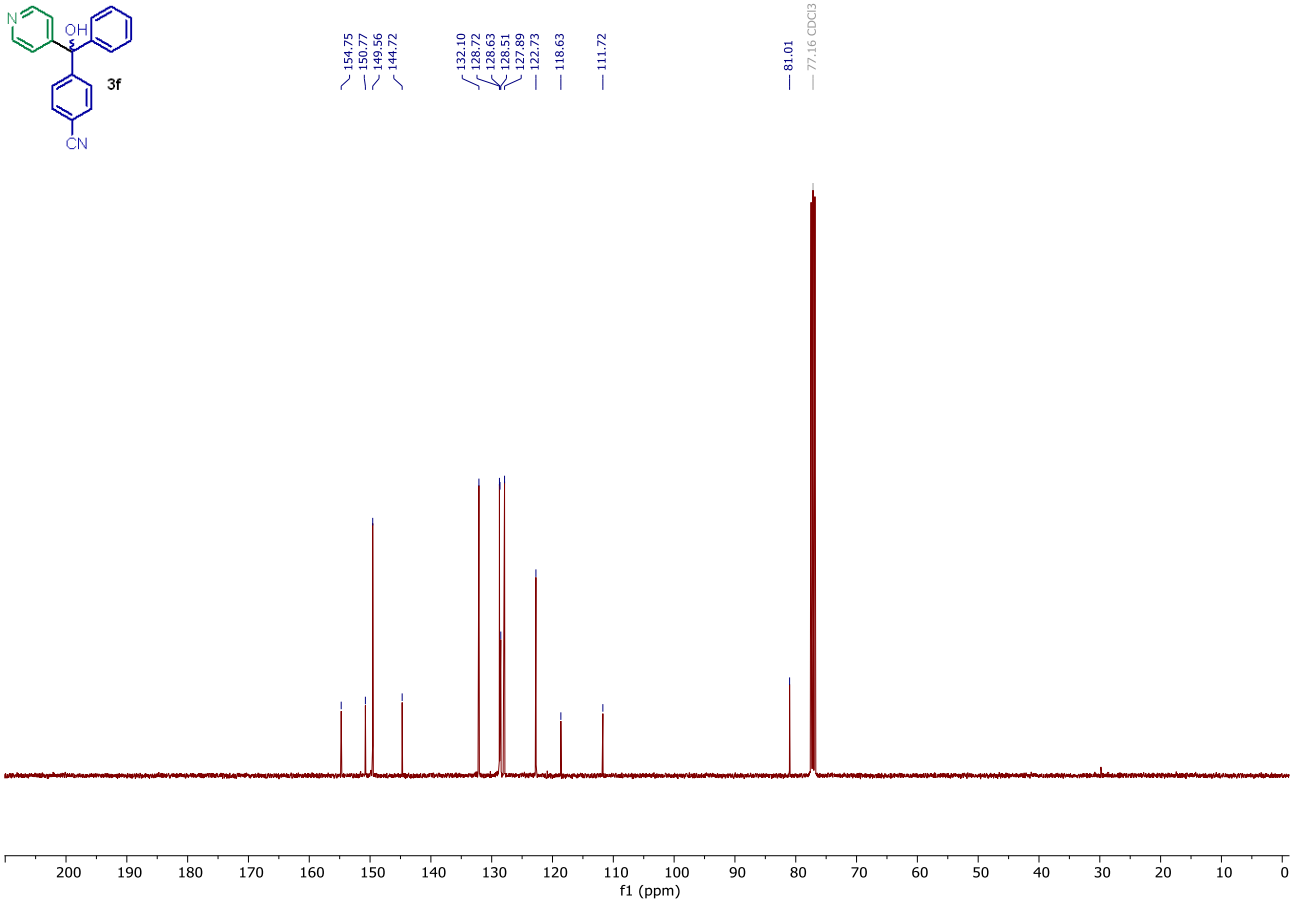
7.19
7.18
7.18
7.17
7.17
7.17
4.30
2.00
2.06
2.04
3.12
2.00
2.02
1.00
f1 (ppm)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149.56
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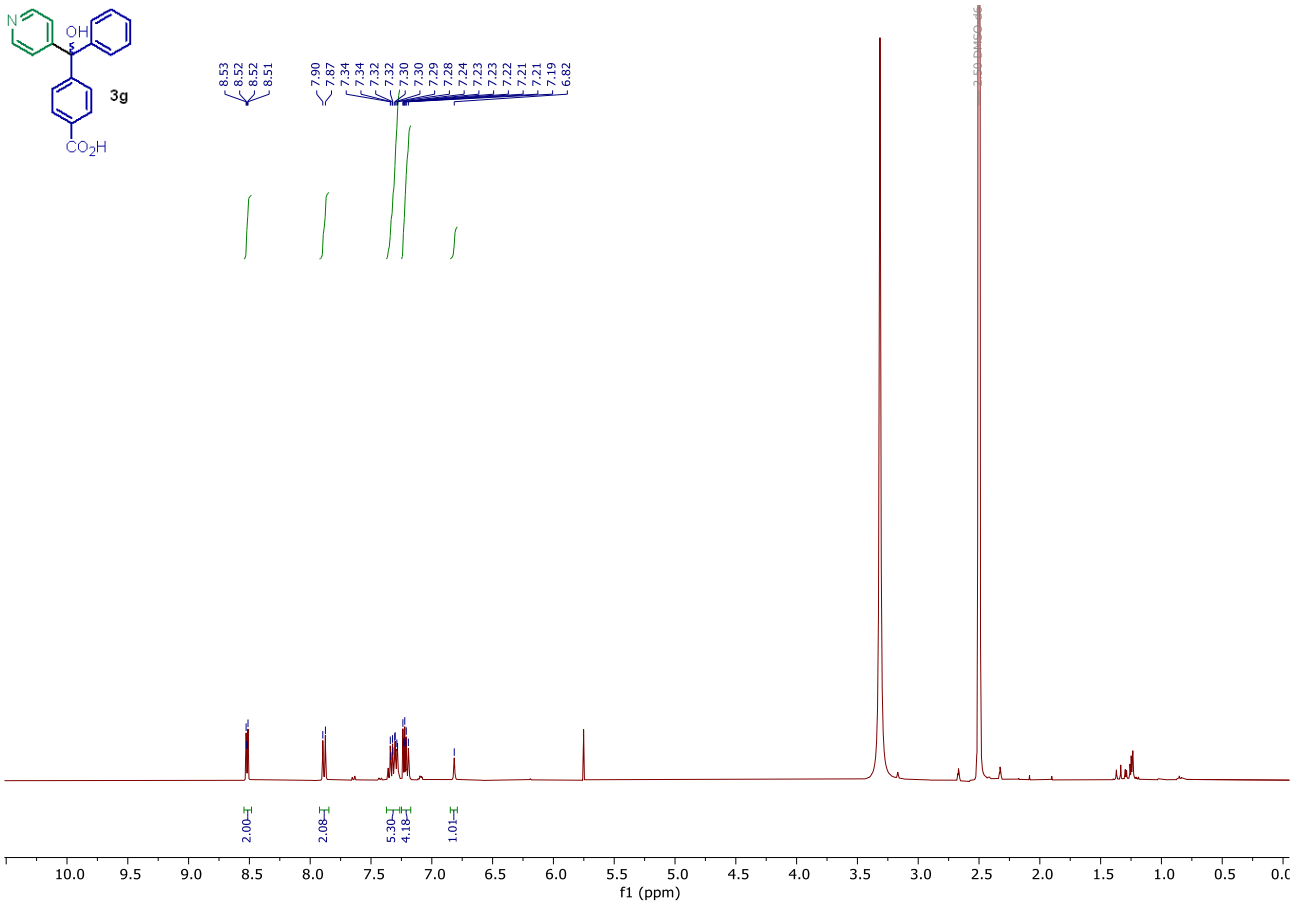
128.72
128.63
128.51
127.89
122.73
118.63
111.72
81.01
77.16 CDCl3
f1 (ppm)


3g
8.53
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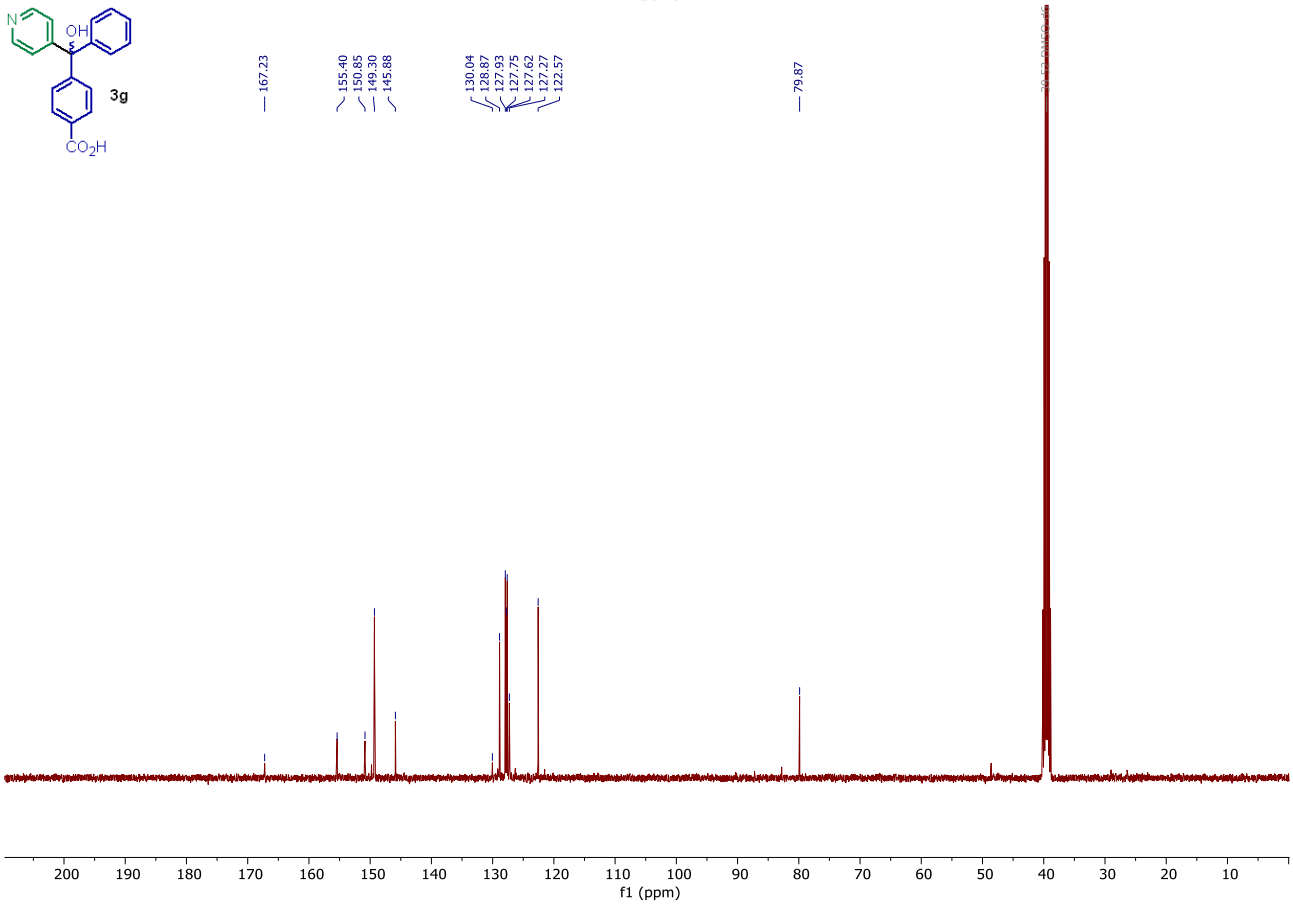
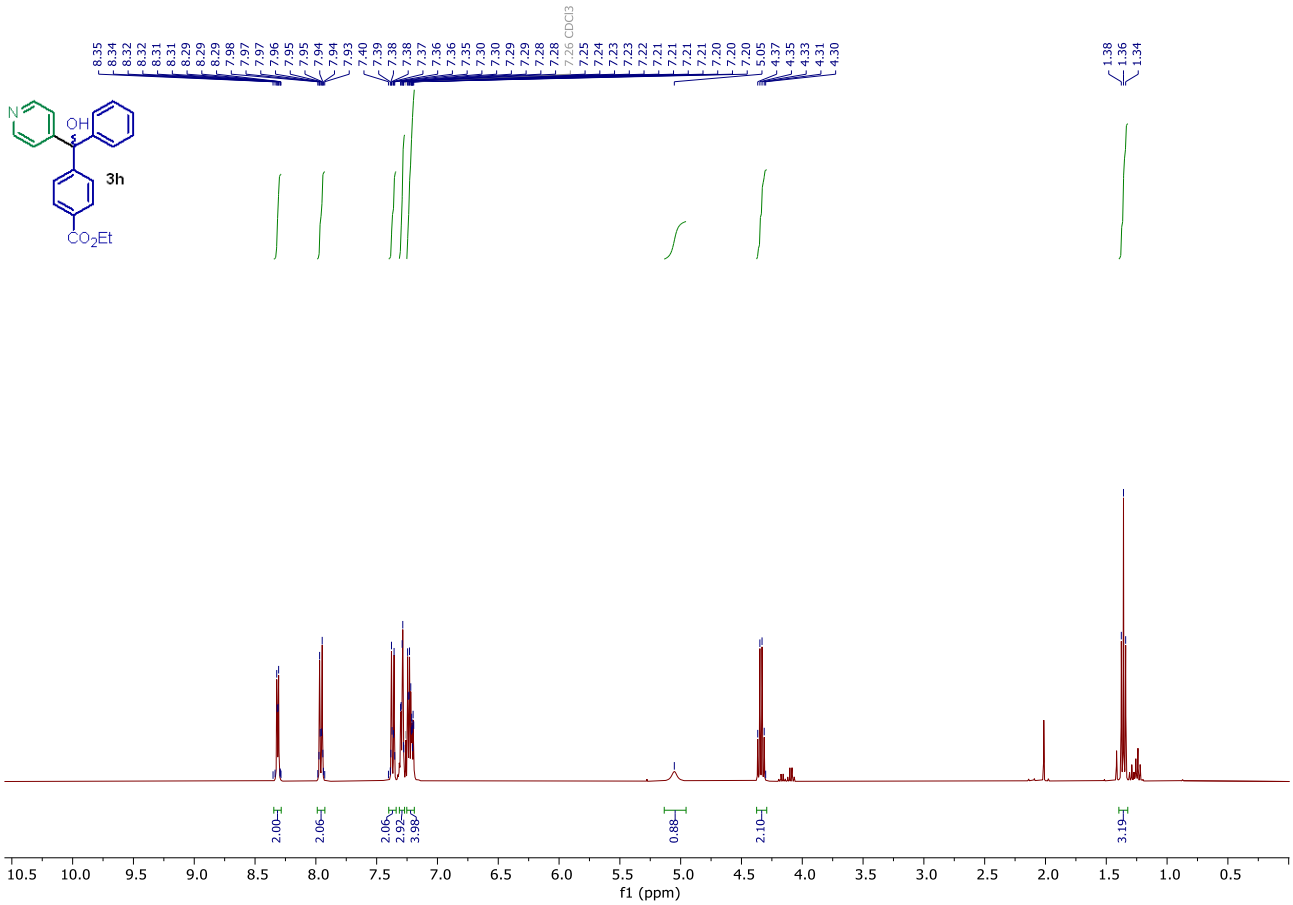
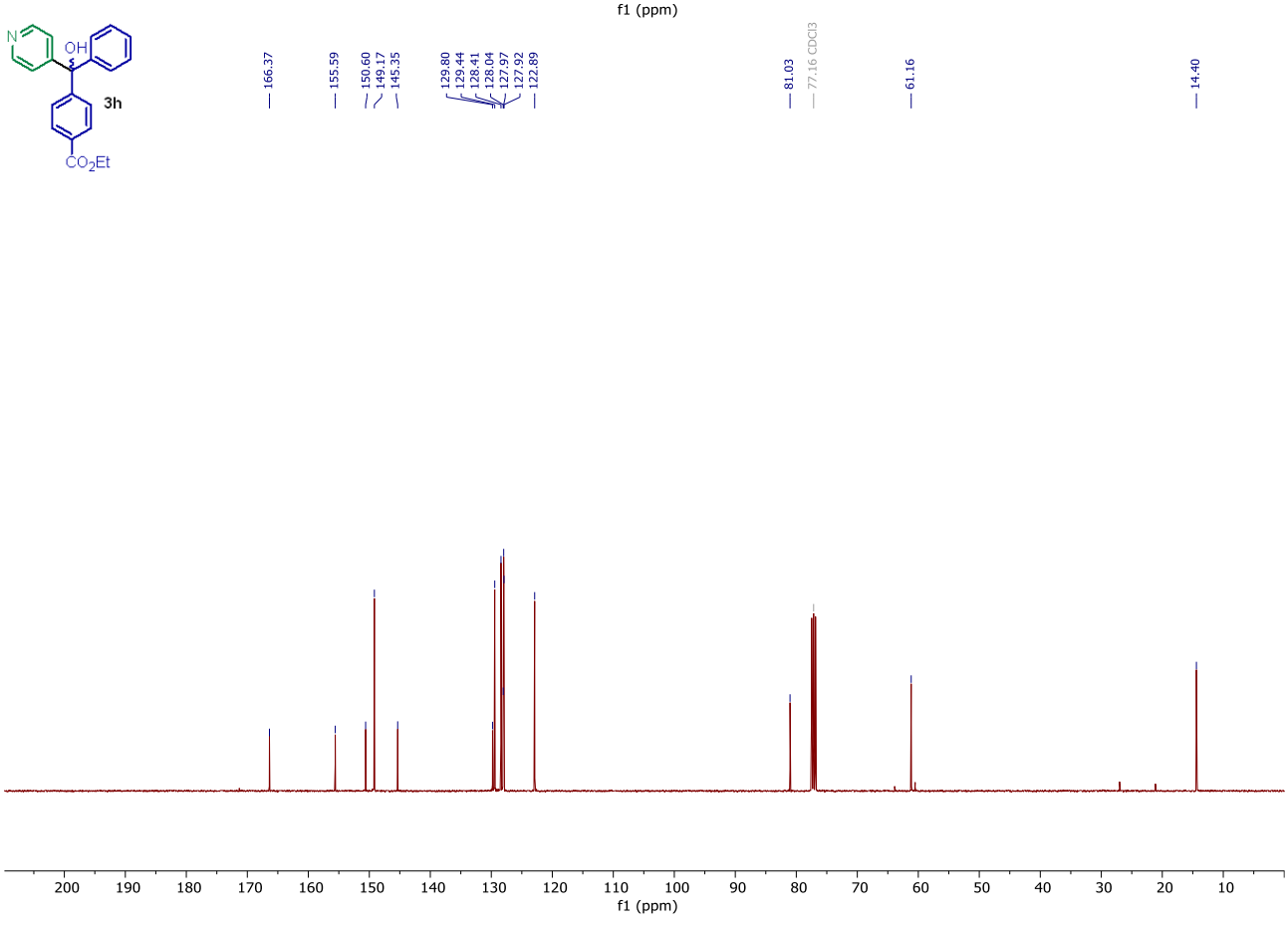
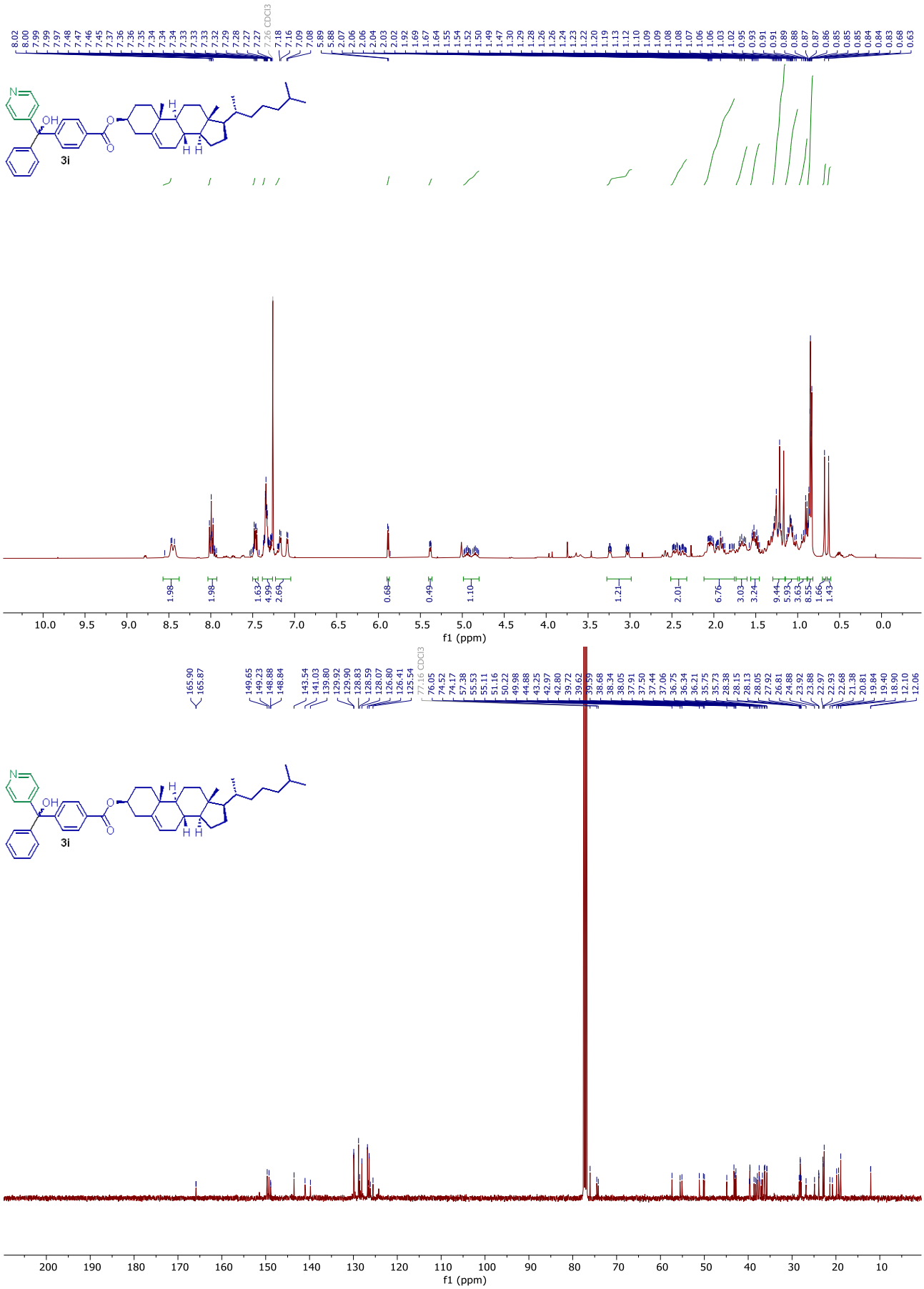
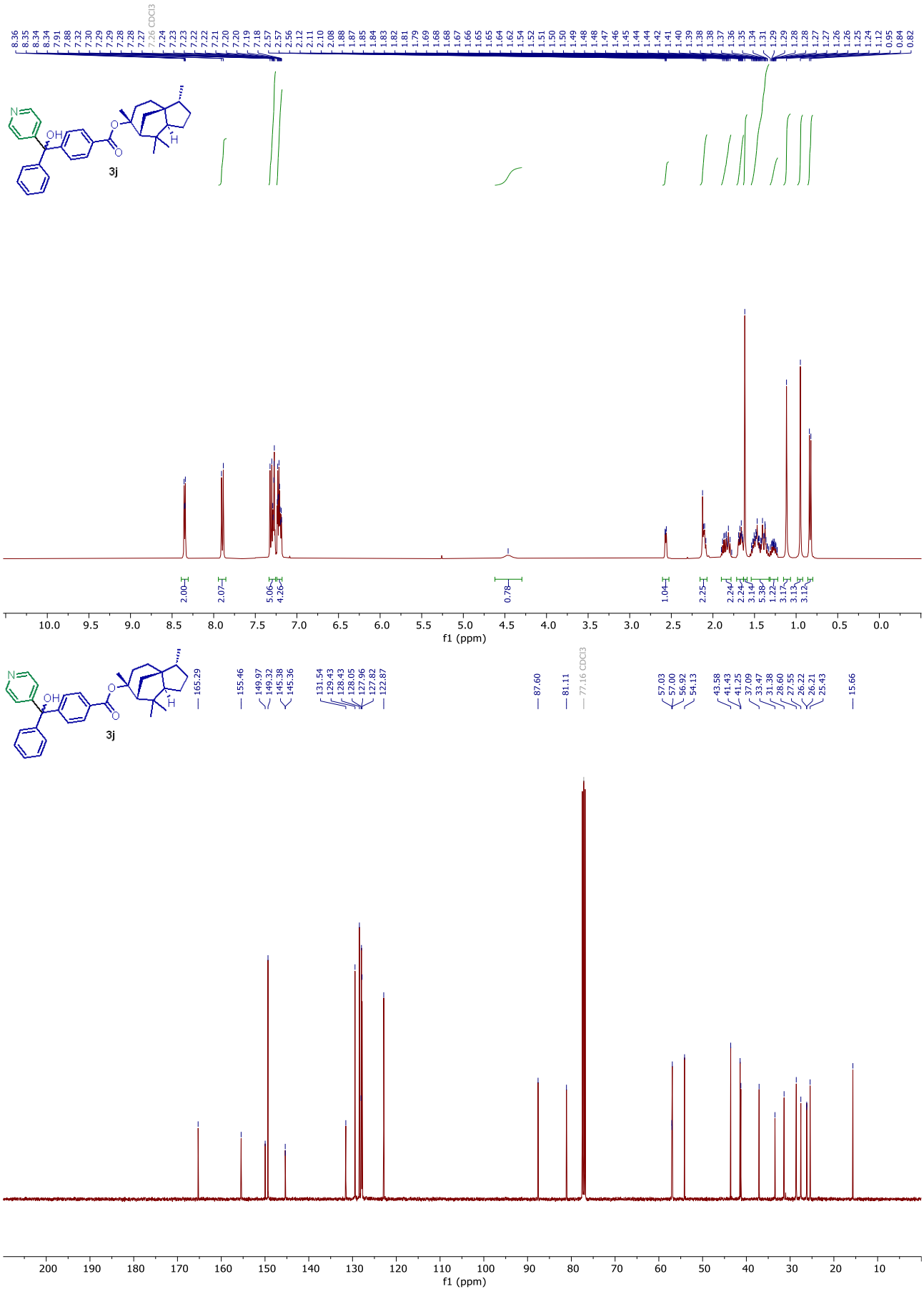
8.52
8.51
7.90
7.87
7.34
7.34
7.32
7.32
7.30
7.30
7.29
7.28
7.24
7.23
7.23
7.22
7.21
7.21
7.19
6.82
2.00
2.08
5.30
4.18
1.01
f1 (ppm)

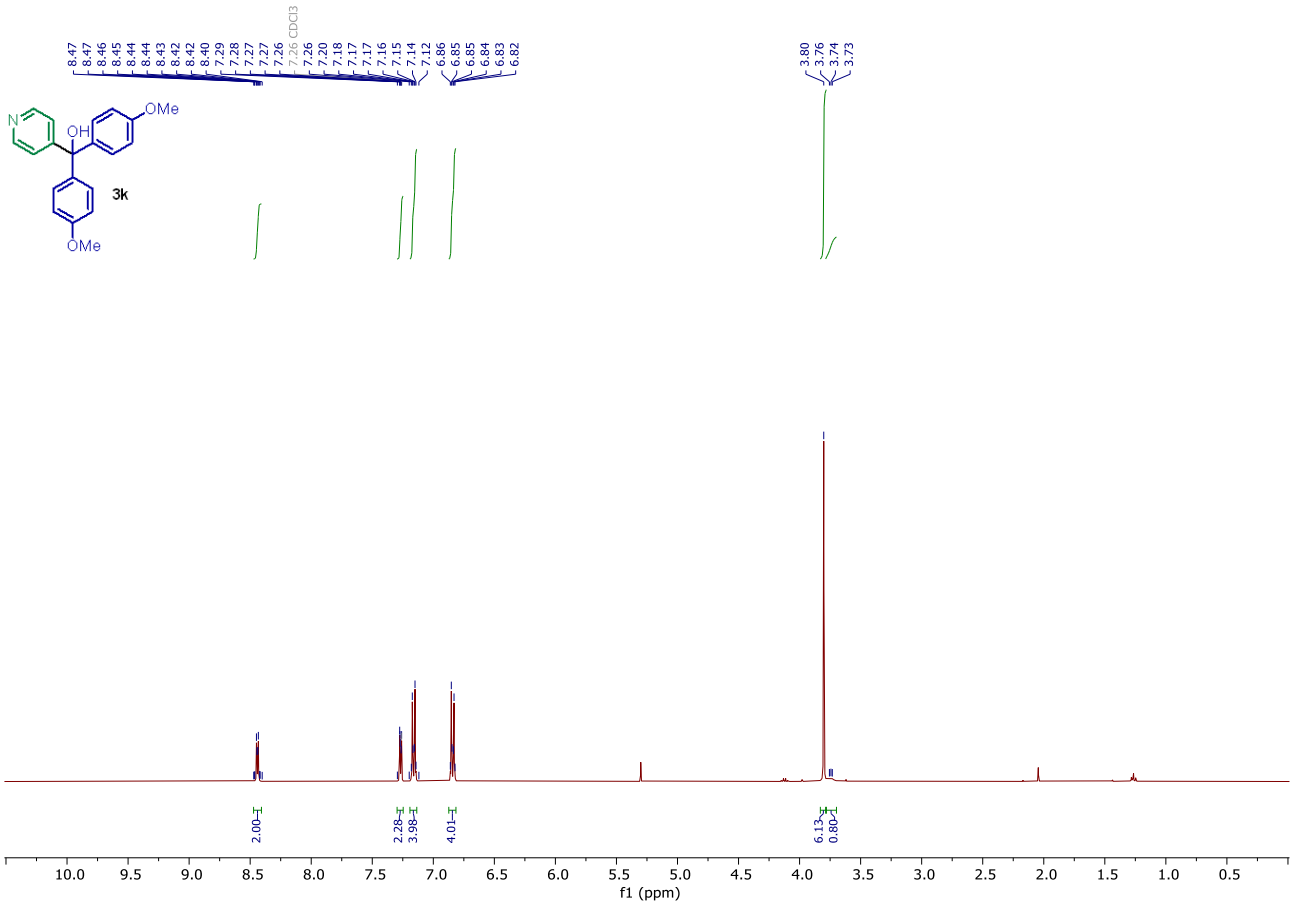

3g
167.23
155.40
150.85
149.30
145.88
130.04
128.87
127.93
127.75
127.62
127.27
122.57
79.87
f1 (ppm)

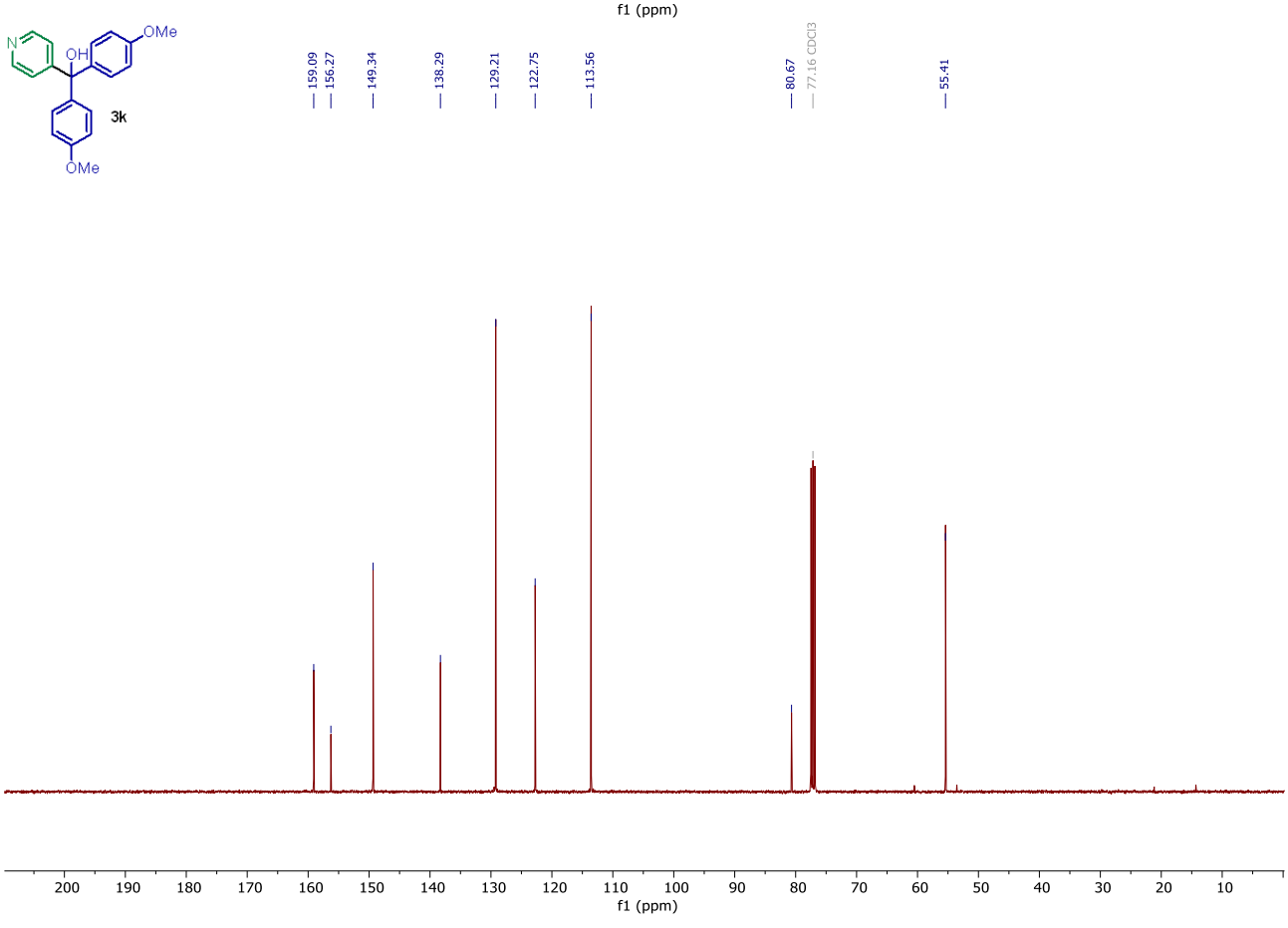

3h
f1 (ppm)

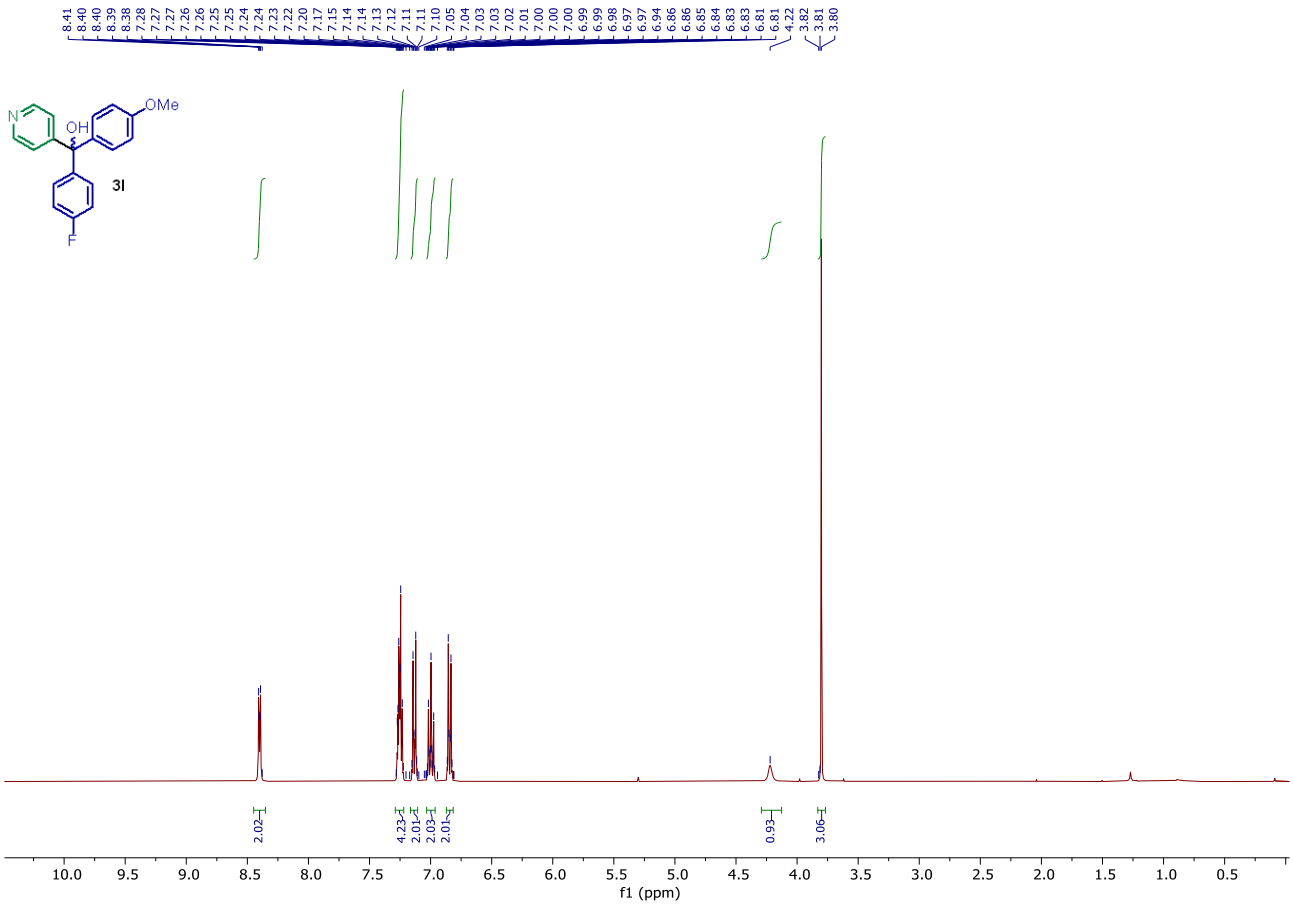

3h
f1 (ppm)

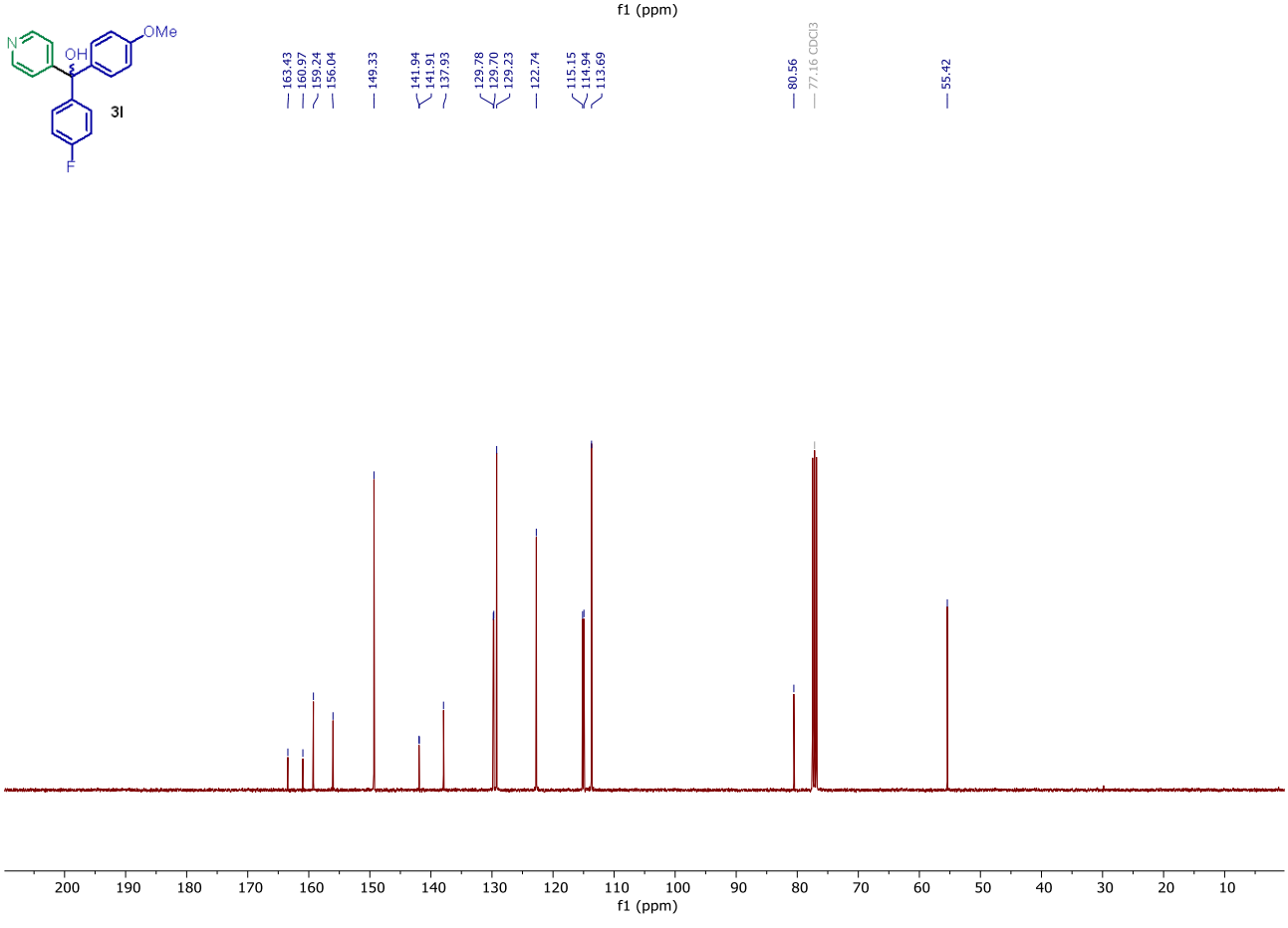

3i
f1 (ppm)
3i
f1 (ppm)

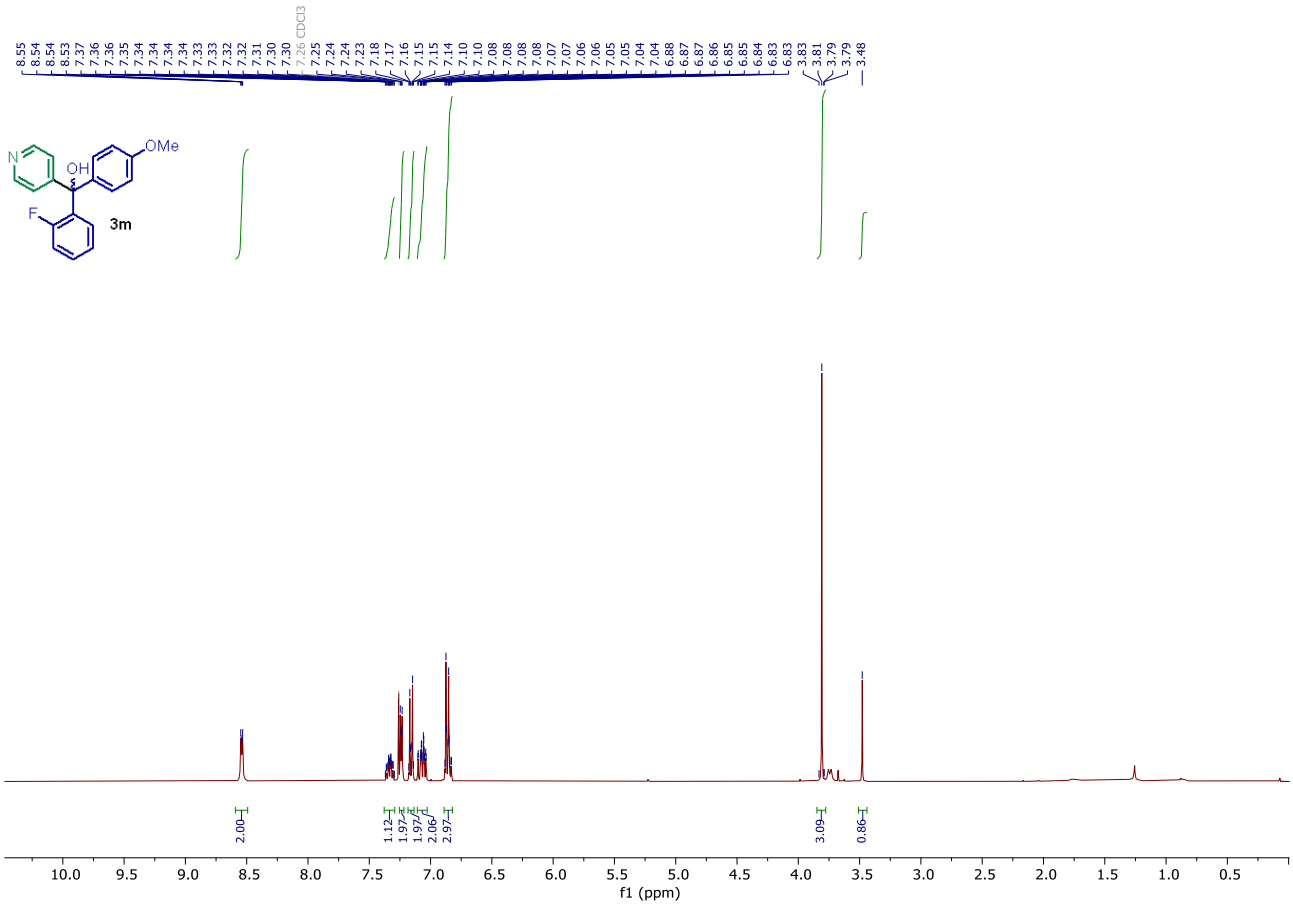

3j
f1 (ppm)
3j
f1 (ppm)

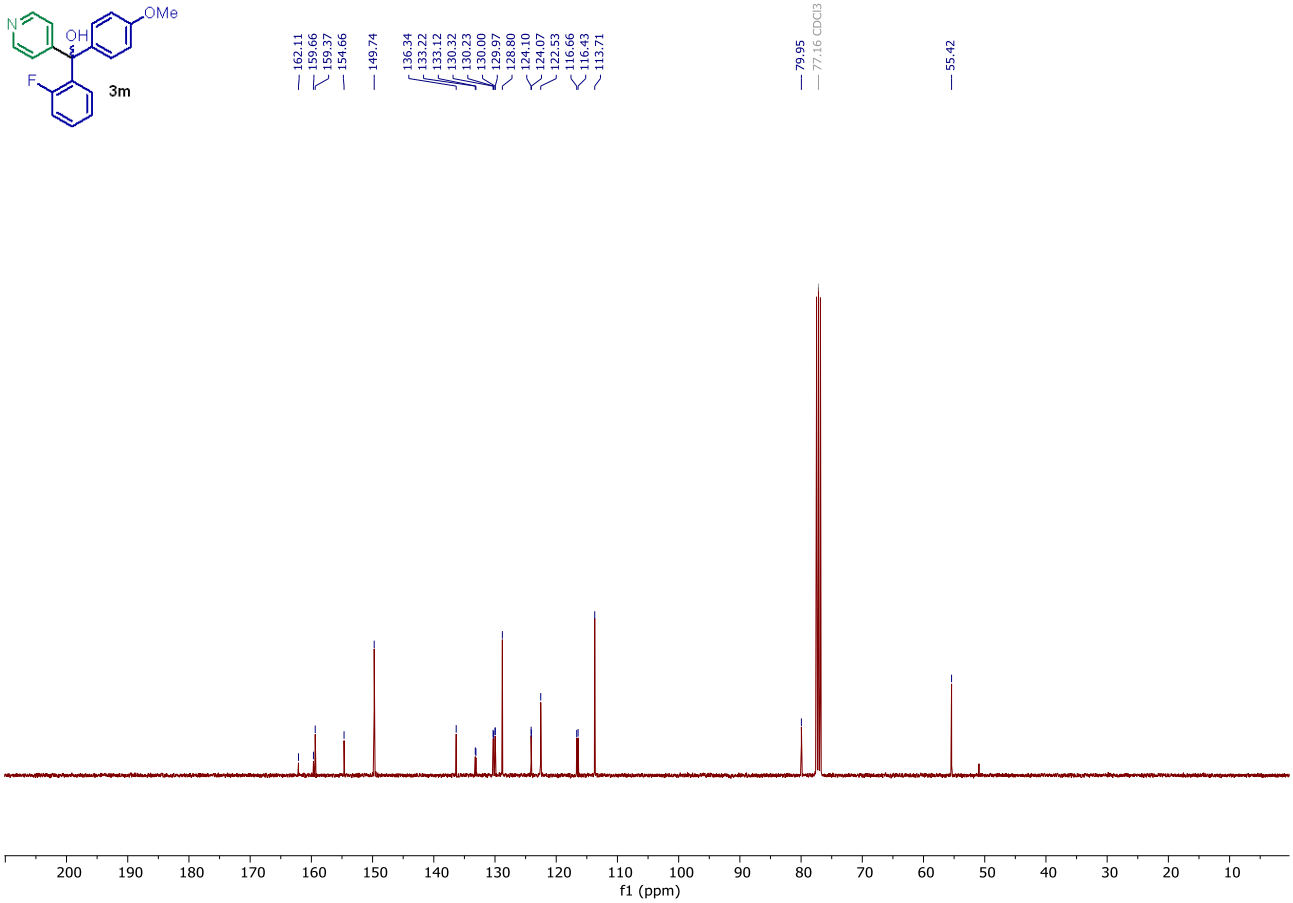

8.47
8.47
8.46
8.45
8.44
8.44
8.43
8.42
8.42
8.40
7.29
7.28
7.27
7.27
7.26
7.26 CDCl3
7.26
7.20
7.18
7.17
7.17
7.16
7.15
7.14
7.12
6.86
6.85
6.85
6.84
6.83
6.82
3.80
3.76
3.74
3.73
N
OH
OMe
OMe
3k
2.00
2.28
3.98
4.01
6.13
0.80
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

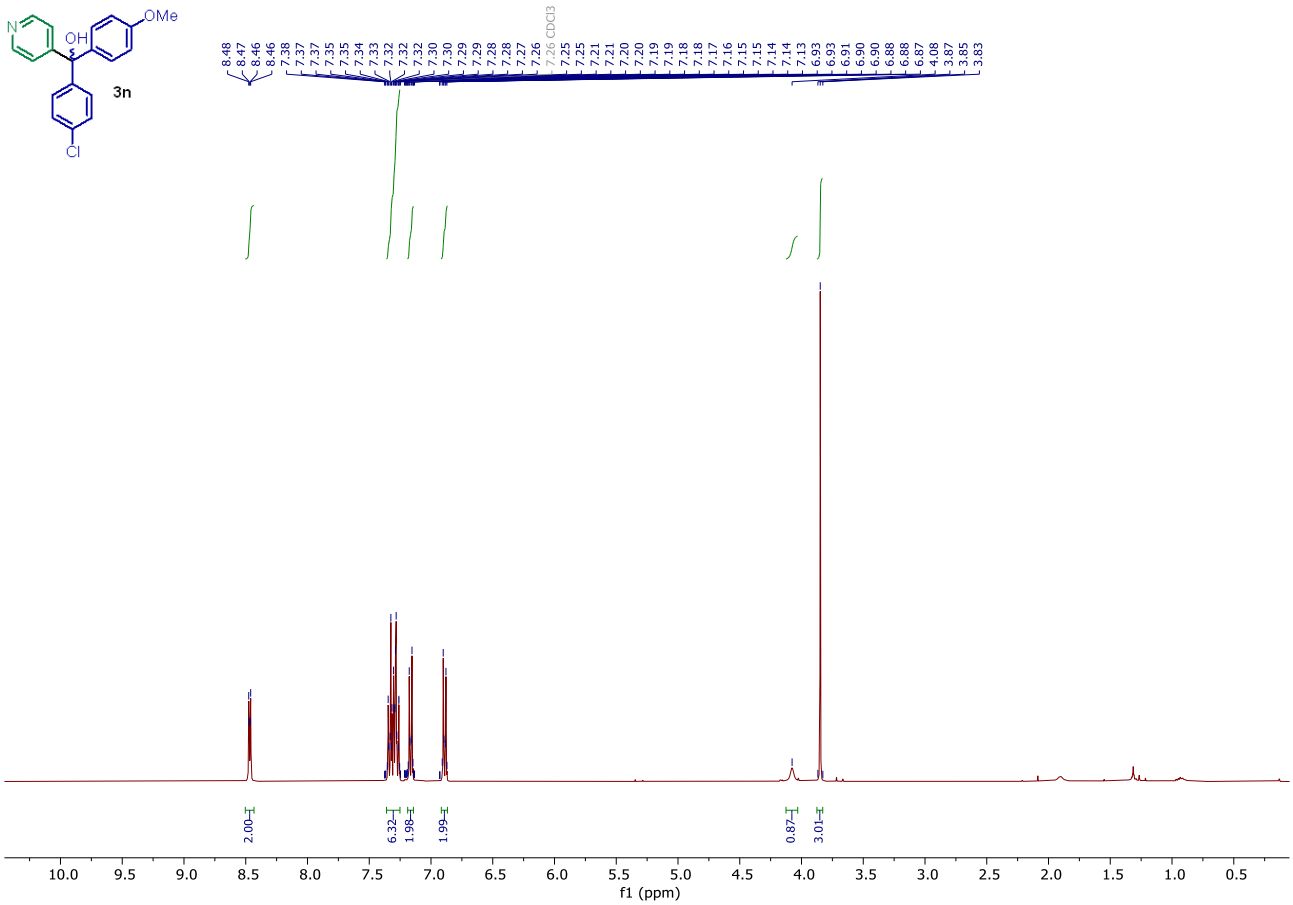

N
OH
OMe
OMe
3k
159.09
156.27
149.34
138.29
129.21
122.75
113.56
80.67
77.16 CDCl3
55.41
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

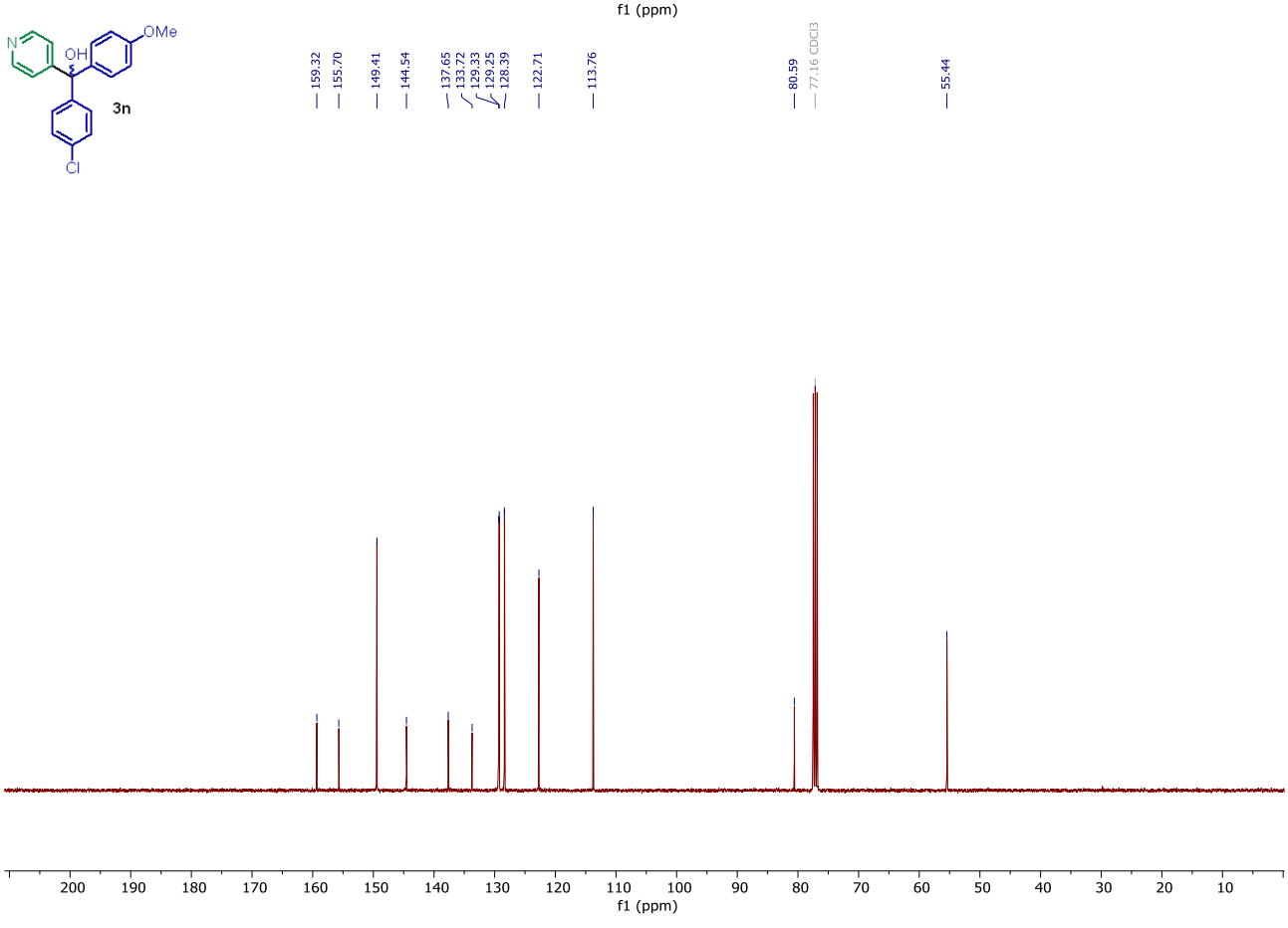

8.41 8.40 8.40 8.39 8.38 7.28 7.27 7.27 7.26 7.25 7.25 7.24 7.24 7.23 7.22 7.20 7.17 7.15 7.14 7.14 7.13 7.12 7.11 7.11 7.10 7.05 7.04 7.03 7.03 7.02 7.01 7.00 7.00 7.00 6.99 6.99 6.98 6.97 6.97 6.94 6.86 6.86 6.85 6.84 6.83 6.83 6.81 6.81 4.22 3.82 3.81 3.80
N
OH
OMe
F
3l
2.02
4.23
2.01
2.03
2.01
0.93
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

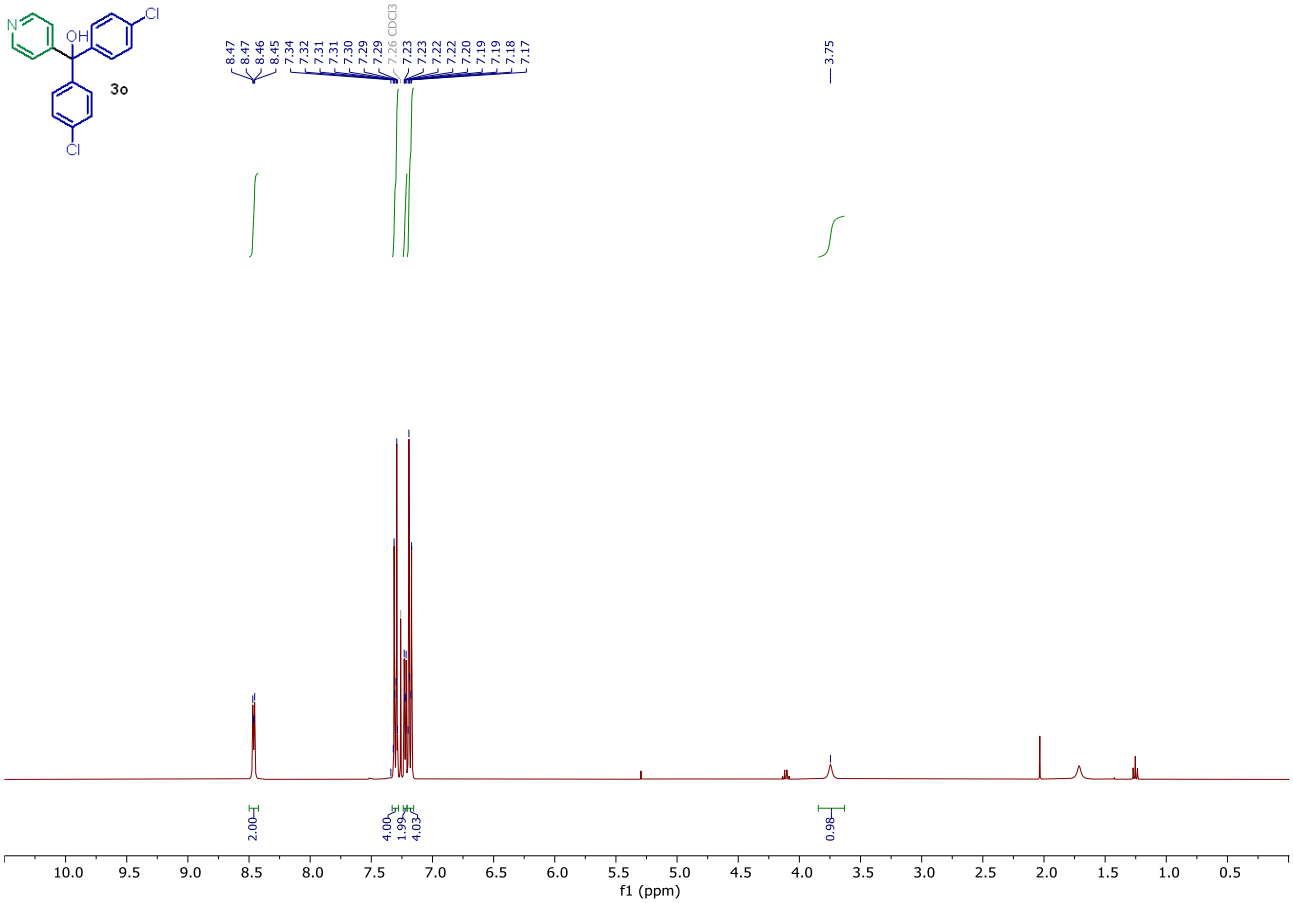

N
OH
OMe
F
3l
163.43
160.97
159.24
156.04
149.33
141.94
141.91
137.93
129.78
129.70
129.23
122.74
115.15
114.94
113.69
80.56
77.16 CDCl3
55.42
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

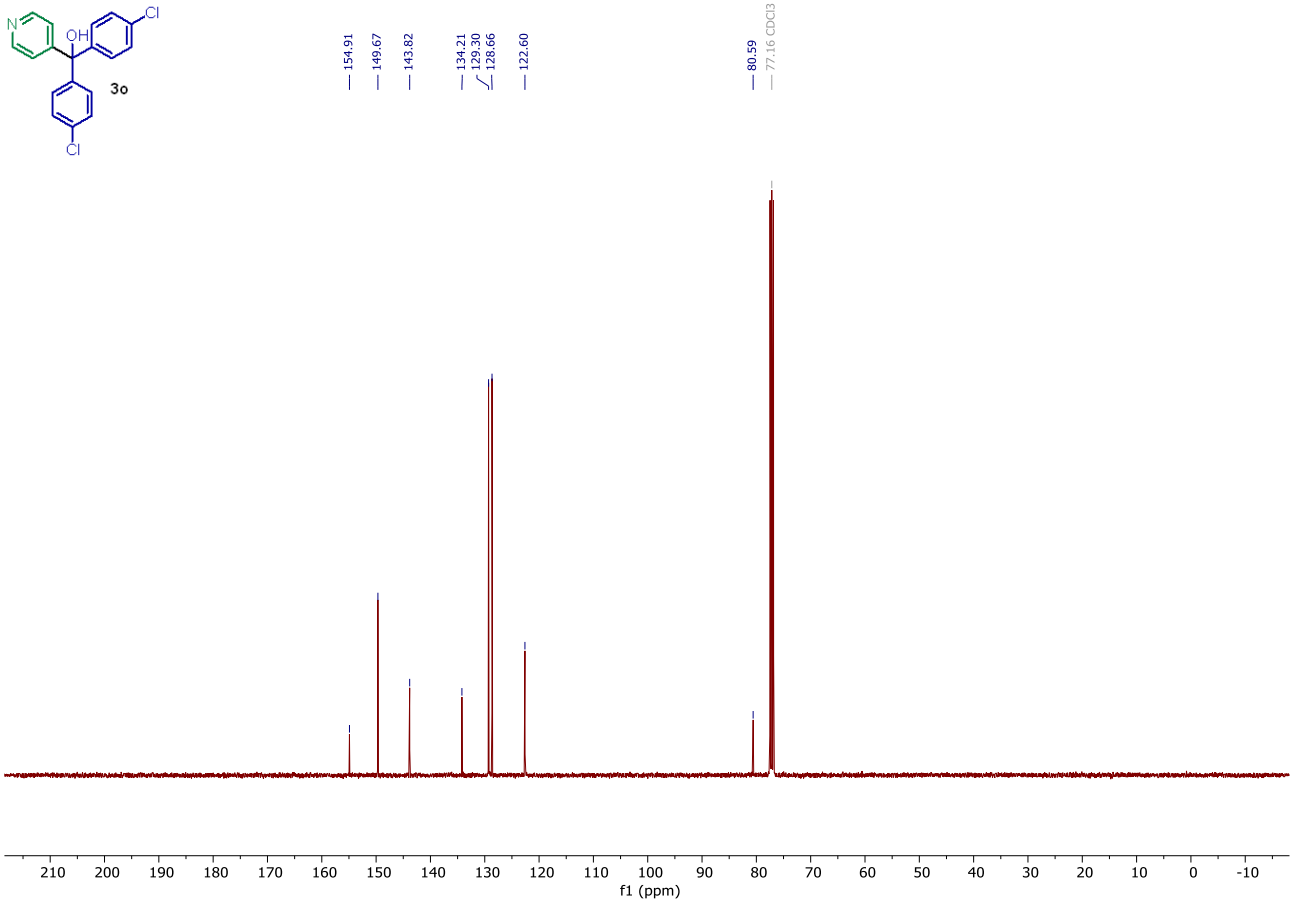

3m
f1 (ppm)

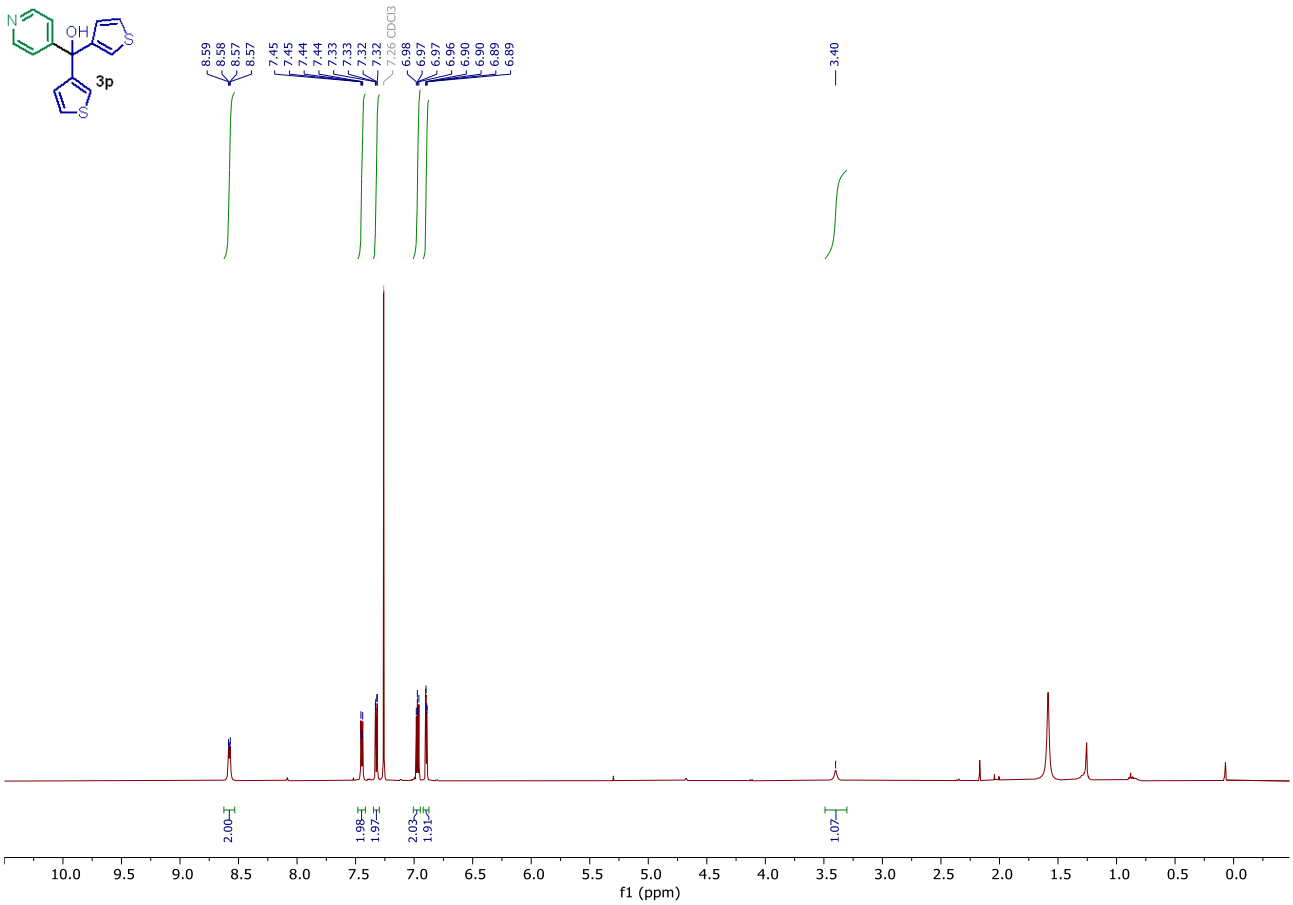

3m
f1 (ppm)

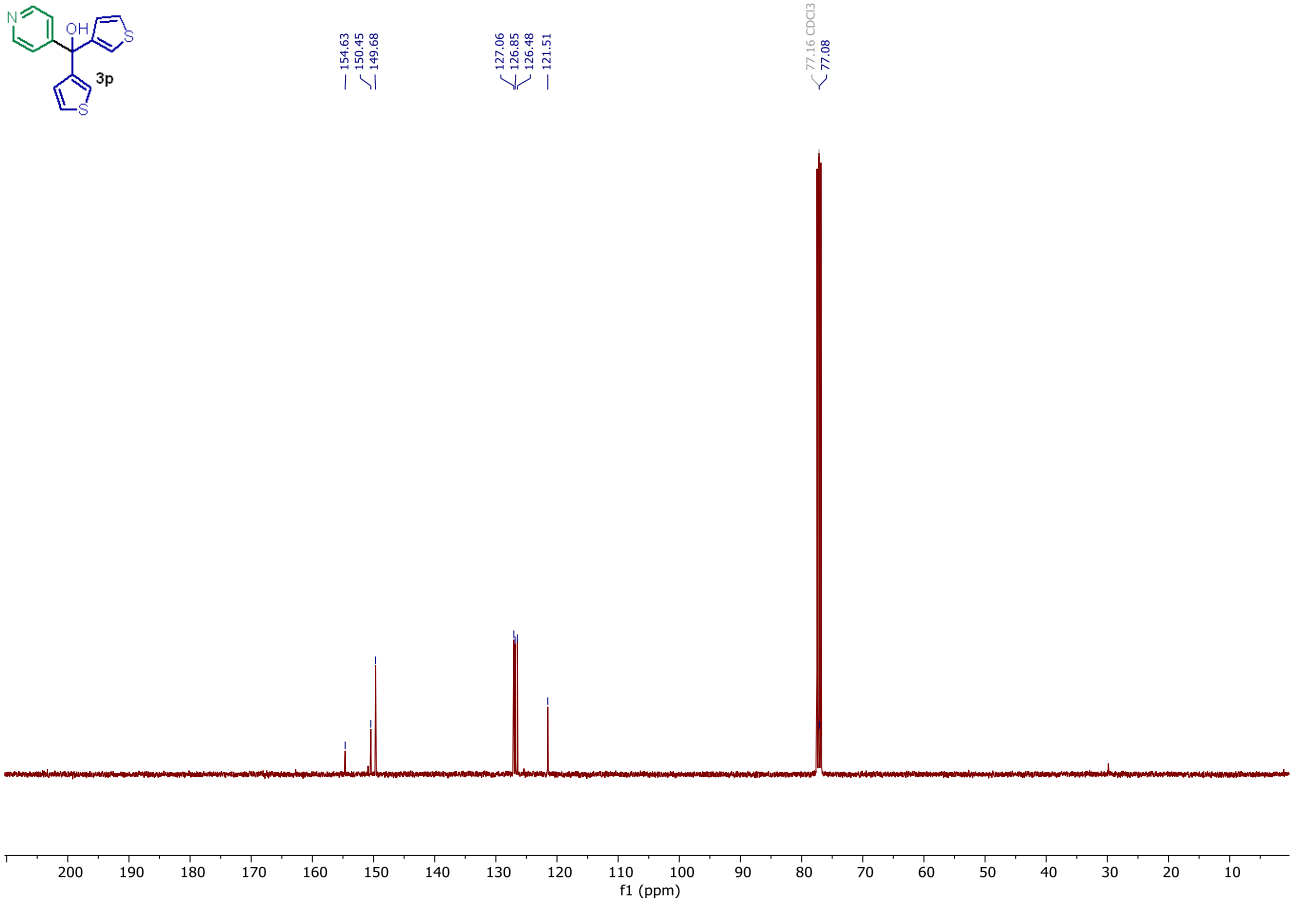

OMe
OH
N
Cl
3n
8.48 8.47 8.46 8.46 7.38 7.37 7.37 7.35 7.35 7.34 7.33 7.32 7.32 7.32 7.30 7.30 7.29 7.28 7.28 7.27 7.26 7.26 CDCl3 7.25 7.25 7.21 7.21 7.20 7.19 7.19 7.18 7.18 7.17 7.16 7.15 7.15 7.14 7.14 7.13 6.93 6.93 6.91 6.90 6.90 6.88 6.88 6.87 4.08 3.87 3.85 3.83
2.00 6.32 1.98 1.99 0.87 3.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


OMe
OH
N
Cl
3n
159.32 155.70 149.41 144.54 137.65 133.72 129.33 129.25 128.39 122.71 113.76 80.59 77.16 CDCl3 55.44
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


3o
8.47
8.47
8.46
8.45
7.34
7.32
7.31
7.31
7.30
7.29
7.29
7.26 CDCl3
7.23
7.23
7.22
7.22
7.20
7.19
7.19
7.18
7.17
3.75
2.00
4.00
1.99
4.03
0.98
f1 (ppm)


3o
154.91
149.67
143.82
134.21
129.30
128.66
122.60
80.59
77.16 CDCl3
f1 (ppm)


3p
8.59
8.58
8.57
8.57
7.45
7.45
7.44
7.44
7.33
7.33
7.32
7.32
7.26 CDCl3
6.98
6.97
6.97
6.96
6.90
6.90
6.89
6.89
3.40
2.00
1.98
1.97
2.03
1.91
1.07
f1 (ppm)


3p
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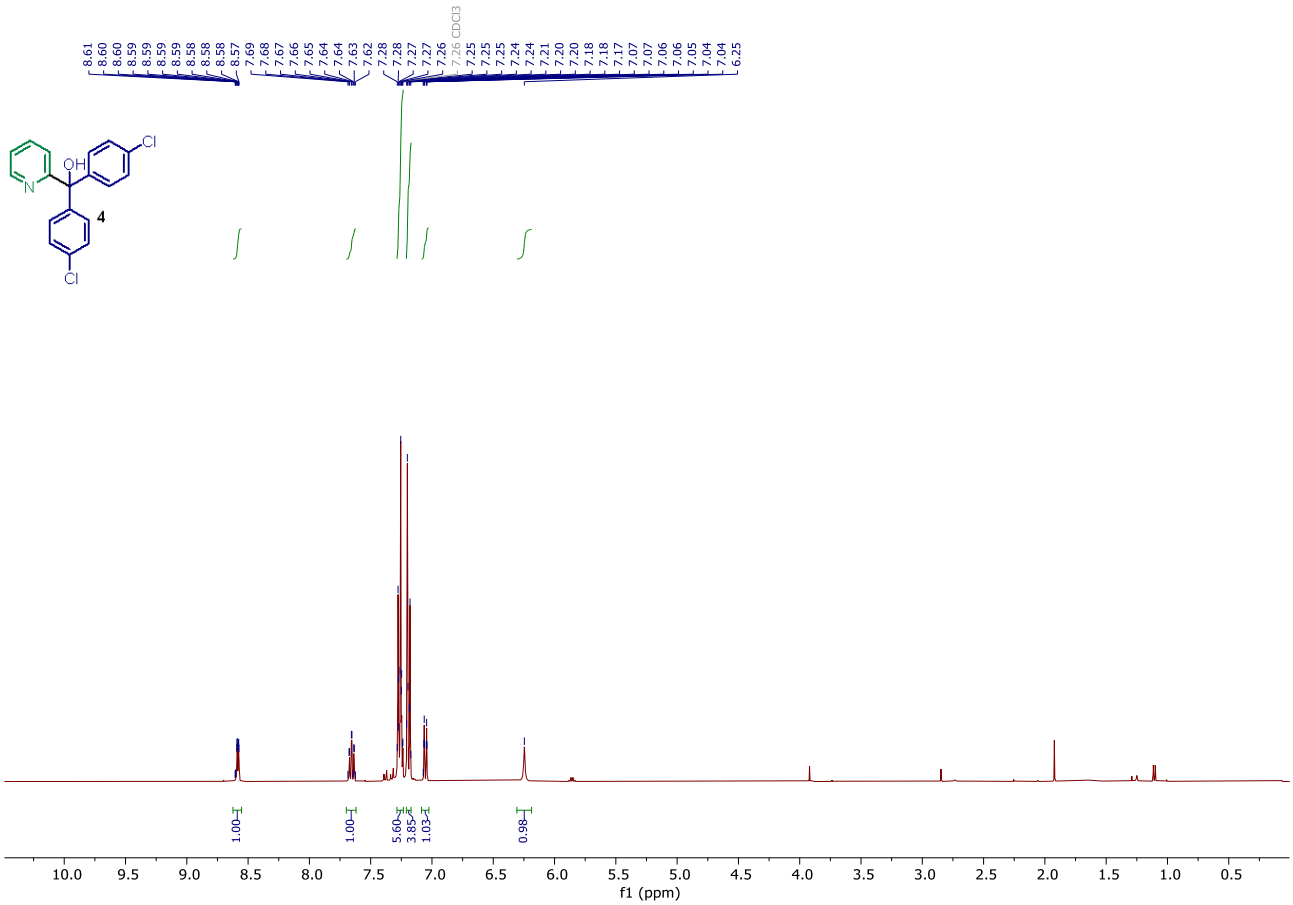
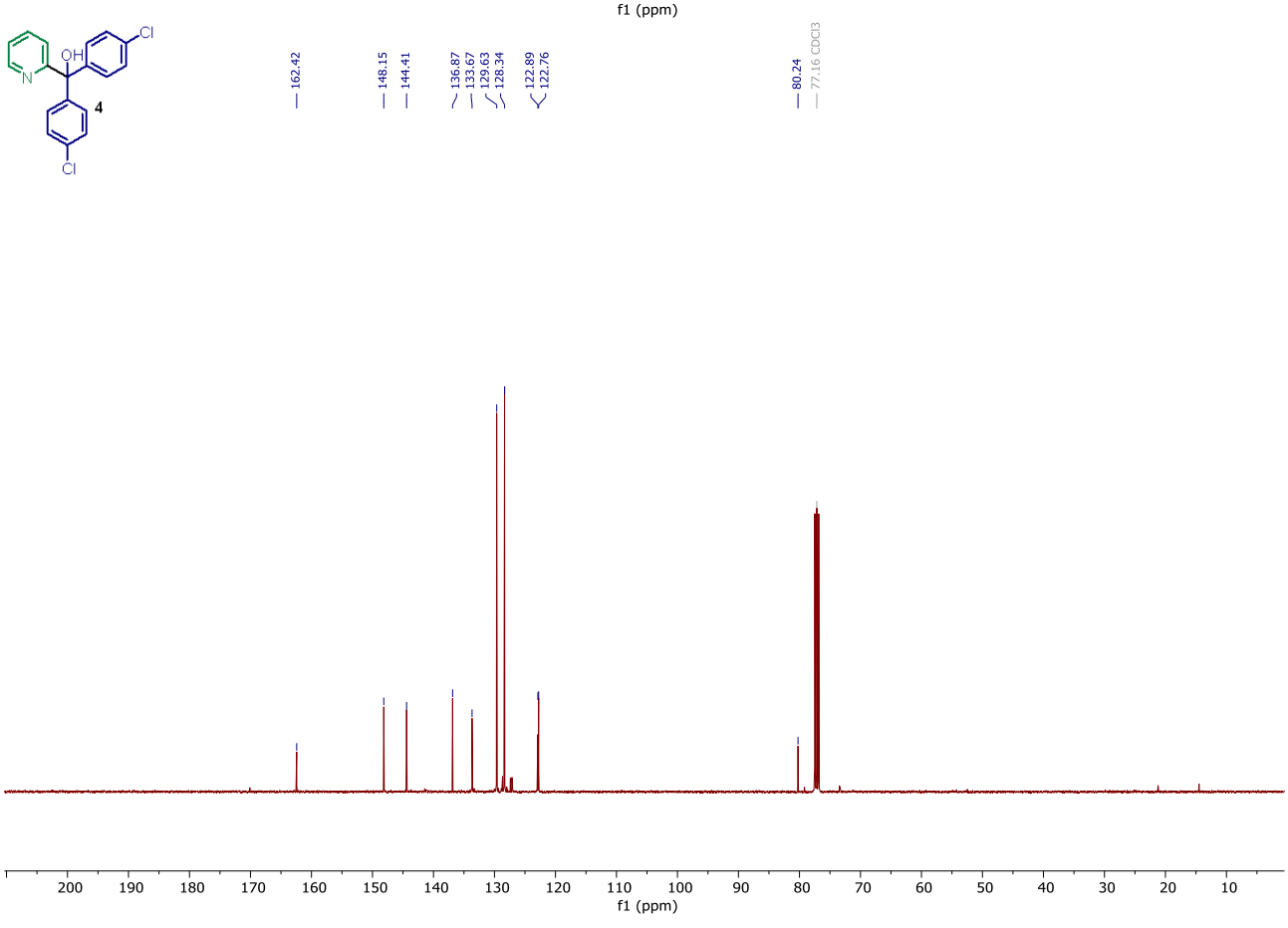
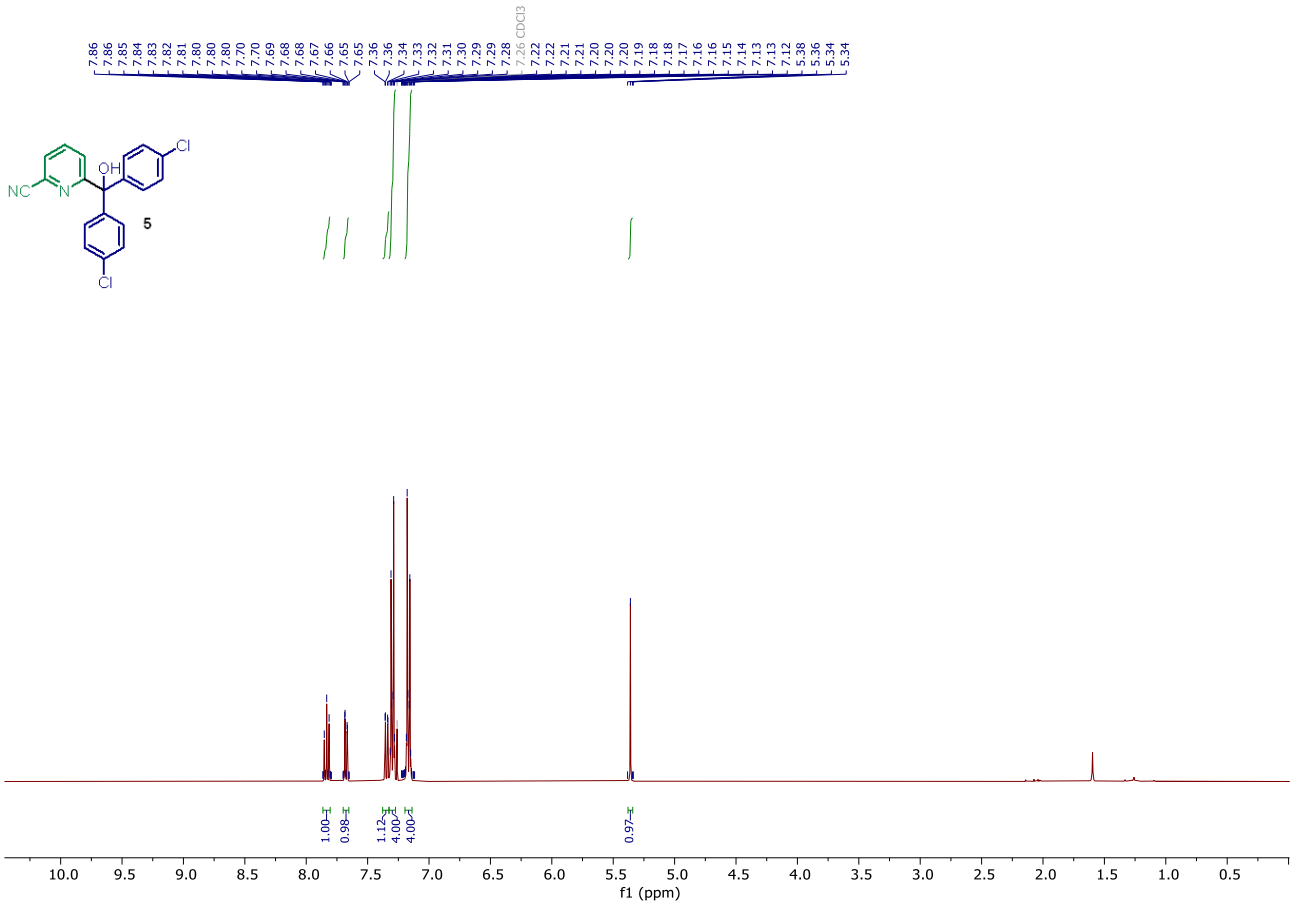
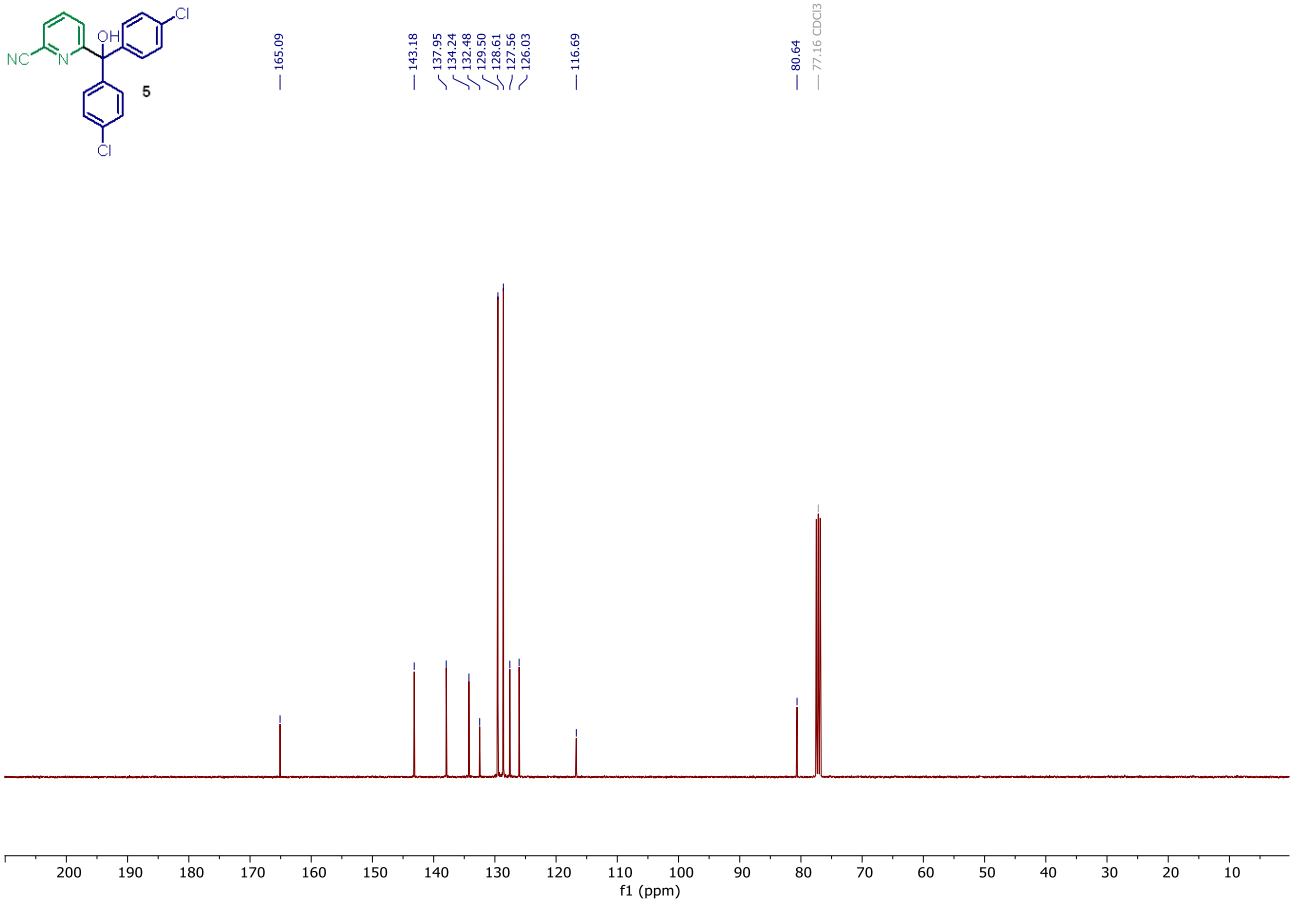
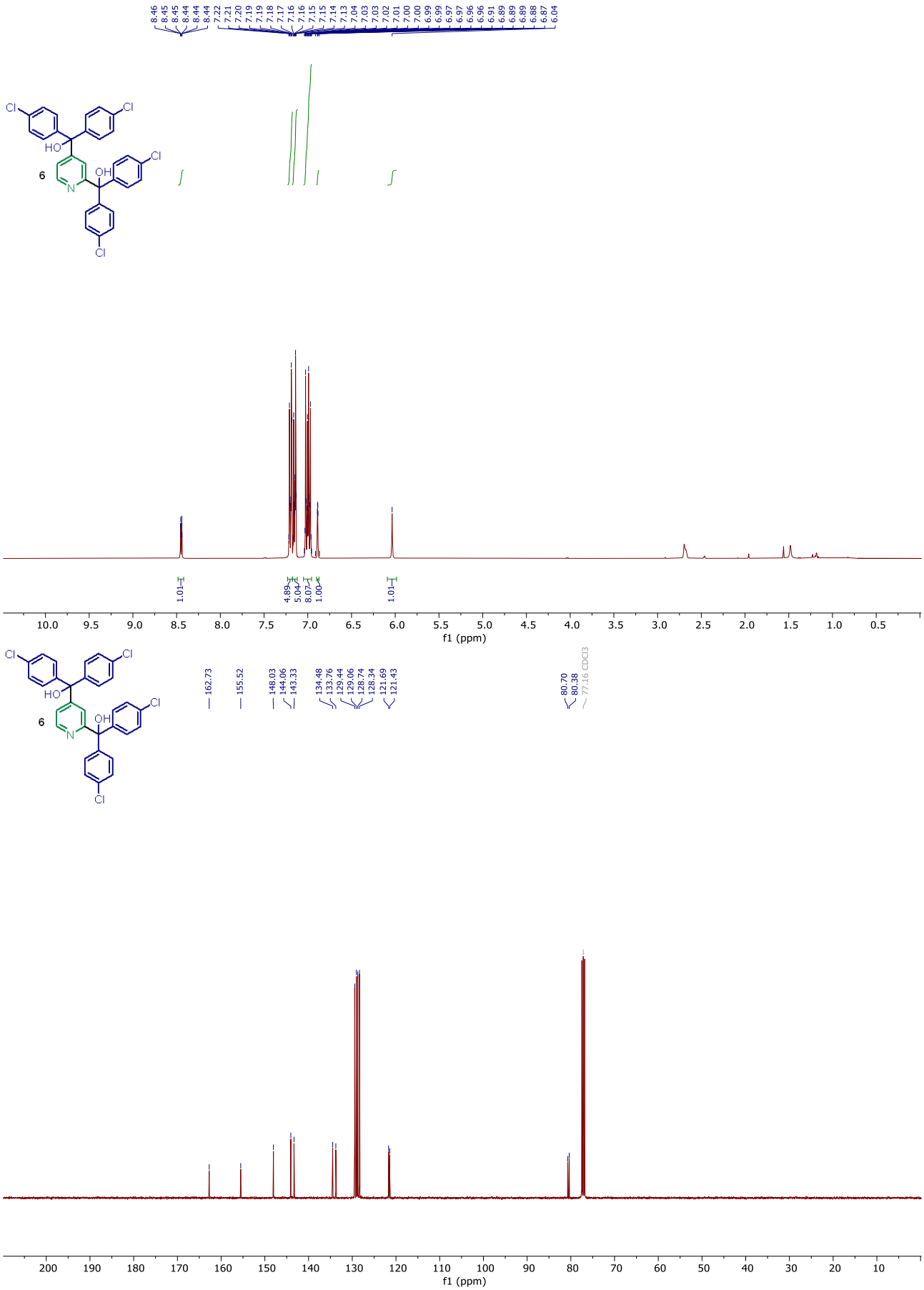
126.85
126.48
121.51
77.16 CDCl3
77.08
f1 (ppm)


8.61 8.60 8.60 8.59 8.59 8.59 8.59 8.58 8.58 8.58 8.58 8.57 7.69 7.68 7.67 7.66 7.65 7.64 7.64 7.63 7.62 7.28 7.27 7.27 7.26 7.26 CDCl3 7.25 7.25 7.25 7.25 7.24 7.24 7.21 7.20 7.20 7.18 7.18 7.17 7.07 7.07 7.06 7.06 7.05 7.04 7.04 6.25
OH
N
Cl
4
Cl
1.00 1.00 5.60 3.85 1.03 0.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


OH
N
Cl
4
Cl
162.42
148.15
144.41
136.87
133.67
129.63
128.34
122.89
122.76
80.24
77.16 CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.86 7.86 7.85 7.84 7.83 7.82 7.81 7.80 7.80 7.80 7.70 7.70 7.69 7.68 7.68 7.67 7.66 7.65 7.65 7.36 7.36 7.34 7.33 7.32 7.31 7.30 7.29 7.29 7.28 7.26 CDCl3 7.22 7.22 7.21 7.21 7.20 7.20 7.20 7.19 7.18 7.18 7.17 7.16 7.16 7.15 7.14 7.13 7.12 5.38 5.36 5.34 5.34
NC
N
OH
Cl
Cl
5
1.00
0.98
1.12
4.00
4.00
0.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


NC
N
OH
Cl
Cl
5
165.09
143.18
137.95
134.24
132.48
129.50
128.61
127.56
126.03
116.69
80.64
77.16 CDCl3
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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7.21
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7.03
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7.02
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6.97
6.97
6.96
6.96
6.91
6.89
6.89
6.89
6.88
6.87
6.04
Cl
Cl
HO
Cl
6
OH
N
Cl
1.01
4.89
5.04
8.07
1.00
1.01
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)
Cl
Cl
HO
Cl
6
OH
N
Cl
162.73
155.52
148.03
144.06
143.33
134.48
133.76
129.44
129.06
128.74
128.34
121.69
121.43
80.70
80.38
77.16 CDCl3
200
190
180
170
160
150
140
130
120
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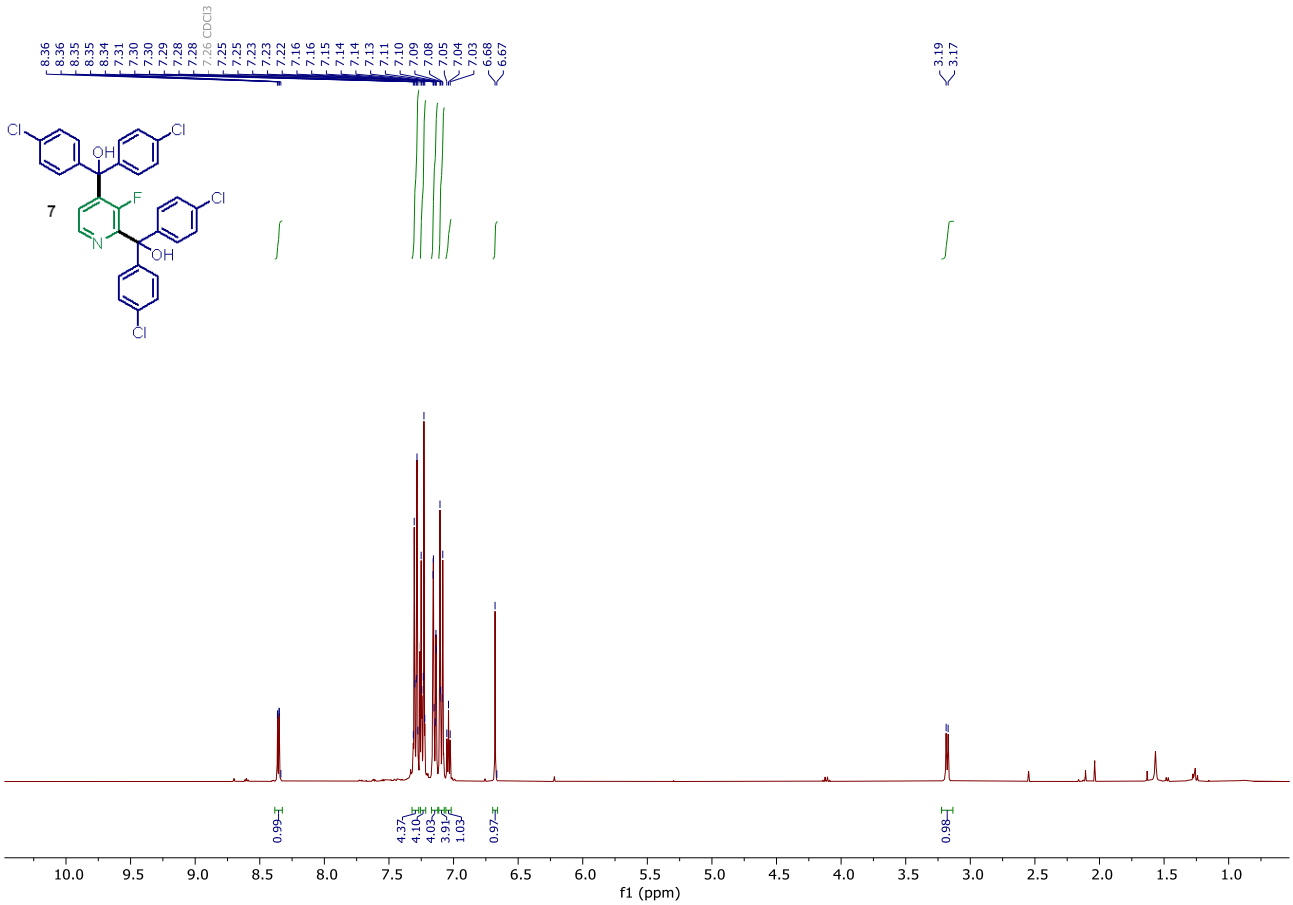
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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8.36
8.35
8.35
8.34
7.31
7.30
7.30
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7.28
7.28
7.26 CDCl3
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Cl
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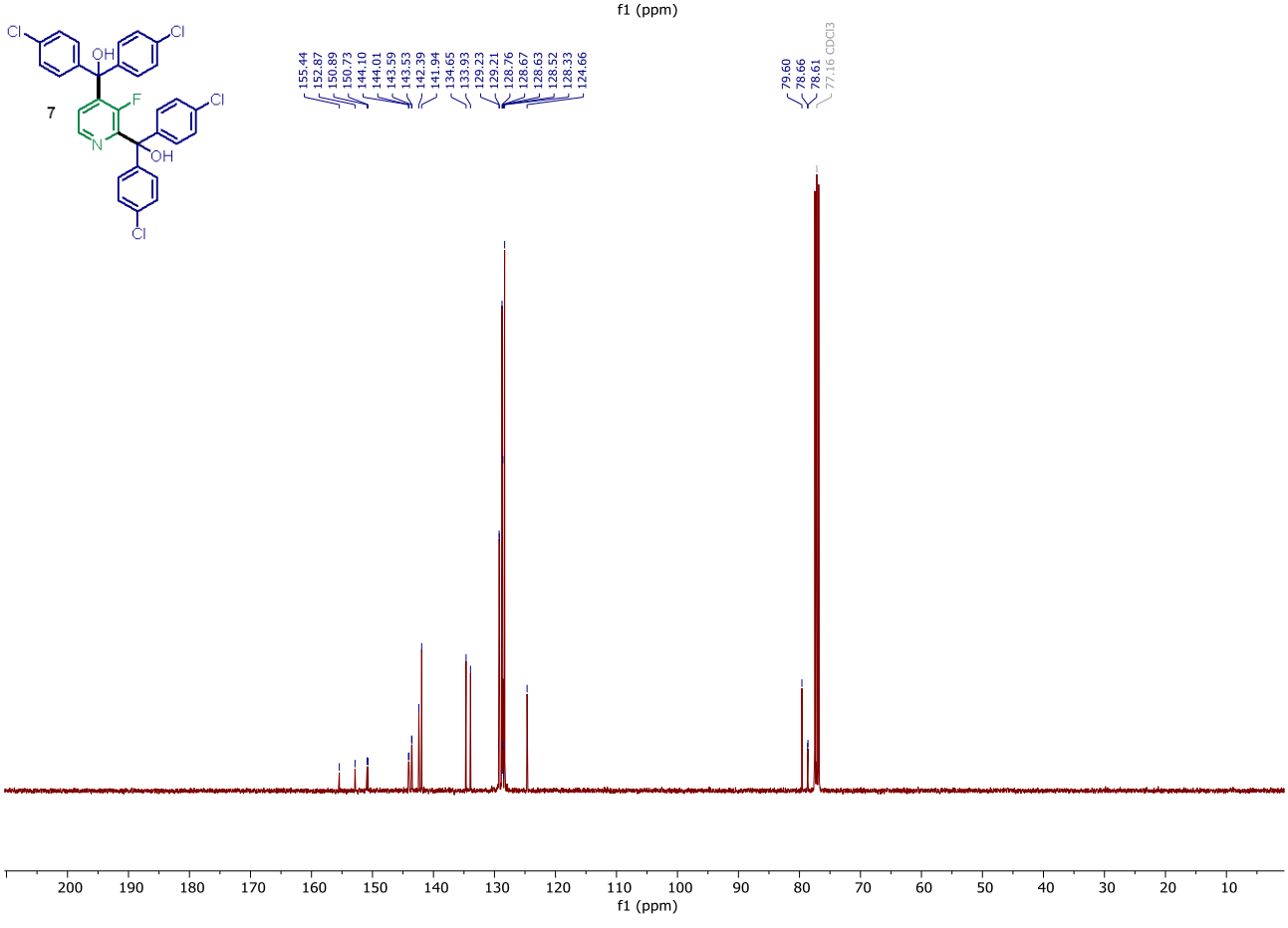
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128.67
128.63
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128.33
124.66
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77.16 CDCl3
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190
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20
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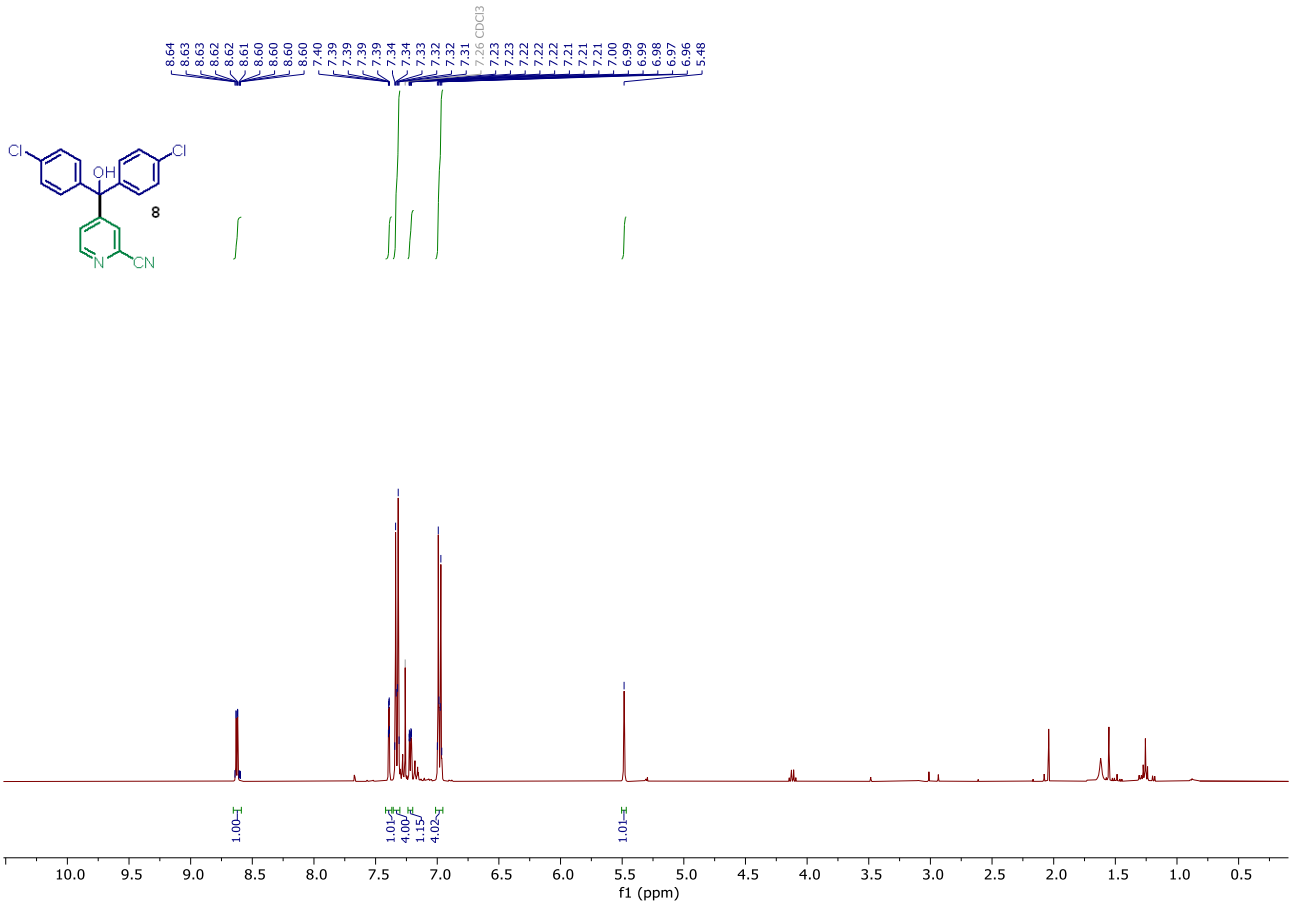
f1 (ppm)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7.31
7.26 CDCl3
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7.22
7.21
7.21
7.21
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6.97
6.96
5.48
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OH
Cl
8
N
CN
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4.00
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4.02
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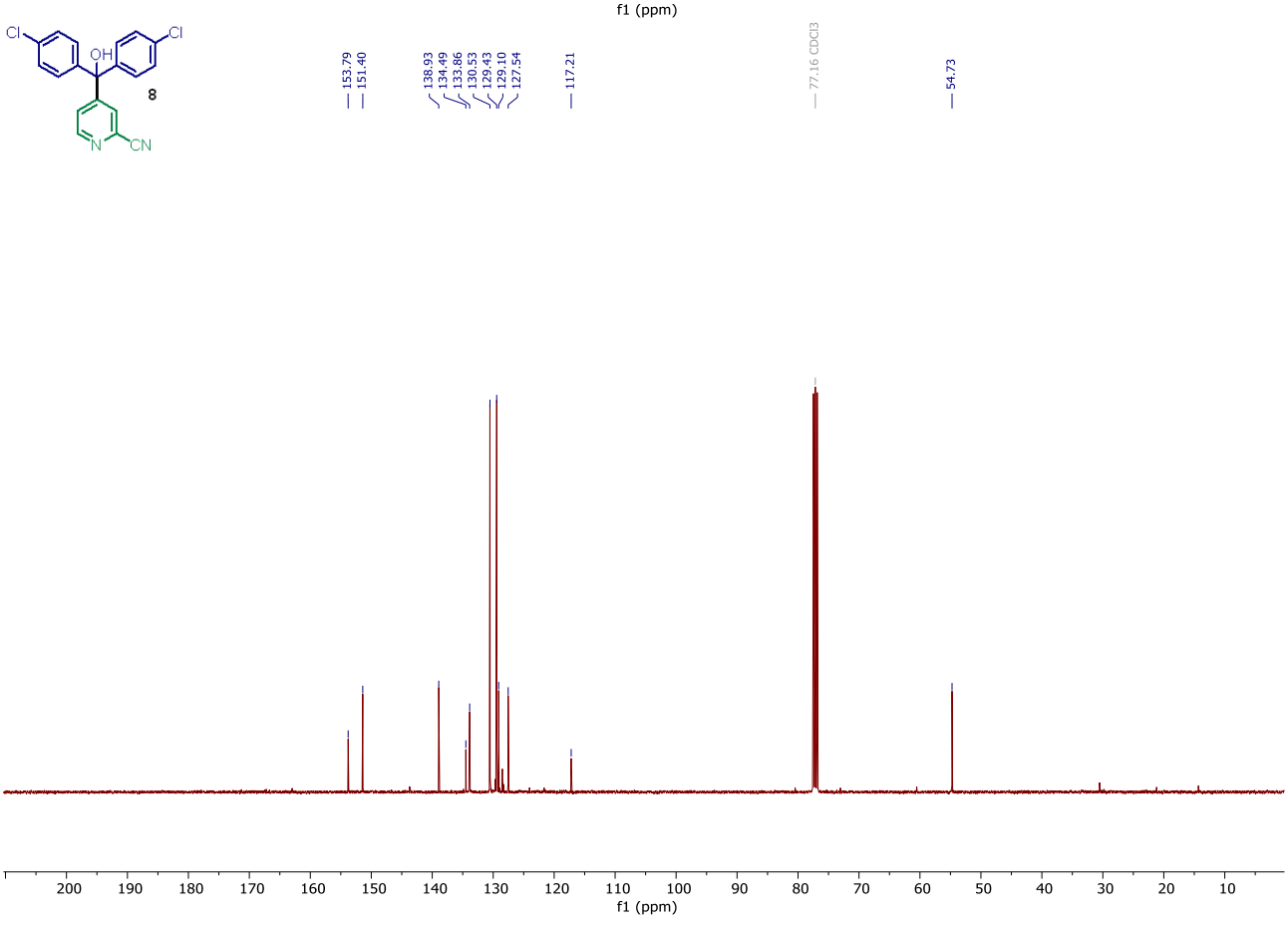
f1 (ppm)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117.21
77.16 CDCl3
54.73
200
190
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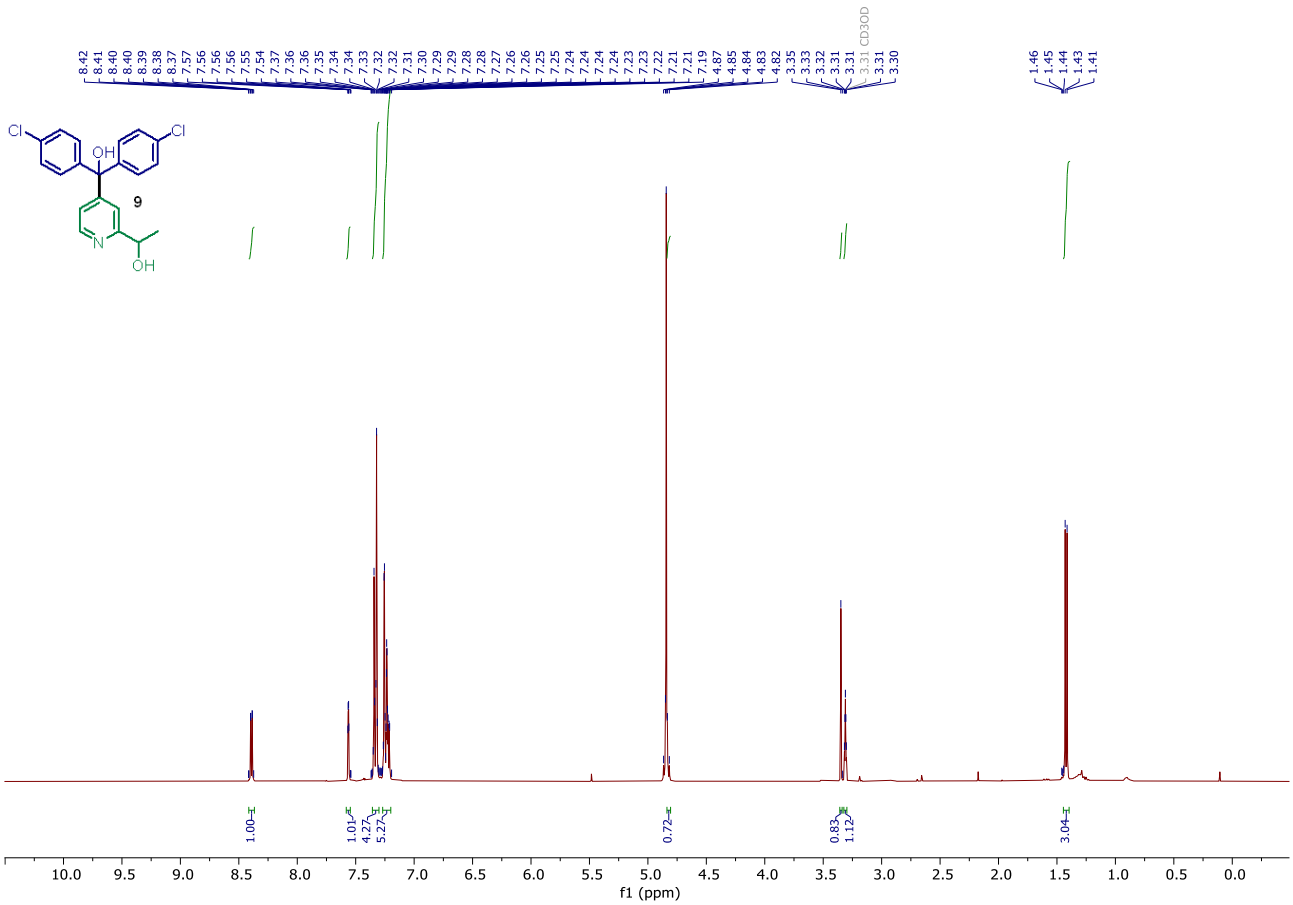
f1 (ppm)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Cl
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OH
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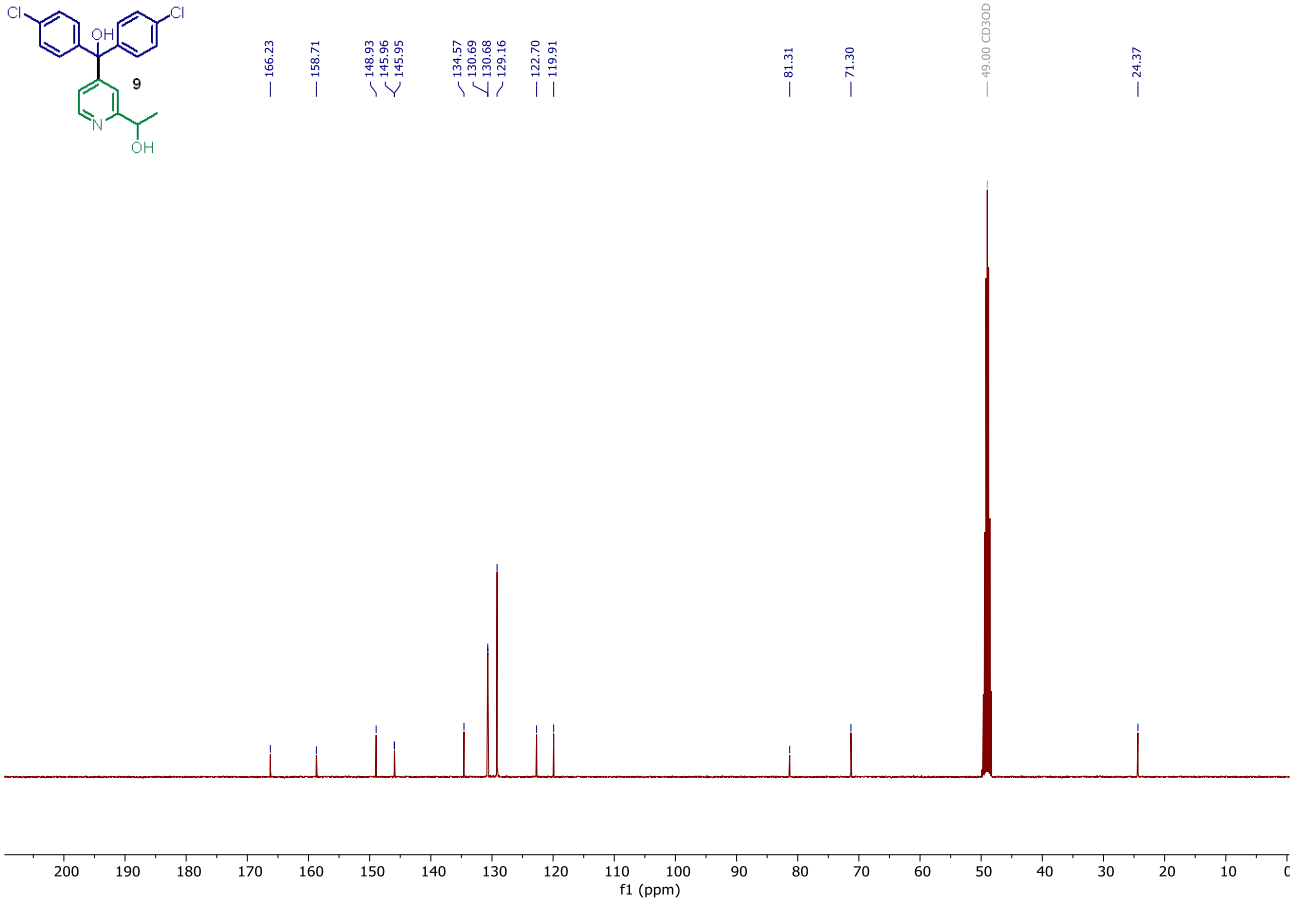
1.46 1.45 1.44 1.43 1.41
1.00 1.01 4.27 5.27 0.72 0.83 1.12 3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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OH
Cl
9
N
OH
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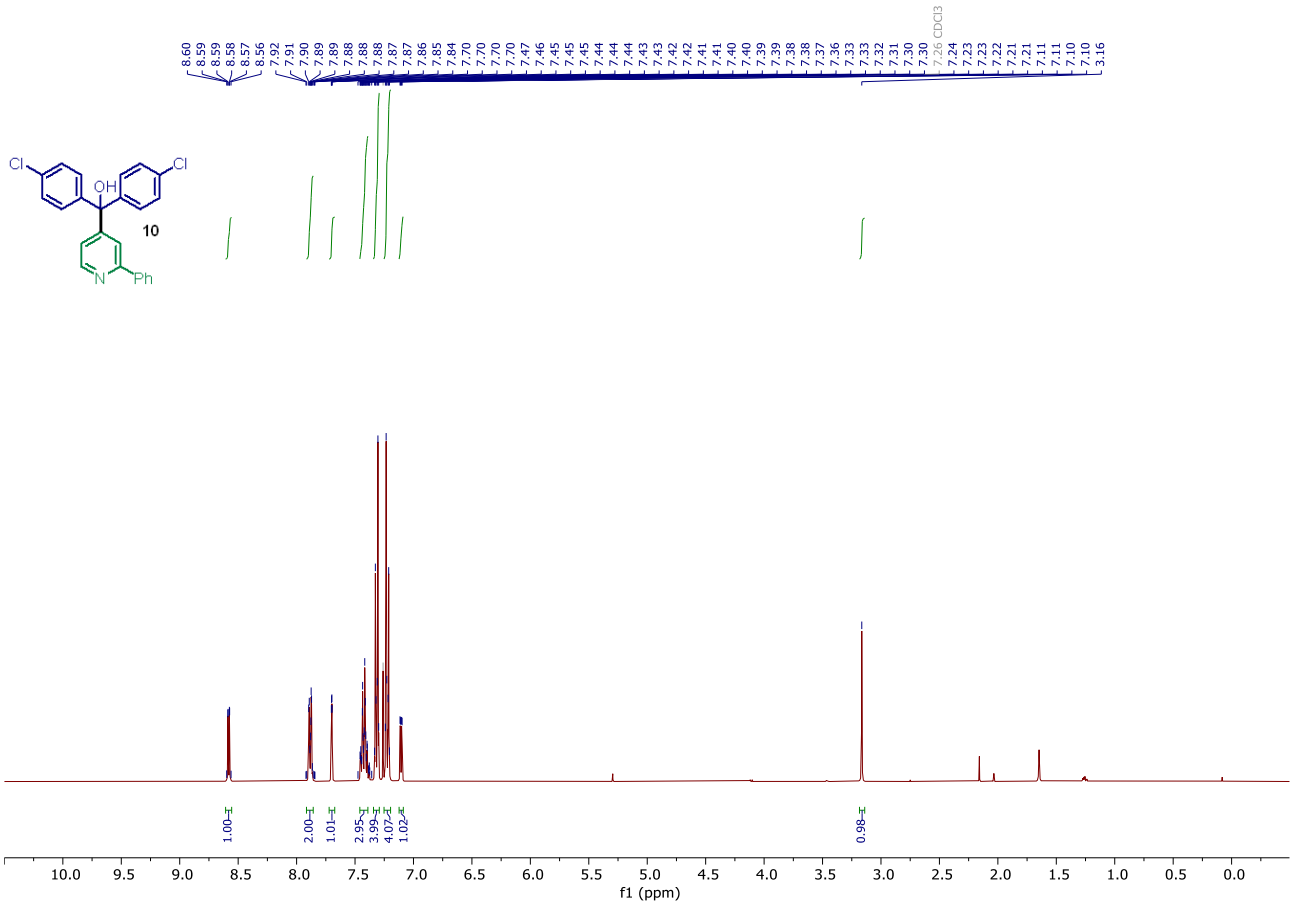
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


Cl
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Cl
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N
Ph
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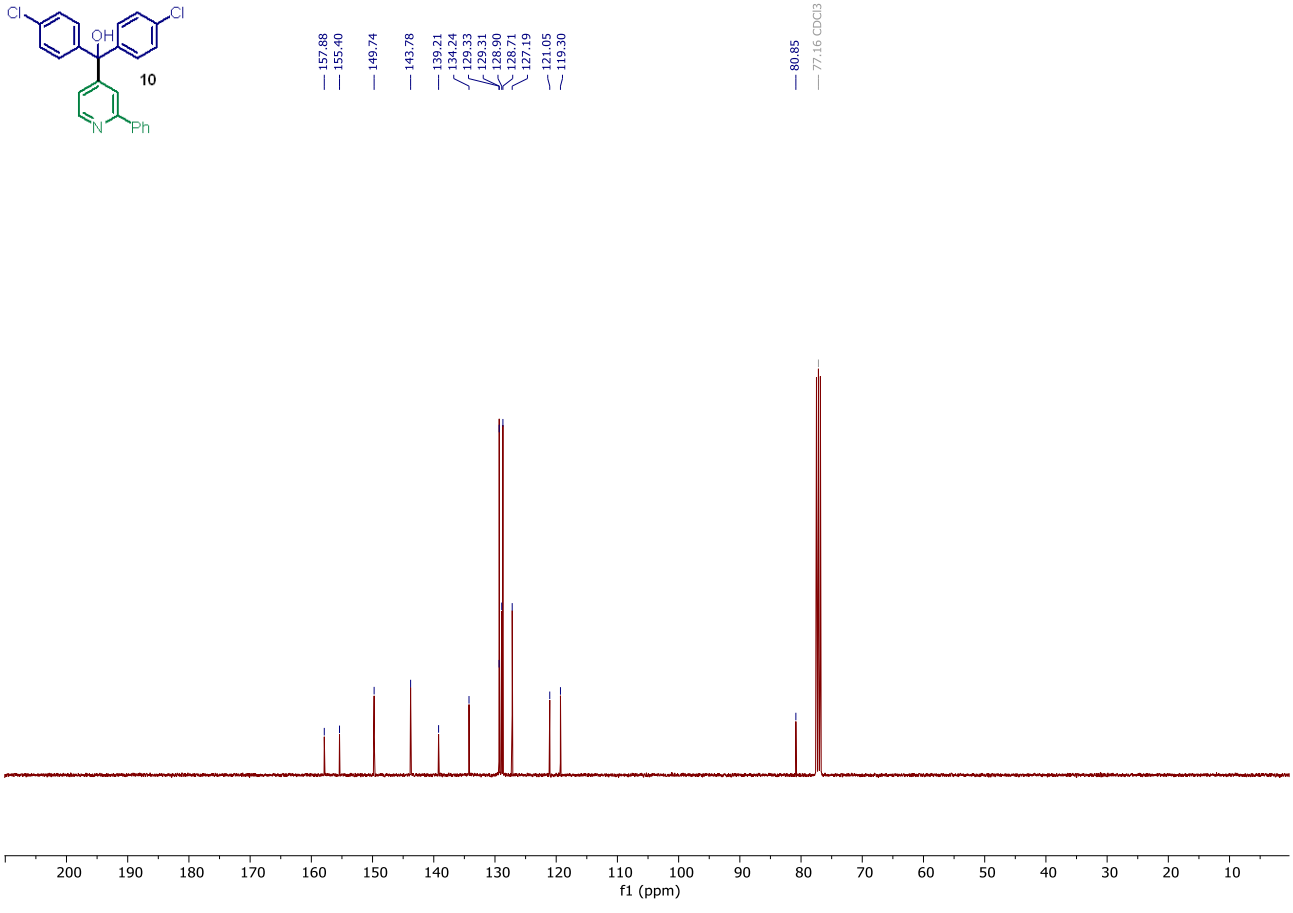
1.00 2.00 1.01 2.95 3.99 4.07 1.02 0.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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OH
Cl
10
N
Ph
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80.85 77.16 CDCl3
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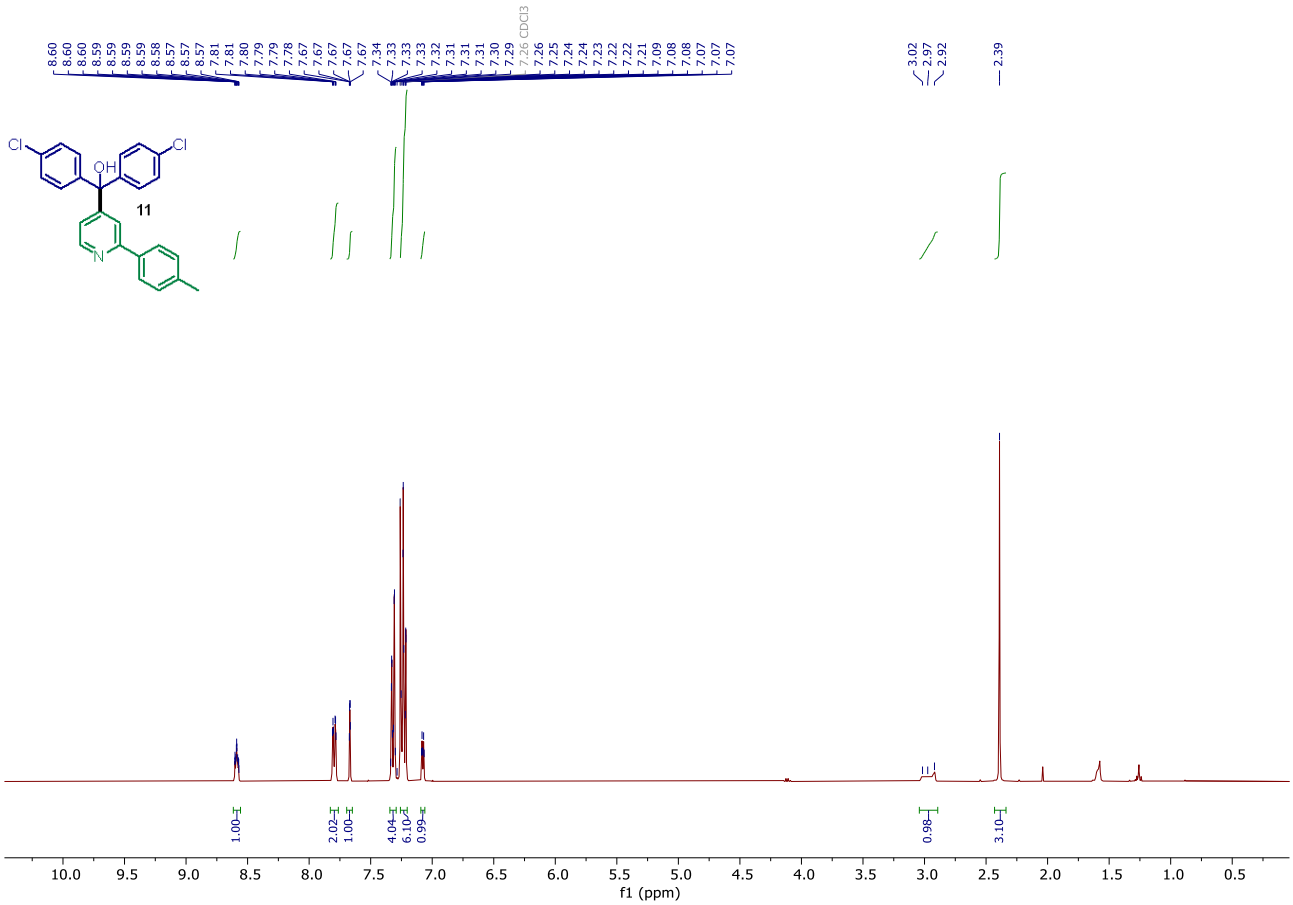
f1 (ppm)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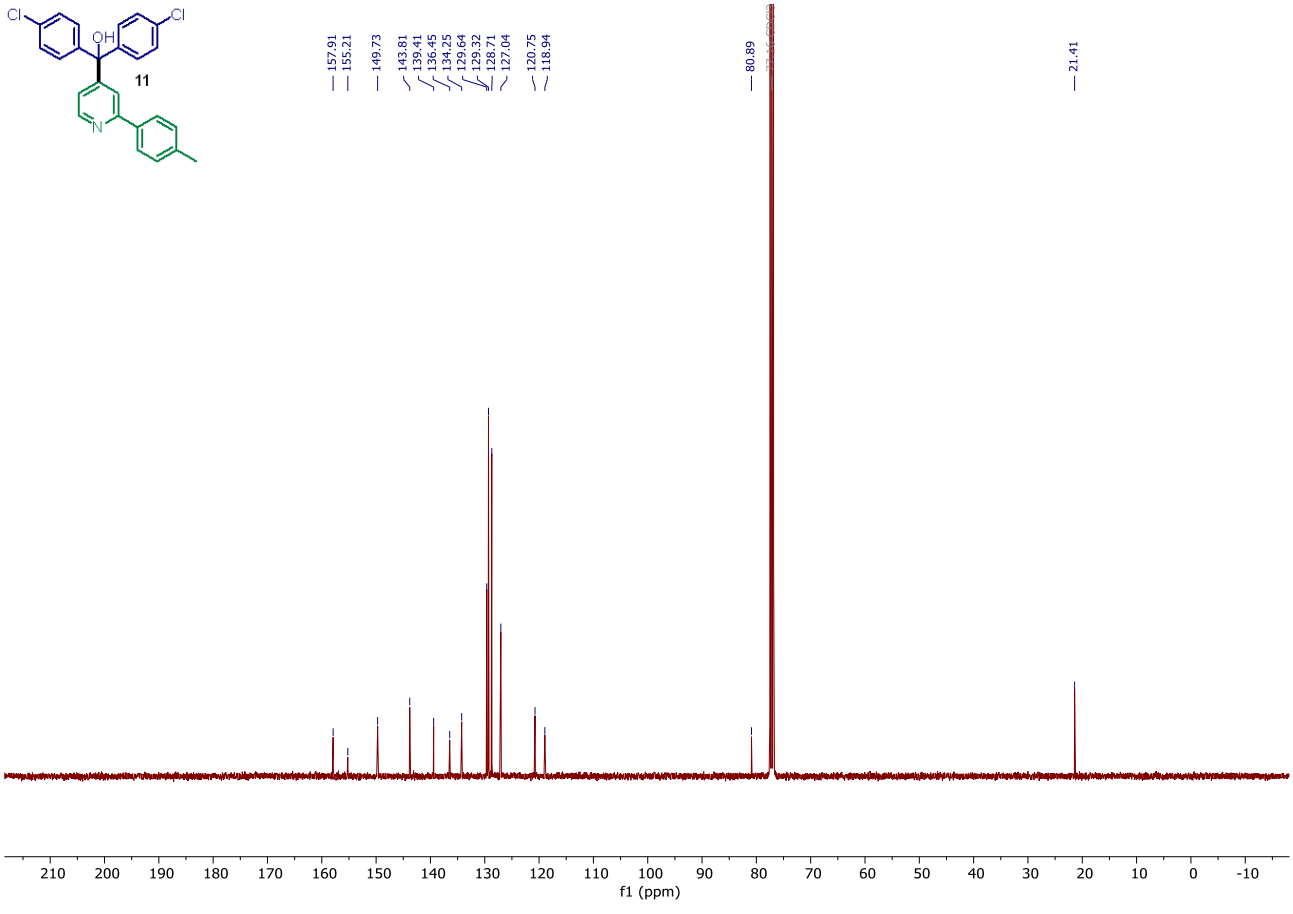
3.02 2.97 2.92
2.39
Cl
OH
Cl
11
N
1.00 2.02 1.00 4.04 6.10 0.99 0.98 3.10
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)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Cl
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N
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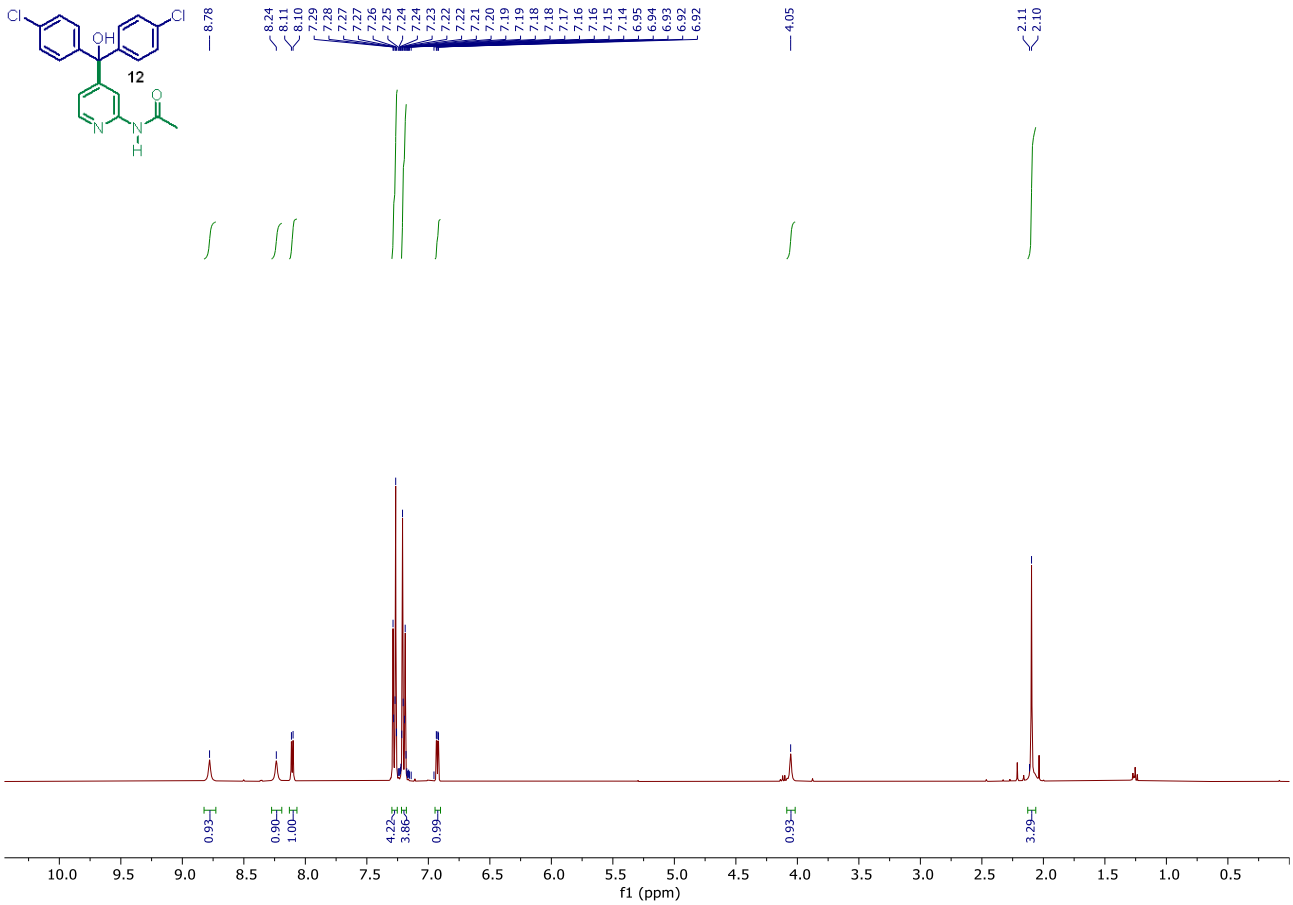
80.89
21.41
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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OH
Cl
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O
N
N
H
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7.29
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7.27
7.26
7.25
7.24
7.24
7.23
7.22
7.22
7.21
7.20
7.19
7.19
7.18
7.18
7.17
7.16
7.16
7.15
7.14
6.95
6.94
6.93
6.92
6.92
4.05
2.11
2.10
0.93
0.90
1.00
4.22
3.86
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0.93
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3.0
2.5
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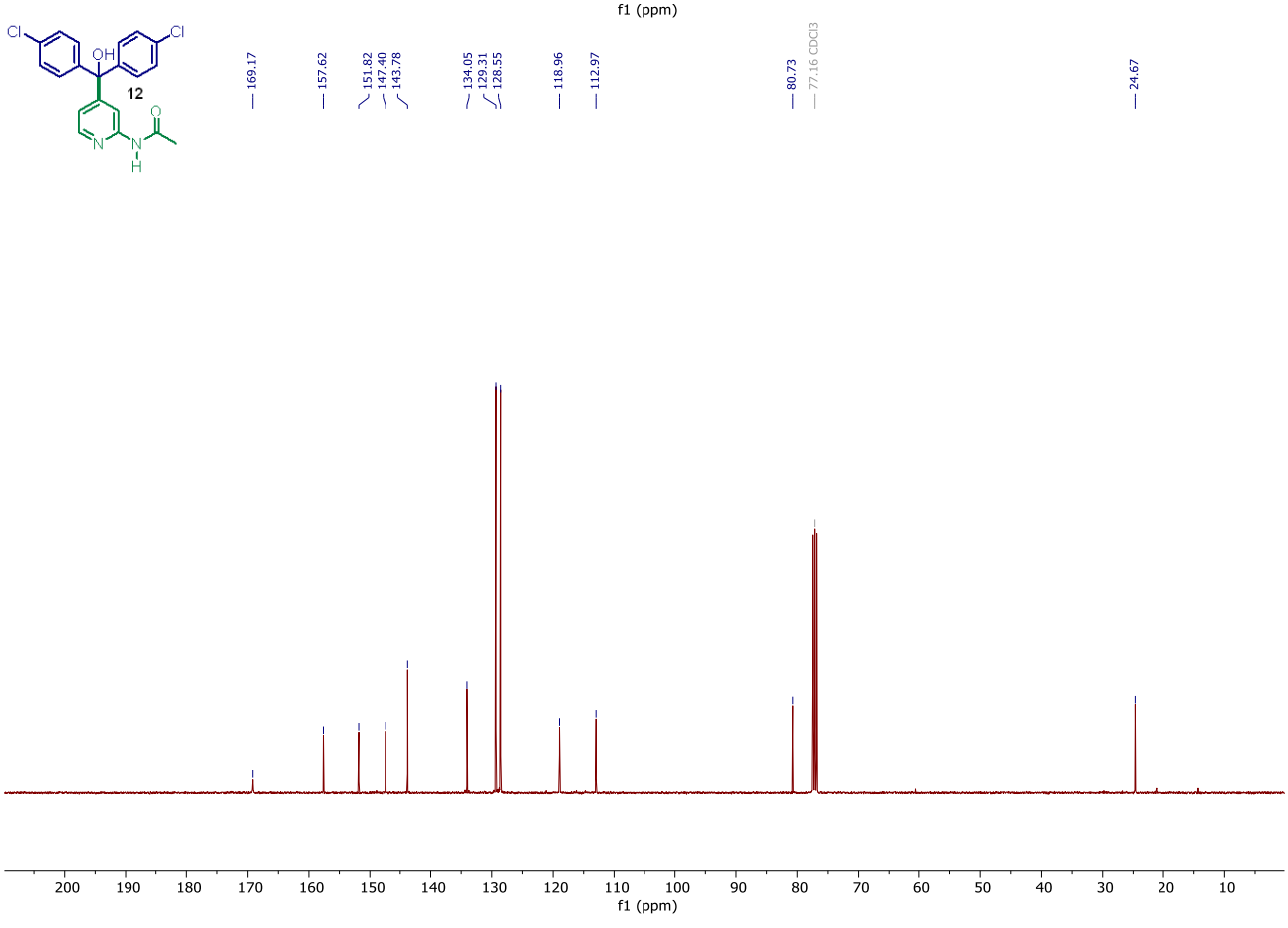
1.5
1.0
0.5
f1 (ppm)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N
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H
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143.78
134.05
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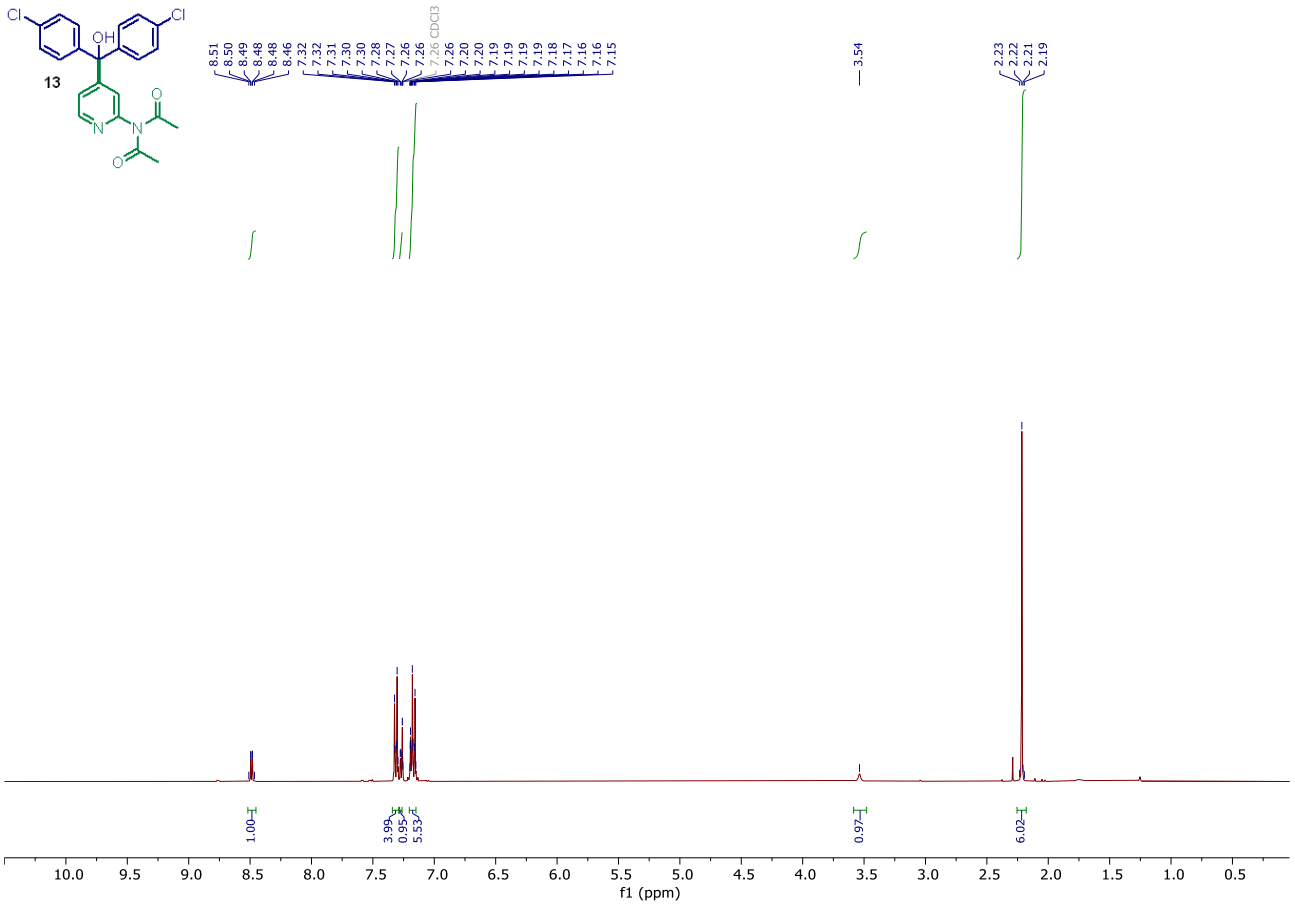
128.55
118.96
112.97
80.73
77.16 CDCl3
24.67
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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7.32
7.31
7.30
7.30
7.28
7.27
7.26
7.26
7.26 CDCl3
7.26
7.20
7.20
7.19
7.19
7.19
7.19
7.18
7.17
7.16
7.16
7.15
3.54
2.23
2.22
2.21
2.19
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3.99
0.95
5.53
0.97
6.02
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3.0
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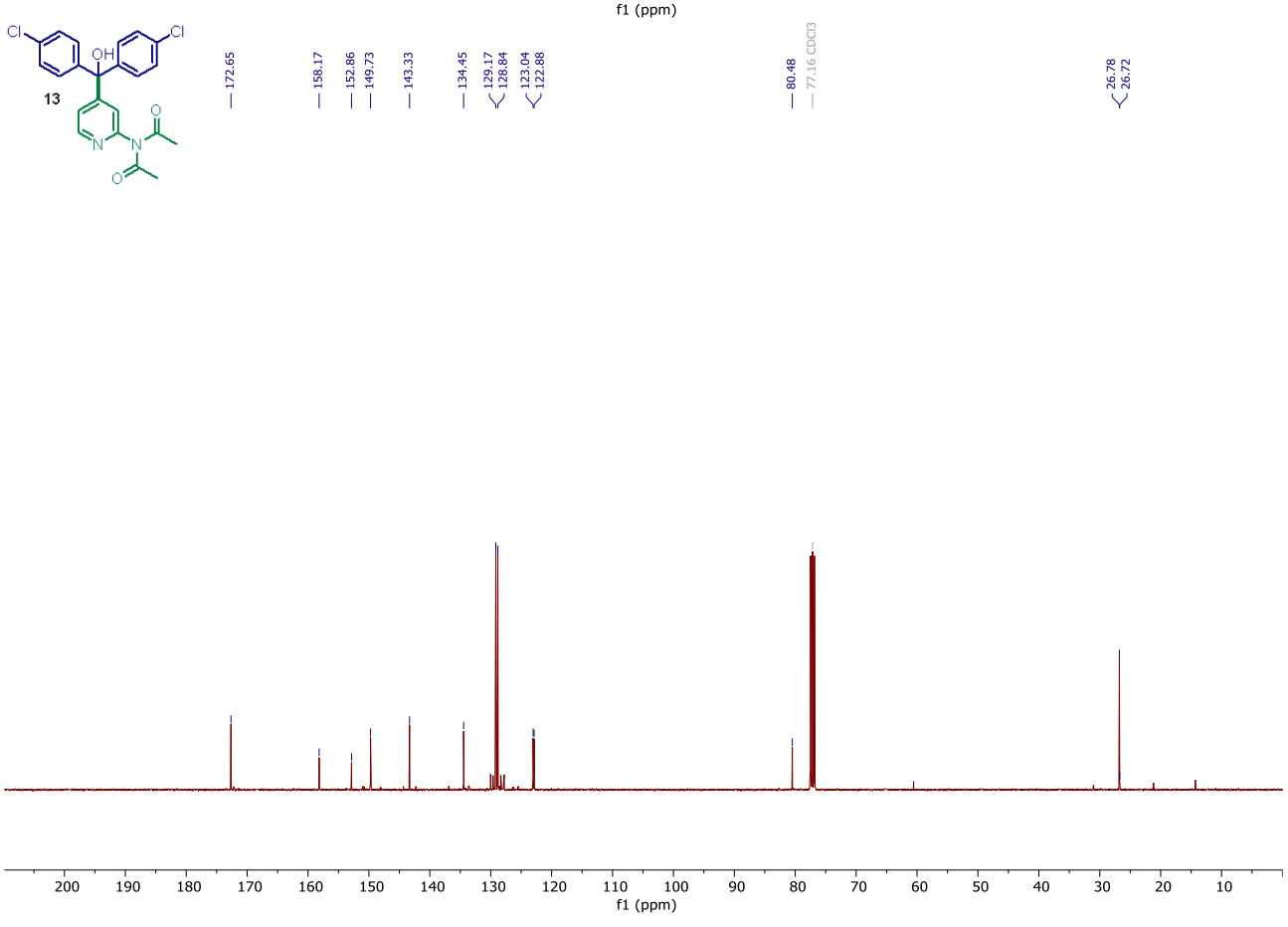
f1 (ppm)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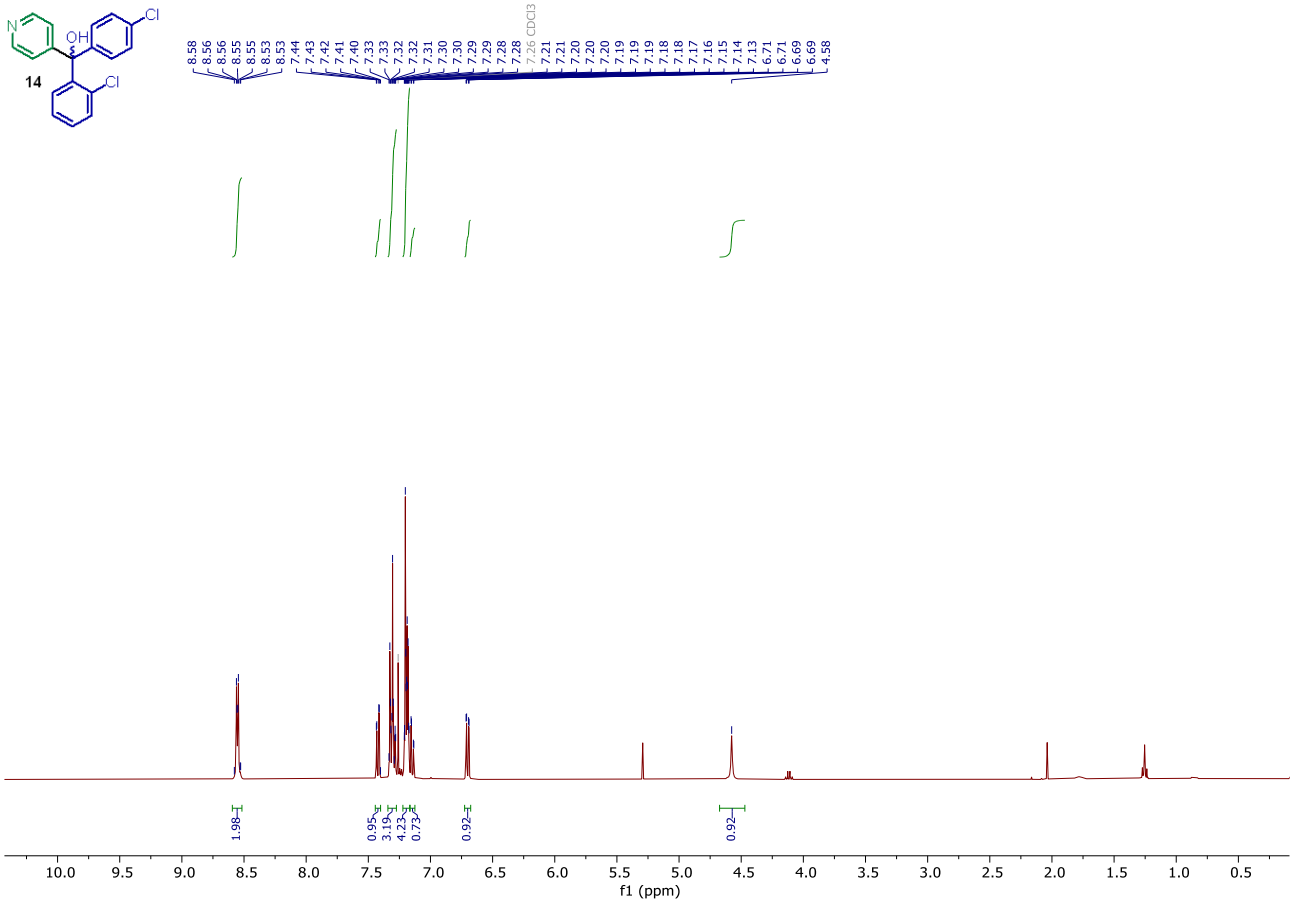
128.84
123.04
122.88
80.48
77.16 CDCl3
26.78
26.72
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


14
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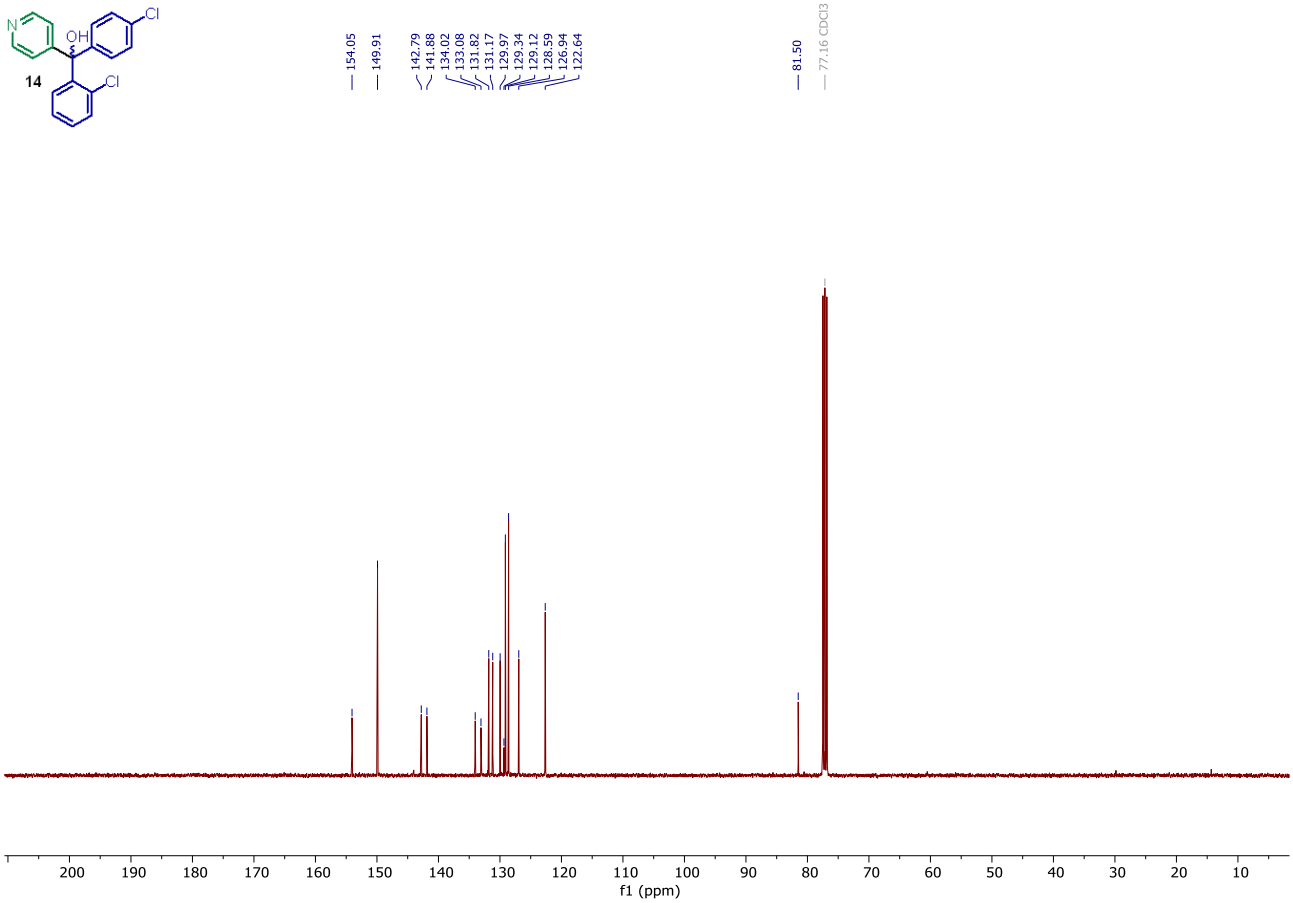
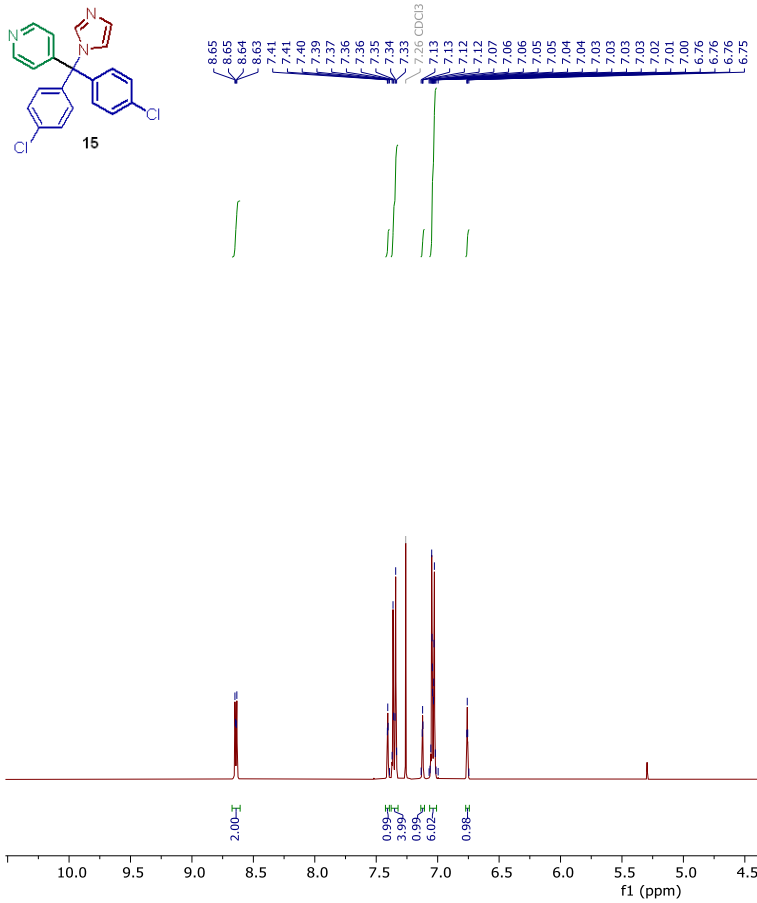
f1 (ppm)


14
154.05 149.91 142.79 141.88 134.02 133.08 131.82 131.17 129.97 129.34 129.12 128.59 126.94 122.64 81.50 77.16 CDCl3
f1 (ppm)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8.65
8.64
8.63
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7.36
7.36
7.35
7.34
7.33
7.26 CDCl3
7.13
7.12
7.12
7.07
7.06
7.06
7.05
7.05
7.04
7.04
7.03
7.03
7.03
7.03
7.02
7.01
7.00
6.76
6.76
6.76
6.75
2.00
0.99
3.99
0.95
6.02
0.98
10.0
9.5
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8.5
8.0
7.5
7.0
6.5
6.0
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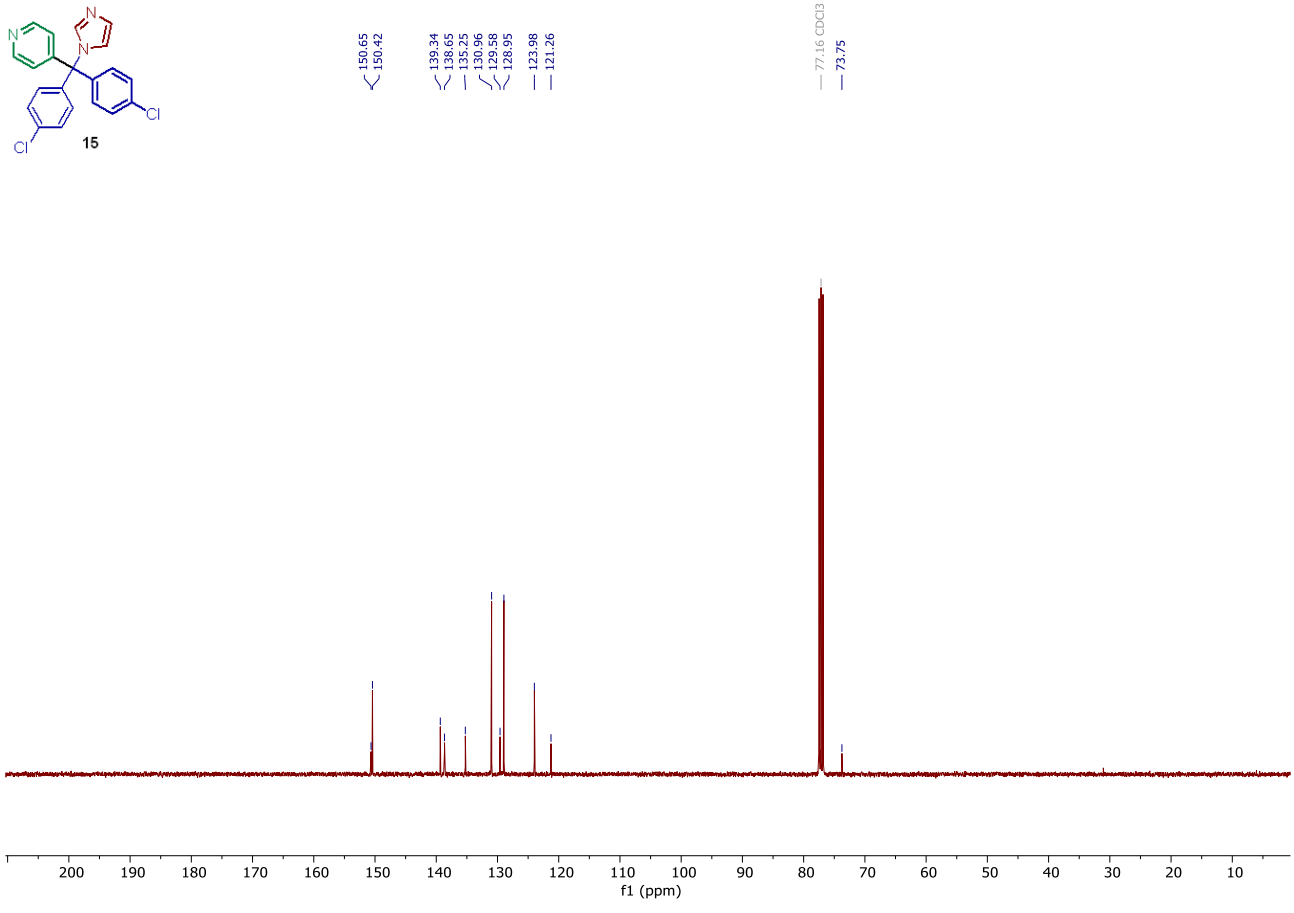
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


15
150.65
150.42
139.34
138.65
135.25
130.96
129.58
128.95
123.98
121.26
77.16 CDCl3
73.75
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

13. References

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