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Deoxyfluorination using CuF₂

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ABSTRACT: Deoxyfluorination is a primary method for the formation of C–F bonds. Bespoke reagents are commonly used due to issues associated with the low reactivity of metal fluorides. Here, we report the development of a simple strategy for deoxyfluorination using first-row transition metal fluorides that overcomes these limitations. Using CuF₂ as an exemplar, activation of an *O*-alkylisourea adduct formed *in situ* allows effective nucleophilic fluoride transfer to a range of primary and secondary alcohols. Spectroscopic investigations have been used to probe the origin of the enhanced reactivity of CuF₂. The utility of the process towards enabling ¹⁸F-radiolabeling is also presented.

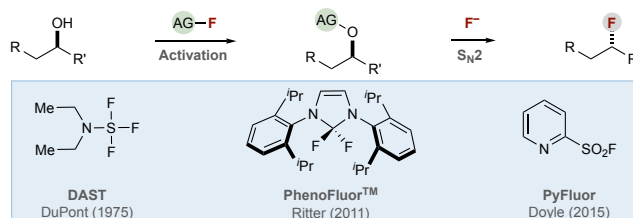
The installation of C–F bonds is a fundamental approach towards the modulation of molecular properties within agrochemicals, pharmaceuticals, and materials.¹ Electronic effects imparted by fluorine have become integral within pharmaceutical and agrochemical development, *e.g.*, enhancing metabolic stability or for radiolabeling applications. In addition, the well-known non-covalent interactions introduced by C–F bonds (*e.g.*, the *gauche* effect),² provides conformational control in a variety of cyclic and acyclic systems and, in turn, exploration of molecular space through the variation in topology that this affords. Accordingly, methods for C–F bond formation are highly valuable and continue to be advanced.

Deoxyfluorination is one of the most widely used methods for conversion of alcohols to the corresponding fluorides, achieved by nucleophilic displacement of the activated alcohol by F[−] (Scheme 1a).³ This suggests that cheap, readily available metal fluorides (MF_n) would be the ideal reagent for deoxyfluorination. However, the intrinsic properties of MF_n have meant that their direct use in these processes is underdeveloped. These species are generally highly solvated, polymeric, hygroscopic, basic, have high lattice energies, and are often poorly soluble in organic solvents.^{1d,3b,4} To circumvent these issues, a number of bespoke reagents have been developed for deoxyfluorination,^{3,5} including diethylaminosulfur trifluoride (DAST),^{5c} PhenoFluorTM,^{5k} and PyFluor,^{5l} amongst others (Scheme 1a). These reagents offer the combined advantages of *in situ* activation of the alcohol with an activating group (AG), while simultaneously addressing the solubility and reactivity problems of fluoride by allowing use of more compatible (organic) media.

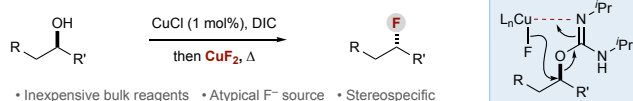
Overcoming the problems with the use of MF_n salts remains a major challenge in this field. There are limited examples of the use of alkali metal fluorides (KF and CsF) for deoxyfluorination.⁶ Recent seminal studies by Gouverneur demonstrated that KF and CsF can also be used for nucleophilic additions,^{7a} including asymmetric ring opening of thionium and aziridinium ions.^{7b,7c} Here, the poor reactivity of F[−] is overcome by the use of a chiral H-bonding phase transfer catalyst that facilitates F[−] transfer. However, the general challenges of MF_n use in deoxyfluorination remain and, despite

recent advances with alkali metal fluorides, readily available transition metal fluorides remain overlooked.⁸ Here we show the development of a simple method for deoxyfluorination with typically unreactive transition metal (TM) fluorides, using CuF₂ as an example (Scheme 1b).

(a) Previous work: Examples of deoxyfluorination reagents



(b) This work: Deoxyfluorination via *O*-alkylisoureas using CuF₂



• Inexpensive bulk reagents • Atypical F[−] source • Stereospecific

Scheme 1. (a) Deoxyfluorination using bespoke reagents. (b) This work. Deoxyfluorination using CuF₂. AG, activating group; DIC, *N,N'*-diisopropylcarbodiimide.

Our approach was based on the proposal that a group used for activation of an alcohol, typical of deoxyfluorination,^{3,5} could be used as a coordinating group for MF_n. Variation of the activating group would provide a Lewis basic site that could, in principle, be tuned for coordination to a specific metal. This approach may assist in overcoming solubility and hydration issues by providing a vector for chelate-directed F[−] transfer, potentially offsetting the issues with F[−] reactivity when used in an intermolecular process.

An initial screen of TM fluorides and alcohol activating groups revealed CuF₂ and DIC-derived *O*-alkylisourea as a promising system for the deoxyfluorination of benchmark substrate **1a** (Table 1; see SI for full details). Optimization delivered a system where Cu(I)-catalyzed formation of *O*-alkylisourea⁹ followed by deoxyfluorination using CuF₂ at 100 °C gave **2a** in 78% isolated yield and with clean S_N2 (entry 1).^{10–12}

Several optimization points are worth noting (for full optimization, see Supporting Information): (1) The reaction required formation of the *O*-alkylisourea prior to addition of CuF₂. Significantly reduced efficiency was observed in experiments where all reagents were combined from the outset (entry 2). (2) The addition of H₂O to anhydrous CuF₂ was essential. Removal of H₂O or use of the known (commercial) dihydrate was less effective (entries 4 and 5; *vide infra*). (3) Alternative activating groups were less effective – acetate, tosylate, methyl xanthate, trichloroacetimidate were largely ineffective (entries 6–10). (4) The urea byproduct was found to inhibit the reaction, suggesting an absence of advantageous

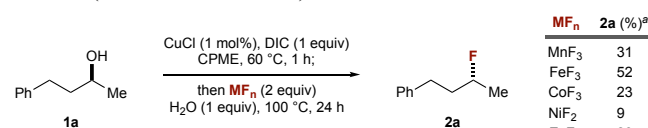
urea•F⁻ H-bonding (entry 10).⁷ The inhibitory effect may be related to interference with substrate-Cu(II) ligation by formation of Cu(II)•urea complexes;¹³ (5) It was possible to use an exogenous fluoride (KF) with stoichiometric Cu(OTf)₂ (entry 11), providing utility within Positron Emission Tomography (PET) radiolabeling (*vide infra*). This process does not operate in the absence of Cu(OTf)₂; however, attempts to render this process catalytic in Cu(OTf)₂ were unsuccessful, possibly due to Cu(II) inhibition as noted above.

Table 1. Reaction development.

	1a	2a
Entry	Deviation from 'optimized conditions'	Yield (%) ^a
1	None	78 ^b (94% <i>es</i>) ^c
2	All reagents present from start	21 (19) ^d
3	Second stage temperature = 80 °C	34
4	No water	22
5	CuF ₂ •2H ₂ O	27
6	Activating group = acetate	0
7	Activating group = tosylate	16
8	Activating group = methyl xanthate	0
9	Activating group = trichloroacetimidate	32
10	<i>N,N'</i> -diisopropylurea (1 equiv) additive	38
11	Cu(OTf) ₂ (1 equiv), KF (2 equiv), 18-crown-6 (2 equiv), 110 °C, 1 h	57

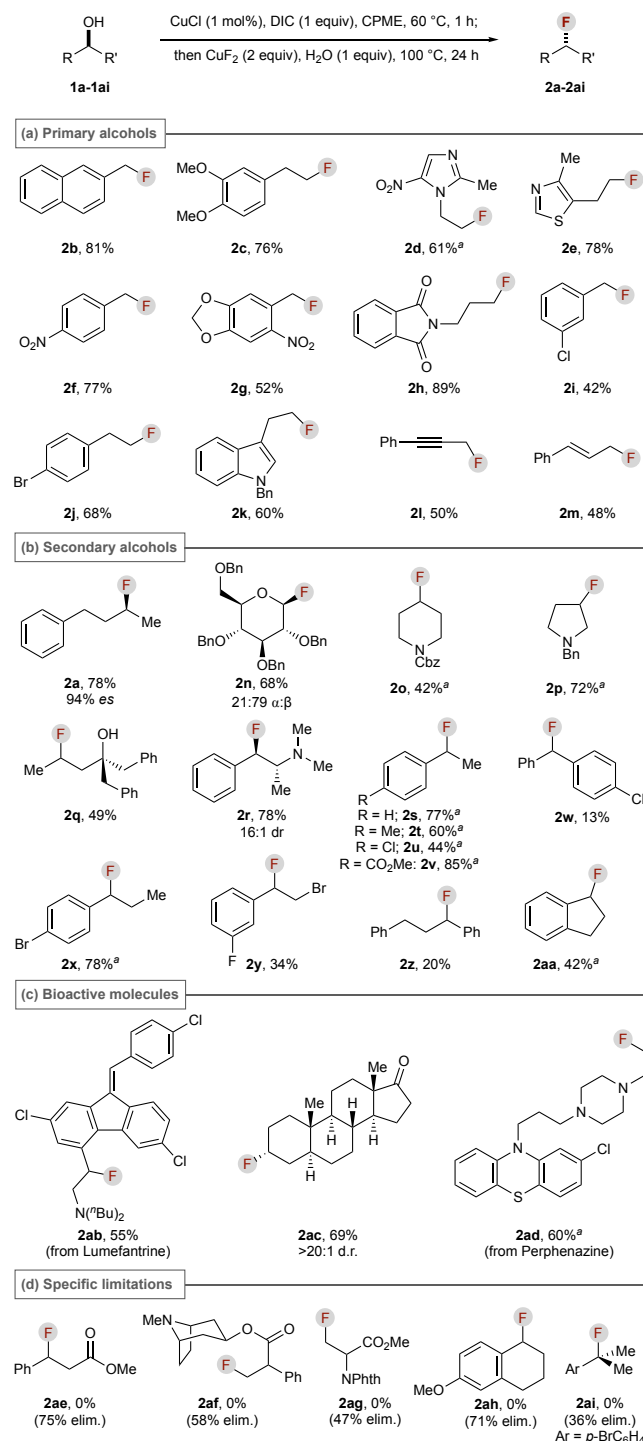
Reactions performed on 1 mmol scale. ^a Determined by ¹H NMR using an internal standard. ^b Isolated yield. ^c Determined by HPLC using a chiral stationary phase. ^d 100 °C from start. CPME, cyclopentyl methyl ether.

Finally, while CuF₂ was selected as an exemplar system, the same process allows deoxyfluorination to proceed using a range of other first row TM fluorides (*e.g.*, Scheme 2). These unoptimized results suggest the method is a viable general approach for developing deoxyfluorination protocols using these atypical fluoride sources (see SI for full details).



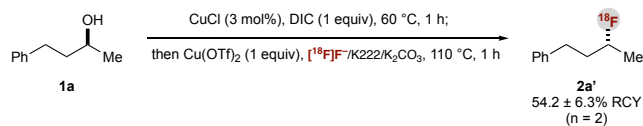
The generality of the optimized CuF₂ process was assessed by deoxyfluorination of a range of alcohol substrates (Scheme 3). Primary alcohols were broadly accommodated in good yield (Scheme 3a). A variety of common functional groups were tolerated in the presence including aryl halides, heterocycles, and amine protecting groups. The reaction was selective for S_N2 vs. potential S_N2' in systems where this is possible (**2l**, **2m**). Similarly, the reaction was broadly tolerant of functionalized secondary alcohols (Scheme 3b). In addition, the reaction demonstrated clean S_N2 with high stereospecificity observed across several substrate types, including simple alcohols (**2a**, 94% *es*) and aminoalcohols (**2r**, 16:1 *dr*), with good diastereoselection also displayed for exemplar sugar substrate **2n** (21:79 α:β). In addition, the reaction was selective for displacement of the *O*-alkylisourea vs. labile alkyl bromides (**2y**), consistent with the experimental design. Substrates more inclined to S_N1 pathways delivered product but in low yield (**2w**). Specific substrates were noted to undergo efficient fluorination but were prone to elimination on silica, leading to diminished isolated yield (*e.g.*, **2z**, **2aa**). The process was assessed on more complex substrates including

marketed drugs, delivering the expected fluoride products in good yield (Scheme 3c). Finally, specific limitations (Scheme 3d) were observed with substrates liable to elimination (**2ae-2ai**).



Scheme 3. Example scope of the deoxyfluorination process. Isolated yields unless noted. ^a Determined by NMR using an internal standard.

As noted in Table 1 (entry 11), the deoxyfluorination can be achieved using Cu(OTf)₂ + KF. This enables application to PET radiolabeling by use of [¹⁸F]fluoride. With minimal optimization (increased CuCl catalyst loading), the [¹⁸F]-labelled benchmark product **2a'** was prepared in 54.2 ± 6.3% (n = 2) radiochemical yield (RCY; Scheme 4).



Scheme 4. Installation of ^{18}F .

Efforts to understand the operation of the process were difficult based on the heterogeneity of the system and the stoichiometry of Cu(II), precluding *in situ* monitoring or meaningful NMR investigations. However, engagement of the *O*-alkylisourea intermediate by Cu(II) was demonstrated by EPR (see SI for full details).

In terms of the engagement/activation of CuF_2 , we were intrigued by the results which showed a critical dependence on H_2O : addition of 1 equiv H_2O to anhydrous CuF_2 was essential, with both an anhydrous reaction and use of the dihydrate significantly less effective (Table 1: entry 1 vs. entries 4 and 5). Accordingly, we sought to interrogate the nature of any possible active copper species generated using a combination of EPR, solid-state NMR, and powder XRD. It was not possible to directly study anhydrous $\text{CuF}_2 + \text{H}_2\text{O}$ due to heterogeneity within the sample; however, “aged” anhydrous CuF_2 (stored on benchtop under air) offered similar performance to anhydrous $\text{CuF}_2 + 1$ equiv H_2O . We therefore used instead the aged sample for analysis. EPR proved uninformative as a result of the lack of resolution of the hyperfine coupling (See SI). Greater insight was obtained through solid-state NMR and powder XRD. The ^1H MAS NMR spectra of each of the three copper samples (Figure 1) displayed distinct differences between the anhydrous and dihydrate samples. For the anhydrous sample, a featureless and low intensity signal attributing to surface hydration was obtained. In contrast, the dihydrate shows an intense signal with an isotropic shift of 45 ppm and a large paramagnetic shift anisotropy ($\Omega = 302$ ppm, $\kappa = 0.0$) which can be attributed to the Cu-bound H_2O . The ^1H MAS NMR spectrum of the aged sample is essentially a superposition of the spectra of the two pure phases, suggesting either a unique phase somewhere between anhydrous and dihydrate or mixture of phases.

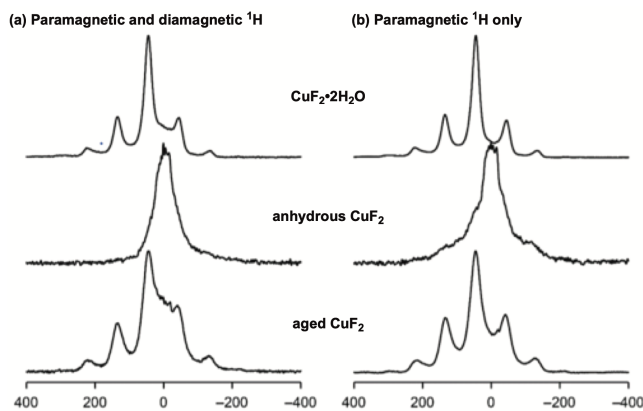


Figure 1. (a) ^1H (14.1 T, 55 kHz MAS) NMR spectra of the three samples with a T_1 relaxation filter chosen to show (a) paramagnetic and diamagnetic H and (b) paramagnetic H.

Powder XRD patterns of the aged sample with both the anhydrous and dihydrate sample displayed similarities but, importantly, there are regions of significant difference. Similar to observations from ^1H MAS NMR, this suggests the aged sample is either a single unique phase or a mixture of phases.

In this regard, it is known that heating $\text{CuF}_2 \cdot 2\text{H}_2\text{O}$ to the threshold temperature of 132°C will produce a $\text{Cu(OH)F} \cdot \text{CuF}_2$ species with the release of HF and H_2O (eqn 1).¹⁴

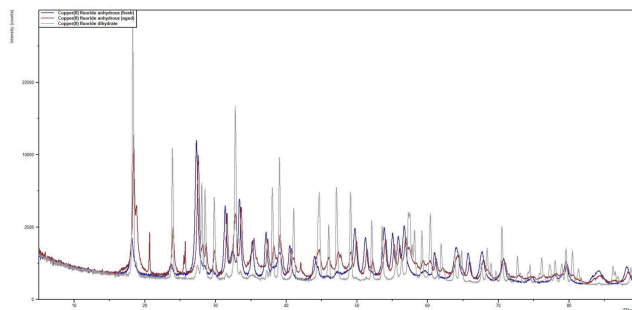
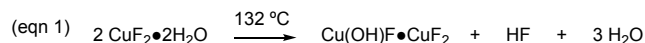


Figure 2. Powder XRD data showing overlay of anhydrous CuF_2 (a), laboratory “in air” aged CuF_2 (b), and $\text{CuF}_2 \cdot 2\text{H}_2\text{O}$ (c) samples.

It is therefore plausible that HF could be produced in small quantities in the present system, which posed the question as to whether the observed reactivity could perhaps be due to formation of HF *in situ*. A series of control reactions were therefore conducted to explore the possibility of CuF_2 acting as a masked HF source. Formation of the *O*-alkylisourea of 1a using DIC as standard (Table 1, entry 1) and treatment with $\text{Et}_3\text{N} \cdot 3\text{HF}$ at 100°C delivered the fluorinated product 2a in 47% conversion (see SI), which, while notably lower than our optimized conditions, could suggest some involvement of HF. However, 100°C is insufficient to induce the formation of HF from CuF_2 (eqn 1).¹⁴ In addition, no issues of acid-induced starting material or product decomposition were observed in the scope: for example, no hydration of olefins/alkynes (2l, 2m), no elimination issues with diols (2q), and no issues over benzyl deprotection (2n, 2p). Elimination issues were largely associated with substrates capable of E_1 or E_1cB , consistent with the presence of reactive F^- , as exemplified in Scheme 3d. It should be noted that NBoc amines did undergo deprotection, although this was also observed under thermal conditions in the absence of CuF_2 in control experiments (see SI). Practical observations for lack of HF generation was also obtained by a notable absence of etched glassware.¹⁵ Attempts to use scavengers to establish HF involvement were inconclusive: addition of organic bases did not impair the reaction (neither did amine substrates 1d, 1e, 1p, 1ab, 1ad, Scheme 3); silylated molecules were deprotected, but this cannot be separated from standard F^- reactivity; and, powdered glass did diminish efficiency but this could not be separated from poor reactivity as a result of exacerbating heterogeneity.¹⁵ Ultimately, while the generation of HF cannot be ruled out conclusively, the totality of the current data suggests that, if present, this contribution appears to be minimal.

In summary, a simple method for deoxyfluorination using first-row transition metal fluorides has been developed and exemplified using CuF_2 . The process is based on a proposed chelate-driven fluoride transfer that effectively overcomes the reactivity issues associated with these fluoride sources. Control experiments and spectroscopic data suggest Cu(II) activation of an *O*-alkylisourea with fluoride transfer from a hydrated Cu(II)F species. The process can also be leveraged to allow ^{18}F installation.

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Deoxyfluorination using CuF₂

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1. General

All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise stated. Purification was carried out according to standard laboratory methods.

1.1. Batch to batch variability of CuF₂

Throughout the duration of this project, batch to batch variability has been observed between CuF₂ samples acquired from different suppliers, and even between different lot numbers from the same supplier. This has resulted in variable conversions being obtained.

1.2. Purification of solvents

All solvents used for dry reactions (THF and Et₂O) were obtained from a PureSolv SPS-400-5 solvent purification system. Anhydrous CPME and 1,4-dioxane were obtained by distillation over CaH₂ or LiAlH₄, respectively, and stored over activated 4 Å molecular sieves under N₂. Et₂O, MeOH, CH₂Cl₂, and petroleum ether 40–60 °C for purification purposes were used as obtained from suppliers without further purification.

1.3. Experimental details

Reactions were carried out using conventional glassware (preparation of starting materials) or in 5 mL capped microwave vials (optimization reactions and substrates). The glassware was oven-dried (150 °C) and cooled under vacuum before use. Room temperature was generally 20 °C. Reactions at elevated temperatures were carried out using a temperature-regulated hotplate/stirrer and a sand bath. Temperature quoted is a measurement of the sand bath heating block. Reactions at 0 °C were carried out using an ice bath. Reactions at –78 °C were carried out using an acetone/dry ice bath.

1.4. Purification of products

Thin layer chromatography (TLC) was carried out using Merck silica plates coated with fluorescent indicator UV254. These were analyzed under 254 nm UV light or developed using potassium permanganate. Column chromatography was carried out using ZEOprep 60 HYD 40-63 µm silica gel.

1.5. Analysis of products

¹⁹F NMR spectra were obtained on either a Bruker AV 400 spectrometer at 376 MHz or Bruker AV 500 at 470 MHz. ¹H and ¹³C NMR spectra were obtained on either a Bruker AV 400 at 400 MHz and 125 MHz or Bruker AV 500 at 500 MHz and 126 MHz, respectively. Chemical shifts are reported in ppm and coupling constants are reported in Hz: CDCl₃ referenced at 7.26 (¹H) and 77.0 ppm (¹³C); NMR conversion for optimization reactions were obtained through addition of a known standard (0.25 M naphthalene standard solution) to the crude reaction

mixture. Solvent was removed under reduced pressure and conversion against the internal standard was determined by ^1H NMR. NMR conversion for products was obtained through the addition of a known standard (trifluorotoluene (41 μL , 0.33 mmol)), referenced at -63.0 ppm) and conversion against the internal standard was determined by ^{19}F NMR.

High performance liquid chromatography (HPLC) was performed on an Agilent 1200 series HPLC using a chiral stationary phase column (Daicel Co. CHIRALCEL OJ-Hor CHIRALCEL IA; eluent: n-hexane/i-PrOH). All solvents used were HPLC-grade solvents purchased from Fisher. The column employed and the respective solvent mixture are indicated for each experiment.

Analytical HPLC was performed with a Dionex Ultimate 3000 HPLC system equipped with a UV detector and a Flow Count radio-HPLC detection system combined with a PMT detector using a Synergi 4 μm Hydro-RP 80 Å column (150 \times 4.6 mm) with 10 mm guard cartridge, UV 254 nm and flow 1 mL/min. The mobile phase for the analysis of substrates was water/acetonitrile. Analysis of the reaction mixture (to assess radiofluoride incorporation) used a gradient profile of water and acetonitrile [30–95% MeCN (0–20 mins), 95% MeCN (20–25 mins), 95–30% MeCN (25–25.5 mins), 30% MeCN (25.5–30 mins)]. Co-elution with the UV signal from the ^{19}F -compound was used to confirm identity of the ^{18}F -product.

Analytical Radio-TLC method for determination of radiofluoride incorporation was performed by spotting a 2 μL reaction sample onto the origin of a TLC plate (Silica Gel, 60 RP-18 F254) and run over a development path of 8 cm using 5:95 (v/v) water:acetonitrile. The plate was left to air dry for 15 mins, then analysed using a MiniGita Dual radio-TLC scanner (Elysia Raytest).

1.6. Analysis of copper sources

EPR spectra of copper(II) fluoride samples were obtained using a Bruker EMX 10/12 spectrometer equipped with ELEXSYS Super High Sensitivity Probehead (Bruker ER4122SHQE) operating at 295 K using 9.824 GHz microwave frequency. Measurements were done using 1 mW microwave power, 0.3 mT modulation amplitude, 100 KHz modulation frequency, 600 mT field sweep centred at 350 mT with 2048 points resolution, a time constant and conversion time of 40.96 ms each. EPR spectra of copper(II) triflate solutions were obtained as above but using a Bruker EMX plus spectrometer operating. Room temperature measurements were done using 9.926 GHz microwave frequency, 1 mW microwave power, 0.3 mT modulation amplitude, 100 KHz modulation frequency, 160 mT field sweep centred at 321 mT with 1600 points resolution, a time constant of 40.96 ms and conversion time of 40.01 ms. Frozen copper(II) triflate solutions were measured using a Bruker ER 4141VT variable

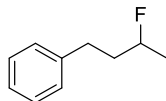
temperature system with liquid nitrogen coolant at 120 K using 9.495 GHz microwave frequency, 20 mW microwave power, 0.3 mT modulation amplitude, 100 KHz modulation frequency, 120 mT field sweep centred at 300 mT with 4000 points resolution, a time constant of 40.96 ms and conversion time of 12.03 ms.

Solid-state NMR spectra were recorded using a Bruker Avance III spectrometer equipped with a 14.1 T wide-bore superconducting magnet (^1H and Larmor frequency of 600.2 MHz). Samples were packed into 1.3 mm zirconia rotors and rotated at the magic angle at a rate of 55 kHz. The sample temperature was maintained at 300(1) K using a Bruker BCU II chiller and BVT/BVTB-3000 heater controller and booster. For ^1H , the spectra were recorded either with signal averaging for 16 transients with a recycle interval of 10 s or with signal averaging 128 transients with a recycle interval of 0.1 s. All spectra were recorded with a spin-echo pulse sequence with a rotor-synchronised echo delay of 18.2 μs . Chemical shifts are reported in ppm relative to $(\text{CH}_3)_4\text{Si}$ using L-aniline ($\delta(\text{NH}_3) = 8.5$ ppm) as a secondary solid reference. Powder patterns were collected at room temperature on a PANalytical Empyrean diffractometer in reflection mode (Bragg-Brentano focusing scheme) using Cu $\text{K}\alpha 1$ radiation. Powder patterns were collected at room temperature on a PANalytical Empyrean diffractometer in reflection mode (Bragg-Brentano focusing scheme) using Cu $\text{K}\alpha 1$ radiation.

2. General experimental procedures

General Procedure A: Deoxyfluorination using first-row metal fluorides: optimization protocol

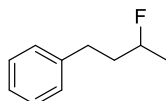
For example, synthesis of compound **2a**



To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), and CPME (2 mL, 0.5 M). The vial was capped and the reaction was heated at 60 °C for 1 h. Once cooled to r.t., the vial was de-capped and then CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.) and H₂O (18.0 µL, 1.0 mmol, 1.0 equiv.) were added. The vial was capped and then the reaction was heated at 100 °C for 24 h. The reaction mixture was cooled to r.t. and naphthalene (1 mL of 0.25 M standard solution) was added. The reaction mixture was then diluted with DCM, filtered through celite, and then concentrated under vacuum. Conversion to the desired product was measured by NMR against a known internal standard (naphthalene for ¹H NMR, trifluorotoluene for ¹⁹F NMR).

General Procedure B: Deoxyfluorination using CuF₂

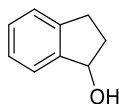
For example, synthesis of compound **2a**



To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), and CPME (2 mL, 0.5 M). The vial was capped and the reaction was heated at 60 °C for 1 h. Once cooled to r.t., the vial was de-capped and then CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.) and H₂O (18.0 µL, 1.0 mmol, 1.0 equiv.) were added. The vial was capped and then the reaction was heated at 100 °C for 24 h. The reaction mixture was cooled to r.t. and diluted with Et₂O before being filtered through celite and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-10% Et₂O in petroleum ether 40-60 °C) to afford the product as a colourless oil (119 mg, 78%).

General Procedure C: Reduction of ketone to alcohol

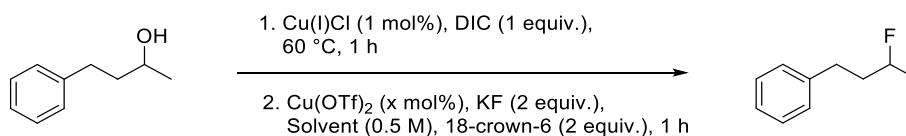
For example, synthesis of compound **S14**



To a round-bottom flask was added 1-indanone (2.0 g, 15.0 mmol, 1.0 equiv.), and MeOH (30.0 mL, 0.5 M). The reaction was cooled to 0 °C and NaBH₄ (870 mg, 23.0 mmol, 1.5 equiv.) was added portion wise before warming to r.t. to stir for 16 h. The reaction mixture was then quenched using NH₄Cl (20.0 mL), and then extracted with Et₂O (2 × 10.0 mL), the combined organic phases were washed with brine (2 × 10.0 mL), dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-50% Et₂O in petroleum ether 40-60 °C) to give the desired product as a white solid (1.6 g, 80%).

General Procedure D: Deoxyfluorination using microwave irradiation

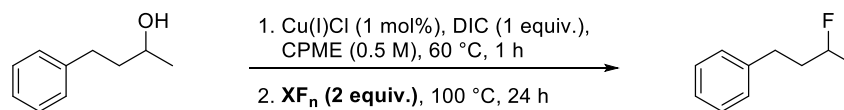
For example, synthesis of compound **2a'**



To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), and DIC (0.15 mL, 1.0 mmol, 1.0 equiv.). The vial was capped and the reaction was heated at 60 °C for 1 h. Once cooled to r.t., the vial was de-capped and then Cu(OTf)₂ (362 mg, 1.0 mmol, 1.0 equiv.), KF (116 mg, 2.0 mmol, 2.0 equiv.), 18-crown-6 (528 mg, 2.0 mmol, 2 equiv.), and MeCN (2 mL, 0.5 M) were added. The vial was capped and then the reaction was heated at 110 °C for 1 h under microwave irradiation. The reaction mixture was cooled and naphthalene (1 mL of 0.25 M standard solution) added. The vial was then de-capped, and the reaction mixture diluted with DCM, filtered through celite, and then concentrated under vacuum. Conversion to the desired product was measured by ¹H NMR against a known internal standard (naphthalene).

3. Reaction optimization data

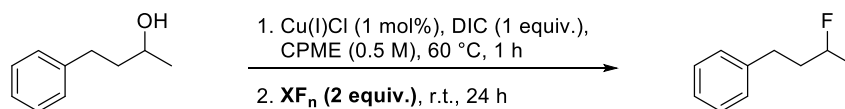
Metal fluoride study at 100 °C



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 0.1 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), and XFn (**xx mg, 2.0 mmol, 2.0 equiv.**). The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Metal Fluoride	Mass (mg)	Conversion (%)
1	CaF ₂	156	0
2	CsF	304	0
3	CuF ₂	203	22
4	CoF ₂	194	0
5	CoF ₃	232	16
6	FeF ₂	188	0
7	FeF ₃	227	0
8	KF	116	0
9	LiF	52	0
10	MgF	125	0
11	MnF ₂	186	0
12	MnF ₃	224	51
13	NiF ₂	193	11
14	ZnF ₂	207	0

Metal fluoride study at room temperature

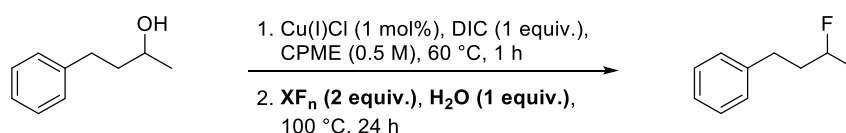


Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 0.15 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), and XFn (**xx mg, 2.0 mmol, 2.0 equiv.**). The reaction was stirred at r.t. for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Metal Fluoride	Mass (mg)	Conversion (%)
1	CaF ₂	156	0

2	CsF	304	0
3	CuF ₂	203	0
4	CoF ₂	194	0
5	CoF ₃	232	0
6	FeF ₂	188	0
7	FeF ₃	227	0
8	KF	116	0
9	LiF	52	0
10	MgF	125	0
11	MnF ₂	186	0
12	MnF ₃	224	0
13	NiF ₂	193	0
14	ZnF ₂	207	0

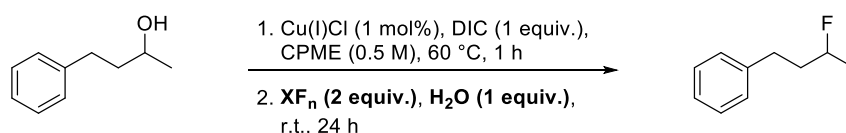
Metal fluoride plus water study at 100 °C



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 0.1 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), XF_n (xx mg, 2.0 mmol, 2.0 equiv.), and H₂O (18.0 μL, 1.0 mmol, 1.0 equiv.). The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Metal Fluoride	Mass (mg)	Conversion (%)
1	CaF ₂	156	0
2	CsF	304	0
3	CuF ₂	203	78
4	CoF ₂	194	0
5	CoF ₃	232	23
6	FeF ₂	188	7
7	FeF ₃	227	52
8	KF	116	0
9	LiF	52	0
10	MgF	125	0
11	MnF ₂	186	0
12	MnF ₃	224	31
13	NiF ₂	193	9
14	ZnF ₂	207	28

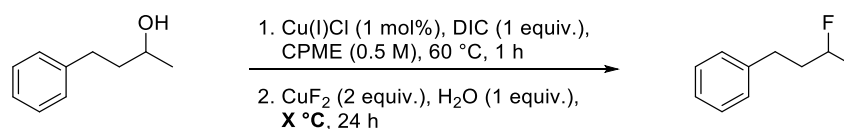
Metal fluoride plus water study at room temperature



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 0.1 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), XF_n (xx mg, 2.0 mmol, 2.0 equiv.), and H_2O (18.0 μL , 1.0 mmol, 1.0 equiv.). The reaction was stirred at r.t. for 24 h, before analysis by ^1H NMR against a known internal standard (naphthalene).

Entry	Fluoride Source	Mass (mg)	Conversion (%)
1	CaF_2	156	0
2	CsF	304	0
3	CuF_2	203	0
4	CoF_2	194	0
5	CoF_3	232	0
6	FeF_2	188	0
7	FeF_3	227	0
8	KF	116	0
9	LiF	52	0
10	MgF	125	0
11	MnF_2	186	0
12	MnF_3	224	0
13	NiF_2	193	0
14	ZnF_2	207	0

Temperature study

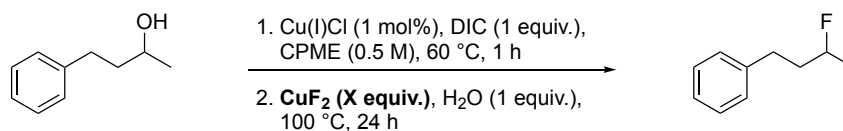


Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18.0 μL , 1.0 mmol, 1.0 equiv.). The reaction was stirred at $X^\circ\text{C}$ for 24 h, before analysis by ^1H NMR against a known internal standard (naphthalene).

Entry	Temperature ($^\circ\text{C}$)	Conversion (%)
1	60	8
2	70	9

3	80	34
4	90	59
5	100	78

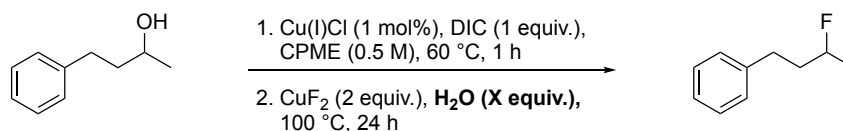
Copper Fluoride Equivalents study



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), **CuF₂ (xx mg, xx mmol, xx equiv.)**, and H₂O (18.0 μ L, 1.0 mmol, 1.0 equiv.). The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	CuF ₂ Equivalents	Mass (mg)	Conversion (%)
1	0.5	51	50
2	1	102	78
3	2	203	65
4	3	305	35

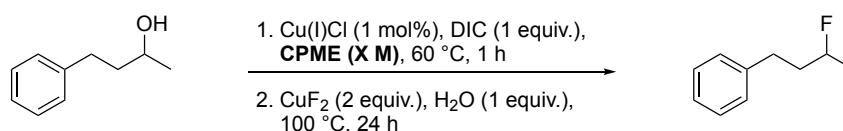
Water Equivalents study



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and **H₂O (xx μ L, xx mmol, 1.0 equiv.)**. The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	H ₂ O Equiv.	Volume (μ L)	Conversion (%)
1	0.5	9	65
2	1	18	78
3	2	36	76
4	3	54	50
5	4	72	33
6	5	90	48

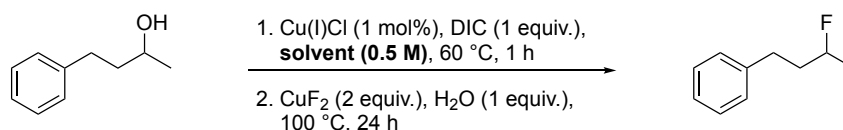
Concentration study



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), **CPME (xx mL, xx M)**, CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18.0 μ L, 1.0 mmol, 1.0 equiv.). The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Concentration (M)	Volume (mL)	Conversion (%)
1	0.1	10	21
2	0.25	4	46
3	0.5	2	78
4	1	1	71
5	2	0.5	68

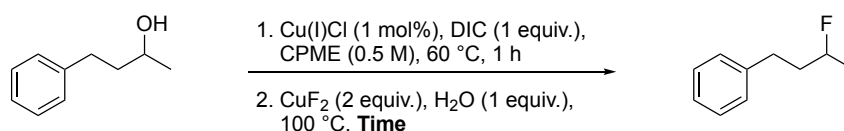
Solvent study



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), **solvent (2 mL, 0.5 M)**, CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18.0 μ L, 1.0 mmol, 1.0 equiv.). The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Solvent	Conversion (%)
1	CPME	78
2	DMSO	19
3	DMF	45
4	1,4-Dioxane	26
5	THF	42
6	CHCl ₃	53
7	Toluene	60
8	MeCN	25

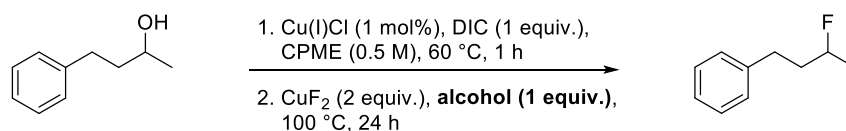
Time study



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18.0 μ L, 1.0 mmol, 1.0 equiv.). The reaction was stirred at 100 °C, for **xx h**, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Time (h)	Conversion (%)
1	1	17
2	2	30
3	3	47
4	5	52
5	8	49
6	16	60
7	24	78
8	48	74

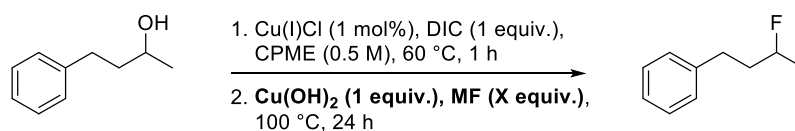
Addition of alcohols



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and **alcohol (xx μ L, 1.0 mmol, 1.0 equiv.)**. The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Alcohol	Volume (μ L)	Conversion (%)
1	Methanol	41	23
2	IPA	76	17

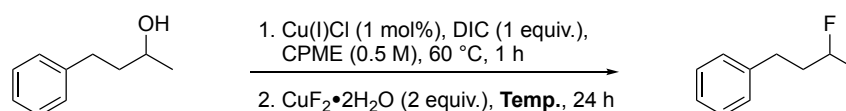
Use of metal fluoride with Cu(OH)₂



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), Cu(OH)₂ (97.6 mg, 1.0 mmol, 1 equiv.), and **MF_n** (**xx mg, 2.0 mmol, 2.0 equiv.**). The reaction was stirred at 100 °C, for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Metal Fluoride	Equiv.	Mass (mg)	Conversion (%)
1	KF	1	58	0
2	KF	2	116	0
3	CsF	1	152	0
4	CsF	2	304	0

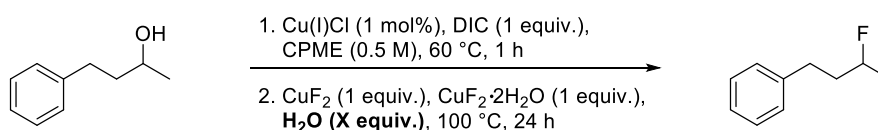
Use of the commercial CuF₂ dihydrate



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), and CuF₂·2H₂O (275 mg, 2.0 mmol, 2.0 equiv.). The reaction was stirred at **XX °C** for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Temperature (°C)	Conversion (%)
1	100	27
2	135	57

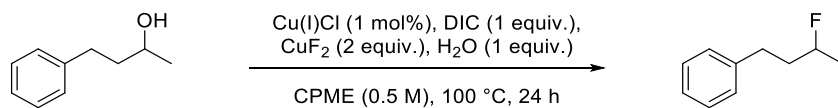
Use of a 1:1 mixture of CuF₂ and CuF₂ dihydrate



Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (102 mg, 1.0 mmol, 1.0 equiv.), CuF₂·2H₂O (138 mg, 1.0 mmol, 1.0 equiv.), and **H₂O (xx μL, xx mmol, xx equiv.)**. The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

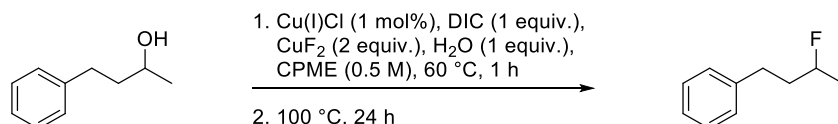
Entry	H ₂ O Equiv	Mass (μL)	Conversion (%)
1	0	0	39
2	1	18	68

One-pot attempt: All reagents present at the beginning of the reaction for 24 h at 100 °C



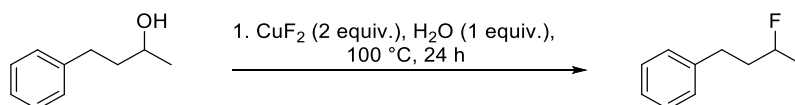
To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.) and H₂O (18.0 µL, 1.0 mmol, 1.0 equiv.). The vial was then capped and the reaction was heated at 100 °C for 24 h before analysis by ¹H NMR against a known standard (naphthalene). Conversion to product determined as 19%.

One-pot attempt: All reagents present at the beginning of the reaction with heating at 60 °C for 1 h, then 100 °C for 24 h



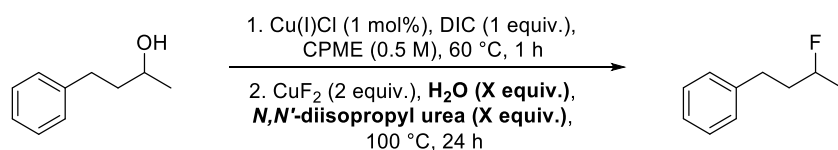
To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.) and H₂O (18.0 µL, 1.0 mmol, 1.0 equiv.). The vial was then capped and the reaction was heated at 60 °C for 1 h, followed by heating at 100 °C for 24 h before analysis by ¹H NMR against a known standard (naphthalene). Conversion to product determined as 21%.

No adduct formation



To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.) and H₂O (18.0 µL, 1.0 mmol, 1.0 equiv.). The vial was then capped and the reaction was heated at 100 °C for 24 h before analysis by ¹H NMR against a known standard (naphthalene). Conversion to product determined as 0%.

Urea addition

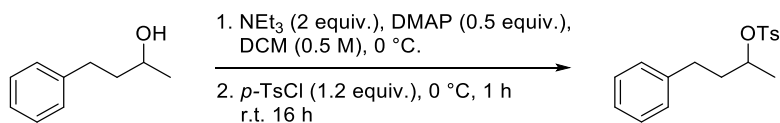


Reactions were carried out according to General Procedure A using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), H₂O (**xx μL, xx mmol, xx equiv.**), and **1,3-diisopropylurea (xx mg, xx mmol, xx equiv.)**. The reaction was stirred at 100 °C for 24 h, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	H ₂ O Equiv	Mass (μL)	Urea Equiv.	Mass (mg)	Conversion (%) ^a
1	0	-	10 mol%	14	23
2	0	-	1 equiv.	144	14
3	1	18	10 mol%	14	48
4	1	18	1 equiv.	144	38

4. Synthesis of Adducts

Synthesis of 4-phenyl-2-butanol tosylate (S1)



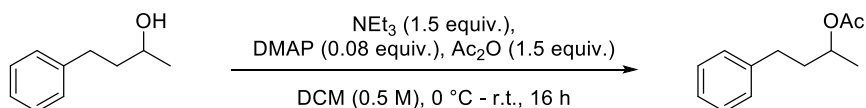
To an oven-dried round-bottom flask was added 4-phenyl-2-butanol (500 mg, 3.3 mmol, 1.0 equiv.), NEt_3 (0.9 mL, 6.66 mmol, 2.0 equiv.), DMAP (204 mg, 1.67 mmol, 0.5 equiv.), and anhydrous DCM (7 mL, 0.5 M). The solution was cooled to 0 °C, and then $p\text{-TsCl}$ (763 mg, 4.0 mmol, 1.2 equiv.) was added portion-wise. The reaction was then stirred for an hour at 0 °C before being stirred at r.t. for 16 h under an N_2 atmosphere. The reaction mixture was washed with H_2O (3×10 mL) and brine (10 mL) and the organic phase dried over Na_2SO_4 , filtered, and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-10% Et_2O in petroleum ether 40-60 °C) to give the desired product as a white solid (820 mg, 82%).

^1H NMR (400 MHz, CDCl_3): δ 7.81 (d, J = 8.3 Hz, 2H), 7.36 – 7.32 (m, 2H), 7.29 – 7.23 (m, 2H), 7.21 – 7.14 (m, 1H), 7.09 – 7.06 (m, 2H), 4.71 – 4.62 (m, 1H), 2.62 (ddd, J = 13.8, 10.1, 6.0 Hz, 1H), 2.51 (ddd, J = 13.9, 10.0, 6.0 Hz, 1H), 2.45 (s, 3H), 1.95 (dddd, J = 14.2, 10.0, 7.3, 6.0 Hz, 1H), 1.82 (dddd, J = 14.2, 10.1, 6.1, 5.0 Hz, 1H), 1.31 (d, J = 6.3 Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3): δ 144.6, 140.9, 134.5, 129.8, 128.5, 128.3, 127.8, 126.1, 79.9, 38.2, 31.2, 21.7, 20.9.

Spectroscopic data were in agreement with literature values.^[2]

Synthesis of 4-phenyl-2-butanol acetate (S2)



To a round-bottom flask was added acetic anhydride (0.29 mL, 3 mmol, 1.5 equiv.), NEt_3 (0.42 mL, 3.0 mmol, 1.5 equiv.), and DCM (4 mL, 0.5 M) followed by the addition of 4-phenyl-2-butanol (300 mg, 2.0 mmol, 1.0 equiv.). The reaction mixture was stirred at r.t. for 16 h before being quenched with 2 M HCl (10 mL) and extracted with Et_2O (3×10 mL). The combined organic phases were washed with saturated NaHCO_3 (10 mL), dried over Na_2SO_4 , filtered, and concentrated under vacuum. The crude residue was purified by column chromatography (silica

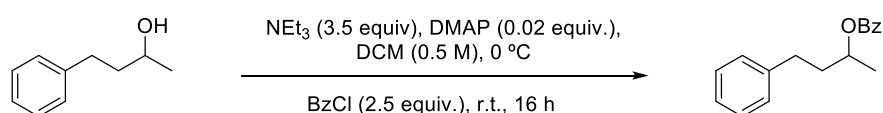
gel, 0-10% Et₂O in petroleum ether 40-60 °C) to give the desired product as a colourless oil (381 mg, 99%).

¹H NMR (400 MHz, CDCl₃): δ 7.34 – 7.25 (m, 2H), 7.24 – 7.14 (m, 3H), 5.01 – 4.87 (m, 1H), 2.66 (m, 2H), 2.04 (m, 3H), 2.00 – 1.89 (m, 1H), 1.87 – 1.76 (m, 1H), 1.26 (d, *J* = 6.3 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 170.9, 141.7, 128.6, 128.5, 126.1, 70.7, 37.7, 32.0, 21.6, 20.2.

Spectroscopic data were in agreement with literature values.^[3]

Synthesis of 4-phenylbutan-2-yl benzoate (S3)



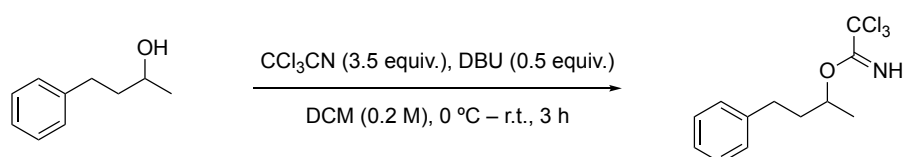
To a round bottom flask was added 4-phenyl-2-butanol (451 mg, 3.0 mmol, 1.0 equiv.), and anhydrous DCM (7 mL, 0.5 M). The mixture was cooled to 0 °C before the addition of NEt₃ (1.46 mL, 10.5 mmol, 3.5 equiv.), and DMAP (7 mg, 0.06 mmol, 0.02 equiv.). The reaction mixture was stirred and benzoyl chloride (0.87 mL, 7.5 mmol, 2.5 equiv.) was added. The reaction mixture was warmed to r.t. and the solution stirred for 16 h. The reaction was quenched using sat. NH₄Cl (20 mL) and then extracted using Et₂O (3 × 10 mL). The combined organic phases were washed with saturated NaHCO₃ (10 mL), dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-10% Et₂O in petroleum ether 40-60 °C) to give the desired product as a colourless oil (671 mg, 88%).

¹H NMR (500 MHz, CDCl₃): δ 8.08 – 8.00 (m, 2H), 7.59 – 7.52 (m, 1H), 7.46 – 7.43 (m, 2H), 7.31 – 7.24 (m, 2H), 7.22 – 7.15 (m, 3H), 5.23 – 5.17 (m, 1H), 2.80 – 2.68 (m, 2H), 2.16 – 2.03 (m, 1H), 1.98 – 1.91 (m, 1H), 1.39 (d, *J* = 6.2 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 166.3, 141.7, 132.9, 130.9, 129.7, 128.6, 128.5, 128.5, 126.1, 71.3, 37.9, 32.0, 20.3.

Spectroscopic data were in agreement with literature values.^[4]

Synthesis of 4-phenylbutan-2-yl trichloroacetimidate (S4)



To a round-bottom flask was added 4-phenyl-2-butanol (225 mg, 1.5 mmol, 1.0 equiv.), trichloroacetonitrile (0.53 mL, 5.25 mmol, 3.5 equiv.), and DCM (7.5 mL, 0.2 M). The reaction was cooled to 0 °C before DBU (114 mg, 0.75 mmol, 0.5 equiv.) was added dropwise. The reaction was warmed to r.t. and stirred for 3 h under a N₂ atmosphere. The reaction mixture was then concentrated under vacuum. The crude residue was purified by column chromatography (0-30% Et₂O in petroleum ether 40-60 °C) to give the desired product as a colourless oil (440 mg, 99%).

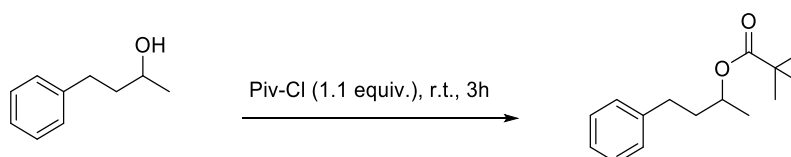
ν_{max} (solid): 3345, 3026, 2976, 2934, 1657, 1603, 1290, 1074, 1047, 791, 646 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 8.26 (br s, 1H), 7.32 – 7.26 (m, 2H), 7.23 – 7.12 (m, 3H), 5.10 – 5.04 (m, 1H), 2.86 – 2.66 (m, 2H), 2.14 – 2.07 (m, 1H), 1.97 – 1.90 (m, 1H), 1.38 (d, J = 6.1 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 162.3, 141.7, 128.6, 128.5, 126.1, 92.2, 75.7, 37.7, 31.8, 19.0.

HRMS (ESI): exact mass calculated for [M+Na]⁺ (C₁₂H₁₄Cl₃NONa) requires m/z 316.0039, found m/z 316.0031.

Synthesis of 1-methyl-3-phenylpropyl 2,2-dimethylpropionate (S5)



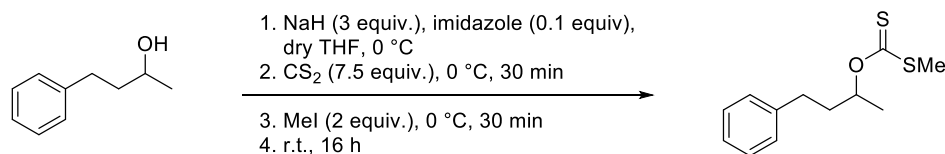
To a round-bottom flask was added 4-phenyl-2-butanol (451 mg, 3.0 mmol, 1.0 equiv.), and pivaloyl chloride (0.41 mL, 3.3 mmol, 1.1 equiv.). The reaction was stirred at r.t. for 3 h and then concentrated under vacuum. The crude residue was purified by column chromatography (10 - 30% Et₂O in petroleum ether 40-60 °C) to give the desired product as a colourless oil (646 mg, 92%).

¹H NMR (400 MHz, CDCl₃): δ 7.31 – 7.25 (m, 2H), 7.22 – 7.14 (m, 3H), 4.97 – 4.87 (m, 1H), 2.73 – 2.57 (m, 2H), 2.00 – 1.75 (m, 2H), 1.23 (d, J = 6.4 Hz, 3H), 1.22 (s, 9H).

¹³C NMR (101 MHz, CDCl₃): δ 178.1, 141.7, 128.5, 128.3, 125.9, 70.0, 38.8, 37.8, 31.8, 27.2, 19.9.

Spectroscopic data were in agreement with literature values.^[5]

Synthesis of *S*-methyl *O*-(4-phenylbutan-2-yl)carbonodithioate (S6)



To a solution of 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.) in anhydrous THF (44 mL, 0.02 M) at 0 °C in a round-bottom flask was added NaH (240 mg, 6.0 mmol, 3.0 equiv.), and imidazole (13.6 mg, 0.2 mmol, 0.1 equiv.). The reaction mixture was stirred at 0 °C for 30 min followed by the addition of CS₂ (0.9 mL, 15.0 mmol, 7.5 equiv.). Following a further 30 min period of stirring at 0 °C, MeI (0.24 mL, 4.0 mmol, 2.0 equiv.), was added, warmed to r.t. and then stirred for 16 h. The reaction was quenched with sat. NH₄Cl (30.0 mL), diluted with EtOAc (20 mL), and washed with brine (3 × 10 mL). The organic phase was dried over Na₂SO₄, filtered and concentrated under vacuum. The crude residue was purified by column chromatography (10 - 80% Et₂O in petroleum ether 40-60 °C) to give the desired product as a yellow oil (227 mg, 96%).

¹H NMR (400 MHz, CDCl₃): δ 7.31 – 7.27 (m, 2H), 7.23 – 7.15 (m, 3H), 5.77 – 5.69 (m, 1H), 2.78 – 2.62 (m, 2H), 2.56 (s, 3H), 2.22 – 2.10 (m, 1H), 2.01 – 1.91 (m, 1H), 1.40 (d, *J* = 6.3 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃): 215.5, 141.3, 128.6, 128.5, 126.1, 80.7, 37.6, 31.8, 19.5, 19.0.

Spectroscopic data were in agreement with literature values.^[6]

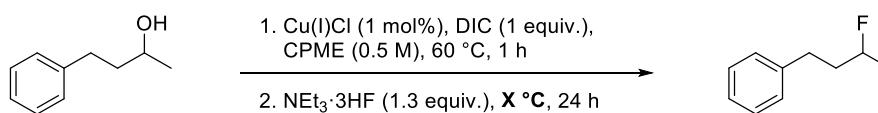
5. Alternative adducts study

To an oven-dried microwave vial was added **adduct (xx mg, 1.0 mmol, 1.0 equiv.)** and CPME (2 mL, 0.5 M). The vial was capped and the reaction was heated at 60 °C for 1 h. Once cooled to r.t., the vial was de-capped and then CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.) and H₂O (18.0 μL, 1.0 mmol, 1.0 equiv.) was added. The vial was capped and then the reaction was heated at 100 °C for 24 h before analysis by ¹H NMR against a known standard (naphthalene).

Entry	Adduct	Mass (mg)	Conversion (%)
1	Tosylate (S1)	304	16
2	Acetate (S2)	192	0
3	Benzoate (S3)	254	0
4	Trichloroacetimidate (S4)	295	32
5	Pivalate (S5)	234	0
6	Carbonodithioate (S6)	240	0

6. HF reactions

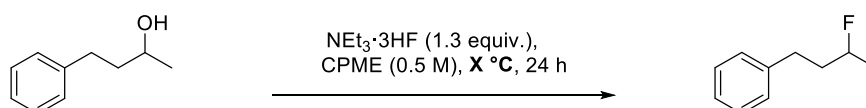
Treatment of DIC adduct with NEt₃·3HF



To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), and CPME (2 mL, 0.5 M). The vial was capped and the reaction was heated at 60 °C for 1 h. Once cooled to r.t., the vial was de-capped and then NEt₃·3HF (0.21 mL, 1.3 mmol, 1.3 equiv.) was added. The vial was capped and then the reaction was heated at X °C for 24 h before analysis by ¹H NMR against a known standard (naphthalene).

Entry	Temperature (°C)	Conversion (%)
1	r.t.	0
2	100	57

Treatment of alcohol with NEt₃·3HF



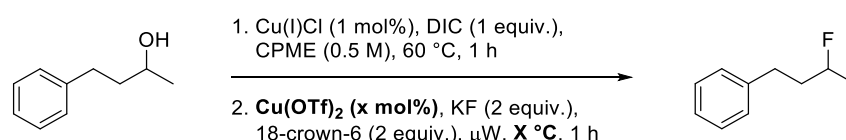
To an oven-dried microwave vial was added 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.) and NEt₃·3HF (0.21 mL, 1.3 mmol, 1.3 equiv.). The vial was capped and then the

reaction was heated at **X °C** for 24 h before analysis by ¹H NMR against a known standard (naphthalene).

Entry	Temperature (°C)	Conversion (%)
1	r.t.	0
2	100	0

7. Optimization with Cu(OTf)₂ and KF

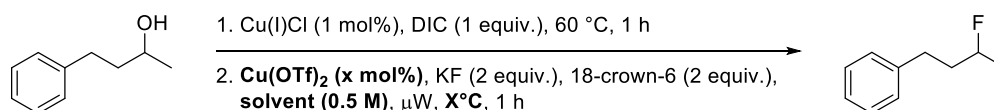
Microwave irradiation with CPME



Reactions were carried out according to General Procedure D using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), Cu(OTf)₂ (xx mg, xx mmol, xx equiv.), KF (116 mg, 2.0 mmol, 2.0 equiv.), and 18-crown-6 (528 mg, 2.0 mmol, 2 equiv.). The reaction was heated at xx °C for 1 h under microwave irradiation, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Cu(OTf) ₂ loading	Mass (mg)	Temperature (°C)	Conversion (%)
1	50 mol%	181	100	0
2	75 mol%	271	100	0
3	1 equiv.	362	100	0
4	50 mol%	181	110	24
5	75 mol%	271	110	0

Microwave irradiation solvent screen



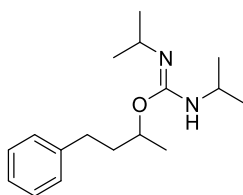
Reactions were carried out according to General Procedure D using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), Cu(OTf)₂ (xx mg, xx mmol, xx equiv.), KF (116 mg, 2.0 mmol, 2.0 equiv.), and 18-crown-6 (528 mg, 2.0 mmol, 2 equiv.), and solvent (2 mL, 0.5 M). The reaction was heated at xx °C, for 1 h under microwave irradiation, before analysis by ¹H NMR against a known internal standard (naphthalene).

Entry	Solvent	Cu(OTf) ₂ loading	Temperature (° C)	Conversion (%)
1	PhMe	50 mol%	100	16
2	MeCN	50 mol%	100	27
3	MeCN	50 mol%	110	36
4	MeCN	75 mol%	110	43
5	MeCN	1 equiv.	110	57
6	MeCN	1 equiv.	100	54

8. Compound characterization data

8.1. Preparation of starting materials

4-Phenylbutan-2-yl (Z)-*N,N'*-diisopropylcarbamimidate, compound **S7**



To an oven-dried microwave vial was added 4-phenol-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), and DIC (0.15 mL, 1.0 mmol, 1.0 equiv.). The vial was capped and the reaction was stirred at 60 °C for 1 h. The reaction mixture was allowed to cool to r.t. and diluted with Et₂O before passing through a pad of celite to remove residual copper. The reaction mixture was concentrated under vacuum and the resulting oil was taken up in CHCl₃, and again passed through a pad of celite to remove the 1,3-diisopropylurea by-product. The desired product was obtained as pale oil (276 mg, quant.) and used in subsequent reactions without further purification.

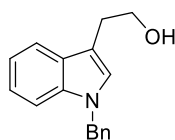
ν_{max} (solid): 3433, 3083, 3059, 3024, 2960, 2927, 2864, 1657, 1605, 1497, 1454 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 7.30 – 7.24 (m, 2H), 7.22 – 7.14 (m, 3H), 5.03 – 4.97 (m, 1H), 3.80 – 3.74 (m, 1H), 3.38 (d, J = 5.8 Hz, 1H), 3.20 – 3.15 (m, 1H), 2.69 (m, 2H), 2.00 – 1.89 (m, 1H), 1.83 – 1.75 (m, 1H), 1.24 (d, J = 6.2 Hz, 3H), 1.20 – 1.05 (m, 12H).

¹³C NMR (101 MHz, CDCl₃): δ 150.8, 142.7, 128.6, 128.4, 69.5, 46.3, 43.4, 38.3, 32.0, 24.5, 24.3, 24.2, 24.1, 19.9.

HRMS (ESI): exact mass calculated for [M⁺H]⁺ (C₁₇H₂₉N₂O) requires m/z 277.2274, found m/z 277.2276.

1-Benzyltryptophol, compound **S8**



To an oven-dried round-bottom flask was added tryptophol (1.0 g, 6.2 mmol, 1.0 equiv.), and anhydrous DMF (16 mL) was added. The solution was cooled to 0 °C and NaH (546 mg, 23.0 mmol, 3.0 equiv.) in anhydrous DMF (4 mL) was then added. The reaction was stirred at 0 °C for 45 min after which, benzyl bromide (1.2 mL, 10.0 mmol, 1.2 equiv.) was added dropwise.

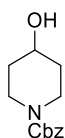
The reaction was allowed to warm to r.t. and stirred for 16 h. The reaction was quenched using sat. NH_4Cl (20 mL), extracted with EtOAc (40 mL) and washed with water (2×30 mL), brine (2×30 mL), dried over Na_2SO_4 , filtered, and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-40% EtOAc in petroleum ether 40-60 °C) to give the desired product as an orange oil (1.39 g, 89%).

^1H NMR (400 MHz, CDCl_3): δ 7.70 (dt, $J = 7.8, 1.1$ Hz, 1H), 7.40 – 7.13 (m, 8H), 7.04 (s, $J = 0.9$ Hz, 1H), 5.30 (s, 1H), 3.93 (t, $J = 6.5$ Hz, 2H), 3.08 (t, $J = 6.2$ Hz, 2H), 1.95 (s, 1H).

^{13}C NMR (101 MHz, CDCl_3): δ 137.6, 136.9, 128.8, 128.2, 127.7, 126.9, 126.7, 122.0, 119.2, 119.1, 111.5, 109.9, 62.8, 50.0, 28.8.

Spectroscopic data were in agreement with literature values.^[7]

Benzyl 4-hydroxy-1-piperidinecarboxylate, compound **S9**



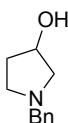
Reaction was carried out according to General Procedure C using 1-Z-4 piperidone (2.0 g, 9.0 mmol, 1.0 equiv.), MeOH (18.0 mL, 0.5 M), and NaBH_4 (488 mg, 23.0 mmol, 1.5 equiv.) The reaction was stirred at r.t. for 3 h. The crude residue was purified by column chromatography (silica gel, 0-50% Et_2O in petroleum ether 40-60 °C) to give the desired product as a colourless oil (1.47 g, 74%).

^1H NMR (400 MHz, CDCl_3): δ 7.40 – 7.28 (m, 5H), 5.12 (s, 2H), 3.92 – 3.85 (m, 3H), 3.20 – 3.09 (m, 2H), 1.91 – 1.73 (m, 2H), 1.49 (br s, 2H). Exchangeable proton not observed.

^{13}C NMR (101 MHz, CDCl_3): δ 155.4, 136.9, 128.6, 128.1, 128.0, 67.5, 67.3, 41.5, 34.2.

Spectroscopic data were in agreement with literature values.^[8]

1-Benzyl-3-pyrrolidinol, compound **S10**



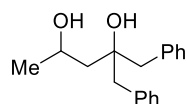
Reaction was carried out according to General Procedure C using 1-benzyl-3-pyrrolidinone (536 mg, 3.6 mmol, 1.0 equiv.), MeOH (13.0 mL, 0.5 M), and NaBH₄ (204 mg, 5.4 mmol, 1.5 equiv.) The reaction was stirred at r.t. for 16 h. The crude residue was purified by column chromatography (silica gel, 0-50% Et₂O in petroleum ether 40-60 °C) to give the desired product as a brown oil (402 mg, 63%).

¹H NMR (400 MHz, CDCl₃): δ 7.46 – 7.19 (m, 5H), 4.31 (ddt, *J* = 7.6, 5.0, 2.4 Hz, 1H), 3.62 (s, 2H), 2.92 – 2.72 (m, 2H), 2.66 (dd, *J* = 10.1, 2.3 Hz, 1H), 2.53 (dd, *J* = 10.1, 5.3 Hz, 1H), 2.30 (td, *J* = 8.9, 6.5 Hz, 1H), 2.18 (dddd, *J* = 13.7, 8.6, 7.3, 4.9 Hz, 1H), 1.81 – 1.64 (m, 1H).

¹³C NMR (101 MHz, CDCl₃): δ 138.7, 129.0, 128.4, 127.2, 71.3, 63.0, 60.3, 52.5, 35.0.

Spectroscopic data were in agreement with literature values.^[9]

2-Benzyl-1-phenylpentane-2,4-diol, compound **S11**



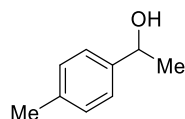
To an oven-dried round bottom flask was added ethyl-3-hydroxybutyrate (1 mL, 7.7 mmol, 1 equiv.), and anhydrous Et₂O (30 mL, 0.25 M) under nitrogen. The reaction mixture was cooled to –78 °C followed by addition of benzyl magnesium chloride (1 M in Et₂O, 27.0 mL, 3.5 equiv.) and then warmed to r.t. for 16 hours. The reaction was quenched using sat. NH₄Cl (200 mL), extracted with Et₂O (2 × 30 mL), and washed with brine (2 × 30 mL), dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-20% Et₂O in petroleum ether 40-60 °C) to give the desired product as a colourless solid (1.76 g, 85%).

¹H NMR (400 MHz, CDCl₃): δ 7.39 – 7.20 (m, 8H), 7.18 – 7.13 (m, 2H), 4.33 (dq, *J* = 8.5, 7.3, 4.2 Hz, 1H), 3.16 (br s, 1H), 3.11 (d, *J* = 13.6 Hz, 1H), 2.90 (d, *J* = 13.5 Hz, 1H), 2.77 (d, *J* = 13.6 Hz, 1H), 2.70 (br s, 1H), 2.62 (d, *J* = 13.7 Hz, 1H), 1.62 – 1.55 (m, 1H), 1.51 (dd, *J* = 14.8, 2.4 Hz, 1H), 1.14 (d, *J* = 6.2 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 137.4, 136.8, 131.0, 131.0, 128.5, 128.4, 126.8, 126.7, 75.4, 65.3, 47.1, 45.8, 45.1, 24.3.

Spectroscopic data were in agreement with literature values.^[10]

1-(*p*-Tolyl)ethanol, compound **S12**



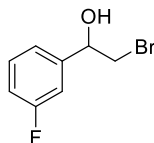
Reaction was carried out according to General Procedure C using 4'-methylacetophenone (2.0 g, 15.0 mmol, 1.0 equiv.), MeOH (30 mL, 0.5 M), and NaBH₄ (204 mg, 5.40 mmol, 1.5 equiv.) The reaction was stirred at r.t. for 16 h. The crude residue was purified by column chromatography (silica gel, 0-30% Et₂O in petroleum ether 40-60 °C) to give the desired product as a colourless oil (1.69 g, 83%).

¹H NMR (500 MHz, CDCl₃): δ 7.26 – 7.24 (m, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 4.85 (q, *J* = 6.4 Hz, 1H), 2.34 (s, 3H), 1.97 – 1.72 (m, 1H), 1.47 (d, *J* = 6.4 Hz, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 143.0, 137.3, 129.3, 125.5, 70.3, 25.2, 21.2.

Spectroscopic data were in agreement with literature values.^[11]

2-bromo-1-(3-fluorophenyl)ethan-1-ol, compound **S13**



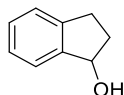
Reaction was carried out according to General Procedure C using 2-bromo-3'-fluoroacetophenone (1.0 g, 4.61 mmol, 1.0 equiv.), MeOH (9 mL, 0.5 M), and NaBH₄ (261 mg, 6.90 mmol, 1.5 equiv.) The reaction was stirred at r.t. for 16 h. The crude residue was purified by column chromatography (silica gel, 0-20% Et₂O in petroleum ether 40-60 °C) to give the desired product as a white solid (872 mg, 86%).

¹H NMR (400 MHz, CDCl₃): δ 7.42 – 7.28 (m, 1H), 7.20 – 7.09 (m, 2H), 7.01 (tdd, *J* = 8.4, 2.6, 1.0 Hz, 1H), 4.91 (dt, *J* = 8.7, 3.3 Hz, 1H), 3.62 (dd, *J* = 10.5, 3.4 Hz, 1H), 3.50 (dd, *J* = 10.5, 8.7 Hz, 1H), 2.86 (d, *J* = 3.4 Hz, 1H).

¹³C NMR (101 MHz, CDCl₃): δ 163.0 (d, ¹*J*_{CF} = 246.7 Hz), 142.9 (d, ³*J*_{CF} = 6.9 Hz), 130.3 (d, ³*J*_{CF} = 8.2 Hz), 121.7, 115.4 (d, ²*J*_{CF} = 21.1 Hz), 113.1 (d, ²*J*_{CF} = 22.3 Hz), 73.2, 39.9.

Spectroscopic data were in agreement with literature values.^[9]

1-Indanol, compound **S14**



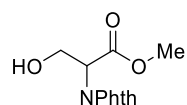
Reaction was carried out according to General Procedure C using 1-indanone (2.0 g, 15.0 mmol, 1.0 equiv.), MeOH (30 mL, 0.5 M), and NaBH₄ (204 mg, 5.40 mmol, 1.5 equiv.) The reaction was at r.t. for 16 h. The crude residue was purified by column chromatography (silica gel, 0-50% Et₂O in petroleum ether 40-60 °C) to give the desired product as a white solid (1.6 g, 80%).

¹H NMR (500 MHz, CDCl₃): δ 7.43 – 7.40 (m, 1H), 7.27 – 7.24 (m, 3H), 5.24 (q, *J* = 6.2 Hz, 1H), 3.09 – 3.09 (m, 1H), 2.85 – 2.79 (m, 1H), 2.52 – 2.45 (m, 1H), 1.99 – 1.90 (m, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 145.1, 143.4, 128.4, 126.8, 125.0, 124.3, 76.5, 36.0, 29.9.

Spectroscopic data were in agreement with literature values.^[1]

Methyl 2-(1,3-dioxoisindolin-2-yl)-3-hydroxypropanoate, compound **S15**



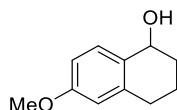
To a solution of serine methyl ester hydrochloride (778 mg, 5.0 mmol, 1.0 equiv.) and phthalic anhydride (740 mg, 5.0 mmol, 1.0 equiv.) in PhMe (20 mL, 0.25 M) was added trimethylamine (0.7 mL, 5.0 mmol, 1.0 equiv.). The reaction mixture was refluxed under Dean-Stark conditions for 2 h. The reaction mixture was concentrated under vacuum and the crude residue was dissolved in EtOAc, washed with 10% citric acid (10 mL), H₂O (10 mL) and the organic phase was dried over Na₂SO₄, filtered and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-30% EtOAc in petroleum ether 40-60 °C) to give the desired product as a white solid (990 mg, 79%).

¹H NMR (400 MHz, CDCl₃): δ 7.87 – 7.78 (m, 2H), 7.76 – 7.68 (m, 2H), 4.99 (dd, *J* = 6.0, 4.7 Hz, 1H), 4.23 – 4.01 (m, 2H), 3.73 (s, 3H), 3.57 (br s, 1H).

¹³C NMR (101 MHz, CDCl₃): δ 168.5, 168.1, 134.5, 131.7, 123.8, 60.8, 54.6, 52.9.

Spectroscopic data were in agreement with literature values.^[12]

6-Methoxy-1,2,3,4-tetrahydronaphthalen-1-ol, compound **S16**



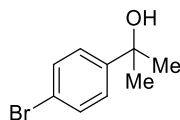
Reaction was carried out according to General Procedure C using 6-methoxy-1-tetralone (2.0 g, 11.0 mmol, 1 equiv.), MeOH (23 mL, 0.5 M), and NaBH₄ (643 mg, 17 mmol, 1.5 equiv.) The reaction was stirred at r.t. for 16 h. The crude residue was purified by column chromatography (silica gel, 0-50% Et₂O in petroleum ether 40-60 °C) to give the desired product as a colourless oil (1.55 g, 79%).

¹H NMR (500 MHz, CDCl₃): δ 7.34 (d, *J* = 8.5 Hz, 1H), 6.77 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.63 (d, *J* = 2.7 Hz, 1H), 4.79 – 4.72 (m, 1H), 3.79 (s, 3H), 2.85 – 2.65 (m, 2H), 1.99 – 1.90 (m, 3H), 1.81 – 1.73 (m, 1H), 1.64 – 1.58 (m, 1H).

¹³C NMR (126 MHz, CDCl₃): δ 159.0, 138.8, 131.4, 130.2, 113.5, 112.6, 67.8, 55.4, 32.5, 29.8, 18.7.

Spectroscopic data were in agreement with literature values.^[13]

2-(4-bromophenyl)propan-2-ol, compound **S17**



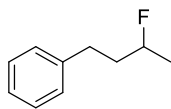
To a round bottom flask was added 4'-bromoacetophenone (2.0 g, 10.0 mmol, 1.0 equiv.), and anhydrous THF (40 mL, 0.25 M). The reaction was stirred at r.t. before the dropwise addition of methyl magnesium bromide (1.27 mL, 11.0 mmol, 1.1 equiv.). Once complete, the reaction was quenched using H₂O (15 mL), extracted with Et₂O (2 × 10 mL), washed with brine (2 × 10 mL), dried over Na₂SO₄, filtered, and concentrated under vacuum. The crude residue was purified by column chromatography (silica gel, 0-30% Et₂O in petroleum ether 40-60 °C) to give the desired product as an orange oil (1.4 g, 66%)

¹H NMR (500 MHz, CDCl₃) δ 7.47 – 7.43 (m, 2H), 7.38 – 7.34 (m, 2H), 1.78 (br s, 1H), 1.56 (s, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 148.3, 131.4, 126.5, 120.7, 72.5, 31.9.

8.2. Substrate scope from Scheme 3

(3-Fluorobutyl)benzene, compound **2a**



Prepared according to General Procedure B, using 4-phenyl-2-butanol (150 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the desired product as a colourless oil (119 mg, 78%).

¹H NMR (500 MHz, CDCl₃): δ 7.35 – 7.27 (m, 2H), 7.25 – 7.19 (m, 3H), 4.79 – 4.56 (m, 1H), 2.85 – 2.68 (m, 2H), 2.09 – 1.75 (m, 2H), 1.37 (dd, J = 23.9, 6.1 Hz, 3H).

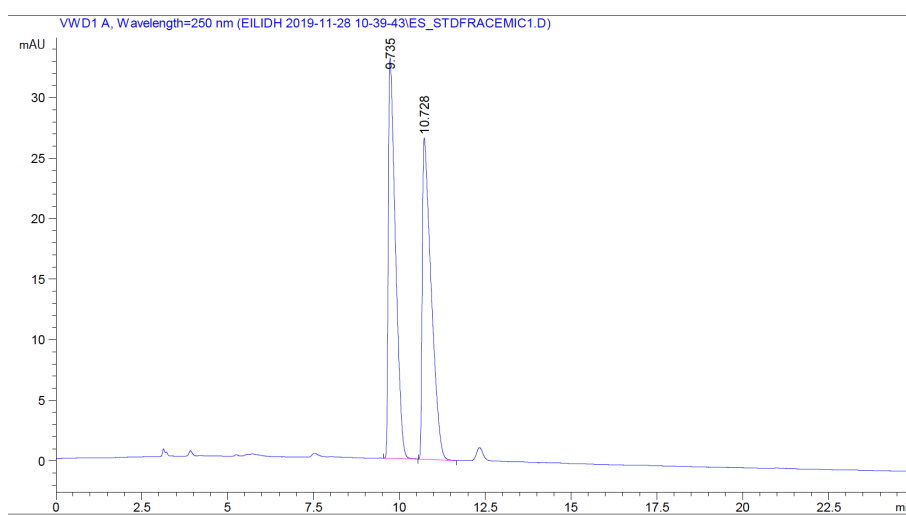
¹³C NMR (101 MHz, CDCl₃): δ 141.6, 128.6, 126.1, 90.2 (d, $^1J_{CF}$ = 164.9 Hz), 38.8 (d, $^2J_{CF}$ = 20.8 Hz), 31.5 (d, $^3J_{CF}$ = 4.8 Hz), 21.1 (d, $^2J_{CF}$ = 22.7 Hz).

¹⁹F NMR (471 MHz, CDCl₃): δ -174.25.

Spectroscopic data were in agreement with literature values.^[14]

To determine the stereochemical outcome, (*S*)-4-phenyl-2-butanol (150 mg, Fluorochem, 98% ee) was fluorinated as described above, affording (*R*)-(3-fluorobutyl)benzene (116 mg, 76%, 92% ee, 94% *es*) ($[\alpha]_D = -18.0^\circ$ (c = 9.9 in CHCl₃)). The enantiomeric excess was determined by HPLC (Chiralcel OJ-H column; Method: 60 min equilibration with 100% hexanes, 20 minute isocratic run with 100% hexanes; elution times: [enantiomers at 10.4 (major) and 11.7 min (minor)]).

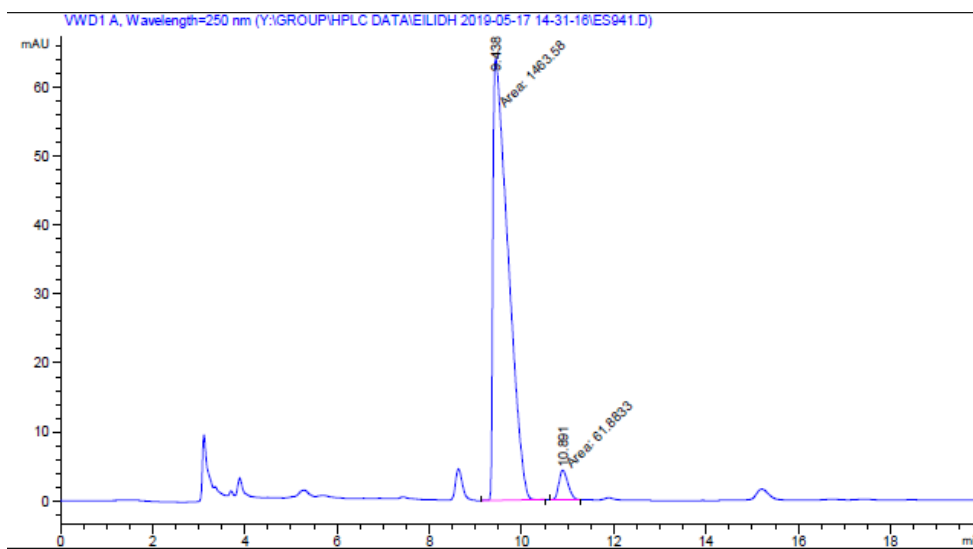
Racemic:



Signal 1: VWD1 A, Wavelength=250 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.735	BB	0.2143	479.06921	33.03362	50.0272
2	10.728	BB	0.2614	478.54877	26.53211	49.9728

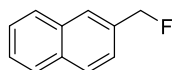
Product:



Signal 1: VWD1 A, Wavelength=250 nm

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.438	NM	0.3808	1463.58484	64.06059	95.9433
2	10.891	NM	0.2369	61.88330	4.35402	4.0567

2-(Fluoromethyl)naphthalene, compound **2b**



Prepared according to General Procedure B, using 2-naphthalenemethanol (158 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the desired product a white solid (130 mg, 81%).

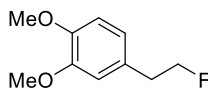
¹H NMR (400 MHz, CDCl₃): δ 7.90 – 7.83 (m, 4H), 7.54 – 7.48 (m, 3H), 5.55 (d, J = 47.7 Hz, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 133.8 (d, $^2J_{\text{CF}}$ = 16.8 Hz), 133.5 (d, $^4J_{\text{CF}}$ = 1.9 Hz), 133.2, 128.6, 128.2, 127.9, 126.8 (d, $^3J_{\text{CF}}$ = 7.5 Hz), 126.6 (d, $^3J_{\text{CF}}$ = 7.4 Hz), 125.1 (d, $^4J_{\text{CF}}$ = 4.7 Hz), 84.9 (d, $^1J_{\text{CF}}$ = 166.4 Hz).

¹⁹F NMR (376 MHz, CDCl₃): δ -206.70.

Spectroscopic data were in agreement with literature values.^[15,16]

4-(2-fluoroethyl)-1,2-dimethoxybenzene, compound **2c**



Prepared according to General Procedure B, using 2-(3,4-dimethoxyphenyl)ethanol (182 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-20% Et₂O in petroleum ether 40-60 °C) to afford the desired product a colourless oil (139 mg, 76%).

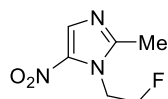
¹H NMR (500 MHz, CDCl₃): δ 6.82 (d, J = 8.0 Hz, 1H), 6.80 – 6.73 (m, 2H), 4.61 (dt, J = 47.2, 6.5 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 2.96 (dt, J = 23.3, 6.5 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 149.0, 147.9, 129.7 (d, $^3J_{\text{CF}}$ = 6.3 Hz), 121.0, 112.2, 111.3, 84.4 (d, $^1J_{\text{CF}}$ = 169.0 Hz), 55.94, 55.87, 36.6 (d, $^2J_{\text{CF}}$ = 20.4 Hz).

¹⁹F NMR (471 MHz, CDCl₃): δ -214.94.

Spectroscopic data were in agreement with literature values.^[10,17]

1-(2-Fluoroethyl)-2-methyl-5-nitro-1*H*-imidazole, compound **2d**



Prepared according to General Procedure B, using metronidazole (171 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μL, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹H NMR against a known standard (naphthalene) determined conversion to product as 61%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% MeOH in DCM) to afford the desired compound as a colourless oil.

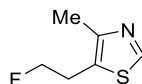
¹H NMR (400 MHz, CDCl₃): δ 7.96 (s, 1H), 4.75 (dt, *J* = 47.0, 3.9 Hz, 2H), 4.61 (dt, *J* = 26.1, 3.9 Hz, 2H), 2.50 (s, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 151.8, 133.4, 82.3 (d, ¹*J*_{CF} = 171.7 Hz), 46.9 (d, ²*J*_{CF} = 20.0 Hz), 14.5.

¹⁹F NMR (376 MHz, CDCl₃): δ -223.93.

Spectroscopic data were in agreement with literature values.^[18]

5-(2-Fluoroethyl)-4-methylthiazole, compound **2e**



Prepared according to General Procedure B, using 4-methyl-5-thiazoleethanol (143 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μL, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-30% Et₂O in petroleum ether 40-60 °C) to afford the desired product as a colourless oil (113 mg, 78%).

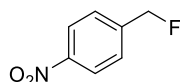
¹H NMR (500 MHz, CDCl₃): δ 8.60 (s, 1H), 4.57 (dt, *J* = 46.8, 6.2 Hz, 2H), 3.16 (dt, *J* = 23.5, 6.2 Hz, 2H), 2.41 (s, 3H).

^{13}C NMR (126 MHz, CDCl_3): δ 150.2, 150.1, 125.9 (d, $^3J_{\text{CF}} = 5.0$ Hz), 83.2 (d, $^1J_{\text{CF}} = 170.9$ Hz), 27.7 (d, $^2J_{\text{CF}} = 22.1$ Hz), 15.0.

^{19}F NMR (471 MHz, CDCl_3): δ -215.35.

Spectroscopic data were in agreement with literature values.^[10,19]

4-Nitrobenzyl fluoride, compound **2f**



Prepared according to General Procedure B, using 4-nitrobenzyl alcohol (153 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% Et_2O in petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a yellow oil (120 mg, 77%).

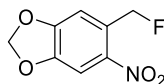
^1H NMR (500 MHz, CDCl_3): δ 8.25 (d, $J = 8.3$ Hz, 2H), 7.53 (d, $J = 8.2$ Hz, 2H), 5.50 (d, $J = 46.8$ Hz, 2H).

^{13}C NMR (101 MHz, CDCl_3): δ 148.0, 143.5 (d, $^2J_{\text{CF}} = 17.6$ Hz), 127.2 (d, $^3J_{\text{CF}} = 7.0$ Hz), 123.8, 83.0 (d, $^1J_{\text{CF}} = 170.8$ Hz).

^{19}F NMR (376 MHz, CDCl_3): δ -215.63.

Spectroscopic data were in agreement with literature values.^[20]

6-Nitropiperonyl fluoride, compound **2g**



Prepared according to General Procedure B, using 6-nitropiperonyl alcohol (197 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-50% hexane in DCM) to afford the desired product as a yellow solid (104 mg, 52%).

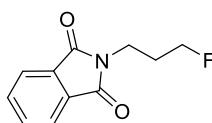
^1H NMR (400 MHz, CDCl_3): δ 7.68 (d, J = 1.0 Hz, 1H), 7.19 (q, J = 0.8 Hz, 1H), 6.16 (s, 2H), 5.79 (dd, J = 48.2, 0.9 Hz, 2H).

^{13}C NMR (101 MHz, CDCl_3): δ 153.4 (d, $^4J_{\text{CF}}$ = 3.6 Hz), 147.5, 139.8, 132.4 (d, $^3J_{\text{CF}}$ = 19.3 Hz), 105.8 (d, $^2J_{\text{CF}}$ = 21.5 Hz), 105.6, 103.4, 81.7 (d, $^1J_{\text{CF}}$ = 173.5 Hz).

^{19}F NMR (376 MHz, CDCl_3): δ -216.26.

Spectroscopic data were in agreement with literature values.^[18]

N-(3-Fluoropropyl)phthalimide, compound **2h**



Prepared according to General Procedure B using *N*-(3-hydroxypropyl)phthalimide (205 mg, 1 mmol, 1 equiv.), Cu(I)Cl (1 mg, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1 mmol, 1 equiv.), CPME (2 mL, 0.5M), CuF_2 (203 mg, 2 mmol, 2 equiv.), and H_2O (18 μL , 1 mmol, 1 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-20% Et_2O in petroleum ether 40-60 $^\circ\text{C}$ with 1% triethylamine) to afford the desired product as a white solid (142 mg, 89%).

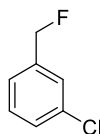
^1H NMR (500 MHz, CDCl_3): δ 7.85 (dd, J = 5.4, 3.1 Hz, 2H), 7.72 (dd, J = 5.5, 3.0 Hz, 2H), 4.52 (dt, J = 47.0, 5.7 Hz, 2H), 3.85 (t, J = 6.9 Hz, 2H), 2.10 (dp, J = 26.3, 6.4 Hz, 2H).

^{13}C NMR (126 MHz, CDCl_3): δ 168.4, 134.2, 132.2, 123.4, 81.8 (d, $^1J_{\text{CF}}$ = 166.1 Hz), 34.8 (d, $^3J_{\text{CF}}$ = 5.3 Hz), 29.6 (d, $^2J_{\text{CF}}$ = 19.9 Hz).

^{19}F NMR (471 MHz, CDCl_3): δ -220.79.

Spectroscopic data were in agreement with literature values.^[21]

1-Chloro-3-(fluoromethyl)benzene, compound **2i**



Prepared according to General Procedure B, using 3-chlorobenzyl alcohol (143 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.),

CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the desired product as a colourless oil (61 mg, 42%).

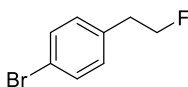
¹H NMR (400 MHz, CDCl₃): δ 7.38 (s, 1H), 7.36 – 7.30 (m, 2H), 7.29 – 7.22 (m, 1H), 5.36 (d, J = 47.4 Hz, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 138.3 (d, $^2J_{CF}$ = 17.5 Hz), 134.6, 130.1, 128.9 (d, $^4J_{CF}$ = 2.6 Hz), 127.4 (d, $^3J_{CF}$ = 6.5 Hz), 125.3 (d, $^3J_{CF}$ = 6.5 Hz), 83.7 (d, $^1J_{CF}$ = 168.4 Hz).

¹⁹F NMR (376 MHz, CDCl₃): δ –209.76.

Spectroscopic data were in agreement with literature values.^[22]

1-Bromo-4-(2-fluoroethyl)benzene, compound **2j**



Prepared according to General Procedure B, using 2-(4-bromophenyl)ethan-1-ol (202 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the desired product as a colourless oil (138 mg, 68%).

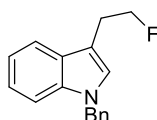
¹H NMR (400 MHz, CDCl₃): δ 7.48 – 7.41 (m, 2H), 7.15 – 7.08 (m, 2H), 4.61 (dt, J = 47.0, 6.4 Hz, 2H), 2.97 (dt, J = 24.2, 6.4 Hz, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 136.3 (d, $^3J_{CF}$ = 5.4 Hz), 131.7, 130.8, 120.7, 83.8 (d, $^1J_{CF}$ = 169.4 Hz), 36.4 (d, $^2J_{CF}$ = 20.5 Hz).

¹⁹F NMR (471 MHz, CDCl₃): δ –215.98.

Spectroscopic data were in agreement with literature values.^[23]

1-Benzyl-3-(2-fluoroethyl)-1*H*-indole, compound **2k**



Prepared according to General Procedure B, using 2-(1-benzyl-1*H*-indol-3-yl)ethanol (251 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-30% Et₂O in petroleum ether 40-60 °C) to afford the desired product as a colourless oil (152 mg, 60%).

ν_{max} (solid): 3057, 3030, 2961, 2926, 2899, 1465, 993 cm⁻¹.

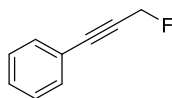
¹H NMR (400 MHz, CDCl₃): δ 7.65 – 7.60 (m, 1H), 7.29 (m, 4H), 7.23 – 7.09 (m, 4H), 7.03 (s, 1H), 5.29 (s, 2H), 4.70 (dt, J = 47.2, 6.7 Hz, 2H), 3.19 (dt, J = 22.0, 6.7 Hz, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 137.7, 136.7, 128.9, 128.2, 127.7, 126.9, 126.7, 122.0, 119.4, 119.0, 110.4 (d, ³ J_{CF} = 8.1 Hz), 109.9, 84.0 (d, ¹ J_{CF} = 168.3 Hz), 50.1, 26.7 (d, ² J_{CF} = 21.4 Hz).

¹⁹F NMR (376 MHz, CDCl₃): δ -212.96.

HRMS (ESI): exact mass calculated for [M+Na]⁺ (C₁₇H₁₆FNNa) requires m/z 276.1164, found m/z 276.1160.

(3-Fluoroprop-1-yn-1-yl)benzene, compound **2l**



Prepared according to General Procedure B, using 3-phenyl-2-propyn-1-ol (132 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-30% Et₂O in petroleum ether 40-60 °C) to afford desired product as a colourless oil (67 mg, 50%).

ν_{max} (solid): 2970, 2928, 2905, 2866, 2835, 1610, 1508, 1240, 1171, 1034, 828, 810 cm^{-1} .

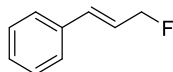
^1H NMR (400 MHz, CDCl_3): δ 7.50 – 7.44 (m, 2H), 7.37 – 7.30 (m, 3H), 5.19 (d, J = 47.6 Hz, 2H).

^{13}C NMR (101 MHz, CDCl_3): δ 131.9 (d, J_{CF} = 3.2 Hz), 129.1, 128.4, 121.8 (d, $^4J_{\text{CF}}$ = 4.2 Hz), 89.5 (d, $^3J_{\text{CF}}$ = 12.1 Hz), 82.6 (d, $^2J_{\text{CF}}$ = 21.4 Hz), 71.2 (d, $^1J_{\text{CF}}$ = 165.0 Hz).

^{19}F NMR (376 MHz, CDCl_3): δ –213.45.

HRMS (EI): exact mass calculated for $[\text{M}]^+$ ($\text{C}_9\text{H}_7\text{F}$) requires m/z 134.0532, found m/z 134.0532.

Cinnamyl fluoride, compound **2m**



Prepared according to General Procedure B, using cinnamyl alcohol (134 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-20% Et_2O in petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a colourless oil (65 mg, 48%).

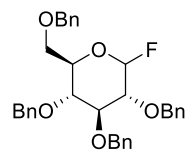
^1H NMR (400 MHz, CDCl_3): δ 7.45 – 7.39 (m, 2H), 7.38 – 7.32 (m, 2H), 7.32 – 7.28 (m, 1H), 6.71 (dd, J = 16.0, 5.2 Hz, 1H), 6.37 (ddt, J = 15.9, 12.1, 6.1 Hz, 1H), 5.09 (dd, J = 6.1, 1.4 Hz, 1H), 4.98 (dd, J = 6.1, 1.4 Hz, 1H).

^{13}C NMR (101 MHz, CDCl_3): δ 136.1 (d, $^4J_{\text{CF}}$ = 2.5 Hz), 134.5 (d, $^2J_{\text{CF}}$ = 12.4 Hz), 128.8, 128.4, 126.9 (d, $^3J_{\text{CF}}$ = 2.2 Hz), 123.7, 83.6 (d, $^1J_{\text{CF}}$ = 162.6 Hz).

^{19}F NMR (376 MHz, CDCl_3): δ –210.46.

Spectroscopic data were in agreement with literature values.^[24]

2,3,4,6-tetra-*O*-benzyl-D-glucopyranosyl fluoride, compound **2n**



Prepared according to General Procedure B, using 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (540 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-20% Et₂O in petroleum ether 40-60 °C) to afford the product as a colourless oil (368 mg, 68%, 21:79 α : β).

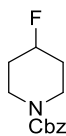
¹H NMR (500 MHz, CDCl₃): [21:79 mixture of α : β anomer]: δ 7.51 – 7.27 (m, 20H α + 20H β), 5.71 (dd, J = 53.2, 2.7 Hz, 1H α), 5.39 (dd, J = 52.8, 6.7 Hz, 1H β), 5.10 (d, J = 10.9 Hz, 1H α), 5.03 (d, J = 11.0 Hz, 1H β), 4.98 (d, J = 11.2 Hz, 1H α + 1H β), 4.96 – 4.88 (m, 3H 2H α + 2H β), 4.83 (d, J = 11.1 Hz, 1H α + 1H β), 4.75 (d, J = 12.1 Hz, 1H β), 4.72 (d, J = 12.1 Hz, 1H α), 4.69 – 4.63 (m, 3H 1 α + 2H β), 4.59 (d, J = 12.1 Hz, 1H α), 4.14 (t, J = 9.4 Hz, 1H α), 4.11 – 4.07 (m, 1H α), 3.93 – 3.90 (m, 1H α), 3.90 – 3.88 (m, 1H α), 3.88 – 3.82 (m, 1H α + 3H β), 3.81 – 3.75 (m, 1H α + 1H β), 3.75 – 3.66 (m, 1H α + 2H β).

¹³C NMR (126 MHz, CDCl₃): [21:79 mixture of α : β anomer]: δ 138.5 (α), 138.3 (β), 138.0 (α), 137.9 (β), 137.8 (β), 137.7 (β), 137.7 (α), 128.6 (α), 128.5 (α + β), 128.4 (α + 3 β), 128.4 (α), 128.2 (β), 128.1 (α), 128.0 (α), 128.0 (2 α + β), 127.9 (β), 127.9 (2 β), 127.9 (α + β), 127.8 (β), 127.8 (α), 127.8 (α), 127.7 (α + β), 109.9 (d, ¹ J_{CF} = 215.9 Hz (β)), 105.5 (d, ¹ J_{CF} = 227.0 Hz (α)), 83.4 (d, ² J_{CF} = 11.2 Hz (β)), 81.5 (d, ² J_{CF} = 21.5 Hz (β)), 81.4 (α), 79.3 (d, ² J_{CF} = 24.7 Hz (α)), 76.9 (β), 76.6 (α), 75.8 (α), 75.4 (β), 75.2 (α), 75.0 (β), 74.8 (d, ³ J_{CF} = 5.0 Hz (β)), 74.4 (d, ³ J_{CF} = 2.2 Hz (β)), 73.5 (β), 73.5 (α), 73.4 (α), 72.7 (d, ³ J_{CF} = 3.8 Hz (α)), 68.3 (β), 67.8 (α).

¹⁹F NMR (471 MHz, CDCl₃): [21:79 mixture of α : β anomer]: δ –137.78 (β), –149.20 (α).

Spectroscopic data were in agreement with literature values.^[18]

Benzyl 4-fluoro-1-piperidinecarboxylate, compound **2o**



Prepared according to General Procedure B, using 1-benzyl-4-hydroxypiperidine (191 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹⁹F NMR against a known standard (trifluorotoluene) determined conversion to product as 42%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% MeOH in DCM) to afford the desired compound as a colourless oil.

ν_{max} (solid): 3343, 3034, 2956, 2937, 2872, 2841, 1697, 1681, 1472, 1222 cm⁻¹.

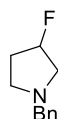
¹H NMR (500 MHz, CDCl₃): δ 7.39 – 7.28 (m, 5H), 5.13 (s, 2H), 4.90 – 4.74 (m, 1H), 3.64 – 3.47 (m, 4H), 1.81 (m, 4H).

¹³C NMR (126 MHz, CDCl₃): δ 138.6, 128.9, 128.5, 127.3, 93.7 (d, ¹J_{CF} = 175.3 Hz), 60.6 (d, ²J_{CF} = 23.0 Hz), 60.3, 52.3, 32.9 (d, ³J_{CF} = 21.9 Hz).

¹⁹F NMR (470 MHz, CDCl₃): δ -182.98.

HRMS (ESI): exact mass calculated for [M-HF+Na]⁺ (C₁₃H₁₅NO₂Na) requires m/z 240.1000, found m/z 240.0992.

1-Benzyl-2-fluoropyrrolidine, compound **2p**



Prepared according to General Procedure B, using 1-benzylpyrrolidin-3-ol (177 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹⁹F NMR against a known standard (trifluorotoluene) determined conversion to product as 72%. The reaction mixture was

subjected to the purification method outlined in the General Procedure (silica gel, 0-10% Et₂O in petroleum ether 40-60 °C) to afford the desired product as a brown oil.

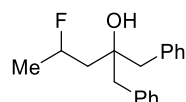
¹H NMR (400 MHz, CDCl₃): δ 7.43 – 7.18 (m, 5H), 5.26 – 5.08 (m, 1H), 3.79 – 3.57 (m, 2H), 2.96 – 2.68 (m, 3H), 2.51 – 2.45 (m, 1H), 2.27 – 1.93 (m, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 138.6, 128.9, 128.5, 127.3, 93.7 (d, ¹J_{CF} = 175.3 Hz), 60.6 (d, ²J_{CF} = 23.0 Hz), 60.3, 52.3, 32.9 (d, ²J_{CF} = 21.9 Hz).

¹⁹F NMR (376 MHz, CDCl₃): δ –168.19.

Spectroscopic data were in agreement with literature values.^[25]

2-Benzyl-4-fluoro-1-phenylpentan-2-ol, compound **2q**



Prepared according to General Procedure B, using 2-benzyl-4-fluoro-1-phenylpentan-2-ol (270 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μL, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% Et₂O in petroleum ether 40-60 °C) to afford the desired product as a colourless oil (133 mg, 49%).

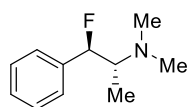
¹H NMR (400 MHz, CDCl₃): δ 7.36 – 7.20 (m, 10H), 5.21 – 4.98 (m, 1H), 2.95 – 2.80 (m, 4H), 1.91 – 1.79 (m, 2H), 1.62 – 1.47 (m, 1H), 1.30 (dd, *J* = 24.2, 6.3 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 137.3, 137.2, 131.0, 130.98, 128.4, 128.3, 126.7, 126.6, 88.7 (d, ¹J_{CF} = 162.7 Hz), 73.6, 46.5, 46.1 (d, ³J_{CF}, *J* = 2.1 Hz), 44.8 (d, ²J_{CF}, *J* = 18.9 Hz), 22.4 (d, ²J_{CF}, *J* = 23.0 Hz).

¹⁹F NMR (376 MHz, CDCl₃): δ –169.77.

Spectroscopic data were in agreement with literature values.^[10]

(1*R*,2*R*)-1-Fluoro-*N,N*-dimethyl-1-phenylpropan-2-amine, compound **2r**



Prepared according to General Procedure B, using (1*S*, 2*R*)-*N*-methylephedrine (180 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% Et₂O in petroleum ether 40-60 °C) to afford the desired product as a yellow oil (141 mg, 78%, 16:1 d.r.).

ν_{max} (solid): 3398, 2976, 2937, 2526, 2783, 1643, 1452.

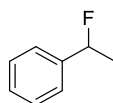
¹H NMR (400 MHz, CDCl₃): δ 7.37 – 7.30 (m, 2H), 7.29 – 7.24 (m, 3H), 5.76 (dd, J = 48.3, 2.7 Hz, 1H), 2.89 (ddd, J = 26.6, 6.9, 2.7 Hz, 1H), 2.40 (s, 6H), 1.01 (dd, J = 6.9, 1.6 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 139.6 (d, $^2J_{\text{CF}}$ = 20.5 Hz), 128.4, 127.8, 125.1 (d, $^3J_{\text{CF}}$ = 8.7 Hz), 94.3 (d, $^1J_{\text{CF}}$ = 178.7 Hz), 64.5 (d, $^2J_{\text{CF}}$ = 21.6 Hz), 41.6 (d, $^4J_{\text{CF}}$ = 2.2 Hz), 7.1 (d, $^3J_{\text{CF}}$ = 6.6 Hz).

¹⁹F NMR (470 MHz, CDCl₃): δ –194.87, –183.49 (*erythro* diastereomer).

HRMS (ESI): exact mass calculated for [M+H]⁺ (C₁₁H₁₇FN) requires m/z 182.1340, found m/z 182.1336.

(1-Fluoroethylbenzene), compound **2s**



Prepared according to General Procedure B, using 1-phenylethanol (122 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹⁹F NMR against a known standard (trifluorotoluene) determined conversion to product as 77%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the desired product as a colourless oil.

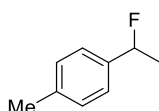
^1H NMR (400 MHz, CDCl_3): δ 7.43 – 7.31 (m, 5H), 5.64 (dq, J = 47.7, 6.4 Hz, 1H), 1.66 (dd, J = 23.9, 6.4 Hz, 3H).

^{13}C NMR (101 MHz, CDCl_3): δ 141.5 (d, $^2J_{\text{CF}}$ = 19.5 Hz), 128.6, 128.3 (d, $^3J_{\text{CF}}$ = 2.1 Hz), 125.3 (d, $^3J_{\text{CF}}$ = 6.7 Hz), 91.1 (d, $^1J_{\text{CF}}$ = 167.4 Hz), 23.07 (d, $^2J_{\text{CF}}$ = 25.3 Hz).

^{19}F NMR (376 MHz, CDCl_3): δ –167.01.

Spectroscopic data were in agreement with literature values.^[26]

1-(1-Fluoroethyl)-4-methylbenzene, compound **2t**



Prepared according to General Procedure B, using 1-(*p*-tolyl)ethanol (136 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ^{19}F NMR against a known standard (trifluorotoluene) determined conversion to product as 60%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a colourless oil.

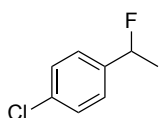
^1H NMR (400 MHz, CDCl_3): δ 7.32 – 7.17 (m, 4H), 5.61 (dq, J = 47.7, 6.4 Hz, 1H), 2.37 (s, 3H), 1.65 (dd, J = 23.8, 6.5 Hz, 3H).

^{13}C NMR (126 MHz, CDCl_3): δ 138.6 (d, $^2J_{\text{CF}}$ = 19.5 Hz), 138.2 (d, $^4J_{\text{CF}}$ = 2.3 Hz), 129.3, 125.5 (d, $^3J_{\text{CF}}$ = 6.3 Hz), 91.1 (d, $^1J_{\text{CF}}$ = 166.4 Hz), 23.0 (d, $^2J_{\text{CF}}$ = 25.5 Hz), 21.3.

^{19}F NMR (376 MHz, CDCl_3): δ –164.91.

HRMS reported previously by Yadav and coworkers: *Chem. Commun.* **2013**, 49, 2154–2156.

1-(1-Fluoroethyl)-4-chlorobenzene, compound **2u**



Prepared according to General Procedure B, using 4-chloro- α -methylbenzyl alcohol (157 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹⁹F NMR against a known standard (trifluorotoluene) determined conversion to product as 44%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% Et₂O in petroleum ether 40-60 °C) to afford the desired product as a colourless oil.

ν_{max} (solid): 2974, 2926, 1489, 1204, 1086, 1013, 825.

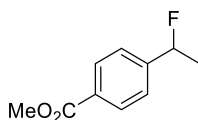
¹H NMR (400 MHz, CDCl₃): δ 7.39 – 7.25 (m, 4H), 5.61 (dq, J = 47.5, 6.4 Hz, 1H), 1.63 (dd, J = 23.9, 6.4 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 140.09 (d, $^2J_{\text{CF}}$ = 19.9 Hz), 134.10 (d, J_{CF} = 2.5 Hz), 128.79, 126.75 (d, $^3J_{\text{CF}}$ = 6.8 Hz), 90.37 (d, $^1J_{\text{CF}}$ = 168.4 Hz), 23.01 (d, $^2J_{\text{CF}}$ = 25.1 Hz).

¹⁹F NMR (471 MHz, CDCl₃): δ –167.46.

HRMS for the exact mass ion of this compound could not be found using either ESI or EI.

Methyl-4-(1-fluoroethyl)benzoate, compound **2v**



Prepared according to General Procedure B, using methyl 4-(1-hydroxyethyl)benzoate (180 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹⁹F NMR against a known standard (trifluorotoluene) determined conversion to product as 85%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% Et₂O in petroleum ether 40-60 °C) to afford the desired product as a colourless oil.

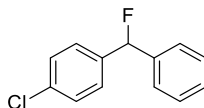
¹H NMR (400 MHz, CDCl₃): δ 8.04 (d, J = 7.6 Hz, 2H), 7.41 (d, J = 8.5 Hz, 2H), 5.67 (dq, J = 47.6, 6.5 Hz, 1H), 3.92 (s, 3H), 1.64 (dd, J = 24.0, 6.5 Hz, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 166.9, 146.6 (d, $^2J_{\text{CF}}$ = 19.6 Hz), 130.0, 125.0 (d, $^3J_{\text{CF}}$ = 7.2 Hz), 90.5 (d, $^1J_{\text{CF}}$ = 169.6 Hz), 52.3, 23.1 (d, $^2J_{\text{CF}}$ = 24.8 Hz).

^{19}F NMR (376 MHz, CDCl_3): δ -171.09.

Spectroscopic data were in agreement with literature values.^[27]

1-Chloro-4-(fluorophenyl)methylbenzene, compound **2w**



Prepared according to General Procedure B, using 4-chlorobenzylhydrol (219 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a white solid (28 mg, 13%).

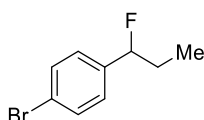
^1H NMR (400 MHz, CDCl_3): δ 7.45 – 7.26 (m, 9H), 6.46 (d, J = 47.3 Hz, 1H).

^{13}C NMR (126 MHz, CDCl_3): δ 139.4 (d, $^2J_{\text{CF}}$ = 21.5 Hz), 138.5 (d, $^2J_{\text{CF}}$ = 22.2 Hz), 134.5, 128.8, 128.7, 128.1 (d, $^3J_{\text{CF}}$ = 6.3 Hz), 126.7 (d, $^3J_{\text{CF}}$ = 6.2 Hz), 93.9 (d, $^1J_{\text{CF}}$ = 173.5 Hz).

^{19}F NMR (376 MHz, CDCl_3): δ -166.66.

Spectroscopic data were in agreement with literature values.^[28]

1-Bromo-4-(1-fluoropropyl)benzene, compound **2x**



Prepared according to General Procedure B, using 1-(4-bromophenyl)propan-1ol (215 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ^{19}F NMR against a known standard (trifluorotoluene) determined conversion to product as 78%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a colourless oil.

ν_{max} (solid): 2955, 2922, 2853, 2363, 2342, 2332, 1734, 1458, 1259 cm^{-1} .

^1H NMR (400 MHz, CDCl_3): δ 7.53 – 7.48 (m, 2H), 7.22 – 7.18 (m, 2H), 5.33 (ddd, $J = 47.5$, 7.5, 5.2 Hz, 1H), 2.05 – 1.74 (m, 2H), 0.97 (t, $J = 7.4$ Hz, 3H).

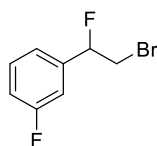
^{13}C NMR (101 MHz, CDCl_3): δ 139.5 (d, $^2J_{\text{CF}} = 20.3$ Hz), 131.7, 127.4 (d, $^3J_{\text{CF}} = 7.0$ Hz), 122.2 (d, $^4J_{\text{CF}} = 2.4$ Hz), 95.2 (d, $^1J_{\text{CF}} = 171.6$ Hz), 30.2 (d, $^2J_{\text{CF}} = 24.1$ Hz), 9.4 (d, $^3J_{\text{CF}} = 5.5$ Hz).

^{19}F NMR (376 MHz, CDCl_3): δ -176.56.

HRMS (EI): exact mass calculated for $[\text{M}]^+$ ($\text{C}_9\text{H}_{10}\text{F}^{79}\text{Br}$) requires m/z 215.9950, found m/z 215.9958.

HRMS (EI): exact mass calculated for $[\text{M}]^+$ ($\text{C}_9\text{H}_{10}\text{F}^{81}\text{Br}$) requires m/z 217.9929, found m/z 217.9928.

1-(2-Bromo-1-fluoroethyl)-3-fluorobenzene, compound **2y**



Prepared according to General Procedure B, using 2-bromo-1-(3-fluorophenyl)ethan-1-ol (219 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a colourless oil (75 mg, 34%).

ν_{max} (solid): 1593, 1489, 1450, 1271, 1250, 1240, 986, 874.

^1H NMR (500 MHz, 400 MHz, CDCl_3): δ 7.41 – 7.33 (m, 1H), 7.15 – 7.05 (m, 3H), 5.63 (ddd, $J = 46.6$, 7.3, 4.5 Hz, 1H), 3.71 – 3.56 (m, 2H).

^{13}C NMR (101 MHz, CDCl_3): δ 163.0 (d, $^1J_{\text{CF}} = 247.4$ Hz), 139.7 (dd, $^2J_{\text{CF}} = 20.8$, $^3J_{\text{CF}} = 7.2$ Hz), 130.6 (d, $^2J_{\text{CF}} = 8.1$ Hz), 121.5 (dd, $^3J_{\text{CF}} = 6.9$, $^4J_{\text{CF}} = 3.1$ Hz), 116.3 (d, $^2J_{\text{CF}} = 21.4$ Hz),

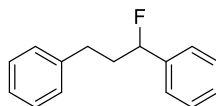
113.0 (dd, $^2J_{\text{CF}} = 22.8$, $^3J_{\text{CF}} = 7.5$ Hz), 92.0 (dd, $^1J_{\text{CF}} = 179.4$, $^4J_{\text{CF}} = 2.0$ Hz), 34.0 (d, $^2J_{\text{CF}} = 28.0$ Hz).

^{19}F NMR (376 MHz, CDCl_3): δ -111.74, -174.93.

HRMS (EI): exact mass calculated for $[\text{M}]^+$ ($\text{C}_8\text{H}_7\text{F}_2^{79}\text{Br}$) requires m/z 219.9699, found m/z 219.9705.

HRMS (EI): exact mass calculated for $[\text{M}]^+$ ($\text{C}_8\text{H}_7\text{F}_2^{81}\text{Br}$) requires m/z 221.9679, found m/z 221.9683.

(1-Fluoropropane-1,3-diyl)dibenzene, compound **2z**



Prepared according to General Procedure B, using 1,3-diphenylpropan-1-ol (212 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a colourless oil (43 mg, 20%).

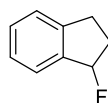
^1H NMR (400 MHz, CDCl_3): δ 7.42 – 7.28 (m, 7H), 7.25 – 7.17 (m, 3H), 5.44 (ddd, $J = 47.8$, 8.5, 4.4 Hz, 1H), 2.90 – 2.66 (m, 2H), 2.43 – 2.24 (m, 1H), 2.24 – 2.03 (m, 1H).

^{13}C NMR (126 MHz, CDCl_3): δ 141.2, 140.3 (d, $^2J_{\text{CF}} = 19.7$ Hz), 128.6, 128.4, 126.2, 125.7 (d, $^3J_{\text{CF}} = 6.7$ Hz), 93.7 (d, $^1J_{\text{CF}} = 170.9$ Hz), 38.9 (d, $^2J_{\text{CF}} = 23.8$ Hz), 31.4 (d, $^3J_{\text{CF}} = 4.0$ Hz).

^{19}F NMR (376 MHz, CDCl_3): δ -175.82.

Spectroscopic data were in agreement with literature values.^[29]

1-Indanyl fluoride, compound **2aa**



Prepared according to General Procedure B, using 1-indanol (134 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL,

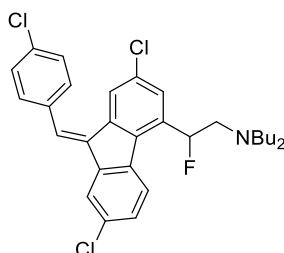
0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹⁹F NMR against a known standard (trifluorotoluene) determined conversion to product as 42%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the desired product as a brown solid. The product was isolated with a 10% impurity of the starting alcohol due to known instability on silica.^[30]

¹H NMR (400 MHz, CDCl₃): δ 7.50 (dtd, J = 7.5, 1.5, 0.7 Hz, 1H), 7.40 – 7.24 (m, 3H), 6.01 (ddd, J = 58.0, 6.1, 2.7 Hz, 1H), 3.29 – 3.11 (m, 1H), 2.99 – 2.78 (m, 1H), 2.57 – 2.24 (m, 2H).
¹³C NMR (101 MHz, CDCl₃): δ 145.0 (d, $^3J_{CF}$ = 4.8 Hz), 140.5 (d, $^2J_{CF}$ = 17.2 Hz), 129.9 (d, $^4J_{CF}$ = 3.9 Hz), 126.9 (d, $^4J_{CF}$ = 3.1 Hz), 125.7 (d, J_{CF} = 1.7 Hz), 125.2 (d, J_{CF} = 2.1 Hz), 97.1 (d, $^1J_{CF}$ = 172.1 Hz), 32.8 (d, $^2J_{CF}$ = 22.7 Hz), 30.1.

¹⁹F NMR (376 MHz, CDCl₃): δ –159.91.

Spectroscopic data were in agreement with literature values.^[30]

Fluorodeoxylumefantrine, compound **2ab**



Prepared according to General Procedure B, using lumefantrine (523 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the desired product as a yellow oil (292 mg, 55%).

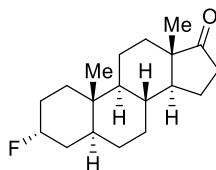
¹H NMR (400 MHz, CDCl₃): δ 7.76 – 7.61 (m, 3H), 7.50 – 7.42 (m, 6H), 7.35 (dd, J = 8.4, 2.0 Hz, 1H), 6.16 (ddd, J = 48.2, 7.4, 2.0 Hz, 1H), 3.03 – 2.78 (m, 2H), 2.71 – 2.49 (m, 4H), 1.49 – 1.26 (m, 8H), 0.91 (t, J = 7.2 Hz, 6H).

^{13}C NMR (101 MHz, CDCl_3): δ 141.5, 138.5, 136.1 (d, $^2J_{\text{CF}} = 20.8$ Hz), 135.8, 135.0, 134.9, 134.7 (d, $^3J_{\text{CF}} = 5.1$ Hz), 134.2, 133.5, 132.9, 130.7, 129.3, 128.8, 128.3, 126.0 (d, $^3J_{\text{CF}} = 13.0$ Hz), 124.6, 123.8, 120.8, 92.2 (d, $^1J_{\text{CF}} = 176.1$ Hz), 59.4 (d, $^2J_{\text{CF}} = 22.1$ Hz), 54.4, 29.1, 20.8, 14.3.

^{19}F NMR (377 MHz, CDCl_3): δ -180.20.

Spectroscopic data were in agreement with literature values.^[18]

3 α -Fluoro-5 α -androstan-17-one, compound **2ac**



Prepared according to General Procedure A, using 3 β -hydroxy-5 α -androstan-17-one (290 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF_2 (203 mg, 2.0 mmol, 2.0 equiv.), and H_2O (18 μL , 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-20% Et_2O in petroleum ether 40-60 $^\circ\text{C}$) to afford the desired product as a colourless oil (201 mg, 69%, >20:1 d.r.).

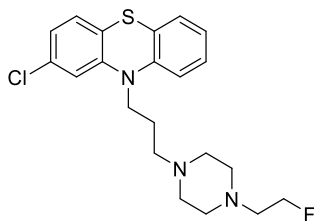
^1H NMR (500 MHz, CDCl_3): δ 4.81 (dt, $J = 48.8, 3.1$ Hz, 1H), 2.43 (dd, $J = 19.2, 8.9$ Hz, 1H), 2.07 (dt, $J = 19.3, 9.1$ Hz, 1H), 1.98 – 1.85 (m, 2H), 1.83 – 1.76 (m, 2H), 1.71 – 1.46 (m, 8H), 1.37 – 1.18 (m, 6H), 1.02 (qd, $J = 12.8, 4.4$ Hz, 1H), 0.86 (s, 3H), 0.81 (s, 4H).

^{13}C NMR (126 MHz, CDCl_3): δ 221.6, 89.5 (d, $^1J_{\text{CF}} = 165.7$ Hz), 54.3, 51.6, 47.9, 39.5, 36.0, 35.1, 34.0 (d, $^2J_{\text{CF}} = 21.1$ Hz), 32.5, 31.7, 30.9, 28.2, 27.2 (d, $^2J_{\text{CF}} = 21.9$ Hz), 21.9, 20.2, 14.0, 11.3.

^{19}F NMR (376 MHz, CDCl_3): δ -181.11.

Spectroscopic data were in agreement with literature values.^[31]

2-Chloro-10-(3-(4(2-fluoroethyl)piperazin-1-yl)propyl)-4a,5a,9a,10a-tetrahydro-10H-phenothiazine, compound **2ad**



Prepared according to General Procedure B, using perphenazine (202 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, analysis by ¹H NMR against a known standard (naphthalene) determined conversion to product determined as 60%. The reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0-10% MeOH in DCM) to afford the desired product as a pale yellow oil.

ν_{max} (solid): 2934, 2810, 2360, 2342, 1661, 1640, 1566, 1456, 1406, 1244 cm⁻¹.

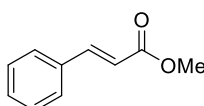
¹H NMR (500 MHz, CDCl₃): δ 7.17 – 7.07 (m, 2H), 7.01 (d, J = 8.1 Hz, 1H), 6.95 – 6.81 (m, 4H), 4.55 (dt, J = 47.6, 4.9 Hz, 2H), 3.90 (t, J = 6.8 Hz, 2H), 2.68 (dt, J = 28.2, 4.9 Hz, 2H), 2.62 – 2.36 (m, 10H), 2.13 – 1.85 (m, 2H).

¹³C NMR (126 MHz, CDCl₃): δ 146.6, 144.6, 133.4, 128.0, 127.7, 127.6, 125.0, 123.7, 123.1, 122.4, 116.0, 115.97, 82.0 (d, $^1J_{\text{CF}}$ = 167.5 Hz), 58.2 (d, $^2J_{\text{CF}}$ = 19.8 Hz), 55.6, 53.4, 53.2, 45.4, 24.2.

¹⁹F NMR (471 MHz, CDCl₃): δ -218.35.

HRMS (ESI): exact mass calculated for [M+H]⁺ (C₂₁H₁₆N₃ClFS) requires m/z 406.1520, found m/z 406.1513.

Methyl cinnamate, compound **2ae**



Prepared according to General Procedure B, using 3-hydroxy-3-phenylpropanoate (180 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0

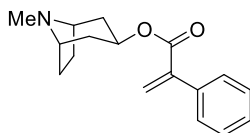
mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the elimination product as a white solid (121 mg, 75%).

¹H NMR (400 MHz, CDCl₃): δ 7.53 (d, *J* = 16.0 Hz, 1H), 7.32 – 7.24 (m, 2H), 7.19 – 7.11 (m, 3H), 6.28 (d, *J* = 16.1 Hz, 1H), 3.59 (s, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 166.6, 144.2, 133.9, 129.7, 128.3, 127.6, 117.3, 50.9.

Spectroscopic data were in agreement with literature values.^[32]

8-Methyl-8-azabicyclo[[3.2.10]octan-3-yl-phenylacrylate, compound **2af**



Prepared according to General Procedure B, using atropine (289 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μL, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the elimination product as a white solid (157 mg, 58%).

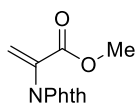
ν_{max} (solid): 2936, 2876, 1710, 1614, 1192 cm⁻¹.

¹H NMR (500 MHz, CDCl₃): δ 7.39 – 7.30 (m, 5H), 6.34 (d, *J* = 1.3 Hz, 1H), 5.86 (d, *J* = 1.3 Hz, 1H), 5.13 (t, *J* = 5.3 Hz, 1H), 3.14 (dq, *J* = 5.4, 2.9 Hz, 2H), 2.29 (s, 3H), 2.24 – 2.17 (m, 2H), 1.96 – 1.91 (m, 2H), 1.80 – 1.72 (m, 4H).

¹³C NMR (126 MHz, CDCl₃): δ 165.9, 142.0, 136.9, 128.4, 128.2, 128.1, 126.8, 67.9, 60.0, 40.3, 36.4, 25.4

HRMS (ESI): exact mass calculated for [M+H]⁺ (C₁₇H₂₂O₂N) requires *m/z* 272.1572, found *m/z* 272.1639.

Methyl 2-(1,3-dioxoisindolin-2-yl)acrylate, compound **2ag**



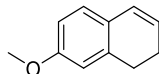
Prepared according to General Procedure B, using methyl-2-(1,3-dioxoisindol-2-yl)-3-hydroxypropanoate (250 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the elimination product as a white solid (109 mg, 47%).

¹H NMR (400 MHz, CDCl₃): δ 7.92 – 7.87 (m, 2H), 7.79 – 7.73 (m, 2H), 6.67 (d, J = 0.7 Hz, 1H), 5.98 (d, J = 0.7 Hz, 1H), 3.80 (s, 3H).

¹³C NMR (126 MHz, CDCl₃): δ 166.5, 162.8, 134.6, 131.9, 129.2, 128.3, 124.0, 52.9.

Spectroscopic data were in agreement with literature values.^[33]

7-Methoxy-1,2-dihydronaphthalene, compound **2ah**



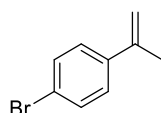
Prepared according to General Procedure B, using 6-methoxy-1,2,3,4-tetrahydronaphthalene-1-ol (178 mg, 1 mmol, 1 equiv.), Cu(I)Cl (1.0 g, 0.01 mmol, 1 mol%), DIC (0.15 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the elimination product as a colourless oil (114 mg, 71%).

¹H NMR (400 MHz, CDCl₃): δ 6.96 (d, J = 9.0 Hz, 1H), 6.69 (m, 2H), 6.43 (dt, J = 9.6, 1.9 Hz, 1H), 5.95 – 5.85 (m, 1H), 3.80 (s, 3H), 2.79 (t, J = 8.2 Hz, 2H), 2.35 – 2.26 (m, 2H).

¹³C NMR (101 MHz, CDCl₃): δ 158.7, 137.3, 127.5, 127.3, 127.0, 126.1, 113.9, 111.2, 55.4, 28.2, 23.1.

Spectroscopic data were in agreement with literature values.^[34]

4-Bromo- α -methylstyrene, compound **2ai**



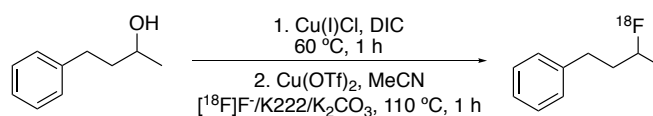
Prepared according to General Procedure B, using 2-(4-bromophenyl)propan-2-ol (215 mg, 1.0 mmol, 1.0 equiv.), Cu(I)Cl (1.0 mg, 0.01 mmol, 1.0 mol%), DIC (0.5 mL, 1.0 mmol, 1.0 equiv.), CPME (2 mL, 0.5 M), CuF₂ (203 mg, 2.0 mmol, 2.0 equiv.), and H₂O (18 μ L, 1.0 mmol, 1.0 equiv.). After the reaction was complete, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 100% petroleum ether 40-60 °C) to afford the elimination product as a white solid (71 mg, 36%).

¹H NMR (400 MHz, CDCl₃): δ 7.48 – 7.41 (m, 2H), 7.37 – 7.30 (m, 2H), 5.37 (s, 1H), 5.11 (s, 1H), 2.13 (s, 3H).

¹³C NMR (101 MHz, CDCl₃): δ 142.3, 140.2, 131.4, 127.3, 121.5, 113.2, 21.8.

Spectroscopic data were in agreement with literature values.^[35]

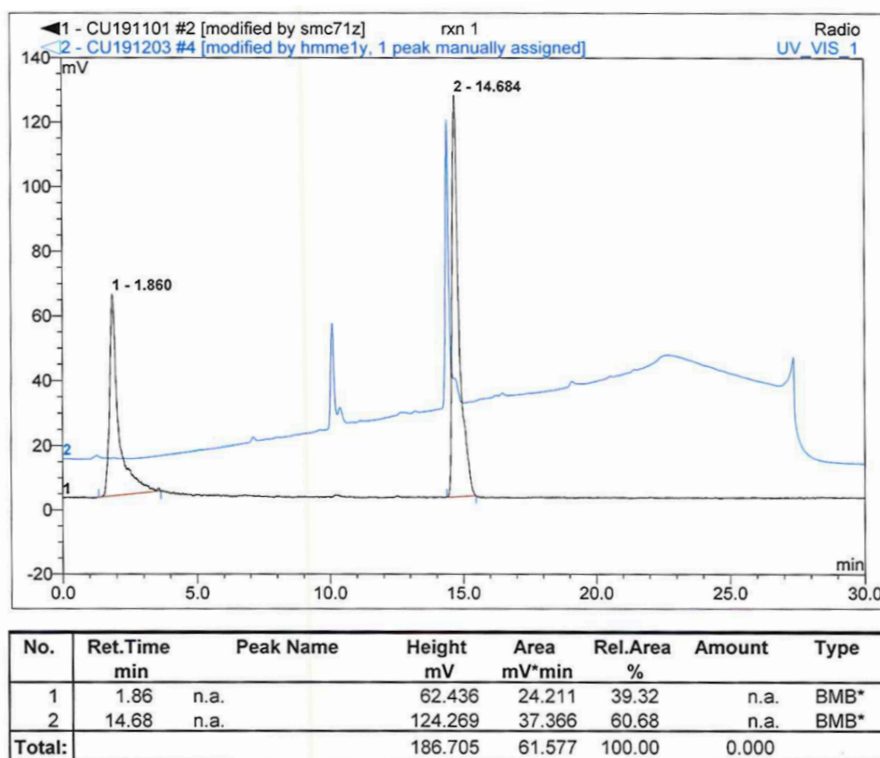
9. Radiochemical experiments from Scheme 4



To a V-vial was added 4-phenyl-2-butanol (0.050 mL, 0.32 mmol, 1 equiv.), Cu(I)Cl (1.0 mg, 0.010 mmol, ca 3 mol%), and DIC (0.050 mL, 0.32 mmol, 1 equiv.). The vial was capped and the reaction mixture was heated at 60 °C for 1 h. The reaction was then cooled to room temperature. Cu(OTf)₂ (50 mg, 0.13 mmol, 0.4 equiv.) was dissolved in MeCN (0.25 mL) and added to the reaction mixture. [¹⁸F]Fluoride was immobilized on a QMA cartridge and then eluted with K222/potassium carbonate in 70:30 MeCN/H₂O solution (1 mL). The [¹⁸F]fluoride/K222/potassium carbonate solution (~0.3 mL, ~180–330 MBq) was then added to the reaction mixture. The mixture was then heated at 110 °C for 1 h. The reaction mixture was then filtered and analysis of the solution by radio-HPLC and radio-TLC showed a radiochemical yield of 54.2 ± 6.3% (n = 2).

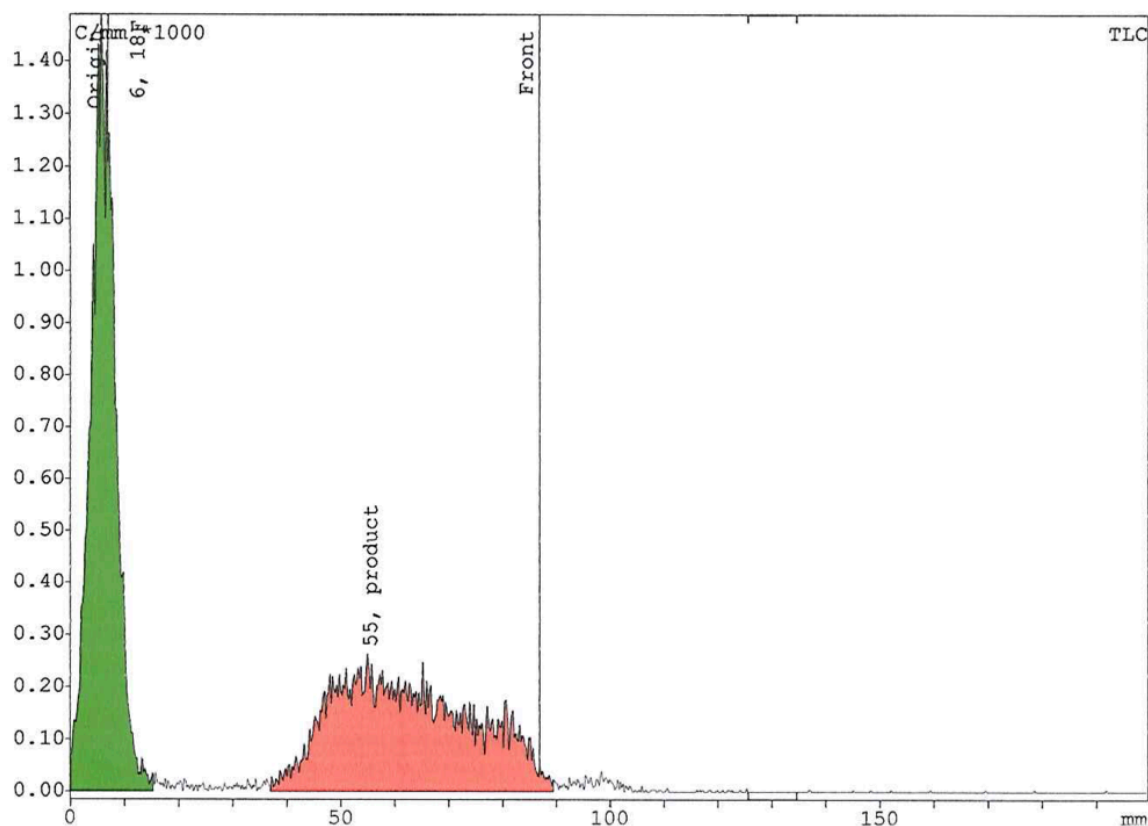
Radio-HPLC and UV-Vis HPLC Chromatograms

Radio-HPLC trace (black) of reaction mixture along with UV-Vis HPLC (blue) of **2a** is provided.



Radio-TLC Scans of Two Selected Reactions

Reaction 1:



Sample description

Study: research
 Measurement: Cu191101_rxn1, started: 01/11/2019 09:53
 Method: FMISO Date: 23/07/2019 11:37
 Instrument: default station
 Origin: 7 mm Front: 87 mm
 Meas. time: 0:03:03 h:m:s
 Integration method: FMISO Date: 06/12/2019 09:26
 Detector: PET - SN: 10108 - Version: 1.00 / Trigger: 16 - Gain: 100
 Collimator: None - Detector height: 4 mm
 Radio detector: Elysia-raytest miniGita Single/Dual Serial Nr: 37026
 Software Version: 6.2, service pack 1, Build 6394

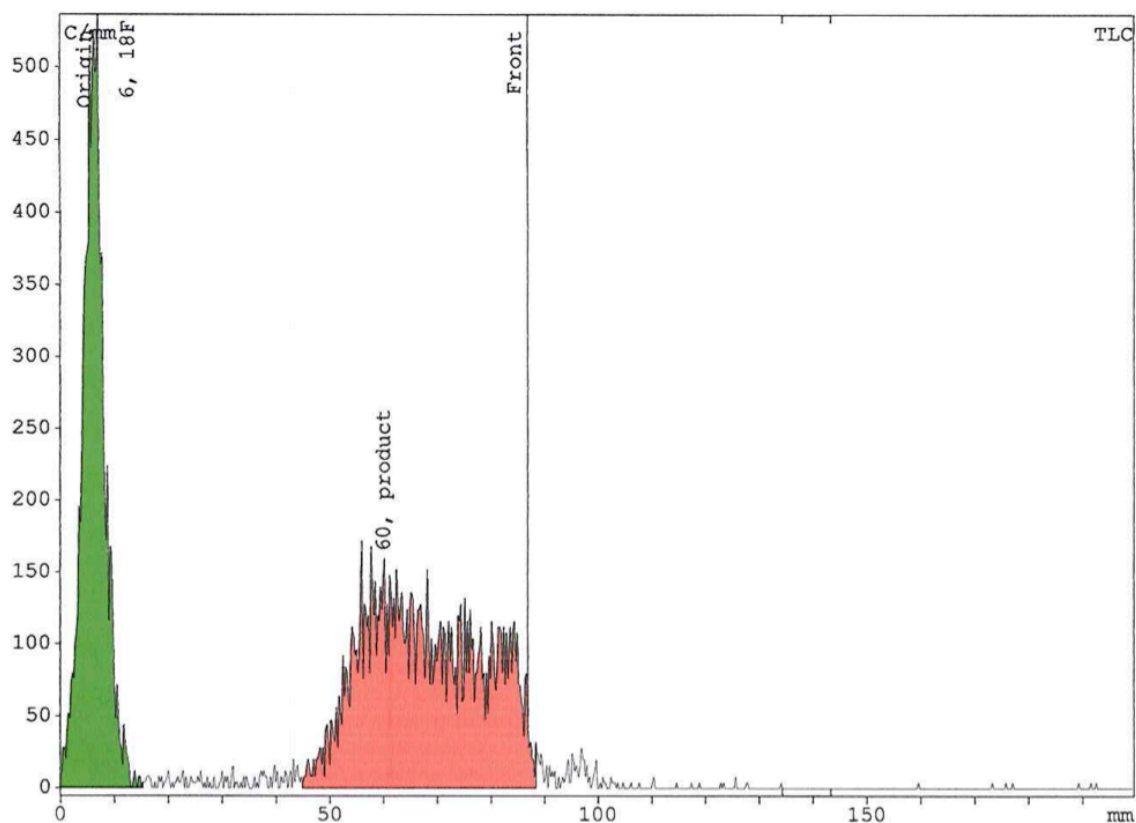
Preparation / SOP

Preparation steps	Sign/Lot
Put plate in	OK
Enter FMISO batch number	OK

Integration TLC

Substance	R/F	%Total %	Type	Area Counts	%Area %	Signal to noise
18F	-0.016	50.40	DD(C)	7754.000	52.10	0.0
product	0.603	46.33	DD(M)	7128.000	47.90	0.0
Sum in ROI	-	-	-	14882.000	100.00	-
Total area	-	-	-	15385.000	-	-
Area (total) RF	-	-	-	10118.000	-	-
1 BKG-ROIs	-	-	-	0.0000	-	-

Reaction 2:



Sample description

Study: research
 Measurement: CU191121, started: 21/11/2019 09:45
 Method: FMISO Date: 23/07/2019 11:37
 Instrument: default station
 Origin: 7 mm Front: 87 mm
 Meas. time: 0:03:03 h:m:s
 Integration method: FMISO Date: 06/12/2019 09:26
 RXn 1
 Detector: PET - SN: 10108 - Version: 1.00 / Trigger: 16 - Gain: 100
 Collimator: None - Detector height: 4 mm
 Radio detector: Elysia-raytest miniGita Single/Dual Serial Nr: 37026
 Software Version: 6.2, service pack 1, Build 6394

Preparation / SOP

Preparation steps	Sign/Lot
Put plate in	OK
Enter FMISO batch number	OK

Integration TLC

Substance	R/F	%Total %	Type	Area Counts	%Area %	Signal to noise
18F	-0.006	37.61	DD(C)	2417.000	39.53	0.0
product	0.659	57.54	DD(R)	3698.000	60.47	0.0
Sum in ROI	-	-	-	6115.000	100.00	-
Total area	-	-	-	6427.000	-	-
Area (total) RF	-	-	-	4691.000	-	-
1 BKG-ROIs	-	-	-	0.0000	-	-

10. EPR analysis of CuF_2 and $\text{Cu}(\text{OTf})_2/\text{S7}$ (Figure 1)

Samples of neat powdered CuF_2 were transferred into 4 mm outer diameter quartz EPR tubes (from Wilmad). Samples of $\text{Cu}(\text{OTf})_2$ were prepared as 5 mM solutions in MeOH:EtOH 1:4 as pure solution, with one equivalent of 1,3-diisopropylurea or with one half and one equivalents of **S7**. Solutions were transferred into custom made 3 mm outer diameter high purity quartz tubes.

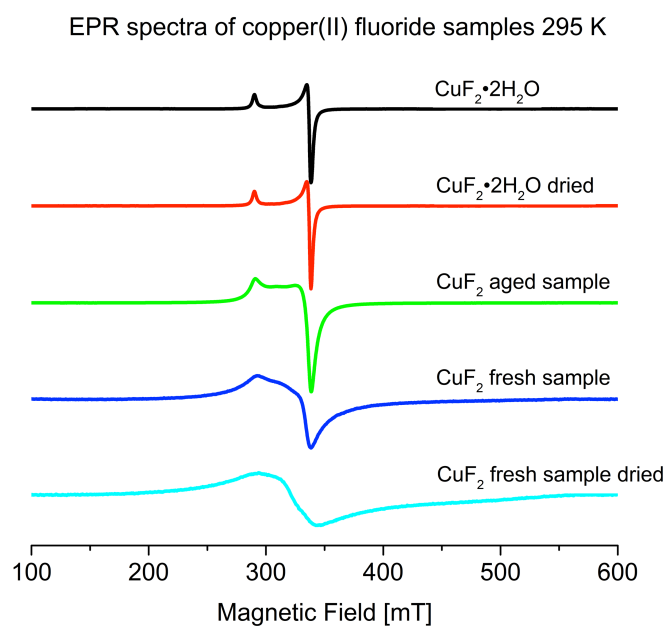


Figure S1. EPR analysis of CuF_2 samples.

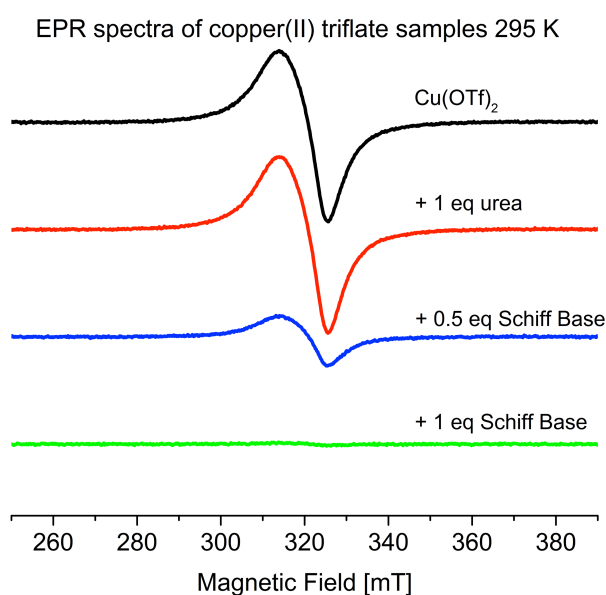


Figure S2. EPR analysis of $\text{Cu}(\text{OTf})_2$ in presence of **S7** at 295 K.

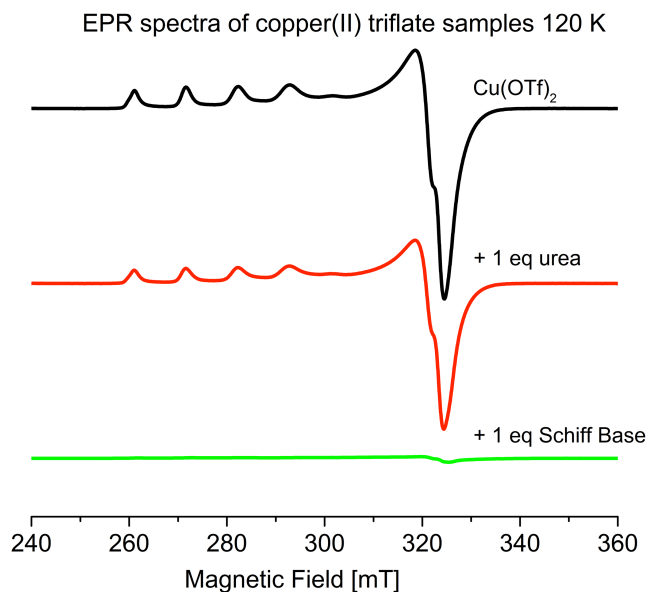


Figure S3. EPR analysis of $\text{Cu}(\text{OTf})_2$ in presence of **S7** at 120 K.

The EPR spectrum of $\text{CuF}_2 \cdot 2\text{H}_2\text{O}$ shows an axial g tensor ($g_{\perp} = 2.417$, $g_{\parallel} = 2.077$) and reproduces an identical spectrum even after heating the sample at 433 K for overnight. This suggests, the water molecular as axial ligands remain bound to the Cu metal ion under these conditions. Notably, the anhydrous CuF_2 obtained from Sigma Aldrich shows different spectra and this can be tentatively attributed to reaction with moisture from air (due to the hygroscopic nature of these complexes) over time. Interestingly, the fresh sample shows broader lines than the aged sample and an even border line is observed on heating in the drying oven at 433 K. Nevertheless, these spectra demonstrate that CuF_2 with water moisture from the air and gives an EPR spectrum similar to $\text{CuF}_2 \cdot 2\text{H}_2\text{O}$. Remarkably, none of the spectra resolve hyperfine interaction with the $^{63/65}\text{Cu}$ nuclei which may be due to the strong interaction between electron spins and/or fast relaxation of these nuclei.

Solution and powder EPR spectra of copper(II) triflate remain unchanged when adding 1,3-diisopropylurea. However, adding **S7** the EPR signal is reduced stoichiometrically. To confirm this is not due broadening due to slower motion the vanishing EPR signal upon addition of one equivalent **S7** was confirmed by frozen solution EPR.

11. ssNMR analysis of CuF₂ samples

This report considers the ¹H and ¹⁹F NMR spectra of anhydrous CuF₂, aged CuF₂, and CuF₂•2H₂O. The crystal structures of the two materials,^{36,37} shows that the Cu(II) is square planar in both cases, with the unpaired electron in the high-energy d(x²–y²) orbital (*i.e.*, the F atoms are in the plane of the unpaired electron). CuF₂•2H₂O has been studied by solid-state NMR spectroscopy,³⁸ and it was reported that the ¹H resonance is not significantly affected by any hyperfine interactions with the unpaired electron, whereas the ¹⁹F nuclei experience a much larger hyperfine interaction (up to ~5000 ppm at 300 K and much larger at lower temperature). Yamakawa *et al.*³⁹ report that the ¹⁹F NMR spectrum of CuF₂ is not readily observed (4.7 T, 20 kHz MAS), but Hua *et al.*⁴⁰ reported a sharp resonance at –190 ppm using more rapid MAS (40 kHz).

¹H MAS NMR

Figure S4 shows the ¹H MAS NMR spectra of the three samples noted above. For the anhydrous CuF₂, the signal is (as might be expected) low intensity and essentially featureless. This signal can presumably be attributed to surface hydration. In CuF₂•2H₂O, a much more intense signal is observed with an isotropic shift of 45 ppm and a large paramagnetic shift anisotropy ($\Omega = 302$ ppm, $\kappa = 0.0$), which can be attributed to the Cu-bound H₂O. The ¹H NMR spectrum of the aged material is essentially a superposition of the spectra of the two pure phases, suggesting that there is no other water containing species formed upon hydration of CuF₂ and the material converts directly to CuF₂•2H₂O.

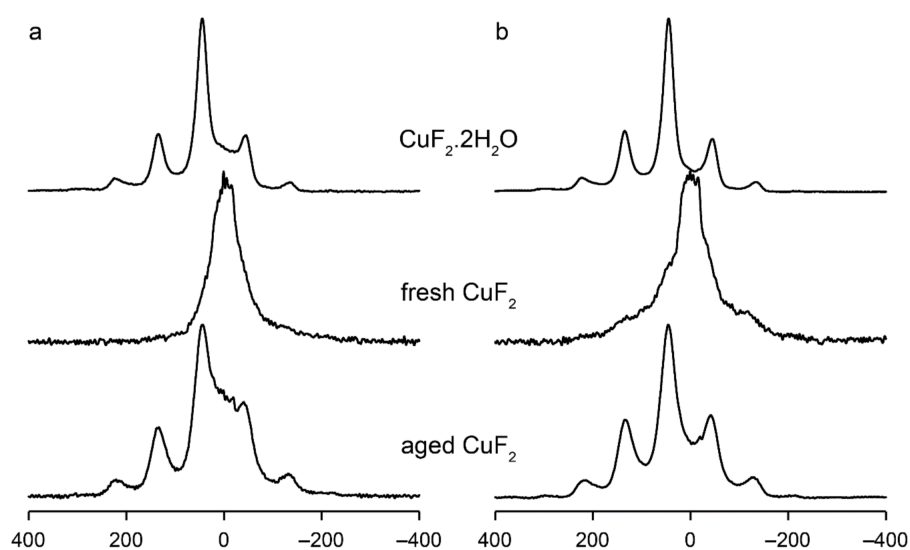


Figure S4. ¹H (14.1 T, 55 kHz MAS) NMR spectra of the three samples with a T1 relaxation filter chosen to show (a) paramagnetic and diamagnetic H and (b) paramagnetic H.

¹⁹F MAS NMR

For $\text{CuF}_2 \cdot 2\text{H}_2\text{O}$, no signal was observed between 0 and 9000 ppm, but a broad signal with isotropic shift of -76 ppm and shift anisotropy $\Omega = 400$ ppm, $\kappa = 0$ was observed, as well as a sharper signal at -152 ppm (Figure S5). However, this sharper signal had a very slow T1 relaxation, characteristic of a diamagnetic rather than a paramagnetic phase, and may arise from reaction of fluoride with the rotor walls (made from zirconia). The fresh anhydrous CuF_2 again showed the broad resonance at -76 ppm, although with much lower signal intensity and much broader lines, suggesting more rapid paramagnetic T2 relaxation. The aged CuF_2 showed only the paramagnetic ^{19}F signal, but with higher intensity and resolution than the anhydrous CuF_2 . Detailed analysis of the ^{19}F NMR spectra is complicated by the fact that it is unlikely that the complete signal is being observed in each case.

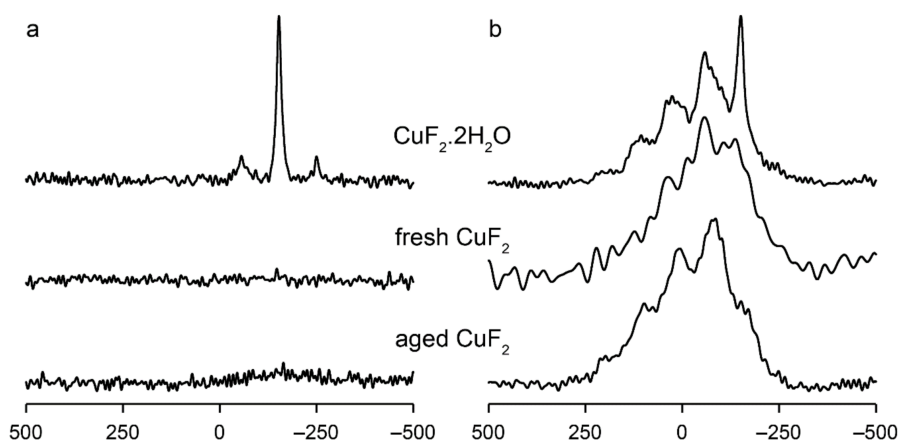


Figure S5. ^{19}F (14.1 T, 55 kHz MAS) NMR spectra of the three samples with a T1 relaxation filter chosen to show (a) paramagnetic and diamagnetic F and (b) paramagnetic F.

12. Powder XRD analysis (Figure 2)

The manuscript Figure 2 is a composite of three individual spectra. These are provided below.

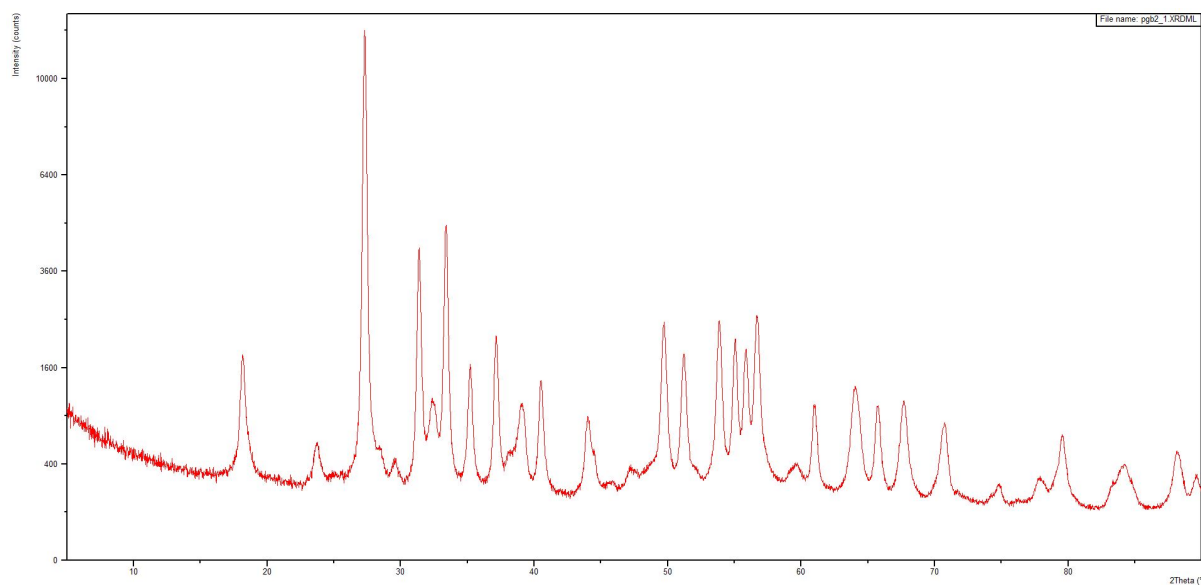


Figure S6. Anhydrous CuF_2 .

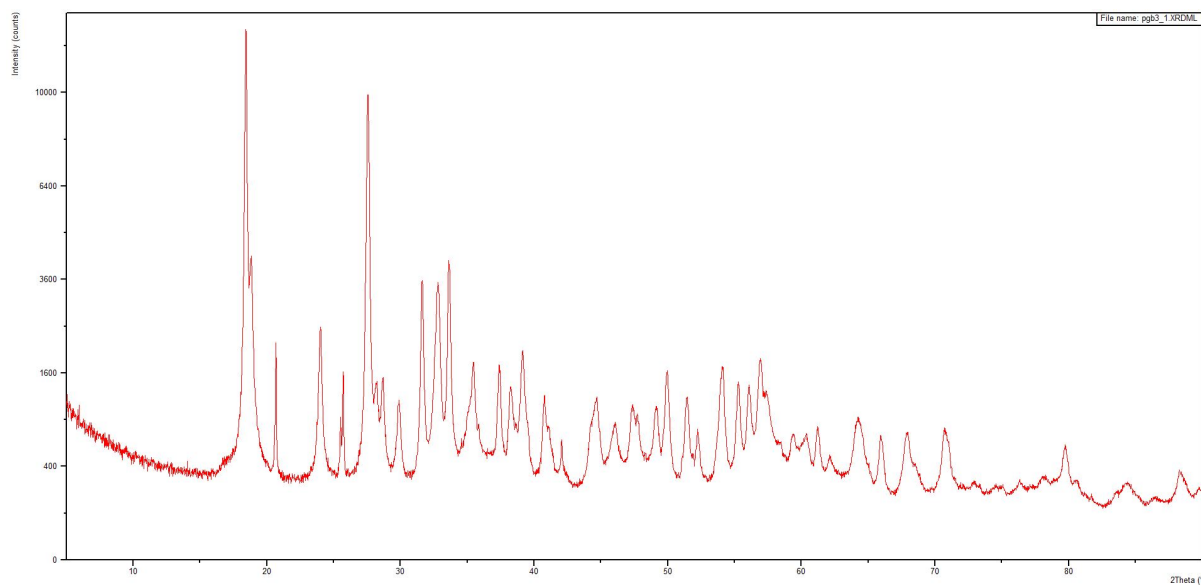


Figure S7. Aged CuF_2 .

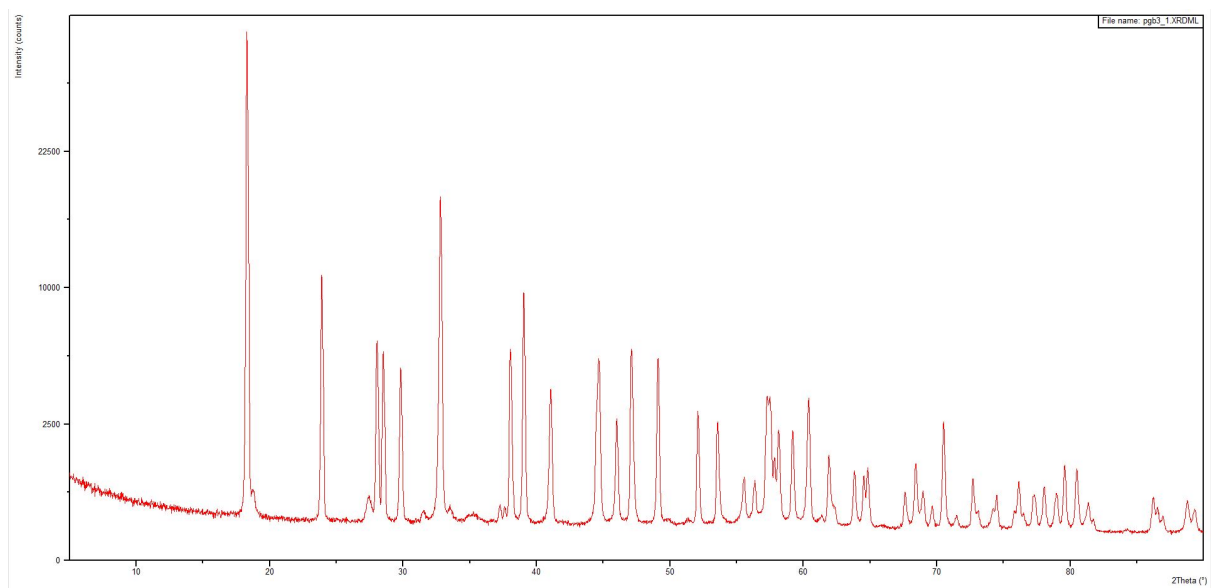


Figure S8. $\text{CuF}_2 \cdot 2\text{H}_2\text{O}$.

13. References

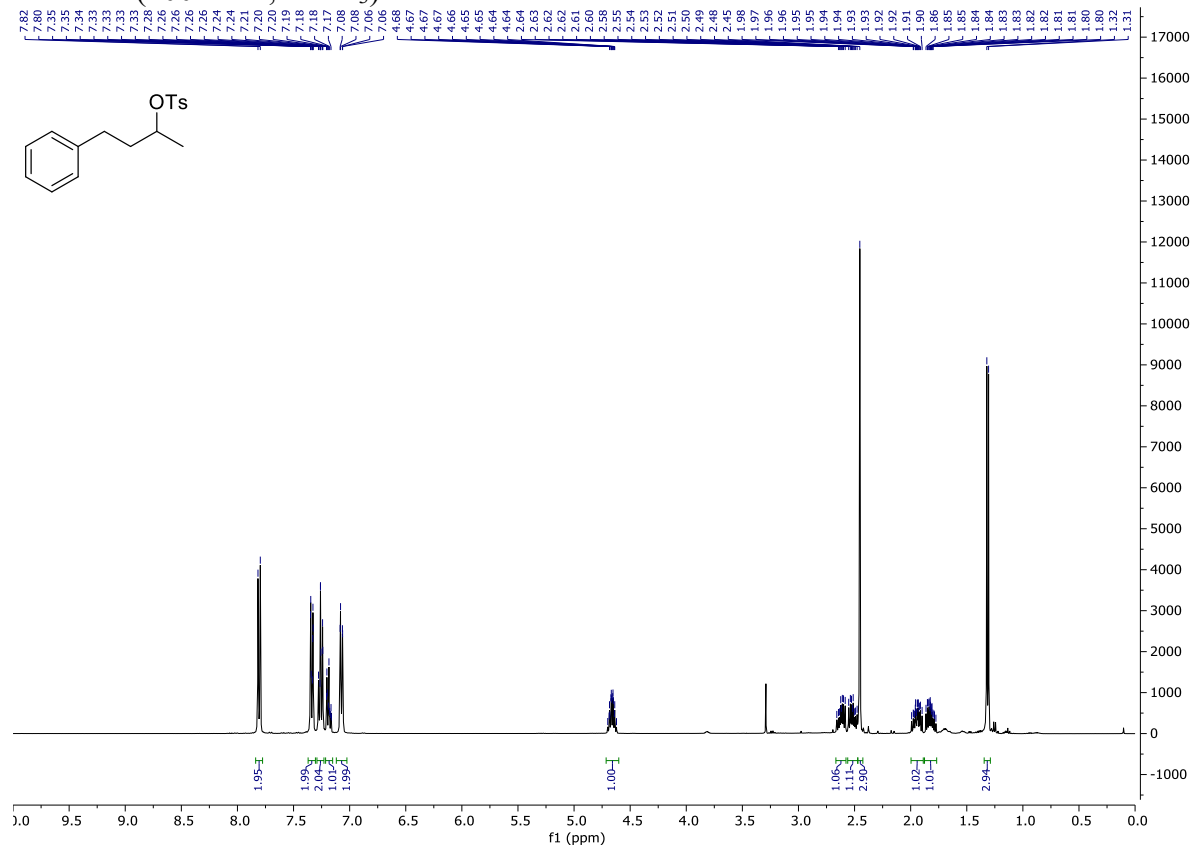
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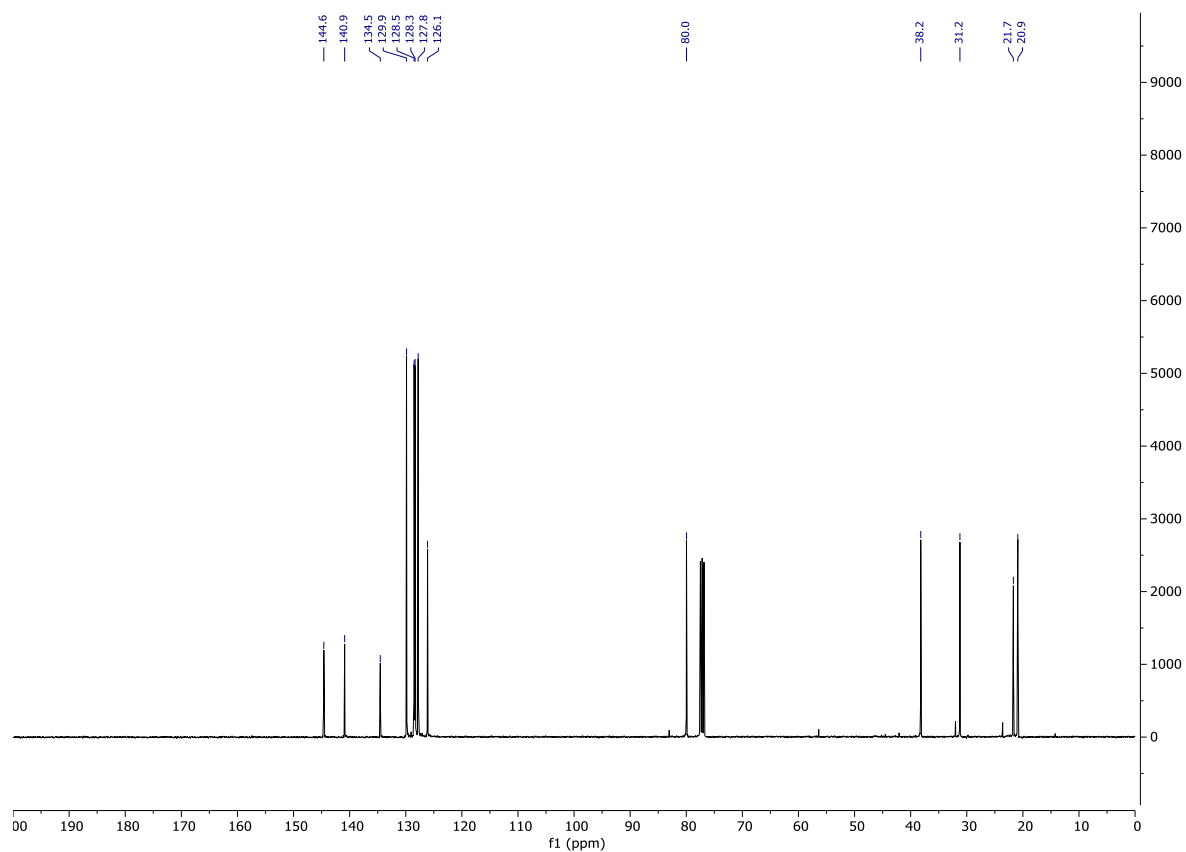
14. Spectra

4-Phenyl-2-butanol tosylate (S1)

^1H NMR (400 MHz, CDCl_3)

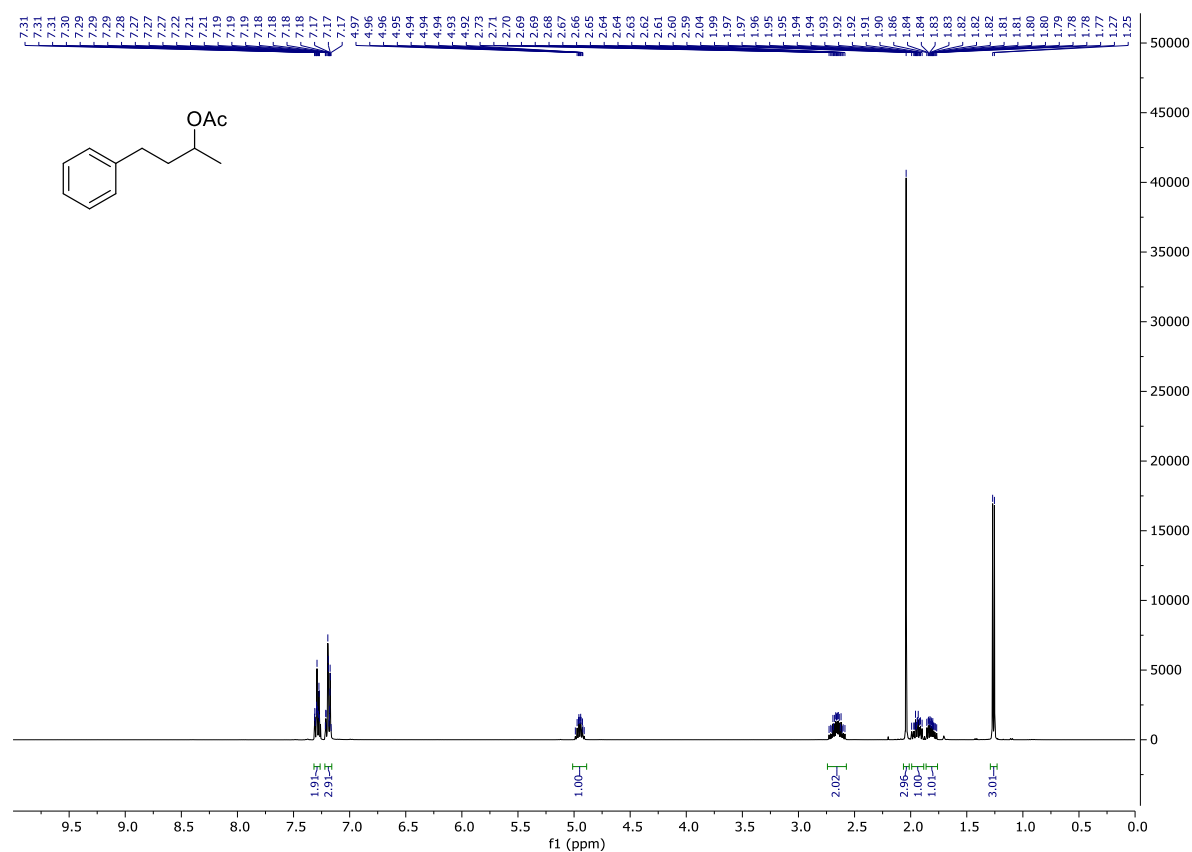


^{13}C NMR (101 MHz, CDCl_3)

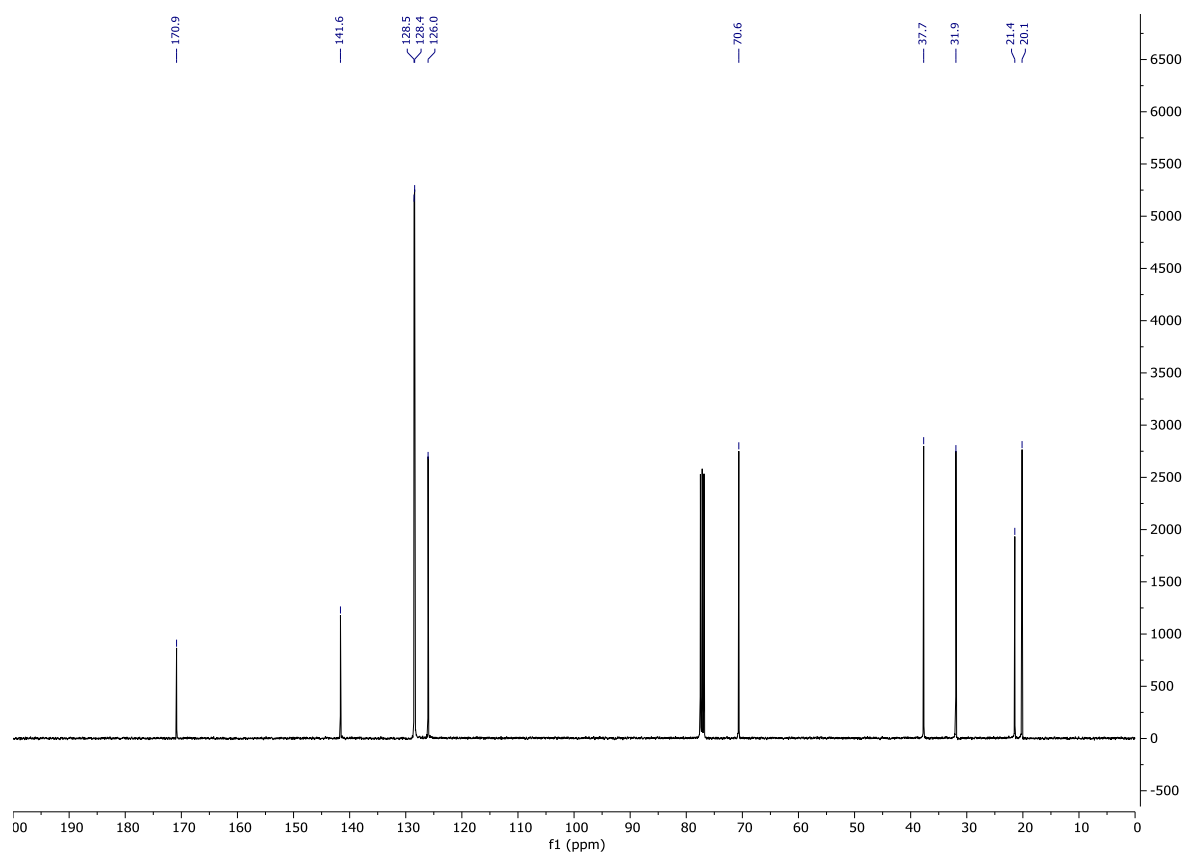


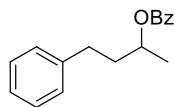
4-Phenylbutan-2-yl acetate (S2)

^1H NMR (400 MHz, CDCl_3)



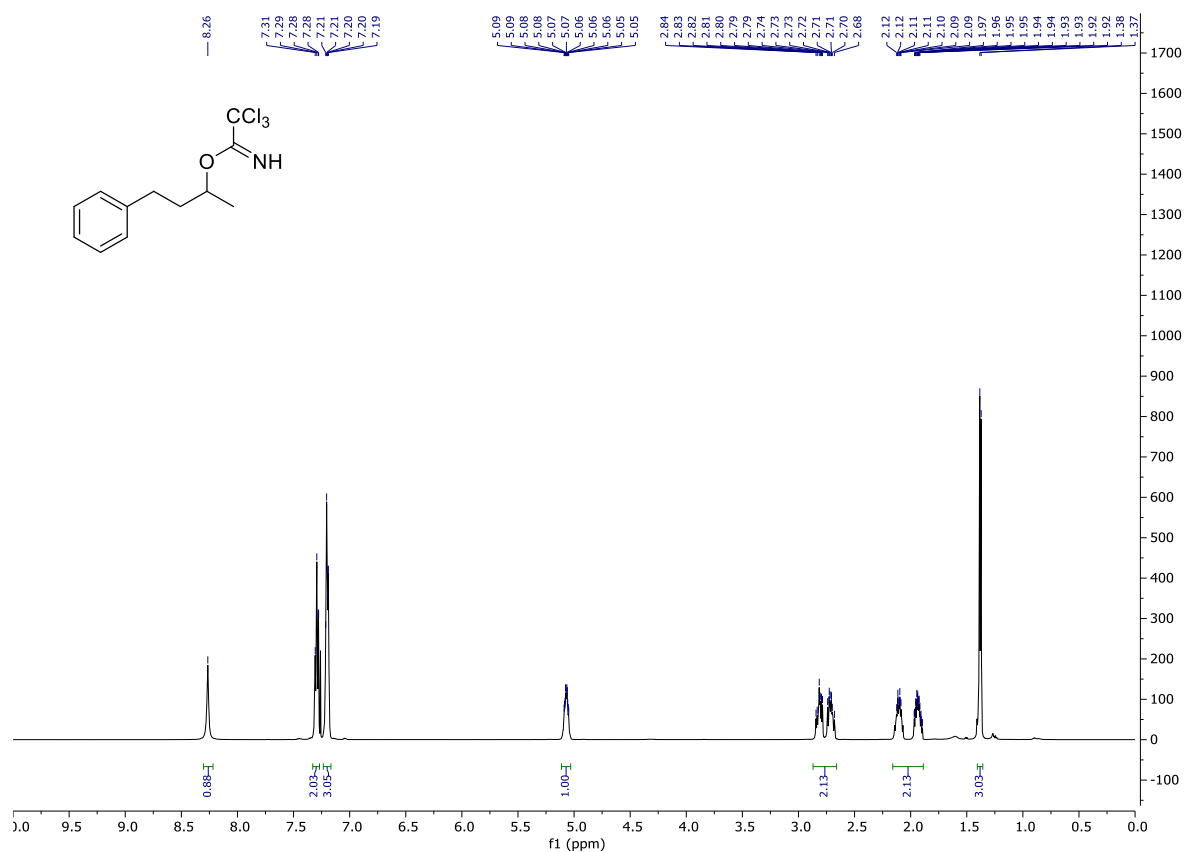
^{13}C NMR (101 MHz, CDCl_3)



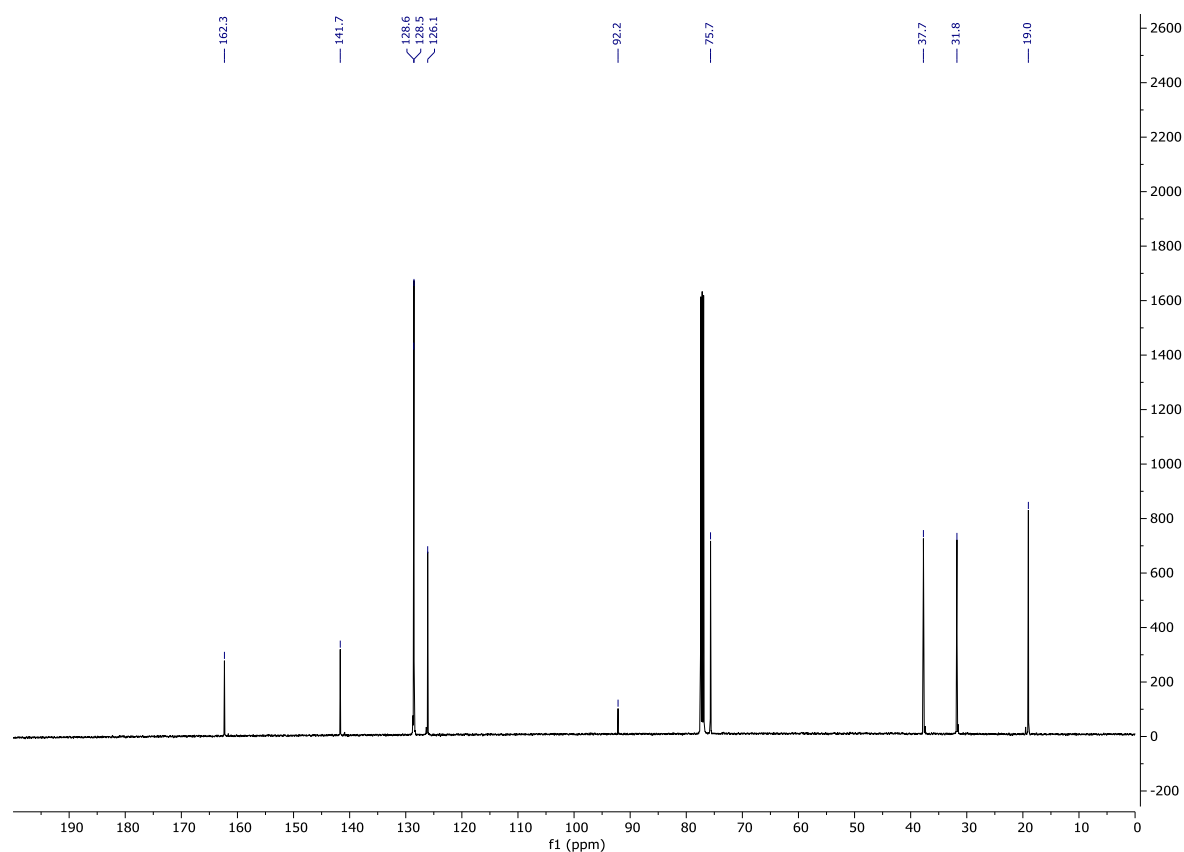
¹H NMR (500 MHz, CDCl₃)

4-Phenylbutan-2-yl trichloroacetimidate (S4)

^1H NMR (500 MHz, CDCl_3)

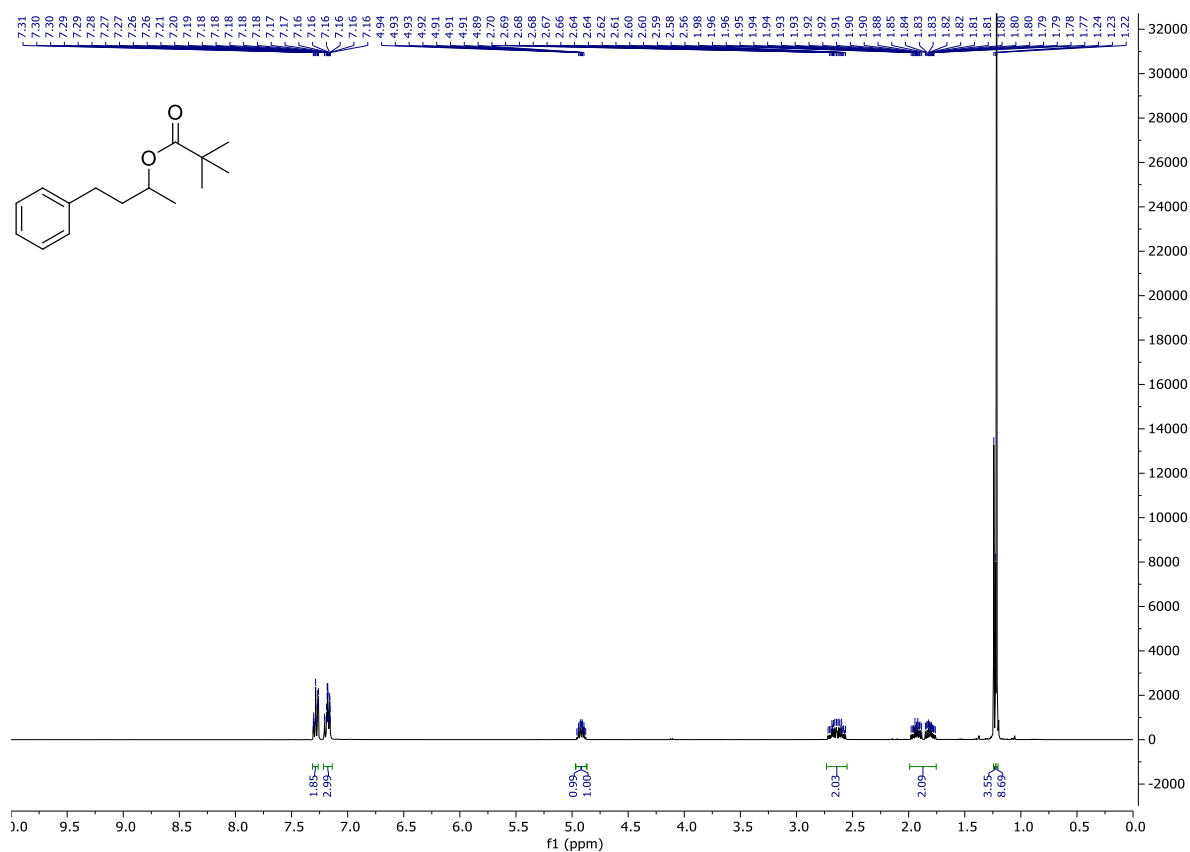


^{13}C NMR (126 MHz, CDCl_3)

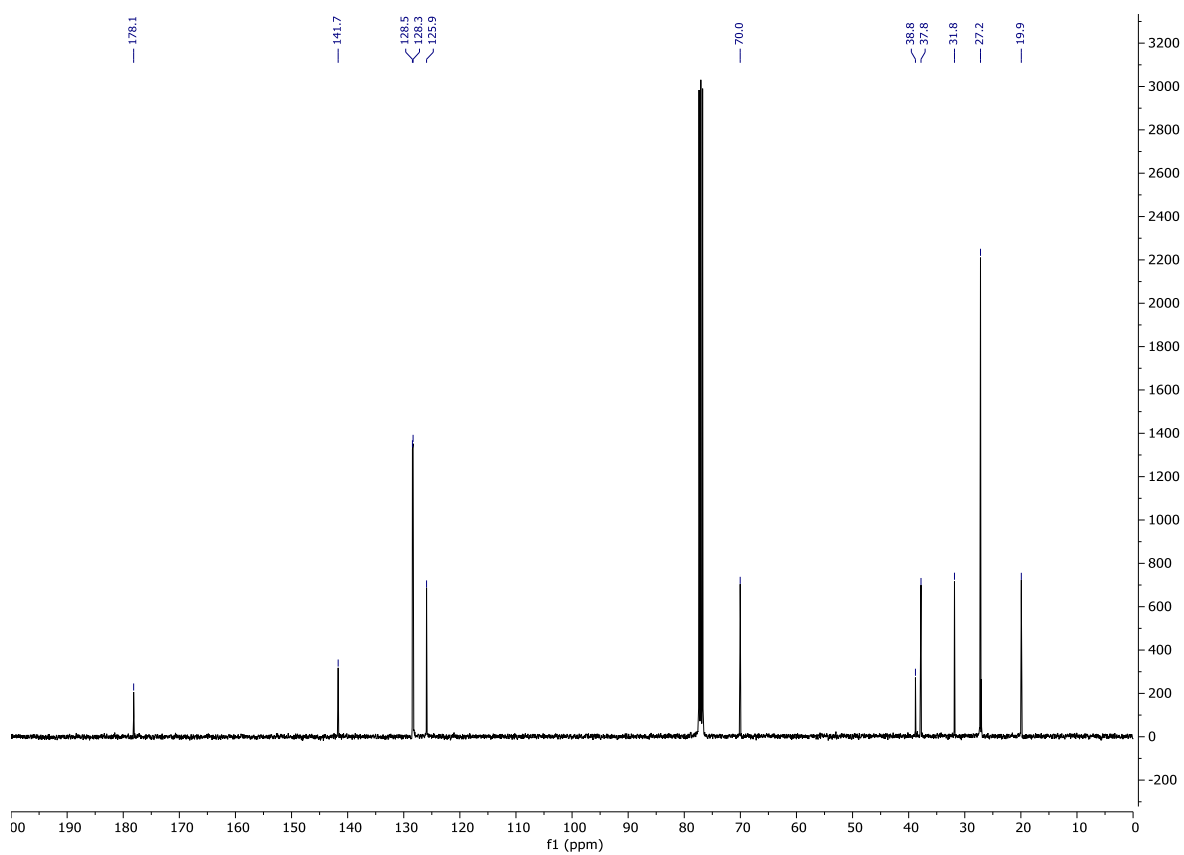


1-Methyl-3-phenylpropyl 2,2-Dimethylpropionate (S5)

^1H NMR (400 MHz, CDCl_3)

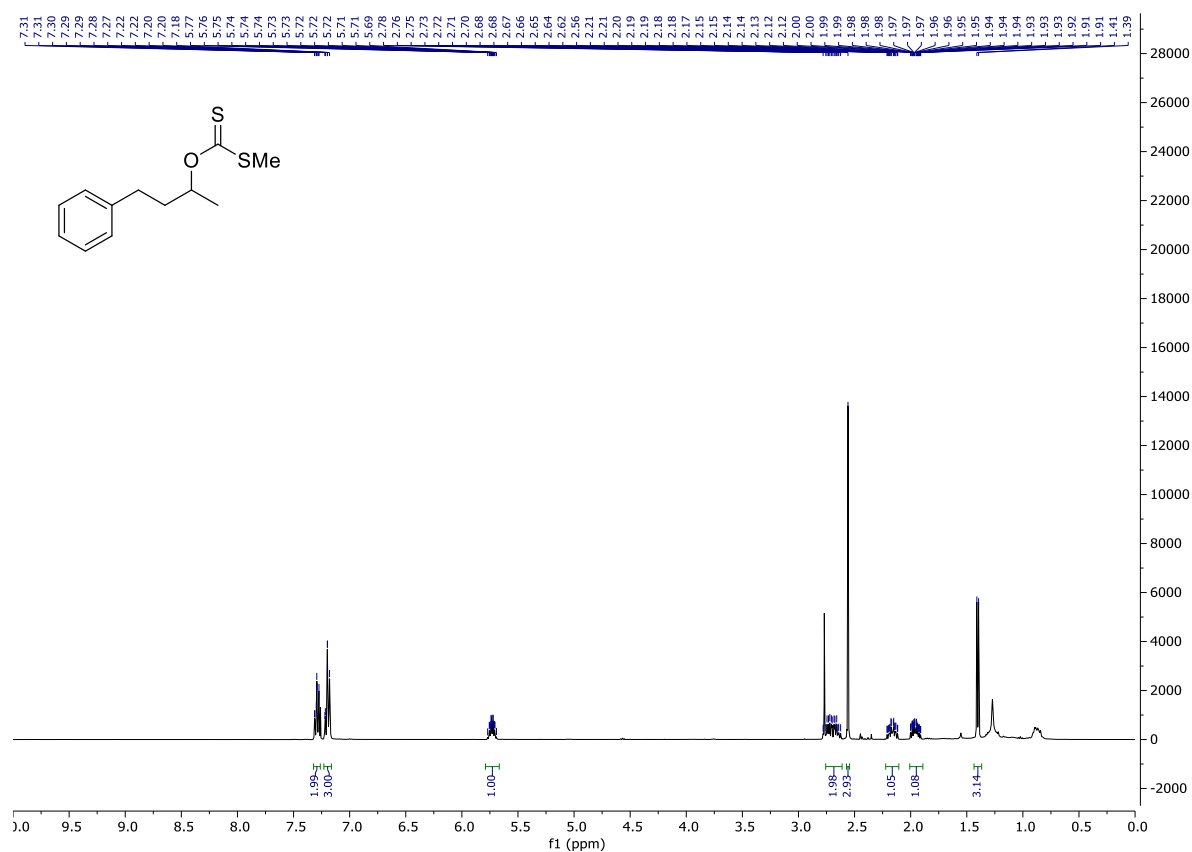


^{13}C NMR (101 MHz, CDCl_3)

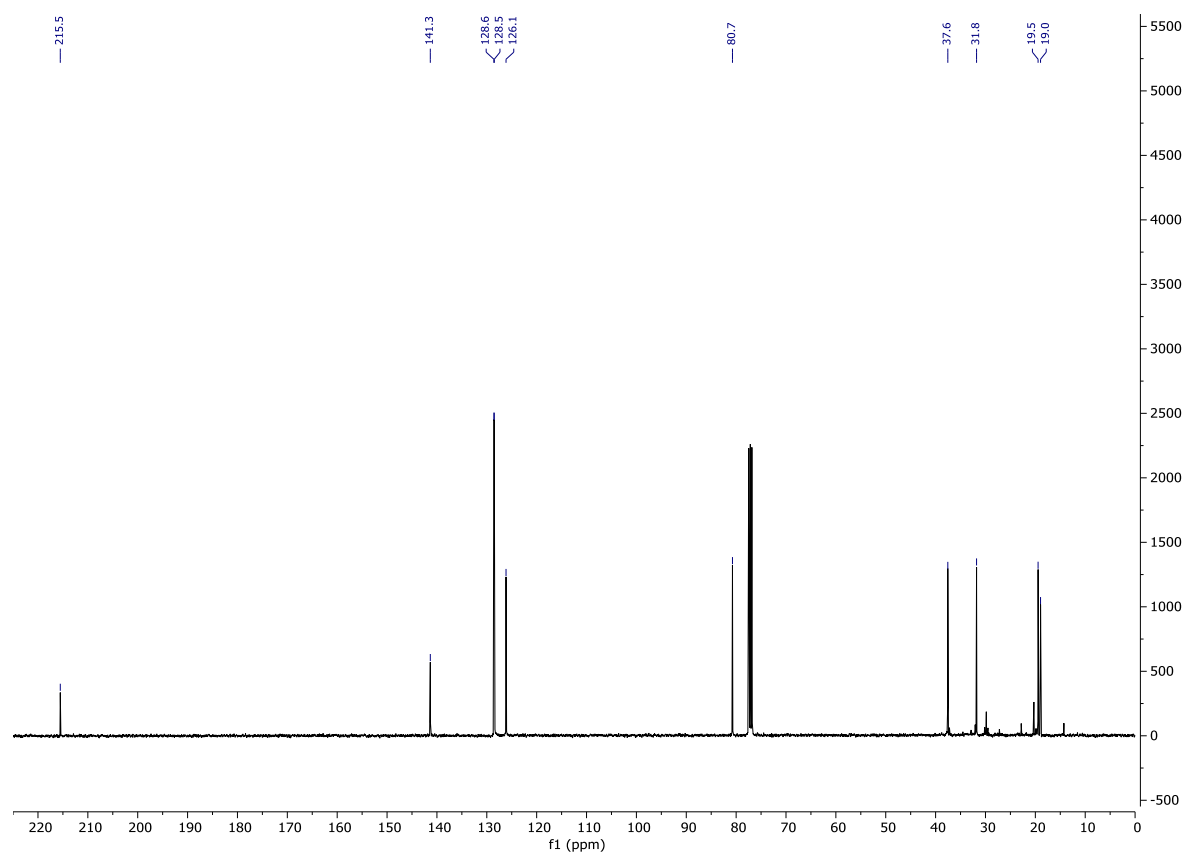


S-Methyl O-(4-phenylbutan-2-yl) carbonodithioate (S6)

^1H NMR (400 MHz, CDCl_3)

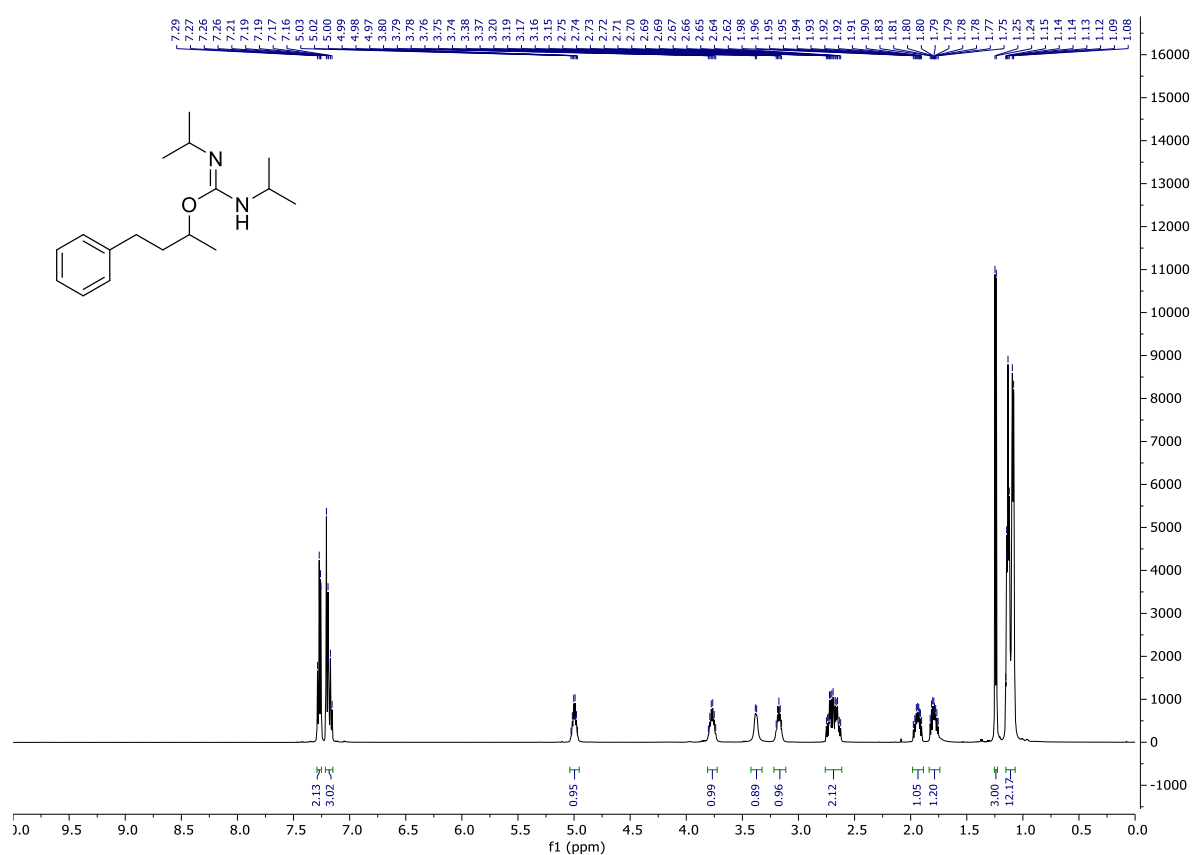


^{13}C NMR (101 MHz, CDCl_3)

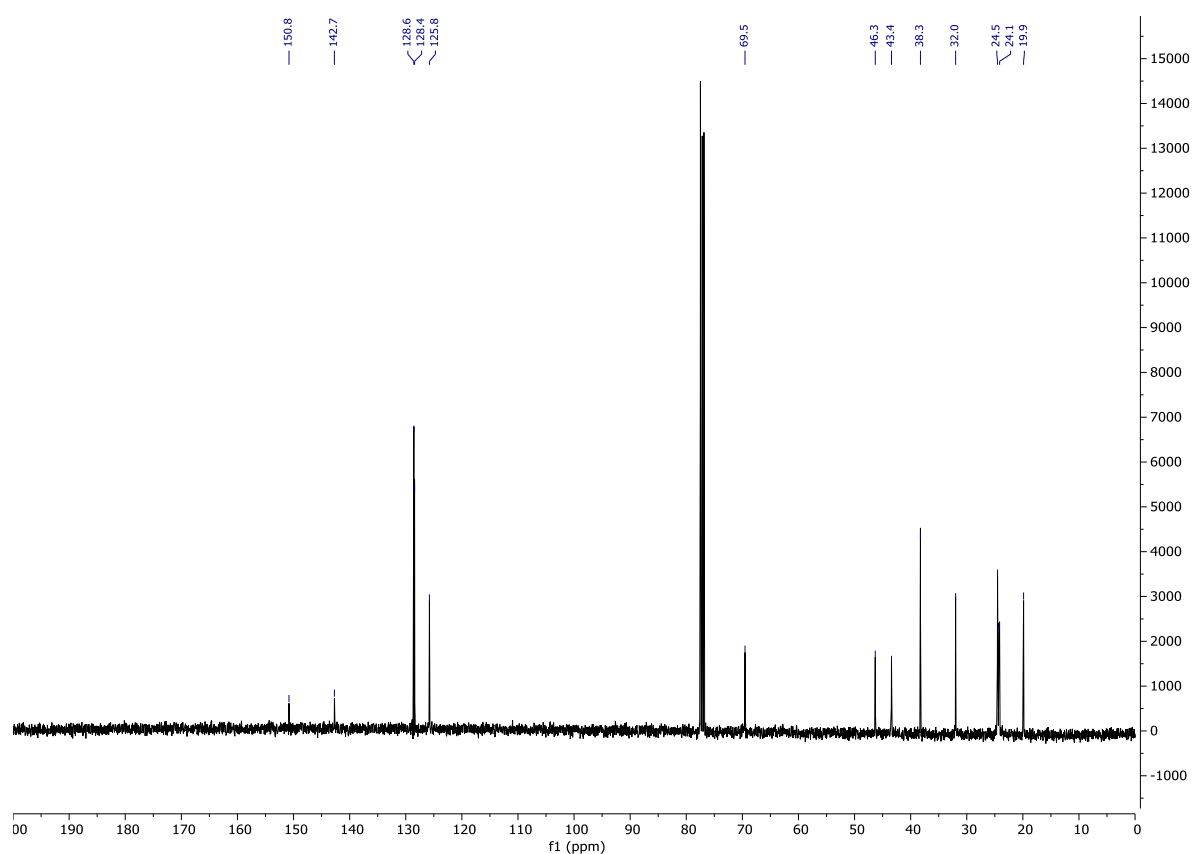


4-Phenylbutan-2-yl (*Z*)-*N,N'*-diisopropylcarbamimidate, compound **S7**

^1H NMR (500 MHz, CDCl_3)

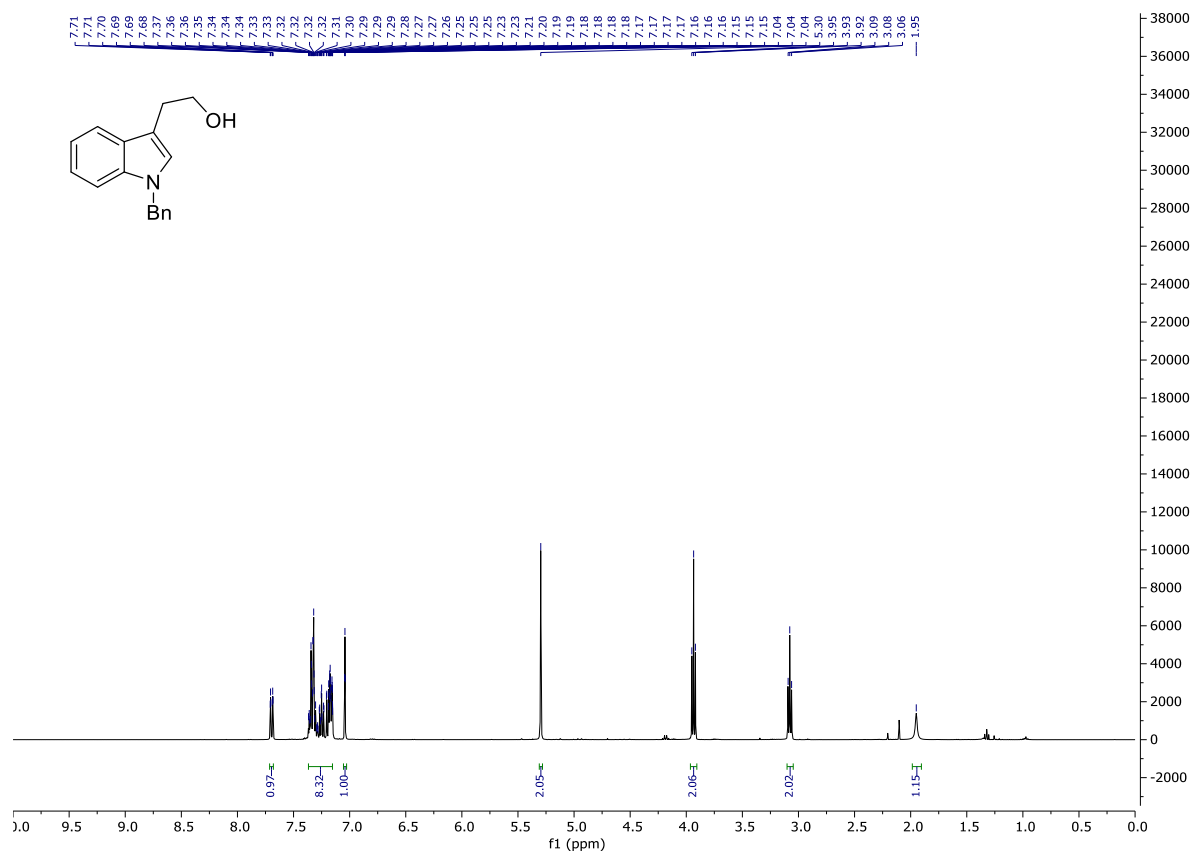


^{13}C NMR (101 MHz, CDCl_3)

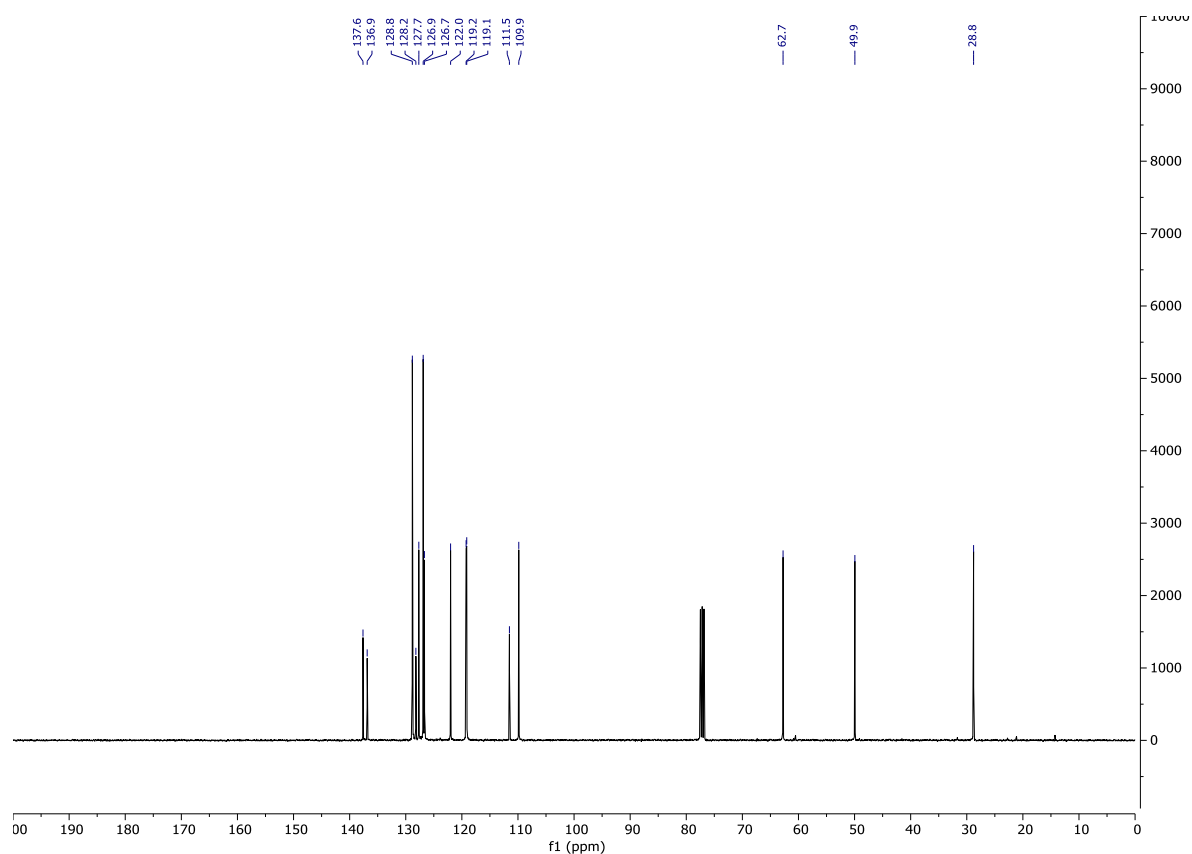


2-(1-Benzyl-1*H*-indol-3-yl)ethanol, compound **S8**

¹H NMR (400 MHz, CDCl₃)

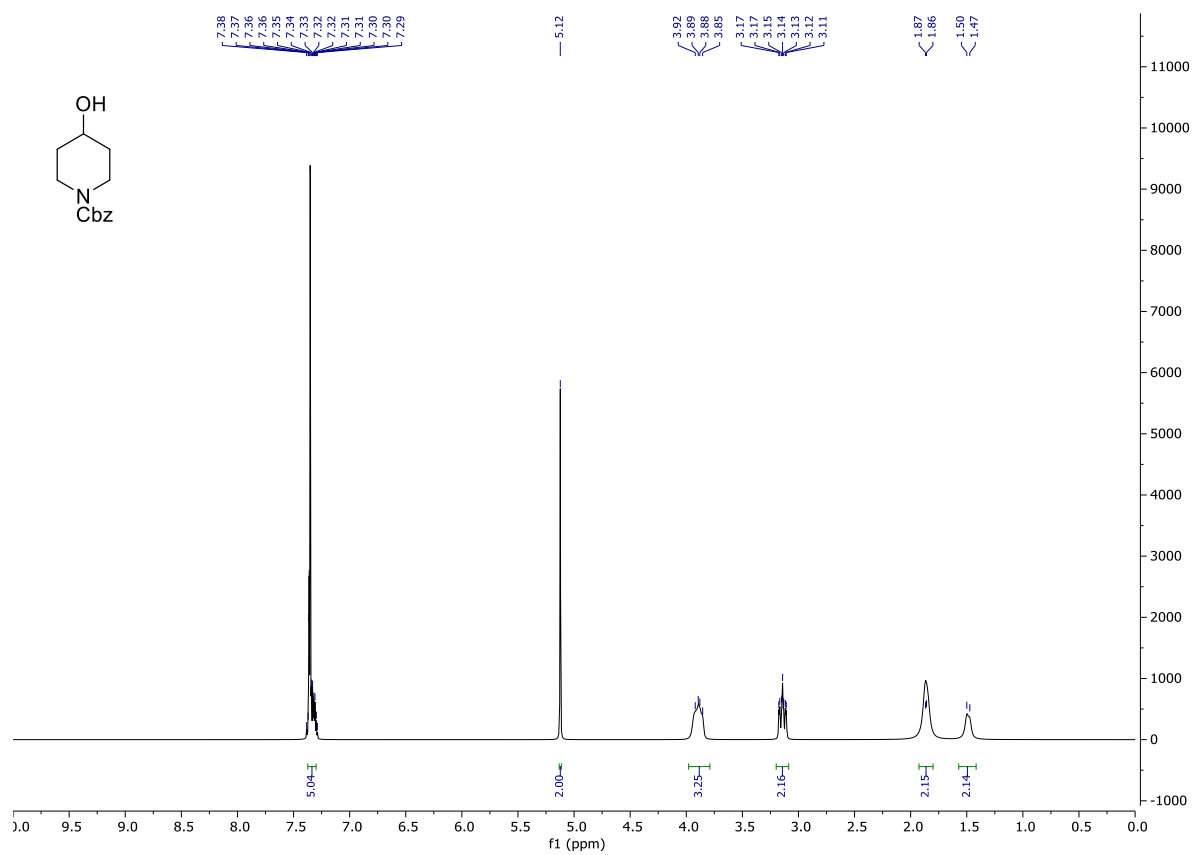


¹³C NMR (101 MHz, CDCl₃)

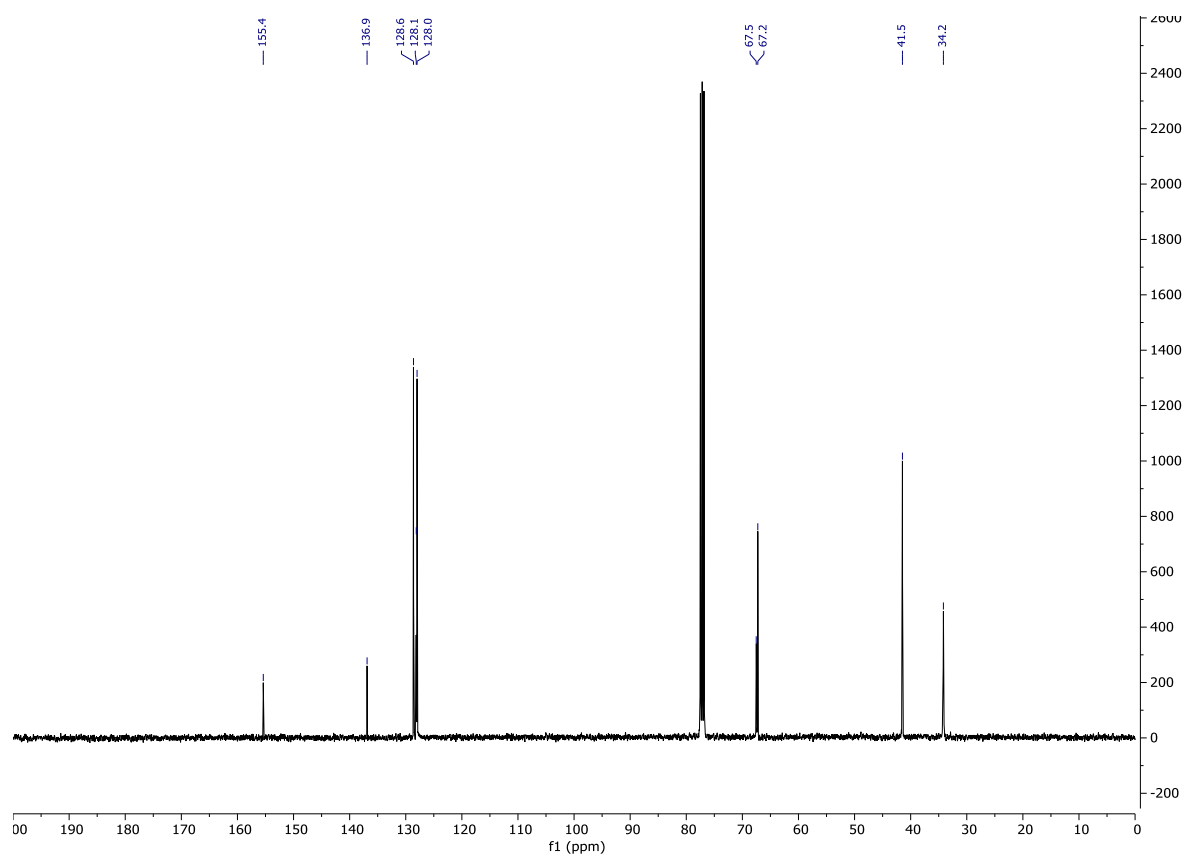


Benzyl 4-hydroxy-1-piperidinecarboxylate, compound **S9**

^1H NMR (400 MHz, CDCl_3)

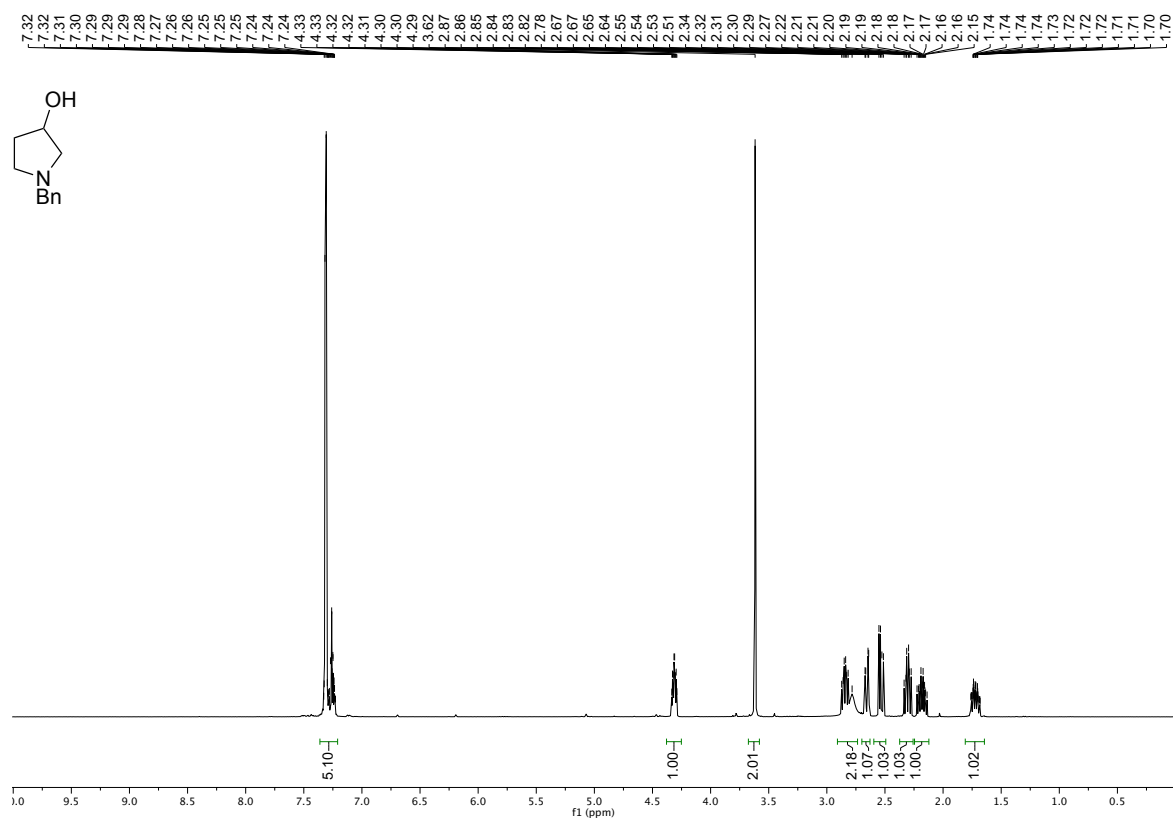


^{13}C NMR (101 MHz, CDCl_3)

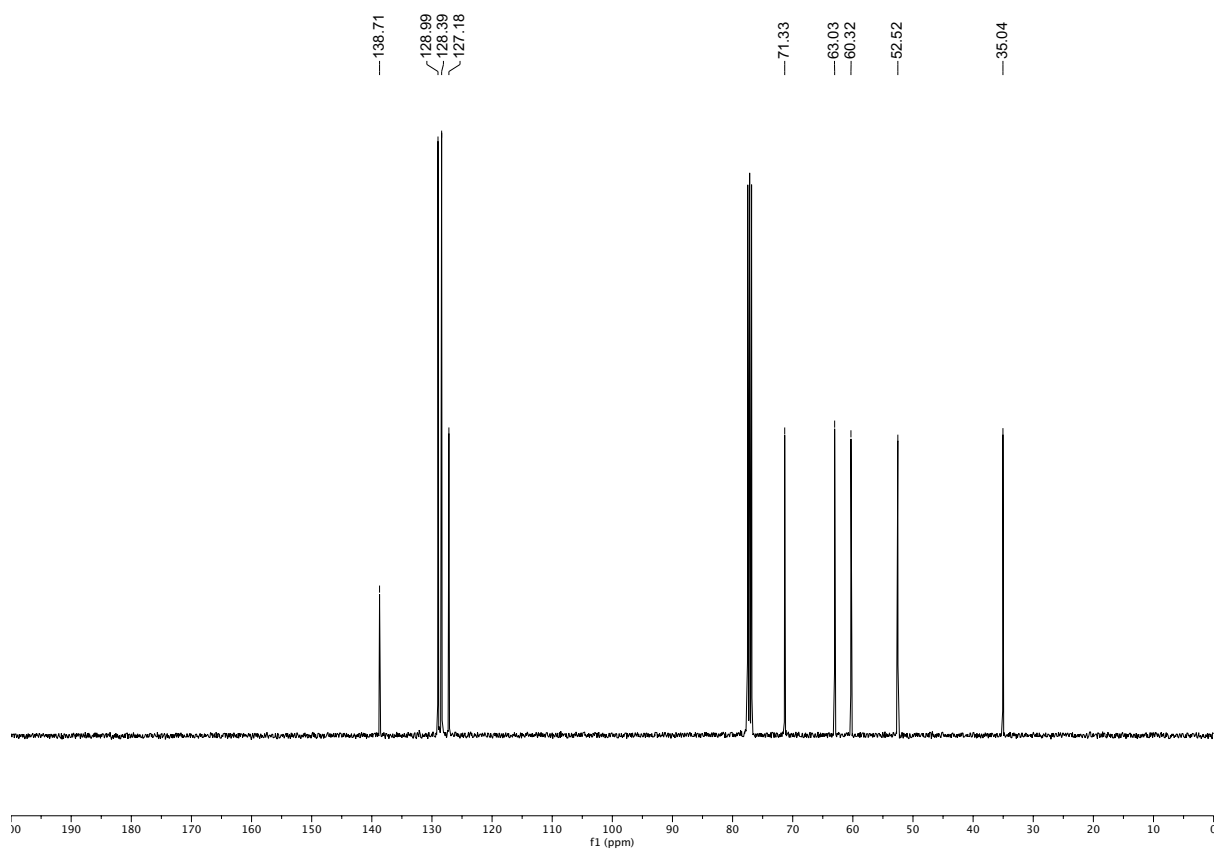


1-Benzyl-3-pyrrolidinol, compound **S10**

^1H NMR (400 MHz, CDCl_3)

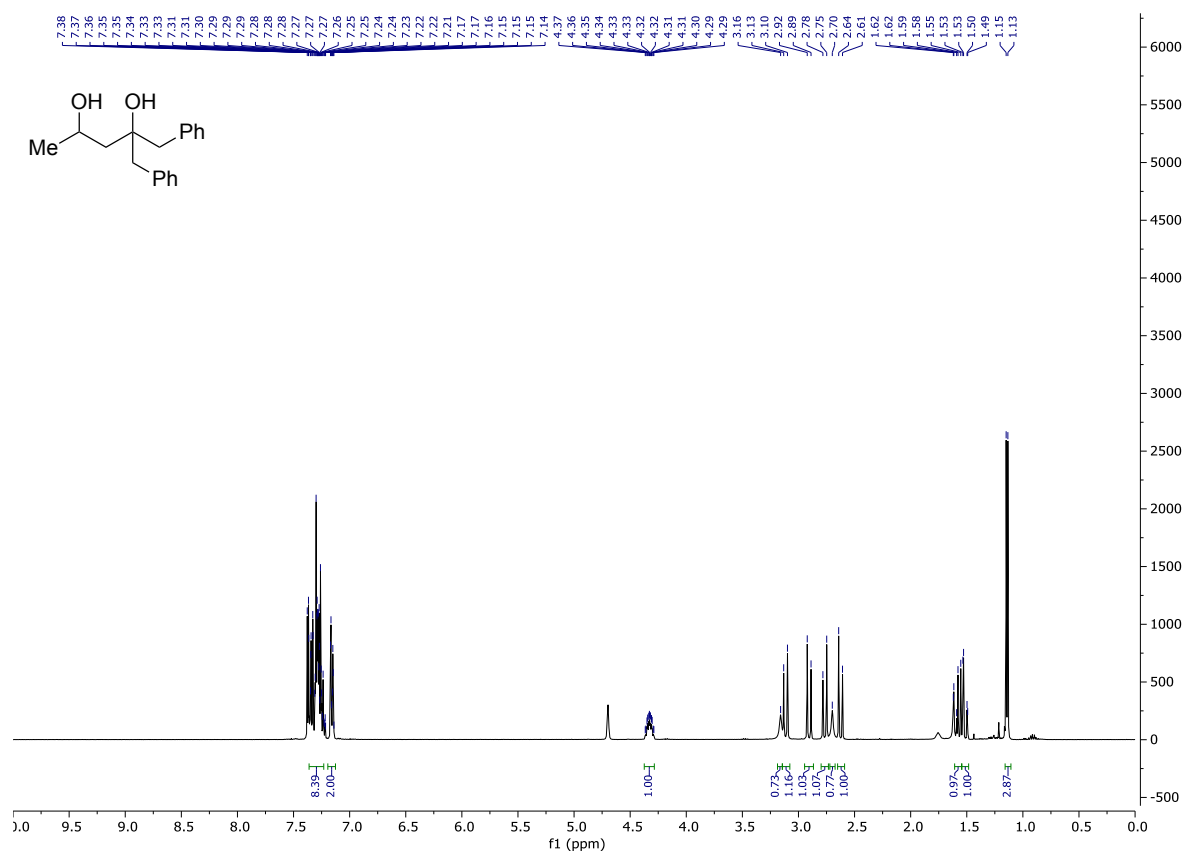


^{13}C NMR (101 MHz, CDCl_3)

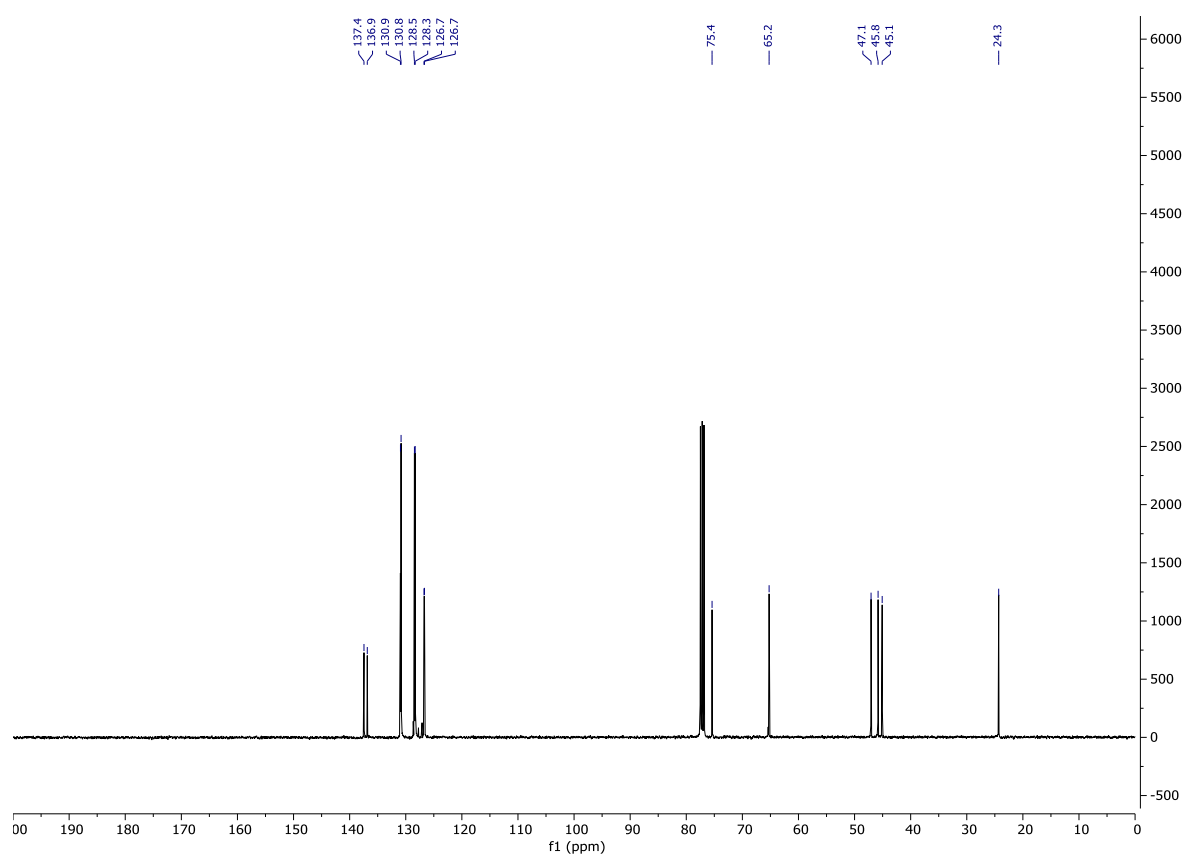


2-Benzyl-1-phenylpentane-2,4-diol, compound S11

^1H NMR (400 MHz, CDCl_3)

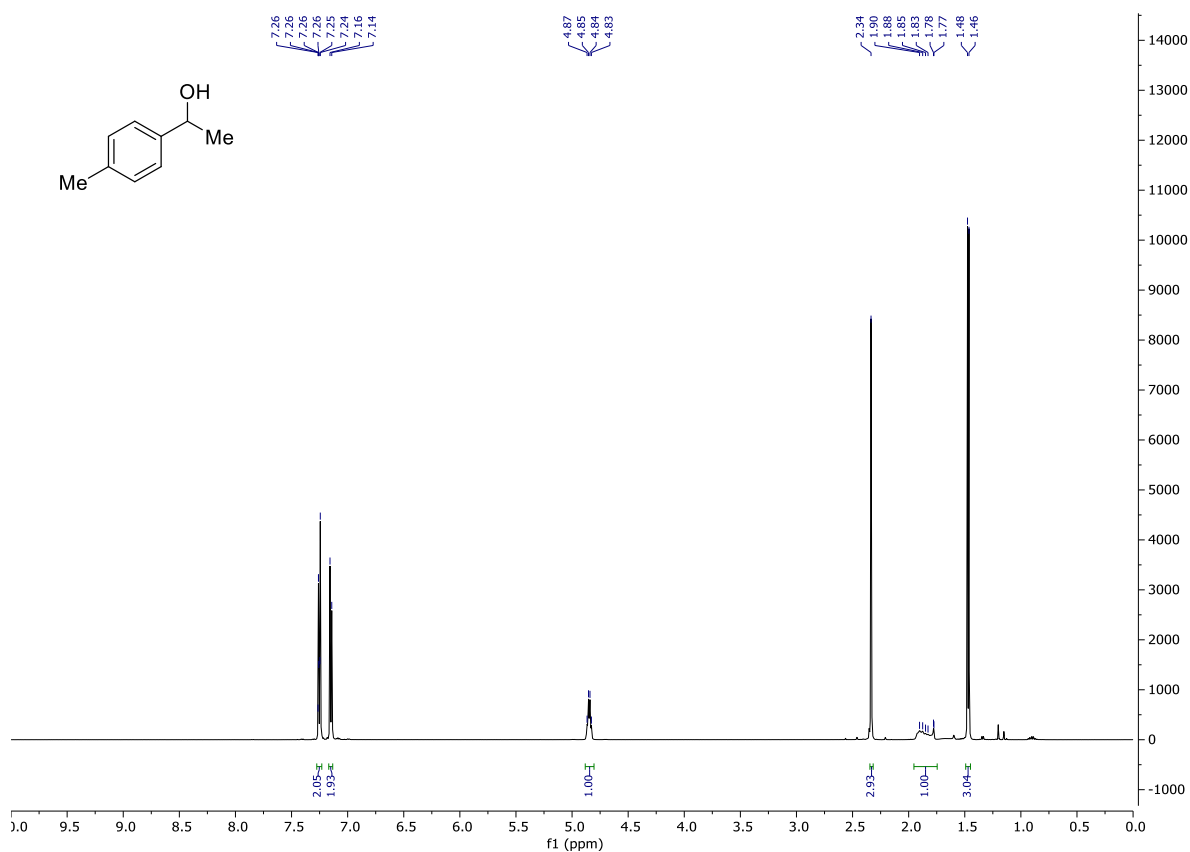


^{13}C NMR (101 MHz, CDCl_3)

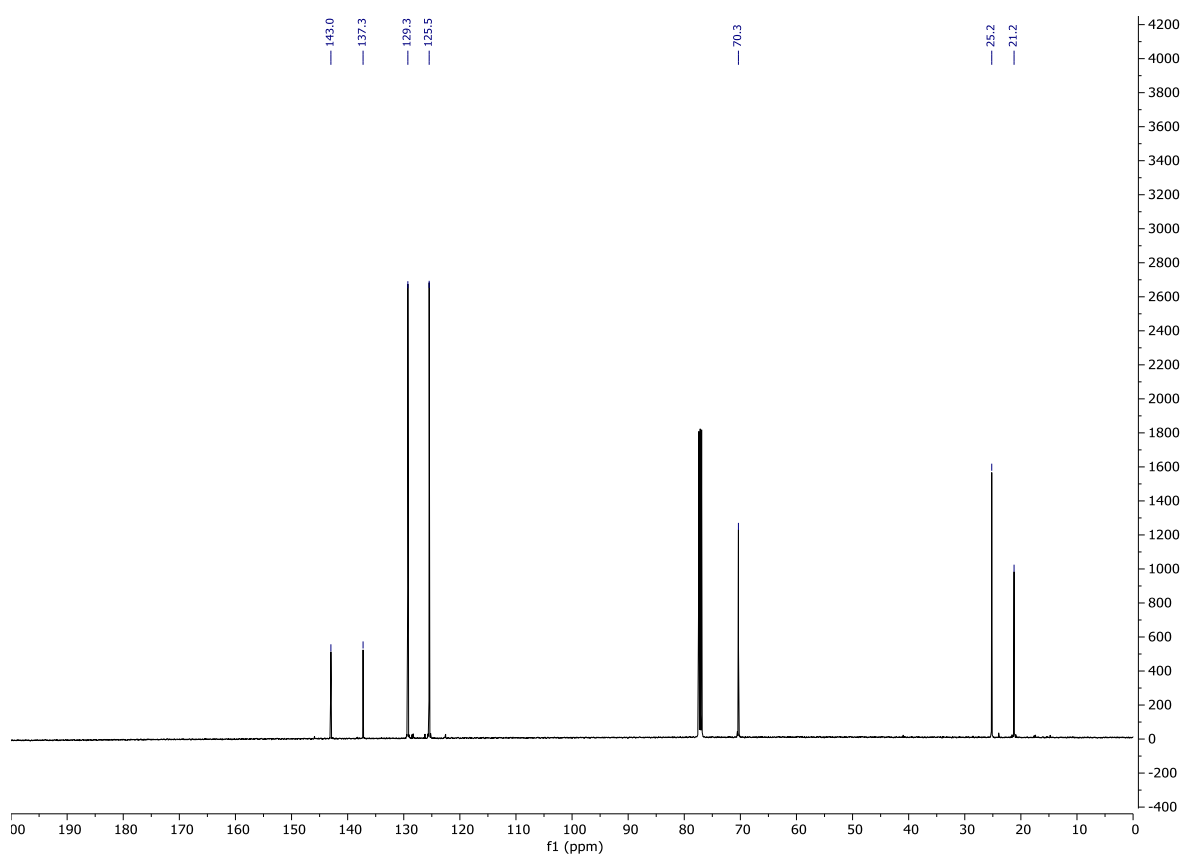


1-(*p*-Tolyl)ethanol, compound **S12**

¹H NMR (500 MHz, CDCl₃)

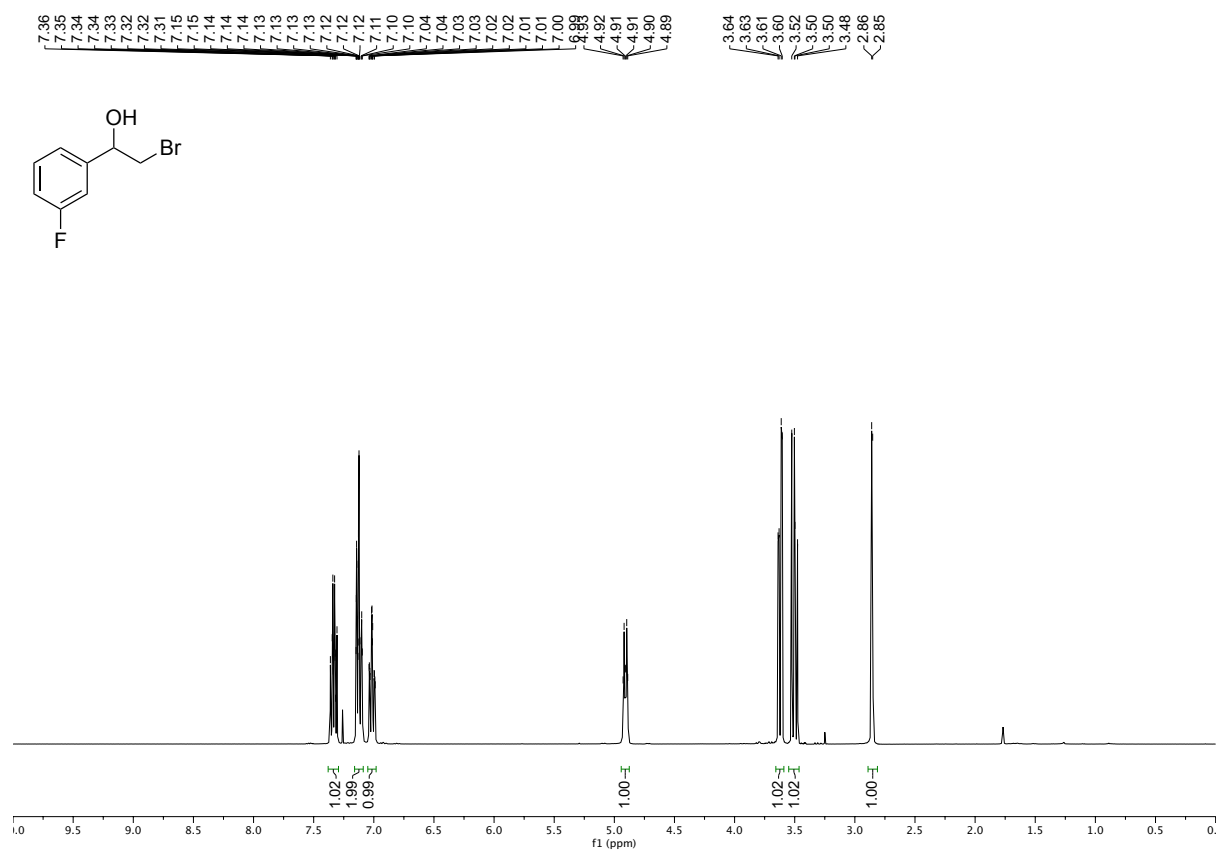


¹³C NMR (126 MHz, CDCl₃)

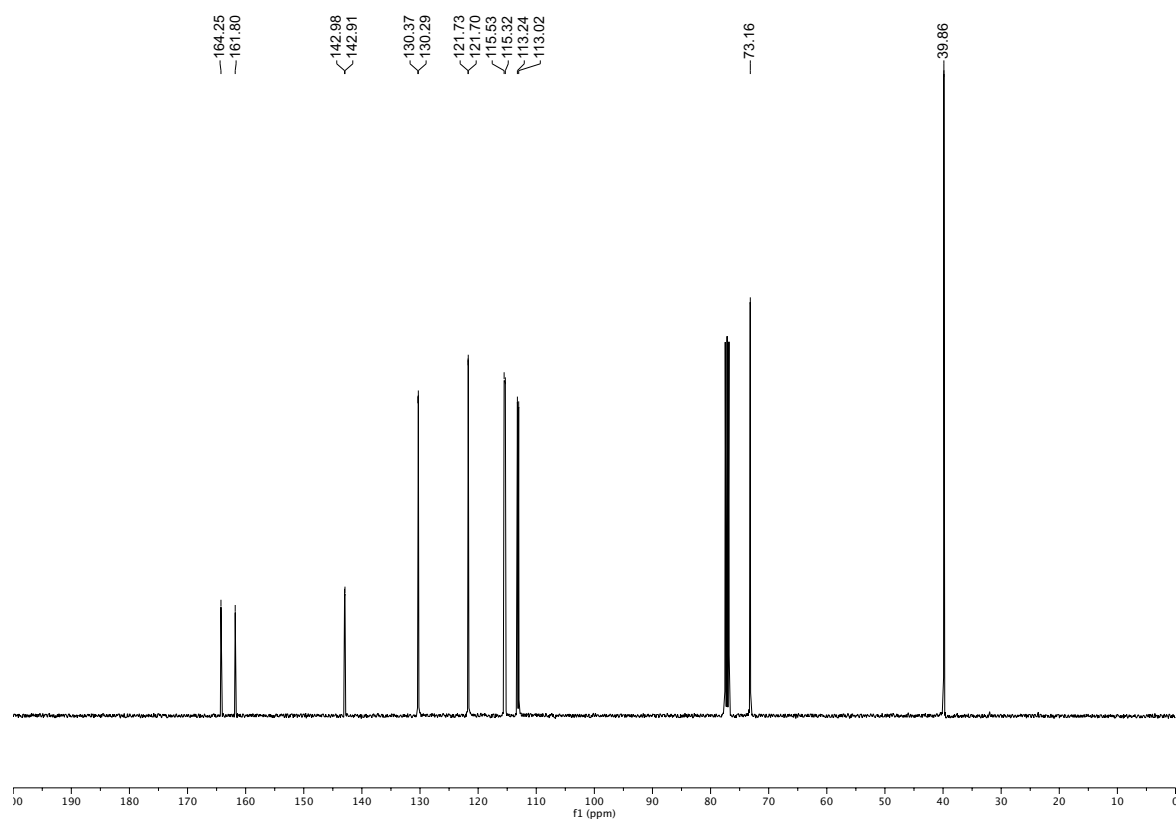


2-Bromo-1-(3-fluorophenyl)ethan-1-ol, compound S13

^1H NMR (400 MHz, CDCl_3)

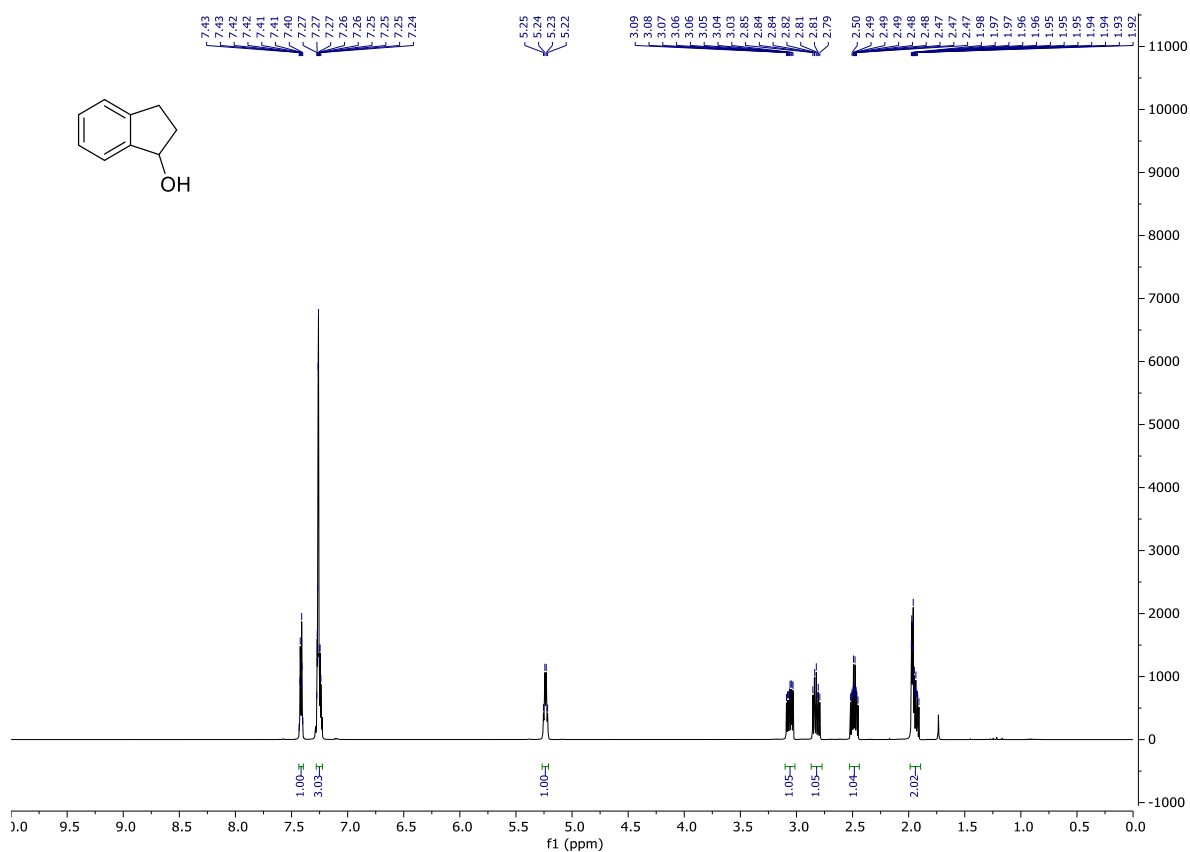


^{13}C NMR (126 MHz, CDCl_3)

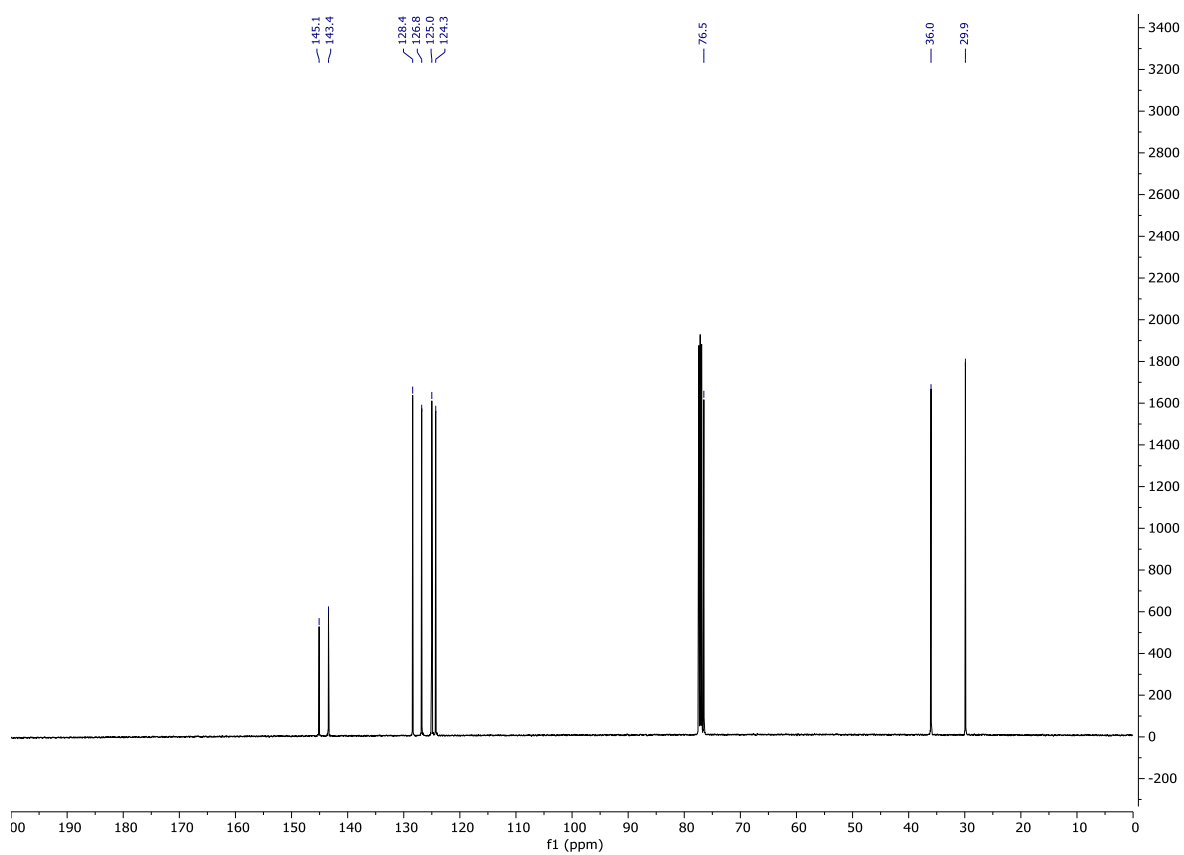


1-Indanol, compound S14

^1H NMR (500 MHz, CDCl_3)

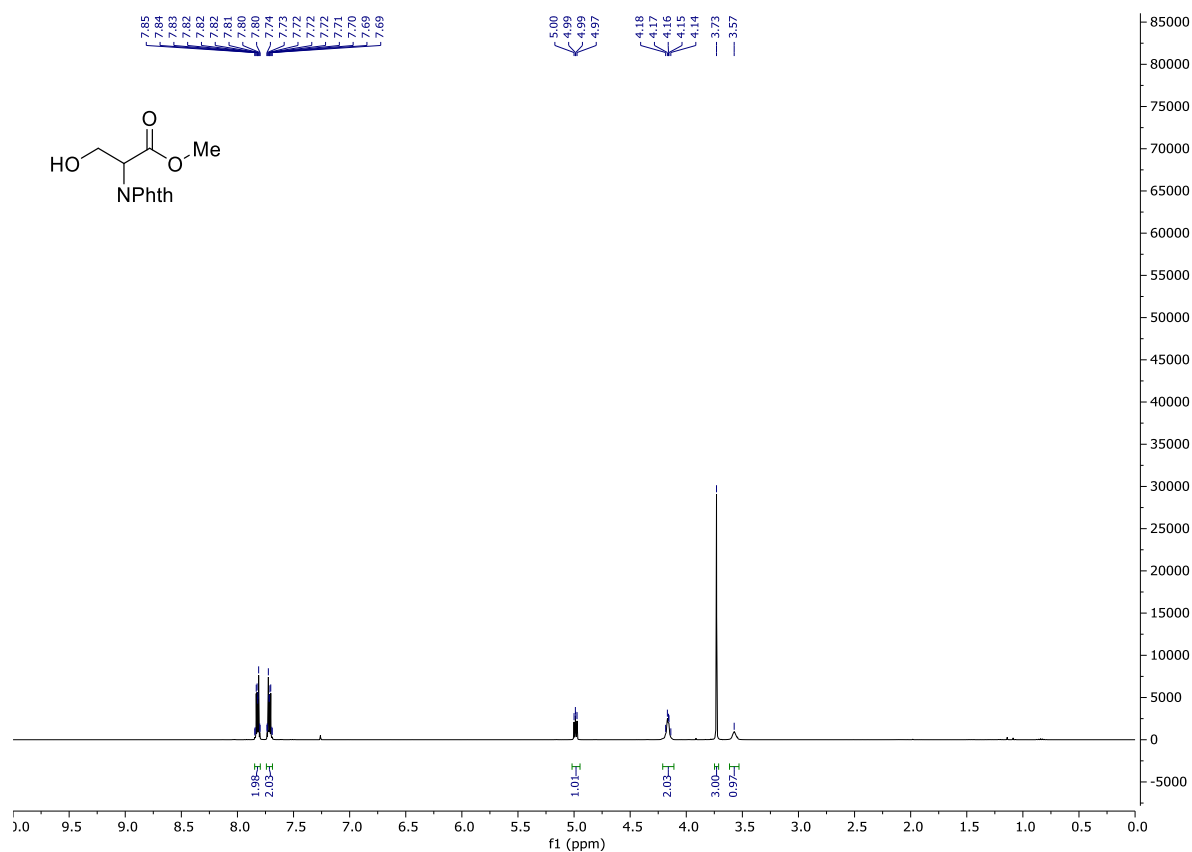


^{13}C NMR (126 MHz, CDCl_3)

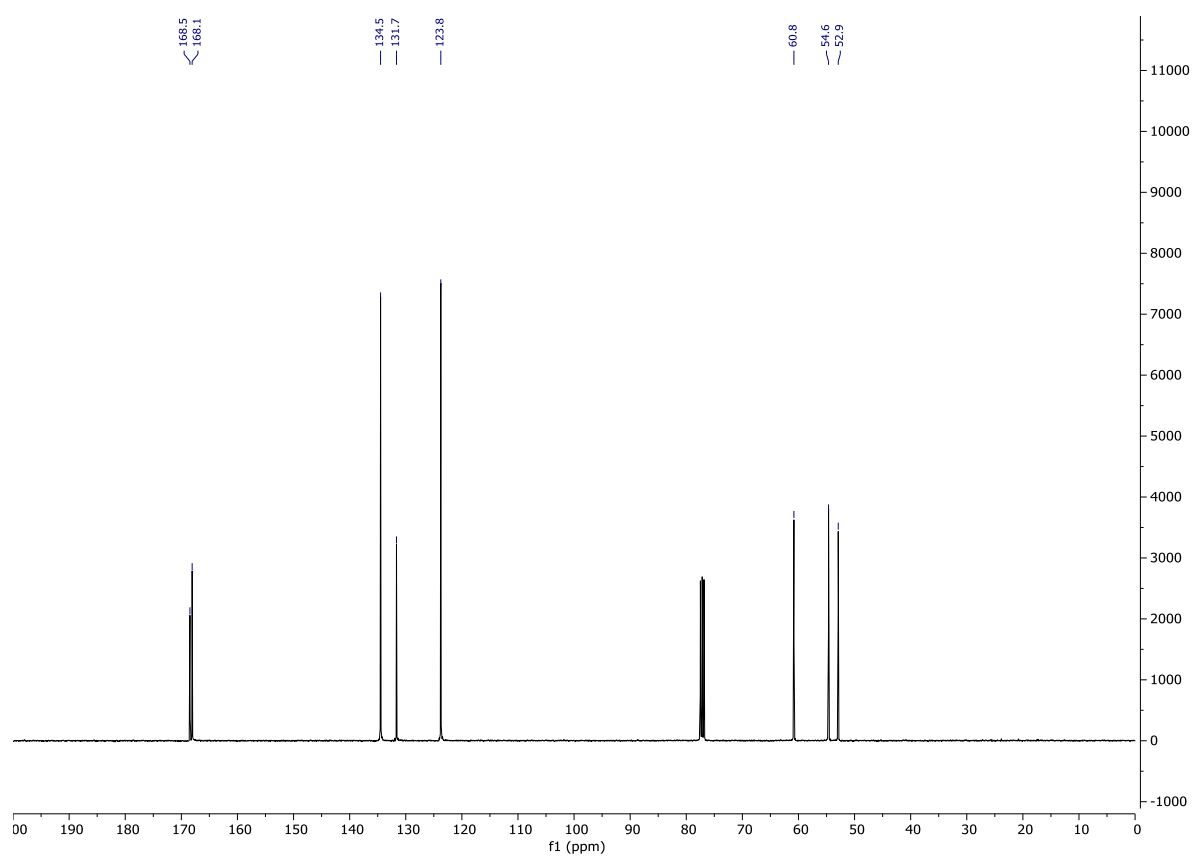


Methyl 2-(1,3-dioxisoindolin-2-yl)-3-hydroxypropanoate, compound **S15**

^1H NMR (400 MHz, CDCl_3)

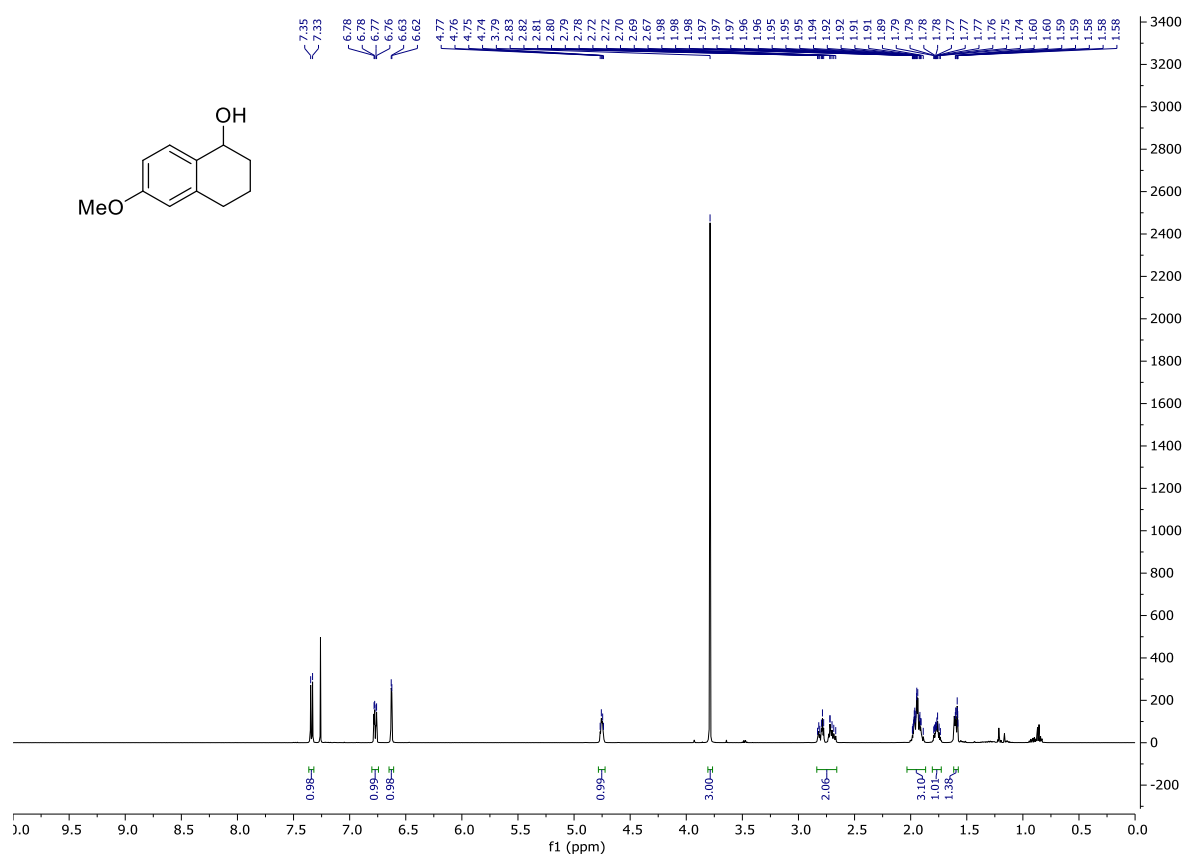


^{13}C NMR (101 MHz, CDCl_3)

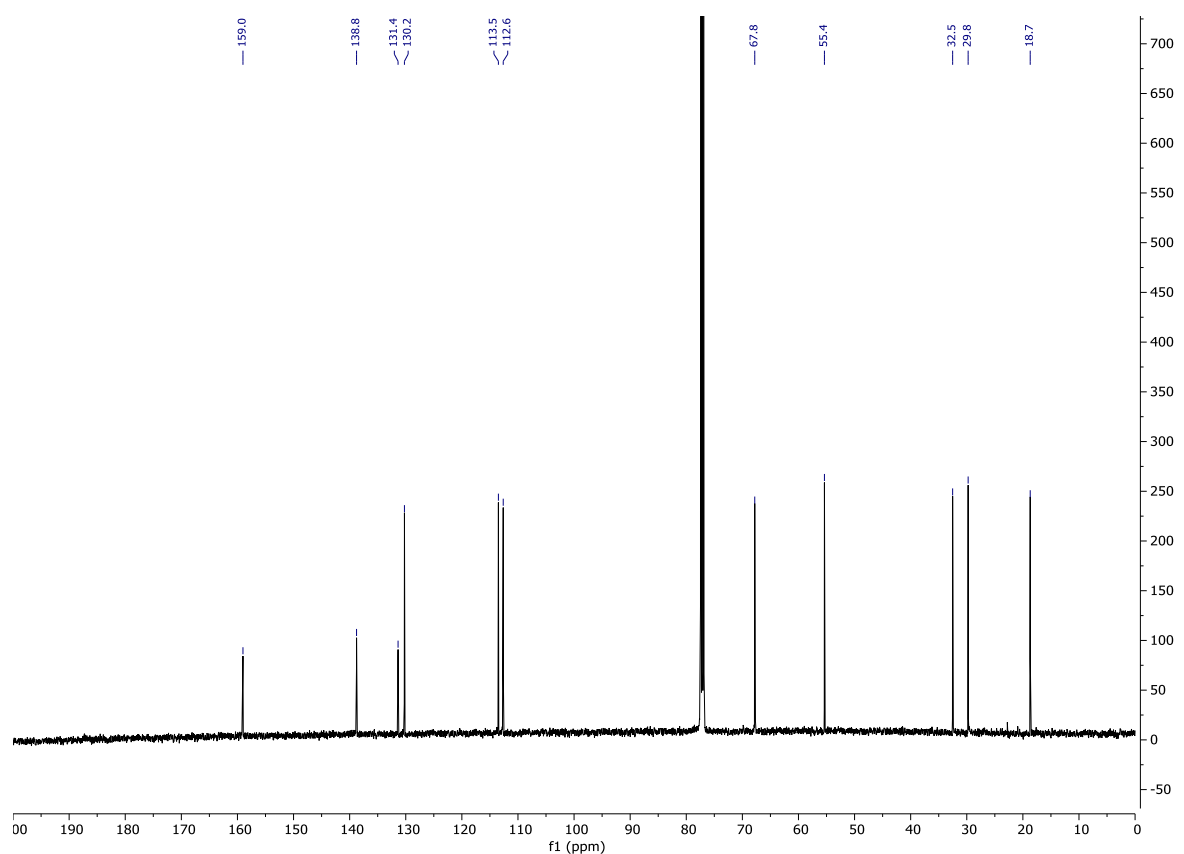


6-Methoxy-1,2,3,4-tetrahydronaphthalen-1-ol, compound S16

^1H NMR (400 MHz, CDCl_3)

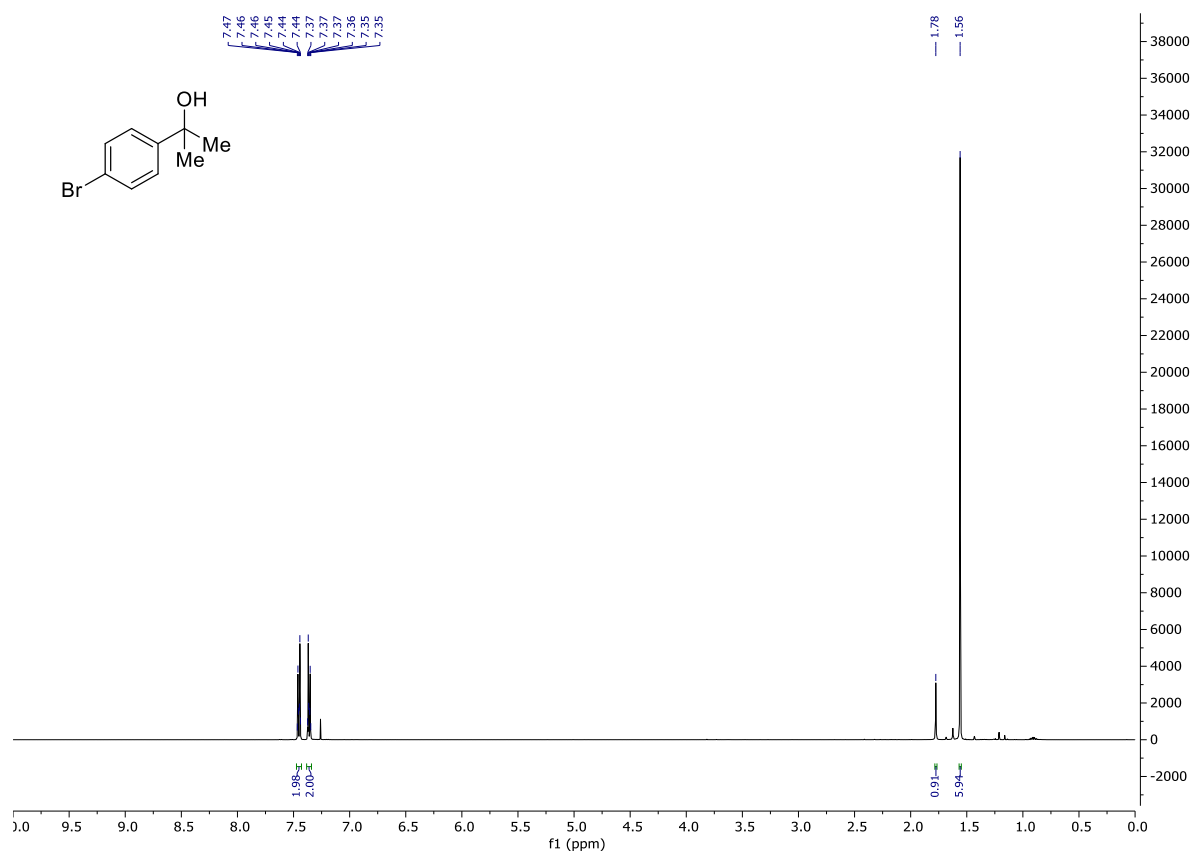


^{13}C NMR (126 MHz, CDCl_3)

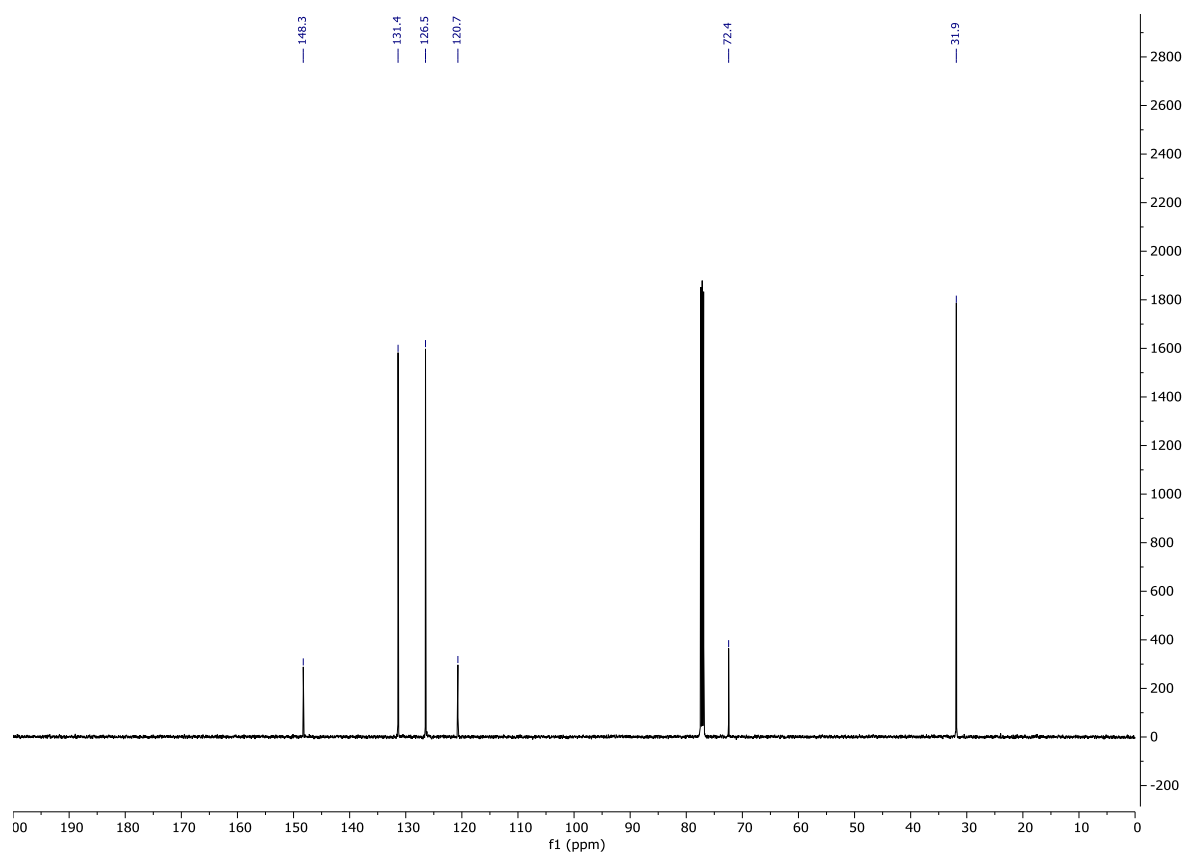


2-(4-Bromophenyl)propan-2-ol, compound **S17**

^1H NMR (500 MHz, CDCl_3)

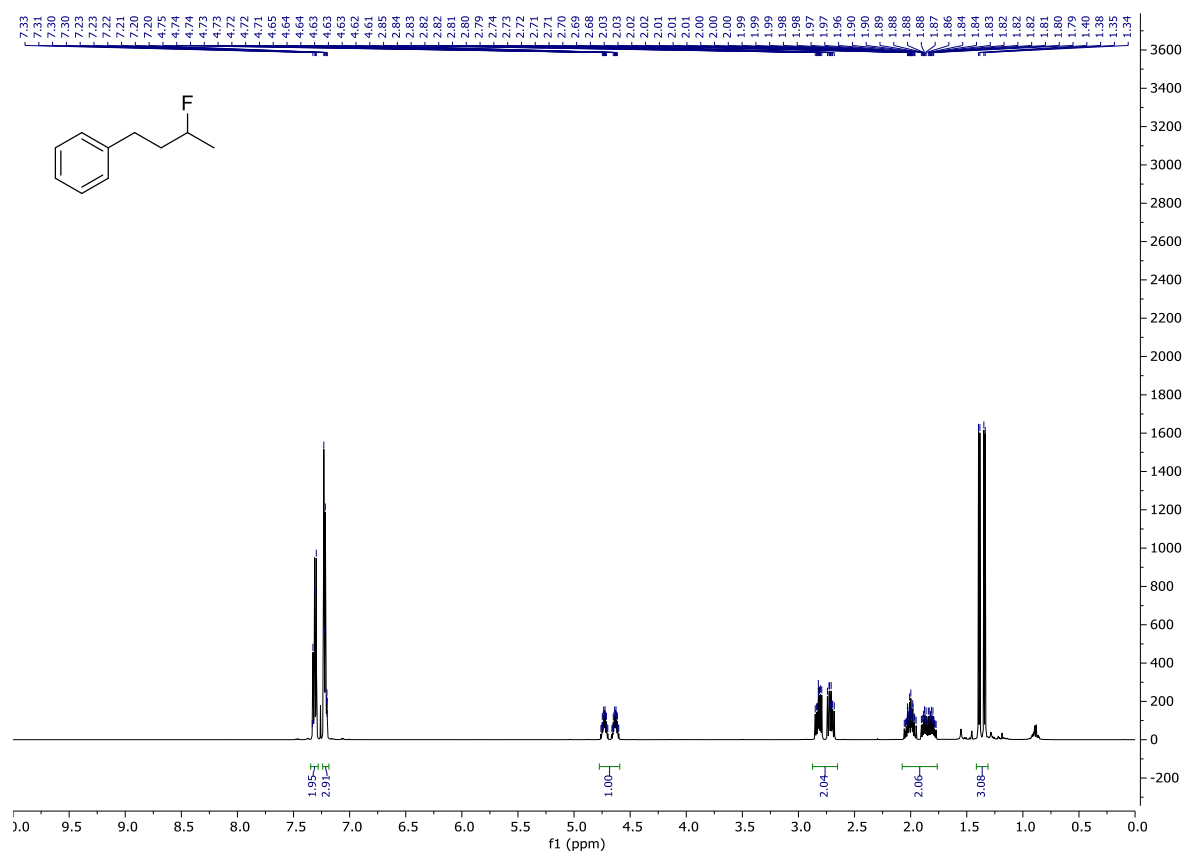


^{13}C NMR (126 MHz, CDCl_3)

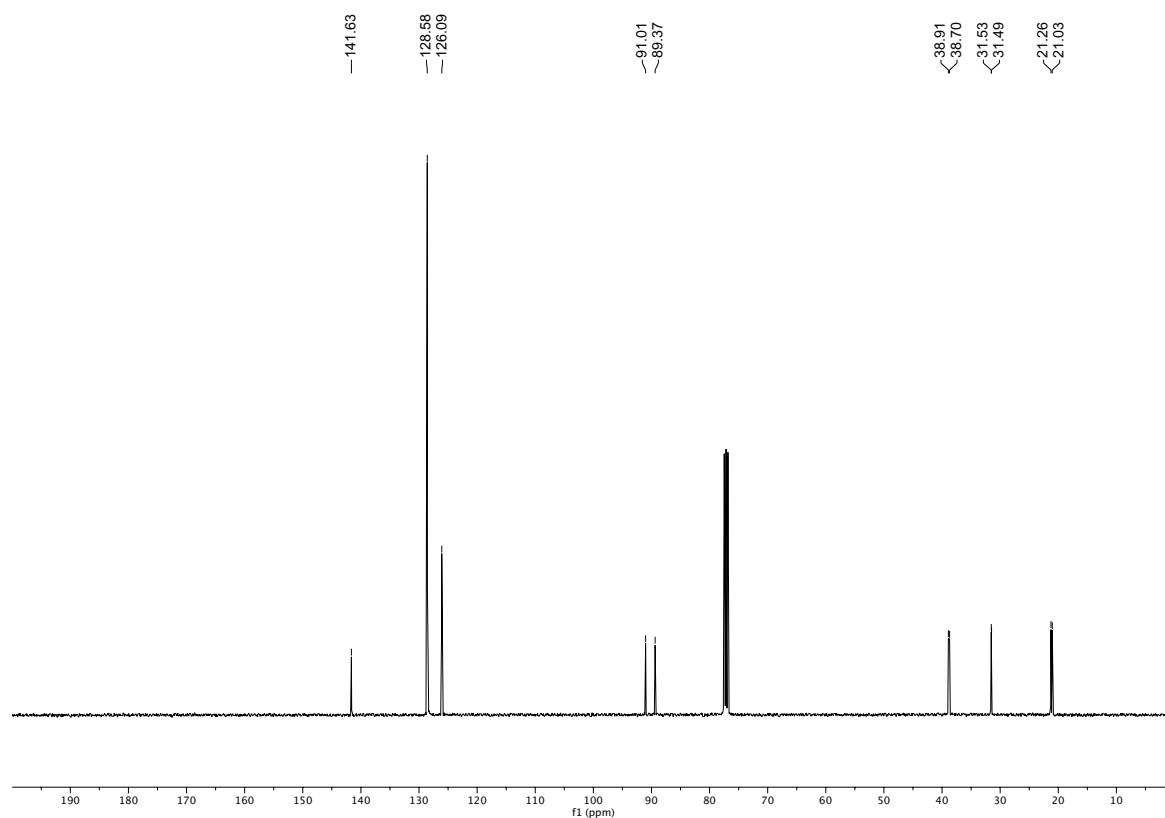


(3-Fluorobutyl)benzene, compound **2a**

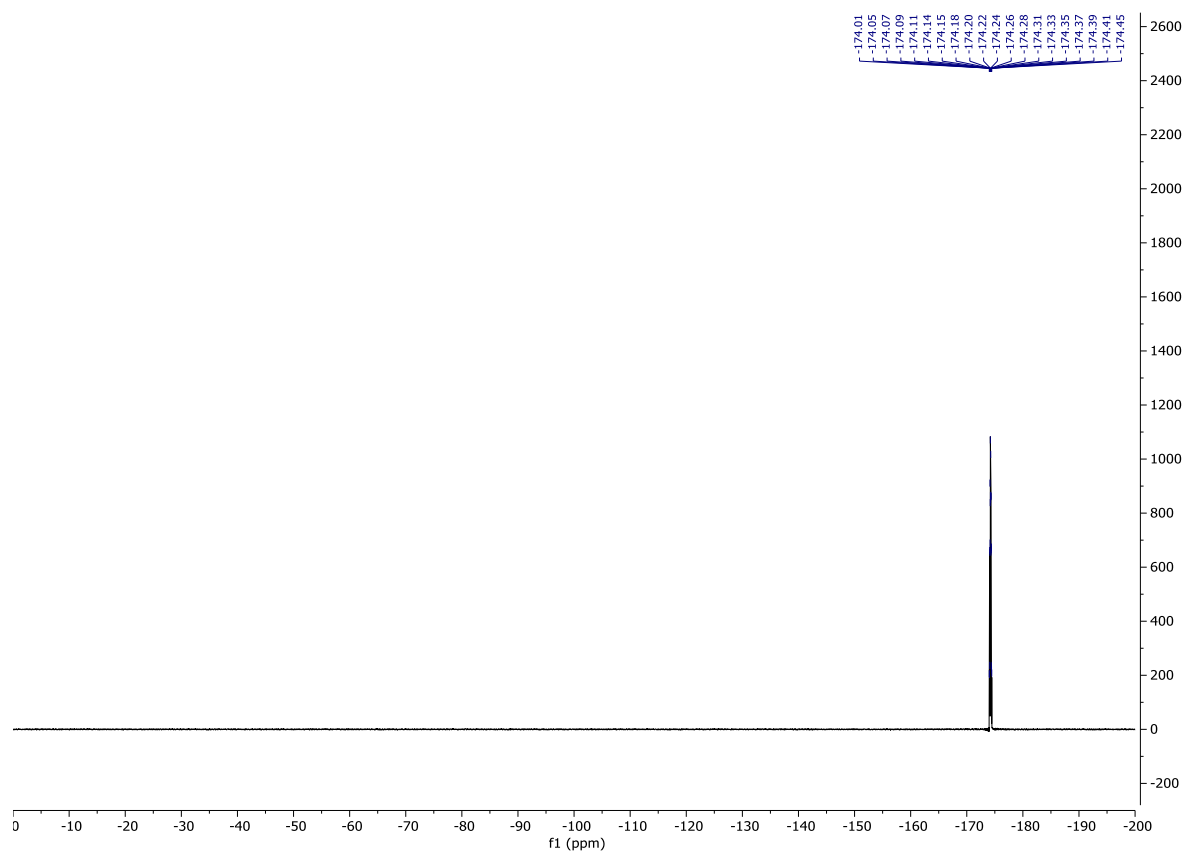
^1H NMR (500 MHz, CDCl_3)



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

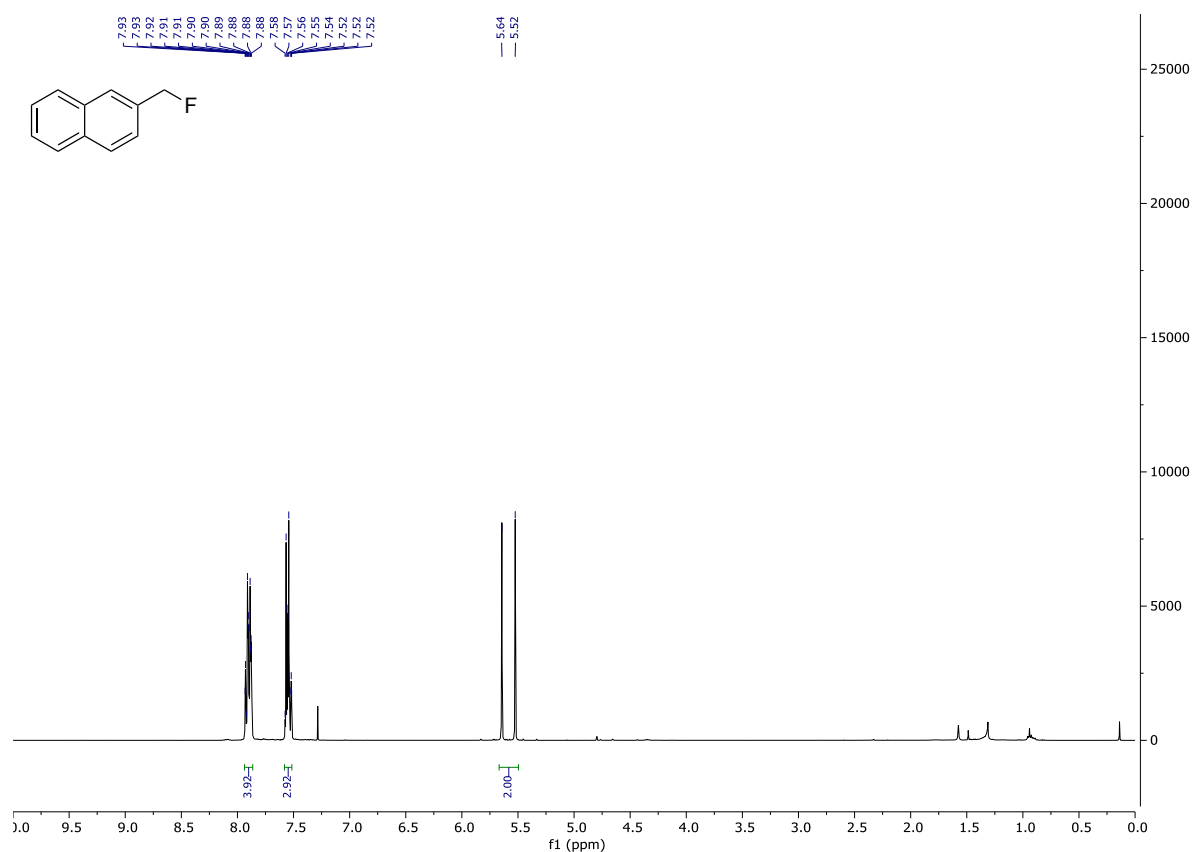


^{19}F NMR (376 MHz, CDCl_3)

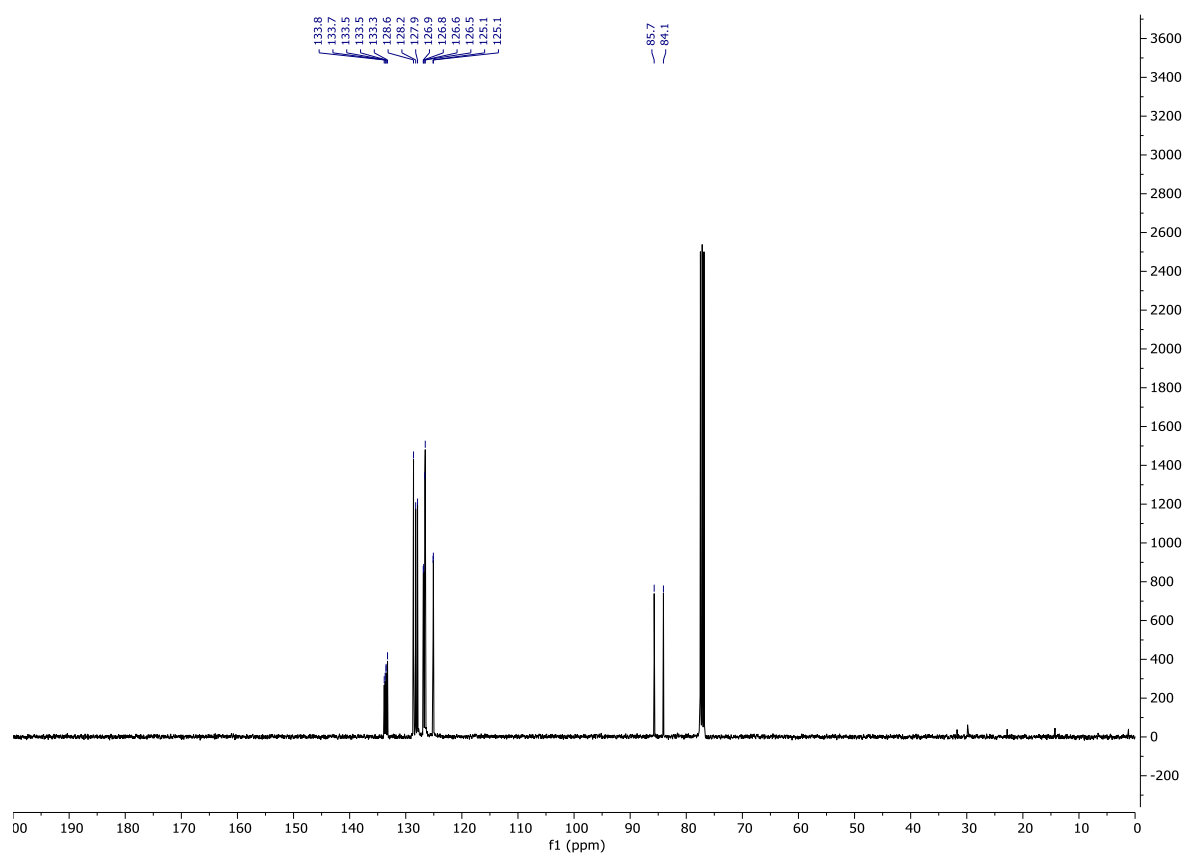


2-(Fluoromethyl)naphthalene, compound **2b**

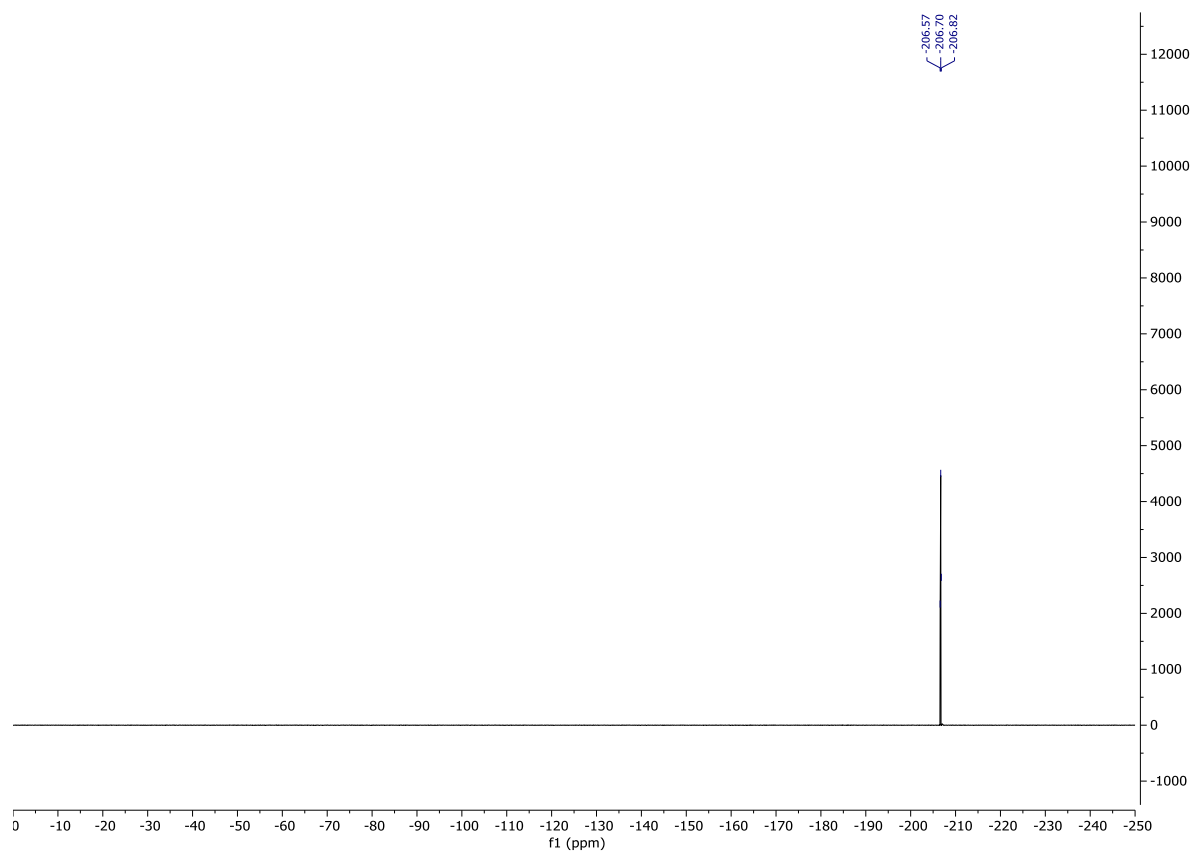
^1H NMR (400 MHz, CDCl_3)



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

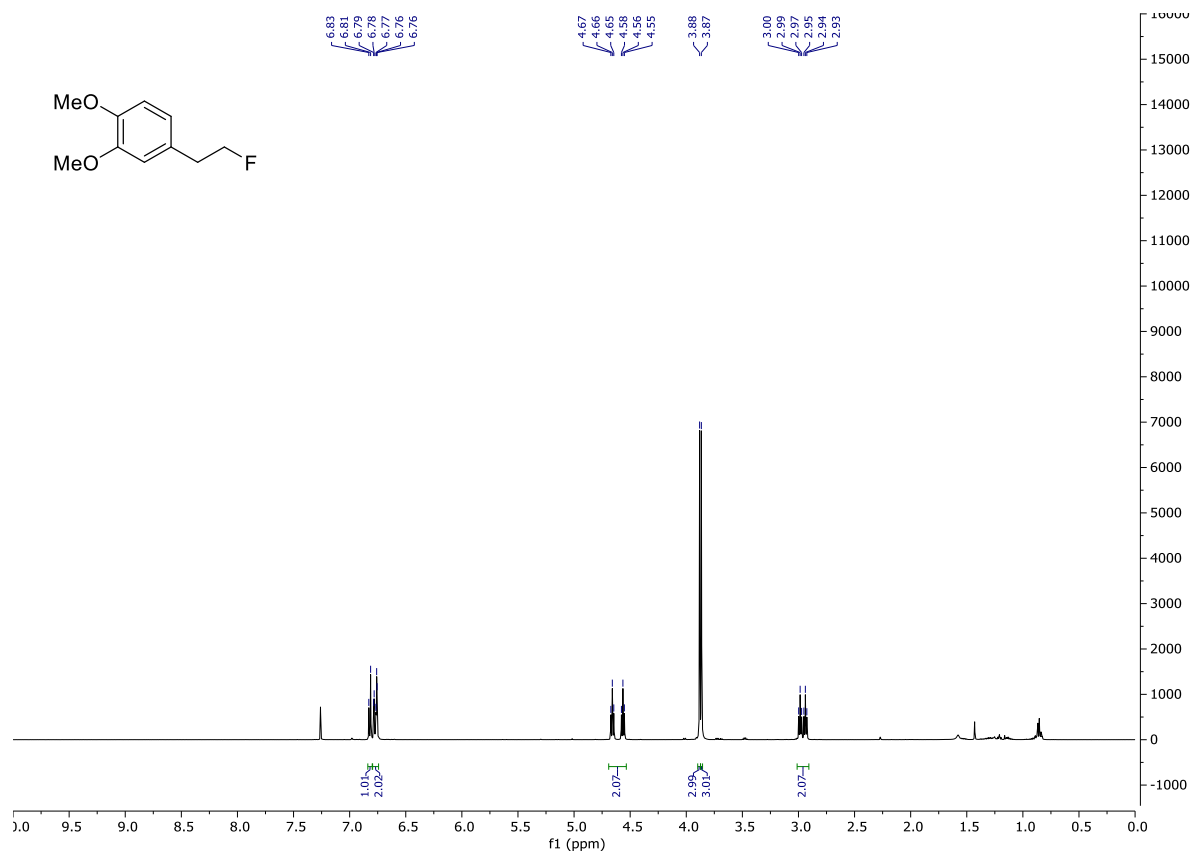


^{19}F NMR (376 MHz, CDCl_3)

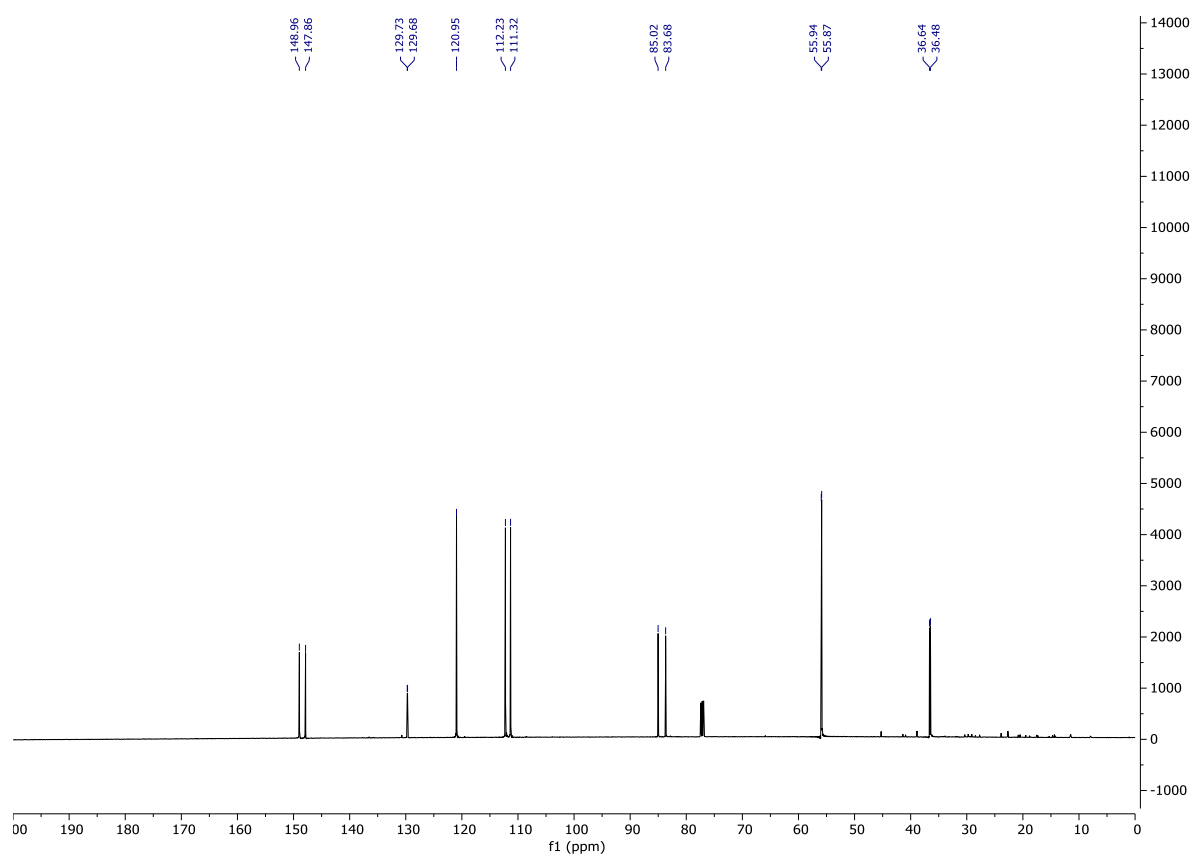


4-(2-Fluoroethyl)-1,2-dimethoxybenzene, compound **2c**

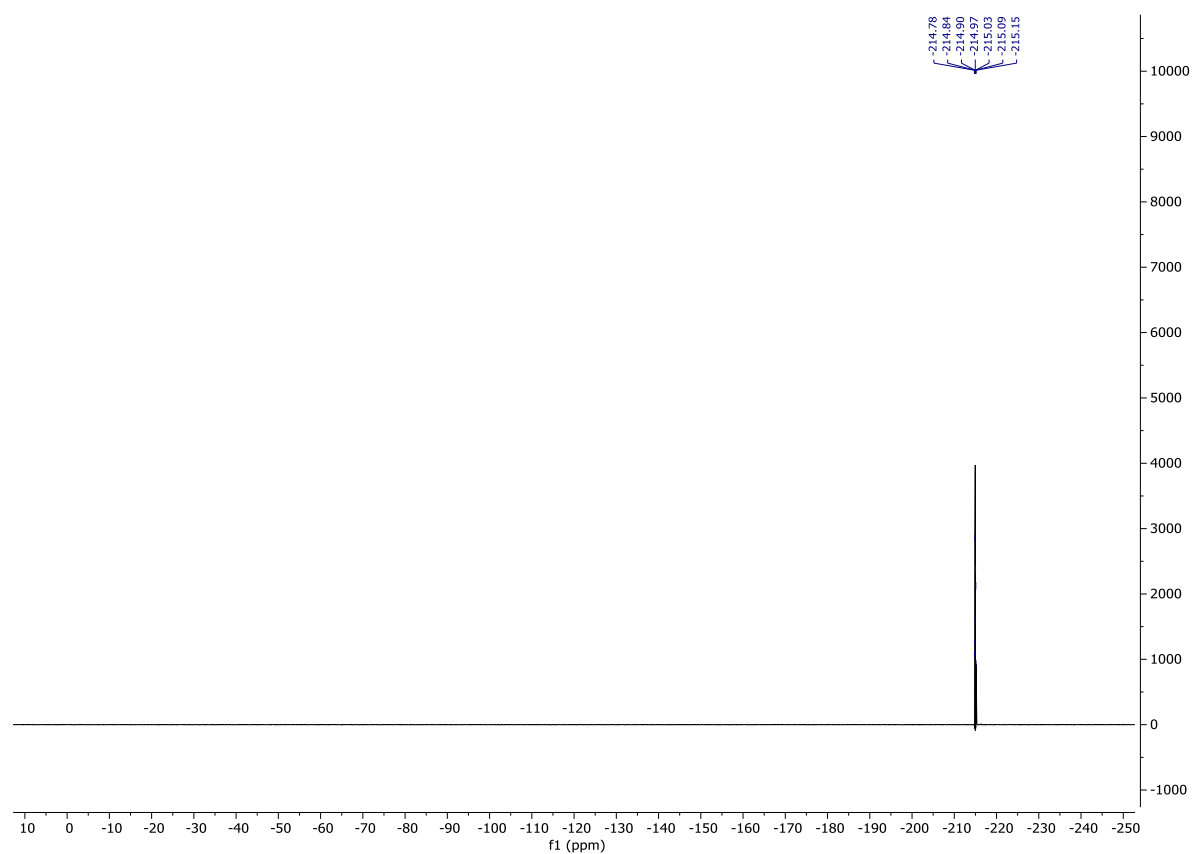
^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

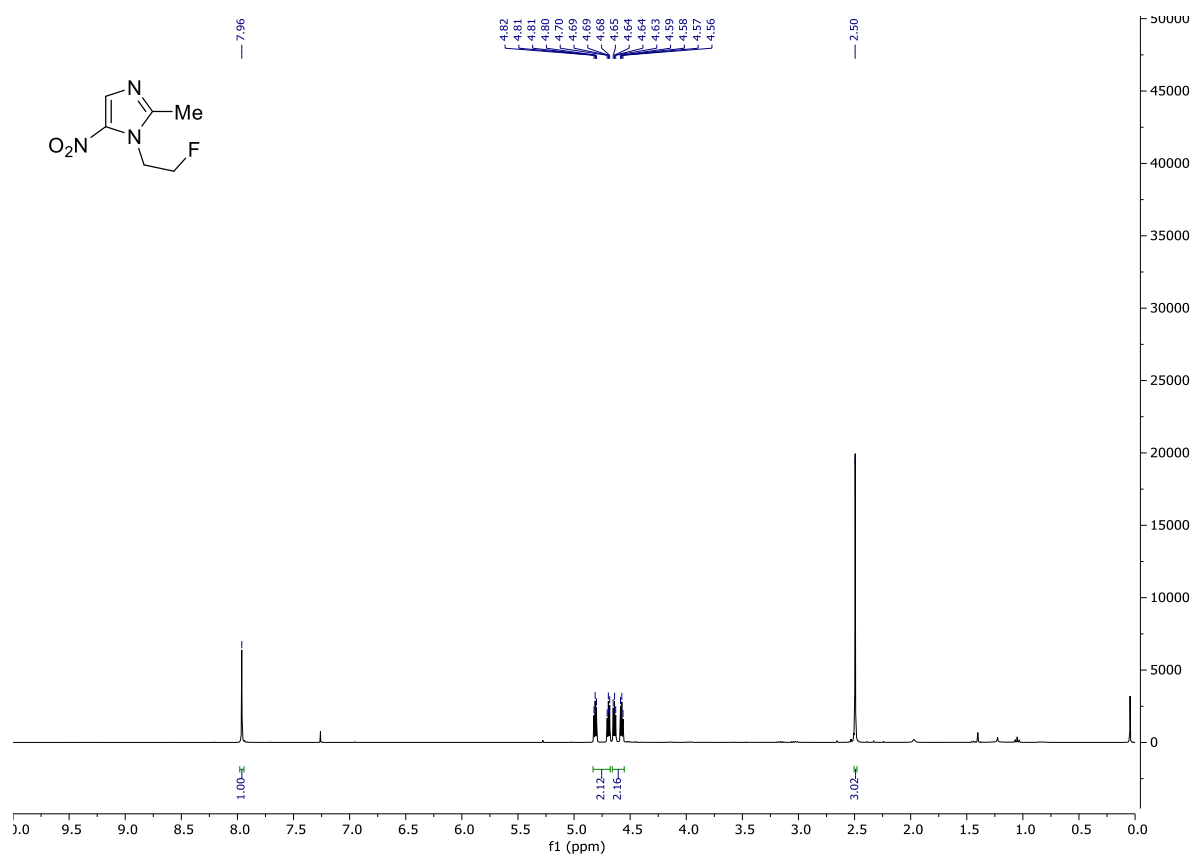


^{19}F NMR (376 MHz, CDCl_3)

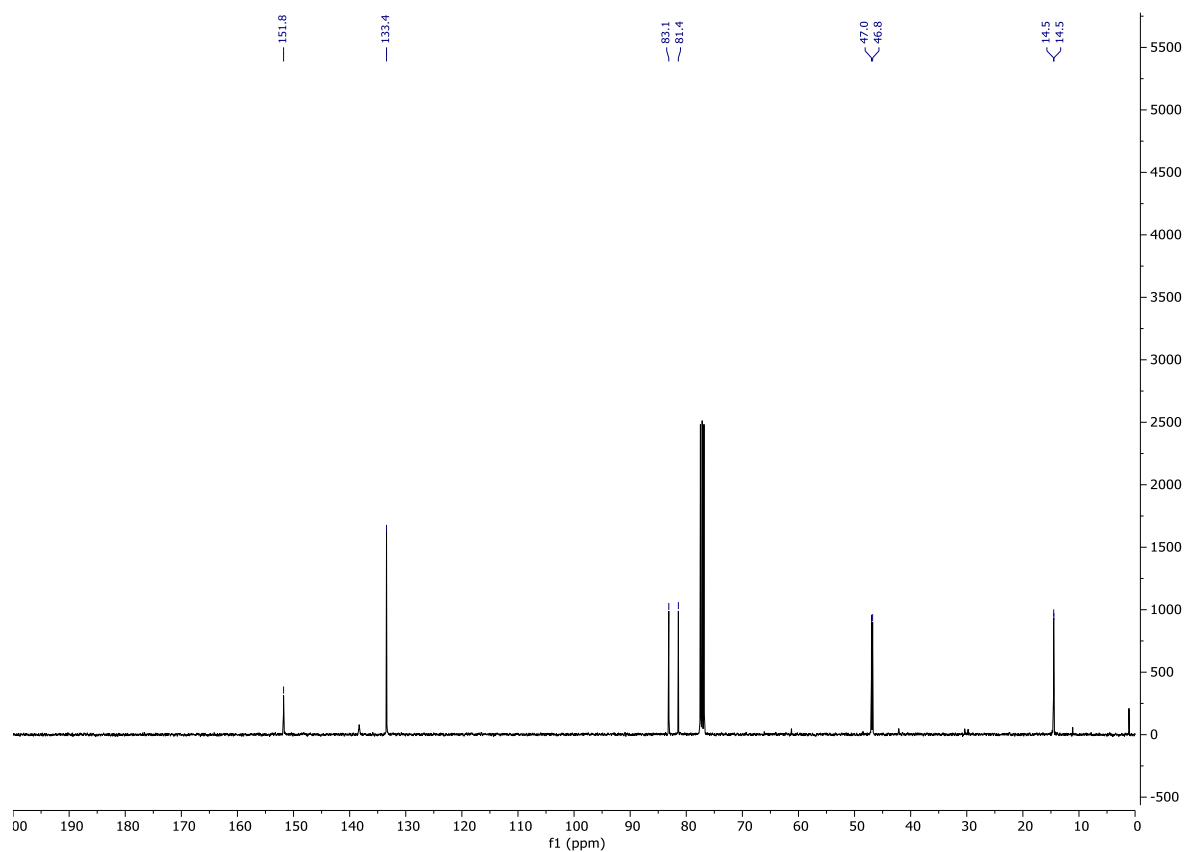


1-(2-Fluoroethyl)-2-methyl-5-nitro-1*H*-imidazole, compound **2d**

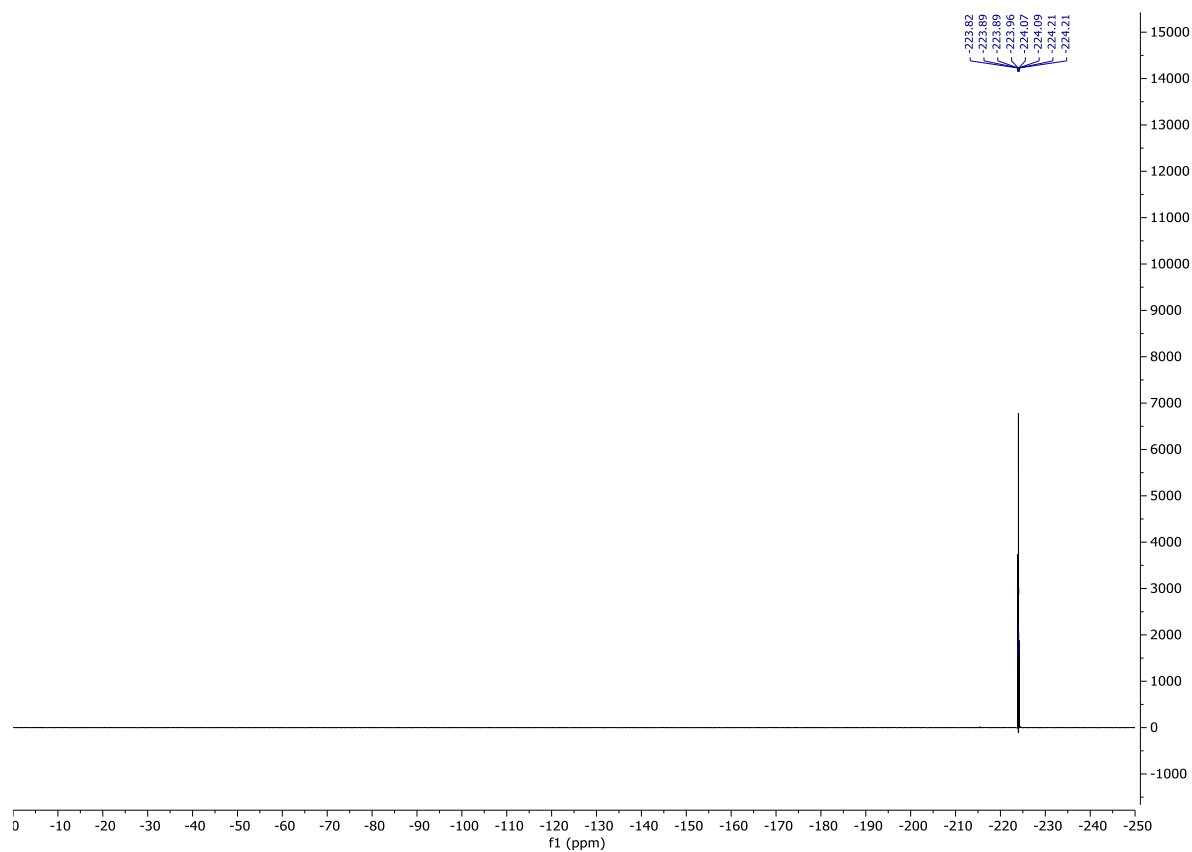
^1H NMR (400 MHz, CDCl_3)



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

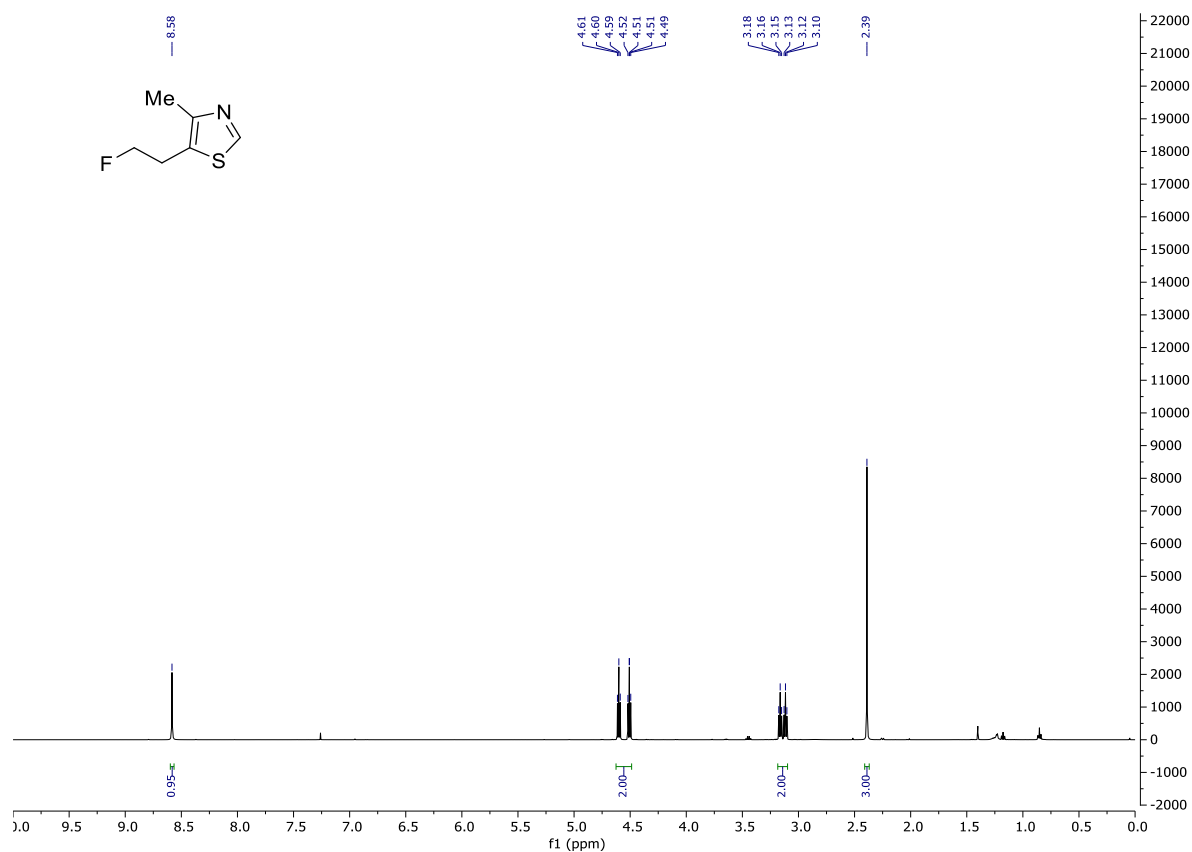


^{19}F NMR (376 MHz, CDCl_3)

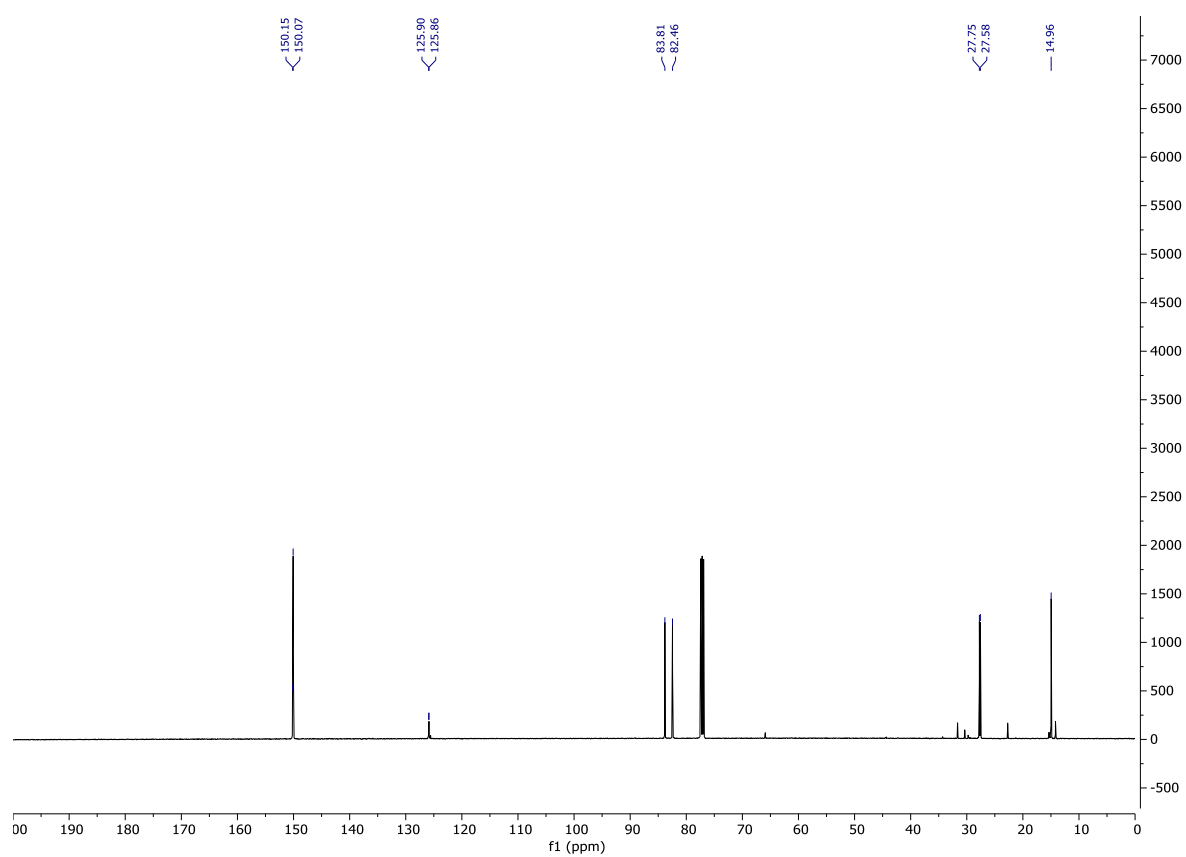


5-(2-Fluoroethyl)-4-methylthiazole, compound **2e**

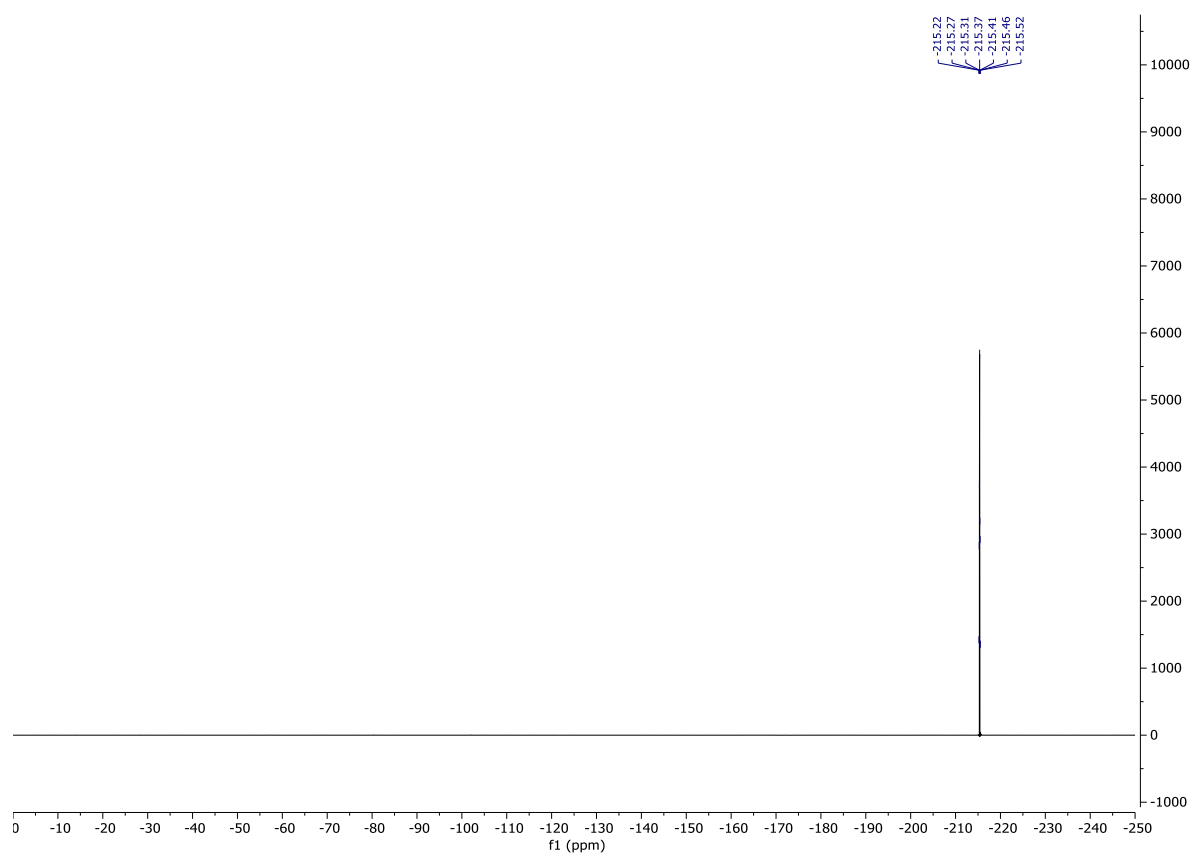
^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

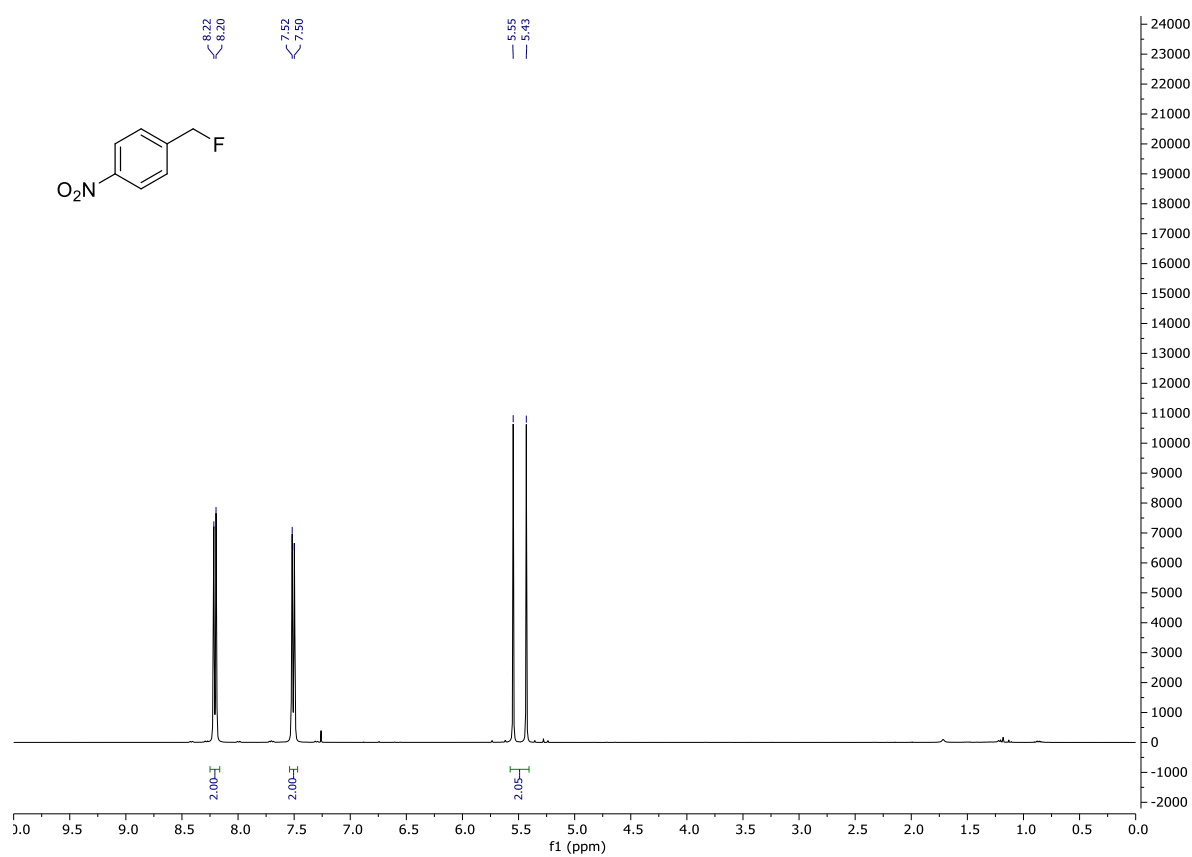


^{19}F NMR (471 MHz, CDCl_3)

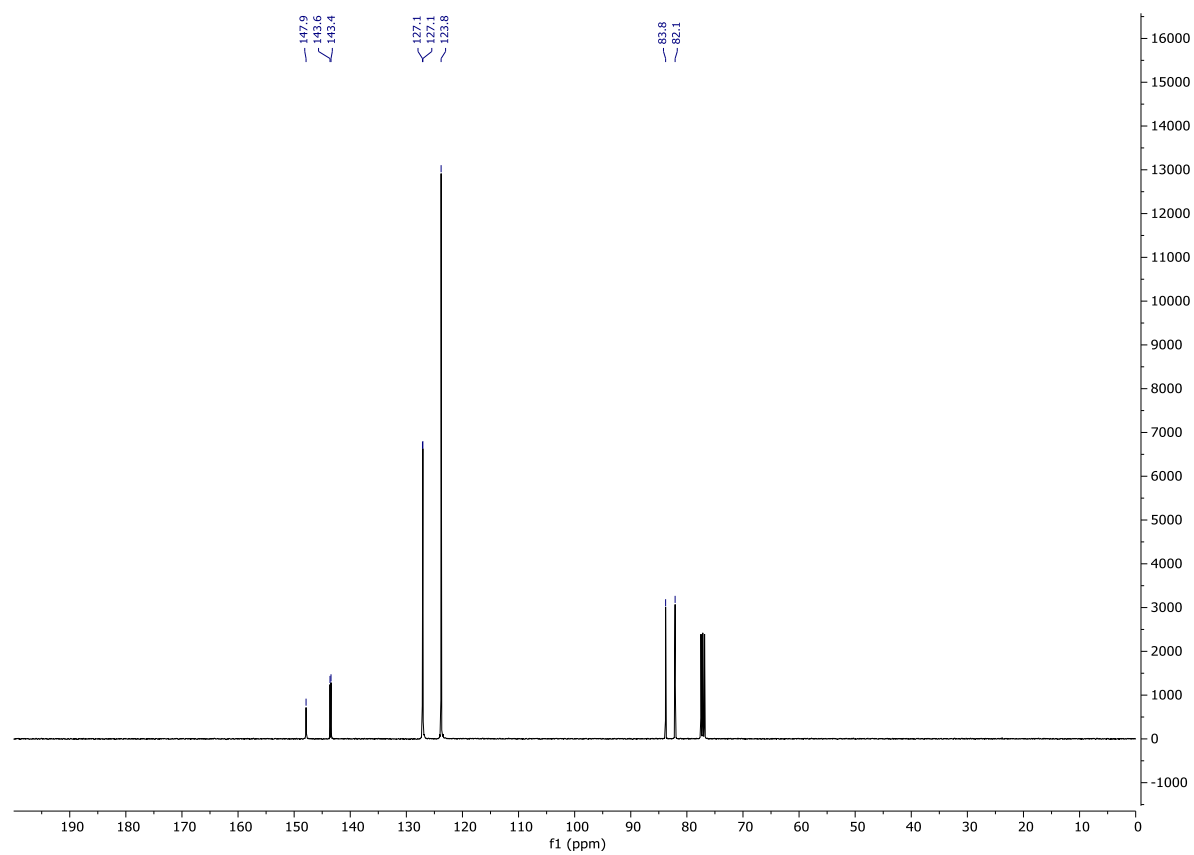


4-Nitrobenzyl fluoride, compound **2f**

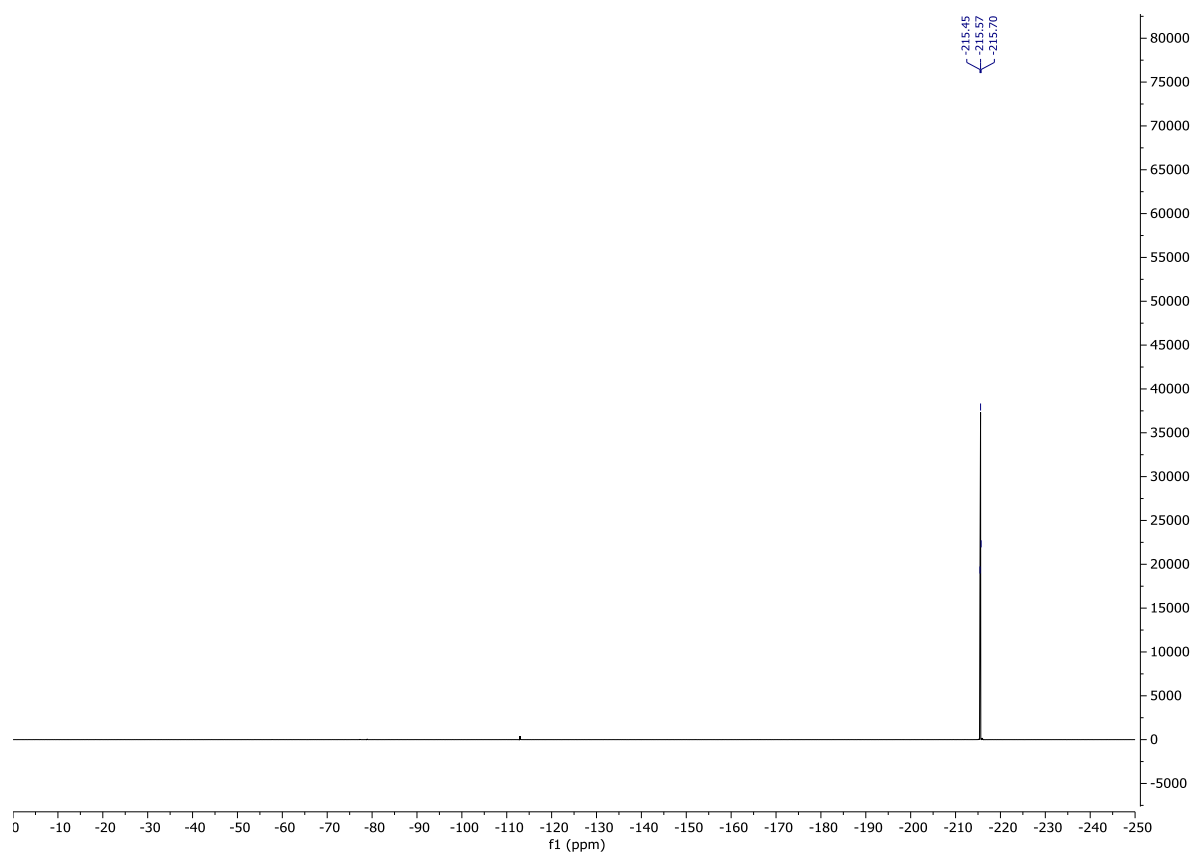
^1H NMR (400 MHz, CDCl_3)



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

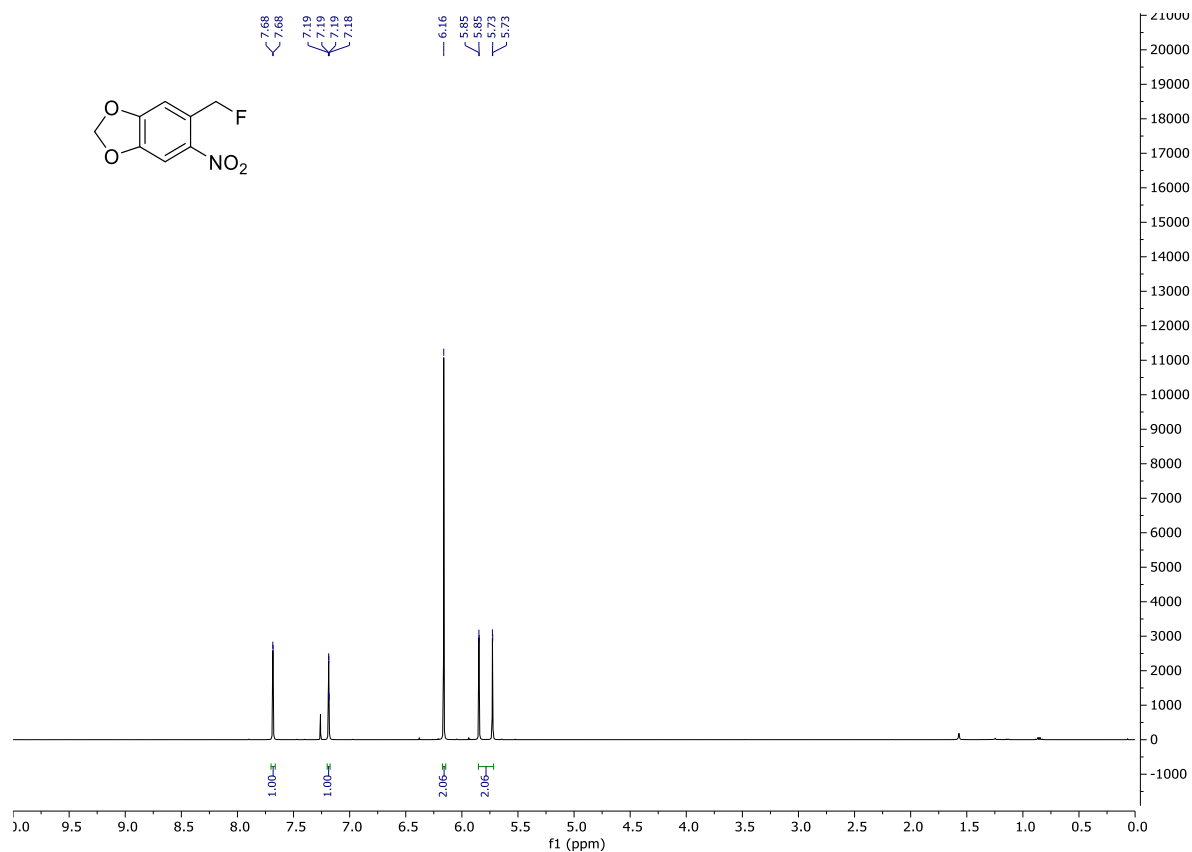


^{19}F NMR (376 MHz, CDCl_3)

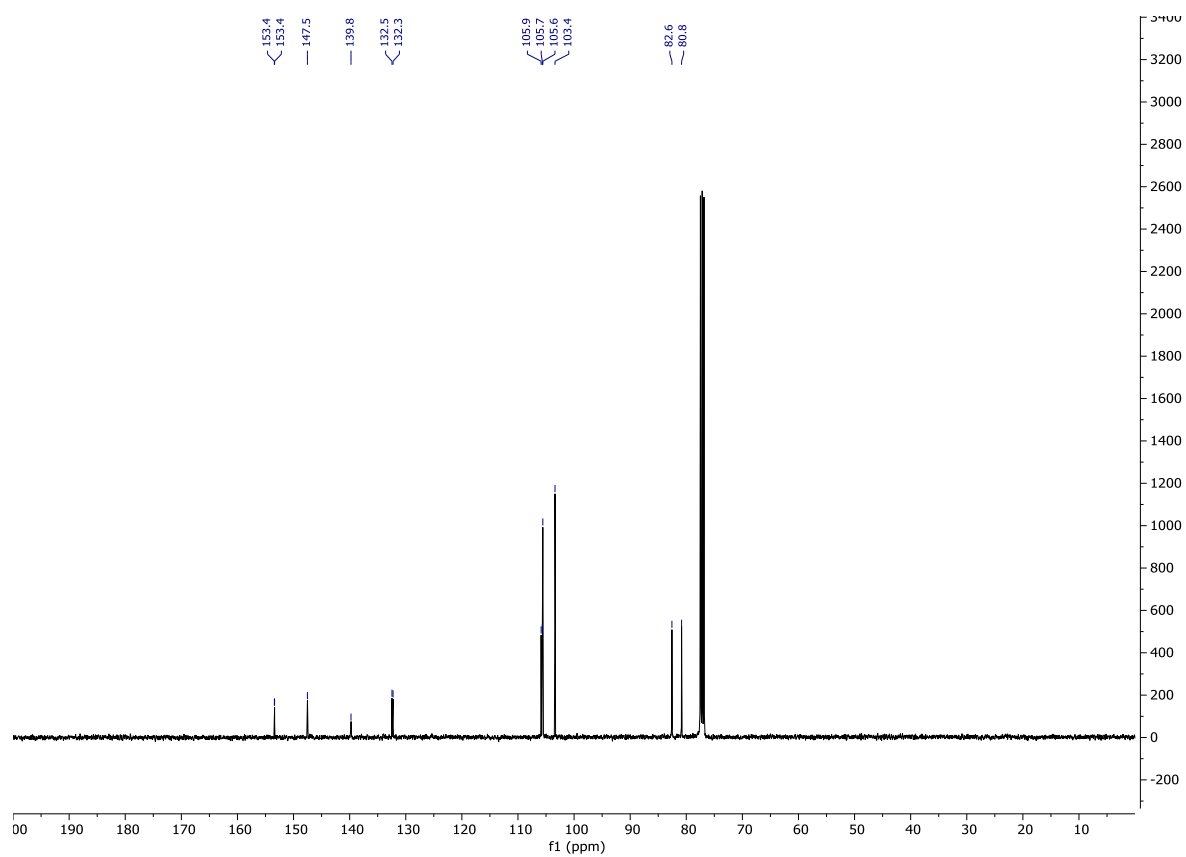


6-Nitropiperonyl fluoride, compound **2g**

^1H NMR (400 MHz, CDCl_3)



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

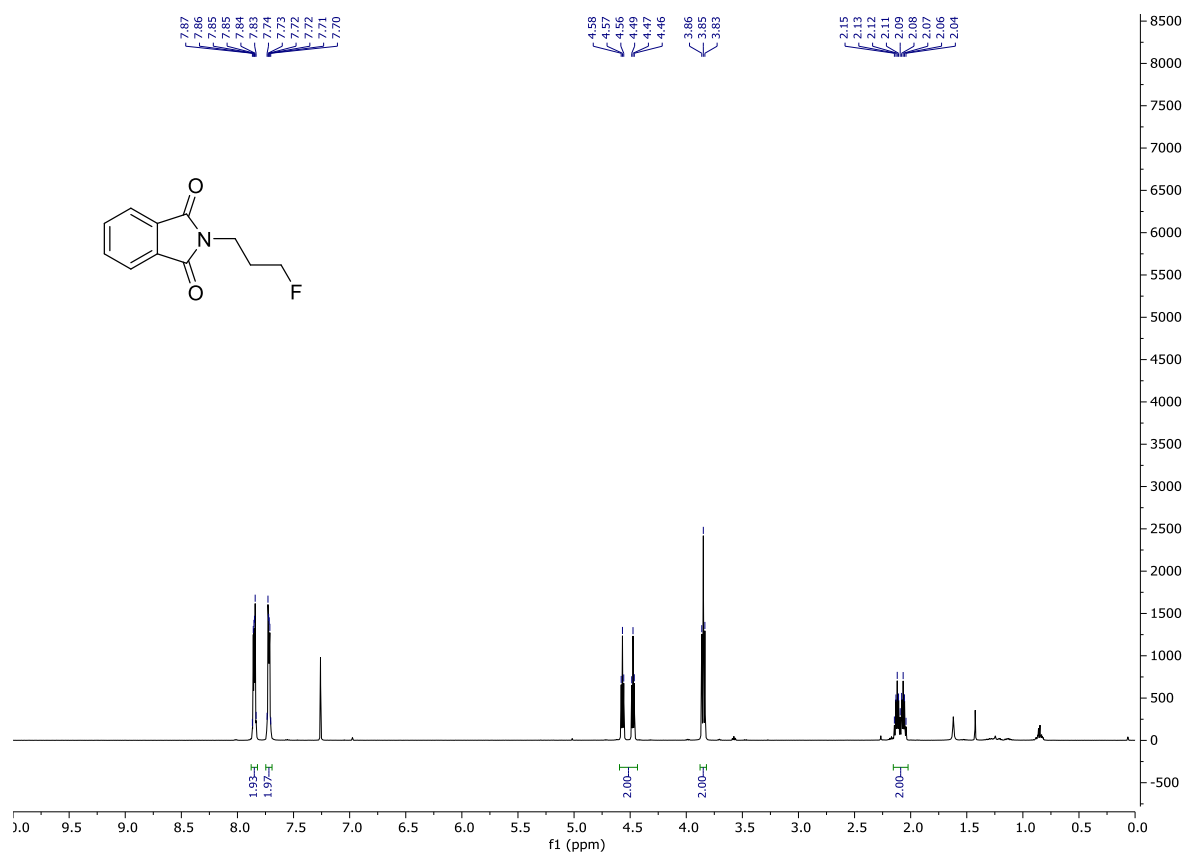


^{19}F NMR (376 MHz, CDCl_3)

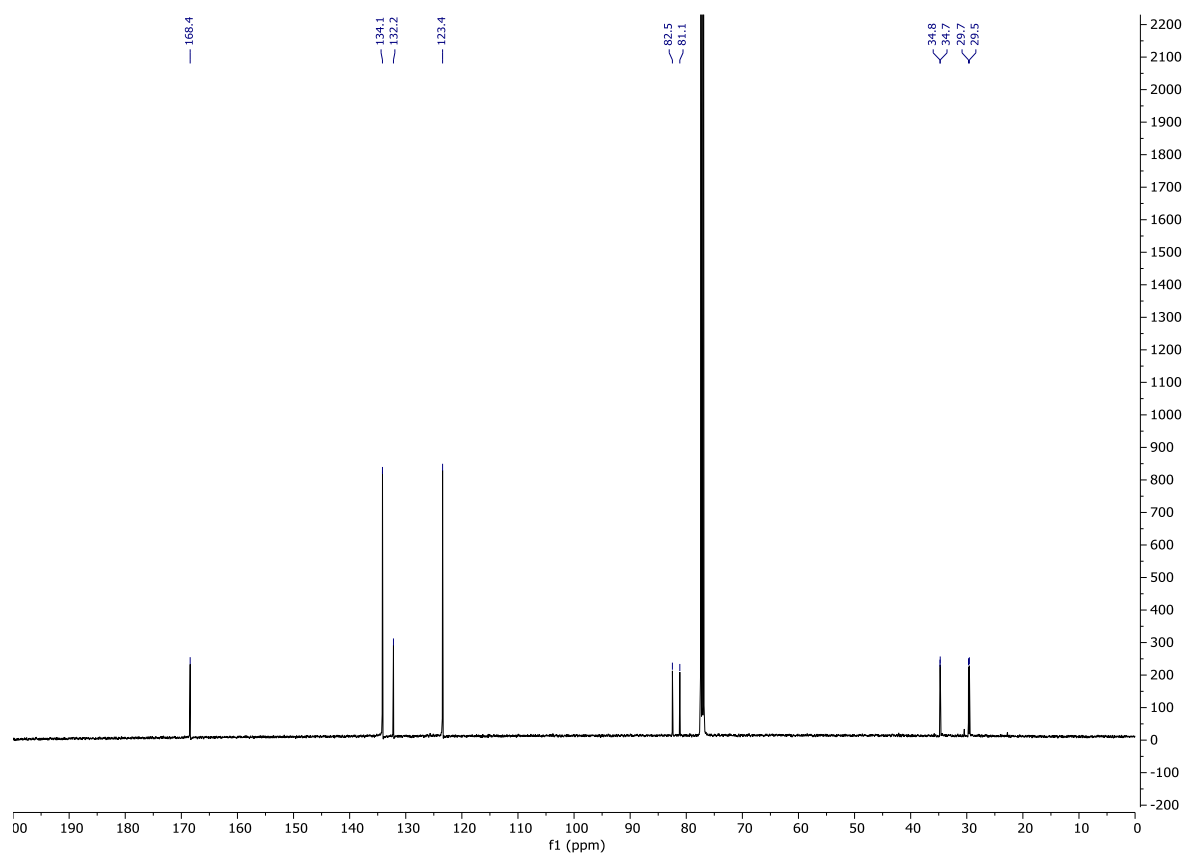


N-(3-Fluoropropyl)phthalimide, compound **2h**

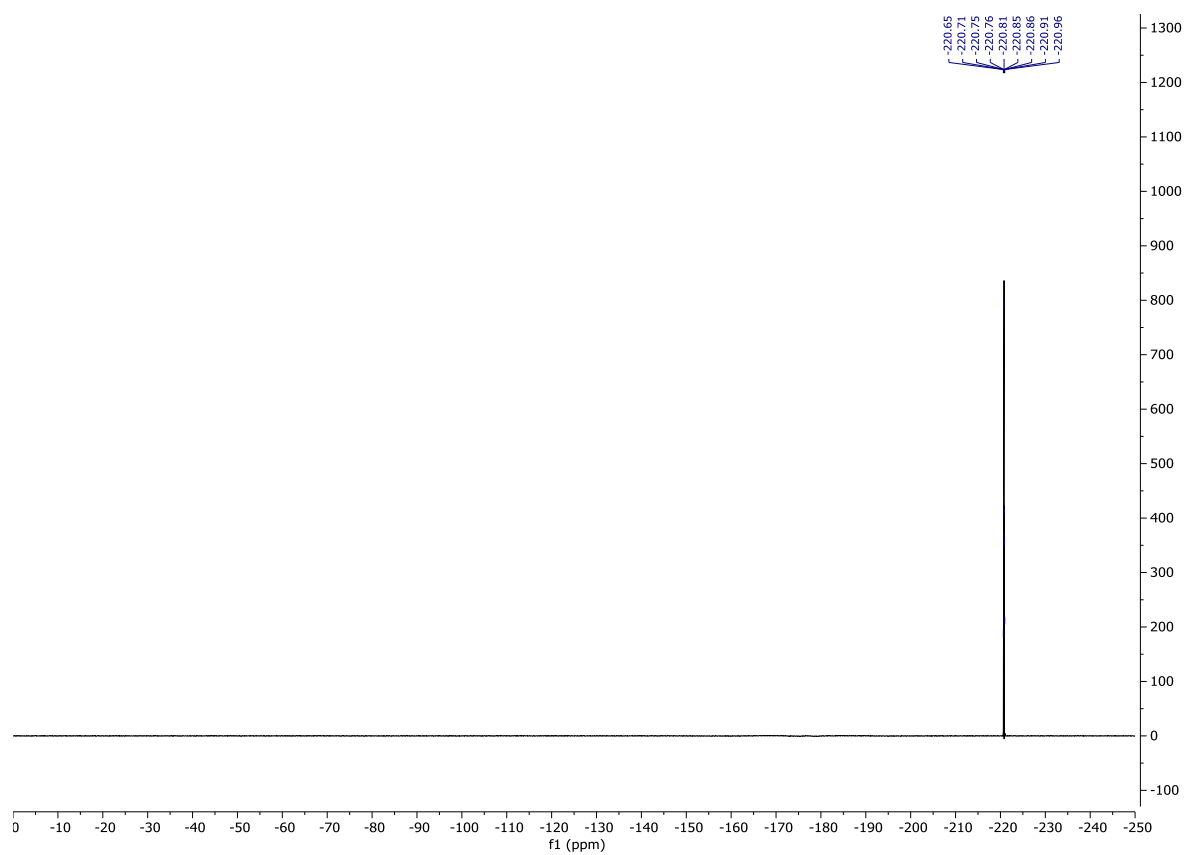
^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

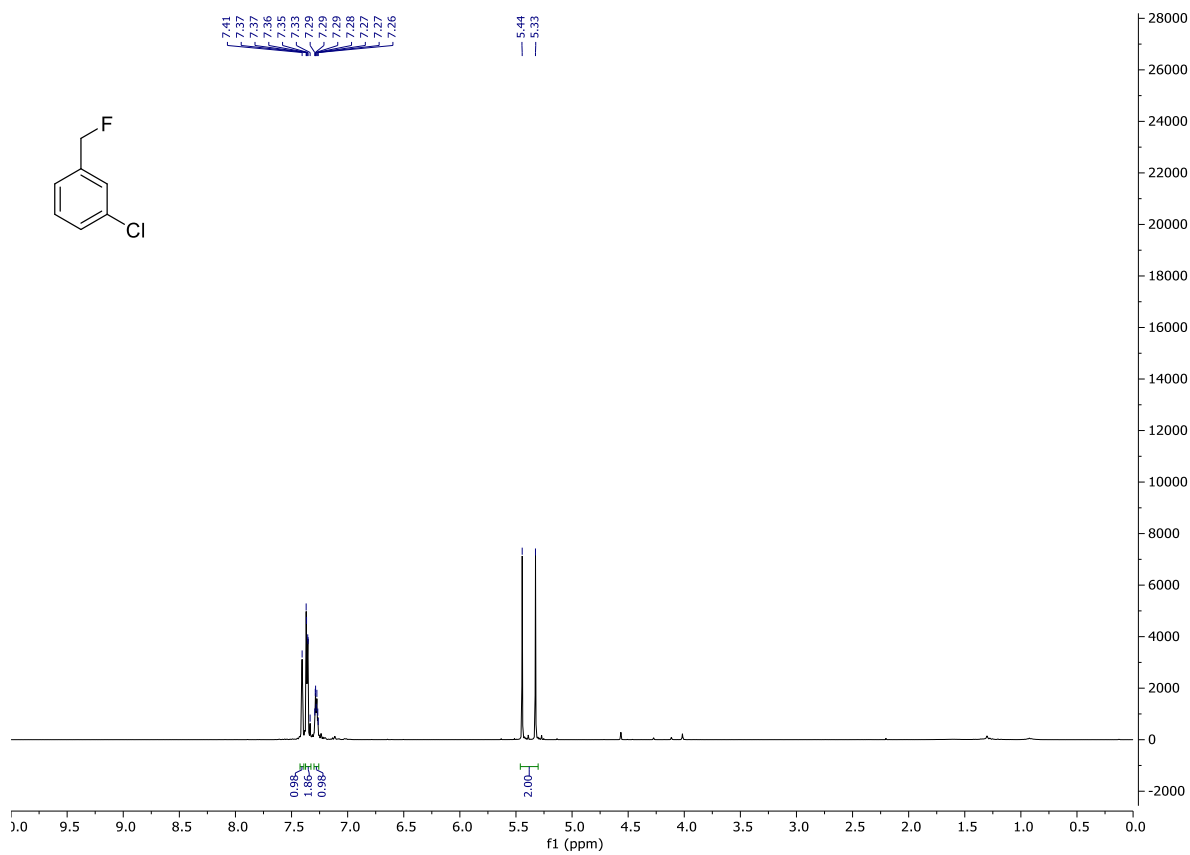


^{19}F NMR (471 MHz, CDCl_3)

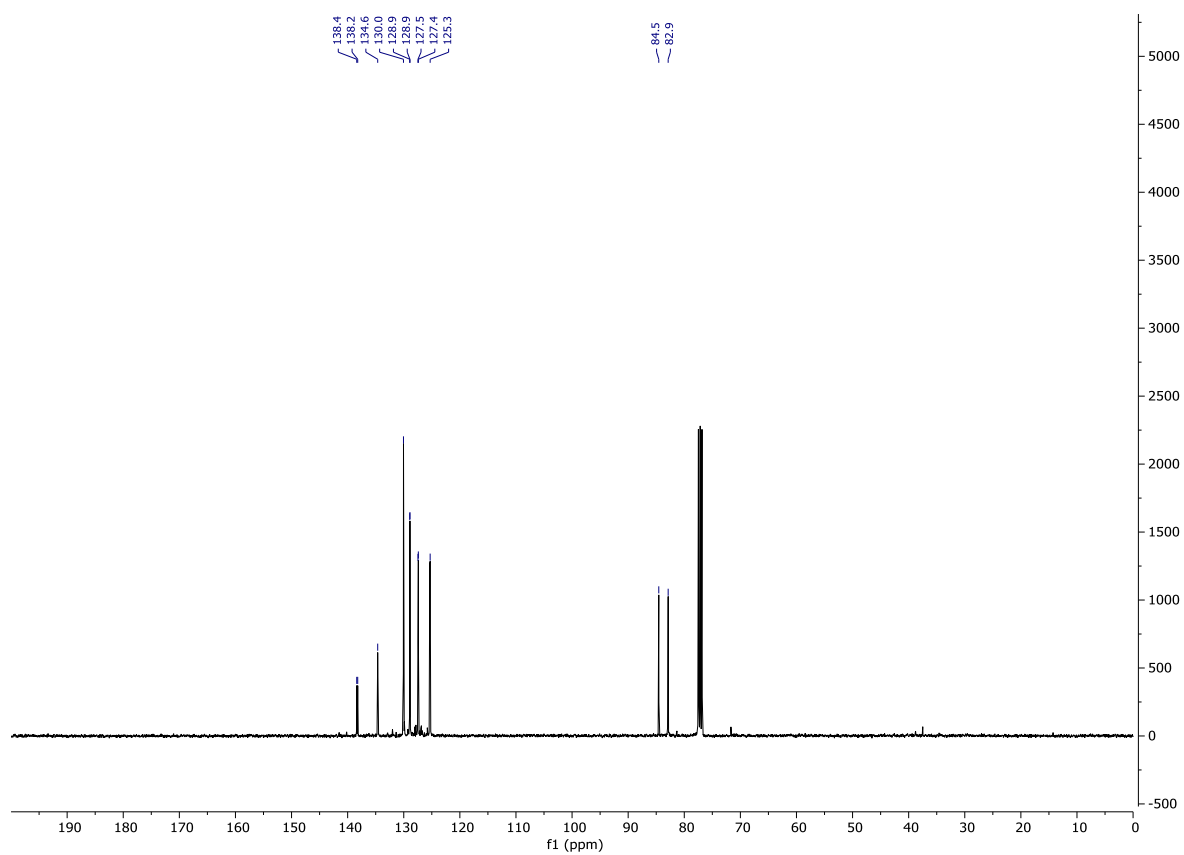


1-Chloro-3-(fluoromethyl)benzene, compound **2i**

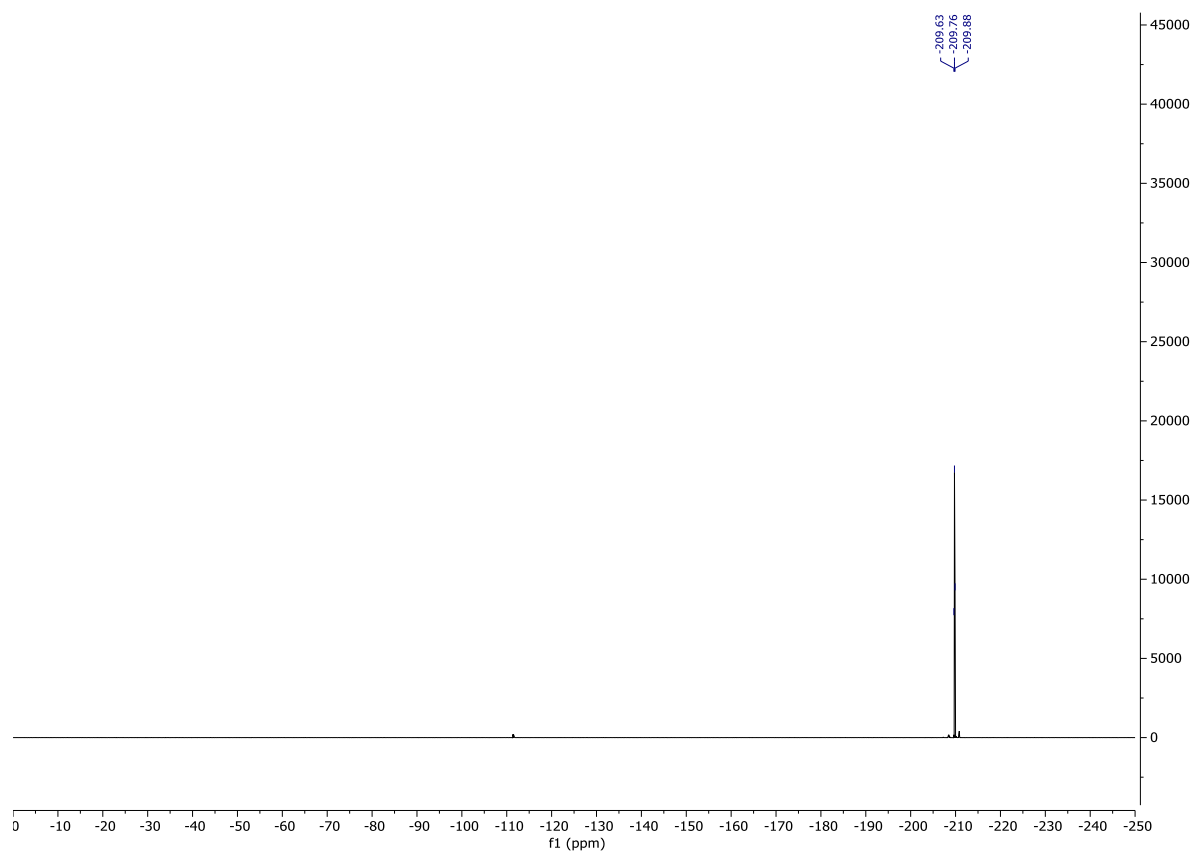
^1H NMR (400 MHz, CDCl_3)



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

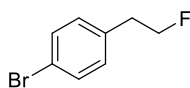
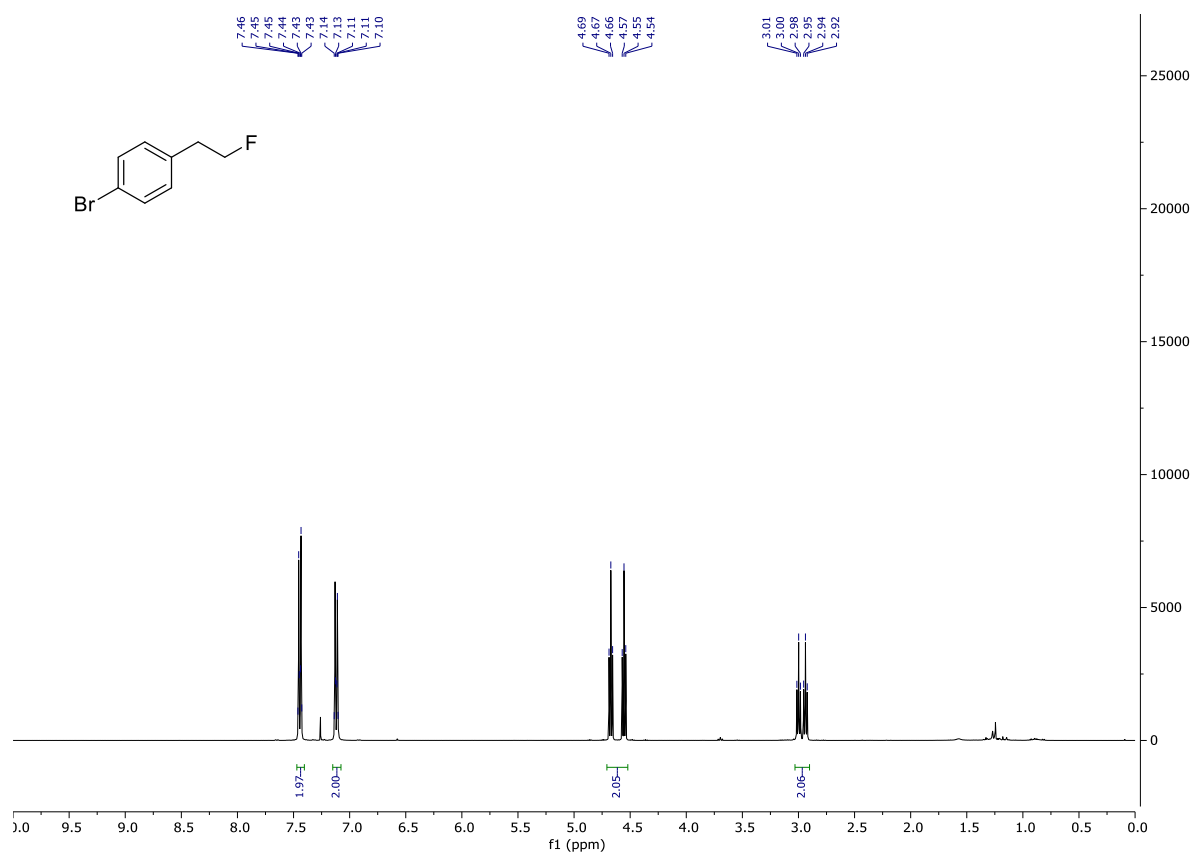


^{19}F NMR (376 MHz, CDCl_3)

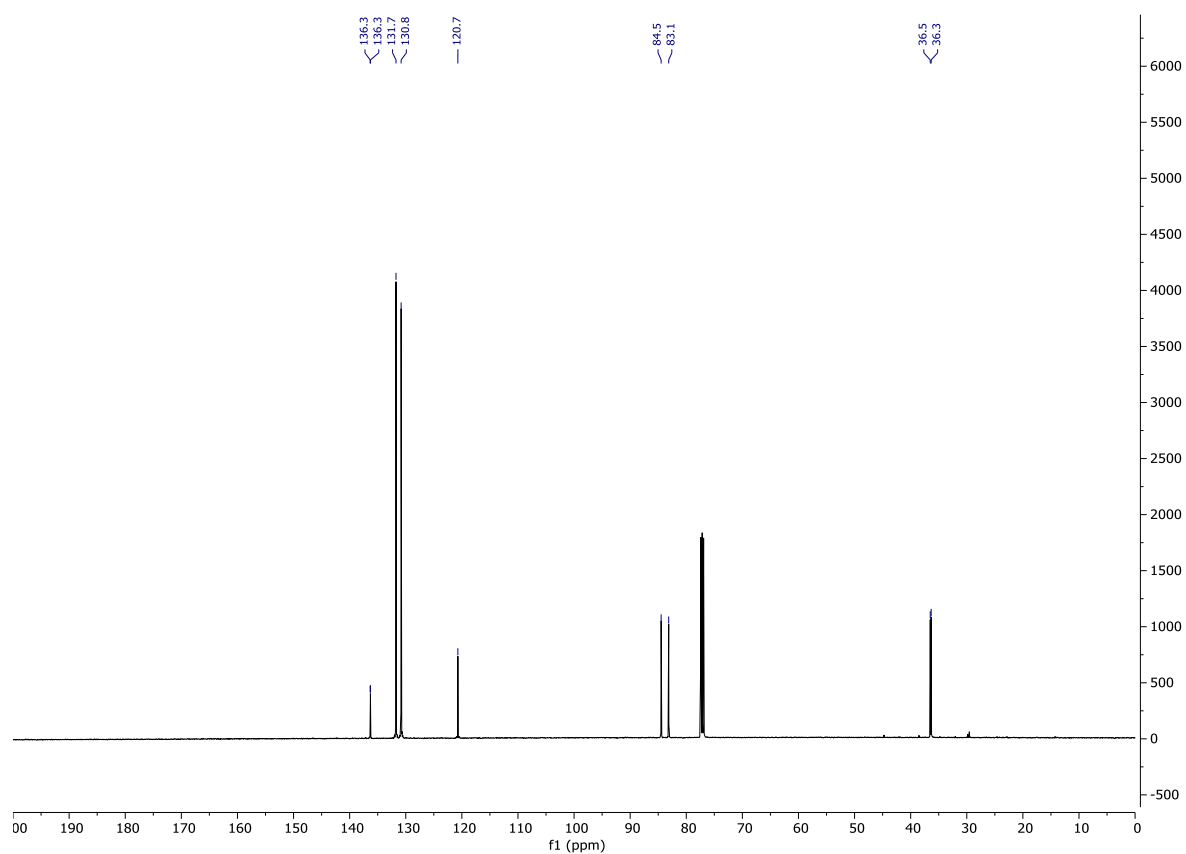


1-Bromo-4-(2-fluoroethyl)benzene, compound **2j**

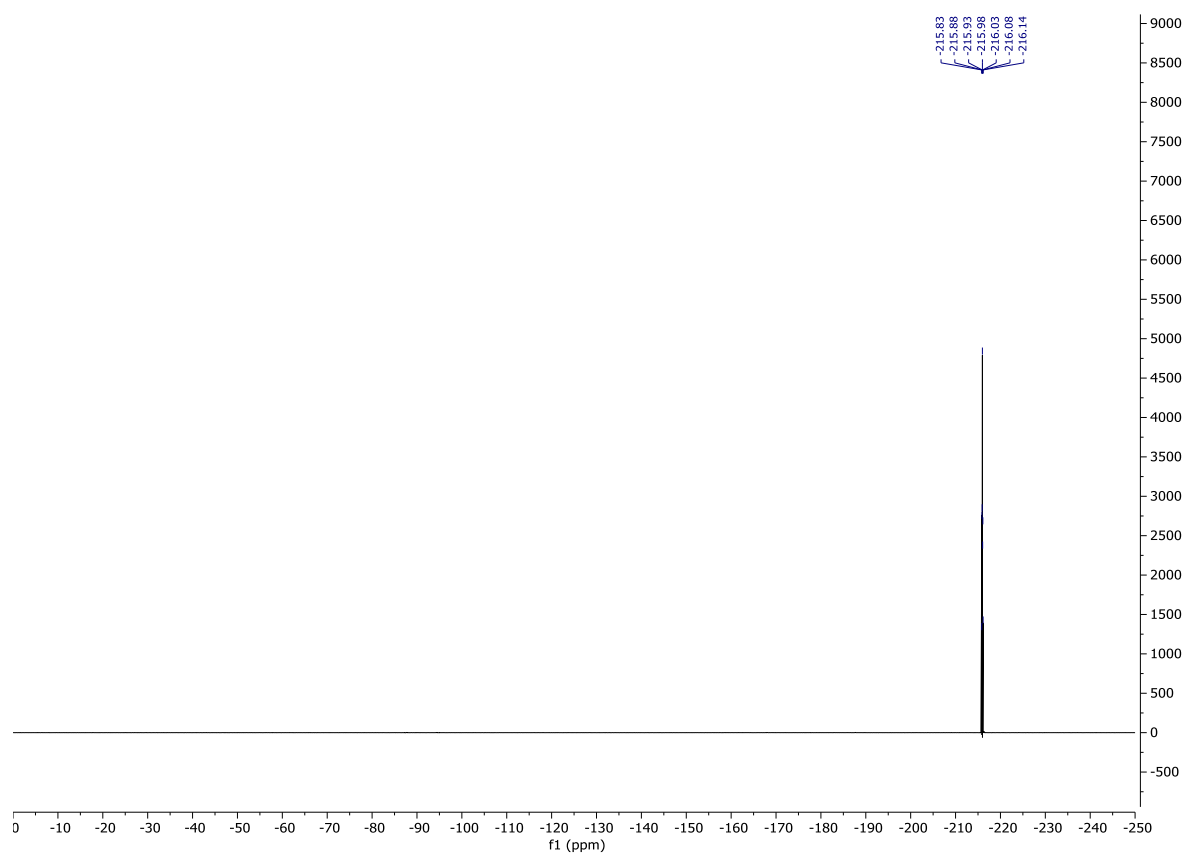
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

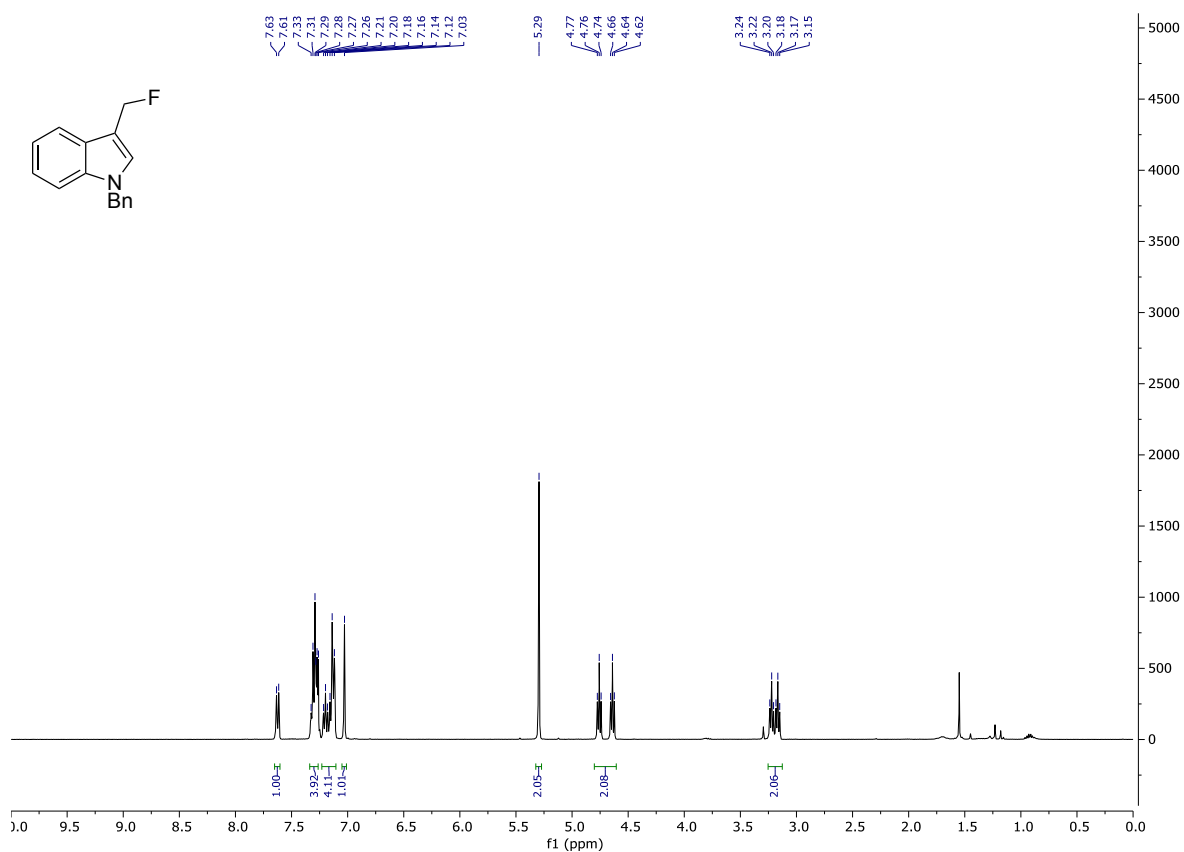


^{19}F NMR (471 MHz, CDCl_3)

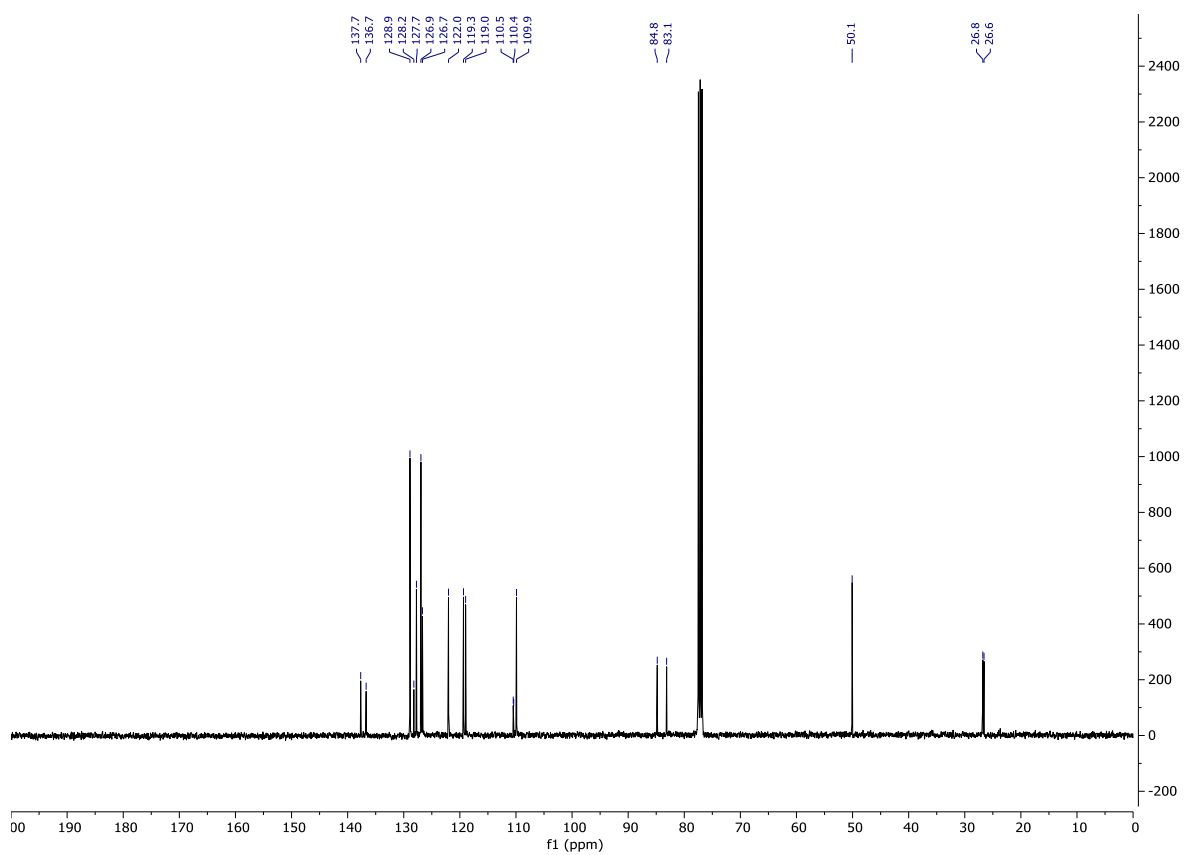


1-Benzyl-3-(2-fluoroethyl)-1*H*-indole, compound **2k**

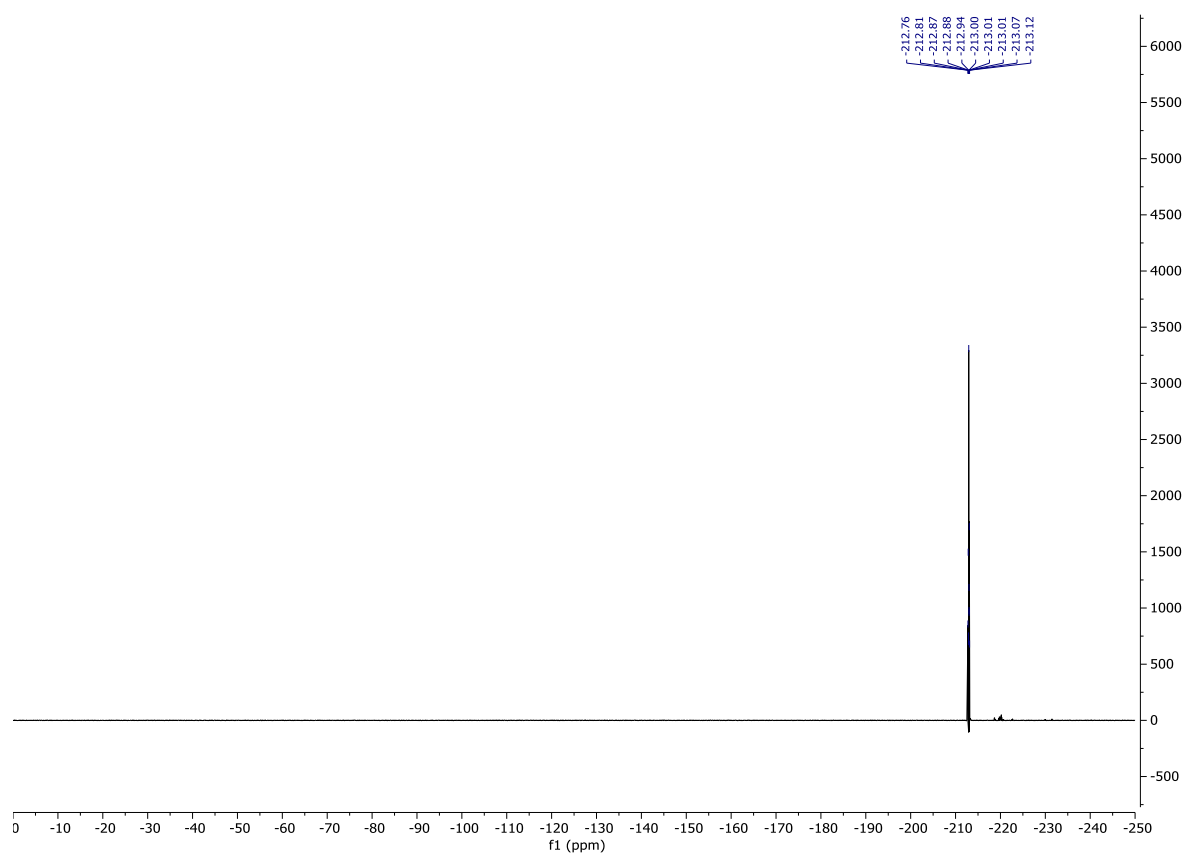
^1H NMR (400 MHz, CDCl_3)



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

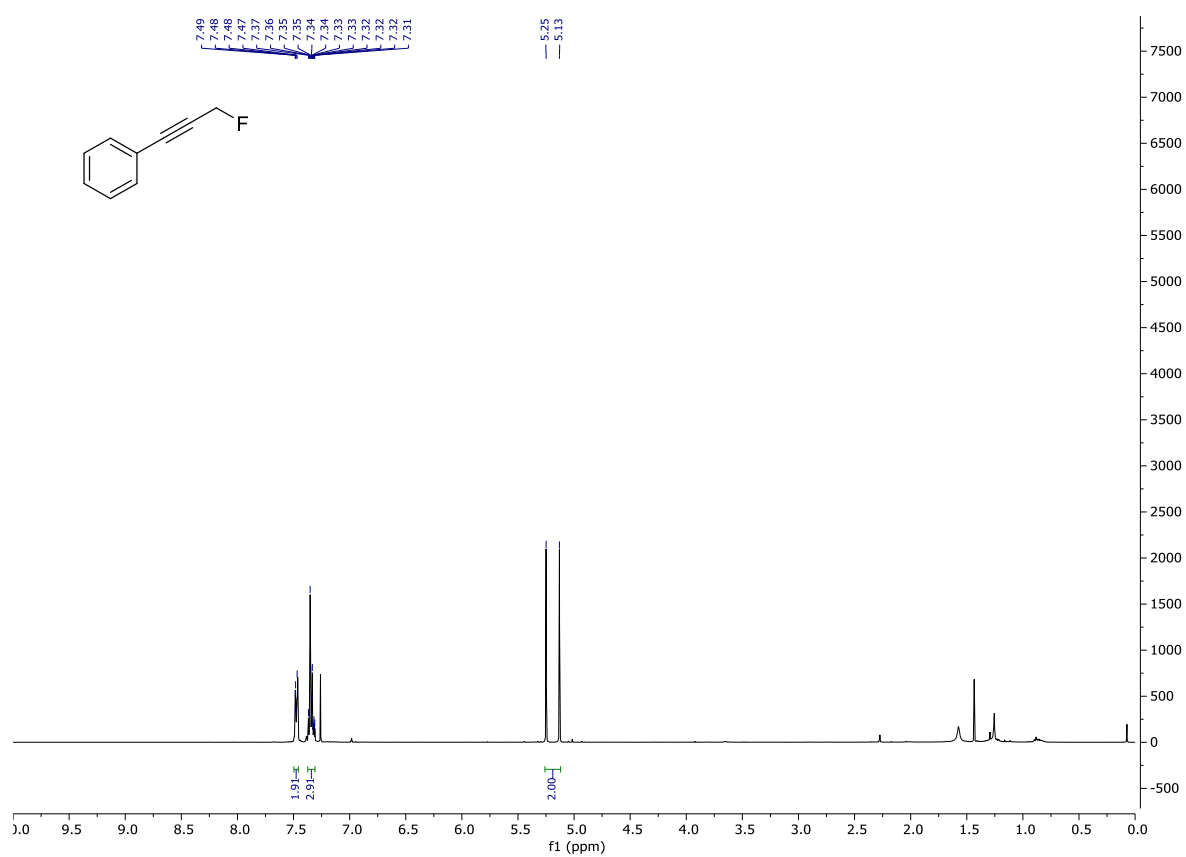


^{19}F NMR (376 MHz, CDCl_3)

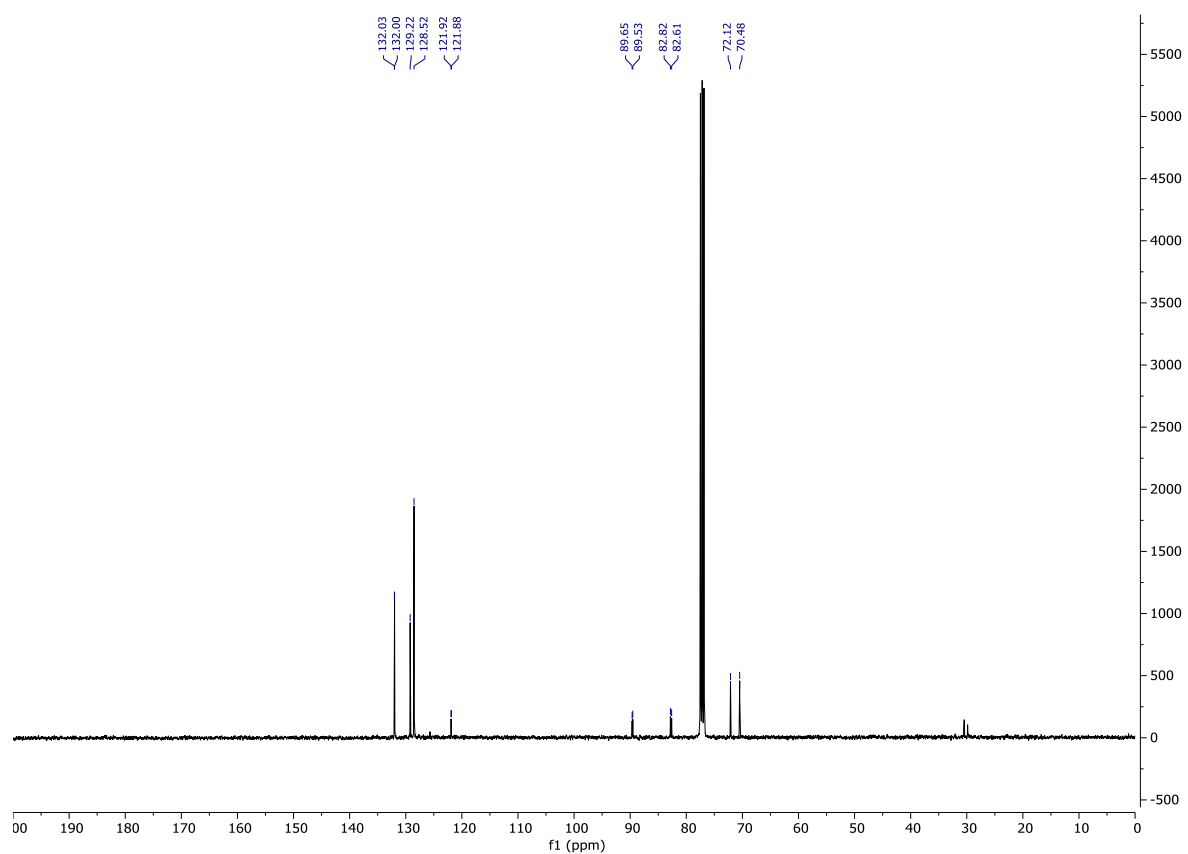


(3-Fluoroprop-1-yn-1-yl)benzene, compound **21**

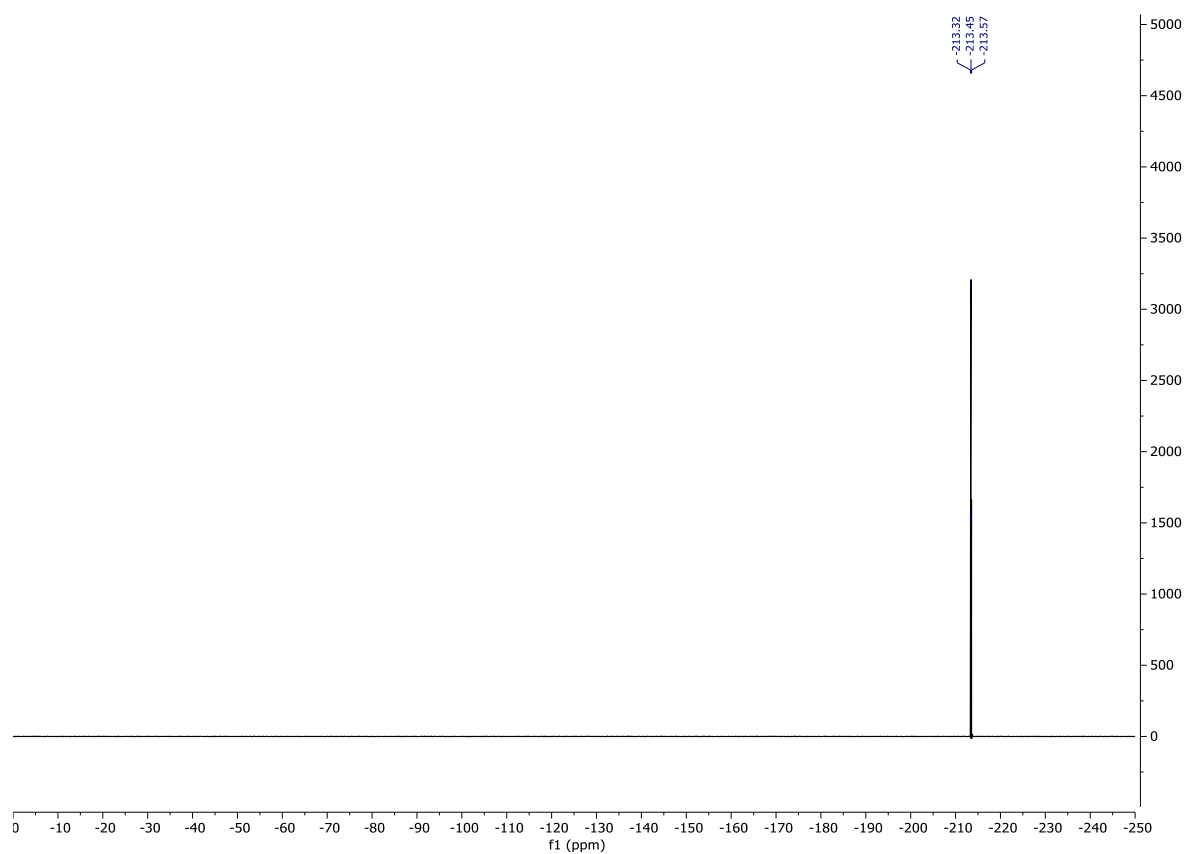
^1H NMR (400 MHz, CDCl_3)



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

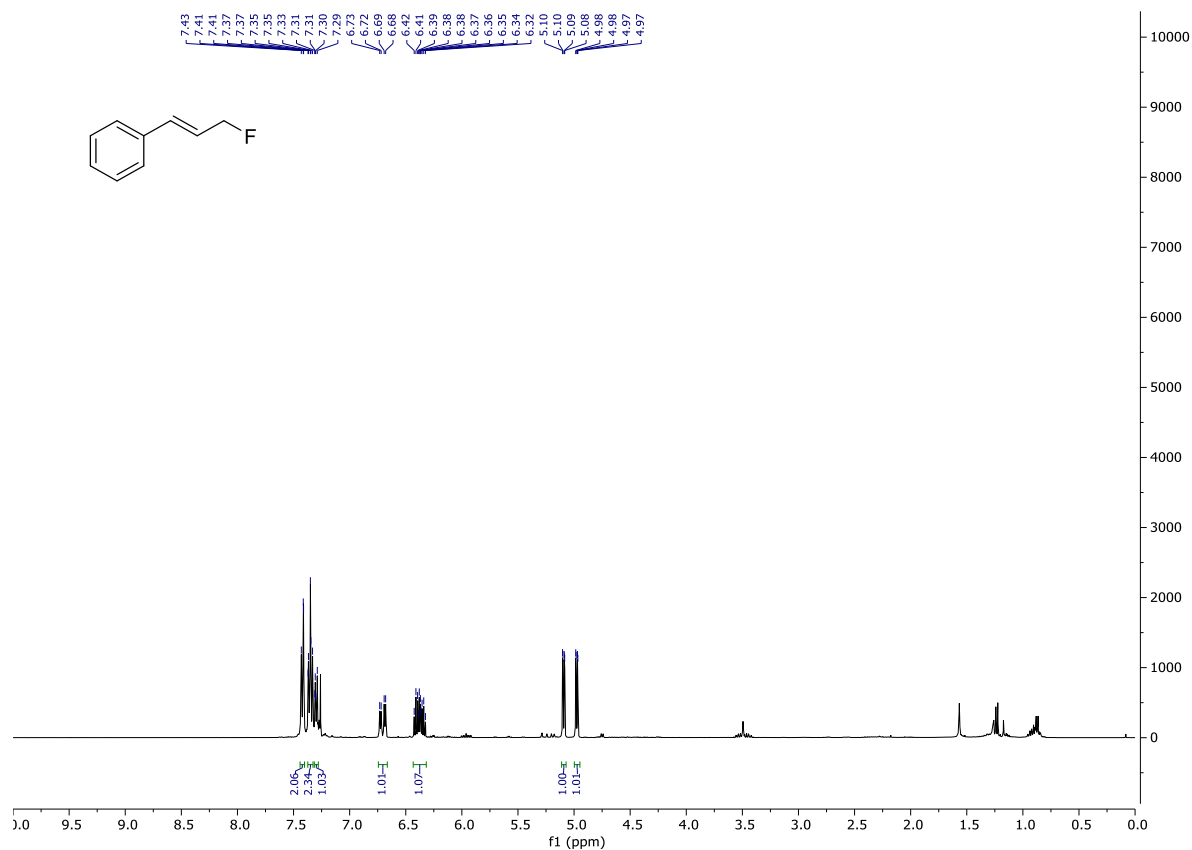


^{19}F NMR (376 MHz, CDCl_3)

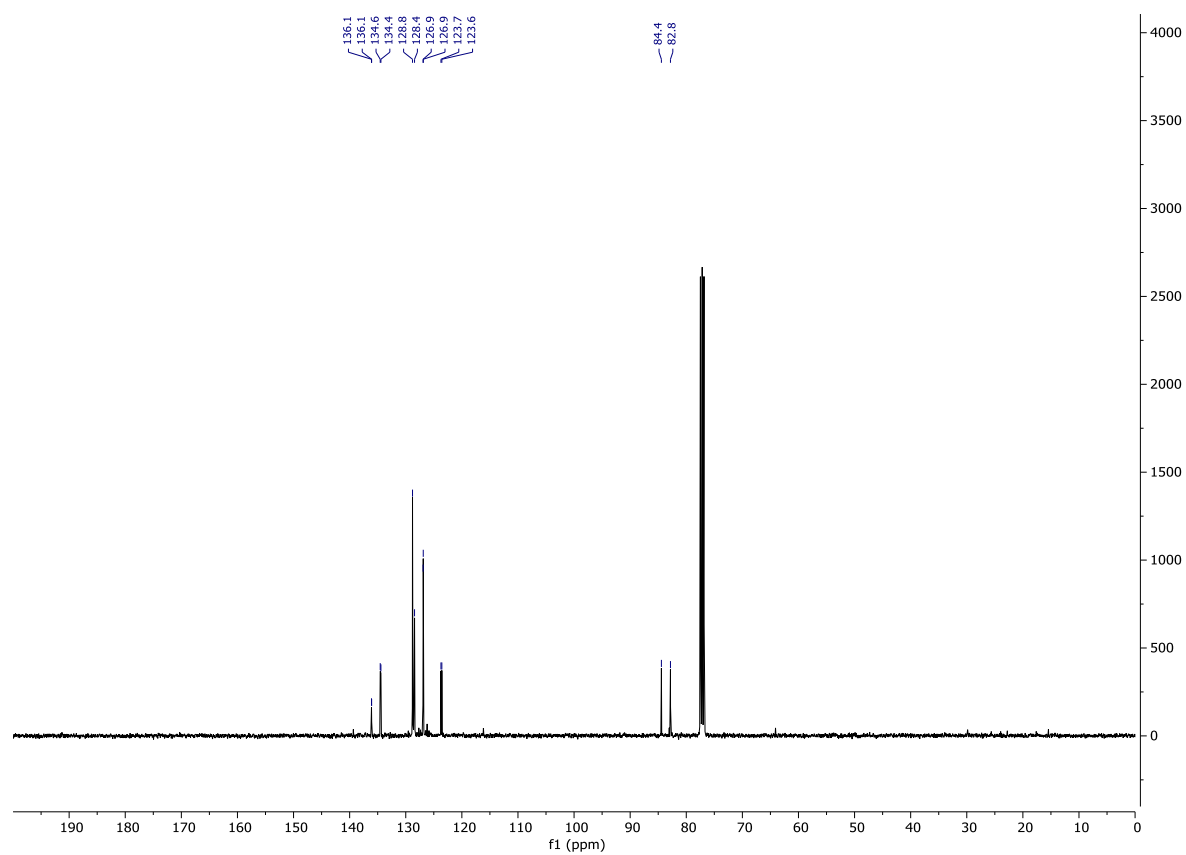


Cinnamyl fluoride, compound **2m**

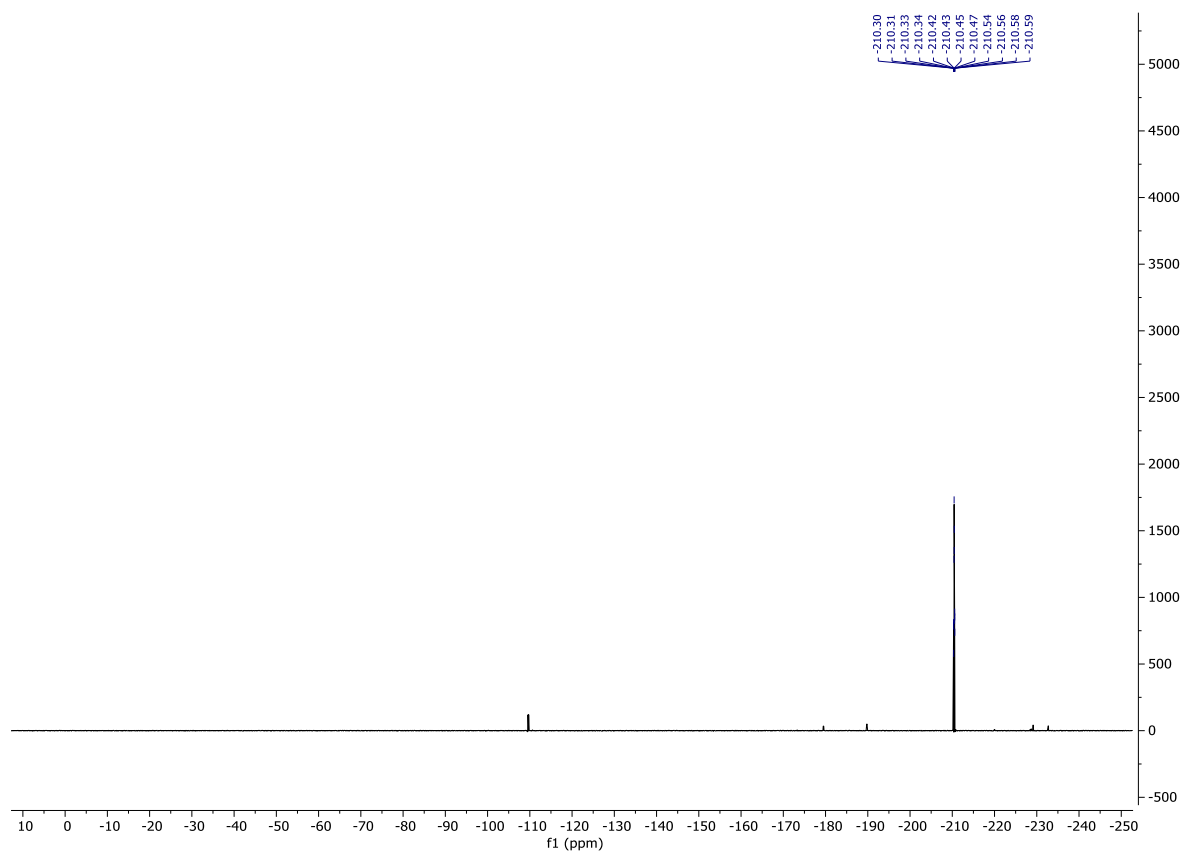
^1H NMR (400 MHz, CDCl_3)



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

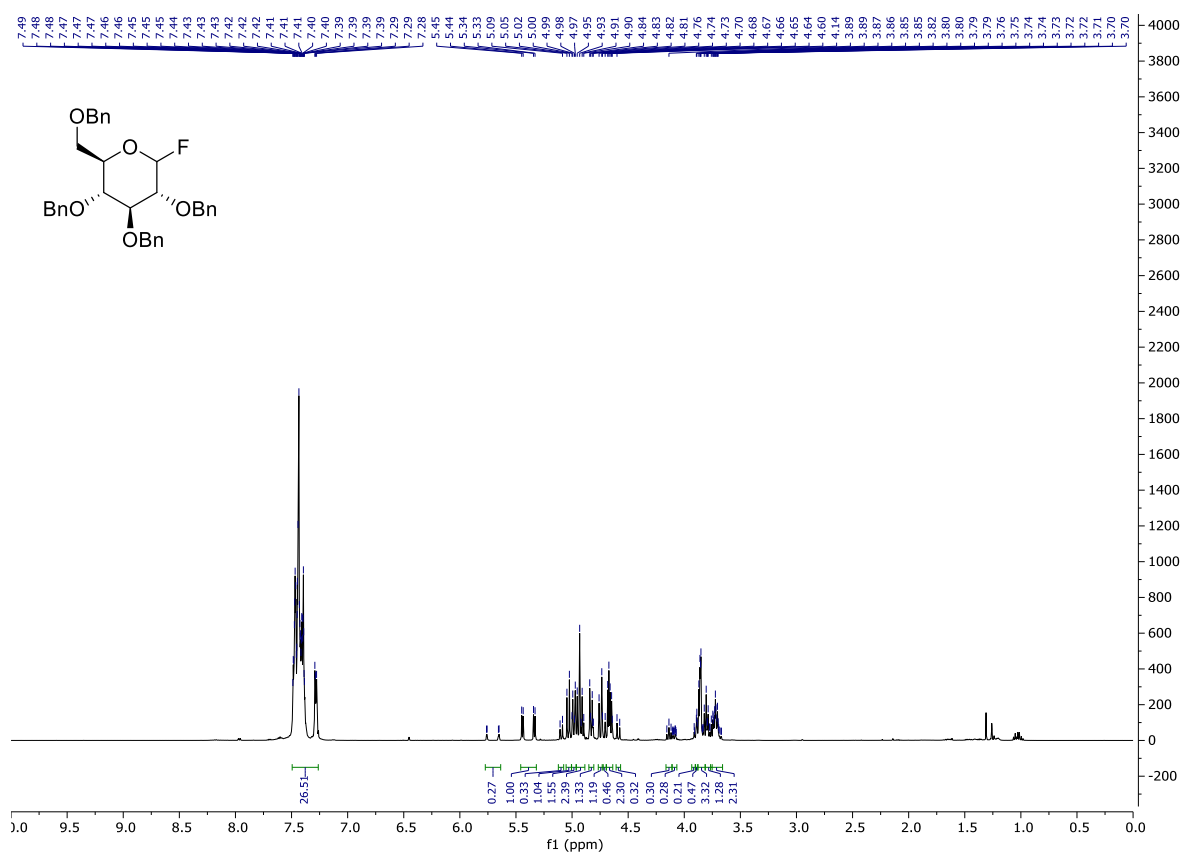


^{19}F NMR (376 MHz, CDCl_3)

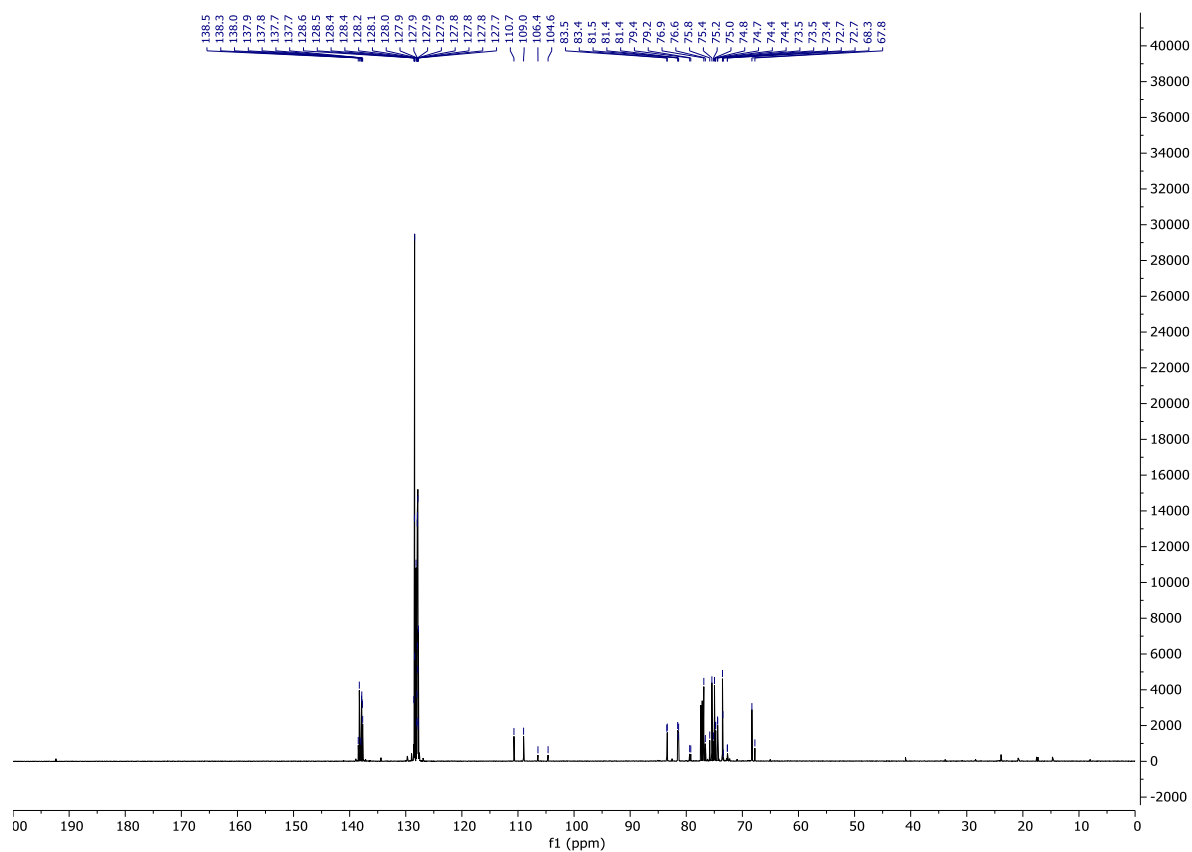


2,3,4,6-Tetra-*O*-benzyl-D-glucopyranosyl fluoride, compound **2n**

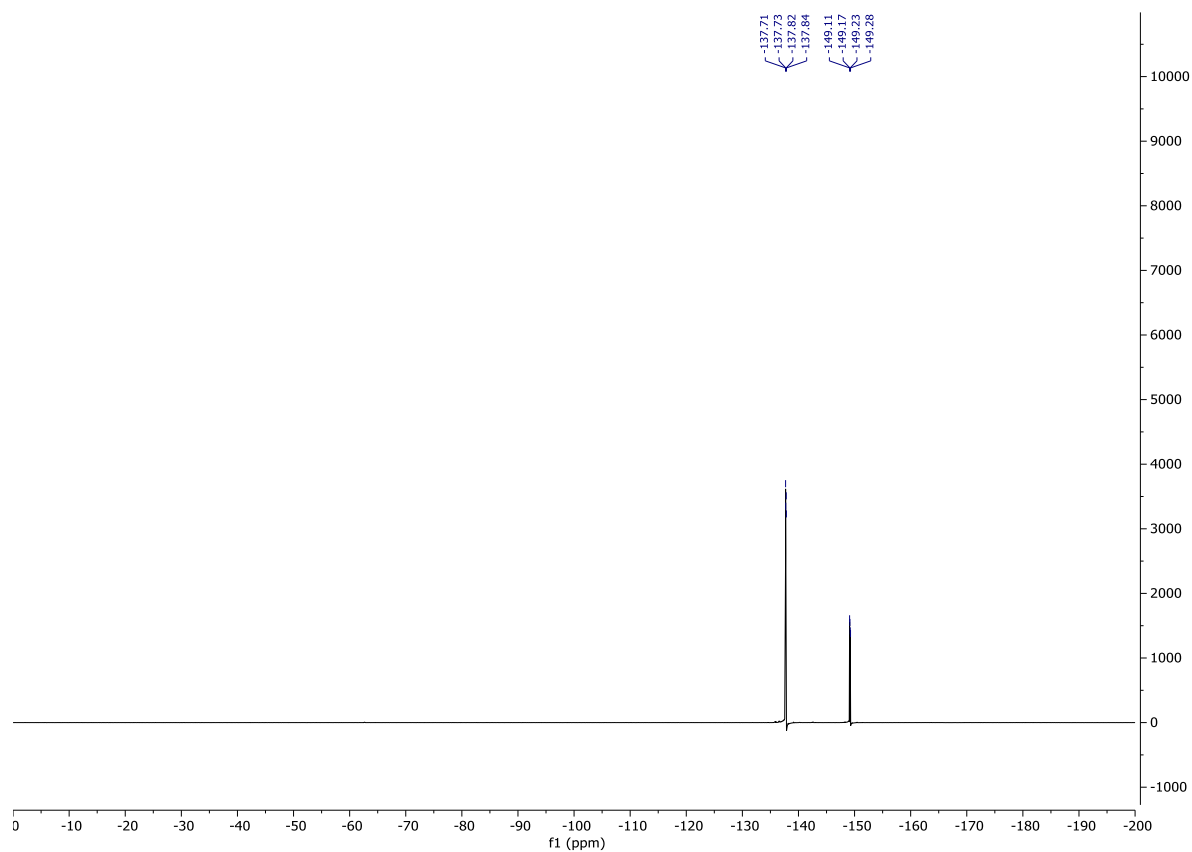
^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

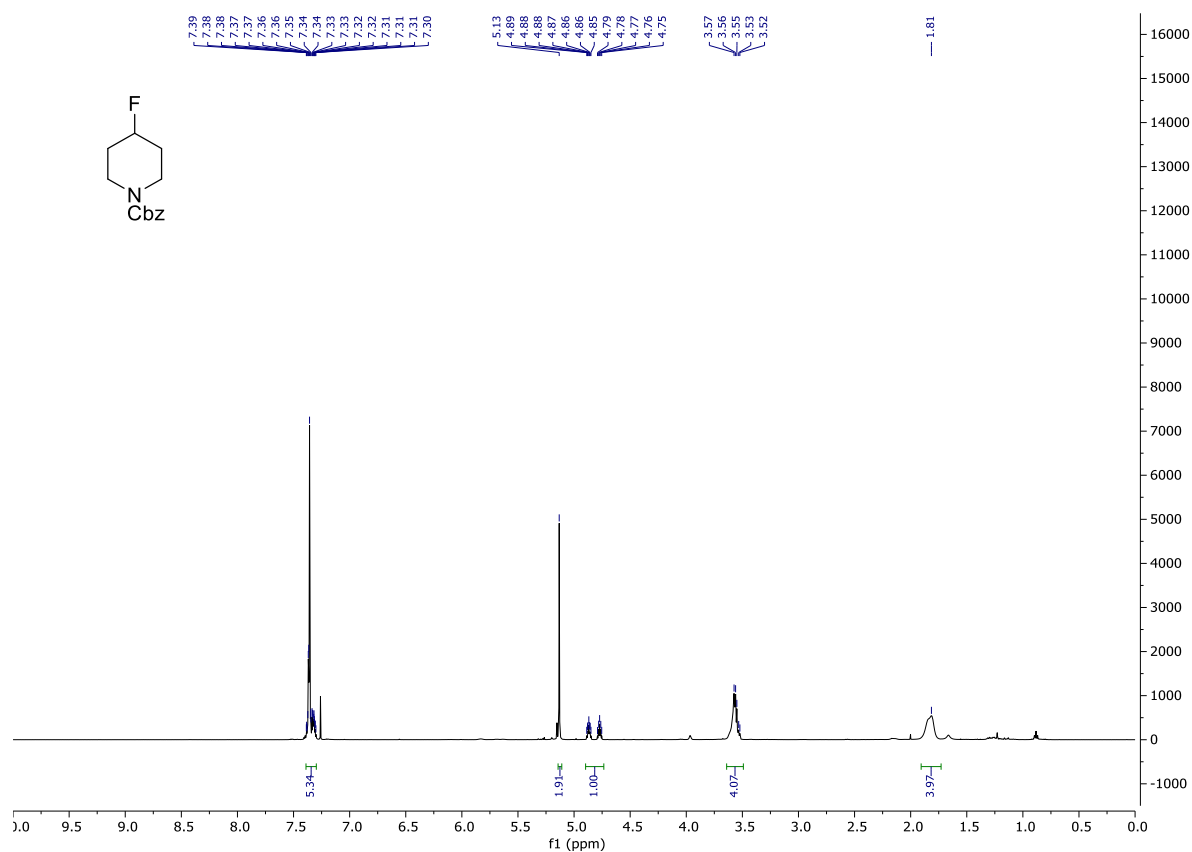


^{19}F NMR (471 MHz, CDCl_3)

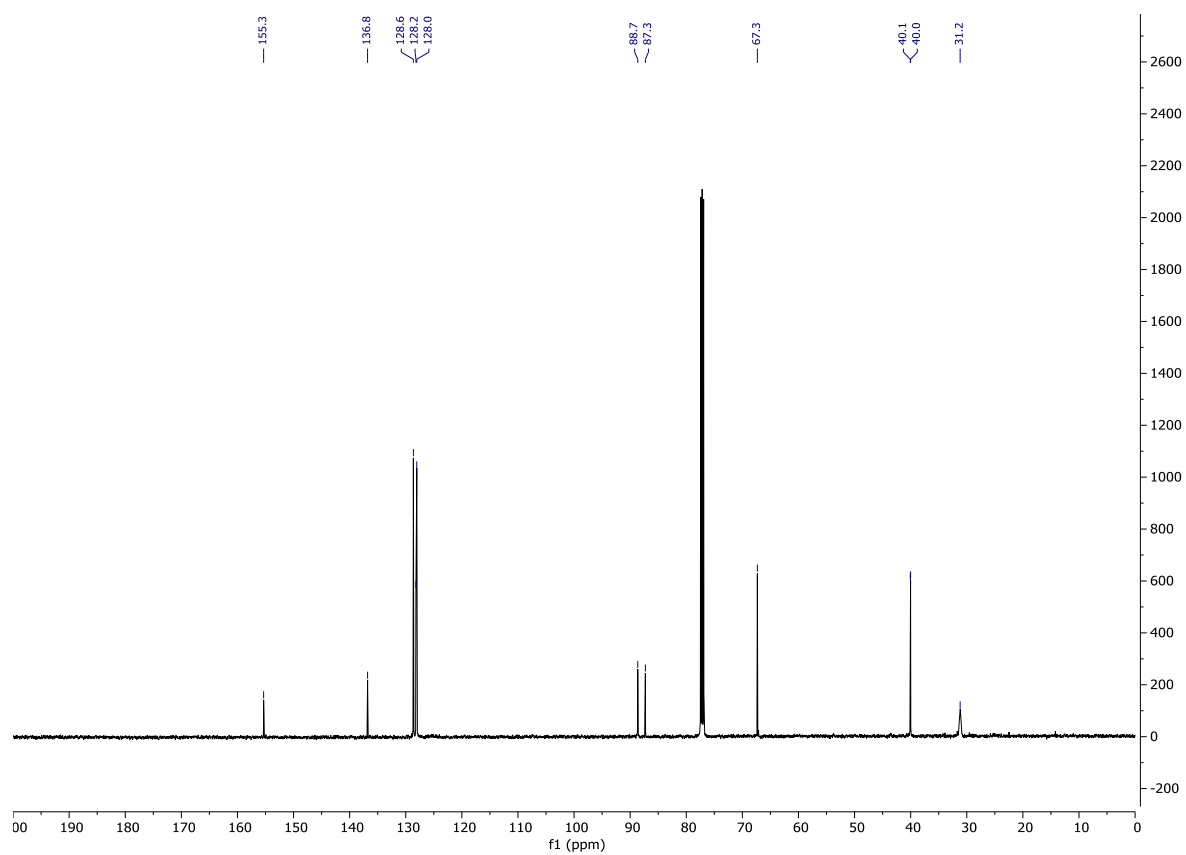


Benzyl 4-fluoro-1-piperidinecarboxylate, compound **2o**

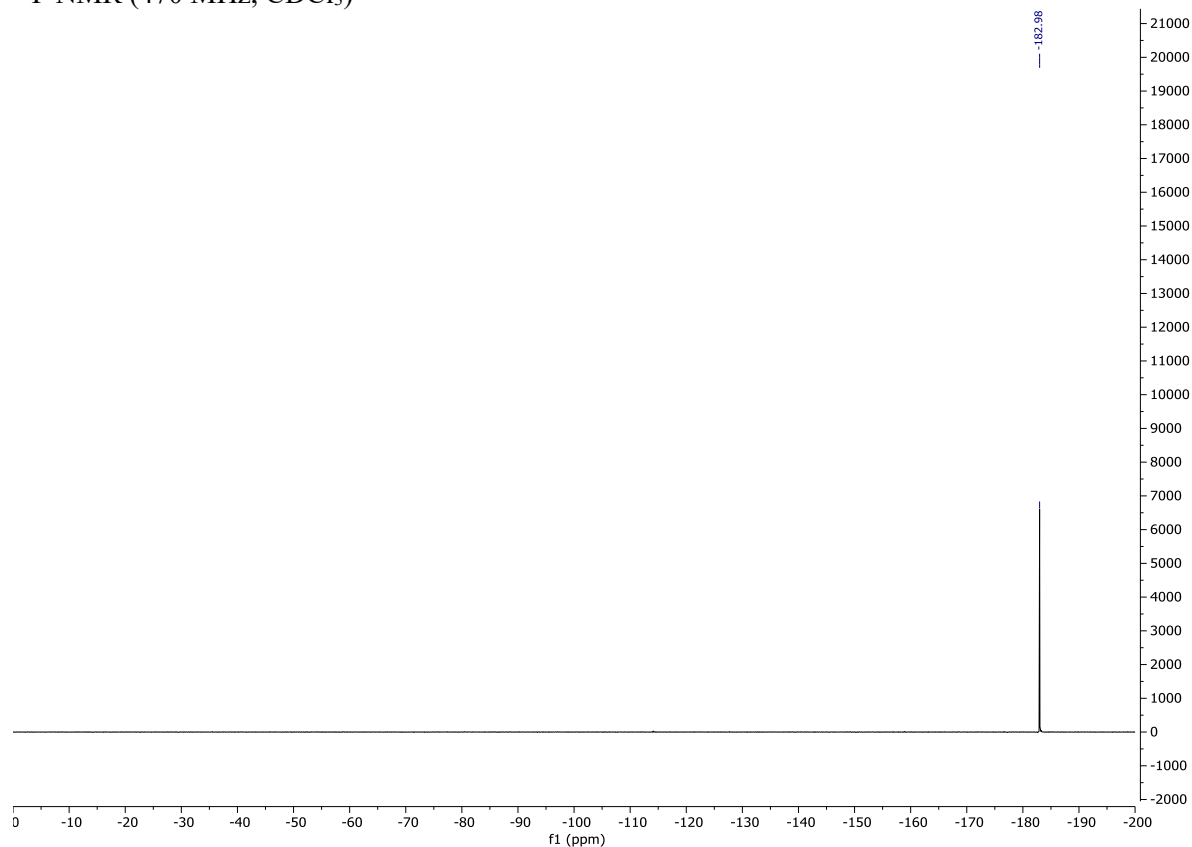
^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

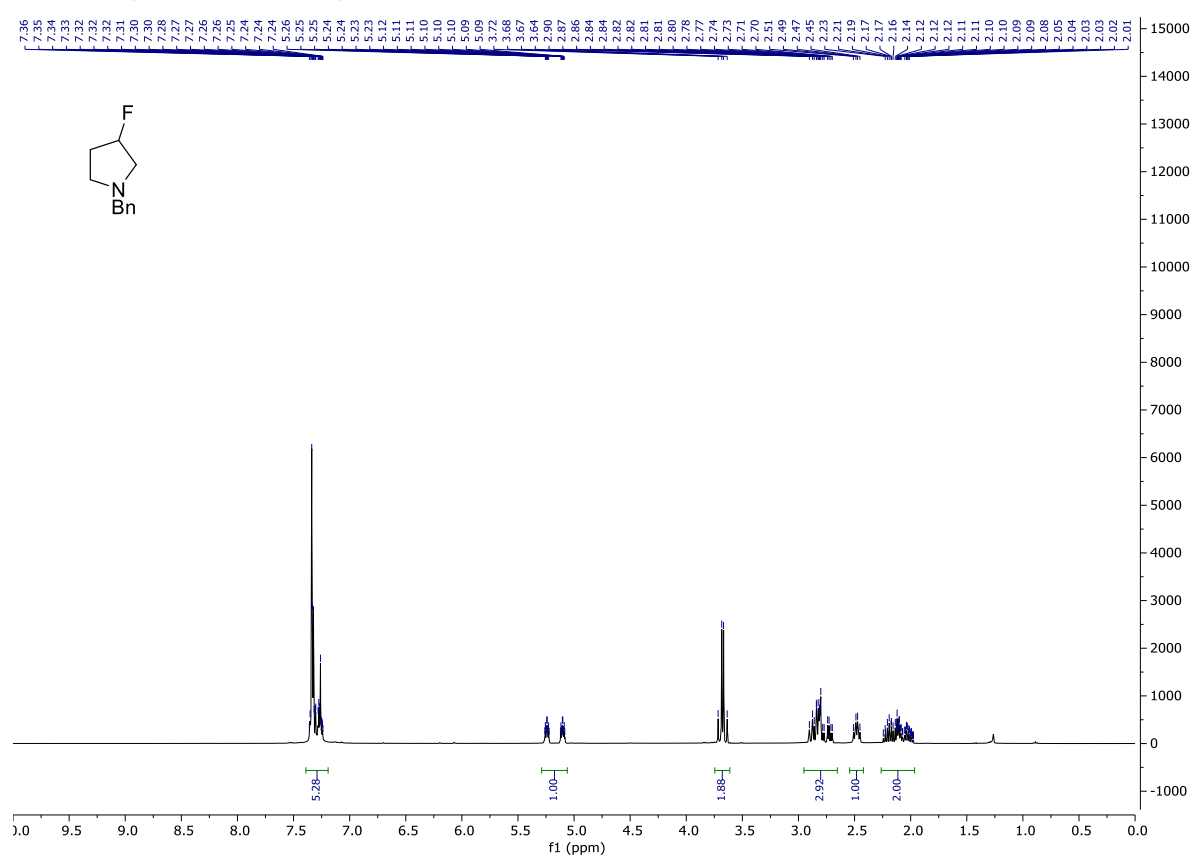


^{19}F NMR (470 MHz, CDCl_3)

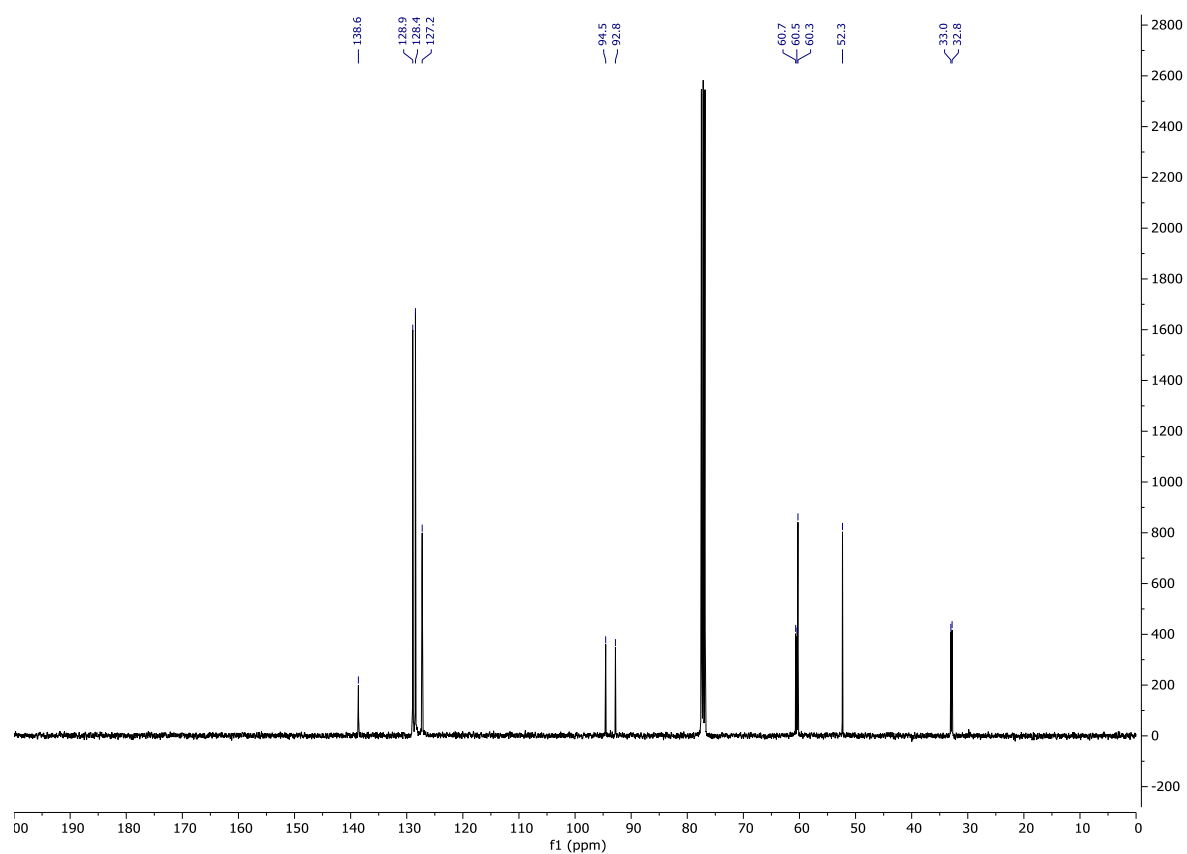


1-Benzyl-2-fluoropyrrolidine, compound **2p**

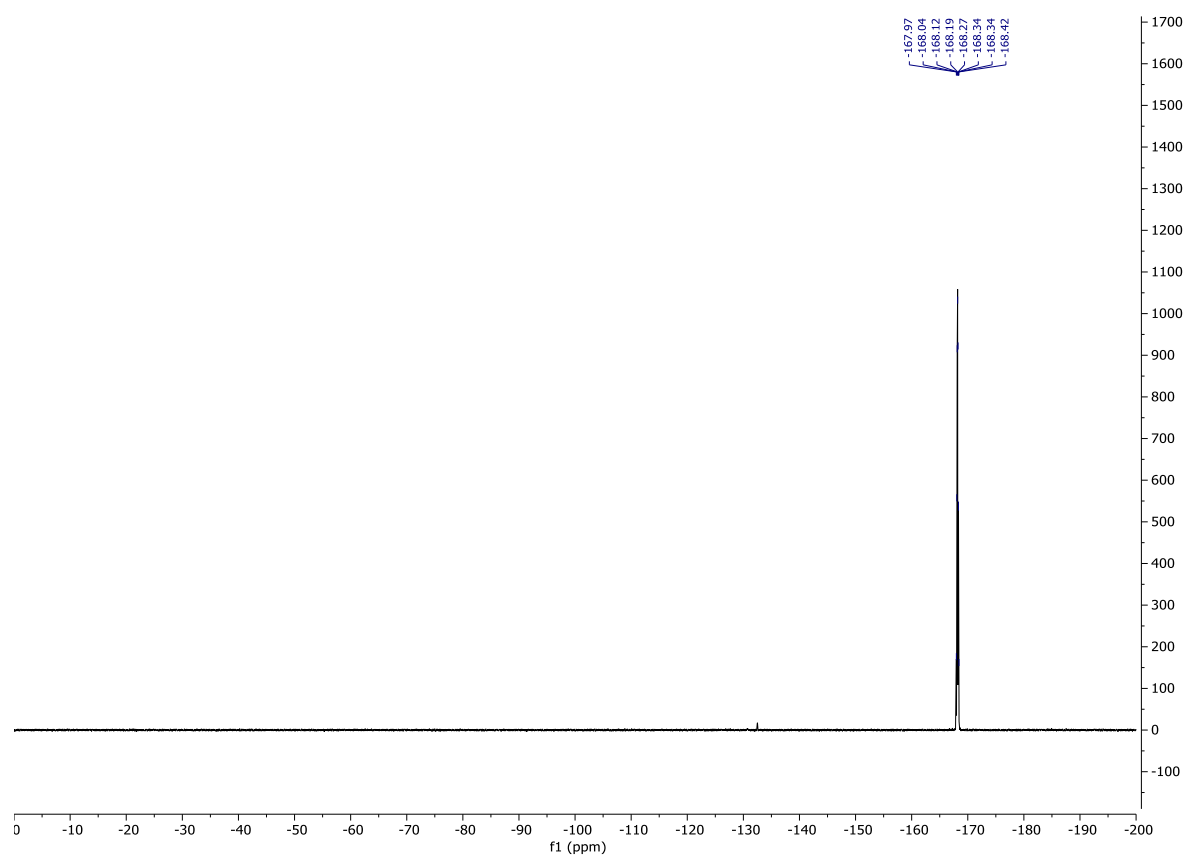
^1H NMR (400 MHz, CDCl_3)



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

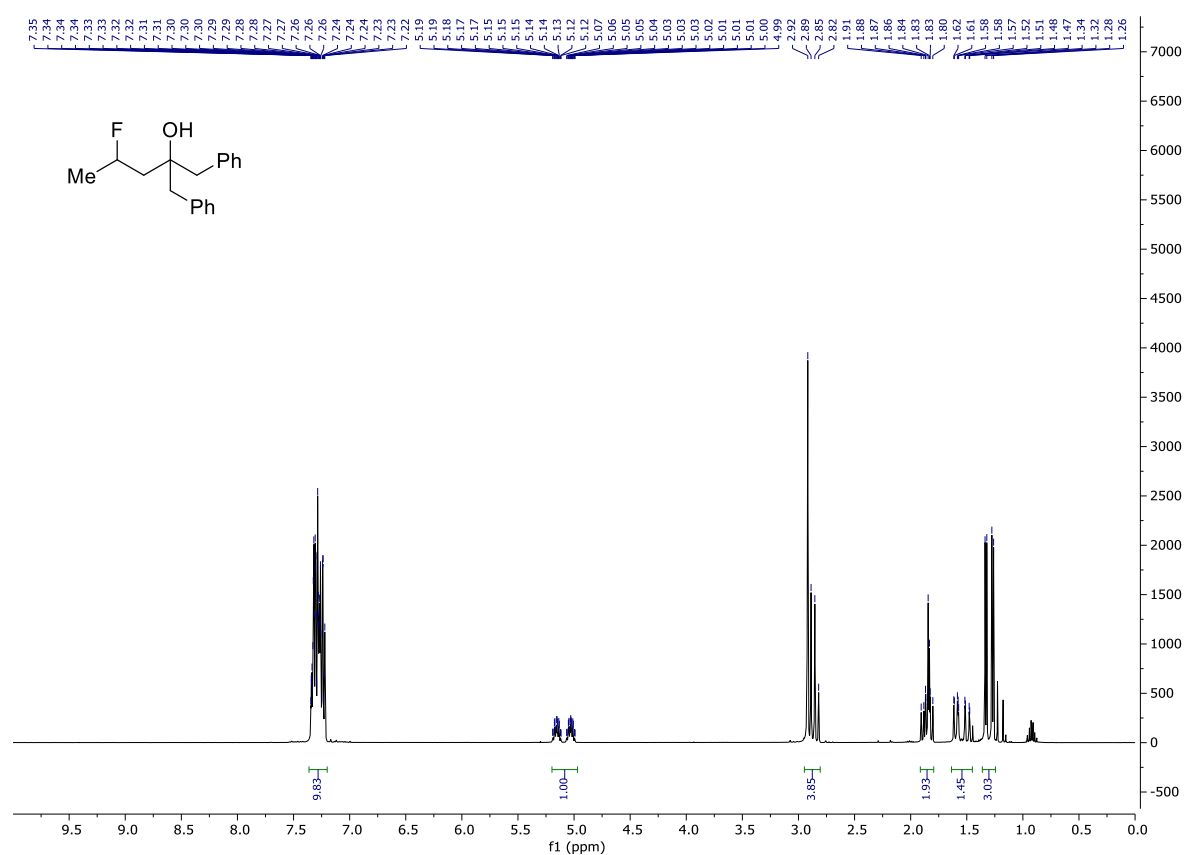


^{19}F NMR (376 MHz, CDCl_3)

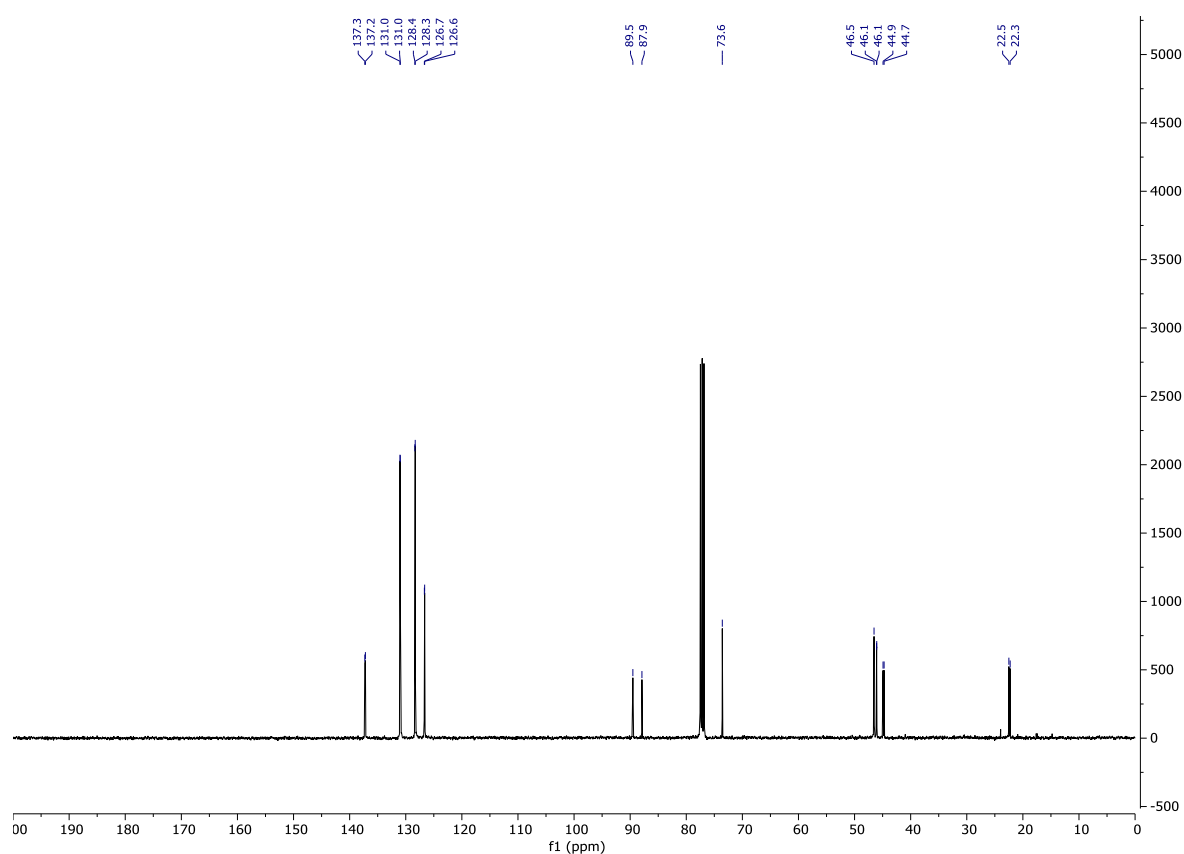


2-Benzyl-4-fluoro-1-phenylpentan-2-ol, compound **2q**

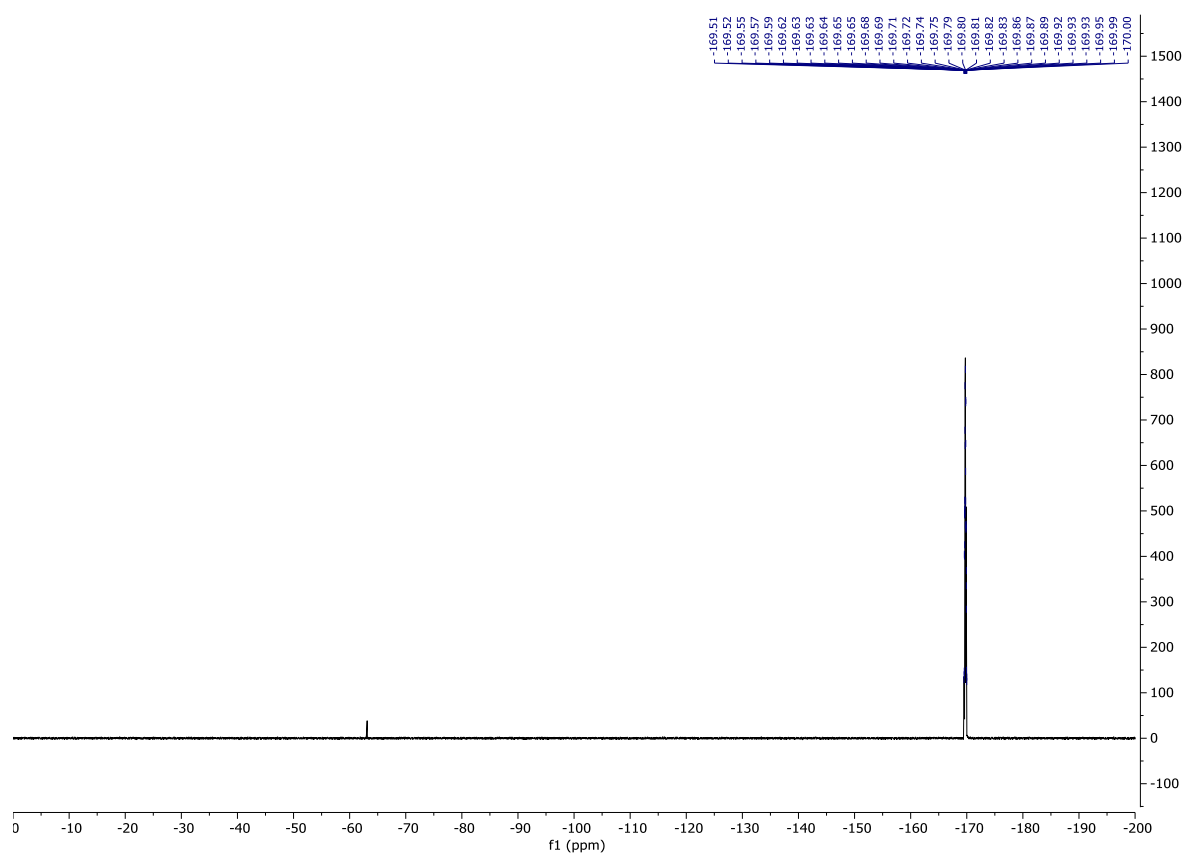
^1H NMR (400 MHz, CDCl_3)



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

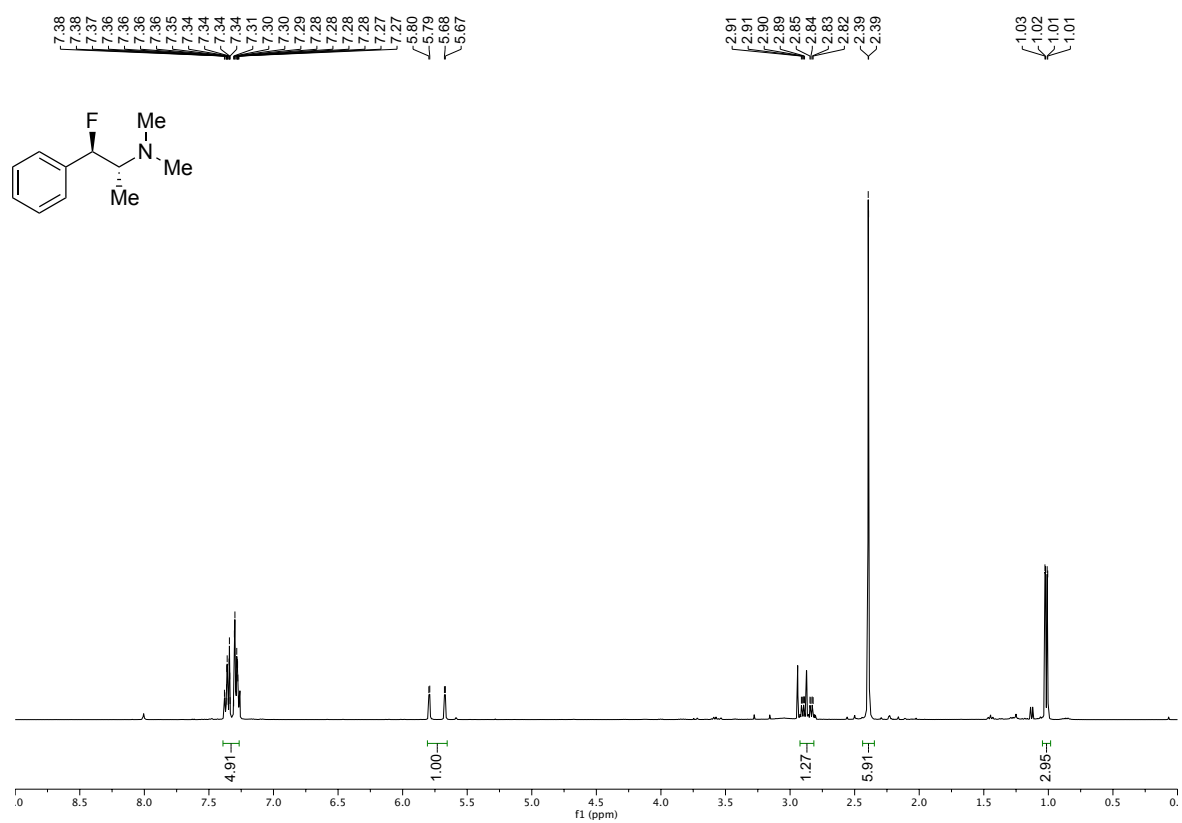


^{19}F NMR (376 MHz, CDCl_3)

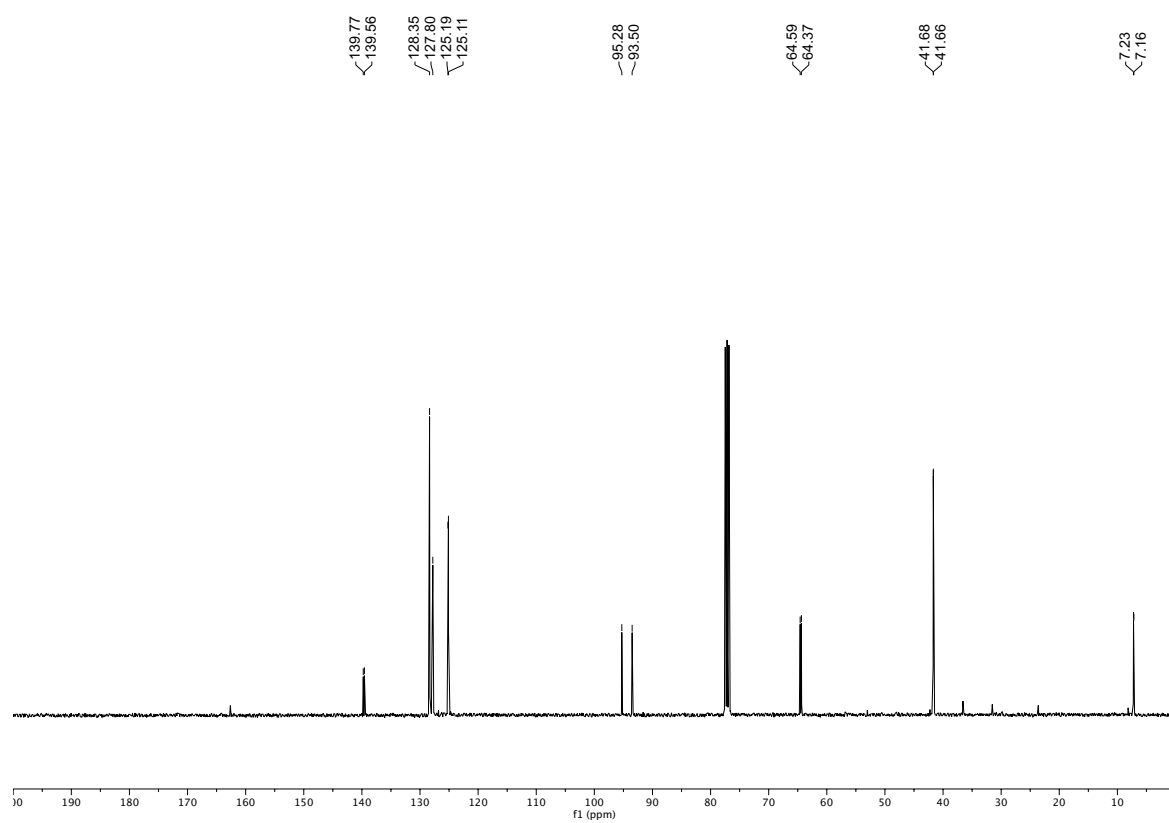


(1*R*,2*R*)-1-Fluoro-*N,N*-dimethyl-1-phenylpropan-2-amine, compound **2r**

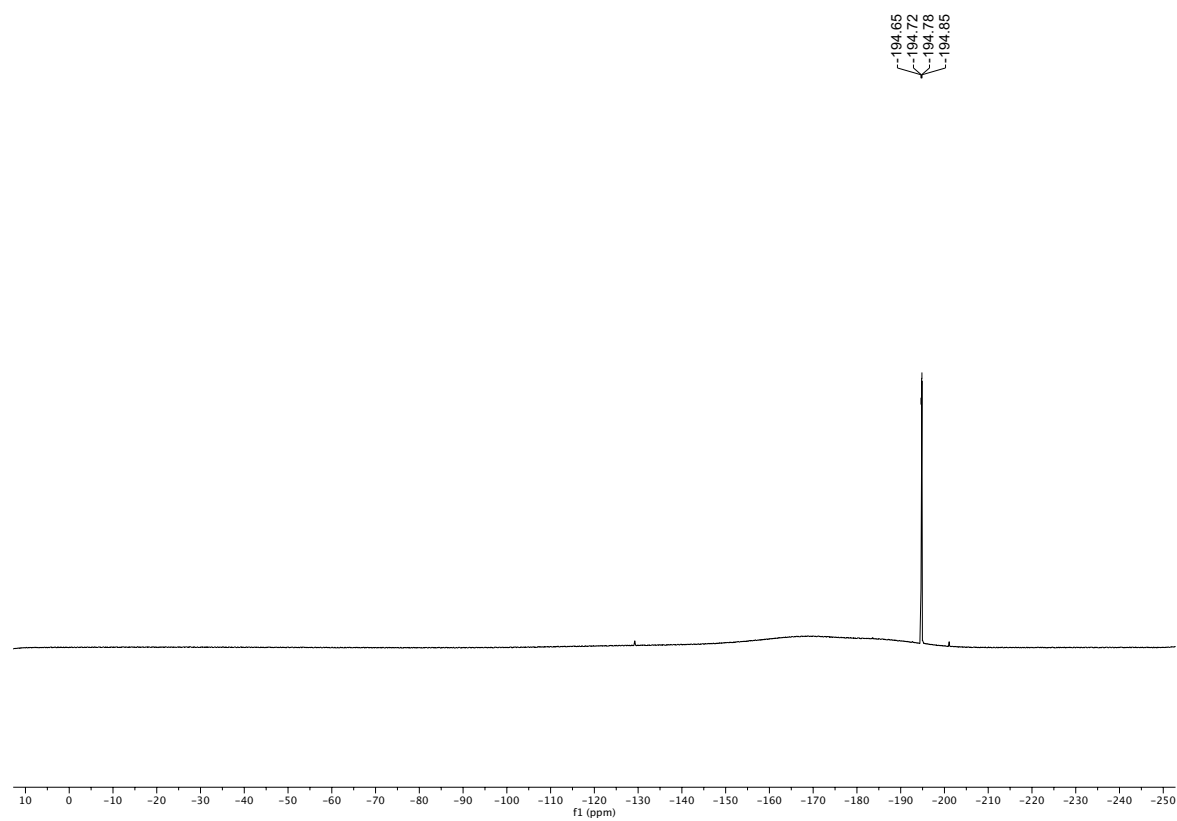
^1H NMR (400 MHz, CDCl_3)



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

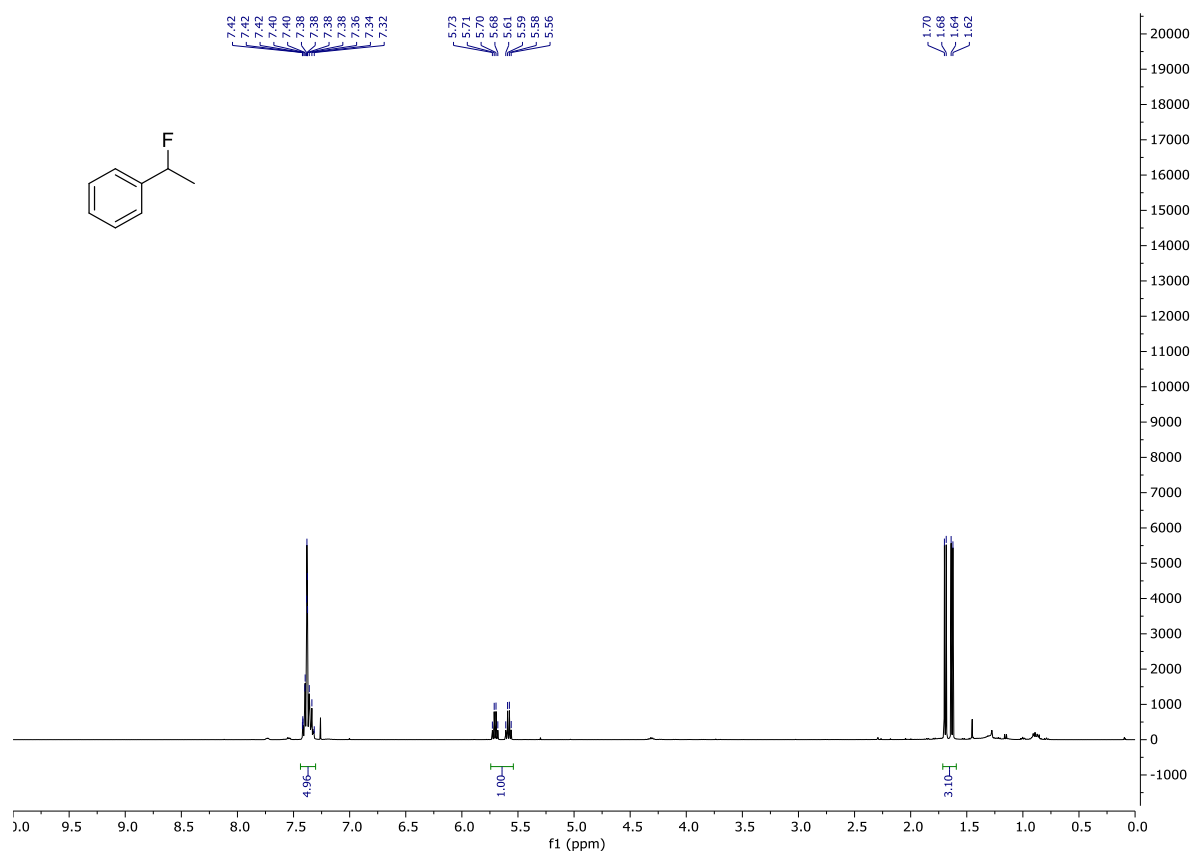


^{19}F NMR (470 MHz, CDCl_3)

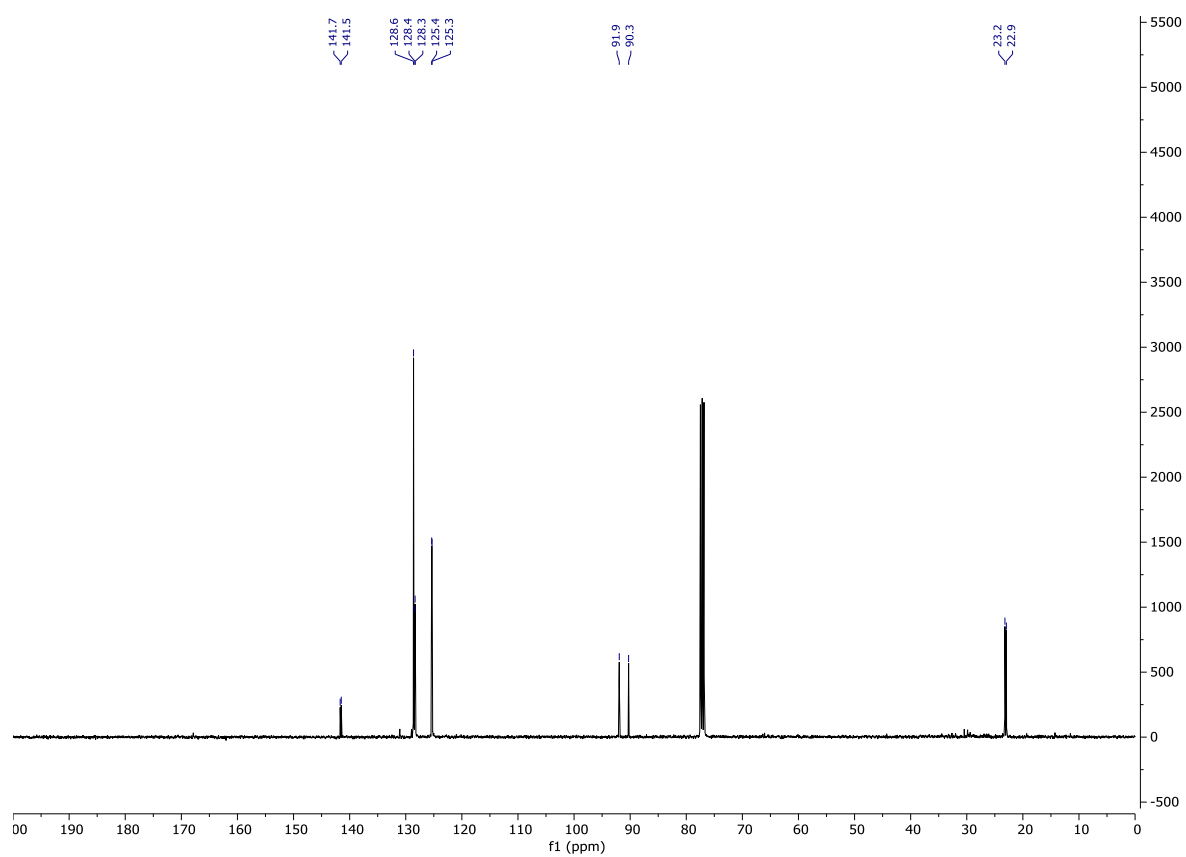


(1-Fluoroethylbenzene)), compound **2s**

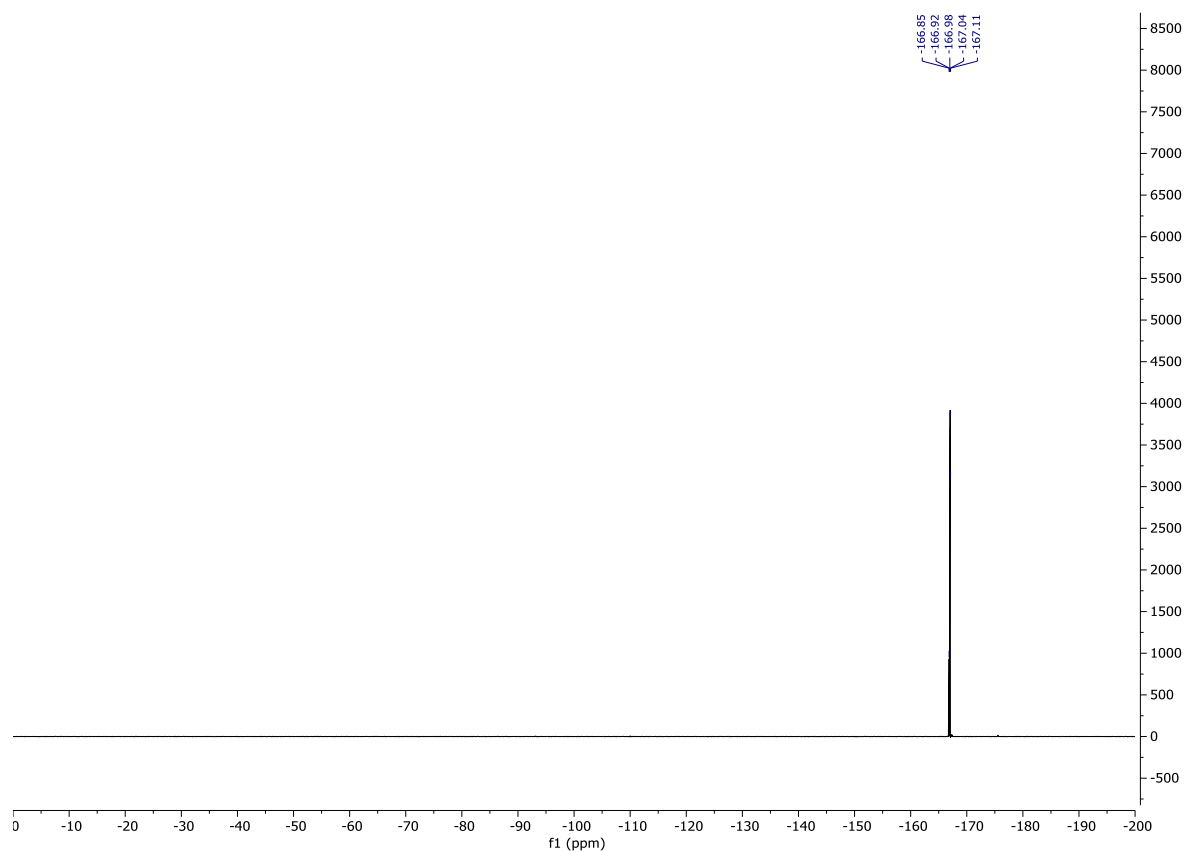
^1H NMR (400 MHz, CDCl_3)



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

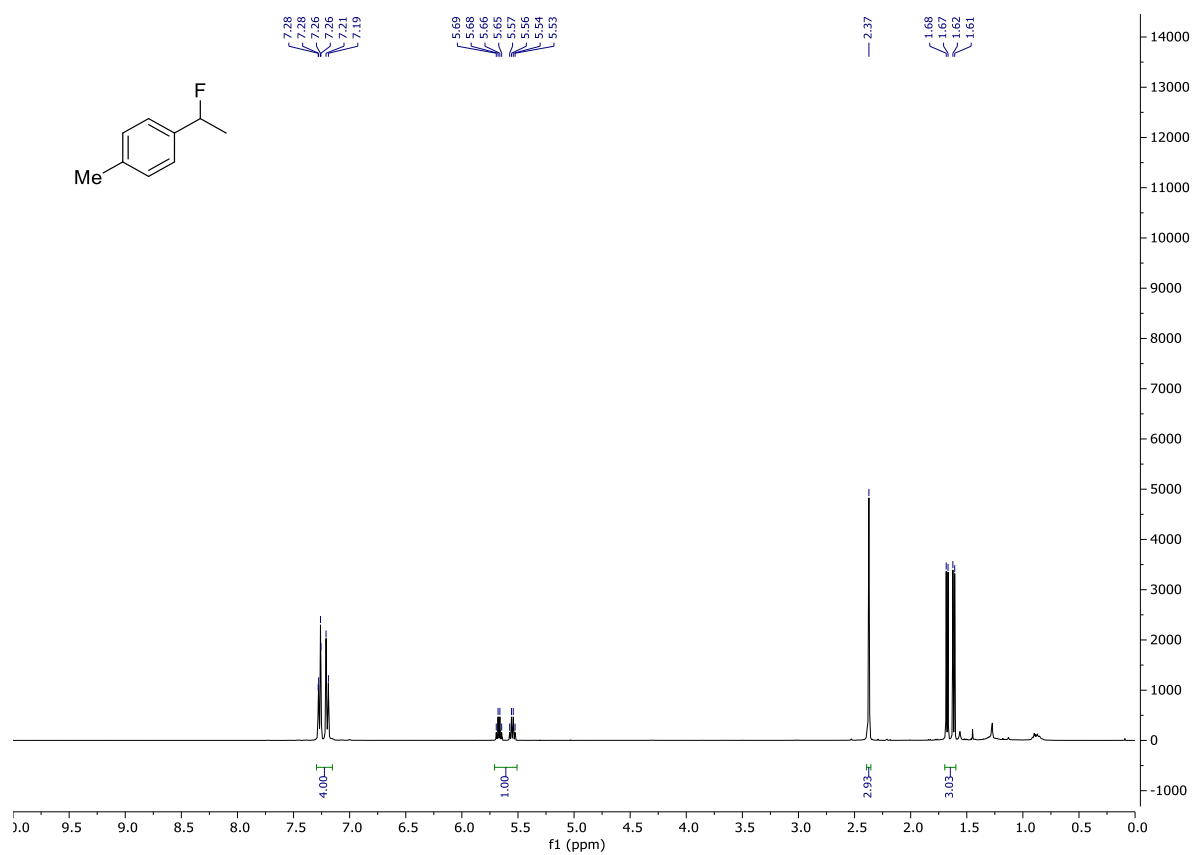


^{19}F NMR (376 MHz, CDCl_3)

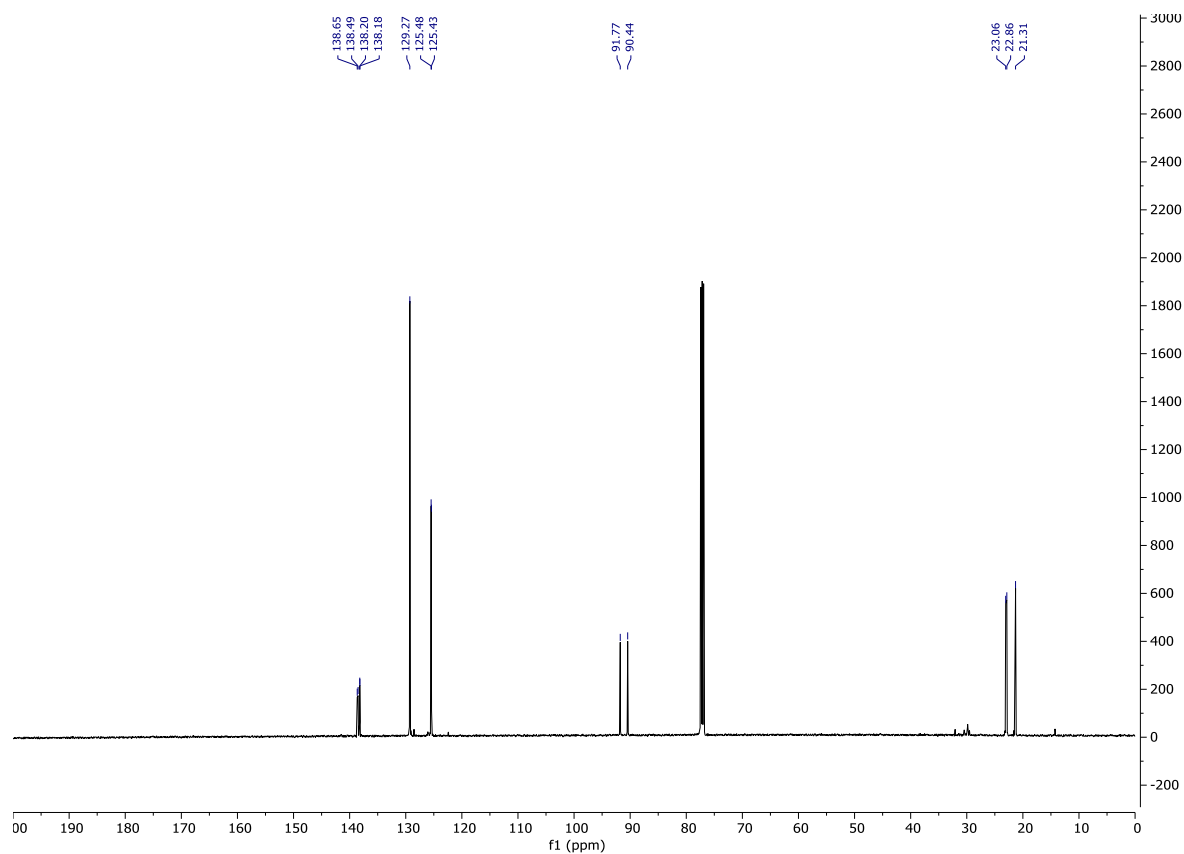


1-(1-Fluoroethyl)-4-methylbenzene, compound **2t**

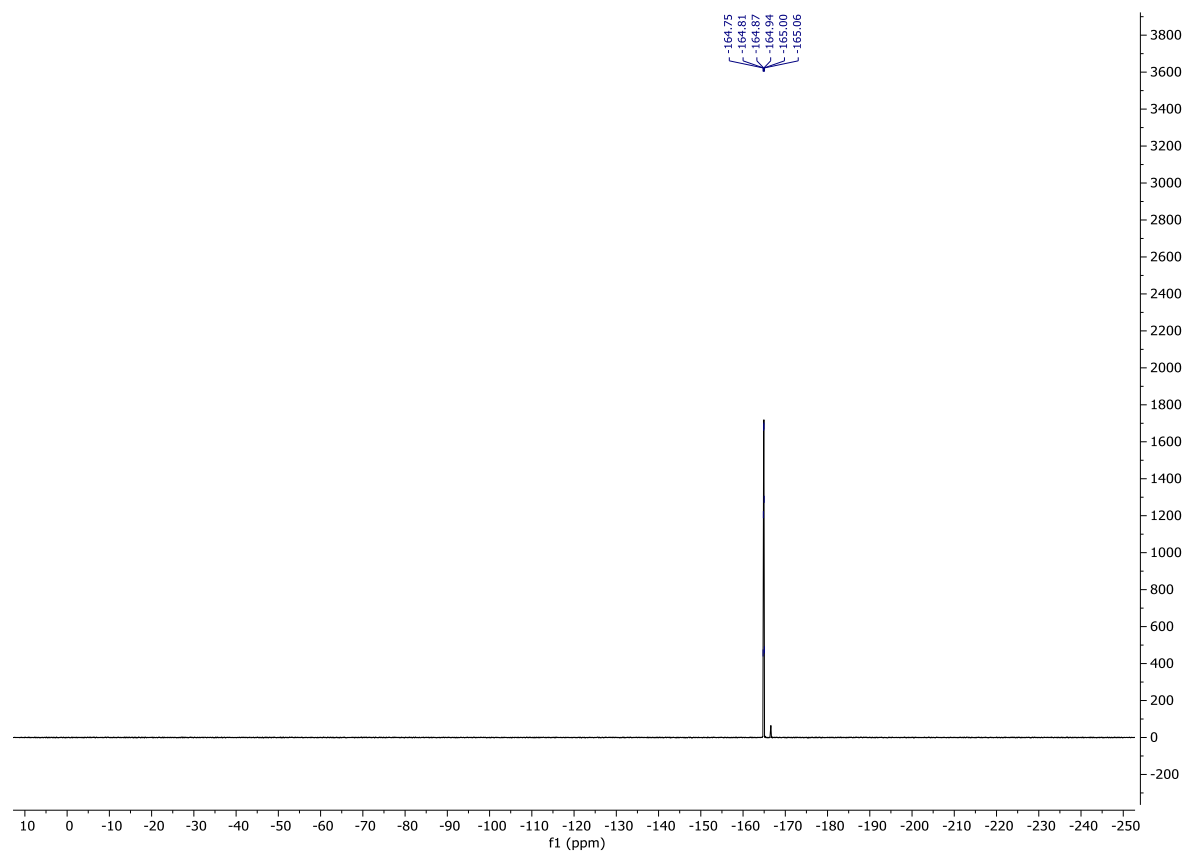
^1H NMR (400 MHz, CDCl_3)



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

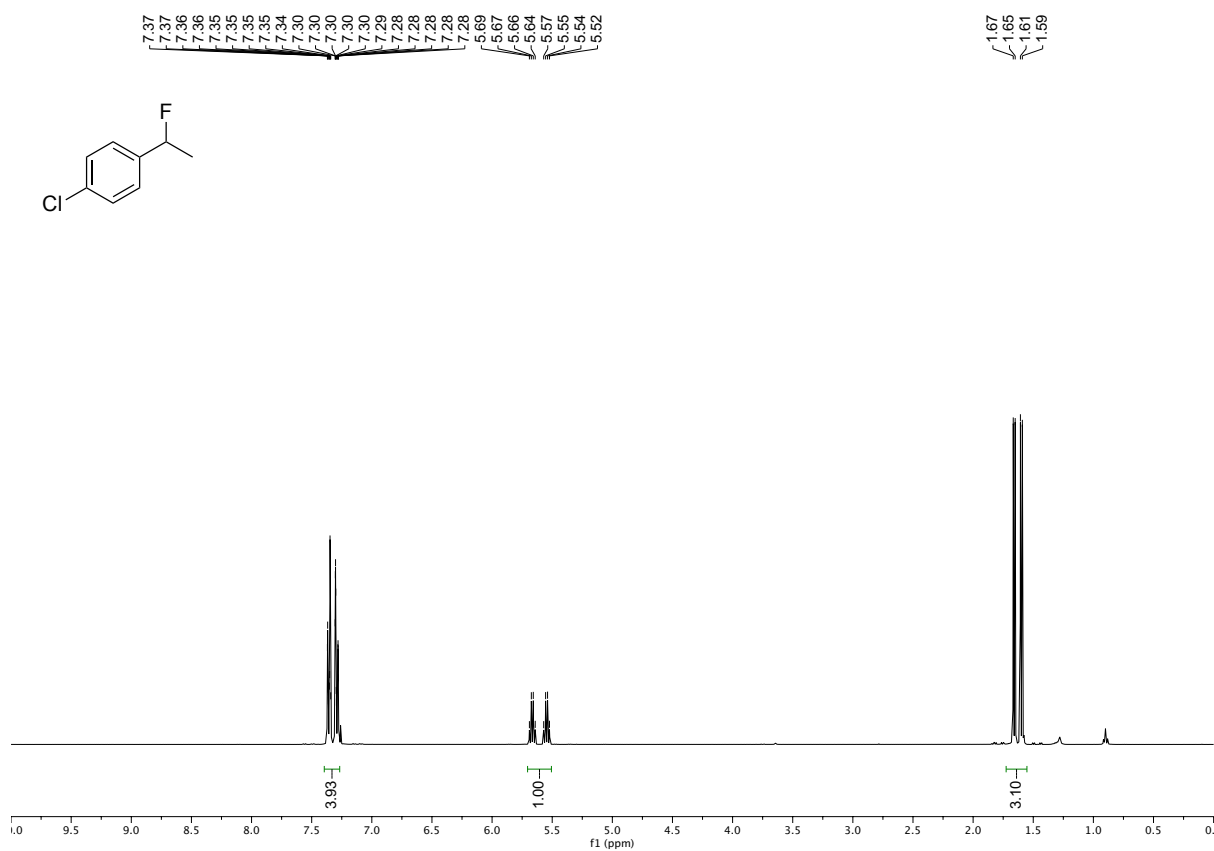


^{19}F NMR (376 MHz, CDCl_3)

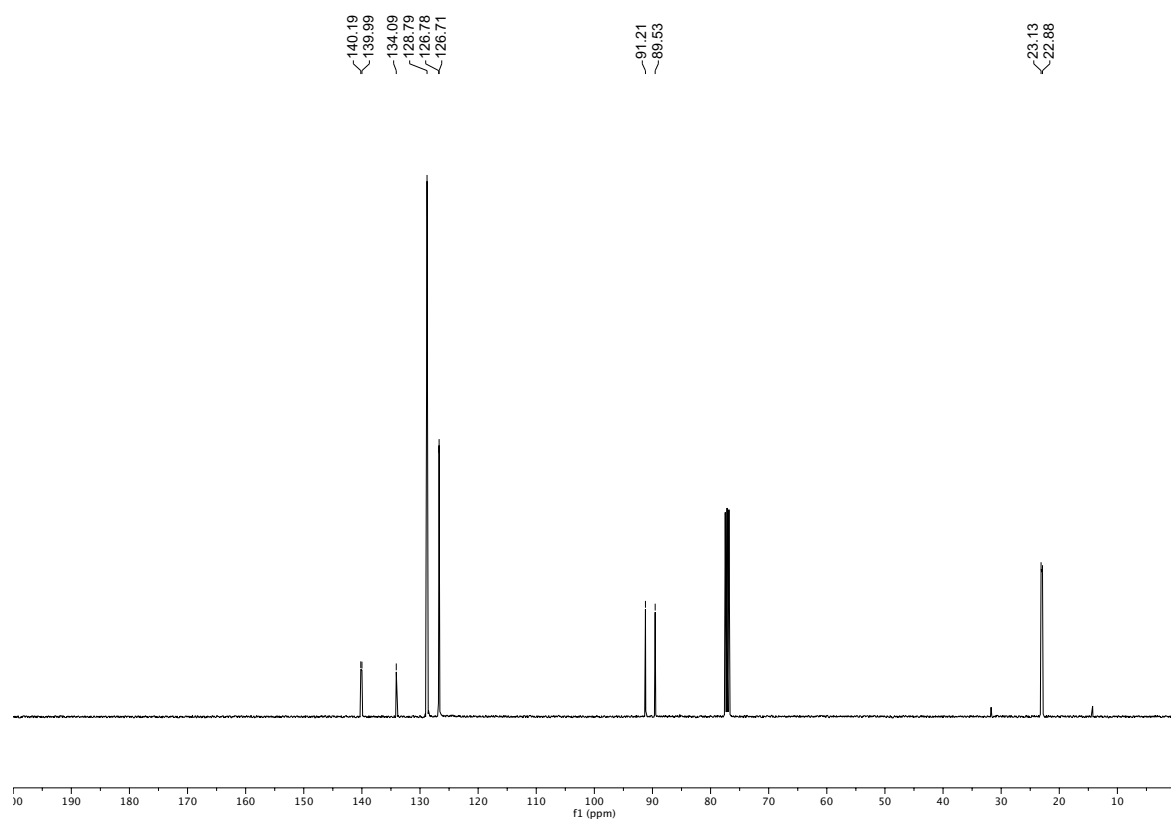


1-(1-Fluoroethyl)-4-chlorobenzene, compound **2u**

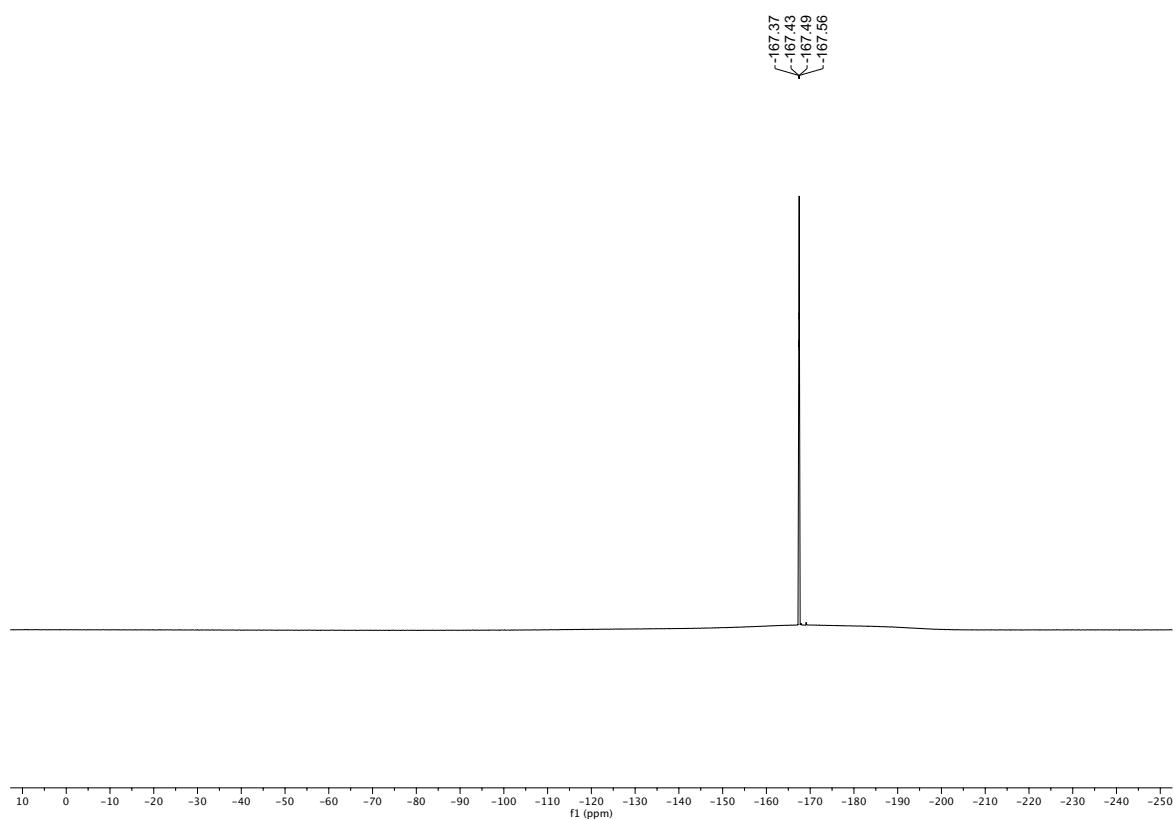
^1H NMR (400 MHz, CDCl_3)



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

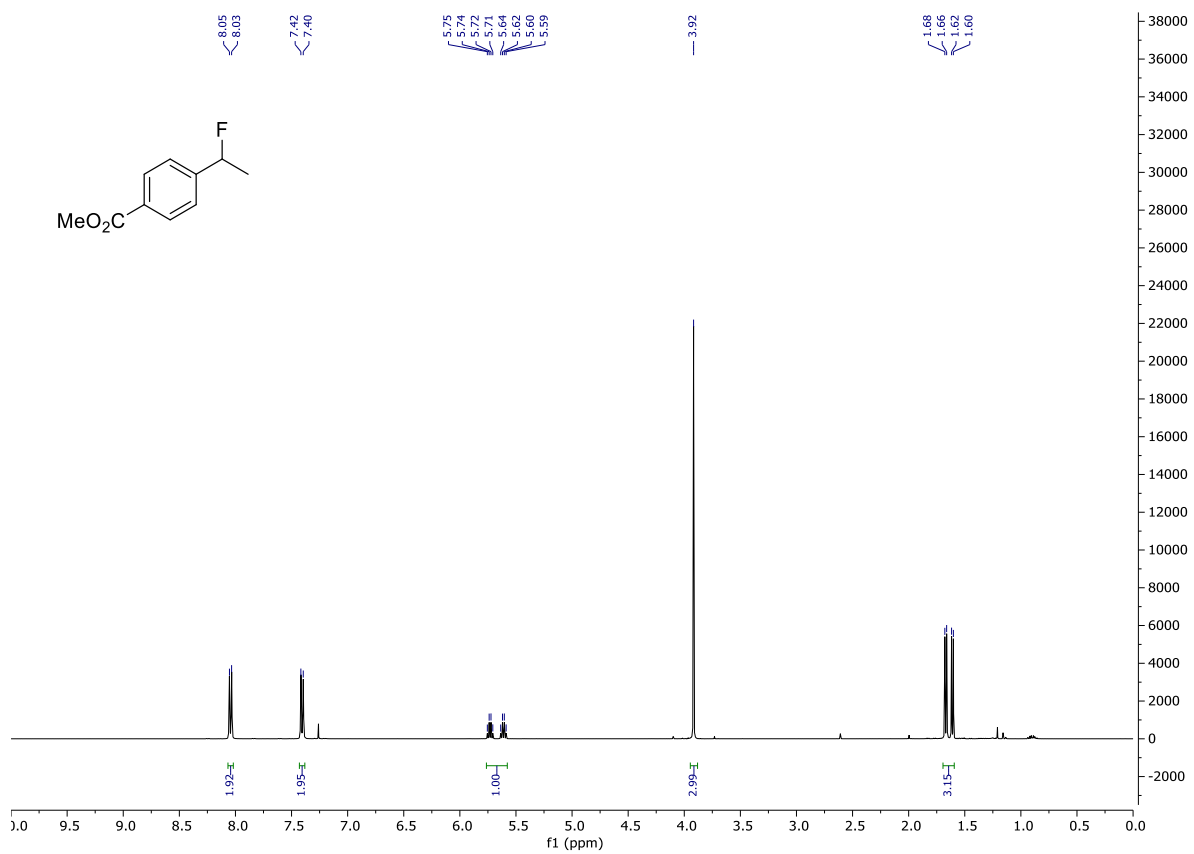


^{19}F NMR (376 MHz, CDCl_3)

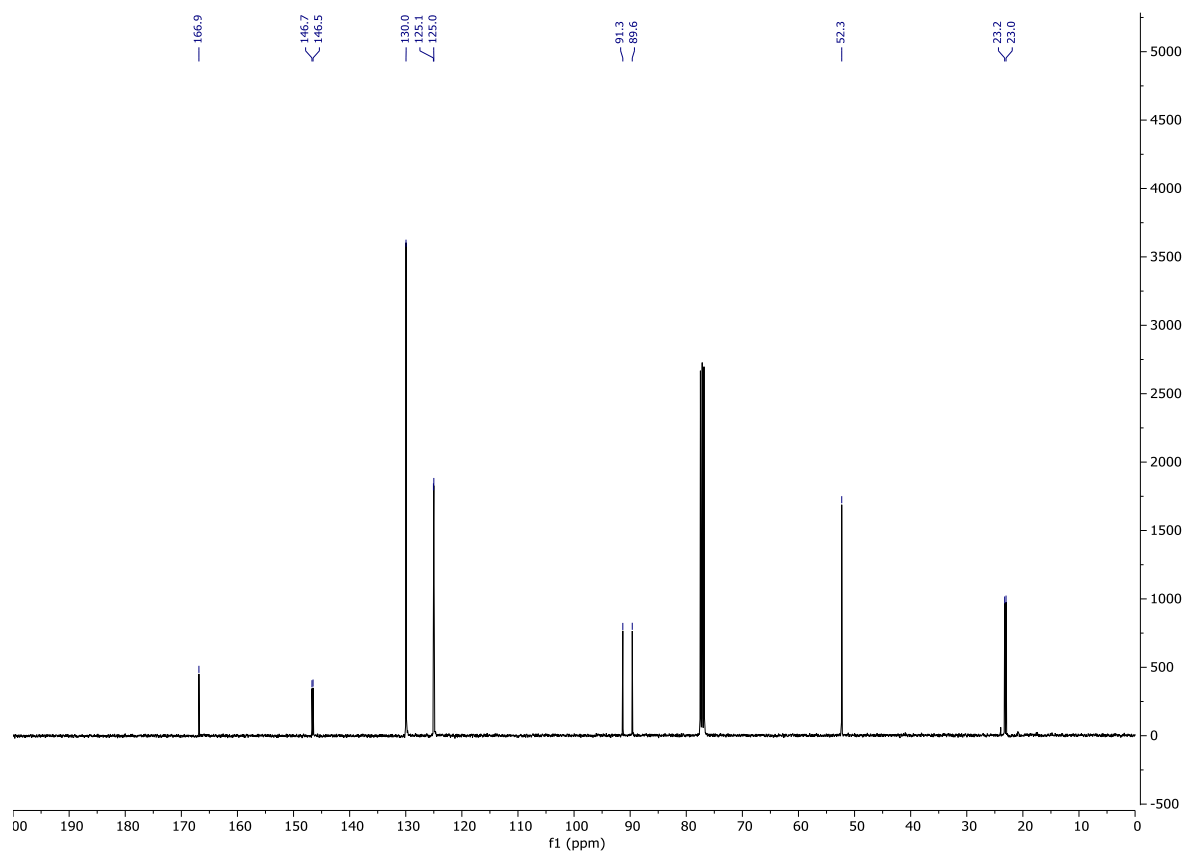


Methyl-4-(1-fluoroethyl)benzoate, compound **2v**

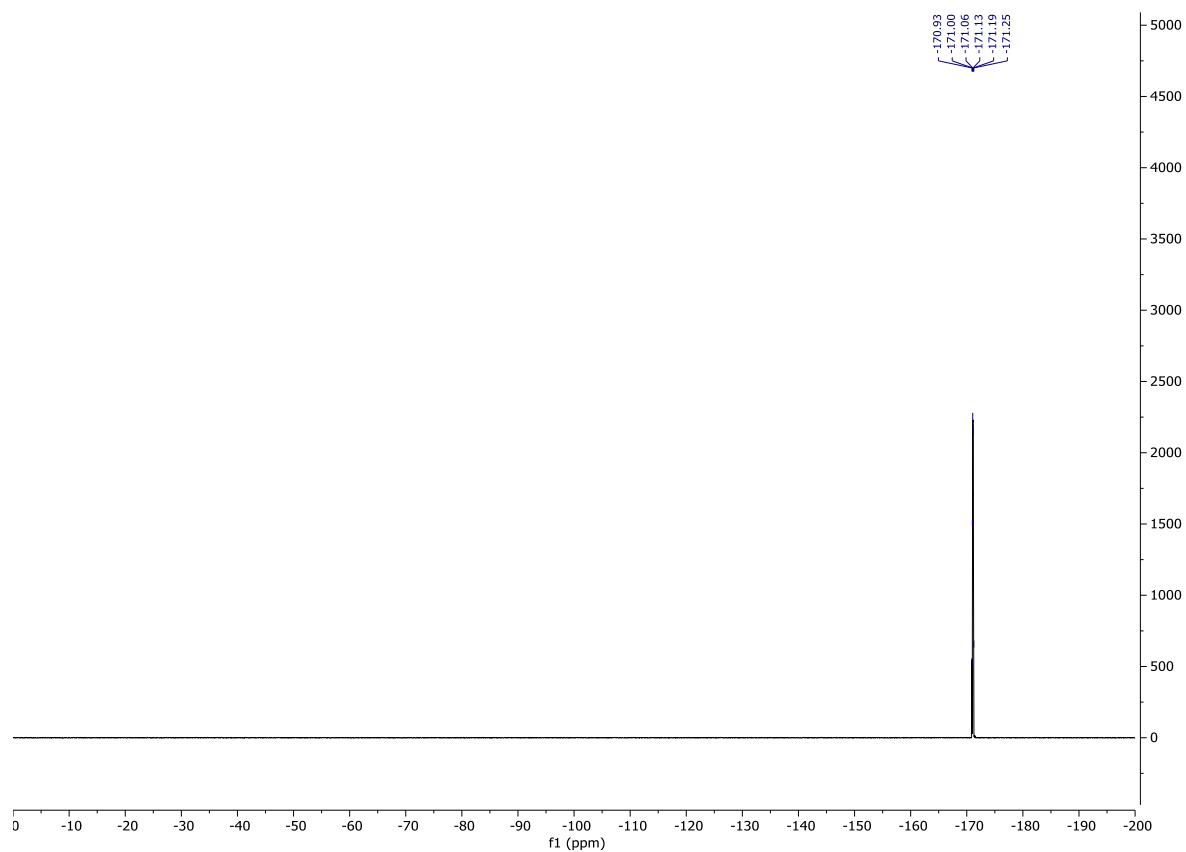
^1H NMR (400 MHz, CDCl_3)



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

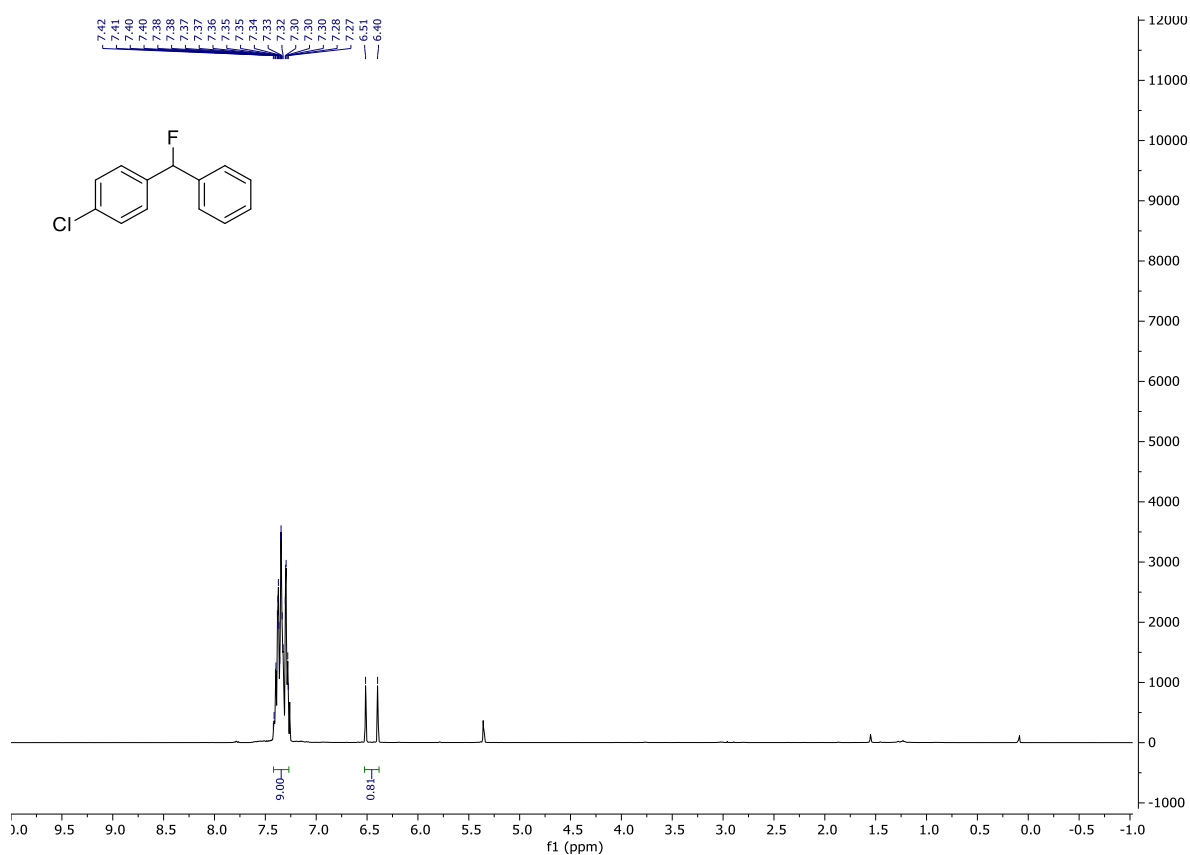


^{19}F NMR (376 MHz, CDCl_3)

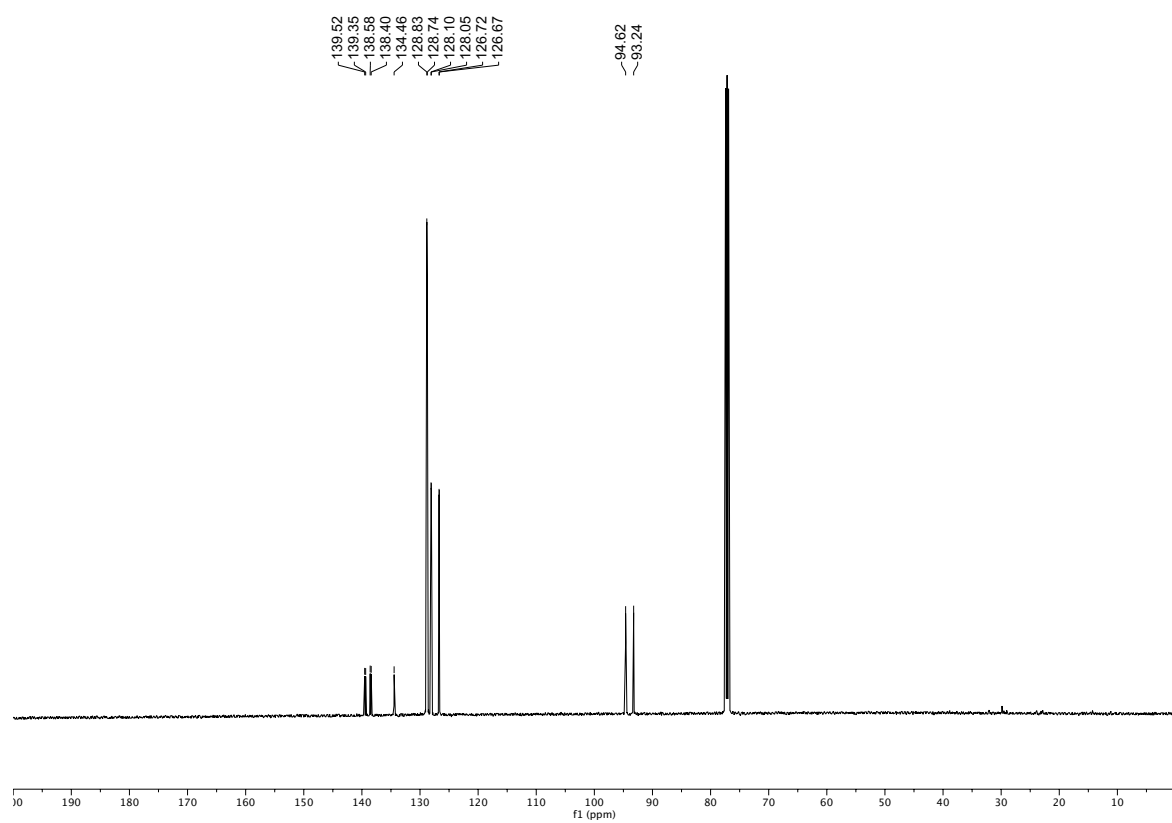


1-Chloro-4-(fluorophenyl)methylbenzene, compound **2w**

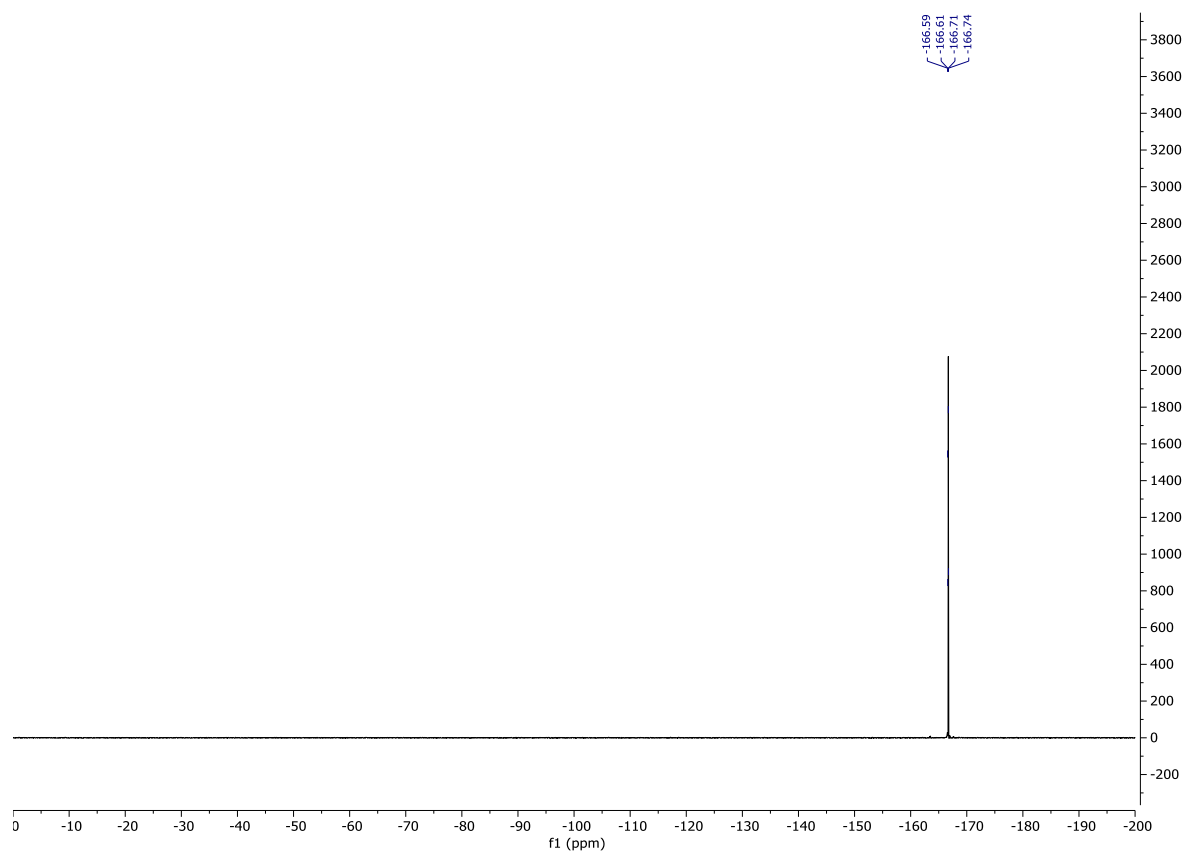
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

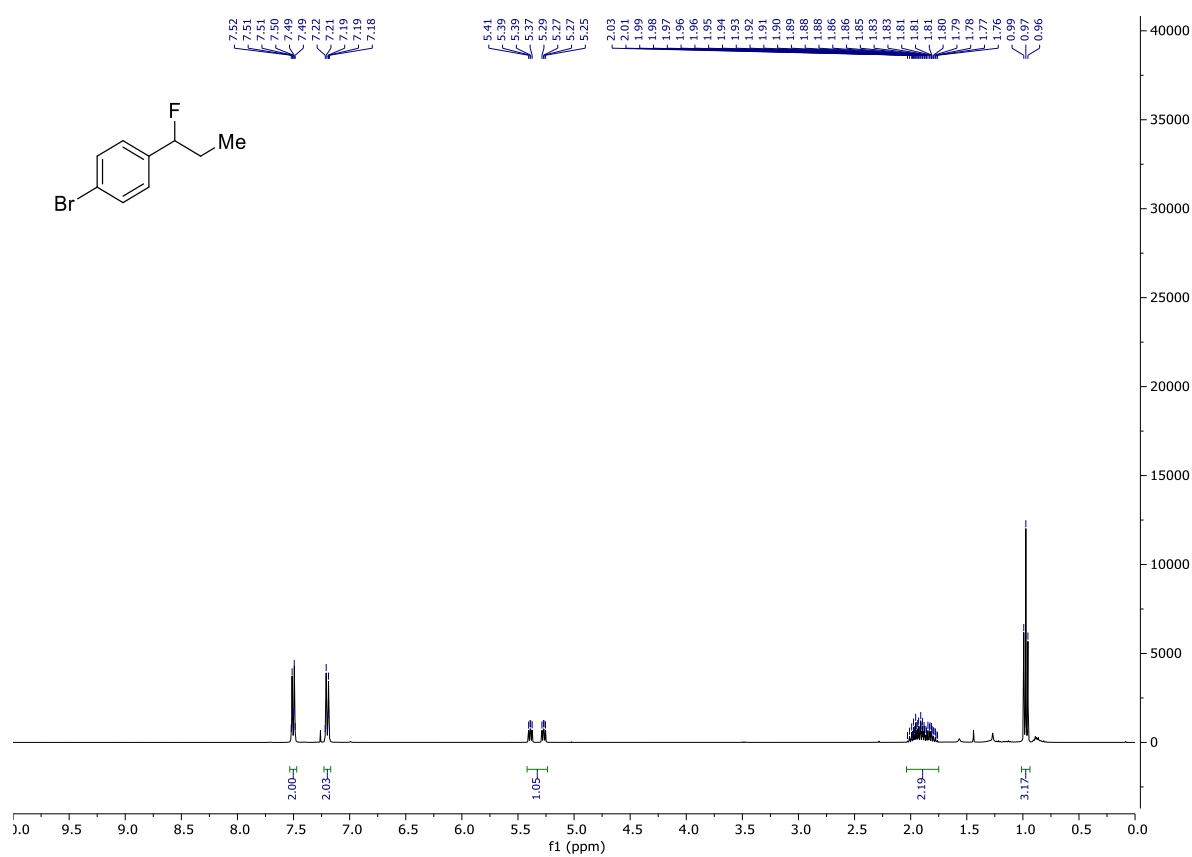


^{19}F NMR (376 MHz, CDCl_3)

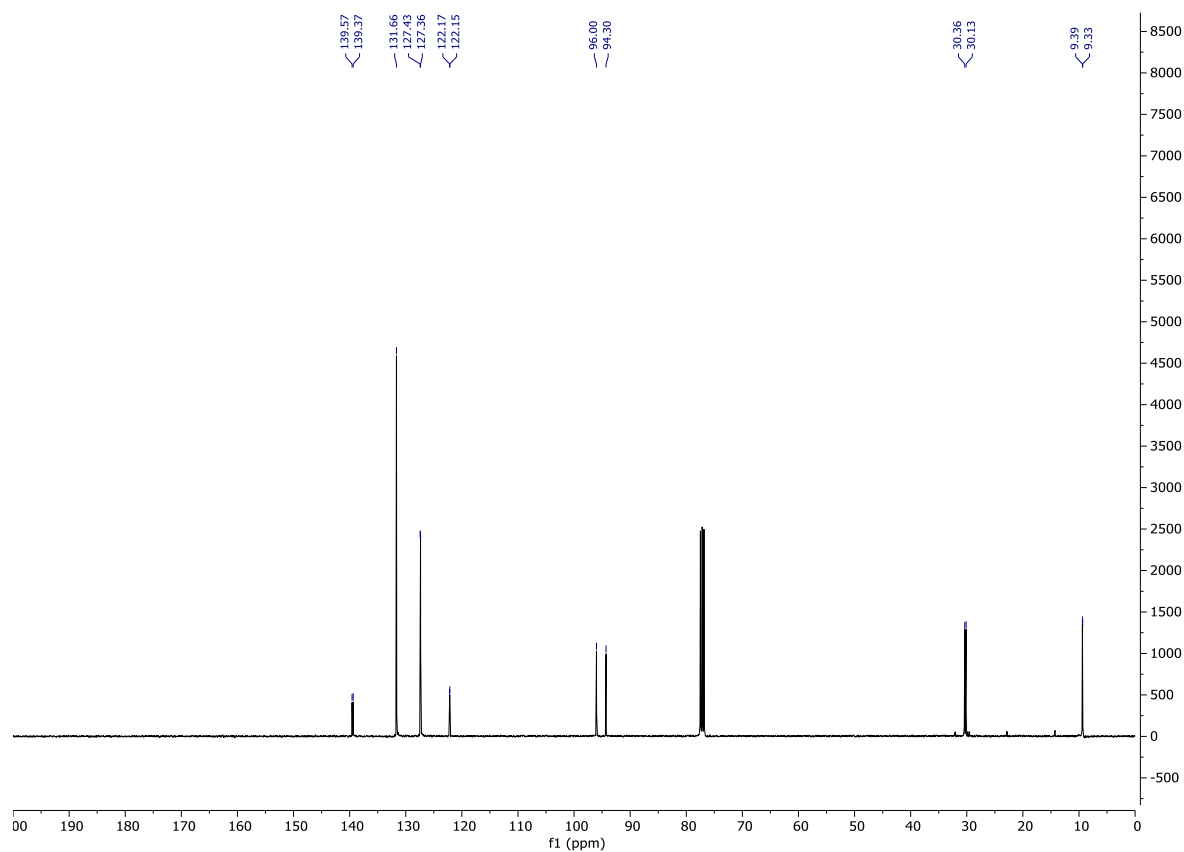


1-Bromo-4-(1-fluoropropyl)benzene, compound **2x**

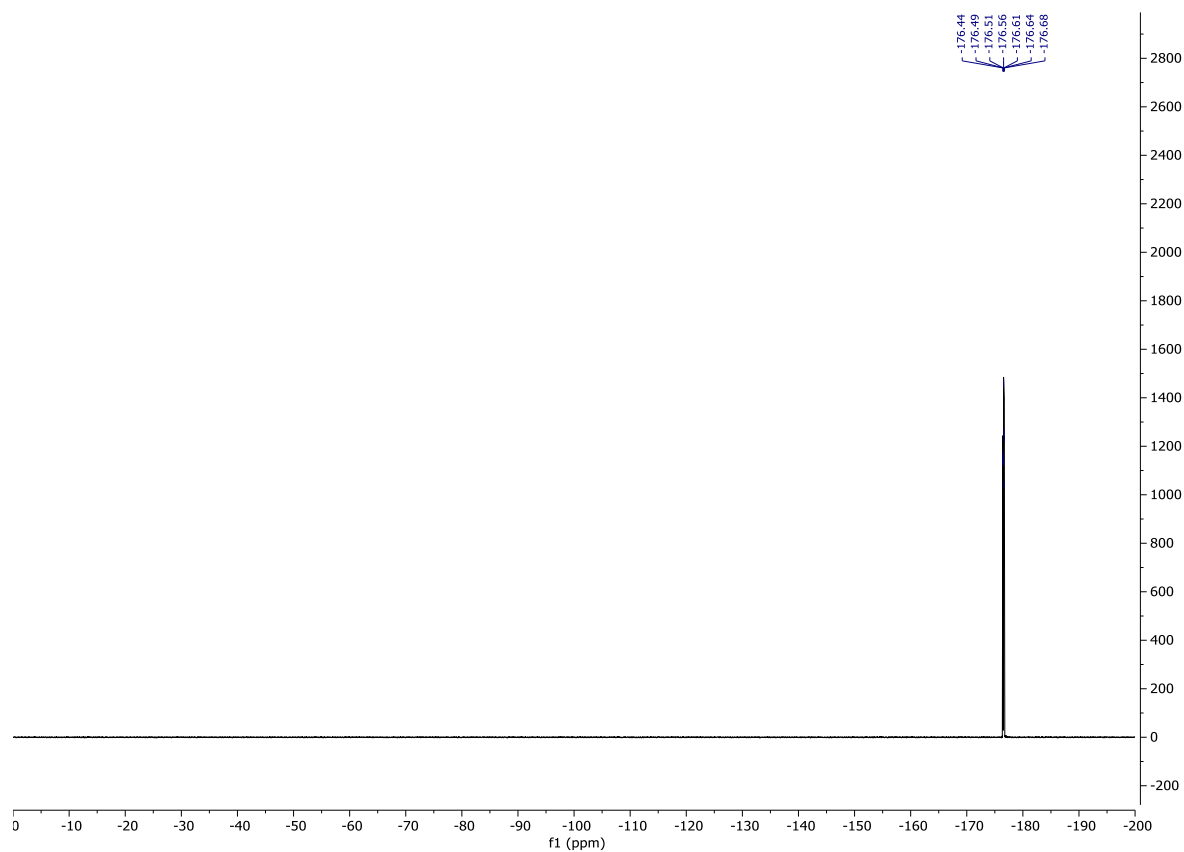
^1H NMR (400 MHz, CDCl_3)



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

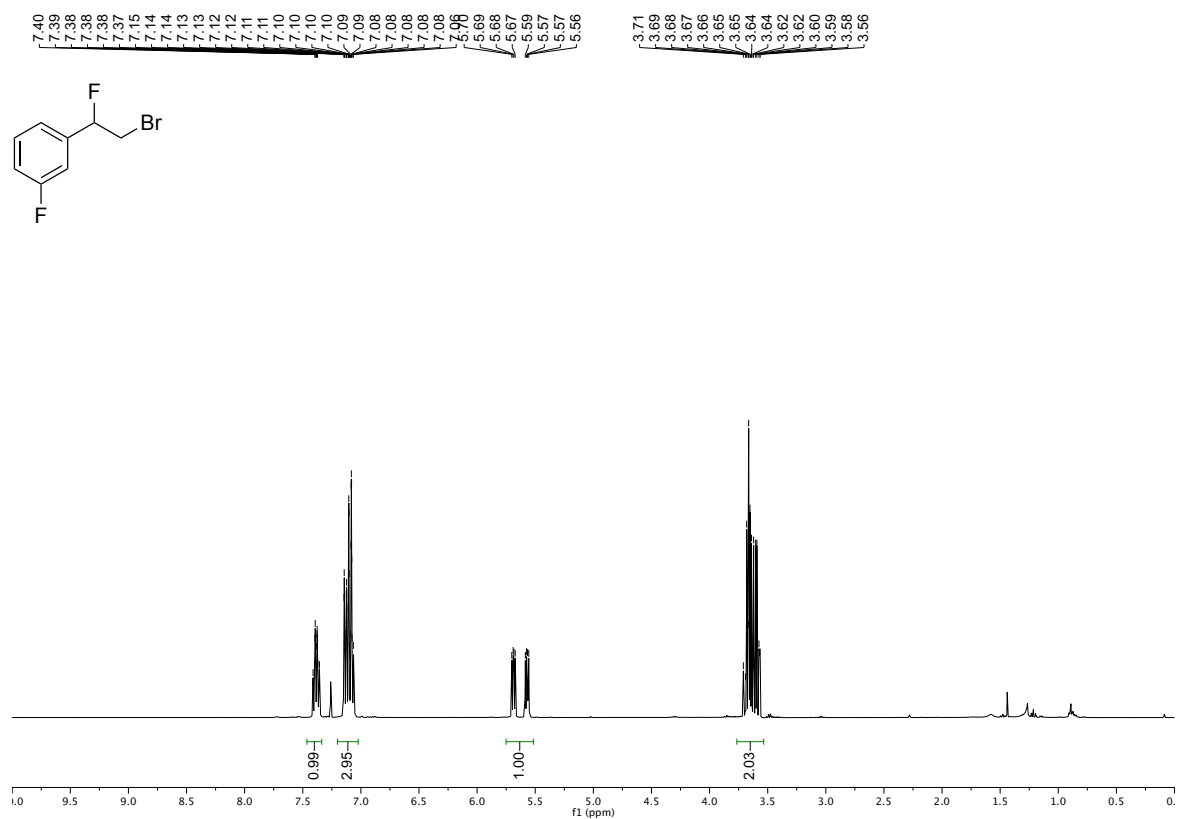


^{19}F NMR (376 MHz, CDCl_3)

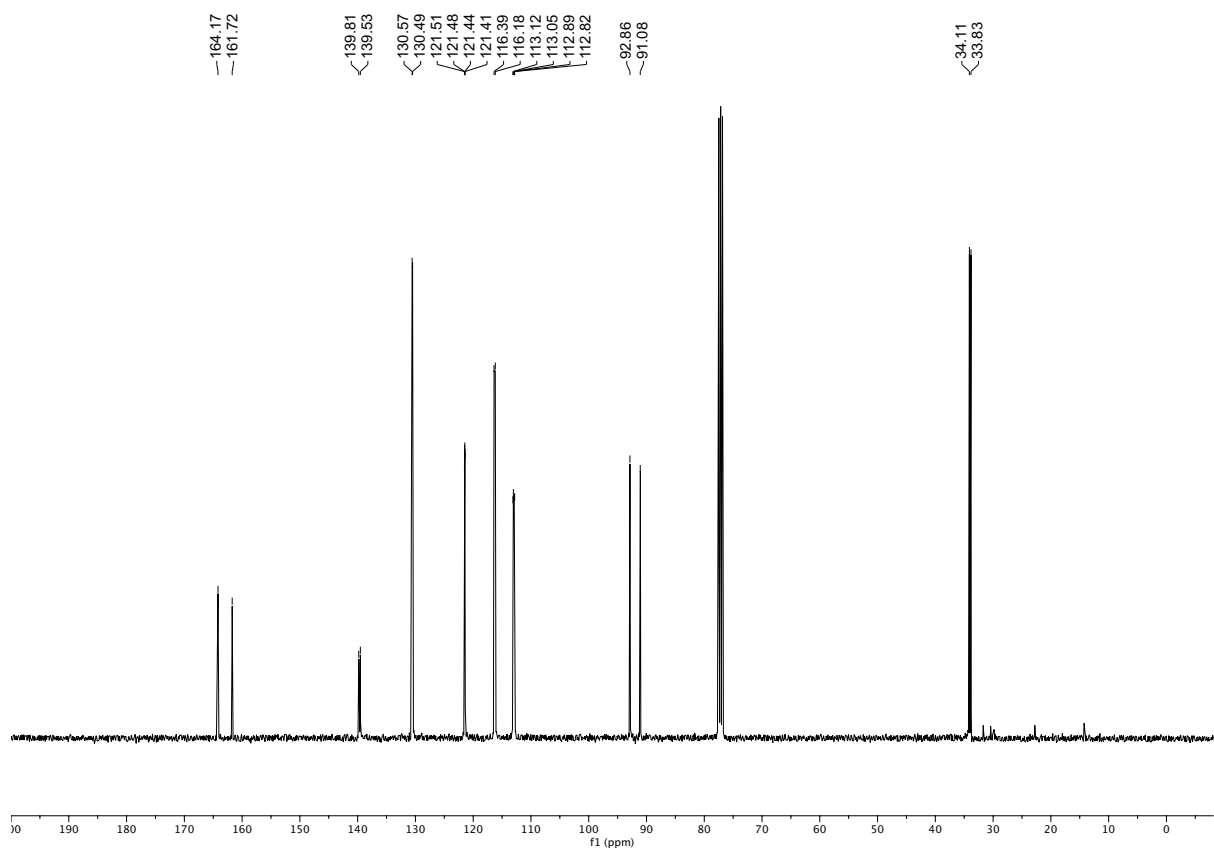


1-(2-Bromo-1-fluoroethyl)-3-fluorobenzene, compound **2y**

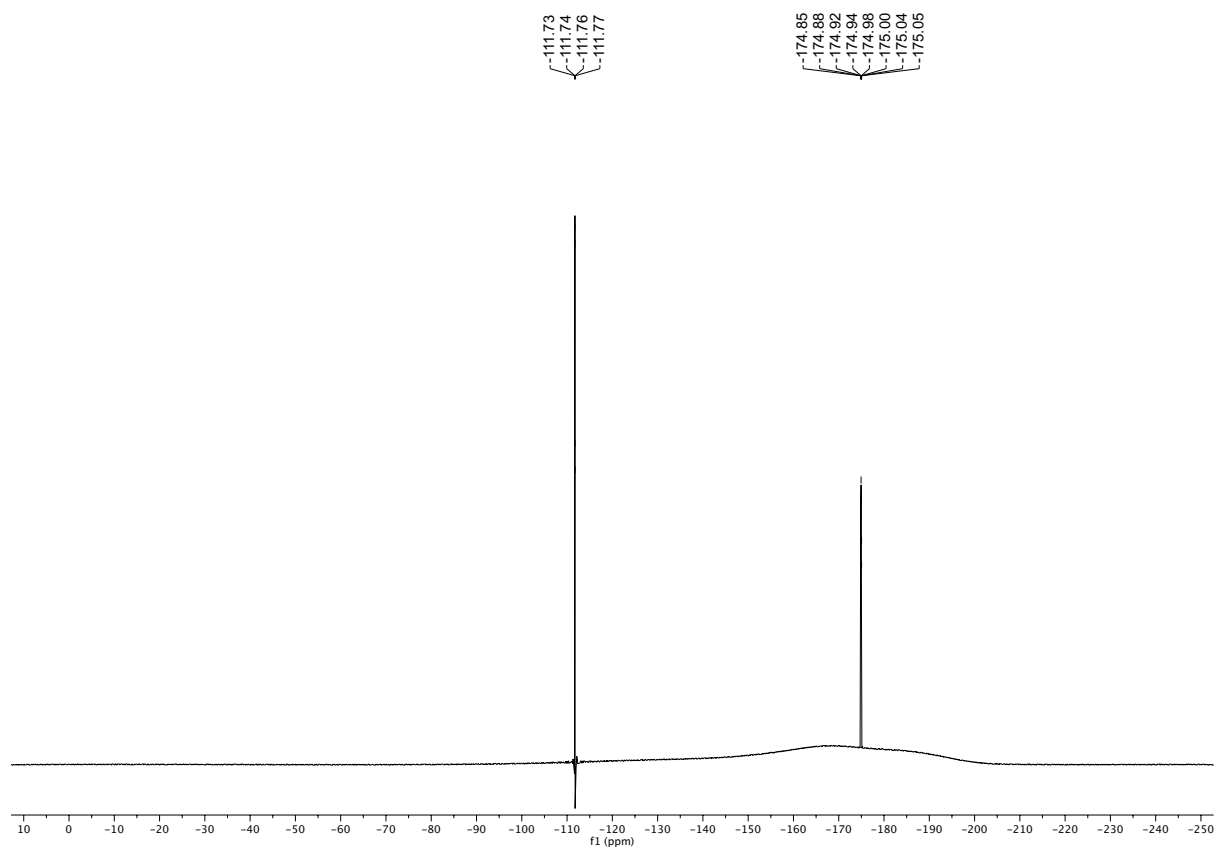
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^{13}C NMR (101 MHz, CDCl_3)

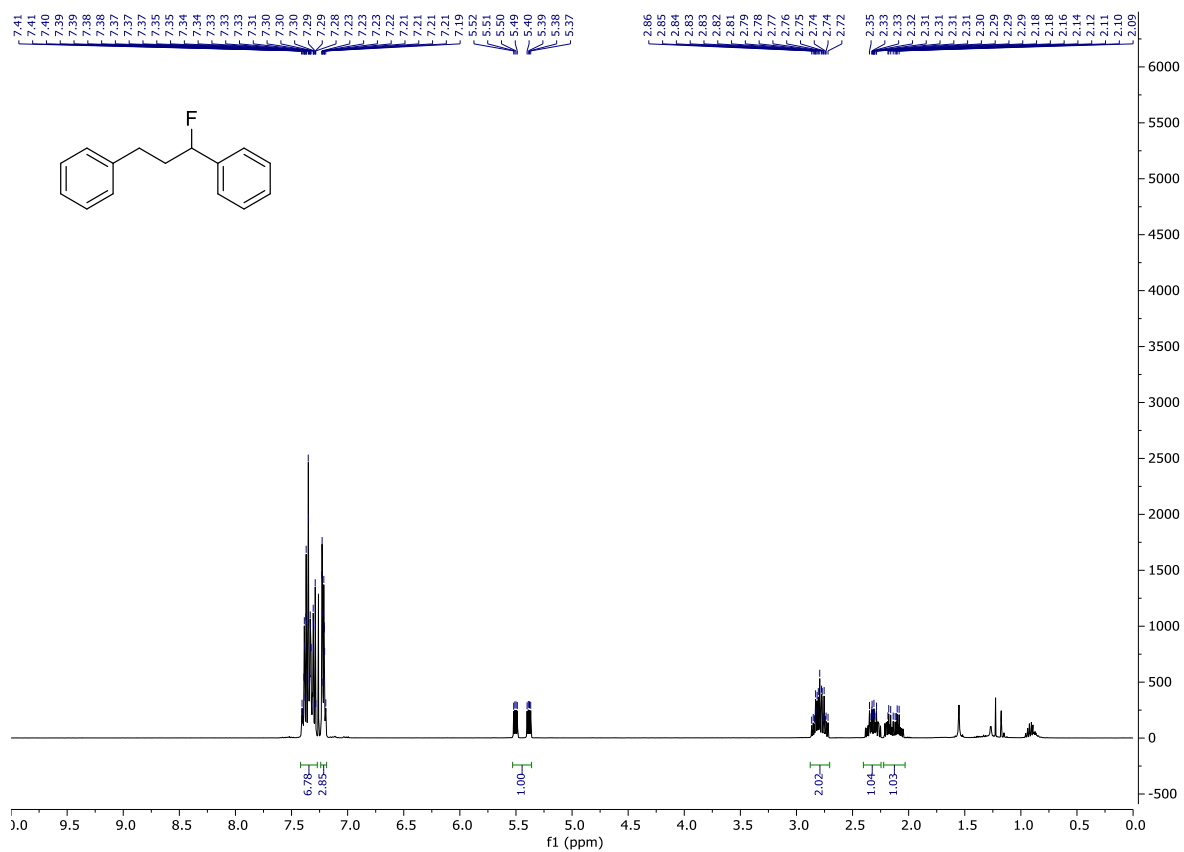


^{19}F NMR (376 MHz, CDCl_3)

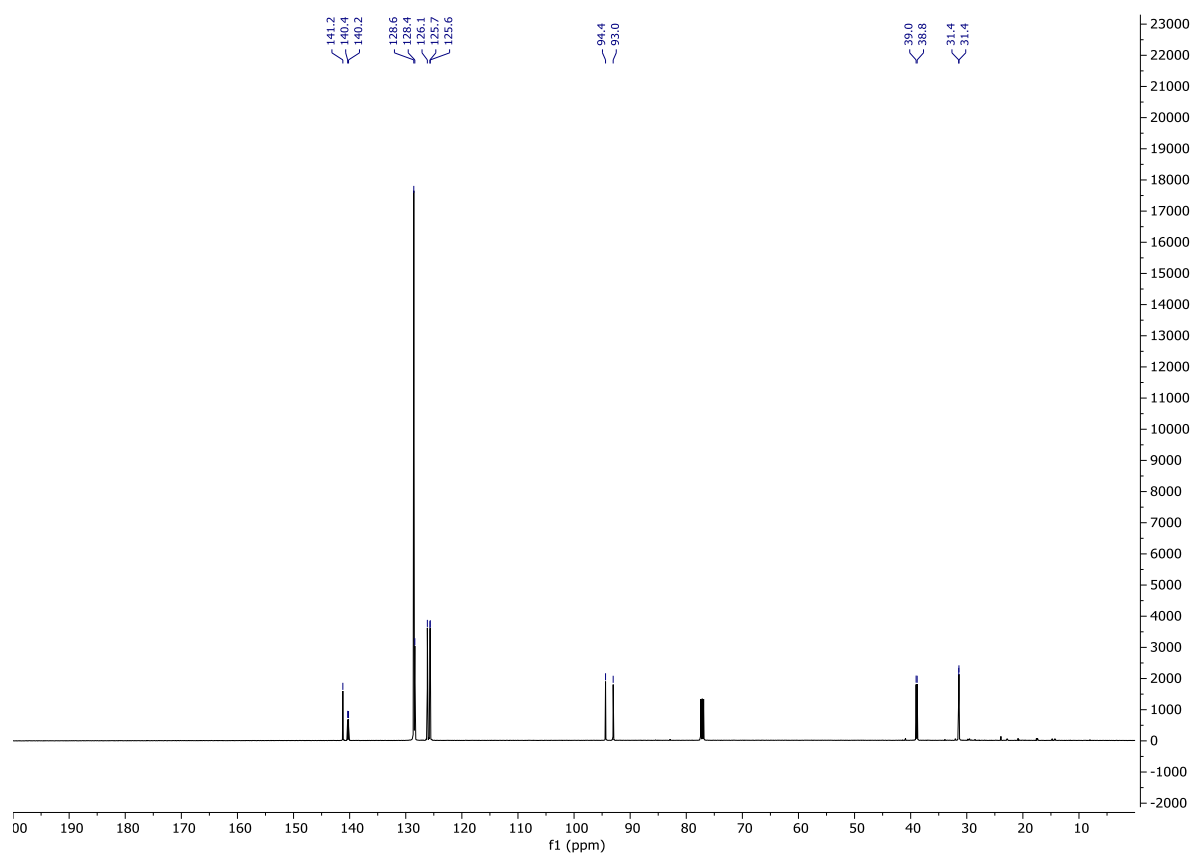


(1-Fluoropropane-1,3-diyl)dibenzene, compound **2z**

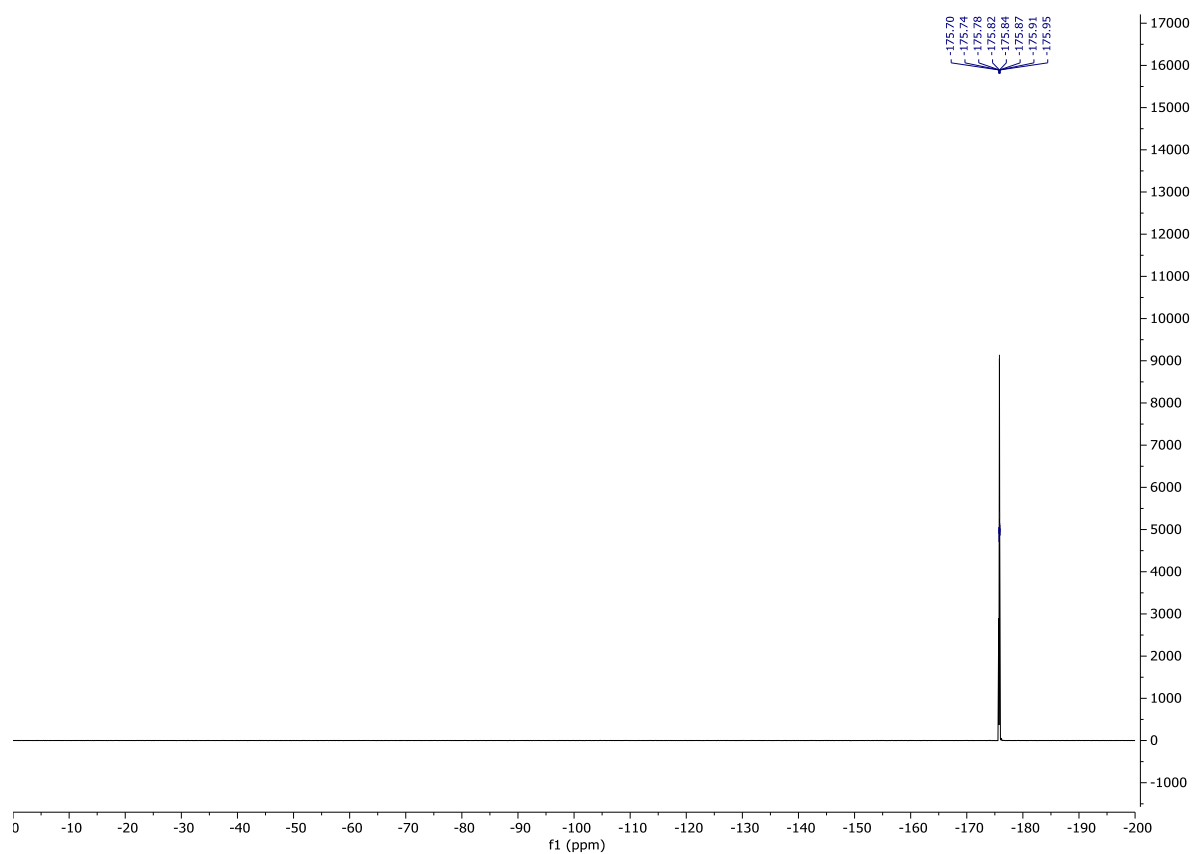
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

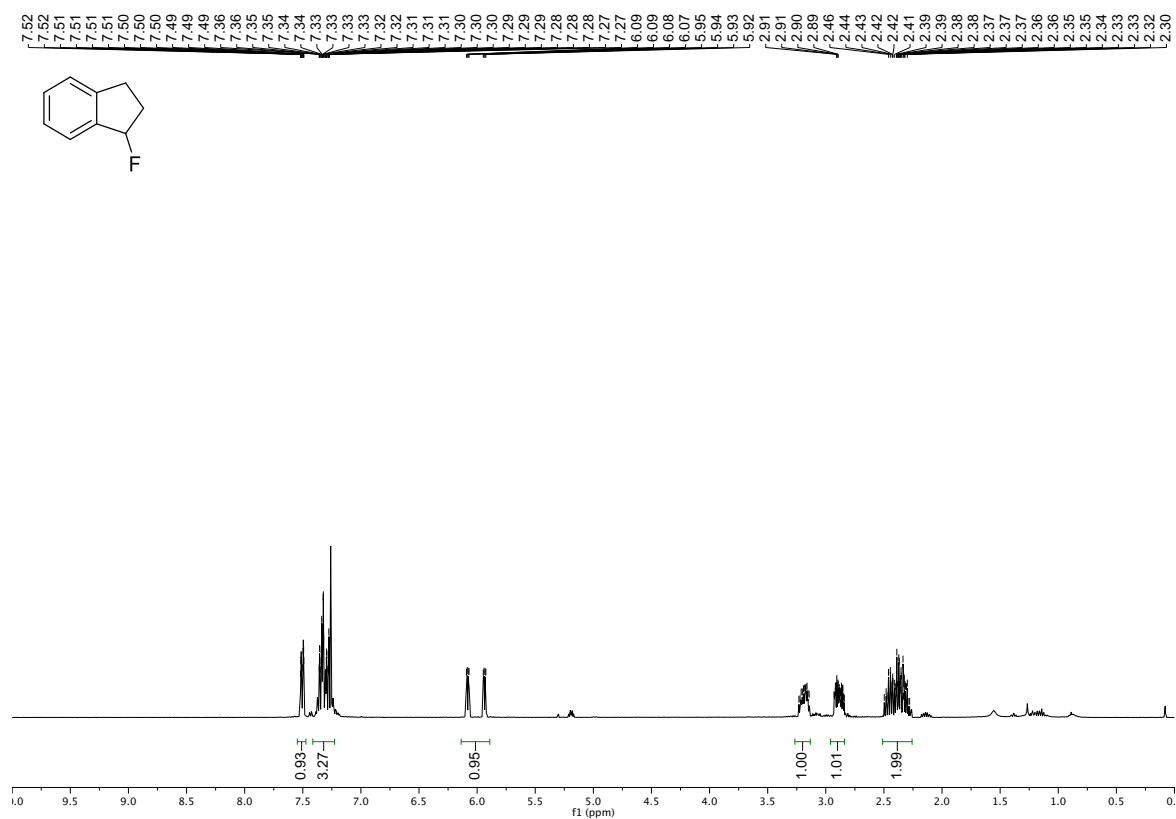


^{19}F NMR (376 MHz, CDCl_3)

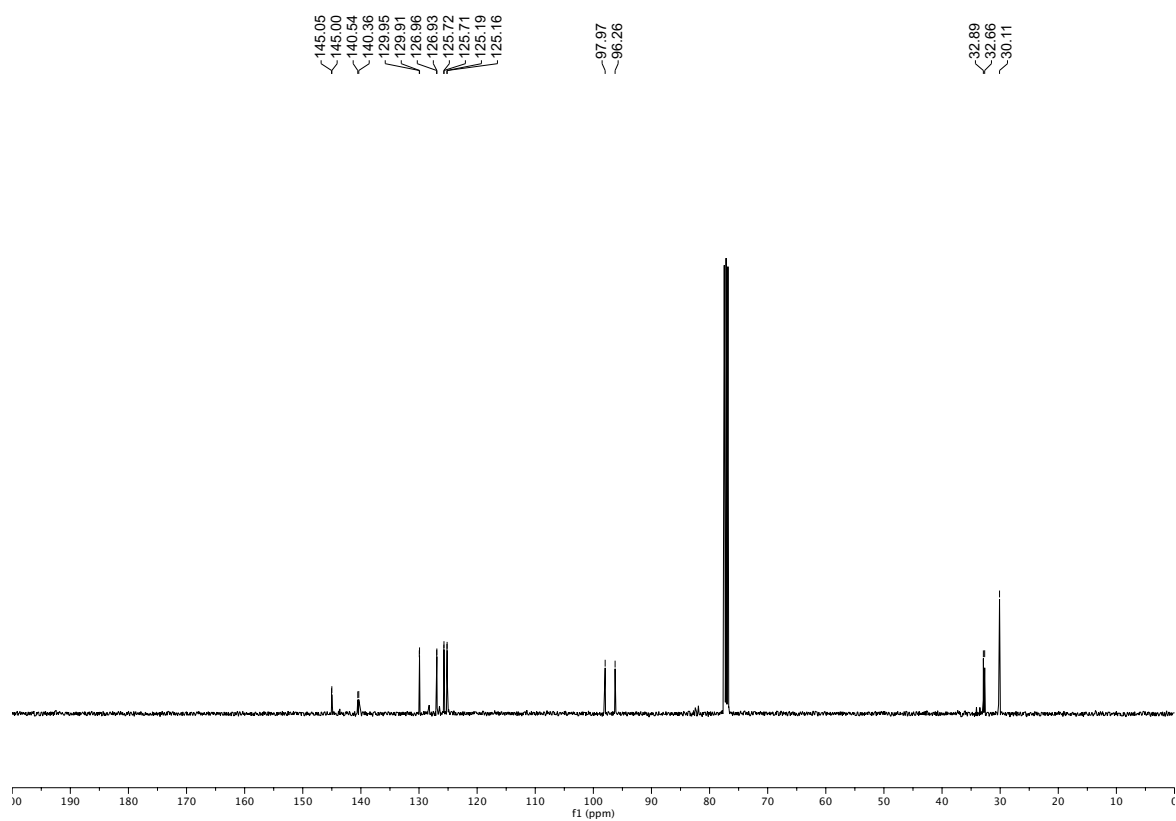


1-Indanyl fluoride, compound **2aa**

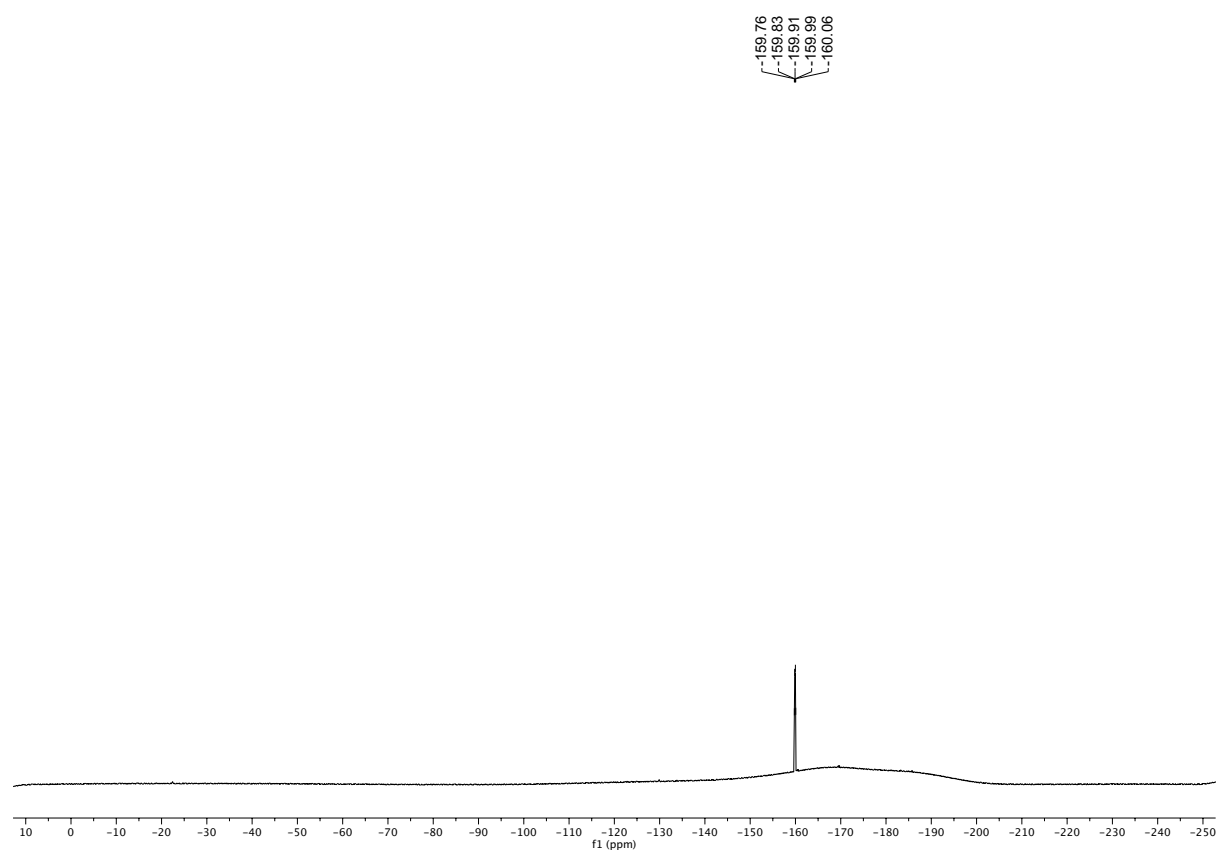
^1H NMR (400 MHz, CDCl_3)



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

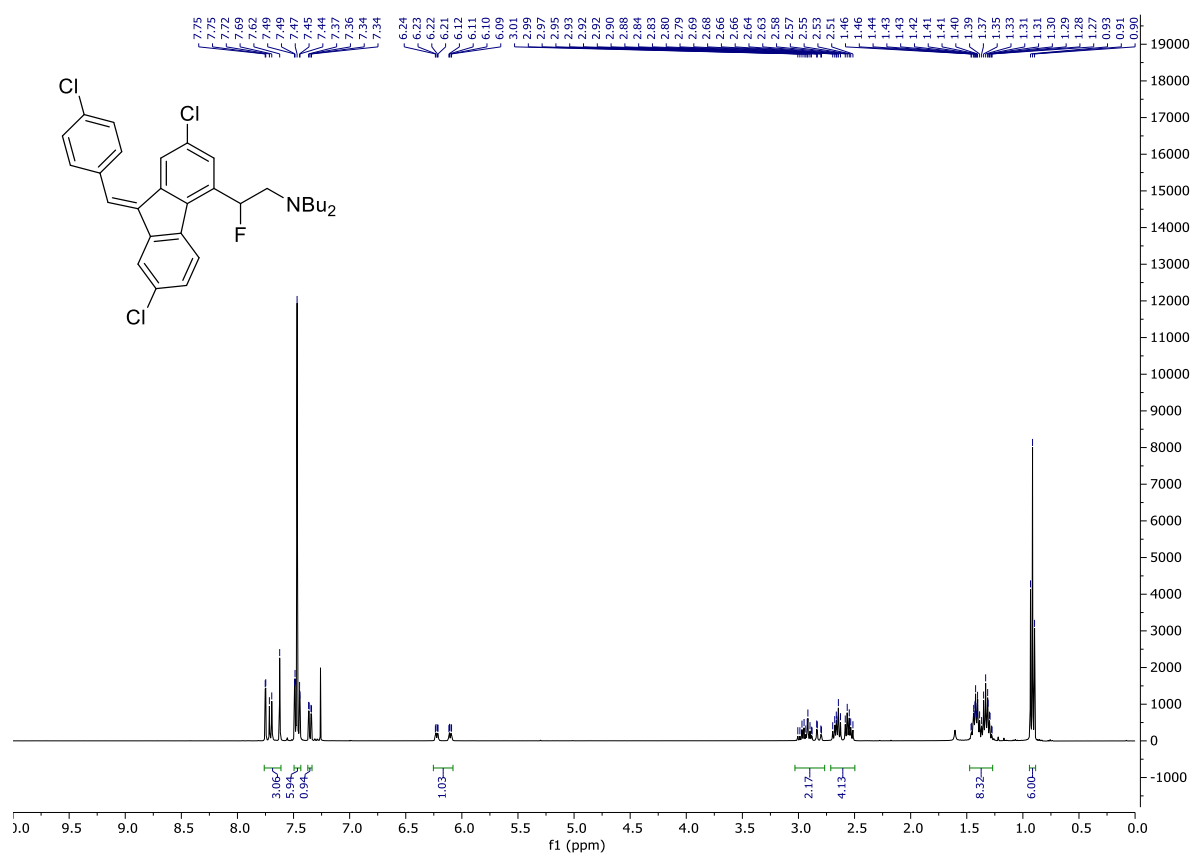


^{19}F NMR (376 MHz, CDCl_3)

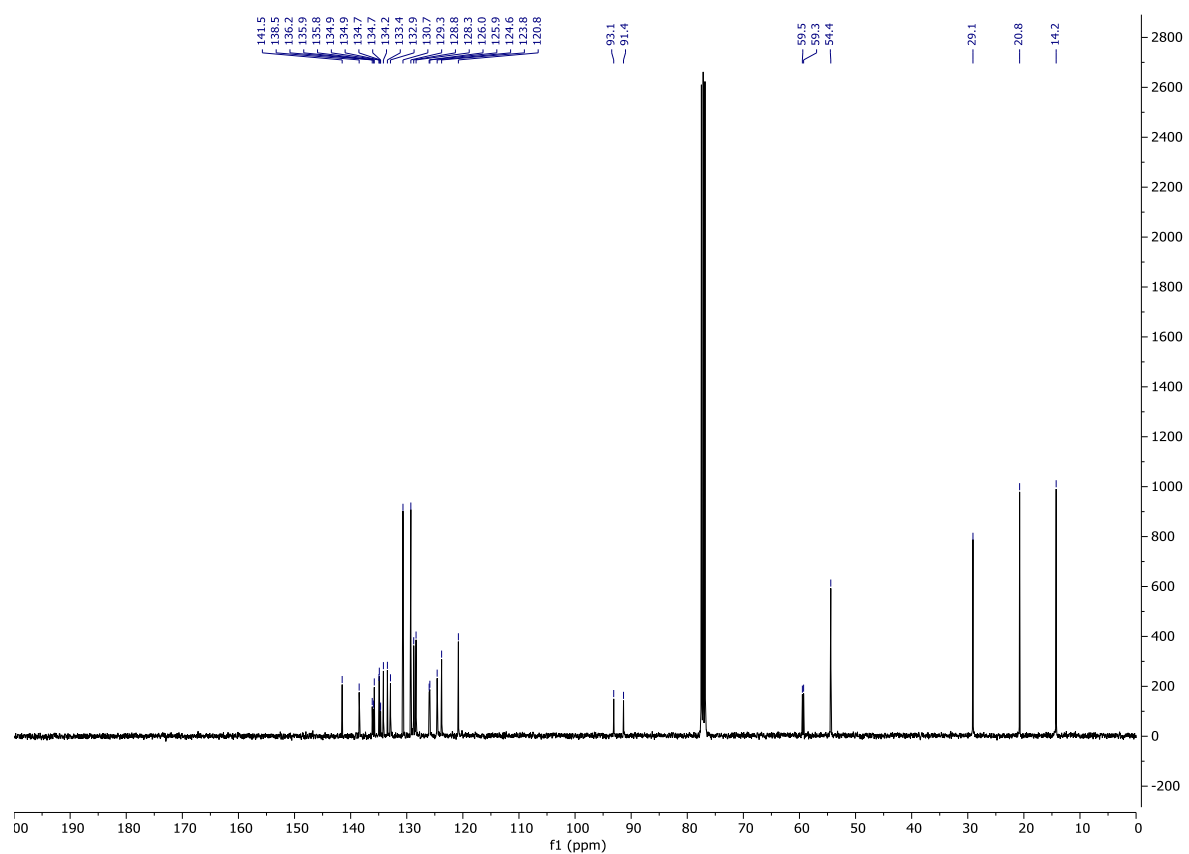


Fluorodeoxylumefantrine, compound **2ab**

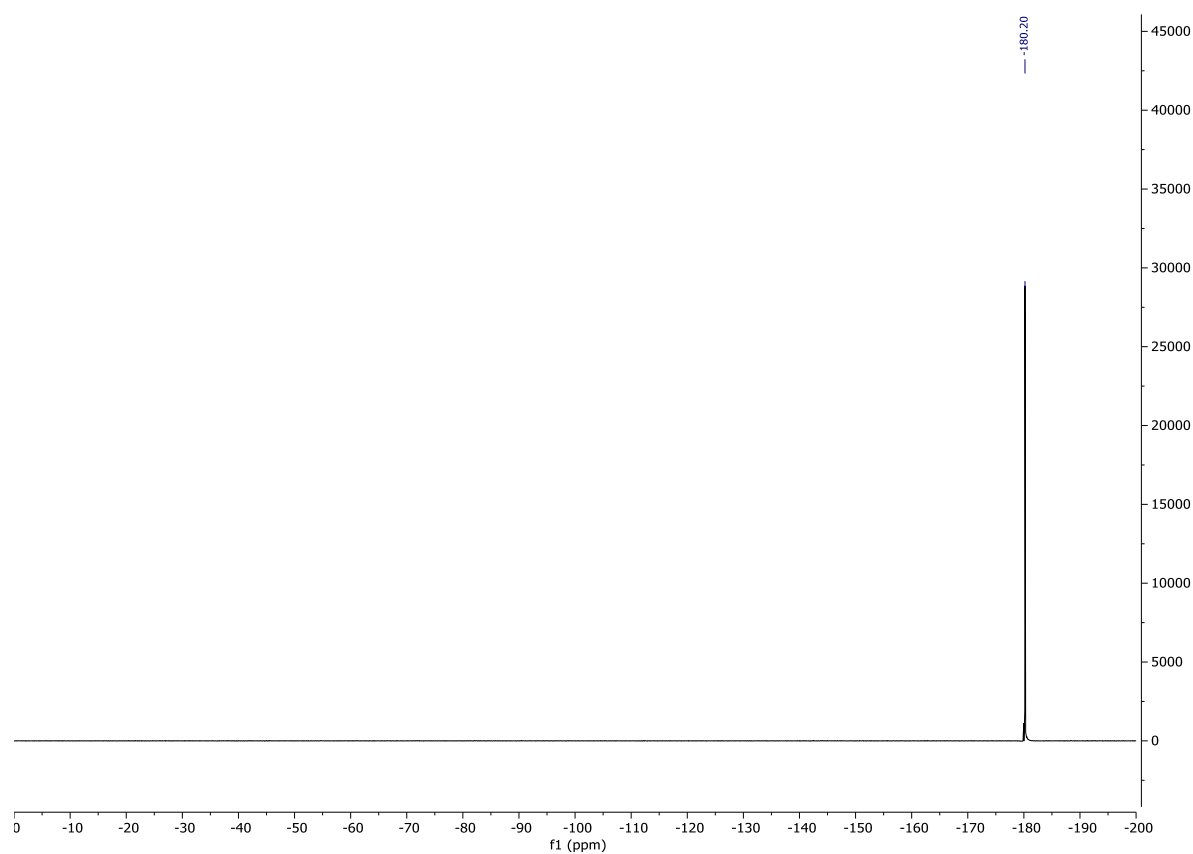
^1H NMR (400 MHz, CDCl_3)



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

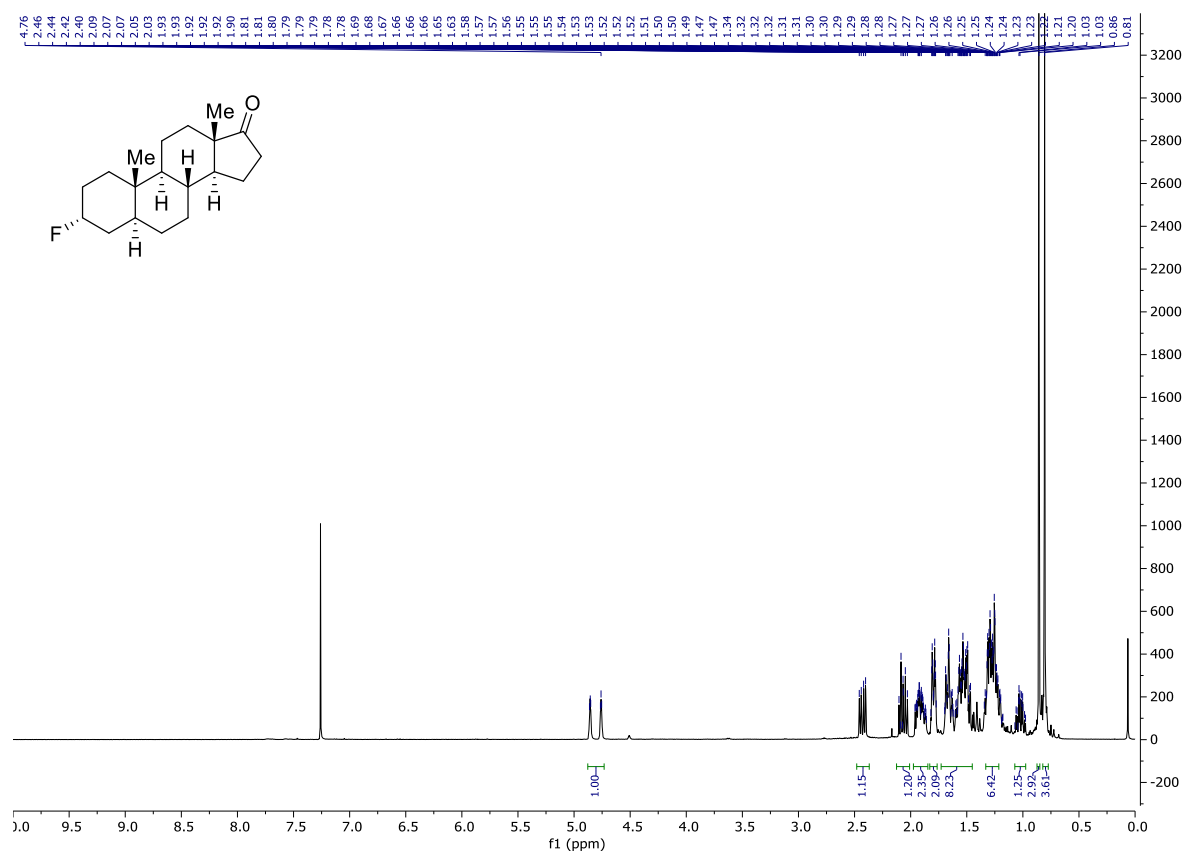


^{19}F NMR (377 MHz, CDCl_3)

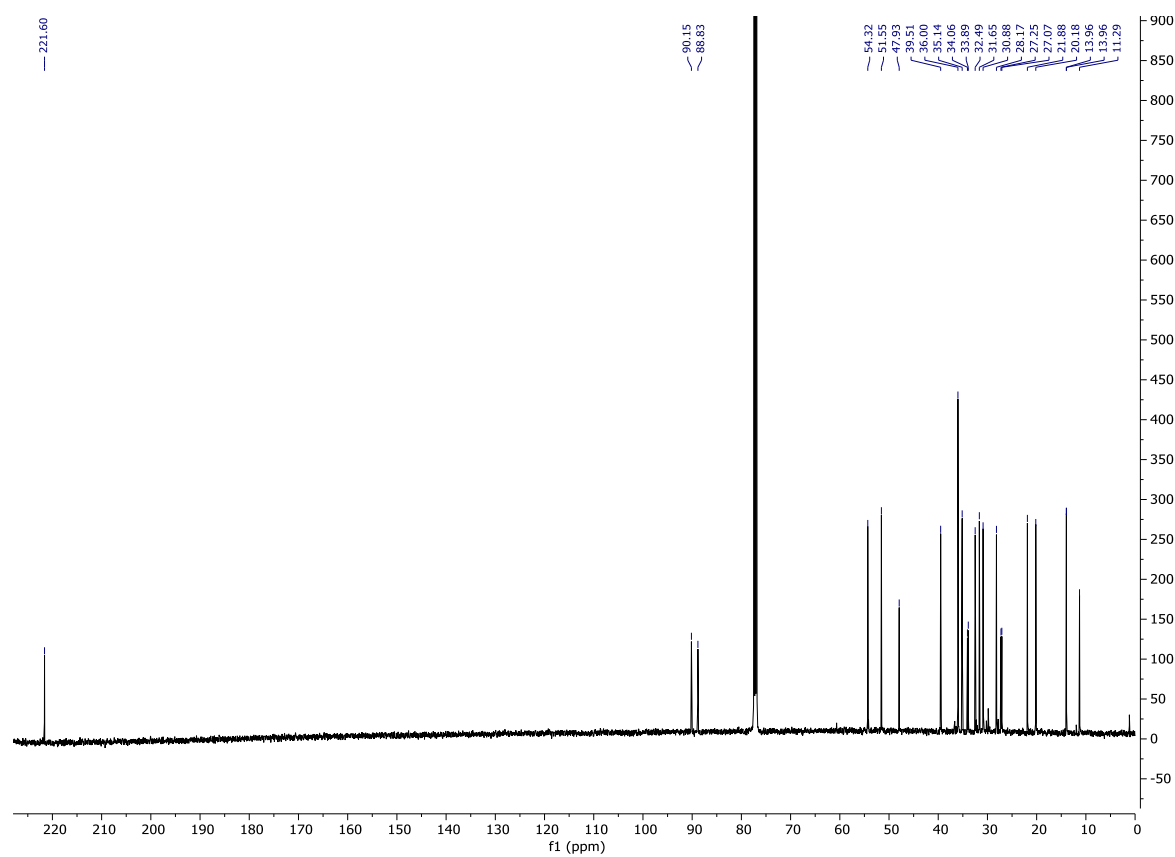


3 α -Fluoro-5 α -androstan-17-one, compound **2ac**

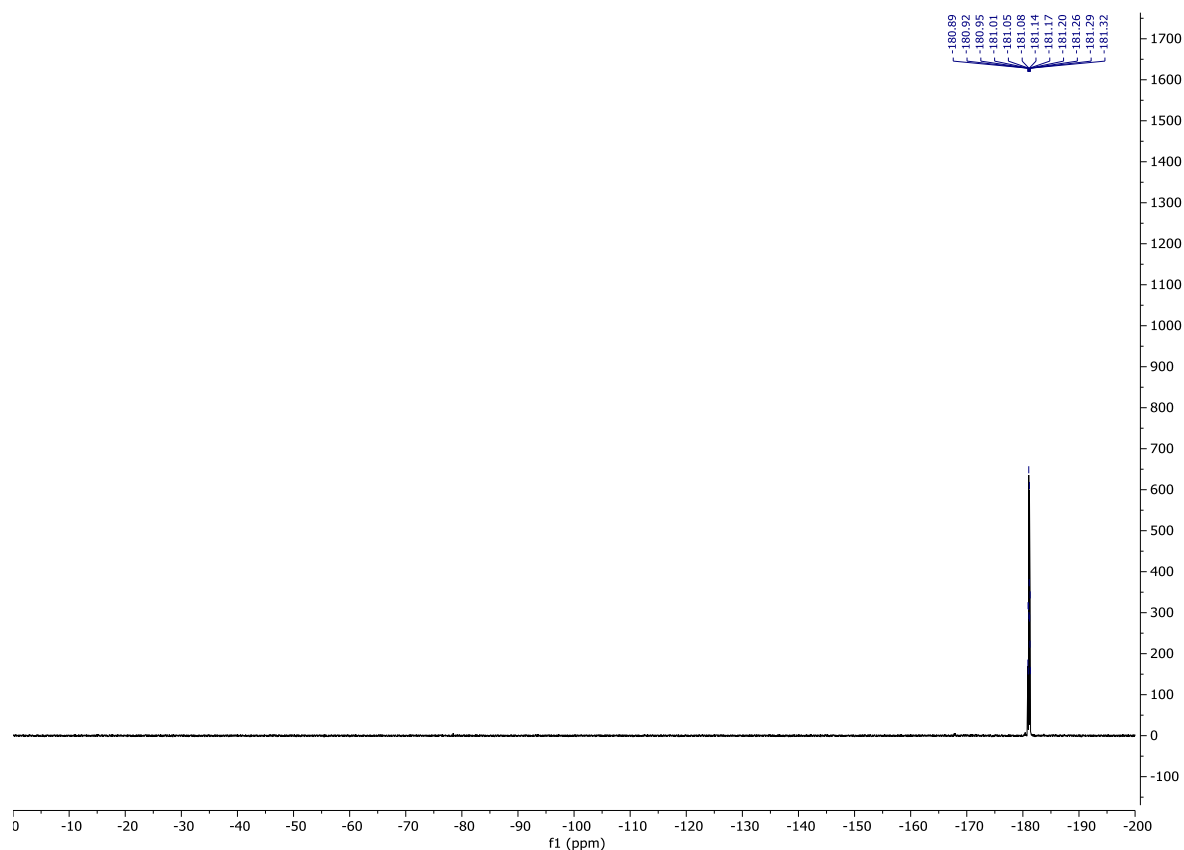
^1H NMR (400 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

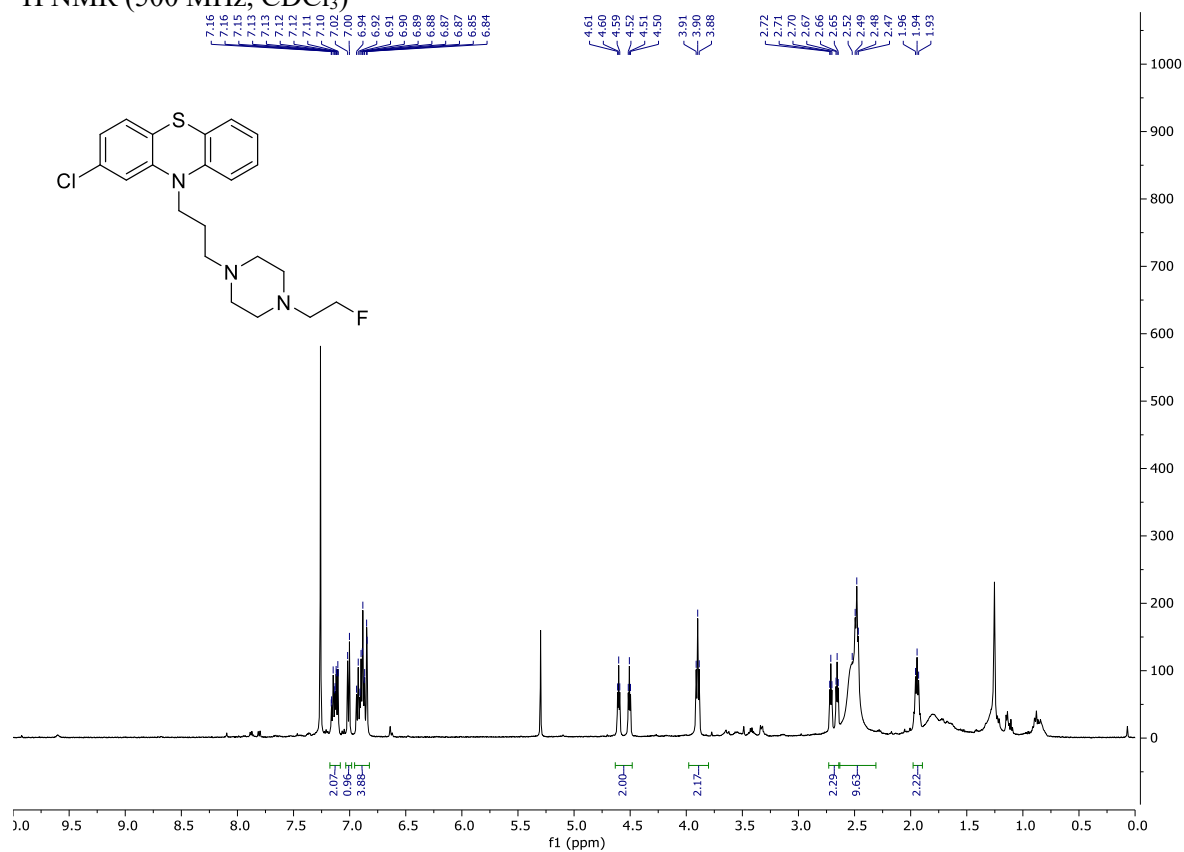


^{19}F NMR (376 MHz, CDCl_3)

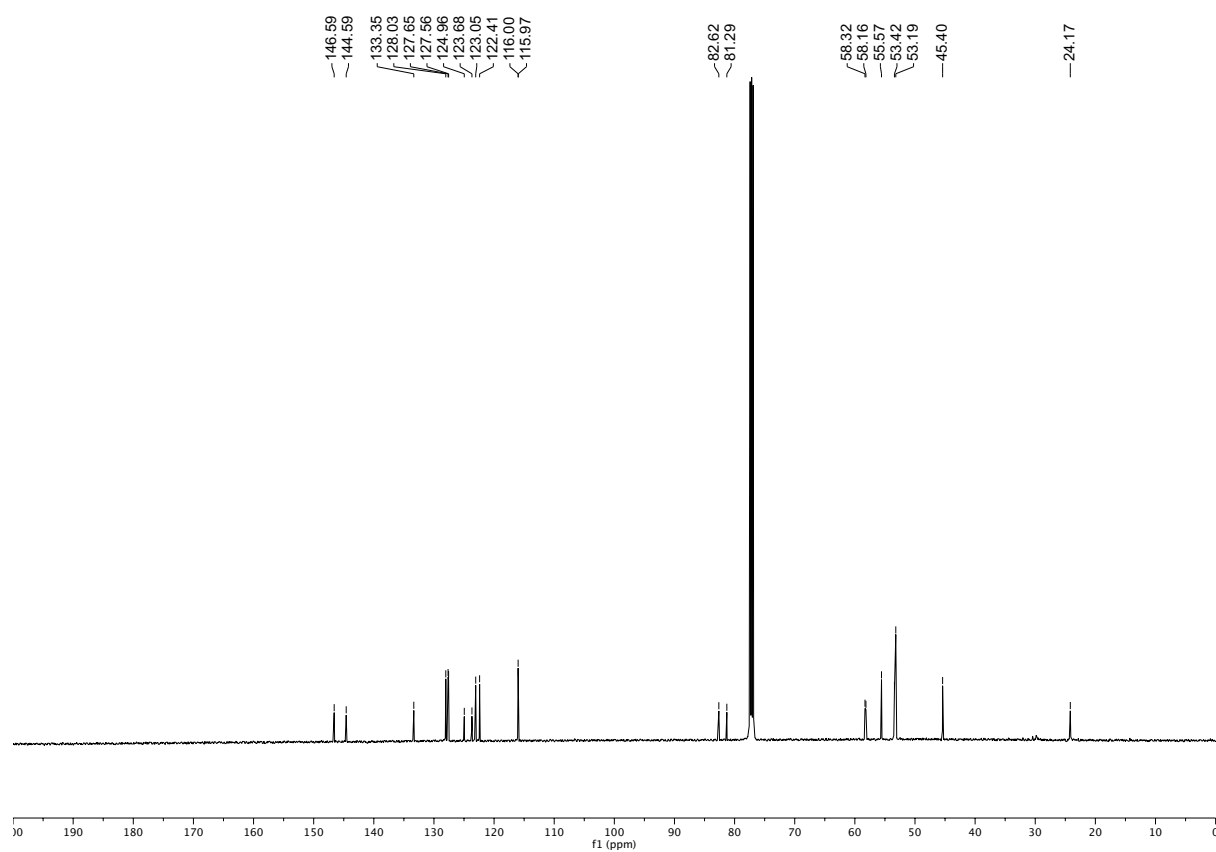


2-Chloro-10-(3-(4(2-fluoroethyl)piperazin-1-yl)propyl)-4a,5a,9a,10a-tetrahydro-10H-phenothiazine, compound **2ad**

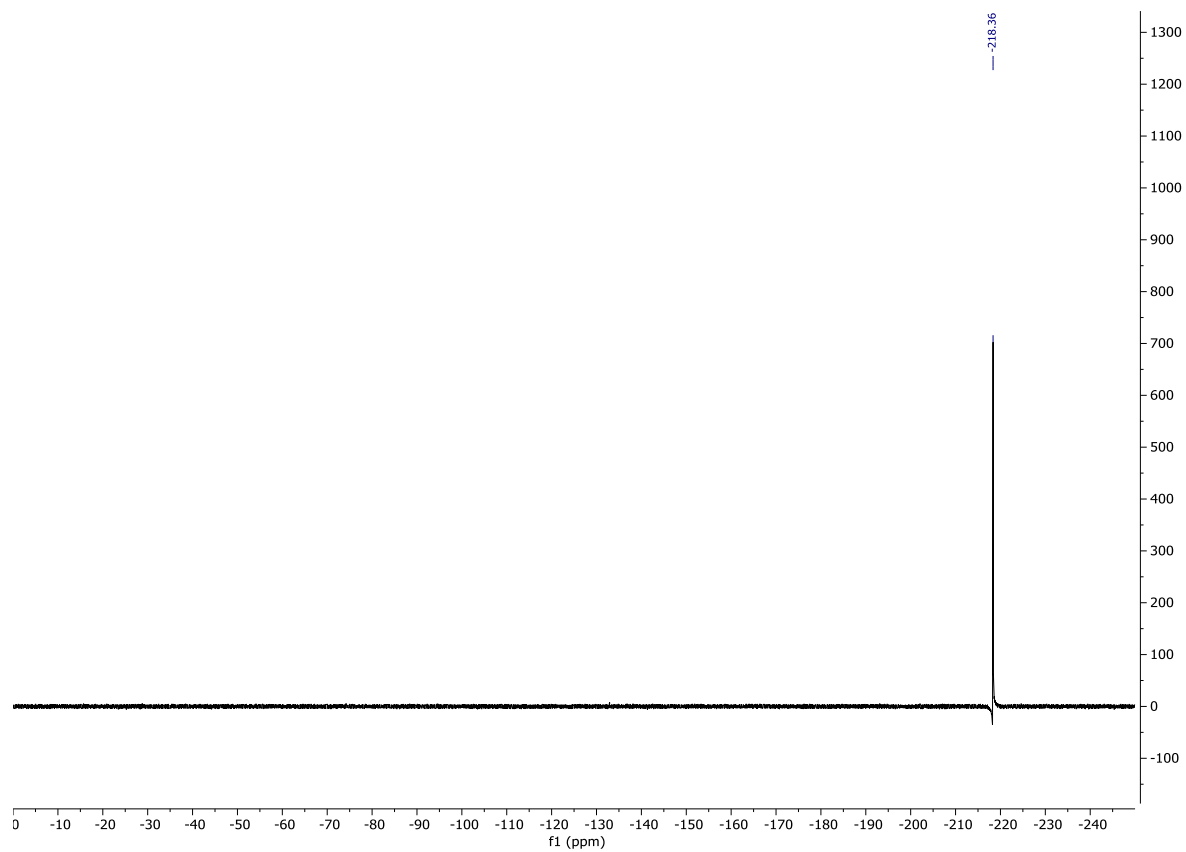
^1H NMR (500 MHz, CDCl_3)



^{13}C NMR (126 MHz, CDCl_3)

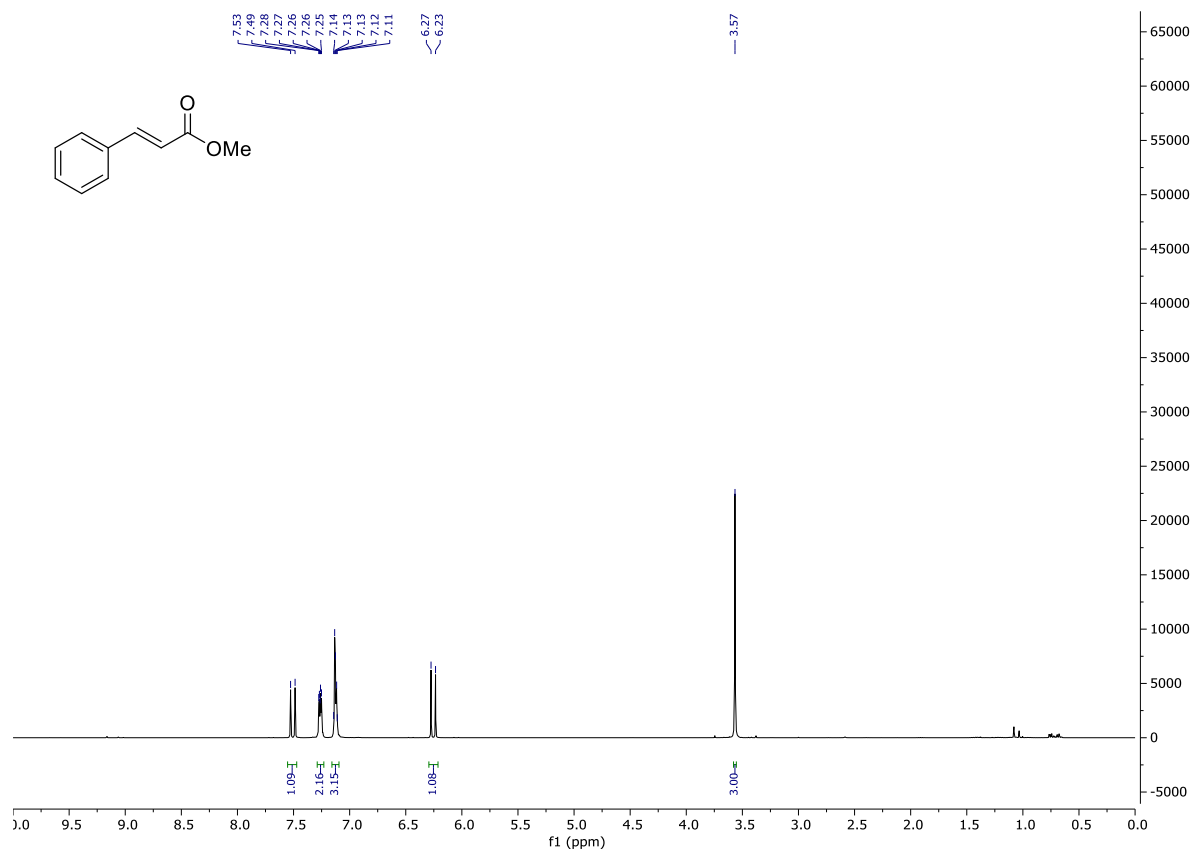


^{19}F NMR (376 MHz, CDCl_3)

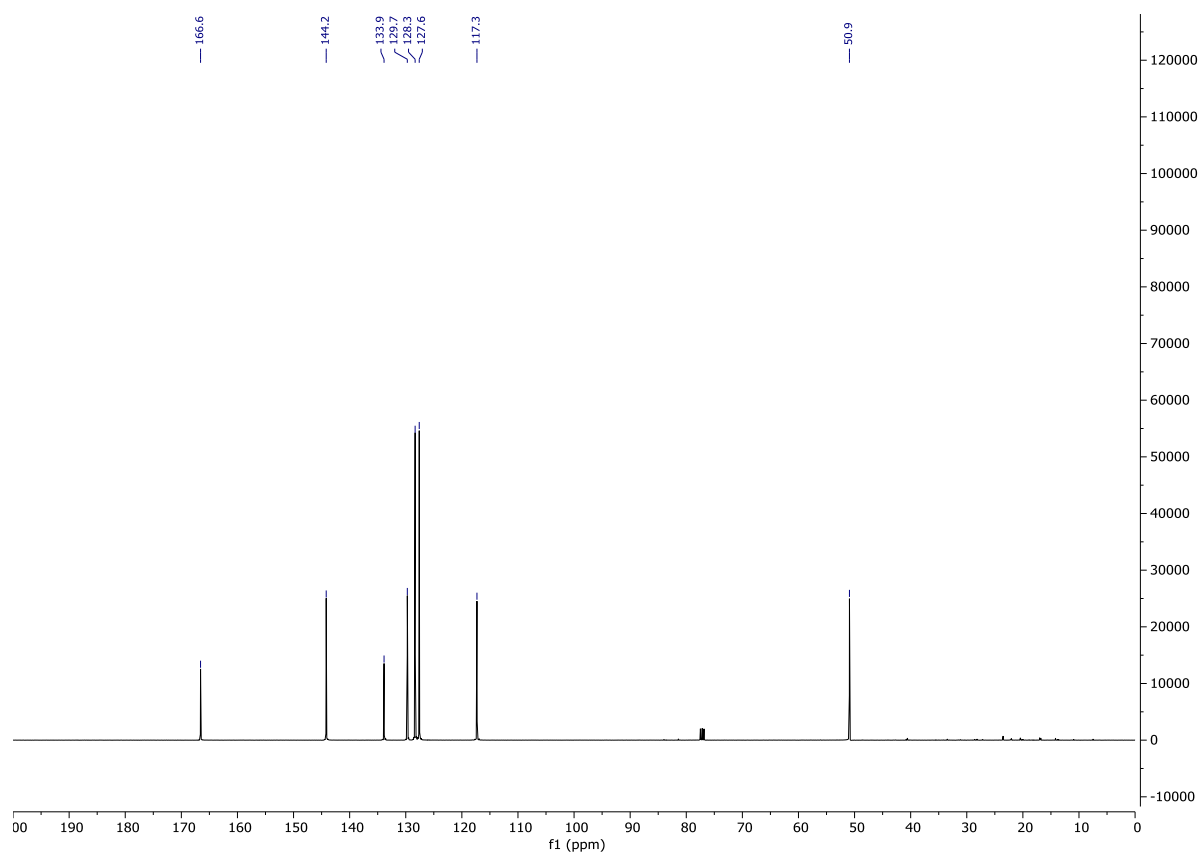


Methyl cinnamate, compound **2ae**

^1H NMR (400 MHz, CDCl_3)

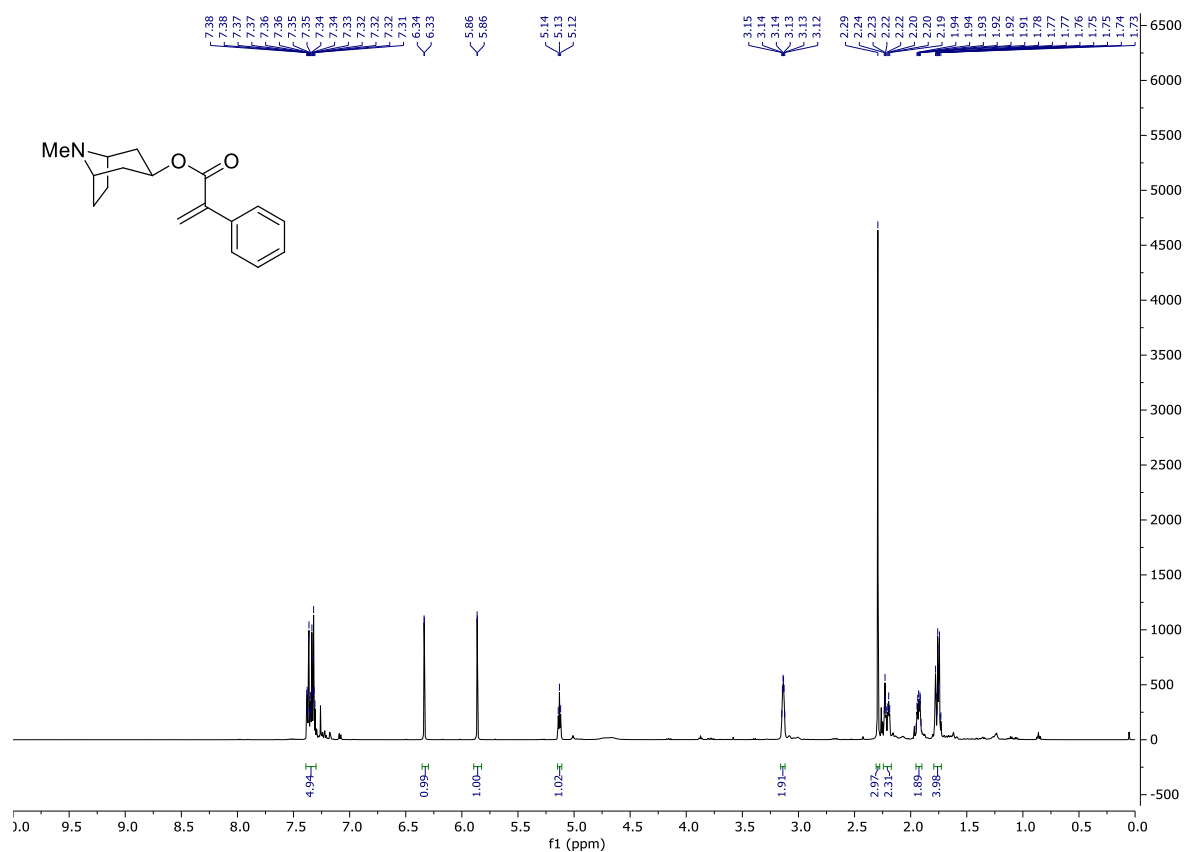


^{13}C NMR (101 MHz, CDCl_3)

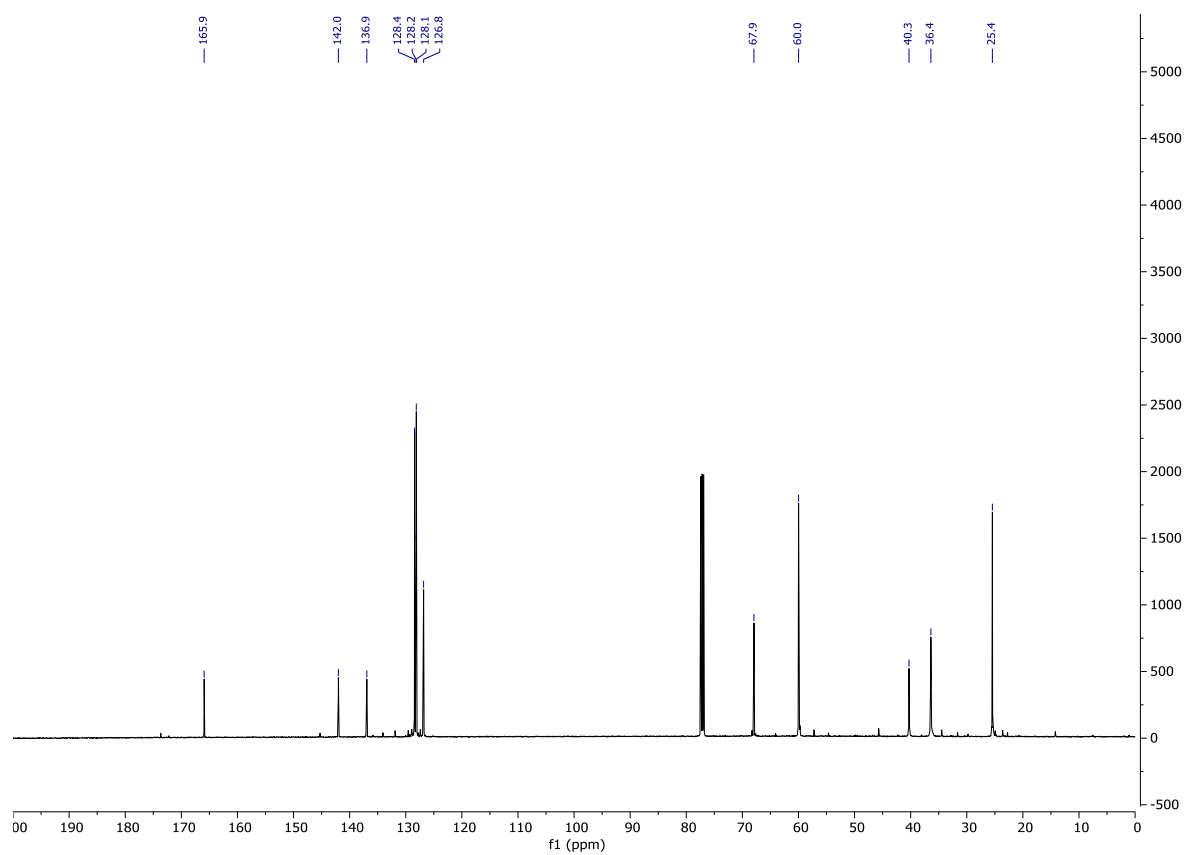


8-Methyl-8-azabicyclo[[3.2.10]octan-3-yl-phenylacrylate, compound **2af**

^1H NMR (500 MHz, CDCl_3)

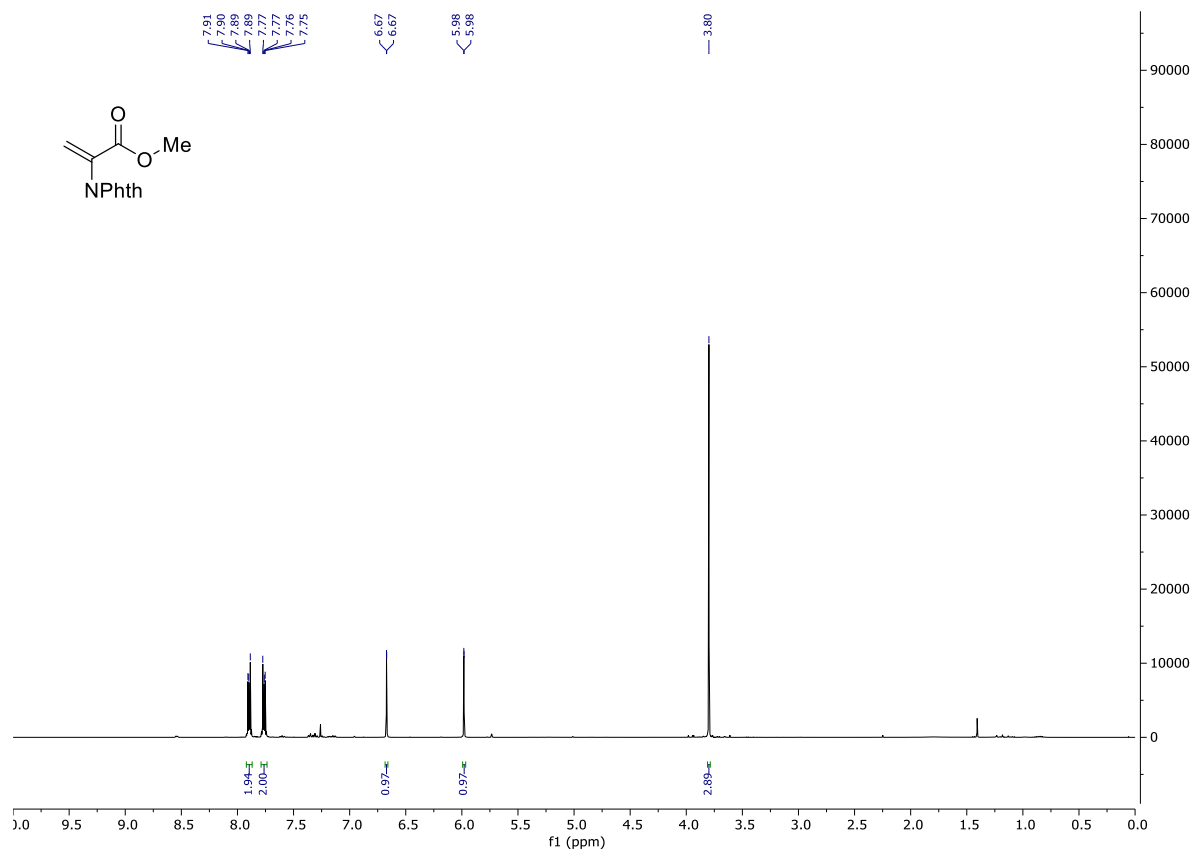


^{13}C NMR (126 MHz, CDCl_3)

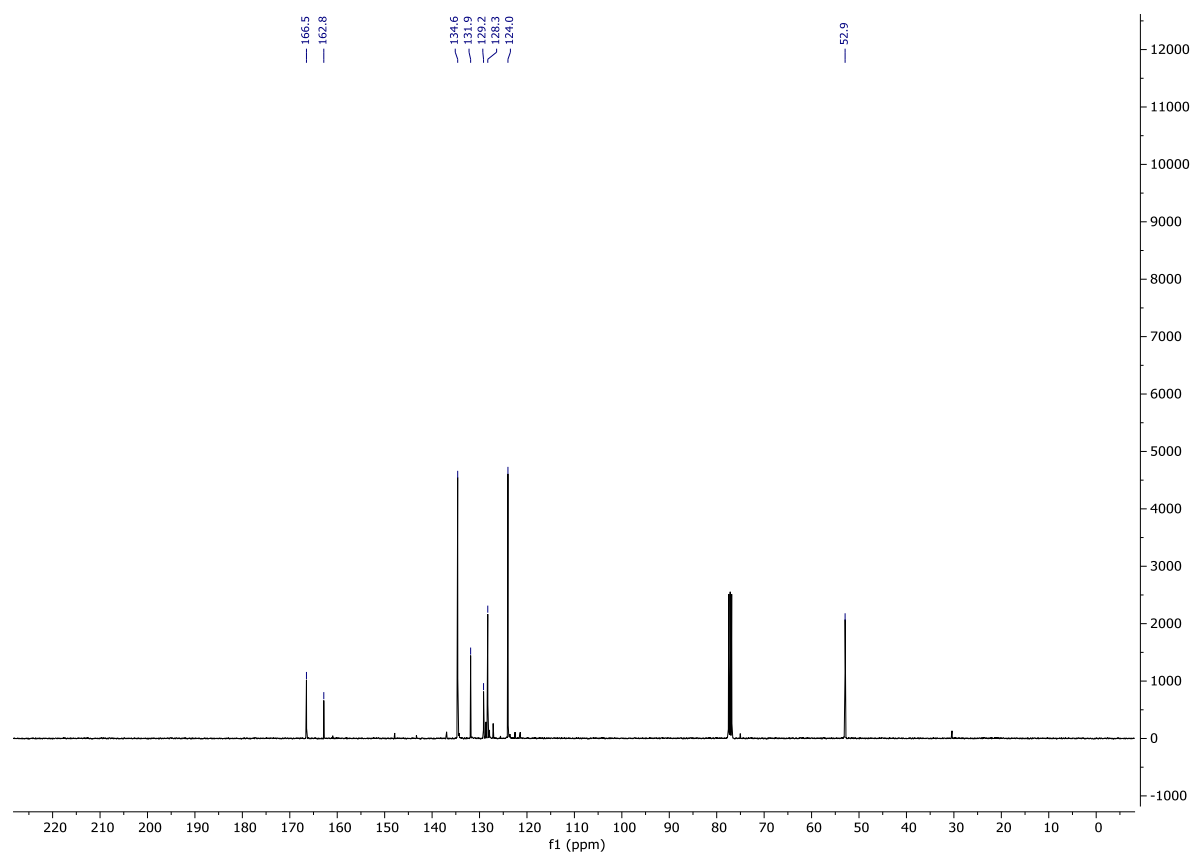


Methyl 2-(1,3-dioxoisindolin-2-yl)acrylate, compound **2ag**

^1H NMR (400 MHz, CDCl_3)

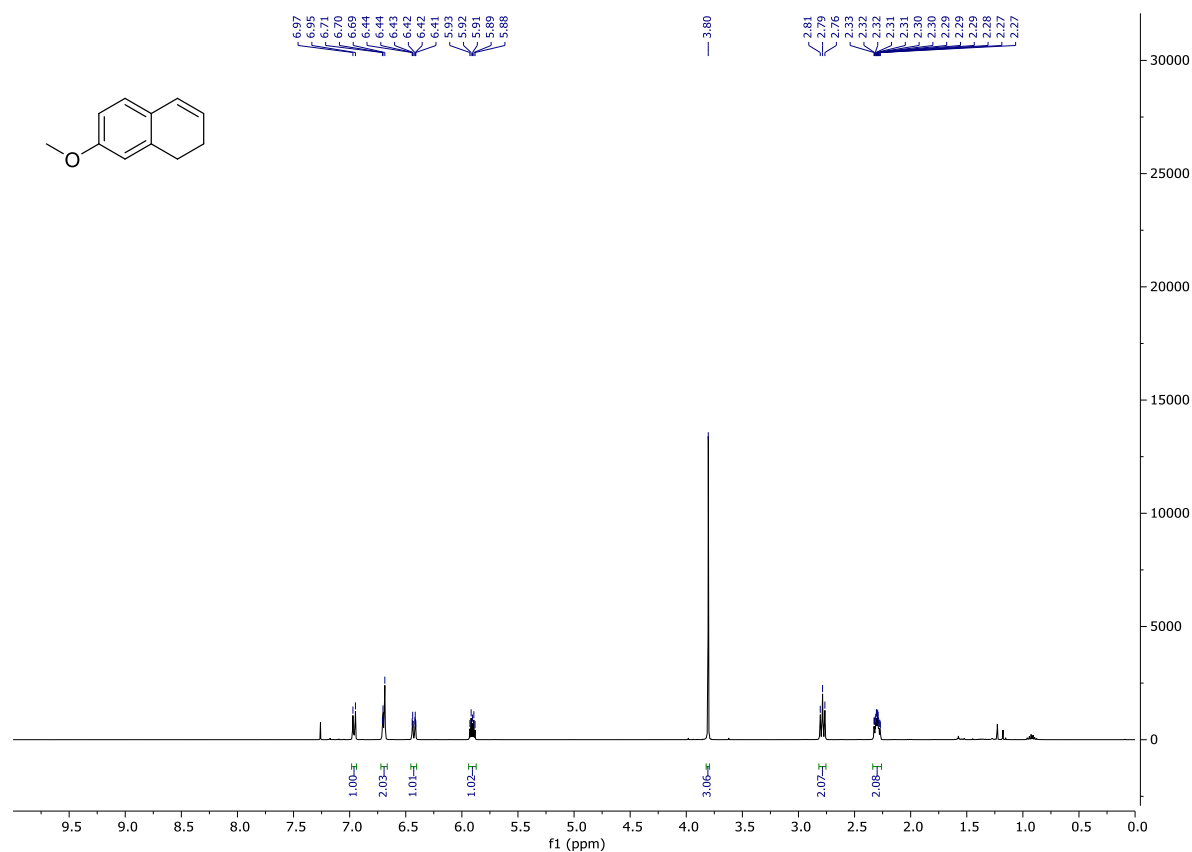


^{13}C NMR (101 MHz, CDCl_3)

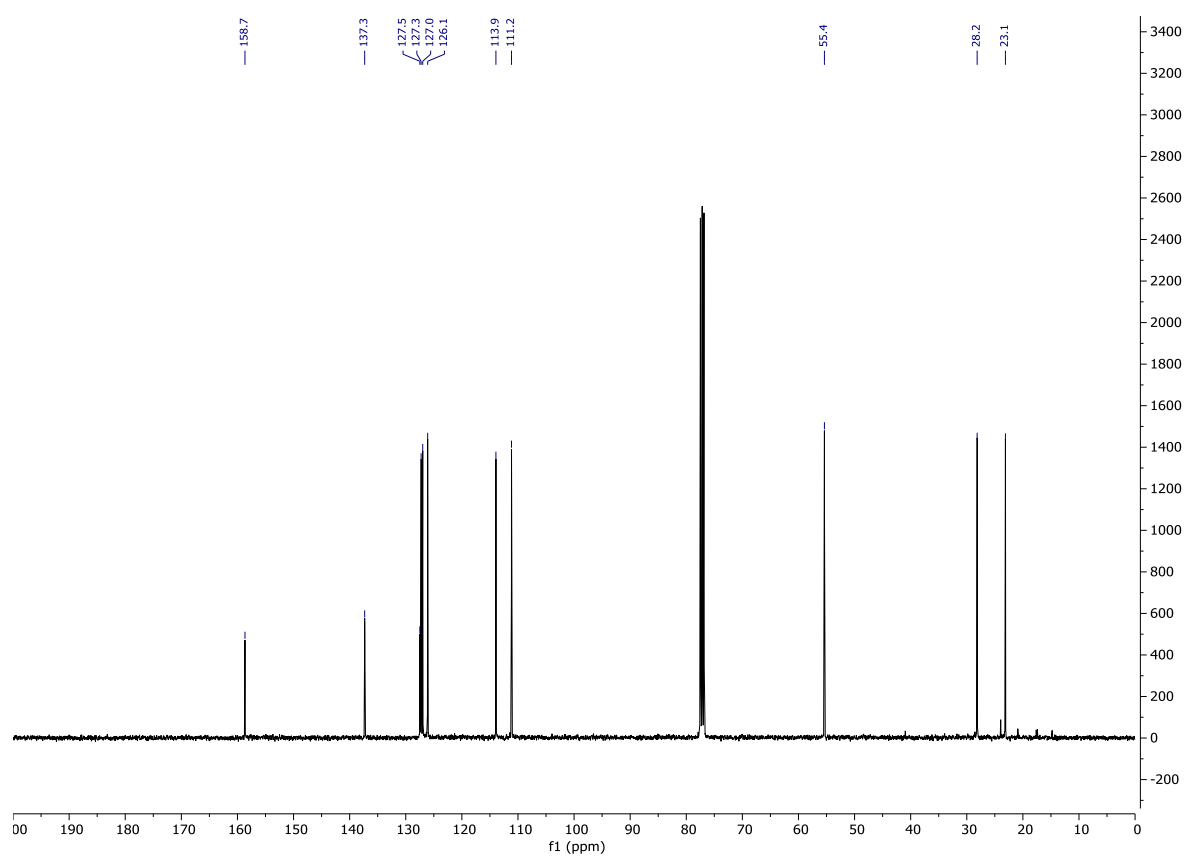


7-Methoxy-1,2-dihydronaphthalene, compound **2ah**

^1H NMR (400 MHz, CDCl_3)

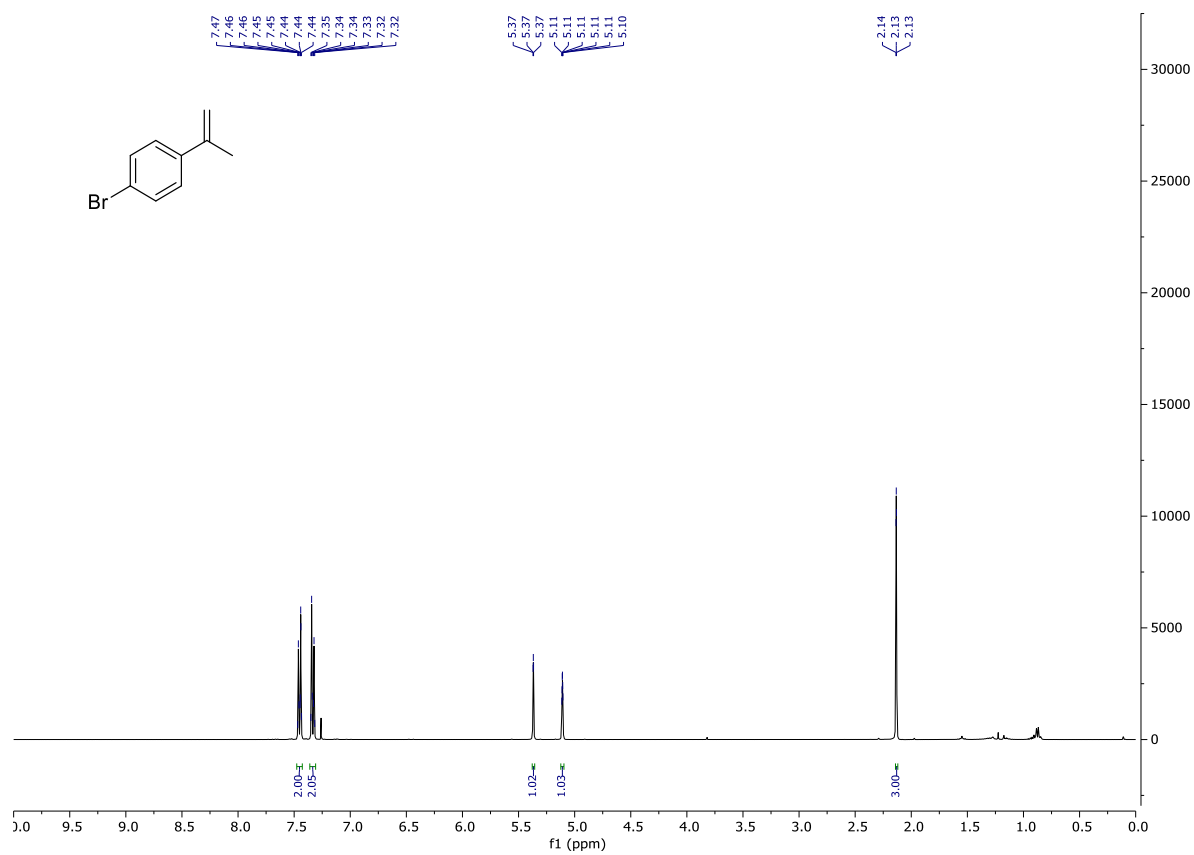


^{13}C NMR (101 MHz, CDCl_3)

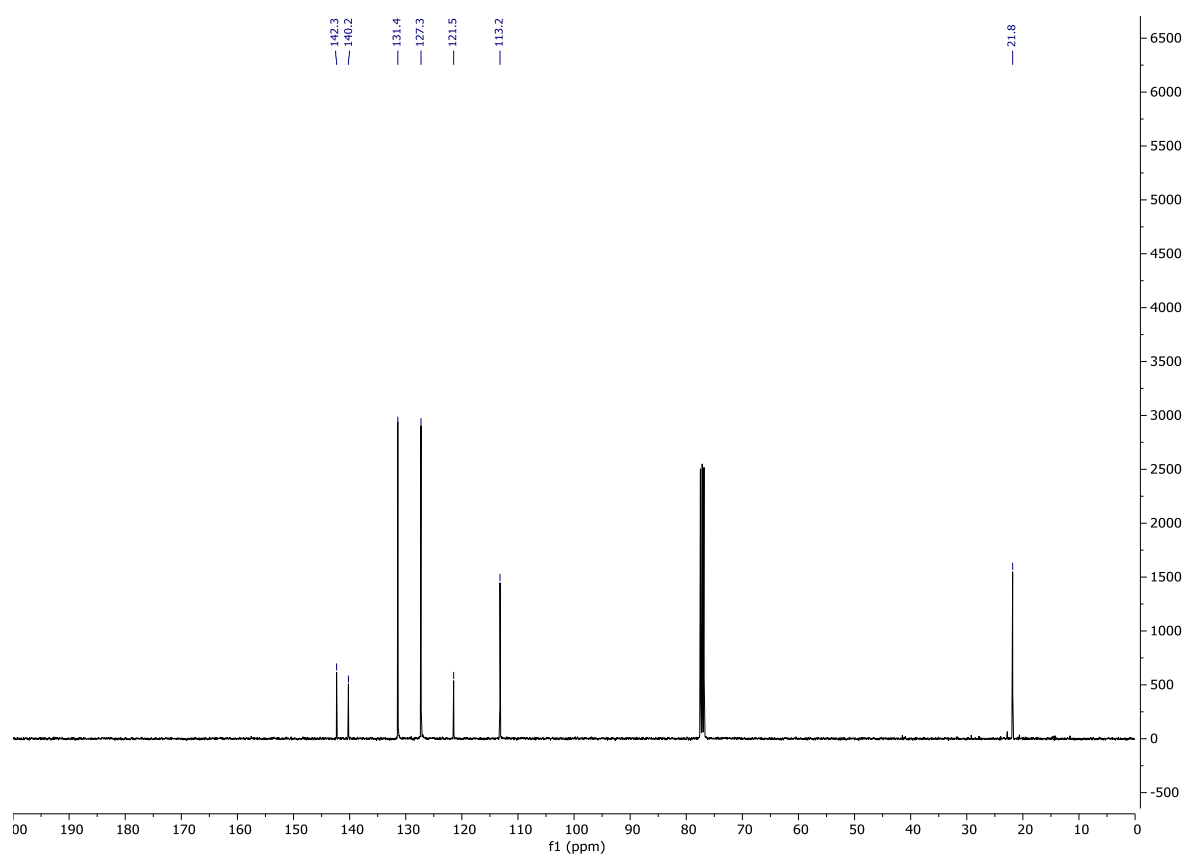


4-Bromo- α -methylstyrene, compound **2ai**

^1H NMR (400 MHz, CDCl_3)



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



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