PRENYL PRAXIS: A METHOD FOR DIRECT PHOTOCATALYTIC DEFLUOROPRENYLATION

By

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Bachelor of Science in Chemistry
University of Delhi
New Delhi, Delhi
2014

Submitted to the Faculty of the
Graduate College of the
Oklahoma State University
in partial fulfillment of
the requirements for
the Degree of
MASTER OF SCIENCE
December, 2018

PRENYL PRAXIS: A METHOD FOR DIRECT

PHOTOCATALYTIC DEFLUOROPRENYLATION

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ACKNOWLEDGEMENTS

I would like to express my gratitude to my advisor Dr. Jimmie D. Weaver for his immense support during my M.S. study. His immense knowledge, skillful guidance and constant motivation to excel in the field of chemistry really helped me to realize my potential.

I would also like to acknowledge my committee members Dr. Richard Bunce and Dr Frank Blum for their valuable inputs and helpful suggestions.

I fully enjoyed working in a healthy research lab environment and must also thank all my lab mates Anuradha, Sameera, Amandeep, Jon, Kamaljeet, Kip, Mo, Manjula, Winston and Ryne. It was a great pleasure sharing ideas and learning from each other.

Name: SONAL PRIYA

Date of Degree: DECEMBER, 2018

Title of Study: PRENYL PRAXIS: A METHOD FOR DIRECT PHOTOCATALYTIC DEFLUOROPRENYLATION

Major Field: CHEMISTRY

Abstract: The prenyl fragment represents the most basic building block in terpenoids, a family of numerous and structurally diverse natural products that are known to possess interesting biological properties. In contrast, multifluorinated arenes are an important class of compounds that have found great utility in agricultural, material, and pharmaceutical industries. Fluorine substitution has been shown to impart a number of positive attributes including resistance to metabolic degradation, enhanced lipophilicity, and improved binding and passive diffusion of compounds across membranes. While allylation chemistry is well developed, effective prenylation strategies have been less forthcoming. Herein, we describe the defluoroprenylation *via* photocatalysis, a powerful method that provides access to "hybrid molecules" containing both the functionality of a prenyl group and fluorinated arenes. This approach involves direct prenyl group transfer under very mild conditions, displays excellent functional group tolerance, and relatively short reaction times (<4 h), which is the fastest photocatalytic C–F functionalization developed to date. Additionally, the strategy can be further extended to include allyl and geranyl (10 carbon fragment) transfer. Another prominent finding is a reagent dependent switch in regioselectivity of the major product from *para* to *ortho* C–F functionalization.

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CHAPTER I

PRENYL PRAXIS: A METHOD FOR DIRECT PHOTOCATALYTIC DEFLUOROPRENYLATION

1.1 Introduction

The prenyl group is the most basic building block of terpenoid natural products and thus possesses interesting biological properties.[1] Terpenes are a large and varied class of organic compounds that are known to possess a variety of impressive biological properties.[2] These diverse bioactive structures have been widely utilized in delivering pharmacological properties,[3] used as natural flavoring compounds in food industry[4] and are the primary constituents of essential oils of a variety of medicinal plants and flowers.[5] Some of the common terpenes (Figure 1.1) include myrcene (known for its highly sedative effects),[6] limonene (common in citrus and a known anti-depressant),[6-7] terpinolene (with woody aroma, slight sedative, antioxidant, anticancer and antibacterial),[8] beta-caryophyllene (gastroprotective and a strong anti-inflammatory with a woody, peppery taste),[9] α-pinene (energetic and therapeutic common in pine needles),[10] humulene (main constituent of hops, strong anti-inflammatory agent and hunger-suppressant).[11] All terpenoids are synthesized from the same five-carbon building blocks (dimethylallyl pyrophosphate and isopentenyl pyrophosphate) but their structures and functions can be manipulated to meet specific requirements.[12] These molecules have led to six major drug classes

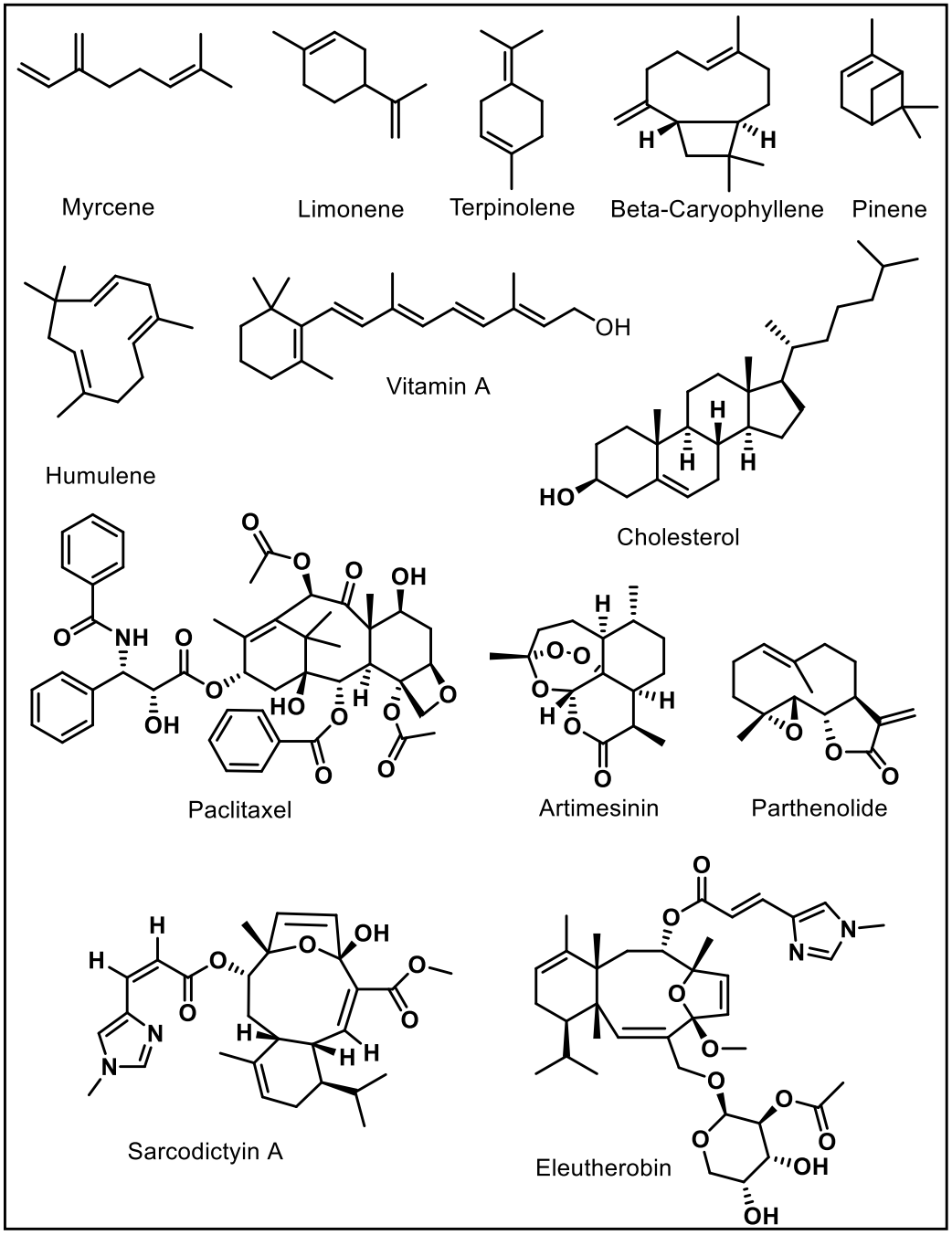


Figure 1.1: Some common examples of Terpenes.

over the last century, namely steroids, artemisinins, tocopherols, taxanes, ingenanes and cannabinoids. Some of the renowned terpene-based drugs include the anticancer drug Taxol (Paclitaxel) and the antimalarial drug Artimesinin (a sesquiterpene lactone).[13] Parthenolide,

another sesquiterpene lactone, exhibits exceptional anticancer and anti-inflammatory properties, that makes it a prominent drug candidate in development studies. Over the last 40 years, a large family of marine terpenes have also received attention for thier promising potential in medical applications. For instance, sarcodictyin A and eleutherobin from the Australian soft coral *eleutherobia sp*. and the stoloniferan coral *sarcodictyon roseum* respectively, are known to exhibit potent antitumor activity against a variety of tumor cells.[14] Thus, there is no doubt that terpenoids will play an increasingly important role in drug development in the future.

Another class of compounds that have found great utility in the medical field are the multifluorinated arenes.[15] They make up an important class of anthropogenic molecules that are highly relevant to the pharmaceutical (Figure 1.2),[16] material[17] and agrichemical industries (Figure 1.3).[18] It is a well-known fact that fluorine's electronegativity, size, imparted lipophilicity, and electrostatic interactions can influence the chemical reactivity of a compound to a great extent.[15a-c, 15e] In the pharmaceutical area, a number of fluorinated compounds with impressive activities have been successfully introduced into the market (Figure 1.2) as anti-depressants, anti-inflammatory agents, antipsychotic drugs, antimalaria compounds, antiviral agents, anaesthetics and steroids.[19] Fluorinated compounds are not only resistant to metabolic degradation, owing to the strong C–F bond (110 kcal/mol for CH_3–F) but also enhance compound lipophilicity. This may result in improved passive diffusion of compounds across membranes which can be highly desirable when synthesizing drugs.[20]

Despite of the great importance that fluorinated molecules demonstrates, methods to build these valuable molecules largely depend on just a handful of rather harsh reactions, such as the Balz-Schiemann decomposition of an aryl diazonium tetrafluoroborate salt,[21] or the high temperature (ca 230 ^{o}C) halex process.[22] This limitation has led to dependence on commercially available pre-fluorinated building blocks that can simply be incorporated into other molecules.

Almost certainly, this leads to incomplete structural activity relationships studies and understanding of fluorine's effects.

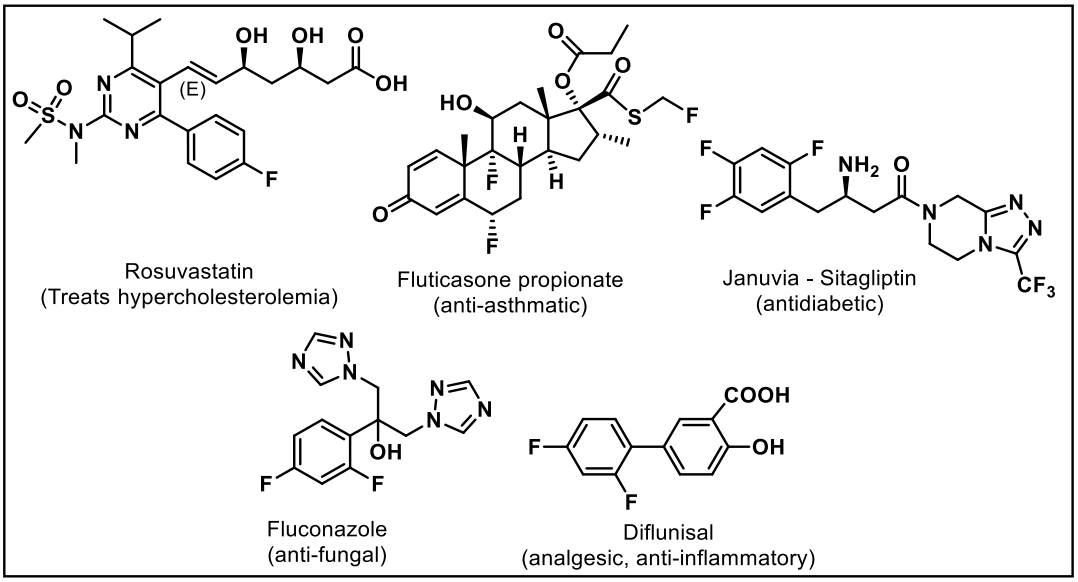


Figure 1.2: Fluorine in pharmaceutical industry

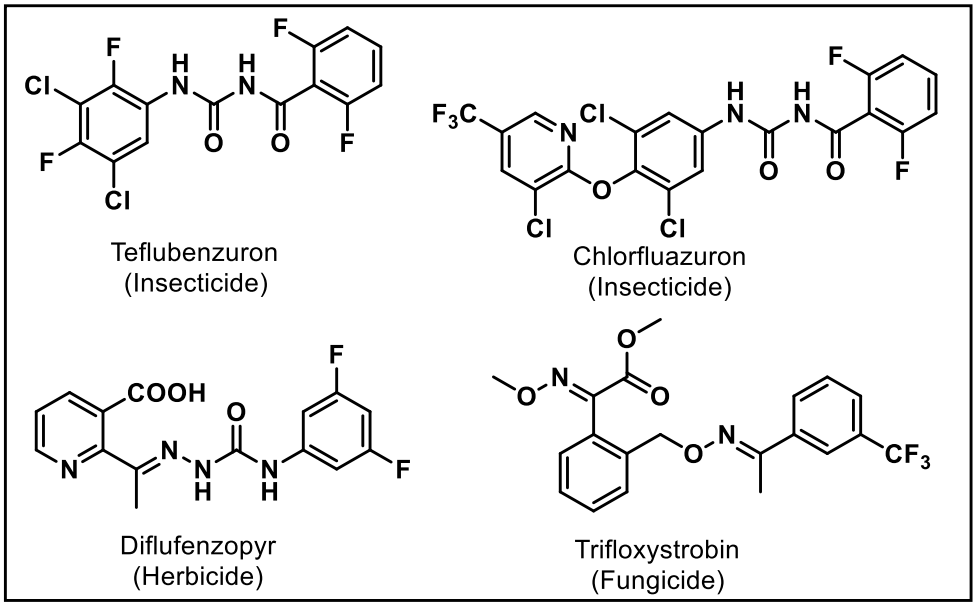
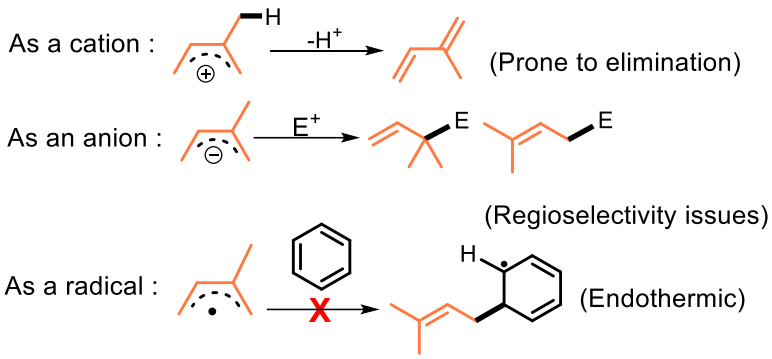


Figure 1.3: Agrochemicals containing fluorinated arenes

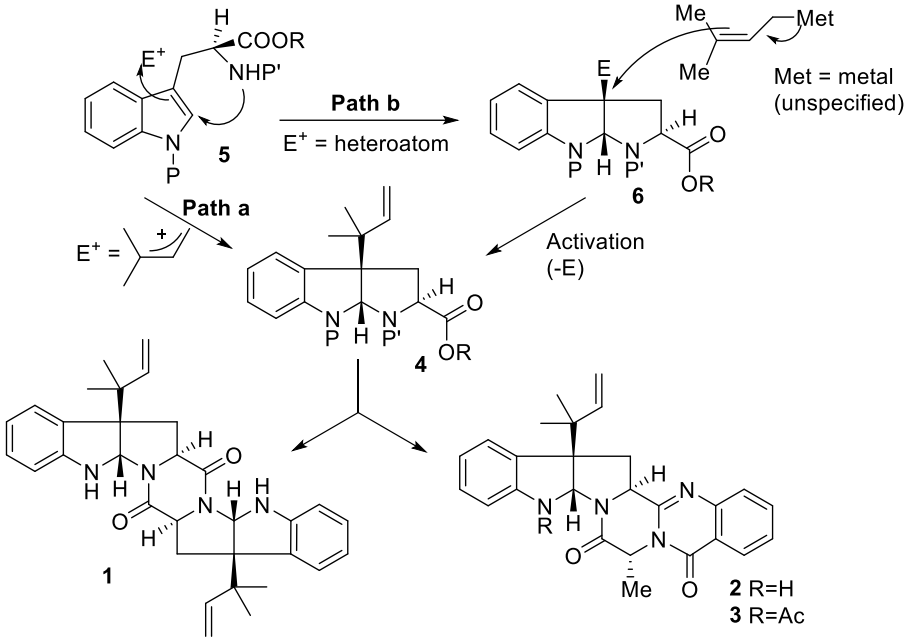
1.2 Development of photocatalytic defluoroprenylation reactions

Building on the C–F functionalization strategy put forth by Braun,[23] Richmond,[24] Uneyama[25] and many others,[26] we developed reactions that start with inexpensive highly fluorinated arenes, and obtain more complex fluorinated arenes *via* selective C–F functionalization. As a result, the complexity of the fluorinated molecules that have now become accessible far exceeds that of previously synthesized derivatives. In this vein, we were drawn to the prenyl motif due to its ubiquity in nature as well as its synthetic versatility. Accomplishing this goal would allow us to wed the natural prenyl group and the unnatural perfluoroarenes to give hybrid molecules.

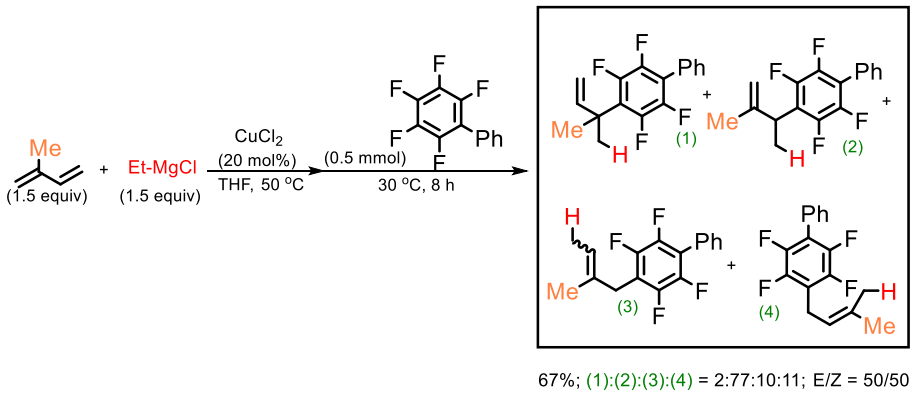
While allylation chemistry is relatively well developed, there are a number of challenges that arise while attempting prenylation (Scheme 1.1). Remarkably, this is a result of the two additional methyl groups found within the prenyl group. As electrophiles, they are prone to elimination.[27] Previously, Danishefsky and co-workers[27a] proposed a cationic prenyl species to access prenylated indole alkaloids (Scheme 1.2), but the use of this synthon in enantioselective transformations has remained undeveloped. As an anion, prenylation causes regioselectivity issues similar to that observed by Kambe.[28] He demonstrated that copper(II) chloride could facilitate the formation of a prenyl magnesiate that would then undergo uncatalyzed addition to the perfluoroarene (Scheme 1.3). The major product results from linear addition of the most stable prenyl metal species, but also gives rise to a total of 4 isomers in substantial quantities in a combined yield (67%), where the major isomer (2) resulted from the reductive coupling at the internal carbon of unsubstituted C–C double bond. Also, the use of a prenyl radical might lead to selectivity in the addition, but addition to arene would be highly endothermic.



Scheme 1.1: Challenges associated with transferring a prenyl group

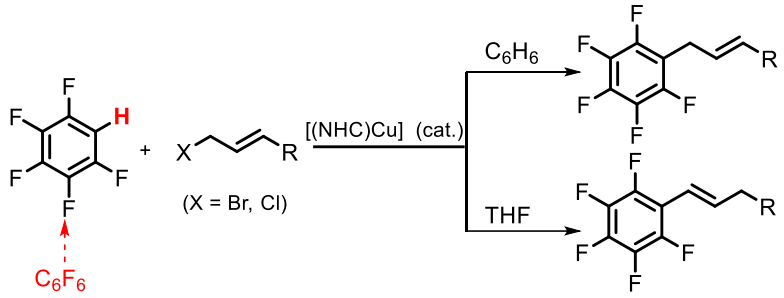


Scheme 1.2: Unfavorable 'path a' to access prenylated indole alkaloids via cationic prenyl species



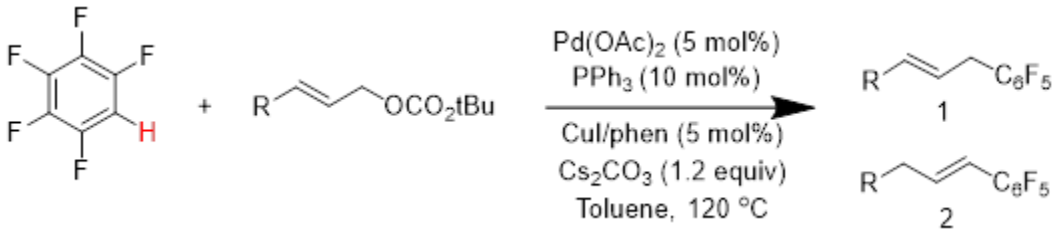
Scheme 1.3: Kambe's approach to achieve prenylation on perfluoroarenes

Several strategies have been explored to achieve related allylation on perfluoroarenes[29] via C–F functionalization both directly and indirectly. Sukbok and co-workers[29f] have shown that C–H functionalization of highly fluorinated arenes could be attained by using a Cu(NHC) catalyst, which has become increasingly relevant with recent improvements to hydrodefluorination technologies,[26b, 30] but at the very least, requires two steps (Scheme 1.4).



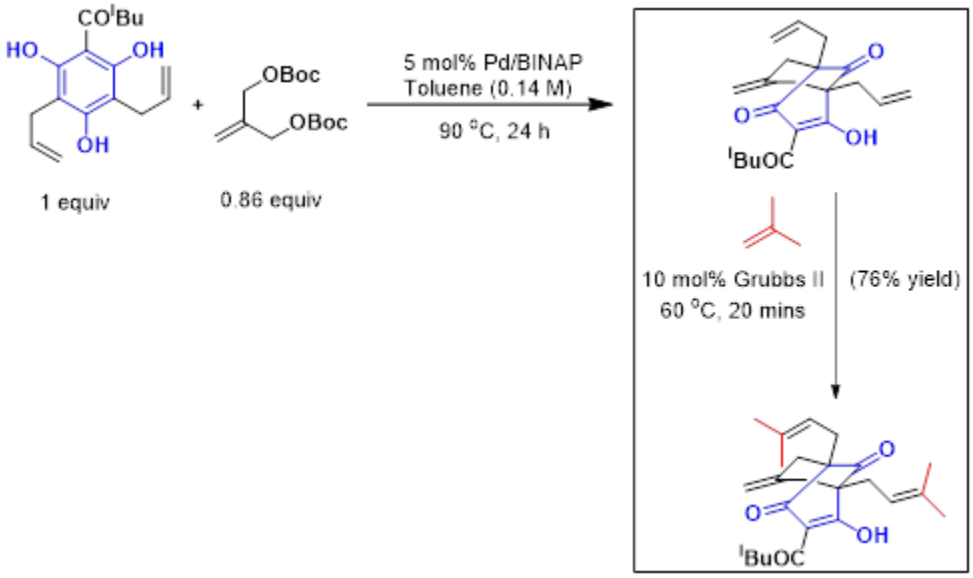
Scheme 1.4: C–H allylation of multifluoroarenes

Allylation on perfluoroarenes has also been achieved by Zhang and co-workers[29b] in 2011 (Scheme 1.5). They employed $Pd(OAc)_2$ to carry out this transformation using allyl carbonates and partially fluorinated arenes. While this was a great strategy, the reaction conditions required relatively high temperatures (over 100 ^oC) for extended periods (12 hours) and its applicability to other fluorinated arenes could only be expanded as far as hydrodefluorination was possible since it took place via C–H functionalization.



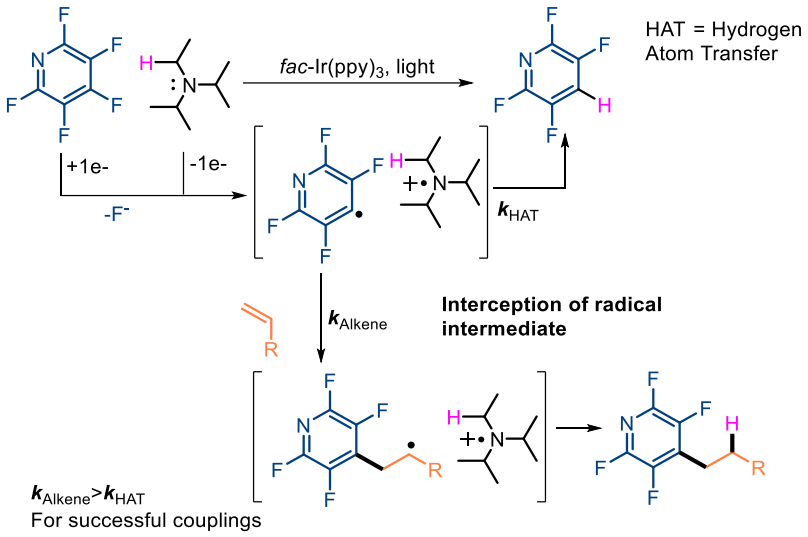
Scheme 1.5: Palladium catalyzed allylation on polyfluoroarenes using allyl carbonates

Other indirect workarounds such as allylation followed by cross-metathesis with isobutene to install the remaining geminal dimethyl group have also been employed to accomplish prenylation. For instance, Porco and co-workers[31] employed indirect allylation followed by cross-metathesis to achieve prenylation in order to access a class of polyprenylated acylphloroglucinols (Scheme 1.6).



Scheme 1.6: Indirect prenylation via cross-metathesis

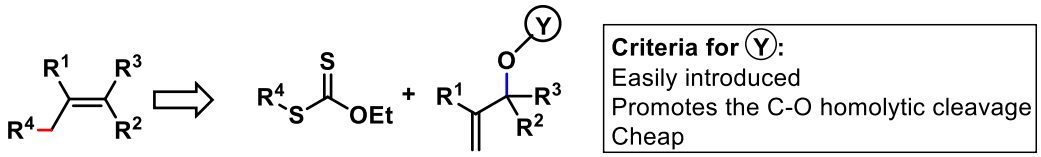
Previously, the Weaver group has shown that upon photocatalytic electron transfer to a perfluoroarene, an unstable radical anion forms, which then undergoes mesolytic cleavage to extrude a fluoride and a perfluoroaryl radical (Scheme 1.7).[30e, 32] This approach solves several challenges associated with the short, remarkably strong, and nonpolarizable C–F bond. As a result, the C–F bond is both kinetically and thermodynamically robust. Furthermore, even if the bond is broken, and fluoride is formed, fluoride often forms strong and stable metal–F bonds that can lead to poor catalyst turnover, thereby making metal-catalyzed processes difficult. Thus, it was possible to achieve hydrodefluorination on perfluoroarenes[30d] by accessing the perfluoroaryl radical generated in the reaction which could abstract a hydrogen atom from amine radical cation. Perfluoroaryl radical was also utilized to intercept with an alkene to form C–C alkylated product with the addition taking place selectively at the unsubstituted position of the alkene.[33]



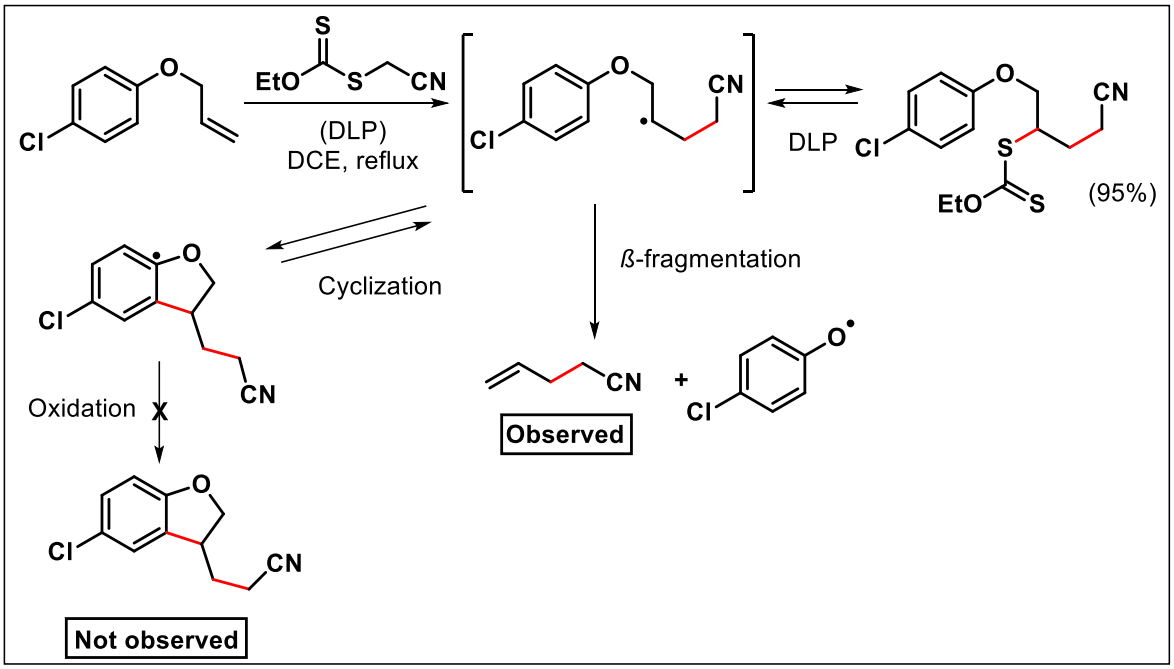
Scheme 1.7: Photocatalytic C–F functionalization of perfluoroarenes

Inspired by the work of Zard who has popularized a number of allyl radicophiles,[34] (olefins with captodative substitution[35]) we envisioned that such a reagent could be designed to facilitate photocatalytic C–F prenylation. Our hope was that this radicophile would intercept the photocatalytically generated perfluoroaryl radical to regioselectively generate the key C–C bond. The addition would result in an alkyl radical intermediate that we hoped to entice to undergo homolytic fragmentation of the ß-leaving group, unmasking the prenyl group. We anticipated that the nature of the leaving group would be key to preventing simple hydrogen atom transfer (HAT) to the radical.[32b] Zard and co-workers developed systems that could combine the use of allylic alcohol derivatives and readily available xanthates under metal-free conditions to make alkenes, aldehydes, saturated and unsaturated ketones through homolytic cleavage of the normally strong C−O or C−C bond.[34b] The activated allylic alcohol derivatives could be synthesized in two steps from aldehydes or ketones. They could also be obtained by base-induced opening of epoxides. In order to use allylic alcohols for allylation, an easily introducible appendage, (Y, Scheme 1.8), was needed that would weaken the strong C−O bond and render it prone to radical fragmentation. In an attempt to construct dihydrobenzofurans *via* a radical addition-cyclization sequence (Scheme 1.9), they observed pent-4-enenitrile instead of the expected dihydrobenzofuran. The β-

fragmentation was seen to be faster than either the reversible cyclization or the oxidation step. Apart from the gain in entropy, the driving force for β-scission could presumably be the relative weakness of the C_{alkyl}–O bond which is weakened due to the formation of a stabilized phenoxyl radical.



Scheme 1.8: Allyl alcohol as a radical allylating agent

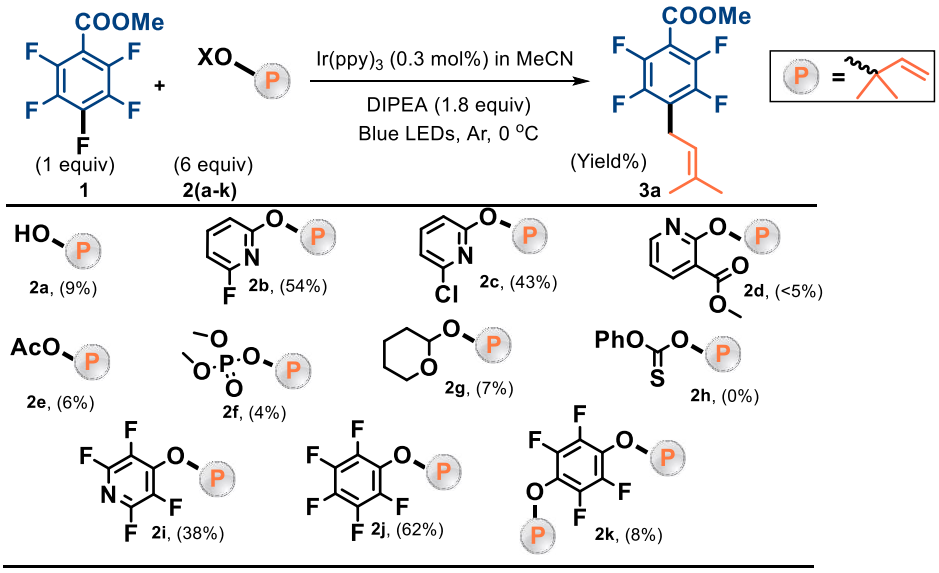


Scheme 1.9: Observation of C–O bond fragmentation

Therefore, Zard demonstrated that the C–O bond of allyl alcohol (80.1 kcal/mol BDE)[36] can be weakened by converting the hydroxy to an aryloxy group; rendering it susceptible to homolytic fragmentation.[34, 37] This stabilization is mirrored by the phenoxy radical (PhO–H BDE = 87.3 kcal/mol) which is more stable than hydroxyl radical (HO–H BDE = 119.3 kcal/mol).[38]

Thus, we began our investigation with the hope of finding a group capable of activating the C–O bond towards homolytic fragmentation (Table 1.1). As expected, reaction with isoprenyl alcohol (Figure 13, **2a**) itself simply results in hydroarylation of the alkene,[32c] highlighting the need for an activating group that can increase the rate of fragmentation. Next, we assessed the 6-halopyridine motif (**2b**, **2c**) previously explored by Zard[37] in lauroyl peroxide mediated transfer of xanthates to olefins. The pyridyl group is conveniently introduced *via* nucleophilic addition of isoprenyl alcohol to the corresponding fluoroarene. We were delighted to see the desired prenylated product (**3a**) in 54% and 43% respectively. The mass balance was primarily comprised of hydrodefluorination (HDF) as well as an oxidized version of the desired product, which was only identified by GCMS. However, reagents **2b** and **2c** both underwent competitive [3,3]-sigmatropic rearrangement, which further complicated the situation and necessitated higher reagent loading to compensate for this background reaction that effectively reduced the concentration of the prenyl transfer reagent present in solution. By blocking the ortho position with an ester group and increasing the steric demand (**2d**), we hoped to curtail both the rearrangement and the oxidation. Indeed, we halted the rearrangement, but unfortunately, this reagent did not deliver the desired prenylated product, but instead yielded only hydrodefluorination (HDF) product. This behavior is perhaps due to competitive and unproductive electron transfer to **2d** rather than the perfluoroarene.

Table 1.1: Screening of prenyl sources



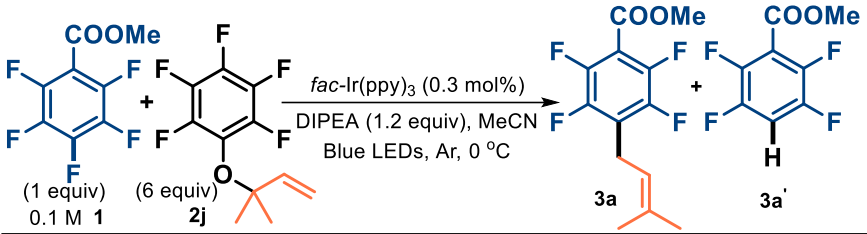
Observed: **2a** - HDF, amine addition, C-O coupling, **2b** and **2c** - HDF, oxidized prenylation, [3,3]-rearrangement, **2d** - >90% HDF, **2e** - HDF, C-O coupling, multiple side products, **2f** - mostly HDF, multiple side products, **2g** - HDF, incomplete conversion, **2h** - HDF, multiple side products, **2i** - HDF, **2j** - HDF, **2k** - HDF.

The importance of a weak C–O bond can be observed in low yields of **2e** and **2f**, which would be expected to work better if the C–O bond were to break heterolytically. However, substrates **2g** and **2h** were expected to have a weaker C–O bond and still failed to give improved yields. We next evaluated aryl ethers formed from the perfluoroarene (**2i** and **2j**). We were pleased to see that these prenyl transfer reagents afforded the desired product, with HDF as the only by-product. It is possible that the fluorines on the reagent serve to prevent rearrangement and sterically reduce the activity of the resulting aryloxy radical, potentially involved in the formation of the previously observed oxidized product. However, **2k** displayed significantly decreased activity even though it contained two prenyl groups. Given the positive results and the simple nature of **2j** we opted to use it for further reaction development.

Using conditions that had facilitated C–F reductive alkylation,[32b] using Blue LEDs we irradiated methyl pentafluorobenzoate and diisopropylethyl amine (DIPEA) as the electron source, along with 6 equiv of **2j** at 0 °C. Previously, we observed that lowering the temperature could reduce the amount of competitive HDF in the related C–F arylation reaction.[32d] We were

pleased to see that the desired C−C-coupled product was formed as the major product in decent yield, albeit along with a significant amount of HDF product (Table 1.2, entry 1). No prenylation or HDF of reagent **2j** was observed. Control studies demonstrated the necessity of light, catalyst, and amine (entry 2-3). Carrying out the reaction at lower temperature increased the reaction time with no significant improvement in **3a**:**3a'** ratio (entry 4). While decreasing the DIPEA loading slowed the reaction, increasing amine resulted in more HDF (entry 5-7); ultimately, 1.8 equivalents of DIPEA produced the optimal yield. There appeared to be a rate dependency on catalyst concentration (entries 8 and 9). Next, we investigated the effect of water on the reaction. Unexpectedly, the presence of water significantly accelerated the reaction from 18 h to less than 4 h and improved product: HDF ratio (entry 10-11). One explanation could be the increase in exothermicity of the reaction due to hydration of fluoride.[39] An alternative explanation is that water acidifies the pentafluorophenol generated in situ. By doping the reaction mixture with pentafluorophenol we observed its inhibitory effect on the reaction progress. This effect was diminished upon addition of water. An alternative explanation could involve the build up of the DIPEA derived iminium, which could competitively quench the photocatalyst. The addition of water could help consume the iminium, preventing unproductive photoquenching. Recently, Wu showed that the competitive reduction product could be minimized by the addition of TEMPO.[40] Therefore, we ran the reaction in the presence of TEMPO and found it initially helped, but ultimately slowed the reaction substantially.

Table 1.2: Optimization of reactions

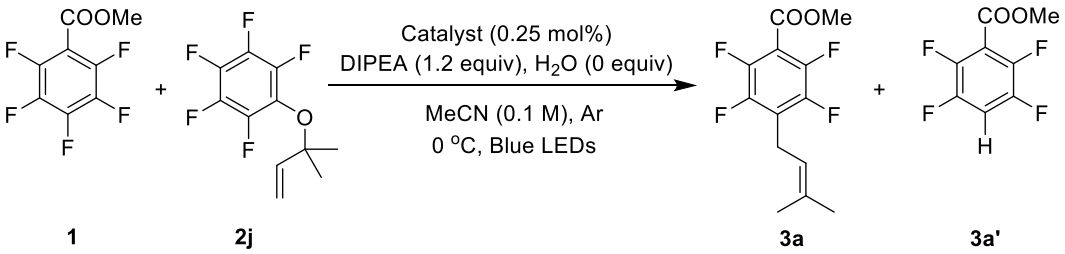


Entry	Modifications	Yield of 3a (%)[a]	3a:3a'[d]	Time (h)
1	none	31/62	1.6:1	5/17
2	no cataylst or in dark	0	na	17[b]
3	without amine	0	na	17[b]
4	-10 °C instead of 0 °C	29/64	1.7:1	5/25
5	DIPEA (1.0 equiv)	25/57	2:1	5/23[b]
6	DIPEA (1.8 equiv)	36/64	1.9:1	5/18
7	DIPEA (2.5 equiv)	38/57	1.3:1	5/15
8	0.25 mol% catalyst, DIPEA (1.8 equiv)	31/58	1.8:1	5/24
9	0.025 mol% catalyst, DIPEA (1.8 equiv)	6/28	1.6:1	5/24[b]
10	H_2O (10 equiv), DIPEA (1.8 equiv)	57/65	1.9:1	3/4
11	H_2O (15 equiv), DIPEA (1.8 equiv)	59/65	1.9:1	3/4
12	Entry 10 with 0.4 equiv TEMPO	39/68	2.1:1	4/10

[a]Determined by ^{19}F NMR analysis. Reaction complete unless otherwise noted. [b]Reaction did not go to completion over extended time, observed 0%, 0%, 83% and 44% conversion of **1** in entries 2, 3, 5 and 9 respectively. [d]Reported for the final time point.

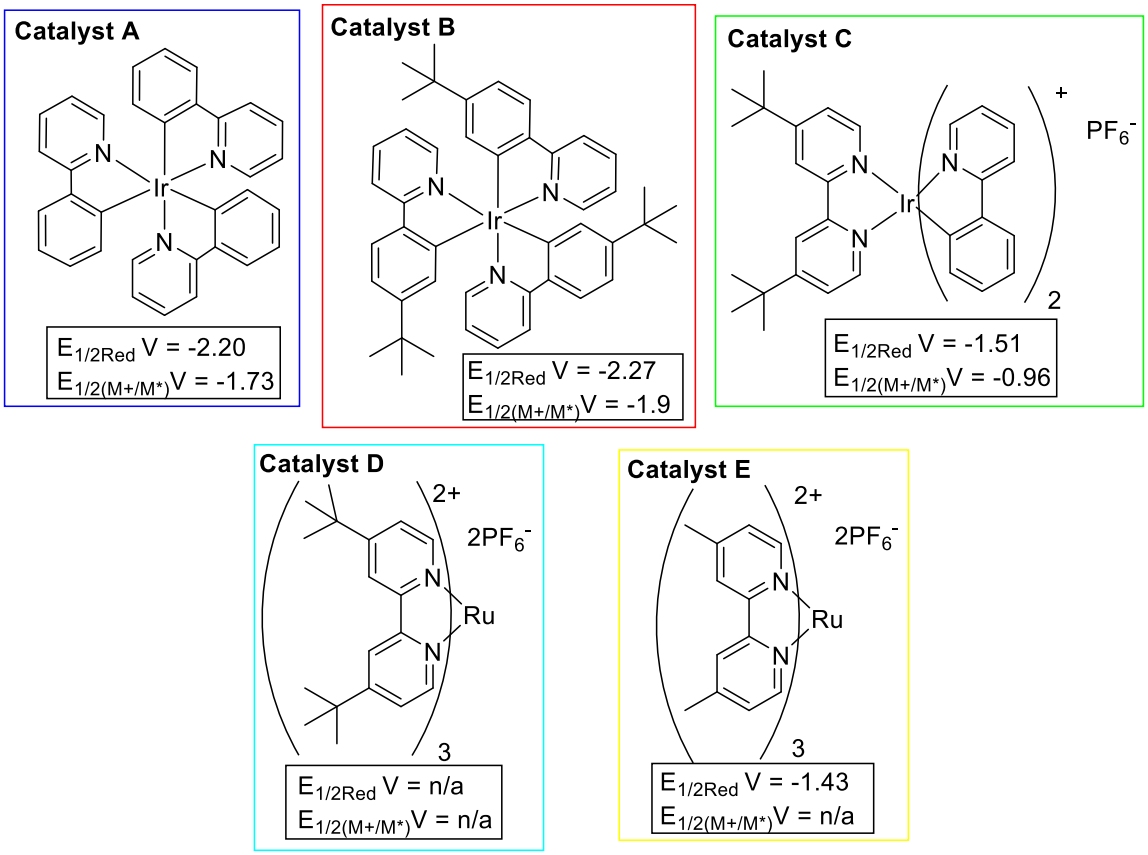
These data were summarized after a more extensive study that included variations in several parameters and careful optimizations.

Table 1.3: Optimization of Catalyst



Entry	modification	Time (h)	1	3a	3a' (% compound)
1.	no catalyst	24	100	-	-
2.	Catalyst A	21	12	58	30
3.	Catalyst B	21	15	53	32
4.	Catalyst C	24	48	29	23
5.	Catalyst D	24	72	17	11
6.	Catalyst E	24	67	20	12

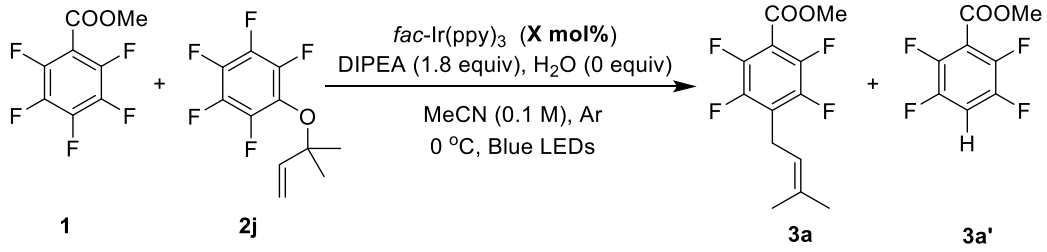
(Determined by 19F NMR)



The presence of the photocatalyst was required, as indicated by the photocatalyst control reaction (Table 1.3, entry 1), in which no conversion was observed. Catalyst A (*fac*-Ir(ppy)$_3$) produced considerable amount of prenylated product (58%) within 21 h. Catalyst B also worked well producing 53% of the desired prenylated product within 21 h, however the Pdt:HDF ratio was observed to be slightly better in case of Catalyst A. Less reducing Catalyst C also facilitated the reaction, resulting in the desired C–C coupled product, albeit at significantly diminished rates and with diminished product selectivity. Remarkably, both Catalyst D and E also facilitated

prenylation despite an anticipated substantial underpotential. The reaction in these cases was slow with no considerable progress after 24 h.

Table 1.4: Catalyst loading



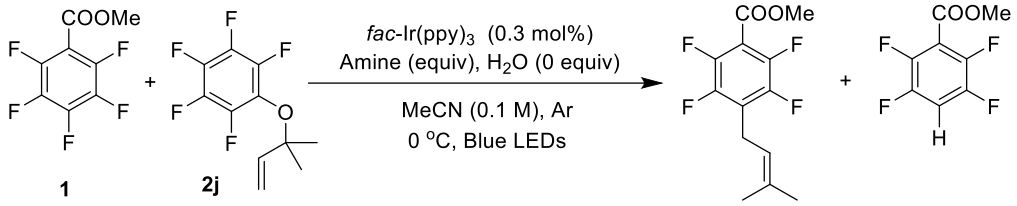
1 **2j** **3a** **3a'**

Entry	X mol%	Time	1	3a	3a'
1.	0.3	18 h	8	61	31
2.	0.25	5 h	46	35	19
		20 h	12	58	30
3.	0.20	20 h	26	41	33
4.	0.10	20 h	38	32	30
5.	0.05	20 h	46	25	39
6.	0.025	5 h	90	4.2	5.5
		20 h	54	17	28
7.	0.0125	20 h	68	12	19
8.	0.25, 10 equiv H_2O	8 h	Trace	64	35
9.	0.025, 10 equiv H_2O	2.5 d	51	30.7	18

(% compound)
(Determined by ^{19}F NMR)

The catalyst loading experiments clearly demonstrated the rate dependency on the concentration of the catalyst. Higher concentrations of the catalyst (Table 1.4, entry 1, 2) produced the fastest reactions with good conversions within 20 h. The rate of reaction significantly dropped with a decrease in concentration of the catalyst. Interestingly, while water seems to accelerate the reaction at 0.25 mol%, this acceleration is reduced at much lower catalyst loadings (compare entries 2 & 8 to 6 & 9). This might be explained by a trace impurity in the reaction mixture that effectively quenches the photocatalyst when it too is present only in very trace amounts.

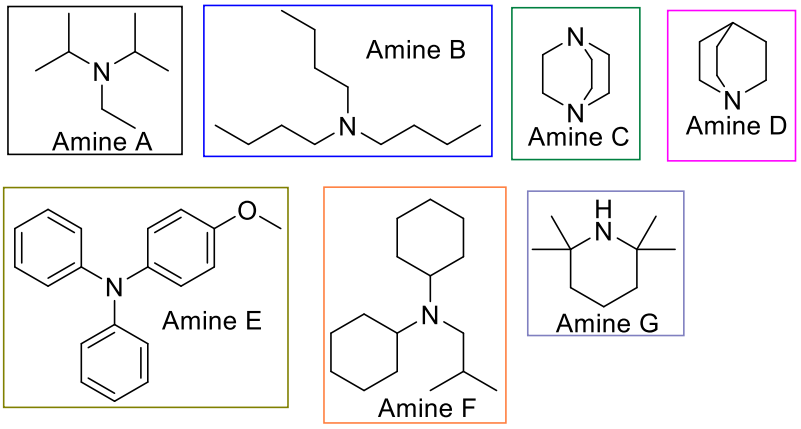
Table 1.5 : Optimization of Amine



(Determined by 19F NMR)

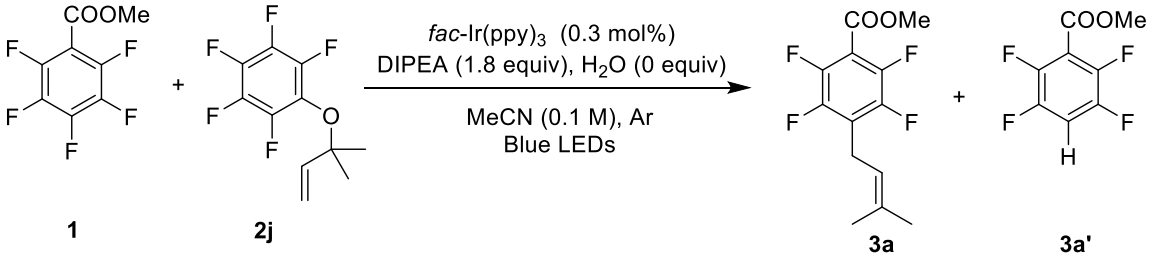
Entry	Amine	Time	1	3a	3a'
1.	Amine A, 1.2 equiv	18 h	8	61	30
2.	Amine A, 1.8 equiv	18 h	2	64	33
3.	Amine A, 2.5 equiv	18 h	-	57	44
4.	Amine B, 1.8 equiv	18 h	17	44	37
5.	Amine C, 1.8 equiv	18 h	100	-	-
6.	Amine C, 1.8 equiv, rt instead of 0 °C	18 h	100	-	-
7.	Amine D, 2.5 equiv, rt instead of 0 °C	18 h	100	-	-
8.	Amine E, 2.5 equiv, rt instead of 0 °C	18 h	100	-	-
9.	Amine F, 2.5 equiv	18 h	95	2	3
10.	Amine F, 2.5 equiv, rt instead of 0 °C	18 h	81	8	11
11.	Amine G, 2.5 equiv, rt instead of 0 °C	18 h	100	-	-

(% compound)



Amine A (DIPEA) produced prenylated products in moderate to high yields in 18 h (Table 1.5, entry 1-3). Increasing amine concentration to 1.8 equiv produced better conversion as compared to 1.2 equiv. When the amine concentration was further increased to 2.5 equiv, it resulted in complete consumption of starting material within 18 h but it also produced more of HDF side-product. Therefore, 1.8 equiv DIPEA was chosen to be the best condition. Amine B (entry 4) was also able to form desired prenylated product but in slightly lower yield. Switching the amine to Amines C-E (entry 5-8) did not result in any product formation even when the reaction was warmed to room temperature (27 ^{o}C) instead of running at 0 ^{o}C. Compared to Amine A, Amine F gave lower conversion of the starting material at 0 ^{o}C, as well as at room temperature (entry 9, 10) probably because of its lower solubility. Amine G did not result in any conversion.

Table 1.6: Temperature Screening



1 2j 3a 3a'

Entry	Temperature (^{0}C)	Time	1	3a	3a'	Other
1.[a]	-10	24 h	19	55	26	
2.	0	18 h	3	63	34	
3.	25	16 h	-	55	36	8
4.	45	12 h	-	32	47	21

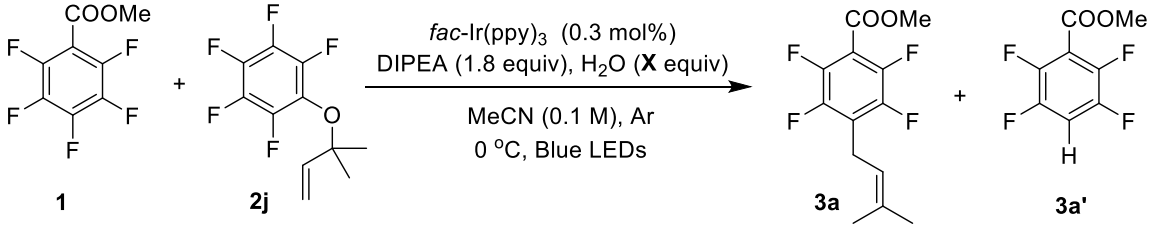
[a]Reaction produced more HDF over extended time.
(Determined by 19F NMR)

Temperature screening revealed yet another important parameter that greatly affected the rate of reactions (Table 1.6). Reaction at -10 ^{o}C was slow, resulting in 55% prenylated product in 24 h. Carrying out the reaction at 0 ^{o}C produced 63% of product with reasonable Pdt:HDF ratio. As expected, at higher temperature the rate increased (entries 3-4). Though the starting material was

fully consumed within 16 h (and 12 h), warmer temperatures always produced relatively more HDF, in addition to another minor side product. Entry 2 was chosen to be the optimal temperature which produced the cleanest reaction within a reasonable time frame.

The inclusion of water also played a very important role in improving the reaction rate significantly (Table 1.7). The presence of 5 equiv of H_2O in the reaction mixture caused the reaction to complete in 8 h, as compared to 18 h when the reaction was carried out in the absence of water. As the amount of water was increased to 10 equiv (entry 3), the reaction completed within 4 h. One plausible explanation could be that the pentafluorophenol (by-product that develops during the course of reaction) produces an inhibitory effect under anhydrous reaction conditions.

Table 1.7: Effect of Water



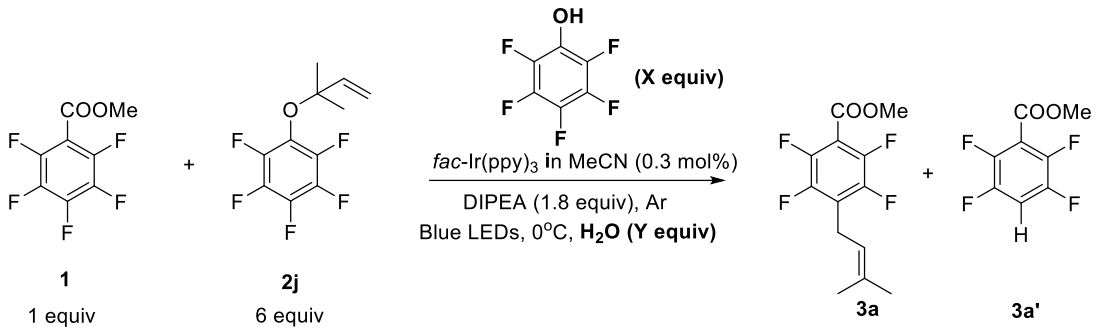
Entry	Equiv of H_2O	Time	1	3a	3a'
1.	0	4 h	79	13	8
		18 h	-	63	36
2.	5	4 h	18	54	28
		8 h	-	63	35
3.	10	4 h	-	65	34
4.	20	4 h	-	65	35

By running an experiment in which pentafluorophenol was intentionally added at the beginning of the reaction, the reaction was retarded (Table 1.8). Upon addition of 10 equiv of H_2O the rate was restored. Furthermore, upon addition of water an improvement can be seen from

1.44:1 (product:HDF) in the absence of H_2O, to 1.8:1 when 10 equivalents H_2O was present (entry 3). For comparison, the Pdt:HDF ratio under the standard conditions is 1.9:1.

One potential explanation is that the water acidifies pentafluorophenol facilitating deprotonation and ionization by DIPEA in the reaction, effectively removing phenol-OH by converting it to phenoxide. We suspect phenol may serve as an HAT shuttle which can facilitate HDF and can generate a problematic persistent radical, which may inhibit catalytic turnover.

Table 1.8: Experiments investigating the inhibitory effect of pentafluorophenol

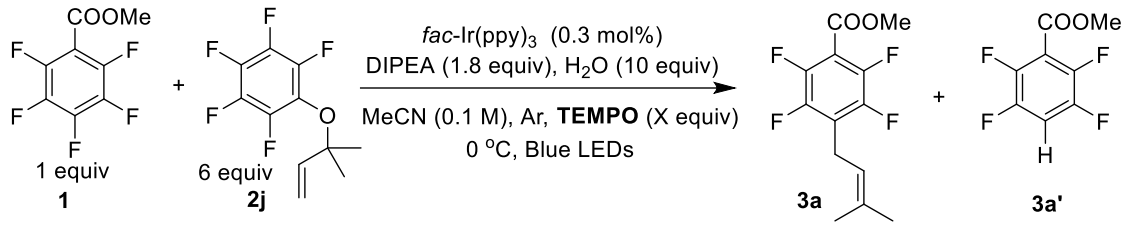


Entry	X equiv	Y equiv	Time	1	3a	3a'	3a:3a'	Other
1.	0.5	0	4 h	71	17	11	1.54:1	
			10 h	66	20	14	1.42:1	
2.	1.0	0	4 h	17	40	29	1.4:1	at least 2 more pdts
			10 h	3	55	38	**1.44:1**	+2 more pdts
3.	1.0	10	4 h	-	47	26	**1.8:1**	+ 2 side pdts

We further tested the possibility of using TEMPO to minimize the formation of the competitive reduction product.[40] TEMPO had a significant effect on the progress of the reaction (Table 1.9). TEMPO could abstract an H-atom from the amine radical cation formed during the reaction forcing the aryl radical to react with the prenyl source. The Pdt:HDF ratio (**3a**:**3a'**) was seen to improve during the initial time points. But as the reaction progressed, the Pdt:HDF ratio eventually returned to almost the same as observed using standard reaction conditions. Also, the presence of TEMPO slowed the overall progress of reaction (from 4 h to 10 h when 0.4 equiv was

used) and increasing the amount of TEMPO more further decreased the rate of reaction, thus causing incomplete conversion of **1a** over extended time possibly due to quenching of the necessary aryl radical intermediate.

Table 1.9: Effect of TEMPO on the rate and selectivity of the reaction



1) 0 equiv TEMPO

Time	1	3a'	3a	3a:3a'
2 h	27%	24%	49%	2.04:1
4 h	-	34%	66%	1.9:1
				(Standard)

2) 0.4 equiv TEMPO

Time	1	3a'	3a	3a:3a'
2 h	86%	4.2%	9.6%	2.25:1
4 h	43%	17%	39%	2.21:1
7 h	23%	24%	52%	2.16:1
10 h	-	32%	68%	2.1:1

3) 1.0 equiv TEMPO

Time	1	3a'	3a	3a:3a'
2 h	94%	1.6%	4.4%	2.75:1
4 h	68%	9%	23%	2.55:1
7 h	41%	16%	42%	2.6:1
10 h	13%	27%	59%	2.2:1
15 h	11%	29%	60%	2.06:1

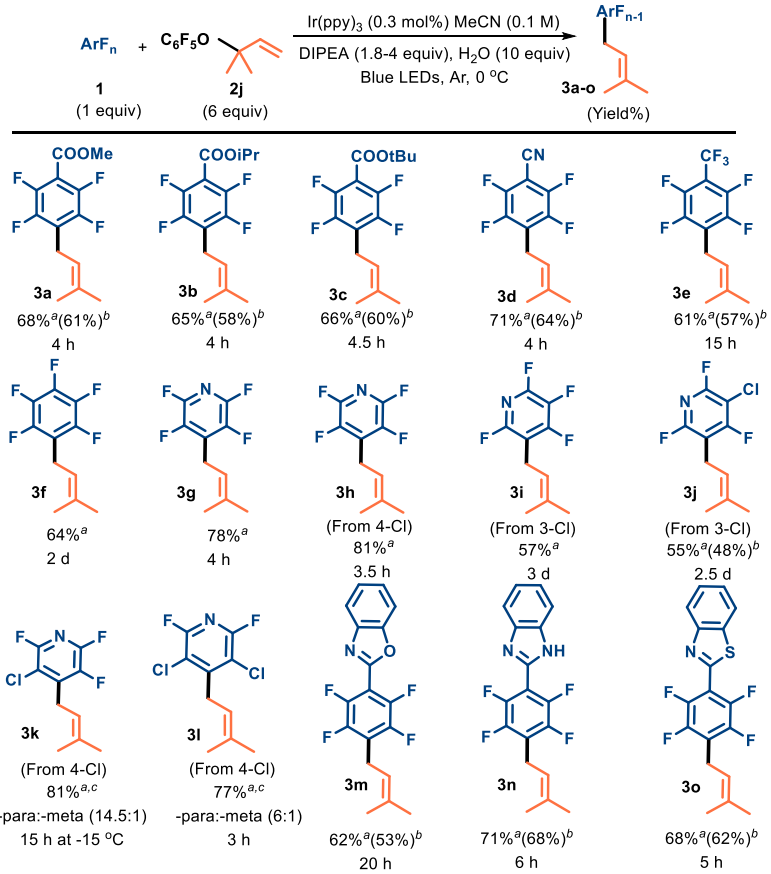
4) 1.5 equiv TEMPO

Time	1	3a'	3a	3a:3a'
2 h	97%	0.8%	2.2%	2.75:1
4 h	91%	2.4%	6.6%	2.71:1
7 h	83%	4.6%	12.4%	2.69:1
10 h	79%	6%	15%	2.5:1
15 h	77%	7.5%	15.6%	2.1:1

Ultimately, using 0.1 M of substrate, 1.8 equiv of DIPEA, 0.3 mol% of *fac*-Ir(ppy)$_3$ and 10 equiv of H_2O, we began evaluating substrate scope. Under these conditions a number of perfluoroarenes smoothly underwent C–F defluoroprenylation in good to modest yields. The reaction tolerates a number of functional groups including esters (Table 1.10, **3a**-**3c**), nitriles (**3d**), CF_3 (**3e**), and perfluoroheterocyclic arenes (**3g**). Hexafluorobenzene, devoid of any additional electron-withdrawing functional group also proceeded to form **3f**, though it required the use of 6-halopyridyl prenyl source **2b** as the prenyl source. Specifically, in the presence of prenyl transfer reagent **2j**, hexafluorobenzene remained unchanged. **3h-l** are noteworthy as they demonstrate the preference for chlorine fragmentation over that of fluorine despite the position on the ring. Given

that many chlorofluoro-starting materials are commercially available, it provides a convenient strategy for accessing complementary regioisomers. When a chlorine was placed at the site of preferential fluorine fragmentation (4 position for pyridine), it displayed moderately shorter reaction time compared to pentafluoropyridine (i.e. **3h** compared to **3g**). This could be because fragmentation of chloride ion is more exothermic than fluoride, resulting in a faster fragmentation event. Furthermore, the presence of chlorine substituents create greater steric demand than fluorine substituents, and could result in a relative increase the ground state energy.[41] Likewise, steric repulsion between the substituents in the radical anion may also accelerate its breakdown, leading to faster fragmentation. Interestingly, prenylation at the meta position was also possible but required longer reaction time (**3i** and **3j** vs **3g**).

Table 1.10: Scope of Prenylation

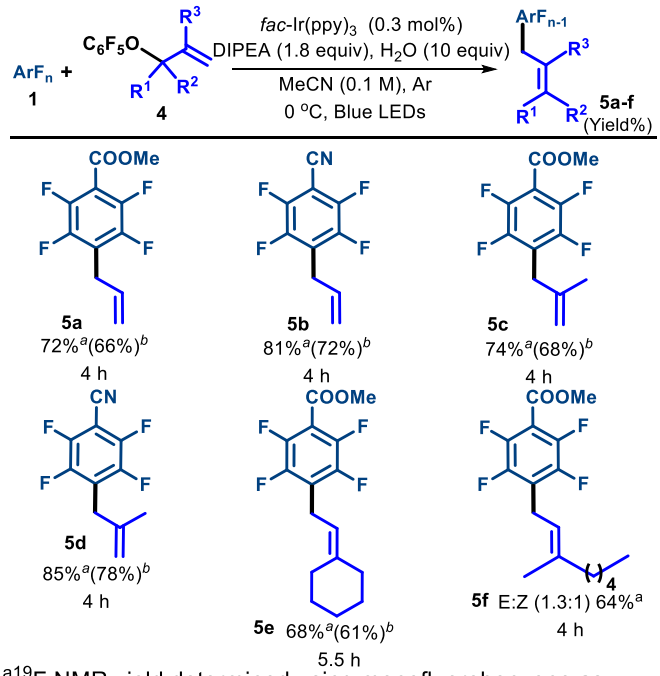


a19F NMR yield determined using monofluorobenzene as internal standard. bIsolated yield. cComprises of both products.

While the photocatalytically enduced mesolytic fragmentation of fluoride has been highly resgioselective, the fragmentation of chloride from multichlorinated arenes is generally less regioselective and displays a temperature dependent behavior (**3g** *vs* **3k** and **3l**), but still results in useful selectivities. This method can be used to access heterocyclic substituted perfluoroarenes like oxazoles (**3m**), benzoimidazoles (**3n**) and benzothiazoles (**3o**). In all these reactions, HDF made up the mass balance.

Looking to expand the utility of the method, we applied this strategy towards allylation of perfluoroarenes. As expected, allylation with transposition of the double bond proceeded smoothly to yield **5a-5f** in good yield (Table 1.11). Substitution at both the ß-position (**5c** and **5d**), and the γ-position were well tolerated (**5e** and **5f**). While the yield was acceptable, in the case of unsymmetric **5f**, the E/Z-selectivity was very modest (1.3:1) and did not display significant temperature dependence, which may limit its use in cases where the olefin geometry is essential.

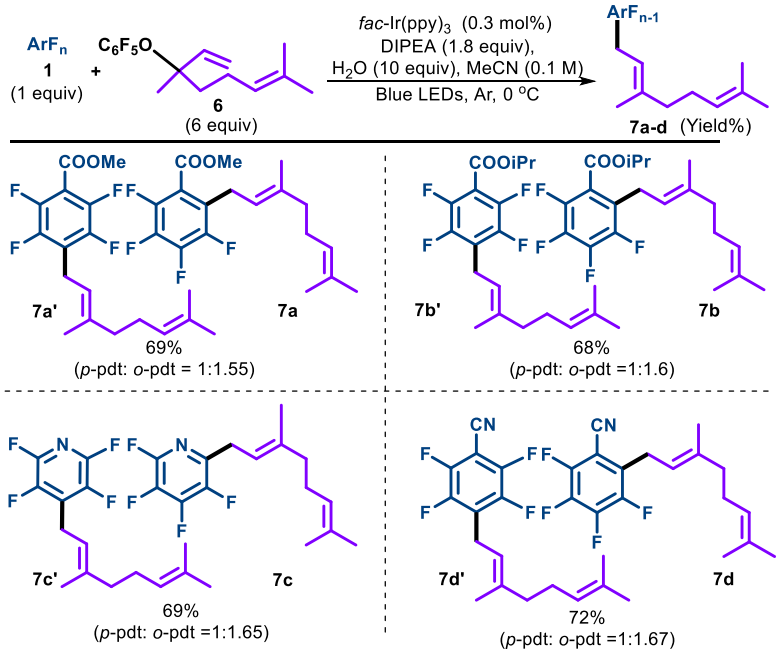
Table 1.11: Scope of Allylation



[a]^{19}F NMR yield determined using monofluorobenzene as internal standard. [b]Isolated yield.

Encouraged by our success with prenyl transfer, we hoped to extend our strategy to geranyl transfer which would add a 10 carbon unit. Using the same optimized conditions, we reacted perfluoroarenes with pentafluoroisogeranyl ether (**6**, Table 1.12). We were concerned that the alkyl radical formed upon addition to the alkene would undergo intramolecular addition to the additional olefin (i.e. 5-exo-trig cyclization) faster than fragmentation of the pentafluorophenoxy radical. Thus, we were pleased to obtain the geranylated product in similar yields to the prenylation reaction. A striking difference, however, was that the reaction took place preferentially at the position ortho to the substituent on the perfluoroaryl ring (c.a. ortho: para 1.6:1). This is particularly noteworthy as it is the first time that we have observed an external reagent capable of influencing the C–F regioselectivity in a photocatalytic C–F functionalization. While we are uncertain about the underlying cause of this change in regioselectivity, our working hypothesis is that there is an attractive interaction between **6** and the radical anion of **1**. This results in an intermolecular complex which sterically perturbs the ortho C–F bond, presumably causing deviation from planarity, and resulting in a faster fragmentation.

Table 1.12: Scope of Geranylation



Determined by ^{19}F NMR. Reactions completed in 6-8 h.

While, **7a**-**7d** were produced as a mixture of ortho-para isomers, it demonstrated perfect diastereoselectivity, giving only the *E*-alkene. This selectivity is in stark contrast to the unsymmetric allyl derivative, **5f**, which was produced as a mixture. Again, the origin of this is not clear.

1.3 Summary

In conclusion, we have developed a strategy and along with reagents that enable photocatalytic defluoro-allylation, -prenylation, and -geranylation of perfluoroarenes. We observed that the addition of water leads to substantial rate enhancements. Further, as we moved from prenylation to geranylation, we observed a change in the regioselectivity of the major product from para-C–F functionalization to ortho-C–F functionalization. Our approach allows direct allyl, prenyl and geranyl substitution of C–F bonds using very mild conditions and short reaction times. This strategy should facilitate investigations involving the synthesis of hybrid fluorinated analogs of natural products. Additionally, this reaction presents a number of interesting mechanistic facets which are currently being studied, and the findings will be reported in due course.

1.4 Experimental Section

General Experimental

All reagents were obtained from commercial suppliers (Sigma-Aldrich, Oakwood chemicals, Alfa Aesar, Matrix Scientific) and used without further purification unless otherwise noted. Acetonitrile (CH_3CN) was dried over molecular sieves. *N*,*N*-diisopropylethylamine was purchased from Sigma-Aldrich and stored over KOH pellets. Photocatalyst tris(2-phenyl pyridinato-C2, N)iridium(III)[$Ir(ppy)_3$], 99%(purity), was synthesized according to a literature procedure.[32c] Photocatalyst tris[4,4'-bis(*tert*-butyl)-2,2'-bipyridine]ruthenium(II) hexafluorophosphate and tris(4,4'-dimethyl-2,2'-bipyridine)ruthenium(II) hexafluorophosphate

were purchased from Aspira Chemical. Isopropyl 2,3,4,5,6-pentafluorobenzoate, *tert*-butyl 2,3,4,5,6-pentafluorobenzoate, 4-chloro-2,3,5,6-tetrafluoropyridine, 3,4-dichloro-2,5,6-trifluoropyridine, 3,4,5-trichloro-2,6-difluoropyridine, 2-(perfluorophenyl)benzo[*d*]oxazole, 2-(perfluorophenyl)-1*H*-benzo[d]imidazole and 2-(perfluorophenyl)benzo[*d*]thiazole were synthesized according to literature procedures.[30d, 42] Reactions were monitored by ^{19}F and GC-MS (QP 2010S, Shimadzu equipped with auto sampler). NMR spectra were obtained on a 400 MHz Bruker Avance III spectrometer and 400 MHz Unity Inova spectrometer. ^{1}H and ^{13}C NMR chemical shifts are reported in ppm relative to the residual protio solvent peak (^{1}H, ^{13}C) and ^{19}F NMR shifts are reported using fluorobenzene as a standard. Melting points were determined on a Mel-Temp apparatus and are uncorrected. GC analyses were carried out using a QP 2010S Shimadzu, equipped with an auto sampler. Isolations were carried out using a Teledyne Isco Combiflash Rf 200i flash chromatograph with Sorbtech Rf normal phase silica (4 g, or 12 g columns). Some isolations were performed using Sorbent Technologies Silica Prep TLC Plates, w/UV254, glass backed, 1000 μm, 20 x 20 cm, and were visualized with ultraviolet light. Substrate syntheses were monitored by thin layer chromatography (TLC) obtained from Sorbent Technologies; Silica XHL TLC Plates, w/UV254, glass backed, 250 μm, and were visualized with ultraviolet light or potassium permanganate. No attempts were made to report ^{13}C spectra of volatile compounds.

Photocatalytic Reaction Set up

Photocatalytic reactions were set up in a light bath as described below. Strips of blue LEDs (18 LEDs/ft.) were purchased from Solid Apollo. The strips (4.9 ft) were wrapped around on the walls of a glass crystallization dish, secured with masking tape and then the dish was wrapped with aluminum foil. A lid which rest on the top was fashioned from cardboard and holes were made such that NMR tubes were held firmly in the cardboard lid which was placed on the top of the bath. Isopropanol/water bath was prepared such that the tubes were submerged, and it was

maintained at 0 °C with the aid of a chiller that circulated coolant through a coil of copper tubing placed in the bath. In some cases, the same light bath set up was used with water in it which was maintained at 45 °C with the aid of a sand bath connected to a thermostat.[30d]

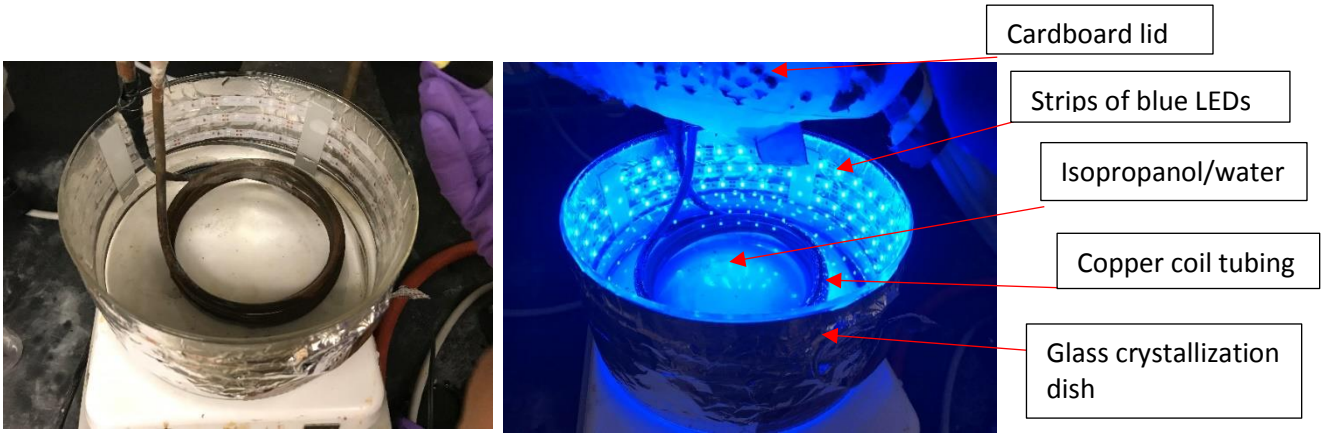


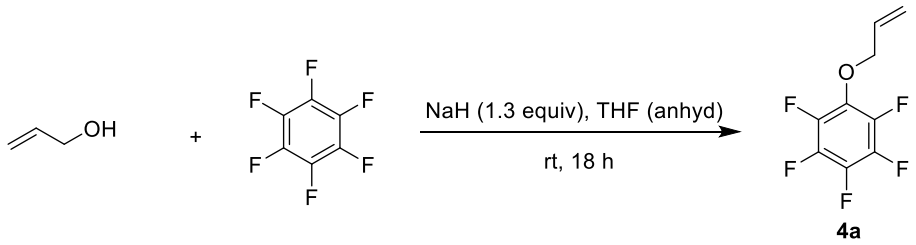
Figure 1.4: Photocatalytic reaction set up using light bath

Synthesis of Substrates

General Procedure A for synthesis of aryl ethers:

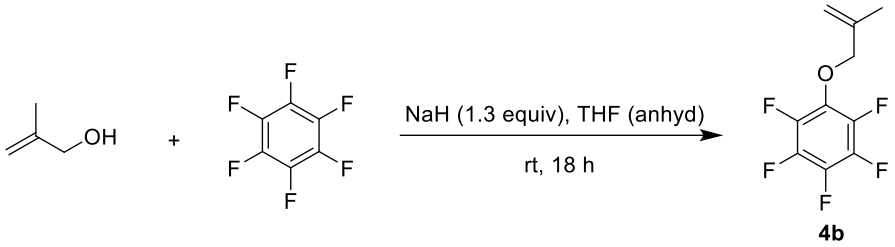
To a stirred solution of alcohol (1.0 equiv) in THF (anhyd) in a flame-dried 250 mL round-bottomed flask, was added NaH (1.3 equiv) portion wise under Ar. The resulting mixture was stirred for 20 minutes at room temperature. Hexafluorobenzene (1.3-4.0 equiv) was then added all at once and the reaction was monitored by TLC until the spot for alcohol disappeared. After completion, the reaction mixture was slowly quenched with water. The aqueous phase was extracted with diethyl ether, and the combined organic extracts were washed with brine (3 x 30 mL), dried over $MgSO_4$, filtered and concentrated in *vacuo*. The crude material was purified by normal phase chromatography using hexane:ethyl acetate.[43]

Synthesis of 1-(allyloxy)-2,3,4,5,6-pentafluorobenzene (4a)



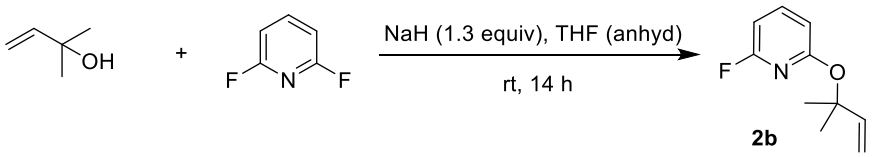
1-(Allyloxy)-2,3,4,5,6-pentafluorobenzene (4a) was synthesized using **general procedure A**. 2-Propen-1-ol (3.51 mL, 51.6 mmol), NaH (1.61 g, 66.6 mmol) was stirred in anhyd. THF (30 mL) at room temperature for 20 minutes. Then hexafluorobenzene (7 mL, 66.6 mmol) was added and stirred for 18 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0 % EtOAc for 0-15 cv and ramped to 50 % EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 85% yield (9.8 g, 43.8 mmol) as a colorless liquid.

Synthesis of 1,2,3,4,5-pentafluoro-6-((2-methylallyl)oxy)benzene (4b)



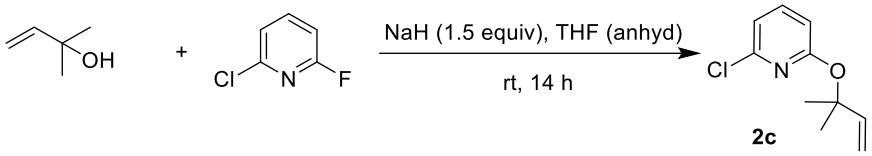
1,2,3,4,5-Pentafluoro-6-((2-methylallyl)oxy)benzene (4b) was synthesized using **general procedure A**. 2-Methylprop-2-en-1-ol (3.51 mL, 41.6 mmol), NaH (1.29 g, 54.1 mmol) was stirred in anhyd. THF (30 mL) at room temperature for 20 minutes. Then hexafluorobenzene (6.24 mL, 54.1 mmol) was added and stirred for 18 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 86% yield (8.52 g, 35.77 mmol) as a colorless liquid.

Synthesis of 2-fluoro-6-((2-methylbut-3-en-2-yl)oxy)pyridine (2b)



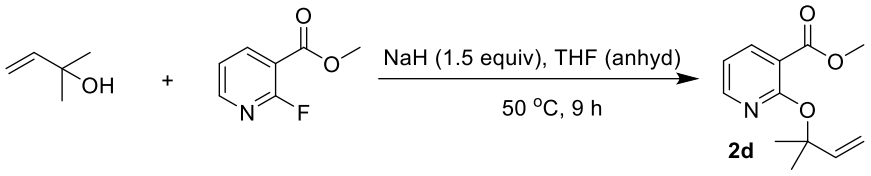
2-Fluoro-6-((2-methylbut-3-en-2-yl)oxy)pyridine (2b) was synthesized using a modified version of **general procedure A**. 2-Methylbut-3-en-2-ol (3 mL, 28.7 mmol), NaH (0.908 g, 37.7 mmol) was stirred in anhyd. THF (35 mL) at room temperature for 20 minutes. Then, 2,6-difluoropyridine (3.12 mL, 34.4 mmol) (rather than C_6F_6) was added and stirred for 14 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 88% yield (4.57 g, 25.26 mmol) as a colorless liquid.

Synthesis of 2-chloro-6-((2-methylbut-3-en-2-yl)oxy)pyridine (2c)



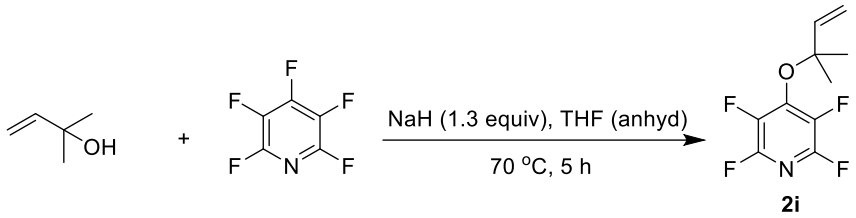
2-Chloro-6-((2-methylbut-3-en-2-yl)oxy)pyridine (2c) was synthesized using a modified version of **general procedure A**. 2-Methylbut-3-en-2-ol (2 mL, 19 mmol), NaH (0.684 g, 28.5 mmol) was stirred in anhyd THF (35 mL) at room temperature for 20 minutes. Then 2-chloro-6-fluoropyridine (3 g, 22.8 mmol) (rather than C_6F_6) was added and stirred for 14 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 87% yield (3.25 g, 16.53 mmol) as a colorless liquid.

Synthesis of methyl 2-((2-methylbut-3-en-2-yl)oxy)nicotinate (2d)



Methyl 2-((2-methylbut-3-en-2-yl)oxy)nicotinate (2d) was synthesized using a modified version of **general procedure A**. 2-methylbut-3-en-2-ol (1.7 mL, 16.11 mmol), NaH (0.58 g, 24.16 mmol) was stirred in anhyd THF (35 mL) at room temperature for 20 minutes. Then methyl 2-fluoronicotinate (3 g, 19.33 mmol) (rather than C_6F_6) was added, heated at 50 °C and stirred for 9 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 44% yield (1.568 g, 7.088 mmol) as a colorless liquid.

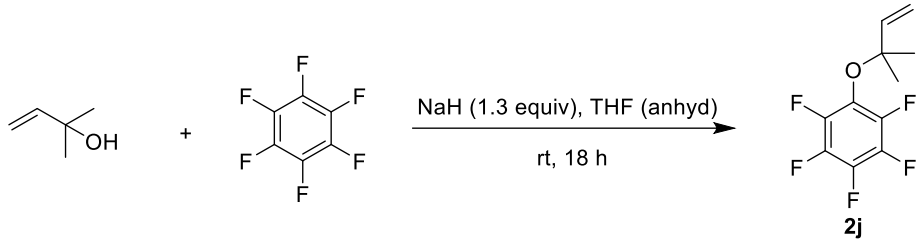
Synthesis of 2,3,5,6-tetrafluoro-4-((2-methylbut-3-en-2-yl)oxy)pyridine (2i)



2,3,5,6-Tetrafluoro-4-((2-methylbut-3-en-2-yl)oxy)pyridine (2i) was synthesized using a modified version of **general procedure A**. 2-methylbut-3-en-2-ol (3 mL, 28.7 mmol), NaH (0.91 g, 37.31 mmol) was stirred in anhyd THF (40 mL) at room temperature for 20 minutes. Then pentafluoropyridine (3.8 mL, 34.44 mmol) (rather than C_6F_6) was added, heated at 70 °C and stirred for 5 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then

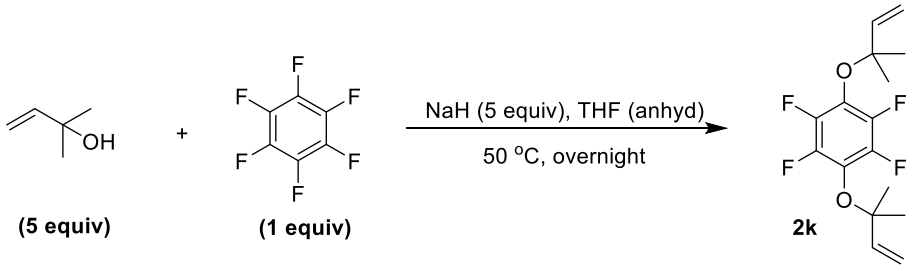
held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 35% yield (2.362 g, 10.04 mmol) as a colorless liquid.

Synthesis of 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (2j)



1,2,3,4,5-Pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (2j) was synthesized using **general procedure A**. 2-Methylbut-3-en-2-ol (5.2 mL, 49.44 mmol), NaH (1.54 g, 64.2 mmol) was stirred in anhyd. THF (40 mL) at room temperature for 20 minutes. Then hexafluorobenzene (8 mL, 69.2 mmol) was added and stirred for 18 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 83% yield (10.3 g, 41.03 mmol) as a colorless liquid.

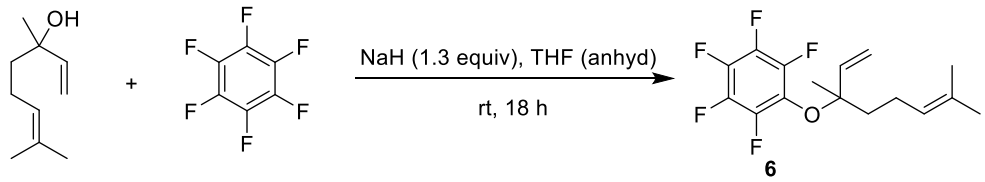
Synthesis of 1,2,4,5-tetrafluoro-3,6-bis((2-methylbut-3-en-2-yl)oxy)benzene (2k)



1,2,4,5-Tetrafluoro-3,6-bis((2-methylbut-3-en-2-yl)oxy)benzene (2k) was synthesized using a modified version of **general procedure A**. 2-Methylbut-3-en-2-ol (5.6 mL, 53.7 mmol), NaH (1.28 g, 53.7 mmol) was stirred in anhyd. THF (40 mL) at room temperature for 20 minutes. Then hexafluorobenzene (1.24 mL, 10.7 mmol) was added and stirred at 50 °C overnight. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc

for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 51% yield (1.74 g, 5.45 mmol) as a colorless liquid.

Synthesis of 1-((3,7-dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (6)



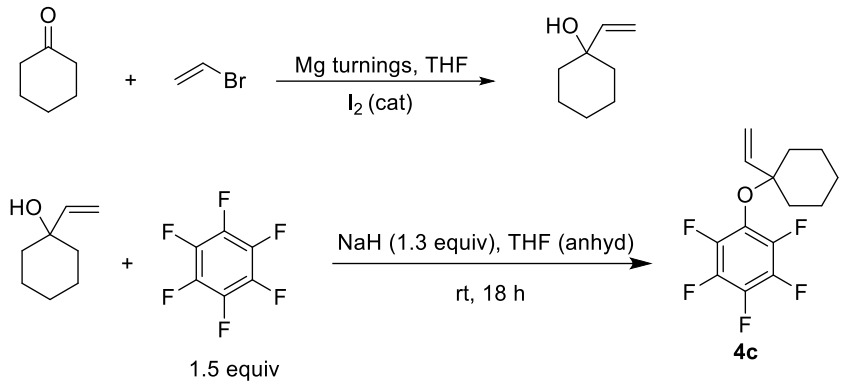
6

1-((3,7-Dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (6) was synthesized using **general procedure A**. Linalool (1.8 mL, 9.9 mmol), NaH (0.31 g, 12.9 mmol) was stirred in anhyd. THF (40 mL) at room temperature for 20 minutes. Then hexafluorobenzene (1.5 mL, 12.9 mmol) was added and stirred for 18 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford the product in 81% yield (2.56 g, 8.02 mmol) as a colorless liquid.

General Procedure B for synthesis of aryl ethers via Grignard reagent:

To a suspension of fresh Mg turnings in anhydrous THF was added catalytic amount of I2. A solution of vinyl bromide (1 M in THF) was then added, and the mixture was heated to initiate the Grignard reaction. The remainder of vinyl bromide solution was added at a rate to maintain gentle reflux. After complete addition, a solution of corresponding ketone in THF was added over 15 minutes and the reaction was left to stir at room temperature overnight. The reaction was carefully quenched with saturated NH4Cl solution, and then extracted with ether (4x40 mL). The ether extract was washed with brine (40 mL), dried over MgSO4 and then concentrated using rotatory evaporator. The product was isolated using column chromatography.

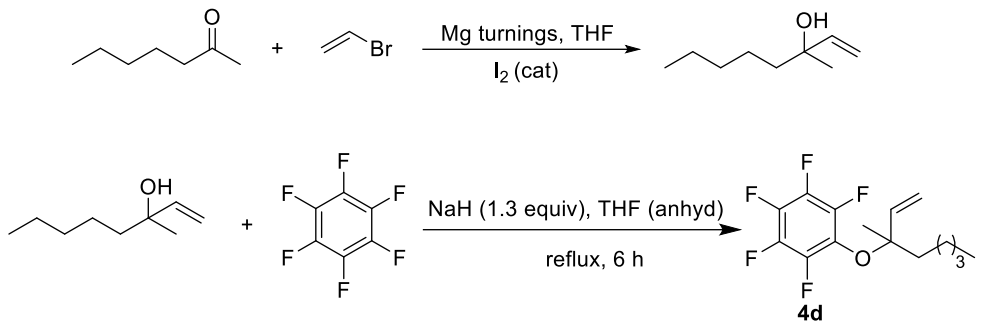
Synthesis of 1,2,3,4,5-pentafluoro-6-((1-vinylcyclohexyl)oxy)benzene (4c)



1,2,3,4,5-pentafluoro-6-((1-vinylcyclohexyl)oxy)benzene (4c) was synthesized using **general procedure B** followed by **general procedure A**. A solution of 1 M vinyl bromide in THF (32 mL, 32 mmol) was added to Mg turnings (0.77 g) in THF (45 mL) and heated to initiate Grignard reaction. It was followed by addition of cyclohexanone (2.54 mL, 24.6 mmol) over 15 minutes and left to stir overnight at room temperature. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-10 cv, ramped to 10% EtOAc for 10-25 cv, ramped again to 50% for 25-30 cv and then held at 100% EtOAc for 30-40 cv) on a 24 g silica column to afford **1-vinylcyclohexan-1-ol** in 29.7% yield (0.92 g, 7.3 mmol) as a pale yellow liquid.

1-vinylcyclohexan-1-ol was then used to carry out **general procedure A** for synthesis of aryl ether. 1-vinylcyclohexan-1-ol (0.96 mL, 7.3 mmol), NaH (0.262 g, 10.94 mmol) was stirred in anhyd. THF (40 mL) at room temperature for 20 minutes. Then hexafluorobenzene (1.26 mL, 10.94 mmol) was added and stirred at the same temperature for 18 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford **1,2,3,4,5-pentafluoro-6-((1-vinylcyclohexyl)oxy)benzene (4c**) in 63% yield (1.34 g, 4.58 mmol) as a colorless liquid.

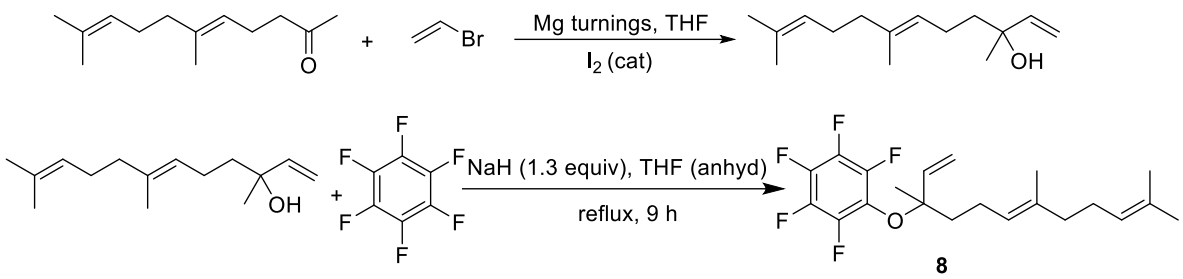
Synthesis of 1,2,3,4,5-pentafluoro-6-((3-methyloct-1-en-3-yl)oxy)benzene (4d)



1,2,3,4,5-pentafluoro-6-((3-methyloct-1-en-3-yl)oxy)benzene (4d) was synthesized using **general procedure B** followed by **general procedure A**. A solution of 1 M vinyl bromide in THF (36 mL, 36 mmol) was added to Mg turnings (0.864 g) in THF (45 mL) and heated to initiate Grignard reaction. It was followed by addition of heptan-2-one (2.8 mL, 20.0 mmol) over 15 minutes and left to stir overnight at room temperature. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-10 cv, ramped to 10% EtOAc for 10-25 cv, ramped again to 50% for 25-30 cv and then held at 100% EtOAc for 30-40 cv) on a 24 g silica column to afford **3-methyloct-1-en-3-ol** in 44% yield (1.25 g, 8.8 mmol) as a colorless liquid.

3-methyloct-1-en-3-ol was then used to carry out **general procedure A** for synthesis of aryl ether. 3-methyloct-1-en-3-ol (1.49 mL, 8.8 mmol), NaH (0.316 g, 13.2 mmol) was stirred in anhyd. THF (40 mL) at room temperature for 20 minutes. Then hexafluorobenzene (4.07 mL, 35.2 mmol) was added and refluxed for 6 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford **1,2,3,4,5-pentafluoro-6-((3-methyloct-1-en-3-yl)oxy)benzene (4d)** in 66% yield (1.78 g, 5.81 mmol) as a colorless liquid.

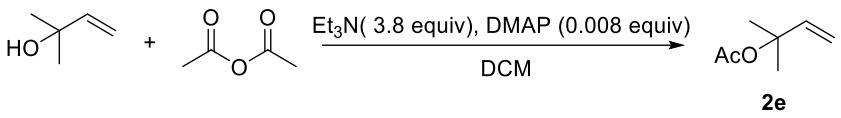
Synthesis of (E)-1,2,3,4,5-pentafluoro-6-((3,7,11-trimethyldodeca-1,6,10-trien-3-yl)oxy)benzene (7)



(E)-1,2,3,4,5-pentafluoro-6-((3,7,11-trimethyldodeca-1,6,10-trien-3-yl)oxy)benzene (8) was synthesized using **general procedure B** followed by **general procedure A**. A solution of 1 M vinyl bromide in THF (25 mL, 25 mmol) was added to Mg turnings (0.519 g) in THF (45 mL) and heated to initiate Grignard reaction. It was followed by addition of (E)-6,10-dimethylundeca-5,9-dien-2-one (3.71 mL, 16.67 mmol) over 15 minutes and left to stir overnight at room temperature. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0 % EtOAc for 0-10 cv, ramped to 10 % EtOAc for 10-25 cv, ramped again to 50% for 25-30 cv and then held at 100% EtOAc for 30-40 cv) on a 24 g silica column to afford **(E)-3,7,11-trimethyldodeca-1,6,10-trien-3-ol** in 32.7% yield (1.21 g, 5.45 mmol) as a pale yellow liquid.

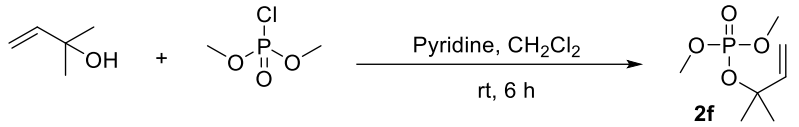
(E)-3,7,11-trimethyldodeca-1,6,10-trien-3-ol was then used to carry out **general procedure A** for synthesis of aryl ether. (E)-3,7,11-trimethyldodeca-1,6,10-trien-3-ol (1.38 mL, 5.45 mmol), NaH (0.261 g, 10.9 mmol) was stirred in anhyd. THF (45 mL) at room temperature for 20 minutes. Then hexafluorobenzene (0.95 mL, 8.17 mmol) was added and refluxed for 9 h. The crude residue was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford **(E)-1,2,3,4,5-pentafluoro-6-((3,7,11-trimethyldodeca-1,6,10-trien-3-yl)oxy)benzene (8)** in 61% yield (1.29 g, 3.32 mmol) as a colorless liquid.

General procedure C for synthesis of aryl ether via acetylation:



To a flame dried 250 mL round bottom flask was added 2-methylbut-3-en-2-ol (2.5 mL, 23 mmol), Et_3N (10.4 mL, 87.4 mmol), DMAP (0.04 mL, 0.184 mmol) and DCM (20 mL) via syringe. Flask was cooled in ice-bath and acetic anhydride (7.2 mL, 87.4 mmol) was added dropwise with constant stirring. The resulting solution was stirred under an Ar atmosphere at room temperature and was monitored by TLC (hexane : ethyl acetate 95:5) until no alcohol was observed. The mixture was washed with $NaHCO_3$ (2 x 150 mL), 10% NaOH (2 x 50 mL), brine (50 mL) and dried over MgSO4. Solvent was removed in vacuo and crude product was obtained as a yellow oil which was distilled (130-150 ^oC at 760 mm Hg) to yield **2-methylbut-3-en-2-yl acetate** in 91% yield (2.9 mL, 20.93 mmol) as a colorless liquid.

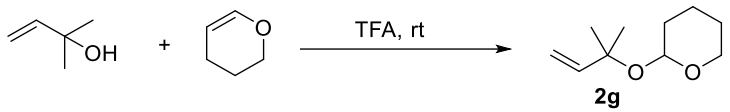
General Procedure D for synthesis of aryl ether using dimethyl phosphorochloridate :



Dimethyl phosphorochloridate (3.61g, 25 mmol) was added to a solution of 2-methylbut-3-en-2-ol (1.94 g, 22.5 mmol) and pyridine (2.0 mL) in CH2Cl2 (30 mL) at 0 oC over 5 minutes. The resulting white slurry was stirred for 6 h at room temperature. The reaction mixture was diluted with diethyl ether and was washed successfully with a 10% HCl solution, saturated $NaHCO_3$ (2 x 50 mL) and brine (3 x 50 mL). The organic layer was dried over anhydrous $MgSO_4$. After removal of the solvent in vacuo, the crude product was purified by automated flash chromatography using hexane:ethyl acetate (0% EtOAc for 0-15 cv and ramped to 50% EtOAc

for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford **dimethyl (2-methylbut-3-en-2-yl) phosphate** in 76% yield (3.32 g, 17.1 mmol) as a colorless liquid.

General Procedure E for synthesis of aryl ether from pyran :



2g

To a solution of 2-methylbut-3-en-2-ol (0.9 ml, 9 mmol) in DCM (30 mL) 2,3-dihydro-4H-pyran (0.8 mL, 9 mmol) and trifluoroacetic acid (0.1 mL, 1.8 mmol) were added. The reaction was stirred at room temperature and monitored by TLC. After completion of the reaction, it was quenched with NaHCO3 and extracted with DCM. The organic phase was then washed with water and brine, dried over MgSO4, and concentrated in vacuo. The crude product was purified by automated flash chromatography using hexane : ethyl acetate (0% EtOAc for 0-15 cv and ramped to 30% EtOAc for 15-25 cv and then held at 100% EtOAc 25-35 cv) on a 24 g silica column to afford **2-((2-methylbut-3-en-2-yl)oxy)tetrahydro-2H-pyran** in 70% yield (1.07 g, 6.3 mmol) as a colorless oil.

<u>Working mechanism</u>

We believe that the reaction progresses with excitation of $Ir(ppy)_3$ in the presence of blue LEDs to form a long lived triplet excited state. This further undergoes endothermic single electron transfer from DIPEA forming the radical anion *via* reductive quenching. It can then transfer an electron exothermically to the perfluoroarene (A) resulting in the formation of a perfluoroaryl radical anion (I1) that causes extrusion of fluoride ion to form a perfluoroaryl radical (I2). This perfluoroaryl radical (I2) in turn attacks the prenylating agent (B) selectively at the unsubsituted terminus of the alkene to generate a new radical (I3) followed by the loss of a phenoxy radical (I4) and results in the desired C–C coupled prenylated product (C).

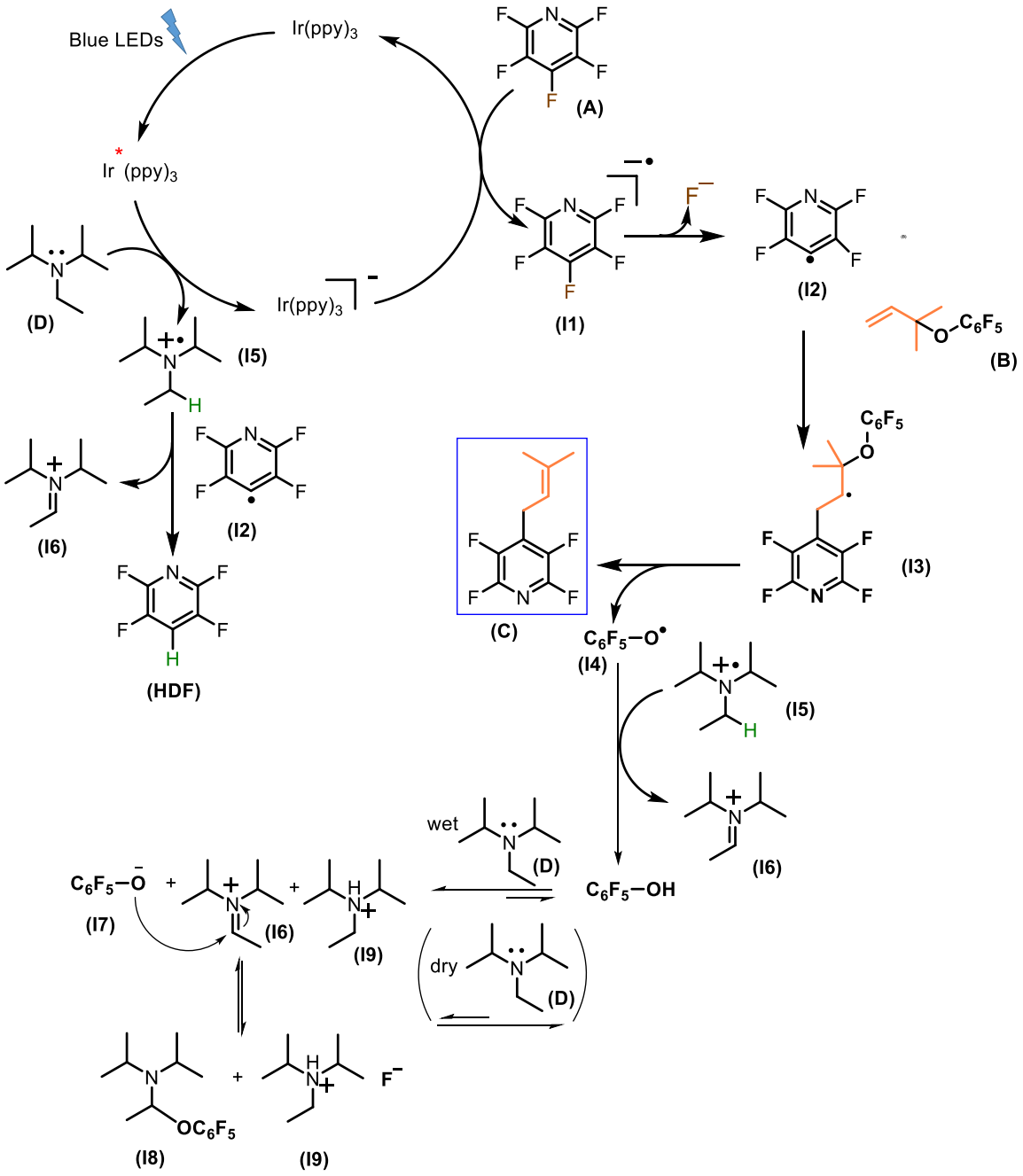


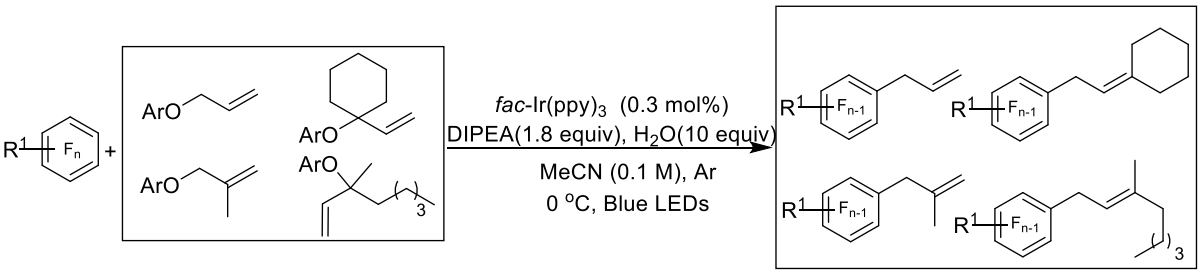
Figure 1.5: Working mechanism

Photocatalytic Reactions on Perfluoroarenes

We believe that the reaction progresses with excitation of $Ir(ppy)_3$ in the presence of blue LEDs to form a long lived triplet excited state. This further undergoes endothermic single electron

transfer from DIPEA forming the radical anion via reductive quenching. It can then transfer an electron exothermically to the perfluoroarene (A) resulting in the formation of a perfluoroaryl radical anion (I1) that causes extrusion of fluoride ion to form a perfluoroaryl radical (I2). This perfluoroaryl radical (I2) in turn attacks the prenylating agent (B) selectively at the unsubsituted terminus of the alkene to generate a new radical (I3) followed by the loss of a phenoxy radical (I4) and results in the desired C–C coupled prenylated product (C). The perfluoroaryl radical (I2) generated upon fluoride fragmentation could also undergo undesired hydrogen atom transfer from the amine radical cation (I5) (and potentially the amine D, α C–H BDE of 91 kcal/mol)[44] to form undesired HDF product. The phenoxy radical (I4) generated (BDE C6H5O–H is 87.6 kcal/mol)[45] during the course of reaction is capable of abstracting hydrogen atom from amine radical cation (I5, α C–H BDE ~ 42 kcal/mol)[46] to form pentafluorophenol and generate an iminium ion (I6). We believe that in the presence of water, the equilibrium is shifted towards the ionic forms (the left). Our control studies with C_6F_5OH demonstrate its inhibitory and deleterious effect in the absence of water (see above). This may be because it serves as a good HAT donor. We speculate that the phenolate (I7) could also have a beneficial role by attacking the iminium ion (I6) to form the N-acetal species (I8).

General procedure F for photocatalytic allylation reaction

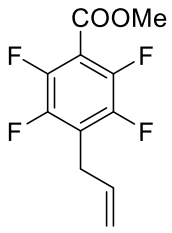


1 **4a-d** **5a-f**

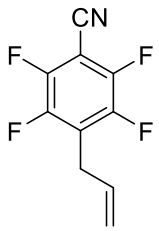
An NMR tube was charged with fluoroarene (0.1 mmol, 1.0 equiv), allyl-OAr (0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (0.18 mmol, 1.8 equiv), distilled water (1 mmol, 10 equiv), *fac*-tris(2- phenyl pyridinato-C2, N) Iridium(III) (Ir(ppy)3) (0.3 mM, 1 mL in MeCN), sealed

glass capillary containing C_6D_6 and was capped with an NMR septum (Ace glass, part no. 9096-25). When reaction was run in greater than 0.1 mmol of fluoroarene, more than one NMR tube was used to set up the reaction and each NMR tube had 1 mL of reaction mixture. The reaction was degassed via Ar bubbling for 15 min at 0 °C (to avoid evaporation of *N,N* diisopropylethylamine and other volatile starting materials) and then placed in a light bath (*vide supra*) such that the lower portion of the tube was submerged under the isopropanol/water bath.

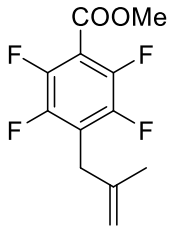
The reaction was monitored periodically by ^{19}F NMR (care was taken to exclude light while in transit). After the complete consumption of starting material, CH_3CN was removed *via* rotavap. The crude material was purified using prep TLC plate 10:1 hexane:ether. If the reaction did not go to completion with the first addition of *N,N* diisopropylethylamine, an additional 0.2 - 1.2 equiv of *N,N* -diisopropylethylamine was added to the reaction. Then the reaction was re-degassed and returned to the light bath. This sequence was repeated until the reaction reached completion as judged by ^{19}F NMR.



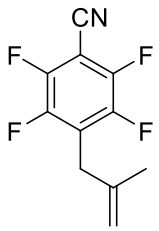
General procedure F was followed using methyl 2,3,4,5,6-pentafluorobenzoate (14.75 μL, 0.1 mmol, 1 equiv), 1-(allyloxy)-2,3,4,5,6-pentafluorobenzene (97.5 μL, 0.6 mmol, 6 equiv), *N,N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **methyl 4-allyl-2,3,5,6-tetrafluorobenzoate (5a)** as a colorless liquid in 72% ^{19}F NMR yield and 66% isolated yield (14.89 mg, 0.06 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.04 – -140.19 (m, 2F), -143.12 (td, *J* = 15.8, 4.8 Hz, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94 – 5.82 (m, 1H), 5.12 (d, 2H), 3.97 (s, 3H), 3.50 (d, *J* = 6.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 146.1 – 143.6 (ddd, *J* = 12.9, 6.4, 4.8 Hz), 145.8 – 143.3 (dt, *J* = 15.9, 4.6 Hz), 132.2, 121.9 (t, *J* 18.4 Hz), 117.6, 110.6 (t, *J* = 15.7 Hz), 53.2, 27.1. GC/MS (m/z, relative intensity) 248 (M+, 48), 229 (2), 217 (100), 169 (28).



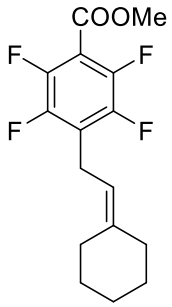
General procedure F was followed using methyl pentafluorobenzonitrile (12.6 µL, 0.1 mmol, 1 equiv), 1-(allyloxy)-2,3,4,5,6-pentafluorobenzene (97.6 µL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 µL, 0.18 mmol, 1.8 equiv), distilled water (18 µL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **4-allyl-2,3,5,6-tetrafluorobenzonitrile (5b)** as a colorless liquid in 81% ^{19}F NMR yield and 72% isolated yield (15.48 mg, 0.07 mmol). Not much effort was given to evaporate the solvents due to low volatility of compound. The crude product also contained hydrodefluorinated product. ^{19}F NMR (376 MHz, $CDCl_3$) δ -132.67 – -133.24 (m, 2F), -133.68 – -134.38 (m, 2F, minor), -140.50 (td, *J* = 15.8, 4.8 Hz, 2F), -140.94 – -141.51 (m, 2F, minor). ^1H NMR (400 MHz, $CDCl_3$) δ 5.89 – 5.68 (m, 1H), 5.09 (d, 2H), 3.47 (d, 2H).



General procedure F was followed using methyl 2,3,4,5,6-pentafluorobenzoate (14.75 µL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylallyl)oxy)benzene (107.3 µL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 µL, 0.18 mmol, 1.8 equiv), distilled water (18 µL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **methyl 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzoate (5c)** as a colorless liquid in 74% ^{19}F NMR yield and 68% isolated yield (18.34 mg, 0.07 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.02 – -140.44 (m, 2F), -142.50 (td, *J* = 15.8, 4.8 Hz, 2F). ^1H NMR (400 MHz, $CDCl_3$) δ 4.85 (s, 1H), 4.65 (s, 1H), 3.98 (s, 3H), 3.44 (s, 2H), 1.78 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 146.2 – 143.8 (ddd, *J* = 12.9, 6.4, 4.8 Hz), 145.8 – 143.2 (dt, *J* = 15.9, 4.6 Hz), 140.4, 121.9 (t, *J* = 18.4 Hz), 112.8, 110.6 (t, *J* = 15.7 Hz), 53.2, 31.3 – 30.6 (m), 22.3. GC/MS (m/z, relative intensity) 262 (M+, 64), 247 (15), 231 (100).

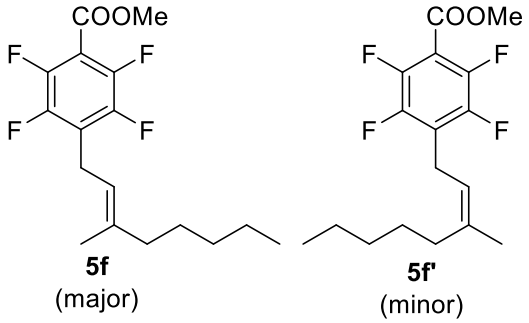


General procedure F was followed using 2,3,4,5,6-pentafluorobenzonitrile (12.6 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylallyl)oxy)benzene (107.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **2,3,5,6-tetrafluoro-4-(2-methylallyl)benzonitrile (5d)** as a colorless liquid in 85% ^{19}F NMR yield and 78% isolated yield (17.86 mg, 0.08 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -133.06 (td, *J* = 17.4, 7.1 Hz, 2F), -139.86 (td, *J* = 16.8, 7.0 Hz, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.88 (s, 1H), 4.66 (s, 1H), 3.48 (s, 2H), 1.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.2 – 145.6 (dt, *J* = 16.4, 3.6 Hz), 146.3 – 143.4 (m), 139.7, 125.8 (t, *J* = 18.4 Hz), 113.5, 107.6 (t, *J* = 3.7 Hz), 92.4, 31.2, 22.3. GC/MS (m/z, relative intensity) 229 (M+, 55), 214 (34), 194 (25).



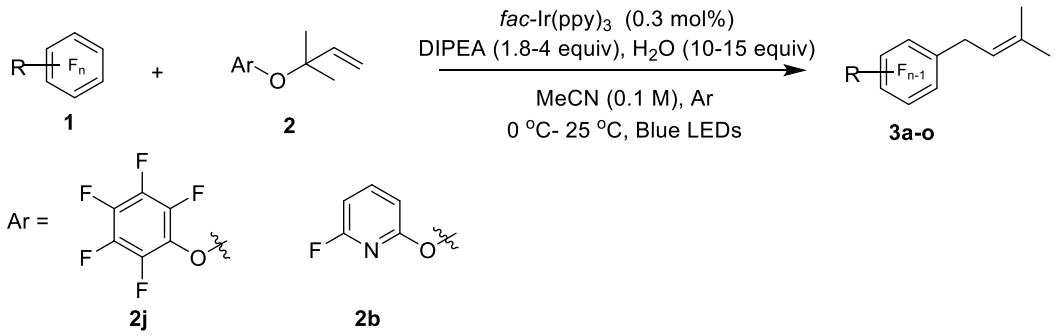
General procedure F was followed using methyl 2,3,4,5,6-pentafluorobenzoate (14.8 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((1-vinylcyclohexyl)oxy)benzene(125 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **methyl 4-(2-cyclohexylideneethyl)-2,3,5,6-tetrafluorobenzoate (5e)** as a colorless liquid in 68% ^{19}F NMR yield and 61% isolated yield (18.96 mg, 0.06 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.24 – -140.41 (m, 2F, major and minor), -143.41 (td, *J* = 15.7, 4.9 Hz, 2F, major and minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, *J* = 7.5 Hz, 1H), 3.96 (s, 3H), 3.45 (d, *J* = 7.5 Hz, 2H), 2.27 (t, *J* = 5.5 Hz, 2H), 2.11 – 2.00 (m, 2H), 1.63 – 1.44 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 146.2 – 143.8 (ddd, *J* = 12.9, 6.4,

4.8 Hz), 145.8 – 143.4 (dt, *J* = 15.9, 4.6 Hz), 143.1, 123.9 (t, *J* = 18.7 Hz), 114.8, 109.7, 53.1, 37.0, 29.7, 28.3, 26.7, 21.3. GC/MS (m/z, relative intensity) 316 (M+, 15), 285 (15), 235 (58).



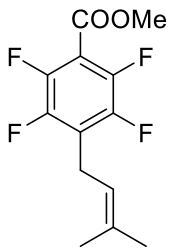
General procedure F was followed using methyl 2,3,4,5,6-pentafluorobenzoate (14.8 μL, 0.1 mmol, 1 equiv1,2,3,4,5-pentafluoro-6-((3-methyloct-1-en-3-yl)oxy)benzene (142 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **methyl (E)-2,3,5,6-tetrafluoro-4-(3-methyloct-2-en-1-yl)benzoate (5f)** with E:Z 1.3:1 as a colorless liquid in 64% ^{19}F NMR yield. Alkene geometry was assigned by NOE correlation of the allylic methylene to the cis substituent. ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.23 – -140.41 (m, 4F, major and minor), -143.13 (tt, *J* = 15.1, 6.7 Hz, 4F, major and minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15 (t, *J* = 7.3 Hz, 2H, major and minor), 3.96 (s, 6H, major and minor), 3.45 (d, *J* = 7.3 Hz, 4H, major and minor), 2.22 – 2.09 (m, 2H, minor), 1.95 (d, *J* = 7.8 Hz, 2H), 1.73 (s, 3H), 1.68 (s, 3H, minor), 1.45 – 1.14 (m, 12H, major and minor), 0.95 (t, *J* = 7.2 Hz, 3H, minor) – 0.83 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 146.2 – 143.6 (ddd, *J* = 12.9, 6.4, 4.8 Hz), 145.8 – 143.1 (dt, *J* = 15.9, 4.6 Hz), 139.5, 139.3, 123.8 (t, *J* = 18.7 Hz), 118.4, 117.8, 110.3 – 109.3 (m), 53.5 – 52.3 (m), 39.8 – 39.1 (m), 31.8 (d, *J* = 9.9 Hz), 31.4, 27.5, 22.5 (d, *J* = 9.3 Hz), 22.2, 15.9, 14.0. GC/MS (m/z, relative intensity) 332 (M+, 18), 301 (22), 256 (30), 216 (68).

General procedure G for photocatalytic prenylation reaction

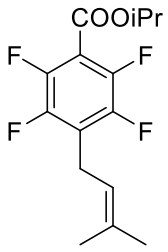


An NMR tube was charged with fluoroarene (0.1 mmol, 1.0 equiv), prenyl-OAr (0.6-0.8 mmol, 6-8 equiv), *N,N*-diisopropylethylamine (0.18-0.4 mmol, 1.8-4 equiv), distilled water (1-1.5 mmol, 10-15 equiv), *fac*-tris(2- phenyl pyridinato-*C*2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.3 mM, 1 mL in MeCN), sealed glass capillary containing C_6D_6 and was capped with an NMR septum (Ace glass, part no. 9096-25). When reaction was run in greater than 0.1 mmol of fluoroarene, more than one NMR tube was used to set up the reaction and each NMR tube had 1 mL of reaction mixture. The reaction was degassed via Ar bubbling for 15 min at 0 °C (to avoid evaporation of *N,N* diisopropylethylamine and other volatile starting materials) and then placed in a light bath (*vide supra*) such that the lower portion of the tube was submerged under the isopropanol/water bath.

The reaction was monitored periodically by ^{19}F NMR (care was taken to exclude light while in transit). After the complete consumption of starting material, CH_3CN was removed via rotavap. The crude material was purified using prep TLC plate. If the reaction did not go to completion with the first addition of *N,N*-diisopropylethylamine, an additional 1 - 3 equiv of *N,N* -diisopropylethylamine was added to the reaction. Then the reaction was re-degassed and returned to the light bath. This sequence was repeated until the reaction reached completion as judged by ^{19}F NMR.

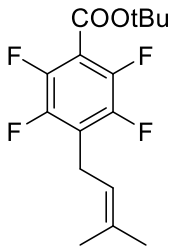


General procedure G was followed using methyl 2,3,4,5,6-pentafluorobenzoate (14.75 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **methyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3a)** as a colorless liquid in 68% ^{19}F NMR yield and 61% isolated yield (16.6 mg, 0.06 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.23 – -140.38 (m, 2F), -143.20 (dd, *J* = 21.4, 12.7 Hz, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15 (t, *J* = 7.4 Hz, 1H), 3.96 (s, 3H), 3.43 (d, *J* = 7.4 Hz, 2H), 1.74 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 146.1 – 143.6 (ddd, *J* = 12.9, 6.4, 4.8 Hz), 145.8 – 143.3 (dt, *J* = 15.9, 4.6 Hz), 135.3, 123.6 (t, *J* = 18.8 Hz), 118.2, 110.0 (t, *J* = 15.7 Hz), 53.1, 25.6, 22.2, 17.6. GC/MS (m/z, relative intensity) 276 (M+, 20), 261 (35), 245 (15). This product was also obtained when 2-fluoro-6-((2-methylbut-3-en-2-yl)oxy)pyridine was used as the prenyl source. However, in this case the reaction produced a significant side-product which we assume it to be methyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-enoyl)benzoate (oxidized product) based on GC/MS (m/z, relative intensity) 290 (M+, 40) which is the mass of the side product.

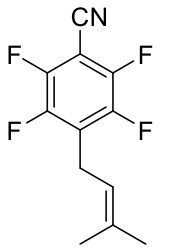


General procedure G was followed using isopropyl 2,3,4,5,6-pentafluorobenzoate (16.6 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **isopropyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3b)** as a colorless

liquid in 65% ^{19}F NMR yield and 58% isolated yield (18.24 mg, 0.06 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -141.03 – -141.16 (m, 2F), -143.39 – -143.52 (m, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.34 – 5.25 (m, 1H), 5.15 (t, *J* = 7.3 Hz, 1H), 3.42 (d, *J* = 7.3 Hz, 2H), 1.74 (s, 3H), 1.69 (s, 3H), 1.37 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 145.9 – 143.6 (ddd, *J* = 12.9, 6.4, 4.8 Hz), 145.6 – 143.1 (dt, *J* = 15.9, 4.6 Hz), 135.2, 123.1 (t, *J* = 18.8 Hz), 118.4, 111.0 (t, *J* = 16.3 Hz), 70.6, 25.6, 22.2, 21.7, 17.6. GC/MS (m/z, relative intensity) 304 (M+, 12), 289 (7), 247 (22).

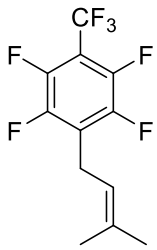


General procedure G was followed using isobutyl 2,3,4,5,6-pentafluorobenzoate (19.8 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **isobutyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3c)** as a colorless liquid in 66% ^{19}F NMR yield and 60% isolated yield (19.08 mg, 0.06 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.84 – -137.99 (m, minor), -141.06 – -141.21 (m, minor), -141.87 – -142.00 (m), -143.61 – -143.73 (m). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15 (t, *J* = 7.4 Hz, 1H), 3.41 (d, *J* = 7.4 Hz, 2H), 1.74 (s, 3H), 1.69 (s, 3H), 1.59 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9 (t, *J* = 3.0 Hz), 145.8 – 143.4 (ddd, *J* = 13.0, 6.8, 4.5 Hz), 145.4 – 142.9 (dt, *J* = 15.9, 4.6 Hz), 135.0, 122.5 (t, *J* = 18.8 Hz), 118.5, 112.1 (t, *J* = 16.8 Hz), 84.3, 28.1, 25.6, 22.1, 17.6. GC/MS (m/z, relative intensity) 318 (M+, 25), 262 (65), 247 (100).

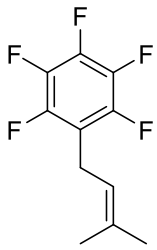


General procedure G was followed using 2,3,4,5,6-pentafluorobenzonitrile (12.9 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL

of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzonitrile (3d)** as a colorless liquid in 71% ^{19}F NMR yield and 64% isolated yield (14.58 mg, 0.06 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -133.13 – -133.26 (m, 2F), -140.61 (td, *J* = 16.4, 6.9 Hz, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.13 (t, *J* = 7.2 Hz, 1H), 3.48 (d, *J* = 7.3 Hz, 2H), 1.75 (s, 3H), 1.71 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3 – 145.7 (dt, *J* = 14.3, 3.8 Hz), 145.9 – 143.4 (m), 136.3, 127.5 (t, *J* = 18.6 Hz), 117.3, 107.7 (t, *J* = 3.7 Hz), 29.7, 25.7, 22.7, 17.7. GC/MS (m/z, relative intensity) 243 (M+, 34), 228 (40), 208 (18), 188 (35).

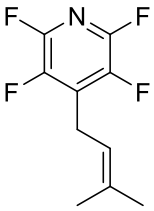


General procedure G was followed using 1,2,3,4,5-pentafluoro-6-(trifluoromethyl)benzene (14.16 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **1,2,4,5-tetrafluoro-3-(3-methylbut-2-en-1-yl)-6-(trifluoromethyl)benzene (3e)** as a colorless liquid in 61% ^{19}F NMR yield and 57% isolated yield (16.3 mg, 0.057 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -56.20 (t, *J* = 21.5 Hz, 3F), -141.39 – -141.69 (m, 2F), -142.17 (td, *J* = 16.0, 6.5 Hz, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16 (t, *J* = 7.5 Hz, 1H), 3.46 (d, *J* = 7.4 Hz, 2H), 1.75 (s, 3H), 1.71 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.2 – 143 (ddd, *J* = 17.1, 6.7, 4.0 Hz), 145.4 – 142.5 (ddd, *J* = 12.6, 7.3, 3.3 Hz), 135.7, 129.0, 128.2, 125.3, 117.8, 25.7, 22.2, 17.7. GC/MS (m/z, relative intensity) 286 (M+, 52), 271 (64), 231 (34).

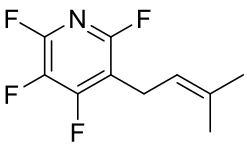


General procedure G was followed using pentafluorobenzene (11.6 μL, 0.1 mmol, 1 equiv), 2-fluoro-6-((2-methylbut-3-en-2-yl)oxy)pyridine (103 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of Ir(ppy)3

(0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 1:1 hexane : DCM to afford **1,2,3,4,5-pentafluoro-6-(3-methylbut-2-en-1-yl)benzene (3f)** as a colorless liquid in 64% ^{19}F NMR yield and 55% isolated yield (13.9 mg, 0.06 mmol). Due to volatile nature of compound, minimal effort was given to remove the solvents. ^{19}F NMR (376 MHz, $CDCl_3$) δ -144.31 (dd, *J* = 22.3, 8.2 Hz, 2F), -158.81 (t, *J* = 20.7 Hz, 1F), -163.29 (td, *J* = 22.3, 8.1 Hz, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.15 (t, *J* = 7.3 Hz, 1H), 3.37 (d, *J* = 7.4 Hz, 2H), 1.74 (s, 3H), 1.69 (s, 3H). GC/MS (m/z, relative intensity) 236 (M+, 70), 221 (85), 201 (20). The compound produced a thermally generated impurity under GC conditions that was otherwise not observed in ^{1}H or ^{19}F NMR.

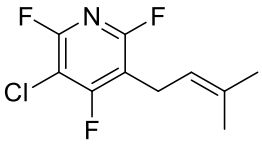


General procedure G was followed using pentafluoropyridine (10.9 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC with 100% hexanes to afford **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)pyridine (3g)** as a colorless liquid in 78% ^{19}F NMR yield and 74% isolated yield (15.33 mg, 0.07 mmol). Minimal effort was given to evaporate the solvent due to volatile nature of the product. ^{19}F NMR (376 MHz, $CDCl_3$) δ -91.72 – -91.93 (m, 2F), -145.20 – -145.42 (m, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.10 (t, *J* = 7.5 Hz, 1H), 3.42 (d, *J* = 7.5 Hz, 2H), 1.69 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7 – 141.3 (m), 141.5 – 138.7 (m), 136.4, 134.3 (t, *J* = 17.3 Hz), 116.9, 25.7, 22.9, 17.7. GC/MS (m/z, relative intensity) 219 (M+, 100), 204 (84), 184 (62), 177 (40).

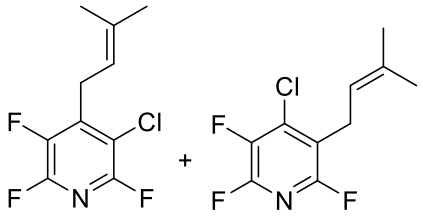


General procedure G was followed using 3-chloro-2,4,5,6-tetrafluoropyridine (12.44 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv),

N,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC with 100% hexanes to **2,3,4,6-tetrafluoro-5-(3-methylbut-2-en-1-yl)pyridine (3i)** as a colorless liquid in 57% ^{19}F NMR yield and 41% isolated yield (8.97 mg, 0.04 mmol). Minimal effort was given to evaporate the solvent due to volatile nature of the product. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.43 – -73.64 (m, 1F), -88.22 – -88.43 (m, 1F), -118.20 (q, *J* = 17.3 Hz, 1F), -167.39 (ddd, *J* = 24.1, 21.7, 19.6 Hz, 1F). ^1H NMR (400 MHz, $CDCl_3$) δ 5.15 (t, *J* = 7.9 Hz, 1H), 3.32 (d, *J* = 7.2 Hz, 2H), 1.74 (s, 3H), 1.70 (s, 3H). GC/MS (m/z, relative intensity) 219 (M+, 95), 204 (80), 184 (60).

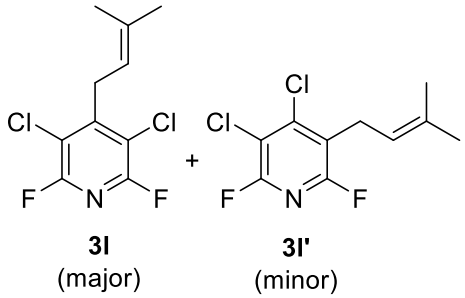


General procedure G was followed using 3,5-dichloro-2,4,6-trifluoropyridine (12.44 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC with 100% hexanes to afford **3-chloro-2,4,6-trifluoro-5-(3-methylbut-2-en-1-yl)pyridine (3j)** as a colorless liquid in 55% ^{19}F NMR yield and 48% isolated yield (11.5 mg, 0.05 mmol). Minimal effort was given to evaporate the solvent due to volatile nature of the product. ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.52 – -71.67 (m, 1F), -72.44 (t, *J* = 13.6 Hz, 1F), -97.91 (dd, *J* = 19.5, 13.8 Hz, 1F). ^1H NMR (400 MHz, $CDCl_3$) δ 5.14 (t, *J* = 7.4 Hz, 1H), 3.32 (d, *J* = 7.4 Hz, 2H), 1.74 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4 – 164.8 (dd, *J* = 10.5, 4.9 Hz), 158.7 – 156.3 (m), 156.5 – 154.1 (m), 135.2, 118.3, 115.4, 110.4 (ddd, *J* = 35.5, 20.0, 7.2 Hz), 25.6, 21.5, 17.7. GC/MS (m/z, relative intensity) 235 (M+, 50), 220 (100), 180 (70).



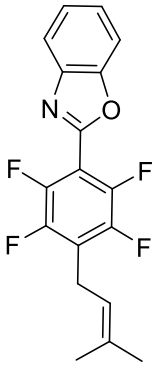
3k (major) **3k'** (minor)

General procedure G was followed using 3,4-dichloro-2,5,6-trifluoropyridine (12.4 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The reaction was run at -15 ºC instead of 0 ºC to control the selectivity, delivering more para substituted product. The crude material was purified by using Prep TLC with 100% hexanes to afford **3-chloro-2,5,6-trifluoro-4-(3-methylbut-2-en-1-yl)pyridine (major, 3k)** as a colorless liquid in 81% ^{19}F NMR yield and 73% isolated yield (16.51 mg, 0.06 mmol). It comprised of a mixture of para substituted product and meta prenylated product in the ratio 14.5:1 (para:meta). Looking at the ^{19}F NMR of both isomers we see that these signals shift very closely to one another. Unfortunately, they shift too close to use recently developed 19F NMR prediction method (*JOC*, 2018, 83, 3220). We unsuccessfully attempted to derivatize the mixture, which might have allowed us to distinguish the molecules so the assignment is unfortunately made based on analogy with **3l/3l'**. In the substrate **3k**, which has one fewer meta chlorines, we assume it follows the same pattern. Minimal effort was given to evaporate the solvent due to volatile nature of the product. ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.85 (dd, *J* = 26.9, 12.3 Hz, 1F, minor), -74.15 (dd, *J* = 27.8, 12.8 Hz, 1F), -89.54 (dd, *J* = 20.9, 14.1 Hz, 1F, minor), -89.91 (dd, *J* = 21.5, 12.8 Hz), -145.00 (dd, *J* = 25.7, 21.3 Hz, 1F, minor), -145.33 (dd, *J* = 27.8, 21.7 Hz). ^1H NMR (400 MHz, $CDCl_3$) δ 5.15 (m, 2H, major and minor), 3.58 (d, *J* = 7.2 Hz, 2H), 3.43 (d, *J* = 7.6 Hz, 2H, minor), 1.77 (s, 6H, major and minor), 1.70 (s, 6H, major and minor). GC/MS (m/z, relative intensity) 235 (M+, 52), 220 (100), 180 (90).



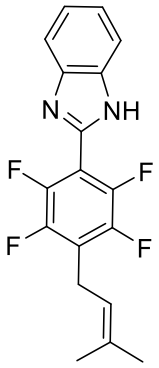
3l (major) **3l'** (minor)

General procedure G was followed using 3,4,5-trichloro-2,6-difluoropyridine (12.44 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC with 100% hexanes to afford **3,5-dichloro-2,6-difluoro-4-(3-methylbut-2-en-1-yl)pyridine (major, 3l)** as a colorless liquid in 77% ^{19}F NMR yield and 69% isolated yield (16.56 mg, 0.06 mmol). It comprised of a mixture of para substituted product (single peak for symmetrical F-atoms at -71.67 ppm) and meta prenylated product in the ratio 6:1 (para:meta), determined by ^{19}F NMR Pdt1:Pdt2 peak integrations. ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.67 (d, *J* = 16.4 Hz, 1F, minor), -71.67(s, 2F), -71.77 (d, *J* = 12.3 Hz, 1F, minor). ^1H NMR (400 MHz, $CDCl_3$) δ 5.07(m, 1H), 4.99 (m, 1H, minor), 3.73 (d, *J* = 7.0 Hz, 2H), 3.49 (d, *J* = 7.1 Hz, 2H, minor), 1.84 (s, 3H), 1.79 (s, 3H, minor), 1.74 (s, 3H), 1.72 (s, 3H, minor). GC/MS (m/z, relative intensity) 251 (M+, 45), 216 (35), 200 (37).

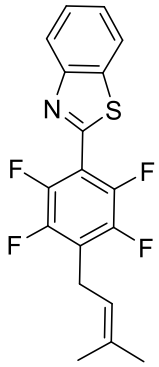


General procedure G was followed using 2-(perfluorophenyl)benzo[d]oxazole (18.6 μL, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC with 1% AcOH in hexanes to afford **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]oxazole (3m)** as a pale yellow solid in 62% ^{19}F NMR yield and 53% isolated yield (17.75 mg, 0.05 mmol), which includes 20%

HDF. ^{19}F NMR (376 MHz, $CDCl_3$) δ -137.11 – -137.33 (m, 2F, minor), -137.68 (tt, *J* = 16.9, 5.2 Hz, 2F, minor), -138.79 – -138.93 (m, 2F), -143.04 (td, *J* = 15.1, 4.8 Hz, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (td, *J* = 7.7, 1.1 Hz, 1H), 7.65 (td, *J* = 7.8, 1.1 Hz 1H), 7.48 – 7.40 (m, 2H), 5.22 (t, *J* = 7.4 Hz, 1H), 3.51 (d, *J* = 7.4 Hz, 2H), 1.78 (s, 3H), 1.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.9 – 153.2 (m), 150.8 – 150.1 (m), 146.6 – 146.0 (m), 143.9 (dd, *J* = 21.2, 11.8 Hz), 141.2, 135.4, 126.6, 126.3, 125.2, 125.0, 123.5, 118.2, 111.0, 25.7, 22.4, 17.7. GC/MS (m/z, relative intensity) 335 (M+, 100), 320 (80), 300 (42), 280 (70).

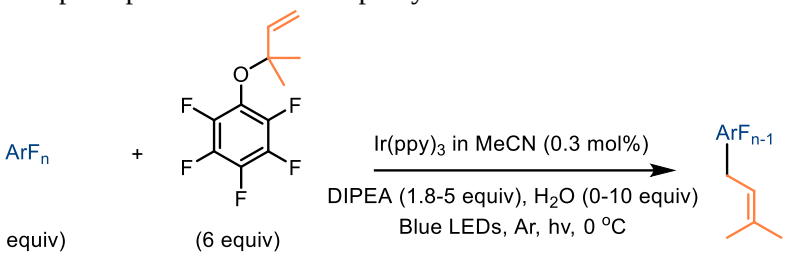


General procedure G was followed using 2-(perfluorophenyl)-1H-benzo[d]imidazole (28.4 mg, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. Due to lower solubility of the perfluoroarene starting material, another 1 mL of dry CH_3CN was added and the reaction mixture (0.05 M) was subjected to sonication after regular intervals. The crude material was purified by using Prep TLC with 100% hexanes followed by re-dipping the plate in 10:1 hexane:ether to afford **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)-1H-benzo[d]imidazole (3n)** as a pale yellow solid in 71% ^{19}F NMR yield and 68% isolated yield (22.7 mg, 0.068 mmol),which includes 12% HDF. ^{19}F NMR (376 MHz, CD_3CN) δ -140.04 – -140.35 (m, 2F, minor), -141.66 – -141.84 (m, 2F, minor), -142.27 – -142.43 (m, 2F), -145.11 – -145.28 (m, 2F). ^{1}H NMR (400 MHz, CD_3CN) δ 7.75 (dd, *J* = 6.1, 3.2 Hz, 2H), 7.38 (dd, *J* = 6.1, 3.2 Hz, 2H), 5.25 (t, *J* = 7.4 Hz, 1H), 3.53 (d, *J* = 7.3 Hz, 2H), 1.79 (s, 3H), 1.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.9 (m), 146.6 – 144.1 (ddt, *J* = 17.1, 12.7, 6.6 Hz), 145.7 – 143.2 (m), 140.3, 135.3, 124.0, 122.1 (t, *J* = 18.8 Hz), 118.3, 115.5 (dd, *J* = 33.9, 24.7 Hz), 107.0, 25.7, 22.3, 17.7. GC/MS (m/z, relative intensity) 334 (M+, 75), 319 (68), 291 (100), 278 (60).

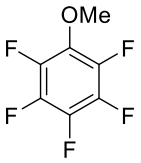
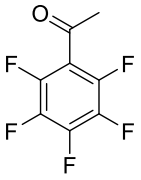
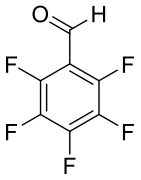
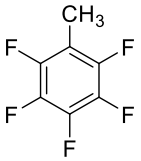
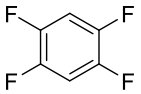
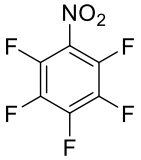
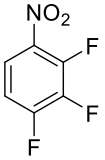


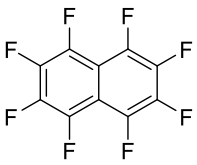
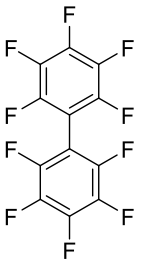
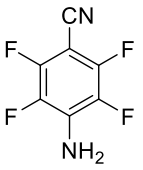
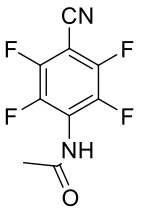
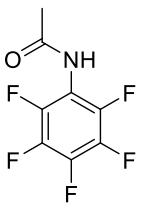
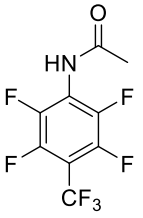
General procedure G was followed using 2-(perfluorophenyl)benzo[d]thiazole (31.76 mg, 0.1 mmol, 1 equiv), 1,2,3,4,5-pentafluoro-6-((2-methylbut-3-en-2-yl)oxy)benzene (117.3 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC with 100% hexanes followed by re-dipping the plate in 10:1 hexane:ether to afford **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]thiazole (3o)** as a white solid in 68% ^{19}F NMR yield and 62% isolated yield (21.76 mg, 0.06 mmol). ^{19}F NMR (376 MHz, $CDCl_3$) δ -140.17 – -140.29 (m, 2F), -143.38 – -143.51 (m, 2F). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 8.1 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.57 (td, *J* = 7.6, 1.2 Hz 1H), 7.48 (td, *J* = 7.7, 1.1 Hz, 1H), 5.23 (t, *J* = 7.4 Hz, 1H), 3.50 (d, *J* = 7.4 Hz, 2H), 1.78 (s, 3H), 1.72 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 152.9, 146.6 – 144.1 (ddd, *J* = 13.0, 6.8, 4.5 Hz), 145.4 – 142.9 (dt, *J* = 15.9, 4.6 Hz), 135.6 (t, *J* = 2.5 Hz), 135.2, 126.6, 126.1, 125.2, 124.1, 122.3 (t, *J* = 18.9 Hz), 121.4, 118.5, 25.7, 22.3, 17.7. GC/MS (m/z, relative intensity) 351 (M+, 100), 336 (70), 316 (46), 296 (73).

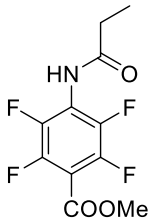
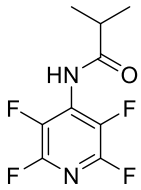
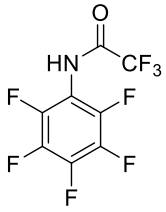
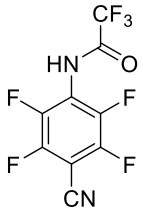
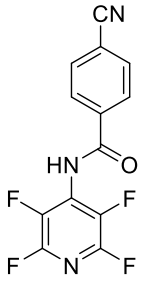
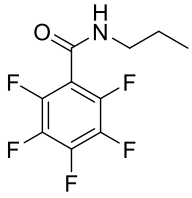
Table 1.13: Scope of perfluoroarenes for prenylation reactions

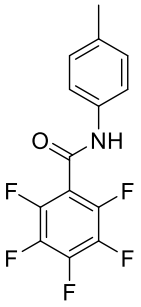
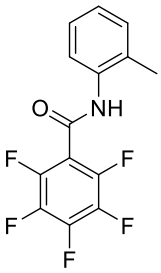
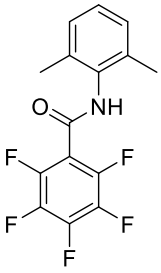
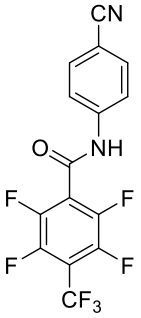
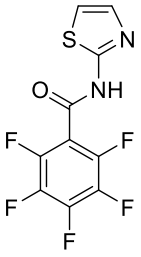


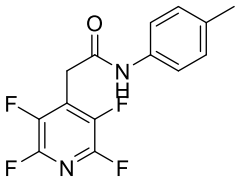
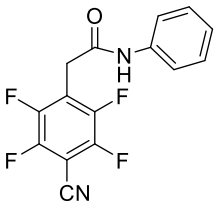
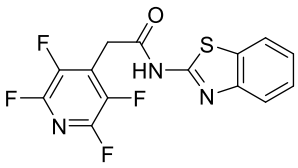
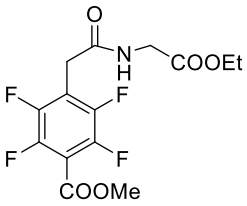
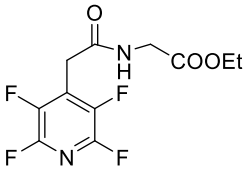
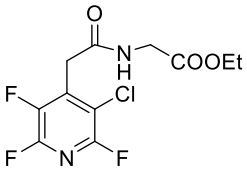
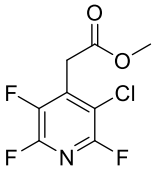
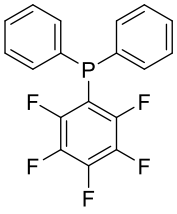
(1 equiv) (6 equiv)

Entry	ArF_n	Result
1		No product
2		19F NMR yield = 52% Isolated yield = 43% 8 h
3		Trace amount of product Multiple side products Mostly HDF
4		Trace amount of product
5		No reaction
6		Messy reaction Multiple side products including HDF
7		No reaction

Entry	ArF_n	Result
8		Reaction goes to 45% conversion in 1 w. Observed mono- and di-prenylated product after keeping it that long
9		65-70% SM remained after 1 w.
10		Reaction undergoes 40% conversion in 6 d. 22% product along with HDF.
11		Messy reaction SM consumed in 6 h
12		4 d : 19F NMR- No reaction
13		Product = 24% HDF = 73% SM = 3% 3d

Entry	ArF_n	Result
14		<15 % conversion in 4d No product
15		No product
16		No product
17		4 d 19F NMR : No reaction
18		4 d 19F NMR : No reaction
19		Slow reaction. >40% SM remained after 5 d <20% product 2 other side products

Entry	ArF_n	Result
20		19F NMR yield : Pdt1 = 27% Pdt2 = 35% Pdt3 = 14% HDF = 24% 4 d
21		Formation of 4 pdts 19F NMR : Pdt1 = 38% Pdt2 = 17% Pdt3 = 37% Pdt4 = 7% 4 d
22		Formation of 4 products including HDF 4 d
23		No product
24		No product

Entry	ArF_n	Result
25		<10 conversion in 4.5 d No product
26		No product
27		No product
28		No product
29		<10% pdt
30		Product = 57% HDF = 28% SM = 15% 4 d
31		6 d : 19F NMR- SM = 34% Product = 55% HDF = 11%
32		1 d :19F NMR- SM = 31% Formation of 2 pdts apart from HDF Not a clean rxn

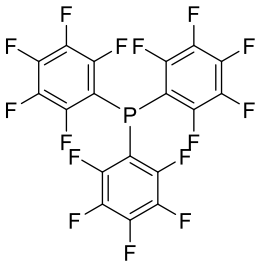
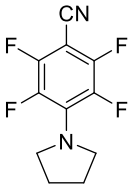
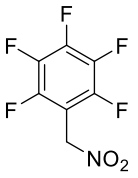
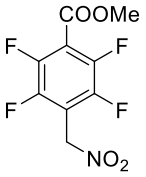
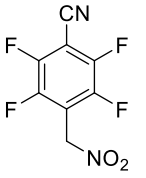
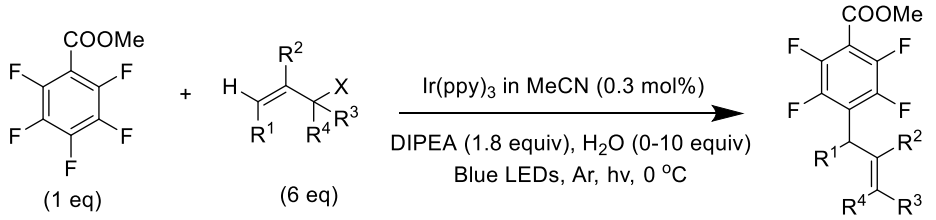
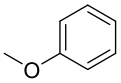
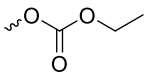
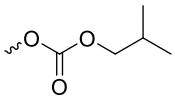
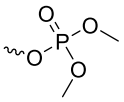
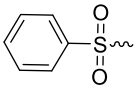
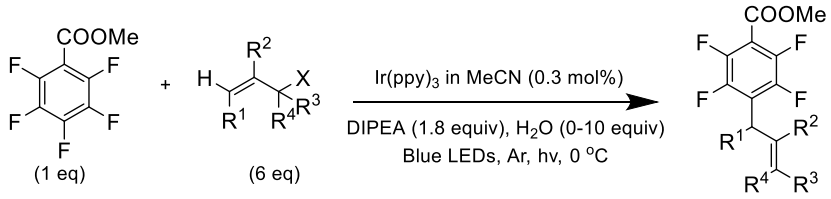
Entry	ArF_n	Result
33		Product formation along with many side products Not a clean reaction
34		No product
35		No product
36		No product
37		No product

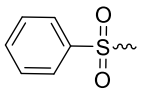
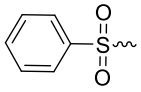
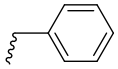
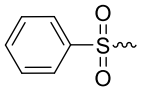
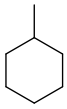
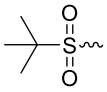
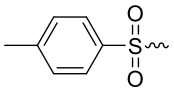
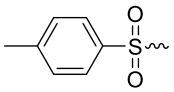
Table 1.14: Scope of prenylating agents

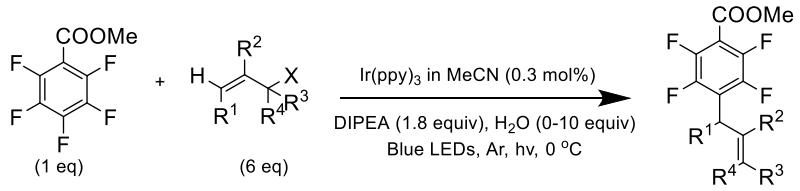


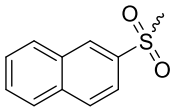
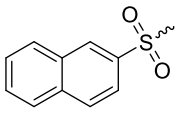
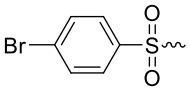
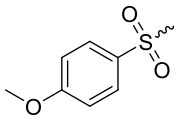
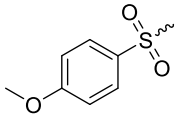
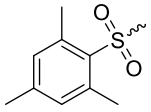
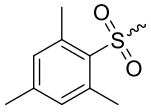
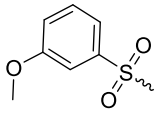
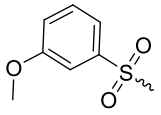
	Entry	R^1	R^2	R^3	R^4	X	Result
With PFP	1.	H	Me	H	H	Cl	41% product with PFP 41% product with MPB (3d)
	2.		H	Me	H	OAc	No product Multiple sideproducts
	3.		H	Me	H	OAc	No product Not a clean reaction
	4.	H	H	Me	Me	OAc	Multiple products
	5.	H	H	Me	Me	OH	19F NMR: Could see the product, reduction,C-O coupling, amine addition GC: Observed peaks for amine addition and product.
	6.	H	H	i-Pr	H		21% product 66% HDF
	7.	H	H	i-Pr	H		13% product 69% HDF
	8.	H	Me	H	H		4% product
	9.	H	Me	H	H		10% product Slow reaction
	10.	H	H	H	H		48% product 47% HDF 18 h

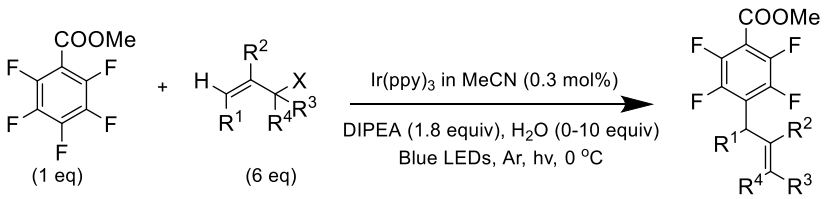
PFP = Pentafluoropyridine
MPB = Methyl Pentafluorobenzoate

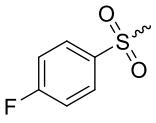
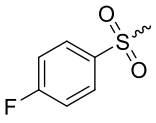
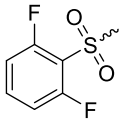
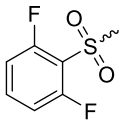
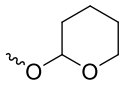
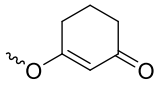
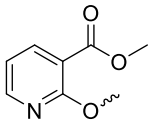
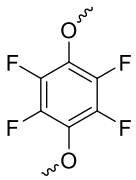


Entry	R^1	R^2	R^3	R^4	X	Result
11	H	H	Me	Me		36% pdt 51% HDF +other 35 h
12	H	Me	Me	Me		23% product 43% HDF 35 h
13	H	H		H		19F NMR: 2d- Observed SM, reduction, C-C coupled product with multiple side products
14	H	Me	H	H		Very slow reaction Good Pdt:HDF ratio
15	H	H	H	H		4 d-19F NMR: SM = 52%, Product= 36%, HDF = 10%
16	H	Me				No Product
17	H	Me	H	H		Clean but slow rxn, pdt more than reduction.
18	H	H	Me	Me		4 d-19F NMR: SM = 61%, Product= 24%, HDF = 15%
19	H	H	H	H		SM HDF Pdt -140.5 Other 1d 28 12 23 20 16 2d 22 14 27 27 10 Did not undergo further conversion
20	H	H	Me	Me		SM HDF Pdt -140.5 Other 5h - 26 21 35 18 Very fast rxn but not clean, with poor Pdt to HDF ratio.

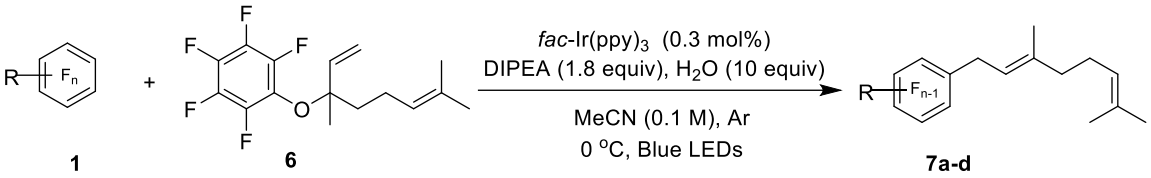


Entry	R^1	R^2	R^3	R^4	X	Result
21	H	H	H	H		SM HDF Pdt Other (%) 18h 10 12 32 47 35h - 13 34 52 Rxn was fast, but observed a number of signicant other peaks
22	H	H	Me	Me		SM HDF Pdt Other (%) 5h 45 7 18 30 21h 18 9 19 54
23	H	H	H	H		SM HDF Pdt Other (%) 1d 40 9 29 22 2d 38 9.3 31 23 5d rxn did not proceed further
24	H	H	H	H		SM HDF Pdt Other (%) 4h 83 9 8 - 2 d 12 36 39 13
25	H	H	Me	Me		SM HDF Pdt Other (%) 15h - 31 18 51
26	H	H	H	H		17% product HDF - major side product
27	H	H	Me	Me		10% product Mostly HDF
28	H	H	H	H		38% product Mostly HDF
29	H	H	Me	Me		18% product Mostly HDF plus other side products



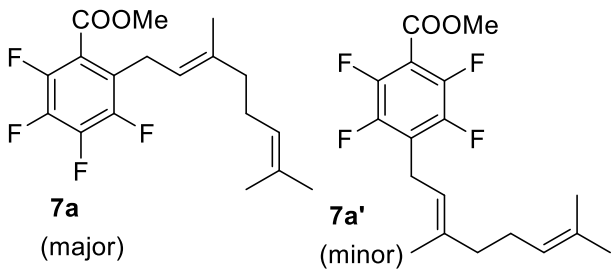
Entry	R^1	R^2	R^3	R^4	X	Result
30	H	H	H	H		31% product Not a clean reaction
31	H	H	Me	Me		17% product Multiple side products
32	H	H	H	H		No product
33	H	H	Me	Me		No product
34	H	H	Me	Me		7% product 4 sets of peaks in C-C range with reduction being the major pdt
35	H	H	Me	Me		No product
36	H	H	Me	Me		No product Major product = HDF
37	H	H	Me	Me		4% product Mostly HDF

General procedure H for photocatalytic geranylation reaction

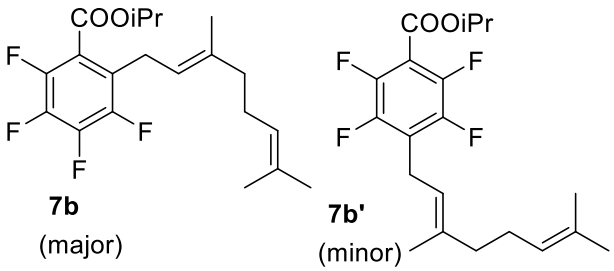


An NMR tube was charged with fluoroarene (0.1 mmol, 1.0 equiv), 1-((3,7-dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (0.18 mmol, 1.8 equiv), distilled water (1 mmol, 10 equiv), *fac*-tris(2- phenyl pyridinato-*C*2, *N*) Iridium(III) ($Ir(ppy)_3$) (0.3 mM, 1 mL in MeCN), sealed glass capillary containing C_6D_6 and was capped with an NMR septum (Ace glass, part no. 9096-25). When reaction was run in greater than 0.1 mmol of fluoroarene, more than one NMR tube was used to set up the reaction and each NMR tube had 1 mL of reaction mixture. The reaction was degassed via Ar bubbling for 15 min at 0 °C (to avoid evaporation of *N*,*N*-diisopropylethylamine and other volatile starting materials) and then placed in a light bath (*vide supra*) such that the lower portion of the tube was submerged under the isopropanol/water bath.

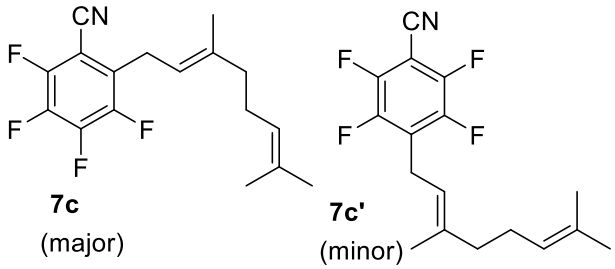
The reaction was monitored periodically by ^{19}F NMR (care was taken to exclude light while in transit). After the complete consumption of starting material, CH_3CN was removed via rotavap. The crude material was purified using prep TLC plate. If the reaction did not go to completion with the first addition of *N*,*N*-diisopropylethylamine, an additional 1-3 equiv of *N*,*N* -diisopropylethylamine was added to the reaction. Then the reaction was re-degassed and returned to the light bath. This sequence was repeated until the reaction reached completion as judged by ^{19}F NMR.



General procedure H was followed using methyl 2,3,4,5,6-pentafluorobenzoate (14.75 μL, 0.1 mmol, 1 equiv), 1-((3,7-dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (147 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')** as a colorless liquid in 42% and 27% ^{19}F NMR yield respectively (*o*-Ger : *p*-Ger = 1.55:1). This was determined using ^{19}F NMR peak integrations (four –F peaks as a result of ortho-substitution and two peaks arising from para-substitution. ^{19}F NMR (376 MHz, $CDCl_3$) δ -134.34 – -134.51 (m, 1F), -138.07 (dd, *J* = 22.8, 12.4 Hz, 1F), -140.14 (ddd, *J* = 21.6, 12.4, 5.2 Hz, 1F), -140.21 – -140.38 (m, 2F, minor), -140.44 (ddd, *J* = 21.8, 12.4, 5.2 Hz, 1F), -142.99 – -143.15 (m, 2F, minor). ^1H NMR (400 MHz, $CDCl_3$) δ 5.44 (t, *J* = 7.0 Hz, 1H), 5.16 (t, *J* = 14.6 Hz, 2H, major and minor), 5.03 (t, *J* = 7.5 Hz, 1H, minor), 3.97 (s, 3H), 3.96 (s, 3H, minor), 3.45 (d, *J* = 7.3 Hz, 2H), 3.19 (d, *J* = 10.7 Hz, 2H, minor), 2.34 – 1.96 (m, 8H, major and minor), 1.77 (d, *J* = 1.5 Hz, 3H), 1.74 (s, 3H, minor), 1.70 (s, 3H), 1.69 (s, 3H, minor), 1.64 (s, 3H), 1.63 (s, 3H, minor).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 160.2, 147.1 – 145.4 (m), 146.4 – 143.5 (m), 145.9 – 143.6 (m), 145.5 – 142.8 (m), 140.2, 138.8 (d, *J* = 13.0 Hz), 132.1, 131.7, 127.4 (t, *J* = 17.2 Hz), 123.9, 123.7, 121.8, 118.7, 118.3, 110.1 (t, *J* = 15.7 Hz), 53.1, 49.2, 41.8, 39.5, 37.2, 34.3, 31.8, 30.4, 26.4, 26.3, 26.1, 25.7, 25.6, 25.2, 22.2, 17.6, 16.1. GC/MS (m/z, relative intensity) 344 (M+, 15), 313 (10), 301 (20).

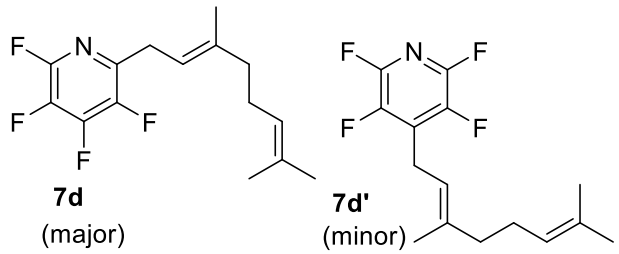


General procedure H was followed using isopropyl 2,3,4,5,6-pentafluorobenzoate (16.7 μL, 0.1 mmol, 1 equiv), 1-((3,7-dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (147 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **isopropyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7b) and isopropyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6- tetrafluorobenzoate (7b')** as a colorless liquid in 42% and 26% ^{19}F NMR yield respectively (*o*-Ger : *p*-Ger = 1.6:1). This was determined using ^{19}F NMR peak integrations (assignment was made based on the analogy with **7a**). ^{19}F NMR (376 MHz, $CDCl_3$) δ -134.55 – -134.77 (m, 1F), -138.32 (dd, *J* = 22.8, 12.4 Hz, 1F), -140.82 – -140.97 (m, 1F), -140.99 – -141.17 (m, 2F, minor), -141.17 – -141.27 (m, 1F), -143.22 – -143.44 (m, 2F, minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (t, *J* = 7.0 Hz, 2H), 5.30 (hept, 2H, major and minor), 5.15 (t, *J* = 9.2 Hz, 2H, major and minor), 5.05 – 5.00 (m, 1H, minor), 3.44 (d, *J* = 7.3 Hz, 3H), 3.18 (d, *J* = 10.7 Hz, 3H, minor), 2.33 – 2.01 (m, 8H, major and minor), 1.76 (s, 3H), 1.73 (s, 3H, minor), 1.70 (d, *J* = 2.3 Hz, 3H, minor), 1.65 (s, 3H), 1.63 (d, 3H, minor), 1.57 (s, 3H), 1.39 (d, 3H), 1.38 (d, 3H, minor), 1.37 (d, 3H), 1.36 (d, 3H, minor). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 159.2, 147.9 – 146.4 (m), 147.2 – 145.8 (m), 147.1 – 143.0 (m), 144.8 – 142.6 (m), 140.2, 138.8, 138.7, 132.1, 131.7, 127.0, 126.6, 123.8, 123.7, 123.1, 121.9, 119.8, 118.9, 118.3, 111.3 – 110.8 (m), 70.7, 70.6, 53.4, 49.2, 41.9, 39.5, 37.2, 34.3, 30.4, 26.3 (d, *J* = 9.9 Hz), 26.1 (d, *J* = 6.7 Hz), 25.7 (d, *J* = 8.6 Hz), 25.3, 22.1 (d, *J* = 5.9 Hz), 21.7, 17.6, 16.0. GC/MS (m/z, relative intensity) 372 (M+, 20), 329 (25), 313 (20).



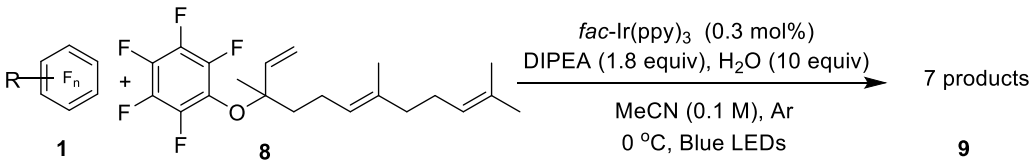
General procedure H was followed using Pentafluorobenzonitrile (12.6 μL, 0.1 mmol, 1 equiv), 1-((3,7-dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (147 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzonitrile (7c) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzonitrile (7c')** as a colorless liquid in 45% and 27% ^{19}F NMR yield respectively (*o*-Ger : *p*-Ger = 1.65:1). This was determined using ^{19}F NMR peak integrations (four –F peaks as a result of *ortho*-substitution and two peaks arising from *para*-substitution). Assignment was made based on the analogy with **7a.** ^{19}F NMR (376 MHz, $CDCl_3$) δ -132.13 (ddt, *J* = 16.9, 11.2, 5.6 Hz, 1F), -133.01 (ddd, *J* = 20.6, 12.1, 7.4 Hz, 1F), -133.22 (tt, *J* = 16.6, 8.4 Hz, 2F, minor), -133.47 (ddd, *J* = 22.0, 12.0, 7.3 Hz, 1F), -135.40 (dd, *J* = 22.1, 12.1 Hz, 1F), -140.50 (tt, *J* = 16.5, 8.5 Hz, 2F, minor). ^1H NMR (400 MHz, $CDCl_3$) δ 5.44 (t, *J* = 7.0 Hz, 2H, major and minor), 5.13 (t, *J* = 7.4 Hz, 1H), 5.01 (t, *J* = 7.5 Hz, 1H, minor), 3.49 (d, *J* = 1.8 Hz, 2H), 3.23 (d, 2H, minor), 2.36 – 1.92 (m, 8H, major and minor), 1.77 (s, 3H), 1.74 (s, 3H, minor), 1.69 (s, 3H), 1.64 (s, 3H, minor), 1.62 (s, 3H, minor), 1.57 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1 (d, *J* = 6.4 Hz), 147.9 (d, *J* = 6.6 Hz), 148.8 – 146.2 (m), 148.1 – 145.8 (m), 144.6 (dt, *J* = 15.9, 4.6 Hz), 143.8 – 142.6 (dt, *J* = 15.9, 4.6 Hz), 140.1, 139.8, 132.2, 131.8, 131.1, 127.7, 127.5, 123.6, 121.7, 117.1, 107.7, 91.8, 49.5, 39.5, 37.4, 34.2, 30.2, 26.2, 25.9 (d, *J* = 6.8 Hz), 25.7, 25.2, 23.2,

22.6, 22.2 (d, *J* = 6.2 Hz), 17.6 (d, *J* = 2.9 Hz), 16.1. GC/MS (m/z, relative intensity) 311 (M+, 15), 296 (5), 268 (35), 255 (10).



General procedure H was followed using Pentafluoropyridine (10.9 μL, 0.1 mmol, 1 equiv), 1-((3,7-dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (147 μL, 0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of Ir(ppy)3 (0.16 mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The crude material was purified by using Prep TLC 10:1 hexane:diethyl ether to afford **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluoropyridine (7d) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluoropyridine (7d')** as a colorless liquid in 43% and 26% ^{19}F NMR yield respectively (*o*-Ger : *p*-Ger = 1.67:1). Assignment was made based on the analogy with **7a**. ^{19}F NMR (376 MHz, $CDCl_3$) δ -91.62 – -92.13 (m, 3F, major and minor), -92.39 (ddd, *J* = 28.6, 21.8, 14.0 Hz, 1F), -136.75 – -136.99 (m, 1F), -140.61 – -140.98 (m, 1F), -145.00 – -145.32 (m, 2F, minor). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48 – 5.39 (m, 1H), 5.22 – 5.14 (m, 1H), 5.14 – 5.08 (m, 1H, minor), 5.02 (dt, *J* = 6.8, 4.1 Hz, 1H, minor), 3.50 (d, *J* = 7.4 Hz, 2H), 3.23 (d, *J* = 10.9 Hz, 2H, minor), 2.38 – 1.96 (m, 8H, major and minor), 1.77 (s, 3H), 1.75 (s, 3H, minor), 1.69 (s, 3H), 1.64 (s, 3H, minor), 1.62 (s, 3H), 1.57 (s, 3H, minor). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.5 – 148.9 (m), 148.6 – 147.9 (m), 147.6 – 147.1 (m), 146.9 – 146.2 (m), 145.7 – 142.7 (m), 144.9 – 142.1 (m), 140.2, 139.9, 139.8, 139.1 (d, *J* = 9.0 Hz), 131.8, 123.6, 123.5, 121.7, 117.5, 116.8, 49.7, 41.8, 39.5, 37.1, 34.1, 26.3, 25.7 – 25.4 (m), 25.2, 22.9 – 22.7 (m), 22.6, 22.1 (d, *J* = 6.0 Hz), 17.6, 16.1. GC/MS (m/z, relative intensity) 287 (M+, 30), 272 (10), 258 (8), 244 (35).

General procedure I for the attempted photocatalytic farnesylation reaction



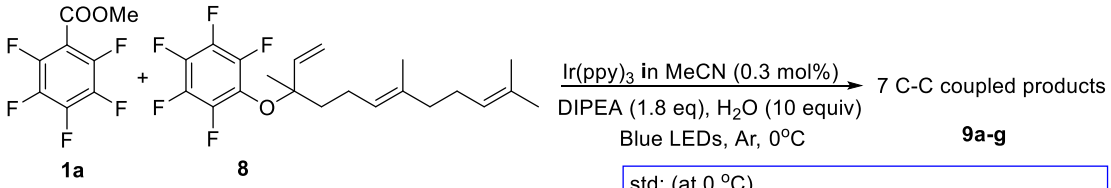
An NMR tube was charged with fluoroarene (0.1 mmol, 1.0 equiv), 1-((3,7-dimethylocta-1,6-dien-3-yl)oxy)-2,3,4,5,6-pentafluorobenzene (0.6 mmol, 6 equiv), *N*,*N*-diisopropylethylamine (0.18 mmol, 1.8 equiv), distilled water (1 mmol, 10 equiv), *fac*-tris(2- phenyl pyridinato-*C*2, *N*) Iridium(III) (Ir(ppy)3) (0.3 mM, 1 mL in MeCN), sealed glass capillary containing C_6D_6 and was capped with an NMR septum (Ace glass, part no. 9096-25). When reaction was run in greater than 0.1 mmol of fluoroarene, more than one NMR tube was used to set up the reaction and each NMR tube had 1 mL of reaction mixture. The reaction was degassed via Ar bubbling for 15 min at 0 °C (to avoid evaporation of *N*,*N* diisopropylethylamine and other volatile starting materials) and then placed in a light bath (*vide supra*) such that the lower portion of the tube was submerged under the isopropanol/water bath.

The reaction was monitored periodically by ^{19}F NMR (care was taken to exclude light while in transit). After the complete consumption of starting material, CH_3CN was removed via rotavap. The crude material was purified using prep TLC plate. If the reaction did not go to completion with the first addition of *N*,*N*-diisopropylethylamine, an additional 1 - 3 equiv of *N*,*N* -diisopropylethylamine was added to the reaction. Then the reaction was re-degassed and returned to the light bath. This sequence was repeated until the reaction reached completion as judged by ^{19}F NMR.

General procedure I was followed using methyl 2,3,4,5,6-pentafluorobenzoate (14.7 μL, 0.1 mmol, 1 equiv), (E)-1,2,3,4,5-pentafluoro-6-((3,7,11-trimethyldodeca-1,6,10-trien-3-yl)oxy)benzene (154 μL, 0.6 mmol, 6 equiv), *N*,*N*diisopropylethylamine (31.3 μL, 0.18 mmol, 1.8 equiv), distilled water (18 μL, 1 mmol, 10 equiv) and 1.0 mL of stock solution of $Ir(ppy)_3$ (0.16

mg, 0.0003 mmol, 0.003 equiv) in CH_3CN was used. The reaction produced 7 products (determined by GC/MS). An attempt was made to improve the selectivity by lowering the temperature to -20 °C and/or varying the amount of farnesyl ether in the reaction but these multiple products were still observed at those conditions.

Table **1.15**: Optimization of attempted farnesylation reaction at -20 °C



std: (at 0 °C)

19F NMR :	Time	1a	HDF	9a-g
	3.5 h	-	38%	59%

Optimizations of above reaction at **-20 °C**

Entry	Conditions	Time	1a	HDF	9a-g
1.	6 equiv ether	5 h	56%	17%	26.7%
2.	3 equiv ether	5 h	24%	56%	21%
3.	1 equiv ether	5 h	9%	83%	8%
4.	6 equiv ether, no water	5 h	62%	22%	16%

Multiple C-C coupled product formations observed from the initial stage of reaction.

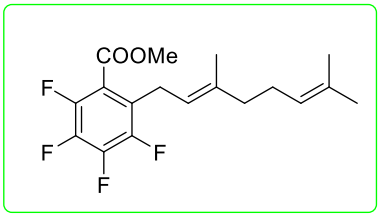
Table **1.16**: Change in product ratios on varying conditions

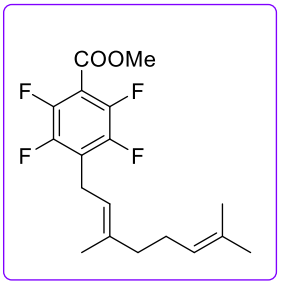
Conditions	9a	9b	9c	9d	9e	9f	9g	
6 equiv B 10 equiv H_2O	8.13		10.9	1.28	1.15	1	16.74	(std)
3 equiv B 10 equiv H_2O	9.19	5.04	12.36	12.64	19.39	1	23.53	
1 equiv B 10 equiv H_2O	8.31		7.96	7.76	13.57	1	16.79	
6 equiv B no H_2O	3.84		3.11	3.17	5.83	1	6.77	
	Ratio of products →							

In some cases **9a** and **9b** did not resolve completely on GCMS and have been represented by a —— to show a combined peak appearing at a specific retention time.

(Determined by calculating peak areas in GC/MS)

Evidence for ortho C-F Functionalization





One interesting feature of this project was the observed change in regioselectivity of the major product upon moving from prenylation to geranylation. This is the first report of preferential ortho fragmentation based on reagent (we have shown that an intramolecular hydrogen bond can cause the ortho fragmentation to occur preferentially). Thus, we approached this with a healthy skepticism. We based the proposed structure on the basis of several arguments which are outlined below. First, we observed 6 peaks in the ^{19}F NMR which could arise from 3 para-substituted products in which 2 of them were produced in the same ratio, or alternatively the reaction produces two products in total, i.e., expected para-geranylated product that accounts for two 1:1 –F signals and an ortho-geranylated product which accounts for four –F signals in a 1:1:1:1 relationship with one another. We ruled out the possibility of formation of 3 para-substituted products as the four –F signals were found to be present in the same spin system as confirmed by ^{19}F-^{19}F TOCSY. Another major evidence that supported ortho-geranylation was that upon running a $AgNO_3$ impregnated silica column chromatography in an attempt to separate the C–C coupled products from one another, we observed that the compound eluted in such a way that each and every fraction (from very early to late fractions) produced four 1:1:1:1 peaks in ^{19}F NMR, suggesting either perfect co-elution of two compounds or that this was a single compound. Other evidences included appropriate and distinct vinyl protons, methyl ester, methylene and methyl peaks in ^{1}H NMR, two separate peaks of same m/z determined by GCMS, genuine 4-bond F–F couplings observed in ^{19}F-^{19}F COSY[47]. Another very important study to validate ortho C-C coupled product was to calculate predicted ^{19}F NMR shifts for ortho-geranylated product. We

observed that the actual ^{19}F NMR shifts fell in the acceptable range of error.[48] Apart from that, we determined that all the F-atoms were attached to distinct C-atoms by ^{19}F-^{13}C HSQC and ^{1}H-^{13}C HSQC further confirmed our assignment of vinyl, methyl ester, benzylic methylene, methylene from geranyl chain and methyl protons on ^{1}H NMR. Alkene geometry was assigned by NOE correlations.

1. ^{19}F NMR

Observation:

- Four distinct 1:1:1:1 peaks with similar splitting pattern supported o-Geranylated pdt (-134.4, -138.2, -140, -140.4)
- Two 1:1 peaks confirmed p-Geranylated pdt (-140.3 and -143.1)

2. ^{1}H NMR

- 4 vinyl protons (5.01-5.5 ppm)
- Methylene (3.2-3.4 ppm and 1.95-2.35 ppm) and methyl peaks (1.55-2.78 ppm) from both compounds

3. GC/MS

- 2 peaks each of M+ 344 (at 17.4 and 17.6 mins retention time)

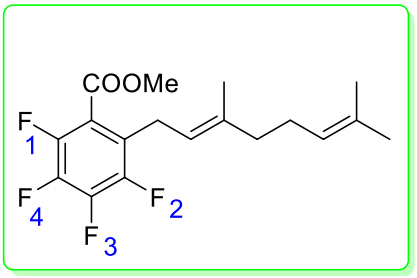
4. Isolation using $AgNO_3$ impregnated silica column

- ^{19}F NMR of various fractions contained either 1:1:1:1 peaks for o-Geranylated product or 1:1 peaks for p-Geranylated product

5. ^{19}F-^{19}F TOCSY

- 4 –F peaks in the same spin-system
- 2 –F peaks within another spin-system

6. ^{19}F-^{19}F COSY



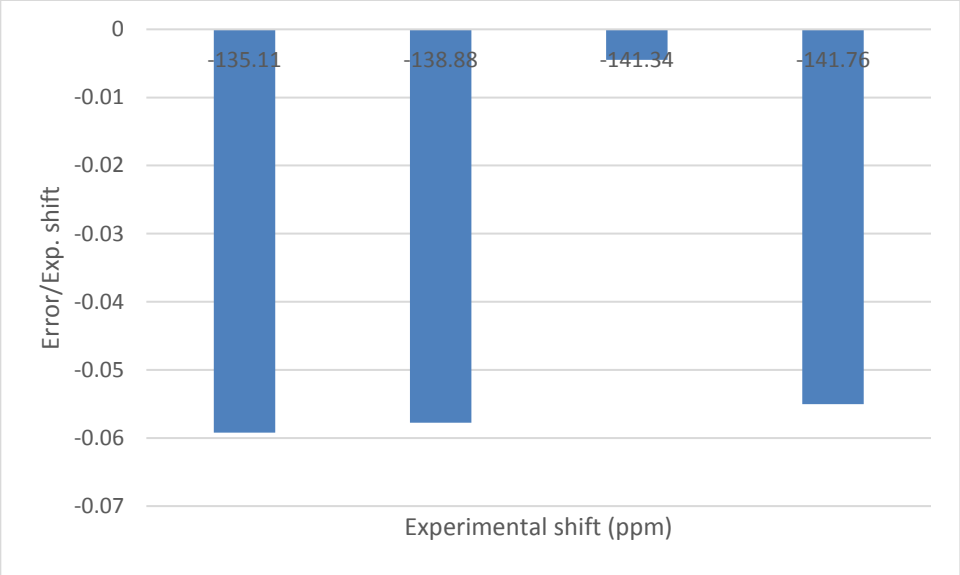
- 4-bond coupling stronger than 3-bond coupling
- F-1 and F-3 showed strong correlation
- F-2 showed strong correlation with F-4
- Weak interaction observed between F-1 and F-4

7. Structure prediction using NMR calculations

Experimental Shift	Isotropic	Calculated Shift	Error	
-135.11	312.5896	-127.3452	8	(ppm)
-138.88	315.2231	-129.9849	8.02	
-141.34	327.1844	-141.9751	0.63	
-141.76	334.8345	-149.6436	7.8	

Calculated isotropic values, and shifts of compounds
Geometry optimizations and NMR calculations run using the B3LYP/6-31+G(d,p) method in gas phase using Gaussian09. The shifts were scaled based on the equation y=-0.9968x+184.92.

- The actual NMR shifts lie within the acceptable error range.



8. $^{19}F - ^{13}C$ HSQC

- The four –F peaks are attached to four different C-atoms

9. $^{1}H-^{13}C$ HSQC

- A total of 4 vinyl protons from both molecules 5.0-5.5 ppm
- 2 separate methyl ester peaks (3.94-4.0 ppm)
- 2 benzylic methylene signals (3.2 and 3.4 ppm)
- Presence of 4 types of alkyl methylene signals (1.95-2.35 ppm)

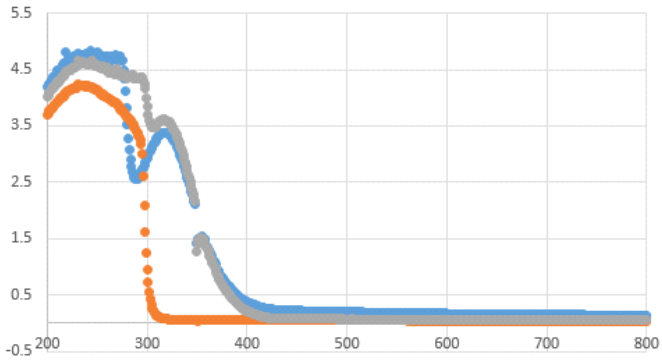
[This region includes peaks from minor side-products]

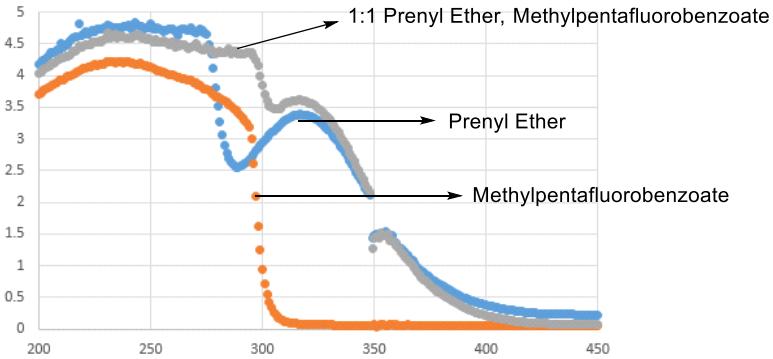
- Both products produces a total of 6 different methyl signals in the alkyl region (1.55-2.78 ppm) [This region also includes peaks from minor side-products]

UV-Vis Experiments:

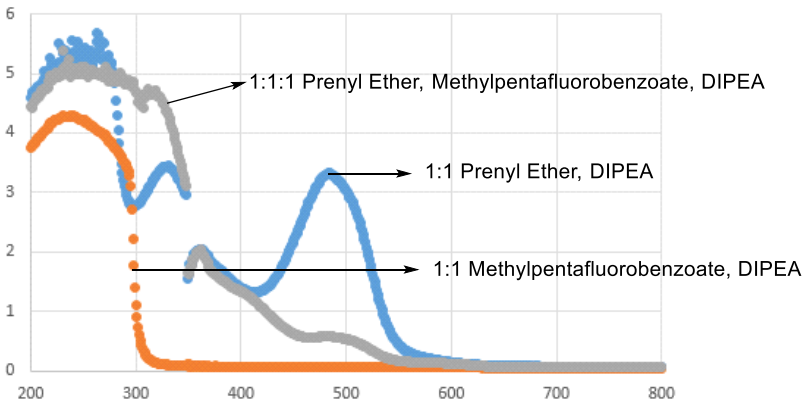
In order to gain a better insight on the interactions between substrates, we carried out UV-Vis experiments. We did not see any interaction between perfluoroarene and prenylating source, but there was a formation of exciplex observed between prenylating source and DIPEA.

Prenyl ether and Methylpentafluoro benzoate in MeCN (0.1 M)

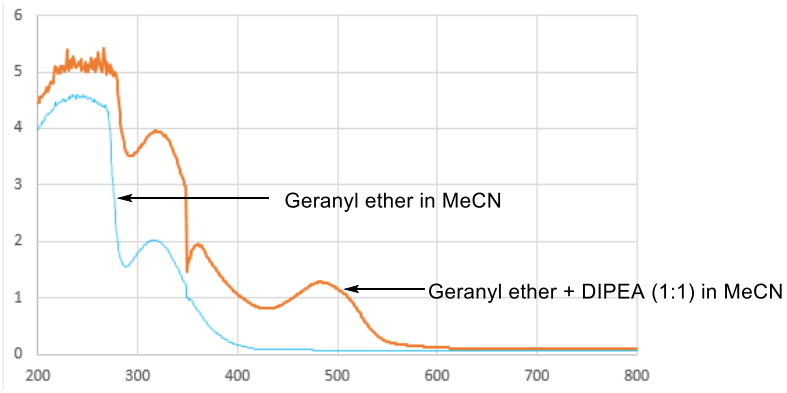


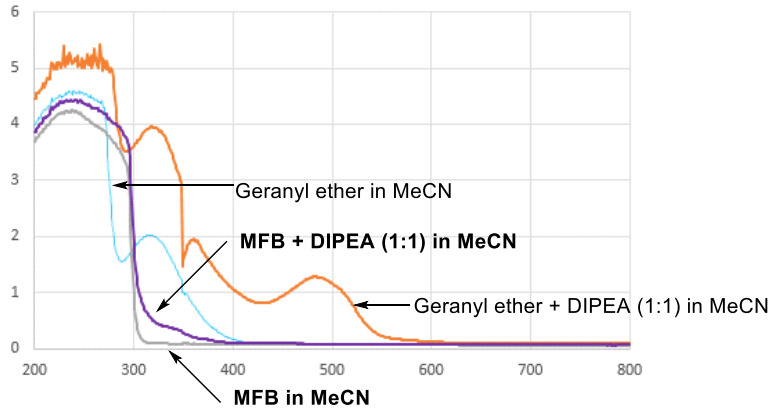


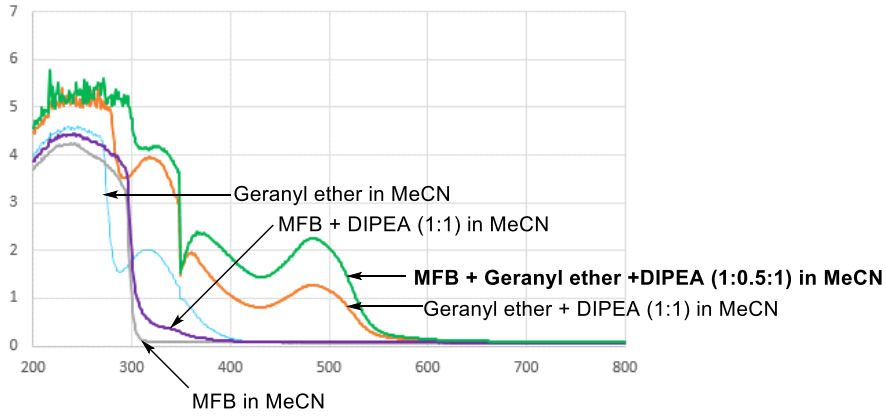
Prenyl Ether Methyl Pentafluorobenzoate DIPEA in MeCN (0.1 M)

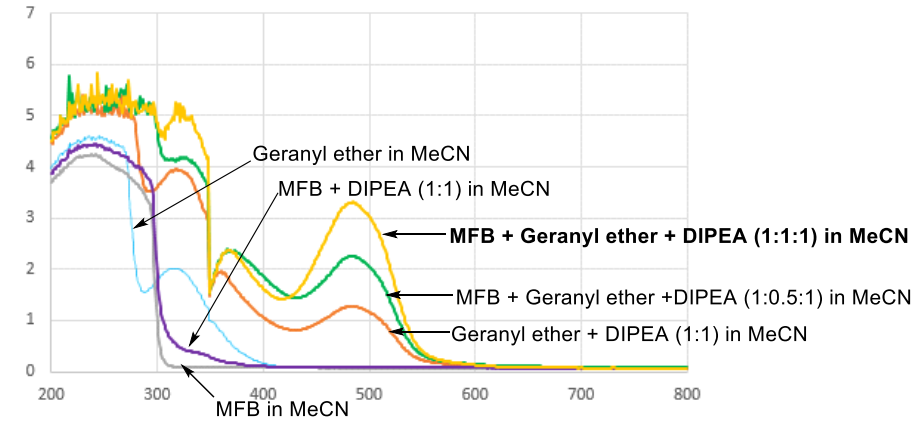


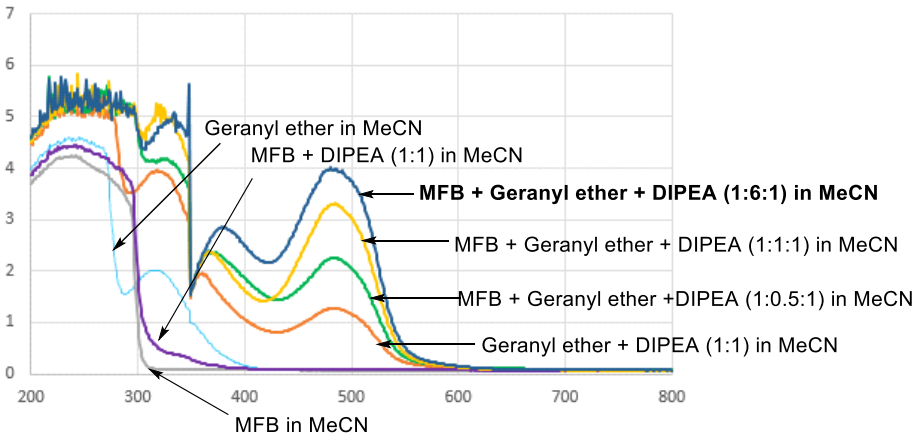
Geranyl ether and methylpentafluoro benzoate (0.1 M) in MeCN

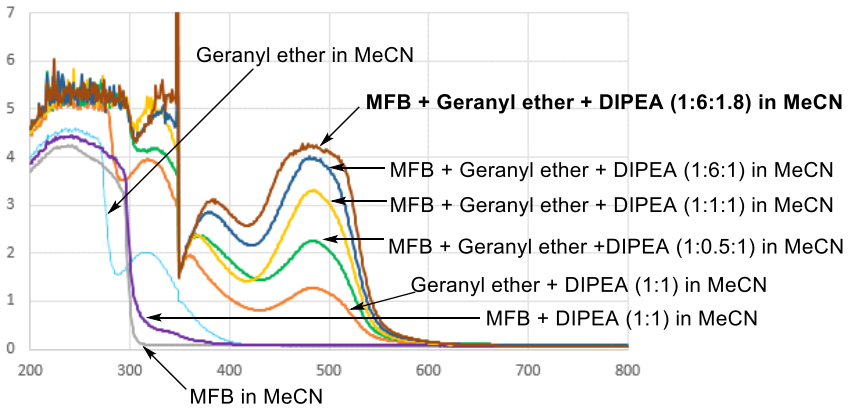







Geranyl ether in MeCN
MFB + DIPEA (1:1) in MeCN
MFB + Geranyl ether + DIPEA (1:1:1) in MeCN
MFB + Geranyl ether +DIPEA (1:0.5:1) in MeCN
Geranyl ether + DIPEA (1:1) in MeCN
MFB in MeCN


Geranyl ether in MeCN
MFB + DIPEA (1:1) in MeCN
MFB + Geranyl ether + DIPEA (1:6:1) in MeCN
MFB + Geranyl ether + DIPEA (1:1:1) in MeCN
MFB + Geranyl ether +DIPEA (1:0.5:1) in MeCN
Geranyl ether + DIPEA (1:1) in MeCN
MFB in MeCN


Geranyl ether in MeCN
MFB + Geranyl ether + DIPEA (1:6:1.8) in MeCN
MFB + Geranyl ether + DIPEA (1:6:1) in MeCN
MFB + Geranyl ether + DIPEA (1:1:1) in MeCN
MFB + Geranyl ether +DIPEA (1:0.5:1) in MeCN
Geranyl ether + DIPEA (1:1) in MeCN
MFB + DIPEA (1:1) in MeCN
MFB in MeCN

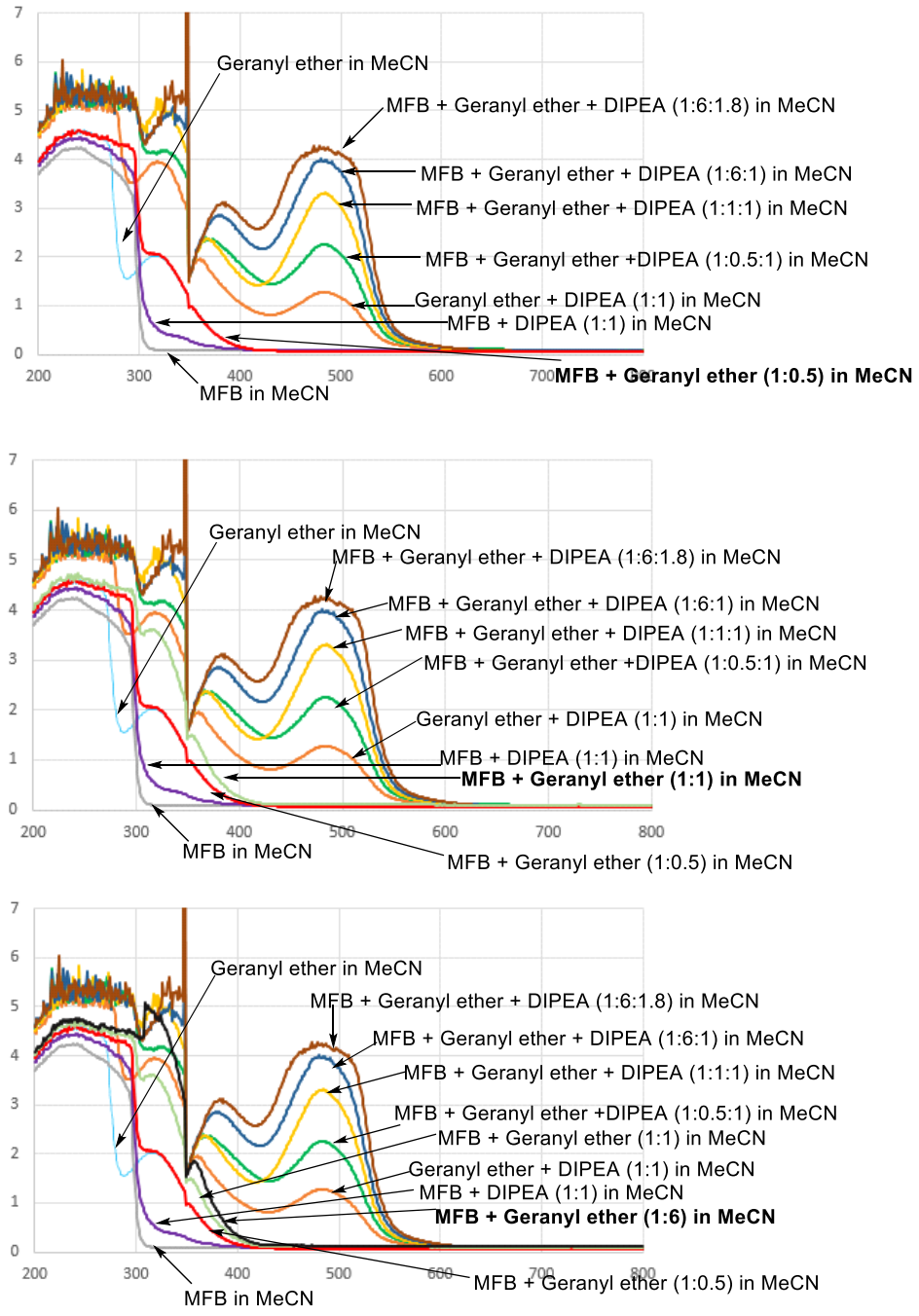
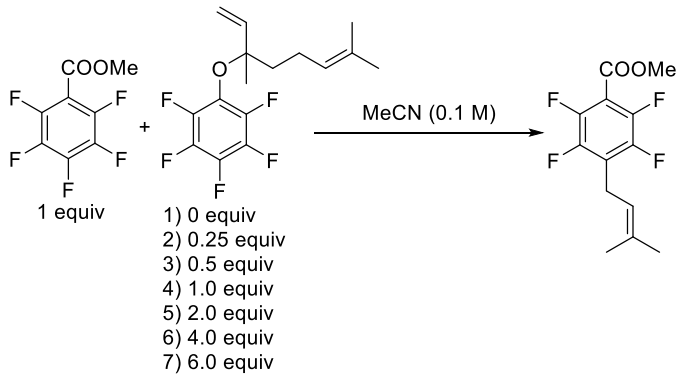


Figure 1.6: UV-Vis experiments

NMR Titration experiments:

Several combinations of ^{19}F NMR titrations were also carried out that in turn demonstrated no significant interactions between perfluoroarene and prenylating agent at ground state.

Variation in Geranyl ether (without DIPEA)
Internal standard - Fluorobenzene



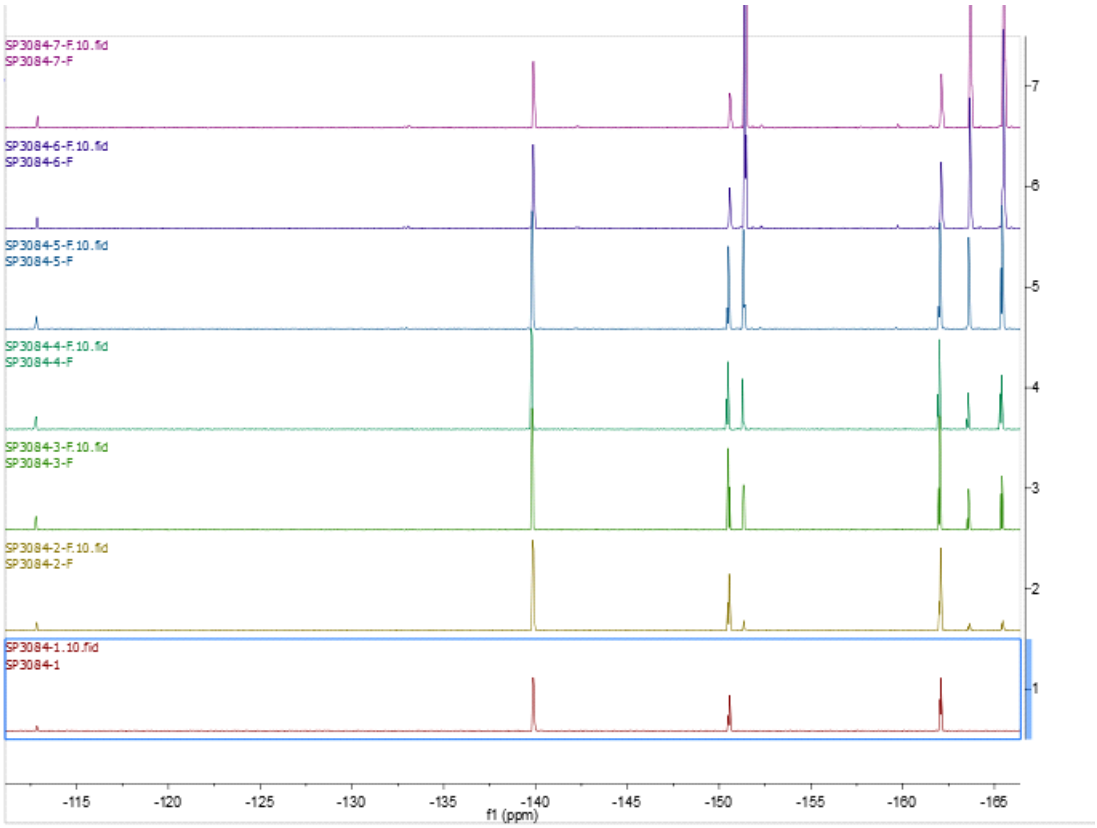
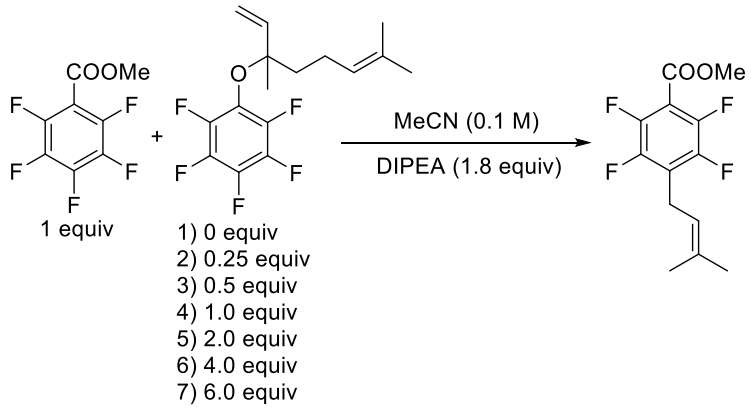


Figure 1.7: NMR titration experiments: variations in geranyl ether (without DIPEA)

NMR Titrations - Variation in Geranyl ether (with DIPEA)



Internal standard - Monofluorobenzene

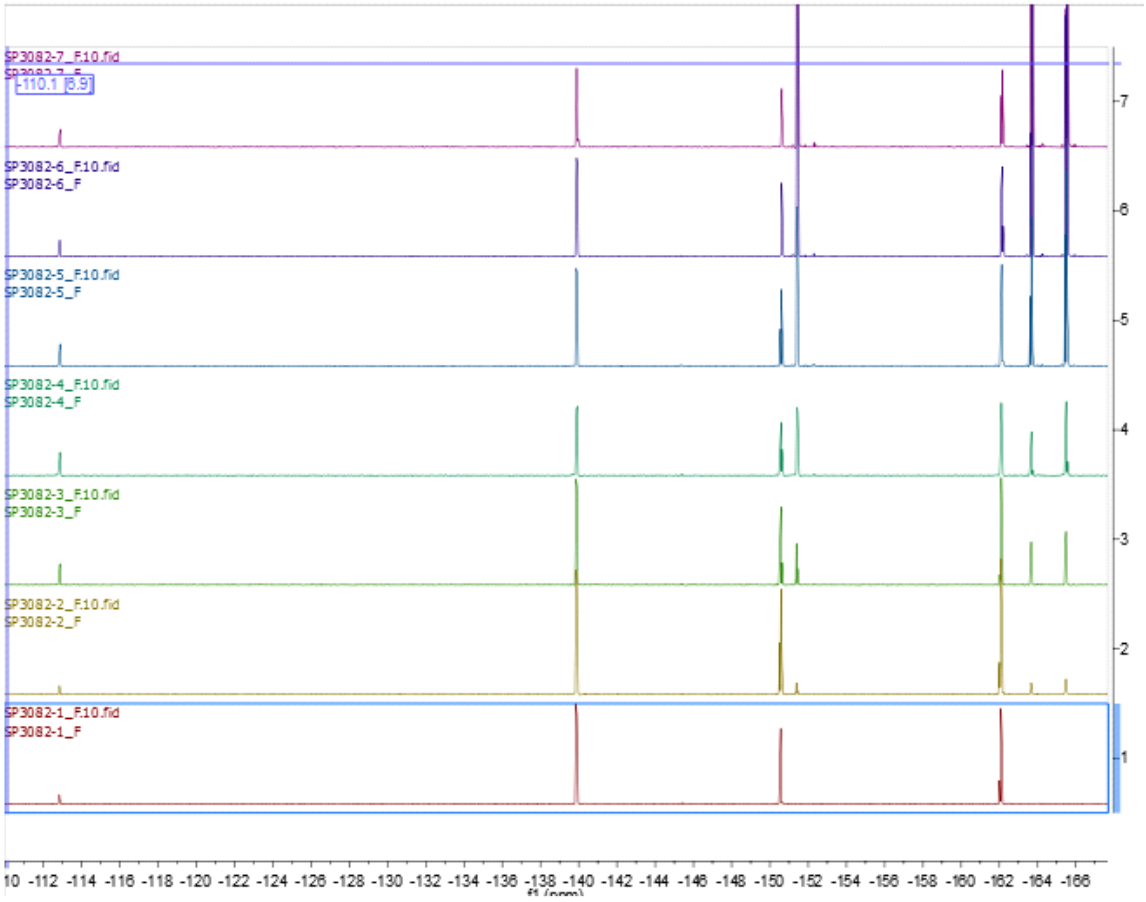
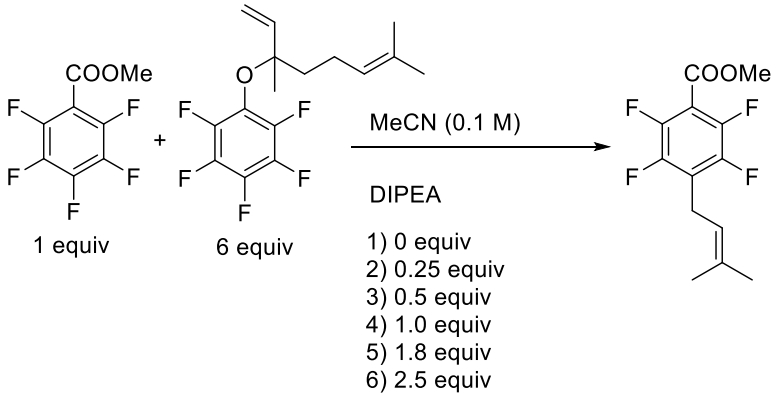


Figure 1.8: NMR titration experiments: variations in geranyl ether (with DIPEA)

Variation in DIPEA



Internal standard - Monofluorobenzene

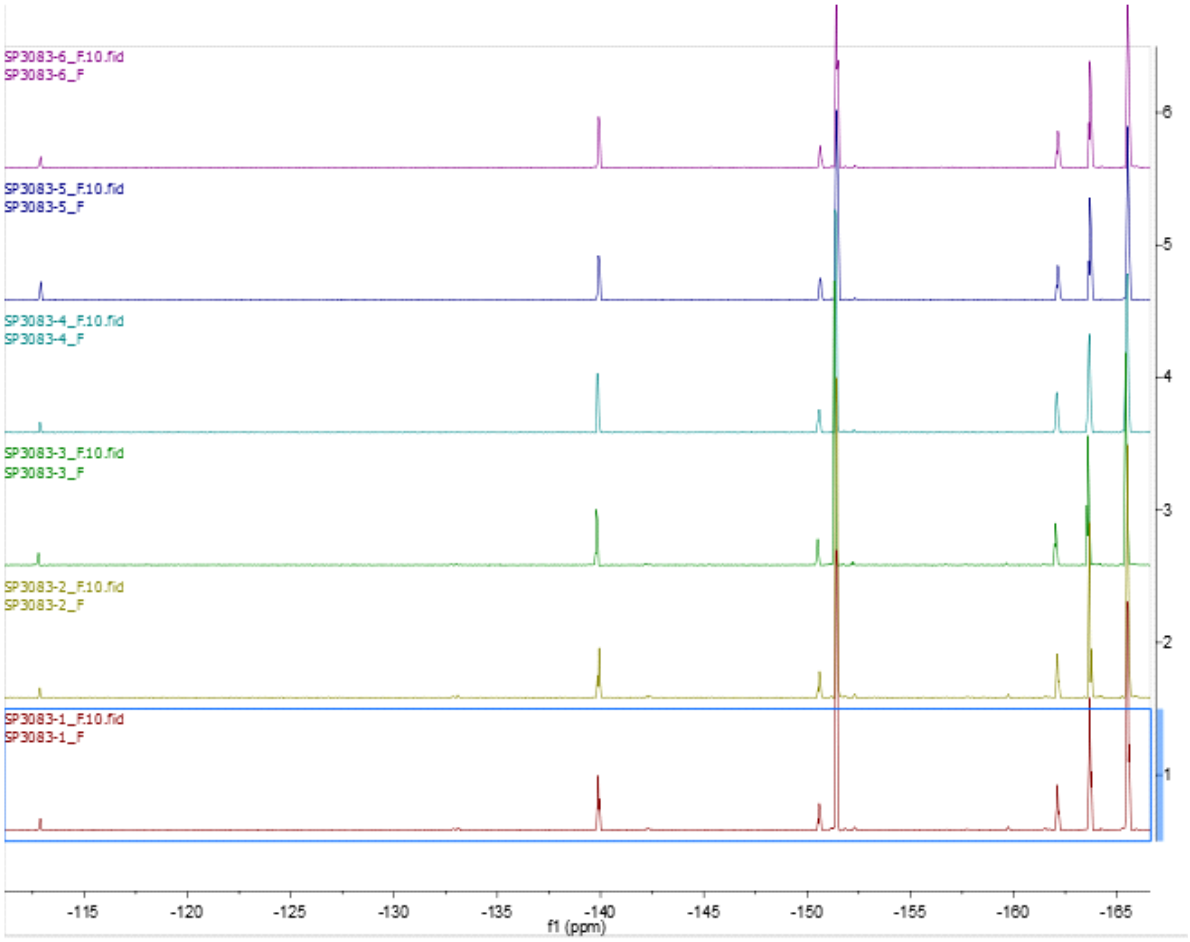


Figure 1.9: NMR titration experiments: variations in DIPEA

Evidence for no post-reaction isomerization in geranylated products:

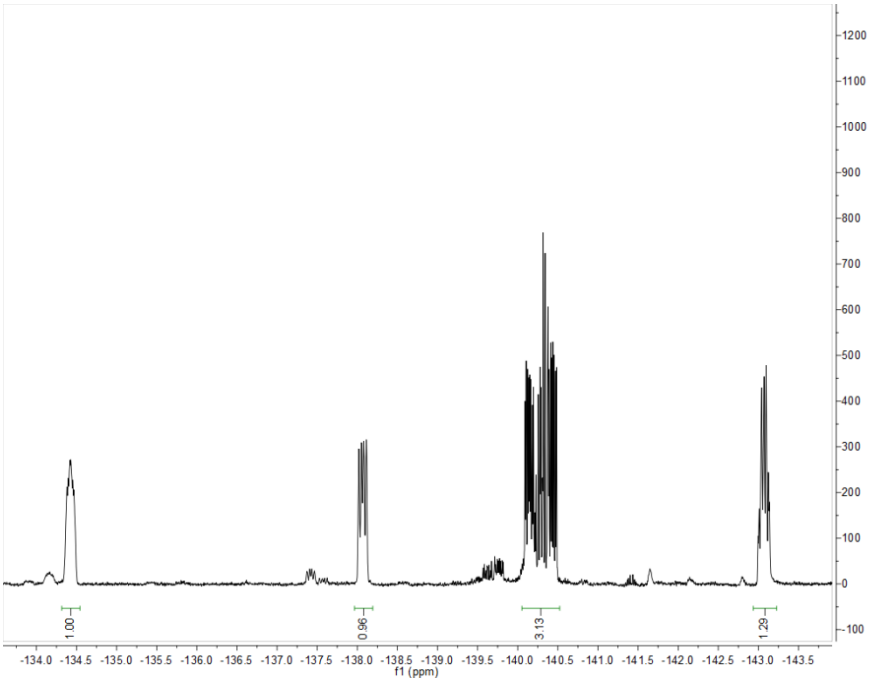
Table 1.17: Evidence for no post-reaction isomerization in geranylated products:

Entry	Conditions 0.025 M MeCN	*ortho*-Ger enriched mixture ortho:para ratio[a]	*para*-Ger enriched mixture ortho-para ratio[a]
1	Mixtures at 22 ^{o}C, 3 h	1:0.65	1:0.96
2.	Mixtures heated to 45 ^{o}C, 3 h	1:0.645	1:0.96
3.	Mixtures, 0.3 mol% fac-Ir(ppy)$_3$ blue LEDs, 3 h in 0 ^{o}C	1:0.64	1:0.96
4.	Mixtures, 0.3 mol% fac-Ir(ppy)$_3$ blue LEDs, 3 h in 22 ^{o}C	1:0.65	1:0.955
5.	Mixtures, 0.3 mol% fac-Ir(ppy)$_3$ blue LEDs, 3 h in 45 ^{o}C	1:0.645	1:0.965

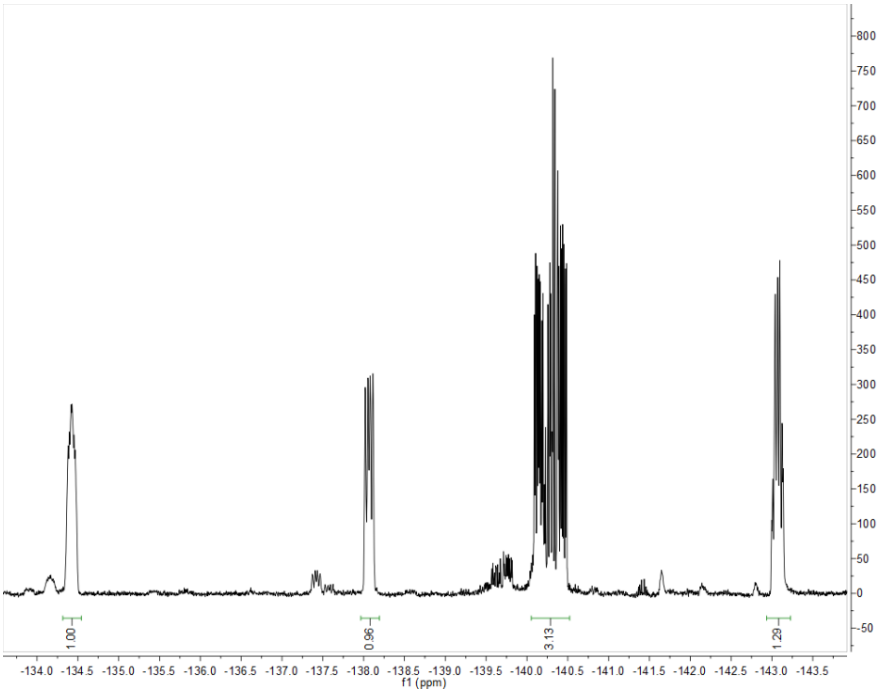
([a]Determined by integration of the ^{19}F NMR signal at -134.4 and -143.1 ppm after normalization)

In order to check for post-reaction isomerization of geranylated products, while we were not able to completely resolve these isomers, we were able to collect samples enriched in one or the other isomers after chromatography by taking early and late fractions. When we re-subjected the enriched mixtures to a number of conditions (see above), we saw that the ratio never changed. This is clear evidence that the selectivity is a kinetic phenomenon and not subject to equilibration.

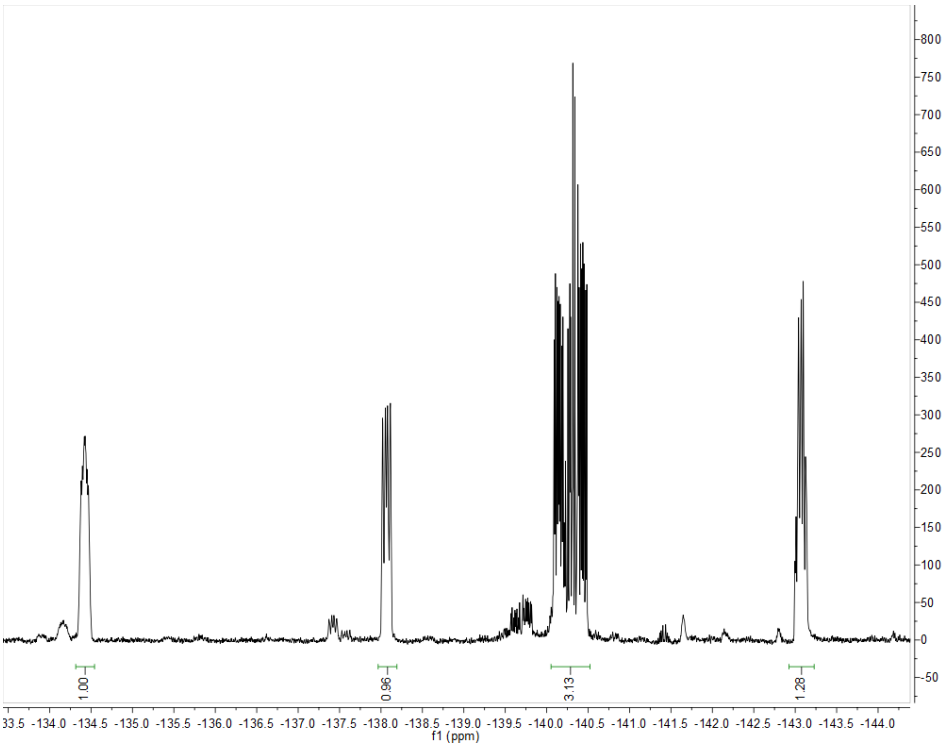
1. ortho-Ger enriched mixture



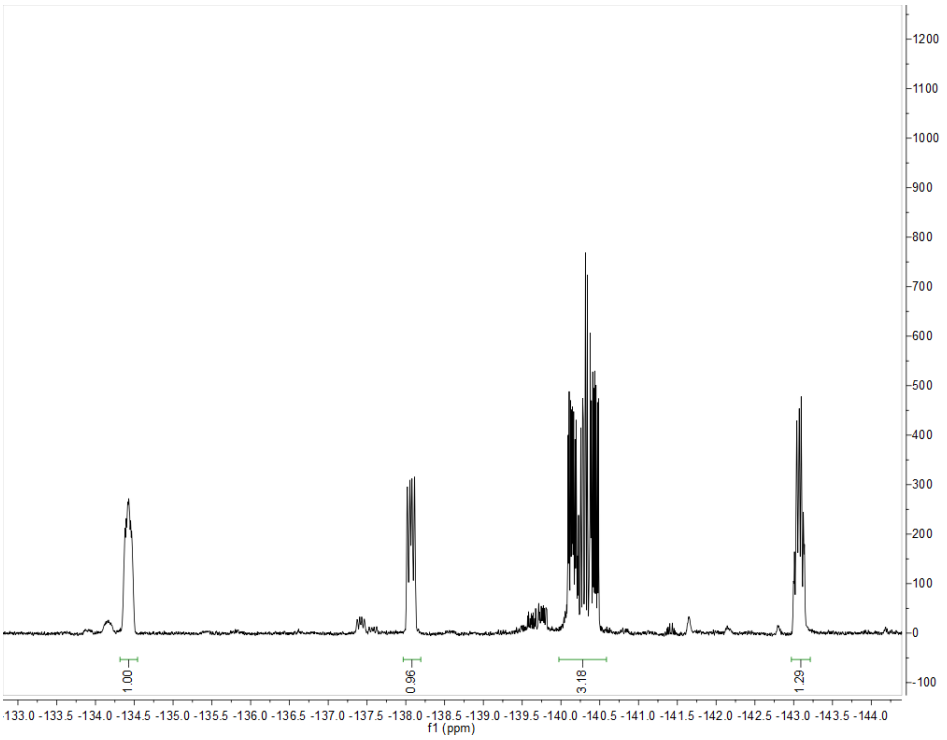
2.



3.



4.



5.

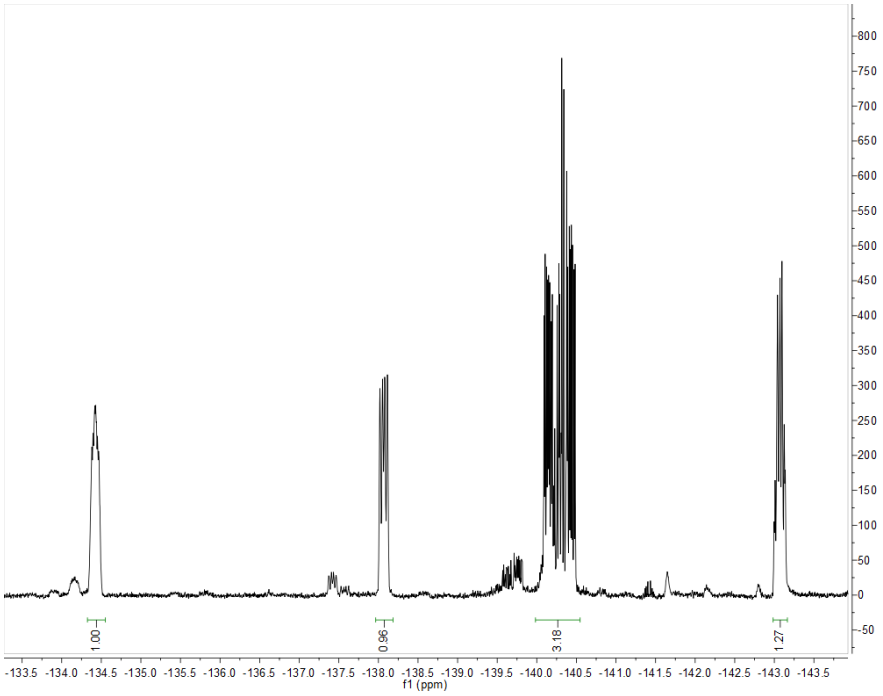
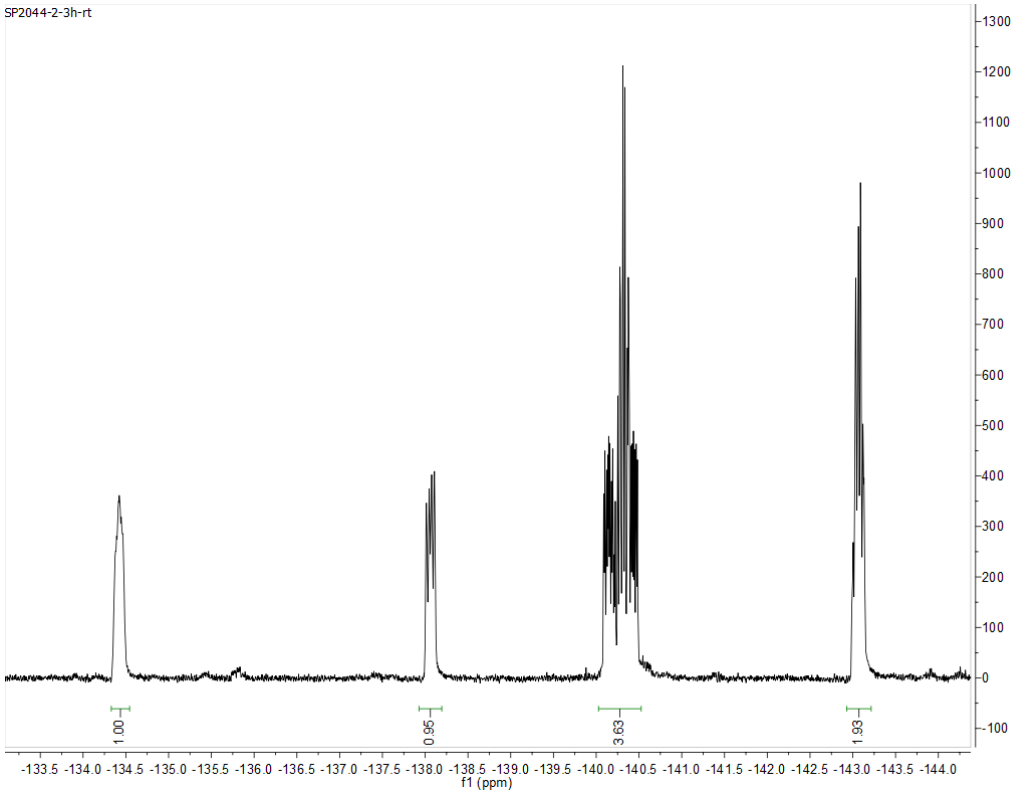
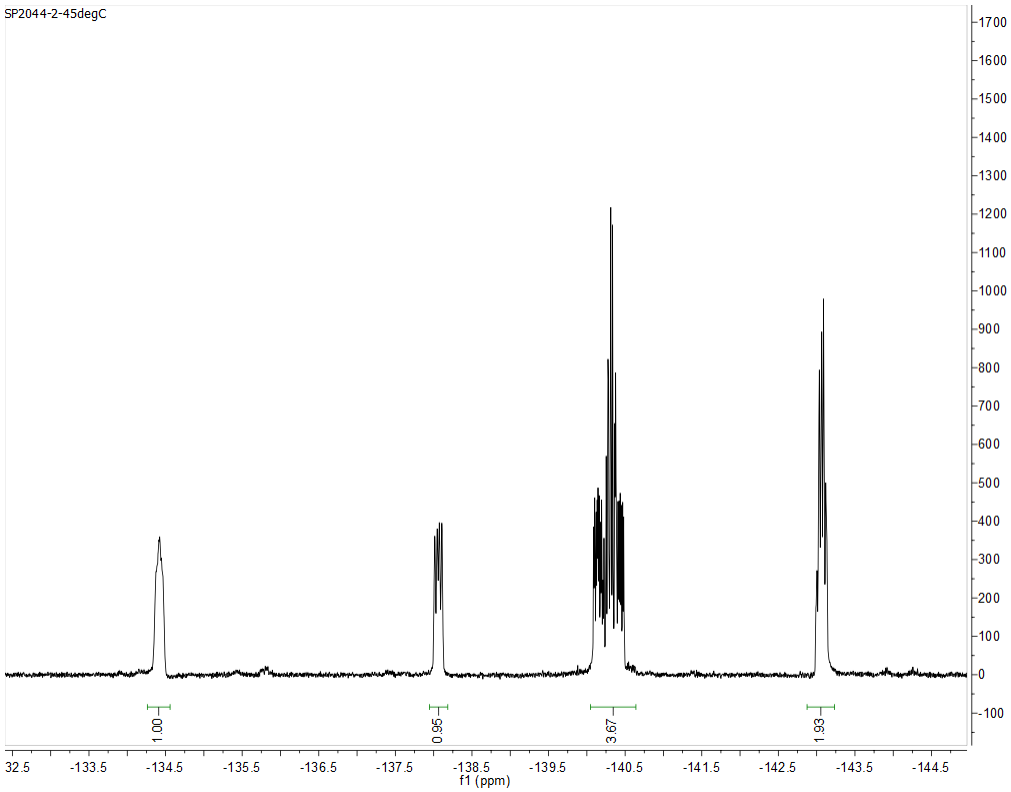


Figure 1.10: *ortho*-Ger enriched mixture

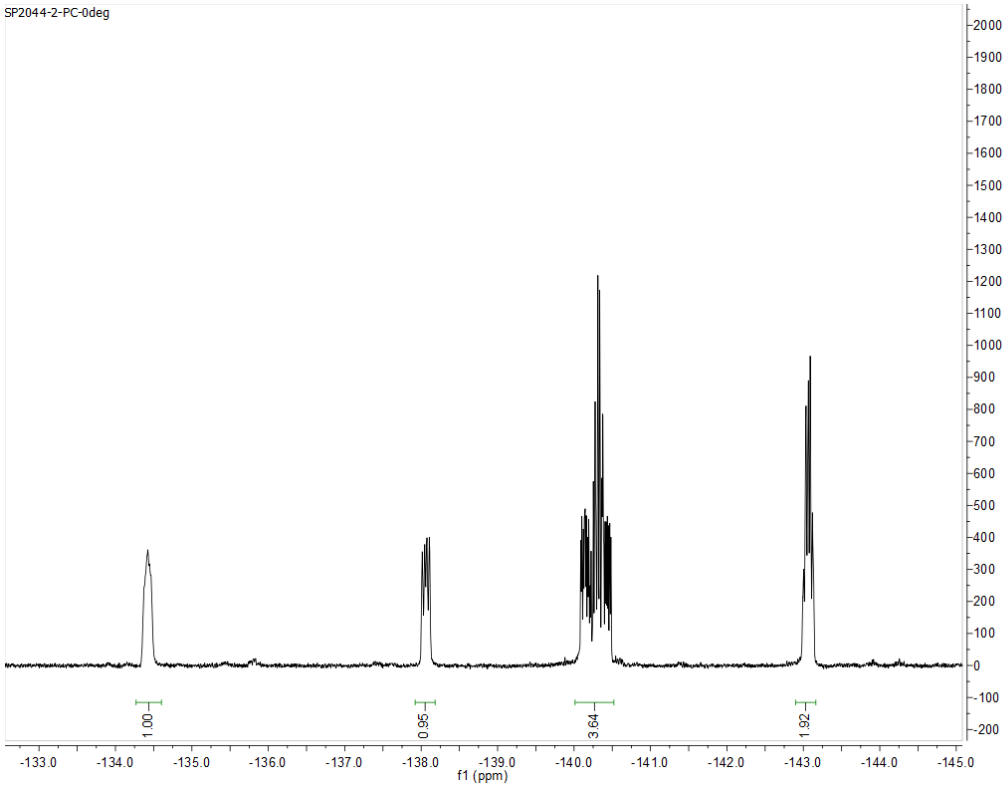
1. *para*-Ger enriched mixture



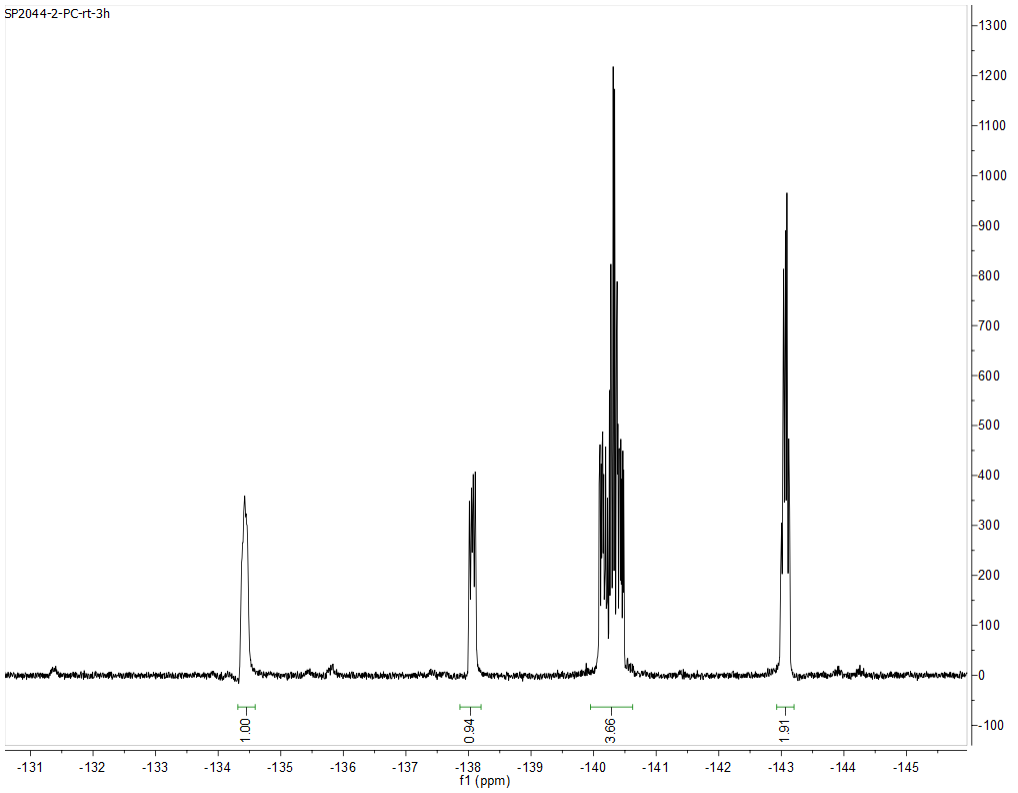
2.


SP2044-2-45degC
1.00
0.95
3.67
1.93
f1 (ppm)

3.


SP2044-2-PC-0deg
1.00
0.95
3.64
1.92
f1 (ppm)

4.



5.

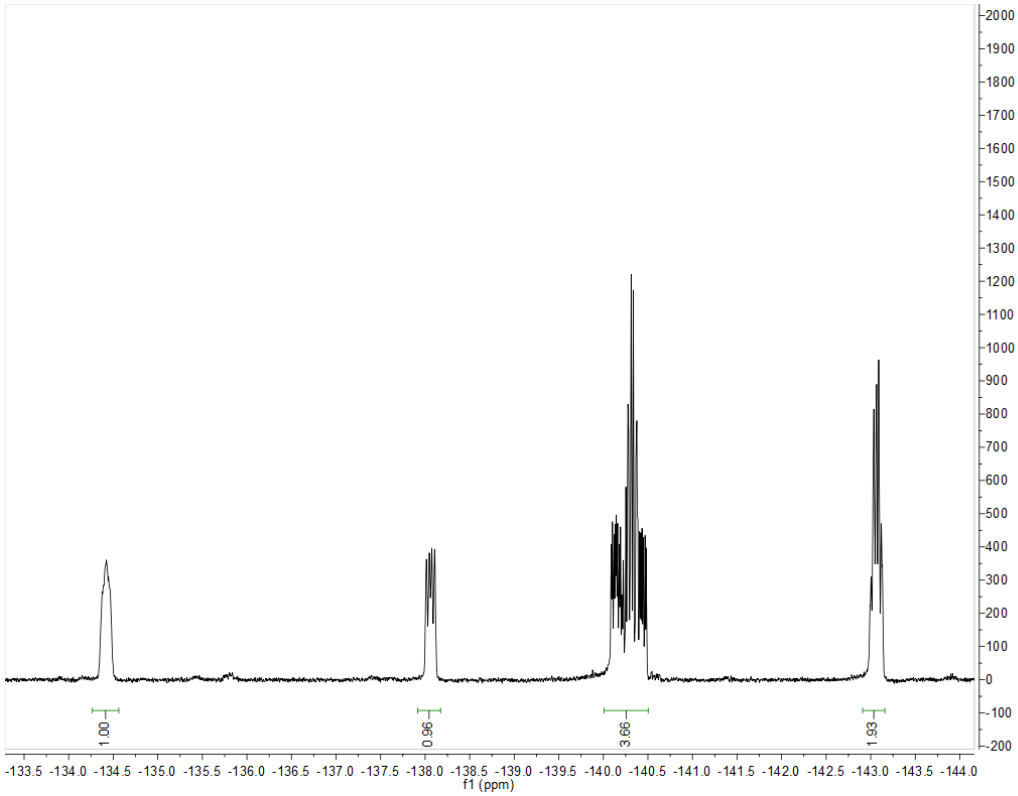
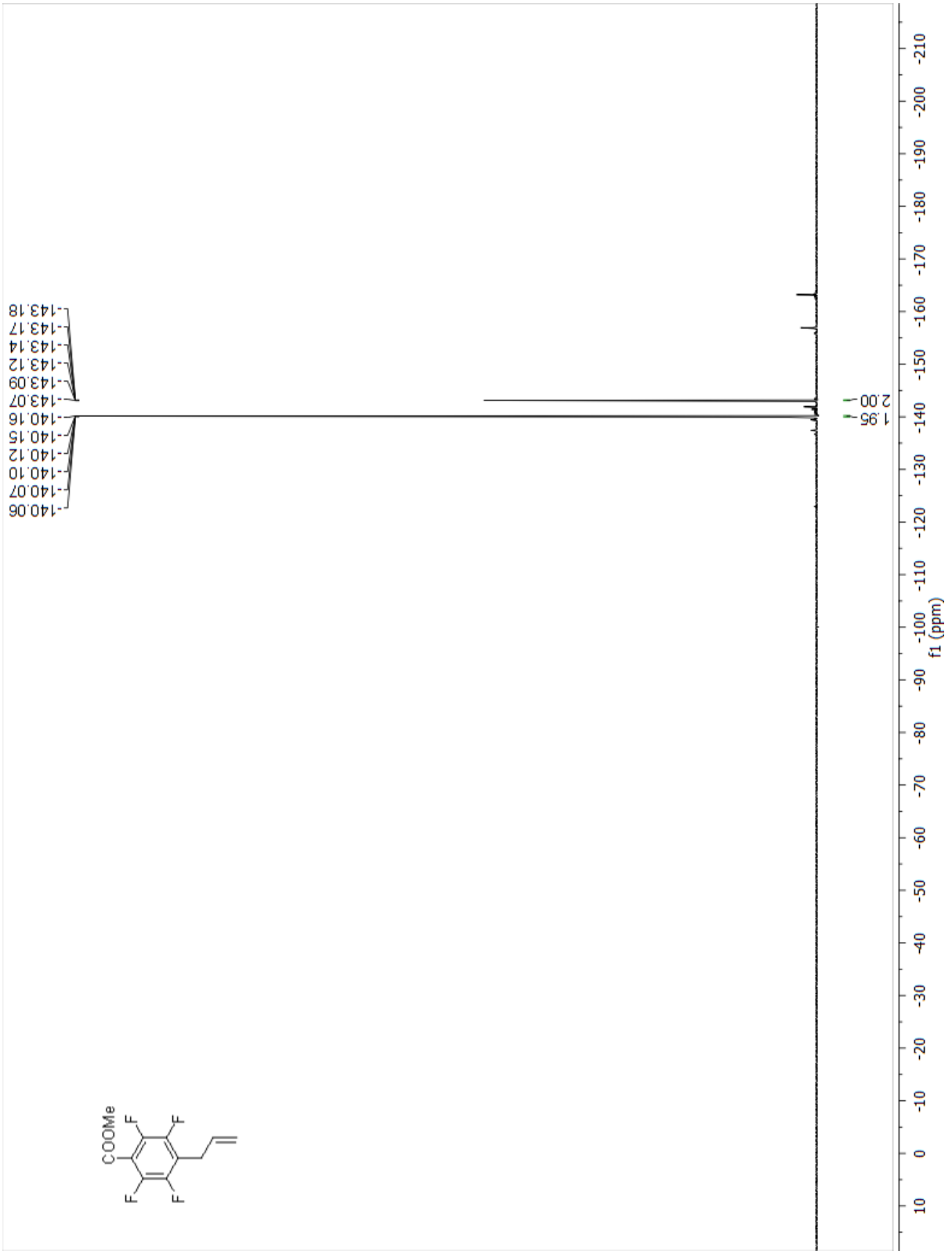
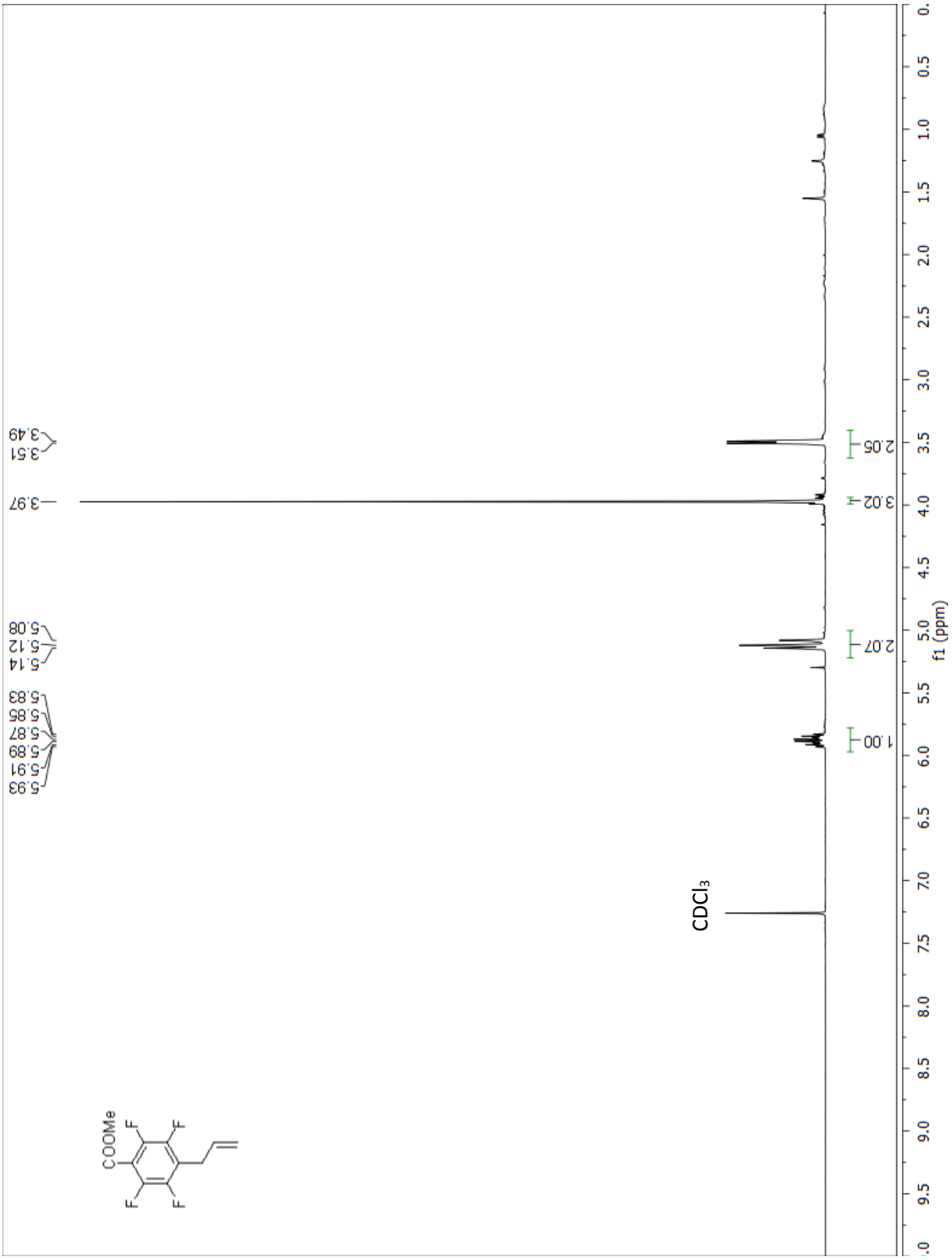


Figure 1.11: *para*-Ger enriched mixture

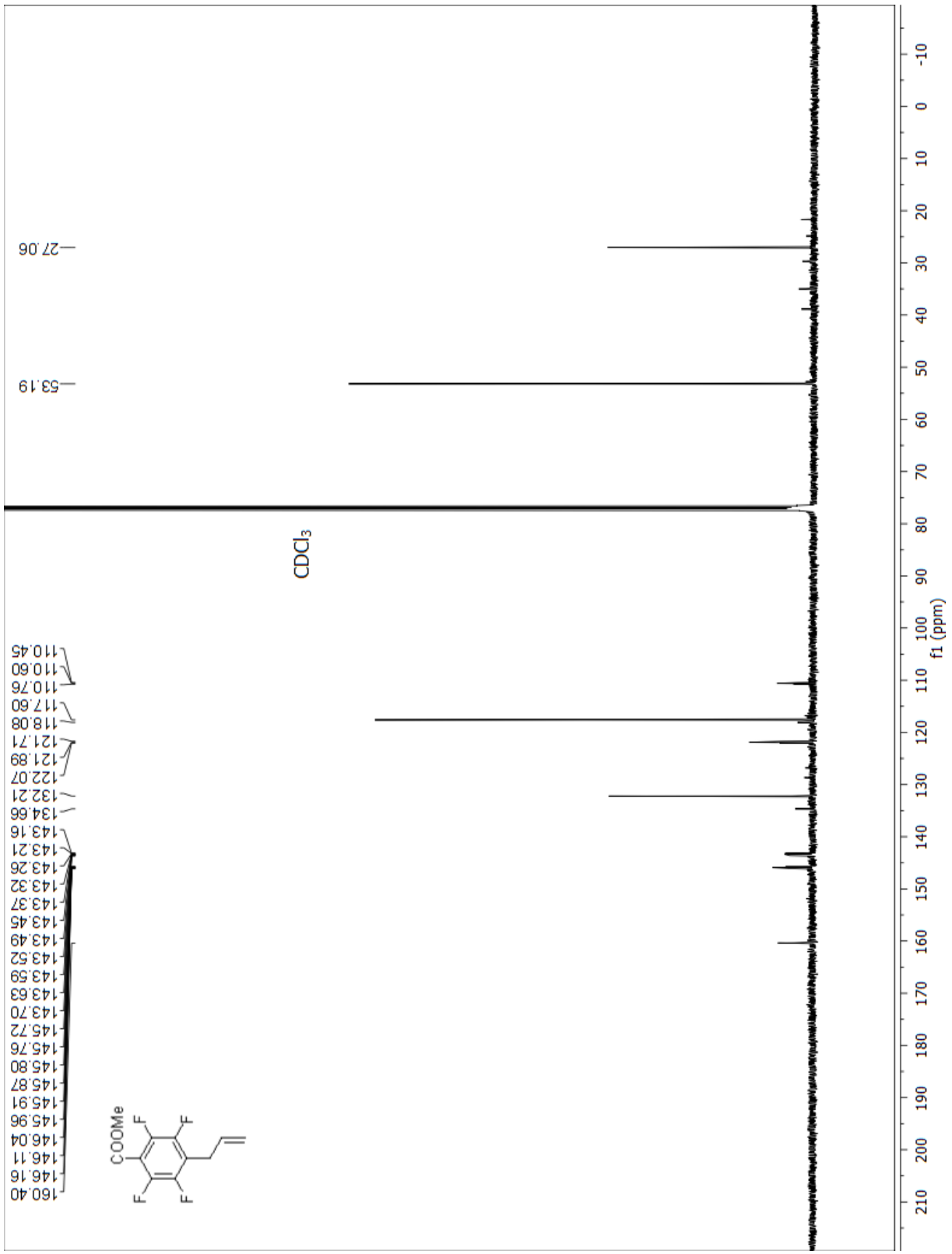
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl 4-allyl-2,3,5,6-tetrafluorobenzoate (5a)**



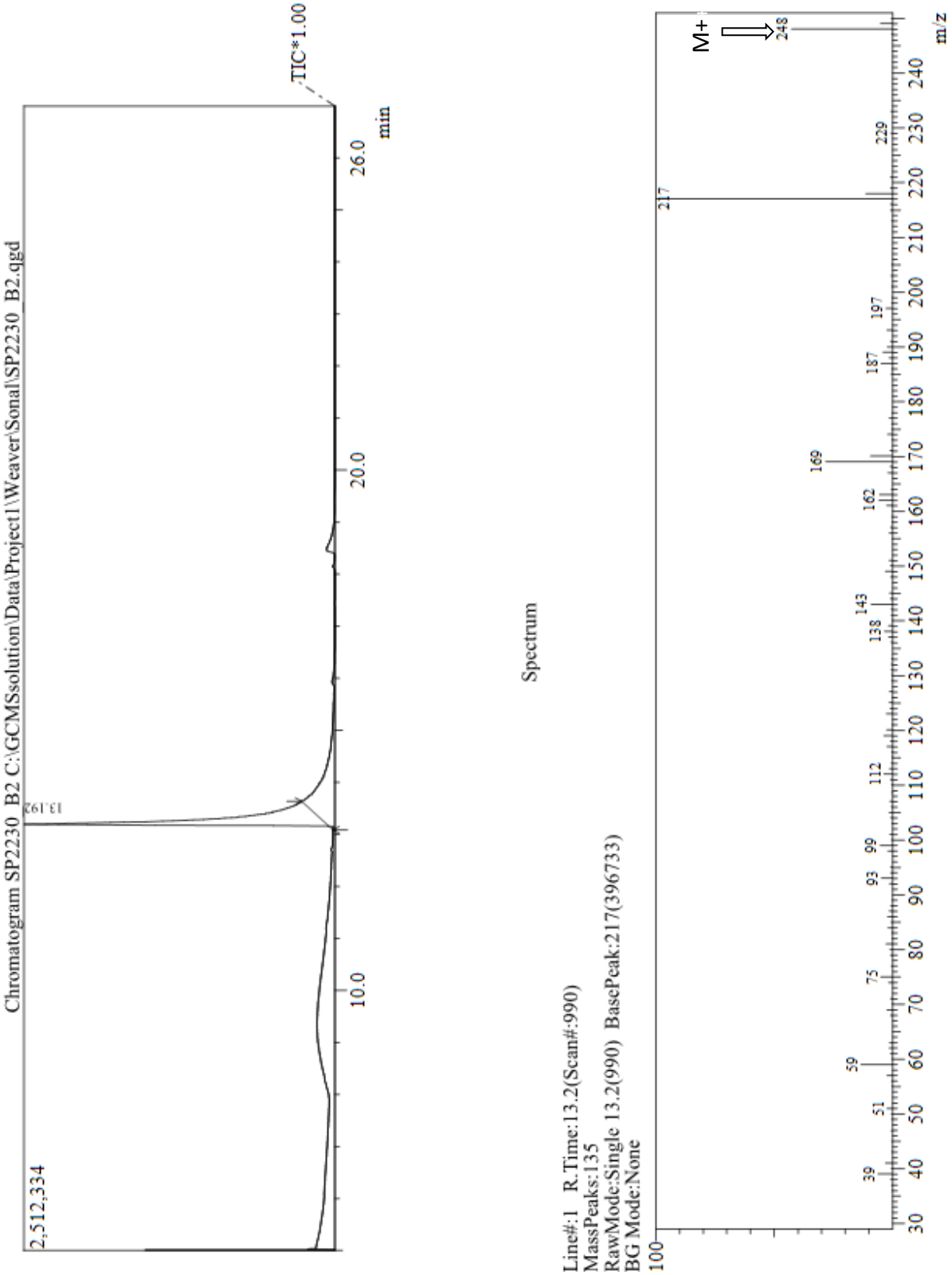
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **methyl 4-allyl-2,3,5,6-tetrafluorobenzoate (5a)**



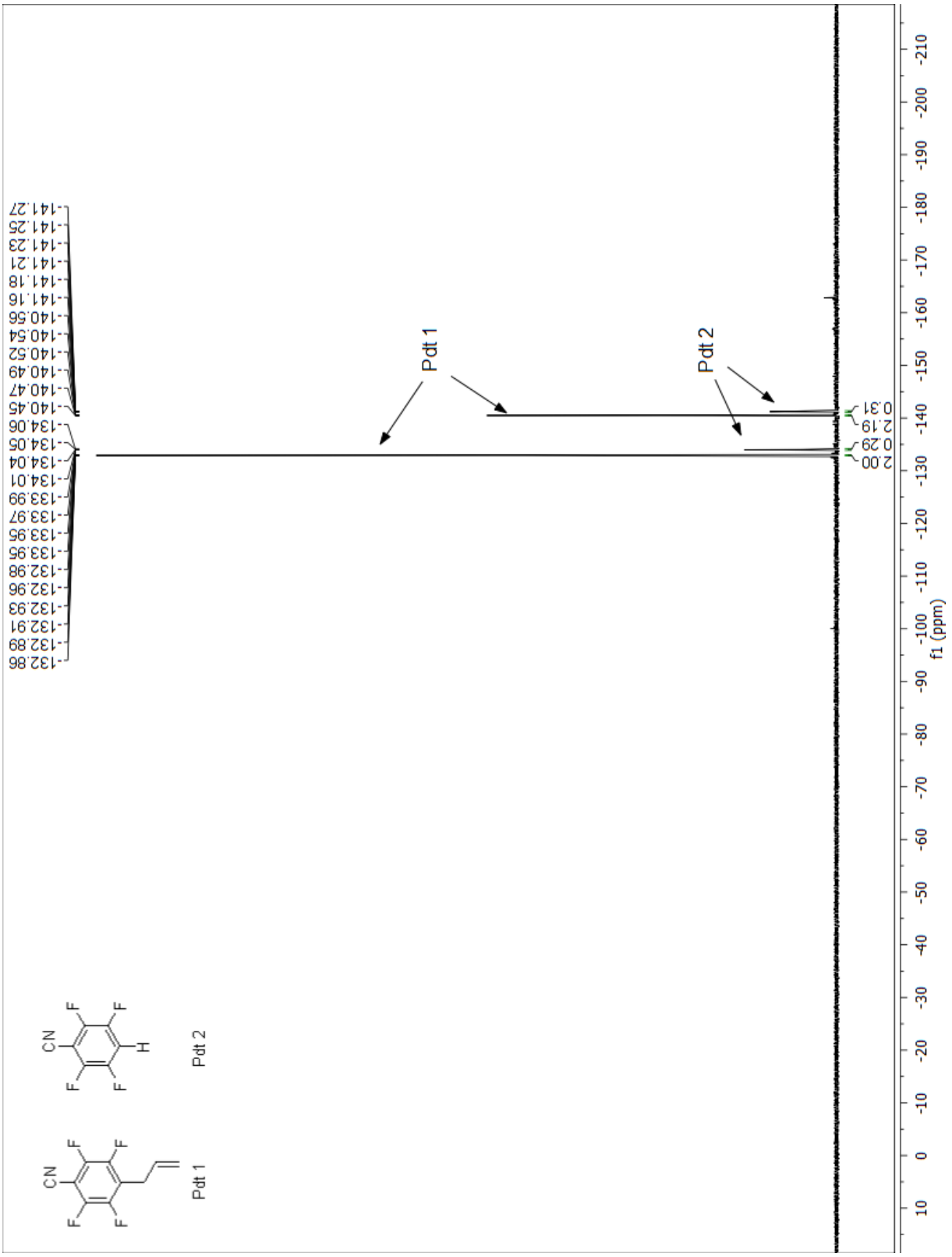
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **methyl 4-allyl-2,3,5,6-tetrafluorobenzoate (5a)**



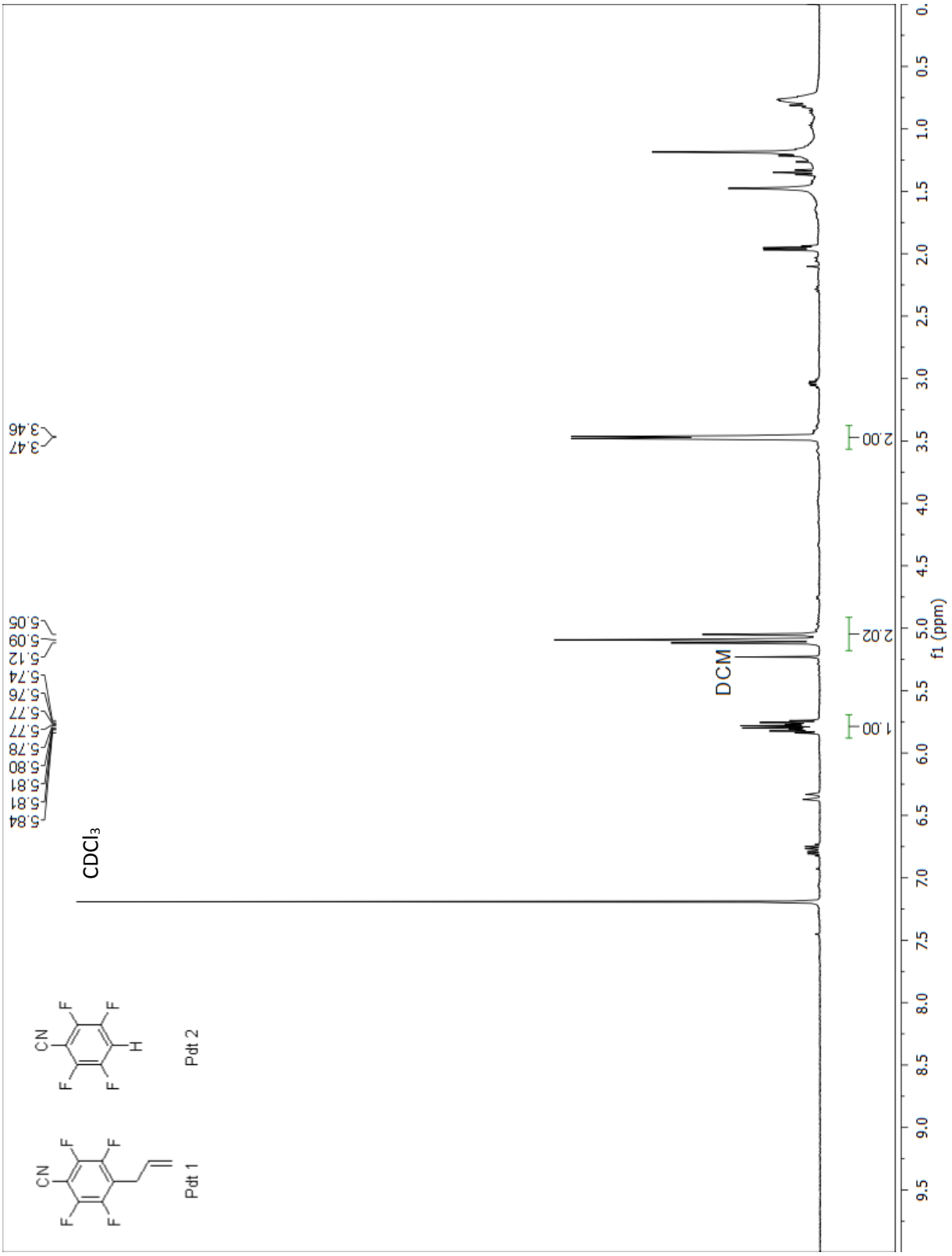
GC and MS of **methyl 4-allyl-2,3,5,6-tetrafluorobenzoate (5a)**



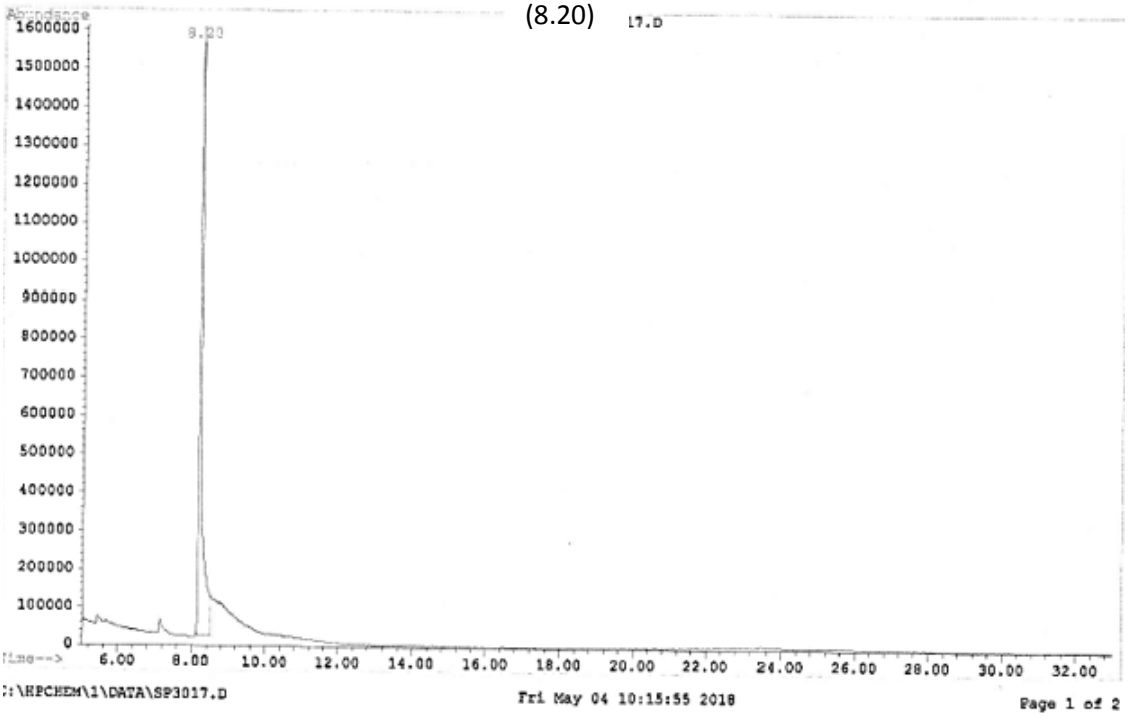
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **4-allyl-2,3,5,6-tetrafluorobenzonitrile (5b)**

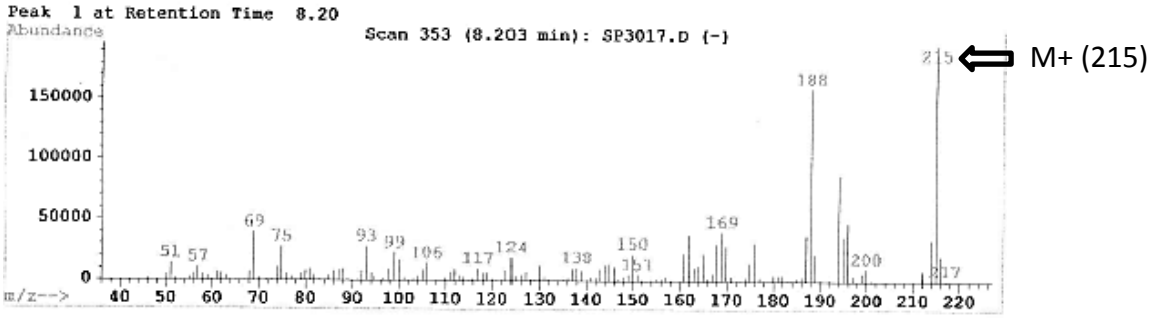


^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **4-allyl-2,3,5,6-tetrafluorobenzonitrile (5b)**

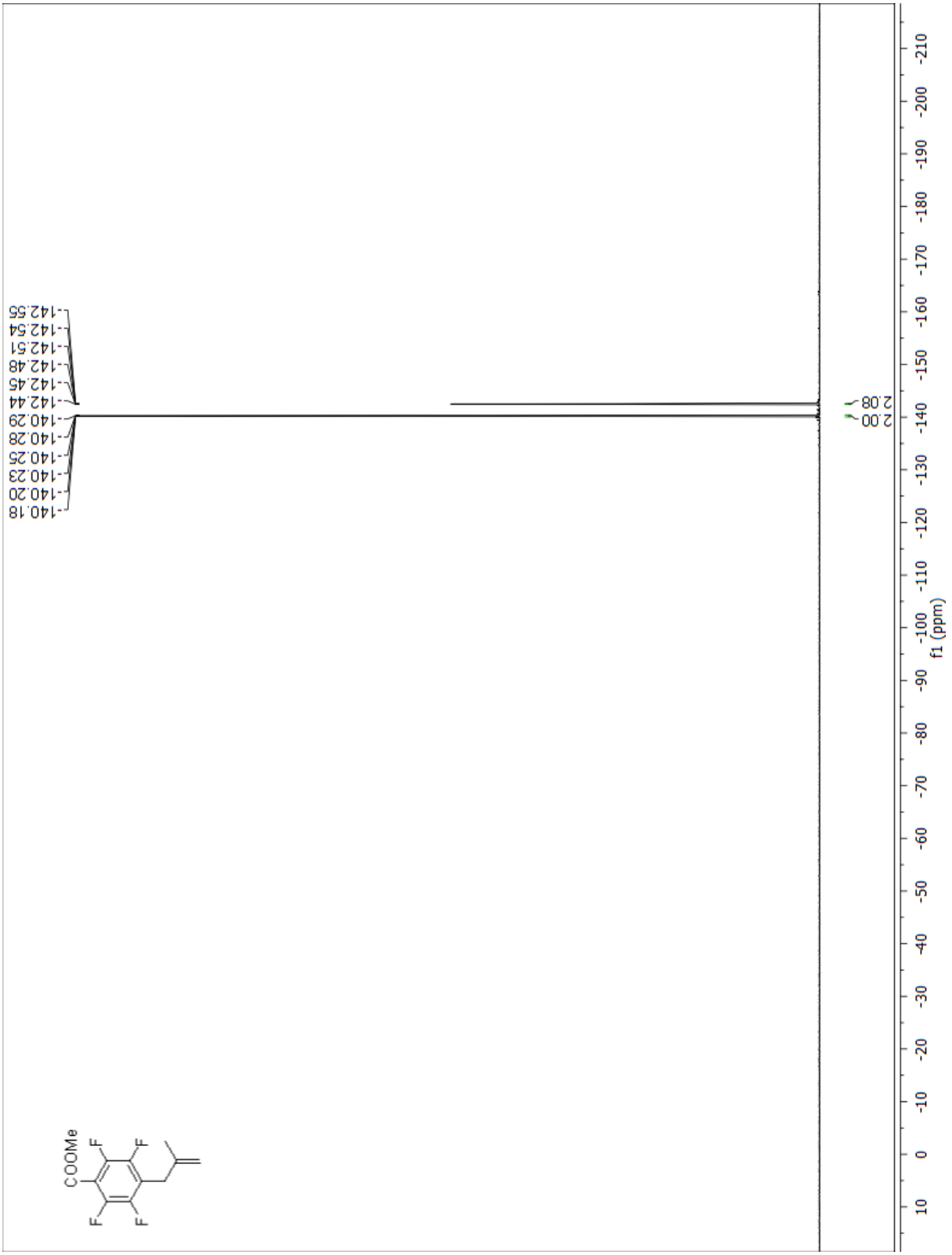


GC and MS of **4-allyl-2,3,5,6-tetrafluorobenzonitrile (5b)**

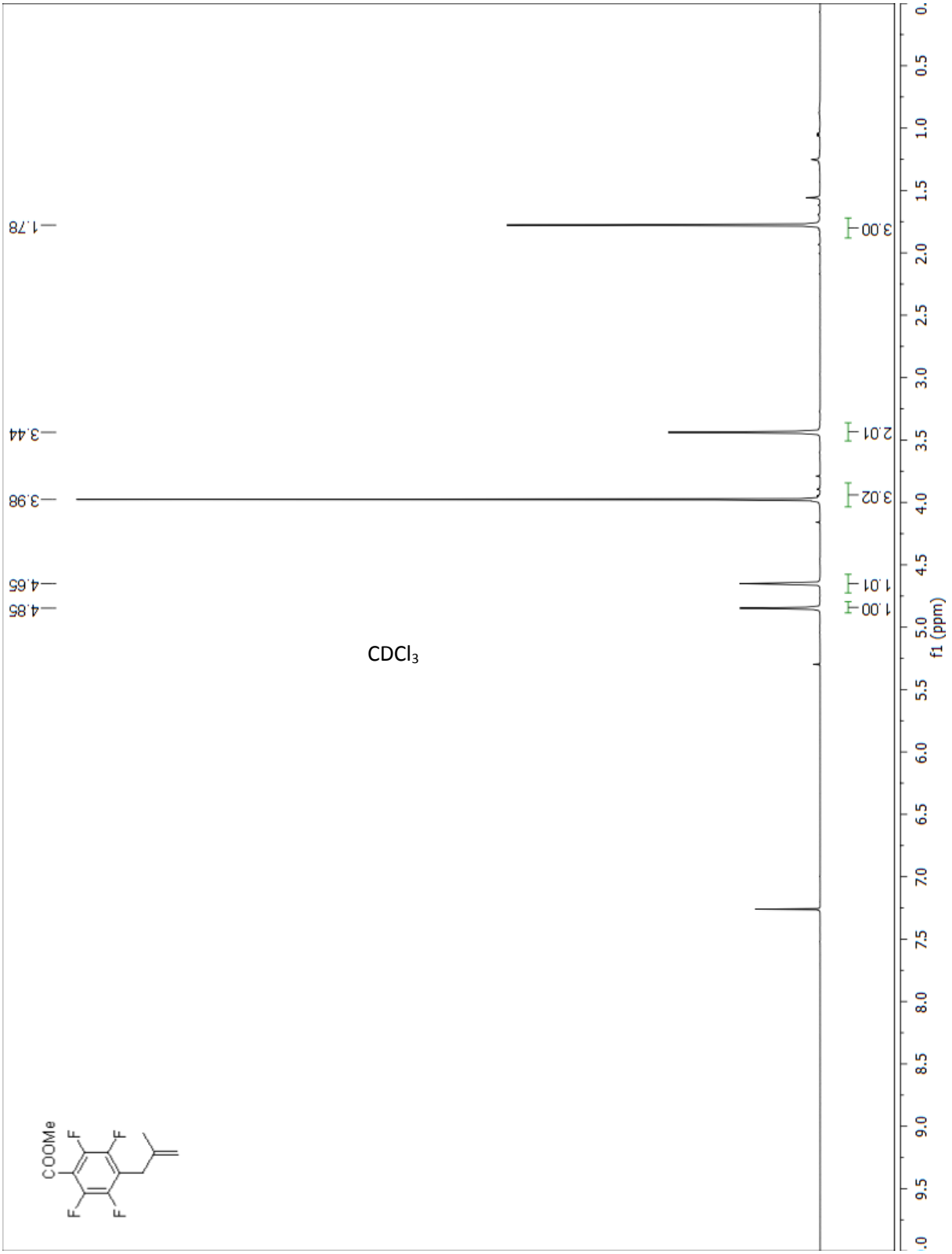




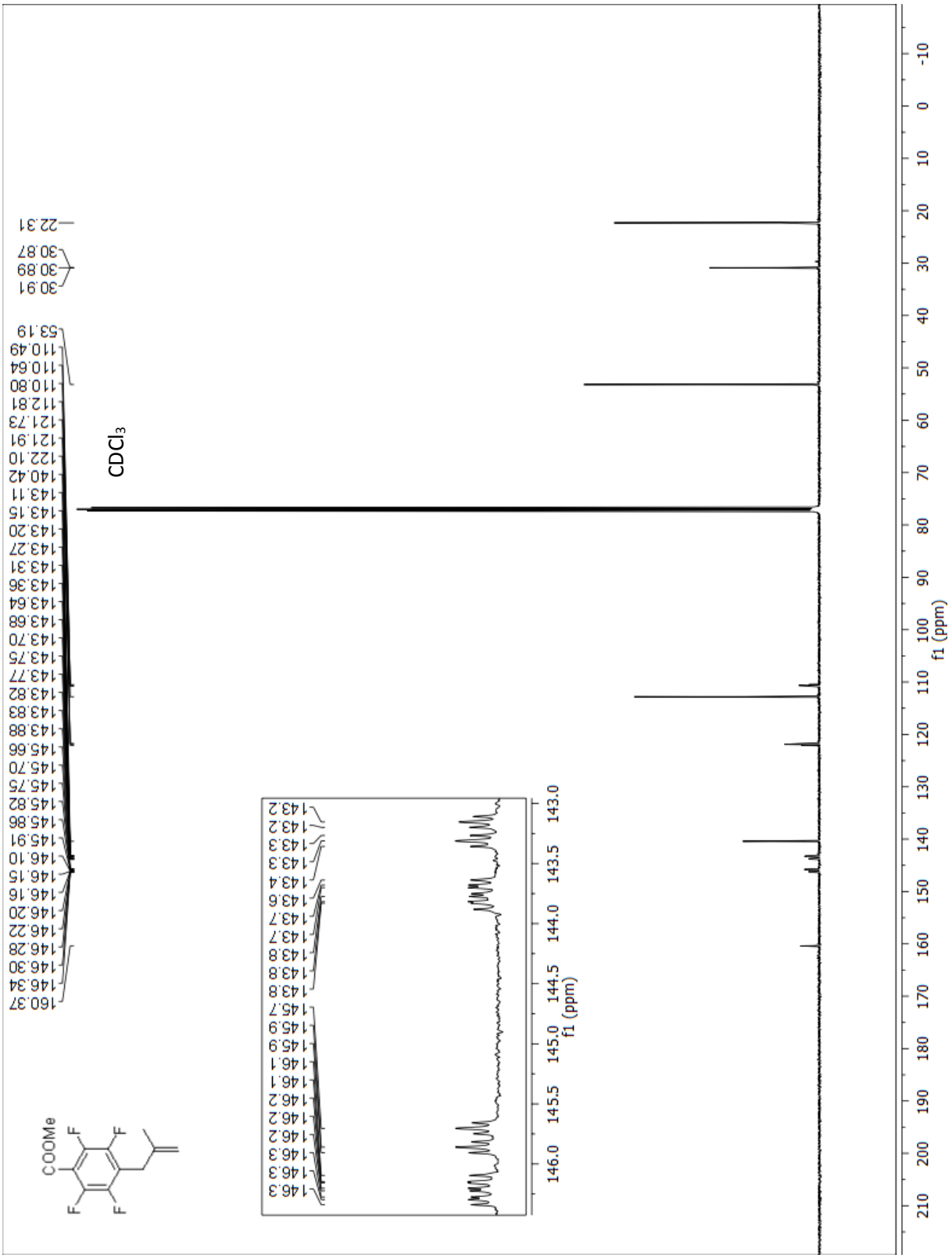
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzoate (5c)**



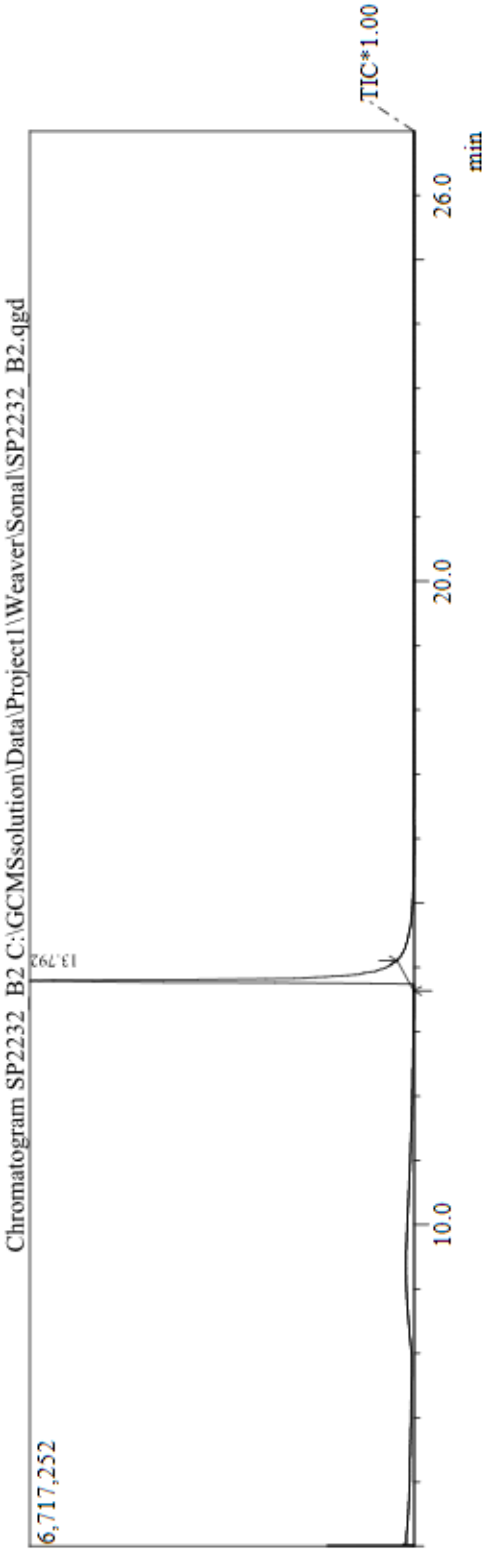
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **methyl 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzoate (5c)**

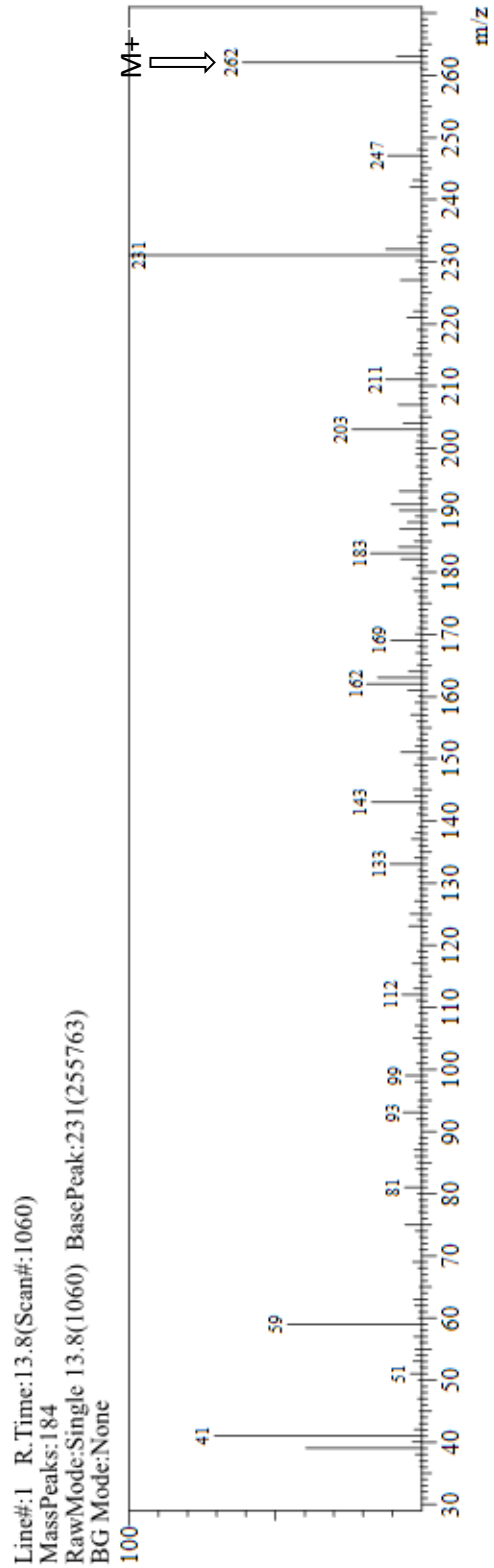


^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **methyl 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzoate (5c)**

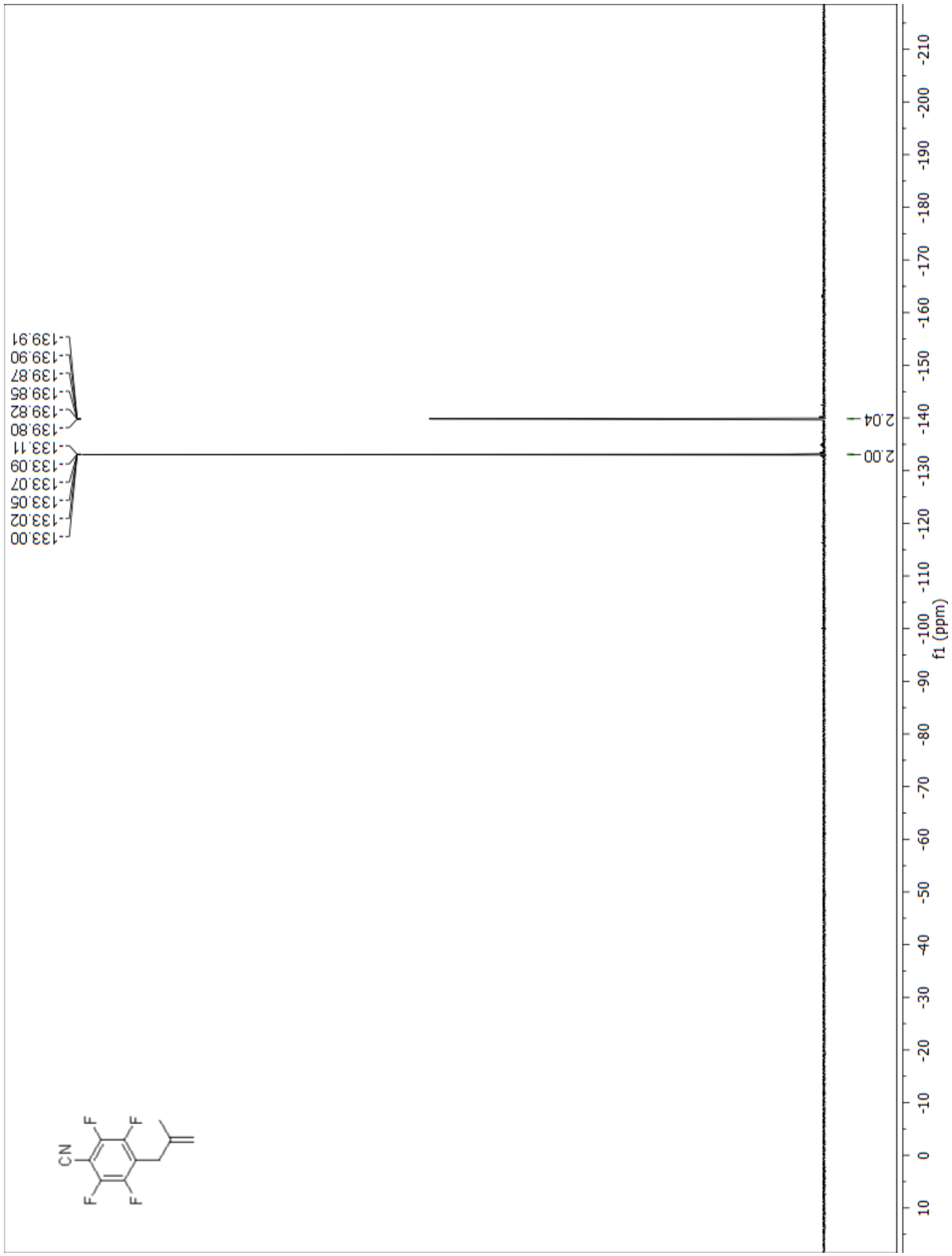


GC and MS of **methyl 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzoate (5c)**

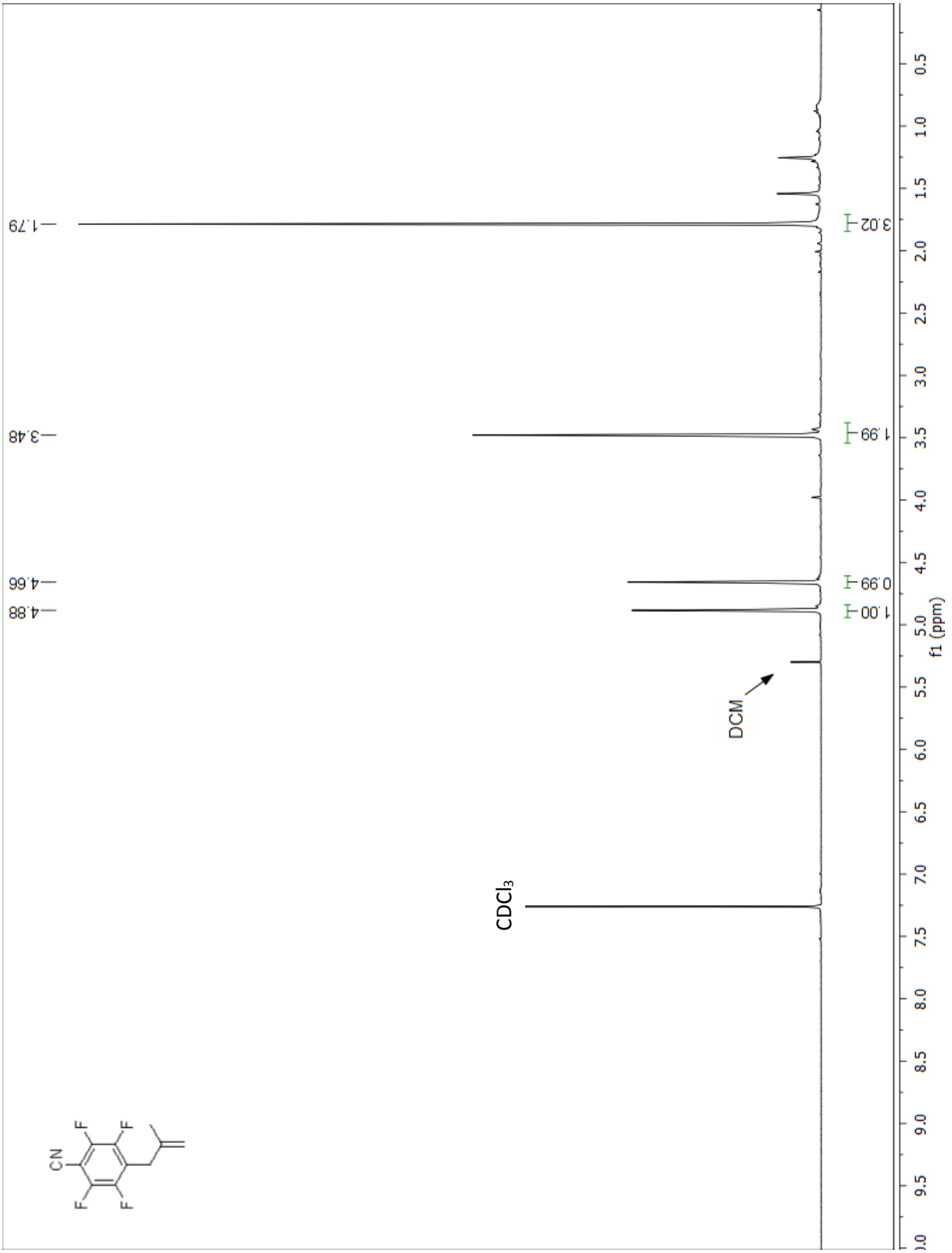




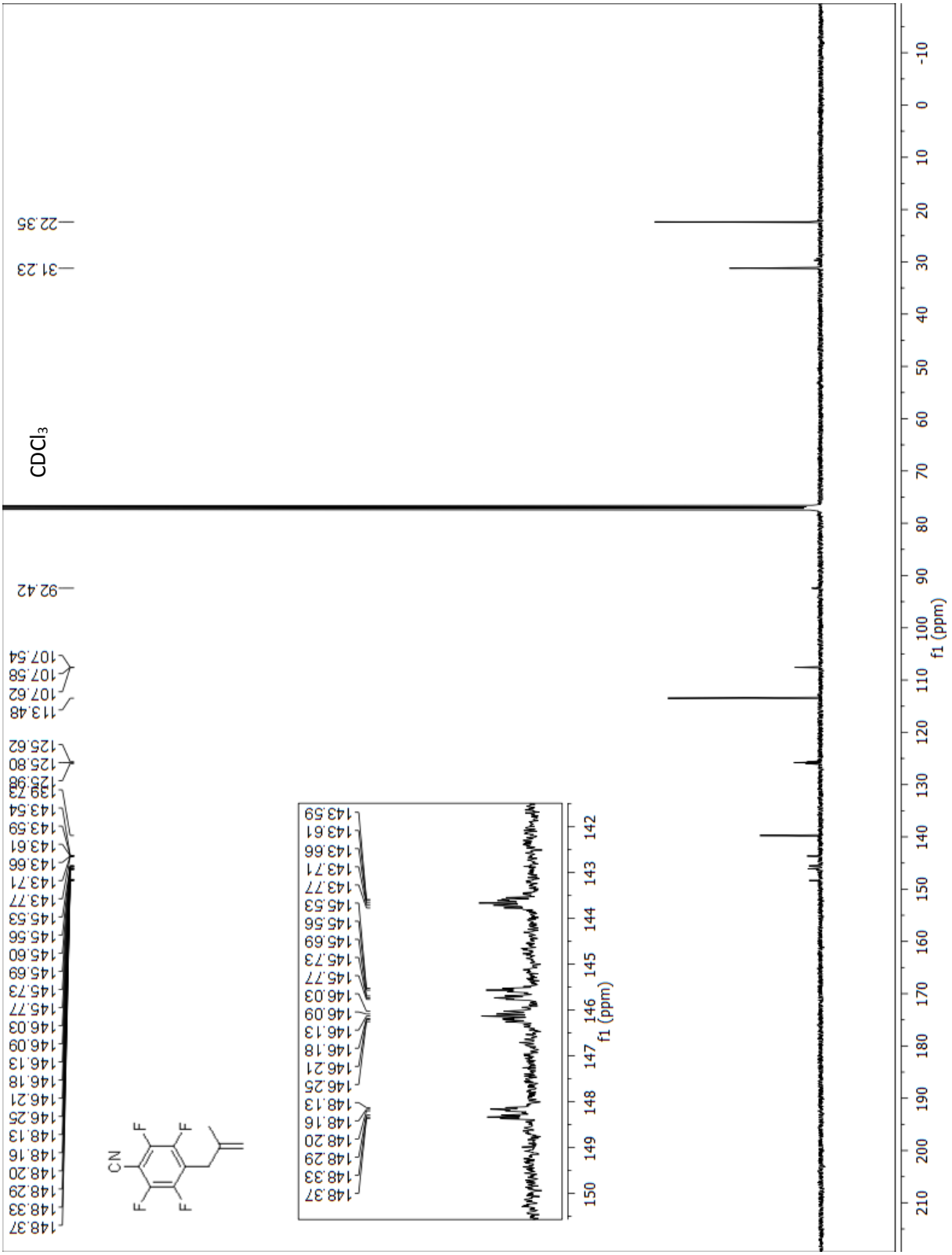
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzonitrile (5d)



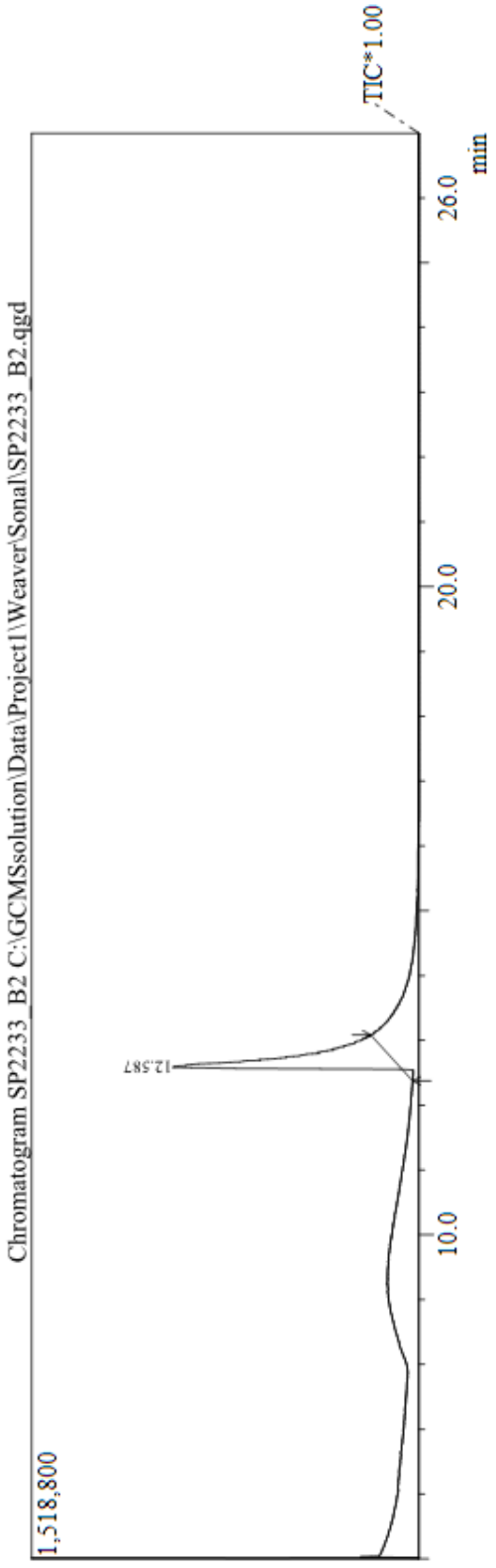
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzonitrile (5d)

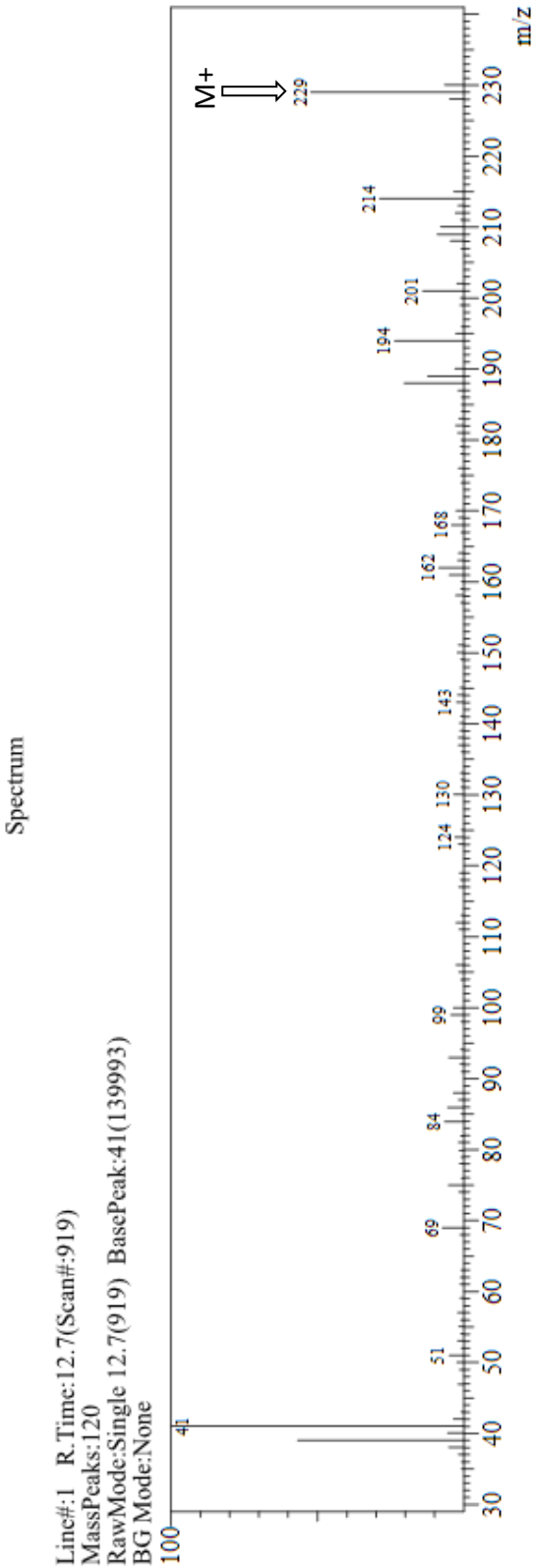


^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzonitrile (5d)

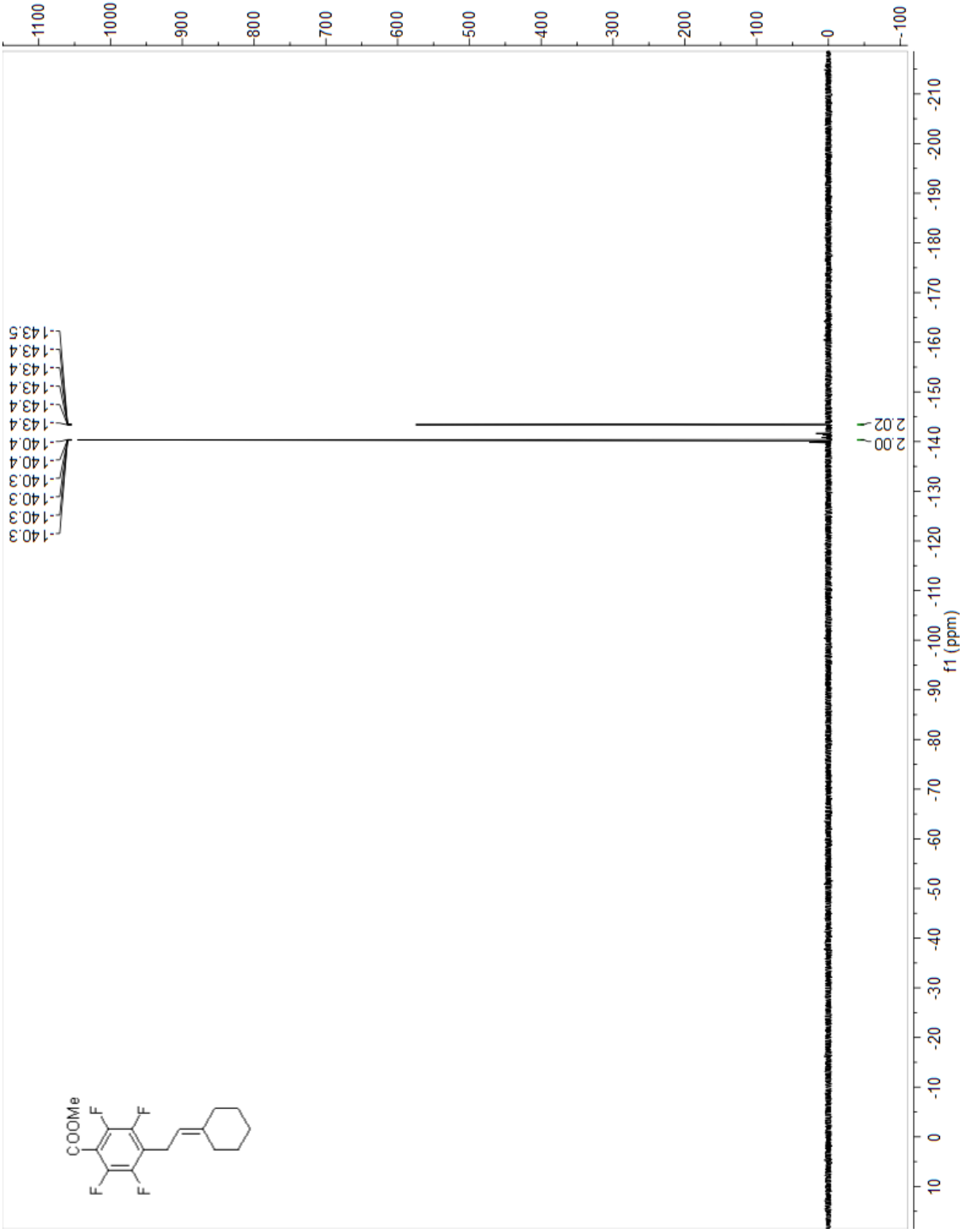


GC and MS of 2,3,5,6-tetrafluoro-4-(2-methylallyl)benzonitrile (5d)

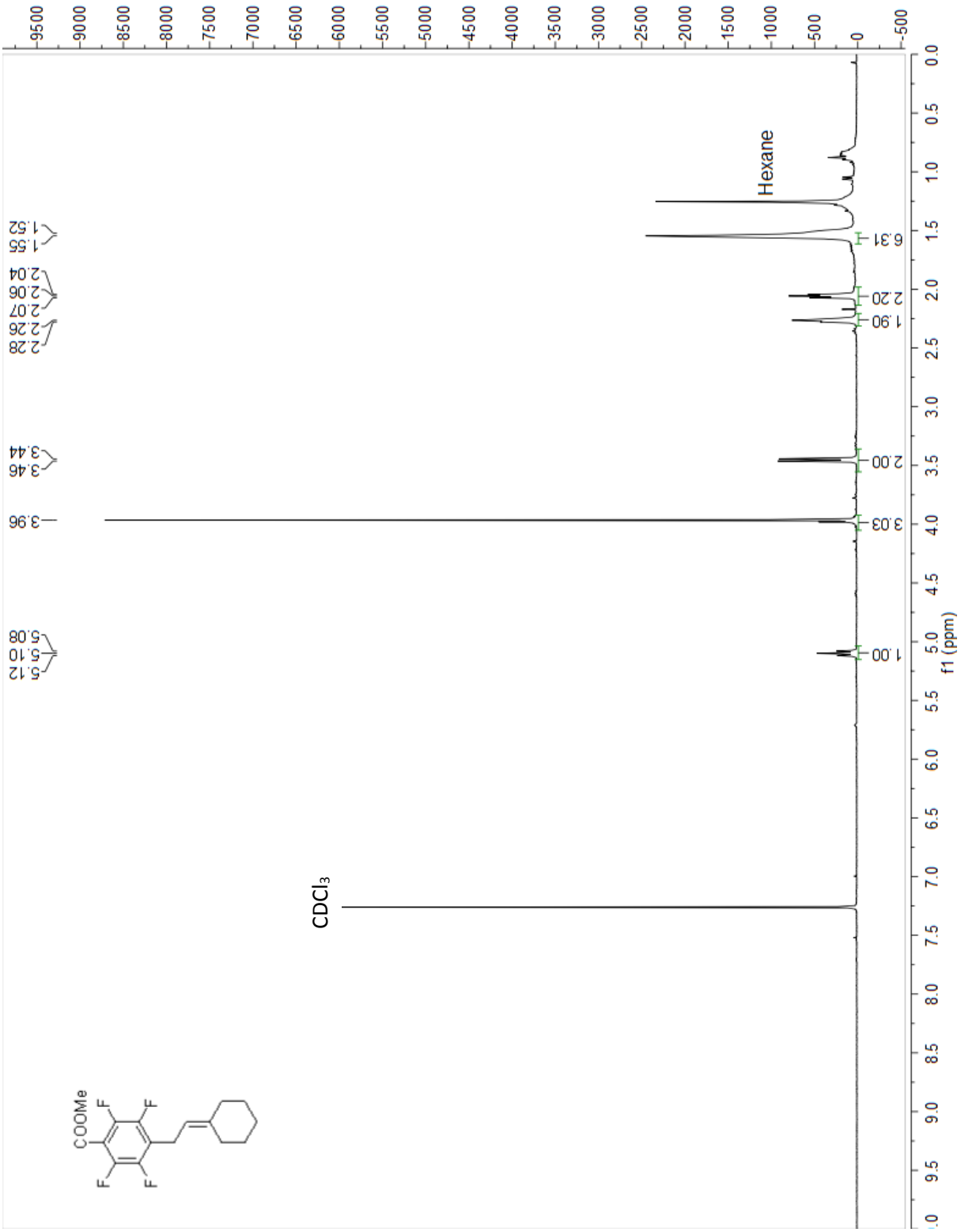




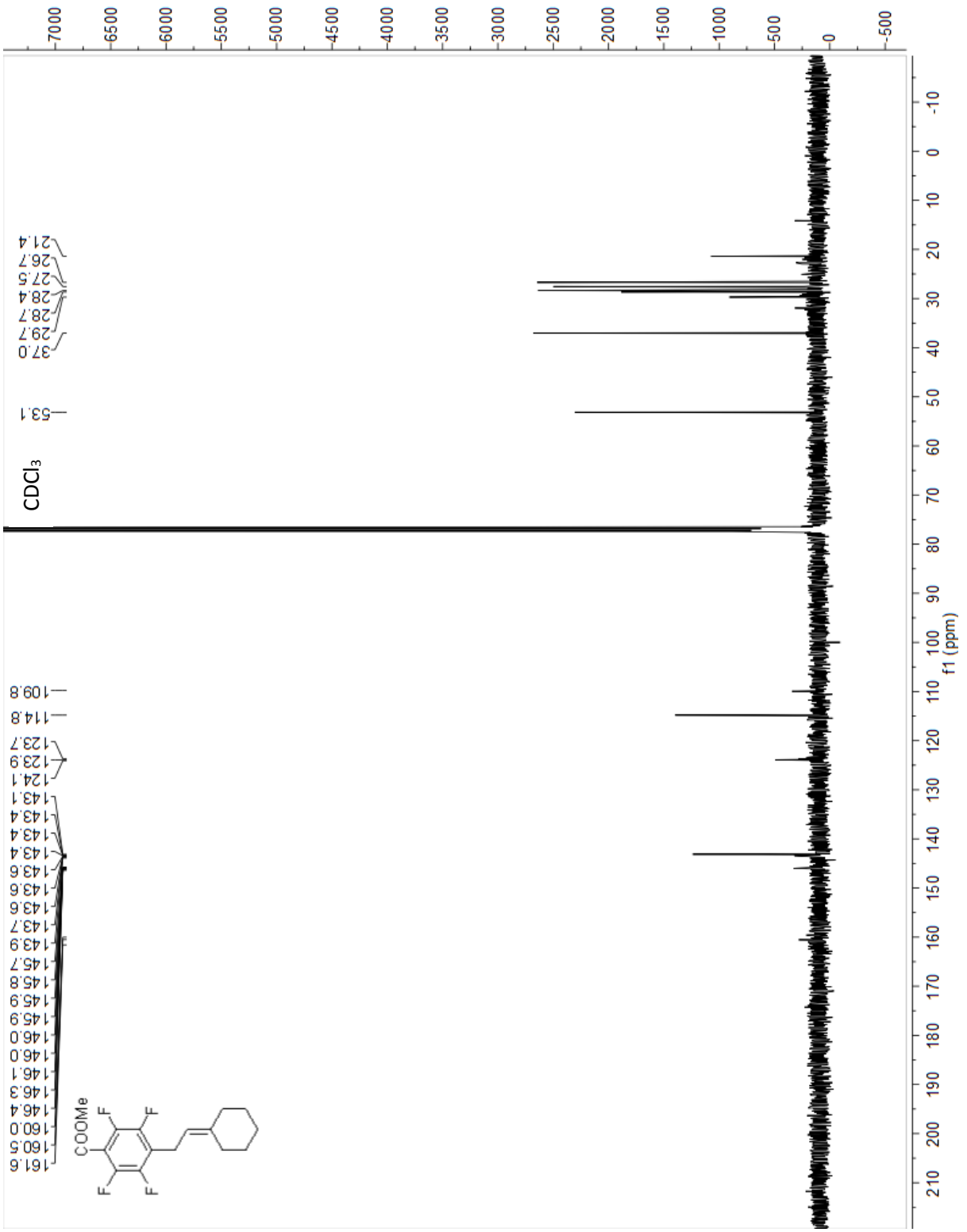
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl 4-(2-cyclohexylideneethyl)-2,3,5,6-tetrafluorobenzoate (5e)**



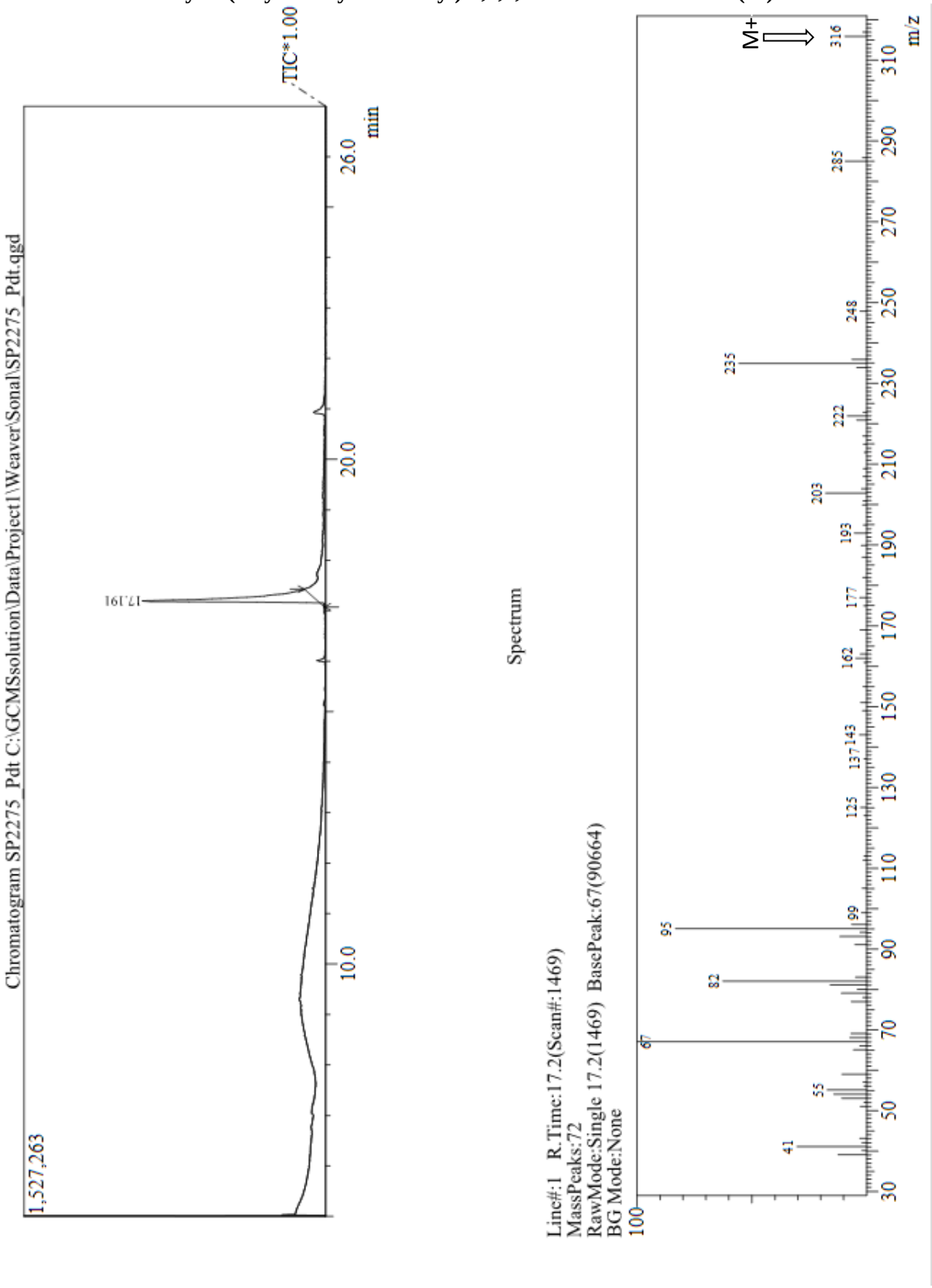
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **methyl 4-(2-cyclohexylideneethyl)-2,3,5,6-tetrafluorobenzoate (5e)**



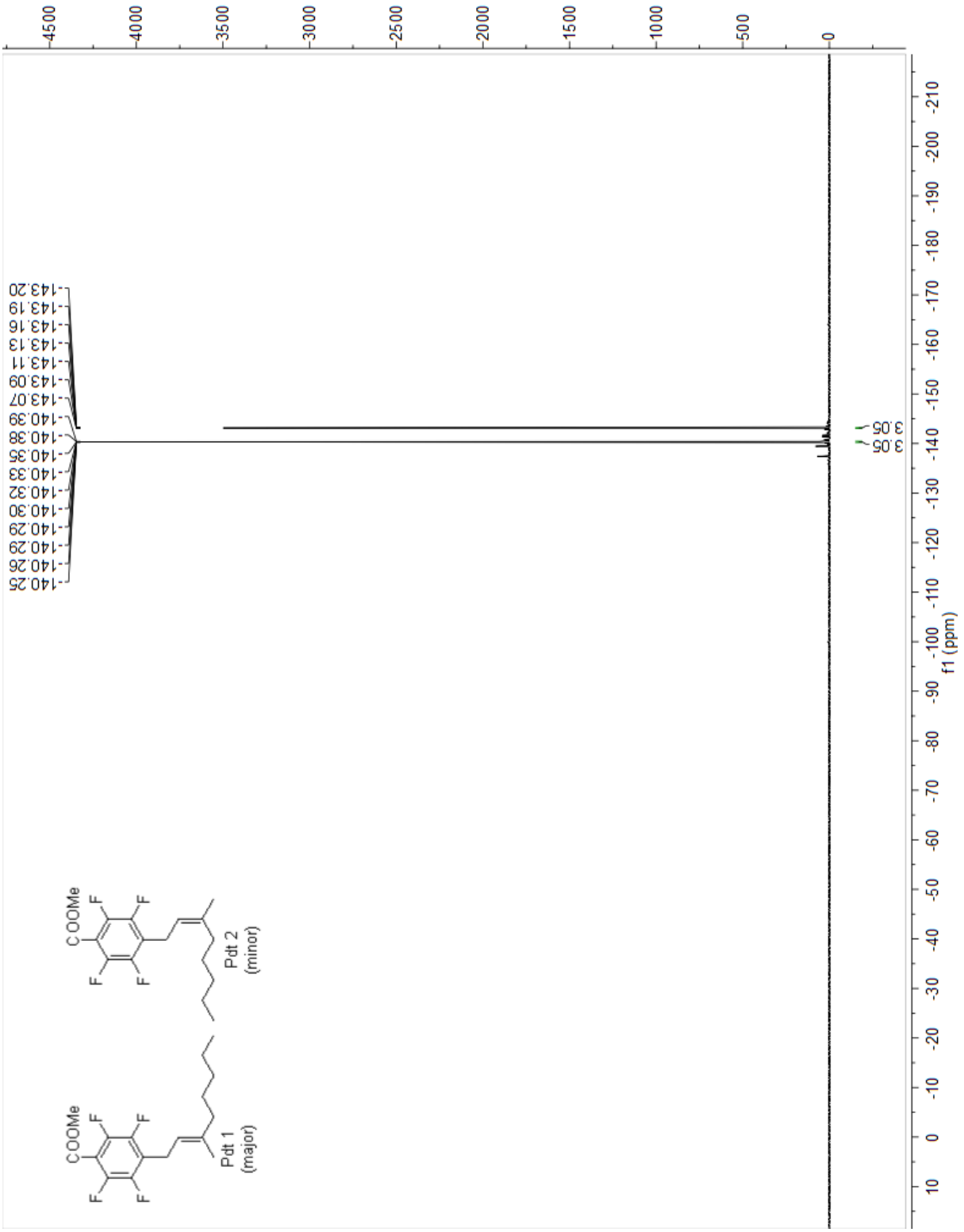
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **methyl 4-(2-cyclohexylideneethyl)-2,3,5,6-tetrafluorobenzoate (5e)**



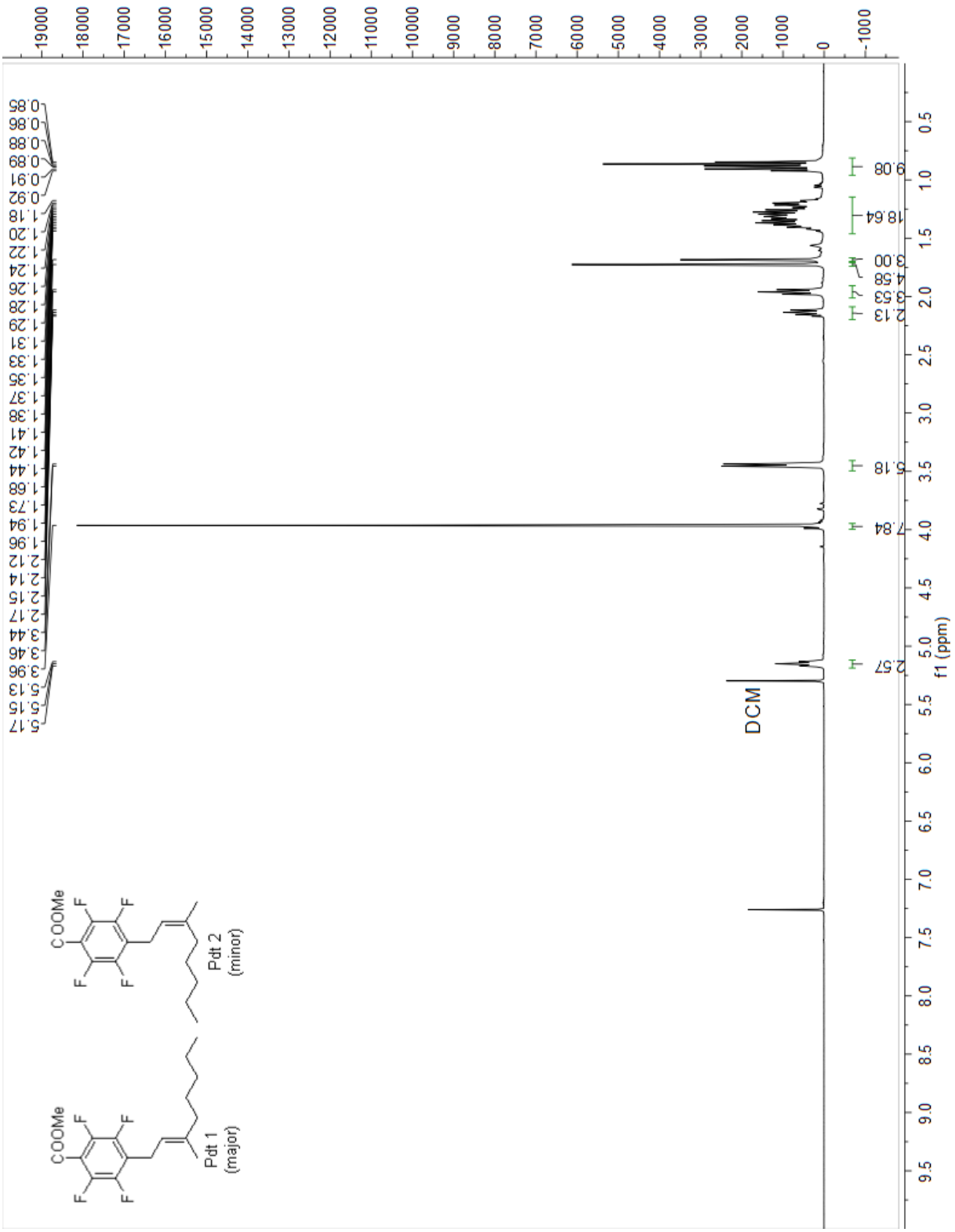
GC and MS of **methyl 4-(2-cyclohexylideneethyl)-2,3,5,6-tetrafluorobenzoate (5e)**



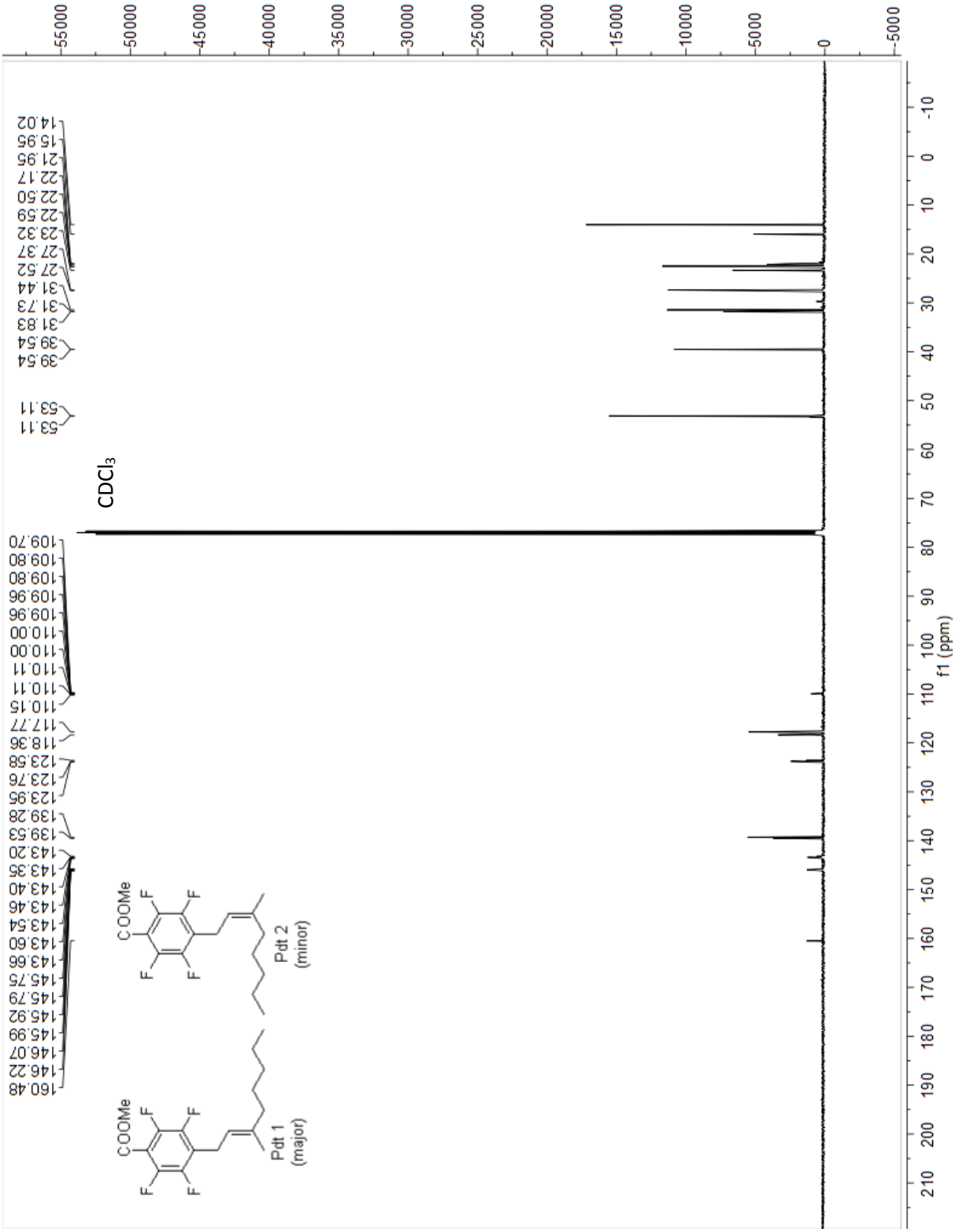
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl (E)-2,3,5,6-tetrafluoro-4-(3-methyloct-2-en-1-yl)benzoate (5f)**



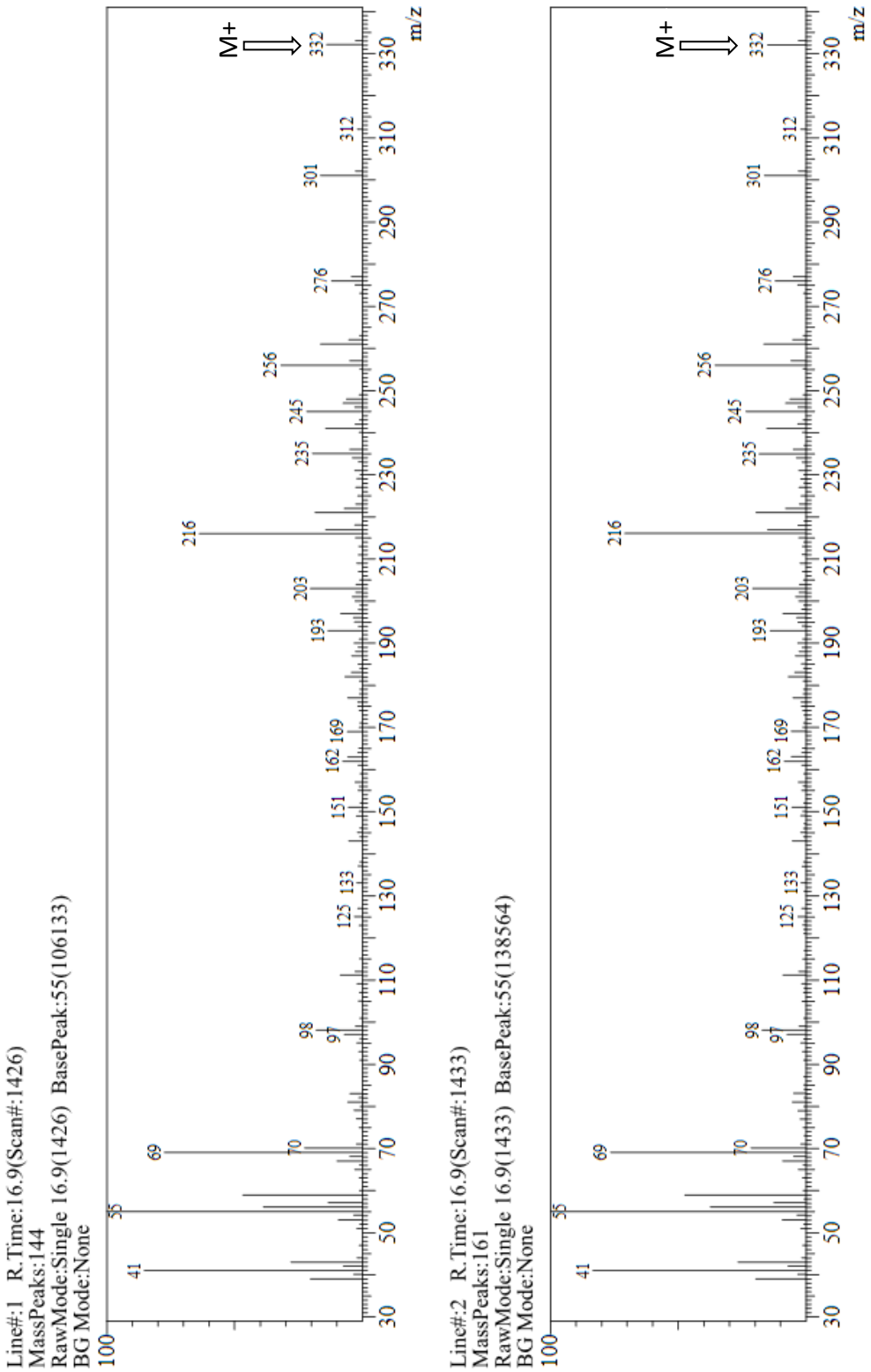
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of methyl **methyl (E)-2,3,5,6-tetrafluoro-4-(3-methyloct-2-en-1-yl)benzoate (5f)**



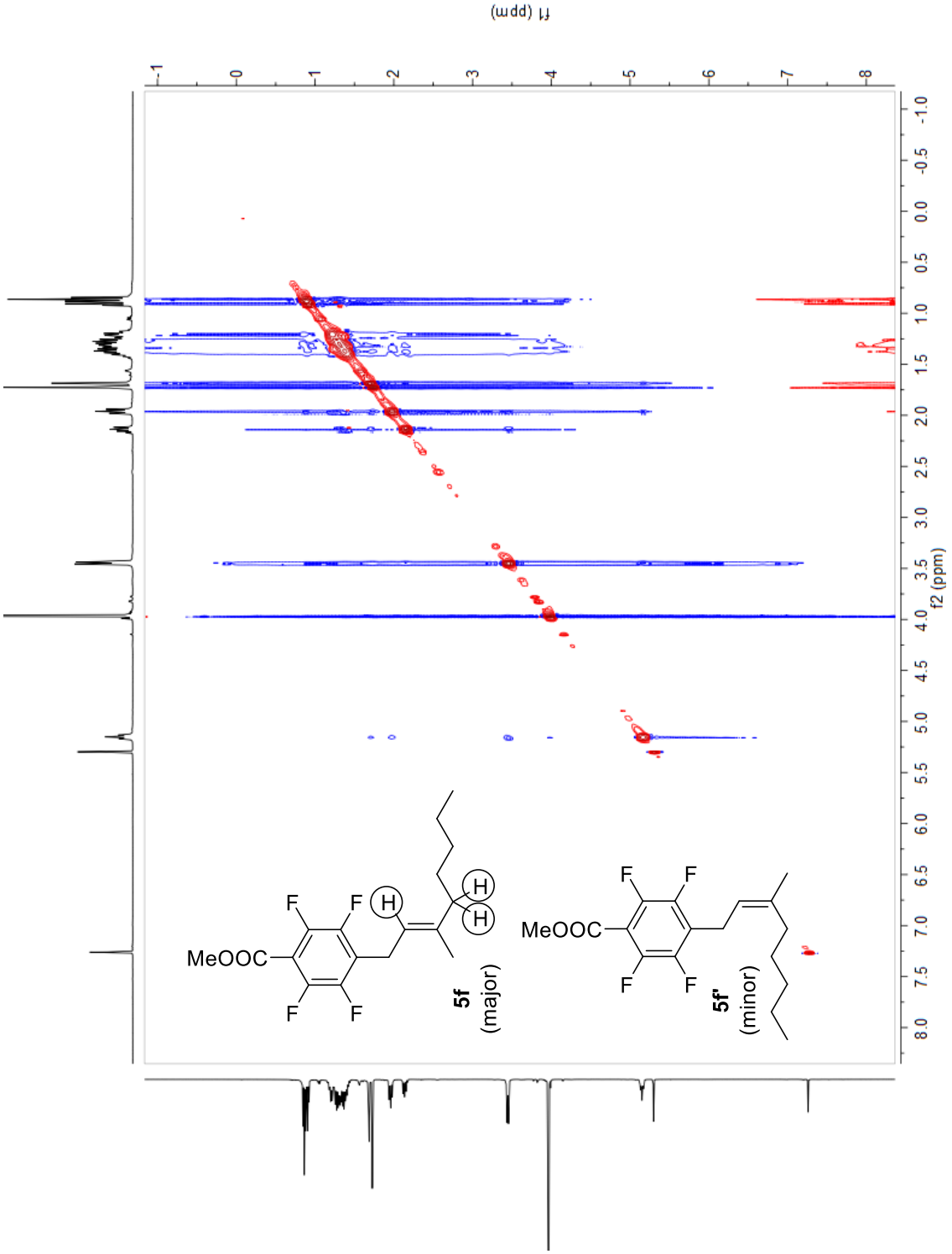
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **methyl (E)-2,3,5,6-tetrafluoro-4-(3-methyloct-2-en-1-yl)benzoate (5f)**



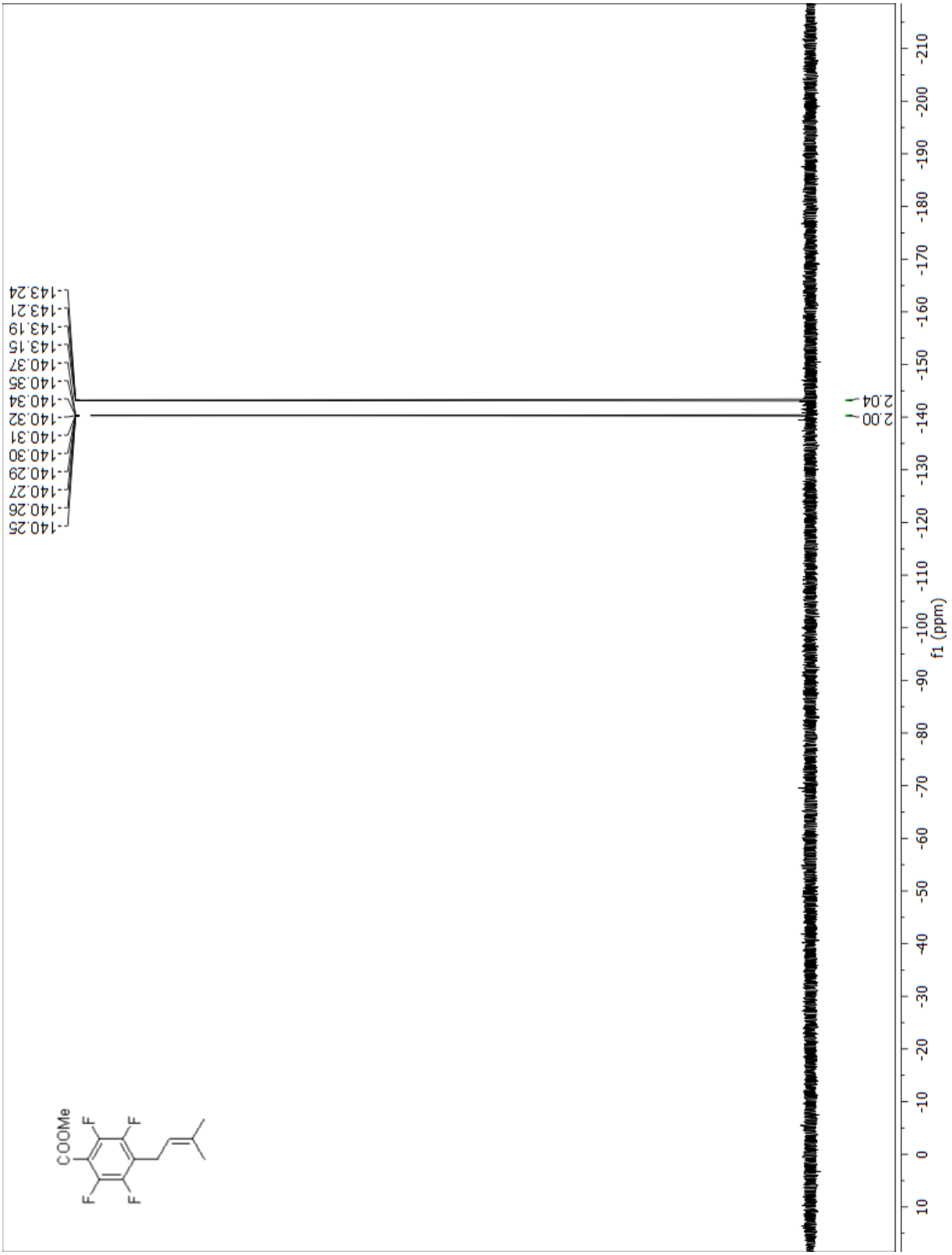
GC and MS of **methyl (E)-2,3,5,6-tetrafluoro-4-(3-methyloct-2-en-1-yl)benzoate (5f)**



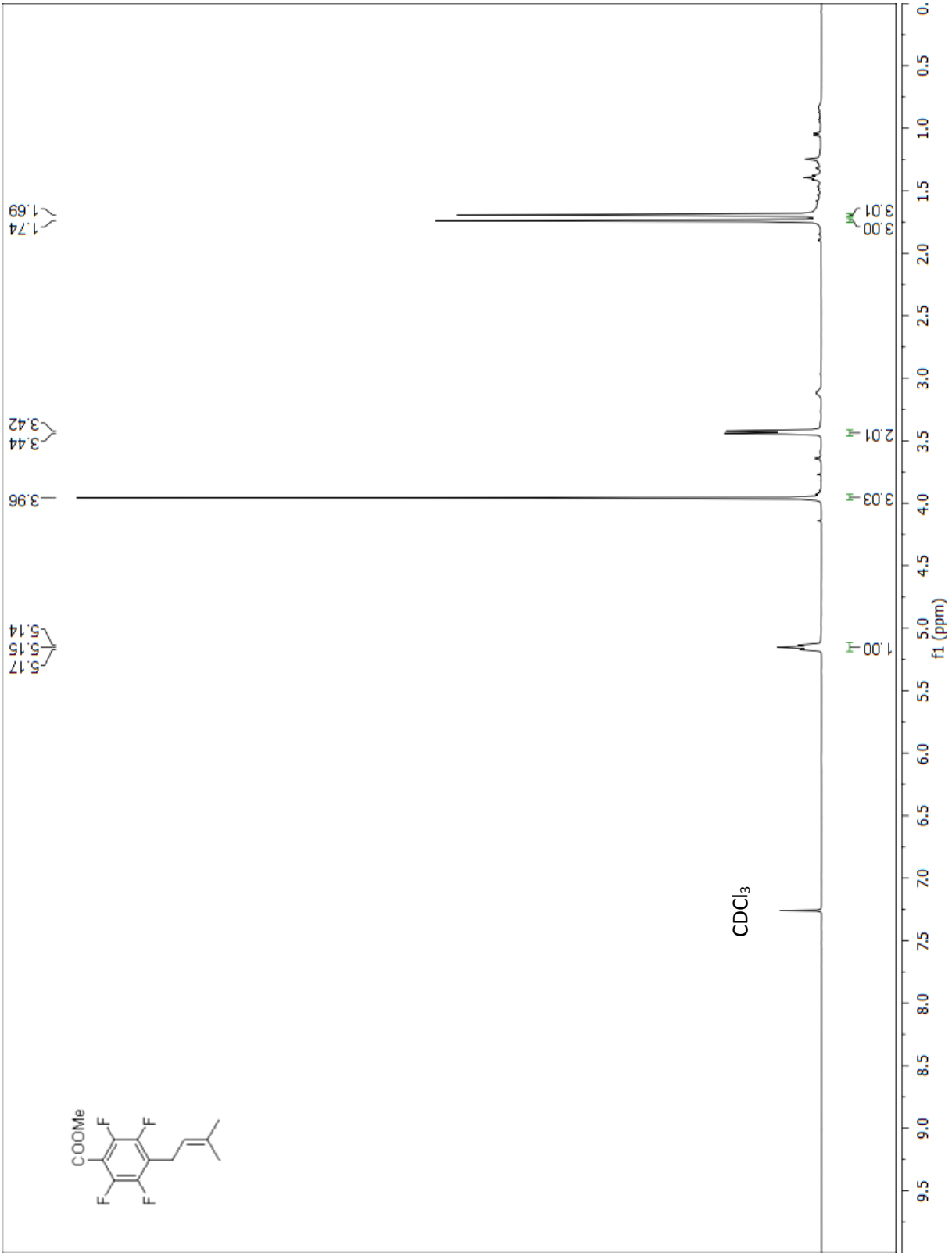
NOESY of **methyl (E)-2,3,5,6-tetrafluoro-4-(3-methyloct-2-en-1-yl)benzoate (5f)**



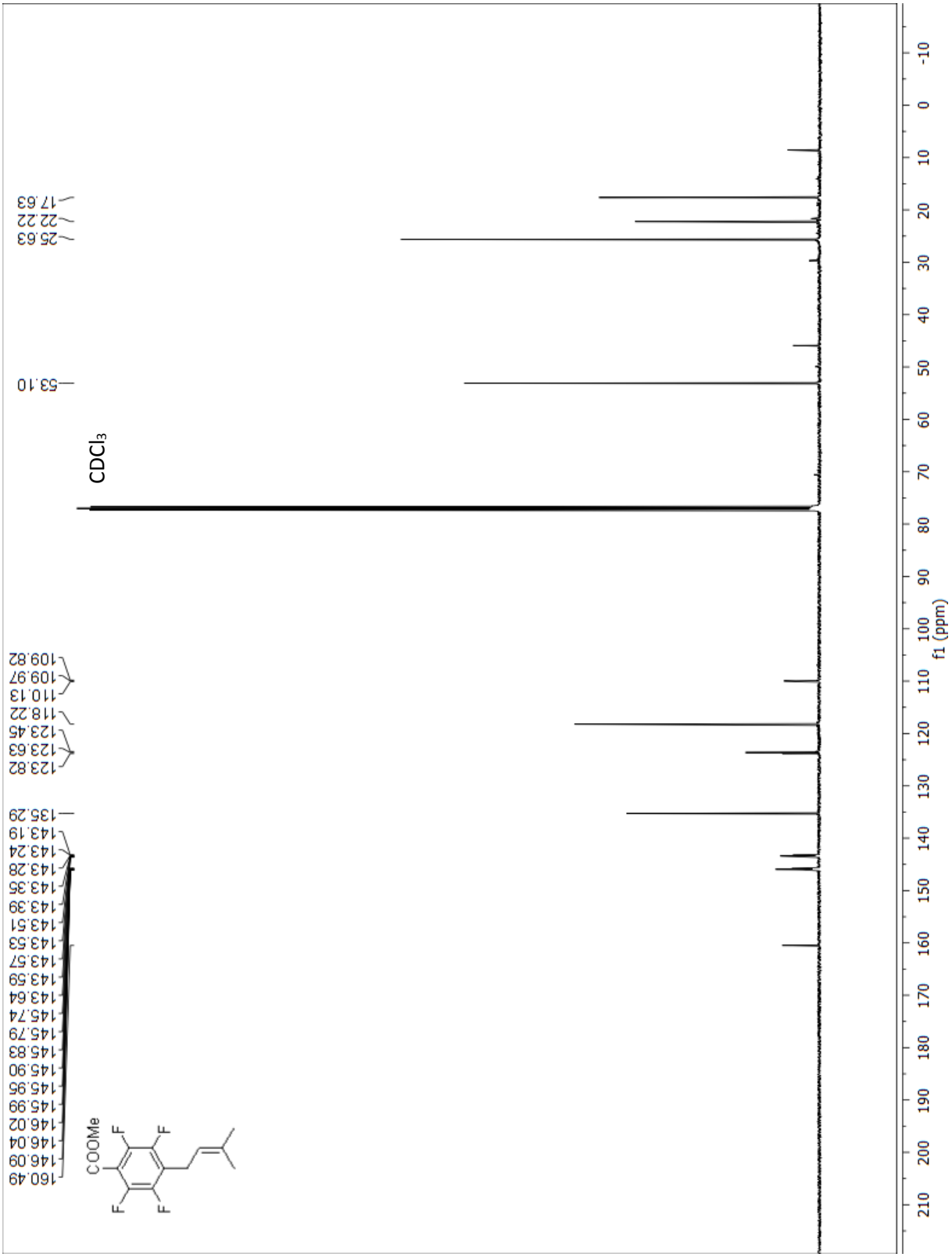
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3a)**



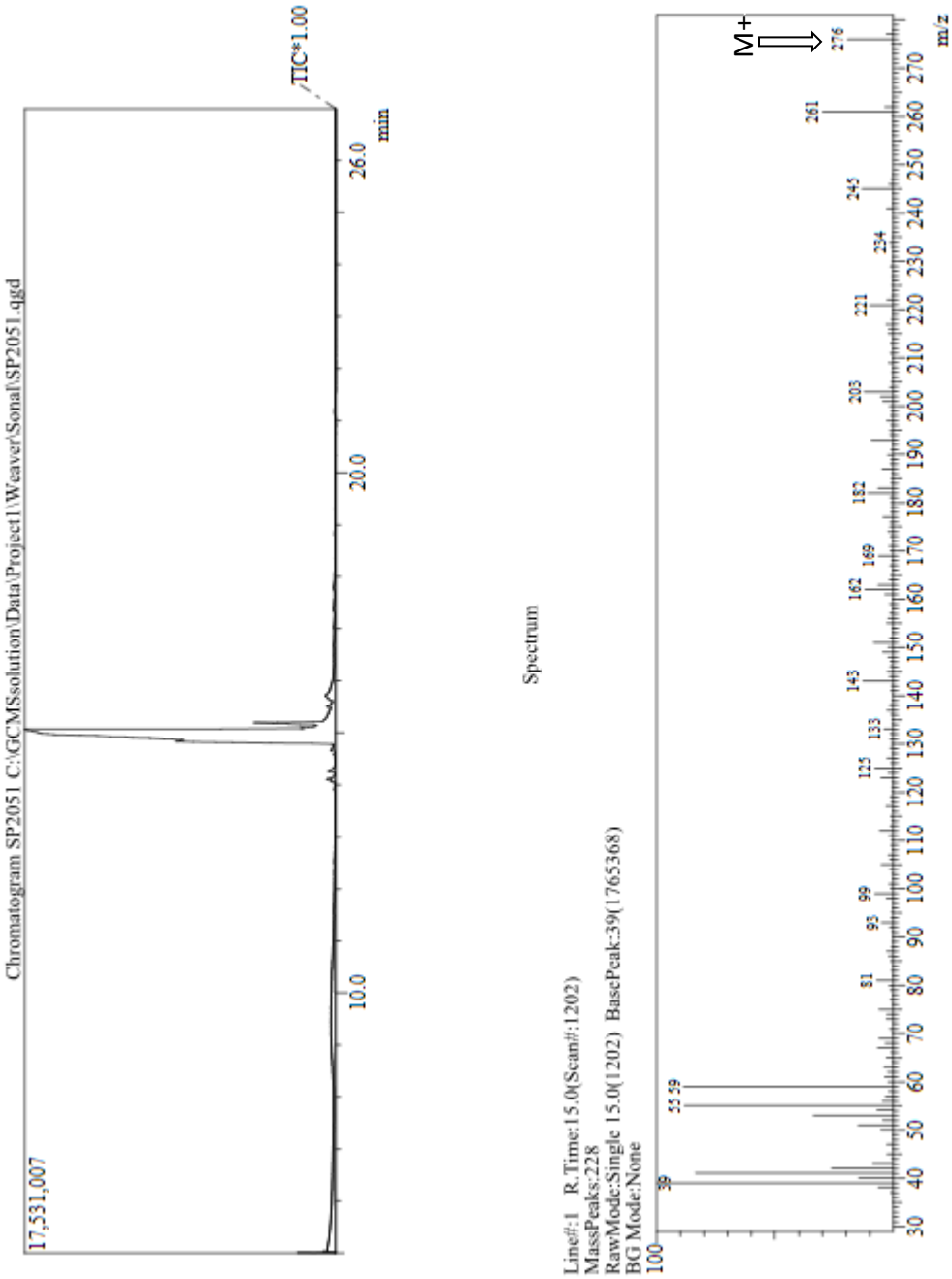
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **methyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3a)**



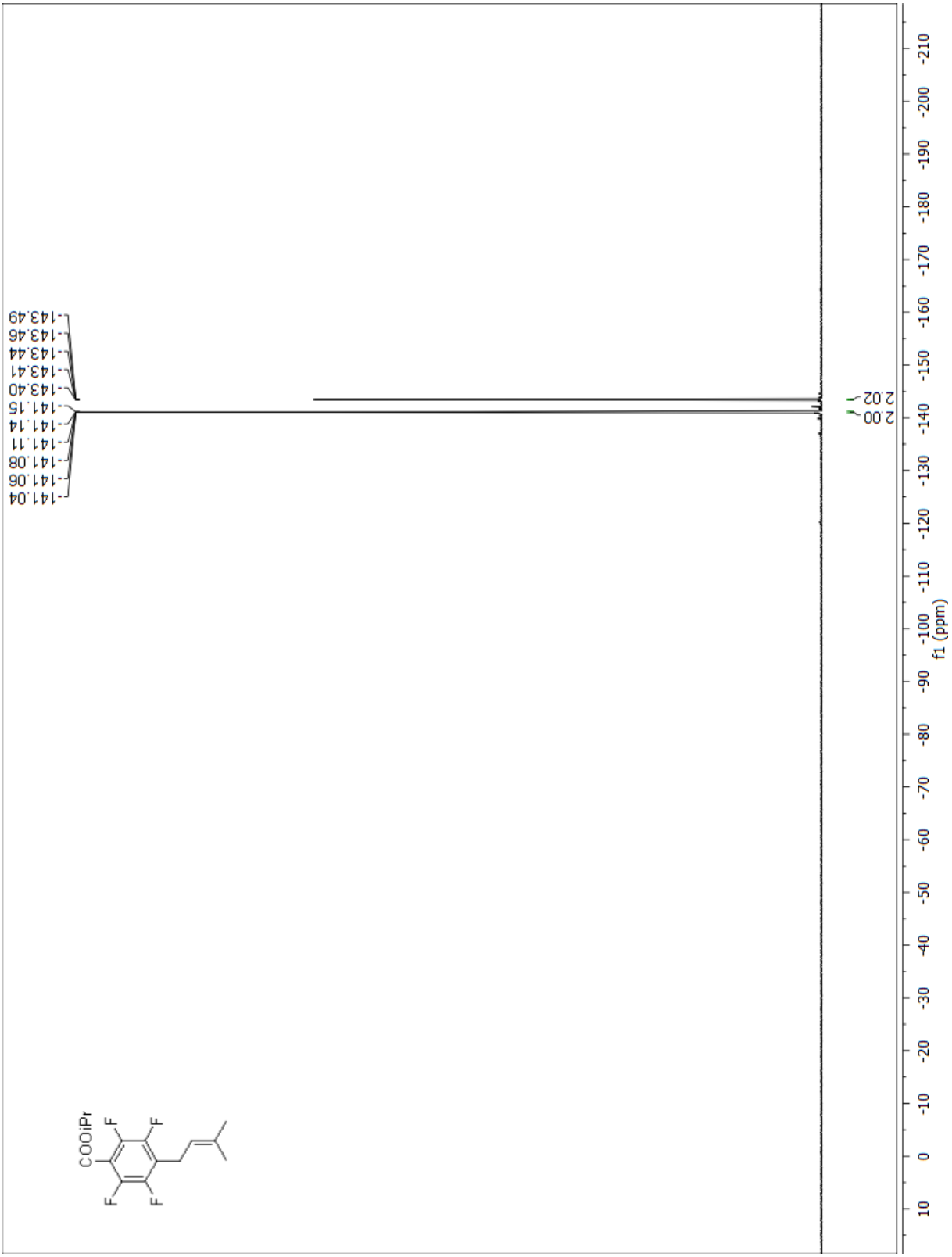
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **methyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3a)**



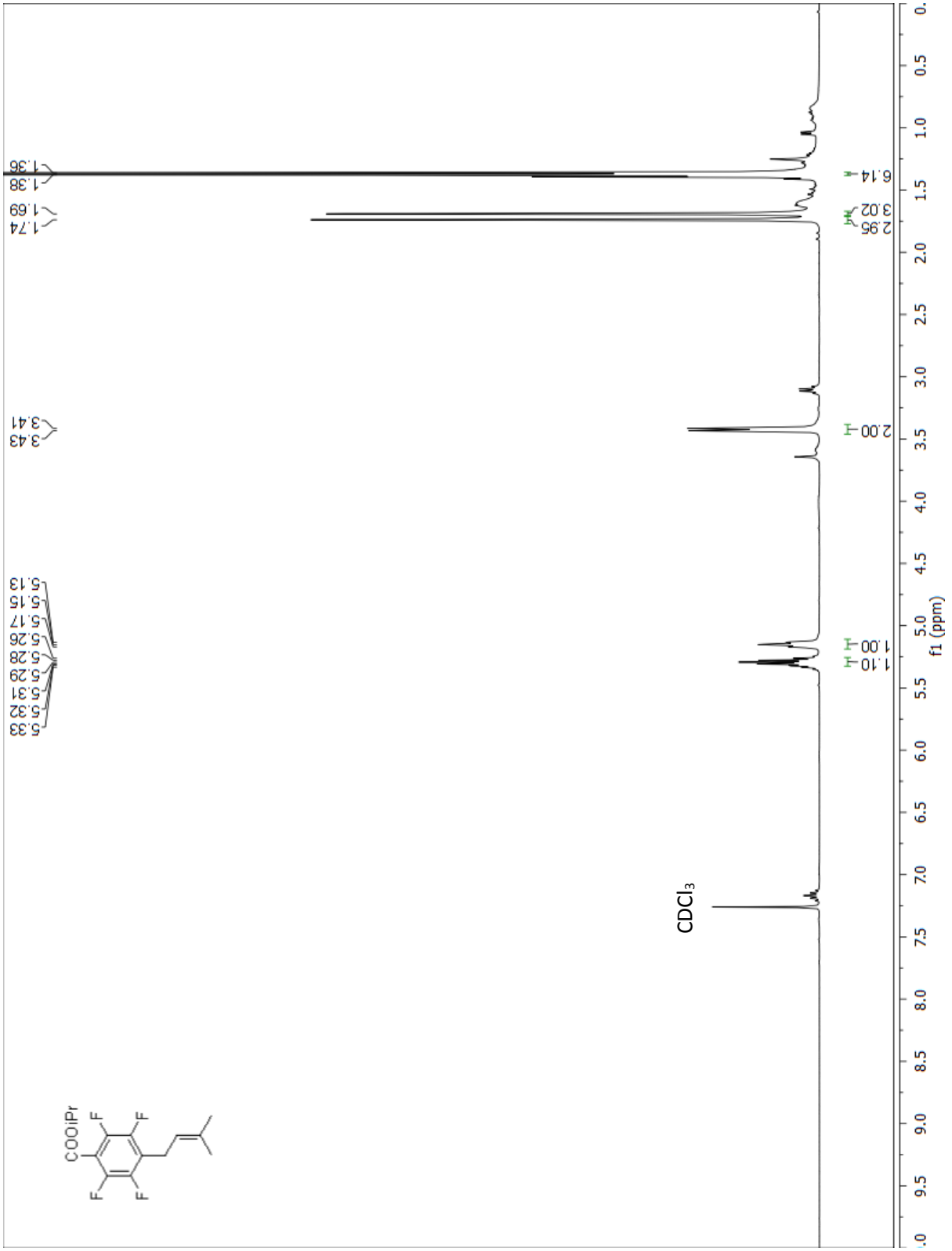
GC and MS of **methyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3a)**



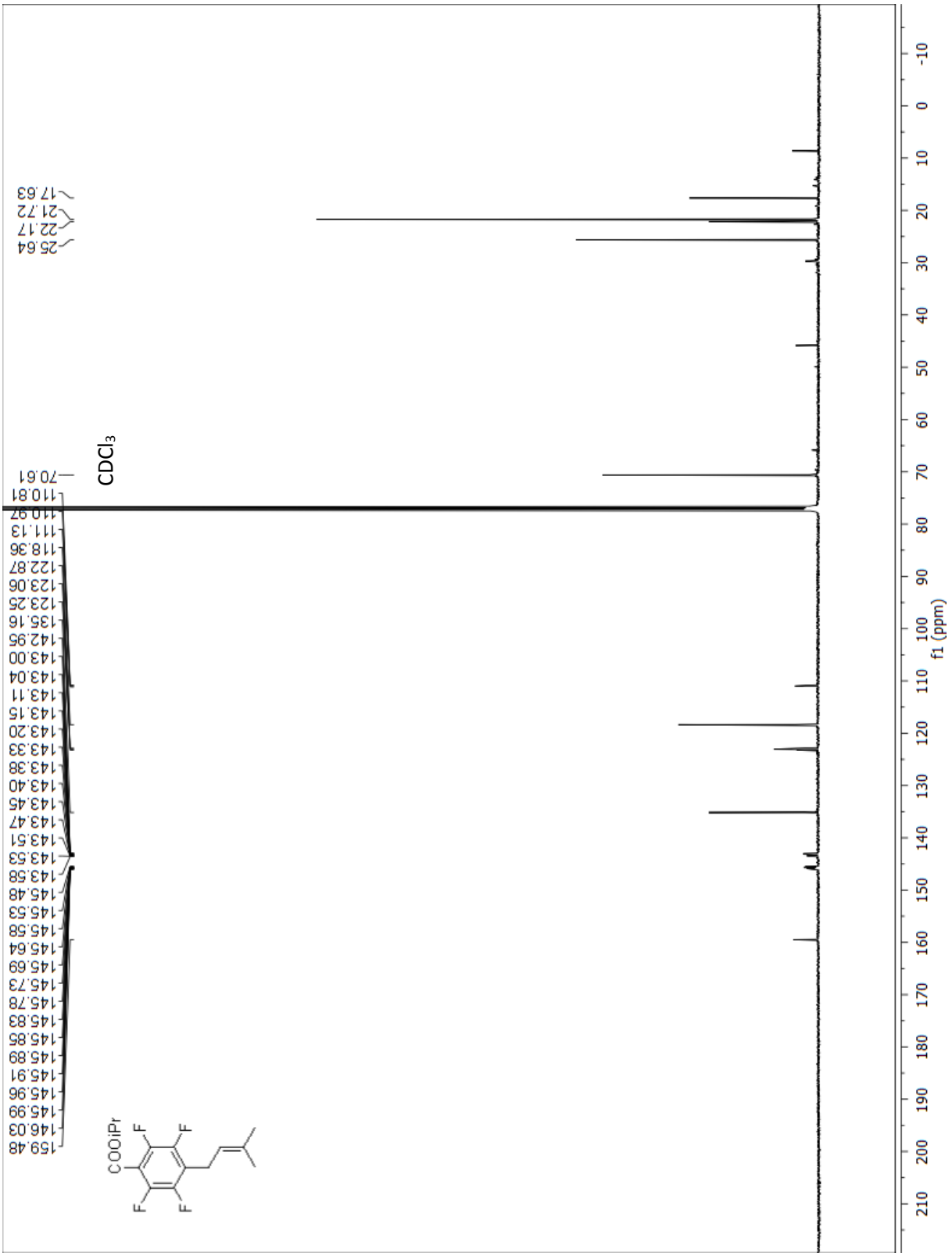
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **isopropyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3b)**



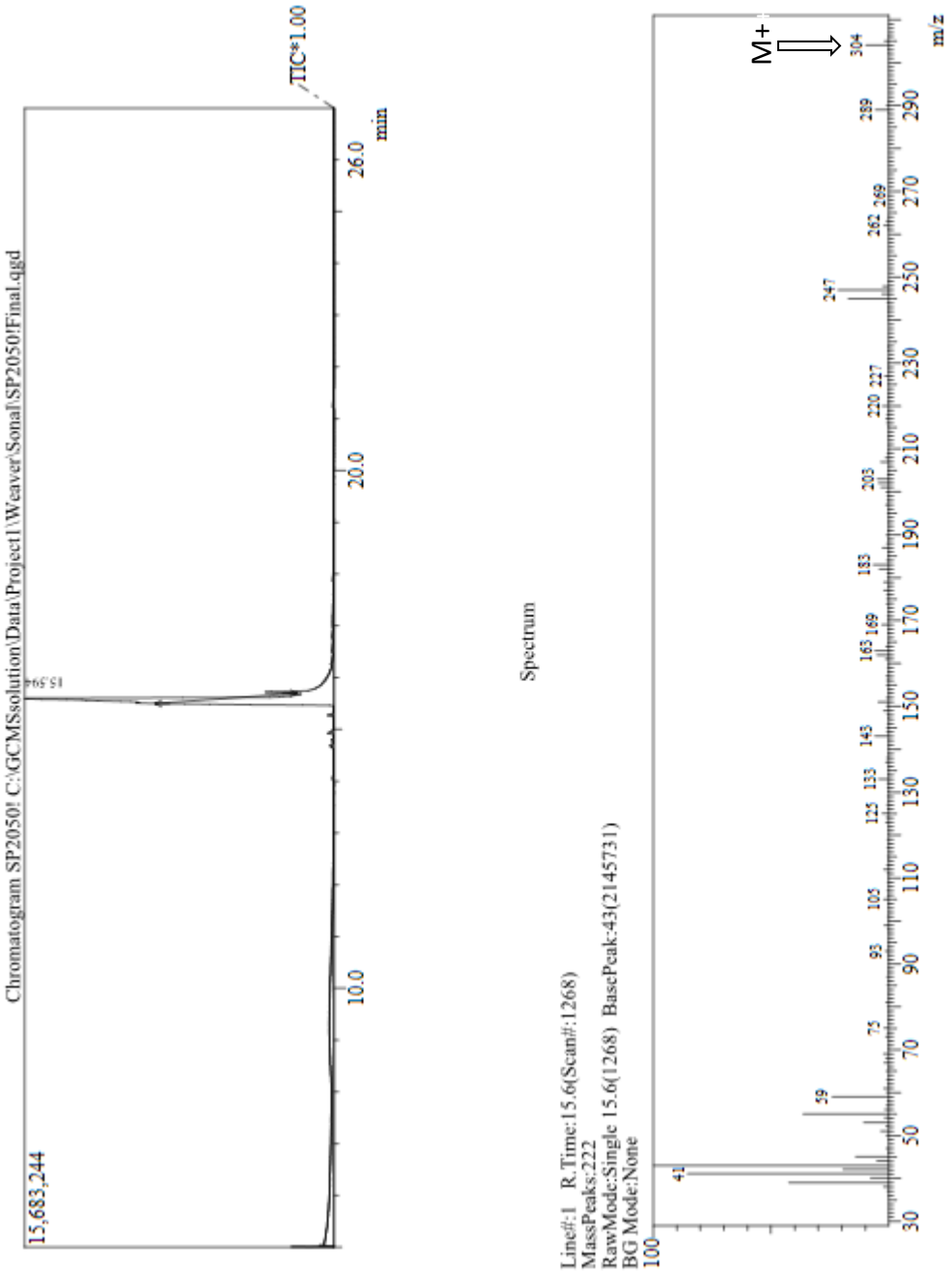
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **isopropyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3b)**



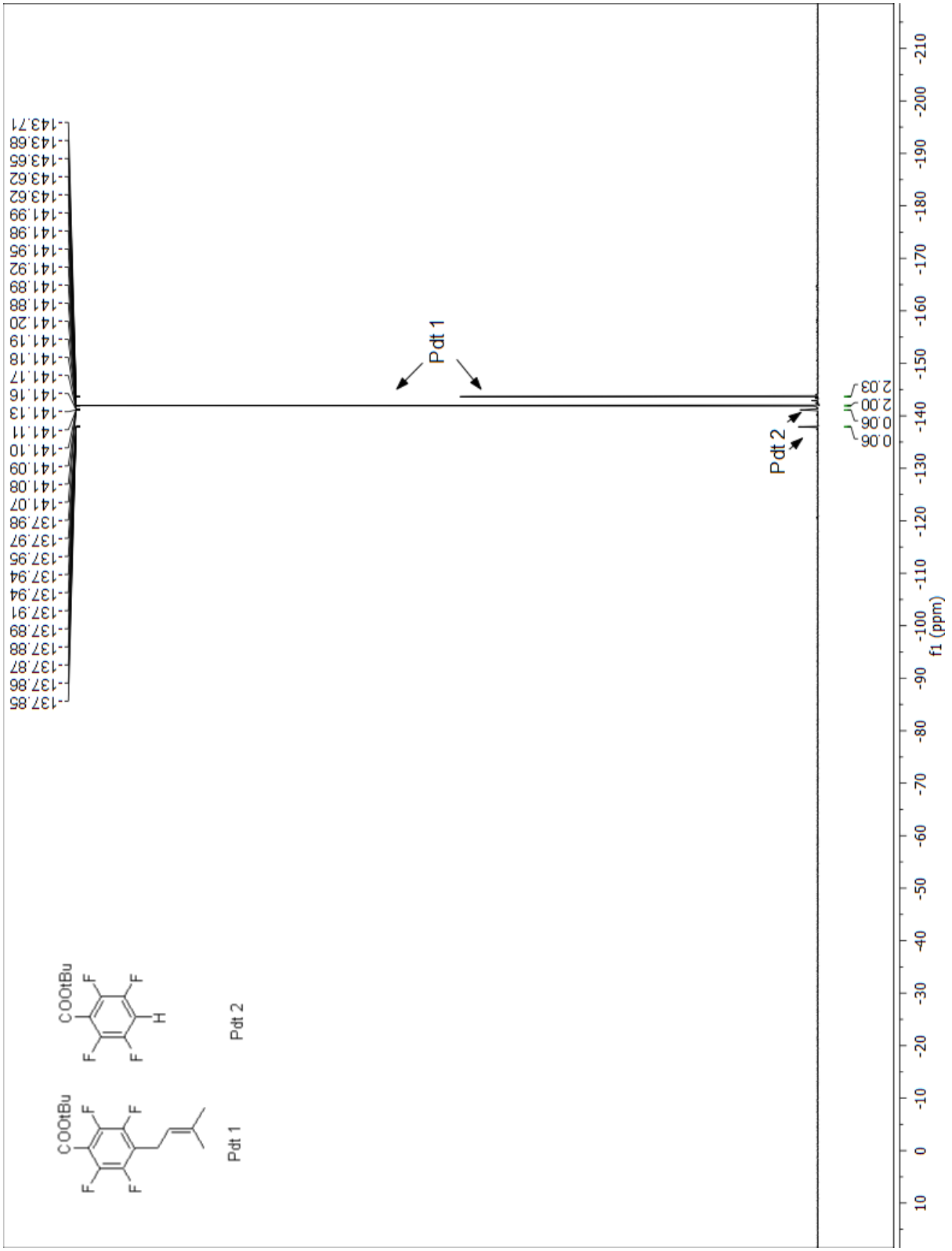
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **isopropyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3b)**



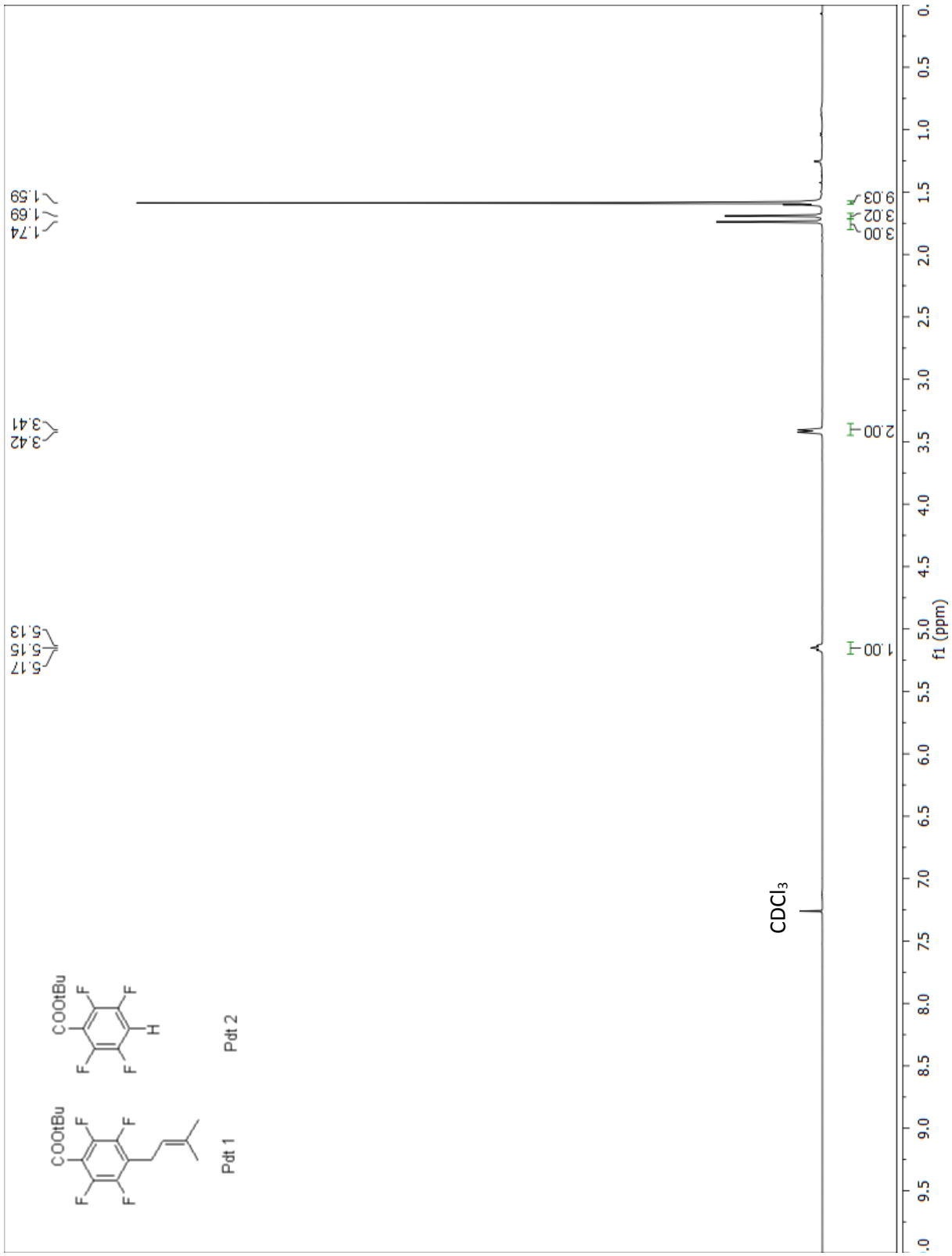
GC and MS of **isopropyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3b)**



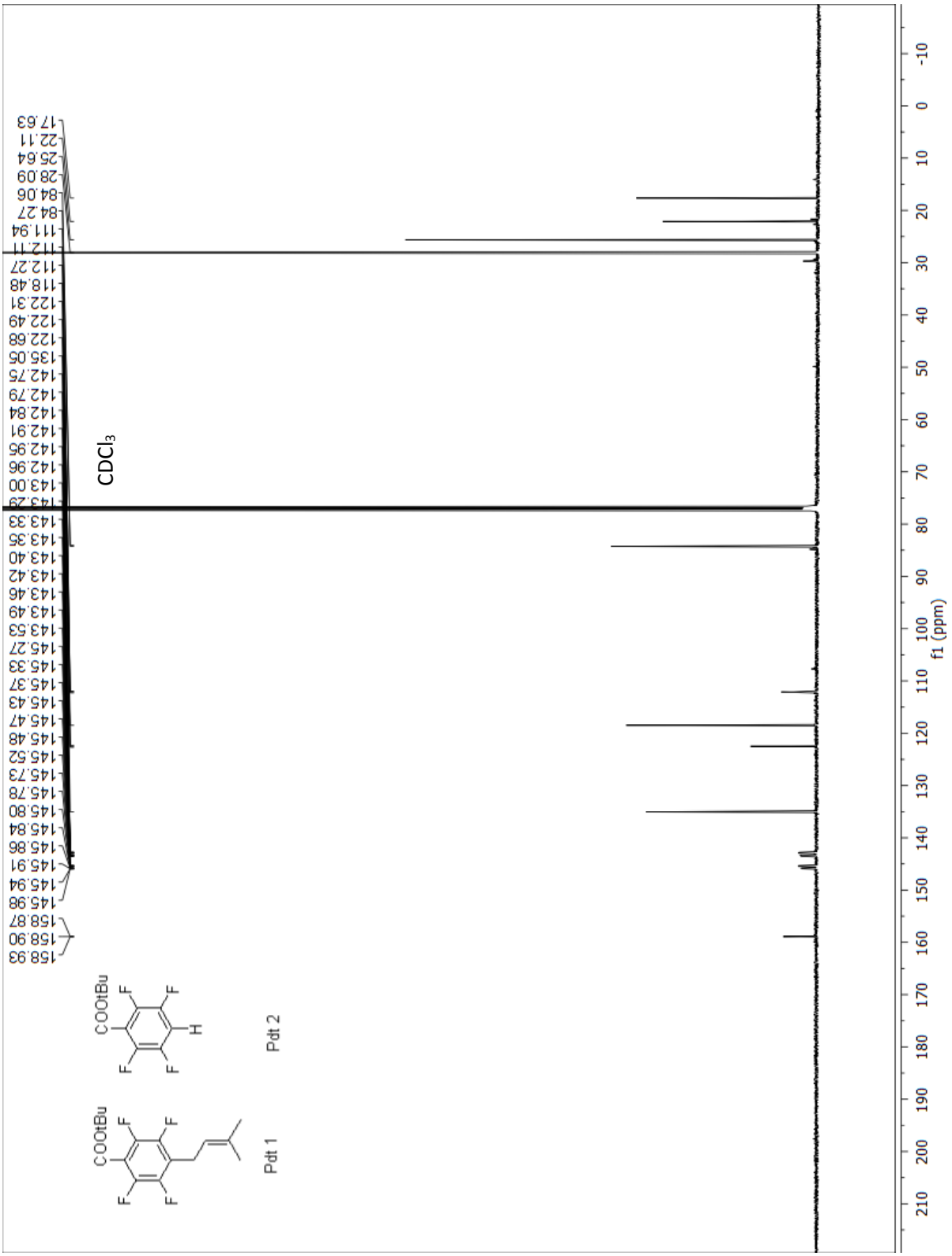
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **isobutyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3c)**



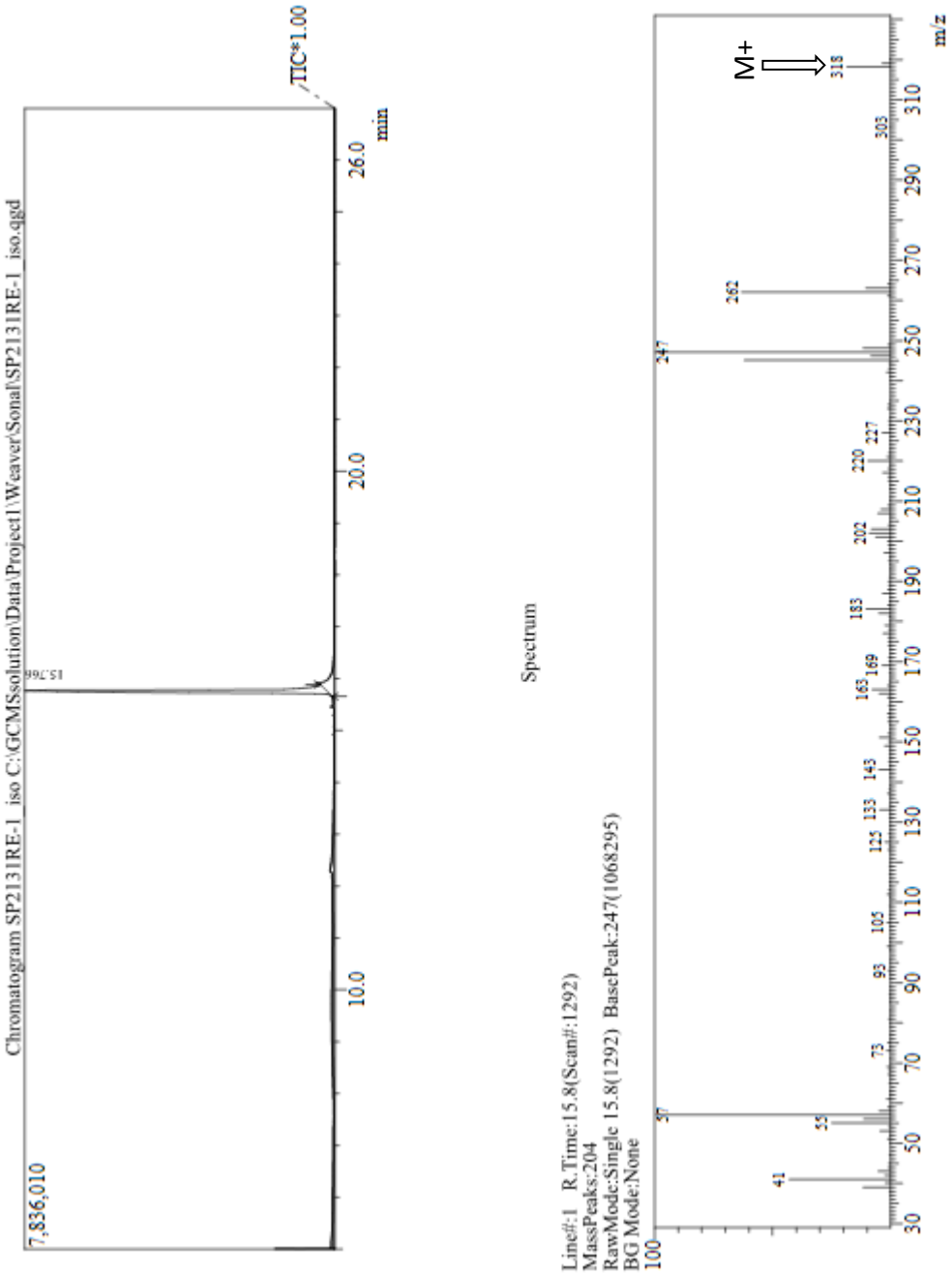
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **isobutyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3c)**



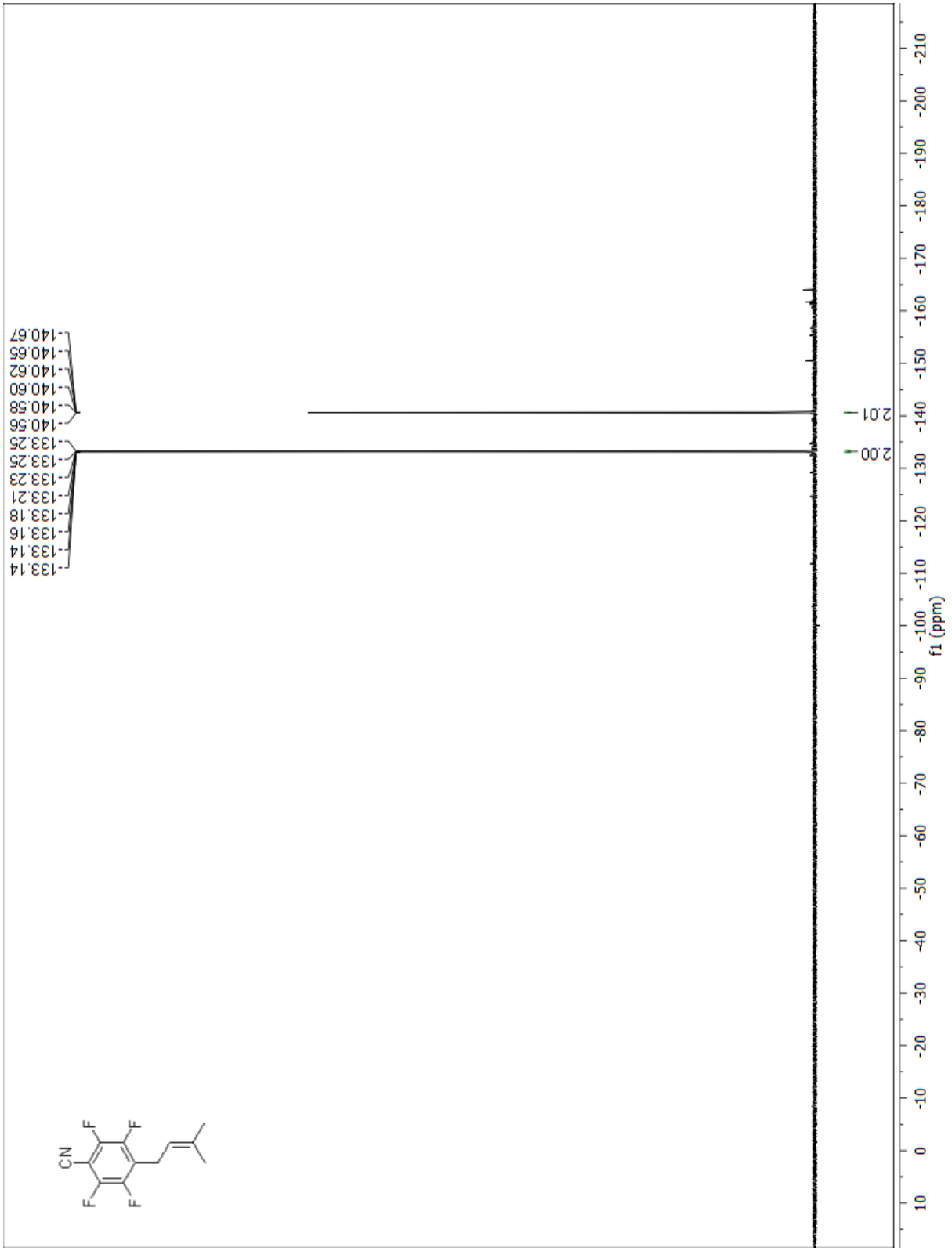
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **isobutyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3c)**



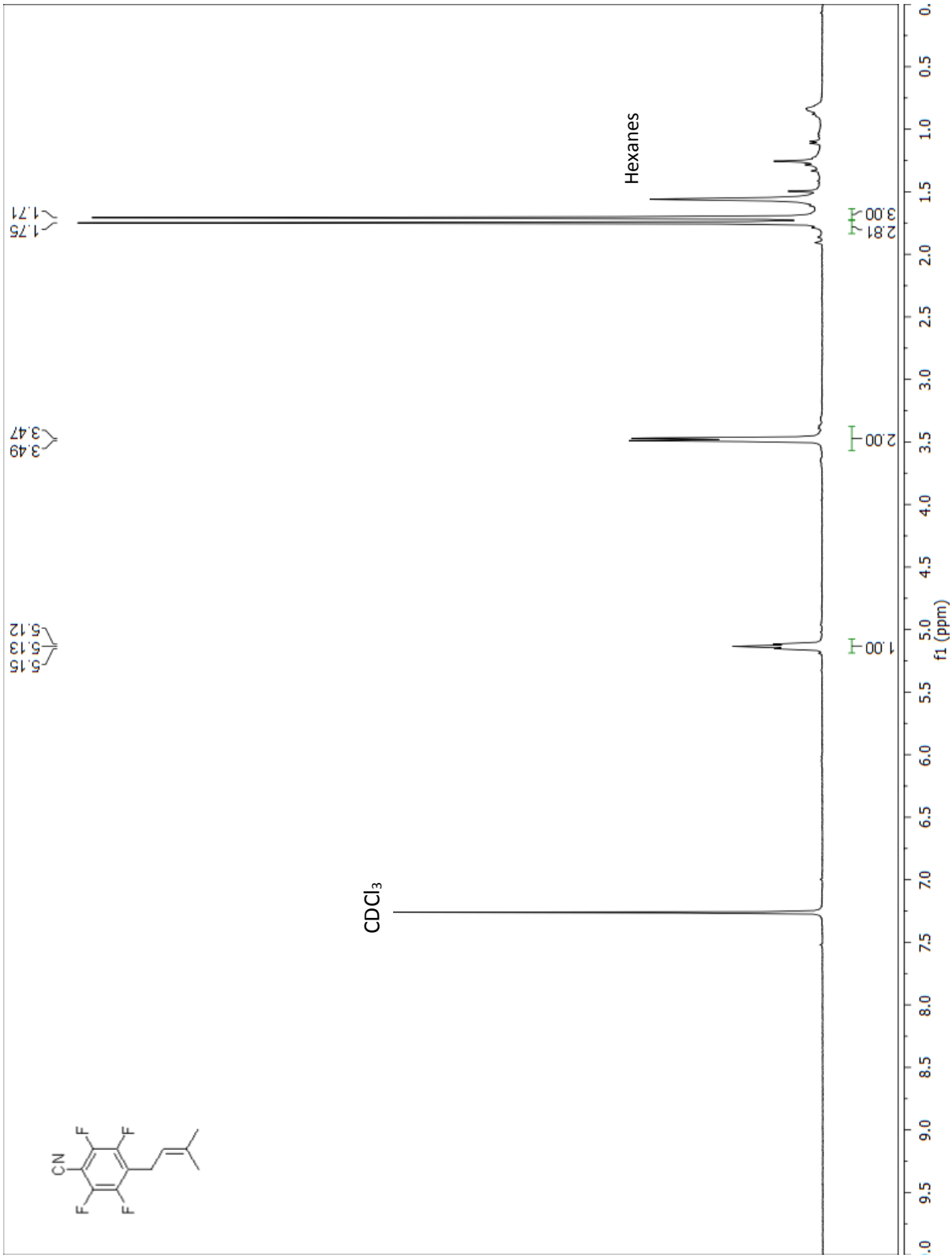
GC and MS of **isobutyl 2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzoate (3c)**



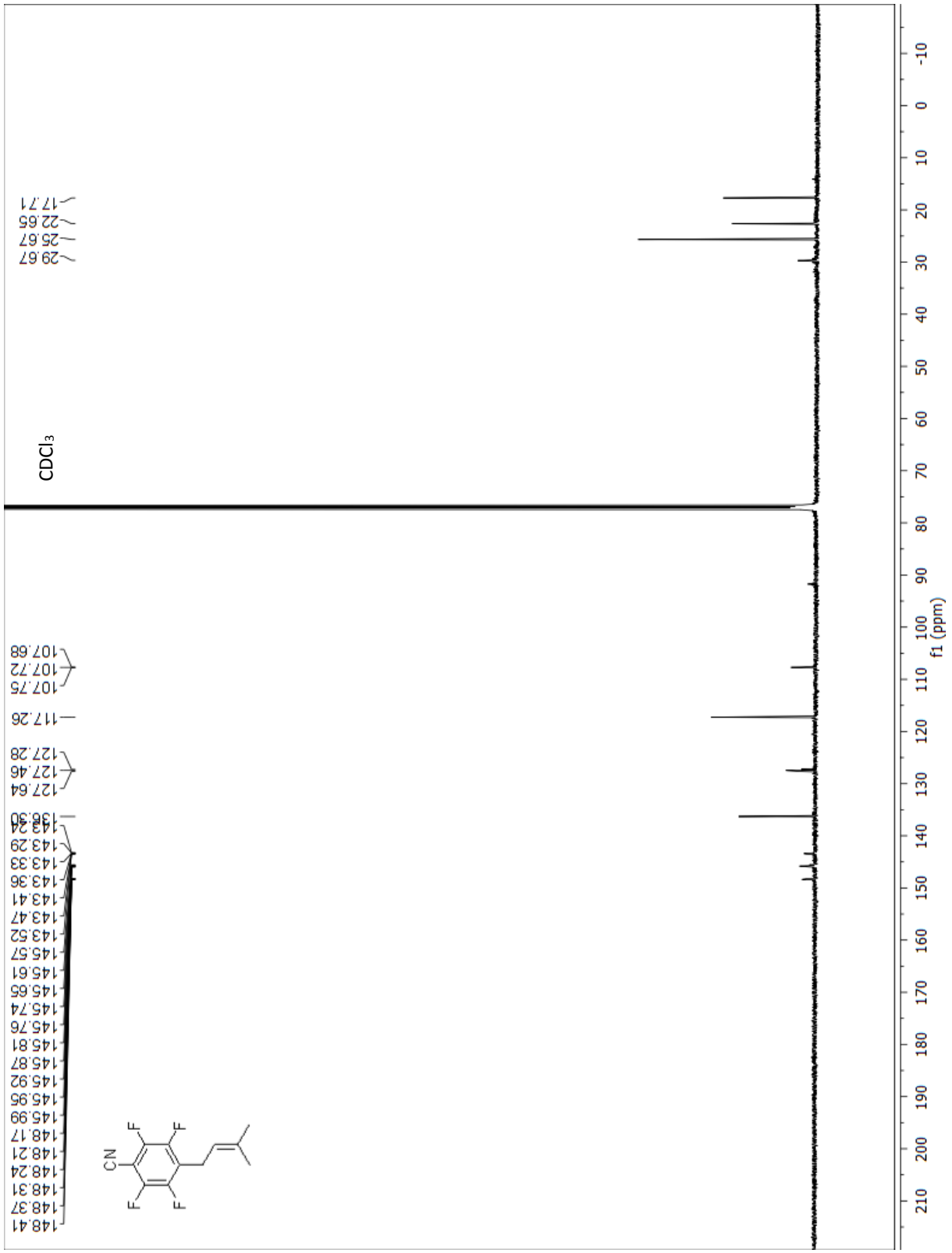
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzonitrile (3d)**



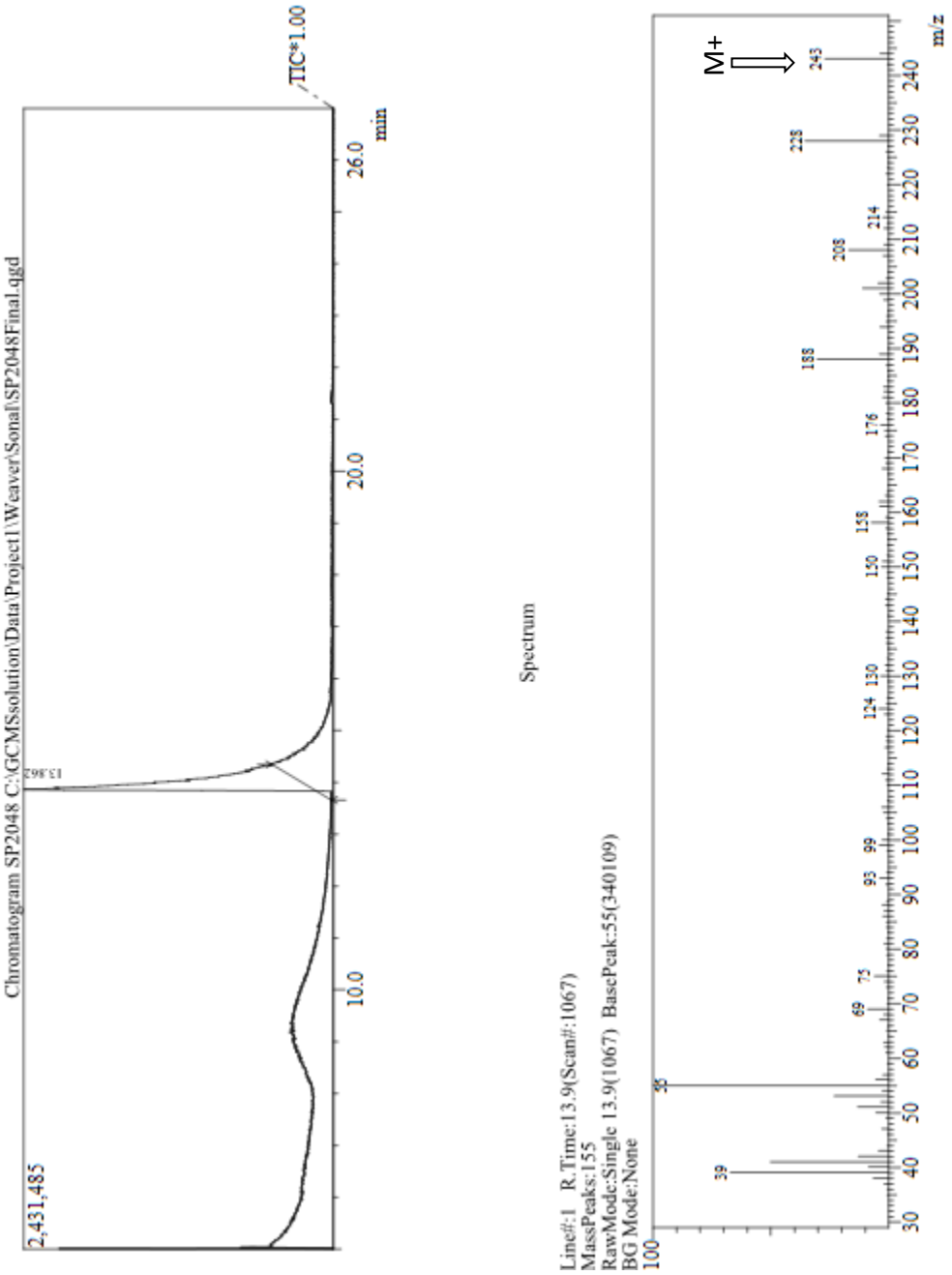
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzonitrile (3d)**



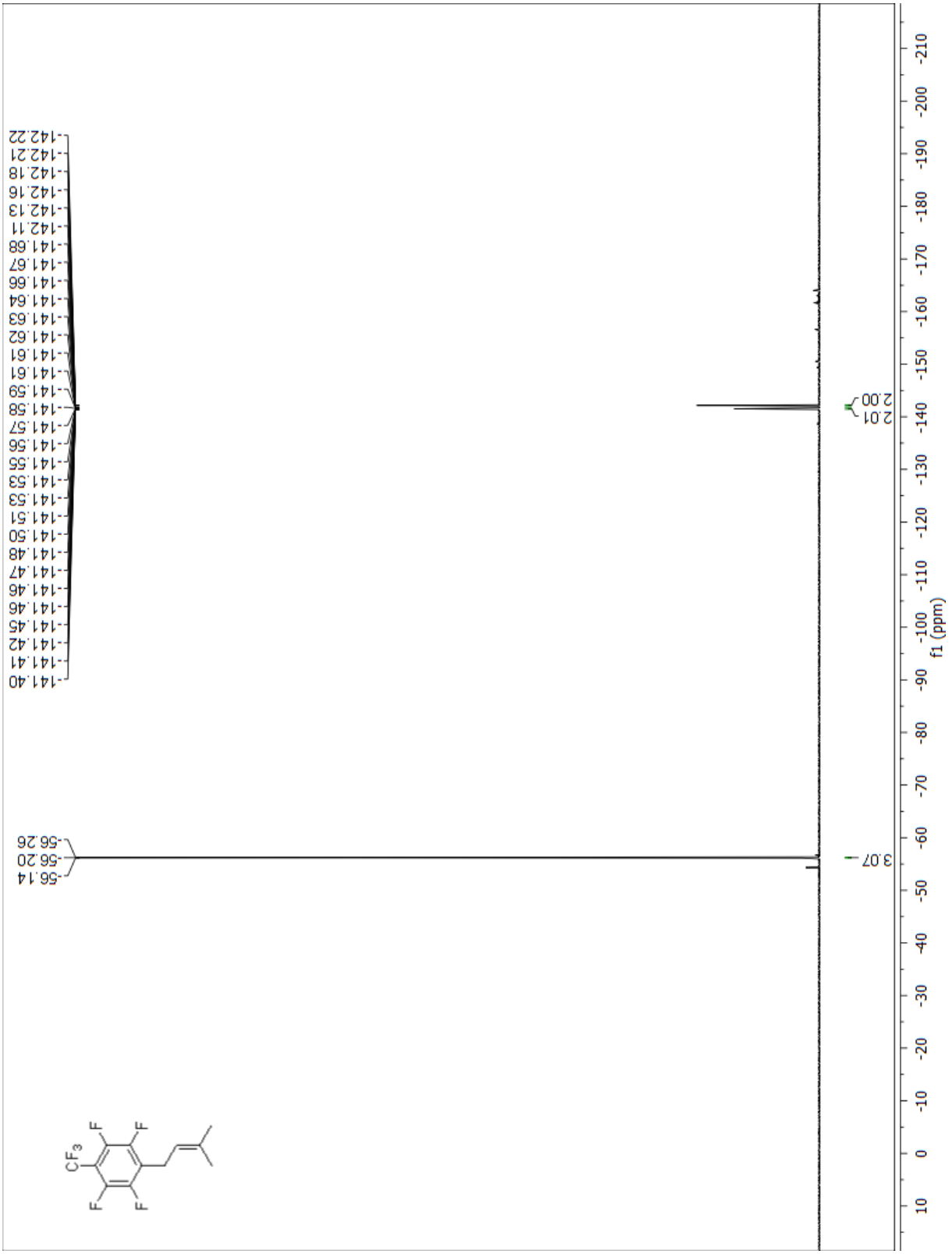
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzonitrile (3d)**



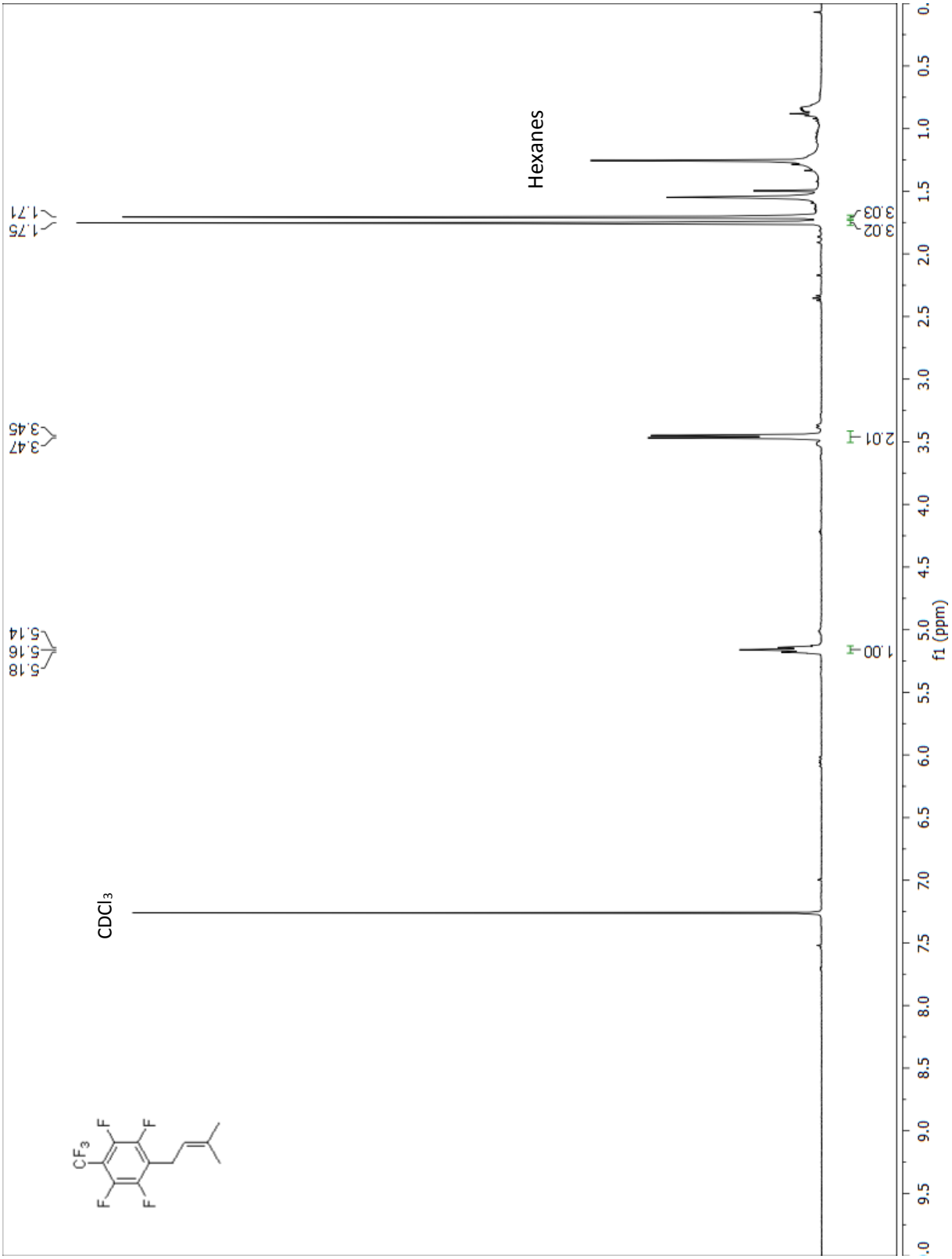
GC and MS of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)benzonitrile (3d)**



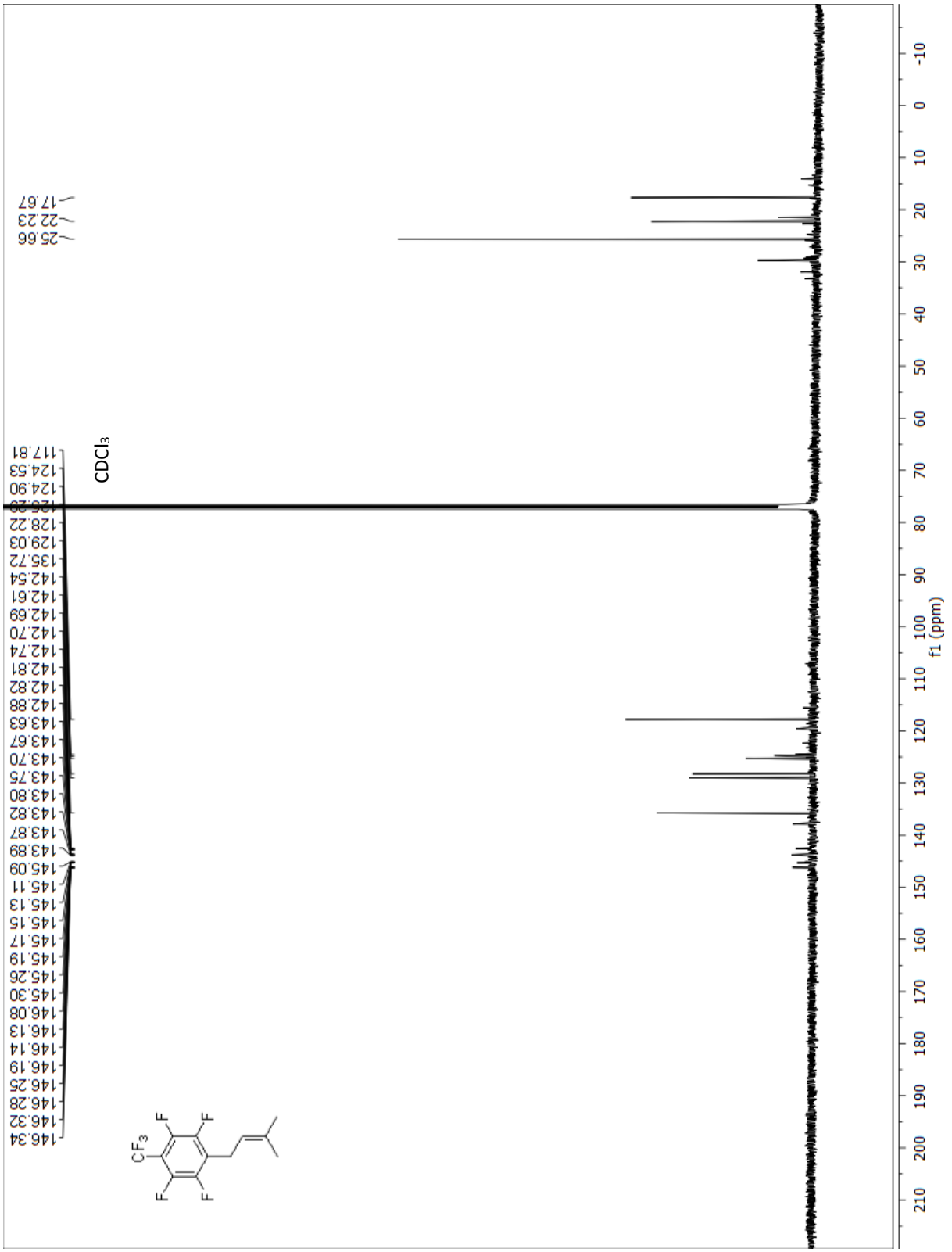
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **1,2,4,5-tetrafluoro-3-(3-methylbut-2-en-1-yl)-6-(trifluoromethyl)benzene (3e)**



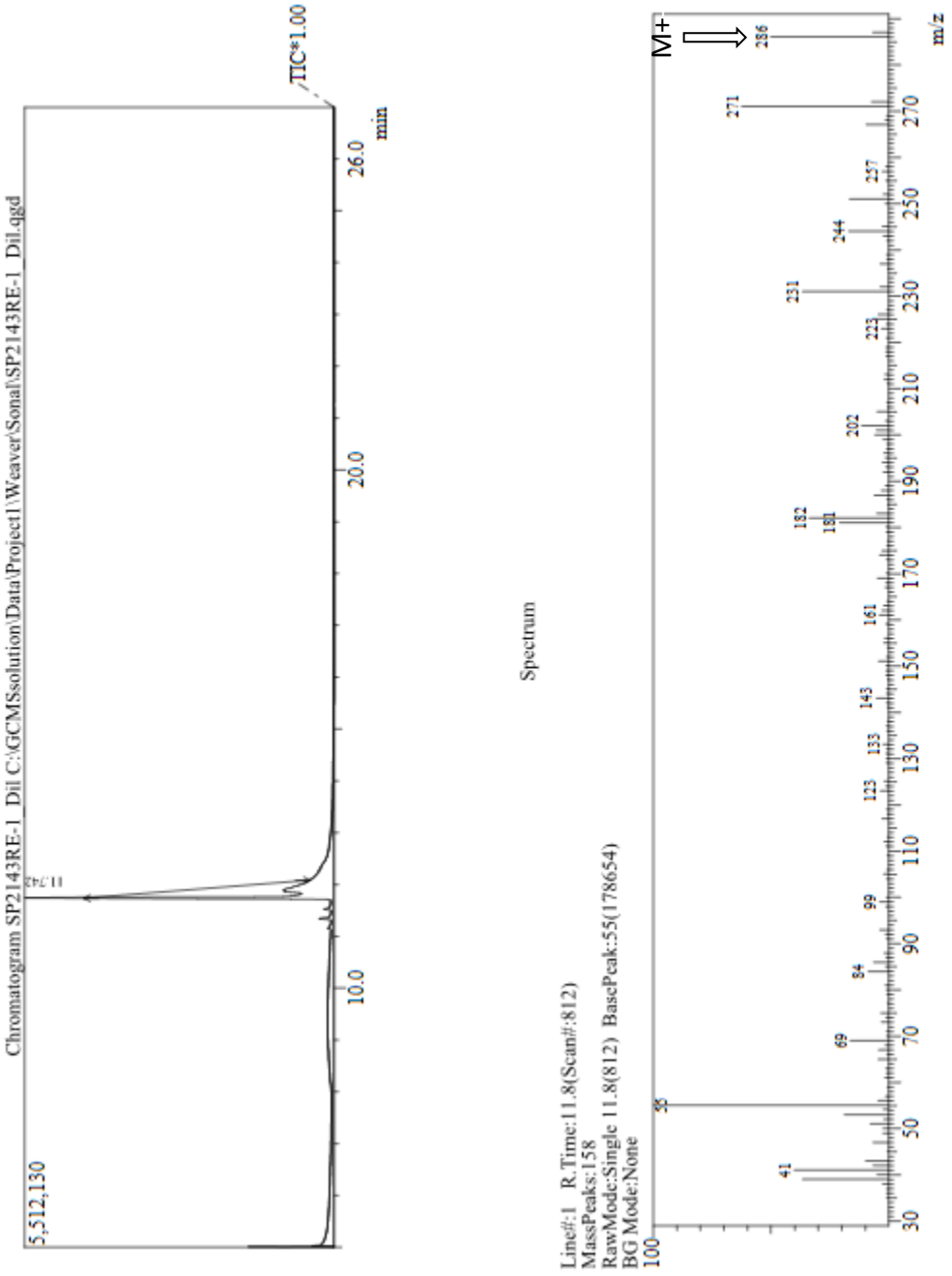
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **1,2,4,5-tetrafluoro-3-(3-methylbut-2-en-1-yl)-6-(trifluoromethyl)benzene (3e)**



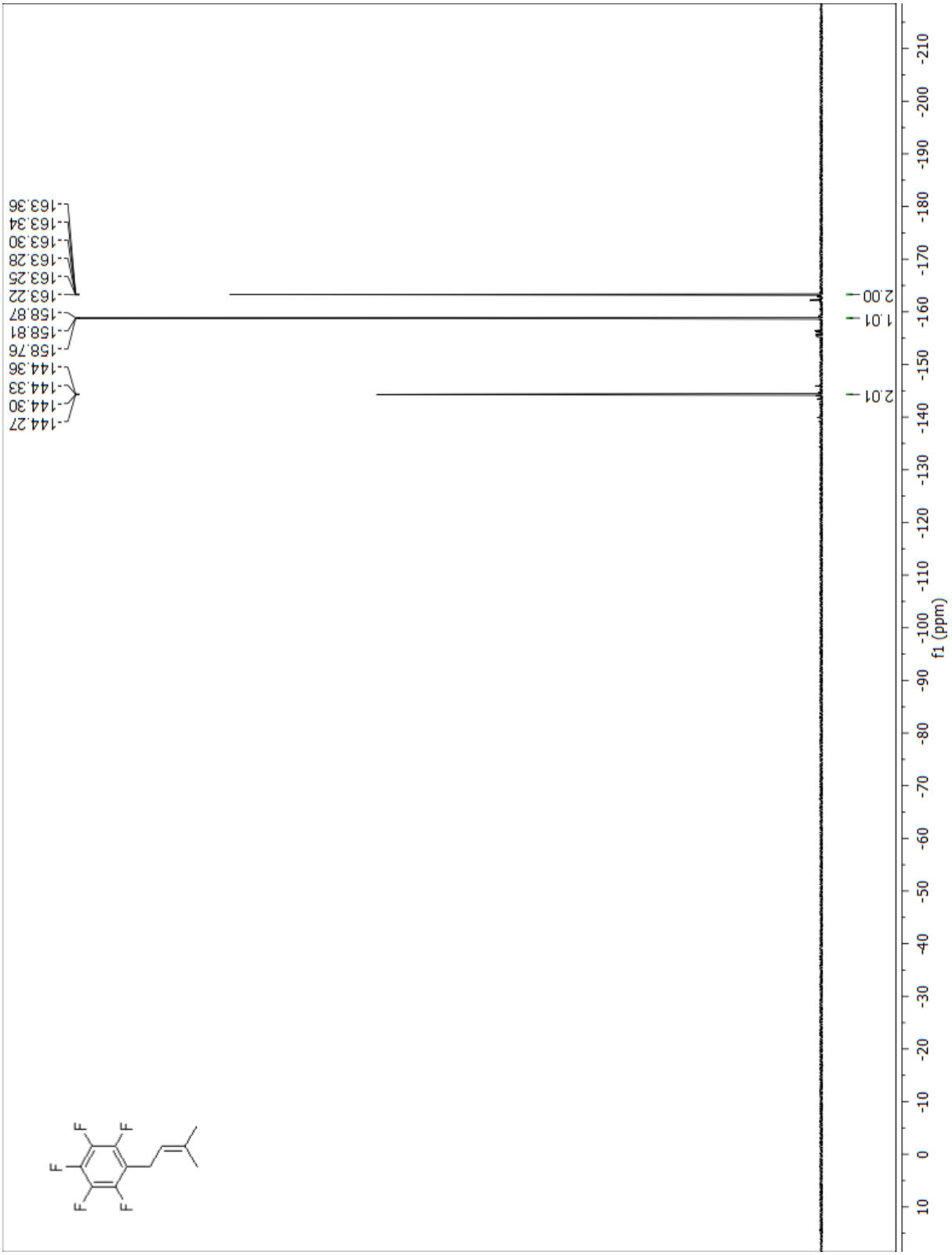
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **1,2,4,5-tetrafluoro-3-(3-methylbut-2-en-1-yl)-6-(trifluoromethyl)benzene (3e)**



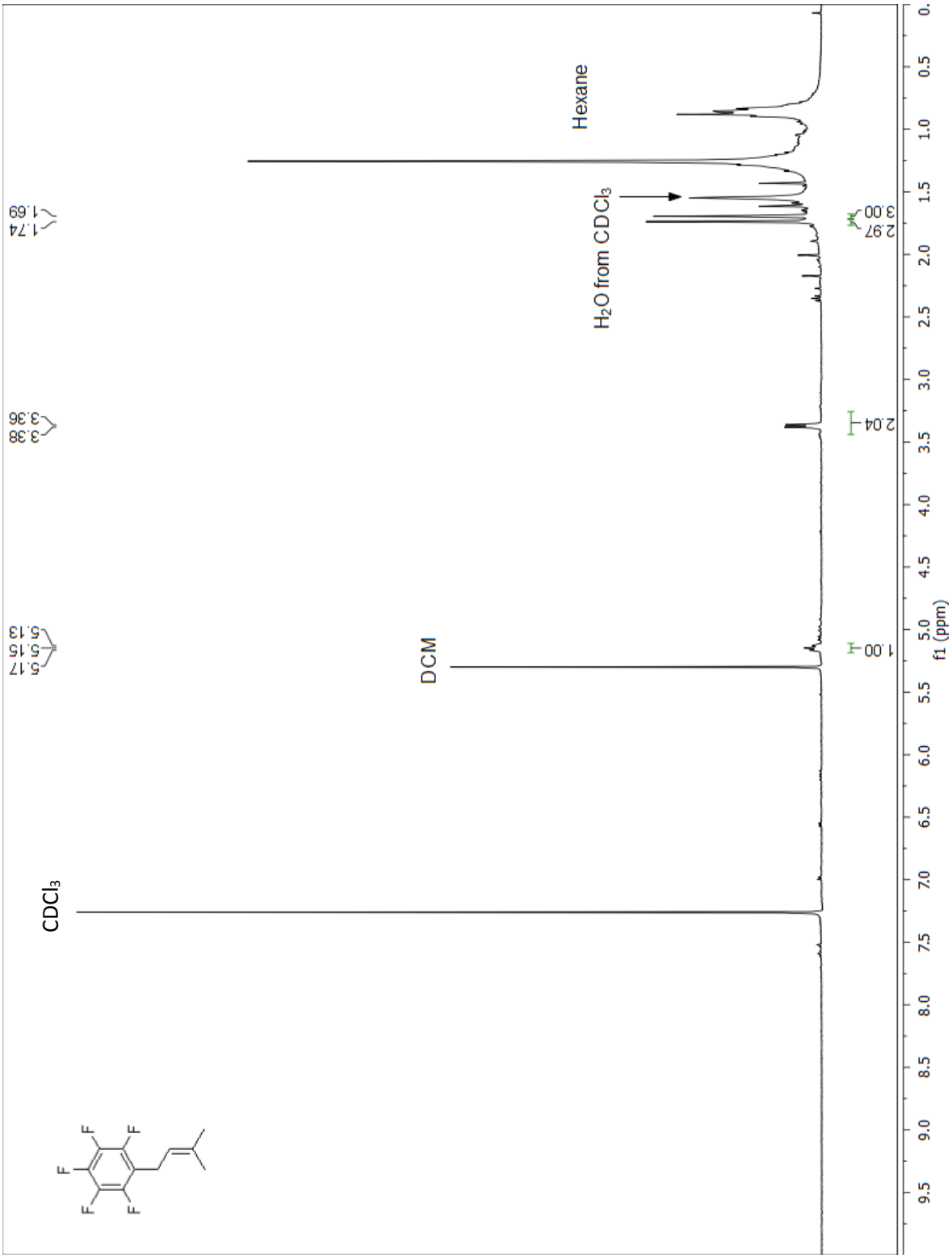
GC and MS of **1,2,4,5-tetrafluoro-3-(3-methylbut-2-en-1-yl)-6-(trifluoromethyl)benzene (3e)**



^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **1,2,3,4,5-pentafluoro-6-(3-methylbut-2-en-1-yl)benzene (3f)**

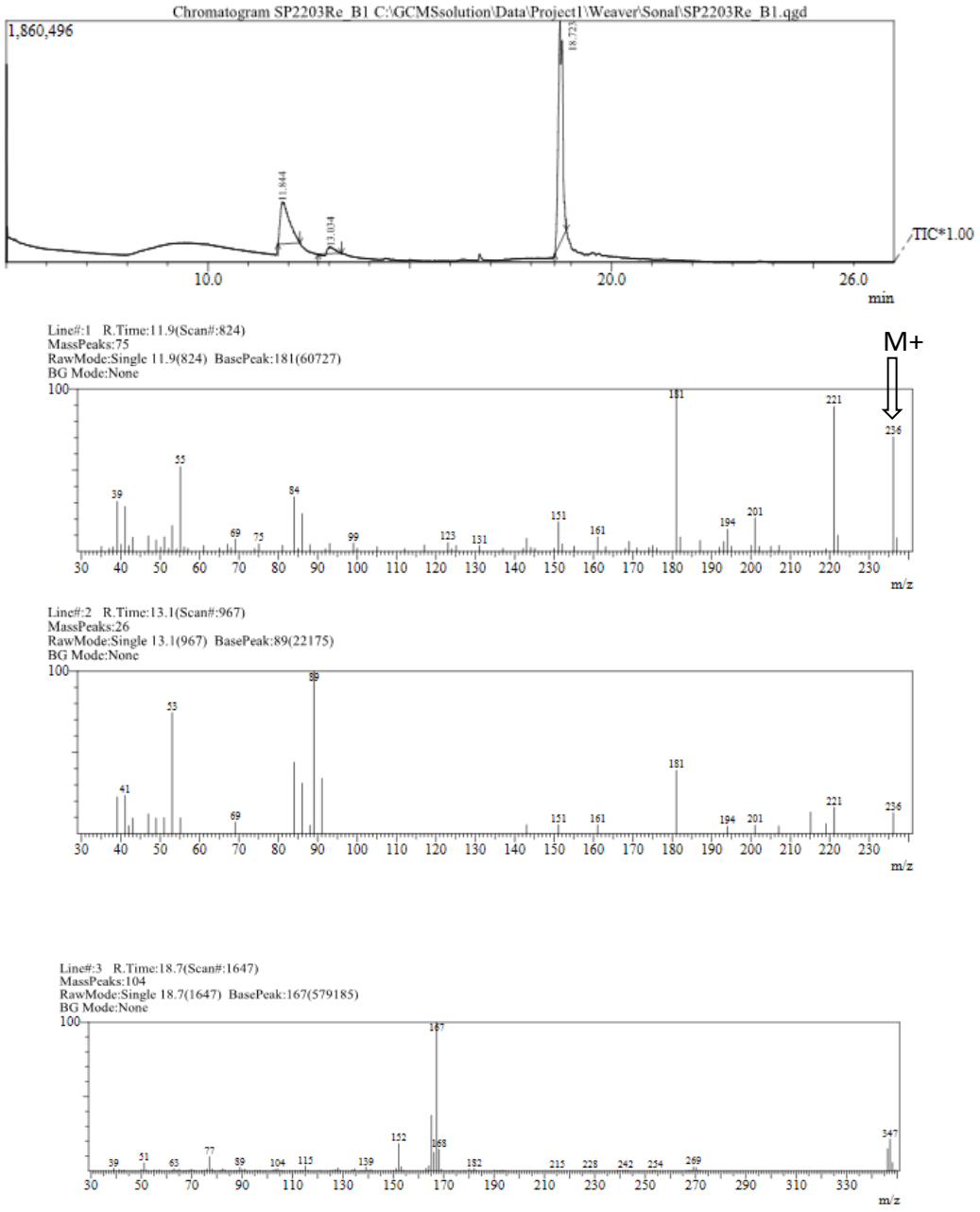


^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **1,2,3,4,5-pentafluoro-6-(3-methylbut-2-en-1-yl)benzene (3f)**

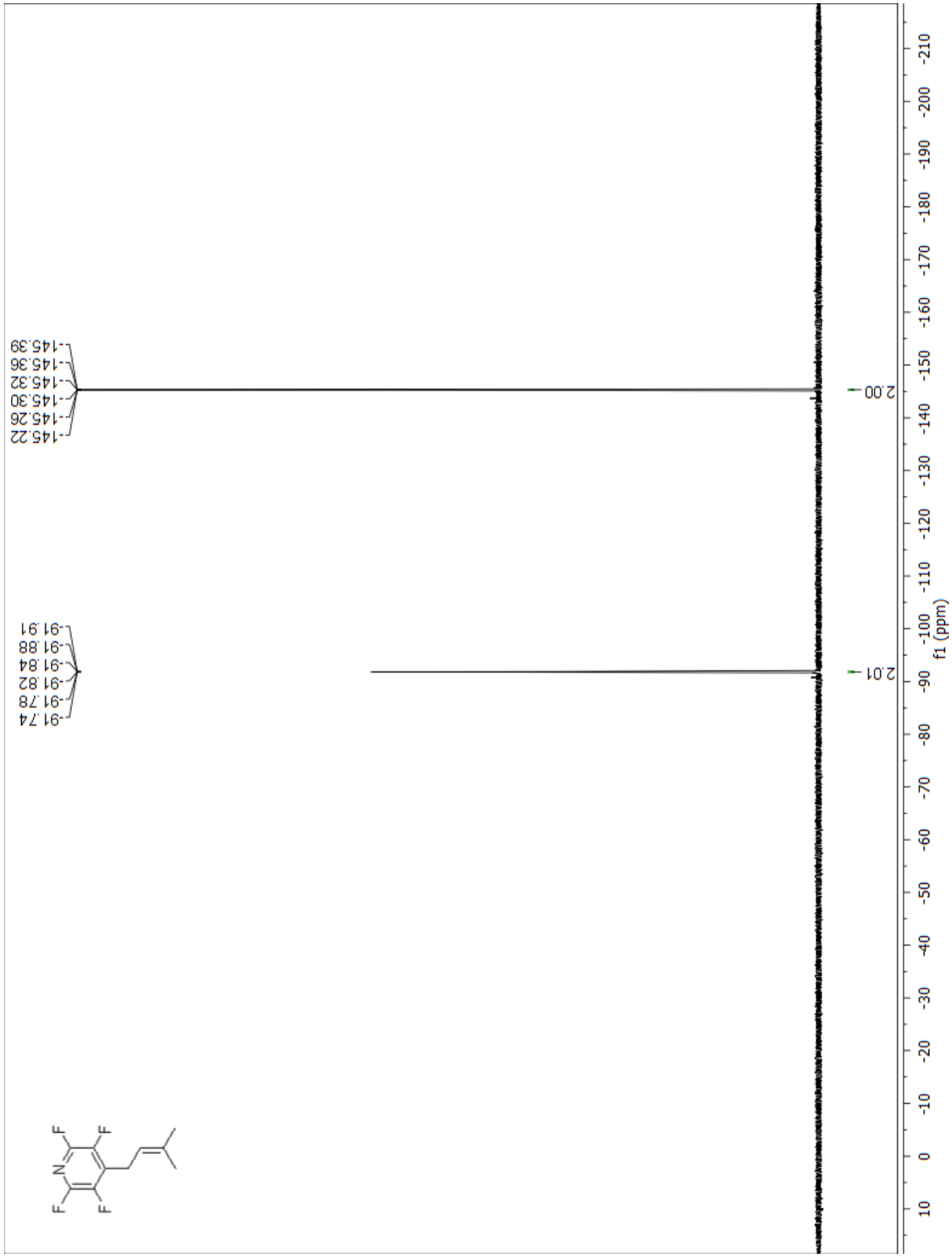


Minimal effort was given to evaporate the solvent due to low volatility of the product.

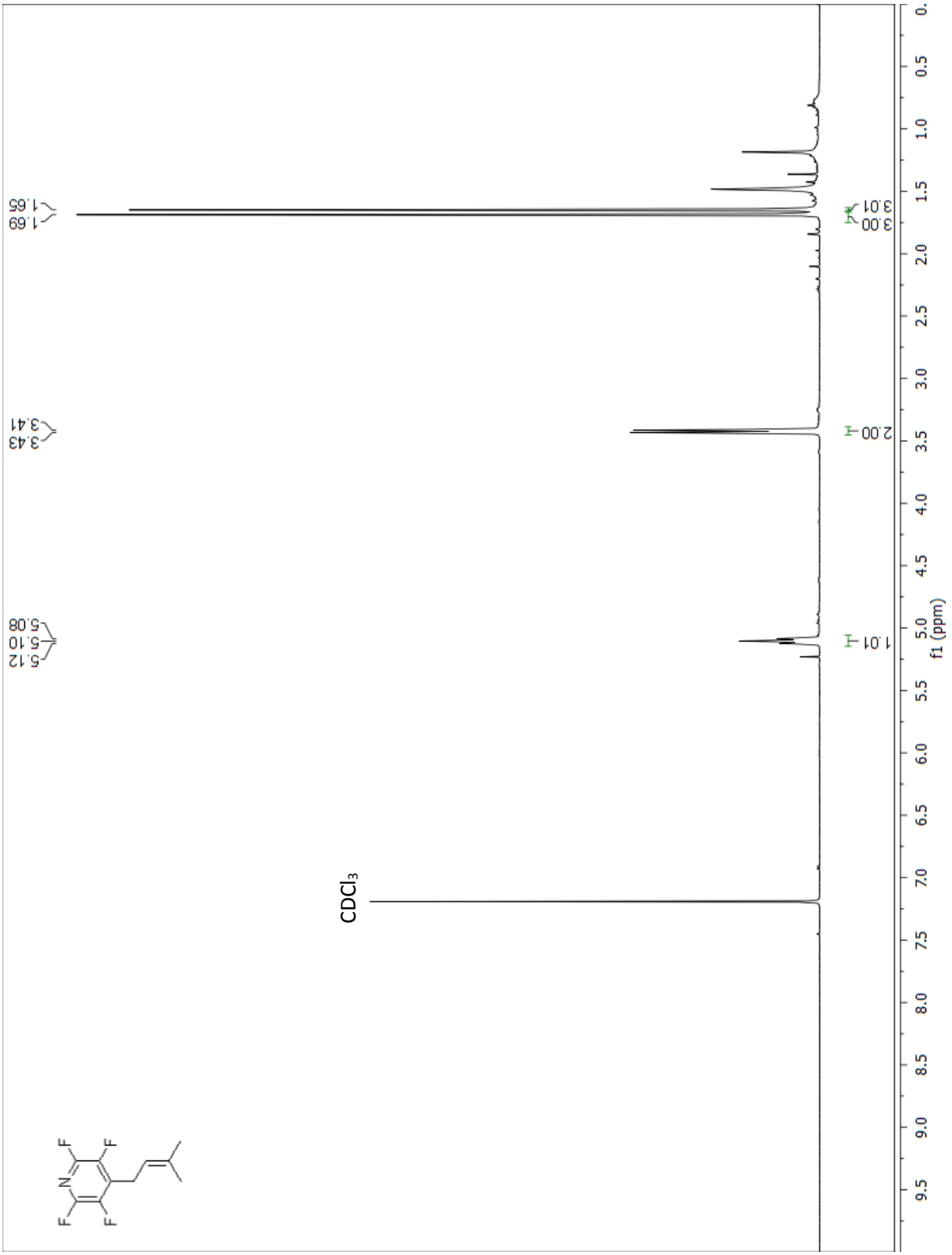
GC and MS of **1,2,3,4,5-pentafluoro-6-(3-methylbut-2-en-1-yl)benzene (3f)**



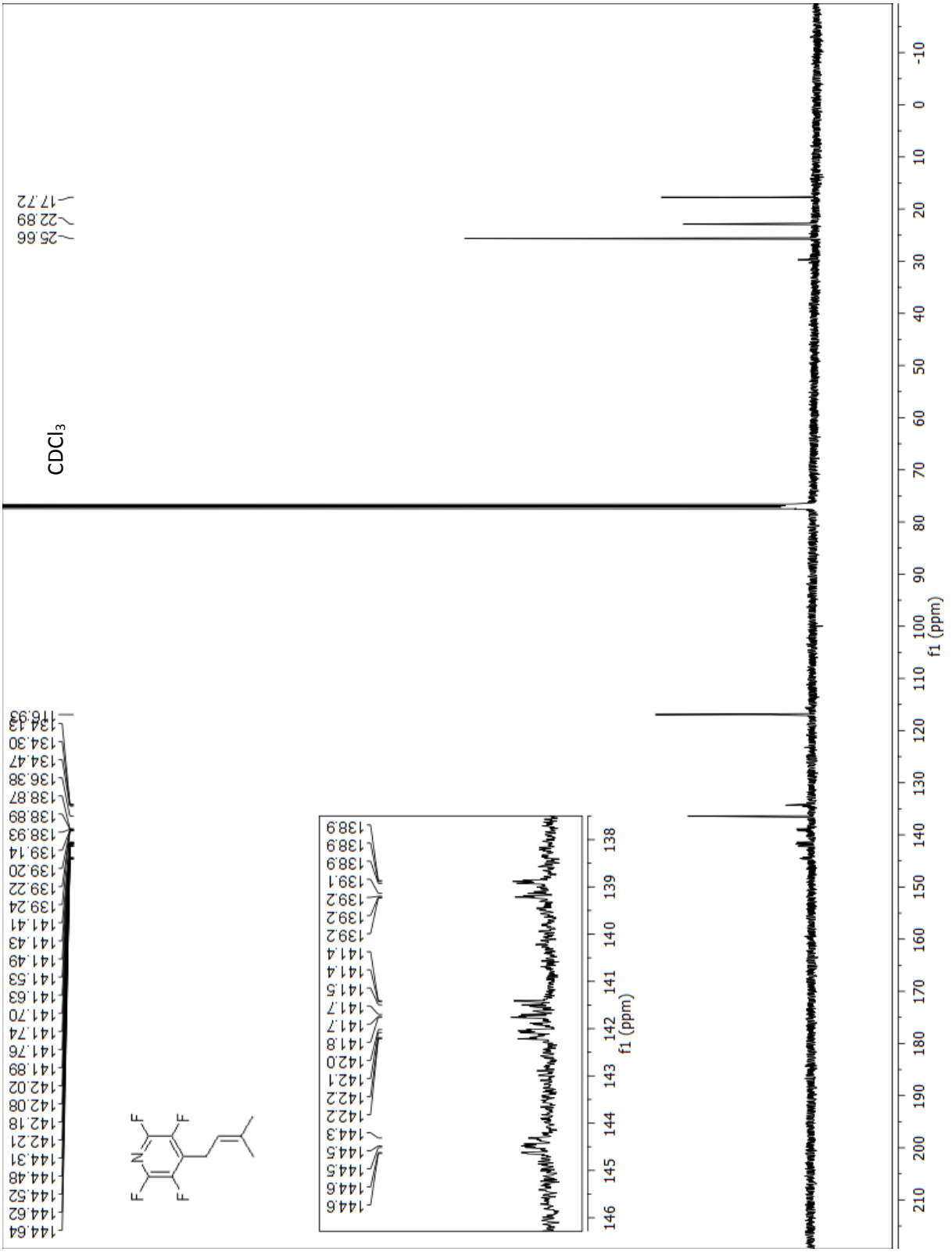
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)pyridine (3g)**



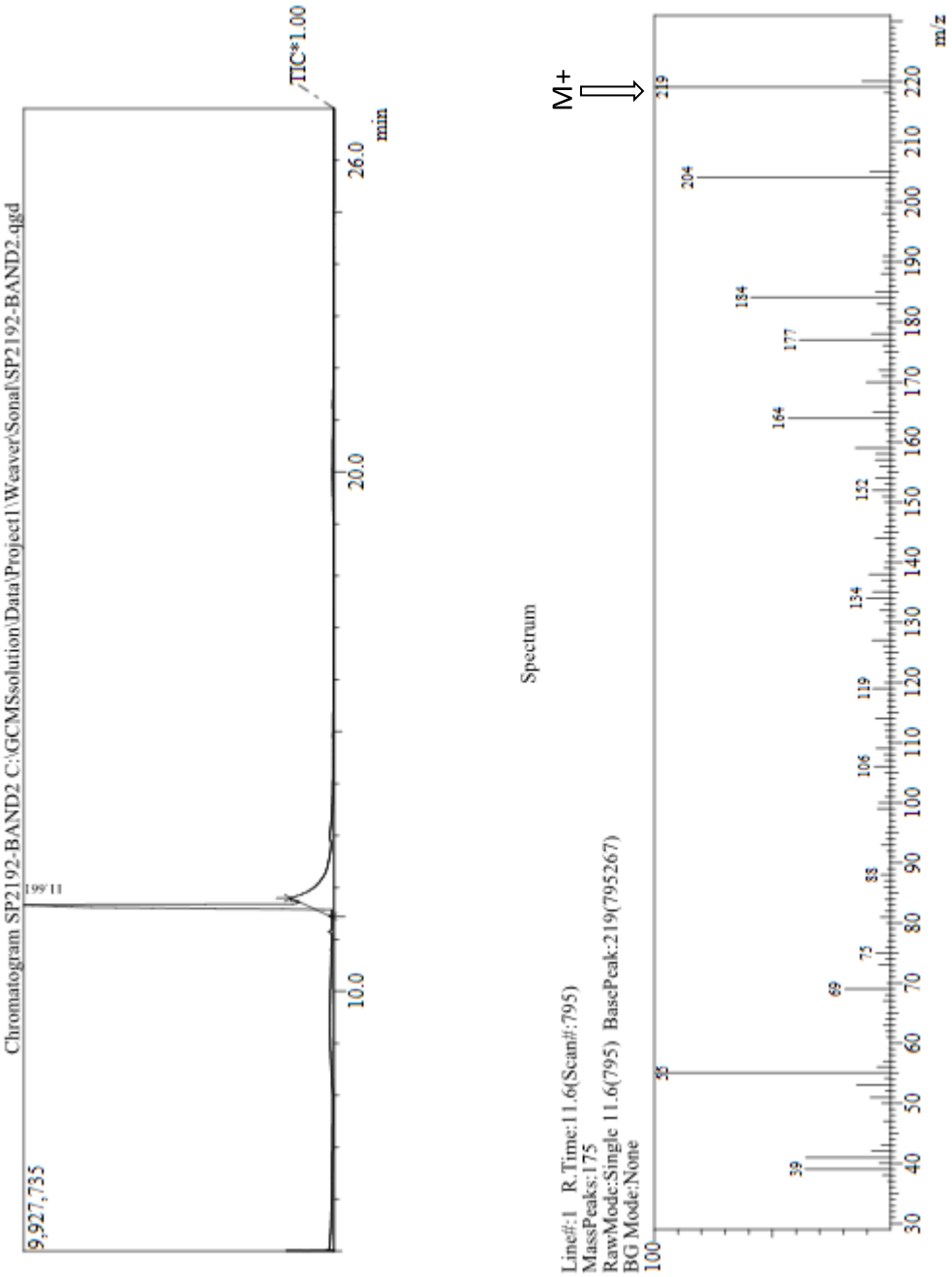
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)pyridine (3g)**



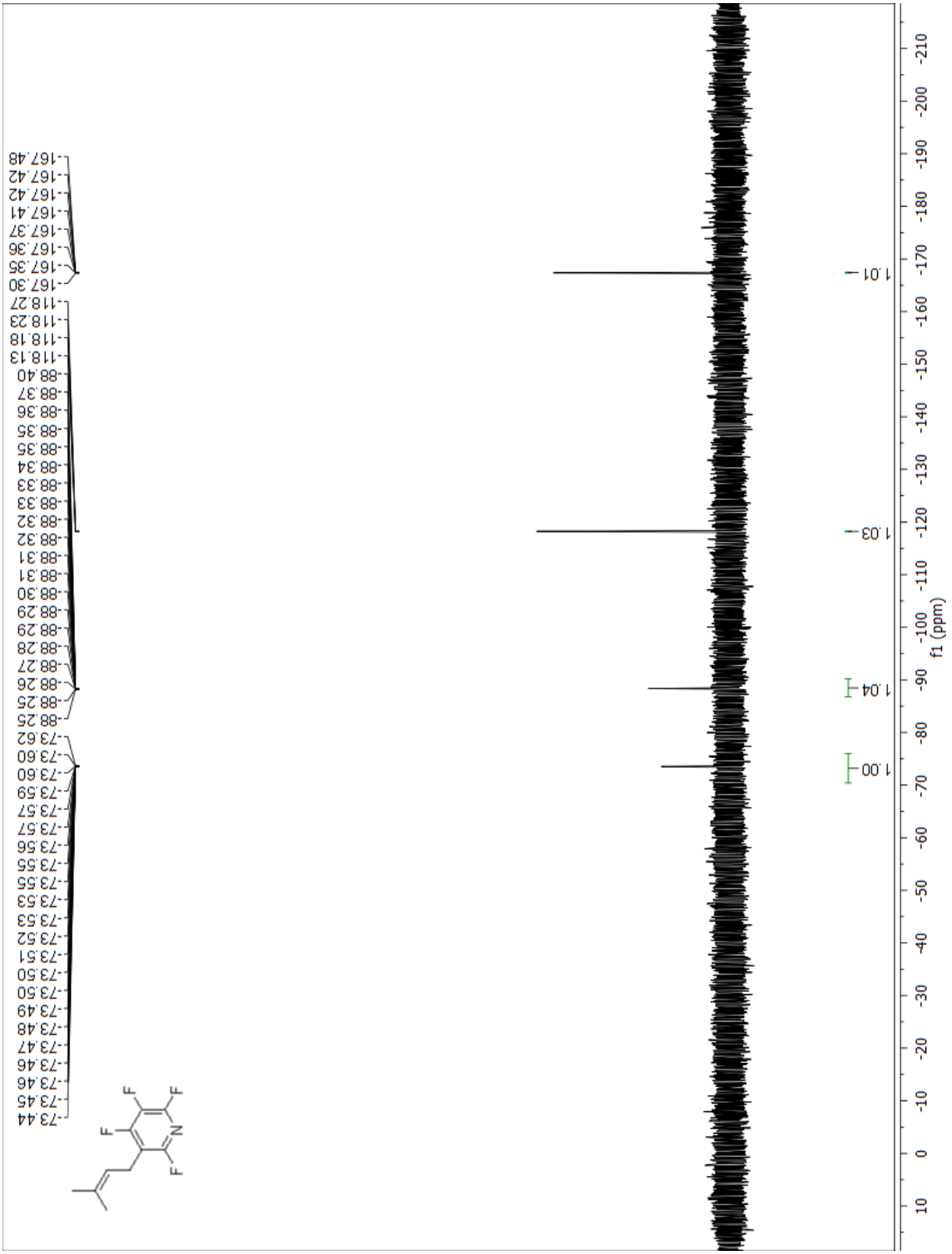
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)pyridine (3g)**



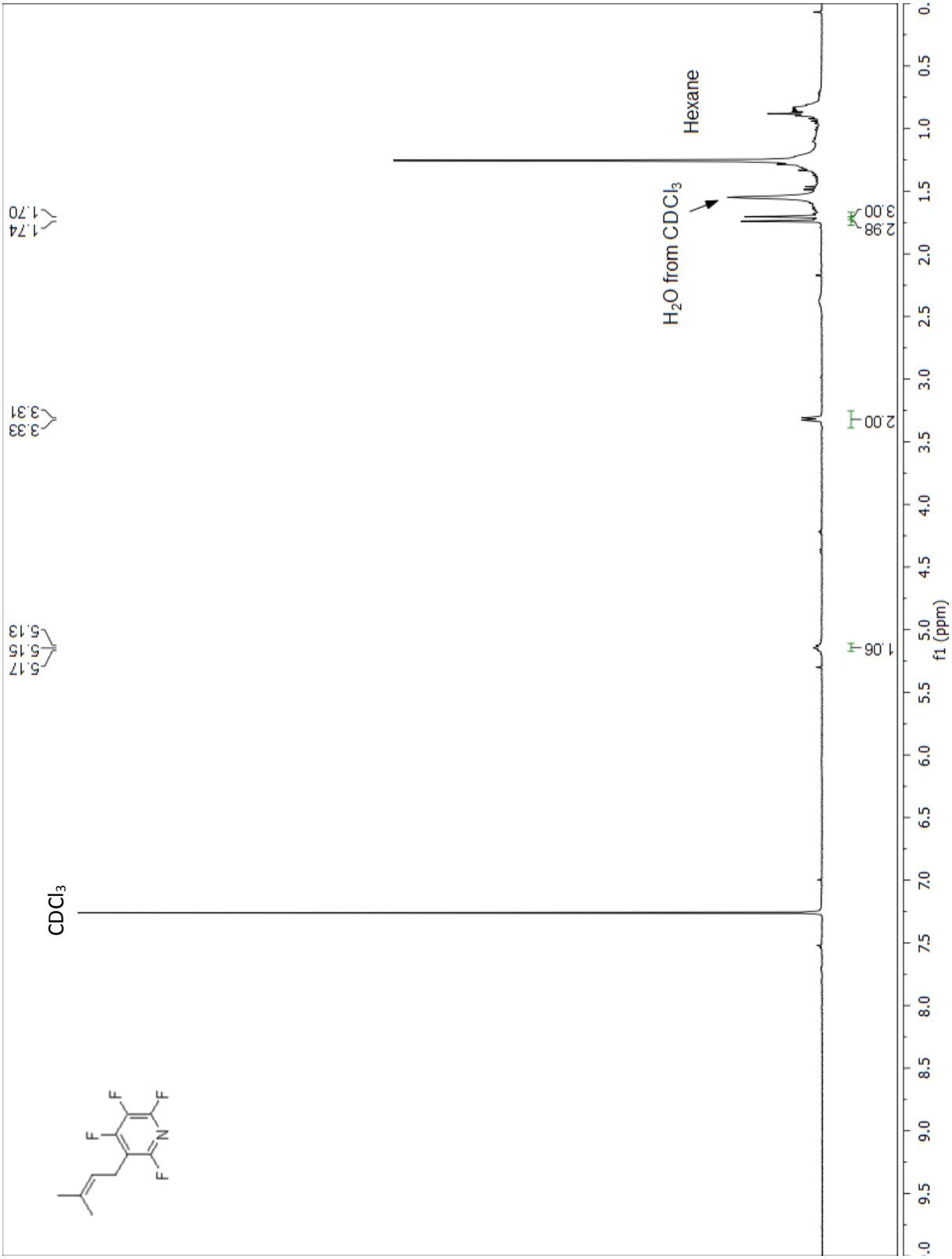
GC and MS of **2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)pyridine (3g)**



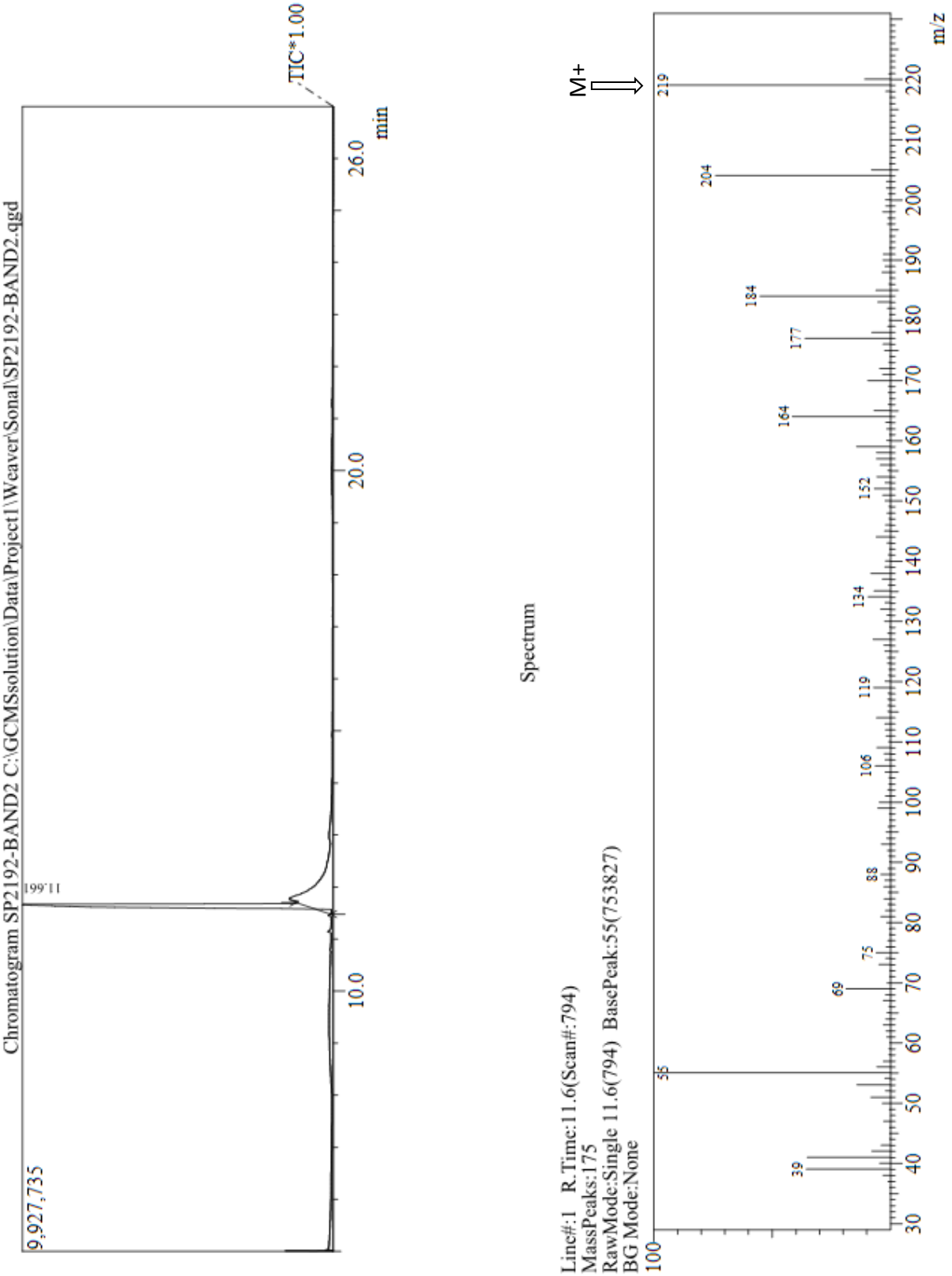
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **2,3,4,6-tetrafluoro-5-(3-methylbut-2-en-1-yl)pyridine (3i)**



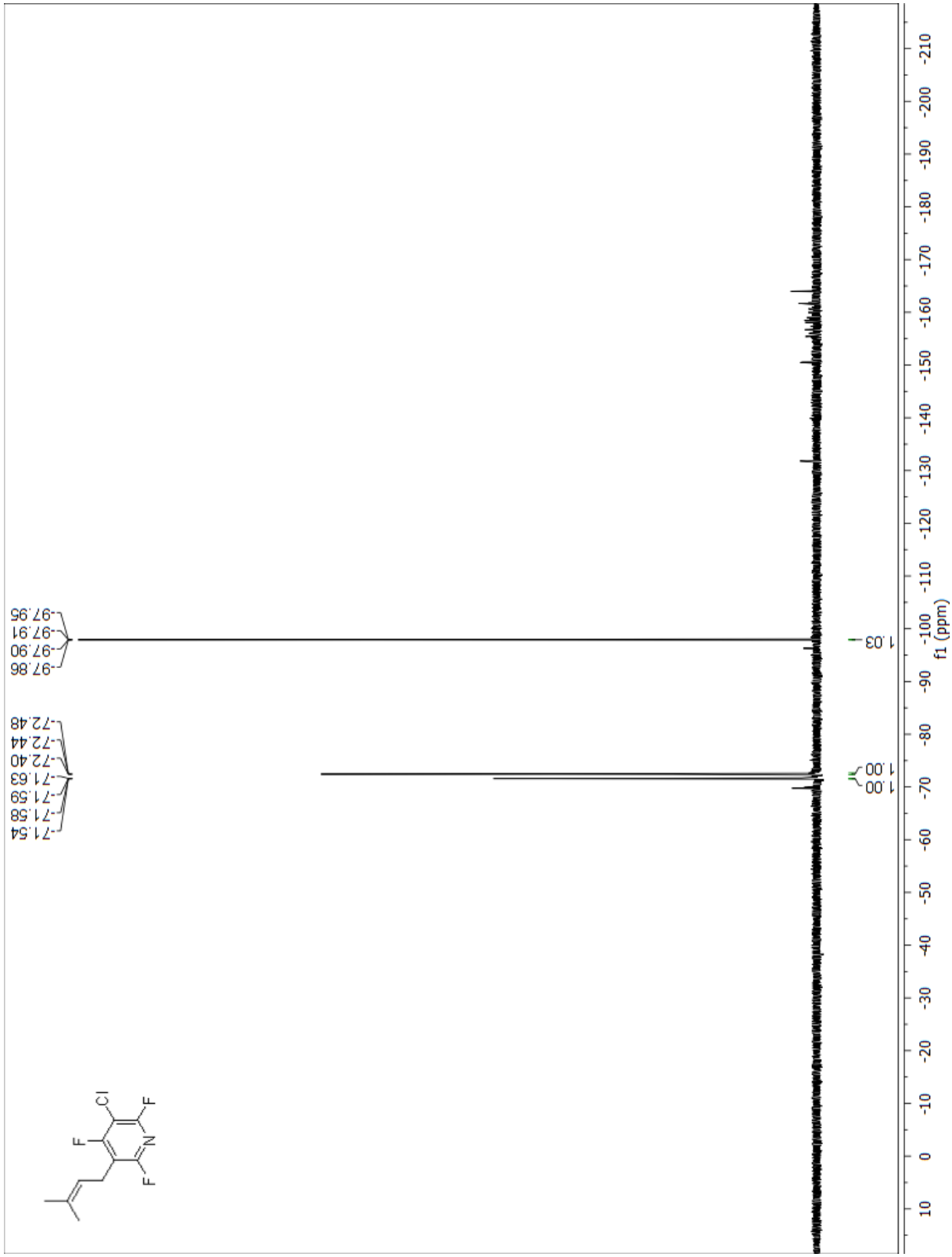
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **2,3,4,6-tetrafluoro-5-(3-methylbut-2-en-1-yl)pyridine (3i)**



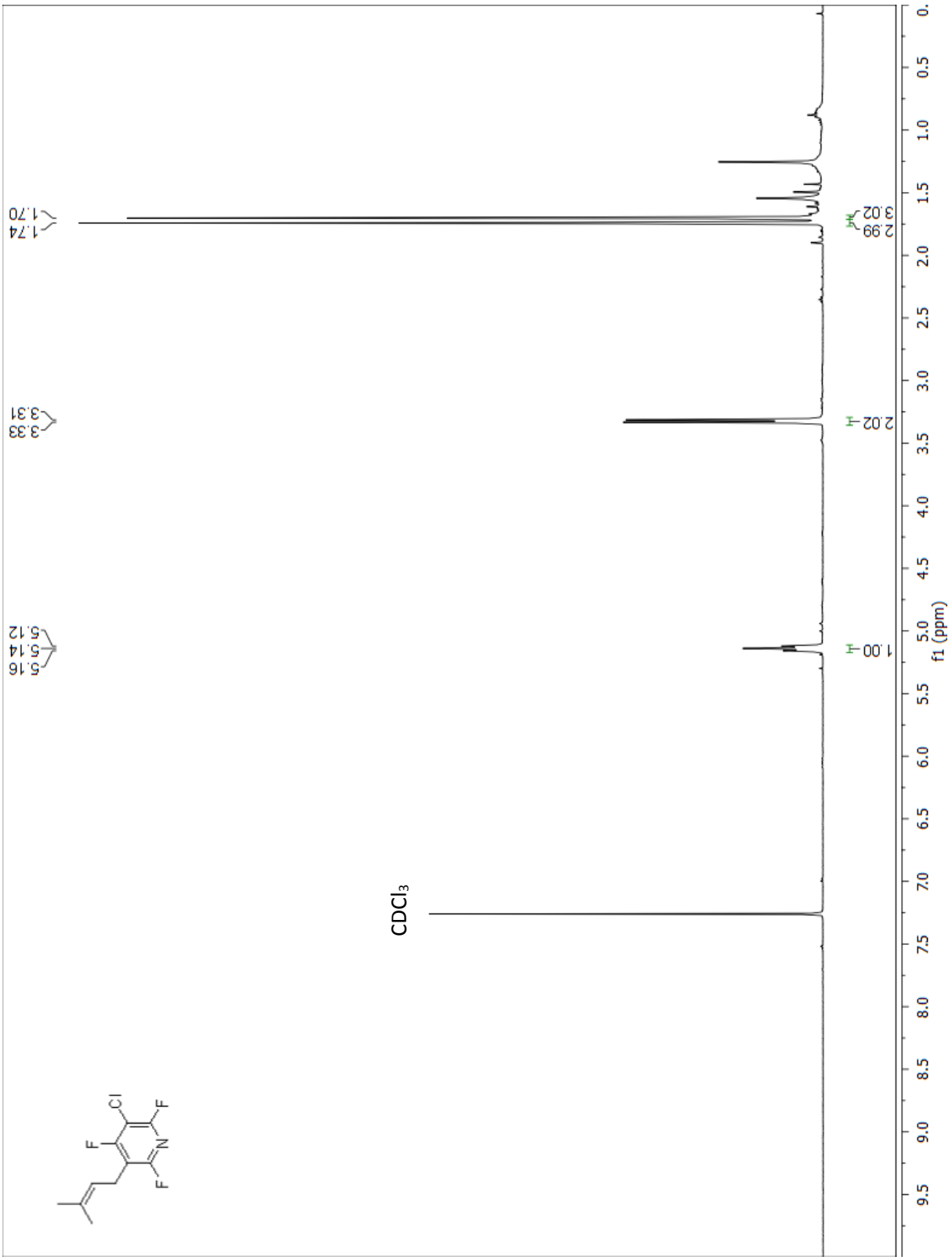
GC and MS of **2,3,4,6-tetrafluoro-5-(3-methylbut-2-en-1-yl)pyridine (3i)**



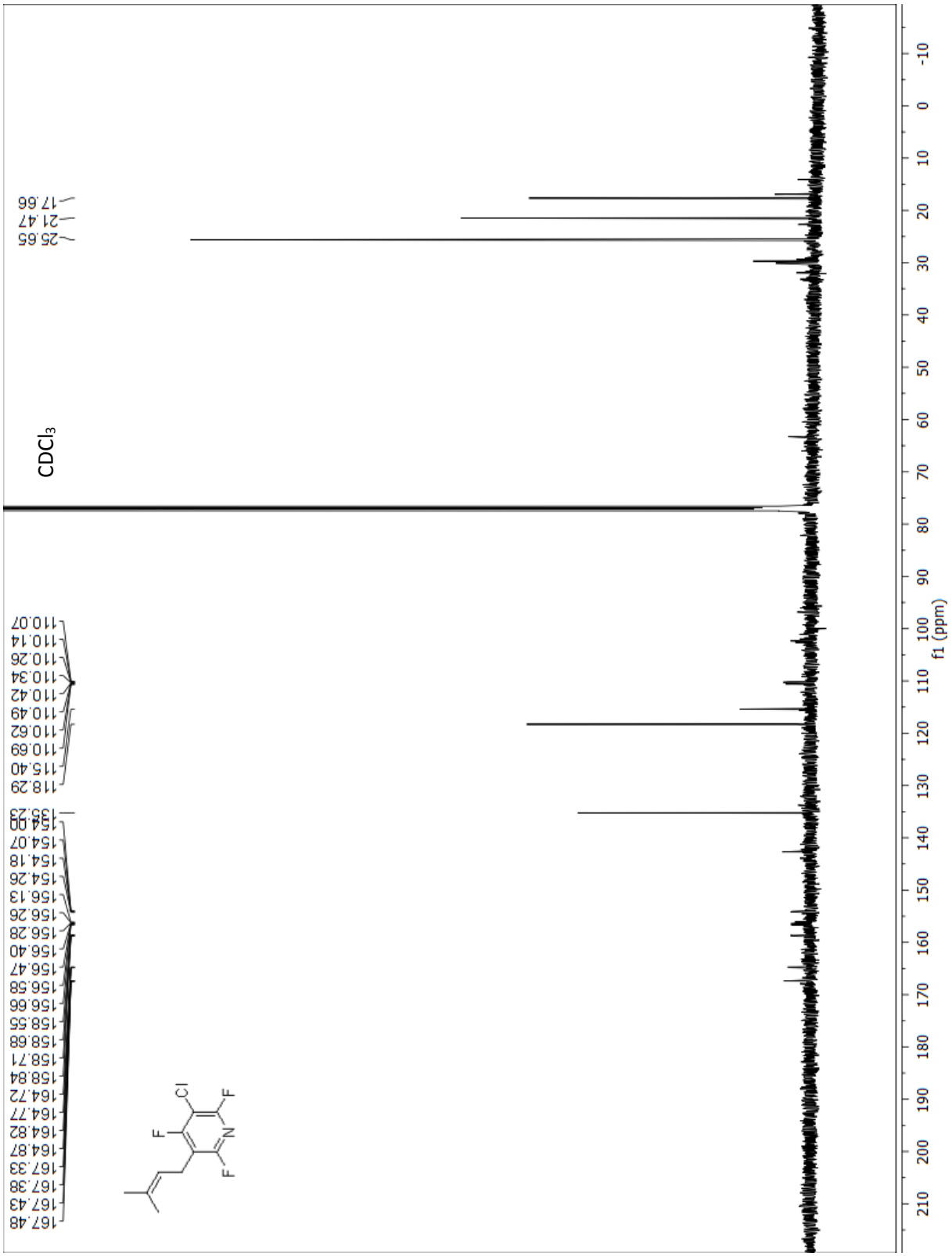
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **3-chloro-2,4,6-trifluoro-5-(3-methylbut-2-en-1-yl)pyridine (3j)**



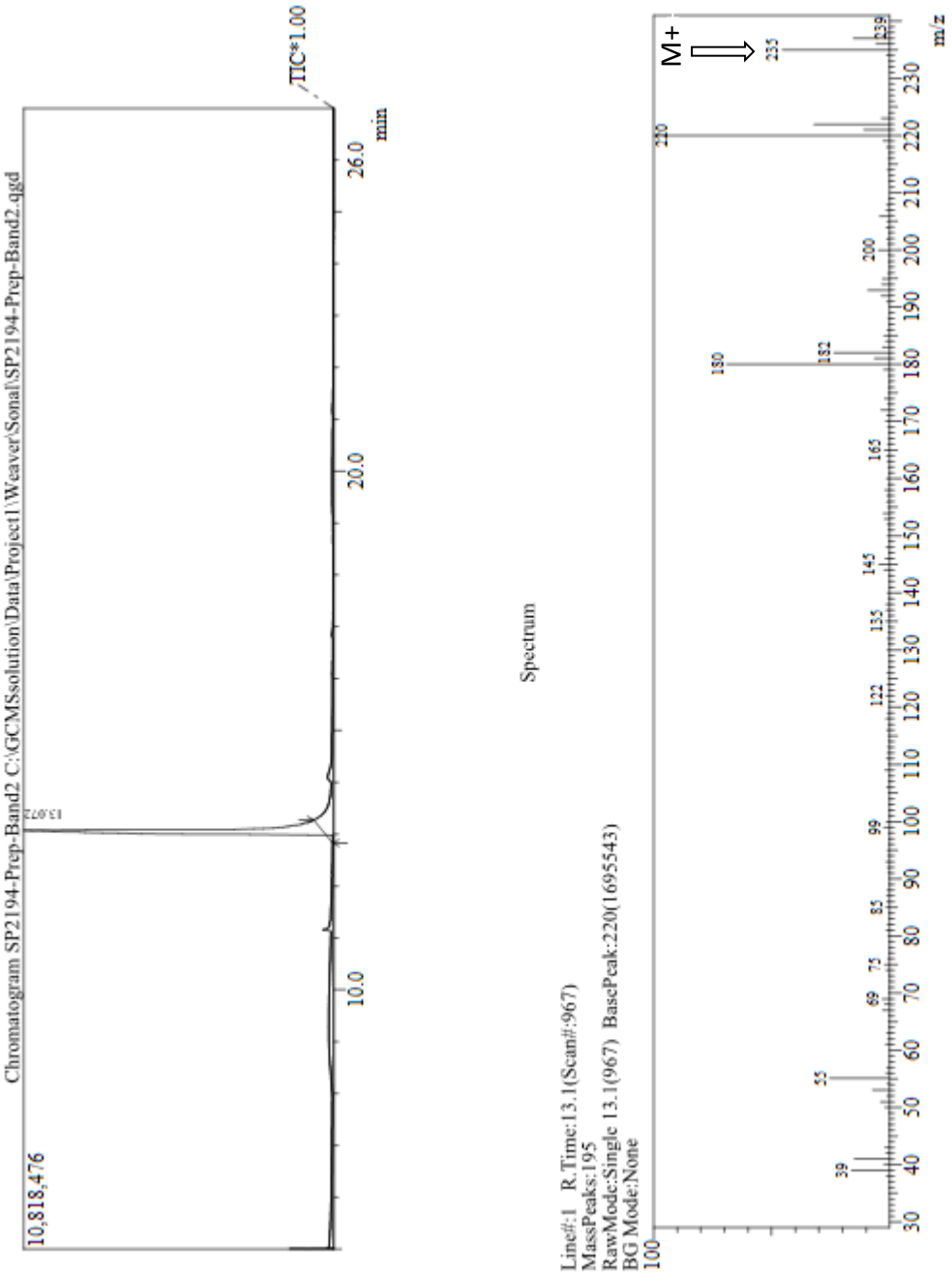
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **3-chloro-2,4,6-trifluoro-5-(3-methylbut-2-en-1-yl)pyridine (3j)**



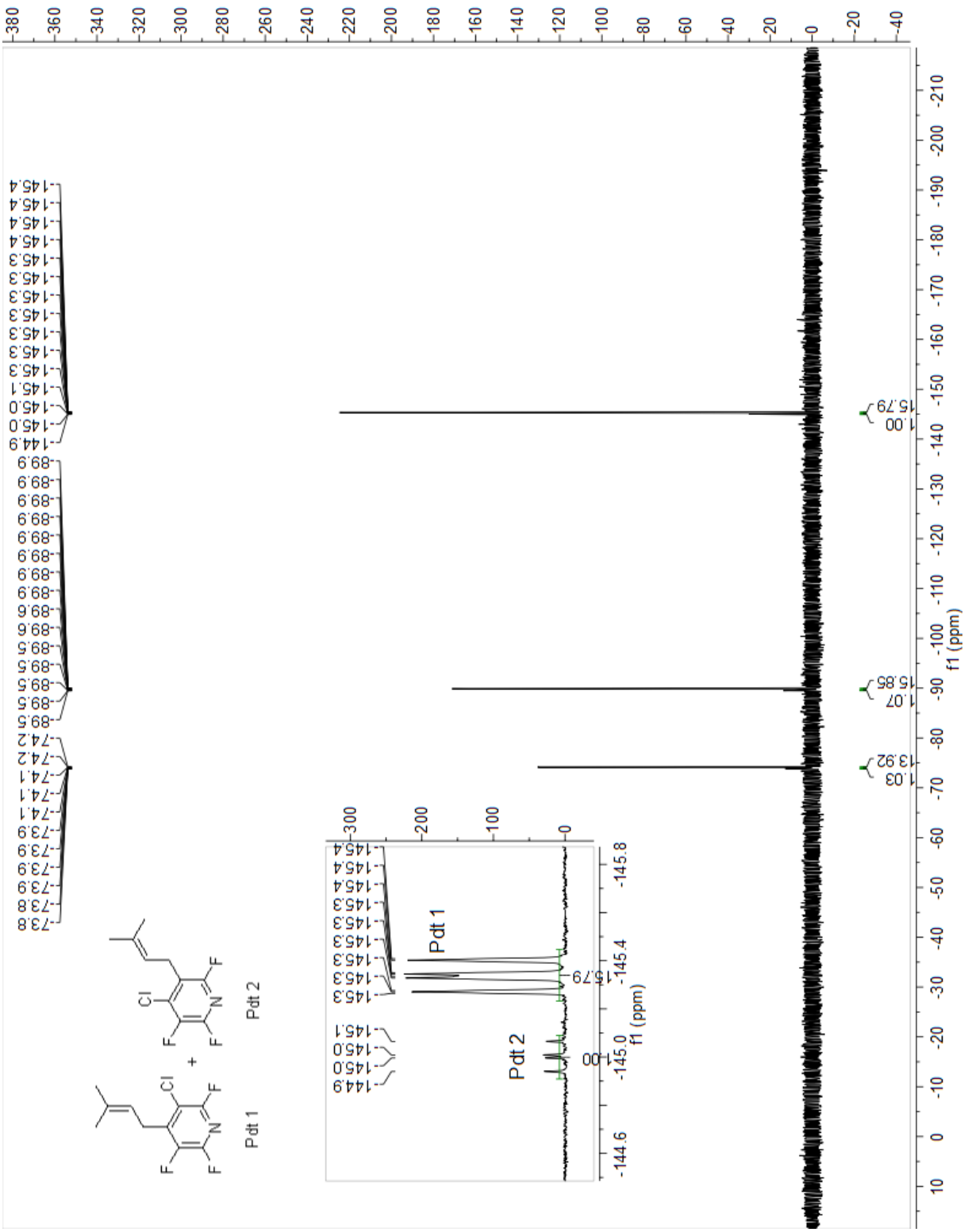
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **3-chloro-2,4,6-trifluoro-5-(3-methylbut-2-en-1-yl)pyridine (3j)**



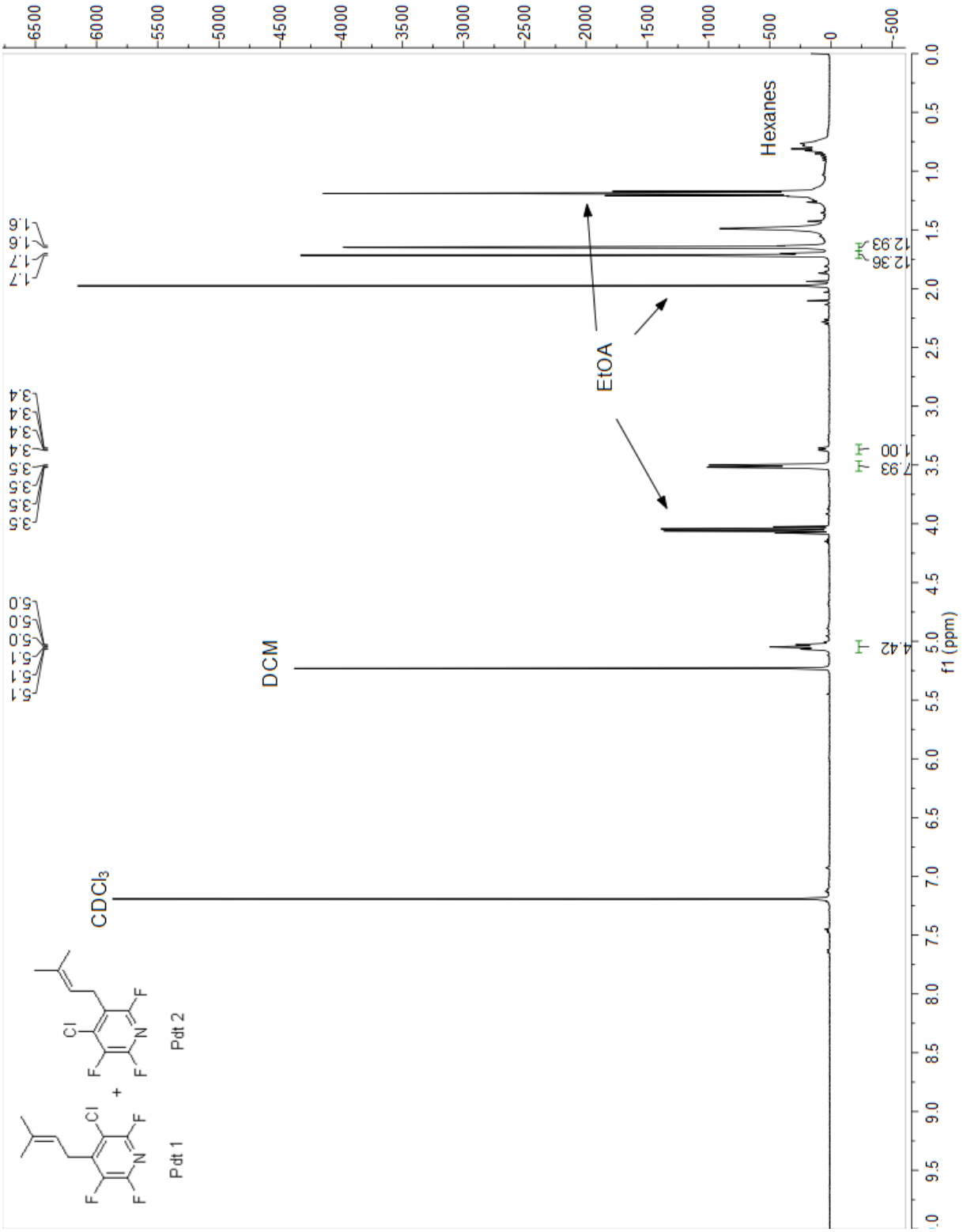
GC and MS of **3-chloro-2,4,6-trifluoro-5-(3-methylbut-2-en-1-yl)pyridine (3j)**



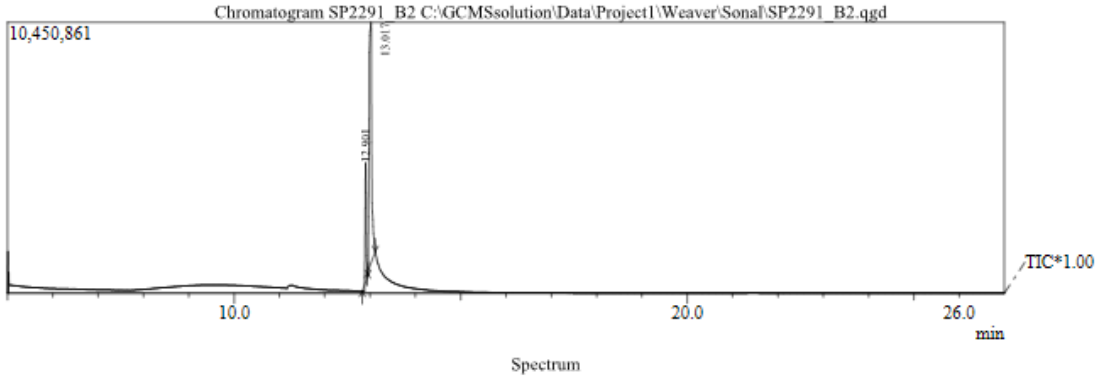
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **3-chloro-2,5,6-trifluoro-4-(3-methylbut-2-en-1-yl)pyridine (3k)**



^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **3-chloro-2,5,6-trifluoro-4-(3-methylbut-2-en-1-yl)pyridine (3k)**

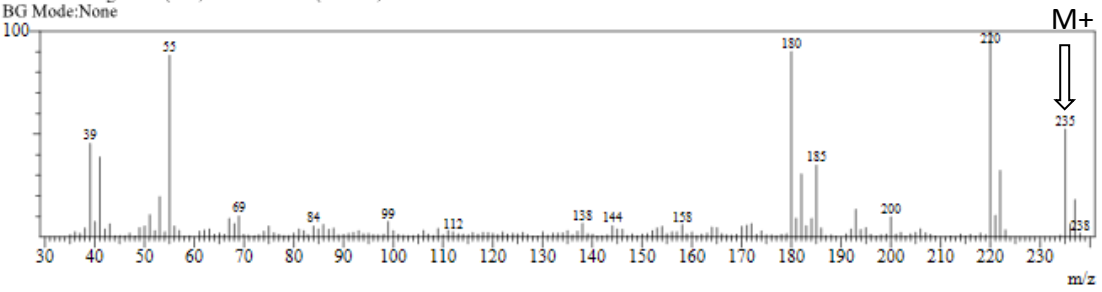


GC and MS of **3-chloro-2,5,6-trifluoro-4-(3-methylbut-2-en-1-yl)pyridine (3k)**

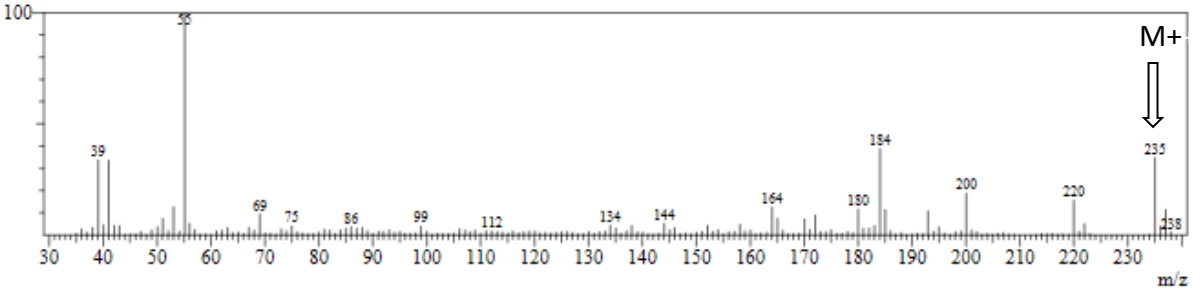


Spectrum

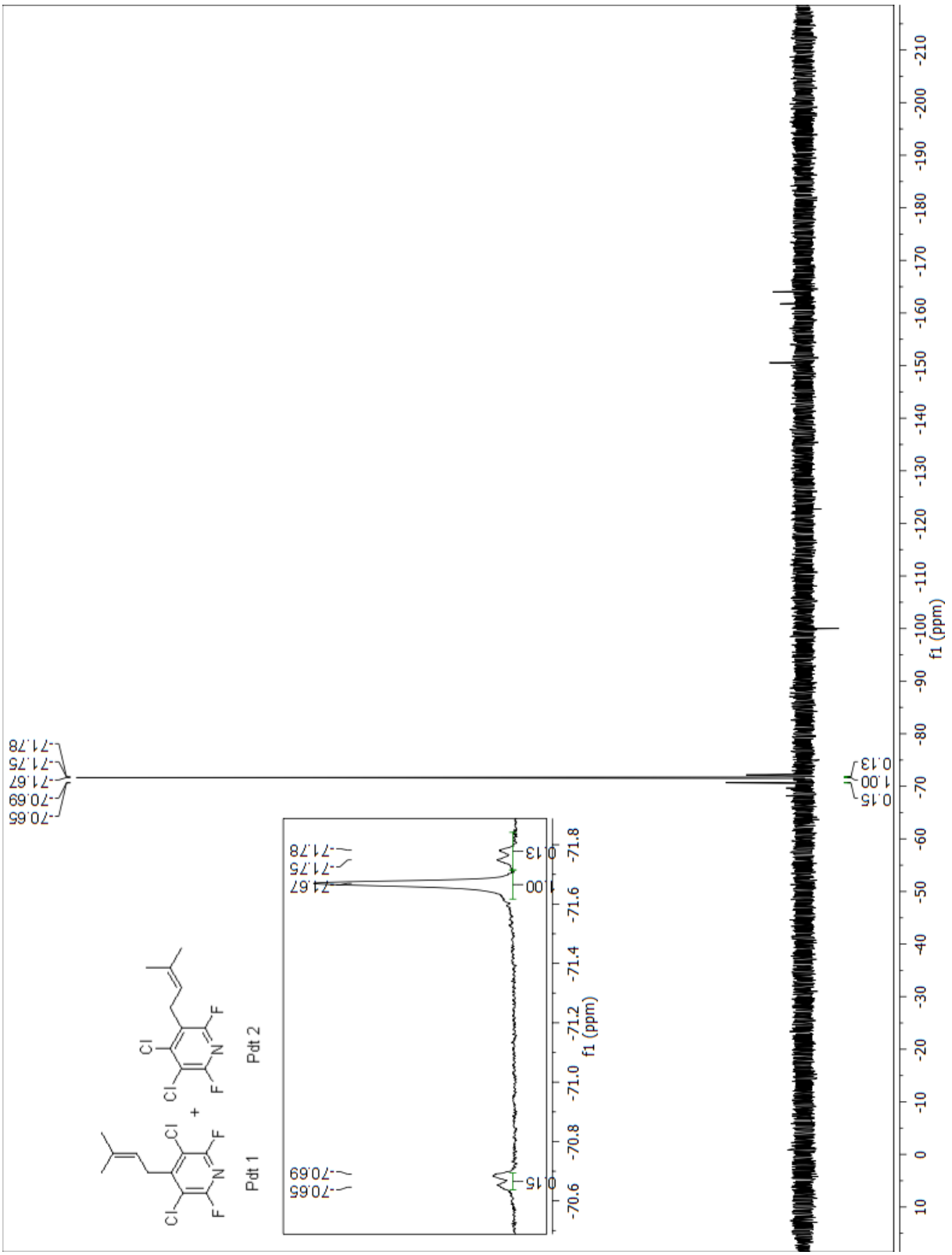
Line#:1 R.Time:12.9(Scan#:950)
MassPeaks:189
RawMode:Single 12.9(950) BasePeak:220(385938)
BG Mode:None



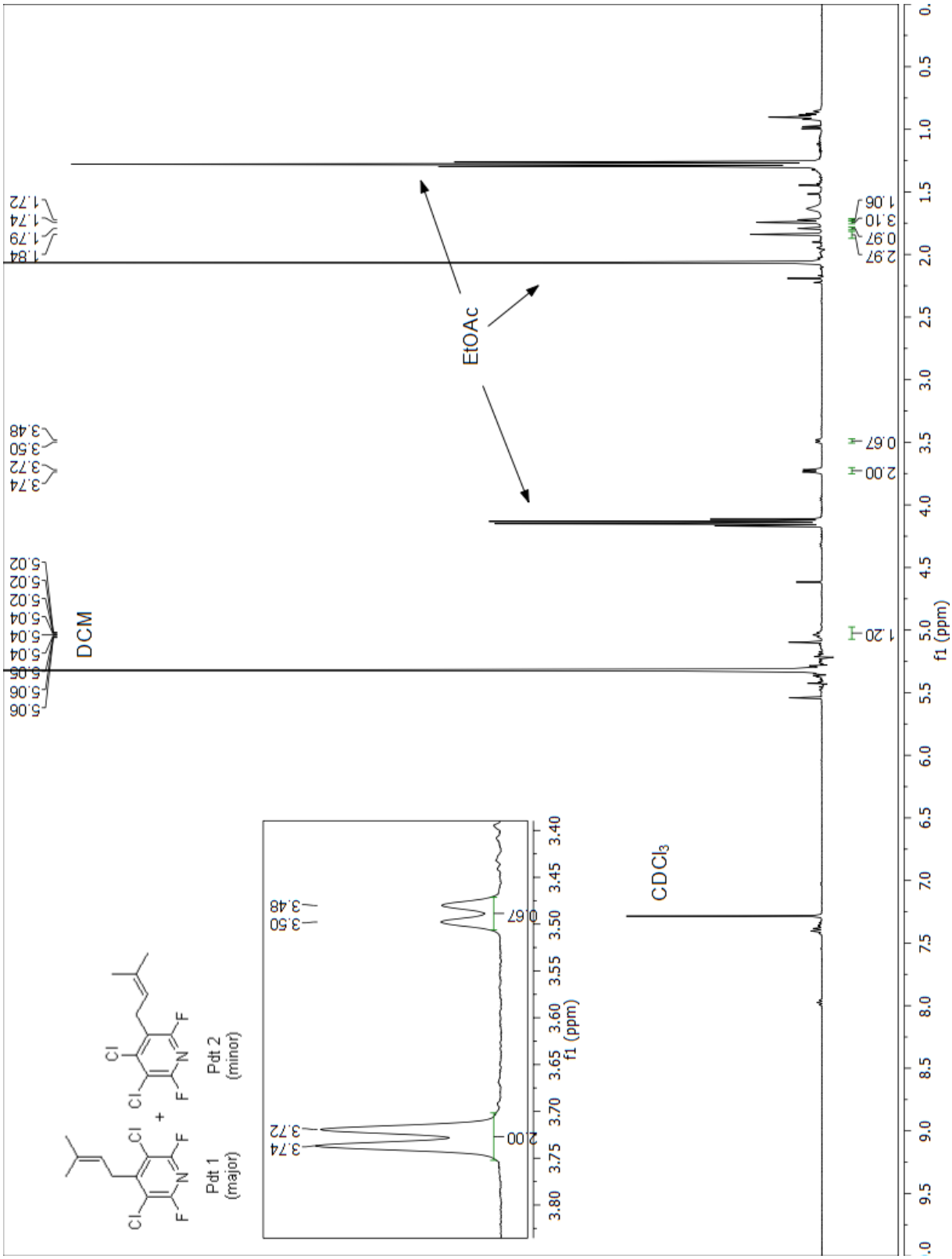
Line#:2 R.Time:13.0(Scan#:965)
MassPeaks:191
RawMode:Single 13.0(965) BasePeak:55(870577)
BG Mode:None



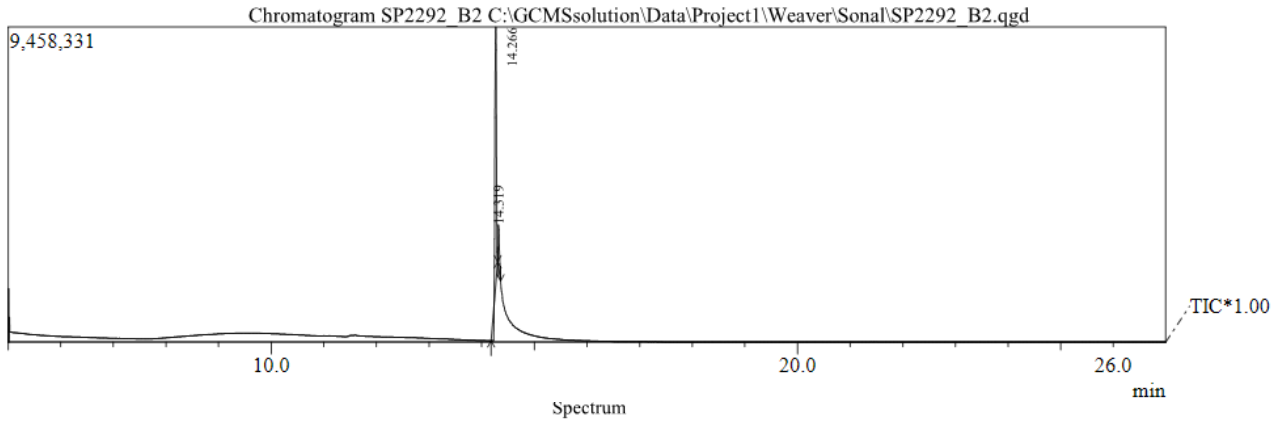
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **3,5-dichloro-2,6-difluoro-4-(3-methylbut-2-en-1-yl)pyridine (3l)**



^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **3,5-dichloro-2,6-difluoro-4-(3-methylbut-2-en-1-yl)pyridine (3l)**

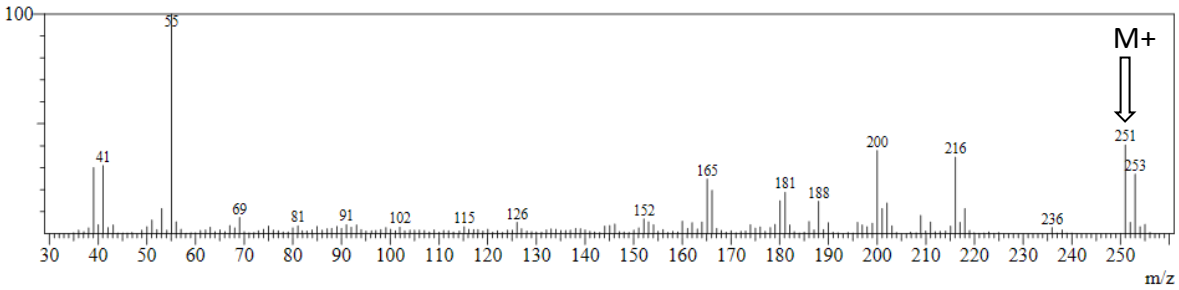


GC and MS of **3,5-dichloro-2,6-difluoro-4-(3-methylbut-2-en-1-yl)pyridine (3l)**

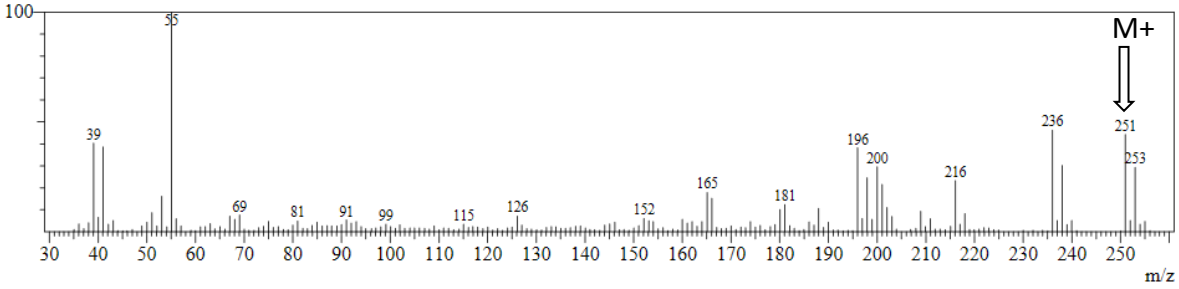


Spectrum

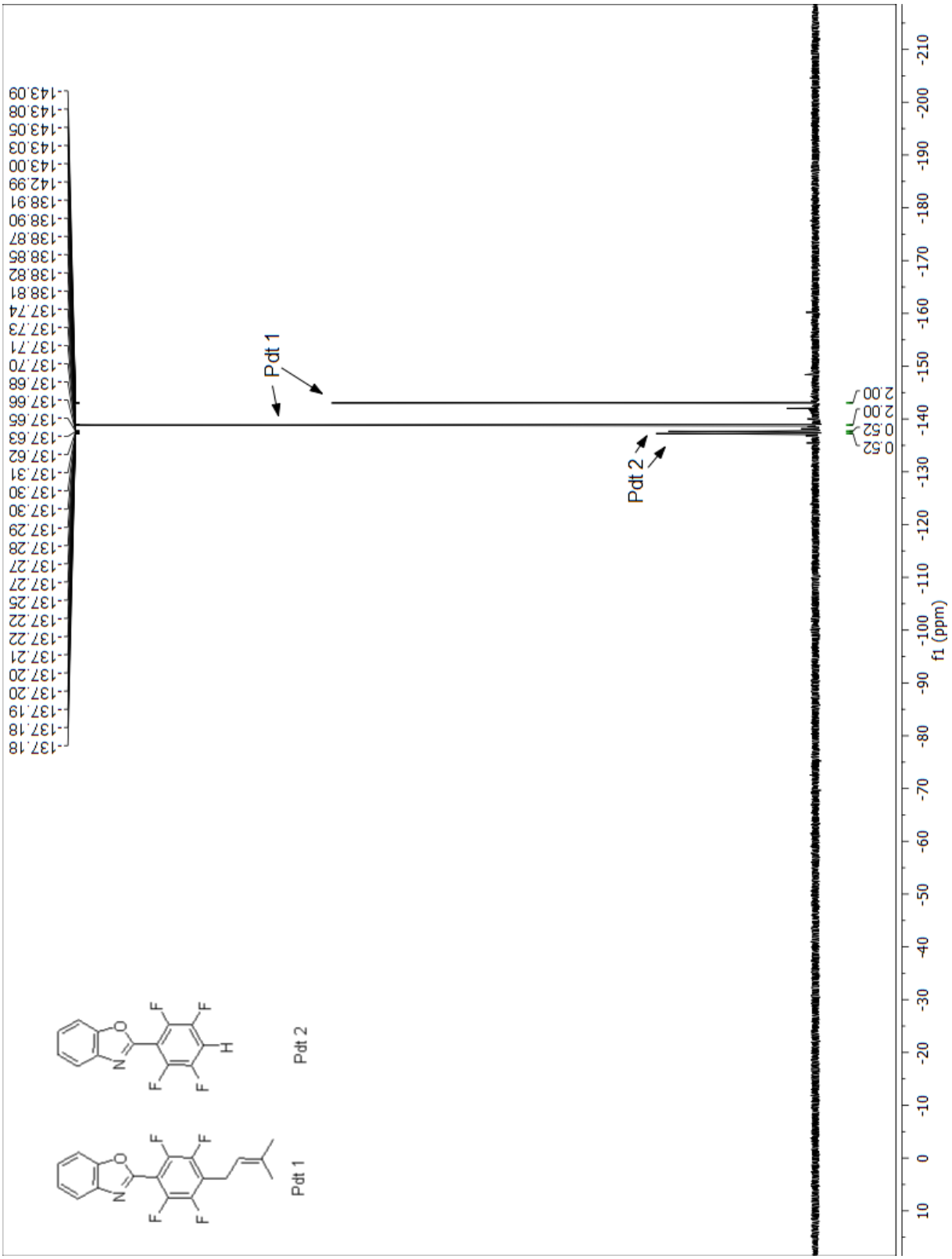
Line#:1 R.Time:14.3(Scan#:1111)
MassPeaks:199
RawMode:Single 14.3(1111) BasePeak:55(830922)
BG Mode:None



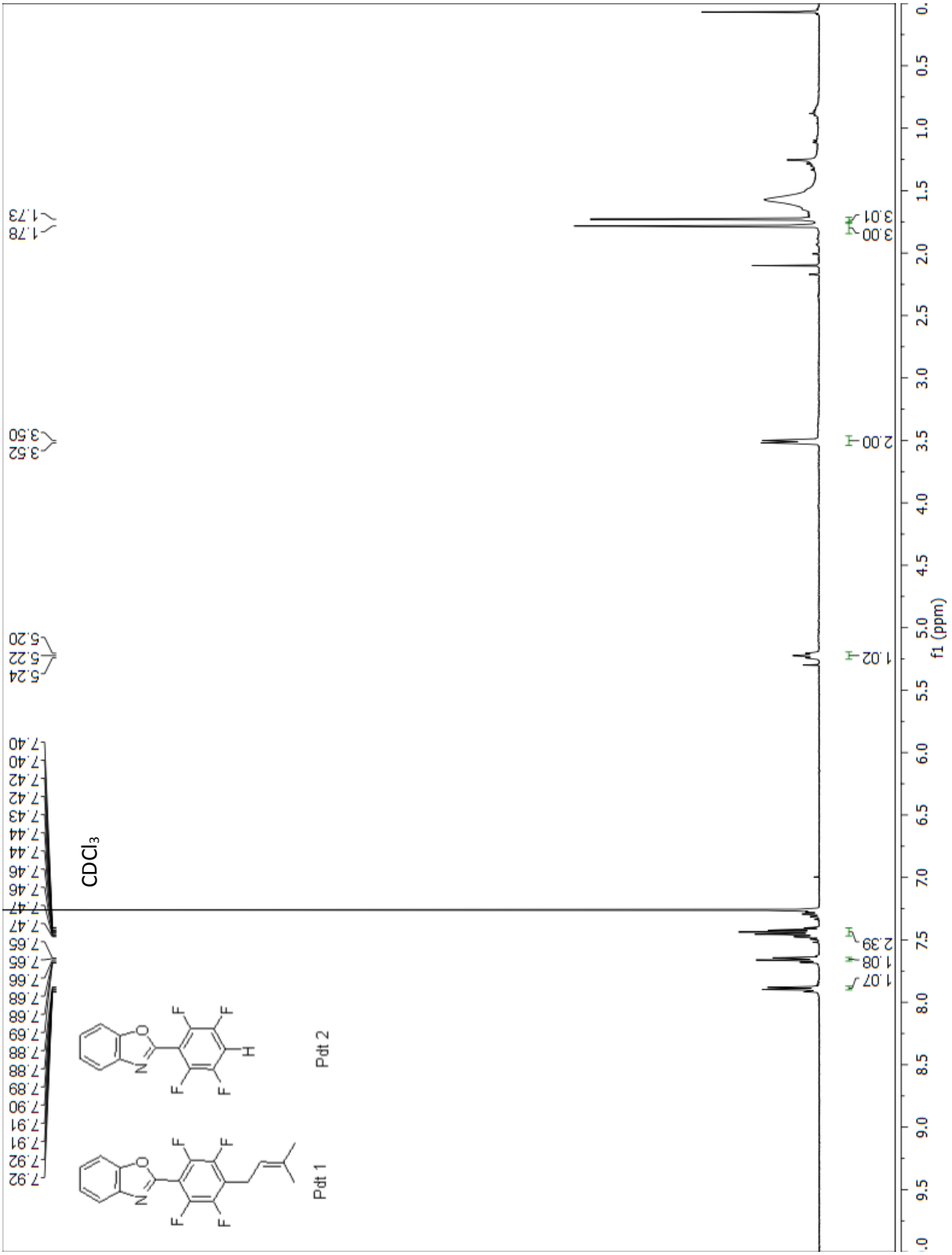
Line#:2 R.Time:14.3(Scan#:1119)
MassPeaks:204
RawMode:Single 14.3(1119) BasePeak:55(346766)
BG Mode:None



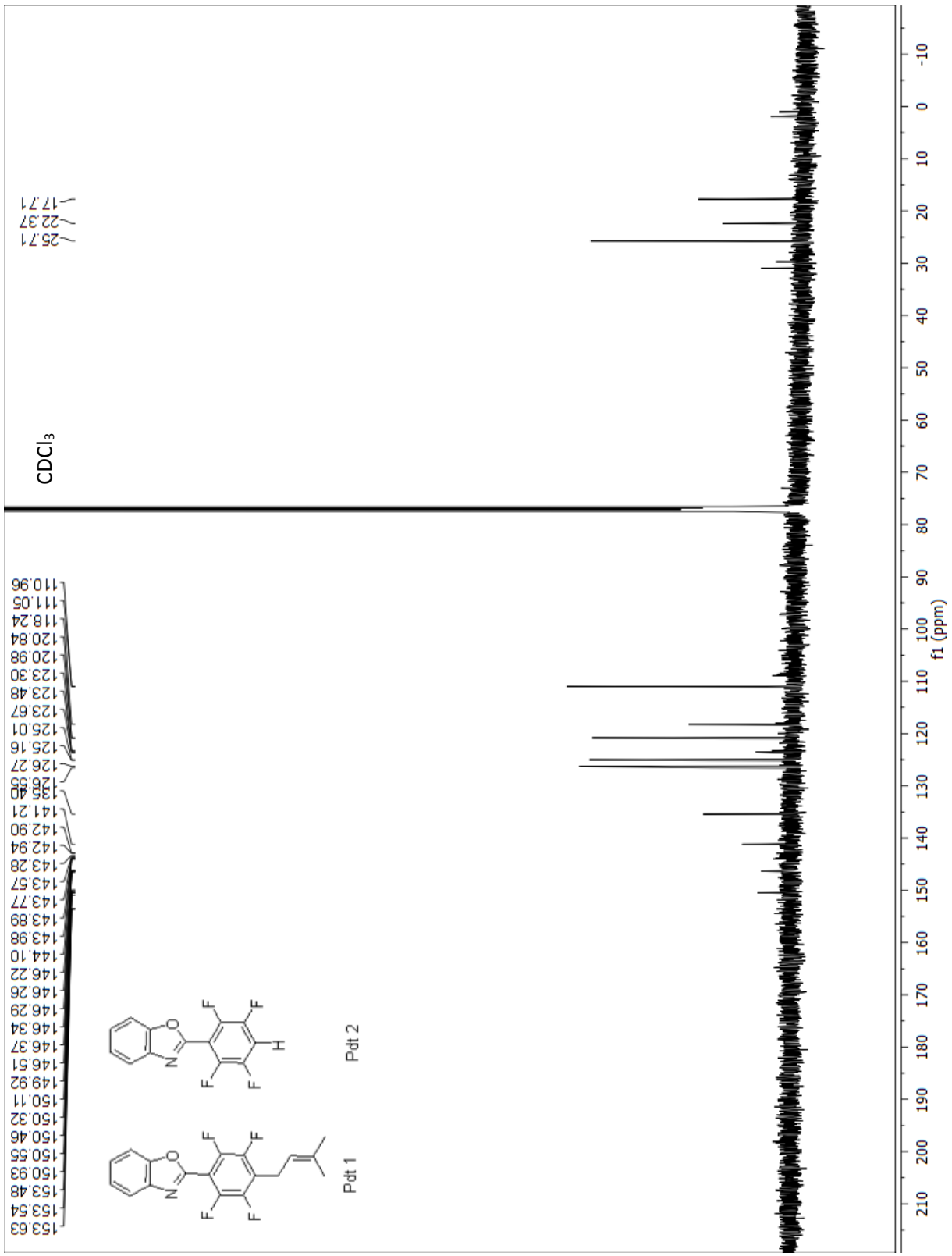
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]oxazole (3m)**



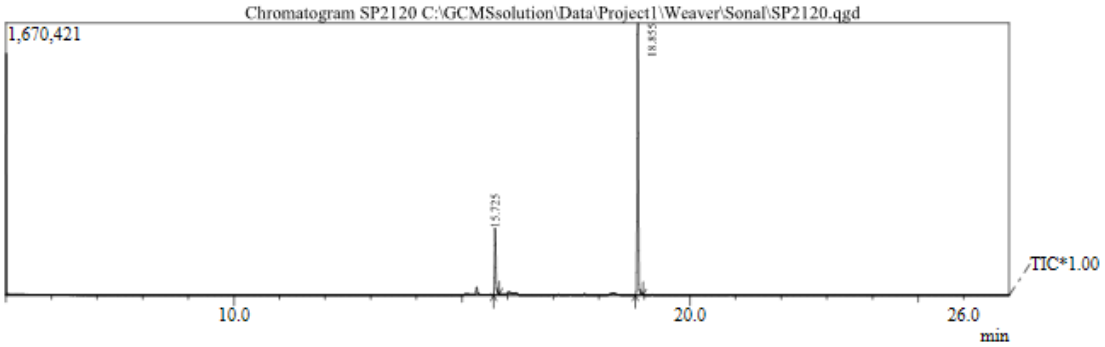
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]oxazole (3m)**

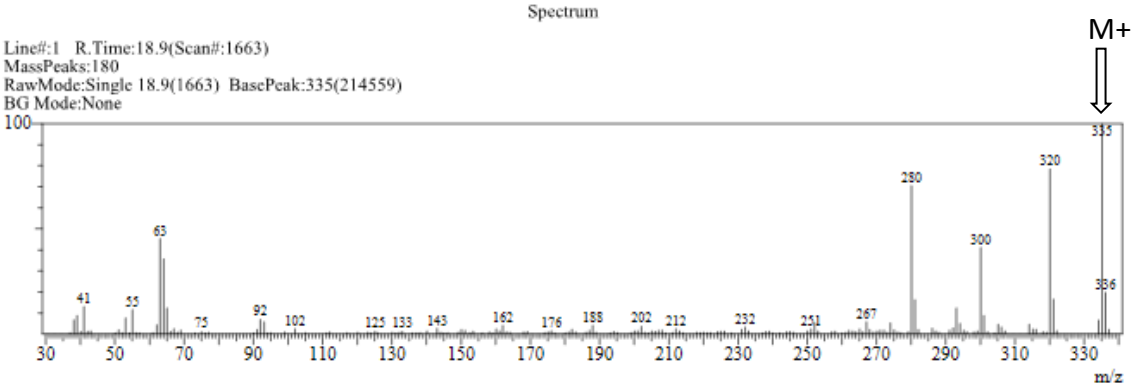


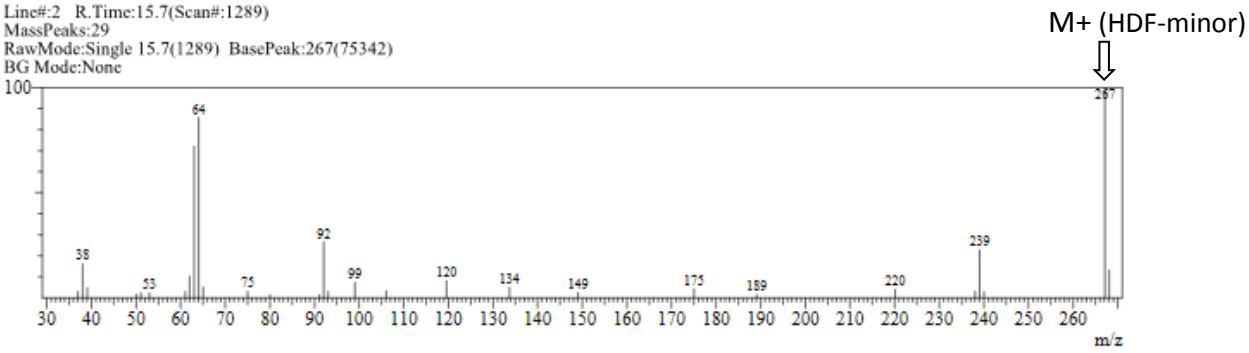
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]oxazole (3m)**



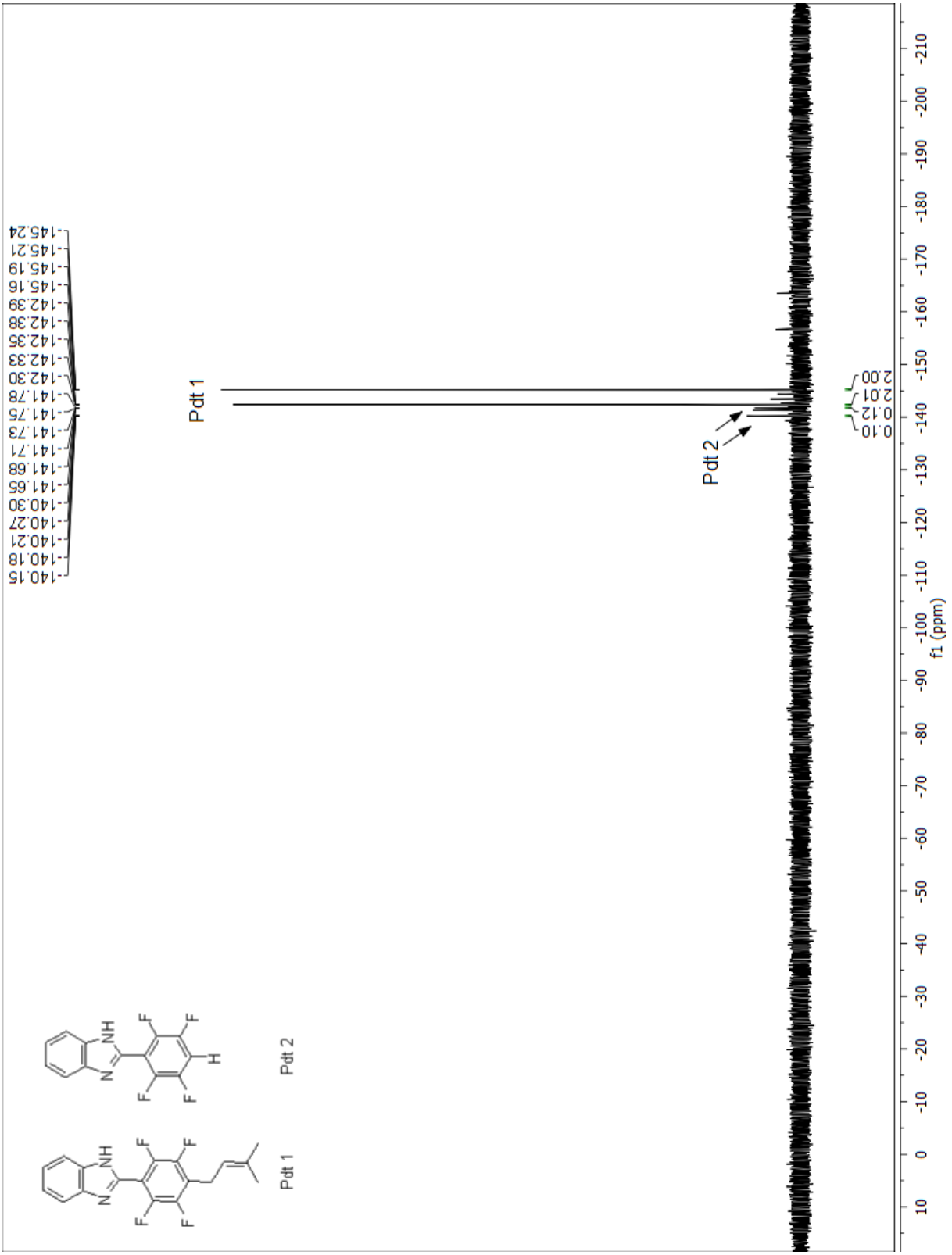
GC and MS of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]oxazole (3m)**



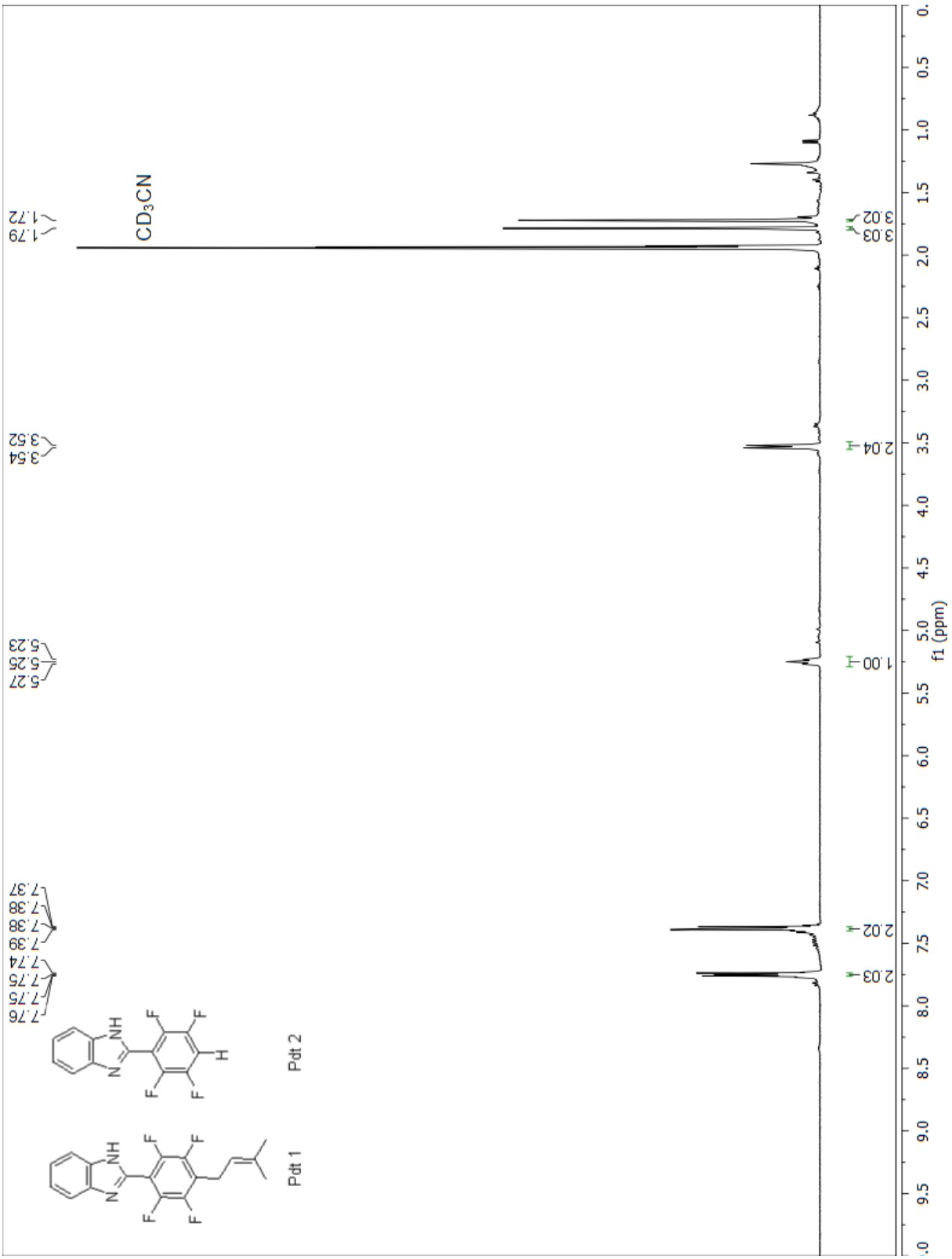




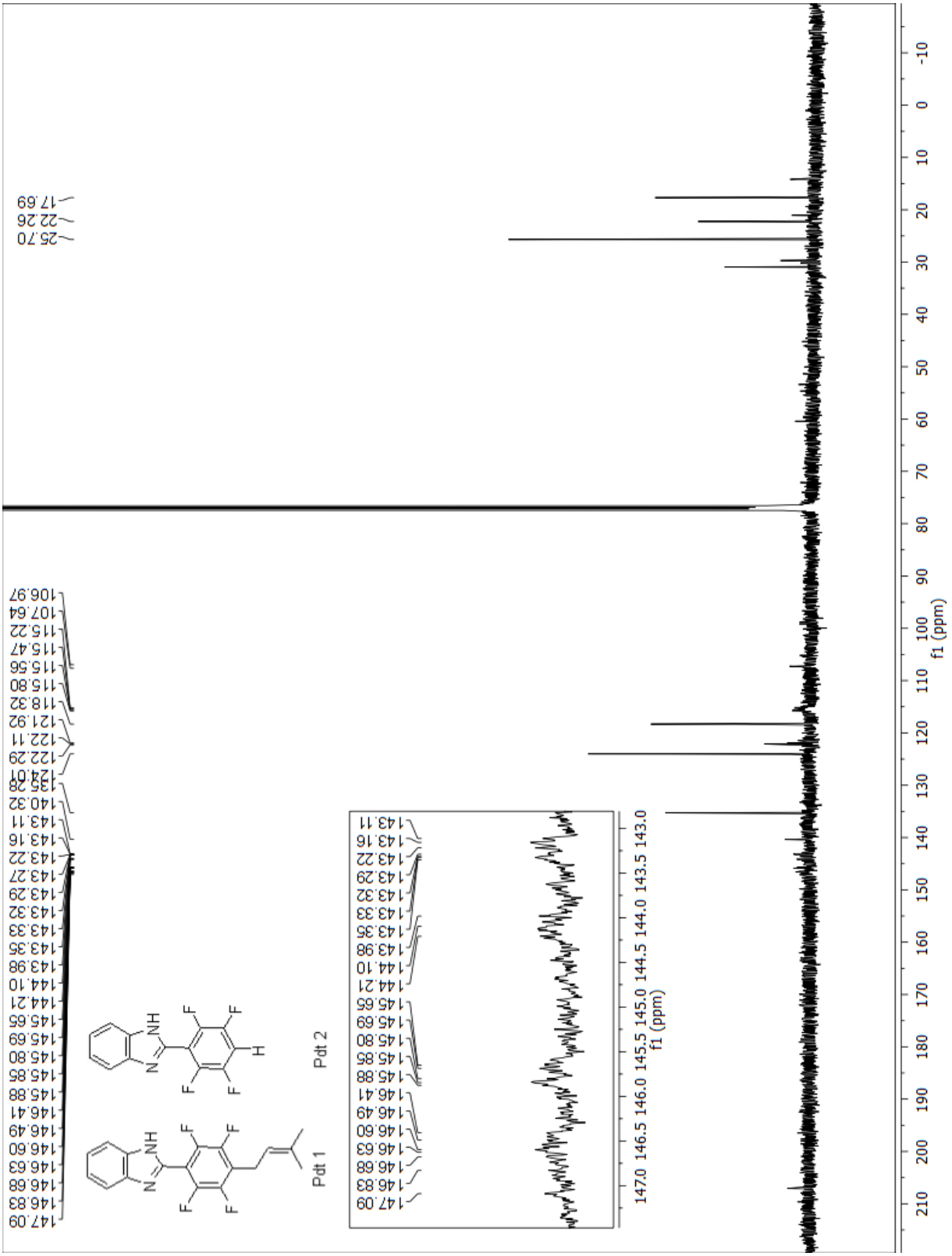
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)-1H-benzo[d]imidazole (3n)**



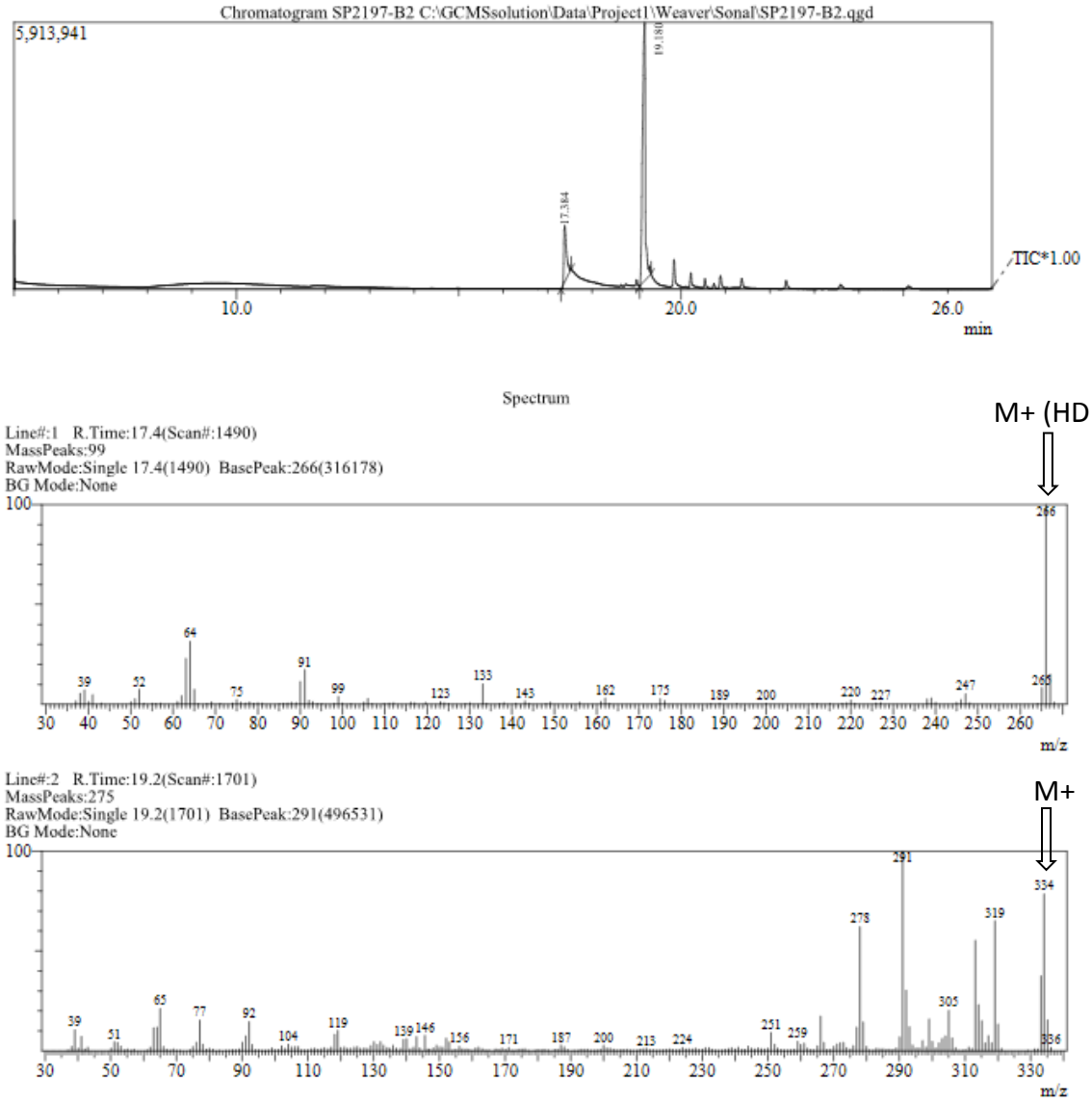
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)-1H-benzo[d]imidazole (3n)**



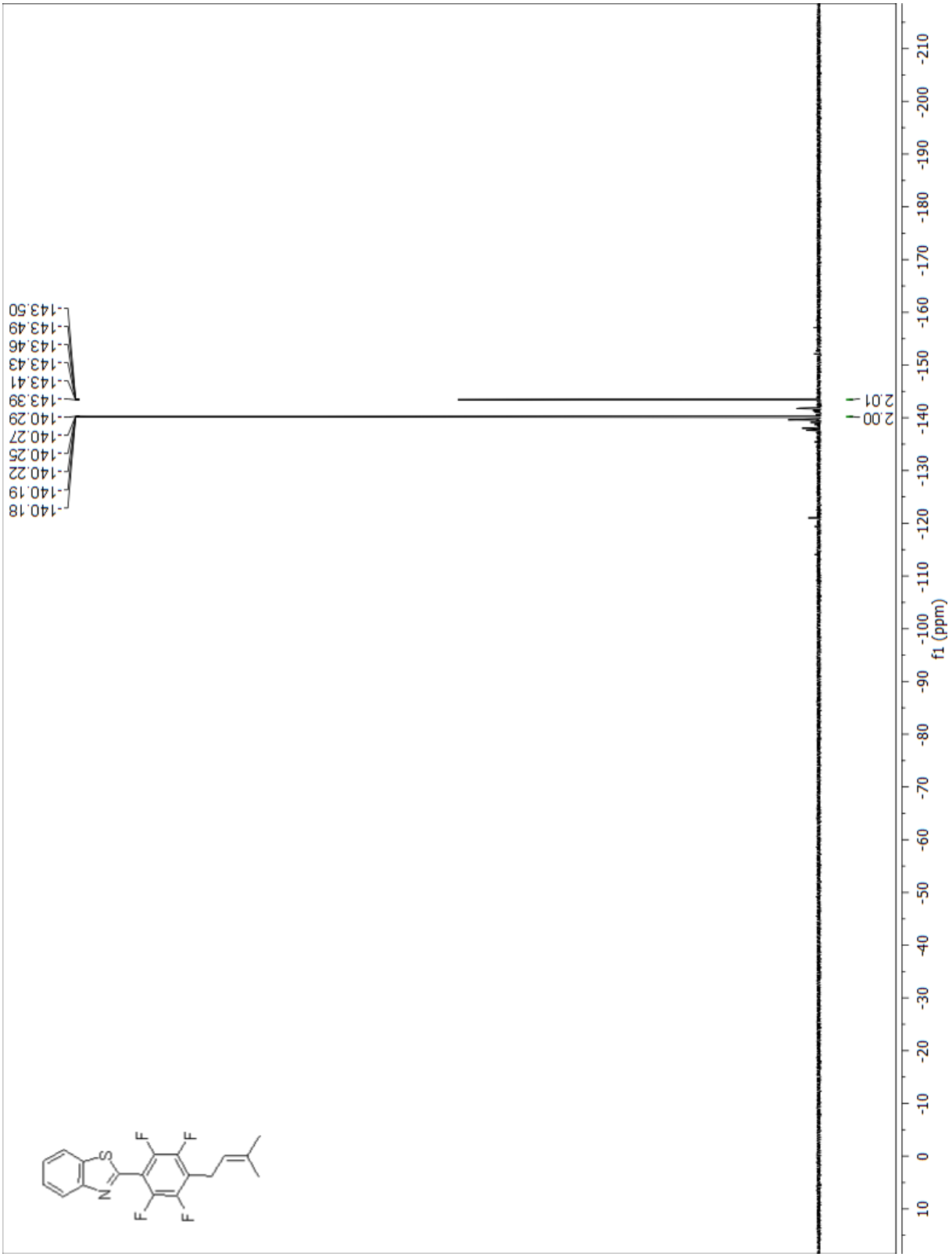
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)-1H-benzo[d]imidazole (3n)**



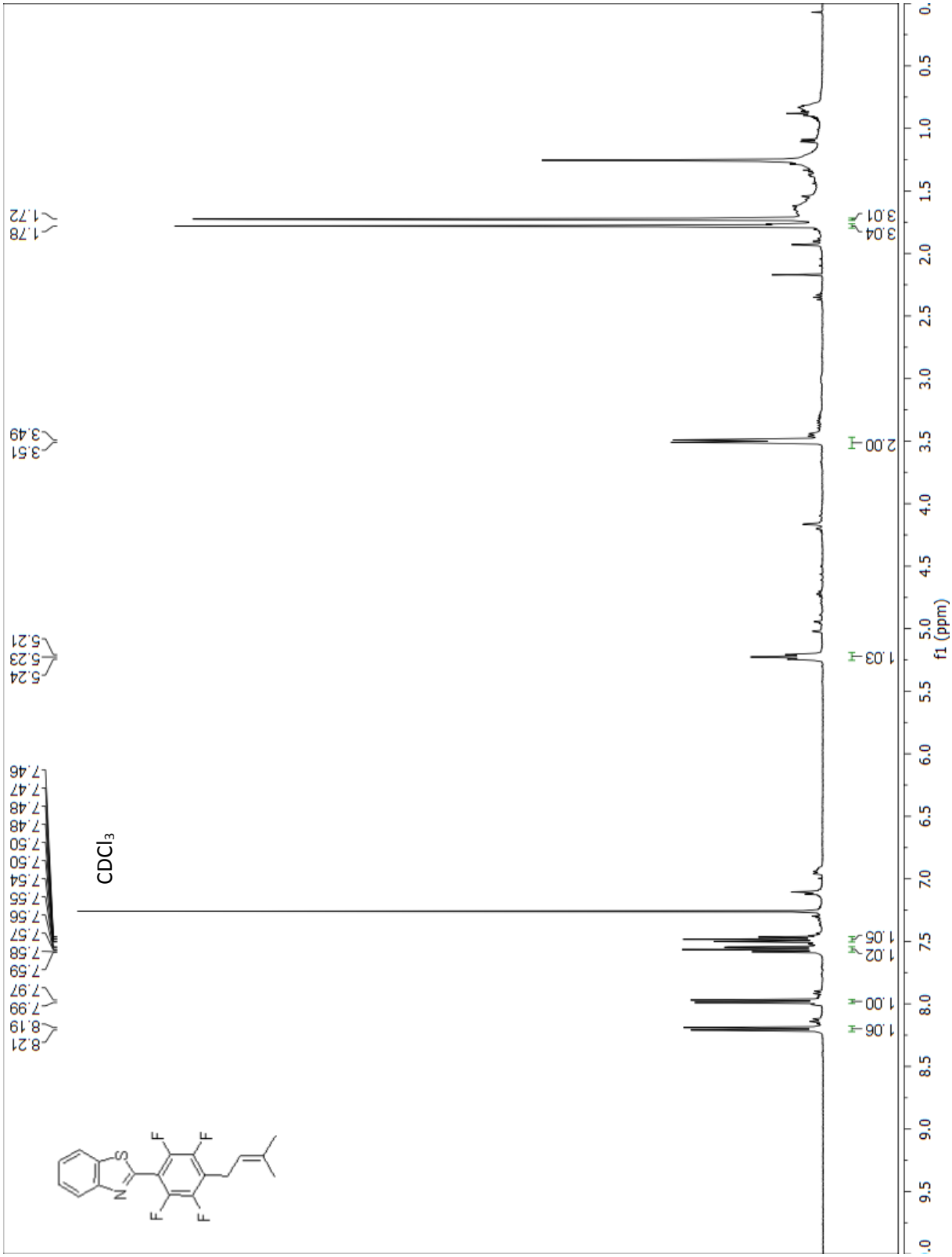
GC and MS of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)-1H-benzo[d]imidazole (3n)**



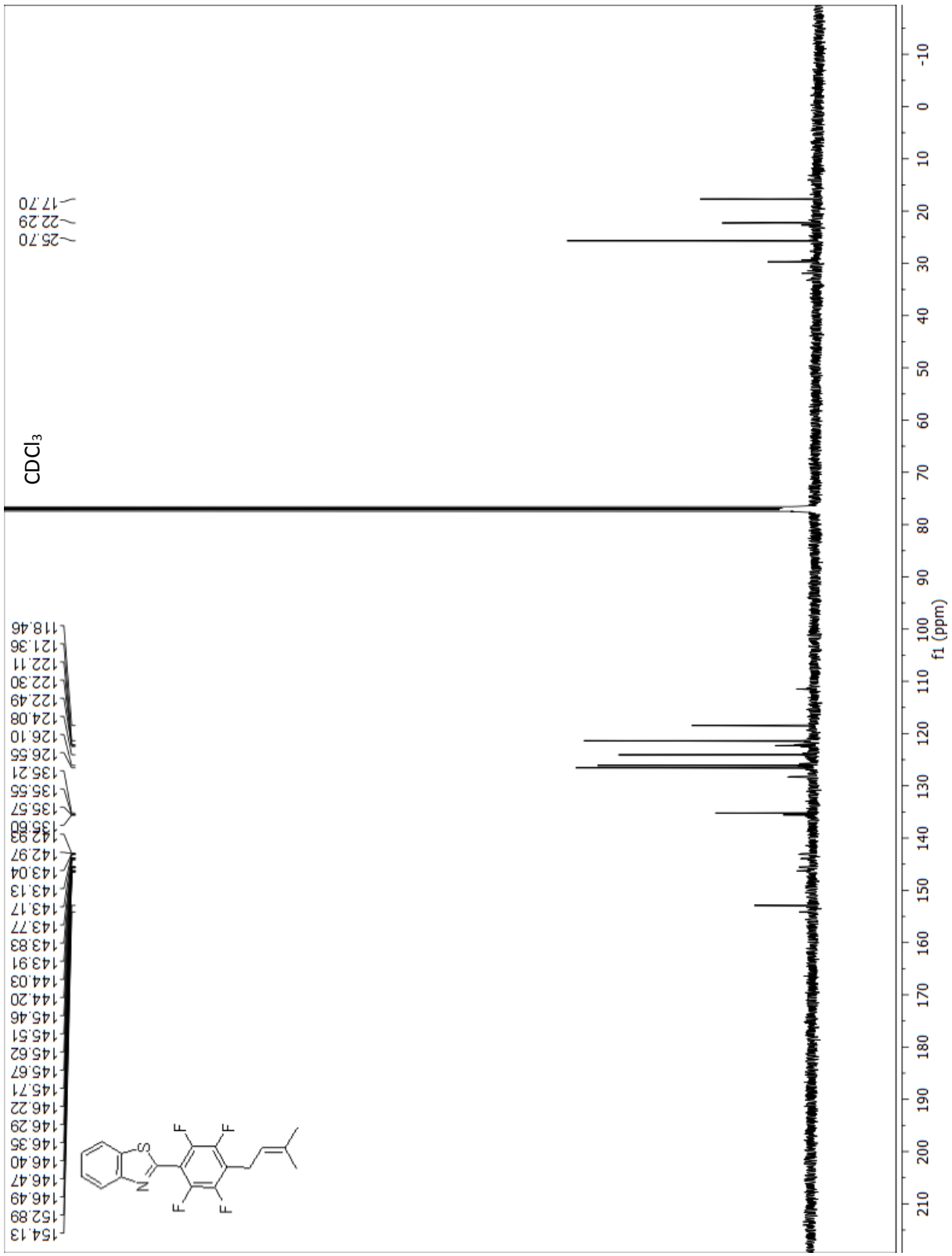
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]thiazole (3o)**



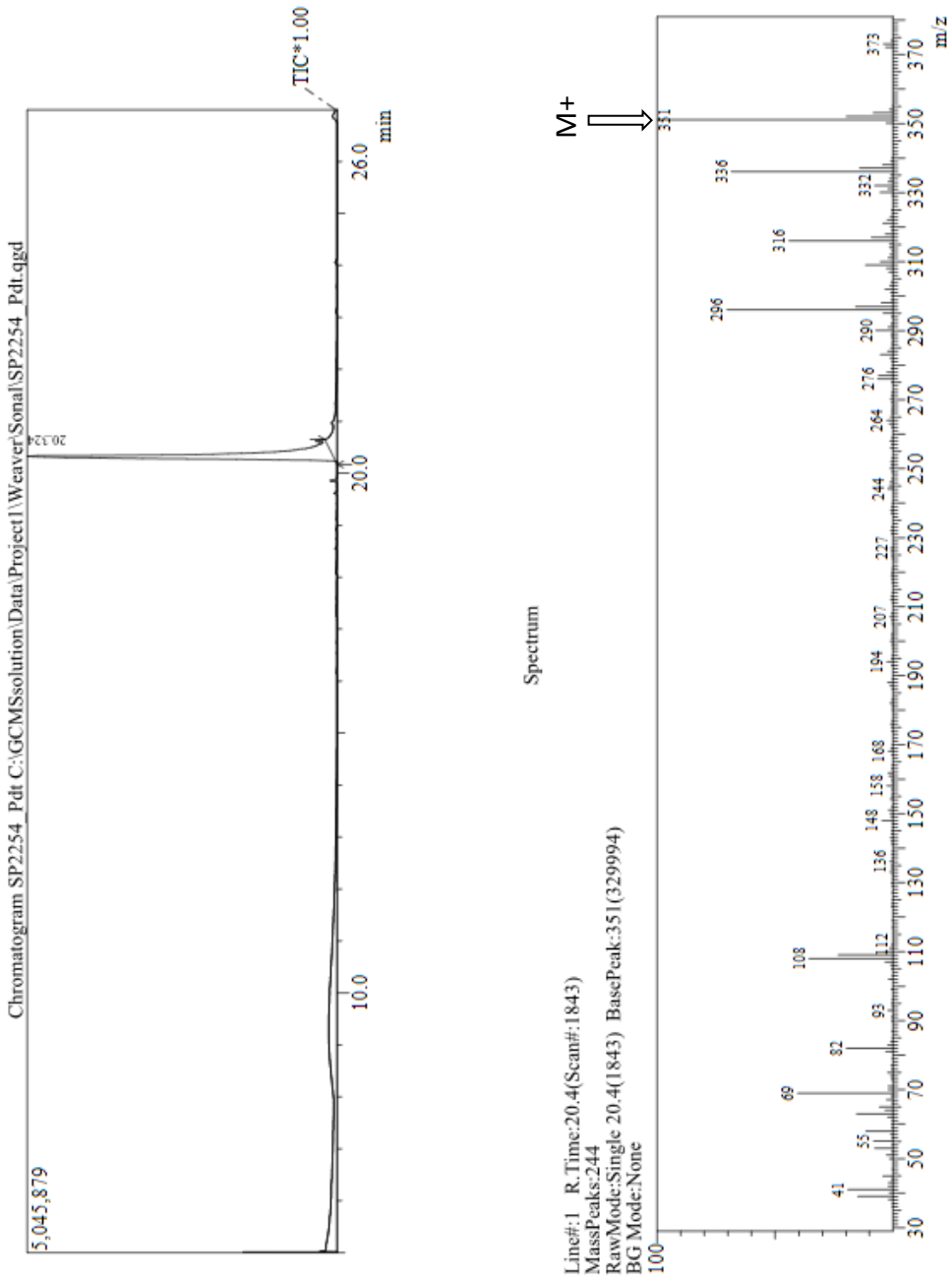
^{1}H NMR (400 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]thiazole (3o)**



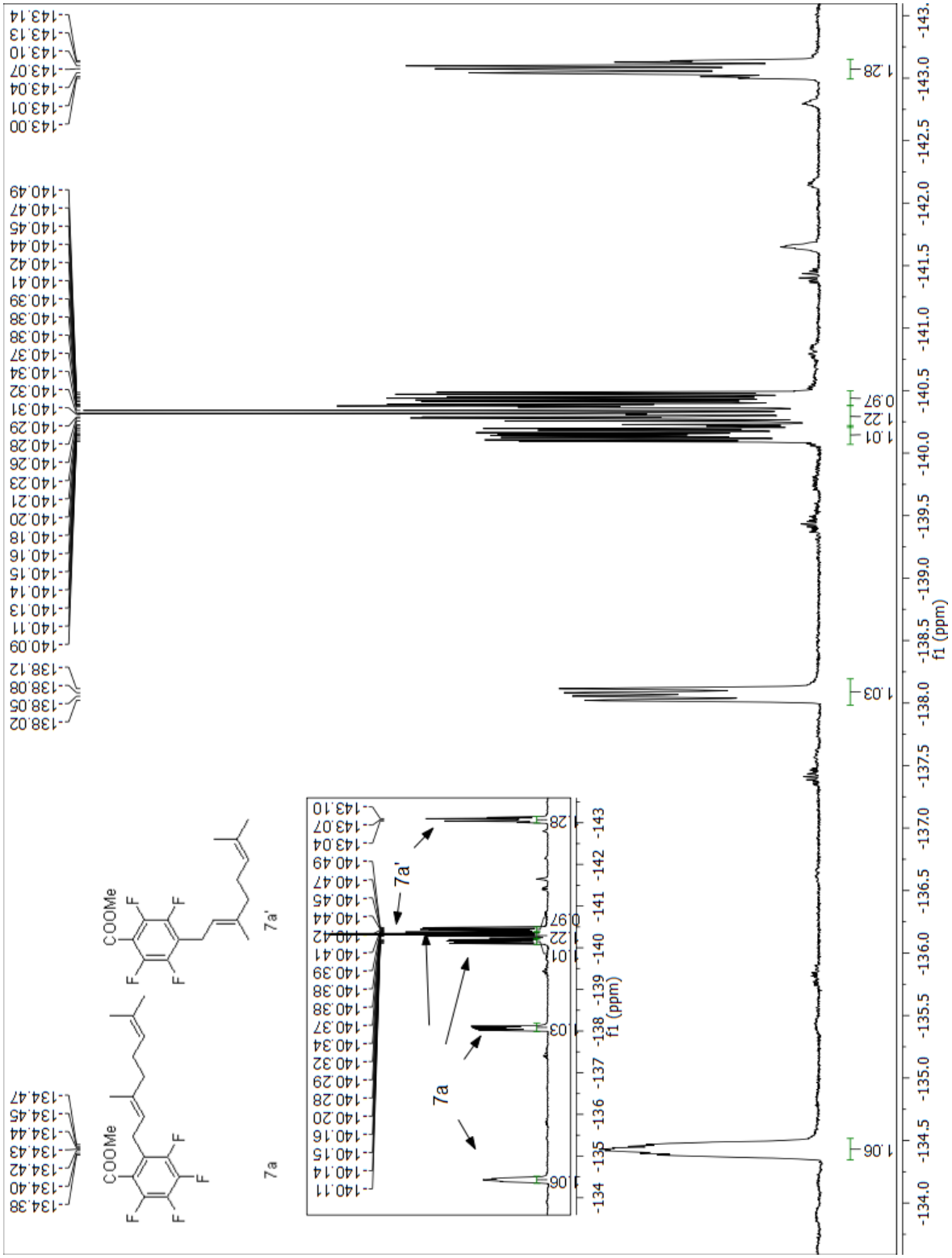
^{13}C NMR (101 MHz, CDCl3, at rt) spectrum of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]thiazole (3o)**



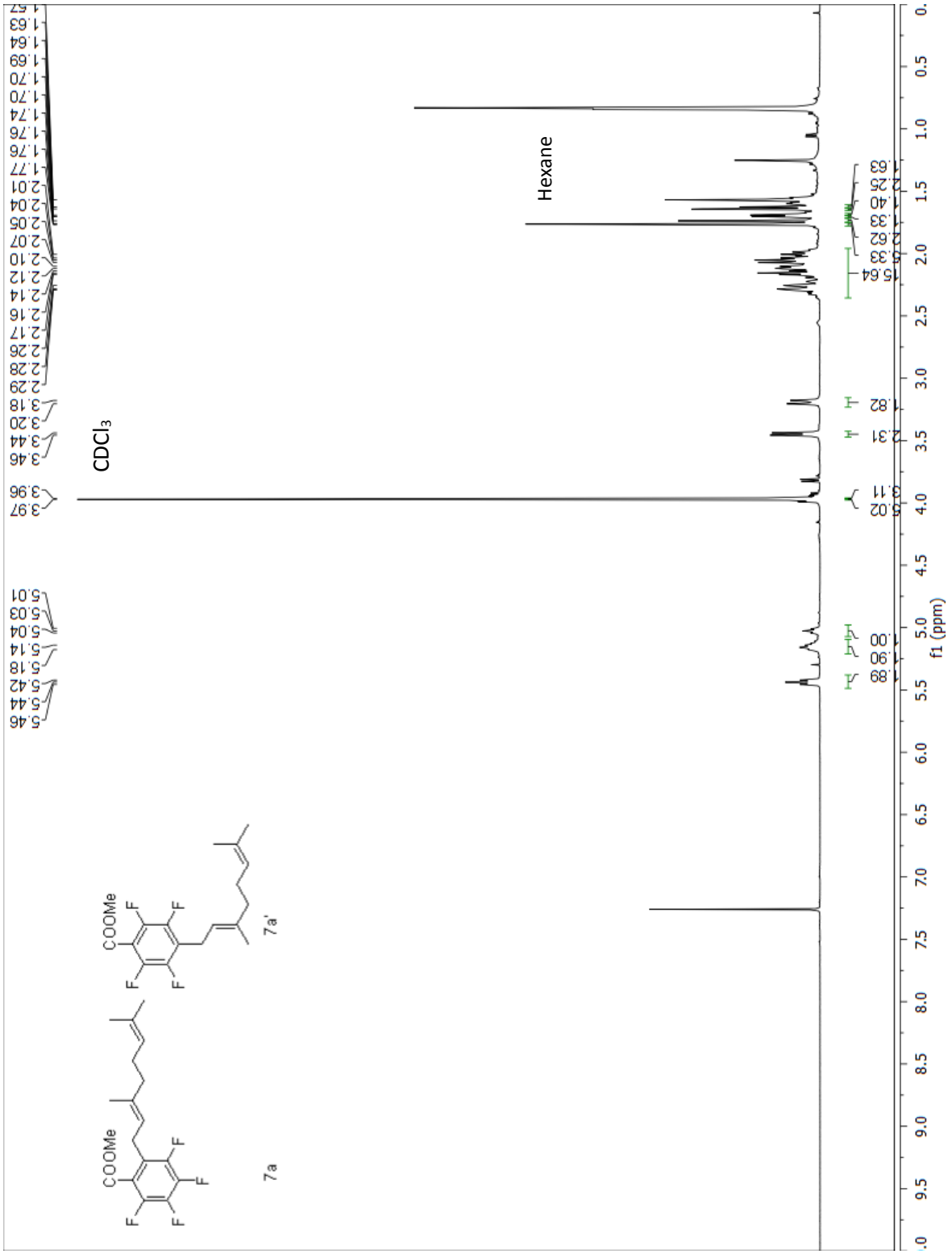
GC and MS of **2-(2,3,5,6-tetrafluoro-4-(3-methylbut-2-en-1-yl)phenyl)benzo[d]thiazole (3o)**



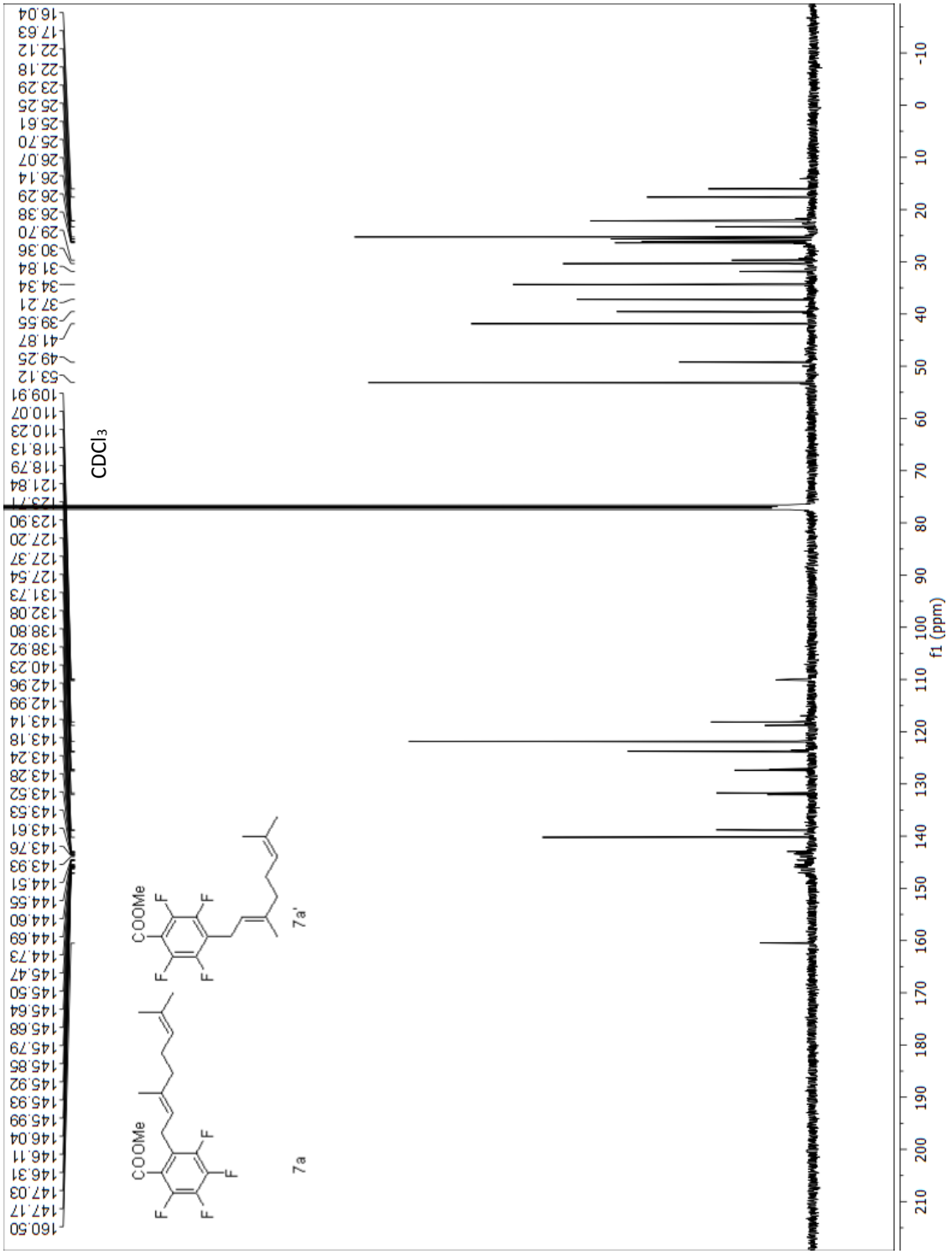
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**



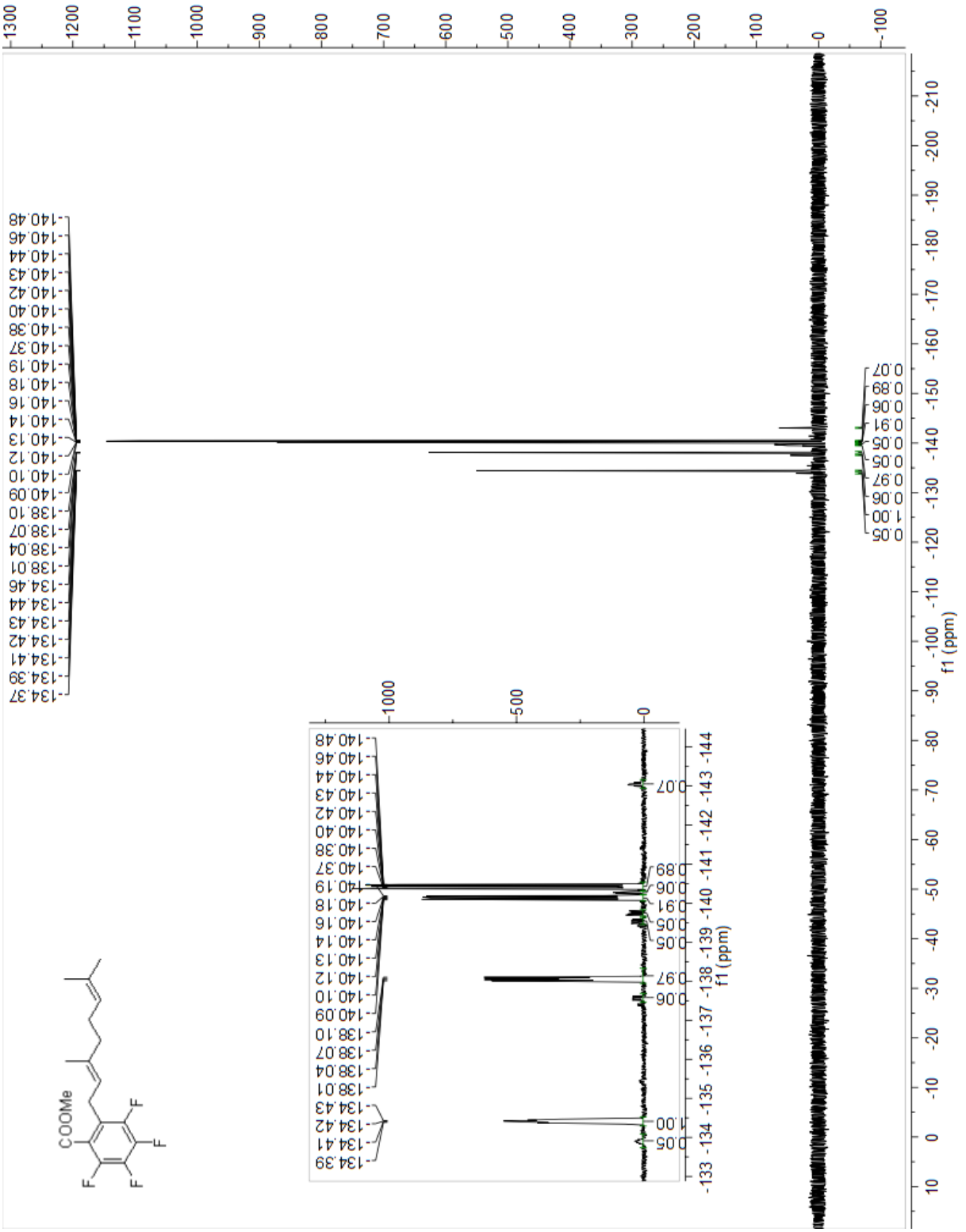
^{1}H NMR (376 MHz, CDCl3, at rt) spectrum of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**



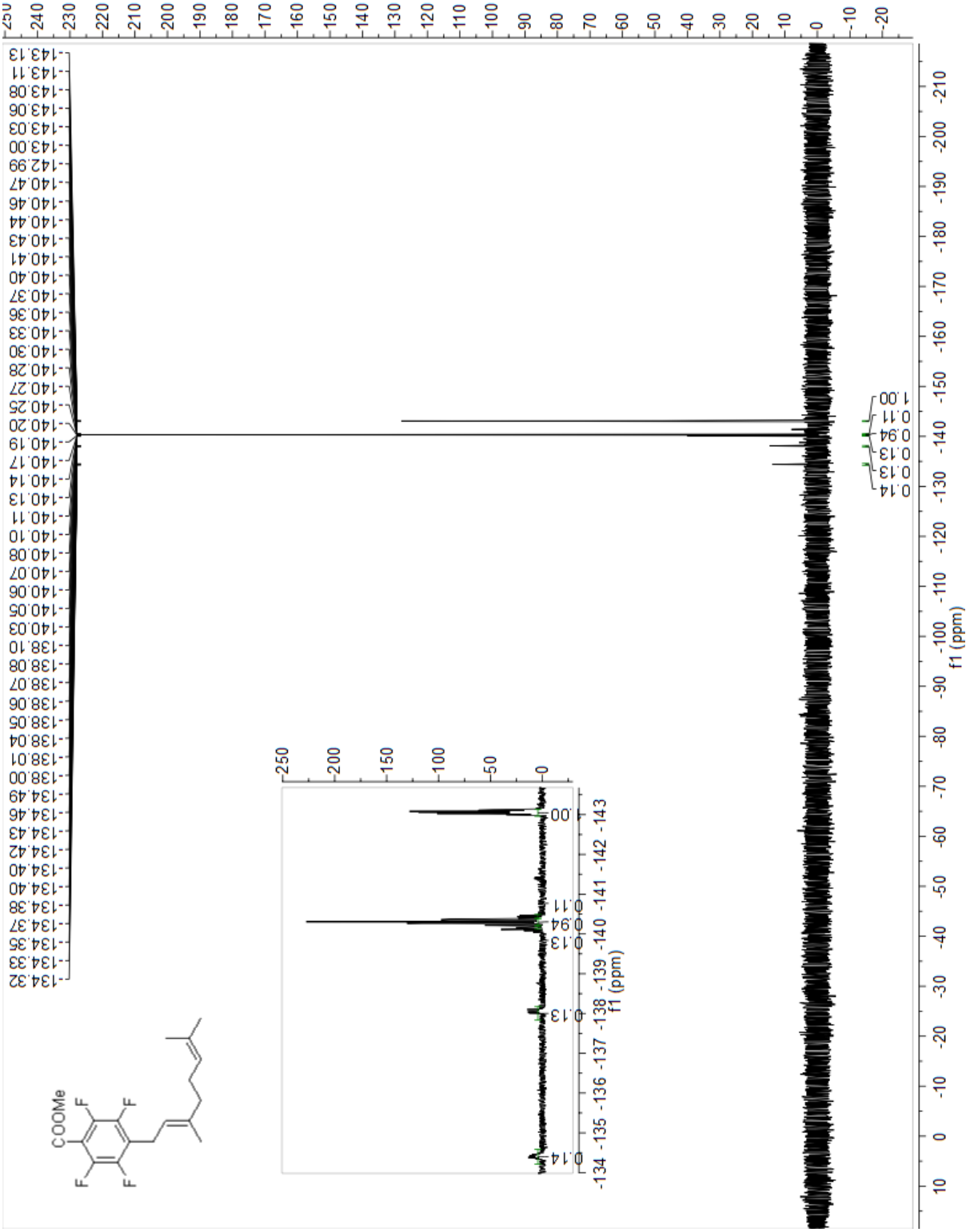
^{13}C NMR (376 MHz, CDCl3, at rt) spectrum of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)- 2,3,5,6-tetrafluorobenzoate (7a')**



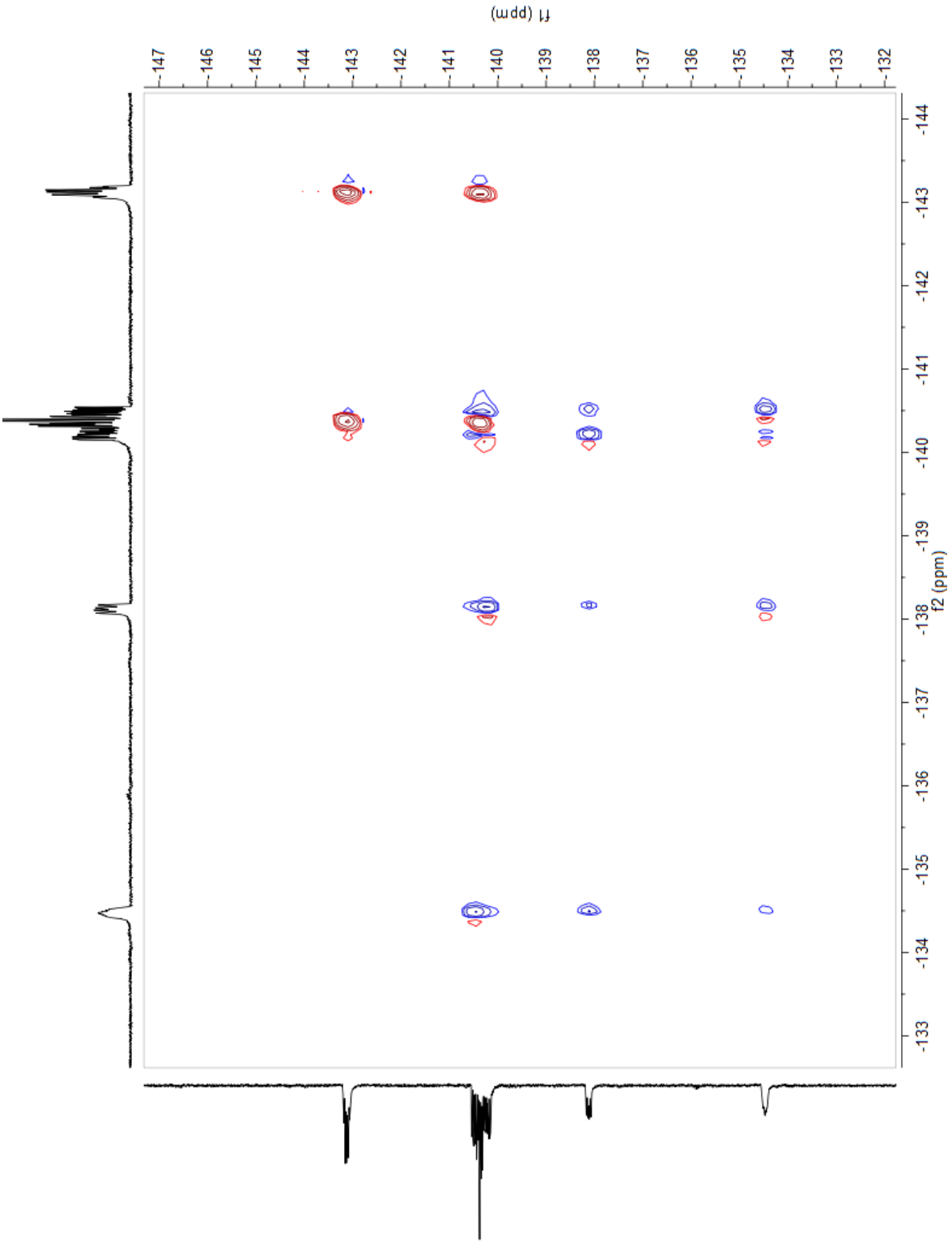
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a)**



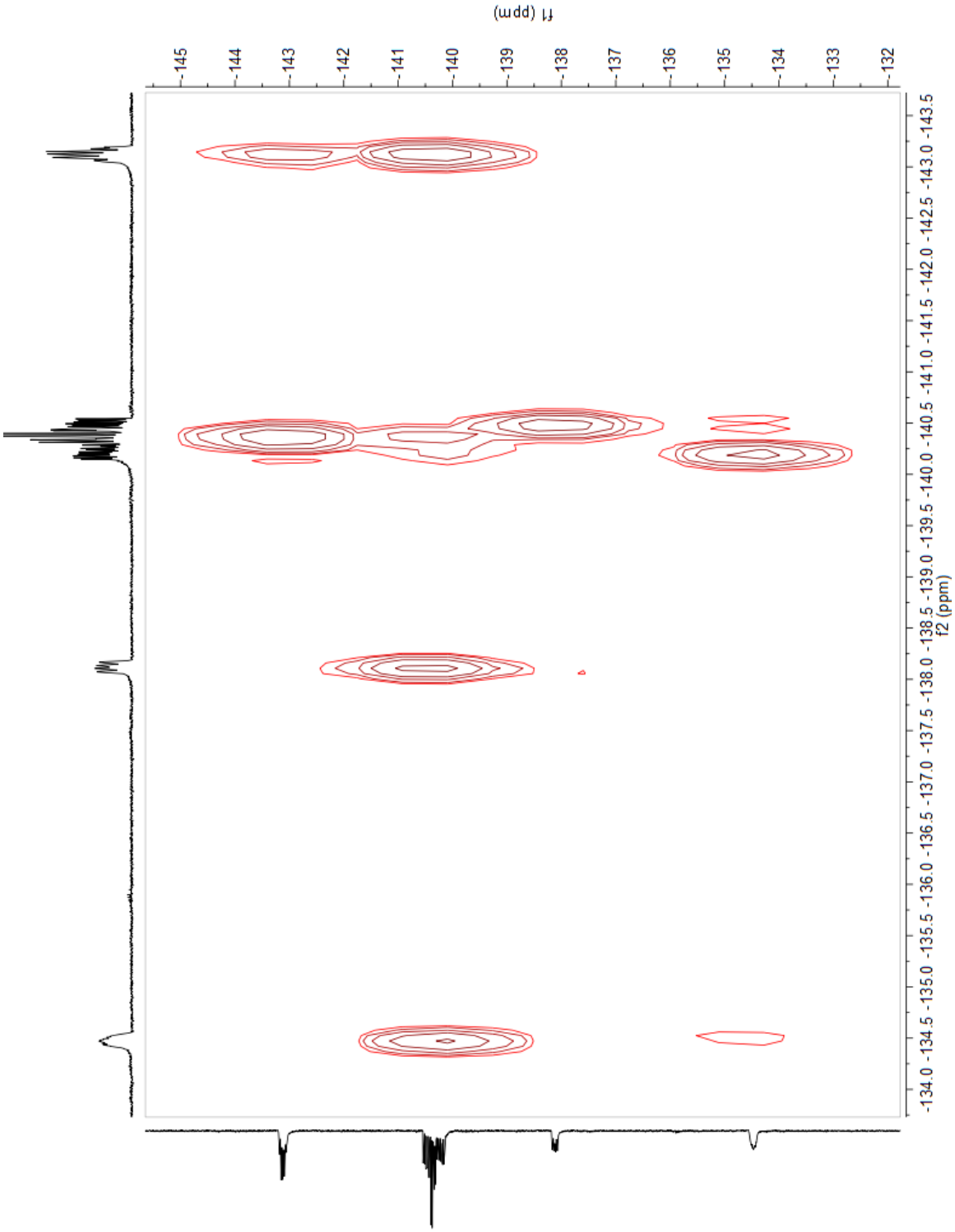
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**



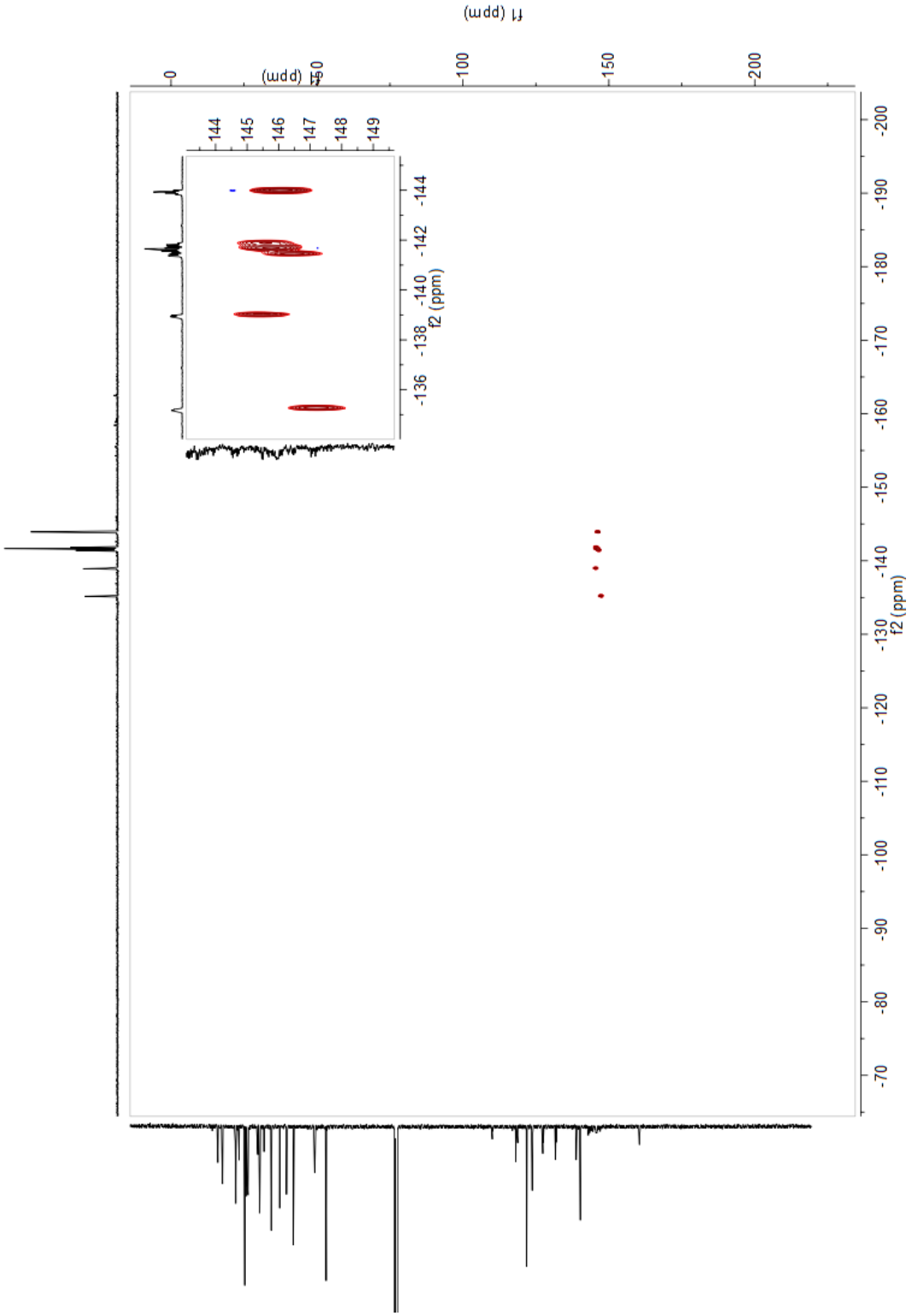
^{19}F -^{19}F TOCSY of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**



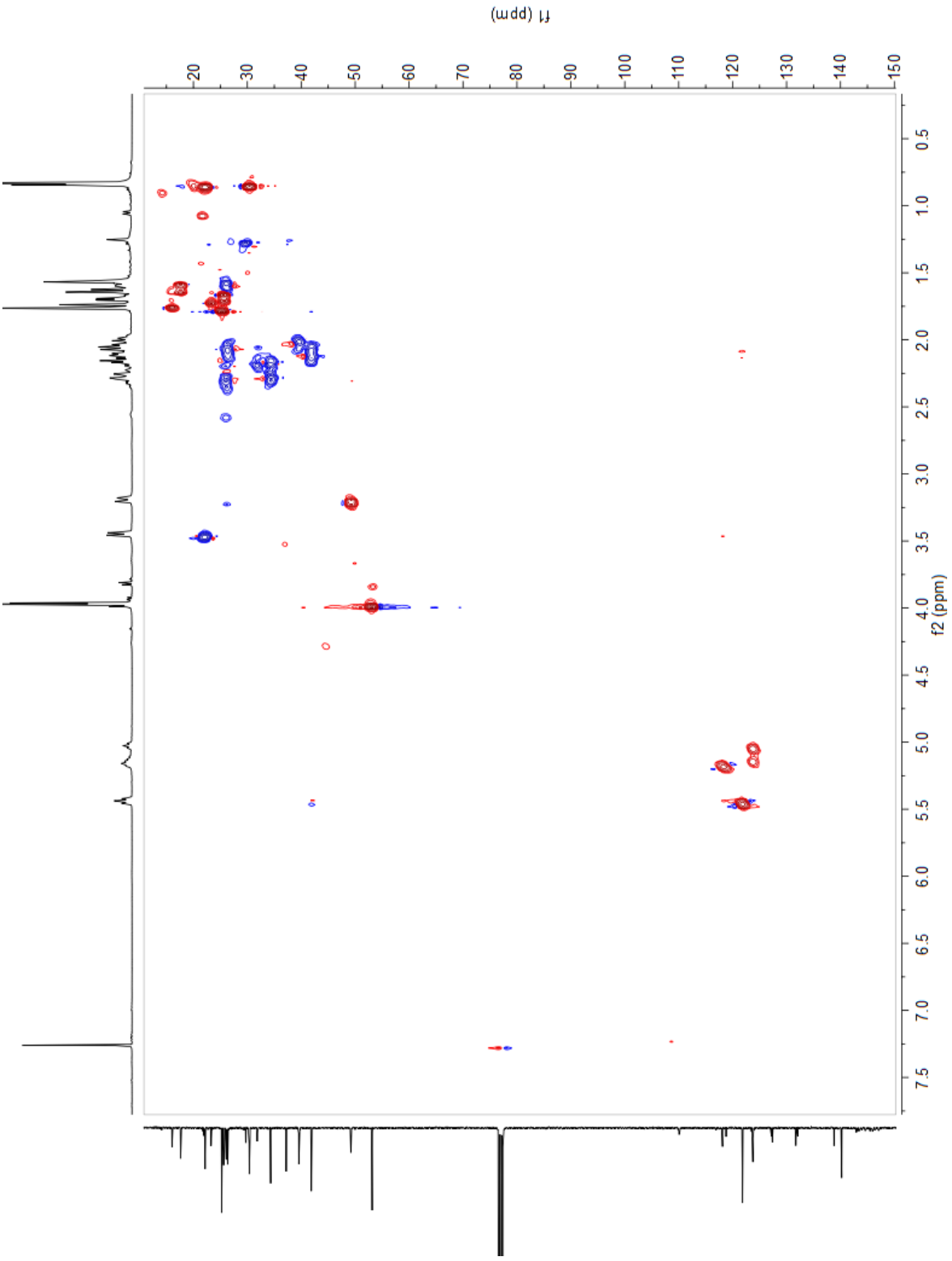
^{19}F -^{19}F COSY of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**



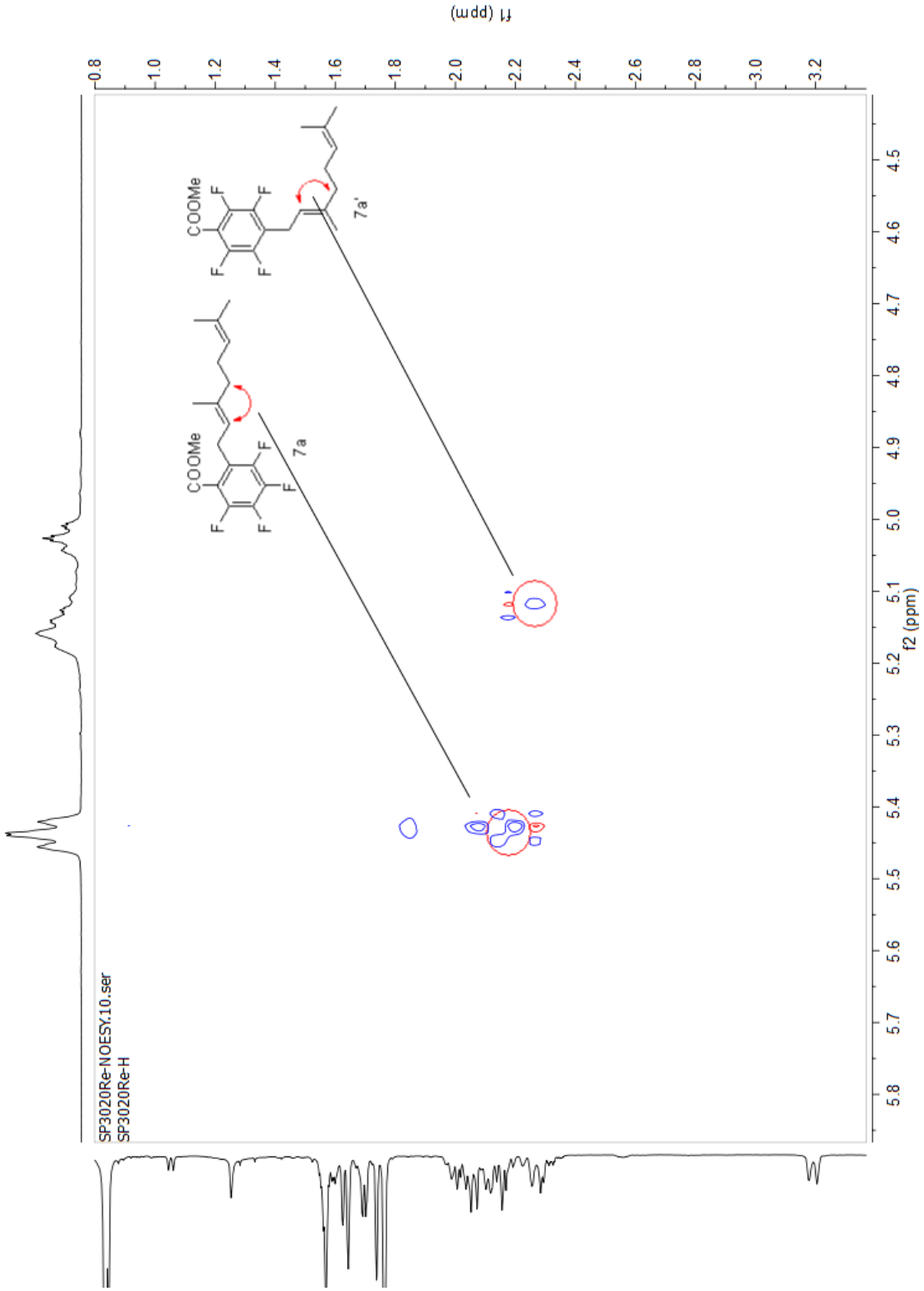
^{19}F-^{13}C HSQC of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')** (in MeCN-d3)



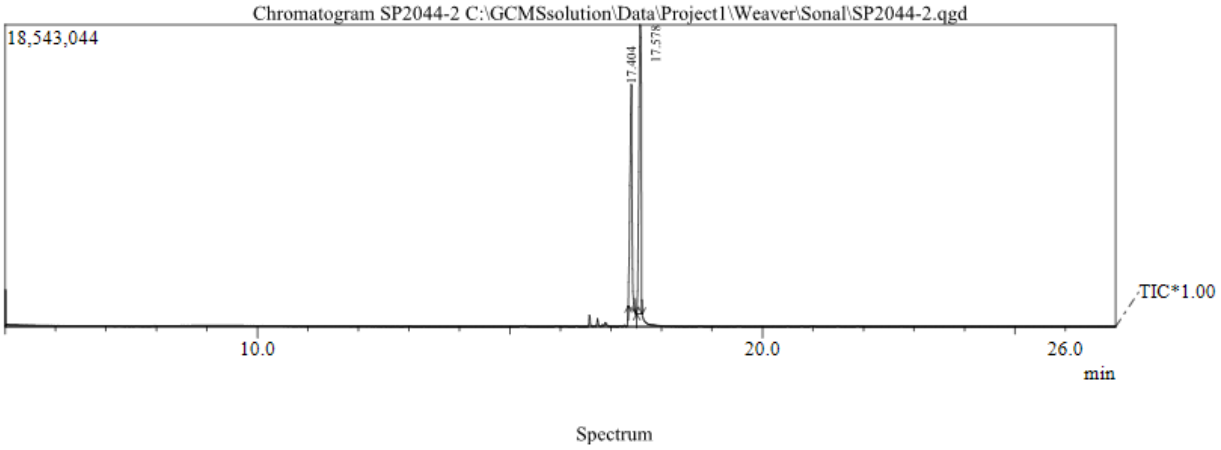
^{1}H-^{13}C HSQC of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**



^{1}H-^{1}H NOESY of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**

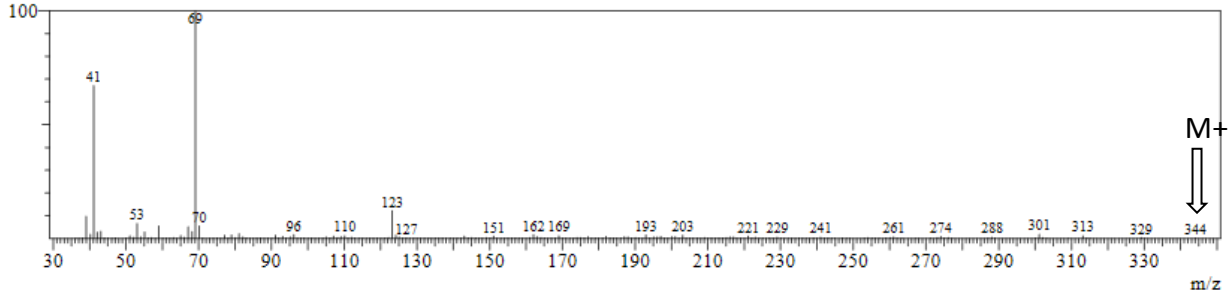


GC and MS of **methyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7a) and methyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7a')**

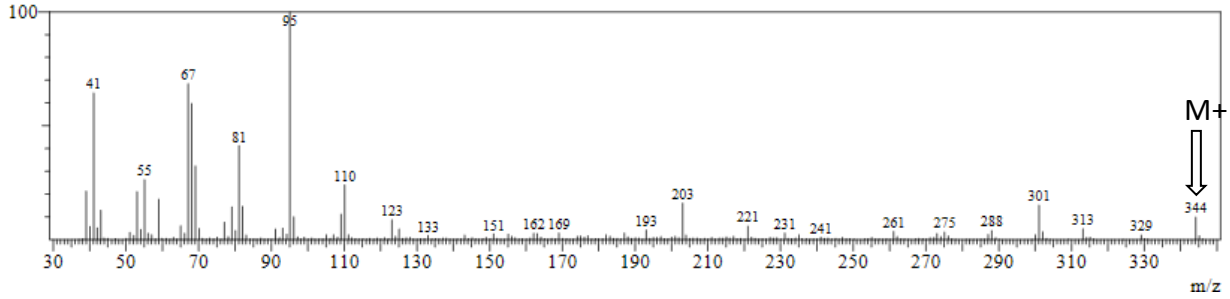


Spectrum

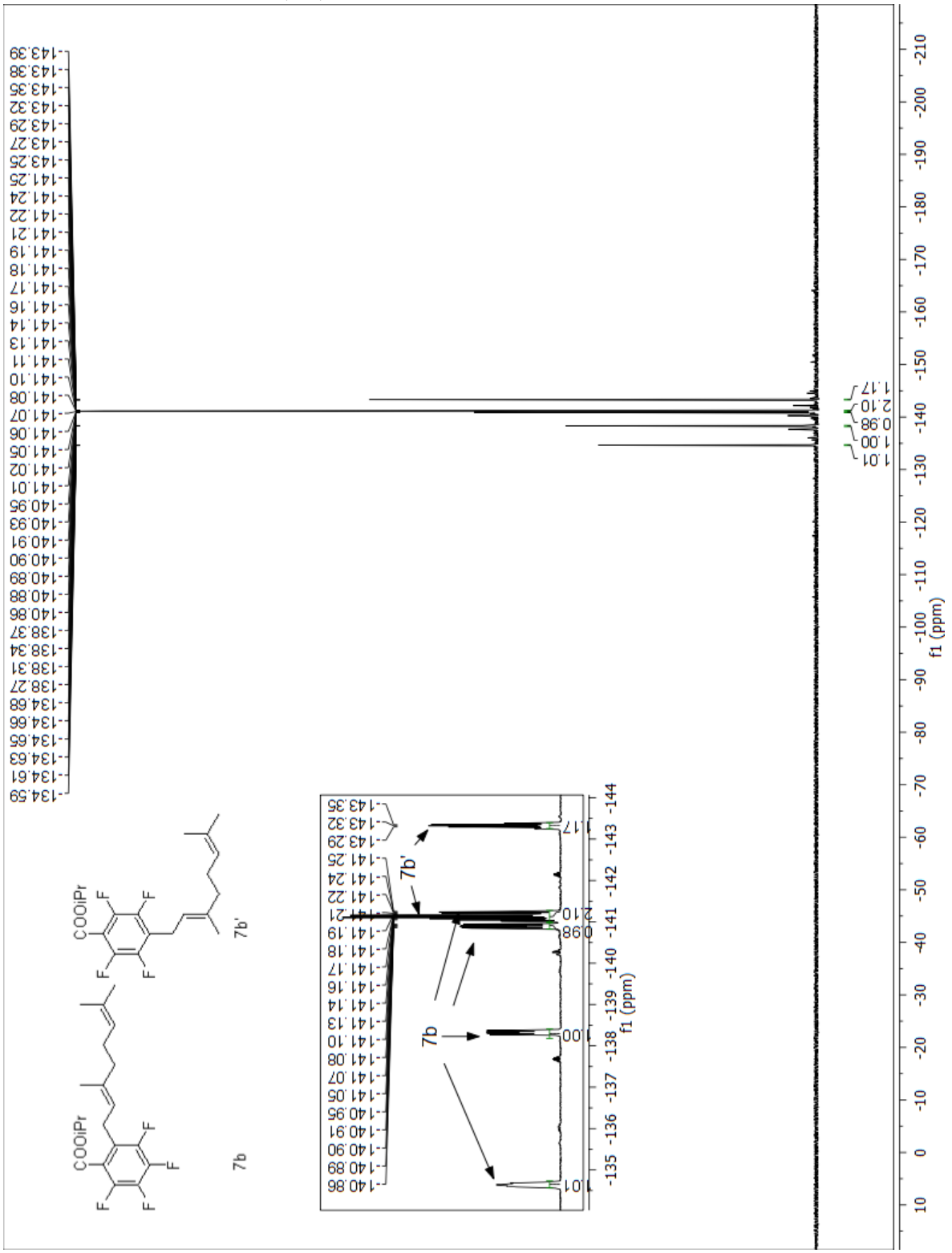
Line#:1 R.Time:17.4(Scan#:1489)
MassPeaks:242
RawMode:Single 17.4(1489) BasePeak:69(4949625)
BG Mode:None



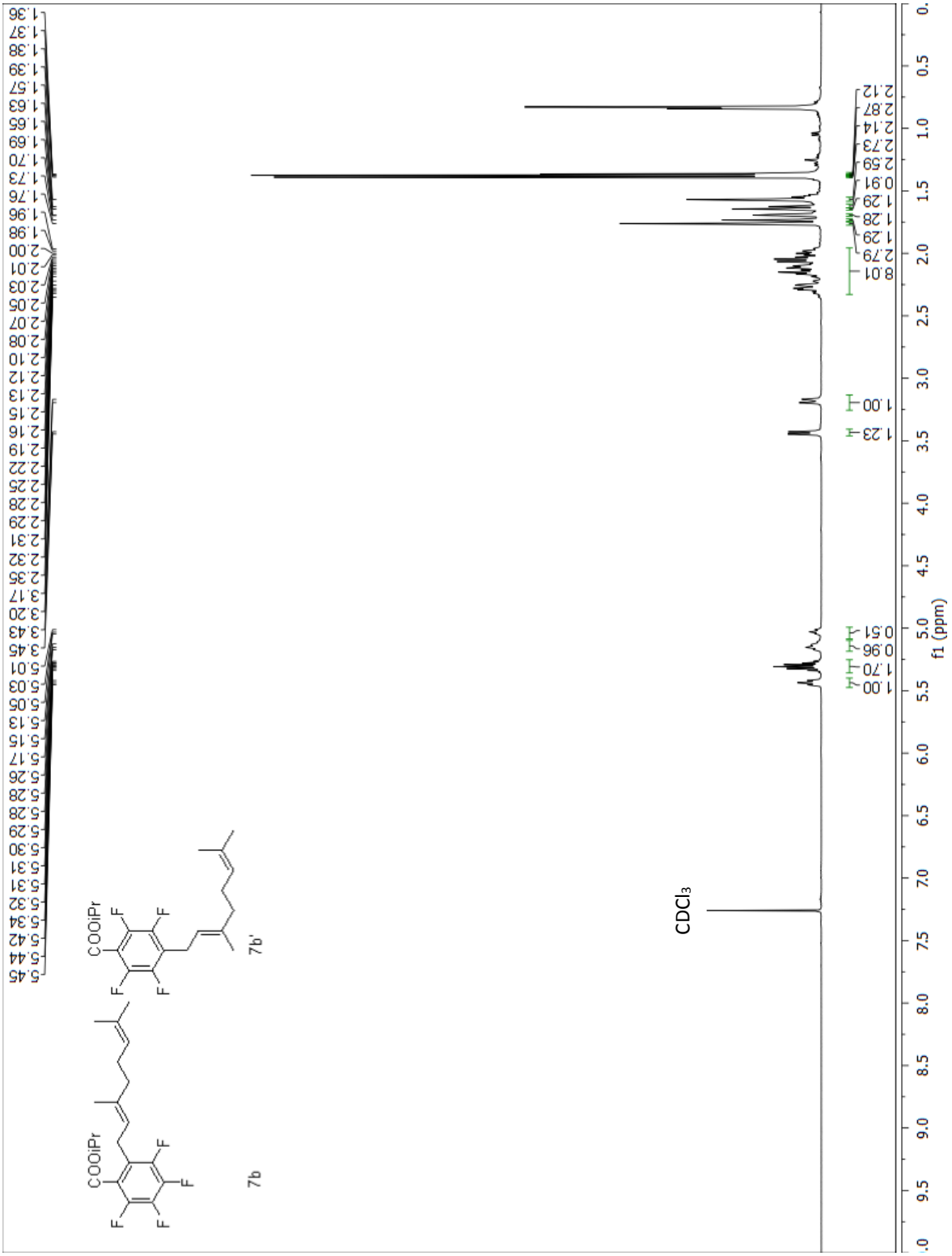
Line#:2 R.Time:17.6(Scan#:1509)
MassPeaks:264
RawMode:Single 17.6(1509) BasePeak:95(2063375)
BG Mode:None



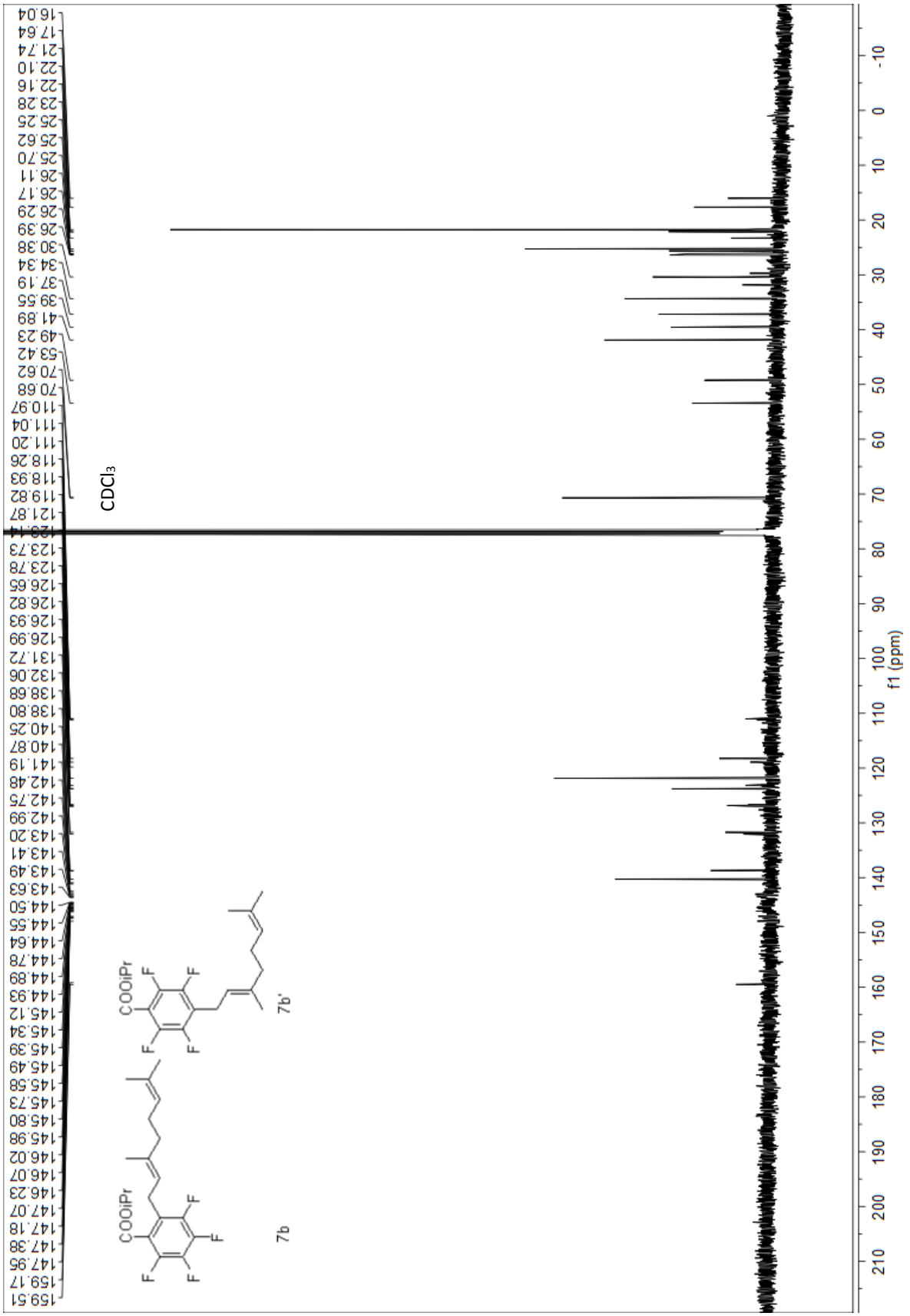
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **isopropyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7b) and isopropyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7b')**



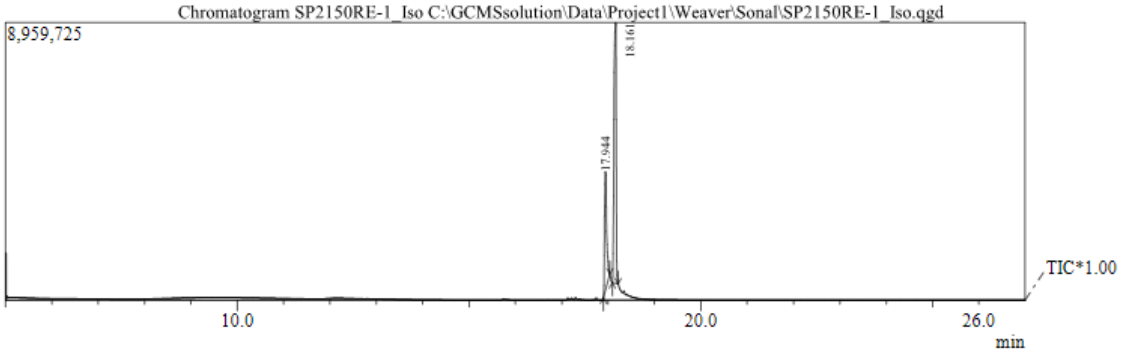
^{1}H NMR (376 MHz, CDCl3, at rt) spectrum of **isopropyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7b) and isopropyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7b')**



^{13}C NMR (376 MHz, CDCl3, at rt) spectrum of **isopropyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7b) and isopropyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7b')**

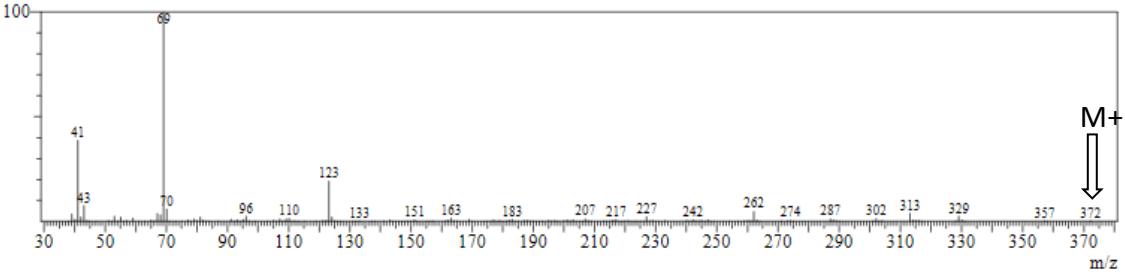


GC and MS of **isopropyl (E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzoate (7b) and isopropyl (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzoate (7b')**

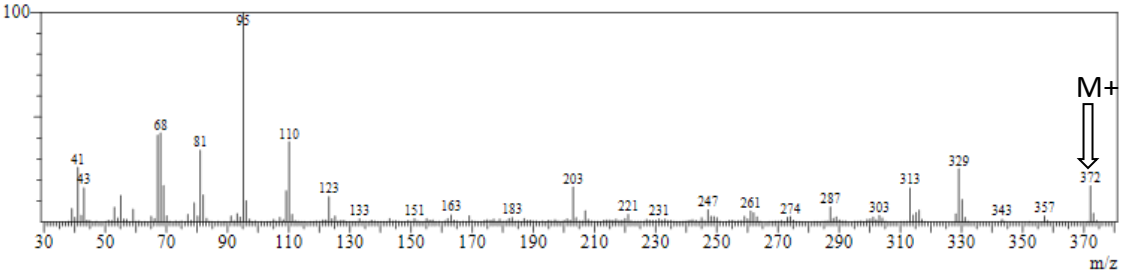


Spectrum

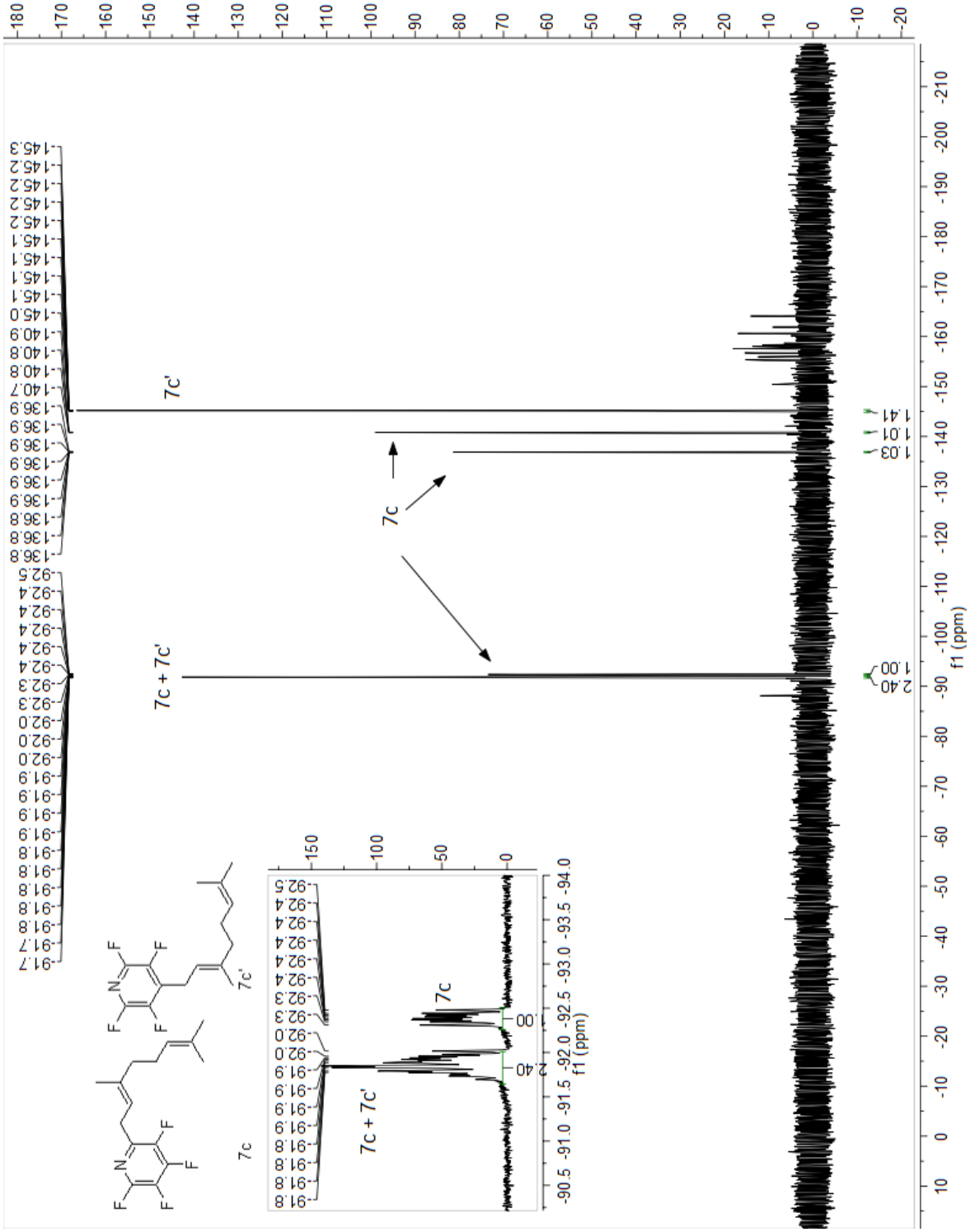
Line#:1 R.Time:17.9(Scan#:1554)
MassPeaks:185
RawMode:Single 17.9(1554) BasePeak:69(1538834)
BG Mode:None



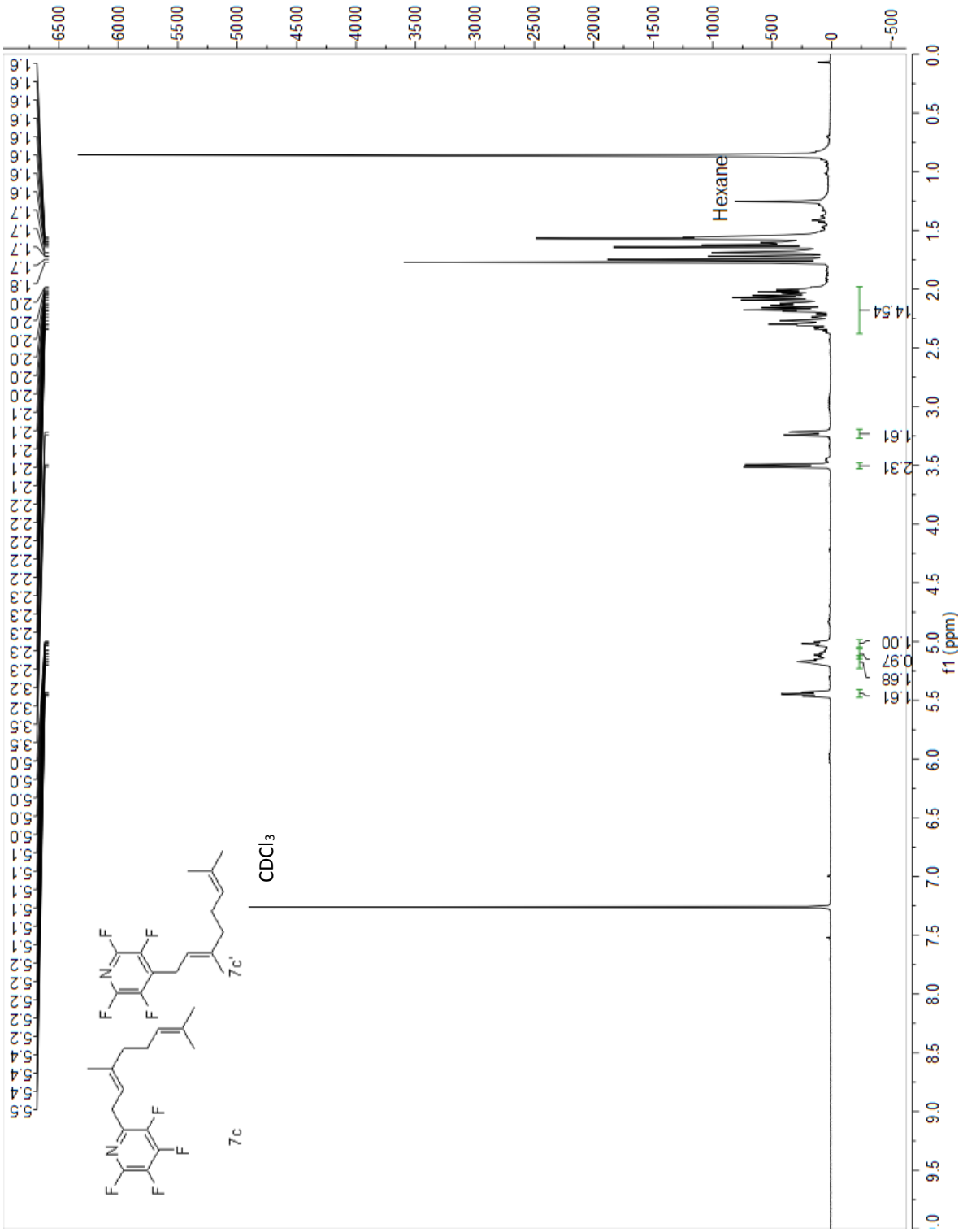
Line#:2 R.Time:18.2(Scan#:1579)
MassPeaks:268
RawMode:Single 18.2(1579) BasePeak:95(1183221)
BG Mode:None



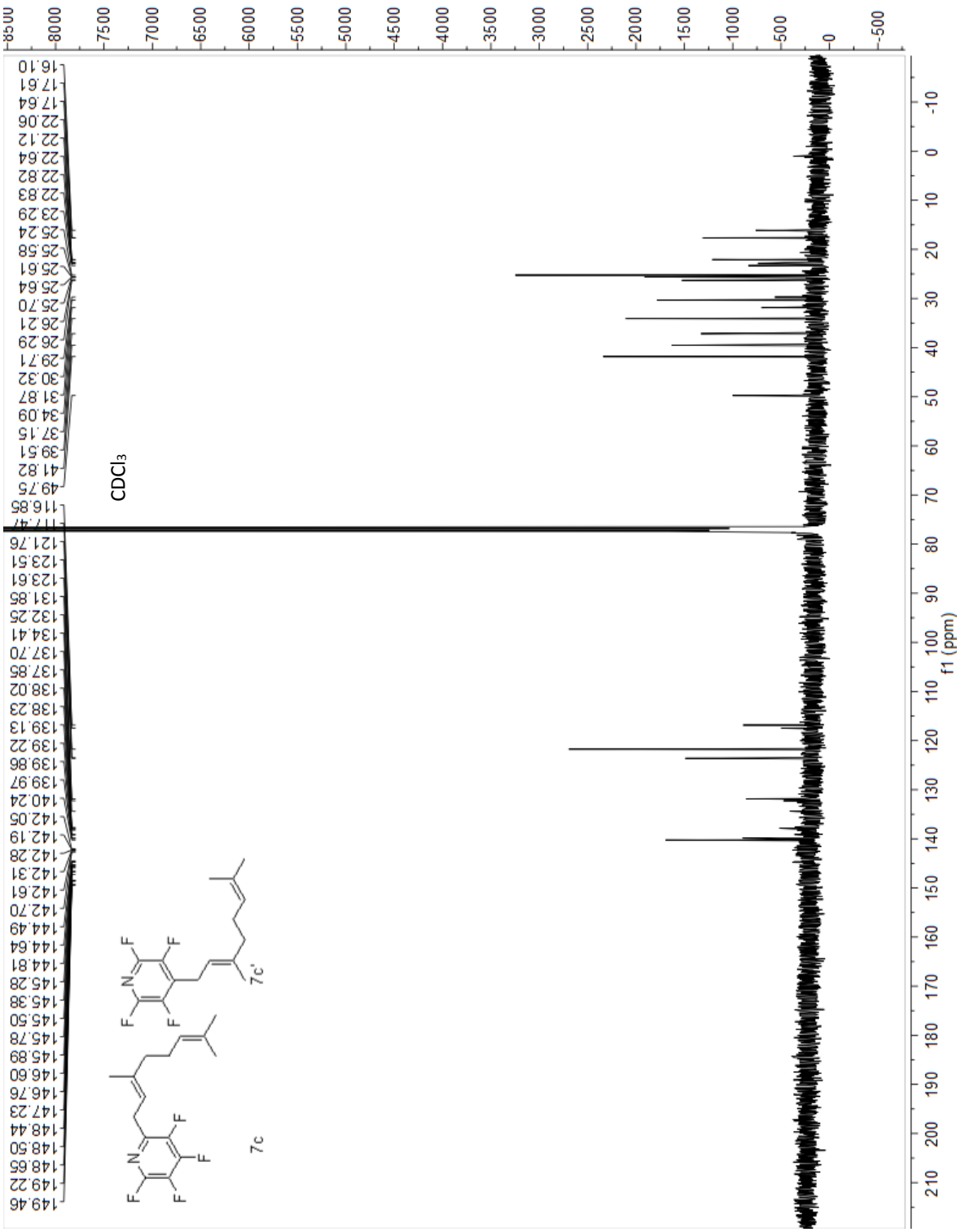
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluoropyridine (7c) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluoropyridine (7c')**



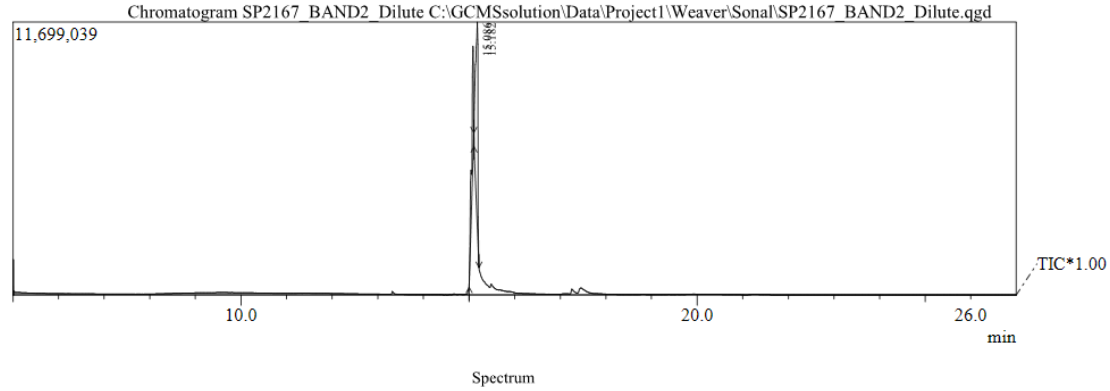
^{1}H NMR (376 MHz, CDCl3, at rt) spectrum of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluoropyridine (7c) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluoropyridine (7c')**



^{13}C NMR (376 MHz, CDCl3, at rt) spectrum of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluoropyridine (7c) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluoropyridine (7c')**

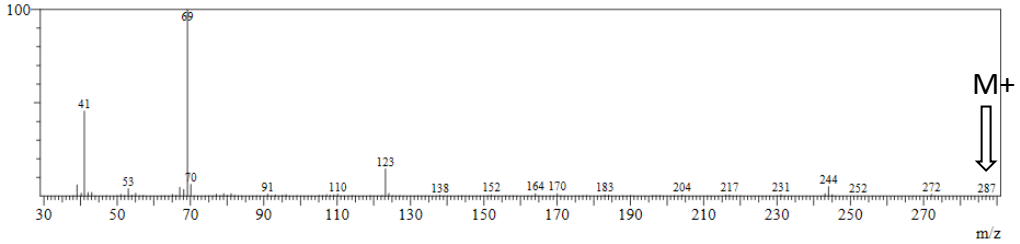


GC and MS of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluoropyridine (7c) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluoropyridine (7c')**

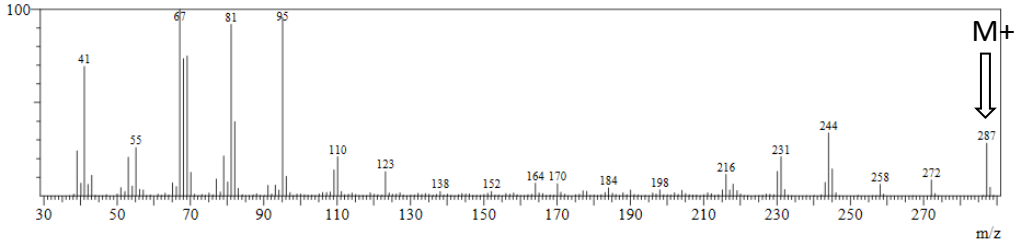


Spectrum

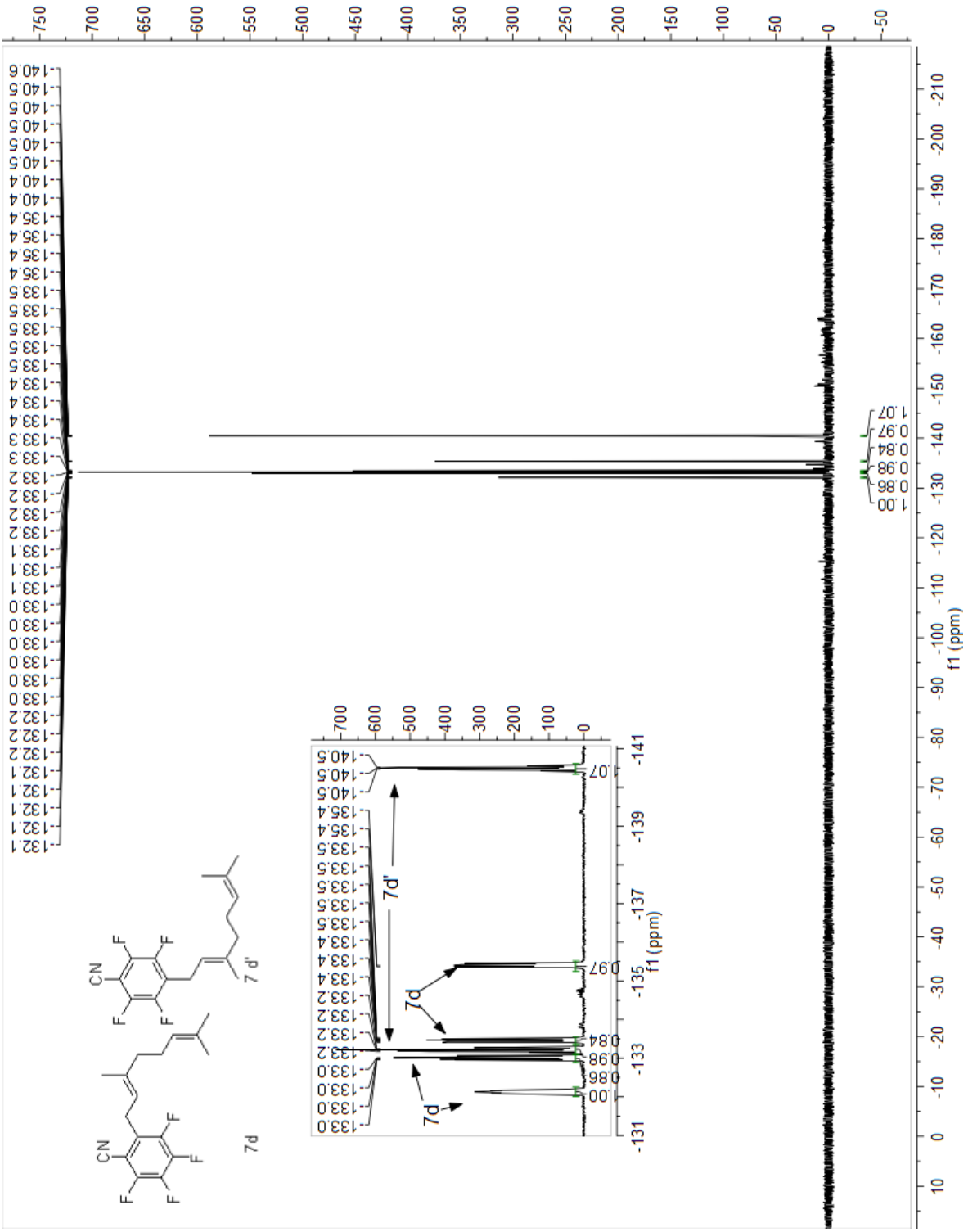
Line#:1 R.Time:15.1(Scan#:1211)
MassPeaks:198
RawMode:Single 15.1(1211) BasePeak:69(4371859)
BG Mode:None



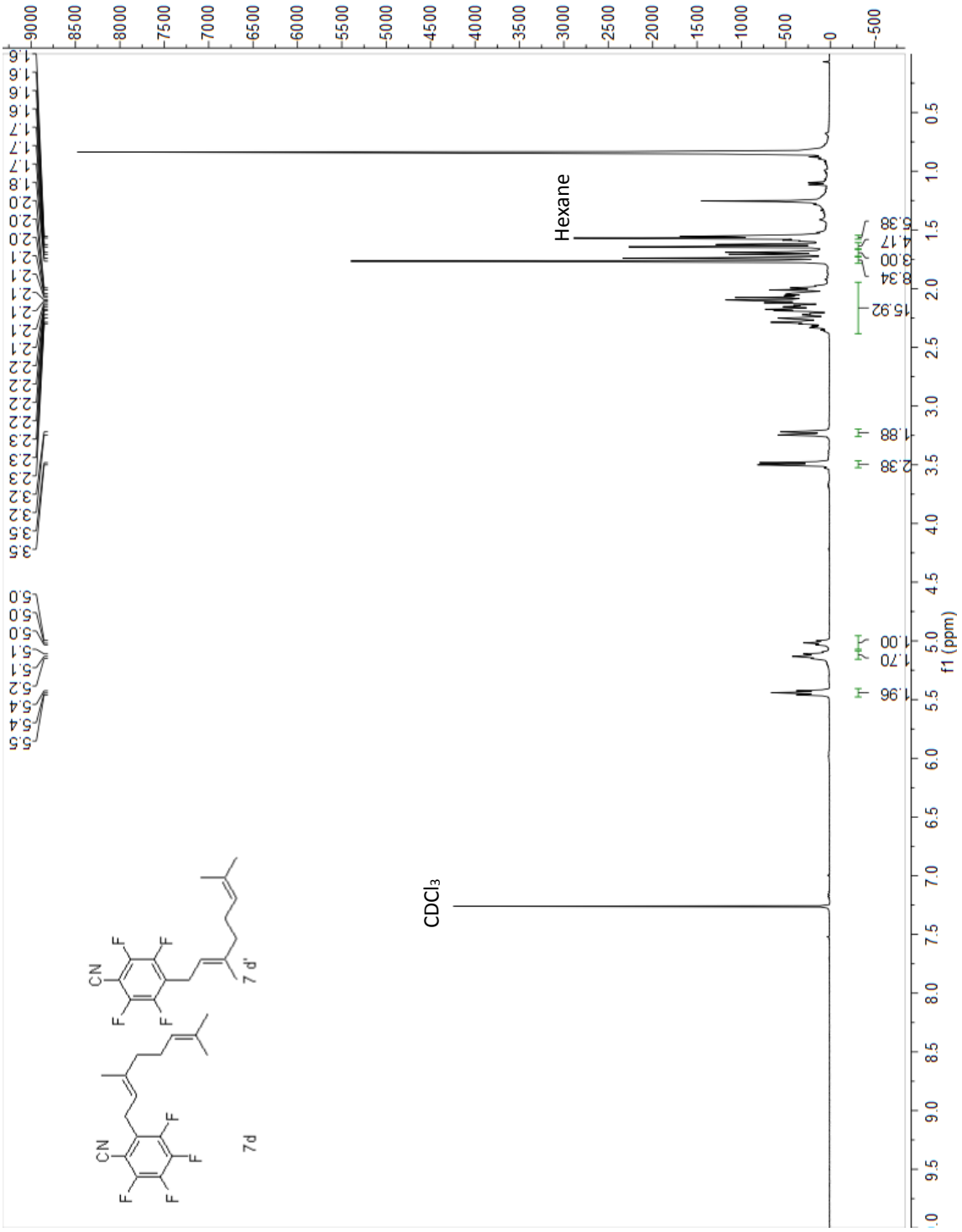
Line#:2 R.Time:15.2(Scan#:1220)
MassPeaks:214
RawMode:Single 15.2(1220) BasePeak:67(947079)
BG Mode:None



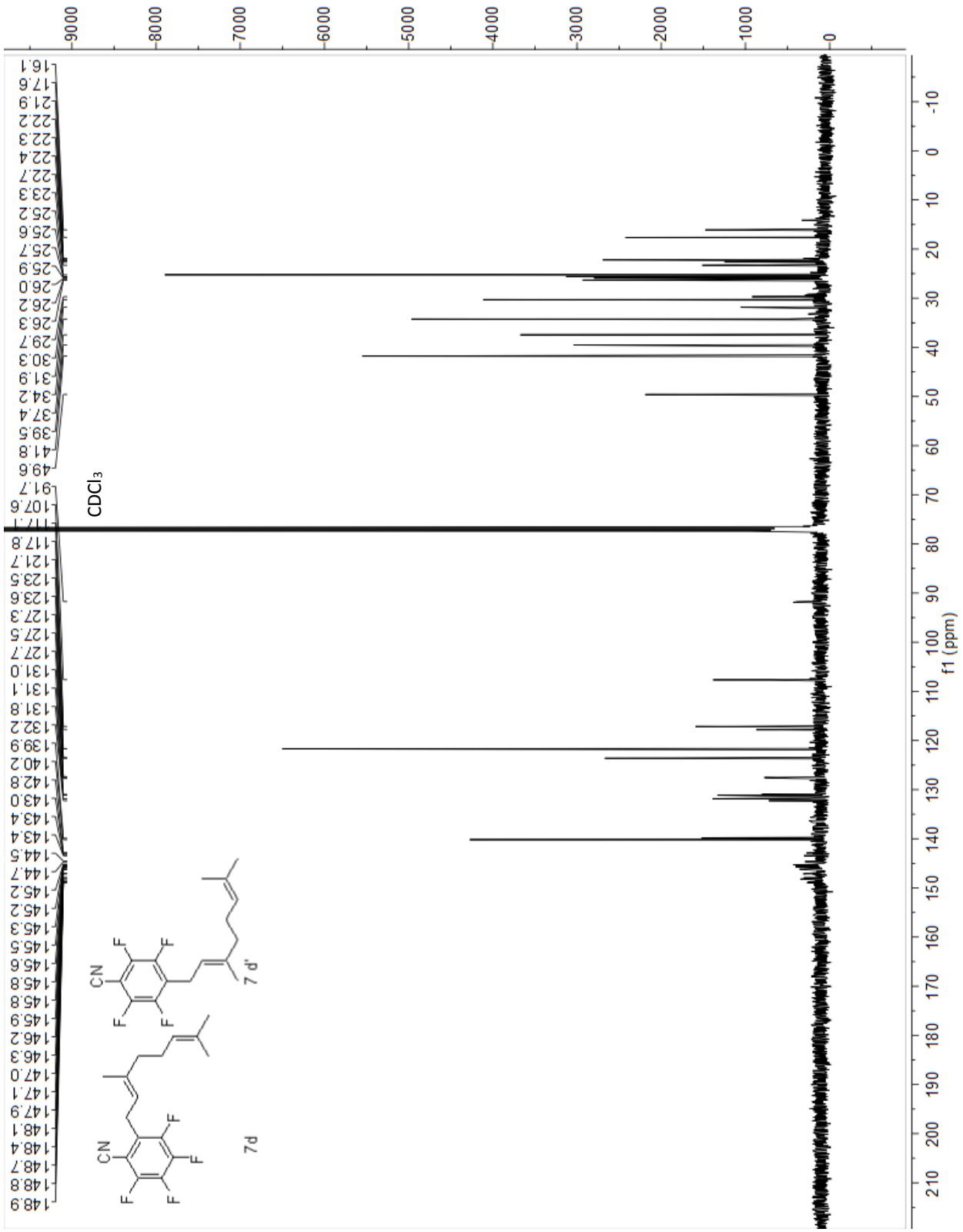
^{19}F NMR (376 MHz, CDCl3, at rt) spectrum of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzonitrile (7d) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzonitrile (7d')**



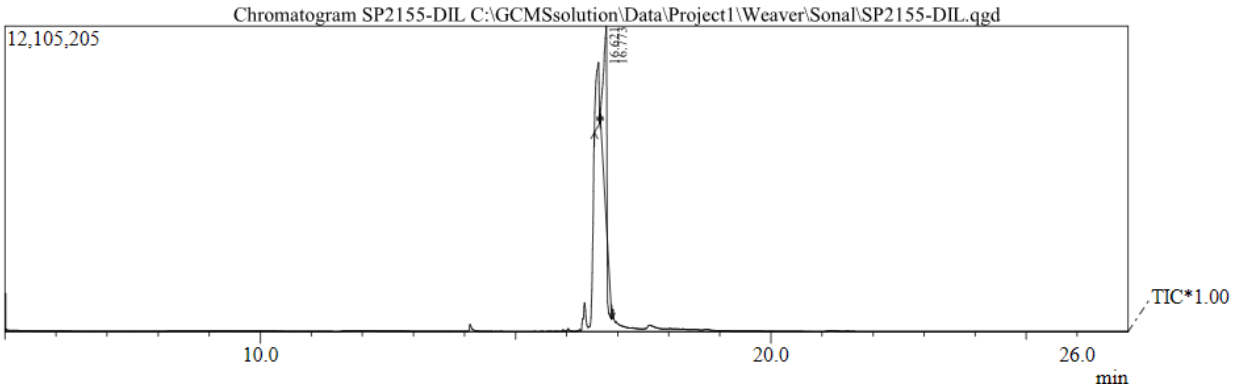
^{1}H NMR (376 MHz, CDCl3, at rt) spectrum of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzonitrile (7d) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzonitrile (7d')**



^{13}C NMR (376 MHz, CDCl3, at rt) spectrum of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzonitrile (7d) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzonitrile (7d')**

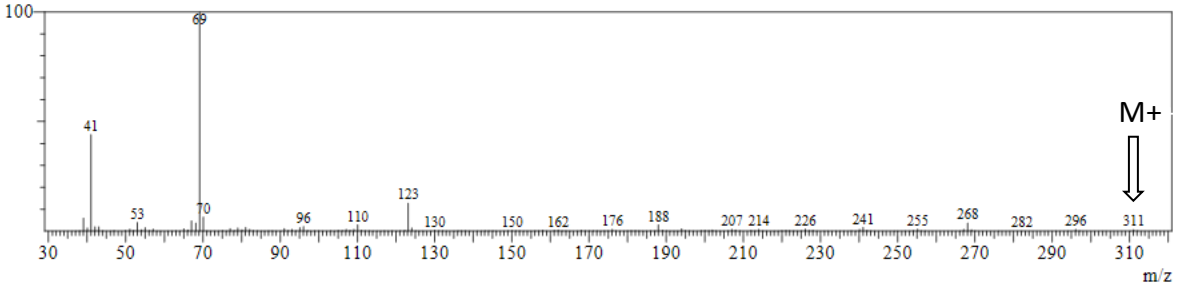


GC and MS of **(E)-2-(3,7-dimethylocta-2,6-dien-1-yl)-3,4,5,6-tetrafluorobenzonitrile (7d) and (E)-4-(3,7-dimethylocta-2,6-dien-1-yl)-2,3,5,6-tetrafluorobenzonitrile (7d')**

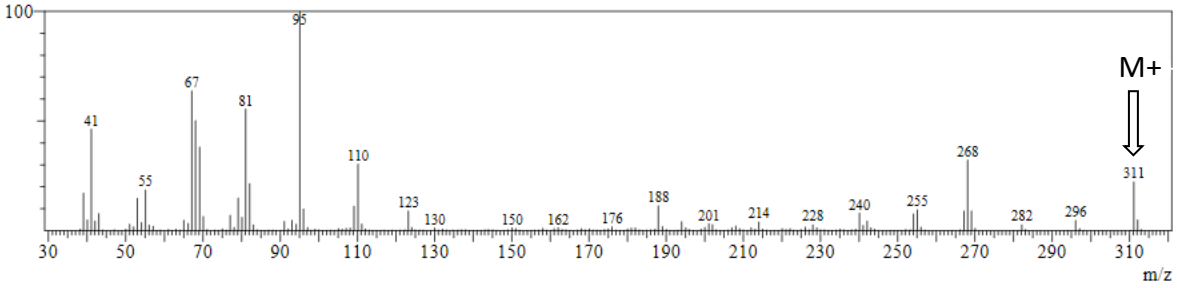


Spectrum

Line#:1 R.Time:16.6(Scan#:1394)
MassPeaks:212
RawMode:Single 16.6(1394) BasePeak:69(4220964)
BG Mode:None



Line#:2 R.Time:16.7(Scan#:1408)
MassPeaks:223
RawMode:Single 16.7(1408) BasePeak:95(1292090)
BG Mode:None



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APPENDICES

Single Electron Transfer (SET)

Trimethylamine (TEA, Et3N)

Di-isoprpylethylamine (DIPEA)

Dichloromethane (DCM)

Acetonitrile (MeCN)

Hydrogen atom transfer (HAT)

Methanol (MeOH)

N, N-Dimethylformamide (DMF)

Tetrahydrofuran (THF)

Thin layer chromatography (TLC)

VITA

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