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Exploring Palladium-Catalyzed Cross-Coupling at Nitrile Groups

A preliminary study on using nitrile groups as the center for cross-coupling reactions

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I Abstract

Carbon-Carbon cross-coupling is a useful method that is used to connect carbons of different molecules to create a larger molecule. This is particularly powerful in synthesis of complicated molecules because it allows for different parts of the target molecule to be worked with separately before they are connected, which reduces the restrictions on the methods used during synthesis. One major drawback of these methods is that the number of functional motifs they work with is quite limited. The earliest reports of metal-catalyzed cross-coupling reactions were in the late 1950s[1] and since then the number of different cross-coupling methods that deal with different functional motifs has steadily increased[1-14]. Aryl nitriles have not yet been reported as one of the viable functional motifs.

In this thesis, the viability of aryl nitriles towards metal-catalyzed cross-coupling was explored, specifically regarding Palladium-catalyzed cross-coupling, and efforts towards optimizing the procedure for this reaction have been made. Conditions, reagents, and starting materials were tested to make progress toward creating an efficient reaction procedure.

Aryl nitriles were shown to be reliably expected to react in the presence of some palladium catalysts, solvent and temperature were optimized, and multiple co-catalysts were shown to either interfere, promote, or not significantly affect the reaction. A reaction procedure that produced high yields was not found, but the yield of the reaction was increased in comparison to the reference reaction and suboptimal conditions were cataloged. Further avenues for the progression of the study of this reaction are discussed.

II Acknowledgements

Any significant amount of work cannot be attributed to just one person and the contributions made by all should be recognized. First, I would like to thank my advisor for this project at UiT The Arctic University of Norway's Tromsø campus Associate Professor Jørn H. Hansen. He kindly endorsed my idea for this project and gave me the opportunity to learn about the scientific process by giving me freedom to choose how to direct this study. He has also come up with several ideas and suggestions toward the progression of the study as well as helped in giving me motivation and direction during the writing of this thesis. Lastly, he continues to push for my success in life by giving and telling me about opportunities.

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III Abbreviations

Ac	Acetyl
Bu	Butyl
Cat.	Catalyst
Co.	Company
DCM	Dichloromethane
DMF	Dimethylformamide
Et	Ethyl
Exp.	Experiment
GC	Gas Chomatography
GCMS	Gas Chromatography Mass Spectrometry
HD	High Definition
HRMS	High Resolution Mass Spectrometry
L	Ligand
LRMS	Low Resolution Mass Spectrometry
MS	Mass Spectrometry
Me	Methyl
NMR	Nuclear Magnetic Resonance
Pr	Propyl
THF	Tetrahydrofuran
Temp.	Temperature
UiT	Universitet i Tromsø
dba	Dibenzylideneacetone
dppf	1,1′-Bis(diphenylphosphino)ferrocene
iPr	isopropyl
tBu	tert-butyl

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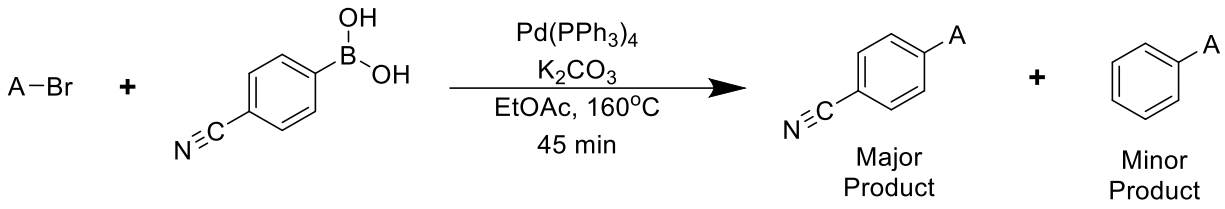
1 Background

1.1 Origins of the Reaction of Study

The reaction being studied was identified during the preliminary work of another study. The study has not been published so specifics of the reaction have not been included to protect the work of those involved in the project. The necessary details of the reaction are shown below (Scheme 1).



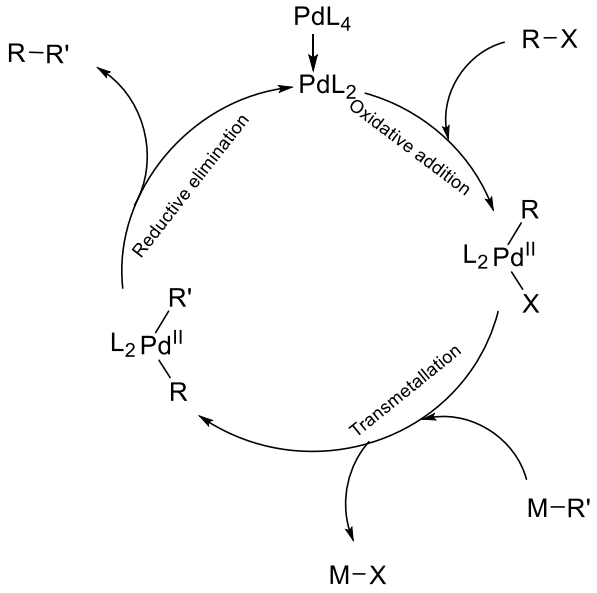
Scheme 1: The reference reaction

This reaction is called "the reference reaction" throughout this study. This is a Suzuki reaction following a typical procedure[9]. This thesis is an attempt at exploring and optimizing the reaction that occurred to produce the minor product. Because Suzuki reactions are typically high yielding and relatively quick[9], it was assumed that the side reaction occurred independently and at a different rate than the main reaction and the reaction mechanism would be relatively the same since other parts of the molecule were not suspected to promote the reaction in any significant way. Because optimizing for the minor product was the goal, it was necessary to remove the main reaction to prevent further complications. Because the minor product had its nitrile group removed, it was suspected that the mechanism followed the general mechanism for palladium-catalyzed cross-coupling instead of the Suzuki because no coupling products with the boronic acid at the site of the nitrile were detected. The original yield for the minor product was 1-2% based on GCMS. After a preliminary reaction, it was determined that the most easily measured product of the reaction being studied with benzonitrile as the starting material was biphenyl. This is what influenced the decision to focus on coupling at the nitrile site instead of removal of the nitrile and replacement with hydrogen.

1.2 Palladium-Catalyzed Cross-Coupling

Palladium catalyzed carbon-carbon cross-coupling reactions follow a general reaction mechanism[15]. Neutral palladium normally has up to four ligands at a time[16]. It must have room for the substrate and the group that is being replaced for the reaction to occur, so the first step is often to lose ligands until it has two or fewer. It can then go through oxidative addition, the

process by which palladium inserts itself between two groups, giving its own electrons to do so[15,17]. The generally accepted next step is to replace the group it substituted with another carbon group by switching ligands with another metal center, called transmetallation, in the case of this thesis it is assumed to be another palladium[15]. Last, the two carbon groups form a bond through reductive elimination, leaving palladium and giving its electrons back in the process, thereby reforming the starting point of the cycle[15].



Scheme 2: General Palladium Cross-Coupling Catalytic Cycle

Cross-coupling is a group of methods that creates connections that would otherwise not be possible[1-14]. For example, the Heck reaction produces substituted alkenes from terminal alkenes and organic halides[5] (Scheme 3). Palladium isn't the only metal used for cross coupling, but it is used in most methods[1-14]. Copper, Iron, Nickel, and Ruthenium have also been used. Palladium is well-studied and there are already a wide variety of palladium catalysts available with unique ligands that modulate their reactivities[18].

1.3 The Use of Nitrile Groups in Synthesis

Nitrile groups are an interesting functional group in synthesis. Being only made up of a carbon and nitrogen, they can be produced entirely from organic components. One example of this is the creation of nitriles from amides[21-25]. They allow for the addition of a single carbon, the one in the nitrile to be exact, adding by nucleophilic attack of the nitrile[26]. Further, their π-system allows for nucleophilic attack, which means they can be transformed relatively easily. An example of this is the conversion of a nitrile to a carboxylic acid[27]. They are also a strong electron withdrawing group. They withdraw electrons through resonance, which allows for

even more possibilities as well as promotes selectivity within reactions[28,29]. This can be employed to allow for deprotonation of nearby carbons[30] and to direct aromatic substitution reactions and other reactions that rely on charge distributions to determine selectivity such as cross-coupling. The last example is the most relevant for the work done here.

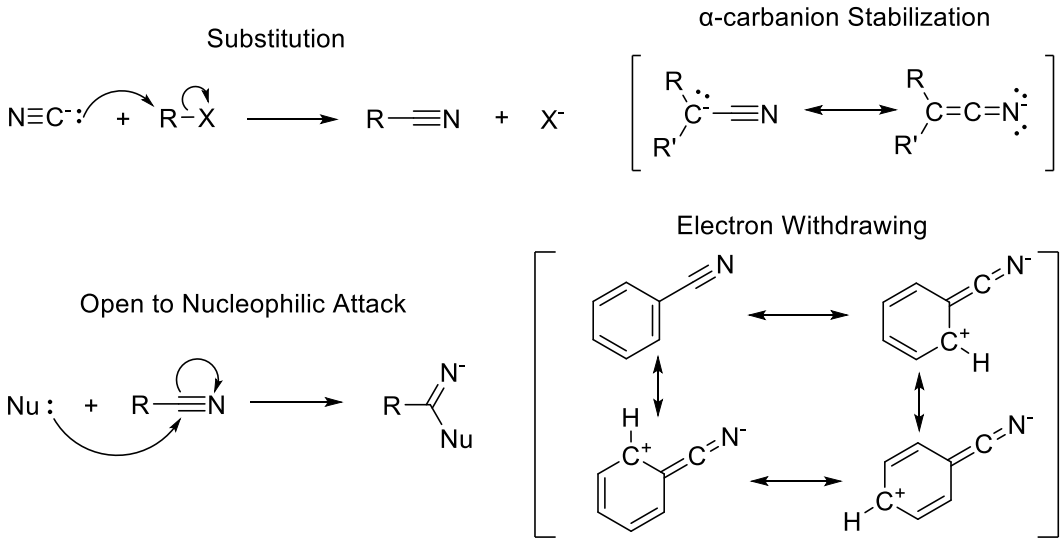


Figure 1: Examples of nitrile group reactivity

Further, metals interact with cyanide and nitrile groups in several ways. Cyanide has a lone pair on each atom as well as two π-bonds that can all interact with metal atoms (Figure 2).

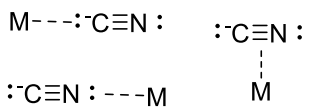


Figure 2: Examples of metal interactions with cyanide

Nitriles have also been shown to undergo oxidative addition decyanation and cross-coupling with various metals[31]. However, most of them do not use palladium.

2 Aims of the Thesis

Metal-catalyzed cross-coupling has yet to see its full potential. Adding aryl nitriles to the list of viable functional motifs that can be used in this group of methods would greatly expand the scope and applicability of the cross-coupling toolkit.

Developing this procedure for aryl nitriles would prove very useful for industrial production because nitrile groups themselves are the center of many useful chemical reactions. Nitriles groups are electron withdrawing, which makes them particularly useful in aromatic substitution reactions since they can significantly affect the position of substitution[28]. For nucleophilic aromatic substitution, nitrile groups are activating as well as *ortho-para* directors[29]. For electrophilic aromatic substitution, nitrile groups are deactivators and *meta* directors. This means that during a synthesis an aryl nitrile can be used to regioselectively add functional groups onto the aryl group before being used in a cross-coupling reaction. Further, if future studies show that alkyl, allyl, and alkynyl nitriles may also go through cross-coupling reactions, then many other nitrile reactions can be incorporated to synthesis procedures.

Nitriles are also one of the few functional groups that can be produced by a wide variety of methods[19-25,32-77]. This makes them a particularly advantageous synthetic intermediate for multiple reasons. Firstly, this means that there are many options when designing a synthesis up to the nitrile intermediate. Secondly, this gives the opportunity to employ selectivities of different functional groups that can be transformed into the nitrile afterward.

With this in mind, the aims of this preliminary study are:

- To determine optimal conditions for the reaction, if feasible
- To explore the effects of selected co-catalysts on the yield
- To determine an optimal catalyst out of many common palladium catalyst

•

3 Reaction Conditions

This chapter details the experiments done to screen for the optimal solvent, temperature, and time of the reaction. The initial testing conditions were based on the reference reaction (Scheme 1) discussed in the background. The tables listed show experiments that vary by only the conditions shown in the tables, while the conditions that were kept the same are shown on the reaction schemes above the tables. Experiment numbers are listed so that the experiment procedures and chromatograms can easily be referenced by interested parties.

3.1 Solvent Screening

The first several experiments were done at a high temperature of 160°C with a few different solvents. All of these reactions produced a black precipitate, which the reference reaction did not. Throughout the study, it was determined through qualitative observation that production of triphenylphosphine oxide, whose presence was indicated by GCMS, was directly related to how dark the solution was. However, triphenylphosphine oxide is reported to be white to pink-brown[78]. It has been assumed that the solution darkening is due to triphenylphosphine oxide being unable to stabilize the homogeneous Pd-complexes, so Pd forms nanoparticles by aggregating with each other. For similar reasons, raising the temperature high enough to dissociate a significant amount of triphenylphosphine ligands could also cause palladium to precipitate. If the palladium precipitated, then it may be less able to catalyze further reactions. This could be causing the low yield of the reaction.

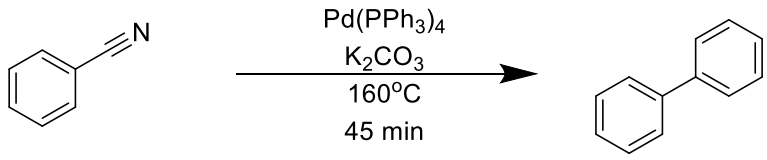


Table 1: Initial solvent screening

Exp. #	Solvent	% yield	Observations
1	MeOH	36	Black ppt, benzamide side product
2	EtOH	3	Black ppt
4	EtOAc+MeOH	8	Black ppt
5	EtOAc	6	Black ppt

Because of the production of black precipitate, further solvent screening was done at the lower temperature of 120°C based on another reaction within the study the reference reaction came from. Ethyl acetate was chosen to be the solvent to test different temperatures with because

methanol produced benzamide as a side product and its peak in the GC chromatogram directly overlapped with biphenyl, meaning the percent yield of biphenyl measured is likely inaccurate. Further, ethyl acetate was the solvent of the reference reaction.

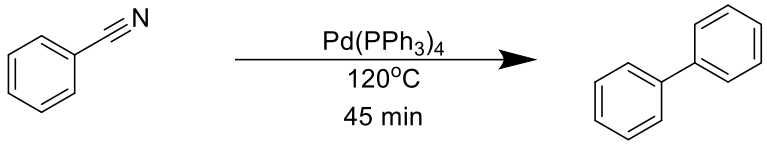


Table 2: Solvent screening continued

Exp. #	Solvent	% yield
92	EtOAc dry	5
16	MeOH	0
17	MeOH	0
18	EtOH	trace
19	DCM	0
20	Acetone	2
21	Heptane	2
102	H_2O	0
106	Toluene	2

3.2 Temperature Screening

The results show that for ethyl acetate, the highest temperature that does not produce a black precipitate was 120°C. Temperatures below this threshold created a yellow precipitate. The catalyst before addition was also yellow and did not fully dissolve in the solution at room temperature. When the vials were taken out of the microwave reactor, no yellow precipitate was seen, but it would form as the vial cooled. This observation likely meant that the yellow precipitate was the original catalyst. The highest temperature producing only yellow precipitate was chosen to be the temperature for future reactions because this would be the temperature at which the reaction would happen fastest and not destroy the catalyst during the reaction.

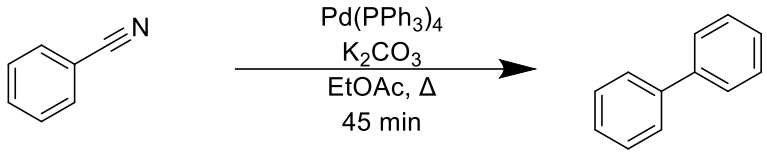


Table 3: Temperature screening

Exp. #	Temp. (°C)	% yield	Observations
5	160	6	Black ppt
22	140	3	Black ppt
23	130	5	Black ppt
27	125	6	Black ppt
25	120	4	Yellow ppt
10	120	14	Yellow ppt
91	120	3	Yellow ppt
28	115	5	Yellow ppt
25	110	4	Yellow ppt
26	100	5	Yellow ppt

Second, it should be noted that the percent yield varies significantly in respect to the total magnitude, even at the same temperature. This can be seen by focusing on the three reactions at 120°C. The three reactions were the same, but had an average yield and standard deviation of 7 and 5, respectively. There are no obvious trends relating temperature to yield here for the range of temperature selected. This can be seen in the graph below. The yield is almost constant for this temperature range. Even if the experiment that appears to be an outlier is taken out, the trendline is relatively flat and has no correlation.

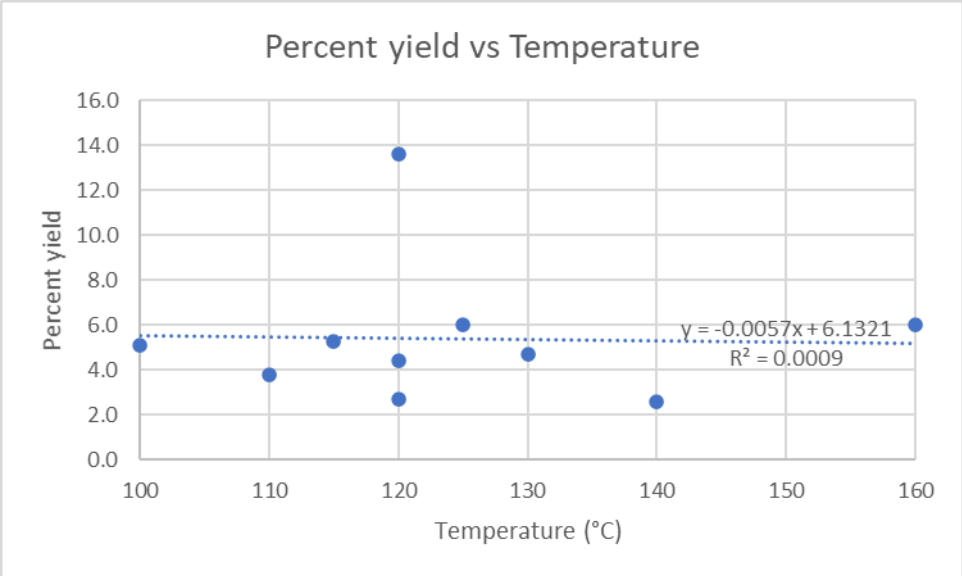


Figure 3: Percent yield vs Temperature

3.3 Catalyst Loading

Table 4 is split into two major sections that will be analyzed separately, one with potassium carbonate and the other without. From the first section, it can be seen in the graph below that yield generally increased logarithmically with catalyst loading, but there is still some variability.

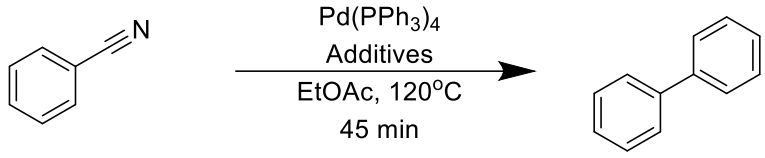


Table 4: Catalyst loading screening

Exp. #	Solvent Volume (mL)	Substrate Volume (mL)	Catalyst Loading	Additives	% yield
29	5	0.25	1.3	K_2CO_3	2
91	5	0.25	1.5	K_2CO_3	3
24	5	0.25	2.5	K_2CO_3	4
10	5	0.25	2.5	K_2CO_3	14
13	5	0.25	5	K_2CO_3	7
72	0	2	0.2	-	0
71	5	0.75	0.5	-	2
90	5	0.25	2.5	-	4
92	5	0.25	2.5	-	5
69	1	0.15	2.5	-	8
93A	5	0.25	5.5	-	10
96	1	0.01	50	-	9
103	5	0.01	50	-	23

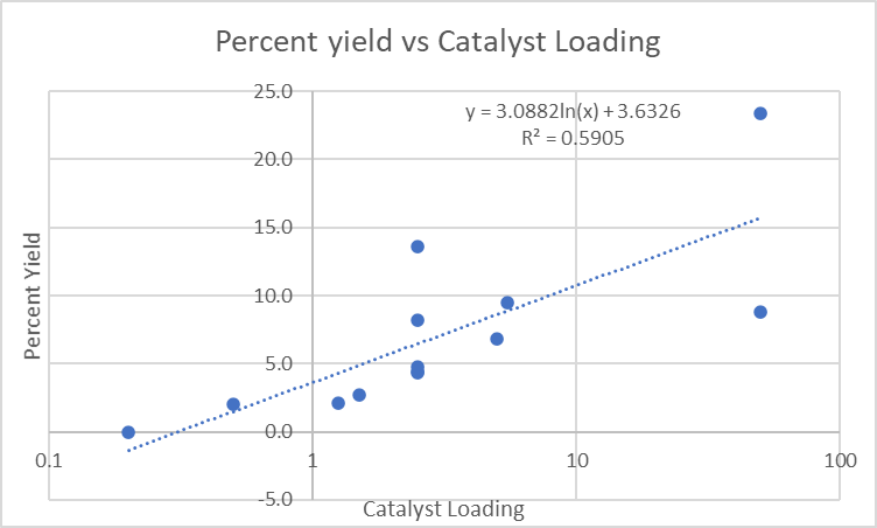


Figure 4: Percent yield vs Catalyst loading

Table 4 shows that catalyst loading was not the only condition that varied so some of the variability can be explained through the variables of solvent, addition of potassium carbonate, and substrate volume. The most notable difference is between experiments 96 and 103. In both of these experiments, a high catalyst loading of 50% was used, but this was achieved by reducing the volume of the substrate to a very small amount. The total amount of catalyst did not differ significantly between these and the average experiment. The difference between these two was the solvent volume. The higher yielding one had more solvent. This could be for multiple reasons. Further study would be required to draw conclusions.

3.4 Reaction time

Table 5 groups all comparable experiments relating time. Experiments such as 73A, 73B, and 73C are done in succession, meaning the vial was sampled, then the reaction was continued. The times listed for these experiments are the total time from the time the reaction was started in 73A to the end of the reaction considered. The data shows that the yield is not benefitted by increasing the reaction time. This suggests that the reaction either quickly reaches equilibrium or is unable to proceed after a relatively short amount of time. After this happens, the product decreases either through further unwanted reactions or by reverting to the substrate.

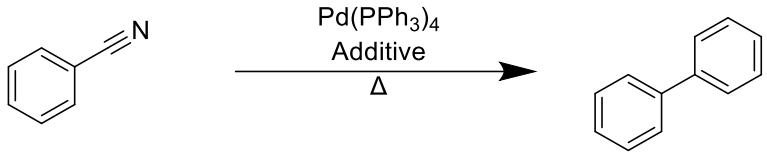


Table 5: Reaction time screening

Exp. #	Solvent	Temp. (C)	Catalyst	Catalyst loading %	Additives	Time	% yield
4	EtOAc+MeOH	160	$Pd(PPh_3)_4$	2.5	K_2CO_3	45 min	8
6	EtOAc+MeOH	160	$Pd(PPh_3)_4$	2.5	K_2CO_3	1.5 hr	5
7	EtOAc	160	$Pd(PPh_3)_2Cl_2$	2.5	K_2CO_3	45 min	8
9	EtOAc	160	$Pd(PPh_3)_2Cl_2$	2.5	K_2CO_3	1.5 hr	trace
10	EtOAc	120	$Pd(PPh_3)_4$	2.5	K_2CO_3	45 min	14
24	EtOAc	120	$Pd(PPh_3)_4$	2.5	K_2CO_3	45 min	4
11	EtOAc	120	$Pd(PPh_3)_4$	2.5	K_2CO_3	1.5 hr	3
73A	EtOAc	120	$Pd(PPh_3)_4$	1.5	$ZnCl_2$	45 min	0
73B	EtOAc	120	$Pd(PPh_3)_4$	1.5	$ZnCl_2$	1.5 hr	trace
73C	EtOAc	120	$Pd(PPh_3)_4$	1.5	$ZnCl_2$	21 hr	1
77A	EtOAc	120	$Tris(dba)Pd_2$	2.5	-	45 min	0
77B	EtOAc	120	$Tris(dba)Pd_2$	2.5	-	21.25 hr	0
93A	EtOAc	120	$Pd(PPh_3)_4$	5.5	-	45 min	10
93B	EtOAc	120	$Pd(PPh_3)_4$	5.5	-	1.5 hr	9
93C	EtOAc	120	$Pd(PPh_3)_4$	5.5	-	22 hr	12

Both further unwanted reactions and product reverting to substrate are interesting conclusions to draw and may very well be the key to further optimization of this reaction. If the reaction is reaching equilibrium, then what needs to be done is to shift the equilibrium towards the products by either adding more substrate or by reducing the amount of products available in the solution. Since the yield is so low and catalyst solubility seems to play a large role in the yield, adding more substrate is not an ideal choice. This is because even a direct linear correlation between substrate amount and total yield would predict to get the full yield of a single reaction with a normal amount of substrate would require roughly 25 times the amount of substrate. Further, adding too much substrate to the solution will affect the solubility of the catalyst. Experiment #72 tested this at the extreme. Benzonitrile is a liquid itself, so the reaction can be attempted without a solvent by dissolving all other reagents in it. In experiment 72, the reaction was performed in 2 mL of benzonitrile with no other solvent and showed no yield of the product. Generally speaking, reactions are done in solvents because the reagents themselves are not good at dissolving the reagents. As the concentration of the substrate increases, the solvent's ability to dissolve the reagents will generally decrease due to the substrate interfering.

With this in mind, the only solution if the system is in equilibrium is to remove products from the system. The expected products in this case are biphenyl and two cyanide ions. Since biphenyl is a liquid at the temperature of the reaction, there is little hope to remove it from the solution by precipitation or evaporation. Biphenyl is also generally unreactive due to its lack of reactive functional groups so temporary modification with a goal of promoting biphenyl to leave the solution is unlikely to work. This leaves the cyanide ions to remove. Luckily, cyanide is a small nucleophilic molecule, meaning it could precipitate as a salt or even be evaporated if it is converted to hydrogen cyanide through acidification, but extra precautions should be taken in this case since hydrogen cyanide is toxic.

In order to precipitate it as a salt, a positive counterion must be supplied and the resulting salt must be insoluble in the solution. Unfortunately, there isn't much information on the solubility of cyanide salts in solvents other than water. Despite this, several options were tried in the later experiments, which are discussed in Chapter 4.

Acidifying the solution poses some possible issues. Having an acidic solution may prevent cross coupling from occurring and oxidize the palladium by the palladium coupled carbon picking up a proton. Further, this could reduce the availability of triphenylphosphine ligands as some will be converted to triphenylphosphonium, which don't have a free lone pair available for interaction with palladium. The listed pKa of triphenylphosphonium is 7.64 in acetonitrile[79], while the pKa of hydrogen cyanide is 9.21[80]. With this information available, one could attempt to convert the cyanide ions and subsequently evaporate them by carefully controlling the acidity of the solution since triphenylphosphine conversion to triphenylphosphonium is around 37 times less likely than that of cyanide to hydrogen cyanide. This was not attempted in this study because the proper equipment required to monitor the pH is incompatible with the reaction setup. Specifically, because the reaction was done sealed under inert conditions and was most often done in a microwave reactor.

The cyanide could also be taken out of the solution by further reactions. Two possibilities are to oxidize it[81] or have it nucleophilically substitute another functional group on another molecule[26]. A commonly used way to get rid of cyanide is to mix it with sodium hypochlorite[81]. This is problematic for the reaction because the palladium catalyst is being used as a reducing agent to initiate its reaction. Oxidizers such as sodium hypochlorite have a chance to oxidize the catalyst and stop the reaction from proceeding. This was tried in experiment #70 and resulted in much lower yields than the reference reaction. Using sodium hypochlorite is also

problematic since it is most often sold dissolved in water, which is immiscible with ethyl acetate. It should be noted that other methods may circumvent this problem, but they were not attempted in this study.

Using nucleophilic substitution to trap cyanide is an interesting possible solution, but it comes with limitations. With a palladium catalyst in the solution, many of the functional groups that could be substituted by cyanide are also receptive to oxidative addition. This means that adding these in may not work effectively as the catalyst couples with them as well and could produce unwanted coupling products. In order to determine what functional groups would be susceptible to nucleophilic attack by cyanide but not oxidative addition by palladium in the reaction conditions given would require further research.

If the reaction is not in equilibrium, but rather the reaction has come to a halt, then the most likely cause is that the catalyst is no longer able to react as expected. There are a few possible reasons for this. First, the palladium may have been oxidized. This is suspected to be at least partially the problem. This is based on the observation that palladium (II) in palladium (II) chloride is red and the reactions that did not produce a black precipitate very often turned from yellow to orange during the reaction. Sometimes, it would even reach red. In many cases when possible oxidizing agents or acids were added, this color change was even more significant, further supporting this theory. Additionally, producing the expected two cyanide ions requires that palladium become oxidized to keep the charge balanced. If palladium being oxidized is the problem, then the solution is to simply reduce it back. This is further discussed in Chapter 4.

Another possible reason for the catalyst not being active anymore is that it no longer has the necessary ligands to have a high enough reduction potential to catalyze the reaction. Bruns et. al. (2020) showed that there is a relationship between ligands and reduction potential of palladium catalysts[82]. This could happen in two ways: oxidizing triphenylphosphine and cyanide becoming a ligand. Triphenylphosphine being oxidized was not a large concern since the reactions are done under inert gas and, as previously mentioned, an increase in triphenylphosphine oxide shows as a darkening of the solution, which normally was not witnessed. Cyanide is likely to have a greater ligand interaction energy with palladium due to its full formal charge and it is more nucleophilic than phosphorous. This is especially likely while palladium has a positive formal charge during its catalytic cycle. Even if this isn't true, it would be expected that as the concentration of cyanide increases it will replace triphenylphosphine more. Dobbs et. al. (2006) showed that excess cyanide during palladium

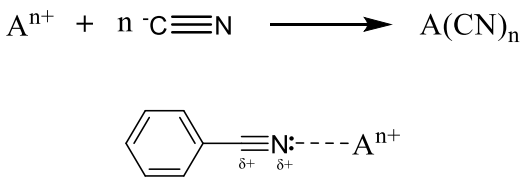
catalyzed cyanation prevents the reaction from proceeding, effectively poisoning the catalyst[83]. The only solution to this would be to remove cyanide, which has already been discussed in detail.

4 Effects of Additives

This chapter details the experiments done to test whether different additives could be used to enhance the yield. Many of the reasons for attempting specific additives were discussed in Chapter 3 as problems encountered. Most notably, many Lewis acids, reducing agents, and salts were tested.

4.1 Lewis acids

Many Lewis acids were tested for several reasons. First, Lewis acids can be used to attempt to remove cyanide from the solution, which may decrease the previously discussed problems it could be causing. This could cause it to precipitate or simply be unavailable to react in other ways. Also, Lewis acids can interact with the nitrile group to reduce the energy barrier to perform oxidative addition by making the nitrile group more electrophilic. Both are shown in Scheme 3.



Scheme 3: Cyanide binding and nitrile activation by Lewis acid

Zinc (II) chloride was focused on specifically because it has been reported by Hoesch (1915) to promote nucleophilic attack on nitriles[84]. Table 6 shows the experiments in detail.

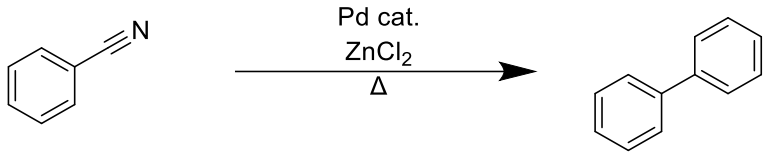


Table 6: Zinc (II) Chloride loading screening

Exp. #	Solvent	Temp. (C)	Catalyst	Catalyst loading %	$ZnCl_2$ Loading %	Time	End Color	% yield
57	EtOAc	120	$Pd(PPh_3)_4$	2.5	94	45 min	dark red	5
58	EtOAc	120	$Pd(PPh_3)_4$	2.5	42	45 min	turns red	1
59	EtOAc	120	$Pd(PPh_3)_4$	2.5	19	45 min	red	4
60	EtOAc	120	$Pd(PPh_3)_4$	2.5	8	45 min	red	2
61	EtOAc	120	$Pd(PPh_3)_4$	2.5	5.5	45 min	red	3
62	EtOAc	120	$Pd(PPh_3)_4$	2.5	2.5	45 min	orange	1
63	EtOAc	120	$Pd(PPh_3)_4$	2.5	2.5	45 min	orange	1
65	EtOAc	120	$Pd(PPh_3)_4$	2.5	2.5	45 min	orange	1
66	EtOAc	120	$Pd(PPh_3)_4$	2.5	2.5	45 min	orange	1
64	EtOAc	120	$Pd(PPh_3)_4$	2.5	1.25	45 min	orange	1
90	EtOAc	120	$Pd(PPh_3)_4$	2.5	0	45 min	-	4
92	EtOAc	120	$Pd(PPh_3)_4$	2.5	0	45 min	-	5
67	EtOAc	80	$Pd(PPh_3)_4$	2.5	2.5	45 min	opaque yellow	trace
68	EtOAc	100	$Pd(PPh_3)_4$	2.5	2.5	45 min	light orange	trace
73C	EtOAc	120	$Pd(PPh_3)_4$	1.5	30	21 hr	-	1
74B	DMF	120	$Pd(PPh_3)_2Cl_2$	3	29	1.5 hr	-	0
56	THF	120	$Pd(PPh_3)_4$	2.5	0.17	45 min	turns red	1

The first group are all directly comparable experiments. The vast majority of them show very low yields even compared to the reference reactions with no zinc (II) chloride. A couple of them are comparable yields, but not significantly larger. There doesn't seem to be any correlation between the yields and zinc (II) chloride loading. This is easy to see from the graph of the data below. No trendline was put in because the high loading experiments have such a wide difference that they would skew the data.

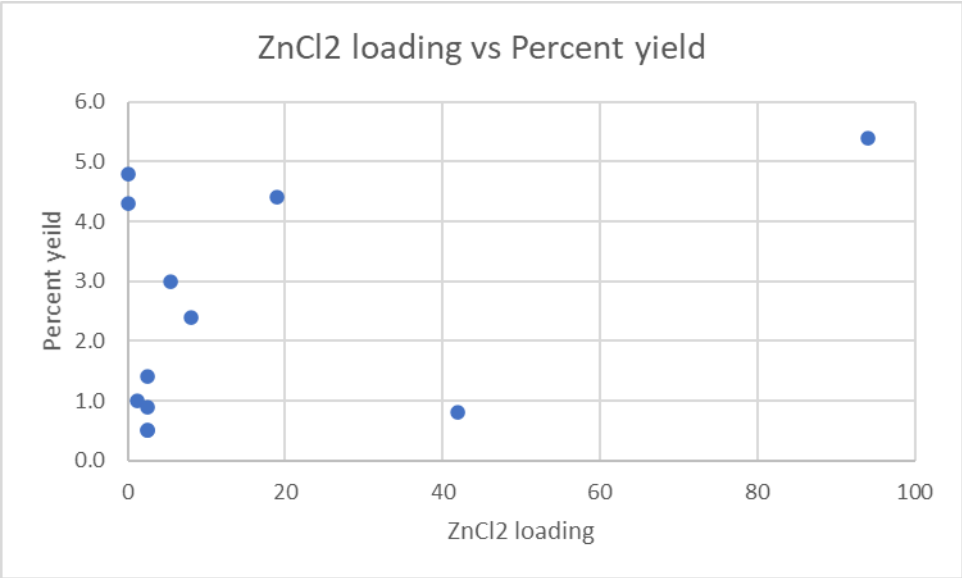


Figure 5: Zinc (II) Chloride loading vs percent yield

The second group contains experiments that aren't directly comparable, but all of them also show low yields. At best, zinc (II) chloride has no effect on the reaction. At worst, it inhibits it. It can also be seen that the higher the concentration of zinc (II) chloride, the redder the solution becomes when the reaction has finished. This may suggest that the zinc (II) chloride was oxidizing the catalyst to palladium (II). Interestingly enough, experiments 31 and 55 showed that Palladium (II) chloride reacts with zinc metal producing bubbles and black precipitate in ethyl acetate and water, respectively. This paired with the respective standard reduction potentials, predicts that zinc metal would react with palladium (II) to form palladium metal and zinc (II). However, the reverse reaction occurs when palladium has triphenylphosphine ligands. This supports that the triphenylphosphine ligands make palladium a better reducing agent as previously discussed. If the standard reduction potential of the catalyst is calculated, perhaps a better Lewis acid can be chosen to promote the reaction without reacting with the catalyst.

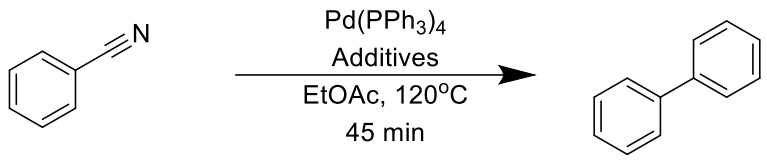


Table 7: Lewis Acid Additive Screening

Exp. #	Catalyst loading %	Additives	Observations	% yield
14	2.5	K_2CO_3, CuI	Brown ppt	1
10	2.5	K_2CO_3	Yellow ppt	14
12	2.5	K_2CO_3	Yellow ppt	4
24	2.5	K_2CO_3	Yellow ppt	4
36	2.5	$B(Et)_3$	turns red then green-yellow when heated	3
75	1.5	$AlCl_3$	-	trace
76	1.5	BF_3	-	trace
94	2.5	CuBr	Multiple color changes	1

Table 7 shows the other Lewis acids that were tested. All of them also showed lower yields than the reference reaction. Lewis acids have shown to consistently decrease the yield despite the possible ways they could have benefitted the reaction.

4.2 Reducing agents

Scheme 2 shows that in the transmetallation step a metal exchanges and alkyl group for X, which is typically a halide or psuedohalide. For the reaction studied here, there are no other metals that we expect to be in the solution so it is assumed that the metal is another palladium complex that has already undergone oxidative addition. Because of this, we expect each cycle produces a $Pd^{II}L_2X_2$ complex. Meaning that only one of two palladium atoms gets reduced back to the neutral state in one cycle. While some sources cite being able to use palladium (II) as a catalyst for similar reactions[85], this may not be possible in all cases. Whether or not palladium (0) can be recovered from this is likely dependent on what X is. If X favors reductive elimination or another method that returns palladium to its neutral state, then little or no catalyst will be lost during the reaction. One example of this is in the Suzuki reaction where a base is used to promote boronic acids from leaving without taking electrons from palladium in the process[9]. In the case that X does not favor this sort of process, another method must be used to ensure there is enough catalyst to complete the reaction. Two of the common methods used are to supply a sacrificial catalyst to supply electrons[86] and to depend on ligands[87]. For example, sometimes zinc is employed to reduce the palladium to its active state[7]. Two metals were tested

here to attempt to reduce palladium back to its neutral state:zince and copper. Zinc was already shown to reduce palladium (II) chloride in experiments 31 and 55. Copper was tested because both copper (I) cyanide and copper (II) cyanide are insoluble in water[88], meaning that if copper were to reduce palladium, the ionic copper could then force some of the cyanide to precipitate if it is also insoluble in the solvent being used.

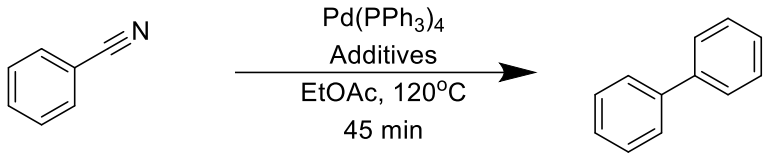


Table 8:Reducing agent screening

Exp. #	Catalyst loading %	Additives	% yield
30	1.25	K_2CO_3, Zinc	2
10	2.5	K_2CO_3	14
12	2.5	K_2CO_3	4
24	2.5	K_2CO_3	4
97	2.5	Zinc powder	4
98	2.5	Copper powder	3
100	2.5	Zinc powder	3
101	2.5	Copper powder	4
90	2.5	-	4
92	2.5	-	5

All the reactions with zinc and copper showed a slight decrease as compared to the reference reactions. This means that either they were unsuccessful in reactivating the catalyst or that the catalyst being oxidized was not a problem in the first place.

4.3 Formic acid

Since it was shown that palladium could perform oxidative addition on benzonitrile, it would be interesting to know how well this method could be used to remove the nitrile group entirely by replacing it with hydrogen. Formic acid is often used as a hydride donor for this[89]. Below shows the data from the experiments using formic acid. There was no detected production of benzene. It is unknown if this is because the GCMS does not detect benzene with the method chosen or if benzene simply was not produced. The percent yields shown are for biphenyl.

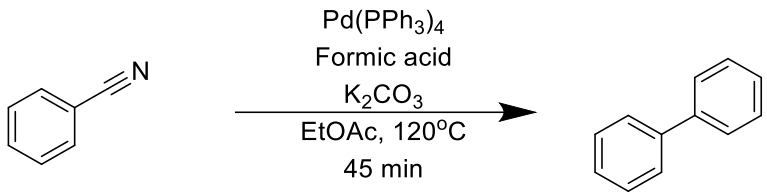


Table 9: Formic Acid screening

Exp. #	Acid equivalents	Base mol %	% Yield	Observations
39	2.7	0	4	orange
41	9	0	2	red
90	0	0	4	dark brown
92	0	0	5	-
40	2.7	30	2	-
43	2.7	75	4	-
42	9	75	2	orange
10	0	45	14	yellow
12	0	22.5	4	yellow
24	0	45	4	yellow

Compared to the reference reactions, the reactions with formic acid generally produced lower yields. The most interesting observation here is that the lower the pH is, the redder the solution turns. This supports the theory that oxidizing the catalyst turns the solution red. However, what is interesting about this is it means that palladium did react with the formic acid, but it gave its own electrons to do so instead of reacting with the hydrogen connected to the carbon of formic acid.

4.4 Suzuki Reactions

Because it was suspected that palladium was being oxidized by the reaction, several Suzuki reactions were tested. This is because Suzuki reactions use a base as an electron source for the reaction[9]. Table 10 shows the data from all the Suzuki reaction experiments. Note that the reference reactions are greyed out because they do not follow the given scheme.

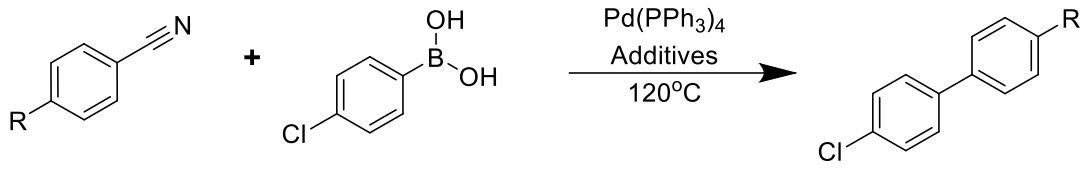


Table 10: Suzuki screening

Exp. #	Solvent	R	Time	% Yield	Additives
33	EtOAc	H	45 min	13	K_2CO_3, 4-chlorophenylboronic acid
34	EtOAc	H	3.5 hr	10	K_2CO_3, 4-chlorophenylboronic acid
48	EtOAc	CN	45 min	8	K_2CO_3, 4-chlorophenylboronic acid
50	EtOAc	OCH_3	45 min	9	K_2CO_3, 4-chlorophenylboronic acid
51	DMF	H	45 min	6	K_2CO_3, 4-chlorophenylboronic acid
52	DMF/Water	H	45 min	9	K_2CO_3, 4-chlorophenylboronic acid
53	Water	H	45 min	11	K_2CO_3, 4-chlorophenylboronic acid
10	EtOAc	H	45 min	14	K_2CO_3
12	EtOAc	H	45 min	4	K_2CO_3
24	EtOAc	H	45 min	4	K_2CO_3
49	EtOAc	OCH_3	45 min	0	4-chlorophenylboronic acid
35	EtOAc	H	45 min	1	4-chlorophenylboronic acid
90	EtOAc	H	45 min	4	
92	EtOAc	H	45 min	5	

The Suzuki reactions performed better than the reference reactions on average. Comparing the first two listed reactions shows that the reaction had likely finished by 45 minutes since adding extra time decreased the yield. The increase in yield may be due the reaction with the boronic acid being more favored than its nitrile counterpart. In fact, this is reflected in the yields of the products. Figure 4 shows the gas chromatogram from experiment 34, which is representative.

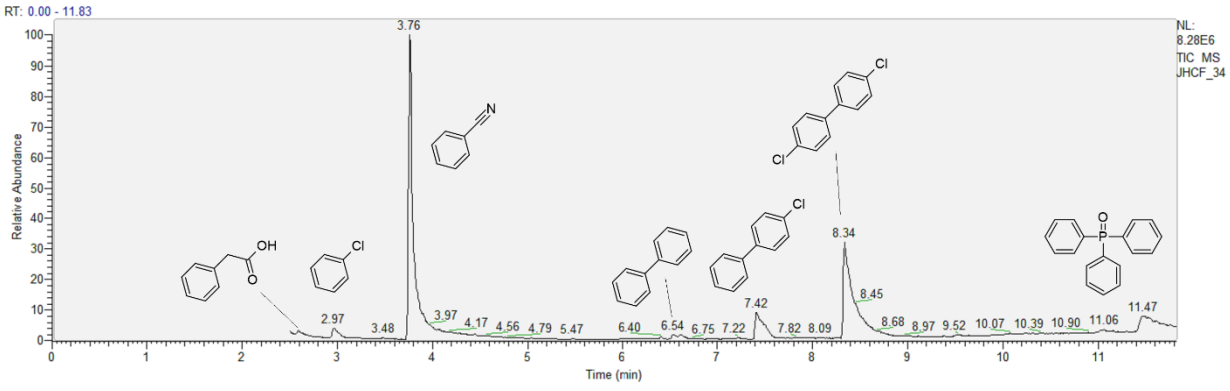


Figure 6: Experiment 34 GC chromatogram

It can be seen here that the homocoupling of the boronic acid happened the most, the heterocoupling happened at an intermediate level, and the homocoupling of the nitrile happened

the least. This supports that the catalytic cycle prefers the boronic acid over the nitrile, either by reacting faster or by having a higher equilibrium concentration. The reason for the increase in yield may be due to this, that palladium does not need to lose electrons to push the reaction due to the base providing them, or both.

The third and fourth reactions are done with substrates that have different functional groups on the ring. This was done to see if electron donating or withdrawing groups affected the yield. It was decided that this would be tested with a Suzuki reaction because the higher reference yield means that differences would more easily be seen. Both were lower than the reference reaction, experiment 33. Further, they both exhibited peculiar behavior. 1,4-dicyanobenzene was measured to have reacted at both nitrile groups to produce a terphenyl product some of the time. Also, neither of these substates produced biphenyl products with the functional groups still attached. For 1,4-dicyanobenzene, this might be expected since oxidative addition followed by picking up a hydrogen from any available protic molecules. However, 4-methoxybenzonitrile also lost its methoxy group, which cannot be explained from anything seen in this study. Perhaps oxidative addition can also happen at the methoxy group? Only further research would tell.

The third group of experiments tests how well DMF, water, and a combination of them work. This was tested because it was found that some Suzuki protocols used those solvents and reported relatively high yields[90,91]. DMF and the DMF/water mixture did not perform as well as ethyl acetate, but water had a similar yield. This contrasts the results of experiment 102 where water had shown no yield of the product. The difference between these two reactions was that one was a Suzuki reaction, and the other was not. This may suggest that the Suzuki reagents assist in dissolving the nitrile and catalyst in water. In any case, this is an exciting development because it may allow for a greener approach to the reaction being studied.

The last group shows that the Suzuki reaction necessarily requires a base for it to work. Without the base, the reaction barely happened at all.

4.5 A nickel co-catalyst

Because Feng et al. (2021) showed that a nickel catalyst could be used to substitute a nitrile group with an isotopically labeled nitrile group[92], the nickel catalyst may also prove useful in this reaction. Table 11 shows the data from the experiments.

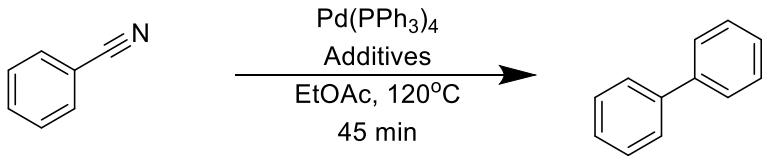


Table 11: Nickel catalyst data

Exp. #	Solvent	Additives	% Yield
90	EtOAc	-	4
92	EtOAc	-	5
105	EtOAc	Bis(1,5-cyclooctadiene)nickel(0)	15
106	Toluene	-	2
107	Toluene	Bis(1,5-cyclooctadiene)nickel(0)	12

The reactions with the nickel catalysts performed better than the reference reactions. However, it should be noted that both reactions with nickel produced a black precipitate. This may suggest that the ligands that the nickel co-catalyst has are not strongly bound. It may be worthwhile to test other nickel catalysts. Also, it cannot be concluded from the data if the nickel catalyst was going through its own catalytic cycle analogous to the one palladium was going through or if it was simply assisting in palladium's cycle. The study this is based on would suggest that it worked through its own cycle. In fact, there may be a much better metal catalyst for this reaction, but this study focused on exploring palladium catalysis for nitrile activation, and other metals were outside the scope of this study.

5 Catalyst Screening

This chapter goes over the experiments that screened different palladium catalysts and experiments using bis(triphenylphosphine)palladium (II) chloride.

5.1 Screening Different Palladium Catalysts

Table 12 shows the data from the screening of many palladium catalysts.

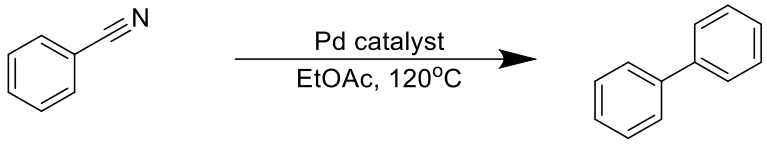


Table 12: Pd catalyst screening

Exp. #	Catalyst	Catalyst loading %	Time	% Yield
77	Tris(dba)Pd_2	2.5	21.25 hr	0
78	$Pd(OAc)_2$	4	45 min	0
79	$[Pd(allyl)Cl]_2$	3.5	45 min	trace
80	tBuXPhosPd G3	4.5	45 min	0
81	$Pd(dppf)_2$ CH_2Cl_2	4.5	45 min	0
82	BrettPhos Pd G1 Methyl t-Butyl Ether Adduct	4.5	45 min	0
83	SPhos Pd G2	3.5	45 min	trace
84	XantPhos Pd G3	4	45 min	1
85	$PdCl_2$	3.5	45 min	0
86	$Pd(OH)_2/C$	6	45 min	0
87	PEPPSI™-IPr catalyst	4	45 min	0
88	Pd/C	18.5	45 min	0
89	SPhos Pd G1 methyl t-butyl ether adduct	4	45 min	trace
104	$Pd(P(tert\text{-}butyl))_2$	2.5	45 min	0
90	$Pd(PPh_3)_4$	2.5	45 min	4
92	$Pd(PPh_3)_4$	2.5	45 min	5

Out of all the catalysts screened for here, the reference catalyst was the highest yielding one. In fact, most of the catalysts showed no yield at all, while a few showed trace or very small yields. This may have to do with many catalysts with ligands being made for specific purposes, while the most important factors here are reduction potential and ability to couple two molecules.

The most similar catalyst to the reference catalyst is Bis(triphenylphosphine)palladium (II) chloride or $Pd(PPh_3)_2Cl_2$. The major difference between it and the reference catalyst are that the palladium has an oxidation state of (II), it has only two triphenylphosphine ligands, and two chloride ligands. A few reactions were done with this catalyst. They are detailed below.

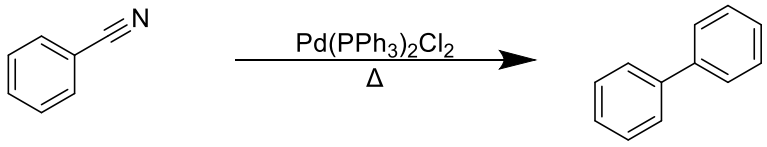


Table 13: Bis(triphenylphosphine)palladium(II) dichloride catalyst data

Exp. #	Solvent	Temp. (C)	Catalyst loading %	Additives	Time	% Yield
8	EtOAc	160	2.5	-	45 min	trace
7	EtOAc	160	2.5	K_2CO_3	45 min	8
9	EtOAc	160	2.5	K_2CO_3	1.5 hr	trace
74A	DMF	120	3	-	45 min	0
74B	DMF	120	3	$ZnCl_2$	1.5 hr	0

Much like the other catalysts, this one did not perform as well as the reference. It did have one relatively high yielding reaction, but the same reaction extended to twice the time reduced the yield drastically. This may suggest that the high yielding reaction was an outlier.

6 Sources of Error

As with any data-driven research, error is an important topic to address. It can be seen from the data that there is quite a bit of variability in the yield between similar or even the same reaction procedures. This variability is likely due to nonsystematic errors such as measurement errors or other human errors. Further study would be required to pin down the exact causes of the variability. However, because the variability is on the same order of magnitude as the measurements, the validity of some conclusions can be drawn into question. Many of the conclusions were based on other factors, such as physical observations, but not all of them. If there isn't any work dedicated to reducing this variability done for future research, it is recommended that experiments and measures are repeated to increase the statistical power of the conclusions.

Systematic error is also a concern here. For the sake of being able to screen many reactions, results were measured by the relatively quick method of GCMS. Specifics about how the results were measured can be found near the beginning of the Experimental Procedures section. To summarize, the measurements were taken unaltered from peak areas in the GC chromatograms. This does not take into account the individual response factors of the molecules being measured. It was attempted to measure response factors two times, but the results varied significantly. It is suspected that this has to do with the replacement of the GCMS measurement filament multiple times over the course of the study. Unfortunately, the response factors for all important molecules were not measured every single time the machine had a new filament for the simple reason of being unaware of the replacement. It was decided that the response factors would not be applied to the data as which response factor curves should be applied to which experiments would be unclear due to the lack of knowledge surrounding the exact dates of filament replacements and some experiments may have no recorded response factor curve to apply at all. Fortunately, only the magnitude of the yields would be changed significantly by the application of response factor curves. The conclusions are based on relative yields so they would stay the same. In future studies, a way to avoid this would be to fully purify and measure the mass of the product.

Further, the identity of some molecules detected in the GCMS measurements were confirmed by low resolution mass spectrometry (LRMS) and their identity was decided by what would make the most sense in the reaction. This was not the case for benzonitrile and biphenyl. This is especially relevant for the unusual products shown in some of the chromatograms and for

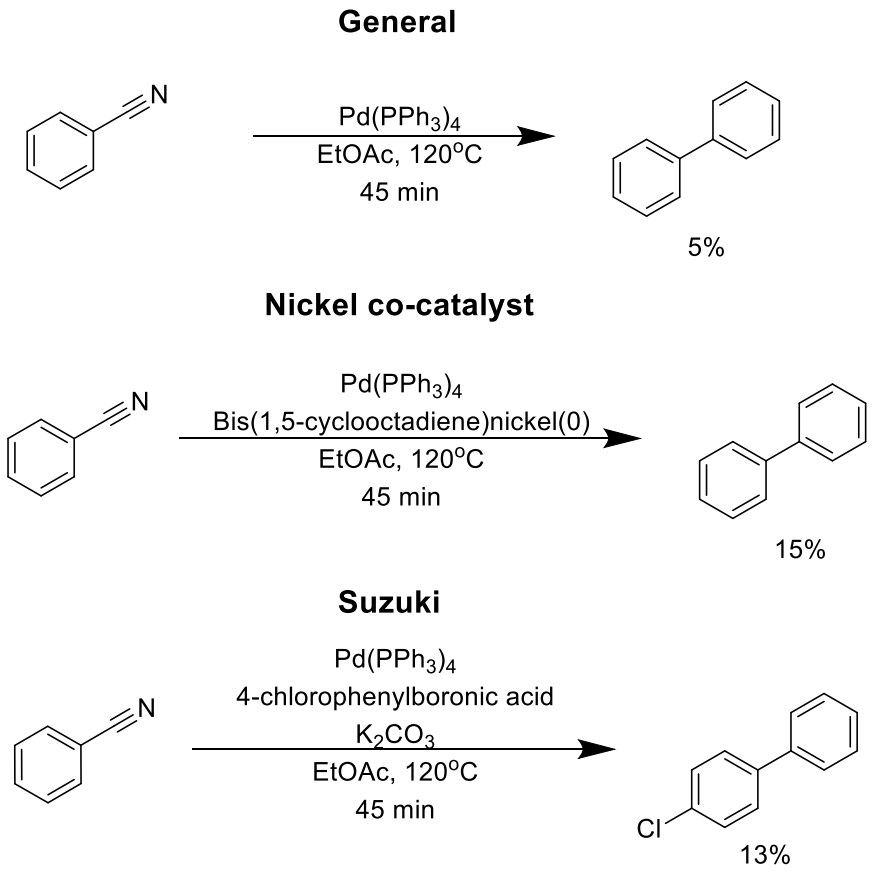
products that have multiple structural isomers. For example, 4-Chloro-1,1'-biphenyl was the reported heterocoupling product from the Suzuki reactions. This is the product that makes the most mechanistic sense, but both 2-Chloro-1,1'-biphenyl and 3-Chloro-1,1'-biphenyl would also have similar MS spectra. This could also be said for other structural isomers. More rigorous identification methods such as NMR and HRMS should be used to confirm all relevant molecules.

Lastly, many of the reactions were done using a microwave reactor, but some were not due to the microwave losing functionality for a few months during the study. There wasn't any observed yield difference between the two methods of heating, but the reactions done on a hot plate had much more variable temperature control. This could play into the variability of the yields. Full details about which heating method was used in each reaction are specified in the Experimental Procedures section under each experiment.

7 Conclusion

7.1 Highest Yielding Methods

The current highest yielding methods produced from this work were shown to follow be the reaction scheme shown below.



Scheme 4: Highest yielding methods

The yield was shown to generally increase with catalyst loading and this effect is suspected to be limited by solubility. Further, using the nickel co-catalyst or following the Suzuki reaction increased the yields, but more research needs to be done to optimize these reactions.

7.2 Avenues for Further Study

Clearly, further work needs to be done to improve on this reaction. There are many areas of study that would benefit the optimization of this reaction. The most obvious ones include testing nickel and alternative metal catalysis and Suzuki type reactions further, as well as expanding the tested solvents. Computational work can also be done to determine the most appropriate catalyst including which metal and ligands would best promote the reaction. Other methods such as photocatalytic methods may also be a possible route of study. Other substrates can also

be tested such as vinyl nitriles and many more substrates with differing substituents than were tested here. Additionally, more work can be done to resolve the problems presented in this thesis such as the apparent maximum yield due to either chemical equilibrium or by catalyst poisoning by cyanide.

8 References

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9 Experimental Procedures

All reagents were purchased from Sigma Aldrich Co. and used as received. All solvents used that aren't specified to be "dry" were obtained from laboratory solvent squeeze bottles that exposes the solvent to ambient atmosphere. These solvents should be assumed to contain some amount of water. Dry solvents were dried using molecular sieves and were kept sealed under either argon or nitrogen gas.

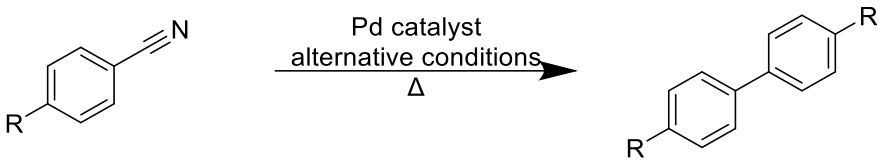
NMR spectra were recorded on a Bruker Avance III HD spectrometer operating at 400 MHz for 1H and 101 MHz for 13C equipped with a two-channel broadband SmartProbe™. Chemical shift values (δ) are reported in parts per million (ppm) relative to tetramethylsilane. All NMR spectra were processed with MestReNova v14.2.0-26256. Reference NMR spectra were taken by dissolving a pure sample of the compound bought from Sigma Aldrich Co. in deuterated trichloromethane.

Gas chromatography – mass spectrometry (GCMS) measurements were done using a Thermo Scientific Trace GC Ultra paired with a Thermo Scientific ITQ 1100. Sampling was done by a Thermo Scientific TriPlus RSH Autosampler. GCMS procedure: Sample volume 1.5 uL, 50°C hold 2 minutes followed by 15°C/min increase until 300°C hold 2 minutes, Mass spectrometry measurements start at 4 minutes scanning from 40 to 400 amu positive ion channel with three microscans per data point. GCMS data was measured by identifying products and reagents detected in the chromatogram, filtering for the main substrate and any products that could have come from it by their molecular mass to reduce baseline noise, then measuring the total area above the baseline of each peak. Yields were calculated from these areas by dividing the amount of substrate require to make the product by the sum of amount of substrate required to make all products of this substrate detected and the amount of substrate itself (Formula 1). For example, the general reaction converts benzonitrile to biphenyl. Two moles of benzonitrile are required to produce one mole of biphenyl, so to calculate the yield two times the area of the biphenyl is divided by the sum of the area of benzonitrile and two times the area of biphenyl. Response factor curves with data ranging from 1% to 100% of yield or leftover concentration after reaction were made for biphenyl and benzonitrile, respectively. These measurements were made at the same time on the same sample to get relative response factors. The equations produced by these curves were not used to modify the data for reasons discussed in the Sources of Error chapter.

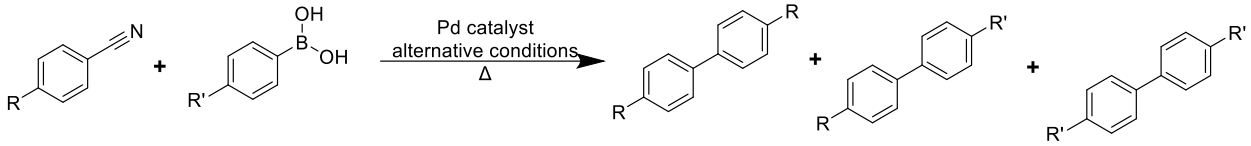
$$\% \text{ yield} = \frac{\chi_P A_P}{A_S + \chi_P A_P + \sum_i \chi_i A_i}$$

Formula 1: % yield calculation where S is substrate,P is product,i represents other products, χ_i is the molar ratio between i and S,and A_i is the measured area of i in the GC chromatogram

Reactions that specify they were done in a microwave reactor were done in an Anton Paar Monowave 300 with a stirring speed of 900 rpm, heated to reacting temperature as quickly as possible, and were cooled to 55°C before release. Time and temperatures of the specific reaction are specified in the descriptions below. Reactions that don't specify that they were done in a microwave were heated in a sand bath on a hot plate with temperature control with the maximum stirring speed that did not introduce bubbles into the solution, determined before the solution heated up and maintained for the rest of the experiment.



Scheme 5: General Palladium-Coupling Reaction



Scheme 6: General Suzuki-Miyaura Reaction

Experiment 1

Using the General Palladium-Coupling Reaction Scheme, 152 mg of Potassium carbonate was dissolved in 5 mL methanol and stirred. 0.25 mL of benzonitrile was added and stirred. 71 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 2

Using the General Palladium-Coupling Reaction Scheme, 155 mg of Potassium carbonate was dissolved in 5 mL ethanol and stirred. 0.25 mL of benzonitrile was added and stirred. 68 mg of

tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 3

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was stirred into 5 mL ethanol. 67 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 4

Using the General Palladium-Coupling Reaction Scheme, 146 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and 1 mL of methanol and stirred. 0.25 mL of benzonitrile was added and stirred. 71 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 5

Using the General Palladium-Coupling Reaction Scheme, 147 mg of Potassium carbonate was dissolved in 5 mL ethanol and stirred. 0.25 mL of benzonitrile was added and stirred. 68 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 6

Using the General Palladium-Coupling Reaction Scheme, 155 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and 1 mL of methanol and stirred. 0.25 mL of benzonitrile was added and stirred. 69 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 1.5 hours. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 7

Using the General Palladium-Coupling Reaction Scheme, 154 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and stirred. 0.25 mL of benzonitrile was added and stirred. 43 mg of bis(triphenylphosphine)palladium (II) dichloride was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 8

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was dissolved in 5 mL ethyl acetate and stirred. 43 mg of bis(triphenylphosphine)palladium (II) dichloride was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 9

Using the General Palladium-Coupling Reaction Scheme, 151 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and stirred. 0.25 mL of benzonitrile was added and stirred. 43 mg of bis(triphenylphosphine)palladium (II) dichloride was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 160°C for 1.5 hours. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 10

Using the General Palladium-Coupling Reaction Scheme, 150 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and stirred. 0.25 mL of benzonitrile was added and stirred. 72 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 11

Using the General Palladium-Coupling Reaction Scheme, 155 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and stirred. 0.25 mL of benzonitrile was added and stirred. 68

mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 1.5 hours. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 12

Using the General Palladium-Coupling Reaction Scheme, 76 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and stirred. 0.25 mL of benzonitrile was added and stirred. 71 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure. The rest of the solution was washed with 30 mL of 1 M hydrochloric acid and 30 mL of brine. The aqueous layer was washed with 30 mL of ethyl acetate twice. A yellow solid was separated from the organic layer via filtration. The solid was washed with methanol, then dissolved in deuterated trichloromethane for NMR analysis. The leftover organic layer was dried with sodium sulfate and a sample was mixed into deuterated trichloromethane for crude NMR analysis.

Experiment 13

Using the General Palladium-Coupling Reaction Scheme, 147 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and stirred. 0.25 mL of benzonitrile was added and stirred. 139 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 14

Using the General Palladium-Coupling Reaction Scheme, 104 mg of Potassium carbonate was dissolved in 5 mL ethyl acetate and stirred. 159 mg of CuI was added and stirred. 0.25 mL of benzonitrile was added and stirred. 64 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 15

Using the General Palladium-Coupling Reaction Scheme, 147 mg of Potassium carbonate was dissolved in 5 mL dry methanol and stirred. 0.25 mL of benzonitrile was added and stirred. 68 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 16

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL dry methanol. 66 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 17

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL methanol. 66 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 18

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethanol. 68 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 19

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL dichloromethane. 70 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 20

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL acetone. 68 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 21

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL heptane. 69 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 22

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 145 mg of Potassium carbonate was stirred in. 65 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 140°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 23

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 144 mg of Potassium carbonate was stirred in. 67 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 130°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 24

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 146 mg of Potassium carbonate was stirred in. 71 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen

gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 25

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 145 mg of Potassium carbonate was stirred in. 65 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 110°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 26

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 150 mg of Potassium carbonate was stirred in. 73 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 100°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 27

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 154 mg of Potassium carbonate was stirred in. 63 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 125°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 28

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 147 mg of Potassium carbonate was stirred in. 66 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 115°C for 45 min. A sample

was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 29

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 145 mg of Potassium carbonate was stirred in. 36 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 30

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 116 mg granular zinc was stirred in. 153 mg of Potassium carbonate was stirred in. 33 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 31

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of benzonitrile was added and stirred into 5 mL ethyl acetate. 100 mg of granular zinc was stirred in. 10 mg of PdCl2 was added and the vial was flushed with nitrogen gas before stirring. The vial was placed in the microwave reactor at 120°C for 45 min. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 32

Using the General Palladium-Coupling Reaction Scheme, 150 mg of potassium carbonate was added and stirred into 5 mL ethanol. 0.25 mL of benzonitrile was added and stirred. 66 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 33

Using the General Palladium-Coupling Reaction Scheme, 344 mg of 4-Chloroyphenylboronic acid was added to and stirred in 5 mL ethyl acetate. 538 mg of potassium carbonate was added and stirred. 0.15 mL benzonitrile was added and stirred. 42 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 34

Using the General Palladium-Coupling Reaction Scheme, 349 mg of 4-chlorophenylboronic acid was added to and stirred in 5 mL ethyl acetate. 544 mg of potassium carbonate was added and stirred. 0.15 mL benzonitrile was added and stirred. 41 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 3.5 hours with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 35

Using the General Palladium-Coupling Reaction Scheme, 343 mg of 4-chlorophenylboronic acid was added to and stirred in 5 mL ethyl acetate. 0.15 mL benzonitrile was added and stirred. 40 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 36

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL benzonitrile was added and stirred into 5 mL ethyl acetate. 0.1 mL of triethylborate was added and stirred. 42 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 37

0.1 mL hydrogen peroxide was added and stirred into 5 mL ethyl acetate. 10 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring.

Experiment 38

1 mL of 2 M hydrochloric acid was added and stirred into 5 mL ethyl acetate. 7 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring.

Experiment 39

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL formic acid was added and stirred into 5 mL ethyl acetate. 0.15 mL benzonitrile was added and stirred. 40 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 40

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL formic acid was added and stirred into 5 mL ethyl acetate. 56 mg of potassium carbonate was added and stirred. 0.15 mL benzonitrile was added and stirred. 42 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 41

Using the General Palladium-Coupling Reaction Scheme, 0.5 mL formic acid was added and stirred into 5 mL ethyl acetate. 0.15 mL benzonitrile was added and stirred. 43 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 42

Using the General Palladium-Coupling Reaction Scheme, 0.5 mL formic acid was added and stirred into 5 mL ethyl acetate. 158 mg of potassium carbonate was added and stirred. 0.15 mL benzonitrile was added and stirred. 41 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 43

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL formic acid was added and stirred into 5 mL ethanol. 154 mg of potassium carbonate was added and stirred. 0.15 mL benzonitrile was added and stirred. 42 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. 3 mL of gas in vial removed due to bubbling. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 44

Using the General Palladium-Coupling Reaction Scheme, 197 mg of 1,4-dicyanobenzene was added and stirred into 5 mL ethyl acetate. 40 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 45

Using the General Palladium-Coupling Reaction Scheme, 206 mg of 4-methoxybenzonitrile was added and stirred into 5 mL ethyl acetate. 44 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 140-150°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 46

25 mg of palladium (II) chloride was mixed into 5 mL dichloromethane. The vial was flushed with nitrogen gas and stirred at 115-125°C for 45 min. The resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 47

Using the General Palladium-Coupling Reaction Scheme, 206 mg of 4-methoxybenzonitrile was added and stirred into 5 mL ethyl acetate. 44 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 48

Using the General Palladium-Coupling Reaction Scheme, 335 mg of 4-chlorophenylboronic acid was added and stirred into 5 mL ethyl acetate. 560 mg of potassium carbonate was added and stirred. 189 mg of 1,4-dicyanobenzene was added and stirred. 39 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 49

Using the General Palladium-Coupling Reaction Scheme, 333 mg of 4-chlorophenylboronic acid was added and stirred into 5 mL ethyl acetate. 212 mg of 4-methoxybenzonitrile was added and stirred. 45 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 50

Using the General Palladium-Coupling Reaction Scheme, 324 mg of 4-chlorophenylboronic acid was added and stirred into 5 mL ethyl acetate. 546 mg of potassium carbonate was added and stirred. 202 mg of 4-methoxybenzonitrile was added and stirred. 45 mg of tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen

gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 51

Using the General Palladium-Coupling Reaction Scheme, 319 mg of 4-chlorophenylboronic acid was added and stirred into 5 mL of dry N,N-dimethylformamide. 553 mg of Potassium carbonate was added and stirred. 0.15 mL of Benzonitrile was added and stirred. 44 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 52

Using the General Palladium-Coupling Reaction Scheme, 2 mL of distilled water was added and stirred into 3 mL of dry N,N-dimethylformamide. 326 mg of 4-chlorophenylboronic acid was added and stirred. 552 mg of Potassium carbonate was added and stirred. 0.15 mL of Benzonitrile was added and stirred. 40 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 53

Using the General Palladium-Coupling Reaction Scheme, 323 mg of 4-chlorophenylboronic acid was added and stirred into 5 mL of distilled water. 528 mg of Potassium carbonate was added and stirred. 0.15 mL of Benzonitrile was added and stirred. 45 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 54

0.1 mL of triethylborate was added and stirred into 5 mL of Dichloromethane. 35 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. 0.7 mL of triethylborate was added and stirred. 76 mg of Zinc (granular) was added and the vial was flushed with nitrogen gas before stirring. The vial was then opened to the atmosphere and stirred.

Experiment 55

88 mg of Zinc (granular) and 32 mg of Palladium (II) Chloride were added and stirred into 5 mL of distilled water.

Experiment 56

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 0.5 M Zinc (II) chloride in tetrahydrofuran. 45 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 57

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 189 mg of Zinc (II) chloride was added and stirred. 41 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 58

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 85 mg of Zinc (II) chloride was added and stirred. 41 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A

sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 59

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 39 mg of Zinc (II) chloride was added and stirred. 42 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 60

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 16 mg of Zinc (II) chloride was added and stirred. 40 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 61

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 11 mg of Zinc (II) chloride was added and stirred. 39 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. The vial was cooled quickly with cold water and left to sit for two days. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 62

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 1 mg/mL Zinc (II) chloride in Ethyl Acetate. 44 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample

was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 63

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 1 mg/mL Zinc (II) chloride in Ethyl Acetate. 45 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 64

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 0.5 mg/mL Zinc (II) chloride in Ethyl Acetate. 45 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 65

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 1 mg/mL Zinc (II) chloride in Ethyl Acetate. 43 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 66

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 1 mg/mL Zinc (II) chloride in Ethyl Acetate. 42 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 10 minutes with stirring. Then the reaction was taken off heating and stirring for 10 minutes before resuming the reaction for

another 35 minutes. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 67

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 1 mg/mL Zinc (II) chloride in Ethyl Acetate. 41 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 75-85°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 68

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 5 mL of 1 mg/mL Zinc (II) chloride in Ethyl Acetate. 43 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 95-105°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 69

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 1 mL of Ethyl Acetate. 46 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 70

Using the General Palladium-Coupling Reaction Scheme, 0.15 mL of Benzonitrile was added and stirred into 1 mL of Ethyl Acetate. 1 mL of 10% sodium hypochlorite in water was added and stirred. 39 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 71

Using the General Palladium-Coupling Reaction Scheme, 0.75 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 45 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring (sample 71). The vial was opened and heated for another 20 minutes at 115-125°C (sample 71B). A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 72

Using the General Palladium-Coupling Reaction Scheme, 39 mg of Tetrakis(triphenylphosphine)-palladium(0) was added into 2 mL of Benzonitrile. The vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 73

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 38 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring (sample 73A). 100 mg of Zinc (II) chloride was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes (73B). 5 mL of Ethyl Acetate was added and the vial was heated at 115-125°C for 19.5 hours (73C). A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 74

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of dry N,N-dimethylformamide. 52 mg of Bis(triphenylphosphine)palladium(II) dichloride was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring (74A). 96 mg of Zinc (II) chloride was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring (74B). A sample was

diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 75

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 92 mg of Aluminum Chloride was added and stirred until completely dissolved. 46 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 76

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 0.5 mL of 1 M Boron trifluoride in ethyl acetate was added and stirred. 42 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 77

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 51 mg of Tris(dibenzylideneacetone)dipalladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring (77A). 5 mL of Ethyl Acetate was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 21.25 hours with stirring (77B). A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 78

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 22 mg of Palladium (II) acetate was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes

with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 79

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 32 mg of [Pd(allyl)Cl]2 was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 80

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 84 mg of tBuXPhosPd G3 was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 81

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 94 mg of [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 82

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 85 mg of BrettPhos Pd G1 Methyl t-Butyl Ether Adduct was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 83

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 62 mg of SPhos Pd G2 was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 84

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 93 mg of XantPhos Pd G3 was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 85

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 15 mg of Palladium (II) Chloride was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 86

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 20 mg of Palladium (II) Hydroxide on carbon was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 87

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 64 mg of [1,3-Bis(2,6-Diisopropylphenyl)imidazol-2-ylidene](3-chloropyridyl)palladium(II) dichloride was added and the vial was flushed with

nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 88

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 48 mg of Palladium on carbon was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 89

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 73 mg of SPhos Pd G1 methyl t-butyl ether adduct was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 90

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 72 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas and sat sealed for 1 hour before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 91

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added into 5 mL of Ethyl Acetate. 148 mg of Potassium carbonate was added and stirred. 41 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 92

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 71 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas and sat sealed for 1 hour before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 93

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 152 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring (93). The vial was heated at 115-125°C for another 45 minutes with stirring (93B). 6 mL of Ethyl Acetate was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 20.5 hours with stirring (93C). A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 94

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added into 5 mL of Ethyl Acetate. 351 mg of Copper (I) Bromide was added and stirred. 72 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 95

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethanol. 73 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas and sat sealed for 1 hour before stirring. The vial was heated at 115-125°C for 45 minutes with stirring. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 96

Using the General Palladium-Coupling Reaction Scheme, 0.01 mL of Benzonitrile was added and stirred into 1 mL of Ethyl Acetate. 54 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 97

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 13 mg of Zinc powder was added and stirred. 69 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 98

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 13 mg of Copper powder was added and stirred. 69 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 99

Using the General Palladium-Coupling Reaction Scheme, 0.21 mL of Butyronitrile was added and stirred into 5 mL of Ethyl Acetate. 71 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 100

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 155 mg of Zinc powder was added and stirred. 75 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 101

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 148 mg of Copper powder was added and stirred. 72 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 102

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of distilled water. 74 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in methanol and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 103

Using the General Palladium-Coupling Reaction Scheme, 0.01 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 61 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 104

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 34 mg of Bis(tri-tert-butylphosphine)palladium(0) was

added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 105

Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of Ethyl Acetate. 38 mg of Bis(1,5-cyclooctadiene)nickel(0) was added and stirred. 74 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 106

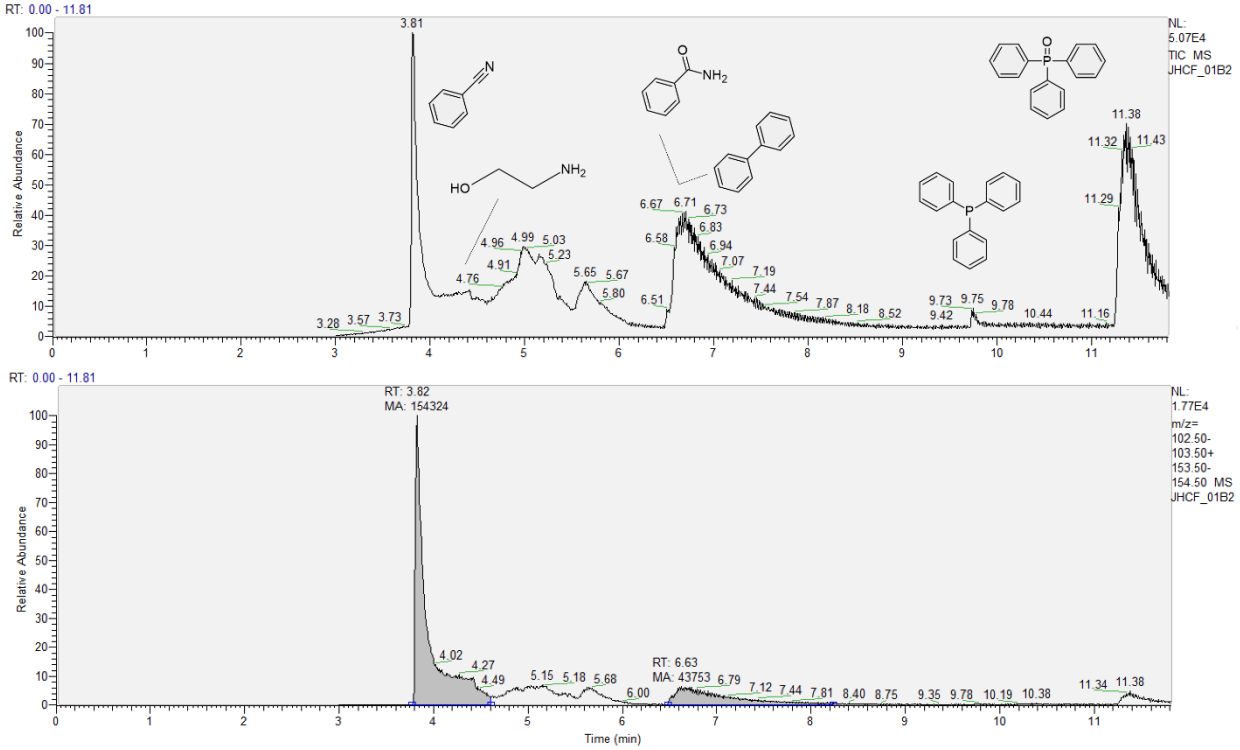
Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of dry toluene. 71 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Experiment 107

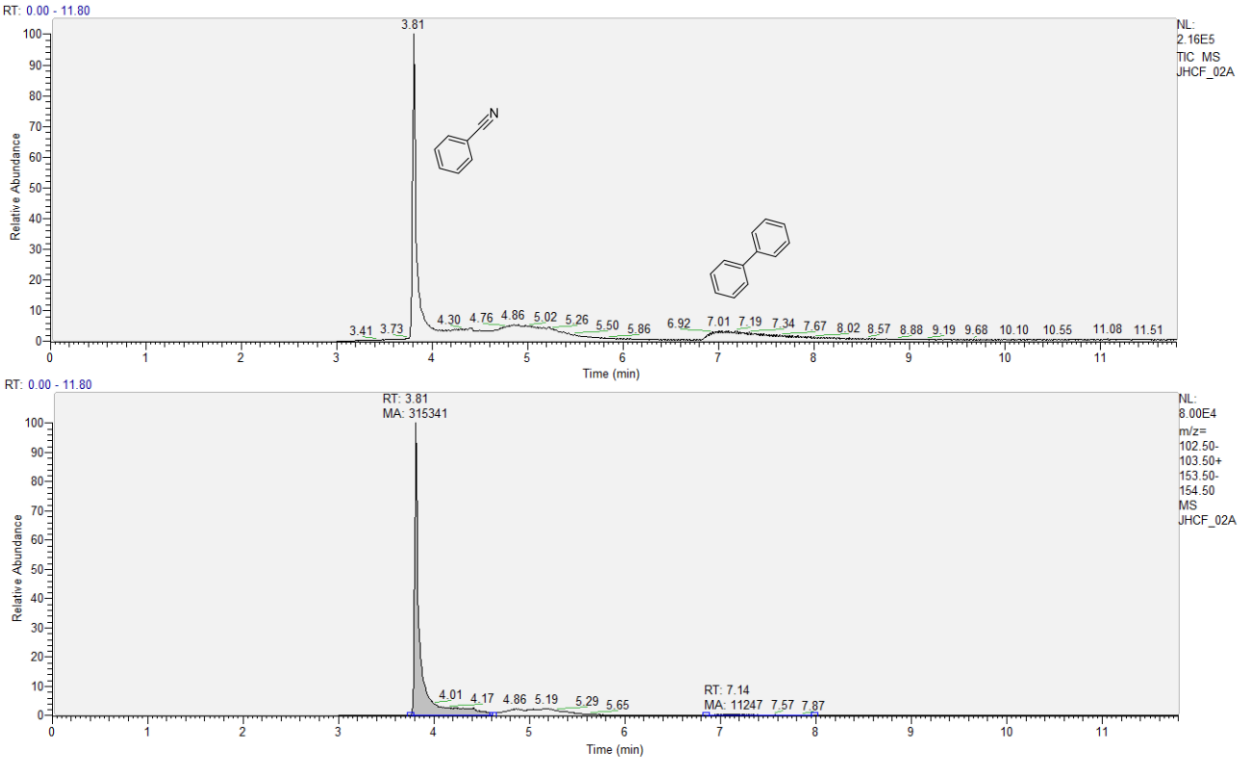
Using the General Palladium-Coupling Reaction Scheme, 0.25 mL of Benzonitrile was added and stirred into 5 mL of dry toluene. 38 mg of Bis(1,5-cyclooctadiene)nickel(0) was added and stirred. 74 mg of Tetrakis(triphenylphosphine)-palladium(0) was added and the vial was flushed with nitrogen gas before stirring. The vial was heated at 120°C for 45 minutes with stirring in the microwave reactor. A sample was diluted 1:2 in dichloromethane and the resulting solution was run on the GCMS using the Standard GCMS Procedure.

Appendix

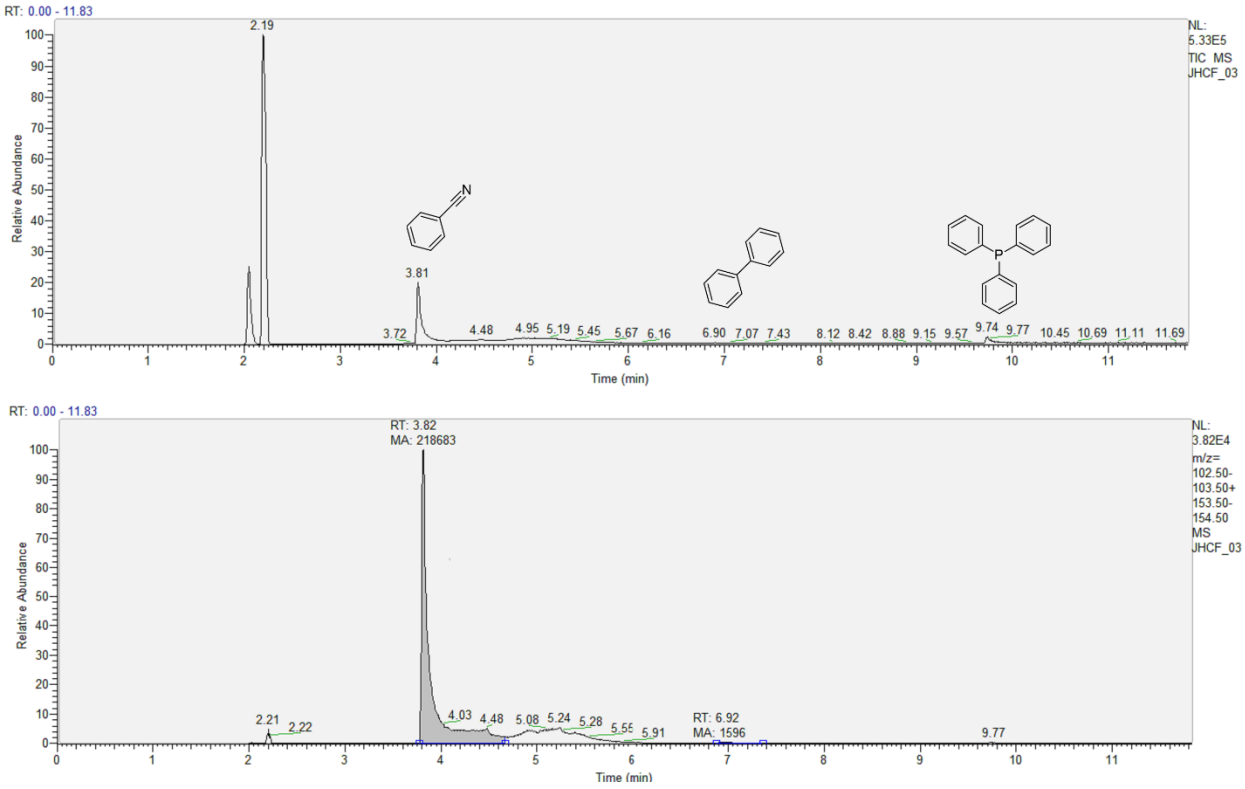
GC unfiltered and filtered chromatogram with area measurements from experiment #1



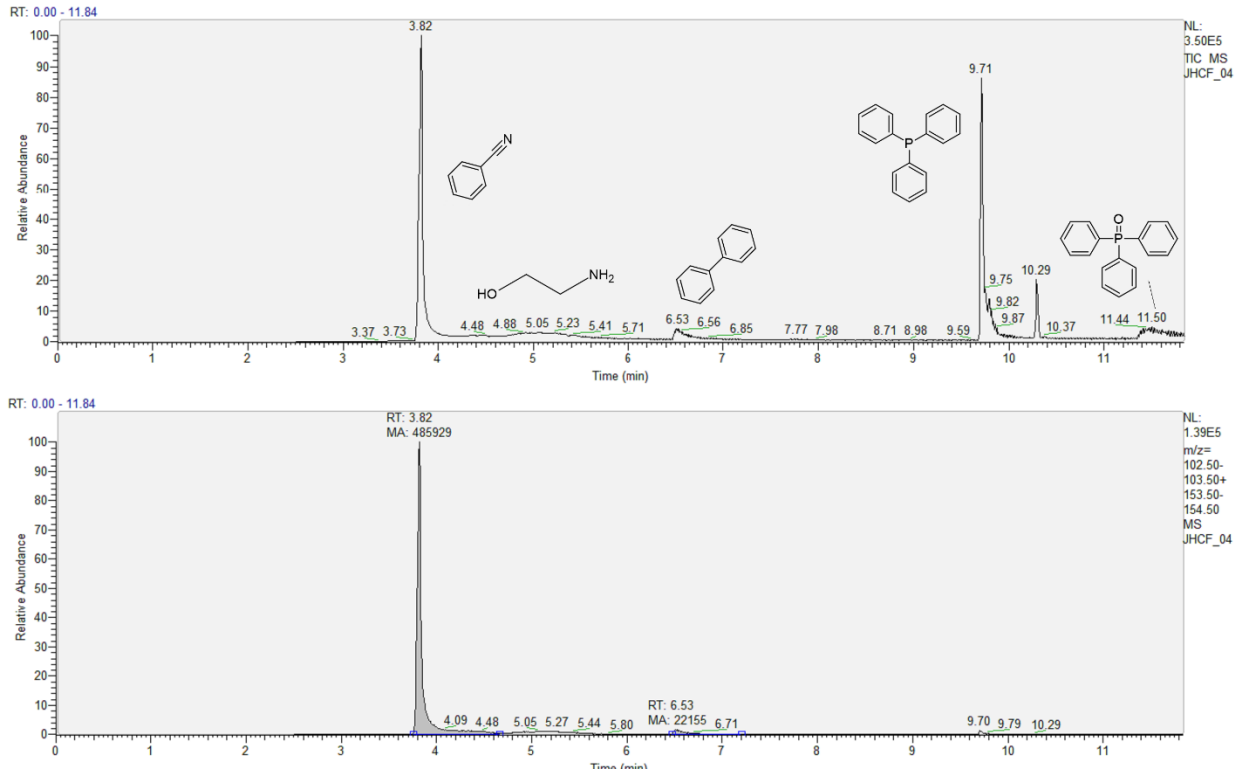
GC unfiltered and filtered chromatogram with area measurements from experiment #2



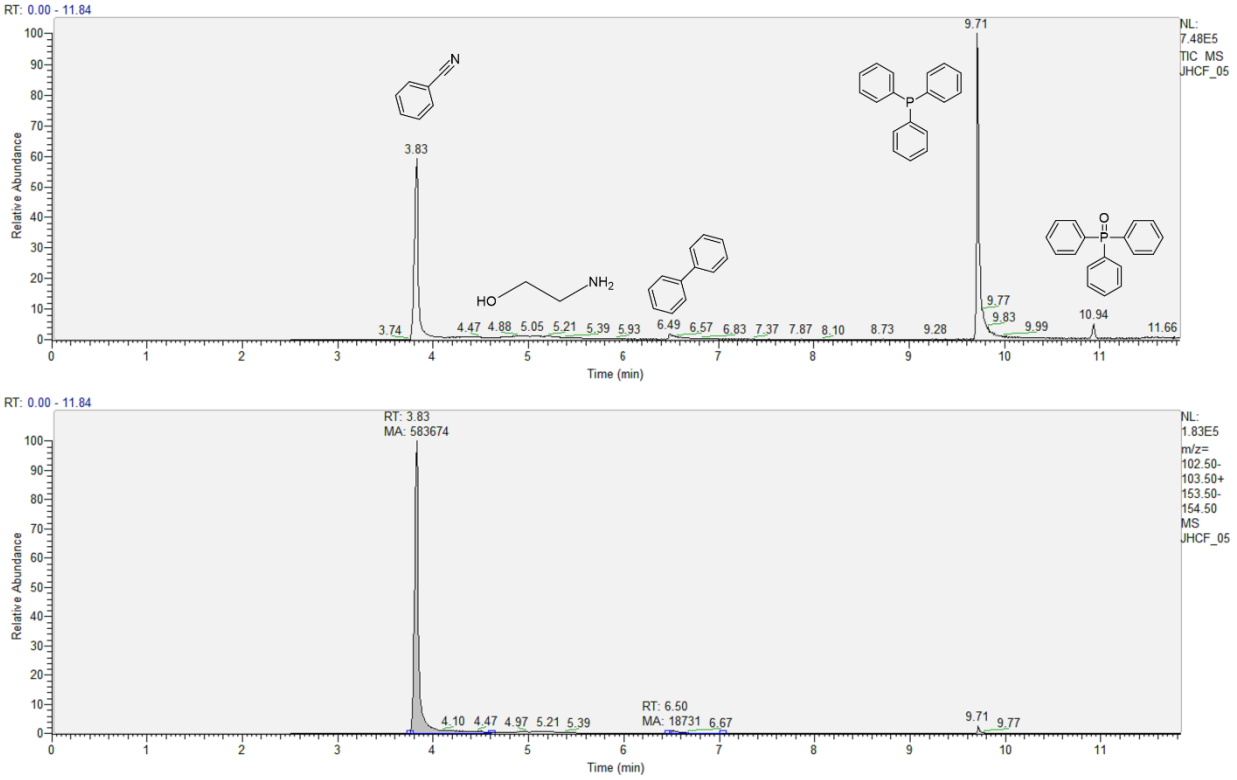
GC unfiltered and filtered chromatogram with area measurements from experiment #3



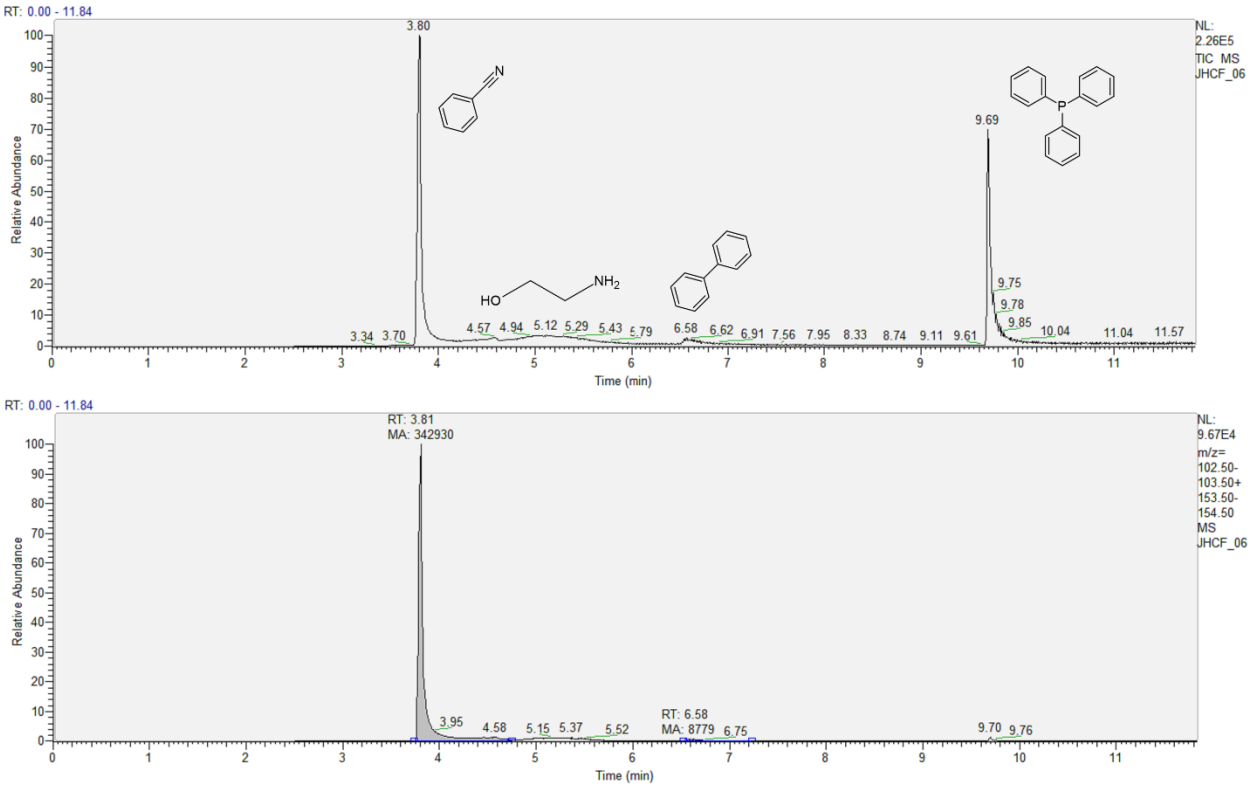
GC unfiltered and filtered chromatogram with area measurements from experiment #4



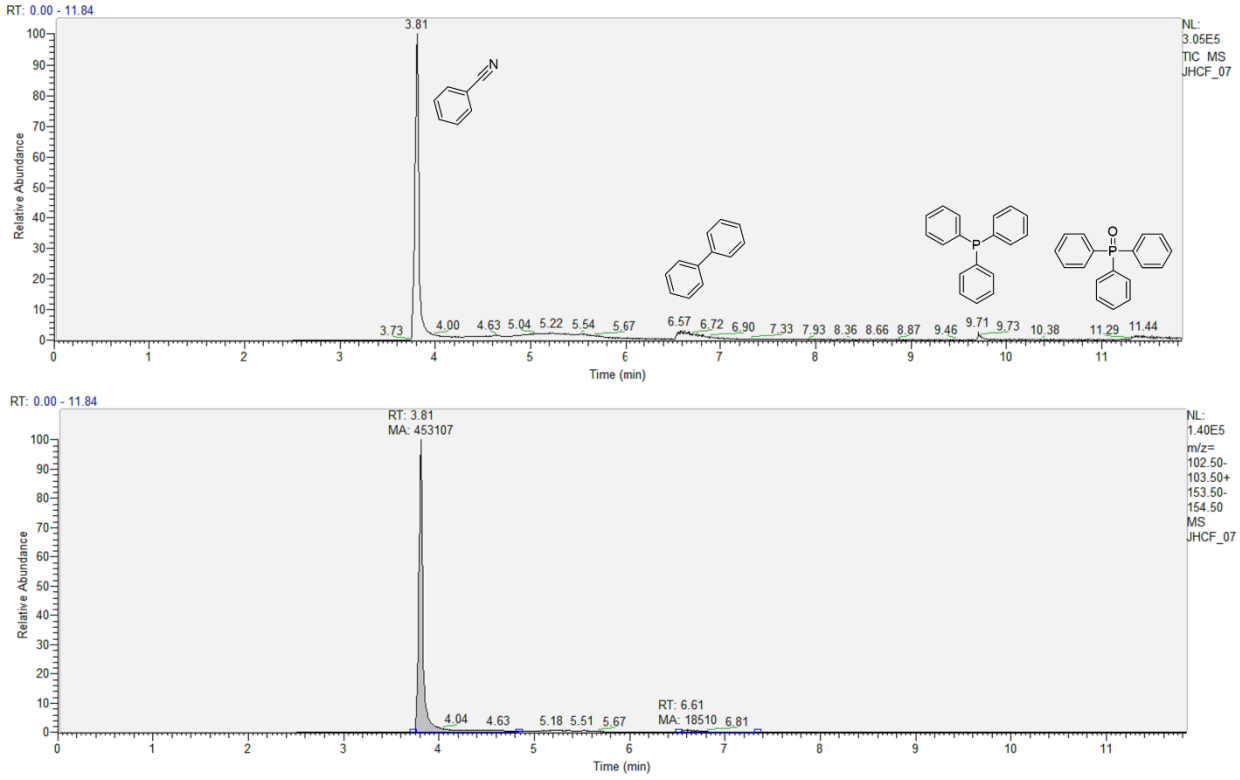
GC unfiltered and filtered chromatogram with area measurements from experiment #5



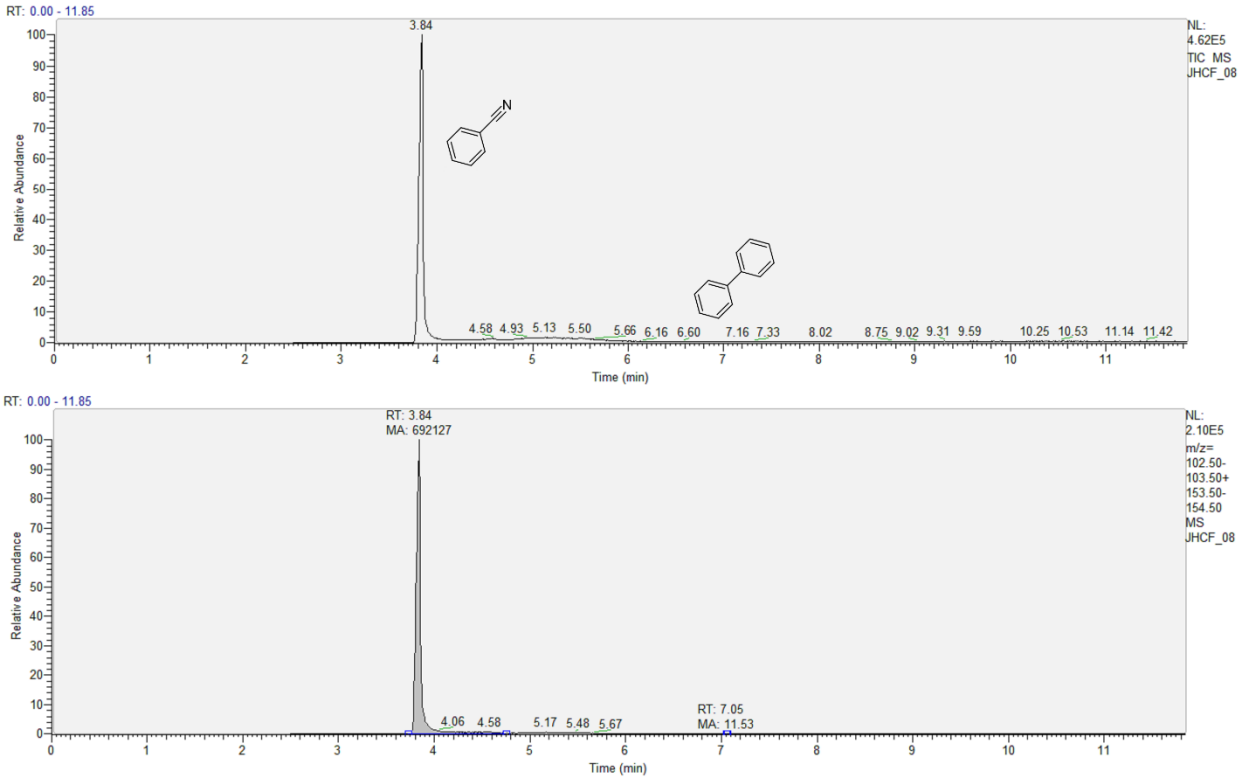
GC unfiltered and filtered chromatogram with area measurements from experiment #6



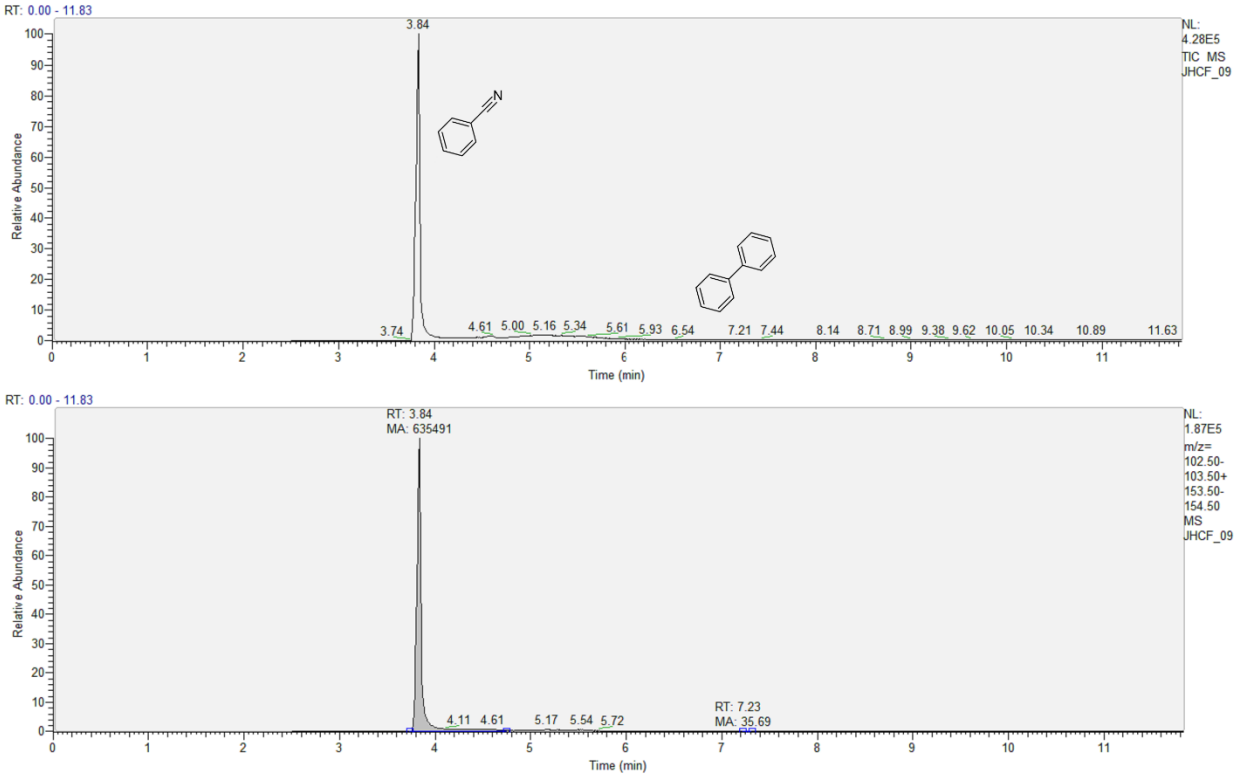
GC unfiltered and filtered chromatogram with area measurements from experiment #7



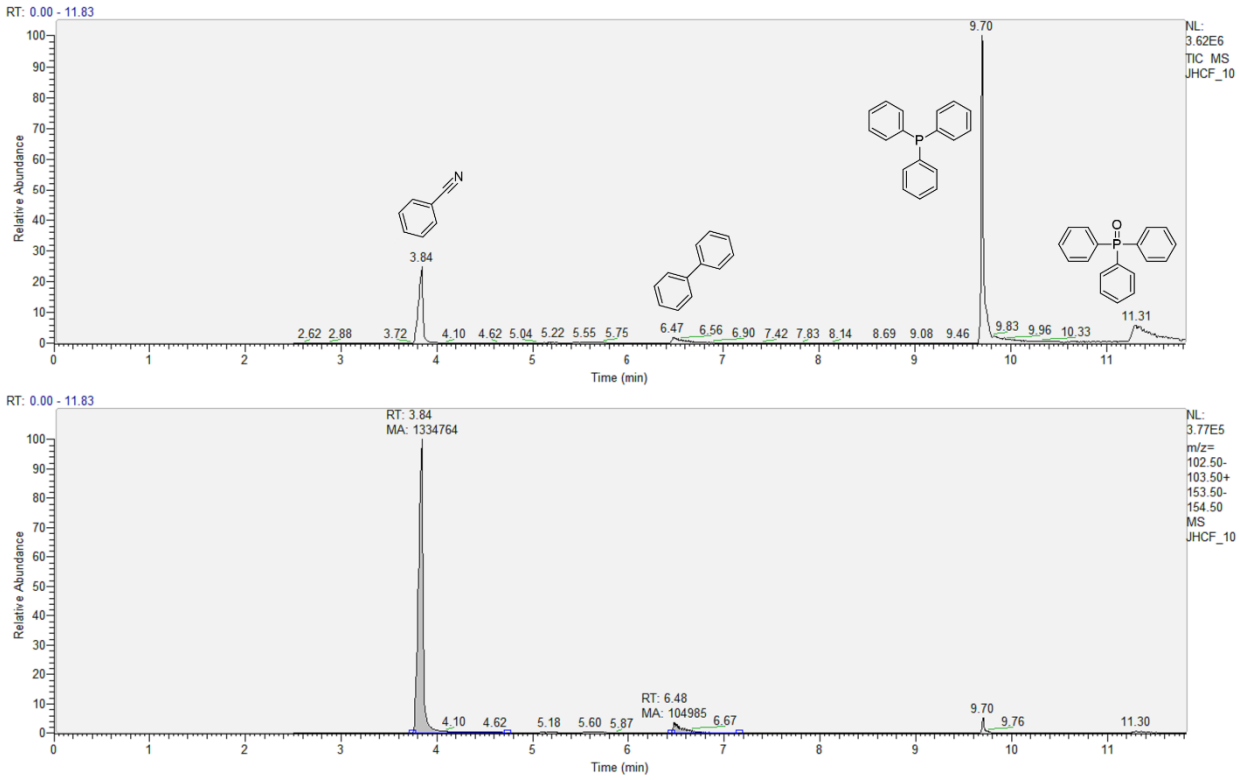
GC unfiltered and filtered chromatogram with area measurements from experiment #8



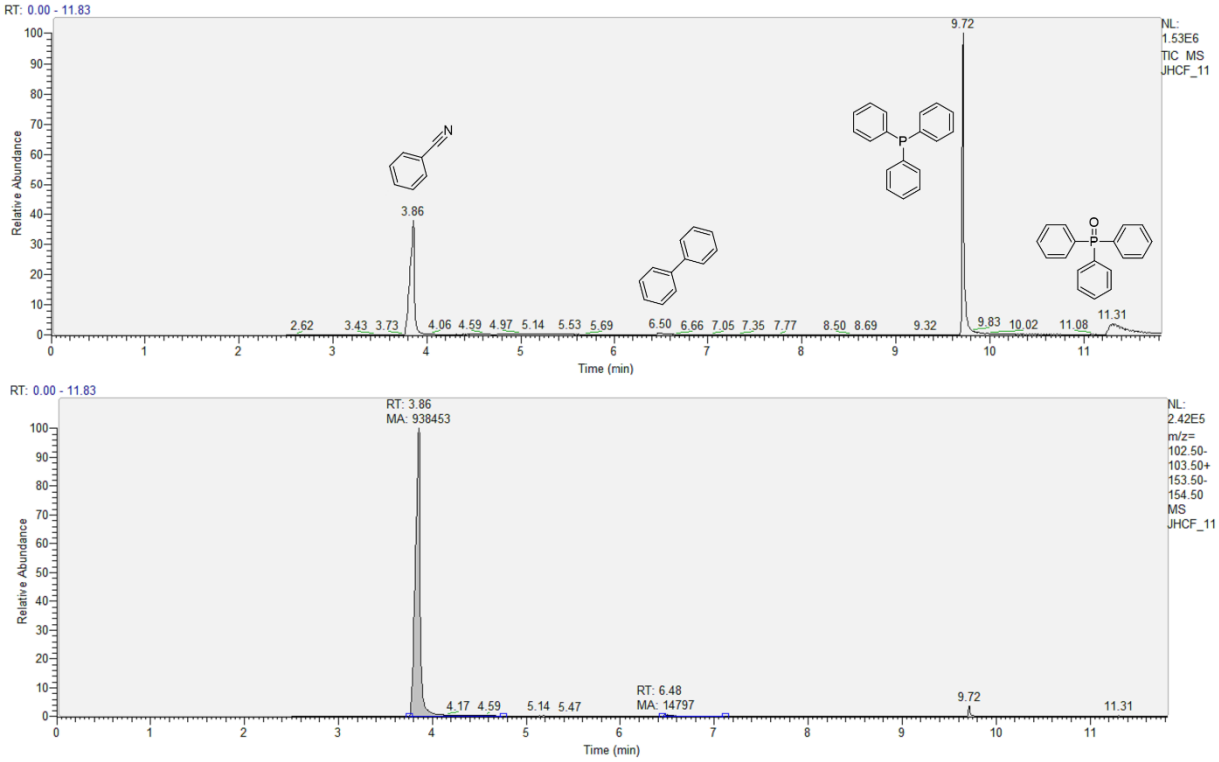
GC unfiltered and filtered chromatogram with area measurements from experiment #9



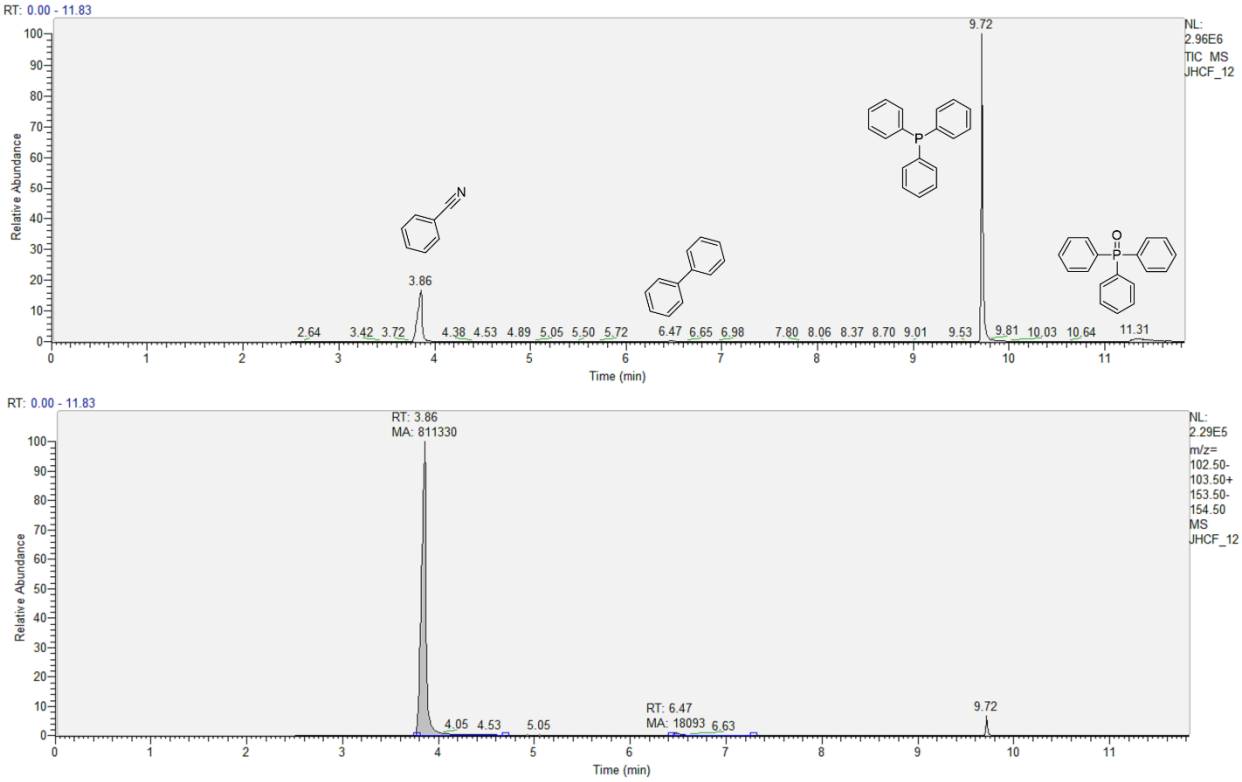
GC unfiltered and filtered chromatogram with area measurements from experiment #10



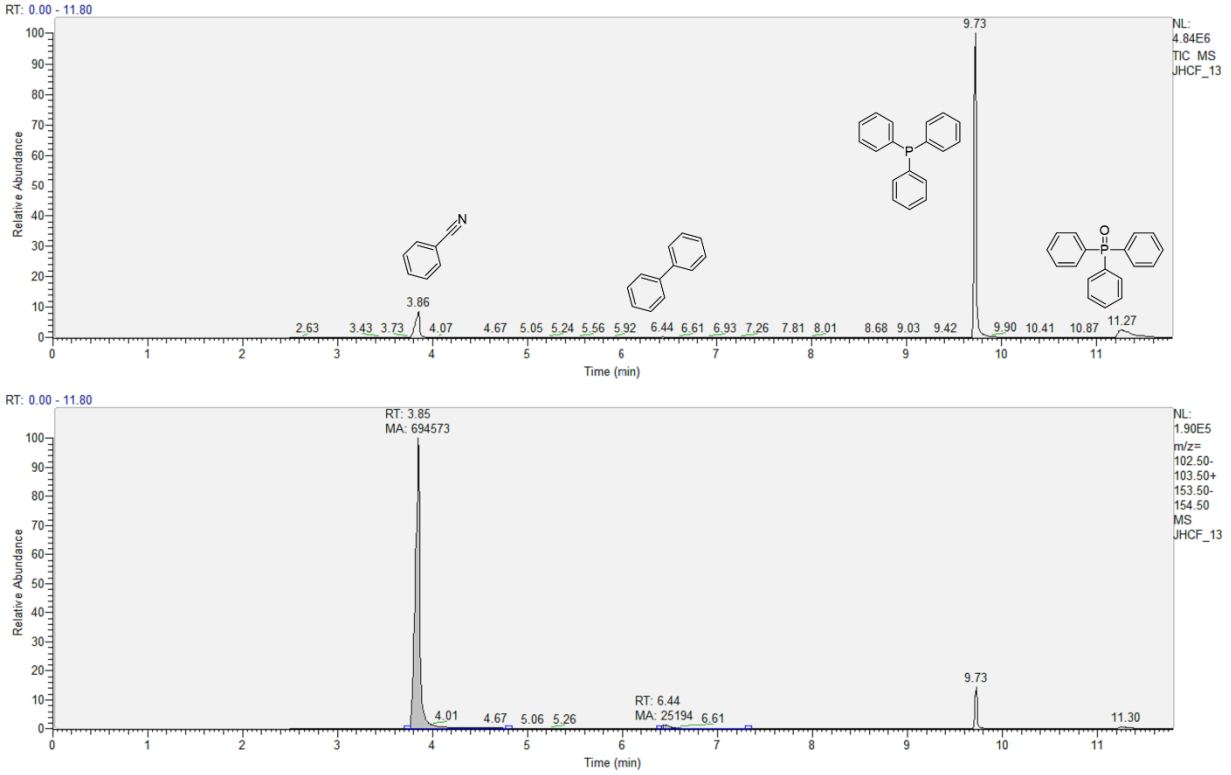
GC unfiltered and filtered chromatogram with area measurements from experiment #11



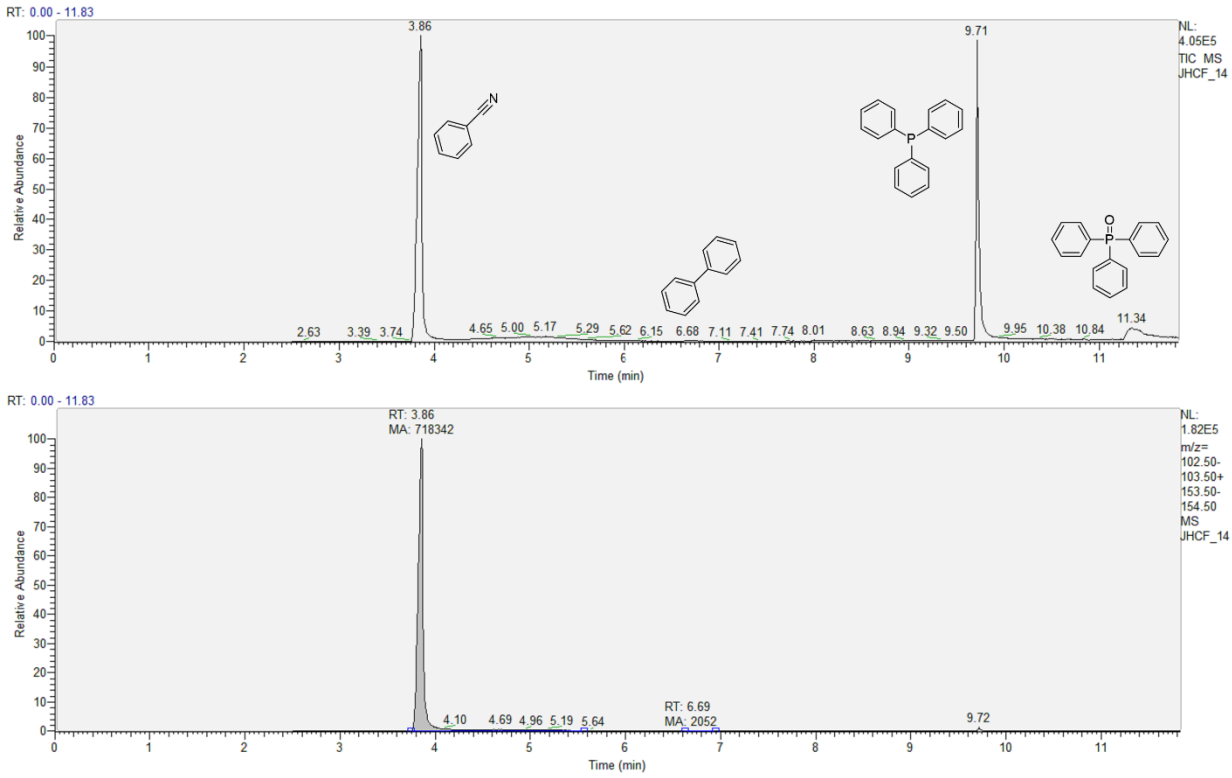
GC unfiltered and filtered chromatogram with area measurements from experiment #12



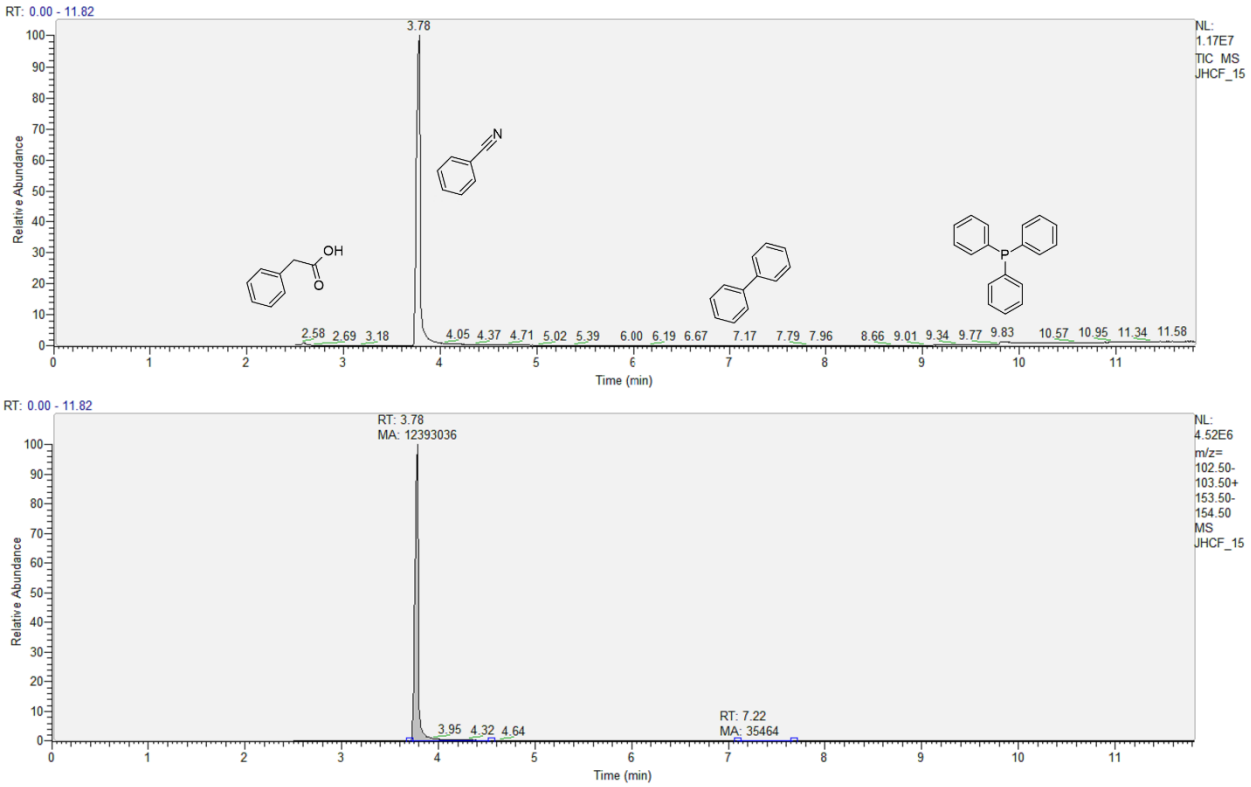
GC unfiltered and filtered chromatogram with area measurements from experiment #13



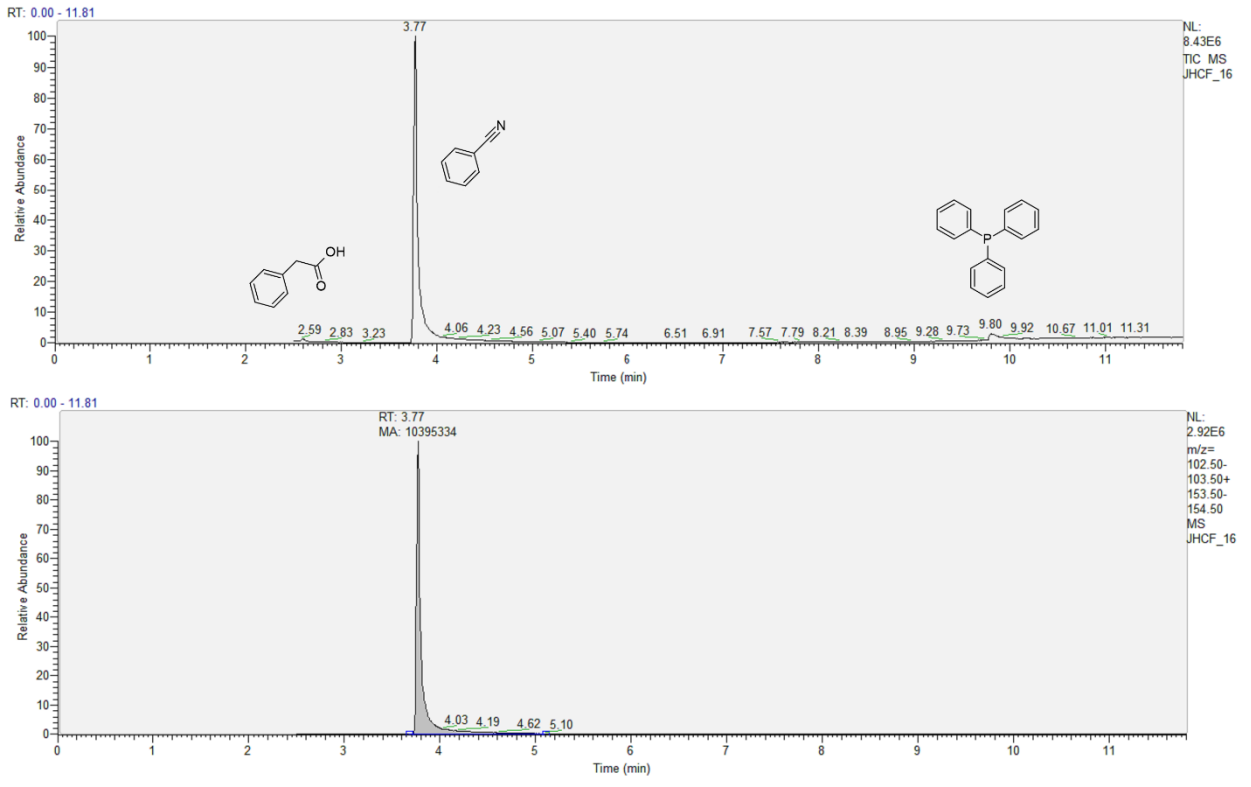
GC unfiltered and filtered chromatogram with area measurements from experiment #14



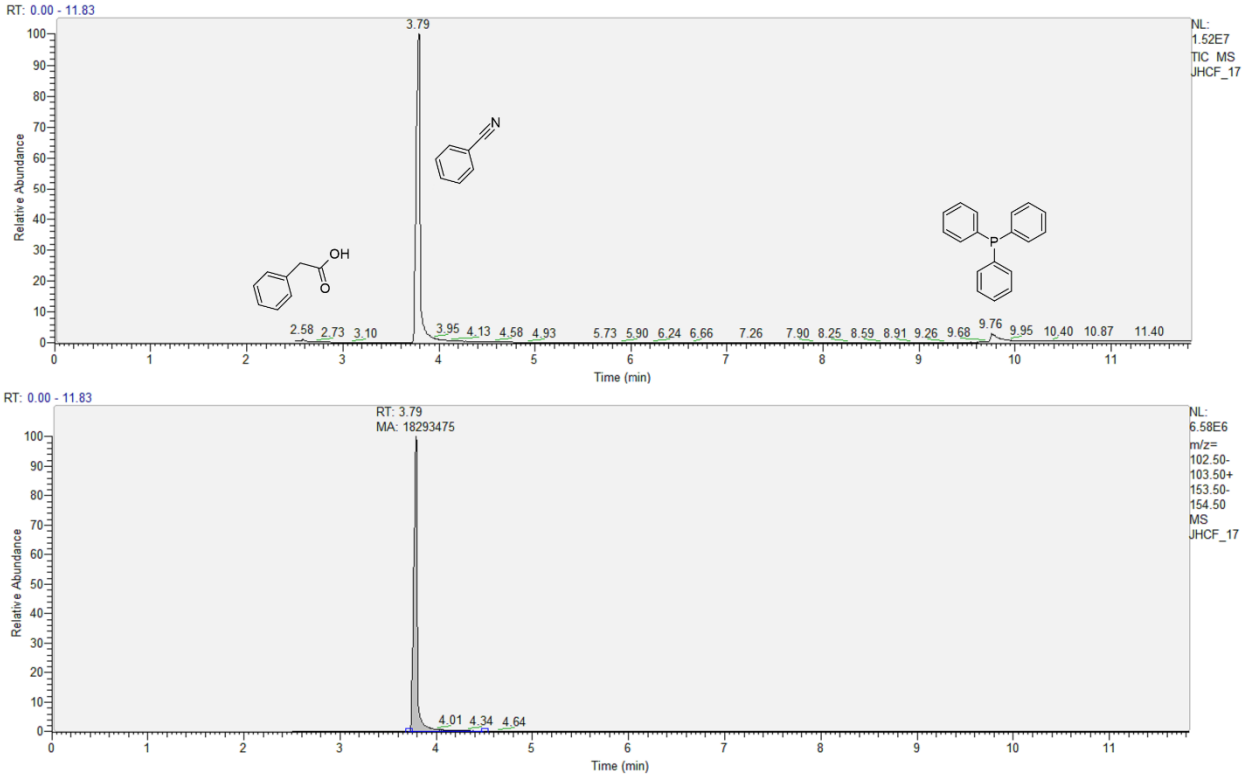
GC unfiltered and filtered chromatogram with area measurements from experiment #15



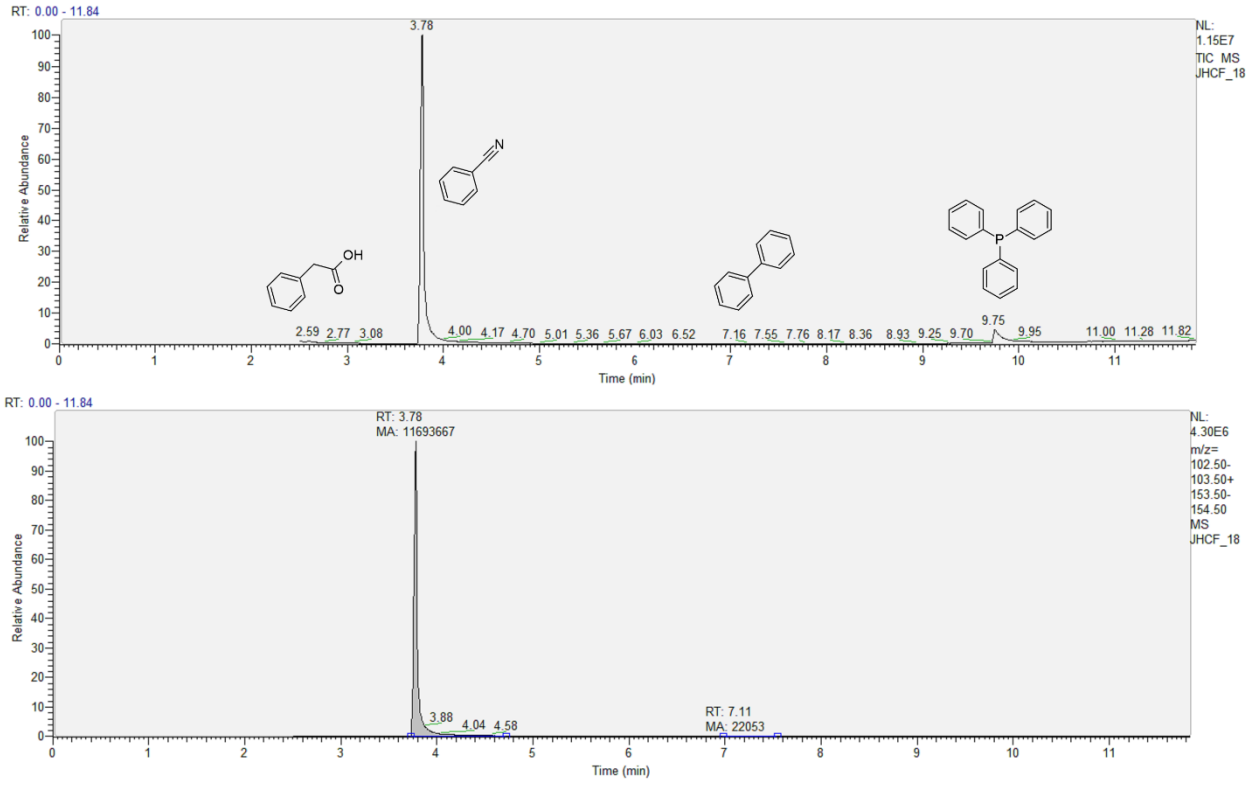
GC unfiltered and filtered chromatogram with area measurements from experiment #16



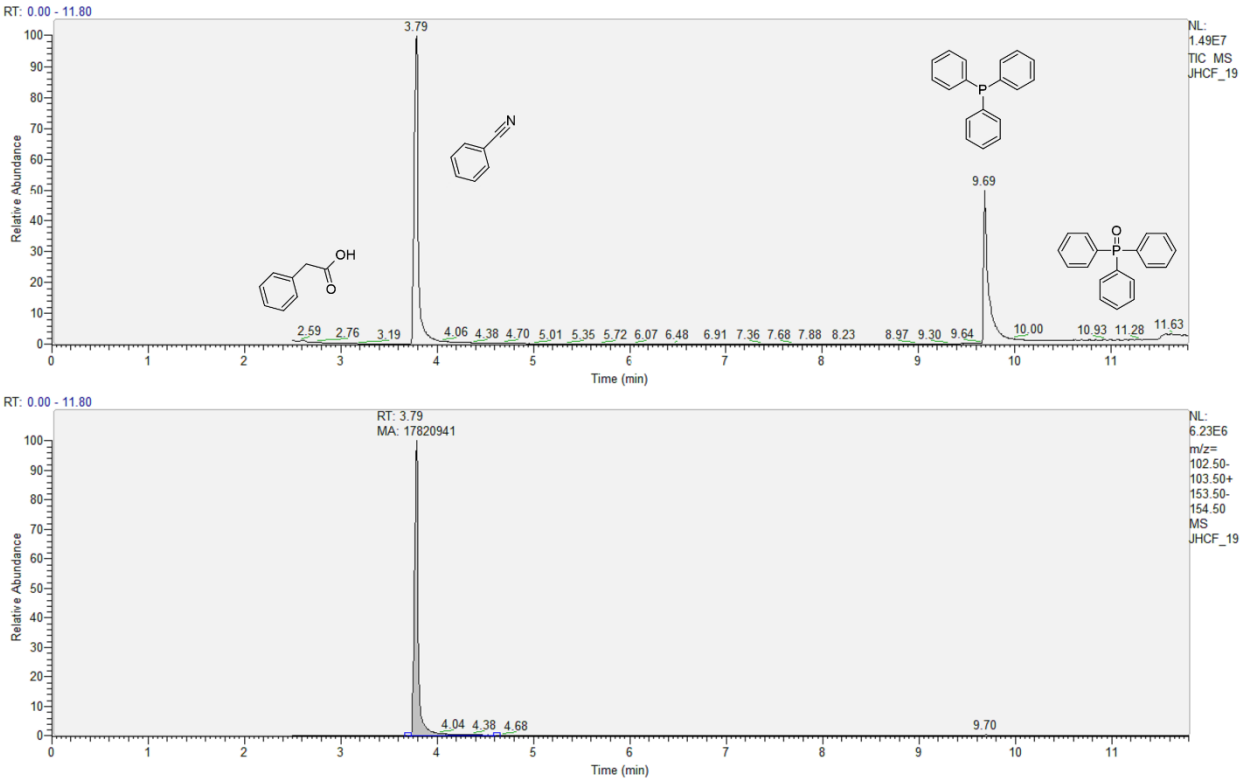
GC unfiltered and filtered chromatogram with area measurements from experiment #17



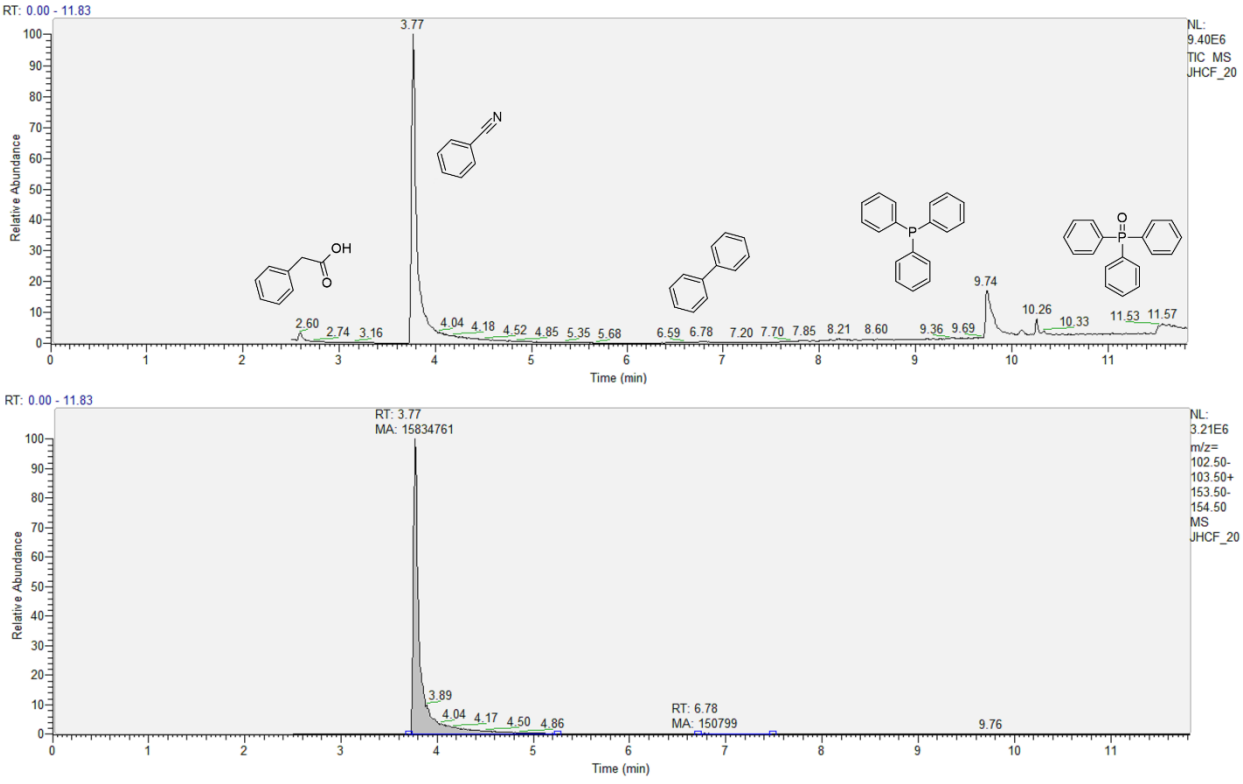
GC unfiltered and filtered chromatogram with area measurements from experiment #18



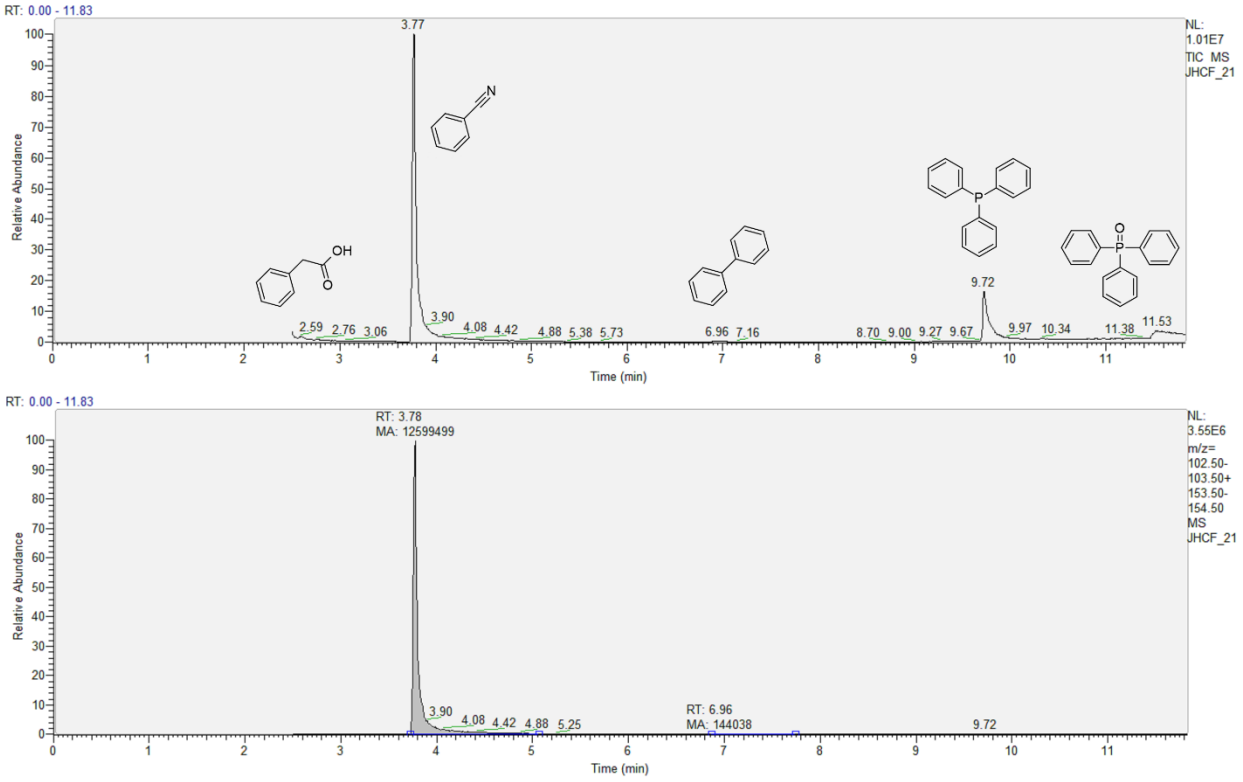
GC unfiltered and filtered chromatogram with area measurements from experiment #19



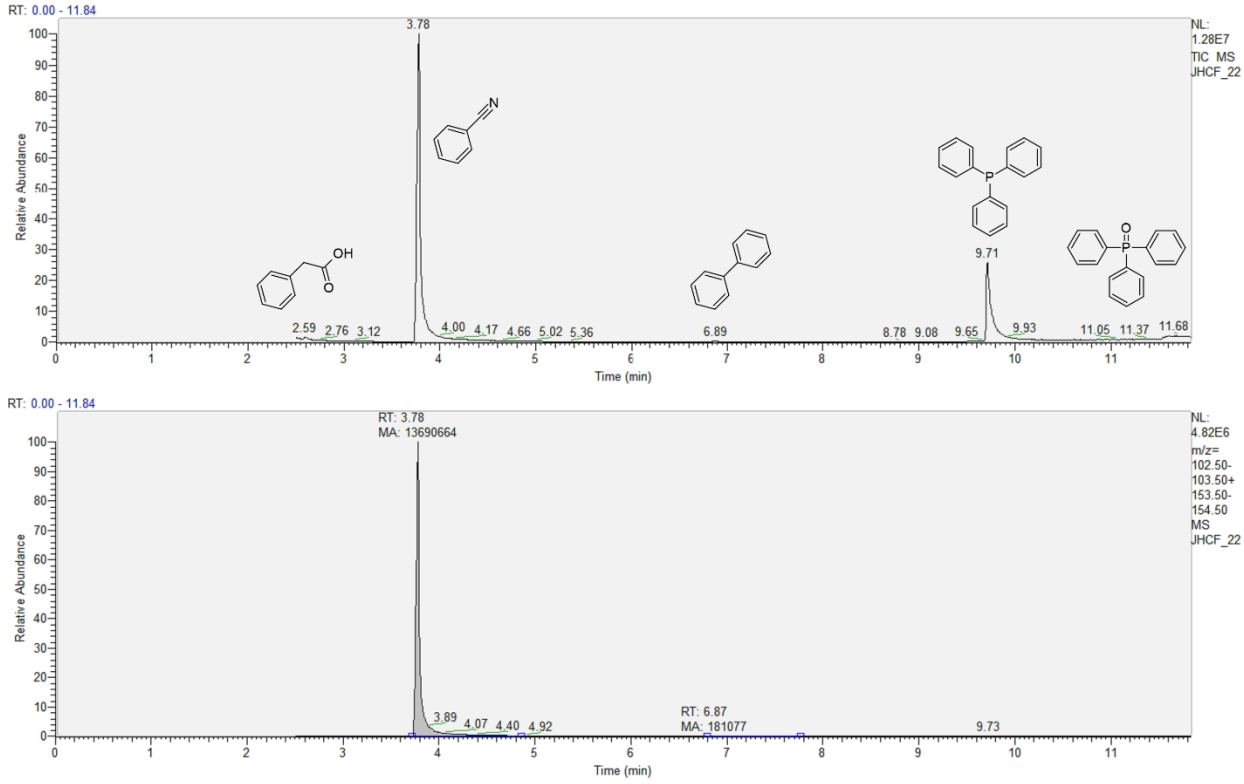
GC unfiltered and filtered chromatogram with area measurements from experiment #20



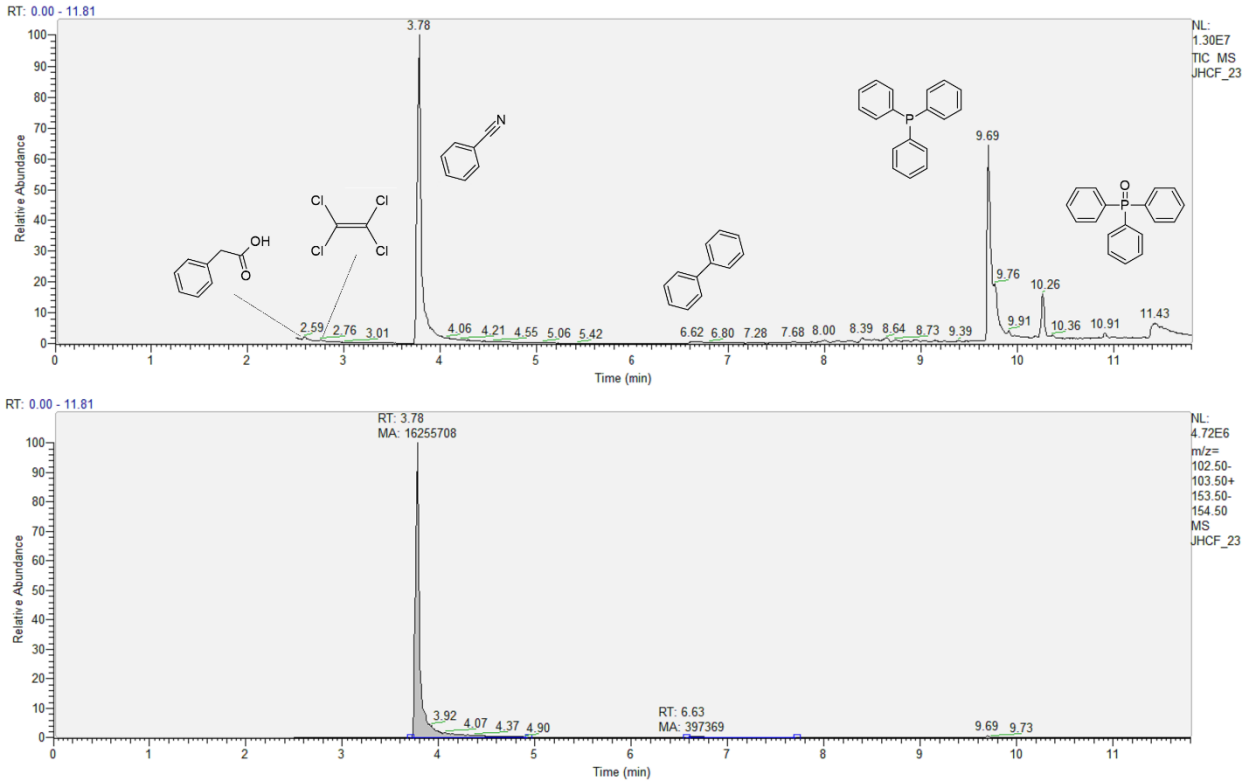
GC unfiltered and filtered chromatogram with area measurements from experiment #21



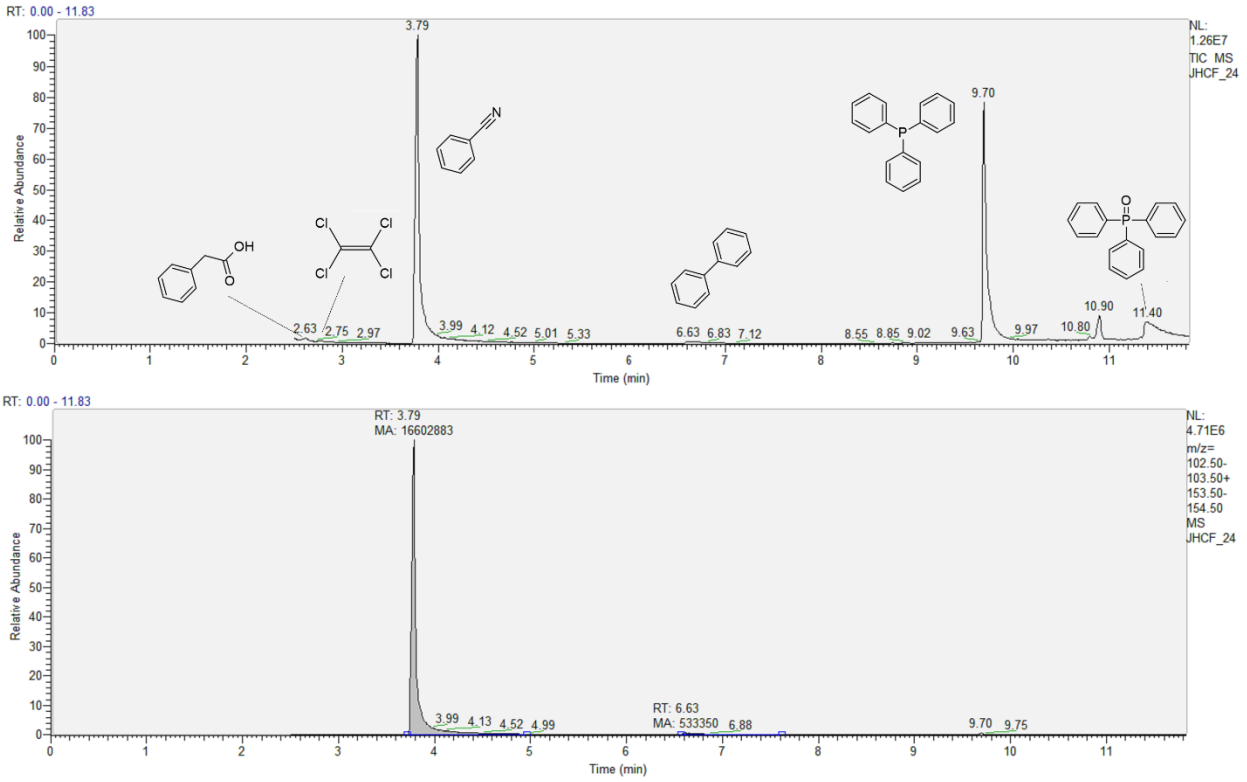
GC unfiltered and filtered chromatogram with area measurements from experiment #22



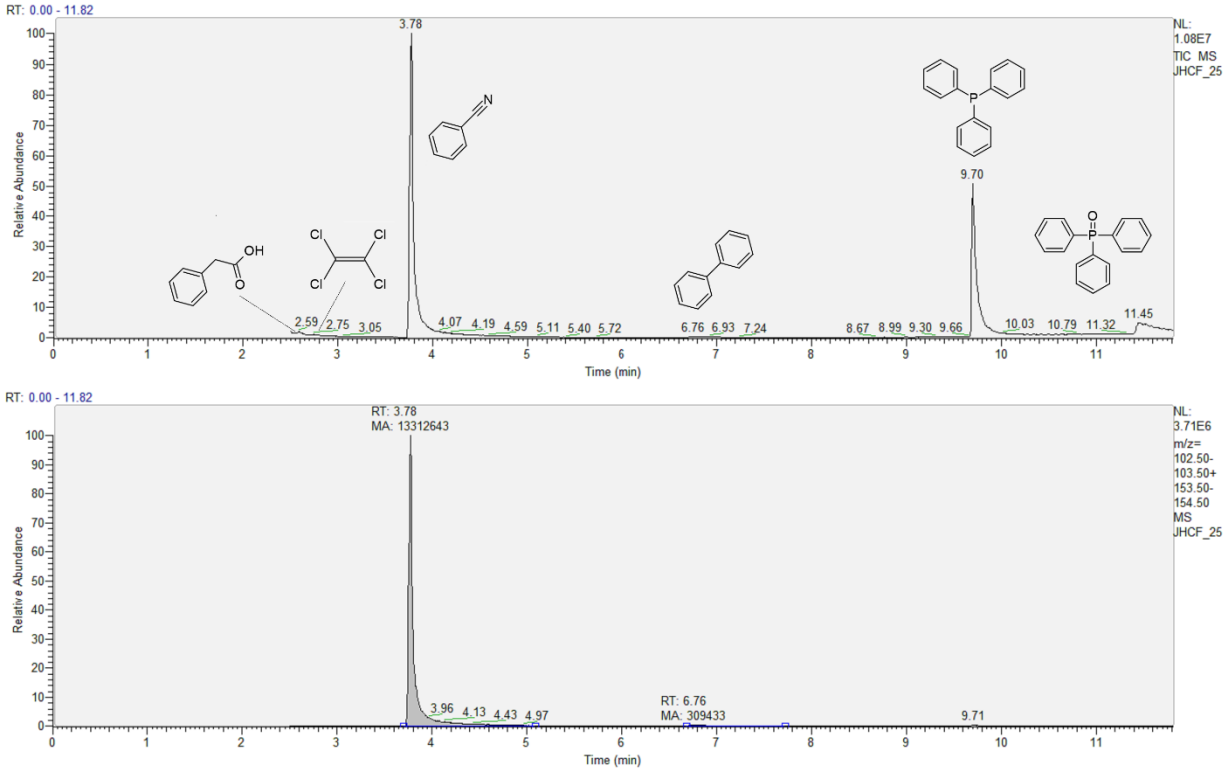
GC unfiltered and filtered chromatogram with area measurements from experiment #23



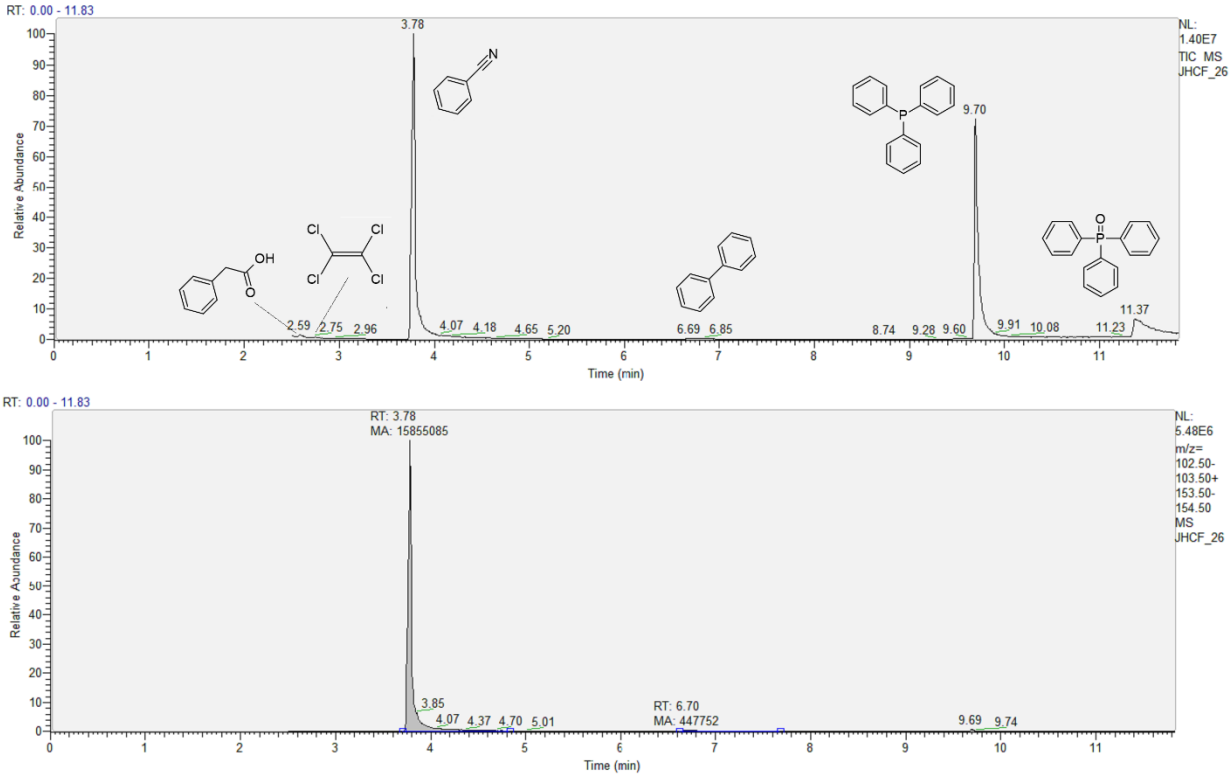
GC unfiltered and filtered chromatogram with area measurements from experiment #24



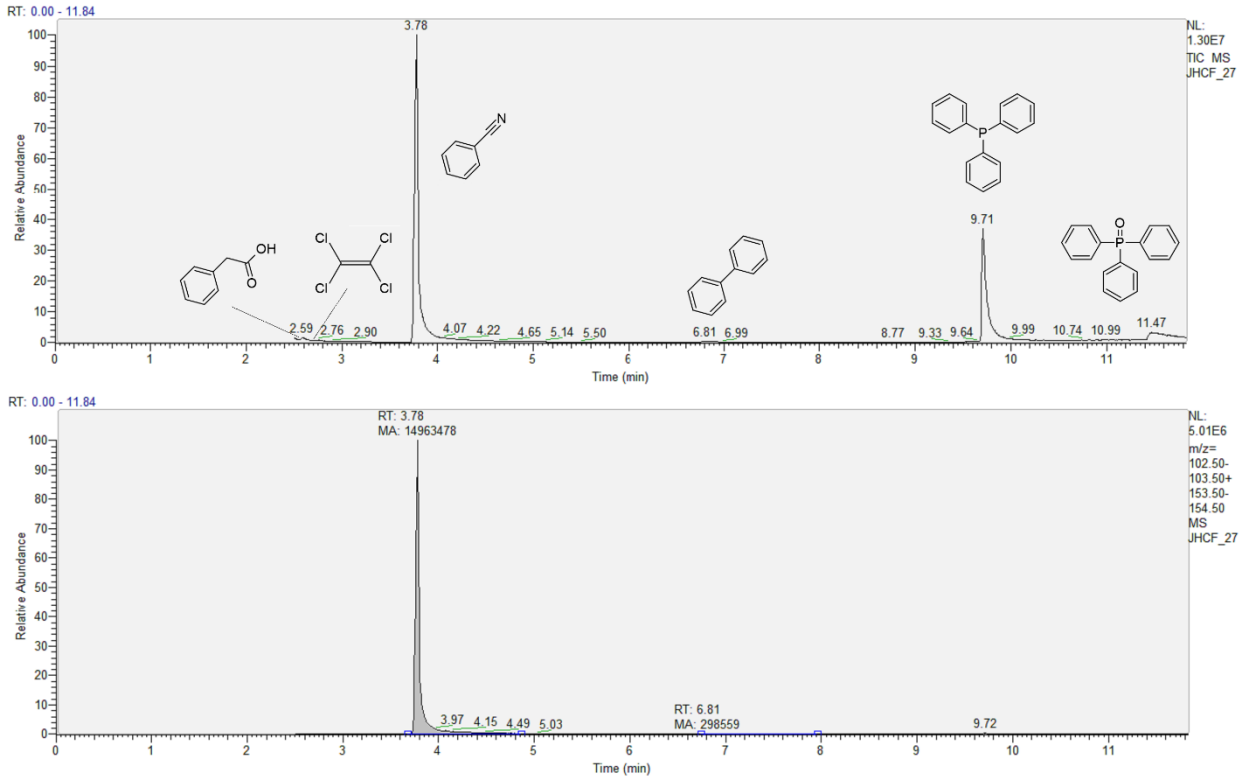
GC unfiltered and filtered chromatogram with area measurements from experiment #25



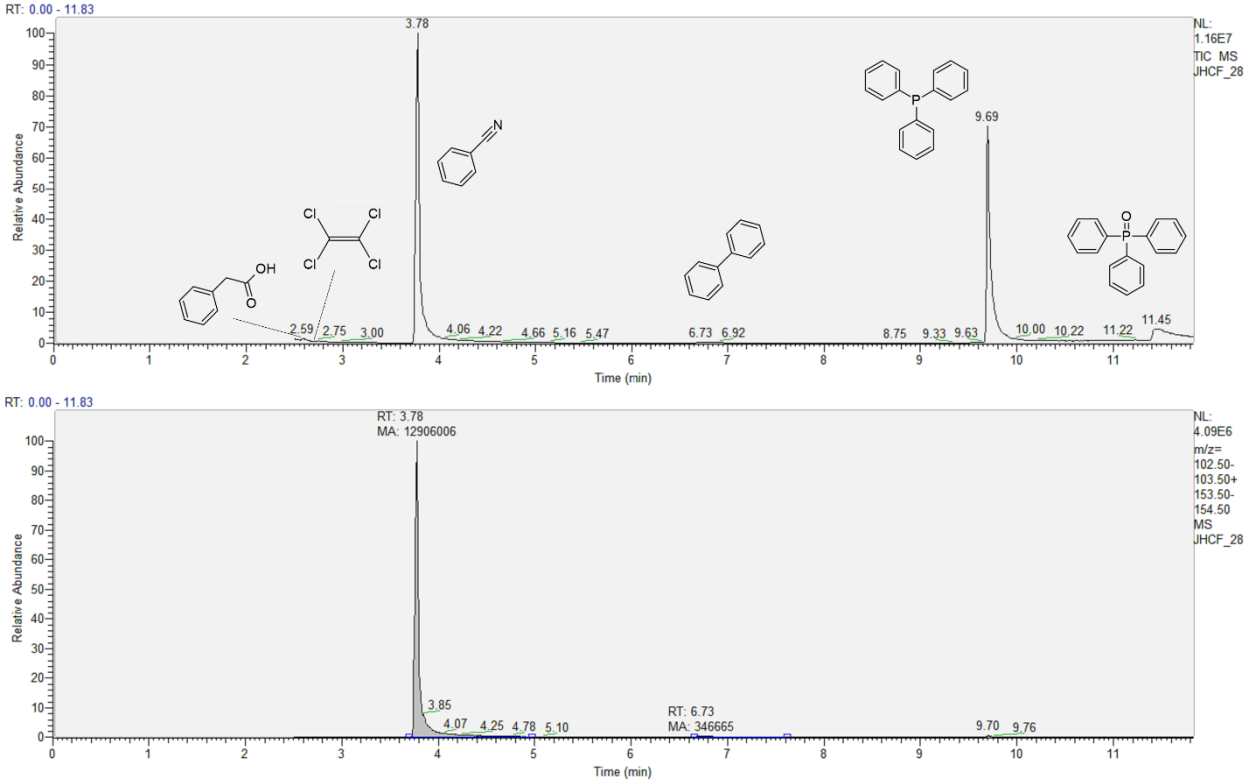
GC unfiltered and filtered chromatogram with area measurements from experiment #26



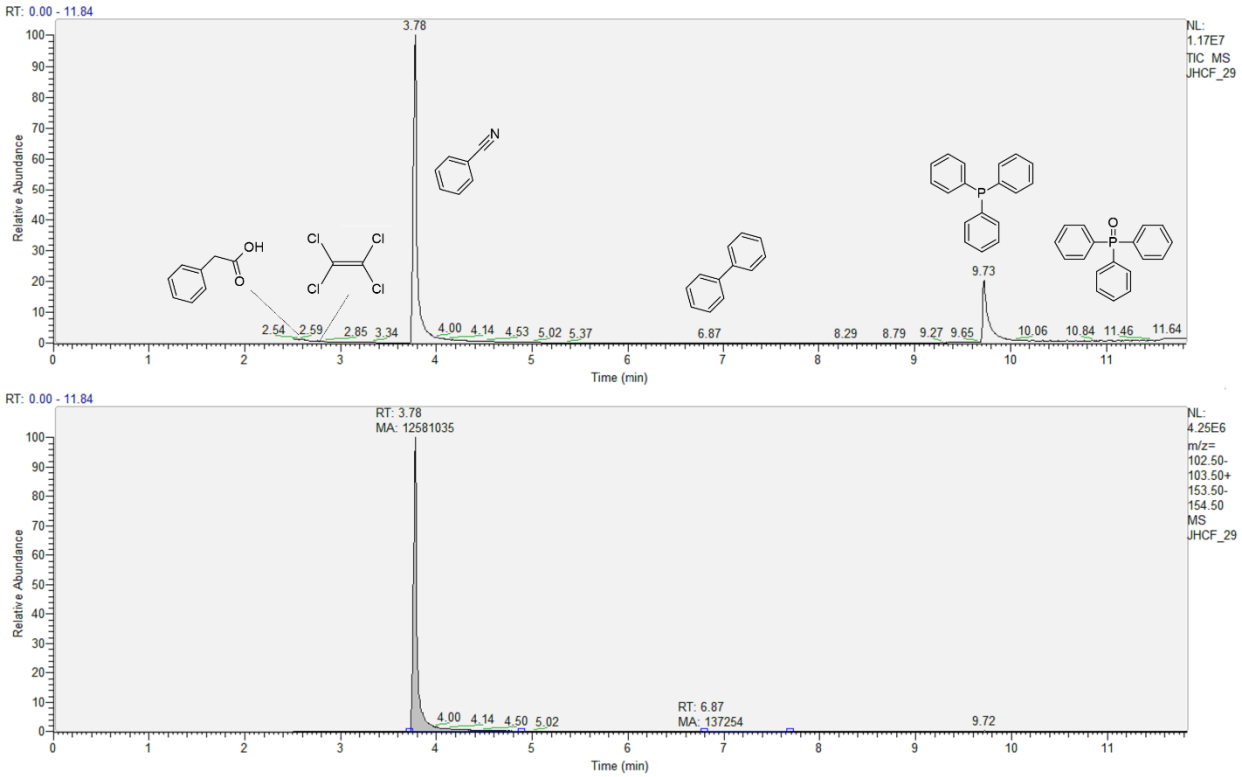
GC unfiltered and filtered chromatogram with area measurements from experiment #27



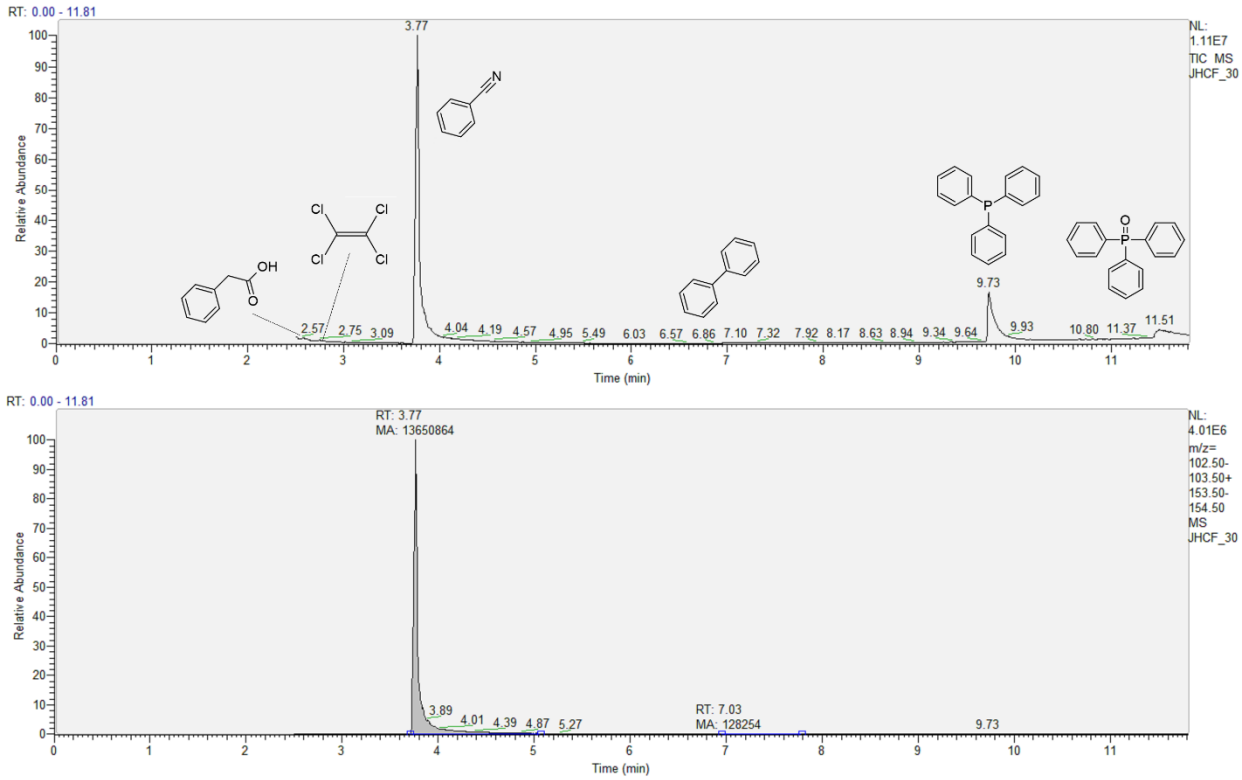
GC unfiltered and filtered chromatogram with area measurements from experiment #28



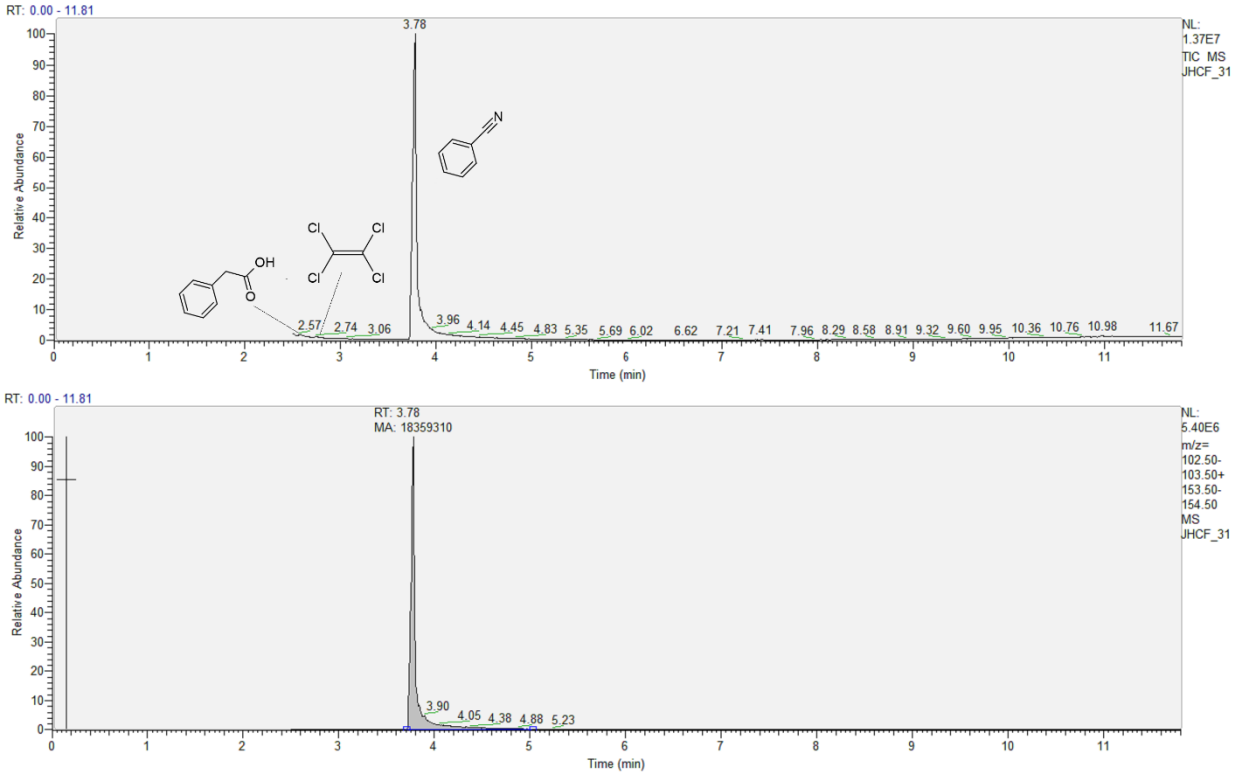
GC unfiltered and filtered chromatogram with area measurements from experiment #29



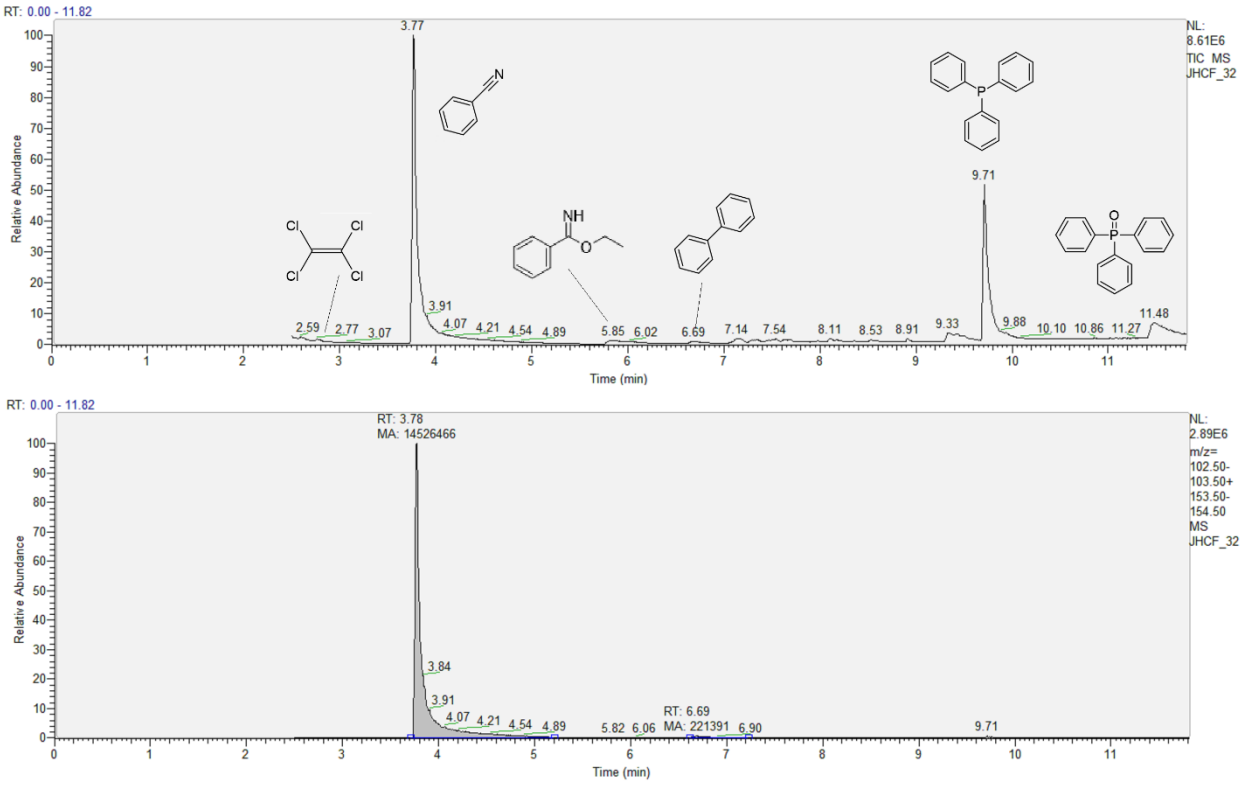
GC unfiltered and filtered chromatogram with area measurements from experiment #30



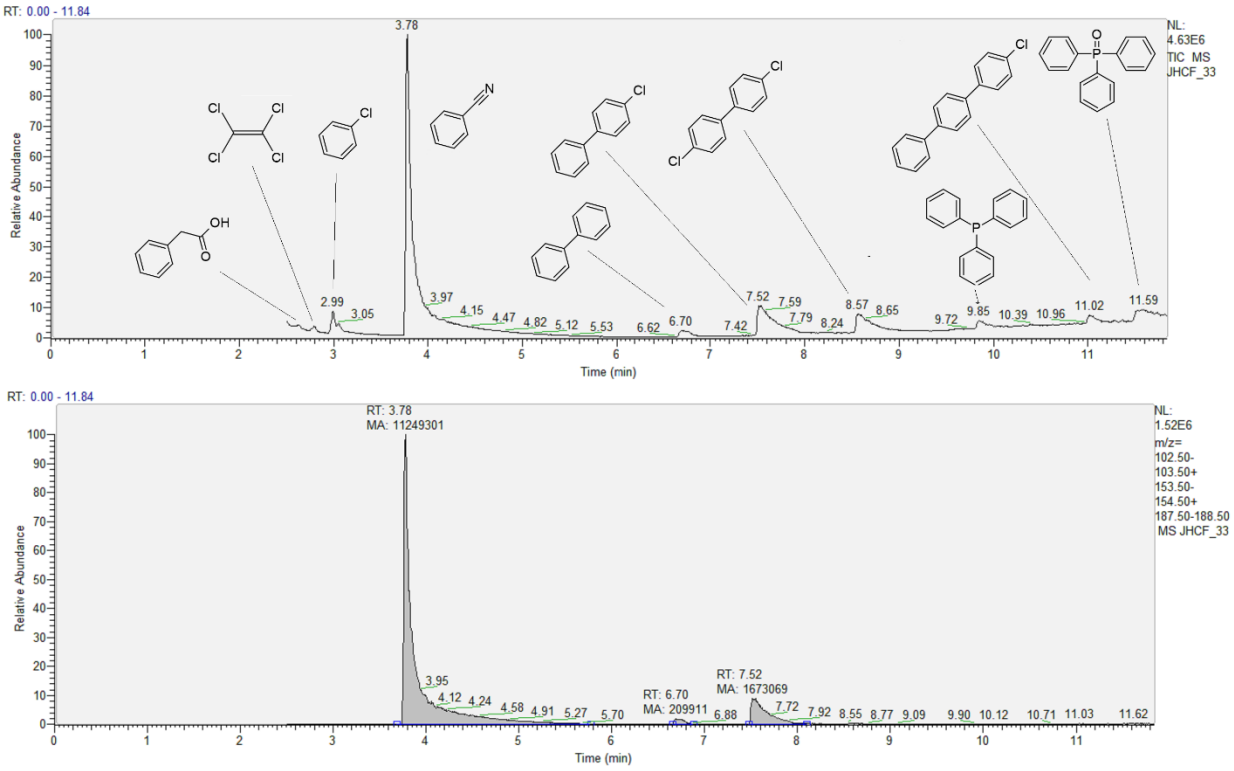
GC unfiltered and filtered chromatogram with area measurements from experiment #31



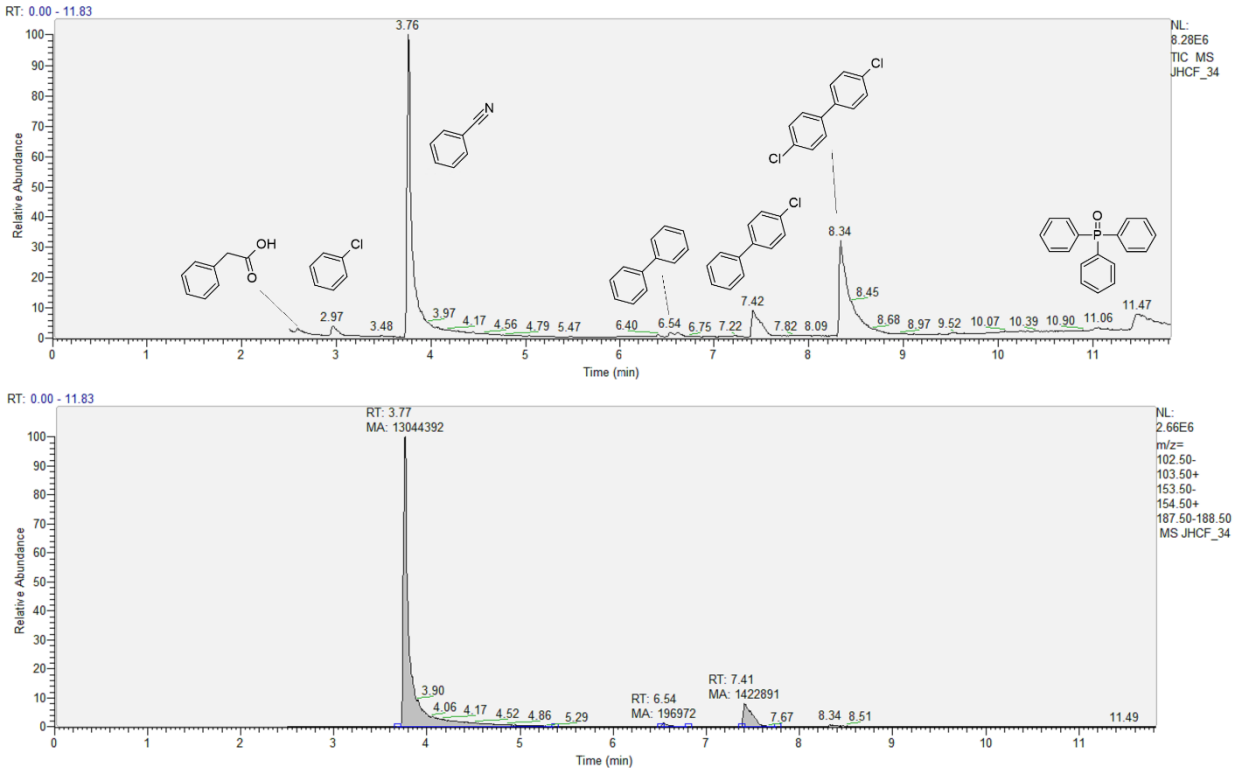
GC unfiltered and filtered chromatogram with area measurements from experiment #32



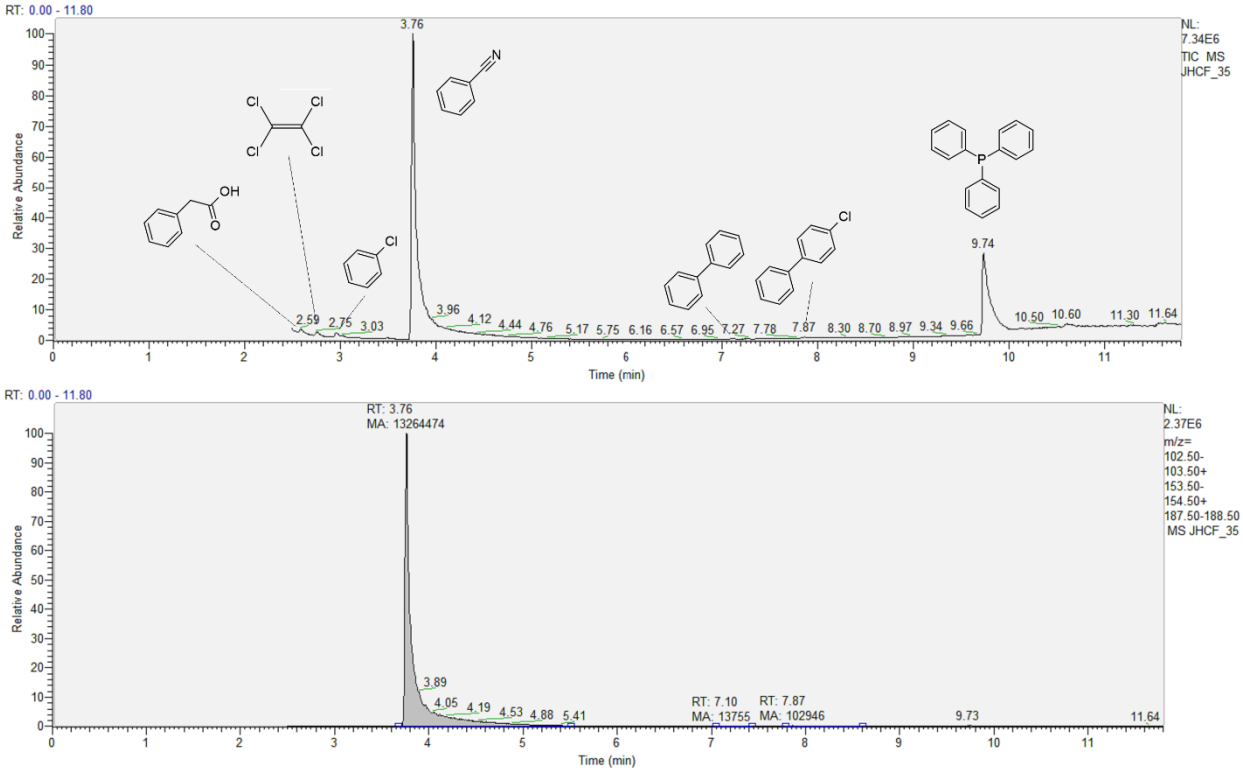
GC unfiltered and filtered chromatogram with area measurements from experiment #33



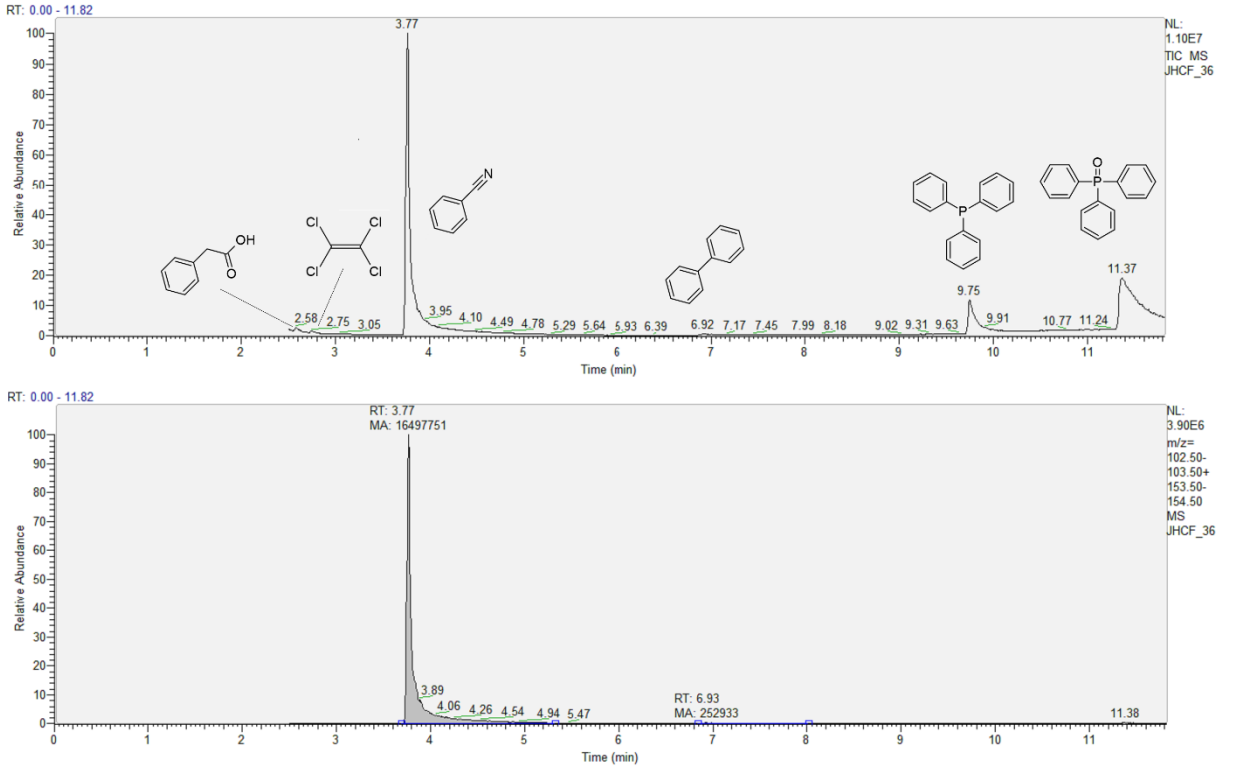
GC unfiltered and filtered chromatogram with area measurements from experiment #34



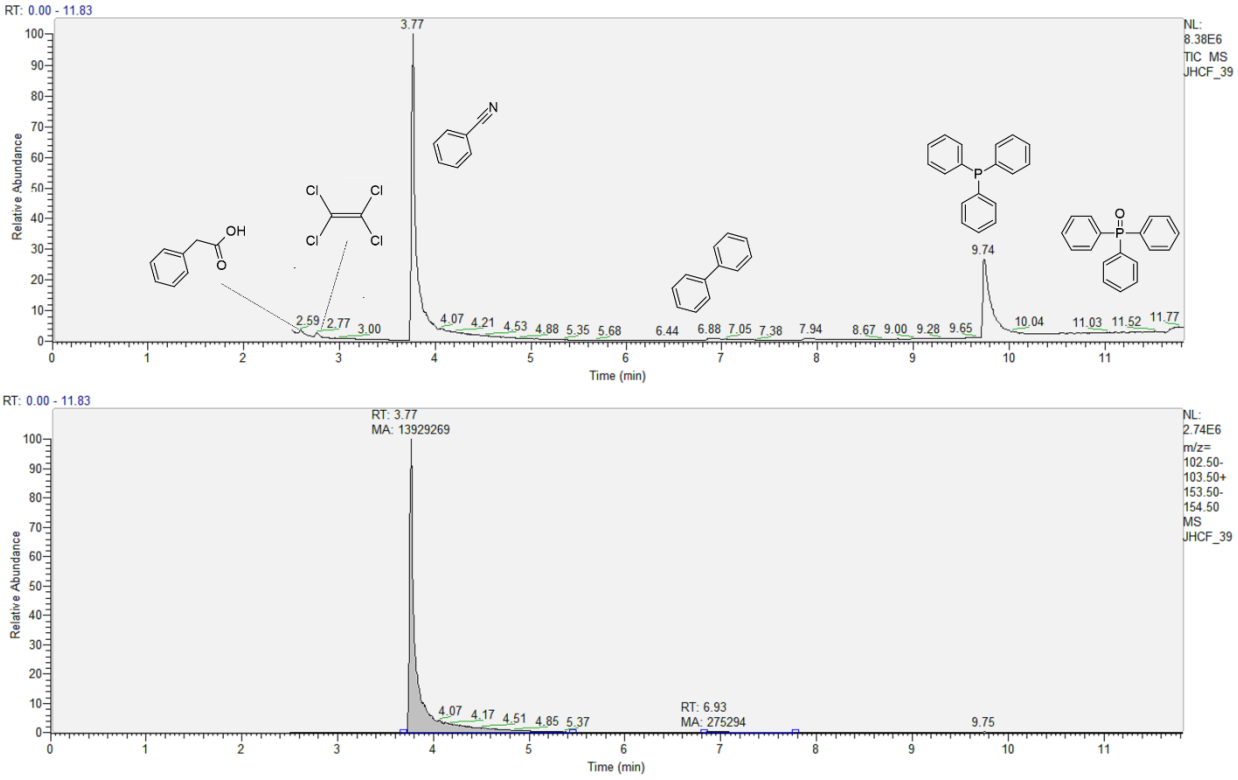
GC unfiltered and filtered chromatogram with area measurements from experiment #35



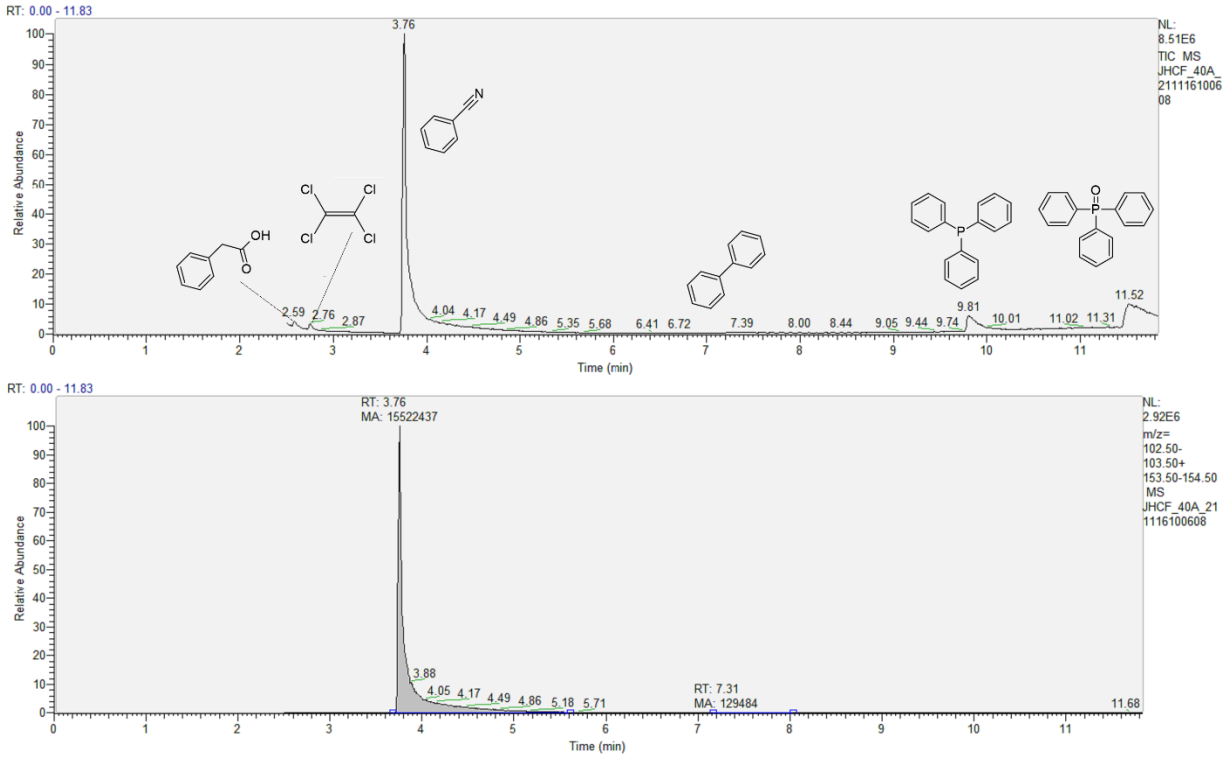
GC unfiltered and filtered chromatogram with area measurements from experiment #36



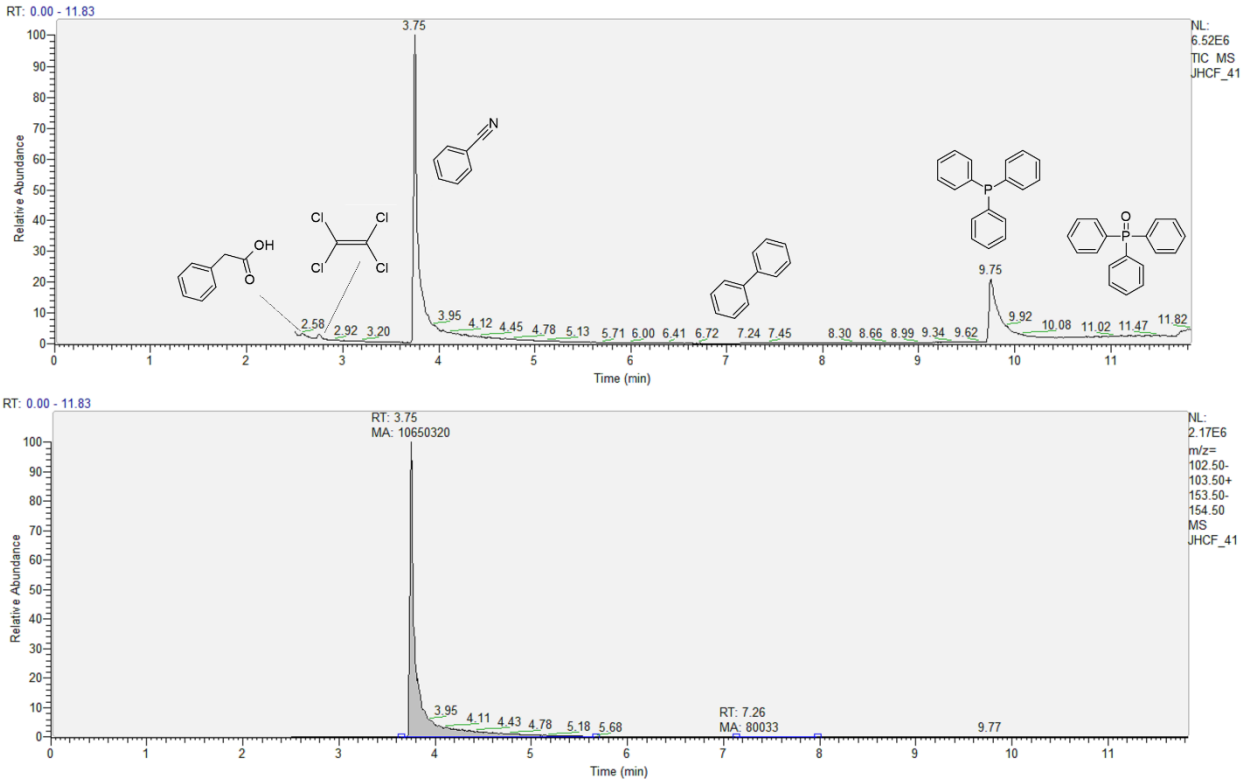
GC unfiltered and filtered chromatogram with area measurements from experiment #39



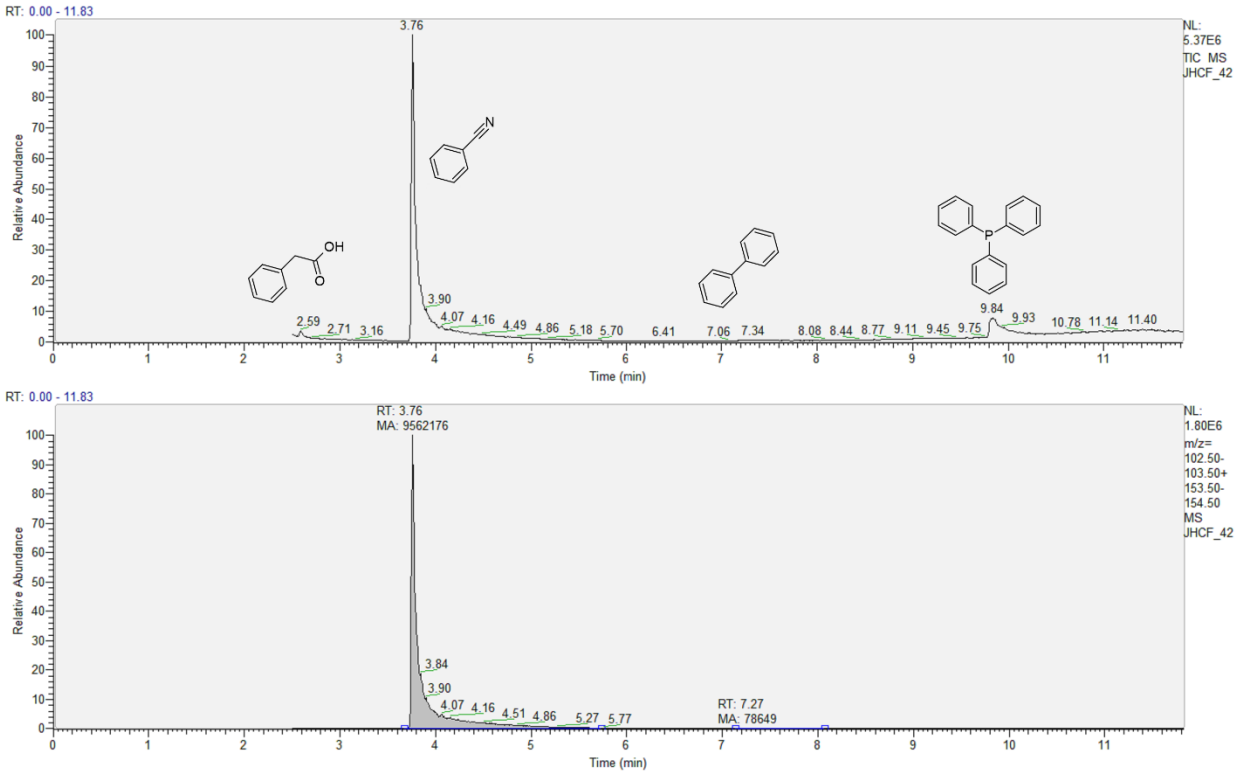
GC unfiltered and filtered chromatogram with area measurements from experiment #40



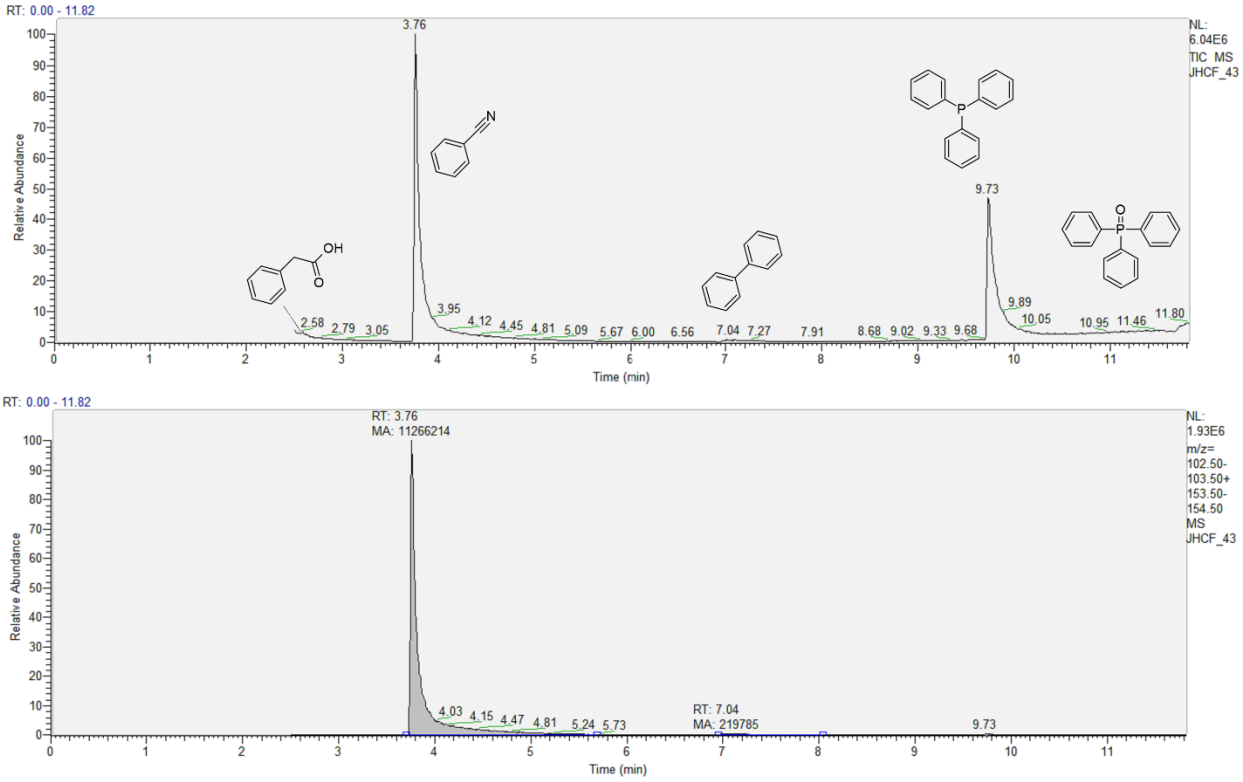
GC unfiltered and filtered chromatogram with area measurements from experiment #41



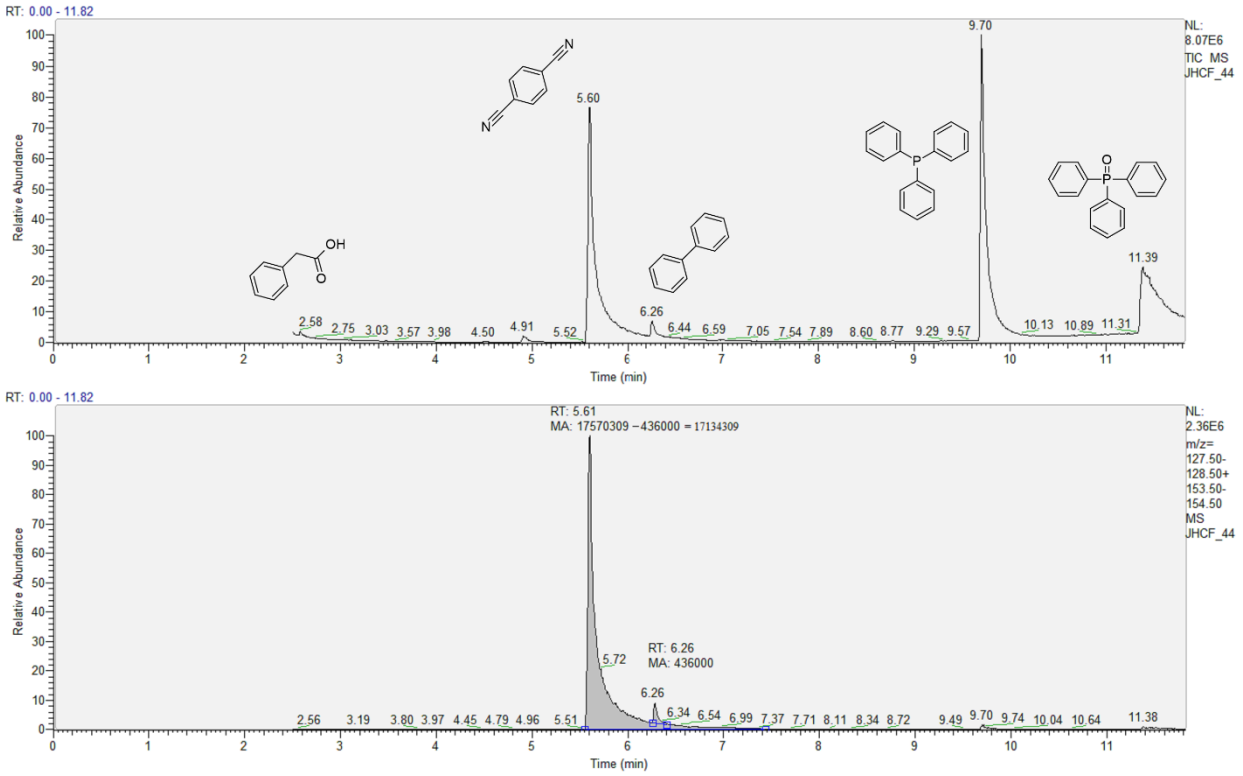
GC unfiltered and filtered chromatogram with area measurements from experiment #42



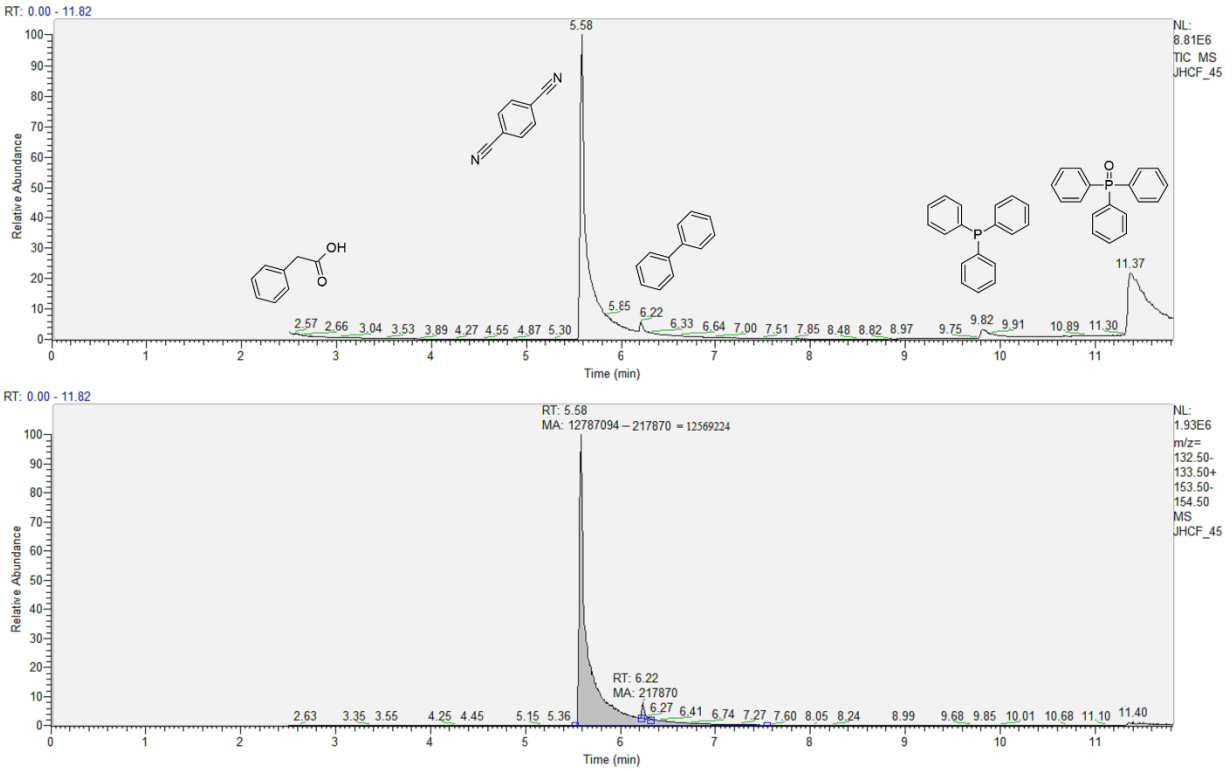
GC unfiltered and filtered chromatogram with area measurements from experiment #43



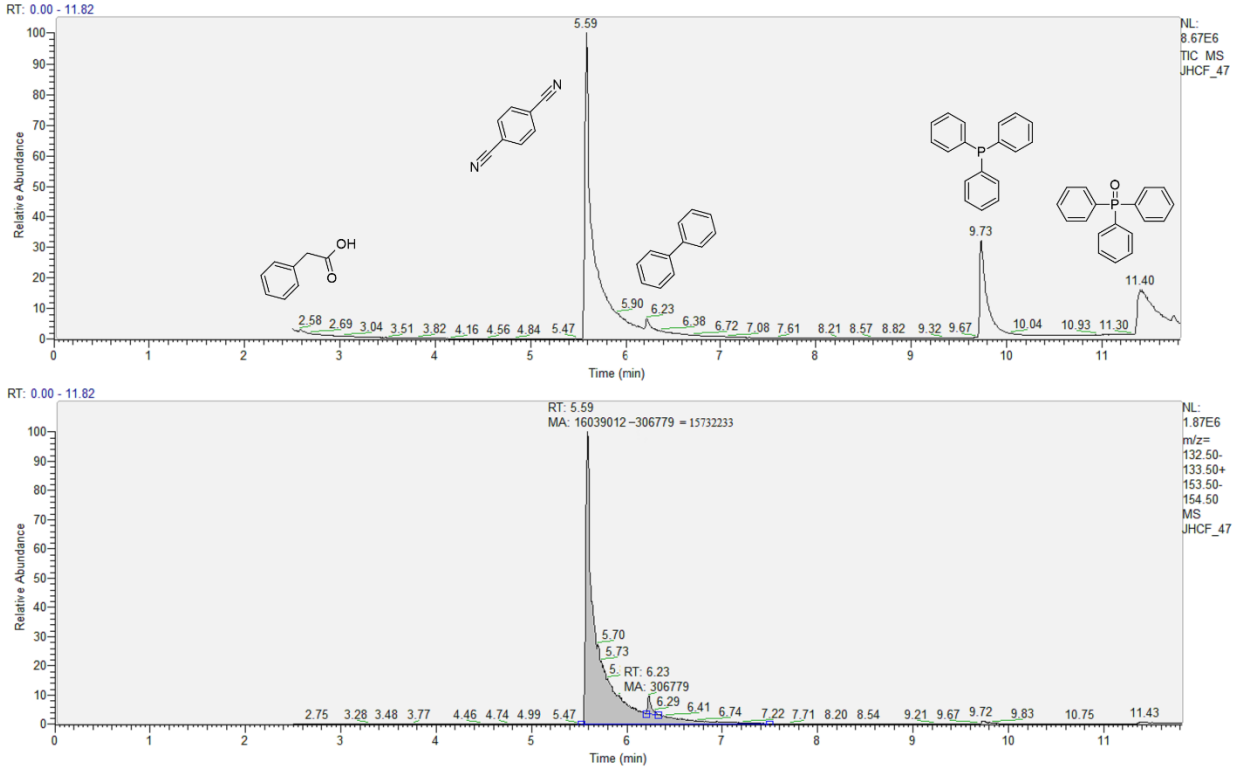
GC unfiltered and filtered chromatogram with area measurements from experiment #44



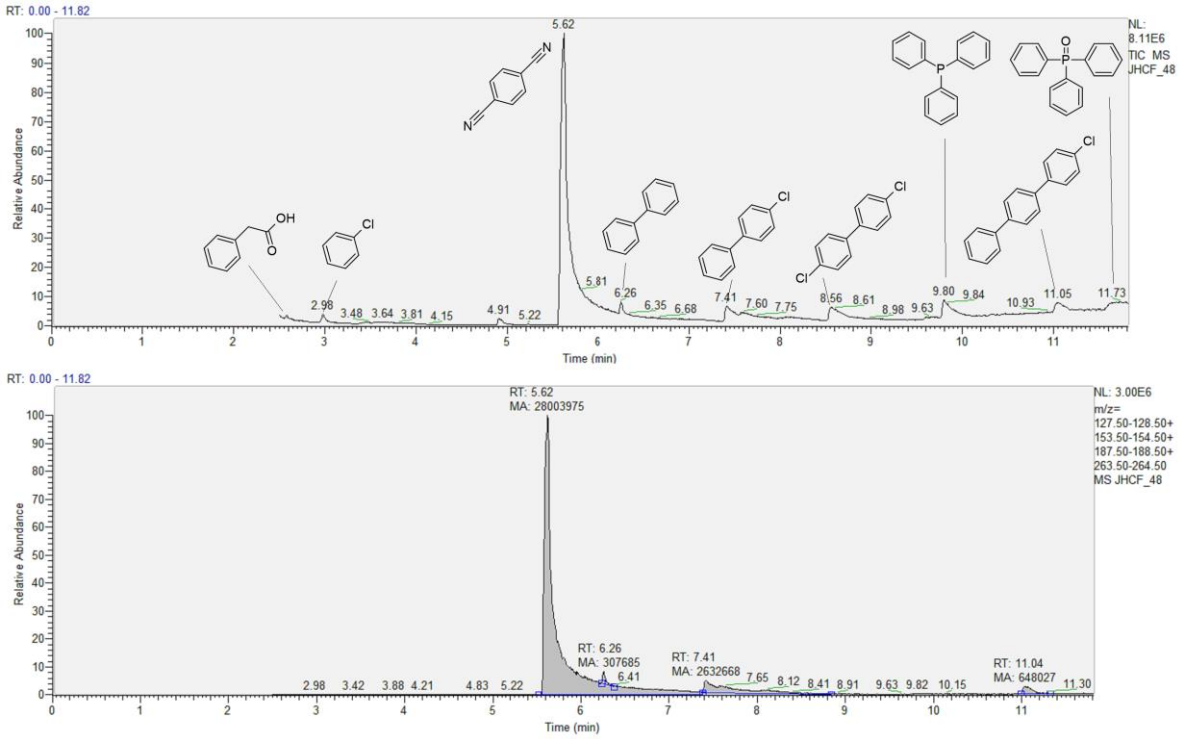
GC unfiltered and filtered chromatogram with area measurements from experiment #45



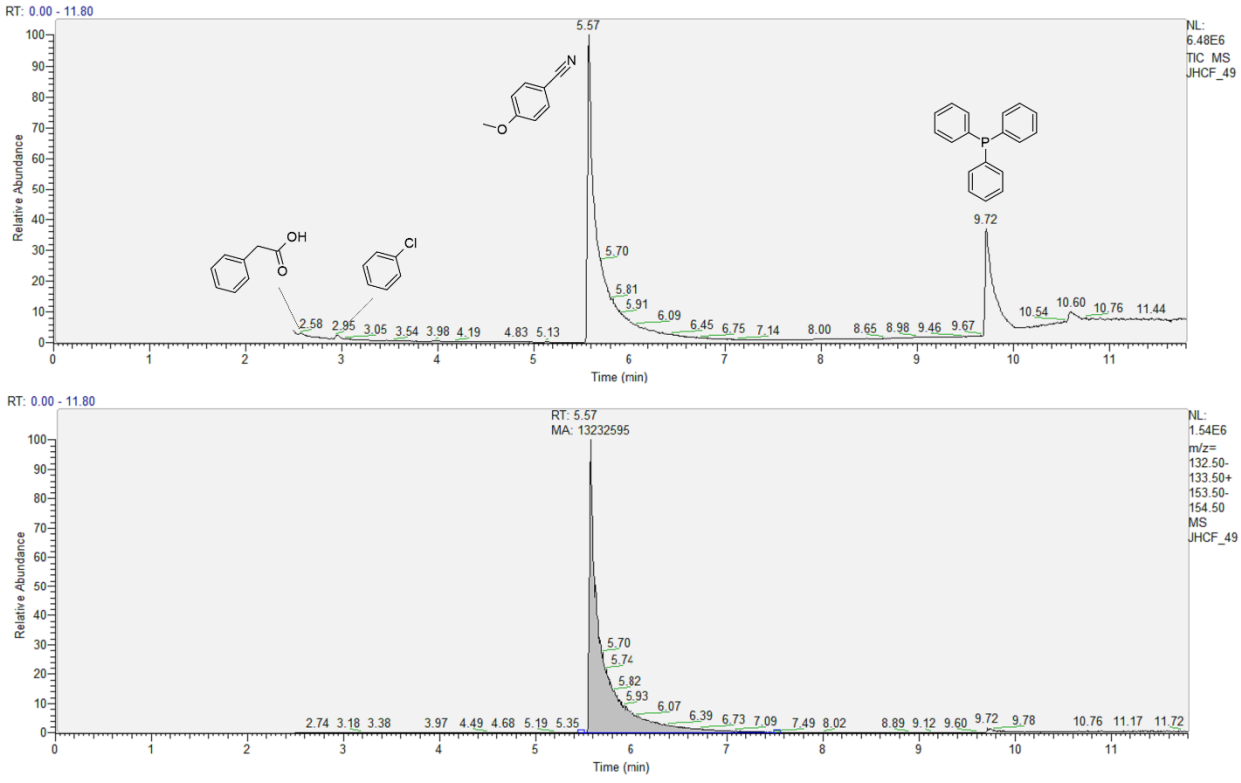
GC unfiltered and filtered chromatogram with area measurements from experiment #47



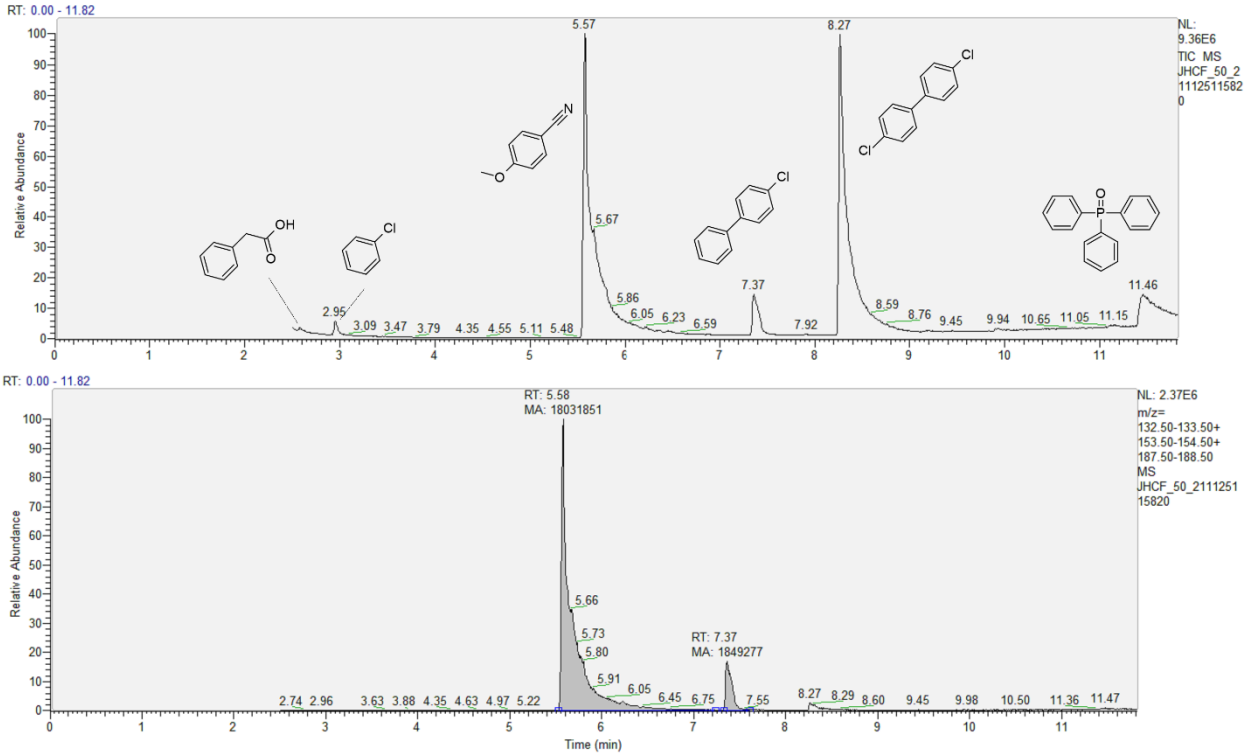
GC unfiltered and filtered chromatogram with area measurements from experiment #48



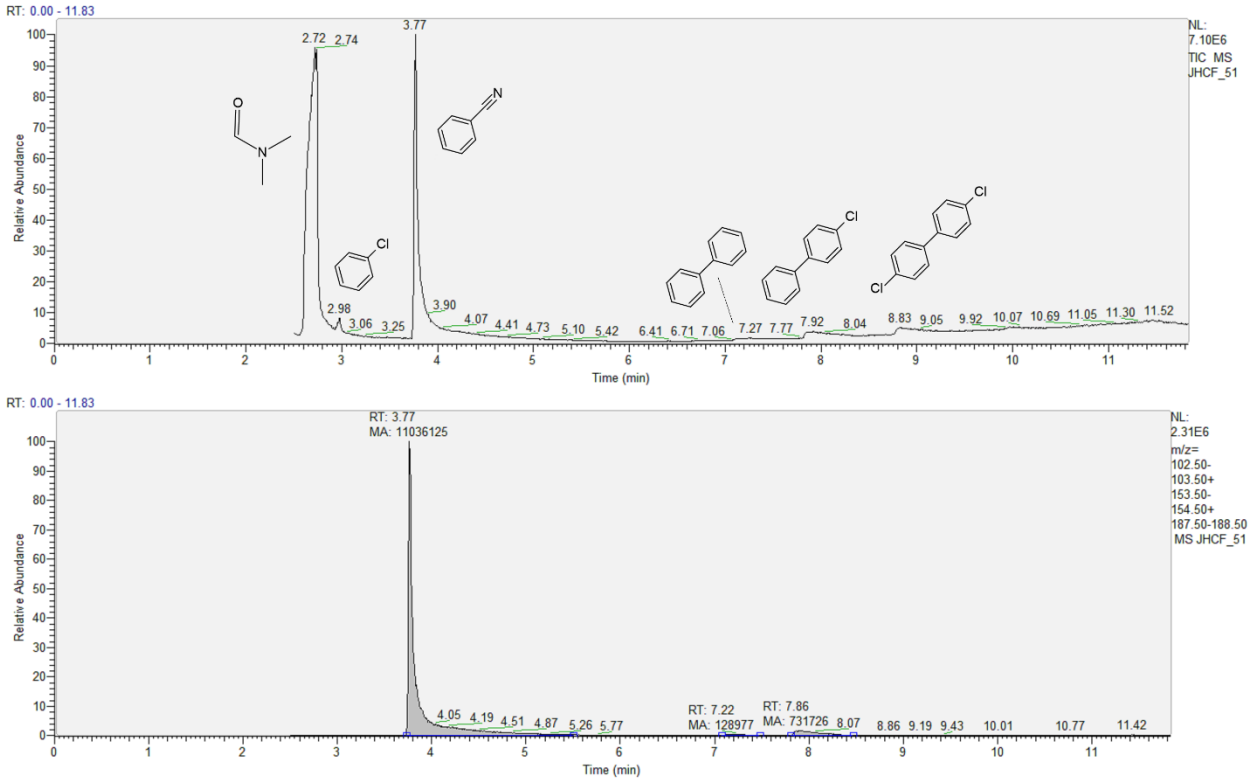
GC unfiltered and filtered chromatogram with area measurements from experiment #49



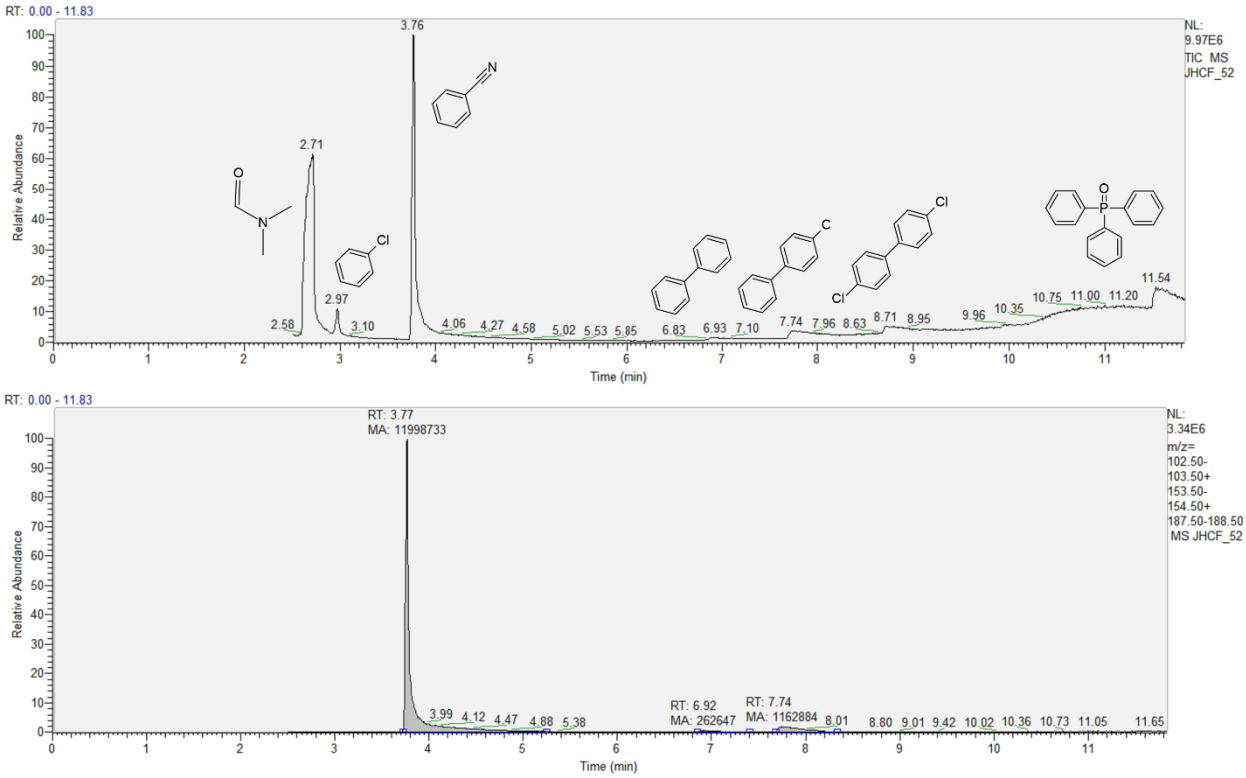
GC unfiltered and filtered chromatogram with area measurements from experiment #50



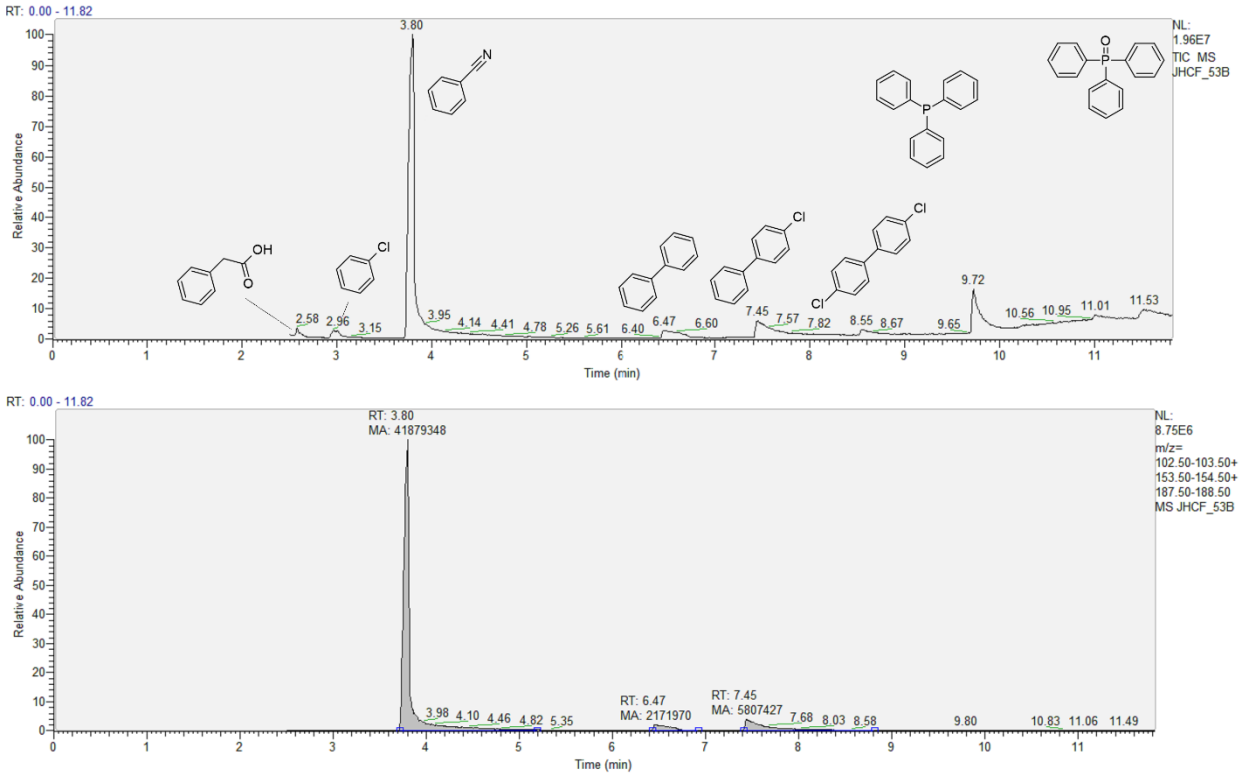
GC unfiltered and filtered chromatogram with area measurements from experiment #51



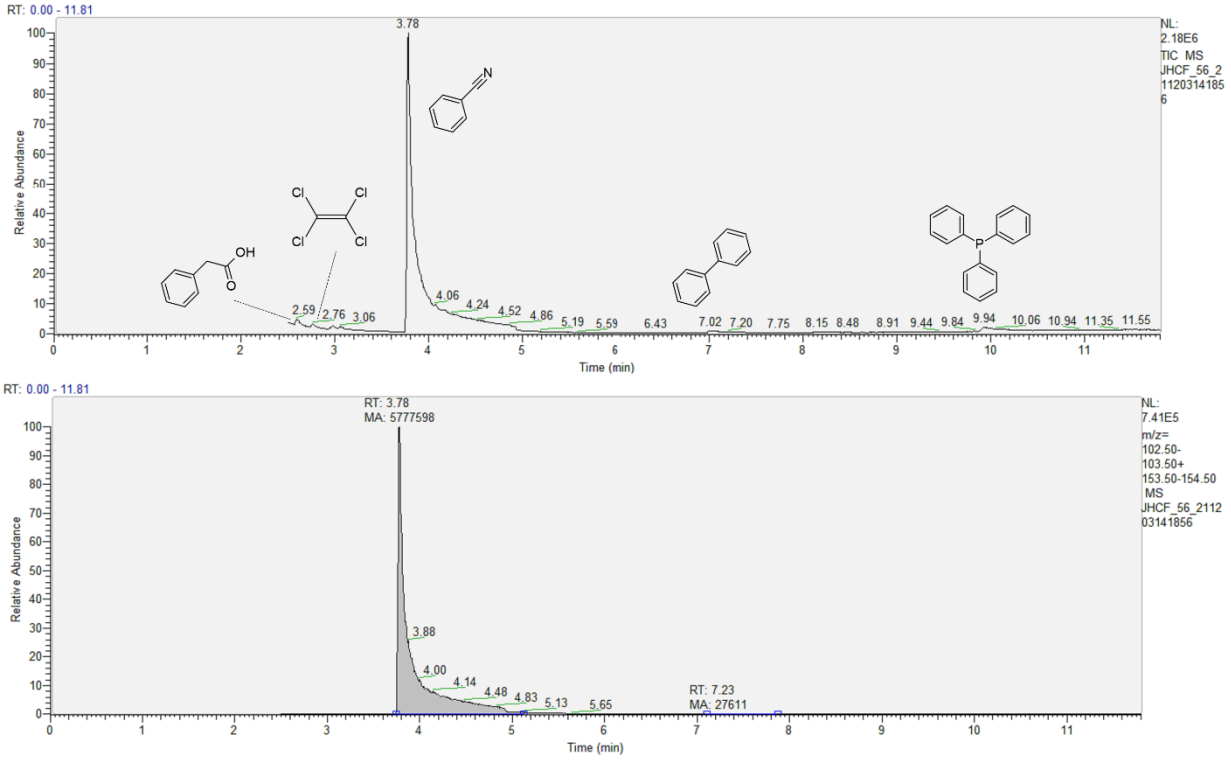
GC unfiltered and filtered chromatogram with area measurements from experiment #52



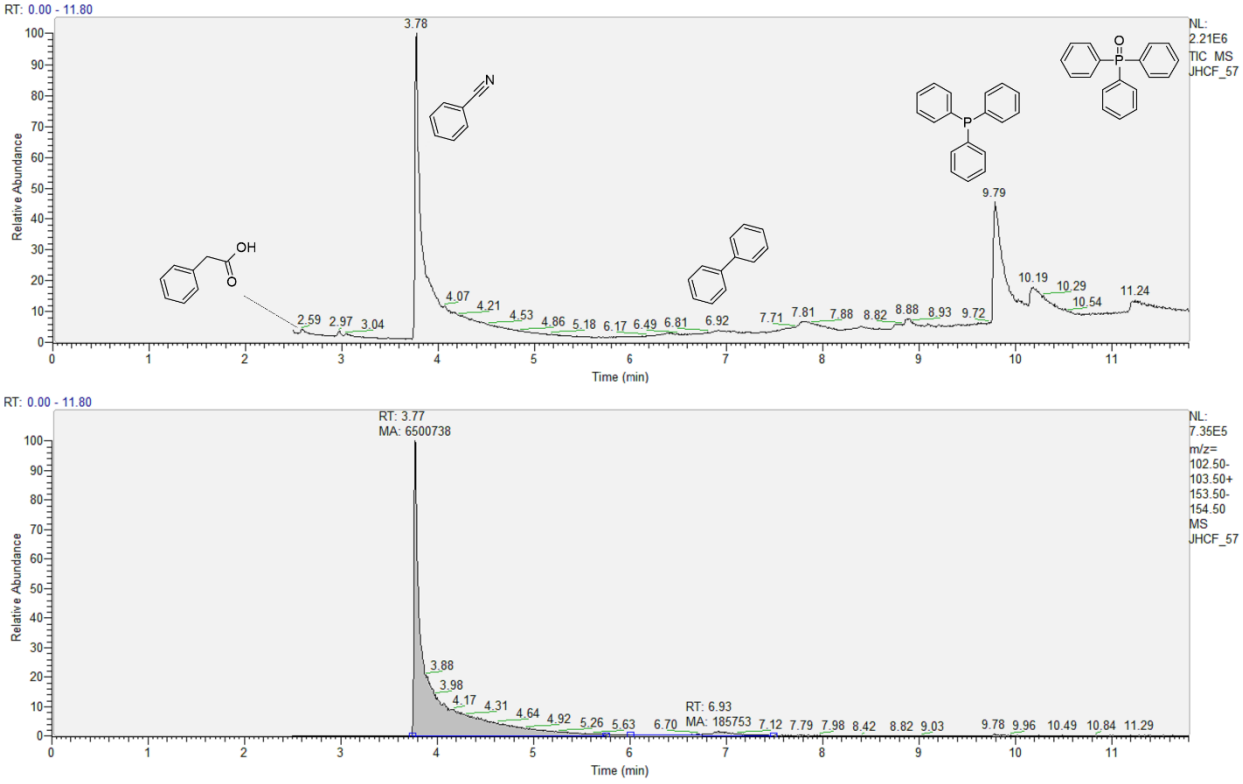
GC unfiltered and filtered chromatogram with area measurements from experiment #53



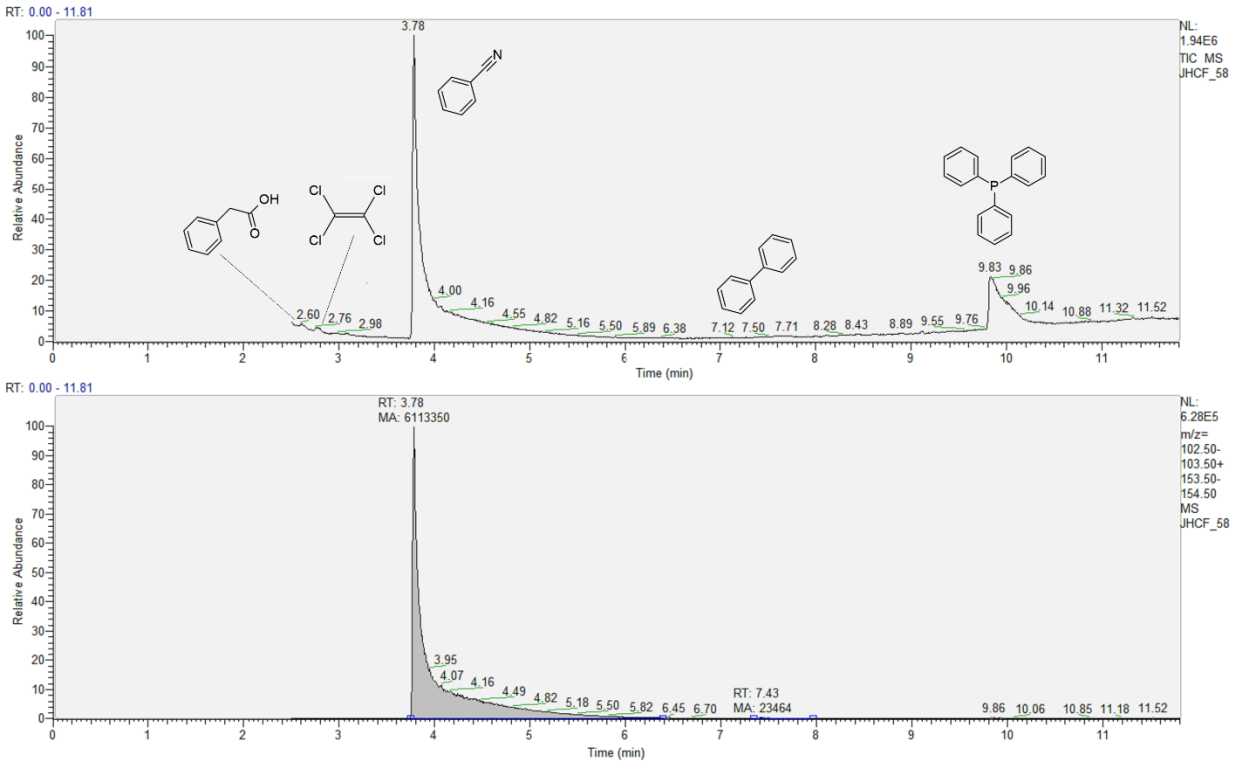
GC unfiltered and filtered chromatogram with area measurements from experiment #56



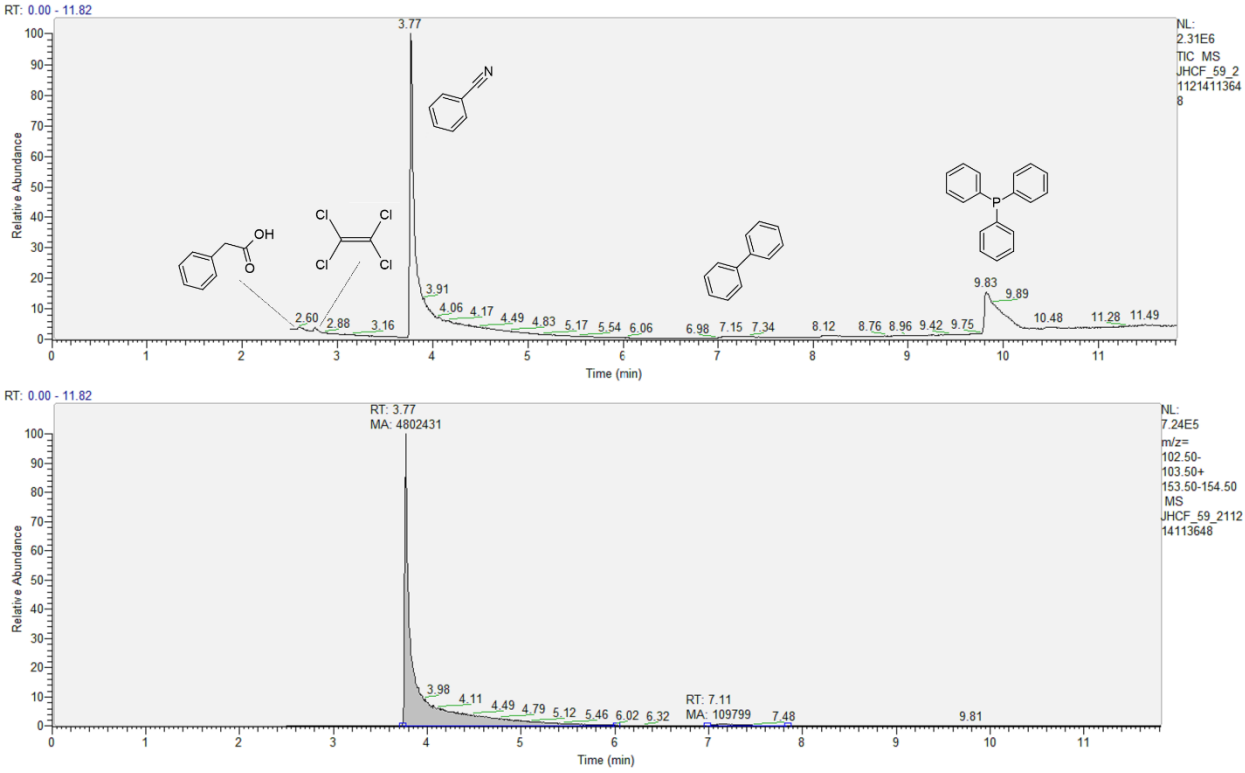
GC unfiltered and filtered chromatogram with area measurements from experiment #57



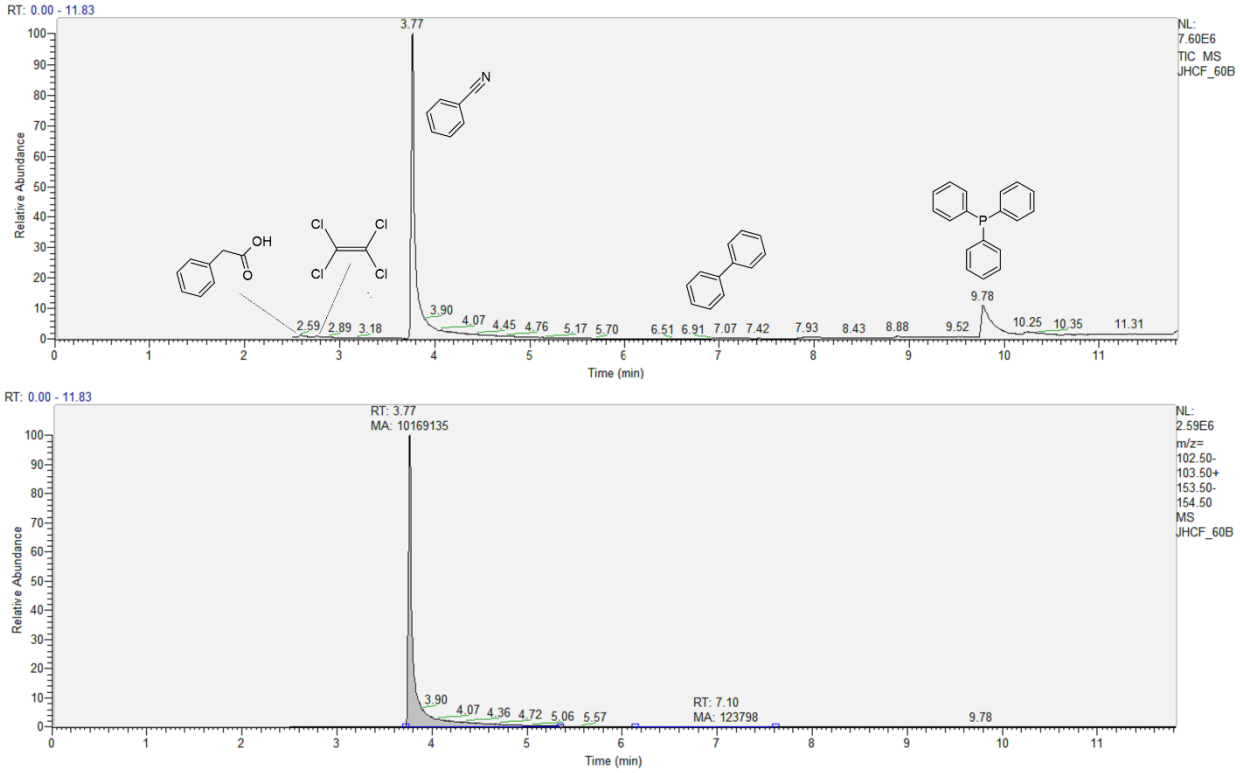
GC unfiltered and filtered chromatogram with area measurements from experiment #58



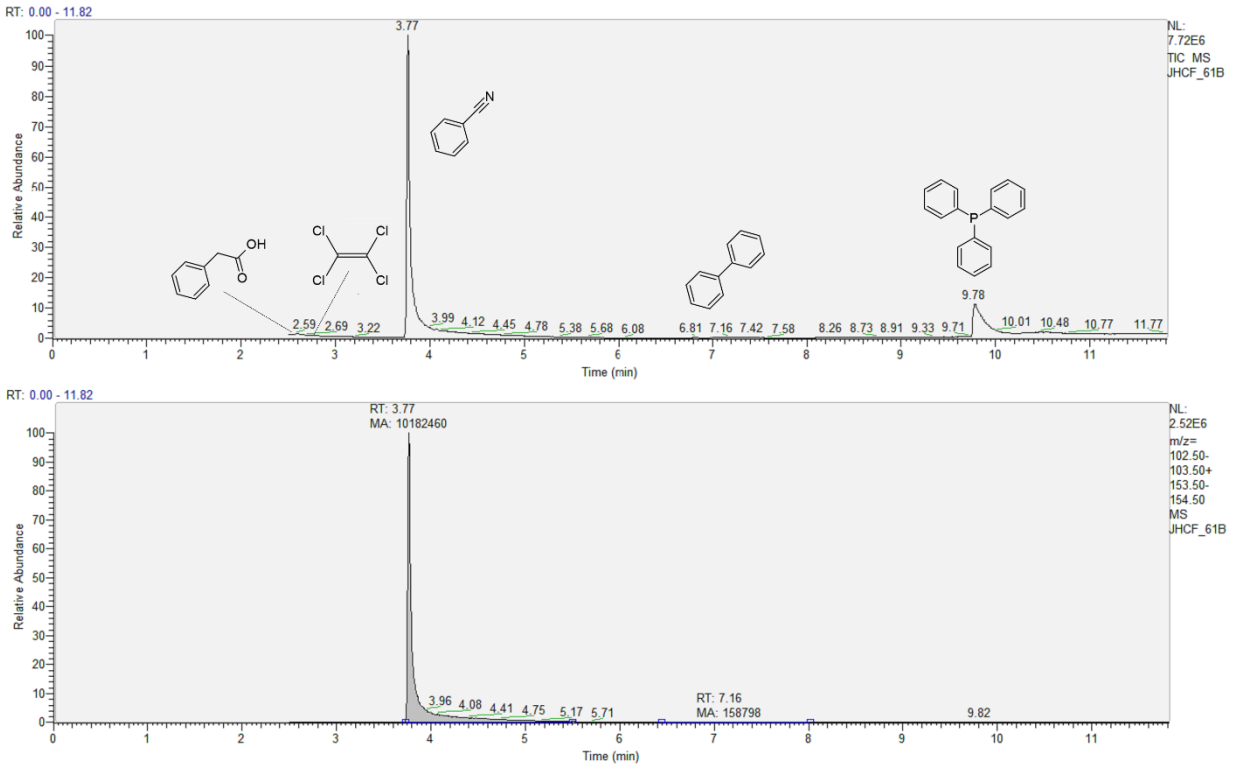
GC unfiltered and filtered chromatogram with area measurements from experiment #59



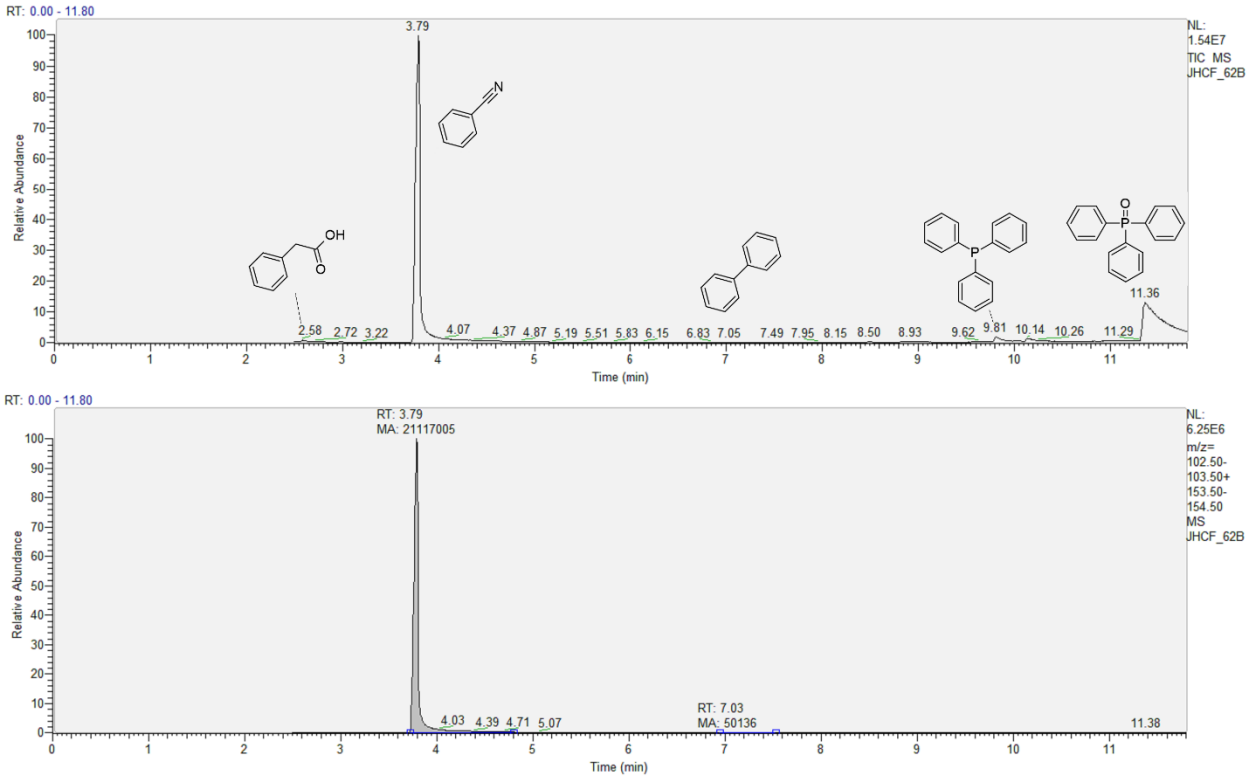
GC unfiltered and filtered chromatogram with area measurements from experiment #60



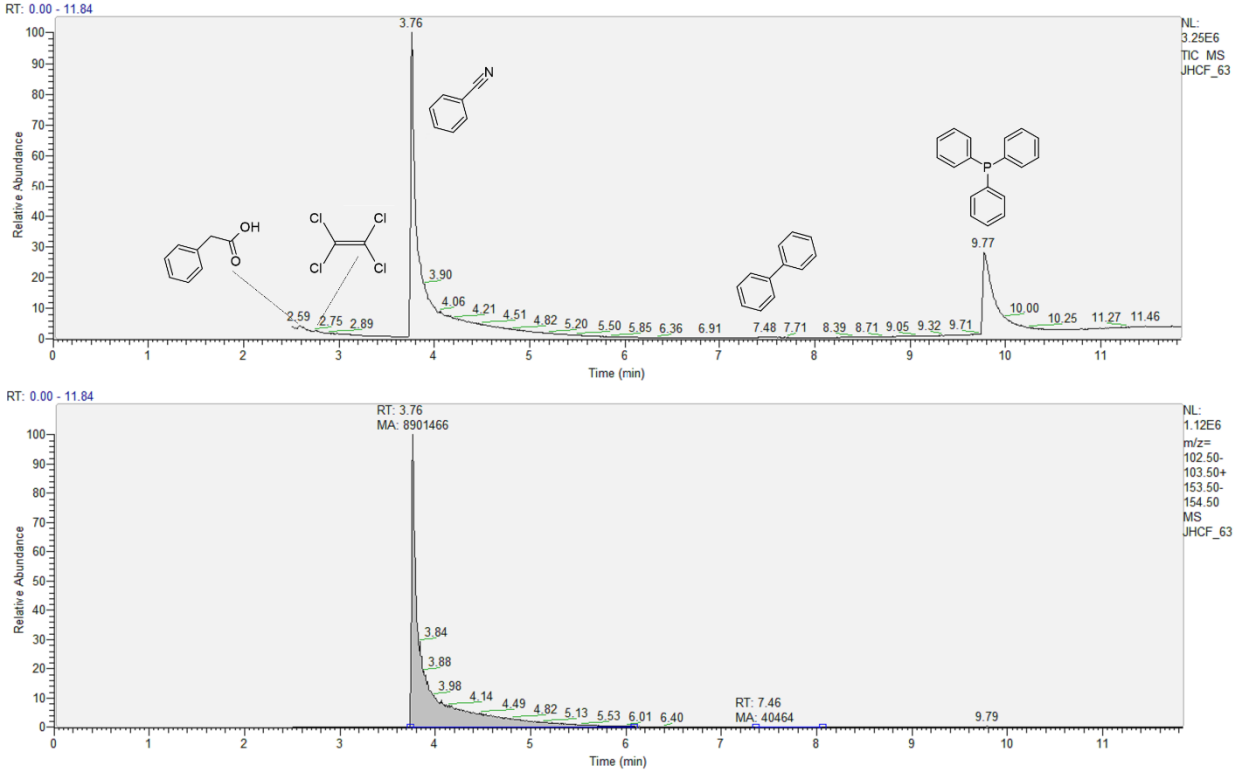
GC unfiltered and filtered chromatogram with area measurements from experiment #61



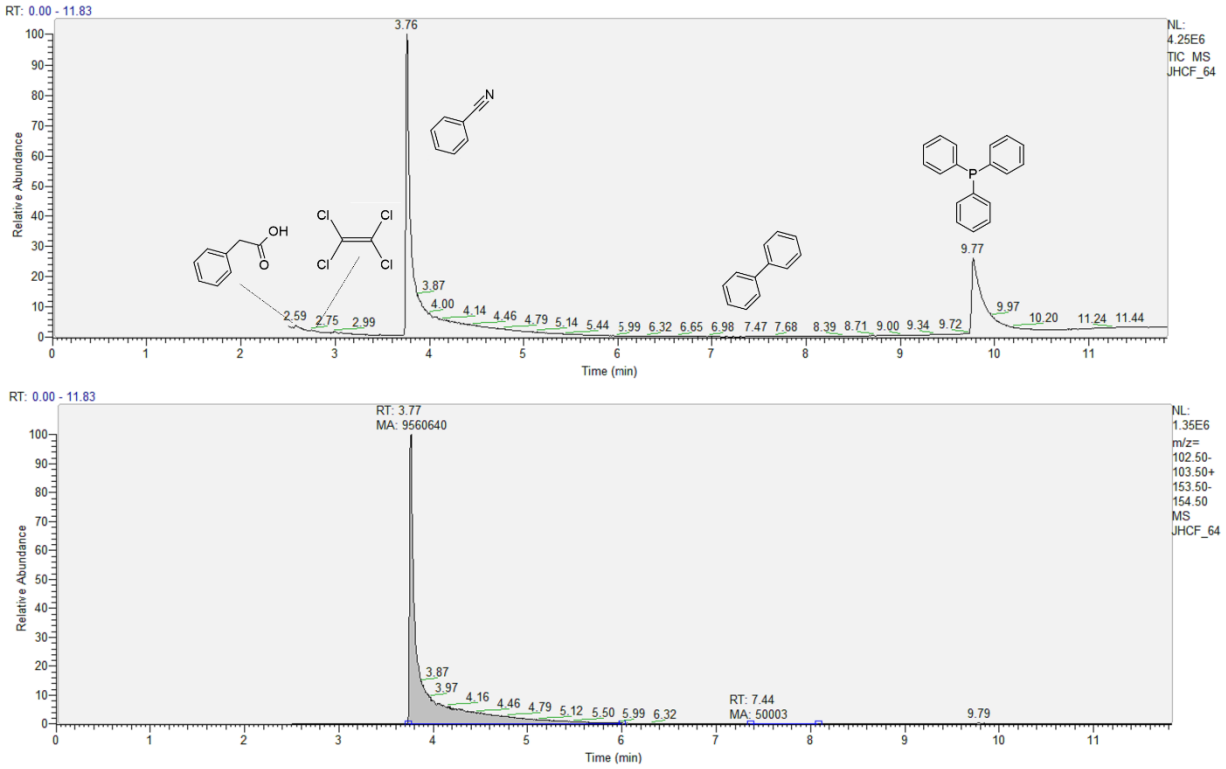
GC unfiltered and filtered chromatogram with area measurements from experiment #62



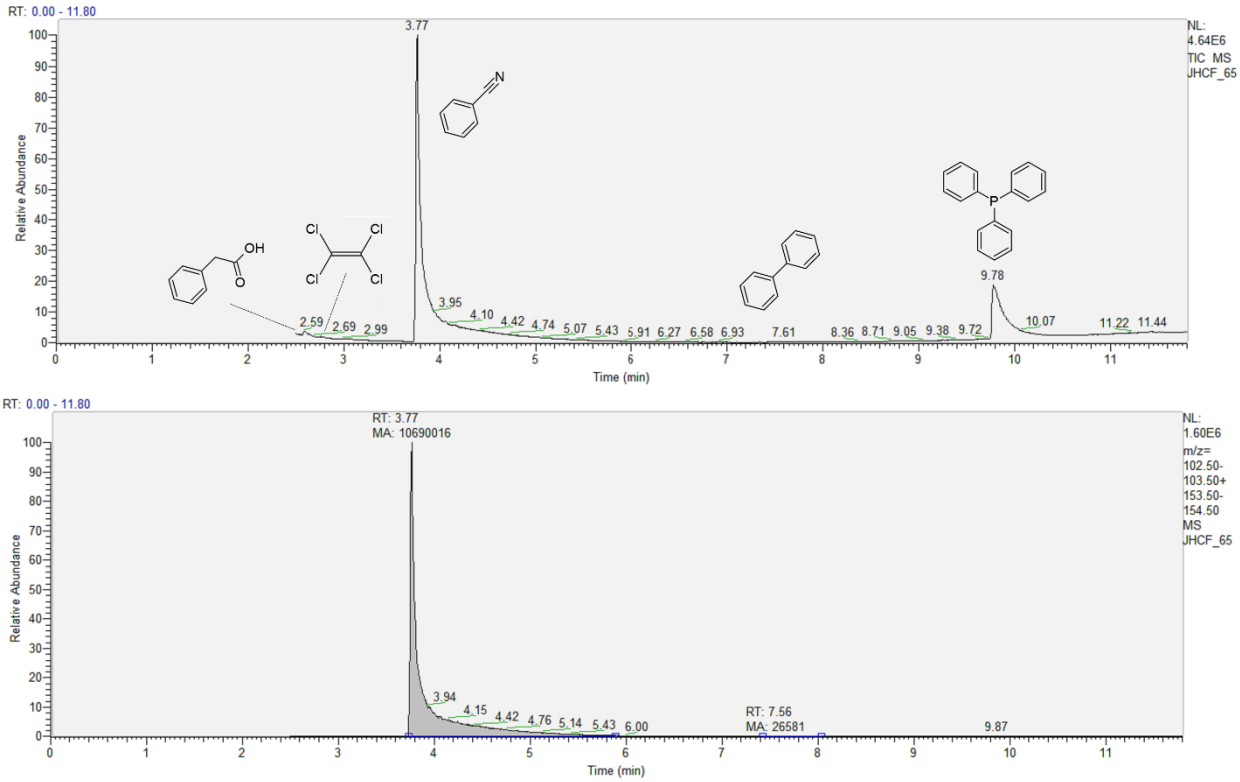
GC unfiltered and filtered chromatogram with area measurements from experiment #63



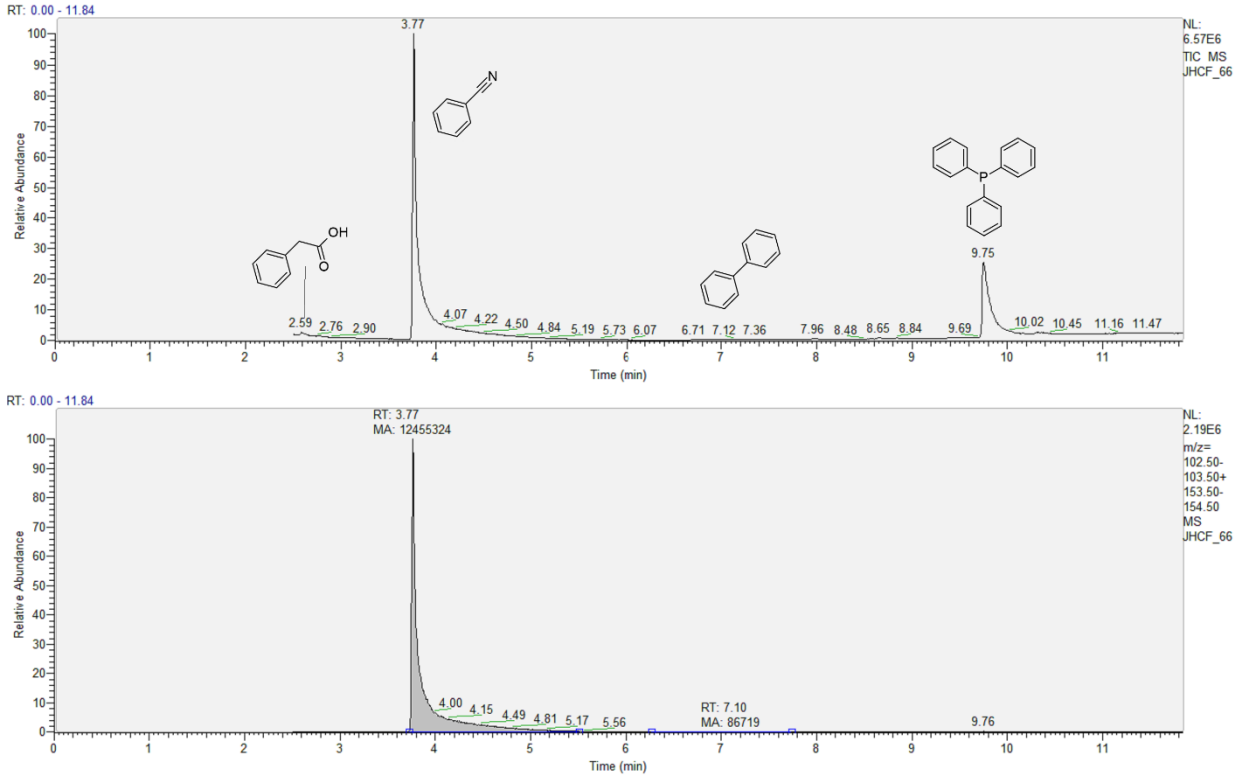
GC unfiltered and filtered chromatogram with area measurements from experiment #64



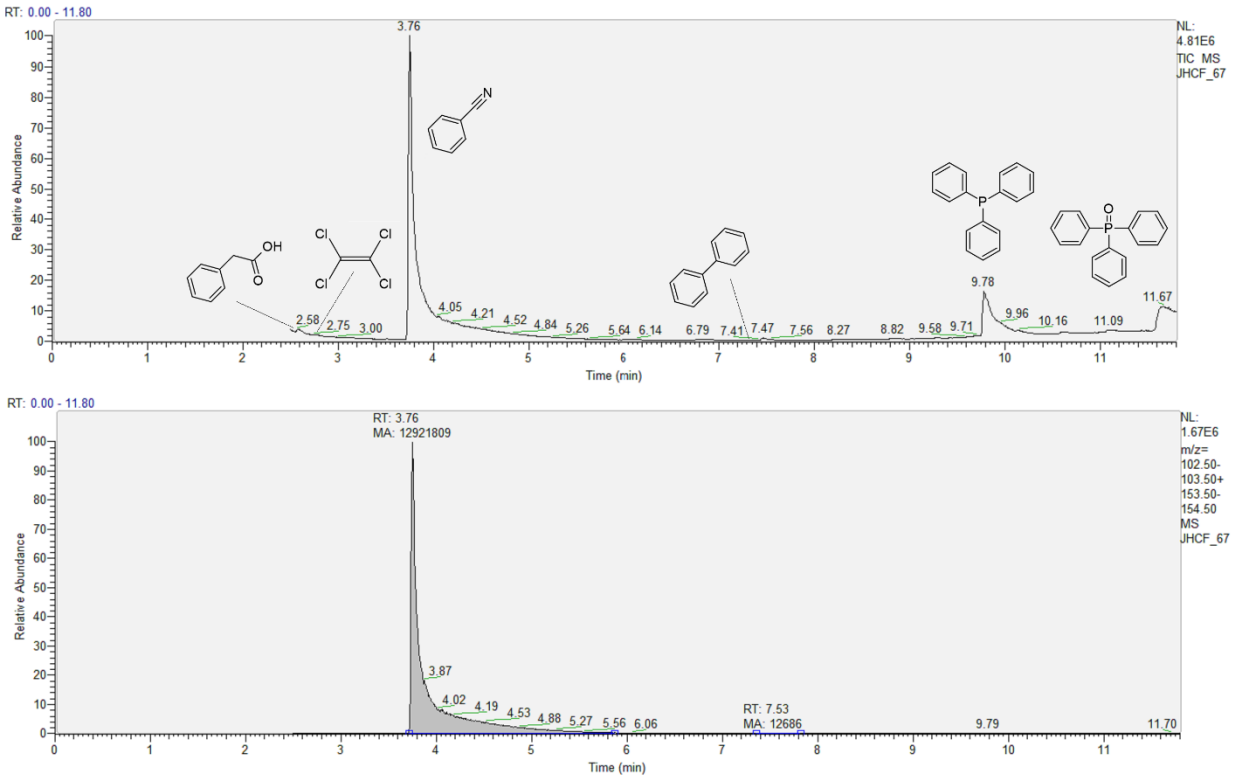
GC unfiltered and filtered chromatogram with area measurements from experiment #65



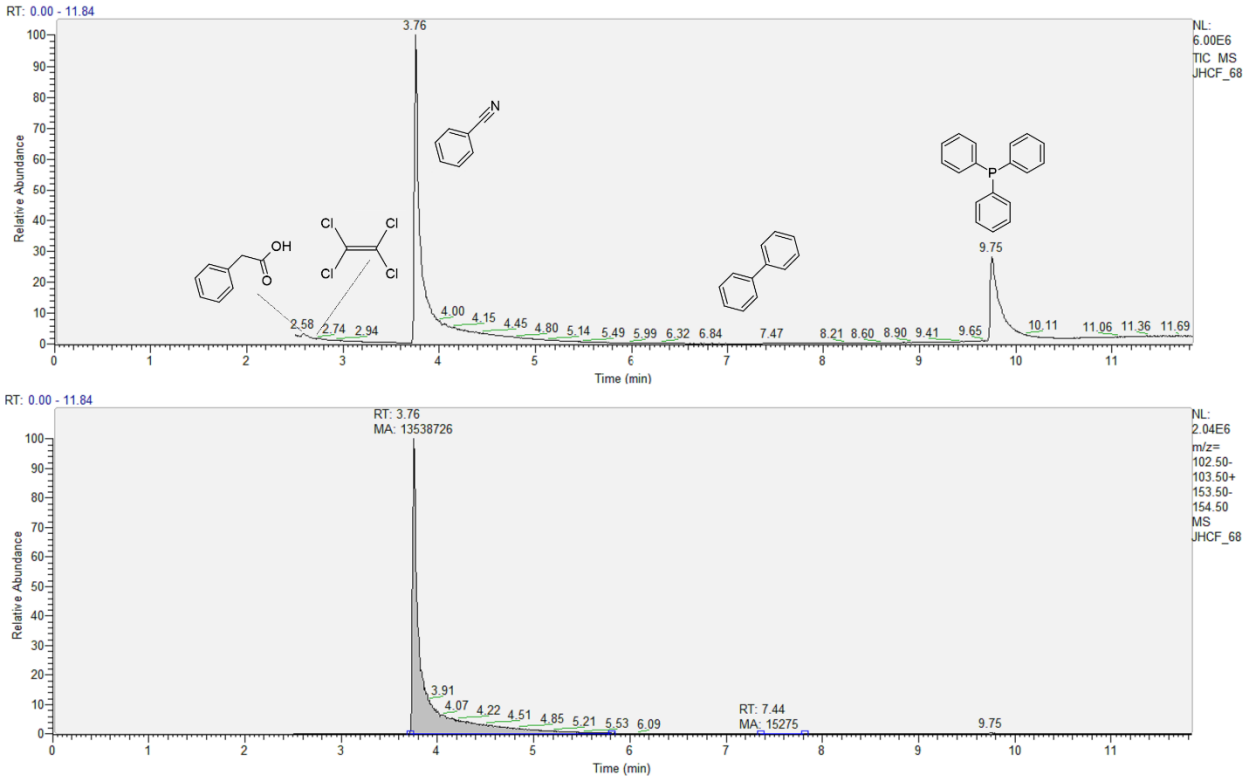
GC unfiltered and filtered chromatogram with area measurements from experiment #66



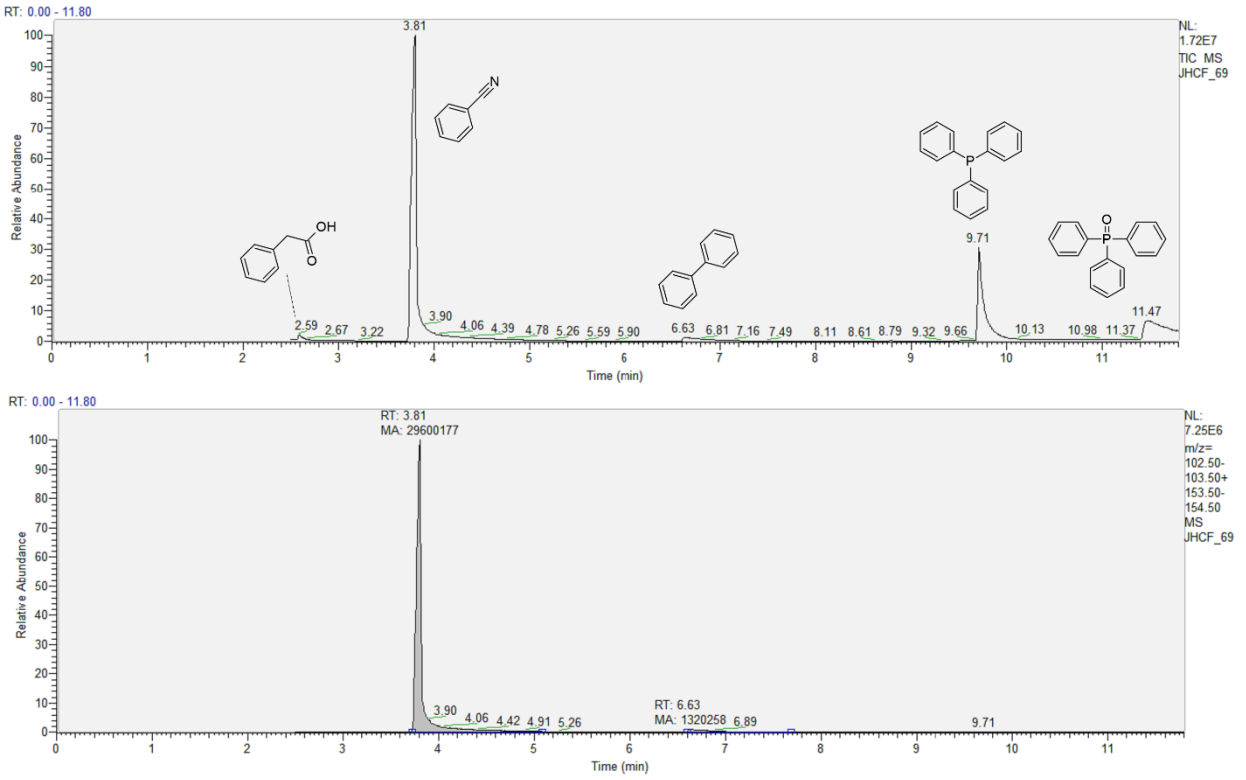
GC unfiltered and filtered chromatogram with area measurements from experiment #67



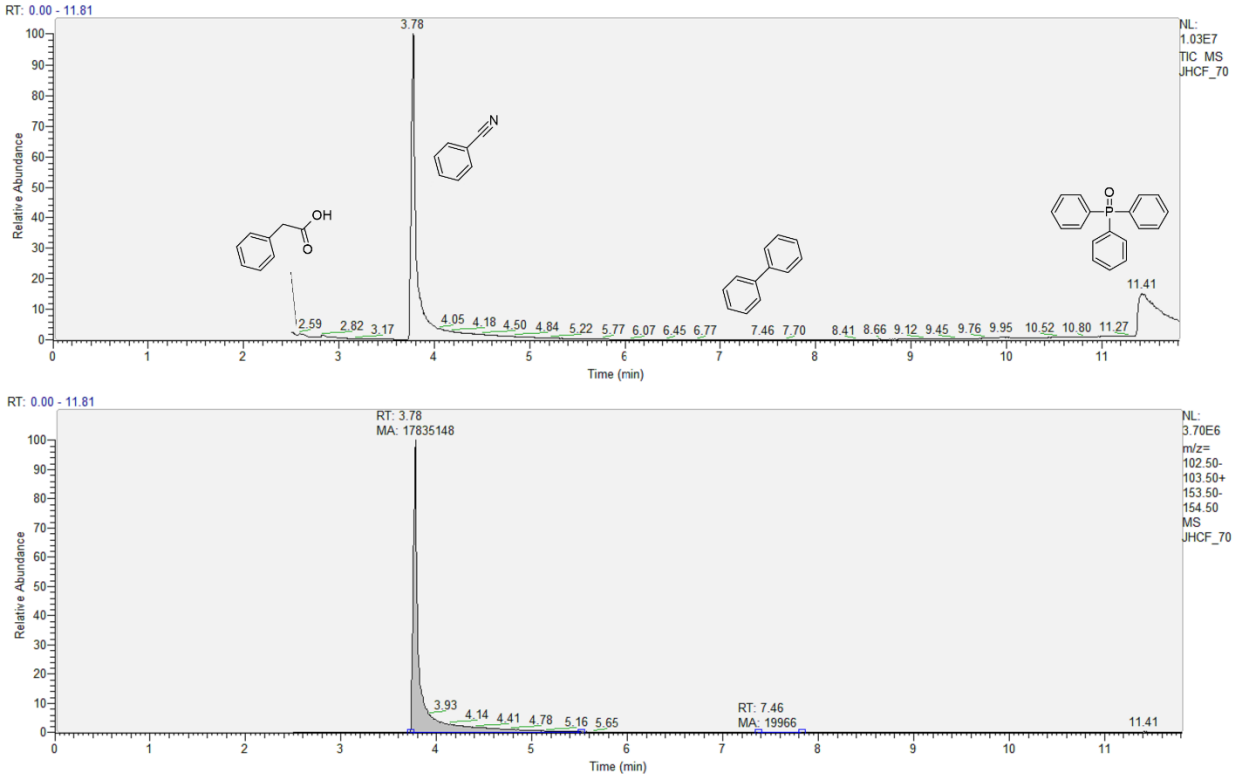
GC unfiltered and filtered chromatogram with area measurements from experiment #68



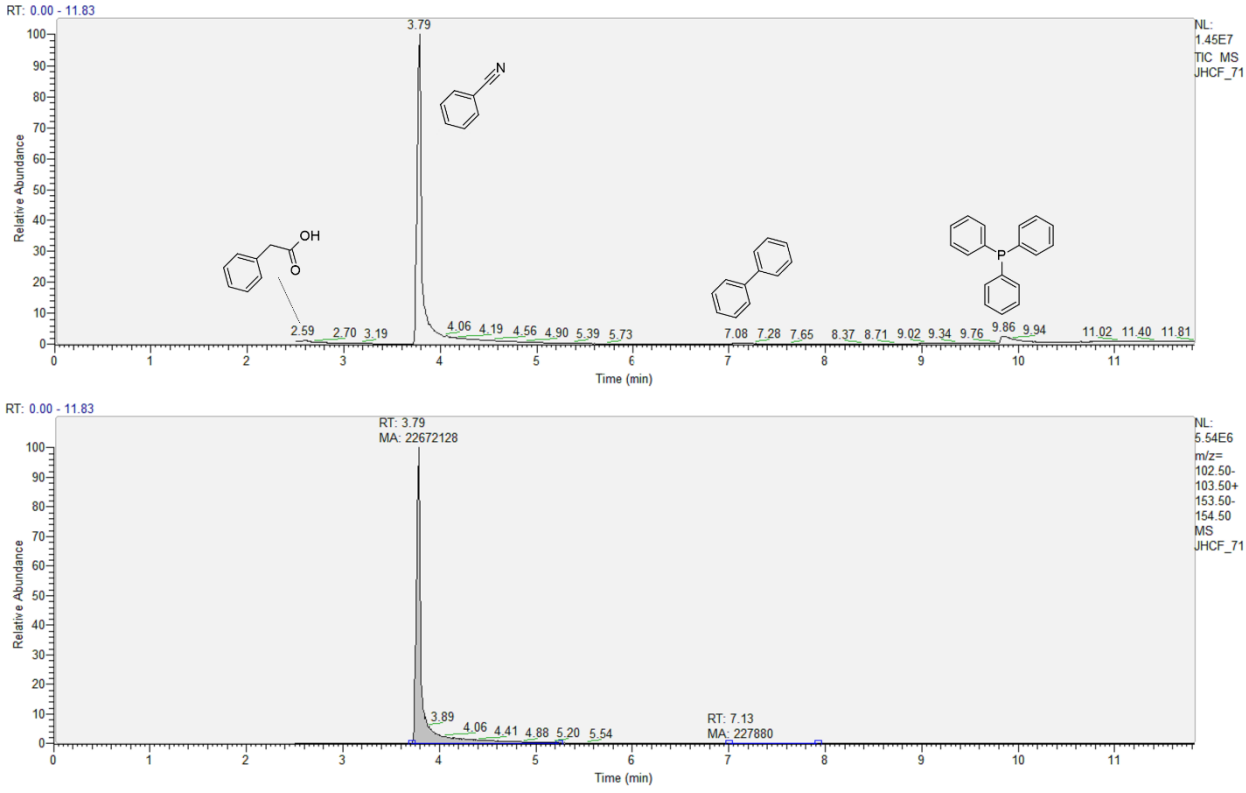
GC unfiltered and filtered chromatogram with area measurements from experiment #69



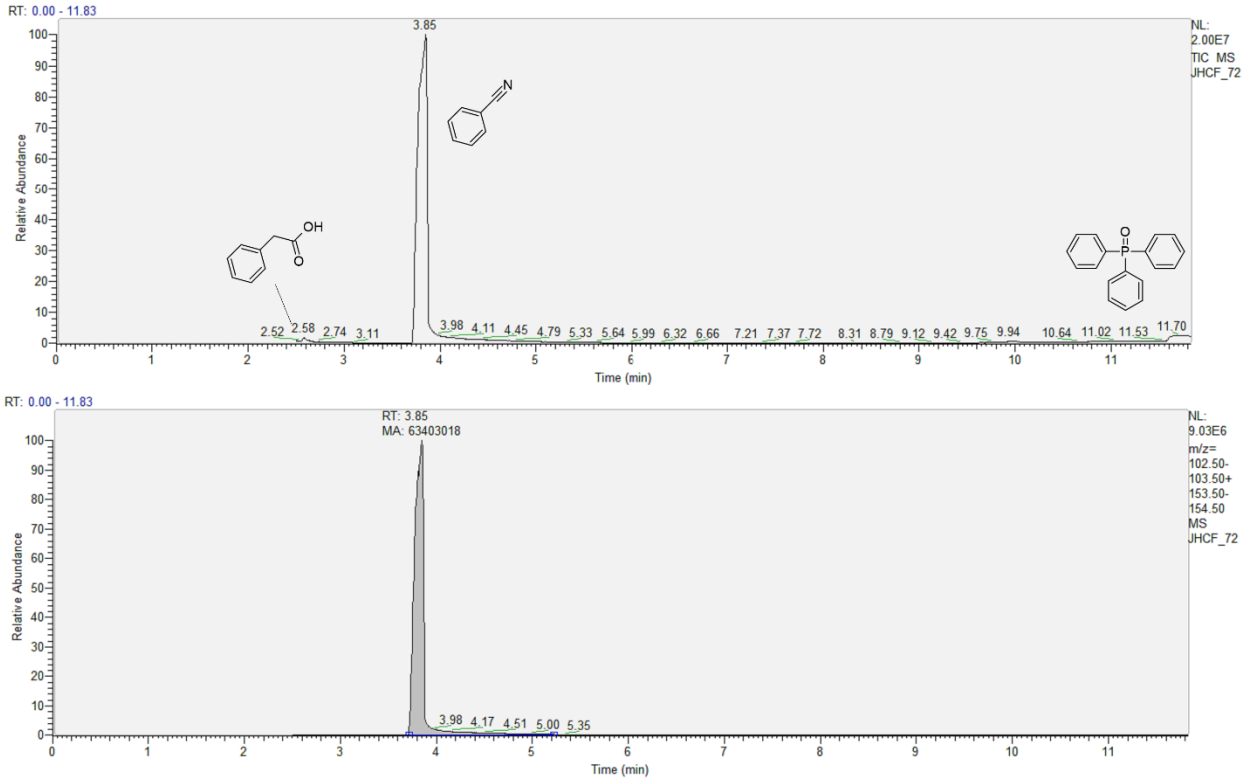
GC unfiltered and filtered chromatogram with area measurements from experiment #70



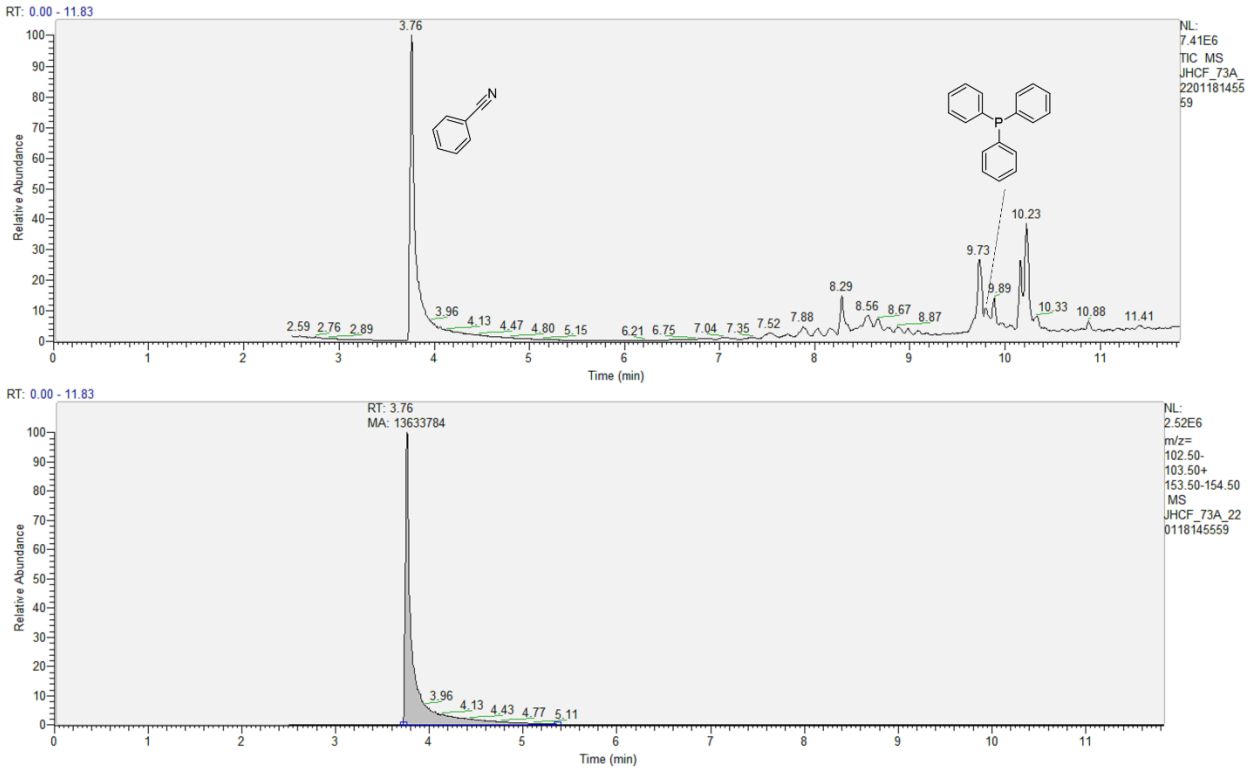
GC unfiltered and filtered chromatogram with area measurements from experiment #71



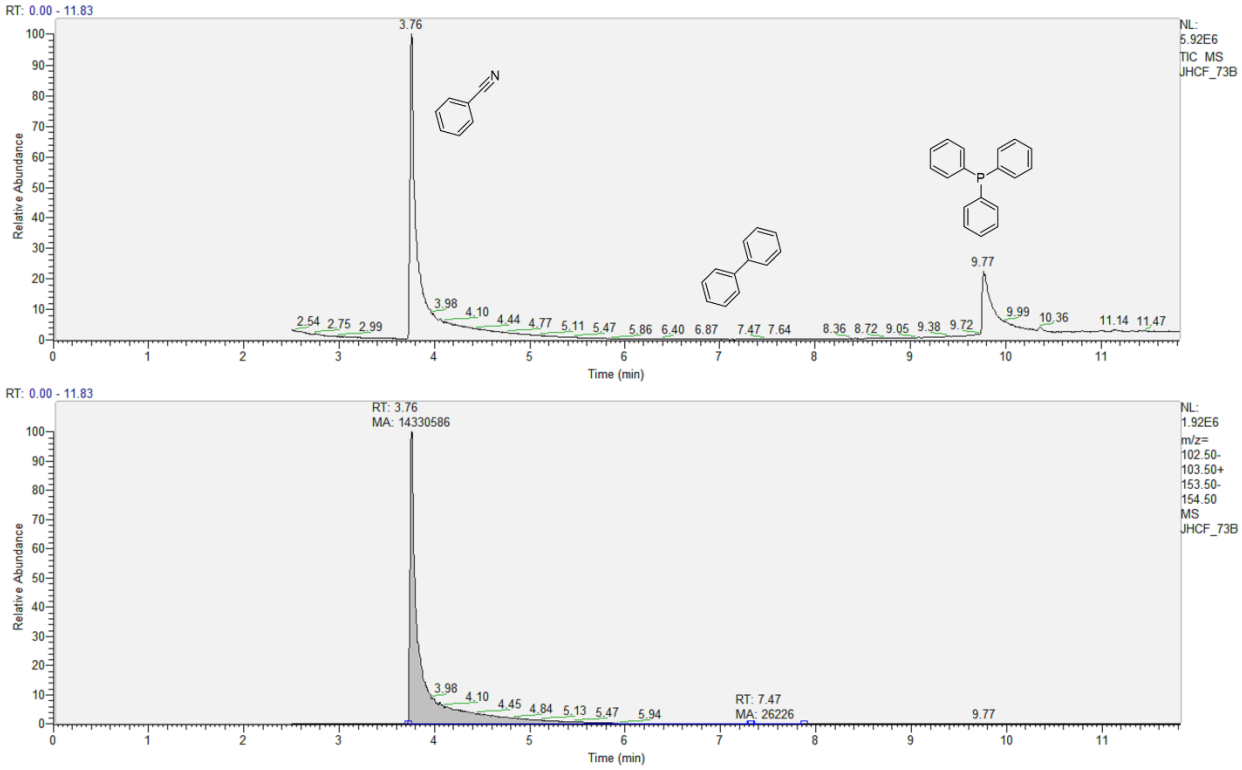
GC unfiltered and filtered chromatogram with area measurements from experiment #72



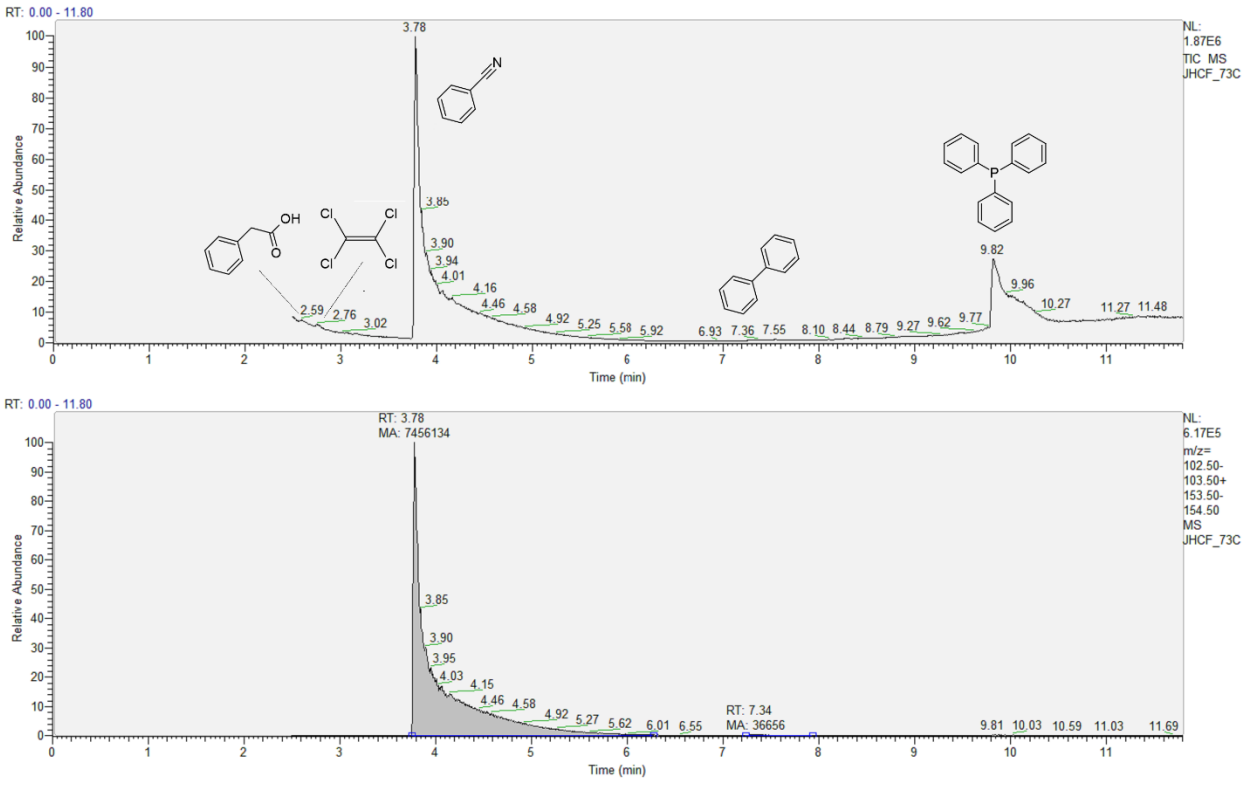
GC unfiltered and filtered chromatogram with area measurements from experiment #73A



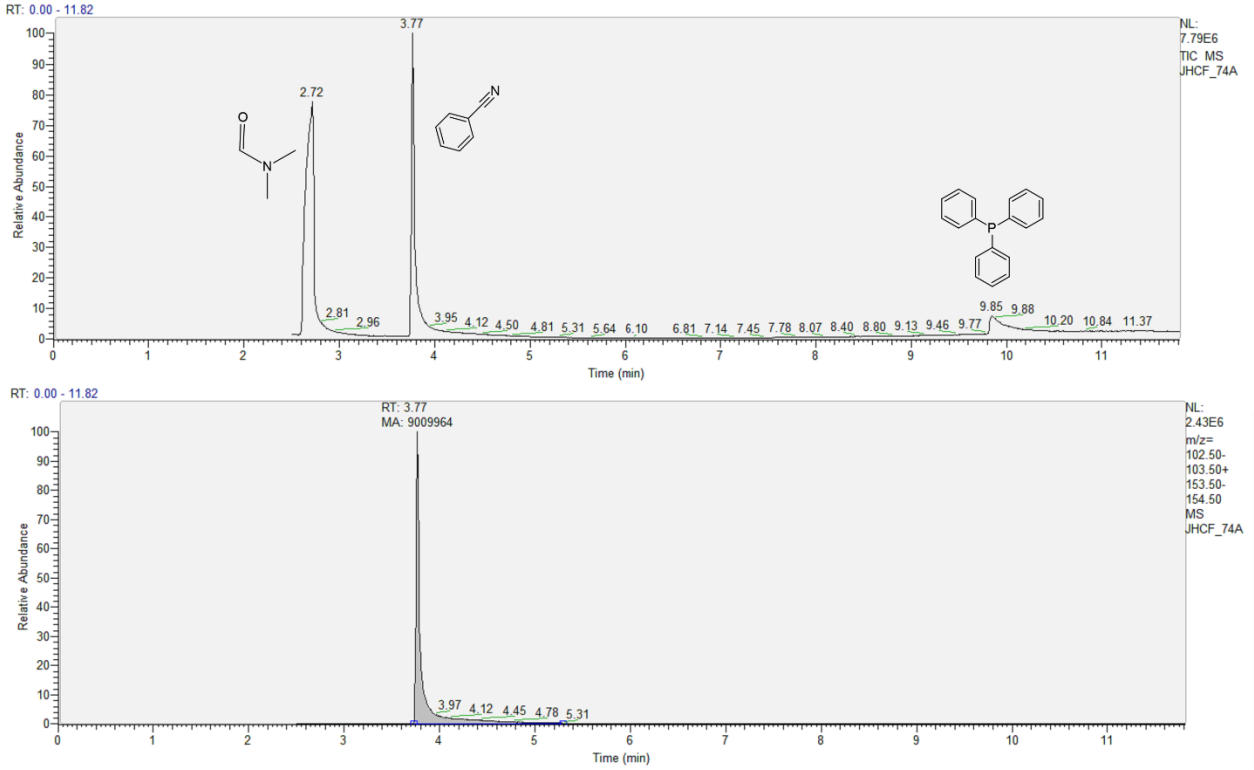
GC unfiltered and filtered chromatogram with area measurements from experiment #73B



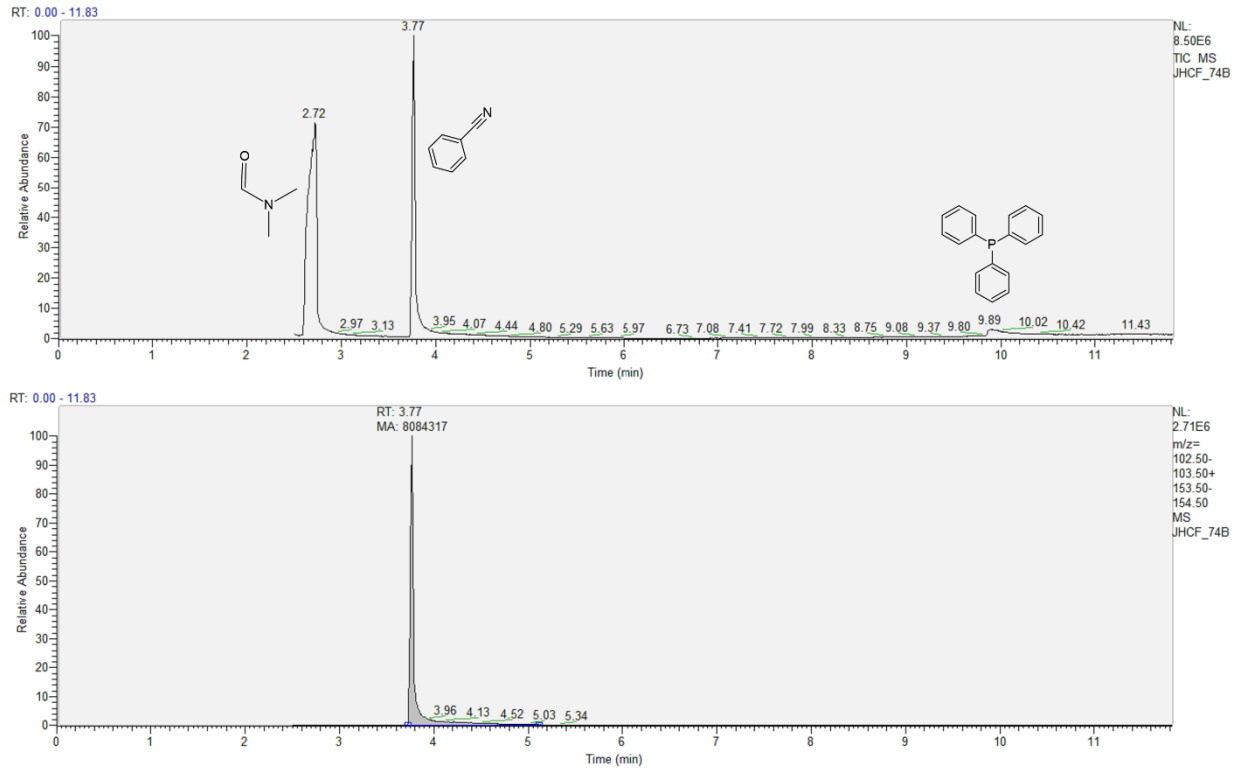
GC unfiltered and filtered chromatogram with area measurements from experiment #73C



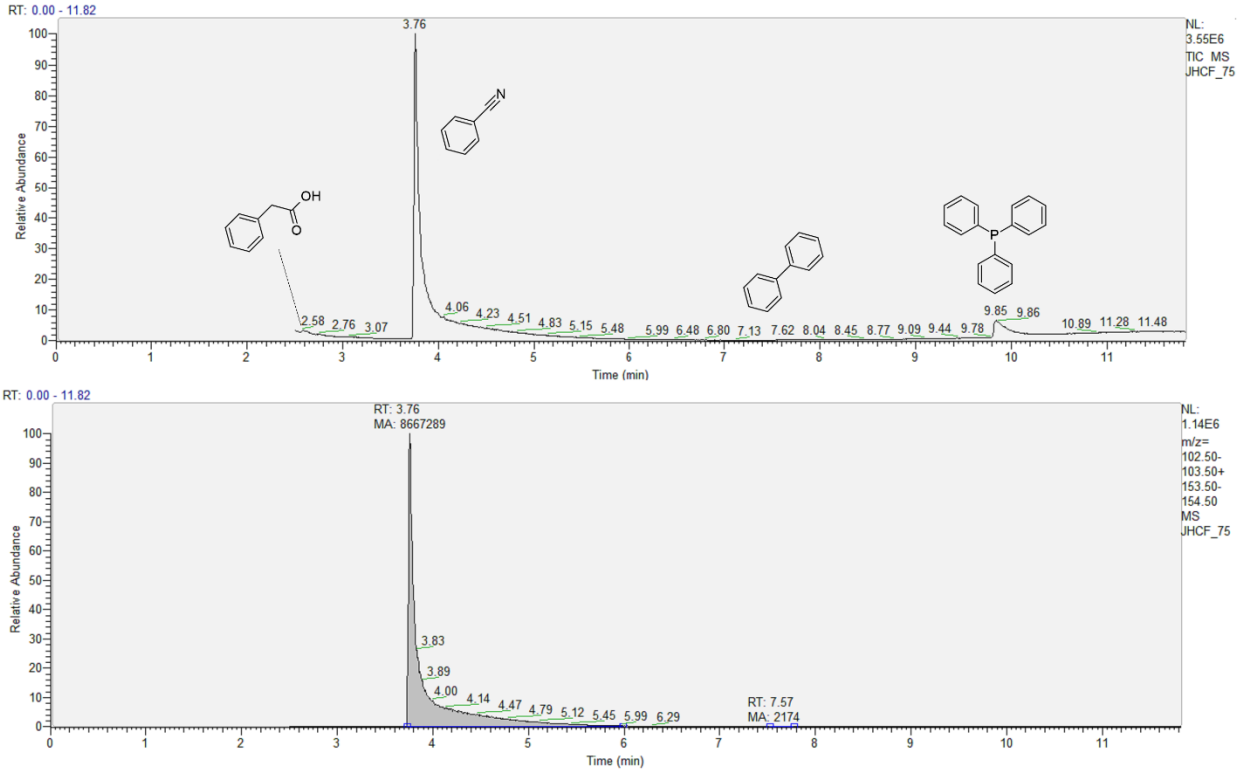
GC unfiltered and filtered chromatogram with area measurements from experiment #74A



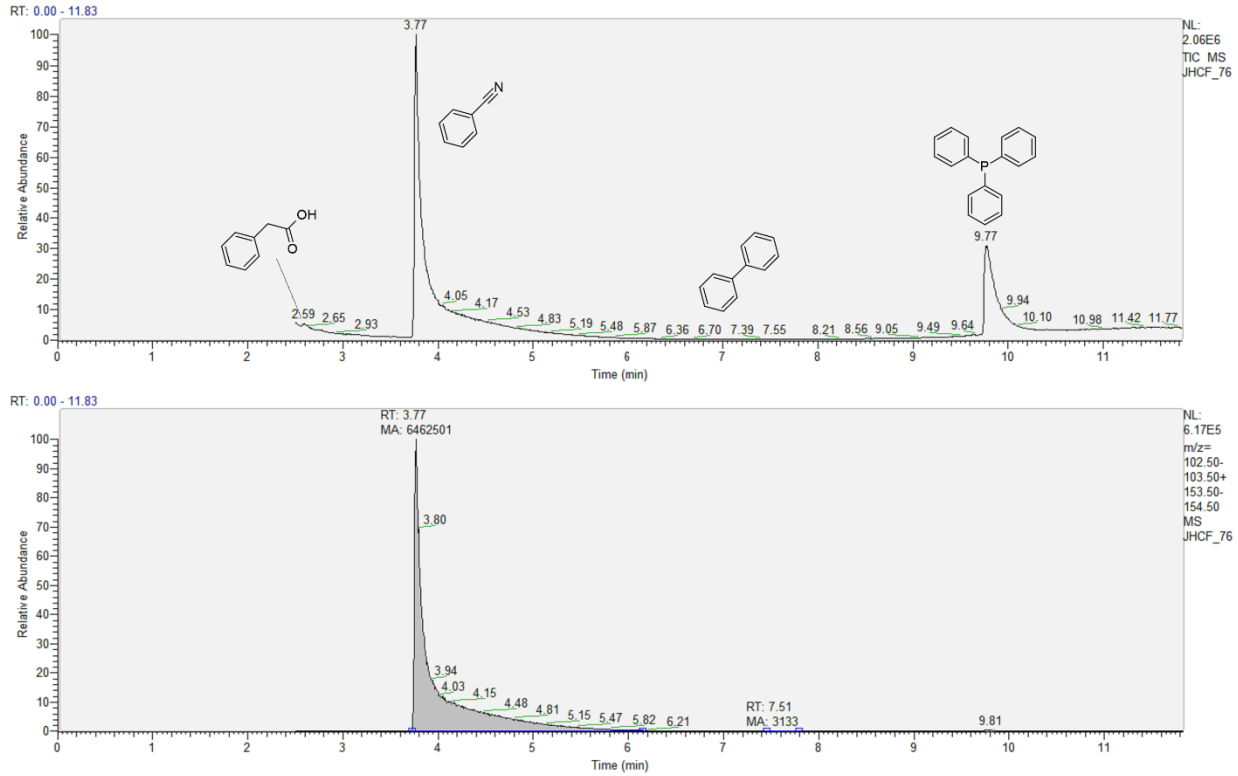
GC unfiltered and filtered chromatogram with area measurements from experiment #74B



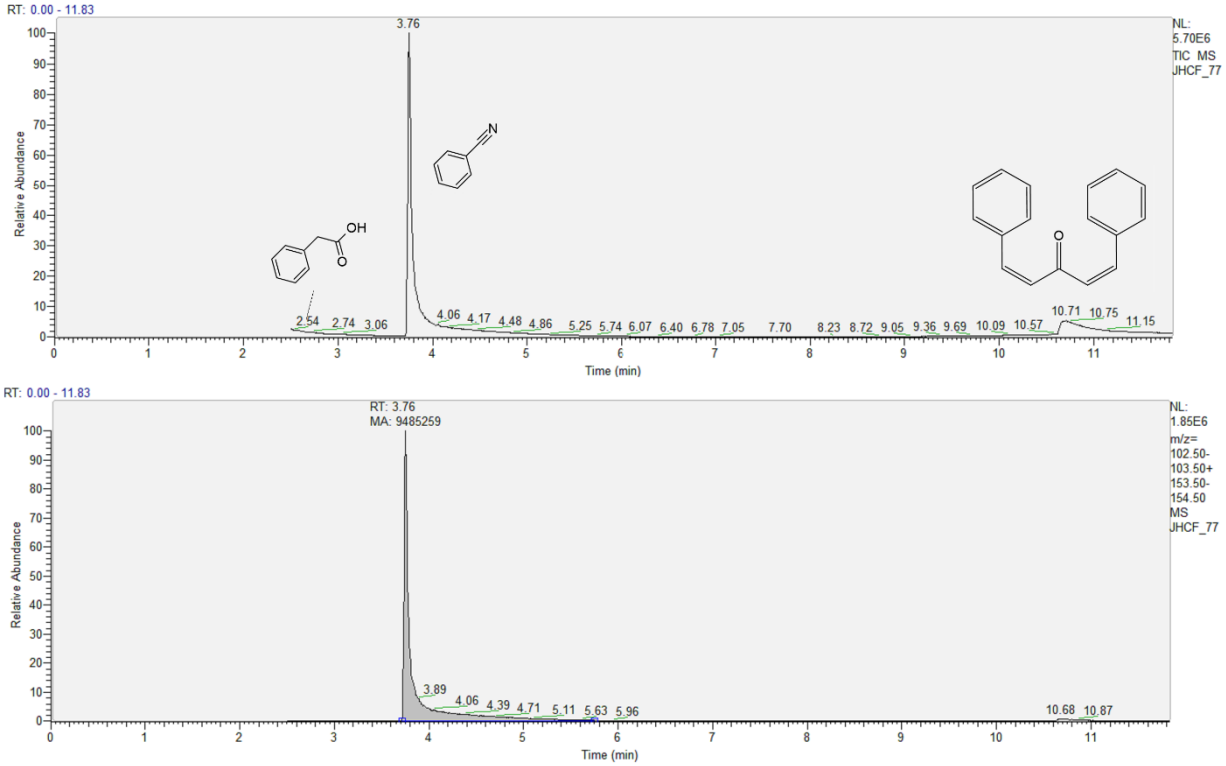
GC unfiltered and filtered chromatogram with area measurements from experiment #75



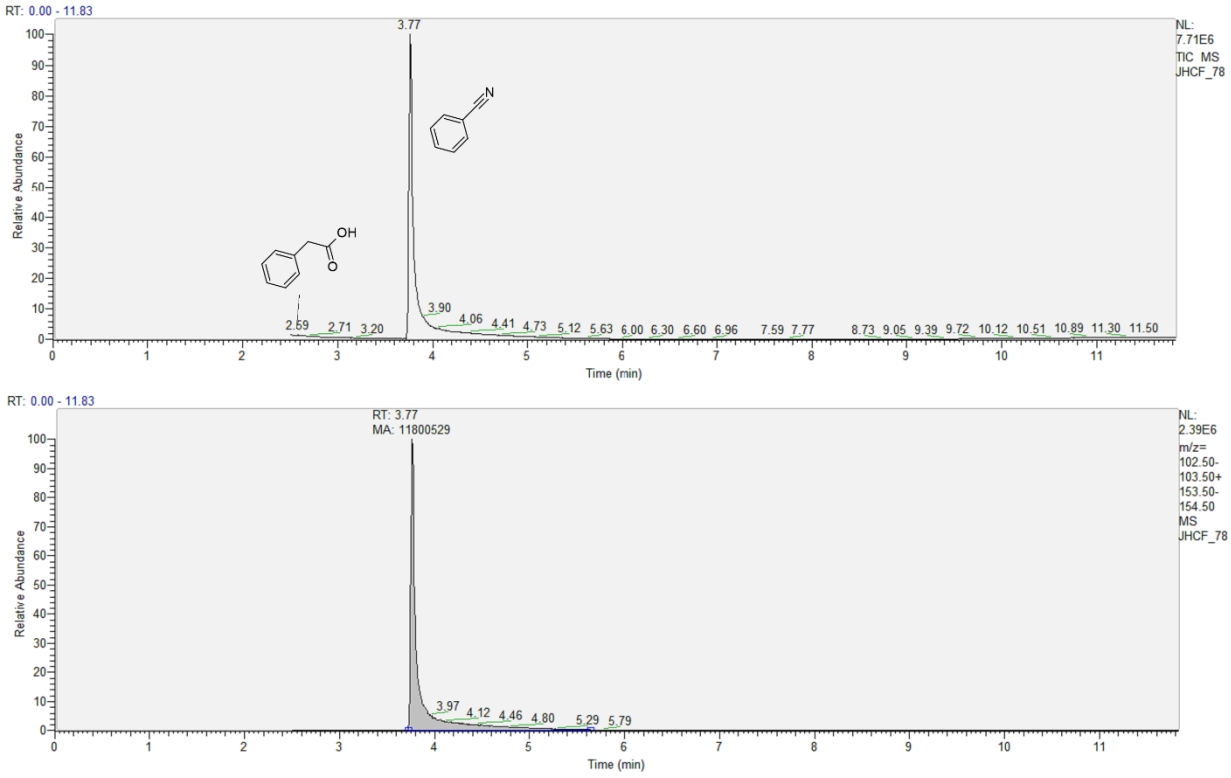
GC unfiltered and filtered chromatogram with area measurements from experiment #76



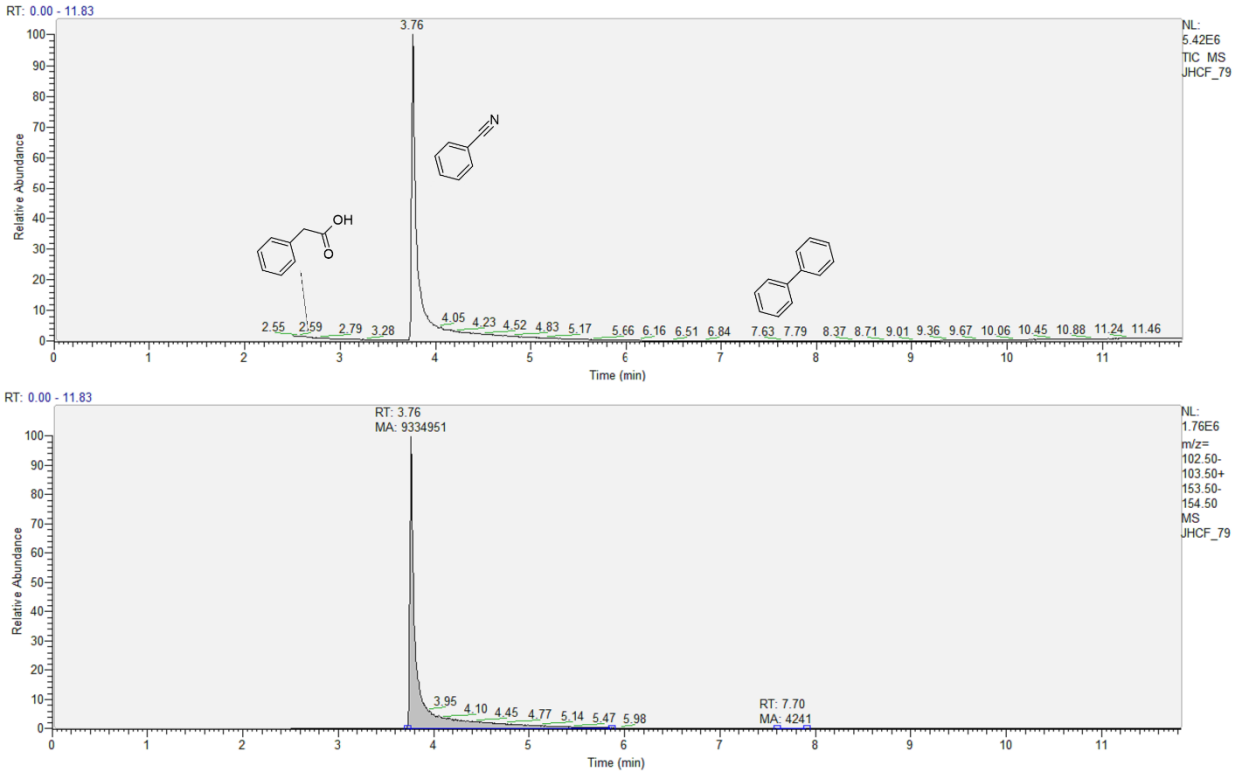
GC unfiltered and filtered chromatogram with area measurements from experiment #77



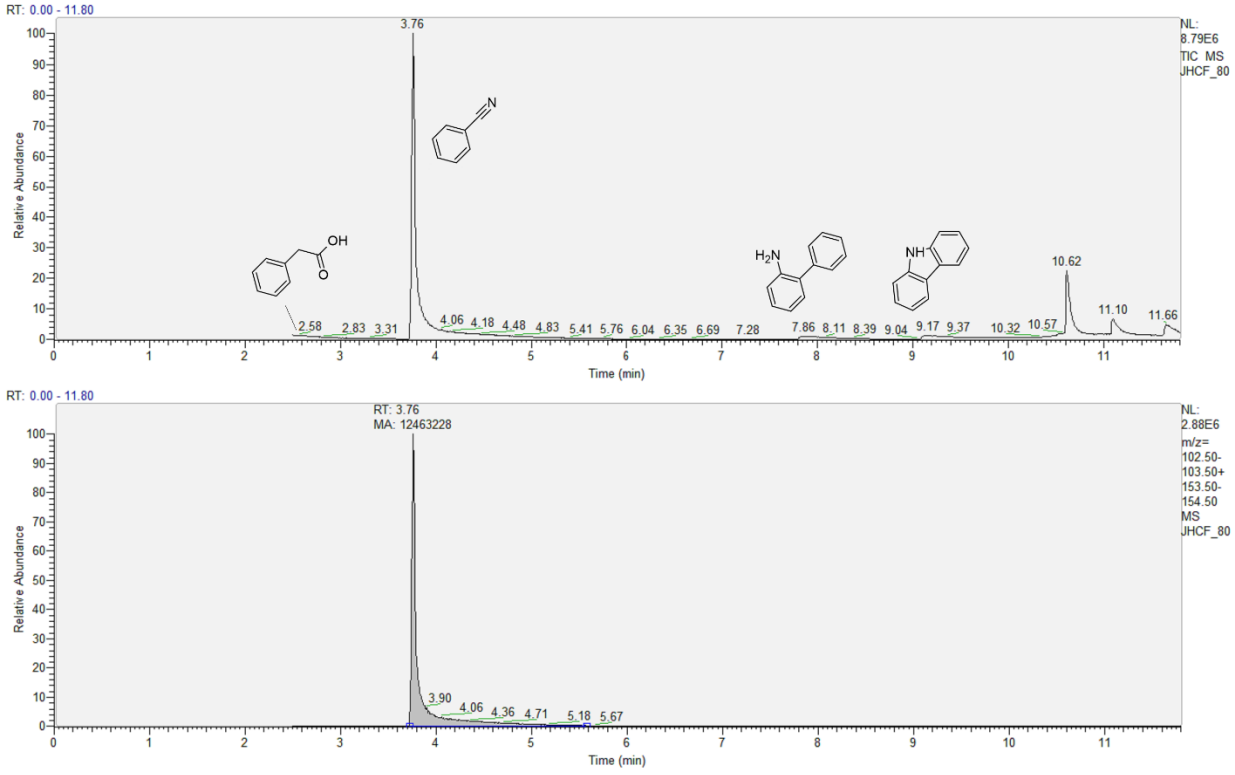
GC unfiltered and filtered chromatogram with area measurements from experiment #78



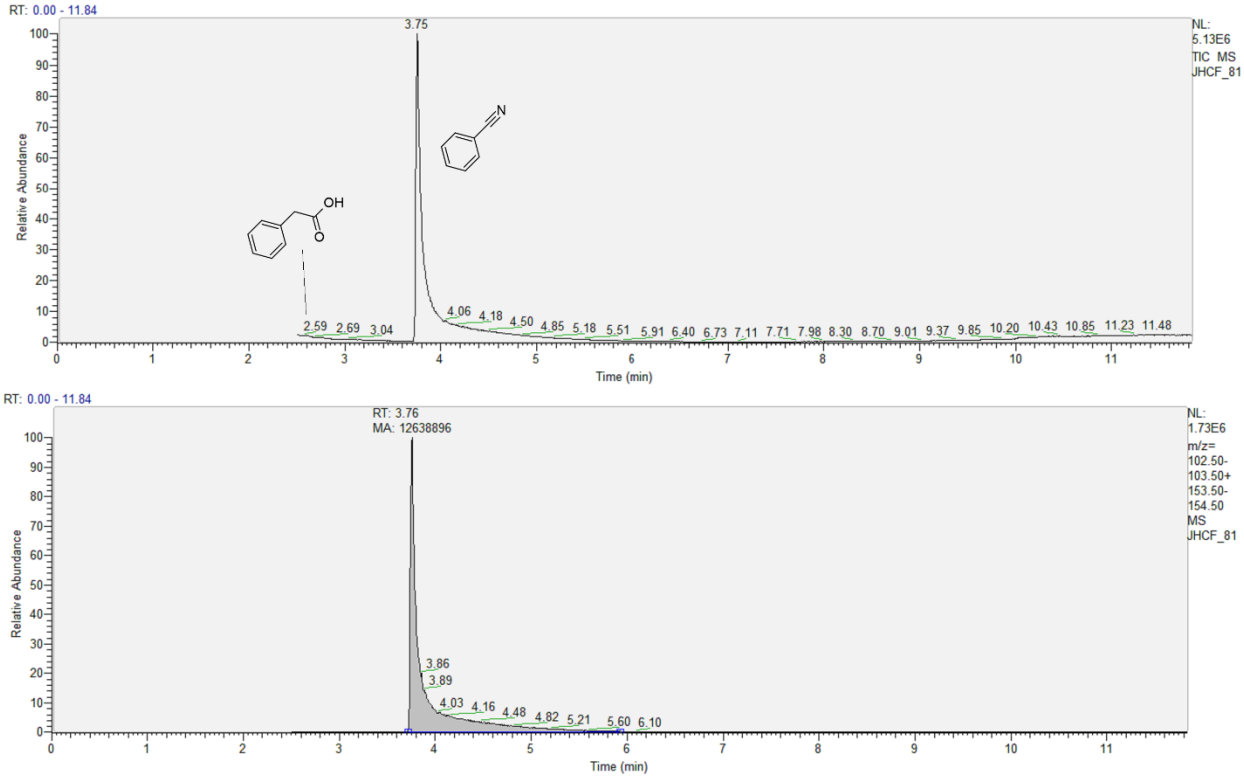
GC unfiltered and filtered chromatogram with area measurements from experiment #79



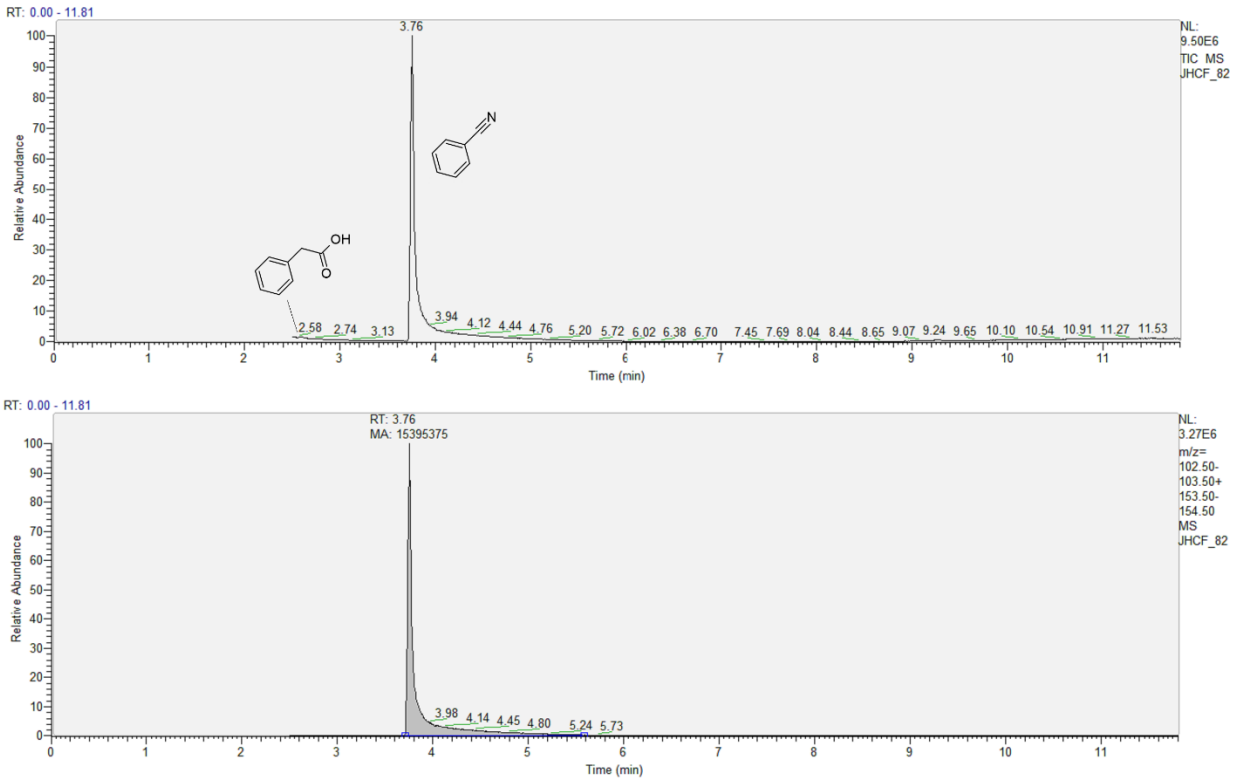
GC unfiltered and filtered chromatogram with area measurements from experiment #80



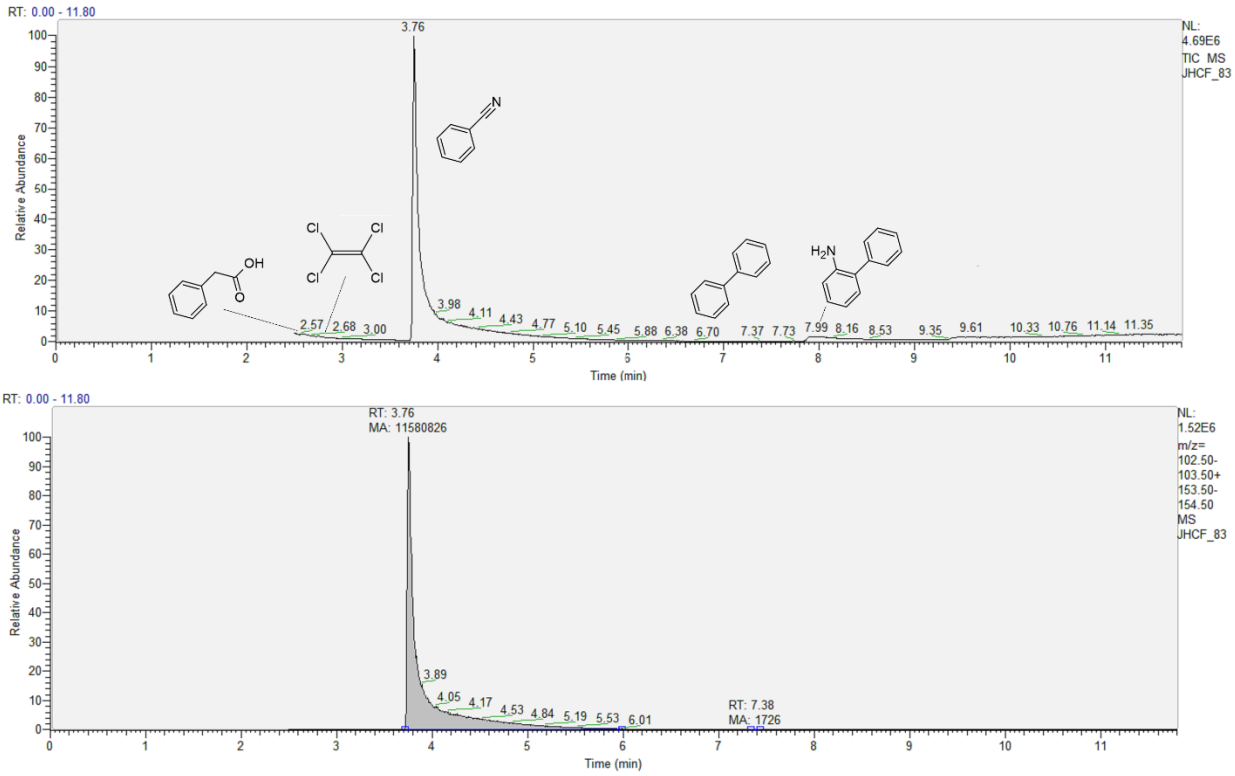
GC unfiltered and filtered chromatogram with area measurements from experiment #81



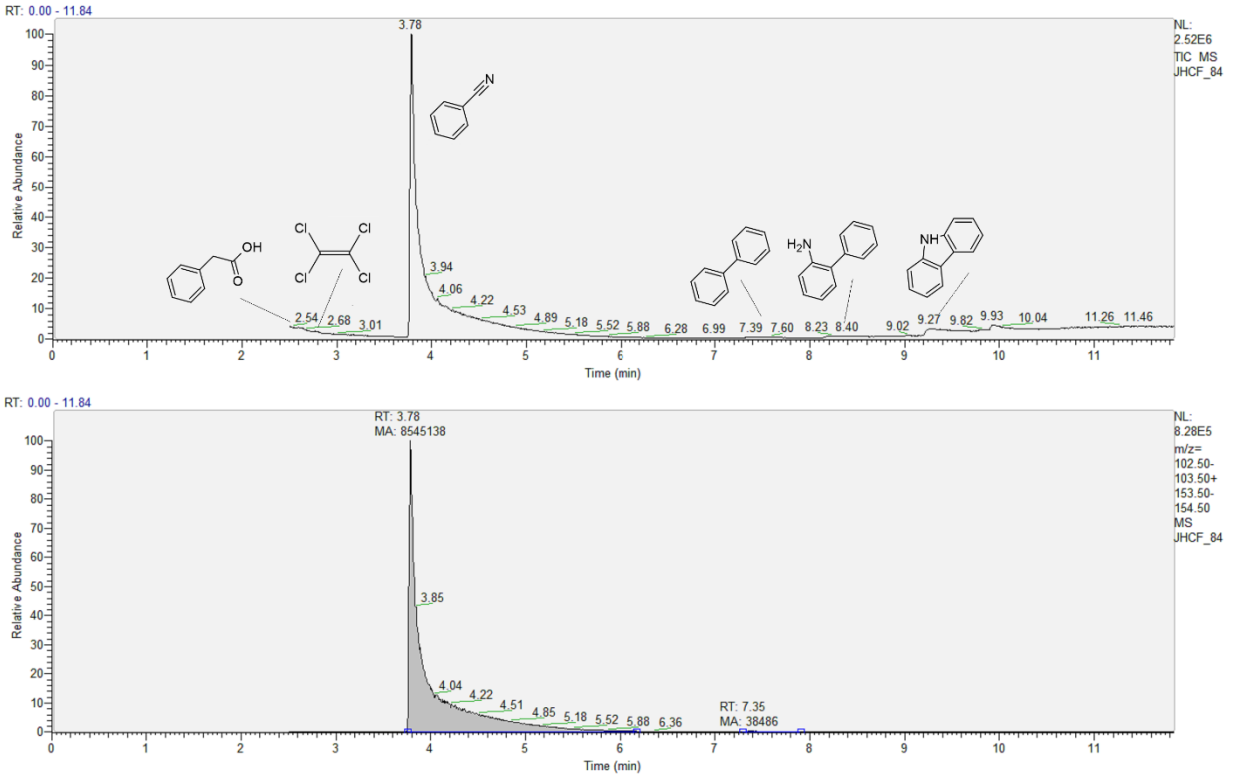
GC unfiltered and filtered chromatogram with area measurements from experiment #82



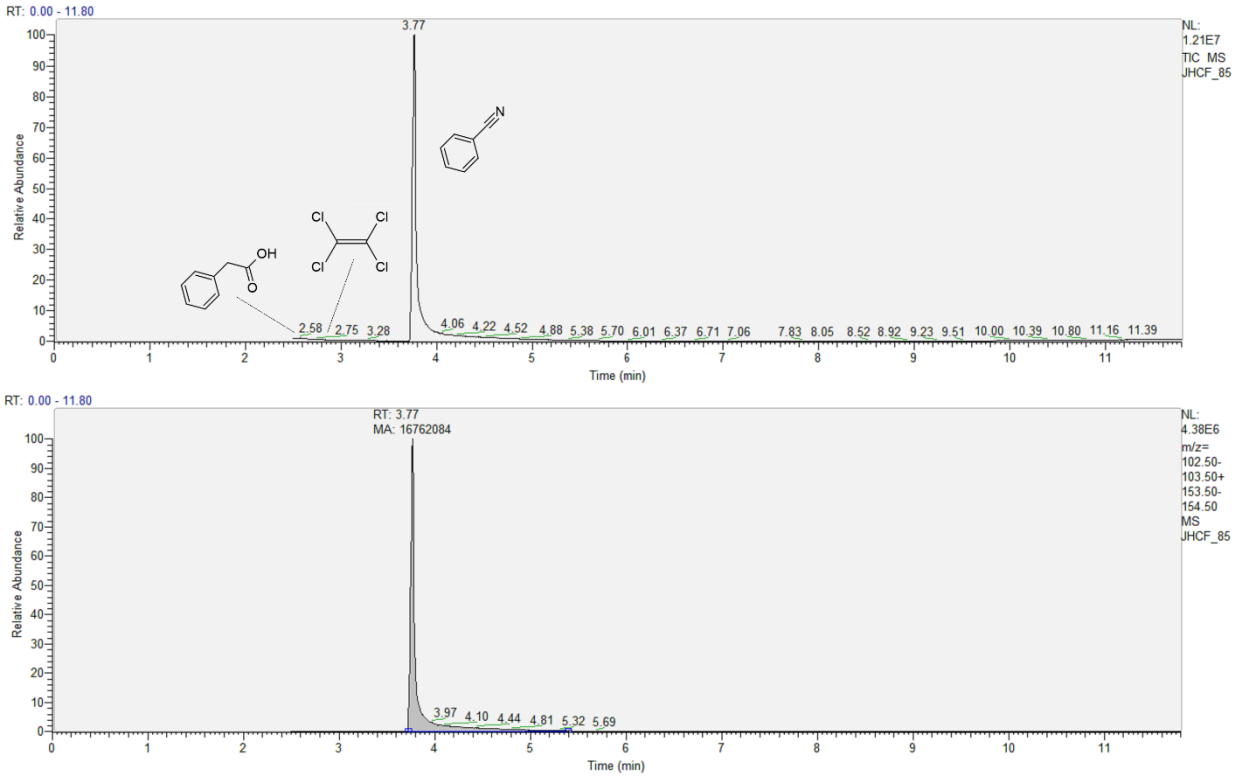
GC unfiltered and filtered chromatogram with area measurements from experiment #83



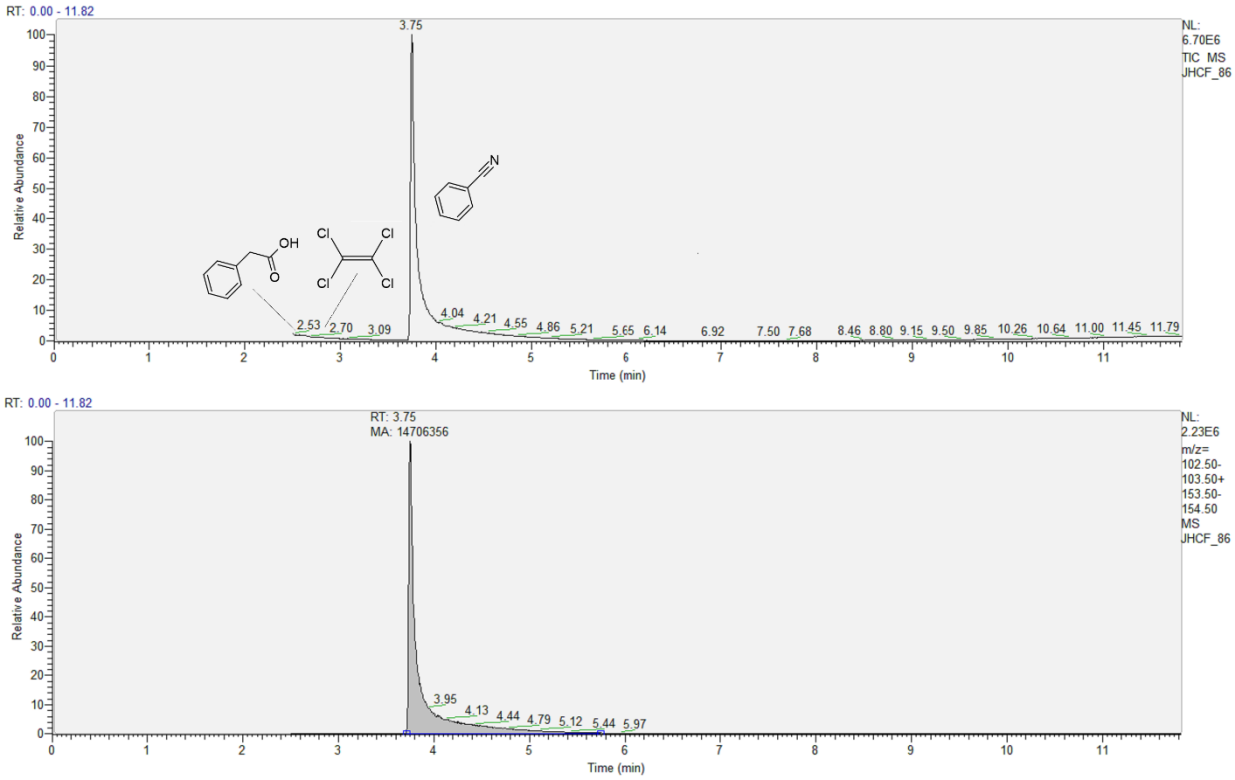
GC unfiltered and filtered chromatogram with area measurements from experiment #84



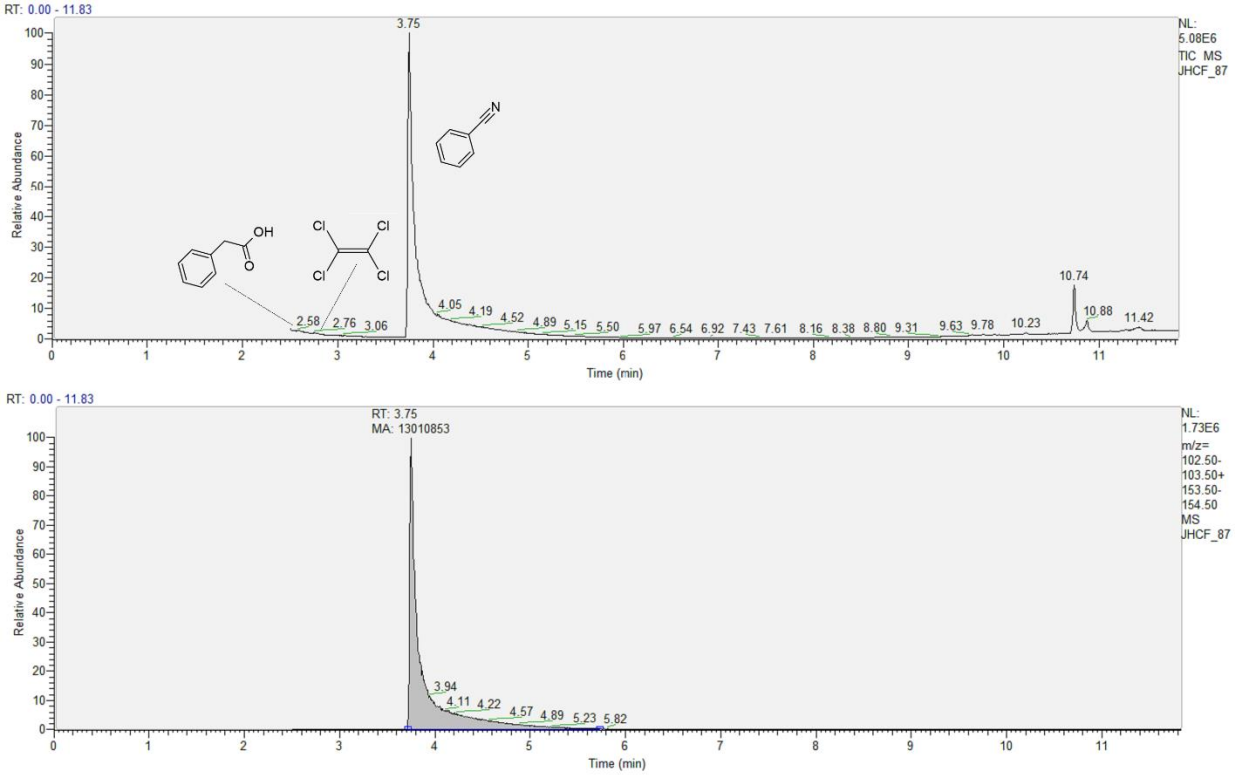
GC unfiltered and filtered chromatogram with area measurements from experiment #85



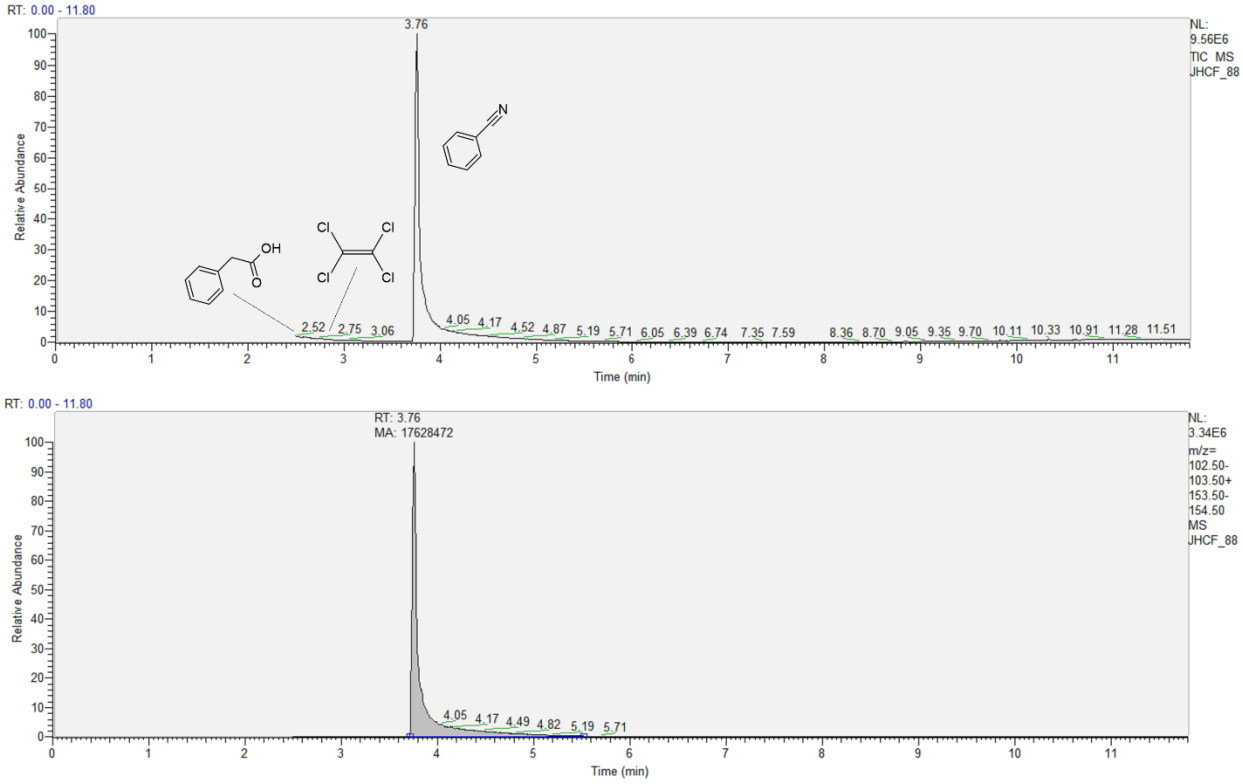
GC unfiltered and filtered chromatogram with area measurements from experiment #86



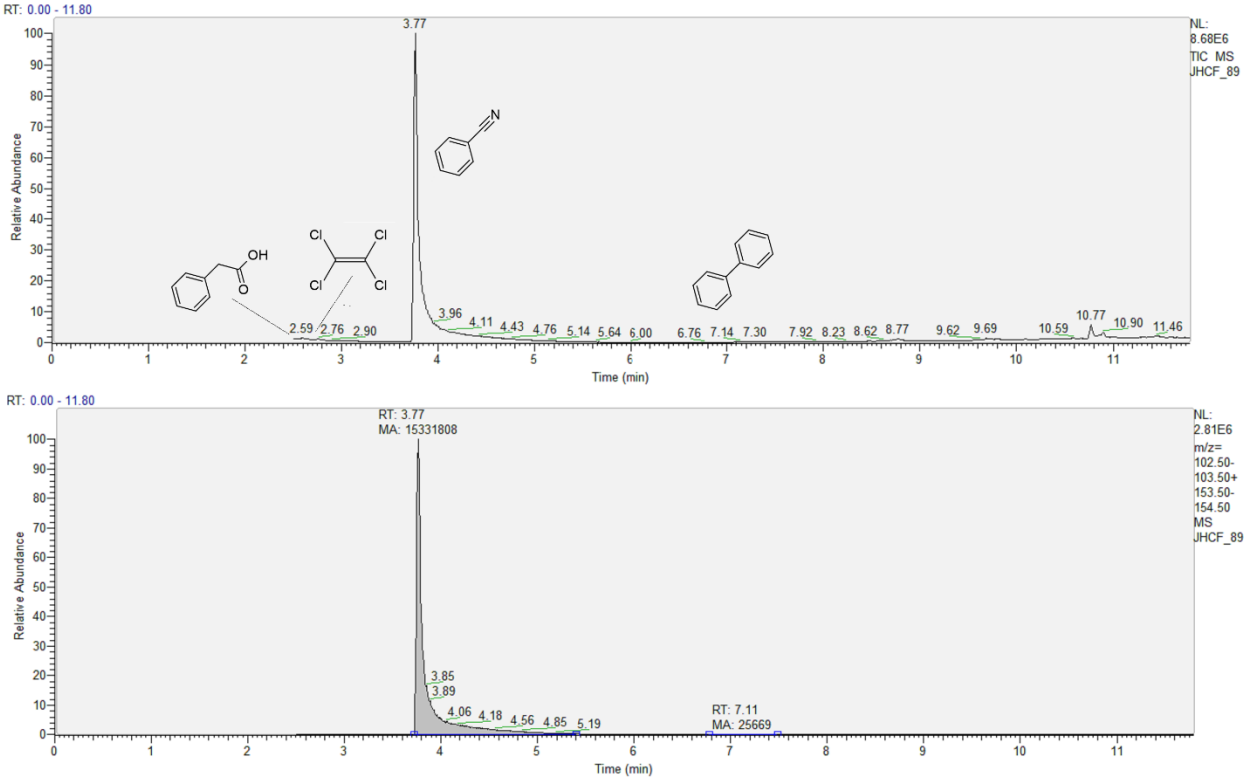
GC unfiltered and filtered chromatogram with area measurements from experiment #87



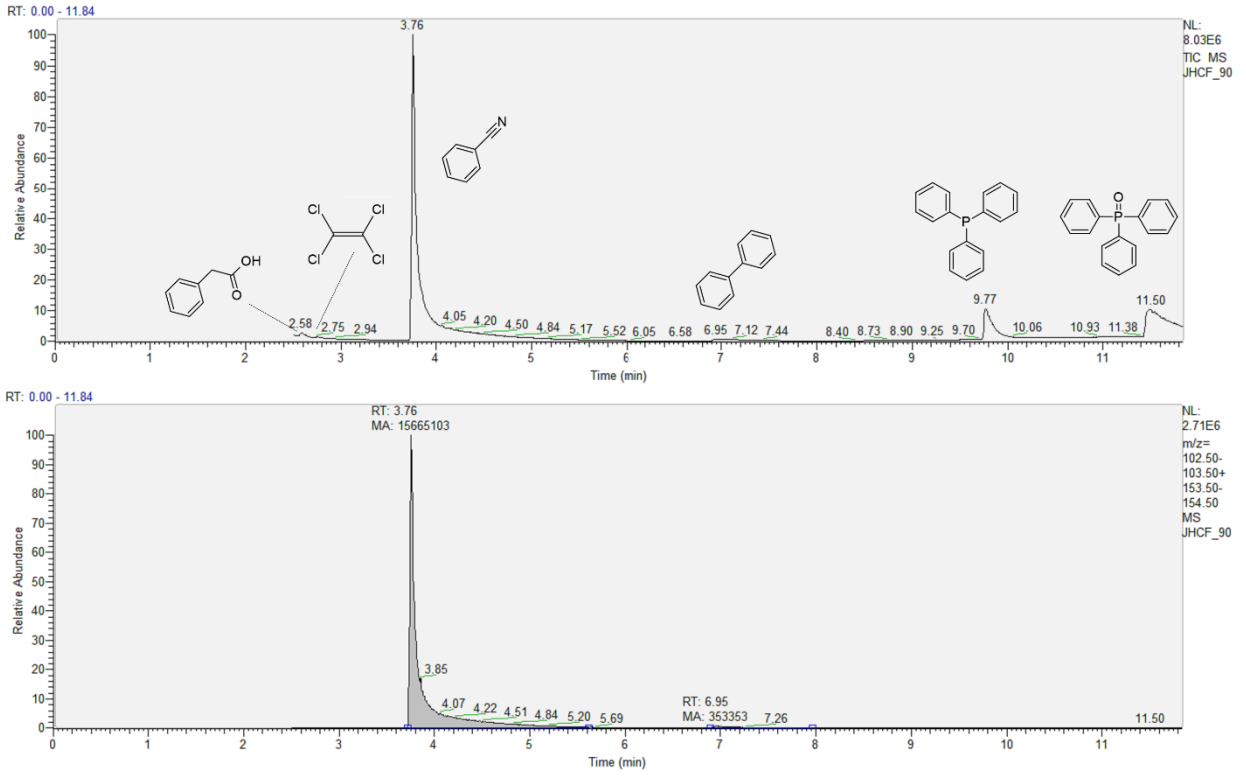
GC unfiltered and filtered chromatogram with area measurements from experiment #88



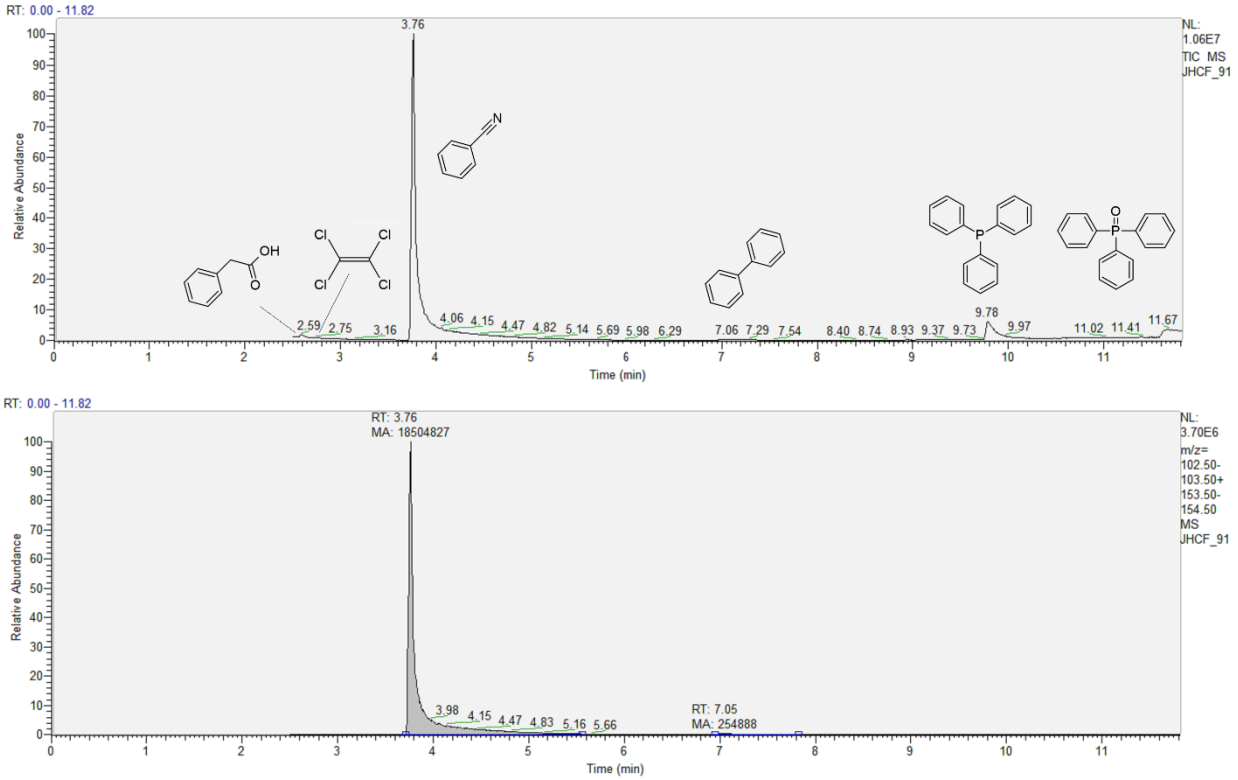
GC unfiltered and filtered chromatogram with area measurements from experiment #89



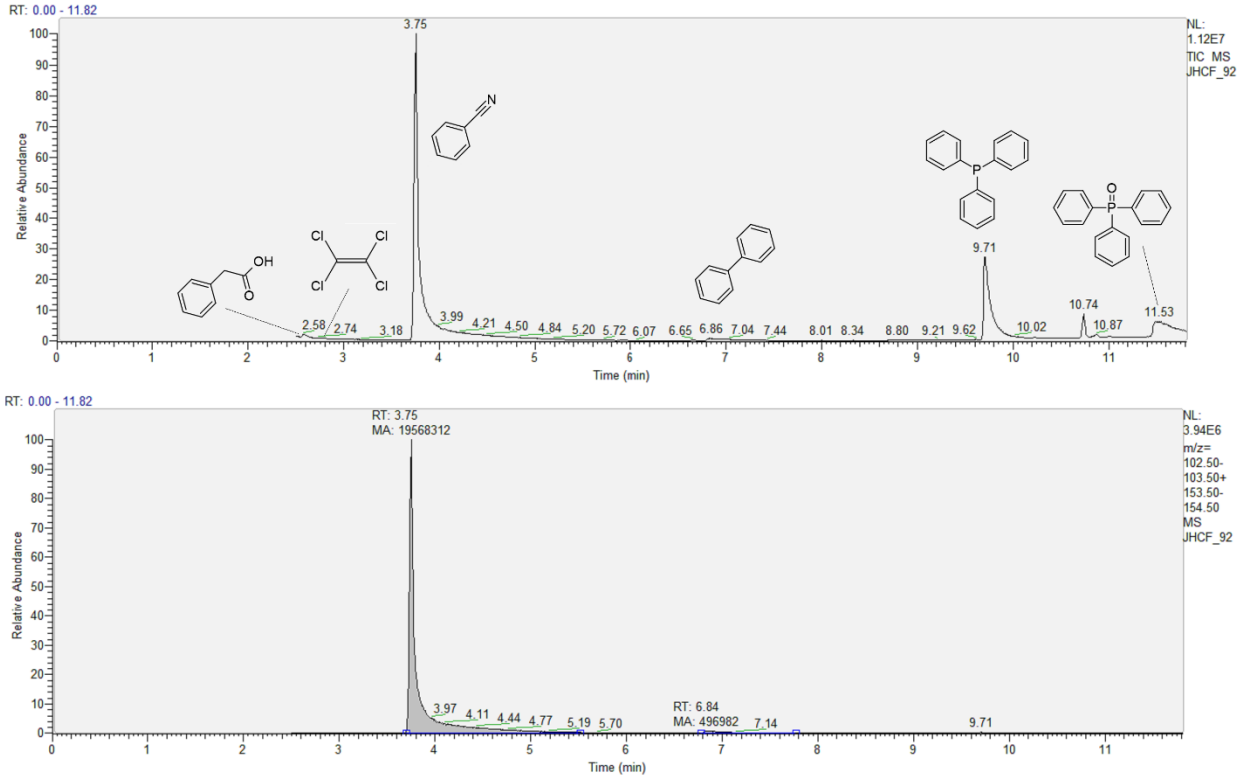
GC unfiltered and filtered chromatogram with area measurements from experiment #90



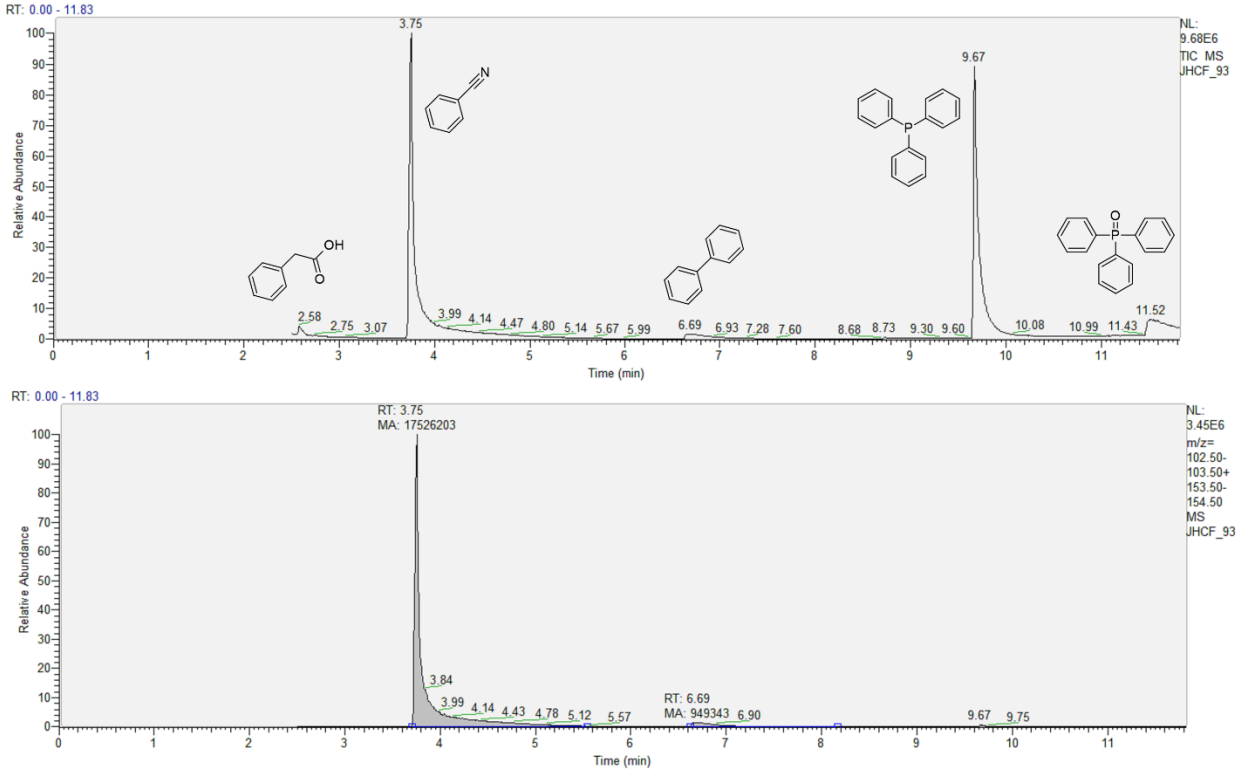
GC unfiltered and filtered chromatogram with area measurements from experiment #91



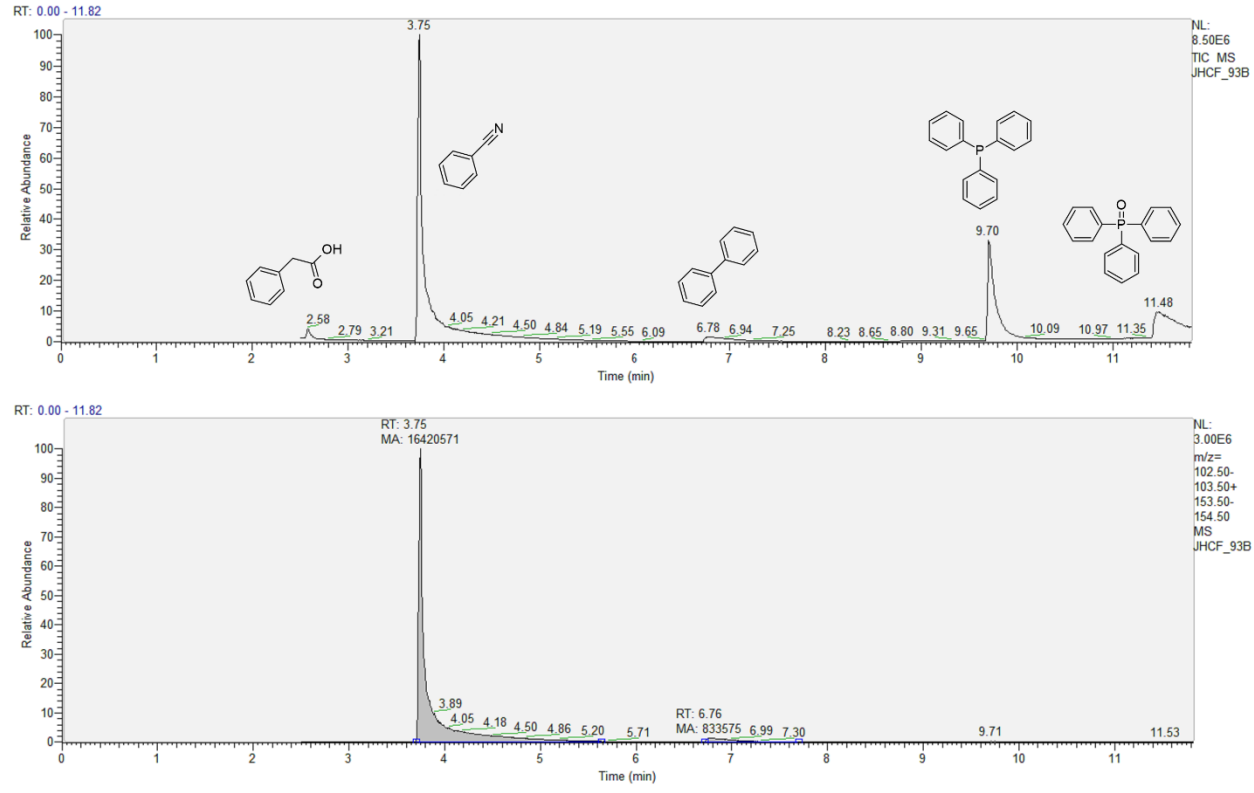
GC unfiltered and filtered chromatogram with area measurements from experiment #92



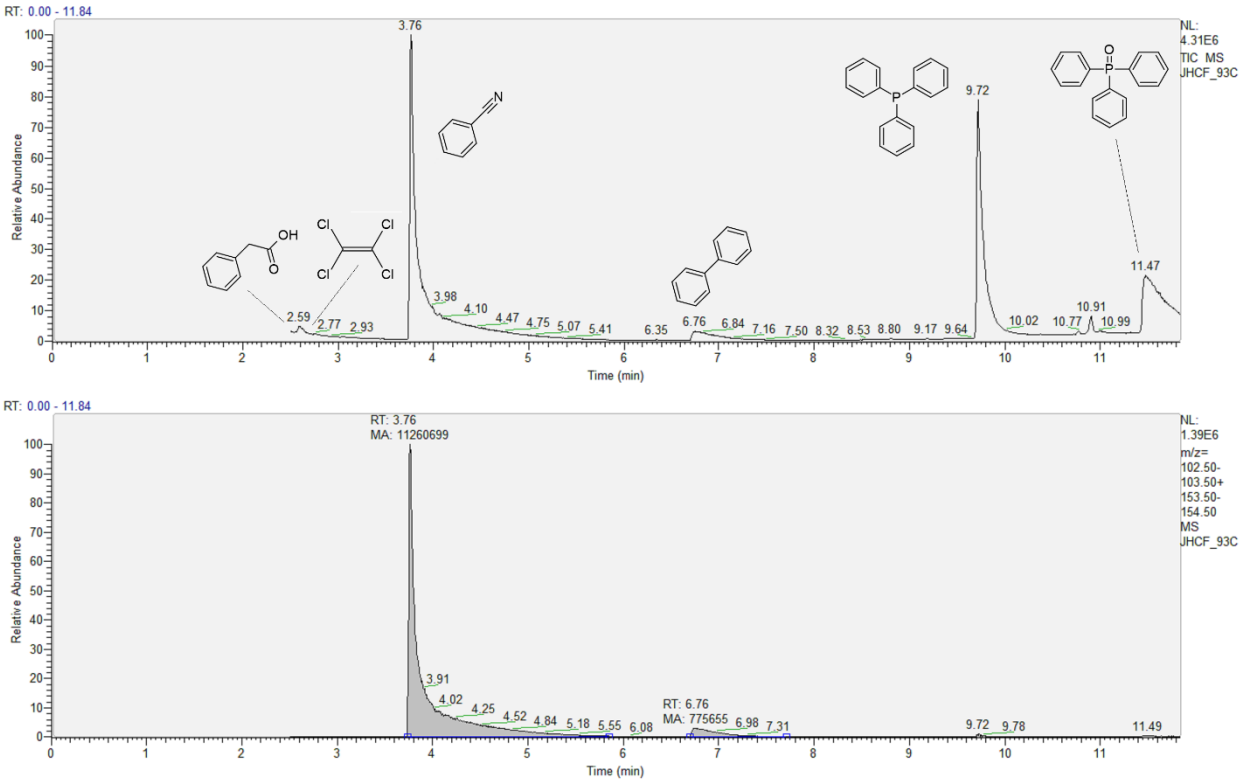
GC unfiltered and filtered chromatogram with area measurements from experiment #93A



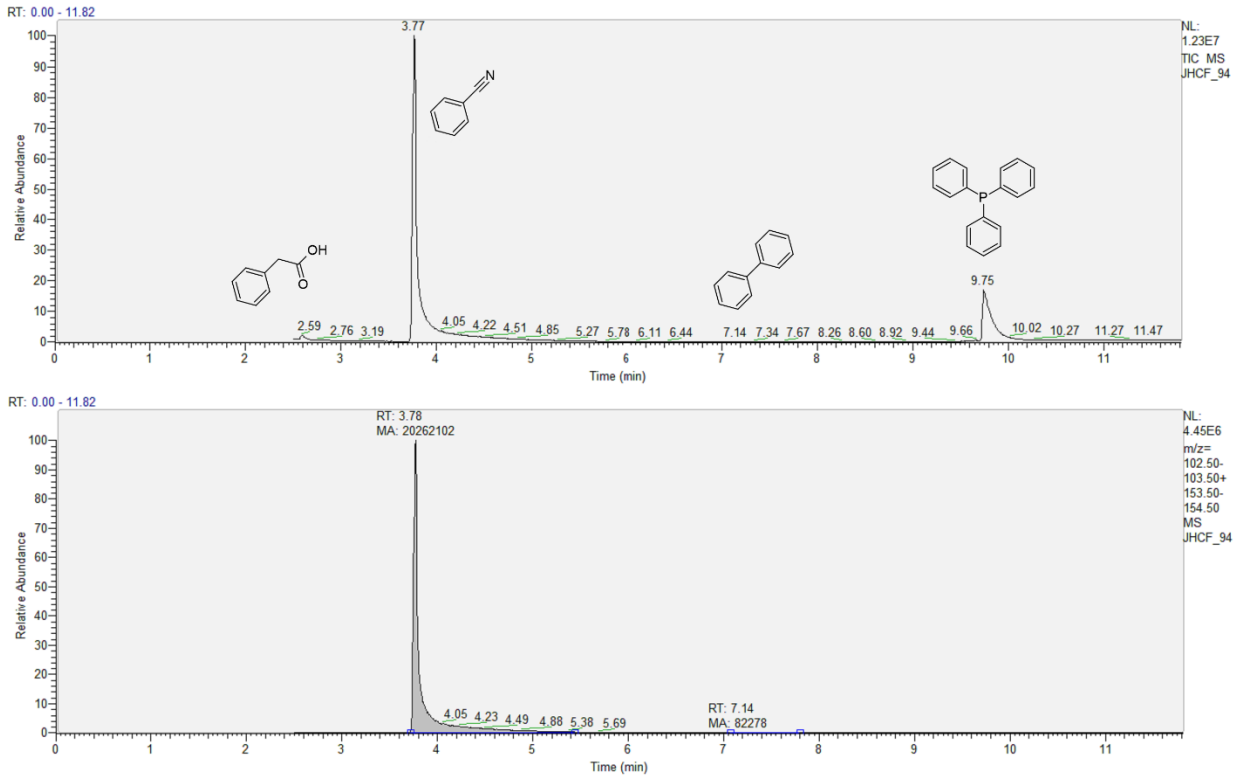
GC unfiltered and filtered chromatogram with area measurements from experiment #93B



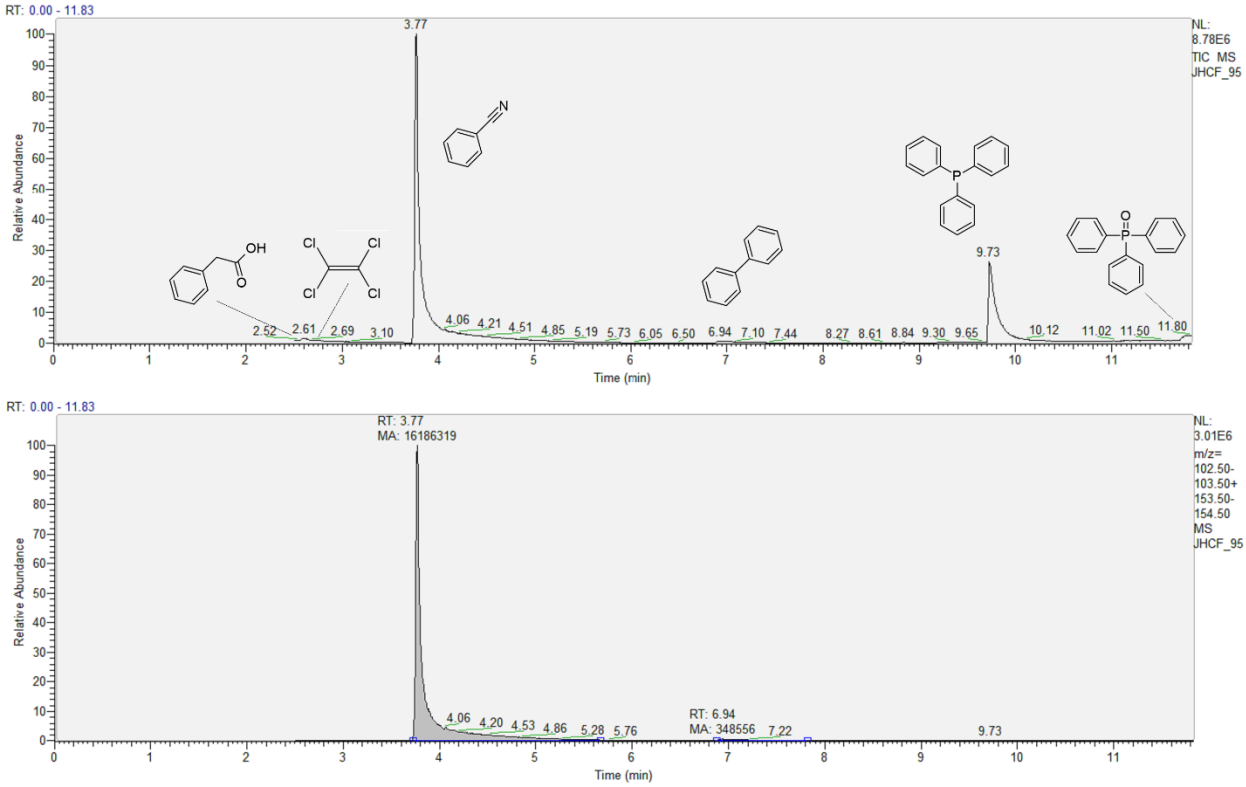
GC unfiltered and filtered chromatogram with area measurements from experiment #93C



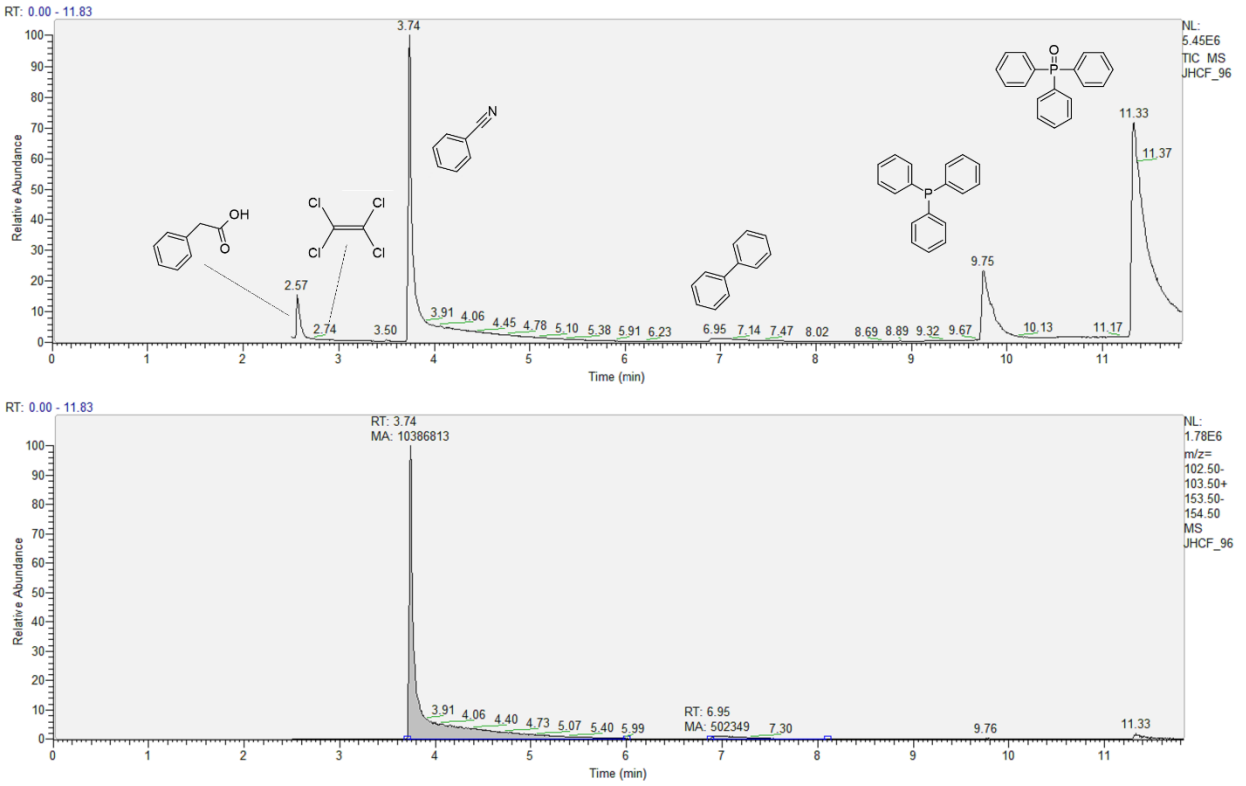
GC unfiltered and filtered chromatogram with area measurements from experiment #94



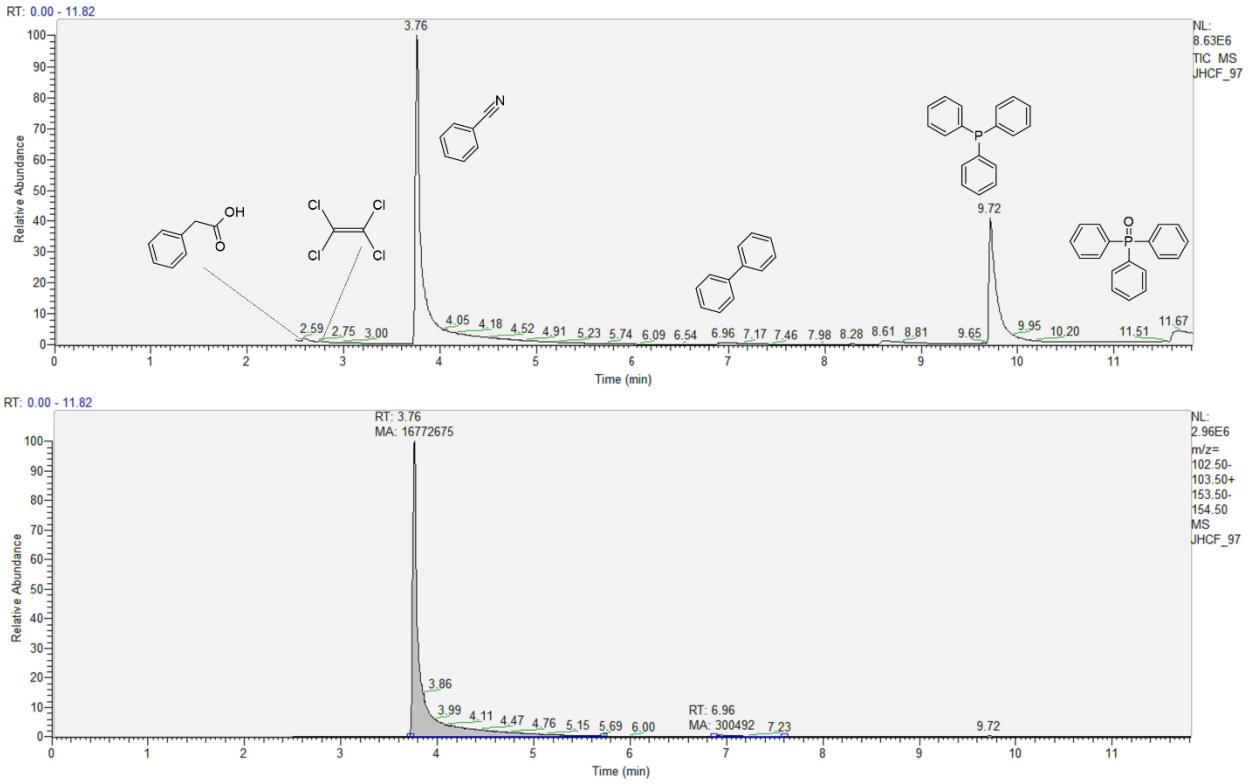
GC unfiltered and filtered chromatogram with area measurements from experiment #95



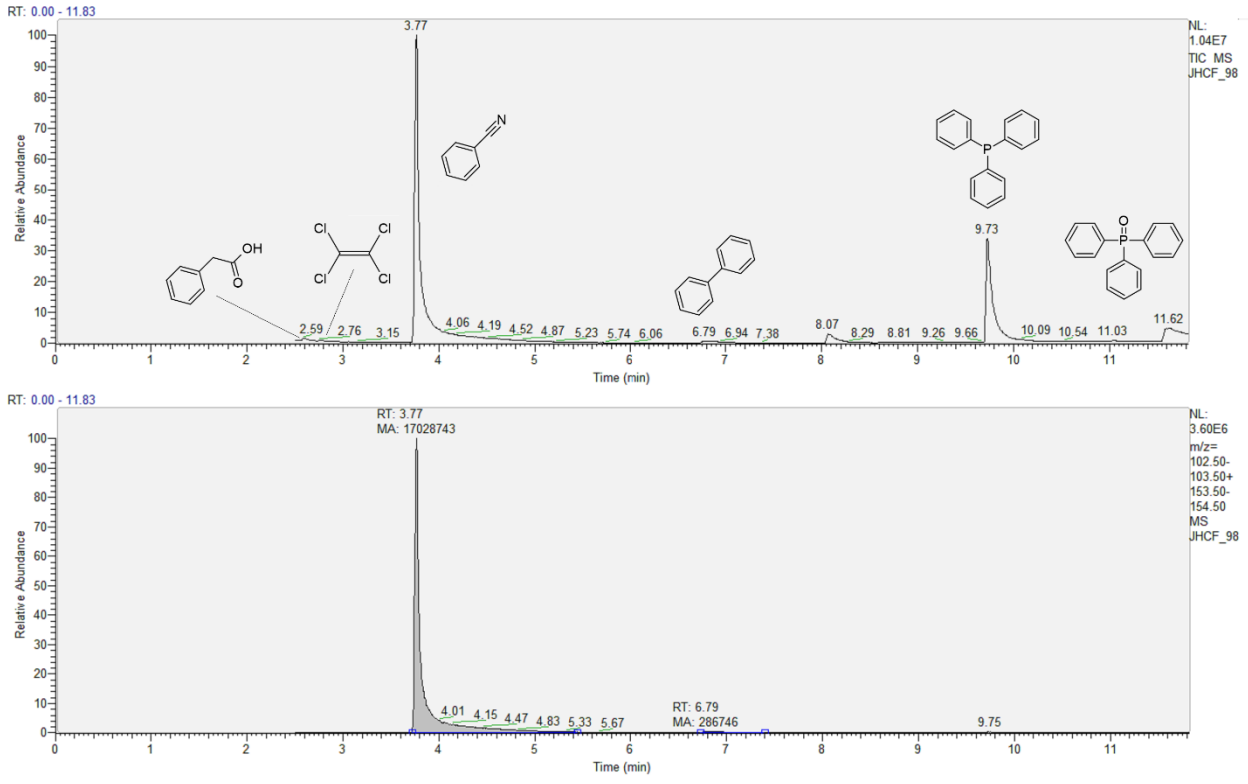
GC unfiltered and filtered chromatogram with area measurements from experiment #96



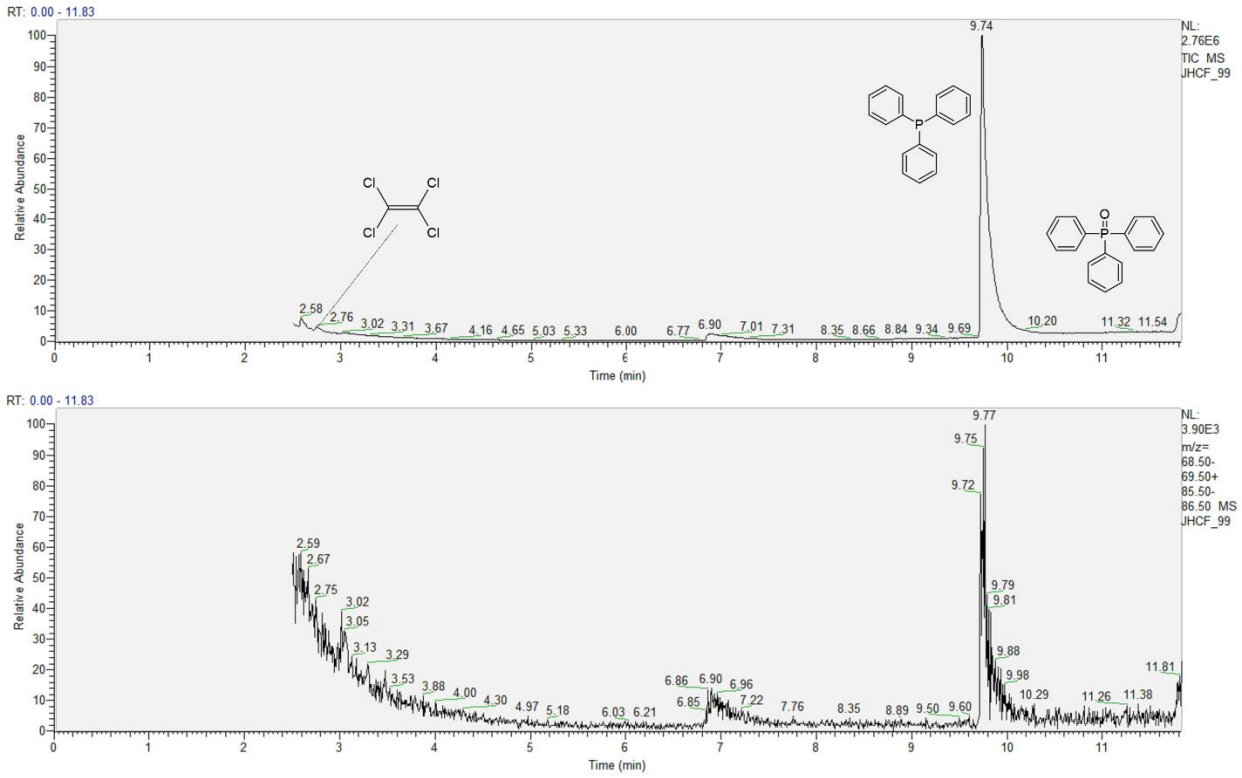
GC unfiltered and filtered chromatogram with area measurements from experiment #97



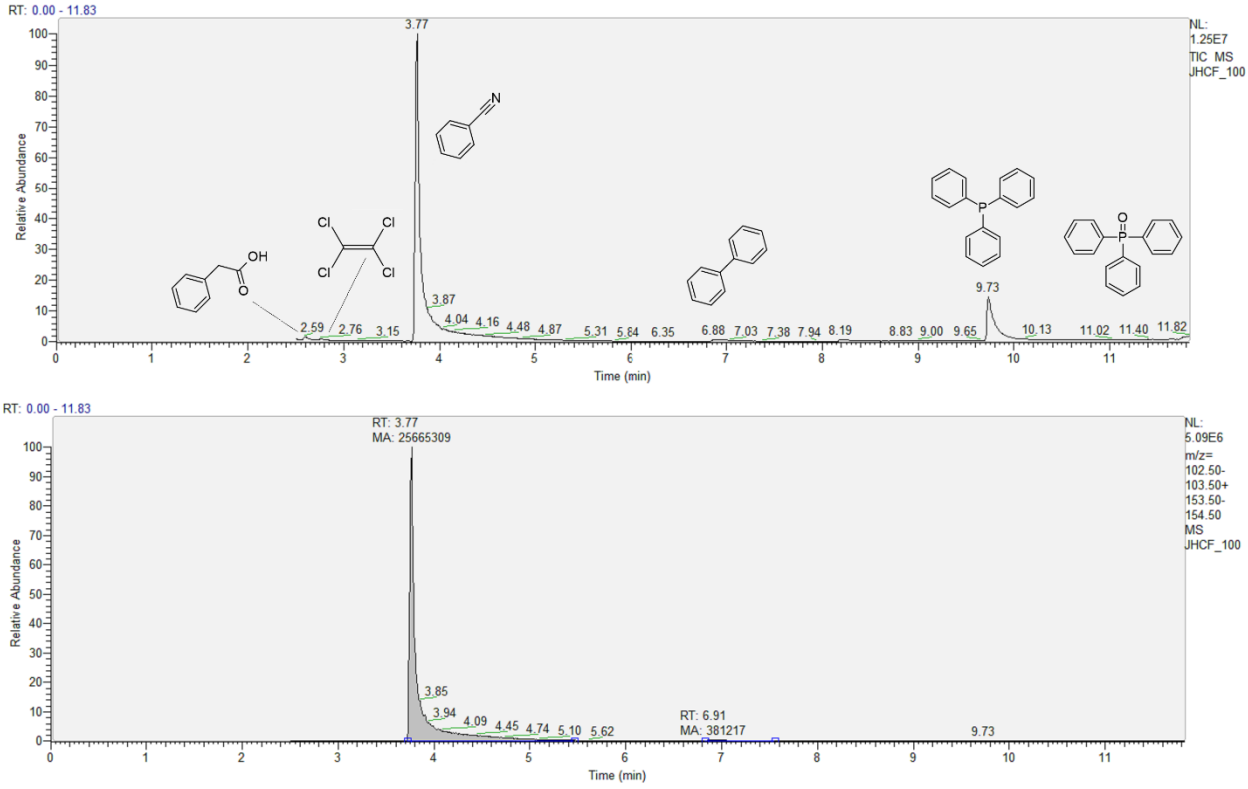
GC unfiltered and filtered chromatogram with area measurements from experiment #98



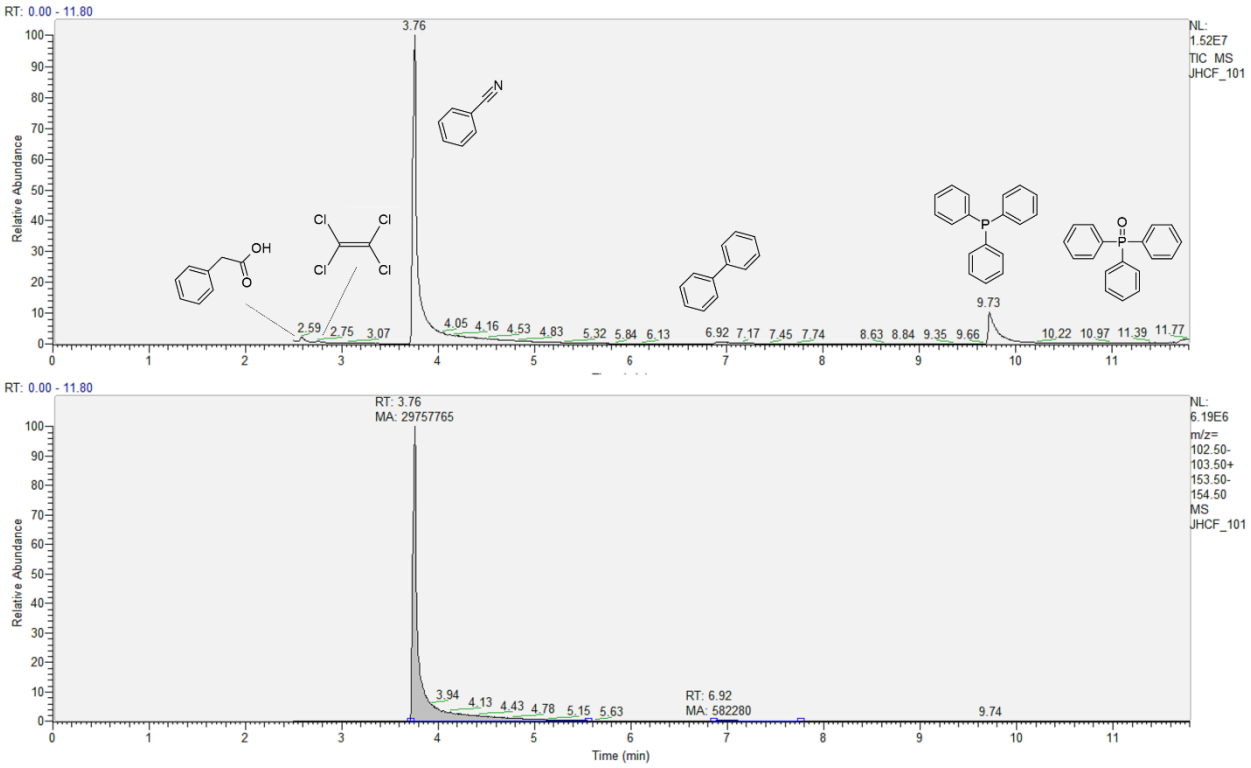
GC unfiltered and filtered chromatogram with area measurements from experiment #99



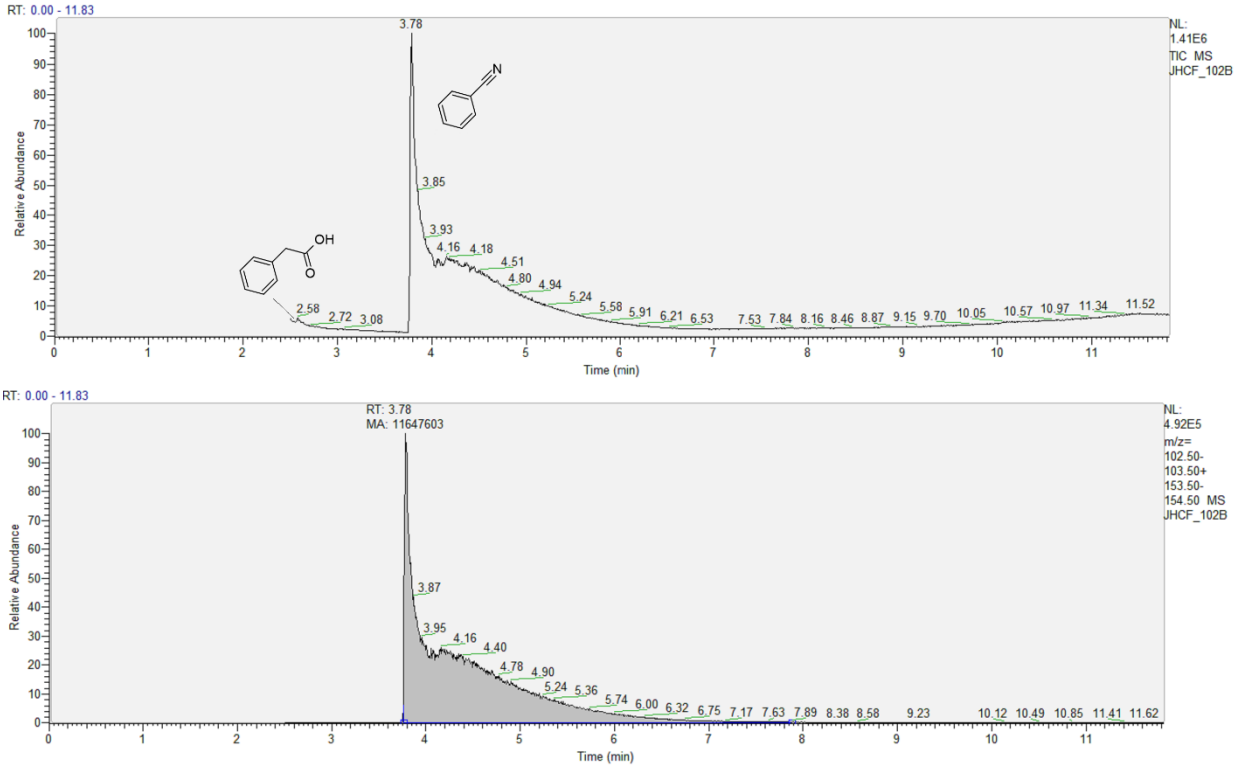
GC unfiltered and filtered chromatogram with area measurements from experiment #100



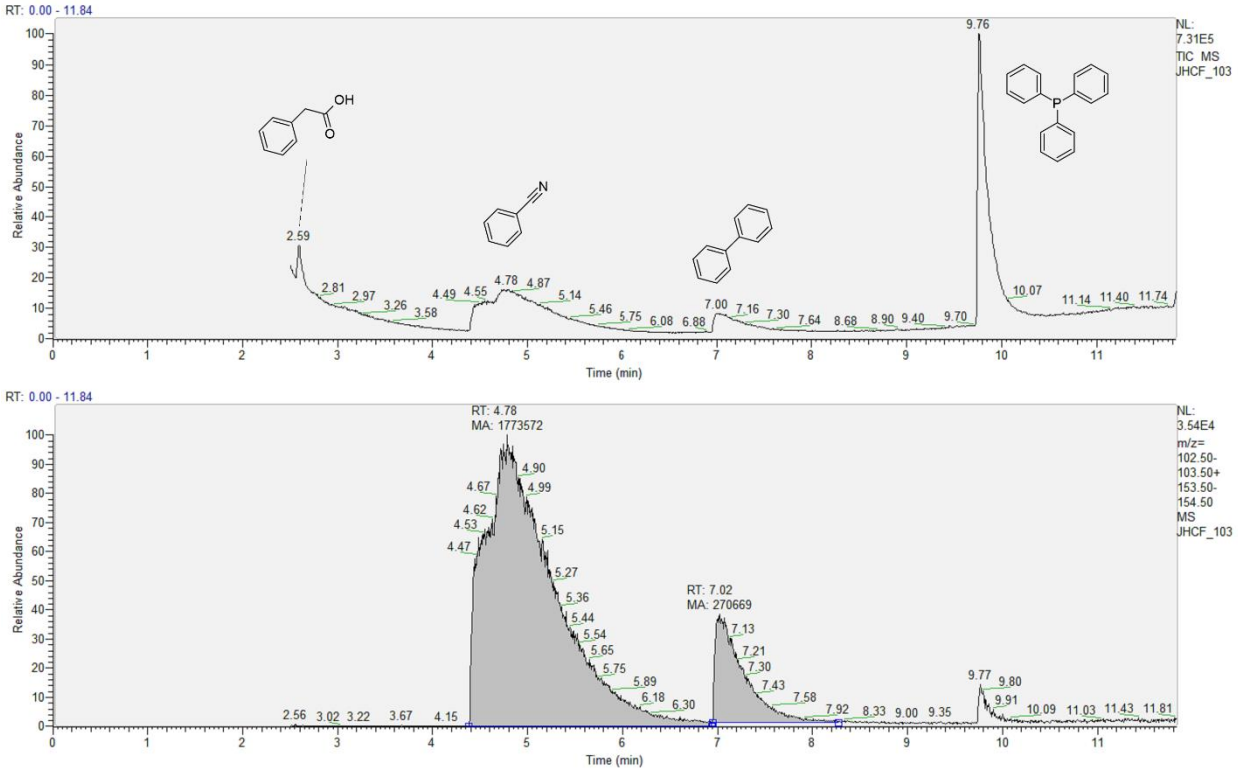
GC unfiltered and filtered chromatogram with area measurements from experiment #101



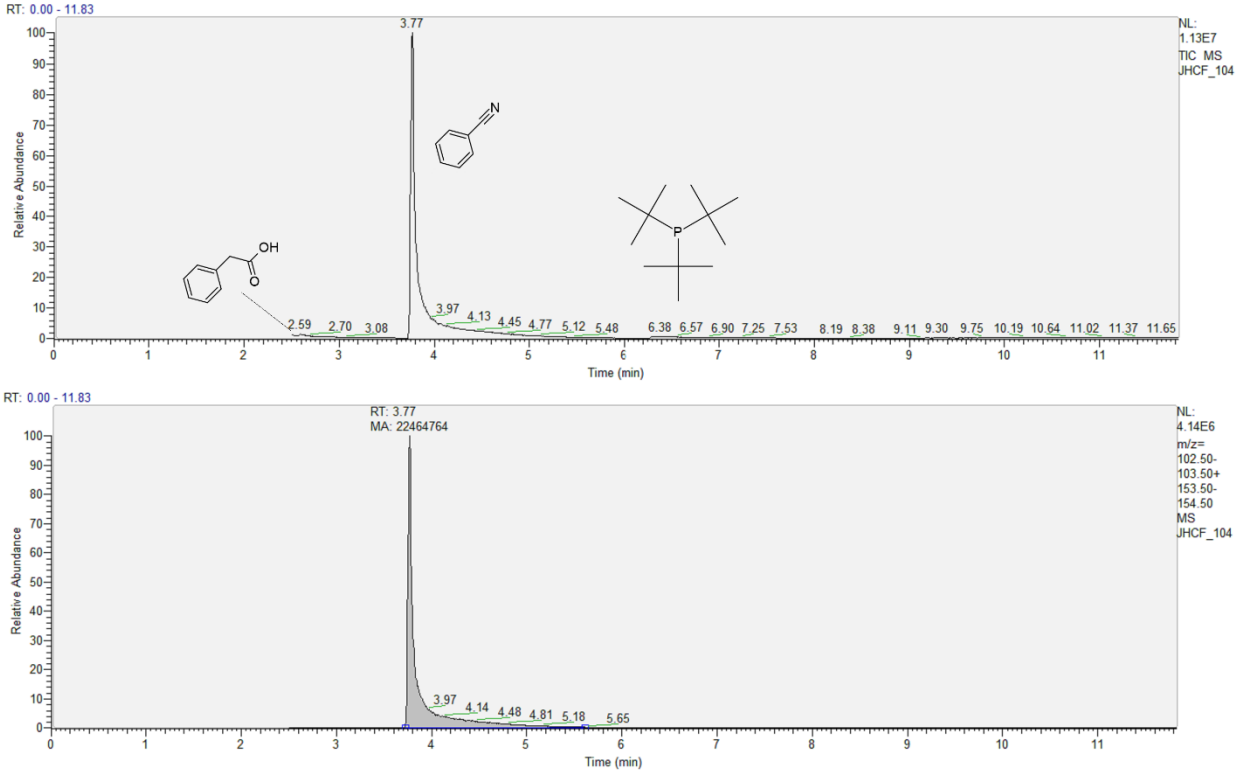
GC unfiltered and filtered chromatogram with area measurements from experiment #102



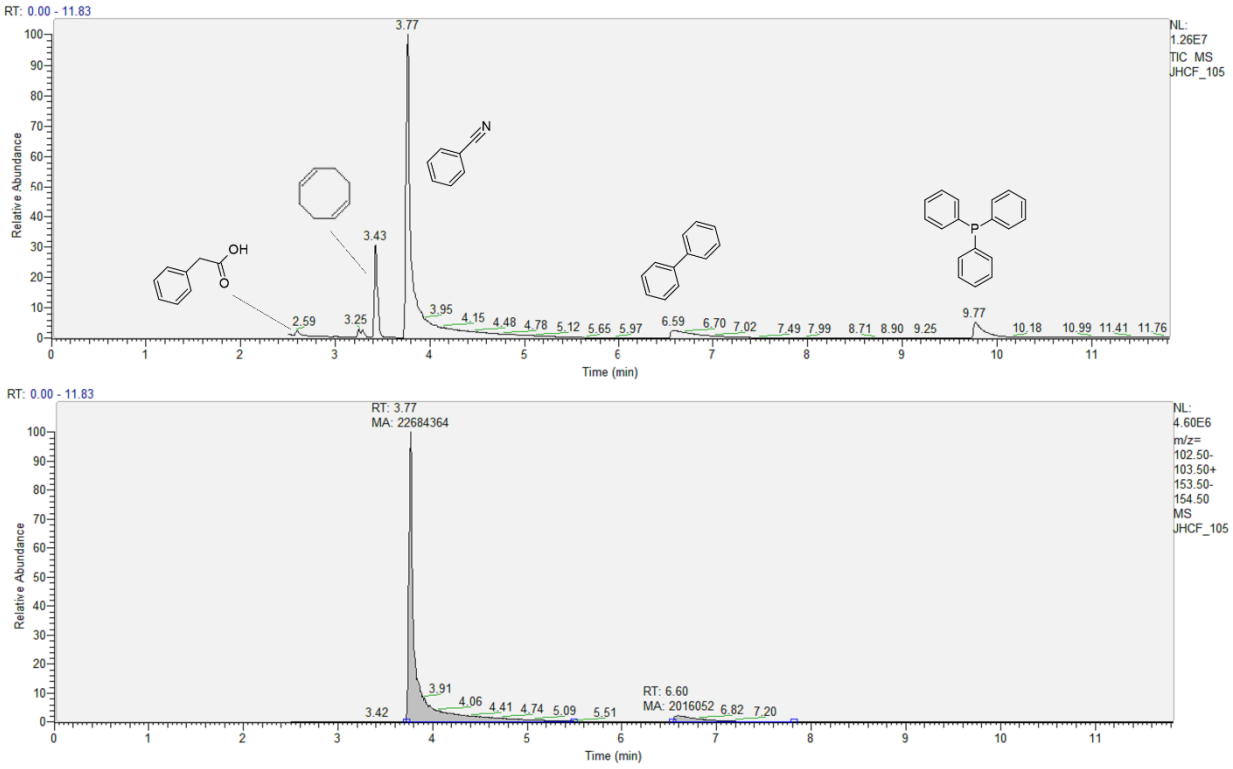
GC unfiltered and filtered chromatogram with area measurements from experiment #103



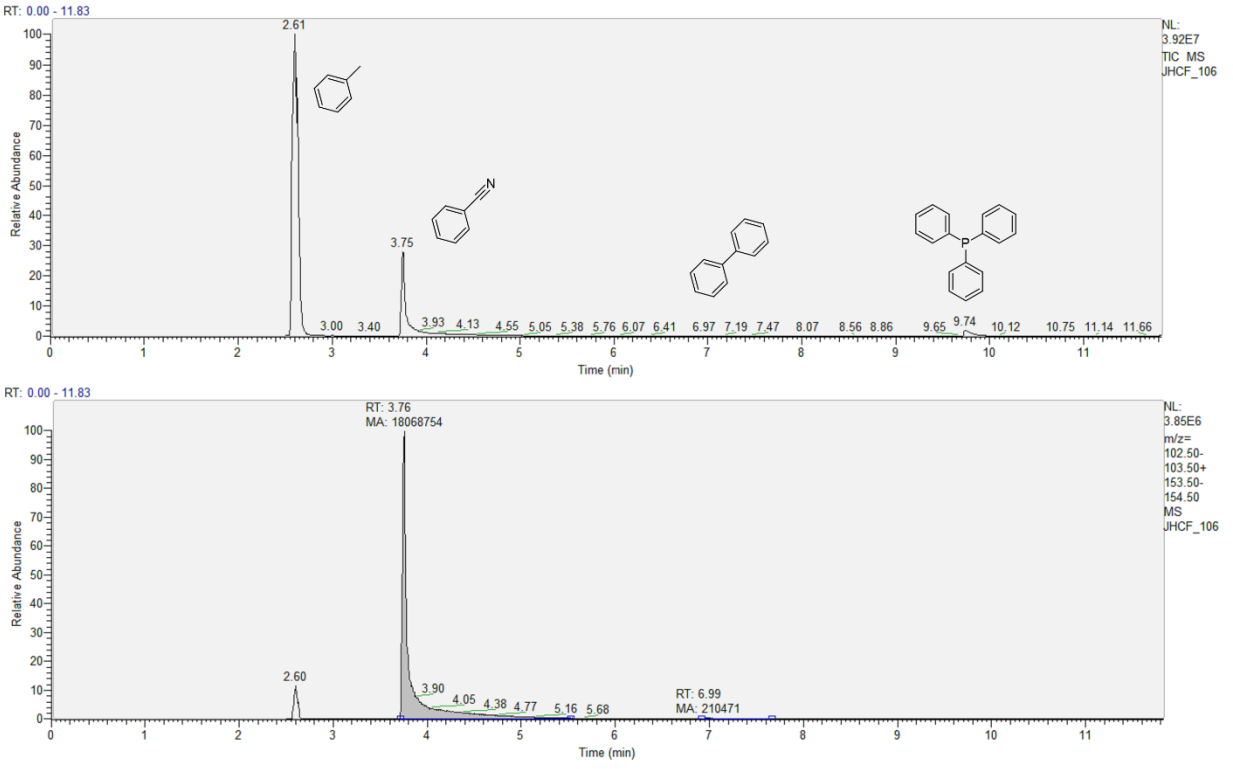
GC unfiltered and filtered chromatogram with area measurements from experiment #104



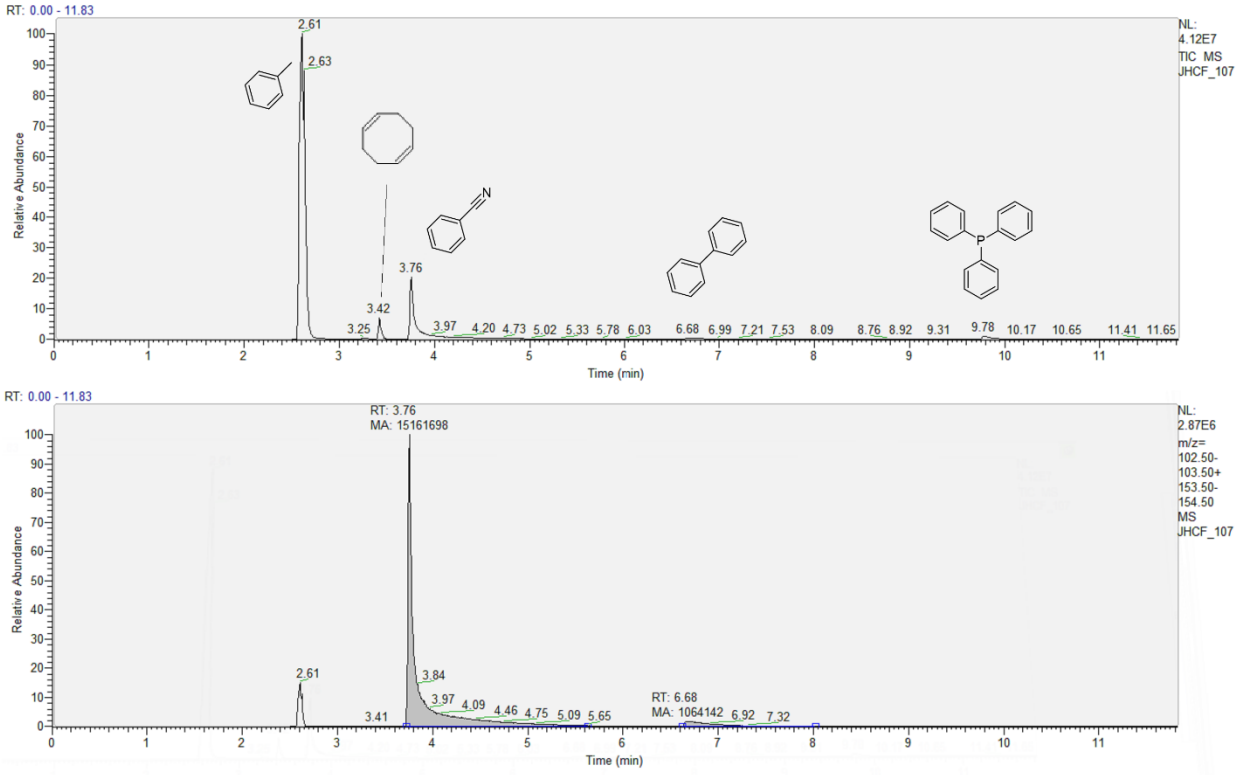
GC unfiltered and filtered chromatogram with area measurements from experiment #105



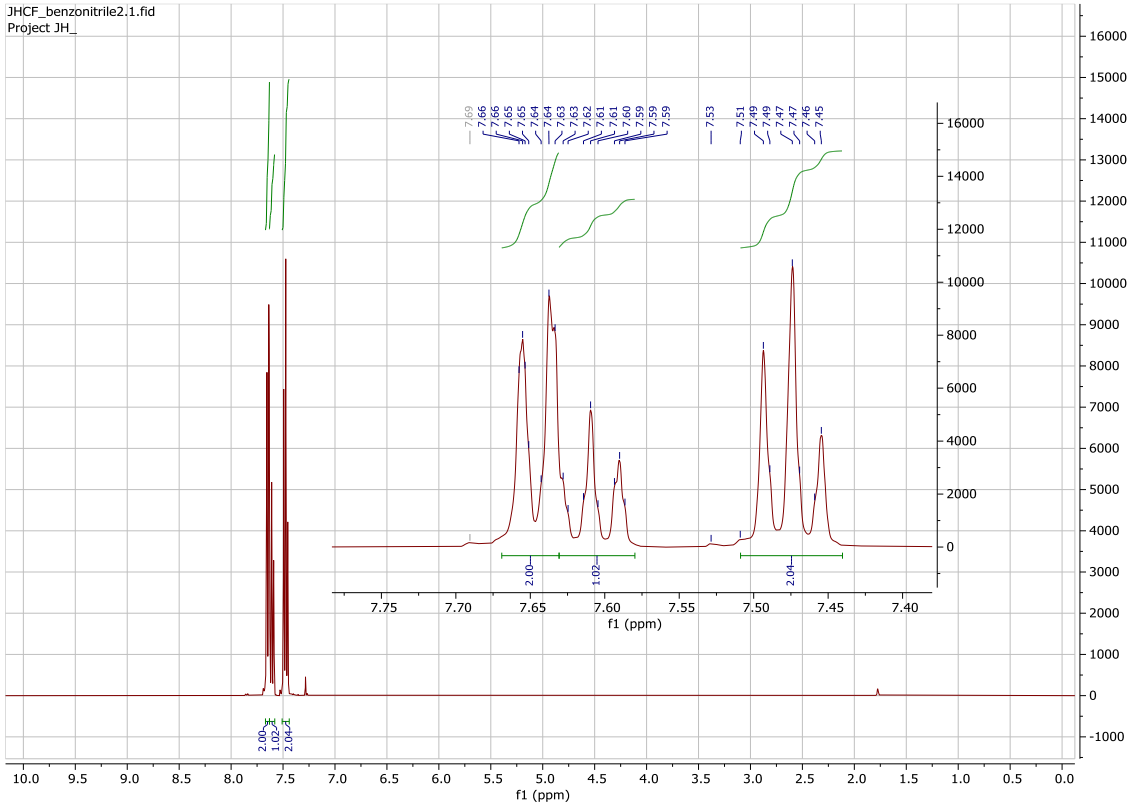
GC unfiltered and filtered chromatogram with area measurements from experiment #106



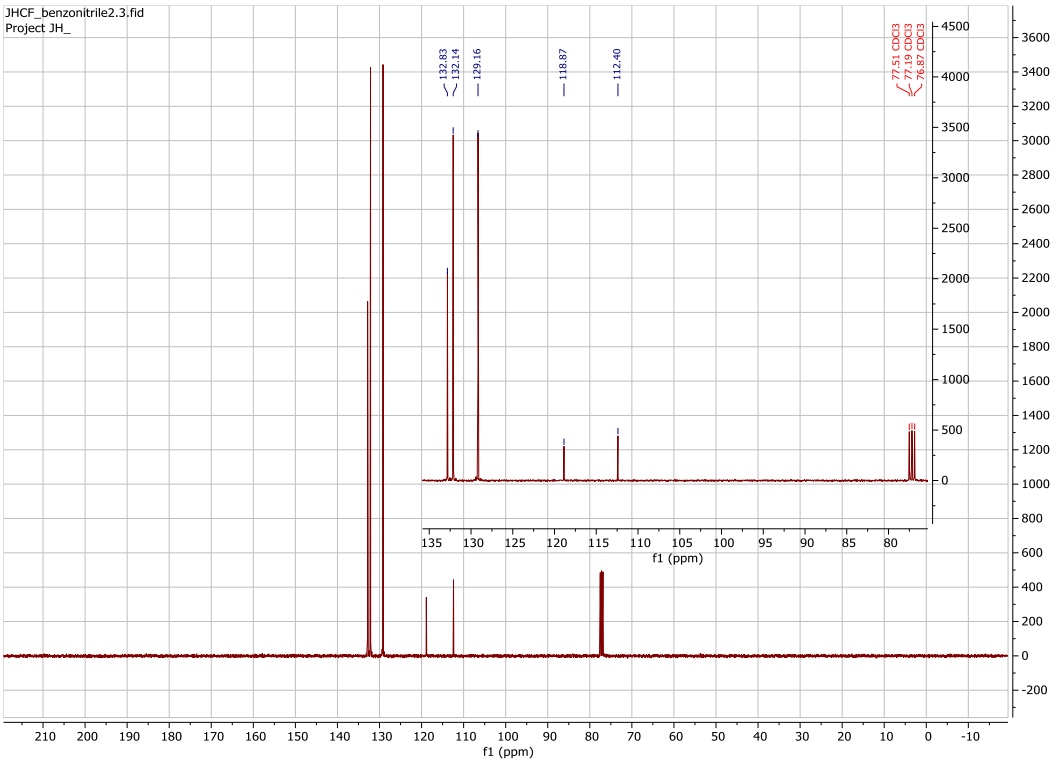
GC unfiltered and filtered chromatogram with area measurements from experiment #107



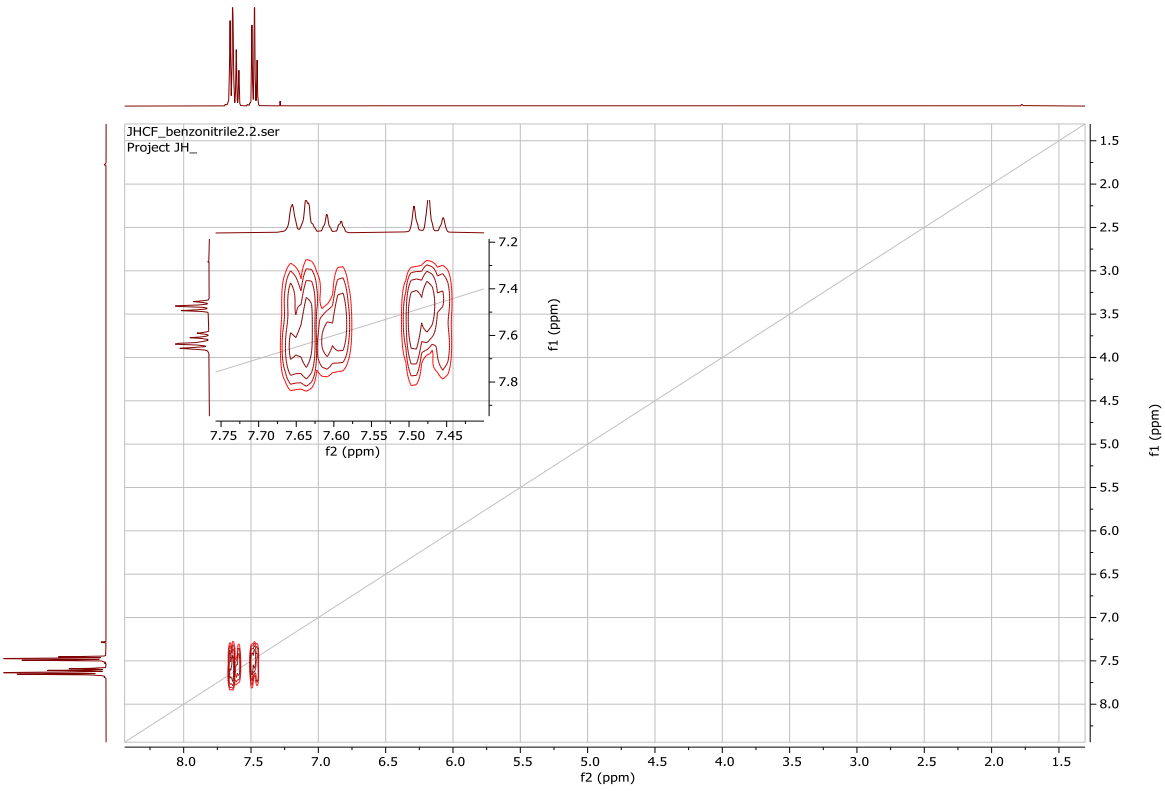
H^1 NMR reference spectrum for benzonitrile



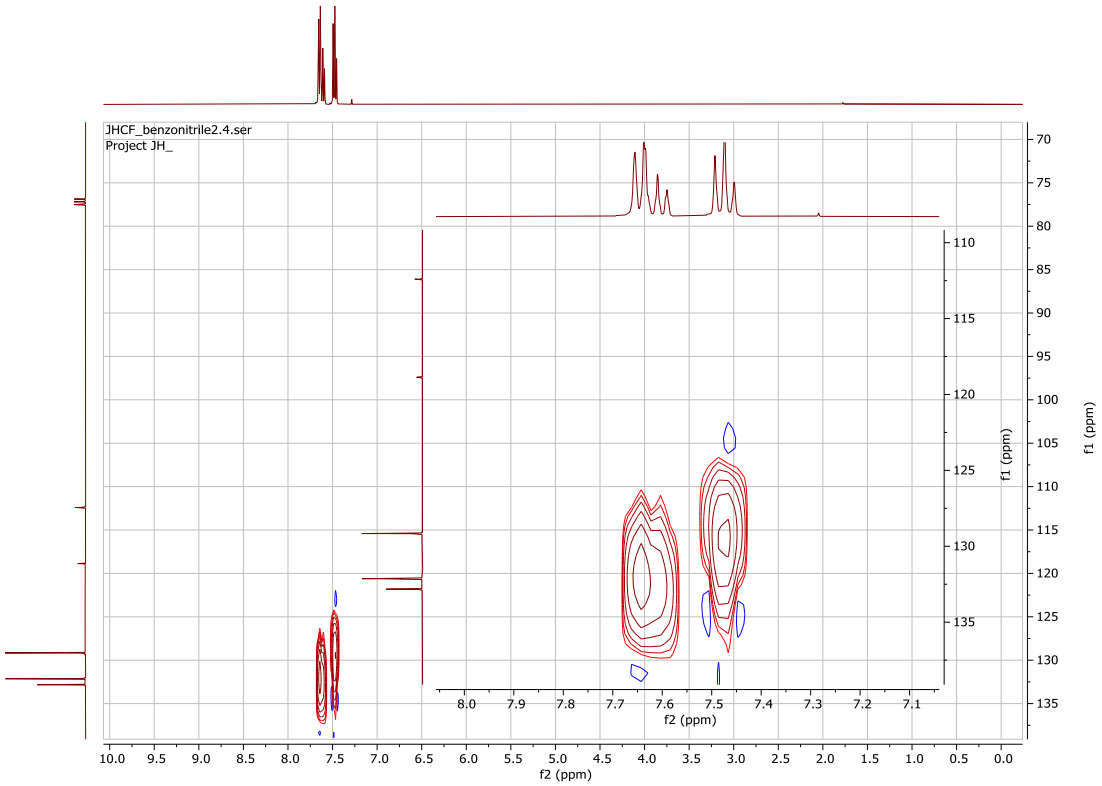
C^{13} NMR reference spectrum for benzonitrile



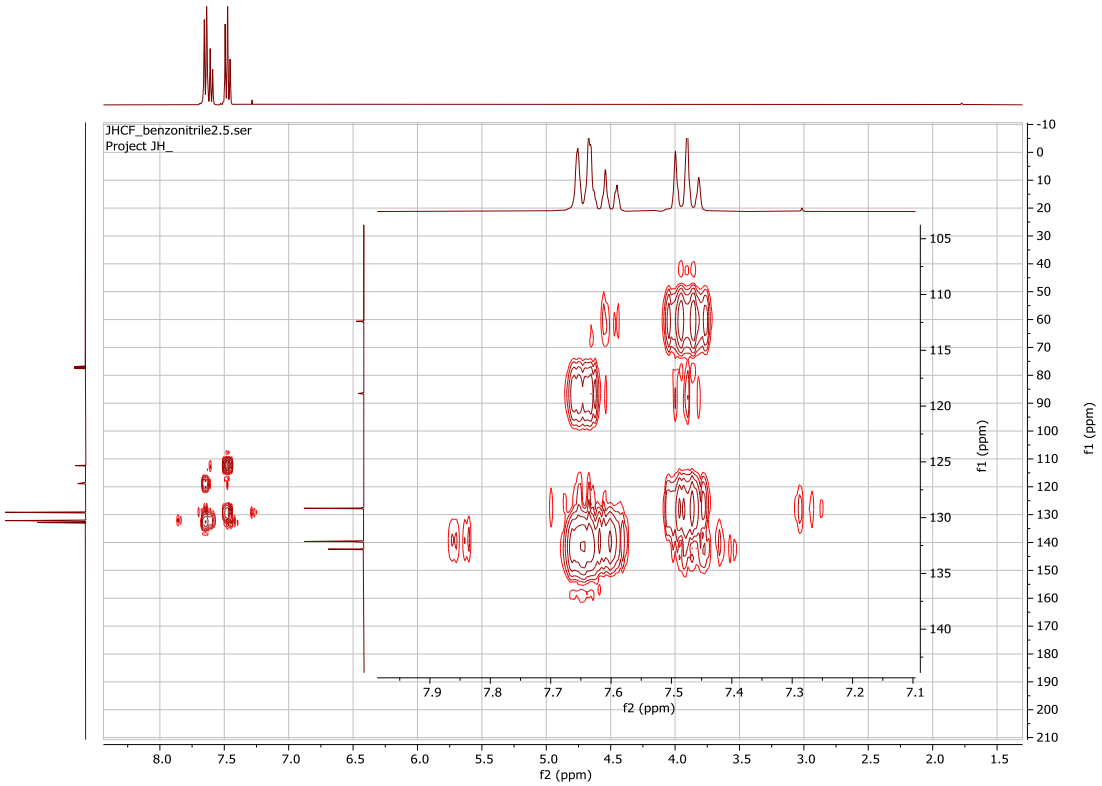
COSY NMR reference spectrum for benzonitrile



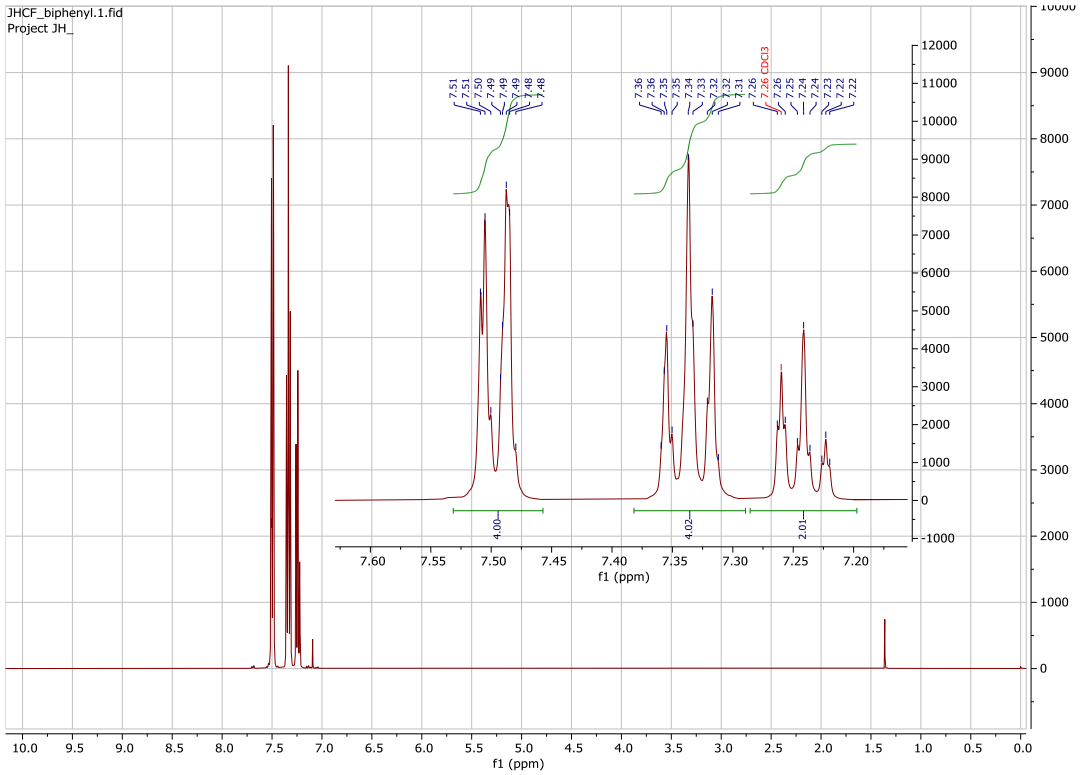
HSQC NMR reference spectrum for benzonitrile



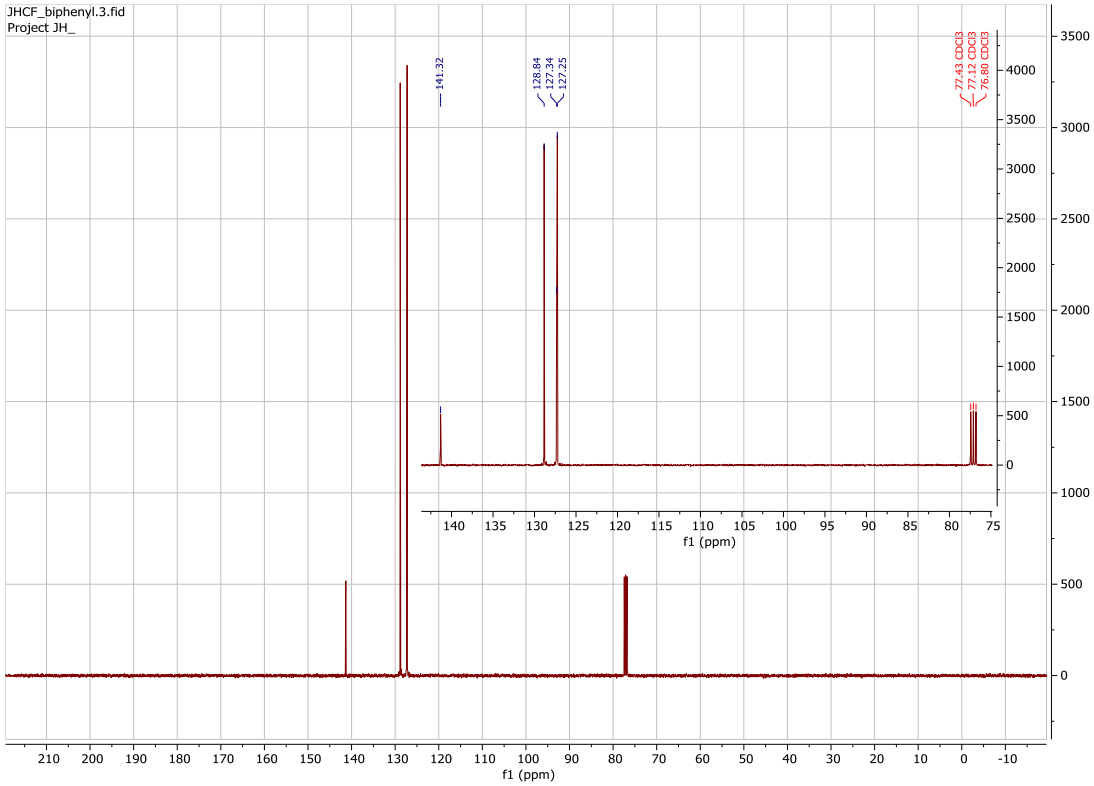
HMBC NMR reference spectrum for benzonitrile



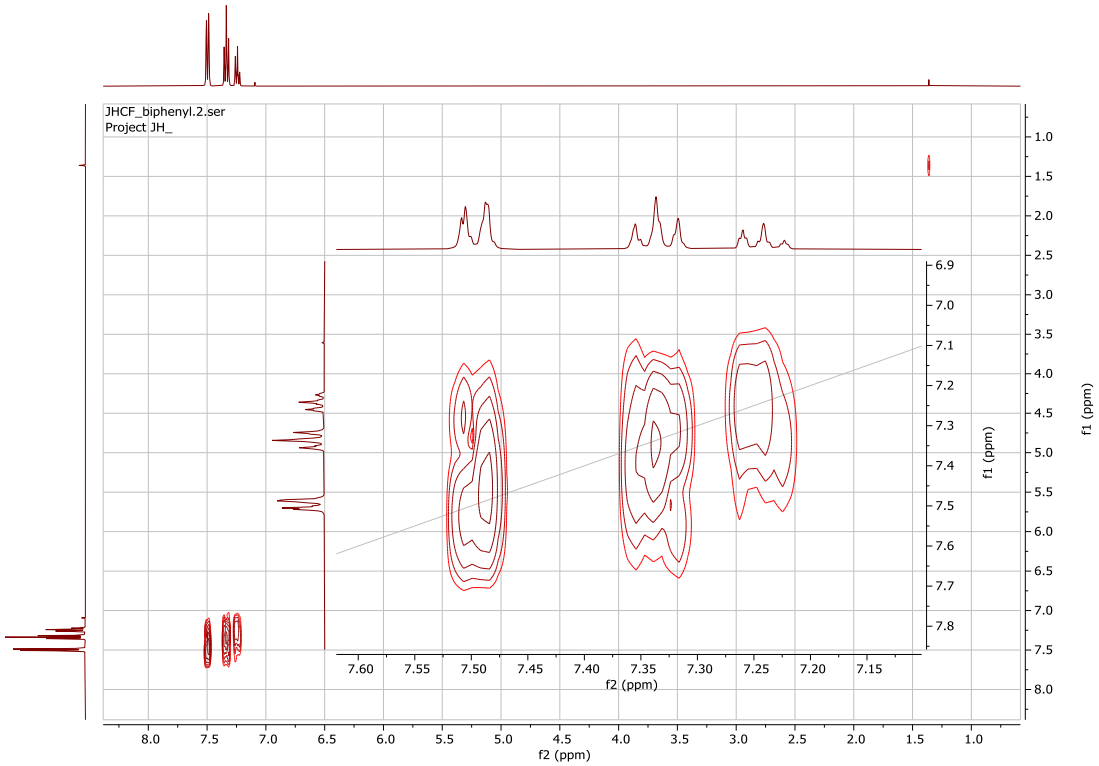
H^1 NMR reference spectrum for biphenyl



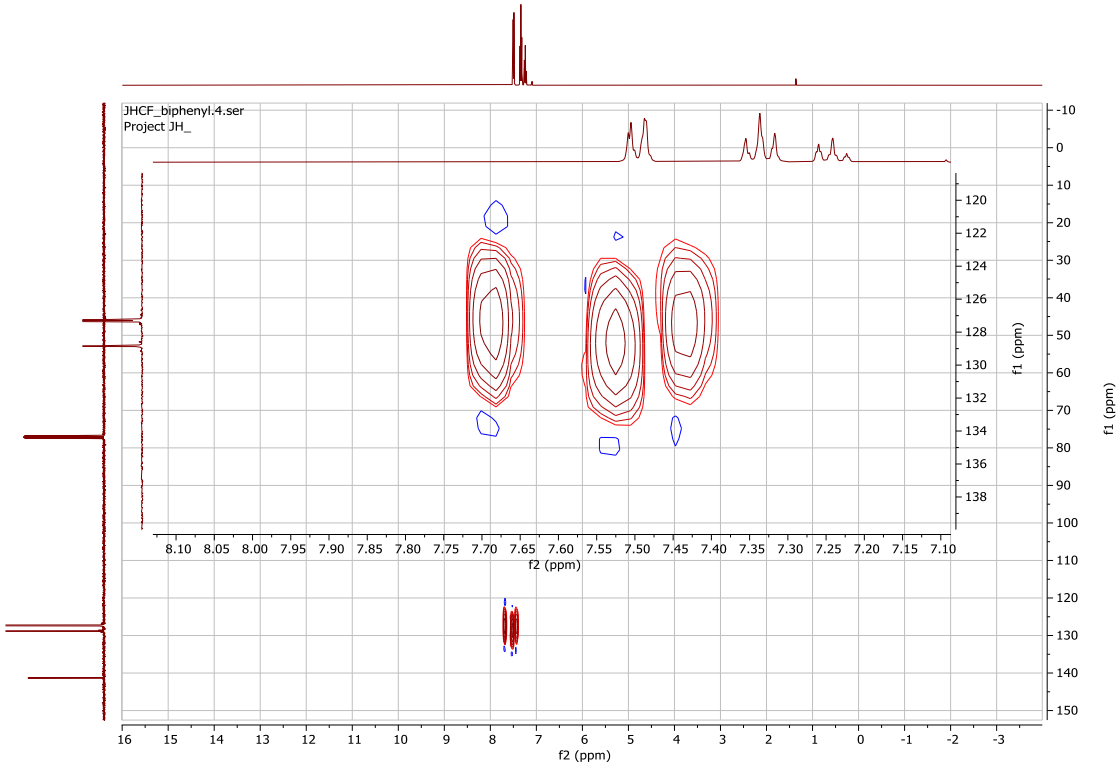
C^{13} NMR reference spectrum for biphenyl



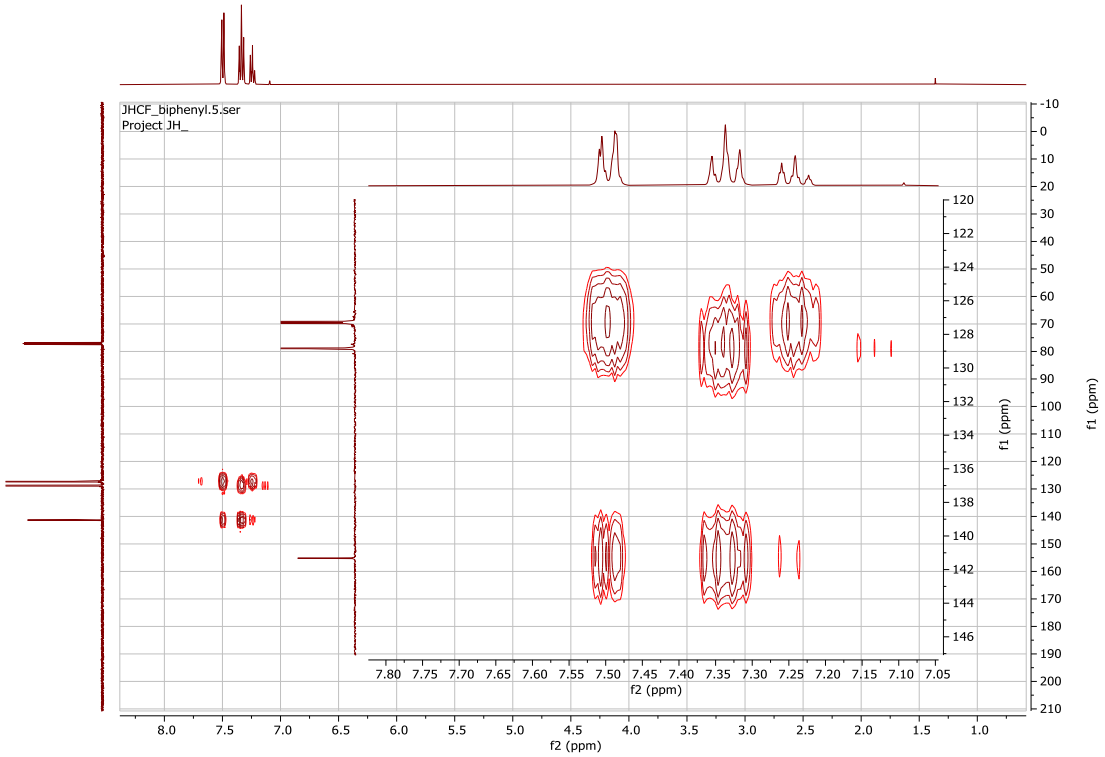
COSY NMR reference spectrum for biphenyl



HSQC NMR reference spectrum for biphenyl



HMBC NMR reference spectrum for biphenyl



Crude H^1 NMR for experiment 11