Synthesis of Medium-Ring Heterocycles via Chelation-Assisted Intramolecular Hydoracylation

Presented to the faculty of Lycoming College in partial fulfillment of the requirements for Departmental Honors in Chemistry

by
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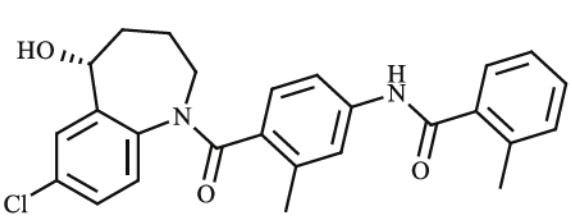
1. Abstract

There are many pharmaceutically useful compounds that contain medium-ring sulfur and nitrogen heterocycles, but these compounds can be difficult to synthesize. Our research focuses on using chelation-assisted intramolecular hydroacylation to construct these medium-ring heterocycles. This project examines the limitations and the extent of success of this type of reaction with allyl amine substrates as well as the optimal conditions and reagents for the intramolecular hydroacylation of allyl sulfides and amines.

2. Introduction and survey of relevant literature

Medium-ring heterocycles are prevalent in natural products and biologically active compounds. A medium ring is defined as a ring of seven to eleven atoms. Medium rings are challenging to prepare due to steric strain associated with the ring size and high entropy of activation for ring-closure reactions to form rings of this size. It would be ideal to formulate a more efficient and versatile pathway to prepare medium rings that could be used in the pharmaceutical industry. A few examples of pharmaceuticals containing medium ring heterocycles include tolvaptan (**1**), which can increase low levels of sodium in the blood for people with heart and liver disease, compound **2** which reduces human oral tumor cell lines, and compound **3** which can lower LDL cholesterol (Scheme 1).[1,2,3]



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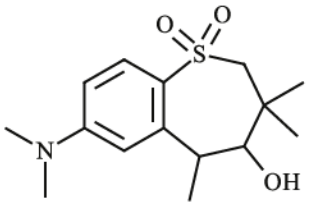

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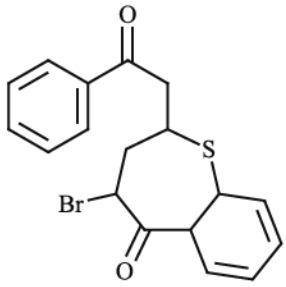

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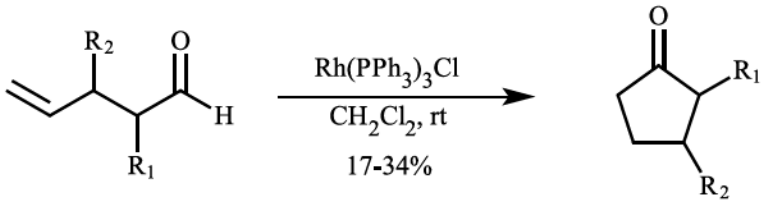
Scheme 1

We propose preparing medium ring heterocycles using rhodium-catalyzed hydroacylation, which is the addition of an aldehyde to an alkene. If this were performed in an intramolecular fashion, with the aldehyde and alkene residing on the same compound, the resulting product would be a ring. In the past, intramolecular hydroacylation has been successful in the formation of smaller rings but has had limited utility in reactions that form medium rings, such as those where the aldehyde and the alkene are separated by more than three carbons. Instead of producing medium rings, attempts have usually resulted in no reaction or a decarbonylation of the aldehyde. Several strategies have been devised to overcome these obstacles to be able to use intramolecular hydroacylation to make medium rings. These strategies include using a conjugated diene to extend the pi system from the alkene, a strained ring to favor ring expansion of the intermediate, a chelating atom in the middle of the molecule as a tether, and finally a chelating imine cocatalyst to encourage hydroacylation.

Emergence of Intramolecular Hydroacylation

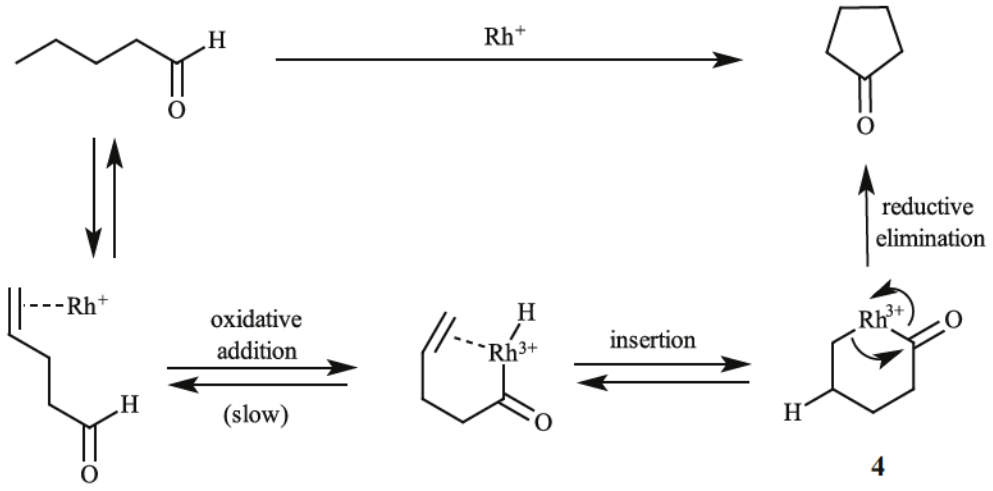
Intramolecular hydroacylation was first used to make cyclopentanone, a small ring, from 4-pentenal by Sakai in 1972 using stoichiometric amounts of the rhodium catalyst (eq. 1).[4] The reaction was successful with 2- and 3-substituted 4-pentenals, but neither increased substitution nor longer carbon chains to make larger rings were explored.



eq. 1

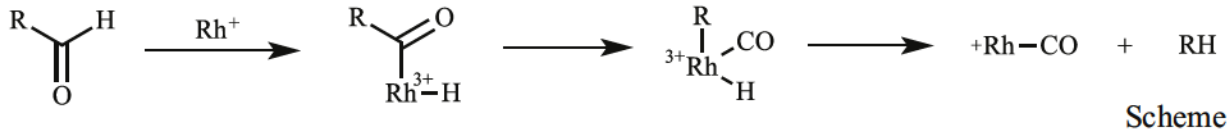
The stoichiometric use of Wilkinson's catalyst by Sakai is unfavorable; rhodium is an expensive metal, therefore, using more than catalytic amounts is impractical. Larock developed

a catalytic variant of the reaction by saturating the solution with ethylene and also proposed a mechanism for intramolecular hydroacylation using catalytic rhodium (Scheme 2).[5] The reaction begins with pre-coordination of the alkene to the rhodium, which positions the aldehyde for oxidative addition to rhodium. The alkene inserts into the rhodium-hydrogen bond to form a metallacyclic intermediate. Subsequent reductive elimination yields the desired cyclized product. Deuterium labeling studies by Bosnich confirmed that all of the steps except the final reductive elimination are reversible and rapid. The final reductive elimination has a significant kinetic barrier and controls the turnover rate of the catalysis for the reaction.[7]



Scheme 2

A competing mechanism in the reaction is decarbonylation of the aldehyde. In the decarbonylation mechanism, there is a carbonyl deinsertion instead of an alkene insertion and subsequent reductive elimination that leaves the carbonyl on the rhodium metal as a ligand (Scheme 3).[6] The rhodium-carbonyl complex with Wilkinson's catalyst, $Rh(PPh_3)_2(CO)Cl$, does not promote hydroacylation.



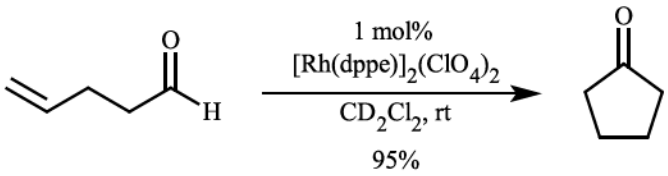
Scheme 3

With the goal of discovering a more active catalyst for intramolecular hydroacylation, Larock screened many analogs of Wilkinson's catalyst by altering the phosphine ligands.[5] There were problems experienced in the attempts to isolate the new catalysts due to their increased solubility and their sensitivity toward oxygen. Because of this, the new catalysts were generated *in situ* (eq. 2).

$$\tfrac{1}{2}\,[RhCl(olefin)_2]_2 \;+\; nL \xrightarrow[n = 1\text{-}3]{} RhCl(olefin)_{3-n}L_n \qquad \text{eq. 2}$$

One, two, and three equivalents of the phosphine ligands were used. The highest yields were obtained when a 2 to 1 ratio of phosphine ligand to rhodium was used. Three useful catalysts were made by adding tri-*p*-tolylphosphine, tri-*p*-anisylphosphine, or tris(*p*-dimethylaminophenyl)phosphine to chlorobis(cyclooctene)rhodium in methylene chloride. These ligands all have electron donating groups that increase electron density on the rhodium, which helps to accelerate the oxidative addition.

Another alteration to the catalytic species was the use of cationic rhodium complexes and bidentate phosphine ligands.[6] It was observed that these complexes could accelerate intramolecular hydroacylation over the unwanted and irreversible decarbonylation and double-bond migration reactions; bidentate coordination of the aldehyde oxygen and the olefin group leads more readily to hydroacylation (eq. 3).[7]



eq. 3

Decarbonylation can also be avoided by adjusting the concentrations of both substrate and catalyst. Decarbonylation is seen more frequently if the amount of substrate is increased

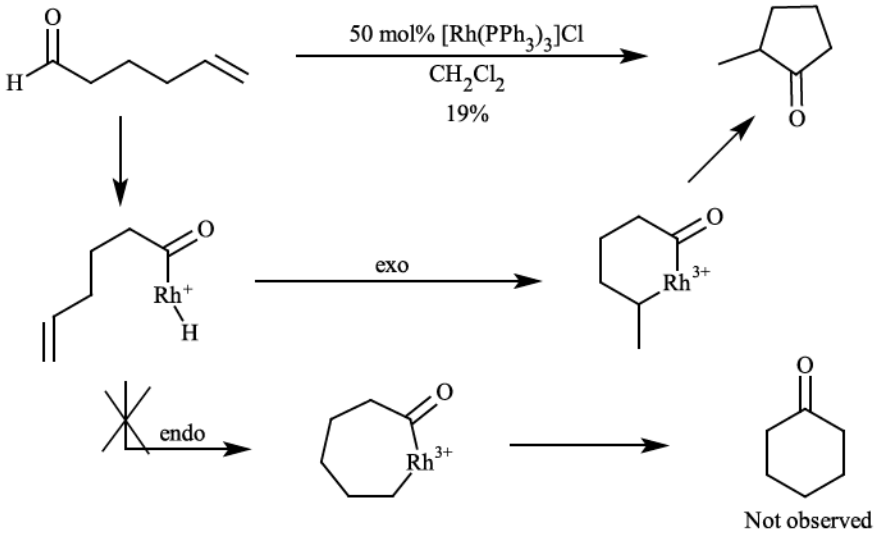
while the concentration of the rhodium stays constant.[6] The rate of the cyclization reaction slows down because coordination sites on the catalyst are occupied by the high concentration of substrate, and there is a greater chance for unproductive substrate-catalyst adducts to form. Therefore, the goal is to increase the rate of formation of the metallacycle intermediate **4** (Scheme 2) so that the decarbonylation step is slower than the metallacycle intermediate formation; this rate difference would ensure that hydroacylation occurs and not decarbonylation. This was achieved by either increasing the concentration of the rhodium or decreasing the concentration of the substrate. The dilute reaction conditions decrease the formation of unwanted substrate-catalyst adducts and increase the rate of the desired reaction.

Reacting 4-pentenal with $[Rh(diphos)]^+$, a cationic catalyst used by Bosnich, or any of the three derivatives of Wilkinson's catalyst used by Larock gave solely the cyclopentanone product in high yields (78-98%).[5,6] The cationic catalyst was effective at loadings as low as 1 mole percent. In contrast, Wilkinson's catalyst derivatives required loadings of 10 mole percent; lower amounts of catalyst resulted in drastically reduced yields.

With Larock's catalysts, substitution on the 3- and/or 4- positions of the 4-pentenal allowed for excellent yields of cyclized product. However, monosubstitution of either the 2- or 5- position cut the yields of cyclized product in half, and disubstitution of the same positions inhibited the reaction altogether. The same pattern was observed when using the cationic catalyst, but only for disubstitution on the 2- and 5- positions; monosubstitution on those positions were not a problem. A reason for this pattern is perhaps that substitution on the 5-position slows down the insertion of the alkene into the rhodium-hydrogen bond, and substitution on the 2- position might induce too much steric hindrance that could interfere with oxidative

addition. The cationic rhodium complex would already be less sterically hindered than a neutral complex and would allow monosubstitution but not disubstitution.

With 5-hexenals, the hydroacylation still occurs; however, the reaction yields a methyl substituted cyclopentanone instead of the expected six-membered ring due to favored exoyclization over the previously seen endocyclization with pentenals (Scheme 4). This difference occurs in the insertion step that forms metallacycle intermediate **4**. Increasing the distance further by using 6-heptenals inhibits the progress of the reaction entirely. When the aldehyde and alkene functional groups are moved further away from each other, the coordination of the rhodium to the alkene is too far to position the aldehyde effectively for oxidative addition. Because of this, it would not be possible to use this mechanism to form medium rings.[5,6]

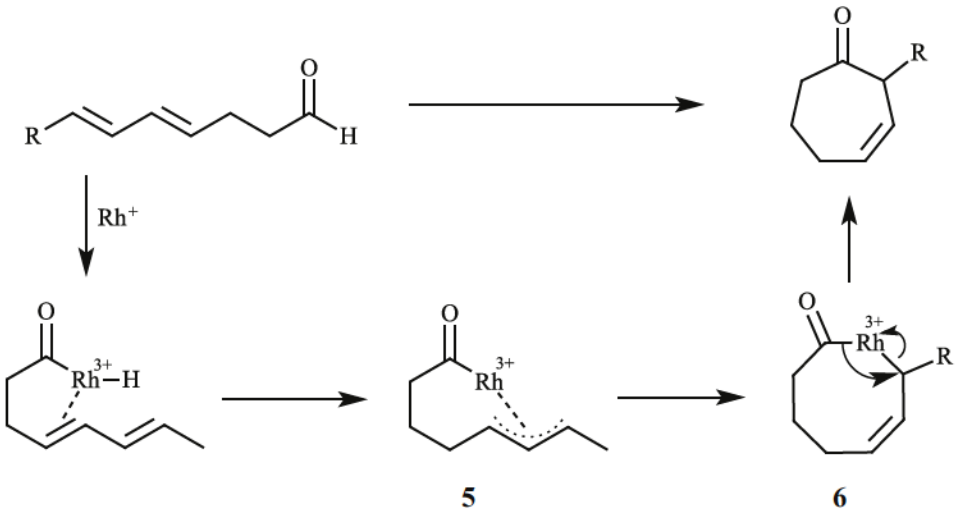


Scheme 4

Formation of Medium Rings Using Conjugated Dienes

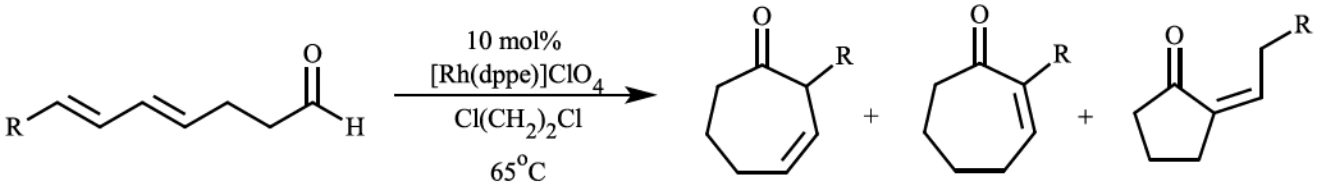
Medium rings can be formed using intramolecular hydroacylation if the 4-pentenal is substituted with another alkene in conjugation. Using the cationic rhodium catalyst $[Rh(dppe)]ClO_4$, dienals were converted to cycloheptenones.[8] In this mechanism (Scheme 5),

the alkene closest to the aldehyde initially coordinates to the rhodium, setting up the oxidative addition of the aldehyde to the rhodium. A π-allyl intermediate, **5**, is formed after insertion into the rhodium-hydrogen bond, and subsequently generates eight-membered metallacycle **6**. Reductive elimination produces a final seven-membered carbocycle. This was the first example of the use of intramolecular hydroacylation to make a seven-membered ring, and the use of a diene is what makes possible the formation of this medium-ring carbocycle.



5 **6** Scheme 5

The geometry of the alkene at the C6 carbon was critical to the success of the reaction. The *E* isomer was able to cyclize to give the desired product, but the *Z* isomer only yielded the cyclopentanone product. This is probably because the *Z* geometry leads to a trans seven-membered ring which is highly strained. Also, the substituent on the C7 carbon needed to be an alkyl group instead of a hydrogen, which can be seen in Table 1. The substituent is necessary to stabilize the accumulation of positive charge on the terminal carbon of the diene.

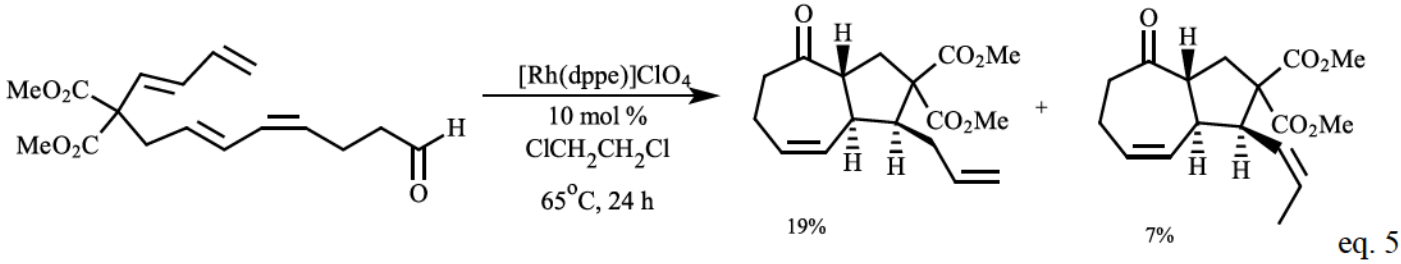


eq. 4

Table 1

R = $CH_2CH_2(C_6H_{11})$	0%	66%	9%
R = CH_2OBn	45%	15%	3%
R = H	7%	0%	45%

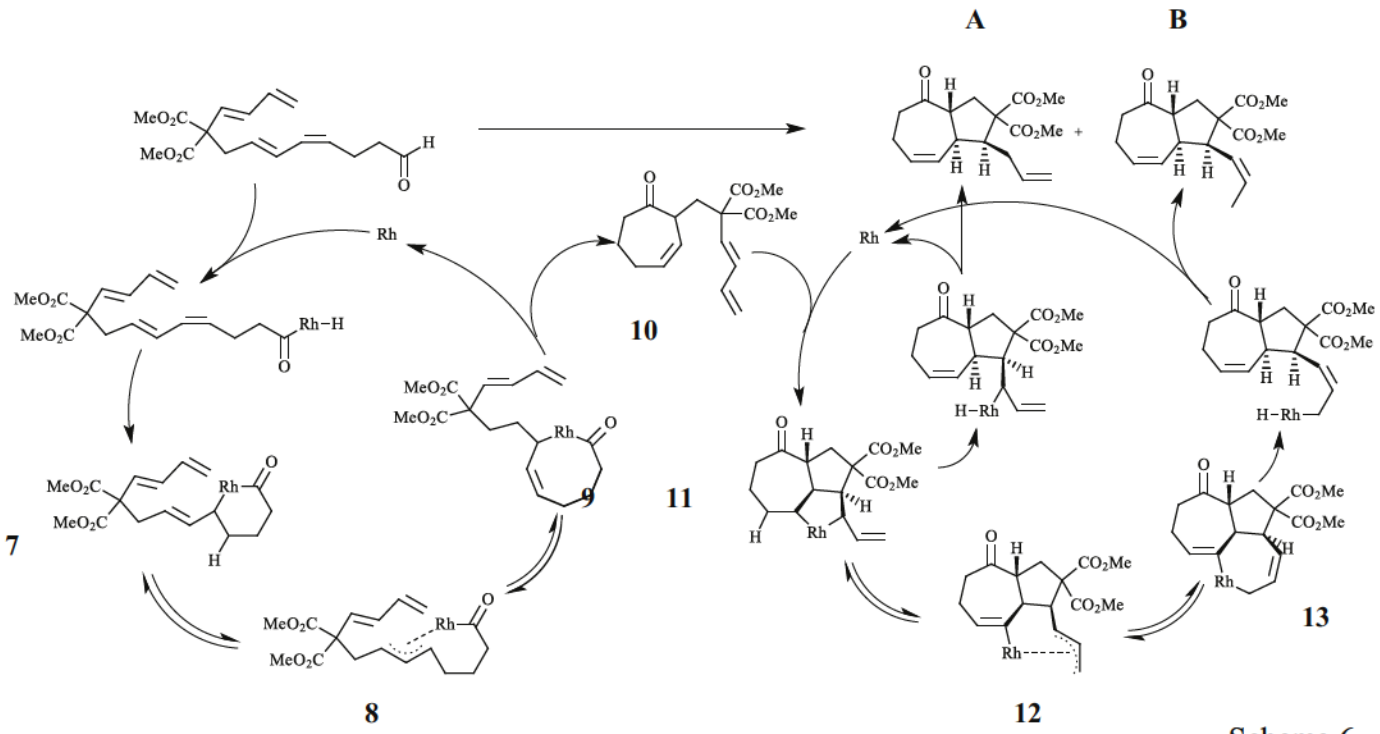
This same reaction was studied in ionic liquids instead of organic solvents.[9] An ionic liquid is of interest because it might facilitate separation of the cationic catalyst, which would remain in the ionic liquid, from the organic compounds, which can be extracted out. This allows for environmentally benign chemical processes and facile recyclization of the catalyst. It was proven that the recovered catalyst could be repeatedly used without a significant decrease in the catalytic activity (eq. 5).



eq. 5

The use of a diene is applicable in a hydroacylation/cycloisomerization cascade reaction.[10] Cascade reactions enable multiple carbon-carbon bonds to be formed in one sequence without having to change the reaction conditions, add reagents, or isolate intermediates. In the mechanism for the cascade reaction (Scheme 6), oxidative addition of the aldehyde to the

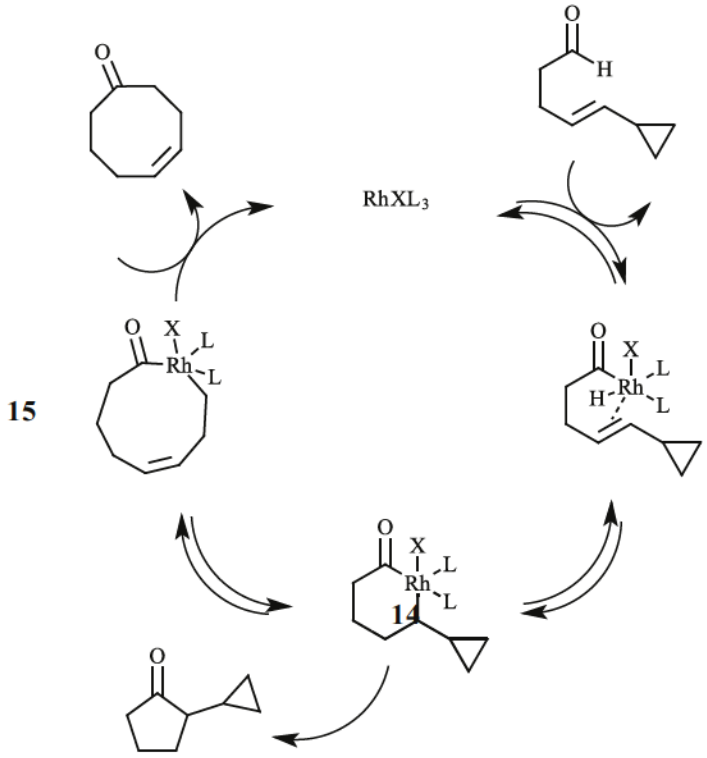
rhodium complex is followed by insertion of the proximal alkene into the rhodium-hydrogen bond to give six-membered rhodacycle intermediate **7**. Intermediate **7** is in equilibrium with π-allyl intermediate **8** and the subsequent eight-membered rhodacycle **9**. Reductive elimination from **9** gives cycloheptanone product **10** and regenerates the rhodium catalyst. Stereoselective oxidative cyclization of cycloheptanone **10** with the rhodium catalyst produces rhodacycle **11**, which can follow two different mechanistic pathways. The first is a β-hydride elimination from **11** followed by reductive elimination to yield bicyclic compound A. Rhodacycle **11** is also in equilibrium with intermediates **12** and **13**, and β-hydride elimination from **13** followed by reductive elimination would yield bicyclic compound B. The resultant structure has been found in a variety of natural product such as hydroazulenes, making this particular cascade very useful.



Scheme 6

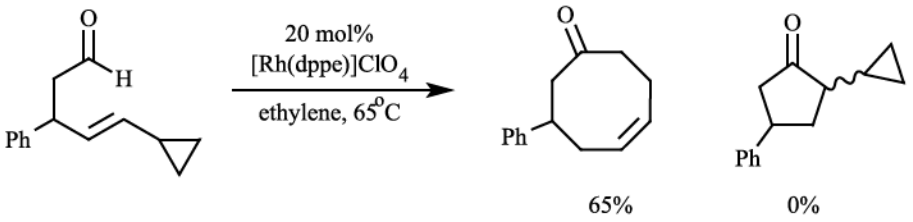
Formation of Medium Rings Using Ring Expansion

A second method capable of forming medium rings via hydroacylation consists of using a ring expansion technique. This strategy involves the use of a strained cyclopropane or cyclobutane ring that will fragment and allow for ring expansion into a medium ring to occur.[11,12,13] The use of cyclopropanes was first examined by Shair.[12] In the proposed mechanism (Scheme 7), oxidative addition of the aldehyde to the cationic rhodium catalyst is followed by insertion of the alkene into the resulting rhodium-hydrogen bond to yield the six-membered metallacycle intermediate, **14**, which can afford two different products. Reductive elimination directly from **14** will give a substituted cyclopentanone. However, ring fragmentation and isomerization can afford the nine-membered metallacycle intermediate **15**, which would result in an eight-membered carbocycle product after reductive elimination.



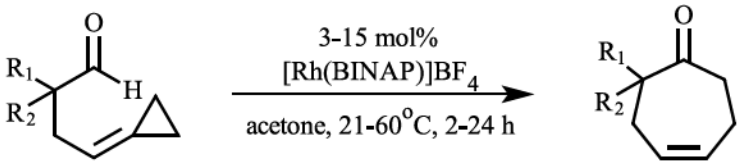
Scheme 7

One technique used to enhance the selectivity of either the cyclopentanone or the cyclooctanone product is by altering the catalyst for the reaction. Wilkinson's catalyst, $Rh(PPh_3)_3Cl$, provided mainly the cyclopentanone while the cationic catalyst $[Rh(dppe)]ClO_4$ favored the medium ring (eq. 6). The ideal conditions for formation of the medium ring used 20 mole percent of the cationic catalyst in dichloroethane at 65°C under an atmosphere of ethylene.

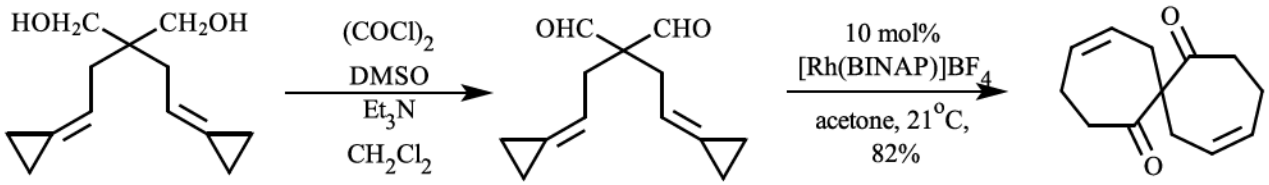


eq. 6

Eliminating sp^3 hybridized carbon that separates the alkene from the cyclopropane ring in the substrate allows for the synthesis of seven-membered rings in place of eight-membered rings.[12] Aissa was able to cyclize these substrates under mild conditions using a modified catalyst (eq. 7). Substitution on the α-carbon was compatible with the reaction, and alkyl, phenyl, silyl, and benzyl ether substitutents were tolerated. The formation of a spiro-bisketone was also achieved via a bidirectional intramolecular hydroacylation reaction (Scheme 8).

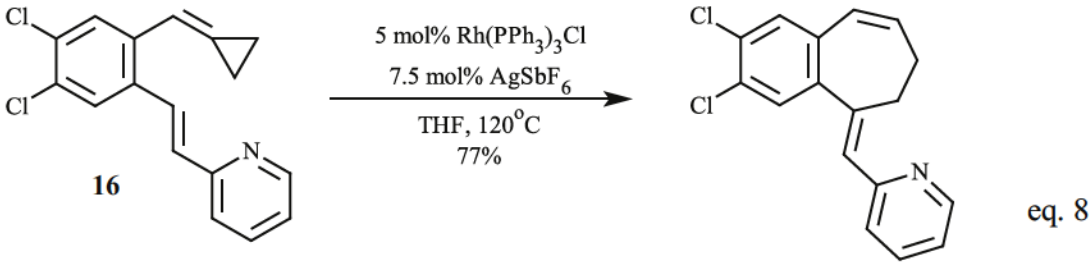


eq. 7



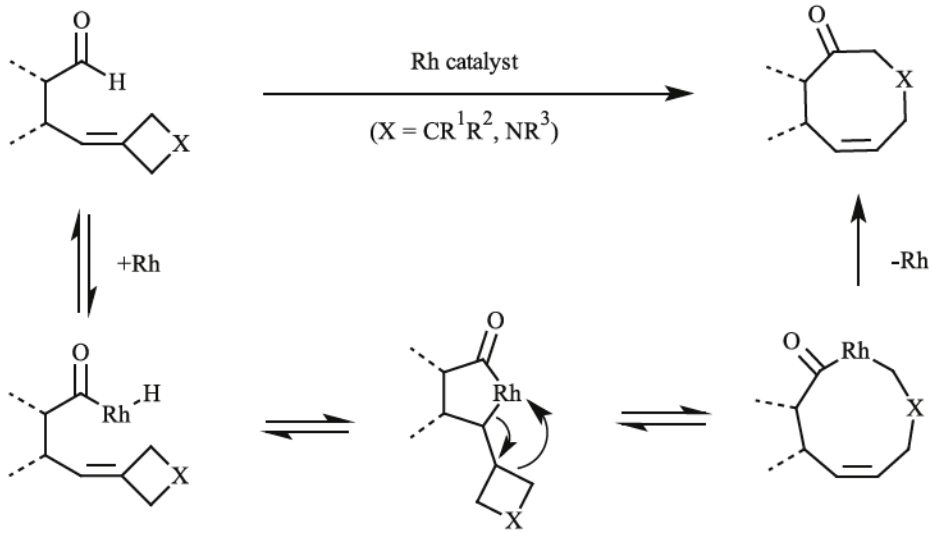
Scheme 8

A related rhodium catalyst which also affords medium ring products is shown in equation 8, although it does not occur via intramolecular hydroacylation.[13] Wilkinson's catalyst can be paired with a second metal cocatalyst, $AgSbF_6$, to form medium rings. The nitrogen in the pyridine ring of compound **16** directs the rhodium to insert into the carbon-hydrogen bond of the upper alkene carbon. Hydrometalation gives a metallacycle intermediate which undergoes ring expansion upon the cleavage of the carbon-carbon bond in the cyclopropane ring to yield a seven-membered carbocycle (eq. 8).[13]

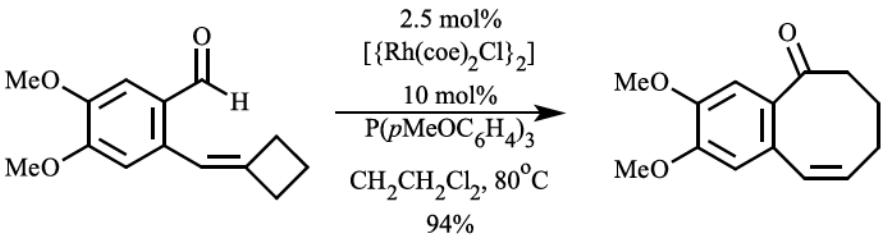


eq. 8

A cyclobutane ring may also be used in place of a cyclopropane ring and yields cyclized product under mild conditions.[14] The use of aldehyde-tethered alkylidenecyclobutanes allow for β-carbon elimination of the metallacyclic intermediate, **17**, to achieve the medium-ring metallacycle before reductive elimination (Scheme 9). Aissa elucidated three different methods, all equally effective for this reaction, with the first outlined in equation 9.



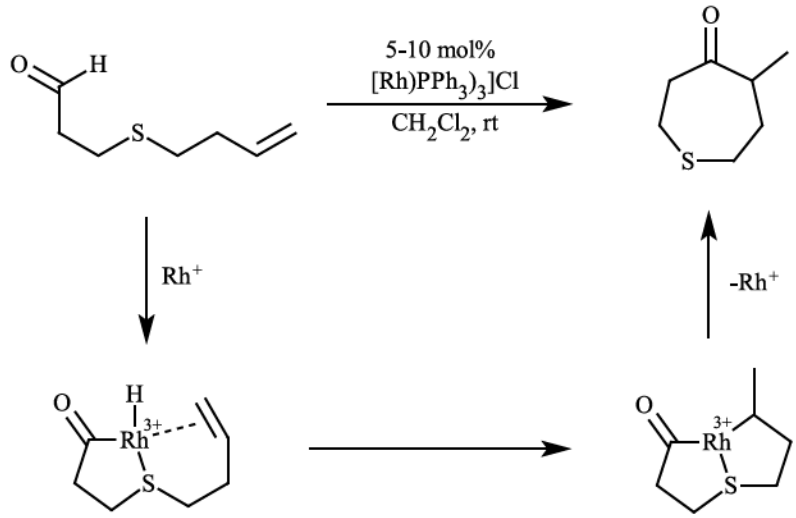
Scheme 9



eq. 9

Formation of Medium-Ring Heteroycles Using Chelating Substrates

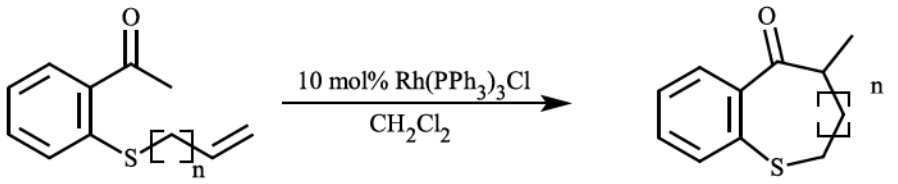
A useful tool in the synthesis of medium-ring heterocycles via intramolecular hydroacylation is the incorporation of a chelating atom, such as sulfur, into the substrate.[15] A Lewis base atom such as sulfur can coordinate to the rhodium catalyst by donating a pair of electrons. Coordination of the sulfur atom positions the aldehyde for oxidative addition and forms a metallabicyclic intermediate (Scheme 10). Oxygen and nitrogen atoms may also be used in place of a sulfur atom.



Scheme 10

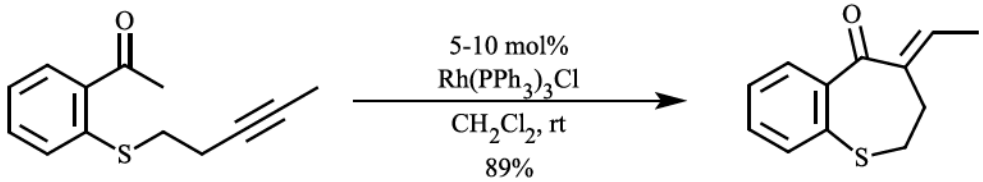
Using this strategy, Bendorf was able to react ω-alkenals and alkynals with Wilkinson's catalyst (eq. 10). However, the distance between the sulfur atom and the alkene and aldehyde is critical. Product was observed only when there were two or three carbons between the sulfur

atom and the alkene. Similarly, the sulfur atom also needed to be three bonds away from the aldehydic carbon.



eq. 10

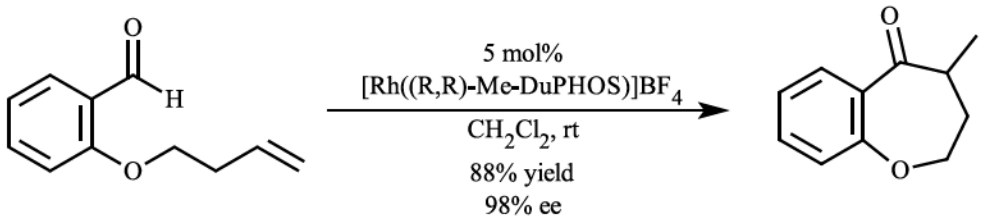
It was observed that the 3-butenyl (n = 2) and 4-pentenyl (n = 3) substituents on the sulfur produced seven- and eight-membered rings respectively. Alkynes could be used in place of alkenes to generate enone products (eq. 11). Internal alkynes gave higher yields of product than terminal alkynes because the enone products of the latter proved to be difficult to isolate and purify. Also noted was the importance of the heteroatom. When the sulfur was replaced with oxygen or a carbon, the once successful cyclization becomes unfavorable. Oxygen, a weaker Lewis base, coordinates more weakly to the rhodium catalyst, and therefore is a less useful chelating atom. This supports the proposed mechanism that suggests that the coordination of the tether atom is required to promote oxidative addition.



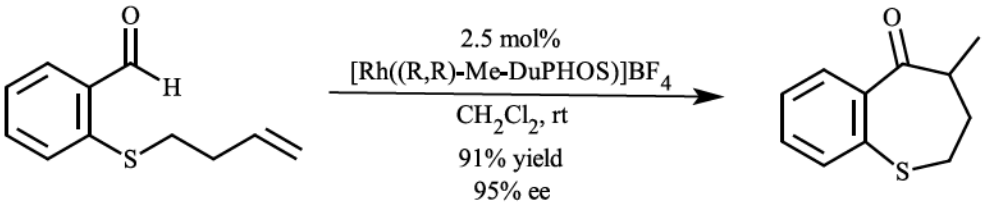
eq. 11

Dong extended the work done by Bendorf by reproducing the cyclizations with chiral catalysts and was also able to obtain the products in high enantiomeric ratios.[16] Dong also reported that hydroacylation is possible for substrates with an ether or sulfoxide group in the place of the sulfide. All tether atoms allowed for cyclizations to form medium-ring heterocycles in good yields. Dong explored different catalysts, including [Rh((*R*,*R*)-Me-DuPHOS)]BF_4 which

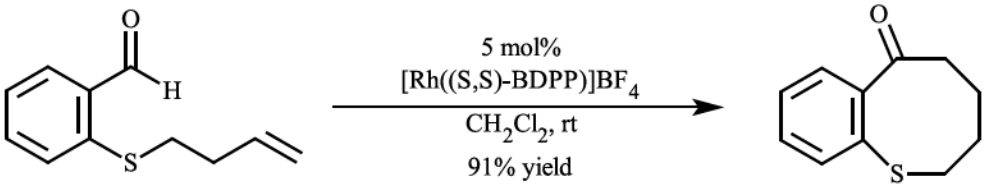
is useful for exocyclization of oxygen- and sulfur-containing substrates (eq. 12 & 13), as well as [Rh((*S*,*S*)-BDPP)]BF_4 which promotes endocyclization of sulfur-containing substrates to provide eight-membered rings (eq. 14).



eq. 12

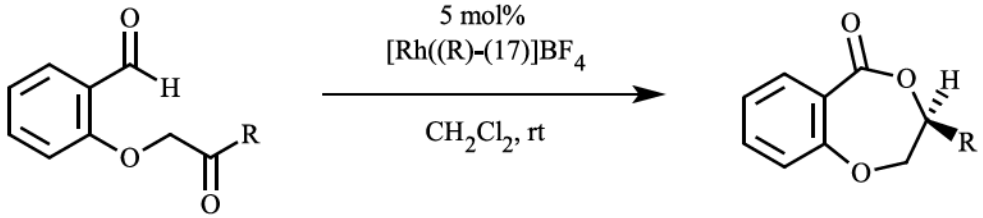


eq. 13



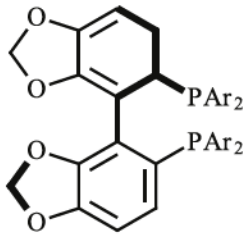
eq. 14

Dong was able to apply this strategy of hydroacylation to ketones in place of the normal alkene.[17] She found that a reaction in dichloromethane at room temperature with [Rh((R)-(14))]BF_4 afforded the optimal results. Aromatic, butyl, benzyl, t-butyl and methyl ketones gave cyclized products in good yields of greater than 84% (eq. 15). The basicity of the phosphine ligand affects the reaction dramatically; highly basic phosphines increase electron density on the rhodium, resulting in sluggish reactions.

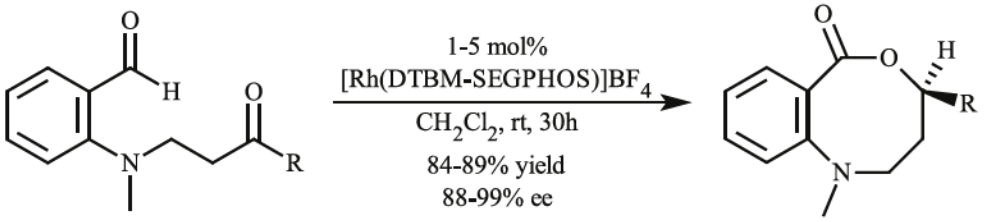


eq. 15

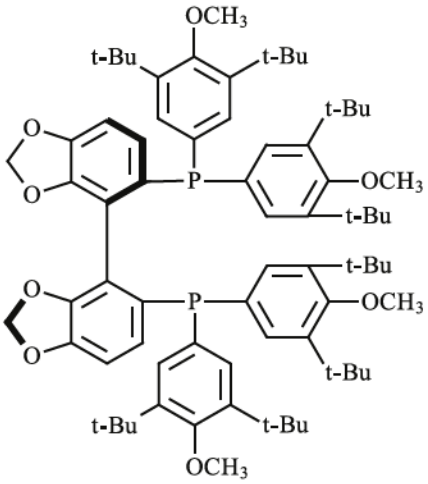
17



The asymmetric synthesis of both seven and eight-membered heterocycles from the hydroacylation of ketones using a homochiral cationic rhodium catalyst is also possible with amine-containing substrates.[18] The use of a nitrogen heteroatom led to greater reactivity, versus the analogous sulfide compound, and no decarbonylation. Dong also examined the effect of the nitrogen substituent that is not directly involved in the cyclization. Strong electron withdrawing groups, such as Ms and Ts, led to loss of reactivity of the amine. However a methyl substituent on the amine yielded product. Keeping the nitrogen three bonds from the aldehydic carbon allowed for any substituent on the nitrogen to cyclize in good yields and produced an excess of one enantiomer (eq. 16).



eq. 16



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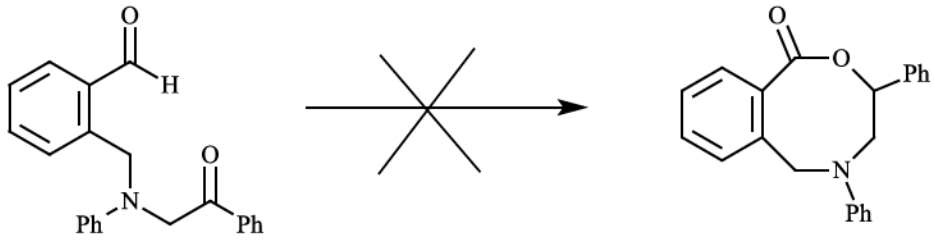
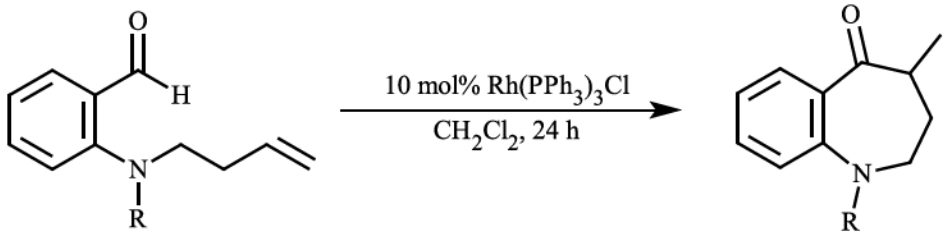
This reaction fails for nine-membered rings. It was also observed that the nitrogen atom must be alpha to the aromatic ring that has the aldehyde for cyclization to an eight-membered ring to occur (eq. 17).



eq. 17

Recent work by the Bendorf group explored the synthesis of medium-ring nitrogen heterocycles by hydroacylation of alkenes and alkynes with Wilkinson's catalyst.[19] Methyl-, benzyl-, homoallyl-, and allyl-substituted amines were examined (eq. 18). Only the allyl-substituted amines produced impressive yields (Table 2). This suggests that the allyl alkene also coordinates to the rhodium and further stabilizes the metal-substrate complex. Although the butenyl can also complex to rhodium, the increased distance of the π-system from the nitrogen may limit the roll it plays in stabilizing the metal-substrate complex. The closer π-system of the benzyl group would alleviate this issue, but it is a weaker π donor due to aromaticity.

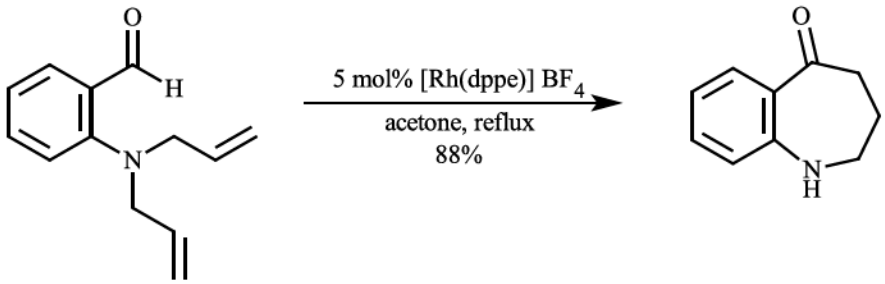


eq. 18

Table 2

Substrate	Yield (%)
R = CH_3	11
R = CH_2Ph	10
R = $CH_2CH_2CH{=}CH_2$	35
R = $CH_2CH{=}CH_2$	72

The reaction was successful with mono-substituted alkenes, cis- and trans-disubstituted alkenes, and terminal alkynes. Substrates that contain aromatic heterocycles also undergo hydroacylation. Interestingly, the bis-allyl substrate failed to cyclize when treated with Wilkinson's catalyst. Upon treatment with a cationic catalyst, $[Rh(dppe)]BF_4$, it underwent intramolecular hydroacylation with an in-situ deprotection of the nitrogen (eq. 19).

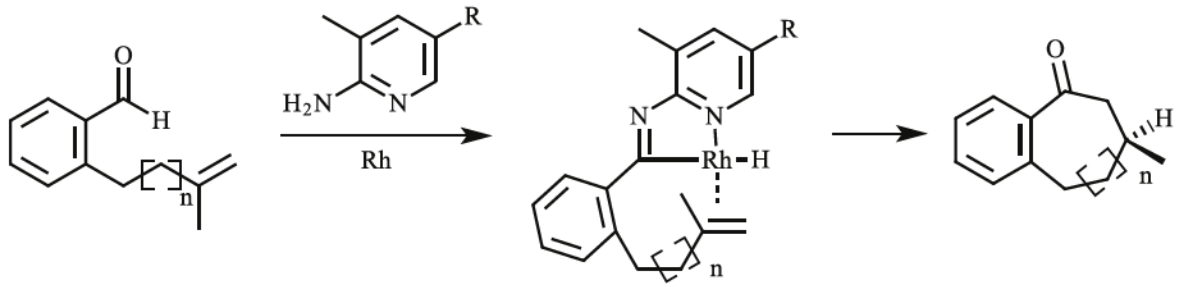


eq. 19

Formation of Medium Rings Using a Chelating Amine Cocatalyst

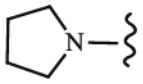
Direct intramolecular hydroacylation to form medium rings is possible for compounds that do not contain dienes, strained rings, or chelating atoms.[20,21,22] By using a chelating amine cocatalyst alongside the rhodium catalyst, an imine intermediate is formed in situ and then undergoes oxidative addition.[20] This imine intermediate can function as a surrogate for the aldehyde in hydroacylation while also suppressing decarbonylation because of the substitution

for the aldehyde (Scheme 11).[21] Previous work with imines examined intermolecular hydroacylation, but Douglas has extended the work to also include intramolecular reactions.[20]

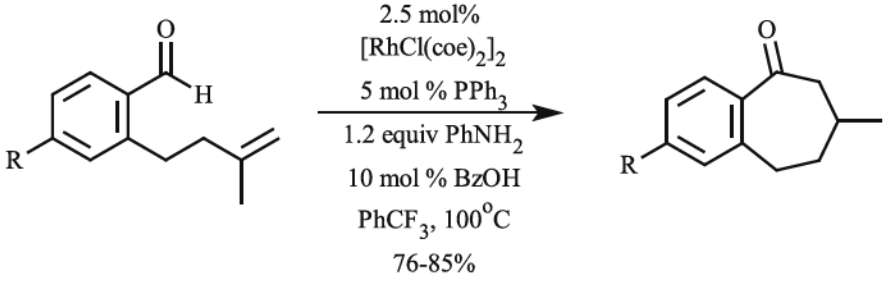


Scheme 11

18, R = H

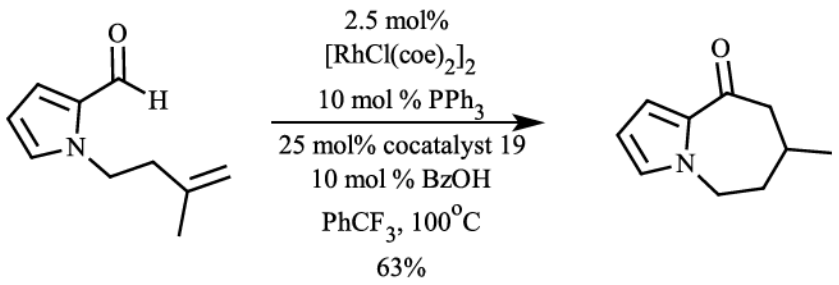
19, R = 

Using the hydrogen-substituted 3-methyl-2-aminopyridyl cocatalyst **18**, a variety of medium ring compounds were prepared (eq. 20). The reaction tolerated a variety of substituents on the benzene rings including a methyl, trifluoromethyl, ether, or fluorine substituent without affecting the yield.



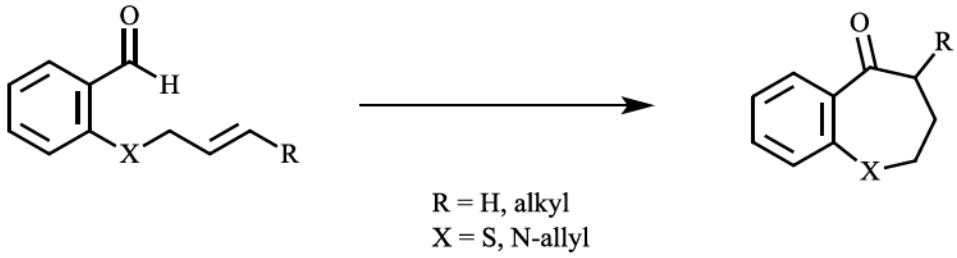
eq. 20

Cocatalyst **19** proved to be the better option because fewer equivalents could be used without sacrificing yield of product. Pyrrole-containing substrates were also compatible with the reaction (eq. 21).



eq. 21

Work on this subject in Dr. Bendorf's lab is now aimed at making the reaction work with allyl-derived substituents of sulfur and nitrogen-containing chelating substrates. This will allow for the formation of a variety of different medium-ring substrates either with or without a substituent on the alpha carbon. The focus is on allyl derivatives due to the ease of installing them on the heteroatom and the commercial availability of said derivatives. Also, hydroacylation with an *in situ* deprotection of diallylamines would further diversification of products.



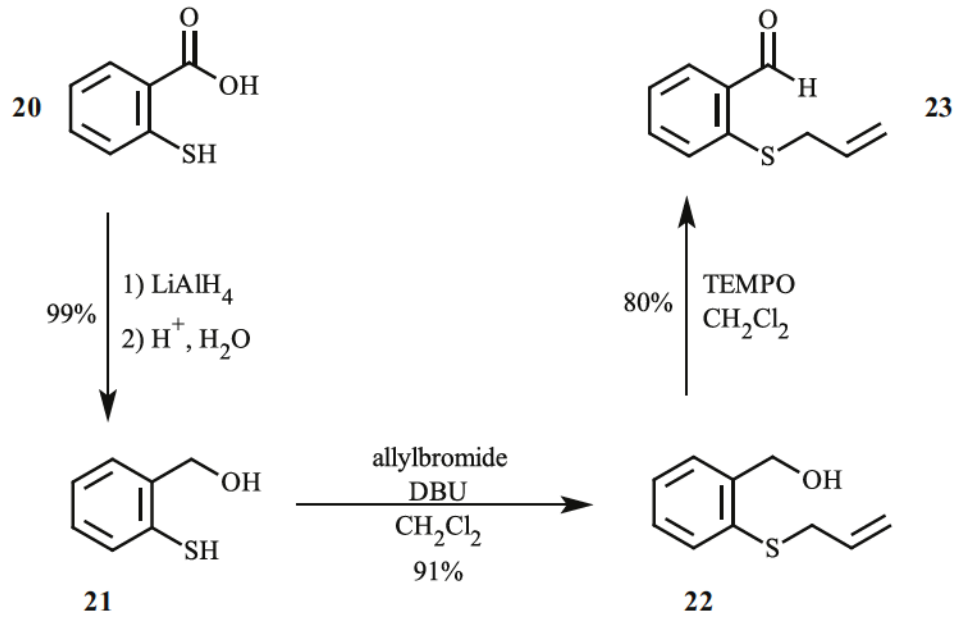
eq. 22

3. Results and discussion

Sulfur Heterocycles

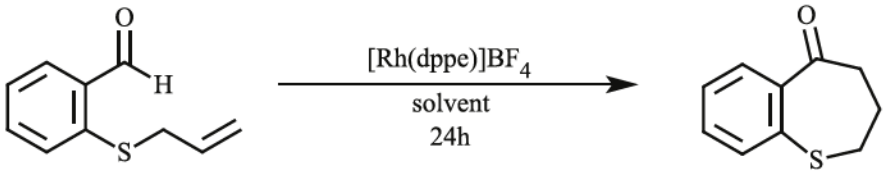
The first substrates investigated were allyl sulfides. The aims of these studies were to optimize the reaction conditions for sulfur-containing substrates and find which substrates were compatible with the reaction. Scheme 12 illustrates a representative synthesis that was used to produce the substrates, beginning with a reduction of thiosalicylic acid, **20**, alkylation with allyl bromide to form compound **22**, and then oxidation of the alcohol to an aldehyde with either

manganese dioxide or TEMPO/iodobenzene diacetate to obtain the hydroacylation substrate, **23**. Manganese dioxide was used in earlier oxidation reactions, but once the catalytic benefits of TEMPO were realized, TEMPO and iodobenzene diacetate were used on all further oxidations.



Scheme 12

Hydroacylation studies examined the effect of the solvent, temperature, and the equivalents of catalyst used (eq. 23). The most successful hydroacylation reaction was run in refluxing CH_2Cl_2 with 5 mol% of catalyst (Table 3). The reaction was not successful in coordinating solvents because the solvent may then occupy any open coordination sites on the rhodium and consequently prevent the coordination of the sulfur atom to the rhodium before oxidative addition.



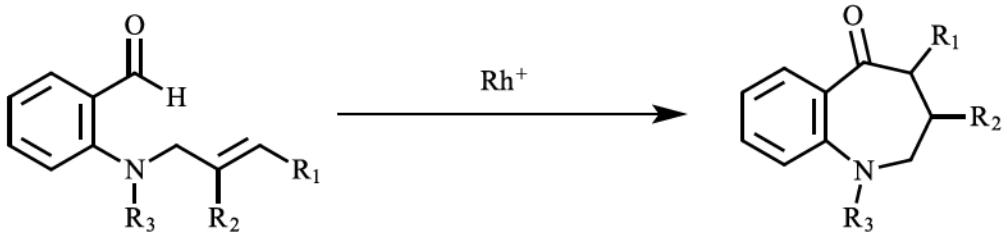
eq. 23

Table 3

Solvent	Equiv of catalyst	Temperature	Yield
CH_2Cl_2	0.05	rt	58%
CH_2Cl_2	0.05	reflux	75%
CH_3CN	0.05	rt	0%
CH_3CN	0.05	reflux	0%
$ClCH_2CH_2Cl$	0.05	reflux	65%
$ClCH_2CH_2Cl$	0.10	reflux	51%

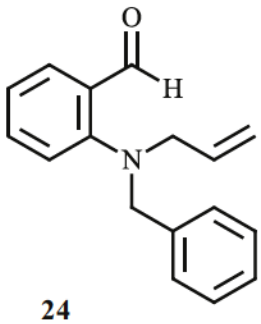
Nitrogen Heterocycles

Changing the chelating atom from a sulfur atom to a nitrogen atom has many benefits.[10,11] There are more pharmaceutical agents that contain nitrogen heterocycles compared to the amount containing sulfur heterocycles. As an added benefit, the hydroacylation of N-allyl substrates is more facile because amine substrates show greater reactivity than the analogous sulfide and ether substrates.[10] One objective with amines is to try to perfect the conditions needed for endocyclization, which is a more difficult pathway than exocyclization. Endocyclization is desired because it will allow for seven-membered rings to be prepared from allyl amines either with or without a substituent next to cyclic carbonyl. Ideally, substituents R_1-R_3 can be varied to produce a variety of different substrates (eq. 24).



eq. 24

The benefits of using an allyl group attached to the nitrogen instead of a butenyl group, which was used previously in our lab,[19] stem from the variety of allyl halides that are commercially available, inexpensive, and easier to install on the heteroatom as compared to an analogous butenyl halide. The final substituent on the nitrogen atom can also be altered; this change can modify the reactivity of the amine and can allow for further synthetic manipulation of the molecule.



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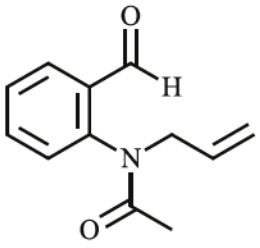
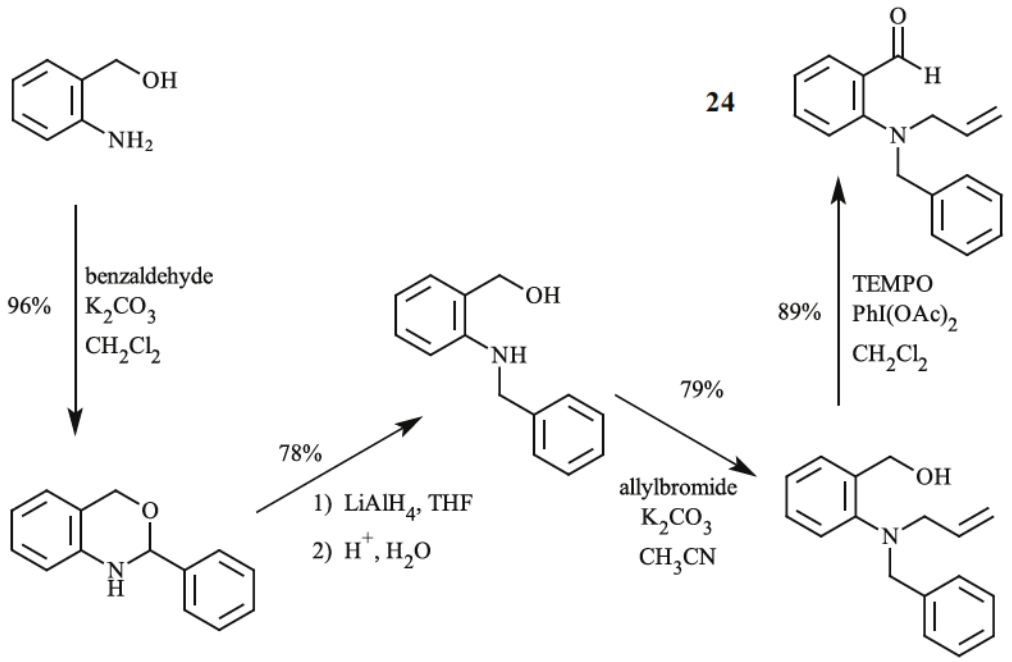


25

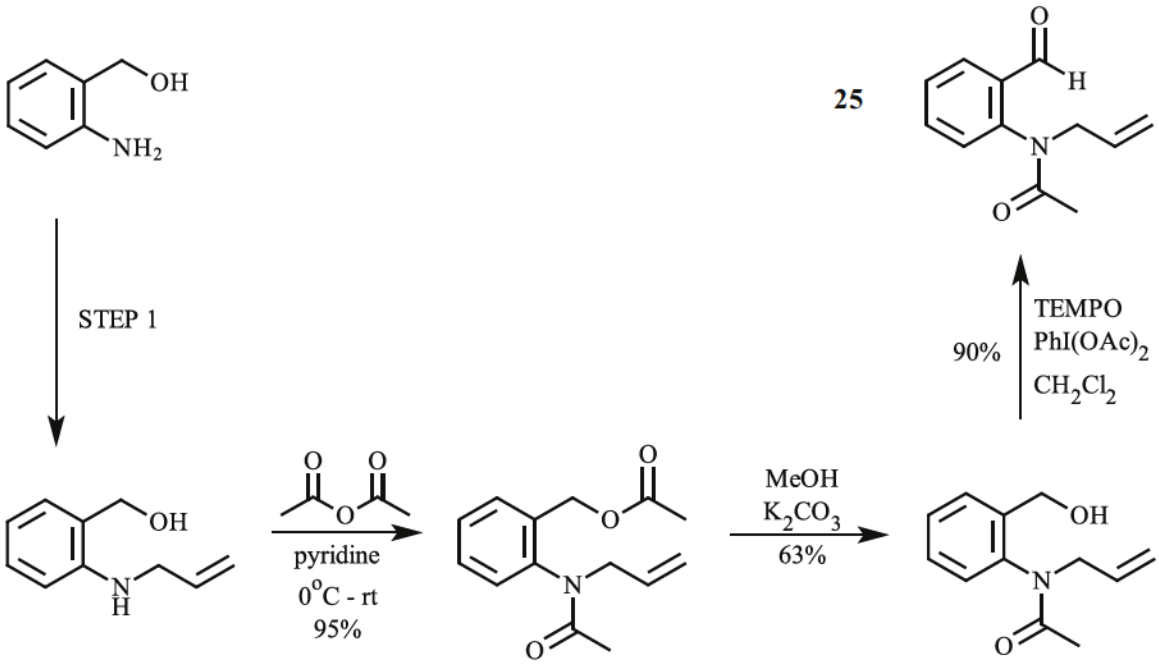
Two different amine substrates, **24** and **25**, were of initial interest. These substrates were of interest because of their differing substitution on the nitrogen, allowing the scope and limitation of the reaction and its proposed mechanism to be tested. Having the benzyl and acetyl functional groups on the nitrogen will allow for further modification of the products to achieve more complex compounds, adding variety and useful applications to the products prepared.

The steps used to prepare the first substrate, **24**, are illustrated in Scheme 13. Aminobenzyl alcohol was reacted with benzaldehyde and potassium carbonate to yield a cyclic aminal, which was reduced using lithium aluminum hydride in tetrahydrofuran to yield a benzyl amine. Alkylation with allyl bromide and oxidation yielded the test substrate.



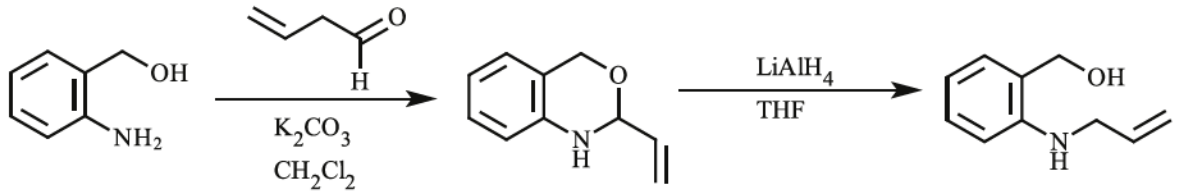
Scheme 13

The second substrate, **25**, has an electron-withdrawing carbonyl attached to the chelating nitrogen atom which may have an effect on the reactivity of the molecule. Scheme 14 exhibits the process used to synthesize this substrate.



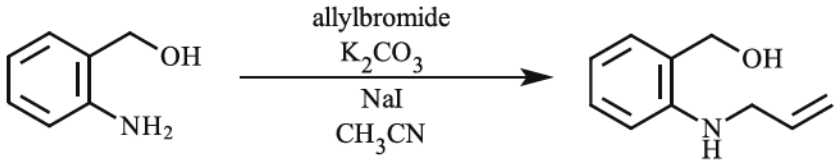
Scheme 14

Three strategies were attempted for step 1 of the synthesis: an aminal-reduction sequence, direct alkylation with allyl bromide, and 9-BBN-mediated allylation. The first strategy employed involved reduction of an aminal formed by the reaction of 3-butenal with aminobenzyl alcohol (eq. 25). This approach worked well for the synthesis of compound **24**, but did not yield any product or any identifiable side product for this compound.



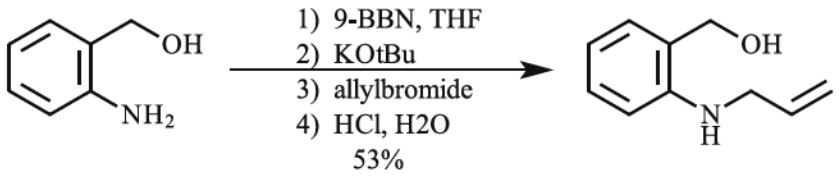
eq. 25

The second strategy was a direct alkylation using allyl bromide (eq. 26). This reaction is an S_N^2 alkylation analogous to those used for the alkylation of sulfides. The reaction yielded low amounts of product, and polymerization of the reagents was an issue. To combat the latter, purification of the allyl bromide reagent by distillation was discontinued in order to retain the radical inhibitor that is present in the commercially available compound. Also, the necessity of sodium iodide was uncertain, and it was not used in early attempts. The addition of sodium iodide converts the allyl bromide to allyl iodide, effectively forming a more reactive electrophile in situ. However, attempts to optimize conditions failed and low yields, less than 10%, were consistently obtained. In addition to low yields of the desired substrate, a second product was obtained due to dialkylation of the nitrogen, which was unfavorable for this synthesis.



eq. 26

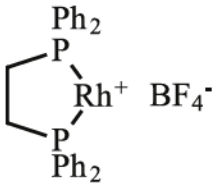
Because of these limitations, step 1 was performed using a 9-BBN-mediated alkylation, which is a labor-intensive method, but it yields enough product to be used in subsequent steps of the synthesis (eq. 27).



eq. 27

After the allylated amine substrate was achieved, it was treated with acetic anhydride in pyridine and then methanol and potassium carbonate to yield an acetyl amine substrate. This compound was then oxidized to an aldehyde using TEMPO and iodobenzene diacetate in methylene chloride.

With the substrates in hand, cyclization experiments used on two different catalysts: [Rh(dppe)]BF_4 (**26**) and [Rh(dppp)]BF_4 (**27**). Each ligand has a different bite angle at the metal which consequently causes a variance in reactivity of the catalyst.



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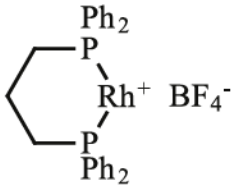
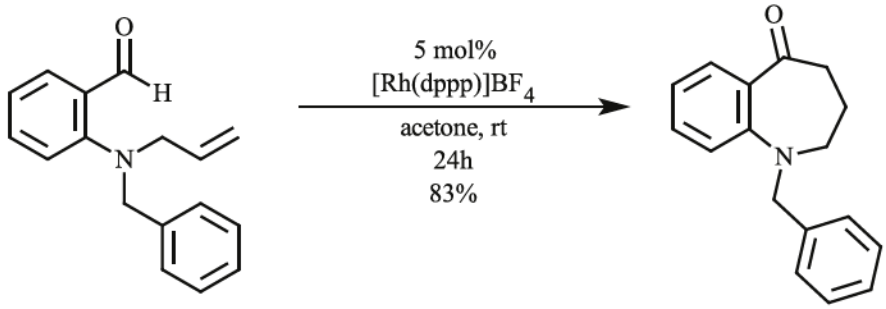


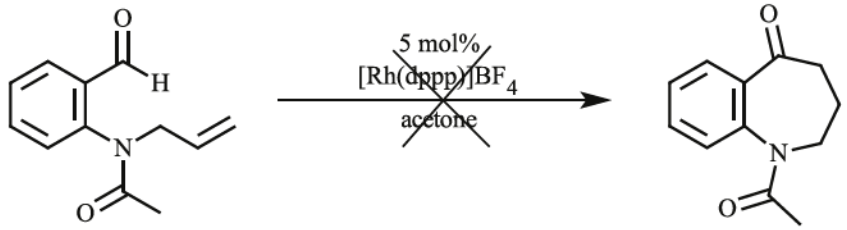
27

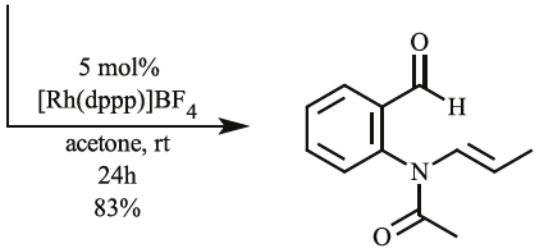
Hydroacylation of substrates **24** and **25** were screened with the [Rh(dppp)]BF_4 catalyst (eq. 27-28). The benzyl amine, **24**, went to completion with an 83% isolated yield of cyclized product. However, the acetyl-substituted amine, **25**, did not yield cyclized product and instead isomerized when exposed to the rhodium catalyst. The presence of the electron withdrawing acetyl group reduces the basicity of the nitrogen and may prevent the pre-coordination of the nitrogen to the rhodium. This observation matches closely with that of Dong, who noted that the

presence of strongly electron-withdrawing substituents on the nitrogen, such as a tosyl or mesyl group, led to no reactivity.[18]



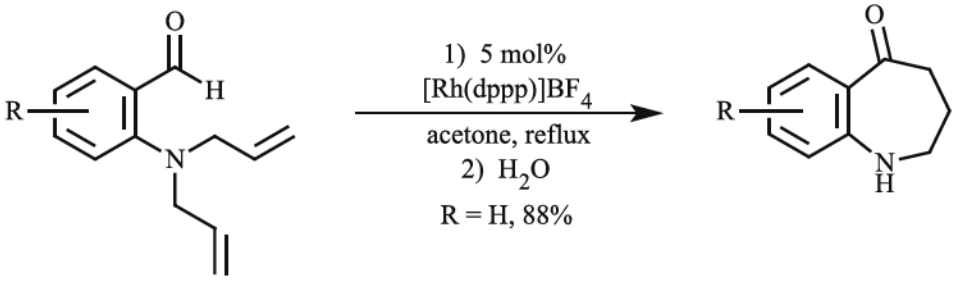
eq. 28





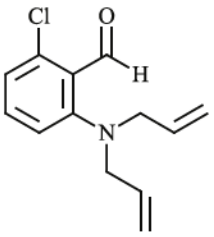
eq. 29

The second goal of studies with nitrogen-containing substrates was to further examine the scope of the reaction by altering the substituent(s) on the phenyl ring; this might alter electron density at the reaction site and change the reactivity (eq. 30). Using diallylamine substrates will also provide an *in situ* deprotection of the nitrogen to yield a secondary amine.[19]



eq. 30

A series of target substrates, 28-32, was identified. It was anticipated that the five substrates could be prepared from commercially available aryl aldehydes in a single step (eq. 31).



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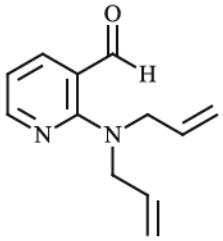

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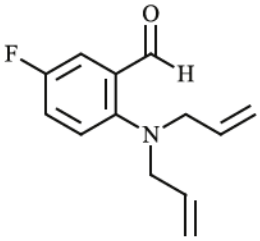

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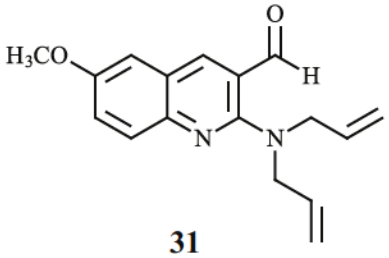

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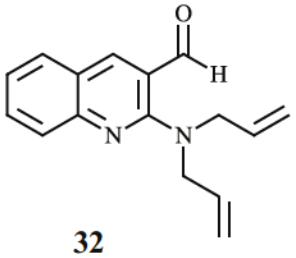

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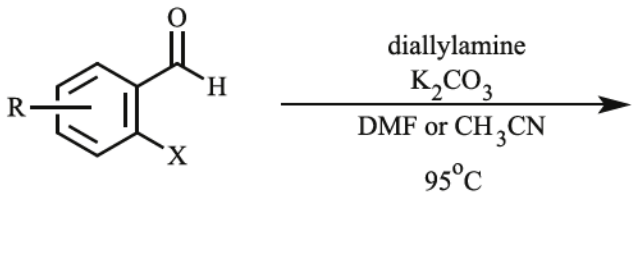
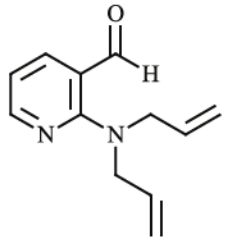


eq. 31

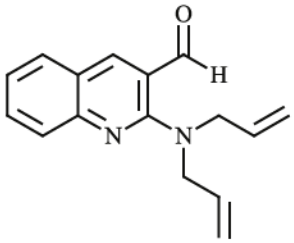
Compound **28** was achieved in good yields (51-73%) by refluxing 2,6-dichlorobenzaldehyde with diallylamine in acetonitrile overnight. Substrates **29** and **32** were difficult to prepare and were only obtained in low yields. Attempts to optimize these reactions are shown in tables 4 and 5.



29

Table 4

Reaction #	Equiv. of diallylamine	Temp. °C	Solvent	Apparatus	Yield
1	1.1	95	DMF	reflux	17%
2	1.1	80	CH_3CN	reflux	<5%
3	1.5	95	DMF	reflux	7%
4	2.0	95	DMF	pressure tube	13%
5	2.0	95	DMF	pressure tube	20%
6	3.0	95	DMF	pressure tube	22%



32

Table 5

7	1.5	95	DMF	reflux	9%
8	2.0	95	DMF	pressure tube	19%
9	2.0	95	DMF	pressure tube	15%
10	2.0	95	DMF	pressure tube	15%
11	2.0*	95	DMF	pressure tube	10%
12	2.0	80	CH_3CN	reflux	<5%
13	3.0	95	DMF	pressure tube	25%

*Freshly distilled diallyl amine was used

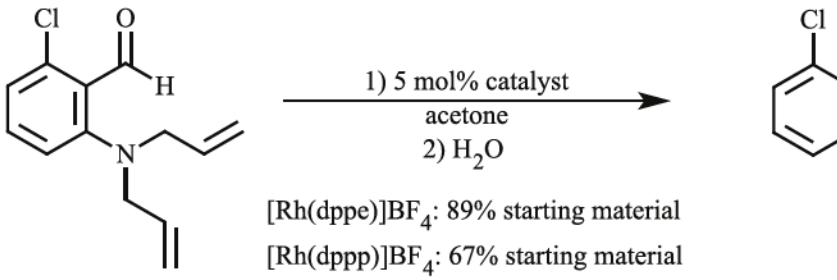
Although refluxing in acetonitrile worked for the synthesis of compound **28**, it provided lower yields for substrates **29** and **32**. There was optimism in the initial attempts to run the reaction in DMF at 95°C in a typical reflux apparatus because the boiling point of diallylamine is around 115°C and would not evaporate out of the vessel. Low yields were obtained using this set up, so pressure tubes were used in all further reactions with DMF as the solvent. Entries 5-6 and 9-13 in Tables 4 and 5 were subjected to a different work-up than the earlier reactions for each substrate to no positive effect. Since the crude product was insoluble in ether, it was thought that the 2:1 ether/hexane mixture was not extracting all of the product. A switch to extracting with ethyl acetate was made since the crude product was soluble in it.[24]

The equivalents of diallylamine necessary for the reaction were also varied. Attempts were made to optimize the reaction by increasing the equivalents of diallylamine. Yields improved slightly, but not dramatically (entries 3-4, 7-8). There was also a concern whether the purity of the diallylamine was a factor due to the presence of the radical inhibitor. The yield with distilled diallylamine was slightly less than that of the reaction with the undistilled diallylamine, proving that distillation was not necessary (entries 10-11).

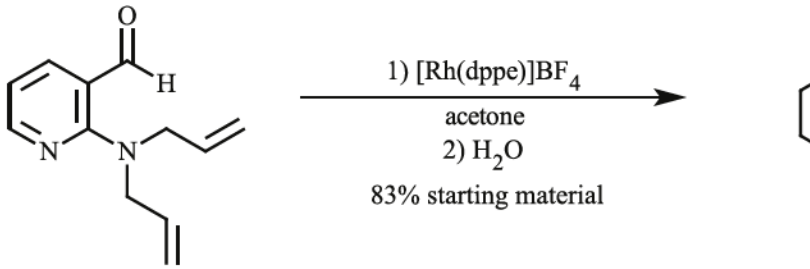
With entries 6 and 13, the reaction was scaled up so that there would be less head space in the pressure tube in order to test whether the diallylamine was in the vapor phase in the space above solution during the reaction and unable to react. This scale up would leave less of a space above solution and hopefully keep more of the diallylamine dissolved in the solvent. To push this concept further, a greater excess of diallylamine and longer reaction times were used. These reactions provided the best, but still disappointing, yields of product.

Substrates **28**, **29**, and **32** were subjected to hydroacylation conditions. Only trace amounts of intramolecular hydroacylation products were observed; the reactions yielded mainly

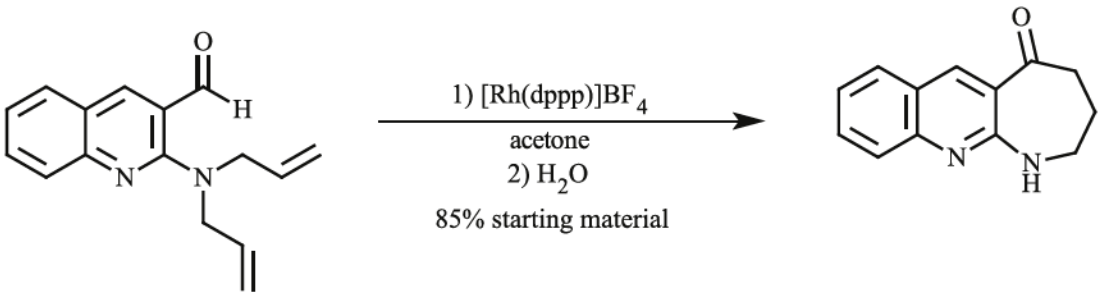
starting material with small amounts of unidentifiable side products (eq. 32-34). Functionalizing the phenyl ring with a chlorine substituent, pyridine, or quinolone appears to shut down the reaction entirely. In the past, butenyl pyridine and quinolone substrates have been cyclized using Wilkinson's catalyst.[19] Perhaps, with the more reactive cationic catalyst, bonds other than the aldehydic carbon-hydrogen bond are breaking in order to follow oxidative addition onto the rhodium. A carbon-chlorine bond is known to do this, but whether a phenyl carbon-chlorine bond is capable of doing this is unknown.



eq. 32



eq. 33



eq. 34

Butenyl ether substrates with a chloro substituent on the phenyl ring underwent hydroacylation using 5 mole percent of [Rh((*R,R*)-Me-DuPHOS)]BF_4 at room temperature.[17]

This is an example of a cationic catalyst being capable of cyclizing a chloro-containing substrate, but this catalyst is also larger and chiral. Having larger ligands that are fixed in place may allow for only the oxidative addition of the aldhydic carbon and hydrogen due to accessibility of the open coordination sites.

4. Conclusions

Useful conditions to cyclize the allyl sulfide compound were successfully determined, and cyclized product was obtained. Substitution of the amine influenced the course of the reaction. A benzyl-substituted amine was very reactive with the reaction going to completion at room temperature in twenty-four hours. An acetyl-substituted allylamine underwent an alkene isomerization instead of the desired hydroacylation. Functionalizing the phenyl ring with a chloro substitutent, pyridine, or quinoline appears to be incompatible with the two cationic catalysts tested. In the future, perhaps different cationic rhodium catalysts will alter the reaction to favor the cyclized product and further extend this chemistry.

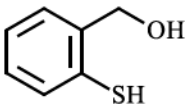
5. Experimental

General Methods:

All reactions were carried out under nitrogen or argon unless otherwise noted. All glassware and syringes were either oven-dried or flame-dried and cooled under nitrogen. Methylene chloride, dichloroethane, and acetonitrile were distilled from calcium hydride and then allowed to cool prior to use. 2-Aminobenzyl alcohol was recrystallized from a 3:1 toluene-hexane mixture and stored under argon prior to use in all reactions. All other commercially available reagents were used as received unless otherwise noted. Reactions were monitored with thin layer chromatography (TLC), using Analtech, silica gel-GF, 250 micron, glass-backed TLC plates. TLC plates were visualized using both ultraviolet (UV) light and iodine (I_2). Products

were purified either by recrystallization or flash chromatography on 70-230 mesh silica gel (Merck, grade 60) with differing ratios of hexane and ethyl acetate as the mobile phase. ^{1}H spectra were acquired with a Bruker Avance DPX-300 Spectrometer using $CDCl_3$ as the solvent and TMS as the reference for $\delta = 0$. IR spectra were obtained using a Thermo Electron IR100 equipped with an ATR device.

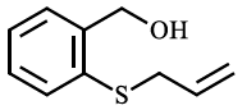
CMD-i-001: **2-mercaptobenzyl alcohol**



$LiAlH_4$ (3.09 g, 81.4 mmol) was added to a 500 mL round bottom flask that was equipped with a dropping funnel. The flask was evacuated and backfilled three times with argon. The round bottom flask was cooled to 0 °C with an ice water bath, and THF (40 mL) was added slowly. Thiosalicylic acid (6.09 g, 39.5 mmol) was dissolved in THF (30 mL) in a 125 mL Erlenmeyer flask and then added to the round bottom flask slowly via the dropping funnel. The Erlenmeyer flask and the dropping funnel were each rinsed with 10 mL of THF, and these rinsings were added to the reaction mixture. The reaction was allowed to warm to room temperature while stirring for 24 h. After reaction completion, it was cooled to 0 °C and treated with ethyl acetate (20 mL) followed with 10% H_2SO_4 (70 mL). The reaction was allowed to warm to room temperature and stir for 15 min. The mixture was then filtered through a celite pad with ethyl acetate. The filtrate was then washed with brine (2x50 mL), and the organic layer was dried over Na_2SO_4 for 1 h and then gravity filtered and concentrated *in vacuo*. The crude product was a clumpy, beige solid (4.89 g, 34.9 mmol, 88%), and was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.36 (m, 2H, phenyl), 7.18 (m, 2H, phenyl), 4.74

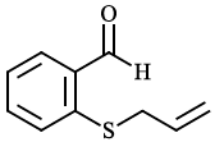
(s, 2H, phenyl-C**H₂**-OH), 3.68 (s, 1H, S**H**), 1.92 (s, 1H, O**H**). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 133.8, 131.3, 130.3, 125.7, 128.4, 125.3, 64.19.

CMD-i-002: **2-(2-propen-1-ylthio)-benzenemethanol**



A 500 mL round bottom flask was charged with product from **001** (0.99 g, 7.09 mmol), CH_2Cl_2 (50 mL), DBU (1.17 mL, 7.8 mmol), and allyl bromide (0.67 mL, 7.8 mmol) and was stirred at room temperature for 24 h. The clear, yellow mixture was extracted with ether (3x15 mL), and then the combined organic layers were washed with water (3x50 mL), 10% HCl (3x50 mL), and brine (2x50 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The product was obtained as a yellow oil (1.07 g, 5.9 mmol, 84%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.37 (m, 2H, phenyl), 7.20 (m, 2H, phenyl), 5.88 (q, J = 9.9 Hz, 1H, alkene C**H**), 5.04 (m, 2H, alkene C**H₂**), 4.73 (s, 2H, phenyl-C**H₂**-OH), 3.50 (d, J = 6.9 Hz, 2H, S-C**H₂**), 2.47 (s, 1H, O**H**). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 141.2, 133.8, 133.3, 130.7, 128.0, 127.9, 126.8, 117.9, 63.2, 37.4. IR (neat, cm^{-1}): 3339, 3059, 2917, 1635, 1589, 1440, 746.

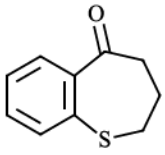
CMD-i-004: **2-(2-propen-1-ylthio)-benzaldehyde**



A 100 mL round bottom flask was charged with pure product from **002** (0.65 g, 3.6 mmol) along with MnO_2 (3.13 g, 36.1 mmol), and methylene chloride (30 mL). The reaction was allowed to stir at room temperature for 24 h, and then filtered through a celite pad and rinsed

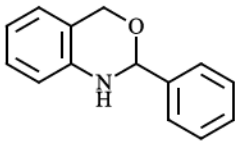
with ether. The filtrate was concentrated and the resulting compound was purified using flash chromatography with a mobile phase ramp from 100% hexane to 98:2 hexane/ethyl acetate. The product was obtained as a yellow oil (0.16 g, 0.65 mmol, 87%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.40 (s, 1H, aldehyde), 7.86 (dd, J = 7.6, 1.5 Hz, 1H, phenyl), 7.51 (m, 2H, phenyl), 7.32 (m, 1H, phenyl), 5.87 (m, 1H, alkene C**H**), 5.11 (m, 2H, alkene C**H$_2$**), 3.58 (d, 2H, S-C**H$_2$**). IR (neat, cm^{-1}): 3060, 2841, 2738, 1687, 1585, 1459, 1194, 748. ^{13}C NMR (75 MHz, $CDCl_3$, δ): 191.7, 140.5, 134.5, 133.3, 132.5, 131.7, 129.5, 125.9, 118.8, 56.7.

CMD-i-010: **3,4-dihydro-1-bensothiepin-5(2*H*)-one**



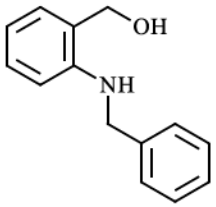
Product from **004** (0.11 g, 0.61 mmol) was added to a 10 mL Schlenk flask. The flask was evacuated and backfilled with argon three times. Methylene chloride (1.5 mL) and [Rh(dppe)]BF_4 (0.030 mmol, 1.5 mL of 0.02 M CH_2Cl_2 solution) were added. The reaction mixture was refluxed gently for 24 h. The mixture was concentrated and purified by flash chromatography with 95:5 hexane/ethyl acetate. The product was obtained as a yellow oil (0.062 g, 0.35 mmol, 75%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.84 (d, J = 1.6 Hz, 1H, phenyl), 7.46 (m, 1H, phenyl), 7.26 (m, 2H, phenyl), 3.08 (t, J = 4.8 Hz, 4H), 2.97 (t, J = 4.8 Hz, 2.28 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 203.0, 142.2, 138.3, 131.0, 130.3, 130.2, 126.0, 40.2, 34.9, 30.0. IR (neat, cm^{-1}): 3055, 2922, 2853, 1673, 1586, 1429, 1285, 740.

CMD-i-037: **1,4-dyhydro-2-phenyl-2*H*-3,1-benzoxazine**



Aminobenzyl alcohol (1.50 g, 12.4 mmol) and methylene chloride (40 mL) were added to a 100 mL round bottom flask. Benzaldehyde (1.32 g, 12.4 mmol) and K_2CO_3 (8.56 g, 61.9 mmol) were added, producing a clear brown reaction mixture. The reaction was stirred at room temperature for 24 h to yield a cloudy, pale yellow mixture. TLC revealed that the starting material had been consumed. The mixture was filtered through a celite pad with ether. The product was concentrated *in vacuo*. The crude product was a light brown powdery solid (2.52 g, 11.9 mmol, 96%) and was used without futher purification. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.57 (m, 2H, phenyl), 7.42 (m, 3H, phenyl), 7.11 (t, J = 7.3 Hz, 1H, phenyl), 6.97 (d, J = 7.7 Hz, 1H, phenyl), 6.87 (td, J = 7.4, 1.1 Hz, 1H, phenyl), 6.73 (d, J = 7.9 Hz, 1H, phenyl), 5.60 (s, 1H, N-**H**), 5.05 (dd, J = 14.7, 55.4 Hz, 1H, phenyl-C**H**$_2$-O-CH-phenyl), 4.12 (s, 1H, NH-C**H**-phenyl). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 141.7, 139.2, 129.1, 128.9, 128.7, 127.5, 126.5, 125.1, 122.2, 119.9, 117.1, 85.3, 67.8. IR (neat, cm^{-1}): 3331, 3038, 2852, 1610, 1590, 1483, 1020, 754, 696.

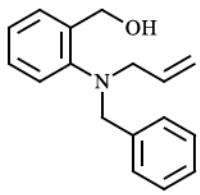
CMD-i-039: **2-[(phenylmethyl)amino]-benzenemethanol**



$LiAlH_4$ (0.87 g, 23.1 mmol) was added to a 250 mL round bottom flask that was equipped with a dropping funnel. The flask was evacuated and backfilled three times with argon. The round bottom flask was cooled to 0 °C with an ice water bath, and THF (30 mL) was

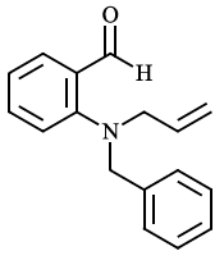
added slowly. The crude product from **037** was dissolved in THF (30 mL) in a 125 mL Erlenmeyer flask and then added to the round bottom flask slowly via the dropping funnel. The Erlenmeyer flask and the dropping funnel were each rinsed with 10 mL of THF, and these rinsings were added to the reaction mixture. The reaction was allowed to warm to room temperature while stirring for 24 h. After reaction completion, it was cooled to 0 °C and treated with ether (30 mL) followed with water (0.9 mL), 10% NaOH (1.4 mL), and then more water (2.7 mL). The reaction was allowed to warm to room temperature and stir for 15 min. $MgSO_4$ (~2.0 g) was added, and the mixture was allowed to stir for another 15 min. It was then filtered through a celite pad with ether. The filtrate was then washed with 10% NaOH (2x30 mL), water (2x20 mL), and brine (2x20 mL). The organic layer was allowed to dry over Na_2SO_4 for 3 h, and then gravity filtered. The crude product was a clumpy white solid at room temperature, and was recrystallized in hexane. The final product was fine white needles (1.92 g, 9.0 mmol, 78%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.37 (m, 4H, phenyl), 7.26 (m, 1H, phenyl), 7.18 (dd, J = 7.8, 6.6 Hz, 1H, phenyl), 7.07 (dt, J = 7.3, 1.6 Hz, 1H, phenyl), 6.67 (m, 2H, phenyl), 5.22 (s, 1H, N**H**), 4.71 (s, 2H, phenyl-C**H$_2$**-OH), 4.39 (s, 2H, NH-C**H$_2$**-phenyl), 1.58 (s, 1H, O-**H**). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 147.4, 139.4, 129.7, 129.1, 128.6, 127.4, 127.1, 124.2, 116.7, 111.0, 64.9, 47.7. IR (neat, cm^{-1}): 3411, 3261, 3052, 2913, 2865, 1605, 1585, 1520, 1446, 988, 743, 694.

CMD-i-041: **2-[(benzyl)(2-propen-1-yl)amino]benzenemethanol**



A 100 mL round bottom flask was charged with pure product from **039** (0.21 g, 0.97 mmol), CH_3CN (30 mL) and K_2CO_3 (0.27 g, 2.0 mmol). The mixture was allowed to stir for 5 min at room temperature. Then allyl bromide (0.10 mL, 1.2 mmol) was added, a condenser was attached, and the reaction was refluxed gently under nitrogen for 24 h. After 24 hours, NaI (0.15 g, 0.97 mmol) and more allyl bromide (0.017 mL, 0.19 mmol) was added and the reaction was left to reflux gently another 24 h. The mixture was cooled and extracted with ether (3x15 mL). The combined organic layers were washed with water (3x15 mL), which was made pH = 9 with a few drops of 10% NaOH, and brine (3x15 mL). The organic layer was dried over Na_2SO_4 and rotovapped. The product was purified using flash chromatography, with a mobile phase ramp of 97:3 to 95:5 hexane/ethyl acetate. The product was obtained as a yellow oil (0.19 g, 0.76 mmol, 79%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.11-7.40 (m, 9H, phenyl), 5.79 (m, 1H, N-CH_2-C**H**=CH_2), 5.16 (d, *J* = 4.5 Hz, 2H, N-CH_2-CH=C**H$_2$**), 4.92 (s, 1H, phenyl-CH_2-O**H**), 4.74 (s, 2H, phenyl-C**H$_2$**-OH), 4.10 (s, 2H, N-C**H$_2$**-phenyl), 3.55 (d, *J* = 6.5 Hz, 2H, N-C**H$_2$**-CH=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 149.0, 137.3, 136.8, 133.9, 129.4, 128.5, 128.4, 127.9, 127.5, 125.1, 123.5, 118.8, 64.5, 58.7, 56.3. IR (neat, cm^{-1}): 3375, 3063, 3028, 2838, 1598, 1490, 1451, 1027, 918, 765, 724, 697.

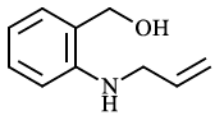
CMD-i-042: **2-[(benzyl)(2-propen-1-yl)amino]benzaldehyde**



A 50 mL round bottom flask was charged with pure product from **041** (0.19 g, 0.76 mmol) along with $PhI(OAc)_2$ (0.30 g, 0.93 mmol), TEMPO (0.023 g, 0.15 mmol), and methylene

chloride (10 mL). The reaction was allowed to stir at room temperature for 24 h, and then extracted with ether (3x15 mL). The combined organic layers were then washed with NaS_2O_3 (3x15 mL) and brine (3x15 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified using flash chromatography with a mobile phase ramp of 100% hexane to 97:3 hexane/ethyl acetate. The product was collected and concentrated to a yellow oil (0.16 g, 0.65 mmol, 87%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.46 (s, 1H, aldehyde), 7.82 (dd, J = 8.2, 1.9 Hz, 1H, phenyl), 7.44 (td, J = 6.5, 1.8 Hz, 1H, phenyl), 7.25 (m, 5H, phenyl), 7.11 (m, 2H, phenyl), 5.86 (m, 1H, N-CH_2-C**H**=CH_2), 5.20 (m, 2H, N-CH_2-CH=C**H$_2$**), 4.35 (s, 2H, N-C**H$_2$**-phenyl), 3.73 (d, J = 6.2 Hz, 2H, N-C**H$_2$**-CH=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 191.5, 154.3, 137.4, 134.4, 133.6, 129.6, 129.5, 128.4, 128.3, 127.3, 122.6, 121.8, 118.5, 58.4, 57.7. IR (neat, cm^{-1}): 3065, 3030, 2842, 1684, 1595, 1480, 1452, 1417, 1279, 1189, 921, 831, 764, 729, 697.

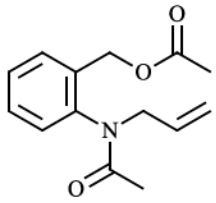
CMD-i-050: **(2-propen-1-yl)aminobenzenemethanol**



A 200 mL Schlenk flask was charged with aminobenzyl alcohol and evacuated and backfilled three times with argon. Then THF (40 mL) and 9-BBN (32.6 mL of 0.5M in THF) were added, and the reaction was stirred at room temperature for 2 h. Potassium t-butoxide (17.9 mL of 1.0M in THF, 17.9 mmol) was added via syringe, and the reaction was stirred at room temperature for 40 min. Allyl bromide (1.7 mL, 19.5 mmol) was added via syringe, and the reaction was stirred at room temperature for 24 h. The mixture was gravity filtered, rotovapped, and added to 1M HCl (200 mL) and stirred at room temperature for 48 h. The mixture was

washed with ether (3x50 mL). The aqueous layer was made basic with 20% NaOH and extracted with ether (4x50mL). The combined organic layers were then washed with brine (3x50 mL). The organic layer was dried over Na_2SO_4 and rotovapped. The crude product was purified by flash chromatography with 95:5 to 90:10 hexane/ethyl acetate. The product was collected as a yellow oil (1.82 g, 11.1 mmol, 68%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.25 (td, J = 7.7, 1.6 Hz, 1H, phenyl), 7.07 (dd, J = 7.7, 1.7 Hz, 1H, phenyl), 6.67 (m, 2H, phenyl), 6.03 (m, 1H, N-CH_2-C**H**=CH_2), 5.29 (dq, J = 17.2, 1.7 Hz, 1H, N-CH_2-CH=C**H$_2$**), 5.18 (dq, J = 10.2, 1.6 Hz, 1H, N-CH_2-CH=C**H$_2$**), 4.92 (s, 1H, N**H**), 4.67 (s, 2H, phenyl-C**H$_2$**-OH), 3.82 (dd, J = 5.2, 1.6 Hz, 2H, NH-C**H$_2$**-CH=CH_2), 1.59 (s, 1H, O**H**). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 147.3, 135.4, 129.6, 129.1, 124.5, 116.9, 116.1, 111.1, 64.7, 45.0. IR (neat, cm^{-1}): 3387, 3077, 2870, 1606, 1586, 1512, 1459, 1416, 1312, 1261, 992, 921, 745.

CMD-i-052: **N-[2-[(acetlyoxy-methyl]phenyl]-N-(2-propen-1-yl) acetamide**



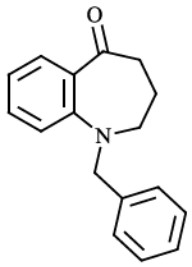
A 50 mL round bottom flask was charged with allylaminobenzyl alcohol (0.58 g, 3.6 mmol) and pyridine (3.6 mL) and cooled to 0 °C. Acetic anhydride (1.08 mL, 11.4 mmol) was added slowly, and the reaction was allowed to stir and warm to room temperature for 24 h. The reaction was poured onto a $NaHCO_3/H_2O$ mixture (15 mL), stirred for 30 min., and then extracted with 2:1 ether/CH_2Cl_2 (3x15 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The product was obtained as a yellow oil (0.85 g, 3.5 mmol, 97%) and was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.49 (m, 1H, phenyl),

7.38 (m, 2H, phenyl), 7.14 (m, 1H, phenyl), 5.91 (m, 1H, N-CH_2-C**H**=CH_2), 5.13 (m, 2H, N-CH_2-CH=C**H$_2$**), 5.08 (m, 2H, N-CH_2-CH=C**H$_2$**), 4.65 (dt, *J* = 5.4, 1.3 Hz, 1H, phenyl-N-C**H$_2$**-CH=CH_2), 3.77 (dd, *J* = 14.4, 7.4 Hz, 2H, phenyl-N-C**H$_2$**-CH=CH_2), 2.10 (s, 3H, O-CO-C**H$_3$**), 1.80 (s, 3H, N-CO-C**H$_3$**). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 170.6, 170.5, 141.4, 133.7, 132.6, 130.6, 129.8, 129.7, 128.8, 118.7, 62.4, 51.9, 22.5, 20.9, 20.5. IR (neat, cm^{-1}): 2934, 1737, 1660, 1601, 1581, 1493, 1381, 1221, 1027, 979, 923, 750.

CMD-i-053: **[Rh(dppp)]BF_4 and [Rh(dppe)]BF_4**

A 25 mL Schlenk flask was charged with anyhydrous acetone and was freeze/thaw/degassed three times. A 10 mL schlenk flask was charged with [Rh(NBD)$_2$]BF_4 (0.0234 g, 0.063 mmol) and dppp (0.026g, 0.063 mmol) and evacuated and backfilled three times with argon. Acetone (6.26 mL) was added to the [Rh(NBD)$_2$]BF_4 and the mixture was bubbled with hydrogen for 5 min. The reaction mixture was freeze/thaw/degassed three times and backfilled with argon. The product was a clear, orange-yellow color and was used without any further purification.

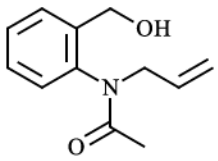
CMD-i-054: **1,2,3,4-tetrahydro-1-(phenylmethyl)-5*H*-1-benzazepin-5-one**



Product from **051** (0.11 g, 0.43 mmol) was added to a 10 mL Schlenk flask. The flask was evacuated and backfilled three times with argon, then acetone (4.3 mL) and [Rh(dppp)]BF_4

(2.15 mL of 0.01 M in acetone, 0.0215 mmol, **053**) were added. The reaction mixture was stirred at room temperature for 24 h. The resulting red mixture was concentrated and purified with flash chromatography using a mobile phase ramp of 100% hexane to 95:5 hexane/ethyl acetate. Product was obtained as a yellow solid (0.0895 g, 0.356 mmol, 83%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.78 (dd, *J* = 7.8, 1.8 Hz, 1H, phenyl), 7.34 (m, 6H, phenyl), 6.82 (m, 2H, phenyl), 4.70 (s, 2H, phenyl-N-C**H$_2$**-phenyl), 3.36 (t, *J* = 6.6 Hz, 2H, N-C**H$_2$**-CH=CH_2), 2.84 (t, *J* = 7.2 Hz, 2H, CO-C**H$_2$**), 2.15 (m, 2H, CO-CH_2-C**H$_2$**-CH_2-N). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 203.2, 153.8, 137.9, 132.5, 129.3, 128.8, 127.3, 127.2, 126.9, 118.3, 115.0, 55.5, 54.5, 41.2, 31.5. IR (neat, cm^{-1}): 3062, 2946, 2924, 2856, 1650, 1591, 1556, 1482, 1441, 1366, 1338, 1293, 1222, 1203, 1160, 1038, 774, 754, 739, 704.

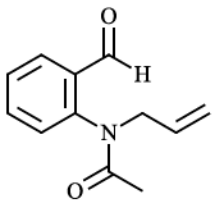
CMD-i-055: **2-[(acetyloxy)(2-propen-1-yl)amino]benzenemethanol**



A 50 mL round bottom flask was charged with product from **052** (0.38 g, 1.5 mmol) and methanol (3.0 mL) and cooled to 0 °C. Potassium carbonate (0.32 g, 2.3 mmol) was added, and the reaction was stirred and allowed to warm to room temperature for 24 h. The reaction mixture was filtered through a celite pad with ether, and the filtrate was removed *in vacuo*. The crude product was purified using flash chromatography with a mobile phase ramp of 85:15 to 60:40 hexane/ethyl acetate. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 7.60 (m, 1H, phenyl), 7.38 (m, 2H, phenyl), 7.09 (m, 1H, phenyl), 5.91 (m, 1H, N-CH_2-C**H**=CH_2), 5.13 (m, 2H, N-CH_2-CH=C**H$_2$**), 4.63 (d, *J* = 5.5 Hz, 2H, phenyl-C**H$_2$**-OH), 4.57 (m, 1H, phenyl-N-C**H$_2$**-CH=CH_2), 3.92 (dd, *J* =

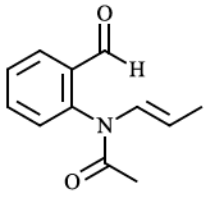
14.4, 7.1 Hz, 1H, phenyl-N-C**H**$_2$-CH=CH$_2$), 2.23 (t, *J* = 5.5 Hz, 1H, phenyl-CH$_2$-O**H**), 1.78 (s, 3H, N-CO-C**H**$_3$).

CMD-i-056: **2-[(acetyloxy)(2-propen-1-yl)amino]benzaldehyde**



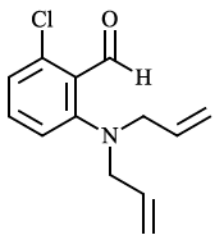
A 50 mL round bottom flask was charged with product from **055** (0.19 g, 0.91 mmol), PhI(OAc)$_2$ (0.37 g, 1.1 mmol), TEMPO (0.028 g, 0.18 mmol), and methylene chloride (5 mL). The reaction was allowed to stir at room temperature for 24 h, and then extracted with ether (3x15 mL). The combined organic layers were then washed with NaS_2O_3 (3x15 mL) and brine (3x15 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified using flash chromatography with a mobile phase ramp of 90:10 to 70:30 hexane/ethyl acetate. The product was collected and concentrated to a yellow oil (0.17 g, 0.82 mmol, 90%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.14 (s, 1H, aldehyde), 7.98 (dd, *J* = 7.7, 1.7 Hz, 1H, phenyl), 7.70 (td, *J* = 1.7, 7.6 Hz, 1H, phenyl), 7.54 (t, *J* = 7.6 Hz, 1H, phenyl), 7.27 (dd, *J* = 7.9, 1.1 Hz, 1H, phenyl), 5.89 (m, 1H, N-CH$_2$-C**H**=CH$_2$), 5.15 (dd, *J* = 10.0, 1.1 Hz, 1H, N-CH$_2$-CH=C**H**$_2$), 5.05 (dq, *J* = 17.1, 1.3 Hz, 1H, N-CH$_2$-CH=C**H**$_2$), 4.48 (dd, *J* = 14.3, 6.7 Hz, 1H, N-C**H**$_2$-CH=CH$_2$), 4.21 (dd, *J* = 14.4, 6.9 Hz, 1H, N-C**H**$_2$-CH=CH$_2$), 1.82 (s, 3H, N-CO-C**H**$_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 189.7, 169.9, 144.5, 135.5, 132.9, 131.9, 130.1, 130.0, 129.0, 119.7, 52.9, 22.8. IR (neat, cm^{-1}): 2856, 1692, 1658, 1595, 1483, 1455, 1383, 1267, 1191, 989, 925, 822, 779, 748.

CMD-i-058: **2-[(acetyloxy)(2-propen-2-yl)amino]benzaldehyde**



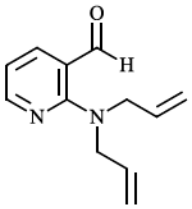
Product from **056** (0.096 g, 0.47 mmol) was added to a 10 mL schlenk flask and evacuated and backfilled three times with argon. Acetone (4.7 mL) and [Rh(dppp)]BF_4 (2.35 mL of 0.01 M in acetone, 0.0235 mmol, **057**) were added. The reaction mixture was stirred and gently heated for 24h. The resulting clear, orange mixture was concentrated and purified with flash chromatography using a mobile phase ramp of 90:10 to 70:30 hexane/ethyl acetate. Product was obtained as a light beige solid (0.079 g, 0.39 mmol, 83%). NMR shows isomerized starting material instead of intented cyclized product. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.14 (s, 1H, aldehyde), 8.07 (dd, J = 7.7, 1.7 Hz, 1H, phenyl), 7.78 (td, J = 7.6, 1.7 Hz, 1H, phenyl), 7.63 (m, 2H, phenyl), 7.27 (dd, J = 7.8, 1.0 Hz, 1H, N-CH=C**H**-CH_3), 4.37 (dq, J = 13.4, 6.7 Hz, 1H, N-C**H**=CH-CH_3), 1.82 (s, 3H, N-CO-C**H$_3$**), 1.62 (dd, J = 6.7, 1.6 Hz, 3H, N-CH=CH-C**H$_3$**). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 189.4, 167.8, 142.2, 135.8, 133.1, 130.3, 129.9, 129.6, 129.4, 110.6, 23.3, 15.2. IR (neat, cm^{-1}): 3082, 2956, 2868, 2360, 1696, 1673, 1654, 1595, 1483, 1458, 1367, 1304, 1273, 1261, 1195, 1125, 1088, 957, 825, 789, 748.

CMD-i-063: **2-chloro-6-(di-2-propen-1-ylamino)-benzaldehyde**



A 25 mL round bottom flask was charged with 2.6-dichlorocarboxaldehyde (0.11 g, 0.70 mmol), K_2CO_3 (0.11 g, 0.77 mmol), diallylamine (0.17 mL, 1.4 mmol), and acetonitrile (3 mL). The reaction was heated to reflux for 24 h, and then extracted with 2:1 ether/hexane (4x10 mL). The combined organic layers were then washed with brine (3x10 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified using flash chromatography with a mobile phase ramp of 100% hexane to 99:1 hexane/ethyl acetate. The product was collected and concentrated to a bright yellow oil (0.12 g, 0.51 mmol, 73%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.31 (s, 1H, aldehyde), 7.31 (t, J = 6.7 Hz, 1H, phenyl), 7.01 (m, 2H, phenyl), 5.78 (m, 2H, N-CH_2-C**H**=CH_2), 5.17 (m, 4H, N-CH_2-CH=C**H$_2$**), 3.76 (dt, J = 6.0, 1.2 Hz, 4H, N-C**H$_2$**-CH=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 189.74, 154.37, 136.00, 133.65, 133.16, 126.11, 123.61, 119.73, 118.46, 56.72. IR (neat, cm^{-1}): 3057.3, 2977.6, 2920.9, 2854.1, 1678.8, 1614.2, 1586.1, 1553.9, 1488.9, 1430.9, 1395.8, 933.4, 919.2, 750.7.

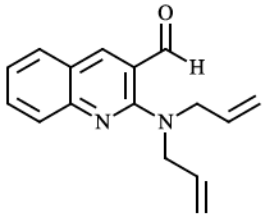
CMD-i-077: **6-(di-2-propen-1-ylamino)-pyridinecarboxaldehyde**



A pressure tube was charged with 2-chloro-3-pyridinecarboxaldehyde (0.30 g, 2.1 mmol), K_2CO_3 (0.44 g, 3.2 mmol), diallylamine (0.78 mL, 6.3 mmol), and DMF (10 mL). The reaction was heated to 95°C for 24 h in a silicon oil bath and then extracted with ethyl acetate (4x10 mL). The combined organic layers were then washed with brine (3x10 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified using flash chromatography with a mobile phase ramp of 100% hexane to 95:5 hexane/ethyl acetate. The

product was collected and concentrated to a pale yellow oil (0.094 g, 0.47 mmol, 22%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.01 (s, 1H, aldehyde), 8.33 (dd, *J* = 4.6, 2.0 Hz, 1H, phenyl), 7.98 (dd, *J* = 7.6, 2.0 Hz, 1H, phenyl), 6.81 (dd, *J* = 7.6, 4.6 Hz, 1H, phenyl), 5.93 (m, 2H, N-CH_2-C**H**=CH_2), 5.27 (m, 4H, N-CH_2-CH=C**H$_2$**), .10 (d, *J* = 6.0 Hz, 4H, N-C**H$_2$**-CH=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 190.17, 160.68, 152.29, 139.88, 133.91, 118.41, 117.83, 114.57, 53.76. IR (neat, cm^{-1}): 3076.5, 2981.6, 2851.9, 1673.5, 1582.7, 1540.4, 1473.7, 1410.1, 1217.6, 921.1, 847.5, 773.9.

CMD-i-078: **6-(di-2-propen-1-ylamino)-quinolinecarboxaldehyde**



A pressure tube was charged with 2-chloro-3-quinolinecarboxaldehyde (0.29 g, 1.5 mmol), K_2CO_3 (0.31 g, 2.2 mmol), diallylamine (0.55 mL, 4.5 mmol), and DMF (7.5 mL). The reaction was heated to 95°C for 24 h in a silicon oil bath and then extracted with ethyl acetate (4x10 mL). The combined organic layers were then washed with brine (3x10 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was purified using flash chromatography with a mobile phase ramp of 100% hexane to 98:2 hexane/ethyl acetate. The product was collected and concentrated to a bright yellow solid (0.095 g, 0.38 mmol, 25%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 10.16 (s, 1H, aldehyde), 8.47 (s, 1H, phenyl), 7.77 (m, 2H, phenyl), 7.66 (m, 1H, phenyl), 7.32 (m, 1H, phenyl), 6.01 (m, 2H, N-CH_2-C**H**=CH_2), 5.27 (m, 4H, N-CH_2-CH=C**H$_2$**), 4.13 (d, *J* = 5.7 Hz, 4H, N-C**H$_2$**-CH=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 190.62, 158.10, 149.27, 141.73, 134.25, 132.38, 129.19, 127.30, 124.07, 123.48, 121.91,

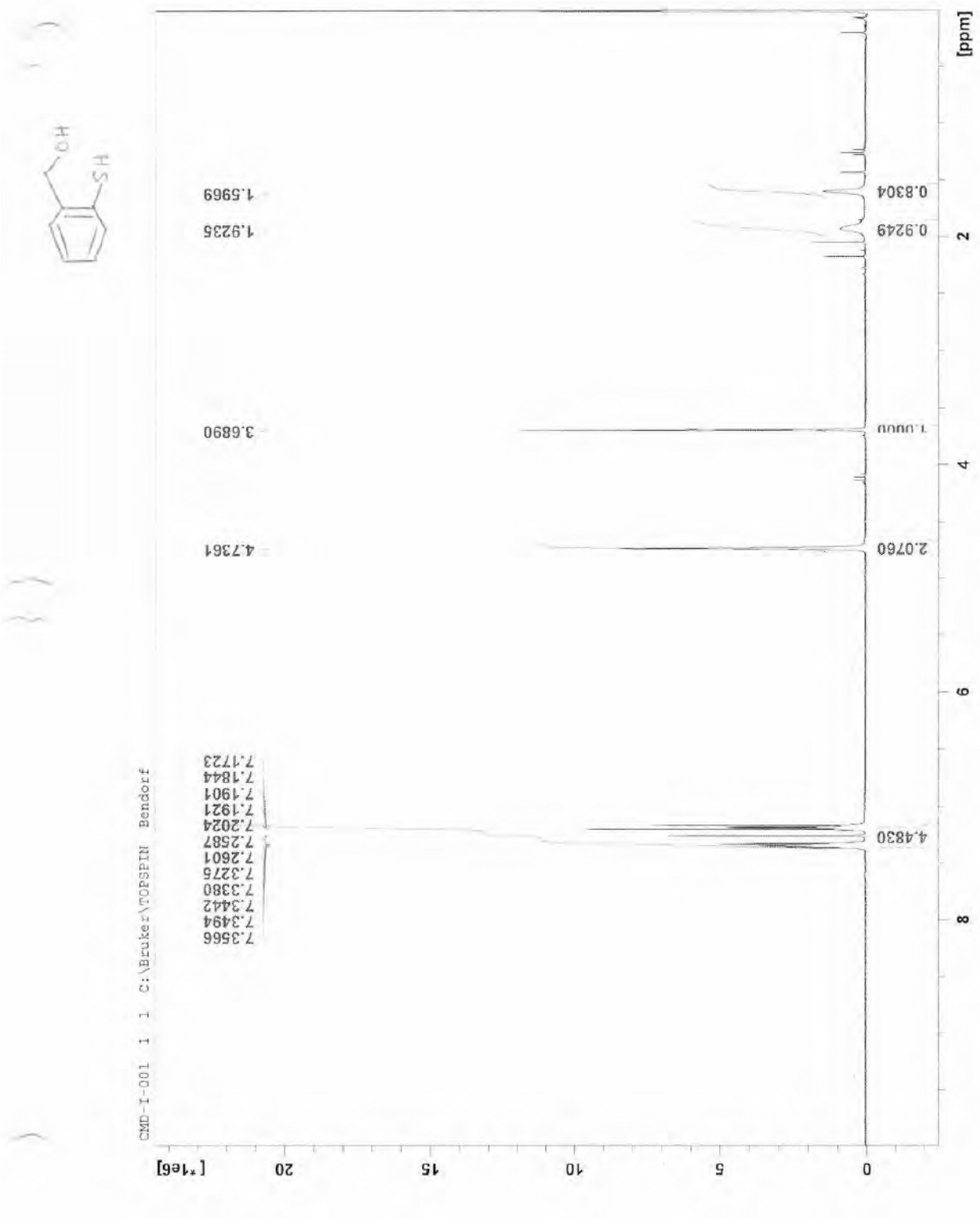
117.96, 53.76. IR (neat, cm^{-1}): 3079.9, 2955.0, 1692.5, 1583.3, 1454.1, 1417.3, 1232.3, 1174.0, 991.5, 921.0, 782.3, 723.2.

References

1. Ghali, Jalal K.; Hamad, Bashar; Yasothan, Uma; Kirkpatrick, Peter. *Nature Reviews Drug Discovery* **2009**, *8,* 611-612.
2. Huang, Horng-Chih, Lee, Len F.; Keller, Bradley T. "Discovery of Potent, Nonsystemic Apical Sodium-Codependent Bile Acid Transporter Inhibitors." *J. Med. Chem.*, **2005**, *48* (18), 5837–5852.
3. National Center for Biotechnology Information http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0004879/ (Accessed February 23, 2012).
4. Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972,** *13*, 1287-1290.
5. Larock, R. C.; Oertle, K.; Potter, G. F. "A Convenient Synthesis of Cyclopentanones via Rhodium(I)-Catalyzed Intramolecular Hydroacylation of Unsaturated Aldehydes." *J. Am. Chem. Soc.* **1980,** *102*, 190-196.
6. Bosnich, B.; Fairlie, Daivd P. "Conversion of 4-Pentenals to Cyclopentanones by Efiicient Rhodium-Catalyzed Hydroacylation." *Organometallics.* **1988,** *7*, 936-945.
7. Bosnich, B.; Fairlie, David P. "Mechanism of Catalytic Hydroacylation: The Conversion of 4-Pentenals to Cyclopentanones." *Organometallics.* **1988,** *7*, 946-954.
8. Sato, Yoshihiro; Mori, Miwako; Oonishi, Yoshihiro. "A New Method for the Synthesis of Cycloheptanones by Rh^{I}-Catalyzed Intramolecular Hydroacylation of 4,6-Dienals." *Angew. Chem. Int. Ed.* **2002,** *41*, 1218-1221.
9. Sato, Yoshihiro; Ogura, Jiro; Oonishi, Yoshihiro. "Rh(I)-catalyzed intramolecular hydroacylation in ionic liquids." *Tetrahedron Lett.* **2007**, *48*, 7505-7507.
10. Sato, Yoshihiro; Mori, Miwako; Oonishi, Yoshihiro. "Rh(I)-catalyzed hydroacylation/cycloisomerization cascade: synthesis of (±)-epiglobulol." *Tetrahedron Lett.* **2006**, *47*, 5617-5621.
11. Shair, Matthew D.; Layton, Mark E.; Aloise, Allen D. "Synthesis of Cyclooctenones Using Intramolecular Hydroacylation." *J. Am. Chem. Soc.* **2000.** *122,* 12610-12611.
12. Aissa, Christophe; Crépin, Damien; Tugny, Coralie; Murray, James H. "Facile and chemoselective rhodium-catalyzed intramolecular hydroacylation of α,α-disubstituted 4-alkylidenecyclopropanals." *Chem. Commun.* **2011**. *47*, 10957-10959.
13. Furstner, Alois; Aissa, Christophe. "A Rhodium-Catalyzed C-H Activation/Cycloisomerization Tandem." *J. Am. Chem. Soc.* **2007.** *129,* 14836-14837.
14. Aissa, Christophe; Crépin, Damien; Dawick, James. "Combined Rhodium-Catalyzed Carbon-Hydrogen Activation and B-Carbon Elimination to access Eight-Membered Rings." *Angew. Chem. Int. Ed.* **2010,** *409*, 620-623.
15. Bendorf, H. D.; Colella, C. M.; Dixon, E. C., Marchetti, M.; Matukonis, A. M.; Musselman, J. D.; Tiley, T. A. "Chelation-Assissted Intramolecular Hydroacylation: Synthesis of Medium-Ring Sulfur Heterocycles." *Tetrahedron Lett.* **2002,** *43*, 7031-7034.
16. Dong, Vy M.; Khan, Hasan A.; Shen, Zengming. "Rh-Catalyzed Carbonyl Hydroacylation: An Enantioselective Approach to Lactones." *J. Am. Chem. Soc.* **2008.** *130,* 2916-2917.

17. Dong, Vy M.; Coulter, Matthew M.; Dornan, Peter K. "Rh-Catalysed Intramolecular Olefin Hydroacylation: Enantioselective Synthesis of Seven- and Eight-Membered Heterocycles." *J. Am. Chem. Soc.* **2009.** *131,* 6932-6933.
18. Dong, Vy M.; Khan, Hasan A.; Kou, Kevin G. M. "Nitrogen-Directed Ketone Hydroacylation: Enantioselective Synthesis of Benzoxazecinones." *Chem. Sci*. **2011,** *2*, 407-410.
19. Bendorf, Holly D.; Ruhl, Kyle E.; Shurer, Andrew J.; Shaffer, Jennie B.; Duffin, Tess O.; LaBarte, Theresa L.; Maddock, Michelle L.; Wheeler, Oscar W. "Amine-Directed Intramolecular Hydroacylation of Alkenes and Alkynes." *Tetrahedron Lett.* **2012**, *53*, 1275-1277.
20. Douglas, Christopher J.; Sudheer, Ch.; Beletskiy, Evgeny V. "Cooperative Catalysis Approach to Intramolecular Hydroacylation." *J. Org. Chem.* **2012**. *77*, 5884-5893.
21. Suggs, J.W. "Activation of Aldehyde C-H Bonds to Oxidative Addition via Formation of 3-Methyl-2-aminopyridyl Aldimines and Related Compounds: Rhodium-Based Catalytic Hydroacylation." *J. Am. Chem. Soc.* **1979.** *101,* 489.
22. Jun, C.-H.; Lee, D.-Y.; Lee, H.; Hong, J.-B. "A Highly Active Catalyst System for Intermolecular Hydroacylation." *Angew. Chem. Int. Ed.* **2000,** *39*, 3070-3072.

Important Spectra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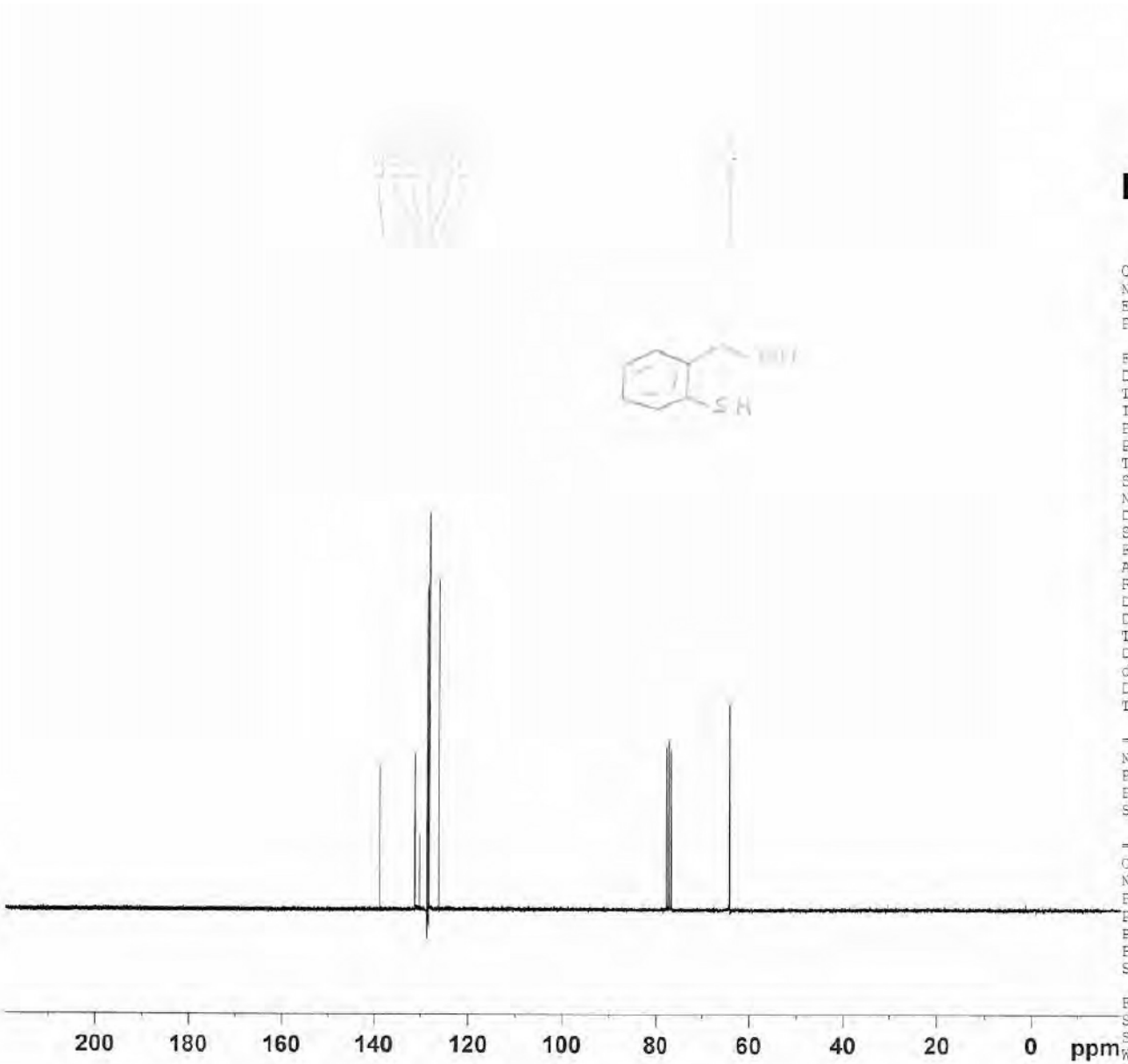

BRUKER

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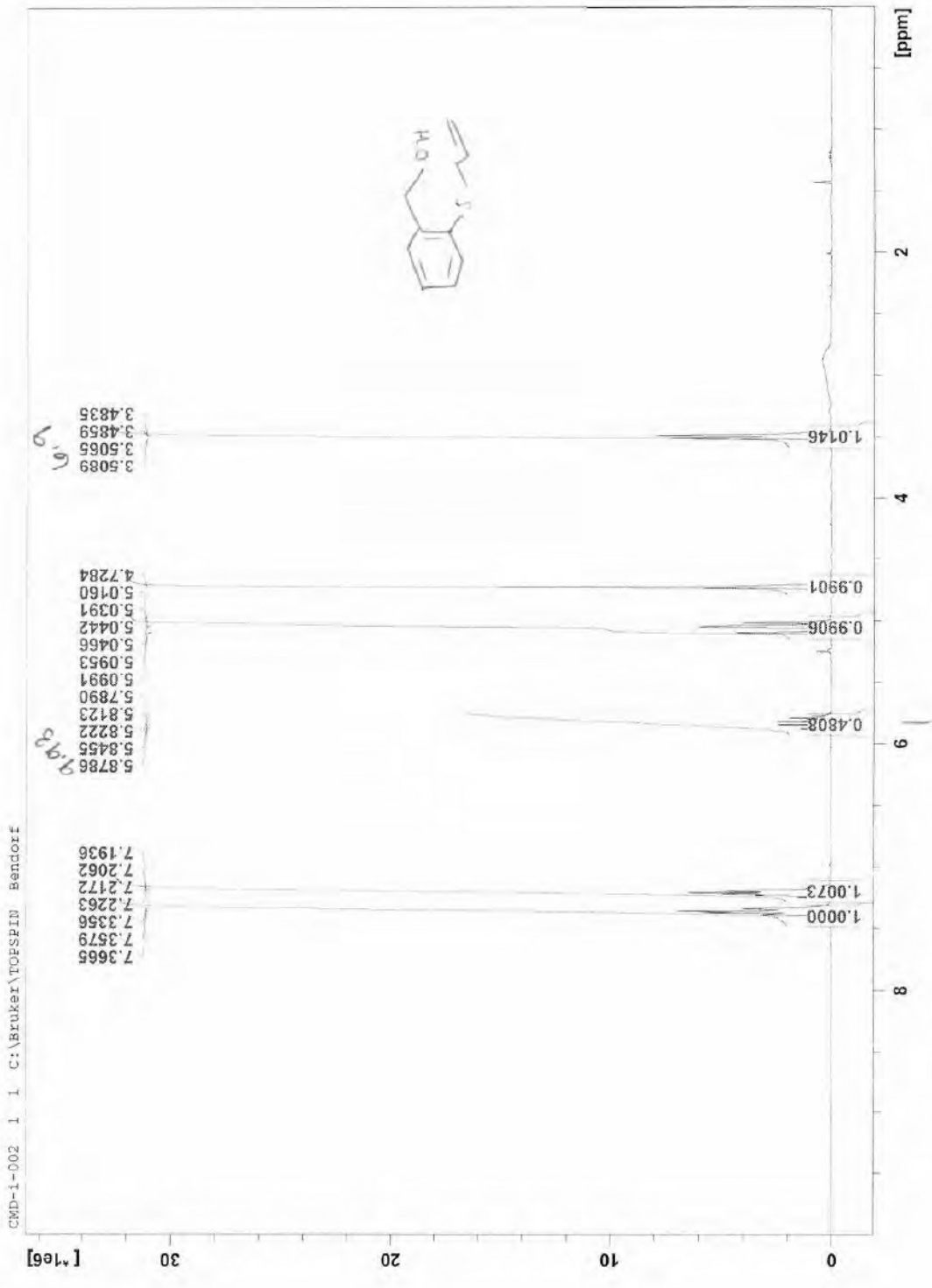
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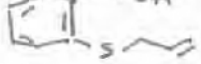

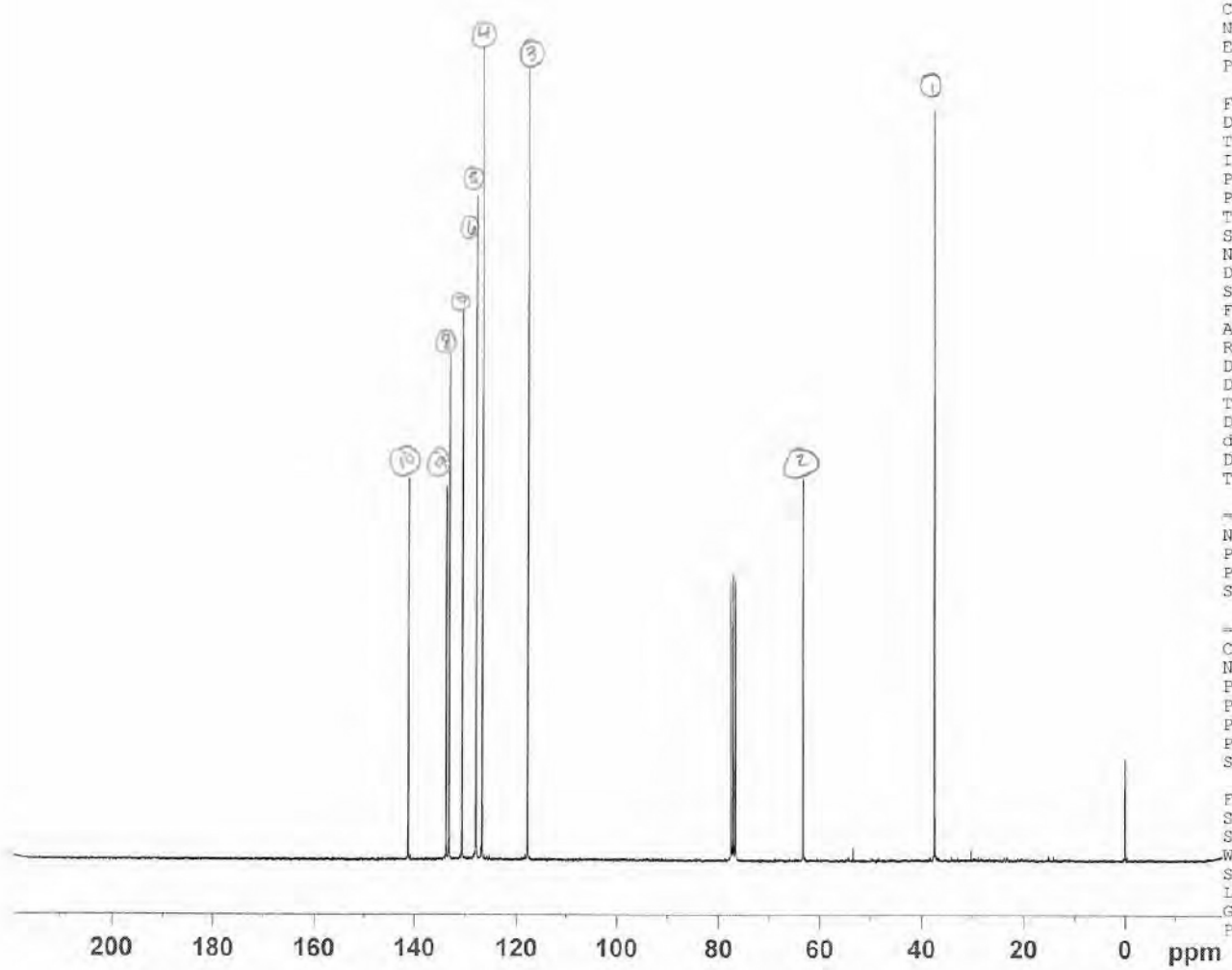

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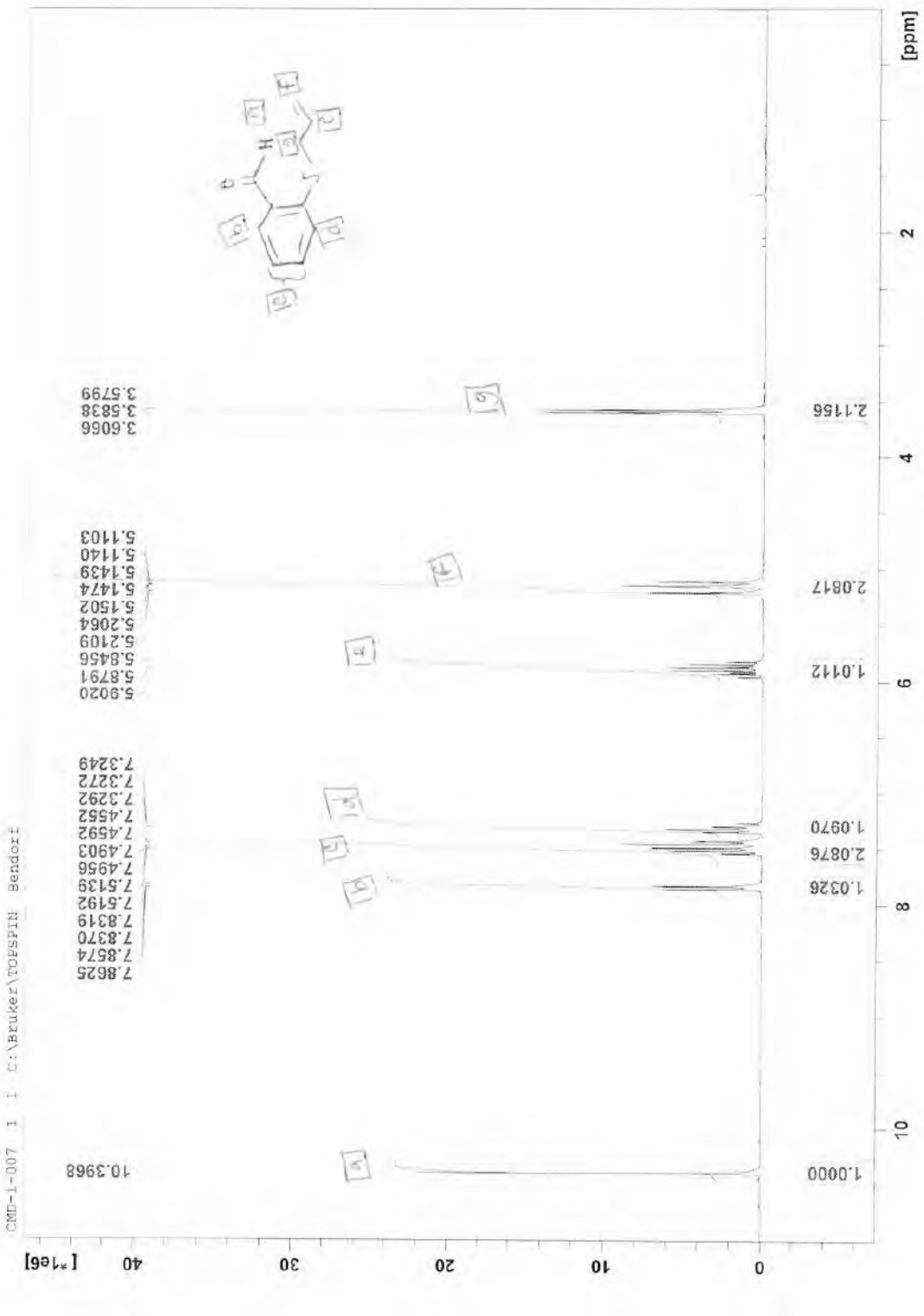
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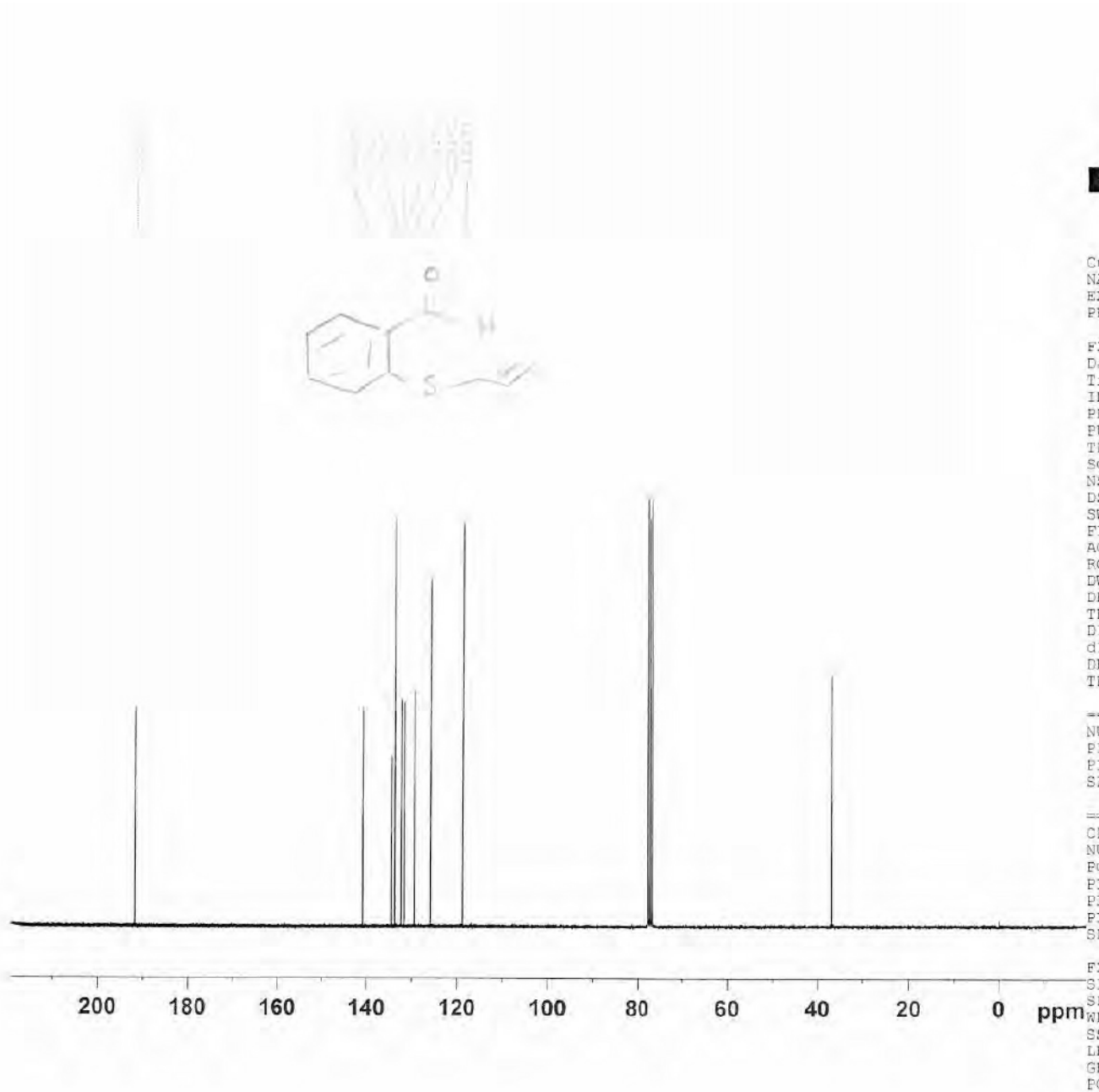
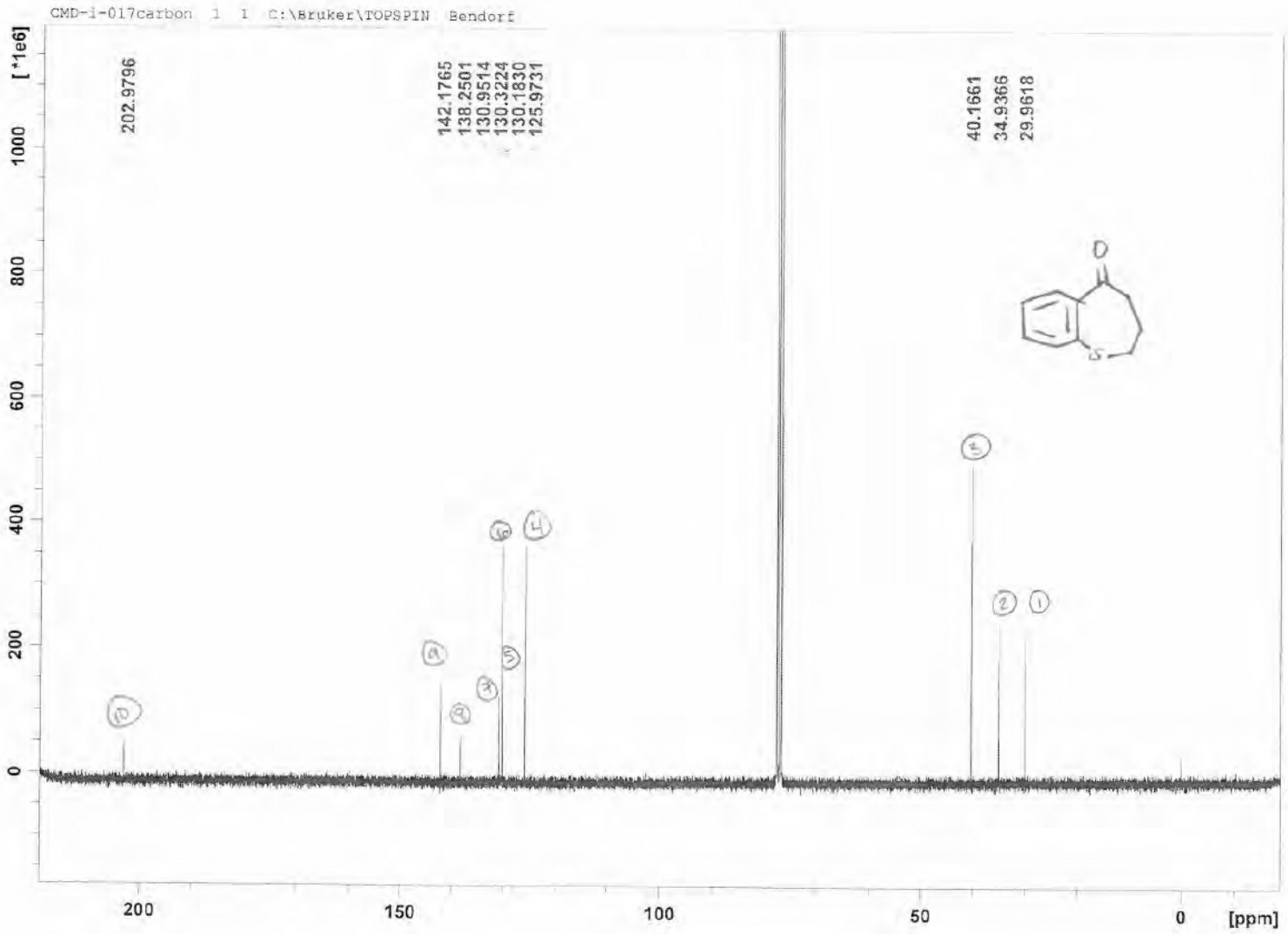
5.8791
1.0112
5.8456
5.2109
5.2064
5.1502
5.1474
2.0817
5.1439
5.1140
5.1103
3.6066
3.5838
3.5799
2.1156



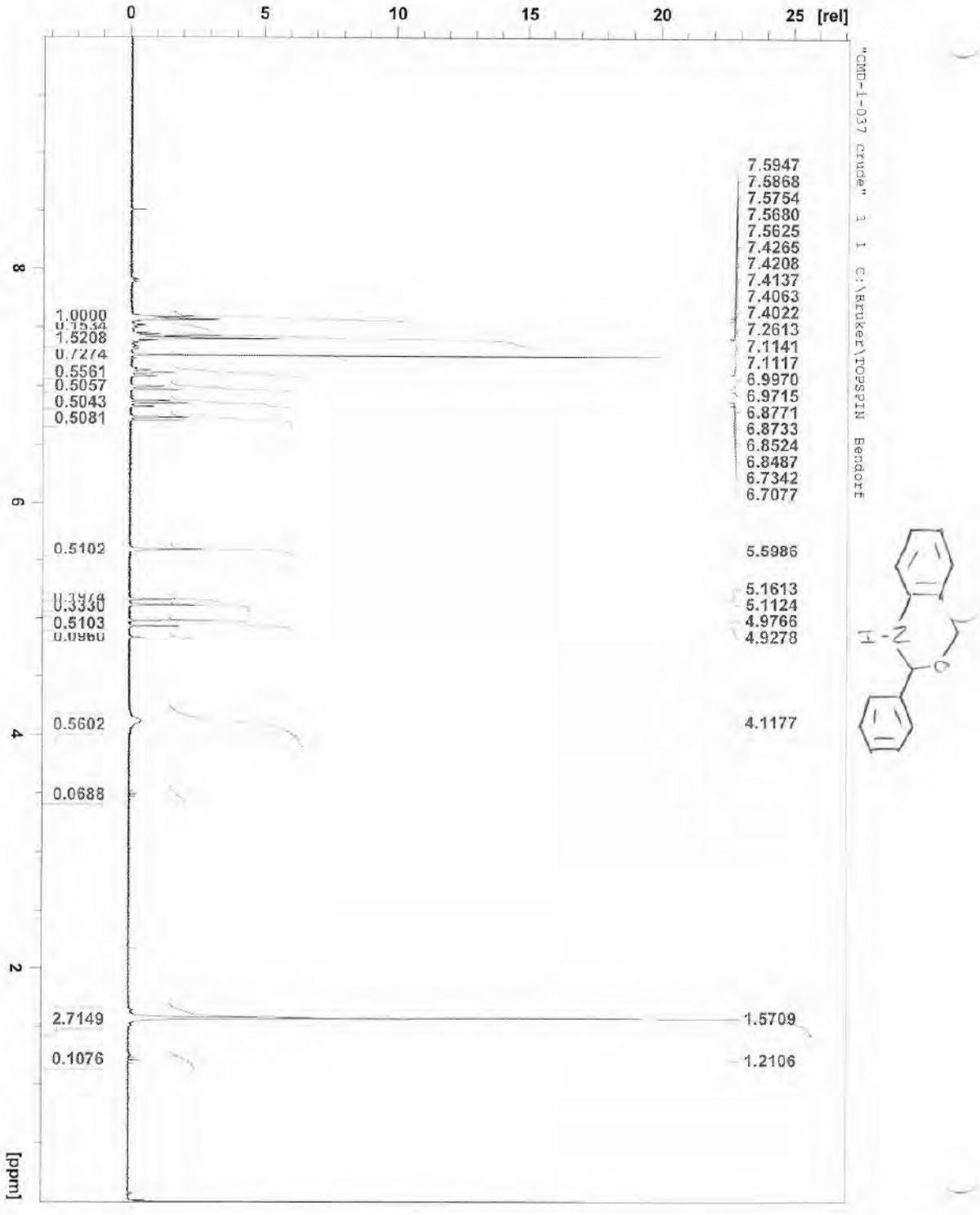
BRUKER

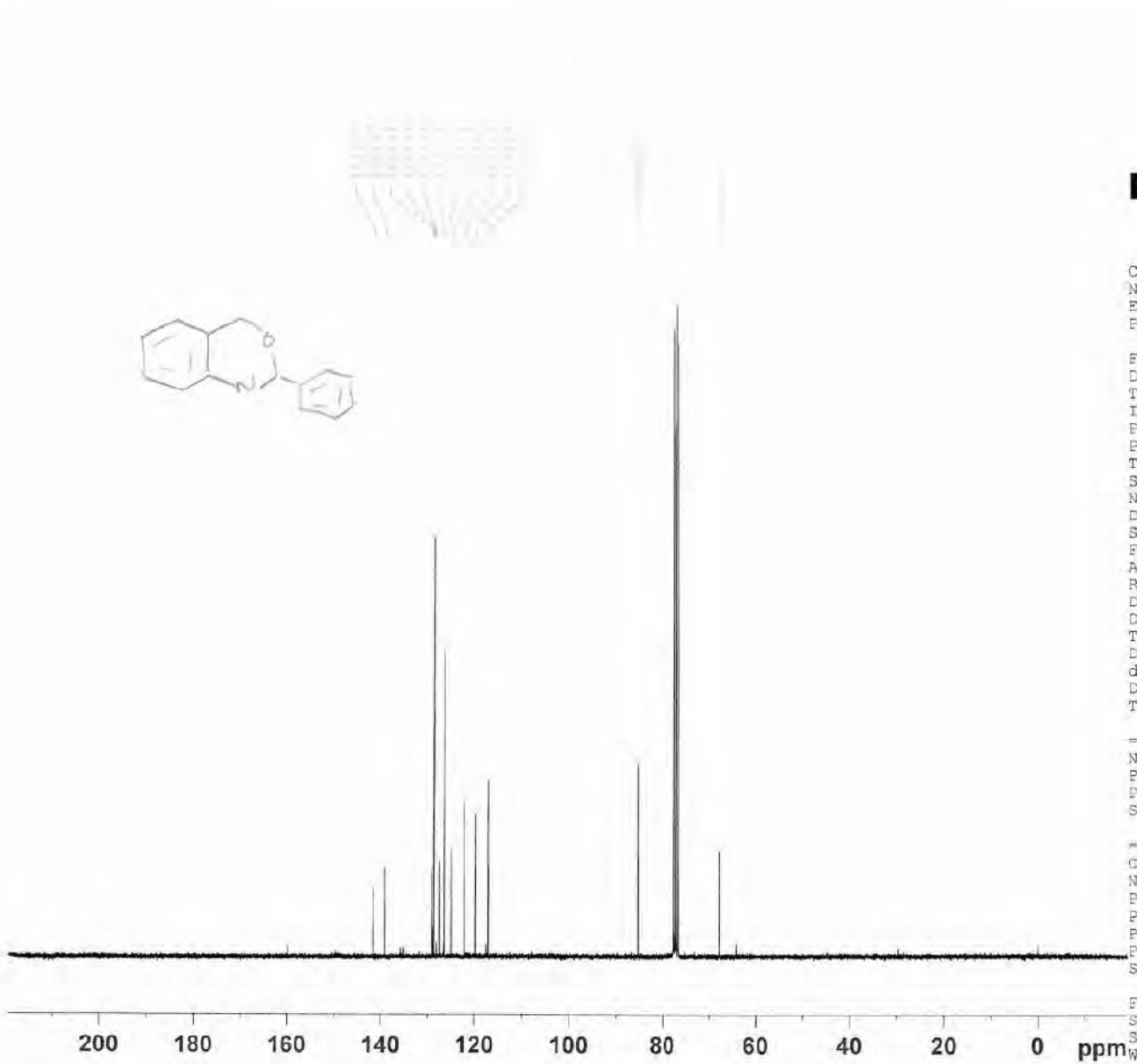
```
Current Data Parameters
NAME       CMD-i-004 c13
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130425
Time              10.09
INSTRUM           spect
PROBHD   5 mm Multinuc1
PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS               10240
DS                   4
SWH          17985.611 Hz
FIDRES         0.274439 Hz
AQ           1.8219508 sec
RG              5792.6
DW              27.800 usec
DE               6.00 usec
TE              293.2 K
D1          2.00000000 sec
d11         0.03000000 sec
DELTA       1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                7.10 usec
PL1               -1.50 dB
SFO1        75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2            80.00 usec
PL2               0.00 dB
PL12             17.23 dB
PL13             19.00 dB
SFO2       300.1312005 MHz

F2 - Processing parameters
SI                32768
SF         75.4677490 MHz
WDW                  no
SSB                   0
LB                0.00 Hz
GB                    0
PC                 1.40
```

CMD-1-010 1 1 C:\Bruker\TOPSPIN Bendorf
7.8345
7.8293
7.8284
7.4581
7.4565
7.4534
7.4526
7.3339
7.3283
7.2748
7.2652
7.2538
7.2495
5.9039
5.8811
5.8475
5.1493
5.1451
3.6082
3.6043
3.5855
3.5816
3.0579
2.9873
2.3039
2.2816
2.2591
1.6115
1.2540
1.0000
1.2014
1.9590
0.3688
0.1842
0.3828
3.4009
1.7062
0.1926
0.1143
[ppm]
[*1e6]


CMD-i-017carbon 1 1 C:\Bruker\TOPSPIN Bendorf
[*1e6]
1000
800
600
400
200
0
202.9796
142.1765
138.2501
130.9514
130.3224
130.1830
125.9731
40.1661
34.9366
29.9618
O
200
150
100
50
0
[ppm]

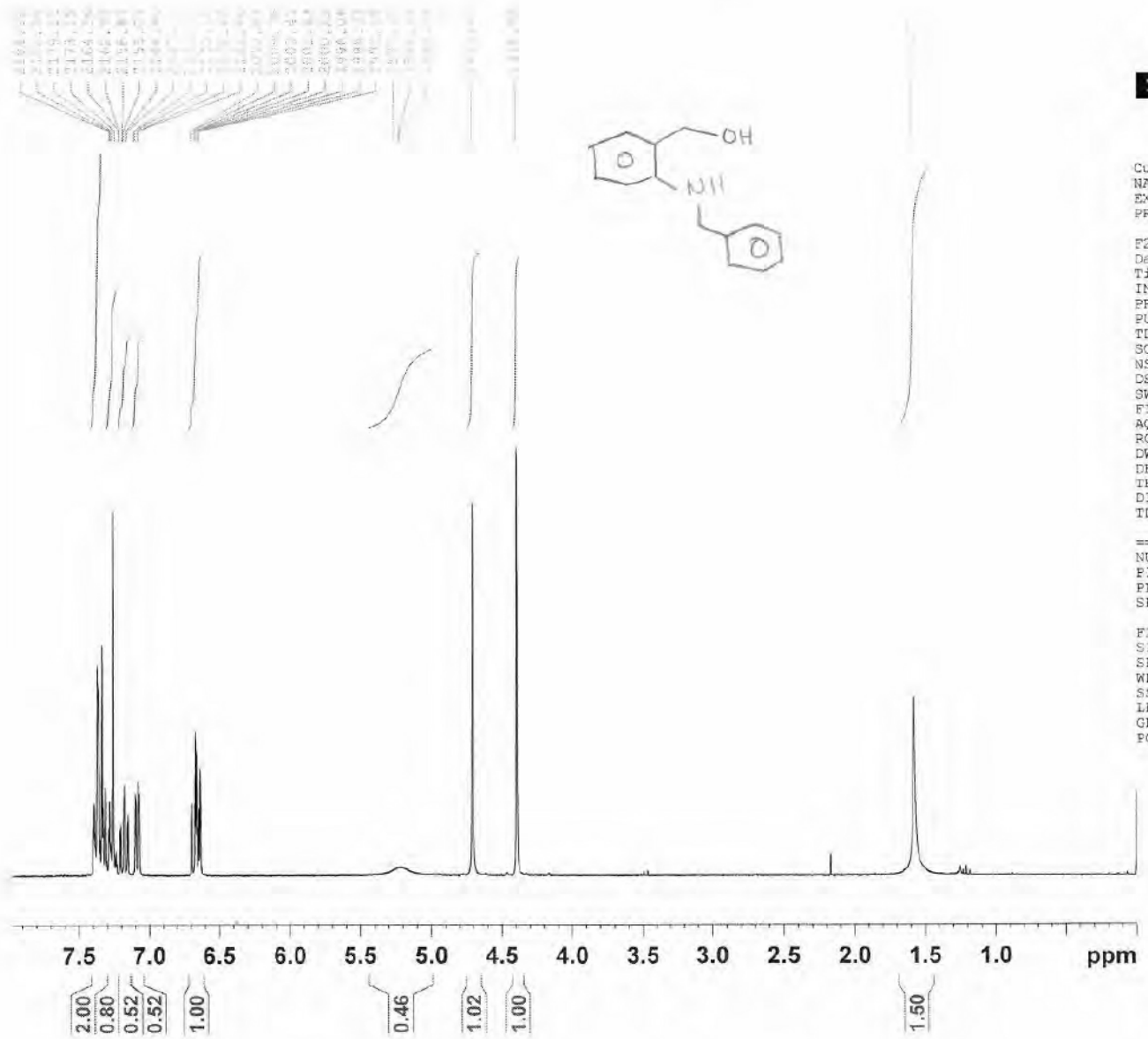
09


0
5
10
15
20
25 [rel]
"CMD-1-037 crude" 1 1 C:\Bruker\TOPSPIN Bendorf
7.5947
7.5868
7.5754
7.5680
7.5625
7.4265
7.4208
7.4137
7.4063
7.4022
7.2613
7.1141
7.1117
6.9970
6.9715
6.8771
6.8733
6.8524
6.8487
6.7342
6.7077
5.5986
5.1613
5.1124
4.9766
4.9278
4.1177
1.5709
1.2106
1.0000
1.5208
0.5561
0.5057
0.5043
0.5081
0.5102
0.3330
0.5103
0.5602
0.0688
2.7149
0.1076
8
6
4
2
[ppm]



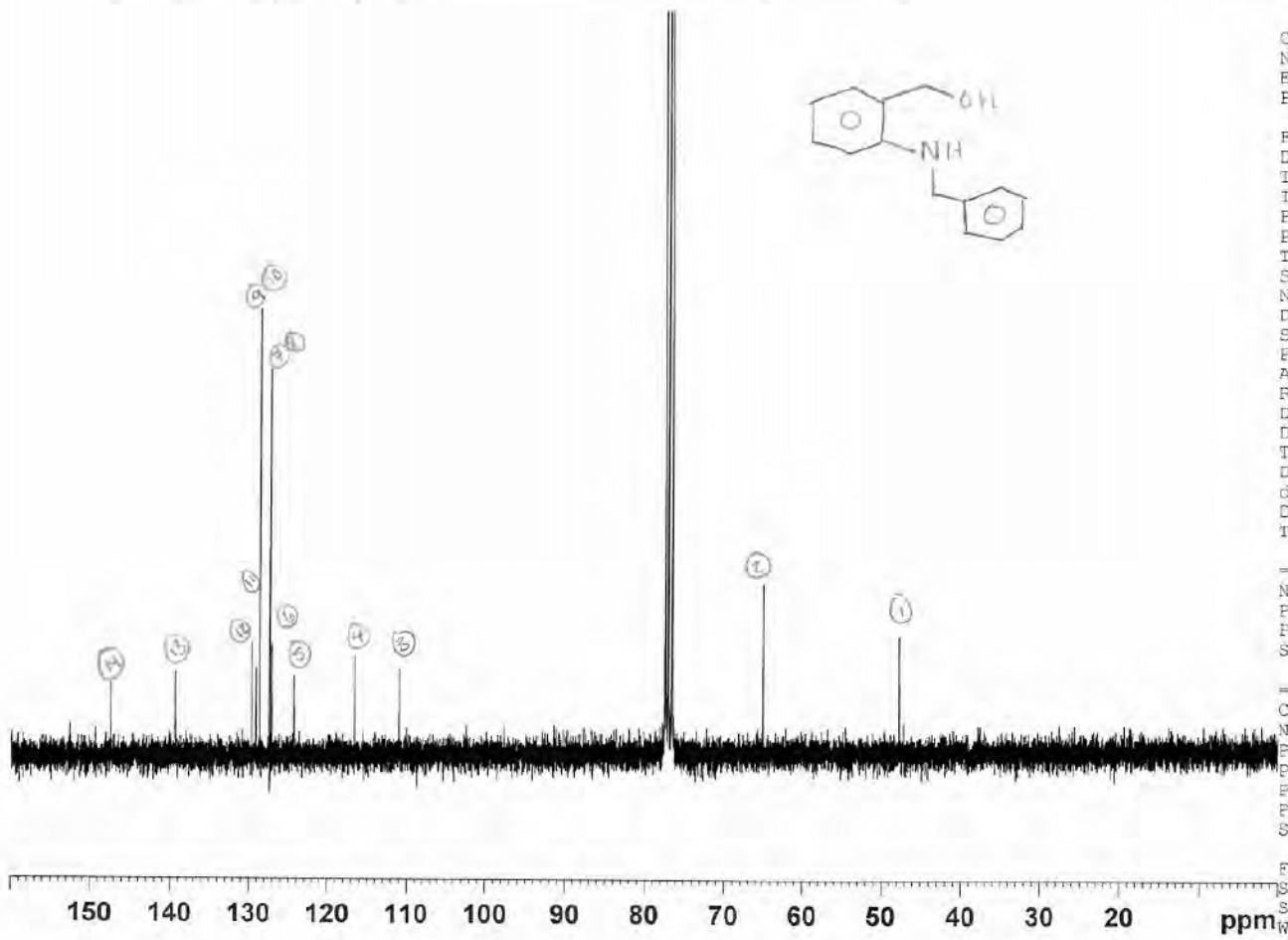
BRUKER

```
Current Data Parameters
NAME       CMD-i-037 c13
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130424
Time              10.20
INSTRUM           spect
PROBHD   5 mm Multinucl
PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS               10240
DS                   4
SWH          17985.611 Hz
FIDRES         0.274439 Hz
AQ           1.8219508 sec
RG              7298.2
DW               27.800 usec
DE                6.00 usec
TE               293.2 K
D1          2.00000000 sec
d11         0.03000000 sec
DELTA       1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                  7.10 usec
PL1                -1.50 dB
SFO1         75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2              80.00 usec
PL2                 0.00 dB
PL12               17.23 dB
PL13               19.00 dB
SFO2        300.1312005 MHz

F2 - Processing parameters
SI                  32768
SF           75.4677490 MHz
WDW                    no
SSB                     0
LB                   0.00 Hz
GB                      0
PC                   1.40
```



BRUKER

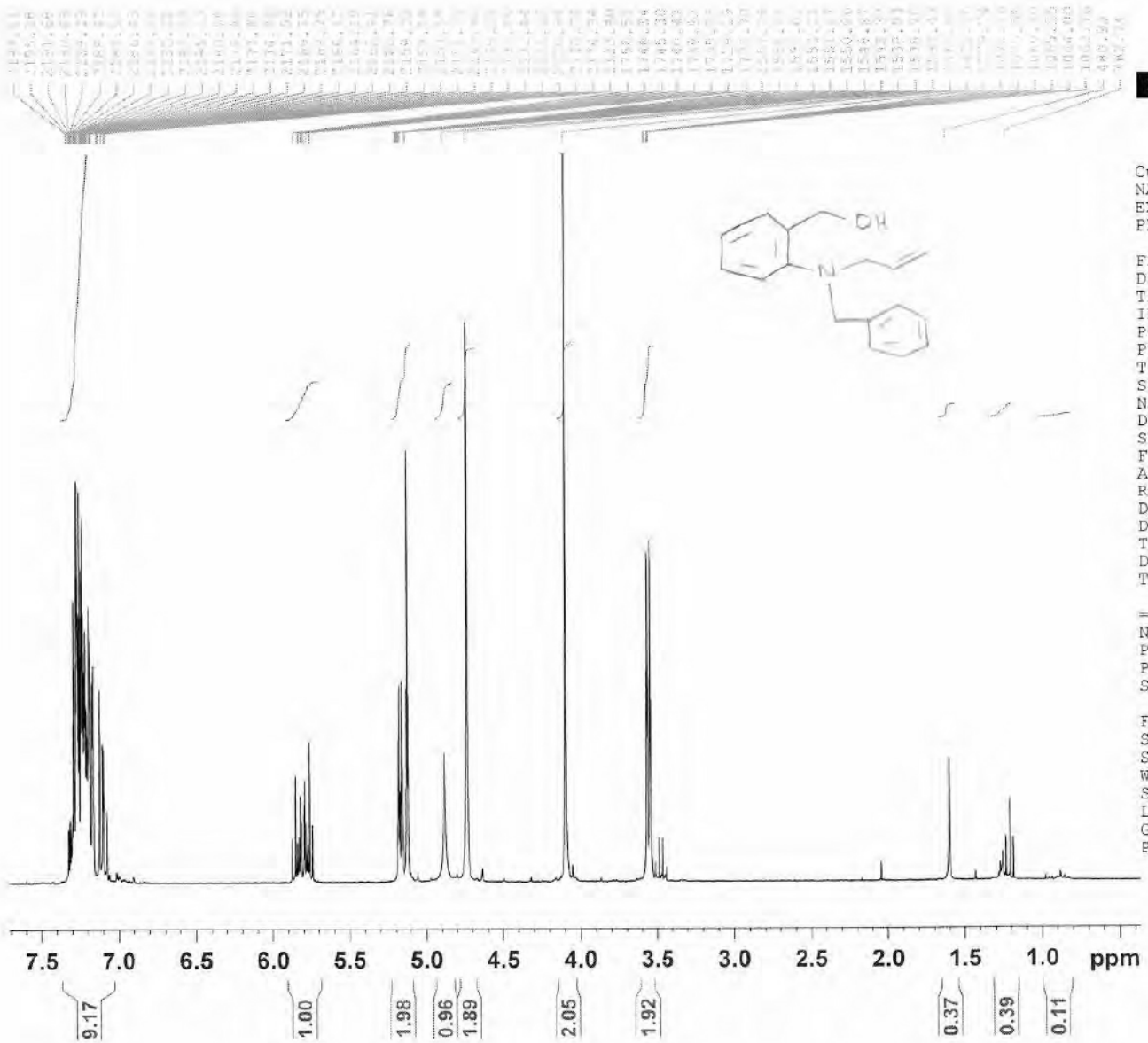
```
Current Data Parameters
NAME      CMD-i-039 recrystallized
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_         20120911
Time              15.20
INSTRUM           spect
PROBHD   5 mm Multinucl
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH            6172.839 Hz
FIDRES         0.094190 Hz
AQ             5.3084660 sec
RG                724.1
DW               81.000 usec
DE                6.00 usec
TE               293.2 K
D1          1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                 1H
P1                11.00 usec
PL1                0.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                32768
SF           300.1300068 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00
```



BRUKER

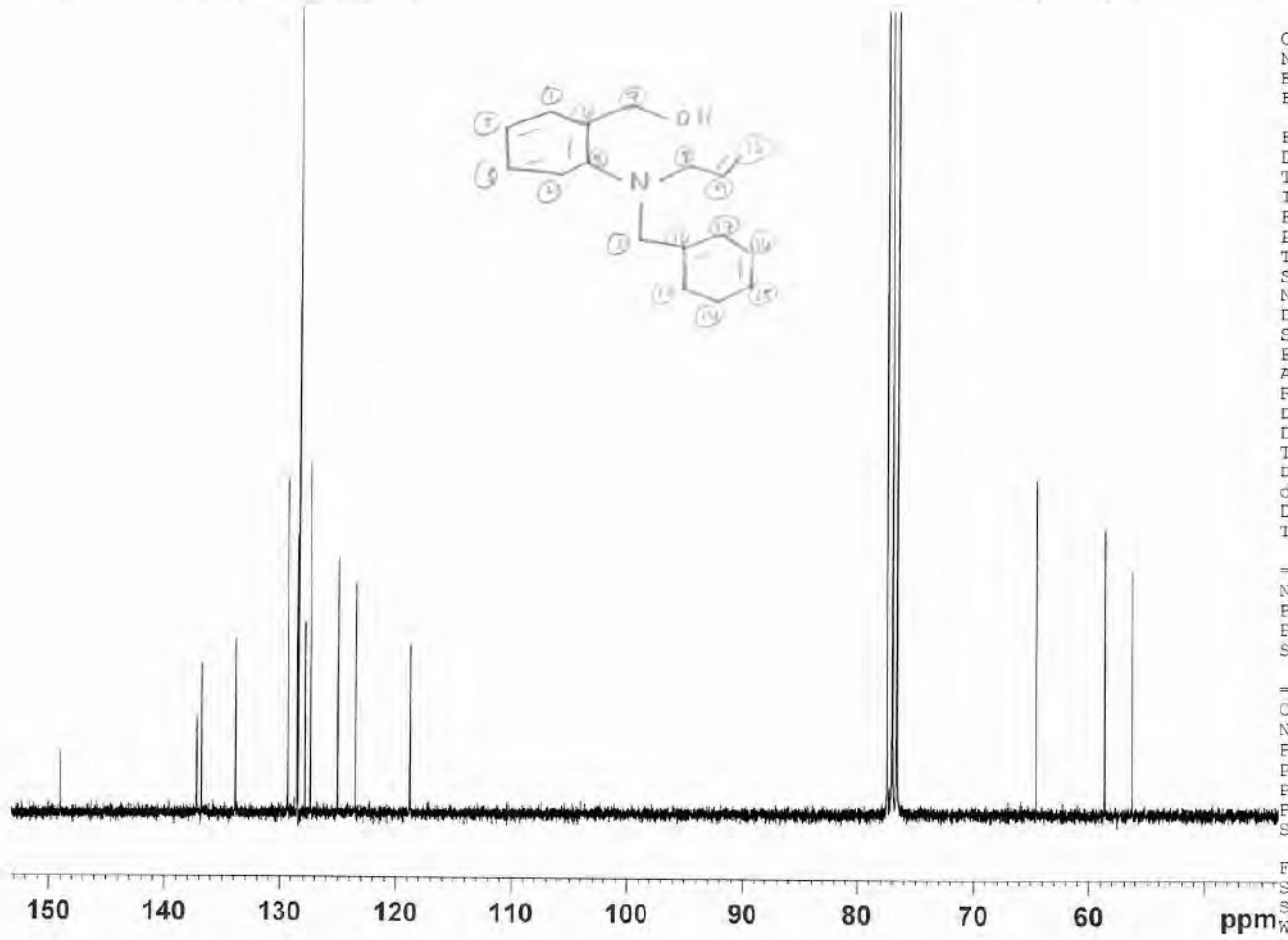
```
Current Data Parameters
NAME        CMD-i-039c13
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20121031
Time               1.51
INSTRUM           spect
PROBHD   5 mm Multinucl
PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS                8192
DS                   4
SWH          17985.611 Hz
FIDRES         0.274439 Hz
AQ            1.8219508 sec
RG                4096
DW              27.800 usec
DE               6.00 usec
TE              295.2 K
D1          2.00000000 sec
d11         0.03000000 sec
DELTA       1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                7.10 usec
PL1               -1.50 dB
SFO1        75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2            80.00 usec
PL2               0.00 dB
PL12             17.23 dB
PL13             19.00 dB
SFO2       300.1312005 MHz

F2 - Processing parameters
SI                32768
SF         75.4677490 MHz
WDW                  no
SSB                   0
LB                0.00 Hz
GB                    0
PC                 1.40
```

039



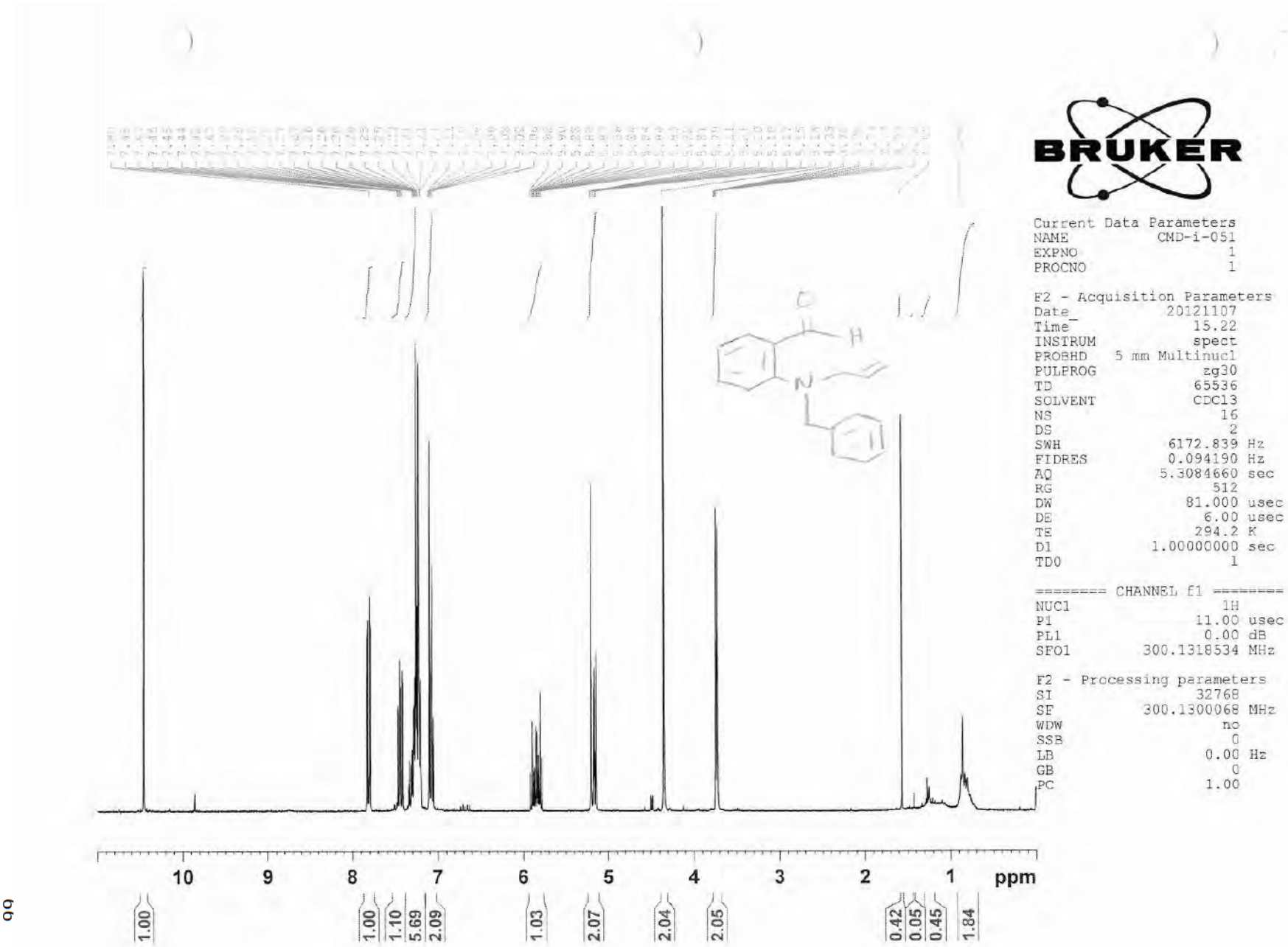
BRUKER

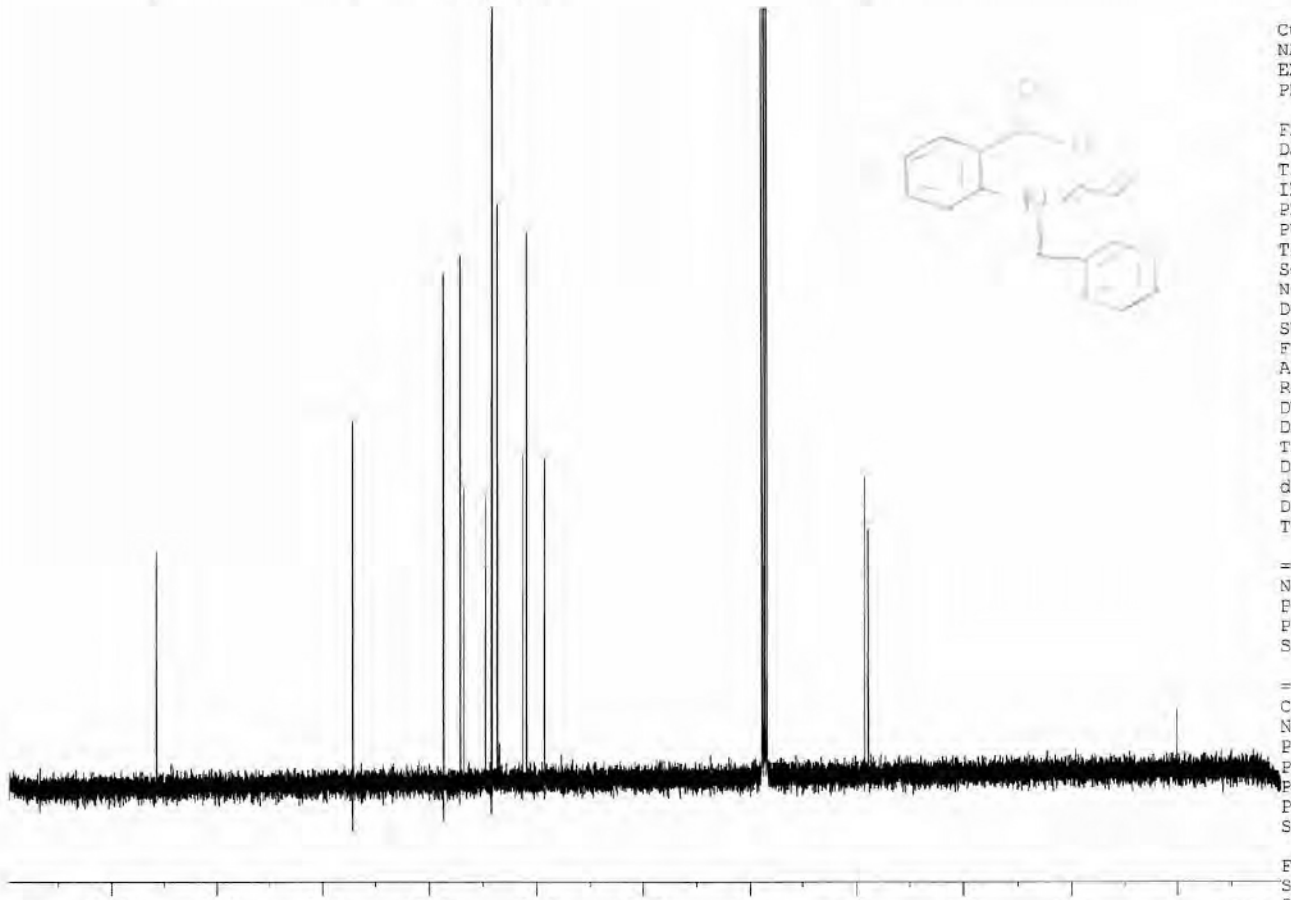
```
Current Data Parameters
NAME      CMD-i-049 purified
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_             20121026
Time                 11.26
INSTRUM              spect
PROBHD    5 mm Multinucl
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              6172.839 Hz
FIDRES           0.094190 Hz
AQ               5.3084660 sec
RG                   406.4
DW                81.000 usec
DE                 6.00 usec
TE                294.2 K
D1           1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 11.00 usec
PL1                 0.00 dB
SFO1         300.1318534 MHz

F2 - Processing parameters
SI                  32768
SF           300.1300076 MHz
WDW                    no
SSB                     0
LB                 0.00 Hz
GB                      0
PC                   1.00
```



BRUKER

```
Current Data Parameters
NAME          CMD-i-049c13
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_              20121030
Time                   1.39
INSTRUM               spect
PROBHD    5 mm Multinucl
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     8192
DS                        4
SWH               17985.611 Hz
FIDRES             0.274439 Hz
AQ                 1.8219508 sec
RG                    4597.6
DW                   27.800 usec
DE                    6.00 usec
TE                   294.2 K
D1                2.00000000 sec
d11               0.03000000 sec
DELTA             1.89999998 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    7.10 usec
PL1                  -1.50 dB
SFO1             75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 17.23 dB
PL13                 19.00 dB
SFO2            300.1312005 MHz

F2 - Processing parameters
SI                      32768
SF               75.4677490 MHz
WDW                        no
SSB                         0
LB                    0.00 Hz
GB                          0
PC                     1.40
```


BRUKER
Current Data Parameters
NAME CMD-i-051
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121107
Time 15.22
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 512
DW 81.000 usec
DE 6.00 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
SF 300.1300068 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
10 9 8 7 6 5 4 3 2 1 ppm
1.00 1.00 1.10 5.69 2.09 1.03 2.07 2.04 2.05 0.42 0.05 0.45 1.84



BRUKER

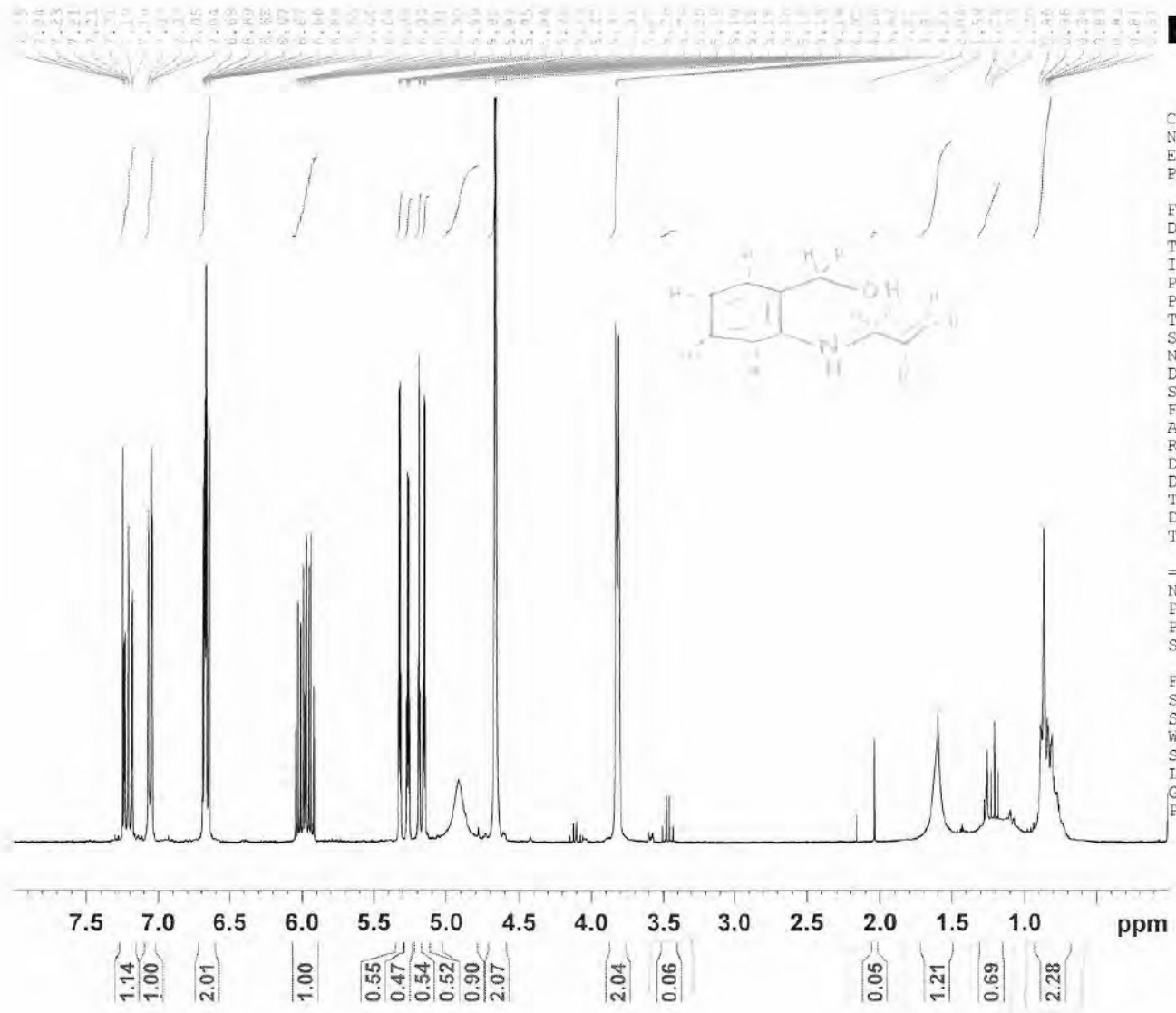
Current Data Parameters
NAME CMD-i-051 c13
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121128
Time 3.21
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 8192
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 2298.8
DW 27.800 usec
DE 6.00 usec
TE 295.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 7.10 usec
PL1 -1.50 dB
SFO1 75.4752953 MHz

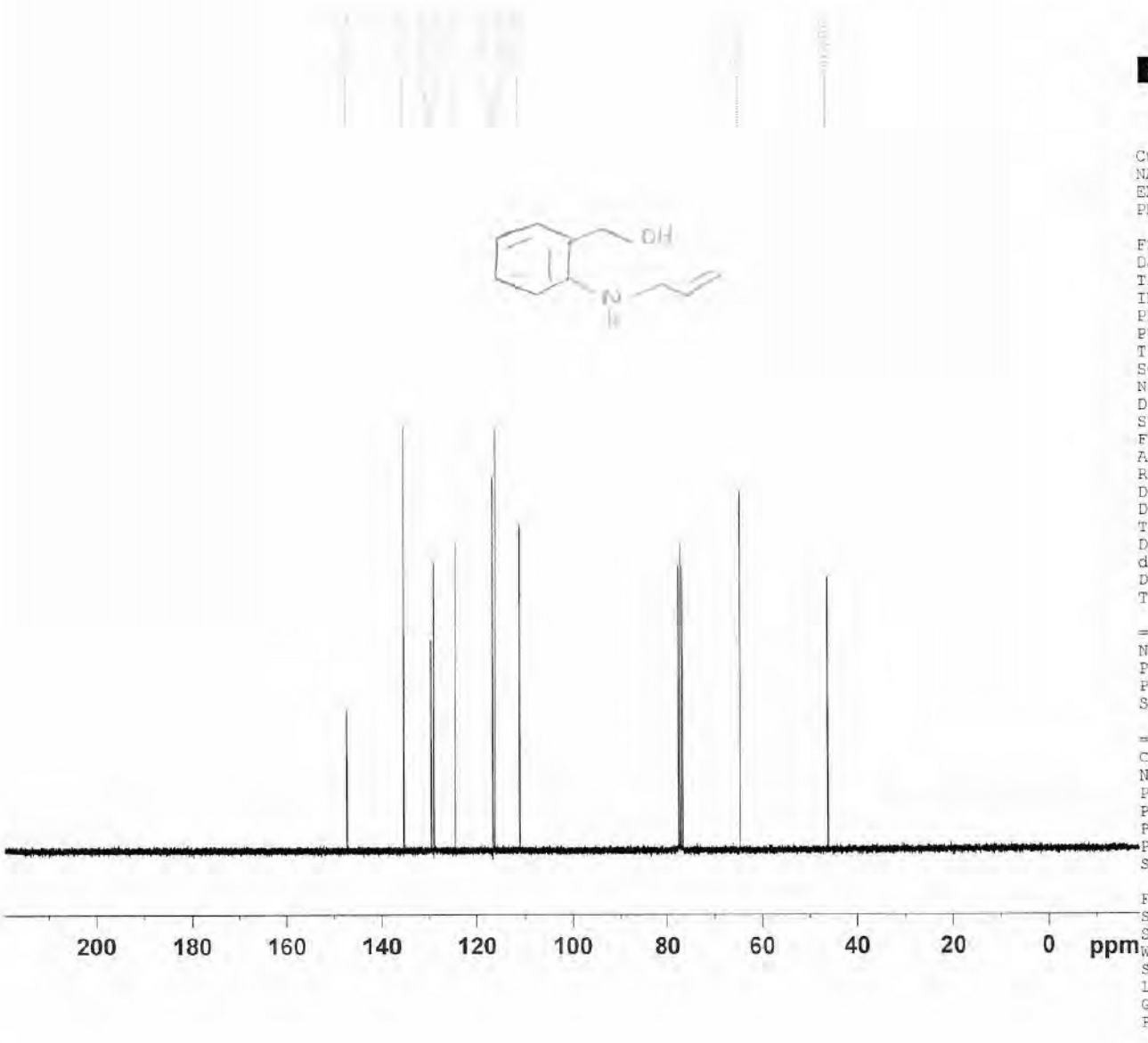
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 17.23 dB
PL13 19.00 dB
SFO2 300.1312005 MHz

F2 - Processing parameters
SI 32768
SF 75.4677499 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40



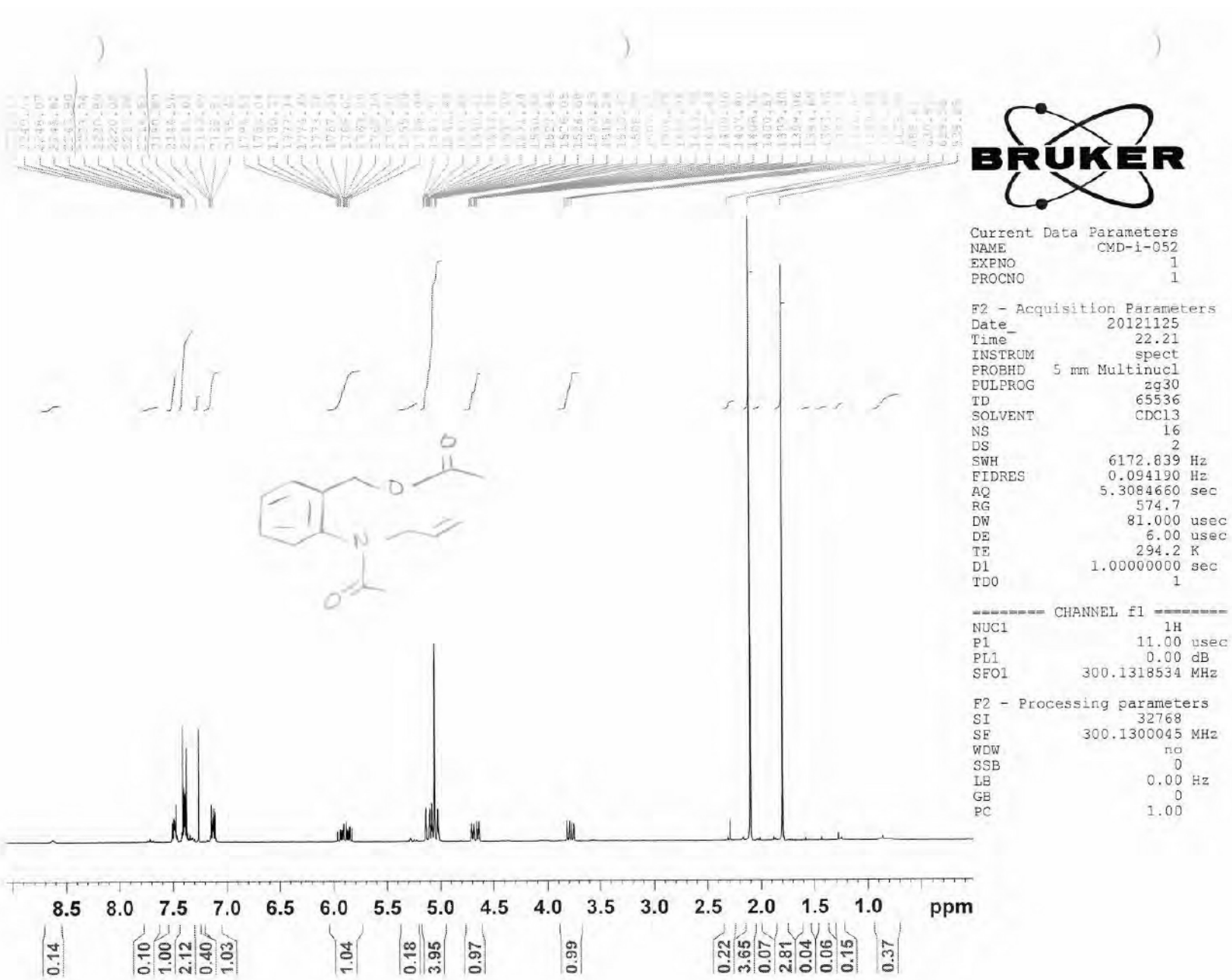
BRUKER

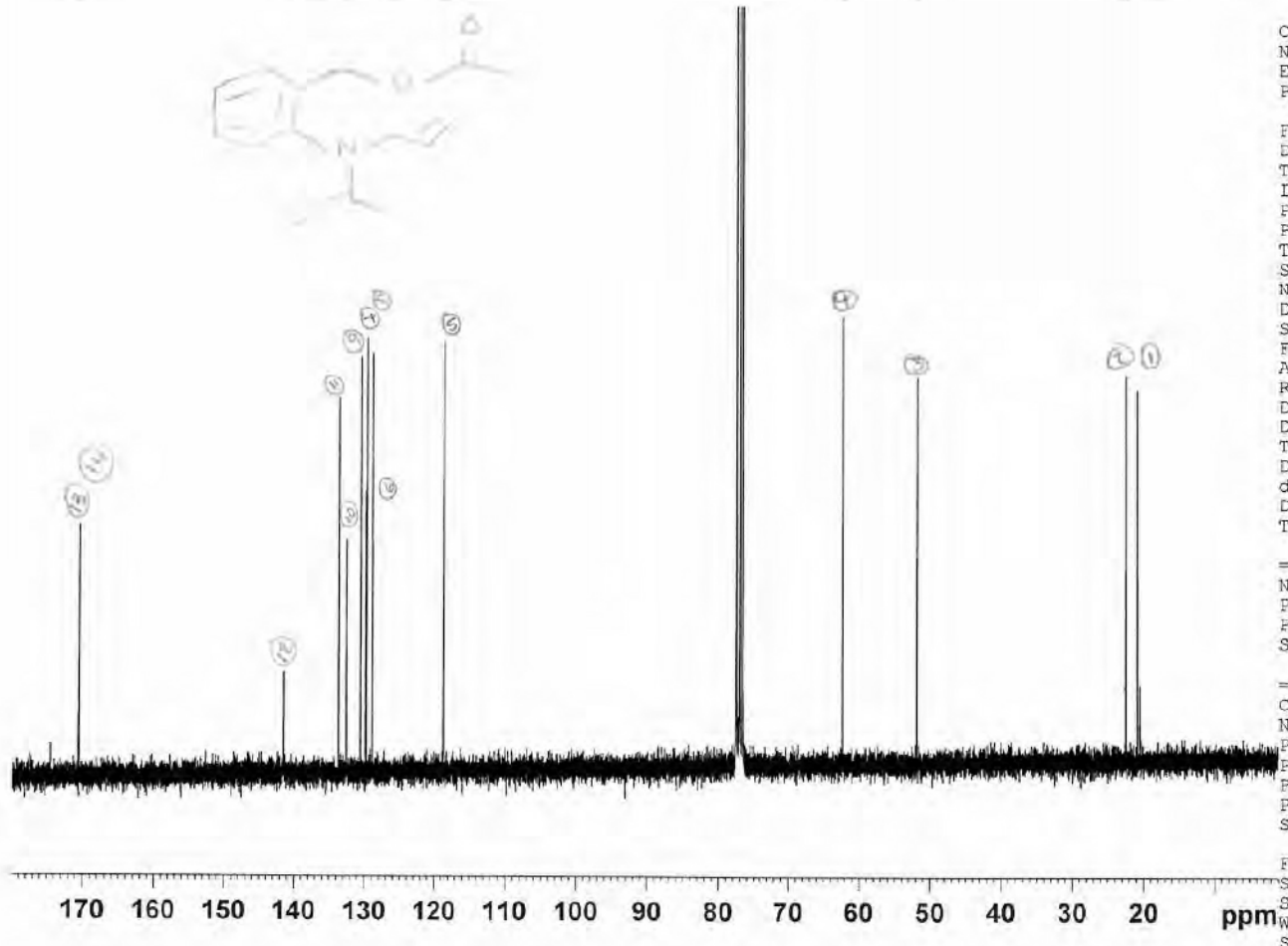
```
Current Data Parameters
NAME                  CMD-i-050
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20121107
Time                      15.07
INSTRUM                   spect
PROBHD    5 mm Multinucl
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                 6172.839 Hz
FIDRES              0.094190 Hz
AQ                  5.3084660 sec
RG                       203.2
DW                    81.000 usec
DE                     6.00 usec
TE                     294.2 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                    11.00 usec
PL1                    0.00 dB
SFO1              300.1318534 MHz

F2 - Processing parameters
SI                       32768
SF                300.1300093 MHz
WDW                         no
SSB                          0
LB                     0.00 Hz
GB                           0
PC                        1.00
```



BRUKER

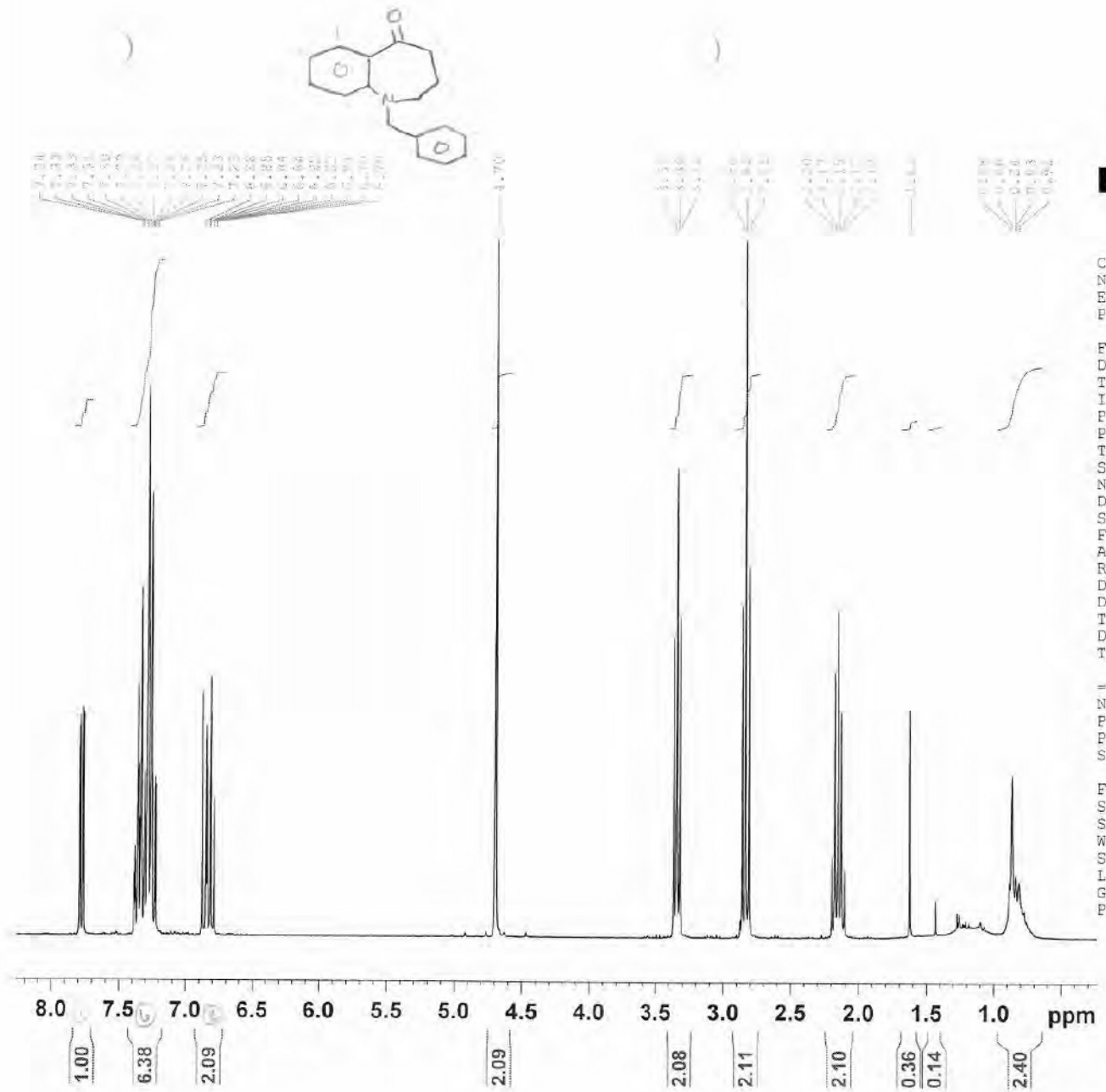
```
Current Data Parameters
NAME        CMD-i-050 c13
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130424
Time              21.41
INSTRUM           spect
PROBHD   5 mm Multinucl
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                 1024
DS                    4
SWH           17985.611 Hz
FIDRES        0.274439 Hz
AQ            1.8219508 sec
RG               7298.2
DW               27.800 usec
DE                6.00 usec
TE               293.2 K
D1           2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                 13C
P1                 7.10 usec
PL1               -1.50 dB
SFO1         75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                 1H
PCPD2             80.00 usec
PL2                0.00 dB
PL12              17.23 dB
PL13              19.00 dB
SFO2         300.1312005 MHz

F2 - Processing parameters
SI                32768
SF         75.4677490 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.40
```


BRUKER
Current Data Parameters
NAME CMD-i-052
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121125
Time 22.21
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 574.7
DW 81.000 usec
DE 6.00 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz
F2 - Processing parameters
SI 32768
SF 300.1300045 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
0.14 0.10 1.00 2.12 0.40 1.03 1.04 0.18 3.95 0.97 0.99 0.22 3.65 0.07 2.81 0.04 0.06 0.15 0.37



BRUKER

```
Current Data Parameters
NAME       CMD-i-052 c13
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20121126
Time               9.31
INSTRUM           spect
PROBHD   5 mm Multinucl
PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS               10240
DS                   4
SWH          17985.611 Hz
FIDRES         0.274439 Hz
AQ           1.8219508 sec
RG                2048
DW               27.800 usec
DE                6.00 usec
TE                295.2 K
D1          2.00000000 sec
d11         0.03000000 sec
DELTA       1.89999998 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1                 7.10 usec
PL1               -1.50 dB
SFO1        75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2             80.00 usec
PL2                0.00 dB
PL12              17.23 dB
PL13              19.00 dB
SFO2       300.1312005 MHz

F2 - Processing parameters
SI                 32768
SF          75.4677493 MHz
WDW                   no
SSB                    0
LB                 0.00 Hz
GB                     0
PC                  1.40
```



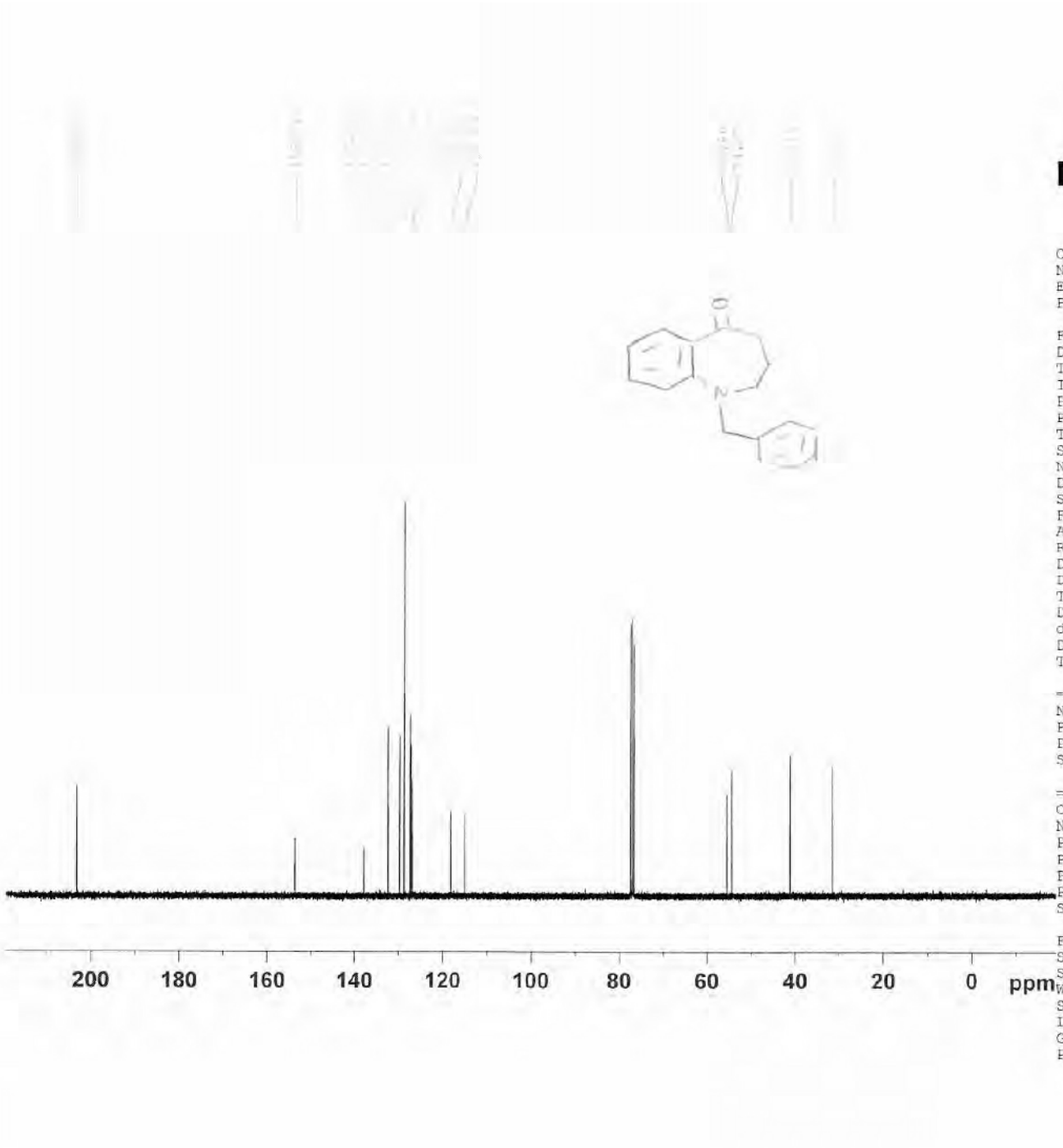
BRUKER

Current Data Parameters
NAME CMD-i-054
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121119
Time 11.25
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 161.3
DW 81.000 usec
DE 6.00 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1

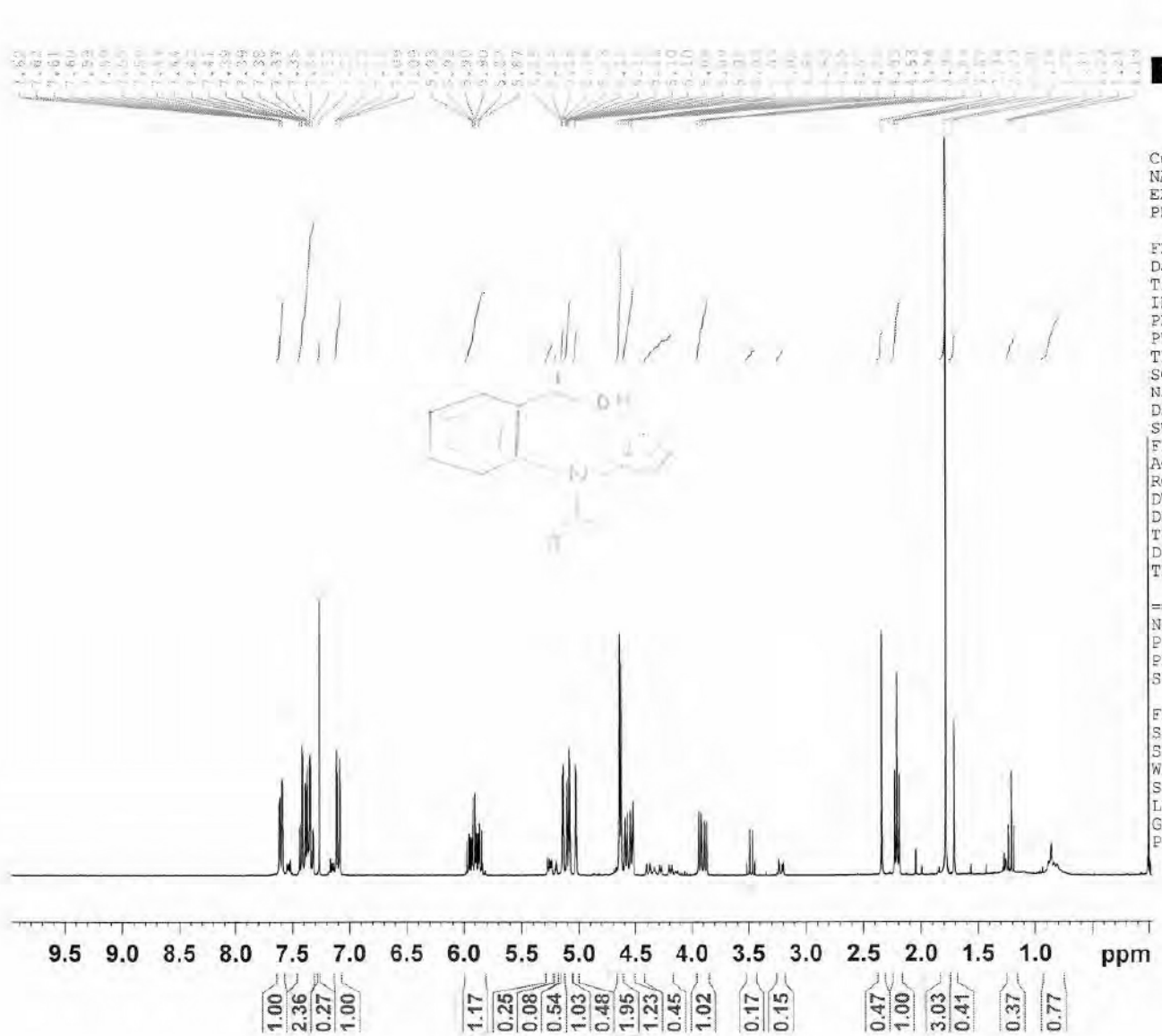
======== CHANNEL f1 ========
NUC1 1H
P1 11.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300073 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00



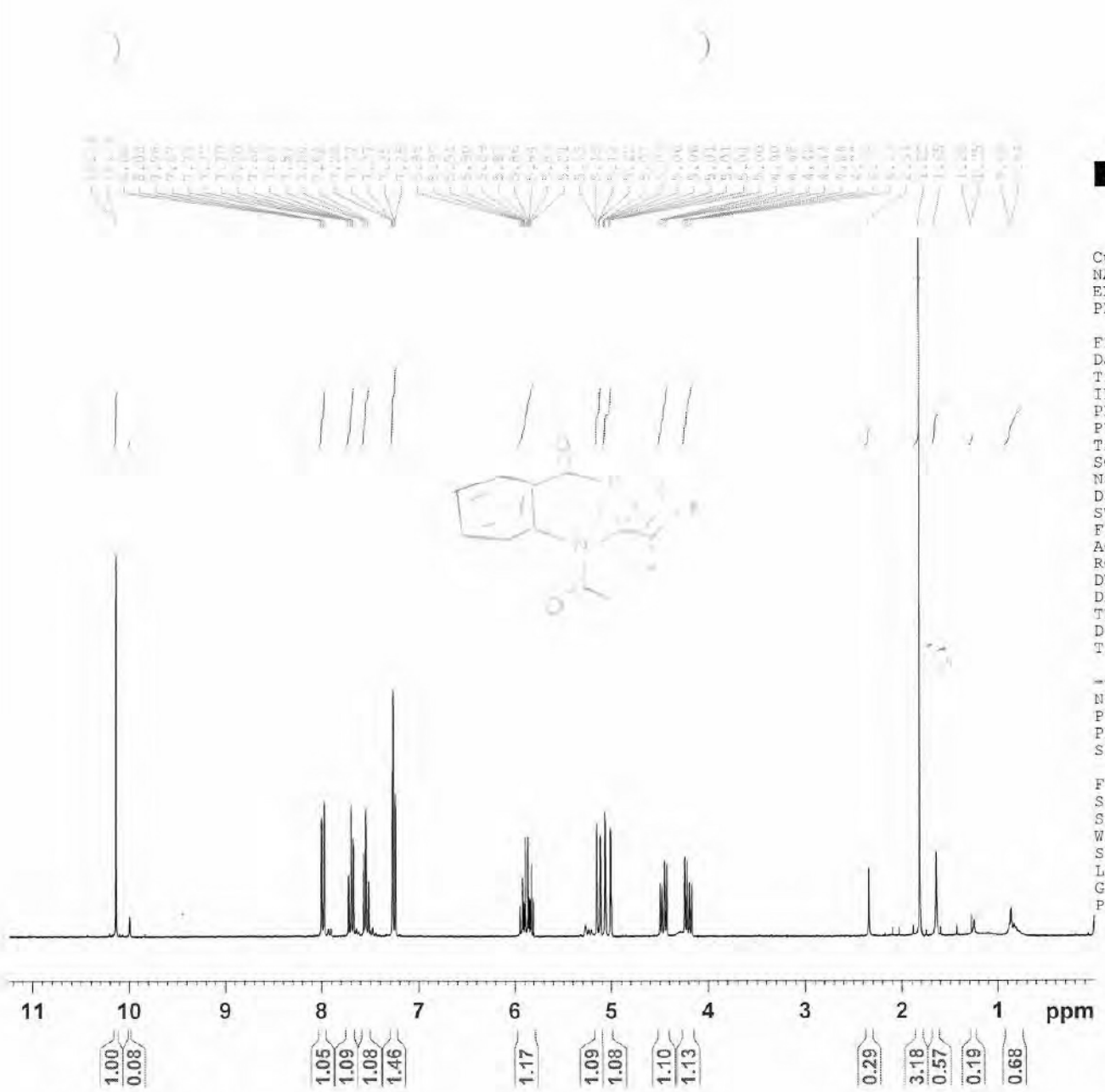
BRUKER

```
Current Data Parameters
NAME      CMD-i-054 c13
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_         20130424
Time            22.55
INSTRUM         spect
PROBHD   5 mm Multinucl
PULPROG        zgpg30
TD              65536
SOLVENT         CDCl3
NS               1024
DS                  4
SWH         17985.611 Hz
FIDRES        0.274439 Hz
AQ            1.8219508 sec
RG               6502
DW              27.800 usec
DE               6.00 usec
TE              293.2 K
D1         2.00000000 sec
d11        0.03000000 sec
DELTA      1.89999998 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               13C
P1                7.10 usec
PL1              -1.50 dB
SFO1       75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2        waltz16
NUC2               1H
PCPD2            80.00 usec
PL2               0.00 dB
PL12             17.23 dB
PL13             19.00 dB
SFO2       300.1312005 MHz

F2 - Processing parameters
SI                32768
SF         75.4677490 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.40
```



BRUKER

```
Current Data Parameters
NAME      CMD-i-055 lower dot
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20121128
Time                   16.30
INSTRUM                spect
PROBHD   5 mm Multinucl
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                6172.839 Hz
FIDRES             0.094190 Hz
AQ                 5.3084660 sec
RG                      512
DW                   81.000 usec
DE                    6.00 usec
TE                   294.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    11.00 usec
PL1                    0.00 dB
SFO1          300.1318534 MHz

F2 - Processing parameters
SI                    32768
SF            300.1300043 MHz
WDW                      no
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.00
```



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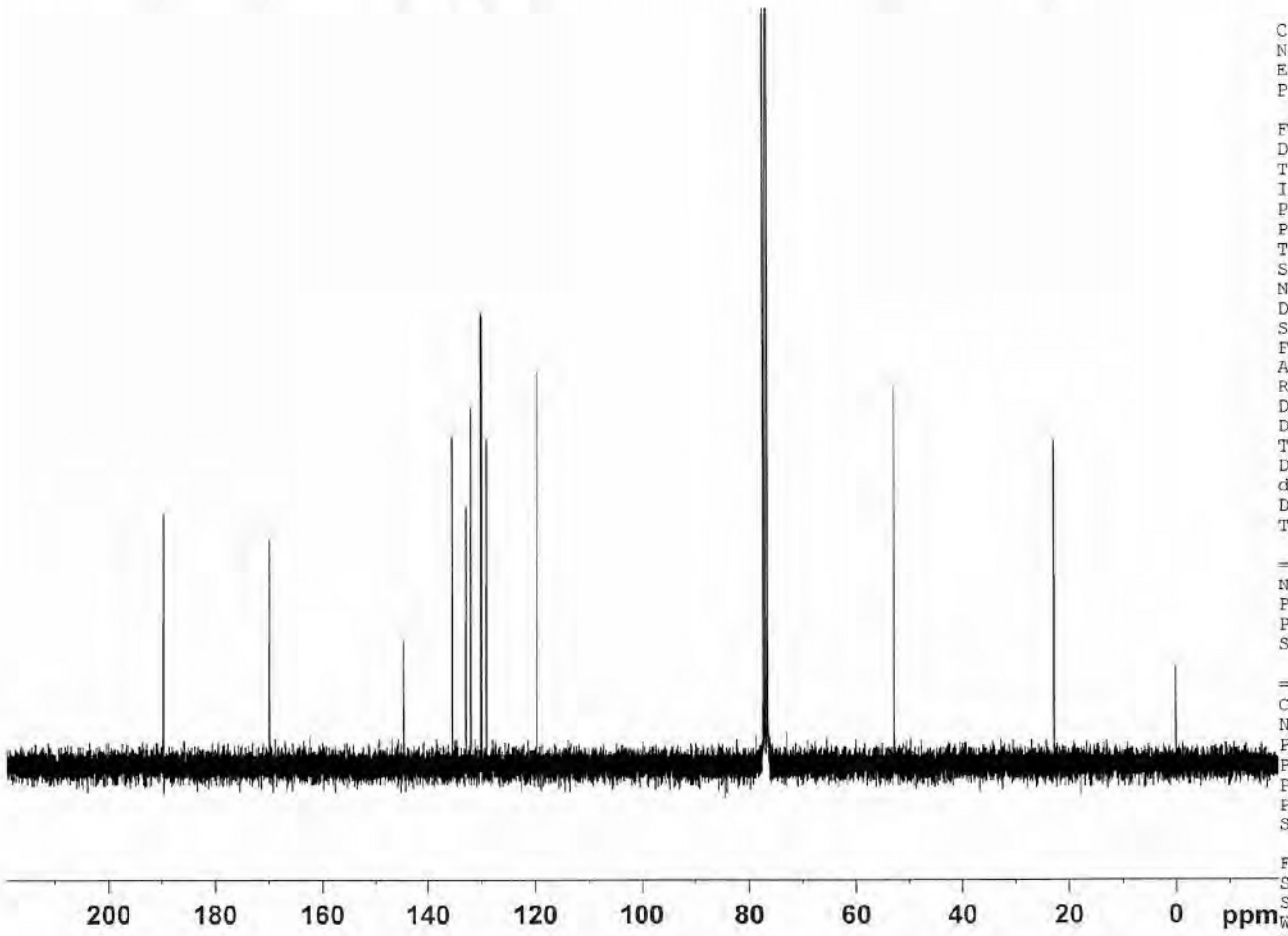
Current Data Parameters
NAME CMD-i-056
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121204
Time 11.04
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 574.7
DW 81.000 usec
DE 6.00 usec
TE 293.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 11.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300039 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00



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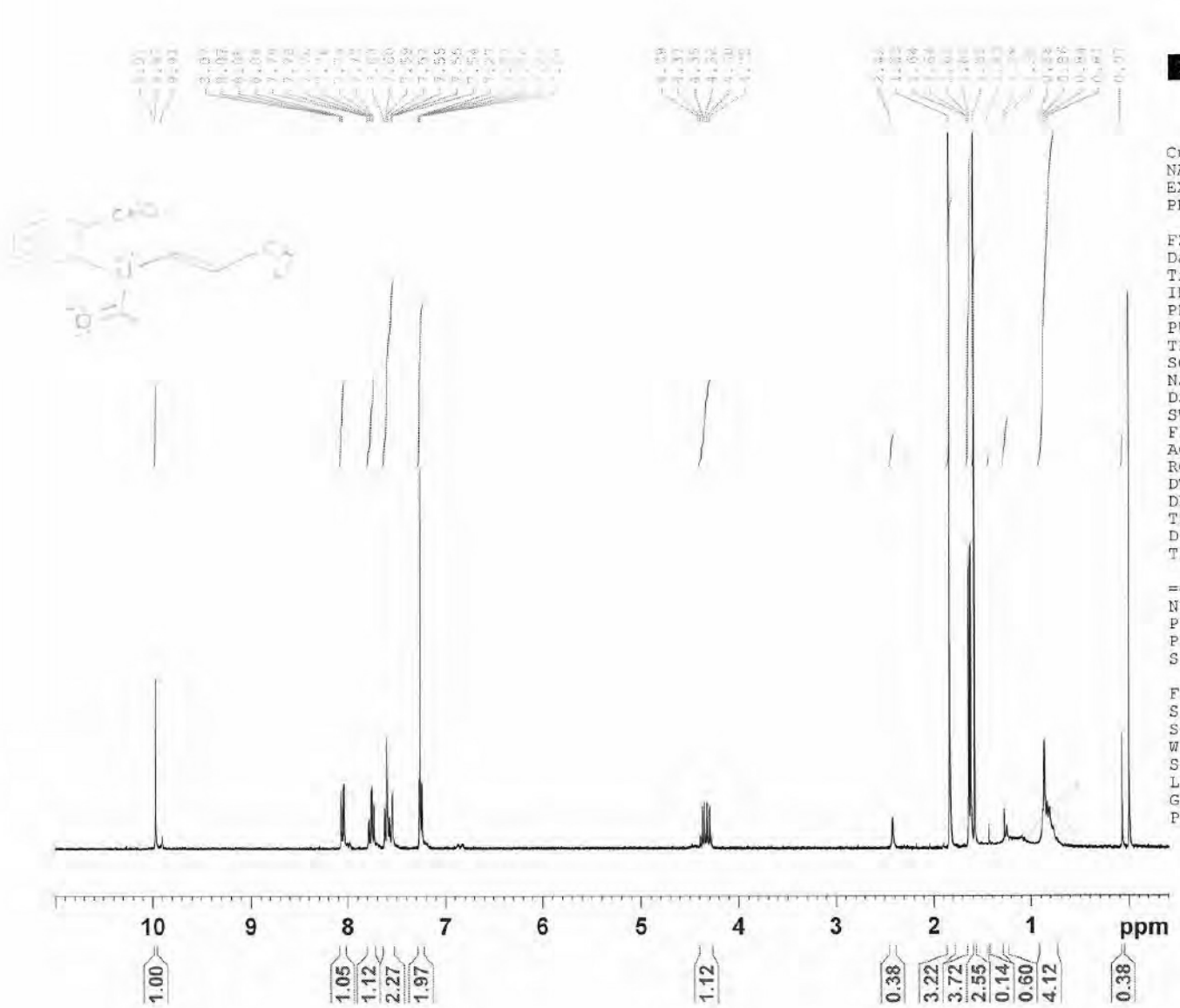
Current Data Parameters
NAME CMD-i-056 c13
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121210
Time 6.36
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 3649.1
DW 27.800 usec
DE 6.00 usec
TE 294.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 7.10 usec
PL1 -1.50 dB
SFO1 75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 17.23 dB
PL13 19.00 dB
SFO2 300.1312005 MHz

F2 - Processing parameters
SI 32768
SF 75.4677493 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40



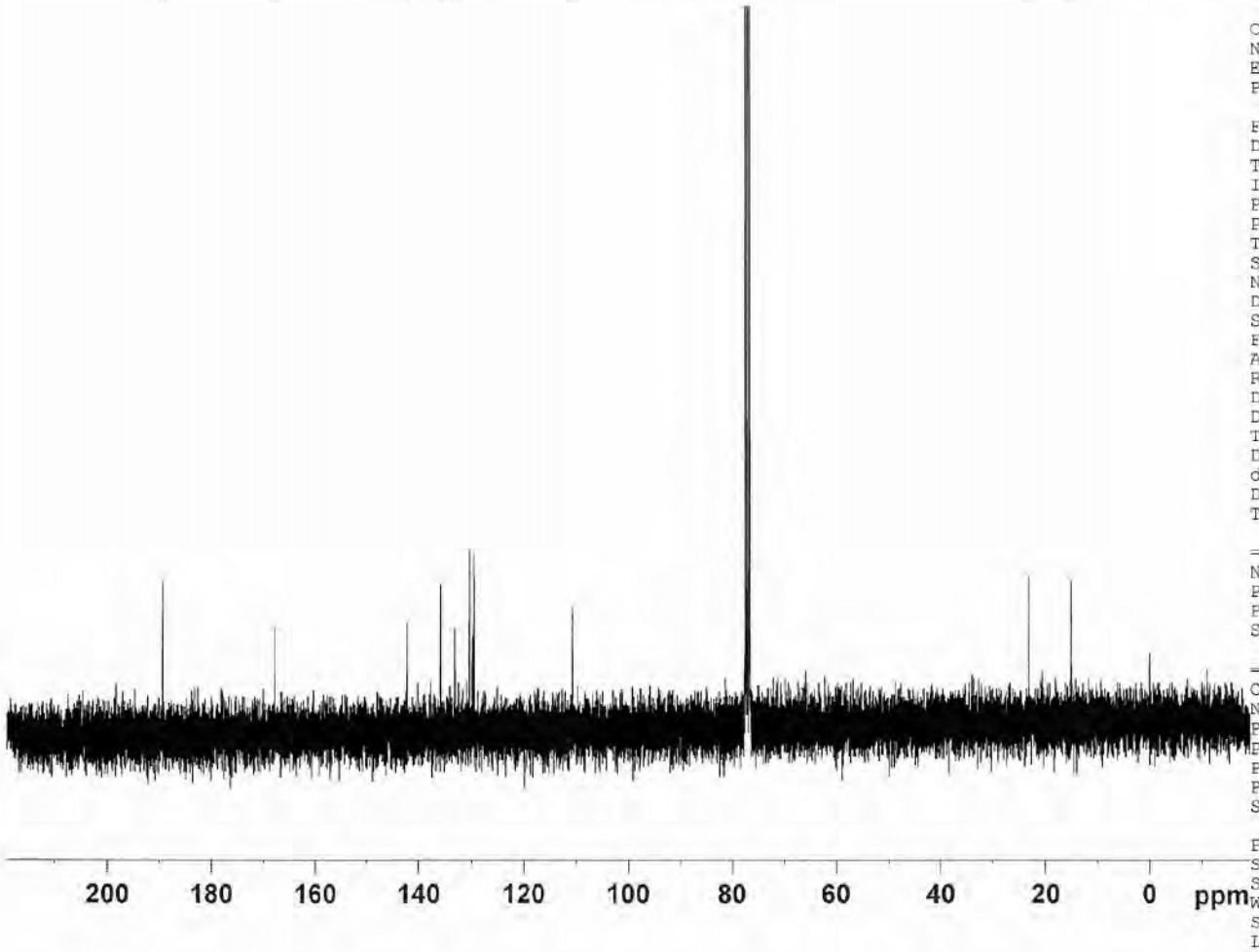
BRUKER

Current Data Parameters
NAME CMD-i-058
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121210
Time 13.03
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 812.7
DW 81.000 usec
DE 6.00 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 11.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300051 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00



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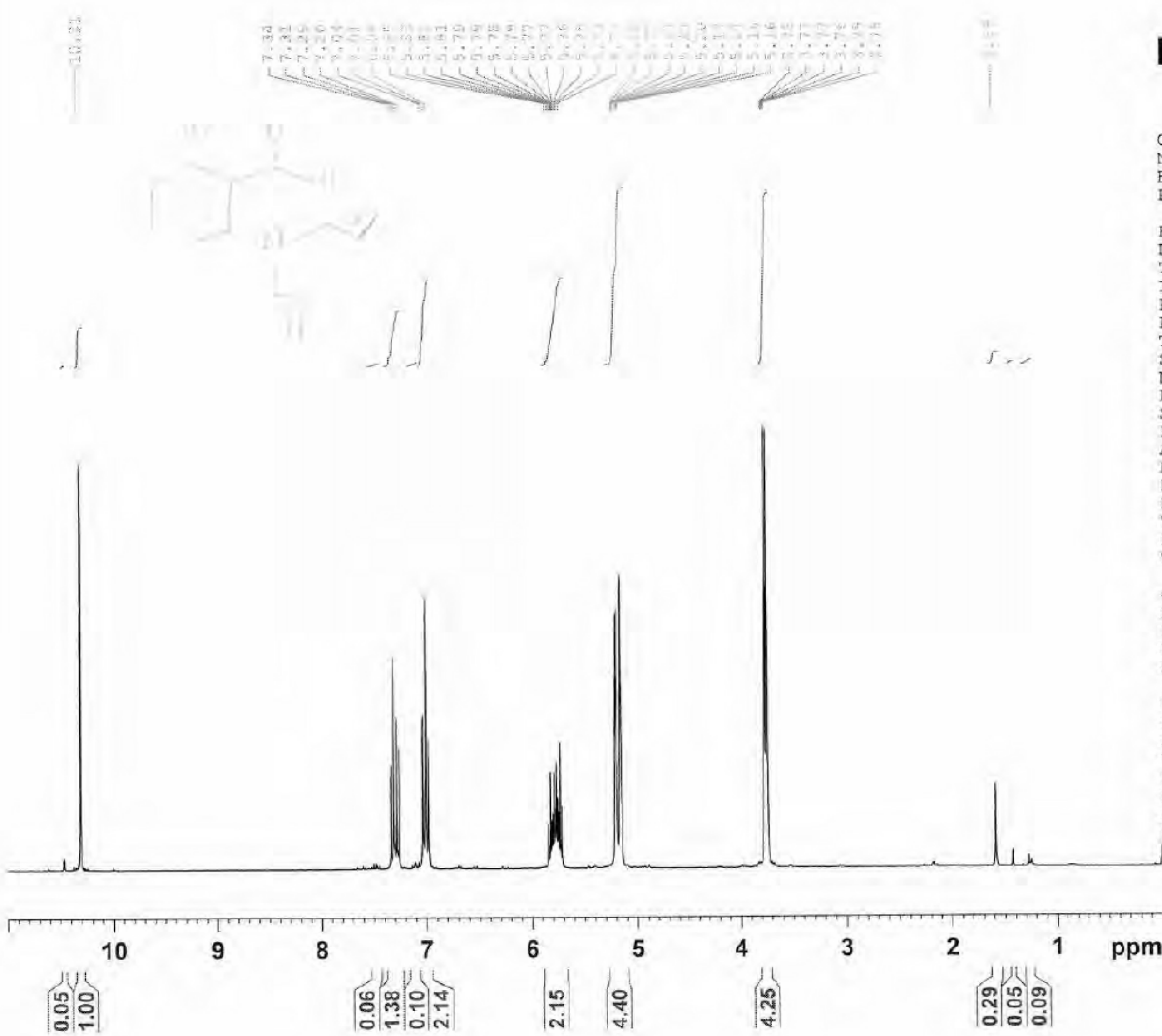
Current Data Parameters
NAME CMD-i-058 c13
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20121210
Time 22.21
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 8192
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 3649.1
DW 27.800 usec
DE 6.00 usec
TE 295.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 7.10 usec
PL1 -1.50 dB
SFO1 75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 17.23 dB
PL13 19.00 dB
SFO2 300.1312005 MHz

F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40

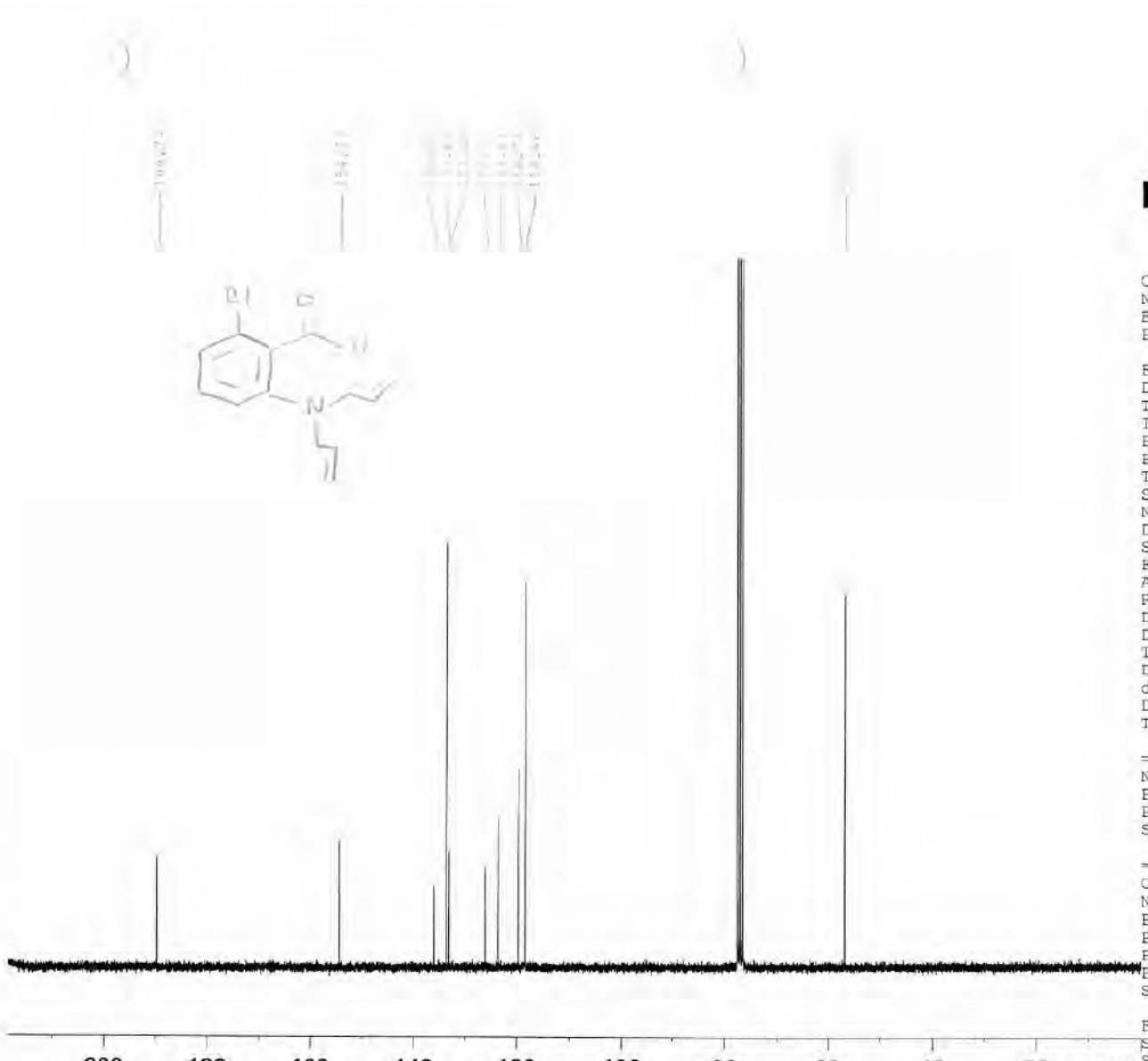


Current Data Parameters
NAME CMD-i-062
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130125
Time 10.29
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 6172.839 Hz
FIDRES 0.094190 Hz
AQ 5.3084660 sec
RG 406.4
DW 81.000 usec
DE 6.00 usec
TE 293.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 11.00 usec
PL1 0.00 dB
SFO1 300.1318534 MHz

F2 - Processing parameters
SI 32768
SF 300.1300050 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00



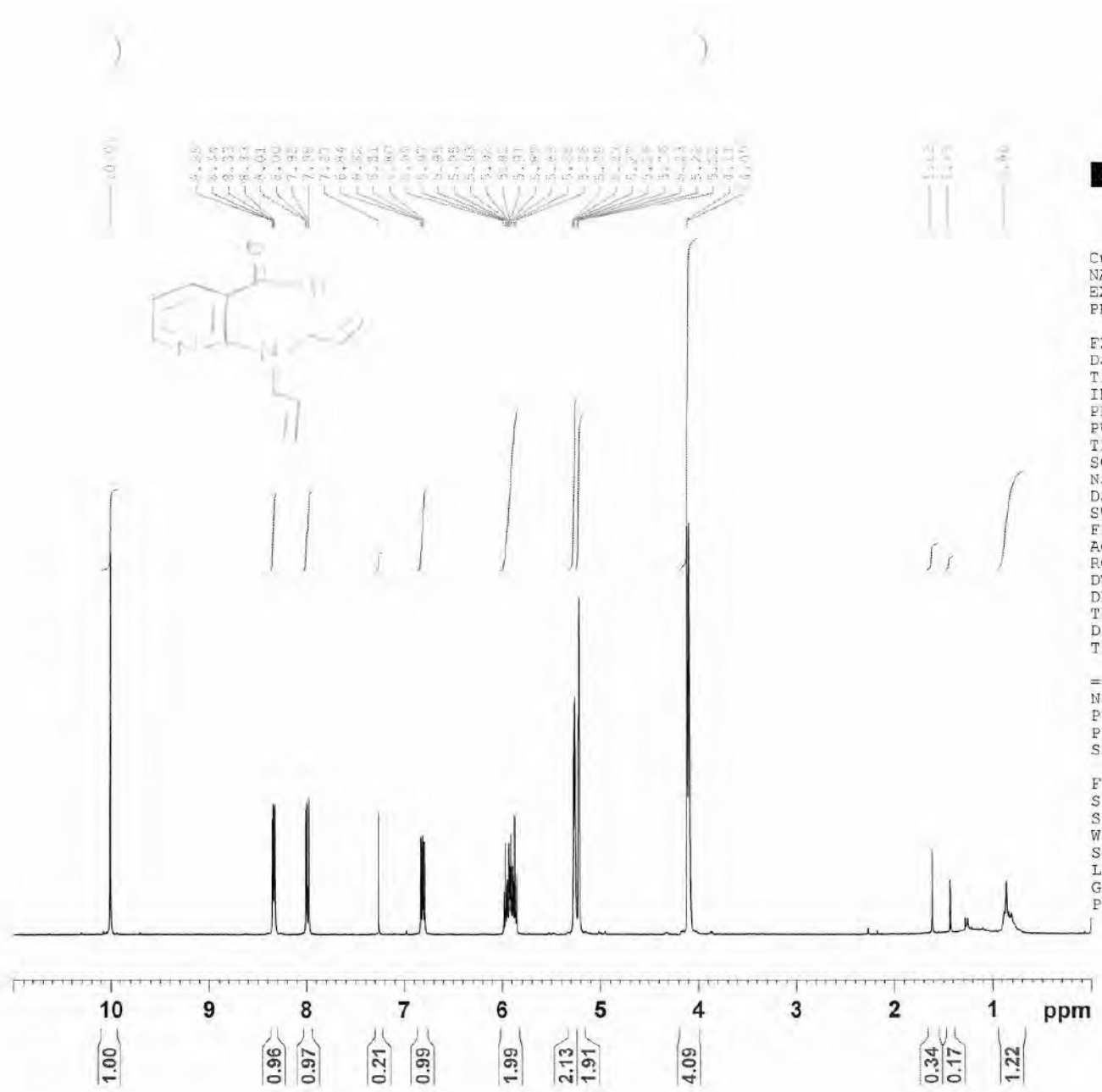
Current Data Parameters
NAME CMD-i-062 c13
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20130126
Time 3.35
INSTRUM spect
PROBHD 5 mm Multinucl
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 17985.611 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 2580.3
DW 27.800 usec
DE 6.00 usec
TE 294.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 7.10 usec
PL1 -1.50 dB
SFO1 75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 0.00 dB
PL12 17.23 dB
PL13 19.00 dB
SFO2 300.1312005 MHz

F2 - Processing parameters
SI 32768
SF 75.4677490 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40



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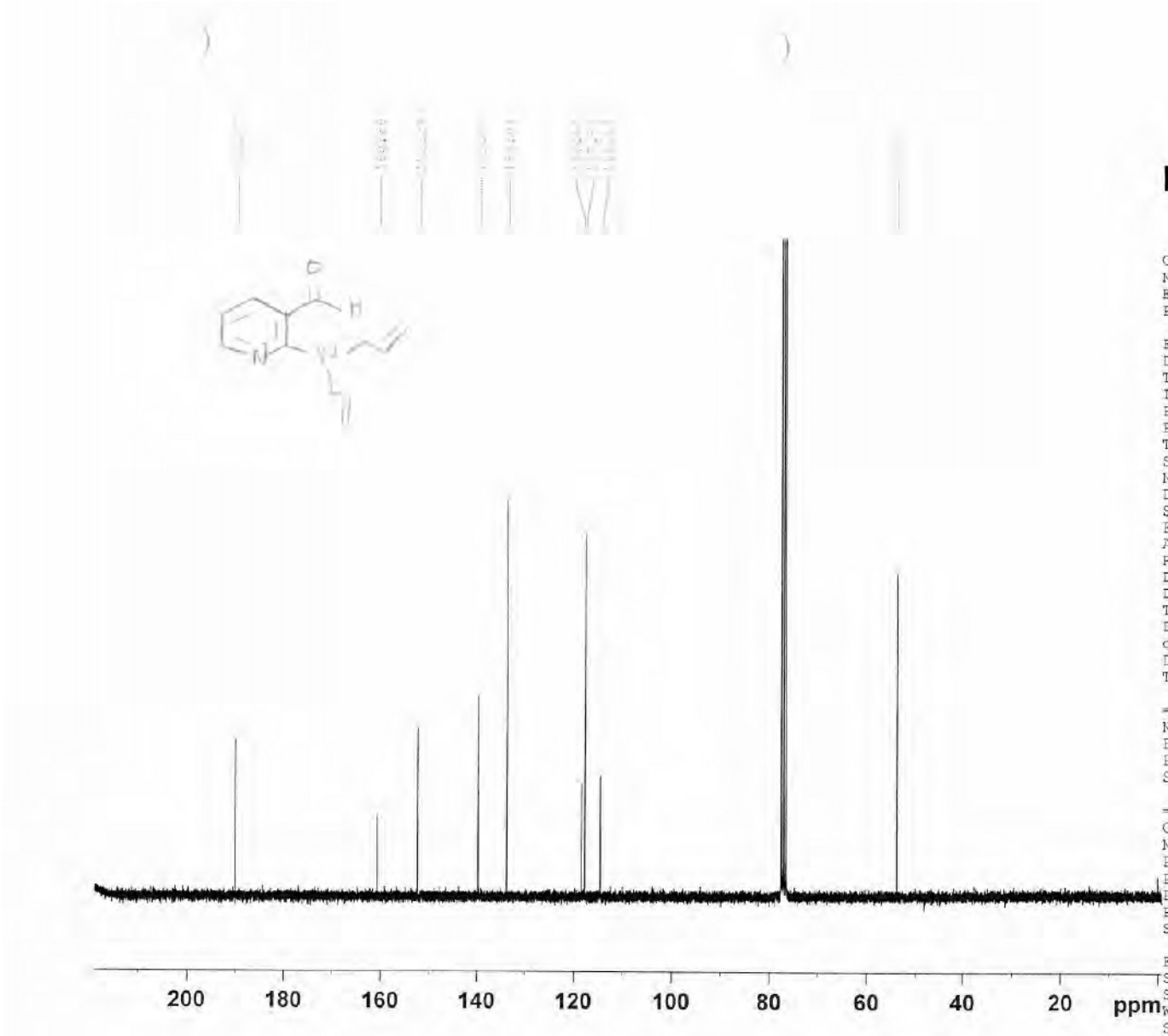
```
Current Data Parameters
NAME      CMD-i-065 top dot
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20130201
Time                  12.49
INSTRUM               spect
PROBHD    5 mm Multinucl
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                6172.839 Hz
FIDRES            0.094190 Hz
AQ                5.3084660 sec
RG                    406.4
DW                   81.000 usec
DE                    6.00 usec
TE                   293.2 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                    11.00 usec
PL1                    0.00 dB
SFO1          300.1318534 MHz

F2 - Processing parameters
SI                    32768
SF            300.1300047 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                     1.00
```



BRUKER

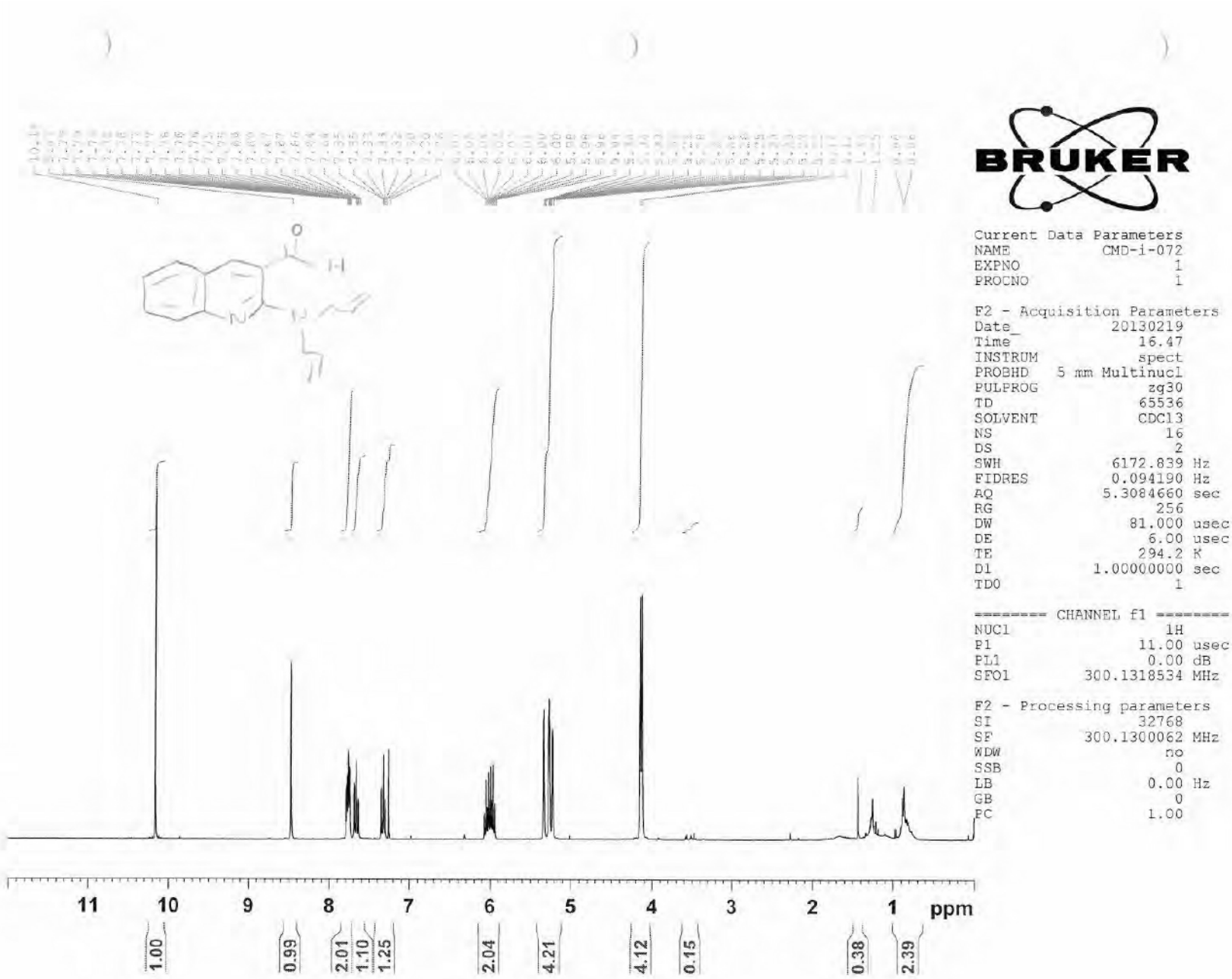
```
Current Data Parameters
NAME       CMD-i-065 c13
EXPNO                 1
PROCNO                1

F2 - Acquisition Parameters
Date_          20130212
Time               3.41
INSTRUM            spect
PROBHD   5 mm Multinucl
PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS               10240
DS                   4
SWH          17985.611 Hz
FIDRES        0.274439 Hz
AQ            1.8219508 sec
RG                4096
DW              27.800 usec
DE               6.00 usec
TE              295.2 K
D1           2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1                7.10 usec
PL1              -1.50 dB
SFO1        75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2            80.00 usec
PL2               0.00 dB
PL12             17.23 dB
PL13             19.00 dB
SFO2       300.1312005 MHz

F2 - Processing parameters
SI                32768
SF          75.4677490 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.40
```



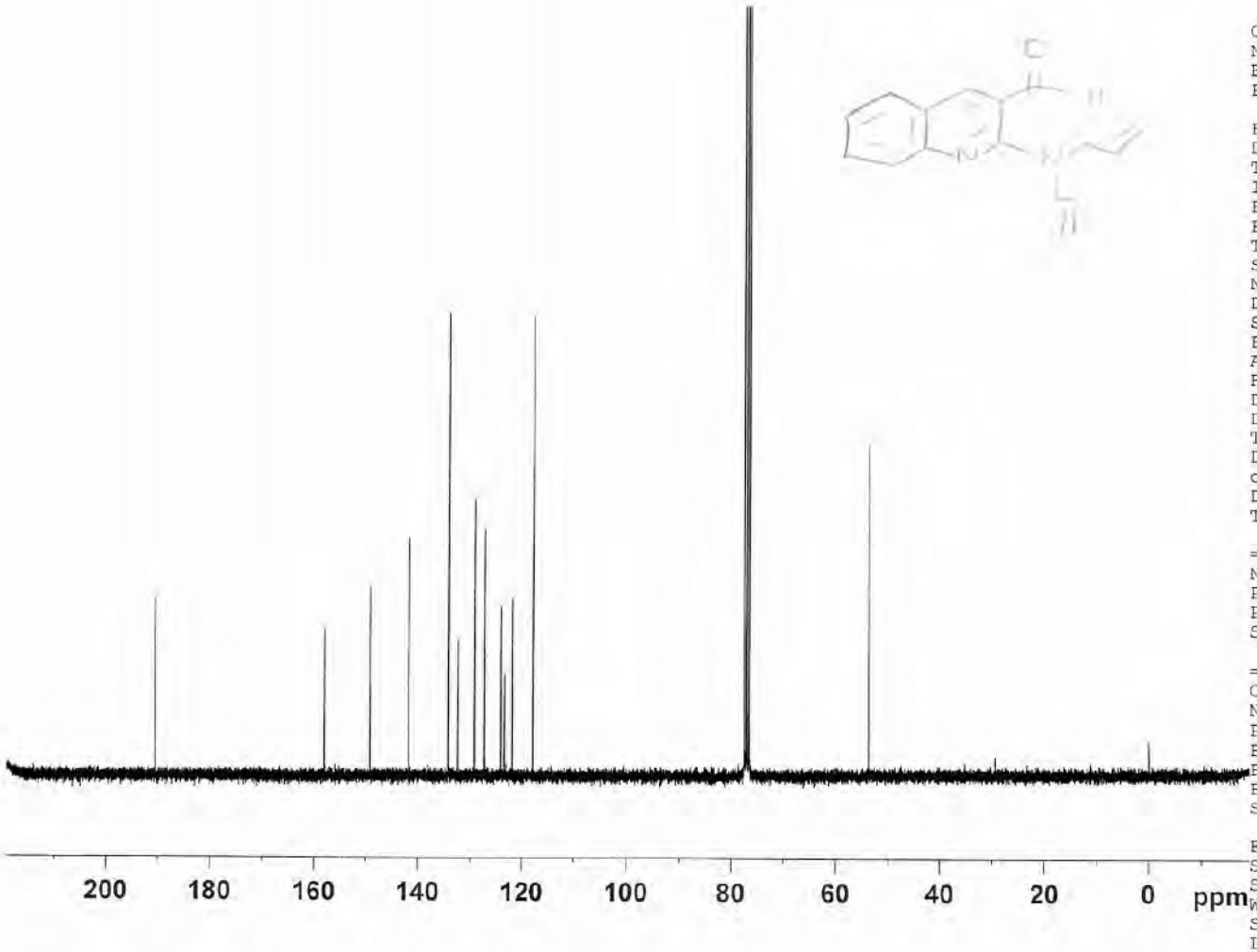
BRUKER

```
Current Data Parameters
NAME                  CMD-i-072
EXPNO                         1
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20130219
Time                      16.47
INSTRUM                   spect
PROBHD     5 mm Multinucl
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                           16
DS                            2
SWH                   6172.839 Hz
FIDRES                0.094190 Hz
AQ                    5.3084660 sec
RG                          256
DW                     81.000 usec
DE                      6.00 usec
TE                      294.2 K
D1                 1.00000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                         1H
P1                     11.00 usec
PL1                     0.00 dB
SFO1              300.1318534 MHz

F2 - Processing parameters
SI                        32768
SF                300.1300062 MHz
WDW                          no
SSB                           0
LB                      0.00 Hz
GB                            0
PC                         1.00
```



BRUKER

```
Current Data Parameters
NAME          cmd66Credo
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130213
Time               6.49
INSTRUM           spect
PROBHD   5 mm Multinucl
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                10000
DS                    4
SWH           17985.611 Hz
FIDRES         0.274439 Hz
AQ             1.8219508 sec
RG                 3251
DW               27.800 usec
DE                6.00 usec
TE                294.2 K
D1           2.00000000 sec
d11          0.03000000 sec
DELTA        1.89999998 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 7.10 usec
PL1               -1.50 dB
SFO1         75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2             80.00 usec
PL2                0.00 dB
PL12              17.23 dB
PL13              19.00 dB
SFO2        300.1312005 MHz

F2 - Processing parameters
SI                 32768
SF          75.4677490 MHz
WDW                   no
SSB                    0
LB                 0.00 Hz
GB                     0
PC                 1.40
```