Formation of Indazoles Through an Unusual Cyclization Reaction of Hydrazones

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Abstract

Antibacterial resistance has become and increasing problem throughout the world. In 2014 an estimated 480,000 deaths occurred due to complications associated with multi-drug resistant strains of tuberculosis (TB) [1]. To combat resistant strains of bacteria, new forms of antibiotics must be utilized. One promising new antibiotic is SAB-P1.

SAB-P1 is an effective antibiotic for both resistant and nonresistant strains of TB. However, it has only been biosynthetically produced in small quantities[2]. In an attempt to couple indole and naphthalene moieties, to produce SAB-P1 like compounds, a Fischer indole synthesis was utilized. This synthesis did not proceed as expected and instead yielded a number a novel indazole compounds.

To further investigate the reaction, 1-acetyl-2-naphtol, 2-hydroxy-napthaldehyde, 1-acetyl-2-methoxy napthalene, and N-(1-acetylnaphthalen-2-yl)acetamide were reacted under Fischer indole synthetic conditions with one or more hydrazine derivative. The resultant compounds were then isolated and characterized.

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1.0 Background

1.1 General

Since the early 1990's indazole chemistry has been gaining notoriety. Indazoles themselves have been shown to be quite biologically active with numerous studies iterating their anti-parasitic, anti-fungal, anti-tumor, cannabinoid, inhibitory, and other pharmacological properties[3].The indazole moiety is that of a bicyclic aromatic compounds comprised of a benzene a pyrrole ring. Indazole moieties appear in nature quite rarely with the three known naturally occurring indazole compounds being Nigellicine, Nigeglanine, and Nigellidine[3]. However, numerous synthetic methods have been developed for the production of indazole based compounds.

1.2 Synthetic production

There are many known synthetic methods for producing indazoles that utilize a wide variety of chemicals and have varying levels of complexity. There are three isomers of the basic indazole ring these being 1H-, 2H-, and 3H-; of these isomers, the most stable are 1-H indazoles and the least stable are 3H-indazoles (Fig.1). Due to the instability of 3H-indazoles there few synthetic methods which are not publicly available due to patent protection. A few select common synthetic methods for the production of indazoles are outlined below.

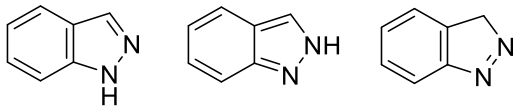


Figure 1: Indazole isomers

1.2.1 1H-indazole syntheses via metallic salts

1H-indazoles are synthesized through numerous methods and many substituents can be added or derivatives produced. Some metal catalyzed reactions are described below.

1.2.1.1 Method 1

One method palladium salts and require a multitude of steps to generate their corresponding indazoles. Lebedev et al (2004) generated indazoles by first synthesizing metallic phenylhydrazones, which were then cyclized under basic conditions[4]. The phenylhydrazones were first generated by the condensation of o-bromobenzaldehyde with phenylhydrazine. Two molar equivalents of the phenylhydrazone in methanol were then complexed to one equivalent of Na_2PdCl_2 and generated the metallic phenylhydrazones[4–6]. The phenyl hydrazones were then cyclized under basic conditions. This synthetic mechanism produced high yields of the indazole product seen in the figure 2.

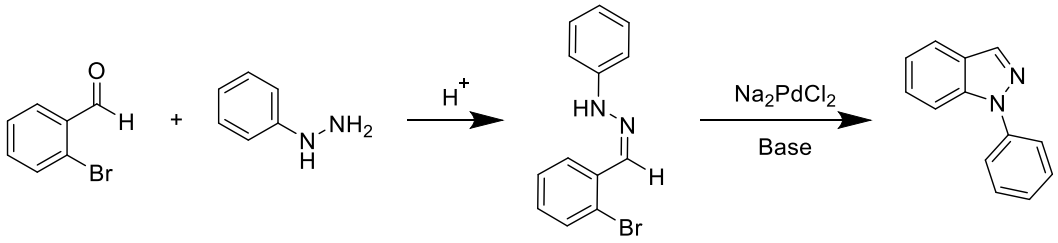


Figure 2: Multi-step production of 1H-phenyl indazole. A phenyl hydrazone is generated through condensation with an acid catalyst and a phenylhydrazine. The phenylhydrazone is cyclized utilizing a palladium catalyst and a base.

1.2.1.2 Method 2

A similar method pioneered by Yeon Kyu Bae and Chan Sik Cho (2012) utilized a copper salt catalyst, in place of a palladium catalyst, to generate aryl indazoles (Fig.3)[7]. The major advantage of the Bae/Cho method, is the fact that it is a one pot synthetic mechanism that produced high yields of the indazole products.

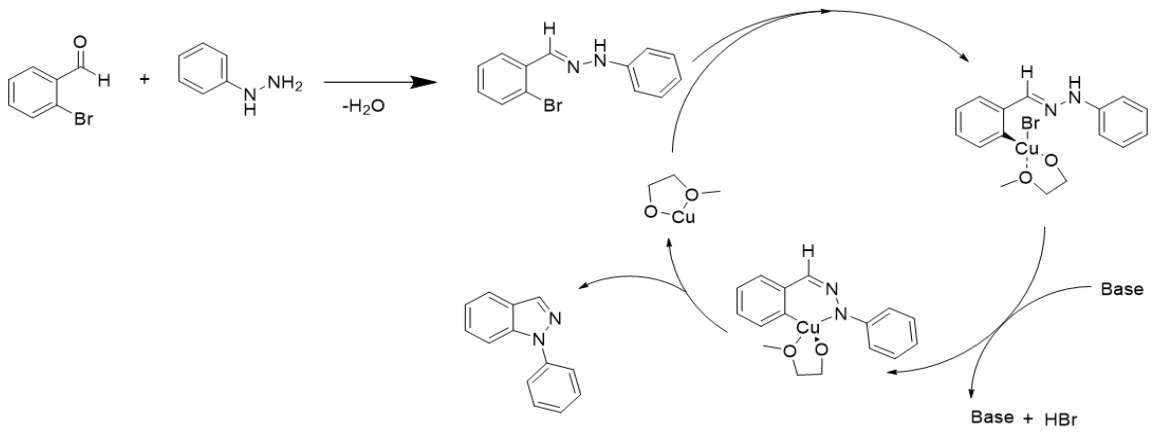


Figure 3: The Bae/Cho catalysis reaction for the one-point production of 1H-aryl-indazoles.

1.2.2 2H-indazole synthesis

There are a far fewer described procedures for the synthesis of 2H-indazoles. Like the 1H-indazoles most methods of synthesis involve metallic salts[3,8]. For instance, one method involves a metallic salt stabilized Coarctate reaction. However, there are instances of acid and base catalyzed Davis-Beirut reaction that generated 2H-indazoles[8,9].

1.2.2.1 Method 1

The Coarctate reaction method poduced 2H-indazoles in high yields when a copper salt was used to stablilze the carbene intermediate[3,10]. In the reaction, (2-ethynylphenyl)-triazenes were heated at 50°C with five equivalents of CuCl in 1,2-dichloroethane for 12 hours to produce 2H-indazoles (Fig.4).

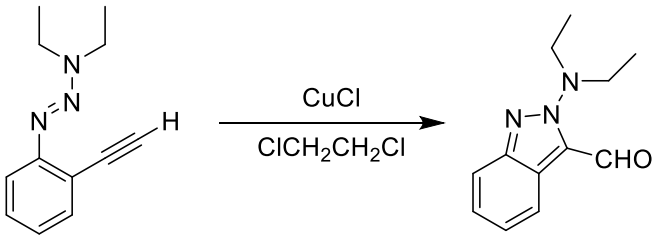


Figure 4: The generation of 2H-indazoles through a Coarctate reaction mechanism.

1.2.2.2 Method 2

The Davis-Beirut reaction base method produces 2H-indazoles in 40-90% yields[8]. In the reaction, nitrobenzyl bromide, in tetrahydrofuran (THF), was added dropwise to an amine, similarily in THF, and allowed to react for four hours[8]. The initial product were 2-nitrobenzylamines. The nitrobenzylamines were added to a 5% KOH alcoholic solution and allowed to react at 60°C for six hours and produced corresponding 2H-indazoles (Fig.5)[8].

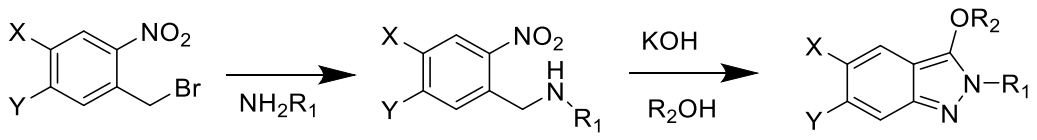


Figure 5*:* A Davis-Beirut base catalyzed production of 2H-indazole products.

1.2.3 3H-benzo[e]indazole synthesis

The naming convention for the indazole compounds change when a napthalene ring replaces the benzene ring; The 1H-indazole moiety seen in figure 1 becomes a 3H-benzo[e]indazole under benzo[e] naming convention, but remains 1H- under benzo[G] and benzo[F] naming conventions (Fig.6). Benzoindazoles were first synthesized, in low yields, by Witt and Braun in 1914. However, there has been little advancements in the production of benzoindazoles and there appear to be no bioactivity studies[11–13].

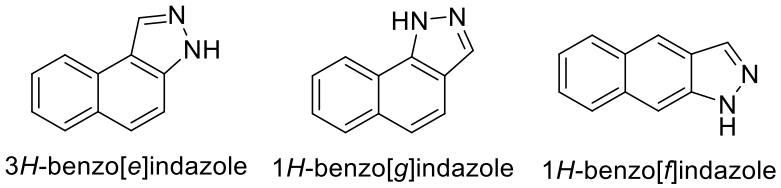


Figure 6: Three different isomers of benzoindazoles

One high yield mechanism for the synthesis of benzoindazoles was introduced by Duewell and Haig (1968)[13]. A mixture of an o-hydroxycarbonyl compound and hydrazine hydrate in diethylene glycol was heated at reflux for three hours. The hydrazine hydrate was added in excess but never allowed to exceed 5% of the solution by volume. The synthesis of 3-methyl-1H-benzo[f]indazole can be seen in figure 7.

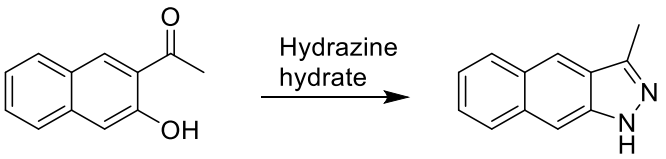


Figure 7*:* The production of 3-methyl-1H-benzo[f]indazole utilizing 1-(3-hydroxynaphthalen-2-yl)ethan-1-one and hydrazine hydrate

2.0 Introduction

Antibacterial resistance has become and increasing problem throughout the world. In 2014 an estimated 480,000 deaths occurred due to complications associated with multi-drug resistant strains of tuberculosis (TB) [1]. To combat resistant strains of bacteria, new forms of antibiotics must be utilized. One promising avenue of study is the production of indole based antibiotics.

Known as a privileged structure, the indole scaffold acts as a ligand for numerous bioreceptors [14]. Indoles have been shown to have anti-inflammatory, antibacterial, and anti-carcinogenic properties[15]. Due to its effectiveness against TB and antibiotic resistant strains of TB, an indole derivative of interest was SAB-P1. For TB, SAB-P1 had a minimum inhibitory concentration (MIC) of 0.16 ± .04 μg/ml, was bactericidal for TB at concentrations of 0.63 μg/ml, and had a 50% inhibitory concentration (IC_{50}) for green monkey kidney cells above 8 μg/ml [2]. SAB-P1 and similar compounds have shown promise as next generation antibiotics due to their low MIC and IC_{50} values.

In the presence of toluene-4-monooxygenase, SAB-P1 was produced biosynthetically by treating *Escherichia coli* with indole and anthranil [2]. However, it was produced in low yields along with a variety of other biproducts. It was hypothesized SAB-

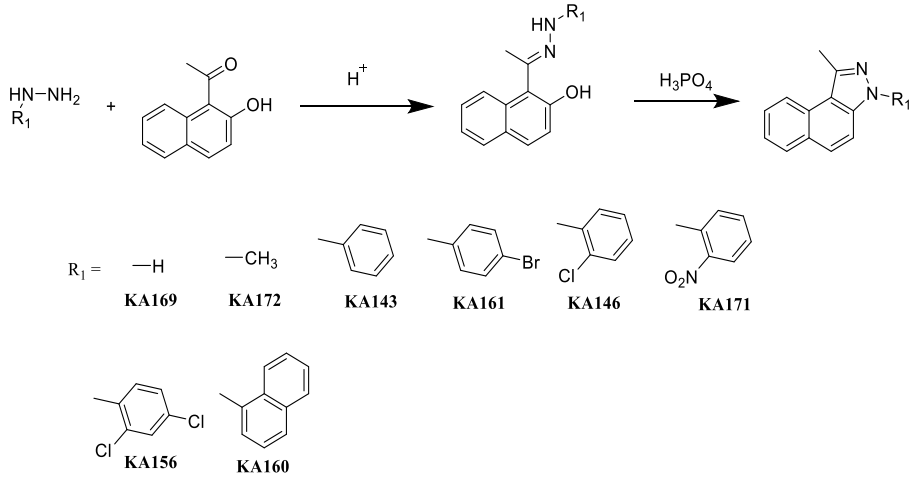


Figure 8: A modified Fischer indole synthesis yielding R1 substituted indazoles, from the corresponding hydrazines and 1-acetyl-2-napthol.

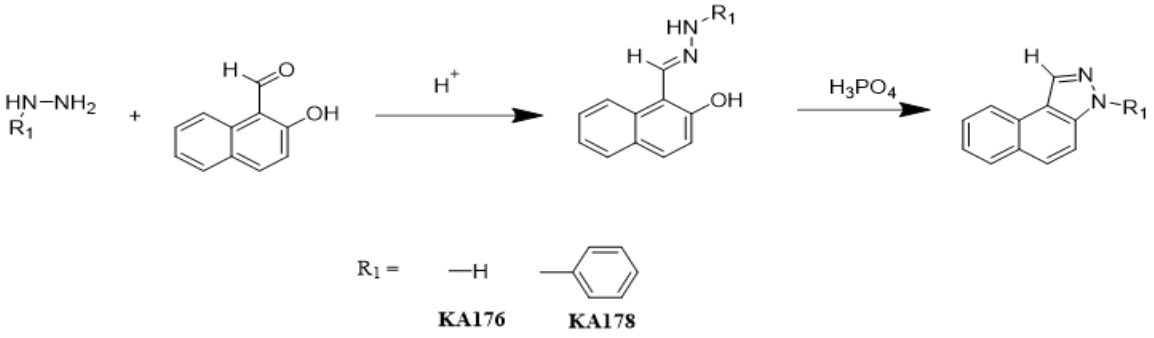


Figure 9: A modified Fischer indole synthesis yielding R1 substituted indazoles, from the corresponding hydrazines and 2-hydroxy-1-acetaldehyde.

P1 could be synthetically produced in high yields utilizing a Fischer indole synthesis followed by oxidation with oxone[16].

In order to utilize the Fischer indole synthesis, two compounds were required: phenylhydrazine which was commercially available, and 5-hydroxy-4-acetyl-indole which, is difficult to synthesize. As plausible substitutes, 2-hydroxyacetophenone and 1-acetyl-2-napthol were utilized as replacements for 5-hydroxy-4-acetyl-indole because of their commercial availability.

When phenylhydrazine was reacted with 1-acetyl-2-napthol, the reaction did not proceed expected and a substituted indazole was produced. This unexpected reaction was further investigated by reacting 1-acetyl-2-napthol and 2-hydroxy-1-napthaldehyde with substituted hydrazines (Fig.8&9). Each reaction produced a corresponding indazole. It was

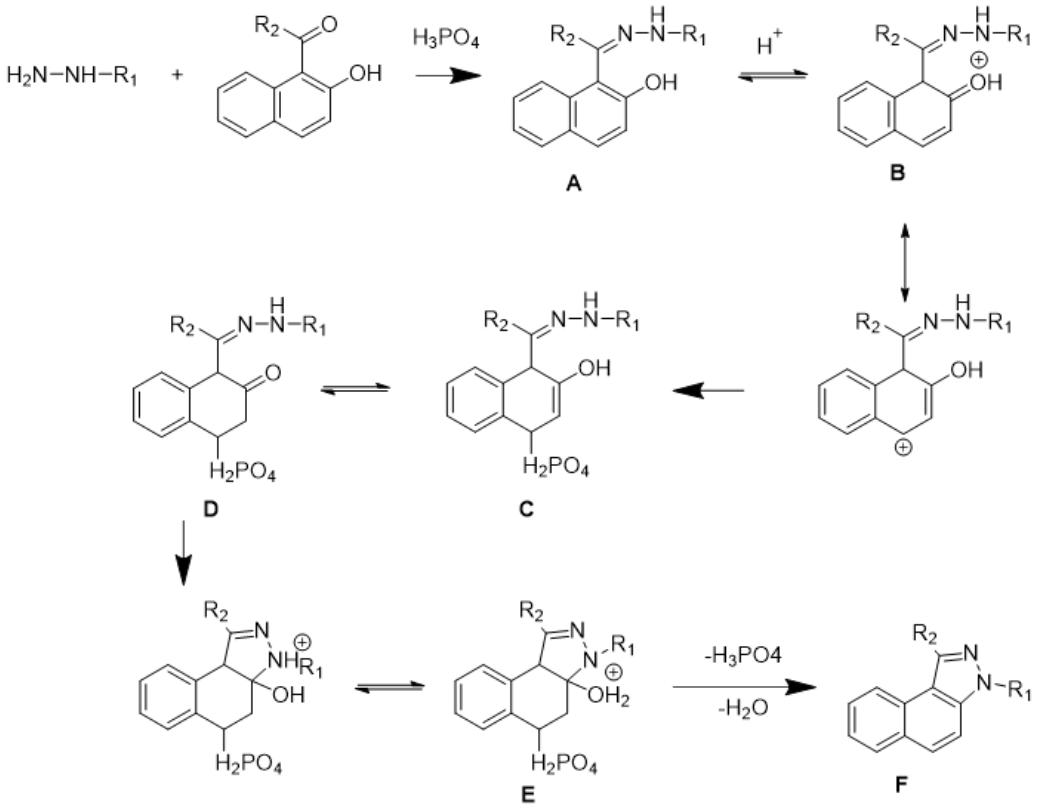


Figure 10: A modified Bucherer reaction. The phosphoric acid acts as a catalyst for the initial reaction between the napthol and hydrazine and produces a hydrazone intermediate (A). With excess H3PO4 the compound is protonated (B). The compound tautomerizes and the phosphoric acid anion attaches to the ring (C). C converts to its keto form (d). The nitrogen attacks the ketone and the oxygen is protonated (E). E regains full aromaticity by losing the attached anion and water forming the stable indazole product (F).

proposed that the reaction proceeded via a modified form of the *Bucherer reaction* (Fig.10)[17].

3.0 Experimental Approach

80 % Phosphoric acid was dried by heating in an oven at 100.0°C for two hours. All samples, unless otherwise noted, were analyzed by: gas chromatography mass spectrometry (GC/MS), high performance mass spec (HPMS), ^{1}H-nulcear magnetic resonance imaging (NMR), ^{13}C-NMR, gradient heteronuclear quantum coherence spectroscopy (gHSQC), gradient heteronuclear multiple bond coherence (gHMBC), and gradient homonuclear correlation spectroscopy (gCOSY). The NMR experiments were run on a 500 MHz instrument. The melting point (MP) range of the indazole products were taken in triplicate (n = 3).

3.1 Compound KA176 (3H-benzo[e]indazole)

A mixture of 243 µl (5 mmol) of hydrazine monohydrate and 0.86 g (5 mmol) of 2-hydroxy-1-napthaldehyde in 10 ml of phosphoric acid were heated at 130°C overnight. To neutralize the acid, 20.0 ml of ammonia hydroxide was added dropwise over a two-hour period. Ethyl acetate was added to the solution and the organic layer was extracted and dried with sodium sulfate. The solution was filtered and the solvent was evaporated under vacuum at 60°C. The crude product was suspended in dichloromethane (DCM) and filtered. The crude GC/MS spectra showed that the product was produced in an 88.7% yield (Appendix A). Dimethyl sulfoxide (DMSO) was added dropwise to the solid until it was completely dissolved. Water was added dropwise to the DMSO solution to precipitate a yellow solid. The solution was filtered and the solid was washed with excess water. The molecular formula was confirmed by HPMS (Appendix A).

3.2 Compound KA178 (3-phenyl-3H-benzo[e]indazole)

A mixture of 1.0 ml (10 mmol) of phenyl hydrazine and 1.72 g (10 mmol) of 2-hydroxy-1-napthaldehyde in 10 ml of phosphoric acid was heated at 130°C overnight. To neutralize the acid, 20.0 ml of ammonia hydroxide was added dropwise over a two-hour period. Chloroform was added to the solution and the organic layer was extracted, filtered, and dried with sodium sulfate. The solution was filtered and the solvent was evaporated

under vacuum at 60°C. The crude GC/MS spectra showed that the product was produced in an 88.7% yield (Appendix B). Column chromatography was run on a 300 mg sample: the stationary silica phase was loaded into the column with hexane and the sample was loaded on to the silica with chloroform. The mobile phase consisted of chloroform, hexane, and triethylamine in an 80:20:1 ratio. The purity of the fractions was assessed with GC/MS data. None of the fractions were clean. The fractions that contained only the two peaks—showing masses of 244 m/z and 258 m/z—were dissolved in chloroform, combined, and dried at 60°C under vacuum. DMSO was added to the solid product dropwise until it fully dissolved. Water was added dropwise to the solution until a yellow/brown solid was precipitated. The solution was filtered and the solid was collected and washed with excess water. The solid was dried at 100°C under vacuum. The dried solid was used for further analysis.

3.3 Compound KA169 (1-methyl-3H-benzo[e]indazole)

A mixture of 0.69 g (13.7 mmol) of hydrazine monohydrate and 1.86 g (10 mmol) of 1-acetyl-2-napthol in 40 ml of phosphoric acid were heated at 120°C for seven days. The solution was filtered and washed with excess water. Ethyl acetate was used to extract the organic matter. Additional organic matter was forced out of the aqueous layer by adding 6.5 g of sodium bicarbonate. The organic matter was again extracted using ethyl acetate. The organic solution was dried with sodium sulfate. The sodium sulfate was filtered and the solvent was removed under vacuum at 60°C. Small crystals were found in the crude product and used for x-ray crystallography. The crystal data and refinement information can be seen in table 1. Complete analysis of the crystal can be found in Appendix C. 300 mg of the product was plated on a high performance thin layer chromatography (HPTLC) plate. The plate was run in a 60 ml:40 ml mix of ethyl acetate and chloroform. The plate was visualized under ultraviolet (UV) light. The product was determined to be between the visible bands. The silica was suspended in ethyl acetate, filtered, and the organic layer was dried under vacuum at 60°C. A heteronuclear single quantum coherence (HSQC) experiment was run in place of a gHSQC experiment.

Table 1: Crystal and refinement information for compound KA169.

Crystal data	*Refinement*
$C_{12}H_{10}N_2$	R[F2 > 2(F2)]= 0.0668
Orthorhombic, $P2_12_12_1$	wR(F2) = 0.1233
a = 5.30400(10) Å	S = 0.9965
b= 10.6855(3) Å	1788 reflections
c = 16.7181(11) Å	127 parameters
α = 90°	$\Delta\rho_{max}$ = 0.33 e A $^{\circ -3}$
β = 90°	$\Delta\rho_{min}$ = -0.22 e A $^{\circ -3}$
γ = 90°	
V = 947.51(7) Å^3	
Z = 4	
Mo Kα radiation	
μ = 1.54	
T = 293 K	

3.4 Compound KA173 (3-ethyl-1-methyl-3H-benzo[e]indazole)

A mixture of 1.5 ml (30 mmol) of hydrazine monohydrate and 4.7 g (25 mmol) of 1-acetyl-2-napthol in 30 ml of phosphoric acid were heated at 120°C overnight. Water and ethyl acetate were added to the solution. The solution was filtered and the ethyl acetate organic layer was extracted. The organic layer was dried under vacuum at 60°C and 1.0912 g of crude was recovered. Approximately 500 mg of the crude was dissolved in 5 ml of DMSO. 0.1414 g of sodium hydride and 239 µl of iodoethane were added to this solution. The solution was reacted overnight. The crude GC/MS spectra showed two products with masses of 210 m/z had yields of 41.8% and 34.1% (Appendix D). Water and ethyl acetate were added to the solution. The ethyl acetate layer was extracted, dried with sodium sulfate, and evaporated under vacuum at 60°C. An HPTLC plate was run with 80 ml of ethyl acetate and 20 ml of hexane. The remaining crude was dissolved in 5 ml of DMSO and reacted with 0.1406 g of sodium hydride and 239 µl of iodoethane. An HPTLC plate was run with 60 ml of hexane, 40 ml of ethyl acetate and 2.0 ml of triethylamine. The plates were visualized under ultraviolet (UV) light. All the distinct bands were scrapped off and the

silica was suspended in ethyl acetate. The silica was filtered and the pure organic layers were analyzed.

3.5 Compound KA172 (1,3-dimethyl-3H-benzo[e]indazole)

A mixture of 52 µl (1 mmol) of methyl hydrazine and 0.1861 g (1 mmol) of 1-acetyl-2-napthol were in 6 ml of ethanol and 4 ml of phosphoric acid was heated at reflux overnight. Water and ethyl acetate were added to the solution. The organic layer was removed, dried with sodium sulfate, and analyzed via GC/MS. No NMR or HPMS data was taken. The crude GC/MS spectra showed the product was produced in a 24.5% yield (Appendix E). The yield was small and due to safety concerns the reaction was not repeated on a larger scale, so no further analysis was completed on the compound.

3.6 Compound KA143 (1-methyl-3-phenyl-3H-benzo[e]indazole)

The compound was synthesized three times: once with 1-acetyl-2-napthol, once with 2-methoxy-1-acetyl naphthalene, and once under argon with 1-acetyl-2-napthol. The reactions utilizing 1-acetyl-2-napthol were combined after they were confirmed via GC/MS to be the same compound. A fourth synthesis was attempted utilizing N-(1-acetylnaphthalen-2-yl)acetamide, but compound KA143 was not produced.

3.6.1 Synthesis with 1-acetyl-2-napthol

A mixture of 1.0 g (10 mmol) of phenyl hydrazine and 1.86 g (10 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and 4 ml of phosphoric acid were heated at reflux overnight. Water and ethyl acetate were added to the solution. The organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C. The crude GC/MS spectra showed that the product was produced in an 73% yield (appendix F). DMSO was added to the crude until it was sufficiently wet. The solution was heated until the product fully dissolved. The solution was left at room temperature until the product crystallized out of solution. The crystallized product was filtered and washed with excess water. The purified product was dried under vacuum at 100°C. A sample was dissolved and crystallized out of excess ethanol. The product was a white crystalline solid.

The x-ray crystal structure of the compound showed the phenyl ring to be bent out of the plane. The phenyl group sits 3° above the indazole moiety, and is rotated out of the plane. The dihedral angle between the indazole and carbon 16 of the phenyl ring was 13°. The dihedral angle between the indazole and carbon 20 of the phenyl ring was 27°. The crystal data and refinement information can be seen in table 2. Complete analysis of the crystal can be found in Appendix F.

3.6.2 Synthesis with 2-methoxy-1-acetyl naphthalene

A mixture of 2.09 g of potassium carbonate and 0.93 g of 1-acetyl-2-napthol were combined in 15 ml of acetone. 1.91 g of dimethylsulfide was added and the solution was heated overnight at 50°C. The acetone was removed under vacuum at 60°C. Ethanol was added to the product creating a cloudy white suspension. The solid was filtered out and confirmed to be 2-methoxy-1-acetyl naphthalene via GC/MS (appendix F). The solid was combined with 0.1342 g of phenyl hydrazine in 6 ml of ethanol and 4 ml of dried phosphoric acid. The reaction was heated at reflux overnight. Water and ethyl acetate were added to the solution. The organic layer was extracted and dried under vacuum at 60°C.

Table 2: Crystal and refinement information for compound KA143

Crystal data	***Refinement***
$C_{18}H_{14}N_2$	R[F2 > 2 (F2)]= 0.1255
Orthorhombic, $Pca2_1$	wR(F2) = 0.1719
a = 11.188(3) Å	S = 0.9965
b = 11.750(3) Å	1862 reflections
c = 10.088(2) Å	181 parameters
α = 90°	$\Delta\rho_{max}$ = 0.30 e A ° $^{-3}$
β = 90°	$\Delta\rho_{min}$ = -0.24 e A ° $^{-3}$
γ = 90°	
V = 1326.2(3) Å3	
Z = 4	
Cu Kα radiation	
μ = 1.54	
T = 293 K	

The product was a black oil and the GC/MS spectra showed multiple products (Appendix F). No NMR or HPMS data was produced.

3.6.3 Synthesis under argon

A mixture of 1.08 g (10 mmol) of phenyl hydrazine and 1.87 g (10 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and 4 ml of dried phosphoric acid were heated at reflux overnight under argon. A small sample was confirmed to be the KA143 product via GC/MS (Appendix F). Excess water and ethyl acetate were added to the solution and the organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C.

3.6.4 Synthesis with N-(1-acetylnaphthalen-2-yl)acetamide

N-(1-acetylnaphthalen-2-yl)acetamide was not commercially available and was synthesizing utilizing Brown et. al (1945)[18]. A mixture of 10.10 g (60 mmol) of 2-acetonapthone, 6.27 g (90 mmol) of hydroxylamine hydrochloride, and 9.04 g (110 mmol) of sodium acetate in 20 ml of ethanol and 4.5 ml of water was heated at 50°C overnight. A white precipitate was collected by filtration and washed with water. The solid was dried under vacuum at a temperature of 80°C. The solid was added to 50 ml of phosphoric acid and reacted for three days. The phosphoric acid solution was poured into 500 ml of deionized water, which produced another white precipitate. The precipitate was collected by filtration and dried again. 1.86 g of the precipitate was added to a mixture of 2 ml of acetic anhydride and 35.5 ml of carbon disulfide under argon. Over a one-hour period, 5.94 g of aluminum chloride was added to the solution. To remove the carbon disulfide, 30 ml of water was added to the mixture. Ethyl acetate was added to the solution and the organic layer was extracted and dried at 60°C under vacuum. The GC/MS spectrum showed a 60% percent yield of N-(1-acetylnaphthalen-2-yl)acetamide (appendix F). 30 ml of phosphoric acid and 592 µl (5 mmol)of phenyl hydrazine were added to the N-(1-acetylnaphthalen-2-yl)acetamide crude. The solution was heated at 130°C overnight. The GC/MS spectrum showed no characteristic compound KA143 peak and no further analysis was done (Appendix F).

3.7 Compound KA161 (3-(4-bromophenyl)-1-methyl-3H-benzo[e]indazole)

A mixture of 0.22 g (1 mmol) of p-bromophenylhydrazine hydrochloride and 0.18 g (1 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and 4 ml of phosphoric acid were heated at reflux overnight. Excess water and ethyl acetate were added to the solution and the organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C. The crude GC/MS spectra showed that the product was produced in an 88.9% yield (Appendix G). An HPTLC plate was run using 60 ml of hexane and 30 ml of ethyl acetate. The plates were visualized under UC light. All the distinct bands were scrapped off and the silica was suspended in ethyl acetate. The silica was filtered and the pure organic layers were analyzed. The product was a brown/yellow solid

.

3.8 Compound KA146 (3-(2-chlorophenyl)-1-methyl-3H-benzo[e]indazole)

A mixture of 1.79 g (10 mmol) of 2-chlorophenyhydrazine and 1.86 g (10 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and 4 ml of phosphoric acid was heated at reflux overnight. Water and ethyl acetate were added to the solution. The organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C. The crude GC/MS spectra showed that the product was produced in an 98.0% yield (appendix H). The crude was purified by washing with hot ethanol. The purified white solid was used for further analysis. A small sample of the compound was dissolved in excess dichloromethane (DCM) and allowed to evaporate slowly to obtain crystals. The crystal data and refinement information can be seen in Table 3. Complete analysis of the crystal can be found in Appendix H.

3.9 Compound KA171 (1-methyl-3-(3-nitrophenyl)-3H-benzo[e]indazole)

A mixture of 1.90 g (10 mmol) of 3-nitrophenylhydrazine hydrochloride and 1.86 g (10 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and 4 ml of phosphoric acid were heated at reflux overnight. Water and ethyl acetate were added to the solution. The organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C. The crude was suspended in ethanol and refluxed. The crude NMR spectra showed that the product was produced in a 68% yield (Appendix I). The solution was

filtered hot, and the yellow solid that remained on the filter paper was dried at 60°C under vacuum. The solid was used for further analysis.

3.10 Compound KA156 (3-(2,4-dichlorophenyl)-1-methyl-3H-benzo[e]indazole)

Table 4: Crystal and refinement information for compound KA146.

Crystal data	***Refinement***
$C_{18}H_{13}Cl_1N_2$	R[F2 > 2 (F2)]=0.2356
Monoclinic, $P2_1/c$	wR(F2) = 0.2860
a = 24.492(8) Å	S = 1.0410
b = 4.3582(16) Å	3769 reflections
c = 28.295(10) Å	379 parameters
α = 90°	$\Delta\rho_{max}$ = 1.36 e A ° -3
β = 112.7(8)°	$\Delta\rho_{min}$ = -1.25 e A ° -3
γ = 90°	
V = 2785.3(10) Å3	
Z = 8	
Mo Kα radiation	
μ = 0.71	
T = 293 K	

A mixture of 2.34 g (10 mmol) of 2,4-dichlorophenylhydrazine hydrochloride and 1.86 g (10 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and three drops of sulfuric acid were heated at reflux overnight. A small sample was removed and allowed to crystallize. The clear crystal was analyzed by x-ray crystallography. The crystal data and refinement information can be seen in table 4. Complete analysis of the crystal can be found in Appendix J.

To the remaining solution 4 ml of phosphoric acid was added. The solution was heated at reflux for two days. Water and DCM were added to the solution and the organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C. The crude was suspended in methanol and refluxed. The solution was filtered hot, and the white solid that remained on the filter paper was dried at 60°C under

vacuum. The crude GC/MS spectra showed that the product was produced in a 78.5% yield (appendix J). The dried solid was used for further analysis.

Table 6: Crystal and refinement information for compound KA156

Crystal data	***Refinement***
$C_{18}H_{12}N_2Cl_2$	R[F2 > 2 (F2)]= 0.0890
Orthorhombic, $Pca2_1$	wR(F2) = 0.2393
a = 14.9397(18) Å	S = 1.0410
b = 67.2222(7) Å	2746 reflections
c = 15.2684(15) Å	175 parameters
α = 90°	$\Delta\rho_{max}$ = 0.79 e A $^{\circ -3}$
β = 109.4°	$\Delta\rho_{min}$ = -0.69 e A $^{\circ -3}$
γ = 90°	
V = 1553.8(3) Å3	
Z = 4	
Mo Kα radiation	
μ = 0.71	
T = 293 K	

3.11 Compound KA160 (1-methyl-3-(naphthalen-2-yl)-3H-benzo[e]indazole)

A mixture of 0.1950 g (1 mmol) of 2-naphthylhydrazine hydrochloride and 0.1864 g (1 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and 4 ml of phosphoric acid were heated at reflux overnight. Water and ethyl acetate were added to the solution. The organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C. The crude was suspended in methanol and refluxed. The solution was filtered hot, and the brown solid that remained on the filter paper was dried at 60°C under vacuum. The crude GC/MS spectra showed that the product was produced in a 90.5% yield (Appendix K). The dried solid was used for further analysis

3.12 Compound KA155 ((Z)-1-(2,4-dinitrophenyl)-2-(1-(naphthalen-1-yl)ethylidene)-hydrazine)

A mixture of 1.99 g (10 mmol) 2,4-Dinitrophenyl hydrazine and 1.86 g (10 mmol) of 1-acetyl-2-napthol in 6 ml of ethanol and 4 ml of phosphoric acid were heated at reflux for 3 days. Water and chloroform were added to the solution. The organic layer was extracted, dried with sodium sulfate, and the solvent was evaporated under vacuum at 60°C. The crude material was dissolved in methanol. The solution was heated and filtered. The methanol evaporated and orange product crystals were collected and analyzed by x-ray crystallography. The product hydrazone did not run through the GC/MS spectrometer or HPMS spectrometer, and no yield was found. The methyl group sat 22° below the plane of the naphthalene ring, and the napthlalene and phenyl rings intersect at a 35° angle. The crystal data and refinement information can be seen in Table 2. Complete analysis of the crystal can be found in Appendix L.

Table 8: Crystal and refinement information for compound KA155

Crystal data	***Refinement***
$C_{18}H_{14}N_4O_5$	R[F2 > 2 (F2)]=0.2356
Orthorhombic, $Pca2_1$	wR(F2) = 0.2860
a = 14.0516(12) Å	S = 1.0410
b = 6.9155(8) Å	2746 reflections
c = 32.938(3) Å	175 parameters
α = 90°	$\Delta\rho_{max}$ = 0.66 e A $^{\circ\ -3}$
β = 90°	$\Delta\rho_{min}$ = -0.73 e A $^{\circ\ -3}$
γ = 90°	
V = 3200.7(3) Å3	
Z = 8	
Mo Kα radiation	
μ = 0.71	
T = 293 K	

4.0 Analysis/Discussion

4.1 KA176

Via the crude GC/MS spectrum **compound KA176** was produced in 85.5% yield from hydrazine monohydrate and 2-Hydroxy-1-naphthaldehyde (appendix A). Compound KA176 MP was 227.0-229.4°C (± 1.2°C). The molecular formula ($C_{11}N_2H_8$) was verified using high performance mass spectrometry (appendix A). The predicted structure is seen in Fig.11. One and two-dimensional NMR spectroscopy were utilized to further evaluate the compound.

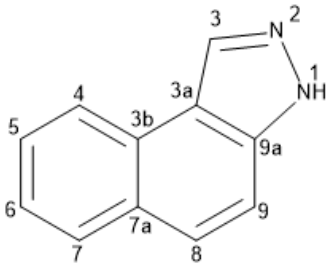


Figure 11: The predicted structure of compound KA176 and its numbering assignments.

Ten peaks were observed in the ^{1}H-NMR spectrum (Fig.11). Eight of the ten peaks were attributed to the compound of interest, while the remaining two peaks were attributed to solvent DMSO and water contamination. The ^{1}H signals, with multiplicities of two

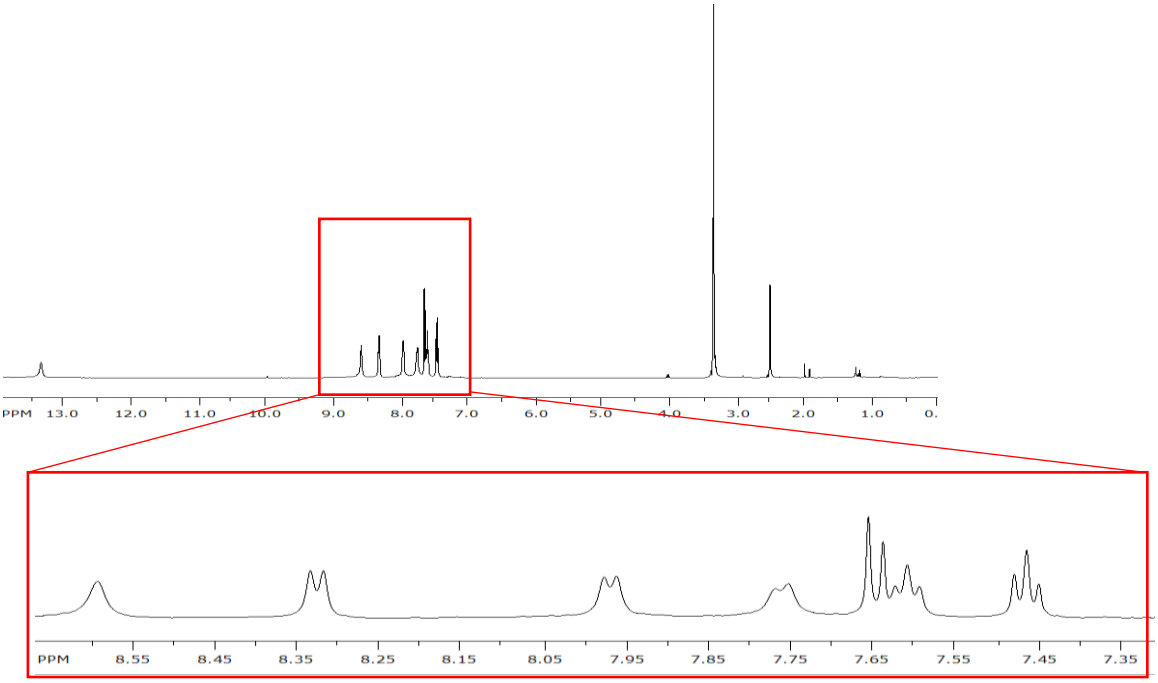


Figure 12: The ^{1}H-NMR spectrum for compound KA176. There are eight hydrogen signals originating from compound KA176, as well as, two signals corresponding to a solvent and water peaks. The peaks of interest include 7.46 ppm (singlet), 7.61 ppm (triplet), 7.65 ppm (doublet), 7.76 ppm (doublet), 7.97 ppm (doublet), 8.33 ppm (doublet), 8.59 ppm (singlet), 13.37 ppm (singlet). (Bottom) The magnified aromatic region of the spectrum with observable multiplicities.

(doublet), had chemical shifts of 7.65 ppm, 7.76 ppm, 7.97 ppm, and 8.33 ppm, and were assigned a relative integration of one. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 7.46 ppm and 7.61 ppm and were integrated to one. The ^{1}H signals, with multiplicities of one (singlet), had chemical shifts of 8.59 ppm and 13.37 ppm and were integrated to one. The experimental ^{1}H signals are congruent with the expected signals in respect to the number, multiplicity, and integration of signals predicted from the proposed structure in Fig.3. The ^{13}C -NMR had 11 unique carbon signals all within the aromatic region (Fig. 13). Several of the ^{13}C signals lacked intensity due to the compound being difficult to purify. Approximately 10 mg of pure compound was isolated.

^{1}H and ^{13}C chemical shifts were correlated via gHSQC and gHMBC spectra. The gHSQC showed coupling over one bond between hydrogens with chemical shifts of 7.46 ppm, 7.61 ppm, 7.65 ppm, 7.76 ppm, 7.97 ppm, 8.33 ppm, and 8.59 ppm to the carbons with chemical shifts of 124.7 ppm, 127.5 ppm, 111.9 ppm, 127.8 ppm, 129.1 ppm, 123.5 ppm, and 133.3 ppm, respectively (Fig.14). The hydrogen signal with a chemical shift of 13.37 ppm showed no coupling over one bond to any carbon and was assigned to position 1 of fig.3. The remaining singlet with a chemical shift of 8.59 ppm was assigned to position

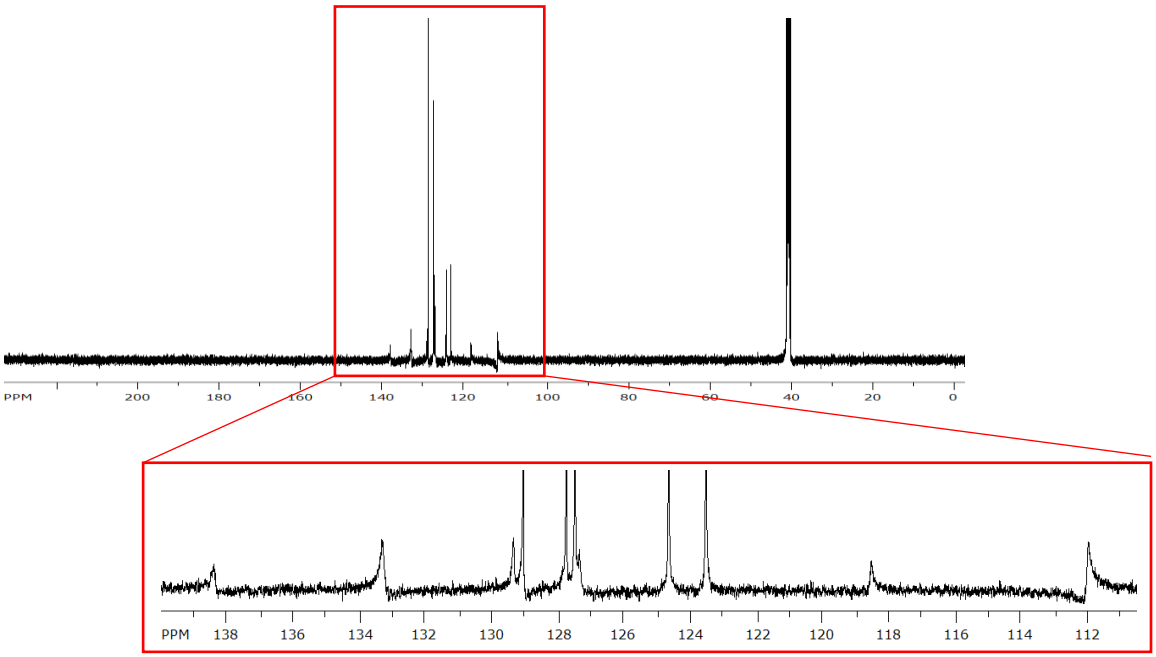


Figure 13: The full ^{13}C-NMR spectrum for compound KA176. There are 11 carbons originating from compound KA176, as well as, one signal corresponding to a solvent peak. The peaks of interest include 111.9 ppm, 118.5 ppm, 123.5 ppm, 124.7 ppm, 127.3 ppm, 127.5 ppm, 127.8 ppm, 129.1 ppm, 129.4 ppm, 133.3 ppm, and 138.5 ppm. (Bottom) The magnified aromatic region of the spectrum.

3 of fig.12 because it coupled over one bond to a carbon signal with a chemical shift of 133.3 ppm (Fig.14). Neither the position 1 or 3 hydrogen showed coupling over three bonds in the gHMBC spectrum (Fig.14). However, the structure was elucidated by observation of specific coupling patterns. Over three bonds, the carbon at position 3a should have coupled to the hydrogens at positions 4 and 9. The only carbon signal that matched the description was the carbon signal with a chemical shift of 118.5 ppm (Fig.15). The 3a carbon was thus assigned the chemical shift of 118.5 ppm.

Over three bonds the 3a carbon coupled to the hydrogen doublet signals with chemical shifts of 8.33 ppm and 7.65 ppm (Fig.16). In turn, the hydrogens signals with

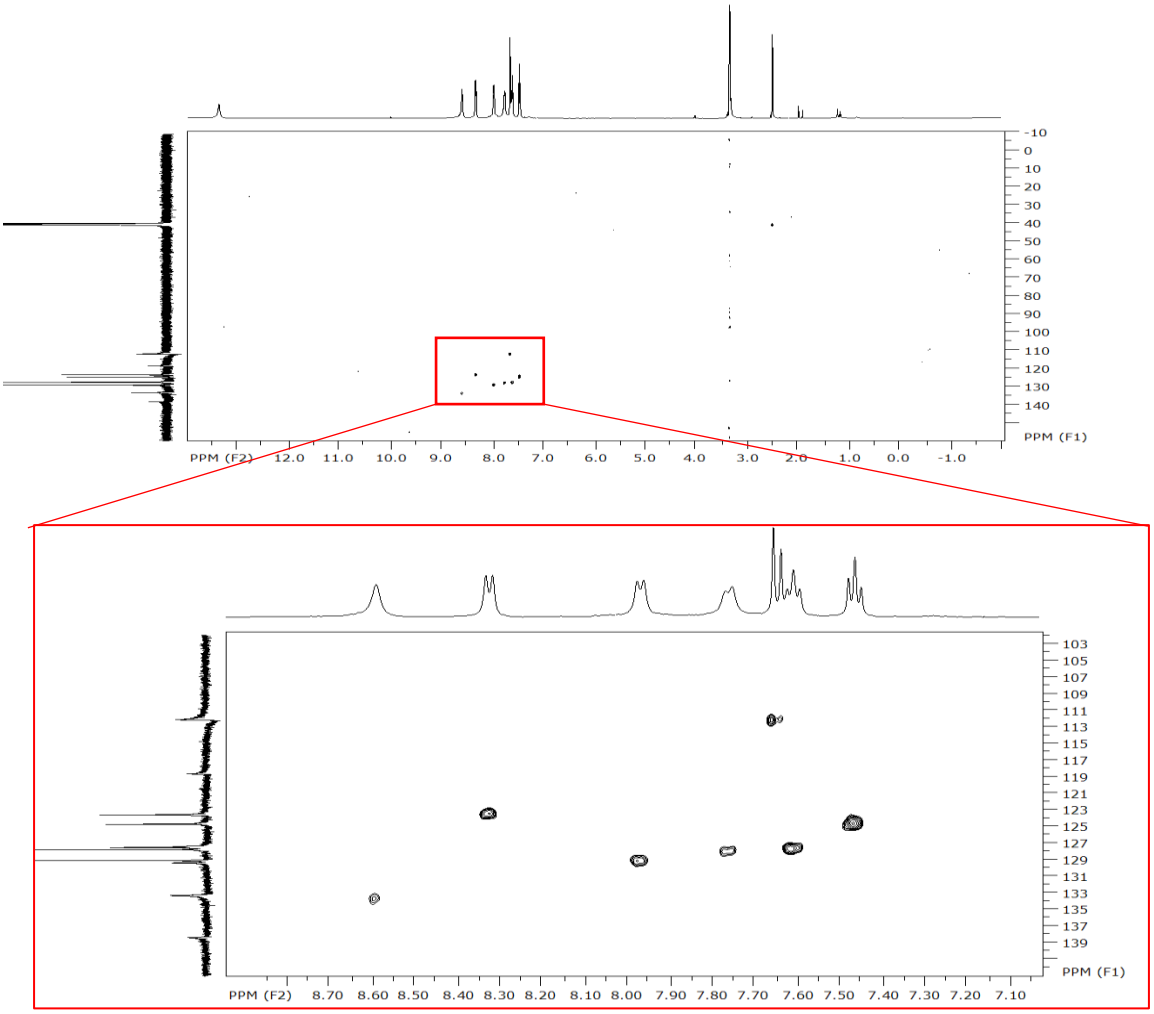


Figure 14: The gHSQC spectrum or compound KA176. (Top) The full gHSQC spectra for compound KA176, showing coupling between carbons and hydrogens over one bond. Signals are observed in only the aromatic region. (Bottom) The magnified aromatic region of the gHMBC spectra.

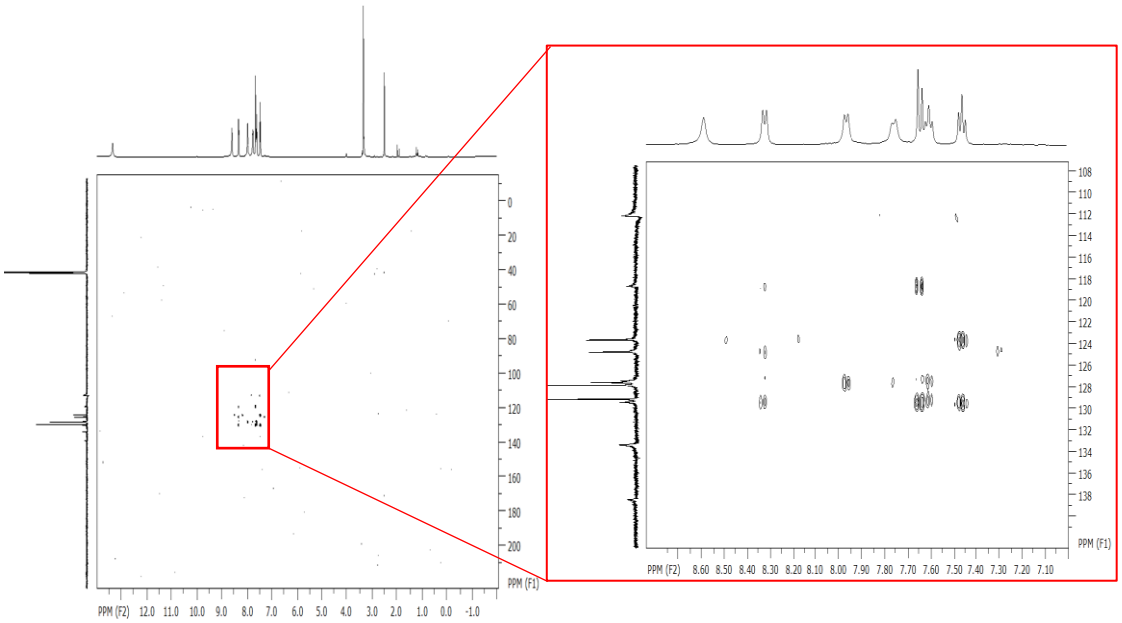


Figure 15: The gHMBC spectrum or KA176. (Left) The full gHMBC spectra for compound KA176, showing coupling between carbons and hydrogens over three bonds. Signals are observed in only the aromatic region. (Right) The magnified aromatic region of the gHMBC spectra.

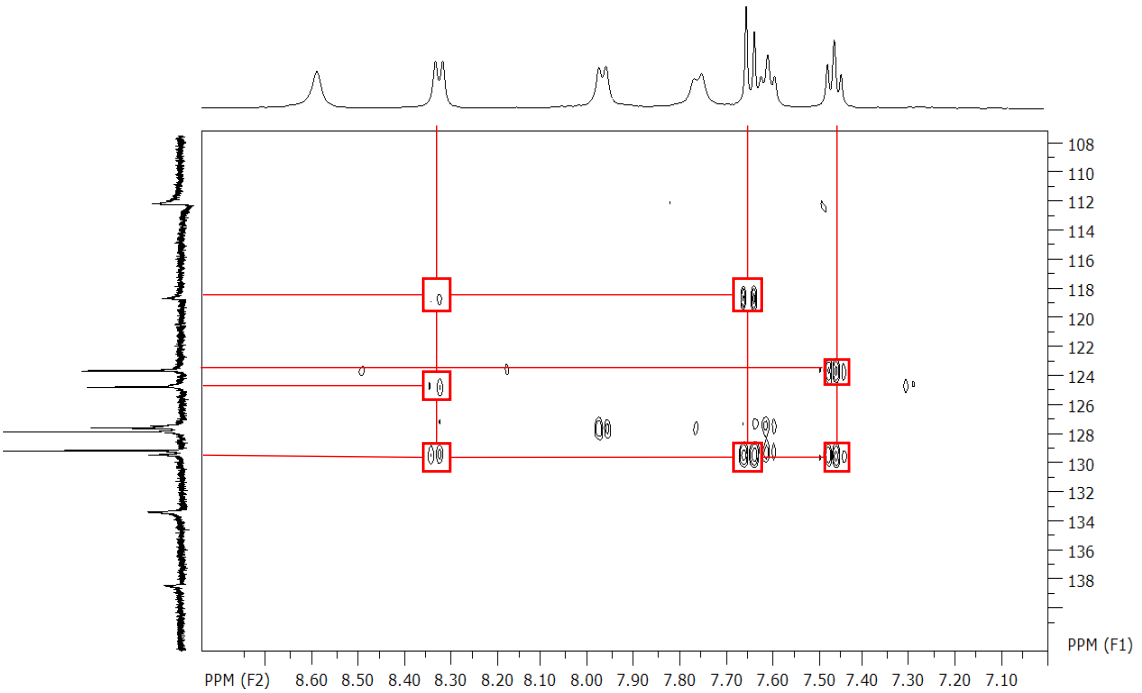


Figure 16: The aromatic region of the gHMBC spectra for compound KA176. Where the horizontal and vertical lines intersect with a box shows coupling over three bonds. The hydrogen signal at a chemical shift of 7.46 ppm couples to the carbon signals with chemical shifts of 123.5 ppm and 129.4 ppm. The hydrogen signal with a chemical shift of 7.65 ppm couples to the carbon signals with chemical shifts of 118.5 ppm and 124.9 ppm. The hydrogen signal with a chemical shift of 8.33 ppm couples to the carbons with chemical shifts of 118.5 ppm, 124.7 ppm, and 129.4 ppm.

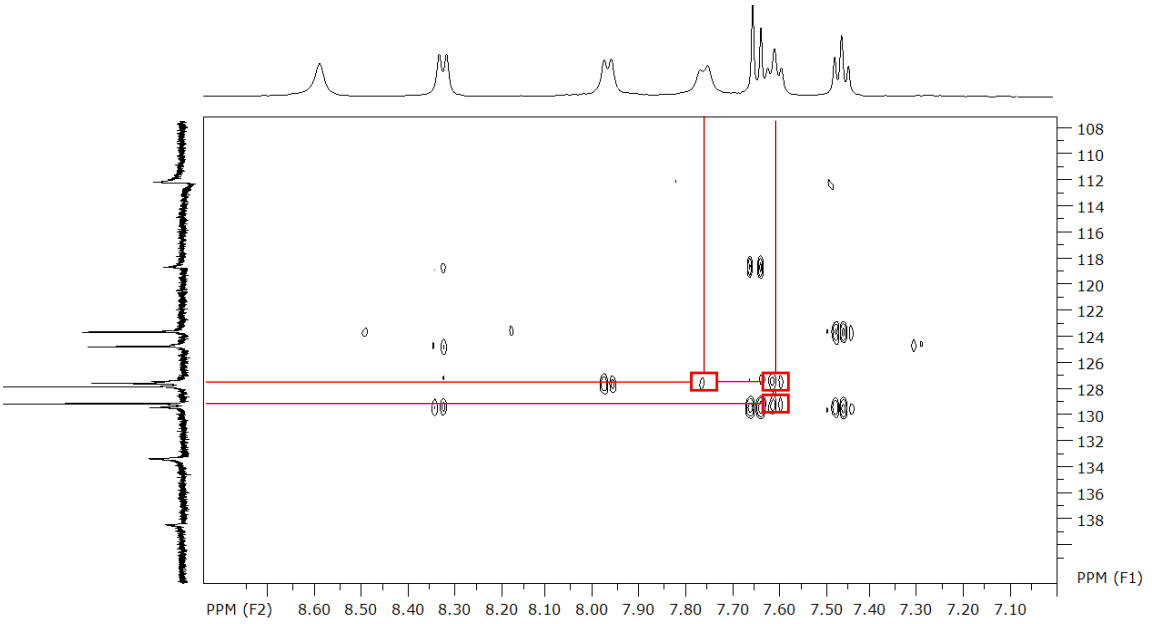


Figure 18: The aromatic region of the gHMBC spectra for compound KA176. Where the horizontal and vertical lines intersect with a box shows coupling over three bonds. The hydrogen signal at a chemical shift of 7.61 ppm couples to the carbons with chemical shifts of 129.1 ppm and 127.3 ppm. The hydrogen with a chemical shift of 7.97 ppm couples to the carbon with a chemical shift of 127.3 ppm.

chemical shifts of 8.33 ppm and 7.65 ppm coupled over one bond to the carbons with chemical shifts of 123.5 ppm and 116.9 ppm respectively (Fig.14). From the predicted structure, it was proposed that the carbon at position 4 would couple to a triplet signal at position 6. Of the two possible carbon signals only the one with a chemical shift of 123.5 ppm coupled over three bonds to the triplet hydrogen signal with a chemical shift of 7.46 ppm (Fig.16). The carbon and hydrogen signals with chemical shifts of 123.5 ppm and 8.33 ppm respectively, were assigned to position 4. By process of eliminations the hydrogen signal with a chemical shift of 7.65 ppm and the carbon signal it coupled to over one bond, chemical shift of 111.9 ppm, were assigned to position 9 (Fig.14).

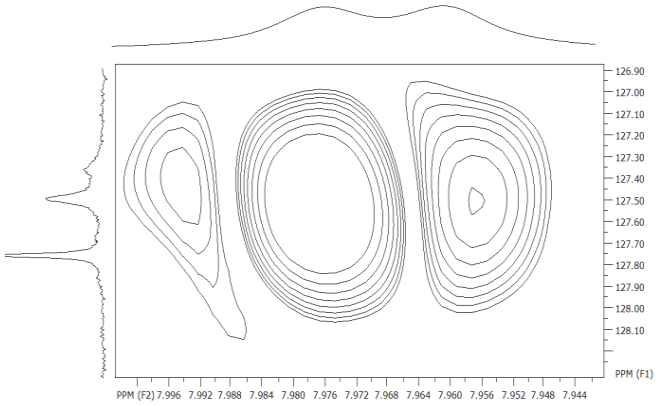
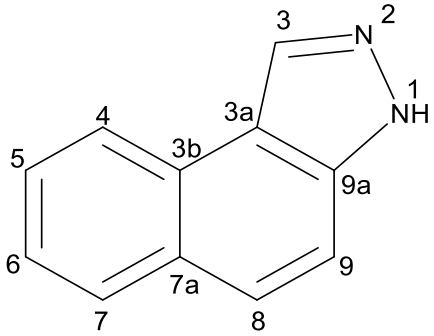


Figure 17*:* A magnified signal within the gHMBC spectra showing distortion in the 2-D signal between the hydrogen signal with a chemical shift of 7.97 ppm and carbon with a chemical shift of 127.3 ppm.

The positions 4, 6, and 9 hydrogens all coupled to the carbon with a chemical shift of 129.4 ppm over three bonds (Fig.16). The carbon signal with a chemical shift of 129.4 ppm coupled to no hydrogens over one bond, and was assigned to position 7a. The remaining triplet, with a chemical shift of 7.61 ppm, was assigned to position 5 because it was the only remaining triplet signal. Over three bonds the position 5 hydrogen coupled to the carbons with chemical shifts of 127.3 ppm and 129.1 ppm (Fig.17).

In turn, the carbon with a chemical shift of 129.1 ppm coupled over one bond to the doublet hydrogen signal with a chemical shift of 7.97 ppm and the carbon with a chemical shift of 127.3 ppm coupled to no hydrogens over one bond (Fig.14). From this, the carbon and hydrogen pair, with chemical shifts of 129.1 ppm and 7.97 ppm respectively, were assigned to position 7. The carbon with a chemical shift of 127.3 ppm was assigned to position 3b. The position 3b carbon couples to the position 5 hydrogen and to the hydrogen signal with a chemical shift of 7.76 ppm. Theoretically the carbon signal with a chemical shift of 127.3 ppm should couple to the position 7 hydrogen, but the 2-D signal between



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	13.37	N/A
2	N/A	N/A
3	8.59	133.3
3a	N/A	118.5
3b	N/A	127.3
4	8.33	123.5
5	7.61	127.5
6	7.46	124.7
7	7.97	129.1
7a	N/A	129.4
8	7.76	127.8
9	7.65	111.9
9a	N/A	138.5

Figure 19: Structural data for KA176. (Left) The proposed structure and number system of compound KA176 (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

the two appears to be buried by the 2-D signal between the position 7 hydrogen and position 5 carbon (Fig.18). The hydrogen with a chemical shift of 7.76 ppm was thus assigned to position 8. Over one bond the position 8 hydrogen couples to the carbon with a chemical shift of 127.8 ppm, which was then assigned as the position 8 carbon (Fig.14). The remaining carbon signal shows no coupling over one or three bonds, but was assigned to position 9a, because it was the only position unaccounted for. The complete position assignments can be seen in Fig.19.

4.2 KA178

Via the crude GC/MS spectrum **compound KA178** was produced in 95% yield from Phenylhydrazine and 2-Hydroxy-1-naphthaldehyde (appendix B). **Compound KA178** MP was 160.5-161.6°C (± 0.9°C). The molecular formula ($C_{17}N_2H_{12}$) was verified using high performance mass spectrometry (appendix B). The predicted structure is seen in Fig.20. One and two-dimensional NMR spectroscopy were utilized to further evaluate the compound.

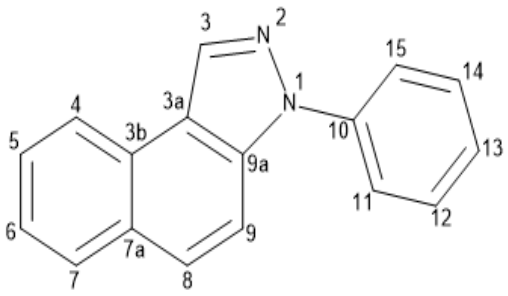


Figure 20:The predicted structure for compound KA178 and its numbering assignments.

Twelve peaks were observed in the ^{1}H-NMR spectrum (Fig.21). Eight of the eleven peaks were attributed to the compound of interest, while the remaining four peaks were attributed solvent contamination. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.95 ppm and 8.30 ppm, and were assigned a relative integration of one. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 7.43 ppm, 7.52 ppm, 7.59 ppm, and 7.67 ppm. All triplets were integrated to one except for the triplet signal with a chemical shift of 7.59 ppm which was integrated to two. The ^{1}H signal, with a multiplicity of one (singlet), had chemical a shift of 8.63 ppm and was integrated to one. The remaining ^{1}H signal at a chemical shift of 7.78 ppm was a multiplet with an integration of four. The integration results were consistent with the what was expected from the predicted structure in fig.20.

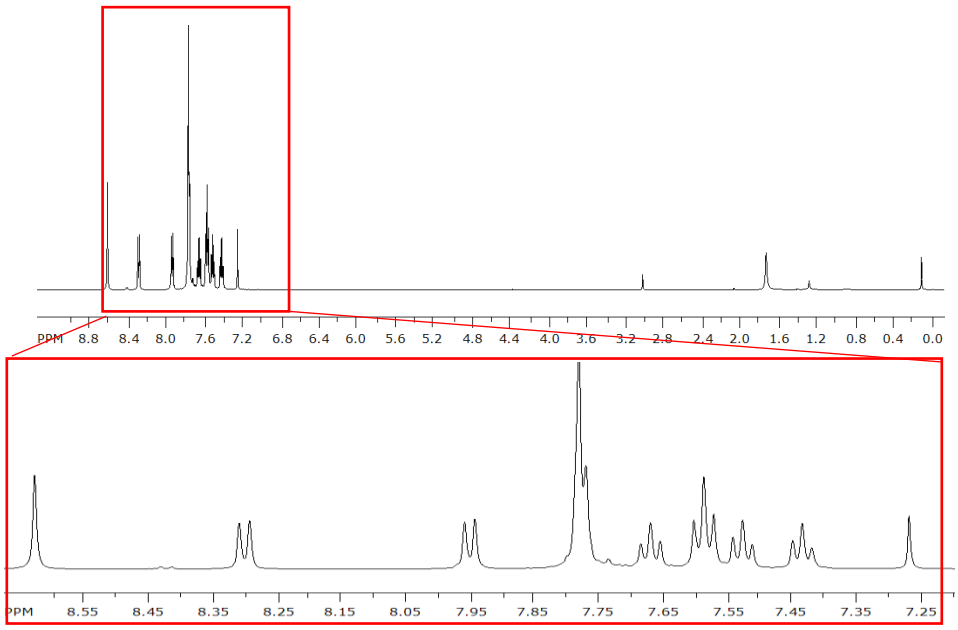


Figure 21: (Top) The full ^{1}H-NMR spectrum for compound KA178. There are eight hydrogen signals originating from compound KA178, as well as, 4 solvent peaks. The peaks of interest include 7.43 ppm (triplet), 7.52 ppm (triplet), 7.59 ppm (triplet), 7.67 ppm (triplet), 7.78 ppm (multiplet), 7.95 ppm (doublet), 8.30 ppm (doublet), and 8.63 ppm (Bottom) The magnified aromatic region of the spectrum with observable multiplicities.

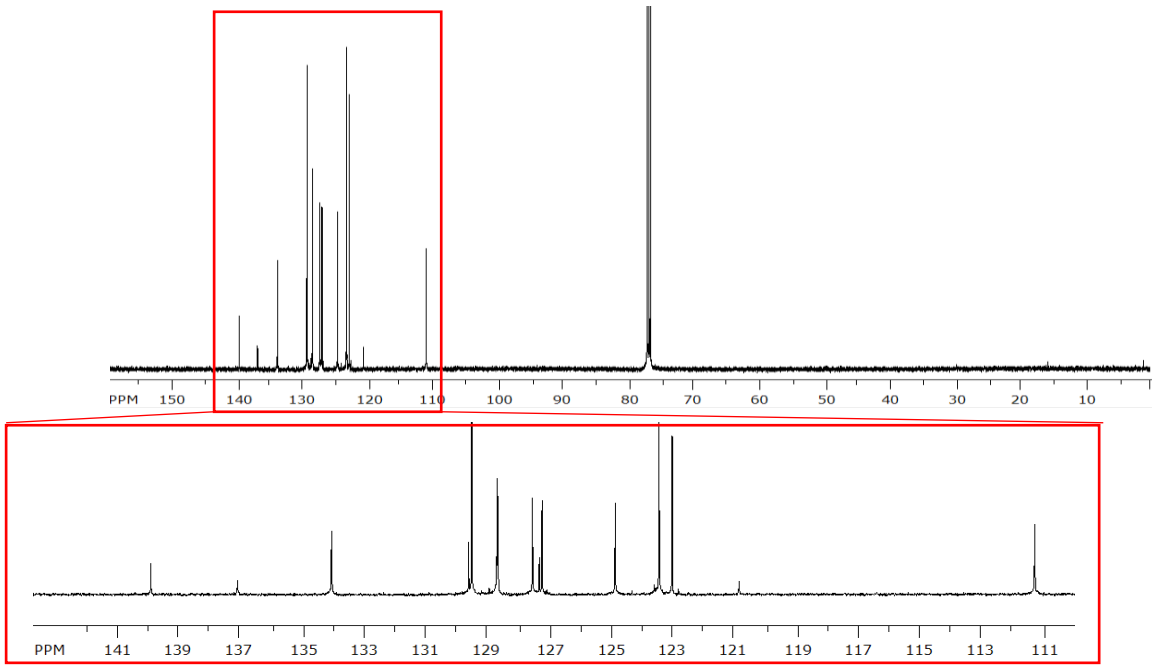


Figure 22: (Top) The full ^{13}C-NMR spectrum for compound KA178. There are 15 carbon signals originating from compound KA178, as well as, one signal corresponding to a solvent peak. The peaks of interest include 111.2 ppm, 120.8 ppm, 123.0 ppm, 123.4 ppm, 124.9 ppm, 127.2 ppm, 127.3 ppm, 127.6 ppm, 128.7 ppm, 128.7 ppm, 129.5 ppm, 129.6 ppm, 134.1 ppm, 137.1 ppm, and 140.0 ppm. (Bottom) The magnified aromatic region of the spectrum.

The ^{13}C -NMR had 15 unique carbon signals all within the aromatic region (Fig.22). Within the ^{13}C -NMR two carbon signals were rounded to the same chemical shift of 128.7 ppm. ^{1}H and ^{13}C chemical shifts were correlated via gHSQC and gHMBC spectra.

The singlet hydrogen signal with a chemical shift of 8.63 ppm coupled over one bond the carbon signal with a chemical shift of 134.1 ppm (Fig.23). Over three bonds, the singlet hydrogen signal coupled to the carbon signals with chemical shifts of 120.8 ppm and 137.1 ppm (Fig.24). Over three bonds the carbon signal with a chemical shift of 120.8 ppm coupled to the doublet hydrogen signal with a chemical shift of 8.30 ppm (Fig.24). With a sufficiently lowered threshold, coupling over three bonds can be observed between the carbon with a chemical shift of 120.8 ppm and the hydrogen signal with a chemical shift of 7.78 ppm (Fig.25). Over three bonds the carbon with a chemical shift of 137.1 ppm coupled to the multiplet hydrogen signal with a chemical shift of 7.78 ppm (Fig.24). Over

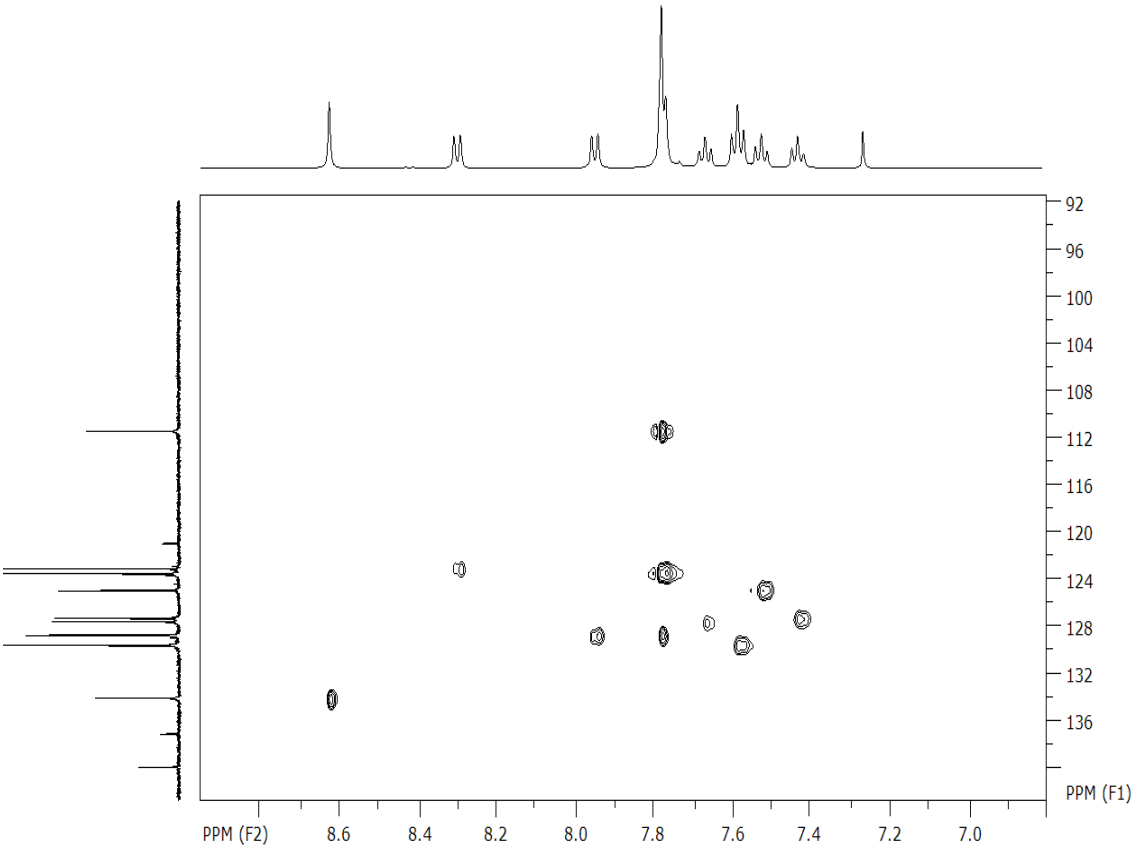


Figure 23: The gHSQC for KA178. Where 2-D signals are present coupling over one bond occurs between hydrogens and carbons. There are eight signals of relevance with hydrogen signals, with chemical shifts of 7.43 ppm, 7.52 ppm, 7.59 ppm, 7.67 ppm, 7.78 ppm, 7.95 ppm, 8.30 ppm, and 8.63 ppm coupling to the carbon signals with chemical shifts of 127.2 ppm, 124.9 ppm, 129.5 ppm, 127.6 ppm, 111.2 ppm, 123.4 ppm, 129.6 ppm, 128.7 ppm, 123.0 ppm, and 134.1 ppm.

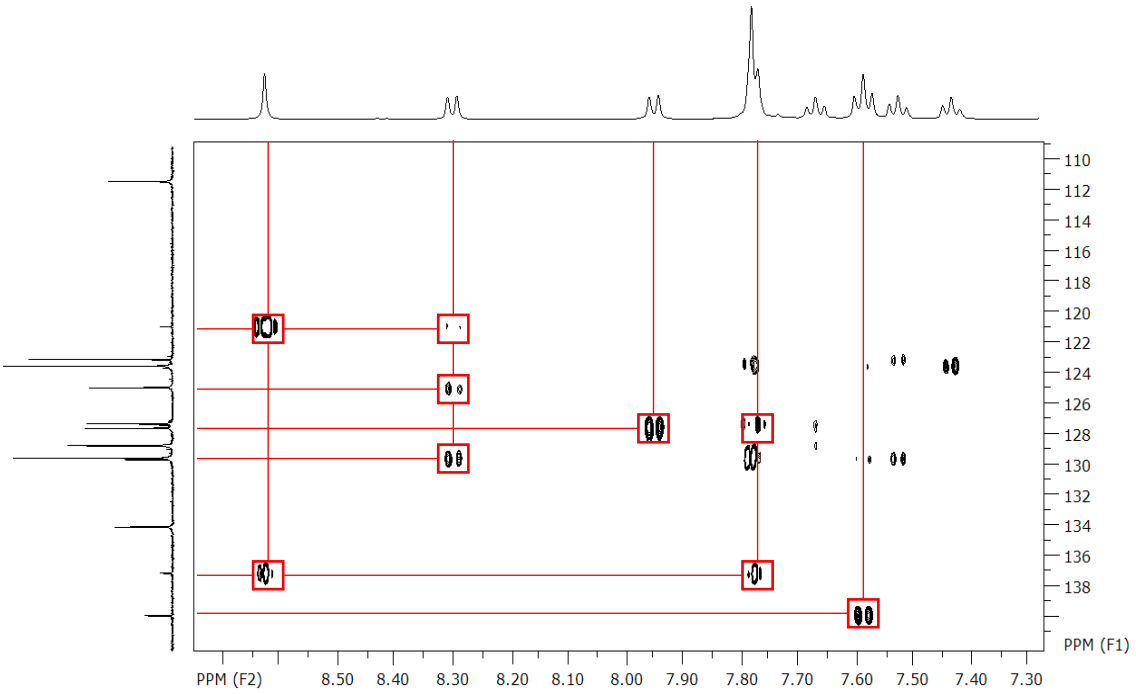


Figure 24: The aromatic region of the gHMBC spectra for compound KA178. Where the horizontal and vertical lines intersect with a box shows the coupling patterns under consideration. Coupling occurs over three bonds between carbon and hydrogen signals. The hydrogen signal with chemical shifts the chemical shift of 7.59 ppm couples to the carbon signals with chemical shifts of 140.0 ppm. The hydrogen signal with a chemical shift of 7.78 ppm couples to the carbon signals with chemical shifts of 127.3 ppm and 137.1 ppm. The hydrogen signals with a chemical shift of 7.95 ppm couples to the hydrogen signal with a chemical shift of 127.3 ppm the hydrogen with a chemical shift of 8.30 ppm couples to the carbon signals with chemical shifts of 120.8 ppm, 124.9 ppm, and 129.6 ppm. The hydrogen with a chemical shift of 8.63 ppm couples to the carbon signals with chemical shifts of 120.8 ppm and 137.1 ppm.

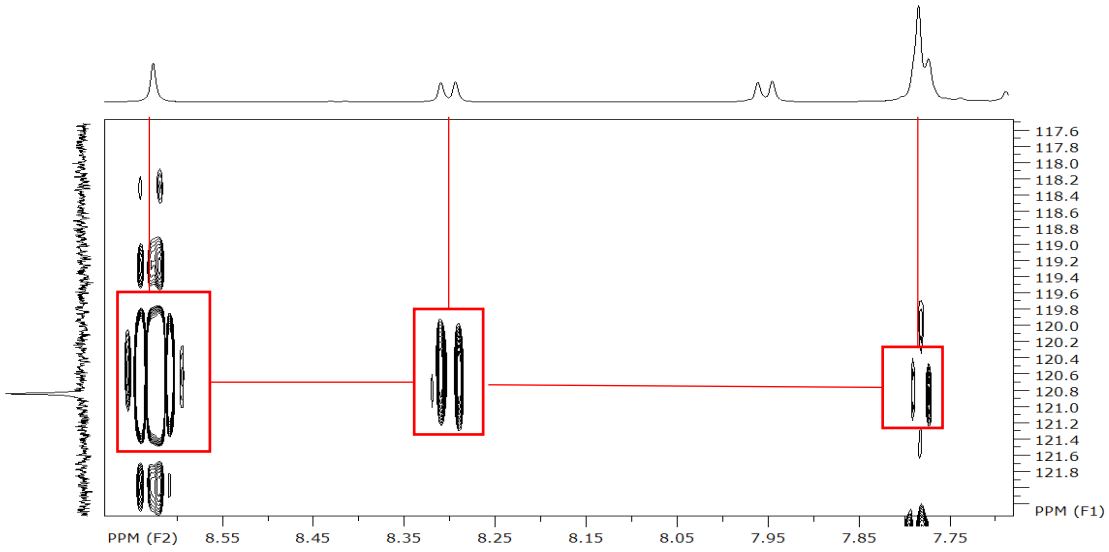


Figure 25*:* A magnified portion of the aromatic region of the gHMBC spectra for compound KA178. Where the horizontal and vertical lines intersect with a box shows the coupling patterns under consideration. Coupling occurs over three bonds between carbon and hydrogen signals. The carbon signal with a chemical shift of 120.8 ppm couples to the hydrogen signals with chemical shifts of 7.78 ppm, 8.30 ppm, and 8.63 ppm

one bond, the hydrogen signal with a chemical shift of 7.78 ppm coupled to the carbon signals with a chemical shift of 111.2 ppm, 123.4 ppm, and 129.6 ppm (Fig.23); This indicated that the multiplet signal was indeed comprised of three different hydrogen signals, which accounted for the three missing hydrogen signals predicted from the structure in fig.20. The doublet hydrogen signal with a chemical shift of 8.30 ppm coupled over one bond to the carbon signal with a chemical shift of 123.0 ppm (Fig.23).

Over three bonds, the hydrogen with a chemical shift of 8.30 ppm coupled to the carbon signals with chemical shifts of 124.9 ppm and 129.6 ppm (Fig.26). Over one bond the carbon with a chemical shift of 124.9 coupled to the triplet hydrogen signal with a chemical shift of 7.52 ppm (Fig.23). The carbon signal with a chemical shift of 129.6 ppm coupled over one bond to the hydrogen signal with a chemical shift of 7.79 ppm (Fig.23).

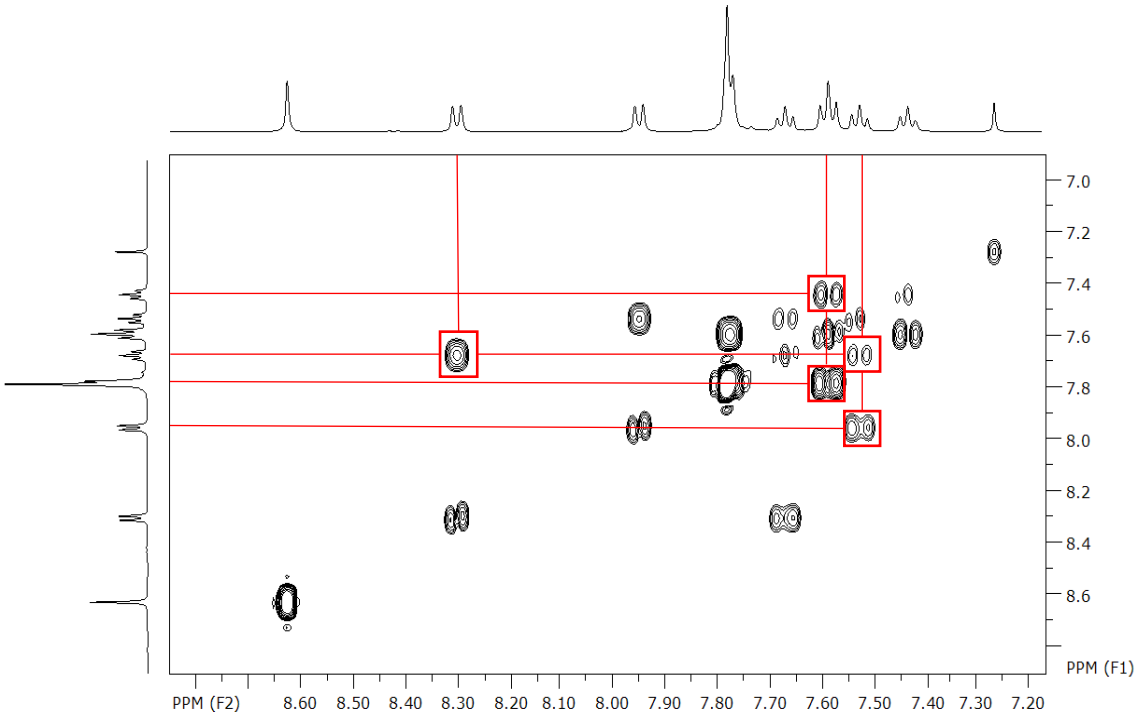


Figure 26: The magnified region of the gCOSY spectra for compound KA178. Where the horizontal and vertical lines intersect with a box shows the coupling patterns under consideration. Coupling occurs between hydrogens within three bonds of each other. The hydrogen signals show interaction with themselves and irrelavent. The hydrogen signal with a chemical shift of 7.52 ppm couples to the hydrogen signals with chemical shifts of 7.67 ppm and 7.95 ppm. The hydrogen signal with a chemical shift of 7.59 ppm couples to the hydrogen signals with chemical shifts of 7.43 ppm and 7.78 ppm. The hydrogen signal with a chemical shift of 8.30 ppm couples to the hydrogen signal with a chemical shift of 7.67 ppm.

Based on the coupling pattern the carbons with chemical shifts of 120.8 ppm, 137.1 ppm, 123.0 ppm, 124.9 ppm, and 129.6 ppm were assigned to positions 3b, 9, 7, 5, and 8. Over three bonds the position 5 hydrogen coupled to the hydrogen signals with chemical shift of 7.67 ppm and 7.95 ppm (Fig.26). The position 7 hydrogen signal coupled over three bonds to the hydrogen signal with a chemical shift of 7.67 ppm (Fig.24). The hydrogen signal

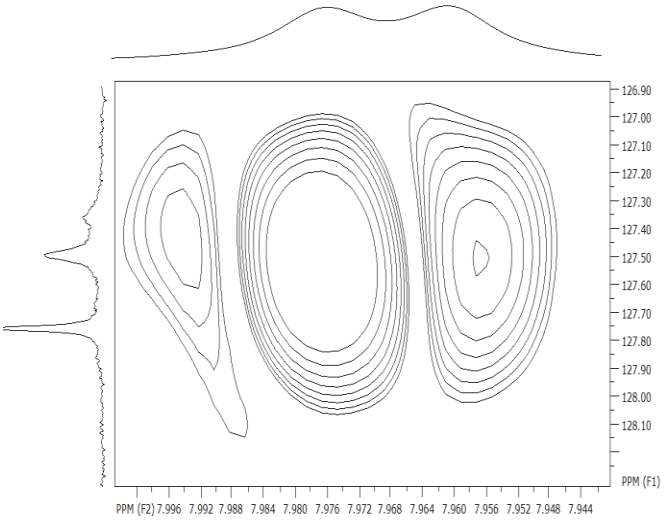


Figure 27: A magnified signal within the gHMBC spectra showing the distortion in a 2-D signal between the hydrogen signal with a chemical shift of 7.95 ppm and carbon with a chemical shift of 127.3 ppm.

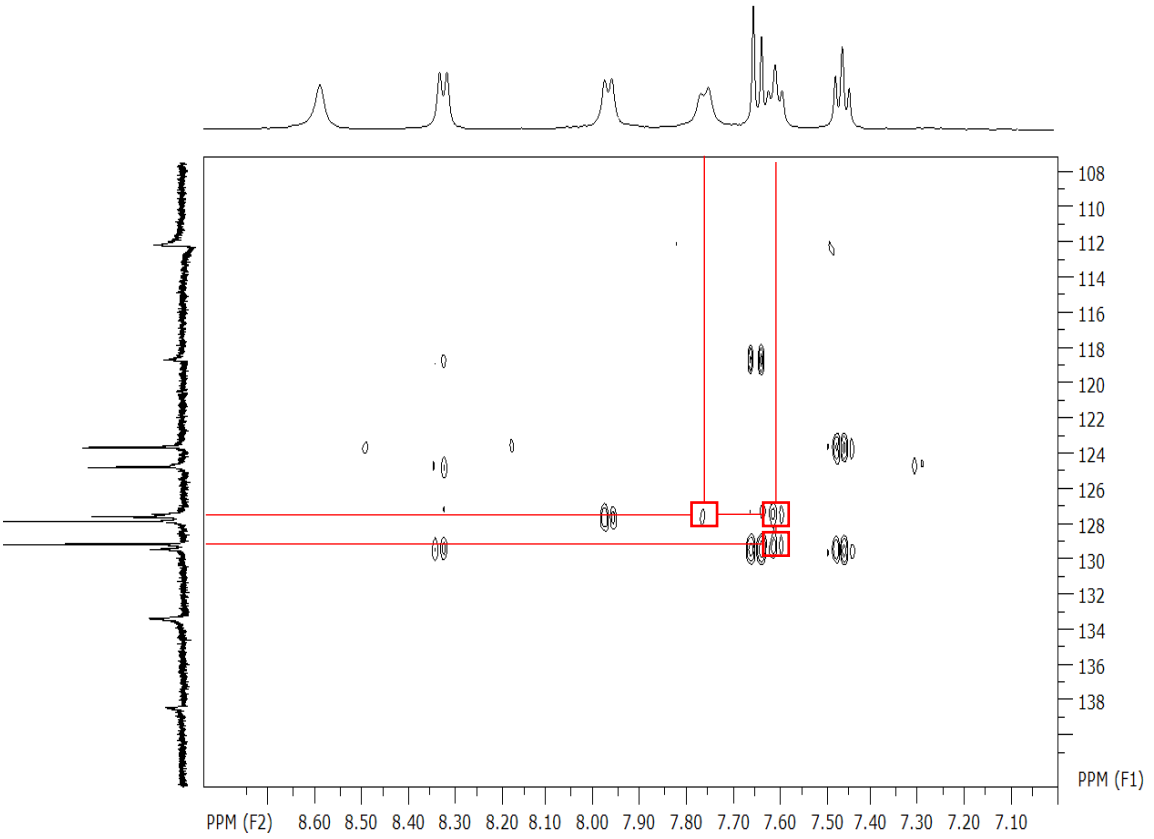
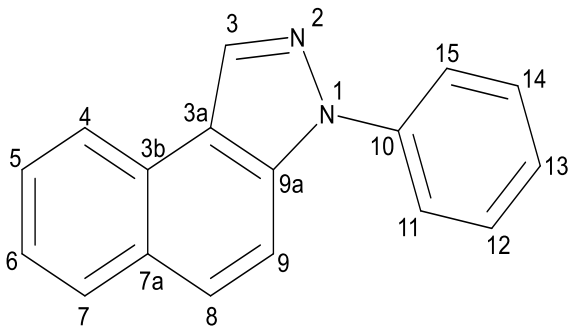


Figure 28: The aromatic region of the gHMBC spectra for compound KA178 Where the horizontal and vertical lines intersect with a box shows coupling over three bonds. The hydrogen signal at a chemical shift of 7.59 ppm couples to the carbons with chemical shifts of 128.7 ppm and 127.3 ppm. The hydrogen with a chemical shift of 7.95 ppm couples to the carbon with a chemical shift of 127.3 ppm

with a chemical shift of 7.67 ppm coupled over one bond to the carbon with a chemical shift of 127.6 ppm, and the two signals were assigned to position 6 (Fig.23). The hydrogen signal with a chemical shift of 7.95 ppm coupled over one bond to the carbon signal with a chemical shift of 128.7 ppm and both signals were assigned to position 4 (Fig,23).

Over three bonds the position 4 hydrogen signal coupled to the carbon signal with a chemical shift of 127.3 ppm (Fig.27&28). Over three bonds the position 6 hydrogen signal coupled to the carbon signal with a chemical shift of 127.3 ppm (Fig.227&28). The carbon with a chemical shift of 127.3 ppm coupled to no hydrogens over one bond and was assigned to position 7a. Over three bonds the position 7a carbon signal coupled to the hydrogen multiplet signal with a chemical shift of 7.78 ppm (Fig.24). The multiplet signal was assigned to position 9. Of the two carbon signals coupling to the position 9 hydrogen over only the carbon signal with a chemical shift of 111.2 ppm coupled to no hydrogens over three bonds and thus was assigned to position 9.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	8.63	134.1
3a	N/A	118.4
3b	120.8	N/A
4	7.95	128.7
5	7.7	124.9
6	7.67	127.6
7	8.04	123
7a	N/A	127.3
8	N/A	129.6
9	7.78	111.2
9a	N/A	140.3
10	N/A	140
11	7.43	123.4
12	7.59	129.5
13	7.43	127.2

Figure 29: Structural data for KA178. (Left) The proposed structure and number system of compound KA178. (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

The triplet signal with a chemical shift of 7.59 was assigned to position 12 and 14 (12/14) because these were the hydrogens with multiplicities of three. Over one bond the position 12/14 hydrogen coupled to the carbon signal with a chemical shift of 129.5 ppm (Fig.23). Thus, the carbon signal with a chemical shift of 129.5 was assigned to position 12/14. Over three bonds, the position 12/14 hydrogen coupled to the carbon with a chemical shift of 140.0 ppm, which was then assigned to position 10 (Fig.24).

Over three bonds the position 12/14 hydrogen coupled to the hydrogen signals with chemical shifts of 7.43 ppm and 7.78ppm (Fig.28). The hydrogen with a chemical shift of 7.43 ppm coupled over one bond to the carbon signal with a chemical shift of 127.2 ppm (Fig.23). From the structure, the only remaining triplet signal would be derived from position 11 and thus the carbon and hydrogen with chemical shifts of 127.2 ppm and 7.43 ppm were assigned to position 13. The multiplet signal and its remaining carbon signal, with a chemical shift of 123.4 ppm, were assigned to position 11. The second carbon signal with a chemical shift of 128.7 ppm was then assigned to position 3a, because it was the only signal to remain unassigned. The complete position assignments can be seen in Fig.29.

4.3 KA169

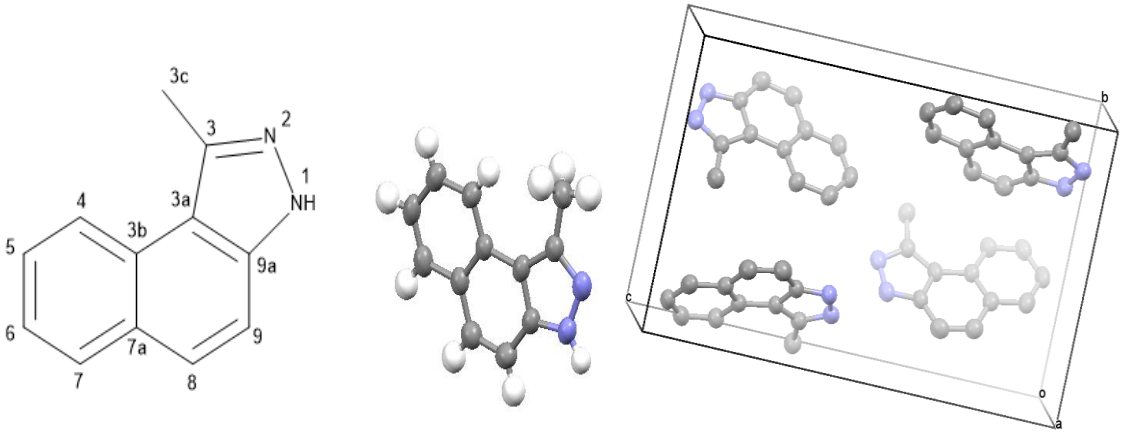


Figure 30: X-ray crystal structure and packing scheme of KA169. Grey, blue, and white ellipsoids are representative of carbon, nitrogen, and hydrogen respectively. (Left) Position numbering and line structure of KA169. (Middle) The crystal solution for the individual molecule. (Right) The packing scheme of KA169 unit cell with denotation of cell lengths a, b, and c (hydrogen solutions are removed for ease of viewing).

Via the crude GC/MS and crude NMR spectrum KA169 was produced in 90.7% yield from 2-napthyl-hydrazine hydrochloride and 1-acetyl-2-napthol (appendix C).

KA169 melting point range (MP) was 180.2-185.4°C (± 3.0°C). As KA169 melted its color profile changed from a white solid to a dark brown. The compound was originally identified using x-ray crystallography. The x-ray structure is represented in Fig.30. The cell lengths and angles were as follows; a = 5.204, b = 10.664, c =16.671, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$. KA169 was shown to pack in an orthorhombic cell with a $P2_12_12_1$ space group packing scheme (Fig.30).

The R, R_w, and GOOF, of the crystal solution, were 0.045, 0.123, and 1.10 respectively. No serious errors were found with the crystal structure. The molecular formula ($C_{12}N_2H_{10}$) was verified using high performance mass spectrometry (appendix C). One and two-dimensional NMR spectroscopy were utilized to further evaluate the compound; in comparison to the x-ray crystal structure the number, multiplicity, and region of the major peaks matched what was theoretically expected in the ^{1}H-NMR. All spectra were run with a sample that was 91% pure by the ^{1}H-NMR.

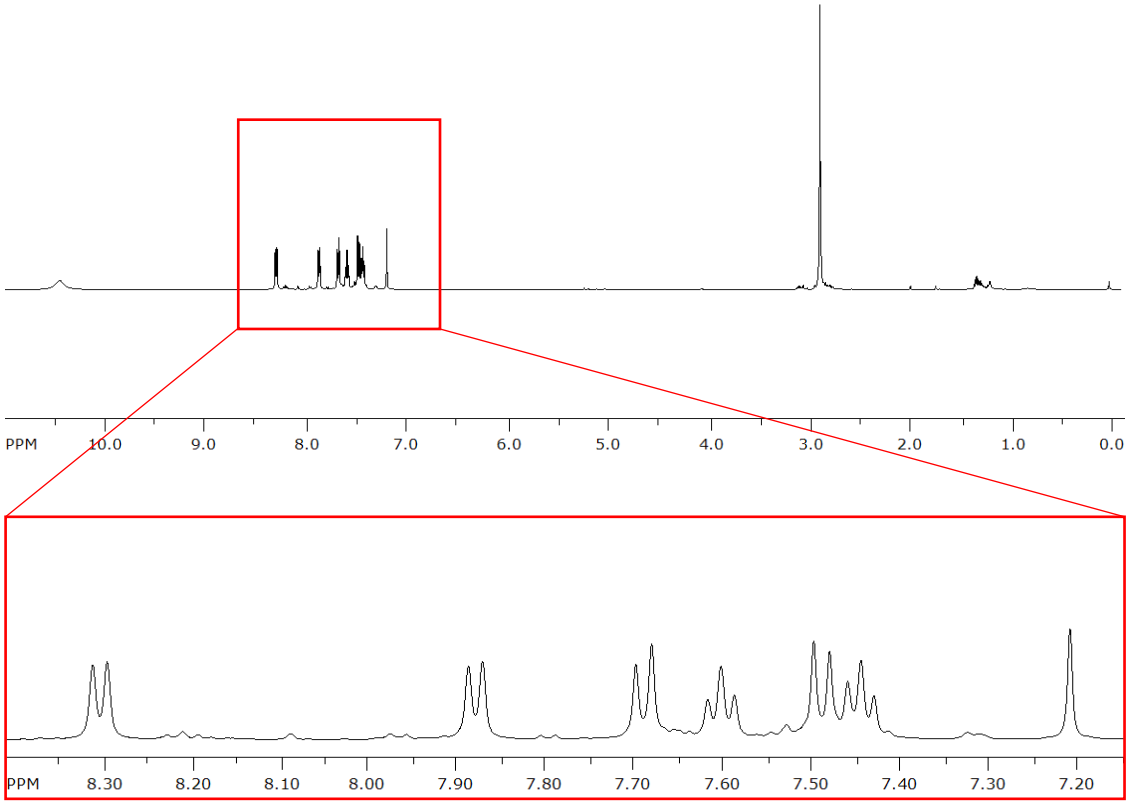


Figure 31: The ^{1}HNMR spectrum for KA169. (Top) The full ^{1}H-NMR spectrum for KA169. There are eight hydrogen signals originating from compound. The peaks of interest include 2.89 ppm (singlet), 7.44 ppm (triplet), 7.49 ppm (doublet), 7.60 ppm (triplet), 7.69 ppm (doublet), 7.88 ppm (doublet), 8.31 ppm (doublet), 7.89 ppm (doublet), 10.47 ppm (singlet). The 7.22 ppm singlet originates from solvent chloroform (Bottom) The magnified aromatic region of the spectrum with observable multiplicities.

Nine peaks were observed in the ^{1}H-NMR spectrum (Fig.31). Eight of the nine peaks were attributed to the compound of interest, while the remaining major peak was indicative of solvent chloroform. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.49 ppm, 7.60 ppm, 7.69 ppm, and 8.31 ppm, and were assigned a relative integration of one. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 7.44 ppm and 7.60 ppm and were integrated to one. The ^{1}H signals, with multiplicities of one (singlet), had chemical shifts of 2.89 ppm and 10.47 ppm. The 2.89 ppm singlet was integrated to three and the 10.47 ppm singlet was integrated to one. The experimental ^{1}H signals are congruent with the expected signals in respect to the number, multiplicity, and integration of the signals predicted from the crystal structure (Fig.30). The ^{13}C -NMR had 12 unique carbon signals: 11 in the aromatic region and one in the alkyl

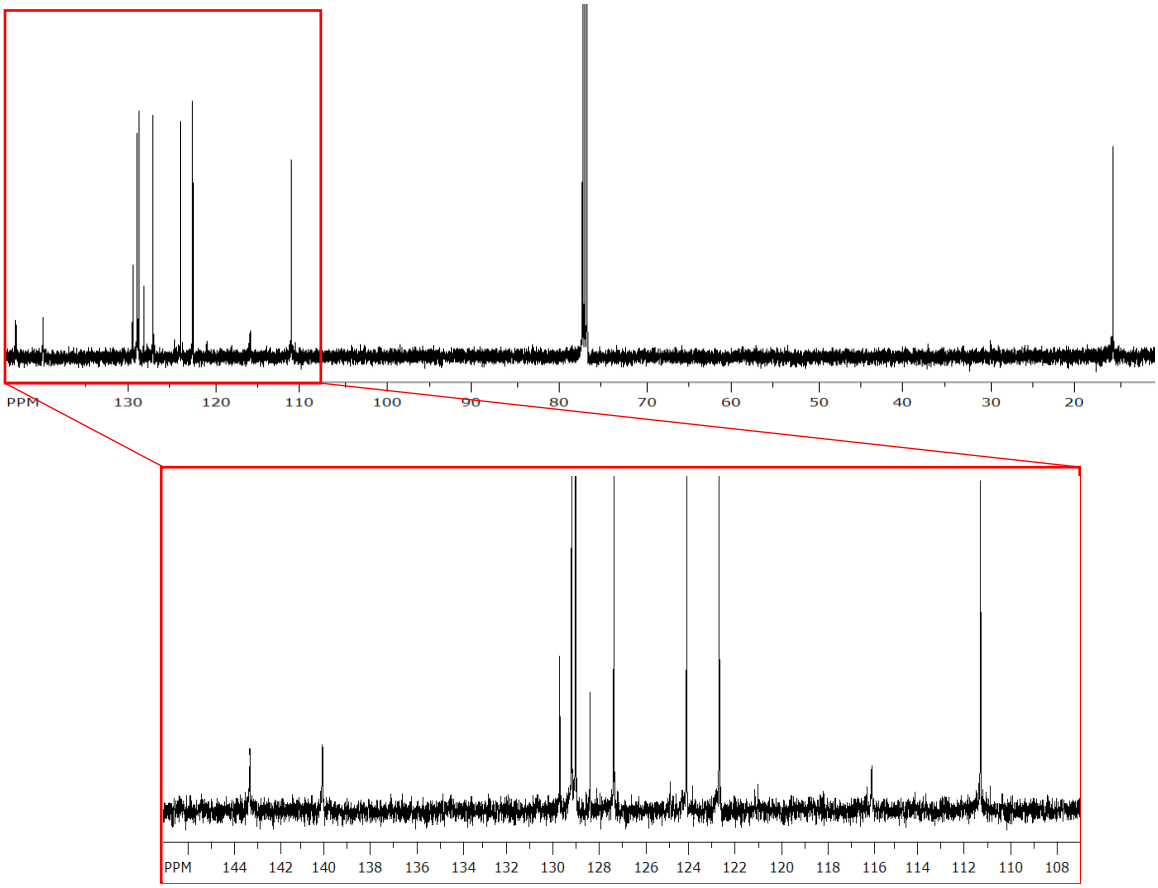


Figure 32: The ^{13}CNMR for KA169. (Top) The full ^{13}C-NMR spectrum for KA169. There are 12 carbons originating from KA169, as well as, one signal corresponding to a solvent peak. The compound peaks include 15.6 ppm, 111.4 ppm, 116.2 ppm, 122.9 ppm, 124.3 ppm, 127.5 ppm, 128.5 ppm, 129.0 ppm, 129.2 ppm, 129.7 ppm, 140.2 ppm, and 143.4 ppm. (Bottom) The magnified aromatic region of the spectrum.

region. Several of the ^{13}C signals lacked intensity and the signal with a chemical shift of 116.2 ppm is near the baseline (Fig.32). The compound was difficult to purify and only 10 mg was isolated.

^{1}H and ^{13}C chemical shifts were correlated via HSQC, HMBC, and gCOSY. The HSQC showed that the alkyl hydrogens, at a chemical shift of 2.89 ppm, and the alkyl carbon, at a chemical shift of 15.6 ppm, coupled over one bond to each other (Fig.33). The alkyl hydrogens and the alkyl carbon were assigned to position 3c in Fig.30. Over three bonds the position 3c carbon did not couple to any hydrogens, but the position 3c

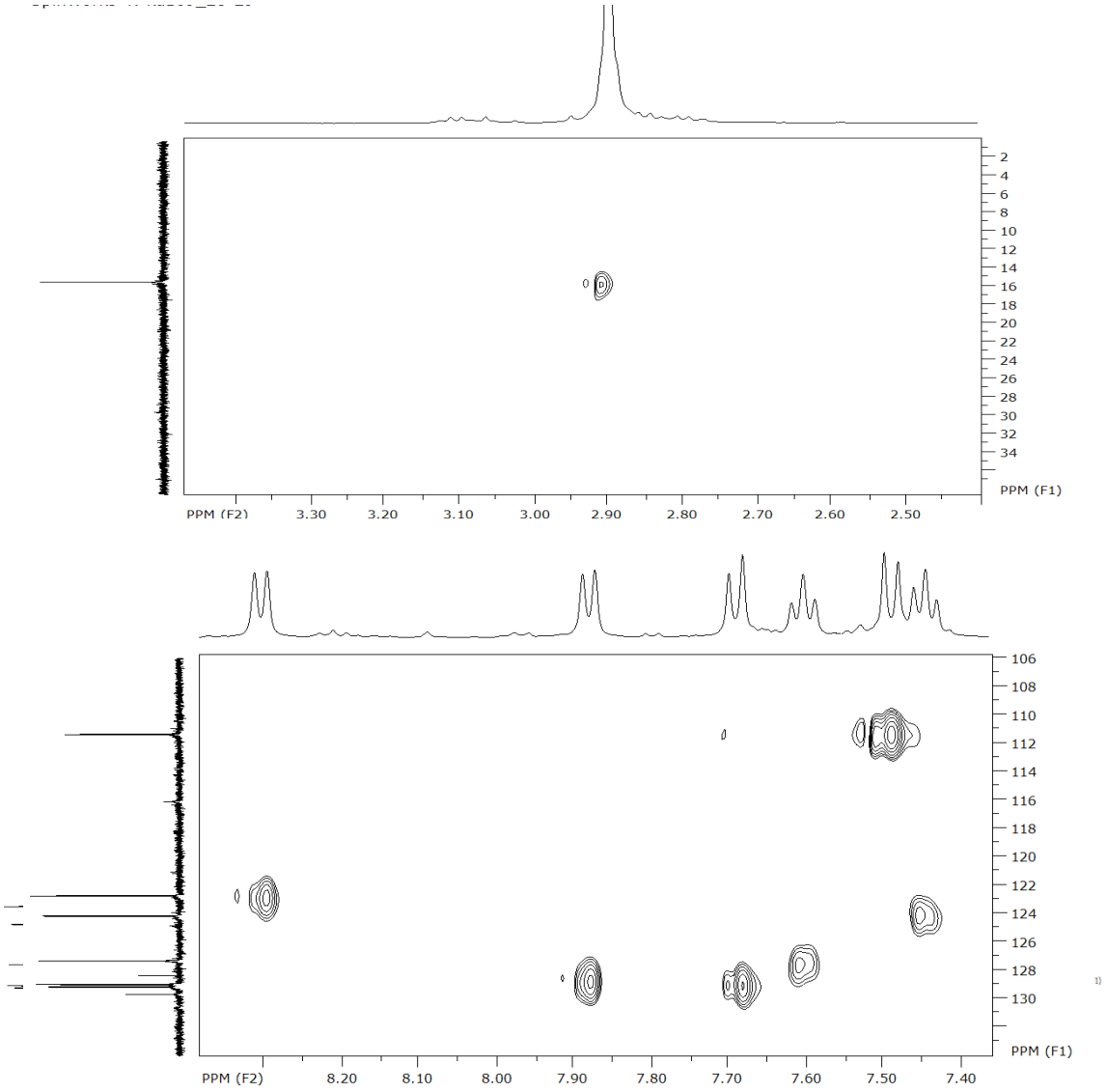


Figure 33: The HSQC for KA169. (Top) The magnified alkyl region). (Bottom) The magnified aromatic region. Coupling over one bond can be seen between hydrogens (x-axis) and carbons (y-axis).

hydrogens coupled to two different carbons (Fig.34). It was not expected for the position 3c hydrogens to couple to two different carbons over three bonds, based on the crystal structure. However, this observation is explained by hydrogen to carbon coupling over two bonds: if coupling over two bonds occurred then the crystal structure does not deviate from the HMBC. The position 3 carbon did not couple to any other hydrogens over two or three bonds (Fig.34). In addition, the carbon coupling over three bonds to the position 3c hydrogens, represented as carbon 3a in fig.30 would couple to the two hydrogen doublet signals at chemical shifts of 7.49 ppm and 8.31 ppm (Fig.34). Based on the gHMBC the previous statements were verified and carbons 3 and 3a were confirmed to be the carbon signals with chemical shifts 143.5 ppm and 116.2 ppm respectively.

Over one bond, the hydrogen signals with chemicals shifts of 7.49 ppm and 8.31 ppm were coupled to the carbon signals with chemical shifts of 111.4 ppm and 122.9 ppm respectively (Fig.35). The 7.49 ppm and 111.4 ppm hydrogen and carbon were assigned to position 9. The 8.31 ppm hydrogen and 122.9 ppm carbon were assigned to position 4. Over three bonds, the carbon at position 4 coupled to the hydrogen triplet signal at a

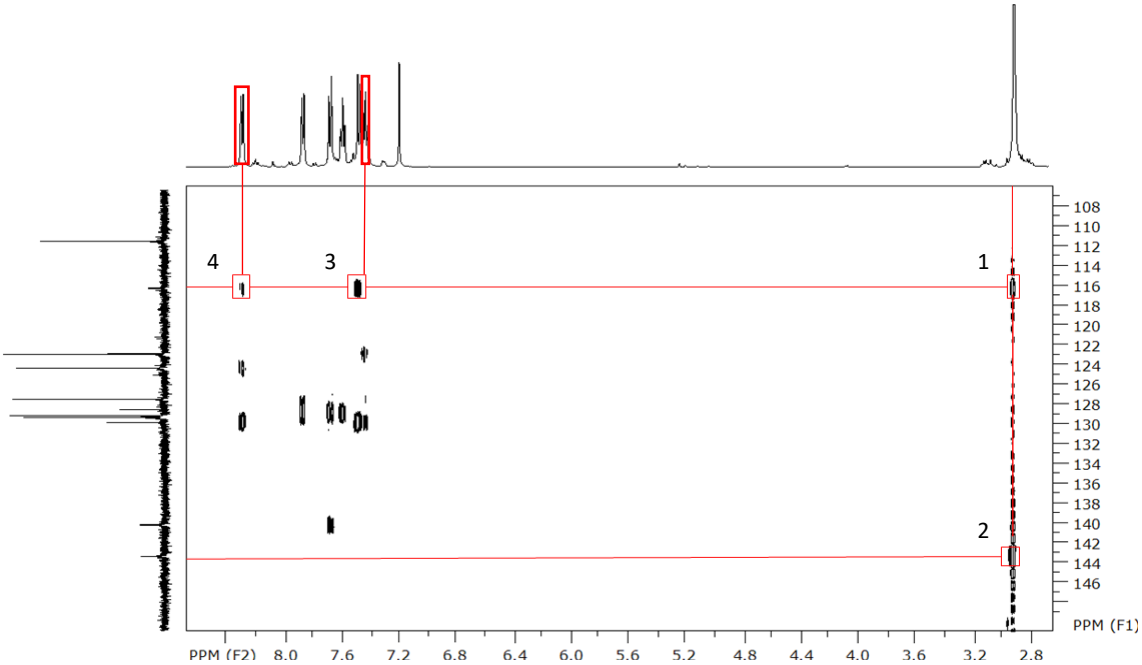


Figure 34: The gHMBC for KA169. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with and chemical shift of 2.88 ppm and the carbons at 116.2 ppm and 143.4 ppm respectively. The horizontal lines intersect other hydrogens that the carbons couple to over three bonds. Boxes 3 and 4 represent carbon/hydrogen coupling over three bonds between the carbon with a chemical shift of 116.2 ppm and the doublet hydrogens with chemical shifts of 7.49 ppm and 8.31 ppm respectively.

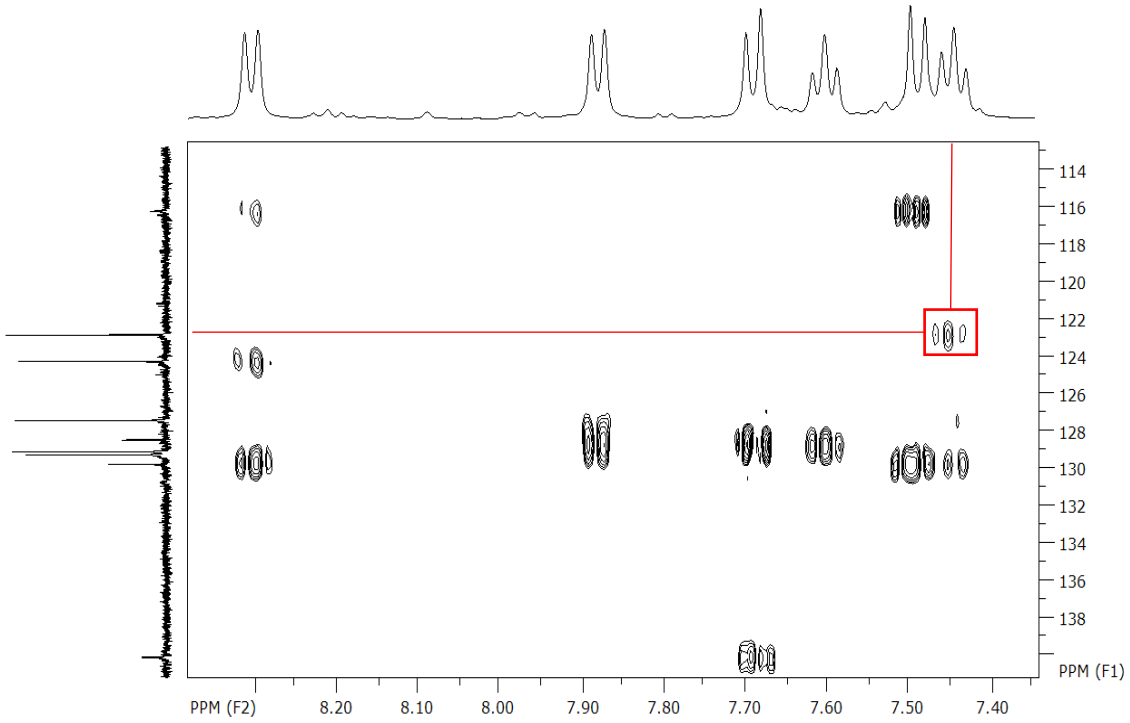


Figure 35: Aromatic region of the gHMBC spectra. The outlined signal shows the coupling over three bonds between the triplet signal with a chemical shift of 7.44 ppm and the carbon signal with a chemical shift of 122.9 ppm.

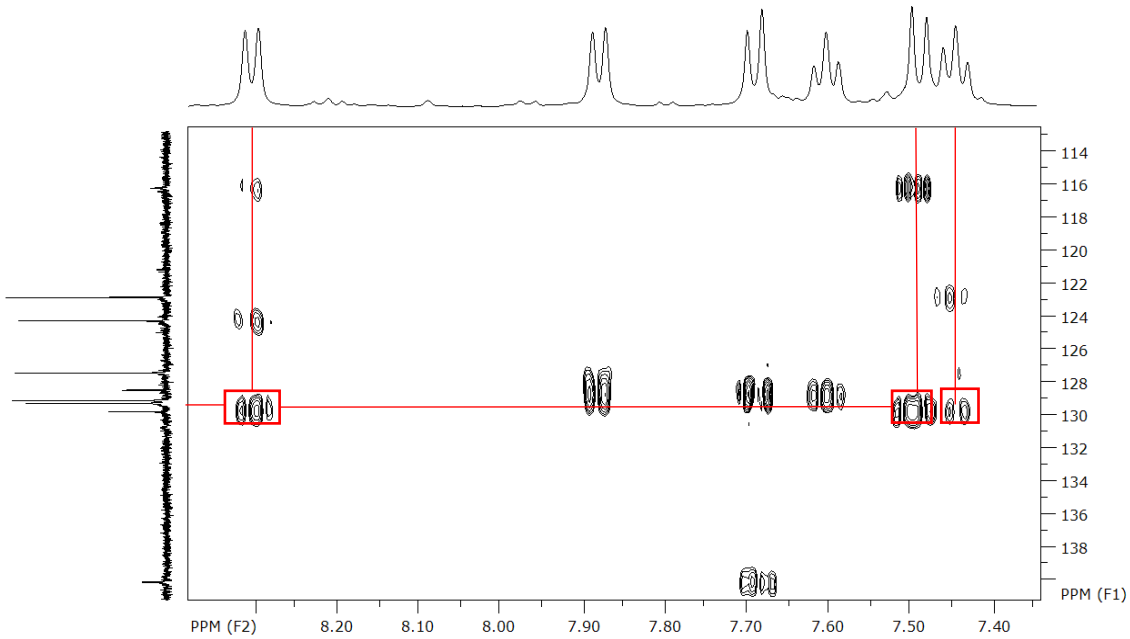


Figure 36: Aromatic region of the gHMBC spectra. The outlined signals show the coupling over three bonds between hydrogen signals at chemical shifts of 7.44 ppm, 7.49 ppm, and 8.31 ppm to the carbon signal with a chemical shift of 129.7 ppm.

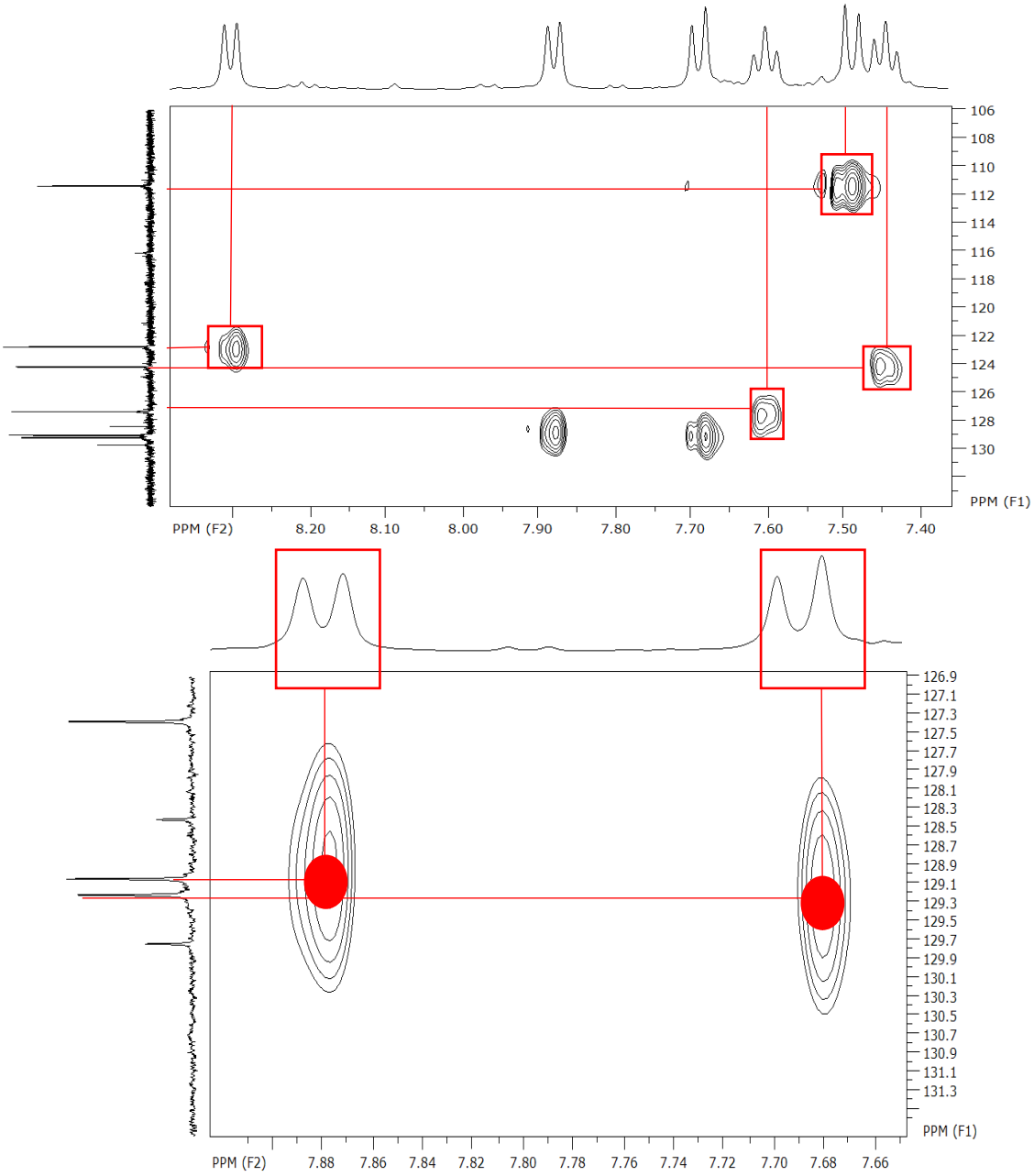


Figure 37: The HSQC for KA169. (Top) The aromatic region of the HSQC. Where the horizontal and vertical lines intersect on a box shows the couple over one bond between a carbon and a hydrogen. (Bottom) Magnified and less intense HSQC spectrum used to distinguish between the carbon hydrogen coupling over one bond for carbon chemical shifts of 129.0 ppm and 129.2 ppm

chemical shift of 7.44 ppm (Fig.36). The triplet signal was then assigned to position 6. The carbon at position 9 should not have coupled to any hydrogens over one or three bonds, and indeed this was observed (Fig.36). The position 4, 6, and 9 hydrogens coupled over three bonds to the carbon signal at a chemical shift 129.9 ppm (Fig.37). Over three bonds

the position 4 hydrogen doublet coupled to a triplet hydrogen signal at a chemical shift of 7.60 ppm (Fig.38). The triplet signal with the chemical shift of 7.60 ppm was assigned to position 5. The 129.9 ppm carbon signal was defined as the carbon at position 7a. Via the HSQC position 5 and 6 carbons are attributed to chemical shifts 127.5 ppm and 124.3 ppm, respectively (Fig.35). The position 5 carbon and position 6 hydrogen couple over three bonds to the hydrogen signal with a chemical shift of 7.88 ppm (Fig.39). Over one bond the hydrogen signal at a chemical shift of 7.88 ppm coupled to the carbon signal at a chemical shift of 129.2 ppm (Fig.35). The position 7 carbon and hydrogen were defined as 129.2 ppm and 7.88 ppm respectively.

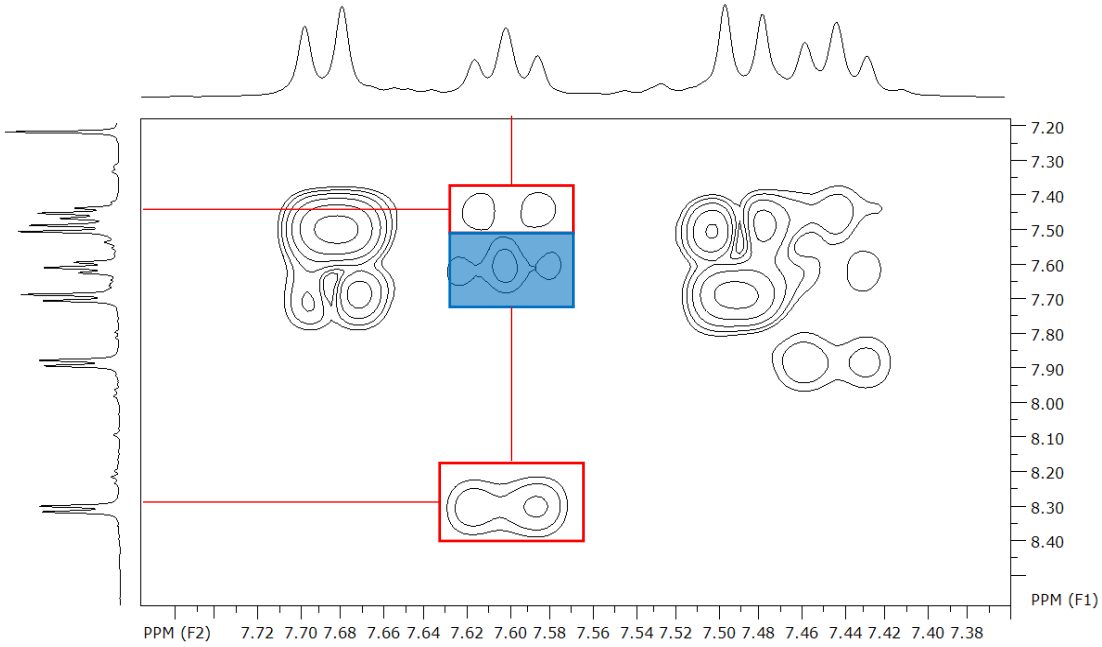


Figure 38: A magnified region of gCOSY spectra. The outlined signals show the coupling over three bonds between the triplet hydrogen signal with a chemical shift of 7.60 ppm and the triplet and doublet signals with chemical shifts of 7.44 ppm 7.88 ppm respectively. The blue highlighted signal is the triplet interacting with itself

Over three bonds, the position 9 hydrogen couples to the position 8 hydrogen doublet signal at a chemical shift of 7.69 ppm (Fig.38). The position 8 hydrogen couples over one bond to the carbon signal at a chemical shift of 129.4 ppm (Fig.35). Over three bonds, the position 5, 7, and 8 hydrogens couple to the carbon signal with a chemical shift of 128.5 ppm (Fig.39). The carbon signal at a chemical shit of 128.5 ppm does not couple

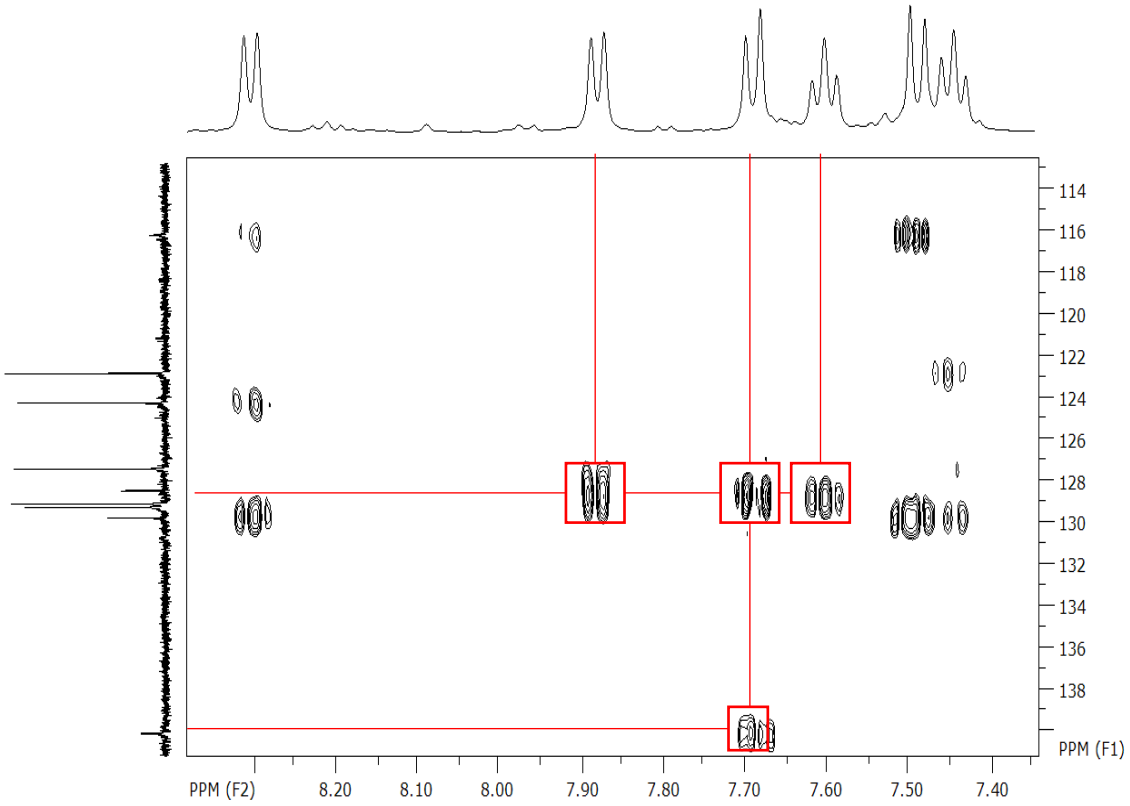
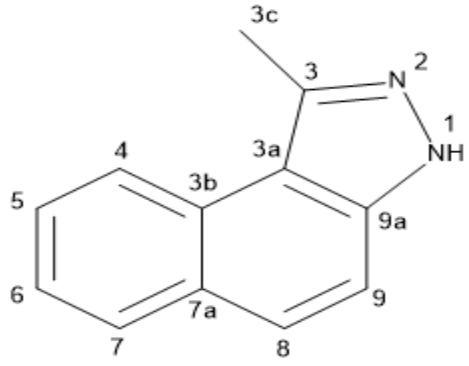


Figure 40: Aromatic region of the gHMBC spectra. The outlined signals show the coupling over three bonds between the hydrogen signals with chemical shifts of 7.88 ppm, 7.69 ppm, and 7.60 ppm with the carbon signal having a chemical shift of 122.9 ppm. The hydrogen signal with a chemical shift of 7.69 ppm couples over three bonds to the carbon signal with a chemical shift of 140.2 ppm.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	10.47	N/A
2	N/A	N/A
3	N/A	144.5
3a	N/A	116.2
3b	N/A	128.5
3c	2.9	15.6
4	8.31	122.9
5	7.6	127.5
6	7.44	124.3
7	7.88	129.2
7a	N/A	129.9
8	7.69	129.4
9	7.49	111.4
9a	N/A	140.3

Figure 39: Structural data for KA169. (Left) The proposed structure and number system of compound KA169. (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

over one bond to any hydrogens, and the signal is assigned to position 3b. The remaining hydrogen signal at a chemical shift of 10.5 ppm was assigned to the position 1 nitrogen and shows no coupling over three bonds. By process of elimination the remaining carbon, with a chemical shift of 140.3 ppm, is assigned position 9a. The assignment is verified by the gHMBC where over three bonds the position 9a carbon couples to the hydrogen doublet signal at position 8 (Fig 37). The complete position assignments can be seen in Fig.40.

4.4 KA173A & B

Via the crude GC/MS spectra, **KA173A** was produced in 41.8% yield and **KA173B** was produced in 34.1% yield from hydrazine monohydrate and 1-acetyl-2-napthol followed by alkylation with iodoethane (appendix C). **KA173A** was a brown solid with a of 62.8-65.8°C (± 0.7°C). The molecular formula for both **KA173A** ($C_{14}H_{14}N_2$) was verified using high performance mass spectrometry (appendix C). **KA173A** and **B** appear to be isomers as they have different elutions in the GC/MS spectr,a but the same molecular weights. The predicted structure is seen in Fig.41. One and two-dimensional NMR spectroscopy were utilized to further evaluate the compounds.

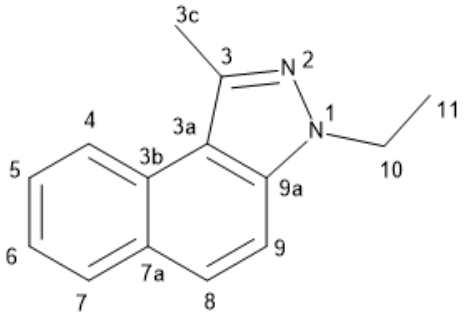


Figure 41*:* The predicted structure for compound KA173A and its numbering assignments.

4.4.1 KA173A

Ten peaks were observed in the ^{1}H-NMR spectrum (Fig.42). Nine of the 10 peaks were attributed to the compound of interest, while the remaining peak was indicative of solvent chloroform. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.44 ppm, 7.71 ppm, 7.93 ppm, and 8.35 ppm, and were assigned a relative integration of one. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 1.54 ppm, 7.47 ppm, and 7.64 ppm and were integrated to three, one, and one respectively. The ^{1}H signal, with a multiplicity of four (quartet), had a chemical shift of 4.46 ppm and was

integrated to two. The ^{1}H signal, with a multiplicity of one (singlet), had a chemical shift of 2.91 ppm and was integrated to three.

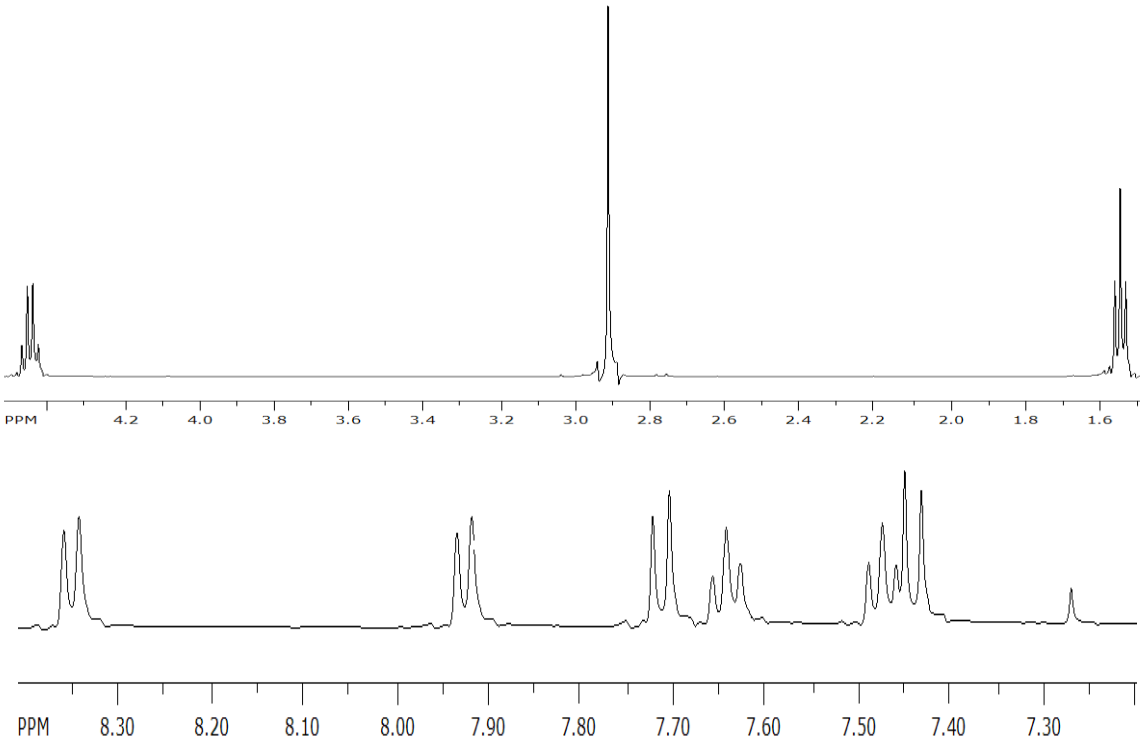


Figure 42: The ^{1}HNMR for KA173A. There are nine hydrogen signals originating from KA173A, as well as, one signal corresponding to a solvent peak. The peaks of interest include 1.54 (triplet), 2.91 ppm (singlet), 4.46 ppm (quartet), 7.44 ppm (doublet), 7.47 ppm (triplet), 7.64 ppm (triplet), 7.71 ppm (doublet), 7.93 ppm (doublet), and 8.35 ppm (doublet). (Top) The magnified alkyl region of the spectrum. (Bottom) The magnified aromatic region of the spectrum.

The experimental ^{1}H signals are congruent with the expected signals in respect to the number, multiplicity, and integration of signals predicted from the predicted structure (Fig.42). The ^{13}C -NMR had 14 unique carbon signals: 11 in the aromatic region and three in the alkyl region (Fig.43). ^{1}H and ^{13}C chemical shifts were correlated via gHSQC and gHMBC. The gHSQC showed that the alkyl hydrogen signals, at a chemical shift of 1.54 ppm, 2.91 ppm, and 4.46 ppm, coupled over one bond to the alkyl carbons at chemical shifts of 15.5 ppm, 15.4 ppm, and 43.6 ppm respectively (Fig.44). In agreement with the proposed structure the hydrogen signals at chemical shifts of 1.54 ppm and 4.46 ppm showed splitting patterns indicative of a triplet and quartet with integrations of three and two respectively. The hydrogen signal at a chemical shift of 2.91 ppm is indicative of an isolated methyl group with no hydrogens within three bonds (Fig.43). The alkyl hydrogen

signals with chemical shifts of 1.54 ppm, 2.91 ppm, and 4.46 ppm and their corresponding carbons at chemical shifts of 15.5 ppm, 15.4 ppm, and 43.6 ppm were assigned to positions 11, 3c, and 10 of Fig.41 respectively (Fig.45).

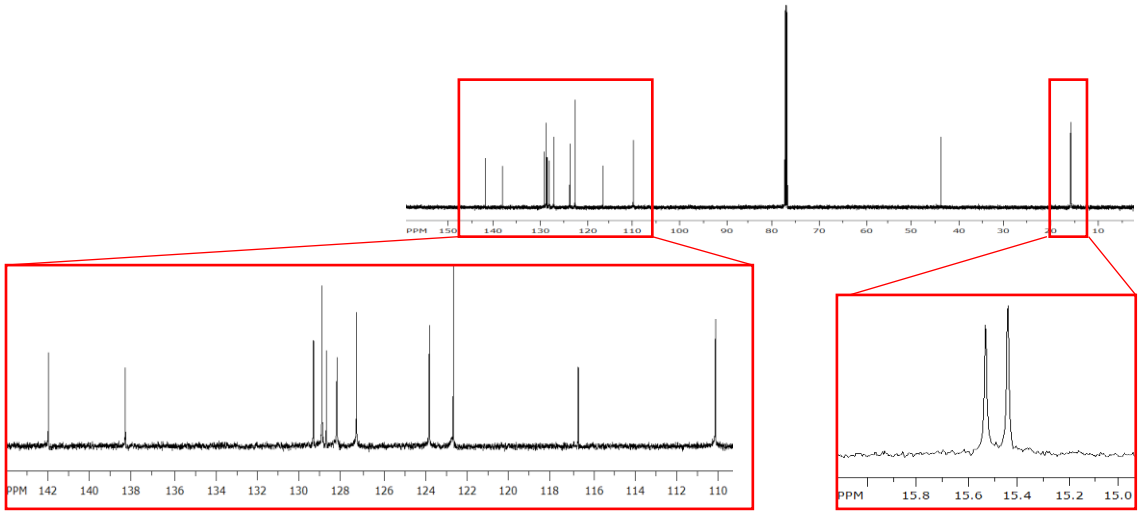


Figure 43: The ^{13}CNMR for compound 173A. (Top) The full ^{13}C-NMR spectrum for KA173A. There are 14 carbons originating from KA173A, as well as, one signal corresponding to a solvent peak. The peaks of interest include 15.4 ppm, 15.5 ppm, 43.6 ppm, 110.1 ppm, 116.7 ppm, 122.6 ppm, 123.8 ppm, 127.3 ppm, 128.2 ppm, 128.7 ppm, 128.9 ppm, 129.3 ppm, 138.4 ppm, and 142.0 ppm (Bottom, Left) The magnified aromatic region of the spectrum. (Bottom, Right) A magnified part of the alkyl region differentiating two peaks.

Over three bonds the position 3c carbon did not couple to any hydrogens, but the position 3c hydrogens coupled to two different carbons (Fig.46). It was not expected for the position 3c hydrogens to couple to two different carbons over three bonds, based on the proposed structure. However, this observation is explained by hydrogen to carbon coupling over two bonds: if coupling over two bonds, between hydrogens at position 3c and the carbon at position 3, occurred then the proposed structure does not deviate from the gHMBC. The suspected position 3 carbon did not couple to any other hydrogens over two or three bonds (Fig.46). In addition, the carbon coupling over three bonds to the position 3c hydrogens, represented as carbon 3a in fig. 2, were expected to couple to two hydrogen doublet signals. Over three bonds, the carbon signal at a chemical shift of 116.7 ppm coupled to the hydrogen doublet signals at chemical shifts of 8.35 ppm and 7.44 ppm. Based on the gHMBC, the previous statements were verified and carbons 3 and 3a were confirmed to be the carbon signals with chemical shifts 145.0 ppm and 116.7 ppm respectively (Fig.46).

The position 11 hydrogens and carbon were not expected to show coupling over three bonds. However, the gHMBC spectrum shows that the position 11 hydrogen signal is coupling to the position 10 carbon signal. Again, if coupling occurred over two bonds there would be no deviation from the proposed structure. This can be verified if the position 10 hydrogen signal couples over three bonds to the position 9a carbon signal.

Over one bond, the hydrogen signals with chemicals shifts of 7.44 ppm and 8.35 ppm were coupled to the carbon signals with chemical shifts of 110.1 ppm and 122.6 ppm respectively (Fig.45). The hydrogen and carbon signals with chemicals shifts of 7.44 ppm and 110.1 ppm assigned to position 9. The hydrogen and carbon signals with chemical

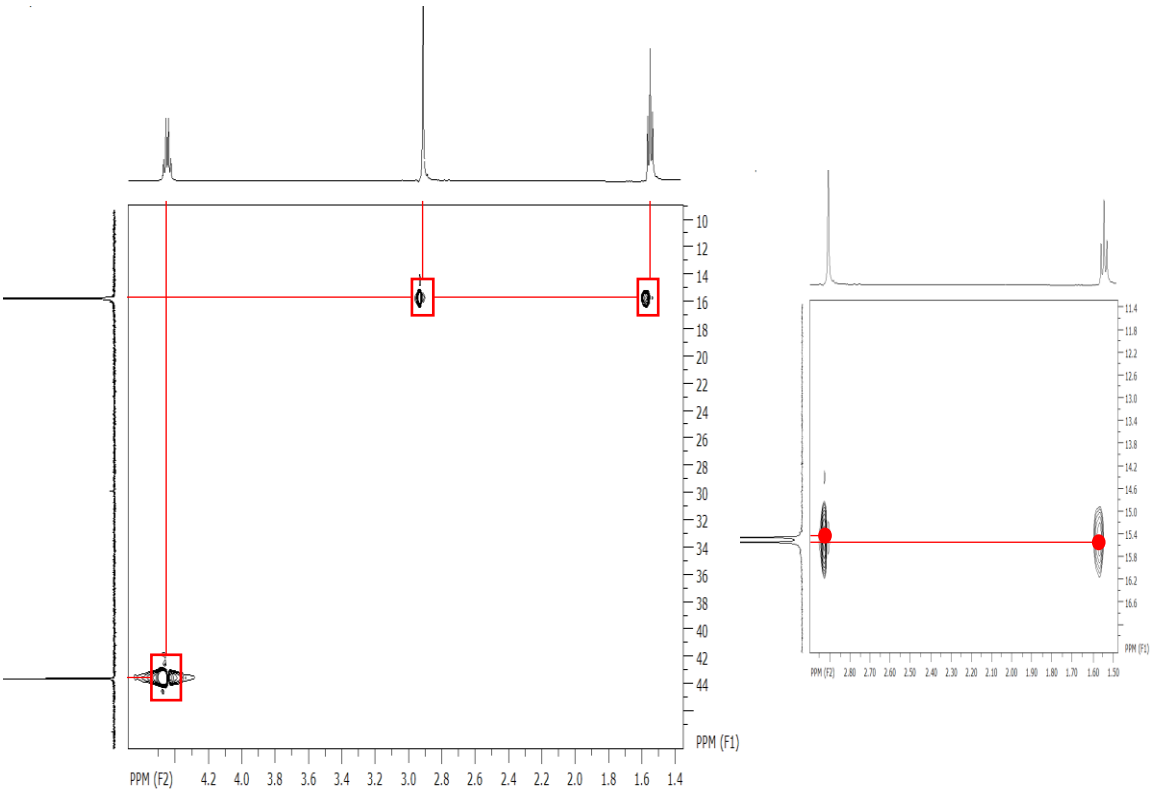


Figure 44: The alkyl region of the gHSQ spectrum. (Left) The alkyl region of the gHSQC spectrum for compound173A. (Right) Magnified portion of the alkyl region, allows for differentiation of carbon/hydrogen interactions at carbon chemical shifts of 15.4 ppm and 15.5 ppm.

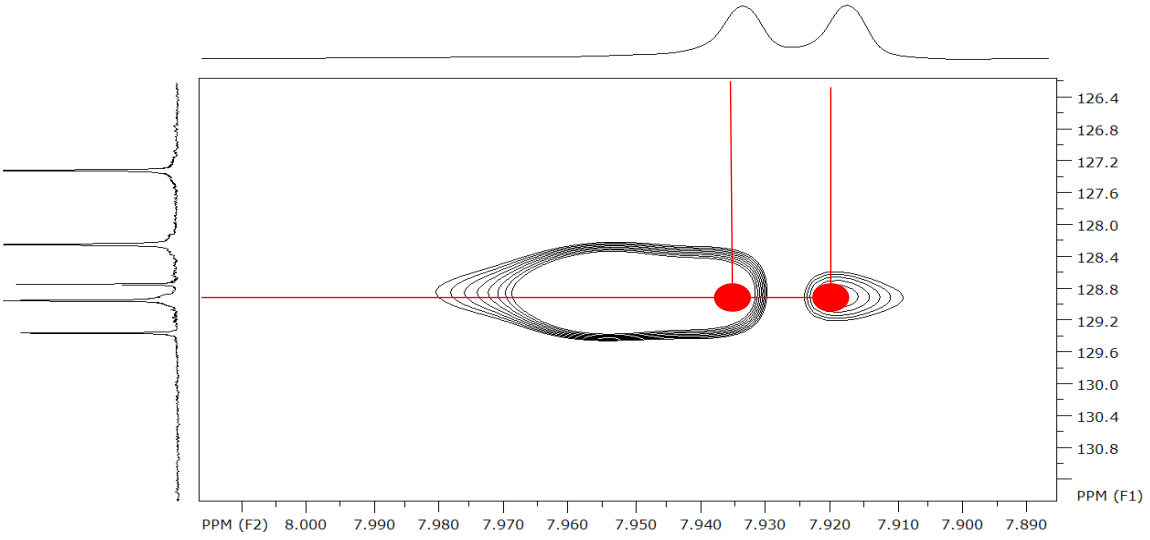


Figure 45: A magnified region of the gHSQC spectra for KA173A specifically showing the coupling over one bond between the hydrogen doublet signal at a chemical shift of 7.93 ppm and the carbon signal at a chemical shift of 128.9 ppm. The red circles indicate high intensity regions of the 2-D signal.

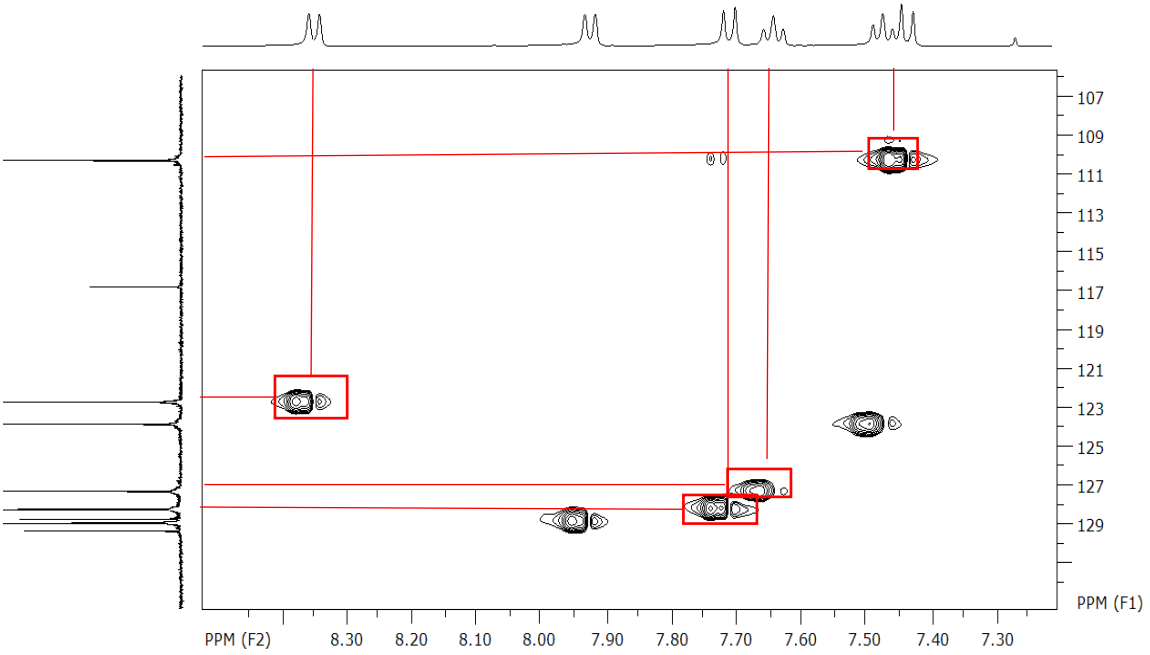


Figure 46: The aromatic region of the gHSQC for KA173A. Where the horizontal and vertical lines intersect with boxes shows coupling over one bond between carbons and hydrogens. Over one bond, the carbons at a chemical shift of 110.1 ppm, 122.6 ppm, 128.2 ppm, and 128.9 ppm are coupling to the hydrogen signals with chemical shifts of 7.44 ppm, 8.35 ppm, and 7.71 ppm, and 7.93 ppm respectively.

shifts of 8.35 ppm and 122.6 ppm were assigned to position 4. Over three bonds the carbon at position 4 coupled to the hydrogen triplet signal at a chemical shift of 7.47 ppm (Fig.41). The triplet signal was then assigned to position 6. The carbon at position 9 should not have coupled to any hydrogens over one or three bonds, and indeed this was observed (Fig.41).

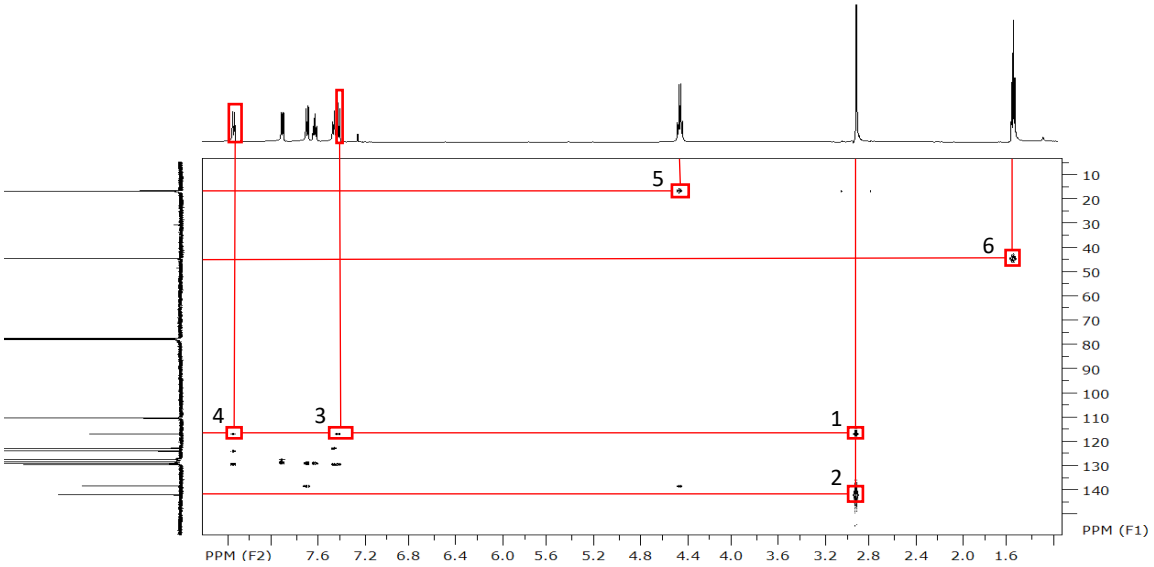


Figure 47: The gHMBC for KA173A. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with and chemical shift of 2.91 ppm and the carbons at 116.7 ppm and 145.0 ppm respectively. The horizontal lines intersect other hydrogens that the carbons couple to over three bonds. Boxes 3 and 4 represent carbon/hydrogen coupling over three bonds between the carbon with a chemical shift of 116.7 ppm and the doublet hydrogen with a chemical shift of 7.44 ppm and 8.35 ppm respectively. Boxes 5 and 6 represent the interactions between the hydrogens at chemical shifts of 1.54 ppm and 4.46 ppm with the carbons at chemical shifts of 43.6 ppm and 15.5 ppm.

The position 4, 6, and 9 hydrogens coupled over three bonds to the carbon signal at a chemical shift 129.3 ppm (Fig.41). The carbon signal at a chemical shift of 129.3 ppm was assigned to position 7a. The remaining triplet signal with a chemical shift of 7.64 ppm was assigned to position 5. The assignment agreed with the proposed structure as the triplet signal coupled over three bonds to a carbon signal at a chemical shift of 128.9, which in turn couples over one bond to the hydrogen doublet signal at a chemical shift of 7.93 ppm (Fig.42, Fig.43). This exact coupling pattern was expected from the proposed structure in Fig. 3. The position 5 hydrogen should have coupled to the position 3b carbon, but only one signal is observed. However, the position 5 hydrogen signal in the gHMBC appears to overlap two carbon signals, one being at a chemical shift of 128.9 ppm and the other at a chemical shift of 128.7 ppm.

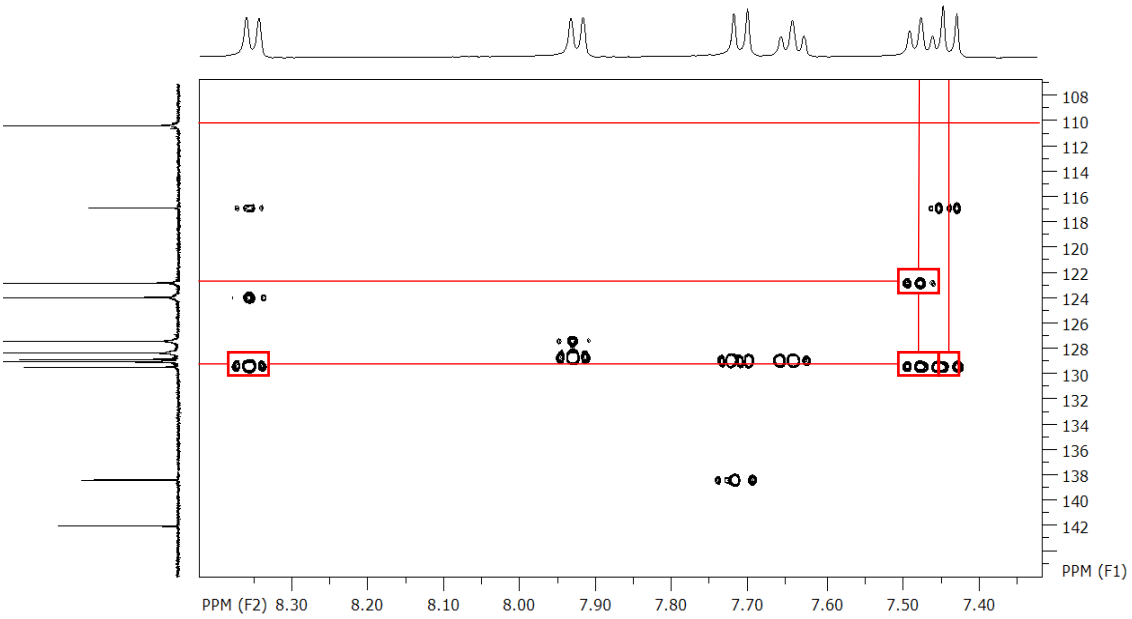


Figure 48: The aromatic region of the gHMBC spectrum for KA173A. Where the horizontal and vertical lines intersect on a box shows the interaction over three bonds between carbons and hydrogens. Over three bonds, the carbon at 110.1 ppm is coupling to no hydrogens. Over three bonds, the carbon at 122.6 ppm is coupling to one hydrogen triplet signal at a chemical shift of 7.47 ppm Over three bonds, the carbon at a chemical shift of 129.3 ppm is coupling to the hydrogens at chemical shifts of 7.43 ppm, 7.47 ppm, and 8.35 ppm.

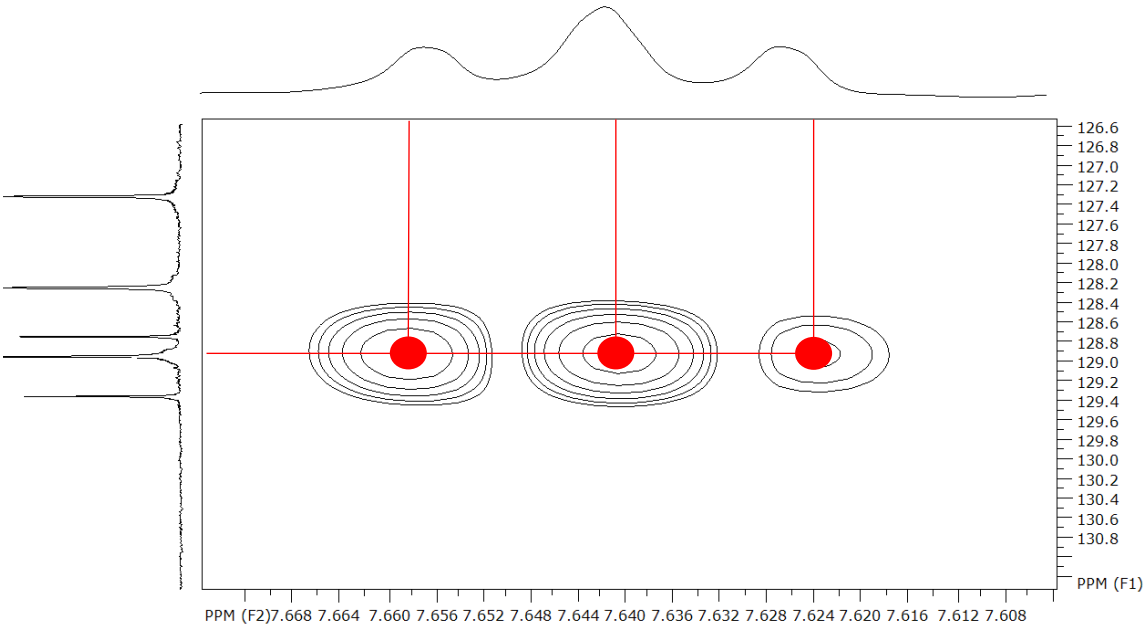
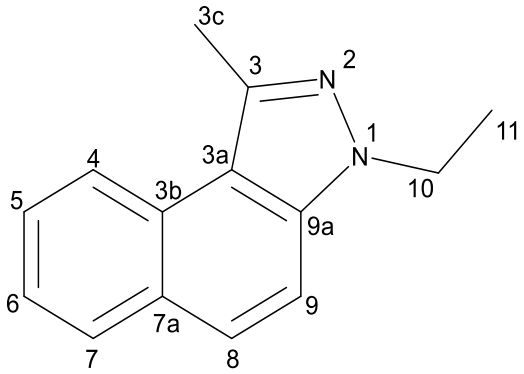


Figure 49: A magnified region of the gHMBC spectrum for KA173A specifically showing the coupling over three bonds between the hydrogen triplet signal at a chemical shift of 7.64 ppm and the carbon signal at a chemical shift of 128.9 ppm. The red circles indicate high intensity regions of the 2-D signal.

It was suspected that the carbon with a chemical shift of 128.7 ppm was the position 3b carbon, and this was verified as it coupled over three bonds to the hydrogen doublet signal at a chemical shift of 7.93 ppm, but to no hydrogens over one bond (Fig.43, Fig. 43). The position 5 hydrogen coupled over one bond to the carbon signal at a chemical shift of 127.3 ppm (Fig.40). The position 5 and 7 hydrogens were defined as having chemical shifts of 7.64 ppm and 7.93 ppm. The position 3b, 5, and 7 carbons were defined as having chemical shifts of 128.7 ppm, 127.3 ppm, and 128.9 ppm. Over three bonds the carbon at position 7 carbon couples to the to the hydrogen doublet signal with a chemical shift of 7.71 ppm (Fig.44).

The hydrogen signal at a chemical shift of 7.71 ppm was thus defined as being the position 8 hydrogen. Over one bond the position 8 hydrogen signal couples to the carbon signal with a chemical shift of 128.2 ppm (Fig.40). The carbon signal at a chemical shift of 128.2 ppm was thus defined as being the position 8 carbon. Over three bonds, the position 8 hydrogen coupled to the carbon signal at a chemical shift of 138.4 ppm, which coupled to no hydrogens over one bond. The carbon signal with a chemical shift of 138.4



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	N/A	142
3a	N/A	116.7
3b	N/A	128.7
3c	2.91	15.4
4	8.35	122.6
5	7.64	127.3
6	7.47	123.8
7	7.93	128.9
7a	N/A	129.3
8	7.71	128.2
9	7.44	110.1
9a	N/A	138.4
10	4.46	43.6
11	1.54	15.4

Figure 50*:* The structural data for KA173A. (Left) The proposed structure and number system for compounds KA173A (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

ppm is assigned as the position 9a carbon. Over three bonds, the position 9a carbon couples to the hydrogen signal at a chemical shift of 4.46 ppm, the position 10 hydrogen (Fig.40).

4.4.2 KA173B

The second isomer was extremely difficult to clean and isolate in any appreciable amount. The ^{1}H-NMR spectra can be seen in Fig. 51. The amount of pure product isolated was not large enough for a ^{13}C-NMR experiment, so no further analysis was done.

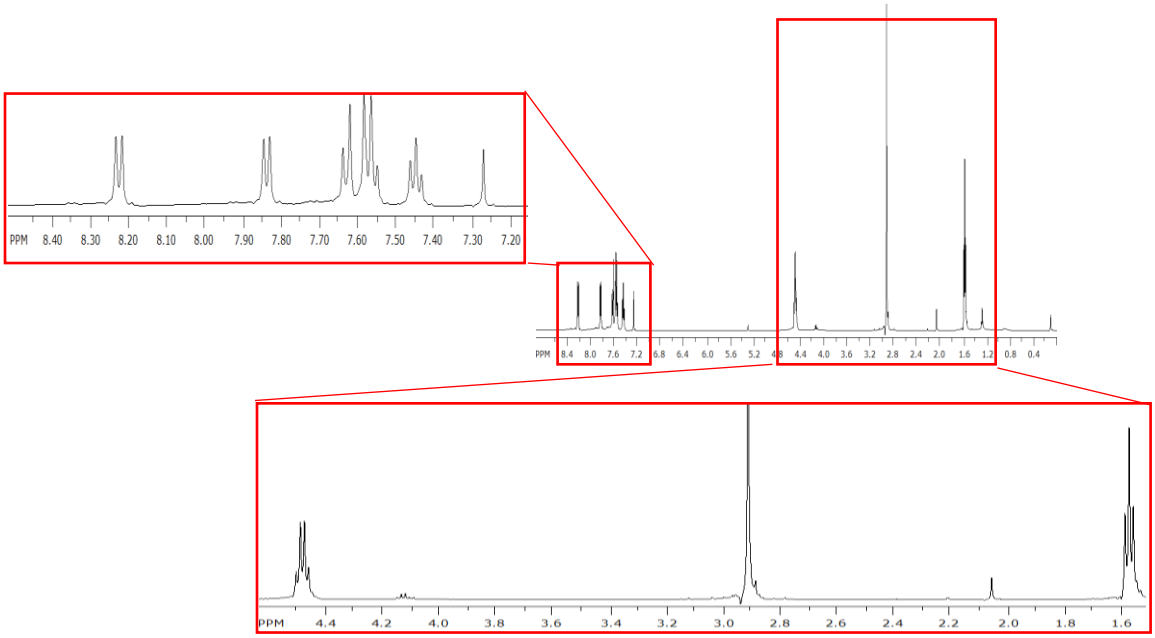


Figure 51: The ^{1}HNMR spectrum for KA173B. (Left) Magnified aromatic region. (Middle) The full spectrum. (Bottom) Magnified alkyl region.

4.5 KA172

The crude GC/MS spectra showed the product was produced in a 24.5% yield (appendix E). The yield was small and due to safety concerns the reaction was not repeated on a larger scale. No further analysis was completed on the compound.

4.6 KA143

Via the crude GC/MS spectrum **KA143** was produced in 80% yields from phenyl hydrazine and 1-acetyl-2-napthol (appendix F). The MP for **KA143** was 99.4-100.4°C (± 0.4°C). As **KA143** melted its color profile changed from a white solid to a dark brown one. The compound was originally identified using x-ray crystallography. The x-ray structure

is represented in Fig.52. The cell lengths and angles were as follows; a = 11.188, b = 11.750, c =10.088, α = 90°, β = 90°, γ = 90°. **KA143** was shown to pack in an orthorhombic cell with a Pca 21 space group (Fig.52). The structure was not flat and the phenyl ring was 3° above the plane. The phenyl ring was rotated 28° out of the plane.

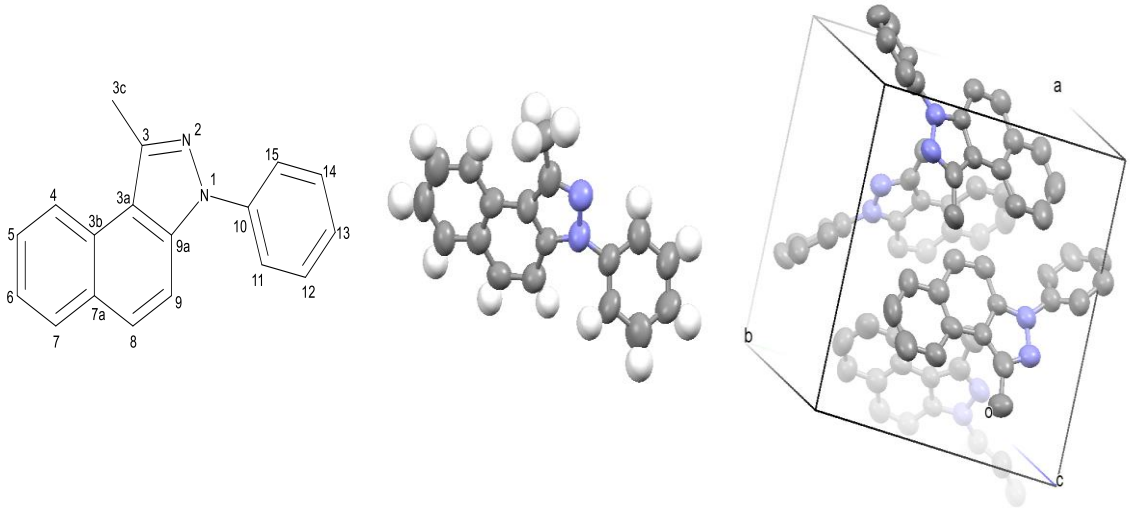


Figure 52: X-ray crystal structure and packing scheme of compound KA143. Grey, blue, and white elipsoids are representative of carbon, nitrogen, and hydrogen respectively. (Left) The numbering and line structure of KA143. (Middle) The crystal solution for the individual molecule. (Right) The packing scheme of KA143 unit cell with denotation of cell lengths a, b, and c (hydrogen solutions are removed for ease of viewing).

The R, R_w, and GOOF, of the crystal solution, were 0.0719, 0.1719, and 0.997 respectively. The .cif file indicated a poorly diffracting crystal with problems giving class A and B warnings (International Union of Crystallography alert level A and B errors : PLAT027_ALERT_3_A THETM01_ALERT_3_B, PLAT340_ALERT_3_B). However, the molecular formula ($C_{18}N_2H_{14}$) was verified using high performance mass spectrometry (appendix F). One and two-dimensional NMR spectroscopy were utilized to further evaluate the compound.

Twelve peaks were observed in the ^{1}H-NMR spectrum (Fig.53). Ten of the twelve peaks were attributed to the compound of interest, while the remaining two were indicative of solvent and water signals. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.82 ppm, 7.89 ppm, 8.06 ppm, and 8.40 ppm, and were assigned a relative integration of one. A doublet with a chemical shift of 7.76 ppm had an integration of two. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 7.43ppm,

7.54ppm, and 7.71ppm and were integrated to one. The triplet signal with a chemical shift of 7.60ppm was integrated to two. The ^{1}H signal, with a multiplicity of one (singlet), at chemical shift 2.88 ppm was integrated to 3. The experimental ^{1}H signals are congruent with the expected signals in respect to the number, multiplicity, and integration of signals predicted from the crystal structure (Fig.53).

Based on the x-ray crystal structure, the ^{13}C -NMR should have had 16 unique carbon signals: 15 in the aromatic region and one in the alkyl region. However, the ^{13}C-NMR spectrum only showed 15 signals (Fig.54). The signal remained absent whether the sample was run in deuterated chloroform or deuterated DMSO. Several of the ^{13}C signals differed by 0.1-0.2 ppm; There is a possibility the sixteenth carbon signal is buried within another signal since the deviations in the chemical shifts are small (Fig.54). ^{1}H and ^{13}C chemical shifts were correlated to the proposed structure by gHSQC, gHMBC, and gCOSY spectra.

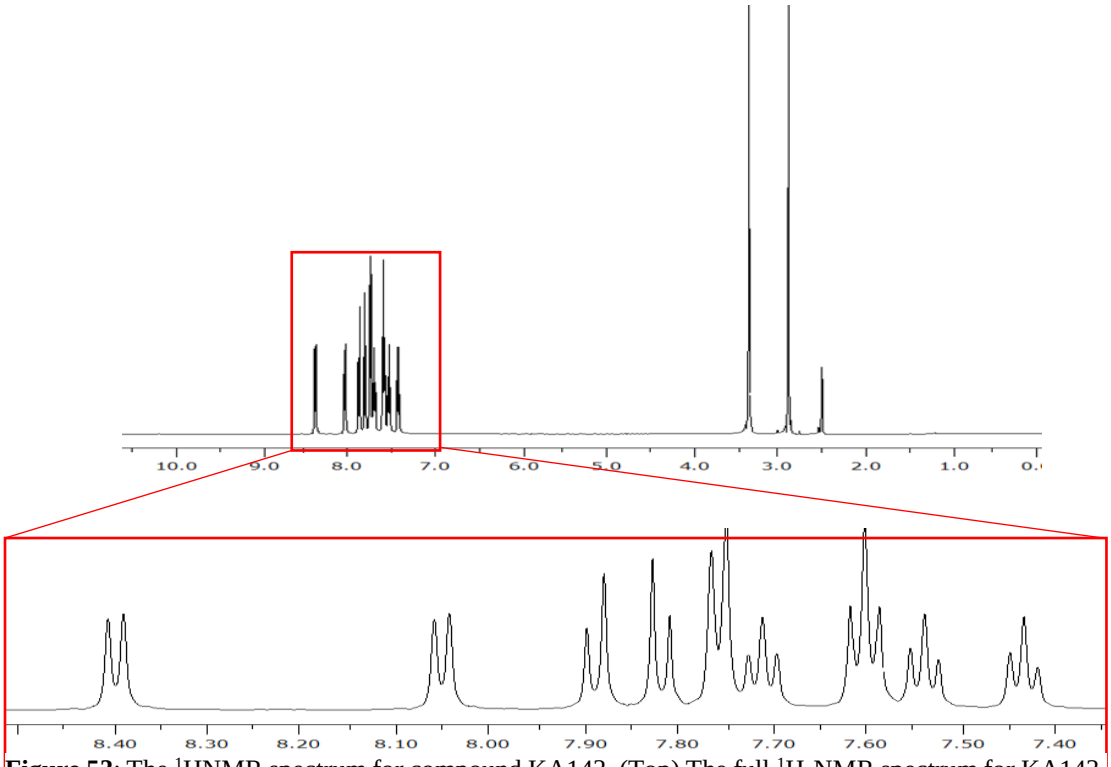


Figure 53: The ^{1}HNMR spectrum for compound KA143. (Top) The full ^{1}H-NMR spectrum for KA143. There are 10 hydrogen signals originating from KA143, as well as, two signals corresponding to a solvent and water peaks. The peaks of interest include 2.88 ppm (singlet), 7.43ppm (triplet), 7.54 ppm (triplet), 7.60 ppm (triplet), 7.71 ppm (triplet), 7.76 ppm (doublet), 7.82 ppm (doublet), 7.89 ppm (doublet), 8.06 ppm (doublet), and 8.40 ppm (doublet). (Bottom) The aromatic region of the spectrum with observable multiplicities.

The ^{13}C signal at chemical shift 15.3 ppm and the ^{1}H signal at chemical shift 2.88 ppm are the only hydrogen and carbon signals within the alkyl region. The gHSQ showed that the alkyl hydrogens and the alkyl carbon coupled over one bond to each other (Fig.55). The alkyl hydrogens and the alkyl carbon were assigned to position 3c in Fig.52. Over three bonds the position 3c carbon did not couple to any hydrogens, but the position 3c hydrogens coupled to two different carbons (Fig.56).

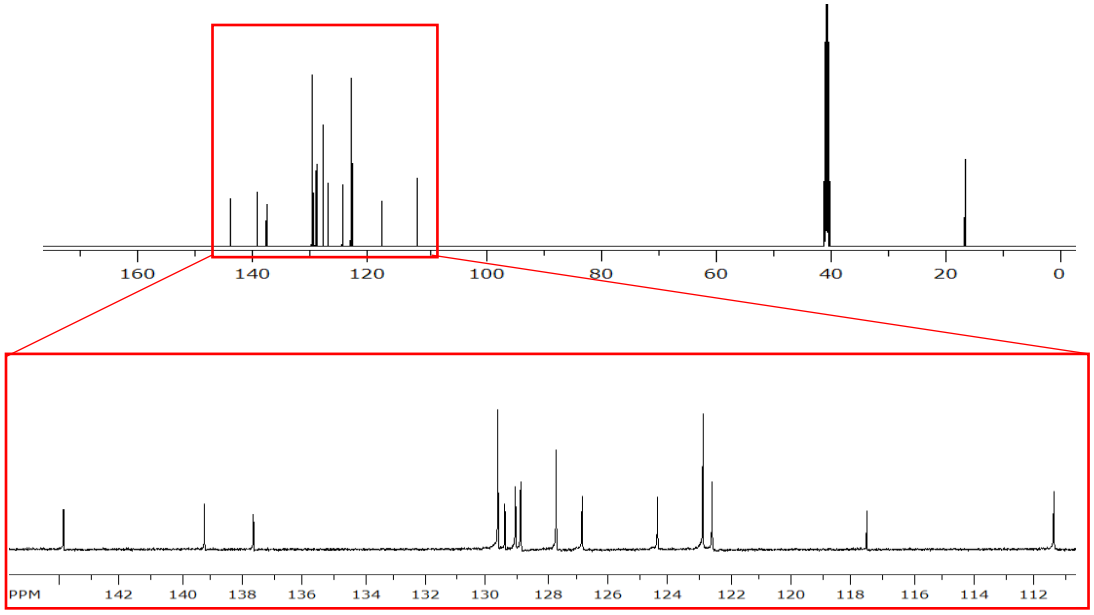


Figure 54: The ^{13}CNMR for compound KA143. (Top) The full ^{13}C-NMR spectrum for compound KA143. There are 15 carbons originating from KA143, as well as, one signal corresponding to a solvent peak. The peaks of interest include 15.3 ppm, 111.3 ppm 117.5 ppm, 122.6 ppm, 122.9 ppm, 124.4 ppm, 126.9 ppm, 127.7 ppm, 128.9 ppm, 129.1 ppm, 129.4 ppm, 129.6 ppm, 137.7 ppm, 139.3 ppm, 143.9 ppm. (Bottom) The magnified aromatic region of the spectrum

From the crystal structure, it was not expected for the position 3c hydrogen signal to couple to two different carbons over three bonds. However, this observation is explained by hydrogen to carbon coupling over two bonds: if coupling over two bonds occurred then the crystal structure does not deviate from the gHMBC. It was expected that the position 3 carbon would not couple to any other hydrogens over two or three bonds; this was observed in the gHMBC (Fig.56). In addition, the carbon coupling over three bonds to the position 3c hydrogens, represented as carbon 3a in fig. 1, would couple to two hydrogen doublet signals over three bonds (Fig.56). Based on the gHMBC the previous statements were verified and carbons 3 and 3a were confirmed to be the carbon signals with chemical shifts 143.9 ppm and 117.5 ppm, respectively.

Over one bond, the hydrogen signals with chemicals shifts of 7.82 ppm and 8.40 ppm are coupled to the carbon signals with chemical shifts of 111.3 ppm and 122.6 ppm respectively (Fig.57). Based on the crystal structure, the doublet hydrogen signals are attached to the carbons at positions 4 and 9 in Fig.52. Over three bonds the carbon at position 4 coupled to the hydrogen triplet signal with a chemical shift of 7.54 ppm (Fig.58). The carbon at position 9 should not be coupled to any hydrogens over one or three bonds, and indeed this is observed (Fig.58).

From this, the carbon and hydrogen at position 4 were defined to have chemical shifts of 122.6 ppm and 8.40 ppm respectively and the carbon and hydrogen at position 9

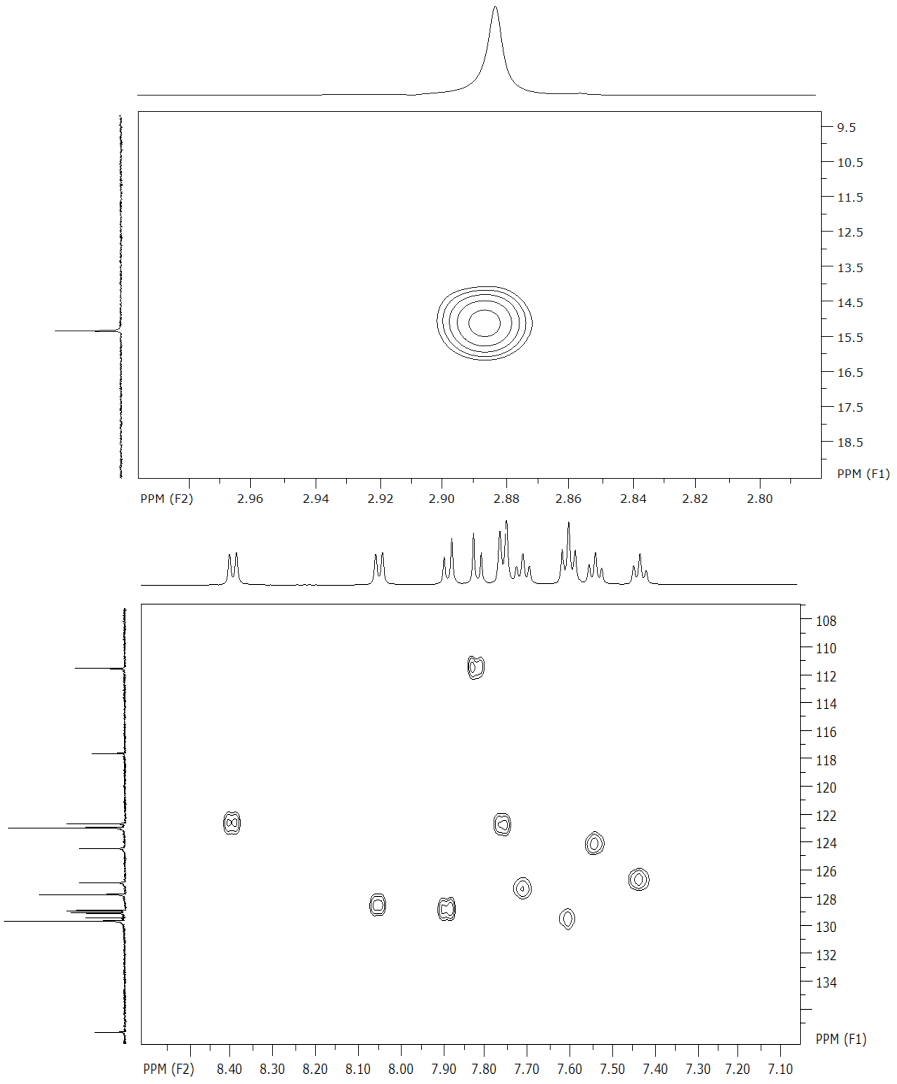


Figure 55: The gHSQC for KA143 with magnified alkyl (Top) and aromatic (Bottom) regions. Coupling over one bond can be seen between hydrogens (x-axis) and carbons (y-axis).

were defined to have chemical shifts of 111.3 ppm and 7.82 ppm respectively. Over three bonds the position 4 hydrogen doublet coupled to a second triplet hydrogen signal at a chemical shift of 7.71 ppm (Fig.59). The position 5 and 6 hydrogens were determined to be 7.71 ppm and 7.54 ppm, respectively. The position 4, 6, and 9 hydrogens coupled over three bonds to the carbon signal at a chemical shift 129.4 ppm (Fig.60). The 129.4 ppm carbon signal couples to no hydrogens over one bond and is defined as the carbon at position 7a.

Via the gHSQC position 5 and 6 carbons are attributed to chemical shifts 127.7 ppm and 124.4 ppm, respectively (Fig.61). The position 5 carbon and position 6 hydrogen couple over three bonds to the hydrogen signal with a chemical shift of 8.06 ppm (Fig.62). Over one bond the hydrogen signal at a chemical shift of 8.06 ppm coupled to the carbon

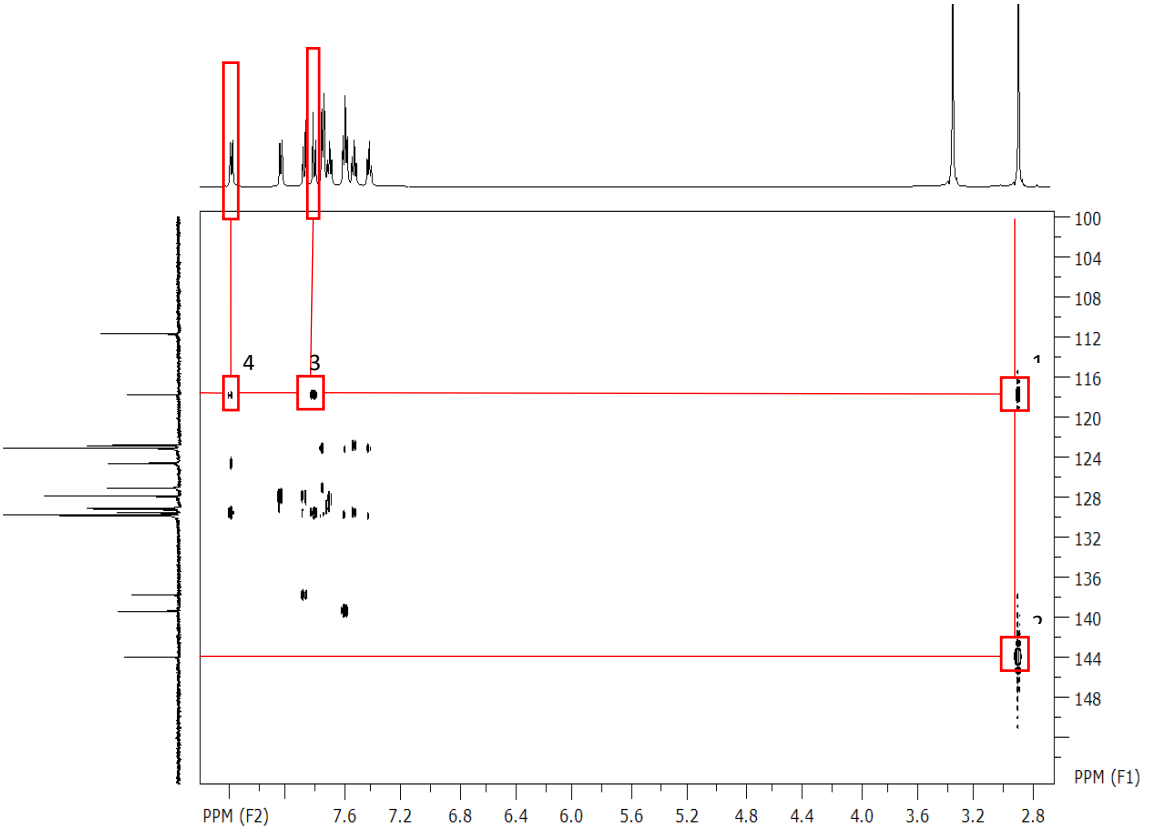


Figure 56: The gHMBC for KA143. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with and chemical shift of 2.88 ppm and the carbons at 117.5 ppm and 143.9 ppm respectively. The horizontal lines intersect hydrogens that the carbons couple to over three bonds. Boxes 3 and 4 represent carbon/hydrogen coupling over three bonds between the carbon with a chemical shift of 117.5 ppm and the doublet hydrogen with a chemical shift of 7.82 ppm and 8.40 ppm respectively

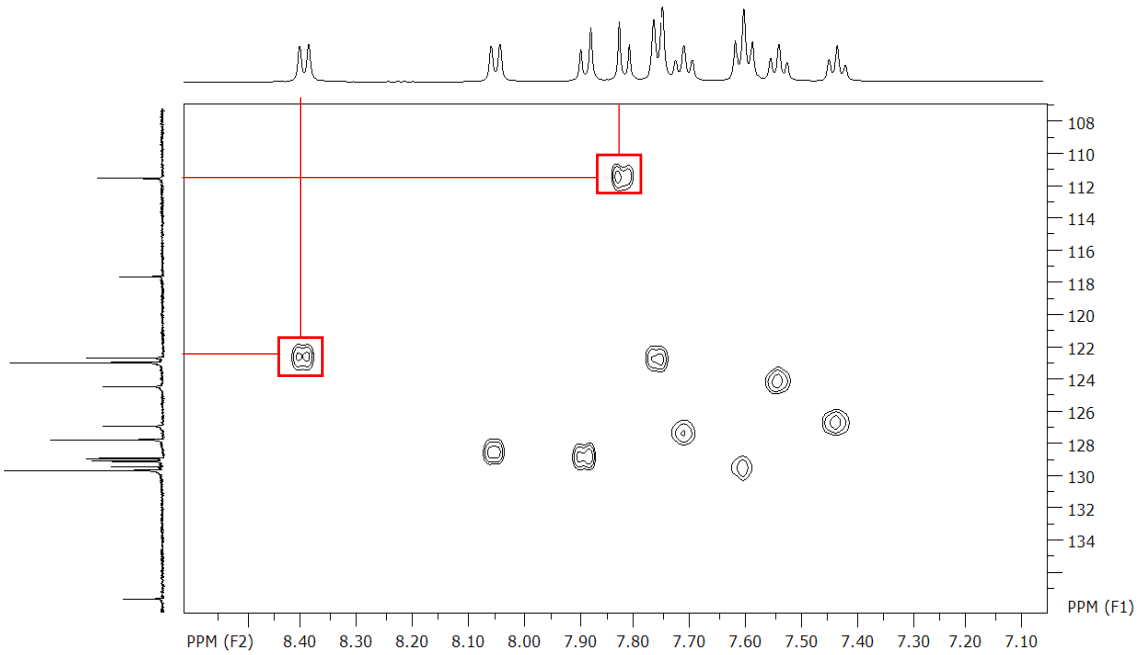


Figure 57: The gHSQC for KA143. Where the horizontal and vertical lines intersect on a box shows the interactions, over one bond, between carbons and hydrogens. Over one bond, the carbon at 111.3 ppm is coupling to the doublet hydrogen signal at 7.82 ppm. Over one bond, the carbon at 122.6 ppm is coupling to the hydrogen doublet signal at 8.40 ppm.

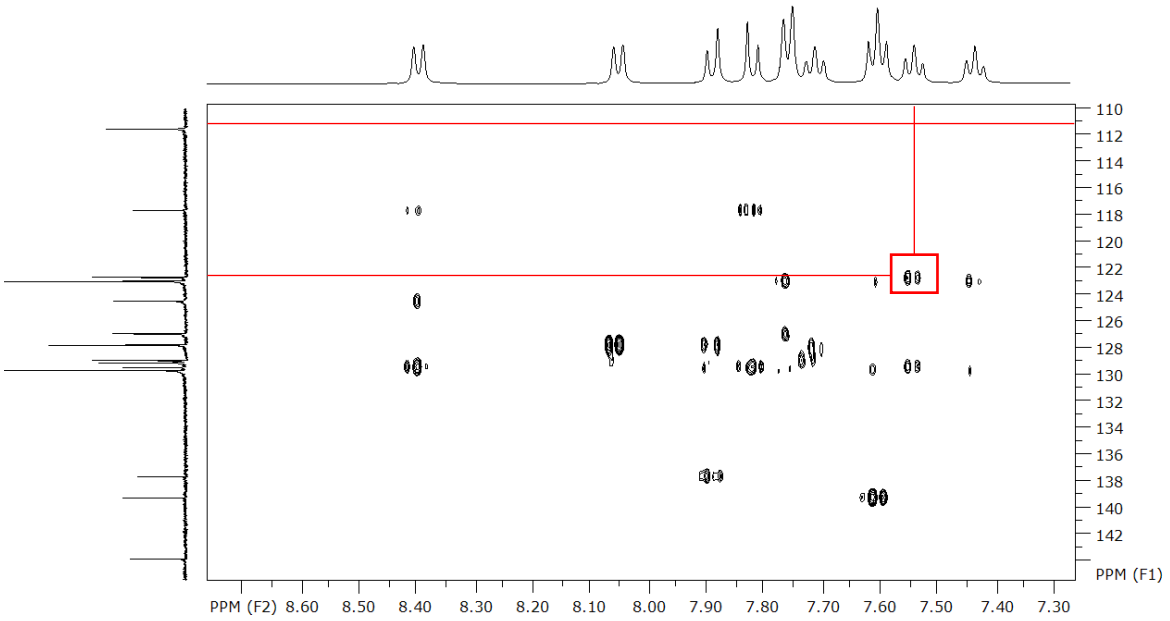


Figure 58: The gHMBC for KA143. Where the horizontal and vertical lines intersect on a box shows the interactions, over three bonds, between carbons and hydrogens. Over three bonds, the carbon at 111.3 ppm is coupling to no hydrogens. Over three bonds, the carbon at 122.9 ppm is coupling to one hydrogen triplet signal.

signal at a chemical shift of 128.9 ppm (Fig.64). The position 7 carbon and hydrogen were defined as 128.9 ppm and 8.06 ppm, respectively.

Over three bonds, the position 9 hydrogen couples to the position 8 hydrogen doublet signal at a chemical shift of 7.89 ppm (Fig.62). The position 8 hydrogen couples over one bond to the carbon signal at a chemical shift of 129.1 ppm (Fig.64). Over three bonds, the position 8 hydrogen couples to the position 3b carbon with a chemical shift of 137.7 ppm (Fig.61). The position 3b carbon cannot be fully verified because the 3b carbon showed no other interactions in the gHMBC spectrum.

The remaining hydrogen signals multiplicities and integrations, one doublet with an integration of two and two triplets with integrations of one and two, are indicative of a singly substituted phenyl ring. Position 11, 12, and 13 hydrogen chemical shifts were designated as 7.76 ppm, 7.60 ppm, and 7.43ppm because of their distinctive integrations

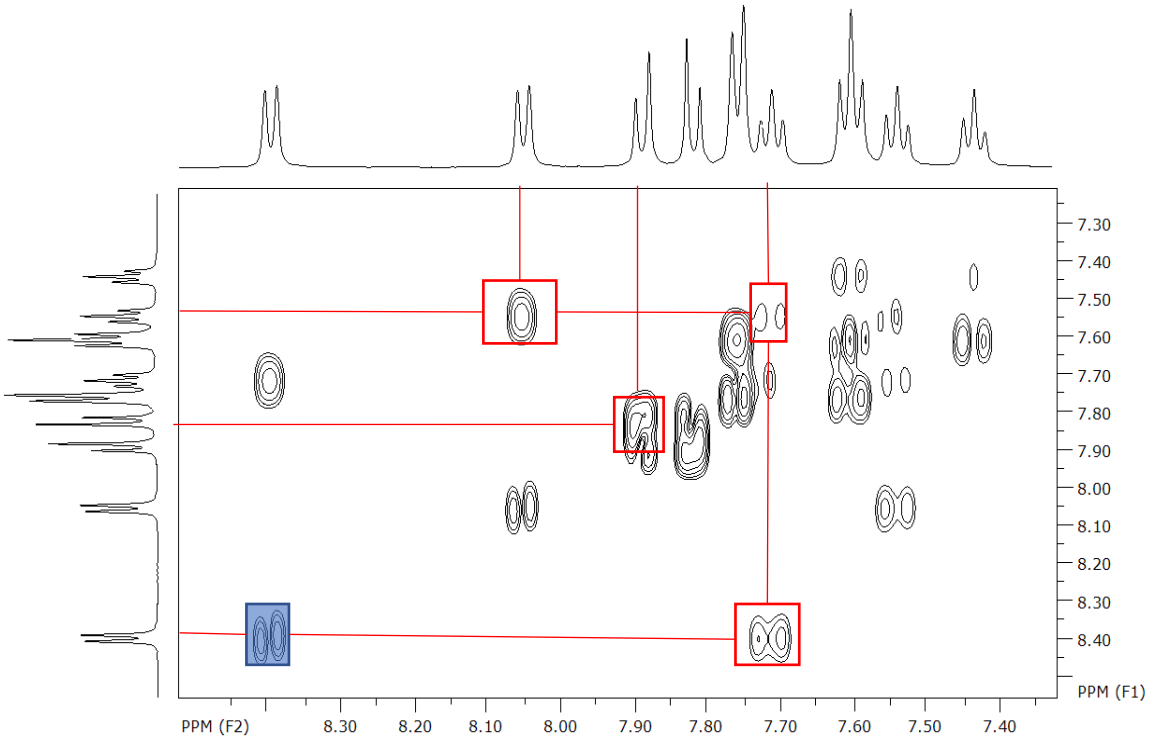


Figure 59: The aromatic region of the gCOSY for KA143. Where the horizontal and vertical lines intersect on a box shows the interactions, over three bonds, between different hydrogens. Over three bonds, the triplet hydrogen signal at chemical shift 7.54 ppm couples to a triplet and doublet signals with chemical shifts of 7.71 ppm and 8.06 ppm respectively. Over three bonds, the hydrogen signal at 7.82 ppm couples to the hydrogen signal at 7.89 ppm. Over three bonds, the doublet hydrogen signal at chemical shift 8.40 ppm couples to the triplet signal at chemical shift 7.71 ppm. The blue boxes are representative of hydrogen signals interacting with themselves.

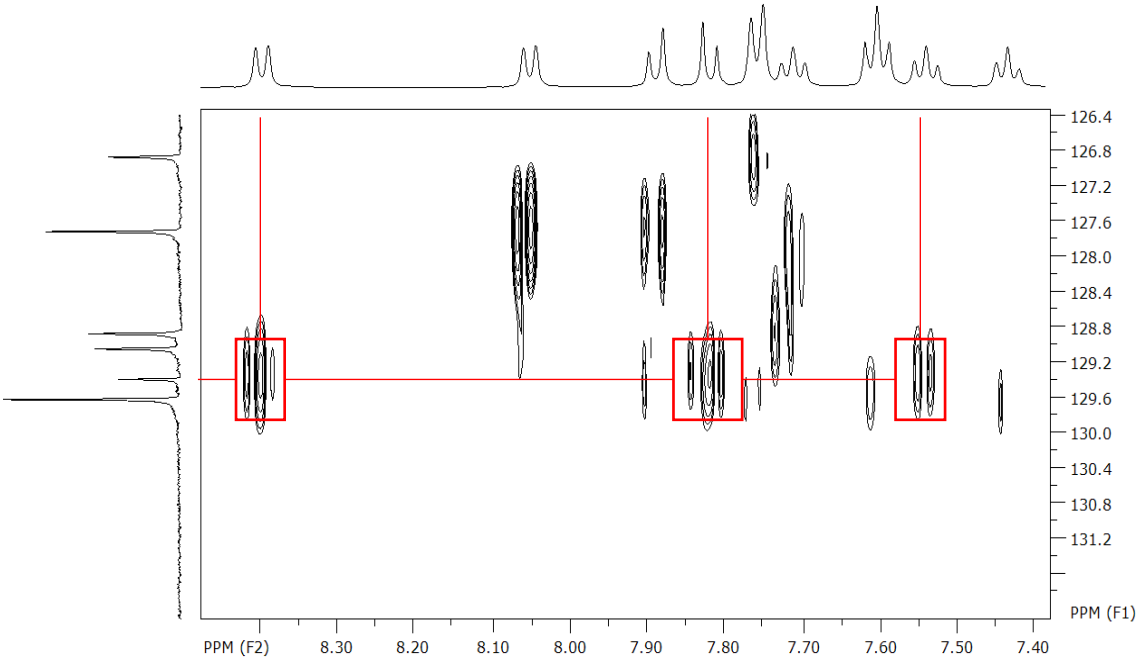


Figure 60: The gHMBC for KA143. Where the horizontal and vertical lines intersect on a box shows the interactions, over three bonds, between carbons and hydrogens. Over three bonds, the carbon at 129.4 ppm is coupling to the doublet hydrogen signals at 7.82 ppm and 8.40 ppm. Over three bonds, the carbon at 129.4 ppm is coupling to the hydrogen triplet signal at 7.54 ppm.

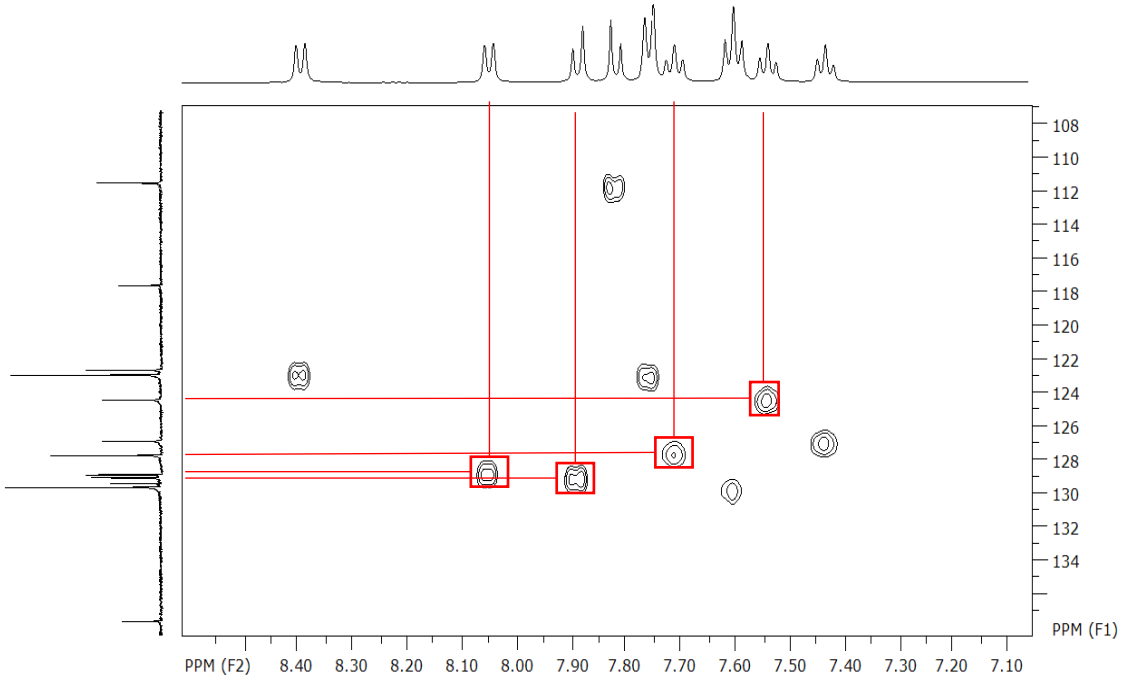


Figure 61*:* The gHSQC spectra for KA143. Where the horizontal and vertical lines intersect with a box shows interactions over one bonds between carbons and hydrogens. Over one bonds, the carbons at chemical shifts of 124.4 ppm, 127.7 ppm, 128.9 ppm, and 128.9 ppm are coupling to the hydrogen signals with chemical shifts of 7.54 ppm, 7.71 ppm, 8.06 ppm, and 7.89 ppm respectively.

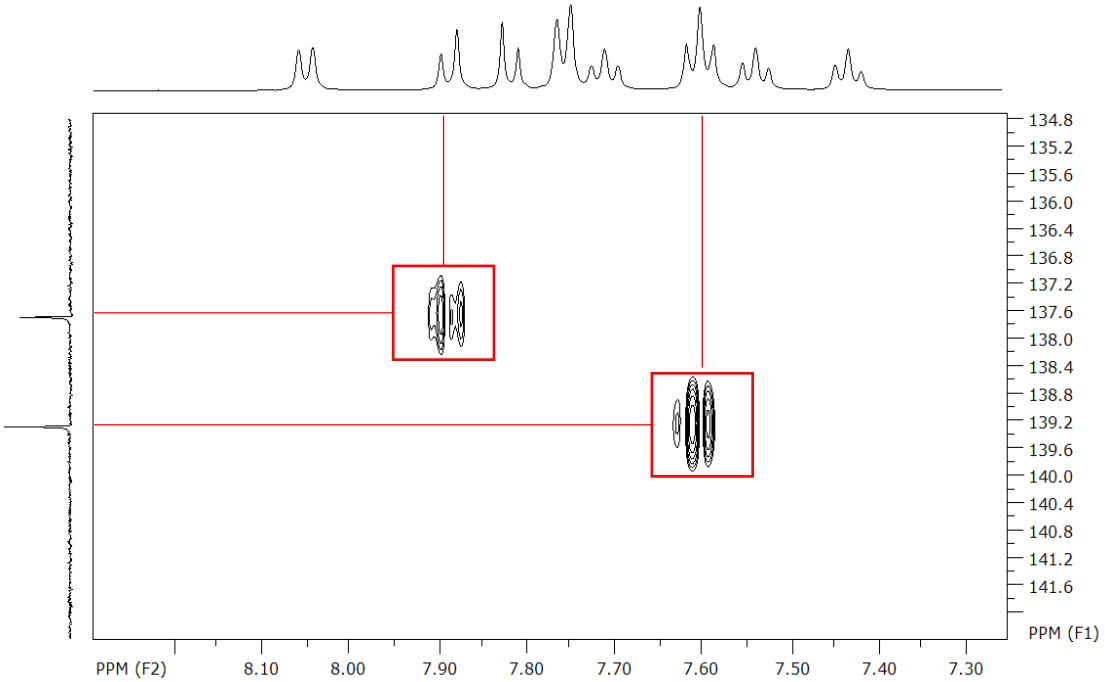


Figure 62: A magnified region of the gHMBC spectra for KA143. Where the horizontal and vertical lines intersect with a box shows interactions over three bonds between carbons and hydrogens. The carbons with chemical shifts of 137.7 ppm and 139.3 ppm couple to the hydrogen signals with chemical shifts of 7.89 ppm and 7.60 ppm respectively.

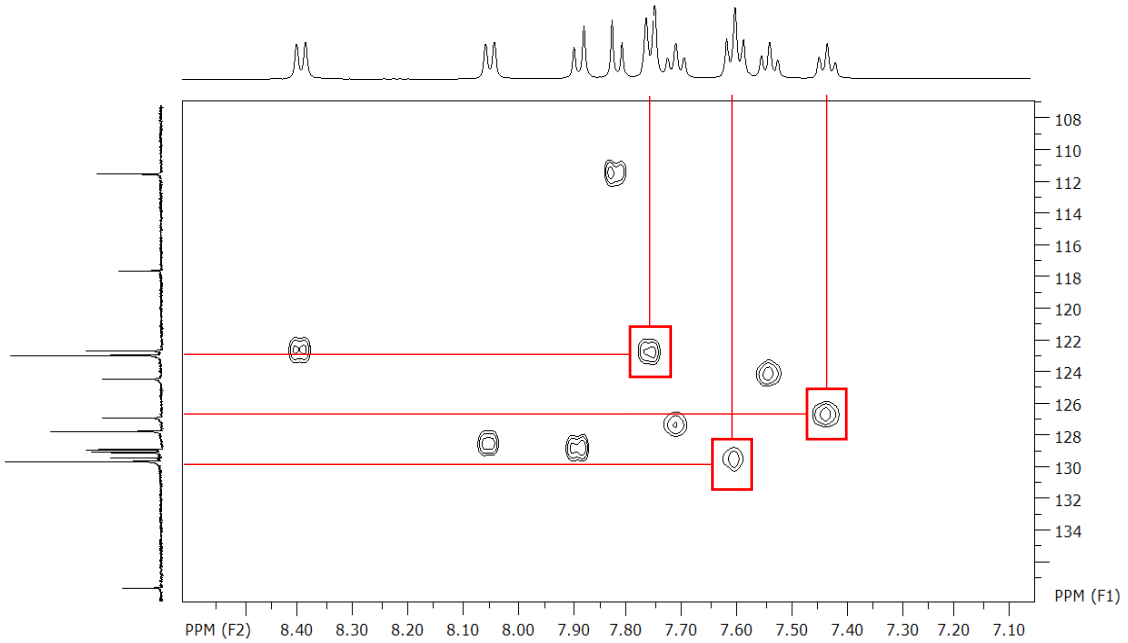
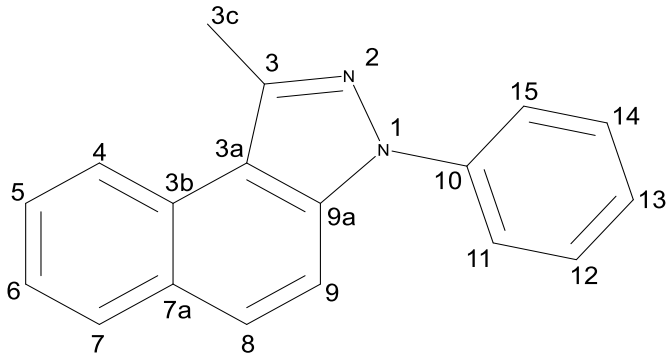


Figure 63: The aromatic region of the gHSQC spectra for KA143. Where the horizontal and vertical lines intersect with a box shows interactions over one bond between carbons and hydrogens. The carbons with chemical shifts of 122.9 ppm, 129.6 ppm, and 126.9 ppm couple to the hydrogen signals with chemical shifts of 7.76 ppm, 7.60 ppm, and 7.43ppm.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	N/A	143.9
3a	N/A	117.5
3b	N/A	138.2
3c	2.88	15.3
4	8.40	123.6
5	7.71	128.2
6	7.54	124.4
7	8.06	128.9
7a	N/A	129.4
8	7.89	129.1
9	7.82	111.3
9a	N/A	N/A
10	N/A	139.9
11	7.76	122.9
12	7.60	129.6
13	7.43	126.9
14	7.60	129.6
15	7.76	122.9

Figure 64: The structural data for KA143. (Left) The proposed structure and number system of KA143. (Right) A table correlating the positions and the chemical shifts of hydrogen and carbon signals assigned to said position.

and multiplicities. Via the gHSQC position 11, 12, and 13 carbon chemical shifts were designated 122.9 ppm 129.6 ppm, and 126.9 ppm (Fig.63). Over three bonds, the at position twelve coupled to the carbon with a chemical shift of 139.3 ppm at position 10 (Fig.62).

Additionally, **KA143** was synthesized using phenylhydrazine and 2-methoxy-1-acetyl - napthalene. The identity of **KA143** was verified via GC/MS fragmentation patterns, which are identical between the two synthetic methods (appendix F). The GC/MS spectrum showed crude

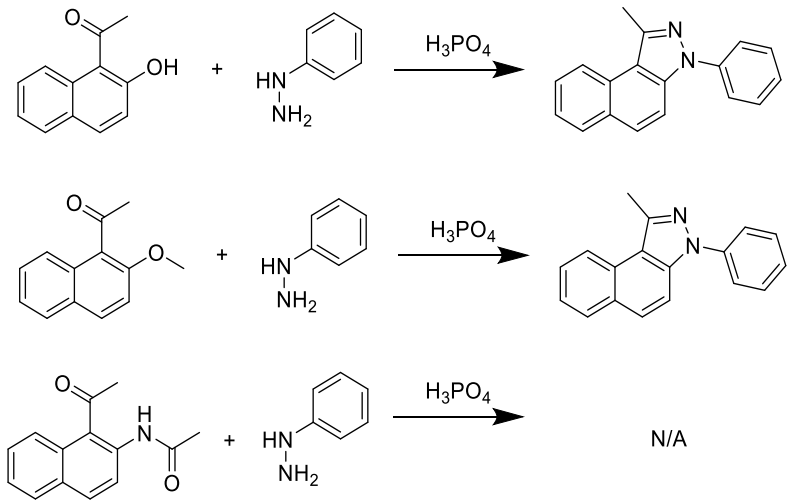


Figure 65: Reactions for the production of KA143. The following naphthalene derivatives were tested as potential starting materials for the production of compound KA143: 1-acetyl-2-napthol, 2-methoxy-1-acetyl-napthalene, N-(1-acetylnaphthalen-2-yl)acetamide respectively.

yields of 40% when synthesized using phenylhydrazine and 1-acetyl-2-methoxy-napthalene. Synthesis of **KA143** was attempted using phenylhydrazine and N-(1-acetylnaphthalen-2-yl)acetamide. The resultant GC/MS spectra gave a singular chromatographic peak with a molecular ion of 143 m/z, which indicated that formation of compound **KA143** did not occur (appendix F). The complete position assignments can be seen in Fig.64. The three different reactions for the attempted synthesis of compound **KA143** can be seen in figure 65.

4.7 KA161

Via the crude NMR compound **KA161** was produced in 88.9% yield from 4-bromo-phenyl hydrazine and 1-acetyl-2-napthol (appendix G). **KA161** MP was 144.2-145.1°C (± 0.8°C). The compound was an off white/brown solid. The molecular formula ($C_{18}H_{13}N_2Br$) was

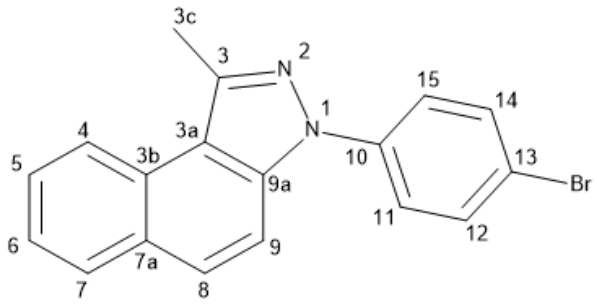


Figure 66: The proposed structure for KA161 and its numbering assignments.

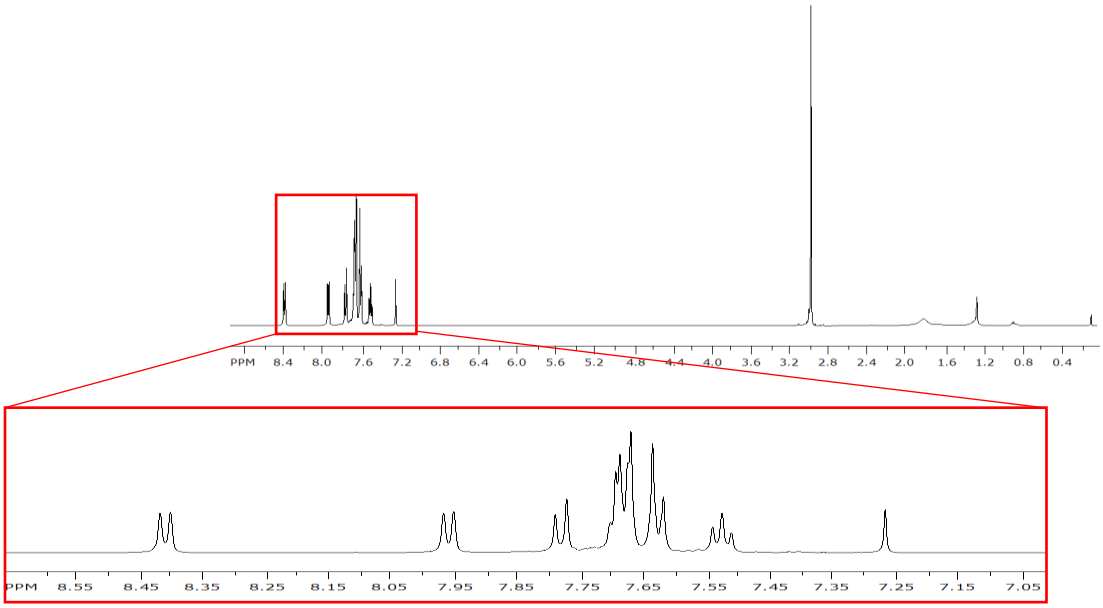


Figure 67: The ^{1}HNMR spectrum for KA161. **(Top)** The full ^{1}H-NMR spectrum for **KA161**. There are seven hydrogen signals originating from **KA161** and one chloroform solvent peak. The peaks of interest include 2.97 ppm (singlet), 7.52 ppm (triplet), 7.62 ppm (doublet), 7.68 ppm (multiplet), 7.78 ppm (doublet) 7.96 ppm (doublet), and 8.41 ppm (doublet) **(Bottom)** The magnified aromatic region of the spectrum with observable multiplicities.

verified using high performance mass spectrometry (appendix G). The compound's proposed structure is seen in Fig.66. Eight peaks were observed in the ^{1}H-NMR spectrum (Fig.67). Seven of the eight peaks were attributed to the compound of interest, while the remaining peak were indicative of solvent chloroform.

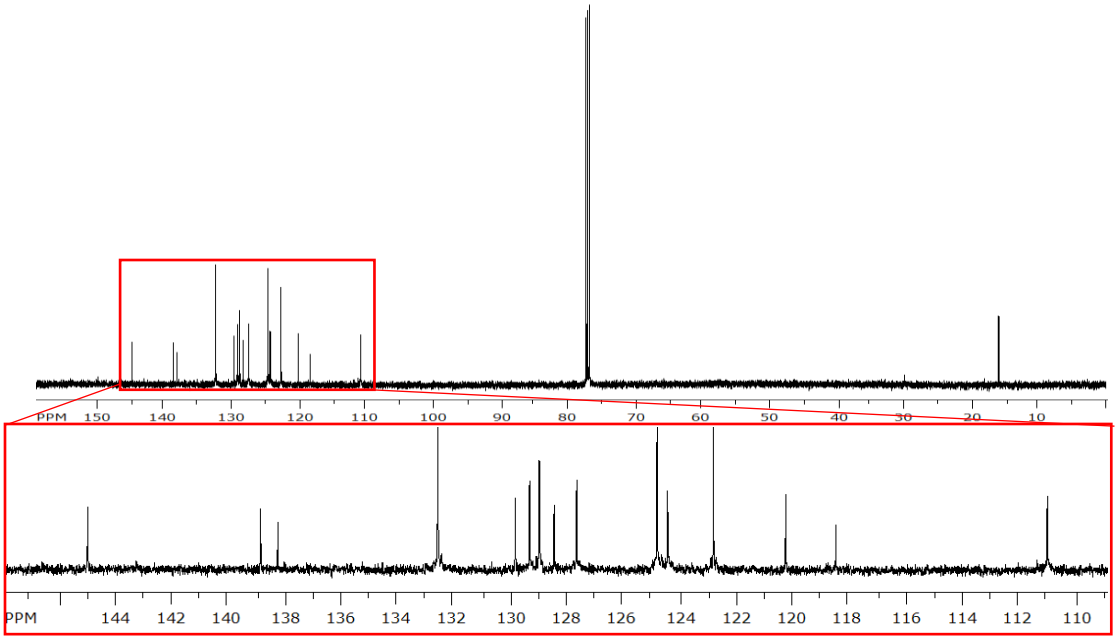


Figure 68: ^{13}CNMR spectrum for KA161. (Top) The full ^{13}C-NMR spectrum for KA161. There are 18 carbons originating from KA161, as well as, one signal corresponding to a solvent peak. The peaks of interest include 15.8 ppm, 111.1 ppm, 118.6 ppm, 120.4 ppm, 122.9 ppm, 124.5 ppm, 124.9 ppm, 127.8 ppm, 128.6 ppm, 129.1 ppm, 129.5 ppm, 130.0 ppm, 132.7 ppm, 138.4 ppm, 139.0 ppm, and 145.2 ppm (Bottom) The magnified aromatic region of the spectrum.

The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.62 ppm, 7.78 ppm, 7.96 ppm, and 8.41 ppm. The doublets with chemical shifts of 7.96 ppm, and 8.41 ppm were assigned a relative integration of one and the doublet with a chemical shift of 7.62 ppm was integrated to two. The ^{1}H signal, with a multiplicity of three (triplet), had a chemical shift of 7.52 ppm and was integrated to one. The hydrogen signal at a chemical shift of 7.68 ppm had an unknown multiplicity, but was considered a multiplet and had an integration of four. The ^{1}H signal, with a multiplicity of one (singlet), had chemical shifts of 2.97 ppm and was integrated to three. The experimental ^{1}H signals are congruent in terms of the summed relative integrations of the signals. The predicted structure should have produced six doublet signals, two triplet signals, and one singlet signal.

The ^{13}C -NMR had 16 unique carbon, which was in agreement with the fig.3 structure (Fig.68). The ^{1}H and ^{13}C chemical shifts were correlated via gHSQC, gHMBC, and gCOSY spectra. The gHSQC spectra showed that the alkyl hydrogens, at a chemical shift of 2.97 ppm, and the alkyl carbon, at a chemical shift of 15.8 ppm, coupled over one bond (Fig.69). The alkyl hydrogen signal and the alkyl carbon signal were assigned to position 3c in Fig.3. Over three bonds the position 3c carbon did not couple to any hydrogens, but the position 3c hydrogens coupled to the carbon signals with chemical shifts of 118.6 ppm and 145.2 ppm (Fig.72). It was not expected for the position 3c hydrogens to

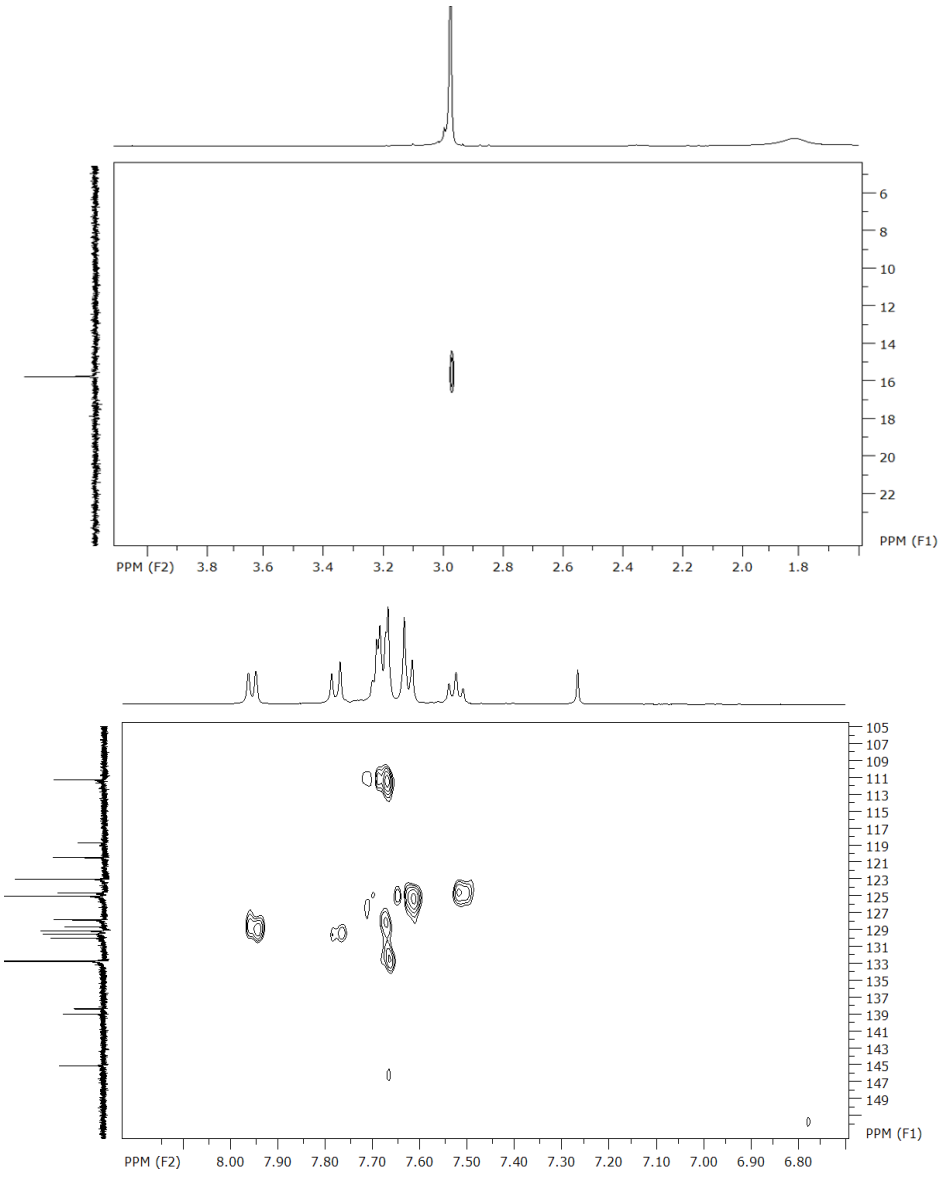


Figure 69: The gHSQC for KA161 with magnified alkyl (Top) and aromatic (Bottom) regions. Coupling over one bond can be seen between hydrogens (x-axis) and carbons (y-axis).

couple to two different carbons over three bonds. However, this observation is explained by hydrogen to carbon coupling over two bonds: if coupling over two bonds occurred then the gHMBC spectra does not deviate from the Fig.68.

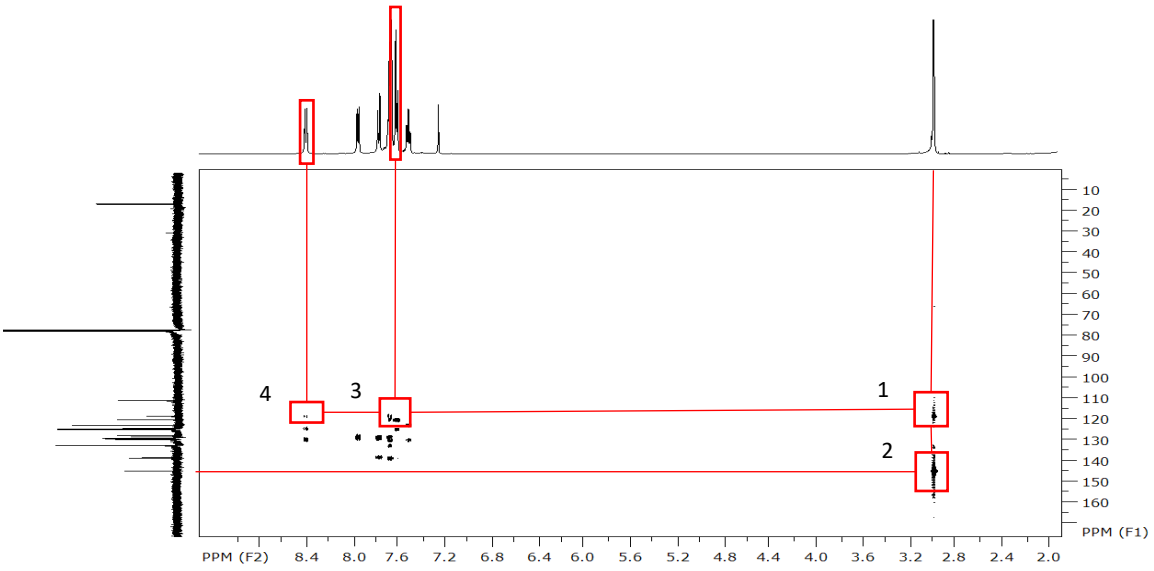


Figure 70: The gHMBC for KA161. The horizontal and vertical lines intersect where the hydrogens and carbons couple over three bonds. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with and chemical shift of 2.88 ppm and the carbons at 118.6 ppm and 145.2 ppm respectively. Boxes 3 and 4 represent carbon/hydrogen coupling between the carbon with a chemical shift of 118.6 ppm and the hydrogen signals with chemical shifts of 7.68 ppm and 8.41 ppm respectively.

The carbon that coupled over two bonds to the hydrogens at position 3c would not have coupled over three bonds to any hydrogens. The carbon that coupled over three bonds to the position 3c hydrogens would have coupled to two different hydrogen signals over three bonds. The carbon signal with a chemical shift of 145.2 ppm coupled over three bonds to no hydrogen signals and the carbon signal with a chemical shift of 118.6 ppm coupled over three bonds to two hydrogen signals with chemical shifts of 7.68 ppm and 8.41 ppm (Fig.70).

The coupling pattern verified that the carbons with chemical shifts of 145.2 ppm and 118.6 ppm coupled over two and three bonds to the position 3c hydrogens respectively. The carbons with chemical shifts of 145.2 ppm and 118.6 ppm were assigned to positions 3 and 3a, respectively. The hydrogen signal with a chemical shift of 8.41 ppm had no carbon signal in the gHSQC spectrum, but coupled over three bonds to the carbon signals with chemical shifts of 124.5 ppm and 130.0 ppm (Fig.71 & 72). Over one bond the carbon

with a chemical shift of 124.5 ppm coupled to a triplet hydrogen signal with a chemical shift of 7.52 ppm (Fig.71). The hydrogen signal with a chemical shift of 7.52 ppm coupled over three bonds to the carbon with a chemical shift of 130.0 ppm (Fig.72). The carbon with a chemical shift of 130.0 ppm coupled to no hydrogens over one bond (Fig.71). Over three bonds, the multiplet signal with a chemical shift of 7.68 ppm coupled to the carbon with a chemical shift of 130.0 ppm (Fig.72). From these data the 4, 6, and 7a positions were assigned to the carbon signals with chemical shifts of 122.9 ppm, 124.5 ppm, and 130.0 ppm, respectively. The hydrogens for positions 4, 6, and 9 were assigned the hydrogen signals with chemical shifts of 8.41 ppm, 7.52 ppm and 7.68 ppm, respectively.

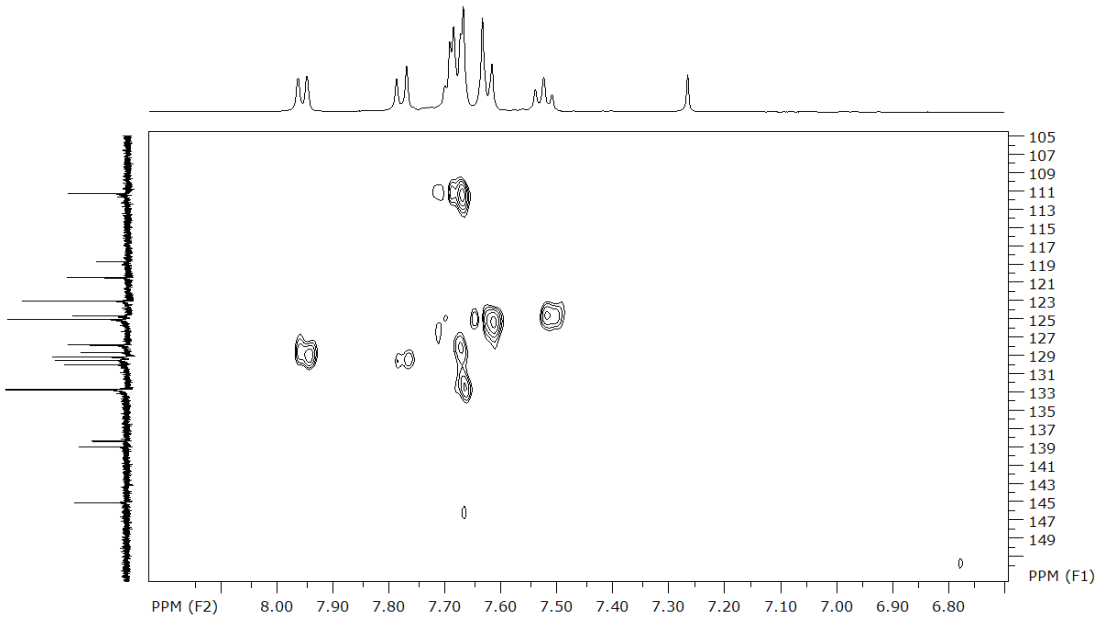


Figure 71: The aromatic region of the gHSQC spectra for KA161. The hydrogen signals with chemical shifts of 7.52 ppm, 7.78 ppm, and 7.96 ppm coupled over one bond to the carbons signals with chemical shifts 124.5 ppm, 129.5 ppm, and 129.1 ppm respectively. The multiplet signal with a chemical shift of 7.68 ppm coupled over one bond to the carbons with chemical shifts of 111.1 ppm, 127.8 ppm, and 132.7 ppm.

The multiplet hydrogen signal with a chemical shift of 7.68 ppm coupled to the three carbons with chemical shifts of 111.1 ppm, 127.8 ppm, and 132.7 ppm, over one bond (Fig.71). The carbon with a chemical shift of 111.1 ppm coupled to no hydrogens over three bonds. The carbon with a chemical shift of 127.8 ppm appeared to couple over three bonds to the hydrogen with a chemical shift of 7.96 ppm, but the 2-D signal spanned multiple carbons and only appeared slightly warped where the signal should’ve been for

the carbon hydrogen pair (Fig.73). The carbon with a chemical shift of 132.7 ppm coupled to no hydrogens over three bonds.

Via the gCOSY, the position 6 hydrogen signal coupled over three bonds to multiplet hydrogen signal with chemical a shift of 7.68 ppm and to the doublet hydrogen signal with a chemical shift of 7.96 ppm (Fig.74). Over one bond the hydrogen with a chemical shift of 7.96 ppm coupled to the carbon signal with a chemical shift of 129.1 ppm (Fig.73). The doublet hydrogen signal with a chemical shift of 7.96 ppm and the carbon with a chemical shift of 129.1 ppm were assigned to position 7. The multiplet hydrogen signal with a chemical shift of 7.68 ppm and the carbon signal with a chemical shift of 127.8 ppm were assigned to position 5.

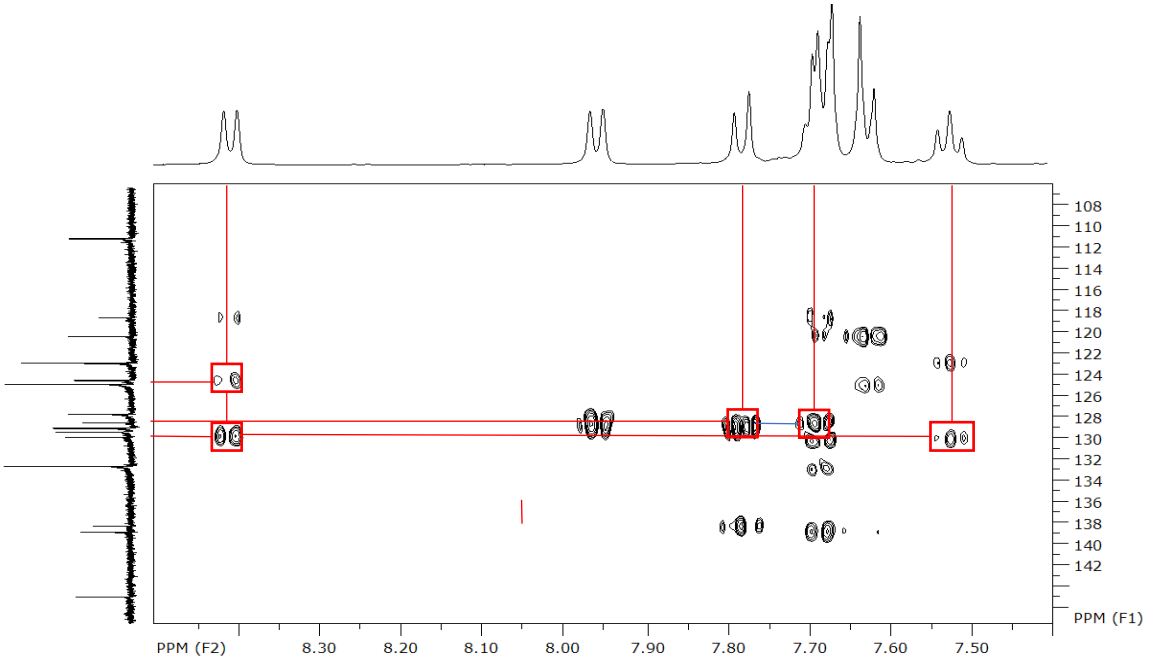


Figure 72: The aromatic region of the gHMBC spectra for KA161. Where the horizontal and vertical lines intersect with a box shows the coupling patterns under consideration. Coupling occurs over three bonds between carbon and hydrogen signals. The hydrogen signals with chemical shifts of 7.52 ppm, 7.68 ppm, and 8.41 ppm couple to the carbon with a chemical shift of 130.0 ppm. The hydrogen signal with a chemical shift of 7.62 ppm coupled over three bonds to the carbon signal with a chemical shift of 120.4 ppm. The hydrogen with a chemical shift of 7.78 ppm couples to the carbon signal with a chemical shift of 129.1 ppm and 138.4 ppmThe hydrogen signal with a chemical shift of 8.41 ppm couples to the carbon with a chemical shift of 124.5 ppm.

Over three bonds, the position 7 carbon signal coupled to the doublet hydrogen signal with a chemical shift 7.78 ppm (Fig.72). Over one bond, the hydrogen with a chemical shift of 7.78 ppm coupled to the carbon signal with a chemical shift of 129.5 ppm.

(Fig.71). The position 7 hydrogen signal and the position 5 hydrogen signal coupled over three bonds to the carbon with a chemical shift of 128.6 ppm (Fig.73). The carbon with a chemical shift of 128.6 ppm coupled to no hydrogens over one bond and was assigned to position 3b. The hydrogen signal with a chemical shift of 7.78 ppm and the carbon with a chemical shift of 129.5 ppm were assigned to position 8. There appeared to be two signals coupling to the carbon with a chemical shift of 129.5 ppm and may indicate bonding to one of the carbon signals with a similar chemical shift (Fig.73). The hydrogen signal at position 8 coupled over three bonds to the carbon with a chemical shift of 138.4 ppm (Fig.72). The carbon with a chemical shift of 138.4 ppm coupled to no other hydrogens over one or three bonds and was assigned to position 9a.

Over three bonds, the position 8 hydrogen coupled to the multiplet hydrogen signal with a chemical shift of 7.68 ppm (Fig.72). The multiplet hydrogen signal with a chemical shift of 7.68 ppm was thus assigned to position 9. The position 9 carbon could not be identified as both remaining carbons it coupled to, with chemical shifts of 111.1 ppm and 132.7 ppm, did not couple to any hydrogens over three bonds. The remaining doublet

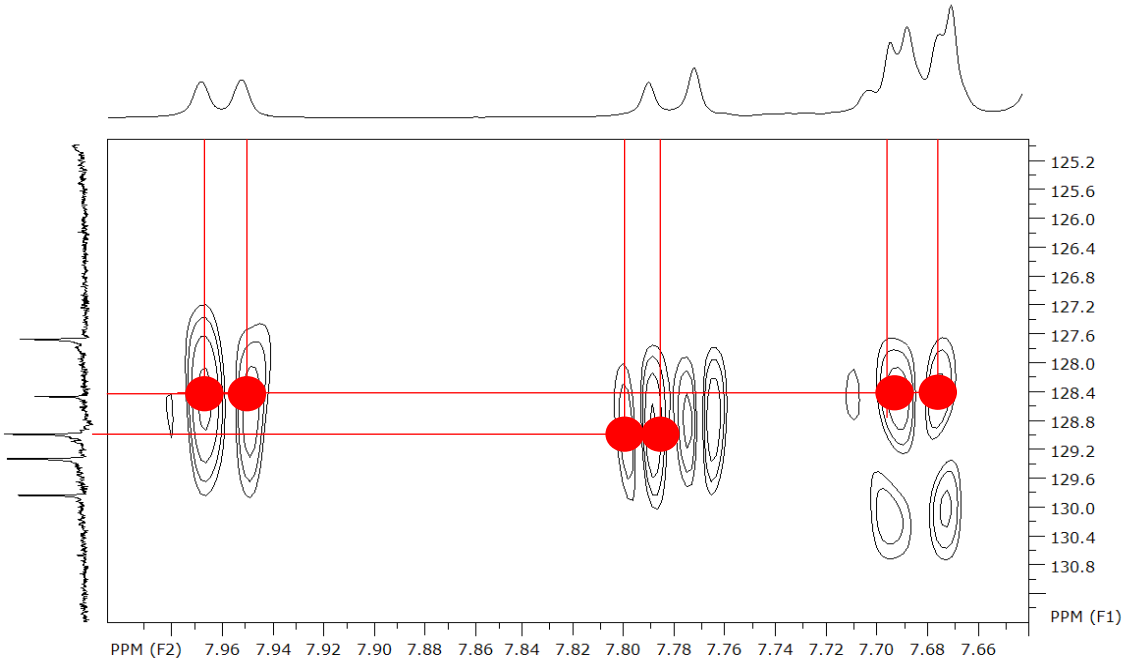


Figure 73: A magnified region of the gHMBC spectrum for KA161. The region specifically shows the coupling over three bonds between the hydrogens signals with a chemical shift of 7.68 ppm, 7.78 ppm, and 7.96 ppm to the carbons with chemical shifts of 128.6 ppm, 129.1 ppm, and 129.1 ppm respectively. The 7.96 ppm hydrogen may couple to the carbon at 127.8 ppm and a slight warping in the 2-D signal can be seen.

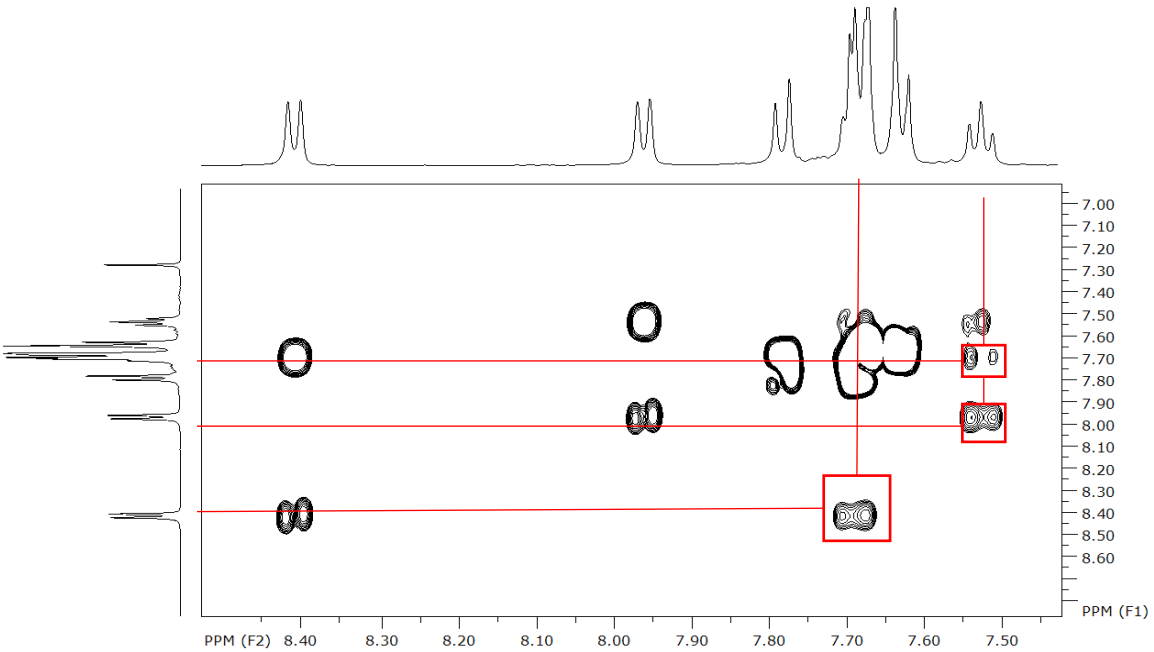
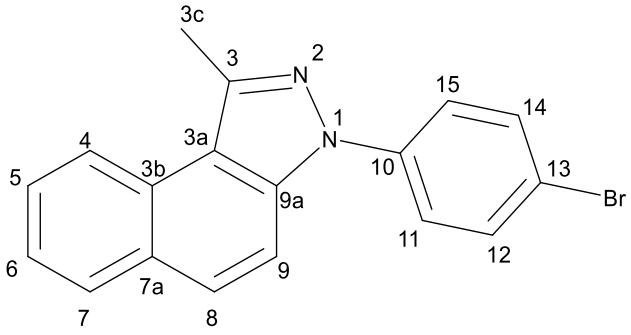


Figure 74: The magnified aromatic region of the gCOSY spectrum for KA161. Where the horizontal and vertical lines intersect shows coupling over three bonds between hydrogens for the signals under consideration. The hydrogen with a chemical shift of 7.52 ppm couples to the hydrogens with chemical shifts of 7.68 ppm and 7.96 ppm. The hydrogen with a chemical shift of 7.68 ppm couples to the hydrogen with a chemical shift of 7.62 ppm as well.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	N/A	15.8
3a	N/A	118.6
3b	N/A	128.6
3c	2.97	15.8
4	8.41	122.9
5	7.68	127.8
6	7.52	124.5
7	7.96	129.1
7a	N/A	129.5
8	7.78	132.7
9	7.68	132.7
9a	N/A	138.3
10	N/A	120.2
11	7.68 or 7.62	111.1 or 124.9
12	7.68 or 7.62	111.1 or 124.9

Figure 75: Structural data for KA161. (Left) The proposed structure and number system for compounds KA161 (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

signals with a chemical shift of 7.62 ppm coupled over three bonds to the carbon with a chemical shift of 120.4 ppm and to the hydrogen multiplet signal with a chemical shift of 7.68 ppm (Fig.73). The hydrogen with a chemical shift of 7.62 ppm coupled over one bond to the carbon with a chemical shift of 124.9 ppm (Fig.72). The multiplet hydrogen signal with a chemical shift of 7.68 ppm couples to the remaining carbon signal with a chemical shift of 139.0 ppm, over one bond (Fig.72). The hydrogens signals with chemical shifts of 7.62 ppm and 7.68 ppm, and the carbons they coupled to over one bond, are assigned to positions 11/15 or 12/14. The complete position assignments can be seen in Fig.73.

4.8 KA146

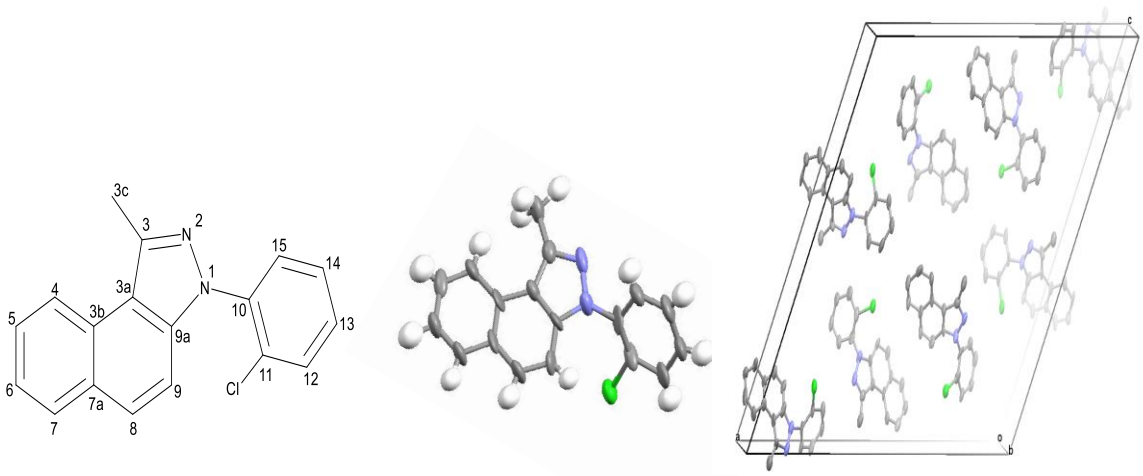


Figure 76: X-ray crystal structure and packing scheme of KA146. Grey, blue, and white elipsoids are representative of carbon, nitrogen, and hydrogen respectively. (Left) The numbering and line structure of KA146. (Middle) The crystal solution for the individual molecule. (Right) The packing scheme of KA146 unit cell with denotation of cell lengths a, b, and c (hydrogen solutions are removed for ease of viewing).

Via the crude GC/MS and crude NMR spectrum **KA146** was produced in 80% yields from 2-chloro-phenyl hydrazine and 1-acetyl-2-napthol (appendix H). **KA146** MP was 89.7-90.0°C (± 0.1°C). The compound was originally identified using x-ray crystallography. The x-ray structure is represented in Fig.76. The cell lengths and angles were as follows; a = 24.492, b = 4.3582, c = 28.295, α = 90°.0, β = 112.7°, γ = 90.0°. **KA146** was shown to pack in a monoclinic cell with a P 21/c space group (Fig.76). The crystal structure was twinned, weakly diffracting, and contained many errors (appendix H). The molecular formula ($C_{18}N_2H_{13}Cl$) was verified using high performance mass

spectrometry (appendix H). No in-depth analysis of the crystal structure was possible, but the chemical structure was identifiable.

Twelve peaks were observed in the ^{1}H-NMR spectrum (Fig.77). Ten of the twelve peaks were attributed to the compound of interest, while the remaining two peaks were indicative of the solvent dimethyl sulfoxide (DMSO) and water contamination. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.25 ppm, 7.65 ppm, 7.77 ppm, 7.85 ppm, 8.04 ppm, and 8.42 ppm, were assigned a relative integration of one. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 7.54 ppm and 7.72 ppm and an integration of one. The hydrogen signal at a chemical shift of 7.60 ppm had an unknow multiplicity, but was considered a multiplet and had an integration of two. ^{1}H signals, with a multiplicity of one (singlet), had chemical shifts of 2.88 ppm and an integration of three. The experimental ^{1}H signals are congruent with the expected signals in respect to the number, multiplicity, and integration of signals predicted from the crystal structure, if the multiplet signal at a chemical shift of 7.60 ppm is representative of two

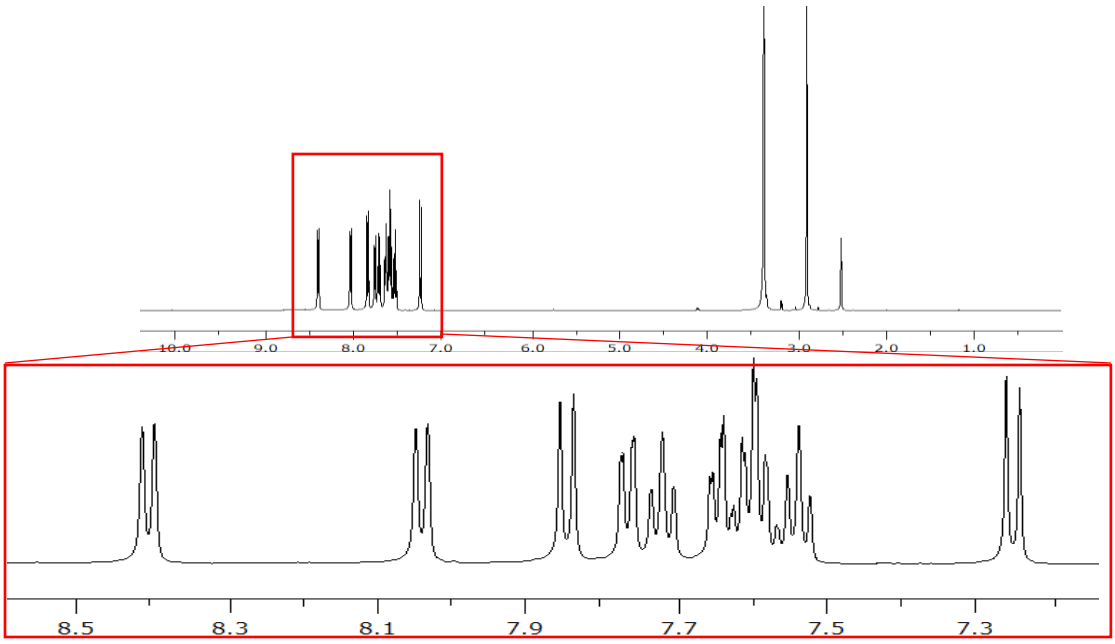


Figure 77: The ^{1}HNMR spectrum for KA146. (Top) The full ^{1}H-NMR spectrum for KA146. There are 10 hydrogen signals originating from KA146, as well as, two signals corresponding to a solvent and water peaks. The peaks of interest include 2.88 ppm (singlet), 7.25 ppm (doublet), 7.54 ppm (triplet), 7.60 ppm (multiplet), 7.65 ppm (doublet), 7.72 ppm (triplet), 7.77 ppm (doublet), 7.85 ppm (doublet), 8.04 ppm (doublet), and 8.42 ppm (doublet). (Bottom) The magnified aromatic region of the spectrum with observable multiplicities.

triplet hydrogen signals (Fig.77). The ^{13}C -NMR had 18 unique carbon signals: 17 in the aromatic region and one in the alkyl region (Fig.78).

^{1}H and ^{13}C chemical shifts were correlated via gHSQC, HMBC, and gCOSY. The gHSQC showed that the alkyl hydrogens, at a chemical shift of 2.88 ppm, and the alkyl carbon, at a chemical shift of 15.4 ppm, coupled over one bond to each other (Fig.79). The alkyl hydrogens and the alkyl carbon were assigned to position 3c in Fig.2. Over three bonds the position 3c carbon did not couple to any hydrogens, but the position 3c hydrogens coupled to two different carbons (Fig.80). It was not expected for the position 3c hydrogens to couple to two different carbons over three bonds, based on the crystal structure. However, this observation is explained by hydrogen to carbon coupling over two bonds: if coupling over two bonds occurred then the crystal structure does not deviate from the gHMBC. The position 3 carbon did not couple to any other hydrogens over two or three bonds (Fig.80). In addition, the carbon coupling over three bonds to the position 3c hydrogens, represented as carbon 3a in fig. 2, would couple to the two hydrogen doublet signals at chemical shifts of 7.25 ppm and 8.42 ppm (Fig.80). Based on the gHMBC the previous statements were verified and carbons 3 and 3a were confirmed to be the carbon signals with chemical shifts 144.0 ppm and 116.5 ppm respectively.

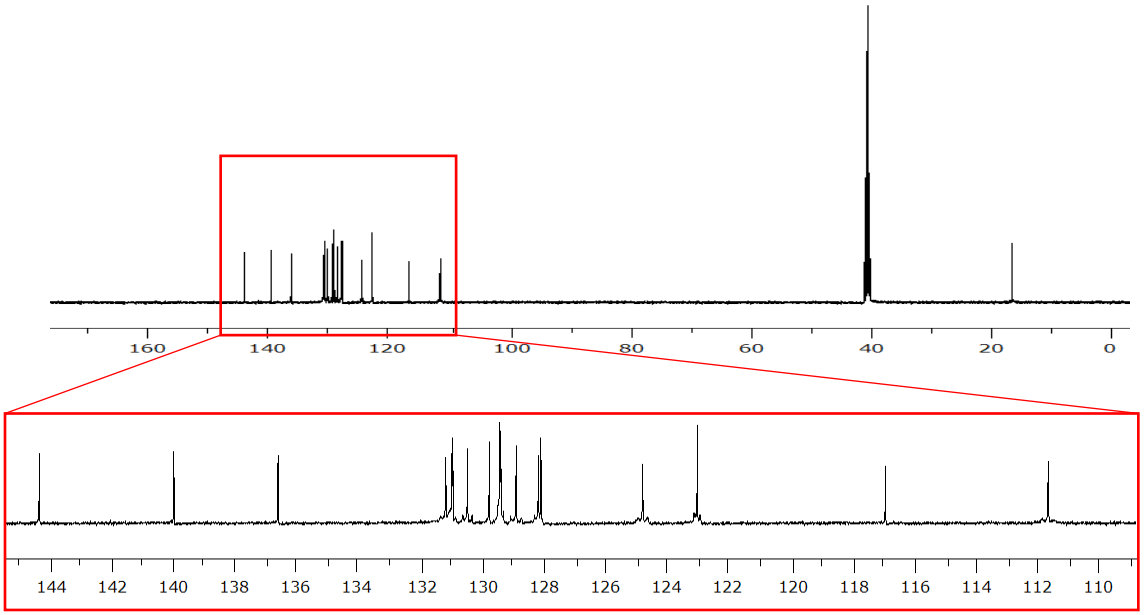


Figure 78: The $^{13}CNMR$ spectrum for KA146. (Top) The full ^{13}C-NMR spectrum for KA146. There are 18 carbons originating from KA146, as well as, one signal corresponding to a solvent peak. The peaks of interest include 15.3 ppm, 111.2 ppm 116.5 ppm, 122.6 ppm, 124.4 ppm, 127.7 ppm, 127.8 ppm, 128.5 ppm, 128.97 ppm, 129.00 ppm, 129.4 ppm, 130.1 ppm, 130.5 ppm, 130.6 ppm, 130.8 ppm, 136.2 ppm, 139.6 ppm, and 144.0 ppm. (Bottom) The magnified aromatic region of the spectrum.

Over one bond, the hydrogen signals with chemicals shifts of 7.25 ppm and 8.42 ppm were coupled to the carbon signals with chemical shifts of 111.2 ppm and 122.6 ppm respectively (Fig.81). The 7.49 ppm and 111.2 ppm hydrogen and carbon were assigned to position 9. The 8.42 ppm hydrogen and 122.6 ppm carbon were assigned to position 4. Over three bonds the carbon at position 4 coupled to the hydrogen triplet signal at a chemical shift of 7.54 ppm (Fig.82). The triplet signal was then assigned to position 6. The

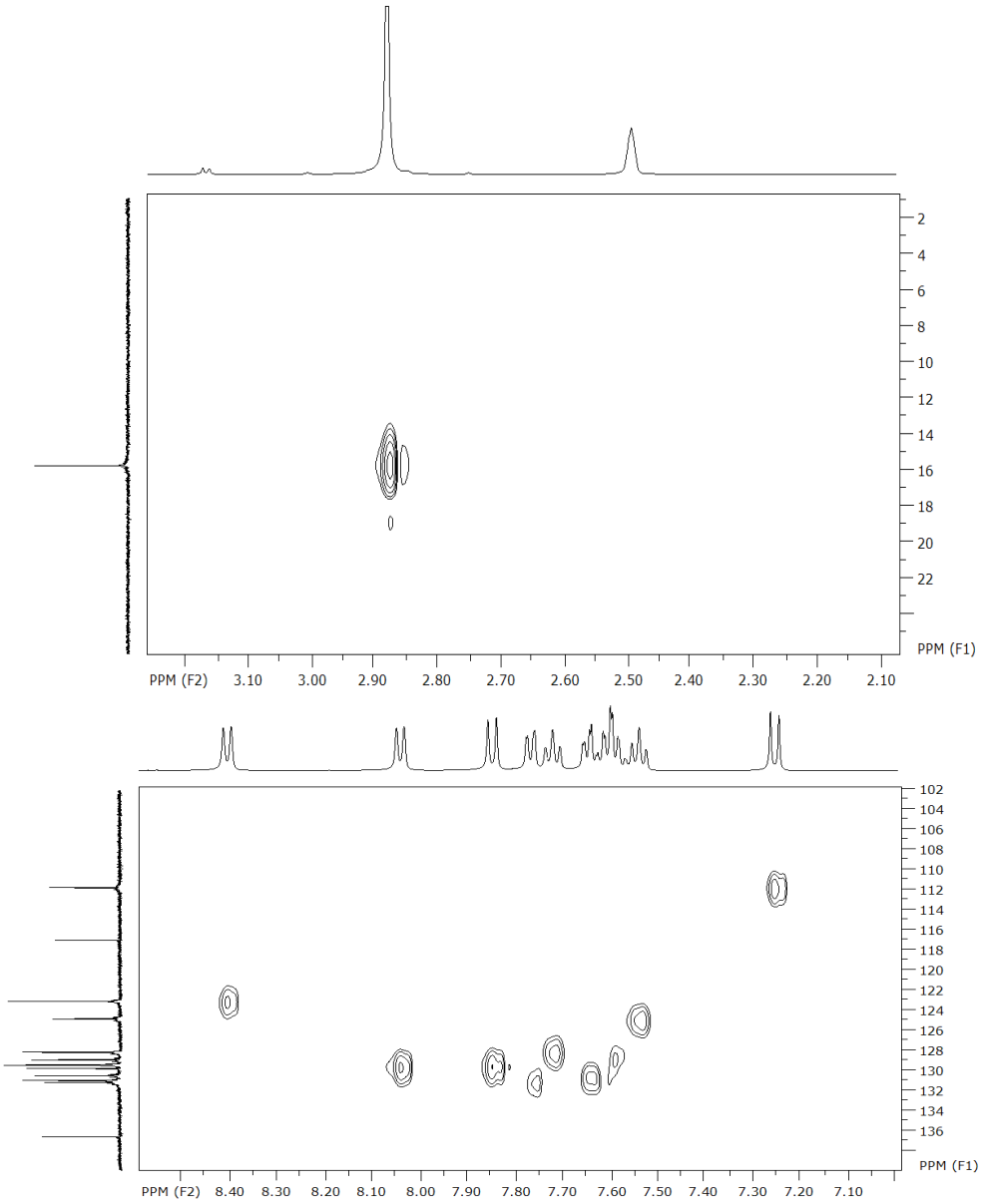


Figure 79: The gHSQC for KA146. (Top) Magnified alkyl region. (Bottom) Magnified aromatic region. Coupling over one bond can be seen between hydrogens (x-axis) and carbons (y-axis).

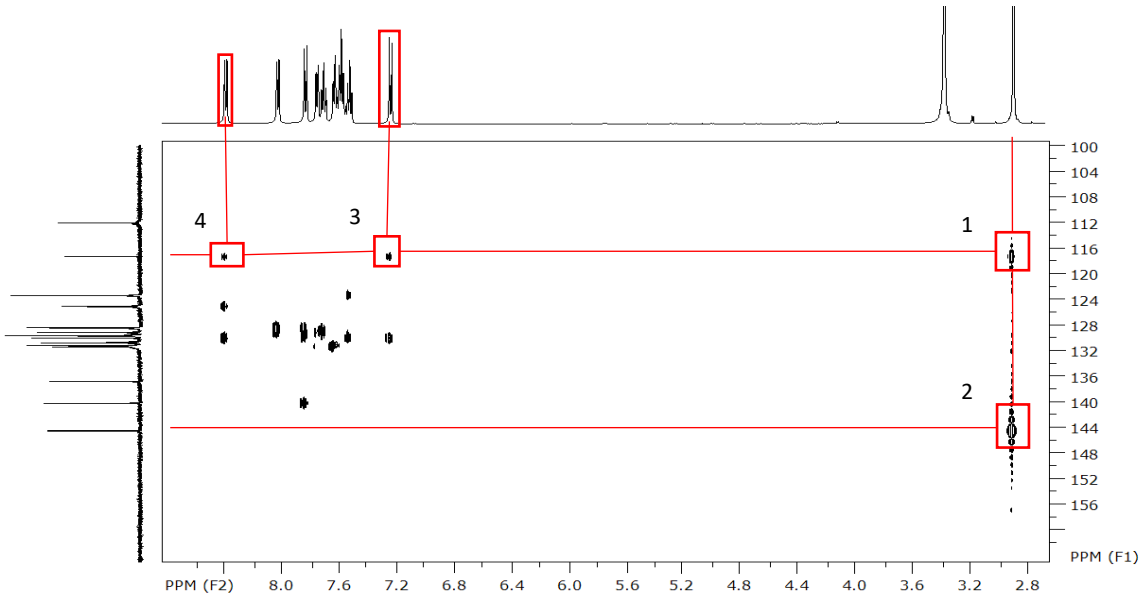


Figure 80: The gHMBC for KA146. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with and chemical shift of 2.88 ppm and the carbons at 116.5 ppm and 144.0 ppm respectively. The horizontal and vertical lines intersect where the hydrogens and carbons couple over three bonds. Boxes 3 and 4 represent carbon/hydrogen coupling between the carbon with a chemical shift of 116.0 ppm and the doublet hydrogens with chemical shifts of 7.25 ppm.

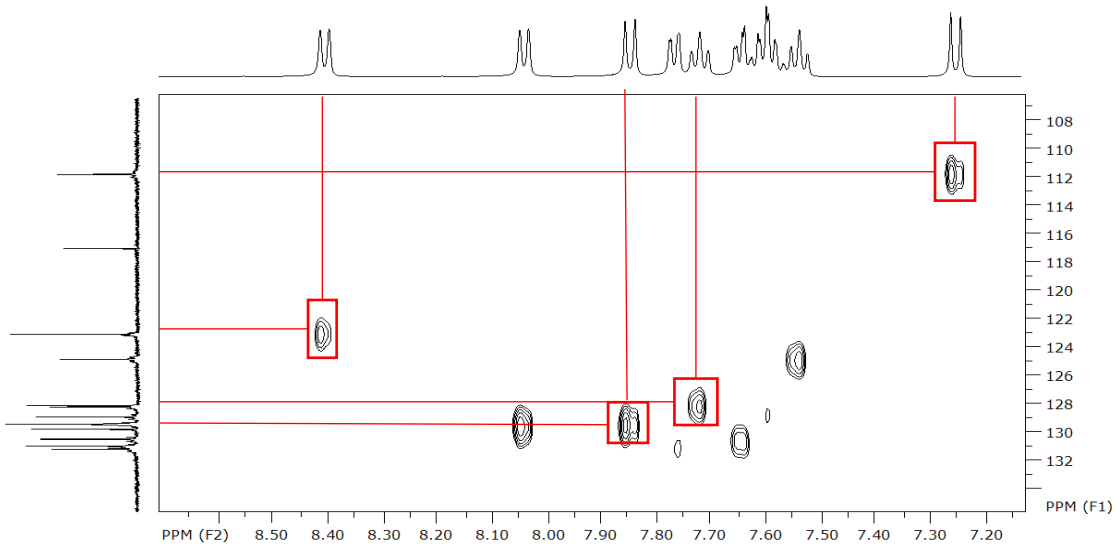


Figure 81: The aromatic region of the gHSQC for KA146. Where the horizontal and vertical lines intersect show coupling over one bond between carbons and hydrogens. Over one bond, the carbon at a chemical shift of 111.2 ppm is coupling to the hydrogen doublet signal at a chemical shift of 7.25. Over one bond, the carbon at a chemical shift of 127.8 ppm is coupling to the hydrogen doublet signal at a chemical shift of 7.72 ppm. Over one bond, the carbon at a chemical shift of 122.6 ppm is coupling to the hydrogen doublet signal at a chemical shift of 8.42 ppm. Over one bond, the carbon at a chemical shift of 129.4 ppm is coupling to the hydrogen doublet signal at a chemical shift of 8.45 ppm.

carbon at position 9 should not have coupled to any hydrogens over one or three bonds, and indeed this was observed (Fig.83 & 84).

The position 4, 6, and 9 hydrogens coupled over three bonds to the carbon signal at a chemical shift 129.4 ppm (Fig.83). Over three bonds the position 6 hydrogen triplet coupled to the triplet and doublet hydrogen signals at chemical shifts of 7.72 ppm and 8.04 ppm respectively (Fig.84). The triplet signal with the chemical shift of 7.72 ppm was assigned to position 5.

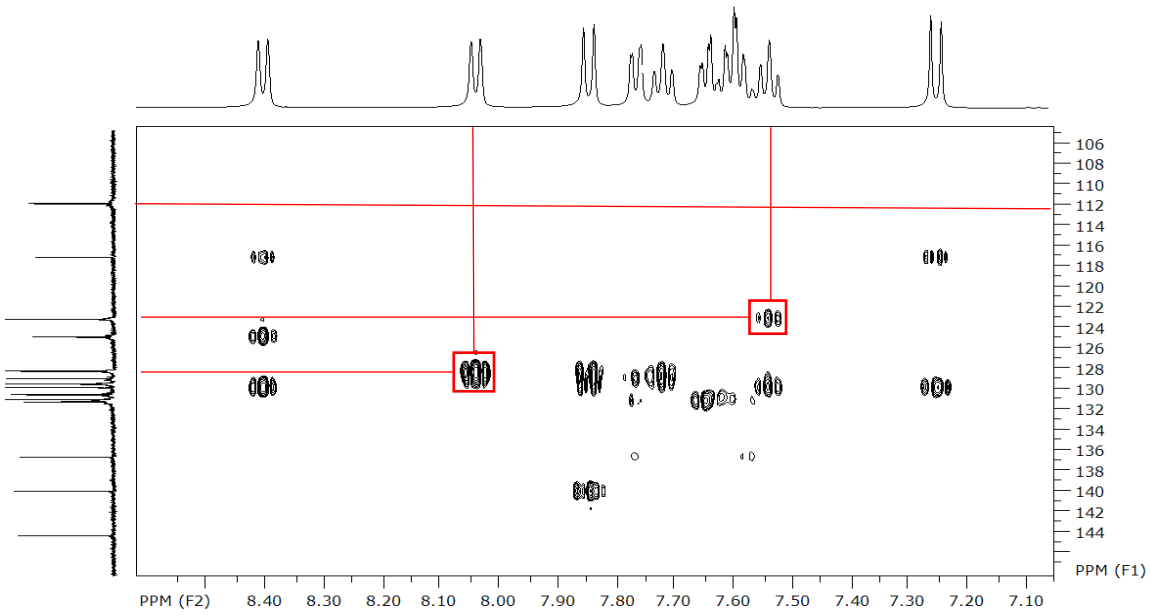


Figure 82: The aromatic region of the gHMBC for KA146. Where the horizontal and vertical lines intersect show interactions over three bonds between carbons and hydrogens. Over three bonds, the carbon at 111.2 ppm is coupling to no hydrogens. Over three bonds, the carbon at 127.8 ppm is coupling to one hydrogen doublet signal at a chemical shift of 8.04 ppm. Over three bonds, the carbon at 124.4 ppm is coupling to one hydrogen triplet signal at a chemical shift of 8.42 ppm.

The 129.4 ppm carbon signal was defined as the carbon at position 7a. Via the gHSQC position 5 and 6 carbons are attributed to chemical shifts 127.8 ppm and 124.4 ppm, respectively (Fig.81). The position 5 carbon and position 6 hydrogen coupled over three bonds to the hydrogen signal with a chemical shift of 8.04 ppm (Fig.84). Over one bond the hydrogen signal at a chemical shift of 8.04 ppm coupled to either the carbon signal with a chemical shift of 128.97 ppm or the carbon signal with a chemical shift of 128.90 ppm (Fig.83). The carbon signals are too close together to distinguish which carbon signal

was coupling to the hydrogen signal at a chemical shift 8.04 ppm. Due to the uncertainty associated with the NMR both signals are referred to as being at a chemical shift of 129.4 ppm. The 129.4 ppm carbon signal and 8.04 ppm hydrogen signal were attributed to position 7 (Fig.83).

Over three bonds, the position 9 hydrogen coupled to the position 8 hydrogen doublet signal at a chemical shift of 7.85 ppm (Fig.84). The position 8 hydrogen couples over one bond to the carbon signal at a chemical shift of 129.4 ppm (Fig.81). Over three bonds, the position 5, 7, and 8 hydrogens couple to the carbon signal with a chemical shift of 127.7 ppm (Fig.85). The hydrogens at position 5, 7, and 8 all appear to be interacting with the carbon signals having chemical shifts of 127.7 ppm, 127.8 ppm, and 127.8 ppm. The highest coupling signal intensity is between the carbon signal with a chemical shift of 127.8 ppm, but this signal is clearly coupling to the multiplet hydrogen signal over one bond.

Via the crystal structure, the position 5, 7, and 8 hydrogens coupled to the position3b carbon and between the three-possible carbon signals the only one not coupling to a hydrogen signal over one bond is the carbon signal at a chemical shift of 127.7 ppm.

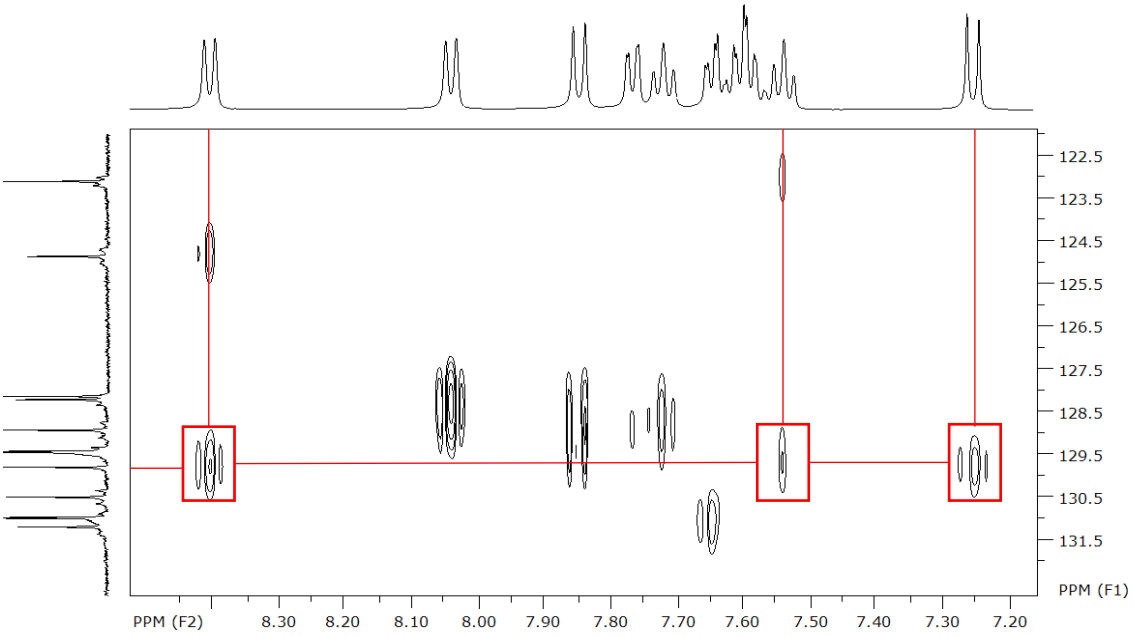


Figure 83: The aromatic region of the gHMBC for KA146. The aromatic region of the gHMBC for KA146. Where the horizontal and vertical lines intersect show interactions over three bonds between carbons and hydrogens. Over three bonds, the carbon at 129.4 ppm is coupling to the three hydrogens at chemical shifts of 7.25 ppm, 7.54 ppm, and 8.42 ppm.

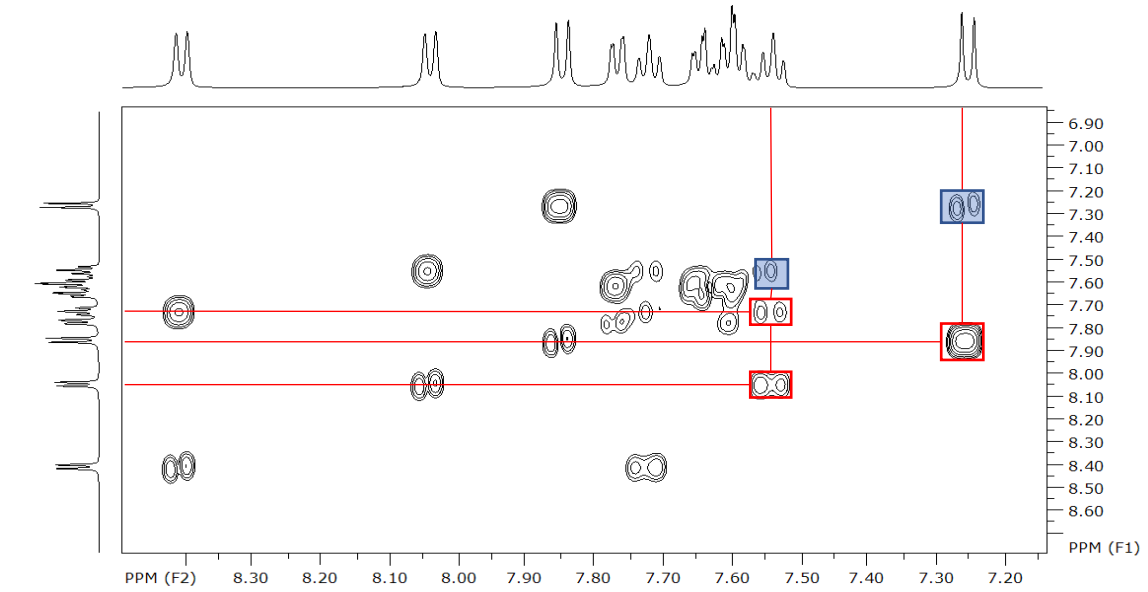


Figure 84: The aromatic region of the gCOSY spectrum for KA146. Where the horizontal and vertical lines intersect show interactions over three bonds between hydrogens. The blue boxes indicate hydrogen interactions with themselves. Over three bonds, the doublet hydrogen signal at a chemical shift of 7.25 couples to a doublet hydrogen couples to the hydrogen doublet signal at a chemical shift of 7.85 ppm. Over three bonds, the triplet hydrogen at a chemical shift 7.54 ppm couples to the triplet and doublet hydrogen signals at chemical shifts of 7.72 ppm and 8.04 ppm respectively.

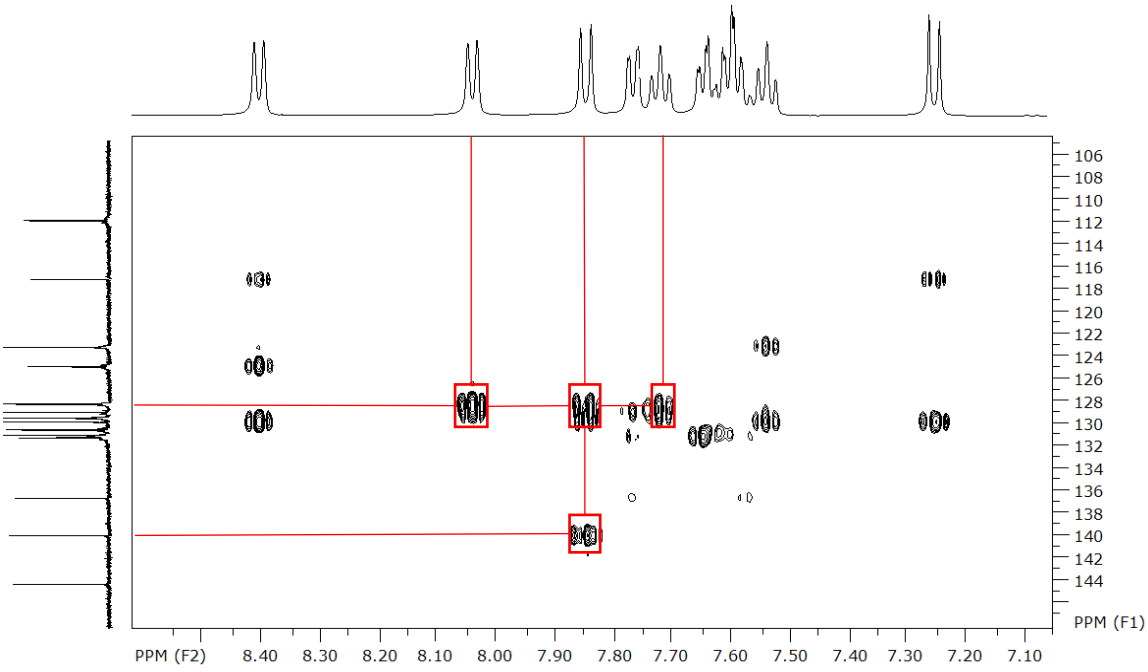
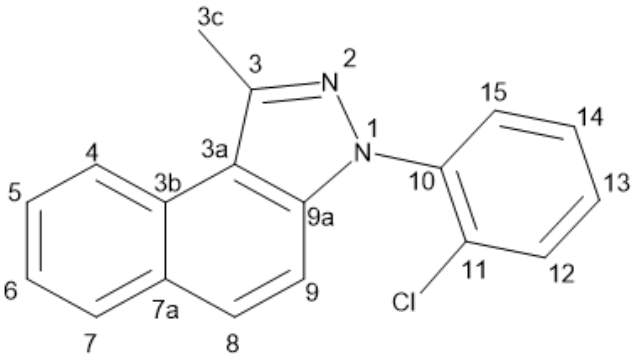


Figure 85: The aromatic region of the gHMBC for KA146. Where the horizontal and vertical lines intersect show interactions over three bonds between carbons and hydrogens. Over three bonds, the carbon at a chemical shift 127.8 ppm couples to the hydrogen signals at chemical shifts of 7.72 ppm (triplet), 7.85 ppm (doublet), and 8.04 ppm (doublet). The doublet hydrogen signal at a chemical shift of 7.85 couples to the carbon signal at a chemical shift of 140.0 ppm.

The carbon signal at a chemical shift of 127.7 ppm was assigned to position 3b. Over three bonds the position 8 hydrogen coupled to the carbon signal with a chemical shift of 139.6 ppm (Fig.85). The carbon signal with a chemical shift of 139.6 ppm couples to no hydrogens over one bond and was assigned to position 9a. The multiplet signal, with an integration of two, was assumed to be the two missing triplet signals overlapping each other and was assigned positions 13 and 14. The hydrogens at position 13 and 14 were assigned to the hydrogen signal with a chemical shift of 7.60 ppm. The remaining hydrogen and carbon signals cannot be distinguished as they show the same coupling patterns over three bonds with respect to both the gCOSY and gHMBC spectra. The unassigned hydrogen signals had chemical shifts of 7.65 ppm and 7.77 ppm. The unassigned carbons had chemical shifts of 130.1 ppm, 130.5 ppm, 130.6 ppm, 130.8 ppm, and 136.2 ppm. The complete position assignments can be seen in Fig.86.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	N/A	144
3a	N/A	116.5
3b	N/A	128.1 or 128.2
3c	2.88	15.3
4	8.42	122.6
5	7.72	128.1 or 128.2
6	7.53	124.4
7	8.04	N/A
7a	N/A	129.4
8	8.85	129
9	7.25	111.2
9a	N/A	139.6
10	N/A	N/A
11	N/A	136.2
12	7.77	N/A
13	7.6	N/A
14	7.60	128.5
15	7.64	N/A

Figure 86: The structural data for KA146. (Left) The proposed structure and number system for compounds KA146 (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position.

4.9 KA171

Via the crude NMR spectrum **KA171** was produced in 70% yields from 3-nitro-phenyl hydrazine and 1-acetyl-2-napthol (appendix I). **KA171** MP was 168.4-168.6°C (± 0.2°C). The compound was a yellow white fluffy solid. The molecular formula ($C_{18}N_3H_{13}O_2$) was verified using high performance mass spectrometry (appendix I). The compounds proposed structure is seen in Fig.87.

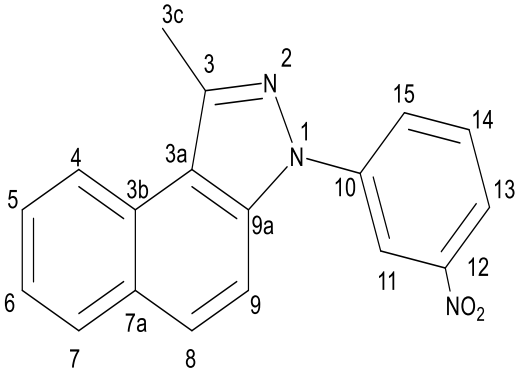


Figure 87:The predicted structure for KA171 and its numbering assignments.

Eleven peaks were observed in the ^{1}H-NMR spectrum (Fig.88). Nine of the eleven peaks were attributed to the compound of interest, while the remaining two peaks were indicative of the solvent dimethyl sulfoxide (DMSO) and water contamination. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 8.21 ppm, 8.26 ppm, and 8.39 ppm, were assigned a relative integration of one. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 7.56 ppm, 7.72 ppm, and 7.85 ppm,

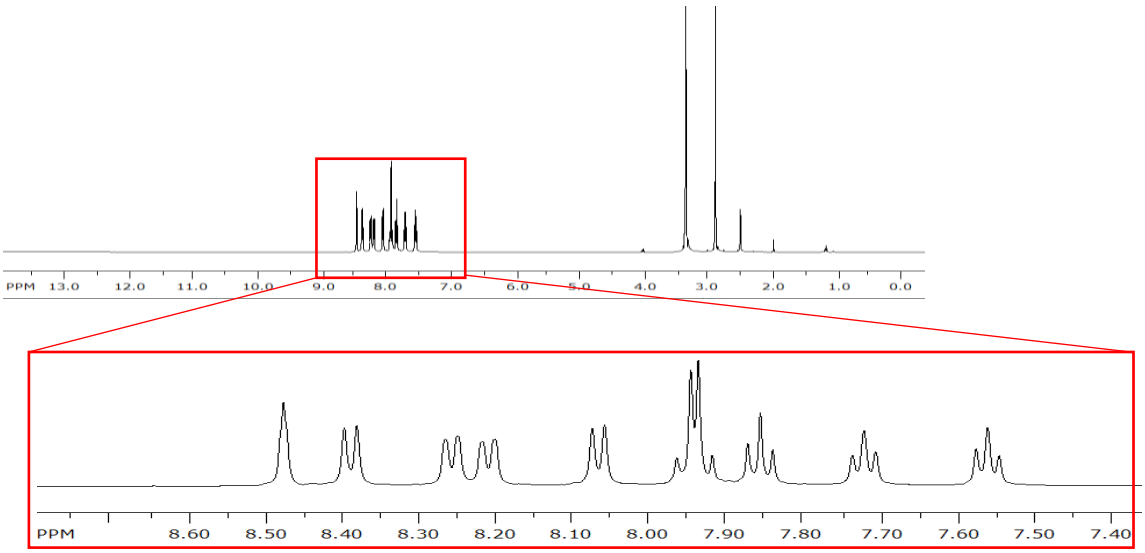


Figure 88: The ^{1}HNMR for KA171. (Top) The full ^{1}H-NMR spectrum for KA171. There are 10 hydrogen signals originating from KA171, as well as, two signals corresponding to a solvent and water peaks. The peaks of interest include 2.88 ppm (singlet), 7.56 ppm (triplet), 7.72 ppm (triplet), 7.86 ppm (triplet), 7.94 ppm (multiplet), 8.07 ppm (doublet), 8.21 ppm (doublet), 8.26 ppm (doublet), 8.39 ppm (doublet), and 8.48 (singlet). (Bottom) The magnified aromatic region of the spectrum with observable multiplicities.

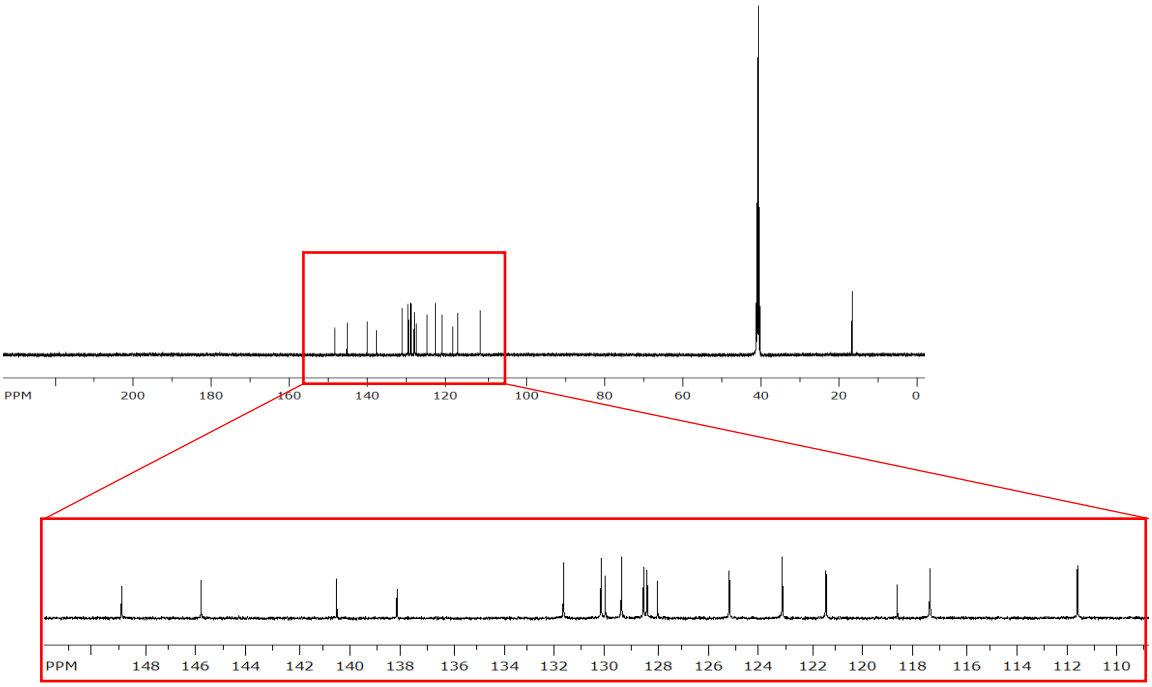


Figure 89: The ^{13}CNMR for KA171. (Top) The full ^{13}C-NMR spectrum for KA171. There are 18 carbons originating from KA171, as well as, one signal corresponding to a solvent peak. The peaks of interest include 15.4 ppm, 111.1 ppm, 116.9 ppm, 118.2 ppm, 120.9 ppm, 122.6 ppm, 124.7 ppm, 127.5 ppm, 127.9 ppm, 128.1 ppm, 128.9 ppm, 129.6 ppm, 129.7 ppm, 131.2 ppm, 137.7 ppm, 140.1 ppm, 145.4 ppm, and 148.5 ppm. (Bottom) The magnified aromatic region of the spectrum.

and had an integration of one. The hydrogen signal at a chemical shift of 7.94 ppm had an unknow multiplicity, but was considered a multiplet and had an integration of two. ^{1}H signals, with a multiplicity of one (singlet), had chemical shifts of 2.88 ppm and 8.48 ppm, and had integrations of three and one respectively. The experimental ^{1}H signals are congruent with the expected signals in respect to the number, multiplicity, and integration of signals predicted from the structure in fig. 2, if the multiplet signal at a chemical shift of 7.94 ppm was representative of two hydrogen doublet signals. The ^{13}C -NMR had 18 unique carbon signals: 17 in the aromatic region and one in the alkyl region (Fig.89).

^{1}H and ^{13}C chemical shifts were correlated via HSQC and gHMBC spectrum. The HSQC spectra showed that the alkyl hydrogens, at a chemical shift of 2.88 ppm, and the alkyl carbon, at a chemical shift of 15.4 ppm, coupled over one bond (Fig.90). The alkyl hydrogen signal and the alkyl carbon signal were assigned to position 3c in Fig.2. Over three bonds the position 3c carbon did not couple to any hydrogens, but the position 3c hydrogens coupled to the hydrogens with chemical shifts of 118.2 ppm and 145.4 ppm

(Fig.91). It was not expected for the position 3c hydrogens to couple to two different carbons over three bonds. However, this observation is explained by hydrogen to carbon coupling over two bonds; if coupling over two bonds occurred, then the structure does not deviate from the gHMBC spectra.

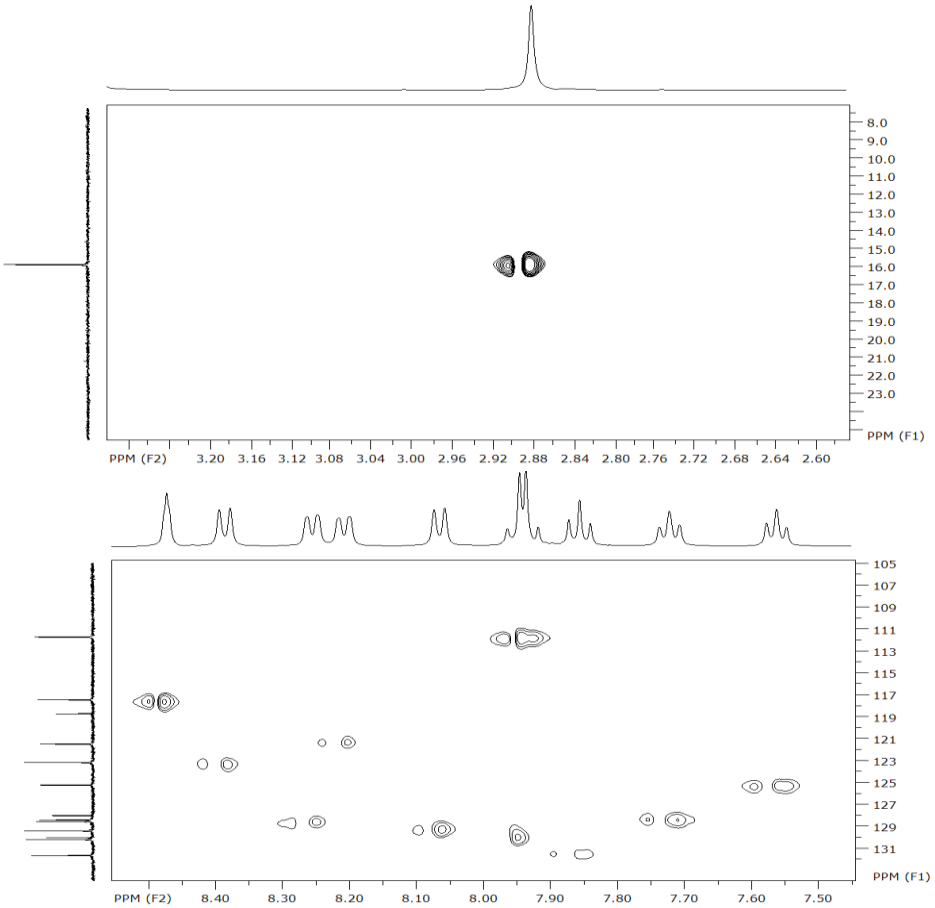


Figure 90: The HSQC sprectra for KA171. (Top) The magnified alkyl region. (Bottom) The magnified aromatic regions. Coupling over one bond can be seen between hydrogens (x-axis) and carbons (y-axis).

A carbon coupling over two bonds to the hydrogens at position 3c would not couple over three bonds to any hydrogens. A carbon coupling over three bonds to the position 3c hydrogens would couple to two different hydrogen signals over three bonds. The carbon signal with a chemical shift of 145.4 ppm coupled over three bonds to no hydrogen signals and the carbon signal with a chemical shift of 118.2 ppm coupled over three bonds to hydrogen signals with chemical shifts of 7.94 ppm and 8.39 ppm (Fig.91). The coupling pattern verified that the carbons with chemical shifts of 145.4 ppm and 118.2 ppm coupled

over two and three bonds to the position 3c hydrogens. The carbons with chemical shifts of 145.4 ppm and 118.2 ppm were assigned to positions 3 and 3a, respectively.

The hydrogen signal with a chemical shift of 8.39 ppm coupled to the carbon with a chemical shift of 122.6 ppm over one bond and over three bonds to the carbon signals with chemical shifts of 124.7 ppm and 129.6 ppm (Fig 92, Fig.93). Over one bond the carbon with a chemical shift of 124.7 ppm coupled to a triplet hydrogen signal with a chemical shift of 7.56 ppm (Fig.92). The hydrogen signal with a chemical shift of 7.56 ppm coupled over three bonds to the carbon with a chemical shift of 129.6 ppm (Fig.9). The carbon with a chemical shift of 129.6 ppm coupled to no hydrogens over one bond (Fig.92). Over three bonds, the multiplet signal with a chemical shift of 7.94 ppm coupled to the carbon with a chemical shift of 129.6 ppm. From these data the 4, 6, and 7a positions were assigned to the carbon chemical shifts of 122.6 ppm, 124.7 ppm, and 129.6 ppm, respectively. The hydrogens for positions 4, 6, and 9 were assigned the hydrogen signals with chemical shifts of 8.39 ppm, 7.56 ppm and 7.94 ppm, respectively.

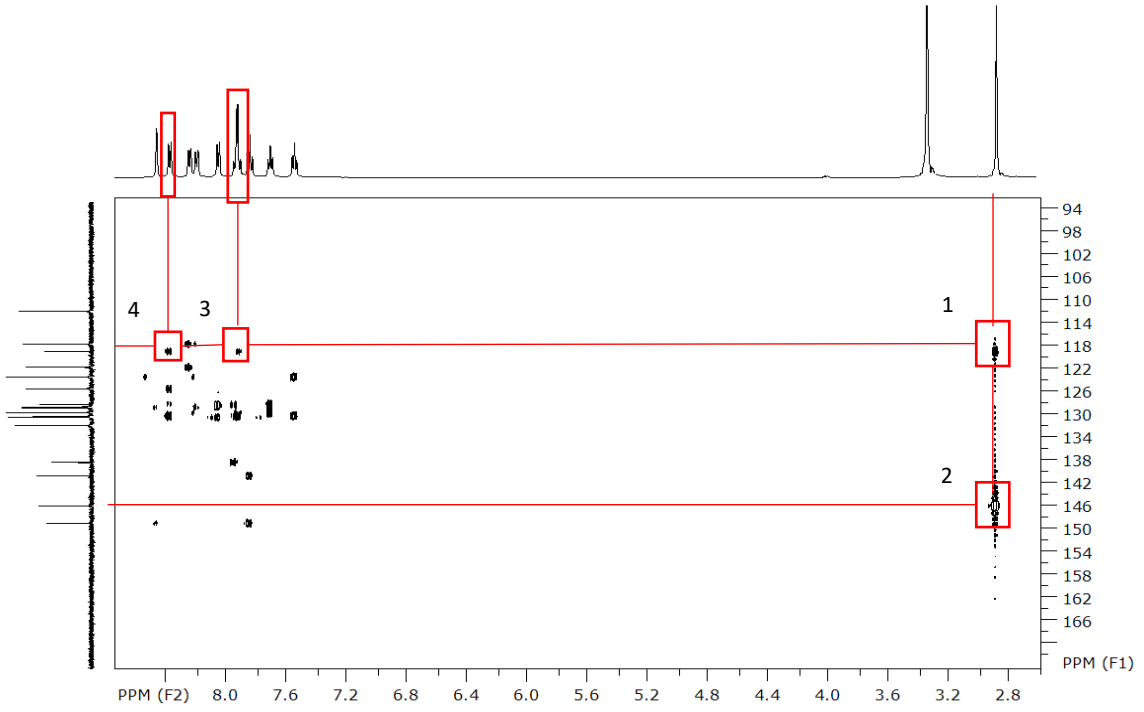


Figure 91: The gHMBC spectra for KA171. Where horizontal and vertical lines intersect with a boxe shows coupling between hydrogen and carbon signals over three bonds. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with a chemical shift of 2.88 ppm and the carbons with chemical shifts of 117.0 ppm and 144.8 ppm respectively. Boxes 3 and 4 represent carbon/hydrogen coupling between the carbon with a chemical shift of 117.0 ppm and the multiplet hydrogen signal with chemical shifts of 8.39 ppm and 7.94 ppm respectively.

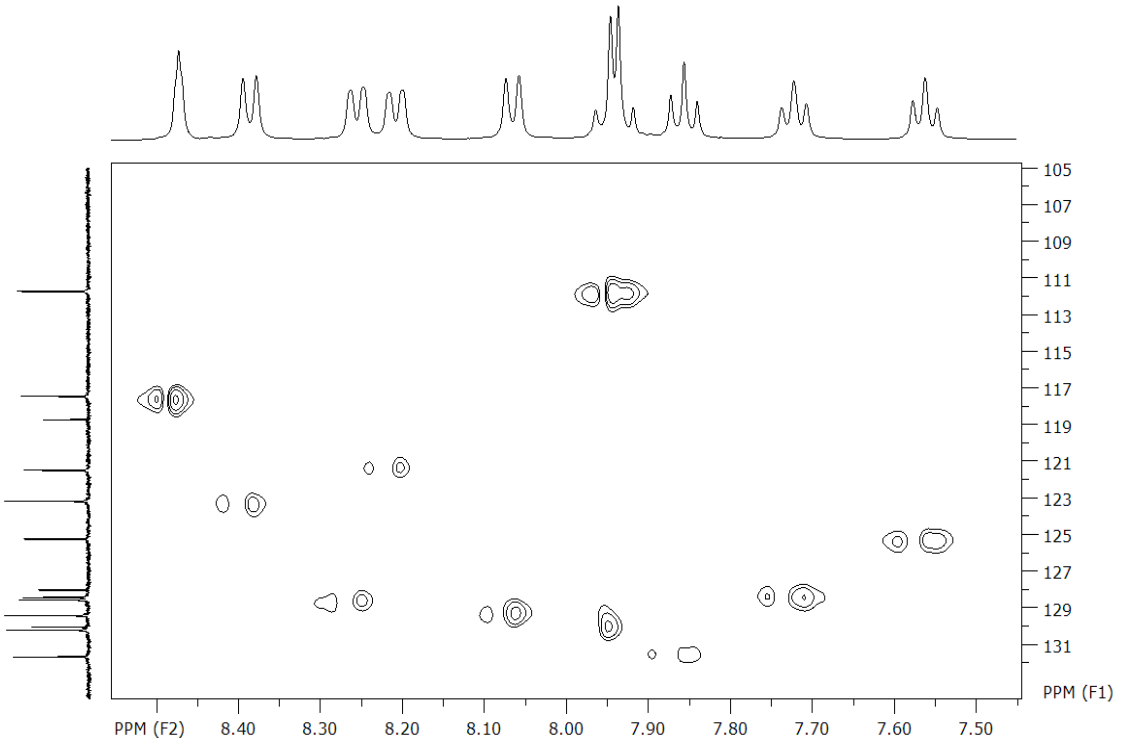


Figure 92: The aromatic region of HSQC spectra for KA171. The hydrogen signals with chemical shifts of 7.56 ppm, 7.72 ppm, 7.86 ppm, 8.07 ppm, 8.21 ppm, 8.26 ppm, 8.39 ppm, and 8.48 ppm couple to the carbons with the chemical shifts of 124.7 ppm, 127.9 ppm, 131.2 ppm, 128.9 ppm, 120.9 ppm, 128.1 ppm, 122.6 ppm, and 116.9 ppm respectively. The multiplet hydrogen signal with a chemical shift of 7.94 couples to the carbon signals with chemical shifts of 111.1 ppm and 129.7 ppm.

The multiplet hydrogen signal with a chemical shift of 7.94 ppm coupled to the two carbons with chemical shifts of 129.7 ppm and 111.1 ppm over one bond (Fig.92). The carbon with a chemical shift of 111.1 ppm coupled to no hydrogens over three bonds. The carbon with a chemical shift of 129.7 ppm coupled over three bonds to the hydrogen with a chemical shift of 8.07 ppm (Fig.94). The hydrogen with a chemical shift of 8.07 ppm coupled over one bond to the carbon with a chemical shift 128.9 ppm (Fig.92). Over three bonds the carbon with a chemical shift of 128.9 ppm coupled to the triplet hydrogen signal with a chemical shift of 7.72 ppm (Fig.94). Over three bonds the hydrogen signal with a chemical shift of 7.72 ppm coupled to the carbon signal with a chemical shift of 127.5 ppm (Fig.94). Over three bonds the carbon with a chemical shift of 127.5 ppm coupled to the hydrogen with a chemical shift of 8.07 ppm (Fig.94). The carbons with chemical shifts of 111.1 ppm, 127.5 ppm, 127.9 ppm, 128.9 ppm, and 129.7 ppm were assigned to positions 9, 3b, 5, 7, and 8; it was the only arrangement that exhibited the coupling patterns described above. Similarly, the hydrogens with chemical shifts of 7.72 ppm and 8.07 ppm were

assigned to positions 5 and 7. The multiplet signal with a chemical shift of 7.94 ppm could only be assigned to positions 8 and 9.

Via the gHMBC, The singlet hydrogen signal with a chemical shift of 8.48 ppm appeared to couple to the four carbon signals with chemical shifts of 120.9 ppm, 128.1 ppm, 140.1 ppm, and 148.5 ppm (Fig.95). This was explained by the hydrogen coupling to carbon signals over two bonds. The carbon signals with chemical shifts of 120.9 ppm and 128.1 ppm coupled over one bond to the doublet hydrogen signals with chemical shifts of 8.21ppm and 8.26 ppm respectively (Fig.92). The remaining triplet signal with a chemical shift of 7.86 ppm coupled over one bond to the carbon with a chemical shift 131.2 ppm and over three bonds to the carbons with chemical shifts of 140.1 ppm and 148.5 ppm (Fig.92, Fig.93).

This verifies that the carbons with chemical shifts of 120.9 ppm and 128.1 ppm were two coupling to the hydrogen signal with a chemical shift of 8.48 ppm over two bonds. The number and multiplicity of the hydrogen signals was indicative of a 1,3-substituted

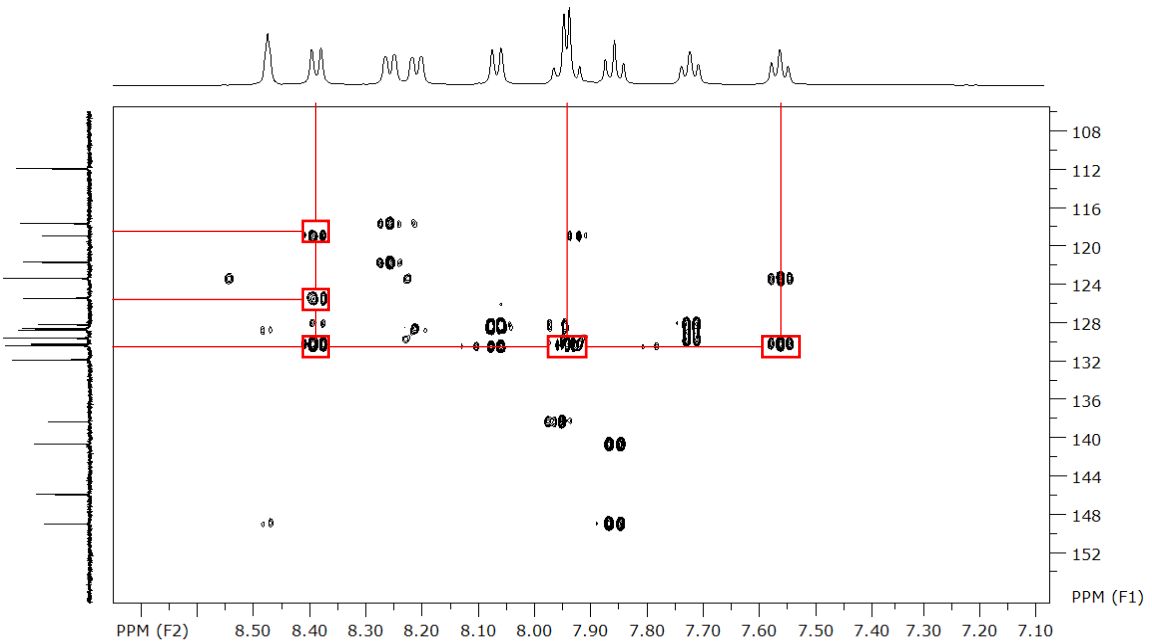


Figure 93: The aromatic region of the gHMBC spectra for KA171. Where the horizontal and vertical lines intersect with a box shows the coupling patterns under consideration. Coupling occurs of 3 bonds. The hydrogen signal with a chemical shift of 7.56 ppm couples to the carbon with a chemical shift of 129.6 ppm. The hydrogen signal with a chemical shift of 7.94 ppm couples to the caqrbon with a chemical shift of 129.6 ppm. The hydrogen at a chemical shift of 8.39 ppm couples to the carbons with chemical shifts of 118.2 ppm, 124.7 ppm, and 129.6 ppm.

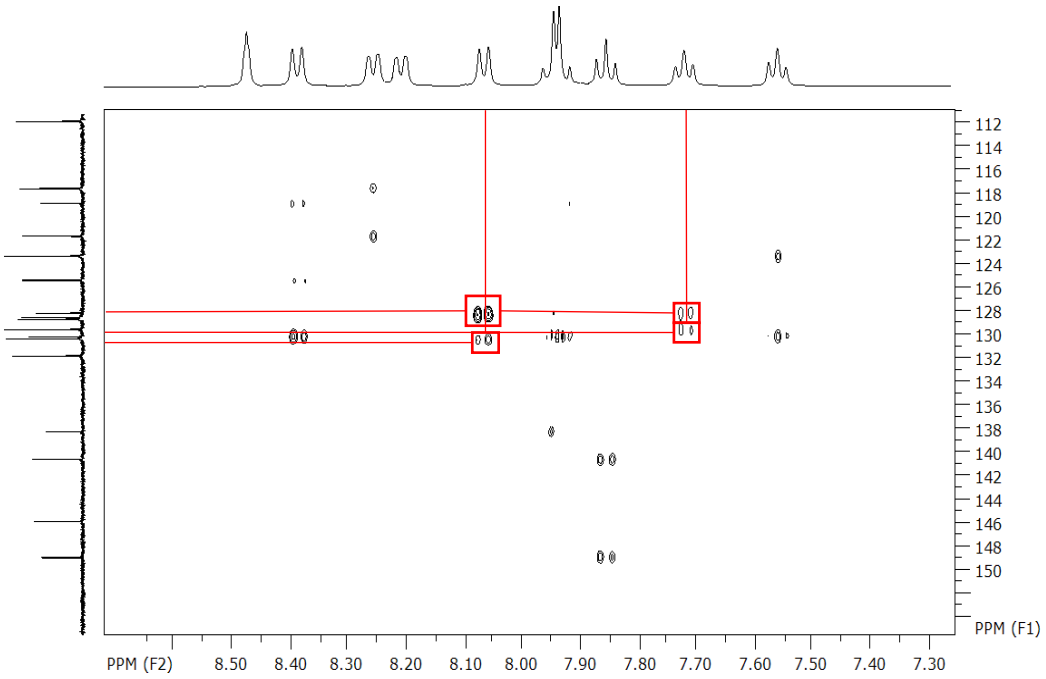


Figure 94: The aromatic region of the gHMBC spectra for KA171. Where the horizontal and vertical lines intersect with a box shows the coupling patterns under consideration. Coupling occurs of 3 bonds. The hydrogen signal with a chemical shift of 7.72ppm couples to the carbons with chemical shifts of 127.5 ppm and 128.9 ppm. The hydrogen with a chemical shift of 8.07 ppm couples to the carbons with chemical shifts of 129.7 ppm and 127.9 ppm.

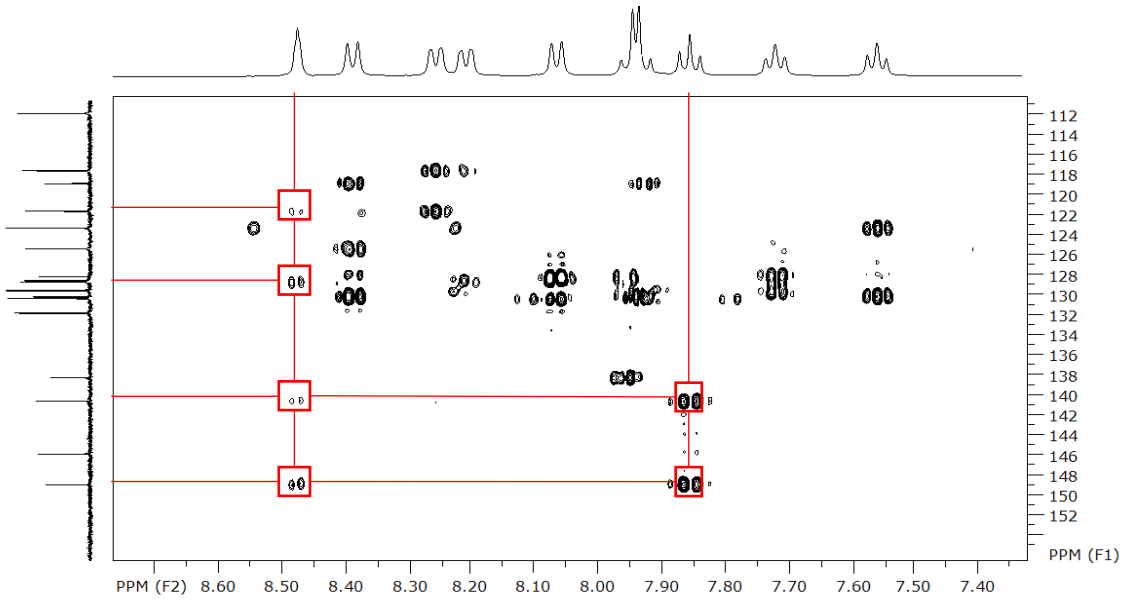
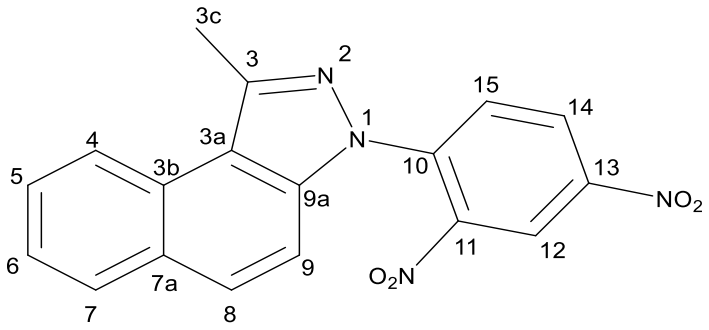


Figure 95: The aromatic region of the gHMBC spectra for KA171. Where the horizontal and vertical lines intersect with a box shows the coupling patterns under consideration. The hydrogen signal with a chemical shift of 7.86 ppm couples to the carbon signals with chemical shifts of 140.1 ppm and 148.5 ppm. The hydrogen signal with a chemical shift of 8.39 ppm couples to the carbon signals with chemical shifts of 118.2 ppm, 124.7 ppm, 127.5 ppm, and 129.6 ppm

phenyl ring. The hydrogen and carbon with chemical shifts of 8.48 ppm and 116.9 ppm were assigned to position 11. The hydrogen and carbon with chemical shifts of 7.86 ppm and 131.2 ppm were assigned to position 14. The hydrogens and carbons at positions 13 and 15 could not be differentiated and were either the hydrogen carbon pair of 8.21 ppm and 120.9 ppm or 8.26 ppm and 128.1 ppm. The remaining carbons with chemical shifts of 140.1 ppm and 148.5 ppm could not be differentiated and belonged to either position 10 or 12. The complete position assignments can be seen in Fig.96.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	N/A	145.4
3a	N/A	118.2
3b	N/A	128.1
3c	2.88	15.4
4	8.39	122.6
5	7.72	128.1
6	7.56	124.7
7	8.07	128.9
7a	N/A	129.6
8	7.94	129.7
9	7.94	111.1
9a	N/A	N/A
10	N/A	N/A
11	8.48	116.9
12	N/A	N/A
13	8.21 or 8.26	128.1 or 120.9
14	7.86	131.2
15	8.21 or 8.26	128.1 or 120.9

Figure 96: The NMR structural data for KA171. (Left) The proposed structure and number system for compounds KA161 (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

4.10 KA156

Via the crude GC/MS spectrum **KA156** was produced in 78.5% yield from 2,4-dichloro-phenylhydrazine and 1-acetyl-2-napthol (appendix J). **KA156** MP was 168.3-173.2°C (± 3.2°C). As **KA156** melted its color profile changed from a white solid to a dark brown solid.

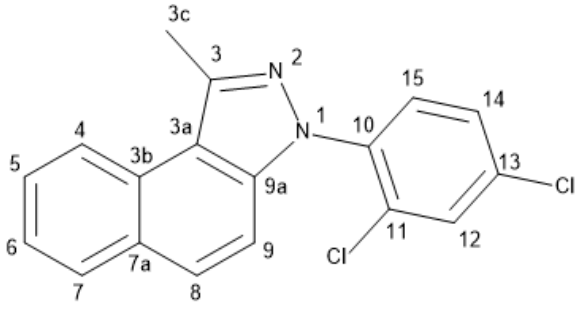


Figure 97: The predicted structure for KA156 and its numbering assignments.

The molecular formula ($C_{18}N_2H_{12}Cl_2$) was verified using high performance mass spectrometry (appendix J). The predicted structure is seen in Fig.97. One and two-dimensional NMR spectroscopy were utilized to further evaluate the compound.

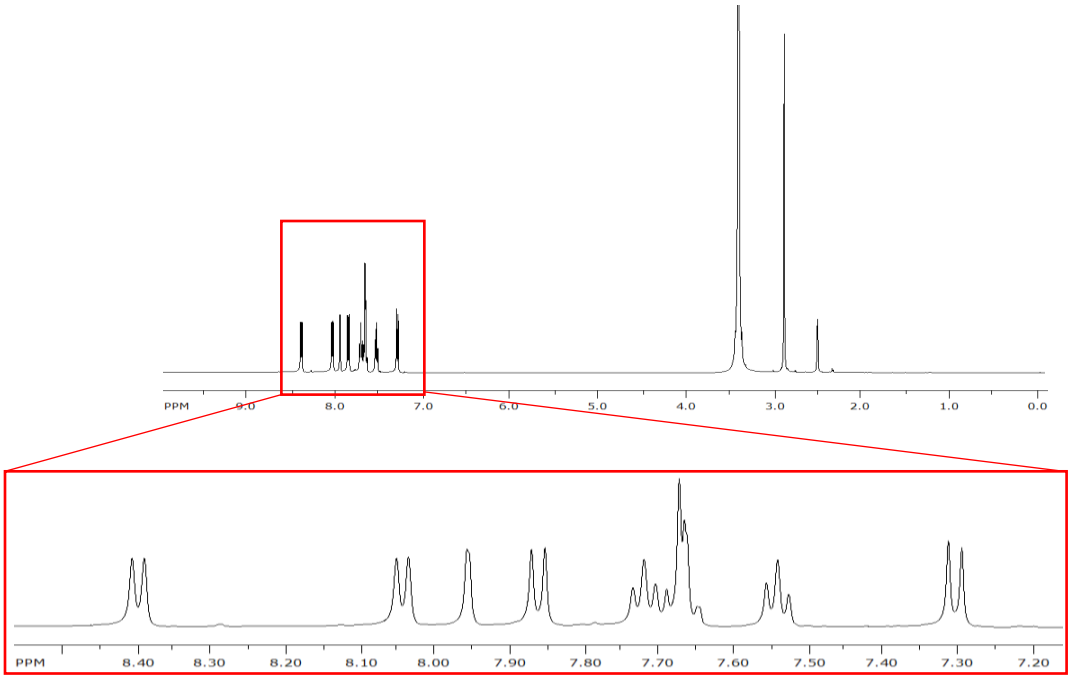


Figure 98: The ^{1}HNMR spectrum for KA156. (Top) The full ^{1}H-NMR spectrum for KA156. There are 10 hydrogen signals originating from KA156, as well as, two signals corresponding to a solvent and water peaks. The peaks of interest include 2.87 ppm (singlet), 7.30 ppm (doublet), 7.54 ppm (triplet), 7.67 ppm (multiplet), 7.72 ppm (triplet), 7.86 ppm (doublet), 7.96 ppm (singlet), 8.04 ppm (doublet), and 8.40 ppm (doublet). (Bottom) The magnified aromatic region of the spectrum with observable multiplicities.

Eleven peaks were observed in the ^{1}H-NMR spectrum (Fig.98). Nine of the eleven peaks were attributed to the compound of interest, while the remaining peaks were indicative of solvent DMSO and water contamination. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.30 ppm, 7.86 ppm, 8.04 ppm, and 8.40 ppm, and were assigned a relative integration of one. The ^{1}H signals, with multiplicities of three (triplet), had chemical shifts of 7.54 ppm and 7.72 ppm and were integrated to one. The ^{1}H signals, with multiplicities of one (singlet), had chemical shifts of 2.87 ppm and 7.96 ppm. The 2.87 ppm singlet was integrated to three and the 7.96 ppm singlet was integrated to one. The final ^{1}H signal was a multiplet at a chemical shift of 7.67 ppm and had an integration of two. If the two doublet signals that are missing from the ^{1}H-NMR spectra were accounted for by the multiplet signal observed in the ^{1}H-NMR spectra, then the

experimental ^{1}H signals are congruent with the expected signals in respect to the number, multiplicity, and integration of signals predicted from the structure in Fig.3. The ^{13}C -NMR spectrum had 18 unique carbon signals: 17 in the aromatic region and one in the alkyl region (Fig.99)

^{1}H and ^{13}C signals were correlated via gHMQC, gHMBC, and gCOSY. The HSQC showed that the alkyl hydrogens, at a chemical shift of 2.87 ppm, and the alkyl carbon, at a chemical shift of 15.3 ppm, coupled over one bond to each other (Fig.100). The alkyl hydrogens and the alkyl carbon were assigned to position 3c in Fig.3. Over three bonds the position 3c carbon did not couple to any hydrogens, but the position 3c hydrogens coupled to two different carbons (Fig.101). It was not expected for the position 3c hydrogens to couple to two different carbons over three bonds. However, this observation was explained by hydrogen to carbon coupling over two bonds: if coupling over two bonds occurred then the predicted structure does not deviate from the gHMBC. The position 3 carbon did not

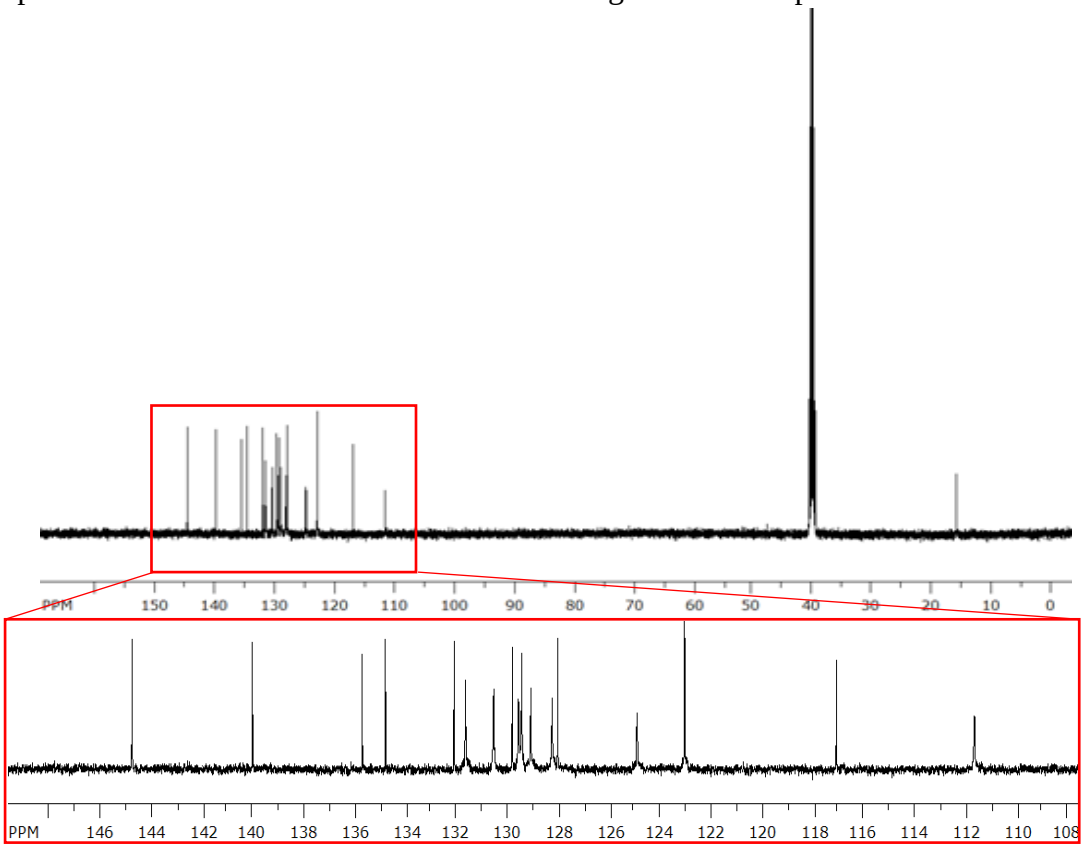


Figure 99: The ^{13}CNMR spectrum for KA156. (Top) The full ^{13}C-NMR spectrum for KA156. There are 18 carbons originating from KA156, as well as, one signal corresponding to a solvent peak. The peaks of interest include 15.3 ppm, 111.2 ppm, 116.6 ppm, 122.6 ppm, 124.5 ppm, 127.6 ppm, 127.8 ppm, 128.7 ppm, 129.0 ppm, 129.1 ppm, 129.4 ppm, 130.1 ppm, 131.3 ppm, 131.7 ppm, 134.4 ppm, 135.3 ppm, 139.7 ppm, and 144.4 ppm. (Bottom) The magnified aromatic region of the spectrum.

couple to any other hydrogens over two or three bonds (Fig.101). In addition, the carbon coupling over three bonds to the position 3c hydrogens, represented as carbon 3a in fig. 2, would couple to the two hydrogen doublet signals at chemical shifts of 7.30 ppm and 8.40 ppm (Fig.101). Based on the gHMBC the previous statements were verified and carbons 3 and 3a were confirmed to be the carbon signals with chemical shifts 144.4 ppm and 116.6 ppm respectively.

Over one bond, the hydrogen signals with chemicals shifts of 7.30 ppm and 8.40 ppm were coupled to the carbon signals with chemical shifts of 111.2 ppm and 122.6 ppm respectively (Fig.102). The 7.30 ppm and 111.2 ppm hydrogen and carbon were assigned to position 9. The 8.40 ppm hydrogen and 122.6 ppm carbon were assigned to position 4. Over three bonds the carbon at position 4 coupled to the hydrogen triplet signal at a

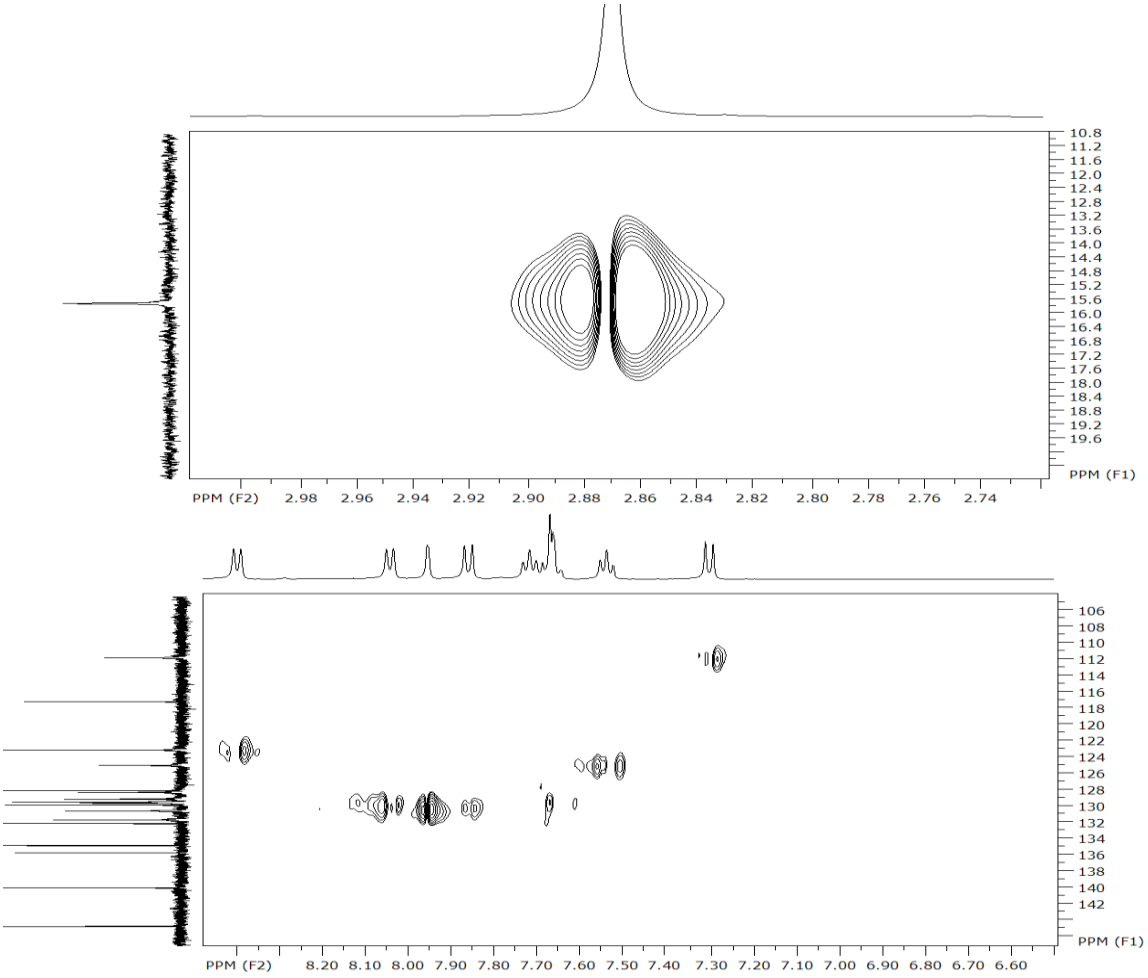


Figure 100: The gHMQC spectra for KA156. (Top) The magnified alkyl and region. (Bottom) The magnified aromatic region. Coupling over one bond can be seen between hydrogens (x-axis) and carbons (y-axis).

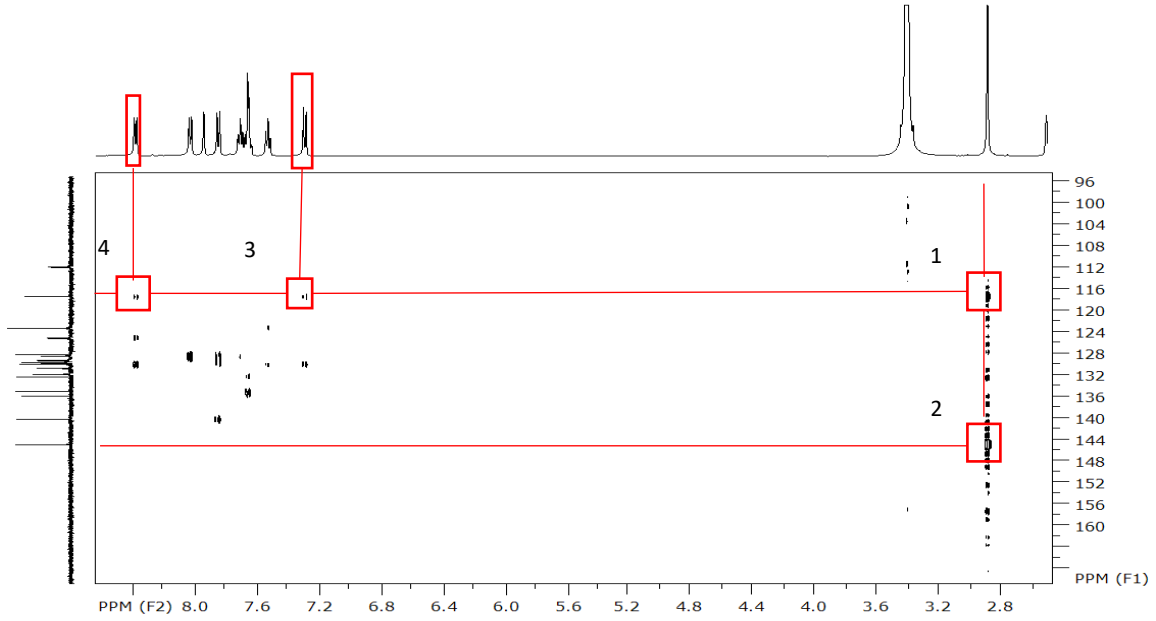


Figure 101: The gHMBC spectrum for KA156. The horizontal and vertical lines intersect where the hydrogens and carbons couple over three bonds. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with a chemical shift of 2.87 ppm and the carbons at 116.6 ppm and 144.4 ppm respectively. Boxes 3 and 4 represent carbon/hydrogen coupling between the carbon with a chemical shift of 116.6 ppm and the doublet hydrogens with chemical shifts of 7.30 ppm and 8.40 ppm respectively.

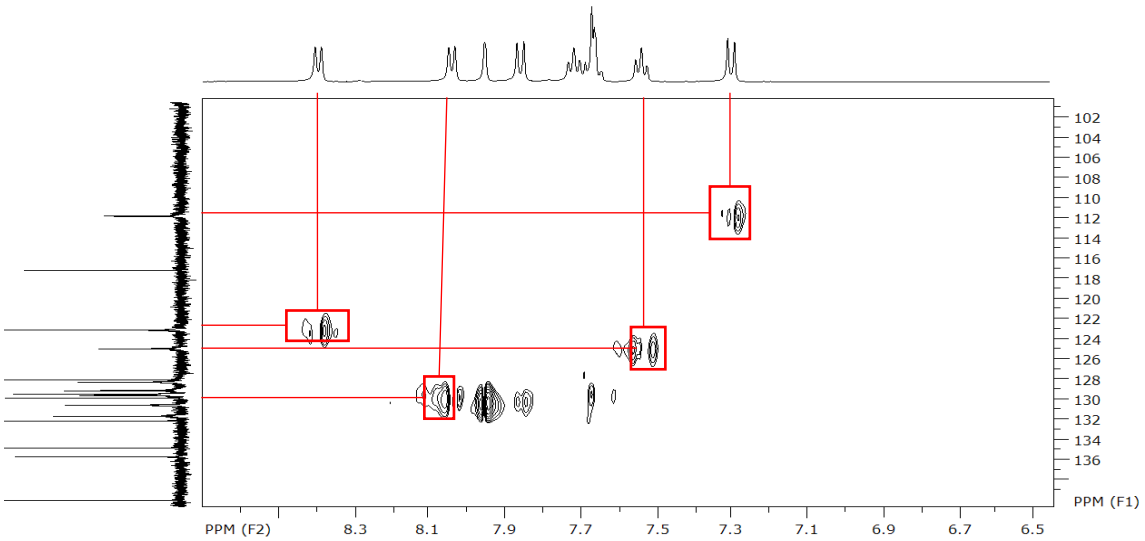


Figure 102: The aromatic region of the gHMQC spectrum for KA156. Where the horizontal and vertical lines intersect show coupling over one bond between carbons and hydrogens. Over one bond, the carbon at a chemical shift of 111.2 ppm is coupling to the hydrogen doublet signal at a chemical shift of 7.30 ppm. Over one bond, the carbon at a chemical shift of 122.6 ppm is coupling to the hydrogen doublet signal at a chemical shift of 8.40 ppm. Over one bond, the carbon at a chemical shift of 124.5 ppm is coupling to the hydrogen triplet signal at a chemical shift of 7.54 ppm. Over one bond, the carbon at a chemical shift of 129.0 ppm couples to the hydrogen doublet at a chemical shift of 8.04 ppm.

chemical shift of 7.54 ppm (Fig.103). The triplet signal was then assigned to position 6. The carbon at position 9 should not have coupled to any hydrogens over one or three bonds, and indeed this was observed (Fig.103).

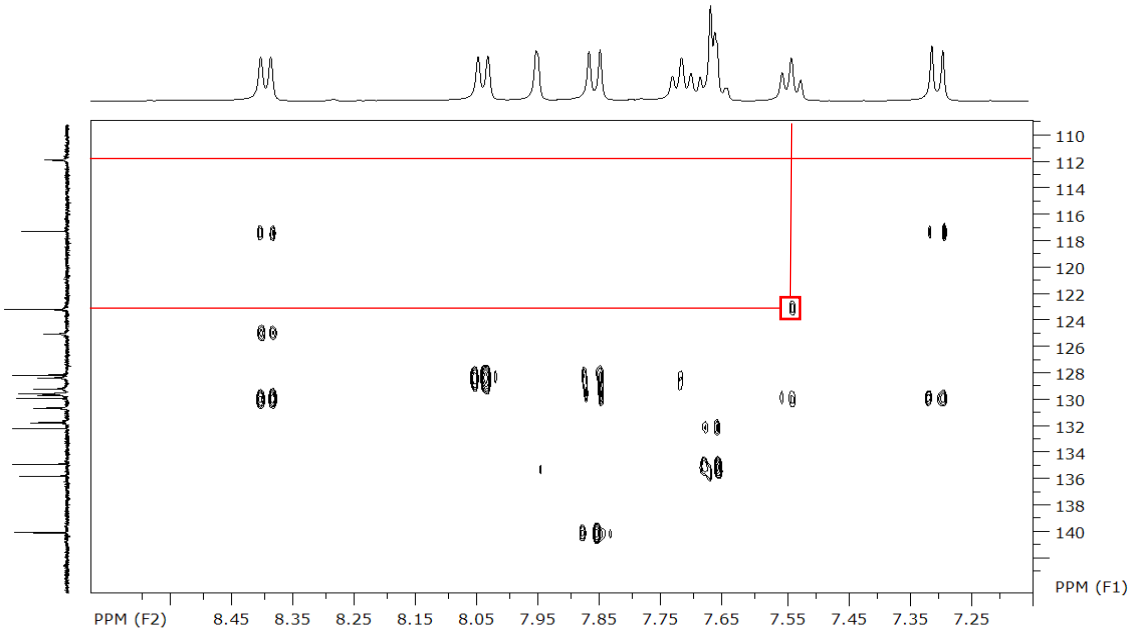


Figure 103: The aromatic region of the gHMBC spectrum for KA156. Where the horizontal and vertical lines intersect show interactions over three bonds between carbons and hydrogens. Over three bonds, the carbon at 111.2 ppm is coupling to no hydrogens. Over three bonds, the carbon at 122.6 ppm is coupling to one hydrogen triplet signal at a chemical shift of 8.40 ppm.

The position 4, 6, and 9 hydrogens coupled over three bonds to the carbon signal at a chemical shift 129.1 ppm (Fig.104). Over three bonds the position 4 hydrogen doublet coupled to a triplet hydrogen signal at a chemical shift of 7.72 ppm (Fig.105). The triplet signal with the chemical shift of 7.72 ppm was assigned to position 5. The 129.1 ppm carbon signal was defined as the carbon at position 7a. Via the gHSQC position 6 carbon is attributed to chemical shift 124.5 ppm (Fig.102). The position 5 hydrogen shows no coupling over one bond, so the position 5 carbon was assigned by first defining the position 7 hydrogen. The position 6 hydrogen coupled over three bonds to the doublet hydrogen signal with a chemical shift of 8.04 ppm (Fig.105). Over one bond the hydrogen signal at a chemical shift of 8.04 ppm coupled to the carbon signal at a chemical shift of 129.2 ppm (Fig.102). The position 7 carbon and hydrogen were defined as 129.2 ppm and 8.04 ppm respectively. The position 7 hydrogen couples over three bonds to a carbon at a chemical

shift of 127.6 ppm (Fig.106). Theoretically, the position 7 hydrogen should be coupling to three different carbons, at positions 3b, 5, and 8, but this is not observed.

The hydrogen at position 5, 7, and 8 all theoretically couple to the position 3b carbon over three bonds. The position 3b carbon couples to no hydrogens over one bond. Over three bonds the position 5 hydrogen should have coupled to the position 3b carbon and the position 7 carbon (already defined). However, the position 5 hydrogen only coupled over three bonds to one observable carbon at a chemical shift of 128.2 ppm (Fig 102). Over three bonds, the position 9 hydrogen couples to the position 8 hydrogen doublet signal at a chemical shift of 7.86 ppm (Fig.105). The position 8 hydrogen couples over one bond to the carbon signal at a chemical shift of 129.4 ppm (Fig.107). Over three bonds, the position 5, 7, and 8 hydrogens couple to the carbon signal with a chemical shift of 128.2 ppm (Fig.106). The carbon signal at a chemical shit o 128.2 ppm does not couple over one bond to any hydrogens, and the signal is assigned to position 3b. Because the 3b carbon is defined as having a chemical shift 128.2 ppm the position 5 carbon cannot be determined directly.

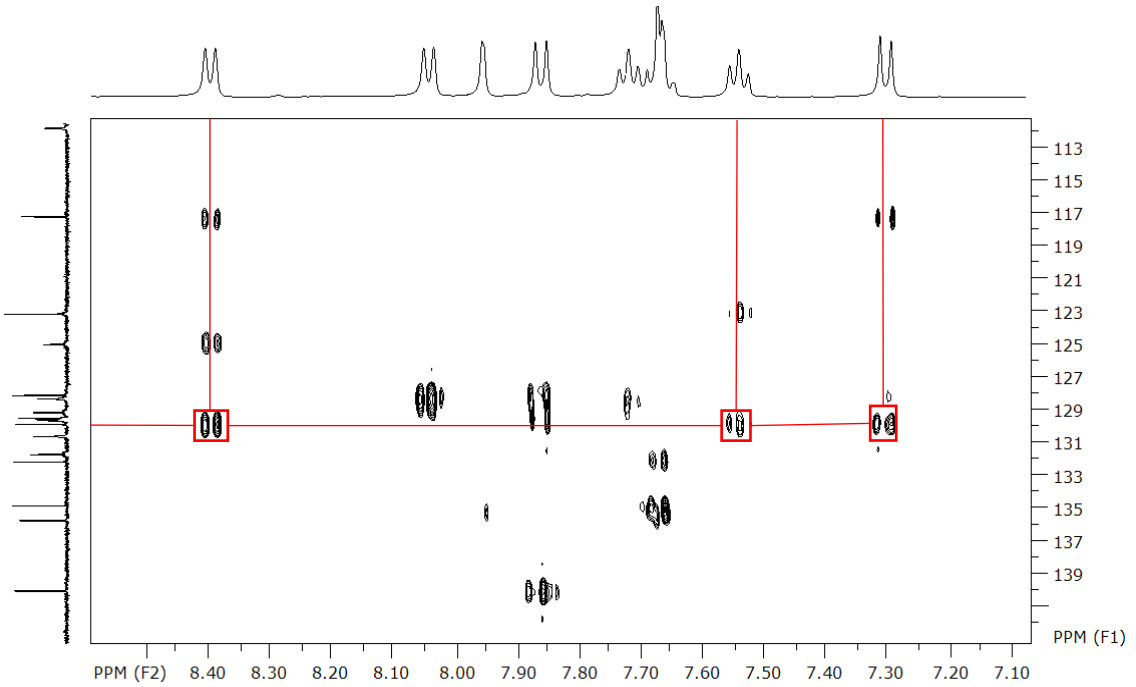


Figure 104: The aromatic region of the gHMBC for KA156. Where the horizontal and vertical lines intersect show interactions over three bonds between carbons and hydrogens. Over three bonds, the carbon signal at a chemical shift of 129.4 ppm is coupling to the three hydrogen signals at chemical shifts of 7.30 ppm, 7.54 ppm, and 8.40 ppm

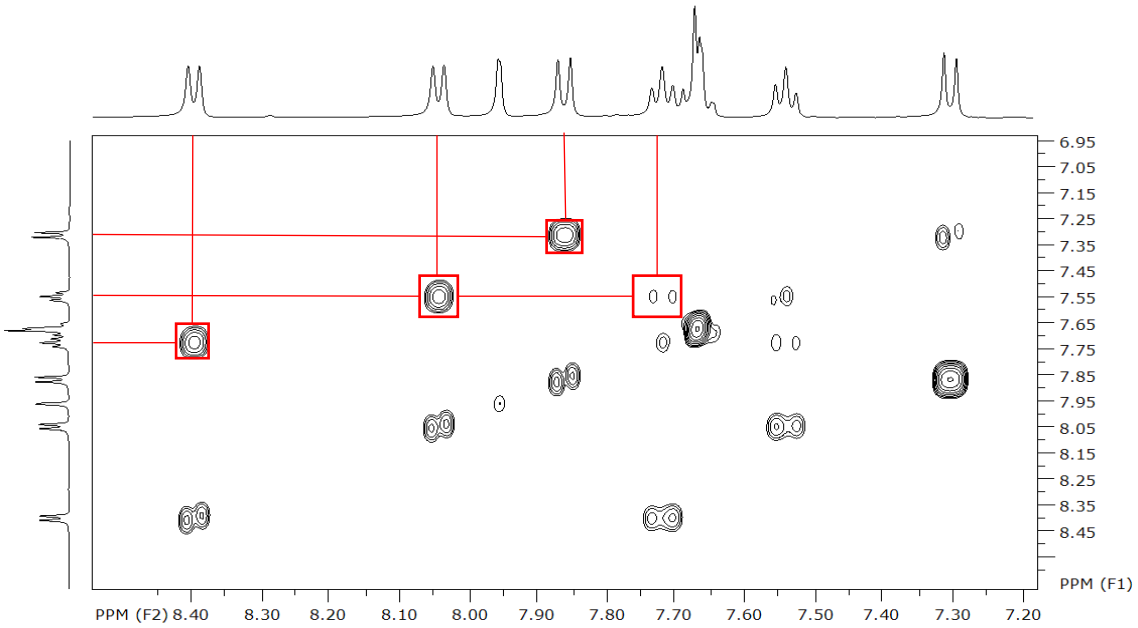


Figure 105: The aromatic region of the gCOSY spectra for KA156. Where the horizontal and vertical lines intersect show interactions over three bonds between hydrogens. Over three bonds, the doublet signal at a chemical shift of 7.30 ppm couples to the doublet signal at a chemical shift of 7.86 ppm. Over three bonds, the triplet hydrogen signal at a chemical shift of 7.54 ppm couples to a doublet signal at a chemical shift of 8.04 ppm and a triplet signal at a chemical shift of 7.72 ppm. Over three bonds, the triplet hydrogen signal at a chemical shift of 7.72 ppm couples to a doublet hydrogen signal with a chemical shift of 8.40 ppm.

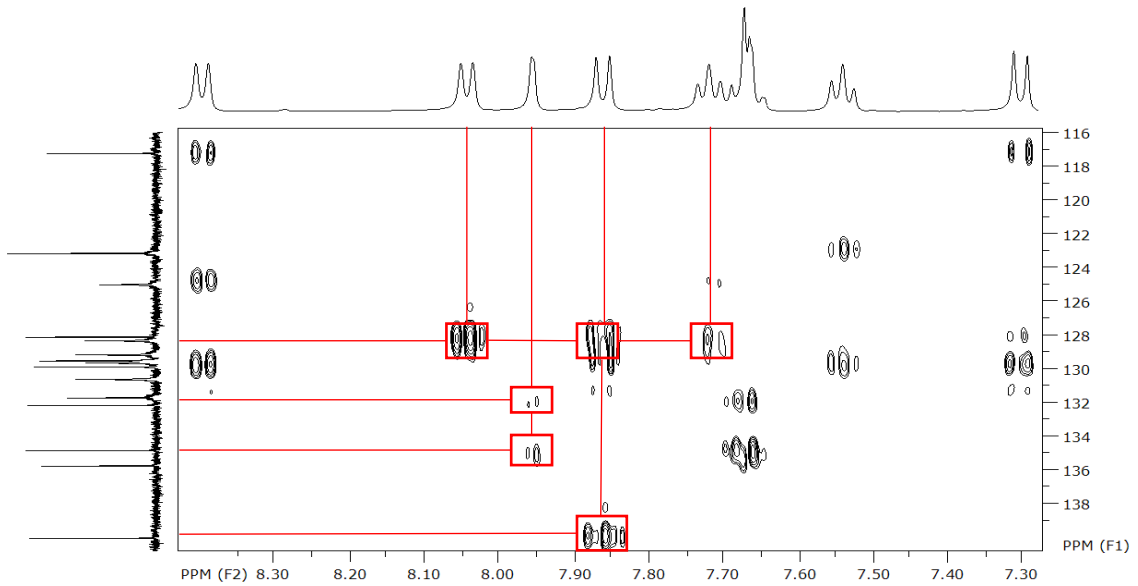


Figure 106: The aromatic region of the gHMBC for KA156. Where the horizontal and vertical lines intersect over a signal shows interaction over three bonds between carbons and hydrogens. Over three bonds, the carbon signal at a chemical shift of 128.2 ppm couples the three hydrogen signals at chemical shifts of 7.72 ppm, 7.86 ppm, and 8.04 ppm. Over three bonds the carbons signal at chemical shifts of 131.3 ppm and 134.4 couple the hydrogen signal at a chemical shift of 7.96 ppm. Over three bonds the carbon signal at a chemical shift of 140.0 ppm couples to the hydrogen signal at a chemical shift of 7.86 ppm.

Over three bonds the position 8 hydrogen couples to a carbon at a chemical shift of 140.0 ppm (Fig.106). The carbon with a chemical shift of 140.0 ppm was assigned to position 9a and shows no coupling over one bond. The designation of the hydrogen and carbon at position 9a is in agreement with the proposed structure. The remaining aromatic singlet has hydrogen and carbon chemical shifts of 7.96 ppm and 130.1 ppm respectively, and is assigned position 12 (Fig.108). Over three bonds the position 12 hydrogen couples to the carbon signals at chemical shifts of 131.7 ppm and 134.4 (Fig.106). The carbon at a chemical shift of 131.7 ppm couples over one bond to the hydrogen multiplet signal at a chemical shift of 7.67 ppm (Fig.107).

The carbon and hydrogen at chemical shifts of 131.3 ppm and 7.67 ppm were assigned to position 14. The carbon at a chemical shift of 134.4 ppm coupled to no hydrogens over one bond and is assigned to position 10. The remaining carbon signal, coupling over one bond to the multiplet, was at a chemical shift of 129.0 ppm and was assigned to position 15 (Fig.107). Over three bonds the multiplet coupled to the carbons at chemical shifts of 135.3 ppm and 131.3 ppm (Fig.108). The two signals cannot be differentiated structurally and are assigned to both position 11 and 13. The remaining

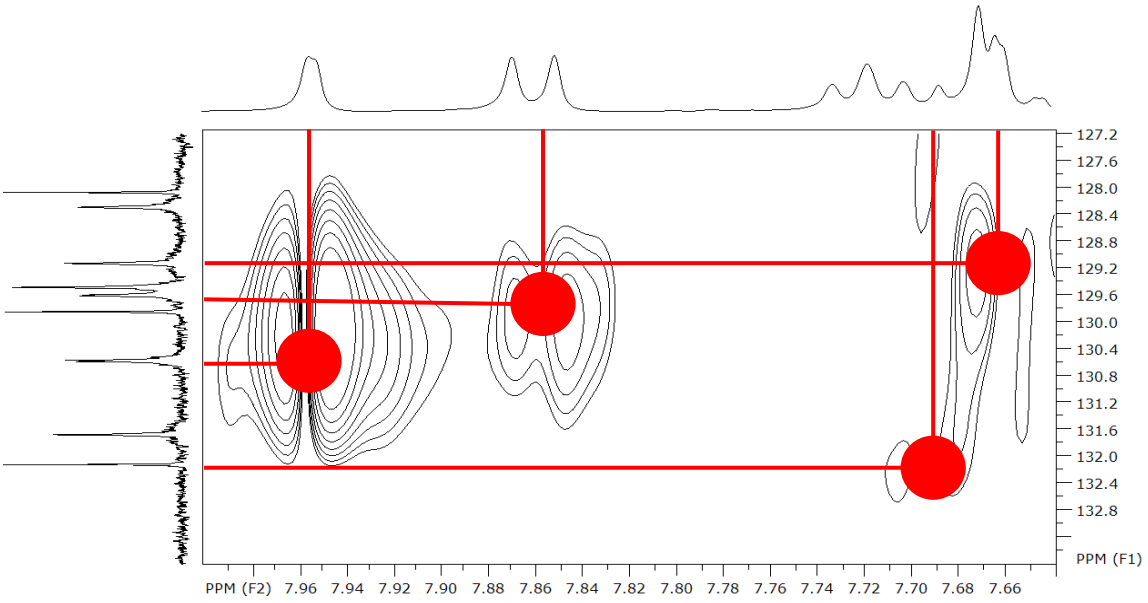


Figure 107: A magnified region of the gHMQC. axis. Where the horizontal and vertical lines intersect on a red circle is representative of high intensity regions of the individual signals. Over one bond the carbons at chemical shifts of 129.0 ppm, 129.4 ppm, 130.1 ppm, 131.7 ppm are coupling to the hydrogens at chemical shifts of 7.67 ppm, 7.86 ppm, 7.96 ppm, and 7.67 ppm.

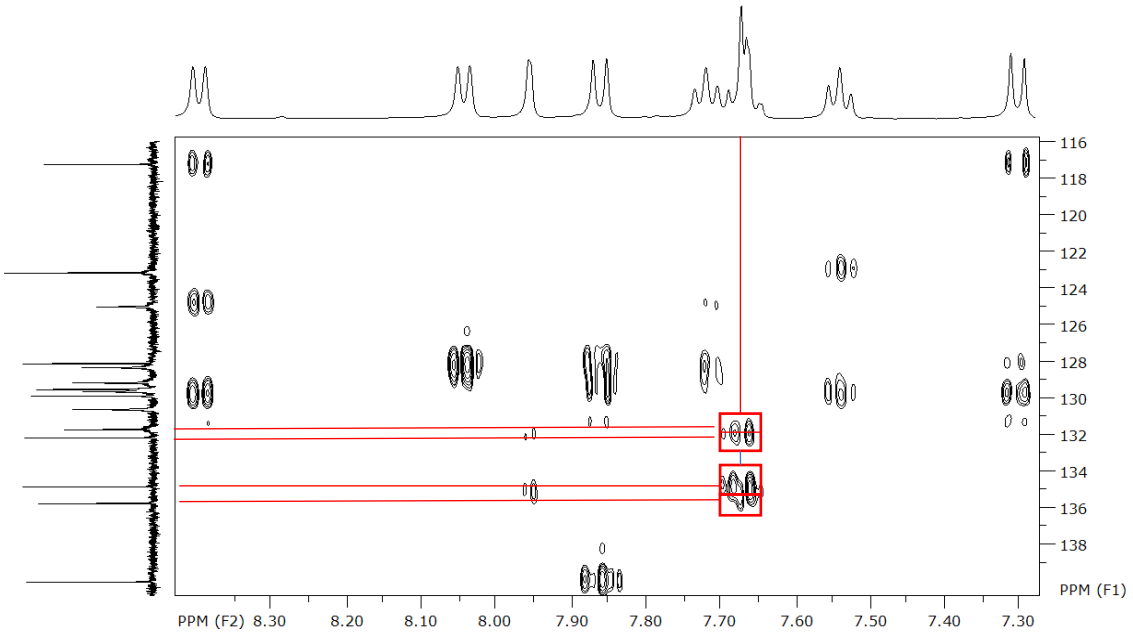
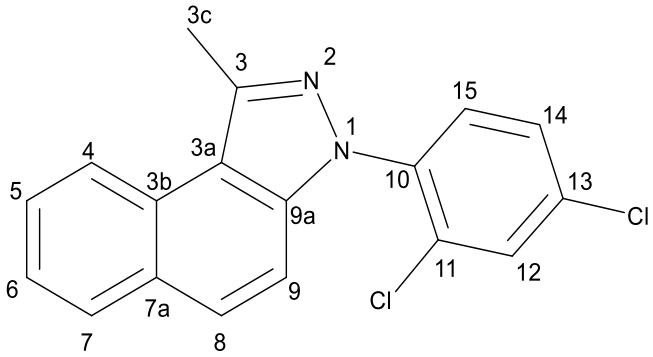


Figure 108: The aromatic region of the gHMBC for KA156. Where the horizontal and vertical lines intersect, over a signal, shows interaction over three bonds between carbons and hydrogens. Over three bonds, the hydrogen signal at a chemical shift of 7.67 ppm couples to four hydrogens at chemical shifts of 131.2 ppm, 132.0 ppm, 134.4 ppm, and 135.3 ppm.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	N/A	144.4
3a	N/A	116.6
3b	N/A	127.8
3c	2.88	15.3
4	8.39	122.6
5	7.72	127.8
6	7.56	124.5
7	8.07	129.2
7a	N/A	129.1
8	7.94	129.4
9	7.94	111.2
9a	N/A	140
10	N/A	134.4
11	8.48	135.3 or 131.3
12	N/A	N/A
13	8.21 or 8.26	135.3 or 131.3
14	7.86	131.2
15	8.21 or 8.26	129

Figure 109: The NMR structural data for KA156. (Left) The proposed structure and number system for compounds KA156 (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

carbon signal at a chemical shift of 127.6 ppm was assigned to position 5 by process of elimination. The complete position assignments can be seen in Fig.109.

4.11 KA160

Via the crude GC/MS and crude NMR spectrum **KA160** was produced in 90.5% yield from 2-napthyl-hydrazine hydrochloride and 1-acetyl-2-napthol (appendix K). **KA160** melting point range (MP) was 108.0-109.9°C (± 1.1°C). As **KA160** melted its color profile changed from an off-white solid to a dark brown one. The molecular formula ($C_{22}N_2H_{16}$) was verified by high performance mass spectrometry (appendix K). The compounds proposed structure is seen in Fig.110.

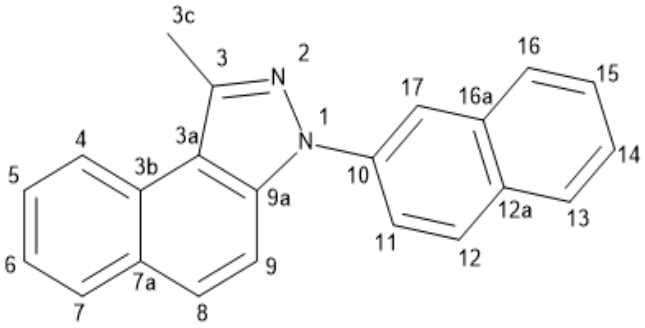


Figure 110: The predicted structure for KA160 and its numbering assignments.

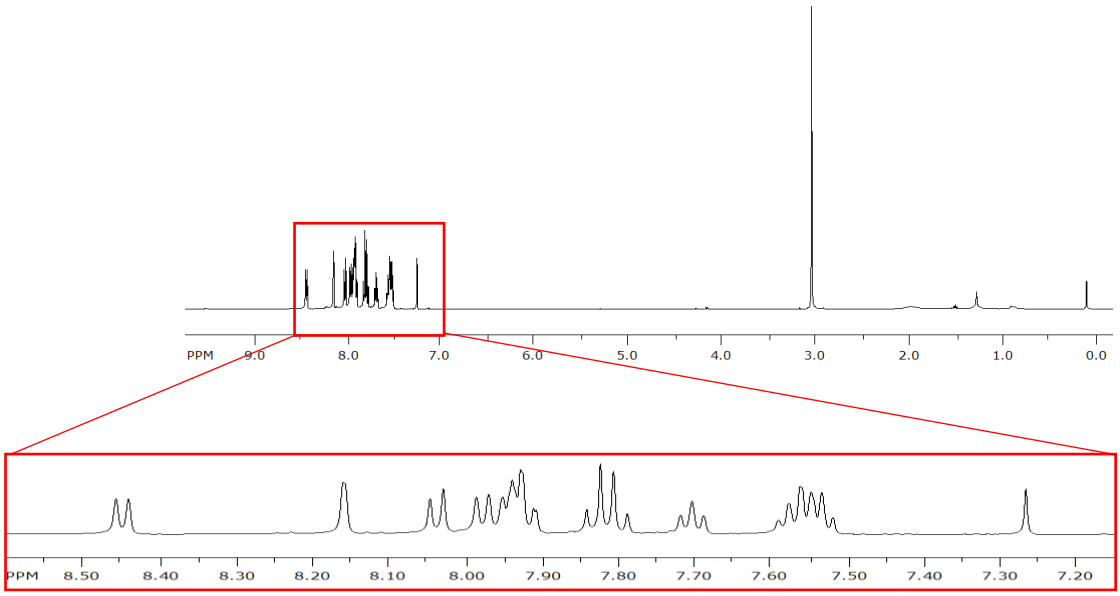


Figure 111: The ^{1}HNMR spectrum for KA160. (Top) The full ^{1}H-NMR spectrum for KA160. There are nine hydrogen signals originating from KA160 and one chloroform solvent peak. The peaks of interest include 3.03 ppm (singlet), 7.55 ppm (multiplet), 7.70 ppm (triplet), 7.82 ppm (multiplet), 7.93 ppm (multiplet), 7.98 ppm (doublet), 8.04 ppm (doublet), 8.16 ppm (singlet), 8.39 ppm (doublet), and 8.48 (singlet). (Bottom) The magnified aromatic region of the spectrum with observable multiplicities.

Ten peaks were observed in the ^{1}H-NMR spectrum (Fig.111). Nine of the ten peaks were attributed to the compound of interest, while the remaining major peak was indicative of solvent chloroform. Fourteen peaks were predicted from the proposed structure in Fig.110. The ^{1}H signals, with multiplicities of two (doublet), had chemical shifts of 7.98 ppm, 8.04 ppm, and 8.45 ppm, and were assigned a relative integration of one. The ^{1}H signal, with a multiplicity of three (triplet), had chemical shifts of 7.70 was integrated to one. The ^{1}H signals, with multiplicities of one (singlet), had chemical shifts of 3.04 ppm and 8.16 ppm. The 3.04 ppm singlet was integrated to three and the 8.16 ppm singlet was integrated to one. The remaining ^{1}H signals were designated as multiplets; The multiplet signals chemical shifts were 7.55 ppm, 7.82 ppm, and 7.93 ppm and their relative integrations were three, two, three respectively. The experimental ^{1}H signals are congruent with the proposed structure in respect to the total relative integration being 18 (Fig.111).

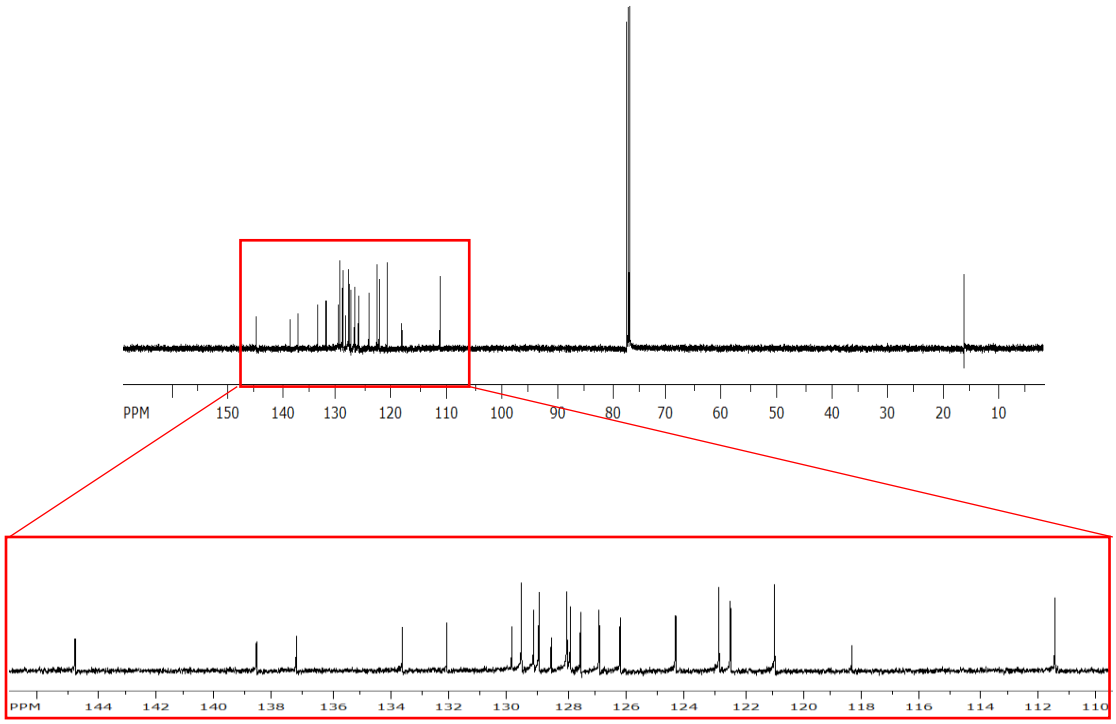


Figure 112: The ^{13}CNMR spectrum for KA160. (Top) The full ^{13}C-NMR spectrum for KA160. There are 11 carbons originating from KA160, as well as, one signal corresponding to a solvent peak. The peaks of interest include 15.9 ppm, 111.5 ppm, 118.4 ppm, 121.1 ppm, 122.6 ppm, 123.0 ppm, 124.5 ppm, 126.3 ppm, 127.1 ppm, 127.5 ppm, 128.2 ppm, 128.2 ppm, 128.5 ppm, 129.1 ppm, 129.3 ppm, 129.7 ppm, 130.0 ppm, 132.3 ppm, 133.8 ppm, 137.4 ppm, 138.8 ppm, and 145.0 ppm. (Bottom) The magnified aromatic region of the spectrum.

The ^{13}C -NMR had 22 unique carbon signals: 21 in the aromatic region and one in the alkyl region (Fig.112). ^{1}H and ^{13}C chemical shifts were correlated via gHSQC, gHMBC, and gCOSY. The HSQC showed that the alkyl hydrogens, at a chemical shift of 3.03 ppm, and the alkyl carbon, at a chemical shift of 15.9 ppm, coupled over one bond to each other (Fig.113). Over three bonds the carbon signal with a chemical shift of 15.9 ppm did not couple to any hydrogens, but the hydrogen signal with a chemical shift of 3.03 ppm coupled to the carbon signals with chemical shifts of 118.4 ppm and 145.0 ppm (Fig.117).

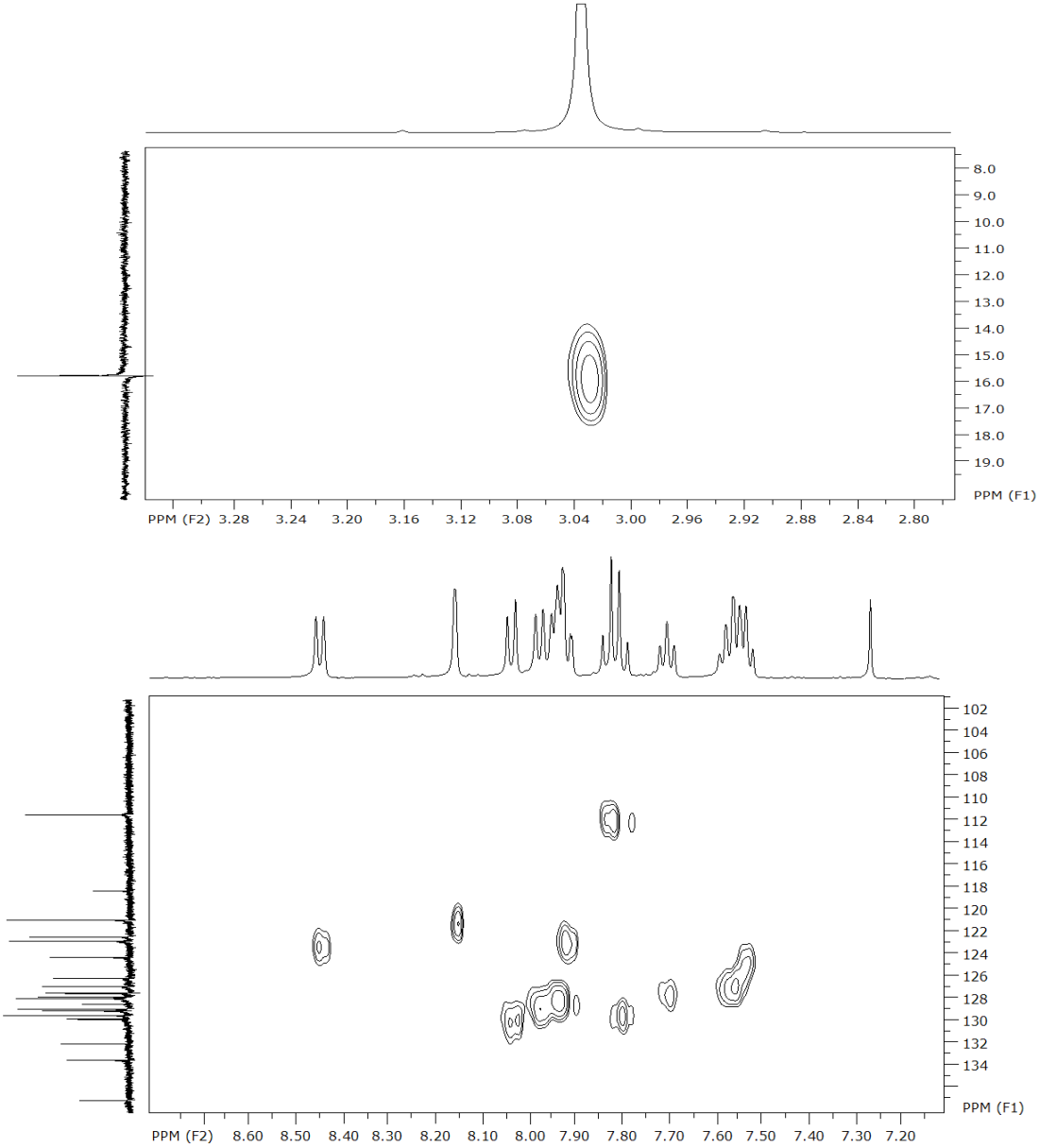


Figure 113: The gHSQC spectra for KA160. (Top) The magnified alkyl region. (Bottom) The Magnified aromatic region. Coupling over one bond can be seen between hydrogens (x-axis) and carbons (y-axis).

It was not expected for the alkyl hydrogens to couple to two different carbons over three bonds, based on the proposed structure. This observation is explained by hydrogen to carbon coupling over two bonds: if coupling over two bonds occurred then the structure does not deviate from the gHMBC.

The carbon signal with a chemical shift of 145.0 ppm did not couple to any other hydrogen signals over three bonds (Fig.114). In addition, the carbon signal coupling over three bonds to the alkyl hydrogens, would couple to the two hydrogen doublet signals. The carbon signal with a chemical shift of 118.4 ppm coupled over three bonds to the two hydrogen signals with chemical shifts of 7.82 ppm and 8.45 ppm (Fig.114). However, the hydrogen signal with a chemical shift of 7.82 ppm was a multiplet signal with an integration of four. The carbons with chemical shifts of 15.9 ppm, 145.0 ppm, and 118.4 ppm were assigned to positions 3c, 3, and 3b respectively.

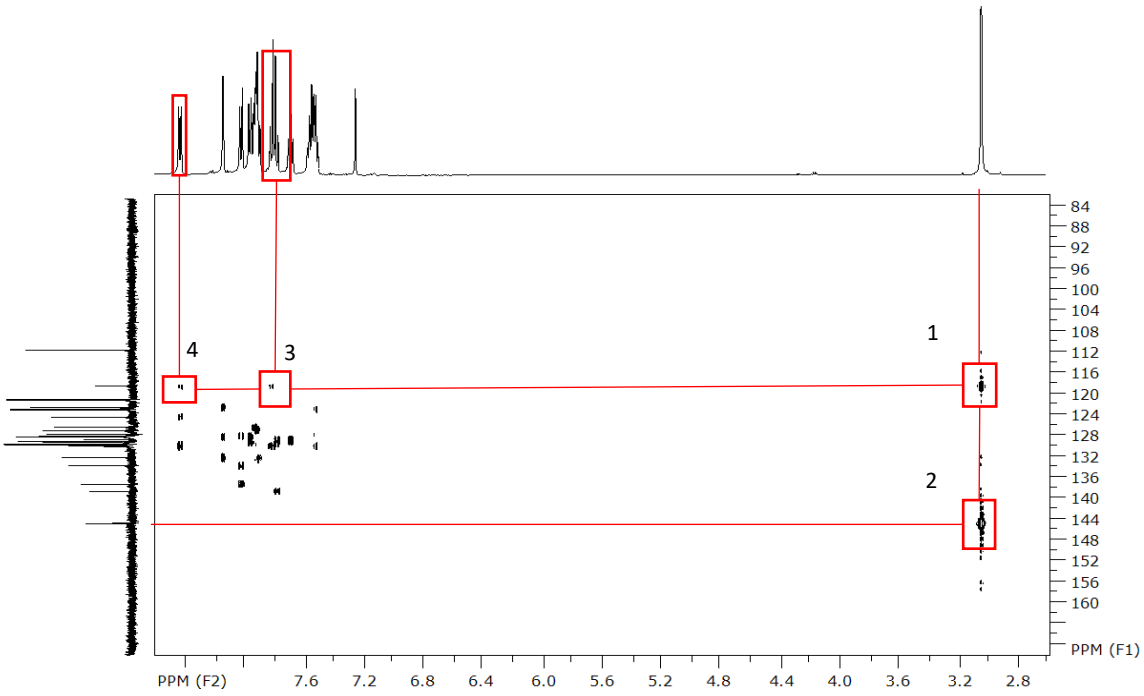
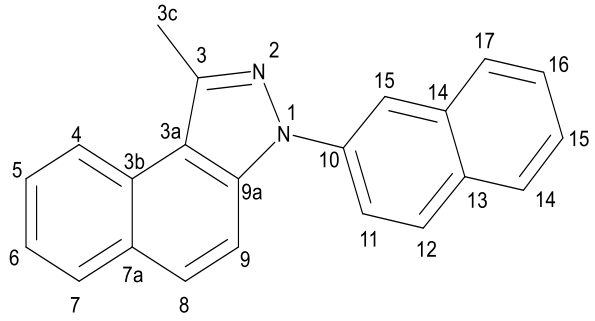


Figure 114: The gHMBC spectra for compound KA160. Boxes 1 and 2 represent the two signals for the carbon/hydrogen coupling over two and three bonds between the hydrogen with and chemical shift of 2.88 ppm and the carbons at 118.4 ppm and 145.0 ppm respectively. The horizontal and vertical lines intersect where the hydrogens and carbons couple over three bonds. Boxes 3 and 4 represent carbon/hydrogen coupling between the carbon with a chemical shift of 11830 ppm and the doublet hydrogens with chemical shifts of 7.82 ppm and 8.45 ppm respectively.

The multiplet signal coupled over one bond to the carbon signals with chemical shifts of 111.5 ppm, 129.1 ppm, and 129.1 ppm (Fig.114). There was one 2-D signal for the carbon signals with chemical shifts of 129.1 ppm and 129.1 ppm, but the most intense region of the signal overlapped both. From the gHSQC spectra it was determined that the multiplet with a chemical shift of 7.82 ppm coupled to at least two carbons and it was likely the multiplet was comprised of two to four unique overlapping hydrogen signals. The carbon signal with a chemical shift of 111.5 ppm coupled to no hydrogens over three bonds and could only be assigned to position 9. The hydrogen signal with a chemical shift of 8.45 ppm was assigned to position 4. The signals seen in Fig.115 are the only assignments that could be distinguished for the compound. Many of the carbon signals were to close together to get an accurate reading.



Posistion	^{1}H signal (ppm)	^{13}C Signal (ppm)
1	N/A	N/A
2	N/A	N/A
3	N/A	145
3a	N/A	118.4
3b	N/A	N/A
3c	3.3	15.9
4	8.45	123
5	7.7	128.2
6	7.55	N/A
7	8.04	129.6
7a	N/A	129.9
8	7.82	N/A
9	7.25	111.5

Figure 115: The NMR structural data for KA160. (Left) The proposed structure and number system for compounds KA160 (Right) A table correlating the positions defined by the compounds number system, and the chemical shifts of hydrogen and carbon signals assigned to said position

5.0 Conclusion

The 1-acetyl-2-napthol derivatives do not undergo a Fischer indole synthesis reaction, but instead cyclize to indazole moieties. The reaction was quite favorable and occurred when utilizing a multitude of hydrazine and naphthalene derivatives. It is unlikely the reaction proceeded using the hydroxy group of the 1-acetyl-2-napthol as a leaving group, as proposed by H. Duewell et. al (1968)[13]. The reaction occurred in high concentration phosphoric acid and proceeded when the 1-acetyl-2-napthol hydroxy group was converted to a methoxy group, but not when replaced with an acetamide group. The Bucherer reaction mechanism seems likely as the reaction has been reported in low yields with 1-acetyl naphthalene, and the hydride leaving group is highly unfavorable[11]. However, the reaction may proceed via an unknown mechanism since it should have occurred utilizing N-(1-acetylnaphthalen-2-yl)acetamide. This may be explained by resonance between the nitrogen and carbonyl group. Some literature shows that similar indazoles display bioactive properties including immune suppressant inhibition and anticarcinogenic characteristics[19–22]. Further analysis would be needed to make any conclusions on the reaction mechanism and biological activity of the compounds generated here.

References

1. Antibiotic Resistance Threats in the United States, 2013 | Antibiotic/Antimicrobial Resistance | CDC. Available at: https://www.cdc.gov/drugresistance/threat-report-2013/index.html. (Accessed: 27th July 2017)

2. McClay, K. *et al.* A novel combinatorial biocatalytic approach for producing antibacterial compounds effective against Mycobacterium tuberculosis (TB). *Appl. Microbiol. Biotechnol.* **97,** 7151–7163 (2013).

3. Recent Advances in the Chemistry of Indazoles - Schmidt - 2008 - European Journal of Organic Chemistry - Wiley Online Library. Available at: http://onlinelibrary.wiley.com/doi/10.1002/ejoc.200800227/full. (Accessed: 19th August 2017)

4. Lebedev, A. Y., Khartulyari, A. S. & Voskoboynikov, A. Z. Synthesis of 1-Aryl-1H-indazoles via Palladium-Catalyzed Intramolecular Amination of Aryl Halides. *J. Org. Chem.* **70,** 596–602 (2005).

5. Espinet, P., Garcia, G., Herrero, F. J., Jeannin, Y. & Philoche-Levisalles, M. (CN)-chelate, N,N'-bridged dimeric palladium complexes derived from hydrazones PhC(R):NN'HPh. X-ray structure of [Pd(o-C6H4C(R):NNPh)L]2 [R = Me, L = P(OMe)3]. *Inorg. Chem.* **28,** 4207–4211 (1989).

6. N. Cockburn, B., V. Howe, D., Keating, T., G. Johnson, B. F. & Lewis, J. Reactivity of co-ordinated ligands. Part XV. Formation of complexes containing Group V donor atoms and metal–carbon σ-bonds. *J. Chem. Soc. Dalton Trans.* **0,** 404–410 (1973).

7. Bae, Y. K. & Cho, C. S. Copper(I) salt/PEG-400 catalysis in one-pot direct synthesis of 1-aryl-1H-indazoles from 2-bromobenzaldehydes and arylhydrazines. *Appl. Organomet. Chem.* **27,** 224–227 (2013).

8. Mills, A. D., Nazer, M. Z., Haddadin, M. J. & Kurth, M. J. N,N-Bond-Forming Heterocyclization: Synthesis of 3-Alkoxy-2H-indazoles. *J. Org. Chem.* **71,** 2687–2689 (2006).

9. Avila, B. *et al.* Acid and base catalyzed Davis-Beirut reaction: experimental and theoretical mechanistic studies and synthesis of novel 3-amino-2H-indazoles. *Tetrahedron Lett.* **53,** 6475–6478 (2012).

10. Kimball, D. B., Herges, R. & Haley, M. M. Two Unusual, Competitive Mechanisms for (2-Ethynylphenyl)triazene Cyclization: Pseudocoarctate versus Pericyclic Reactivity. *J. Am. Chem. Soc.* **124,** 1572–1573 (2002).

11. Dennler, E. B. & Frasca, A. R. Synthesis of fused heterocyclic compounds with polyphosphoric acid. *Can. J. Chem.* **45,** 697–705 (1967).

12. Jordan, D. B. *et al.* Structure-based design of inhibitors of the rice blast fungal enzyme trihydroxynaphthalene reductase. *J. Mol. Graph. Model.* **19,** 434–447 (2001).

13. Duewell, H. & Haig, T. J. The synthesis of heterocyclic compounds. Part III. Studies on Xanthorrhoea resins. Part IV. Some simple benzindazoles. *J. Chem. Soc. C Org.* **0,** 169–172 (1968).

14. de Sa Alves, F. R., Barreiro, E. J. & Manssour Fraga, C. A. From Nature to Drug Discovery: The Indole Scaffold as a 'Privileged Structure'. *Mini Rev. Med. Chem.* **9,** 782–793 (2009).

15. Abele, E., Abele, R., Dzenitis, O. & Lukevics, E. Indole and Isatin Oximes: Synthesis, Reactions, and Biological Activity. (Review). *Chem. Heterocycl. Compd.* **39,** 3–35 (2003).

16. Fischer, E. & Jourdan, F. Ueber die Hydrazine der Brenztraubensäure. *Berichte Dtsch. Chem. Ges.* **16,** 2241–2245 (1883).

17. Bucherer, H. T. Über die Einwirkung schwefligsaurer Salze auf aromatische Amido- und Hydroxylverbindungen. *J. Für Prakt. Chem.* **69,** 49–91 (1904).

18. BROWN, R. F., JACOBS, T. L., WINSTEIN, S., MOSS, E. F. L. R. & OTT, M. SUBSTITUTED α-DIALKYLANOALKYL-1-NAPHTHALENEMETHANOLS. V. THE [ILL] OF SOME α-DIALKYLAMINOMETHYL-2-CHLORO- AND BMO-1-NAPHTHALENEMETHANOLS1. *J. Org. Chem.* **11,** 163–169 (1946).

19. Cui, J. *et al.* Optimization of 1H-indazol-3-amine derivatives as potent fibroblast growth factor receptor inhibitors. *Bioorg. Med. Chem. Lett.* **27,** 3782–3786 (2017).

20. Cabrera, A. R. *et al.* New imidoyl-indazole platinum (II) complexes as potential anticancer agents: Synthesis, evaluation of cytotoxicity, cell death and experimental-theoretical DNA interaction studies. *J. Inorg. Biochem.* **174,** 90–101 (2017).

21. Patch, R. J. *et al.* Indazole-based ligands for estrogen-related receptor α as potential anti-diabetic agents. *Eur. J. Med. Chem.* **138,** 830–853 (2017).

22. Pradhan, N. *et al.* Identification of Substituted 1H-Indazoles as Potent Inhibitors for Immunosuppressive Enzyme Indoleamine 2,3-Dioxygenase 1. *ChemistrySelect* **2,** 5511–5517 (2017).

Appendix A: Supplementary data KA176

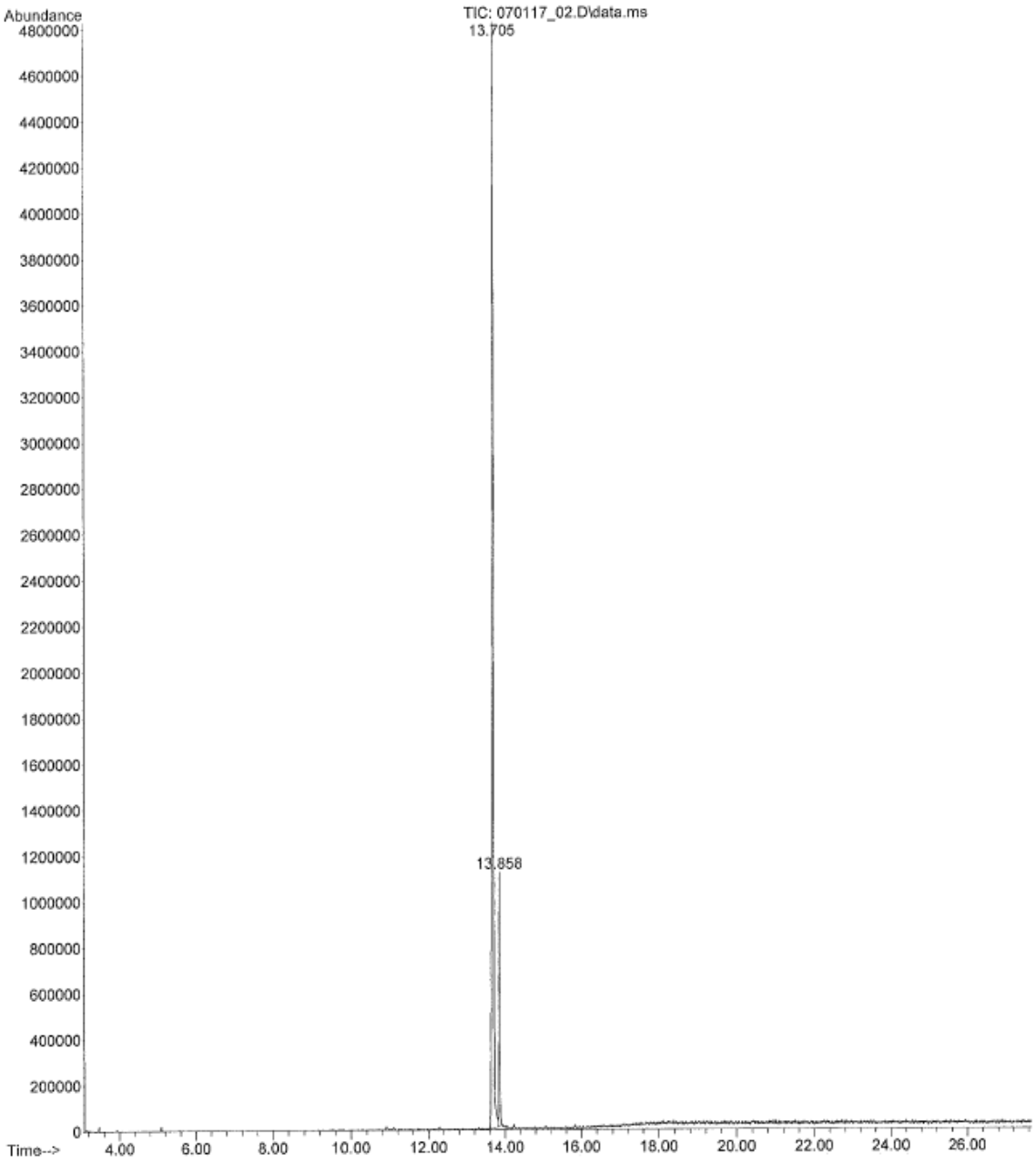


Figure 116: Gas chromatographic spectrum for KA176.

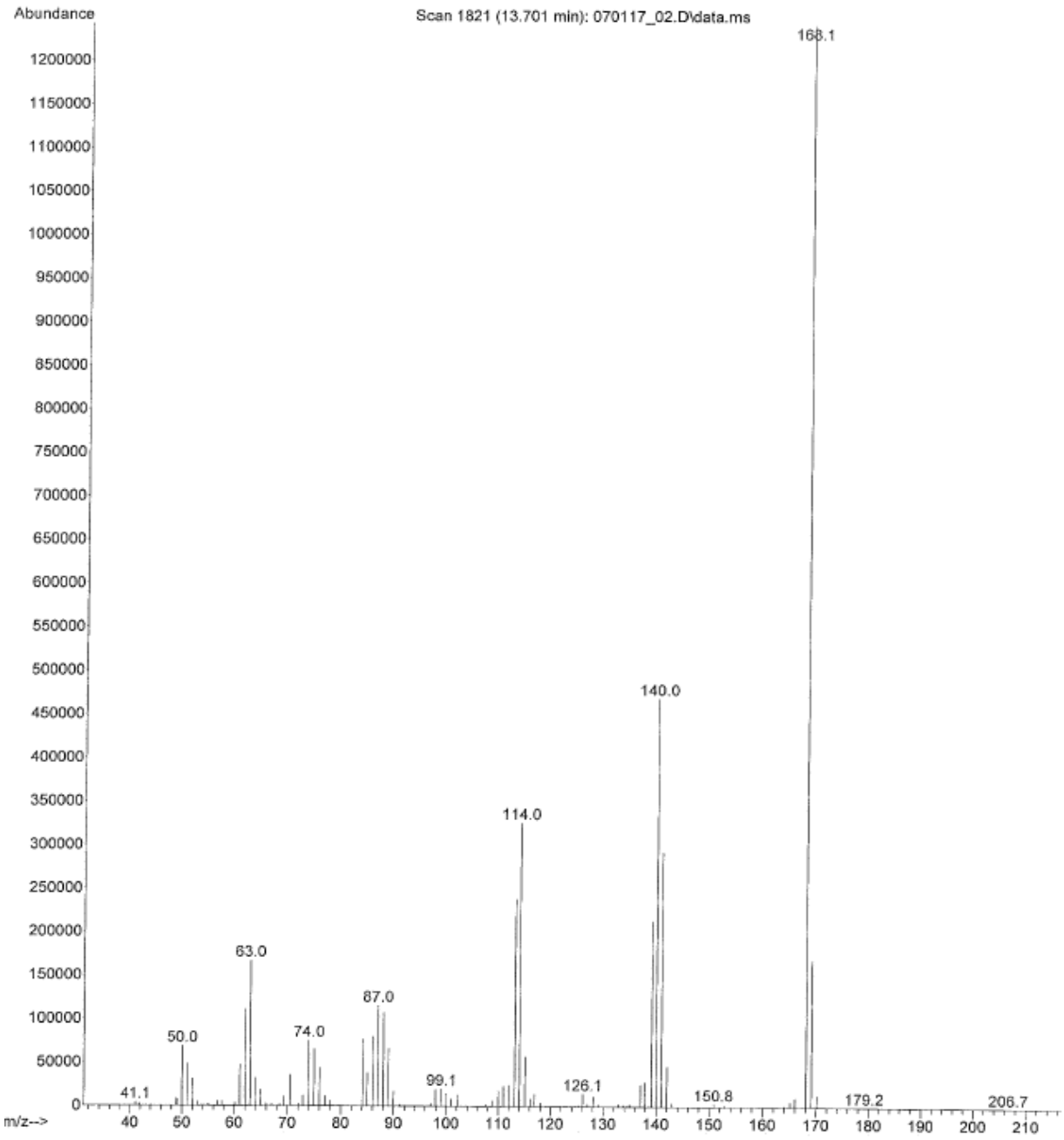


Figure 117: Mass spectrum for KA176.

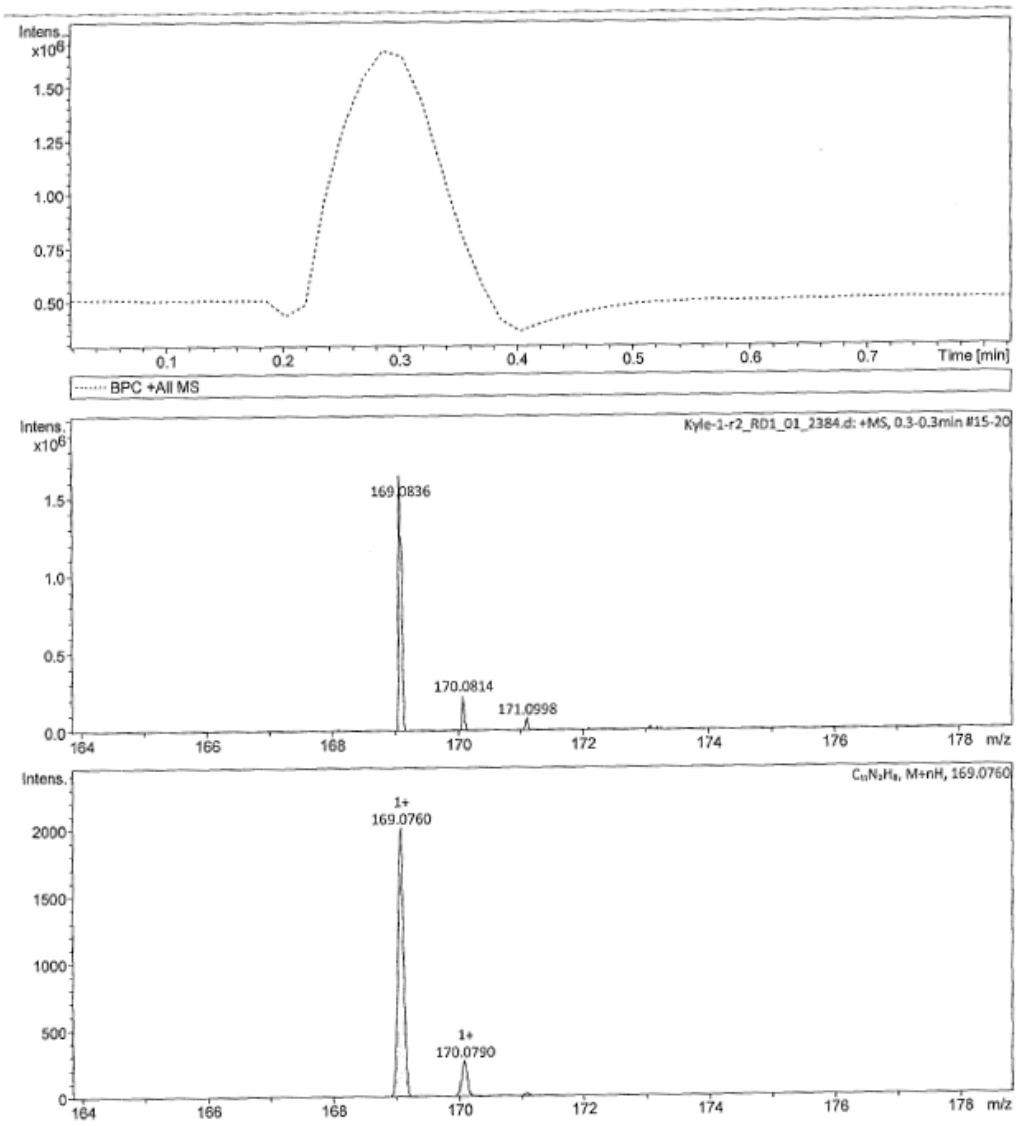


Figure 118: High performace mass spectrum for KA176. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix B: Supplementary data KA178

KA178

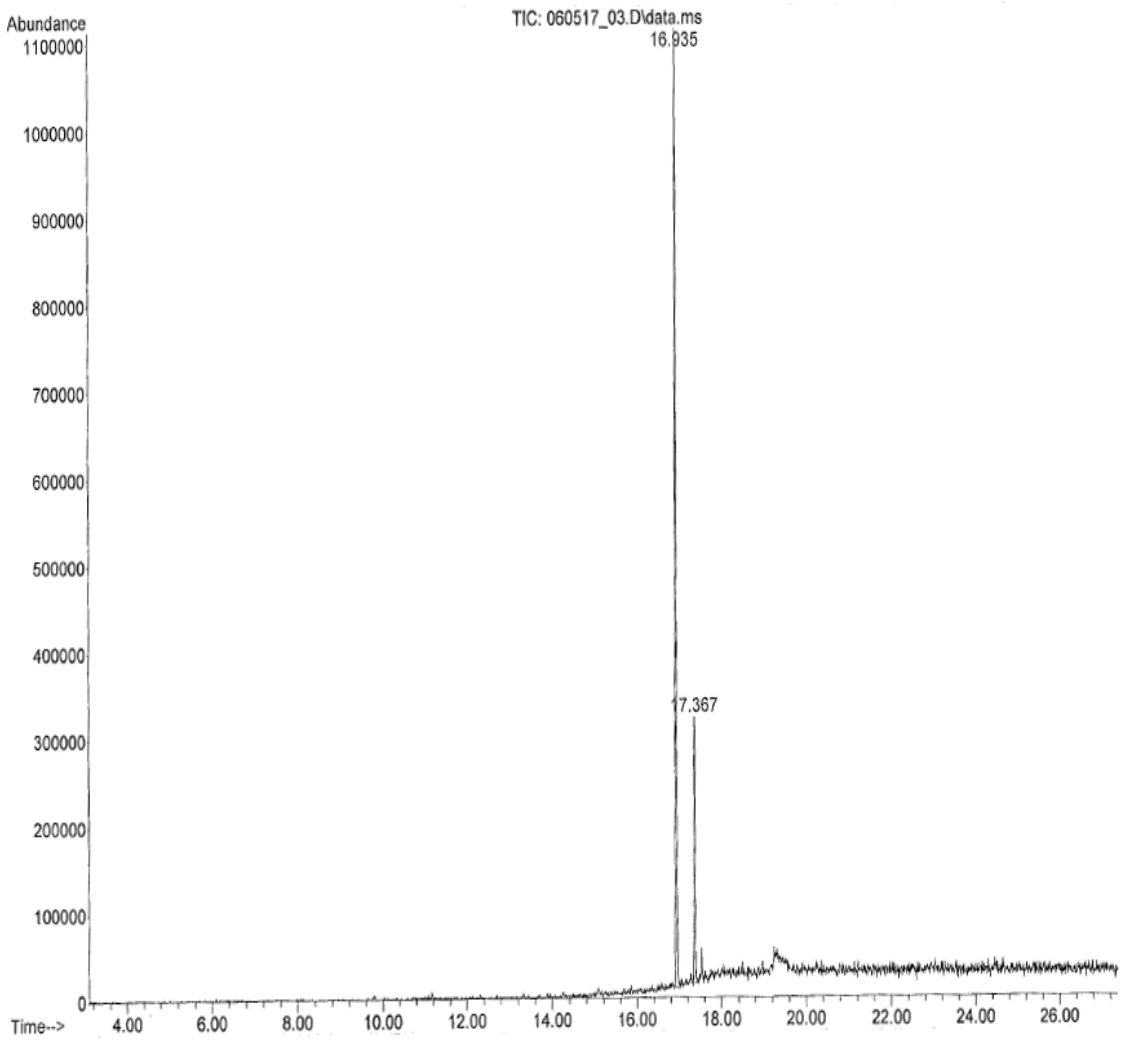


Figure 119: Gas chromatographic spectrum for KA178.

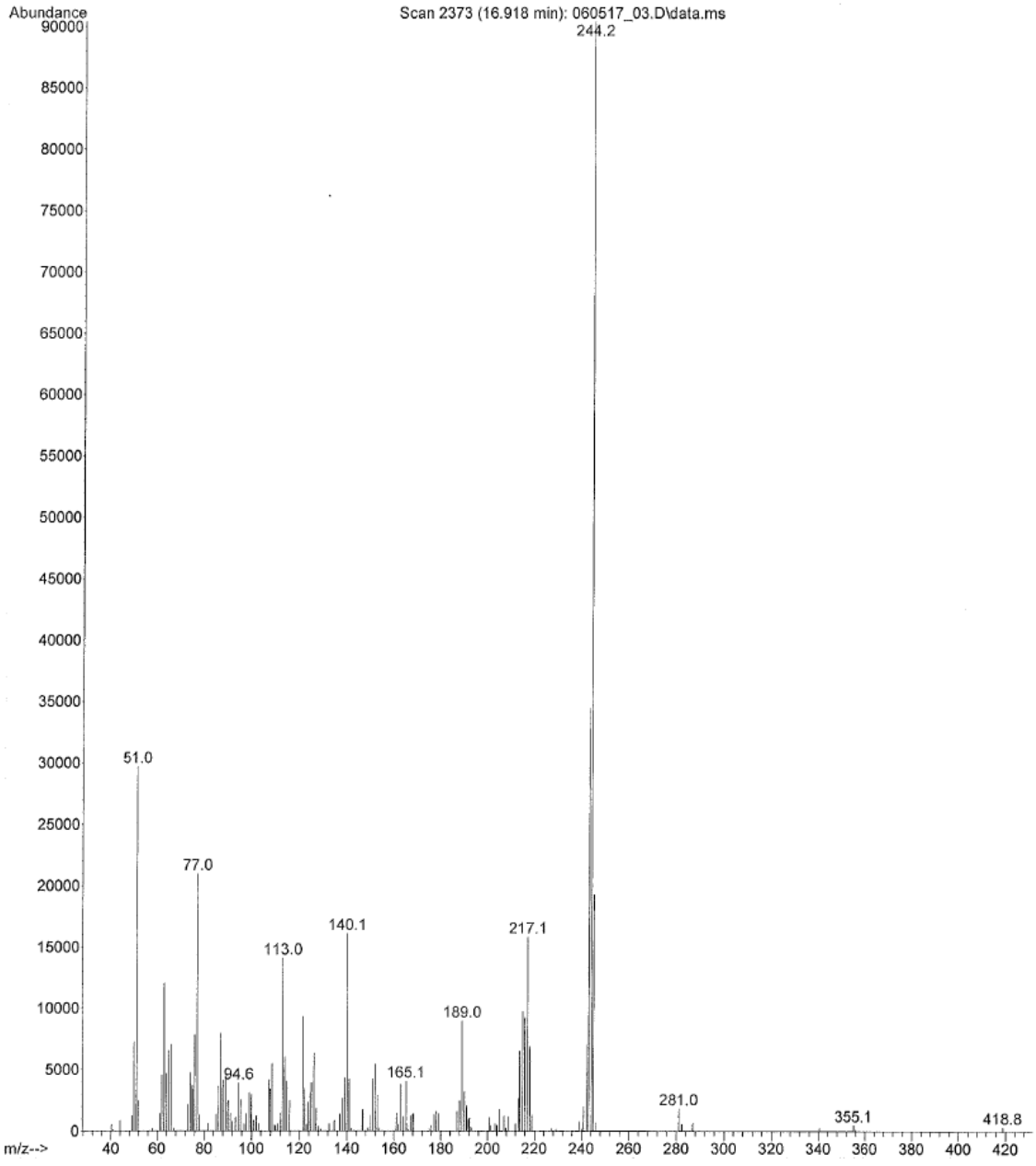


Figure 120: Mass spectrum for KA176

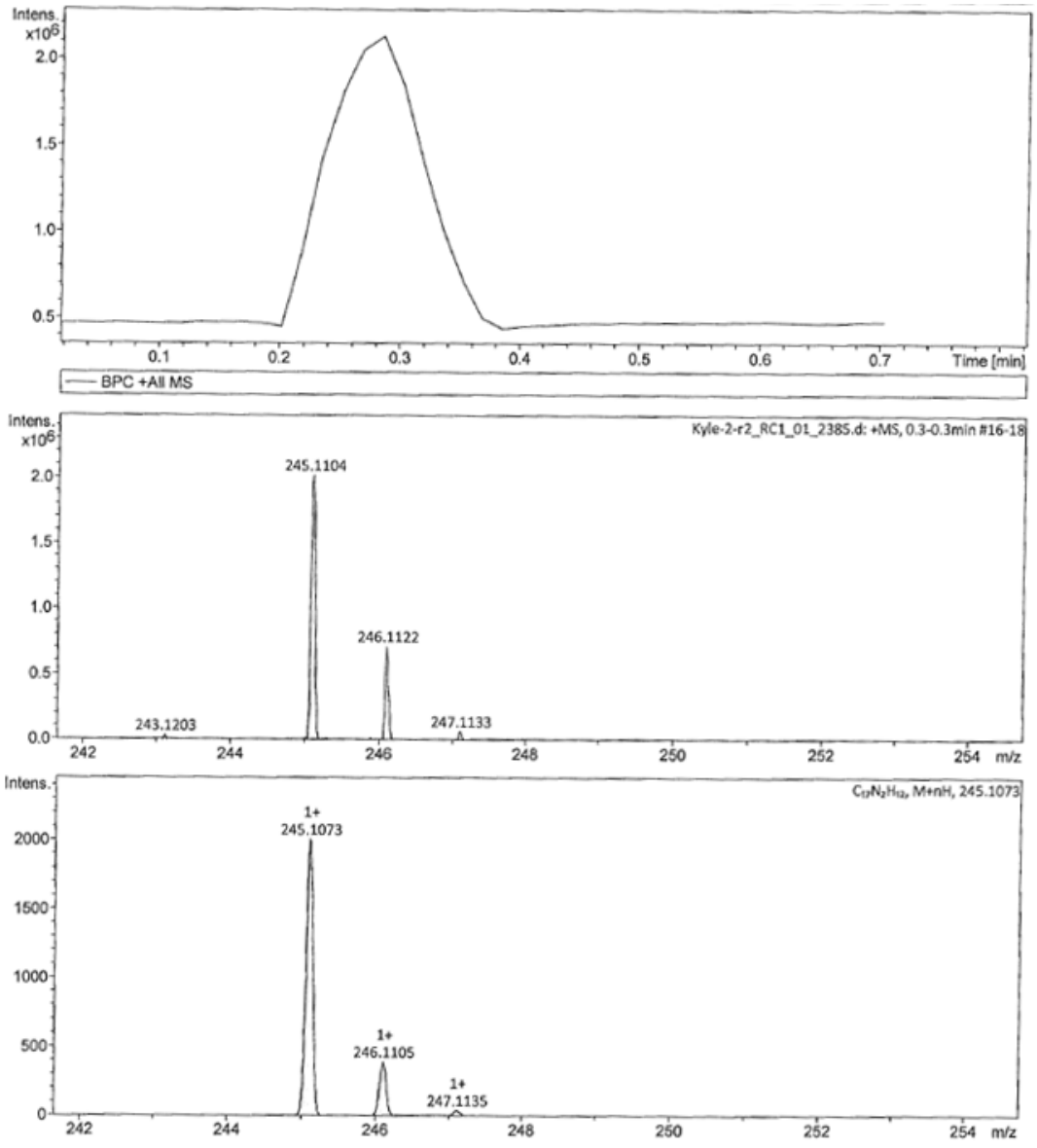


Figure 121: High performace mass spectrum for KA178. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix C: Supplementary data KA169

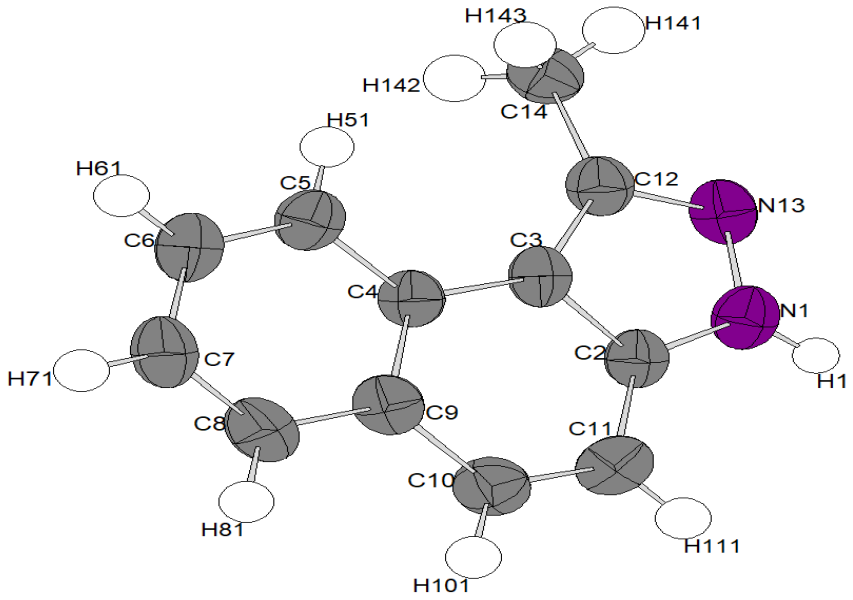


Figure 122: The crystal structure of KA169, for crystal solutions.

Table 9: *Crystal Data KA169*

Empirical Formula	$C_{12}H_{10}N_2$
Formula Weight	182.22
Crystal Color, Habit	white, platelet
Crystal Dimensions	0.20 X 0.20 X 0.20 mm
Crystal System	orthorhombic
Lattice Type	Primitive

Lattice Parameters	a = 5.30400(10) Å
	b = 10.6855(3) Å
	c = 16.7181(11) Å
	V = 947.51(7) Å^3
Space Group	$P2_12_12_1$ (#19)
Z value	2
D_{calc}	1.026 g/cm^3
F_{000}	304.00
w (CuKα)	17.337 cm^{-1}

Table 10: *Intensity Measurements KA169*

Diffractometer	Rigaku RAXIS
Radiation	CuKα (γ = 1.54187 Å)
	graphite mo chromated
Voltage, Current	50kV, 40mA
Temperature	20.0°C
Detector Aperture	460 x 256 mm
Data Images	139 exposures
w oscillation Range	20.0 - 200.0°

Exposure Rate	48.0 sec./^{o}
w oscillation Range	24.0 - 194.0^{o}
Exposure Rate	48.0 sec./^{o}
w oscillation Range	20.0 - 125.0^{o}
Exposure Rate	48.0 sec./^{o}
w oscillation Range	50.0 - 110.0^{o}
Exposure Rate	48.0 sec./^{o}
w oscillation Range	20.0 - 200.0^{o}
Exposure Rate	48.0 sec./^{o}
w oscillation Range	20.0 - 200.0^{o}
Exposure Rate	48.0 sec./^{o}
w oscillation Range	24.0 - 194.0^{o}
Exposure Rate	48.0 sec./^{o}
w oscillation Range	20.0 - 125.0^{o}
Exposure Rate	48.0 sec./^{o}
w oscillation Range	50.0 - 110.0^{o}
Exposure Rate	48.0 sec./^{o}
Detector Position	127.40 mm

Pixel Size	0.100 mm
$2q_{max}$	143.8°
-of Reflections Measured	Total: 6567
	Unique: 1788 (R_{int} = 0.117)
	Friedel pairs: 692
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.230 - 0.707)

***Table 11**: Structure Solution and Refinement*

Structure Solution	Direct Methods
Refinement	Full-matrix least-squares on F^2
Function Minimized	S w (Fo^2 - Fc^2)^2
Least Squares Weights	w = 1/ [$s^2(Fo^2)$ + (0.1000-P)^2 + 0.0000 - P]
	where P = (Max(Fo^2,0) + 2Fc^2)/3
$2q_{max}$ cutoff	143.8°
A malous Dispersion	All n-hydrogen atoms
-Observations (All reflections)	1788
-Variables	127
Reflection/Parameter Ratio	14.08

Residuals: R1 (I>2.00□(I))	0.1326
Residuals: R (All reflections)	0.2235
Residuals: wR2 (All reflections)	0.4137
Goodness of Fit Indicator	1.060
Flack Parameter (Friedel pairs = 692)	-2(3)
Max Shift/Error in Final Cycle	0.019
Maximum peak in Final Diff. Map	0.24 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.34 $e^-/Å^3$

Table 12: *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å2) KA169*

atom	x	y	z	*/Ueq
N(1)	0.1799(16)	0.2432(6)	0.0766(4)	0.106(3)
N(13)	0.3699(16)	0.1692(7)	0.0546(4)	0.111(3)
C(1)	0.3123(17)	0.1594(6)	0.1892(5)	0.093(3)
C(2)	0.1424(16)	0.2390(7)	0.1578(5)	0.092(3)
C(3)	0.6635(18)	0.0203(7)	0.1167(5)	0.109(3)
C(4)	0.3222(17)	0.1359(7)	0.2742(4)	0.085(3)
C(5)	0.4866(17)	0.0589(8)	0.3121(4)	0.102(3)
C(6)	-0.0422(18)	0.2818(8)	0.2846(5)	0.108(3)
C(7)	0.134(2)	0.1729(9)	0.4057(4)	0.122(4)

C(8)	0.458(2)	0.1117(8)	0.1206(4)	0.105(3)
C(9)	-0.0331(20)	0.3045(8)	0.2042(5)	0.110(3)
C(10)	0.1414(18)	0.1976(9)	0.3195(5)	0.107(3)
C(11)	0.482(2)	0.0362(10)	0.3934(5)	0.123(4)
C(12)	0.302(2)	0.0977(9)	0.4391(5)	0.122(4)
H(1)	0.0921	0.2879	0.0442	0.128
H(3A)	0.7715	0.0305	0.1623	0.131
H(3B)	0.7591	0.0334	0.0687	0.131
H(3C)	0.5948	-0.0628	0.1165	0.131
H(5)	0.6093	0.0191	0.2816	0.123
H(6)	-0.1642	0.3198	0.3163	0.129
H(7)	0.0100	0.2102	0.4371	0.147
H(9)	-0.1414	0.3623	0.1808	0.132
H(11)	0.5964	-0.0187	0.4168	0.147
H(12)	0.2989	0.0858	0.4942	0.146

Table 13: *Atomic displacement parameters (Å2) KA169*

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	0.1(2)	0.0987	0.0808	-0.0008	-0.0264	0.0047
N(13)	0.1(3)	0.1118	0.0767	-0.0068	-0.0049	0.0103
C(1)	0.11(20)	0.0817	0.0900	-0.0221	0.0107	0.0024

C(2)	0.1(2)	0.0869	0.0833	0.0182	0.0001	0.0042
C(3)	0.1(3)	0.0985	0.1048	-0.0033	0.0121	0.0008
C(4)	0.1(2)	0.0889	0.0550	0.0150	0.0017	-0.002
C(5)	0.1(3)	0.1133	0.0749	-0.0066	-0.0073	-0.003
C(6)	0.1(3)	0.1121	0.1062	0.0258	0.0036	-0.010
C(7)	0.2(3)	0.1306	0.0699	-0.0087	0.0254	-0.013
C(8)	0.1(3)	0.1071	0.0758	-0.0115	0.0115	0.0064
C(9)	0.1(3)	0.1052	0.1096	0.0099	-0.0289	0.0036
C(10)	0.1(3)	0.1086	0.0835	-0.0204	0.0040	-0.021
C(11)	0.1(3)	0.1518	0.0794	0.0027	-0.0121	0.0016
C(12)	0.2(3)	0.1106	0.0787	-0.0217	-0.0212	0.0145

Table 14: *Geometric parameters (Å, °) KA169*

N(1)-N(13)	1.333(9)	C(4)-C(5)	1.356(8)
N(1)-C(2)	1.372(10)	C(4)-C(10)	1.389(10)
N(13)-C(8)	1.347(7)	C(5)-C(11)	1.381(11)
C(1)-C(2)	1.346(9)	C(6)-C(9)	1.366(12)
C(1)-C(4)	1.444(12)	C(6)-C(10)	1.449(9)
C(1)-C(8)	1.472(13)	C(7)-C(10)	1.465(11)
C(2)-C(9)	1.399(12)	C(7)-C(12)	1.323(10)
C(3)-C(8)	1.466(10)	C(11)-C(12)	1.390(15)

N(13)-N(1)-C(2)	111.4(6)
N(1)-N(13)-C(8)	107.7(7)
C(2)-C(1)-C(4)	121.2(7)
C(2)-C(1)-C(8)	105.4(7)
C(4)-C(1)-C(8)	133.4(7)
N(1)-C(2)-C(1)	108.0(7)
N(1)-C(2)-C(9)	128.9(7)
C(1)-C(2)-C(9)	123.1(7)
C(1)-C(4)-C(5)	126.1(7)
C(1)-C(4)-C(10)	115.5(7)
C(5)-C(4)-C(10)	118.5(6)
C(4)-C(5)-C(11)	123.8(8)
C(9)-C(6)-C(10)	118.9(8)
C(10)-C(7)-C(12)	120.4(9)
N(13)-C(8)-C(1)	107.4(8)
N(13)-C(8)-C(3)	121.6(7)
C(1)-C(8)-C(3)	130.9(7)
C(2)-C(9)-C(6)	118.7(8)
C(4)-C(10)-C(6)	122.6(7)
C(4)-C(10)-C(7)	118.1(8)
C(6)-C(10)-C(7)	119.3(8)
C(5)-C(11)-C(12)	118.1(9)
C(7)-C(12)-C(11)	121.2(8)

Table 15: *Hydrogen bond geometry (Å, °) KA169*

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···N13	162(2)	0.889	2.041	2.900(6)

Symmetry codes: (i) x+1, y, z; (ii) −x+2, −y+1, −z+1.

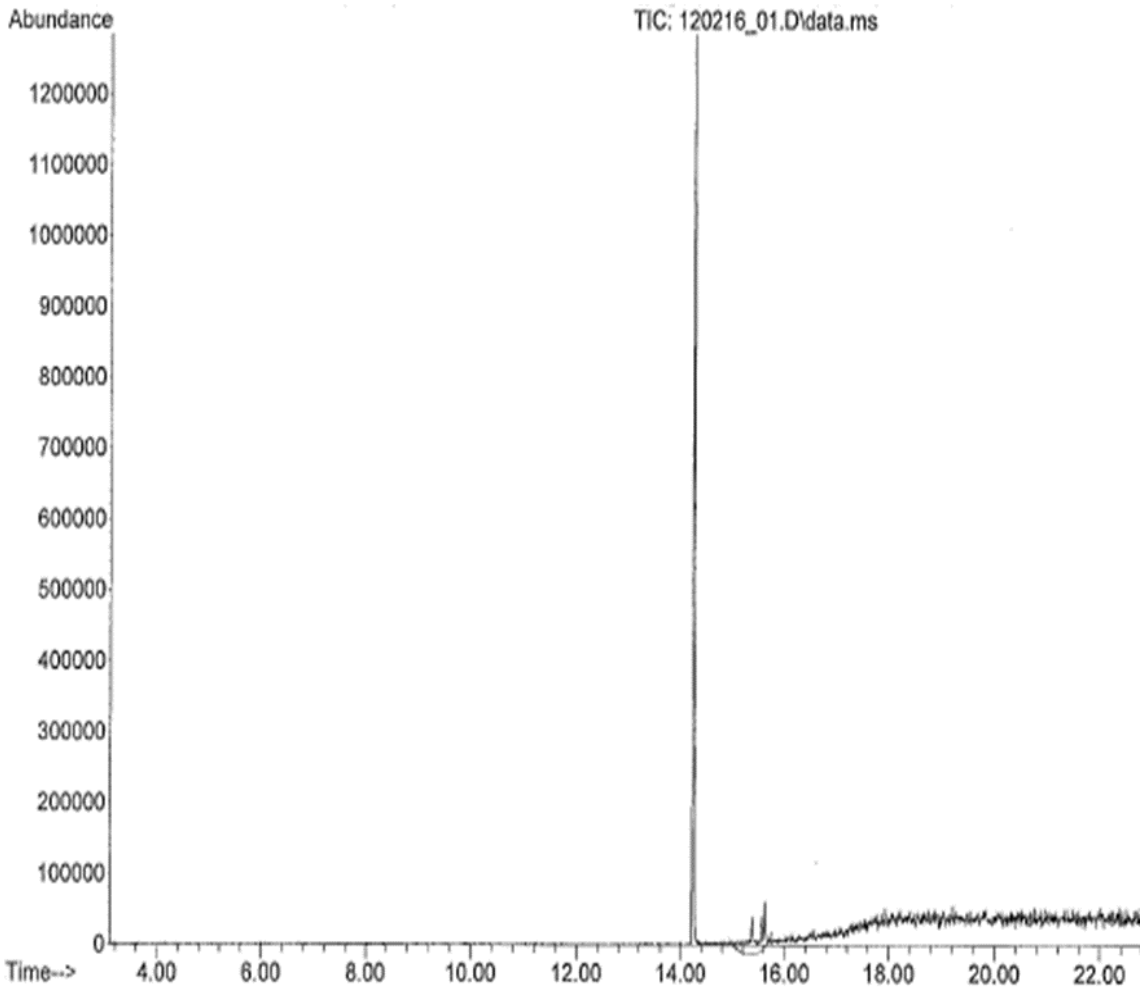


Figure 123: Gas chromatographic spectrum for KA169

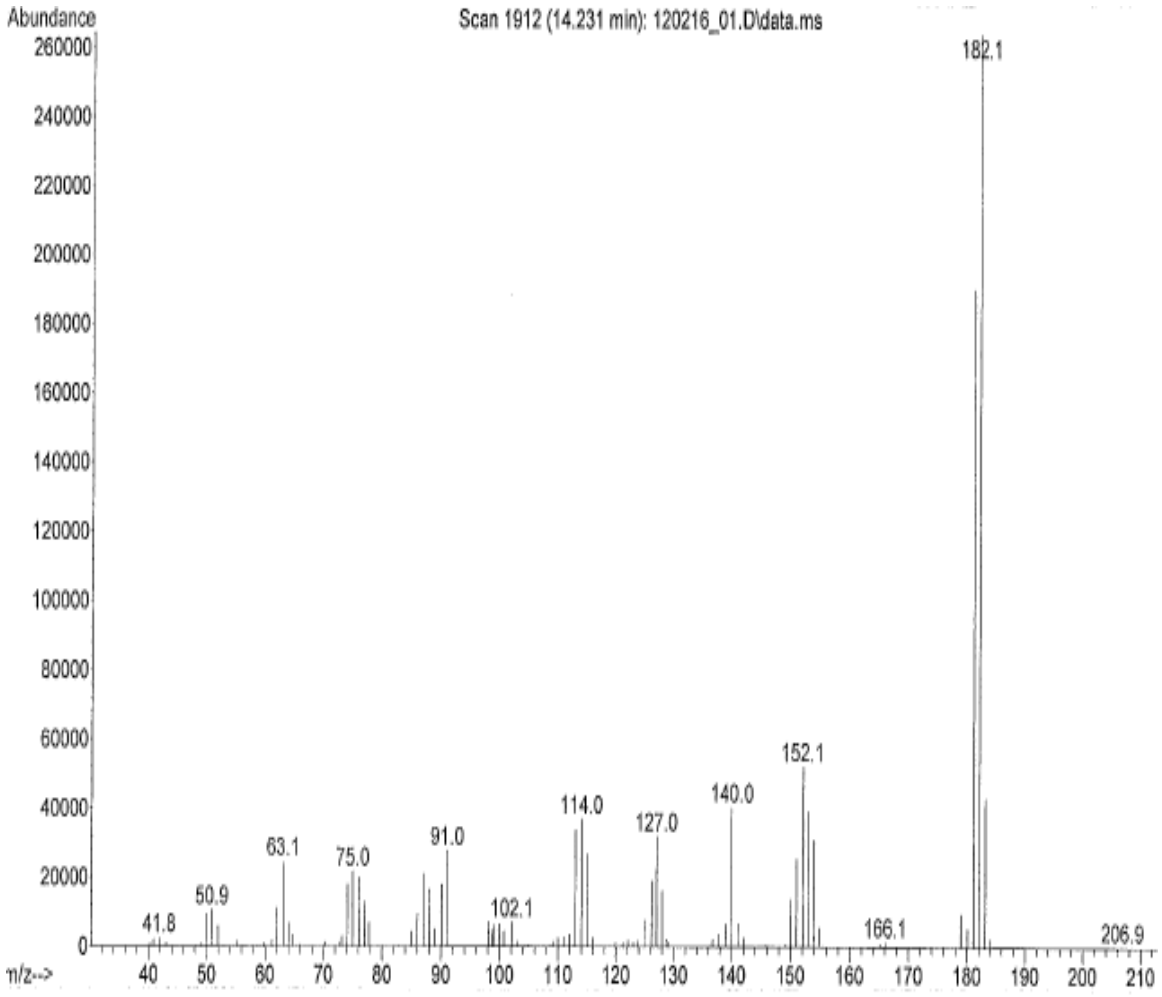


Figure 124: Mass spectrum for KA169

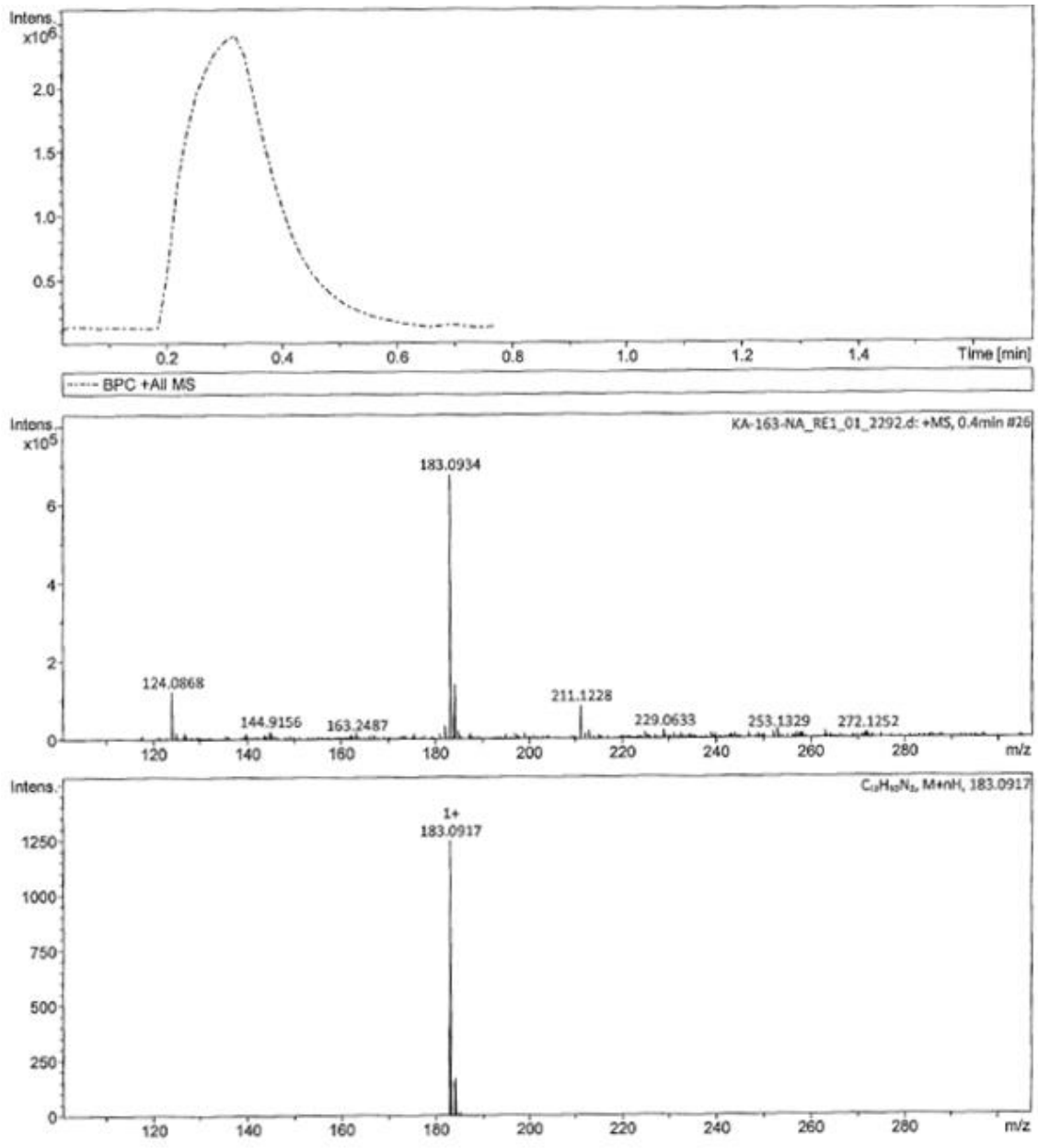


Figure 125: High performace mass spectrum for KA169. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix D: Supplementary data KA173

KA173

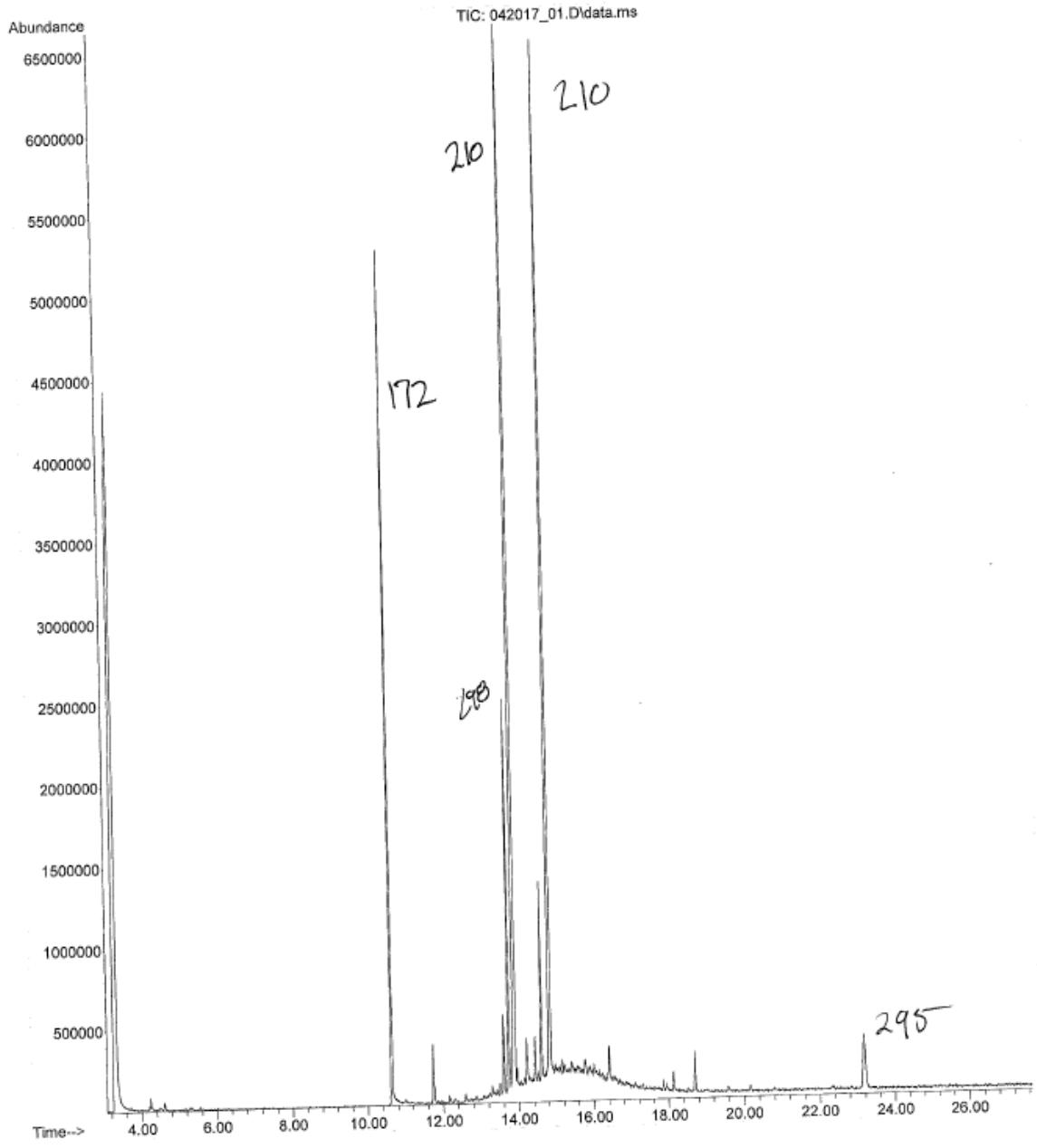


Figure 126: Gas chromatographic spectrum for KA173

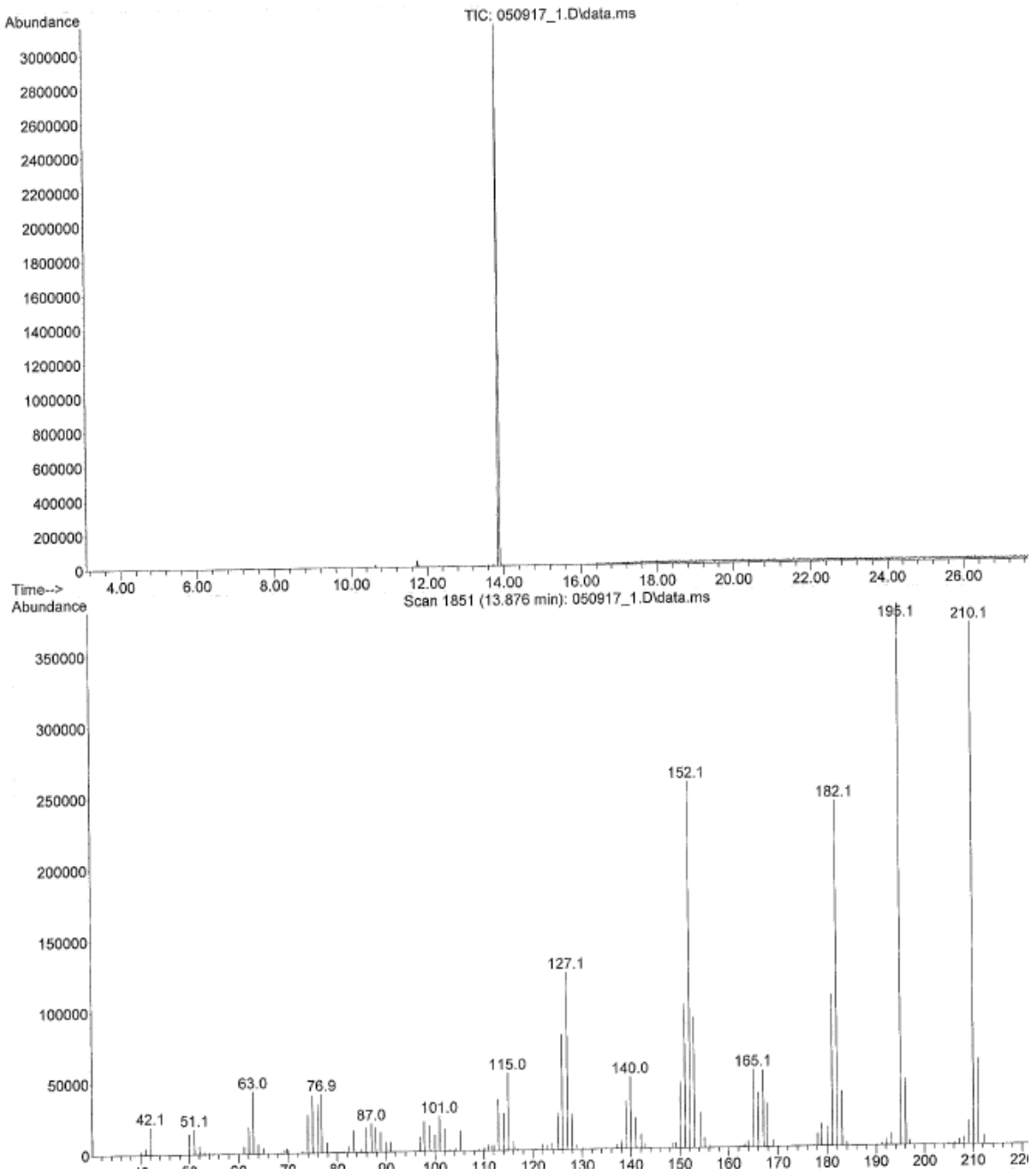


Figure 127: (Top) Gas chromatographic spectrum for KA173A. (Bottom) Mass spectrum for KA173A

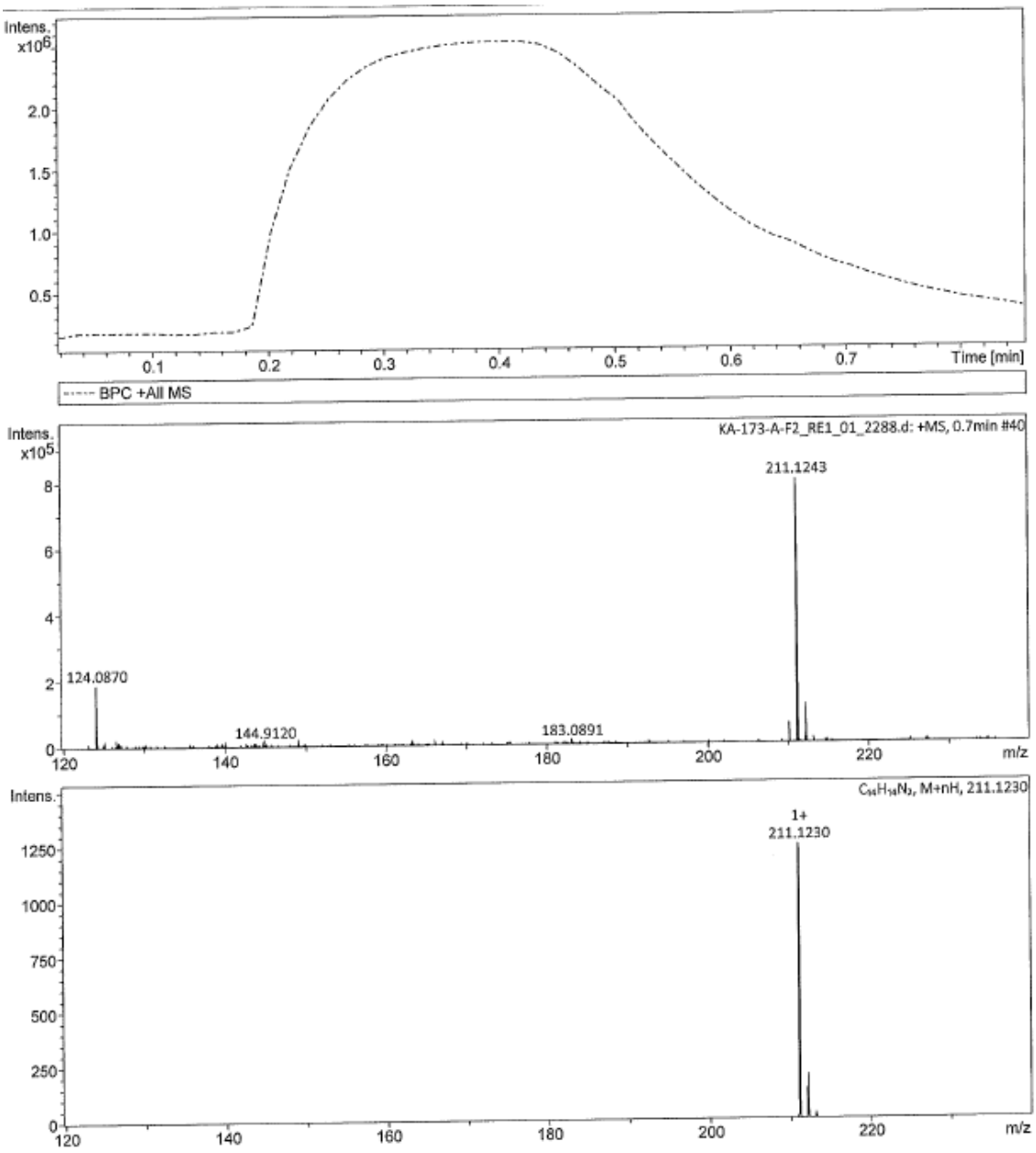


Figure 128: High performace mass spectrum for KA173A. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

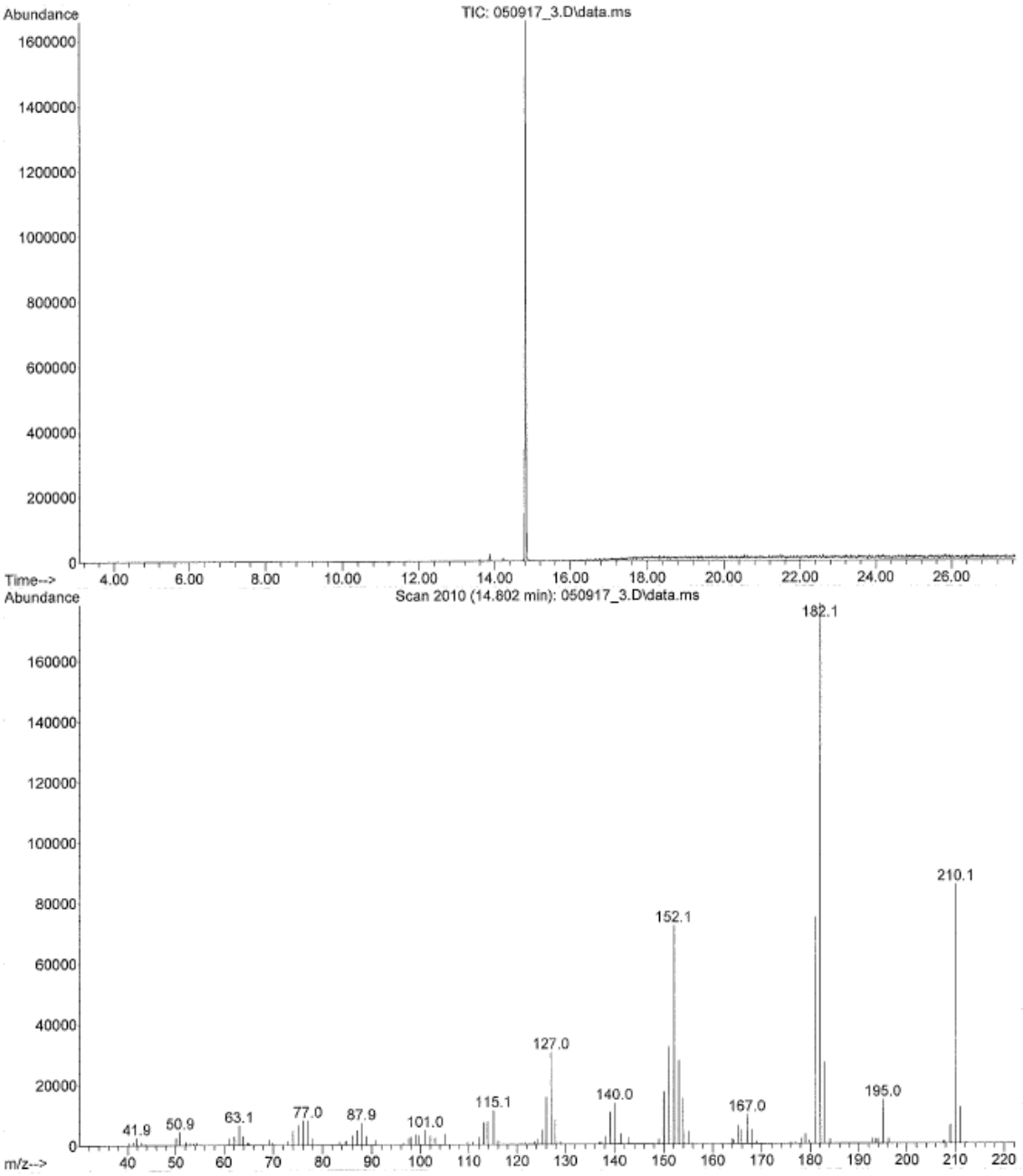


Figure 129: (Top) Gas chromatographic spectrum for KA173B. (Bottom) Mass spectrum for KA173B

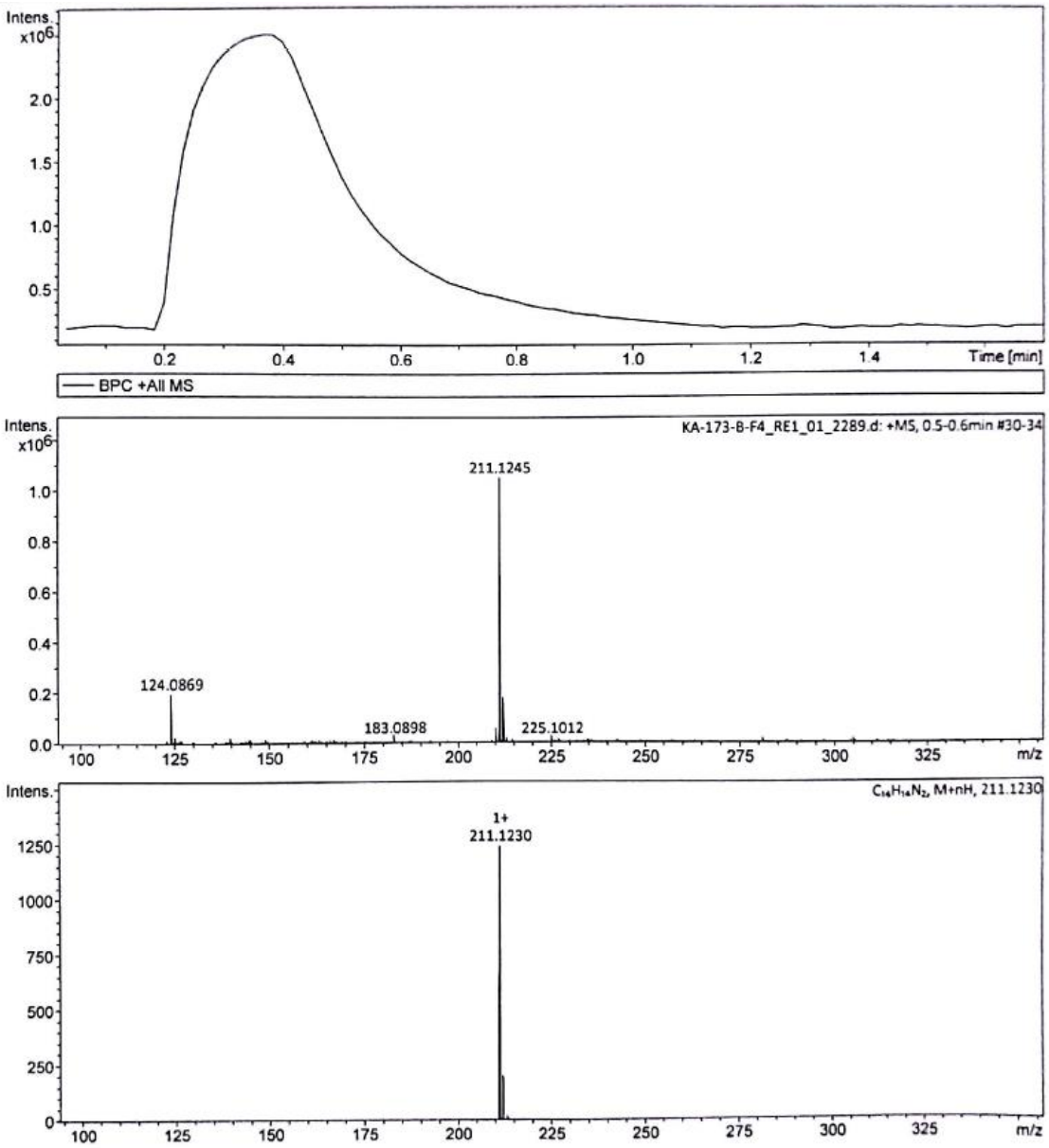


Figure 130: High performace mass spectrum for KA178. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix E: Supplementary data KA172

KA172

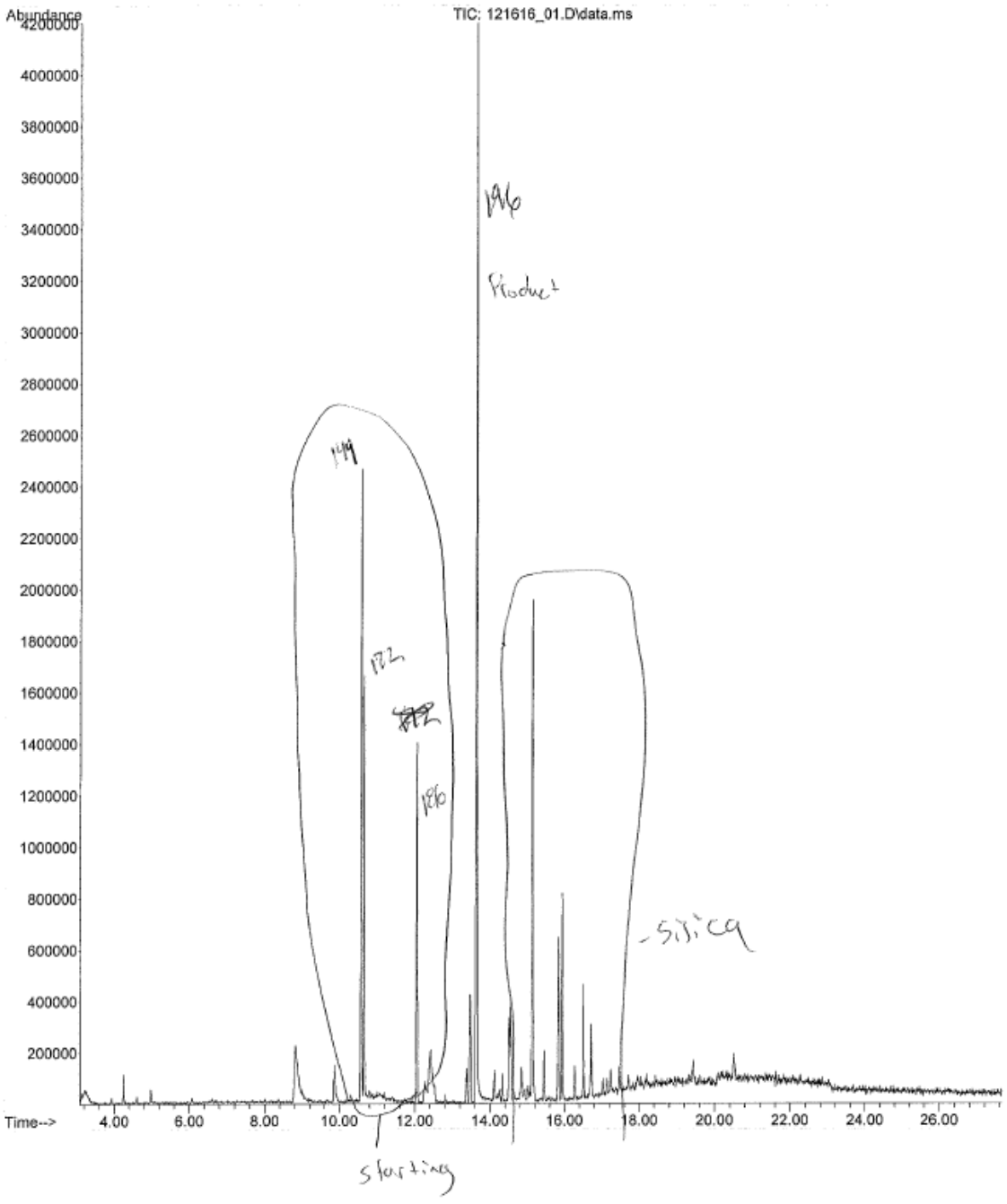


Figure 131: Gas chromatographic spectrum for KA172.

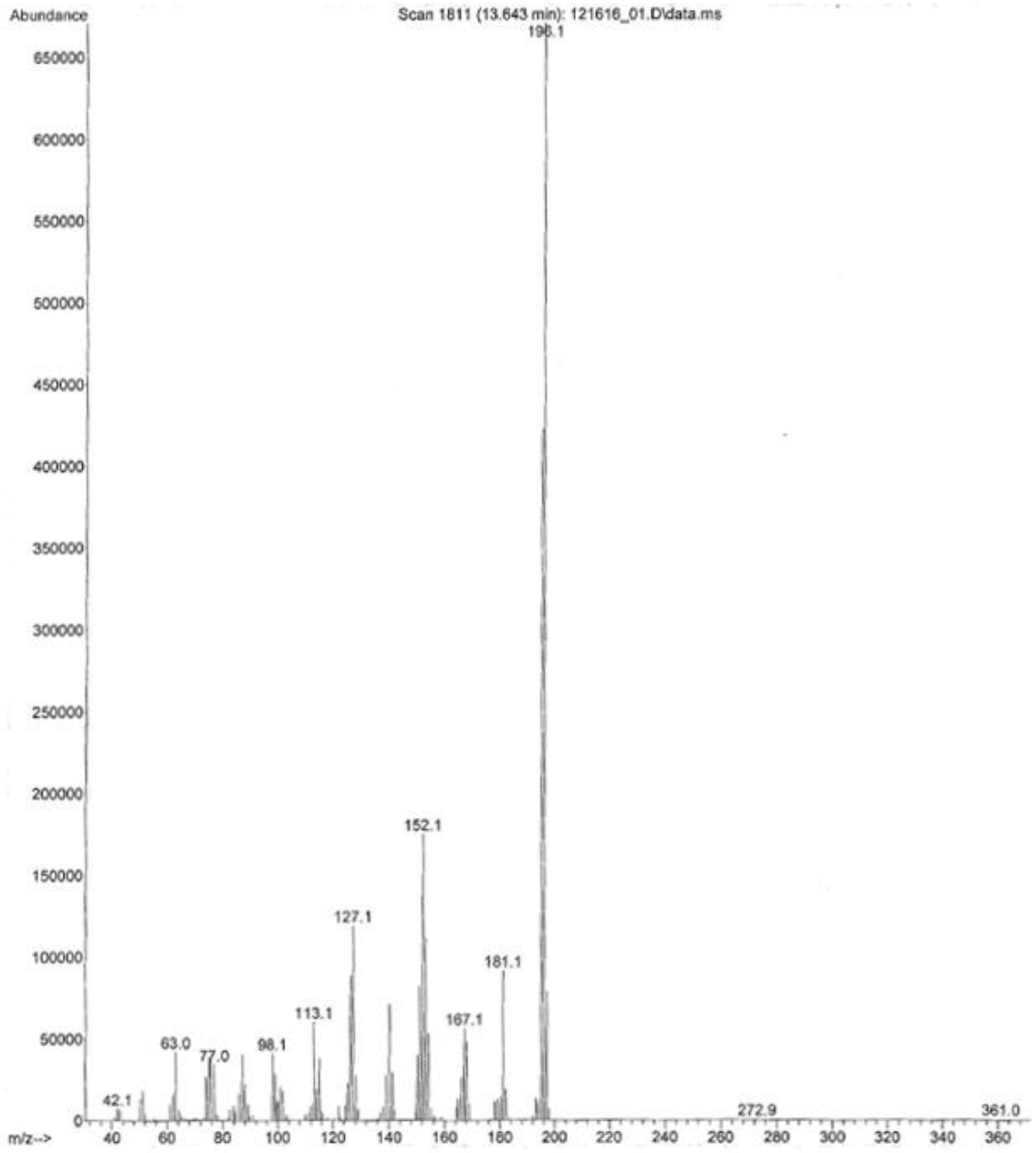


Figure 132: Mass spectrum for KA172

Appendix F: Supplementary data KA143

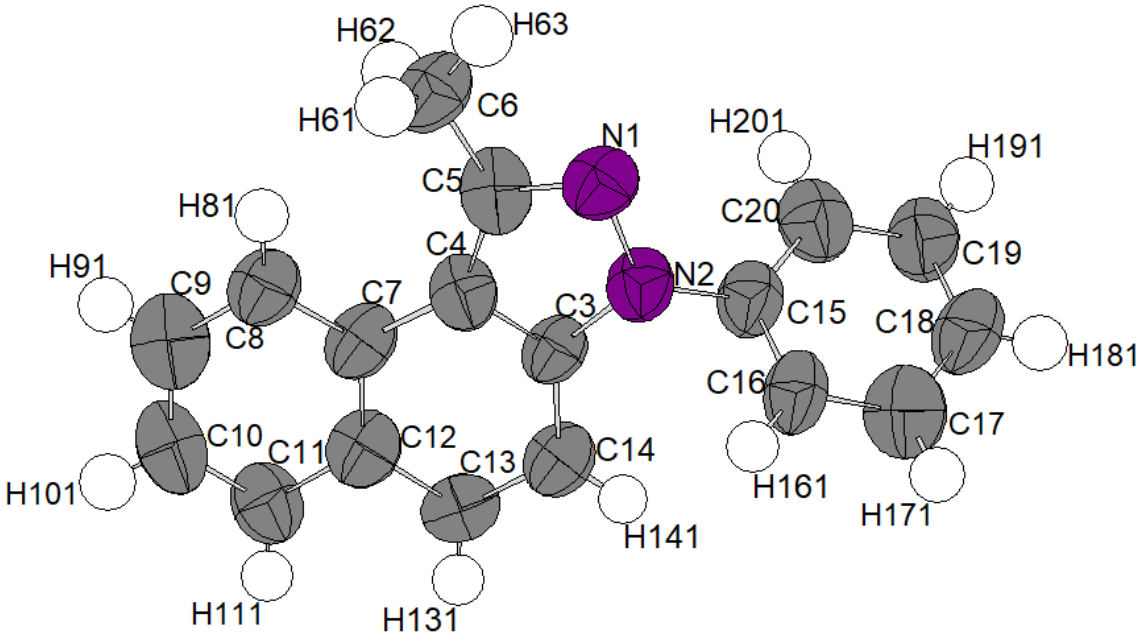


Figure 133: The crystal structure of KA143, for crystal solutions.

Table 16: *Crystal Data KA143*

Empirical Formula	$C_{18}H_{14}N_2$
Formula Weight	258
Crystal Color, Habit	colorless, platelet
Crystal Dimensions	0.20 X 0.20 X 0.20 mm
Crystal System	orthorhombic
Lattice Type	Primitive

Lattice Parameters	a = 11.188(3) Å
	b = 11.750(3) Å
	c = 10.088(2) Å
	V = 1326.2(6) Å^3
Space Group	Pca2$_1$ (#29)
Z value	4
D_{calc}	1.299 g/cm^3
F_{000}	544.00
m(CuKa)	6.352 cm^{-1}

Table 17: *Intensity Measurements KA143*

Diffractometer	Rigaku RAXIS
Radiation	CuKa (l = 1.54187 Å)
	graphite mo chromated
Voltage, Current	50kV, 40mA
Temperature	-150.0^{o}C
Detector Aperture	460 x 256 mm
Data Images	144 exposures
w oscillation Range	-85.0 - 265.0^o
Exposure Rate	60.0 sec./^{o}

w oscillation Range	-18.0 - 122.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	14.0 - 94.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	18.0 - 98.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	24.0 - 94.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	-85.0 - 265.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	-18.0 - 122.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	14.0 - 94.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	18.0 - 98.0^{o}
Exposure Rate	60.0 sec./^{o}
w oscillation Range	24.0 - 94.0^{o}
Exposure Rate	60.0 sec./^{o}

Detector Position	127.40 mm
Pixel Size	0.100 mm
$2q_{max}$	122.1^{o}
-of Reflections Measured	Total: 10451
	Unique: 1873 (R_{int} = 0.177)
	Friedel pairs: 823
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.223 - 0.881)

Table 18: *Structure Solution and Refinement KA143*

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F^2
Function Minimized	S w $(Fo^2 - Fc^2)^2$
Least Squares Weights	w = 1/ [$s^2(Fo^2)$ + $(0.1000-P)^2$
	+ 0.0000- P]
	where P = $(Max(Fo^2,0) + 2Fc^2)/3$
$2q_{max}$ cutoff	122.1^{o}
A malous Dispersion	All n-hydrogen atoms
-Observations (All reflections)	1873
-Variables	181

Reflection/Parameter Ratio	10.35
Residuals: R1 (I>2.00s(I))	0.0741
Residuals: R (All reflections)	0.1298
Residuals: wR2 (All reflections)	0.2122
Goodness of Fit Indicator	0.876
Flack Parameter (Friedel pairs = 823)	1(2)
Max Shift/Error in Final Cycle	0.059
Maximum peak in Final Diff. Map	0.20 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.17 $e^-/Å^3$

Table 19: *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å2) KA143*

atom	x	y	z	*/Ueq
N1	0.6452(6)	0.7765(6)	0.5369(8)	0.0863 1.0000
N2	0.5497(6)	0.7607(6)	0.4495(8)	0.0822 1.0000
C3	0.5421(6)	0.6462(7)	0.4224(9)	0.0694 1.0000
C4	0.6316(7)	0.5917(7)	0.4872(11)	0.0799 1.0000
C5	0.6909(8)	0.6748(8)	0.5568(11)	0.0902 1.0000
C6	0.7996(8)	0.6689(9)	0.6441(11)	0.1000 1.0000
C7	0.6418(7)	0.4695(8)	0.4790(11)	0.0822 1.0000
C8	0.7256(8)	0.4055(8)	0.5475(10)	0.0894 1.0000

C9	0.7277(9)	0.2887(9)	0.5330(13)	0.1083 1.0000
C10	0.6497(11)	0.2352(9)	0.4507(13)	0.1111 1.0000
C11	0.5656(9)	0.2967(8)	0.3803(11)	0.0951 1.0000
C12	0.5610(9)	0.4160(8)	0.3955(10)	0.0888 1.0000
C13	0.4696(8)	0.4756(8)	0.3257(9)	0.0843 1.0000
C14	0.4578(7)	0.5934(7)	0.3376(10)	0.0833 1.0000
C15	0.4795(8)	0.8534(8)	0.4158(11)	0.0855 1.0000
C16	0.4329(8)	0.8641(8)	0.2918(11)	0.0917 1.0000
C17	0.3595(9)	0.9543(10)	0.2544(12)	0.1104 1.0000
C18	0.3299(8)	1.0328(10)	0.3538(11)	0.1042 1.0000
C19	0.3753(9)	1.0229(8)	0.4764(14)	0.1055 1.0000
C20	0.4485(8)	0.9337(8)	0.5125(13)	0.1013 1.0000
H61	0.8647	0.6365	0.5961	0.1518 1.0000
H63	0.8196	0.7447	0.6725	0.1516 1.0000
H62	0.7818	0.6225	0.7186	0.1521 1.0000
H81	0.7808	0.4415	0.6019	0.1137 1.0000
H91	0.7814	0.2456	0.5828	0.1218 1.0000
H101	0.6518	0.1568	0.4432	0.1288 1.0000
H111	0.5111	0.2592	0.3249	0.1057 1.0000
H131	0.4178	0.4361	0.2709	0.1038 1.0000

H141	0.3974	0.6330	0.2917	0.0949 1.0000
H161	0.4503	0.8093	0.2272	0.1091 1.0000
H171	0.3287	0.9628	0.1698	0.1247 1.0000
H181	0.2781	1.0913	0.3345	0.1210 1.0000
H191	0.3574	1.0788	0.5424	0.1205 1.0000
H201	0.4777	0.9256	0.5989	0.1121 1.0000

Table 20: *Atomic displacement parameters (Å2) KA143*

atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N1	0.062(4)	0.098(5)	0.099(6)	0.005(5)	-0.001(4)	-0.010(4)
N2	0.061(4)	0.082(5)	0.103(7)	0.004(4)	0.000(4)	0.002(3)
C3	0.049(4)	0.080(5)	0.079(6)	0.008(5)	-0.001(4)	-0.001(4)
C4	0.055(5)	0.075(5)	0.109(8)	0.001(5)	0.010(5)	-0.003(4)
C5	0.072(5)	0.086(6)	0.113(8)	0.016(6)	0.027(6)	-0.003(5)
C6	0.070(6)	0.111(7)	0.119(9)	0.028(7)	-0.013(6)	-0.015(5)
C7	0.053(4)	0.102(6)	0.091(7)	0.012(6)	0.004(5)	0.002(4)
C8	0.065(5)	0.101(7)	0.102(8)	0.006(6)	0.001(5)	0.003(5)
C9	0.091(7)	0.106(8)	0.127(11)	0.017(7)	0.036(7)	0.001(6)
C10	0.114(8)	0.080(6)	0.139(12)	-0.003(7)	0.024(8)	0.013(7)
C11	0.091(7)	0.085(6)	0.109(10)	-0.004(6)	0.013(6)	0.003(6)

C12	0.074(6)	0.098(7)	0.094(8)	0.008(6)	0.006(5)	-0.001(5)
C13	0.076(6)	0.103(7)	0.074(7)	0.002(5)	0.000(5)	-0.007(5)
C14	0.062(5)	0.098(6)	0.090(7)	0.007(6)	0.001(5)	0.003(5)
C15	0.071(5)	0.079(6)	0.106(8)	0.009(6)	-0.004(6)	0.003(5)
C16	0.068(6)	0.090(6)	0.117(9)	0.013(6)	0.002(6)	0.017(5)
C17	0.076(6)	0.130(9)	0.125(10)	0.001(8)	0.031(7)	0.010(6)
C18	0.068(6)	0.118(8)	0.127(10)	0.013(8)	-0.011(6)	0.017(6)
C19	0.083(6)	0.084(7)	0.150(10)	0.005(7)	-0.012(7)	-0.002(5)
C20	0.086(6)	0.086(6)	0.132(9)	-0.001(7)	0.005(6)	-0.005(5)

Table 21: *Geometric parameters (Å, °) KA143*

N1-C2	1.347(5)	C5-C6	1.373(5)
N1-N13	1.363(5)	C5-H51	0.969
N1-H1	0.889(18)	C6-C7	1.386(7)
C2-C3	1.391(5)	C6-H61	0.941
C2-C11	1.418(6)	C7-C8	1.362(6)
C3-C4	1.445(5)	C7-H71	0.945
C3-C12	1.414(5)	C8-C9	1.418(5)
C4-C5	1.406(5)	C8-H81	0.958
C4-C9	1.409(6)	C9-C10	1.436(6)

C10-C11	1.361(5)	C4-C5-C6	120.2(4)
C10-H101	0.959	C4-C5-H51	118.8
C11-H111	0.938	C6-C5-H51	121.0
C12-N13	1.332(5)	C5-C6-C7	120.9(5)
C12-C14	1.488(6)	C5-C6-H61	121.3
C14-H141	0.987	C7-C6-H61	117.8
C14-H142	0.966	C6-C7-C8	120.3(4)
C14-H143	0.993	C6-C7-H71	120.6
C2-N1-N13	110.8(3)	C8-C7-H71	119.1
C2-N1-H1	124.9(13)	C7-C8-C9	120.7(4)
N13-N1-H1	123.9(12)	C7-C8-H81	120.2
N1-C2-C3	107.6(4)	C9-C8-H81	119.1
N1-C2-C11	129.1(4)	C8-C9-C4	118.7(4)
C3-C2-C11	123.2(3)	C8-C9-C10	120.7(4)
C2-C3-C4	119.5(4)	C4-C9-C10	120.6(3)
C2-C3-C12	104.8(3)	C9-C10-C11	122.3(4)
C4-C3-C12	135.7(4)	C9-C10-H101	117.9
C3-C4-C5	123.5(4)	C11-C10-H101	119.8
C3-C4-C9	117.3(4)	C2-C11-C10	117.1(4)
C5-C4-C9	119.3(4)	C2-C11-H111	120.7

C10-C11-H111	122.1	C12-C14-H142	107.7
C3-C12-N13	110.2(4)	H141-C14-H142	111.2
C3-C12-C14	130.6(4)	C12-C14-H143	110.0
N13-C12-C14	119.2(4)	H141-C14-H143	111.3
N1-N13-C12	106.6(3)	H142-C14-H143	105.9
C12-C14-H141	110.6		

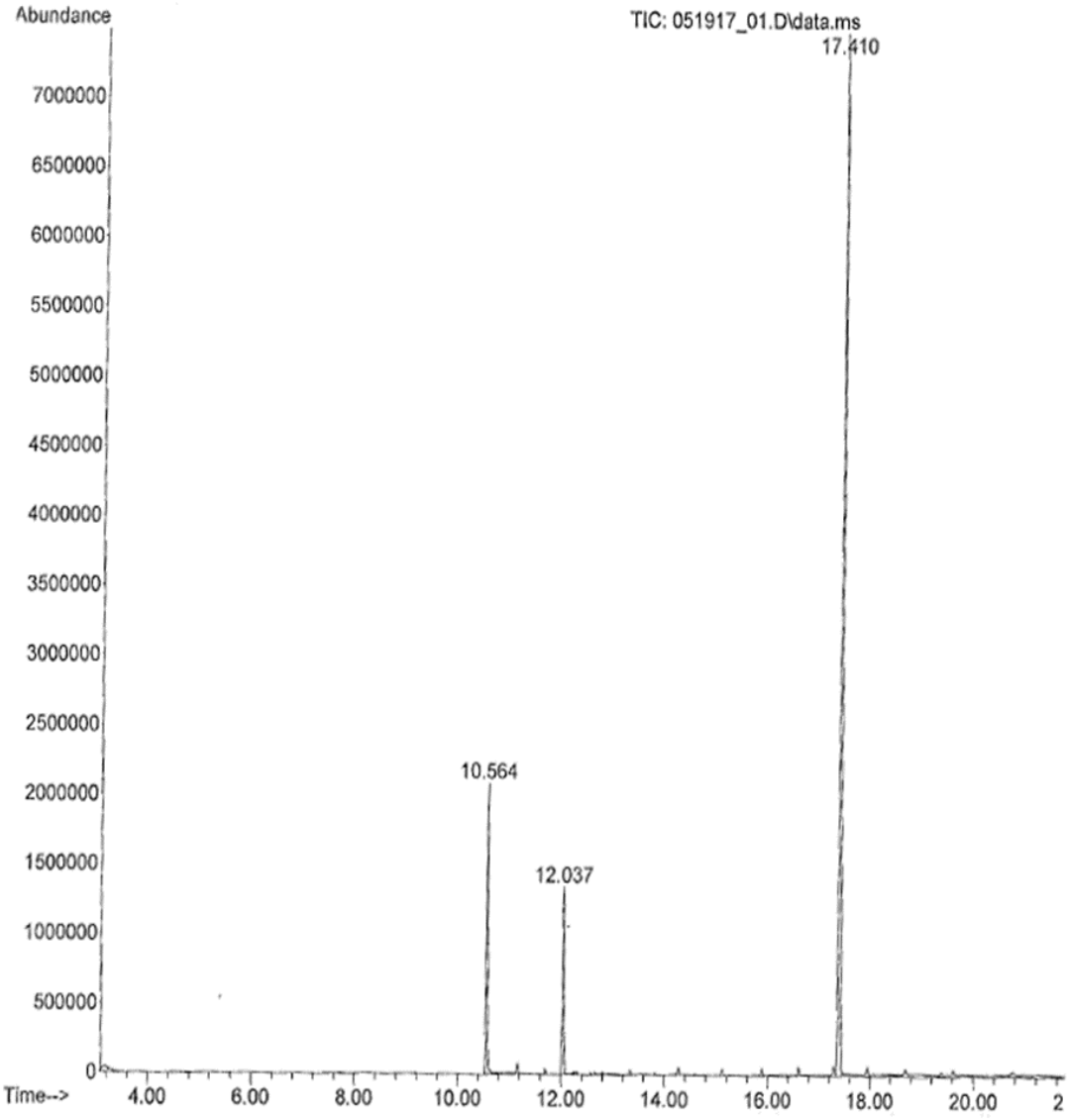


Figure 134 : Gas chromatographic spectrum for KA143.

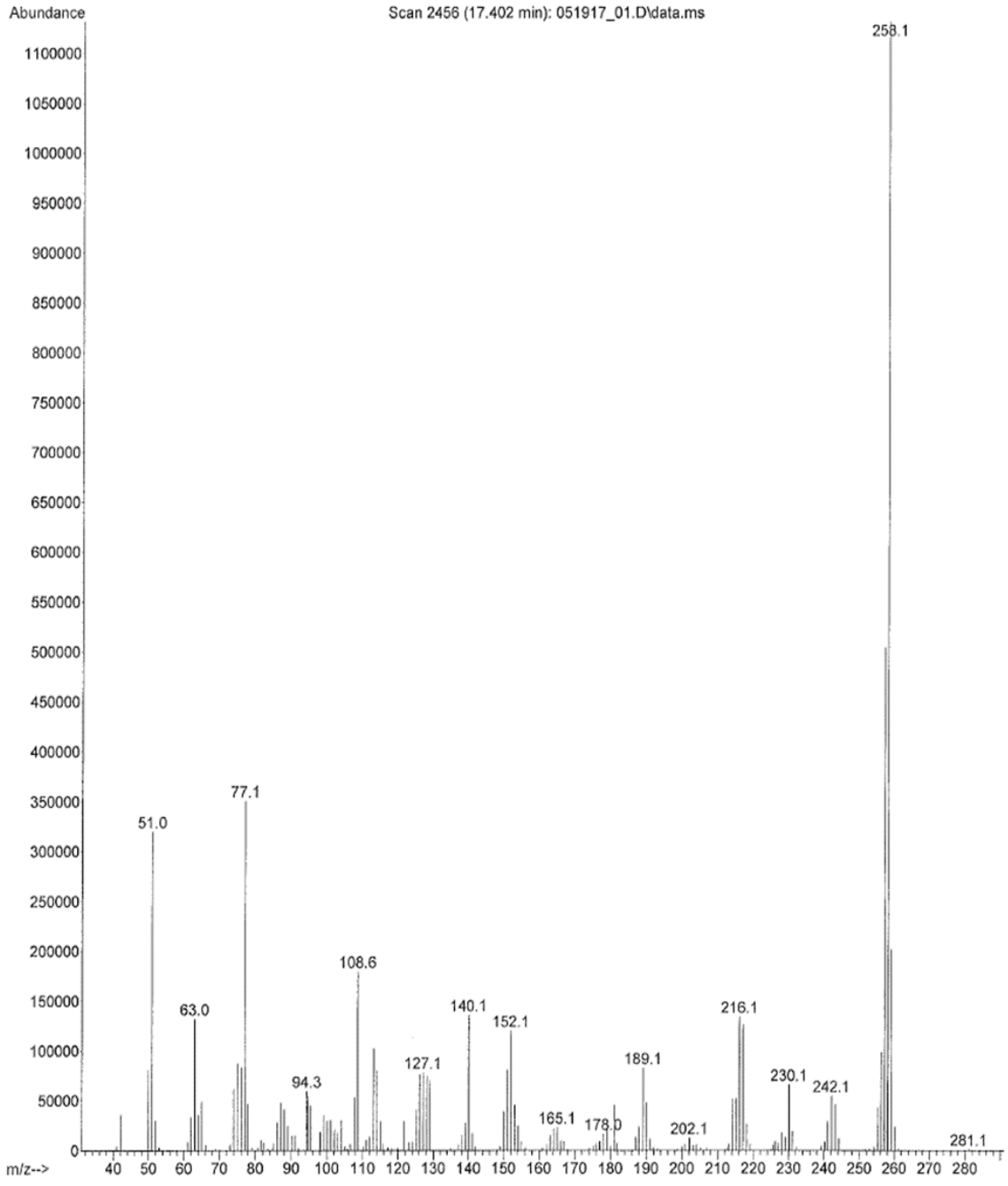


Figure 135: Mass spectrum for KA143

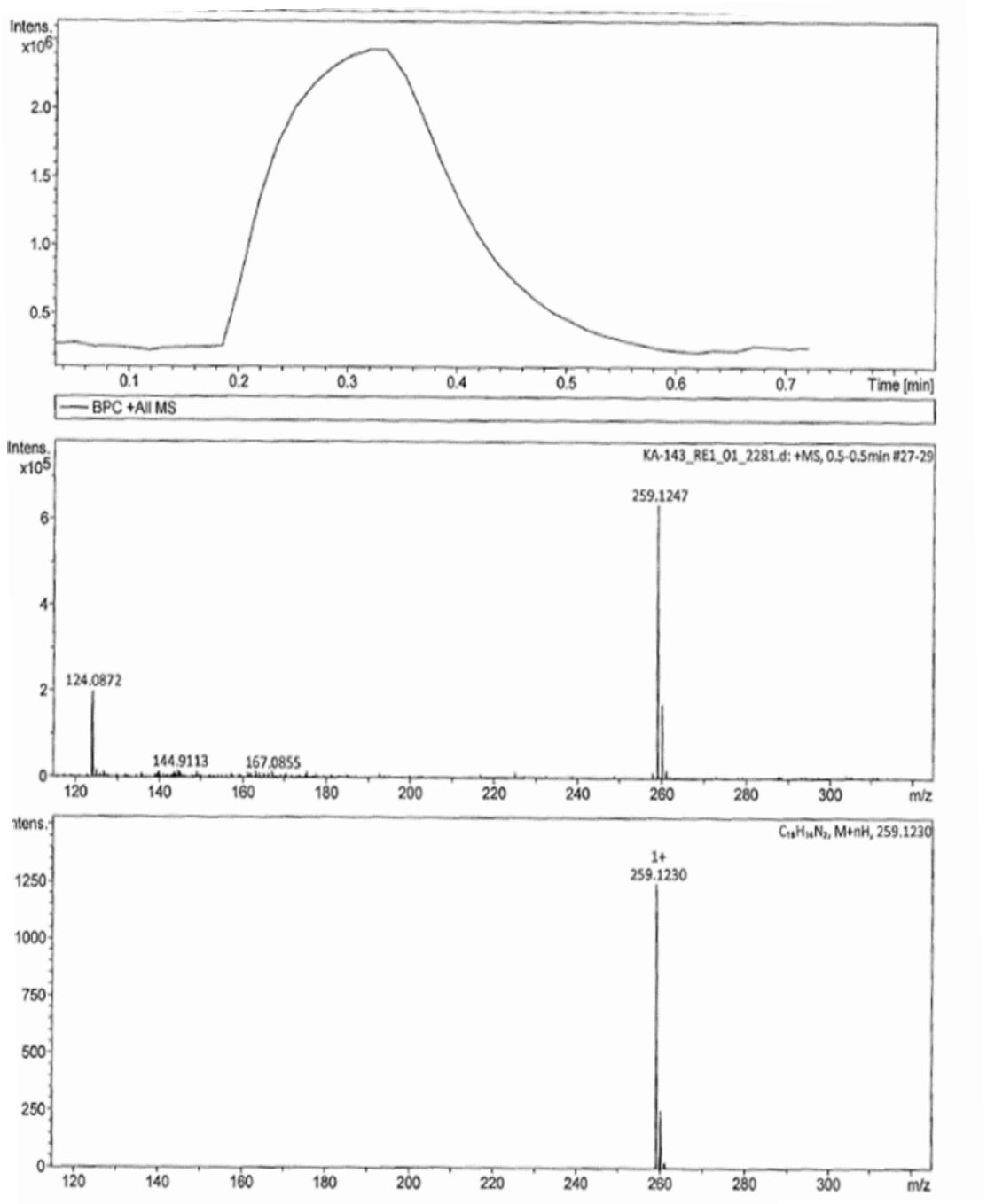


Figure 136: High performace mass spectrum for KA143. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix G: Supplementary data KA161

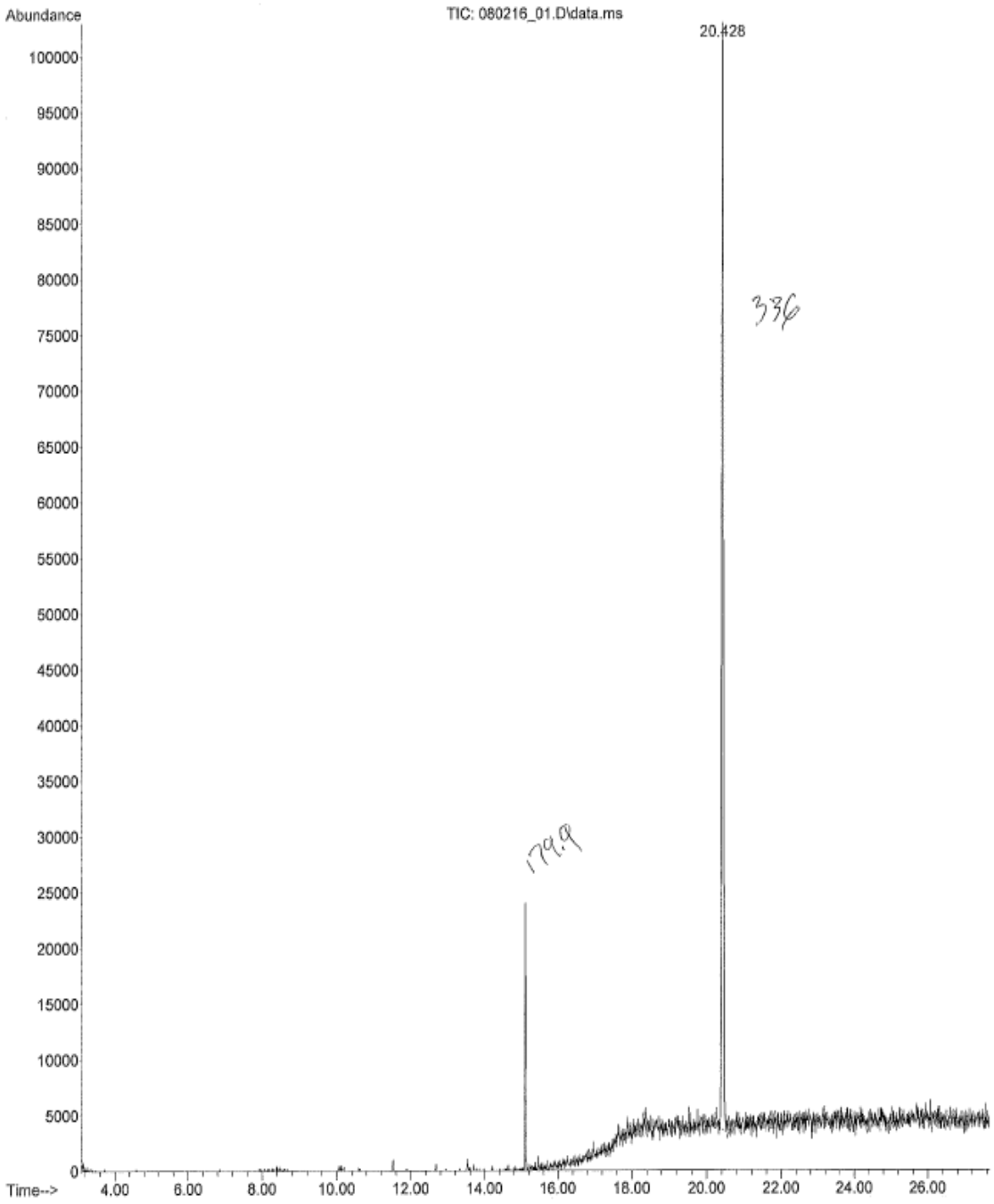


Figure 137: Gas chromatographic spectrum for KA161.

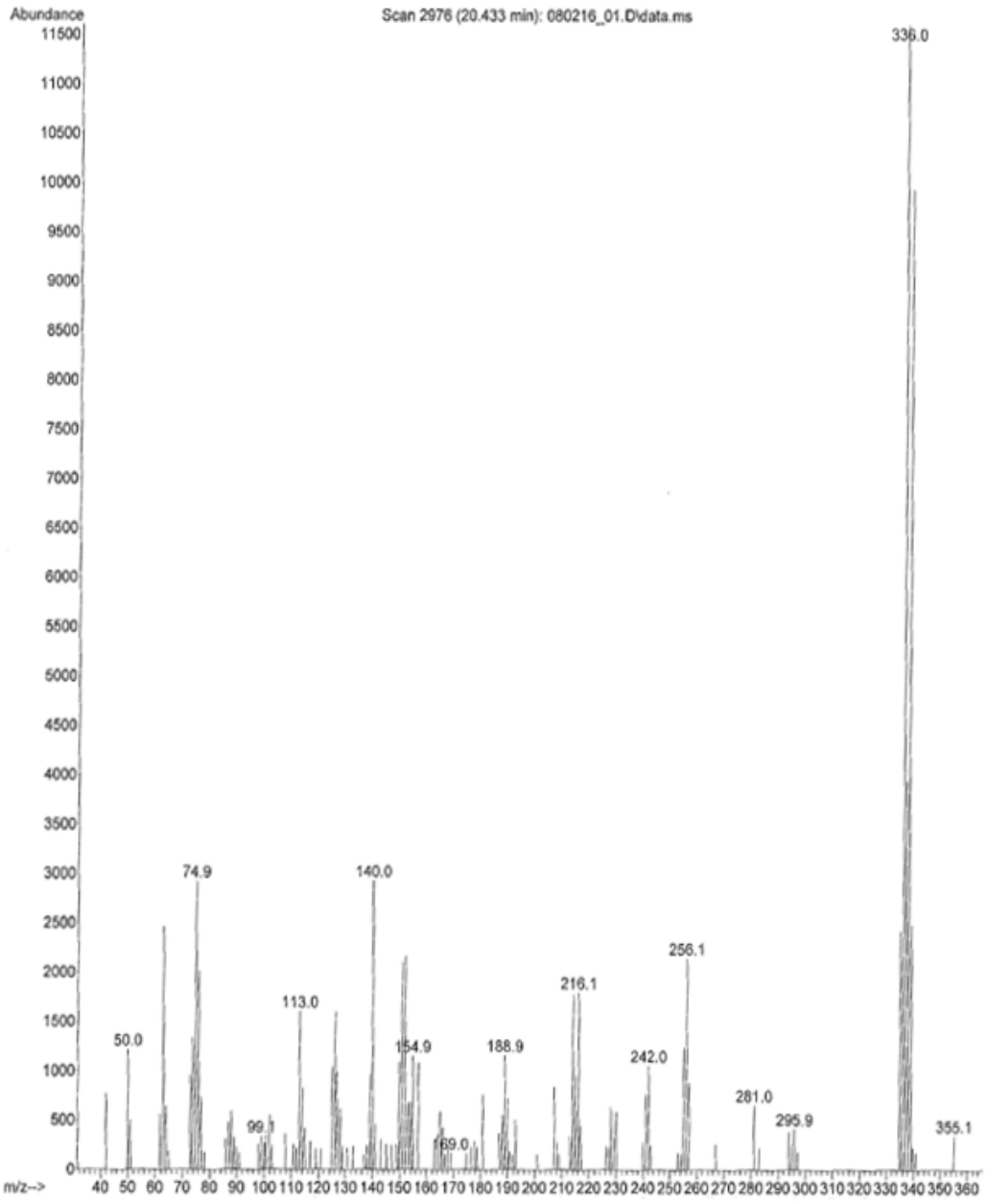


Figure 138: Mass spectrum for KA161

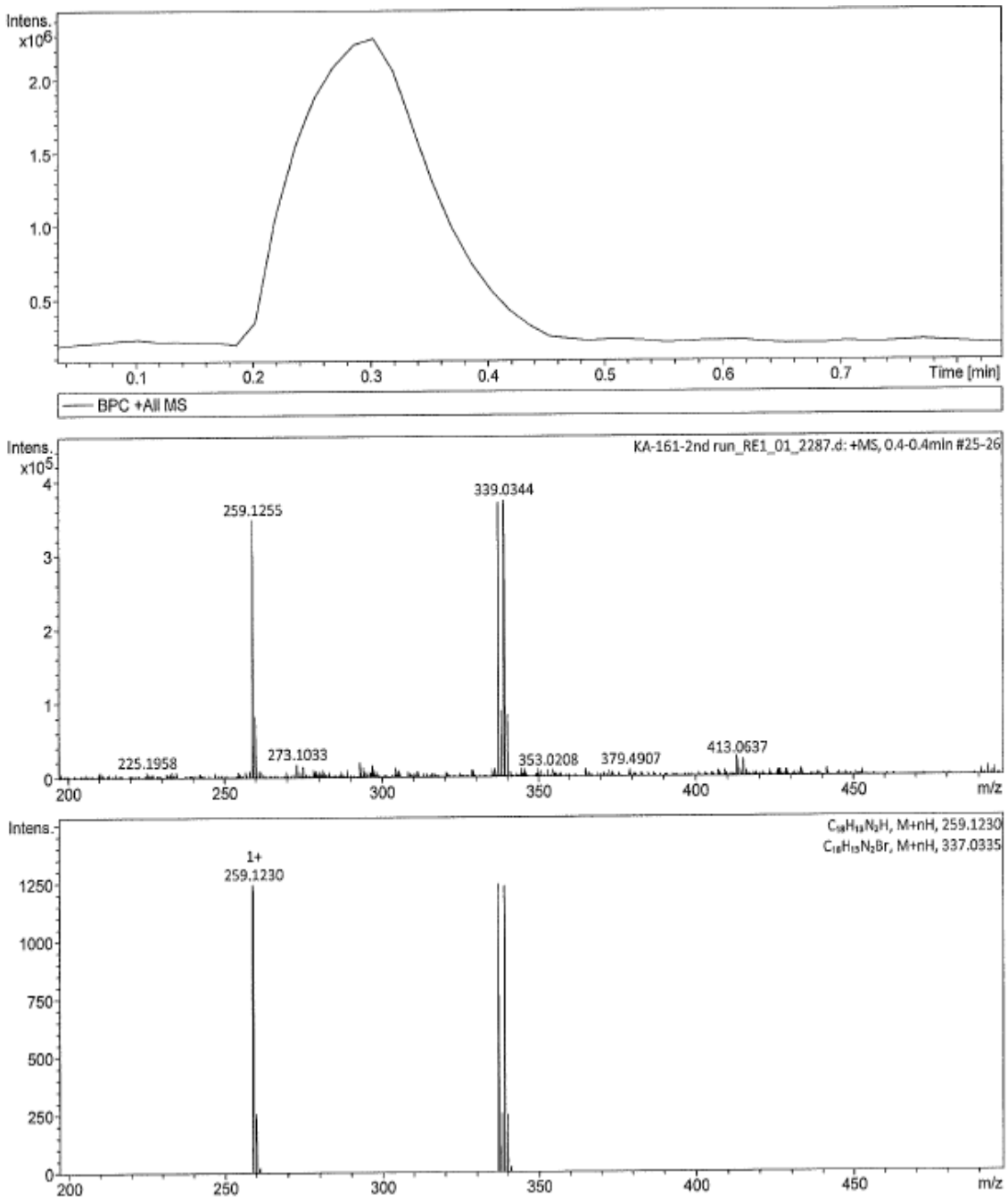


Figure 139: High performace mass spectrum for KA161. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix H: Supplementary data KA146

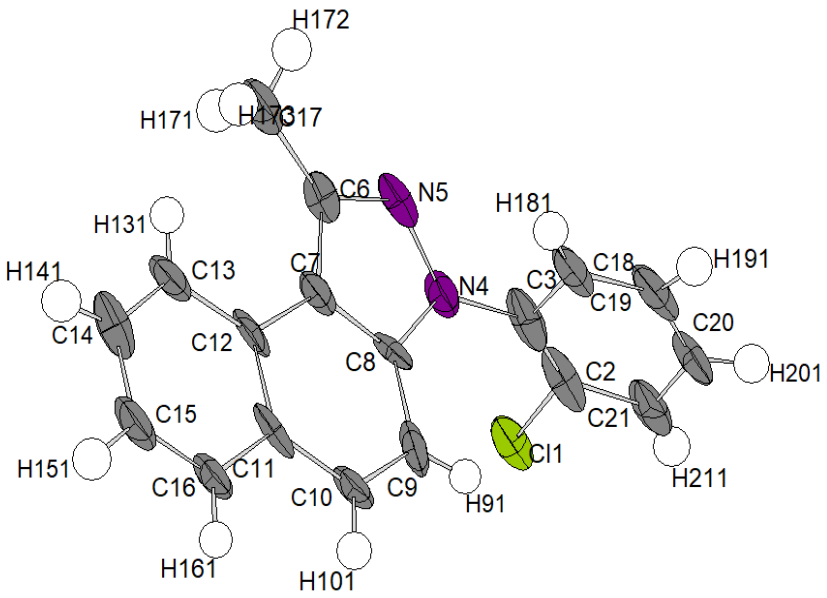


Figure 140: The crystal structure of KA146, for crystal solutions.

Table 22: *Crystal Data KA146*

Empirical Formula	$C_{18}H_{13}Cl_1N_2$
Formula Weight	292.77
Crystal Color, Habit	colorless, platelet
Crystal Dimensions	0.10 X 0.10 X 0.10 mm
Crystal System	monclinic
Lattice Type	Primitive
Lattice Parameters	a = 24.492(8)Å
	b = 4.3582(16)Å

	c = 28.295(10)Å
	β= 112.747 (8) ^{o}
	V = 2785.3(10)Å^{3}
Space Group	$P2_1/c$
Z value	8
D_{calc}	1.40 g/cm^{3}
F_{000}	1216.00
m(MoKa)	2.68 cm^{-1}

Table 23: *Intensity Measurements KA146*

Diffractometer	Rigaku RAXIS
Radiation	MoKa (l = 0.71075 Å)
	graphite monochromated
Voltage, Current	50kV, 40mA
Temperature	-150.0^{o}C
Detector Aperture	280 x 256 mm
Data Images	25 exposures
w oscillation Range	29.0 - 154.0^{o}
Exposure Rate	120.0 sec./^{o}

w oscillation Range	29.0 - 154.0^{o}
Exposure Rate	120.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2q_{max}$	55.0^{o}
-of Reflections Measured	Total: 9755
	Unique: 3769 (R_{int} = 0.195)

Table 24: *Structure Solution and Refinement KA146*

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F^2
$2q_{max}$ cutoff	55.0^{o}
Residuals: R1 (I>2.00s(I))	0.1161
Residuals: R (All reflections)	0.2356
Residuals: wR2 (All reflections)	0.2860
Goodness of Fit Indicator	1.0410
Maximum peak in Final Diff. Map	-1.25 e^{-}/Å^3
Minimum peak in Final Diff. Map	- 1.36 e^{-}/Å^3

Table 25: *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å2) KA146*

atom	x	y	z	*/Ueq
Cl1	0.32537(13)	0.3340(11)	0.15649(18)	0.0586
C2	0.2853(5)	0.542(4)	0.1828(7)	0.0577
C3	0.2982(5)	0.606(4)	0.2392(7)	0.0592
N4	0.3430(4)	0.487(3)	0.2837(6)	0.0547
N5	0.3410(4)	0.315(3)	0.3301(5)	0.0521
C6	0.3891(5)	0.276(4)	0.3694(6)	0.0453
C7	0.4230(5)	0.433(4)	0.3473(7)	0.0463
C8	0.3935(4)	0.568(4)	0.2950(6)	0.0509
C9	0.4118(5)	0.755(4)	0.2613(6)	0.0568
C10	0.4644(5)	0.802(4)	0.2836(7)	0.0579
C11	0.4965(5)	0.658(4)	0.3363(7)	0.0571
C12	0.4785(5)	0.471(4)	0.3707(7)	0.0565
C13	0.5130(5)	0.337(4)	0.4247(6)	0.0549
C14	0.5648(5)	0.396(4)	0.4420(7)	0.0558
C15	0.5832(5)	0.577(4)	0.4076(7)	0.0666
C16	0.5513(5)	0.717(4)	0.3571(7)	0.0613
C17	0.3981(5)	0.088(4)	0.4214(7)	0.0636
C18	0.2635(5)	0.770(4)	0.2561(7)	0.0581

C19	0.2195(5)	0.889(4)	0.2150(8)	0.0705
C20	0.2077(5)	0.826(5)	0.1558(7)	0.0674
C21	0.2401(5)	0.662(4)	0.1363(7)	0.0620
Cl22	0.17526(13)	-0.0499(11)	0.33780(19)	0.0630
C23	0.2087(4)	0.163(4)	0.3990(7)	0.0561
C24	0.1917(4)	0.205(4)	0.4445(7)	0.0488
N25	0.1437(4)	0.083(3)	0.4419(6)	0.0575
N26	0.1418(4)	-0.103(3)	0.4853(6)	0.0562
C27	0.0927(5)	-0.167(4)	0.4717(6)	0.0488
C28	0.0623(5)	-0.015(4)	0.4191(7)	0.0531
C29	0.0961(5)	0.139(4)	0.3997(7)	0.0558
C30	0.0805(5)	0.340(4)	0.3499(6)	0.0507
C31	0.0302(5)	0.353(4)	0.3163(7)	0.0557
C32	-0.0070(5)	0.191(4)	0.3327(6)	0.0498
C33	0.0077(5)	0.007(3)	0.3819(6)	0.0404
C34	-0.0297(5)	-0.154(4)	0.3984(7)	0.0579
C35	-0.0813(5)	-0.123(4)	0.3581(8)	0.0732
C36	-0.0963(5)	0.054(4)	0.3089(7)	0.0578
C37	-0.0601(5)	0.212(4)	0.2942(7)	0.0719
C38	0.0771(5)	-0.372(4)	0.5100(7)	0.0667

C39	0.2211(5)	0.359(4)	0.4950(7)	0.0572
C40	0.2680(5)	0.491(4)	0.5002(7)	0.0674
C41	0.2839(5)	0.460(4)	0.4539(8)	0.0682
C42	0.2555(5)	0.291(4)	0.4032(8)	0.0616
H161	0.5703	0.8351	0.3408	0.0692
H173	0.4192	0.2125	0.4512	0.1002
H172	0.3612	0.0277	0.4232	0.1000
H171	0.4207	-0.0935	0.4225	0.1002
H181	0.2696	0.7955	0.2907	0.0805
H191	0.1932	1.0209	0.2212	0.0822
H201	0.1740	0.9188	0.1318	0.0813
H211	0.2341	0.6292	0.1022	0.0854
H301	0.1101	0.4553	0.3452	0.0651
H311	0.0185	0.4573	0.2849	0.0731
H341	-0.0205	-0.2578	0.4296	0.0892
H351	-0.1132	-0.2185	0.3622	0.0980
H361	-0.1350	0.0409	0.2855	0.0820
H371	-0.0683	0.3174	0.2638	0.1011
H382	0.0500	-0.5308	0.4906	0.1060
H381	0.0588	-0.2486	0.5285	0.1060

H383	0.1122	-0.4659	0.5342	0.1062
H391	0.2055	0.3540	0.5208	0.0772
H401	0.2903	0.6003	0.5300	0.0843
H421	0.2712	0.2862	0.3778	0.0951
H101	0.4850	0.9242	0.2690	0.0762
H91	0.3881	0.8281	0.2290	0.0650
H141	0.5905	0.3213	0.4736	0.0987
H131	0.4943	0.2235	0.4419	0.0731
H151	0.6233	0.6264	0.4214	0.0958
H411	0.3185	0.5631	0.4573	0.0720

Table 26: *Atomic displacement parameters (Å2) KA146*

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Cl1	0.0294(14)	0.062(3)	0.085(3)	-0.005(3)	0.0220(17)	0.0033(18)
C2	0.023(6)	0.045(12)	0.099(15)	-0.034(11)	0.016(7)	-0.002(6)
C3	0.016(5)	0.058(13)	0.086(14)	-0.023(11)	0.000(7)	-0.012(6)
N4	0.024(5)	0.052(10)	0.085(11)	0.021(9)	0.017(6)	0.003(5)
N5	0.020(4)	0.056(10)	0.076(10)	-0.014(9)	0.014(5)	-0.002(5)
C6	0.029(6)	0.046(12)	0.058(11)	-0.007(10)	0.014(6)	0.006(6)
C7	0.021(5)	0.039(11)	0.082(13)	0.007(10)	0.024(7)	0.003(6)
C8	0.019(5)	0.070(13)	0.073(12)	0.012(11)	0.027(7)	-0.001(6)
C9	0.018(5)	0.068(14)	0.073(13)	0.010(11)	0.006(6)	0.014(7)

C10	0.022(5)	0.052(12)	0.105(15)	0.020(12)	0.030(7)	-0.001(6)
C11	0.015(5)	0.073(14)	0.085(14)	-0.013(12)	0.021(7)	0.004(7)
C12	0.018(5)	0.063(13)	0.095(14)	0.011(12)	0.029(7)	0.012(6)
C13	0.022(5)	0.068(13)	0.079(13)	0.001(11)	0.025(7)	-0.002(7)
C14	0.028(6)	0.043(12)	0.084(14)	-0.037(11)	0.008(7)	0.004(6)
C15	0.021(6)	0.071(15)	0.106(16)	0.009(13)	0.022(8)	0.000(7)
C16	0.020(5)	0.067(14)	0.099(15)	0.019(12)	0.026(7)	0.000(7)
C17	0.027(6)	0.055(13)	0.104(15)	0.003(12)	0.019(8)	-0.002(7)
C18	0.023(6)	0.060(13)	0.094(14)	0.001(12)	0.026(7)	0.003(7)
C19	0.026(6)	0.074(15)	0.118(17)	-0.001(14)	0.035(8)	0.004(8)
C20	0.017(5)	0.092(16)	0.091(14)	0.006(14)	0.019(7)	0.002(7)
C21	0.019(5)	0.059(13)	0.100(15)	-0.006(12)	0.014(7)	-0.012(7)
Cl22	0.0281(14)	0.071(3)	0.095(3)	-0.011(3)	0.0287(18)	0.0047(18)
C23	0.016(5)	0.051(11)	0.106(15)	0.005(11)	0.028(7)	-0.002(6)
C24	0.011(4)	0.050(11)	0.088(13)	0.008(11)	0.021(6)	0.001(6)
N25	0.021(5)	0.052(10)	0.097(12)	0.005(10)	0.020(6)	0.002(5)
N26	0.022(5)	0.050(10)	0.090(11)	0.003(9)	0.015(6)	0.005(5)
C27	0.025(6)	0.055(12)	0.070(12)	0.022(11)	0.022(7)	0.013(6)
C28	0.019(5)	0.053(12)	0.095(14)	-0.003(11)	0.030(7)	-0.008(6)
C29	0.018(5)	0.040(11)	0.097(14)	0.003(11)	0.009(7)	0.003(6)
C30	0.018(5)	0.043(11)	0.085(13)	0.008(10)	0.013(6)	-0.004(6)
C31	0.029(6)	0.038(11)	0.105(15)	0.008(11)	0.031(8)	0.003(6)
C32	0.021(5)	0.053(12)	0.076(13)	0.011(11)	0.021(6)	-0.005(6)
C33	0.028(5)	0.020(9)	0.079(12)	0.007(9)	0.026(7)	-0.006(5)

C34	0.032(6)	0.042(12)	0.112(15)	0.012(11)	0.041(8)	-0.004(6)
C35	0.020(6)	0.044(12)	0.16(2)	-0.034(13)	0.038(9)	-0.019(6)
C36	0.027(6)	0.062(13)	0.088(14)	0.020(12)	0.026(7)	0.008(7)
C37	0.023(6)	0.082(15)	0.116(16)	0.045(14)	0.032(8)	0.015(7)
C38	0.034(7)	0.067(14)	0.104(15)	0.004(13)	0.031(8)	-0.003(8)
C39	0.018(5)	0.051(12)	0.102(15)	0.027(11)	0.022(7)	0.007(6)
C40	0.018(5)	0.062(13)	0.109(16)	-0.015(12)	0.010(7)	-0.004(7)
C41	0.023(6)	0.057(13)	0.131(18)	0.014(13)	0.036(9)	0.011(7)
C42	0.029(6)	0.044(12)	0.122(17)	-0.007(12)	0.039(8)	-0.004(7)

Table 27: *Atomic displacement parameters (Å2) KA146*

Cl1-C2-	1.703(15)	C7-C8-	1.49(2)
C2-C3-	1.53(2)	C7-C12-	1.271(15)
C2-C21-	1.45(2)	C8-C9-	1.45(2)
C3-N4-	1.410(19)	C9-C10-	1.213(16)
C3-C18-	1.33(2)	C9-H91-	0.930
N4-N5-	1.530(17)	C10-C11-	1.53(2)
N4-C8-	1.205(14)	C10-H101-	0.930
N5-C6-	1.279(16)	C11-C12-	1.46(2)
C6-C7-	1.40(2)	C11-C16-	1.266(15)
C6-C17-	1.62(2)	C12-C13-	1.55(2)

C13-C14-	1.197(15)	C24-N25-	1.267(15)
C13-H131-	0.930	C24-C39-	1.49(2)
C14-C15-	1.46(2)	N25-N26-	1.489(18)
C14-H141-	0.930	N25-C29-	1.329(18)
C15-C16-	1.47(2)	N26-C27-	1.146(14)
C15-H151-	0.930	C27-C28-	1.53(2)
C16-H161-	0.928	C27-C38-	1.56(2)
C17-H173-	0.967	C28-C29	-1.34(2)
C17-H172-	0.962	C28-C33-	1.349(17)
C17-H171-	0.958	C29-C30-	1.58(2)
C18-C19-	1.35(2)	C30-C31-	1.233(17)
C18-H181-	0.937	C30-H301-	0.933
C19-C20-	1.61(2)	C31-C32-	1.368(19)
C19-H191-	0.928	C31-H311-	0.939
C20-C21-	1.34(2)	C32-C33-	1.53(2)
C20-H201-	0.934	C32-C37-	1.338(18)
C21-H211-	0.930	C33-C34-	1.370(17)
Cl22-C23-	1.853(18)	C34-C35-	1.34(2)
C23-C24-	1.51(2)	C34-H341-	0.939
C23-C42-	1.238(16)	C35-C36-	1.51(2)

C35-H351-	0.932	C3-N4-N5-	132.5(10)
C36-C37-	1.31(2)	C3-N4-C8-	119.6(16)
C36-H361-	0.925	N5-N4-C8-	106.6(13)
C37-H371-	0.928	N4-N5-C6-	119.1(11)
C38-H382-	0.968	N5-C6-C7-	93.1(13)
C38-H381-	0.974	N5-C6-C17-	127.6(13)
C38-H383-	0.960	C7-C6-C17-	139.3(11)
C39-C40-	1.243(17)	C6-C7-C8-	119.5(11)
C39-H391-	0.945	C6-C7-C12-	121.9(16)
C40-C41-	1.51(2)	C8-C7-C12-	118.5(14)
C40-H401-	0.938	C7-C8-N4-	101.7(14)
C41-C42-	1.52(2)	C7-C8-C9-	135.9(11)
C41-H411-	0.930	N4-C8-C9-	122.4(15)
C42-H421-	0.939	C8-C9-C10-	107.0(15)
Cl1-C2-C3-	129.2(11)	C8-C9-H91-	127.2
Cl1-C2-C21-	99.4(13)	C10-C9-H91-	125.8
C3-C2-C21-	131.1(14)	C9-C10-C11-	118.5(15)
C2-C3-N4-	129.8(14)	C9-C10-H101-	121.1
C2-C3-C18-	124.8(14)	C11-C10-H101-	120.3
N4-C3-C18-	105.0(16)	C10-C11-C12-	134.9(11)

C10-C11-C16-	115.0(16)	C6-C17-H171-	108.8
C12-C11-C16-	110.1(16)	H173-C17-H171-	109.2
C11-C12-C7-	105.1(15)	H172-C17-H171-	108.3
C11-C12-C13-	132.6(11)	C3-C18-C19-	107.7(17)
C7-C12-C13-	122.3(15)	C3-C18-H181-	124.9
C12-C13-C14-	114.4(16)	C19-C18-H181-	127.4
C12-C13-H131-	121.8	C18-C19-C20-	126.5(15)
C14-C13-H131-	123.8	C18-C19-H191-	117.1
C13-C14-C15-	113.2(17)	C20-C19-H191-	116.3
C13-C14-H141-	122.5	C19-C20-C21-	128.7(15)
C15-C14-H141-	124.2	C19-C20-H201-	115.9
C14-C15-C16-	133.7(11)	C21-C20-H201-	115.5
C14-C15-H151-	113.2	C2-C21-C20-	100.8(16)
C16-C15-H151-	113.0	C2-C21-H211-	130.0
C15-C16-C11-	115.9(16)	C20-C21-H211-	129.2
C15-C16-H161-	122.2	Cl22-C23-C24-	133.6(9)
C11-C16-H161-	121.9	Cl22-C23-C42-	112.0(15)
C6-C17-H173-	110.3	C24-C23-C42-	114.4(16)
C6-C17-H172-	112.7	C23-C24-N25-	117.1(15)
H173-C17-H172-	107.6	C23-C24-C39-	133.1(11)

N25-C24-C39-	109.8(14)	C31-C32-C33-	128.9(12)
C24-N25-N26-	120.4(13)	C31-C32-C37-	104.8(15)
C24-N25-C29-	116.5(16)	C33-C32-C37-	126.1(12)
N26-N25-C29-	123.1(11)	C32-C33-C28-	124.3(11)
N25-N26-C27-	102.6(13)	C32-C33-C34-	128.9(12)
N26-C27-C28-	106.0(15)	C28-C33-C34-	106.8(14)
N26-C27-C38-	114.3(15)	C33-C34-C35-	101.1(15)
C28-C27-C38-	139.7(11)	C33-C34-H341-	128.2
C27-C28-C29-	118.0(11)	C35-C34-H341-	130.7
C27-C28-C33-	138.8(12)	C34-C35-C36-	130.5(13)
C29-C28-C33-	103.2(14)	C34-C35-H351-	114.1
C28-C29-N25-	90.3(14)	C36-C35-H351-	115.3
C28-C29-C30-	132.2(11)	C35-C36-C37-	127.5(14)
N25-C29-C30-	136.9(13)	C35-C36-H361-	116.6
C29-C30-C31-	122.6(13)	C37-C36-H361-	115.9
C29-C30-H301-	119.7	C32-C37-C36-	105.7(16)
C31-C30-H301-	117.7	C32-C37-H371-	125.5
C30-C31-C32-1	08.3(16)	C36-C37-H371-	128.8
C30-C31-H311-	126.9	C27-C38-H382-	108.3
C32-C31-H311-	124.8	C27-C38-H381-	110.0

H382-C38-H381-	110.1	C39-C40-H401-	122.0
C27-C38-H383-	110.3	C41-C40-H401-	124.8
H382-C38-H383-	109.3	C40-C41-C42-	133.2(13)
H381-C38-H383-	108.8	C40-C41-H411-	113.2
C24-C39-C40-	113.8(16)	C42-C41-H411-	113.6
C24-C39-H391-	122.7	C41-C42-C23-	112.3(17)
C40-C39-H391-	123.5	C41-C42-H421-	124.0
C39-C40-C41-	113.2(16)	C23-C42-H421-	123.7

Table 28: *Hydrogen-bond geometry (Å, °). KA146*

D—H···A	D—H	H···A	D···A	D—H···A
C36—H361···C19	124.8(6)	0.925	2.563	3.18(2)
C42—H421···N5	163.5(5)	0.94	2.56	3.47(2)
C13—H131···C17	132.4(6)	0.93	2.276 2	.98(2)

Symmetry codes: (i) x+1, y, z; (ii) −x+2, −y+1, −z+1.

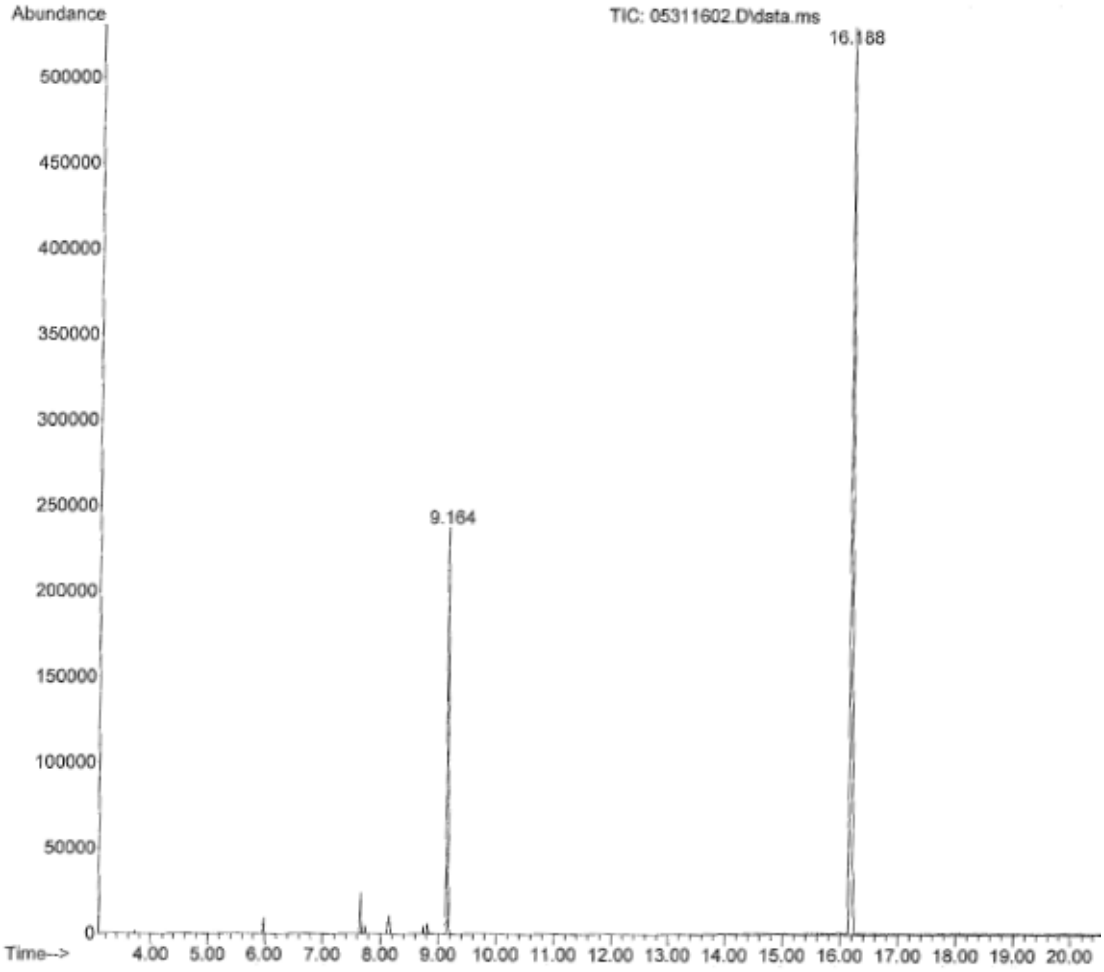


Figure 141: Gas chromatographic spectrum for KA146.

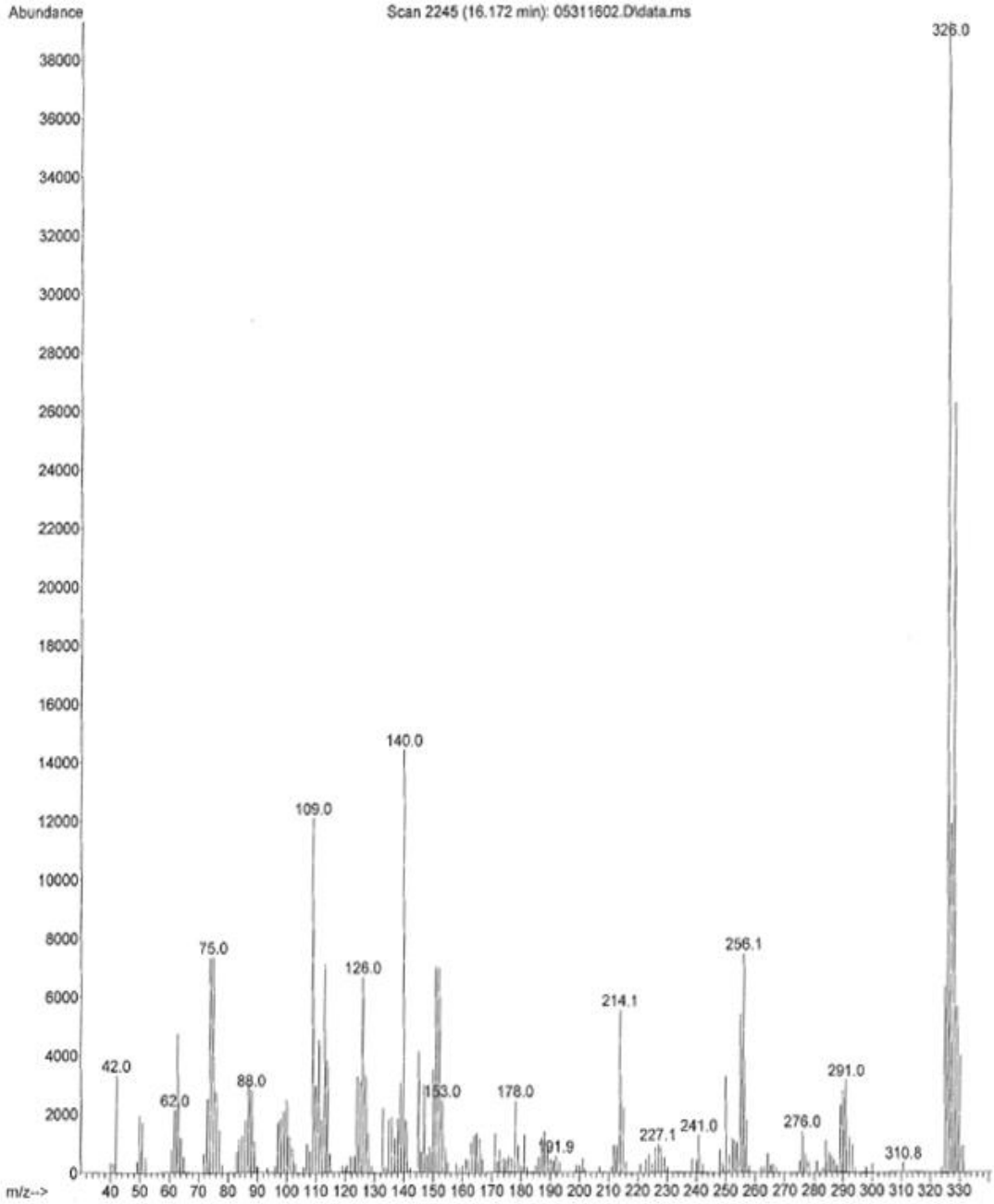


Figure 142: Mass spectrum for KA146

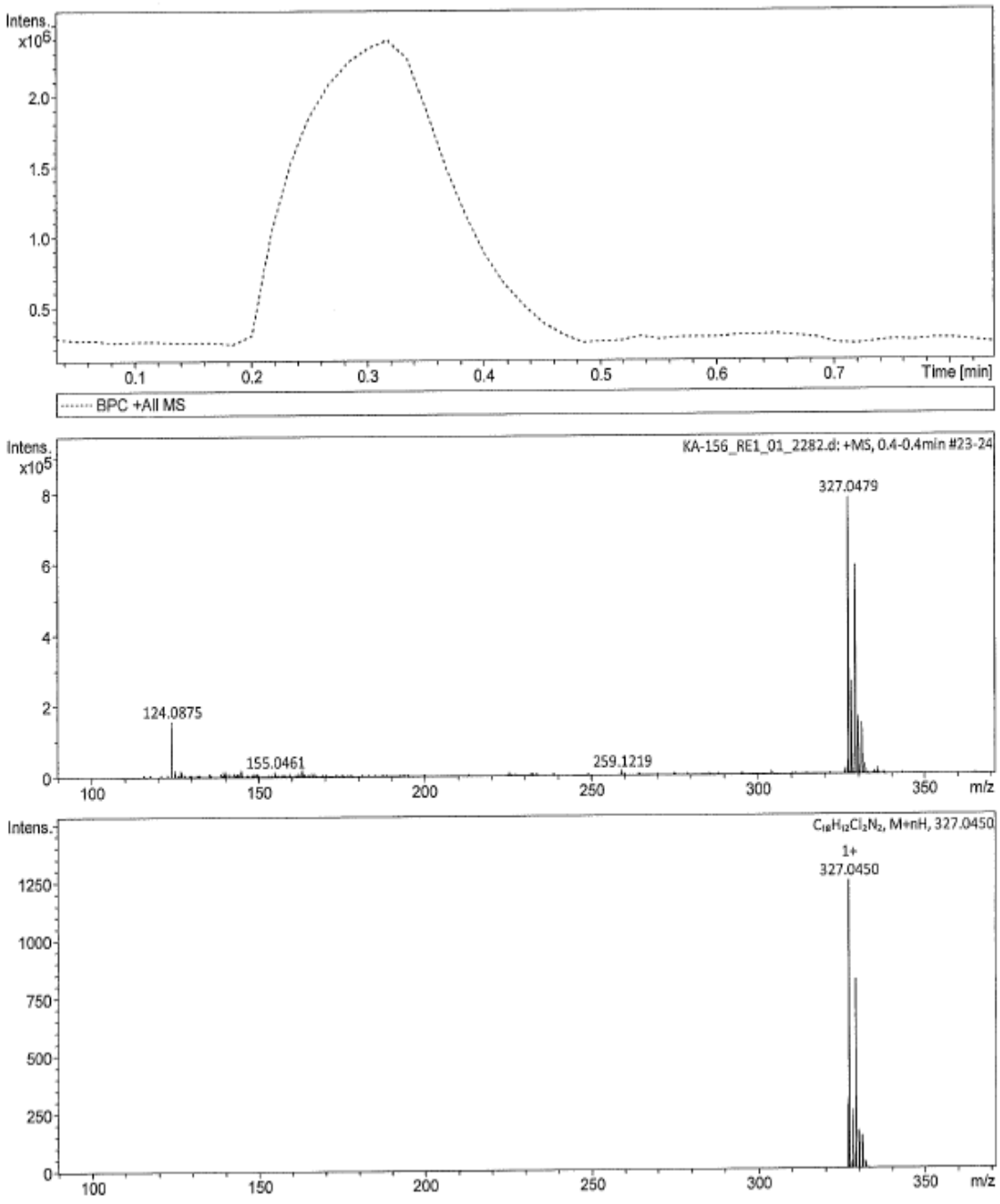


Figure 143: High performace mass spectrum for KA146. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix I: Supplementary data KA171

KA171

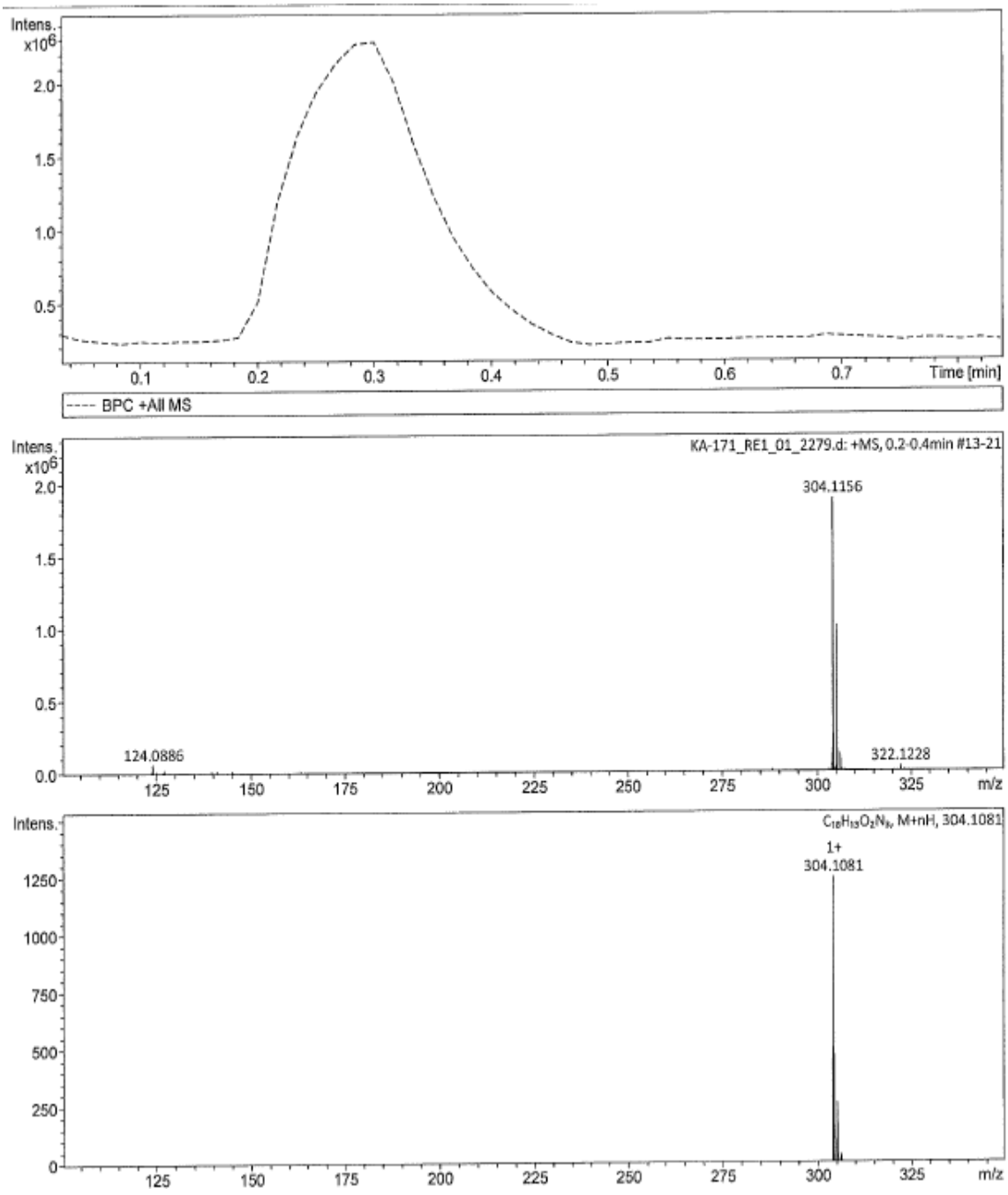


Figure 144: High performace mass spectrum for KA171. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

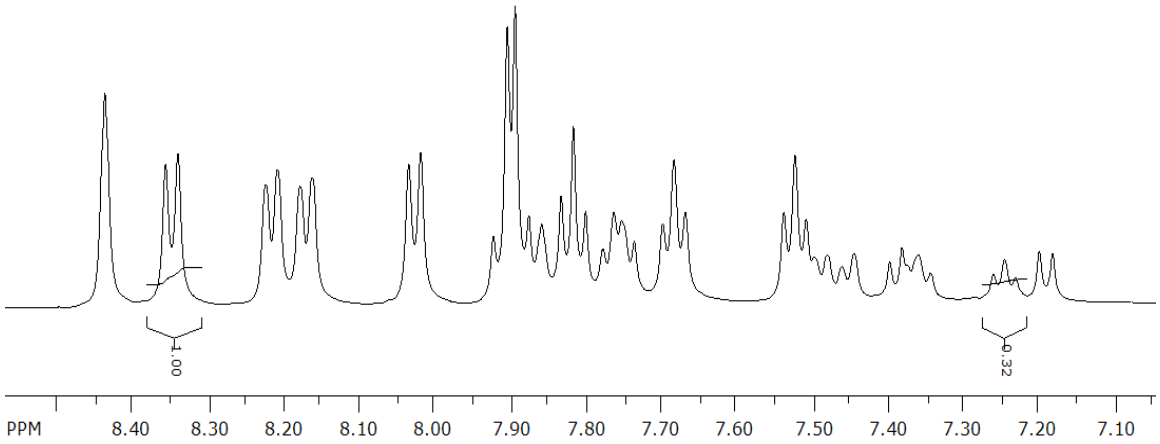


Figure 145: Aromatic region of the 1H-NMR showing relative integrations for the two compounds that appear in the crude mixture. The yield was approximately 68% for compound KA171.

Appendix J: Supplementary data KA156

KA156 Hydrazone

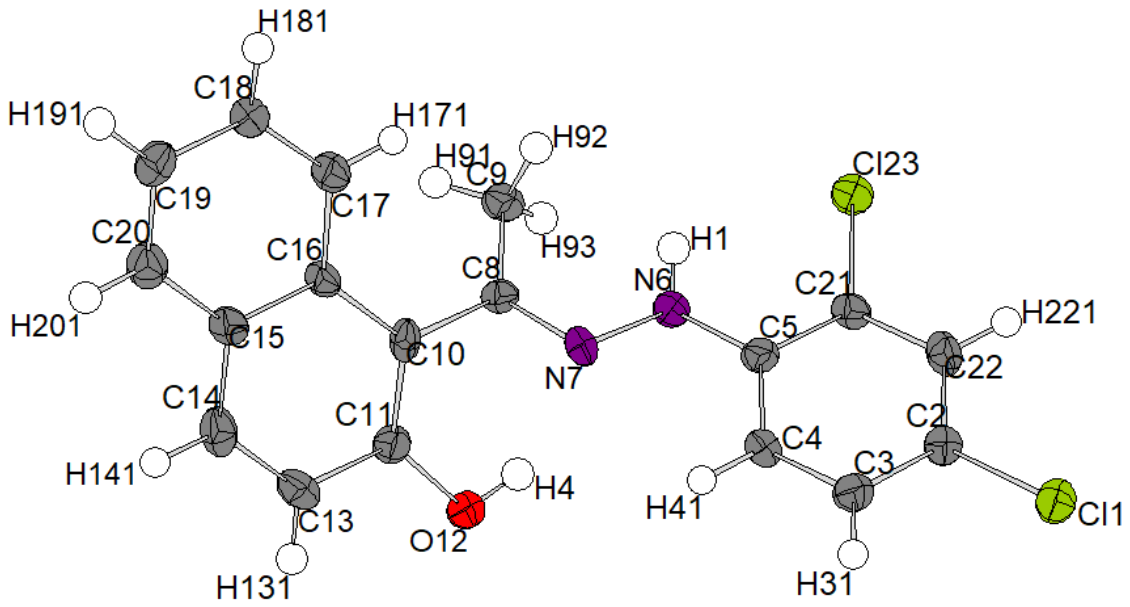


Figure 146: The crystal structure of KA156, for crystal solutions.

Table 29: *Crystal Data KA156 Hydrazone*

Empirical Formula	$C_{18}H_{12}Cl_2N_2$
Formula Weight	327.21
Crystal Color, Habit	colorless, platelet
Crystal Dimensions	0.20 X 0.20 X 0.20 mm
Crystal System	mo clinic
Lattice Type	Primitive

Lattice Parameters	a = 14.9397(18) Å
	b = 7.2222(7) Å
	c = 15.2684(15) Å
	b = 109.404(8) ^{o}
	V = 1553.8(3) Å^{3}
Space Group	P2$_{1}$/c (#14)
Z value	4
D_{calc}	1.399 g/cm^{3}
F_{000}	672.00
m(MoKa)	4.138 cm^{-1}

Table 30: *Intensity Measurements KA156 Hydrazone*

Diffractometer	Rigaku RAXIS
Radiation	MoKa (l = 0.71075 Å)
	graphite mo chromated
Voltage, Current	50kV, 40mA
Temperature	-150.0^{o}C
Detector Aperture	280 x 256 mm
Data Images	25 exposures
w oscillation Range	29.0 - 154.0^{o}

Exposure Rate	120.0 sec./^{o}
w oscillation Range	29.0 - 154.0^{o}
Exposure Rate	120.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2q_{max}$	55.0^{o}
-of Reflections Measured	Total: 8260
	Unique: 3490 (R_{int} = 0.108)
Corrections	Lorentz-polarization
	Absorption
	(trans. factors: 0.038 - 0.921)

Table 31: *Structure Solution and Refinement KA156 Hydrazone*

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F^2
Function Minimized	S w (Fo^2 - Fc^2)^2
Least Squares Weights	w = 1/ [$s^2(Fo^2)$ + (0.0000-P)^2 + 0.0000- P]
	where P = (Max(Fo^2,0) + 2Fc^2)/3

$2q_{max}$ cutoff	55.0^{o}
A malous Dispersion	All n-hydrogen atoms
-Observations (All reflections)	3490
-Variables	208
Reflection/Parameter Ratio	16.78
Residuals: R1 (I>2.00s(I))	0.0890
Residuals: R (All reflections)	0.1655
Residuals: wR2 (All reflections)	0.2393
Goodness of Fit Indicator	1.160
Max Shift/Error in Final Cycle	0.005
Maximum peak in Final Diff. Map	0.79 $e^{-}/Å^{3}$
Minimum peak in Final Diff. Map	-0.69 $e^{-}/Å^{3}$

Table 32: *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å2) KA156 Hydrazone*

atom	x	y	z	*/Ueq
Cl1	0.53067(14)	0.4066(3)	0.38281(15)	0.0402
C2	0.4147(5)	0.3375(11)	0.3299(5)	0.0296
C3	0.3524(5)	0.3376(11)	0.3796(5)	0.0301
C4	0.2598(5)	0.2844(12)	0.3377(5)	0.0307
C5	0.2267(5)	0.2267(11)	0.2438(5)	0.0272

N6	0.1349(4)	0.1678(10)	0.1994(4)	0.0291
N7	0.0681(4)	0.1915(10)	0.2426(4)	0.0290
C8	-0.0195(5)	0.1527(10)	0.1962(5)	0.0253
C9	-0.0465(6)	0.0732(12)	0.0988(5)	0.0321
C10	-0.0875(5)	0.1699(11)	0.2454(5)	0.0260
C11	-0.0615(5)	0.1218(12)	0.3387(5)	0.0292
O12	0.0284(4)	0.0700(9)	0.3901(4)	0.0345
C13	-0.1274(6)	0.1162(12)	0.3864(5)	0.0319
C14	-0.2192(6)	0.1683(12)	0.3433(6)	0.0356
C15	-0.2495(5)	0.2320(11)	0.2503(5)	0.0267
C16	-0.1833(5)	0.2336(11)	0.2008(5)	0.0266
C17	-0.2163(5)	0.3077(12)	0.1080(5)	0.0315
C18	-0.3086(5)	0.3593(12)	0.0674(6)	0.0327
C19	-0.3743(6)	0.3489(12)	0.1159(6)	0.0357
C20	-0.3439(6)	0.2888(13)	0.2053(6)	0.0364
C21	0.2910(5)	0.2268(10)	0.1965(5)	0.0251
C22	0.3854(5)	0.2817(12)	0.2368(6)	0.0321
Cl23	0.25366(14)	0.1631(4)	0.07950(13)	0.0400
H31	0.3723	0.3760	0.4428	0.0406
H41	0.2174	0.2847	0.3713	0.0377

H91	-0.1118	0.0301	0.0788	0.0473
H93	-0.0045	-0.0288	0.0997	0.0477
H92	-0.0401	0.1704	0.0570	0.0471
H131	-0.1075	0.0772	0.4480	0.0425
H141	-0.2638	0.1654	0.3756	0.0406
H171	-0.1739	0.3172	0.0748	0.0379
H181	-0.3270	0.4059	0.0073	0.0433
H191	-0.4389	0.3840	0.0858	0.0456
H201	-0.3867	0.2845	0.2389	0.0456
H221	0.4285	0.2792	0.2031	0.0406
H4	0.060(6)	0.093(15)	0.356(6)	0.0500
H1	0.1162(18)	0.149(11)	0.1401(17)	0.0500

Table 33: *Atomic displacement parameters (Å2) KA156 Hydrazone*

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
Cl1	0.0288(10)	0.0563(14)	0.0351(10)	-0.0048(10)	0.0101(8)	0.0039(9)
C 2	0.026(4)	0.034(4)	0.028(4)	0.000(3)	0.010(3)	0.000(3)
C 3	0.029(4)	0.033(4)	0.027(4)	-0.001(3)	0.007(3)	0.001(3)
C 4	0.027(4)	0.041(5)	0.026(4)	0.002(3)	0.012(3)	0.000(3)
C 5	0.024(3)	0.036(4)	0.021(3)	0.000(3)	0.008(3)	0.005(3)
N 6	0.025(3)	0.042(4)	0.022(3)	-0.003(3)	0.009(2)	0.001(3)

N 7	0.025(3)	0.039(4)	0.027(3)	0.001(3)	0.015(3)	0.001(3)
C 8	0.025(3)	0.027(4)	0.023(3)	0.005(3)	0.005(3)	0.002(3)
C 9	0.033(4)	0.040(4)	0.024(4)	-0.001(3)	0.011(3)	0.003(3)
C 1	0 0.020(3)	0.032(4)	0.030(4)	-0.011(3)	0.012(3)	0.003(3)
C 11	0.026(3)	0.037(4)	0.024(3)	-0.005(3)	0.008(3)	0.000(3)
O 12	0.025(3)	0.053(4)	0.025(3)	0.000(3)	0.008(2)	0.001(3)
C 13	0.040(4)	0.033(4)	0.027(4)	-0.002(3)	0.018(3)	0.003(4)
C 14	0.032(4)	0.039(5)	0.040(4)	-0.011(4)	0.018(3)	0.011(4)
C 15	0.031(4)	0.028(4)	0.023(3)	-0.009(3)	0.011(3)	0.002(3)
C 16	0.027(4)	0.035(4)	0.021(3)	-0.004(3)	0.012(3)	0.003(3)
C 17	0.031(4)	0.041(5)	0.026(4)	-0.006(3)	0.013(3)	0.001(3)
C 18	0.030(4)	0.039(5)	0.029(4)	0.001(3)	0.010(3)	0.002(3)
C 19	0.027(4)	0.039(5)	0.039(4)	0.001(4)	0.009(3)	0.005(3)
C 20	0.033(4)	0.042(5)	0.036(4)	-0.007(4)	0.014(3)	0.004(4)
C 21	0.030(4)	0.025(4)	0.022(3)	-0.004(3)	0.012(3)	0.003(3)
C 22	0.028(4)	0.036(4)	0.038(4)	0.004(3)	0.018(3)	0.005(3)
Cl 23	0.0321(10)	0.0633(15)	0.0257(9)	-0.0067(9)	0.0111(7)	0.0018(10)

Table 34: *Geometric parameters (Å, °) KA156 Hydrazone*

Cl1 -C2	1.725(8)	C2 -C22	1.400(11)
C2 -C3	1.382(10)	C3 -C4	1.372(10)

C3 -H31	0.950	C14 -C15	1.416(11)
C4 -C5	1.415(10)	C14 -H141	0.952
C4 -H41	0.940	C15 -C16	1.431(10)
C5 -N6	1.381(9)	C15 -C20	1.408(11)
C5 -C21	1.380(10)	C16 -C17	1.439(10)
N6 -N7	1.377(8)	C17 -C18	1.363(11)
N6 -H1	0.86(2)	C17 -H171	0.936
N7 -C8	1.295(9)	C18 -C19	1.414(11)
C8 -C9	1.518(10)	C18 -H181	0.928
C8 -C10	1.455(10)	C19 -C20	1.359(12)
C9 -H91	0.970	C19 -H191	0.955
C9 -H93	0.965	C20 -H201	0.945
C9 -H92	0.975	C21 -C22	1.395(10)
C10 -C11	1.389(11)	C21 -Cl23	1.747(7)
C10 -C16	1.440(10)	C22 -H221	0.947
C11 -O12	1.365(9)	Cl1 -C2 -C3	119.8(6)
C11 -C13	1.405(10)	Cl1 -C2 -C22	119.0(6)
O12 -H4	0.83(2)	C3 -C2 -C22	121.2(7)
C13 -C14	1.362(11)	C2 -C3 -C4	120.1(7)
C13 -H131	0.930	C2 -C3 -H31	121.0

C4 -C3 -H31	118.9	C8 -C10 -C11	120.1(7)
C3 -C4 -C5	121.0(7)	C8 -C10 -C16	122.5(7)
C3 -C4 -H41	120.2	C11 -C10 -C16	117.4(6)
C5 -C4 -H41	118.8	C10 -C11 -O12	123.0(7)
C4 -C5 -N6	123.0(6)	C10 -C11 -C13	122.2(7)
C4 -C5 -C21	117.3(7)	O12 -C11 -C13	114.8(7)
N6 -C5 -C21	119.7(6)	C11 -O12 -H4	104(7)
C5 -N6 -N7	119.1(6)	C11 -C13 -C14	120.5(7)
C5 -N6 -H1	119.0(17)	C11 -C13 -H131	119.3
N7 -N6 -H1	119.2(17)	C14 -C13 -H131	120.2
N6 -N7 -C8	118.2(6)	C13 -C14 -C15	120.6(7)
N7 -C8 -C9	120.6(7)	C13 -C14 -H141	120.6
N7 -C8 -C10	116.8(6)	C15 -C14 -H141	118.7
C9 -C8 -C10	122.2(6)	C14 -C15 -C16	119.0(7)
C8 -C9 -H91	110.0	C14 -C15 -C20	121.2(7)
C8 -C9 -H93	108.4	C16 -C15 -C20	119.7(7)
H91 -C9 -H93	109.9	C10 -C16 -C15	120.0(7)
C8 -C9 -H92	108.5	C10 -C16 -C17	123.1(6)
H91 -C9 -H92	109.4	C15 -C16 -C17	116.9(7)
H93 -C9 -H92	110.7	C16 -C17 -C18	120.9(7)

C16 -C17 -H171	119.2
C18 -C17 -H171	119.9
C17 -C18 -C19	121.4(7)
C17 -C18 -H181	118.1
C19 -C18 -H181	120.5
C18 -C19 -C20	118.9(7)
C18 -C19 -H191	120.0
C20 -C19 -H191	121.0
C15 -C20 -C19	122.0(8)
C15 -C20 -H201	118.4
C19 -C20 -H201	119.7
C5 -C21 -C22	123.2(7)
C5 -C21 -Cl23	119.5(6)
C22 -C21 -Cl23	117.3(5)
C2 -C22 -C21	117.2(7)
C2 -C22 -H221	121.2
C21 -C22 -H221	121.6

Table 35: *Hydrogen-bond geometry (Å, °) KA156 Hydrazone*

D—H···A	D—H	H···A	D···A	D—H···A
C13—H131···O12	168.7(2)	0.93	2.588	3.505(12)
O12—H4···N7	. 150(10)	0.83	1.91	2.659(12)

Symmetry codes: (i) x+1, y, z; (ii) −x+2, −y+1, −z+1.

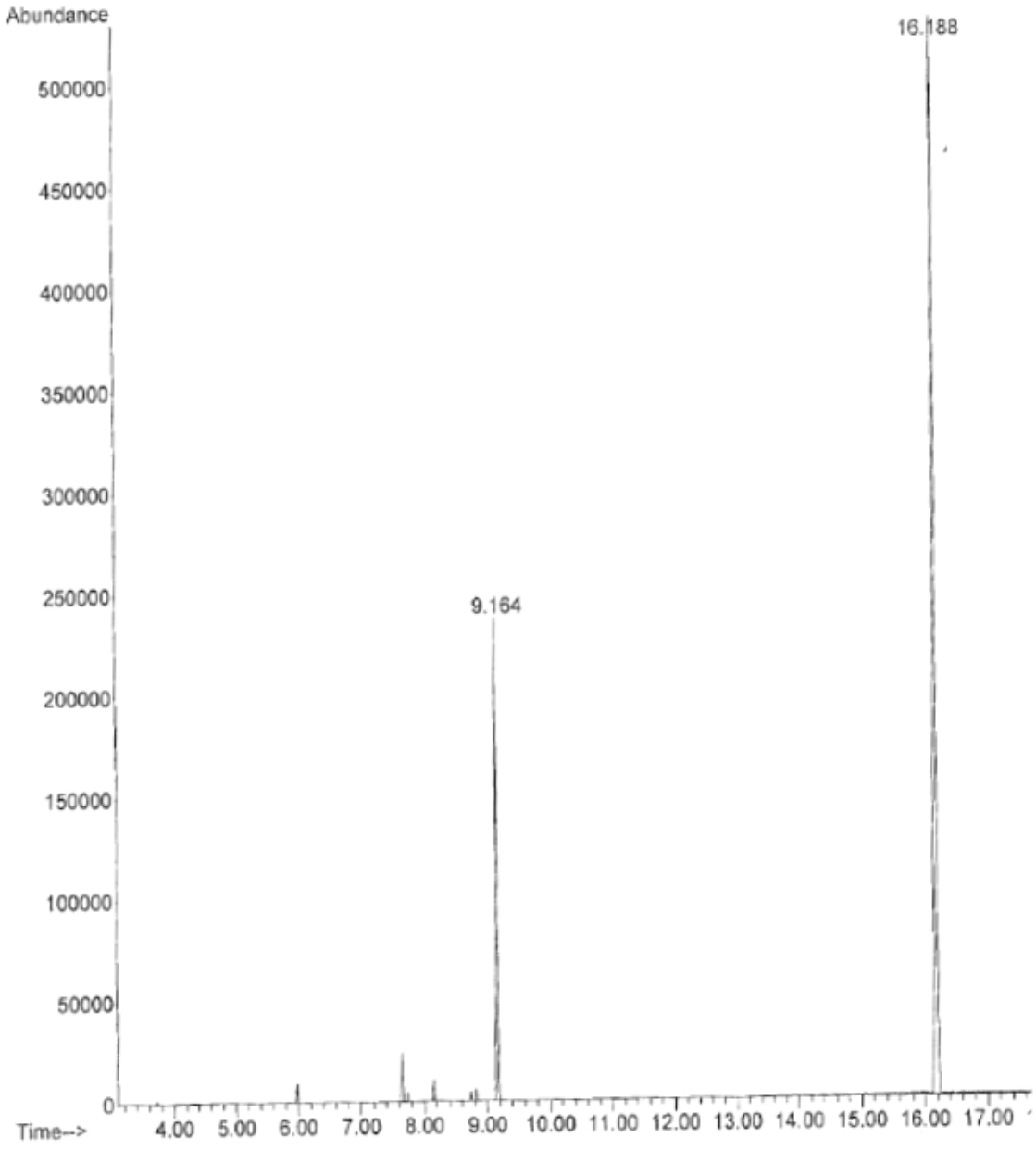


Figure 147: Gas chromatographic spectrum for KA156

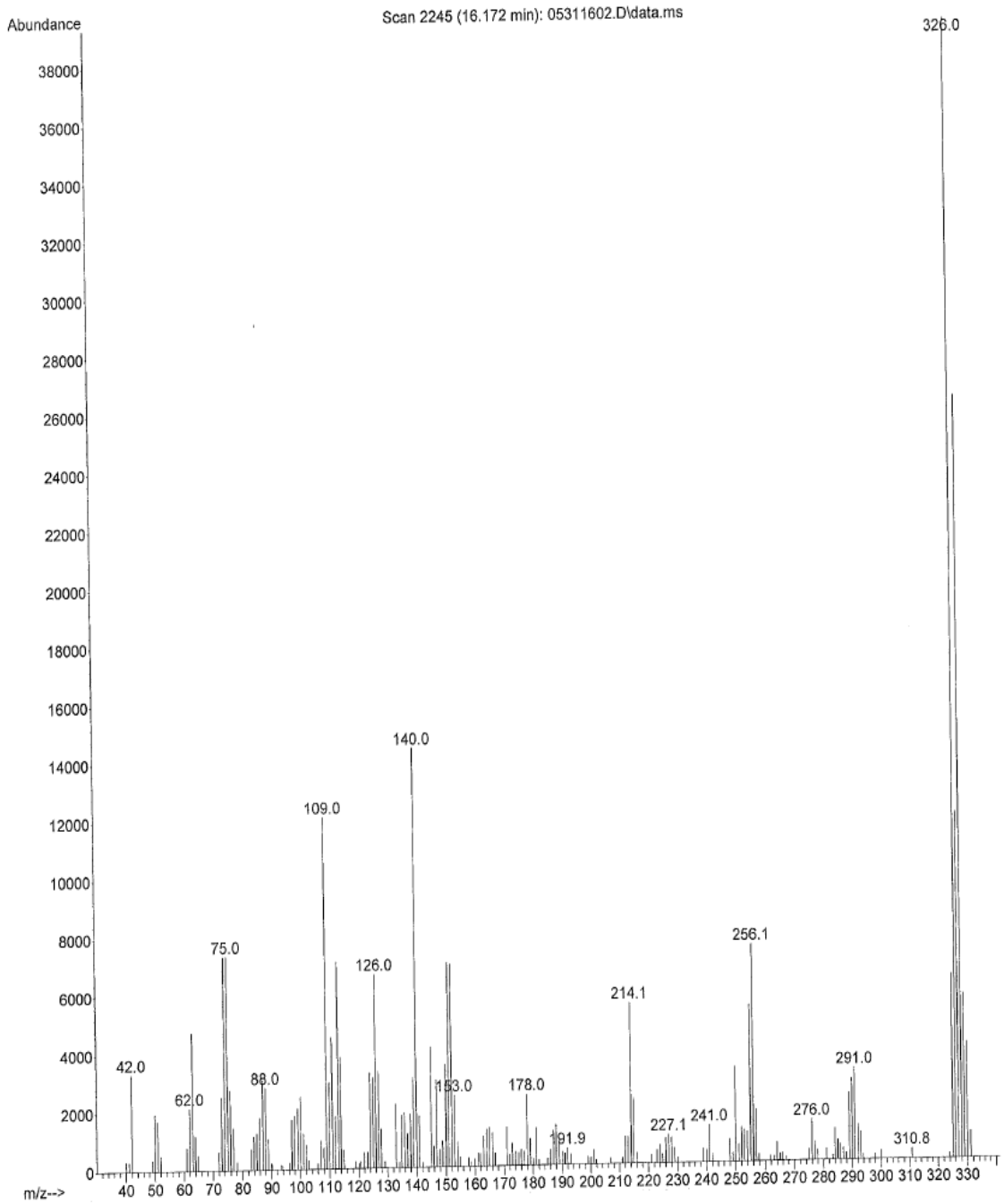


Figure 148: Mass spectrum for KA156

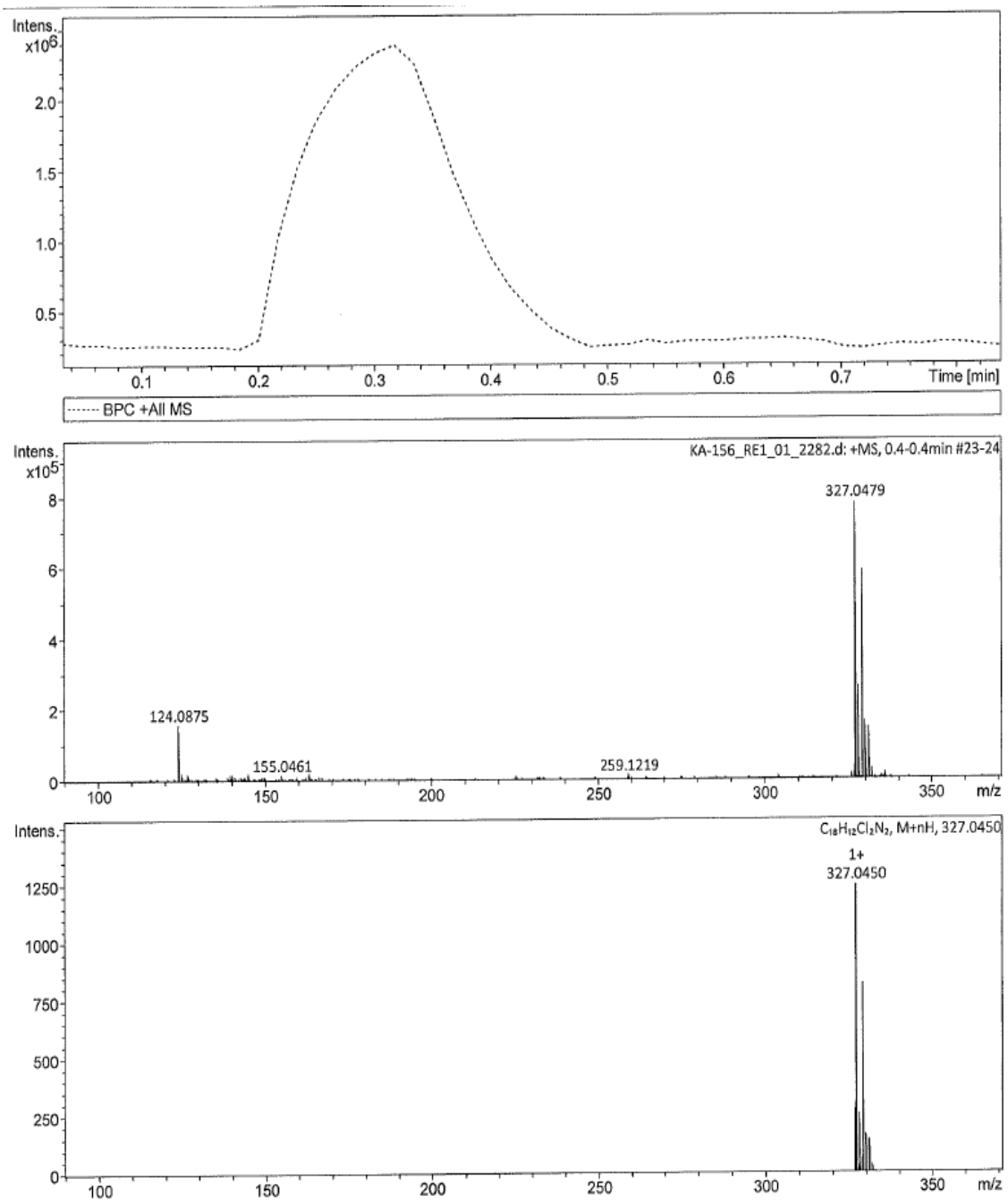


Figure 149: High performace mass spectrum for KA156. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix K: Supplementary data KA160

KA160

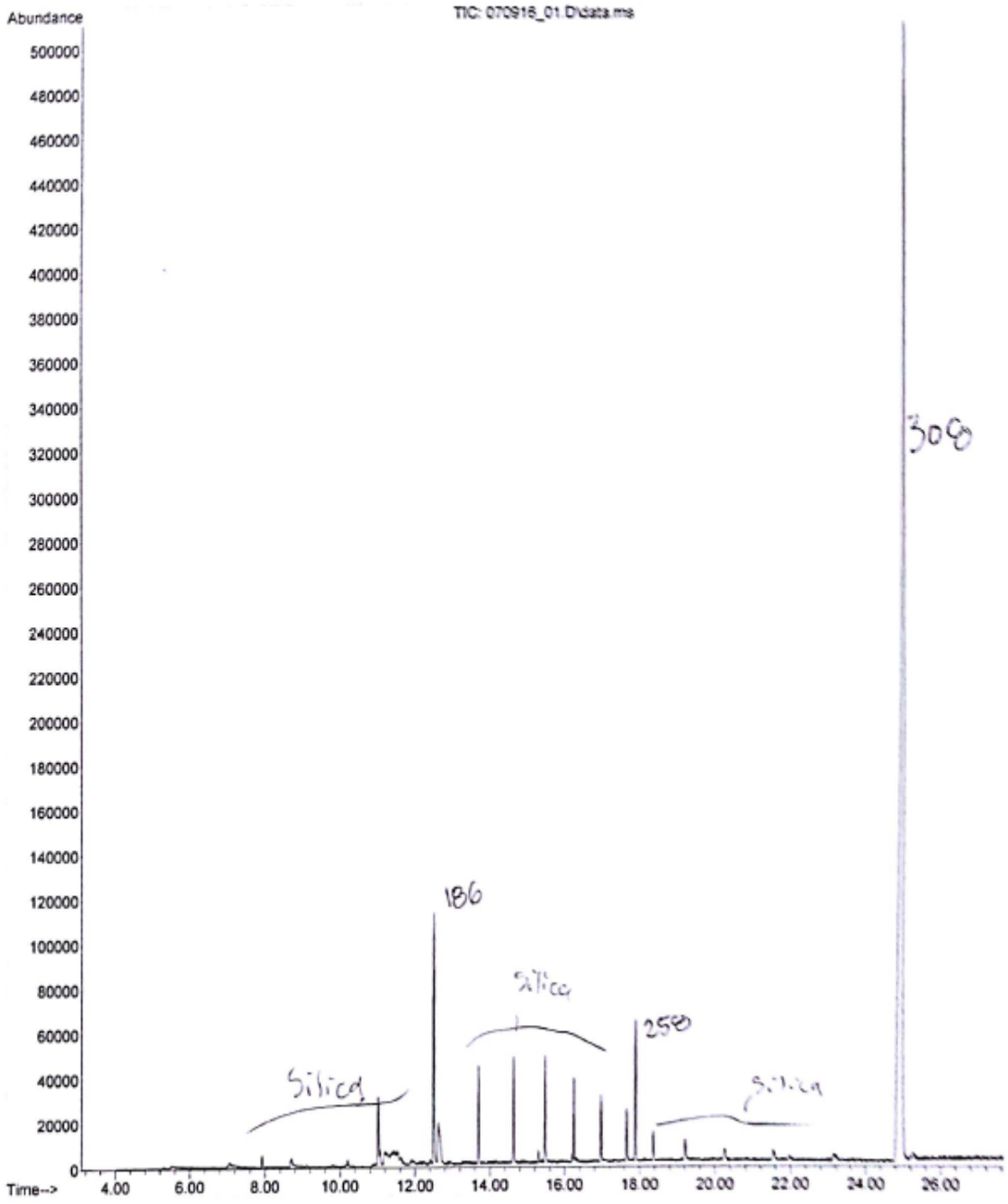


Figure 150: Gas chromatographic spectrum for KA160

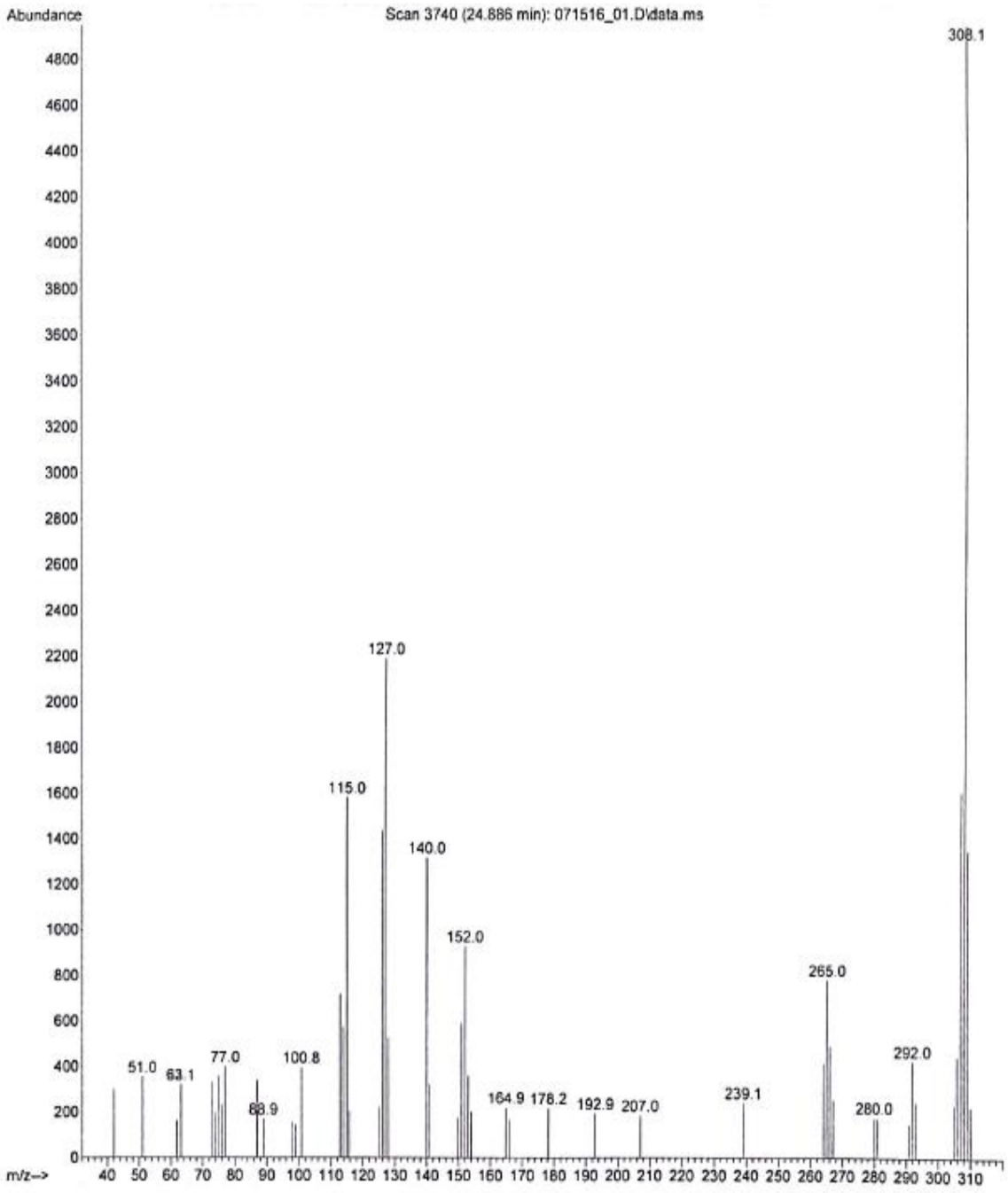


Figure 151: Mass spectrum for KA160

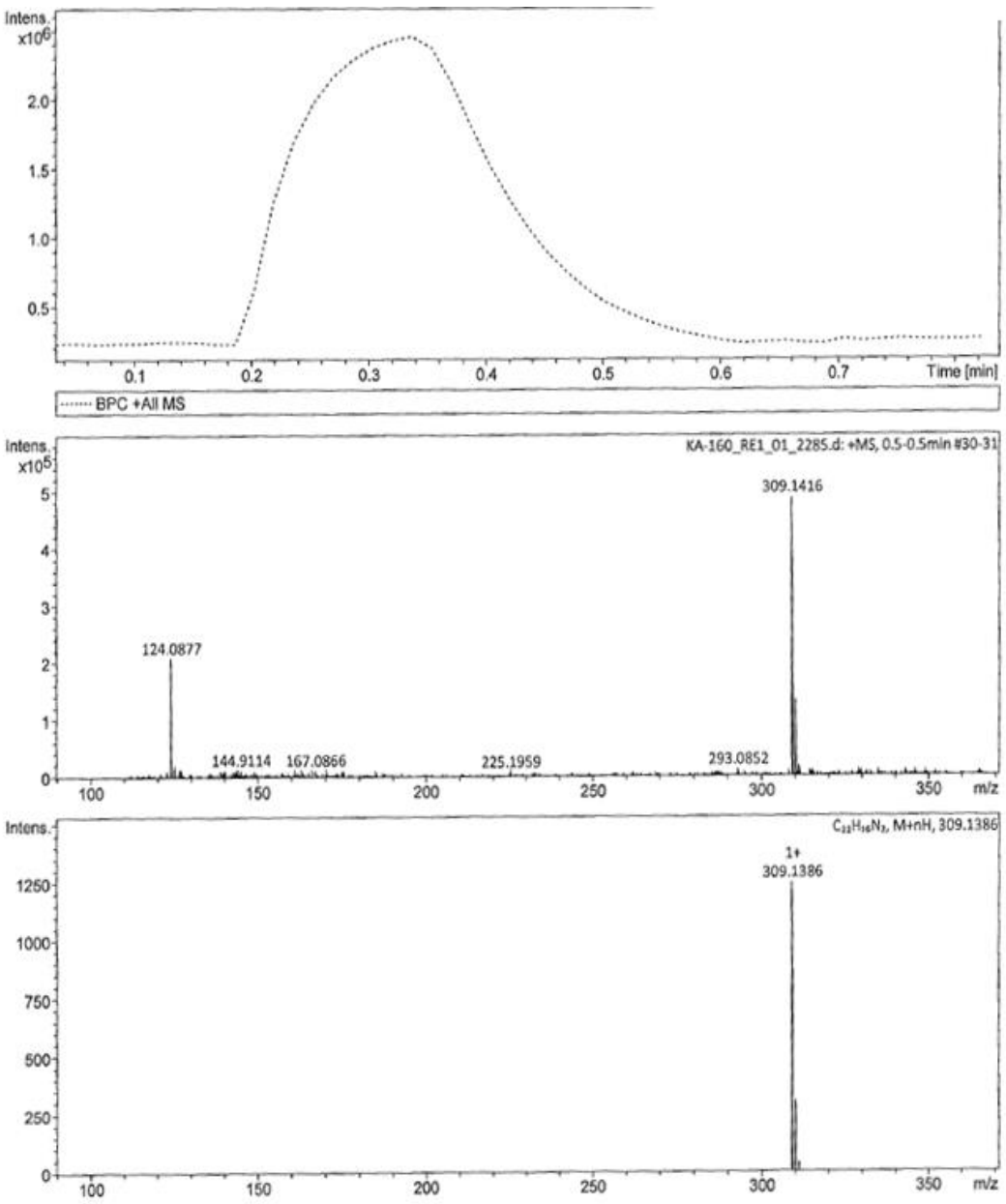


Figure 152: High performace mass spectrum for KA160. (Top) Liquid chromatographic spectrum. (Middle) Experimental mass spectrum. (Bottom) Theoretical mass spectrum based on molecular formula.

Appendix L: Supplementary data KA155

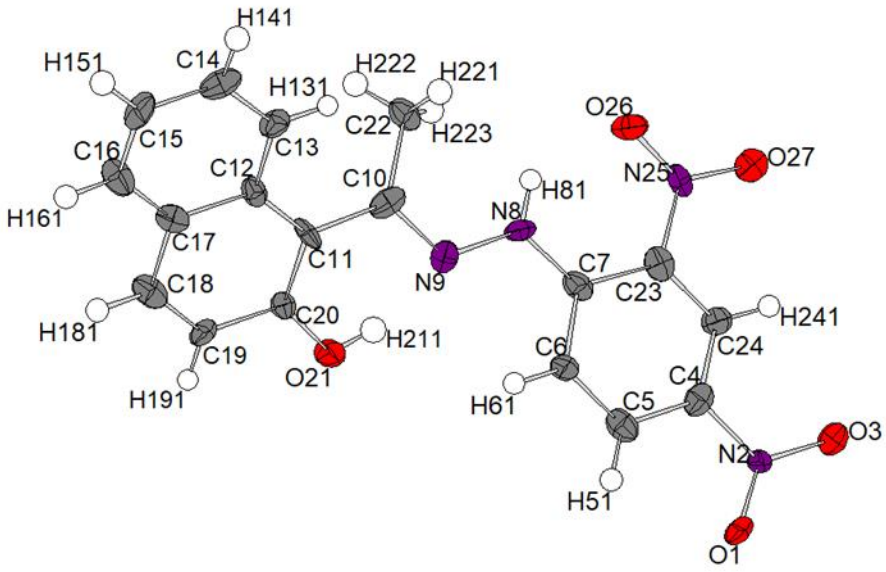


Figure 153: The crystal structure of KA143, for crystal solutions.

Table 36: *Crystal Data KA155*

Empirical Formula	$C_{18}H_{14}N_4O_5$
Formula Weight	366.3
Crystal Color, Habit	orange, platelet
Crystal Dimensions	0.10 X 0.10 X 0.10 mm
Crystal System	mo clinic
Lattice Type	Primitive

Lattice Parameters	a = 14.9397(18) Å
	b = 7.2222(7) Å
	c = 15.2684(15) Å
	b = 109.404(8)
	V = 1553.8(3) $Å^3$
Space Group	$Pca2_1$
Z value	8
D_{calc}	1.52 g/cm^3
F_{000}	1520.00
m(MoKa)	1.14 cm^{-1}

Table 37: *Intensity Measurements KA155*

Diffractometer	Rigaku RAXIS
Radiation	MoKa (l = 0.71075 Å)
	graphite mo chromated
Voltage, Current	50kV, 40mA
Temperature	-150.0°C

Detector Aperture	280 x 256 mm
Data Images	25 exposures
w oscillation Range	29.0 - 154.0^{o}
Exposure Rate	120.0 sec./^{o}
w oscillation Range	29.0 - 154.0^{o}
Exposure Rate	120.0 sec./^{o}
Detector Position	127.40 mm
Pixel Size	0.100 mm
$2q_{max}$	55.0^{o}
-of Reflections Measured	Total: 7208
	Unique: 2758 (R_{int} = 0.088)

Table 38: *Structure Solution and Refinement KA155*

Structure Solution	Direct Methods (SHELX97)
Refinement	Full-matrix least-squares on F^2
$2q_{max}$ cutoff	55.0^{o}
Residuals: R1 (I>2.00s(I))	0.0582

Residuals: R (All reflections)	0.1324
Residuals: wR2 (All reflections)	0.1937
Goodness of Fit Indicator	0.9973
Max Shift/Error in Final Cycle	0.005
Maximum peak in Final Diff. Map	0.66 $e^-/Å^3$
Minimum peak in Final Diff. Map	-0.73 $e^-/Å^3$

Table 39: *Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å2) KA155*

atom	x	y	z	*/Ueq
O1 O	0.7880(5)	0.5003(10)	0.3715(2)	0.0327
N2 N	0.7510(6)	0.4746(10)	0.4040(3)	0.0216
O3 O	0.6594(5)	0.4824(11)	0.4097(3)	0.0371
C4 C	0.8107(6)	0.4194(12)	0.4380(3)	0.0262
C5 C	0.9095(7)	0.4360(14)	0.4325(3)	0.0288
C6 C	0.9672(6)	0.3903(13)	0.4648(3)	0.0262
C7 C	0.9322(6)	0.3236(12)	0.5020(3)	0.0254
N8 N	0.9903(5)	0.2782(12)	0.5330(2)	0.0252
N9 N	1.0878(5)	0.2922(10)	0.5270(2)	0.0242
C10 C	1.1442(7)	0.2398(12)	0.5569(3)	0.0274

C11 C	1.2464(6)	0.2474(12)	0.5483(3)	0.0202
C12 C	1.3136(6)	0.2990(12)	0.5777(3)	0.0218
C13 C	1.2913(7)	0.3820(13)	0.6162(2)	0.0258
C14 C	1.3589(8)	0.4293(13)	0.6443(3)	0.0333
C15 C	1.4569(6)	0.3992(14)	0.6356(3)	0.0321
C16 C	1.4823(7)	0.3304(14)	0.5990(3)	0.0326
C17 C	1.4138(6)	0.2778(11)	0.5696(3)	0.0227
C18 C	1.4412(7)	0.2085(12)	0.5298(3)	0.0298
C19 C	1.3755(6)	0.1668(13)	0.5014(3)	0.0241
C20 C	1.2772(6)	0.1883(12)	0.5097(2)	0.0216
O21 O	1.2197(4)	0.1412(10)	0.47810(18)	0.0306
C22 C	1.1020(7)	0.1604(13)	0.5963(3)	0.0280
C23 C	0.8284(6)	0.3125(12)	0.5055(3)	0.0255
C24 C	0.7719(6)	0.3636(12)	0.4738(3)	0.0259
N25 N	0.7850(5)	0.2481(11)	0.5431(2)	0.0256
O26 O	0.8338(5)	0.2019(10)	0.57235(19)	0.0308
O27 O	0.6955(5)	0.2441(10)	0.5443(2)	0.0356
O28 O	0.5822(4)	0.7100(9)	0.23956(19)	0.0289
N29 N	0.5336(5)	0.7579(11)	0.2698(2)	0.0279
O30 O	0.4461(5)	0.7550(10)	0.2691(2)	0.0350

C31 C	0.5800(6)	0.8240(12)	0.3064(2)	0.0211
C32 C	0.6794(6)	0.8356(11)	0.3099(3)	0.0211
N33 N	0.7384(5)	0.7819(11)	0.2793(2)	0.0258
N34 N	0.8365(5)	0.7928(10)	0.2857(2)	0.0222
C35 C	0.8884(6)	0.7388(12)	0.2547(3)	0.0248
C36 C	0.8520(6)	0.6580(14)	0.2163(3)	0.0281
C37 C	0.9938(6)	0.7372(12)	0.2643(3)	0.0194
C38 C	1.0271(6)	0.6763(12)	0.3016(3)	0.0242
O39 O	0.9679(5)	0.6263(10)	0.33304(19)	0.0334
C40 C	1.1250(7)	0.6549(12)	0.3093(3)	0.0275
C41 C	1.1915(6)	0.7023(13)	0.2804(3)	0.0253
C42 C	1.1623(6)	0.7748(13)	0.2428(3)	0.0237
C43 C	1.0638(7)	0.7926(12)	0.2335(3)	0.0230
C44 C	1.0375(7)	0.8802(13)	0.1959(3)	0.0282
C45 C	1.1058(7)	0.9267(14)	0.1677(3)	0.0323
C46 C	1.2035(7)	0.9001(14)	0.1760(3)	0.0335
C47 C	1.2319(7)	0.8268(11)	0.2128(3)	0.0303
C48 C	0.7199(7)	0.9011(13)	0.3476(3)	0.0284
C49 C	0.6594(7)	0.9575(14)	0.3785(3)	0.0288
C50 C	0.5619(6)	0.9497(13)	0.3734(3)	0.0248

C51 C	0.5219(7)	0.8806(14)	0.3384(3)	0.0311
N52 N	0.5002(9)	1.0112(13)	0.4061(3)	0.0422
O53 O	0.5390(6)	1.0587(12)	0.4394(3)	0.0565
O54 O	0.4171(5)	1.0149(10)	0.4015(3)	0.0402
H51 H	0.9350	0.4777	0.4079	0.0350
H61 H	1.0325	0.4056	0.4619	0.0338
H131 H	1.2275	0.4061	0.6221	0.0311
H141 H	1.3405	0.4809	0.6692	0.0419
H151 H	1.5029	0.4278	0.6552	0.0419
H161 H	1.5464	0.3161	0.5927	0.0409
H181 H	1.5057	0.1912	0.5240	0.0371
H191 H	1.3943	0.1236	0.4759	0.0312
H222 H	1.1515	0.1067	0.6131	0.0441
H221 H	1.0704	0.2613	0.6109	0.0440
H223 H	1.0565	0.0609	0.5902	0.0439
H241 H	0.7060	0.3602	0.4766	0.0332
H361 H	0.9039	0.6095	0.2002	0.0461
H363 H	0.8194	0.7576	0.2015	0.0459
H362 H	0.8086	0.5547	0.2220	0.0460
H401 H	1.1446	0.6093	0.3345	0.0380

H411 H	1.2562	0.6865	0.2858	0.0311
H441 H	0.9736	0.9073	0.1905	0.0362
H451 H	1.0874	0.9782	0.1427	0.0399
H461 H	1.2491	0.9311	0.1564	0.0420
H471 H	1.2967	0.8108	0.2186	0.0359
H481 H	0.7858	0.9055	0.3509	0.0359
H491 H	0.6845	0.9997	0.4031	0.0400
H511 H	0.4560	0.8699	0.3359	0.0410
H81 H	0.9672(16)	0.245(14)	0.5564(11)	0.0339
H331 H	0.7158(16)	0.733(13)	0.2571(13)	0.0330
H391 H	0.997(7)	0.585(15)	0.353(2)	0.0542
H211 H	1.166(3)	0.156(15)	0.488(3)	0.0480

Table 40: *Atomic displacement parameters (Å2) KA155*

Atom	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O1	0.0234	0.0536	0.0211	0.0079	-0.0090	0.0008
N2	0.0161	0.0339	0.0148	0.0000	0.0000	0.0000
O3	0.0253	0.0596	0.0264	-0.0001	-0.0084	0.0000
C4	0.0307	0.0185	0.0293	-0.0021	-0.0057	0.0049
C5	0.0249	0.0293	0.0321	-0.0042	0.0053	-0.0075

C6	0.0201	0.0343	0.0241	0.0104	0.0031	-0.0041
C7	0.0245	0.0229	0.0287	0.0030	0.0079	-0.0027
N8	0.0278	0.0328	0.0152	0.0076	-0.0014	-0.0024
N9	0.0207	0.0173	0.0346	0.0072	-0.0025	-0.0047
C10	0.0429	0.0134	0.0261	0.0009	-0.0095	0.0021
C11	0.0167	0.0199	0.0240	-0.0155	0.0102	-0.0034
C12	0.0186	0.0167	0.0300	0.0026	0.0052	0.0017
C13	0.0298	0.0291	0.0185	-0.0053	-0.0059	0.0035
C14	0.0530	0.0198	0.0271	0.0054	-0.0094	-0.0043
C15	0.0239	0.0366	0.0359	0.0001	-0.0182	-0.0100
C16	0.0266	0.0359	0.0352	-0.0160	0.0049	-0.0049
C17	0.0304	0.0133	0.0243	-0.0010	0.0047	-0.0059
C18	0.0358	0.0198	0.0337	-0.0055	0.0115	0.0015
C19	0.0218	0.0316	0.0191	0.0033	-0.0068	0.0002
C20	0.0230	0.0210	0.0208	-0.0015	0.0036	0.0093
O21	0.0241	0.0522	0.0156	-0.0077	-0.0027	-0.0045
C22	0.0297	0.0209	0.0335	0.0006	0.0112	0.0030
C23	0.0279	0.0153	0.0333	-0.0080	0.0030	0.0025
C24	0.0283	0.0269	0.0225	0.0008	-0.0006	0.0020
N25	0.0174	0.0259	0.0336	-0.0002	0.0067	0.0025

O26	0.0368	0.0363	0.0194	0.0039	-0.0011	-0.0059
O27	0.0331	0.0417	0.0319	0.0039	-0.0022	0.0012
O28	0.0306	0.0350	0.0210	-0.0082	-0.0016	0.0011
N29	0.0255	0.0238	0.0344	-0.0016	-0.0054	-0.0018
O30	0.0253	0.0389	0.0408	-0.0087	-0.0144	-0.0024
C31	0.0255	0.0274	0.0104	-0.0044	0.0046	0.0027
C32	0.0250	0.0112	0.0272	-0.0042	0.0087	0.0011
N33	0.0298	0.0235	0.0241	-0.0025	0.0021	0.0041
N34	0.0206	0.0240	0.0220	-0.0030	0.0030	0.0038
C35	0.0133	0.0214	0.0398	-0.0036	-0.0026	-0.0003
C36	0.0267	0.0388	0.0187	-0.0050	0.0060	-0.0098
C37	0.0213	0.0148	0.0221	-0.0035	-0.0010	0.0128
C38	0.0250	0.0227	0.0250	0.0011	0.0042	-0.0001
O39	0.0406	0.0411	0.0186	0.0028	-0.0023	0.0024
C40	0.0444	0.0148	0.0234	-0.0023	-0.0075	-0.0002
C41	0.0211	0.0255	0.0292	-0.0009	0.0033	0.0032
C42	0.0240	0.0256	0.0215	-0.0026	0.0049	0.0032
C43	0.0318	0.0216	0.0158	0.0011	0.0109	-0.0022
C44	0.0348	0.0198	0.0302	-0.0026	-0.0015	0.0067
C45	0.0436	0.0316	0.0219	0.0012	0.0008	0.0072

C46	0.0405	0.0320	0.0280	-0.0017	0.0008	0.0042
C47	0.0418	0.0126	0.0366	-0.0107	0.0033	0.0048
C48	0.0343	0.0243	0.0265	0.0042	-0.0096	0.0024
C49	0.0421	0.0282	0.0160	-0.0025	0.0104	0.0015
C50	0.0234	0.0340	0.0171	-0.0033	0.0003	-0.0027
C51	0.0291	0.0328	0.0315	0.0087	0.0016	-0.0011
N52	0.0479	0.0467	0.0319	-0.0006	-0.0025	0.0074
O53	0.0494	0.0850	0.0353	-0.0289	-0.0069	0.0171
O54	0.0231	0.0563	0.0411	-0.0014	0.0071	0.0041

Table 41: *Atomic displacement parameters (Å2) KA155*

O1 -N2	1.204(11)	C7 -N8	1.344(12)
N2 -O3	1.302(12)	C7 -C23	1.465(12)
N2 -C4	1.450(13)	N8 -N9	1.387(10)
C4 -C5	1.406(13)	N8 -H81	0.87(2)
C4 -C24	1.355(13)	N9 -C10	1.314(11)
C5 -C6	1.375(13)	C10 -C11	1.464(12)
C5 -H51	0.931	C10 -C22	1.530(13)
C6 -C7	1.399(12)	C11 -C12	1.399(12)
C6 -H61	0.929	C11 -C20	1.405(11)

C12 -C13	1.425(12)	C23 -C24	1.358(12)
C12 -C17	1.440(12)	C23 -N25	1.451(12)
C13 -C14	1.366(13)	C24 -H241	0.931
C13 -H131	0.933	N25 -O26	1.225(9)
C14 -C15	1.422(14)	N25 -O27	1.258(10)
C14 -H141	0.931	O28 -N29	1.253(10)
C15 -C16	1.346(14)	N29 -O30	1.229(10)
C15 -H151	0.934	N29 -C31	1.446(11)
C16 -C17	1.412(12)	C31 -C32	1.403(12)
C16 -H161	0.930	C31 -C51	1.389(12)
C17 -C18	1.449(12)	C32 -N33	1.357(11)
C18 -C19	1.346(13)	C32 -C48	1.439(12)
C18 -H181	0.934	N33 -N34	1.396(10)
C19 -C20	1.416(12)	N33 -H331	0.87(2)
C19 -H191	0.931	N34 -C35	1.309(11)
C20 -O21	1.358(10)	C35 -C36	1.475(12)
O21 -H211	0.82(2)	C35 -C37	1.514(11)
C22 -H222	0.963	C36 -H361	0.962
C22 -H221	0.958	C36 -H363	0.960
C22 -H223	0.961	C36 -H362	0.958

C37 -C38	1.379(12)	C48 -H481	0.933
C37 -C43	1.464(12)	C49 -C50	1.382(13)
C38 -O39	1.373(11)	C49 -H491	0.931
C38 -C40	1.408(13)	C50 -C51	1.370(13)
O39 -H391	0.82(2)	C50 -N52	1.444(14)
C40 -C41	1.375(13)	C51 -H511	0.931
C40 -H401	0.929	N52 -O53	1.268(14)
C41 -C42	1.395(13)	N52 -O54	1.179(14)
C41 -H411	0.933	O1 -N2 -O3	123.2(9)
C42 -C43	1.423(12)	O1 -N2 -C4	118.5(8)
C42 -C47	1.437(13)	O3 -N2 -C4	118.2(9)
C43 -C44	1.428(13)	N2 -C4 -C5	116.7(9)
C44 -C45	1.374(13)	N2 -C4 -C24	121.0(8)
C44 -H441	0.934	C5 -C4 -C24	122.3(9)
C45 -C46	1.413(14)	C4 -C5 -C6	117.6(9)
C45 -H451	0.933	C4 -C5 -H51	121.3
C46 -C47	1.373(14)	C6 -C5 -H51	121.2
C46 -H461	0.934	C5 -C6 -C7	123.2(8)
C47 -H471	0.936	C5 -C6 -H61	118.5
C48 -C49	1.382(13)	C7 -C6 -H61	118.4

C6 -C7 -N8	122.0(8)	C13 -C14 -H141	119.7
C6 -C7 -C23	115.9(8)	C15 -C14 -H141	120.1
N8 -C7 -C23	122.1(8)	C14 -C15 -C16	119.2(8)
C7 -N8 -N9	118.3(7)	C14 -C15 -H151	120.1
C7 -N8 -H81	120.7(14)	C16 -C15 -H151	120.7
N9 -N8 -H81	121.0(14)	C15 -C16 -C17	121.6(8)
N8 -N9 -C10	118.0(7)	C15 -C16 -H161	119.6
N9 -C10 -C11	116.0(8)	C17 -C16 -H161	118.8
N9 -C10 -C22	120.1(8)	C12 -C17 -C16	120.9(8)
C11 -C10 -C22	123.7(8)	C12 -C17 -C18	117.5(8)
C10 -C11 -C12	122.6(7)	C16 -C17 -C18	121.5(8)
C10 -C11 -C20	117.7(8)	C17 -C18 -C19	121.2(9)
C12 -C11 -C20	119.5(8)	C17 -C18 -H181	119.2
C11 -C12 -C13	124.7(8)	C19 -C18 -H181	119.6
C11 -C12 -C17	120.4(8)	C18 -C19 -C20	120.9(8)
C13 -C12 -C17	114.8(8)	C18 -C19 -H191	120.1
C12 -C13 -C14	123.1(9)	C20 -C19 -H191	119.0
C12 -C13 -H131	118.0	C19 -C20 -C11	120.4(8)
C14 -C13 -H131	118.9	C19 -C20 -O21	114.1(7)
C13 -C14 -C15	120.2(9)	C11 -C20 -O21	125.5(7)

C20 -O21 -H211	103(7)	N29 -C31 -C51	117.1(8)
C10 -C22 -H222	110.2	C32 -C31 -C51	120.5(8)
C10 -C22 -H221	110.2	C31 -C32 -N33	122.2(8)
H222 -C22 -H221	109.1	C31 -C32 -C48	118.8(8)
C10 -C22 -H223	109.7	N33 -C32 -C48	119.0(8)
H222 -C22 -H223	109.0	C32 -N33 -N34	118.5(7)
H221 -C22 -H223	108.6	C32 -N33 -H331	120.6(14)
C7 -C23 -C24	120.5(8)	N34 -N33 -H331	120.7(14)
C7 -C23 -N25	120.1(8)	N33 -N34 -C35	114.7(7)
C24 -C23 -N25	119.3(8)	N34 -C35 -C36	125.7(7)
C23 -C24 -C4	120.5(9)	N34 -C35 -C37	112.6(8)
C23 -C24 -H241	120.1	C36 -C35 -C37	121.1(7)
C4 -C24 -H241	119.4	C35 -C36 -H361	109.9
C23 -N25 -O26	121.1(7)	C35 -C36 -H363	109.2
C23 -N25 -O27	117.1(7)	H361 -C36 -H363	109.5
O26 -N25 -O27	121.9(7)	C35 -C36 -H362	109.5
O28 -N29 -O30	121.8(8)	H361 -C36 -H362	109.3
O28 -N29 -C31	120.0(7)	H363 -C36 -H362	109.4
O30 -N29 -C31	118.2(7)	C35 -C37 -C38	121.4(8)
N29 -C31 -C32	122.4(7)	C35 -C37 -C43	120.7(8)

C38 -C37 -C43	117.9(8)	C44 -C45 -C46	121.1(9)
C37 -C38 -O39	122.9(8)	C44 -C45 -H451	119.5
C37 -C38 -C40	121.7(8)	C46 -C45 -H451	119.4
O39 -C38 -C40	115.3(8)	C45 -C46 -C47	120.2(9)
C38 -O39 -H391	113(8)	C45 -C46 -H461	120.1
C38 -C40 -C41	120.9(8)	C47 -C46 -H461	119.7
C38 -C40 -H401	119.2	C42 -C47 -C46	120.1(9)
C41 -C40 -H401	120.0	C42 -C47 -H471	119.6
C40 -C41 -C42	120.0(8)	C46 -C47 -H471	120.3
C40 -C41 -H411	120.0	C32 -C48 -C49	118.7(8)
C42 -C41 -H411	119.9	C32 -C48 -H481	120.3
C41 -C42 -C43	120.5(8)	C49 -C48 -H481	121.0
C41 -C42 -C47	119.9(8)	C48 -C49 -C50	120.7(9)
C43 -C42 -C47	119.5(8)	C48 -C49 -H491	119.8
C37 -C43 -C42	118.8(8)	C50 -C49 -H491	119.5
C37 -C43 -C44	122.6(8)	C49 -C50 -C51	121.4(8)
C42 -C43 -C44	118.4(7)	C49 -C50 -N52	119.6(8)
C43 -C44 -C45	120.4(9)	C51 -C50 -N52	118.9(9)
C43 -C44 -H441	119.9	C31 -C51 -C50	119.7(9)
C45 -C44 -H441	119.7	C31 -C51 -H511	119.8

C50 -C51 -H511	120.5
C50 -N52 -O53	117.6(10)
C50 -N52 -O54	120.3(11)
O53 -N52 -O54	122.1(12)

Table 42: *Hydrogen-bond geometry (Å, °) KA155*

D—H···A	D—H	H···A	D···A	D—H···A
C6—H61···O3	141.4(3)	0.929	2.594	3.371(13)
C19—H191···O53	138.8(3)	0.931	2.404	3.165(13)
C19—H191···O54	170.3(2)	0.931	2.584	3.505(13)
C40—H401···O13	141.7(3)	0.929	2.473	3.254(13)
C40—H401···O3	165.9(3)	0.929	2.563	3.472(13)
C48—H481···O54	143.5(3)	0.933	2.545	3.341(13)
N8—H81···O26	129.3(20)	0.867	1.97	2.607(13)
N33—H331···O28	129(2)	0.866	1.971	2.604(13)
O21—H211···N9	150(10)	0.825	1.944	2.667(13)
O21—H211···C10	121(9)	0.825	2.376	2.884(13)

Symmetry codes: (i) x+1, y, z; (ii) −x+2, −y+1, −z+1.