

Synthesis of aminocyclobutanes through ring expansion of *N*-vinyl- β -lactams

Lawrence L.W. Cheung and Andrei K. Yudin*

Table of Contents

Page

S2	General comments
S2	General procedure for β -lactam synthesis
S3	General procedure for vinyl iodide synthesis
S5	General procedure for β -lactam cross coupling
S5	General procedure for microwave reactions
S6	Product characterizations
S36, S42	X-ray data
S49	References
S50	^1H , ^{13}C NMR Spectra

General comments

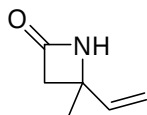
THF was distilled from sodium benzophenone ketyl under sodium prior to use. Anhydrous toluene was purchased from Aldrich and was used as received. All other solvents were used as received. Column chromatography was carried out using Silicycle 230-400 mesh silica gel. Analytical thin layer chromatography was performed on precoated glass-backed plates manufactured by EMD Chemicals, with a pore size of 60 Å and visualized using iodine stain or UV lamp (254 nm). All microwave experiments were performed with a Biotage Initiator Sixty using DMF as the solvent.

Nuclear magnetic resonance: ^1H and ^{13}C NMR were recorded on Varian Mercury 300 SMS sample changer, Mercury 400 SMS sample changer, Varian NMR System 400 or Varian Unity 500. ^1H and ^{13}C were referenced to TMS (0 ppm). Peak multiplicities are designated by the following abbreviations: s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets; dm, doublet of multiplets; ddd, doublet of doublet of doublets; ddt, doublet of doublet of triplets; td, triplet of doublets; dqd, doublet of quartet of doublets; br, broad; and J , coupling constant in Hz.

Mass Spectroscopy: High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV or on an ABI/Sciex Qstar mass spectrometer with ESI source, MS/MS and accurate mass capabilities.

General procedures

Synthesis of β -lactams:

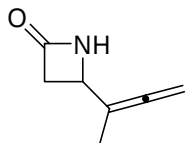


4-methyl-4-vinylazetidin-2-one

A) Synthesis of the β -lactams used a modified procedure from that of Moriconi.¹ A 500 mL three-neck round bottom flask equipped with a 125 mL pressure equalized addition funnel, stir bar, glass stopper and an outlet to an oil bubbler was flame dried and allowed to cool. The flask was then placed under nitrogen and 117 mL of isoprene and 125 mL of diethyl ether were added through the addition funnel. The solution was then placed in a dry ice acetone bath and allowed to cool. 10 mL of chlorosulfonyl isocyanate was added to a closed addition funnel followed by 20 mL of diethyl ether. The addition funnel was then opened to allow addition of the isocyanate solution in a quick drop wise manner. After the addition was complete the flask was removed from the cold bath and stirred for 1 hour, the flask was then placed in an ice bath. Reduction of the *N*-chlorosulfonyl β -lactam followed the procedure of Durst.² 125 g of Na_2SO_3 , 250 mL of diethyl ether and 375 mL of water were combined in a one neck 2 litre round bottom flask. The mixture was stirred and the β -lactam solution was transferred in 20 mL batches by a syringe. KOH flasks were added to the solution to keep the pH of the mixture around 8. The

mixture was then gravity filtered and the organic layer and aqueous layer were separated with a separatory funnel. The aqueous layer was washed twice with diethyl ether and the combined organic layers were dried over magnesium sulphate and concentrated. The resulting β -lactam (76 %) can be used without any purification.

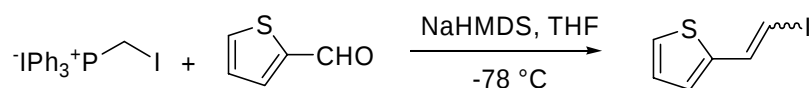
Synthesis of 4-(buta-2,3-dien-2-yl)azetidin-2-one:



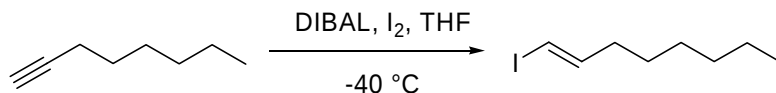
4-(buta-2,3-dien-2-yl)azetidin-2-one

B) The synthesis of 4-(buta-2,3-dien-2-yl)azetidin-2-one was done using a procedure described by Lee³ and requires 4-oxoazetidin-2-yl acetate which can be purchased or made using the procedure described by Miller.⁴

Procedures for vinyl iodide synthesis

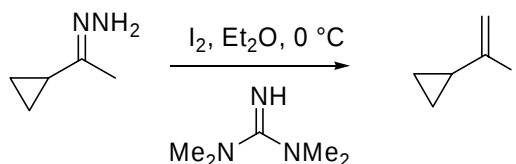


C) Representative procedure⁵: To a flame dried 250 mL round bottom flask equipped with a stir bar was added 5.67 g of iodomethylenetriphenylphosphonium iodide. The flask was then placed under vacuum for five minutes then purged with nitrogen. 35 mL of THF was added and the suspension was cooled to -20 °C. 11.4 mL of NaHMDS (1 M) was added drop wise along the flask wall and after the addition was complete the solution was allowed to stir at -20 °C for 5 minutes. The flask was then cooled to -78 °C and a 0.84 mL of thiophene-2-carboxaldehyde in 15 mL of THF was added along the wall of the flask. The reaction was allowed to stir for 10 minutes and then quenched with saturated aqueous ammonium chloride. Diethyl ether was added to the mixture and the layers were separated with a separatory funnel. The aqueous layer was washed twice with diethyl ether and the combined organic layers were dried with magnesium sulphate and concentrated. The crude product was column with 9:1 (Hex:EtOAc) to give 0.90 g of product. Synthesis of iodomethylenetriphenylphosphonium iodide was done as described by Urch.⁶

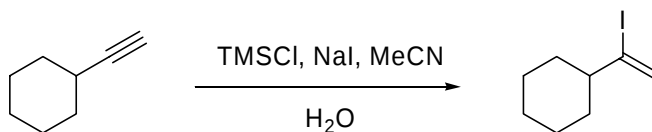


D) Representative procedure⁷: A 250 mL flame dried round bottom flask equipped with a stir bar was flame dried under vacuum and allowed to cool to room temperature. The flask was then purged with nitrogen and 6.7 mL of 1-octyne was charged into the flask. The flask was then cooled in a -40 °C bath and DIBAL (1.5 M, 30 mL) was added drop

wise. The reaction is then heated to 50 °C for 3 hours and then cooled to room temperature and the solvent removed under vacuum. THF (20 mL) is then added and cooled to -50 °C, iodine in THF (20 mL) is then added drop wise. The mixture is then warmed to room temperature and then cooled back down to 0 °C in an ice bath. 20 % aqueous sulphuric acid was then added drop wise until there was no visible exotherm, then the reaction was poured into a mixture of ice and 20 % sulphuric acid. The aqueous layer was extracted twice with pentane and the combined organic layers were washed twice with aqueous saturated sodium thiosulfate, dried with magnesium sulphate and concentrated. 10.3 g (95 %) of crude material was isolated and used without any further purification.



E) Representative procedure⁸: 8.5 g of iodine was added to a flame dried 250 mL 2-neck round bottom flask equipped with a stir bar and a pressure equalized addition funnel (The addition funnel had a rubber septa for addition of liquids via a syringe). 15 mL of ether was added and the mixture was stirred in an ice bath. 9.6 mL of 1,1,3,3-tetramethylguanidine was added to the addition funnel along with 15 mL of ether. The guanidine solution was added to the iodine solution dropwise. After the guanidine solution was added the mixture was stirred for 15 minutes in the ice bath. 1.6 g of the 1-(1-cyclopropylethylidene)hydrazine was added as a solution, in 10 mL of ether, dropwise to the reaction mixture and was allowed to stir for 15 minutes in the ice bath after addition was complete. After the addition was complete, stirring continued for 10 minutes, after which 20 mL of 10 % HCl was added to quench the reaction. The contents of the reaction flask were poured into a separatory funnel. The organic layer was washed with water, then saturated sodium thiosulfate, then twice 10 % HCl. The organic layer was dried with magnesium sulphate and concentrated. 1.2 g of crude material (40 %) was collected and used immediately without any purification. The hydrazone was synthesized by combining 3.4 mL of 1-cyclopropylethanone, 4 mL of hydrazine monohydrate and 15 mL of methanol and refluxing for 45 minutes.⁹



F) Representative procedure:¹⁰ At room temperature TMSCl (2.35 mL) was added to a solution of NaI (3.2 g) in MeCN (18 mL), followed by water (0.2 mL). The reaction was allowed to stir for 10 minutes, then cyclohexylacetylene (1.21 mL) was added and the reaction was stirred for 1 hour at room temperature. The reaction was then quenched with water. The aqueous layer was washed twice with diethyl ether and the combined organic layers were washed twice with aqueous saturated sodium thiosulfate. The organic layer was concentrated to half volume and washed three times with water to

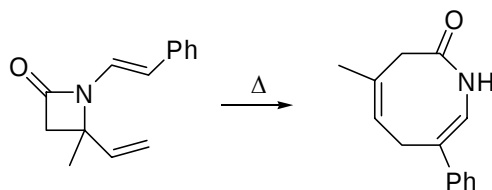
remove any excess MeCN. 2.14 g of crude material (98 %) was collected and was used immediately without any purification.

Cross-coupling β -lactams with vinyl iodides

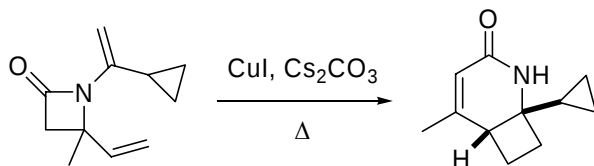
G) Representative procedure for synthesis of *N*-vinyl β -lactams:¹¹ A Schlenk flask charged with a stir bar was flame dried under vacuum. After cooling the Schlenk flask was charged with 281 mg of CuI and 1.45 g of cesium carbonate and equipped with a rubber septum and placed under vacuum. The vessel was purged with nitrogen after being under vacuum for 5 minutes and 1 mL of PhMe was added followed by the 320 μ L *N,N'*-dimethylethylenediamine, 410 mg of the β -lactam and 910 mg of 1-(3-iodobut-3-enyl)benzene. An additional 1 mL of PhMe was used to rinse the vials holding the vinyl iodide and lactam. The flask was lowered into a 75 °C preheated oil bath and allowed to stir overnight. After the reaction was complete, as judged by TLC, the flask contents was allowed to cool. The flask was then emptied into a separatory funnel by rinsing with DCM and water. The aqueous layer was washed twice with DCM. The combined organic layers were dried with magnesium sulphate and concentrated and purified by flash column chromatography.

Microwave Experiments:

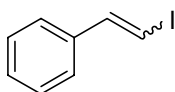
All microwave experiments were performed using sealed reaction vessels inside a Biotage Initiator Sixty microwave reactor.



H) Representative procedure for [3, 3] sigmatropic rearrangement: A 20 mg solution of an *N*-vinyl β -lactam in 450 μ L of DMF was charged in a Biotage Microwave vial of 0.2-0.5 mL capacity. The vial was capped and microwave heated for 30 minutes with the following settings: without pre-stirring, with absorption level of high and with fix hold time on. The temperature used is listed with the characterization of the compound. After the microwave heating is complete the contents of the vial were emptied into a test tube, rinsing the vial with water and DCM. The organic layer is removed and the aqueous layer was washed twice with DCM. The combined organic layers were dried with magnesium sulphate, concentrated and purified by column chromatography.

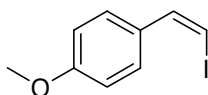


I) Representative procedure for electrocyclization: 10 mol % CuI, 1.5 eq of Cs₂CO₃ were charged into a Biotage Microwave vial of 0.2-0.5 mL capacity. A 20 mg solution of an *N*-vinyl β -lactam in 450 μ L of DMF was added and vial was capped. Microwave heating was performed with the following settings: without pre-stirring, with absorption level of high and with fix hold time on. The temperature used is listed with the characterization of the compound. After the microwave heating is complete the contents of the vial were emptied into a test tube, rinsing the vial with water and DCM. Aqueous ammonium chloride was added and the organic layer was extracted. The organic layer was washed twice with brine. The combined aqueous layers were washed with DCM to extract any organic product that remained. The combined organic layers were dried with magnesium sulphate and concentrated.



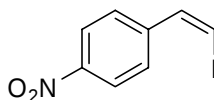
1-(2-iodovinyl)benzene:¹² Employing procedure C) with 481 μ L of benzaldehyde, 1.3 eq of iodomethylenetriphenylphosphonium iodide and 1.3 eq of 1M NaHMDS. The crude material was columned with 8:2 (Hex:EtOAc), 542 mg of product collected, 50 % with an *E:Z* ratio of 3:1.

¹H NMR 400 MHz (CDCl₃) δ : 7.43 (d, *J* = 14.8 Hz, 1H), 7.34-7.28 (m, 5H), 6.83 (d, *J* = 14.8 Hz, 1H)



1-((*Z*)-2-iodovinyl)-4-methoxybenzene:¹³ Employing procedure C) with 365 μ L of *p*-methoxybenzaldehyde, 1.3 eq of iodomethylenetriphenylphosphonium iodide and 1.3 eq of 1 M NaHMDS. The crude material was columned with 8:2 (Hex:EtOAc), to afford 0.406 g of product, 52 %, *R*_f = 0.72 eluent 8:2 (Hex:EtOAc), *E:Z* ratio was greater than 20:1.

¹H NMR 400 MHz (CDCl₃) δ : 7.63 (d, *J* = 8.8 Hz, 2H), 7.25 (d, *J* = 8.8 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.41 (d, *J* = 8.8 Hz, 1H), 3.83 (s, 3H)



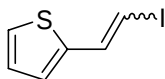
1-((*Z*)-2-iodovinyl)-4-nitrobenzene: Employing procedure C) with 453 mg of *p*-nitrobenzaldehyde, 1.3 eq of iodomethylenetriphenylphosphonium iodide and 1.3 eq of 1 M NaHMDS. The crude material was columned with 7:3 (Hex:EtOAc), *R*_f = 0.75 using 7:3 (Hex:EtOAc). 0.315 g of product was collected (38 %), with an *E:Z* ratio of 7:1

¹H NMR 400 MHz (CDCl₃) δ : 8.25 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 8.8 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 1H)

¹³C NMR 100 MHz (CDCl₃) δ : 143.2, 136.9, 133.0, 129.1, 123.6, 84.1

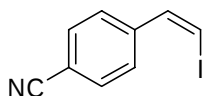
High Resolution MS:

Calculated: 274.9443, Actual: 274.9450



2-(2-iodovinyl)thiophene:¹⁴ Employing procedure C) with 0.84 mL of thiophene-2-carbaldehyde, 1.3 eq of iodomethylenetriphenylphosphonium iodide and 1.3 eq of 1 M NaHMDS. The crude was purified by column chromatography using 8:2 (Hex:EtOAc), 0.8992 g of product collect, 42 % (1:1 mixture of *E* and *Z*).

¹H NMR (CDCl₃) 400 MHz δ : 7.64 (d, *J* = 8.8 Hz), 7.48 (d, *J* = 14.8 Hz), 7.37-7.36 (m), 7.21 (d, *J* = 4.8 Hz), 7.09 (dd, *J* = 4.0, 5.0 Hz), 6.99-6.95 (m), 6.63 (d, *J* = 14.8 Hz), 6.44 (d, *J* = 8.8 Hz)



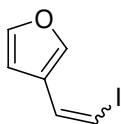
4-(2-iodovinyl)benzonitrile: Employing procedure C) with 393 mg of *p*-cyanobenzaldehyde, 1.3 eq of iodomethylenetriphenylphosphonium iodide 1.3 eq of 1 M NaHMDS. The crude material was columned with, 25 % (*E*:*Z* ratio 1:6.71), 0.191 g collected, 25 %.

¹H NMR 400 MHz (CDCl₃) δ : 7.72 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 1H)

¹³C NMR 100 MHz (CDCl₃) δ : 141.3, 137.2, 132.1, 128.9, 118.7, 111.8, 83.3

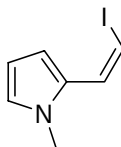
High Resolution MS:

Calculated: 254.9545, Actual: 254.9548



3-(2-iodovinyl)furan: Employing procedure C) with 520 μ L of furan-3-carbaldehyde, 1.3 eq of iodomethylenetriphenylphosphonium iodide and 1.3 eq of 1 M NaHMDS. The crude was purified using 9:1 (Hex:Et₂O), 430 mg collected, 33 %, *R*_f = 0.81 Eluent 7:3 (Hex:EtOAc).

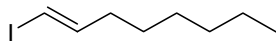
¹H NMR (CDCl₃) 300 MHz δ : 8.00 (s, 1H), 7.42 (t, *J* = 2.0 Hz, 1H), 7.23 (s, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 11.2 Hz, 1H)



2-(2-iodovinyl)-1-methyl-1H-pyrrole: Employing procedure C) with 645 μ L of furan-3-carbaldehyde, 1.3 eq of iodomethylenetriphenylphosphonium iodide and 1.3 eq of 1 M

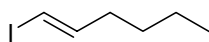
NaHMDS. The crude was purified using 8:2 (Hex:Et₂O), 479 mg collected, 34 %, R_f = 0.86 Eluent 7:3 (Hex:EtOAc).

¹H NMR (CDCl₃) 300 MHz δ: 7.24-7.21 (m, 2H), 6.68-6.67 (m, 1H), 6.30 (d, *J* = 8.4 Hz, 1H), 6.23-6.20 (m, 1H), 3.59 (s, 3H)



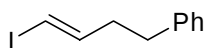
(E)-1-iodooct-1-ene:¹⁵ Employing procedure D) with 6.69 mL of 1-octyne, 30 mL of DIBAL (1.5 M in PhMe), and 11.75 g of I₂. The crude product was used without any purification. 10.3 g collected, 95 %.

¹H NMR 400 MHz (CDCl₃) δ: 6.51 (dt, *J* = 7.2, 14.4 Hz, 1H), 5.97 (dt, *J* = 1.6, 14.4 Hz, 1H), 1.70 (qd, *J* = 3.2, 12.4 Hz, 2H), 1.40-1.27 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H)



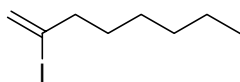
(E)-1-iodohex-1-ene:¹⁶ Employing procedure D) with 2.8 mL of 1-hexyne, 16 mL of DIBAL (1.5 M in PhMe), and 6.15 g of I₂. The crude was purified by column chromatography using 9:1 (Hex:EtOAc) as the eluent, 3.6 g collected, 71 %. R_f = 0.88 Eluent 9:1 (Hex:EtOAc).

¹H NMR (CDCl₃) 300 MHz δ: 6.51 (dt, *J* = 7.2, 14.4 Hz, 1H), 5.97 (dt, *J* = 1.2, 14.4 Hz, 1H)



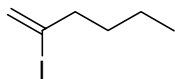
1-((E)-4-iodobut-3-enyl)benzene:¹⁷ Employing procedure D) with 2.2 mL of 1-(but-3-ynyl)benzene, 10.2 mL of DIBAL (1.5 M in PhMe) and 3.92 g of I₂. The crude was columned with 8:2 (Hex:EtOAc), 2.8683 g collected, 71 %.

¹H NMR (CDCl₃) 400 MHz δ: 7.31-7.26 (m, 2H), 7.20 (tt, *J* = 1.6, 7.2 Hz, 1H), 7.17-7.15 (m, 2H), 6.55 (dt, *J* = 7.2, 14.4 Hz, 1H), 6.02 (dt, *J* = 1.6, 14.4 Hz, 1H), 2.71 (t, *J* = 7.6 Hz, 2H), 2.40-2.34 (m, 2H)

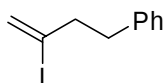


2-iodooct-1-ene:¹⁸ Employing procedure F) with 1.5 mL of 1-octyne, 1.5 mL of TMSCl, 1.8 g of NaI and 100 μL of water. 1.78 g of crude was collected, 73 %.

¹H NMR 300 MHz (CDCl₃) δ: 6.00 (m, 1H), 5.68 (m, 1H), 2.40-2.36 (m, 2H), 1.53-1.44 (m, 2H), 1.41-1.29 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H)

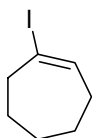


2-iodohex-1-ene:¹⁸ Employing procedure F) with 5.7 mL of 1-hexyne, 7.6 mL of TMSCl, 9. ¹H NMR (CDCl₃) 300 MHz δ: 6.01-6.00 (m, 1H), 5.68 (m, 1H), 2.41-2.36 (m, 2H), 1.53-1.43 (m, 2H), 1.38-1.26 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H)



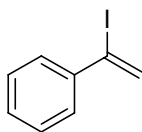
1-(3-iodobut-3-enyl)benzene:¹⁹ Employing procedure F) with 2.1 mL of 1-(but-3-ynyl)benzene, 7.6 mL of TMSCl, 9.46 g of NaI and 0.54 mL of water. 3.19 g of crude was collected, 70 %.

¹H NMR (CDCl₃) 300 MHz δ : 7.31-7.26 (m, 2H), 7.22-7.18 (m, 3H), 5.96 (d, J = 1.2 Hz, 1H), 5.68 (d, J = 1.2 Hz, 1H), 2.86-2.81 (m, 2H), 2.72-2.67 (m, 2H)



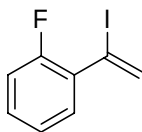
(*E*)-1-iodocyclohept-1-ene:²⁰ Employing procedure E) with 2.74 g of 1-cycloheptylidenehydrazine, 8.94 g of I₂ and 24 mL of 1,1,3,3-tetramethylguanidine. 1.95 g of crude product was collected, 55 %.

¹H NMR (CDCl₃) 300 MHz δ : 6.51 (t, J = 6.6 Hz, 1H), 2.78-2.74 (m, 2H), 2.08-2.02 (m, 2H), 1.76-1.69 (m, 2H), 1.58-1.51 (m, 4H)



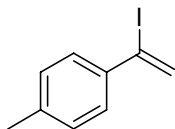
1-(1-iodovinyl)benzene:²¹ Employing procedure E) with 2.2 g of 1-(1-phenylethylidene)hydrazine, 8.37 g of I₂, and 22.5 mL of 1,1,3,3-tetramethylguanidine. 3.77 g of crude product was collected, 48 %.

¹H NMR (CDCl₃) 200 MHz δ : 7.54-7.26 (m, 5H), 6.46 (d, J = 1.8 Hz, 1H), 6.08 (d, J = 1.8 Hz, 1H)



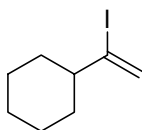
1-fluoro-2-(1-iodovinyl)benzene: Employing procedure E) with 2.09 g of 1-(1-(2-fluorophenyl)ethylidene)hydrazine, 7.55 g of I₂, and 10 mL of 1,1,3,3-tetramethylguanidine. 2.62 g of crude product was collected, 77 %.

¹H NMR (CDCl₃) 300 MHz δ : 7.38 (td, J = 1.8, 7.8 Hz, 1H), 7.17-7.09 (m, 2H), 7.05-6.98 (m, 1H), 6.45-6.44 (m 1H), 6.30-6.29 (m, 1H)



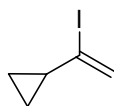
1-(1-iodovinyl)-4-methylbenzene: Employing procedure E) with 3.00 g of 1-(1-p-tolylolethylidene)hydrazine, 10.0 g of I₂, and 10 mL of 1,1,3,3-tetramethylguanidine. 2.47 g of crude product was collected, 50 %.

¹H NMR (CDCl₃) 400 MHz δ : 7.40 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 6.42 (d, *J* = 2.0 Hz, 1H), 6.03 (d, *J* = 2.0 Hz, 1H), 2.35 (s, 3H)



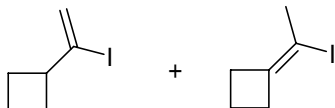
(1-iodovinyl)cyclohexane:²² Employing procedure F) with 1.21 mL of Cyclohexylacetylene, 2.35 mL of TMSCl, 3.2 g of NaI and 0.2 mL of water. 2.142 g of crude product was collected, 98 %.

¹H NMR (CDCl₃) 300 MHz δ : 6.06 (s, 1H), 5.70 (d, *J* = 1.5 Hz, 1H), 2.20-2.16 (m, 1H), 1.87-1.45 (m, 5H), 1.46-1.09 (m, 5H)



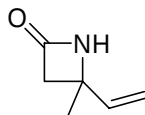
(1-iodovinyl)cyclopropane:²³ Employing procedure E) with 1.5 g of 1-(1-cyclopropylethylidene)hydrazine, 8.5 g of I₂, and 9.6 mL of 1,1,3,3-tetramethylguanidine. 1.2 g of crude was collected, 40 %.

¹H NMR (CDCl₃) 200 MHz δ : 6.08 (t, *J* = 1.2 Hz, 1H), 5.67 (d, *J* = 1.4 Hz, 1H), 1.62-1.43 (m, 1H), 0.79-0.70 (m, 2H), 0.68-0.63 (m, 2H)



(1-iodovinyl)cyclobutane and (1-iodoethylidene)cyclobutane: Employing procedure E) with 1.33 g of 1-(1-cyclobutylethylidene)hydrazine, 5.32 g of I₂ and 6.4 mL of 1,1,3,3-tetramethylguanidine. 1.80 g of crude was collected, 85 %. The ratio of (1-iodovinyl)cyclobutane to (1-iodoethylidene)cyclobutane was 1.00:0.71.

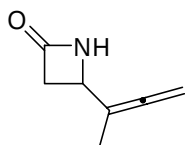
¹H NMR (CDCl₃) 400 MHz δ : 5.96 (t, *J* = 2.0 Hz, 1H), 5.67 (t, *J* = 2.0 Hz, 1H), 3.12-3.03 (m), 2.84 (s, 3H), 2.68-2.63 (m), 2.52-2.48 (m), 2.26-2.24 (m), 2.00-1.92 (m), 1.88-1.75 (m), 1.71-1.64 (m)



4-methyl-4-vinylazetidin-2-one:² Employing procedure A).

^1H NMR (CDCl_3) 400 MHz δ : 6.06 (dd, $J = 10.8, 17.2$ Hz, 1H), 5.26 (dd, $J = 0.8, 17.2$ Hz, 1H), 5.16 (dd, $J = 0.8, 10.8$ Hz, 1H), 2.85 (d, $J = 1.6$ Hz, 2H), 1.55 (s, 3H)

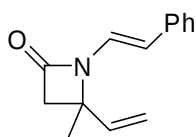
^{13}C NMR (CDCl_3) 75 MHz δ : 167.0, 141.2, 113.9, 54.5, 51.0, 24.8



4-(buta-2,3-dien-2-yl)azetidin-2-one:³ Employing procedure B).

^1H NMR (CDCl_3) 400 MHz δ : 5.89 (bs, 1H), 4.82-4.79 (m, 2H), 4.11-4.08 (m, 1H), 3.15 (ddd, $J = 1.6, 5.2, 14.8$ Hz, 1H), 2.83 (ddd, $J = 1.6, 2.4, 14.8$ Hz, 1H), 1.72 (t, $J = 3.2$ Hz, 3H)

^{13}C NMR 75 MHz (CDCl_3) δ : 205.6, 167.4, 104.8, 98.4, 48.8, 43.4, 14.0



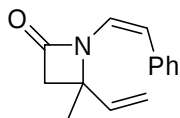
4-methyl-1-styryl-4-vinylazetidin-2-one (**1a**): Employing procedure G) with 103 mg of 4-methyl-4-vinylazetidin-2-one, 229 mg of 1-(2-iodovinyl)benzene (mixture of *E* and *Z* isomers), 8.8 mg of CuI, 480 mg of Cs_2CO_3 , 10 μL of *N,N'*-dimethylethylenediamine and 1 mL of PhMe. The crude was columned with 8:2 (Hex:EtOAc), 71.2 mg of product collected, 36 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.28-7.27 (m, 4H), 7.21-7.16 (m, 1H), 6.98 (d, $J = 14.8$ Hz, 1H), 6.13 (d, $J = 6.13$ Hz, 1H), 6.06 (dd, $J = 10.8, 17.2$ Hz, 1H), 5.38 (d, $J = 17.6$ Hz, 1H), 5.33 (d, $J = 10.8$ Hz, 1H), 3.00 (d, $J = 14.8$ Hz, 1H), 2.96 (d, $J = 14.8$ Hz, 1H)

^{13}C NMR (CDCl_3) 75 MHz δ : 163.3, 139.3, 136.0, 128.7, 126.8, 125.4, 119.5, 116.5, 113.2, 59.4, 51.9, 21.1

HR-MS: $\text{C}_9\text{H}_{13}\text{NO}$

Calculated: 213.1154, Actual: 213.1156



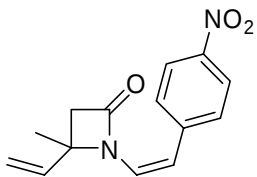
4-methyl-1-styryl-4-vinylazetidin-2-one (**1a**): Employing procedure G) with 103 mg of 4-methyl-4-vinylazetidin-2-one, 229 mg of 1-(2-iodovinyl)benzene (mixture of *E* and *Z* isomers), 8.8 mg of CuI, 480 mg of Cs_2CO_3 , 10 μL of *N,N'*-dimethylethylenediamine and 1 mL of PhMe. The crude was columned with 8:2 (Hex:EtOAc), 47.2 mg of product collected, 24 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.32-7.31 (m, 4H), 7.24-7.20 (m, 1H), 6.07 (d, $J = 10.0$ Hz, 1H), 5.97 (dd, $J = 10.8, 17.6$ Hz, 1H), 5.76 (d, $J = 10.0$ Hz, 1H), 5.29-5.22 (m, 2H), 2.94 (d, $J = 14.8$ Hz, 1H), 2.86 (d, $J = 15.2$ Hz, 1H), 1.53 (s, 3H)

^{13}C NMR (CDCl_3) 75 MHz δ : 163.3, 139.6, 135.7, 128.9, 128.0, 127.3, 121.4, 118.3, 116.3, 58.9, 50.5, 21.7

HR-MS: $\text{C}_9\text{H}_{13}\text{NO}$

Calculated: 213.1154, Actual: 213.1155



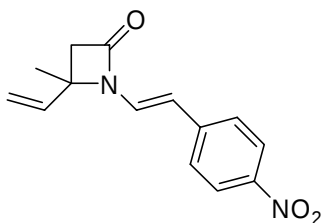
1-(4-nitrostyryl)-4-methyl-4-vinylazetidin-2-one (**2a**): Employing procedure G) with 275 mg of 1-(2-iodovinyl)-4-nitrobenzene, 113.6 mg of 4-methyl-4-vinylazetidin-2-one, 500 mg of Cs_2CO_3 , 9.9 mg of CuI , 15 μL of N,N' -dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 6:4 (Hex:EtOAc), 123.5 mg collected, 48 %.

^1H NMR (CDCl_3) 400 MHz δ : 8.17 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 8.8 Hz, 2H), 6.03 (d, J = 9.6 Hz, 1H), 6.01 (dd, J = 10.8, 17.2 Hz, 1H), 5.86 (d, J = 9.6 Hz, 1H), 5.35 (d, J = 17.2 Hz, 1H), 5.33 (d, J = 10.8 Hz, 1H), 2.99 (d, J = 15.6 Hz, 1H), 2.94 (d, J = 15.6 Hz, 1H), 1.62 (s, 3H)

^{13}C NMR (CDCl_3) MHz δ :

HR-MS: $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3$

Calculated: 258.1004, Actual: 258.1005



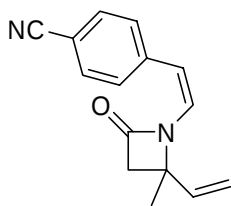
1-(4-nitrostyryl)-4-methyl-4-vinylazetidin-2-one (**2a**): Employing procedure G) with 275 mg of 1-(2-iodovinyl)-4-nitrobenzene, 113.6 mg of 4-methyl-4-vinylazetidin-2-one, 500 mg of Cs_2CO_3 , 9.9 mg of CuI , 15 μL of N,N' -dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 6:4 (Hex:EtOAc), 123.5 mg collected, 48 %.

^1H NMR (CDCl_3) 400 MHz δ : 8.14 (d, J = 8.8 Hz, 2H), 7.38 (d, J = 8.8 Hz, 2H), 7.11 (d, J = 14.8 Hz, 1H), 6.17 (d, J = 15.2 Hz, 1H), 6.07 (dd, J = 10.4, 17.2 Hz, 1H), 5.40 (d, J = 17.2 Hz, 1H), 5.37 (d, J = 10.4 Hz, 1H), 3.06 (d, J = 15.6 Hz, 1H), 3.02 (d, J = 15.6 Hz, 1H), 1.72 (s, 3H)

^{13}C NMR (CDCl_3) 75 MHz δ : 163.6, 162.6, 146.2, 146.1, 143.2, 142.9, 139.3, 138.8, 129.4, 125.6, 124.2, 123.2, 123.1, 121.5, 117.2, 116.9, 110.7, 59.8, 58.7, 52.2, 50.7, 21.8, 21.2

HR-MS: $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3$

Calculated: 258.1004, Actual: 258.1006



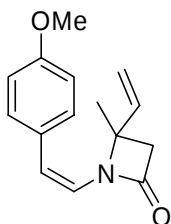
4-((Z)-2-(2-methyl-4-oxo-2-vinylazetidin-1-yl)vinyl)benzonitrile (**3a**): Employing general procedure G) with 268 mg of 4-(2-iodovinyl)benzonitrile, 118 mg of 4-methyl-4-vinylazetidin-2-one, 500 mg of Cs_2CO_3 , 10.1 mg of CuI, 15 μL of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 7:3 (Hex:EtOAc), 105 mg of product collected, 68 %.

^1H NMR (CDCl_3) 400 MHz δ : (cis) 7.58 (d, $J = 8.4$ Hz, 2H), 7.35 (d, $J = 8.4$ Hz, 2H), 6.00 (dd, $J = 10.4, 17.2$ Hz, 1H), 5.99 (d, $J = 9.6$ Hz, 1H), 5.82 (d, $J = 9.6$ Hz, 1H), 5.33 (d, $J = 17.2$ Hz, 1H), 5.32 (d, $J = 10.4$ Hz, 1H), 2.98 (d, $J = 15.2$ Hz, 1H), 2.93 (d, $J = 15.2$ Hz, 1H), 1.60 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 162.7, 140.8, 139.3, 131.7, 129.3, 120.9, 119.1, 117.9, 116.8, 110.2, 58.7, 50.7, 21.8

HR-MS: $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}$

Calculated: 238.1109, Actual: 238.1106



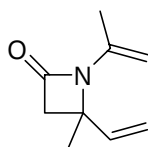
1-(4-methoxystyryl)-4-methyl-4-vinylazetidin-2-one (**4a**): Employing procedure G) with 159 mg of 1-((Z)-2-iodovinyl)-4-methoxybenzene, 1.2 eq of the 4-methyl-4-vinylazetidin-2-one, 1.5 eq of Cs_2CO_3 , 5 mol % CuI and 10 mol % *N,N'*-dimethylethylenediamine and 2 mL PhMe. The crude was columned with 8:2 (Hex:EtOAc), 70 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.29 (d, $J = 8.80$ Hz, 2H), 6.85 (d, $J = 8.80$ Hz, 2H), 6.03 (d, $J = 9.60$ Hz, 1H), 5.97 (dd, $J = 10.8, 17.4$ Hz, 1H), 5.65 (d, $J = 9.60$ Hz, 1H), 5.28 (d, $J = 17.4$ Hz, 1H), 5.23 (d, $J = 10.8$ Hz, 1H), 3.80 (s, 3H), 2.95 (d, $J = 15.2$ Hz, 1H), 2.89 (d, $J = 15.2$ Hz, 1H), 1.54 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 163.4, 158.8, 139.7, 130.3, 128.2, 122.0, 116.6, 116.2, 113.5, 58.8, 55.2, 50.4, 21.6

HR-MS: $\text{C}_{15}\text{H}_{17}\text{NO}_2$

Calculated: 243.1253, Actual: 243.1259



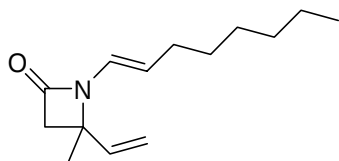
4-ethenyl-4-methyl-1-(1-methylethenyl)azetidin-2-one (**5a**): Employing procedure G) with a temperature change, using 100 °C, 110 mg of 4-methyl-4-vinylazetidin-2-one, 273 mg of K₂CO₃, 9.1 mg of CuI, 12 µL of *N,N'*-dimethylethylenediamine, 450 µL of 2-bromopropene. The crude was columned with 8:2 (Hex:EtOAc), 102.4 mg collected, 68 %.

¹H NMR 300 MHz (CDCl₃) δ: 6.03 (dd, *J* = 10.8, 17.6 Hz, 1H), 5.30 (d, *J* = 17.6 Hz, 1H), 5.26 (d, *J* = 10.8 Hz, 1H), 4.32 (s, 1H), 4.12 (s, 1H), 2.84 (s, 2H), 2.12 (s, 3H), 1.64 (s, 3H)

¹³C NMR 100 MHz (CDCl₃) δ: 163.8, 140.2, 139.0, 115.9, 94.9, 58.6, 51.1, 20.7, 20.1

HR-MS: C₉H₁₃NO

Calculated: 151.0997, Actual: 151.0998



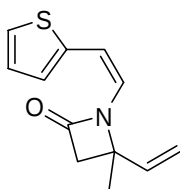
4-methyl-1-((*E*)-oct-1-enyl)-4-vinylazetidin-2-one (**6a**): Employing procedure G) with 1.51 g of (*E*)-1-iodooct-1-ene, 497 mg of 4-methyl-4-vinylazetidin-2-one, 2.25 g of Cs₂CO₃, 50 µL of *N,N'*-dimethylethylenediamine, 42 mg of CuI and 2 mL of PhMe. The crude was columned with 7:3 (Hex:EtOAc), 0.85 g collected, 85 %.

¹H NMR (CDCl₃) 400 MHz δ: 6.22 (dt, *J* = 1.2, 14.4 Hz, 1H), 5.98 (dd, *J* = 10.8, 17.6 Hz, 1H), 5.29 (dd, *J* = 0.8, 17.6 Hz, 1H), 5.25 (d, *J* = 0.8, 10.8 Hz, 1H), 5.18 (dt, *J* = 7.2, 14.4 Hz, 1H), 2.89 (d, *J* = 14.8 Hz, 1H), 2.85 (d, *J* = 14.8 Hz, 1H), 1.97 (qd, *J* = 1.2, 7.2 Hz, 2H), 1.58 (s, 3H), 1.35-1.26 (m, 8H), 0.88 (t, *J* = 7.2 Hz, 3H)

¹³C NMR (CDCl₃) 100 MHz δ: 162.8, 139.6, 119.6, 115.9, 114.6, 58.7, 51.4, 31.6, 30.2, 29.6, 28.7, 22.6, 20.8, 14.1

HR-MS: C₁₄H₂₃NO

Calculated: 221.1780, Actual: 221.1786



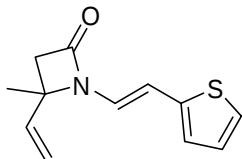
4-methyl-1-((*Z*)-2-(thiophen-2-yl)vinyl)-4-vinylazetidin-2-one (**7a**): Employing procedure G) with 236 mg of 2-(2-iodovinyl)thiophene (*E*:*Z* = 1:1), 1.2 eq of 4-methyl-4-vinylazetidin-2-one, 1.5 eq of Cs₂CO₃, 5 mol % CuI, 10 mol % *N,N'*-dimethylethylenediamine and 2 mL PhMe. The crude was columned with 6:4 (Hex:EtOAc), 67 % yield combining both *E* and *Z* isomers.

¹H NMR (CDCl₃) 400 MHz δ: 7.29 (d, *J* = 4.8 Hz, 1H), 7.07 (d, *J* = 3.20 Hz, 1H), 6.98 (dd, *J* = 4.0, 4.8 Hz, 1H), 6.43 (d, *J* = 8.8 Hz, 1H), 6.03 (dd, *J* = 10.8, 17.6 Hz, 1H), 6.03 (d, *J* = 5.62, 1H), 5.31 (d, *J* = 17.6 Hz, 1H), 5.26 (d, *J* = 10.8 Hz, 1H), 3.01 (d, *J* = 15.2 Hz, 1H), 2.96 (d, *J* = 15.2 Hz, 1H), 1.60 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 164.0, 139.5, 137.5, 129.0, 126.4, 119.3, 116.5, 115.8, 59.2, 50.7, 21.4

HR-MS: $\text{C}_{12}\text{H}_{13}\text{NOS}$

Calculated: 219.0718, Actual: 219.0716



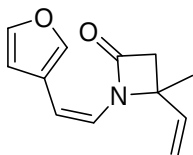
4-methyl-1-((*E*)-2-(thiophen-2-yl)vinyl)-4-vinylazetidin-2-one (**7a**): Employing procedure G) with 236 mg of 2-(2-iodovinyl)thiophene (*E*:*Z* = 1:1), 1.2 eq of 4-methyl-4-vinylazetidin-2-one, 1.5 eq of Cs_2CO_3 , 5 mol % CuI , 10 mol % *N,N'*-dimethylethylenediamine and 2 mL PhMe. The crude was columned with 6:4 (Hex:EtOAc), 67 % combining both *E* and *Z* isomers.

^1H NMR (CDCl_3) 400 MHz δ : 7.08 (d, J = 5.2 Hz, 1H), 6.94-6.91 (m, 1H), 6.87 (d, J = 3.2 Hz, 1H), 6.82 (d, J = 14.8 Hz, 1H), 6.31 (d, J = 14.8 Hz, 1H), 6.04 (dd, J = 10.8, 17.6 Hz, 1H), 5.38 (d, J = 17.6 Hz, 1H), 5.33 (d, J = 10.8 Hz, 1H), 2.99 (d, J = 2.99 Hz, 1H), 2.95 (d, J = 2.95 Hz, 1H), 1.67 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz: 163.1, 140.4, 139.2, 127.5, 124.6, 123.0, 119.2, 116.6, 107.5, 59.4, 51.9, 21.1

HR-MS: $\text{C}_{12}\text{H}_{13}\text{NOS}$

Calculated: 219.0718, Actual: 219.0717



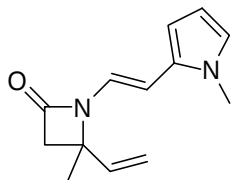
1-((*Z*)-2-(furan-3-yl)vinyl)-4-methyl-4-vinylazetidin-2-one (**9a**): Employing procedure G) with 430 mg of 3-(2-iodovinyl)furan (mixture of *E* and *Z* isomers), 222.3 mg of 4-methyl-4-vinylazetidin-2-one, 21 mg of CuI , 975 mg of Cs_2CO_3 , 22 μL of *N,N'*-dimethylethylenediamine, and 2 mL of PhMe. The crude was columned using 7:3 (Hex:EtOAc), 327.2 mg collected, 79 % total, (*E*:*Z* ratio 1:4).

^1H NMR (CDCl_3) 300 MHz δ : 7.51 (s, 1H), 7.38-7.37 (m, 1H), 6.49 (d, J = 1.2 Hz, 1H), 6.03 (d, J = 9.0 Hz, 1H), 5.98 (dd, J = 10.8, 17.2 Hz, 1H), 5.61 (d, J = 9.0 Hz, 1H), 5.28 (d, J = 17.2 Hz, 1H), 5.24 (d, J = 10.8 Hz, 1H), 2.98 (d, J = 14.7 Hz, 1H), 2.92 (d, J = 14.7 Hz, 1H), 1.56 (s, 3H)

Mixture of cis/trans olefins ^{13}C NMR (CDCl_3) 75 MHz δ : 163.7, 143.7, 142.84, 142.77, 139.8, 139.65, 169.64, 139.3, 122.2, 120.6, 119.3, 117.1, 116.5, 116.2, 114.8, 110.6, 106.7, 103.6, 59.2, 58.8, 51.8, 50.6, 21.6, 21.0

HR-MS: $\text{C}_{12}\text{H}_{13}\text{NO}_2$

Calculated: 203.0946, Actual: 203.0943



4-methyl-1-((E)-2-(1-methyl-1H-pyrrol-2-yl)vinyl)-4-vinylazetidin-2-one **(8a)**:

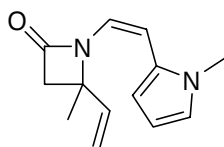
Employing procedure G) with 479 mg of 2-(2-iodovinyl)-1-methyl-1H-pyrrole (mixture of *E* and *Z* isomers), 223 mg of 4-methyl-4-vinylazetidin-2-one, 21 mg of CuI, 993 mg of Cs₂CO₃, 22 μL of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned using 7:3 (Hex:EtOAc), 327.2 mg collected, 86 % yield, (*E*:*Z* ratio 3:1).

¹H NMR (CDCl₃) 400 MHz δ: 6.65 (d, *J* = 14.8 Hz, 1H), 6.58-6.57 (m, 1H), 6.19 (dd, *J* = 1.2, 4.0 Hz, 1H), 6.14 (d, *J* = 14.8 Hz, 1H), 6.09-6.07 (m, 1H), 6.04 (dd, *J* = 10.8, 17.2 Hz, 1H), 5.36 (d, *J* = 17.2 Hz, 1H), 5.30 (d, *J* = 10.8 Hz, 1H), 3.54 (s, 3H), 2.98 (d, *J* = 15.2 Hz, 1H), 2.93 (d, *J* = 15.2 Hz, 1H), 1.65 (s, 3H)

¹³C NMR (CDCl₃) 100 MHz δ: 162.9, 139.5, 129.8, 122.9, 118.0, 116.3, 108.0, 104.8, 103.8, 59.0, 51.7, 34.0, 21.1

HR-MS: C₁₃H₁₆N₂O

Calculated: 216.1263, Actual: 216.1263



4-methyl-1-((Z)-2-(1-methyl-1H-pyrrol-2-yl)vinyl)-4-vinylazetidin-2-one **(8a)**:

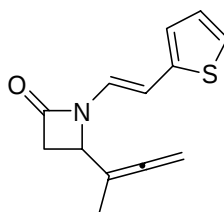
Employing procedure G) with 479 mg of 2-(2-iodovinyl)-1-methyl-1H-pyrrole (mixture of *E* and *Z* isomers), 223 mg of 4-methyl-4-vinylazetidin-2-one, 21 mg of CuI, 993 mg of Cs₂CO₃, 22 μL of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned using 7:3 (Hex:EtOAc), 327.2 mg collected, 86 % yield, (*E*:*Z* ratio 3:1).

¹H NMR (CDCl₃) 300 MHz δ: 6.60-6.59 (m, 1H), 6.29-6.28 (m, 1H), 6.16-6.14 (m, 1H), 5.98 (d, *J* = 9.6 Hz, 1H), 5.94 (dd, *J* = 10.8, 17.1 Hz, 1H), 5.64 (d, *J* = 9.6 Hz, 1H), 5.24 (d, *J* = 17.1 Hz, 1H), 5.21 (d, *J* = 10.8 Hz, 1H), 3.58 (s, 3H), 2.96 (d, *J* = 15.0 Hz, 1H), 2.90 (d, *J* = 15.0 Hz, 1H), 1.52 (s, 3H)

¹³C NMR (CDCl₃) 100 MHz δ: 163.1, 139.6, 127.6, 122.9, 116.0, 115.0, 111.6, 111.4, 108.1, 59.2, 50.5, 34.0, 21.6

HR-MS: C₁₃H₁₆N₂O

Calculated: 216.1263, Actual: 216.1264



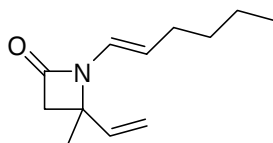
4-(buta-2,3-dien-2-yl)-1-((E)-2-(thiophen-2-yl)vinyl)azetidin-2-one (**10a**): Employing procedure G) with 374 mg of 2-(2-iodovinyl)thiophene, 97.2 mg of 4-(buta-2,3-dien-2-yl)azetidin-2-one, 8.1 mg of CuI, 390 mg of Cs₂CO₃, 10 µL of *N,N'*-dimethylethylenediamine, and 2 mL of PhMe. The crude was columned with 7:3 (Hex:EtOAc) 91.3 mg collected, 50 %.

¹H NMR (CDCl₃) 400 MHz δ: 7.09 (d, *J* = 5.2 Hz, 1H), 7.00 (d, *J* = 14.4 Hz, 1H), 6.93 (dd, *J* = 3.6, 5.2 Hz, 1H), 6.88 (d, *J* = 3.6 Hz, 1H), 6.25 (d, *J* = 14.4 Hz, 1H), 4.88 (dq, *J* = 0.8, 3.2, 10.8 Hz, 1H), 4.82 (dq, *J* = 1.2, 3.2, 10.8 Hz, 1H), 4.41 (dd, *J* = 2.8, 5.6 Hz, 1H), 3.25 (dd, *J* = 5.6, 15.6 Hz, 1H), 2.94 (dd, *J* = 2.8, 15.6 Hz, 1H), 1.70 (t, *J* = 3.2 Hz, 3H)

¹³C NMR (CDCl₃) 100 MHz δ: 207.2, 163.3, 140.2, 127.5, 124.7, 123.2, 120.5, 106.6, 95.6, 76.6, 54.1, 42.2, 12.4

HR-MS: C₁₃H₁₃NOS

Calculated: 231.0718, Actual: 231.0718



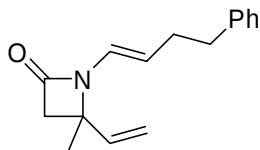
1-((E)-hex-1-enyl)-4-methyl-4-vinylazetidin-2-one (**12a**): Employing procedure G) with 1.14 g of (*E*)-1-iodohex-1-ene, 414 mg of 4-methyl-4-vinylazetidin-2-one, 1.76 g of Cs₂CO₃, 34.9 mg of CuI, 39 µL of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 7:3 (Hex:EtOAc), 271 mg collected, 38 %.

¹H NMR (CDCl₃) 400 MHz δ: 6.22 (dt, *J* = 1.6, 14.8 Hz, 1H), 5.98 (dd, *J* = 10.8, 17.2 Hz, 1H), 5.29 (dd, *J* = 0.8, 17.2 Hz, 1H), 5.25 (dd, *J* = 0.8, 10.8 Hz, 1H), 5.19 (dt, *J* = 7.2, 14.8 Hz, 1H), 2.89 (d, *J* = 14.8 Hz, 1H), 2.85 (d, *J* = 14.8 Hz, 1H), 1.98 (qd, *J* = 1.2, 7.2 Hz, 2H), 1.58 (s, 3H), 1.37-1.24 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H)

¹³C NMR (CDCl₃) 100 MHz δ: 162.8, 139.6, 119.6, 115.9, 114.6, 58.7, 51.4, 31.8, 29.8, 22.1, 20.8, 13.9

HR-MS: [M+H]⁺

Calculated: 194.1539, Actual: 194.1541



4-methyl-1-((E)-4-phenylbut-1-enyl)-4-vinylazetidin-2-one (**13a**): Employing procedure G) with 980 mg of 1-((E)-4-iodobut-3-enyl)benzene, 298 mg of 4-methyl-4-vinylazetidin-2-one, 28 mg of CuI, 1.36 g of Cs₂CO₃, 30 µL of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 8:2 (Hex:EtOAc), 263 mg collected, 41 %.

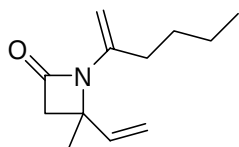
¹H NMR (CDCl₃) 400 MHz δ: 7.29-7.25 (m, 2H), 7.20-7.13 (m, 3H), 6.22 (dt, *J* = 1.2, 14.8 Hz, 1H), 5.95 (dd, *J* = 10.8, 17.6 Hz, 1H), 5.25 (dd, *J* = 0.8, 8.4 Hz, 1H), 5.27-5.15

(m, 3H), 2.88 (d, $J = 14.8$ Hz, 1H), 2.84 (d, $J = 14.8$ Hz, 1H), 2.67 (t, $J = 7.6$ Hz, 2H), 2.30 (qd, $J = 1.2, 7.2$ Hz, 2H), 1.55 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 162.8, 141.4, 139.5, 128.5, 128.3, 125.9, 120.2, 116.0, 113.3, 58.7, 51.4, 36.3, 32.2, 20.8

HR-MS: $[\text{M}+\text{Na}]^+$

Calculated: 264.1358, Actual: 264.1363



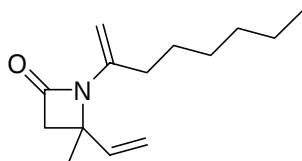
1-(hex-1-en-2-yl)-4-methyl-4-vinylazetidin-2-one (**14a**): Employing procedure G) with 650 mg of 2-iodohex-1-ene, 412 mg of 4-methyl-4-vinylazetidin-2-one, 1.49 g of Cs_2CO_3 , 320 μL of N,N' -dimethylethylenediamine, 290 mg of CuI and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 350 mg collected, 59 %.

^1H NMR (CDCl_3) 400 MHz δ : 6.02 (dd, $J = 10.8, 17.6$ Hz, 1H), 5.29 (dd, $J = 0.4, 17.6$ Hz, 1H), 5.26 (dd, $J = 0.4, 10.8$ Hz, 1H), 4.27 (s, 1H), 4.14 (s, 1H), 2.82 (s, 2H), 2.57-2.50 (m, 1H), 2.46-2.39 (m, 1H), 1.62 (s, 3H), 1.53-1.46 (m, 2H), 1.41-1.31 (m, 2H), 0.92 (t, $J = 7.2$ Hz, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 163.3, 143.6, 140.4, 115.9, 93.9, 58.4, 50.8, 32.7, 30.2, 22.1, 20.4, 13.9

HR-MS: $\text{C}_{12}\text{H}_{19}\text{NO}$

Calculated: 193.1467, Actual: 193.1461



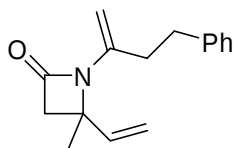
4-methyl-1-(oct-1-en-2-yl)-4-vinylazetidin-2-one (**15a**): Employing procedure G) with 787 mg of 2-iodooct-1-ene, 418 mg of 4-methyl-4-vinylazetidin-2-one, 1.49 mg of Cs_2CO_3 , 290 mg of CuI , 320 μL of N,N' -dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 571 mg collected, 78 %.

^1H NMR (CDCl_3) 400 MHz δ : 6.02 (dd, $J = 10.8, 17.2$ Hz, 1H), 5.29 (d, $J = 17.2$ Hz, 1H), 5.26 (d, $J = 10.8$ Hz, 1H), 4.27 (s, 1H), 4.14 (s, 1H), 2.82 (s, 2H), 2.57-2.49 (m, 2H), 2.45-2.37 (m, 2H), 1.62 (s, 3H), 1.54-1.46 (m, 2H), 1.37-1.25 (m, 6H), 0.88 (t, $J = 7.2$ Hz, 3H)

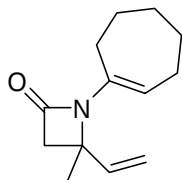
^{13}C NMR (CDCl_3) 100 MHz δ : 163.2, 143.7, 140.4, 115.9, 93.9, 58.4, 20.8, 33.0, 31.7, 28.7, 28.0, 22.6, 20.4, 14.0

HR-MS: $\text{C}_{14}\text{H}_{23}\text{NO}$

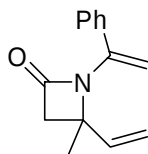
Calculated: 221.1780, Actual: 221.1781



4-methyl-1-(4-phenylbut-1-en-2-yl)-4-vinylazetidin-2-one (**16a**): Employing procedure G) with 910 mg of 1-(3-iodobut-3-enyl)benzene, 410 mg of 4-methyl-4-vinylazetidin-2-one, 281 mg of CuI, 1.45 g of Cs₂CO₃, 320 μ L of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 431 mg collected, 56 %. ¹H NMR (CDCl₃) 400 MHz δ : 7.30-7.16 (m, 5H), 6.03 (dd, *J* = 10.8, 17.6 Hz, 1H), 5.29 (d, *J* = 17.6 Hz, 1H), 5.26 (d, *J* = 10.8 Hz, 1H), 4.25 (s, 1H), 4.11 (s, 1H), 2.92-2.67 (m, 6H), 1.63 (s, 3H). ¹³C NMR (CDCl₃) 75 MHz δ : 163.2, 142.7, 141.3, 140.2, 128.6, 128.3, 125.9, 116.0, 94.4, 58.4, 50.9, 35.2, 34.8, 20.4. HR-MS: C₁₆H₁₉NO. Calculated: 241.1467, Actual: 241.1470.



1-(*E*)-cycloheptenyl-4-methyl-4-vinylazetidin-2-one (**17a**): Employing procedure G) with 670 mg of (*E*)-1-iodocyclohept-1-ene, 320 mg of 4-methyl-4-vinylazetidin-2-one, 285 mg of CuI, 1.47 g of Cs₂CO₃, 320 μ L of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 8:2 (Hex:EtOAc), 465 mg collected, 74 %. ¹H NMR (CDCl₃) 300 MHz δ : 6.03 (dd, *J* = 10.8, 17.4 Hz, 1H), 5.51 (t, *J* = 6.9 Hz, 1H), 5.26 (d, *J* = 17.4 Hz, 1H), 5.23 (d, *J* = 10.8 Hz, 1H), 2.78 (s, 2H), 2.70-2.64 (m, 2H), 2.11-2.04 (m, 2H), 1.76-1.66 (m, 2H), 1.60 (s, 3H), 1.58-1.56 (m, 2H), 1.52-1.44 (m, 2H). ¹³C NMR (CDCl₃) 100 MHz δ : 163.9, 141.2, 140.6, 115.5, 115.0, 58.9, 50.5, 32.0, 28.8, 27.1, 26.2, 25.7, 20.9. HR-MS: C₁₃H₁₉NO. Calculated: 205.1467, Actual: 205.1469.



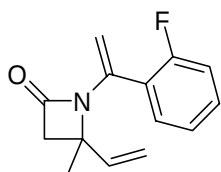
4-methyl-1-(1-phenylvinyl)-4-vinylazetidin-2-one (**18a**): Employing procedure G) with 656 mg of 1-(1-iodovinyl)benzene, 394 mg of 4-methyl-4-vinylazetidin-2-one, 337 mg of CuI, 1.43 g of Cs₂CO₃, 320 μ L of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 257 mg collected, 42 %.

^1H NMR (CDCl_3) 300 MHz δ : 7.38-7.31 (m, 5H), 6.11 (dd, $J = 10.5, 17.4$ Hz, 1H), 5.28 (d, $J = 17.4$ Hz, 1H), 5.24 (d, $J = 10.5$ Hz, 1H), 5.00 (s, 1H), 4.75 (s, 1H), 2.95 (s, 2H), 1.62 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 164.1, 142.1, 140.6, 135.8, 128.7, 127.9, 127.6, 116.0, 102.5, 59.8, 50.8, 21.1

HR-MS: $\text{C}_{14}\text{H}_{15}\text{NO}$

Calculated: 213.1154, Actual: 213.1148



1-(1-(2-fluorophenyl)vinyl)-4-methyl-4-vinylazetidin-2-one (**19a**): Employing procedure G) with 1.20 g of 1-fluoro-2-(1-iodovinyl)benzene, 415 mg of 4-methyl-4-vinylazetidin-2-one, 336 mg of CuI , 1.85 g of Cs_2CO_3 , 400 μL of N,N' -dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 415 mg collected, 48 %.

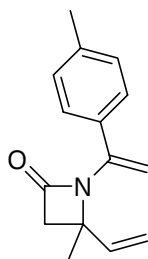
^1H NMR (CDCl_3) 400 MHz δ : 7.36-7.27 (m, 2H), 7.12 (td, $J = 1.2, 7.6$ Hz, 1H), 7.05-7.00 (m, 1H), 6.10 (dd, $J = 10.8, 17.6$ Hz, 1H), 5.31 (d, $J = 17.6$ Hz, 1H), 5.25 (d, $J = 10.8$ Hz, 1H), 4.94 (s, 1H), 4.55 (s, 1H), 2.92 (s, 2H), 1.65 (s, 3H)

^{19}F NMR (CDCl_3) 375 MHz δ : -115.14 (ddd, $J = 3.75, 7.50, 11.25$ Hz, 1F)

^{13}C NMR (CDCl_3) 100 MHz δ : 163.3, 160.0 (d, $J = 247.4$ Hz), 140.3, 136.7, 130.6 (d, $J = 3.3$ Hz), 130.5 (d, $J = 8.2$ Hz), 124.1 (d, $J = 14.5$ Hz), 123.8 (d, $J = 3.7$ Hz), 116.1, 115.2 (d, $J = 21.6$ Hz), 101.5, 59.7, 51.2, 20.3

HR-MS: $\text{C}_{14}\text{H}_{14}\text{NOF}$

Calculated: 231.1059 Actual: 231.1053



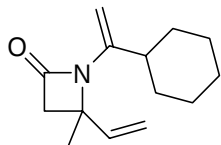
4-methyl-1-(1-(p-tolyl)vinyl)-4-vinylazetidin-2-one (**20a**): Employing procedure G) with 738 mg of 1-(1-iodovinyl)-4-methylbenzene, 405 mg of 4-methyl-4-vinylazetidin-2-one, 335 mg of CuI , 1.45 g of Cs_2CO_3 , 390 μL of N,N' -dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 300 mg collected, 44 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.25 (d, $J = 8.4$ Hz, 2H), 7.13 (d, $J = 8.4$ Hz, 2H), 6.11 (dd, $J = 10.8, 17.2$ Hz, 1H), 5.28 (d, $J = 17.2$ Hz, 1H), 5.24 (d, $J = 10.8$ Hz, 1H), 4.94 (s, 1H), 4.71 (s, 1H), 2.94 (s, 2H), 2.35 (s, 3H), 1.63 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 164.1, 142.1, 140.7, 138.6, 133.0, 128.7, 127.5, 116.0, 101.9, 59.7, 50.8, 21.3, 21.1

HR-MS: $\text{C}_{15}\text{H}_{17}\text{NO}$

Calculated: 227.1310 Actual: 227.1315



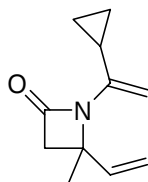
1-(1-cyclohexylvinyl)-4-methyl-4-vinylazetidin-2-one (**21a**): Employing procedure G) with 1.15 g of (1-iodovinyl)cyclohexane, 395 mg of 4-methyl-4-vinylazetidin-2-one, 328 mg of CuI, 1.73 g of Cs₂CO₃, 302 μ L of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 489 mg collected, 63 %.

¹H NMR (CDCl₃) 400 MHz δ : 6.03 (dd, *J* = 10.8, 17.6 Hz, 1H), 5.28 (d, *J* = 17.6 Hz, 1H), 5.24 (d, *J* = 10.8 Hz, 1H), 4.28 (s, 1H), 4.21 (s, 1H), 2.84 (tt, *J* = 2.8, 11.6 Hz, 1H), 2.80 (s, 2H), 1.93-1.89 (m, 2H), 1.78-1.67 (m, 3H), 1.61 (s, 3H), 1.36 (qt, *J* = 3.3, 12.6 Hz, 2H), 1.24-1.01 (m, 3H)

¹³C NMR (CDCl₃) 100 MHz δ : 163.3, 149.5, 140.7, 115.8, 91.8, 58.4, 50.6, 39.0, 32.5, 31.8, 26.4, 20.4

HR-MS: C₁₄H₂₁NO

Calculated: 219.1623 Actual: 219.1617



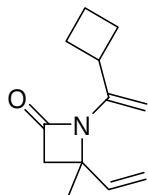
1-(1-cyclopropylvinyl)-4-methyl-4-vinylazetidin-2-one (**22a**): Employing procedure G) with 1.2 g of (1-iodovinyl)cyclopropane, 380 mg of 4-methyl-4-vinylazetidin-2-one, 341 mg of CuI, 1.78 g of Cs₂CO₃, 390 μ L of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 409 mg collected, 68 %.

¹H NMR (CDCl₃) 300 MHz δ : 6.05 (dd, *J* = 10.8, 17.4 Hz, 1H), 5.29 (dd, *J* = 0.8, 17.6 Hz, 1H), 5.25 (dd, *J* = 0.8, 10.8 Hz, 1H), 4.45 (s, 1H), 4.13 (s, 1H), 2.86 (s, 2H), 1.95-1.85 (m, 1H), 1.65 (s, 3H), 0.79-0.72 (m, 2H), 0.55-0.51 (m, 2H)

¹³C NMR (CDCl₃) 100 MHz δ : 163.8, 144.9, 140.6, 115.8, 92.1, 58.7, 50.9, 20.9, 12.8, 7.2, 6.5

HR-MS: C₁₁H₁₅NO

Calculated: 177.1154, Actual: 177.1157



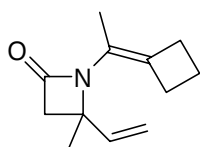
1-(1-cyclobutylvinyl)-4-methyl-4-vinylazetidin-2-one (**23a**): Employing procedure G) with a 1.80 g mixture of (1-iodovinyl)cyclobutane (1.00) and (1-iodoethylidene)cyclobutane (0.71), 383 mg of 4-methyl-4-vinylazetidin-2-one, 1.74 g of Cs₂CO₃, 332 mg of CuI, 320 μ L of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 209 mg was collected, 31 %.

¹H NMR (CDCl₃) 400 MHz δ : 6.01 (dd, *J* = 10.8, 17.6 Hz, 1H), 5.29 (d, *J* = 17.6 Hz, 1H), 5.26 (d, *J* = 10.8 Hz, 1H), 4.32 (s, 1H), 4.25 (s, 1H), 3.63-3.55 (m, 1H), 2.80 (s, 2H), 2.24-2.17 (m, 2H), 1.97-1.84 (m, 3H), 1.79-1.73 (m, 1H), 1.61 (s, 3H)

¹³C NMR (CDCl₃) 100 MHz δ : 162.9, 146.8, 140.4, 115.9, 91.4, 58.1, 50.7, 36.9, 27.8, 27.2, 20.4, 17.6

HR-MS: C₁₂H₁₇NO

Calculated: 191.1310, Actual: 193.1315



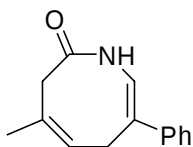
1-(1-cyclobutylideneethyl)-4-methyl-4-vinylazetidin-2-one (**24a**): Employing procedure G) with a 1.80 g mixture of (1-iodovinyl)cyclobutane (1 parts) and (1-iodoethylidene)cyclobutane (0.71 parts), 383 mg of 4-methyl-4-vinylazetidin-2-one, 1.74 g of Cs₂CO₃, 332 mg of CuI, 320 μ L of *N,N'*-dimethylethylenediamine and 2 mL of PhMe. The crude was columned with 9:1 (Hex:EtOAc), 194 mg was collected, 28 %.

¹H NMR (CDCl₃) 400 MHz δ : 6.04 (dd, *J* = 10.8, 17.6 Hz, 1H), 5.26 (d, *J* = 17.6 Hz, 1H), 5.20 (d, *J* = 10.8 Hz, 1H), 2.82 (d, *J* = 14.4 Hz, 1H), 2.76 (d, *J* = 14.4 Hz, 1H), 2.72-2.65 (m, 4H), 1.98-1.90 (m, 2H), 1.59-1.58 (m, 3H), 1.56 (s, 3H)

¹³C NMR (CDCl₃) 100 MHz δ : 163.5, 141.6, 134.6, 121.0, 115.3, 59.0, 49.7, 30.5, 28.7, 22.3, 16.1, 15.0

HR-MS: C₁₂H₁₇NO

Calculated: 191.1310, Actual: 193.1306



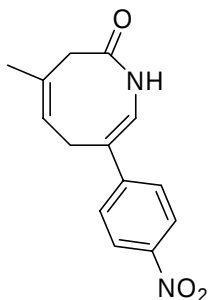
(4*Z*,7*E*)-4-methyl-7-phenylazocin-2-one (**1b**): Employing procedure H) with 20 mg of 4-methyl-1-styryl-4-vinylazetidin-2-one and 450 μ L of DMF at 200 °C. The crude was columned with 1:1 (Hex:EtOAc), 16.3 mg collected, 86 %.

¹H NMR (CDCl₃) 500 MHz δ : 7.40-7.30 (m, 5H), 6.74 (bs, 1H), 6.49 (s, 1H), 5.57 (tq, *J* = 1.6, 6.2 Hz, 1H), 3.22 (d, *J* = 6.0 Hz, 2H), 3.14 (s, 2H), 1.85 (s, 3H)

¹³C NMR (CDCl₃) 125 MHz δ : 170.7, 138.9, 133.9, 132.5, 128.6, 127.9, 126.5, 121.4, 118.9, 41.0, 28.7, 27.1

HR-MS: C₁₄H₁₅NO

Calculated: 213.1154, Actual: 213.1148



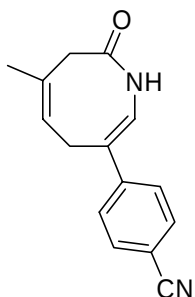
(4Z,7E)-4-methyl-7-(4-nitrophenyl)azocin-2-one (**2b**): Employing procedure H) with 21.8 mg of 1-(4-nitrostyryl)-4-methyl-4-vinylazetidin-2-one and 450 μ L of DMF at 170 $^{\circ}$ C. The crude was columned with 6:4 (Hex:EtOAc) then 95:5 (DCM:MeOH), 10.4 mg collected, 48 %.

^1H NMR (CDCl_3) 400 MHz δ : 8.21 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 8.8 Hz, 2H), 7.09 (bs, 1H), 6.65 (s, 1H), 5.60 (tq, J = 1.2, 4.8 Hz, 1H), 3.23 (d, J = 5.6 Hz, 1H), 3.15 (s, 2H), 1.88 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 170.4, 147.2, 145.7, 133.3, 131.6, 127.1, 124.4, 123.9, 118.2, 41.2, 28.6, 26.9

HR-MS: $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3$

Calculated: 258.1004, Actual: 258.1014



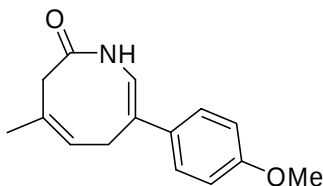
4-((2E,5Z)-1,4,7,8-tetrahydro-6-methyl-8-oxoazocin-3-yl)benzonitrile (**3b**): Employing procedure H) with 18.6 mg of 4-(2-(2-methyl-4-oxo-2-vinylazetidin-1-yl)vinyl)benzonitrile and 450 μ L of DMF at 200 $^{\circ}$ C. The crude was columned with 6:4 (Hex:EtOAc) then 95:5 (DCM:MeOH), 11.5 mg collected, 62 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.64 (d, J = 8.8 Hz, 2H), 7.47 (d, J = 8.8 Hz, 2H), 6.99 (bs, 1H), 6.59 (d, J = 1.6 Hz, 1H), 5.57 (tq, J = 1.6, 4.8 Hz, 1H), 3.21 (d, J = 6.0 Hz, 1H), 3.14 (s, 2H), 1.87 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 170.3, 143.7, 133.2, 132.4, 132.0, 127.0, 123.8, 118.6, 118.3, 111.4, 41.1, 28.5, 26.9

HR-MS: $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}$

Calculated: 238.1106, Actual: 238.1102



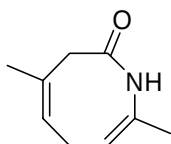
(4Z,7E)-7-(4-methoxyphenyl)-4-methylazocin-2-one (**4b**): Employing procedure H) with 19 mg of 1-(4-methoxystyryl)-4-methyl-4-vinylazetidin-2-one and 450 μ L of DMF at 200 $^{\circ}$ C. The crude was columned with 6:4 (Hex:EtOAc), 11.0 mg collected, 58 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.32 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 6.84 (bs, 1H), 6.42 (d, J = 1.2 Hz, 1H), 5.55 (dq, J = 1.6, 6.3 Hz, 1H) 3.82 (s, 3H), 3.19 (d, J = 6.0 Hz, 1H), 3.13 (s, 2H), 1.84 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 170.7, 159.5, 133.6, 132.5, 131.2, 127.6, 119.9, 118.9, 114.0, 55.3, 40.9, 28.7, 27.0

HR-MS: $[\text{M}+\text{H}]^+$

Calculated: 224.1332, Actual: 244.1333



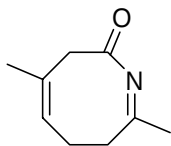
(4Z,7Z)-4,8-dimethylazocin-2-one (**5b**): Employing procedure H) with 19.7 mg of 4-methyl-1-(prop-1-en-2-yl)-4-vinylazetidin-2-one and 450 μ L of DMF at 140 $^{\circ}$ C. The crude was columned with 6:4 (Hex:EtOAc), 7.3 mg collected, 37 %.

^1H NMR 400 MHz (CDCl_3) δ : 6.60 (bs, 1H), 5.40 (tq, J = 1.6, 6.0 Hz, 1H), 5.13 (td, J = 1.2, 8.0 Hz, 1H), 3.03 (s, 2H), 2.71 (t, J = 6.8 Hz, 2H), 1.86 (s, 3H), 1.83 (s, 3H)

^{13}C NMR 100 MHz (CDCl_3) δ : 170.4, 133.9, 131.9, 119.7, 116.5, 40.3, 27.0, 25.6, 21.3

HR-MS: $\text{C}_9\text{H}_{13}\text{NO}$

Calculated: 151.0997, Actual: 151.1000

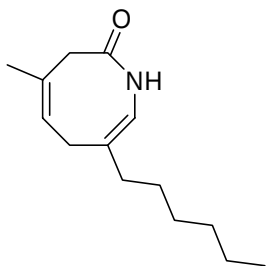


(1Z,4Z)-6,7-dihydro-4,8-dimethylazocin-2-one (**5b**): Employing procedure H) with 19.7 mg of 4-methyl-1-(prop-1-en-2-yl)-4-vinylazetidin-2-one and 450 μ L of DMF at 140 $^{\circ}$ C. The crude was columned with 6:4 (Hex:EtOAc), 3.8 mg collected, 19 %.

^1H NMR 400 MHz (CDCl_3) δ : 5.38 (tq, J = 2.0, 11.2 Hz, 1H), 3.18 (s, 2H), 2.54 (t, J = 8.0 Hz, 2H), 2.25-2.19 (m, 2H), 2.01 (s, 3H), 1.73 (s, 3H)

^{13}C NMR 100 MHz (CDCl_3) δ : 208.9, 173.1, 131.0, 127.5, 42.7, 40.0, 30.2, 23.6, 22.1

Calculated: 151.0997, Actual: 151.1003



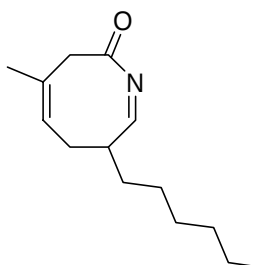
(4Z,7Z)-7-hexyl-4-methylazocin-2-one (**6c**): Employing procedure H) with 20.8 mg of 4-methyl-1-((E)-oct-1-enyl)-4-vinylazetidin-2-one and 450 μ L of DMF at 200 $^{\circ}$ C. The crude was columned with 7:3 (Hex:EtOAc) then 95:5 (DCM:MeOH), 8.3 mg collected, 40 %.

^1H NMR (CDCl_3) 300 MHz δ : 6.56 (bs, 1H), 5.95 (s, 1H), 5.40 (tq, J = 1.5, 6.3 Hz, 1H), 3.06 (s, 2H), 2.77, (d, J = 6.0 Hz, 2H), 2.04 (q, J = 7.0 Hz, 2H), 1.82 (s, 3H), 1.44-1.21 (m, 8H), 0.88 (t, J = 6.6 Hz, 3H)

^{13}C NMR (CDCl_3) 75 MHz δ : 170.9, 136.0, 131.7, 119.5, 119.0, 40.6, 35.3, 31.7, 29.0, 28.9, 27.8, 27.0, 22.6, 14.1

HR-MS: $\text{C}_{14}\text{H}_{23}\text{N}_2\text{O}$

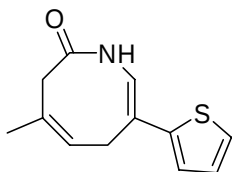
Calculated: 221.1780, Actual: 221.1774



(1Z,4Z)-7-hexyl-6,7-dihydro-4-methylazocin-2-one (**6b**): Employing procedure H) with 20.8 mg of 4-methyl-1-((E)-oct-1-enyl)-4-vinylazetidin-2-one and 450 μ L of DMF at 200 $^{\circ}$ C. The crude was columned with 7:3 (Hex:EtOAc) then 95:5 (DCM:MeOH), 2.4 mg collected, 12 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.40 (d, J = 2.8 Hz, 1H), 5.38 (t, J = 8.8 Hz, 1H), 3.22 (d, J = 18.4 Hz, 1H), 3.14 (d, J = 18.0 Hz, 1H), 2.55-2.47 (m, 1H), 1.73 (s, 3H), 1.47-1.38 (m, 2H), 1.33-1.28 (8H), 0.9-0.87 (m, 3H)

Calculated: 221.1780, Actual: 221.1778



(4Z,7E)-4-methyl-7-(thiophen-2-yl)azocin-2-one (**7b**): Employing procedure H) with 21.6 mg of 4-methyl-1-(2-(thiophen-2-yl)vinyl)-4-vinylazetidin-2-one and 450

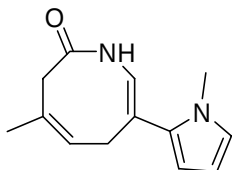
μL of DMF at 200 °C. The crude was columned with 7:3 (Hex:EtOAc), 15.7 mg collected, 73 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.31 (bs, 1H), 7.20 (dd, $J = 1.2, 5.2$ Hz, 1H), 7.08 (dd, $J = 0.8, 3.6$ Hz, 1H), 7.00 (dd, $J = 3.6, 5.2$ Hz, 1H), 6.62 (s, 1H), 5.55 (tq, $J = 1.6, 6.2$ Hz, 1H), 3.24 (d, $J = 6.0$ Hz, 2H), 3.13 (s, 2H), 1.82 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 170.7, 142.2, 132.6, 127.5, 127.2, 124.6, 124.5, 119.8, 118.5, 41.1, 28.8, 26.9

HR-MS: $[\text{M}+\text{H}]^+$

Calculated: 220.0791, Actual: 220.0790



(4Z,7E)-4-methyl-7-(1-methyl-1H-pyrrol-2-yl)azocin-2(1H,3H,6H)-one (**8b**): Employing procedure H) with 22.0 mg of 4-methyl-1-(2-(1-methyl-1H-pyrrol-2-yl)vinyl)-4-vinylazetidin-2-one and 450 μL of DMF at 170 °C. The crude was columned with 1:9 (Hex:EtOAc), 4.5 mg collected, 21 %.

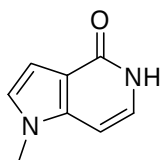
^1H NMR (CDCl_3) 300 MHz δ : 6.96 (bs, 1H), 6.62 (t, $J = 2.2$ Hz, 1H), 6.23 (d, $J = 1.6$ Hz, 1H), 6.15 (dd, $J = 1.8, 3.8$ Hz, 1H), 6.12 (dd, $J = 2.8, 3.6$ Hz, 1H), 5.48 (tq, $J = 1.6, 6.0$ Hz, 1H), 3.65 (s, 3H), 3.16 (s, 2H), 3.15 (d, $J = 6.0$ Hz, 2H), 1.84 (d, $J = 1.2$ Hz, 3H)

(8JA24R2C3C.fid) ^{13}C NMR (CDCl_3) 100 MHz δ : 170.5, 132.1, 126.1, 124.8, 121.4, 119.4, 110.1, 107.6, 104.8, 40.8, 35.8, 29.9, 27.0

(8JA30R2C1F1C.fid) ^{13}C NMR (CDCl_3) 75 MHz δ : 170.3, 132.2, 126.2, 124.8, 121.3, 119.3, 110.1, 107.7, 104.8, 40.8, 35.8, 29.9, 27.0

HR-MS: $[\text{M}+\text{H}]^+$

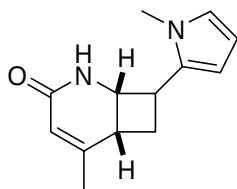
Calculated: 217.1344, Actual: 217.1335



1-methyl-1H-pyrrolo[3,2-c]pyridin-4(5H)-one (**8d**):²⁵ Employing procedure H) with 22.0 mg of 4-methyl-1-(2-(1-methyl-1H-pyrrol-2-yl)vinyl)-4-vinylazetidin-2-one and 450 μL of DMF at 170 °C. The crude was columned with 1:9 (Hex:EtOAc), 5.6 mg collected, 37 %.

^1H NMR 300 MHz (CDCl_3) δ : 11.30 (bs, 1H), 7.15 (d, $J = 6.6$ Hz, 1H), 6.86 (d, $J = 3.0$ Hz, 1H), 6.82 (d, $J = 3.0$ Hz, 1H), 6.41 (d, $J = 7.2$ Hz, 1H), 3.74 (s, 3H)

^{13}C NMR 100 MHz (CDCl_3) δ : 161.9, 140.1, 127.2, 126.0, 115.8, 104.1, 94.2, 33.3



5-methyl-8-(1-methyl-1*H*-pyrrol-2-yl)-2-azabicyclo[4.2.0]oct-4-en-3-one **(8c)**:

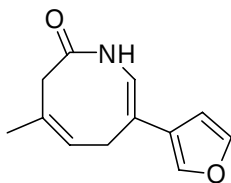
Employing procedure H) with 22.0 mg of 4-methyl-1-(2-(1-methyl-1*H*-pyrrol-2-yl)vinyl)-4-vinylazetidin-2-one and 450 μ L of DMF at 170 $^{\circ}$ C. The crude was columned with 1:9 (Hex:EtOAc), 5.8 mg collected, 27 %.

^1H NMR (CDCl_3) 400 MHz δ : 6.56-6.55 (m), 6.09 (t, J = 2.8 Hz), 6.07-6.04, 6.01-5.99 (m), 5.79-5.78 (m), 5.54-5.53 (m), 5.06 (bs), 4.40-4.35 (m), 4.05-4.00 (m), 3.80-3.71 (m), 3.52 (s), 3.50 (s), 2.81-2.74 (m), 2.55-2.47 (m), 2.40-2.25 (m), 1.93 (s), 1.85-1.84 (m)

^{13}C NMR (CDCl_3) 75 MHz δ : 172.7, 165.2, 153.7, 152.6, 134.3, 122.69, 122.67, 120.0, 118.3, 109.0, 107.5, 107.3, 105.2, 55.9, 53.0, 41.1, 36.9, 35.8, 34.3, 34.2, 33.92, 33.85, 29.8, 20.9, 20.5

High Resolution MS: $[\text{M}+\text{H}]^+$

Calculated: 217.1335, Actual: 217.1356



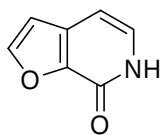
(4*Z*,7*E*)-7-(furan-3-yl)-4-methylazocin-2(1*H*,3*H*,6*H*)-one **(9b)**: Employing procedure H) with 20.1 mg of 1-(2-(furan-3-yl)vinyl)-4-methyl-4-vinylazetidin-2-one and 450 μ L of DMF at 170 $^{\circ}$ C. The crude was columned with 1:9 (Hex:EtOAc) followed by 95:5 (DCM:MeOH), 8.3 mg collected, 41 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.47 (s, 1H), 7.40 (t, J = 1.6 Hz, 1H), 6.86 (bs, 1H), 6.52 (dd, J = 0.8, 1.6 Hz, 1H), 6.45 (s, 1H), 5.51 (tq, J = 1.2, 6.4 Hz, 1H), 3.11 (s, 2H), 3.09 (d, J = 6.0 Hz, 2H), 1.82 (s, 3H)

^{13}C NMR (CDCl_3) 75 MHz δ : 170.6, 143.8, 139.9, 132.5, 125.2, 124.5, 119.4, 118.5, 107.6, 41.0, 27.9, 26.9

HR-MS: $[\text{M}+\text{H}]^+$

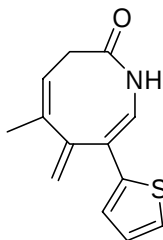
Calculated: 204.1013, Actual: 204.1019



furo[2,3-*c*]pyridin-7(6*H*)-one **(9c)**:²⁴ Employing procedure H) with 20.1 mg of 1-(2-(furan-3-yl)vinyl)-4-methyl-4-vinylazetidin-2-one and 450 μ L of DMF at 170 $^{\circ}$ C. The crude was columned with 1:9 (Hex:EtOAc) followed by 95:5 (DCM:MeOH), 7.2 mg collected, 54 %.

^1H NMR (CDCl_3) 400 MHz δ : 11.94 (bs, 1H), 7.78 (d, J = 2.8 Hz, 1H), 7.20 (d, J = 8.8 Hz, 1H), 6.72 (d, J = 2.8 Hz, 1H), 6.58 (d, J = 8.8 Hz, 1H)

^{13}C NMR 100 MHz (CDCl_3) δ : 155.1, 148.5, 134.6, 128.5, 107.5, 104.8, 101.4



(4Z,7E)-5-methyl-6-methylene-7-(thiophen-2-yl)azocin-2(1H,3H,6H)-one **(10b)**:

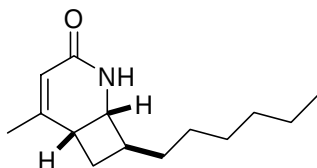
Employing procedure H) with 20.6 mg of 4-(buta-2,3-dien-2-yl)-1-(2-(thiophen-2-yl)vinyl)azetidin-2-one and 450 μL of DMF at 200 $^\circ\text{C}$. The crude was columned with EtOAc then 95:5 (DCM:MeOH), 8.9 mg collected, 43 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.22 (dd, J = 1.2, 5.2 Hz, 1H), 7.05 (dd, J = 0.8, 3.6 Hz, 1H), 6.99 (dd, J = 3.6, 5.2 Hz, 1H), 6.75 (bs, 1H), 6.58 (d, J = 2.0 Hz, 1H), 5.63 (t, J = 7.2 Hz, 1H), 5.53 (s, 1H), 5.20 (s, 1H), 3.18 (dd, J = 0.8, 6.8 Hz, 2H), 2.04 (d, J = 1.6 Hz, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 170.8, 143.7, 141.6, 135.5, 130.9, 127.7, 125.5, 125.4, 120.1, 118.8, 118.7, 35.3, 24.1

HR-MS: $\text{C}_{13}\text{H}_{13}\text{NOS}$

Calculated: 231.0718, Actual: 231.0715



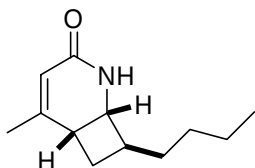
8-hexyl-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one **(11b)**: Employing procedure I) with 20 mg of 4-methyl-1-((E)-oct-1-enyl)-4-vinylazetidin-2-one, 2.0 mg of CuI, 50 mg of Cs_2CO_3 and 450 μL of DMF at 190 $^\circ\text{C}$. 19.8 mg collected, 99 % yield.

^1H NMR (CDCl_3) 400 MHz δ : 5.68 (s, 1H), 5.65, 3.62, (td, J = 4.0, 8.4 Hz, 1H), 3.04-2.99 (m, 1H), 2.64-2.53 (m, 1H), 2.06-2.00 (m, 1H), 1.85 (t, J = 1.2 Hz, 3H), 1.52-1.43 (m, 1H), 1.31-1.17 (m, 8H), 0.88 (t, J = 6.8 Hz, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 165.3, 153.9, 104.8, 54.2, 44.9, 35.5, 34.7, 31.8, 29.8, 29.3, 27.2, 22.6, 20.2, 14.1

HR-MS: $[\text{M}+\text{H}]^+$

Calculated: 222.1851, Actual: 221.1841



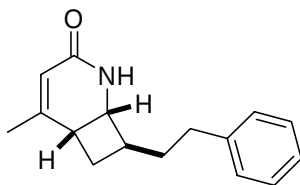
8-butyl-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**12b**): Employing procedure I) with 21.5 mg of 1-((*E*)-hex-1-en-1-yl)-4-methyl-4-vinylazetidin-2-one, 2.0 mg of CuI, 52 mg of Cs₂CO₃ and 450 μ L of DMF at 190 °C. 21.2 mg collected, 98 % yield.

¹H NMR (CDCl₃) 400 MHz δ : 5.98 (bs, 1H), 5.67 (s, 1H), 3.63 (td, J = 4.0, 12.4 Hz, 1H), 3.05-2.96 (m, 1H), 2.63-2.53 (m, 1H), 2.06-2.00 (m, 1H), 1.85 (t, J = 1.2 Hz, 3H), 1.53-1.43 (m, 1H), 1.40-1.15 (m, 6H), 0.87 (t, J = 7.6 Hz, 3H)

¹³C NMR (CDCl₃) 100 MHz δ : 165.4, 153.9, 119.2, 54.1, 44.9, 35.5, 34.3, 29.8, 29.4, 22.6, 20.2, 14.0

HR-MS: [M+H]⁺

Calculated: 194.1539, Actual: 194.1533



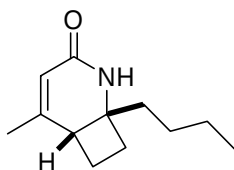
5-methyl-8-(2-phenylethyl)-2-azabicyclo[4.2.0]oct-4-en-3-one (**13b**): Employing procedure I) with 21.2 mg of 4-methyl-1-((*E*)-4-phenylbut-1-en-1-yl)-4-vinylazetidin-2-one, 1.9 mg of CuI, 42 mg of Cs₂CO₃ and 450 μ L of DMF at 190 °C. 19.7 mg collected, 93 %.

¹H NMR (CDCl₃) 400 MHz δ : 5.73 (bs, 1H), 5.65 (q, J = 1.2 Hz, 1H), 3.63-3.57 (m, 1H), 3.02-2.97 (m, 1H), 2.68-2.45 (m), 2.05-1.99 (m, 1H), 1.91-1.80 (m), 1.82 (t, J = 1.2, 3H), 1.75-1.66 (m)

¹³C NMR (CDCl₃) 100 MHz δ : 165.2, 153.6, 141.7, 128.4, 128.3, 126.0, 119.2, 54.2, 44.6, 36.3, 35.5, 33.7, 29.6, 20.2

HR-MS: [M+H]⁺

Calculated: 242.1539, Actual: 242.1552



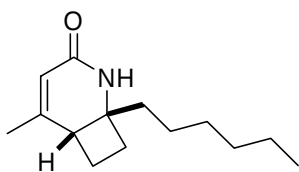
1-butyl-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**14b**): Employing procedure I) with 20.4 mg of 1-(hex-1-en-2-yl)-4-methyl-4-vinylazetidin-2-one, 2.0 mg of CuI, 52 mg of Cs₂CO₃ and 450 μ L of DMF at 160 °C. 16.9 mg collected, 83 %.

¹H NMR (CDCl₃) 400 MHz δ : 5.65 (m, 1H), 5.48 (bs, 1H), 2.74-2.71 (m, 1H), 2.05-1.89 (m, 2H), 1.83 (m, 3H), 1.70 (ddd, J = 5.2, 11.2, 14.0 Hz, 1H), 1.58 (ddd, J = 4.4, 11.6, 14.0 Hz, 1H), 0.91 (t, J = 7.2 Hz, 3H)

¹³C NMR (CDCl₃) 75 MHz δ : 165.6, 153.2, 118.0, 57.5, 42.1, 40.4, 35.0, 25.3, 24.2, 22.8, 20.4, 14.0

HR-MS: C₁₂H₁₉NO

Calculated: 193.1467, Actual: 193.1467



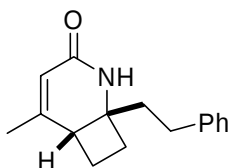
1-hexyl-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**15b**): Employing procedure I) with 21.3 mg of 4-methyl-1-(oct-1-en-2-yl)-4-vinylazetidin-2-one, 1.7 mg of CuI, 69 mg of Cs₂CO₃ and 450 μ L of DMF at 170 °C. 19.3 mg collected, 91 %.

¹H NMR (CDCl₃) 400 MHz δ : 5.65 (m, 1H), 5.43 (bs, 1H), 2.73-2.70 (m, 2H), 2.32-2.23 (m, 2H), 2.05-1.98 (m, 1H), 1.96-1.88 (m, 1H), 1.83 (m, 3H), 1.73-1.65 (m, 1H), 1.61-1.54 (m, 1H), 1.39-1.23 (m, 8H), 0.89 (t, *J* = 6.8 Hz, 3H)

¹³C NMR (CDCl₃) 75 MHz δ : 165.6, 153.2, 118.0, 57.5, 42.2, 40.7, 35.0, 31.7, 29.4, 24.2, 23.1, 22.6, 20.4, 14.0

HR-MS: C₁₄H₂₃NO

Calculated: 221.1780, Actual: 221.1781



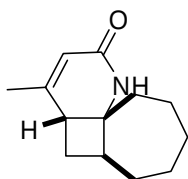
5-methyl-1-(2-phenylethyl)-2-azabicyclo[4.2.0]oct-4-en-3-one (**16b**): Employing procedure I) with 20.3 mg of 4-methyl-1-(4-phenylbut-1-en-2-yl)-4-vinylazetidin-2-one, 2.7 mg of CuI, 42 mg of Cs₂CO₃ and 450 μ L of DMF at 160 °C. 16.6 mg collected, 82 %

¹H NMR (CDCl₃) 400 MHz: 7.31-7.26 (m, 2H), 7.21-7.17 (m, 3H), 5.72 (bs, 1H), 5.68 (m, 1H), 2.75-2.72 (m, 1H), 2.68 (ddd, *J* = 5.2, 11.2, 14.0 Hz, 1H), 2.59 (ddd, *J* = 6.0, 11.0, 14.0 Hz, 1H), 2.35-2.26 (m, 2H), 1.99-1.88 (m, 2H), 1.81 (s, 3H)

¹³C NMR (CDCl₃) 75 MHz δ : 165.7, 153.2, 141.3, 128.5, 128.3, 126.1, 118.1, 57.5, 42.6, 41.9, 35.2, 29.8, 24.3, 20.4

HR-MS: C₁₆H₁₉NO

Calculated: 241.1467, Actual: 241.1461



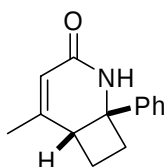
4-methyl-4a,5,5a,6,7,8,9,10-octahydrocyclohepta[1,4]cyclobuta[1,2-b]pyridin-2(1H)-one (**17b**): Employing procedure I) with 20.2 mg of 1-(*E*)-cycloheptenyl-4-methyl-4-vinylazetidin-2-one, 2.0 mg of CuI, 66 mg of Cs₂CO₃ and 450 μ L of DMF at 190 °C. 16.9 mg collected, 84 %.

^1H NMR (CDCl_3) 400 MHz: 5.80 (bs, 1H), 5.63-5.62 (m, 1H), 2.63-2.53 (m, 2H), 2.07 (ddd, J = 5.6, 9.6, 11.6 Hz, 1H), 1.96-1.77 (m, 7H), 1.75-1.70 (m, 1H), 1.38-1.33 (m, 3H), 1.22-1.14 (m, 1H)

^{13}C NMR (CDCl_3) 100 MHz δ : 164.9, 153.4, 117.4, 59.4, 47.5, 40.6, 38.9, 33.7, 31.8, 30.8, 28.0, 23.6, 20.4

HR-MS: $\text{C}_{13}\text{H}_{19}\text{NO}$

Calculated: 205.1467, Actual: 205.1471



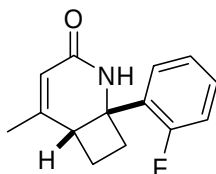
5-methyl-1-phenyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**18b**): Employing procedure I) with 20.2 mg of 4-methyl-1-(1-phenylvinyl)-4-vinylazetidin-2-one, 1.8 mg of CuI , 46 mg of Cs_2CO_3 and 450 μL of DMF at 150 $^\circ\text{C}$. The crude was columned with 1:1 (Hex:EtOAc), 8.5 mg collected, 42 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.40-7.35 (m, 4H), 7.33-7.28 (m, 1H), 5.77 (bs, 1H), 5.75 (s, 1H), 3.05 (t, J = 8.4 Hz, 1H), 2.83-2.76 (m, 1H), 2.51-2.44 (m, 1H), 2.43-2.34 (m, 1H), 2.21-2.12 (m, 1H)

^{13}C NMR (CDCl_3) 100 MHz δ : 165.3, 152.6, 144.9, 128.8, 127.7, 125.1, 118.0, 60.5, 44.8, 34.3, 24.9, 20.8

HR-MS: $\text{C}_{14}\text{H}_{15}\text{NO}$

Calculated: 213.1154 Actual: 213.1154



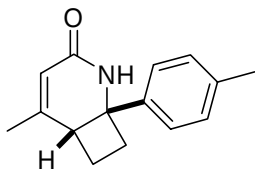
1-(2-fluorophenyl)-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**19b**): Employing procedure I) with 20.6 mg of 1-(1-(2-fluorophenyl)vinyl)-4-methyl-4-vinylazetidin-2-one, 2.9 mg of CuCl , 46 mg of Cs_2CO_3 and 450 μL of DMF at 140 $^\circ\text{C}$. The crude was columned with 6:4 (Hex:EtOAc), 5.6 mg collected, 27 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.31-7.25 (m, 1H), 7.19-7.12 (m, 2H), 7.10-7.03 (m, 1H), 5.72 (s, 1H), 5.68 (bs, 1H), 3.32 (t, J = 8.8 Hz, 1H), 2.69-2.62 (m, 1H), 2.57-2.50 (m, 1H), 2.45-2.37 (m, 1H), 2.31-2.22 (m, 1H), 1.92 (m, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 164.9, 160.5 (d, J = 245.9 Hz), 152.4, 131.8 (d, J = 13.9 Hz), 129.7 (d, J = 8.4 Hz), 126.2 (d, J = 4.6 Hz), 124.3 (d, J = 3.4 Hz), 118.0, 116.4 (d, J = 21.6 Hz), 58.6, 41.2, 35.4 (d, J = 2.4 Hz), 26.0, 20.9

HR-MS: $\text{C}_{14}\text{H}_{14}\text{NOF}$

Calculated: 231.1059 Actual: 231.1049



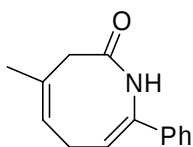
5-methyl-1-(4-methylphenyl)-2-azabicyclo[4.2.0]oct-4-en-3-one (**20b**): Employing procedure I) with 20.5 mg of 4-methyl-1-(1-p-tolylvinyl)-4-vinylazetidin-2-one, 3.0 mg of CuI, 48 mg of Cs₂CO₃ and 450 μ L of DMF at 160 °C. The crude was columned with 1:1 (Hex:EtOAc), 7.0 mg collected, 34 %.

¹H NMR (CDCl₃) 400 MHz δ : 7.28 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 5.75 (s, 1H), 5.62 (bs, 1H), 3.02 (t, *J* = 8.0 Hz, 1H), 2.81-2.74 (m, 1H), 2.52-2.32 (m, 3H), 2.35 (s, 3H), 2.18-2.09 (m, 1H), 1.84 (m, 3H)

¹³C NMR (CDCl₃) 100 MHz δ : 165.3, 152.7, 142.0, 137.5, 129.5, 125.1, 118.0, 60.3, 45.1, 34.4, 24.9, 21.0, 20.8

HR-MS: C₁₅H₁₇NO

Calculated: 227.1310 Actual: 227.1313



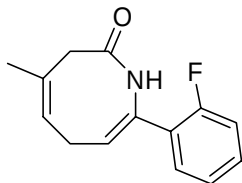
(4Z,7Z)-4-methyl-8-phenylazocin-2(1H,3H,6H)-one: Employing procedure I) with 20.2 mg of 4-methyl-1-(1-phenylvinyl)-4-vinylazetidin-2-one, 1.8 mg of CuI, 46 mg of Cs₂CO₃ and 450 μ L of DMF at 150 °C. The crude was columned with 1:1 (Hex:EtOAc), 4.2 mg collected, 21 %.

¹H NMR (CDCl₃) 400 MHz δ : 7.51-7.48 (m, 2H), 7.40-7.34 (m, 3H), 6.77 (bs, 1H), 5.82 (t, *J* = 8.4 Hz, 1H), 2.96 (s, 2H), 2.95 (t, *J* = 7.6 Hz, 2H), 1.85 (s, 3H)

¹³C NMR (CDCl₃) 100 MHz δ : 171.2, 137.2, 136.1, 132.8, 128.797, 128.769, 125.6, 119.2, 117.3, 40.1, 27.0, 26.2

HR-MS: C₁₄H₁₅NO

Calculated: 213.1154 Actual: 213.1164



(4Z,7Z)-8-(2-fluorophenyl)-4-methylazocin-2(1H,3H,6H)-one: Employing procedure I) with 20.6 mg of 1-(1-(2-fluorophenyl)vinyl)-4-methyl-4-vinylazetidin-2-one, 2.9 mg of CuCl, 46 mg of Cs₂CO₃ and 450 μ L of DMF at 140 °C. The crude was columned with 6:4 (Hex:EtOAc), 6.8 mg collected, 33 %.

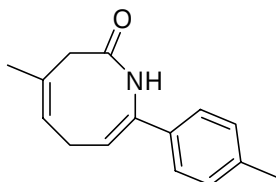
¹H NMR (CDCl₃) 400 MHz δ : 7.39 (td, *J* = 1.6, 7.6 Hz, 1H), 7.33-7.27 (m, 1H), 7.15 (td, *J* = 1.2, 7.6 Hz, 1H), 7.15 (td, *J* = 1.2, 7.6 Hz, 1H), 7.09 (ddd, *J* = 1.2, 8.4, 11.6 Hz, 1H),

6.92 (bs, 1H), 5.88 (t, $J = 8.4$ Hz, 1H), 5.47 (tq, $J = 1.6, 4.4$ Hz, 1H), 3.13 (s, 2H), 2.97 (t, $J = 7.2$ Hz, 2H), 1.86 (m, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 171.0, 160.3 (d, $J = 249.1$ Hz), 133.8, 132.9, 132.2 (d, $J = 2.4$ Hz), 130.0 (d, $J = 8.7$ Hz), 129.1 (d, $J = 2.9$ Hz), 124.3 (d, $J = 3.7$ Hz), 122.5 (d, $J = 7.1$ Hz), 118.9, 116.4 (d, $J = 22.5$ Hz), 40.3, 27.0, 26.2

HR-MS: $\text{C}_{14}\text{H}_{14}\text{NOF}$

Calculated: 231.1059 Actual: 231.1068



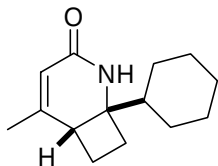
(4Z,7Z)-4-methyl-8-*p*-tolylazocin-2(1H,3H,6H)-one: Employing procedure I) with 20.5 mg of 4-methyl-1-(1-*p*-tolylvinyl)-4-vinylazetidin-2-one, 3.0 mg of CuI, 48 mg of Cs_2CO_3 and 450 μL of DMF at 160 $^\circ\text{C}$. The crude was columned with 1:1 (Hex:EtOAc), 4.1 mg collected, 20 %.

^1H NMR (CDCl_3) 400 MHz δ : 7.38 (d, $J = 8.0$ Hz, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 6.76 (bs, 1H), 5.76 (t, $J = 8.4$ Hz, 1H), 5.48 (tq, $J = 1.6, 4.4$ Hz, 1H), 3.07 (s, 2H), 2.92 (t, $J = 7.6$ Hz, 1H), 2.37 (s, 3H), 1.84 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 171.2, 138.8, 137.2, 133.3, 132.7, 129.4, 125.5, 119.3, 116.3, 40.1, 27.0, 26.2, 21.2

HR-MS: $\text{C}_{15}\text{H}_{17}\text{NO}$

Calculated: 227.1310 Actual: 227.1302



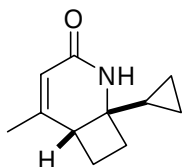
1-cyclohexyl-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**21b**): Employing procedure I) with 21 mg of 1-(1-cyclohexylvinyl)-4-methyl-4-vinylazetidin-2-one, 2.0 mg of CuI, 47 mg of Cs_2CO_3 and 450 μL of DMF at 200 $^\circ\text{C}$. 17.7 mg collected, 84 %.

^1H NMR (CDCl_3) 400 MHz δ : 5.59 (s, 1H), 5.32 (bs, 1H), 2.71 (t, $J = 8.4$ Hz, 1H), 2.30-2.22 (m, 1H), 2.13-2.09 (m, 2H), 2.04-1.95 (m, 1H), 1.83-1.76 (m, 5H), 1.69-1.58 (m, 3H), 1.40 (tt, $J = 2.8, 12.0$ Hz, 1H), 1.27-0.87 (m, 5H)

^{13}C NMR (CDCl_3) 100 MHz δ : 166.0, 153.5, 117.6, 60.8, 48.2, 41.0, 33.3, 26.3, 26.2, 26.1, 25.8, 24.9, 24.6, 20.6

HR-MS: $[\text{M}+\text{H}]^+$

Calculated: 220.1695, Actual: 220.1706



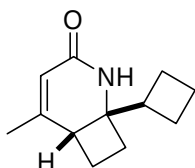
1-cyclopropyl-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**22b**): Employing procedure I) with 19.6 mg of 1-(1-cyclopropylvinyl)-4-methyl-4-vinylazetidin-2-one, 3.3 mg of CuI, 60 mg of Cs₂CO₃ and 450 μ L of DMF at 175 °C. 17.5 mg collected, 89 %.

¹H NMR (CDCl₃) 400 MHz δ : 5.65 (m, 1H), 5.48 (bs, 1H), 2.80-2.77 (m, 1H), 2.24-2.15 (m, 1H), 2.12-2.05 (m, 1H), 1.92-1.86 (m, 1H), 1.83 (dd, *J* = 0.8, 1.2 Hz, 1H), 1.81-1.74 (m, 1H), 1.13-1.06 (m, 1H), 0.60-0.48 (m, 2H), 0.45-0.39 (m, 1H), 0.28-0.22 (m, 1H)

¹³C NMR (CDCl₃) 100 MHz δ : 165.5, 153.2, 118.2, 57.7, 43.0, 31.1, 24.5, 20.6, 19.5, 1.3, 0.2

HR-MS: [M+H]⁺

Calculated: 178.1226, Actual: 178.1230



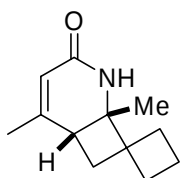
1-cyclobutyl-5-methyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**23b**): Employing procedure I) with 21.1 mg of 1-(1-cyclobutylvinyl)-4-methyl-4-vinylazetidin-2-one, 2.4 mg of CuI, 56 mg of Cs₂CO₃ and 450 μ L of DMF at 160 °C. 20.0 mg collected, 95 %.

¹H NMR (CDCl₃) 400 MHz δ : 5.64 (q, *J* = 1.2 Hz, 1H), 5.52 (bs, 1H), 2.76-2.72 (m, 1H), 2.65-2.56 (m, 1H), 2.26-2.05 (m, 3H), 2.01-1.85 (m, 5H), 1.80-1.73 (m, 2H)

¹³C NMR (CDCl₃) 100 MHz δ : 165.7, 153.2, 117.9, 58.6, 43.1, 39.8, 31.9, 24.4, 22.0, 21.9, 20.4, 17.0

HR-MS: [M+H]⁺

Calculated: 192.1382, Actual: 192.1389



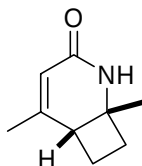
2,6-dimethyl-5-azaspiro[bicyclo[4.2.0]octane-7,1'-cyclobutane]-2-en-4-one (**24b**): Employing procedure I) with 20.7 mg of 1-(1-cyclobutylideneethyl)-4-methyl-4-vinylazetidin-2-one, 3.0 mg of CuI, 55.0 mg of Cs₂CO₃ and 450 μ L of DMF at 160 °C. 19.0 mg collected, 93 %.

¹H NMR (CDCl₃) 400 MHz δ : 5.77 (bs, 1H), 5.59 (m, 1H), 2.60 (dd, *J* = 4.0, 9.6 Hz, 1H), 2.34 (dd, *J* = 9.6, 12.0 Hz, 1H), 2.30-2.22 (m, 1H), 2.08-1.98 (m, 1H), 2.02 (dd, *J* = 4.0, 12.0 Hz, 1H), 1.87-1.69 (m, 2H), 1.81 (m, 3H), 1.66-1.57 (m, 2H), 1.30 (s, 3H)

^{13}C NMR (CDCl_3) 100 MHz δ : 166.0, 153.5, 118.3, 56.8, 51.5, 41.5, 38.2, 31.2, 29.0, 23.3, 20.2, 15.0

HR-MS: $[\text{M}+\text{H}]^+$

Calculated: 192.1382, Actual: 192.1377



1,5-dimethyl-2-azabicyclo[4.2.0]oct-4-en-3-one (**25**): To a flame dried schlenk flask charged with a stir bar added 11.5 mg of CuI , 341 mg of K_2CO_3 , the flask was placed under vacuum for 10 minutes and then purged with nitrogen. 117 mg of 4-methyl-4-vinylazetidin-2-one, 106 μL of 2-bromopropene, 11 μL of *N,N*'-dimethylethylenediamine, and 1 mL of xylenes were injected into the flask and were lowered into a preheated 180 $^\circ\text{C}$ oil bath for 12 hours. After allowing the contents of the flask to cool the material was rinsed out with water and DCM into a separatory funnel, the organic layer was collected and the aqueous layer was washed twice with DCM and collected. The organic layer was dried with magnesium sulphate, filtered and concentrated and columned with 7:3 (Hex:EtOAc) and then 9:1 (DCM:MeOH) to afford 5.7 mg of product, 4 %.

^1H NMR 400 MHz (CDCl_3) δ : 5.86 (bs, 1H), 5.68 (s, 1H), 2.72-2.68 (m, 1H), 2.41-2.24 (m, 2H), 2.01-1.95 (m, 1H), 1.90-1.83 (m, 1H) 1.84 (s, 3H), 1.43 (s, 3H)

^{13}C NMR 75 MHz (CDCl_3) δ : 165.4, 153.0, 118.3, 54.3, 44.2, 36.0, 27.6, 23.2, 20.3

High Resolution MS: $[\text{M}+\text{H}]^+$

Calculated: 152.1069, Actual: 152.1063

X-Ray data for 1,5-dimethyl-2-azabicyclo[4.2.0]oct-4-en-3-one (25)

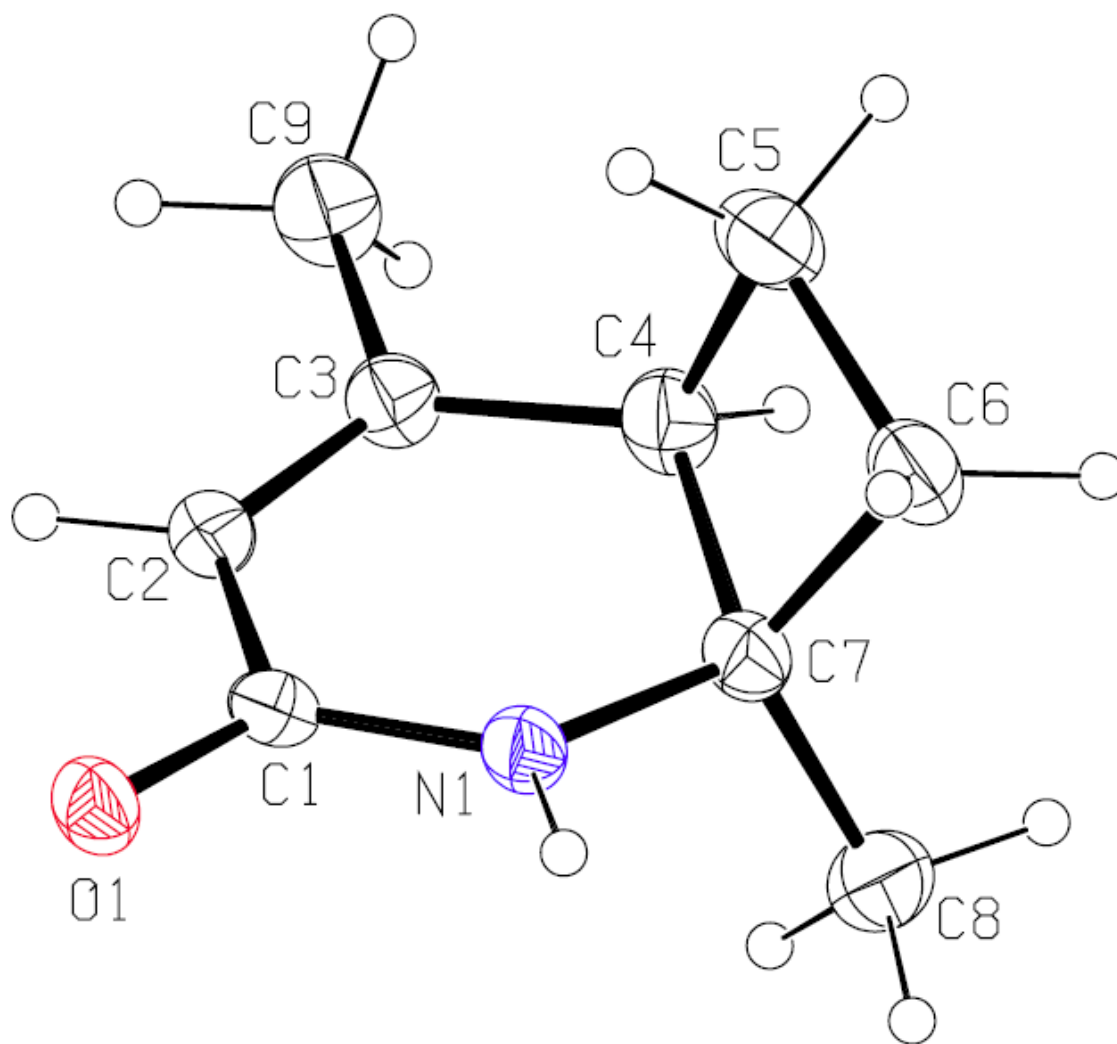


Table 1. Crystal data and structure refinement for k07293a.

Identification code	k07293a	
Empirical formula	C ₉ H ₁₃ N O	
Formula weight	151.20	
Temperature	150(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/n	
Unit cell dimensions	a = 8.0963(7) Å	α = 90°.
	b = 9.7756(6) Å	β = 97.923(4)°.
	c = 10.6313(8) Å	γ = 90°.
Volume	833.39(11) Å ³	

Z	4
Density (calculated)	1.205 Mg/m ³
Absorption coefficient	0.079 mm ⁻¹
F(000)	328
Crystal size	0.30 x 0.27 x 0.16 mm ³
Theta range for data collection	2.84 to 25.07°.
Index ranges	-9<=h<=9, -11<=k<=11, -12<=l<=12
Reflections collected	7680
Independent reflections	1473 [R(int) = 0.0616]
Completeness to theta = 25.07°	99.3 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.000 and 0.860
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	1473 / 0 / 106
Goodness-of-fit on F ²	1.074
Final R indices [I>2sigma(I)]	R1 = 0.0623, wR2 = 0.1664
R indices (all data)	R1 = 0.0884, wR2 = 0.1875
Largest diff. peak and hole	0.516 and -0.236 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for k07293a. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	7301(2)	4932(2)	5260(2)	44(1)
N(1)	5610(3)	6159(2)	3805(2)	38(1)
C(1)	7120(3)	5750(2)	4344(2)	36(1)
C(2)	8589(3)	6252(2)	3801(2)	38(1)
C(3)	8456(3)	6986(3)	2735(2)	41(1)
C(4)	6774(3)	7304(3)	2042(2)	48(1)
C(5)	5921(4)	6229(3)	1062(3)	58(1)
C(6)	4275(3)	6480(3)	1588(2)	50(1)
C(7)	5262(3)	7157(3)	2777(2)	41(1)
C(8)	4569(4)	8466(3)	3273(3)	53(1)
C(9)	9947(3)	7408(3)	2137(3)	54(1)

Table 3. Bond lengths [Å] and angles [°] for k07293a.

O(1)-C(1)	1.253(3)
N(1)-C(1)	1.337(3)
N(1)-C(7)	1.463(3)
C(1)-C(2)	1.476(3)
C(2)-C(3)	1.333(3)
C(3)-C(4)	1.489(4)
C(3)-C(9)	1.498(3)
C(4)-C(7)	1.548(3)
C(4)-C(5)	1.571(4)
C(5)-C(6)	1.534(4)
C(6)-C(7)	1.548(4)
C(7)-C(8)	1.520(4)
C(1)-N(1)-C(7)	126.2(2)
O(1)-C(1)-N(1)	121.7(2)
O(1)-C(1)-C(2)	120.1(2)
N(1)-C(1)-C(2)	118.1(2)
C(3)-C(2)-C(1)	122.5(2)
C(2)-C(3)-C(4)	119.6(2)
C(2)-C(3)-C(9)	122.3(2)
C(4)-C(3)-C(9)	117.9(2)
C(3)-C(4)-C(7)	117.7(2)
C(3)-C(4)-C(5)	118.5(2)
C(7)-C(4)-C(5)	88.1(2)
C(6)-C(5)-C(4)	88.6(2)
C(5)-C(6)-C(7)	89.4(2)
N(1)-C(7)-C(8)	110.13(19)
N(1)-C(7)-C(4)	110.8(2)
C(8)-C(7)-C(4)	116.9(2)
N(1)-C(7)-C(6)	110.5(2)
C(8)-C(7)-C(6)	118.0(2)
C(4)-C(7)-C(6)	88.99(18)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for k07293a. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	43(1)	53(1)	35(1)	12(1)	5(1)	2(1)
N(1)	35(1)	47(1)	32(1)	8(1)	8(1)	2(1)
C(1)	41(2)	41(1)	27(1)	-3(1)	6(1)	0(1)
C(2)	36(1)	45(1)	34(1)	-1(1)	3(1)	2(1)
C(3)	38(2)	44(1)	40(1)	3(1)	7(1)	-4(1)
C(4)	41(2)	58(2)	46(1)	13(1)	9(1)	-2(1)
C(5)	56(2)	80(2)	37(1)	-2(1)	5(1)	-2(2)
C(6)	44(2)	67(2)	38(1)	9(1)	2(1)	-3(1)
C(7)	42(2)	47(1)	33(1)	8(1)	7(1)	3(1)
C(8)	60(2)	50(2)	54(2)	9(1)	18(1)	10(1)
C(9)	44(2)	66(2)	53(2)	12(1)	11(1)	-9(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for k07293a.

	x	y	z	U(eq)
H(2A)	9670	6045	4227	46
H(4A)	6774	8228	1639	58
H(5A)	5897	6506	164	69
H(5B)	6360	5288	1204	69
H(6A)	3689	5630	1774	60
H(6B)	3511	7114	1065	60
H(8A)	5454	8942	3827	80
H(8B)	3657	8241	3756	80
H(8C)	4148	9059	2557	80
H(9A)	10961	7056	2643	81
H(9B)	10000	8409	2102	81
H(9C)	9856	7036	1274	81
H(1N)	4720(40)	5860(30)	4120(30)	49(8)

Table 6. Hydrogen bonds for k07293a [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(1)#1	0.88(3)	2.01(3)	2.886(3)	176(3)

Symmetry transformations used to generate equivalent atoms:

#1 $-x+1, -y+1, -z+1$

X-Ray data for 2,6-dimethyl-5-azaspiro[bicyclo[4.2.0]octane-7,1'-cyclobutane]-2-en-4-one (**24b**)

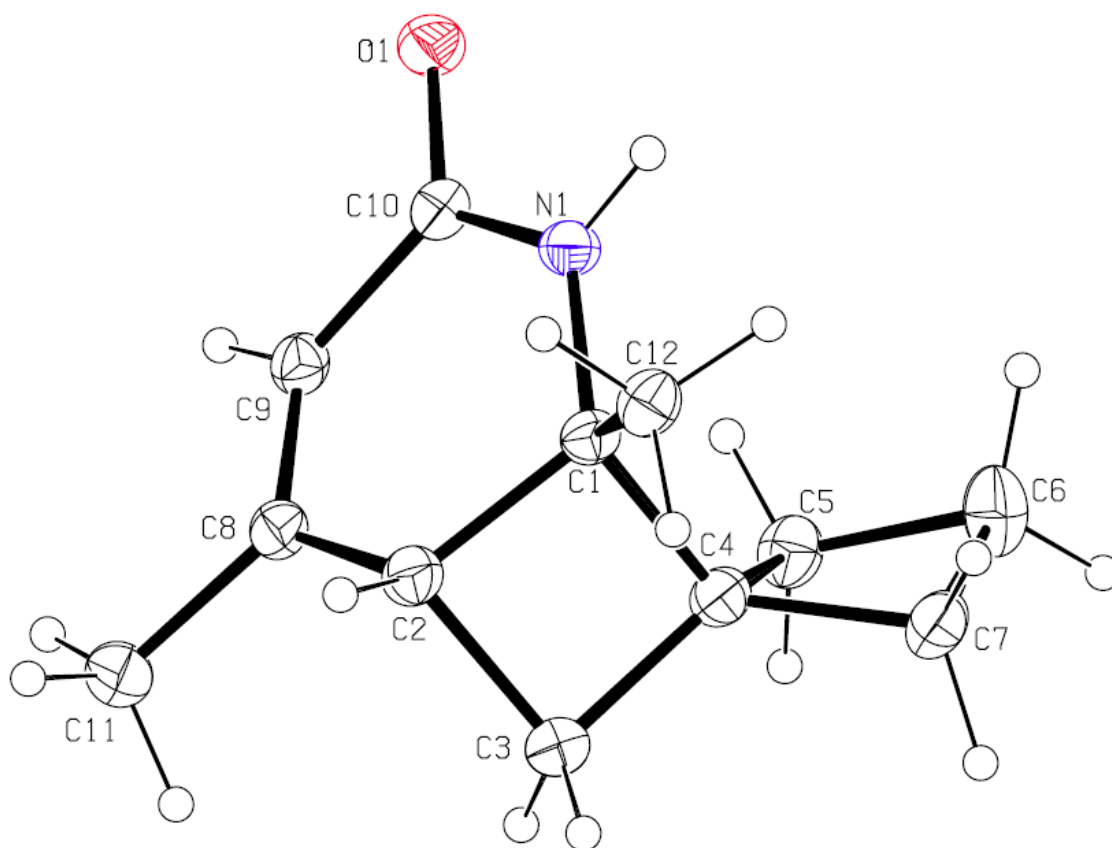


Table 1. Crystal data and structure refinement for k08286.

Identification code	k08286
Empirical formula	C ₁₂ H ₁₇ N O
Formula weight	191.27
Temperature	150(1) K

Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.3068(6) Å	$\alpha = 91.359(4)^\circ$.
	b = 7.7198(8) Å	$\beta = 110.180(5)^\circ$.
	c = 10.0156(7) Å	$\gamma = 95.337(4)^\circ$.
Volume	527.03(8) Å ³	
Z	2	
Density (calculated)	1.205 Mg/m ³	
Absorption coefficient	0.076 mm ⁻¹	
F(000)	208	
Crystal size	0.23 x 0.20 x 0.14 mm ³	
Theta range for data collection	2.65 to 27.56°.	
Index ranges	-9<=h<=9, -10<=k<=10, -12<=l<=12	
Reflections collected	5685	
Independent reflections	2375 [R(int) = 0.0438]	
Completeness to theta = 27.56°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.990 and 0.863	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	2375 / 0 / 130	
Goodness-of-fit on F ²	1.042	
Final R indices [I>2sigma(I)]	R1 = 0.0561, wR2 = 0.1362	
R indices (all data)	R1 = 0.0907, wR2 = 0.1591	
Largest diff. peak and hole	0.224 and -0.247 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for k08286. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6768(2)	6784(2)	5782(1)	37(1)
N(1)	7295(2)	3945(2)	5909(2)	30(1)
C(1)	8532(3)	2556(2)	6397(2)	29(1)
C(2)	10764(3)	3114(2)	6877(2)	32(1)
C(3)	11051(3)	2005(3)	8205(2)	37(1)
C(4)	8846(3)	1934(2)	7942(2)	31(1)
C(5)	8075(3)	3033(3)	8905(2)	38(1)
C(6)	6371(3)	1588(3)	8642(3)	50(1)
C(7)	7576(3)	334(3)	8165(2)	38(1)
C(8)	11351(3)	5021(2)	7257(2)	30(1)
C(9)	10003(3)	6139(2)	6988(2)	31(1)
C(10)	7904(3)	5643(2)	6203(2)	30(1)
C(11)	13509(3)	5591(3)	7903(2)	39(1)
C(12)	7851(3)	1065(2)	5265(2)	35(1)

Table 3. Bond lengths [Å] and angles [°] for k08286.

O(1)-C(10)	1.247(2)
N(1)-C(10)	1.337(2)
N(1)-C(1)	1.451(2)
C(1)-C(12)	1.517(3)
C(1)-C(2)	1.548(3)
C(1)-C(4)	1.578(2)
C(2)-C(8)	1.497(3)
C(2)-C(3)	1.563(2)
C(3)-C(4)	1.536(3)
C(4)-C(7)	1.542(3)
C(4)-C(5)	1.546(2)
C(5)-C(6)	1.538(3)
C(6)-C(7)	1.539(3)
C(8)-C(9)	1.331(2)
C(8)-C(11)	1.501(3)
C(9)-C(10)	1.470(3)
C(10)-N(1)-C(1)	124.53(16)
N(1)-C(1)-C(12)	108.54(15)
N(1)-C(1)-C(2)	115.21(15)
C(12)-C(1)-C(2)	112.85(14)
N(1)-C(1)-C(4)	117.75(14)
C(12)-C(1)-C(4)	112.83(15)
C(2)-C(1)-C(4)	88.70(13)
C(8)-C(2)-C(1)	114.74(15)
C(8)-C(2)-C(3)	113.18(16)
C(1)-C(2)-C(3)	88.74(13)
C(4)-C(3)-C(2)	89.67(13)
C(3)-C(4)-C(7)	124.64(15)
C(3)-C(4)-C(5)	120.99(17)
C(7)-C(4)-C(5)	88.20(14)
C(3)-C(4)-C(1)	88.63(13)
C(7)-C(4)-C(1)	120.54(17)
C(5)-C(4)-C(1)	117.22(14)

C(6)-C(5)-C(4)	88.45(15)
C(5)-C(6)-C(7)	88.64(15)
C(6)-C(7)-C(4)	88.54(15)
C(9)-C(8)-C(2)	120.68(17)
C(9)-C(8)-C(11)	122.64(18)
C(2)-C(8)-C(11)	116.65(16)
C(8)-C(9)-C(10)	123.64(18)
O(1)-C(10)-N(1)	121.93(18)
O(1)-C(10)-C(9)	120.42(17)
N(1)-C(10)-C(9)	117.58(16)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for k08286. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	34(1)	26(1)	48(1)	6(1)	10(1)	7(1)
N(1)	27(1)	26(1)	32(1)	3(1)	5(1)	3(1)
C(1)	30(1)	26(1)	32(1)	6(1)	11(1)	7(1)
C(2)	32(1)	34(1)	32(1)	6(1)	14(1)	8(1)
C(3)	34(1)	38(1)	39(1)	12(1)	11(1)	7(1)
C(4)	34(1)	30(1)	31(1)	6(1)	12(1)	5(1)
C(5)	43(1)	39(1)	32(1)	1(1)	17(1)	1(1)
C(6)	51(1)	48(1)	59(1)	0(1)	33(1)	-3(1)
C(7)	44(1)	34(1)	39(1)	10(1)	17(1)	3(1)
C(8)	30(1)	36(1)	25(1)	5(1)	10(1)	2(1)
C(9)	32(1)	26(1)	32(1)	2(1)	9(1)	-1(1)
C(10)	34(1)	28(1)	29(1)	4(1)	12(1)	3(1)
C(11)	34(1)	44(1)	36(1)	4(1)	8(1)	0(1)
C(12)	40(1)	30(1)	36(1)	3(1)	15(1)	4(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for k08286.

	x	y	z	U(eq)
H(1A)	6057	3648	5383	35
H(2A)	11371	2645	6208	38
H(3A)	11495	851	8103	44
H(3B)	11890	2633	9115	44
H(5A)	8968	3196	9910	45
H(5B)	7658	4158	8520	45
H(6A)	5148	1817	7876	60
H(6B)	6112	1263	9516	60
H(7A)	6818	-379	7278	46
H(7B)	8302	-402	8924	46
H(9A)	10421	7322	7321	37
H(11A)	13714	6841	8176	59
H(11B)	14138	5365	7205	59
H(11C)	14084	4940	8748	59
H(12A)	8046	1450	4394	52
H(12B)	6457	697	5061	52
H(12C)	8612	83	5609	52

Table 6. Hydrogen bonds for k08286 [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1A)...O(1)#1	0.88	1.98	2.858(2)	174.6

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+1

¹ Moriconi, E.J.; Meyer, W.C. *Tetrahedron Lett.* **1968**, 35, 3823

² Durst, T.; O'Sullivan, M.J. *J. Org. Chem.* **1970**, 35, 2043

³ Lee, P.H.; Kim, H.; Lee, K.; Kim, M.; Noh, K.; Kim, H.; Seomoon, D. *Angew. Chem. Int. Ed.* **2005**, 44, 1840

⁴ Mickel, S.J.; Hsiao, S.-N.; Miller, M.J. *Org. Synth.* **1987**, 65, 135

⁵ Harried, S.S.; Lee, C.P.; Yang, G.; Lee, T.I.H.; Myles, D.C. *J. Org. Chem.* **2003**, 68, 6646

⁶ Conway, J.C.; Quayle, P.; Regan, A.C.; Urch, C.J. *Tetrahedron* **2005**, 61, 11910

⁷ Trost, B. M.; Rudd, M. T. *Org. Lett.* **2003**, 5, 4599

⁸ Barton, D.H.R.; Bashardes, G.; Pourrey, J.L. *Tetrahedron Lett.* **1983**, 24, 1605

⁹ Blaskovicova, M.; Gaplovsky, A.; Blasko, J. *Molecules* **2007**, 11, 188

¹⁰ Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, 675

¹¹ Jiang, L.; Job, G.E.; Klapers, A.; Buchwald, S.L. *Org. Lett.* **2003**, 5, 3667

¹² Lee, G.C.M.; Tobias, B.; Holmes, J.M.; Harcourt, D.A.; Garst, M.E. *J. Am. Chem. Soc.* **1990**, 112, 9330

¹³ Pan, X.; Cai, Q.; Ma, D.; *Org. Lett.* **2004**, 6, 1809

¹⁴ Naskar, D.; Roy, S. *Tetrahedron*. **2000**, 56, 1369

¹⁵ Trost, B.M.; Rudd, M.T. *Org. Lett.* **2003**, 5, 4599

¹⁶ Zhang, W.; Sun, M.; Salomon, R.G. *J. Org. Chem.* **2006**, 71, 5607

¹⁷ Spino, C.; Genbhau, V.; Gund, G.; Nadeau, C. *J. Comb. Chem.* **2005**, 7, 345

¹⁸ Kamiya, N.; Chikami, Y.; Ishii, Y. *Synlett* **1990**, 675

¹⁹ Devine, S.K.J.; Van Vranken, D.L. *Org. Lett.* **2007**, 9, 2047

²⁰ Bottini, A.T.; Frostll, K.A.; Anderson, B.R.; Dev, V. *Tetrahedron*. **1973**, 29, 1975

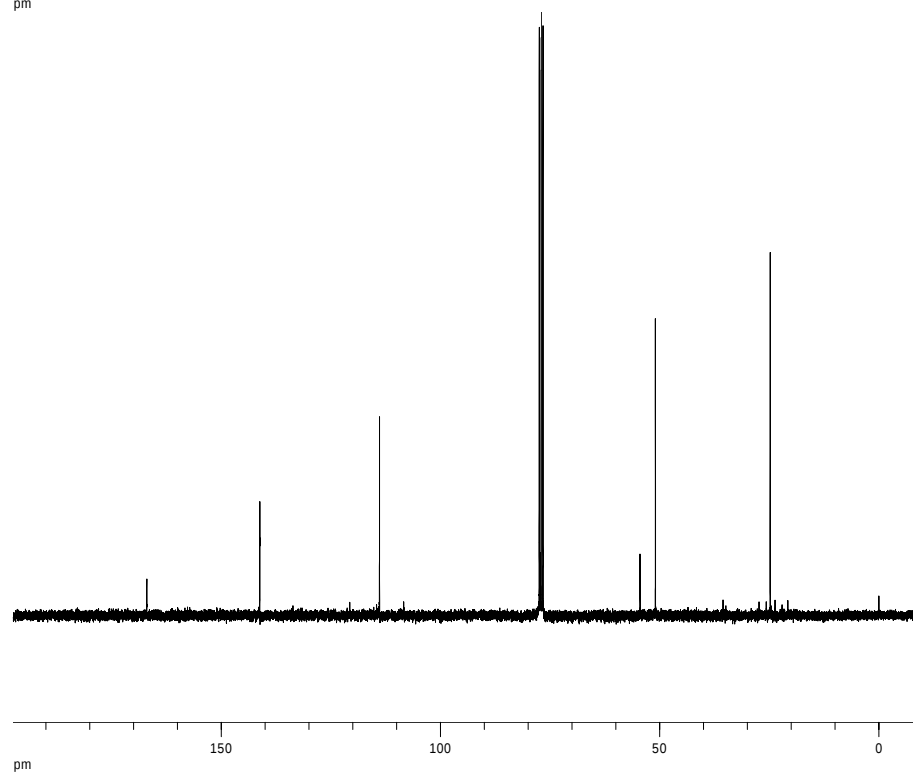
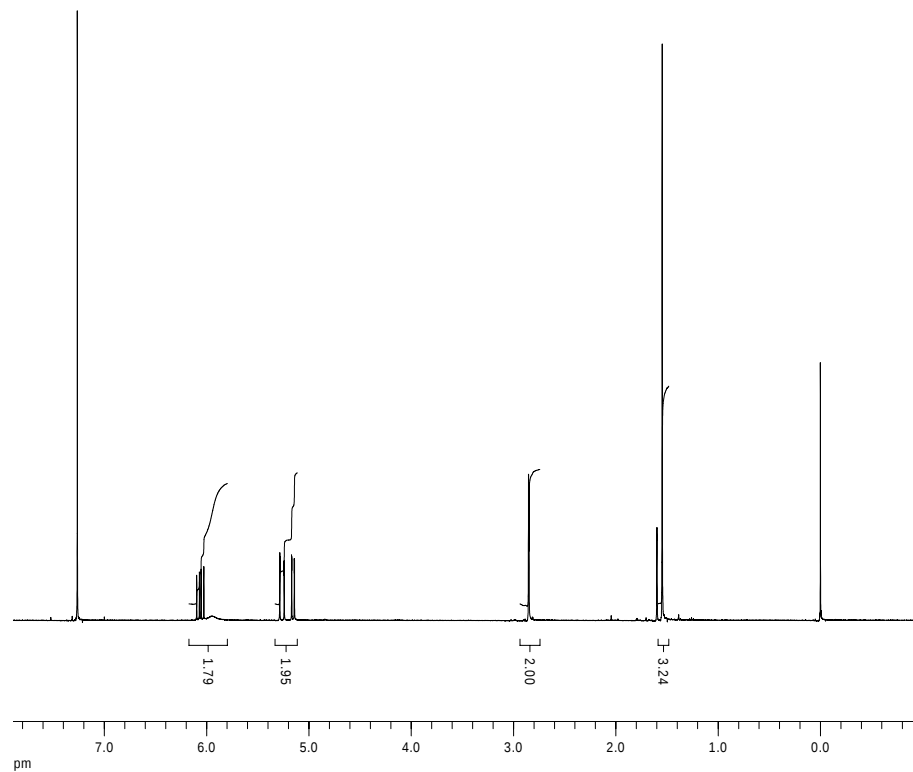
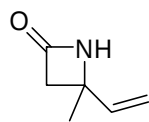
²¹ Shimizu, M.; Toyoda, T.; Baba, T. *Synlett* **2005**, 2516

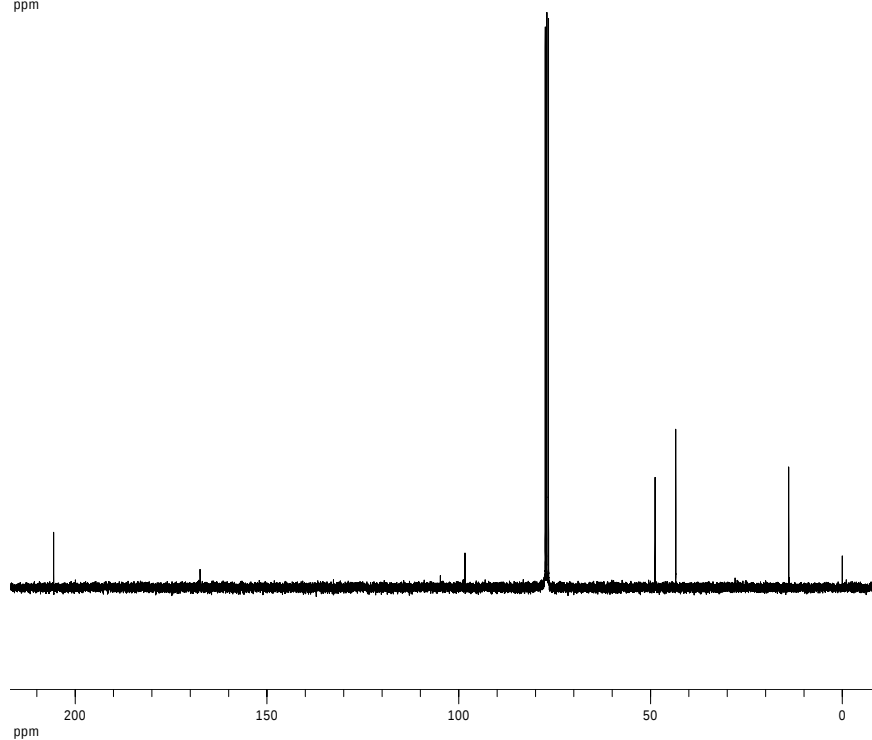
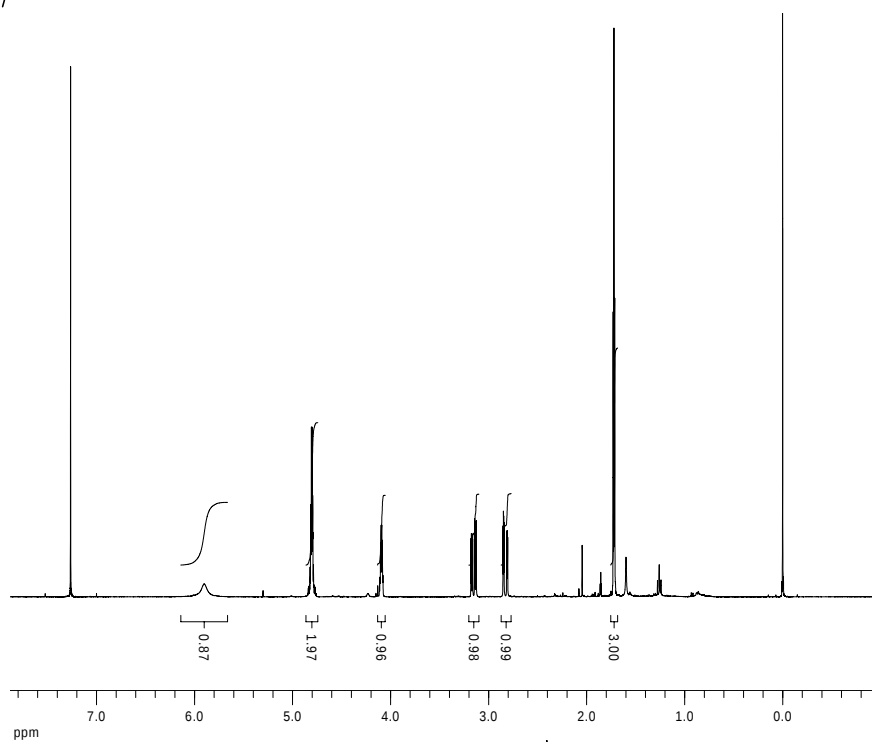
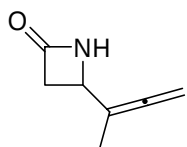
²² Hara, S.; Takinami, S.; Hyuga, S.; Suzuki, A. *Chem. Lett.* **1984**, 345

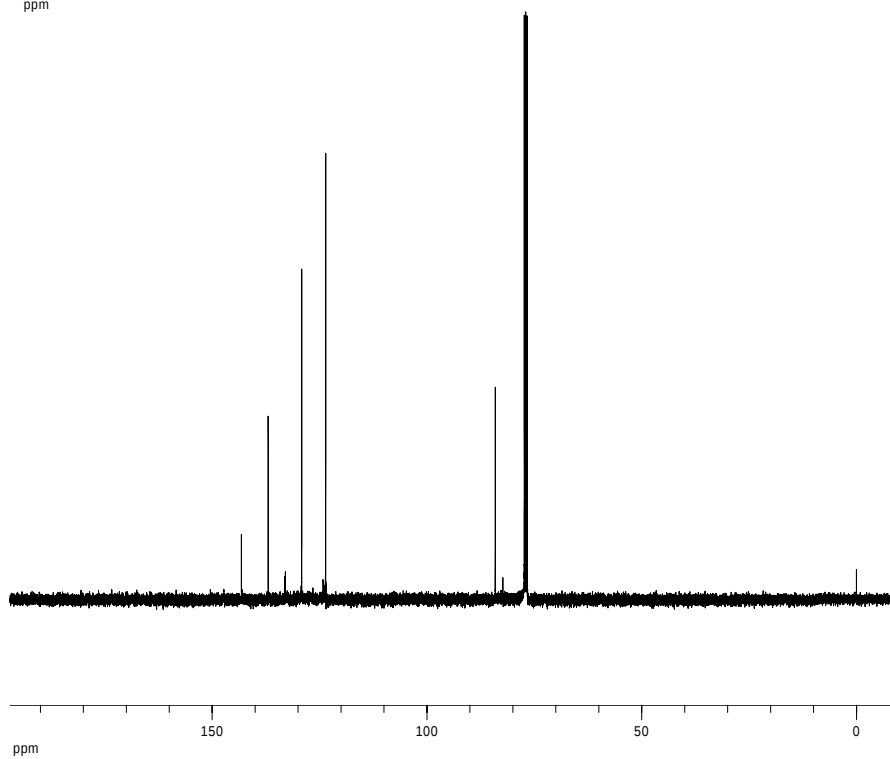
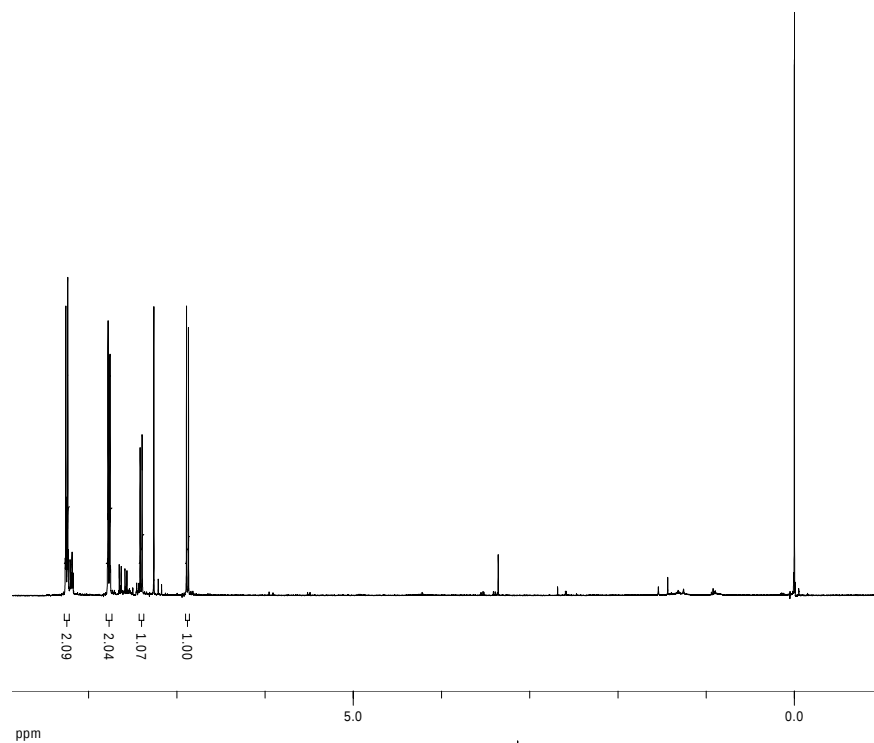
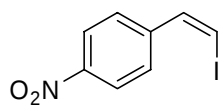
²³ Bergman, R.G.; Sherrod, S.A. *J. Am. Chem. Soc.* **1971**, 93, 1925

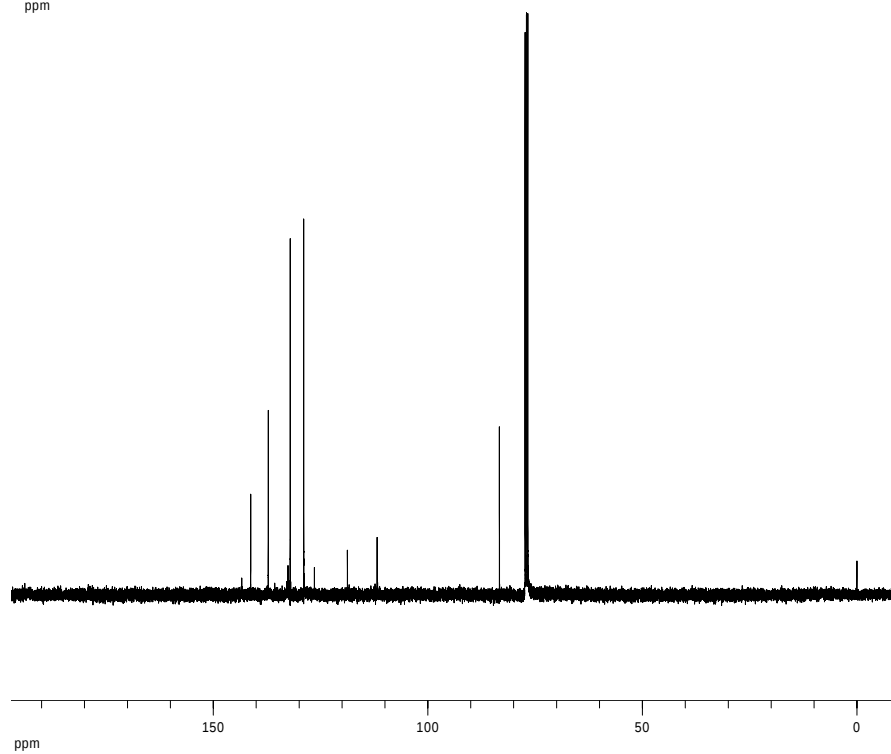
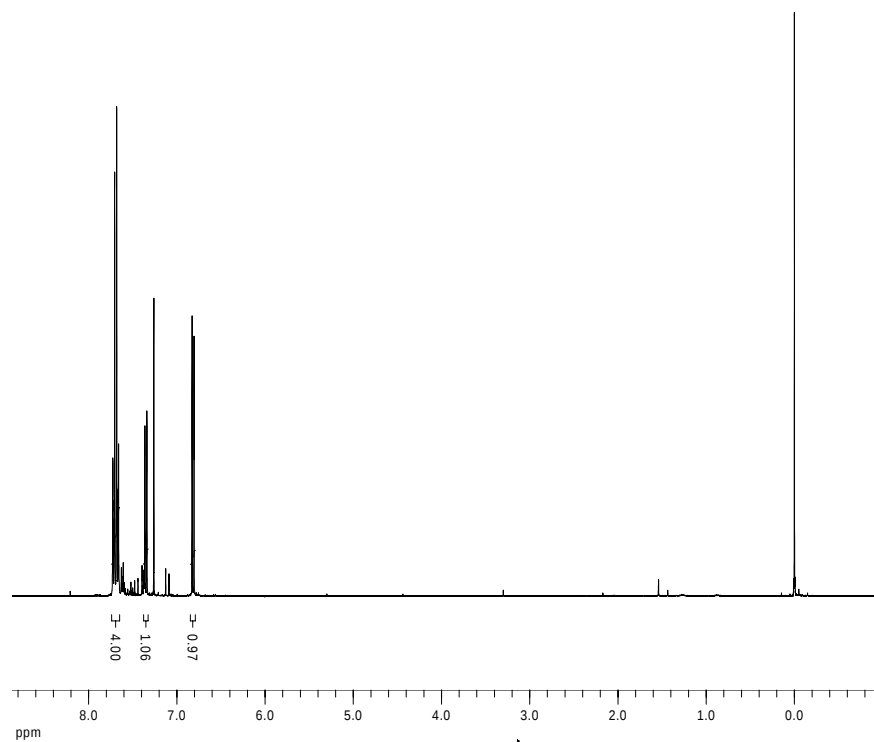
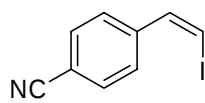
²⁴ Buckley, G.M.; Cooper, N.; Davenport, R.J.; Dyke, H.J.; Galleway, F.P.; Gowers, L.; Haughan, A.F.; Kendall, H.J.; Lowe, C.; Montana, J.G.; Oxford, J.; Peake, J.C.; Picken, L.; Richard, M.D.; Sabin, V.; Sharpe, A.; Warneck, J.B.H. *Bioorg. Med. Chem. Lett.* **2002**, 12, 509

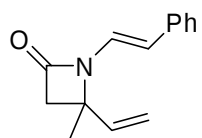
²⁵ New, J.S.; Christopher, W.L.; Yevich, J.P.; Butler, R.; Schlemmer Jr, F.; VanderMaelen, C.P.; Cipollina, J.A. *J. Med. Chem.* **1989**, 32, 1147



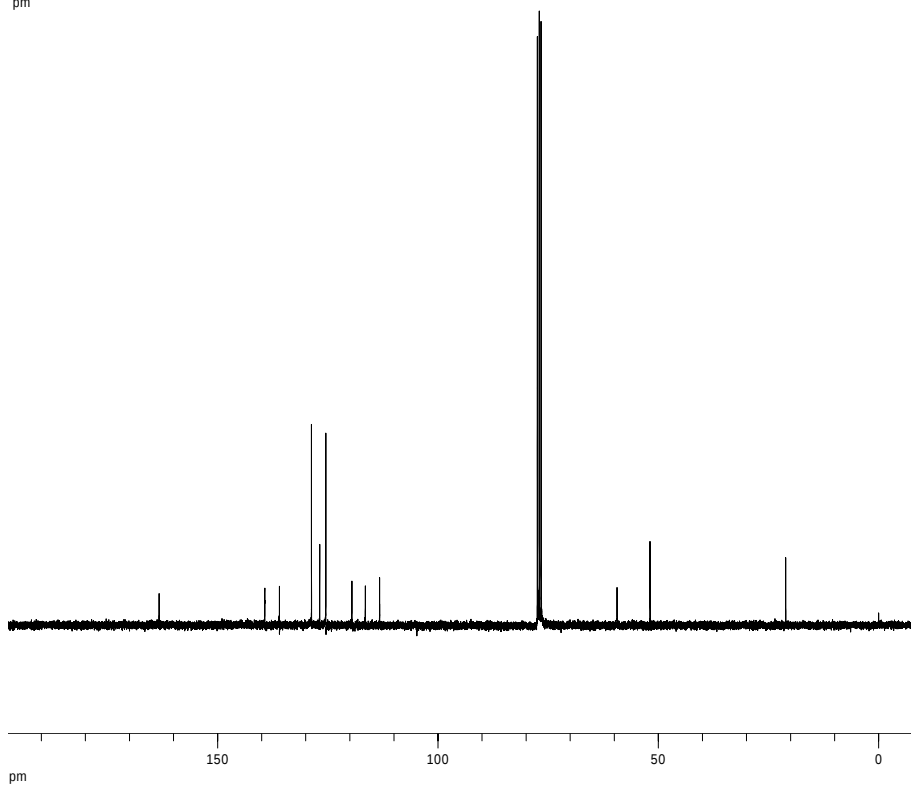
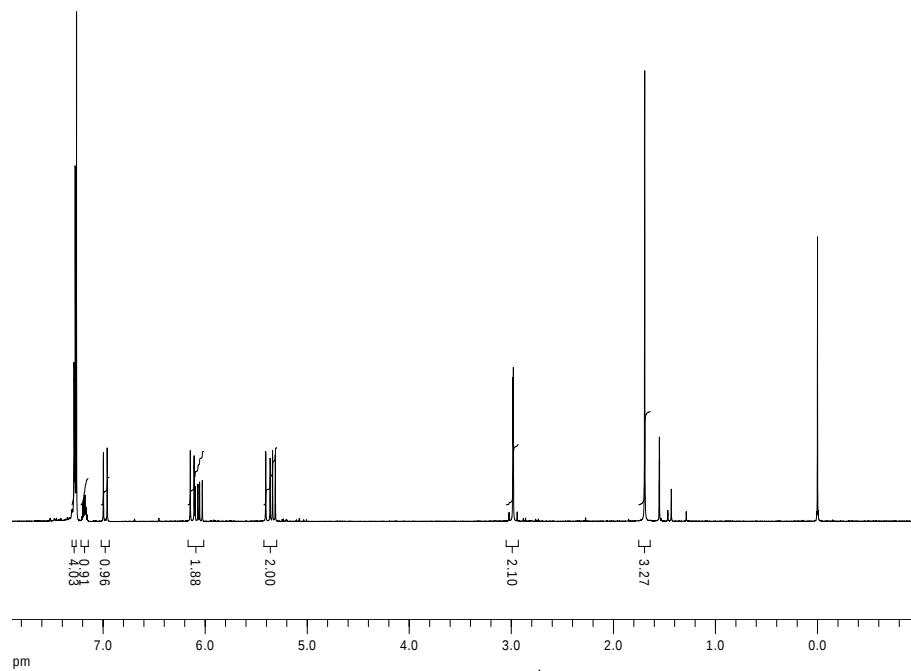


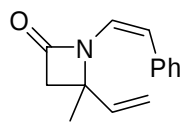




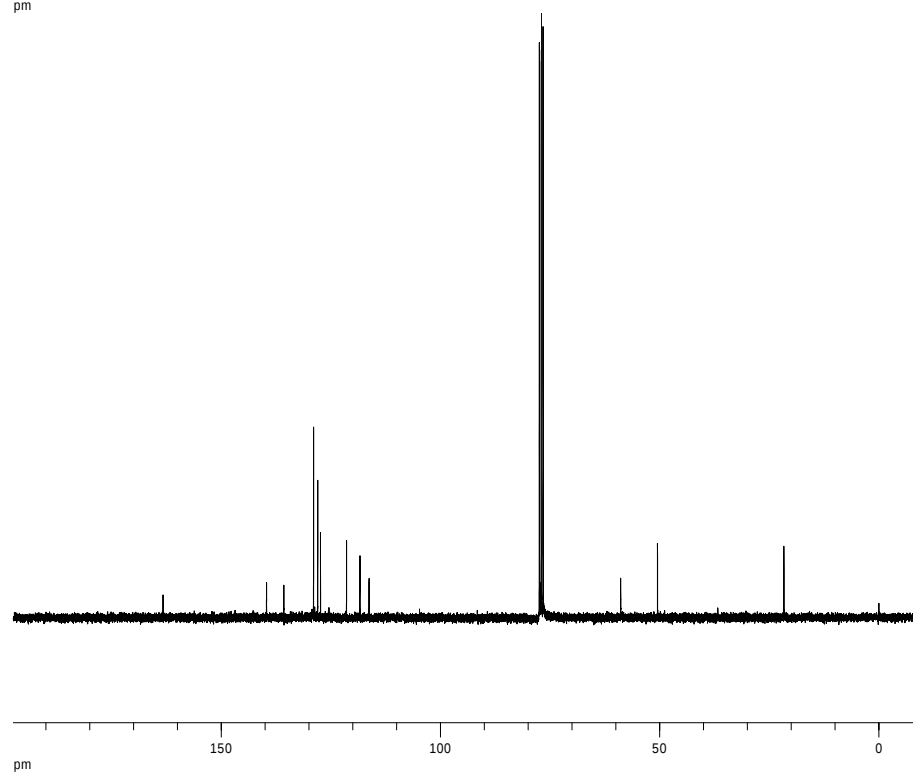
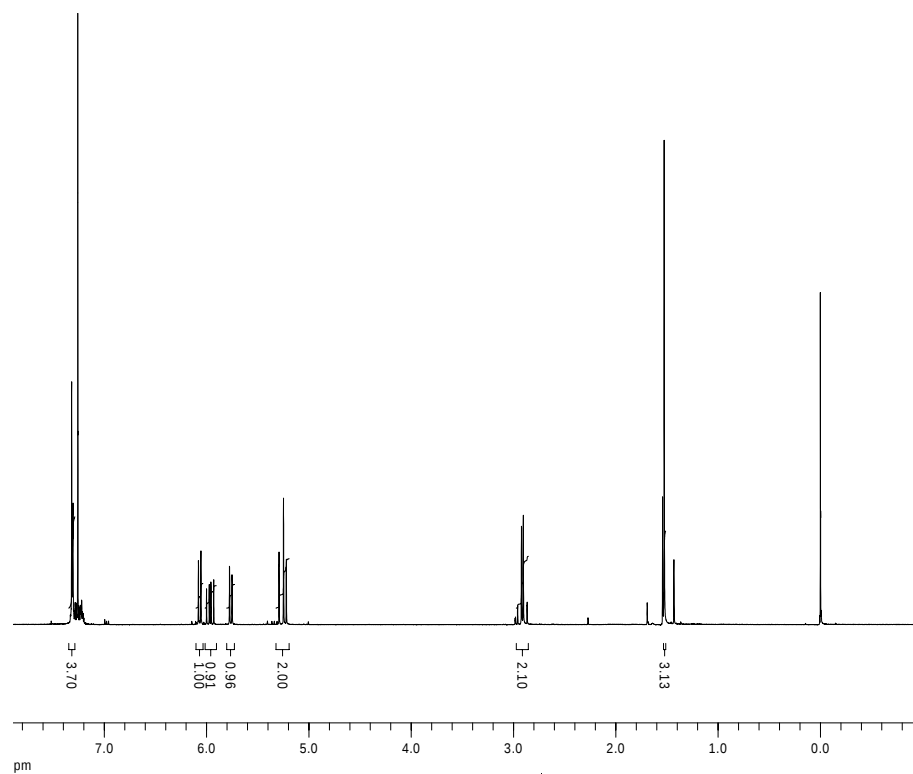


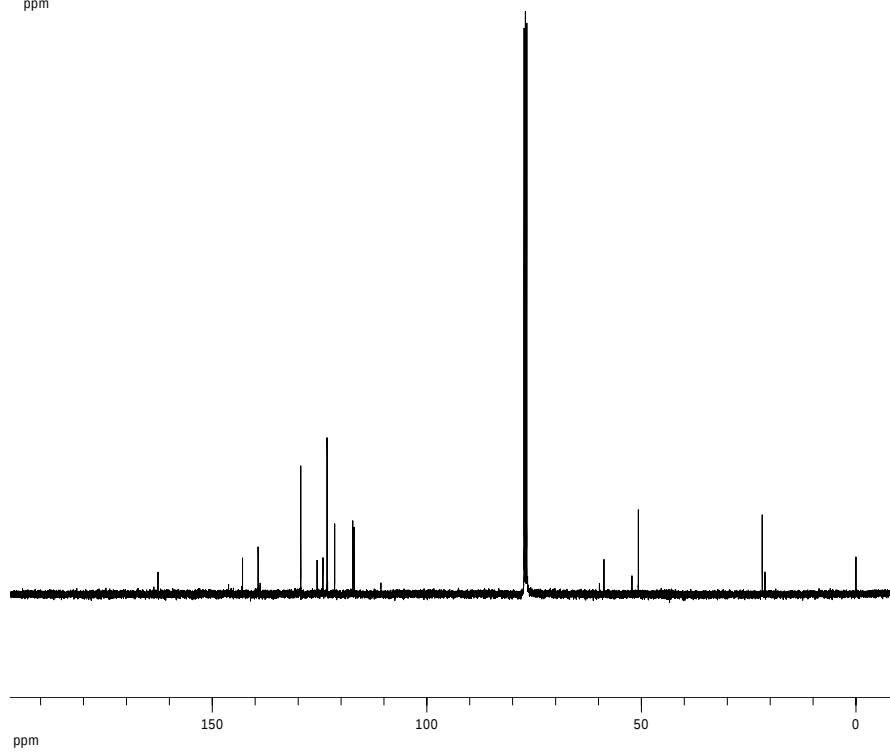
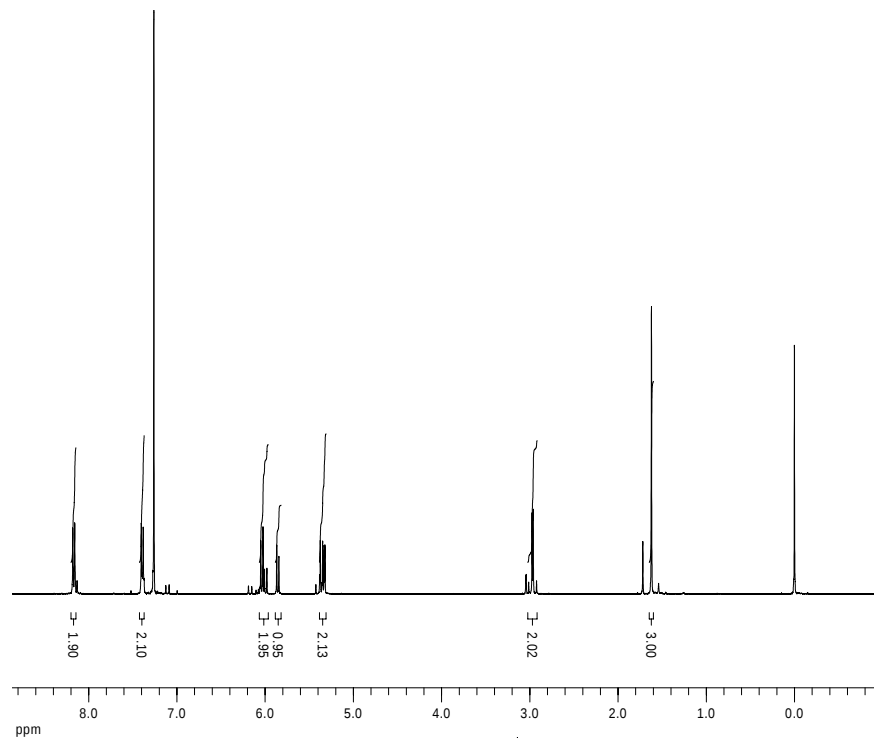
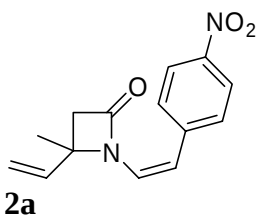
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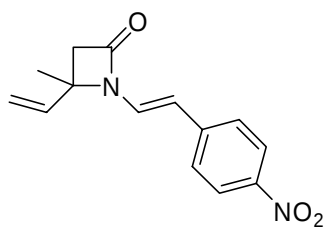




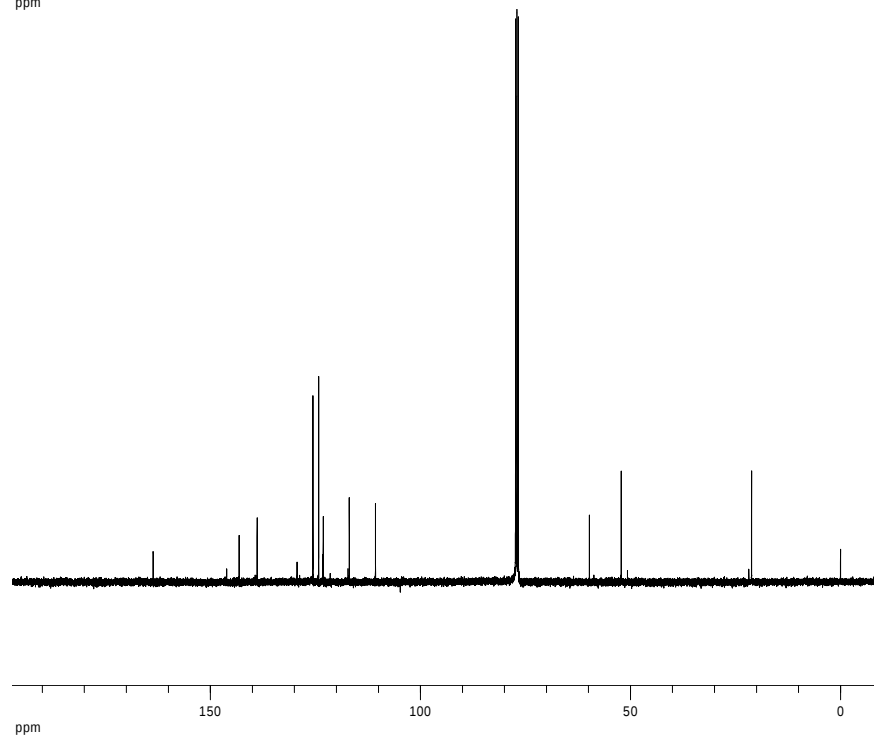
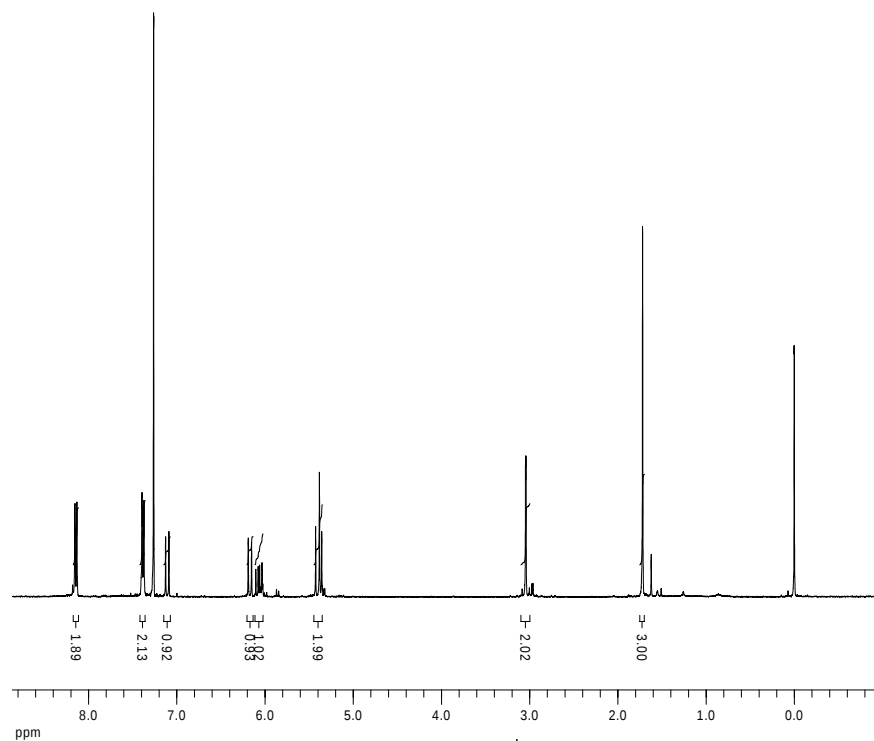
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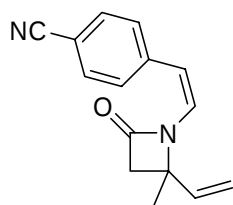




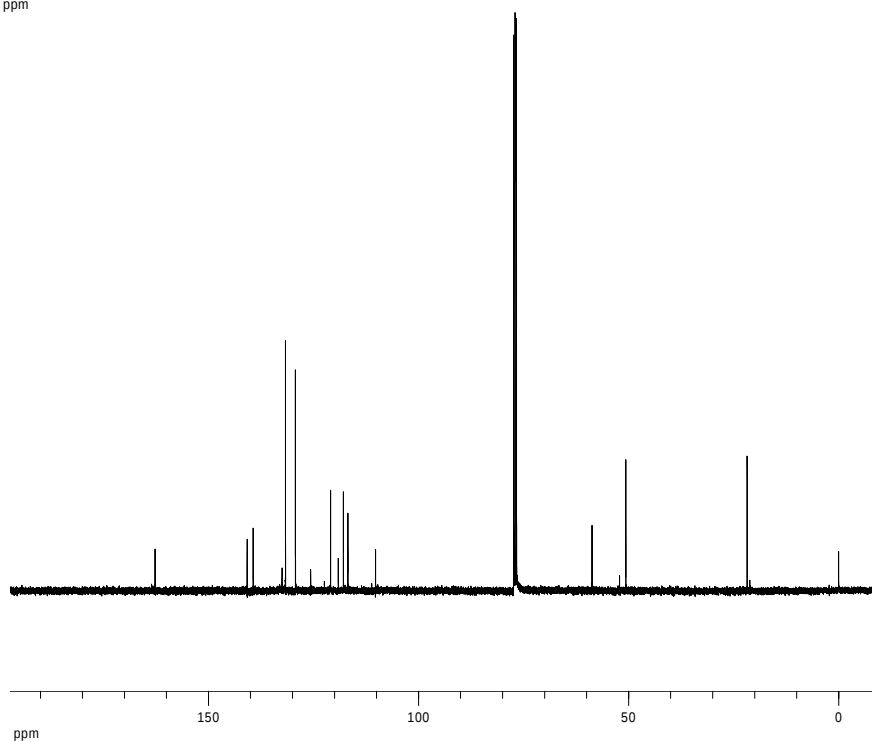
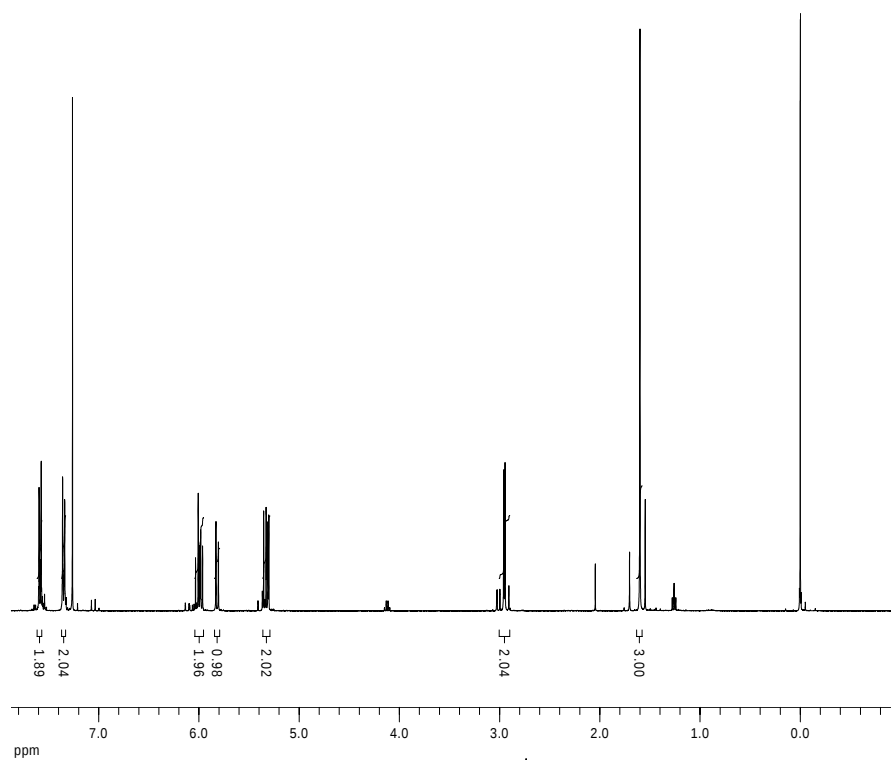


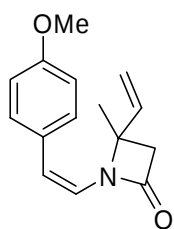
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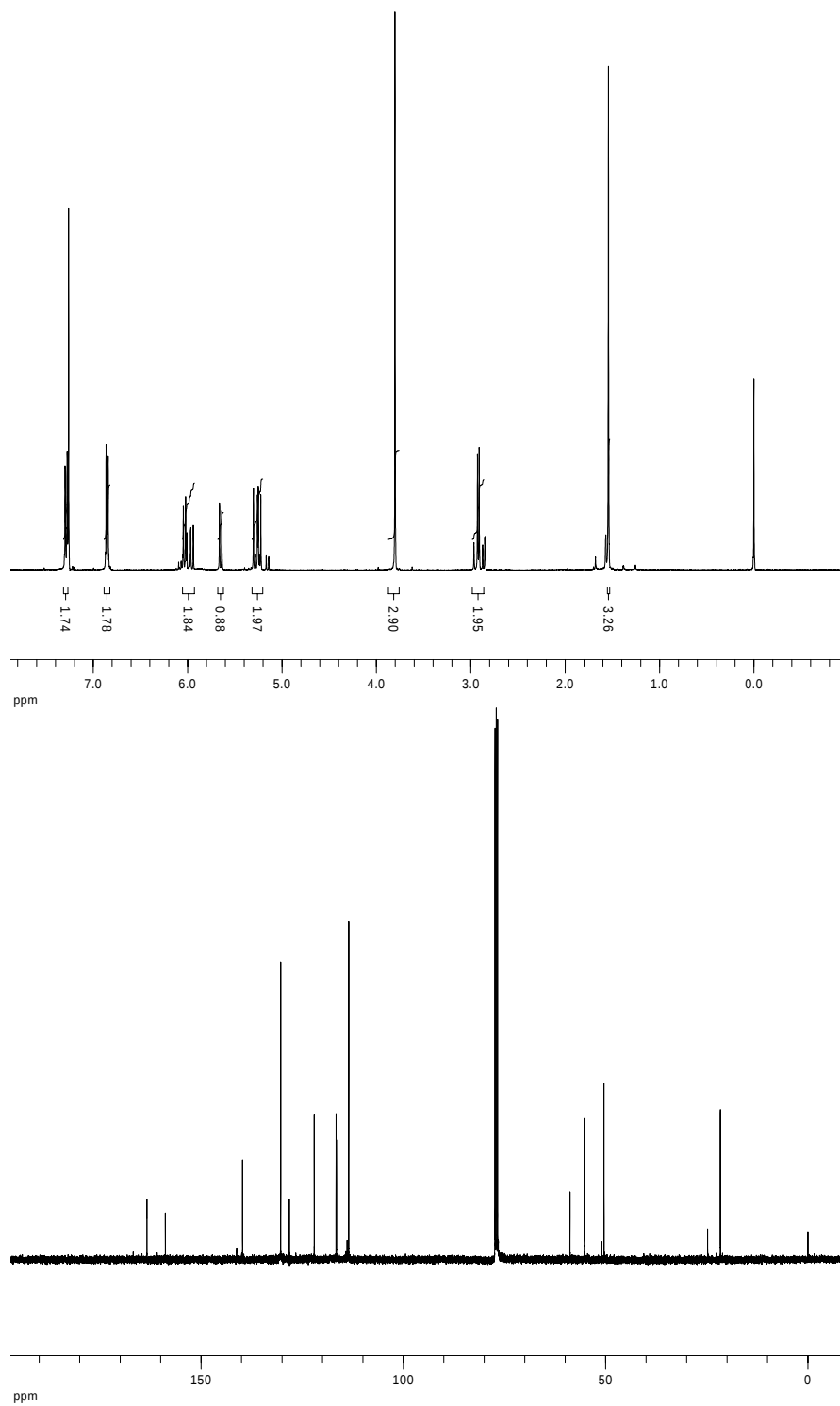


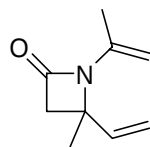
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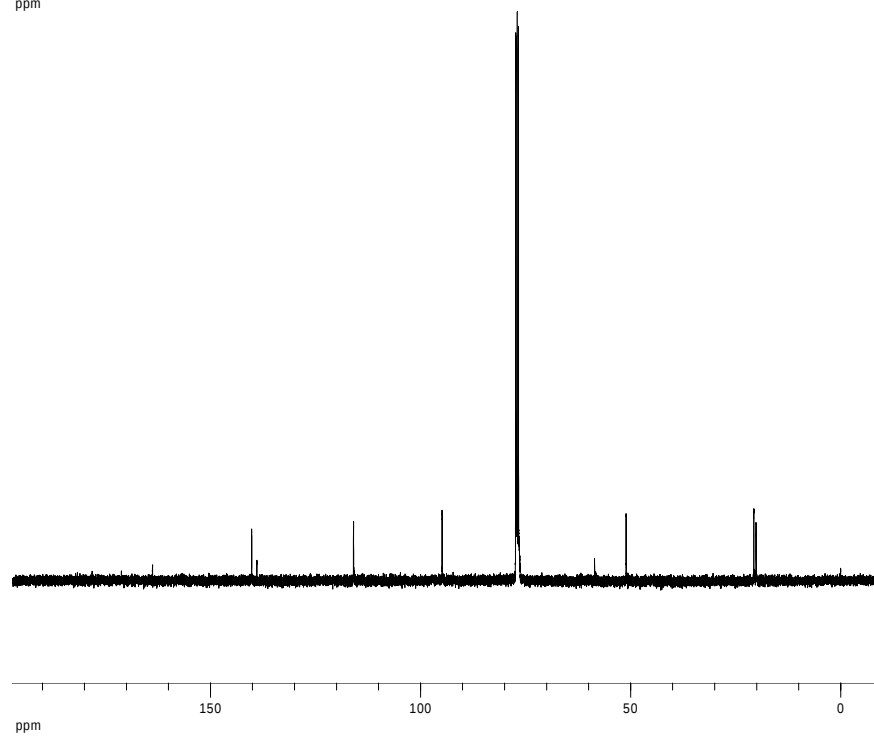
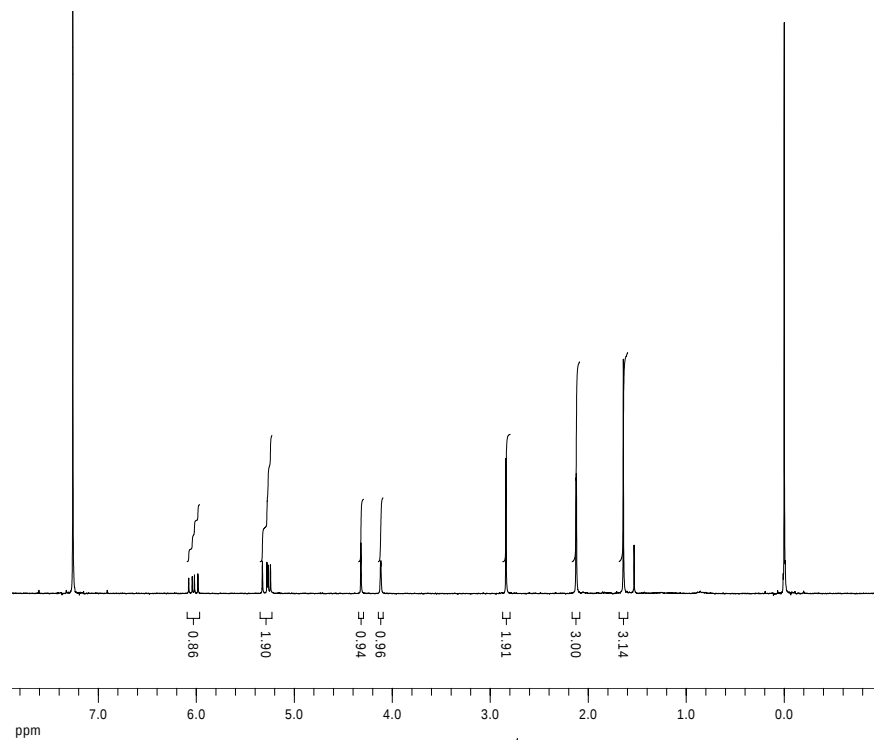


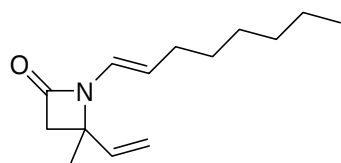
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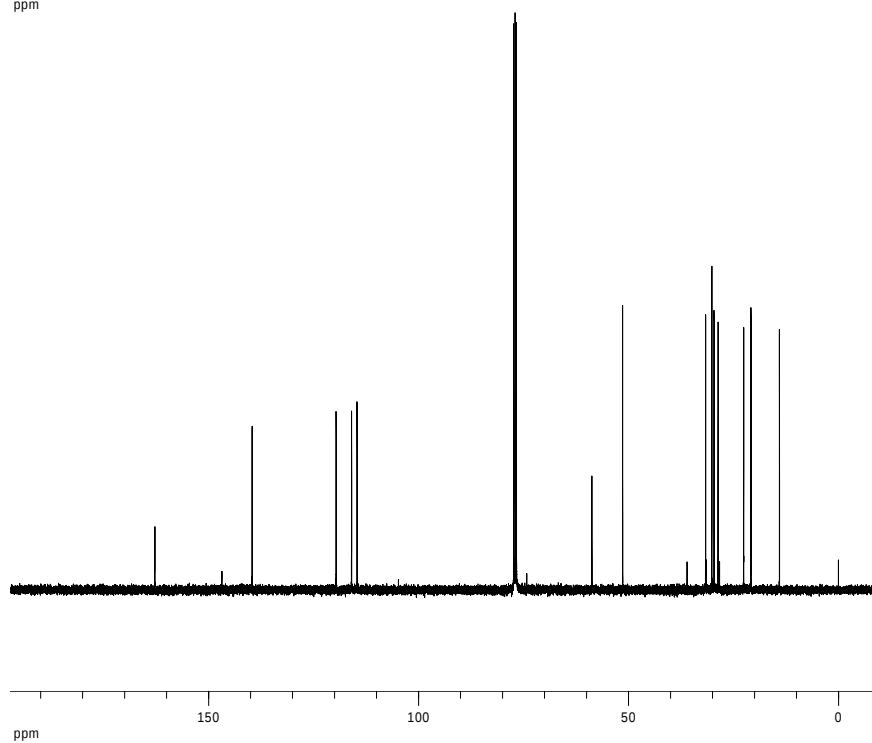
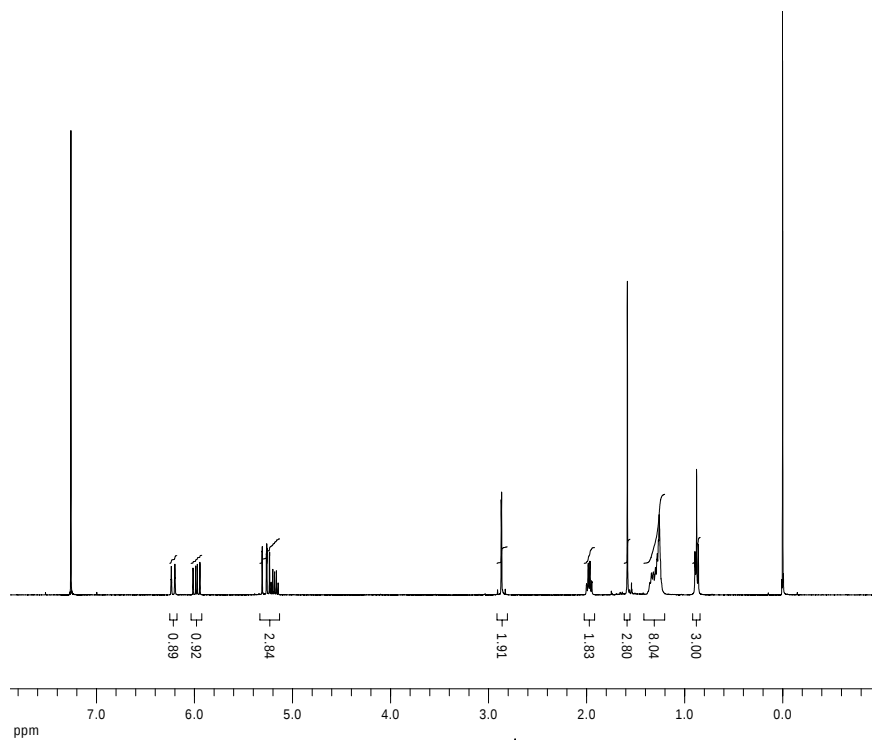


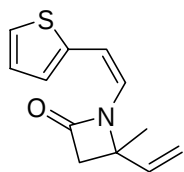
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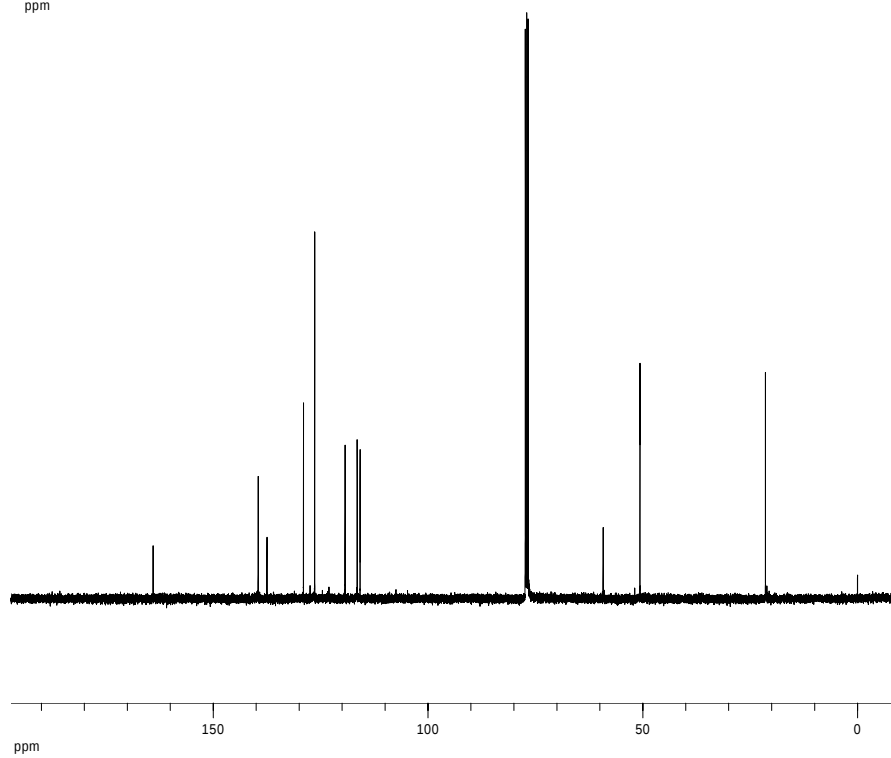
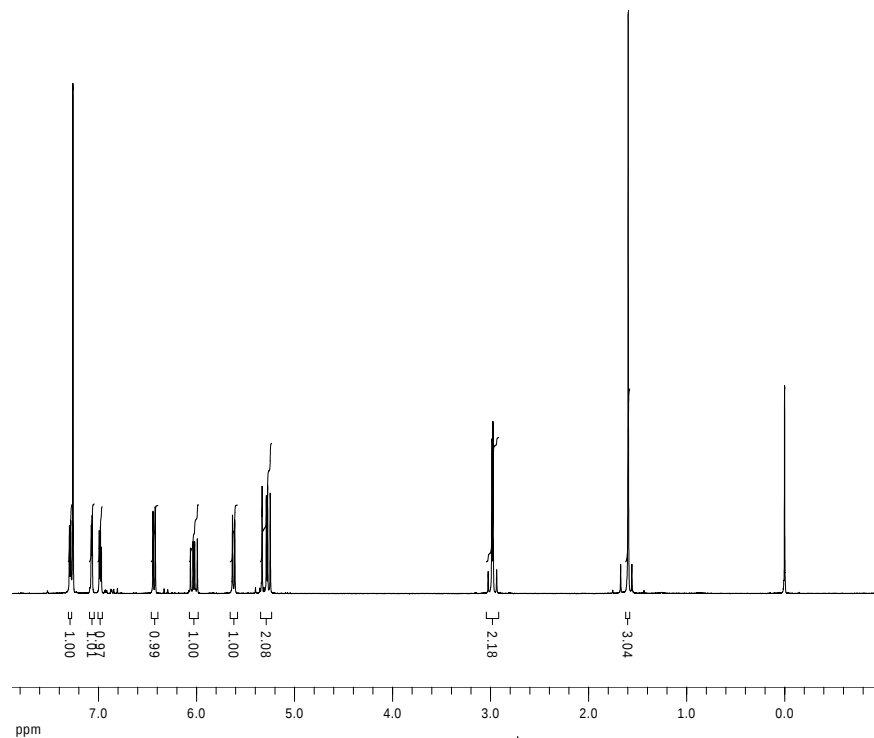


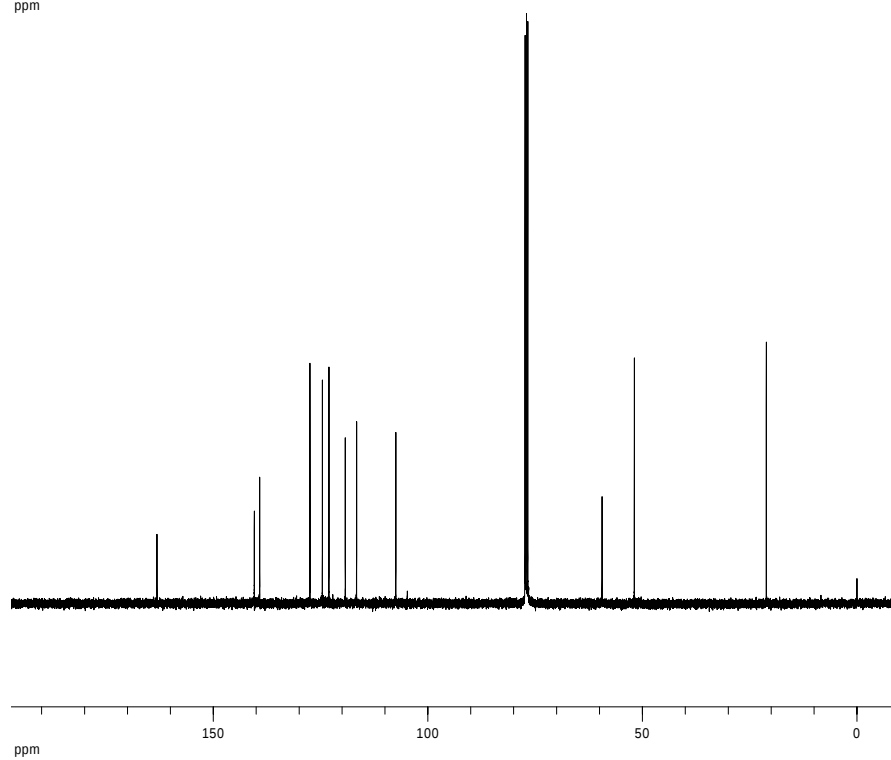
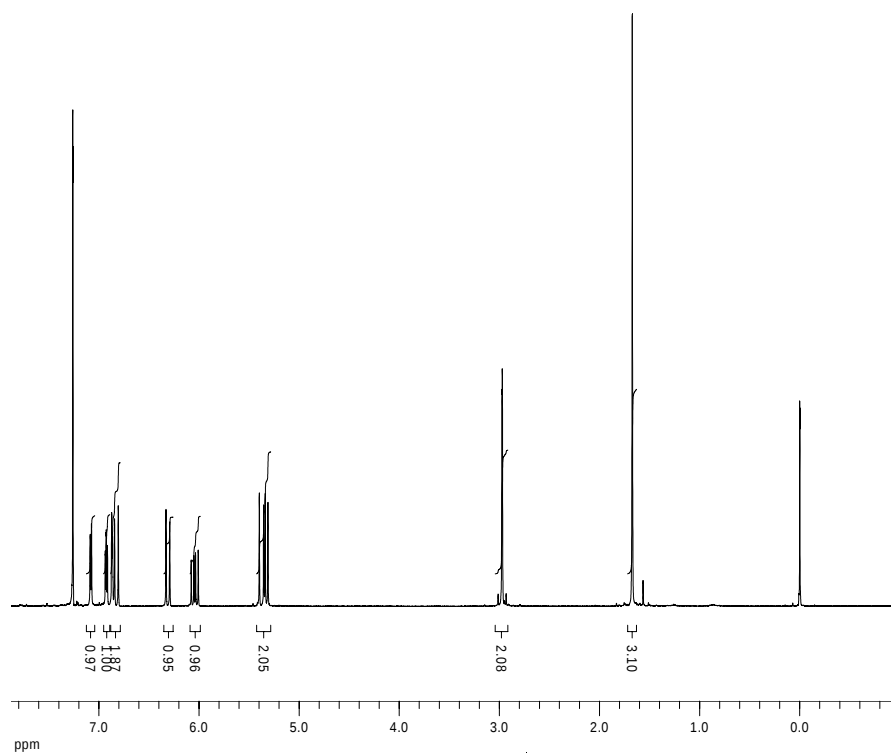
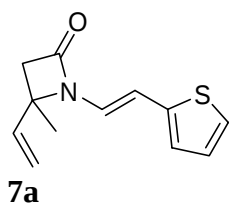
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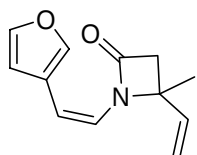




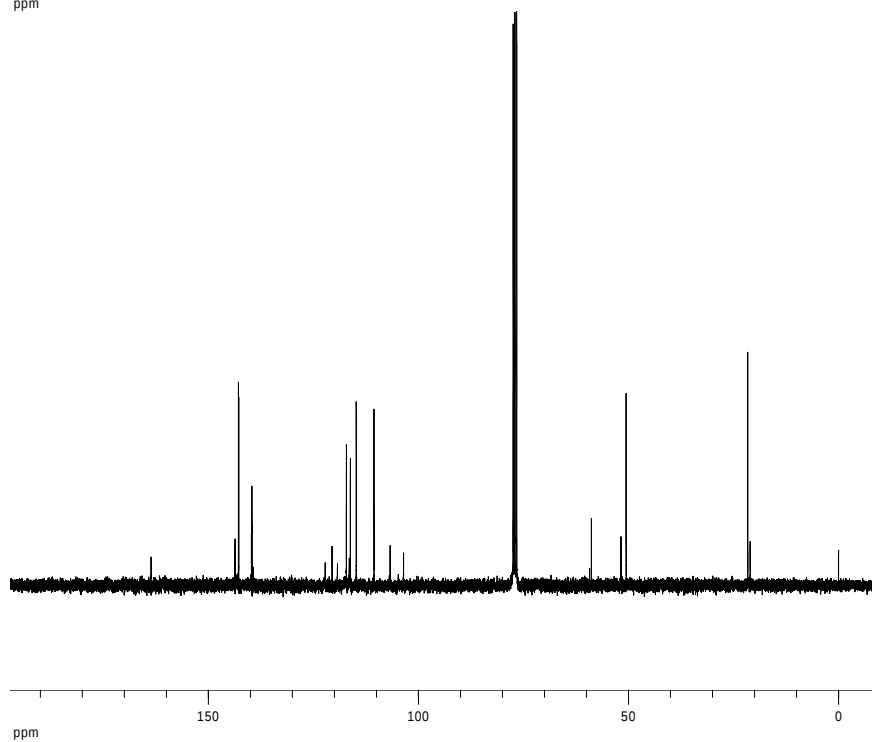
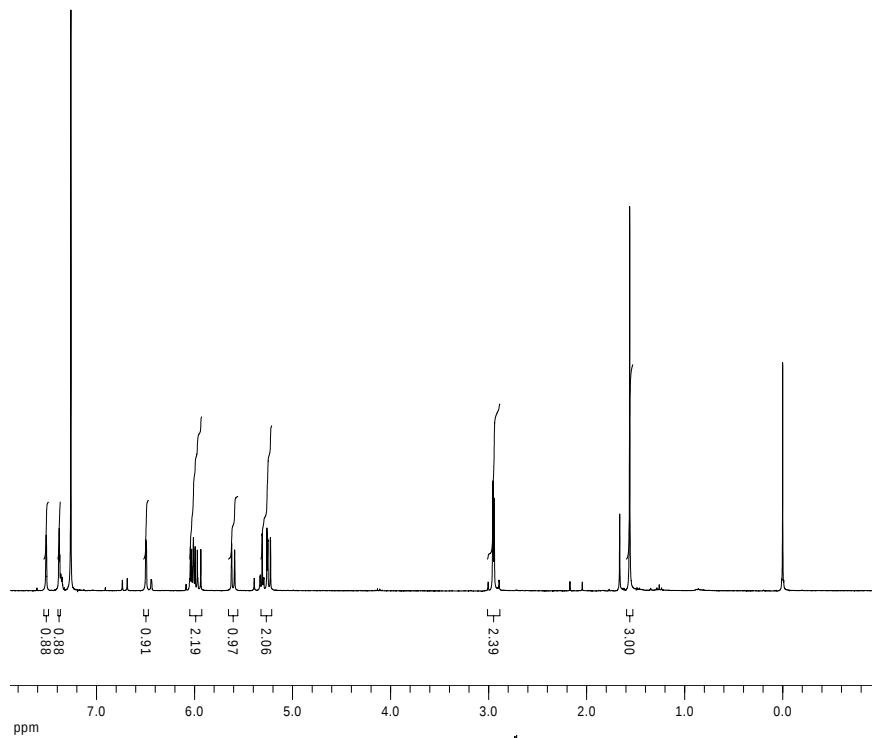
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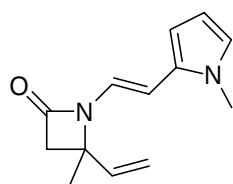




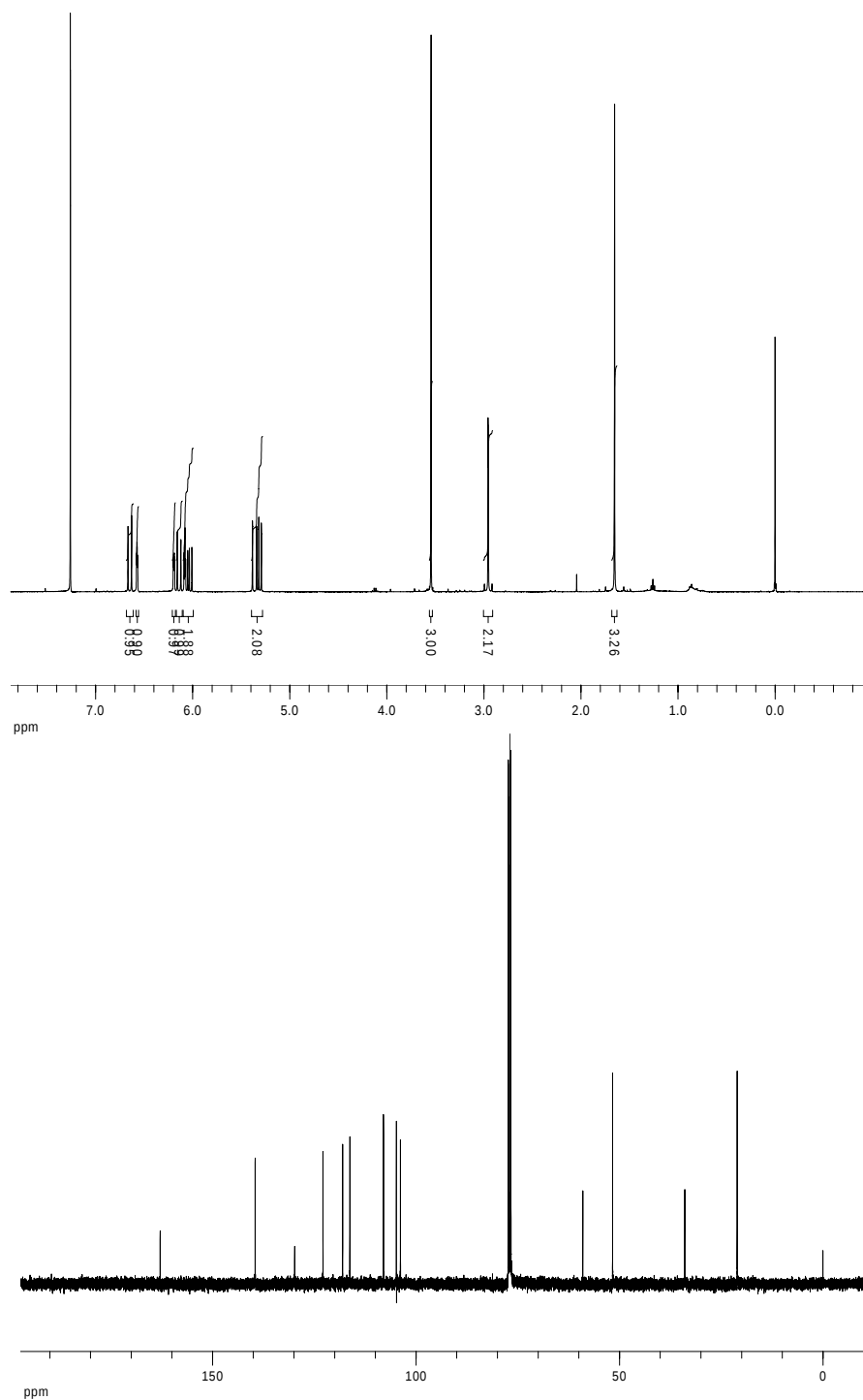


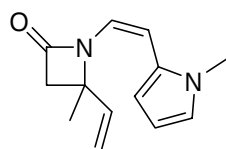
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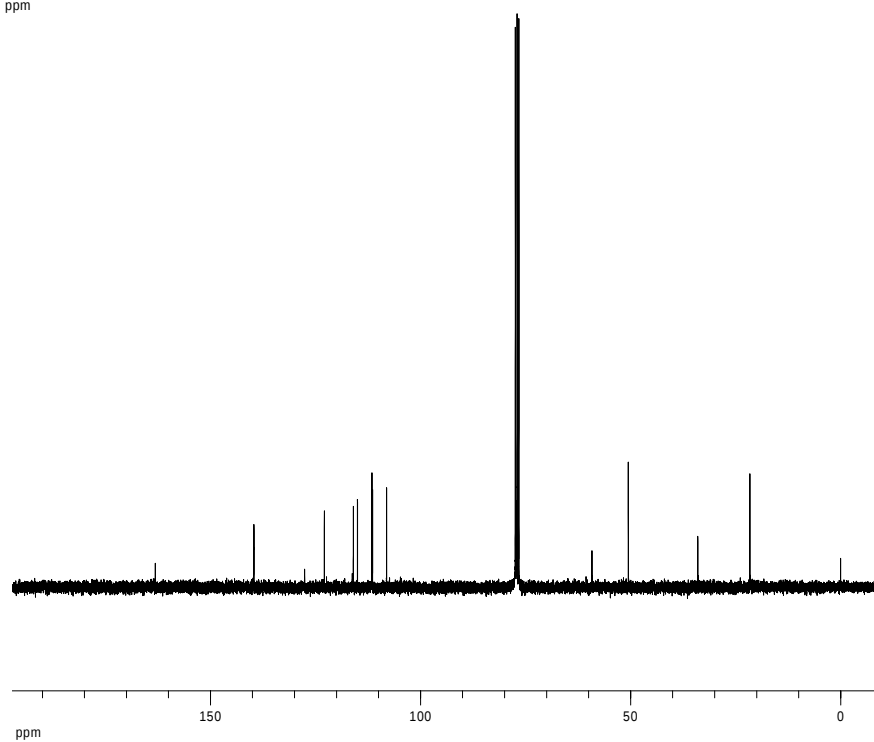
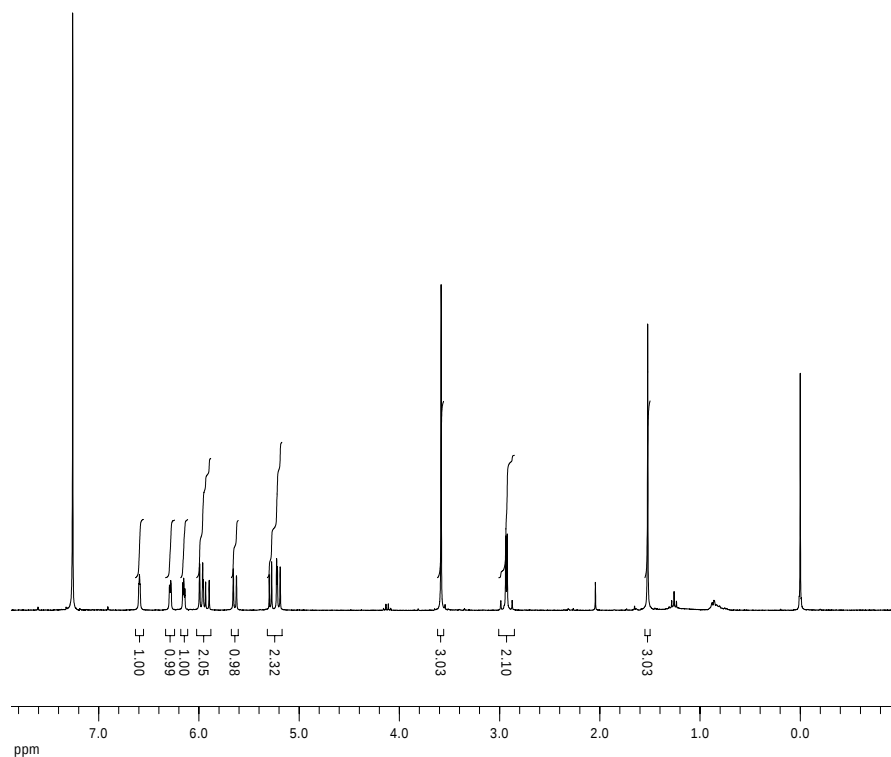


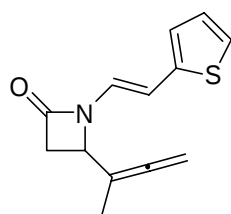
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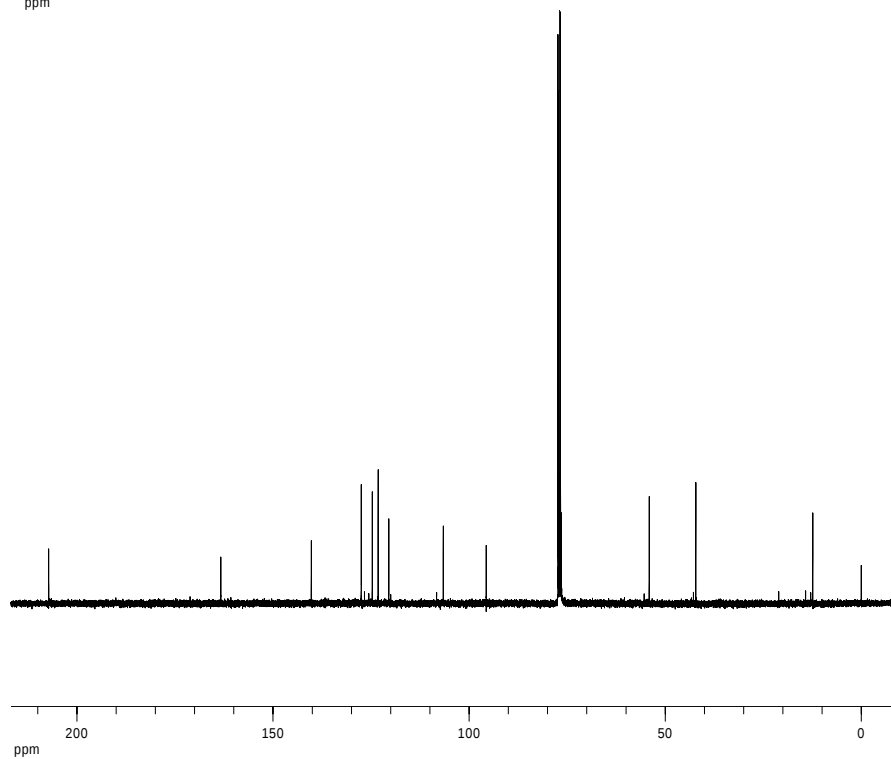
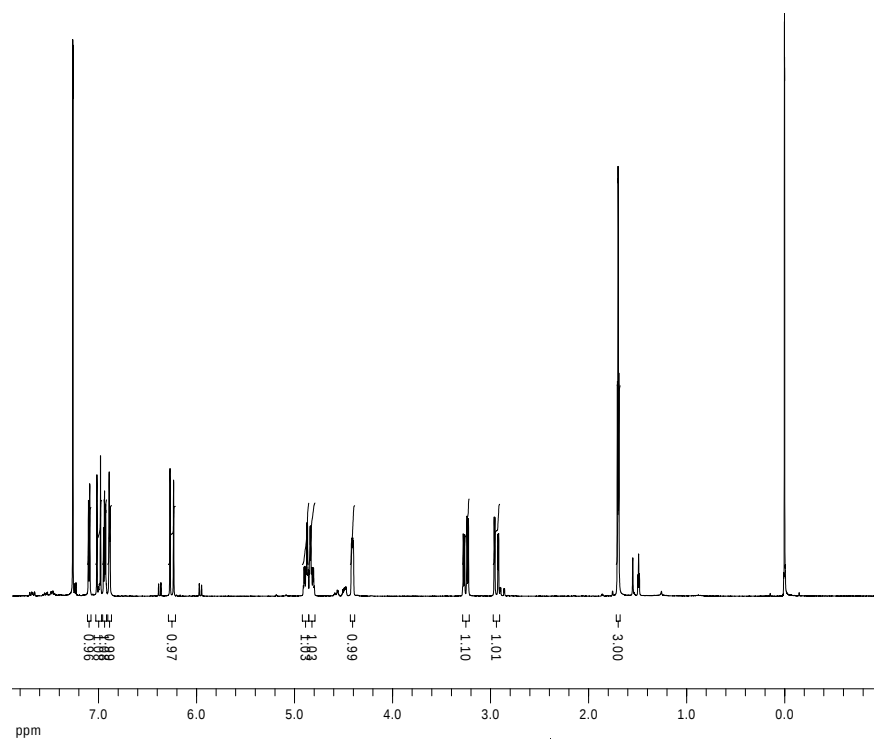


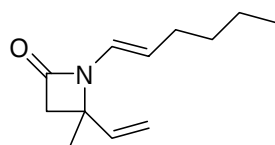
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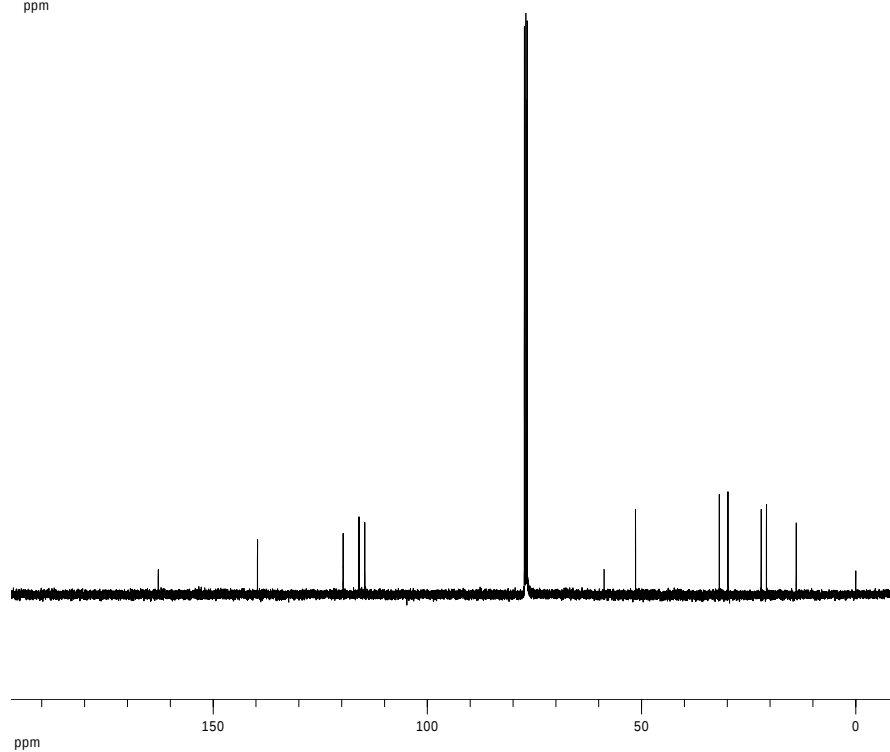
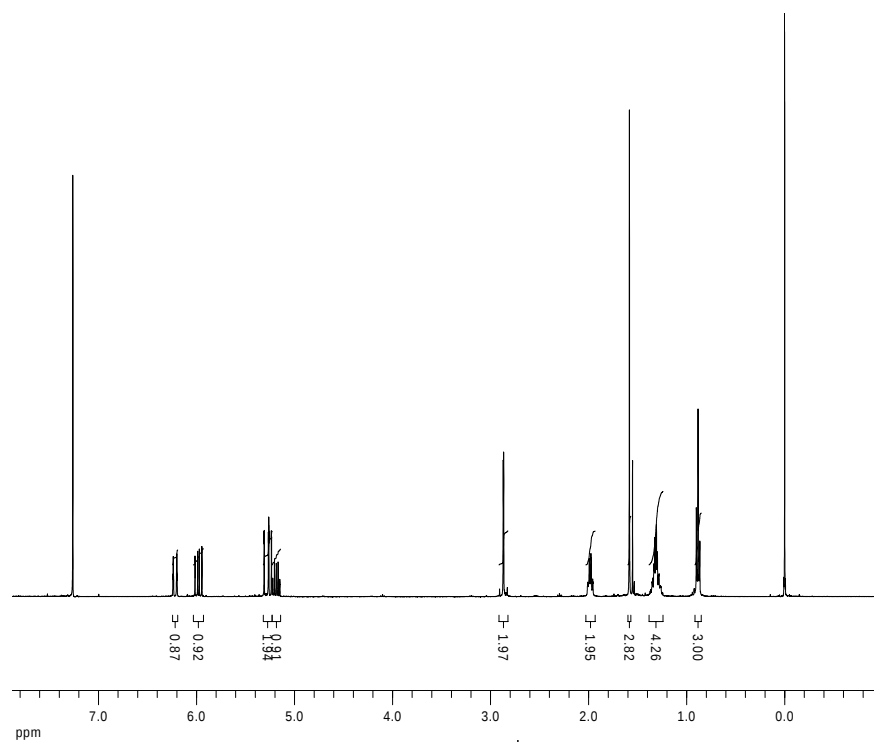


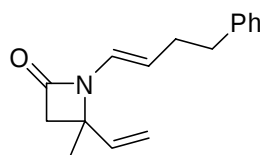
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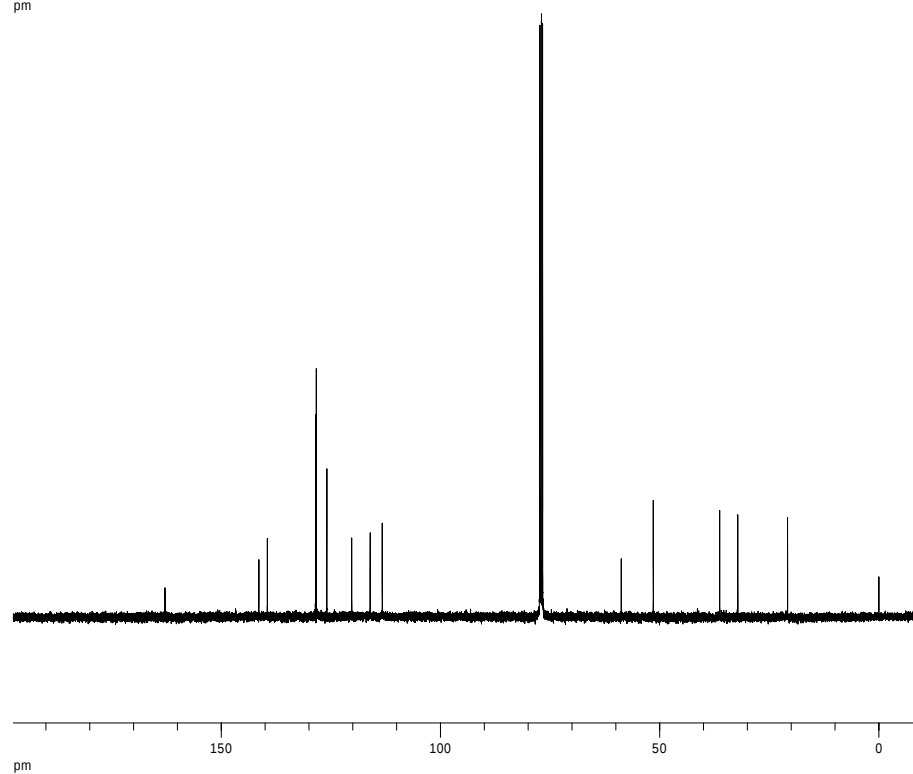
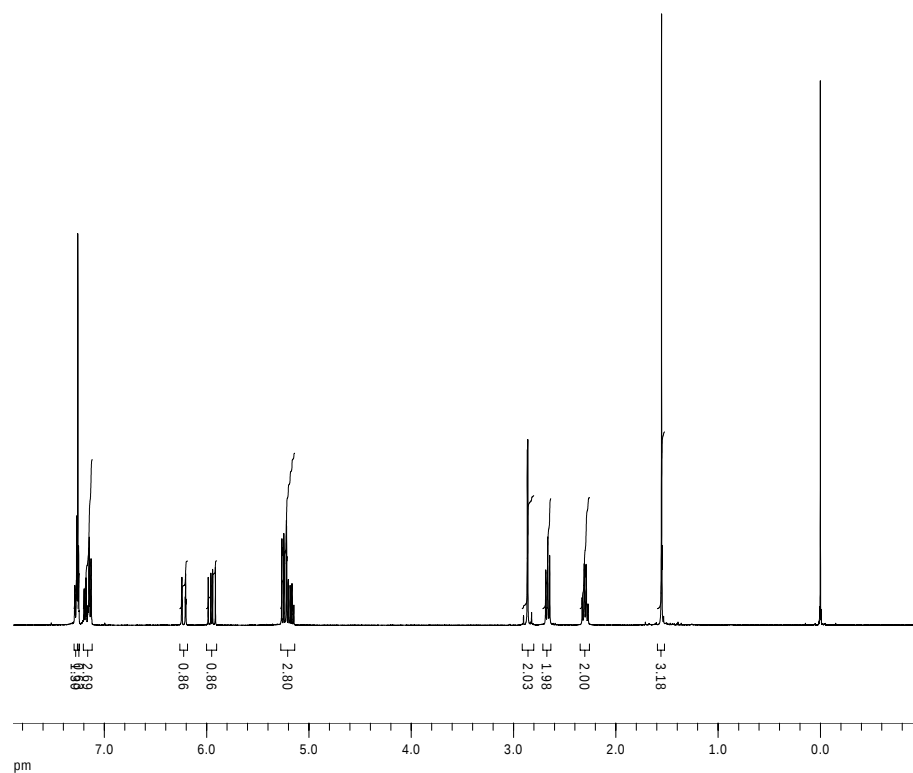


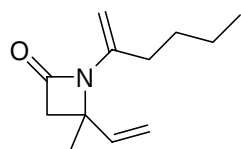
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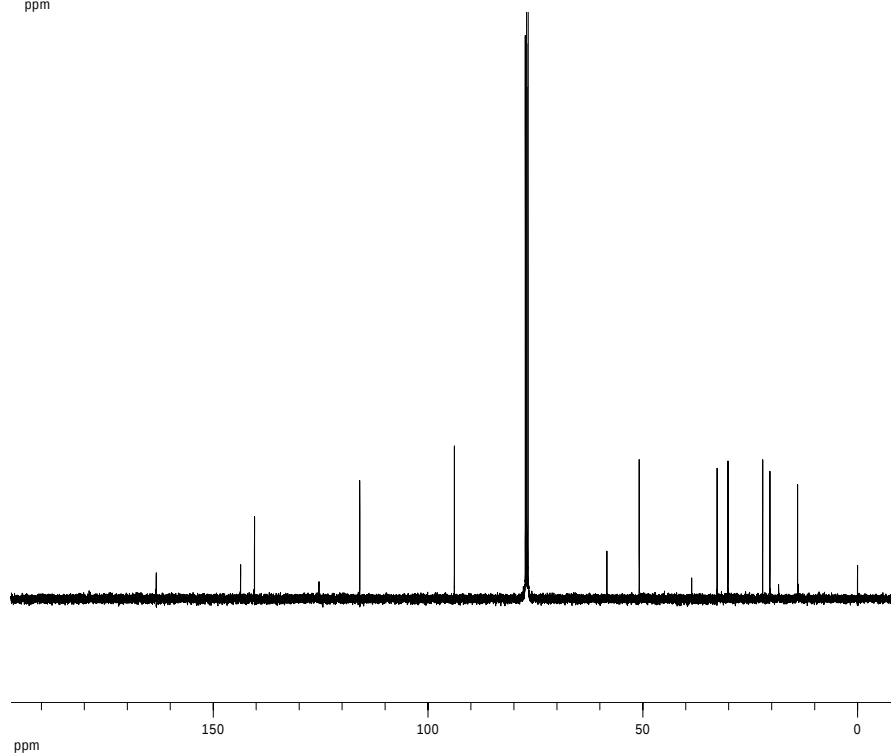
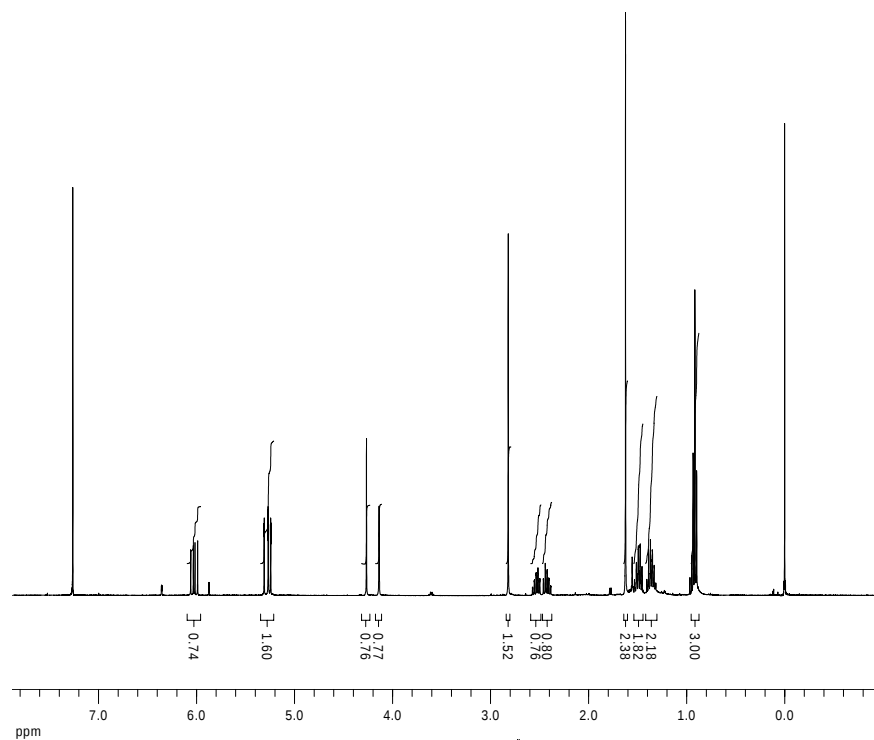


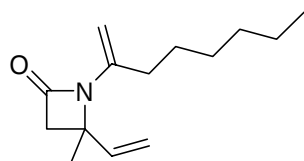
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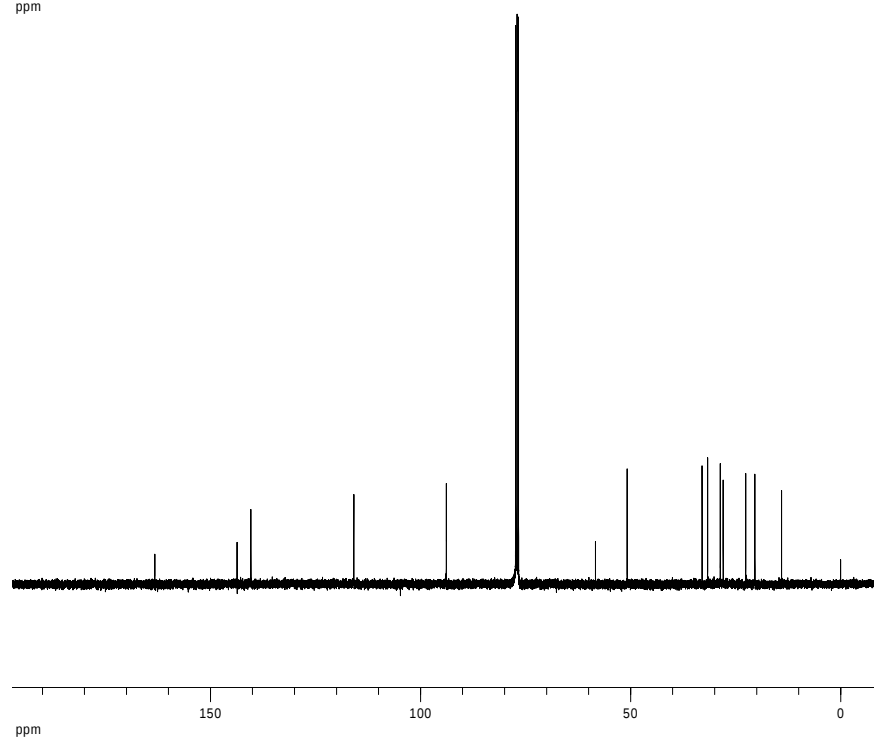
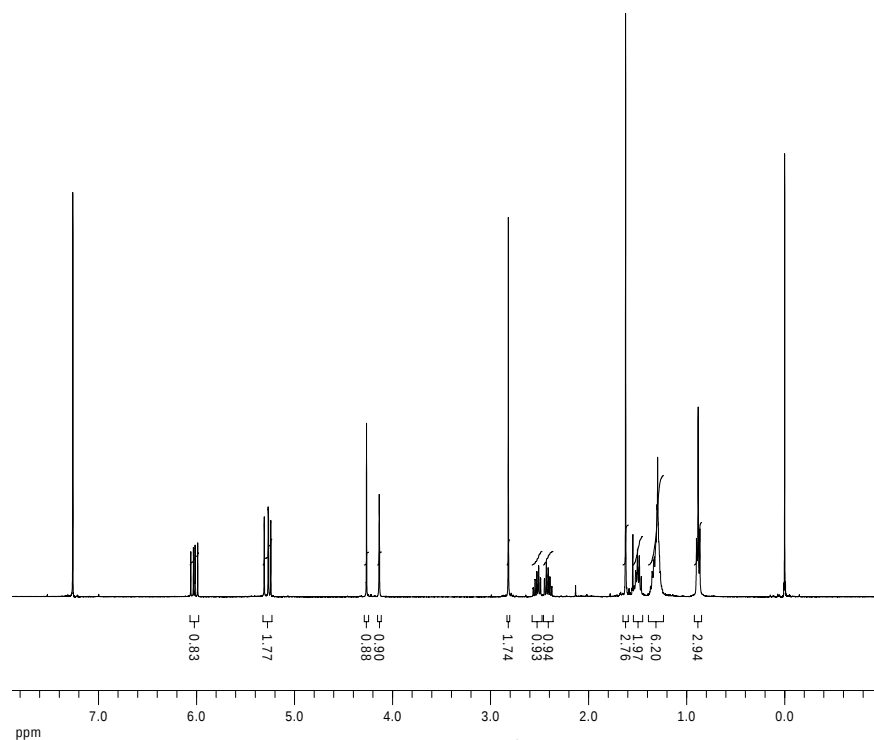


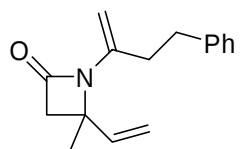
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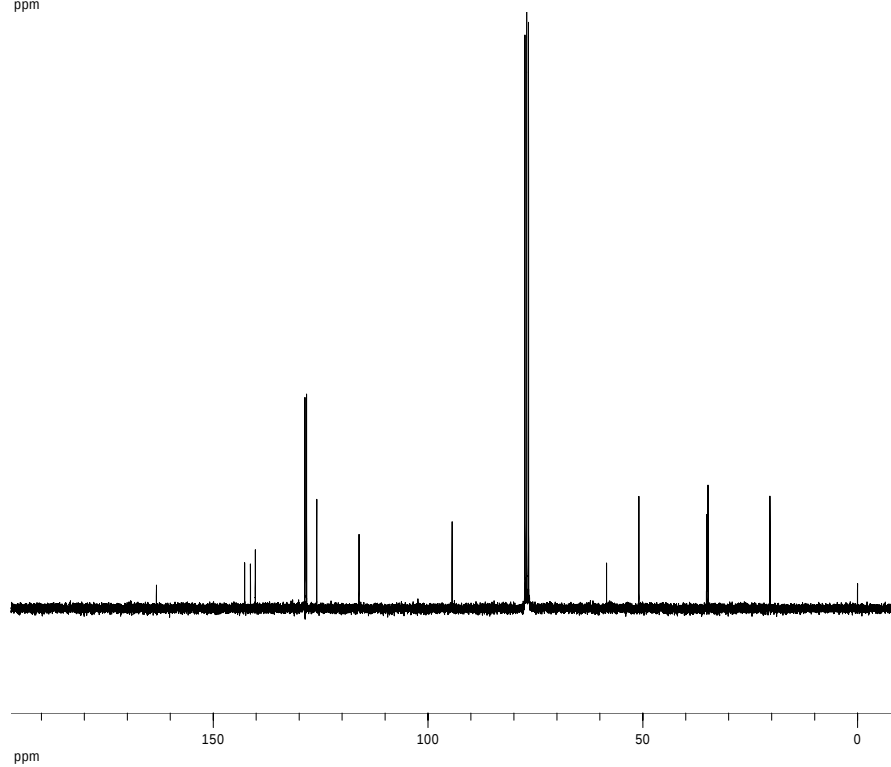
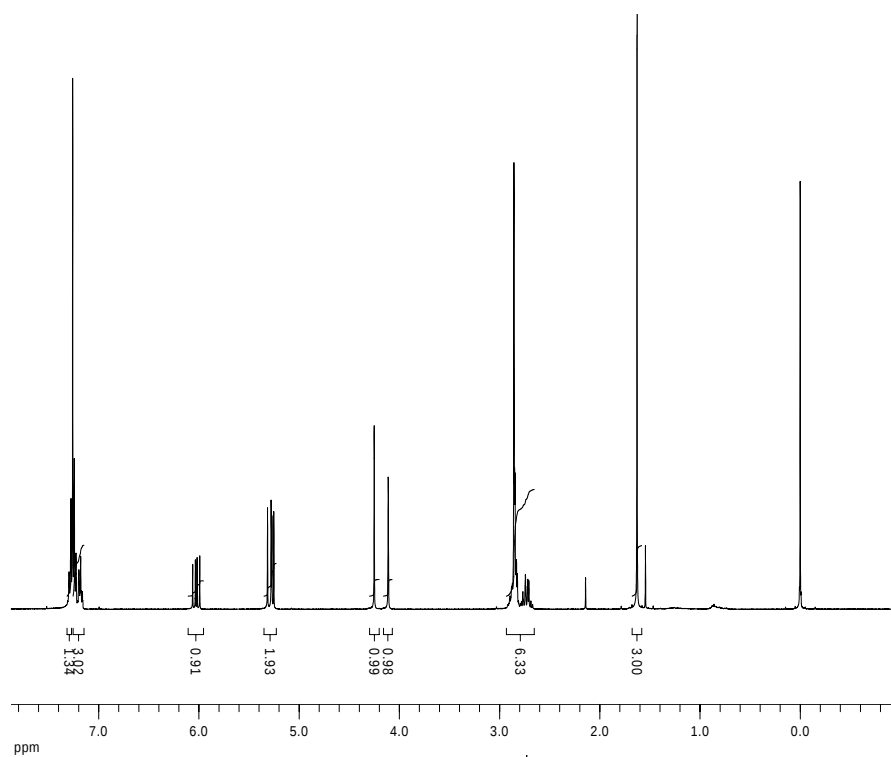


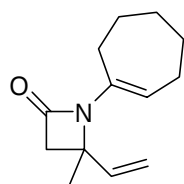
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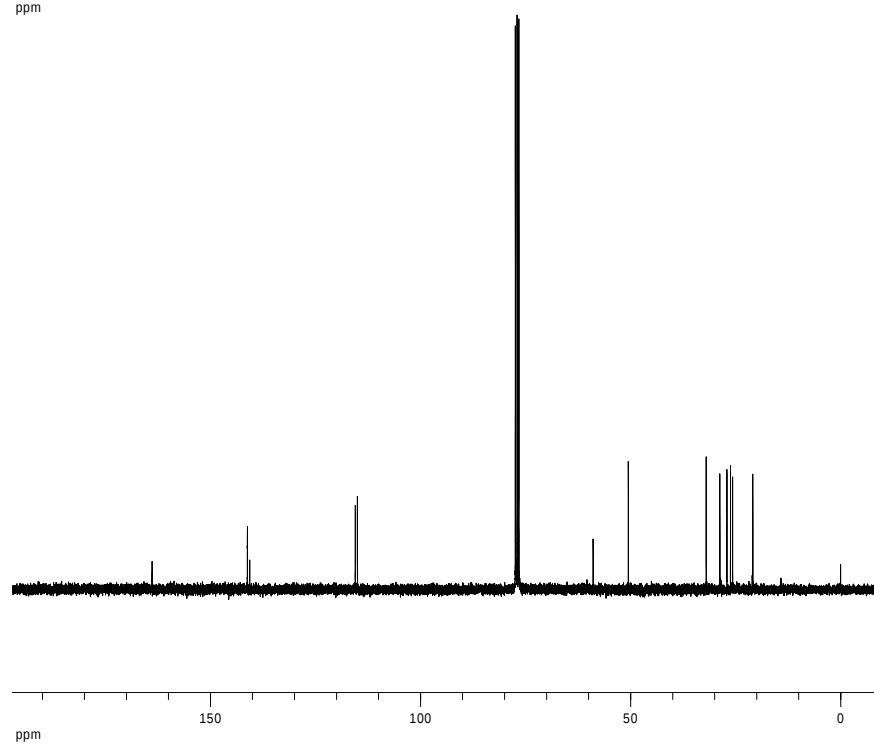
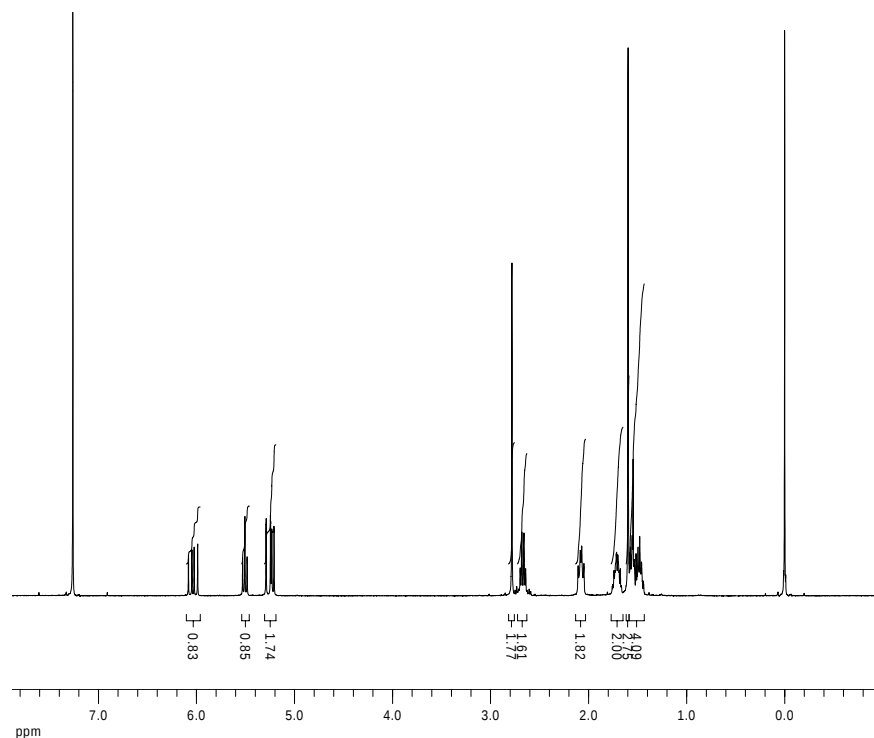


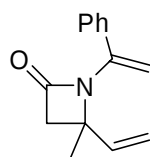
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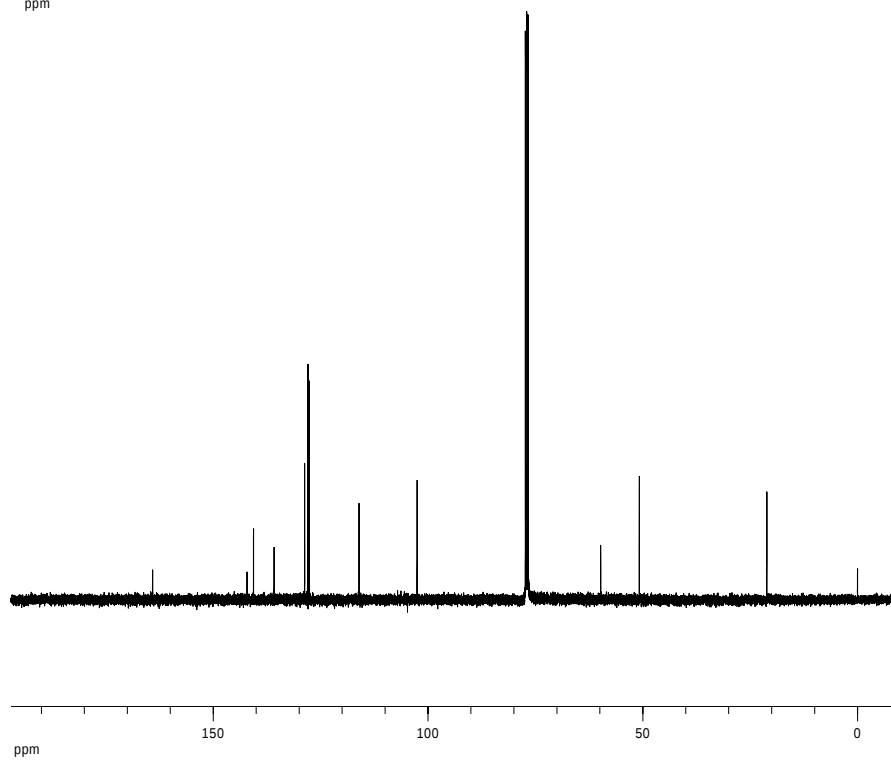
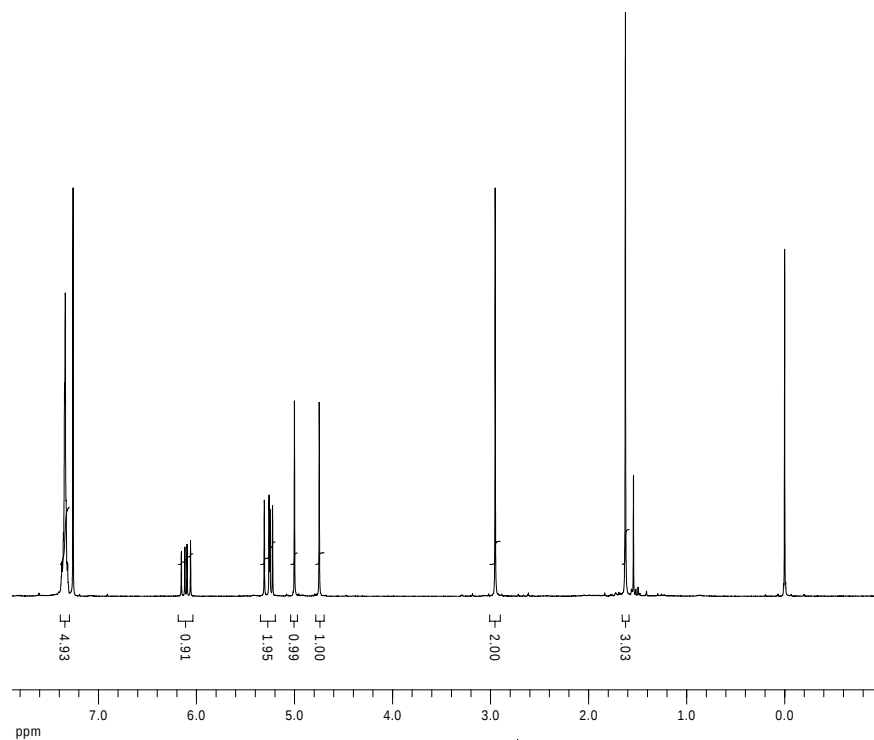


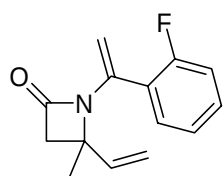
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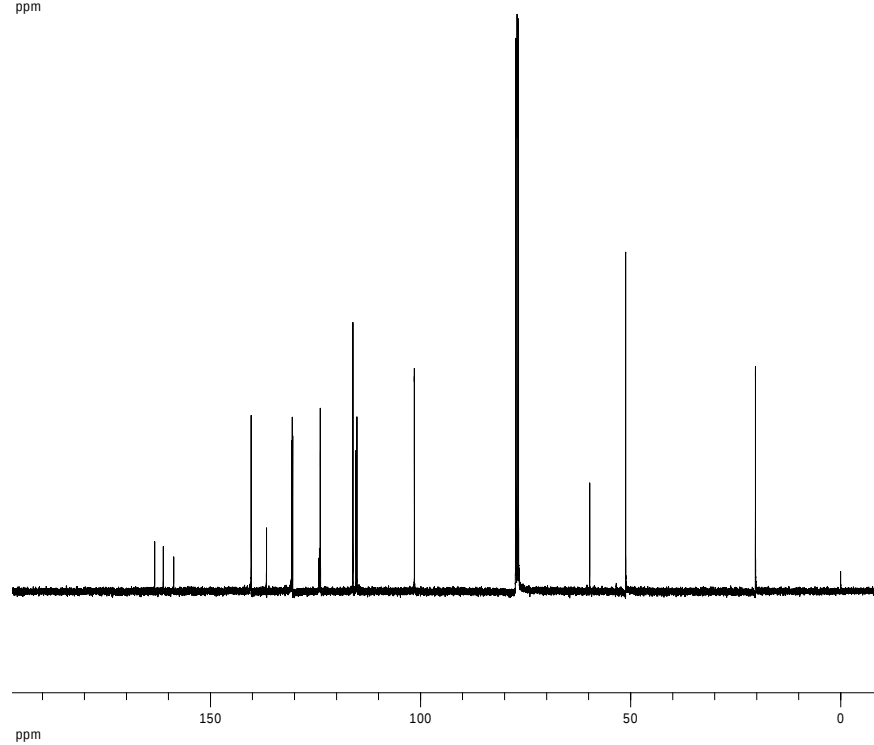
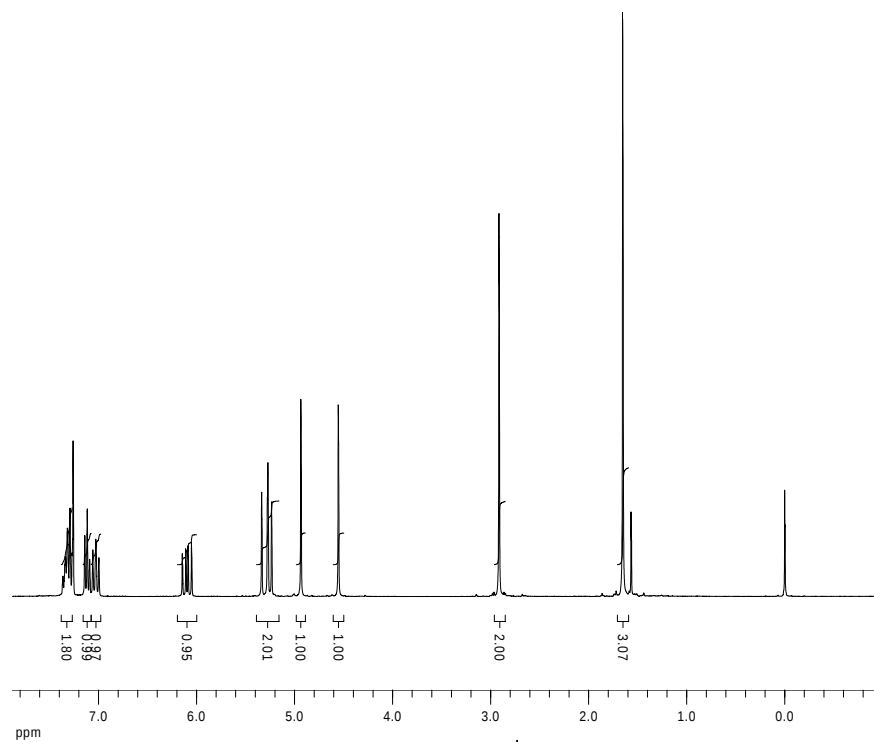


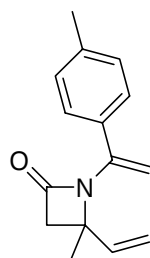
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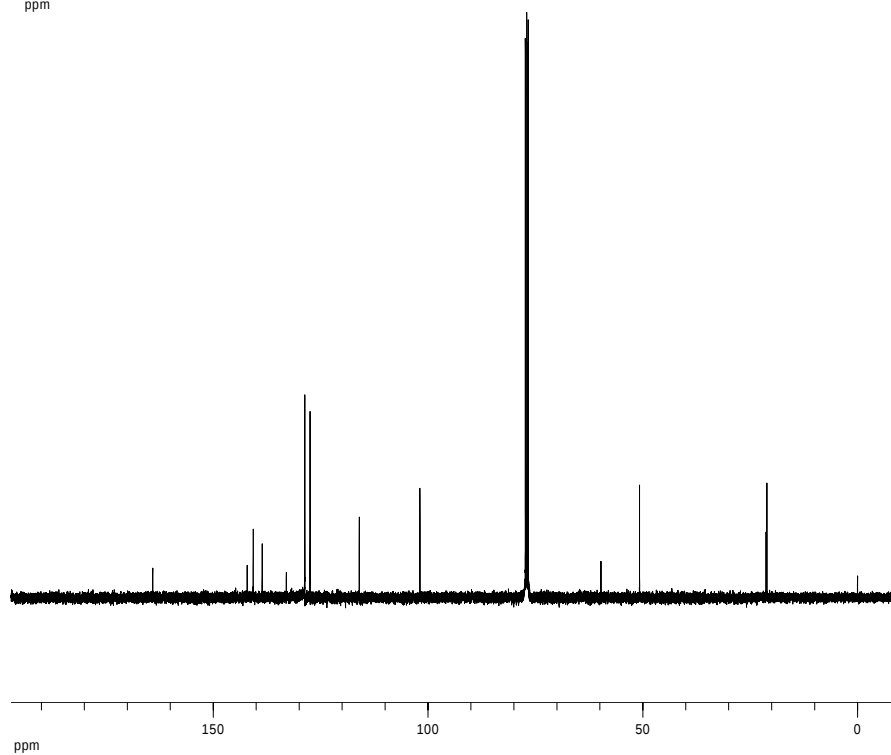
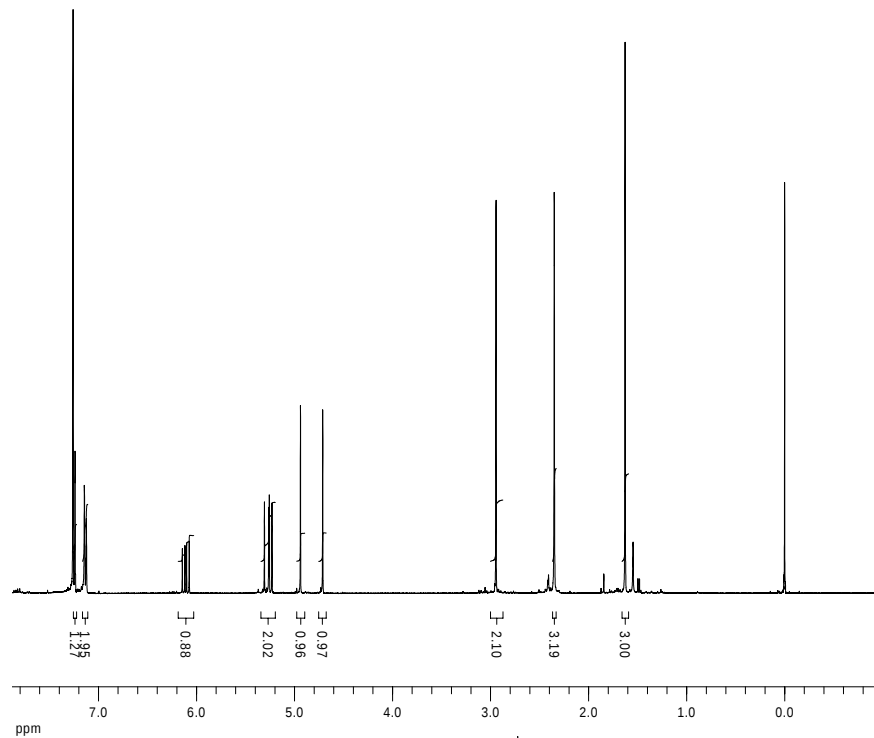


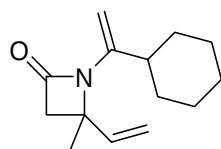
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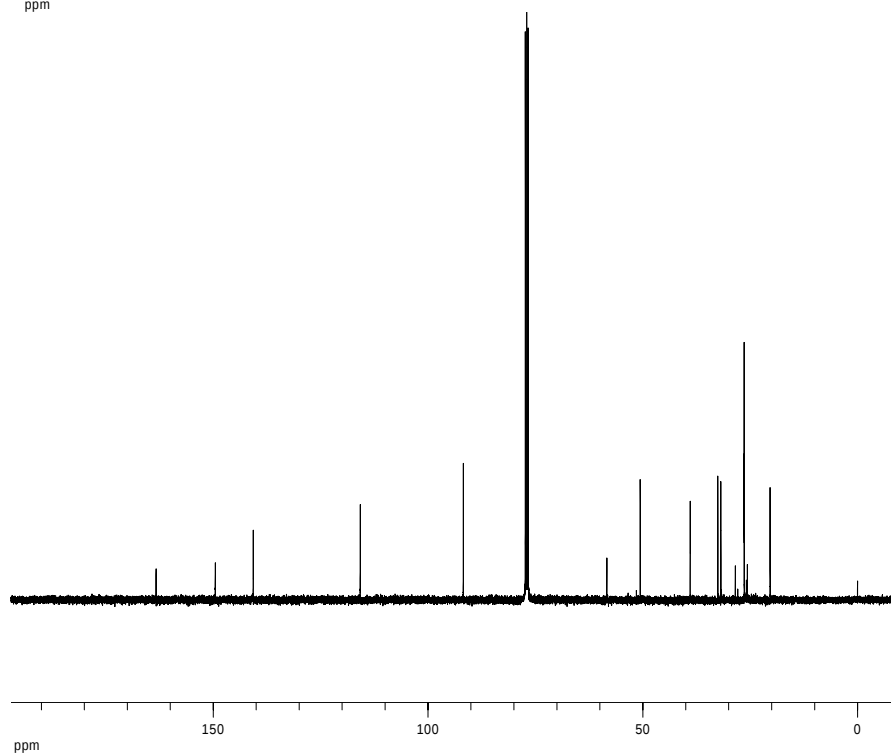
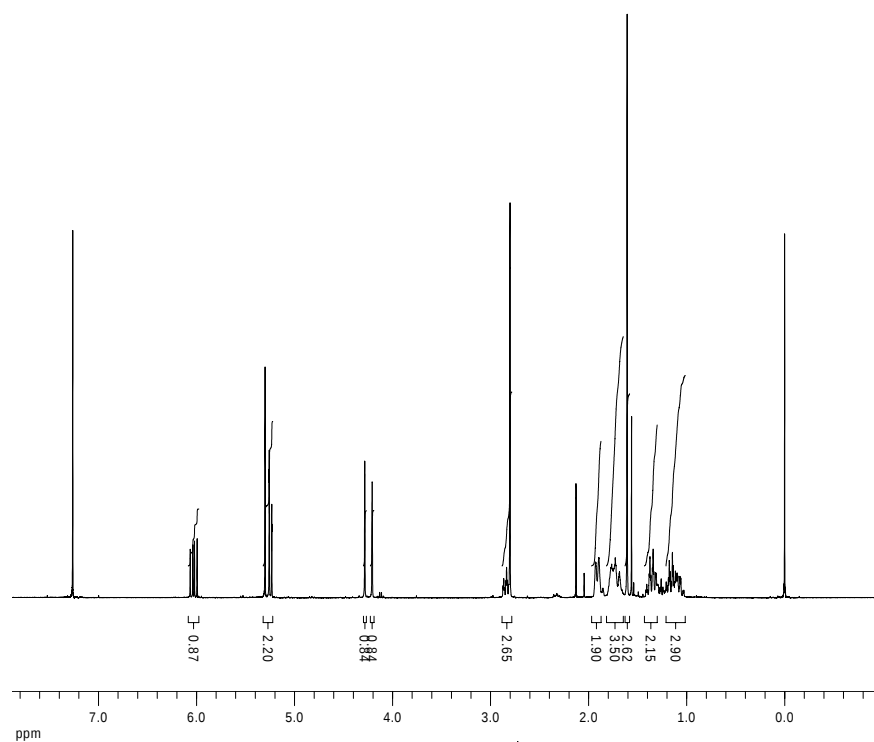


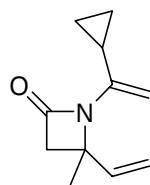
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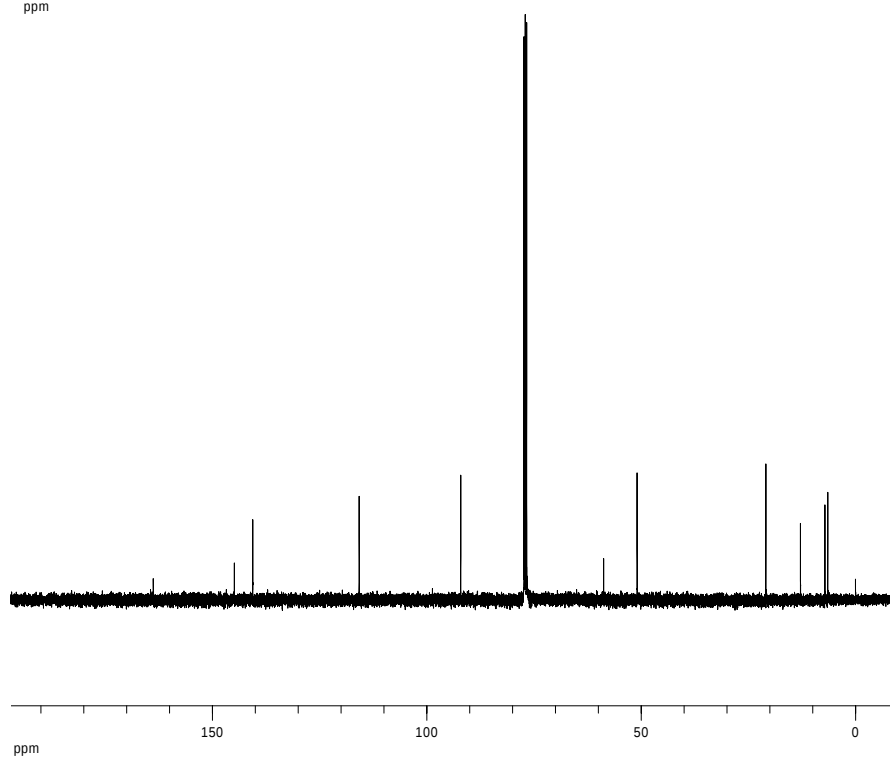
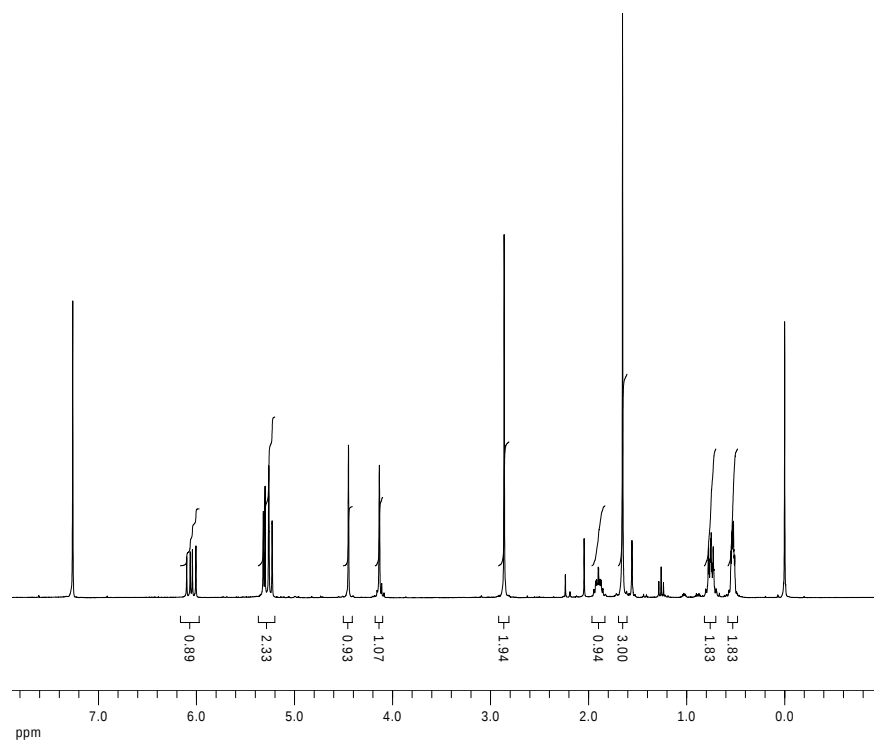


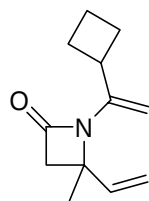
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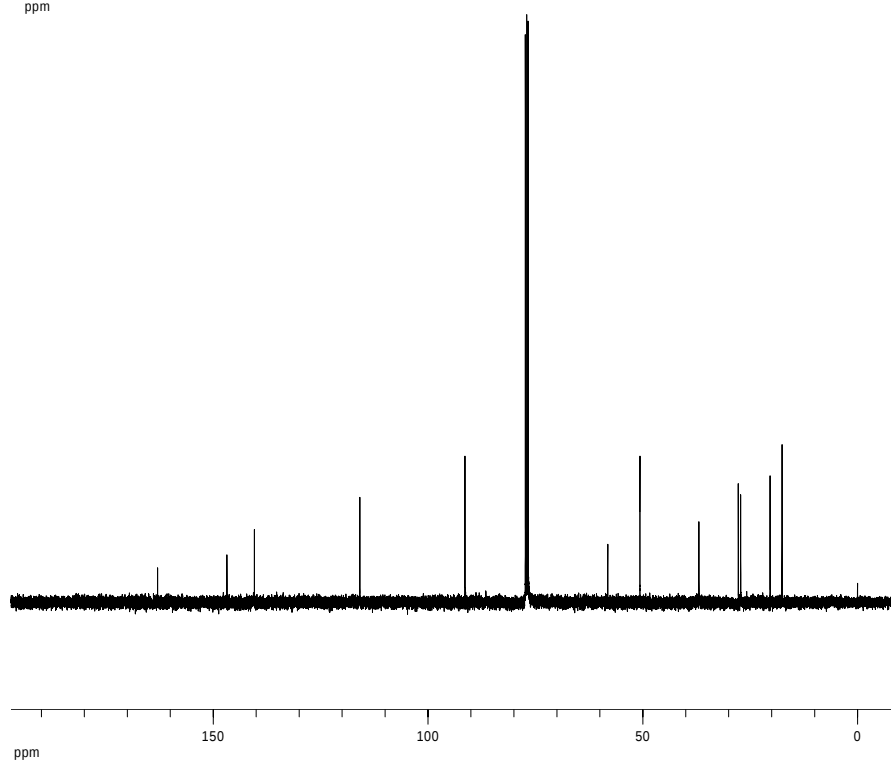
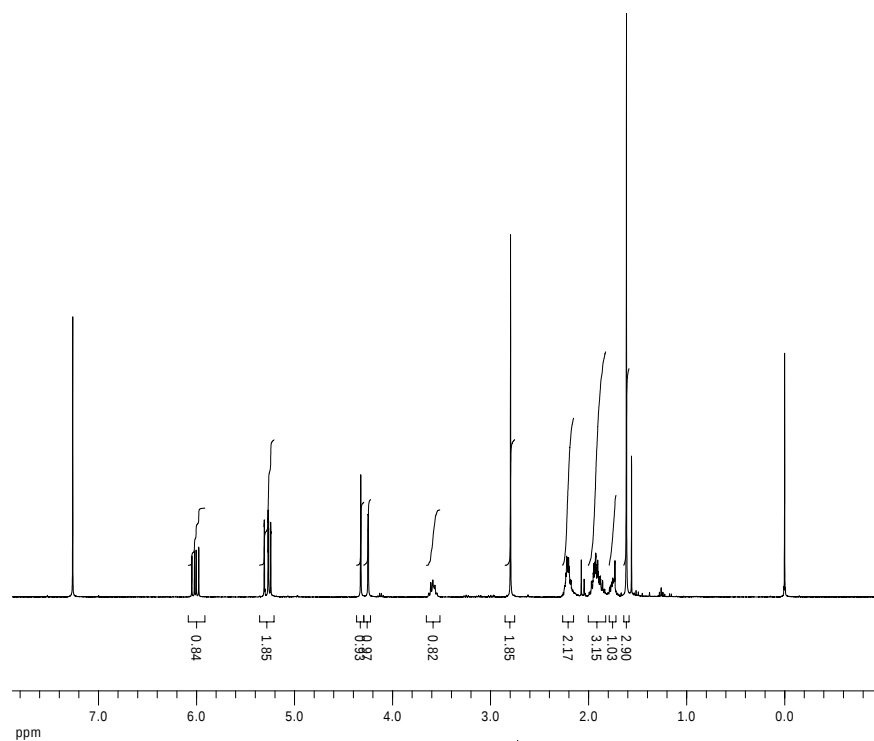


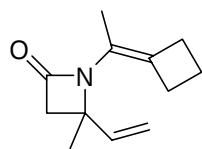
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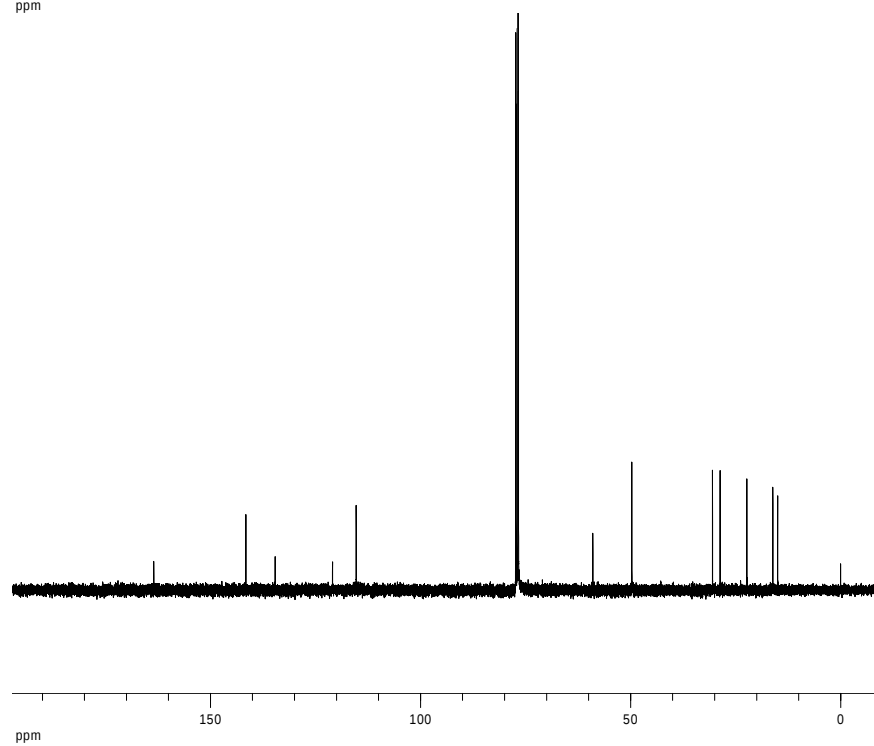
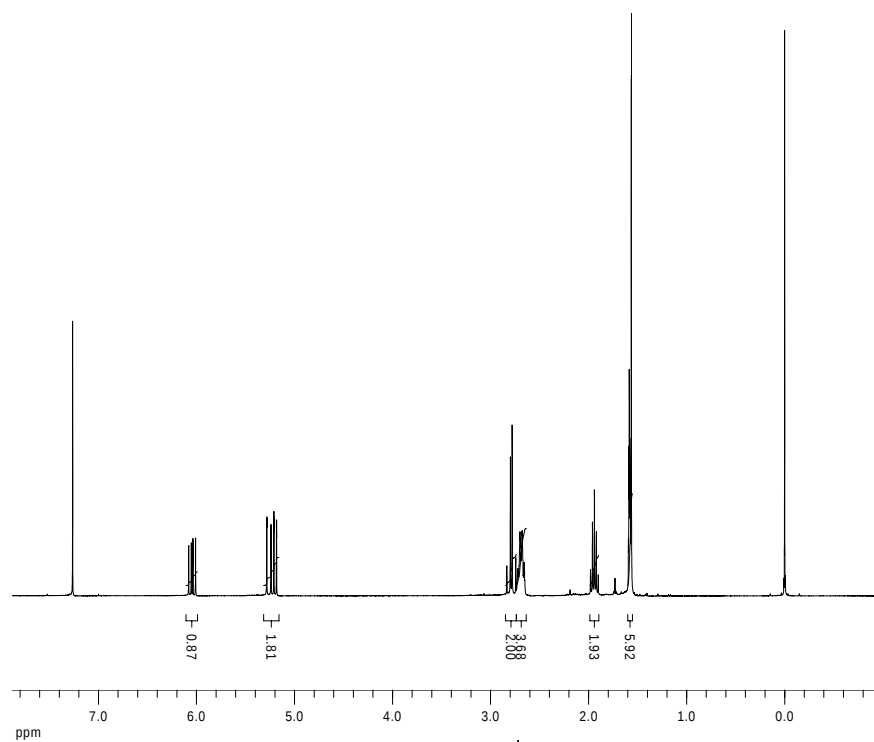


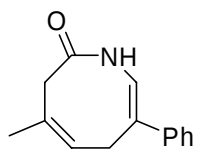
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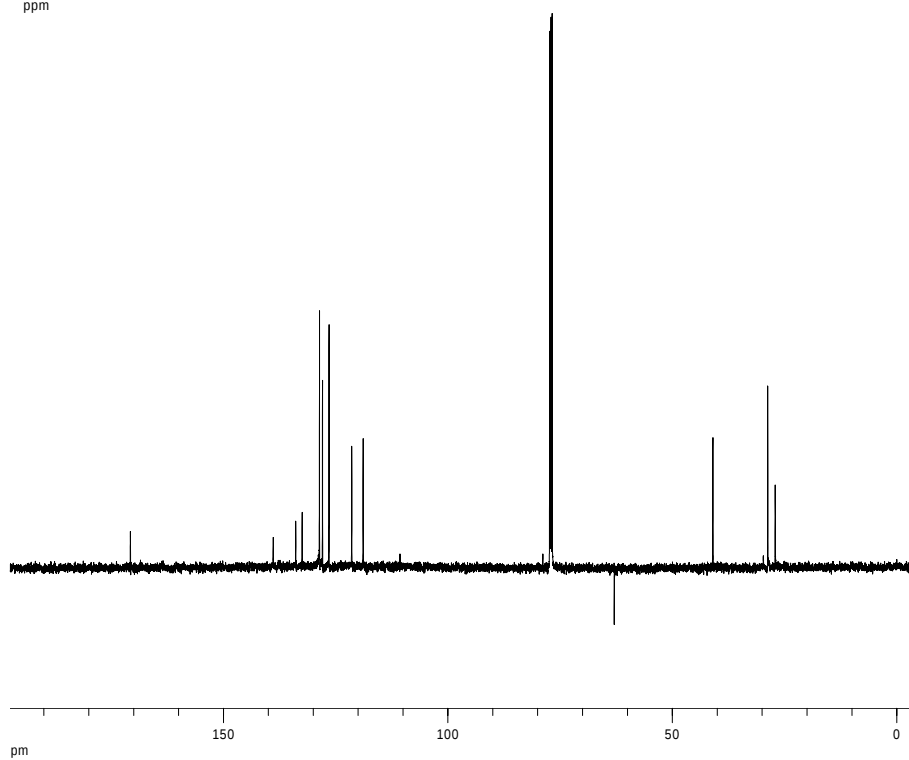
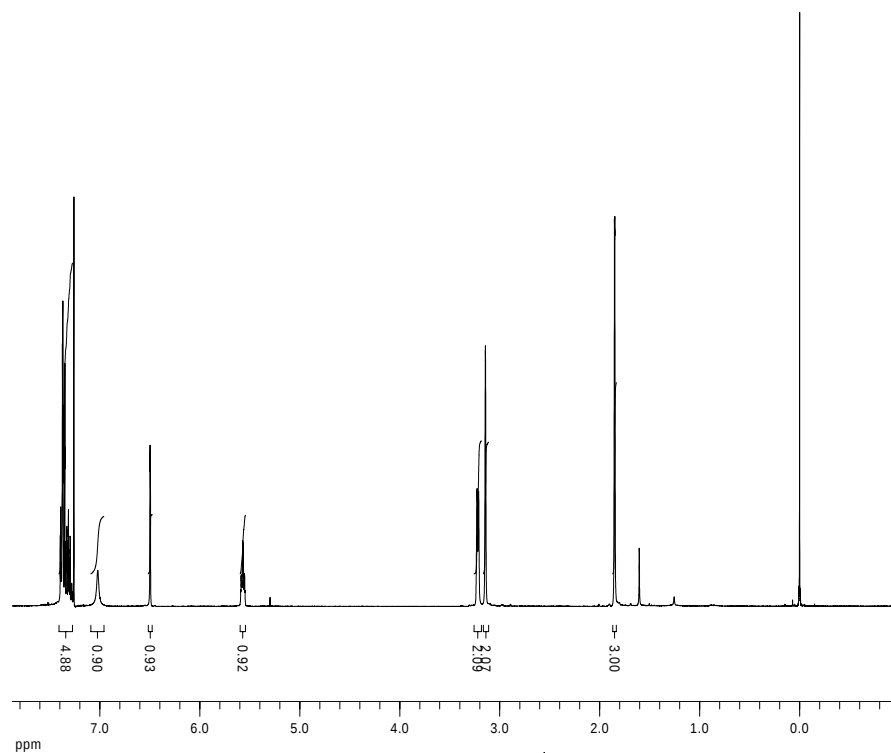


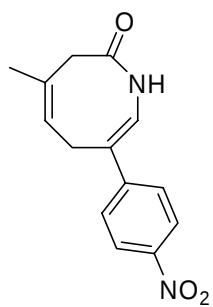
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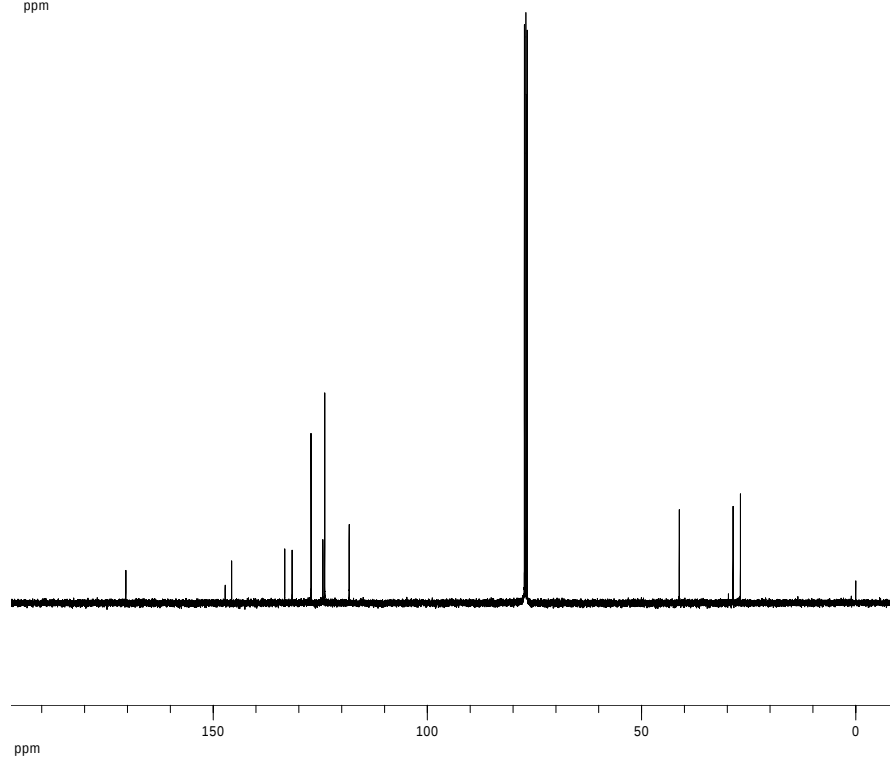
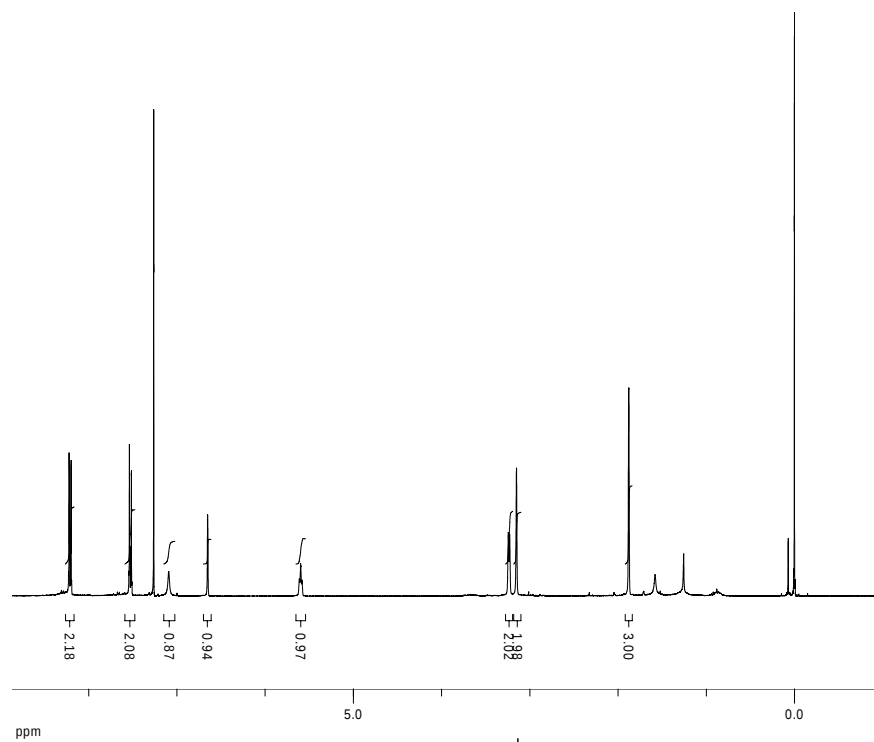


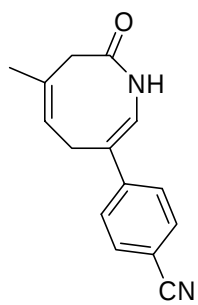
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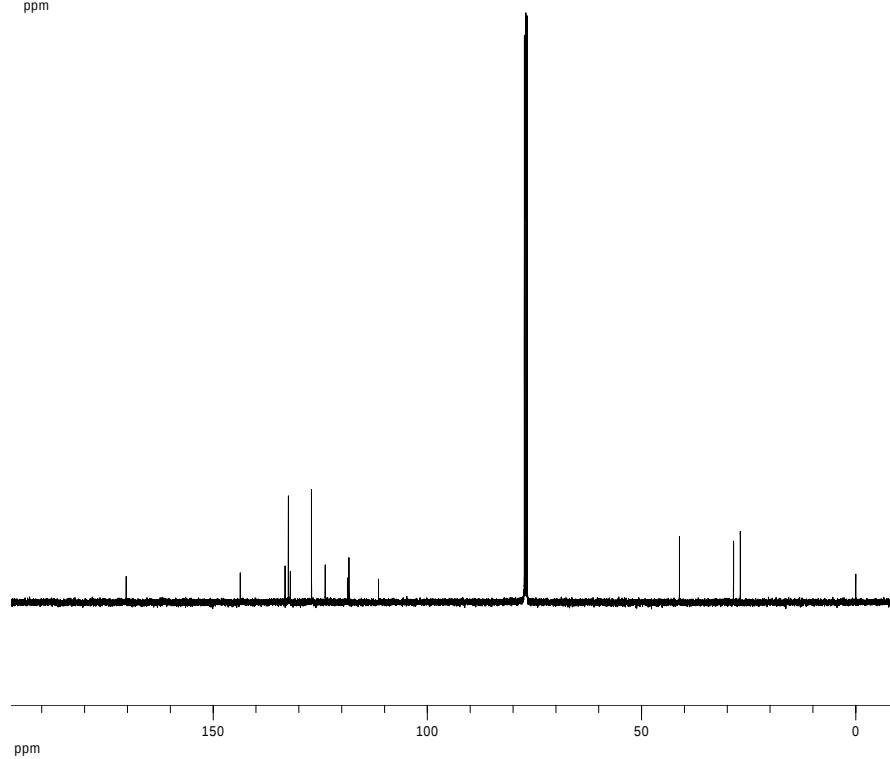
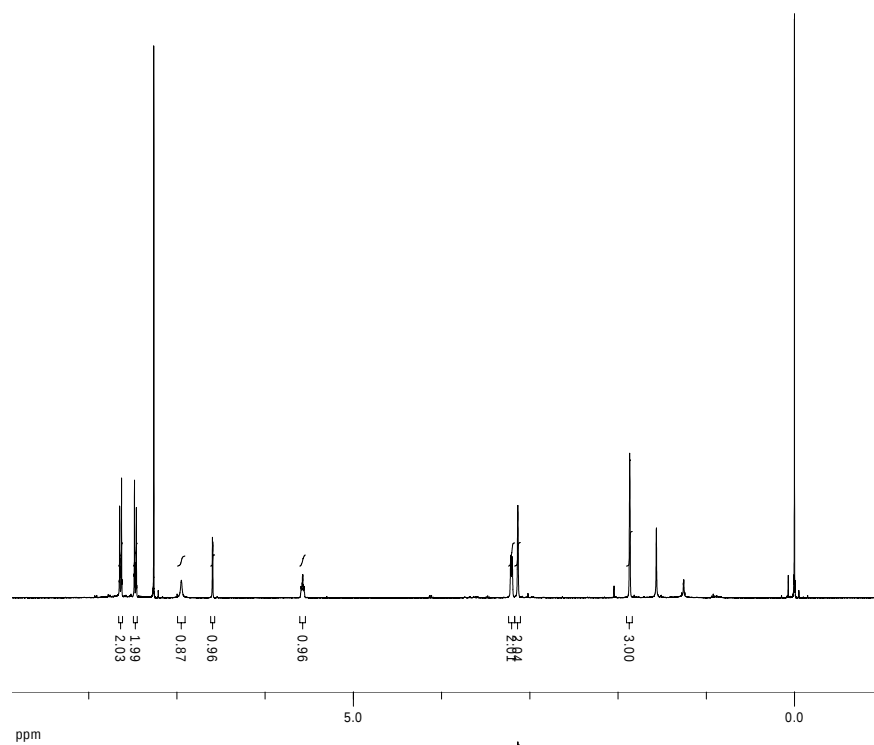


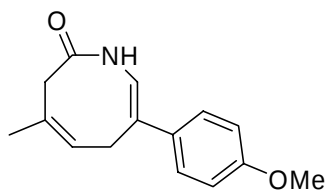
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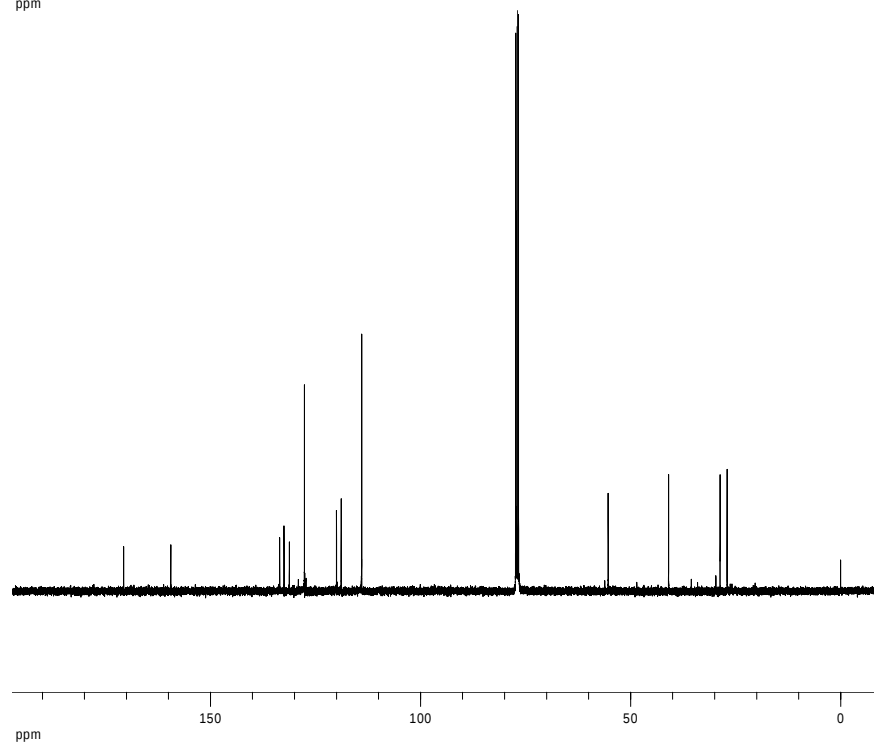
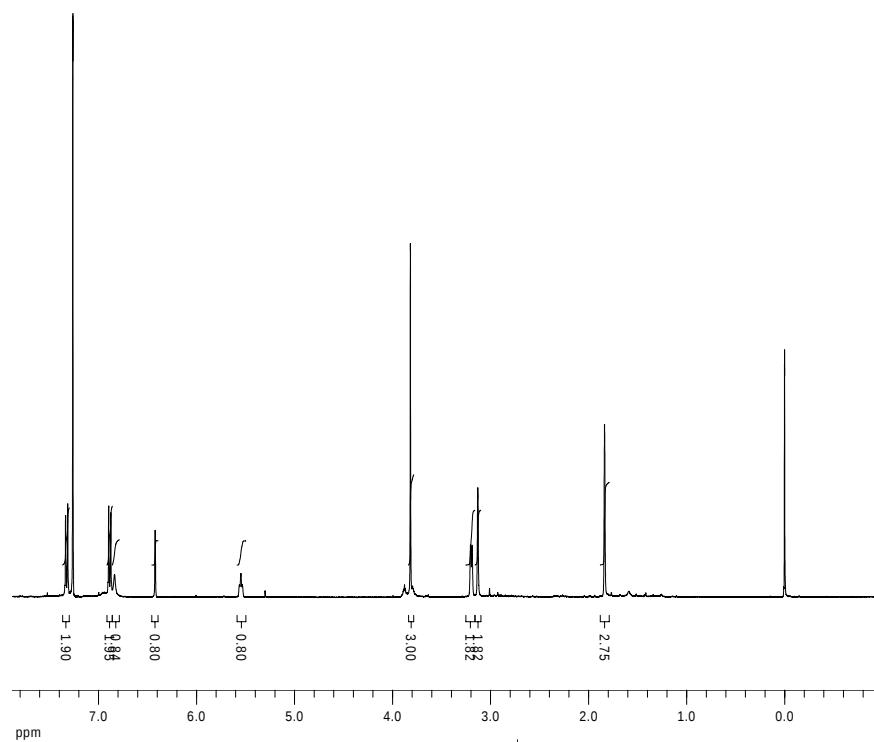


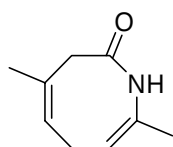
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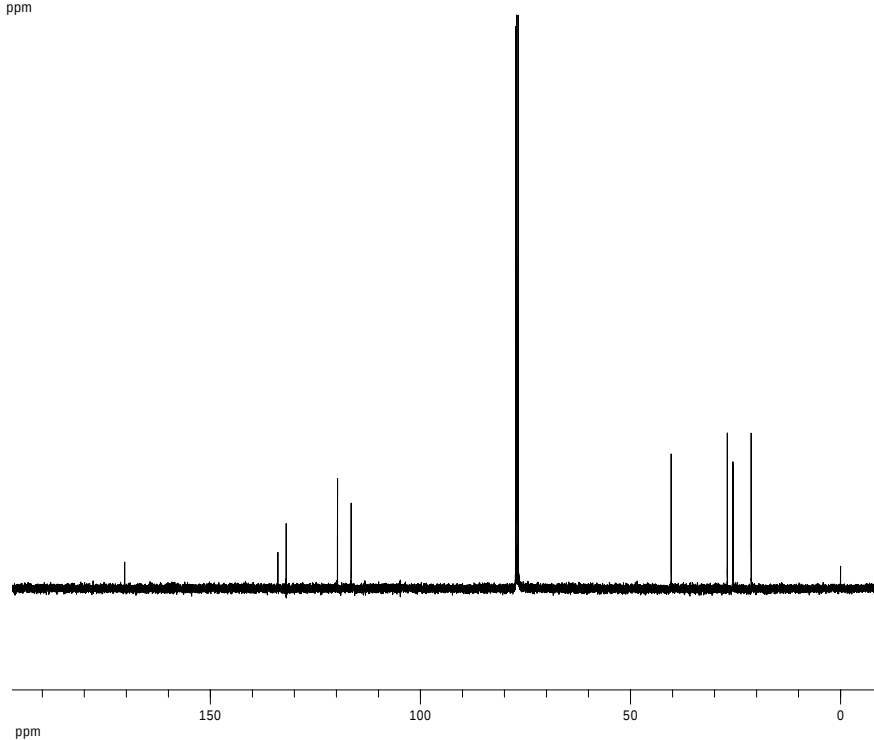
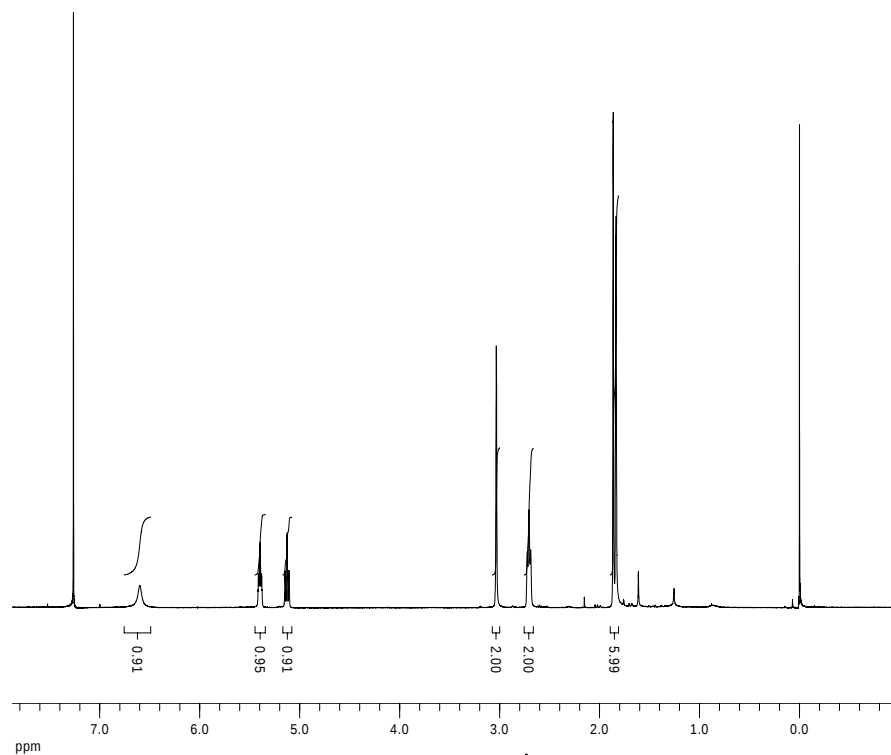


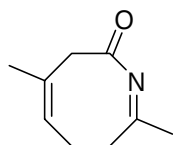
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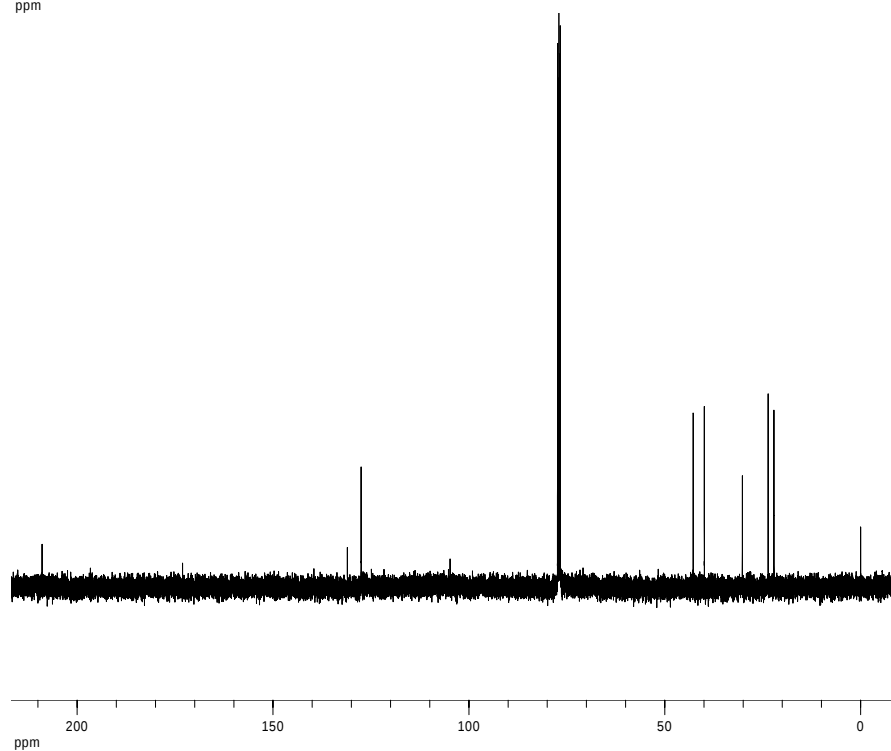
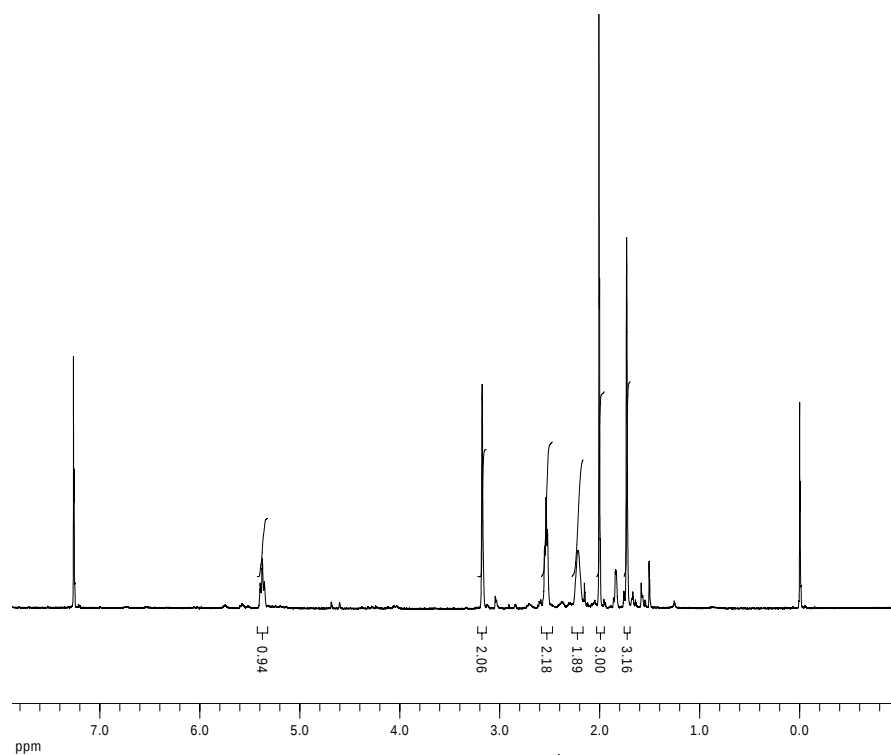


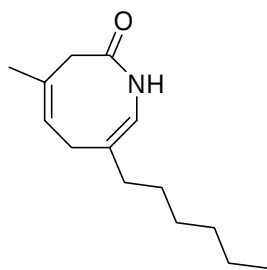
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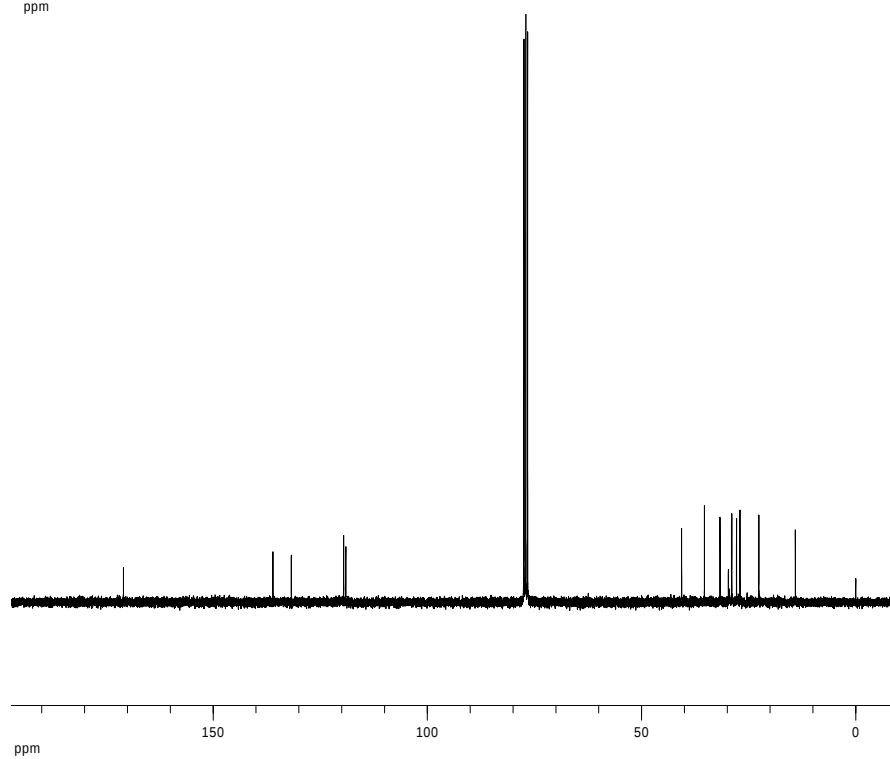
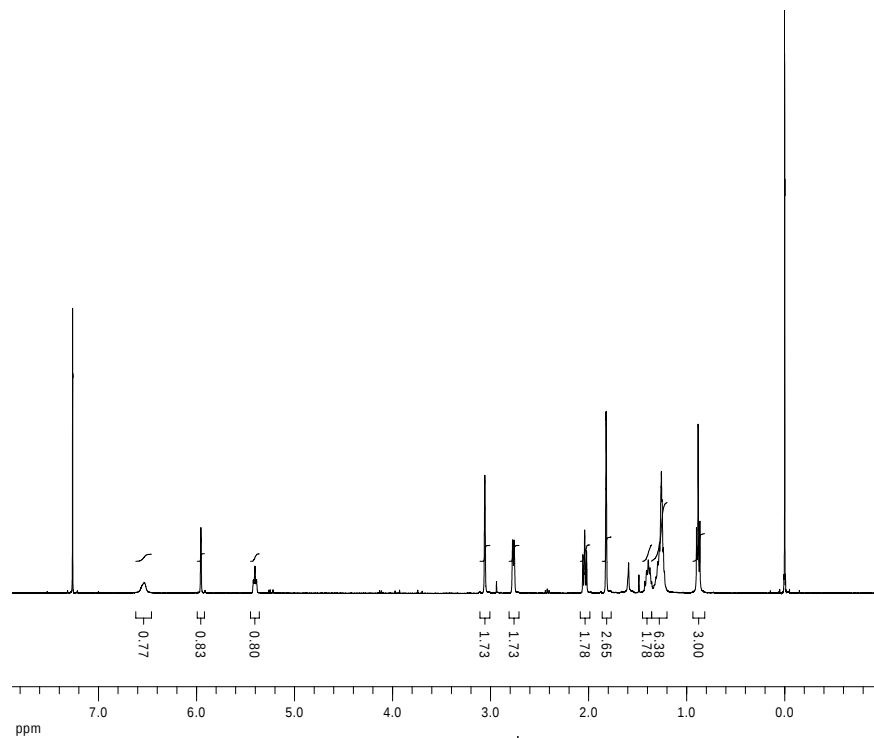


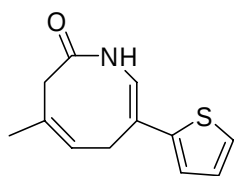
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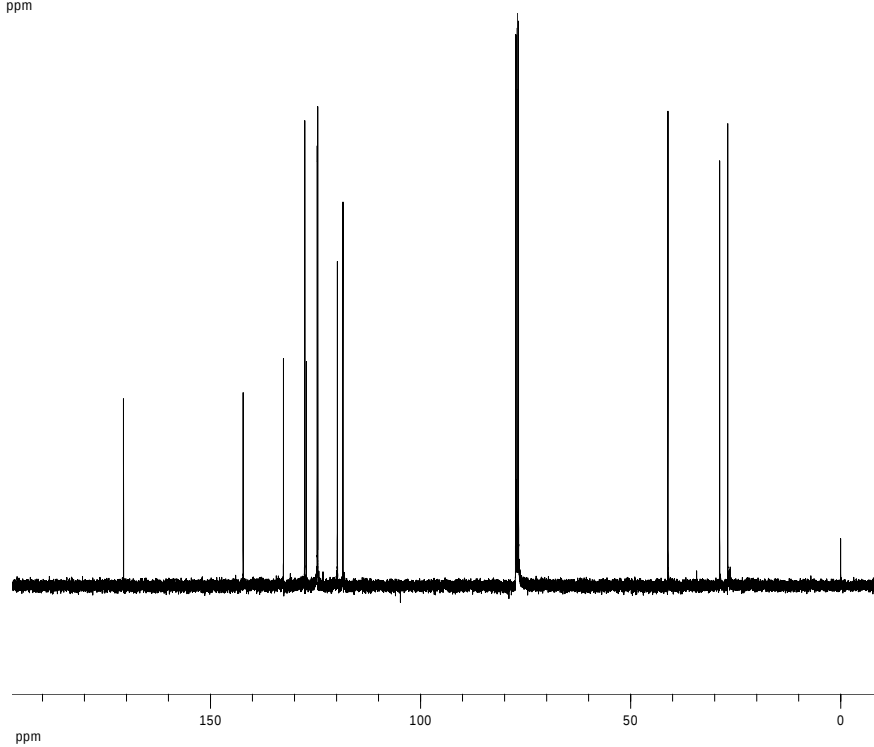
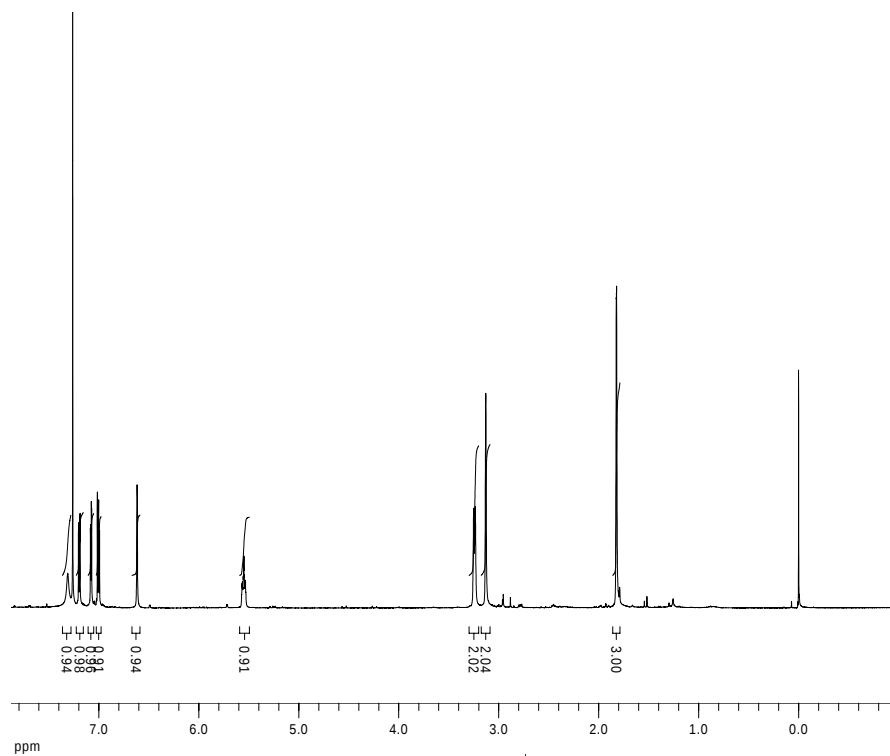


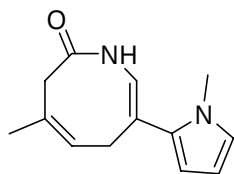
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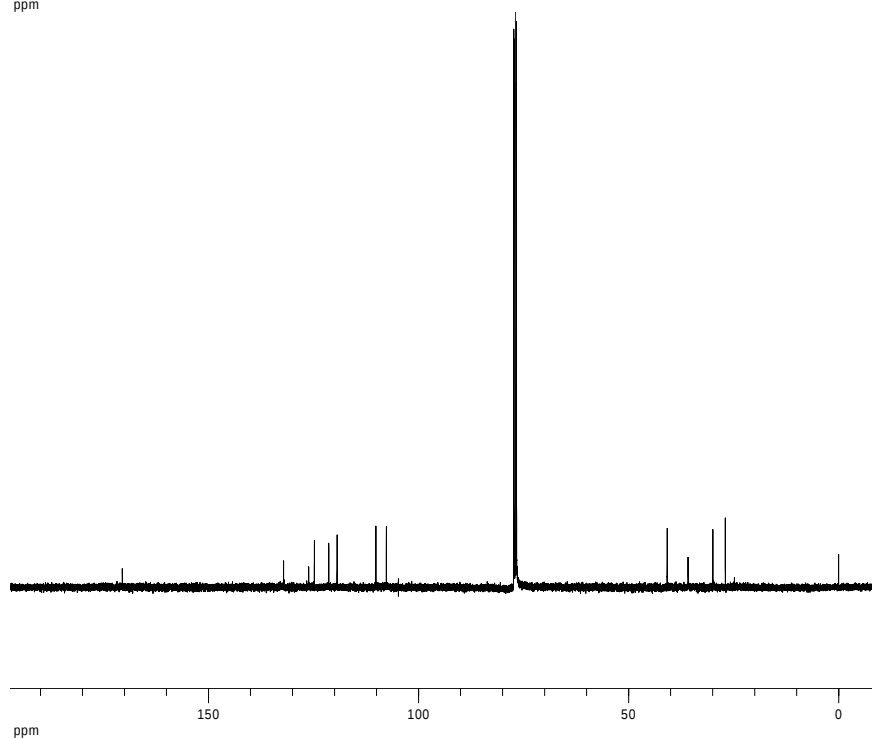
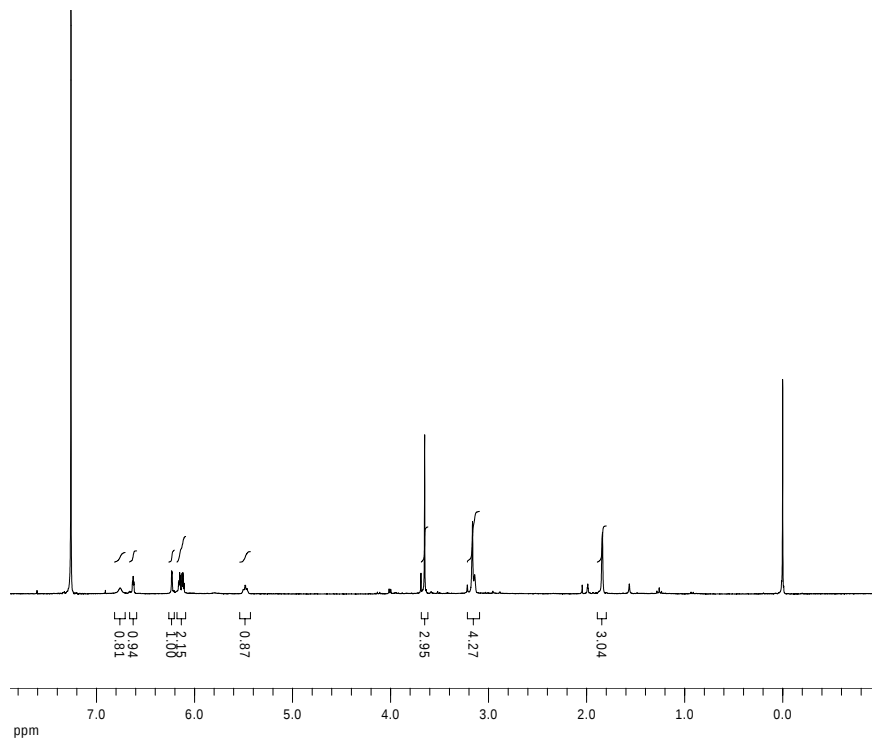


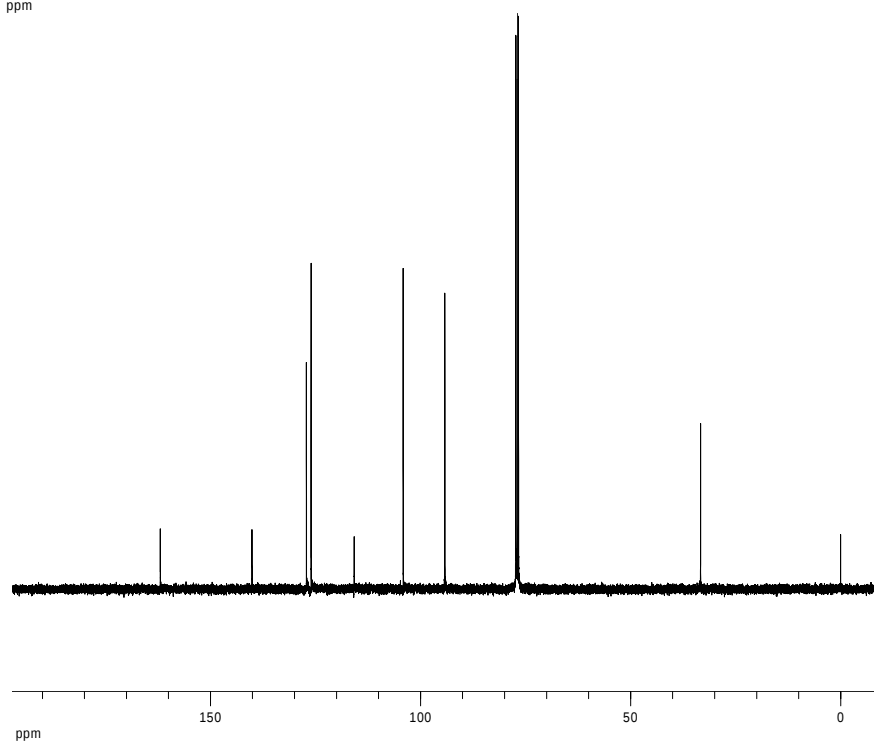
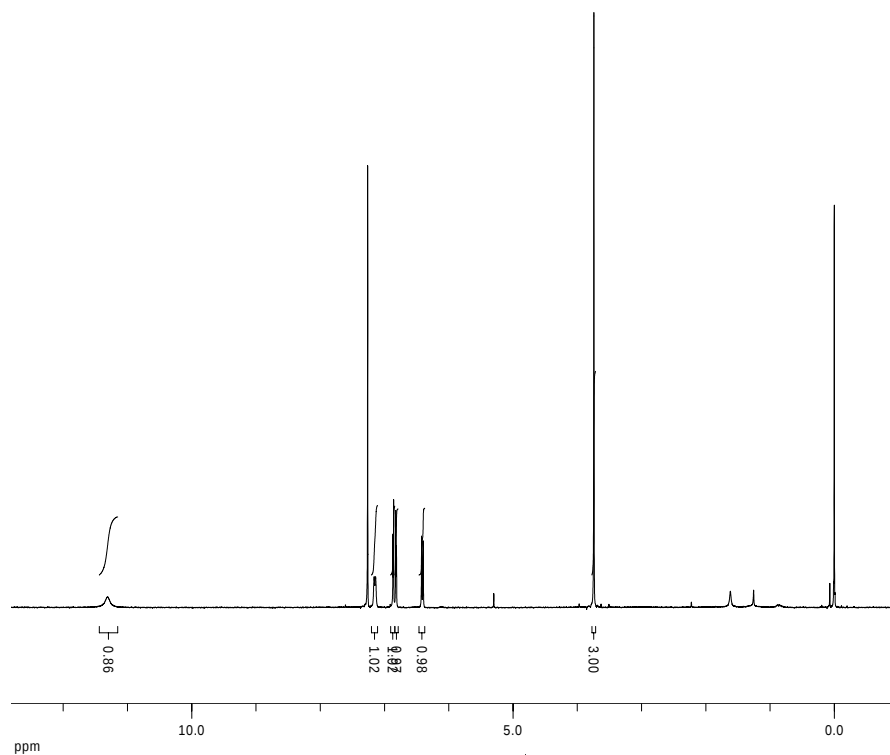
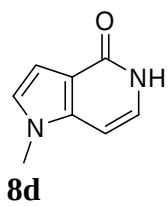
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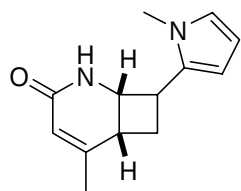




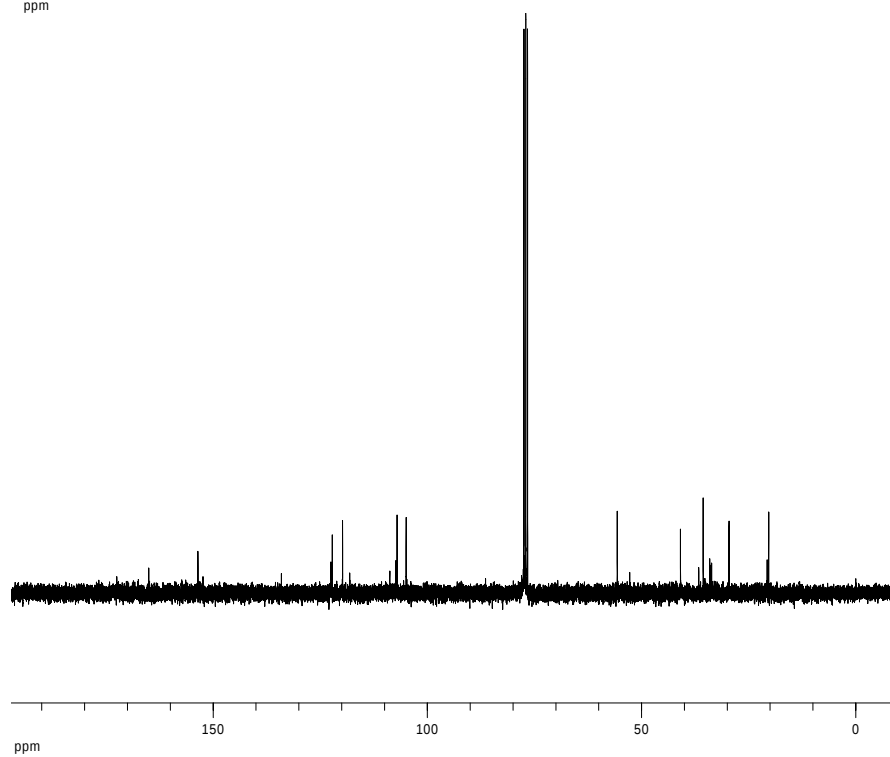
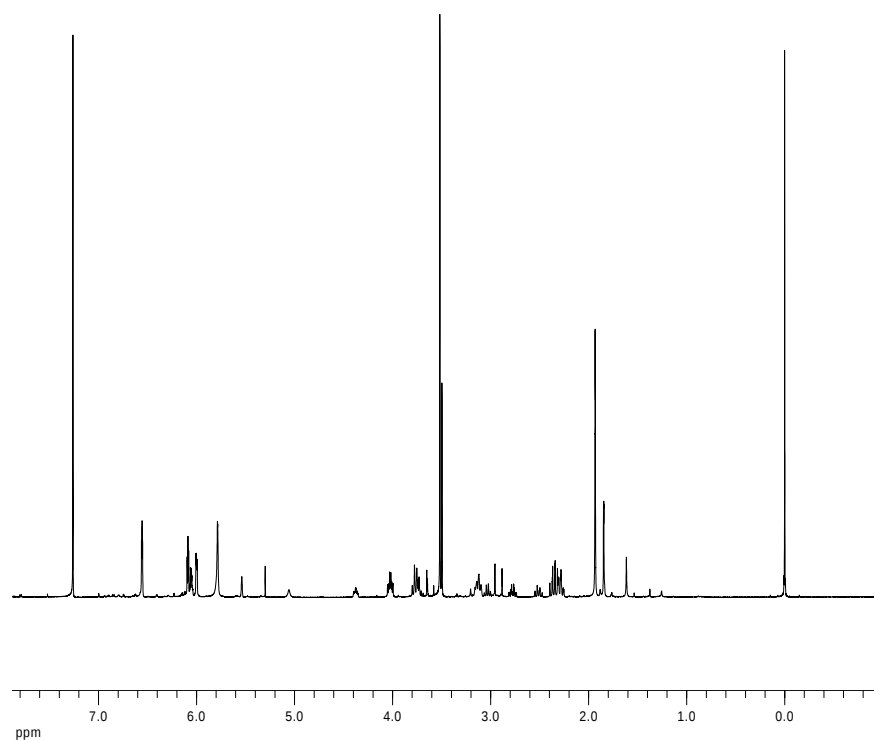
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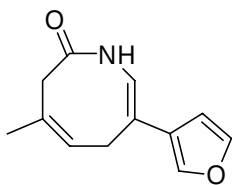




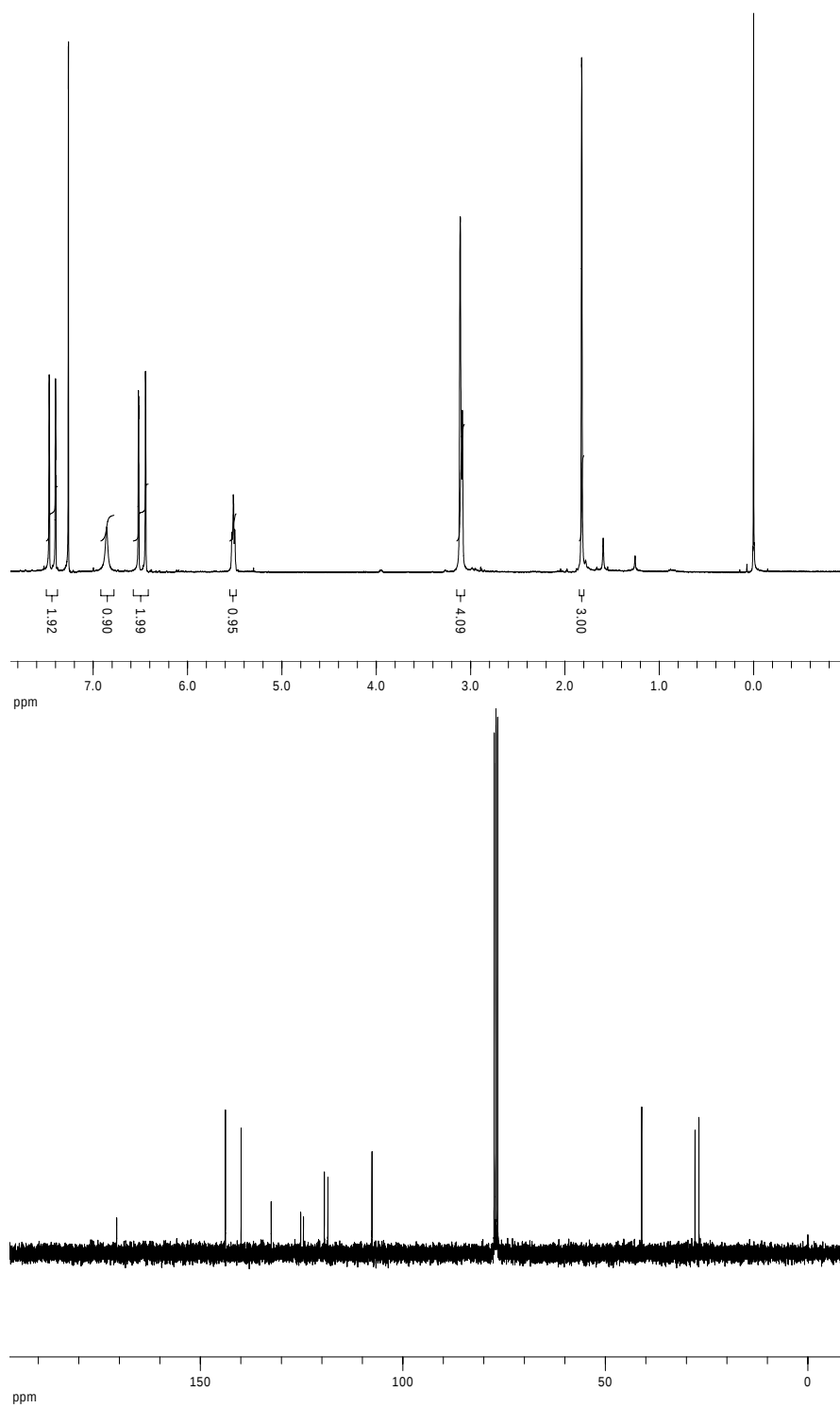


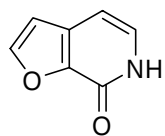
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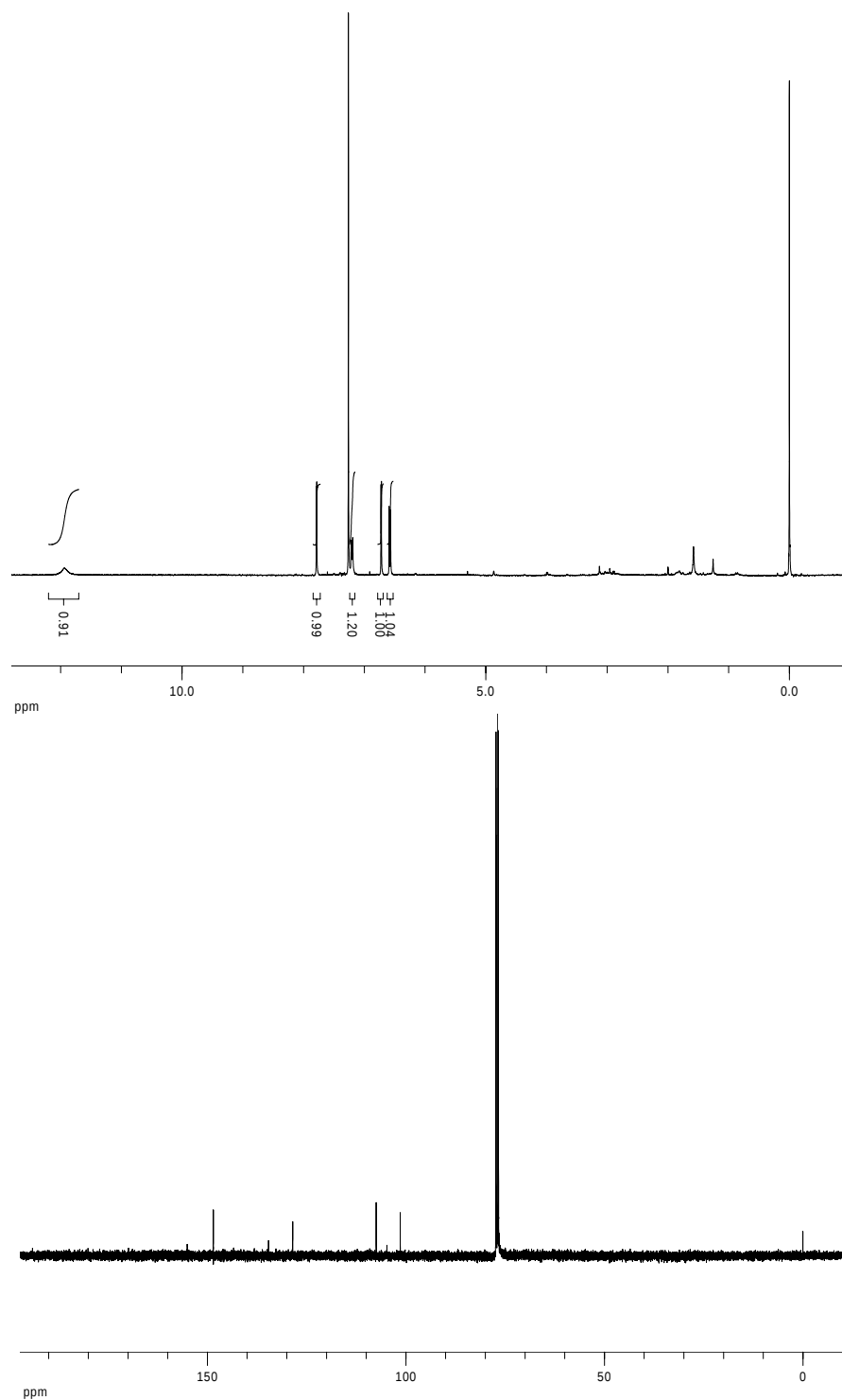


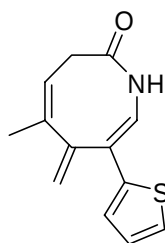
9b



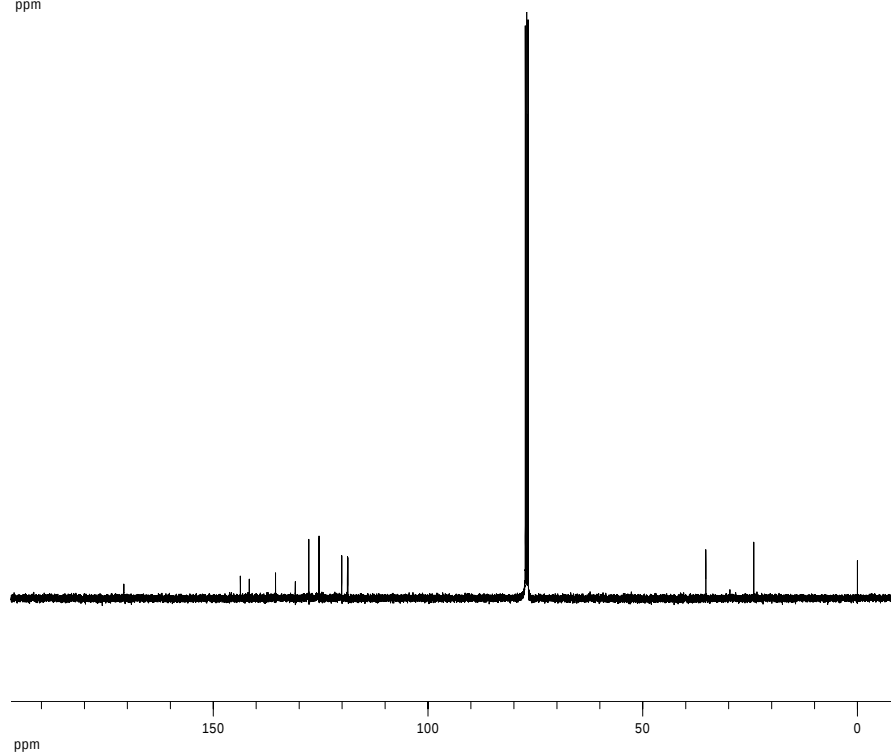
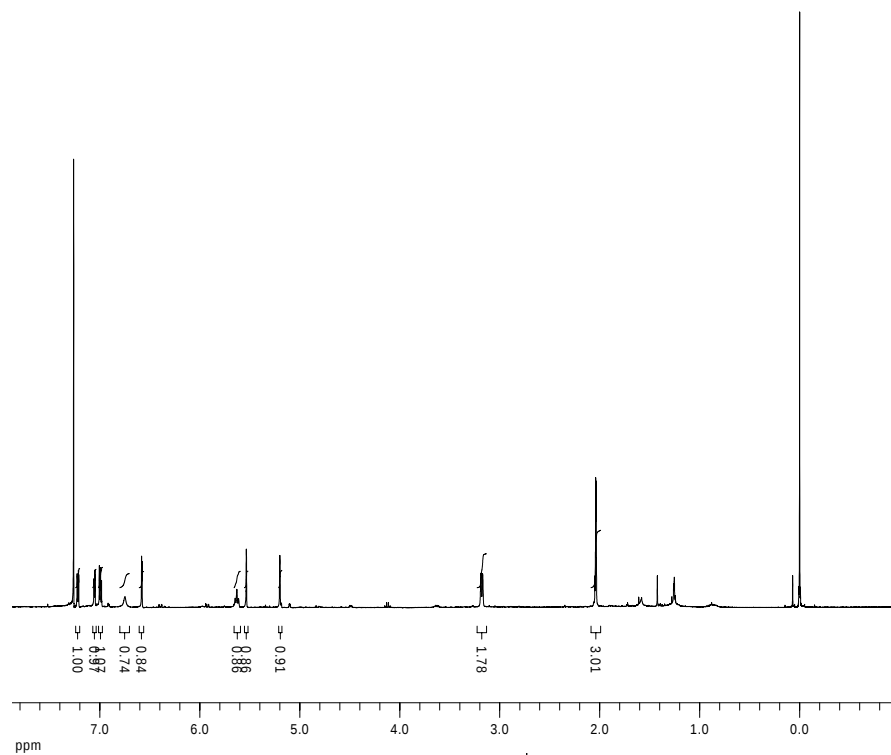


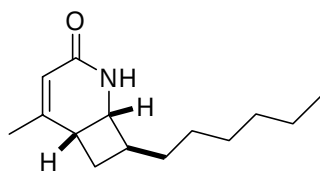
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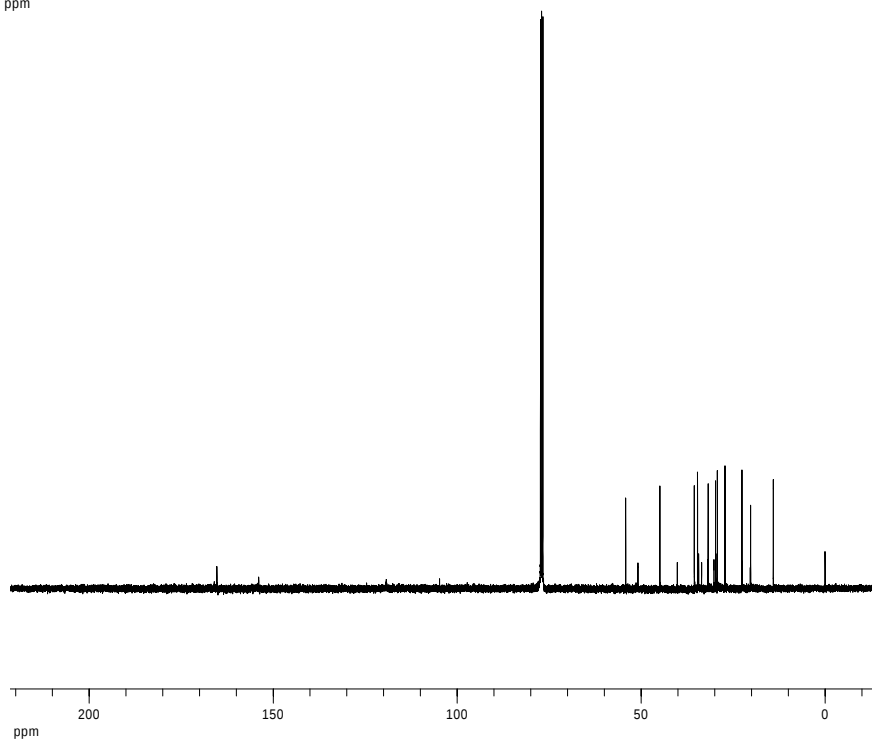
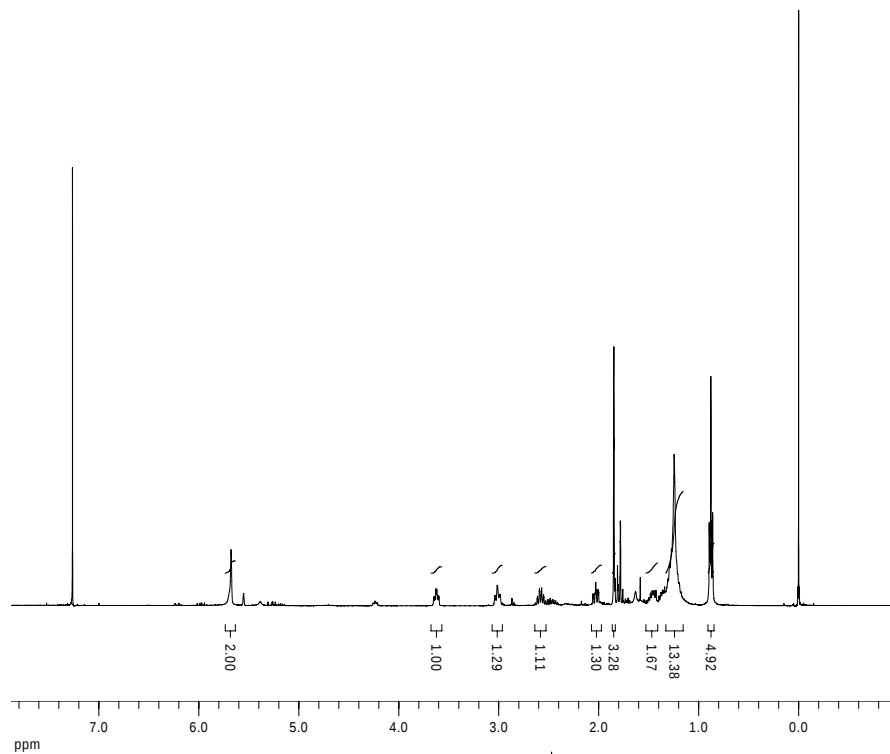


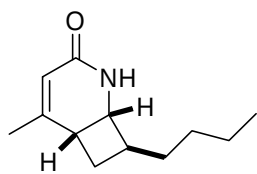
10b



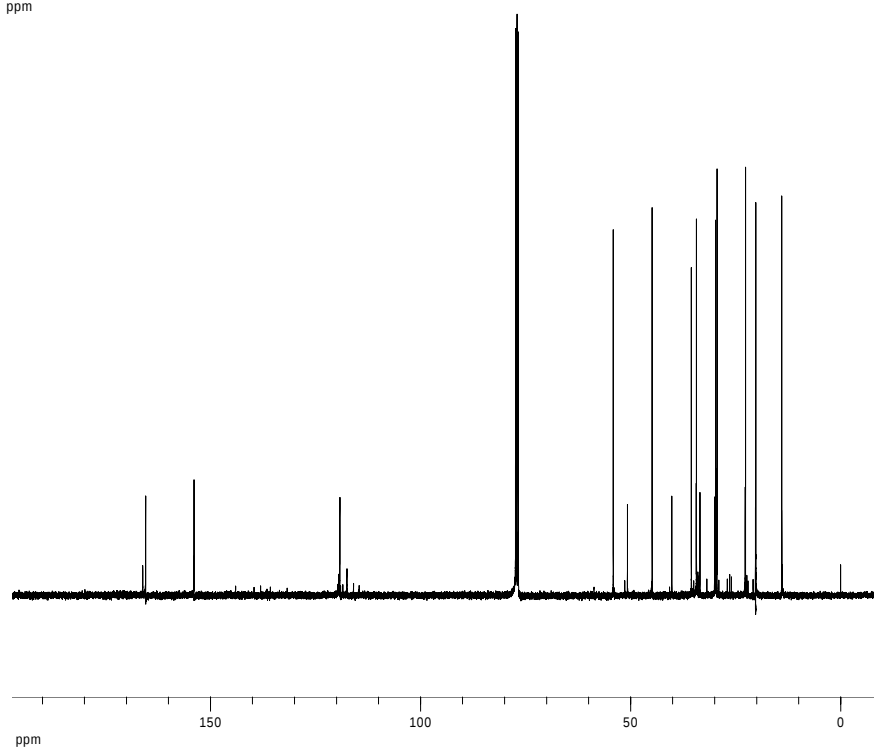
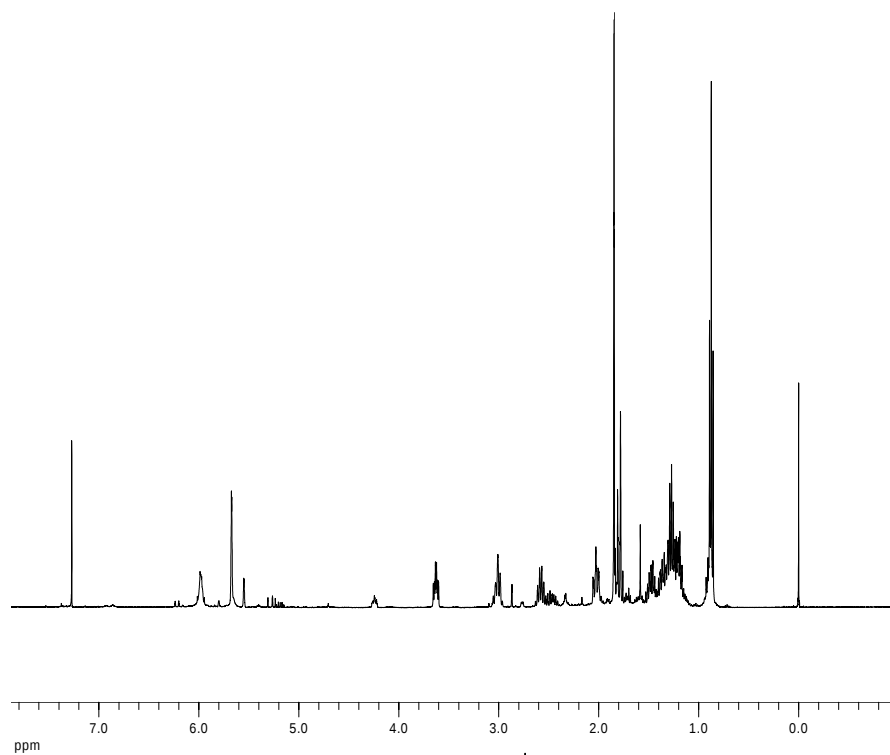


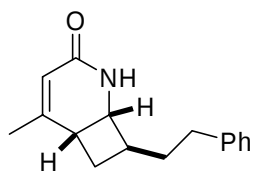
11b



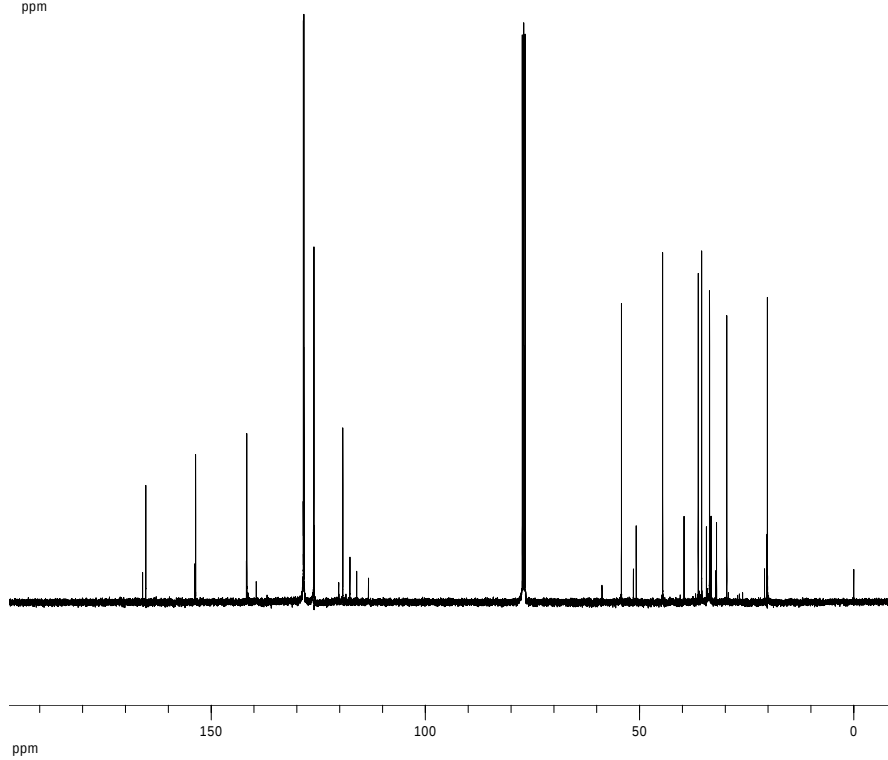
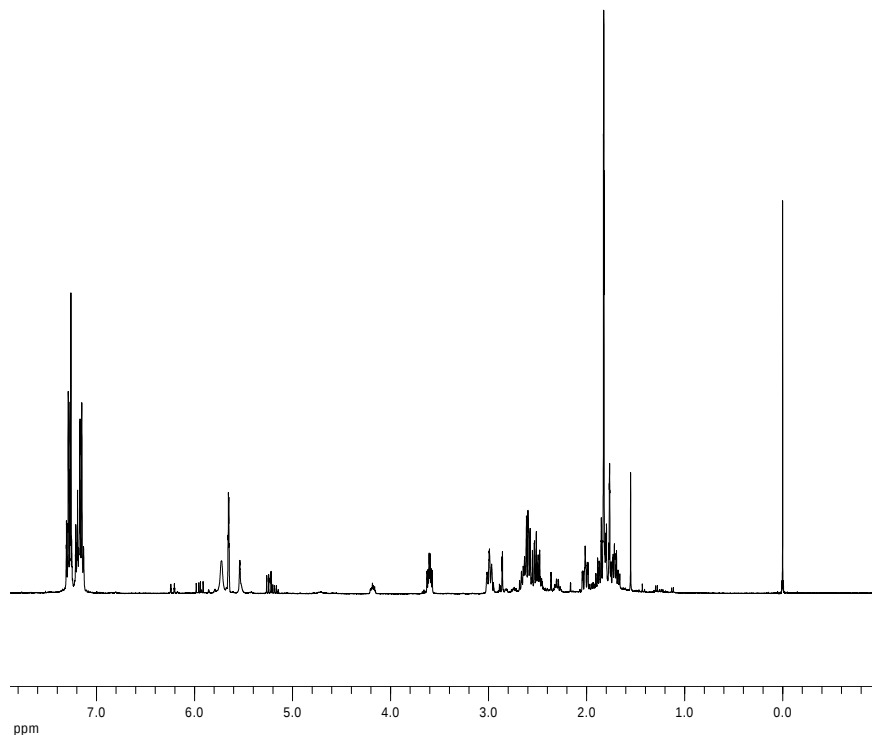


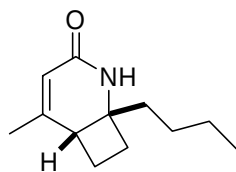
12b



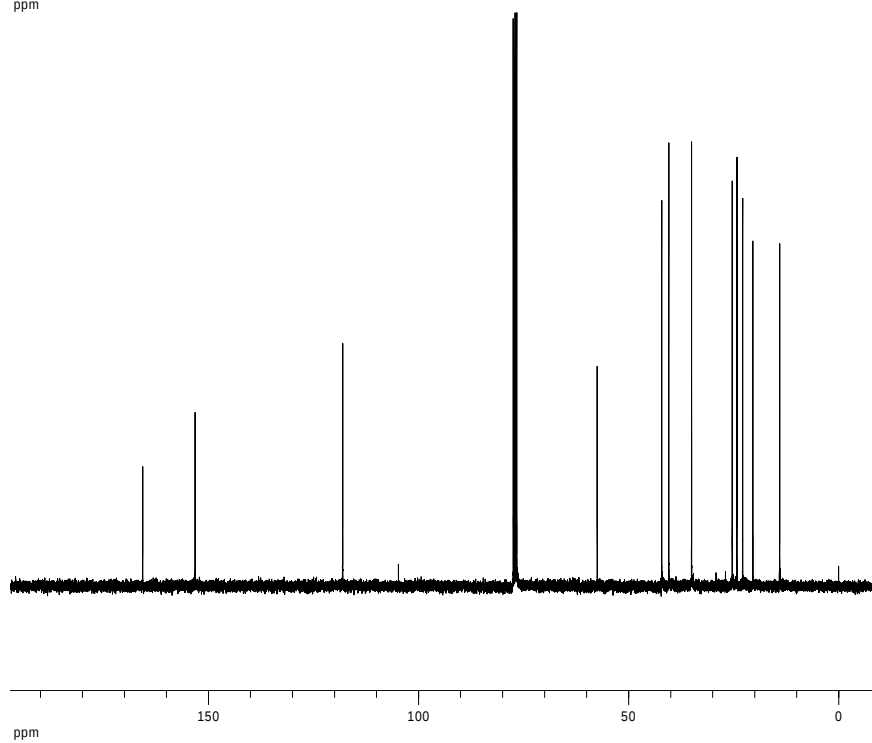
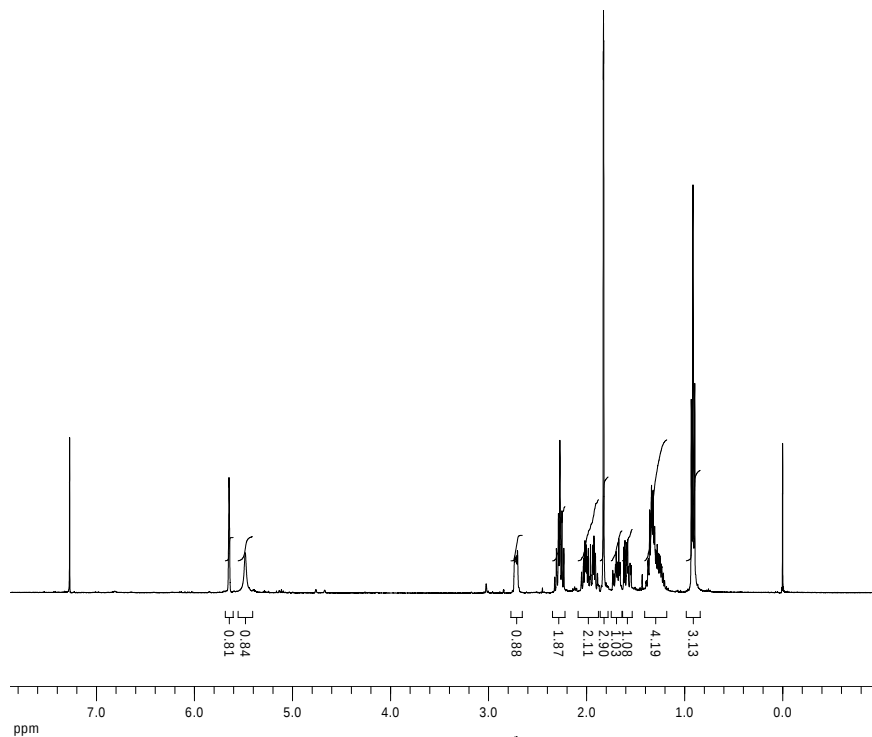


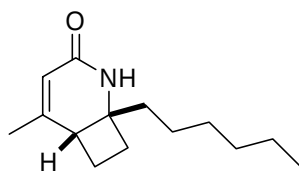
13b



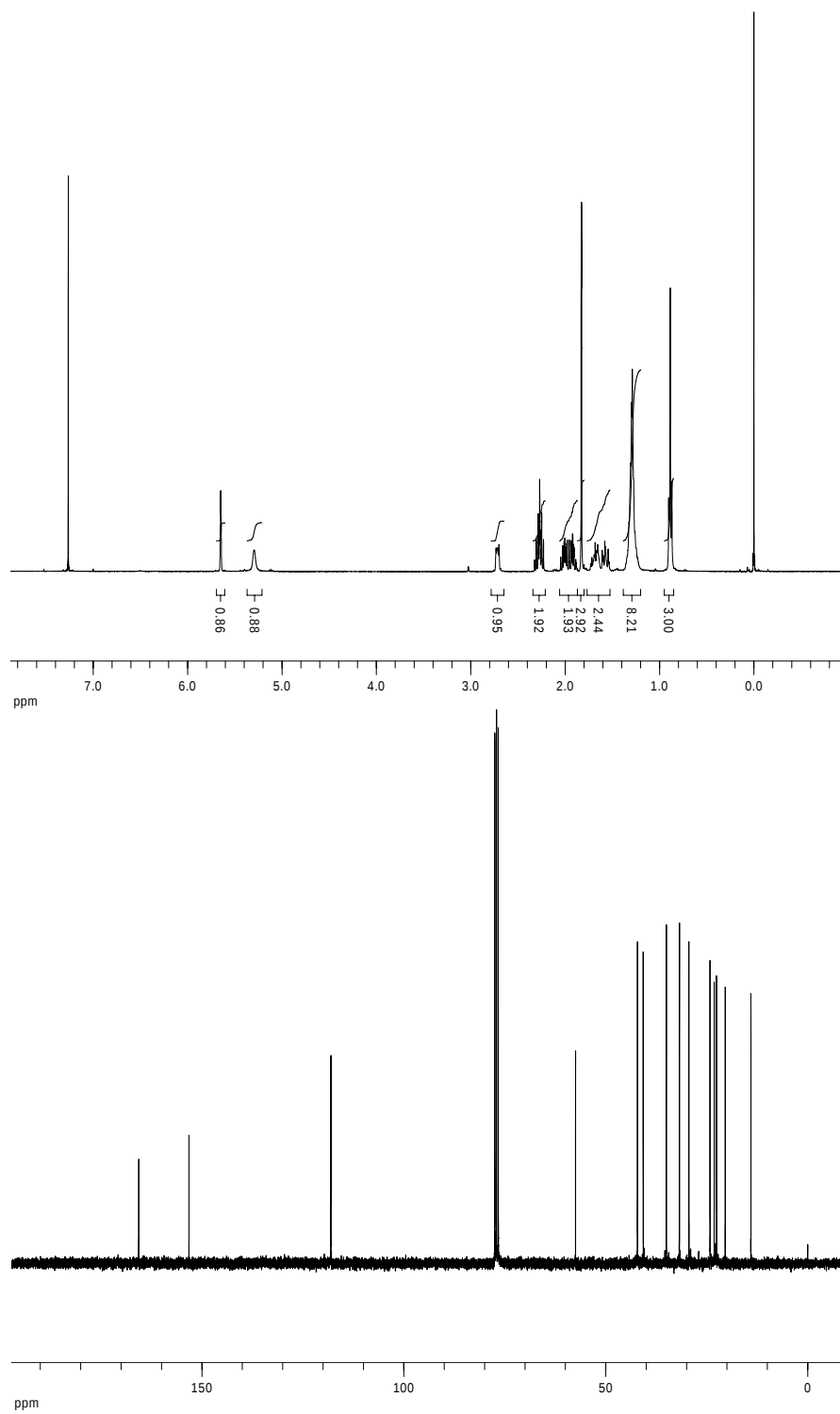


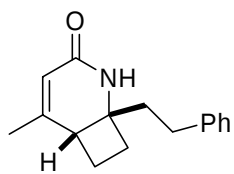
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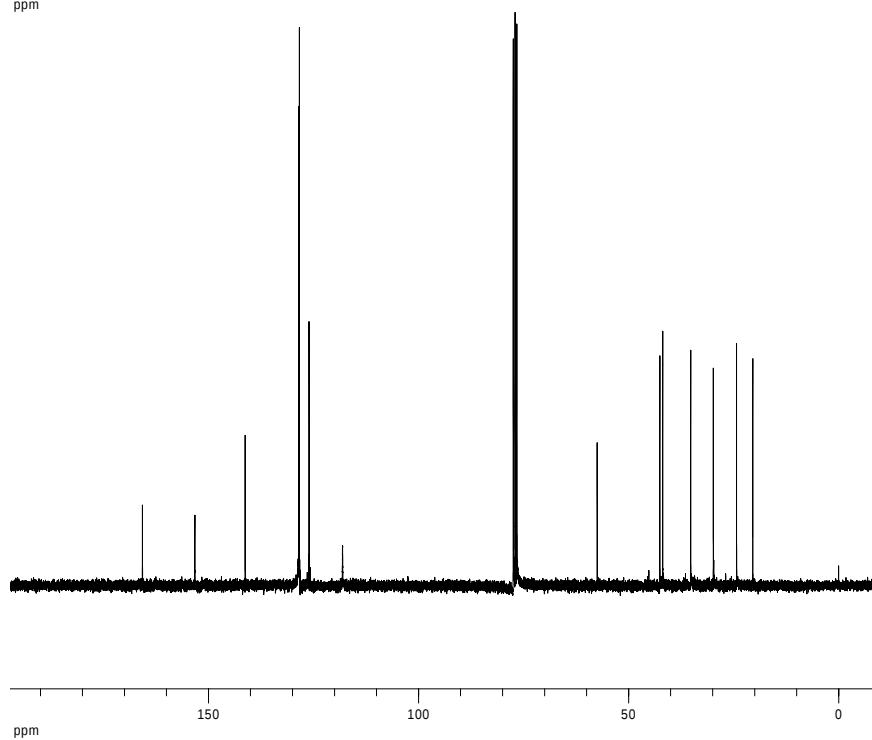
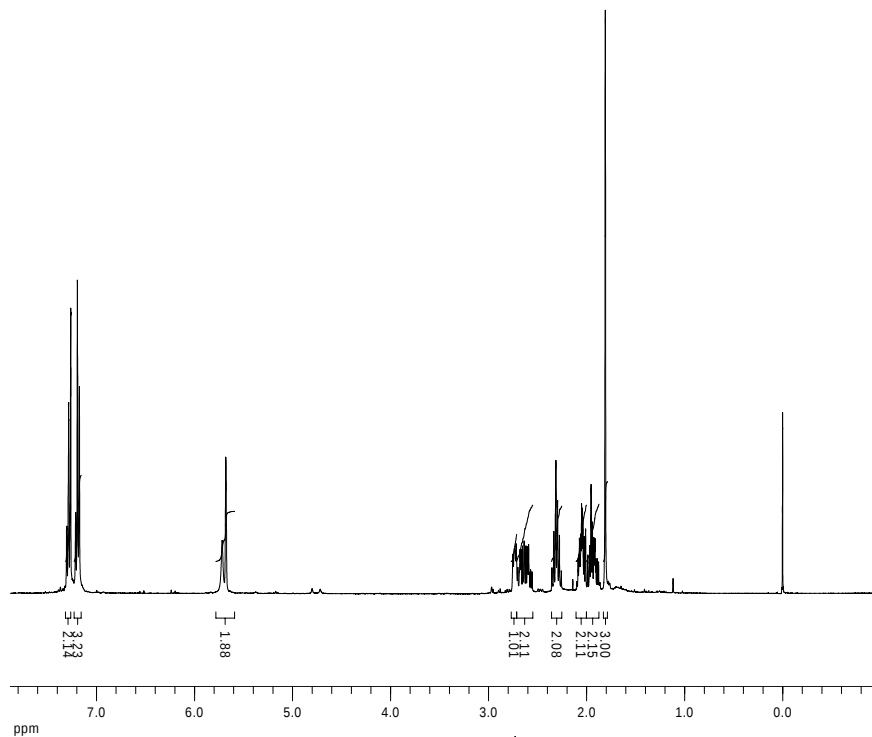


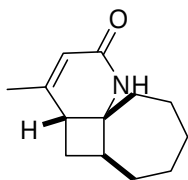
15b



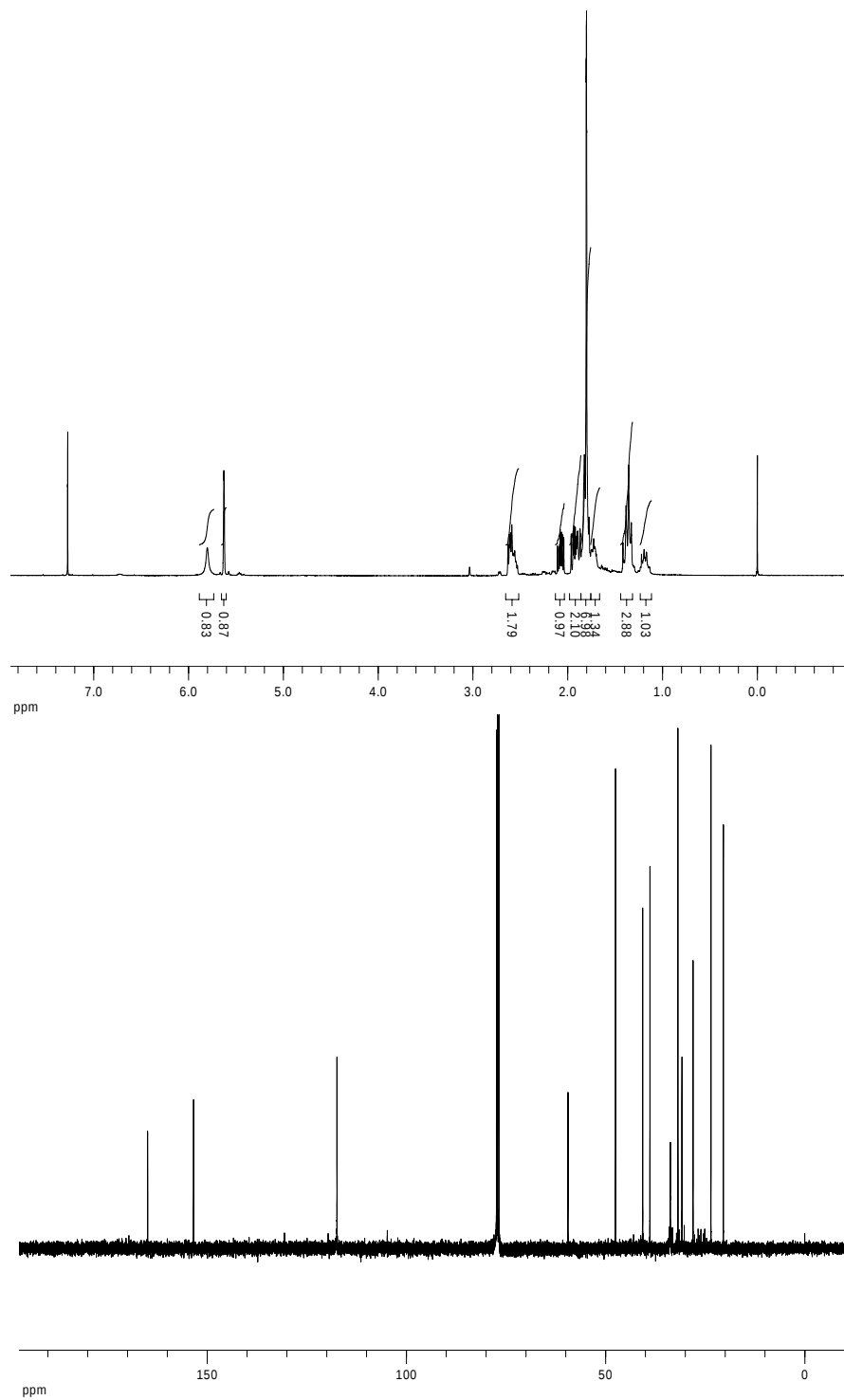


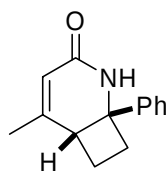
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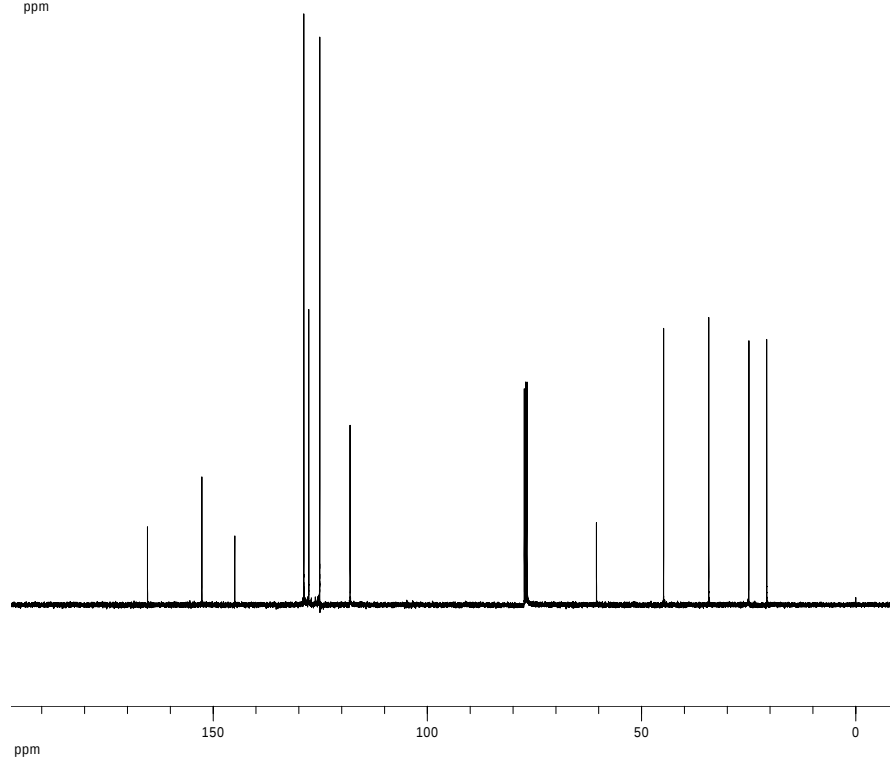
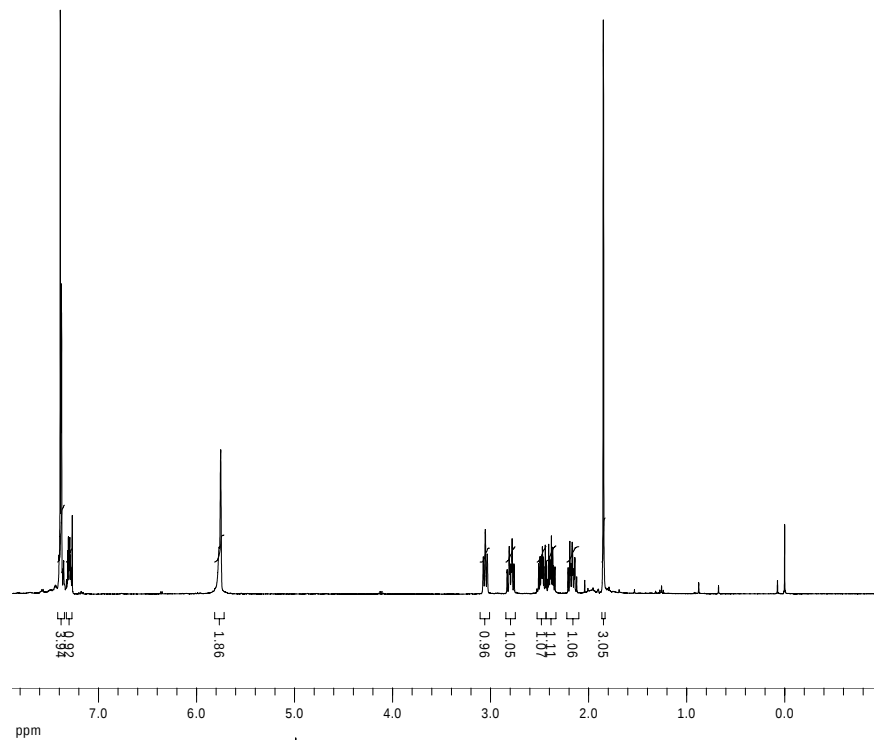


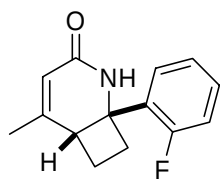
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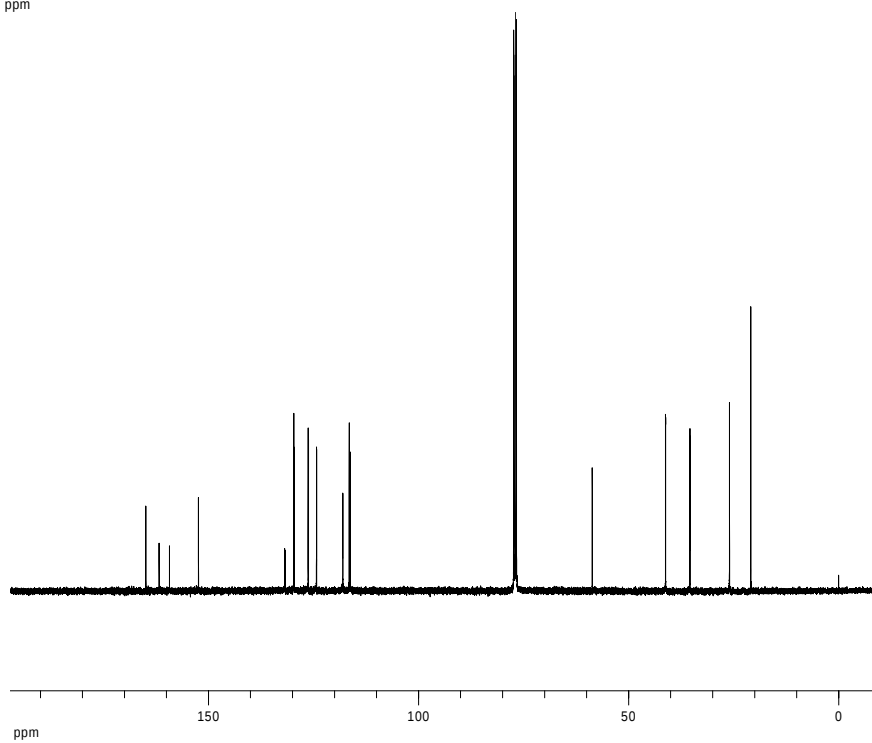
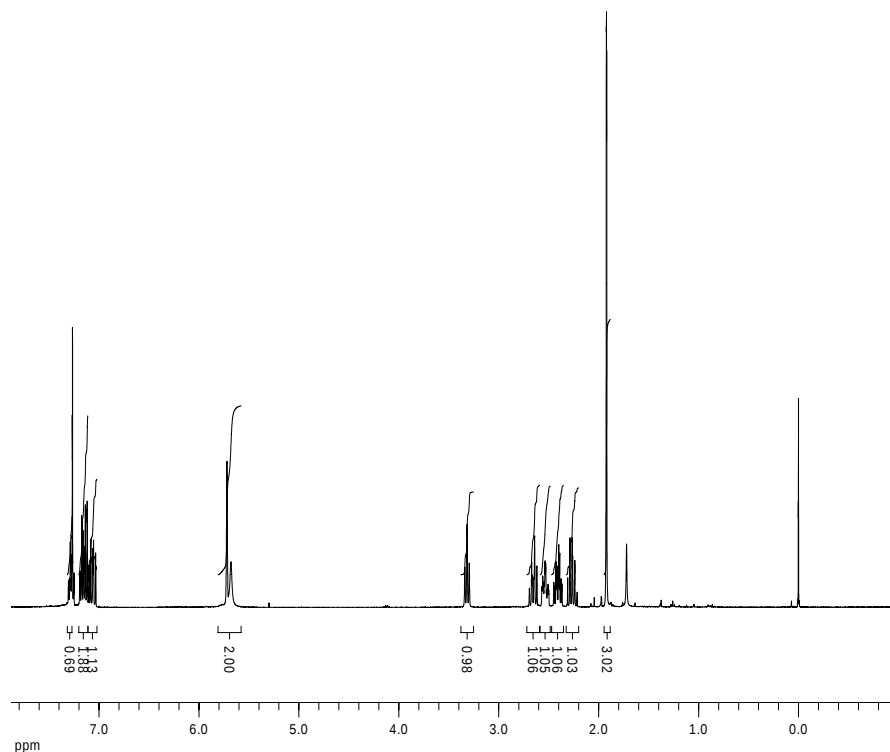


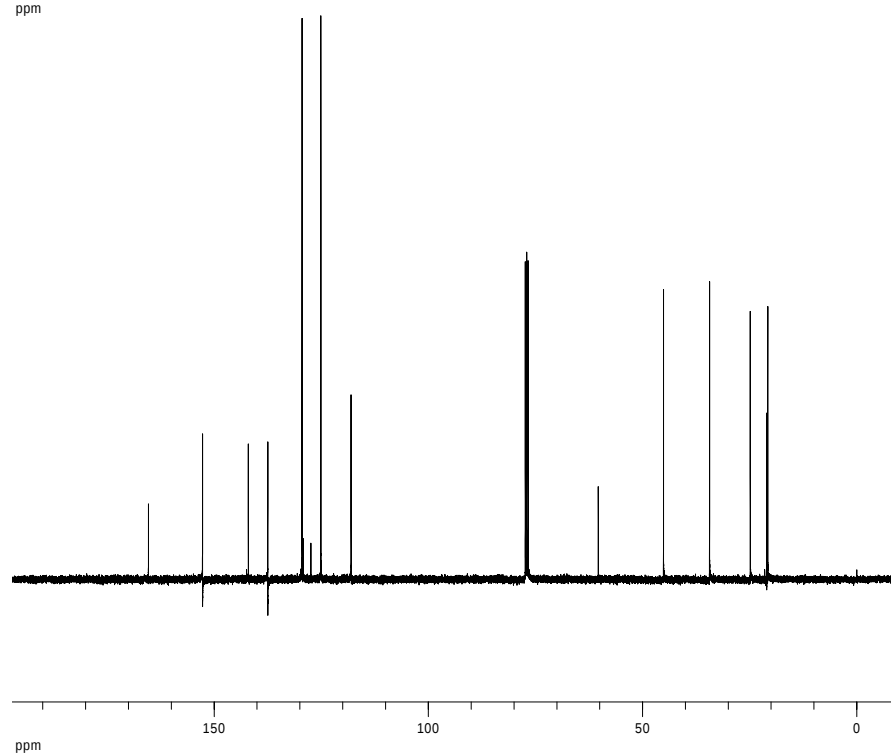
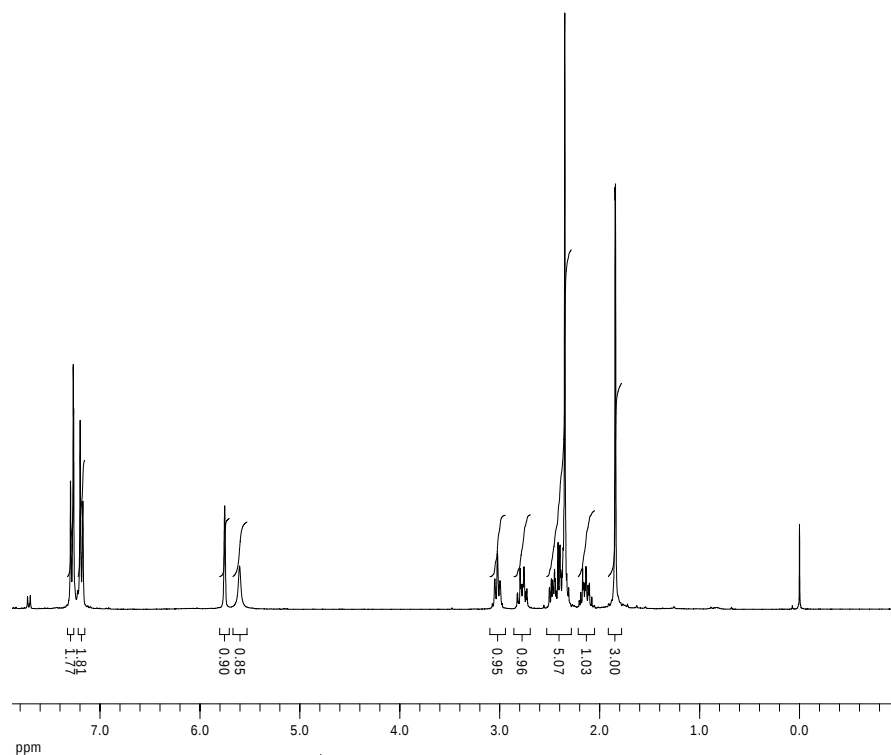
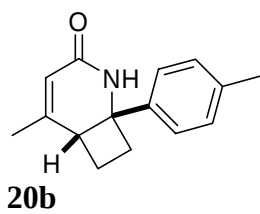
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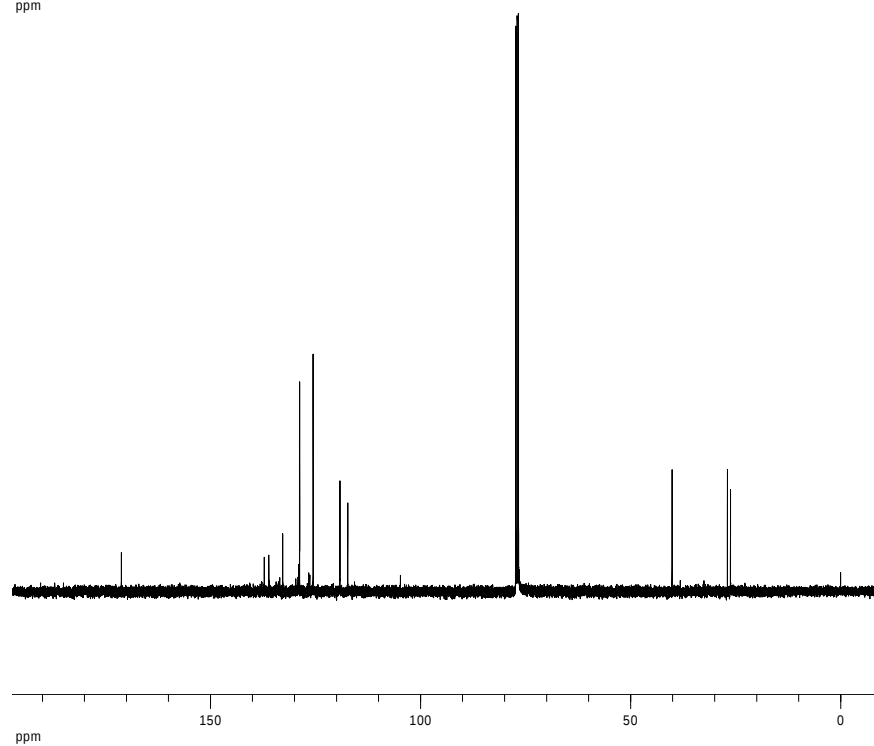
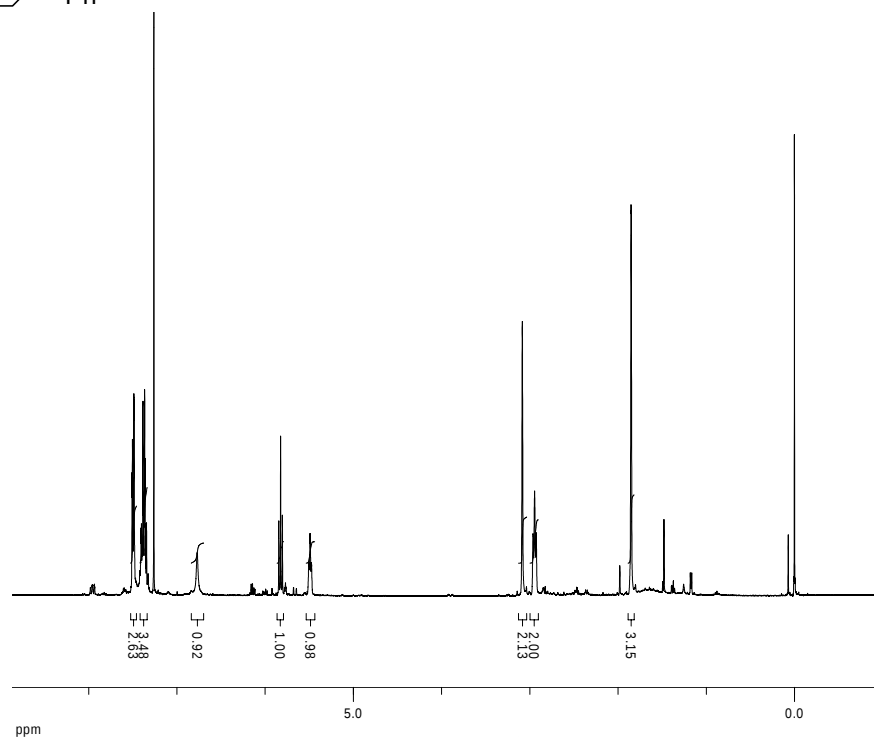
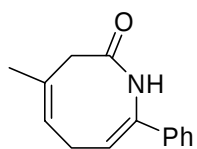


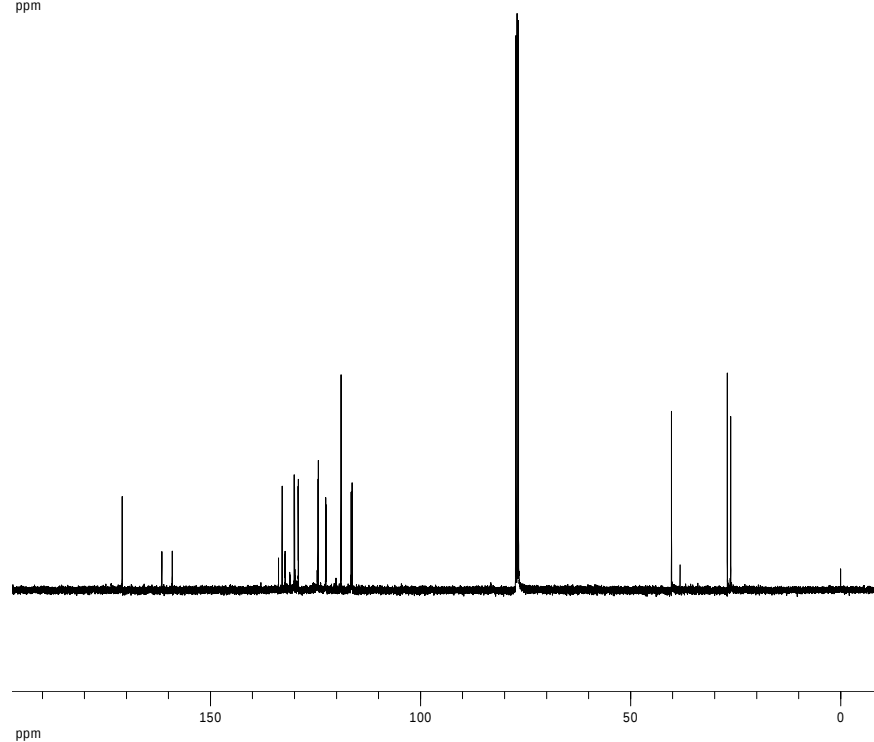
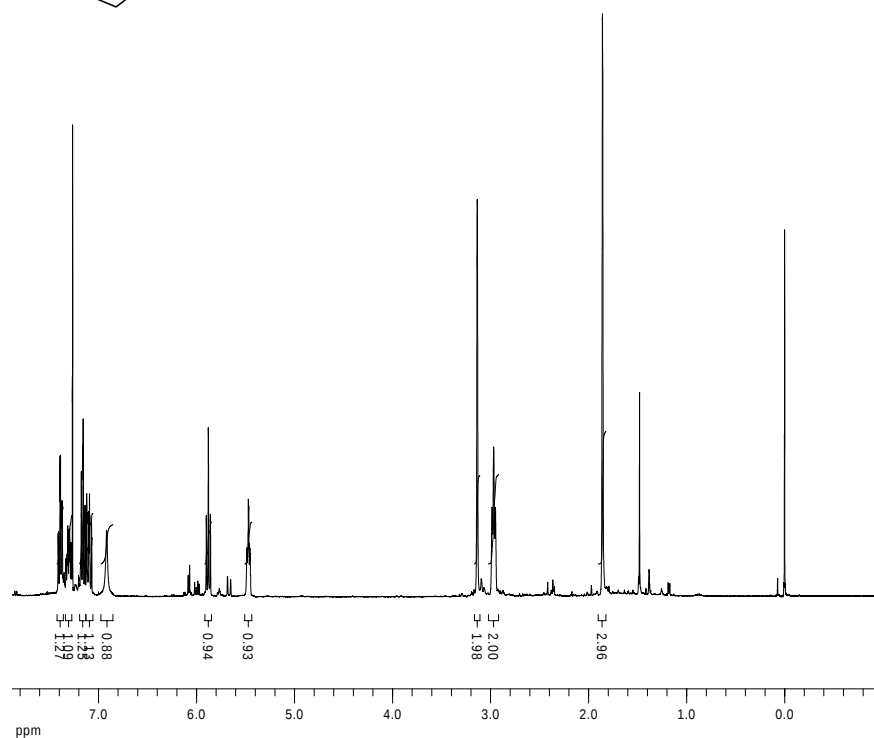
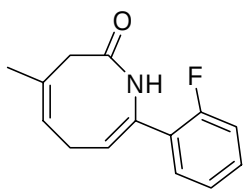


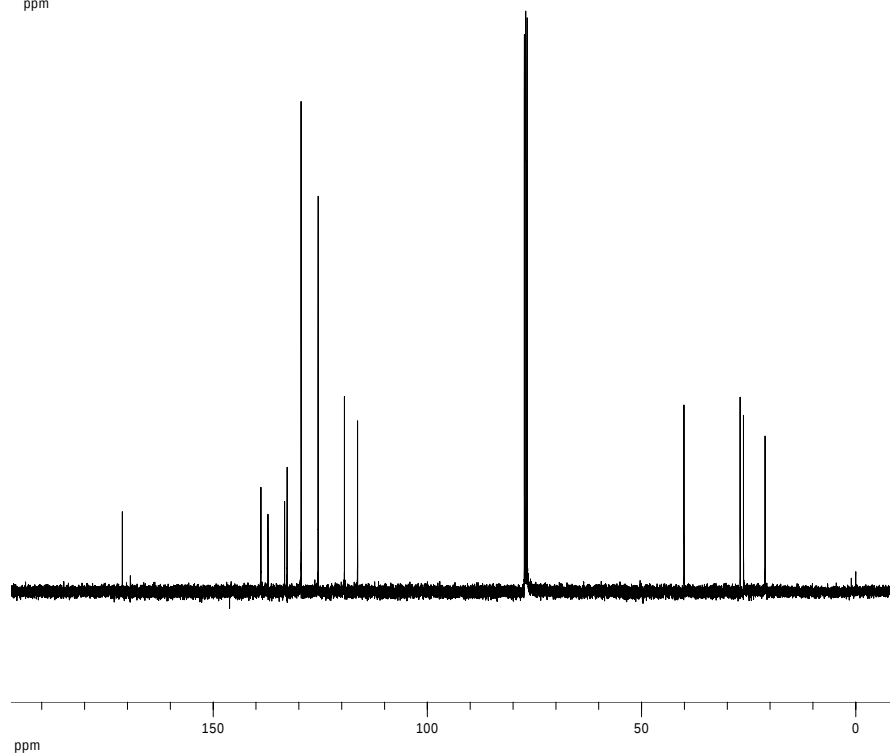
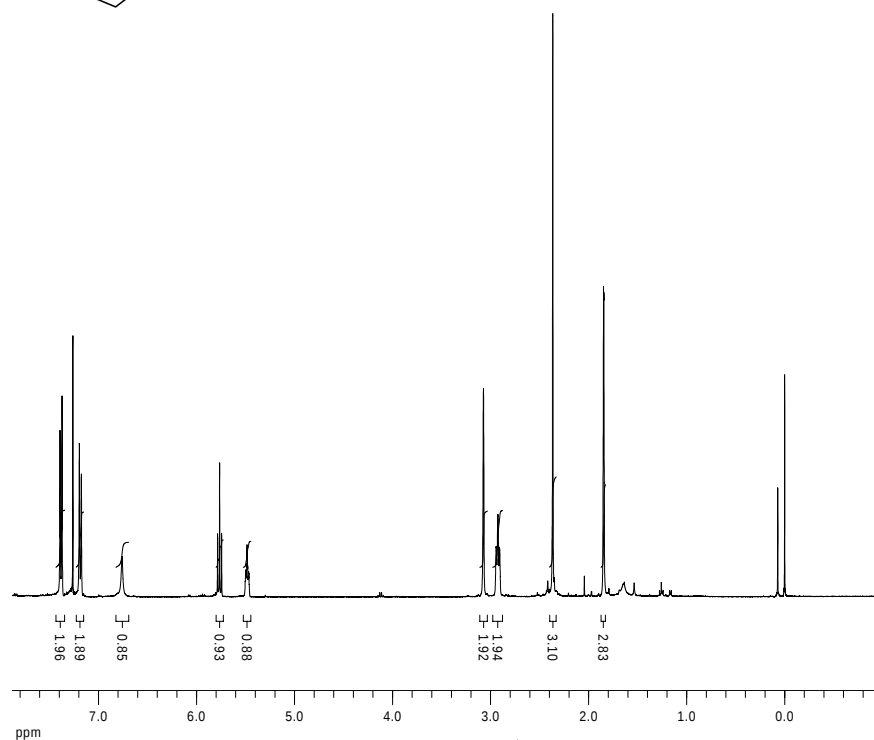
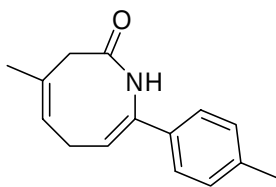
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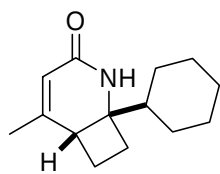




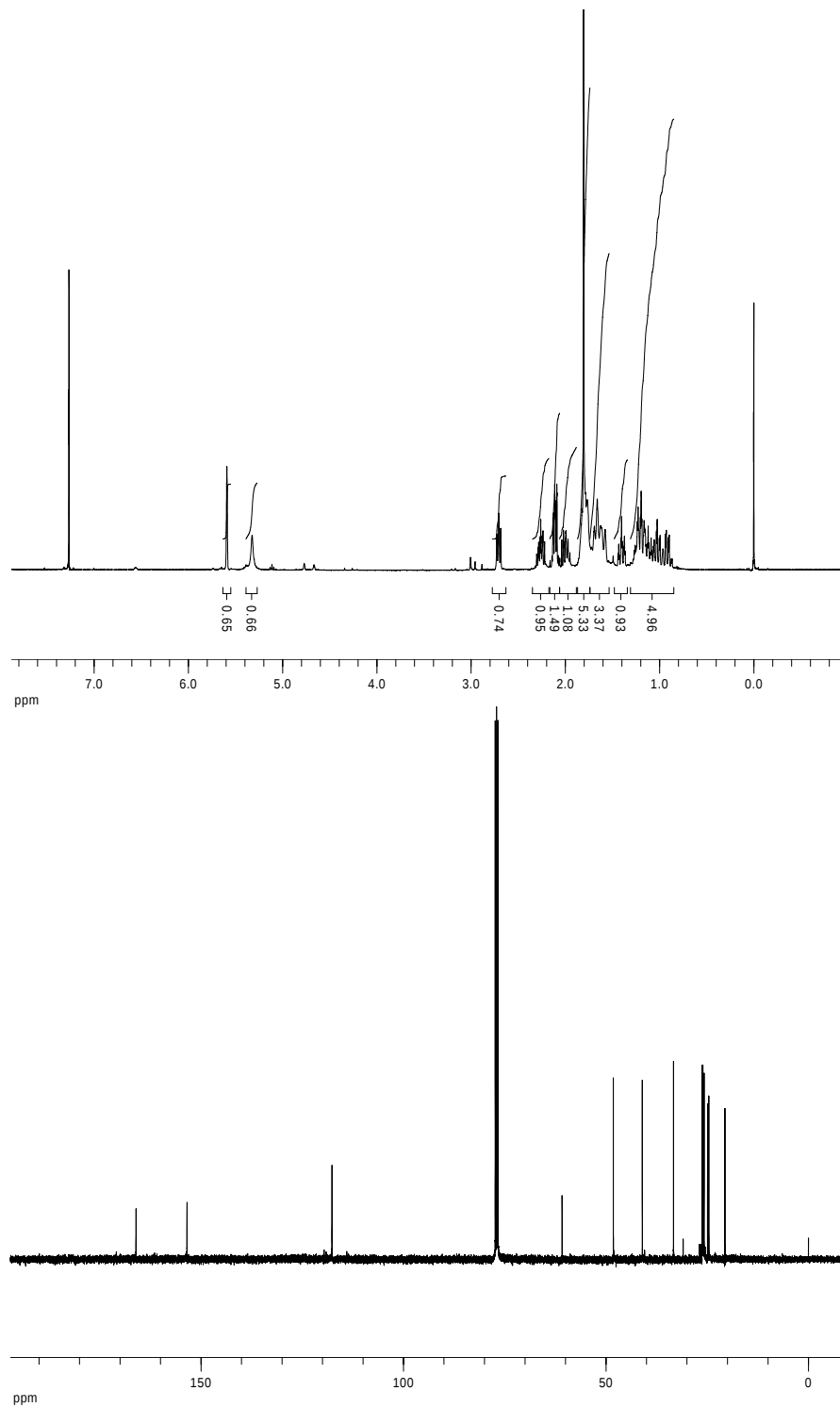


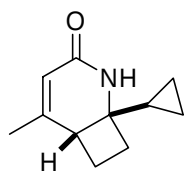




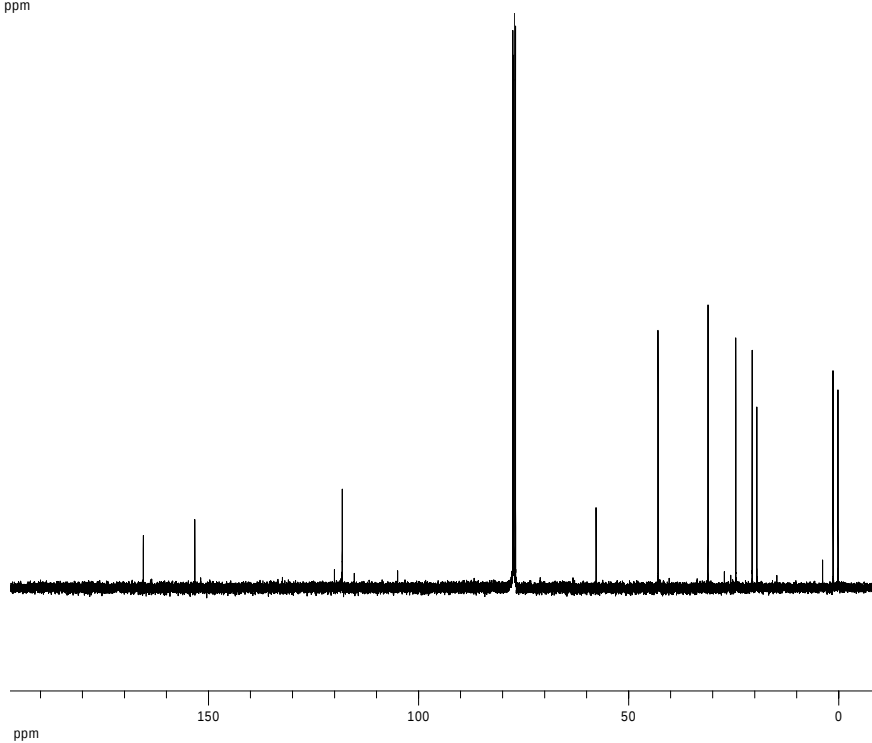
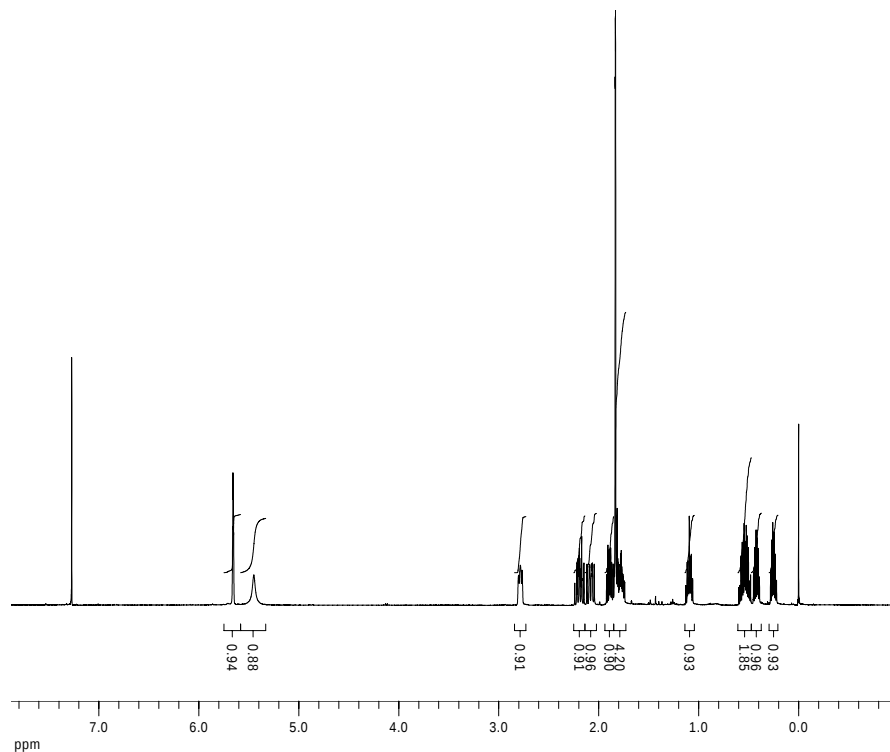


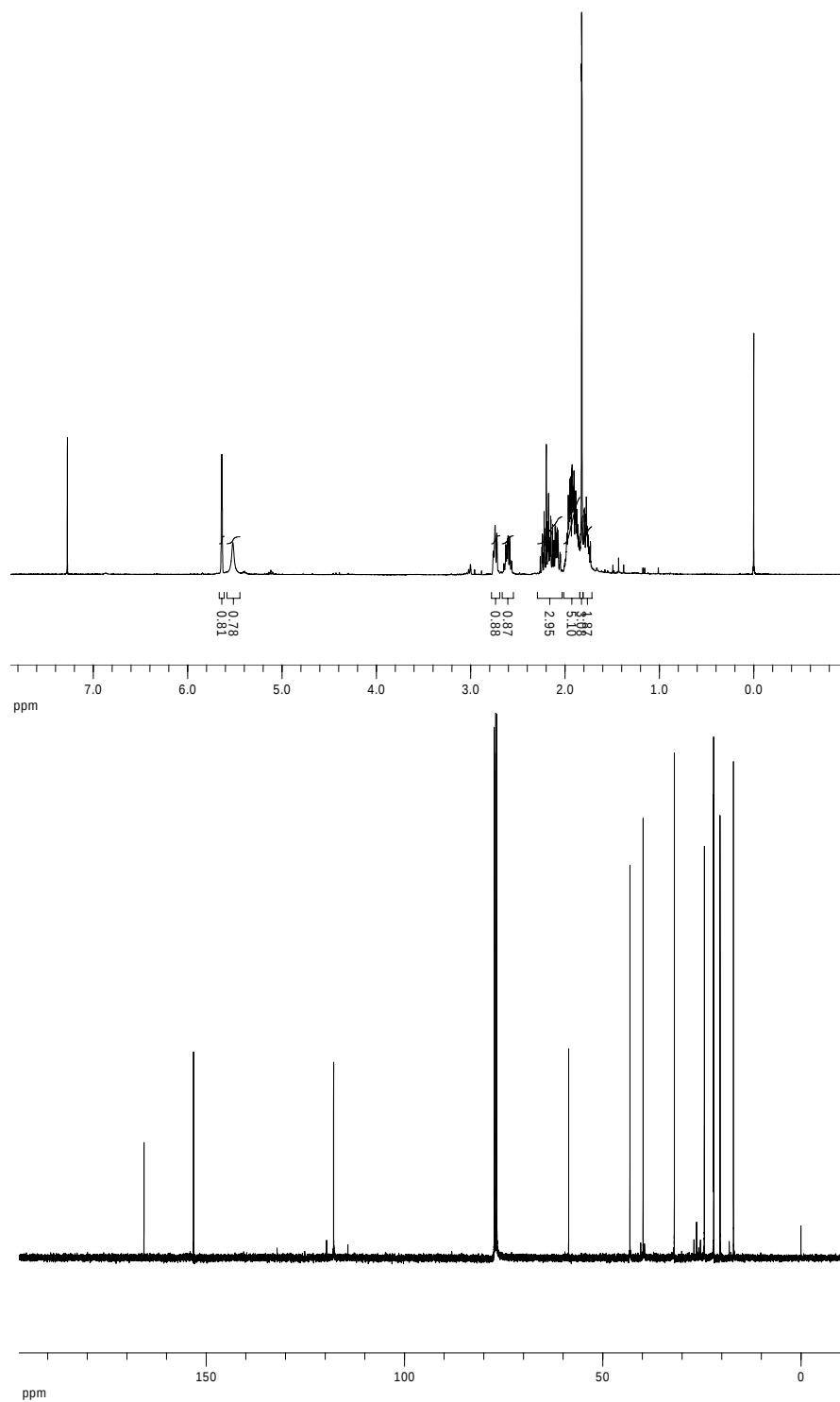
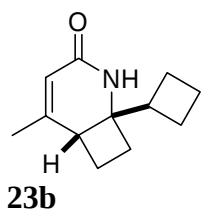
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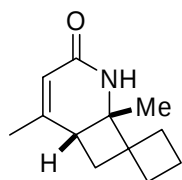




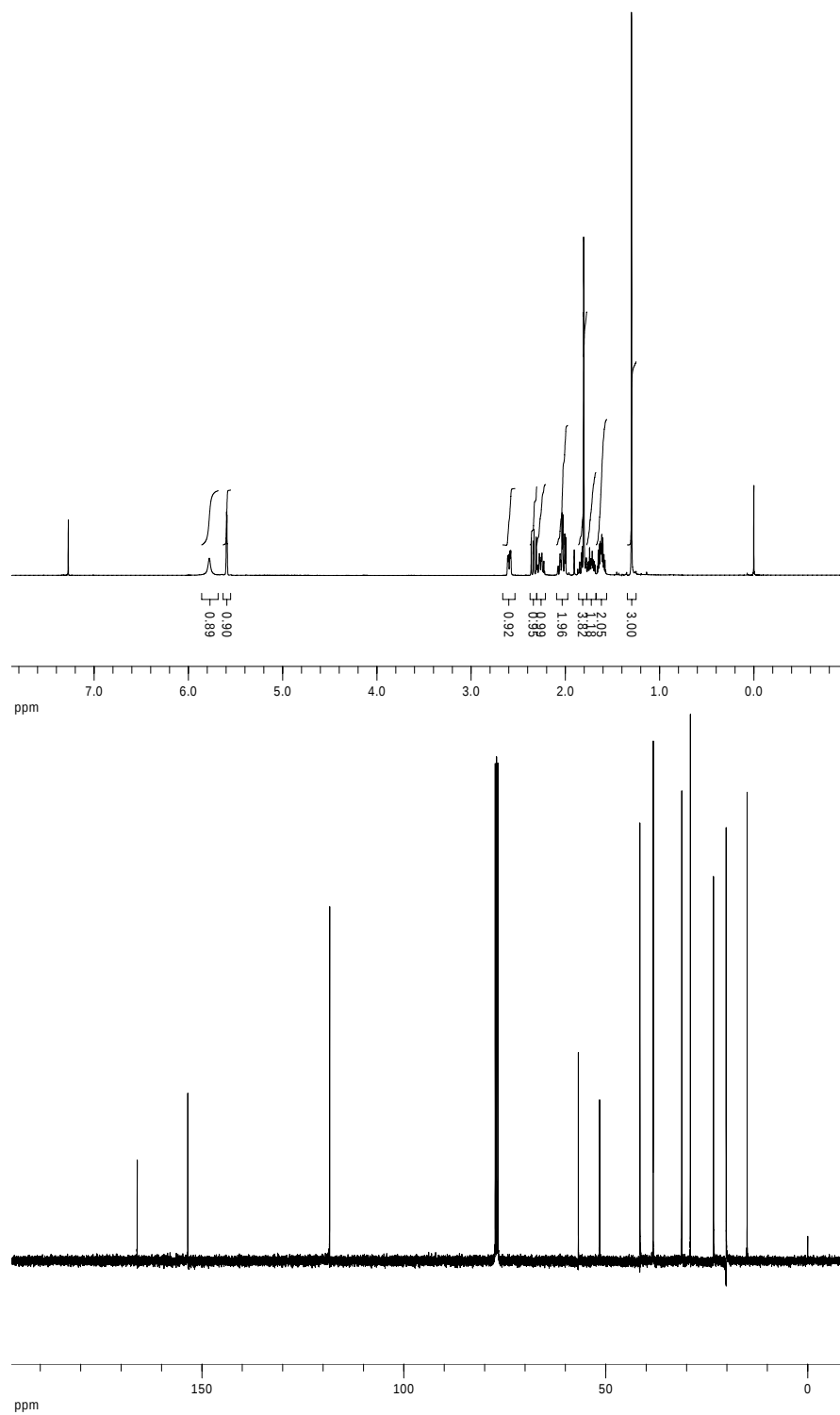
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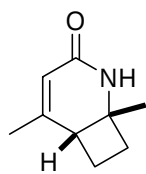






24b





25

