Short communication

Improved Protocol Toward 1,3,4-Oxadiazole-2(3*H*)-thiones and Scale-up Synthesis in the Presence of SDS as a Micelle Promoted Catalyst

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Abstract

Convenient procedure for *in situ* cyclization of hydrazinecarbodithioate potassium salts to 1,3,4-oxadiazole-2(3*H*)-thiones under normal phase micellar media catalysis promoted by sodium dodecyl sulfate (SDS) as an anionic surfactant is reported. The main advantage of this procedure is to provide shorter reaction time for the completion of cyclization; scale-up synthesis is possible and the oxadiazoles were obtained in high to excellent yields (87–100%), making the protocol an attractive alternative to the available methods.

Keywords: Hydrazides; cyclization; 1,3,4-oxadiazoles; surfactant; catalysis.

1. Introduction

The importance of the 1,3,4-oxadiazole ring is well established in industrial, agricultural and pharmaceutical chemistry as demonstrated by the use of its derivatives as antipyretic, analgesic, antidepressant and antimicrobial agents. As an important class of five membered heterocycles, 5-substituted-1,3,4-oxadiazole-2(3*H*)-thiones show a broad spectrum of biological activities. Earlier it was reported that a number of novel quinoline analogs possessing 1,3,4-oxadiazole moiety have been synthesized and screened for their potential antitumor activity.[1] A series of 1,3,4-oxadiazole-2-thiones with salicylate moiety have been synthesized and evaluated for their *in vitro* anticancer activity.[2] Jakubkiene et al. have reported that pyrimidine ring bearing 1,3,4-oxadiazole-2-thiones and their 3-morpholinomethyl derivatives possess anti-inflammatory activity *in vivo*.[3] In addition, some 1,3,4-oxadiazole-2(3*H*)-thiones showed *in vitro* antimycobacterial activity against *Mycobacteriumtuberculosis* $H_{37}Rv$.[4] On the other hand, fatty acid based 1,3,4-oxadiazoles have been synthesized with an objective to study their corrosion inhibiting properties on N-80 steel and mild steel in HCl.[5]

The common synthetic approaches to the 1,3,4-oxadiazole-2(3*H*)-thiones involve cyclization of acylhydrazines in the presence of carbon disulfide in ethanolic solution of potassium hydroxide. However, this classical method of preparation generally requires a long period of time (9–36 h).[6–11] Long chain aliphatic hydrazinecarbodithioate intermediates have to be heated under reflux for a long time. To the best of my knowledge, however, few studies have reported alternative synthesis methods for the preparation of 1,3,4-oxadiazole derivatives.[12–15] Shahzad et al. reported an efficient solvent-free microwave assisted synthesis of 5-substituted-1,3,4-oxadiazole-2(3*H*)-thiones.[12] They also reported that conversion of aromatic hydrazides into 1,3,4-oxadiazoles is more convenient (89–98% yield) but in the case of aliphatic hydrazide conversion is poor and lower yield is obtained (73%). Joshi and Karnik[13] have reported microwave irradiated preparation of oxadiazoles from aromatic hydrazides. Beigi et al. reported a novel practical and efficient catalyst-free method for the synthesis of 1,3,4-oxadiazoles, which is assisted by DMF as a reaction solvent.[14] But one disadvantage of this method is the use of a toxic solvent. Liu et al. developed a new strategy for solid-phase synthesis of 1,3,4-oxadiazoles from resin-bound acylhydrazines, but this method also requires 8 hours for cyclization.[15]

Synthesizing new compounds is a common task for chemists active in preparing various drugs and special industrial chemicals. However, when large-scale synthesis

reaction is performed, some changes in reaction kinetics may occur. In addition low reaction yields, toxicity and abundant hazardous by-products may occur.On the other hand, separation and purification steps play an important role in scale-up of any synthesis.

Therefore, after the evaluation of the disadvantages of the previously published procedures, an alternative procedure involving less toxic, readily available surfactant catalyst, taking place efficiently and quickly in a micellar media, applicable for the synthesis of long-chain aliphatic carboxylic acid hydrazide derived mono and (bis-) 1,3,4-oxadiazole-2(3*H*)-thiones was developed. Furthermore, this strategy also provided the opportunity for clean scale-up synthesis.

2. Results and Discussion

Fatty acid methyl esters were prepared by sulfuric acid catalyzed esterification. For the preparation of fatty acid hydrazides **1a**–**i**, a solution of fatty acid methyl esters in EtOH was mixed with excess of hydrazine hydrate (100%) and the reaction mixture was refluxed for appropriate time. It was cooled and the crystalline solid separated was collected, washed and crystallized from EtOH.

The conventional method applied for the synthesis of the previously known 1,3,4-oxadiazole-2(3*H*)-thiones **2a-i**[18–27] is shown in Scheme 1. The potassium hydrazinecarbodithioates required 24 h for complete cyclization in the absence of SDS.

The optimized SDS catalyzed reaction conditions were determined (Table 1).

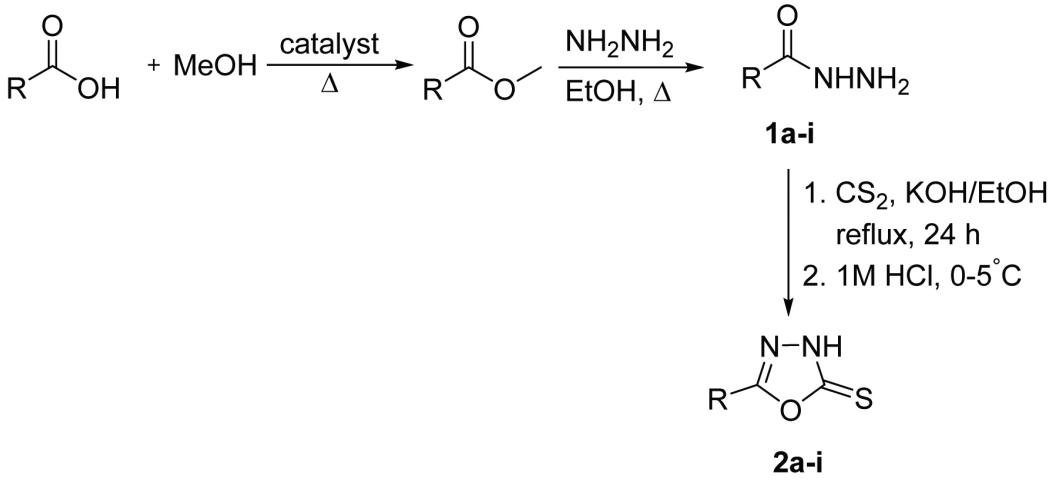
Dodecanehydrazide **1c** was selected as the model substrate for optimization of the micellar media reaction conditions. It was found that the SDS plays a crucial role in the success of the reaction in terms of the rate enhancement. When the reaction was carried out in the absence of SDS for 2 h and in the presence of SDS for 1 h, the conversion is incomplete with starting acyl hydrazine **1c** still available in the reaction medium (entries 1 and 2, Table 1). But after heating for additional 1 h in the presence of SDS, it is found that complete conversion could be obtained. Finally, it was found that for complete conversion in the presence of SDS the optimum reaction time is 2 h (entry 3, Table 1 and Scheme 2).

Table 1. Optimization of the reaction conditions for the preparation of compound **2c**.[19–21]

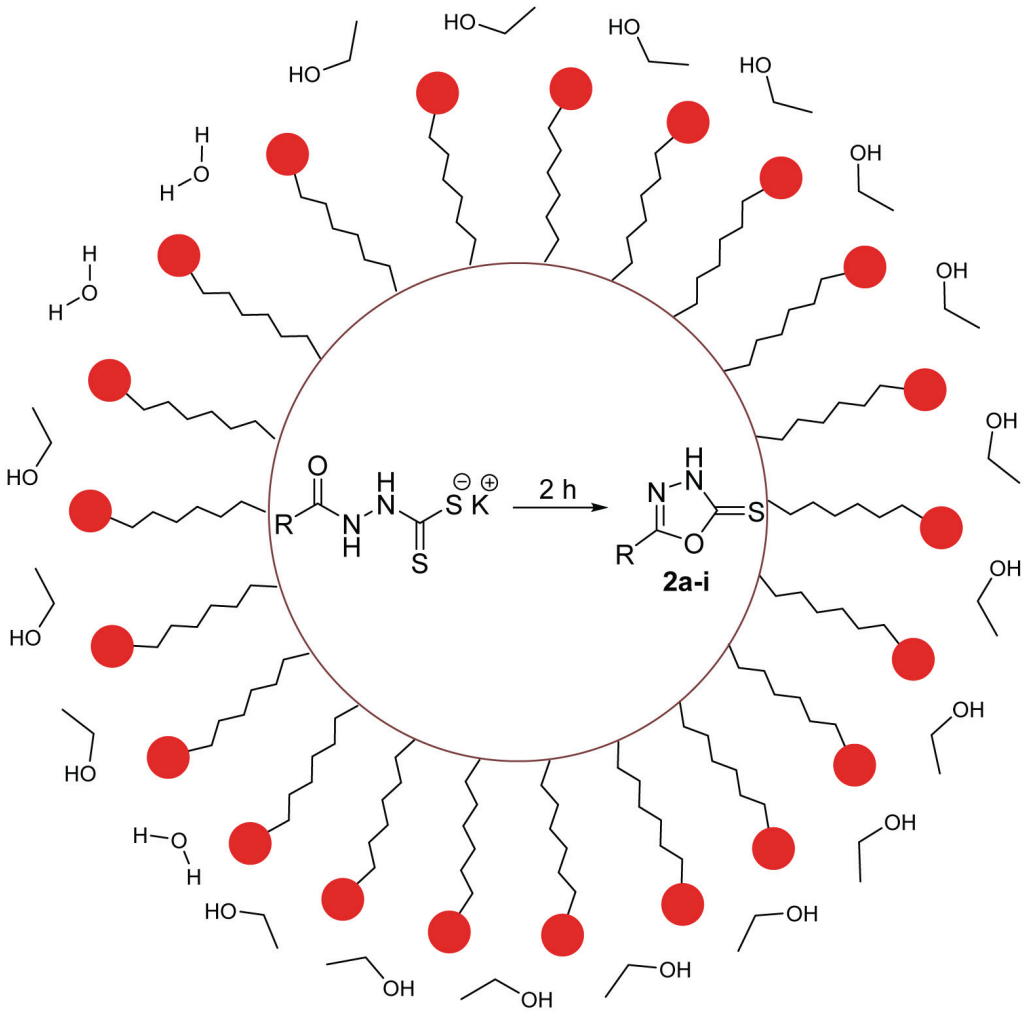
Entry	Catalyst (10% mmol/mmol)	Solvent	Time (h)	Yield (%)
1	–	EtOH + H_2O	2	53
2	SDS	EtOH + H_2O	1	64
3	SDS	EtOH + H_2O	2	100
4	SDS	H_2O	2	Not isolated

When water was used as a solvent in the presence of SDS under reflux conditions for 2 h, the reaction medium was checked by TLC (Thin Layer Chromatography) and the desired cyclization product was detected but the isolation of the product **2c**[19, 20, 21] was very difficult due to the tedious and ineffective vacuum filtration caused by the detergent effect of SDS in water (entry 4, Table 1). One alternative solution to this problem is the extraction of the product from the aqueous medium by using a suitable organic solvent, but this is not practical for scale-up synthesis and is also not eco-friendly. Therefore, EtOH was selected as a suitable recrystallization solvent.

In some cases the yields obtained by micelle catalysis were better than those achieved by the conventional method (Table 2). Typically, surface active compounds have enough solubility in polar organic solvents



Scheme 1. Conventional synthesis of oxadiazoles.



Scheme 2. Micellar media synthesis of oxadiazoles.

Table 2. Synthesis of higher 5-substituted-1,3,4-oxadiazole-2(3*H*)-thiones in micellar media.

Entry	Product	Time [h][a]	Yield [%][a,b]	Time [h][c]	Yield [%][b,c]
1	**2a**[20,21]	24	91	2	92
2	**2b**[19–21]	24	100	2	99
3	**2c**[19–21]	24	95	2	100
4	**2d**	24	87	2	87
5	**2e**[19,20]	24	82	2	100
6	**2f**[27]	24	89	2	99
7	**2g**[27]	24	85	2	90
8	**2h**[23]	24	80	2	96
9	**2i**	24	84	2	99

[a] Conventional method. [b] Yield after crystallization. [c] Micellar media method.

such as lower alcohols. Depending on the alcohol concentration the surface tension is varied.[16] For example, the change of critical micelle concentration (cmc) of SDS in water, depending on the concentration of EtOH is shown in Figure 1.

The cmc reaches a minimum at 5% of EtOH (marked area I), and increases from that point.[16] The reason for this minimum is association of EtOH with the SDS micelle. But then solubility of SDS increases with an increase in the EtOH concentration. Thus at constant temperature

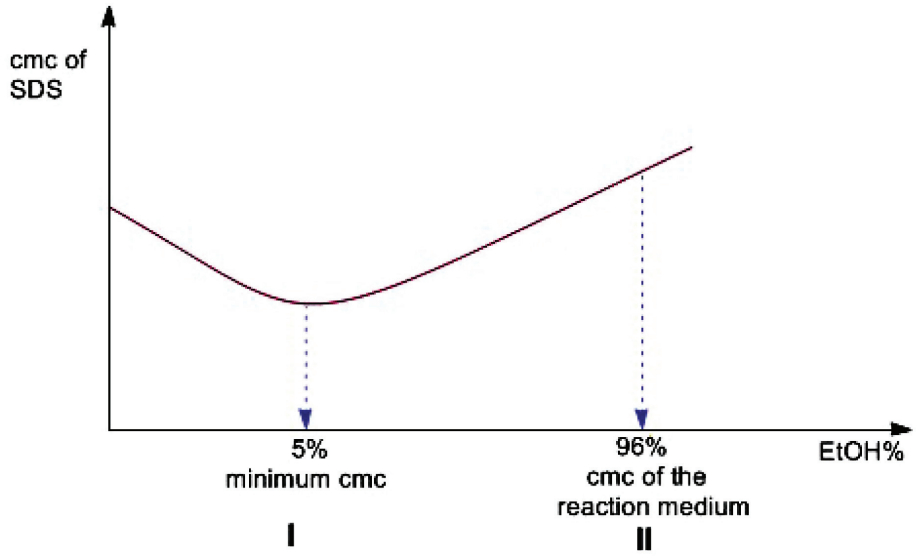
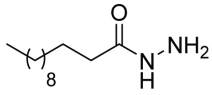
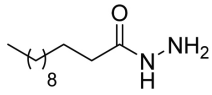
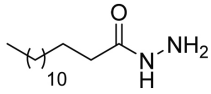
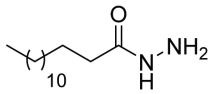
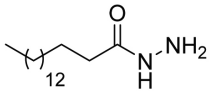
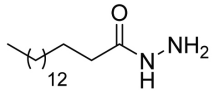
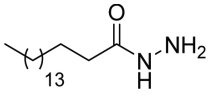
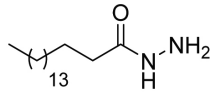
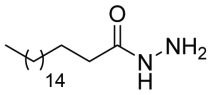
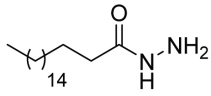
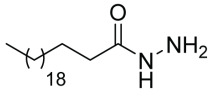
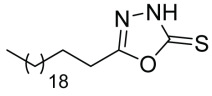
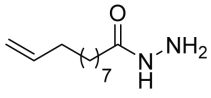
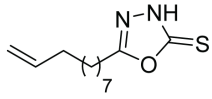
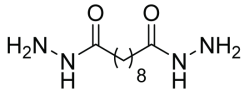
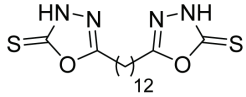
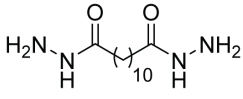
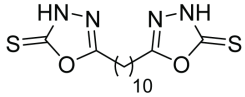


Figure 1. Cmc value of SDS according to EtOH concentration in water.

Table 3. Structures of the synthesized oxadiazoles.

Entry	Substrate 1	Product 2
1	**1a** 	**2a** 
2	**1b** 	**2b** 
3	**1c** 	**2c** 
4	**1d** 	**2d** 
5	**1e** 	**2e** 
6	**1f** 	**2f** 
7	**1g** 	**2g** 
8	**1h** 	**2h** 
9	**1i** 	**2i** 

minor amounts of EtOH lower the cmc of SDS, but when EtOH is available in large amounts the value rises.[17] In Figure 1 the area marked II shows concentration of EtOH where the reaction takes place.

In comparison with the reported conventional methods for the preparation of oxadiazoles, the present method was found to be advantageous in terms of scale up as well as easy isolation of pure products. On the other hand, this method offers a number of attractive advantages such as short reaction time, non-hazardous solvents, and cost effectiveness. The structures of the oxadiazoles prepared in this study are given in Table 3. The synthesis of **2c**[19–21] was performed on a multi-gram scale and high yield of the product was obtained (95%). ^{1}H NMR and ^{13}C NMR data were in good agreement with the literature.[18–27]

3. Conclusions

The present approach furnished mono and bis-1,3,4-oxadiazole-2(3*H*)-thiones with high yields and is, to the best of my knowledge, the first economically SDS catalyzed route to date to prepare above-mentioned heterocyclic compounds in a convenient manner. The heterocyclic compounds could be obtained from readily available reagents and solvents with simple workup, rendering this improved protocol highly amenable to the large-scale synthesis of 1,3,4-oxadiazole-2(3*H*)-thiones.

4. Experimental

4. 1. General

All reagents and solvents were purchased from either Merck or Sigma-Aldrich and used without further purification. TLC was performed using silica gel (60 F_{254}, Merck, Darmstadt, Germany) plates. Melting points were recorded by Büchi melting point B-540 apparatus (Büchi Labortechnik AG in Flawil, Switzerland). The NMR spectra were measured using Varian Mercury plus spectrometer (400 MHz) (Varian Inc., California, USA) in $CDCl_3$ using TMS as the internal standard. Chemical shifts (d) are reported in ppm and *J* values in Hertz.

4. 2. Typical Experimental Procedures for the Synthesis of 5-Substituted-1,3,4 -oxadiazole-2(3H)-thiones

4. 2. 1. Micellar Media Method (2c[19–21])

Potassium hydroxide (0.2 g, 3.6 mmol) was dissolved in 1 mL of water and absolute ethanol (25 mL) was added. Hydrazide **1c** (0.6 g, 2.2 mmol) and SDS (0.06 g, 10% mmol/mmol) were added to the above basic solution. After the formation of a clear solution, CS_2 (0.3 g, 0.24 mL, 3.9 mmol) was added dropwise and the mixture stirred at reflux for 2 h. The reaction mixture was concentrated under vacuum, and 10 mL of ice-cooled water was added. Afterwards, the solution was acidified with cooled 1M HCl(aq). The obtained solid was filtered under vacuum and dried at room temperature and ambient pressure for 24 h. It was crystallized from EtOH/H_2O as a white crystalline solid; yield 0.69 g (100%); mp 83–84°C; IR (KBr): 3205, 1620, 1176, 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.93 (s, 1H, -NH), 2.69 (t, J 7.6 Hz, 2H, -CH_2-het), 1.74 (quin, J 7.5 Hz, 2H, -$CH_2CH_2CH_2$-het), 1.43–1.22 (m, 24H, -CH_2-), 0.87 (t, J 6.4 Hz, 3H, -CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.54, 164.90, 31.87, 29.54, 29.52, 29.32, 29.29, 28.99, 28.76, 25.67, 25.53, 22.66, 14.10. Anal. Calcd for $C_{17}H_{32}N_2OS$: C, 65.34; H, 10.32; N, 8.96; S, 10.26. Found: C, 65.15; H, 10.09; N, 8.49; S, 10.28.

4. 2. 2. Scale-up of Micellar Media Method (2c[19–21])

Potassium hydroxide (6.75 g, 120 mmol) was dissolved in 25 mL of water and absolute ethanol (400 mL) was added. Hydrazide **1c** (20 g, 73.9 mmol) and SDS (2.13 g, 10% mmol/mmol) were added to the above basic solution. After the formation of a clear solution, CS_2 (10 g, 7.9 mL, 131.3 mmol) was added and the mixture stirred at reflux for 2 h. The reaction mixture was concentrated under vacuum, and 150 mL of ice-cooled water was added. Afterwards, the solution was acidified with cooled 1M HCl(aq). The obtained solid was filtered under vacuum and dried at room temperature and ambient pressure for 24 h. It was crystallized from EtOH/H_2O as a white crystalline solid; yield 22 g (95%)

4. 3. 3. Conventional Method (2c[19–21])

Potassium hydroxide (0.2 g, 3.6 mmol) was dissolved in 1 mL of water and absolute ethanol (25 mL) was added. Hydrazide **1c** (0.6 g, 2.2 mmol) was added to the above basic solution. After the formation of a clear solution, CS_2 (0.3 g, 0.24 mL, 3.9 mmol) was added dropwise and the mixture stirred at reflux for 24 h. The reaction mixture was concentrated under vacuum, and 10 mL of ice-cooled water was added. Afterwards, the solution was acidified with cooled 1M HCl(aq). The observed solid was filtered under vacuum and dried at room temperature and ambient pressure for 24 h. It was crystallized from EtOH/H_2O as a white crystalline solid; yield 0.66 g (95%).

5. References

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Povzetek

Poročam o priročnem postopku *in situ* ciklizacije kalijevih hidrazinkarboditioatnih soli v 1,3,4-oksadiazol-2(3*H*)-tione pod pogoji katalize v micelnem mediju z normalno fazo ob sodelovanju natrijevega dodecil sulfata (SDS) kot anionskega surfaktanta. Glavna prednost tega postopka je skrajšanje reakcijskih časov, ki so potrebni za popolno ciklizacijo; možno je tudi izvajanje sintez z večjimi količinami; ker je oksadiazole mogoče pripraviti z visokimi do odličnimi izkoristki (87–100%), to še dodatno poveča zanimivost predstavljenega protokola kot atraktivne alternative obstoječim metodam.

Supplementary material

Improved Protocol Toward 1,3,4-Oxadiazole-2(3*H*)-thiones and Scale-up Synthesis in the Presence of SDS as a Micelle Promoted Catalyst

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Spectroscopic characterization of compounds:

Compound 2a: IR (KBr): 3205, 1620, 1173, 1057 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.97 (*s*, 1H, −NH), 2.69 (*t*, *J* 7.6 Hz, 2H, $-CH_2-$het), 1.75 (*quin*, *J* 7.6 Hz, 2H, $-CH_2CH_2CH_2-$het), 1.43-1.23 (*m*, 16H, $-CH_2-$), 0.87 (*t*, *J* 6.8 Hz, 3H, $-CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.54, 164.90, 31.87, 29.54, 29.52, 29.32, 29.29, 28.99, 28.76, 25.67, 25.53, 22.66, 14.10. Anal. Calcd for $C_{13}H_{24}N_2OS$: C, 60.90; H, 9.43; N, 10.93; S, 12.50. Found: C, 60.85; H, 9.40; N, 10.56; S, 12.70.

Compound 2b: IR (KBr): 3205, 1620, 1176, 1065 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.91 (*s*, 1H, −NH), 2.69 (*t*, *J* 7.5 Hz, 2H, $-CH_2-$het), 1.73 (*quin*, *J* 7.2 Hz, 2H, $-CH_2CH_2CH_2-$het), 1.43-1.21 (*m*, 20H, $-CH_2-$), 0.87 (*t*, *J* 6.8 Hz, 3H, $-CH_3$); ^{13}C NMR (100, MHz, $CDCl_3$): δ 178.54, 164.90, 31.90, 29.63, 29.62, 29.59, 29.52, 29.33, 29.00, 28.77, 25.67, 25.53, 22.67, 14.11. Anal. Calcd for $C_{15}H_{28}N_2OS$: C, 63.34; H, 9.92; N, 9.85; S, 11.27. Found: C, 63.20; H, 9.87; N, 9.63; S, 11.59.

Compound 2c: IR (KBr): 3205, 1620, 1176, 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.93 (*s*, 1H, −N<u>H</u>), 2.69 (*t*, *J* 7.6 Hz, 2H, −C<u>H</u>$_2$−het), 1.74 (*quin*, *J* 7.5 Hz, 2H, −CH$_2$C<u>H</u>$_2$CH$_2$−het), 1.43-1.22 (*m*, 24H, −CH$_2$−), 0.87 (*t*, *J* 6.4 Hz, 3H, −C<u>H</u>$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.54, 164.90, 31.87, 29.54, 29.52, 29.32, 29.29, 28.99, 28.76, 25.67, 25.53, 22.66, 14.10. Anal. Calcd for $C_{17}H_{32}N_2OS$: C, 65.34; H, 10.32; N, 8.96; S, 10.26. Found: C, 65.15; H, 10.09; N, 8.49; S, 10.28.

Compound 2d: IR (KBr): 3205, 1624, 1165, 1072 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.96 (*s*, 1H, −N<u>H</u>), 2.69 (*t*, *J* 7.6 Hz, 2H, −C<u>H</u>$_2$−het), 1.74 (*quin*, *J* 7.4 Hz, 2H, −CH$_2$C<u>H</u>$_2$CH$_2$−het), 1.43-1.18 (*m*, 26H, −CH$_2$−), 0.87 (*t*, *J* 6.8 Hz, 3H, −C<u>H</u>$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.54, 164.89, 31.92, 29.69, 29.68, 29.65, 29.60, 29.54, 29.36, 29.34, 29.01, 28.78, 25.68, 25.53, 22.69, 14.13. Anal. Calcd for $C_{18}H_{34}N_2OS$: C, 66.21; H, 10.50; N, 8.58; S, 9.82. Found: C, 66.26; H, 10.65; N, 8.13; S, 9.52.

Compound 2e: IR (KBr): 3205, 1612, 1165, 1053 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.93 (*s*, 1H, −N<u>H</u>), 2.69 (*t*, *J* 7.5 Hz, 2H, −C<u>H</u>$_2$−het), 1.75 (*quin*, *J* 7.4 Hz, 2H, −CH$_2$C<u>H</u>$_2$CH$_2$−het), 1.43-1.22 (*m*, 28H, −CH$_2$−), 0.87 (*t*, *J* 6.8 Hz, 3H, −C<u>H</u>$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.54, 164.89, 31.92, 29.68, 29.65, 29.60, 29.53, 29.35, 29.33, 29.01, 28.77, 25.68, 25.53, 22.68, 14.12. Anal. Calcd for $C_{19}H_{36}N_2OS$: C, 67.01; H, 10.66; N, 8.23; S, 9.41. Found: C, 66.90; H, 10.66; N, 8.04; S, 9.64.

Compound 2f: IR (KBr): 3205, 1620, 1165, 1060 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.93 (*s*, 1H, −N<u>H</u>), 2.69 (*t*, *J* 7.6 Hz, 2H, −C<u>H</u>$_2$−het), 1.74 (*quin*, *J* 7.4 Hz, 2H, −CH$_2$C<u>H</u>$_2$CH$_2$−het), 1.43-1.22 (*m*, 36H, −CH$_2$−), 0.88 (*t*, *J* 6.8 Hz, 3H, −C<u>H</u>$_3$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.54, 164.89, 31.92, 29.68, 29.65, 29.60, 29.53, 29.35,

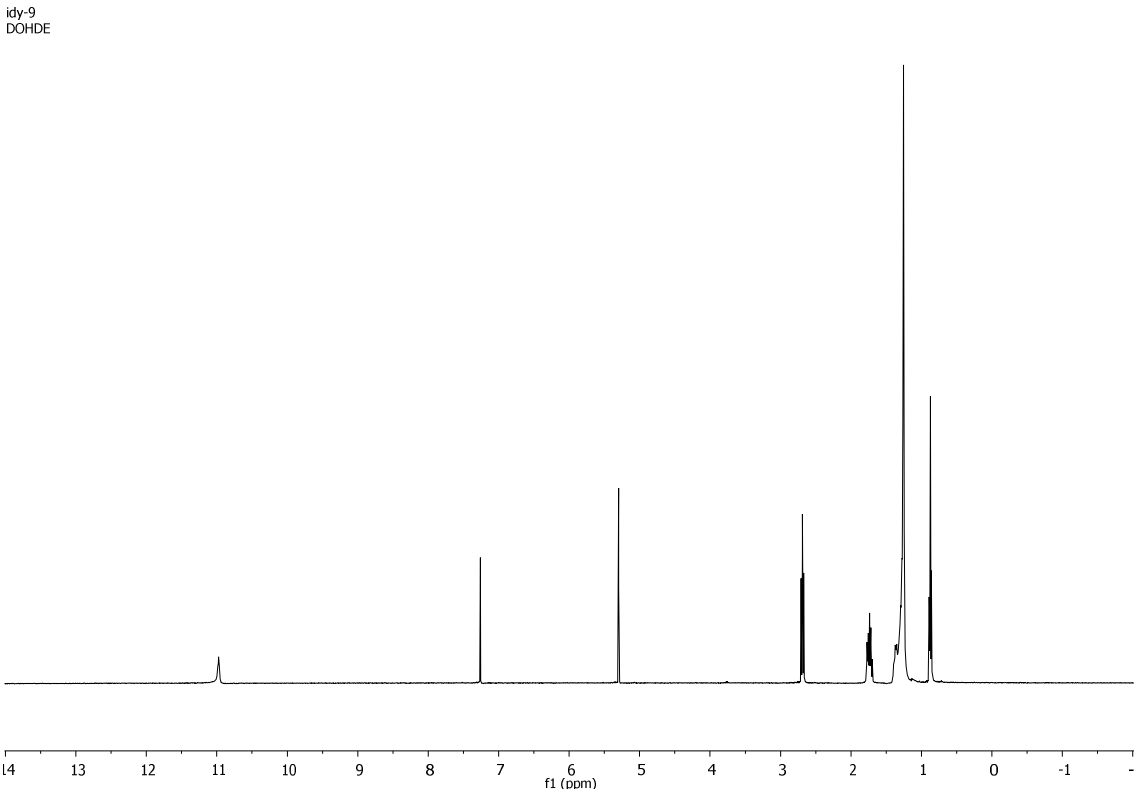
29.33, 29.28, 29.17, 29.01, 28.77, 25.70, 25.68, 25.53, 22.68, 14.12. Anal. Calcd for $C_{23}H_{44}N_2OS$: C, 69.64; H, 11.18; N, 7.06; S, 8.08. Found: C, 69.80; H, 10.76; N, 7.34; S, 8.45.

Compound 2g: IR (KBr): 3190, 1642, 1624, 1611, 1160, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.86-5.76 (*m*, 1H, CH_2=C<u>H</u>-), 5.02-4.97 (*m*, 1H, C<u>H</u>H=CH-), 4.95-4.92 (*m*, 1H, CH<u>H</u>=CH), 2.70 (*t*, *J* 7.6 Hz, 2H, −C<u>H</u>$_2$−het), 2.07-2.02 (*m*, 2H, CH_2=CH-C<u>H</u>$_2$-), 1.74 (*quin*, *J* 7.6 Hz, 2H, −CH_2C<u>H</u>$_2CH_2$−het), 1.39-1.25 (*m*, 10H, −CH_2−); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.56, 164.83, 139.10, 114.23, 33.75, 31.85, 29.78, 29.48, 29.16, 28.97, 28.82, 25.67. Anal. Calcd for $C_{12}H_{20}N_2OS$: C, 59.96; H, 8.39; N, 11.65; S, 13.34. Found: C, 60.15; H, 8.42; N, 11.36; S, 13.29.

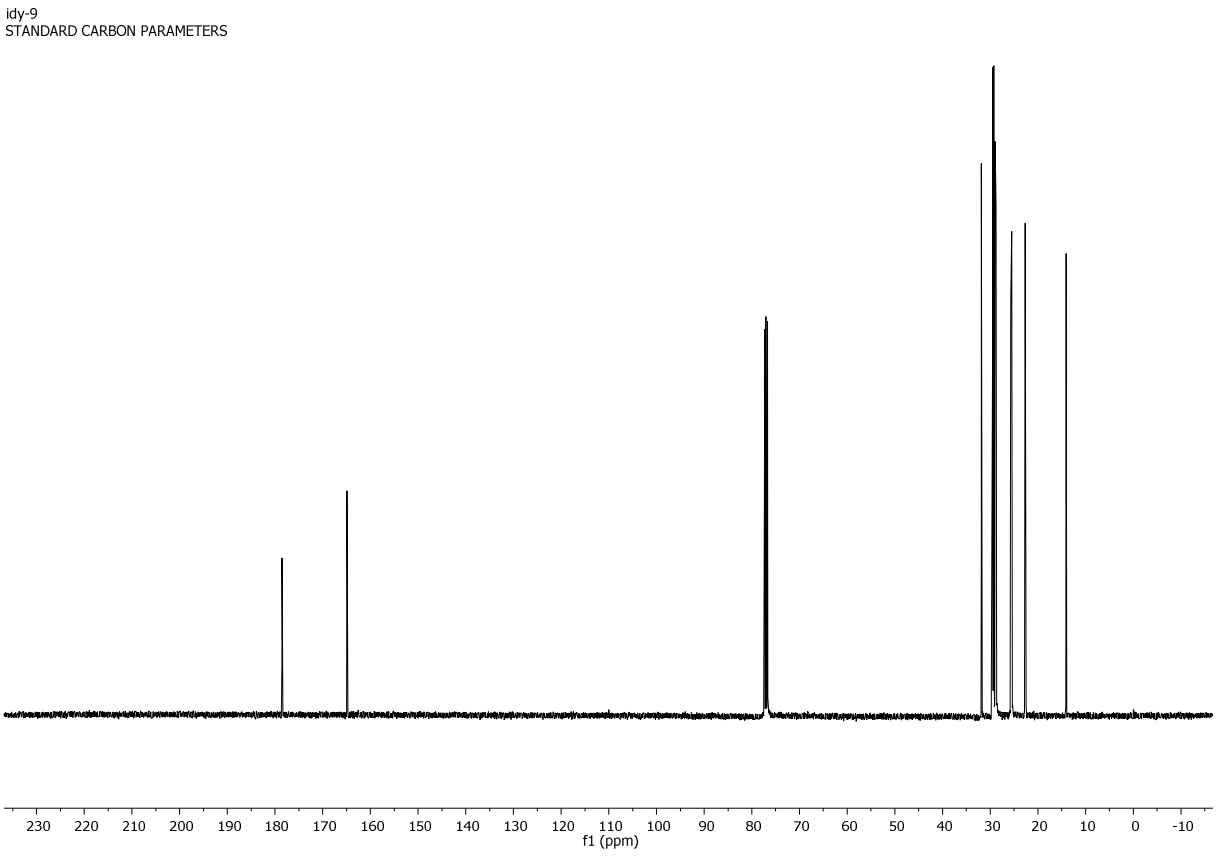
Compound 2h: IR (KBr): 3181, 1626, 1609, 1160, 1065 cm^{-1}; ^1H NMR (400 MHz, DMSOd_6): δ 2.64 (*t*, *J* 7.6 Hz, 4H, 2x−C<u>H</u>$_2$−het), 1.57 (*t*, *J* 6.4 Hz, 4H, 2x−CH_2C<u>H</u>$_2CH_2$−het), 1.23-1.18 (*m*, 8H, −CH_2−); ^{13}C NMR (100 MHz, DMSOd_6): δ 178.09, 164.63, 28.68, 28.49, 25.34, 25.14. Anal. Calcd for $C_{12}H_{18}N_4O_2S_2$: C, 45.84; H, 5.77; N, 17.82; S, 20.39. Found: C, 45.57; H, 5.91; N, 17.86; S, 20.22.

Compound 2i: IR (KBr): 3180, 1626, 1608, 1160, 1064 cm^{-1}; ^1H NMR (400 MHz, DMSOd_6): δ 2.64 (*t*, *J* 7.6 Hz, 4H, 2x−C<u>H</u>$_2$−het), 1.57 (*t*, *J* 6.4 Hz, 4H, 2x−CH_2C<u>H</u>$_2CH_2$−het), 1.23-1.18 (*m*, 12H, −CH_2−); ^{13}C NMR (100 MHz, DMSOd_6): δ 178.09, 164.63, 28.64, 28.48, 25.36, 25.14. Anal. Calcd for $C_{14}H_{22}N_4O_2S_2$: C, 49.10; H, 6.48; N, 16.36; S, 18.72. Found: C, 49.35; H, 6.43; N, 16.37; S, 18.59.

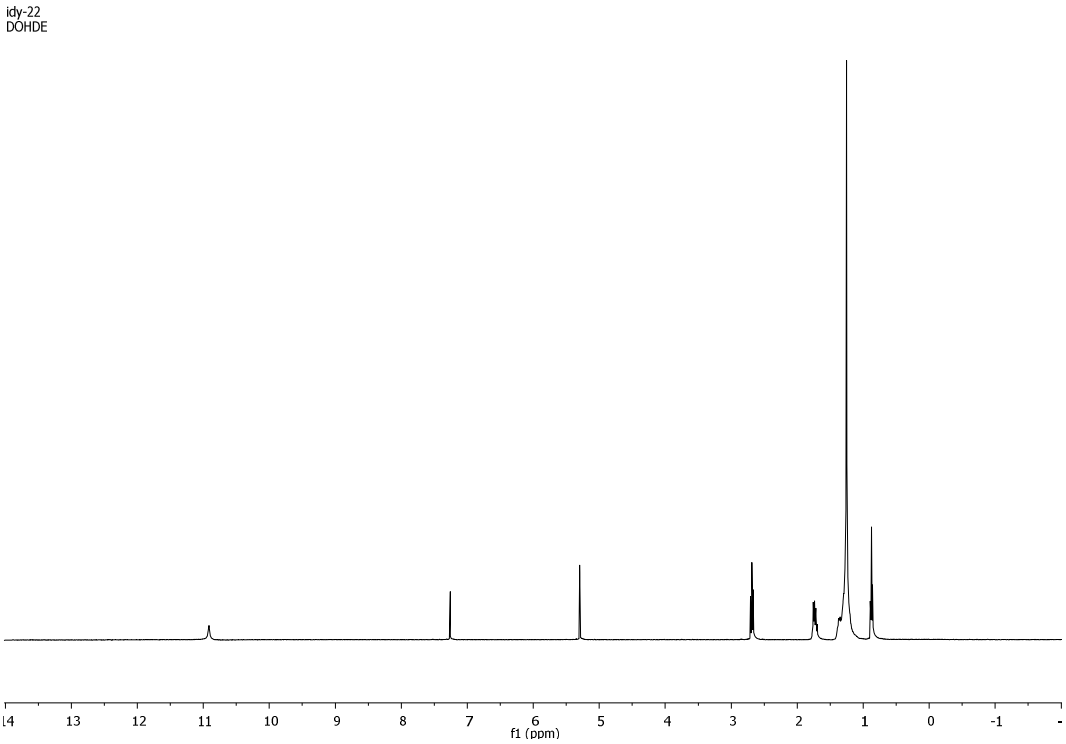
H-NMR Spectrum: **2a**



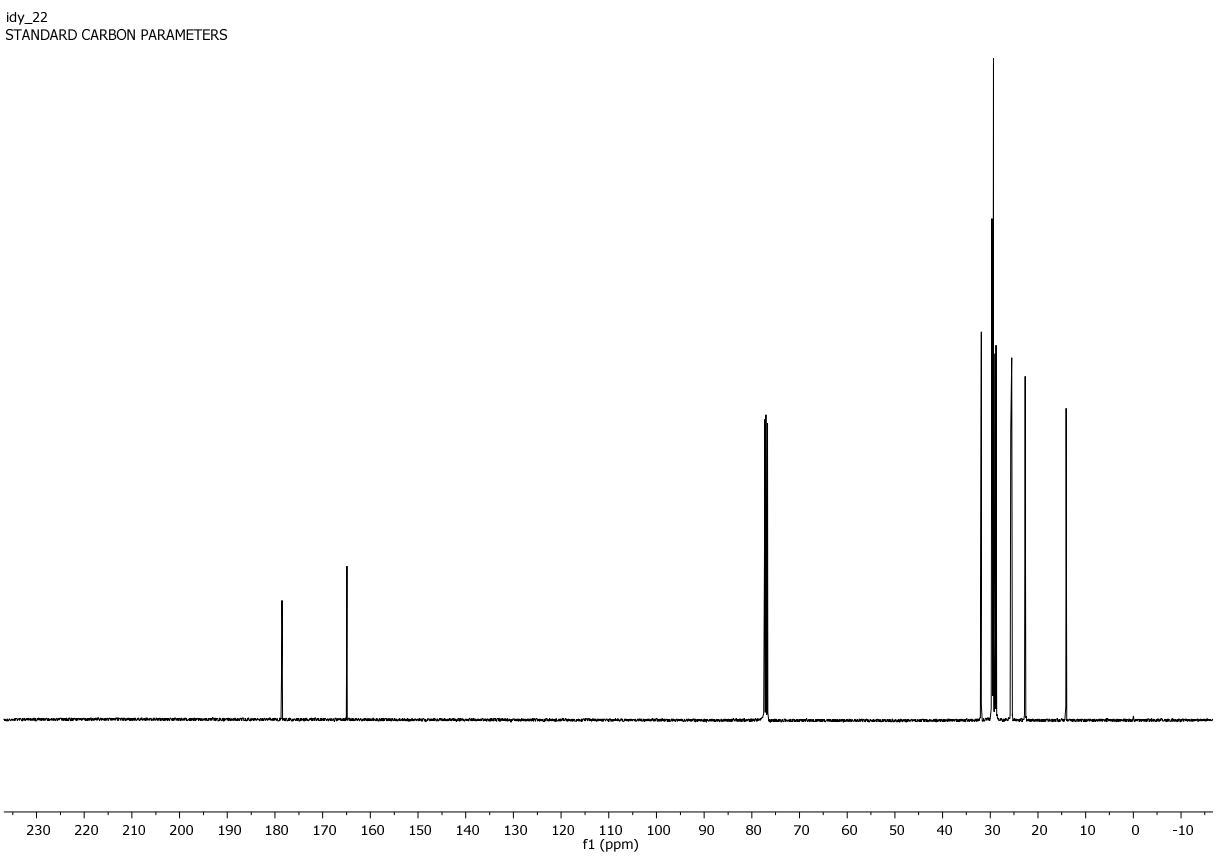
C-NMR Spectrum: **2a**



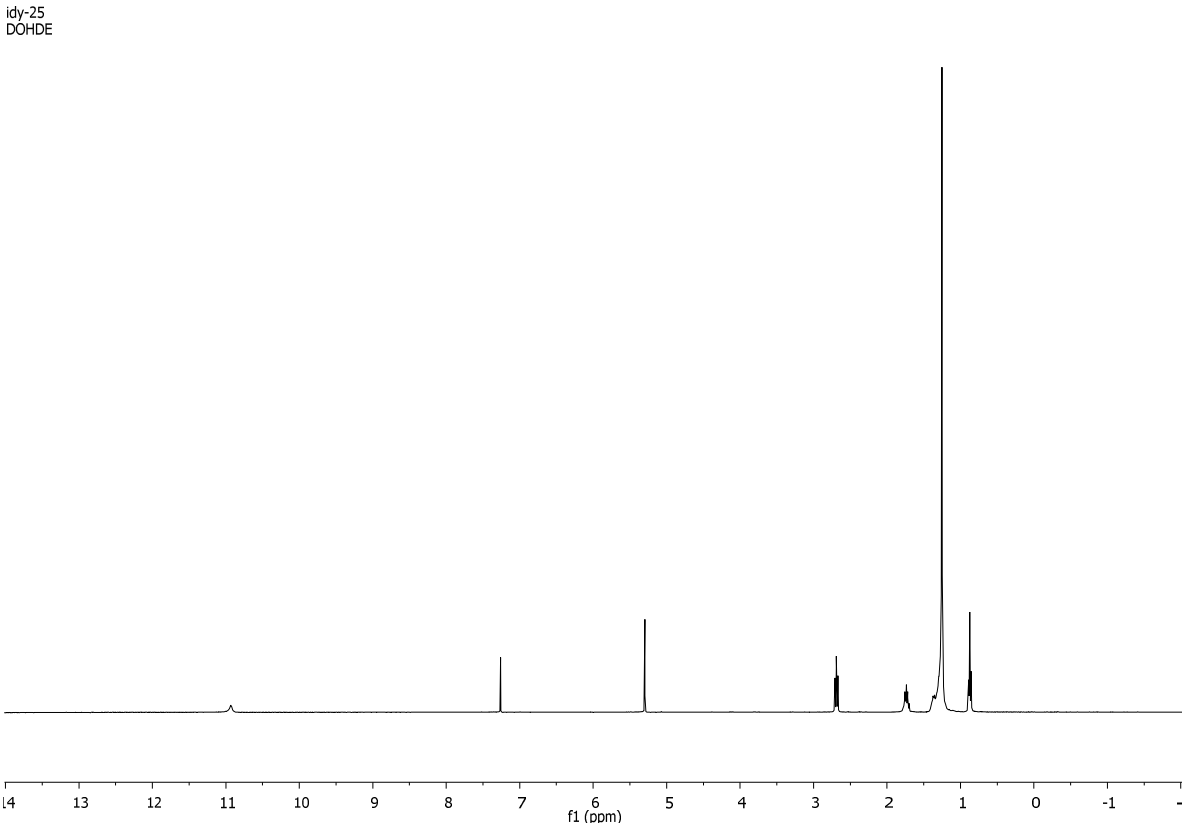
H-NMR Spectrum: **2b**



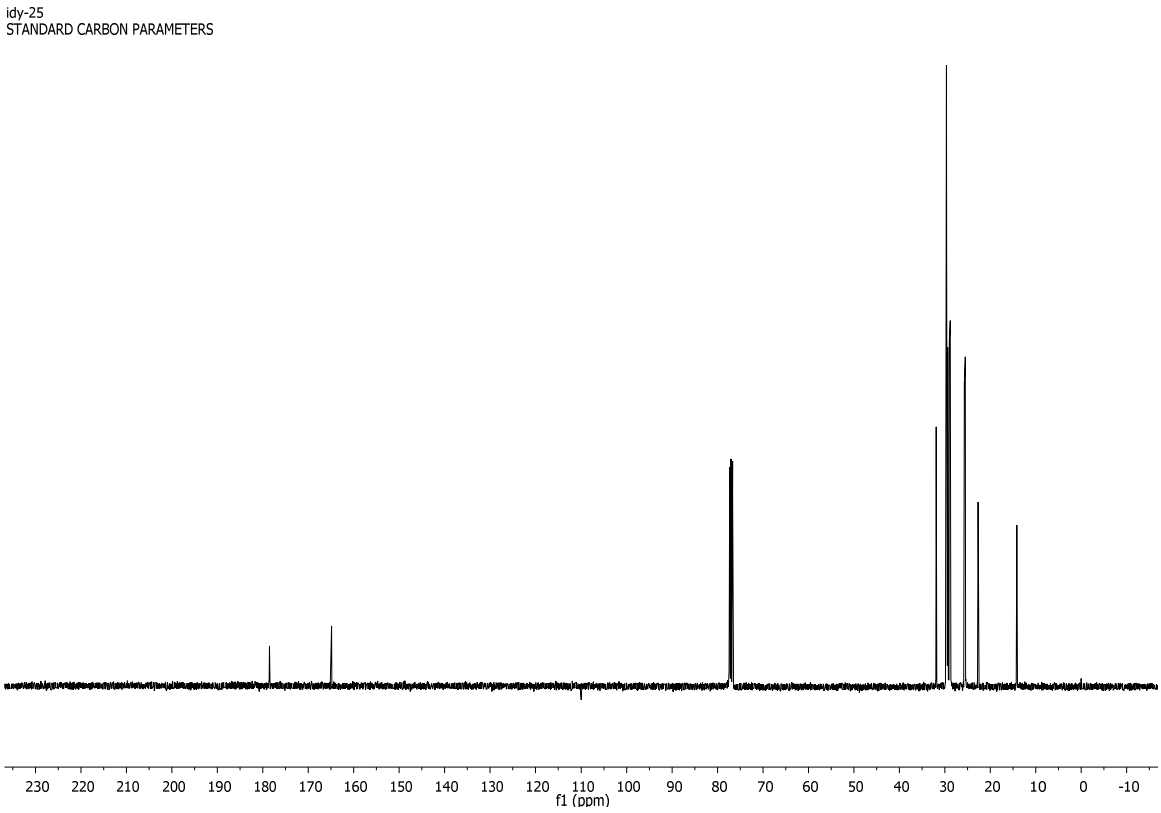
C-NMR Spectrum: **2b**



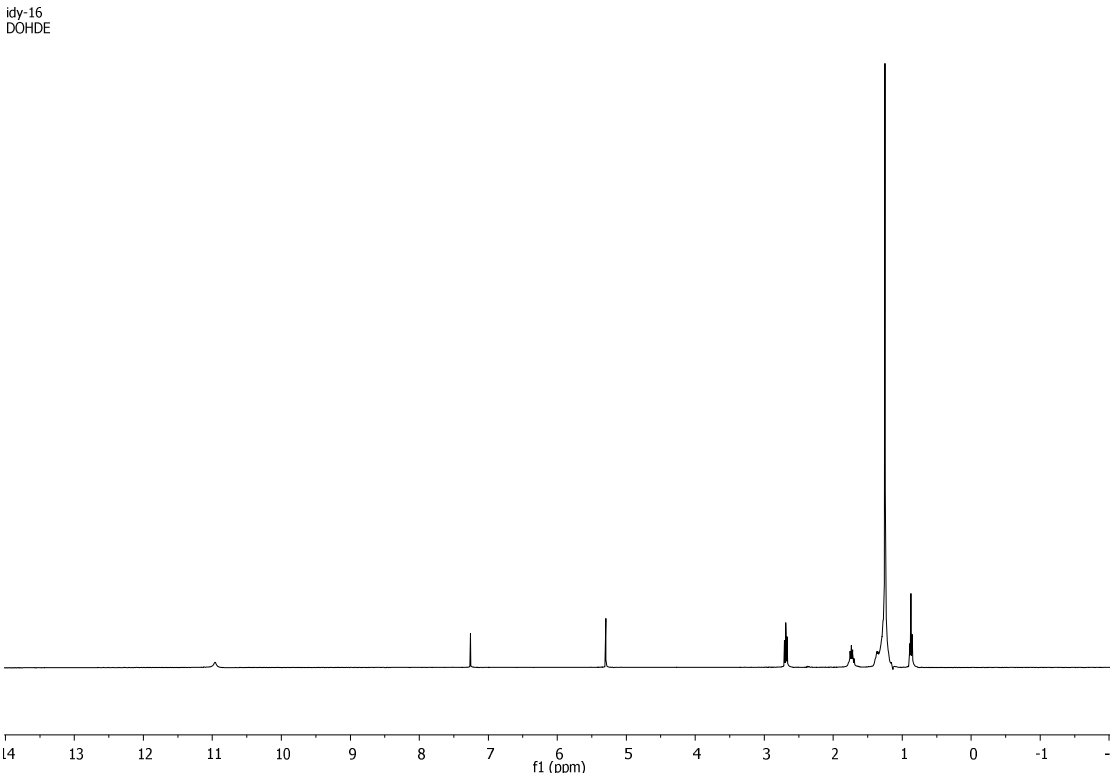
H-NMR Spectrum: **2c**



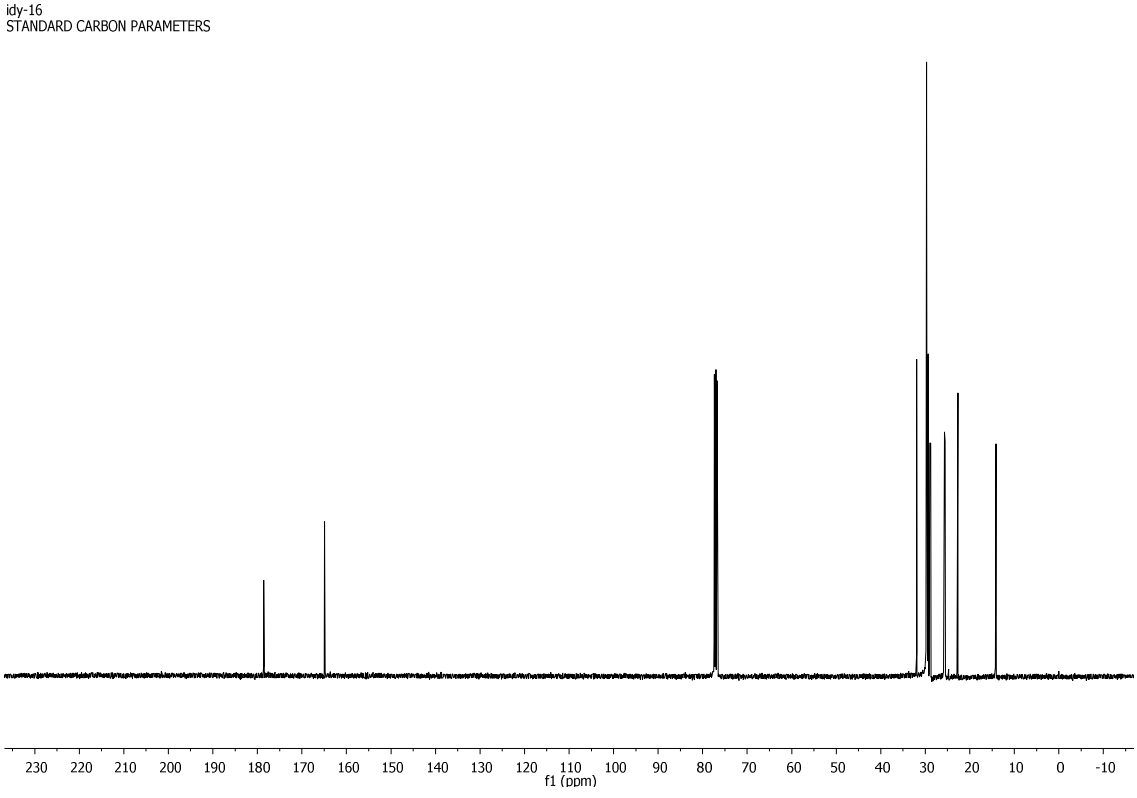
C-NMR Spectrum: **2c**



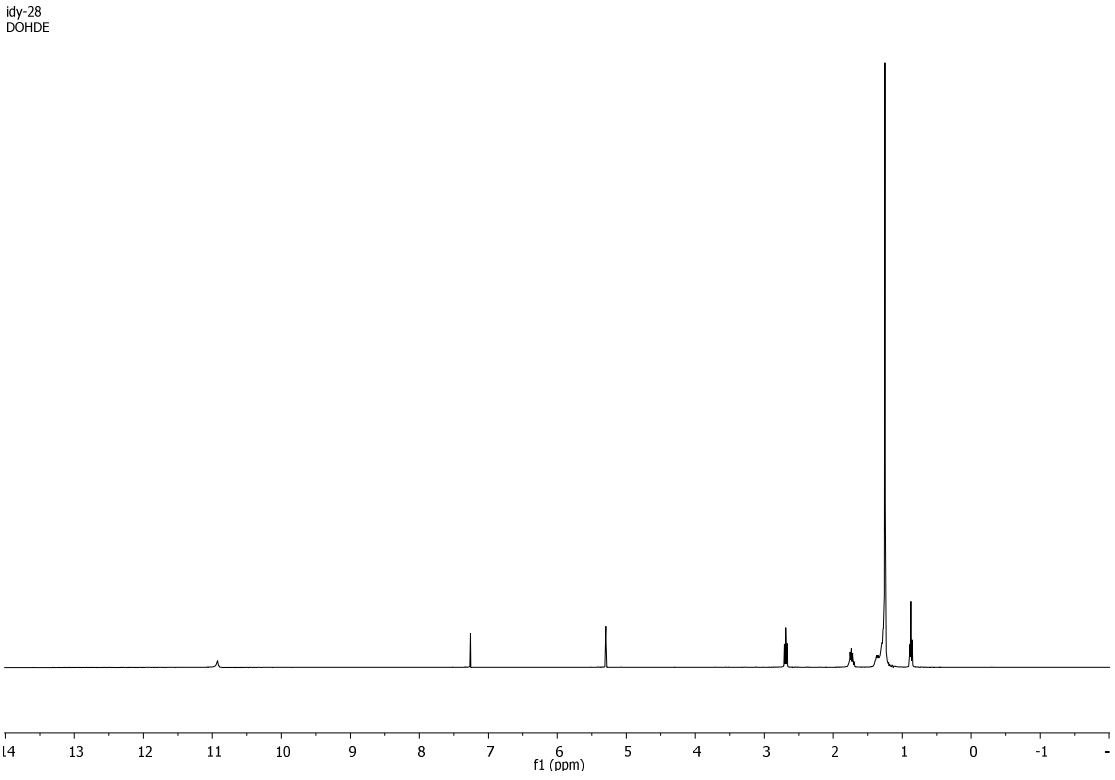
H-NMR Spectrum: **2d**



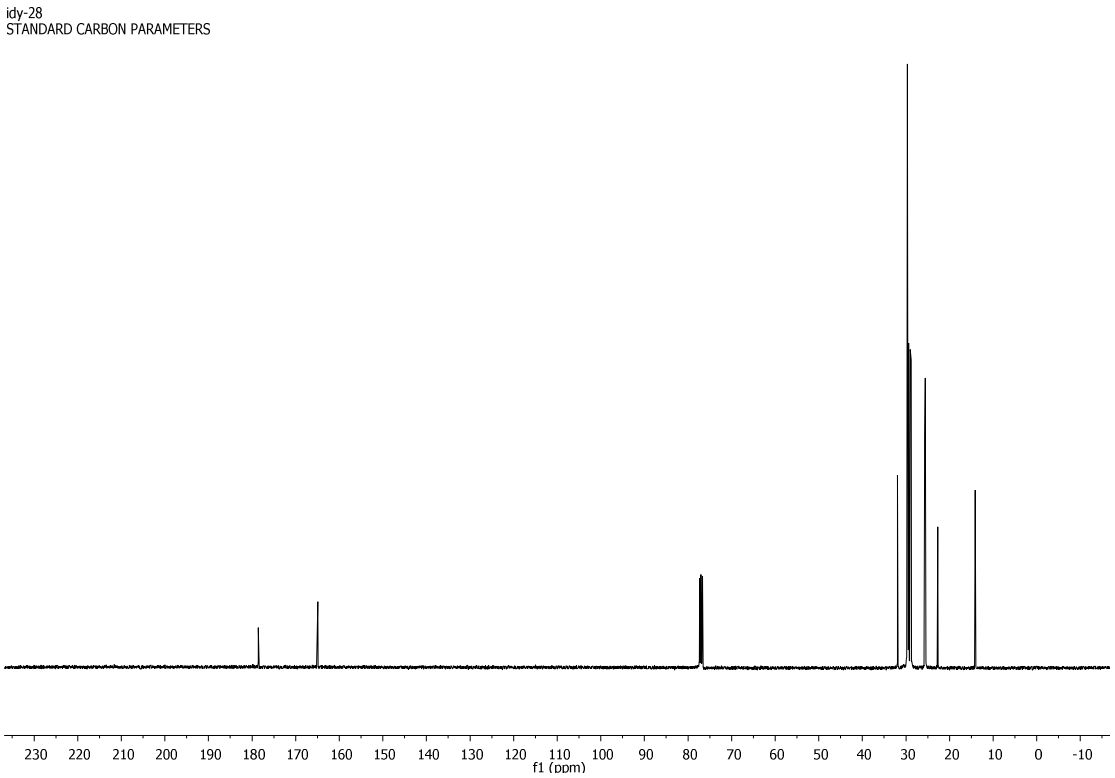
C-NMR Spectrum: **2d**



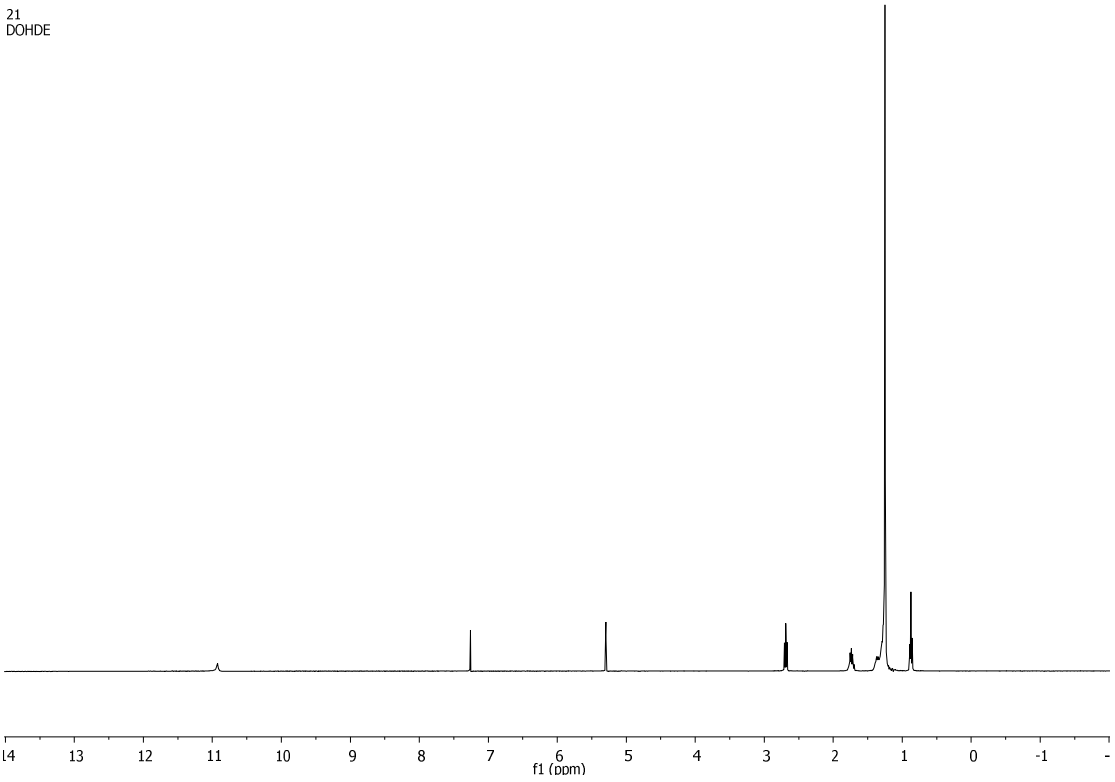
H-NMR Spectrum: **2**



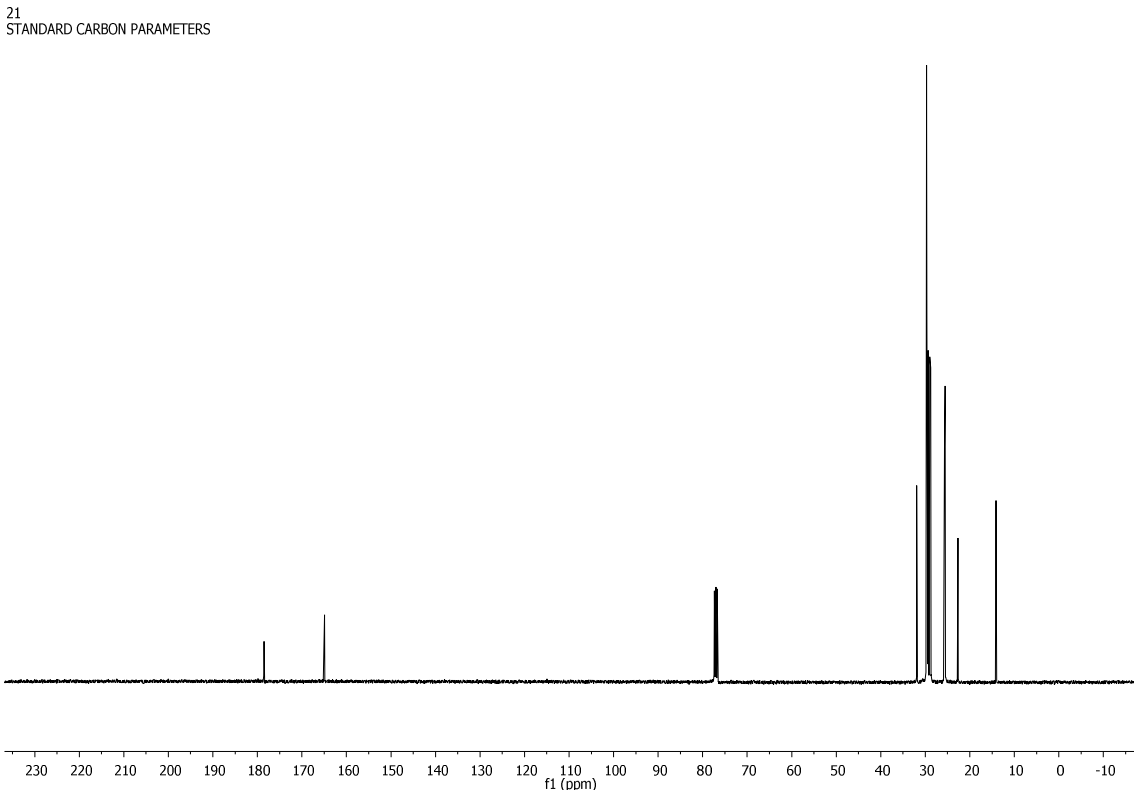
C-NMR Spectrum: **2e**



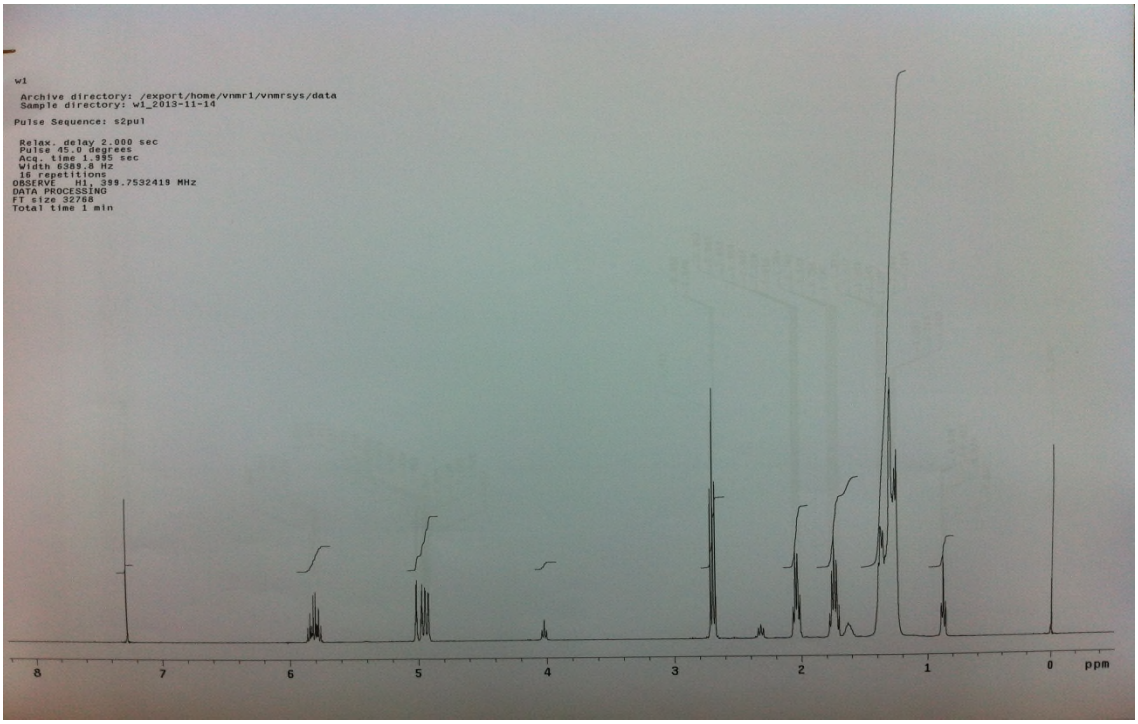
H-NMR Spectrum: **2f**



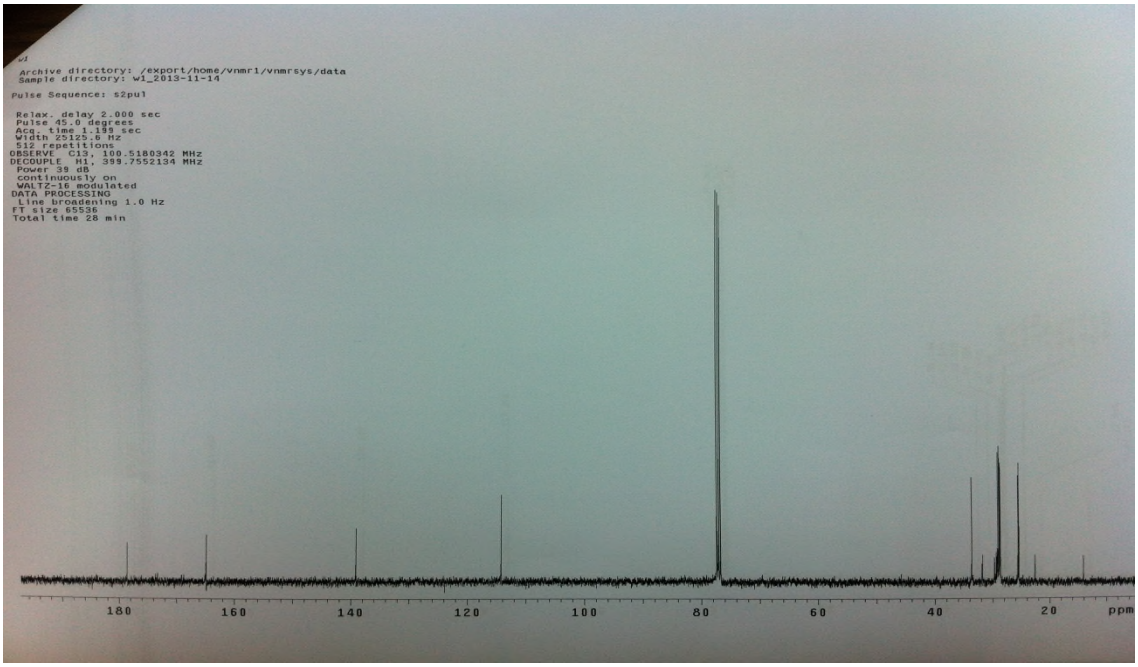
C-NMR Spectrum: **2f**



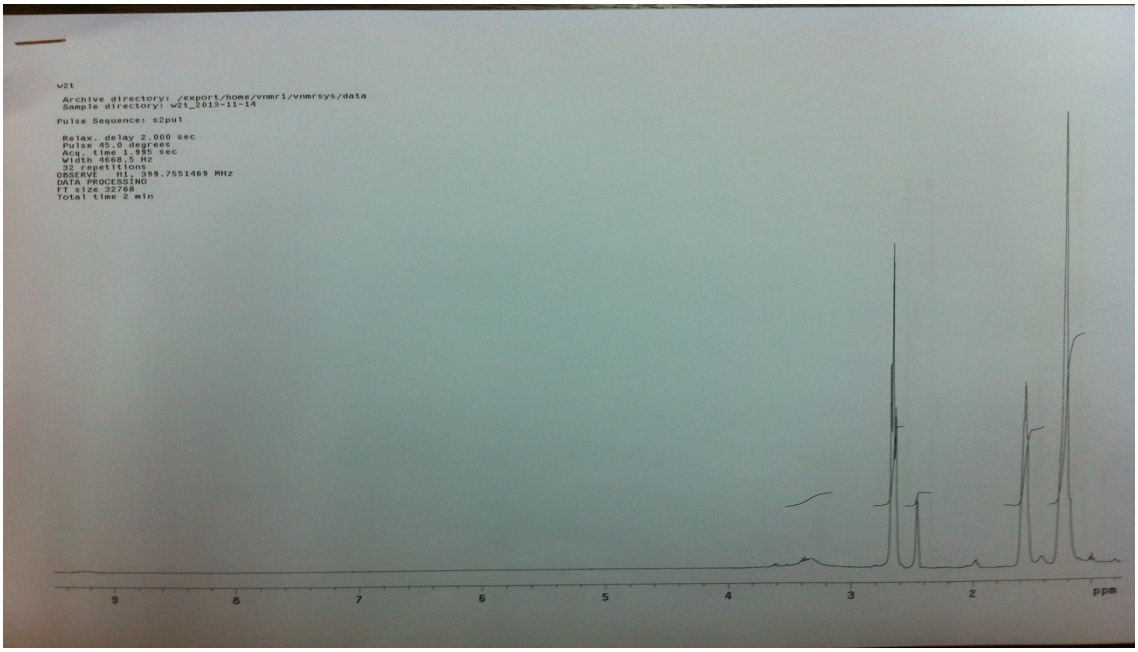
H-NMR Spectrum: **2g**



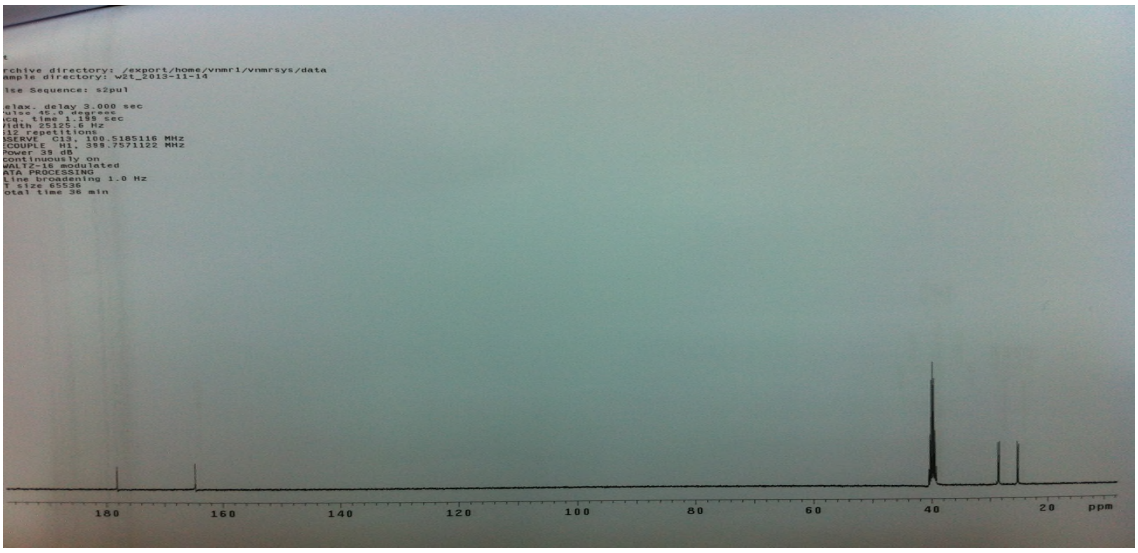
C-NMR Spectrum: **2g**



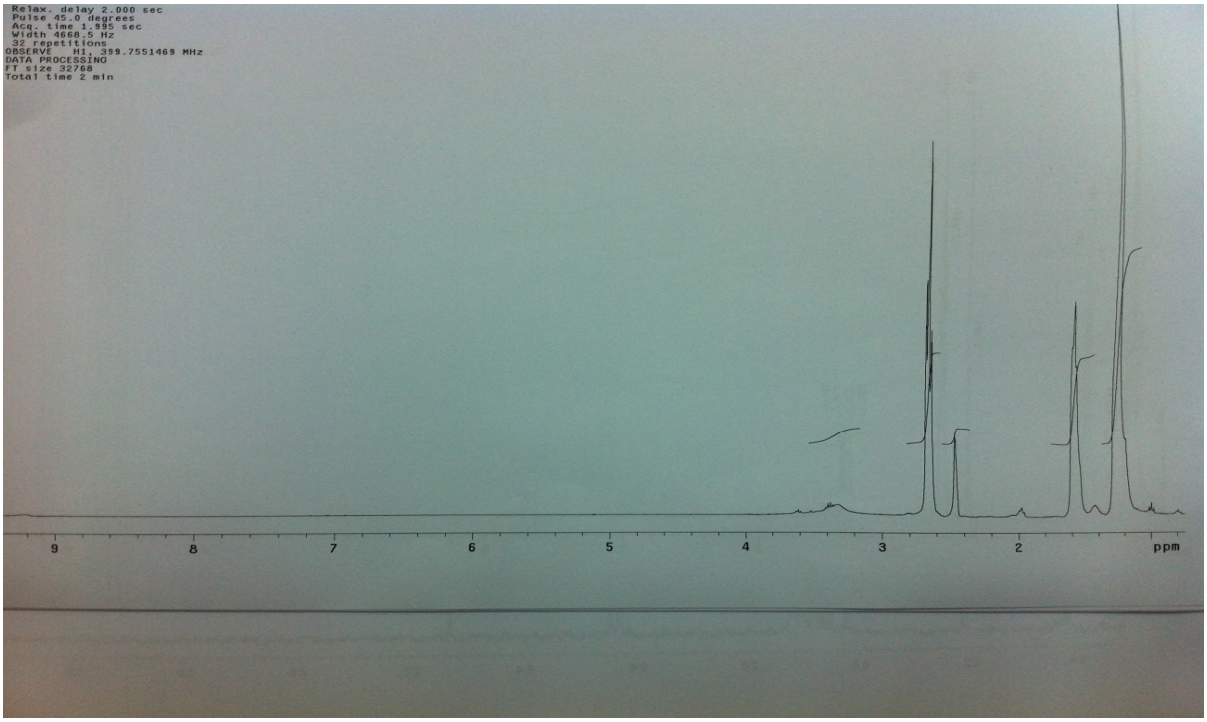
H-NMR Spectrum: **2h**



C-NMR Spectrum: **2h**



H-NMR Spectrum: **2i**



C-NMR Spectrum: **2i**