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SYNTHESIS OF 4-IODO-3-(2-IODOARYL) AND 4-BROMO-3-(2-BROMOARYL) SYDNONES AND THEIR REACTION WITH SODIUM SULFITE, SODIUM BOROHYDRIDE AND IODINE MONOCHLORIDE

A thesis submitted in partial fulfillment of the

requirements for the degree of

Master of Science

By

KYLE JACOB LIDDY

B.S., Wright State University, 2015

2017

Wright State University

WRIGHT STATE UNIVERSITY

GRADUATE SCHOOL

7/25/2017

I hereby recommend that the thesis prepared under my supervision by Kyle Jacob Liddy entitled SYNTHESIS OF 4-IODO-3-(2-IODOARYL) AND 4-BROMO-3-(2-BROMOARYL) SYDNONES AND THEIR REACTION WITH SODIUM SULFITE, SODIUM BOROHYDRIDE AND IODINE MONOCHLORIDE be accepted in partial fulfillment of the requirements for the degree of Master of Science

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ABSTRACT

Liddy, Kyle Jacob. M.S. Department of Chemistry, Wright State University, 2017. *Synthesis of 4-iodo-3-(2-iodoaryl) and 4-bromo-3-(2-bromoaryl)sydnones and their Reactions with Sodium Sulfite, Sodium Borohydride, and Iodine Monochloride.*

One goal of the Turnbull research group has been the synthesis of dihalogenated arylsydnones; *i.e.* sydnones with halogen substitution on the sydnone ring itself, as well as at the position on the aryl ring *ortho* to the sydnone. Further, it has been of interest to explore the reactivity of these compounds, once obtained. The present study examined the synthesis of 4-iodo-3-(2-iodoaryl)-, or "diiodo", and 4-bromo-3-(2-bromoaryl)-, or "dibromo", sydnones and the reactions of these compounds with Na_2SO_3 (sodium sulfite) and $NaBH_4$ (sodium borohydride) to create a better understanding of the reactivity of diiodo and dibromo arylsydnones in general. Additionally, the reactivity of these compounds toward ICl (iodine monochloride) was examined, with the expectation that a sydnone ring iodine atom would be replaced with a chlorine atom. The expected products could be useful in carbon-carbon bond forming reactions where substitution of the more labile iodine atom and retention of the less reactive chlorine atom would result.

The results of the present study showed the effectiveness of Na_2SO_3 in removing an iodine or bromine from the C-4 position of the sydnone ring, with this process leading to

high product purity and respectable yields. Second, the use of $NaBH_4$ to remove iodine from both the sydnone C4 position and the *ortho* position of the aryl ring attached to the sydnone ring was exhibited for several diiodo sydnones. Extension to similar dibromo sydnones resulted in removal of only the sydnone-attached bromine atom, with both sodium sulfite and sodium borohydride. Lastly, the use of a newly developed process for chlorination of sydnones with ICl was extended to diiodo sydnones, resulting in differentiated halogen substitution (replacement of the sydnone-attached iodine with a chlorine atom) in high yield and purity.

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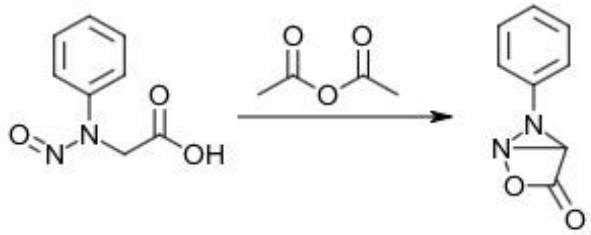
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Introduction

I. Historical Background

In 1935, work by Earl and Mackney[1] in Sydney, Australia led to the synthesis of a stable white crystalline solid upon treatment of N-nitroso-N-phenylglycine **1** with acetic anhydride. They concluded that the product had a bicyclic structure **2** and named the ring system "sydnone" to pay homage to Sydney, Australia where the work had been done. This transformation can be seen in Scheme 1 below. The conclusions drawn about the product's structure would later be refuted, nonetheless, the discovery would prove to be important in the world of synthetic organic chemistry.

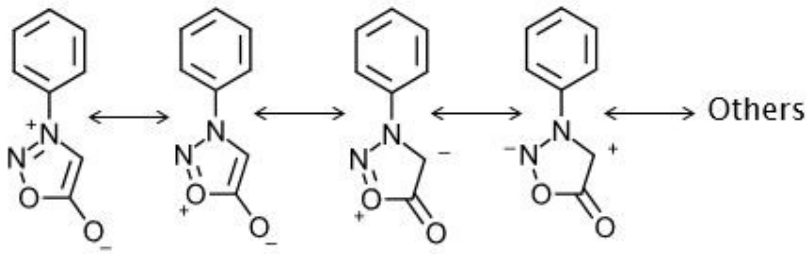


1 **2**

Scheme 1 - Earl and Mackney's proposed results[1]

Starting in the early 1940s, Baker, Ollis, and Poole[2,3,4] proposed, through examination of both the various types of reactions undergone by sydnones and the physical properties of the ring system, that the sydnone could not be a strained, bicyclic structure. It was

expected that a compound with structure **2** would be rather unstable, but sydnones in general were quite stable. Based on their findings, Baker et al. arrived at the conclusion that the structure must be an aromatic, monocyclic, dipolar ring, and attributed its stability to several possible resonance forms. This conclusion led to the creation of a new class of compounds called “mesoionic”, meaning mesomeric and ionic. While this designation was postulated for sydnones initially, Baker, Ollis and Poole recognized that there could be many such mesoionic systems and, accordingly, they assigned a set of rules for the designation of such species. According to these rules, for a compound to be mesoionic it must exhibit all of the following characteristics[4]: 1) contain fully delocalized charges, 2) be a planar, 5-membered heterocycle with an exocyclic atom capable of bearing a partial negative charge, and 3) have a high resonance energy.



3a **3b** **3c** **3d**

Structures **3a-3d** above represent four of the possible nine resonance forms that can be drawn for a sydnone ring. Resonance forms **3a** and **3b** show the most aromatic

character, which is important to note because any level of aromaticity contributes to the sydnone ring's stability. These two resonance structures also show the exocyclic oxygen as bearing a partial negative charge, which is one of the criteria for a compound to be mesoionic. Resonance forms **3c** and **3d** display very little aromatic character, but do show the presence of a carbon-oxygen double bond, which is important when it comes to a discussion of the spectroscopic properties of sydnones. The nine resonance forms that can be drawn for a sydnone ring largely serve to explain why the ring system is so stable, despite bearing both a positive and negative charge.

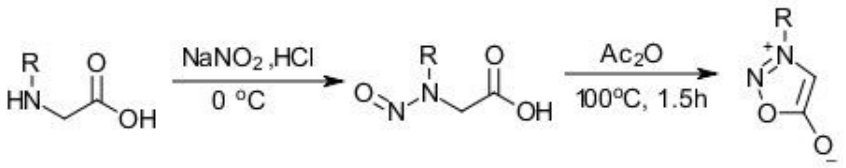
II. Chemical Properties of Sydnones

i. Synthetic Routes to the Sydnone Ring

a) From N-substituted glycines

A long-standing method for the formation of the sydnone ring system involves a procedure based on that reported by Earl and Mackney in 1935. Thus, nitrosation of an N-alkyl or N-arylglycine **4** affords the desired N-nitrosoglycine **5**, which can then be cyclized to the sydnone **6** using a dehydrating agent. The first step involves the reaction of **4** with a source of NO^+, either sodium nitrite ($NaNO_2$) in a strong acid such as HCl at 0^oC or isoamyl nitrite under neutral conditions[5]. The resulting N-nitroso compound **5** is

then cyclized to the desired N-substituted sydnone **6** using either acetic anhydride (Ac_2O) in the presence of heat, or trifluoroacetic anhydride (TFAA) at room temperature.



4 **5** **6**

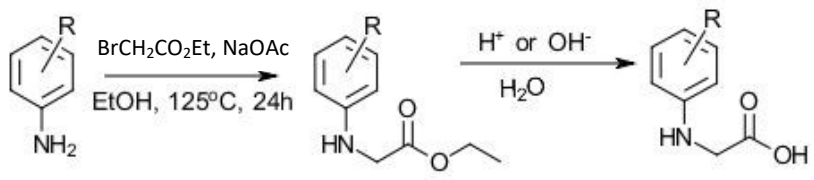
Scheme 2 - Synthesis of sydnone ring from N-substituted glycine

The method outlined in Scheme 2 above is practical and useful for the synthesis of N-alkyl or N-arylsydnones when the appropriate N-substituted glycine is available. For situations where the appropriate N-substituted glycine is not commercially available, which is often the case when preparing N-arylsydnones, an additional step is necessary (see below).

b) N-Arylsydnones from substituted anilines

As mentioned above, when the requisite N-arylglycine is not commercially available, one can begin with the appropriately substituted aniline derivative **7**, as shown in Scheme 3 below[6]. The first step involves reaction of **7** with ethyl bromoacetate in ethanol with sodium acetate added as a base to react with any acid formed during the reaction. Once

the appropriate glycine ester **8** is formed from step one, the ester is hydrolyzed to the desired N-arylglycine **9** under either aqueous acidic or basic conditions.



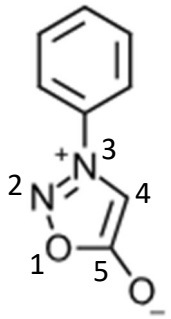
7 **8** **9**

Scheme 3 - Synthesis of N-arylglycines from aniline derivatives

Once the desired N-arylglycine has been prepared, it can then be used in the process previously discussed for the preparation of a sydnone using nitrosation followed by cyclization.

ii. Sydnone Reactions

In order to effectively explain the types of reactions sydnones undergo, it is important to understand the numbering of the sydnone ring, as shown in structure **10** below.



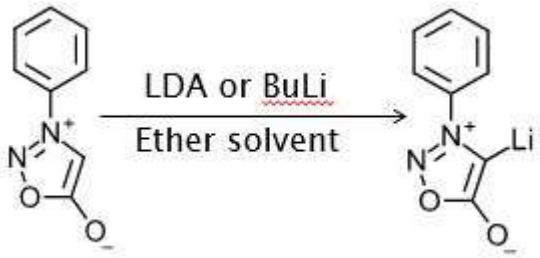
10

Structure **10** shows 3-phenylsydnone, with the sydnone ring numbered. Numbering of the sydnone ring follows the general rules for numbering heterocyclic compounds. Each atom of the ring is assigned priority based on its atomic number. For the sydnone ring specifically, the oxygen atom within the ring is numbered as 1 because it has the highest atomic number (8) of the atoms contained in the ring. Nitrogen comes next, having an atomic number of 7, so going clockwise on the ring from oxygen, the two nitrogens are labeled as 2 and 3, respectively.

The majority of reactions performed on sydnones take place at the C4 position of the sydnone ring, and are often electrophilic aromatic substitution type reactions. However, there are several different, less studied types of reactions that can take place with compounds containing a sydnone ring. The latter will be discussed first in the following section.

a) Metalation at the C-4 position

Electrophilic aromatic substitution is by far the most studied type of reaction involving sydnones, especially when it comes to adding substituents at the C4 position. However, there is another method that has been studied that involves adding a metal, such as lithium, to the C4 position of the sydnone ring[7,8]. In general, this transformation involves reacting a sydnone such as 3-phenylsydnone (**10**) with a strong base such as lithium diisopropylamide (LDA) or BuLi in an ether type solvent. This results in the formation of the C4-lithiated intermediate, **11**, where the metal now attached to the sydnone ring at the C4 position is from the strong base that was used.



10 **11**

Scheme 4 - C4 metalation of 3-phenylsydnone

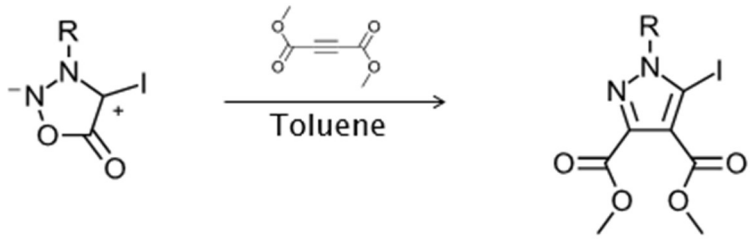
The specific reactions shown in Scheme 4 above are just one example of the many different types of C4 metalation reactions that sydnones can undergo. Mechanistically, this reaction works by the LDA (or BuLi) acting as a strong base to remove the hydrogen

from the C4 position of the sydnone, leaving behind a negative charge that then attracts the positively charged lithium that was ionically bound in the reagent. This transformation takes place because of the relative pKa's of the species involved. The hydrogen at the C4 position of the sydnone ring has a pKa estimated to be 18, whereas LDA is the conjugate base of diisopropylamine, which has a pKa of ~35, and BuLi is the conjugate base of butane, which has a pKa of ~50-60. This means that both bases are more than strong enough to remove the proton from the sydnone ring under rather mild conditions (usually -78°C).

b) 1,3-Dipolar cycloadditions

The second of the four most studied reactions involving sydnones is the 1,3-dipolar cycloaddition process[9]. This type of procedure involves reaction of a 1,3-dipole with an unsaturated species; the latter usually electron deficient. Sydnones make good 1,3-dipoles for this type of reaction as can be seen from resonance structure **3d**, wherein the 1,3-dipolar arrangement of the charges in the sydnone ring is apparent. Most such reactions with sydnones have been performed with alkynes or alkenes as substrates and the value of the protocol stems from the resultant high yields of valuable pyrazoles that result from extrusion of carbon dioxide from the initial cycloaddition intermediate. A typical example is shown in the scheme below, which shows the reaction of a 4-iodo- N-

substituted sydnone **12** with an electron deficient alkyne in toluene to yield a functionalized pyrazole **13**.



12 **13**

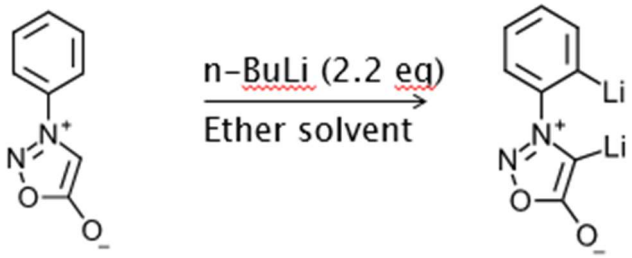
Scheme 5 - Sydnone 1,3-dipolar cycloaddition

The transformation shown in Scheme 5 above is just one example of many variations that can be employed to yield different pyrazoles, mostly by changing the alkyne that is used in the reaction. In recent years considerable effort has gone into exploring the pyrazole regiochemical consequences resulting from the use of different unsymmetrical alkynes under different reaction conditions.[9]

c) Dilithiation at C4 and C2' positions

A third, much less studied type of reaction that aryl sydnones undergo is dilithiation[10]. This transformation is of specific interest and importance to the work reported later in this thesis and is similar to C4 metalation, but with metalation also occurring at the 2' or

ortho position of the aryl ring attached to the sydnone. The transformation involves the reaction of a 3-arylsydnone, *e.g.* **10**, with a strong base such as *n*-butyllithium or another, similar lithiating agent such as *sec*-butyllithium. These reactions, like most metalation processes, are performed in ethereal solvents since the latter are stable to strong nucleophiles and bases. The process yields an unstable dilithio intermediate, *cf*. **14**, which can be reacted *in situ* with electrophiles to yield otherwise difficultly accessible sydnone derivatives.



10 **14**

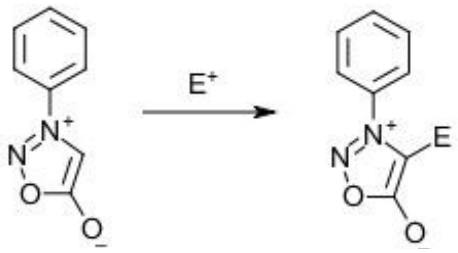
Scheme 6 - Dilithiation of 3-phenylsydnone

The mechanism undoubtedly involves initial removal of the most acidic sydnone ring proton by the first equivalent of n-butyllithium to form a 4-lithio species. It is conjectured that the next step is coordination of the latter to another equivalent of n-butyllithium such that the base is now proximate to the *ortho* proton (C2'). The latter is sufficiently acidic (pKa ~35) to be abstracted by the very strong base and its removal

creates the dianion **14**. In order to avoid decomposition of the very unstable dianion **14** the reaction mixture must be cooled to very low temperatures (usually -78°C), moisture must be excluded rigorously and subsequent reactions must be amenable to these conditions.

d) Electrophilic aromatic substitution (EAS)

The fourth, and most studied type of reaction involving sydnones is electrophilic aromatic substitution at the C4 position of the sydnone ring. This transformation, like the dilithiations mentioned in part c), is of particular interest for the work reported in this thesis. Mechanistically this process occurs because the C4 position of the sydnone ring is the most electron rich part of the system, making this site the most reactive to electrophiles. The electron rich nature of the C4 position is best illustrated by resonance contributor **3c**. The general scheme for electrophilic aromatic substitution involving the sydnone is shown below.



10 **15**

Scheme 7 - Electrophilic aromatic substitution at C4 position

Over the years, several different methods for electrophilic substitution of sydnones have been discovered and perfected, leading to numerous different groups that can be added to the C4 position of the sydnone ring. Acylation[11], and halogenation[12,13] are the two most studied processes for reaction with the sydnone ring. The most relevant for the present study is halogenation and, accordingly, the previous work of relevance involving EAS and halogenation will be discussed in further depth in a later section.

III. Physical Properties of Sydnones[14, 15]

To complete the discussion of the important background information on sydnones, it is necessary to mention their physical properties. These characteristics are useful when it comes to the synthesis and characterization of sydnones. Three valuable physical properties of sydnones are their solubilities, melting points and spectral characteristics, particularly IR and NMR.

i. Solubility

Molecules containing the sydnone ring are soluble in most moderately polar to polar organic solvents such as dichloromethane, ethyl acetate and ethanol. When it comes to non-polar organic solvents such as hexane, and very polar solvents such as water, the

majority of sydnones have virtually no solubility, the exceptions being cases where unusually non-polar or polar functionalities are present.

ii. Melting Point

There exists a general trend when it comes to the melting point of compounds containing a sydnone ring. Pure N-alkylsydnones are either very low melting solids or, in most cases, liquids at room temperature. Pure N-arylsydnones on the other hand are almost always colorless, crystalline solids, and can have a wide range of melting points from low to moderate temperatures. The properties of N-arylsydnones are the most relevant to the present work and, in general, as the degree of substitution on the aryl ring increases, the melting point increases as well. This is not always the case, however, making it difficult to predict what the melting point will be for a particular N-arylsydnone.

iii. Spectral Characteristics

a) Infrared (IR) spectroscopy

One of the most important tools when it comes to the characterization of compounds containing a sydnone ring is infrared spectroscopy. For the latter there are two specific functionalities that are reasonably specific to sydnones, the C-H and C=O stretches of

the C4 and C5 positions, respectively. The best way to illustrate these spectral characteristics is with the simplest case, an IR spectrum of 3-phenylsydnone.

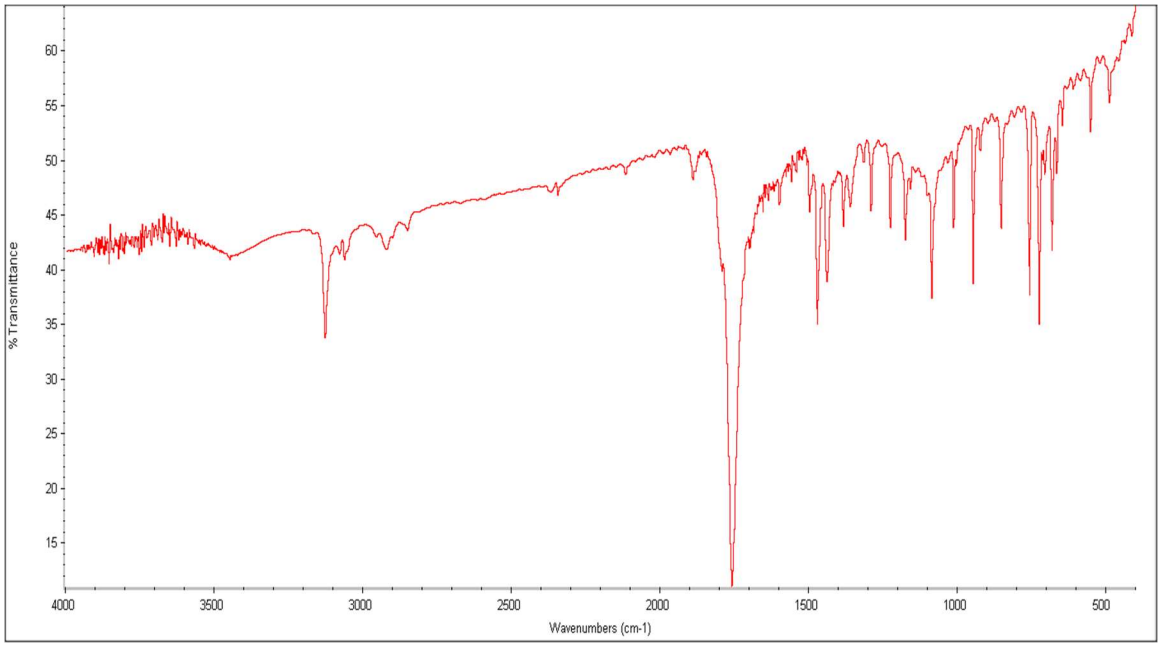


Figure 1 *- IR spectrum of 3-phenylsydnone*

Figure 1 shows the IR spectrum of 3-phenylsydnone. There are two specific peaks that are indicative of the presence of a sydnone ring in a molecule. The first is the C-H stretch of the C4 position, which appears around 3150 cm^{-1} and the second is the C=O stretch of the C5 position which comes around 1760 cm^{-1}. These two peak positions are interesting because the C-H stretch appears close to the area where aromatic C-H stretches occur, but slightly higher. This indicates there may be some aromatic character, but the higher wavenumber for the peak indicates a lower degree of conjugation than there is in

"normal" aromatic molecules like benzene and derivatives. The C=O stretch of the sydnone ring also comes at a relatively unusual position, 1760 cm^{-1}, which is generally where lactone type C=O stretches appear. These two IR characteristics alone do not definitively identify the presence of a sydnone ring but, when used in conjunction with other spectra such as NMR, they provide strong evidence. One of the most useful applications of IR spectroscopy in sydnone chemistry is in identifying the absence of a C-H stretch when it is suspected that a substitution reaction has occurred at the C4 position. This will be illustrated later, as it is an important aspect to the present study.

b) Nuclear Magnetic Resonance (NMR) Spectroscopy

Another useful source of spectral data for compounds containing a sydnone ring is nuclear magnetic resonance spectroscopy. This is perhaps the most useful tool when it comes to sydnone chemistry since several relatively unique peaks can be observed in both ^{1}H and ^{13}C NMR spectra. To illustrate the utility of NMR in sydnone chemistry, it is best to look at the ^{1}H and ^{13}C NMR spectra for the simplest aryl sydnone, *viz.* 3-phenylsydnone.

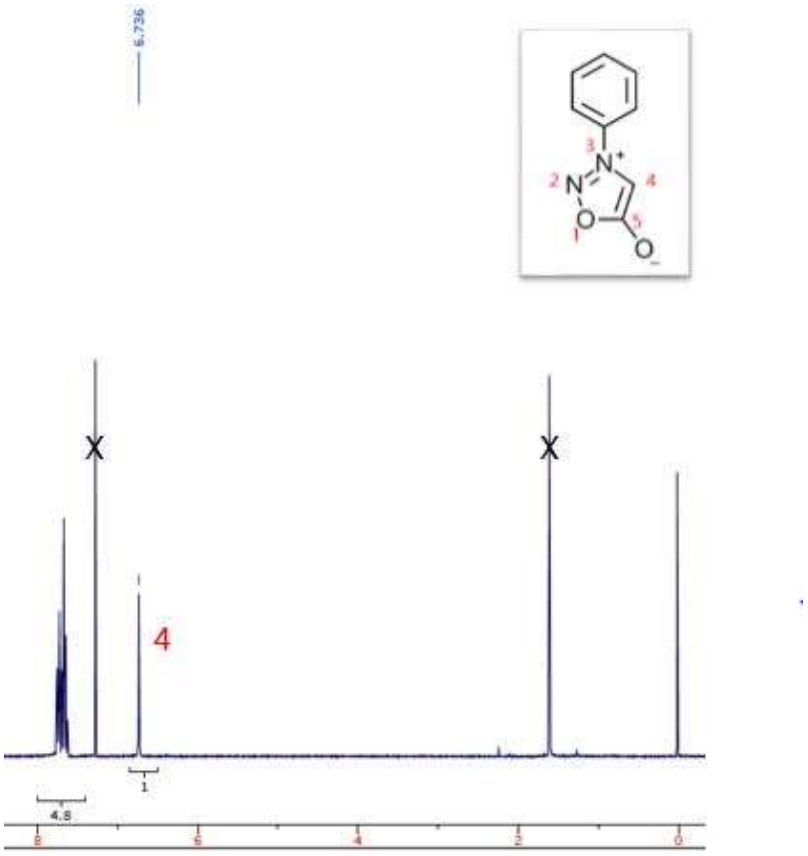


Figure 2 - ^{1}H NMR spectrum of 3-phenylsydnone

Figure 2 shows the ^{1}H NMR spectrum of 3-phenylsydnone collected in deuteriochloroform ($CDCl_3$). The peaks at about 7.2 δ and 1.7 δ represent chloroform and water, respectively. The first peak of importance is the singlet at 6.7 δ which represents the C4 hydrogen of the sydnone ring. This location (in $CDCl_3$) is particularly unusual and is therefore very helpful in assessing the presence, or otherwise, of a sydnone ring proton. The group of peaks just below 8 δ represents the aromatic

hydrogens within the molecule. The integration ratio of this group of peaks in the aromatic region relative to the sydnone C4 is 5:1, which is what is expected since five hydrogens are present in the aromatic ring. The aromatic hydrogen characteristics can vary widely between different molecules depending on the substitution nature and pattern on the aromatic ring.

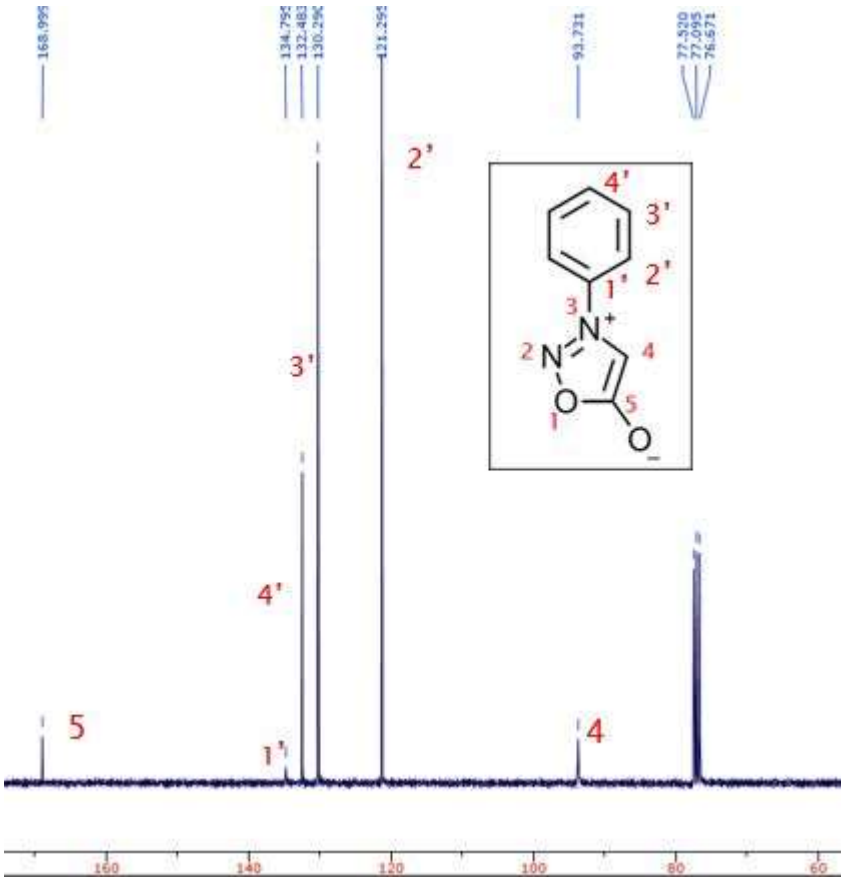


Figure 3 - ^{13}C NMR spectrum of 3-phenylsydnone

Figure 3 shows the ^{13}C NMR spectrum of 3-phenylsydnone. The group of three peaks around 77 represents chloroform. From the molecule itself, 6 peaks in the 13C NMR are expected. There are two unique carbons contained within the sydnone ring, the C4 and C5 (C=O), which come at 94 ppm and 168 ppm, respectively, positions, which are particularly helpful in assessing the presence of the sydnone ring. Due to free rotation around the bond connecting the sydnone ring to the aryl ring, there is a plane of symmetry, leading to four unique aromatic carbon signals. These are labeled 1', 2', 3' and 4', and appear at 135 ppm, 121 ppm, 130 ppm, and 132 ppm, respectively.

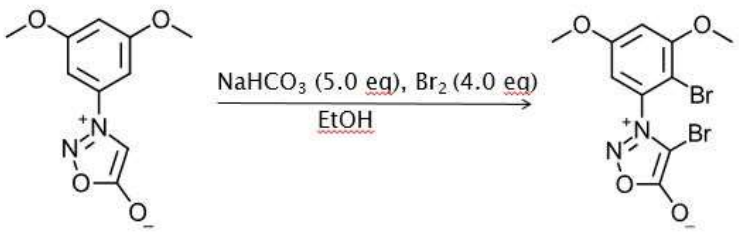
These spectral characteristics are for 3-phenylsydnone, the simplest molecule of interest for this present study. Substituents can have varying effects on the spectral representations of these compounds, and some of these effects will be illustrated later.

IV. Background to, and Aims of, the present research

i. Halogenation of N-arylsydnones

Halogenation reactions of sydnones, particularly at the C4 position of the sydnone ring, have been among the most studied reactions involving sydnones. It has long been a goal of researchers working with sydnones to make dihalogenated N-aryl species, with halogen substitution not only at the C4 position, but also at the C2' position of the aryl

ring system. Early work in the area was accomplished by Turnbull in 1985[6]. It was discovered that an N-arylsydnone system with strong activating groups such as 3-(3,5-dimethoxyphenyl)sydnone (**16**) could effectively be brominated at the C4 and C2' by dissolving the sydnone in a solution of ethanol with 5.0 eq. of sodium bicarbonate ($NaHCO_3$) and subsequently adding a solution of 4.0 eq Br_2 in ethanol. This led to dibromination and formation of 4-bromo-3-(2-bromo-3,5-dimethoxyphenyl)sydnone (**17**).



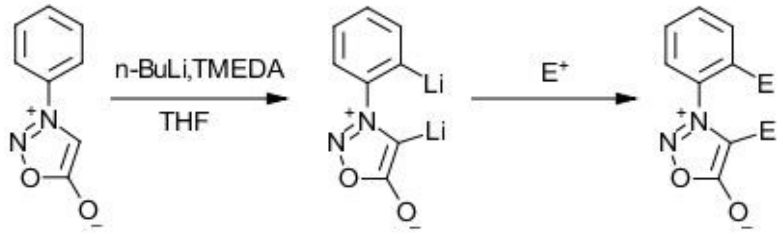
16 **17**

Scheme 8 - Bromination of 3-(3,5-dimethoxyphenyl)sydnone

This transformation is only useful in a scenario where two very strong electron-donating groups are activating the aryl ring system. Accordingly, an effective method for dihalogenation when such groups are not attached to the aryl ring was desired.

Through work in the years following, it would be discovered and reported in 1997 by Krein and Turnbull[10], that the sydnone ring acts as an ortho director in lithiation

reactions. The work reported the reaction of 3-phenylsydnone with 2.2 eq n-Butyllithium and N-N-N'-N'-tetramethylethylenediamine (TMEDA) in tetrahydrofuran (THF) to generate a dilithio species **18**, followed by addition of 2.2 eq of various electrophiles to yield disubstituted sydnones **19**, consisting of E=TMS, CHO, CH(OH)Ph, I, SPh, CH_3, Br.

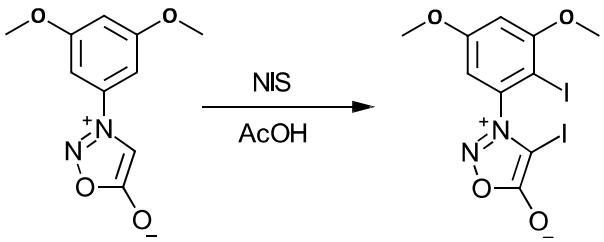


10 **18** **19**

Scheme 9 - Dilithiation of 3-phenylsydnone

This work is very useful in the synthesis of dihalogenated sydnones, and has led to studies that further expand the principal reaction. Thus, subsequent work in the Turnbull research group led to lithiation and halogenation from starting materials with a variety of groups substituted on the aryl ring, including p-CH_3, p-Cl and p-OCH_3. These transformations were expected to be particularly useful in the present research for the preparation of starting materials of interest.

Further expansion of the dihalogenation of N-arylsydnones came in a paper published by Brown and Turnbull in 2013[16]. This work, much like the dibromination work reported in 1985, took advantage of the presence of a strong activating group on the aryl ring of the sydnone compound. It was found that if a starting material such as 3-(3,5-dimethoxy-phenyl)sydnone **16** was treated with 3.0 eq. of N-iodosuccinimide (NIS) in acetic acid, the strong activating effects of the substituents allowed for dihalogenation, leading to a diiodo species **20.**

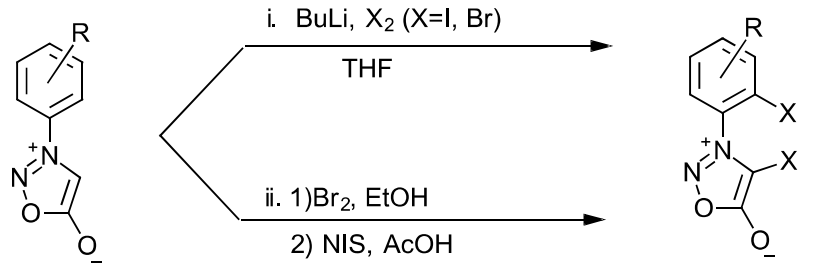


16 **20**

Scheme 10 - Iodination of 3-(3,5-dimethoxyphenyl)sydnone

This work was an extension of Brown and Turnbull's initial findings wherein 1.1 eq of NIS in acetic acid was used as an effective method for iodination at only the C4 position of N-arylsydnones not having strong electron donating substituents attached to the aryl ring. This process led to a library of 4-iodo-3-arylsydnone derivatives. Each of these processes is of particular relevance to the present study for the preparation of desired dihalogenated N-arylsydnones as starting materials.

The aims of this present project begin with the synthesis of dihalogenated N-arylsydnones *via* one of the previously mentioned pathways, with the goal of creating a library of dihalogenated compounds (see Scheme 11) that can then be used as starting materials for further study.



10 **31-36 & 55-58**

i. **a**)R=H, **b**)p-Cl, **c**)p-CH_3, **d**)p-OCH_3,
e)m-OCH_3

ii. **f**)R=3,5-di-OCH_3

Scheme 11 - Dihalogenated sydnone synthesis

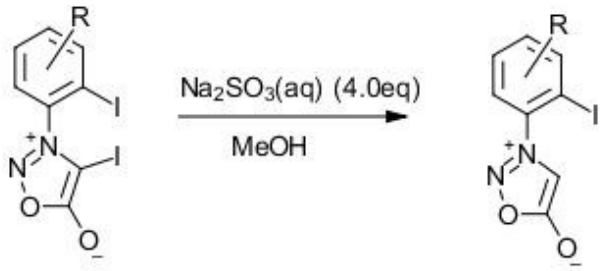
Illustrated in Scheme 11 above are the various methods by which the dihalogenated N-arylsydnones were expected to be prepared based on previously published work. It is important to note that dibromination via dilithiation has been completed previously only for 3-phenylsydnone (R=H). It was planned, then, in this work, to explore other

instances of this process with different R groups as an expansion of the process of dilithiation reported by Krein and Turnbull in 1985.

ii. Reactions of Dihalogenated Sydnones with $NaBH_4$ and Na_2SO_3

Since halogenated sydnones have become readily accessible, their further reactivity has been a topic of much research, particularly within the Turnbull research group. For the latter, more specifically, it has been shown that halogens at the C4 position of the sydnone ring (particularly Br and I) can be removed under mild conditions and this aspect has been examined briefly as a route to ortho-halogenated sydnones from dihalogenated sydnones (*cf*. **21**).

Thus, by exploring the reactivity of dihalogenated sydnones (*cf*. **21**) with Na_2SO_3 and other, mild reducing agents such as $NaBH_4$, it was discovered by Weisner and Turnbull that, while Na_2SO_3 removed only the C4-attached halogen, $NaBH_4$ removed both the C4 halogen and the halogen ortho to the sydnone ring, if the latter were an iodine atom. This was a surprising discovery and led to a more thorough study of the reactions of diiodiinated sydnones with sodium sulfite and sodium borohydride[17]. Through this work, it was found that reacting the appropriate diiodo species **21** with 4.0 molar eq. of Na_2SO_3 removed only the iodine from the C4 position, leading to the expected ortho iodo species **22** as a product.

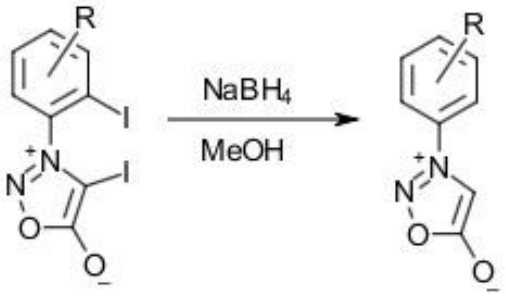


21 **22**

R=H, p-Cl, p-CH_3, p-OCH_3, 3,5-di-OCH_3

Scheme 12 - Diiodo species with sodium sulfite

Reactions of the same diiodo sydnones **21** with sodium borohydride were explored and it was found that reaction with one weight eq. of $NaBH_4$ in methanol led to the removal of both iodine atoms, yielding the parent substituted N-arylsydnone **23**.



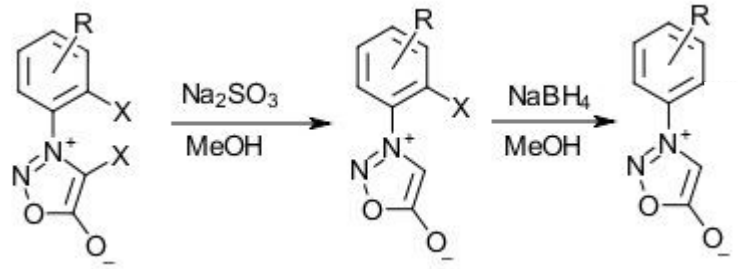
20 **23**

R=H, p-Cl, p-CH_3, p-OCH_3, 3,5-di-OCH_3

Scheme 13 - Diiodo sydnones with sodium borohydride

With the effects of sodium sulfite and sodium borohydride on diiodo compounds well documented, it was of interest in the present study to test the effects of sodium borohydride on ortho-iodo compounds to see if there is any effect on the removability of an iodine ortho to the sydnone ring when the group attached to the aryl ring is changed, and when the iodine from the C4 position is removed before reaction with sodium borohydride (see Scheme 14).

Further, it was of interest to apply the same reaction conditions to a library of dibrominated compounds (see Scheme 14), and observe whether the same results are observed when the halogen present in the starting material is different. The general reaction scheme (Scheme 14) for this portion of the project can be seen below.



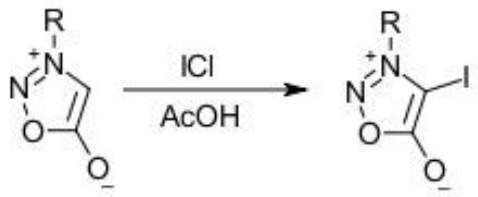
Scheme 14 - Overall sodium sulfite and sodium borohydride aims

It was planned to prepare the dihalo species by one of the previously mentioned methods then react subsequently with sodium sulfite and sodium borohydride, in the manner represented in Scheme 14 above, using the methods reported by Turnbull et al.

iii. Reactions of Dihalogenated Sydnones with ICl

In 1997, Dumitrascu et al.[12] showed that iodine monochloride (ICl) in acetic acid at room temperature could be used as an iodinating agent for sydnones (*cf.* **24** to **25)**.

As an extension to Dumitrascu's findings, Nashishibi[18] and Turnbull pursued the use of this process for the preparation of several hitherto unavailable 4-iodosydnones.

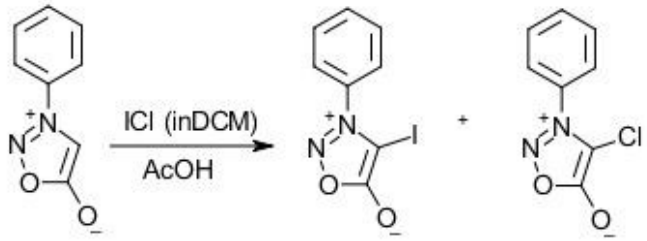


24 **25**

Scheme 15 - Dumitrascu's reported reaction with ICl

While it had been expected that the ICl would be somewhat unstable, it became clear that some of Nashishibi's early results were essentially irreproducible, yielding mixtures of starting material and desired product, due to rather rapid decomposition of the ICl used. A satisfactory alternate solution appeared to be the availability from Aldrich

Chemical Company of ICl in methylene chloride in SureSeal bottles. It was anticipated that this form of ICl would be more stable than the neat liquid and, accordingly, several iodination reactions were attempted with it in the same manner as performed previously (*viz.* in AcOH). Through these trials, it was discovered that not only did iodination (to yield **26**) occur but the 4-chloro product **27** was formed as well.

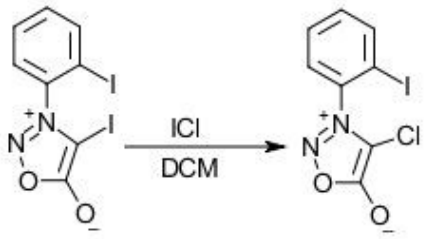


26 **27**

Scheme 16 - ICl (1.0M in DCM) with 3-phenylsydnone in AcOH

It seemed reasonable to assume that the presence of DCM was the cause of this modification and, accordingly, the experiment was repeated with the ICl in DCM reagent, and DCM as reaction solvent. It was discovered that this process yielded almost completely the chlorinated product **27**. Further reactions regarding this transformation were carried out by Nashishibi during his time in the lab. including the intriguing finding that the reaction of 2.0 eq. of ICl in DCM with 4-iodo-3-(2-iodophenyl)sydnone (**28**) in a

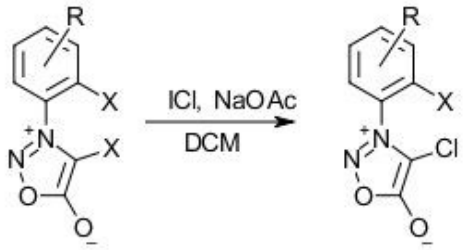
solution of DCM yielded 4-chloro-3-(2-iodophenyl)sydnone (**29**), albeit in low yield and purity.



28 **29**

Scheme 17 - 4-Iodo-3-(2-iodophenyl)sydnone with ICl in DCM

While this unique chlorination protocol was surprising, its ramifications were not pursued further until recently when Tumey and Owens from our lab set out to optimize the process[19]. Through several trials, the latter was found to be the use of 3.0 eq. of ICl, along with 3.0 eq. of sodium acetate (NaOAc) in anhydrous DCM at room temperature under an atmosphere of anhydrous nitrogen. The anhydrous conditions were important to stop hydrolysis of ICl into HI and HCl, which are detrimental to the sydnone ring system and the NaOAc was added to react with any residual acidic byproducts. This optimized process was of interest for the present study since it was anticipated that libraries of 4-chloro-3-(2-iodoaryl) and 4-chloro-3-(2-bromoaryl) sydnones would thus be accessible from 4-iodo-3-(2-iodoaryl) or “diiodo” and 4-bromo-3-(2-bromoaryl) or “dibromo” sydnones (see Scheme 18).



31-36 & 55-58 **49-54 & 62-64**

Scheme 18 - Overall aims of ICl reactions with dihalo sydnones

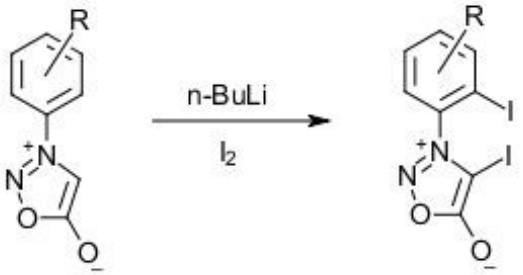
These products are of interest for their potential applications in carbon-carbon bond forming coupling reactions, such as Sonogashira coupling, since the resultant differentiation in the halogen groups will create the potential for selective coupling at specific sites on the sydnone ring.

Results and Discussion

I. Preparation and reactions of 4-iodo-3-(2-iodoaryl)sydnones

i. Preparation of 4-iodo-3-(2-iodoaryl)sydnones

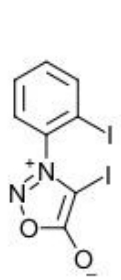
The preliminary portion of this project was to prepare dihalogenated 3-arylsydnones for further study. It was decided that 4-iodo-3-(2-iodoaryl)sydnones would be the most logical compounds to start with, due to the fact that all of the compounds of interest had been prepared in our lab previously, thus providing more straightforward identification. Of the six 4-iodo-3-(iodoaryl)sydnones that were desired (*viz.* R=H, p-CH_3, p-Cl, p-OMe, m-OMe, and 3,5-diOMe), three (**31-33**) were prepared *via* lithiation at -78°C using 3.0 equivalents of n-butyllithium followed by reaction with 3.0 equivalents of iodine (see Scheme 19).



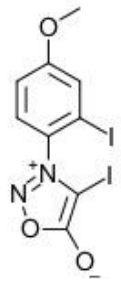
10 a(R=H)**,d**(R=4-OMe)**,e** (R=3-OMe) **31-33**

Scheme 19-Lithiation followed by iodination

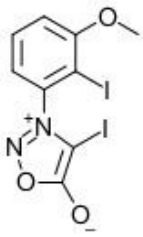
For 3-phenylsydnone (**10a**), 3-(4-methoxyphenyl)sydnone (**10d**), and 3-(3-methoxyphenyl)sydnone (**10e**) dilithiation/iodination was the only satisfactory approach to the diiodo species. Fortunately, the corresponding reactions led to the appropriate diiodo compounds **31**-**33** in good yield with comparable TLC and melting point values to known products previously made in our lab[17]. Their structures were confirmed by ^{13}C and ^{1}H NMR spectroscopy.



31



32

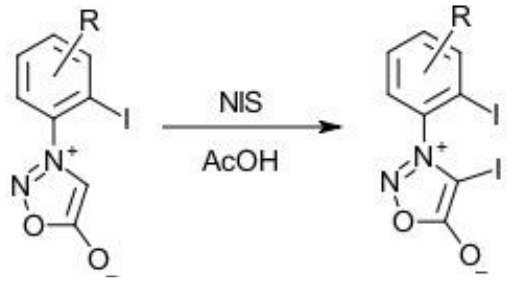


33

Compound	% Yield	Melting Point(°C) (exp.)	Melting Point(°C) (Lit.)[17]
31	**53.1**	**190-191**	**190-191**
32	**65.0**	**127-128**	**128-130**
33	**42.5**	**171-172**	**169-171**

Table 1- diiodinated sydnones via lithiation

For the three additional 4-iodo-3-(2-iodoaryl)sydnones **34-36**, which were to be made from the parent compounds 3-(4-methylphenyl)sydnone (**10c**), 3-(4-chlorophenyl)sydnone (**10b**) and 3-(3,5-dimethoxyphenyl)sydnone (**10f**) the lithiation approach was not necessary because of the availability of certain intermediates in our lab, as well as the special reactivity of the latter. Thus, samples of 3-(4-methyl-2-iodophenyl)sydnone (**38**) and 3-(4-chloro-2-iodophenyl)sydnone (**39**) were available in our lab. From previous work and it was expected that they could be treated with 1.1 eq. of N-iodosuccinimide (NIS) in acetic acid to iodinate at the C4 position of the sydnone ring and generate the desired diiodo sydnones **34** and **35**.



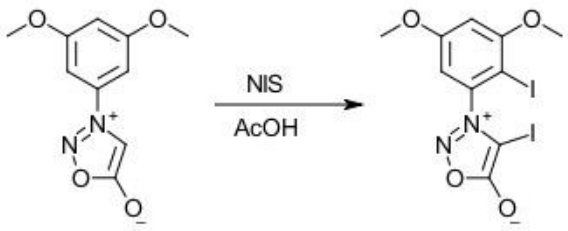
38 (R=4-CH_3) **34-35**

39 (R=4-Cl)

Scheme 20 - C4 iodination using NIS

Similarly, when there are very strong activating groups present on the aryl ring, such as is the case in 3-(3,5-dimethoxyphenyl)sydnone (**10f**), 3.3 eq of NIS in acetic acid can be used to iodinate at the C4 position of the sydnone ring, as well as one of the ortho

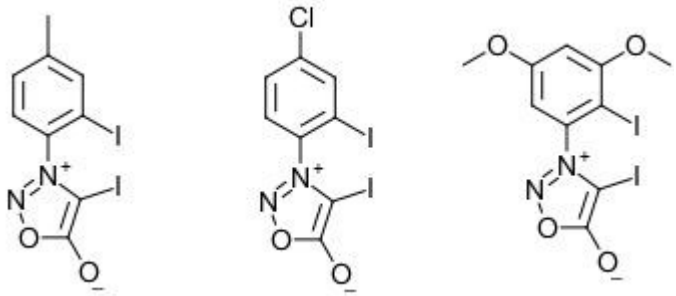
positions of the aryl ring, leading to 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**36**). This reaction was performed and is outlined below.



10f **36**

Scheme 21 - diiodination using NIS

Overall, the two reaction pathways discussed above led to the remaining three desired 4-iodo-3-(2-iodoaryl)sydnones **34**-**36**. These compounds, once obtained were compared to authentic samples previously prepared in our lab[16], and their structures were confirmed via ^{13}C and ^{1}H NMR spectroscopy.



34 **35** **36**

Compound	% yield	Melting Point(°C) (exp.)	Melting Point(°C) (lit.)[16]
34	**83.2**	**187-188**	**188-190**
35	**43.0**	**176-178**	**178-180**
36	**69.2**	**230-231**	**231-233**

Table 2 - NIS reactions leading to diiodinated sydnones

While the spectral characteristics of **31-36** varied slightly with each compound depending on the R group attached to the aryl ring, there existed some general spectral characteristics spanning all six different compounds that could be used in their classification. In IR spectroscopy the two characteristics most useful in characterization of all six compounds was the presence of a sydnone C=O stretch in the region around 1720-1760 cm^{-1}. Further, it was expected to see an absence of the peak that would normally represent the sydnone C-H stretch in the region around 3150 cm^{-1}. All six compounds **31-36** had IR spectral characteristics fitting these expectations (Appendix A, Section I).

Characterization by ^{1}H and ^{13}C NMR was also very useful in confirming the structure of these compounds. While the ^{1}H NMR characteristics varied from one compound to another in substitution pattern and integration in the aromatic region, one

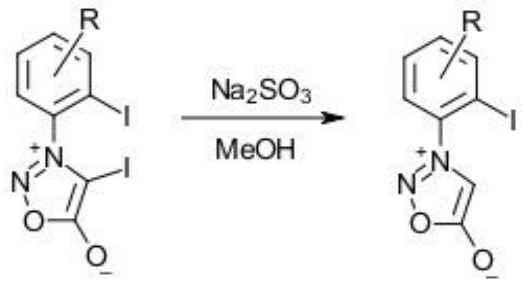
characteristic that was constant through all spectra was the absence of a sydnone C-H singlet peak, which normally comes around 6.7 ppm. The absence of this peak in the ^{1}H NMR is indicative of substitution at the C-4 position, a characteristic, which compounds **31-36** all displayed when their respective ^{1}H NMR spectra were collected (Appendix A, Section I).

The third, and perhaps most useful spectral characterization for compounds **31-36**, involved the use of ^{13}C NMR. Again, each compound had its own characteristics which differed depending on the level of substitution on the aryl ring. However, there were some constant characteristics which proved useful in confirming that the desired compound had been made. The first of these is the presence of six unique peaks corresponding to the six carbons within the aryl ring. The position of these peaks changes depending on substitution, but the number of peaks remains constant due to asymmetry in the molecule. Second, is the presence of the C=O carbon of the sydnone ring, which always comes at around 168 ppm in the ^{13}C spectrum. The third, and most telling ^{13}C NMR spectral characteristic of compounds **31-36**, arises from the substitution of an iodine at the ortho aryl ring position and at the C4 position of the sydnone ring itself. Iodine causes a rather large upfield shift on attached carbons, thus, causing the ortho position to shift from 121 ppm (3-phenylsydnone) to about 90 ppm when an iodine is substituted. Similarly, at the C4 position of the sydnone ring, an even larger

shift is seen from about 95 ppm (3-phenylsydnone) to about 55 ppm when an iodine is present. All diiodo compounds prepared via the methods outlined above had spectral characteristics fitting these general trends (Appendix A, Section I).

ii. Reactions of 4-iodo-3-(2-iodoaryl)sydnones 31-36 with $NaBH_4$ and Na_2SO_3

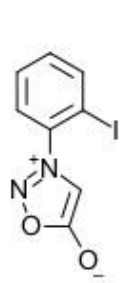
After the desired 4-iodo-3-(2-iodoaryl)sydnones **31-36** were prepared, it was of interest to observe their reactivity with sodium sulfite based on our previous observation that a C4 attached halogen (Br or I) could be removed with this reagent. Further, a reaction pathway that had not been reported previously was the reaction of 3-(2-iodoaryl)sydnones **37-42** with sodium borohydride in order to assess whether or not the ortho-attached iodine could be removed with this reagent, yielding the parent compound **43-48**. The 3-(2-iodoaryl)sydnones **37-42** were prepared via the reaction process shown below, using 4.0 eq of aqueous Na_2SO_3 in methanol.



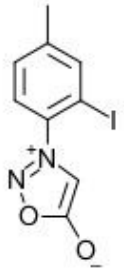
31-36 **37-42**

Scheme 22 - diiodo sydnones with sodium sulfite

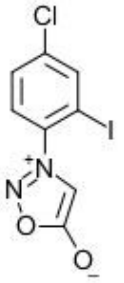
The six 4-iodo-3-(2-iodoaryl)sydnones **31-36** prepared previously were subjected to these reaction conditions, leading to the expected products **37-42**. All of the products **37-42** were known entities except for 3-(3-methoxy-2-iodophenyl)sydnone (**41**) and, accordingly, all but the latter were compared to authentic samples[17] via TLC, melting point and IR spectroscopy to confirm their identities. In the case of 3-(3-methoxy-2-iodophenyl)sydnone (**41**), ^{13}C, ^{1}H NMR, and IR spectroscopy were used to confirm its identity.



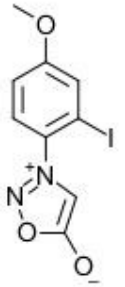
37



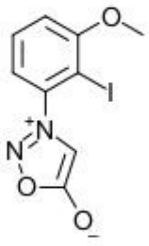
38



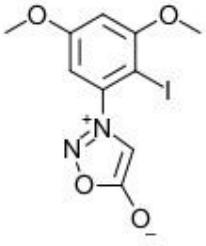
39



40



41



42

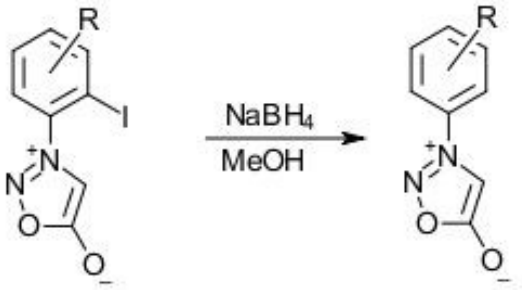
Compound	% yield	Melting Point(°C) (exp)	Melting Point(°C) (lit)[17]
37	**61.3**	**80-81**	**80-81**
38	**57.4**	**133-135**	**134-135**
39	**37.6**	**178-180**	**179-181**
40	**91.5**	**138-140**	**139-141**
41	**60.0**	**149-150**	**-**
42	**75.7**	**191-192**	**194-196**

Table 3 – Na_2SO_3 reactions leading to ortho iodinated sydnones

For confirmation that the expected 3-(2-iodoaryl)sydnones **37-42** had been prepared, comparison by TLC and melting point to authentic samples was deemed useful but not absolute. Further confirmation was found in the collection of IR (KBr) spectra and ^1H NMR spectra for each compound. While characteristics varied slightly between individual compounds, there existed some generalities that remained constant in each of the types of spectra for each compound. In the IR spectrum it was expected to see the sydnone C=O stretch around 1750 cm^{-1}, as well as the reemergence of the sydnone C-H stretch about 3150 cm^{-1}. All compounds met this expectation (Appendix A, Section II).

Similarly, in their ^{1}H NMR spectra, though substitution and integration patterns within the aromatic region varied, the reemergence of the sydnone C-H peak at about 6.7 ppm was observed in each of the compounds **37-42**. This served as further confirmation that the desired compounds had been achieved (Appendix A, Section II).

After reacting each compound with sodium sulfite and confirming removal of the iodine from the C4 position of the sydnone ring, each product was purified *via* recrystallization and subsequently reacted with 1 weight equivalent of sodium borohydride in methanol to test whether or not the *ortho*-attached iodine could be removed with this reagent to afford the parent sydnone , as had been observed with the diiodo sydnones (see Scheme 23).

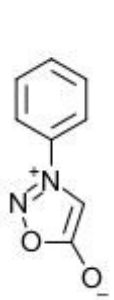


37-42 **43-48**

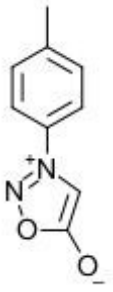
Scheme 23 - ortho iodo sydnones with sodium borohydride

Ultimately, in all six cases, the iodine ortho to the sydnone ring was removed, yielding the parent compounds **43-48** in good yields. The products were compared *via* melting

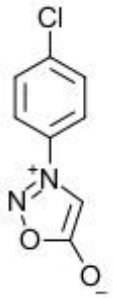
point and TLC to authentic samples of the corresponding 3-arylsydnones **43-48** to confirm that the expected transformation shown above had taken place.



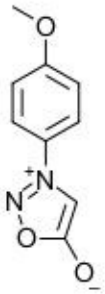
43



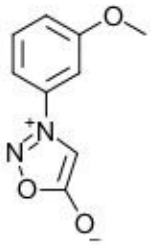
44



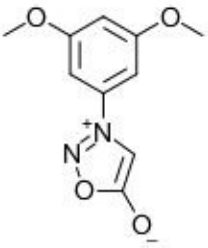
45



46



47



48

Compound	% yield	Melting Point(°C) (exp.)	Melting Point(°C) (lit.)
43	**53.4**	**130-132**	**130-132**
44	**87.5**	**141-143**	**142-143**
45	**82.3**	**108-110**	**111-113**

46	**88.0**	**123-125**	**125-126**
47	**66.8**	**134-135**	**134-135**
48	**77.2**	**164-165**	**163-165**

Table 4 - $NaBH_4$ reactions leading to parent sydnones

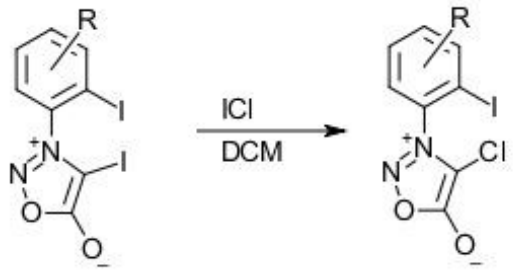
While confirmation by comparison with authentic samples of **43-48** was useful, it was not deemed absolute. Thus, IR (KBr) and ^{1}H NMR spectra were collected also. The characteristics present in the IR spectra of each compound were much the same as in the previous section. It was expected to see the sydnone C=O stretch, as well as the sydnone C-H stretch in the IRs of these compounds (Appendix A, Section III).

Similarly, with ^{1}H NMR spectral analysis it was expected to see the sydnone C-H at about 6.7 ppm. More importantly, it was expected to see a reemergence of symmetry in the aromatic region due to the removal of iodine from the ortho position of the aryl ring. The ^{1}H NMR spectra for each compound **43-48** met these characteristics (Appendix A, Section III).

iii. Reactions of 4-iodo-3-(2-iodoaryl)sydnones 31-36 with ICl

Based on the discovery in our lab of iodine monochloride (ICl) as an effective reagent for chlorination at the C4 position of sydnones (Schemes 16 and 17), it was of interest to expand on this process. As mentioned earlier, one example of a diiodo sydnone (**31**) had been converted to the corresponding 4-Cl analog (**49**) using this process, however, the

yield was extremely low, and the generality of the process had not been assessed. Accordingly, in the present work, it was elected to extend the improved protocol to the use of compounds with different R groups substituted on the aryl ring, (*cf*. **31-36**) such that the synthesis of 4-chloro-3-(2-iodoaryl)sydnones **49-54** would result (see Scheme 24).



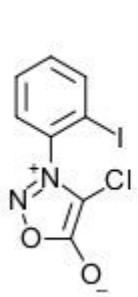
31-36 **49-54**

Scheme 24 - diiodo sydnones with ICl

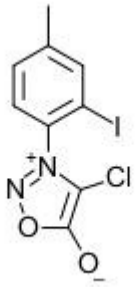
For these reactions, 3.0 eq of ICl (1.0M in DCM) was used, along with 3.0 eq of NaOAc to mitigate the formation of HI and HCl from hydrolysis of ICl. The reactions were performed under an atmosphere of nitrogen in a flame dried flask using dry reagents including anhydrous DCM and NaOAc.

Ultimately, in all six cases, the expected 4-chloro-3-(2-iodoaryl)sydnones **49-54** were prepared with high levels of purity and in good yield. In all cases, except **49**, the product was a new compound, and thus was fully characterized by melting point, ^{1}H and ^{13}C

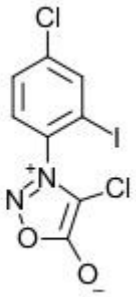
NMR, IR spectra and elemental analysis. In the case of **49**, the product was identical to an authentic sample[18] by melting point, TLC, IR, ^{1}H and ^{13}C NMR comparison.



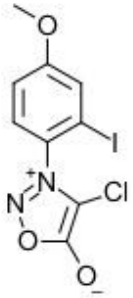
49



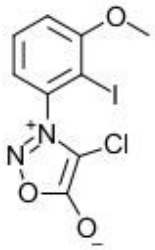
50



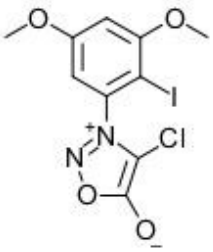
51



52



53



54

Compound	% yield	Melting Point(°C) (exp)	Melting Point(°C) (lit)[18]
49	**71.4**	**101-102**	**100-102**
50	**68.4**	**128-129**	-
51	**68.8**	**163-164**	-

52	**71.5**	**111-112**	-
53	**76.1**	**107-108**	-
54	**79.3**	**217-218**	-

Table 5 - 4-chloro sydnones from ICl reactions

As mentioned above, compounds **49-54** were fully characterized by IR, ^{1}H and ^{13}C NMR. In their IR spectra, a similar trend was observed as for the diiodo compounds **31-36** discussed previously. In their ^{1}H and ^{13}C NMR spectra the characteristics were similar to those for the diiodo compounds **31-36**, with one small difference, namely, in their ^{13}C NMR spectra, the C4 position of the sydnone ring shifted from approximately 55 ppm to about 99 ppm, indicative of a change at that position from iodine to chlorine. All compounds **49-54** met these characteristics (Appendix A, Section IV).

iv. Conclusion For Part I

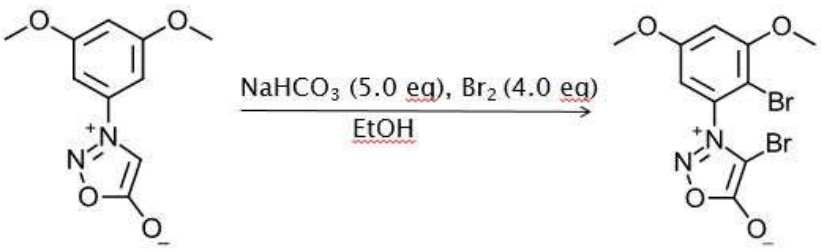
Through the work outlined above, much about the preparation and reactivity of 4-iodo-3-(2-iodoaryl)sydnones has been determined. First, it was further confirmed in support of previous work that 4-iodo-3-(2-iodoaryl)sydnones can be prepared via several different processes in respectable yield with relatively high purity. These processes for preparation of compounds **31-36** were well documented before the present work was performed, but the results outlined herein serve to further confirm the reproducibility of these synthetic routes, as well as lead to precursors for the work to be performed

thereafter. Further, several reaction pathways involving 4-iodo-3-(2-iodoaryl)sydnones were observed, leading to a more complete understanding of the reactivity of sydnones and leading to precursors for potential future work. The work involving reactions of 4-iodo-3-(2-iodoaryl) sydnones with Na_2SO_3 and 3-(2-iodoaryl)sydnones with $NaBH_4$ was important in building upon the work performed by Turnbull et al., wherein Na_2SO_3 was shown to remove an iodine from the sydnone ring, and one weight equivalent of $NaBH_4$ would remove both iodines. The conclusion from similar work reported in this thesis is that the presence of an iodine on the sydnone ring does not affect the ability of $NaBH_4$ to remove the iodine from the aryl ring. The mechanism of these transformations is still unclear, however, it is to be hoped that this work will stimulate mechanistic studies to provide further understanding. Lastly, the work involving electrophilic aromatic substitution of a chlorine at the C4 position, displacing an iodine, builds upon work that, until this point, was only partially explored. With a viable route to 4-chloro analogs using ICl, this work creates an opportunity for expansion and further exploration of such reactions with sydnones, namely, producing differentiated halogen substitution, which should be useful in carbon-carbon bond forming coupling reactions in which a terminal halogen is a necessary part of one reagent.

II. Preparation and reactions of 4-bromo-3-(2-bromoaryl)sydnones

i. Preparation of 4-bromo-3-(2-bromoaryl)sydnones (see Scheme 11, X = Br)

As shown by Turnbull in 1985[6], when there are very strong activating groups present on the aryl ring, such as is the case in 3-(3,5-dimethoxyphenyl)sydnone (**10f**), 4.0 eq of Br_2 in ethanol along with 5.0 eq of $NaHCO_3$ can be used to brominate at the C4 position of the sydnone ring, as well as one of the *ortho* position of the aryl ring leading to 4-bromo-3-(3,5-dimethoxy-2-bromophenyl)sydnone (**55**). This reaction was performed and is outlined below.



10f **55**

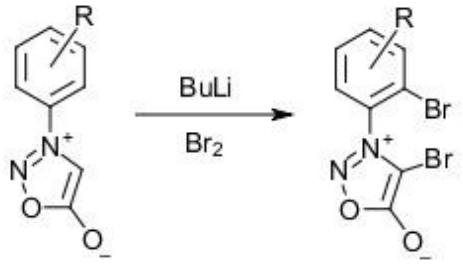
Scheme 25 - bromination of 3-(3,5-dimethoxyphenyl)sydnone

The reaction pathway discussed above led to **55**, and this compound was identical to an authentic sample previously prepared in our lab[6] by TLC, melting point, IR, and ^{1}H and ^{13}C NMR spectroscopy comparison.



55

For preparation the remaining 4-bromo-3-(2-bromoaryl)sydnones **56-58**, the process of lithiation was required. Lithiation with 3.0 eq. of BuLi in THF followed by reaction with 3.0 eq. of bromine is a process that was reported by Krein and Turnbull in 1997, but only for 3-phenylsydnone (**10a**).

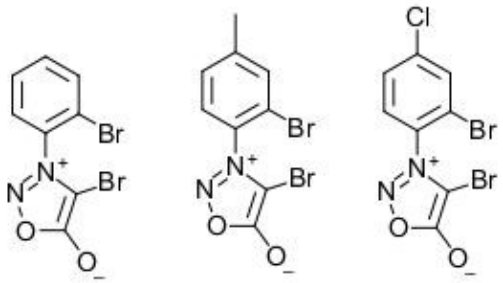


10a, b, c **56-58**

Scheme 26 - lithiation/bromination of sydnones

Originally, the process of lithiation and bromination of sydnones outlined above was desired for the same six parent compounds as had been used for diiodination. However, while the first transformation was performed with 3-phenylsydnone (**10a**) and was shown to be moderately successful in leading to 4-bromo-3-(2-bromophenyl)sydnone (**56**) after several trials, attempts to expand this process to compounds with substituents on the aryl ring, such as in **10b** (*p*-Cl) and **10c** (*p*-CH_3), led only to limited amounts of pure material after column chromatography and recrystallization. Due to this difficulty, the preparation of dibrominated compounds was pursued for a more limited number of compounds. It was deemed important to at include the parent compound **10a** and to include sydnones with groups exhibiting different electronic effects, as in **10b** and **10c.**

The process outline above was thus attempted with 3-(4-methylphenyl) (**10c**) and 3-(4-chlorophenyl)sydnone (**10b**), leading to the corresponding dibromo substituted sydnones **57** and **58.**



56 **57** **58**

The structures of **57** and **58** were verified by IR, ^{1}H and ^{13}C NMR. As mentioned above, these compounds had not been prepared in our lab or any other previously, thus, full characterization, including elemental analysis, was required. Both compounds provided satisfactory elemental analysis results confirming the expected compounds had been prepared.

Compound	**%yield**	**Melting Point(°C) (exp)**	**Melting Point(°C) (lit)[6,10]**
55	**60.4**	**201-202**	**200-202**

56	**63.8**	**93-95**	**94-96**
57	**27.9**	**129-130**	**-**
58	**20.3**	**101-102**	**-**

Table 6 – 4-bromo-3-(2-bromoaryl)sydnone products

In order to prove that the appropriate 4-bromo-3-(2-bromoaryl)sydnones **55-58** were prepared as expected, compounds **55** and **56** were compared to authentic samples *via* TLC, melting point IR, ^{1}H and ^{13}C NMR. Compounds **57** and **58** were fully characterized as new compounds. While their spectral characteristics varied slightly with each compound, depending on the R group attached to the aryl ring, general patterns existed. In their IR spectra the two characteristics most useful in characterization of all four compounds was the presence of a sydnone C=O stretch at 1720-1760 cm^{-1}. Further, it was expected that the peak that would normally represent the sydnone C-H stretch around 3150 cm^{-1} would be absent due to substitution at the C-4 position. All four compounds **55-58** had IR spectral characteristics that fit these expectations (Appendix A).

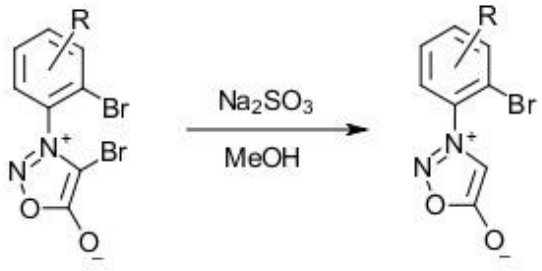
Characterization by ^{1}H and ^{13}C NMR spectroscopy was also useful in confirming the structure of these compounds. While the ^{1}H NMR characteristics varied from one compound to another in substitution pattern and integration in the aromatic region, one characteristic that was constant throughout was the absence around 6.7 ppm of a

sydnone proton singlet, indicative of substitution at the C-4 position. All prepared compounds **55-58** displayed this characteristic in their respective ^{1}H NMR spectra (Appendix A).

The third, and most useful, spectral characterization for compounds **55-58** involved the use of ^{13}C NMR. Again, each compound had its own characteristics which differed depending on the level of substitution on the aryl ring, but there existed constants for each. The first of these is the presence of six unique peaks corresponding to the six carbons within the aryl ring, due to asymmetry in the molecule. Second, is the presence of the C=O carbon of the sydnone ring, which always comes at around 168 ppm in the ^{13}C spectrum. The third, and most telling, ^{13}C NMR spectral characteristics of compounds **55-58** arise from the substitution of bromine atoms at the *ortho* position of the aryl ring and at the C4 position of the sydnone ring. Bromine has a slight upfield effect on these carbons, causing the *ortho* position to shift from 121 ppm (in 3-phenylsydnone) to about 119 ppm when a bromine atom is present. Similarly, at the C4 position of the sydnone ring, a shift from about 95 ppm (in 3-phenylsydnone) to about 86 ppm is observed when a bromine atom is present. All dibromo compounds prepared *via* the methods outline above had spectral characteristics that met these general trends. All spectra for these compounds are assembled in Appendix A.

ii. Reactions of 4-bromo-3-(2-bromoaryl)sydnones 55-58 with $NaBH_4$ and Na_2SO_3

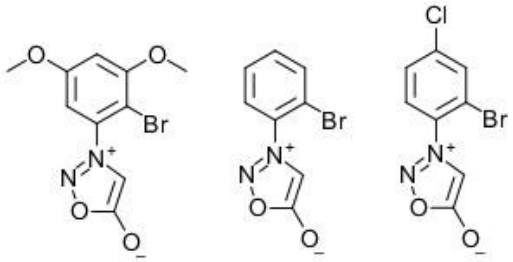
After the desired 4-bromo-3-(2-bromoaryl)sydnones **55-58** were prepared, it was of interest to observe their reactivity with sodium sulfite, and subsequently, that of the 3-(2-bromoaryl) product **59-61** with sodium borohydride. The first such reaction pathway was with sodium sulfite, based on our previous observation that a C4 attached halogen (Br or I) could be removed with this reagent. Further, a reaction pathway that had not been reported was the reaction of 3-(2-bromoaryl)sydnones **59-61** with sodium borohydride to observe if the parent compound **43-48** could be obtained. The 3-(2-bromoaryl)sydnones **59-61** were prepared *via* the reaction process shown below, using 4.0 eq of aqueous Na_2SO_3 in methanol. It is important to note that this process was only completed for 4-bromo-3-(2-bromophenyl) (**56**), 4-bromo-3-(4-chloro-2-bromophenyl) (**58**), and 4-bromo-(3,5-dimethoxy-2-bromophenyl) (**55**) sydnone due to limited availability of 4-bromo-3-(4-methyl-2bromophenyl)sydnone (**57**).



55-58 **59-61**

Scheme 27 - dibromo sydnones with sodium sulfite

This process was completed using 4.0 eq. of aqueous sodium sulfite in methanol, leading to the expected compounds **59**-**61**. In the cases of compounds **59** and **60** where R=3,5-di-OMe and R=H, these compounds were prepared previously, thus comparison by TLC, melting point and IR was sufficient to prove the expected transformation had taken place in each case. Compound **61**, where R=Cl, this had not been previously prepared, thus ^{1}H, ^{13}C NMR as well as elemental analysis were required for confirmation. It was determined in all cases that the expected transformation had taken place, thus **59**-**61** were successfully obtained *via* the process discussed.



59 **60** **61**

Compound	%yield	Melting Point(°C) (exp)	Melting Point(°C) (lit)
59	**90.9**	**160-162**	**162-164**

60	**61.3**	**78-79**	**78-79**
61	**76.3**	**131-132**	**-**

Table 7 – 3-(2-bromoaryl)sydnone products

For confirmation that the expected 3-(2-bromoaryl)sydnone **59-61** had been prepared, comparison by TLC and melting point to authentic sample was deemed useful but not absolute. Further confirmation was found in the collection of IR (KBr) and ^{1}H NMR spectra for compounds **59** and **60**. Compound **61** was fully characterized as a new compound wirh IR, ^{1}H and ^{13}C NMR as well as elemental analysis. While characteristics can vary slightly between individual compounds, there existed some generalities. In the IR spectra it was expected to see the sydnone C=O stretch around 1760 cm^{-1}, as well as the reemergence of the sydnone C-H stretch around 3150 cm^{-1}. All compounds met this expectation and their IR spectra can be seen in Appendix A.

Similarly, in ^{1}H NMR, though substitution and integration patterns within the aromatic region varied, the reemergence of the sydnone C-H peak at about 6.7 ppm was observed in each of the compounds **59-61**. This served as further confirmation that the desired compound had been achieved, and the ^{1}H NMR spectrum for each compound as well as ^{13}C NMR spectrum for **61** can be observed in Appendix A.

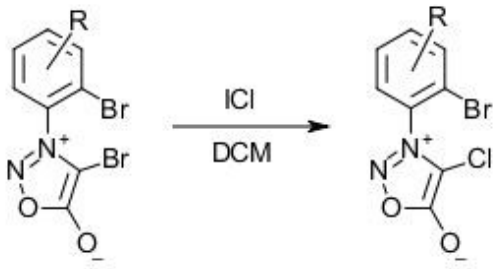
After reacting each compound with sodium sulfite and confirming removal of the bromine from the C4 position of the sydnone ring, each product was purified *via*

recrystallization and subsequently reacted with 1 weight equivalent of sodium borohydride in methanol to test whether or not the *ortho*-attached bromine could be removed with this reagent to afford the parent sydnone, as had been observed with the ortho-iodo sydnones.

Ultimately, in all three cases, the bromine ortho to the sydnone ring was not removed, leading to recovery of starting materials **59**-**61**. The products were compared *via* melting point and TLC to authentic samples of the starting materials to confirm that no reaction had taken place.

iii. Reactions of 4-bromo-3-(2-bromoaryl)sydnones with ICl

Based on the discovery in our lab of iodine monochloride (ICl) as an effective reagent for chlorination at the C4 position of sydnones (Schemes 16 and 17), it was of interest to expand on this process, and prove that similar compounds can be achieved with different R groups substituted on the aryl ring *cf.* **62**-**64** (Scheme 28).

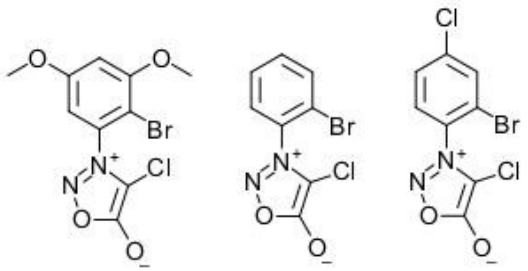


55-58 **62-64**

Scheme 28 - dibromo sydnones with ICl

For these reactions, 3.0 eq. of ICl (1.0M in DCM) was used, along with 3.0 eq. of NaOAc to mitigate the formation of HI and HCl from hydrolysis of ICl. The reactions were done under an atmosphere of nitrogen in a flame dried flask using dry reagents including anhydrous DCM and NaOAc.

Ultimately in all three cases, the expected 4-chloro-3-(2-bromoaryl)sydnones **62-64** were achieved with high levels of purity and in good yields. Products **63** and **64** were new compounds and thus were fully characterized by melting point, ^{1}H and ^{13}C NMR, IR and elemental analysis. In the case of **62**, comparison by melting point and TLC with an authentic sample, as well as structural confirmation by ^{1}H and ^{13}C NMR spectra helped to confirm its identity.



62 **63** **64**

Compoumd	%yield	Melting Point (exp)	Melting Point (lit)
62	**45.1**	**188-190**	**190-191**
63	**63.6**	**89-90**	**-**
64	**34.2**	**110-111**	**-**

Table 8 – 4-chloro-3-(2-bromoaryl)sydnone products

As mentioned above, compounds **62-64** were fully characterized by IR, ^{1}H and ^{13}C NMR. In the IR spectra, a similar trend was observed as was observed in the dibromo compound **55-58** studied previously. Their ^{1}H and ^{13}C NMR spectral characteristics were similar to dibromo compounds, with one difference. In ^{13}C NMR, at the C4 position of the sydnone ring, instead of an upfield shift of about 10 ppm indicating substitution of a bromine atom, a slight downfield shift to about 99 ppm was observed, due to the presence of a chlorine atom at the C4 position. All compounds **62-64** met these expectations, and their spectra and elemental analysis results can be observed in Appendix A.

iv. Conclusion For Part II

Through the work outlined above, much about the preparation and reactivity of 4-bromo-3-(2-bromoaryl)sydnones was discovered. First, it was further confirmed in support of previous work that 4-bromo-3-(2-bromoaryl)sydnones can be prepared via several different processes in respectable yield with relatively high purity. These processes for preparation of compounds **55** and **56** were well documented before the present work was performed, but the results outlined above serve to further confirm the reproducibility of these synthetic routes, as well as lead to precursors for the work to be performed thereafter. In the case of compounds **57** and **58** it was observed that dibromo compounds can be obtained via lithiation/bromination, but the yield and purity was limited and difficult to achieve. It is hypothesized that, due to the instability and difficulty in using Br_2, this process is not optimal. This, potentially, creates the need for a more optimized procedure, or the exploration of other sources of bromine. Further, several synthetic pathways involving 4-bromo-3-(2-bromoaryl)sydnones were observed, leading to a more complete understanding of the reactivity of sydnones and leading to precursors for potential future work. The work involving reactions of 4-bromo-3-(2-bromoaryl) sydnones with Na_2SO_3 and 3-(2-bromoaryl)sydnones with $NaBH_4$ was important in building upon the work performed by Turbull et al., wherein Na_2SO_3 was shown to remove an iodine from the sydnone ring, and one weight equivalent of $NaBH_4$

would remove both. The conclusion from similar work reported in this thesis is that bromine can be removed from the C4 position of the sydnone ring using Na_2SO_3, but $NaBH_4$ does not remove the bromine from the aryl ring, indicating some difference in the nature of dibromo compounds versus their diiodo counterparts. The mechanism of these transformations is still unclear, however, this work could lead to a mechanistic study to further understand these transformations. Lastly, the work involving electrophilic aromatic substitution of a chlorine at the C4 position, displacing a bromine, builds upon work that, up to point, was only partially explored. With a viable method for 4-chloro analog production using ICl, this work creates an opportunity for expansion and further exploration of such reactions with sydnones in producing differentiated halogen substitution, which is hypothesized to be useful in carbon-carbon bond forming coupling reactions in which a terminal halogen is a necessary part of one reagent.

Experimental

I. Notes

All starting reagents were purchased from commercial sources and used without further purification. Where applicable (i.e. reactions with BuLi and ICl), all glassware was flame-dried under an atmosphere of nitrogen prior to the use of dry reagents. Melting points were determined on a Mel-Temp melting point apparatus and are uncorrected. Infrared spectra were acquired on a Nicolet FTIR manufactured by Thermo-Fisher Scientific. NMR spectra were acquired on a Bruker Advance 300MHz NMR. Elemental analyses were performed by Midwest Microlab LLC, Indianapolis, Indiana.

II. Synthesis of 4-iodo-3-(2-iodoaryl)sydnones

Synthesis of 4-iodo-3-(2-iodophenyl)sydnone (**31**) via lithiation

To a stirred solution of 3-phenylsydnone (0.2042 g, 0.0013 mol) in dry THF (30 mL) under an atmosphere of nitrogen at -78^{o}C were added three equivalents of n-butyllithium (1.6 M in cyclohexane, 2.4 mL, 0.0039 mol). The solution was allowed to stir for 15 minutes at which point excess iodine (0.9955 g, 0.0039 mol) was added and the reaction was continued for one hour. Subsequently, the reaction was warmed to -10^{o}C and quenched with ice cold saturated brine solution (50 mL). The solution volume was

reduced overnight with stirring to allow THF to evaporate completely. At this point the remaining mixture was transferred to a separatory funnel with DCM (30 mL). The organic layer was separated and washed with of 2% aqueous Na_2SO_3 (50 mL). The aqueous layer was extracted with DCM (3x20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a light yellow oily solid. Recrystallization from 95% ethanol yielded the desired compound (0.2871 g, 0.00069 mol, 53.1%), with a melting point of 190-191^oC, identical (TLC, IR, m.p.) to an authentic sample previously prepared in our lab.

IR (KBr): 1751.8 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 8.1 (dd, 1H), 7.65 (td, 1H), 7.4-7.5 (m, 2H) ppm.

^{13}C-NMR ($CDCl_3$): 168.5 (C=O), 140.7, 138.1, 133.7, 129.8, 127.5, 93.8, 52.9 ppm.

Synthesis of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone (**32**) via lithiation

To a stirred solution of 3-(4-methoxyphenyl)sydnone (0.1969 g, 0.0010 mol) in dry THF (30 mL) under an atmosphere of nitrogen at -78^{o}C were added three equivalents of n-butyllithium (1.6 M in cyclohexane, 1.9 mL, 0.0031 mol). The solution was allowed to stir for 15 minutes at which point excess iodine (0.7900 g, 0.0031 mol) was added and the solution stirred for one hour. Subsequently, the reaction was warmed to -10^{o}C and

quenched with ice cold saturated brine solution (50 mL). The solution volume was reduced overnight with stirring to allow THF to evaporate completely. At this point the remaining mixture was transferred to a separatory funnel with DCM (30 mL). The organic layer was extracted and washed with 2% aqueous Na_2SO_3 (50 mL). Aqueous layer was extracted with DCM (3x20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a light brown oily solid. Recrystallization from 95% ethanol yielded the desired compound (0.2906 g, 0.00065 mol, 65.0%), with a melting point of 127-128^oC, identical (TLC, IR, m.p.) to an authentic sample previously prepared in our lab.

IR (KBr): 1744.8 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.55 (m, 1H), 7.30 (dd, 1H), 7.1 (m, 1H), 3.9 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 162.3 (C=O), 130.8, 128.0, 126.5, 125.6, 115.3, 94.3, 56.1, 53.7 ppm.

Synthesis of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone (**33**) via lithiation

To a stirred solution of 3-(3-methoxyphenyl)sydnone (0.1903 g, 0.00099 mol) in dry THF (40 mL) under an atmosphere of nitrogen at -78^oC were added three equivalents of n-butyllithium (1.6 M in cyclohexane, 1.9 mL, 0.0030 mol). The solution was allowed to stir for 15 minutes at which point excess iodine (0.7744 g, 0.0033 mol) was added and the

solution was stirred for one hour. Subsequently, the reaction was warmed to -10°C and quenched with ice cold saturated brine solution (50 mL). The solution volume was reduced overnight with stirring to allow THF to evaporate completely. At this point the remaining mixture was transferred to a separatory funnel with DCM (30 mL). The organic layer was extracted and washed with 2% aqueous Na_2SO_3 (50 mL). Aqueous layer was extracted with DCM (3x20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a light brown solid. Recrystallization from 90% ethanol yielded the desired compound (0.1879 g, 0.00080 mol, 42.5%), with a melting point of 171-172°C, identical (TLC, IR, m.p.) to an authentic sample previously prepared in our lab.

IR (KBr): 1761.7 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.6 (td, 1H), 7.0-7.2 (m, 2H), 4.0 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 168.6 (C=O), 160.1, 139.3, 130.7, 119.4, 113.9, 87.2, 57.2, 52.8 ppm.

Synthesis of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone (**34**) via iodination with NIS

To a stirred solution of 3-(4-methyl-2-iodophenyl)sydnone (0.1161 g, 0.00038 mol) in concentrated acetic acid (3 mL) was added N-iodosuccinimide (1.1 eq, 0.0985 g, 0.00042 mol). The mixture was allowed to react for 4 hours with constant stirring, at which point

TLC in DCM showed complete conversion of starting material to a higher running product. At this point, DI H_2O (10 mL) was added slowly to the reaction mixture, leading to precipitation. The white precipitated solid was isolated by vacuum filtration and dried under vacuum to yield the title compound, 0.1362 g, 0.00032 mol, 83.2%, m.p. 187-188^oC. Identical to authentic sample previously prepared in our lab (TLC, IR, m.p.).

IR (KBr): 1715.6 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.9 (d, 1H), 7.4 (dd, 1H), 7.3 (d, 1H), 2.5 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 168.6 (C=O), 144.8, 141.0, 135.6, 130.4, 127.0, 93.5, 53.1, 21.0 ppm.

Synthesis of 4-iodo-3-(4-chloro-2-iodophenyl)sydnone (**35**) via iodination with NIS

To a stirred solution of 3-(4-chloro-2-iodophenyl)sydnone (0.0559 g, 0.00017 mol) in concentrated acetic acid (3 mL) was added N-iodosuccinimide (1.1 eq, 0.0449 g, 0.00019 mol). The mixture was allowed to react for 4 hours with constant stirring, at which point TLC in DCM showed complete conversion of starting material to a higher running product. At this point, DI H_2O (10 mL) was added slowly to the reaction mixture, leading to precipitation. The white precipitated solid was isolated by vacuum filtration and dried to yield the title compound, 0.0330 g, 0.000073 mol, 43.0%, m.p. 176-178^oC. Identical to authentic sample previously prepared in our lab (TLC, IR, m.p.).

IR (KBr): 1740.5 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 8.1 (d, 1H), 7.65 (dd, 1H), 7.4 (d, 1H) ppm.

^{13}C-NMR ($CDCl_3$): 168.4 (C=O), 140.3, 139.4, 136.6, 130.1, 128.2, 94.5, 53.0 ppm.

Synthesis of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**36**) via iodination with NIS

To a stirred solution of 3-(3,5-dimethoxyphenyl)sydnone (0.1268 g, 0.00057 mol) in concentrated acetic acid (7 mL) was added N-iodosuccinimide (5.0 eq, 0.6371 g, 0.0028 mol). The mixture was allowed to react for 24 hours with constant stirring, at which point TLC in DCM showed complete conversion of starting material to a higher running product. At this point, DI H_2O (30 mL) was slowly added to the reaction mixture, leading to precipitation. The white precipitated solid was isolated by vacuum filtration and dried yielding the title compound, 0.1865 g, 0.00039 mol, 69.2%, m.p. 230-231^{o}C. Identical to authentic sample previously prepared in our lab (TLC, IR, m.p.).

IR (KBr): 1741.4 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.2 (d, 1H), 6.9 (d, 1H), 3.9 (s, 3H), 3.8 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 169.3 (C=O), 161.9, 160.5, 139.6, 106.2, 102.2, 77.7, 59.6, 57.7, 56.8 ppm.

III. Reaction of 4-iodo-3-(2-iodoaryl)sydnones with Na_2SO_3

Reaction of 4-iodo-3-(2-iodophenyl)sydnone (**31**) with Na_2SO_3

To a stirred solution of 4-iodo-3-(2-iodophenyl)sydnone (0.0306 g, 0.000074 mol) in methanol (3mL) was added Na_2SO_3 (0.0390 g, 0.0003 mol, in 2 mL H_2O). The mixture was allowed to react for 30 minutes, at which point the volume of methanol was allowed to evaporate. The remaining aqueous layer was washed with DCM (3x5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a pale brown solid. Confirmed by TLC, IR, m.p to be identical to a sample of 3-(2-iodophenyl)sydnone (**37**), 0.0131 g, 0.000045 mol, 61.3%, m.p. 80-81^oC.

IR (KBr): 1751.8 (C=O), 3117.7 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 8.5 (dd, 1H), 7.6 (td, 1H), 7.5 (dd, 1H), 7.4 (td, 1H), 6.5 (s, 1H) ppm.

Reaction of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone (**34**) with Na_2SO_3

To a stirred solution of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone (0.0037 g, 0.0000086 mol) in methanol (3mL) was added Na_2SO_3 (0.0043 g, 0.00034 mol, in 2 mL H_2O). The mixture was allowed to react for 30 minutes, at which point the volume of methanol

was allowed to evaporate. The remaining aqueous layer was washed with DCM (3x5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a white solid. Confirmed by TLC, IR, m.p to be identical to a sample of 3-(4-methyl-2-iodophenyl)sydnone (**38**), 0.0015 g, 0.0000049 mol, 57.4%, m.p. 133-135^oC.

IR (KBr): 1734.9 (C=O), 3137.0 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.9 (dd, 1H), 7.3-7.5 (d, 2H), 6.5 (s, 1H), 2.5 (s, 3H) ppm.

Reaction of 4-iodo-3-(4-chloro-2-iodophenyl)sydnone (**35**) with Na_2SO_3

To a stirred solution of 4-iodo-3-(4-chloro-2-iodophenyl)sydnone (0.0330 g, 0.000073 mol) in methanol (3mL) was added Na_2SO_3 (0.0442 g, 0.00029 mol, in 2 mL H_2O). The mixture was allowed to react for 30 minutes, at which point the volume of methanol was allowed to evaporate. The remaining aqueous layer was washed with DCM (3x5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a pale orange solid. Confirmed by TLC, IR, m.p to be identical to a sample of 3-(4-chloro-2-iodophenyl)sydnone (**39**), 0.0089 g, 0.000027 mol, 37.6%, m.p 178-180^oC.

IR (KBr): 1734.4 (C=O), 3138.0 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 8.1 (d, 1H), 7.6 (dd, 1H), 7.45 (d, 1H), 6.55 (s, 1H) ppm.

Reaction of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone (**32**) with Na_2SO_3

To a stirred solution of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone (0.0310 g, 0.000069 mol) in methanol (5mL) was added Na_2SO_3 (0.0350 g, 0.00028 mol, in 3 mL H_2O). The mixture was allowed to react for 20 minutes, at which point the volume of methanol was allowed to evaporate. The remaining aqueous layer was washed with DCM (3x5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a tan solid. Confirmed by TLC, IR, m.p to be identical to a sample of 3-(4-methoxy-2-iodophenyl)sydnone (**40**), 0.0202 g, 0.000063 mol, 91.5%, m.p 138-140^oC.

IR (KBr): 1741.3 (C=O), 3105.8 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.5 (m, 1H), 7.4 (m, 1H), 7.1 (m, 1H), 6.5 (s, 1H), 3.9 (s, 3H) ppm.

Reaction of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone (**33**) with Na_2SO_3

To a stirred solution of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone (0.0397 g, 0.000089 mol) in methanol (5mL) was added Na_2SO_3 (0.0442 g, 0.00029 mol, in 5 mL H_2O). The mixture was allowed to react for 30 minutes, at which point the volume of methanol was allowed to evaporate. The remaining aqueous layer was washed with DCM (3x5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to

yield a pale tan solid. Recrystallization from 90% ethanol yielded a white solid (**41**) as the title compound, 0.0171 g, 0.000053 mol, 60.0%, m.p 149-150^{o}C.

IR (KBr): 1734.8 (C=O), 3151.4 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.55 (td, 1H), 7.15 (dd, 1H), 7.05 (dd, 1H), 6.55 (s, 1H), 4.0 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 168.7 (C=O), 160.0, 139.1, 130.6, 118.9, 113.8, 97.7, 85.8, 57.2 ppm.

Reaction of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**36**) with Na_2SO_3

To a stirred solution of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone (0.0112 g, 0.000024 mol) in methanol (2mL) was added aqueous Na_2SO_3 (0.0121 g, 0.000096 mol in 5 mL H_2O). The mixture was allowed to react for 20 minutes, at which point the volume of methanol was allowed to evaporate. The remaining aqueous layer was washed with DCM (3x5 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a yellow solid. Confirmed by TLC, IR, m.p to be identical to a sample of 3-(3,5-dimethoxy-2-iodophenyl)sydnone (**42**) previously prepared in our lab, 0.0062 g, 0.000018 mol, 75.7%, m.p 191-192^{o}C.

IR (KBr): 1734.9 (C=O), 3145.9 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 6.7 (d, 1H), 6.6 (d, 1H), 6.5 (s, 1H), 4.0 (s, 3H), 3.9 (s, 3H) ppm.

IV. Reaction of 3-(2-iodoaryl)sydnones with $NaBH_4$

Reaction of 3-(2-iodophenyl)sydnone (**37**) with $NaBH_4$

To a stirred solution of 3-(2-iodophenyl)sydnone (**37**) (0.0317 g, 0.00011 mol) in MeOH (2 mL) was added $NaBH_4$ (0.0320 g, 0.00085 mol) slowly over a period of about 10 minutes. After complete addition of $NaBH_4$, the reaction was left stirring for 30 minutes, at which point TLC showed remaining starting material. An additional portion of $NaBH_4$ (0.0215 g) was added and the reaction was allowed to sit stirring for an additional 1.5 hours, at which point TLC indicated complete conversion of starting material. Volume of MeOH was reduced, leaving behind a solid. Solid transferred to vacuum funnel using DI water (2 mL), dried for one hour and collected to yield 3-phenylsydnone (**43**) Identical by IR, TLC, m.p. to authentic sample, 0.0095 g, 0.000059 mol, 53.4%, mp of 130-132^{o}C.

IR (KBr): 1758.8 (C=O), 3127.7 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.7 (m, 5H), 6.7 (s, 1H) ppm.

Reaction of 3-(4-methyl-2-iodophenyl)sydnone (**38**) with $NaBH_4$

To a stirred solution of 3-(4-methyl-2-iodophenyl)sydnone (**38**) (0.0662 g, 0.00022 mol) in MeOH (3 mL) was added $NaBH_4$ (0.0832 g, 0.0018 mol) slowly over a period of about 5 minutes. After complete addition of $NaBH_4$, the reaction was left stirring for 30 minutes, at which point TLC indicated complete conversion of starting material. Volume of MeOH was reduced, leaving behind a solid. Solid transferred to vacuum funnel using DI water (3 mL), dried for three hours and collected, Identical by IR, TLC, m.p. to authentic sample of 3-(4-methylphenyl)sydnone (**44**) previously prepared in our lab, 0.0341 g, 0.00019 mol, 87.5%, mp of 141-143^{o}C.

IR (KBr): 1730.3 (C=O), 3139.9 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.6 (dd, 2H), 7.4 (dd, 2H), 6.7 (s, 1H), 2.5 (s, 3H) ppm.

Reaction of 3-(4-chloro-2-iodophenyl)sydnone (**39**) with $NaBH_4$

To a stirred solution of 3-(4-chloro-2-iodophenyl)sydnone (**39**) (0.0501 g, 0.00015 mol) in MeOH (2 mL) was added $NaBH_4$ (0.0535 g, 0.0014 mol) slowly over a period of about 10 minutes. After complete addition of $NaBH_4$, the reaction was left stirring for 30 minutes, at which point TLC indicated complete conversion of starting material. Volume of MeOH was reduced, leaving behind a solid. Solid transferred to vacuum funnel using

DI water (2 mL), dried for 16 hours and collected, identical by IR, TLC, m.p. to authentic sample of 3-(4-chlorophenyl)sydnone (**45**) previously prepared in our lab, 0.0251 g, 0.00013 mol, 82.3%, mp of 108-110^{o}C.

IR (KBr): 1734.7 (C=O), 3121.6 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.7 (dd, 2H), 7.65 (dd, 2H), 6.75 (s, 1H) ppm.

Reaction of 3-(4-methoxy-2-iodophenyl)sydnone (**40**) with $NaBH_4$

To a stirred solution of 3-(4-methoxy-2-iodophenyl)sydnone (**40**) (0.0200 g, 0.00010 mol) in MeOH (3 mL) was added $NaBH_4$ (0.0206 g, 0.0007 mol) slowly over a period of about 5 minutes. After complete addition of $NaBH_4$, the reaction was left stirring for 15 minutes, at which point TLC indicated complete conversion of starting material. Volume of MeOH was reduced, leaving behind a solid. Solid transferred to vacuum funnel using DI water (2 mL), dried for one hour and collected, dentical by IR, TLC, m.p. to authentic sample of 3-(4-methoxyphenyl)sydnone (**46**) previously prepared in our lab, 0.0171 g, 0.000089 mol, 88.0%, mp of 123-125^{o}C.

IR (KBr): 1753.1 (C=O), 3151.1 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.7 (dd, 2H), 7.1 (dd, 2H), 6.7 (s, 1H), 3.9 (s, 3H) ppm.

Reaction of 3-(3-methoxy-2-iodophenyl)sydnone (**41**) with $NaBH_4$

To a stirred solution of 3-(3-methoxy-2-iodophenyl)sydnone (**41**) (0.0100 g, 0.000031 mol) in MeOH (2 mL) was added $NaBH_4$ (0.0140 g, 0.00024 mol) slowly over a period of about 5 minutes. After complete addition of $NaBH_4$, the reaction was left stirring for 20 minutes, at which point TLC indicated complete conversion of starting material. Volume of MeOH was reduced, leaving behind a solid. Solid transferred to vacuum funnel using DI water (2 mL), dried for 30 minutes and collected, identical by IR, TLC, m.p. to authentic sample of 3-(3-methoxyphenyl)sydnone (**47**) previously prepared in our lab, 0.0040 g, 0.000021 mol, 66.8%, mp of 134-135^oC.

IR (KBr): 1761.8 (C=O), 3143.0 (C-H) cm^{-1}.

^1H-NMR ($CDCl_3$): 7.5 (td, 1H), 7.3 (m, 2H), 7.2 (dd, 1H), 6.7 (s, 1H), 3.9 (s, 3H) ppm.

Reaction of 3-(3,5-dimethoxy-2-iodophenyl)sydnone (**42**) with $NaBH_4$

To a stirred solution of 3-(3,5-dimethoxy-2-iodophenyl)sydnone (**42**) (0.0059 g, 0.000017 mol) in MeOH (2 mL) was added $NaBH_4$ (0.0061 g, 0.00015 mol) slowly over a period of about 5 minutes. After complete addition of $NaBH_4$, the reaction was left stirring for 30 minutes, at which point TLC indicated complete conversion of starting

material. Volume of MeOH was reduced, leaving behind a solid. Solid transferred to vacuum funnel DI water (2 mL), dried for 16 hours and collected, identical by IR, TLC, m.p. to authentic sample of 3-(3,5-dimethoxyphenyl)sydnone (**48**) previously prepared in our lab, 0.0029 g, 0.000013 mol, 77.2%, mp of 164-165^{o}C.

IR (KBr): 1735.6 (C=O), 3144.6 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 6.8 (m, 2H), 6.7 (s, 1H), 6.6 (t, 1H), 3.9 (s, 6H) ppm.

V. Reaction of 4-iodo-3-(2-iodoaryl)sydnones with ICl

Reaction of 4-iodo-3-(2-iodophenyl)sydnone (**31**) with ICl

To a stirred solution of 4-iodo-3-(2-iodophenyl)sydnone (**31**) (0.1073 g, 0.00026 mol) and NaOAc (0.0654 g, 0.00077 mol) in anhydrous DCM (6 mL) at room temperature was added ICl (1.0M in DCM, 0.7700 mL, 0.00077 mol) slowly via syringe. The mixture was allowed to react for 30 minutes at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 2% aqueous Na_2SO_3 (30 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to of 2% aqueous $NaHCO_3$ (30 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with

$MgSO_4$ and concentrated under vacuum to yield a white solid. Immediate recrystallization from 95% ethanol yielded a white solid. Identical by m.p., TLC and IR to authentic sample of 4-chloro-3-(2-iodophenyl)sydnone (**49**) previously prepared in our lab, 0.0600 g, 0.00018 mol, 71.4%, m.p. 101-102^{o}C.

IR (KBr): 1773.1 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 8.1 (d, 1H), 7.65 (td, 1H), 7.4-7.5 (m, 2H) ppm.

^{13}C-NMR ($CDCl_3$): 163.7 (C=O), 140.8, 135.8, 134.0, 129.8, 127.5, 99.9, 93.4 ppm.

Reaction of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone (**34**) with ICl

To a stirred solution of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone (**34**) (0.0838 g, 0.00019 mol) and NaOAc (0.0518 g, 0.00019 mol) in anhydrous DCM (10 mL) at room temperature was added ICl (1.0M in DCM, 0.5800 mL, 0.00058 mol) slowly via syringe. The mixture was allowed to react for 30 minutes at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 4% aqueous Na_2SO_3 (30 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 5% aqueous $NaHCO_3$ (30 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried

with $MgSO_4$ and concentrated under vacuum to yield a yellow oily solid. Immediate recrystallization from 95% ethanol yielded a white solid. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) and elemental analysis to be the title compound, 4-chloro-3-(4-methyl-2-iodophenyl)sydnone (**50**), 0.0423 g, 0.00012 mol, 68.4% yield, m.p. 128-129^{o}C.

IR (KBr): 1745.5 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.9 (m, 1H), 7.35 (m, 1H), 7.25 (d, 1H), 2.5 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 163.5 (C=O), 145.1, 141.1, 133.3, 130.5, 126.9, 100.6, 93.1, 21.0 ppm.

Elemental analysis calculated for $C_9H_6ClIN_2O_2$ (339.4): C: 32.12, H: 1.80, N: 8.32. Found C: 32.05, H: 1.90, N: 8.03.

Reaction of 4-iodo-3-(4-chloro-2-iodophenyl)sydnone (**35**) with ICl

To a stirred solution of 4-iodo-3-(4-chloro-2-iodophenyl)sydnone (**35**) (0.1111 g, 0.00025 mol) and NaOAc (0.0672 g, 0.00074 mol) in anhydrous DCM (5 mL) at room temperature was added ICl (1.0M in DCM, 0.7500 mL, 0.00075 mol) slowly via syringe. The mixture was allowed to react for 30 minutes at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 2% aqueous Na_2SO_3 (30 mL) and stirred until mixture turned completely

from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 2% aqueous $NaHCO_3$ (30 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to yield a yellow oily solid. Immediate recrystallization from 95% ethanol yielded a white solid. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) and elemental analysis to be title compound, 4-chloro-3-(4-chloro-2-iodophenyl)sydnone (**51**), 0.0609 g, 0.00017 mol, 68.8% yield, m.p. 163-164^{o}C.

IR (KBr): 1740.0 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 8.1 (d, 1H), 7.65 (dd, 1H), 7.45 (d, 1H) ppm.

^{13}C-NMR ($CDCl_3$): 163.5 (C=O), 140.3, 139.8, 134.3, 130.2, 128.1, 99.9, 94.0 ppm.

Elemental analysis calculated for $C_8H_3Cl_2IN_2O_2$ (359.9): C: 26.92, H: 0.85, N: 7.85. Found: C: 26.94, H: 0.87, N: 7.81.

Reaction of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone (**32**) with ICl

To a stirred solution of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone (**32**) (0.0988 g, 0.00022 mol) and NaOAc (0.0562 g, 0.00066 mol) in anhydrous DCM (10 mL) at room temperature was added ICl (1.0M in DCM, 0.6600 mL, 0.00066 mol) slowly via syringe. The mixture was allowed to react for 30 minutes at which point TLC showed complete

conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 2% aqueous Na_2SO_3 (30 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 2% aqueous $NaHCO_3$ (30 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to yield a yellow oily solid. Immediate recrystallization from 80% ethanol yielded a white solid. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) and elemental analysis to be title compound 4-chloro-3-(4-methoxy-2-iodophenyl)sydnone (**52**), 0.0559 g, 0.00016 mol, 71.5% yield, m.p. 111-112^{o}C.

IR (KBr): 1766.5 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.55 (d, 1H), 7.4 (d, 1H), 7.1 (dd, 1H), 3.9 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 163.8 (C=O), 162.5, 128.4, 127.9, 125.7, 115.2, 99.9, 93.9, 56.2 ppm.

Elemental analysis calculated for $C_9H_6ClIN_2O_3$ (355.5): C: 30.66, H: 1.72, N: 7.95. Found C: 30.54, H: 1.69, N: 7.70.

Reaction of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone (**33**) with ICl

To a stirred solution of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone (**33**) (0.0806 g, 0.00018 mol) and NaOAc (0.0442 g, 0.00054 mol) in anhydrous DCM (8 mL) at room temperature was added ICl (1.0M in DCM, 0.5400 mL, 0.00054 mol) slowly via syringe. The mixture was allowed to react for 30 minutes at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 2% aqueous Na_2SO_3 (30 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 2% aqueous $NaHCO_3$ (30 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to yield a yellow solid. Immediate recrystallization from 80% ethanol yielded a white solid. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) and elemental analysis to be title compound, 4-chloro-3-(3-methoxy-2-iodophenyl)sydnone (**53**), 0.0487 g, 0.00014 mol, 76.1% yield, m.p. 107-108^{o}C.

IR (KBr): 1744.9 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.6 (t, 1H), 7.05-7.15 (m, 2H), 4.0 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 163.8 (C=O), 160.2, 137.1, 130.8, 119.3, 114.1, 99.9, 86.8, 57.2 ppm.

Elemental analysis calculated for $C_9H_6ClIN_2O_3 \cdot 1/5\ H_2O$ (355.5):C: 31.21, H: 2.01, N: 7.74. Found: C: 31.39, H: 2.21, N: 7.51.

Reaction of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**36**) with ICl

To a stirred solution of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**36**) (0.0438 g, 0.000092 mol) and NaOAc (0.0441 g, 0.00054 mol) in anhydrous DCM (5 mL) at room temperature was added ICl (1.0M in DCM, 0.4000 mL, 0.00040 mol) slowly via syringe. The mixture was allowed to react for 30 minutes at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 5% aqueous Na_2SO_3 (5 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 5% aqueous $NaHCO_3$ (50 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to yield a tan oily solid. Immediate recrystallization from 80% ethanol yielded a white solid. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) and elemental analysis to be title compound, 4-chloro-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**54**), 0.0276 g, 0.000072 mol, 79.3% yield, m.p. 217-218^{o}C.

IR (KBr): 1758.4 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 6.7 (d, 1H), 6.6 (d, 1H), 4.0 (s, 3H), 3.9 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 163.7 (C=O), 161.9, 160.6, 137.1, 104.3, 101.9, 99.9, 75.8, 57.0, 56.2 ppm.

Elemental analysis calculated for $C_{10}H_8ClIN_2O_4$ (382.6): C: 31.40, H: 2.11, N: 7.32. Found: C: 31.11, H: 1.97, N: 7.13.

VI. Synthesis of 4-bromo-3-(2-bromoaryl)sydnones

Synthesis of 4-bromo-3-(3,5-dimethoxy-2-bromophenyl)sydnone (**55**) via Br_2 in ethanol

To a stirred solution of 3-(3,5-dimethoxyphenyl)sydnone (0.1145 g, 0.00051 mol) in ethanol (10 mL) was added $NaHCO_3$ (0.2082 g, 0.0025 mol in 5 mL H_2O), along with Br_2 (0.3326 g, 0.0021 mol in 5 mL ethanol). The mixture was allowed to react with constant stirring for 30 minutes, at which point TLC in DCM showed complete conversion of starting material into less polar material. At this point, H_2O (20 mL) was added to the reaction mixture and precipitation of solid occurred. The solid was dried via vacuum filtration and recrystallized from 95% ethanol to yield two crops of a white solid, which was identical by melting point, IR and TLC to an authentic sample of **55** previously prepared in our lab, 0.1185 g, 0.00031 mol, 60.4% yield, m.p. 201-202^{o}C.

IR (KBr): 1764.2 (C=O) cm^{-1}.

^{1}H-NMR (DMSO): 7.3 (d, 1H), 7.1 (d, 1H), 3.95 (s, 3H), 3.85 (s, 3H) ppm.

^{13}C-NMR (DMSO): 165.5 (C=O), 160.8, 157.9, 134.4, 106.1, 103.8, 99.6, 87.9, 57.7, 56.8 ppm.

Synthesis of 4-bromo-3-(2-bromophenyl)sydnone (**56**) via lithiation

To a stirred solution of 3-phenylsydnone (0.2396 g, 0.0015 mol) in dry THF (40 mL) under an atmosphere of nitrogen at -78^{o}C were added three equivalents of n-butyllithium (1.6 M in cyclohexane, 2.8 mL, 0.0044 mol). The solution was allowed to stir for 15 minutes at which point excess bromine (0.7031 g, 0.0044 mol) was added and the reaction was continued for two hours. Subsequently, the reaction was warmed to -10^{o}C and quenched with ice cold saturated brine solution (40 mL). The solution volume was reduced overnight with stirring to allow THF to evaporate completely. At this point the remaining mixture was transferred to a separatory funnel with DCM (30 mL). The organic layer was separated and washed with of 2% aqueous Na_2SO_3 (50 mL). The aqueous layer was extracted with DCM (3x10 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a dark brown oil. Silica column chromatography (DCM), followed by recrystallization from 95% ethanol yielded

the desired compound as a light orange solid identical (TLC, IR, m.p.) to an authentic sample of **56** previously made in our lab, 0.3076 g, 0.00096 mol, 63.8%, m.p. of 93-95^{o}C.

IR (KBr): 1766.1 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.9 (m, 1H), 7.65 (m, 2H), 7.5 (m, 1H) ppm.

^{13}C-NMR ($CDCl_3$): 165.3 (C=O), 134.4, 133.9, 133.2, 128.9, 127.9, 119.7, 86.2 ppm.

Synthesis of 4-bromo-3-(4-methyl-2-bromophenyl)sydnone (**57**) via lithiation

To a stirred solution of 3-(4-methylphenyl)sydnone (0.1535 g, 0.00087 mol) in dry THF (40 mL) under an atmosphere of nitrogen at -78^{o}C were added three equivalents of n-butyllithium (1.6 M in cyclohexane, 1.6 mL, 0.0026 mol). The solution was allowed to stir for 15 minutes at which point excess bromine (0.4148 g, 0.0026 mol) was added and the reaction was continued for two hours. Subsequently, the reaction was warmed to -10^{o}C and quenched with ice cold saturated brine solution (50 mL). The solution volume was reduced overnight with stirring to allow THF to evaporate completely. At this point the remaining mixture was transferred to a separatory funnel with DCM (30 mL). The organic layer was separated and washed with of 2% aqueous Na_2SO_3 (50 mL). The aqueous layer was extracted with DCM (3x20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a dark orange oil. Silica

column chromatography, followed by recrystallization from 95% ethanol yielded the title compound as a white solid, 0.0812 g, 0.00024 mol, 27.9%, m.p. 129-130^{o}C.

IR (KBr): 1781.9 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.7 (d, 1H), 7.4 (m, 2H), 2.5 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 165.4 (C=O), 145.3, 134.7, 130.6, 129.6, 127.5, 119.1, 86.3, 21.3 ppm.

Elemental analysis calculated for $C_9H_6Br_2N_2O_2$ (337.0): C: 32.37, H: 1.81, N: 8.39. Found: C: 32.31, H: 1.69, N: 8.20.

Synthesis of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone (**58**) via lithiation

To a stirred solution of 3-(4-chlorophenyl)sydnone (0.3709 g, 0.0019 mol) in dry THF (40 mL) under an atmosphere of nitrogen at -78^{o}C was added excess n-butyllithium (1.6 M in cyclohexane, 4.75 mL, 0.0076 mol). The solution was allowed to stir for 20 minutes at which point excess bromine (1.3408 g, 0.0079 mol) was added and the reaction was continued for two hours. Subsequently, the reaction was warmed to -10^{o}C and quenched with ice cold saturated brine solution (50 mL). The solution volume was reduced overnight with stirring to allow THF to evaporate completely. At this point the remaining mixture was transferred to a separatory funnel with DCM (30 mL). The organic layer was separated and washed with of 2% aqueous Na_2SO_3 (50 mL). The

aqueous layer was extracted with DCM (3x20 mL), and the combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a dark orange oil. Silica column chromatography, followed by recrystallization from 95% ethanol yielded the title compound as a white solid, 0.1368 g, 0.00038 mol, 20.3%, m.p. 101-102^oC.

IR (KBr): 1768.1 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.9 (dd, 1H), 7.65 (dd, 1H), 7.5 (d, 1H) ppm.

^{13}C-NMR ($CDCl_3$): 165.1 (C=O), 140.0, 134.2, 131.6, 129.4, 128.8, 120.5, 86.4 ppm.

Elemental analysis calculated for $C_8H_3Br_2ClN_2O_2$ (357.9): C: 27.11, H: 0.85, N: 7.90. Found: C: 27.09, H: 0.95, N: 7.80.

VII. Reaction of 4-bromo-3-(2-bromoaryl)sydnones with Na_2SO_3

Reaction of 4-bromo-3-(3,5-dimethoxy-2-bromophenyl)sydnone (**55**) with Na_2SO_3

To a stirred solution of 4-bromo-3-(3,5-dimethoxy-2-bromophenyl)sydnone (0.0121 g, 0.000032 mol) in methanol (2 mL) was added Na_2SO_3 (0.0161 g, 0.00013 mol in 2 mL H_2O). The mixture was allowed to react for 20 minutes at which point TLC in DCM showed complete conversion of starting material to a more polar product. The volume was reduced until all methanol was presumed gone, and the aqueous layer was

extracted with DCM (3x2 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a light yellow solid, which was identical by melting point, IR and TLC to an authentic sample of **59** previously prepared in our lab, 0.0087 g, 0.000029 mol, 90.9% yield, m.p. 161-162^oC.

IR (KBr): 1763.7 (C=O), 3160.7 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 6.55 (m, 1H), 6.5 (m, 1H), 6.5 (s, 1H), 4.0 (s, 3H), 3.9 (s, 3H) ppm.

Reaction of 4-bromo-3-(2-bromophenyl)sydnone (**56**) with Na_2SO_3

To a stirred solution of 4-bromo-3-(2-bromophenyl)sydnone (0.0201 g, 0.000062 mol) in methanol (2 mL) was added Na_2SO_3 (0.0312 g, 0.00025 mol in 2 mL H_2O). The mixture was allowed to react for 15 minutes at which point TLC in DCM showed complete conversion of starting material to a more polar product. The volume was reduced until all methanol was presumed gone, and the aqueous layer was extracted with DCM (3x2 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield an off white solid, which was identical by melting point, IR and TLC to an authentic sample of **60** previously prepared in our lab, 0.0092 g, 0.000038 mol, 61.3% yield, m.p. 78-79^oC.

IR (KBr): 1773.5 (C=O), 3158.8 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.85 (m, 1H), 7.6 (m, 3H), 6.6 (s, 1H) ppm.

Reaction of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone (**58**) with Na_2SO_3

To a stirred solution of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone (0.0538 g, 0.00015 mol) in methanol (5 mL) was added Na_2SO_3 (0.0808 g, 0.00060 mol in 5 mL H_2O). The mixture was allowed to react for 20 minutes at which point TLC in DCM showed complete conversion of starting material to a more polar product. The volume was reduced until all methanol was presumed gone, and the aqueous layer was extracted with DCM (3x2 mL). The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo to yield a white solid, which was recrystallized from 95% ethanol. Confirmed by ^{1}H and ^{13}C NMR (Appendix A) to be 3-(4-chloro-2-bromophenyl)sydnone (**61**), 0.0318 g, 0.00011 mol, 76.3% yield, m.p. 131-132^{o}C.

IR (KBr): 1734.5 (C=O), 3135.7 (C-H) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.85 (d, 1H), 7.85 (m, 2H), 6.65 (s, 1H) ppm.

^{13}C-NMR ($CDCl_3$): 168.3 (C=O), 139.5, 134.4, 129.3, 128.1, 118.9, 97.9 ppm.

VIII. Reaction of 3-(2-bromoaryl)sydnones with $NaBH_4$

Reaction of 3-(3,5-dimethoxy-2-bromophenyl)sydnone (**59**) with $NaBH_4$

To a stirred solution of 3-(3,5-dimethoxy-2-bromophenyl)synone (0.0087 g, 0.000029 mol) in methanol (2 mL) was added $NaBH_4$ (0.0101 g) over a period of about 5 minutes. After 30 minutes, TLC in DCM showed no conversion of starting material, so the mixture was left to react overnight, and TLC in DCM still showed no conversion of starting material. The methanol was allowed to evaporate and H_2O (2 mL) was used to transfer solid to a vacuum funnel where is was dried for 20 minutes. The solid was identical by melting point and TLC to an authentic sample of **59**, thus it was determined that no reaction had occurred. The solid melted from 158-160^oC and weighed 0.0078g, 0.000025 mol, 87.4% recovery of starting material.

Reaction of 3-(2-bromophenyl)sydnone (**60**) with $NaBH_4$

To a stirred solution of 3-(2-bromophenyl)synone (0.0376 g, 0.00012 mol) in methanol (2 mL) was added $NaBH_4$ (0.0408 g) over a period of about 5 minutes. After 30 minutes, TLC in DCM showed no conversion of starting material, so the mixture was left to react overnight, and TLC in DCM still showed no conversion of starting material. The methanol was allowed to evaporate and H_2O (2 mL) was used to transfer solid to a vacuum funnel where is was dried for 20 minutes. The solid was identical by melting point and TLC to an authentic sample of **60**, thus it was determined that no reaction had occurred. The

solid melted from 76-78°C and weighed 0.0175 g, 0.000072 mol, 60.3% recovery of starting material.

Reaction of 3-(4-chloro-2-bromophenyl)sydnone (**61**) with $NaBH_4$

To a stirred solution of 3-(4-chloro-2-bromophenyl)synone (0.0158 g, 0.000057 mol) in methanol (2 mL) was added $NaBH_4$ (0.0163 g) over a period of about 5 minutes. After 30 minutes, TLC in DCM showed no conversion of starting material, so the mixture was left to react overnight, and TLC in DCM still showed no conversion of starting material. The methanol was allowed to evaporate and H_2O (2 mL) was used to transfer solid to a vacuum funnel where is was dried for 20 minutes. The solid was identical by melting point and TLC to an authentic sample of **61**, thus it was determined that no reaction had occurred. The solid melted from 131-132°C and weighed 0.0125 g, 0.000045 mol, 79.1% recovery of starting material.

IX. Reaction of 4-bromo-3-(2-bromoaryl)sydnones with ICl

Reaction of 4-bromo-3-(3,5-dimethoxy-2-bromophenyl)sydnone (**55**) with ICl

To a stirred solution of 4-bromo-3-(3,5-dimethoxy-2-bromophenyl)sydnone (0.0320 g, 0.000083 mol) and NaOAc (0.0205 g, 0.00025 mol) in anhydrous DCM (5 mL) at room

temperature was added ICl (1.0M in DCM, 0.25 mL, 0.00025 mol) slowly via syringe. The mixture was allowed to react for one hour at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 2% aqueous Na_2SO_3 (50 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 2% aqueous $NaHCO_3$ (50 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to yield a yellow oily solid. Immediate recrystallization from 80% ethanol yielded a white solid. The solid was identical by melting point, TLC and IR to authentic sample of **62** previously prepared in our lab. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) to be 4-chloro-3-(3,5-dimethoxy-2-bromophenyl)sydnone (**62**), 0.0127 g, 0.000037 mol, 45.1% yield, m.p. 188-190^{o}C.

IR (KBr): 1769.4 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 6.75 (d, 1H), 6.65 (d, 1H), 4.0 (s, 3H), 3.9 (s, 3H) ppm.

^{13}C-NMR ($CDCl_3$): 163.6 (C=O), 160.5, 158.1, 133.4, 103.9, 103.1, 100.7, 99.9, 56.9, 56.2 ppm.

Reaction of 4-bromo-3-(2-bromophenyl)sydnone (**56**) with ICl

To a stirred solution of 4-bromo-3-(2-bromophenyl)sydnone (0.0737 g, 0.00023 mol) and NaOAc (0.0566 g, 0.00069 mol) in anhydrous DCM (8 mL) at room temperature was added ICl (1.0M in DCM, 0.69 mL, 0.00069 mol) slowly via syringe. The mixture was allowed to react for four hours at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 2% aqueous Na_2SO_3 (50 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 5% aqueous $NaHCO_3$ (50 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to yield a yellow oily solid. Immediate recrystallization from 95% ethanol yielded a white solid. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) and elemental analysis to be title compound 4-chloro-3-(2-bromophenyl)sydnone (**63**), 0.0406 g, 0.00015 mol, 63.6% yield, m.p. 89-90^{o}C.

IR (KBr): 1773.8 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.9 (m, 1H), 7.65 (m, 2H), 7.55 (m, 1H) ppm.

^{13}C-NMR ($CDCl_3$): 163.5 (C=O), 134.5, 134.1, 132.2, 129.0, 127.9, 119.6, 107.9 ppm.

Elemental analysis calculated for $C_8H_4BrClN_2O_2$ (277.5): C: 34.88, H: 1.46, N: 10.17. Found: C: 35.08, H: 1.58, N: 9.89.

Reaction of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone (**58**) with ICl

To a stirred solution of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone (0.0503 g, 0.00014 mol) and NaOAc (0.0370 g, 0.00042 mol) in anhydrous DCM (5 mL) at room temperature was added ICl (1.0M in DCM, 0.42 mL, 0.00042 mol) slowly via syringe. The mixture was allowed to react for one hour at which point TLC showed complete conversion of starting material into a higher running product. The reaction mixture was then poured slowly into 2% aqueous Na_2SO_3 (50 mL) and stirred until mixture turned completely from dark purple to pale yellow. This mixture was extracted with DCM (3x10 mL) and combined organic layers were transferred to 5% aqueous $NaHCO_3$ (50 mL). Mixture extracted again with DCM (3x10mL), then combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to yield a brown oil. Immediate recrystallization from DCM/Hexanes yielded a white solid. Confirmed by ^{13}C and ^{1}H NMR, as well as IR (Appendix A) and elemental analysis to be title compound 4-chloro-3-(4-chloro-2-bromophenyl)sydnone (**64**), 0.0171 g, 0.000055 mol, 34.2% yield, m.p. 110-111°C.

IR (KBr): 1743.9 (C=O) cm^{-1}.

^{1}H-NMR ($CDCl_3$): 7.9 (d, 1H), 7.6 (dd, 1H), 7.5 (d, 1H) ppm.

^{13}C-NMR ($CDCl_3$): 163.3 (C=O), 140.2, 134.3, 130.7, 129.4, 128.7, 120.5, 99.8 ppm.

Elemental analysis calculated for $C_8H_3BrCl_2N_2O_2$ (312.9): C: 31.00, H: 0.98, N: 9.04.

Found: C: 31.12, H: 1.01, N: 8.94.

References

[1] Earl, J. C., Mackney, A. W. *J. Chem. Soc*., 899 (1935).

[2] Baker,W, Ollis, D.W., Poole, V.D., *J. Chem. Soc*., 307 (1949).

[3] Baker,W, Ollis, D.W., Poole, V.D., *Nature*, **158**, 703 (1946).

[4] Baker,W, Ollis, D.W., Poole, V.D., *Chem. Ind*. (London), 910 (1955).

[5] Applegate, J., Turnbull, K., *Synthesis*, 1011 (1988).

[6] Turnbull, K., *J. Heterocycl. Chem.*, **22**, 965 (1985).

[7] Fuchigami, T., Chen, C.S., Nonaka, T., Yeh, M.Y., Tien, H.J., *Bull. Chem. Soc. Jpn.* ,**59**, 483 (1986).

[8] Fuchigami, T., Chen, C.S., Nonaka, T., Yeh, M.Y., Tien, H.J., *Bull. Chem. Soc. Jpn.* **59**, 487 (1986).

[9] Huisgen, R., Gotthardt, H., Grashley, R., *Angew. Chem. Int. Ed. Engl.*, **1**, 48, (1962).

[10] Turnbull, K., Krein, D.M, *Tetrahedron Lett.,* **38**, 1165 (1997).

[11] Tien, H., Fang, G.M., Lin, S.T., Tien, L.L., J. *Chin. Chem. Soc.,* **39**, 443 (1992).

[12] Dumitrascu, F., Draghici, C., Dumitrescu, D., Tarko, L. , Raileanu, D., *Liebigs Ann.,* 2613 (1997).

[13] Dumitrascu, F., Mitan, C., Caprioui, M.T., Draghici, C., Dumitrescu, D., *Arkivoc, **2**, 80* (2002).

[14] Stewart, F. H. C., *Chem. Rev.,* **64**, 129 (1964).

[15] Browne, D.L., Harrity, J.P., Tetrahedron, **66**, 553 (2010).

[16] Brown, D. C., Turnbull, K., *Synth. Commun.*, **43**, 3233 (2013).

[17] Chitiyo, N.N, Dossa, A.Y., Jackson, C.M., Sun, L., Turnbull, K., *Org. Prep. Proced. Int.*, **48**, 405 (2016).

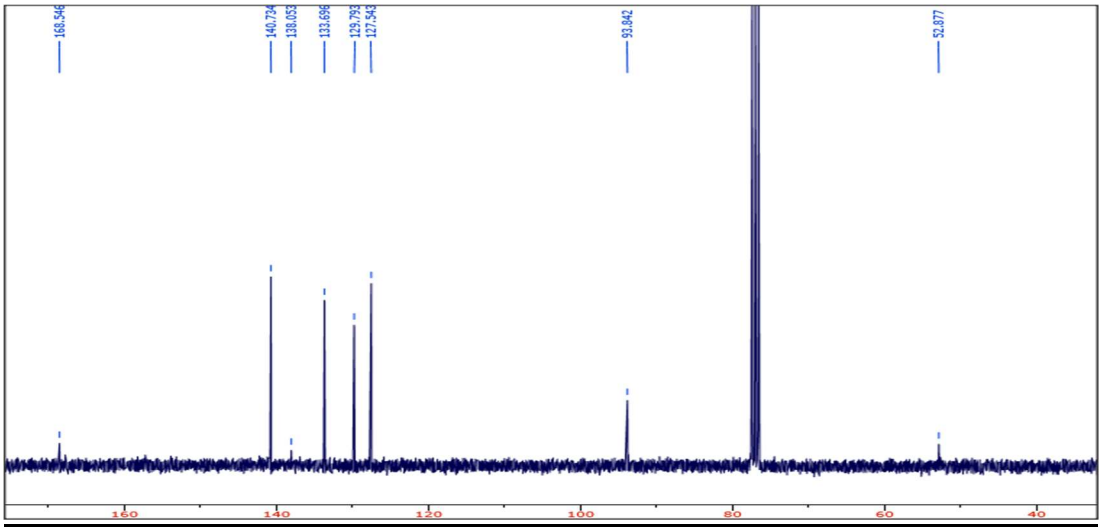
[18] Nashishibi, I., Master's Thesis, "Preparation and Reactions of Halogeno Sydnones", Wright State University (2000).

[19] Nashashibi, I.F., Tumey, J.M., Owens, B.L., Turnbull, K., *Org. Prep. Proced. Int.,* **49**, 59 (2016).

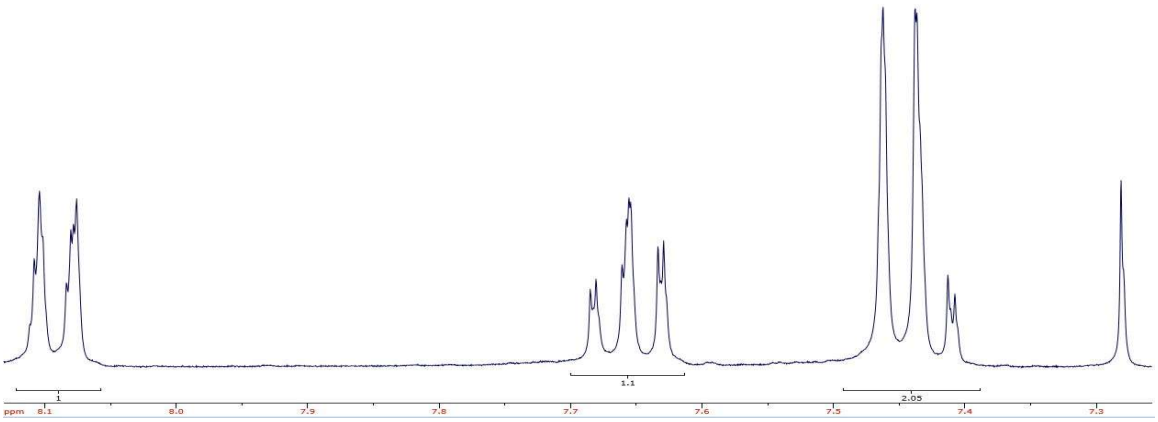
Appendix A

I. 4-iodo-3-(2-iodoaryl)sydnone spectra

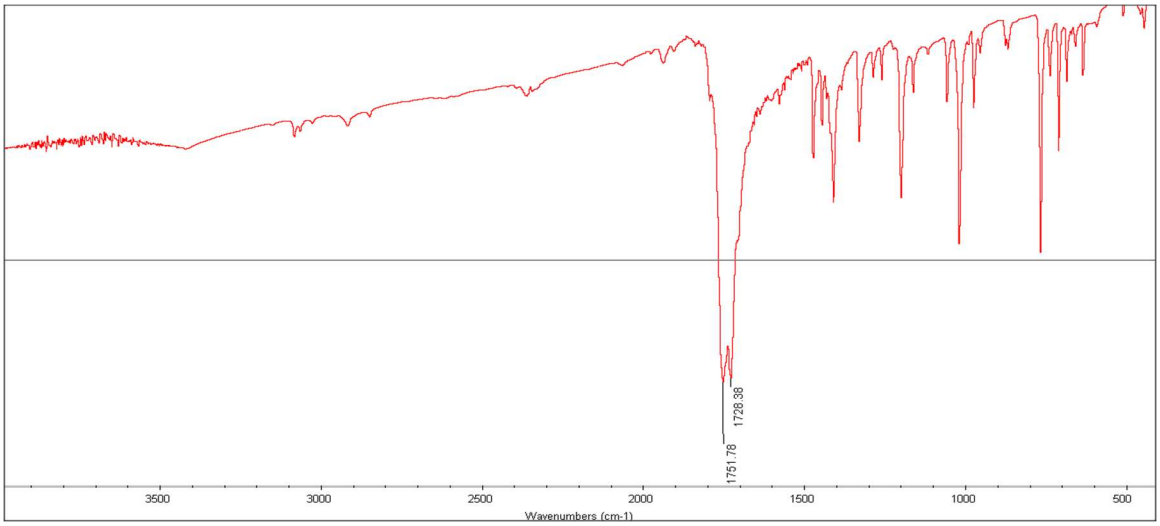
4-iodo-3-(2-iodophenyl)sydnone (**31**)



Spectrum 1 - ^{13}C NMR of 4-iodo-3-(2-iodophenyl)sydnone

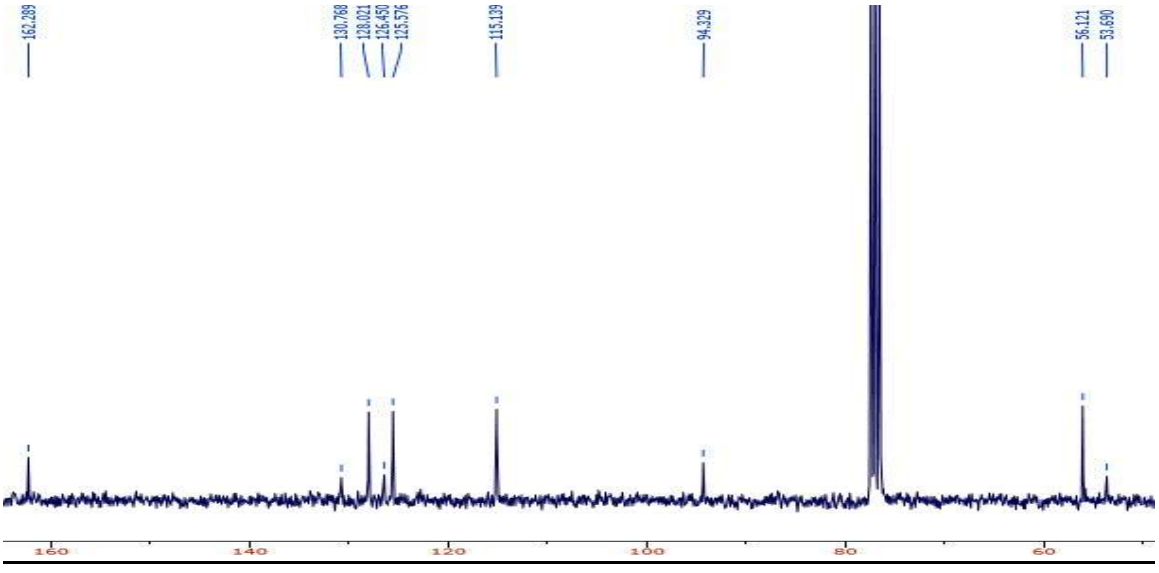


Spectrum 2 - ^{1}H NMR of 4-iodo-3-(2-iodophenyl)sydnone

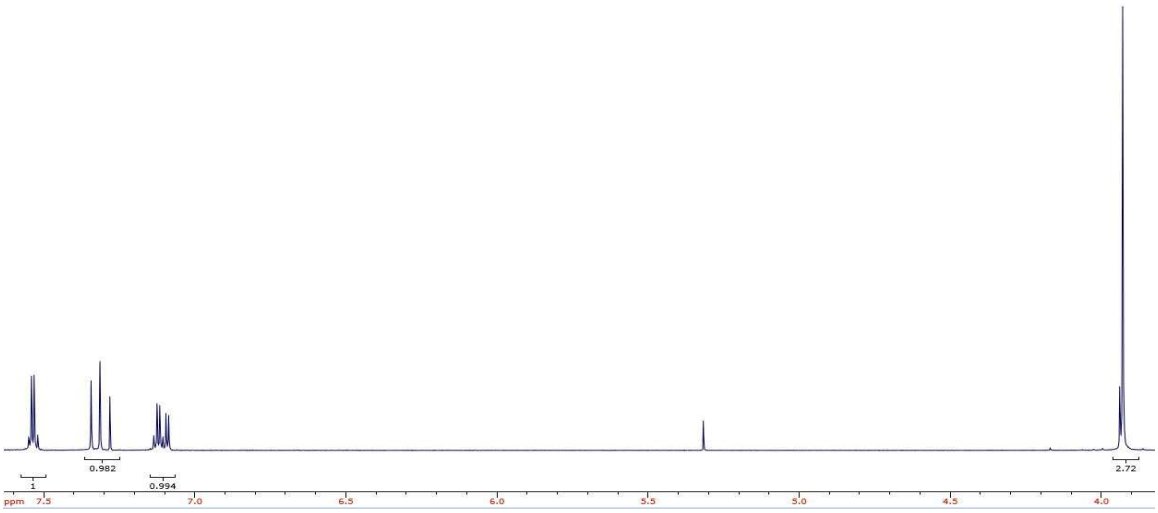


Spectrum 3 - IR (KBr) of 4-iodo-3-(2-iodophenyll)sydnone

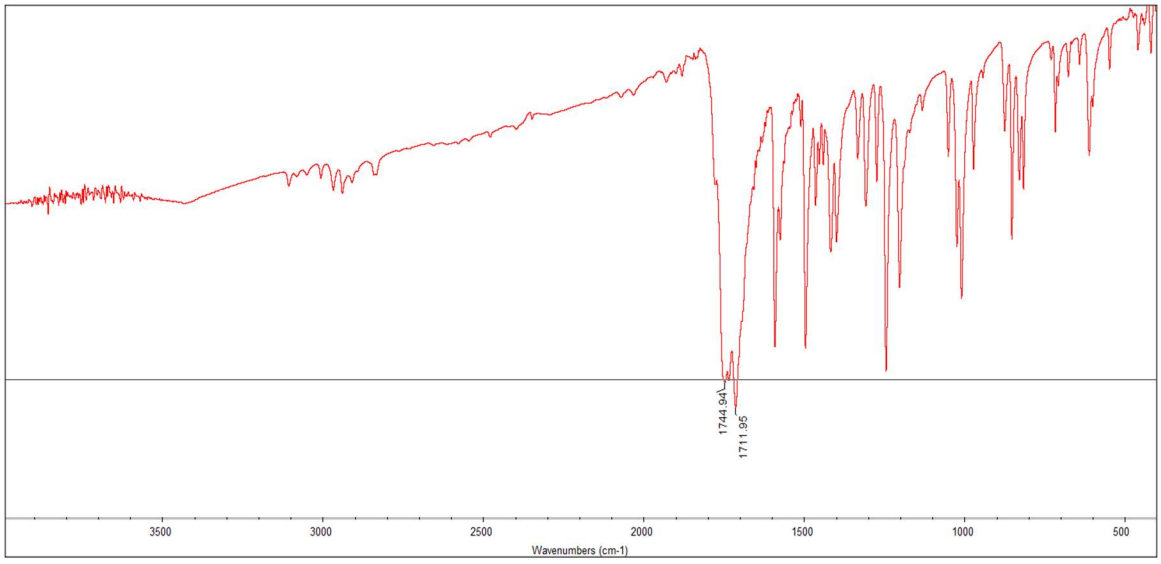
4-iodo-3-(4-methoxy-2-iodophenyl)sydnone (**32**)



Spectrum 4 - ^{13}C NMR of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone

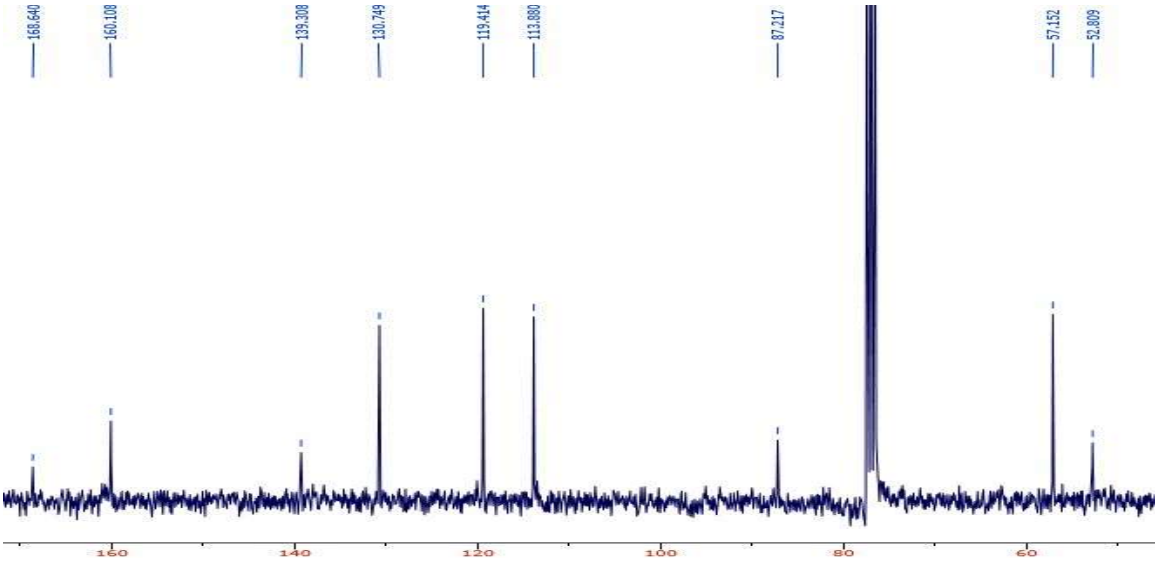


Spectrum 5 - ^{1}H NMR of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone

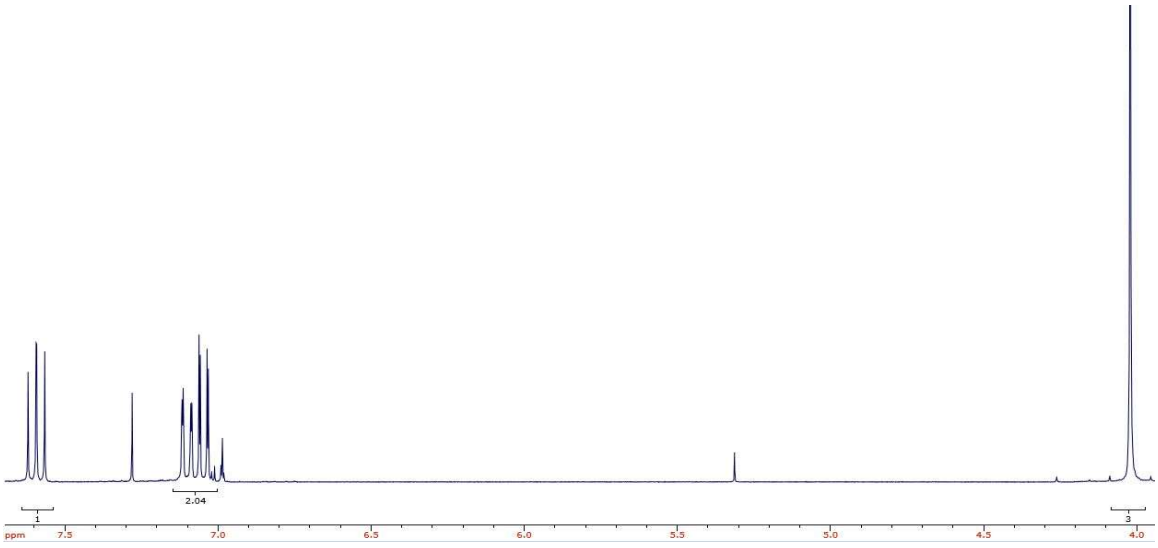


Spectrum 6 - IR (KBr) of 4-iodo-3-(4-methoxy-2-iodophenyl)sydnone

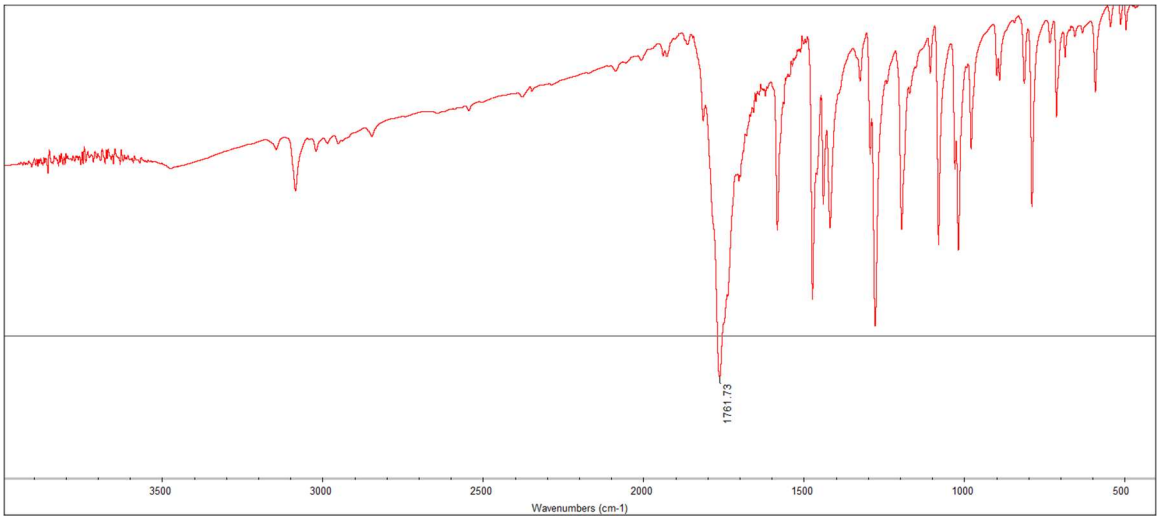
4-iodo-3-(3-methoxy-2-iodophenyl)sydnone (**33**)



Spectrum 7 - ^{13}C NMR of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone

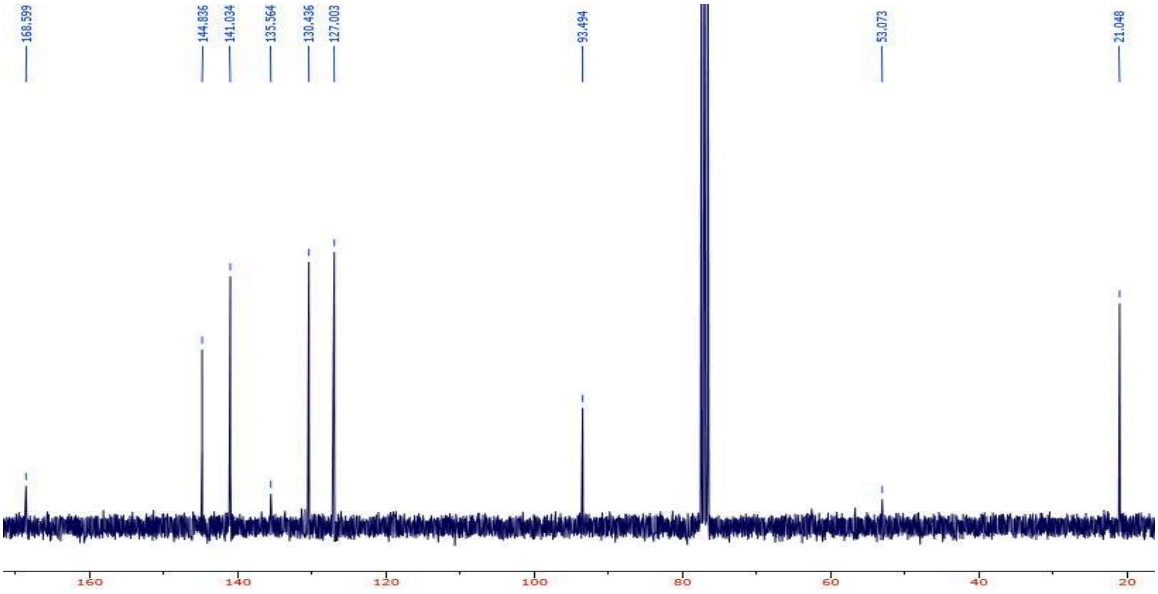


Spectrum 8 - ^{1}H NMR of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone

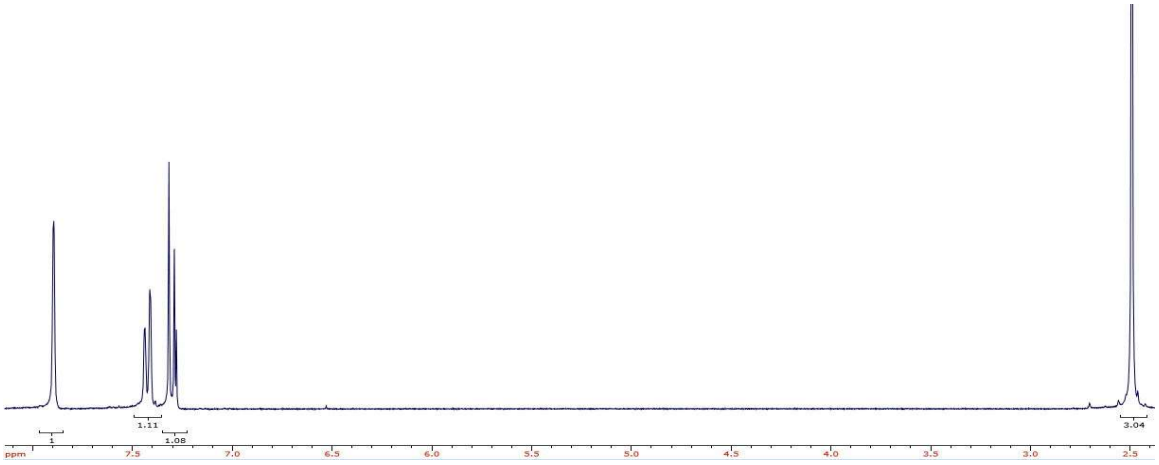


Spectrum 9 - IR (KBr) of 4-iodo-3-(3-methoxy-2-iodophenyl)sydnone

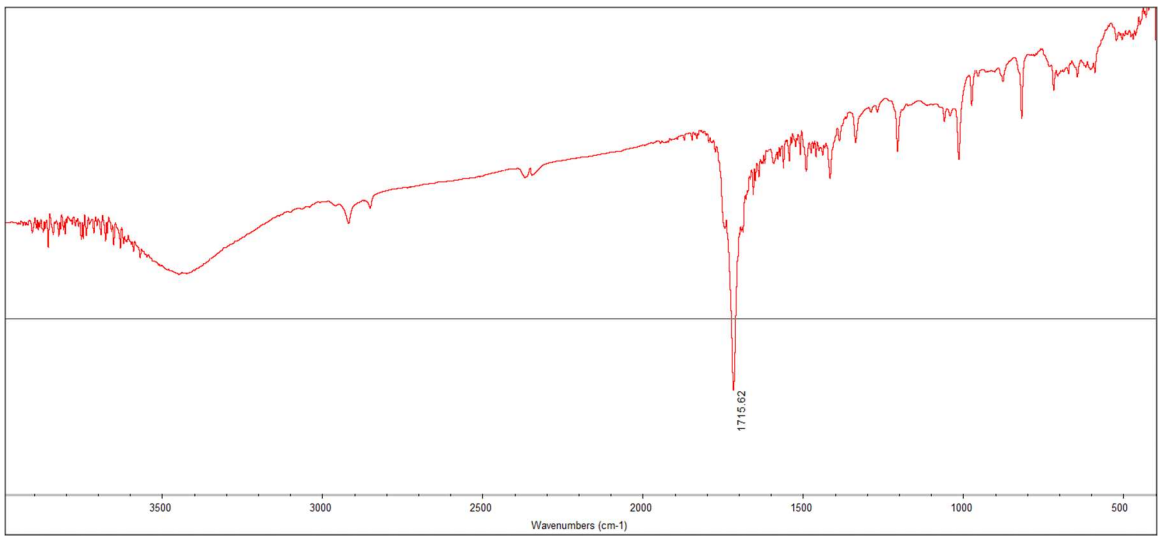
4-iodo-3-(4-methyl-2-iodophenyl)sydnone (**34**)



Spectrum 10 - ^{13}C NMR of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone

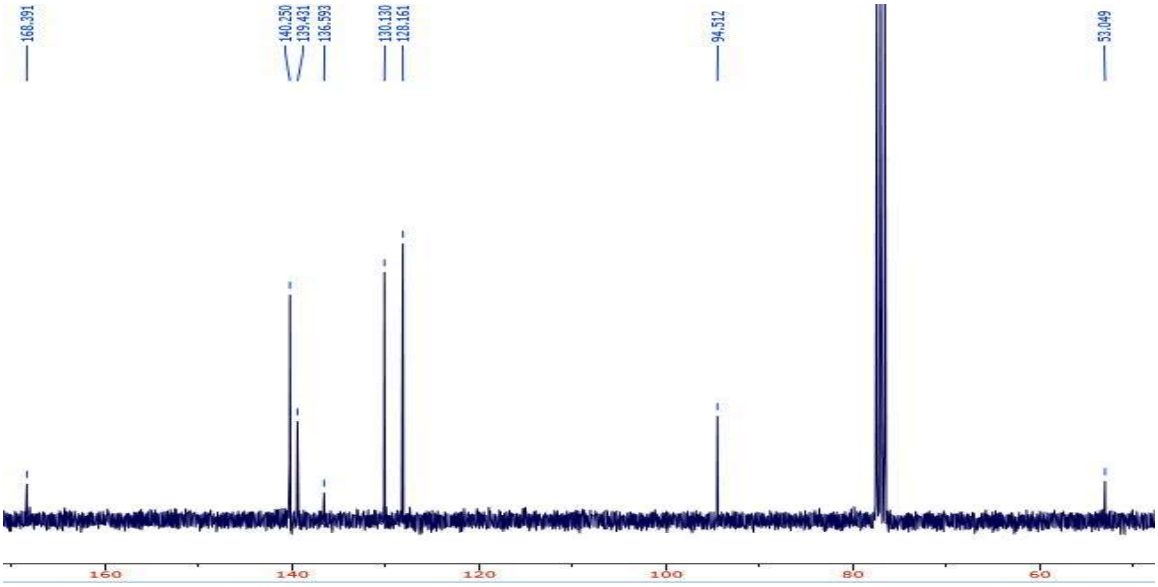


Spectrum 11 - ^{1}H NMR of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone

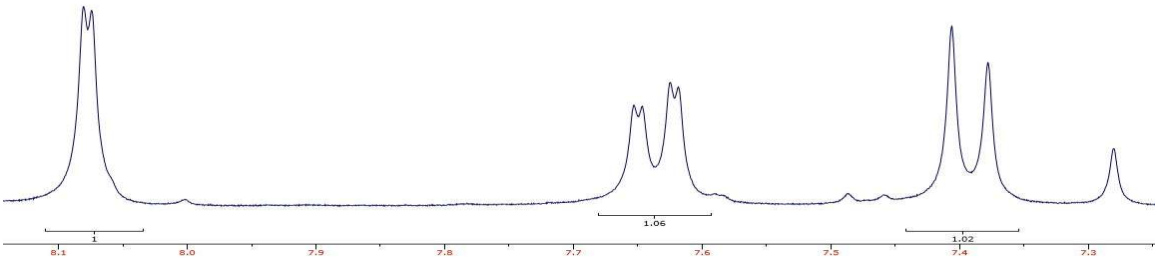


Spectrum 12 – IR (KBr) of 4-iodo-3-(4-methyl-2-iodophenyl)sydnone

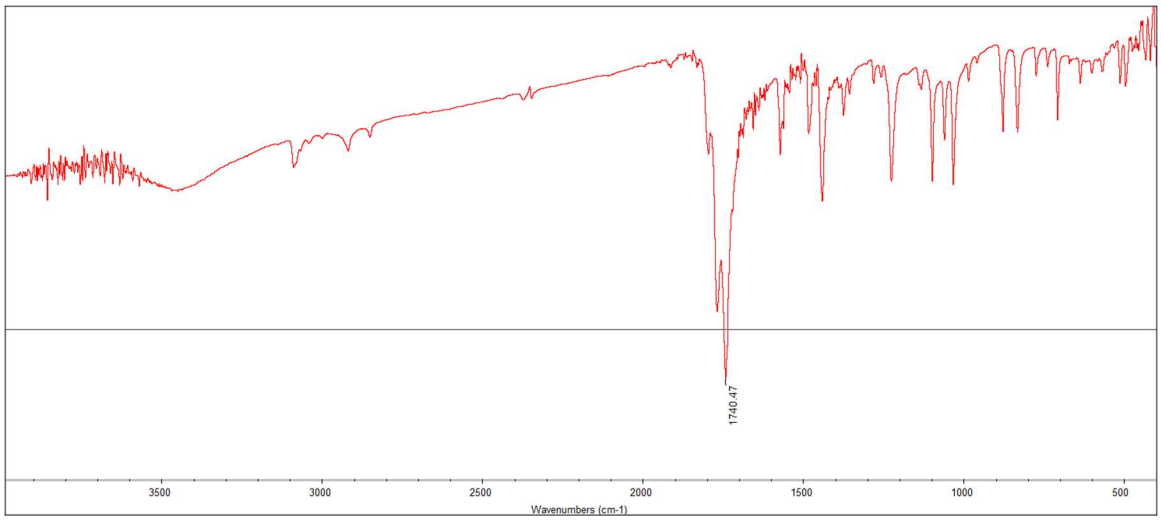
4-iodo-3-(4-chloro-2-iodophenyl)sydnone (**35**)



Spectrum 13 - ^{13}C NMR of 4-iodo-3-(4-chloro-2-iodophenyl)sydnone

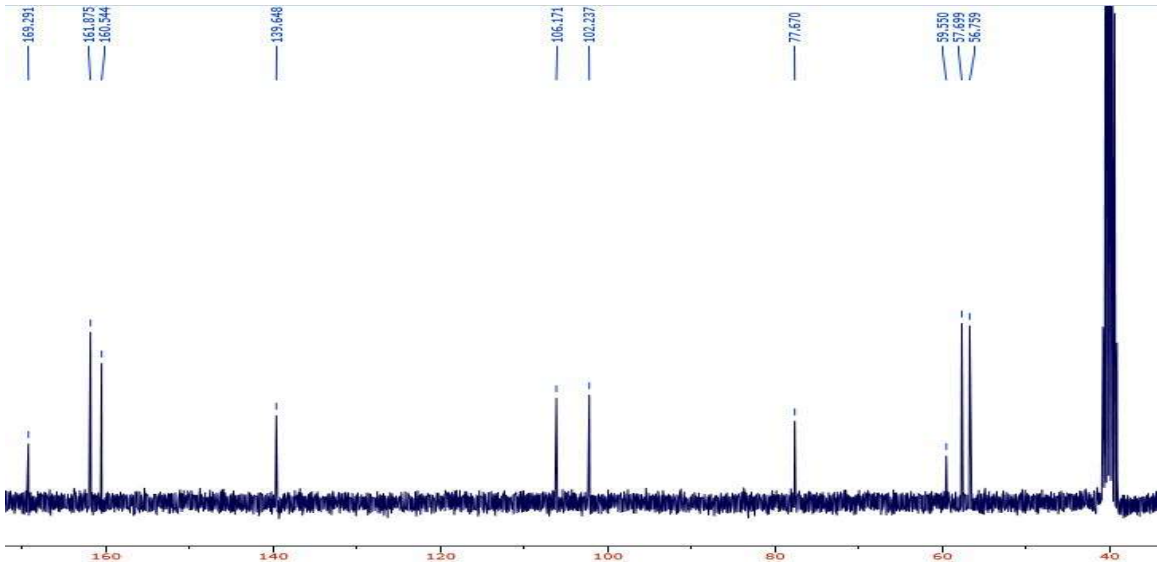


Spectrum 14 - ^{1}H NMR of 4-iodo-3-(4-chloro-2-iodophenyl)sydnone

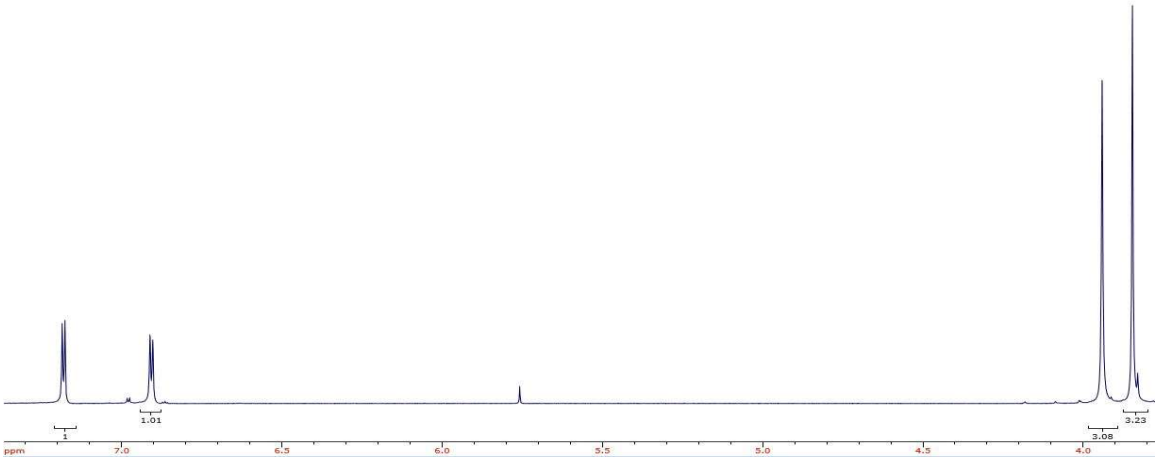


Spectrum 15 - IR (KBr) 4-iodo-3-(4-chloro-2-iodophenyl)sydnone

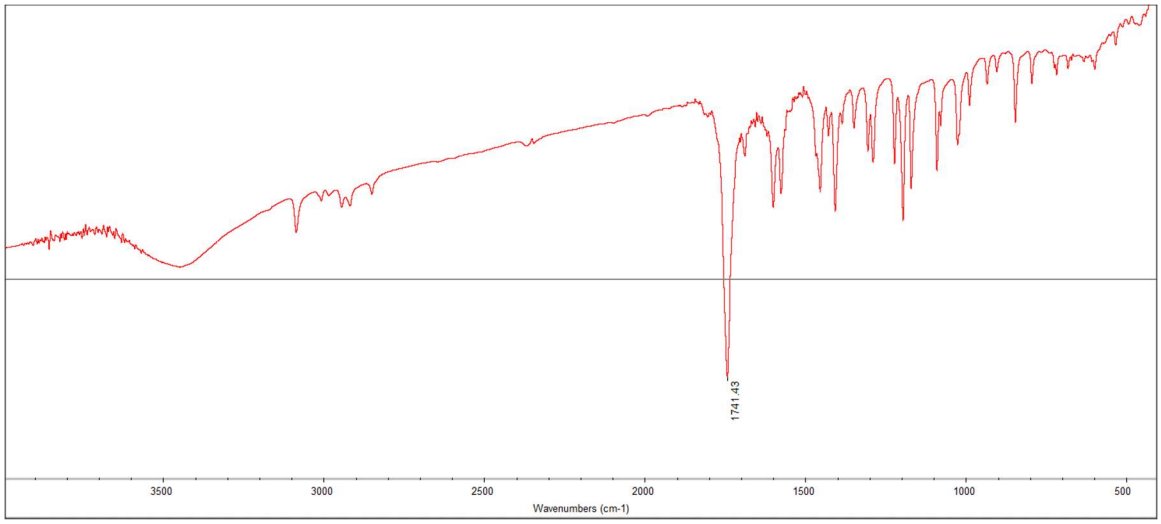
4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**36**)



Spectrum 16 - ^{13}C NMR of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone



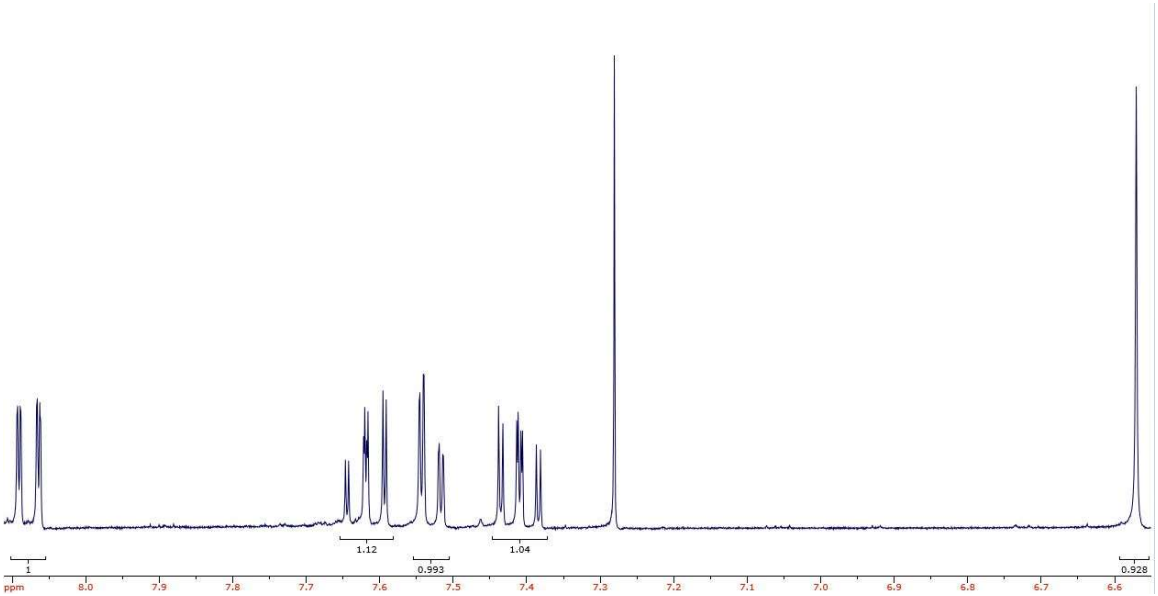
Spectrum 17 - ^{1}H NMR of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone



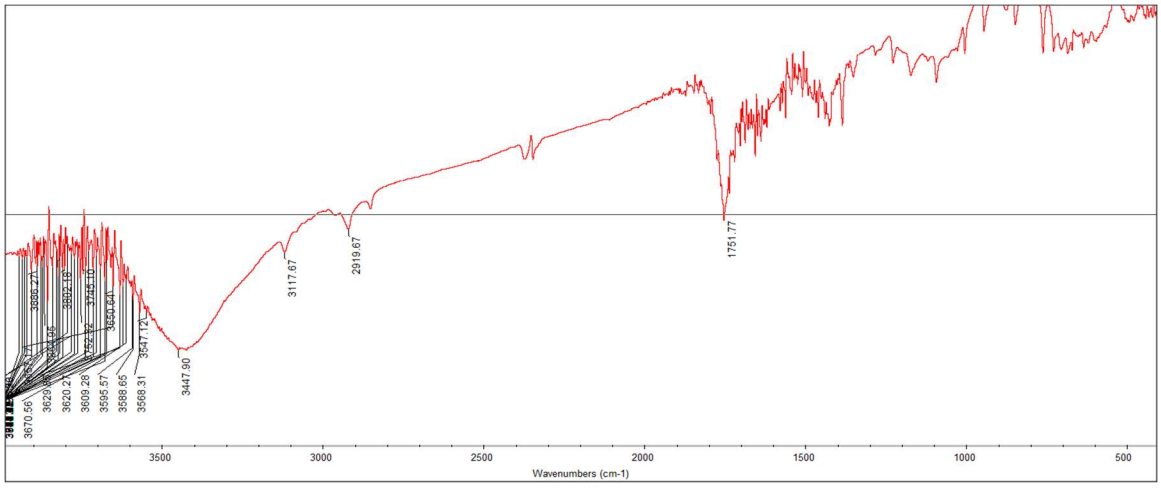
Spectrum 18 - IR (KBr) of 4-iodo-3-(3,5-dimethoxy-2-iodophenyl)sydnone

II. 3-(2-iodoaryl)sydnone spectra

3-(2-iodophenyl)sydnone (**37**)

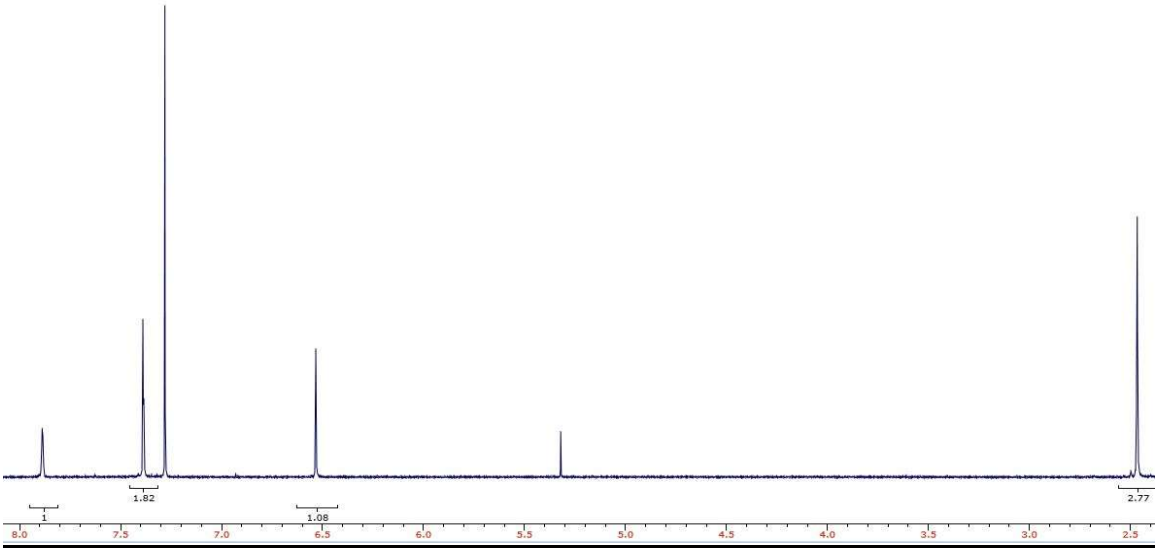


Spectrum 19 - ^{1}H NMR of 3-(2-iodophenyl)sydnone

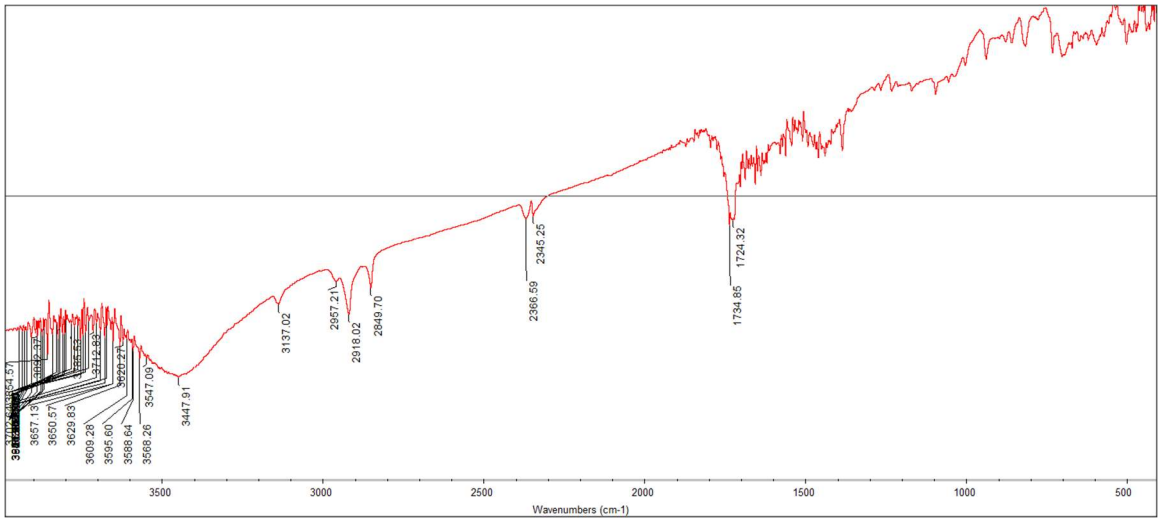


Spectrum 20 - IR (KBr) of 3-(2-iodophenyl)sydnone

3-(4-methyl-2-iodophenyl)sydnone (**38**)

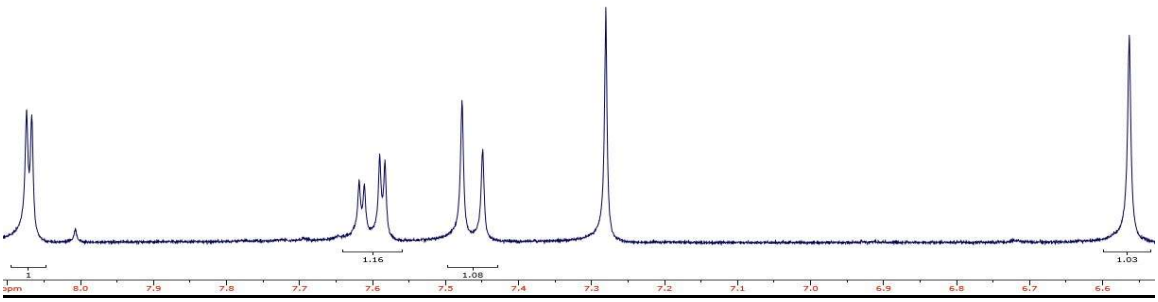


Spectrum 21 - ^{1}H NMR of 3-(4-methyl-2-iodophenyl)sydnone

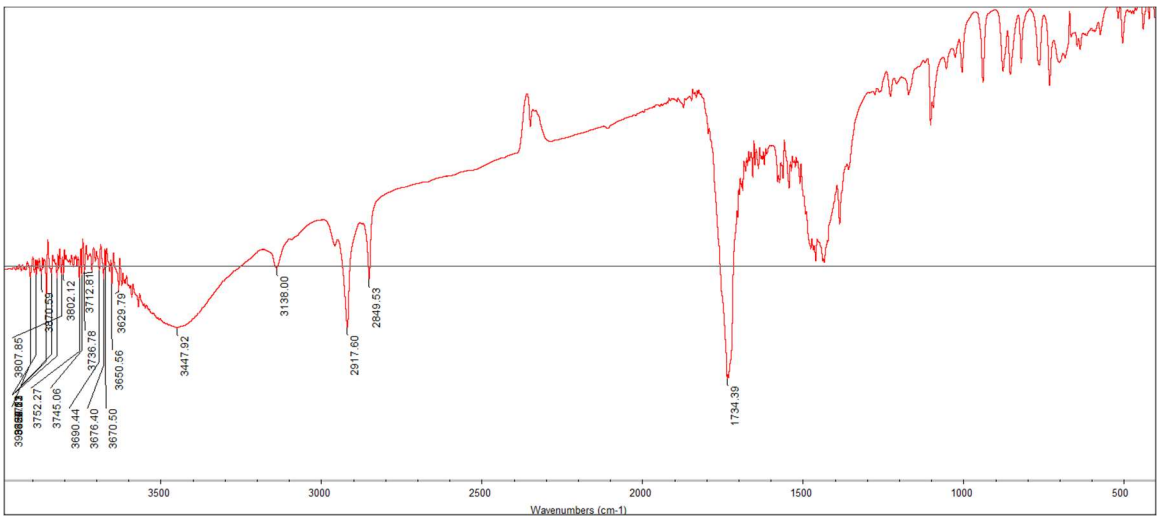


Spectrum 22 - IR (KBr) of 3-(4-methyl-2-iodophenyl)sydnone

3-(4-chloro-2-iodophenyl)sydnone (**39**)

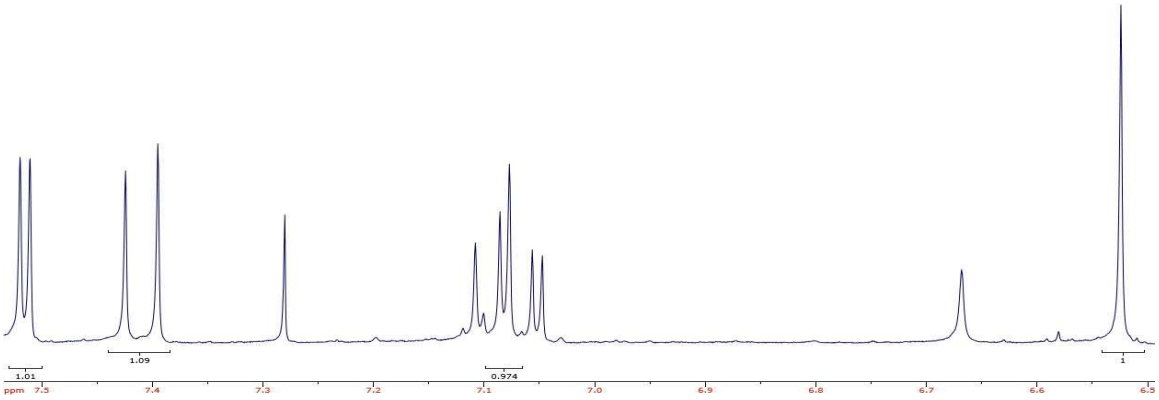


Spectrum 23 - ^{1}H NMR of 3-(4-chloro-2-iodophenyl)sydnone

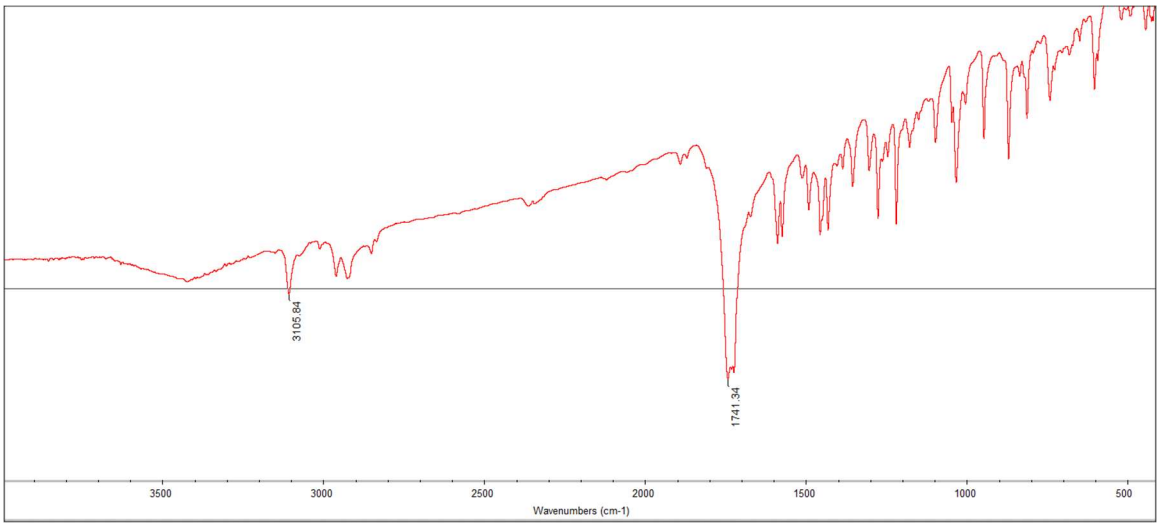


Spectrum 24 - IR (KBr) of 3-(4-chloro-2-iodophenyl)sydnone

3-(4-methoxy-2-iodophenyl)sydnone (**40**)

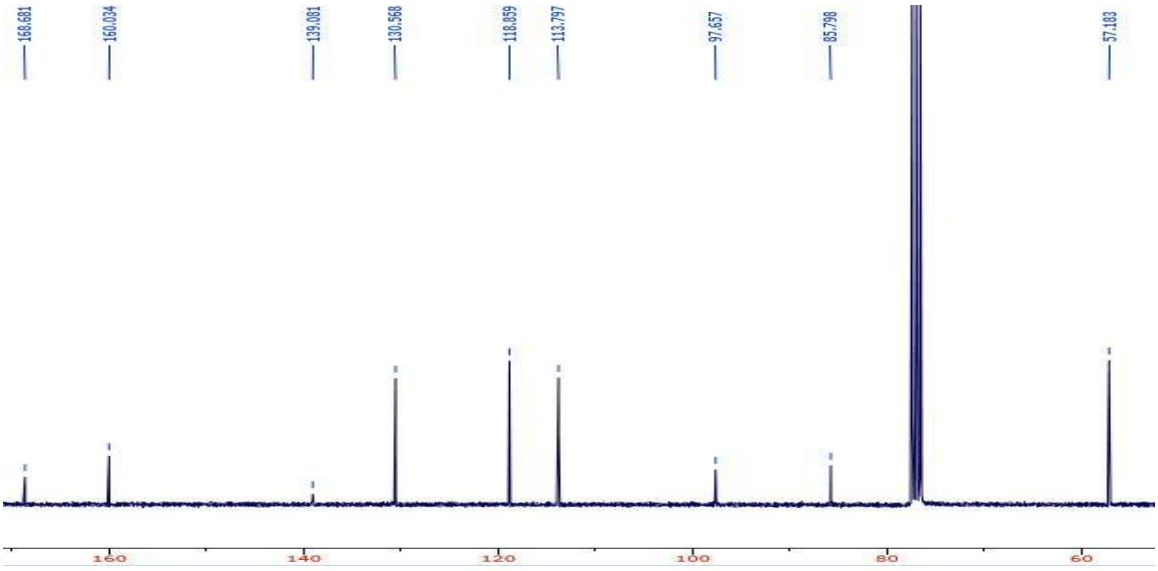


Spectrum 25 - ^{1}H NMR of 3-(4-methoxy-2-iodophenyl)sydnone

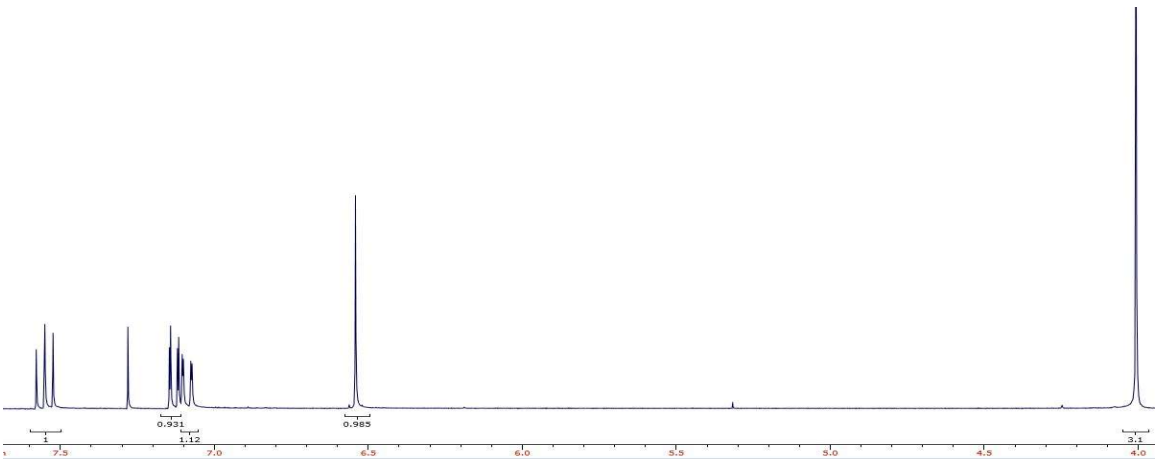


Spectrum 26 - IR (KBr) of 3-(4-methoxy-2-iodophenyl)sydnone

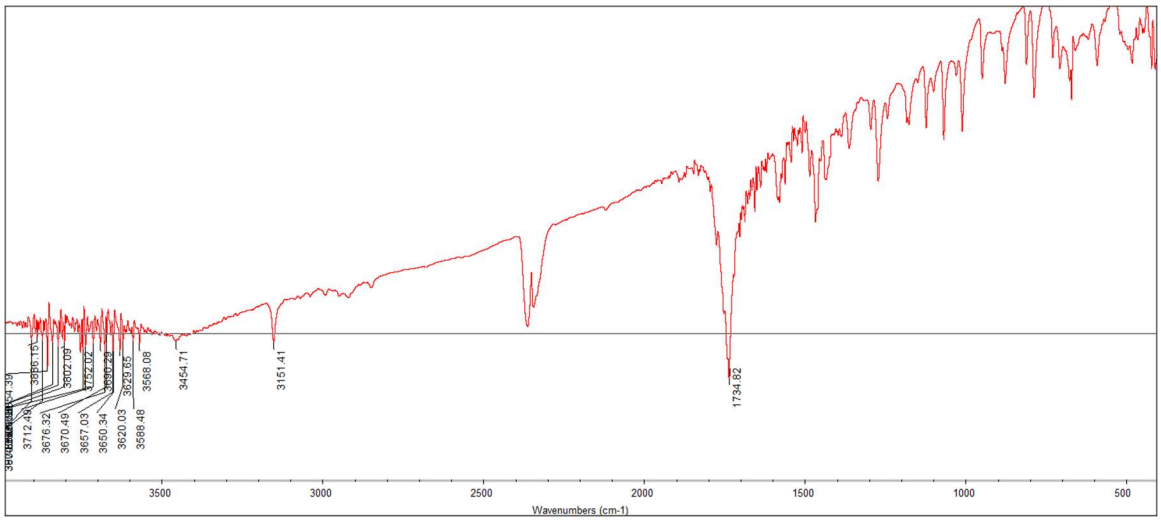
3-(3-methoxy-2-iodophenyl)sydnone (**41**)



Spectrum 27 - ^{13}C NMR of 3-(3-methoxy-2-iodophenyl)sydnone

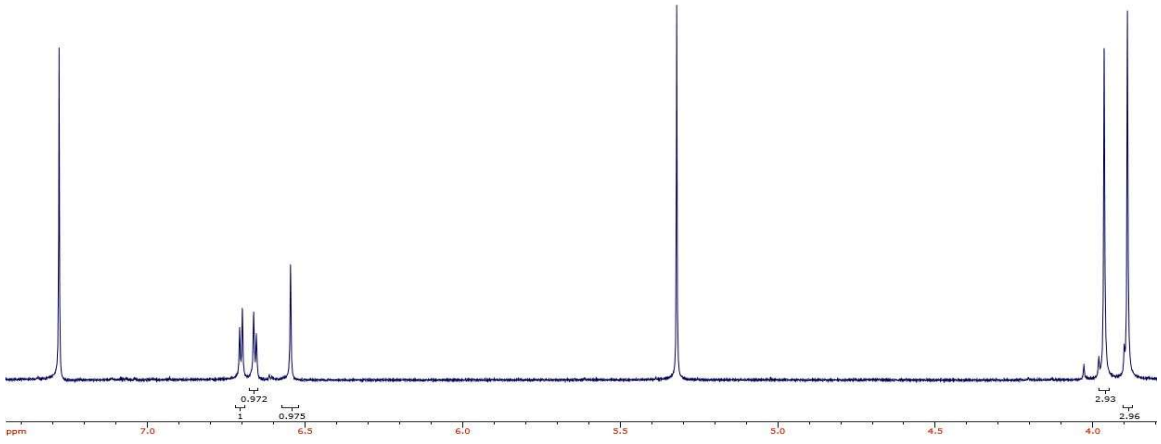


Spectrum 28 - ^{1}H NMR of 3-(3-methoxy-2-iodophenyl)sydnone

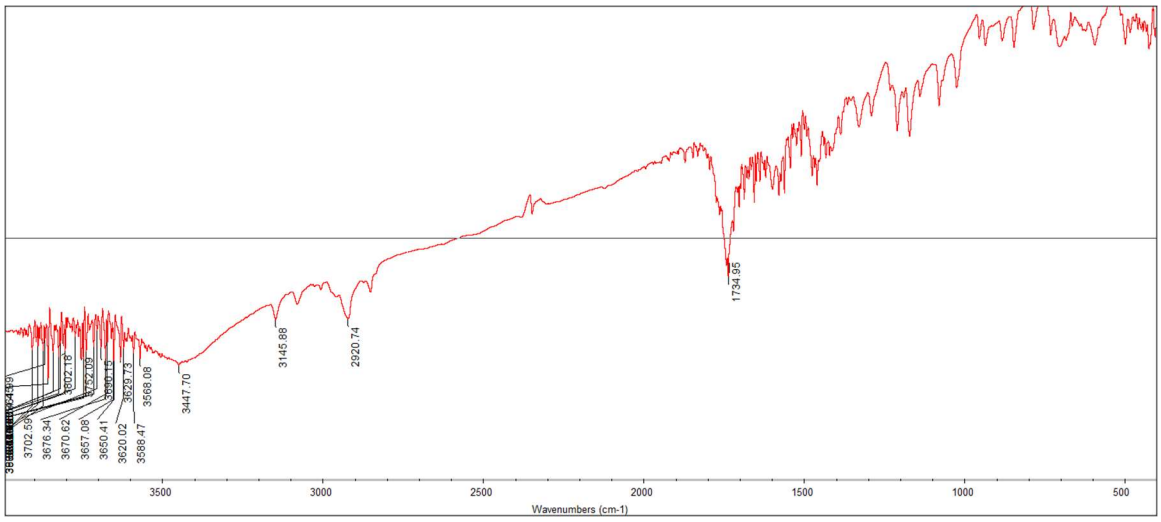


Spectrum 29 - IR (KBr) of 3-(3-methoxy-2-iodophenyl)sydnone

3-(3,5-dimethoxy-2-iodophenyl)sydnone (**42**)



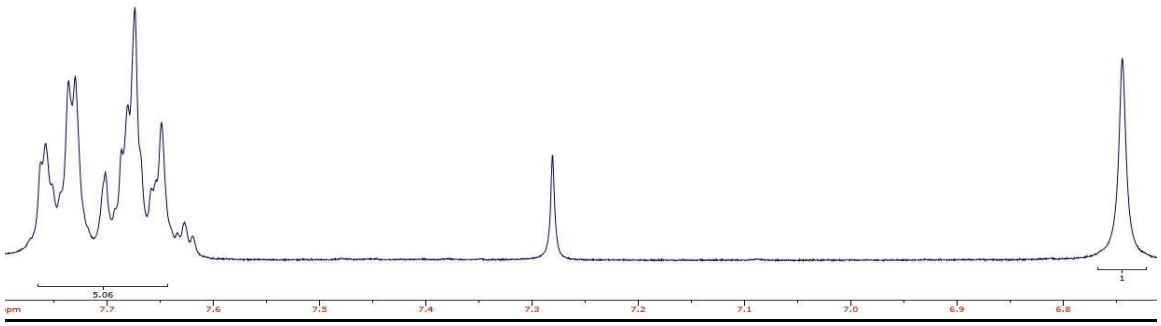
Spectrum 30 - ^{1}H NMR of 3-(3,5-dimethoxy-2-iodophenyl)sydnone



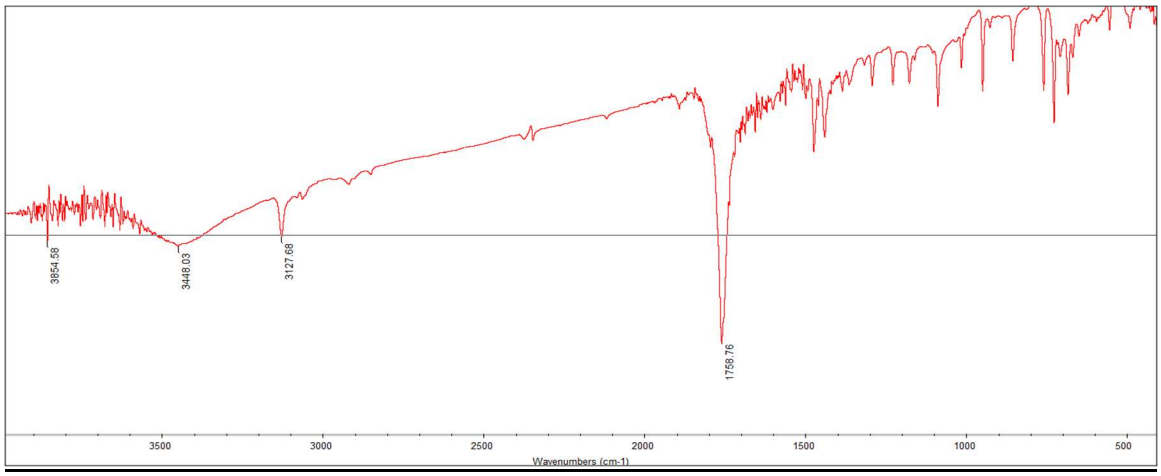
Spectrum 31 - IR (KBr) of 3-(3,5-dimethoxy-2-iodophenyl)sydnone

III. 3-arylsydnone spectra

3-phenylsydnone (**43**)

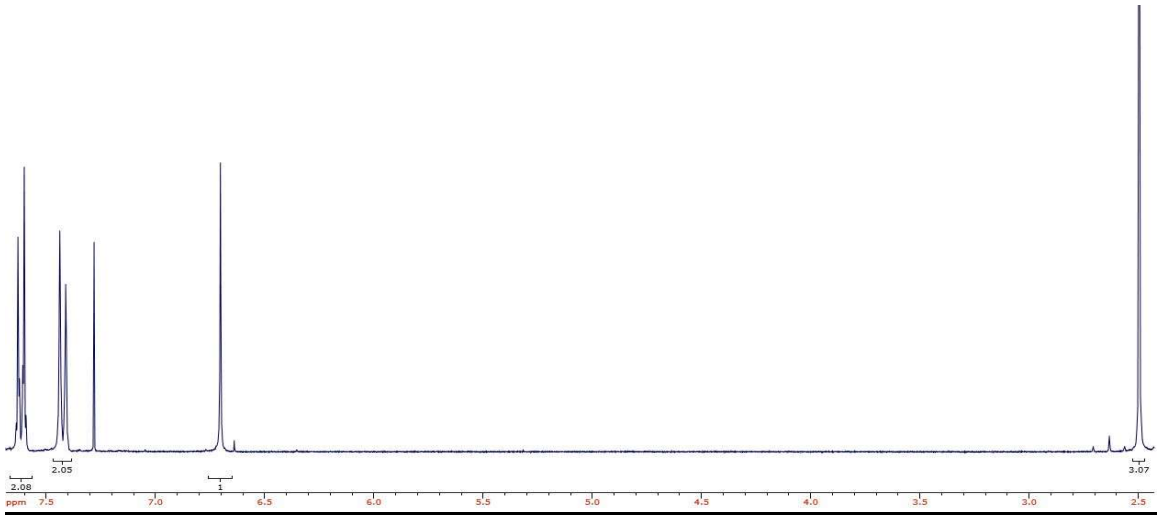


Spectrum 32 - ^{1}H NMR of 3-phenylsydnone

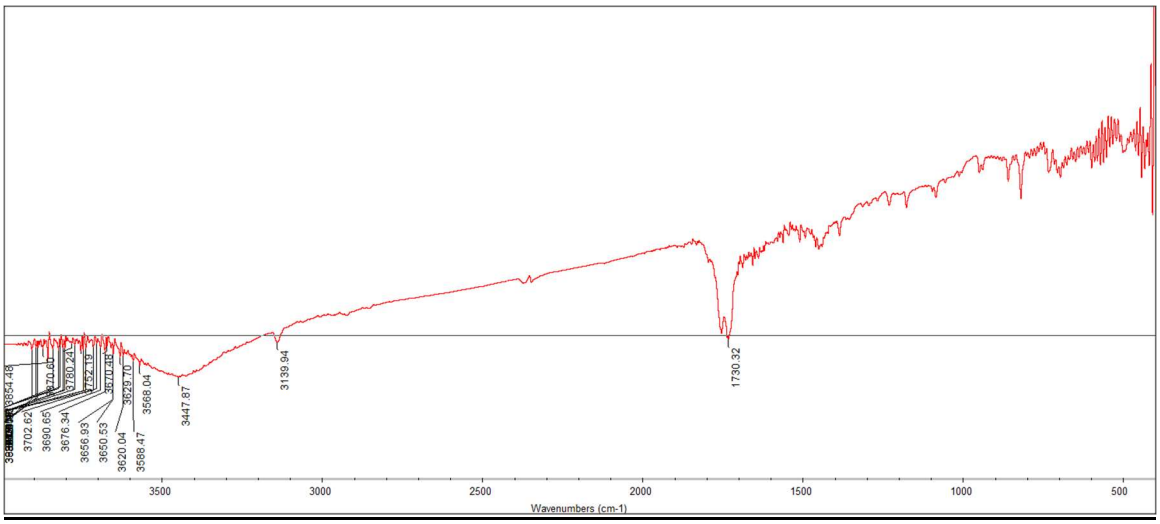


Spectrum 33 - IR (KBr) of 3-phenylsydnone

3-(4-methylphenyl)sydnone (**44**)

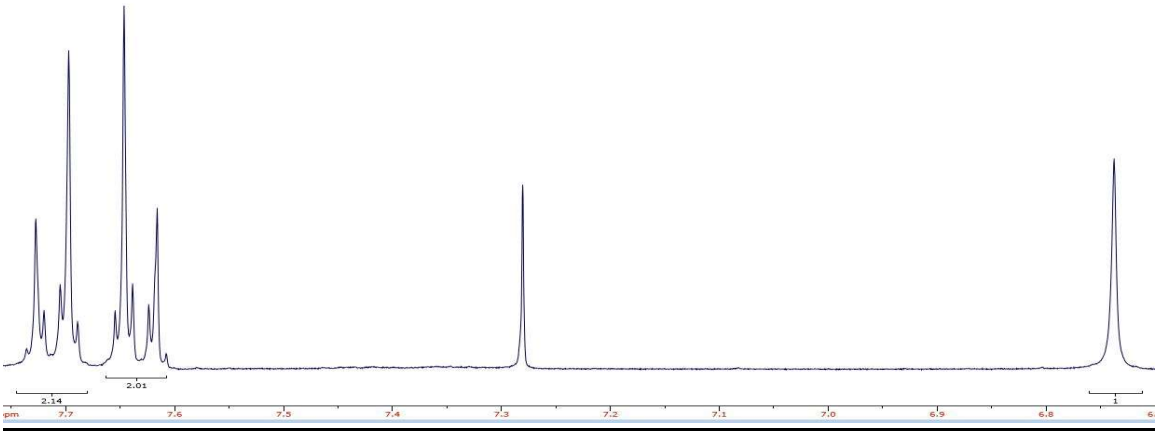


Spectrum 34 - ^{1}H NMR of 3-(4-methylphenyl)sydnone

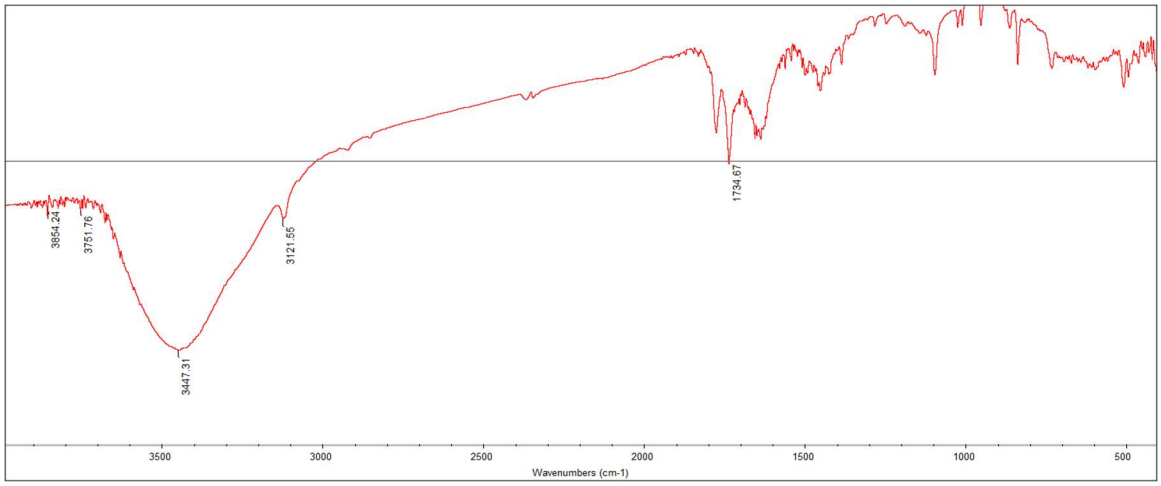


Spectrum 35 - IR (KBr) of 3-(4-methylphenyl)sydnone

3-(4-chlorophenyl)sydnone (**45**)

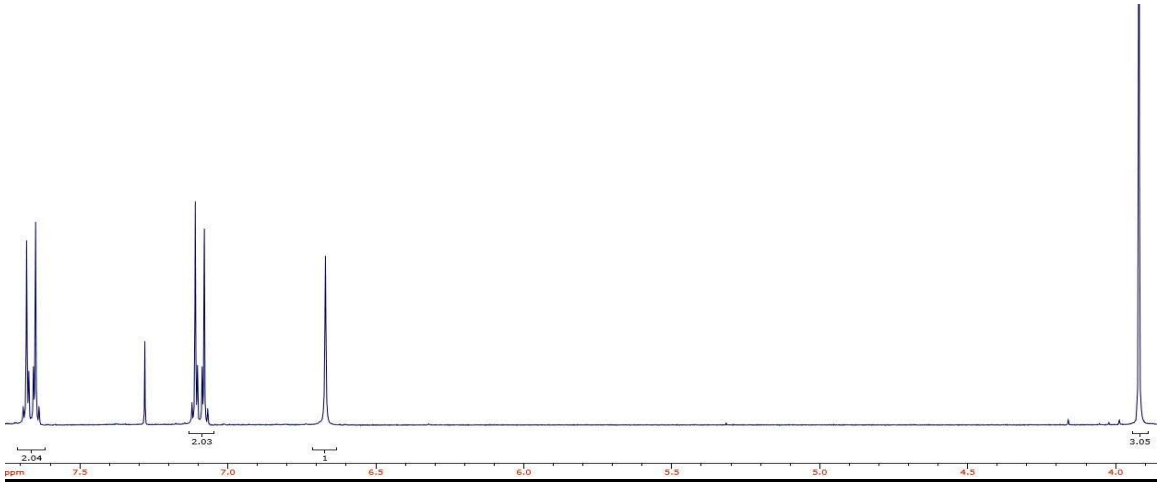


Spectrum 36 - ^{1}H NMR of 3-(4-chlorophenyl)sydnone

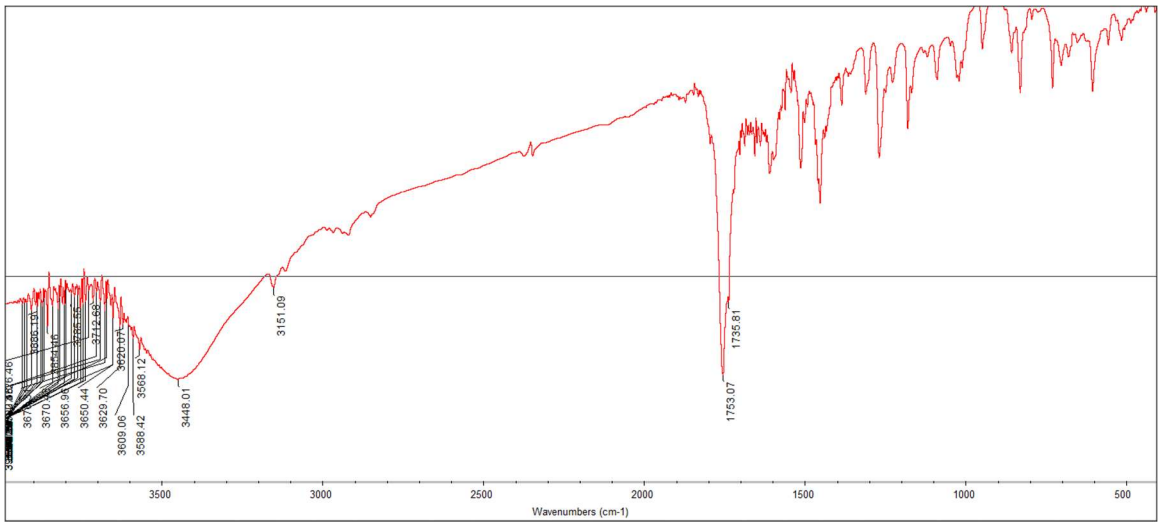


Spectrum 37 - IR (KBr) of 3-(4-chlorophenyl)sydnone

3-(4-methoxyphenyl)sydnone (**46**)

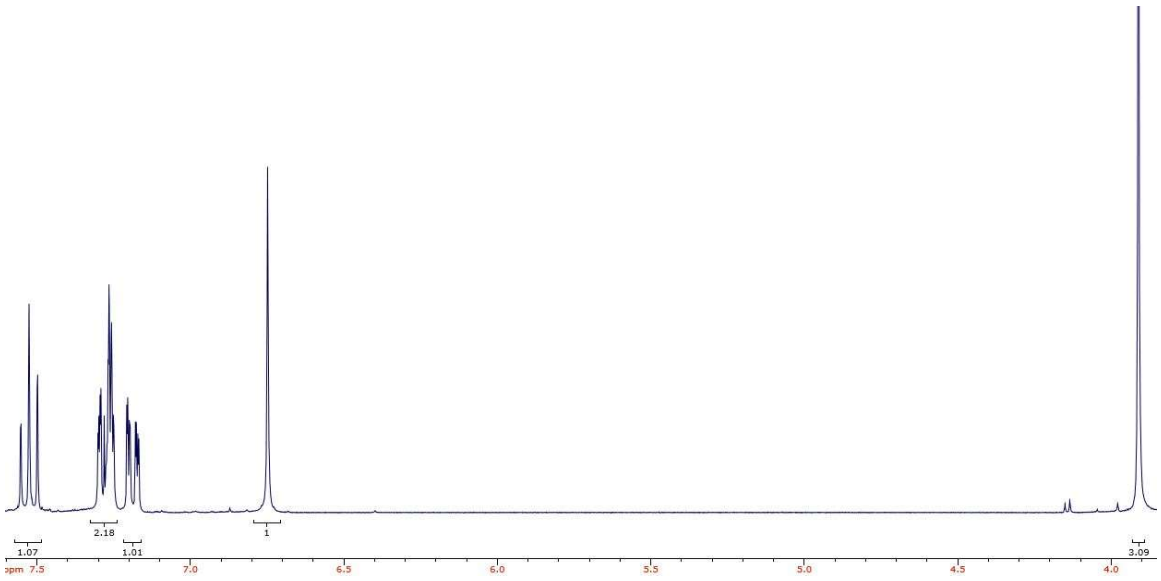


Spectum 38 - ^{1}H NMR of 3-(4-methoxyphenyl)sydnone

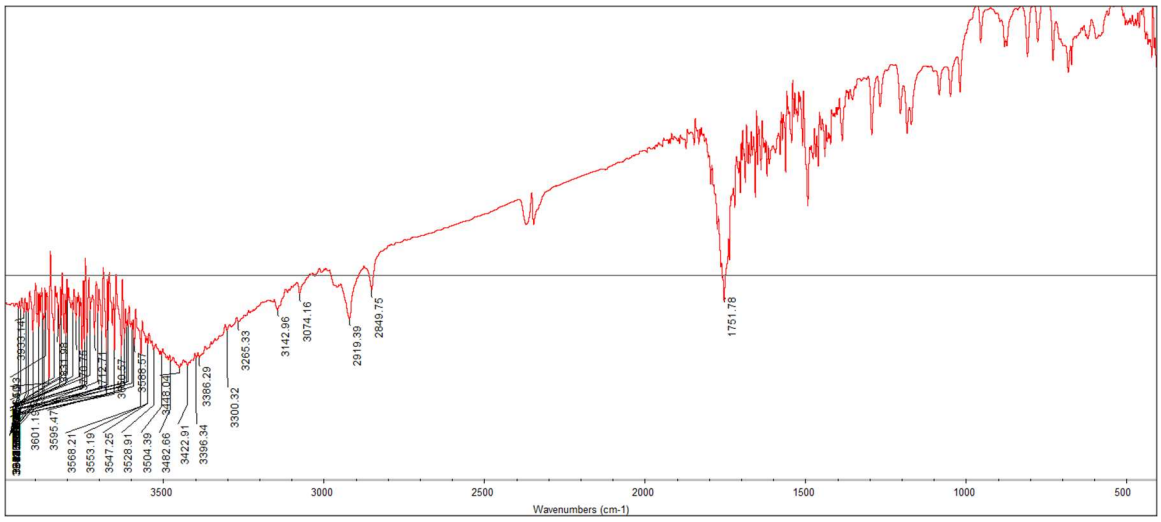


Spectrum 39 - IR (KBr) of 3-(4-methoxyphenyl)sydnone

3-(3-methoxyphenyl)sydnone (**47**)

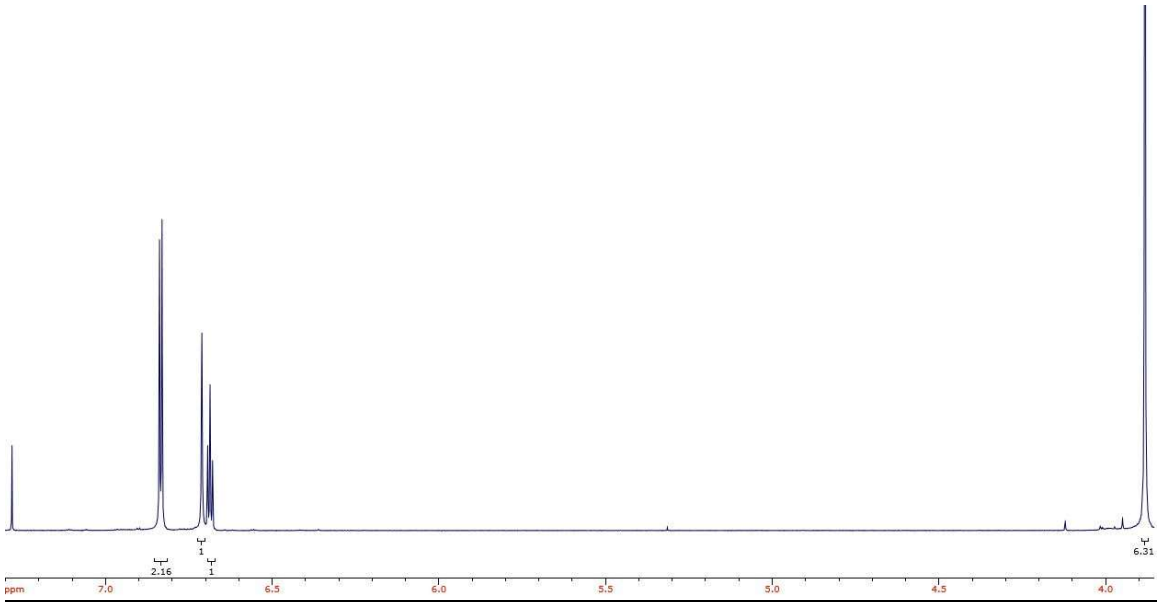


Spectrum 40 - ^{1}H NMR of 3-(3-methoxyphenyl)sydnone

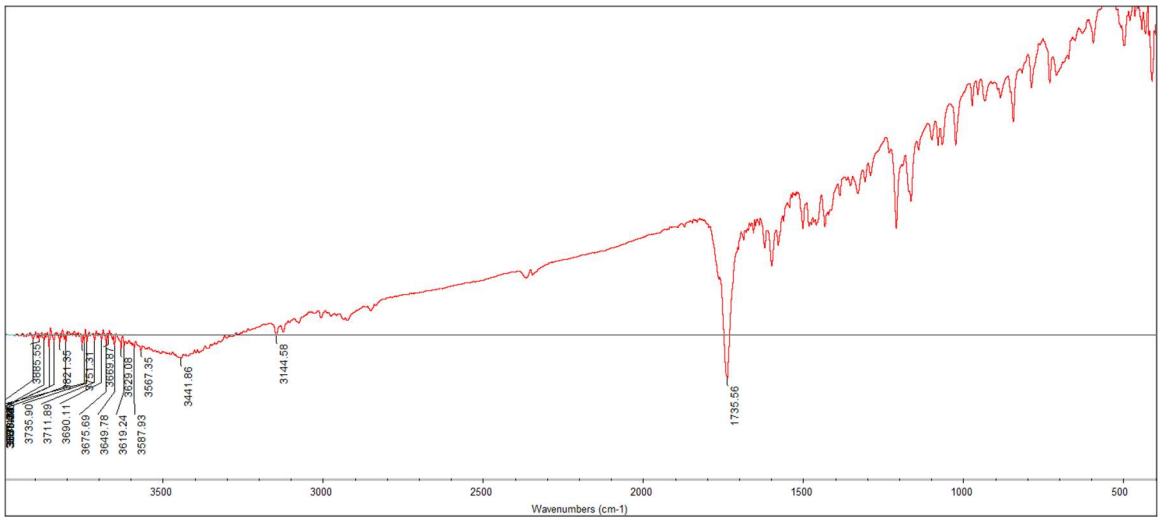


Spectrum 41 - IR (KBr) of 3-(3-methoxyphenyl)sydnone

3-(3,5-dimethoxyphenyl)sydnone (**48**)



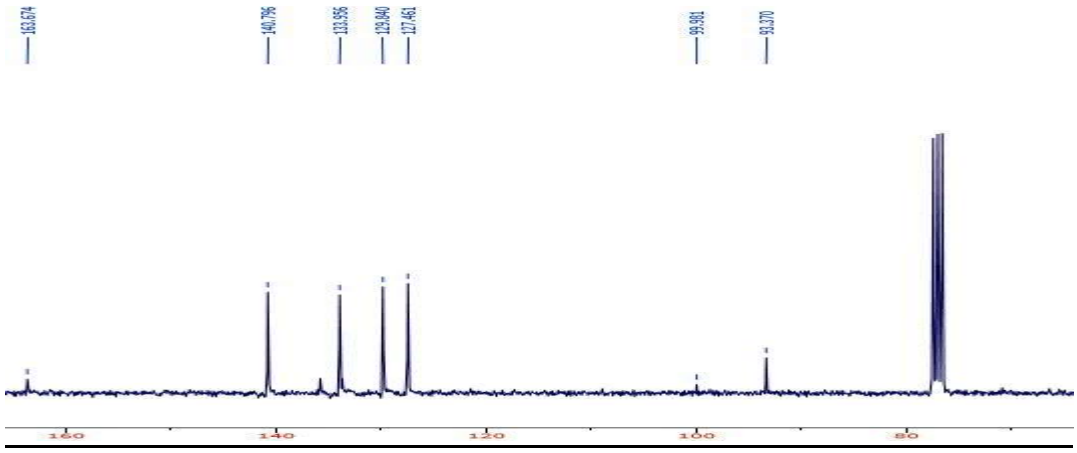
Spectrum 42 - ^{1}H NMR of 3-(3,5-dimethoxyphenyl)sydnone



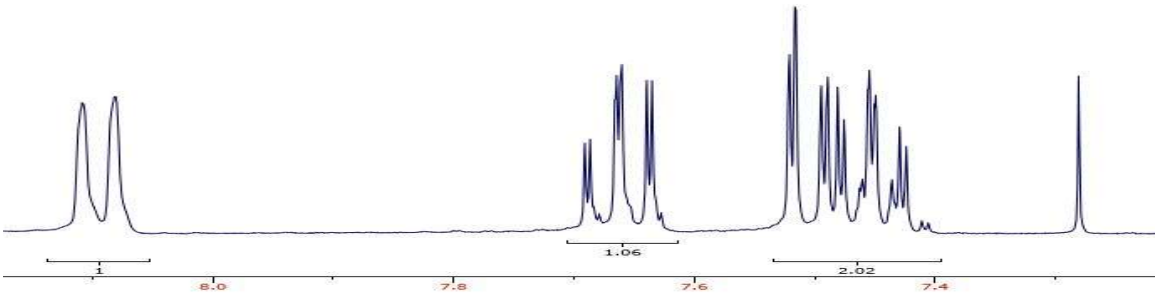
Spectrum 43 - IR (KBr) of 3-(3,5-dimethoxyphenyl)sydnone

IV. 4-chloro-3-(2-iodoaryl)sydnone spectra

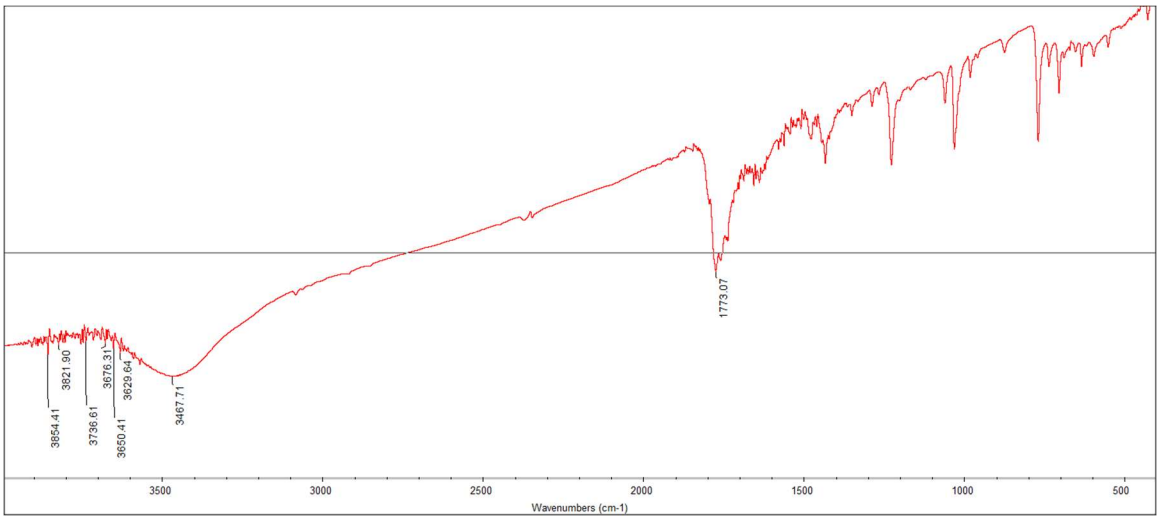
4-chloro-3-(2-iodophenyl)sydnone (**49**)



Spectrum 44 - ^{13}C NMR of 4-chloro-3-(2-iodophenyl)sydnone

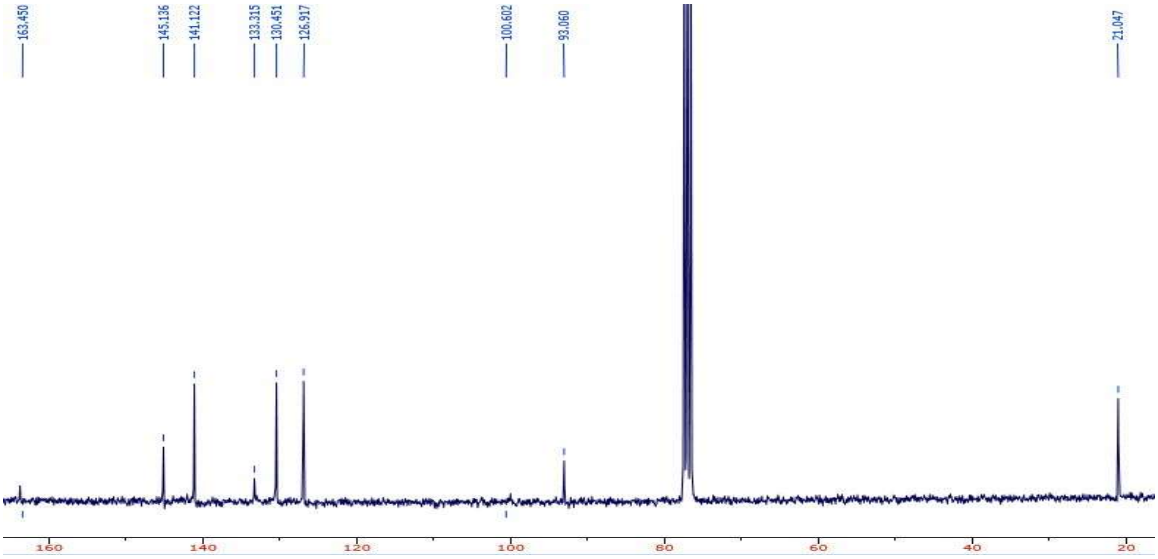


Spectrum 45 - ^{1}H NMR of 4-chloro-3-(2-iodophenyl)sydnone

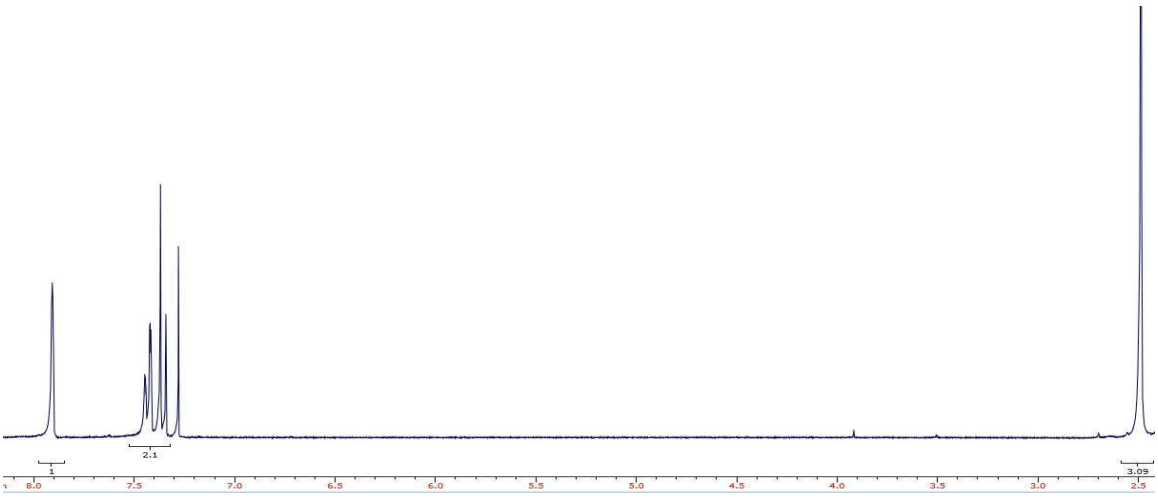


Spectrum 46 - IR (KBr) of 4-chloro-3-(2-iodophenyl)sydnone

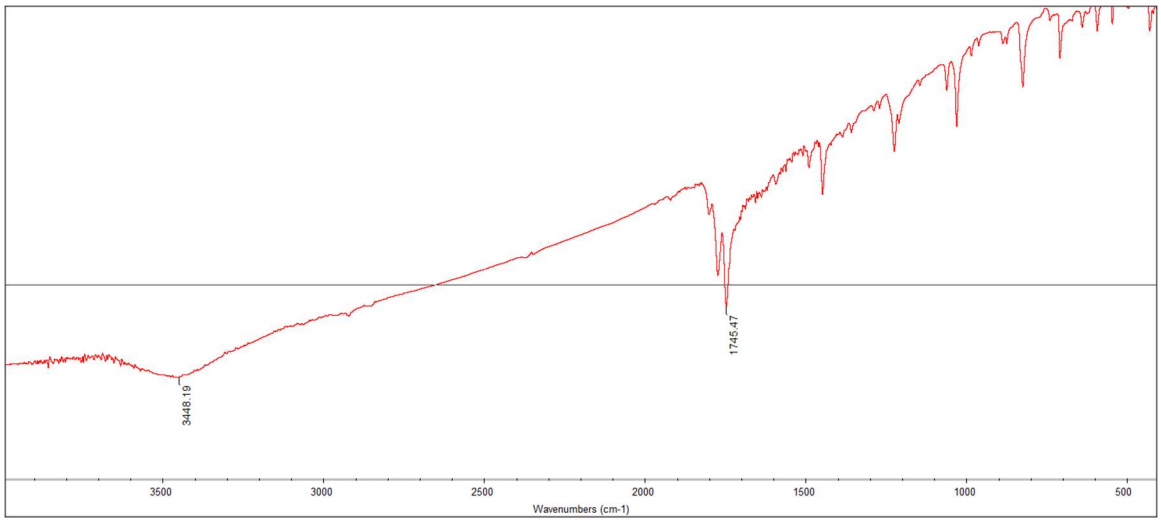
4-chloro-3-(4-methyl-2-iodophenyl)sydnone (**50**)



Spectrum 47 - ^{13}C NMR of 4-chloro-3-(4-methyl-2-iodophenyl)sydnone

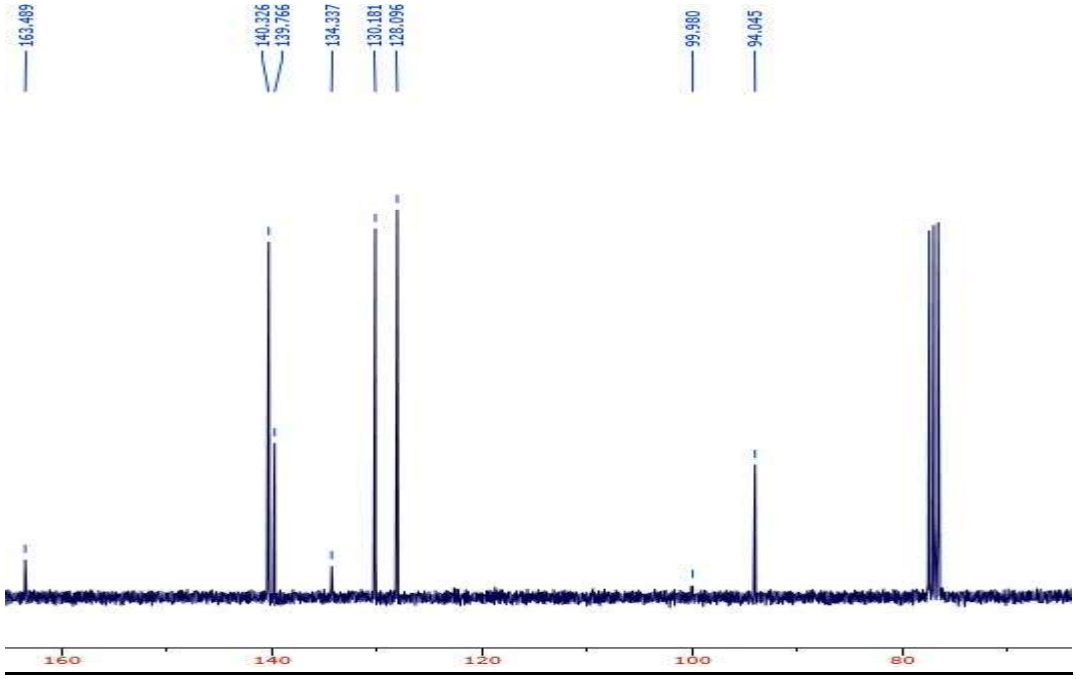


Spectrum 48 - ^{1}H NMR of 4-chloro-3-(4-methyl-2-iodophenyl)sydnone

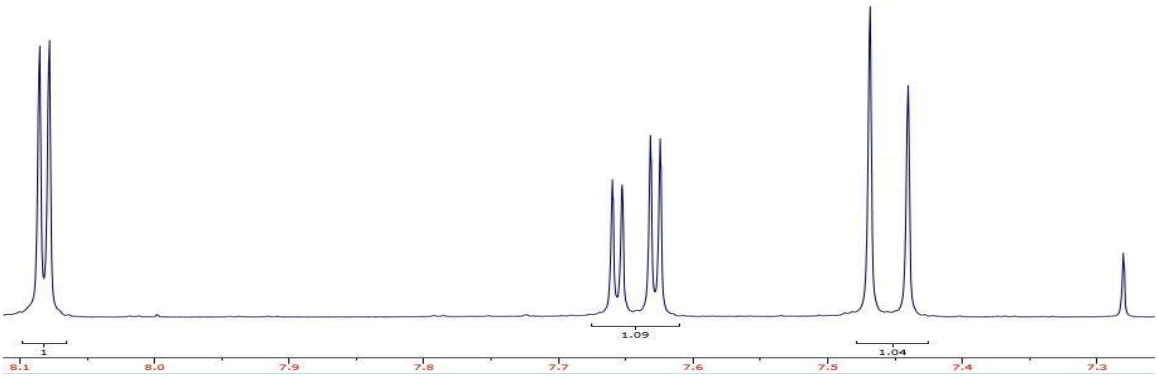


Spectrum 49 - IR (KBr) of 4-chloro-3-(4-methyl-2-iodophenyl)sydnone

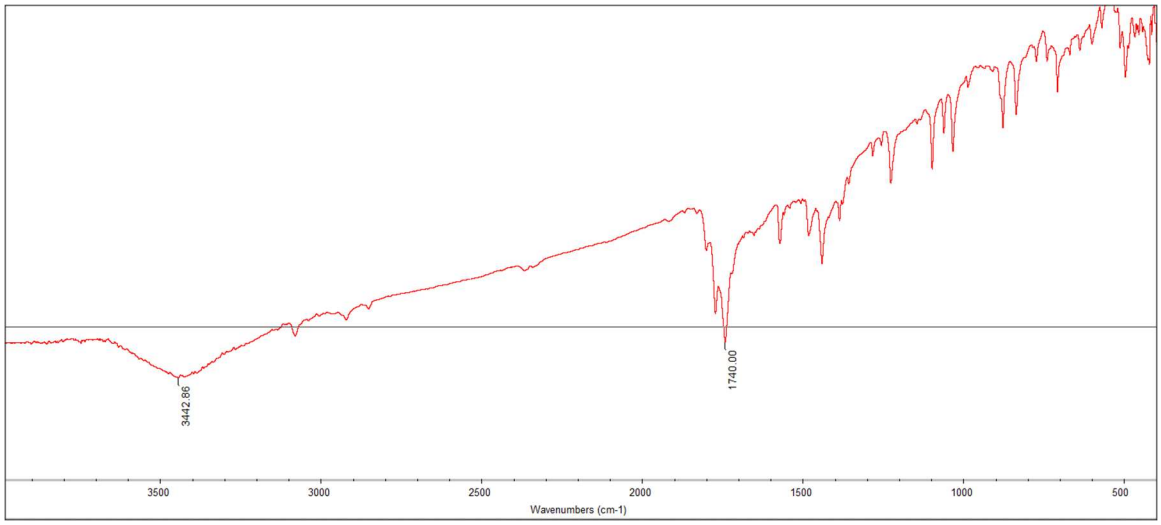
4-chloro-3-(4-chloro-2-iodophenyl)sydnone (**51**)



Spectrum 50 - ^{13}C NMR of 4-chloro-3-(4-chloro-2-iodophenyl)sydnone

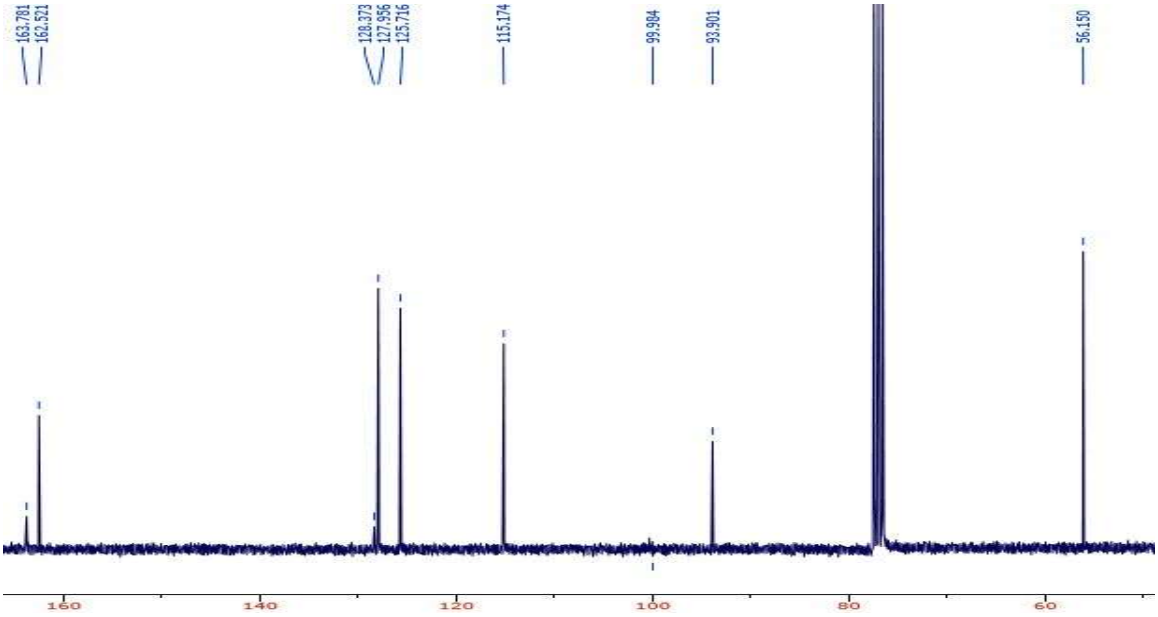


Spectrum 51 - ^{1}H NMR of 4-chloro-3-(4-chloro-2-iodophenyl)sydnone

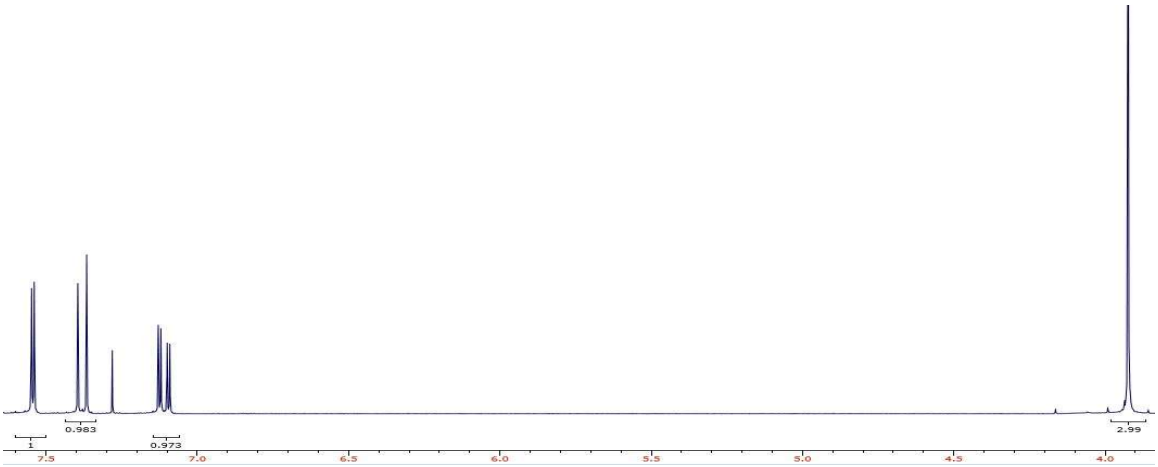


Spectrum 52 - IR (KBr) of 4-chloro-3-(4-chloro-2-iodophenyl)sydnone

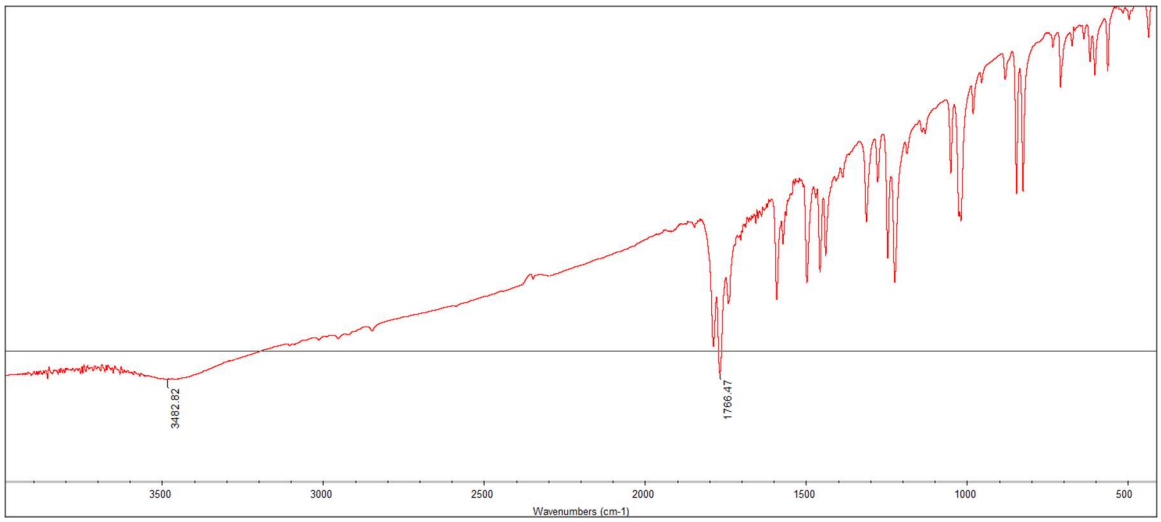
4-chloro-3-(4-methoxy-2-iodophenyl)sydnone (**52**)



Spectrum 53 - ^{13}C NMR of 4-chloro-3-(4-methoxy-2-iodophenyl)sydnone

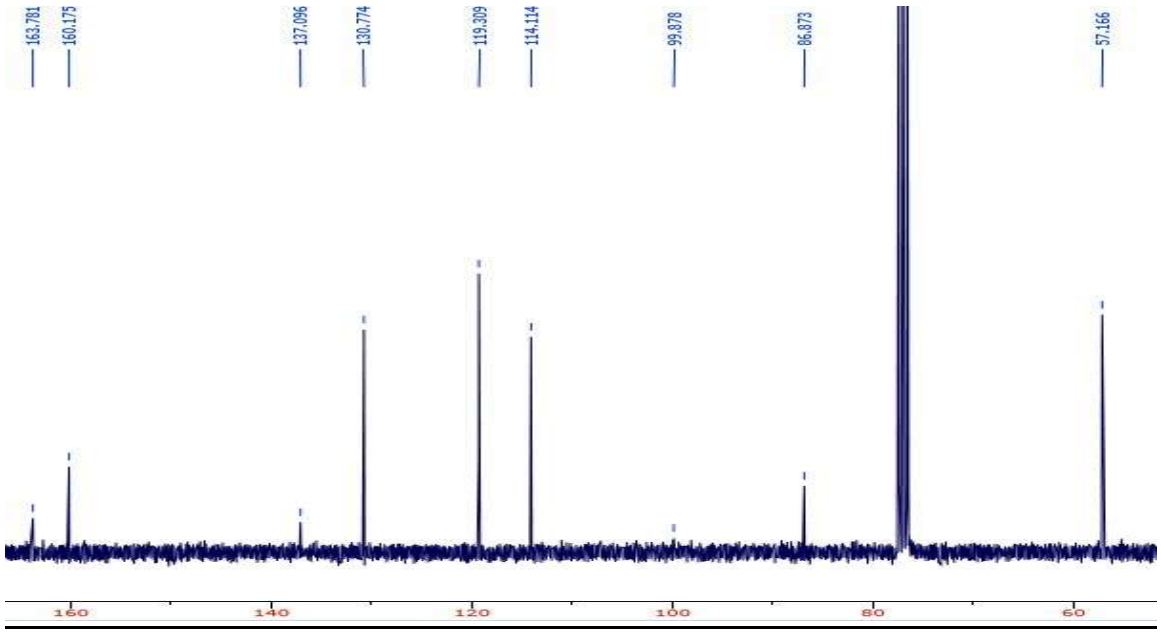


Spectrum 54 - ^{1}H NMR of 4-chloro-3-(4-methoxy-2-iodophenyl)sydnone

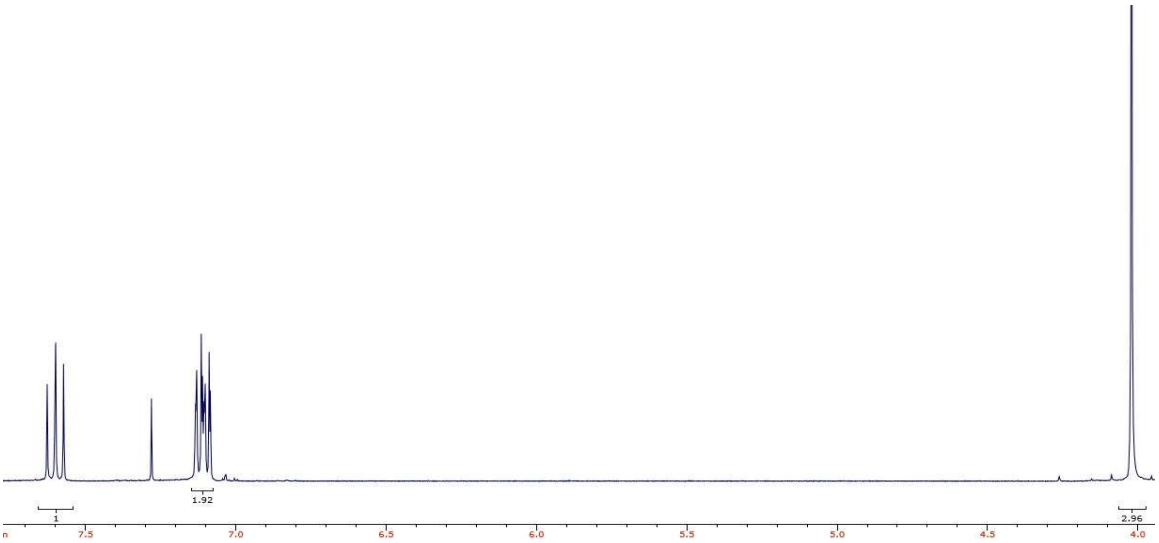


Spectrum 55 - IR (KBr) of 4-chloro-3-(4-methoxy-2-iodophenyl)sydnone

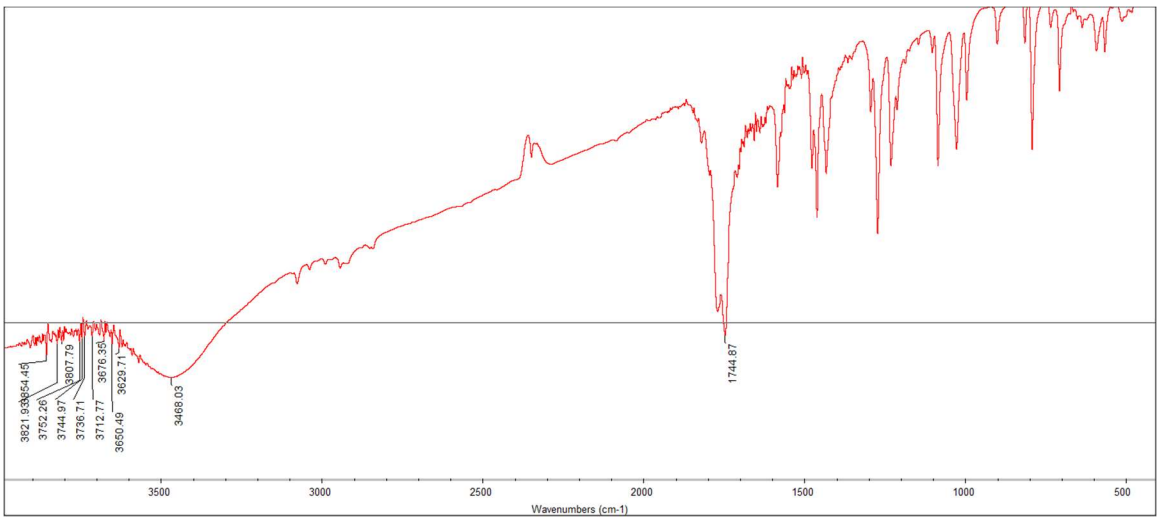
4-chloro-3-(3-methoxy-2-iodophenyl)sydnone (**53**)



Spectrum 56 - ^{13}C NMR of 4-chloro-3-(3-methoxy-2-iodophenyl)sydnone

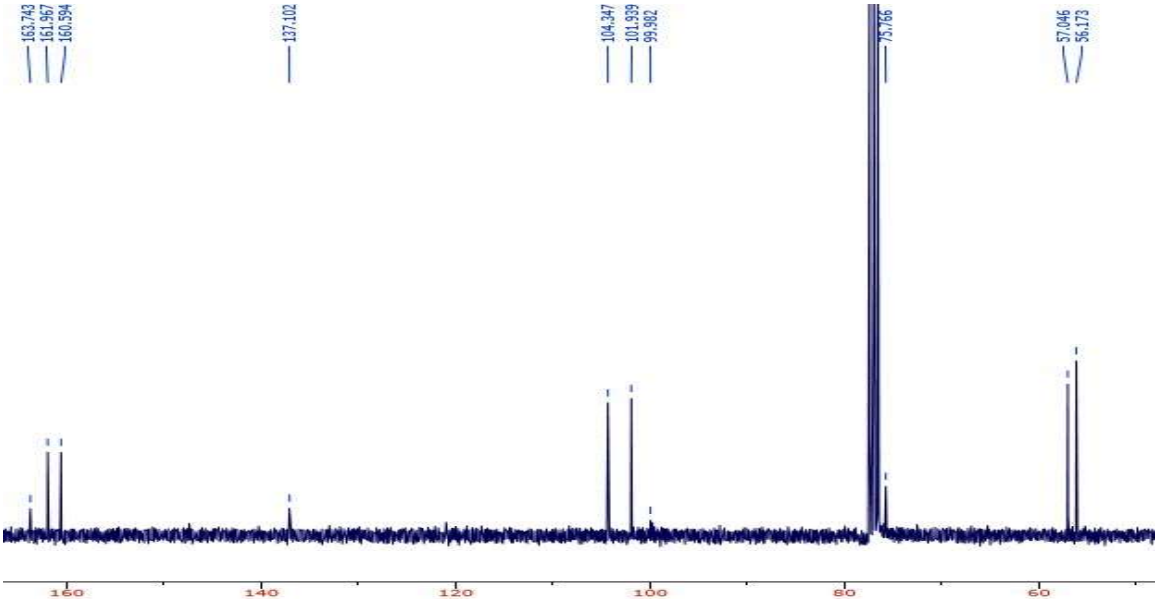


Spectrum 57 - ^{1}H NMR of 4-chloro-3-(3-methoxy-2-iodophenyl)sydnone

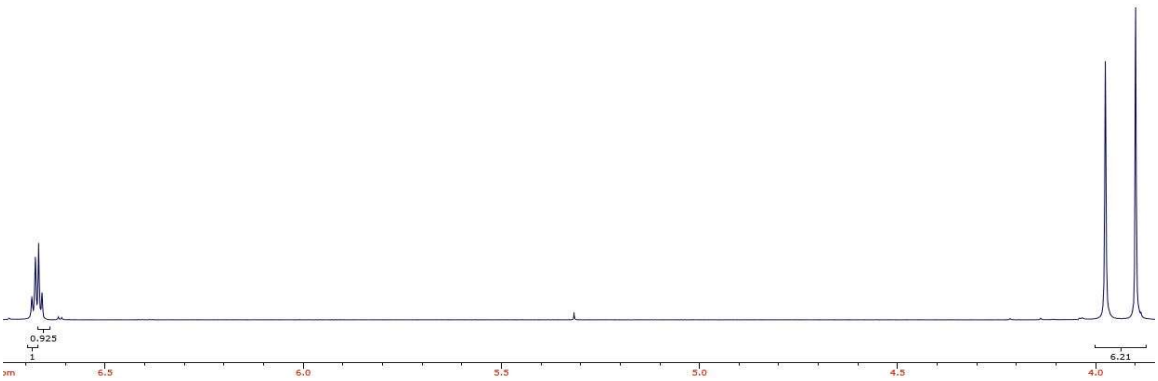


Spectrum 58 - IR (KBr) of 4-chloro-3-(3-methoxy-2-iodophenyl)sydnone

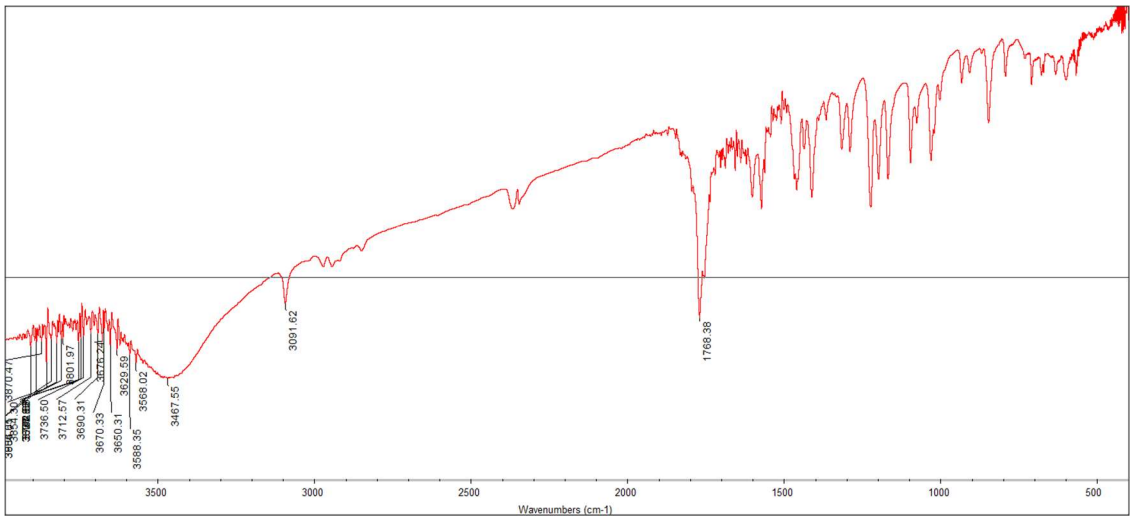
4-chloro-3-(3,5-dimethoxy-2-iodophenyl)sydnone (**54**)



Spectrum 59 - ^{13}C NMR of 4-chloro-3-(3,5-dimethoxy-2-iodophenyl)sydnone



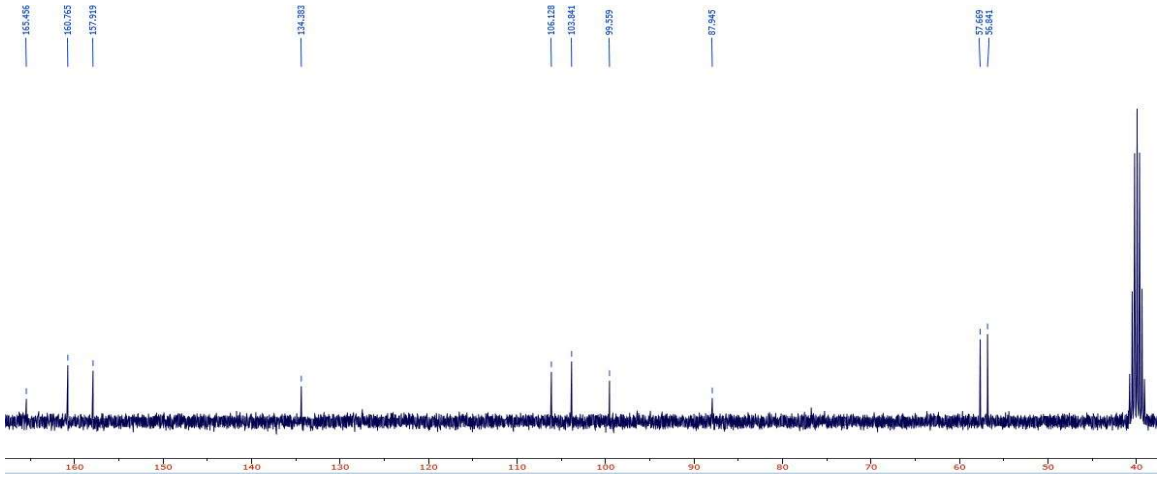
Spectrum 60 - ^{1}H NMR of 4-chloro-3-(3,5-dimethoxy-2-iodophenyl)sydnone



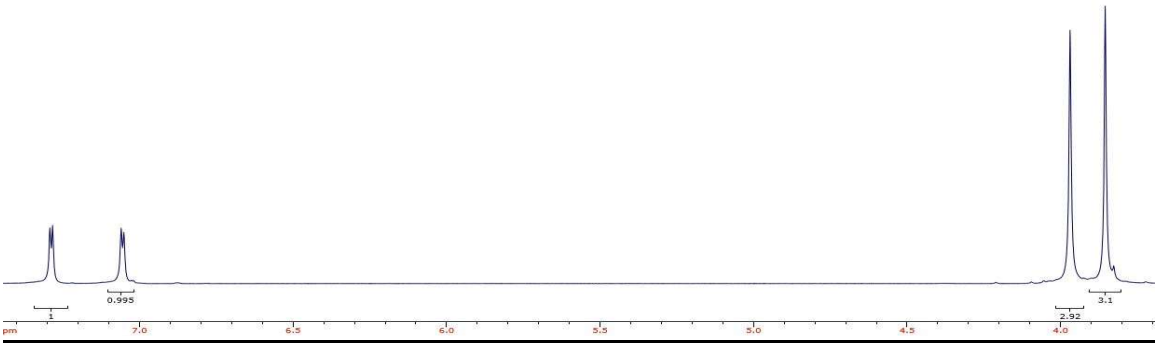
Spectrum 61 - IR (KBr) of 4-chloro-3-(3,5-dimethoxy-2-iodophenyl)sydnone

V. 4-bromo-3-(2-bromoaryl)sydnone spectra

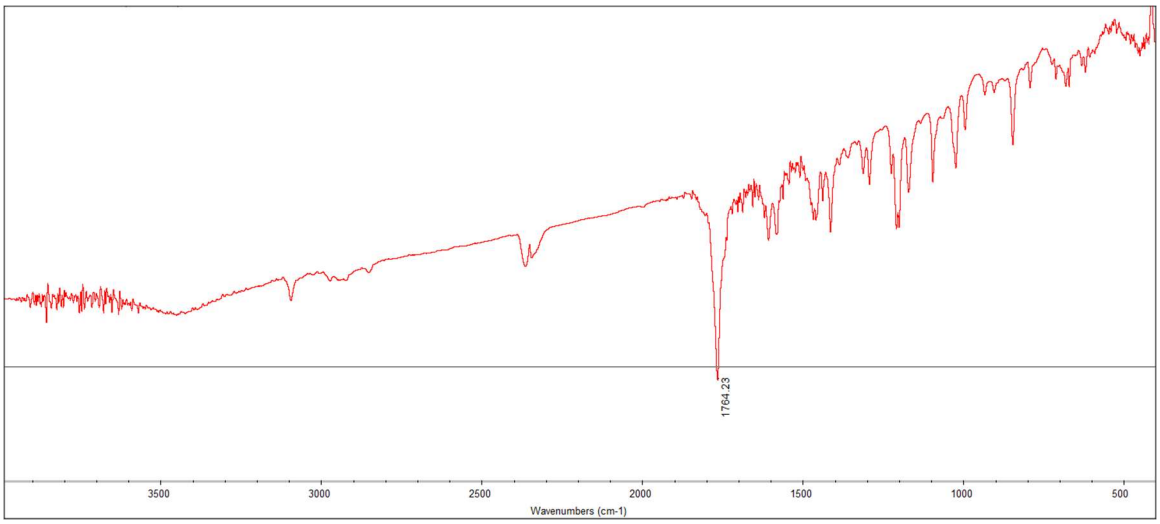
4-bromo-3-(3,5-dimethoxy-2-bromophenyl)sydnone (**55**)



Spectrum 62 - ^{13}C NMR of 4-bromo-3-(3,5-dimethoxy-2-bromohenyl)sydnone

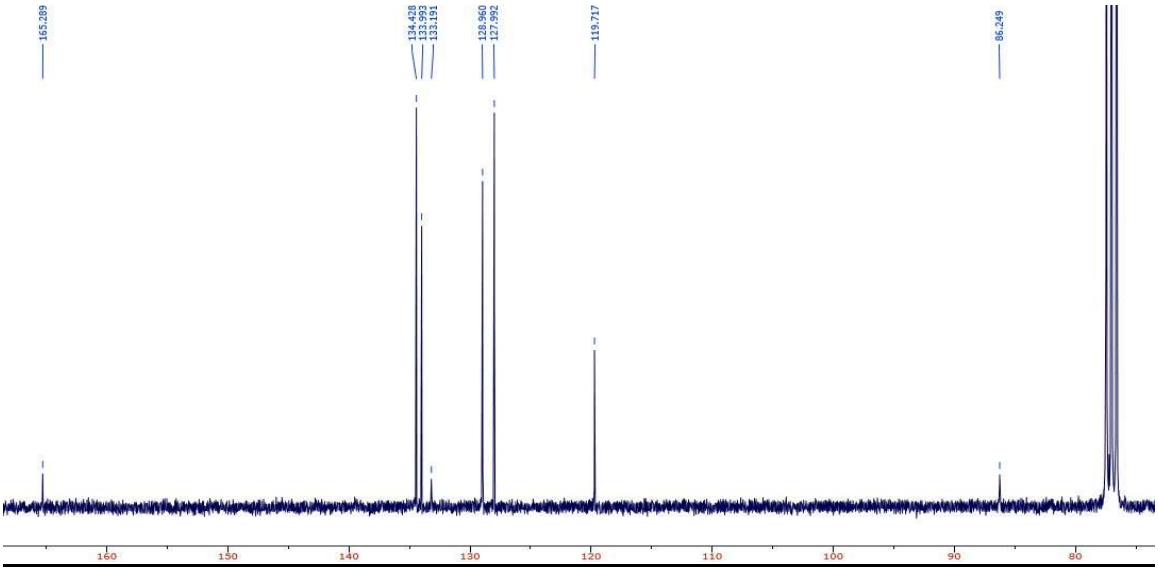


Spectrum 63 - ^{1}H NMR of 4-bromo-3-(3,5-dimethoxy-2-bromohenyl)sydnone

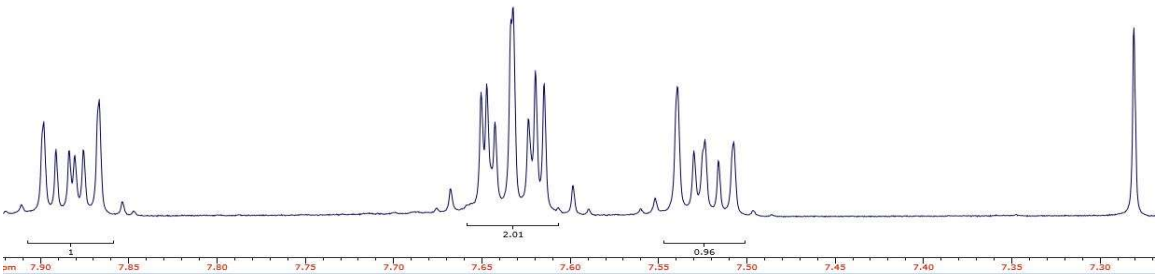


Spectrum 64 - IR (KBr) of 4-bromo-3-(3,5-dimethoxy-2-bromohenyl)sydnone

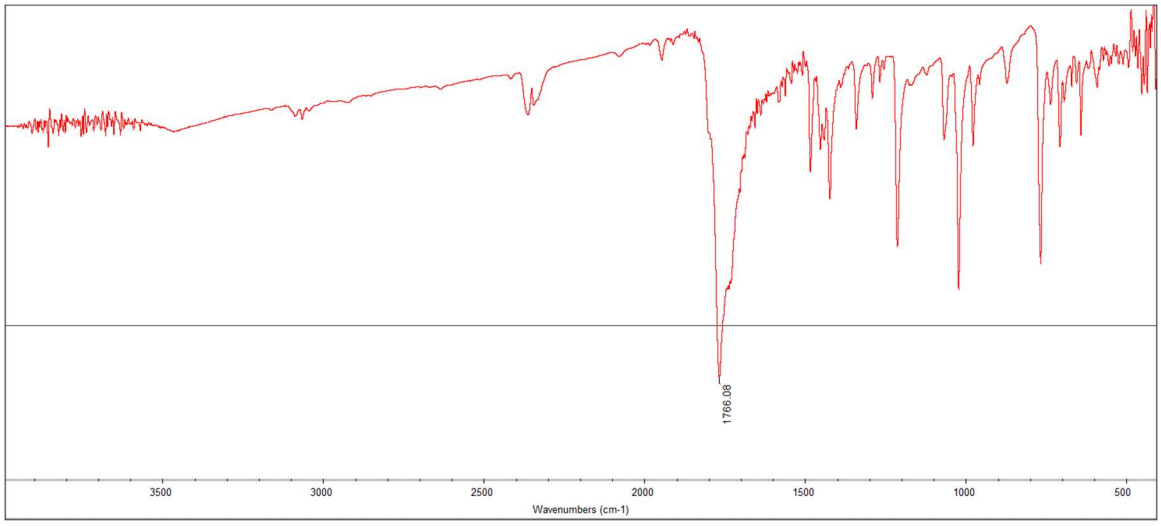
4-bromo-3-(2-bromophenyl)sydnone (**56**)



Spectrum 65 - ^{13}C NMR of 4-bromo-3-(2-bromophenyl)sydnone

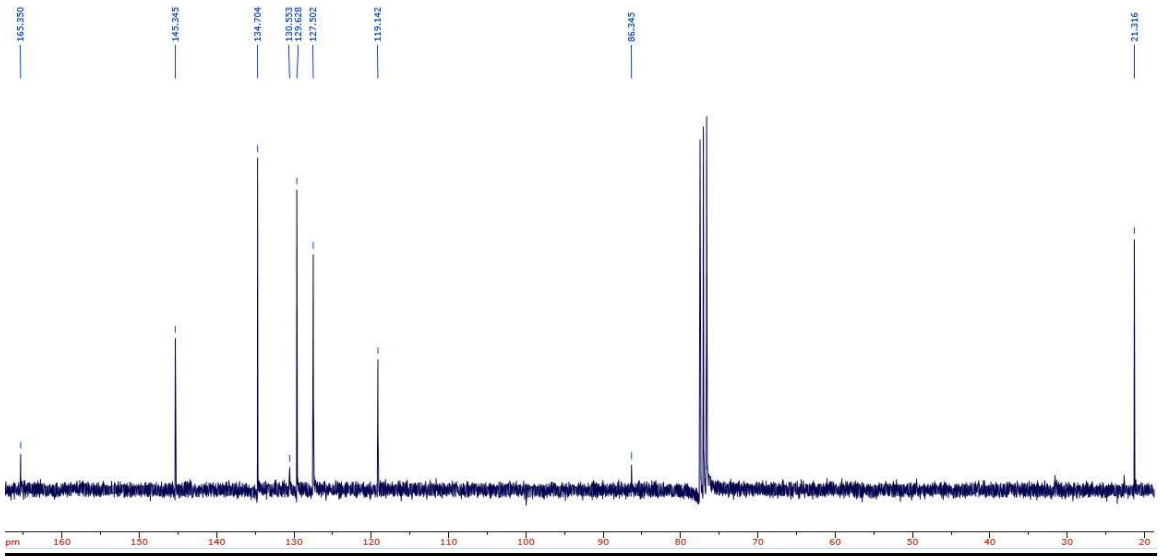


Spectrum 66 - ^{1}H NMR of 4-bromo-3-(2-bromophenyl)sydnone

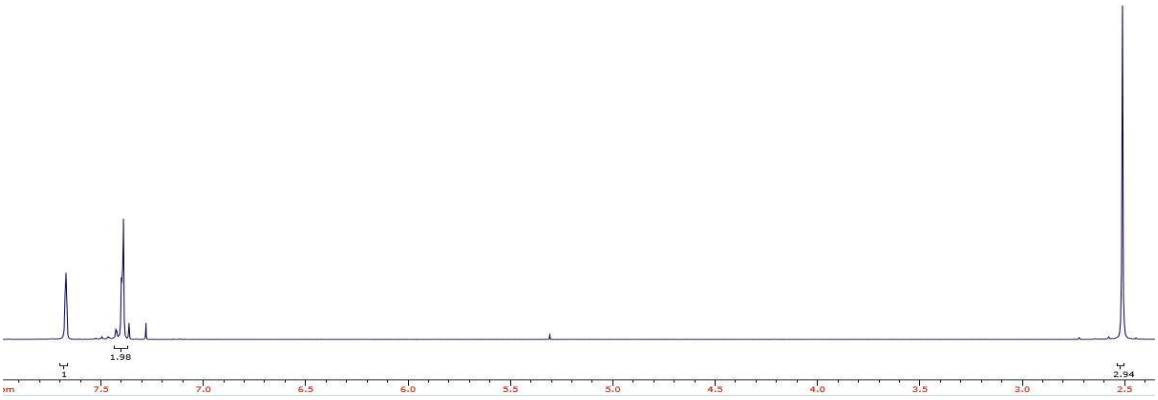


Spectrum 67 - IR (KBr) of 4-bromo-3-(2-bromophenyl)sydnone

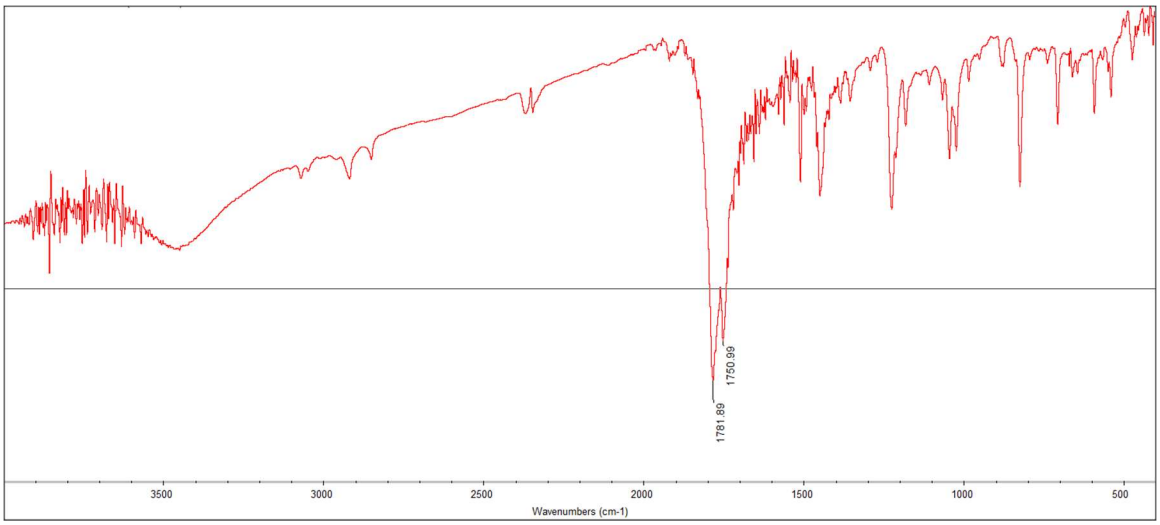
4-bromo-3-(4-methyl-2-bromophenyl)sydnone (**57**)



Spectrum 68 - ^{13}C NMR of 4-bromo-3-(4-methyl-2-bromophenyl)sydnone

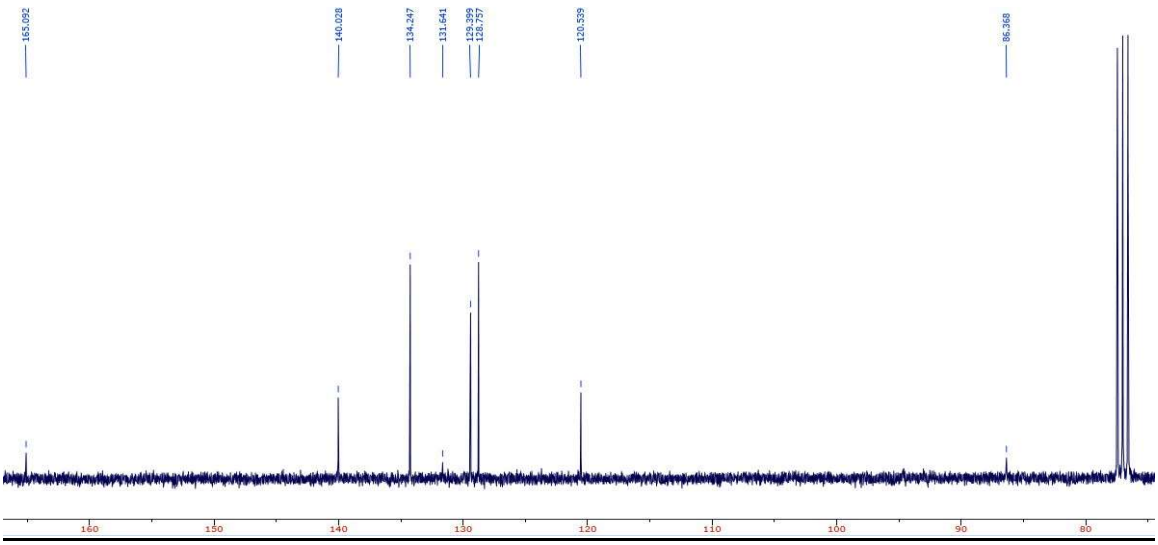


Spectrum 69 - ^{1}H NMR of 4-bromo-3-(4-methyl-2-bromophenyl)sydnone

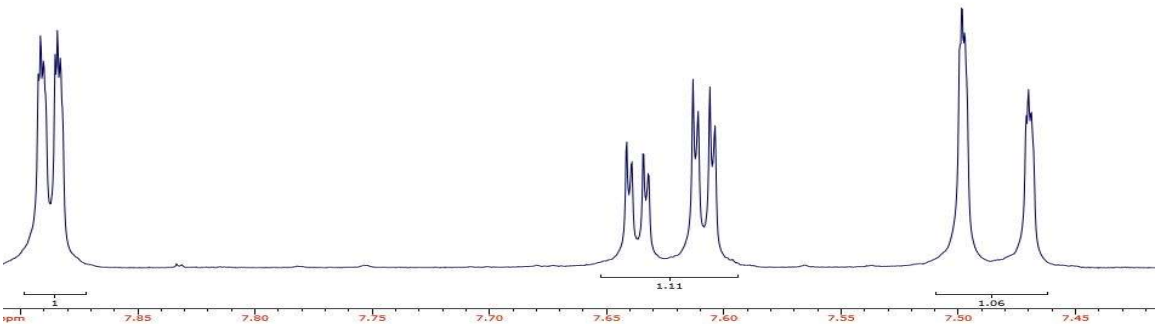


Spectrum 70 - IR (KBr) of 4-bromo-3-(4-methyl-2-bromophenyl)sydnone

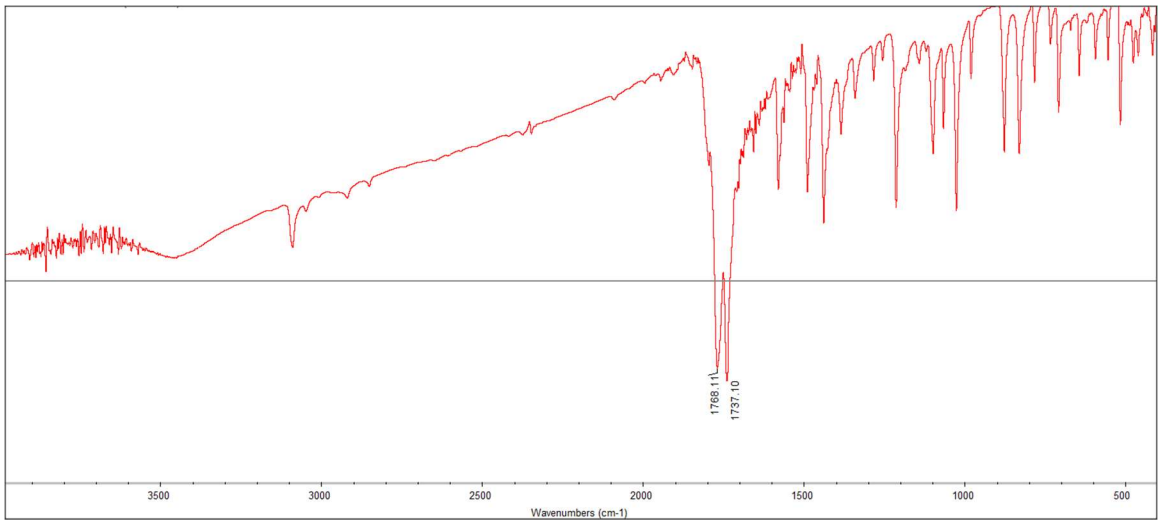
4-bromo-3-(4-chloro-2-bromophenyl)sydnone (**58**)



Spectrum 71 - ^{13}C NMR of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone



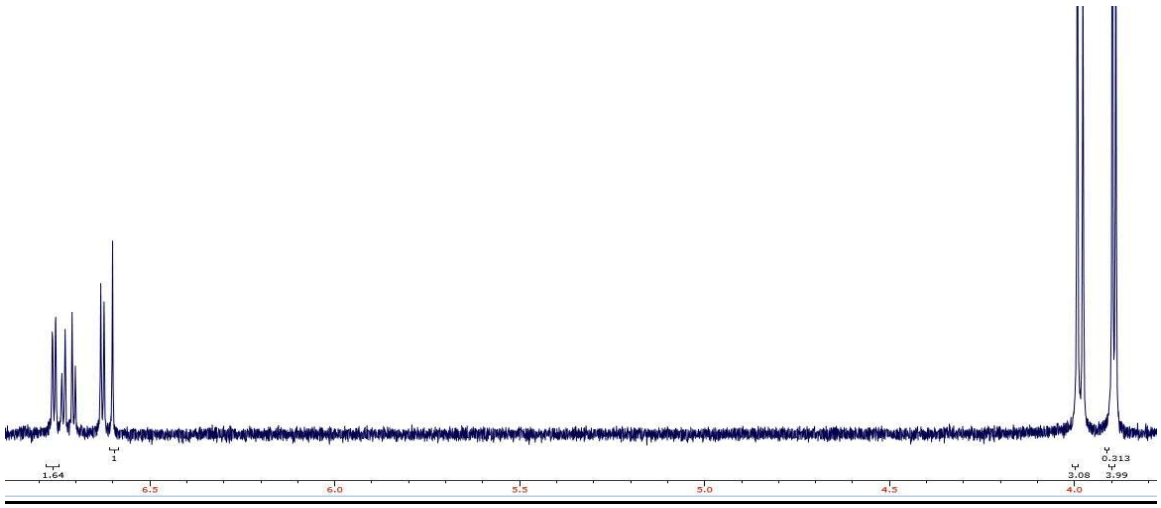
Spectrum 72 - ^{1}H NMR of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone



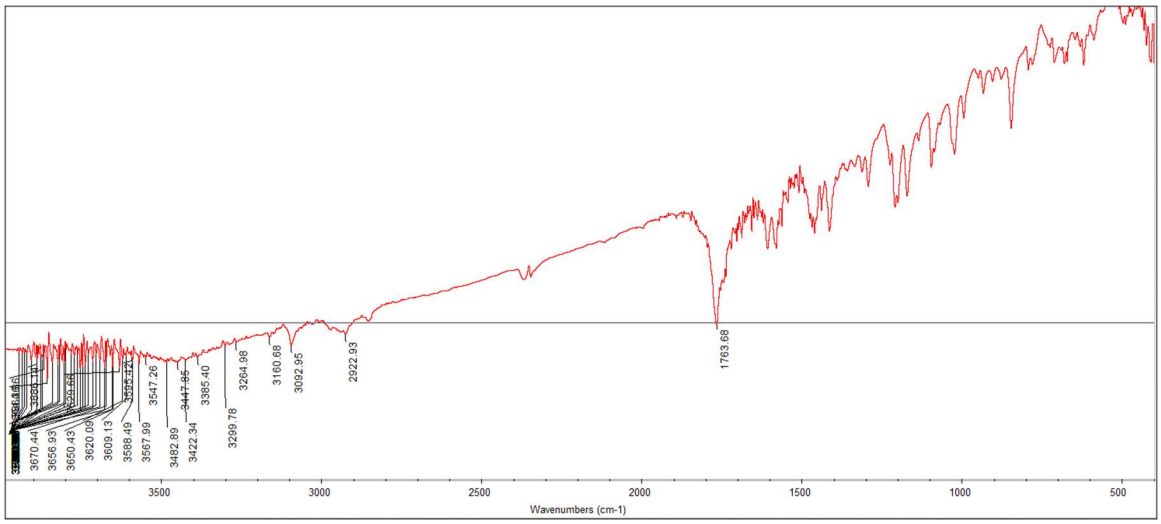
Spectrum 73 - IR (KBr) of 4-bromo-3-(4-chloro-2-bromophenyl)sydnone

VI. 3-(2-bromoaryl)sydnone spectra

3-(3,5-dimethoxy-2-bromoaryl)sydnone (**59**)

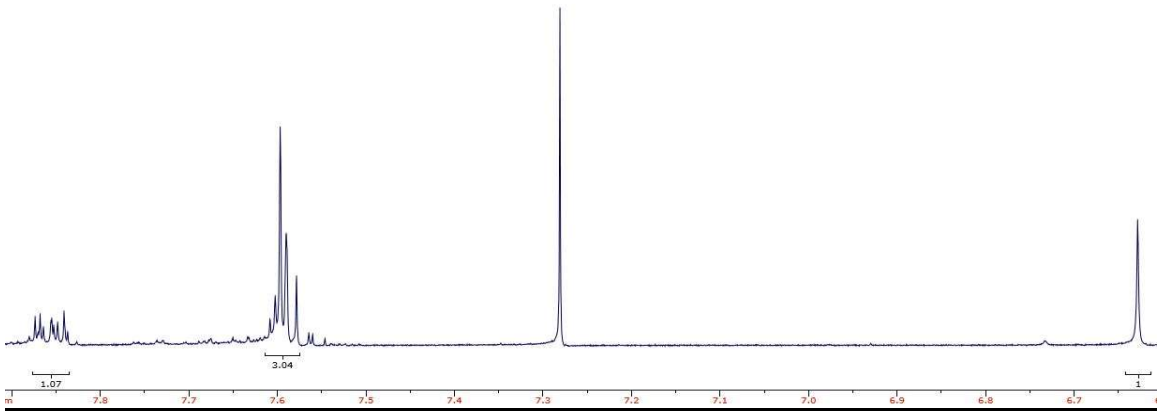


Spectrum 74 - ^{1}H NMR of 3-(3,5-dimethoxy-2-bromoaryl)sydnone

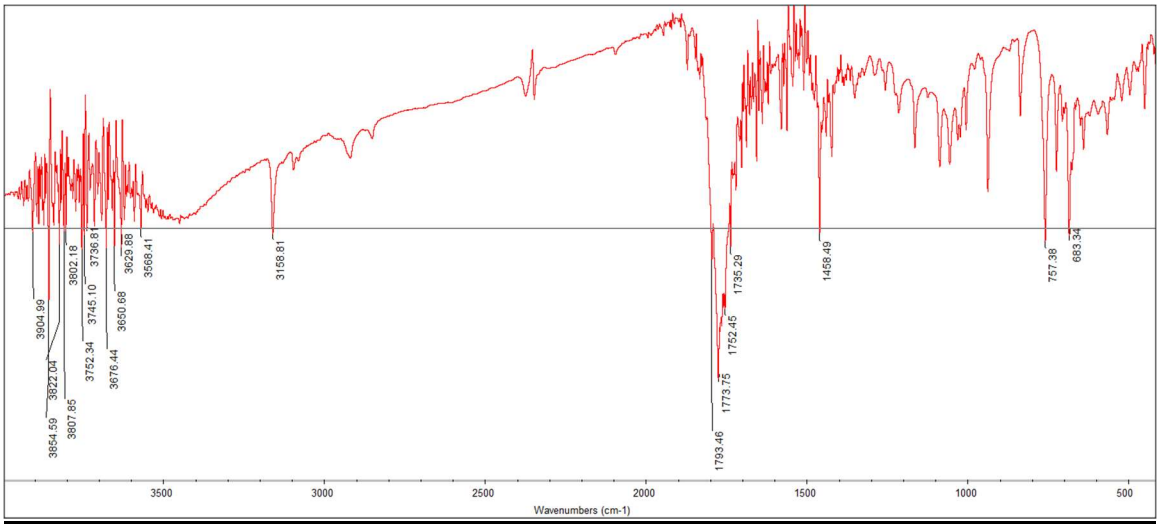


Spectrum 75 - IR (KBr) of 3-(3,5-dimethoxy-2-bromoaryl)sydnone

3-(2-bromophenyl)sydnone (**60**)

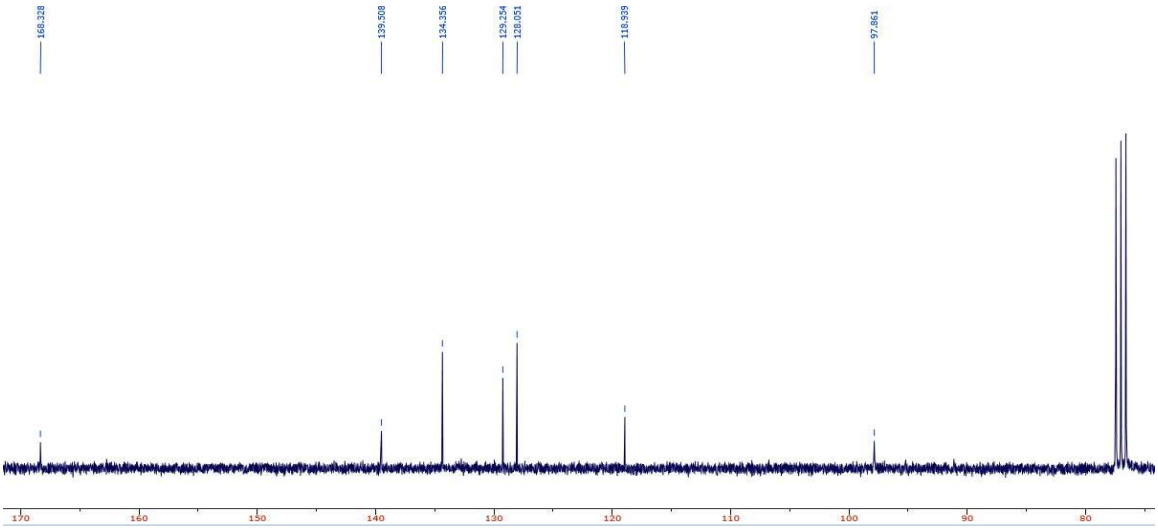


Spectrum 76 - ^{1}H NMR of 3-(2-bromophenyl)sydnone

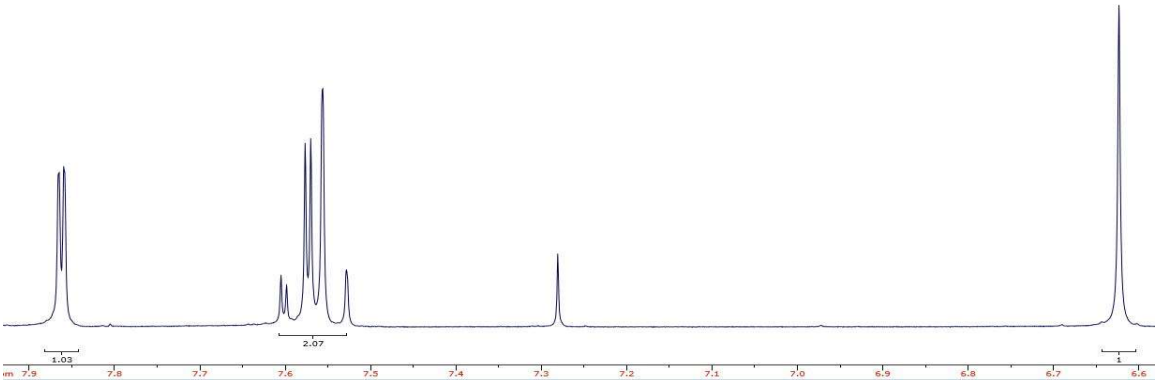


Spectrum 77 - IR (KBr) of 3-(2-bromophenyl)sydnone

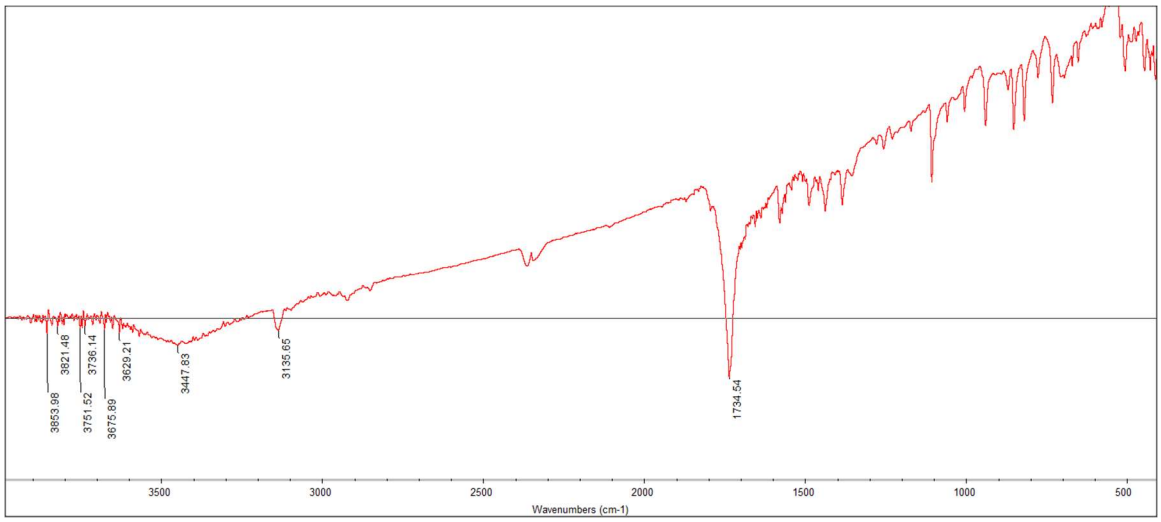
3-(4-chloro-2-bromophenyl)sydnone (**61**)



Spectrum 78 - ^{13}C NMR of 3-(4-chloro-2-bromophenyl)sydnone



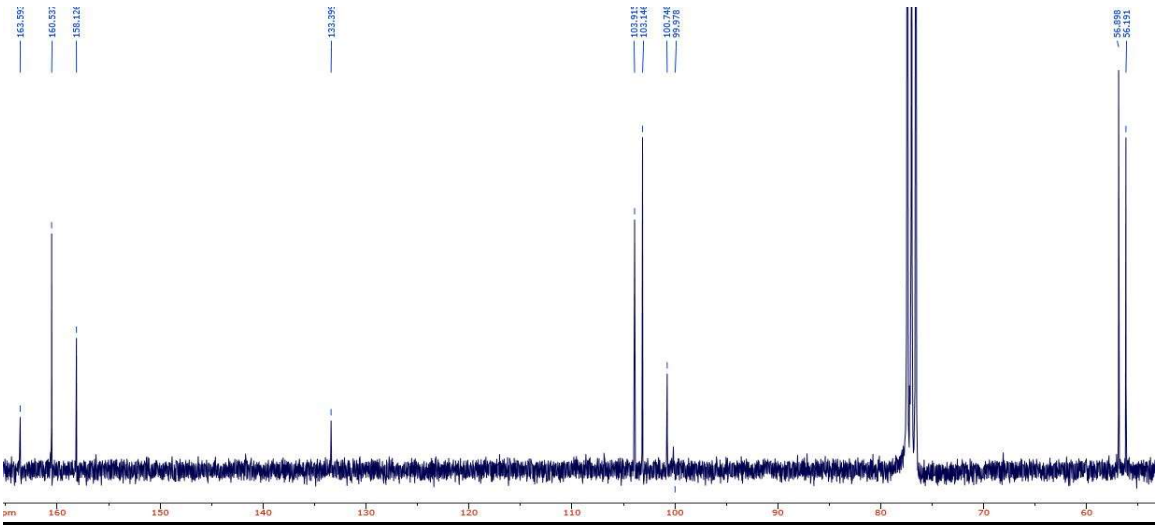
Spectrum 79 - ^{1}H NMR of 3-(4-chloro-2-bromophenyl)sydnone



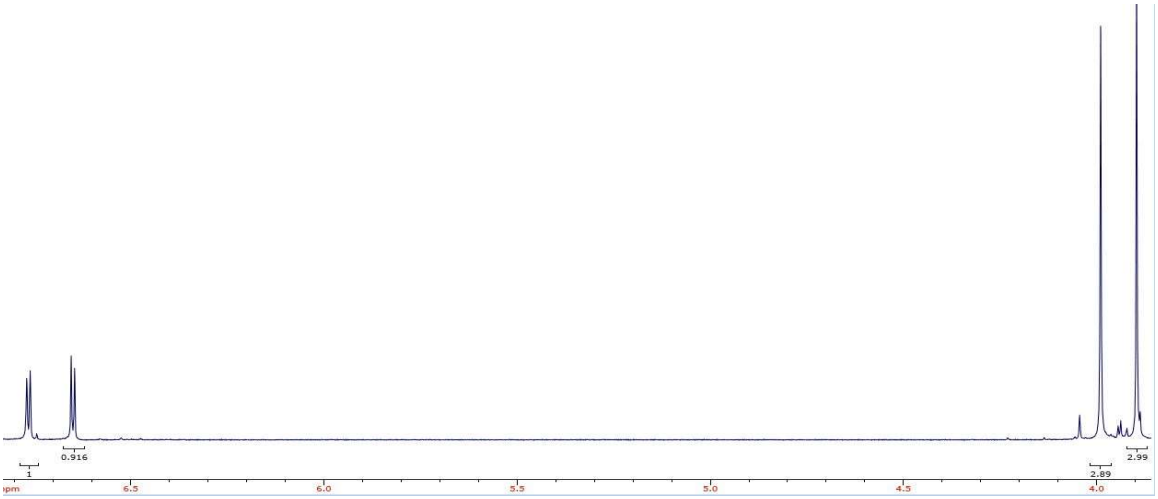
Spectrum 80 - IR (KBr) of 3-(4-chloro-2-bromophenyl)sydnone

VII. 4-chloro-3-(2-bromoaryl)sydnone spectra

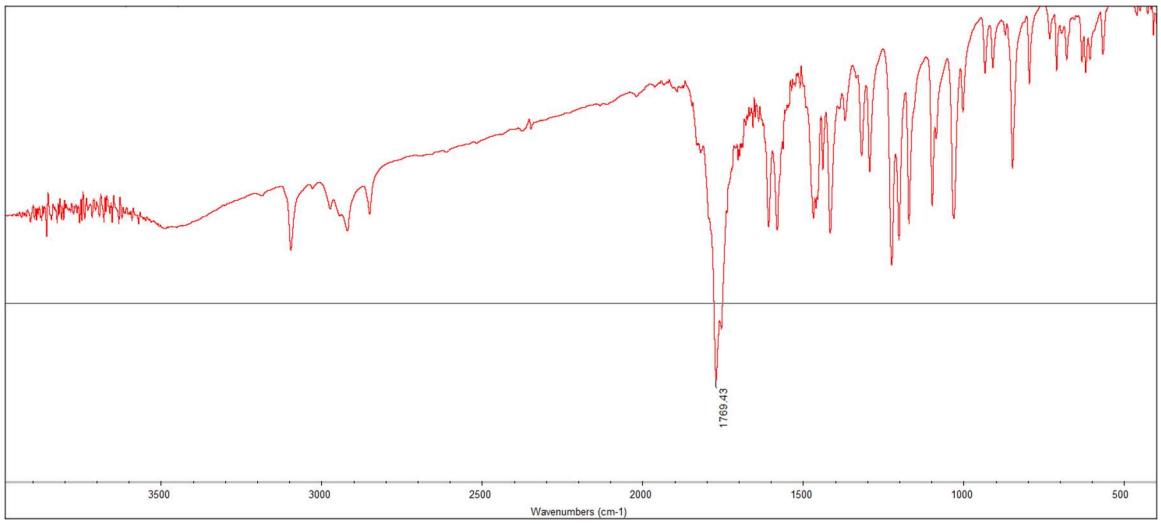
4-chloro-3-(3,5-dimethoxy-2-bromophenyl)sydnone (**62**)



Spectrum 81 - ^{13}C NMR of 4-chloro-3-(3,5-dimethoxy-2-bromophenyl)sydnone

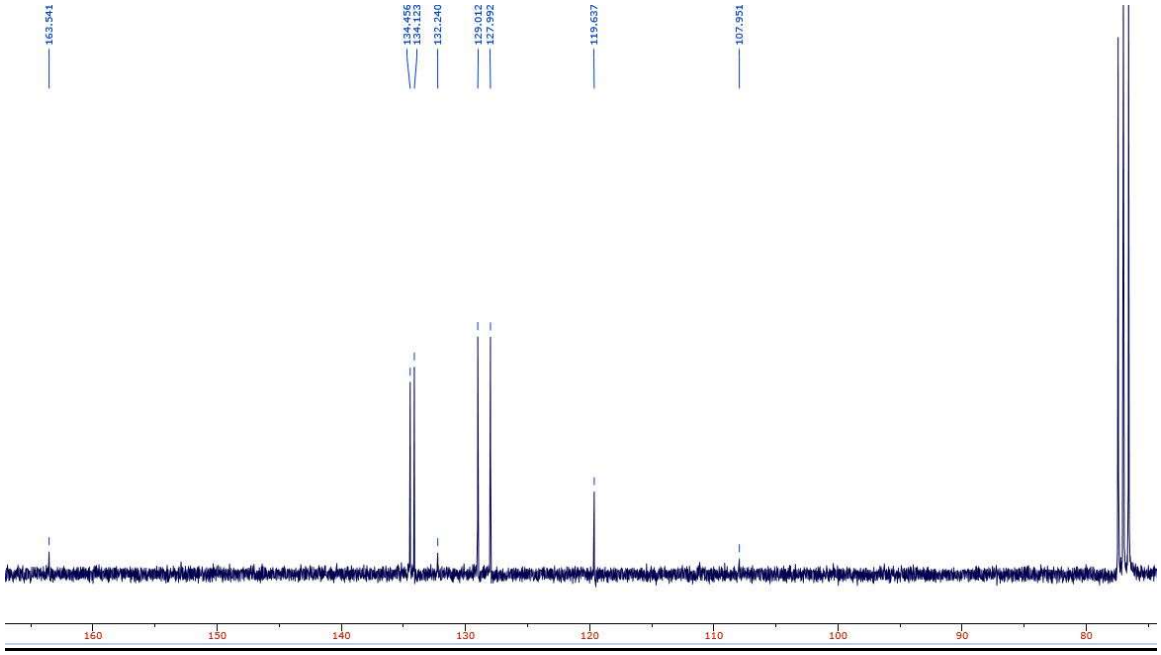


Spectrum 82 - ^{1}H NMR of 4-chloro-3-(3,5-dimethoxy-2-bromophenyl)sydnone

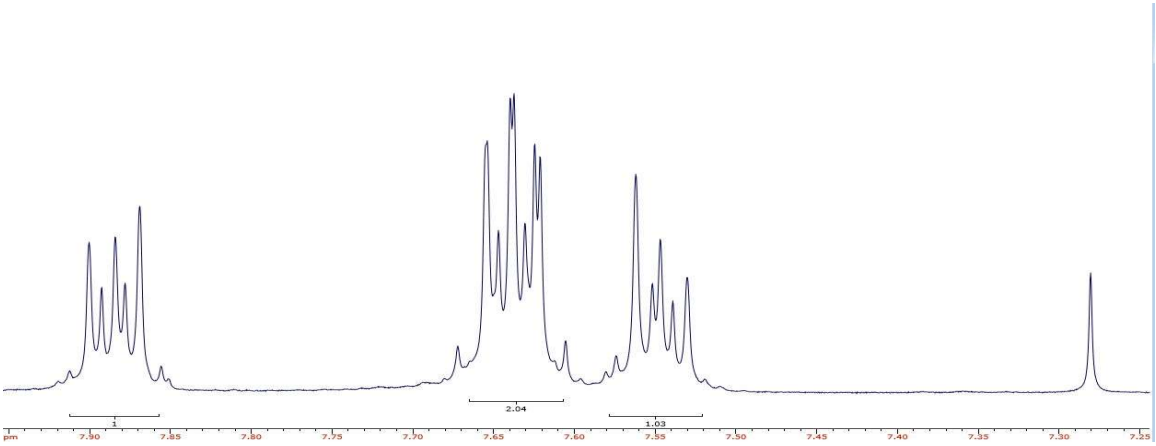


Spectrum 83 - IR (KBr) of 4-chloro-3-(3,5-dimethoxy-2-bromophenyl)sydnone

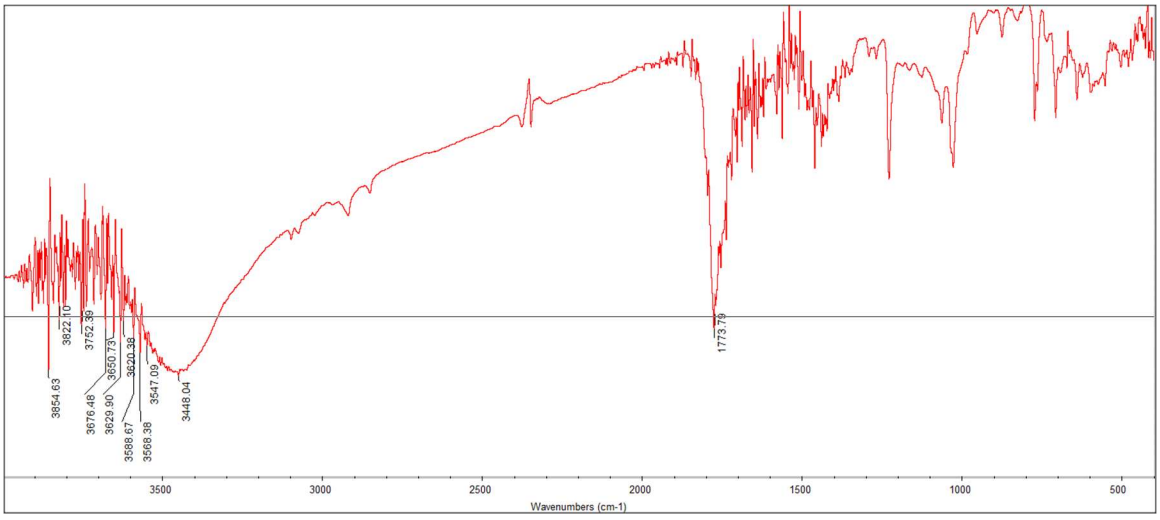
4-chloro-3-(2-bromophenyl)sydnone (**63**)



Spectrum 84 - ^{13}C NMR of 4-chloro-3-(2-bromophenyl)sydnone

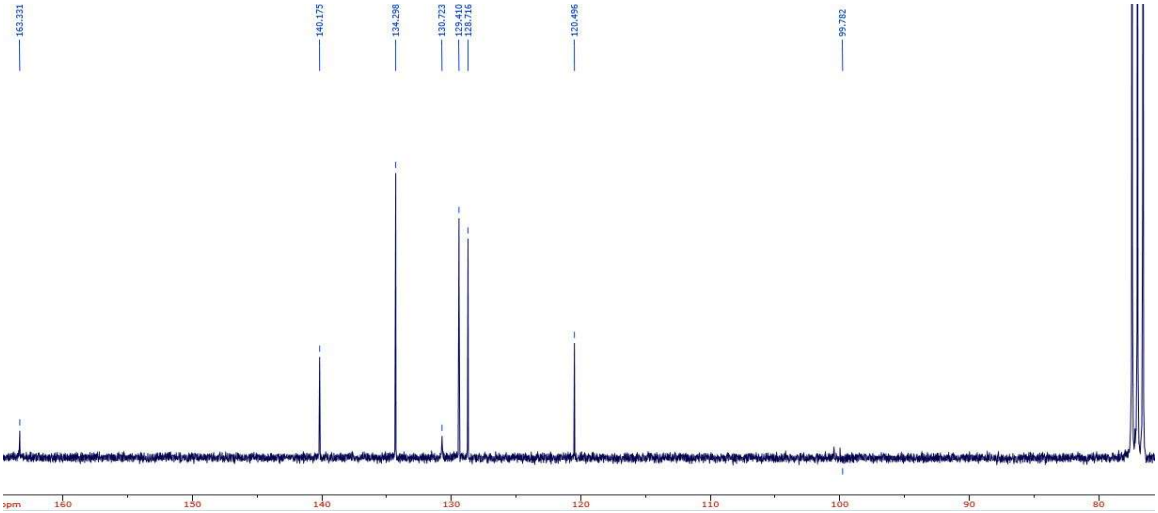


Spectrum 85 - ^{1}H NMR of 4-chloro-3-(2-bromophenyl)sydnone

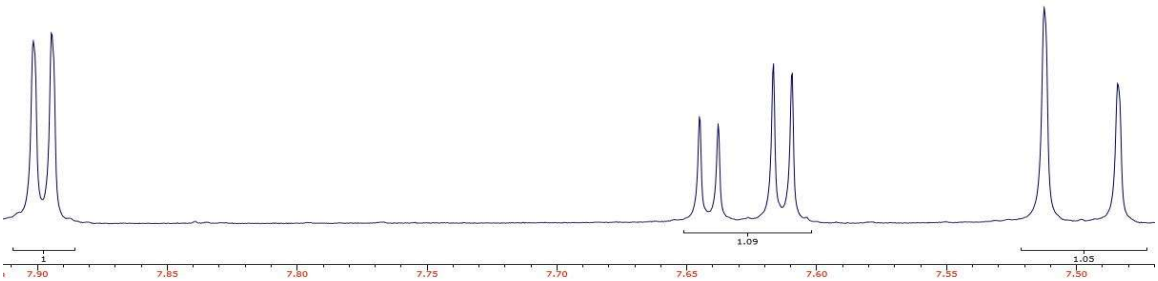


Spectrum 86 - IR (KBr) of 4-chloro-3-(2-bromophenyl)sydnone

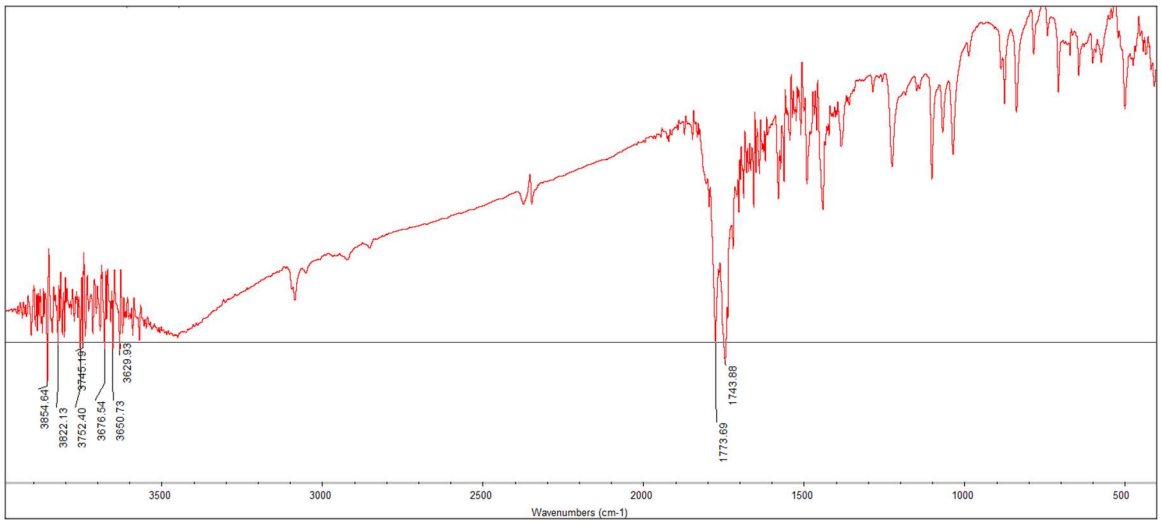
4-chloro-3-(4-chloro-2-bromophenyl)sydnone (**63**)



Spectrum 87 - ^{13}C NMR of 4-chloro-3-(4-chloro-2-bromophenyl)sydnone



Spectrum 88 - ^{1}H NMR of 4-chloro-3-(4-chloro-2-bromophenyl)sydnone



Spectrum 89 - IR (KBr) of 4-chloro-3-(4-chloro-2-bromophenyl)sydnone