IMIDATION OF SILYL ENOL ETHERS USING A NEW HYPERVALENT IODINE REAGENT

A THESIS
SUBMITTED TO THE FACULTY OF
UNIVERSITY OF MINNESOTA
BY

STEVEN ROBERT KOSKI

IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
MASTER OF SCIENCE

Thesis Adviser: Dr. Viktor Zhdankin

August 2014

ACKNOWLEDGEMENTS

First of all, I would like to thank Dr. Viktor Zhdankin for allowing me to pursue research in his well-equipped organic chemistry lab and for all of his excellent guidance as a research adviser throughout the past two years. His advice and expertise in hypervalent iodine chemistry has truly been remarkable.

I would like to thank Andrey Maskaev for helping me learn new organic chemistry techniques as I first entered Dr. Zhdankin's lab. His instruction was invaluable during my first year as I became accustomed to many new organic chemistry practices.

Next, I wish to thank Dr. Akira Yoshimura who has been instrumental with his hands-on teaching within the research lab. My research would not have progressed as far as it had without his expert guidance and ability to find answers to my many daily questions.

I would also like to thank the other members of Dr. Zhdankin's research group, both past and present, including Dr. Mekhman Yusubov, Dr. Nicholas Jones, Brent Kastern, Scott Klasen, Jonathan Fuchs, Anthony Todora, and Paul Vue for their collaboration. I also wish to thank Dr. Viktor Nemykin for helping with X-ray crystallography analysis.

Lastly, I wish to thank the University of Minnesota Duluth and the Chemistry Department as a whole for allowing me the opportunity pursue graduate studies.

This work was supported through a research grant from the National Science Foundation (CHE 1262579)

DEDICATION

This thesis is dedicated to my beloved parents, Jack and Kerry Koski, as none of this would have been possible without their love and support.

ABSTRACT

Hypervalent iodine compounds have been known for their remarkable reactivity as powerful reagents in the field of organic chemistry. They present a class of compounds that are typically benign when compared to their metal containing counterparts and also allow ease of handling. The focus of this research has been to find a new way to produce an imide transfer reaction using hypervalent iodine reagents. Two new reagents were discovered during the process and one was chosen as the focus reagent for the imide transfer. Optimized conditions were found to produce the functional group transfer using the novel mu-oxo type reagent with good yields, which varied depending on the starting substrate. The desired products from the reaction are important because some of the compounds have found possible application in the treatment of certain diseases. This research presents an interesting look into a relatively undeveloped area of hypervalent iodine chemistry.

TABLE OF CONTENTS

LIST OF TABLES

Table **Page**

LIST OF SCHEMES

Scheme **Page**

LIST OF ABBREVIATIONS

AcOOH = peracetic acid

AcOH = Acetic Acid

Alk = alkyl

Ar = aryl

d = doublet

dd = doublet of doublets

DIB = (diacetoxyiodo)benzene

DMP = Dess-Martin Periodinane

DMSO = dimethyl sulfoxide

h = hour

Hz = hertz

ESI-HRMS = electrospray ionization-high resolution mass spectrometry

IBX = 2-iodoxybenzoic acid

IR = infrared

IUPAC = International Union of Pure and Applied Chemistry

min = minute

mL = milliliter

mmol = millimole

NMR = nuclear magnetic resonance

PIFA = (bis(trifluoroacetoxy)iodo)benzene

ppm = parts per million

TBHP = tert-butyl hydroperoxide

THF = tetrahydrofuran

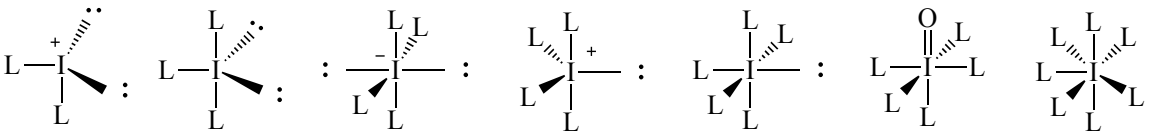
TMS = trimethylsilane

q = quartet

CH. 1 INTRODUCTION

1.1 Background and Classification of Hypervalent Iodine

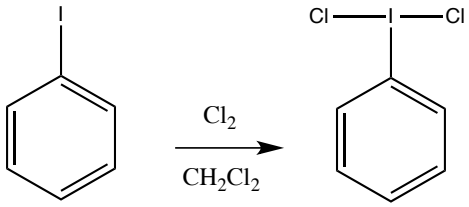
Iodine is a very unique element. When looking at the periodic table, one can note that it is found toward the lower middle portion on the right side with other p-block elements. It can be described as the heaviest non-radioactive element that is a non-metal, and other important characteristics include it being the least electronegative and most polarizable of the halogens.[1,2] It is because of these unique properties that iodine can exist in compounds with oxidation states that can vary from +3 (on the left **1**) to +7 (on the right **2**) as seen in **Scheme 1** below.



1 **2**

Scheme 1[1]

The first hypervalent iodine compound was first discovered in 1886 by C. Willgerodt, who reacted iodobenzene with chlorine gas to give the desired (dichloroido)benzene **3** in **Scheme** 2.[3]



3

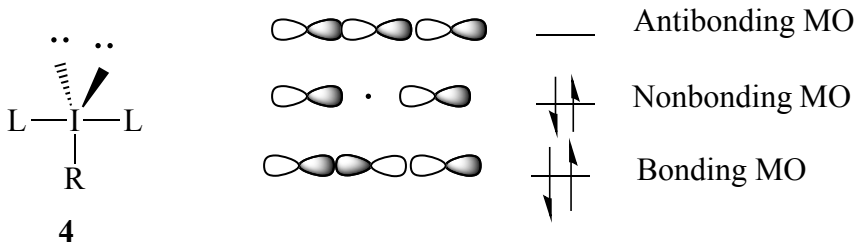
Scheme 2

During that period of time many new hypervalent iodine compounds, including iodosylbenzene, (diacetoxyiodo)benzene, and 2-idoxybenzoic acid (IBX) were

discovered characterized and then the area of hypervalent iodine chemistry seemed to slow.[4] Although hypervalent iodine compounds have been known since the 19th century, it wasn't until recently hypervalent iodine chemistry has seen a large resurgence in interest with countless new reagents such as the famous Dess-Martin reagent for the oxidation of alcohols, along with countless journal articles and a number of books being published.[1,4,5,6,7,8,9,10] These compounds are of great importance because hypervalent iodine containing compounds can be used for a variety of reactions such as C-C bond formations, iodinations, and oxidations, while maintaining a benign environmental character and easy commercial availability compared to other reagents containing heavy metals such as palladium, chromium or lead.[1,2,10]

The term hypervalent comes from the ability of the iodine in the molecule to exceed its normal octet of eight valence electrons, commonly containing ten or twelve electrons instead.[11] **Scheme 3**[1] below depicts a general structure of a hypervalent iodine molecule **4**. The bonding in a hypervalent iodine-containing molecule is quite unique. Two electrons reside in bonding and non-bonding molecular orbitals, while the antibonding orbitals remain empty. This gives rise to what is known as a three-center, four-electron bond (3c-4e) where two electrons are delocalized to the ligands giving rise to a charge distribution of approximately +1 on the central iodine atom and -0.5 on each of the ligands.[1] Because of this special bonding, the iodine to ligand (L) bonds are longer and weaker, thus giving important reactive character to the molecule in consideration. A normal covalent bond exists between iodine and the least electronegative element, depicted in the **Scheme 3** as R, and the molecule takes on a distorted, trigonal

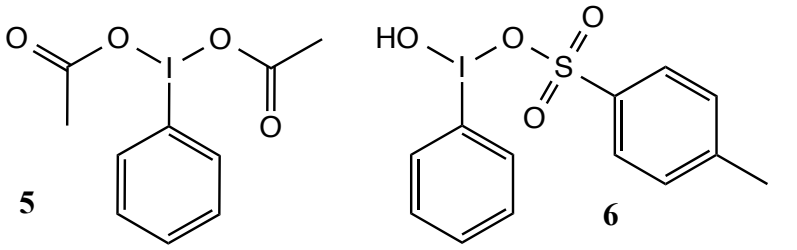
bipyramidal geometry with an over all T-shape[1].



4

Scheme 3[1]

Most commonly, iodine (III) and iodine (V) reagents are used in organic chemistry today and some examples be seen in **Schemes 4** and **5** respectively below.

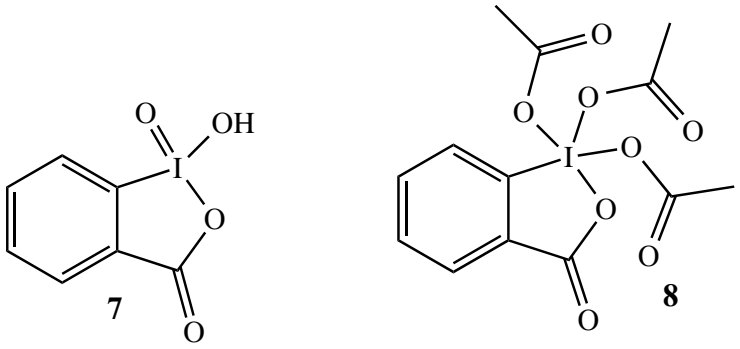


5 (Diacetoxyiodo)benzene (DIB)

6 Hydroxy(tosyloxy)iodobenzene (Koser's Reagent)

Scheme 4

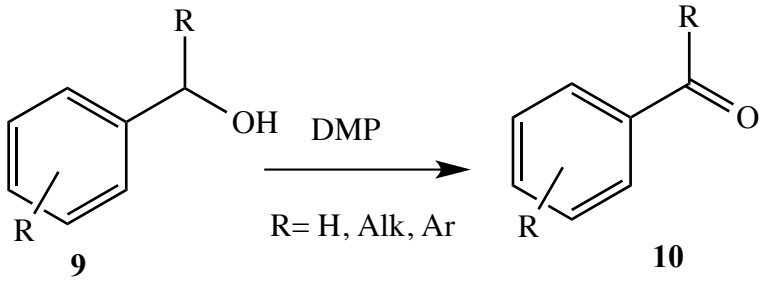
(Diacetoxyiodo)benzene **5** and Koser's Reagent **6** are very common λ^3-iodanes and have found use in such reactions as oxidations of olefins, ring expansions and contractions, synthesis of iodonium salts, and oxidations.[12] The IUPAC nomenclature uses the λ^n notation to designate a heteroatom in a non-standard valence state n.[1]



2-Iodoxybenzoic Acid (IBX) Dess-Martin Periodinane

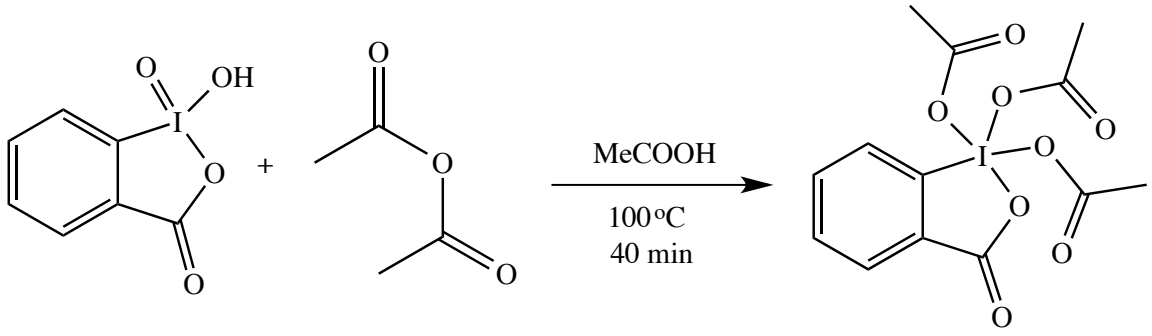
Scheme 5

Two examples of λ^5-iodanes, 2-iodoxybenzoic acid (IBX) **7** and its derivative Dess-Martin Periodinane (DMP) **8**, are shown in **Scheme 5**. These two reagents are most commonly used as efficient oxidants in organic chemistry with the most common application being the oxidation of alcohols **9** to their carbonyl derivative **10**, **Scheme** 6.[10]



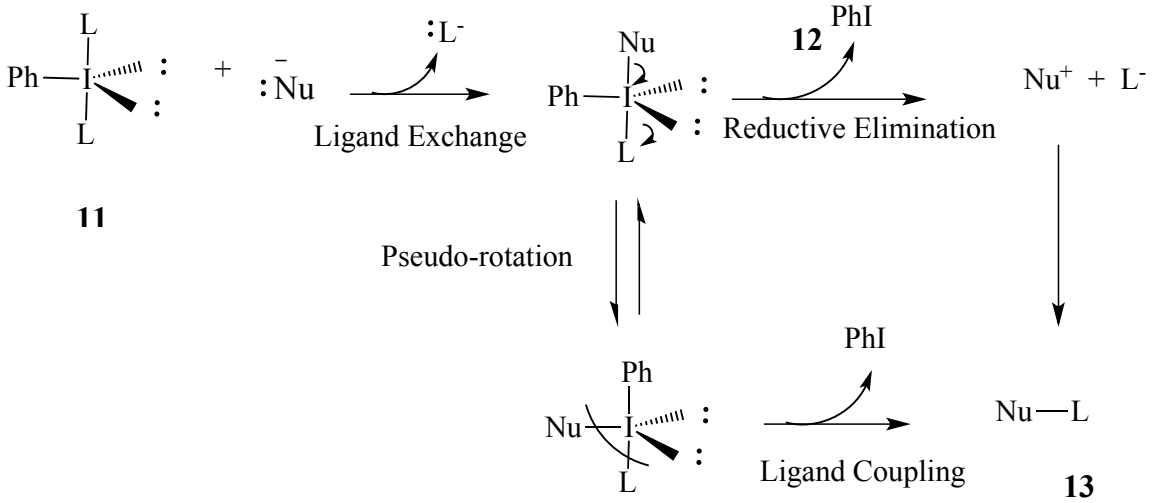
Scheme 6[10]

DMP was synthesized by heating IBX in an acetic anhydride/acetic acid mixture as shown in **Scheme** 7.[10,13] The synthesis of DMP was found to be extremely important because of its increased solubility compared to IBX, which is insoluble in most organic solvents and water, besides dimethyl sulfoxide (DMSO).[10,13]



Scheme 7

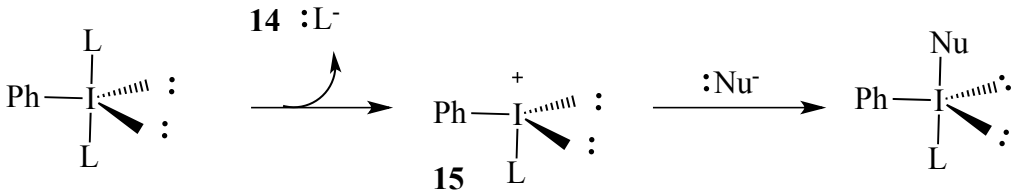
Since the focus of this thesis is on λ^3-iodanes, only the reactivity of this hypervalent iodine species will be discussed. The reactivity of λ^3-iodanes can be seen in a more detailed mechanism in **Scheme 8** and take into account the special characteristics of the iodine-ligand bonds and can be viewed as a ligand exchange process.[1] A nucleophile attacks the iodine center in **11** causing exchange of one of the ligands. This step is then followed by immediate reductive elimination of iodobenzene **12**, or pseudo rotation to a more favorable conformation followed by reductive elimination of iodobenzene **12** to



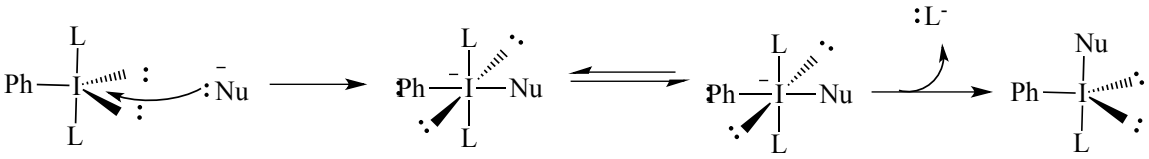
Scheme 8[1]

give the coupled nucleophile-ligand product **13**. This is a very favorable process as

iodobenzene **12** is a very good leaving group, approximately a million times greater than triflate.[1] **Schemes 9** and **10** depict the two possible pathways of reaction. In **Scheme 9**, the dissociative pathway, a dissociated ligand **14** creates a positive iodine species **15**, which is then attacked by a nucleophile. In the **Scheme 10**, the associative pathway, a nucleophile attacks the partially positive iodine center, followed by pseudo rotation and elimination of a ligand.



Scheme 9[1]



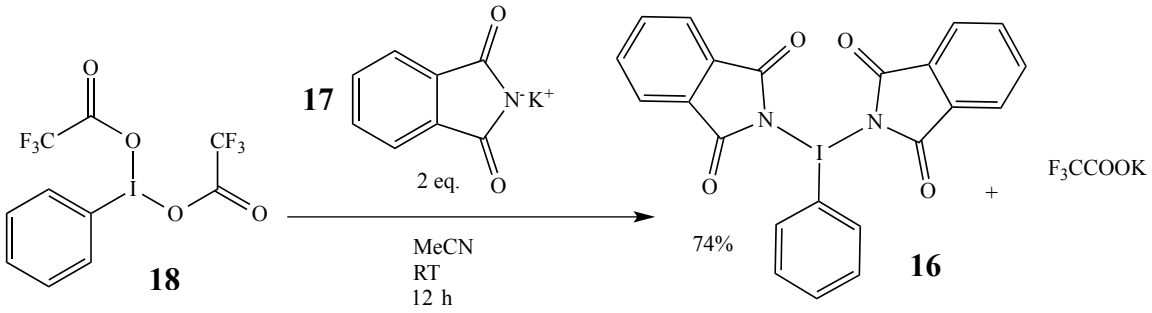
Scheme 10[1]

The next parts of this chapter will deal specifically with hypervalent iodine and imide chemistry as it relates closely to the focus of this research.

1.2 Hypervalent Iodine and Imides

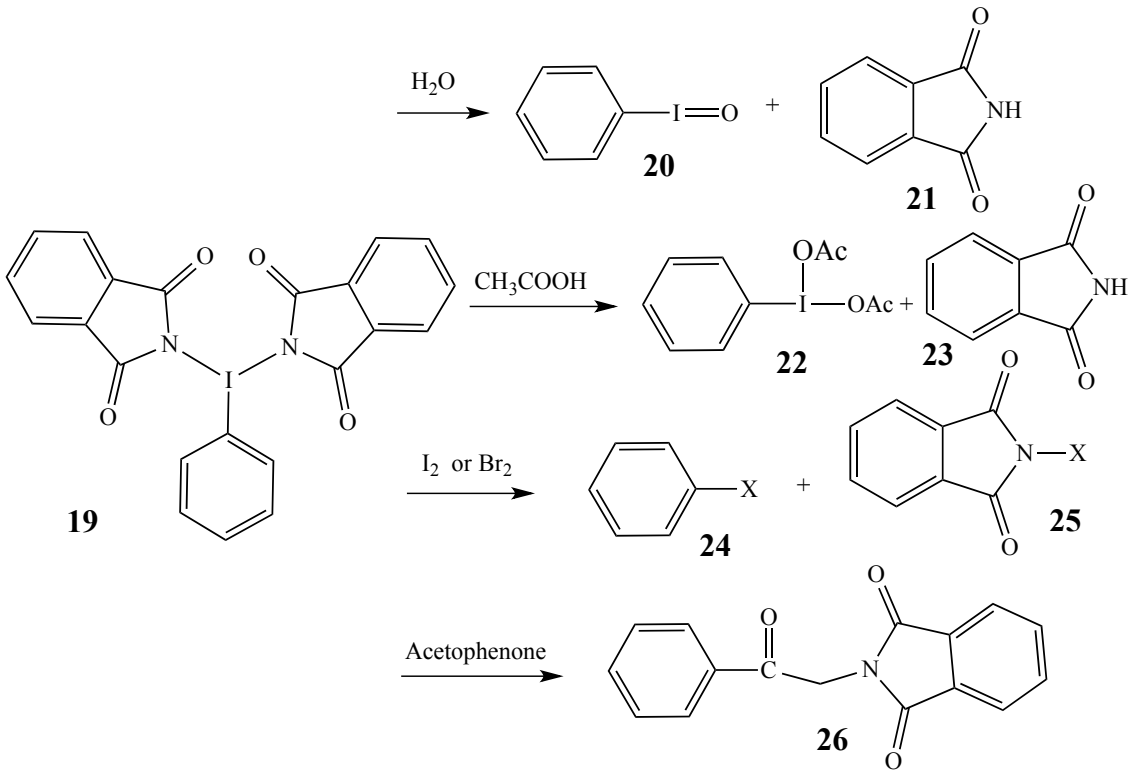
As previously stated, λ^3-iodane compounds have been known for quite awhile, but aryl iodine(III) compounds containing two nitrogen bonds weren't discovered until 1983 when the research group of Varvoglis discovered bis(phthalimidate) **16**, through a ligand exchange reaction of potassium phthalimidate **17** with

[bis(trifluoroacetoxy)iodo]benzene) (PIFA) **18** in acetonitrile as shown in **Scheme 11**.[14]



Scheme 11

The compound was noted to be very insoluble in typical organic solvents and was characterized through elemental analysis and infrared spectroscopy. Afterwards, the bis(phthalimidate) **16** was shown to have interesting reactive properties. As described in the same article, **Scheme 12** demonstrates various reactions that were possible between water, acetic acid, molecular iodine and bromine, and also acetophenone with the new bis(phthalimidate) **16**.[14] In water the bis(phthalimidate) reagent **19** is hydrolyzed slowly and thus converted to idosylbenzene **20** and phthalimide **21** over time. When reacted with acetic acid, the bis(phthalimidate) **19** undergoes ligand exchange to give (diacetoxyido)benzene **22** and phthalimide **23** by the usual ligand exchange mechanism previously discussed for λ^3-iodane compounds.

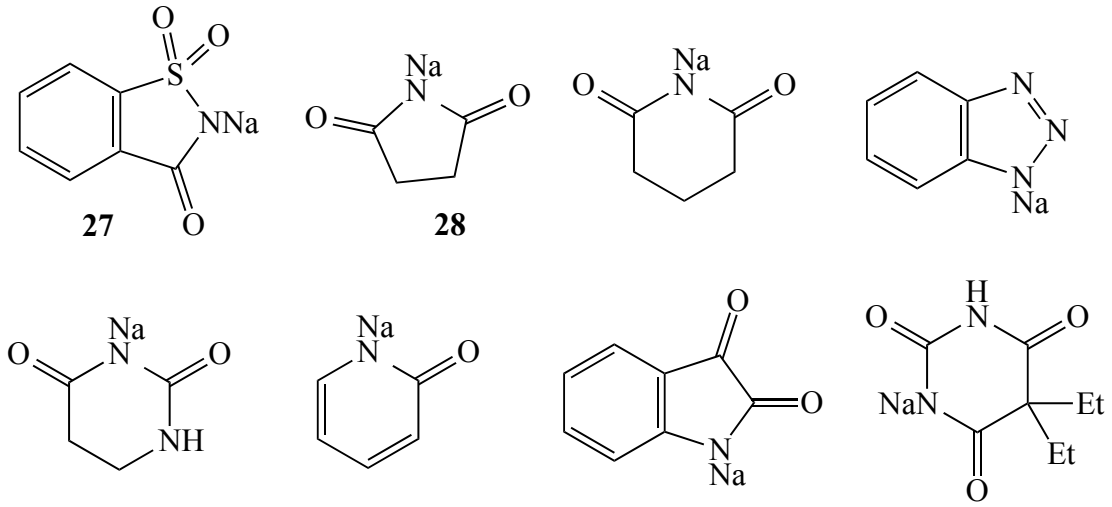


Scheme 12[14]

When reacted with elemental iodine or bromine, the reagent affords iodobenzene **24** and either *N*-bromo- or *N*-iodophthalimide **25**. Interestingly, when bis(phthalimidate) was reacted with acetophenone at high temperatures in carbon tetrachloride, *N*-phenacylphthalimide **26** was found to be produced in low yields.

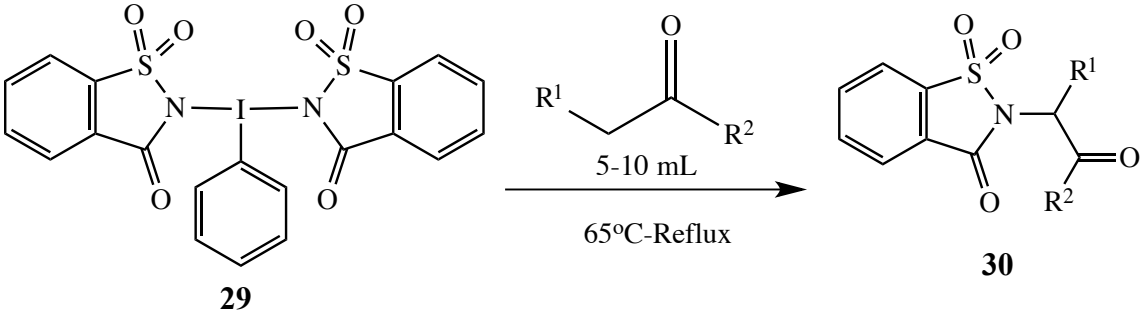
In the same year, the research group of Varvoglis later expanded on the project and created a variety of phenyl iodine(III) bisimidates using the sodium salts of several more imides shown in **Scheme 13**[15]. Some imides used in the general synthesis of **Scheme 13** included saccharin **27** and succinimide **28**. As before, the resulting compounds were typically insoluble in ordinary organic solvents and were characterized by infrared spectroscopy, melting point, and elemental analysis. Similar reactions as found in

Scheme 12 were applied once again with similar results.



Scheme 13

A year later, the same group reported on the reaction of (disaccharinyliodo)benzene **29** with various ketones as shown in **Scheme 14** to afford the corresponding α-saccharin derivatives **30**.[16]



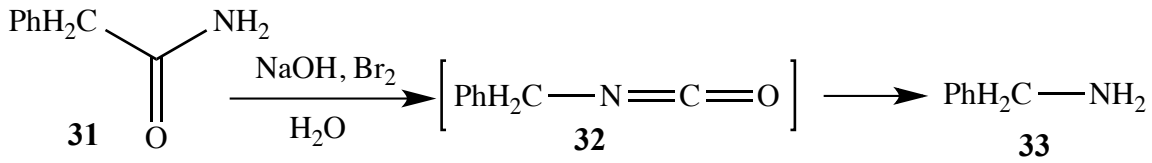
Scheme 14

The reaction was carried out using 1 equivalent of the (disaccharinyliodo)benzene **29** 5-10 mL of the ketone, which was used neat as a solvent. A total of seven examples were shown with yields ranging from 18-75%, however acetophenones containing electron-withdrawing groups were found to be unreactive. The authors hypothesized that this

reaction takes place via a free-radical mechanism.

1.3 Hofmann Rearrangement of Phthalimide

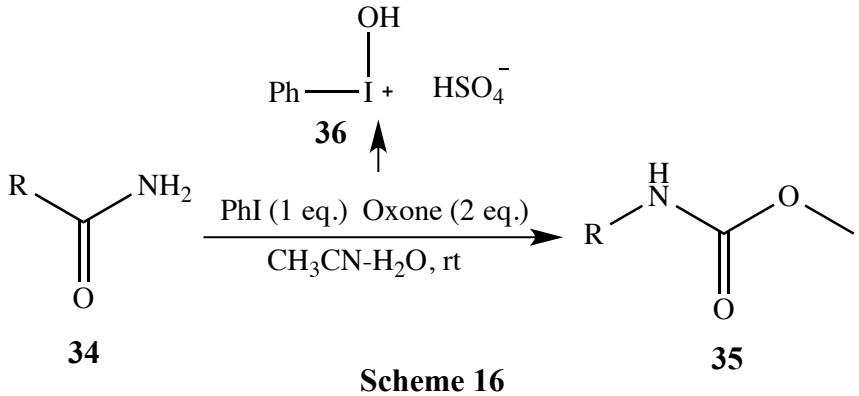
Another interesting reaction utilizing imides and hypervalent iodine is known as the Hofmann Rearrangement. The Hofmann Rearrangement is a useful reaction that traditionally allows for the conversion of an amide (benzyl amide **31**) in a basic solution containing elemental bromine into a carbamate **32** and followed decarboxylation to give the respective amine **33** as shown in **Scheme 15**.[17]



31 **32** **33**

Scheme 15[17]

In 2010, Zhdankin et al. reported that alkyl carboxamides **34** could be converted to their corresponding amines **35** through the Hofmann Rearrangement by using an in situ generated hypervalent iodine species $PhI(OH)^+$ **36** from Oxone and iodobenzene in an aqueous acetonitrile solution as shown in **Scheme 16** with excellent yields (75-97%).[17]



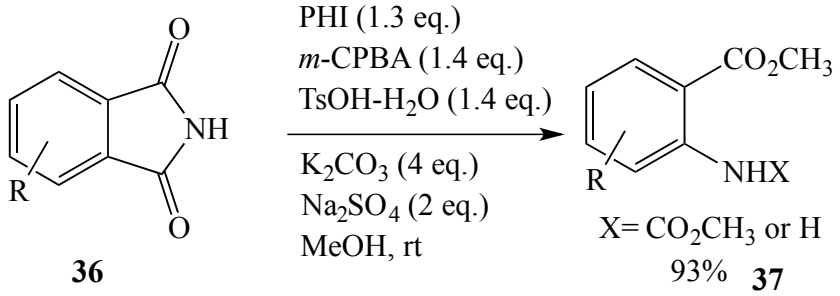
36

34 **35**

Scheme 16

In 2012 Togo et al. described the Hofmann-type reaction of phthalimides **36**, as well as

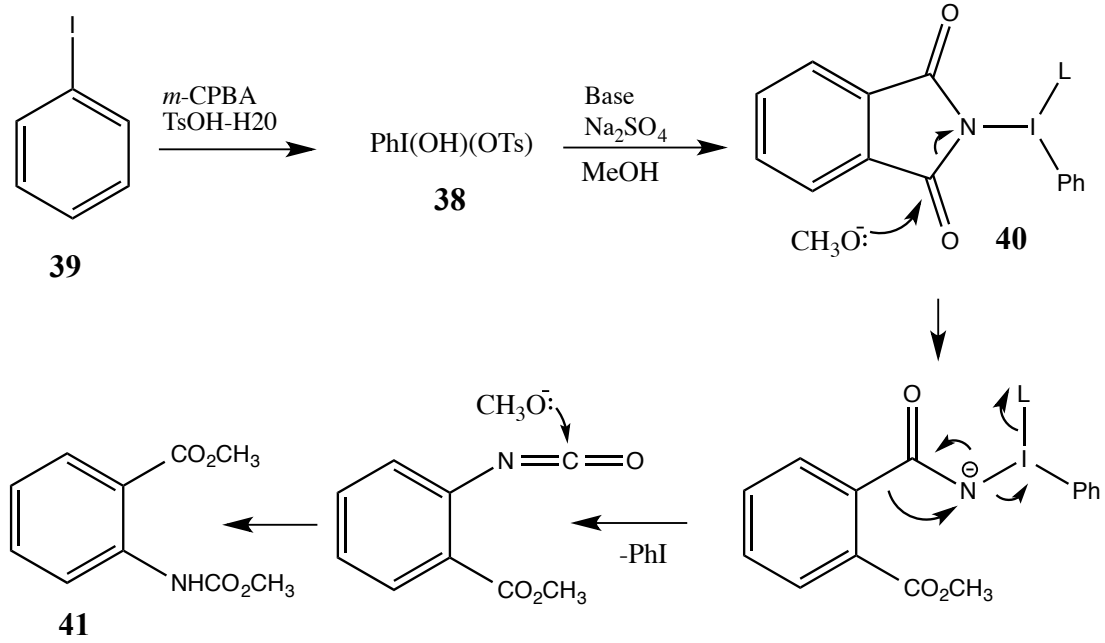
other various aliphatic imides, as shown in **Scheme 17** to afford the corresponding anthracilic and amino acid derivatives **37** in good yields.[18]



36 **37**

Scheme 17[18]

The reaction is proposed to proceed through an in situ generated iodine(III) reagent **38** that is created through the reaction of iodobenzene **39**, *m*-CPBA, and *p*-toluenesulfonic acid.[18] The generated Koser's reagent **38** reacts in a basic solution with the imide to afford an imide-combined hypervalent structure **40**. Reaction with methanol allows for ring opening, followed by rearrangement and leaving of iodobenzene. The desired



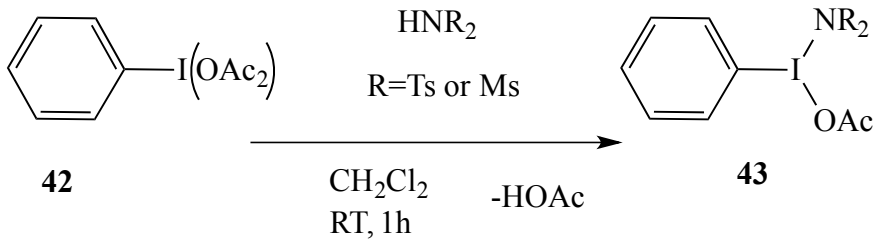
39 **38** **40** **41**

Scheme 18

carbamate **41** is achieved by further reaction with an alcohol. The final products from Hofmann-type rearrangements have important use in the pharmaceutical industry.[17,18,19]

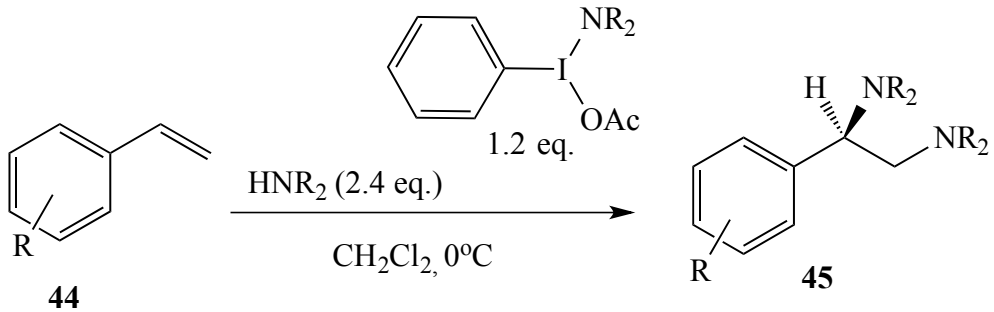
1.4 Metal-Free Diamination of Styrenes

Carbon-nitrogen bond formation was further explored by the Muniz research group through the reaction of an iodine(III) reagent containing a bissulfonimide moiety with various alkenes.[20,21] This paralleled previous diamination reactions that utilized palladium, thallium, mercury, or copper in catalytic amounts.[21]



Scheme 19

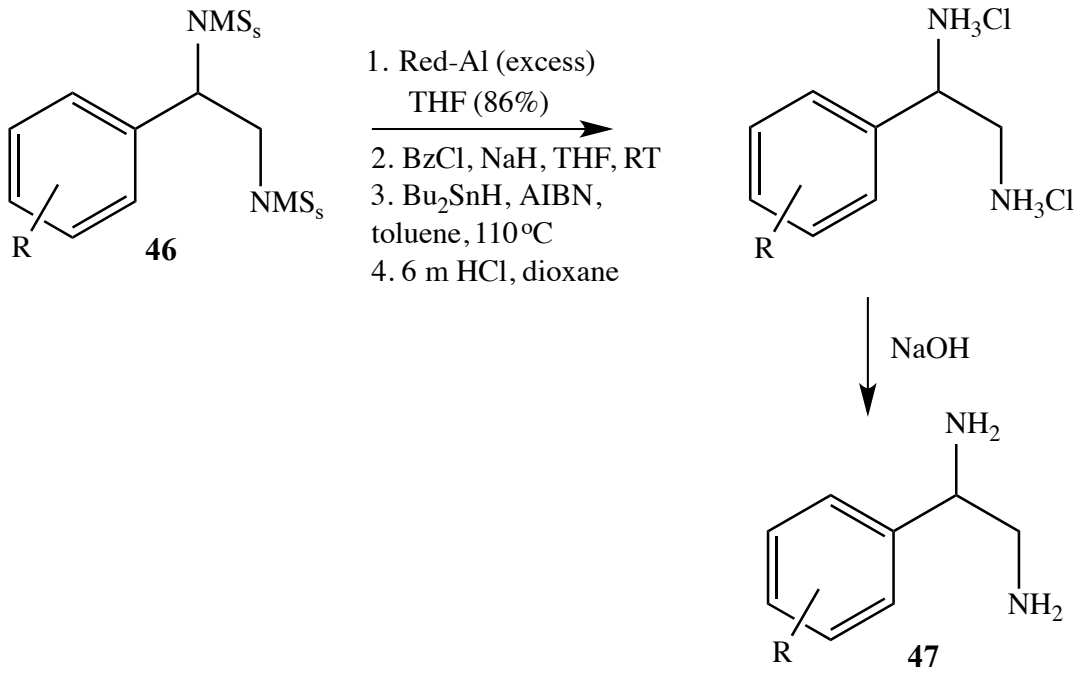
The reaction of (diacetoxyiodo)benzene **42** with a bissulfonimide in **Scheme 19** results in the formation of a monosubstituted-bissulfonimide hypervalent iodine compound **43** via ligand exchange.



Scheme 20

The formed reagent **43** is then used to react with various styrenes and alkenes **44** which

attack the iodine center, generate an iodo(III)amine which forms an aziridium intermediate which undergoes nucleophilic opening by a bissulfonimide ion to generate the corresponding diamine **45**.[20]

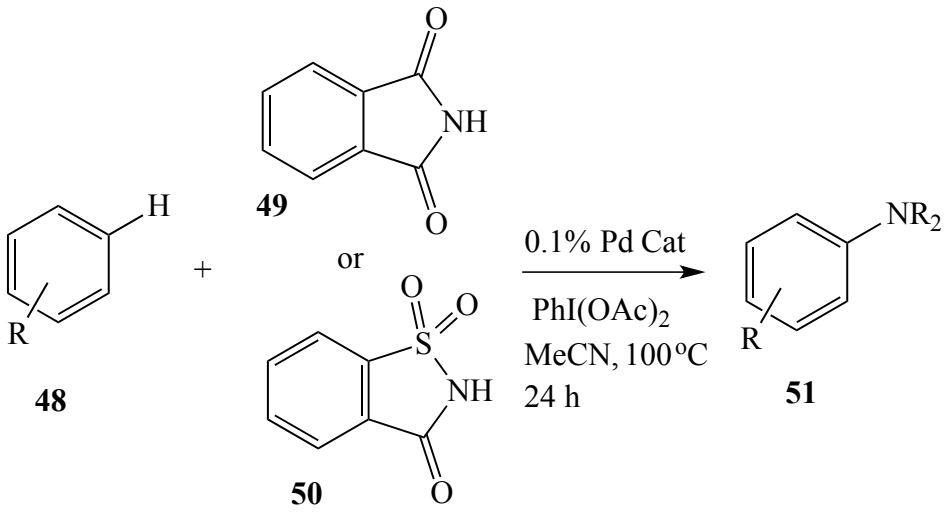


Scheme 21

Scheme 21 above shows the utility of a diamination reaction utilizing bissulfonimide groups as they can be deprotected and converted into the corresponding diamines **47**, which are useful as precursors to pharmaceutical agents such as (S)-levamisole.[20]

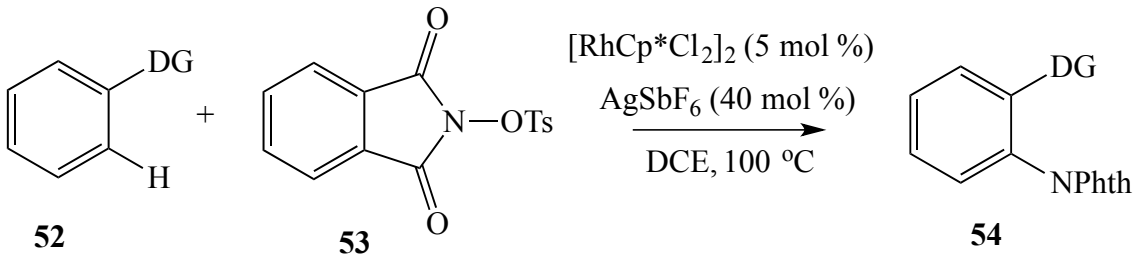
1.5 C-H Insertion of Arenes Using Imides

Another important reaction of hypervalent iodine reagents and imides is the C-H insertion reaction. This reaction is important as it gives a way for C-N bond formation on an aromatic ring, which is typically performed using heavy metal catalysts, which are shown in the following schemes.



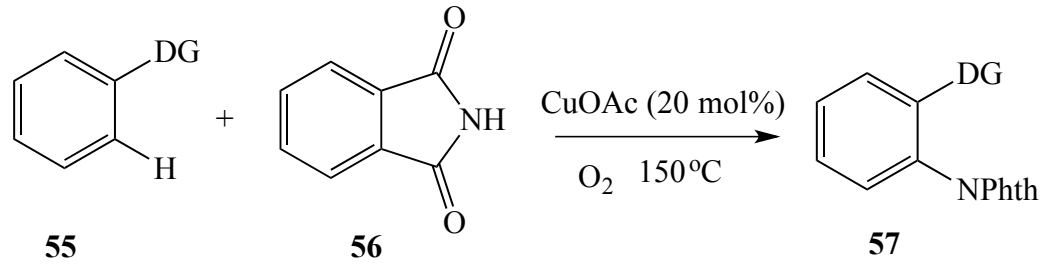
Scheme 22

In 2013, Hartwig, et al. demonstrated that various arenes **48** could be reacted with phthalimide **49** or saccharin **50** with a palladium catalyst and (diacetoxyiodo)benzene to afford the desired aminated arene **51** in good yields.[22]



Scheme 23

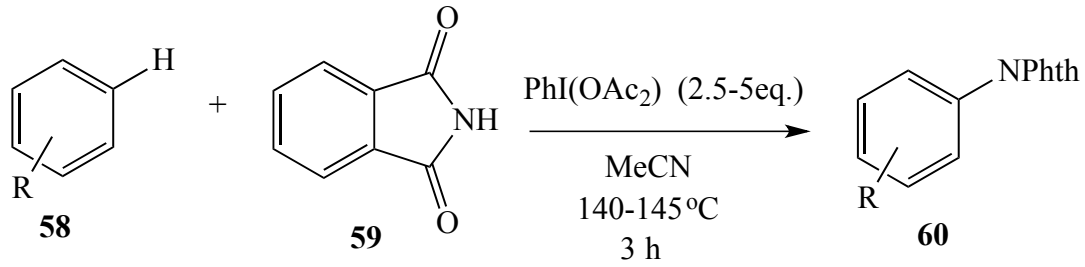
Research by Li et al. has shown an efficient amination of various arenes **52** with *N*-arenesulfonated imides **53** using rhodium and gold catalysts to yield twenty-three examples of phthalimide aminated arenes **54** in good yields (48-87%).[23]



55 **56** **57**

Scheme 24

Another parallel reaction using an arene **55** and phthalimide **56** is shown in **Scheme 24** above and uses a copper catalyst to achieve desired products of arene amination **57** at a lower cost than the previously mentioned methods.[24]



58 **59** **60**

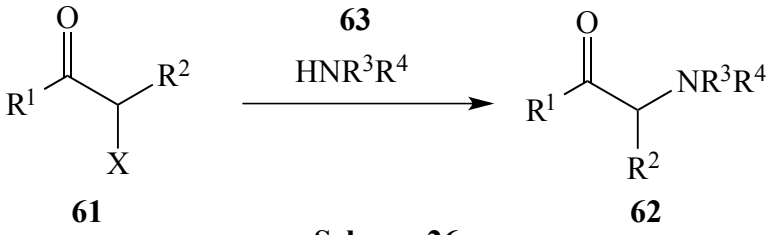
Scheme 25

DeBoef et al. performed a metal-free version of the amination of substituted arenes reactions previously described, in 2011, using a hypervalent iodine reagent ((diacetoxyiodo)benzene) as an oxidant.[25] This method, which is outlined in **Scheme 25**, provides good yields up to 90% without using excess arenes or metal catalysts to achieve C-N bond formation. As shown, various substituted arenes **58** were used along with phthalimide **59** to achieve the substituted arene **60**. The reaction was also shown to work with succinimide and other substituted phthalimides, but in lower yields. Each of these papers mentions the importance of (hetero)arylamines, as they are valuable targets due to their use as agrochemicals, pharmaceuticals, and other natural and biologically active

products.[22,23,24,25]

1.6 Imidation of Ketones with Imides

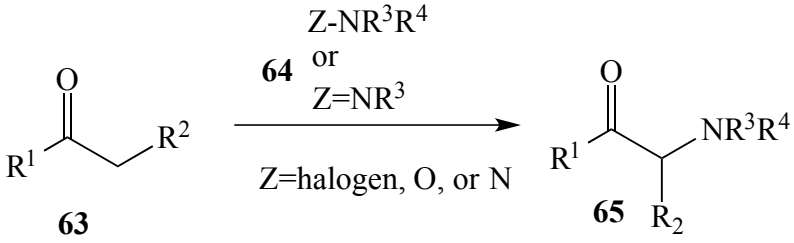
Other than the previous work done by Varvoglis on the α-saccharin imidation of ketones previously described,[16] there currently exists three different pathways for the imidation of ketones and these are outlined in **Schemes 26-28**.



61 **62**

Scheme 26

Scheme 26 describes the first general route for the generation of α-amino ketones. This method utilizes a previously prepared α-halogenated ketone **61** followed by reaction with a nucleophilic nitrogen source **63** to afford the α-amino ketone **62** via nucleophilic substitution.[26]

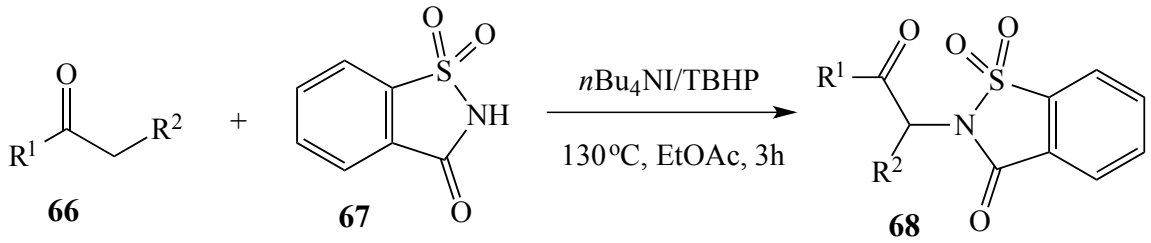


63

Scheme 27

Another variation is shown in **Scheme 27** above. This is a well-described general reaction that utilizes a previously prepared, halogenated nitrogen source **64** as an electrophile, which is reacted with a ketone **63** to afford the desired α-amino ketone **65**,

via electrophilic substitution.[26,27]



Scheme 28

Lastly, Zhang et al. have recently reported on the nBu$_4$NI-catalyzed oxidative imidation of ketones **66** with various imides such as saccharin **67** to afford α-imido ketones **68**.[26] The reaction likely proceeds via a radical mechanism and worked well with various imides such as phthalimide, saccharin, and succinimide while reacting with various ketones such as acetone. This work parallels other nBu$_4$NI-catalyzed coupling reactions such as the coupling of aldehydes and aromatic tertiary amines and the synthesis of α-ketoamides from aryl methyl ketones with dialkylformamides.[28,29]

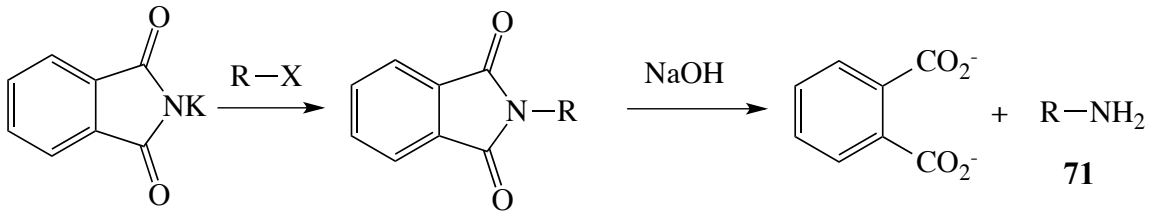
CHAPTER 2

RESULTS AND DISCUSSION

2.1 Synthesis of Hypervalent Iodine Compounds Containing Imides

A. Introduction

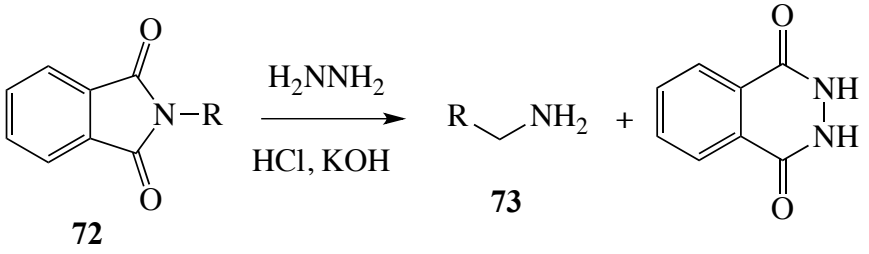
Following previously mentioned work by Varvoglis and Muniz groups,[14,20] we set out to explore hypervalent iodine compounds using imides, with hopes of obtaining a metal-free imidation reaction of alkenes. This would then allow for a much easier deprotection of the imide groups into the corresponding diamines. General imide deprotection would follow the process known as Gabriel synthesis. **Scheme 29** below depicts the simple process of this reaction.



69 **70** **71**

Scheme 29

Potassium phthalimidate **69** and an alkyl halide are reacted to give alkyl phthalimide **70**, which is then hydrolyzed under basic conditions to release the primary amine. Another variation of this reaction, shown in **Scheme 30**, includes the formation of the alkyl phthalimide **72** via nucleophilic substitution with an alkyl chloride and phthalimide, followed by deprotection with hydrazine and hydrochloric acid to give the primary amine **73**, and is common enough to be performed as an undergraduate experiment.[30]

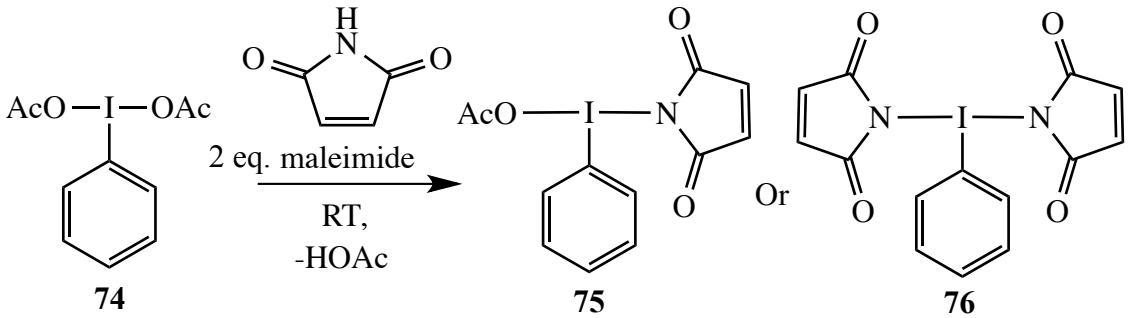


Scheme 30

It was first chosen to try to work with an imide that had not been previously described in the literature as having been incorporated into a hypervalent iodine compound. Maleimide was chosen as the starting imide as it has a unique double bond, which could potentially allow for further reactions such as Diels-Alder or Michael additions and broaden the scope of any subsequent reaction.

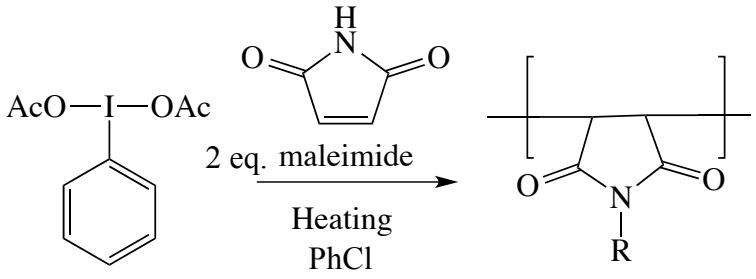
B. Results and Discussion

Initially, the goal was to provide an easier ligand exchange reaction with an imide functional group, HNR_2, and a hypervalent iodine reagent to produce a new hypervalent iodine reagent with an incorporated imide group. Rather than working with potassium or sodium salt versions of the imides as previously described by Varvoglis, it was hypothesized that by reacting an imide with (diacetoxyiodo)benzene **74**, it would undergo a ligand exchange reaction as shown in **Scheme 31** under mild conditions to afford either



Scheme 31

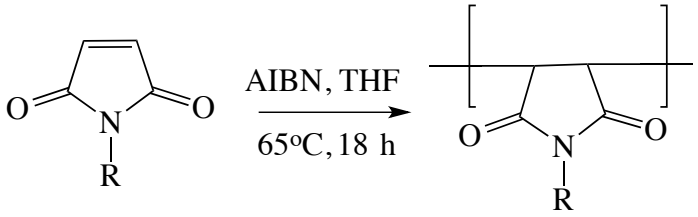
a singly **75** or doubly **76** substituted iodine(III) compound, leaving acetic acid as a byproduct, which could easily be removed under deep vacuum. Unfortunately, after trying many variations including changing solvents, times, and temperature, the reaction failed to progress successfully. In fact, when the reaction was heated to help facilitate ligand exchange, maleimide appeared to form a polymeric structure **77** as hypothesized in **Scheme 32**.



77

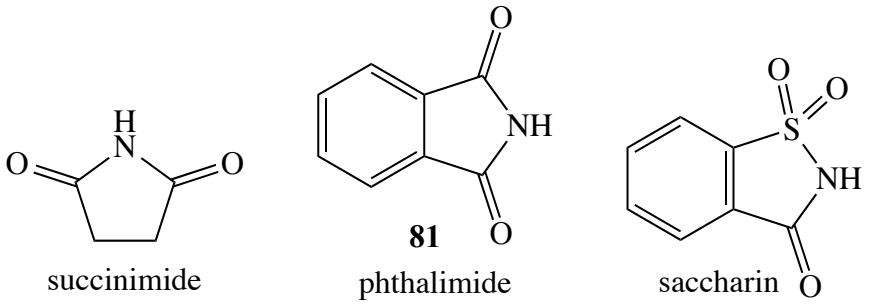
Scheme 32

A polymeric structure is plausible as the reaction yielded a yellow solid, which was insoluble in organic solvents and had a melting point greater than 300 ^{0}C. Literature sources also explained that maleimide and its derivatives **78** can form polymers **79** from the internal double bond, and an example as shown in below in **Scheme 33**.[31]



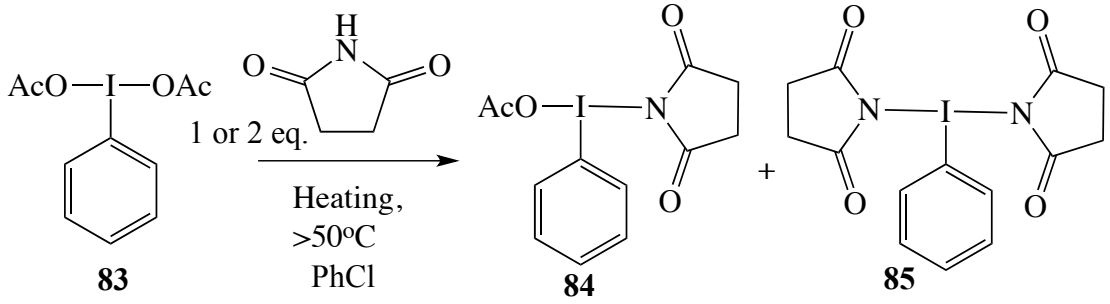
78 **79**

Scheme 33



Scheme 34

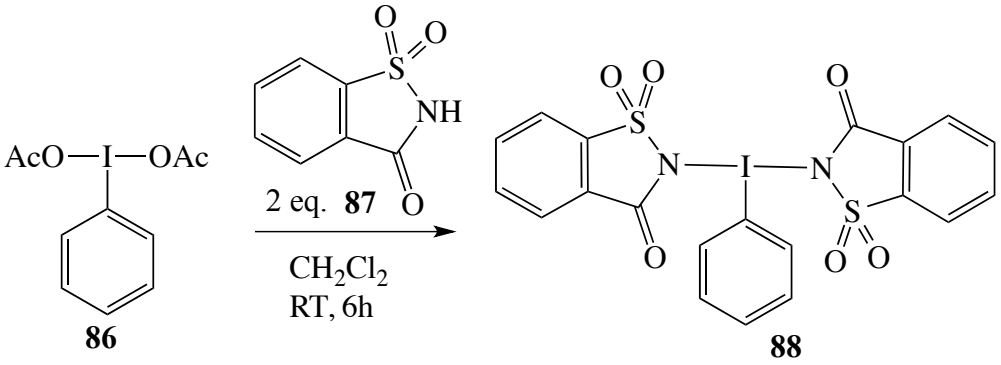
After these results, it was decided to move on to trying other imides. The imides listed in **Scheme 26**, succinimide **80**, phthalimide **81**, and saccharin **82**, were each tried under the same conditions as in **Scheme 31** and **Scheme 32** with various results. **Scheme 35** demonstrates the results of the reaction with succinimide. Under room temperature and varied solvent conditions, both of the desired mono-substituted **84** and di-substituted **85** products were obtained in mixture in low yields. Upon heating and rotary evaporation at



Scheme 35

temperatures greater than 50 ^{o}C, in chlorobenzene, using 1 or 2 equivalents of succinimide, the major product of the reaction was the mono-substituted product **84**, but the resulting solid also contained di-substituted product **85** as well as unreacted (diacetoxyiodo)benzene **83**, which were impossible to remove under varying recrystallization and washing methods as the solubility of the molecules appeared to be

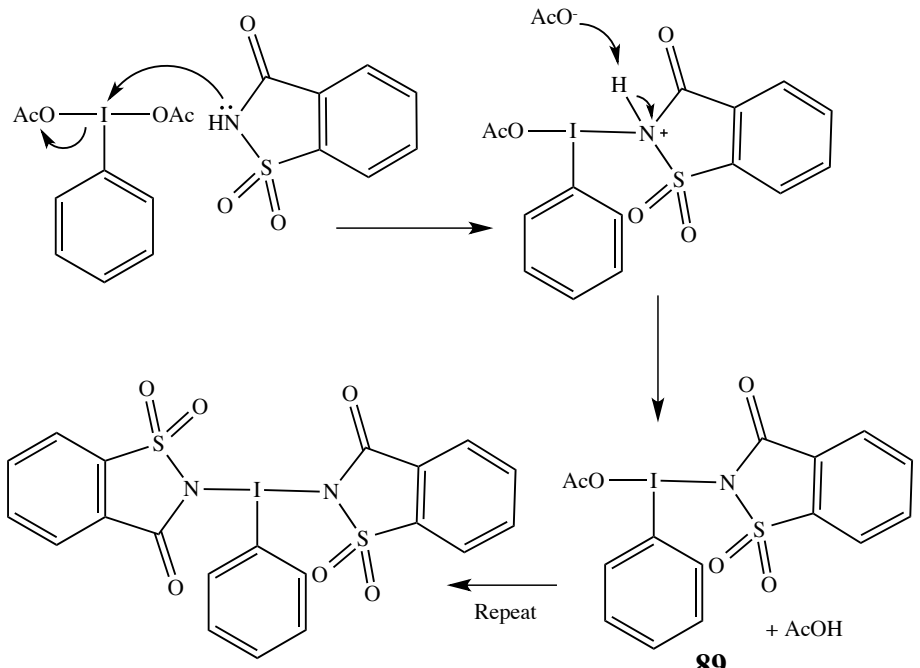
similar. Subsequent reactions with phthalimide **81** resulted in a mainly di-substituted product, but we were unable to purify well enough to get a reliable elemental analysis.



86 **88**

Scheme 36

Upon reacting DIB **86** with two equivalents of saccharin **87** in dichloromethane, as shown in **Scheme 36**, after 6 hours the desired highly insoluble di-substituted product **88**

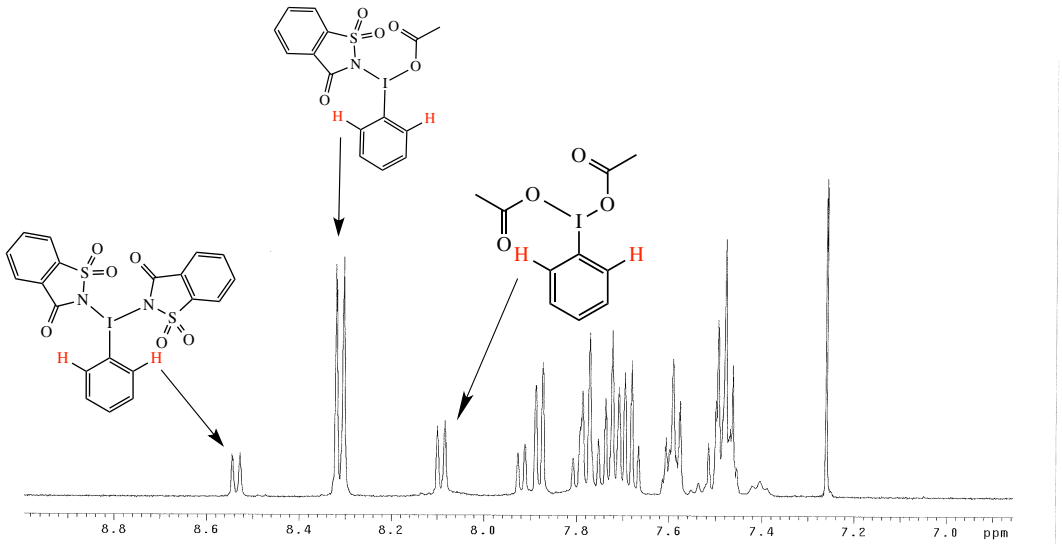


89

Scheme 37

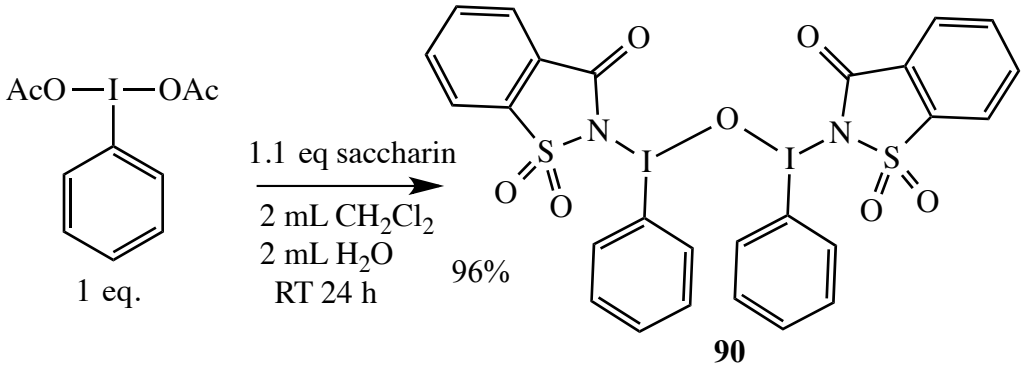
was achieved in yields greater than 90% and the result was confirmed via elemental, NMR, and IR analyses. A detailed mechanism of the ligand exchange is given in

Scheme 37. To help prove that the mechanism goes through a mono-substituted product **89**, the reaction time was shortened to a half-hour and the ^{1}H NMR analysis is shown below in **Scheme 38**. After reacting for a half hour, it is possible to see three different compounds present in ^{1}H NMR analysis, unreacted DIB, and the mono and di-substituted products. Unfortunately, only the di-saccharin product could be purely obtained as varying the time and amount of starting reagents always led to a mixture, unless enough time had elapsed to fully convert the starting materials to the insoluble di-product, which could be purified via washing with organic solvents and filtering.



Scheme 38

Lastly, a mu-oxo variation of the di-saccharin product **88** was synthesized by **Scheme 39**.



Scheme 39

The new mu-oxo di-saccharin product **90** was afforded in good yields through the reaction of DIB and saccharin in water and dichloromethane solution. This reaction paralleled a similar reaction with bistosylimide.[21] These oxygen-bridged molecules have been noted by Kita et al. to be very reactive.[32]

C. Summary

When trying to find a hypervalent iodine reagent containing an imide functional group under mild reaction conditions, maleimide polymerized upon heating and succinimide provided a mono-substituted product, but could not be isolated due to impurities that could not be removed due to their similar solubility. Column chromatography was not a feasible answer as hypervalent iodine compounds readily degrade on acidic silica gel. Phthalimide was found to predominately form a di-substituted iodine(III) compound, but could not be purified as well. Saccharin readily formed a di-substituted iodine(III) product under mild conditions in good yields when reacted with DIB, and when water was added at the start of the reaction, a novel oxygen-bridged molecule was formed. The observed reactivity of the imides with DIB was most

likely due to their pKa values, saccharin 1.8, maleimide 9.5, phthalimide 8.3, and succinimide 9.6. The extra electron-withdrawing group on saccharin helps make the N-H bond more acidic and allows for ease of ligand exchange.

2.2 Imidation of Silyl Enol Ethers

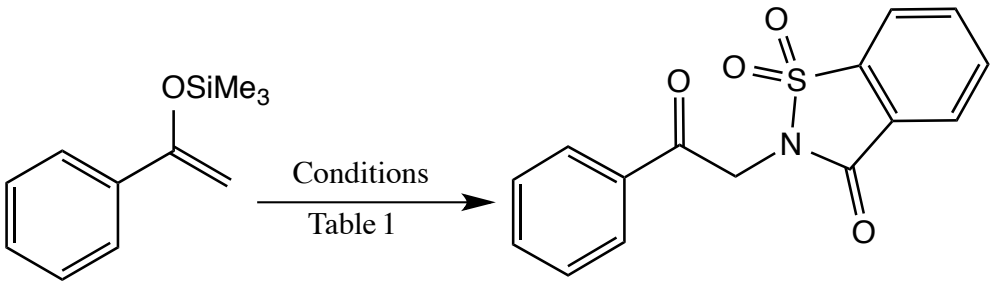
A. Introduction

Now that two good starting materials were characterized, both of which contained saccharin as the imide, the next step was to determine if they were valuable as reagents. As stated previously, the goal was to create a metal-free imidation of alkenes reaction with an imide-containing iodine(III) reagent similar to the ones described by the Muniz research group.[20,21] A series of attempted reactions and the results are discussed in the following section.

B. Results and Discussion

Using the previously mentioned reagents, many attempts were made to react them with various alkenes including styrenes, aliphatic alkenes, and cyclic alkenes with no apparent success. This included varying solvents, temperatures, and even using Lewis acid catalysts. Other attempts were made with alkynes and C-H insertions, with negative results as well. Upon heating the mu-oxo reagent **90** at reflux in benzene to attempt a C-H insertion reaction, the compound was deoxygenated back into the di-saccharin **88** molecule. Finally, after many negative results, a reaction with 1-phenyl-1-trimethylsiloxyethylene **91** was noted with the mu-oxo reagent **90** as shown in the

generalized **Scheme 40** to give the α-imido ketone **92** and the conditions of this first reaction are described in entry 1 of **Table 1**. At this time, it was believed that a strong acid was necessary to break the apart the starting saccharin containing reagent in order to catalyze the reaction.



91 **92**

Scheme 40

Table 1

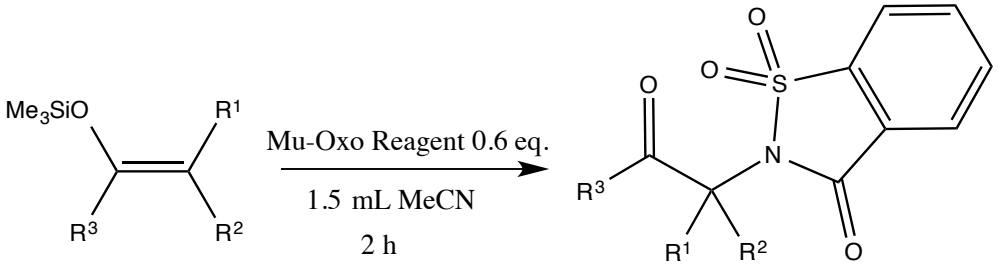
Entry	Starting Material (eq.)	Excess Saccharin (eq.)	Solvent 1.5mL	Acid (1 eq.)	Temp ^{o}C	Time	Yield [%][a,b]
1*	mu-oxo (1)	1	CH_2Cl_2	TFOH	RT	12 h	5[b]
2	mu-oxo (1)	1	CH_2Cl_2	TFOH	RT	24 h	15
3	mu-oxo (1)	1	CH_2Cl_2	TFOH	$0^0C\rightarrow$ RT	24 h	3
4	mu-oxo (2)	0	CH_2Cl_2	TFOH	RT	24 h	13
5*	mu-oxo (1)	0	MeCN	TFOH	RT	24 h	56
6	mu-oxo (1)	0	Et_2O	TFOH	RT	24 h	Trace
7	mu-oxo (1)	0	$CHCl_3$	TFOH	RT	24 h	Trace
8	mu-oxo (1)	0	acetone	TFOH	RT	24 h	23
9	mu-oxo (1)	0	MeOH	TFOH	RT	24 h	17
10	mu-oxo (1)	0	EtOAc	TFOH	RT	24 h	0

11*	None	1	MeCN	None	RT	24 h	0
12*	None	1	MeCN	TFOH	RT	24 h	0
13*	di-saccharin (0.6)	0	MeCN	None	RT	24 h	54
14*	mu-oxo (1)	0	MeCN	None	RT	12 h	69
15*	mu-oxo (0.6)	0	MeCN	None	RT	2 h	66
16*	mu-oxo (0.6)	0	MeCN	None	RT	2h	70 (68[b])
17*	acetophenone (No silyl enol ether)	1	MeCN	None	RT	2 h	0
18*	acetophenone mu-Oxo (1) (No silyl enol ether)	0	MeCN	None	RT	2 h	0

[a]Yields are calculated with ^{1}H NMR using tetrachloroethane as a standard. [b]Isolated yields after purification.

1-Phenyl-1-trimethylsiloxyethylene **91** was chosen as a starting silyl enol ether for optimization because of its simple structure and commercial availability. Upon further optimization, it was found that acetonitrile gave the best yield as a solvent, entry 5, and that a strong acid was in fact not needed for the reaction to occur, entry 14. Optimized time was two hours and entries 11, 12, 17, and 18 were included as blank reactions to show that the starting hypervalent reagent and silyl enol ether were both necessary for the reaction to occur. Di-saccharin reagent **88** gave an approximately 15% lower yield when compared to the mu-oxo type, entries 13 and 16, which corresponds to the high reactivity of these reagents described by Kita et al.[32] It is most likely due to increased nucleophilicity at the iodine center when compared to the di-saccharin compound with

two stabilizing imide groups at the iodine center. It was also important to note that only 0.6 equivalent of the reagent was required for the reaction to occur, which was helpful with describing the mechanism. **Scheme 41** describes the optimized reaction condition between a generic silyl enol ether substrate **93** and our starting reagent, which allowed for the conversion to the corresponding α-imido ketone **94**.

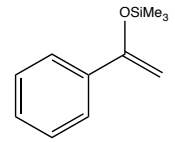
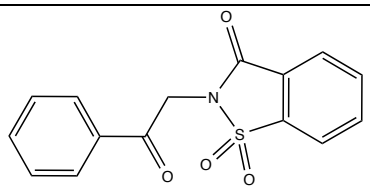
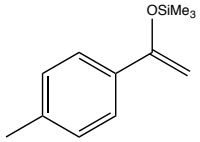
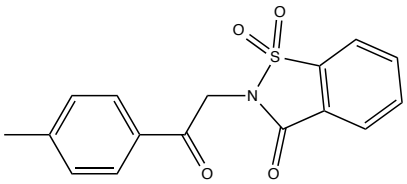
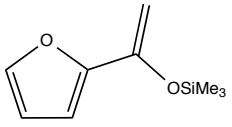
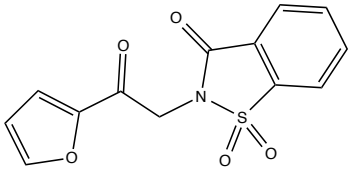


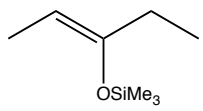
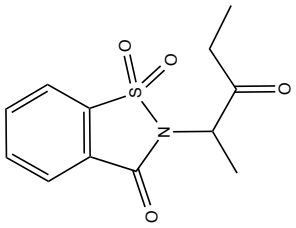
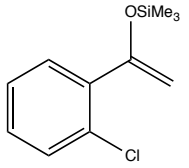
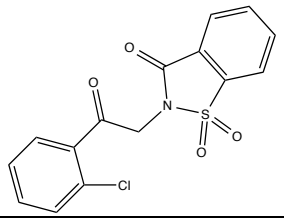
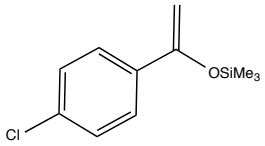
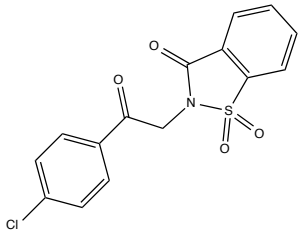
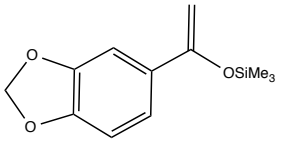
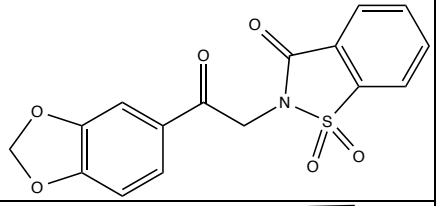
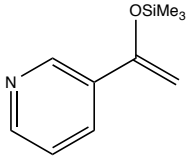
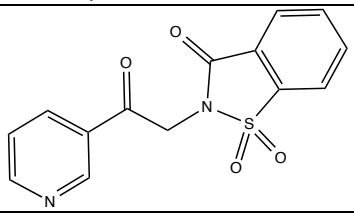
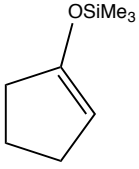
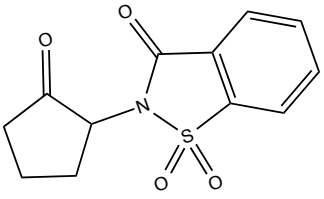
93 **94**

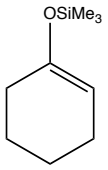
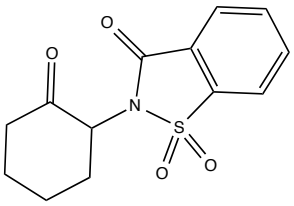
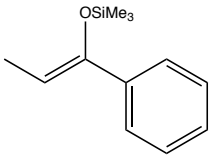
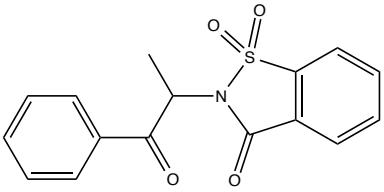
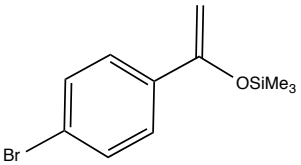
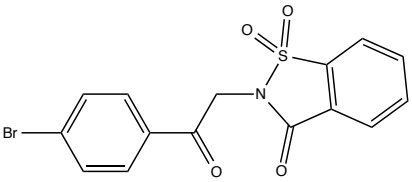
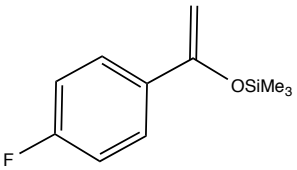
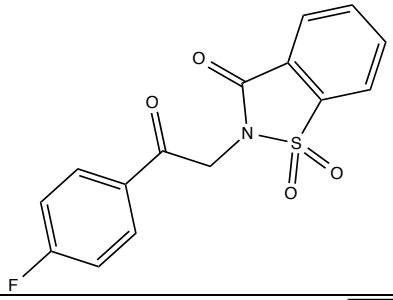
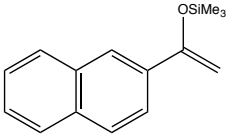
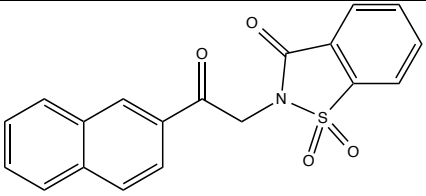
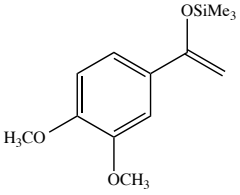
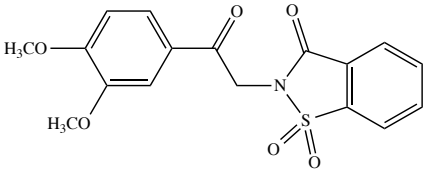
Scheme 41

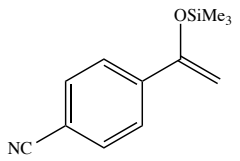
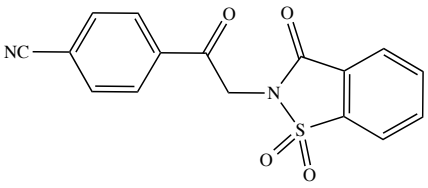
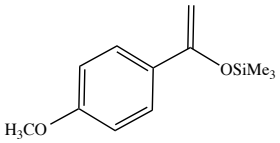
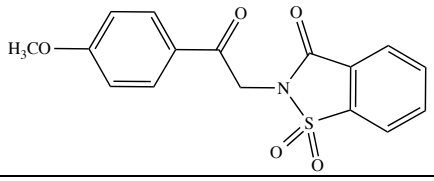
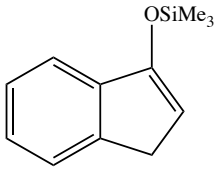
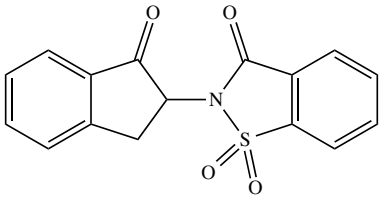
Table 2 below describes the results of the optimized reaction with varying substrates.

Table 2

Substrate	Product	Yield [%][a]
		68
		66
		71

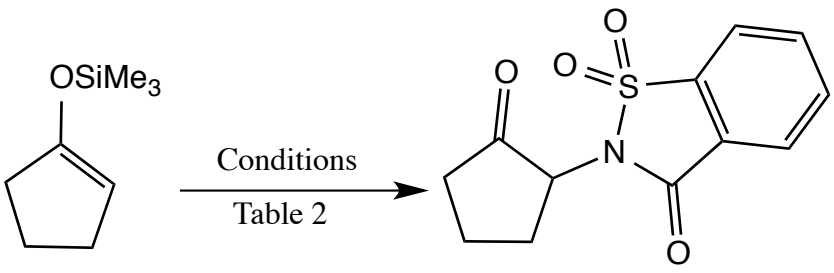
		24
		57
		65
		52
		48
		33

		18
		24
		72
		74
		38[b]
		60[b]

		78[b]
		42[b]
		19[b]

[a] Isolated yields after purification. [b] Yields determined by ^{1}H NMR using a tetrachloroethane standard.

An attempt to increase the yields of a reaction with a substrate **95** that had given low yields for this reaction is shown in **Scheme 42** and **Table 3**. The tested reactions still utilized the same mu-oxo reagent, but the amount used, temperature, and time conditions were varied. The change in yields was determined to negligible.



95

Scheme 42

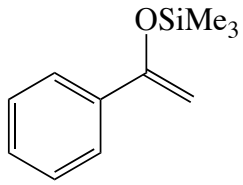
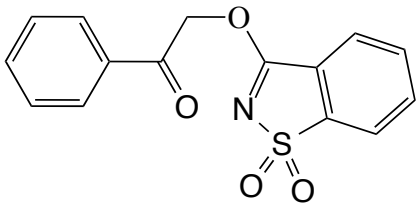
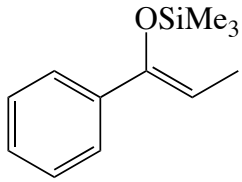
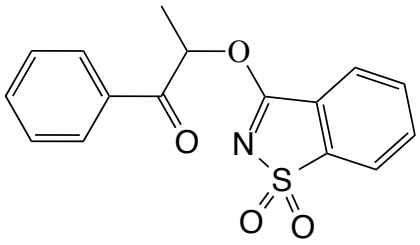
Table 3

Entry	Starting Material (eq.)	Temp ^{o}C	Time	Yield [%][a,b]
1	0.6	RT	15 h	34
2	1.2	RT	5 h	37
3	0.6	Hot Plate 100 ^{o}C	2 h	32
4	0.6	0^{o} C to RT	5 h	30
5	0.6	RT	2 h	36 (33[b])

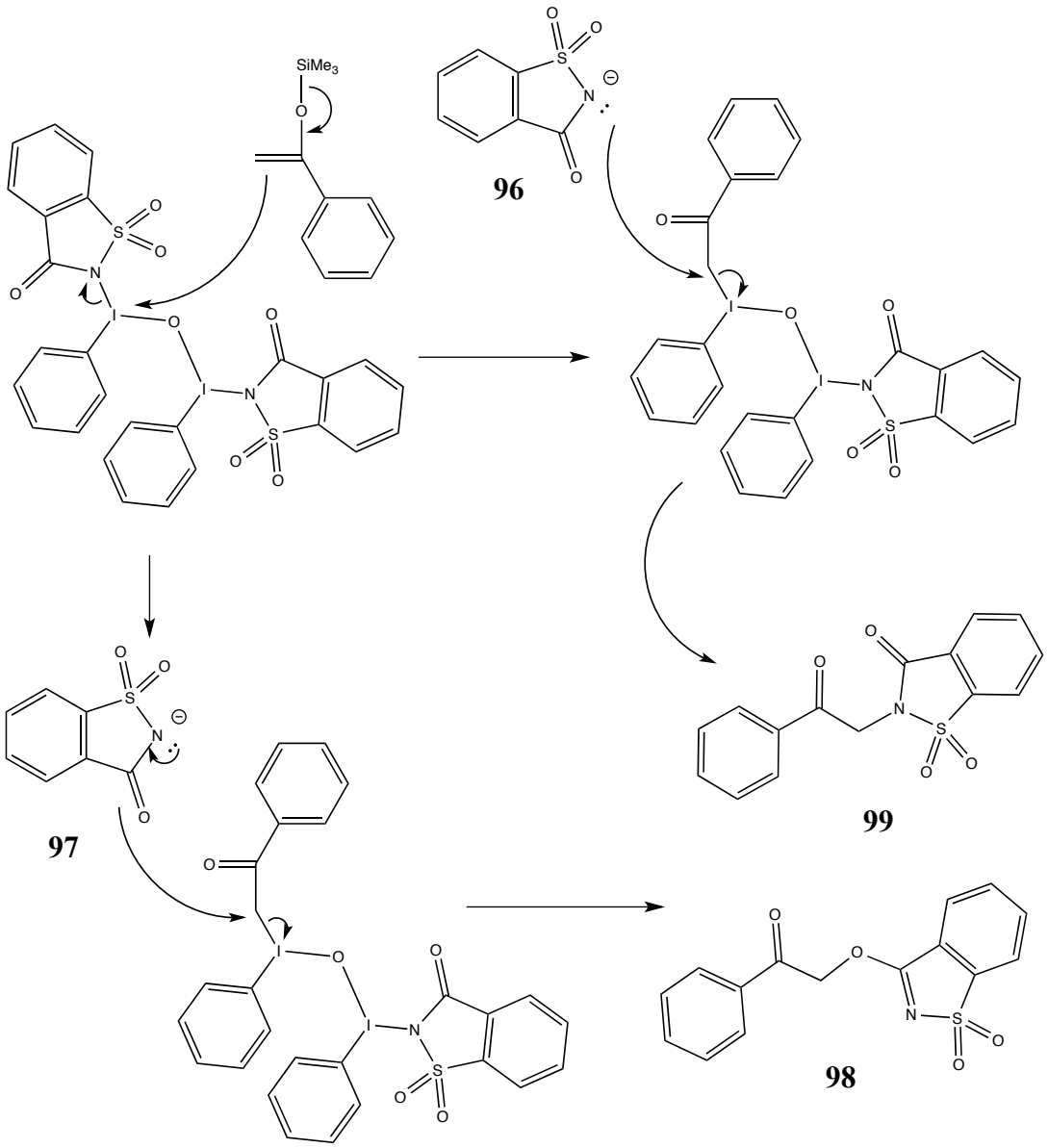
[a]Yields are ^{1}H NMR yields calculated using tetrachloroethane as a standard. [b]Isolated yields after purification.

Because the yields were not 100%, it was unsure what exactly was happening to the remaining starting substrate if it was not being completely converted into its α-imido ketone, but still being transformed into something other than the methyl ketone from which it was derived. Upon careful chromatography, we elucidated what appears to be a rearrangement of the saccharin moiety, which is bound to the substrate via a carbon-oxygen bond, rather than by a carbon-nitrogen bond. Two examples of this are shown in **Table 4** and these products appear to be where the rest of the reaction proceeds, if not bound to the substrate via a carbon-nitrogen bond. Also, only a few examples of these products were obtained, as these compounds appeared to decompose or bind to alumina gel during chromatography and were often difficult to purify when compared to their nitrogen bound counter part. The mechanism that is proposed for this reaction to yield these results is shown in **Scheme 43**.

Table 4

Substrate	Product	Yield [%][a]
		29
		67

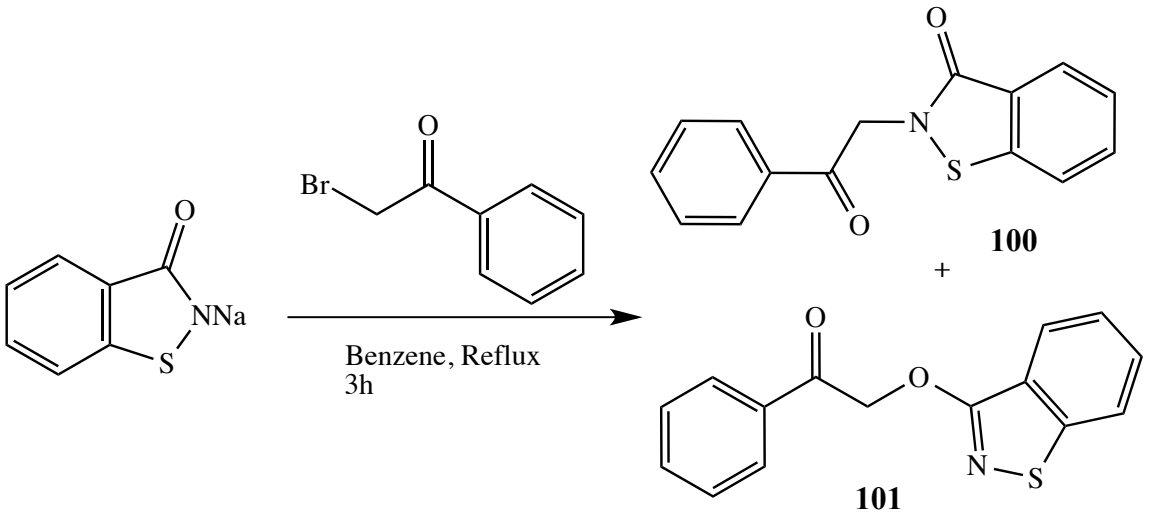
[a] Isolated yields after purification.



Scheme 43

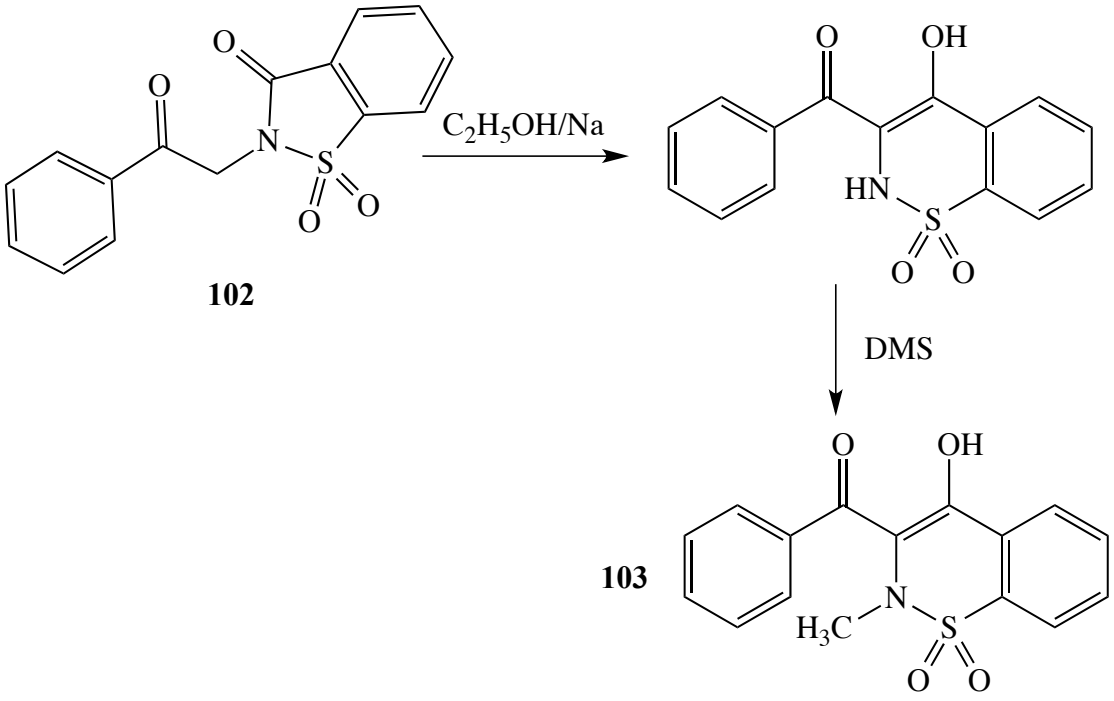
As with most reactions with λ^3-iodane species, the mechanism uses a ligand exchange explanation at the iodine center. The double bond from the silyl enol ether acts as the nucleophile, which attacks the iodine center. Ligand exchange causes the formation of a saccharin nucleophile, which can attack the electrophilic carbon via a nitrogen nucleophile **96** or rearrange and react as an oxygen-based nucleophile **97** followed by

reduction of the hypervalent iodine to afford either the α-imido ketone **99** or the oxygen-bridging α-imido ketone **98**. Both α-nitrogen **100** and α-oxygen bound **101** ketone products have been reported in a previous literature article describing the synthesis of a similar molecule as shown in **Scheme 44**.[33] The reaction is predicted to proceed in a similar fashion at the iodine on the other side of the mu-oxo reagent, as only 0.6 equivalents are needed for the optimized reaction.



Scheme 44

As for importance of this reaction, the desired products from our reported method have recently found use as precursors to many new possible pharmaceutical agents.[34,35,36,37,38] As an example, Shahwar et al. utilized compound **102** to prepare benzothiazine derivatives such as **103** in **Scheme 45**, which are noted to be active acetylcholinesterase inhibitors and have found application in the treatment of Alzheimer and Parkinson's disease.[34]

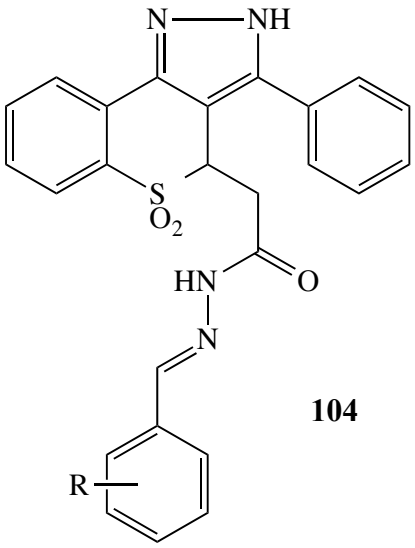


102

103

Scheme 45

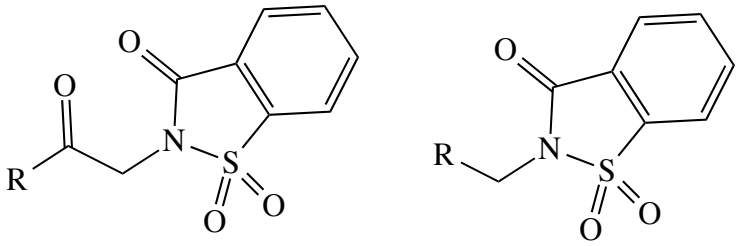
Schninazi et al. has also reported on the synthesis of benzothiazine derivatives **104** shown in **Scheme 46** below utilizing the same precursor **102** for use as potent anti-HIV-1 agents.[35]



104

Scheme 46

Alkylated saccharin derivatives, **105** and **106**, which are similar to the ones synthesized by our new method, were also used in studied by Supuran et al. as selective inhibitors of tumor-associated carbonic anhydrase[36]. These were synthesized by saccharin alkylation using alkyl bromides.



105 **106**

Scheme 47

C. Summary

Herein we present a new imidation reaction of silyl enol ethers to afford α-saccharin ketones in moderate yields, under mild conditions without the use of metal catalysts. These imido ketones were synthesized from aliphatic, aromatic, and heterocyclic starting substrates, with aromatic substrates giving the best yields. The reaction mechanism is hypothesized using a traditional ligand-exchange explanation at the hypervalent iodine center of the starting reagent. Both nitrogen-bound and oxygen-bound products were noted in the reactions. It has been hypothesized that this mixture occurs due to a rearrangement of the nucleophile to a more favorable conformation that allows the saccharin molecule to get closer to the substrate to react, as this has been shown to be the more favorable product in sterically hindered substrates. Higher yields of α-imido ketones from the aromatic precursors most likely occurs from their higher reactivity, which stems from electron donation into the double bond from the aromatic

ring. The synthesized products are important precursors to biologically active compounds.

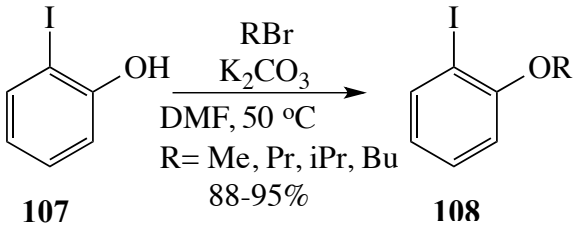
2.4 Preparation of a New, Soluble Mu-Oxo Hypervalent Reagent

A. Background

Even though the reaction in **Scheme 41** proceeded effectively, it was important to determine the exact structure of the reagent to show that these theorized hypervalent iodine-imide bonds do exist. As previously discussed and also explained by the Varvoglis research group, bis(imidates) were found to be very insoluble in ordinary organic solvents and crystallization was not possible.[14] This prompted us to attempt to synthesize a similar molecule, which would be soluble in ordinary organic solvents to allow crystallization and thus analysis by x-ray crystallography. One attempt at a soluble reagent was based on results obtained from Zhdankin's research group, while the other attempt was based on results from Kita's research group, who recently discovery hypervalent iodine compounds of the mu-oxo variety containing two acetate groups as well as a bridging oxygen atom in 2012.[39,32] These mu-oxo type reagents were found to be much more reactive than their normal iodine(III) counterparts. It was hypothesized that these reagents could undergo a similar ligand exchange reaction as we had found with (diacetoxyiodo)benzene and saccharin, while being able to obtain a more soluble compound.

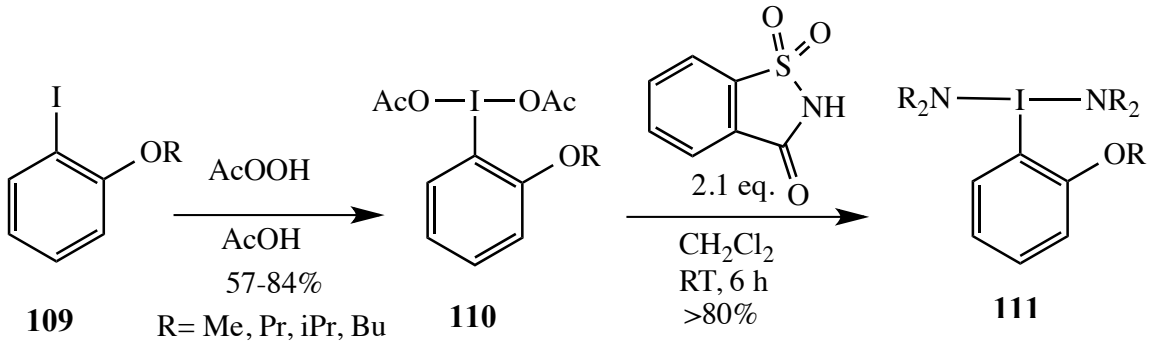
B. Results and Discussion

Recently, Zhdankin et al. reported on the preparation of a highly soluble carbene precursor.[39] Using the steps in their proposed schemes, we first synthesized iodobenzene with ortho-alkoxy groups **108** from 2-iodophenol **107** as shown in **Scheme 48**.



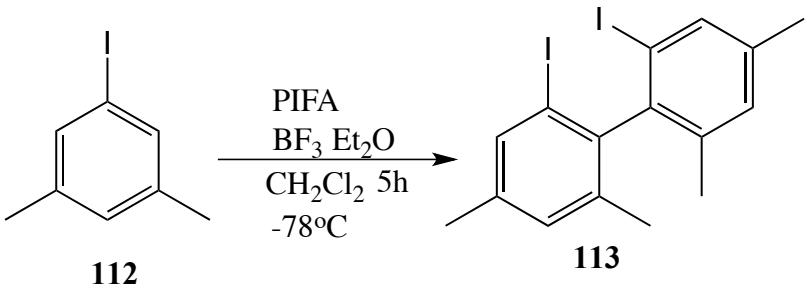
Scheme 48

The *o*-alkoxy iodobenzene **109** was oxidized leading to the diacetate iodine(III) reagent **110,** which was then reacted with two equivalents of saccharin to undergo ligand exchange and afford the new di-saccharin reagents **111** in good yields.



Scheme 49

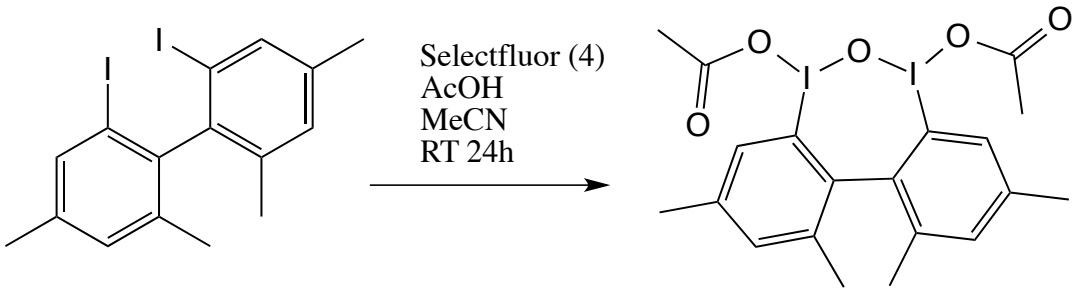
Unfortunately, the introduction of an *o*-alkoxy group did not appear to greatly increase solubility. The second attempt at making a soluble reagent is shown in **Schemes 50-52**.



112 **113**

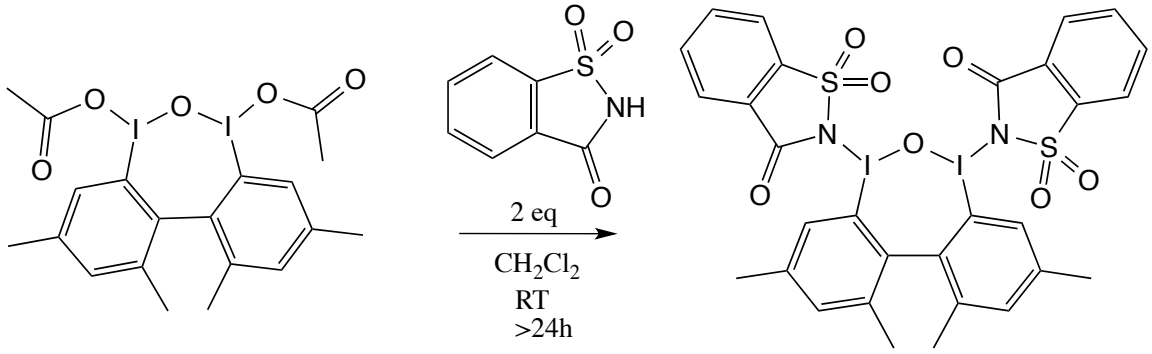
Scheme 50

Scheme 50 and **51** are followed from the literature.[38] The first step, was a coupling reaction of 1-iodo-3,5-dimethybenzene **112** shown in **Scheme 50** using PIFA and a Lewis acid catalyst. The resulting product **113** could be oxidized as shown in **Scheme 51** to afford the μ-oxo bridged hypervalent iodine(III) molecule **114**, which is reacted with 2 equivalents of saccharin to afford **115** in **Scheme 52** in a 63% yield.



114

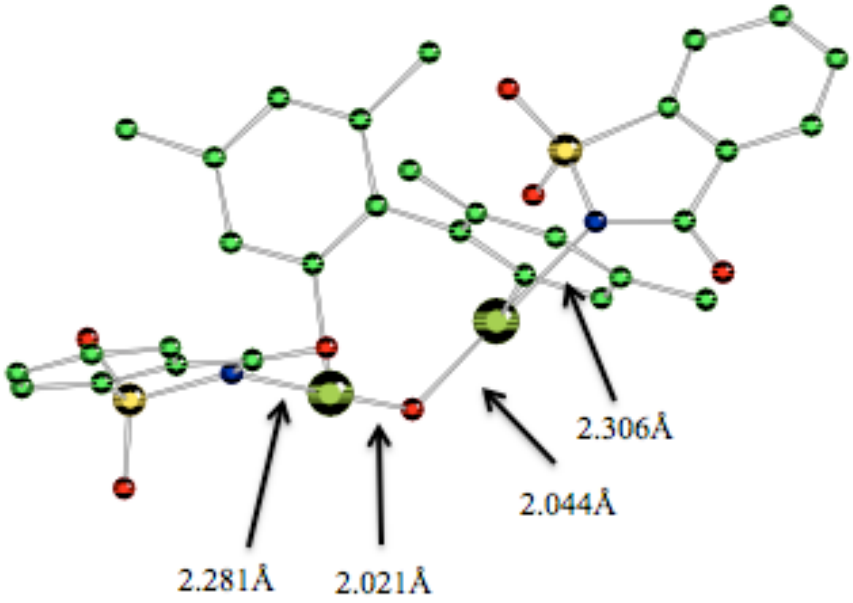
Scheme 51



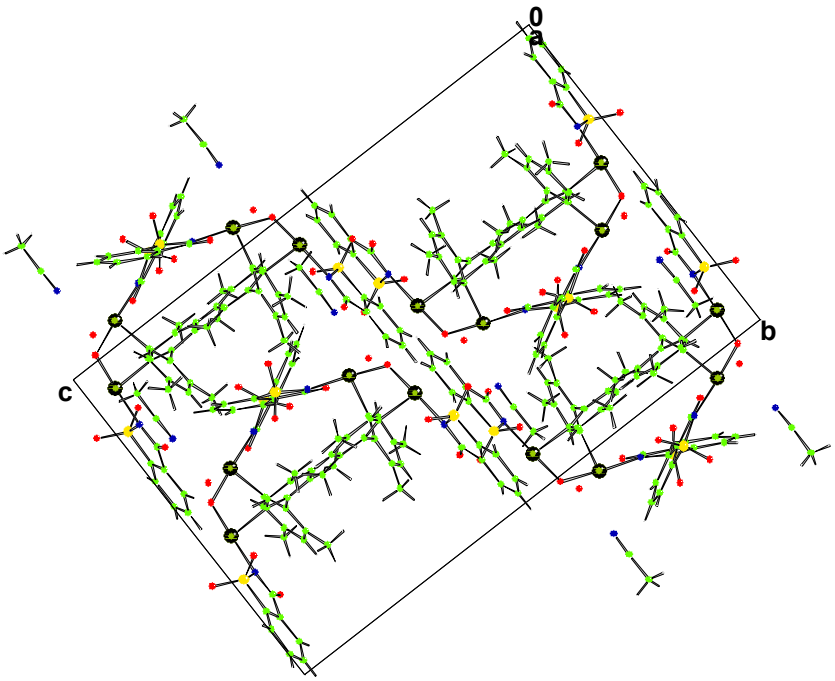
115

Scheme 52

The resulting structure **115** was isolated in 63% yield and found to be easily soluble in ordinary organic solvents such as acetonitrile and chloroform. Immediately, the compound was characterized and then began the attempt at obtaining a crystal suitable for x-ray analysis. Recrystallization in acetonitrile yielded single crystals suitable for x-ray crystallographic analysis. **Scheme 53** shows the structure of the resulting crystal with important bond lengths shown and **Scheme 54** shows the packing arrangement of the molecules.

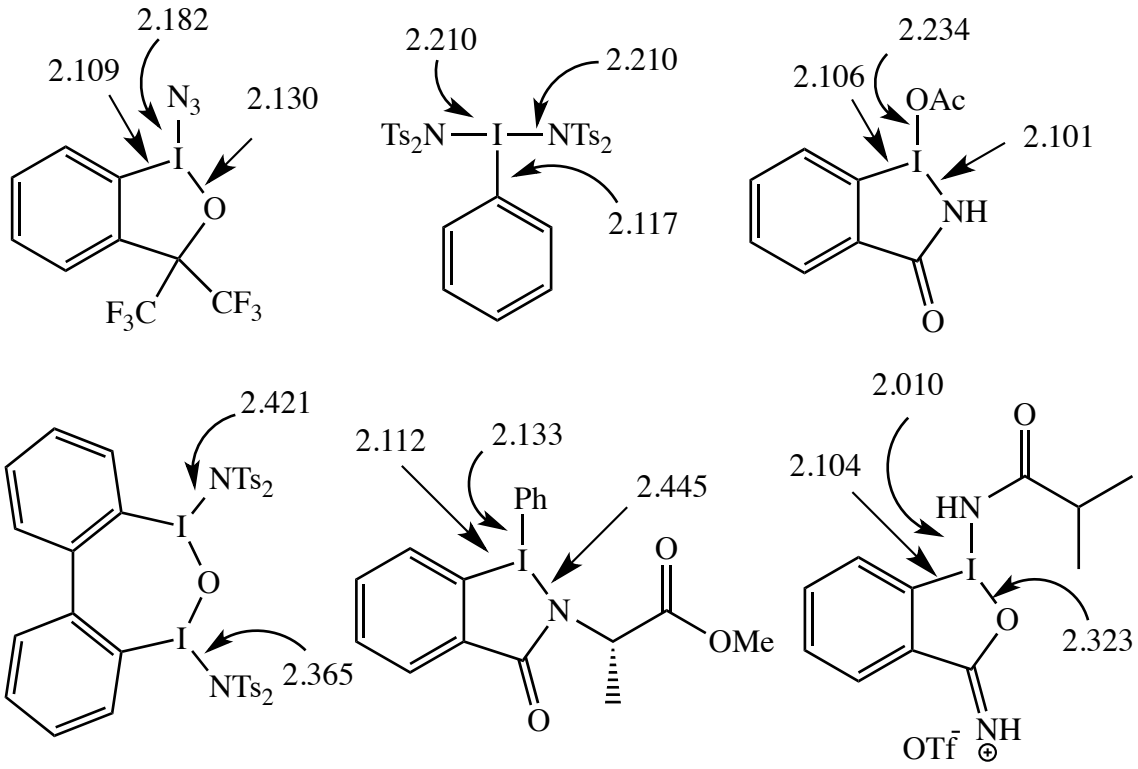


Scheme 53



Scheme 54

To our knowledge, this is the first x-ray to show a hypervalent iodine to imide bond. Other published structures containing hypervalent iodine-nitrogen bonds are shown in **Scheme 55** with their important bond lengths noted.[40,41,42,43,44,45]



Scheme 55

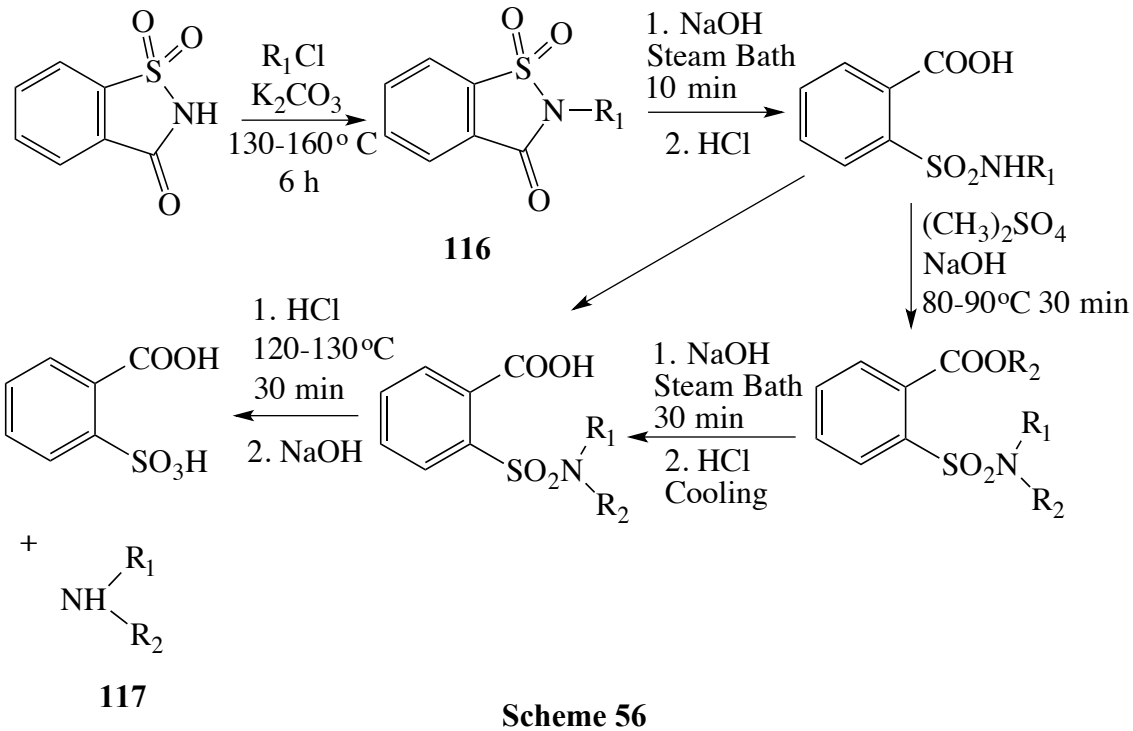
2.5 Summary

Di-saccharin iodine(III) molecules containing an o-alkoxy group did not appear to show significant solubility in organic solvents. Adapting a synthetic method from Kita et al., we were able to synthesize a di-saccharin reagent soluble in ordinary organic solvents.[32] The valuable crystal structure in **Scheme 53** helps to support our hypothesis of our precursor μ-oxo reagent also containing two iodine-nitrogen bonds and is the first of its type to be proven via x-ray analysis. The structure is also compared to compounds containing similar bonding as shown in **Scheme 55**.

2.6 Future Directions

As a continuation of this project, it will be important to finish fully characterizing and obtaining isolated yields from the reaction of the substrates on the bottom of **Table 2** to show its broad applicability. In addition, single crystals of compound **3s** have been grown in acetonitrile and await x-ray analysis. These crystals will be important, as they will be able to prove that the rearrangement of the saccharin nucleophile shown in **Scheme 43** does exist, and that some of the reaction progresses toward an oxygen-bound product as shown in **97**, as well as the desired C-N bond formation.

As another future direction, it would be interesting to explore the deprotection of the saccharin moiety, giving rise to either primary or secondary amines, which are extremely useful as pharmaceutical agents.[46] The deprotection of saccharin is a fairly unexplored area, with only a few papers fully describing its reaction process. As seen in **Scheme 56** below, Abe and Sugasawa have developed a simple method for the preparation of primary and secondary amines from alkylated saccharin.[47] The alkylated saccharin **116** was first alkaline-hydrolyzed using aqueous sodium hydroxide, alkalized a second time to eventually afford a secondary amine or left as is and then treated under basic and acidic conditions yielding either the primary or secondary amines **117**.


R1Cl
K2CO3
130-160° C
6 h
116
1. NaOH
Steam Bath
10 min
2. HCl
COOH
SO2NHR1
(CH3)2SO4
NaOH
80-90°C 30 min
COOR2
1. NaOH
Steam Bath
30 min
2. HCl
Cooling
1. HCl
120-130°C
30 min
2. NaOH
SO3H
117

Scheme 56

CHAPTER 3

EXPERIMENTAL

3.1 General Methods

NMR Spectra were recorded using a Varian ^{UNITY} INOVA 500 MHz NMR spectrometer operating at 500 MHz (^{1}H NMR) and 125 MHz (^{13}C NMR) with ^{1}H and ^{13}C chemical shifts referenced to the corresponding solvent and recorded in parts per million (ppm). Each of the melting points was determined with an open capillary tube with a Mel-temp II® melting point apparatus and the values are uncorrected. High-resolution mass Spectra (HRMS) was determined with a Bruker BioTOF II Reflectron ESI-TOF instrument at the University of Minnesota Twin-Cities campus. Microanalysis was performed by Atlantic Microlab Inc., Norcross, Georgia. IR Spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR Spectrophotometer scanned from 4000 cm^{-1} to 450 cm^{-1} and the peaks were recorded in inverse centimeters (cm^{-1}). Pre-coated silica gel 60 F254 plates from MERCK were used to determine proper separation and reaction completion conditions and the spot markings were distinguished using UV light at 254 nm.

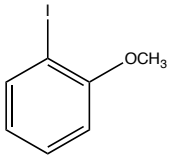
3.2 Materials

All of the commercial reagents and solvents were ACS grade and used without any further purification or distillation. For column chromatography, silica gel was

obtained from Dynamic Adsorbents Inc., 63-200μm, 60A and basic alumina oxide, 50-200μm, 60A, was obtained from Acros Organics.

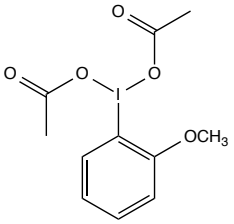
3.3 Synthesis of Compounds

1-iodo-2-methoxybenzene (3a)[39]



Synthesized according to the literature procedure by Zhdankin et al.[39] 10.0 mmol of 2-iodophenol was mixed with 50.0 mmol potassium carbonate in 10 mL DMF and allowed to stir for 10 minutes. 15.0 mmol of methyl bromide was added and the reaction was stirred at 50 ^{o}C for 3 h. The mixture was purified via column chromatography (3:1 hexanes/ ethyl acetate) to afford pure 1-iodo-2-methoxybenzene**.** The product was confirmed via ^{1}H NMR and the spectrum was included for reference.

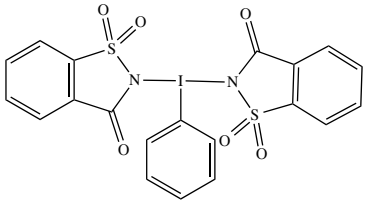
(2-methoxyphenyl)-λ^{3}-iodanediyl diacetate (3b)[39]



Synthesized according to the literature procedure by Zhdankin et al.[39] Peracetic acid was formed by the reaction of 30 mL of acetic anhydride and 10 mL of 30% H_2O_2 at 40^{o}C with stirring overnight. Afterwards, 5.0mmol of 1-iodo-2-methoxybenzene **3a** was added

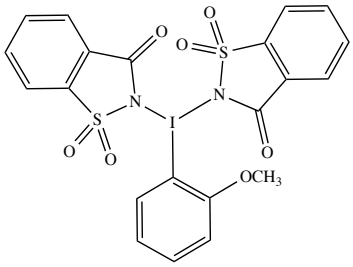
to the peracetic acid and the mixture was stirred for 8 h at 40°C. The mixture was then evaporated under reduced pressure and then washed with water and hexanes. Upon drying under vacuum, (2-methoxyphenyl)-λ^3-iodanediyl diacetate, was isolated as a yellow solid and verified via ^{1}H NMR. The spectrum is included for reference.

2,2'-(phenyl-λ^3-iodanediyl)bis(benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide) (3c)[14]



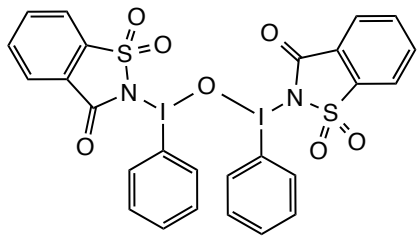
To a 10 ml round bottom flask, 1 mmol (322 mg) of (diacetoxyiodo)benzene was added along with 2 mL of dichloromethane and the mixture was stirred until all of the (diacetoxyiodo)benzene was dissolved. Afterwards, 2.1 mmol (385 mg) of saccharin was added and the mixture was allowed to stir overnight. The solvent was removed under reduced pressure and the residue was washed with acetonitrile and diethyl ether, filtered, and then dried under vacuum to afford 500 mg (96%) the desired product. Isolated as a white solid; mp 214.5-215.3°C; ^{1}H NMR (CD_3OD): δ 8.32-8.31 (d 2H), 7.92-7.80 (2d 4H, 2t 4H), 7.68-7.65 (t 1H), 7.58-7.55 (t 2H); ^{13}C NMR (CD_3OD): δ 163.7, 141.0, 134.4, 134.2, 133.6, 132.1, 130.8, 128.9, 124.2, 122.8, 120.3; IR (KBr) cm^{-1} 3099, 1698, 1590, 1456, 1300, 1169; Elemental analysis calcd. for $C_{20}H_{13}IN_2O_6S_2$: C, 42.27; H, 2.31; I, 22.33; N, 4.93; O, 16.89; S, 11.28. Found: C, 42.12; H, 2.31; N, 4.93.

2,2'-((2-methoxyphenyl)-λ^3-iodanediyl)bis(benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide) (3d)



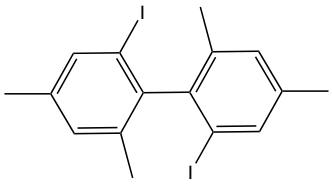
To a 10 mL round bottom flask, 1 mmol of (2-methoxyphenyl)-λ^3-iodanediyl diacetate **3b** was added along with 2 mL dichloromethane. The mixture was allowed to stir until fully dissolved, and then 2.1 mmol (385 mg) of saccharin was added. The mixture was allowed to stir overnight. The solvent was removed under reduced pressure and the residue was washed with acetonitrile and diethyl ether, filtered, and then dried under vacuum to afford 527 mg (88%) the desired product. Isolated as a pale yellow solid; mp 169.5-170.3 ^{o}C; ^{1}H NMR (CD_3OD): δ 8.36-8.45 (d 1H), 7.90-7.79 (2d 4H, 2t 4H), 7.71-7.69 (t 1H), 7.38-7.36 (d 1H), 7.10-7.07 (t 1H), 4.06 (s 3H); ^{13}C NMR (CD_3OD): δ 156.7, 141.4, 137.5, 135.4, 133.9, 133.4, 124.0, 122.3, 120.2, 114.8, 112.1, 105.0, 56.2; IR (KBr) cm^{-1} 3091, 3009, 2970, 2940, 2836, 1720, 1640, 1584, 1475, 1338, 1267, 1153.

,2'-(oxybis(phenyl-λ^3-iodanediyl))bis(benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide) (3f)



To a 10 ml round bottom flask, 1 mmol (322 mg) of (diacetoxyiodo)benzene was added along with 1 mL of dichloromethane and the mixture was stirred until all of the (diacetoxyiodo)benzene was dissolved. Afterwards, 2.0 mL of water was added along with 1.1 mmol (202 mg) of saccharin. 1 mL of dichloromethane was added to wash down any remaining reagents from the sides of the flask and the reaction was allowed to stir for 24 h, making certain the solid residue remains in the liquid portion of the mixture and does not build up on the sides of the flask. The solvent was removed under reduced pressure and the residue was gently washed with acetonitrile and diethyl ether, filtered, and then dried under vacuum to afford 378 mg (96%) of the desired product. Isolated as a pale yellow solid; mp 175.9-176.6 ^{o}C; ^{1}H NMR (CD_3OD): δ 8.28-8.26 (d 4H), 7.84-7.74 (2d 4H, 2t 4H), 7.68-7.65 (t 2H), 7.59-7.55 (t 4H); ^{13}C NMR (CD_3OD): δ 166.3, 141.9, 134.2, 133.6, 133.3, 131.9, 130.8, 129.8, 123.9, 122.8, 120.1; IR (KBr) cm^{-1} 3081, 3054, 1670, 1485, 1471, 1458, 1305, 1240, 1154, 950; Elemental analysis calcd. for $C_{26}H_{18}I_2N_2O_7S_2$: C, 39.61; H, 2.30; I, 32.19; N, 3.55; O, 14.21; S, 8.13. Found: C, 39.79; H, 2.33; I, 32.08; N, 3.65; S, 8.17.

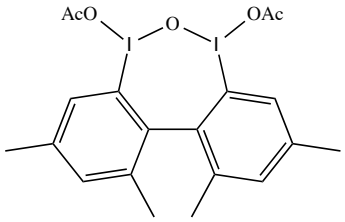
2,2'-diiodo-4,4',6,6'-tetramethyl-1,1'-biphenyl (3g)[32]



Compound **3g** was synthesized using a procedure from Kita et al.[32] 7 mmol of 3,5-dimethyliodobenzene in 8.75 mL CH_2Cl_2 was added drop wise to a stirring solution of 3.5 mmol PIFA and 7 mmol $BF_3 \bullet Et_2O$ in 8.75 mL CH_2Cl_2 under argon atmosphere at -

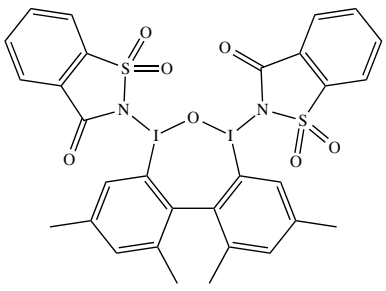
78 °C. The reaction was maintained under these conditions for 5 h and then quenched with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The desired product **3g** was obtained by column chromatography using hexanes/ethyl acetate and confirmed via ^1H NMR. The spectrum is included for reference.

1,3,9,11-tetramethyl-5λ^3,7λ^3-dibenzo[*d*,*f*][1,3,2]diodaoxepine-5,7-diyl diacetate (3h)[32]



Following the same article by Kita et al., 17.1 mL of AcOH and 1.9 mmol of **3g** was added successively to a stirring solution of Selectfluor™ (7.6 mmol) in 47.5 mL of acetonitrile. The reaction was stirred overnight at room temperature and the solvent was removed under reduced pressure. The solid was dried and then dissolved in a minimum amount of CH_2Cl_2 and hexane was added drop-wise to precipitate out the desired product. This was then dried under vacuum and its identity was confirmed via ^1H NMR. The spectrum is included for reference.

2,2'-(1,3,9,11-tetramethyl-5λ^3,7λ^3-dibenzo[*d*,*f*][1,3,2]diodaoxepine-5,7-diyl)bis(benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide) (3i)



To a 10 ml round bottom flask, 0.17 mmol (103 mg) of **3h** was added along with 1.5 mL of CH_2Cl_2 and the mixture was stirred until dissolved. 0.34 mmol (62 mg) of saccharin was added and the reaction was allowed to stir for 24 h. The solvent was removed under reduced pressure and the residue was gently washed with diethyl ether and dried under vacuum to afford 90mg (63%) of the desired product. Isolated as a pale yellow solid; mp 130.1-131.2 $^{\circ}$C; ^{1}H NMR ($CDCl_3$): δ 8.42 (s 2H), 7.84-7.83 (d 2H), 7.74-7.66 (d 2H, 2t 4H), 7.54 (s 2H), 2.52, (s 6H), 2.27 (s 6 H); ^{13}C NMR ($CDCl_3$): δ 177.3, 143.7, 141.6, 139.9, 137.9, 136.4, 135.0, 133.6, 133.3, 129.7, 128.7, 124.6, 120.6, 21.4, 21.3; IR (KBr) cm^{-1} 3413, 3070, 3014, 2918, 2863, 1637, 1585, 1458, 1334, 1255, 1154; Elemental analysis calcd. for: $C_{30}H_{24}I_2N_2O_7S_2 \cdot H_2O$: C, 41.02; H, 3.21; I, 28.89; N, 3.19; O, 16.39; S, 7.30; Found: C, 40.72; H, 3.06; I, 28.78; N, 2.98; S, 7.28.

Single crystals of **3i** suitable for X-ray crystallographic analysis were obtained by slow recrystallization from acetonitrile. X-ray diffraction data was collected on Rigaku RAPID II Image Plate system using graphite-monochromated MoKα radiation (λ=0.71073 Å). Crystal data for **3i** $C_{32}H_{27}I_2N_3O_8S_2$: M 842.46, a = 16.0540(8), b = 16.6646(7), c = 25.6470 (18) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 6861.43 Å^3, Z = 8, R-Factor = 7.73.

General Procedure for Synthesis of Silyl Enol Ethers[48,49]

All of the silyl enol ethers were freshly prepared according to a general procedure except for 1-phenyl-1-trimethylsiloxyethylene, 1-(trimethylsiloxy)cyclopentene, and 1-(trimethylsiloxy)cyclohexene, which were commercially available from Sigma Aldrich®.

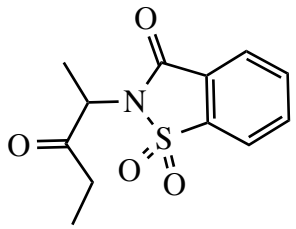
The general procedure was adapted from two articles by Boto et al. where the silyl enol ethers were prepared from their corresponding methyl ketones.[48,49] TMSOTF (0.804 mL, 4.2 mmol) was added to 3 mL of dichloromethane and this solution was added drop wise to a solution of the triethylamine (1.1mL) and the methyl ketone in (3.5 mmol) in 15 mL of dichloromethane which was cooled to 0 °C. The solution was allowed to stir for 30 minutes at 0°C and then brought to room temperature (25 °C) and continued to stirring for 1 h. Afterwards, the mixture was diluted with hexanes and washed with a saturated aqueous sodium bicarbonate solution and water. The organic layer was extracted and dried over anhydrous sodium sulfate, followed by filtration and rotary evaporation. The resulting oil was then dried under deep vacuum to remove any solvent impurities and then used without further purification in the imide transfer reaction. Confirmation of the correct structures was confirmed via ^{1}H NMR and the corresponding spectra are included for reference.

General Procedure for Imide Transfer Reaction

To a 10 mL pear-shaped round bottom flask, 0.15 mmol (0.6 equivalent) of the mu-oxo starting material was added along with 1.5 mL of dry acetonitrile. A stir bar was added and the solution was stirred for 1 minute before the addition of 0.25 mmol (1 equivalent) of the silyl enol ether, which was added via an Eppendorf pipette. The solution was stirred and monitored via TLC for full conversion of the silyl enol ether. When complete, the solution was evaporated under reduced pressure and the NMR yield was determined using a 1,1,2,2-Tetrachloroethane standard. Purification of the desired products was achieved using column chromatography with alumina or silica gel and

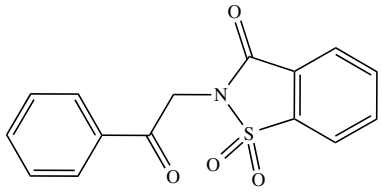
eluting with hexanes/ethyl acetate. The products were then dried under deep vacuum to remove any trace solvent impurities.

2-(3-oxopentan-2-yl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3j)[26]



Reaction of (*Z*)-trimethyl(pent-2-en-3-yloxy)silane according to the general procedure afforded 16 mg (24%) of product after column chromatography using silica gel (1:2.5 hexanes/ethyl acetate). Isolated as a pale-yellow liquid. ^{1}H NMR ($CDCl_3$): δ 8.071-8.054 (d 1H), 7.95-7.93 (d 1H), 7.92-7.84 (2t 2H), 4.65-4.61 (q 1H), 2.59-2.55 (m 2H), 1.79-1.77 (d 3H), 1.10-1.07 (t 3H). ^{13}C NMR ($CDCl_3$): δ 204.5, 158.8, 137.9, 135.0, 134.5, 126.9, 125.4, 121.0, 56.1, 31.6, 13.8, 7.5; IR (CH_2Cl_2) cm^{-1} 3039, 2974, 2942, 2875, 1730, 1460, 1343, 1299, 1260, 1214, 1187.

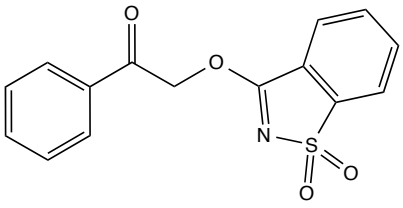
2-(2-oxo-2-phenylethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3k)[26]



Reaction of trimethyl((1-phenylvinyl)oxy)silane according to the general procedure afforded 51 mg (68%) of product after column chromatography using silica gel (3:1 hexanes/ethyl acetate). Isolated as a white solid; mp 193.0-194.0 ^{o}C; ^{1}H NMR ($CDCl_3$): δ

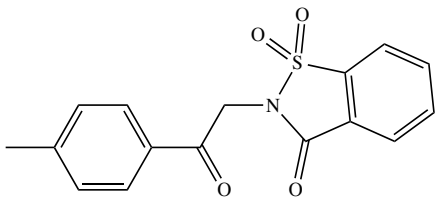
8.11-8.10 (d 1H), 8.02-8.01 (d 2H), 7.98-7.96 (d 1H), 7.92-7.89 (t 1H), 7.88-7.85 (t 1H), 7.66-7.63 (t 1H), 7.54-7.51 (t 2H), 5.15 (s 2H); ^{13}C NMR ($CDCl_3$): δ 188.7, 159.1, 138.0, 134.9, 134.5, 134.2, 134.1, 129.0, 128.2, 127.4, 125.5, 121.2, 44.5; IR (KBr) cm^{-1} 3069, 2970, 2928, 2857, 1736, 1701, 1595, 1450, 1417, 1335, 1229, 1182; HRMS (ESI): calcd for $C_{15}H_{11}NNaO_4S$ ($M+ Na^+$): 324.0306; found: 324.0294.

2-((1,1-dioxidobenzo[*d*]isothiazol-3-yl)oxy)-1-phenylethan-1-one (3l)[33]



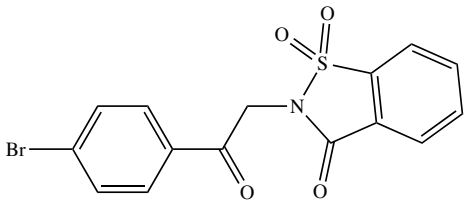
Reaction of trimethyl((1-phenylvinyl)oxy)silane according to the general procedure afforded 22 mg (29%) of product after column chromatography using silica gel (3:1 hexanes/ethyl acetate). Isolated as a white solid; mp 180.3-181.1 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 7.97-7.95 (d 2H), 7.92 (d 1H), 7.91-7.90 (d 1H), 7.82-7.79 (t 1H), 7.77-7.74 (t 1H), 7.68-7.65 (t 1H), 7.56-7.53 (t 2H), 5.86 (s 2H); ^{13}C NMR ($CDCl_3$): δ 189.4, 169.2, 143.9, 134.5, 134.4, 133.6, 133.6, 129.1, 127.9, 126.4, 123.8, 122.1, 71.6; IR (KBr) cm^{-1} 3094, 3069, 2944, 1709, 1616, 1569, 1556, 1471, 1435, 1399, 1325, 1230, 1177, 1057.

2-(2-oxo-2-(*p*-tolyl)ethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3m)[16]



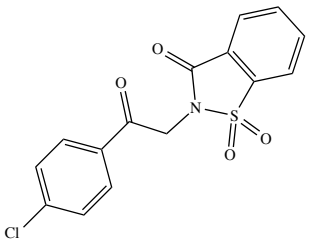
Reaction of trimethyl((1-(*p*-tolyl)vinyl)oxy)silane according to the general procedure afforded 52 mg (66%) of product after column chromatography using alumina gel (1:1 hexanes/ethyl acetate). Isolated as a white solid; mp 183.1-183.9 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 8.12-8.11 (d 1H), 7.98-7.96 (d 1H), 7.92-7.85 (d 2H, 2t 2H), 7.33-7.31 (d 2H), 5.13 (s 2H), 2.45 (s 3H); ^{13}C NMR ($CDCl_3$): δ 188.3, 159.2, 145.3, 138.0, 134.9, 134.4, 131.7, 129.7, 128.3, 127.5, 125.5, 121.2, 44.4, 21.8; IR(KBr) cm^{-1} 3092, 3040, 2972, 2930, 1736, 1698, 1606, 1463, 1423, 1335, 1267, 1183.

2-(2-(4-bromophenyl)-2-oxoethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3n)[50]



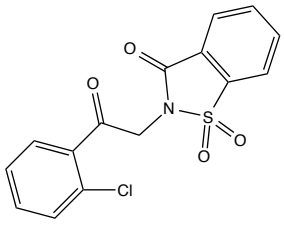
Reaction of ((1-(4-bromophenyl)vinyl)oxy)trimethylsilane according to the general procedure afforded 68 mg (72%) of product after column chromatography using alumina gel (1:1 hexanes/ethyl acetate). Isolated as a white solid; mp 191.3-192 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 8.13-8.11 (d 1H), 7.98-7.97 (d 1H), 7.93-7.87 (2t 2H, d 2H), 7.69-7.62 (d 2H), 5.10 (s 2H); ^{13}C NMR ($CDCl_3$): δ 188.0, 159.1, 138.0, 135.0, 134.5, 132.8, 132.4, 129.7, 127.3, 125.5, 121.3, 44.3; IR (KBr) cm^{-1} 3091, 2983, 2944, 1743, 1693, 1587, 1467, 1425, 1329, 1225, 1185, 590.

2-(2-(4-chlorophenyl)-2-oxoethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3o)[26]



Reaction of ((1-(4-chlorophenyl)vinyl)oxy)trimethylsilane according to the general procedure afforded 55 mg (65%) of product after column chromatography using silica gel (4:1 hexanes/ethyl acetate). Isolated as a white solid; mp 184.5-185.1°C; ^{1}H NMR ($CDCl_3$): δ 8.12-8.10 (d 1H), 7.98-7.58 (d 1H, d 2H, 2t 2H), 7.51-7.49 (d 2H), 5.11 (s 2H). ^{13}C NMR ($CDCl_3$): δ 187.8, 159.1, 140.9, 137.9, 135.0, 134.5, 132.4, 129.6, 129.4, 127.3, 125.5, 121.2, 44.3. IR (KBr) cm^{-1} 3094, 2987, 2935, 1746, 1694, 1591, 1458, 1329, 1227, 749.

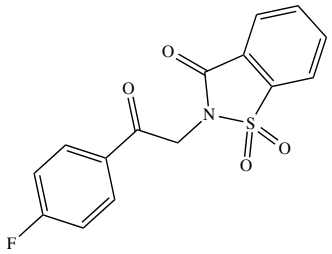
2-(2-(2-chlorophenyl)-2-oxoethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3p)[26]



Reaction of ((1-(2-chlorophenyl)vinyl)oxy)trimethylsilane according to the general procedure afforded 48 mg (57%) of product after column chromatography using silica gel (4:1 hexanes/ethyl acetate). Isolated as a white solid; mp 119.0-119.7 °C; ^{1}H NMR ($CDCl_3$): δ 8.11-8.10 (d 1H), 7.97-7.96 (d 1H) 7.92-7.85 (2t 2H) 7.74-7.73 (d 1H), 7.49-7.48 (d 2H), 7.41-7.38 (m 1H), 5.11 (s 2H). ^{13}C NMR ($CDCl_3$): δ 191.5, 159.0, 137.9,

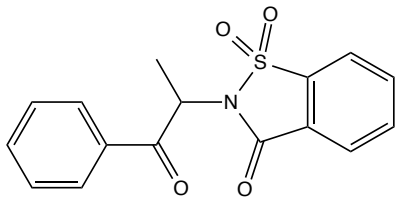
135.5, 135.0, 134.5, 133.3, 132.0, 130.9, 130.6, 127.3, 127.2, 125.5, 121.2, 47.1. IR (KBr) cm^{-1} 3097, 3034, 2973, 2929, 1740, 1717, 1697, 1598, 1464, 1434, 1213, 751.

2-(2-(4-fluorophenyl)-2-oxoethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3q)[50]



Reaction of ((1-(4-fluorophenyl)vinyl)oxy)trimethylsilane according to the general procedure afforded 59 mg (74%) of product after column chromatography using alumina gel (1:1 hexanes/ethyl acetate). Isolated as a white solid; mp 176.8-177.5°C; ^{1}H NMR ($CDCl_3$): δ 8.13-8.11 (d 1H), 8.07-8.04 (dd 2H), 7.98-7.7.97 (d 1H), 7.93-7.86 (2t 2H), 7.23-7.19 (dd 2H), 5.12 (s 2H); ^{13}C NMR ($CDCl_3$): δ 187.3, 167.4, 165.3, 159.1, 137.9, 135.0, 134.5, 131.0, 130.9, 130.6, 130.6, 127.3, 125.5, 121.2, 116.4, 116.2, 44.3. IR (KBr) cm^{-1} 3103, 2988, 2942, 1743, 1694, 1579, 1505, 1467, 1333, 1224.

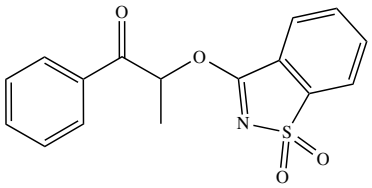
2-(1-oxo-1-phenylpropan-2-yl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3r)[51]



Reaction of (*Z*)-trimethyl((1-phenylprop-1-en-1-yl)oxy)silane according to the general procedure afforded 20 mg (24%) of product after column chromatography using silica gel

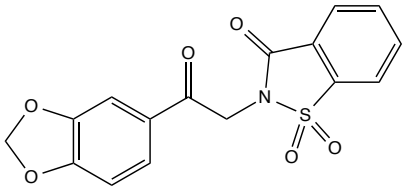
(3:1 hexanes/ethyl acetate). Isolated as a white solid; mp 154.9-155.5 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 7.99-7.97 (d 1H, d 2H), 7.92-7.90 (d 1H), 7.88-7.84 (t 1H), 7.82-7.79 (t 1H), 7.57-7.54 (t 1H), 7.47-7.44 (t 2H), 5.62-5.57 (q 1H), 1.93-1.91 (d 3H); ^{13}C NMR ($CDCl_3$): δ 194.2, 158.7, 138.0, 134.9, 134.6, 134.3, 133.4, 128.8, 128.4, 126.8, 125.3, 120.9, 53.4, 14.6; IR (KBr) cm^{-1} 3095, 3089, 2948, 2904, 1725, 1699, 1597, 1460, 1331, 1294, 1261, 1191.

2-((1,1-dioxidobenzo[*d*]isothiazol-3-yl)oxy)-1-phenylpropan-1-one (3s)



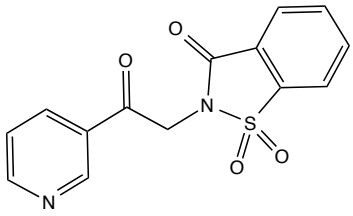
Reaction of (*Z*)-trimethyl((1-phenylprop-1-en-1-yl)oxy)silane according to the general procedure afforded 57 mg (67%) of product after column chromatography using silica gel (3:1 hexanes/ethyl acetate). Isolated as a white solid; mp 171.7-172.6 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 7.98-7.96 (d 2H), 7.89-7.86 (2d 2H), 7.80-7.72 (2t 2H), 7.66-7.62 (t 1H), 7.53-7.50 (t 1H), 6.48-6.44 (q 1H), 1.79-1.77 (d 3H); ^{13}C NMR ($CDCl_3$): δ 194.3, 168.5, 143.7, 134.3, 134.2, 133.8, 133.5, 129.1, 129.0, 128.6, 128.6, 126.5, 123.7, 122.0, 78.0, 17.7; IR (KBr) cm^{-1} 3074, 3004, 2944, 1697, 1615, 1598, 1557, 1469, 1406, 1333, 1228, 1084; HRMS (ESI): calcd for $C_{16}H_{13}NO_4SNa$ (M+ Na^+): 338.0463, found: 338.0450.

2-(2-(benzo[*d*][1,3]dioxol-5-yl)-2-oxoethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3t)[50]



Reaction of ((1-(benzo[*d*][1,3]dioxol-5-yl)vinyl)oxy)trimethylsilane according to the general procedure afforded 45 mg (52%) of product after column chromatography using silica gel (3:1 hexanes/ethyl acetate). Isolated as a white solid; mp 202.3-203.3 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 8.11-8.10 (d 1H), 7.97-7.95 (d 1H), 7.92-7.85 (2t 2H), 7.62-7.59 (d 1H), 7.46 (s 1H), 6.91-6.90 (d 1H), 6.08 (s 2H), 5.07 (s 2H); ^{13}C NMR ($CDCl_3$): δ 186.8, 159.2, 152.7, 148.5, 137.9, 134.9, 134.4, 128.9, 127.4, 125.4, 124.6, 121.2, 108.2, 108.0, 102.1, 44.2. IR(KBr) cm^{-1} 3099, 3069, 2929, 1741, 1688, 1616, 1505, 1451, 1340, 1265, 1184.

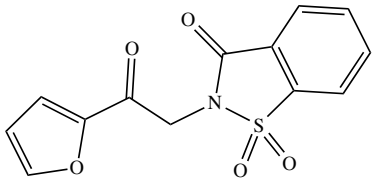
2-(2-oxo-2-(pyridin-3-yl)ethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3u)



Reaction of 3-(1-((trimethylsilyl)oxy)vinyl)pyridine according to the general procedure afforded 36 mg (48%) of product after column chromatography using silica gel (1:1 hexanes/ethyl acetate). Isolated as a white solid; mp 206.5-207.2 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 9.25 (s 1H), 8.88-8.87 (d 1H), 8.31-8.29 (d 1H), 8.14-8.12 (d 1H), 7.99-7.98 (d 1H), 7.94-

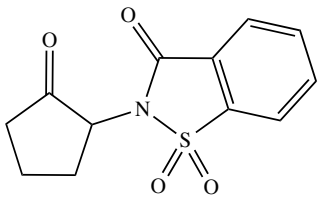
7.87 (2t 2H), 7.52-7.49 (t 1H), 5.15 (s 2H); ^{13}C NMR ($CDCl_3$): δ 188.1, 159.1, 154.6, 149.4 137.9, 135.6, 135.1, 134.6, 129.8, 127.2, 125.6, 124.0, 121.3, 44.4. IR(KBr) cm^{-1} 3095, 3078, 2965, 2927, 1737, 1709, 1589, 1464, 1418, 1332, 1317, 1234, 1182; HRMS (ESI): calcd for $C_{14}H_{10}N_2NaO_4S$ (M+ Na^+): 325.0259, found: 325.0251.

2-(2-(furan-2-yl)-2-oxoethyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3v)[26]



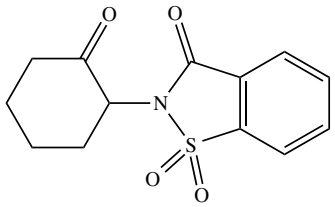
Reaction of ((1-(furan-2-yl)vinyl)oxy)trimethylsilane according to the general procedure afforded 52 mg (71%) of product after column chromatography using alumina gel (1:1 hexanes/ethyl acetate). Isolated as a white solid; mp 181.3-182.4 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 8.12-10 (d 1H), 7.97-7.95 (d 1H), 7.92-7.85 (2t 2H), 7.66 (d 1H), 7.36-7.35 (d 1H), 6.63-6.62 (t 1H), 5.03 (s 2H); ^{13}C NMR ($CDCl_3$): δ 178.4, 159.0, 150.7, 147.1, 137.9, 135.0, 134.5, 127.3, 125.5, 121.2, 118.3, 112.8, 43.8; IR (KBr) cm^{-1} 3124, 3097, 2968, 2934, 1737, 1685, 1594, 1465, 1349, 1299, 1187, 1045.

2-(2-oxocyclopentyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3w)[26]



Reaction of (cyclopent-1-en-1-yloxy)trimethylsilane according to the general procedure afforded 22 mg (33%) of product after column chromatography using silica gel (2:1 hexanes/ethyl acetate). Isolated as a white solid; mp 165.3-166.0 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 8.03-8.02 (d 1H), 7.93-7.91 (d 1H), 7.89-7.82 (2t 2H), 4.38-4.34 (dd 1H), 2.56-2.44 (m 4H), 2.31-2.25(m 1H), 1.99-1.88 (m 1H); ^{13}C NMR ($CDCl_3$): δ 209.5, 158.2, 137.8, 134.9, 134.5, 127.1, 125.3, 121.1, 56.3, 35.6, 26.7, 19.1; IR (KBr) cm^{-1} 3095, 3073, 2961, 2897, 1756, 1732, 465, 1456, 1333, 1313, 1187.

2-(2-oxocyclohexyl)benzo[*d*]isothiazol-3(2*H*)-one 1,1-dioxide (3x)[26]



Reaction of (cyclohex-1-en-1-yloxy)trimethylsilane according to the general procedure afforded 13 mg (18%) of product after column chromatography using silica gel (2:1 hexanes/ethyl acetate). Isolated as a white solid; mp 183.7-184.7 ^{o}C; ^{1}H NMR ($CDCl_3$): δ 8.06-8.04 (d 1H), 7.91-7.81 (d 1H, 2t 2H), 4.67-4.63 (dd 1H), 2.70-2.67 (td 1H), 2.65-2.59 (td 1H), 2.55-2.51 (m 1H), 2.47-2.40 (td 1H), 2.17-2.12 (m 2H). 1.88-1.80 (qtd 2H); ^{13}C NMR ($CDCl_3$): δ 200.2, 159.0, 137.8, 134.8, 134.3, 127.3, 125.3, 120.9, 60.0, 40.8, 30.3, 25.9, 25.0; IR (KBr) cm^{-1} 3099, 3030, 2950, 2927, 2901, 2866, 1740, 1718, 1355, 1333, 1304, 1180.

REFERENCES

1. V.V.Zhdankin. Hypervalent Iodine Chemistry: Preparation, Structure, and Synthetic Applications of Polyvalent Iodine Compounds, Wiley, Chichester, UK, **2013.**

2. Kuepper, F.C., Feiters, M.C., Olofsson, B., et al. *Angew. Chem., Int. Ed*. **2011,** *50*, 11598.

3. C. Willgerodt, Tageblatt der 58. Vers. deutscher Naturforscher u. Aertzte, Strassburg **1885**.

4. A. Varvoglis, *Tetrahedron.* **2010**, *66*, 5739.

5. Zhdankin, V. V., Stang, P. J. *Chem. Rev.* **2002,** *102*, 2523.

6. Ladziata, U.; Zhdankin, V. V. ARKIVOC **2006**, (ix), 26-58.

7. Zhdankin, V.V., Stang, P. J. *Chem. Rev*. **2008**, *108*, 5299.

8. Zhdankin, V. V. ARKIVOC **2009**, (i), 1-62.

9. Moriaty, R., Prakash, O. *Acc. Chem. Res.* **1986**, *19,* 244.

10. Satam, V., Harad, A., Rajule, R., Pati, H. *Tetrahedron.* **2010**, *66,* 7659.

11. Musher, J.I. *Angew. Chem. Int. Ed.* **1969**, *8*, 54.

12. Merrit, E., Carneiro, V., Silva, L., Olofsson, B. *J. Org. Chem.* **2010,** *75,* 7416.

13. Dess, B., Martin, J. *J. Org. Chem.* **1983,** *48*, 4155.

14. Hadjiarapoglou, L., Spyroudis, S., Varvoglis, A. *Synth.* **1983**, *3*, 207.

15. Papadopoulou, M., Varvoglis, A. *J. Chem. Research*. **1983**, *3,* 66.

16. Papadopoulou, M., Varvoglis, A. *J. Chem. Research.* **1984**, *5,* 166.

17. Zagulyaeva, A. A.; Banek, C. T.; Yusubov, M. S.; Zhdankin, V. V. *Org Lett.* **2010**, *12*, 4644.

18. Moriyama, K., Ishida, K., Togo, H. *Org. Lett.* **2012,** *14,* 946.

19. Miyamoto, K., Sakai, Y., Goda, S., Ochiai, M. *Chem. Comm.* **2012**, *48*, 982.

20. Roben, C., Souto, J., Gonzales, Y., Lishchynskyi, A., Muniz, K. *Angew. Chem. Int. Ed.* **2011**, *50*, 9478.

21. Souto, J., Gonzalez, Y., Iglesias, A., Zian, D., Lishchynskyi, A., Muniz, K. *Chem. Asian J.* **2012**, *7*, 1103.

22. Shrestha, R.; Mukherjee, P.; Tan, Y.; Litman, Z. C.; Hartwig, J. F. *J. Am. Chem. Soc*. **2013**, *135*, 8480.

23. Yu, S.; Wan, B.; Li, X. *Org. Lett*. **2013**, *15*, 3706.

24. Xu, H., Qiao, X., Yang, S., Shen, Z. *J. Org. Chem.* **2014**, *79*, 4414.

25. Kantak, A. A.; Potavathri, S.; Barham, R. A.; Romano, K. M.; DeBoef, B. *J. Am. Chem. Soc*. **2011**, *133*, 19960.

26. Lv, Y., Li, Y., Xiong, T., Lu, Y., Liu, Q., Zhang, Q. *Chem. Comm.* **2014,** *50*, 2367.

27. Erdik, E. *Tetrahedron.* **2004**, *60,* 8747.

28. Mai, W., Song, G., Yuan, J., Yang, L., Sun, G., Xiao, Y., Mao, P., Qu, L. *RSC Advances.* **2013**, *3*, 3869.

29. Mai, W., Wang, H., Li, Z., Yuan, J., Xiao, Y., Yang, L., Mao, P., Qu, L. *Chem. Comm.* **2012**, *48*, 10117.

30. Nigh, W. *J. Chem. Ed.* **1975**, *52*, 670.

31. Hiran, B., Boriwal, R., Bapana, S., Paliwal, S. *J. Chem. Technol. Metall.* **2010**, *45*, 127.

32. Dohi, T., Takenaga, N., Fukushima, K., Uchiyama, T., Kato, D., Motoo, S., Fujioka, H., Kita, Y. *Chem. Comm.* **2010**, *46*, 7697.

33. Grivas, J. *J. Org. Chem*. **1976**, *41,* 1325.

34. Shahwar, D., Sana, U., Ahmad, N., *Turk. J. Chem.* **2013**, *37*, 262.

35. Ahmad, M., Aslam, S., Bukhari, M., Montero, C., Detorio, M., Parvez, M., Schinazi, R. *Med. Chem. Res.* **2014**, *23*, 1309.

36. D'Ascenzio, M., Carradori, S., De Monte, C., Secci, D., Ceruso, M., Supuran, C. *Bioorg. Med. Chem*. **2014**, *22*, 1821.

37. Kim, S., Ramu, R., Kwon, S., Lee, S., Kim, C., Kang, S., Rhee, S., Bae, M., Ahn, S., Ha, D., Cheon, H., Kim, K., Ahn, J. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1065.

38. Aslam, S., Zaib, S., Ahmad, M.Gardiner, J., Ahmad, A., Hameed, A., Furtman, N., Gutschow, M., Bajorath, J., Iqbal, J. *Eur. J. Med. Chem.* **2014**, *78*, 106.

39. Zhu, C., Yoshimura, A., Ji, Lei, Wei, Y., Nemykin, V., Zhdankin, V. *Org. Lett.* **2012**, *14*, 3170.

40. Krasutsky, A., Kuehl, C., Simonsen, A., Woodward, J., Mismash, B., Bolz, J., Zhdankin, V. *J. Am. Chem. Soc.* **1996**, *118*, 5192.

41. Souto, J., Martinez, C., Velilla, I., Muniz, K. *Angew. Chem. Int. Ed.* **2013**, *52*, 1324.

42. Arbit, R., McSherry, M., Mismash, B., Young, V., Zhdankin, V. *J. Am. Chem. Soc.* **1997**, *119*, 7408.

43. Roben, C., Souto, J., Escudero-Adan, E., Muniz, K. *Org. Lett.* **2013**, *15*, 1008.

44. Koposov, A., Su, L., Boyarskikh, V., Netzel, B., Young, V., Zhdankin, V. *Org. Lett.* **2003**, *5*, 1583.

45. Arbit, R., Lynch, B., Kiprof, P., Young, V., Zhdankin, V. *J. Org. Chem.* **1998**, *63,* 6590.

46. Salvatore, R., Yoon, C., Jung, K. *Tetrahedron*. **2001**, *57*, 7785.

47. Sugasawa, S., Abe, K. *Yakugaku Zasshi.* **1952**, *72*, 270.

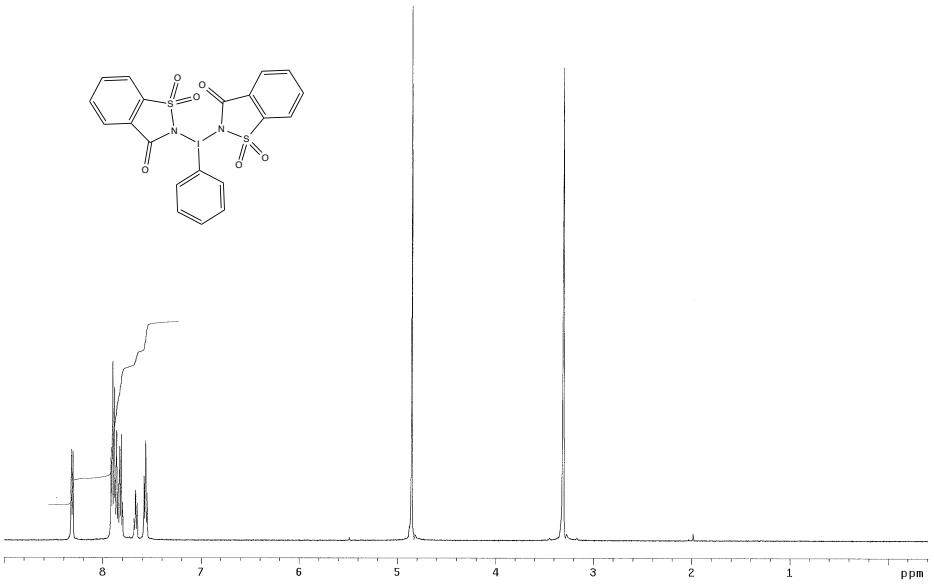
48. Miguelez, J., Batchu, V., Boto, A. *J. Org. Chem.* **2012**, *77*, 7652.

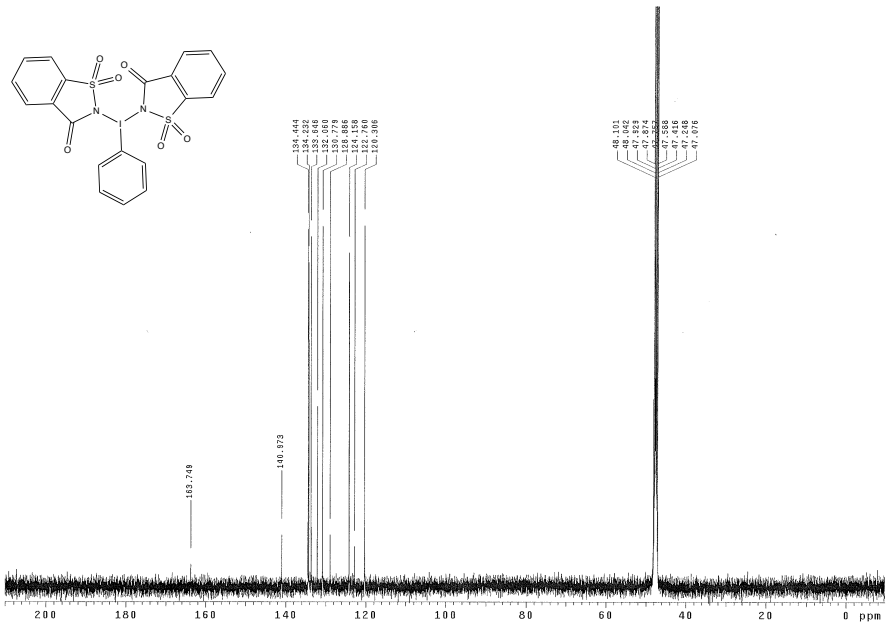
49. Miguelez, J., Boto, A., Marin, R., Diaz, M. *Eur. J. Med. Chem.* **2013**, *66*, 540.

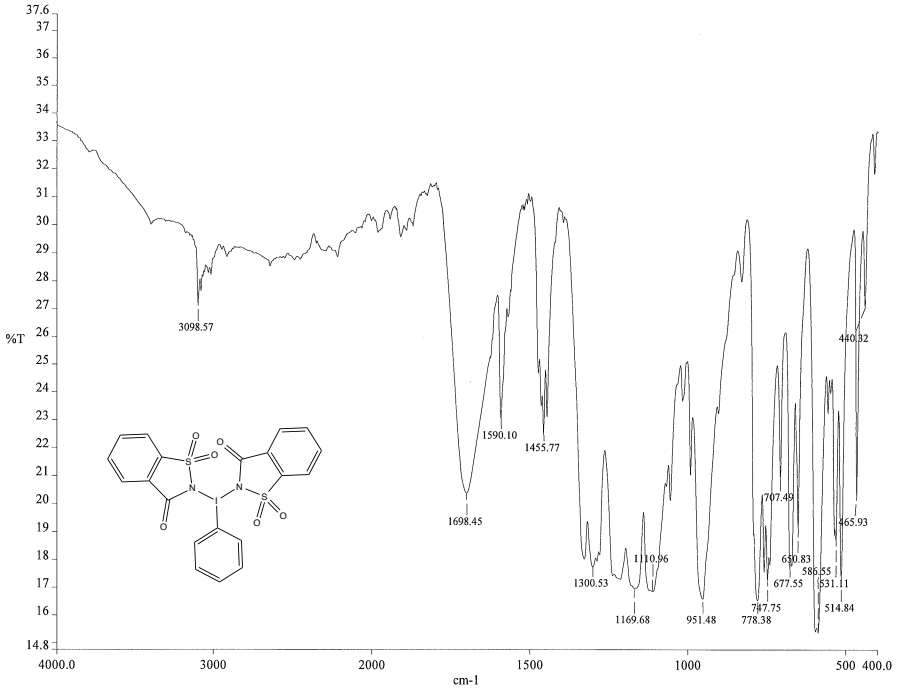
50. Aurora Fine Chemicals. www.aurorafinechemicals.com.

51. Sugasawa, S., Abe, K. *Yakugaku Zasshi.* **1955**, *75*, 168.

APPENDIX

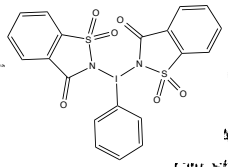

8
7
6
5
4
3
2
1
ppm


134.444
134.232
133.848
133.640
130.779
128.866
128.158
122.760
120.306
48.101
48.042
47.874
47.657
47.588
47.466
47.248
47.076
163.748
140.973
200
180
160
140
120
100
80
60
40
20
0 ppm



Minnesota Duluth.tif

Sample No. DKK 3313



6180 Atlantic Blvd. Suite M
Norcross, GA 30071
www.atlanticmicrolab.com

Company/School University of MN-Duluth
Dept. Chemistry & Biochemistry
Address 246 chem 1039 University Dr.
City, State, Zip Duluth, MN 55812
Name Steven Koski Date 7/3/13
Phone

Professor/Supervisor: Viktor Zhdankin
PO# / CC# Chg to card on file P. Siffert-Quinn

Element	Theory	Found	
C	42.27	42.12	41.99
H	2.31	2.18	2.16
N	4.93	4.78	4.76

Single ☐ Duplicate ☑

Elements Present: C, H, I, N, O, S

Analyze for: C, H, N

Hygroscopic ☐ Explosive ☐

M.P. _____ B.P. _____

To be dried: Yes ☑ No ☐

Temp. R.T. Vac. ☑ Time 2hr

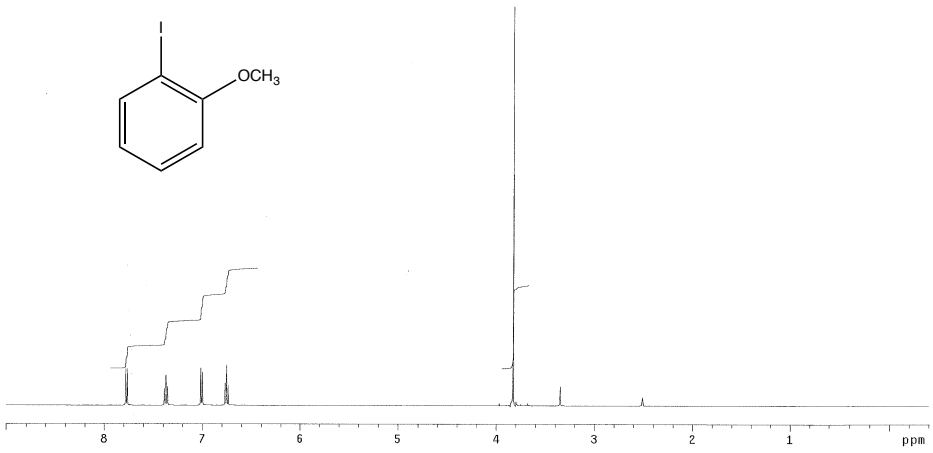
Rush Service ☐ Rush service guarantees analyses will be completed and results available by 5 PM EST on the day the sample is received by 11 AM.

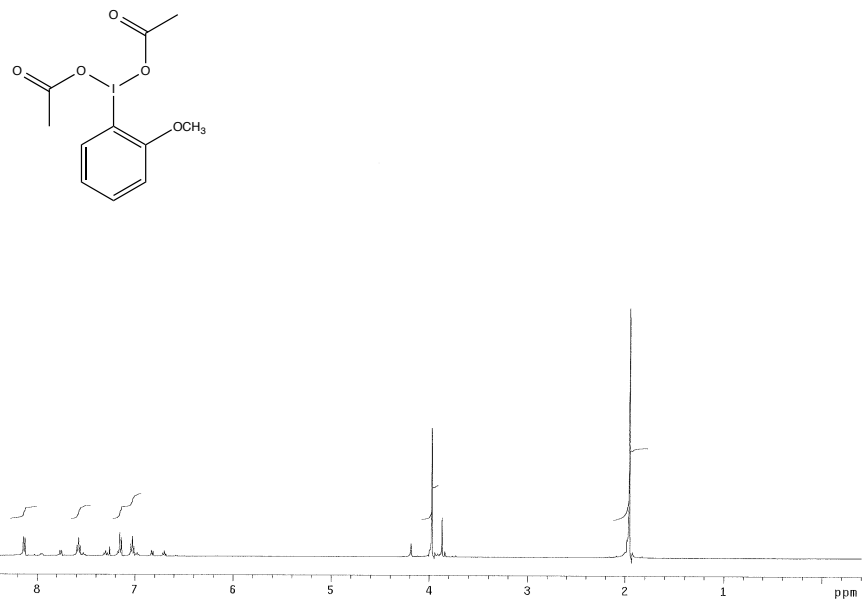
Include Email Address or FAX # Below

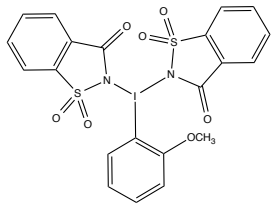
koski117@d.umn.edu

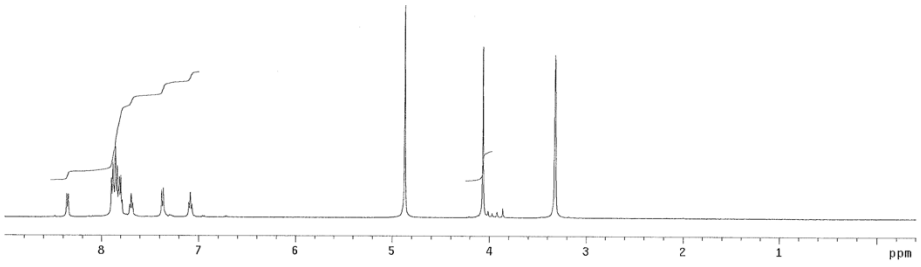
Date Received JUL 11 2013 Date Completed JUL 12 2013

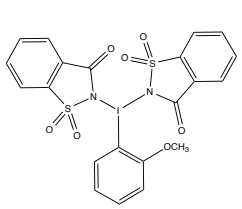
Remarks:


I
OCH3
8
7
6
5
4
3
2
1
ppm

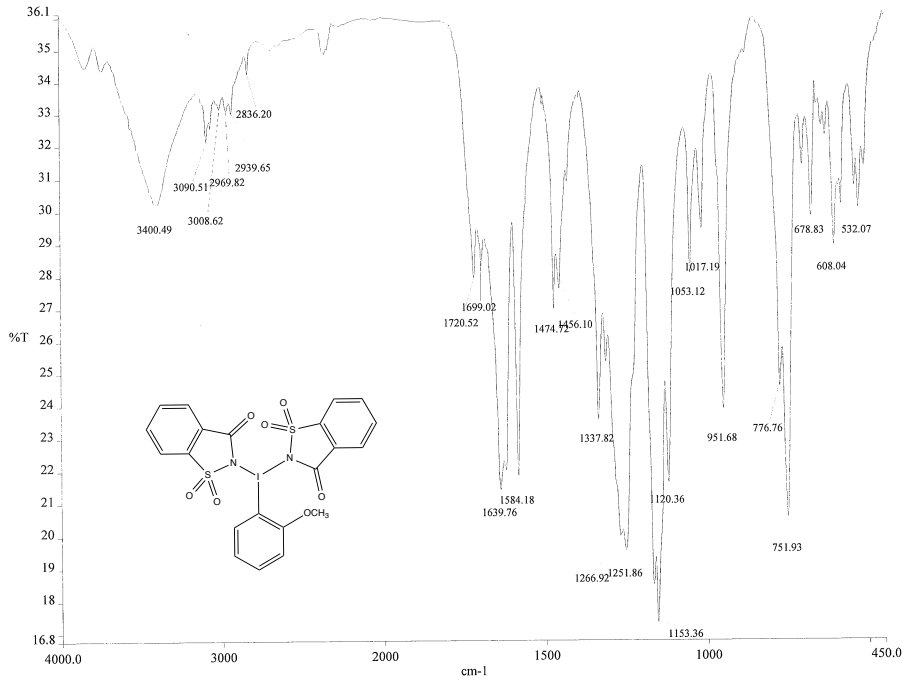

O
O
O
O
I
OCH3
8
7
6
5
4
3
2
1
ppm

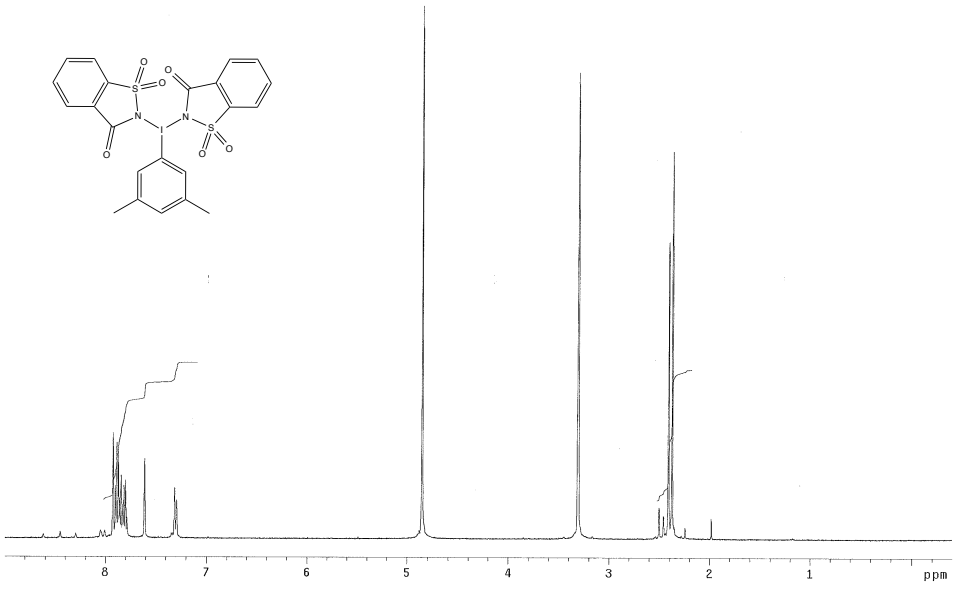

O
O
S
N
I
O
O
O
O
S
N
O
O
OCH3

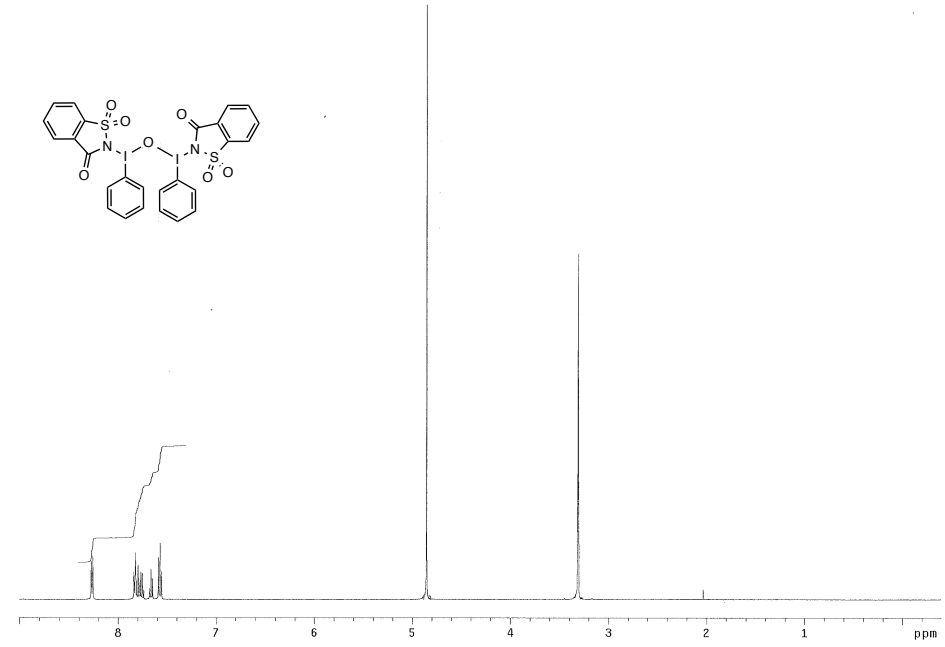

8
7
6
5
4
3
2
1
ppm

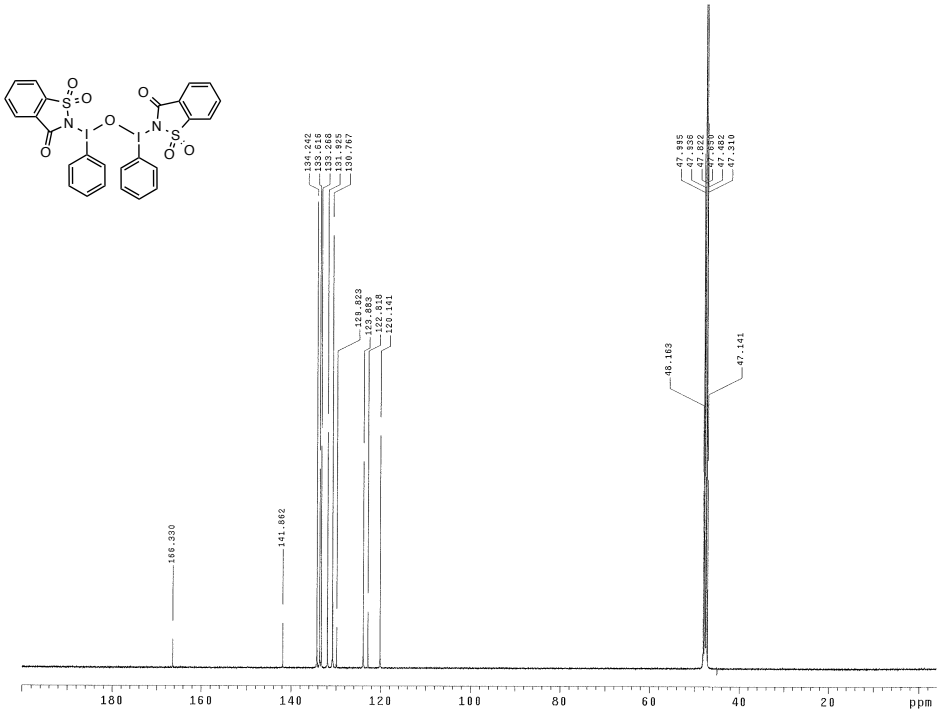

O
O
S
N
I
O
O
O
O
S
N
O
O
OCH3

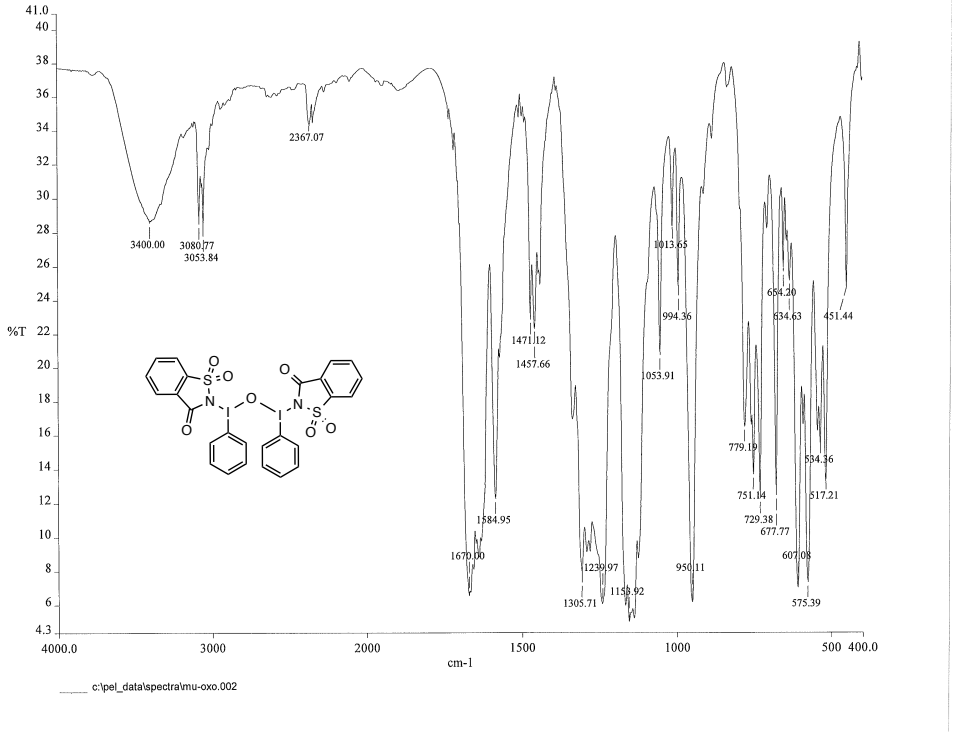
158.700
141.390
137.535
135.400
133.917
133.437
129.385
123.975
122.313
120.160
114.755
112.080
105.000
56.190
48.105
47.996
47.878
47.764
47.537
47.424
47.251
47.083
200
180
160
140
120
100
80
60
40
20
0 ppm


%T
cm-1
4000.0
3000
2000
1500
1000
450.0
3400.49
3090.51
3008.62
2969.82
2939.65
2836.20
1720.52
1699.02
1639.76
1584.18
1474.72
1456.10
1337.82
1266.92
1251.86
1153.36
1120.36
1053.12
1017.19
951.68
776.76
751.93
678.83
608.04
532.07
OCH3
c:\pel_data\spectra\orthomethoxydiproduct.005


8
7
6
5
4
3
2
1
ppm


8
7
6
5
4
3
2
1
ppm


166.330
141.662
134.242
133.616
133.268
131.995
130.767
129.823
129.063
122.858
120.141
47.985
47.838
47.692
47.545
47.398
47.252
47.105
48.163
47.141
180
160
140
120
100
80
60
40
20
ppm



ATLANTIC MICROLAB, INC.

Sample No. Mu-oxo Saccharin (SRK-107)

SUBMIT

6180 Atlantic Blvd. Suite M
Norcross, GA 30071

www.atlanticmicrolab.com

PROFESSOR/SUPERVISOR: Viktor Zhdankin

PO# / CC#: V

Company / School University of

Dept Chemistry

Address 246 Chem 1039 University Dr.

City, St, Zip Duluth, MN 55812

NAME Steven Koski DATE 10/30/13

PHONE 218-969-0641

Element	Theory	Found	
C	39.61	39.79	39.82
H	2.30	2.33	2.33
I	32.19	32.08	31.99
N	3.55	3.65	3.69
O	14.21		
S	8.13	8.17	8.04

Single ☐ Duplicate ☒

Elements Present: C,H,I,N,O,S

Analyze for: C, H, I, N, O, S

Hygroscopic ☐ Explosive ☐

M.P. _____ B.P. _____

To be dried: Yes ☐ No ☐

Temp. r.t. Vac. ✓ Time _____

RUSH SERVICE ☐ Rush service guarantees analyses will be completed and results available by 5pm EST on the day the sample is received by 11am.

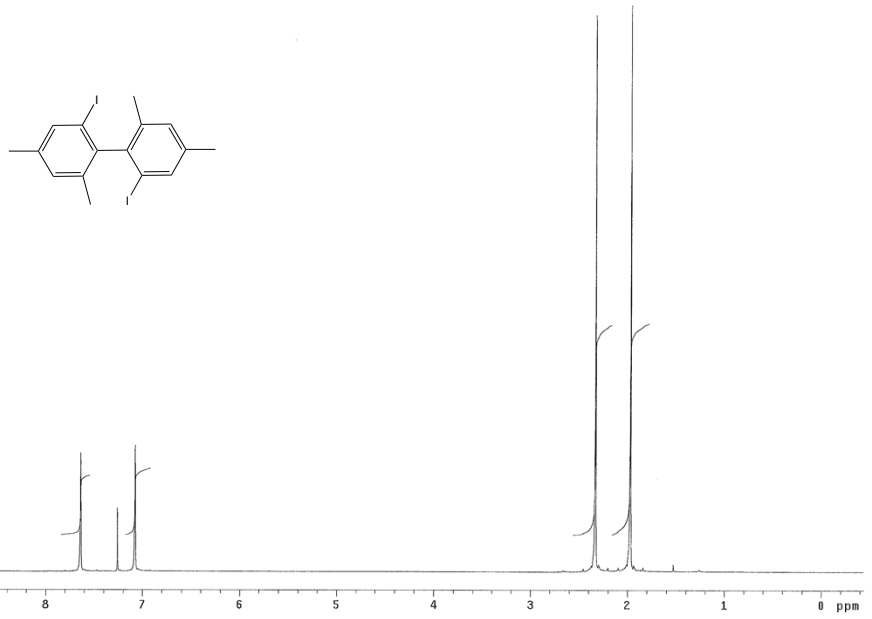
Include Email Address or Fax # Below

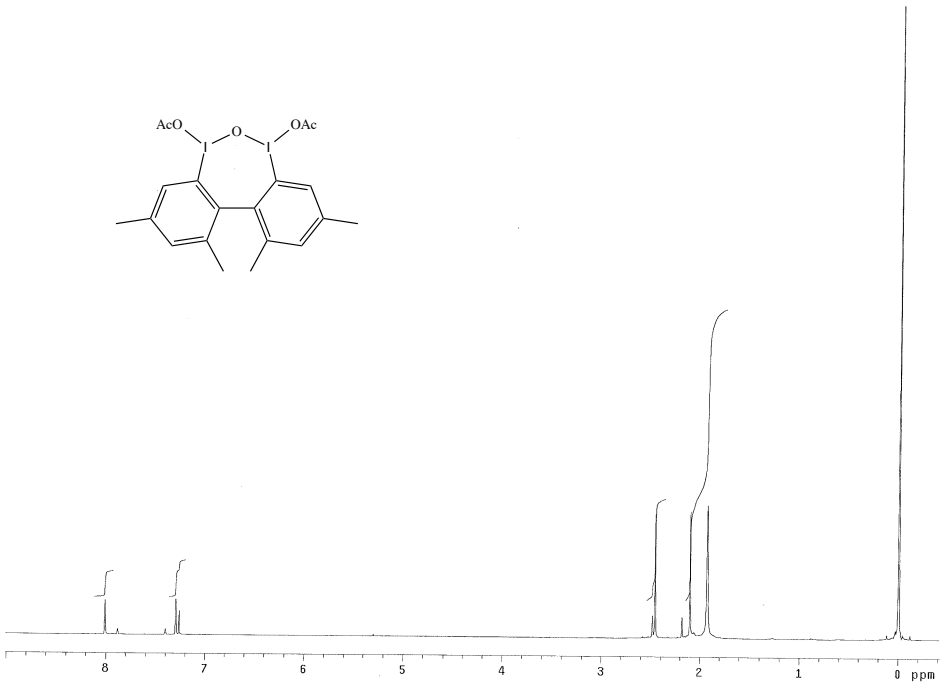
Koski117@d.umn.edu

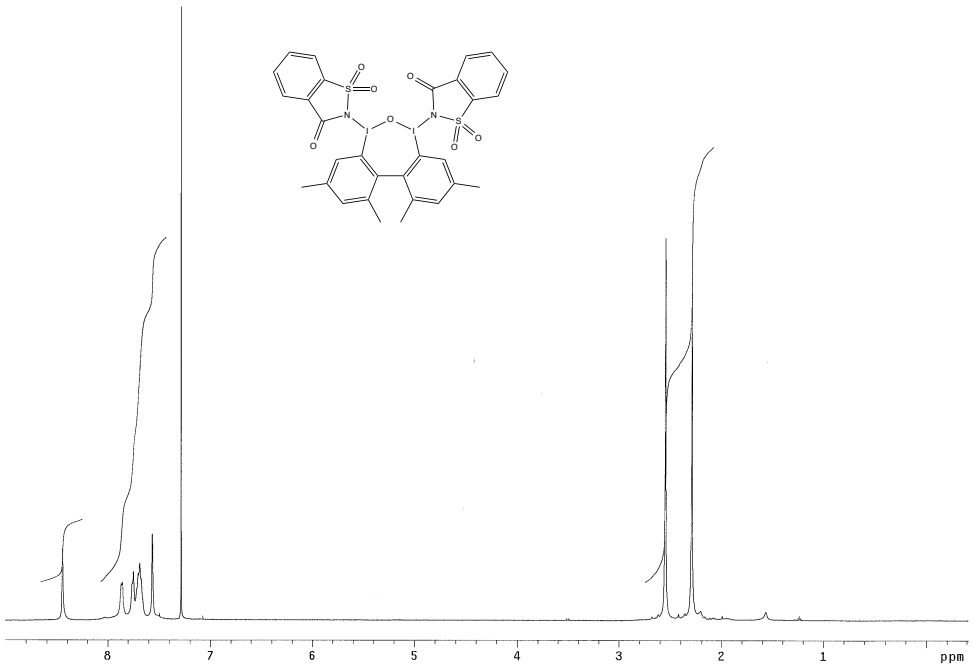
Date Received NOV 04 2013 Date Completed NOV 05 2013

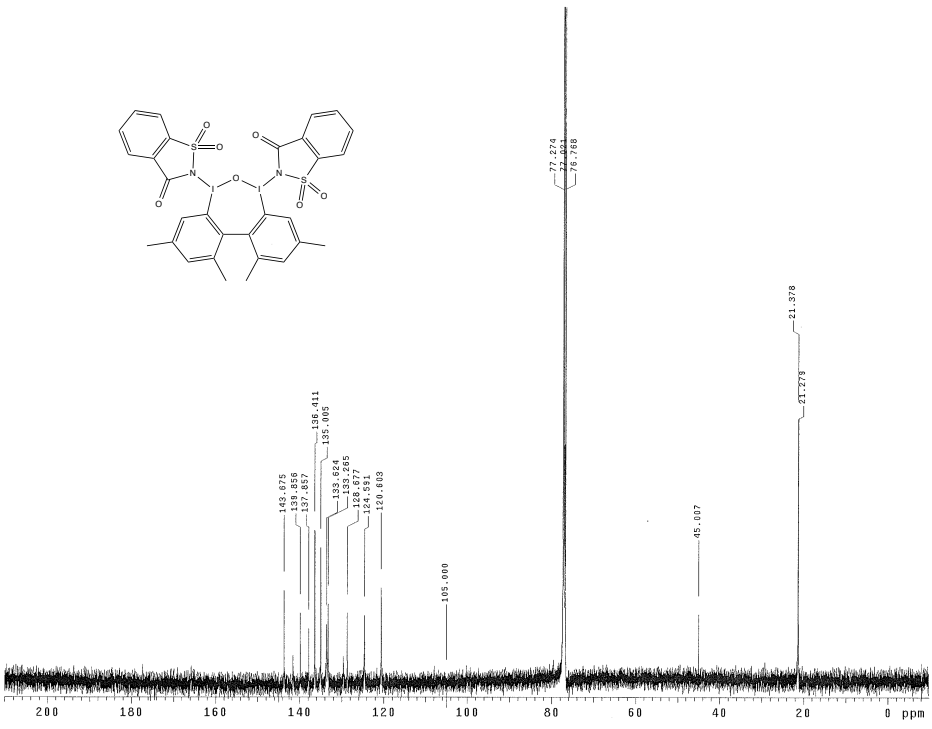
Remarks:

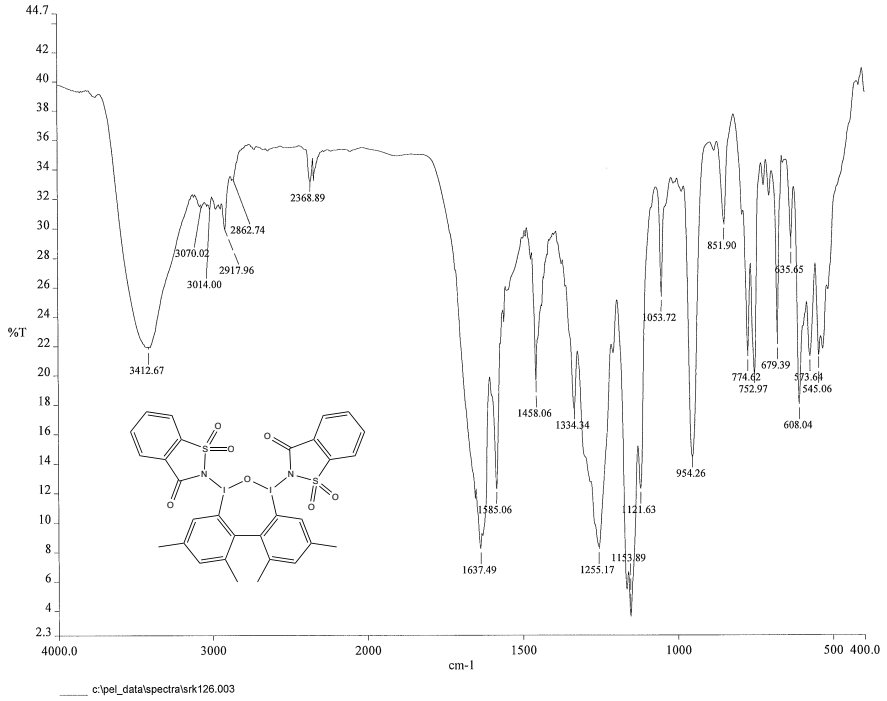
email invoice to psopoien@d.umn.edu


I
I
8
7
6
5
4
3
2
1
0 ppm


AcO
I
O
I
OAc
8
7
6
5
4
3
2
1
0 ppm


8
7
6
5
4
3
2
1
ppm


143.675
139.856
137.857
136.411
135.005
133.624
132.965
128.877
124.591
120.603
105.000
77.274
77.021
76.768
45.007
21.378
21.279
200
180
160
140
120
100
80
60
40
20
0 ppm



Atlantic Microlab, Inc.

6180 Atlantic Blvd. Suite M
Norcross, GA 30071
www.atlanticmicrolab.com

Sample No. SRK 126

Professor/Supervisor: Vikt. [illegible]

PO# / CC#

Company/School University of MN-Duluth
Dept. of Chemistry + Biochemistry
Address 246 Chem 1039 University Dr.
City, State, Zip Duluth, MN 55812
Name Steven Koski Date 1/10/14
Phone 218-969-0641

Element	Theory	Found	
C	42.77	40.72	40.83
H	2.87	3.06	3.04
I	30.13	28.78	INSUFFICIENT SAMPLE
N	3.33	2.98	3.02
O	13.29	OUR LAB DOES NOT PERFORM OXYGEN ANALYSIS	
S	7.61	7.28	7.39

Single ☐ Duplicate ☒

Elements Present: C, H, I, N, O, S

Analyze for: C, H, I, N, O, S

Hygroscopic ☐ Explosive ☐
M.P. _____ B.P. _____

To be dried: Yes ☒ No ☐
Temp. r.t. Vac. _____ Time 2 hr

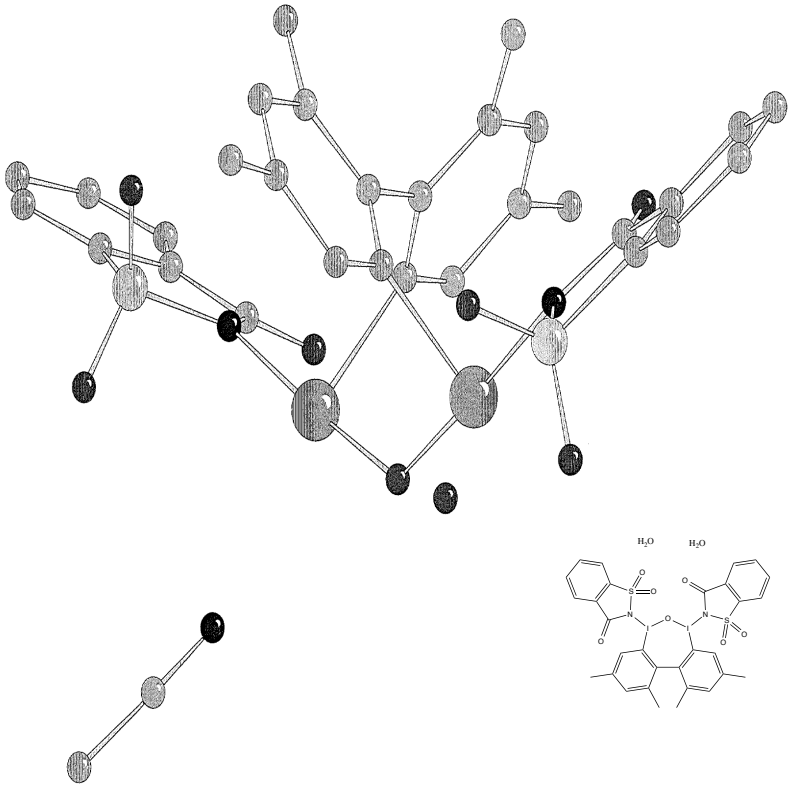
Rush Service ☐ Rush service guarantees analyses will be completed and results available by 5 PM EST on the day the sample is received by 11 AM.

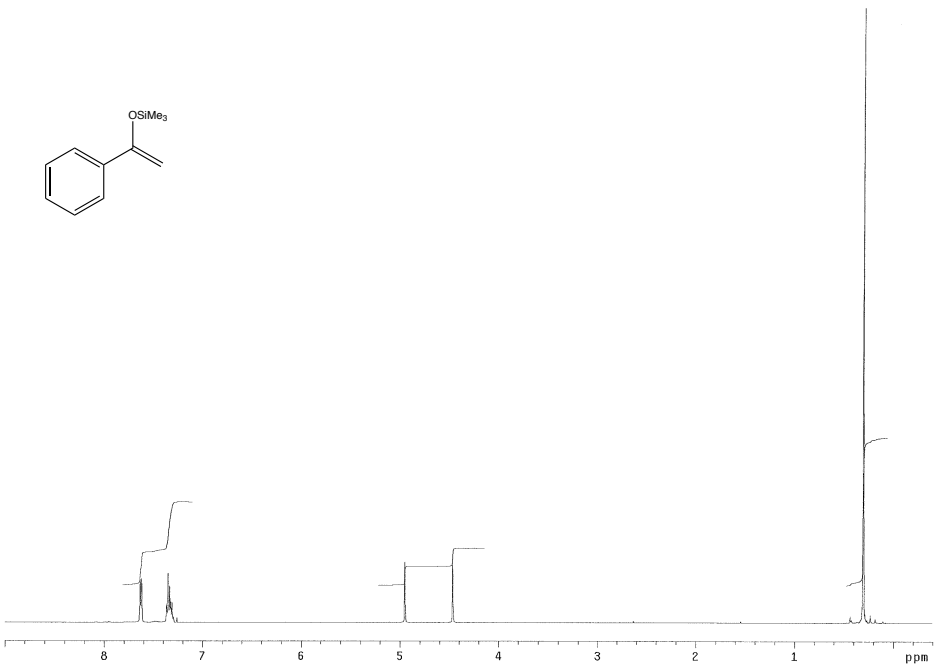
Include Email Address or FAX # Below

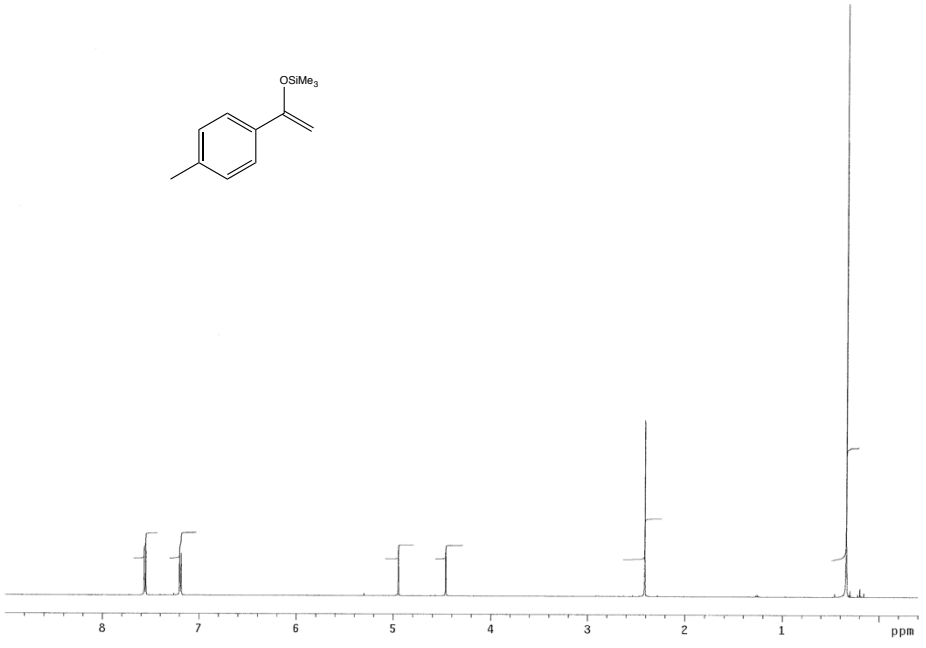
Koski117@d.umn.edu

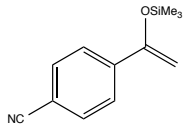
Date Received JAN 14 P.M. Date Completed JAN 15 2014

Remarks:
charge card on file - email invoice to psopo.ier@d.umn.edu

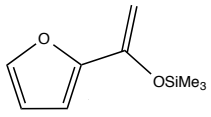



OSiMe3
8
7
6
5
4
3
2
1
ppm

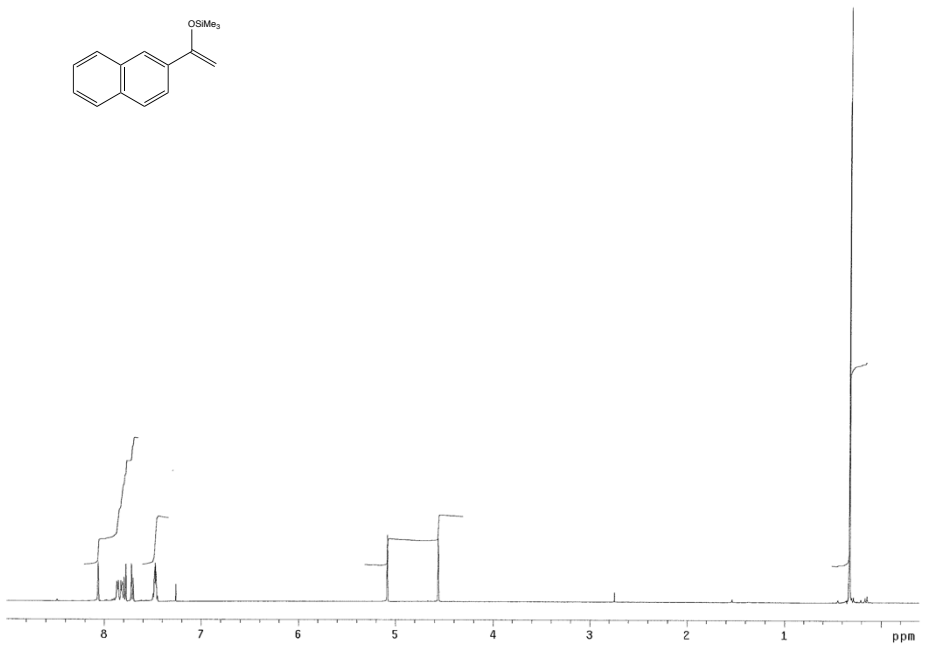

OSiMe3
8
7
6
5
4
3
2
1
ppm

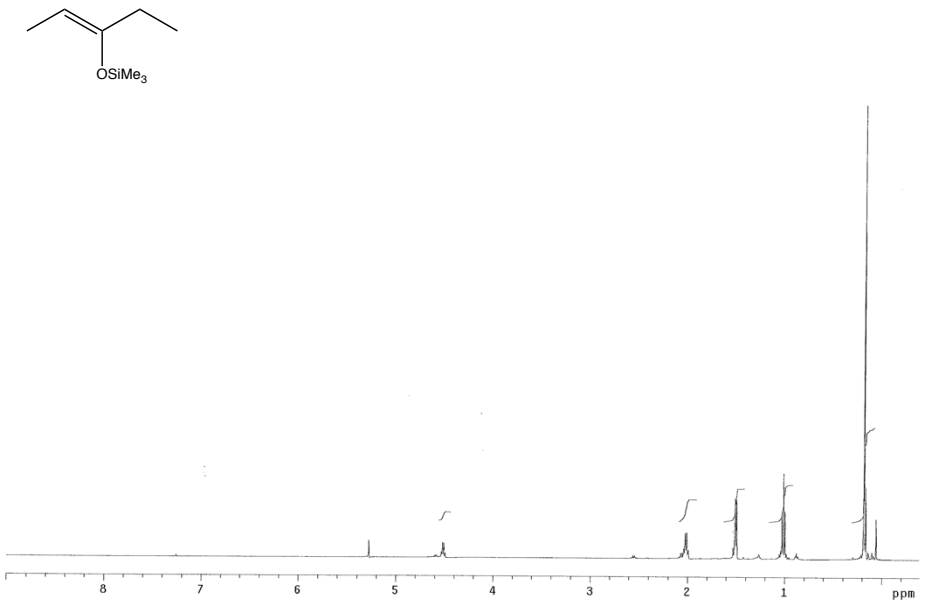

OSiMe3
NC

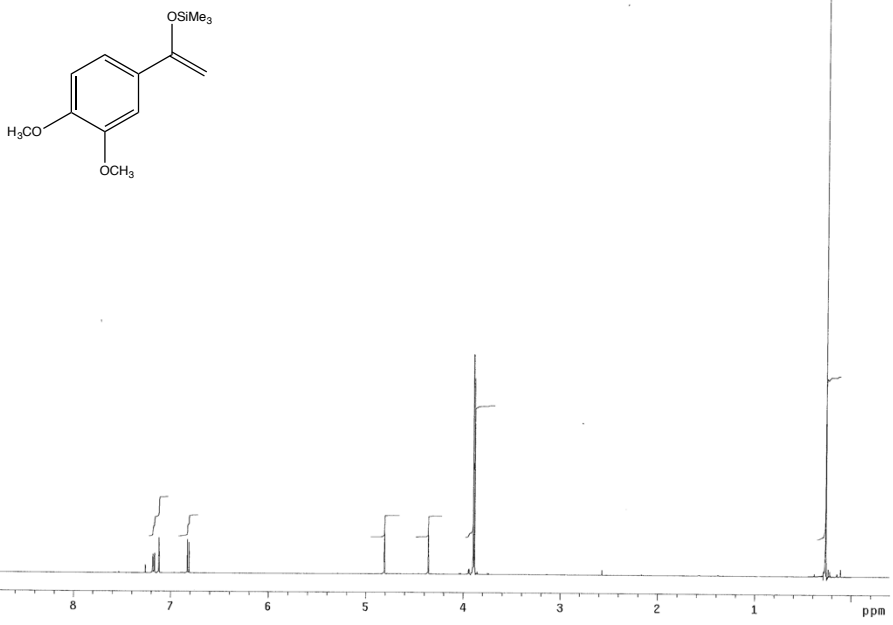
8
7
6
5
4
3
2
1
ppm

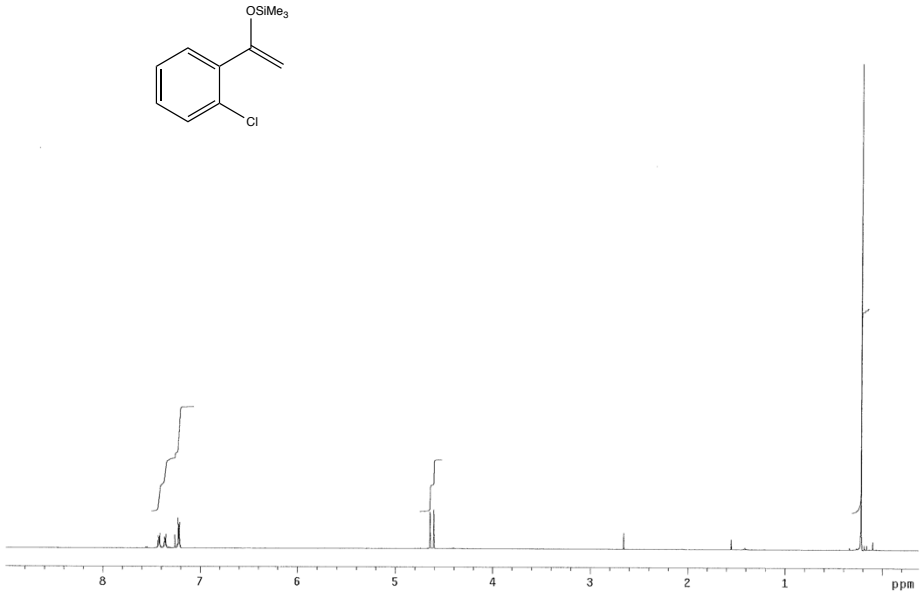

O
OSiMe3

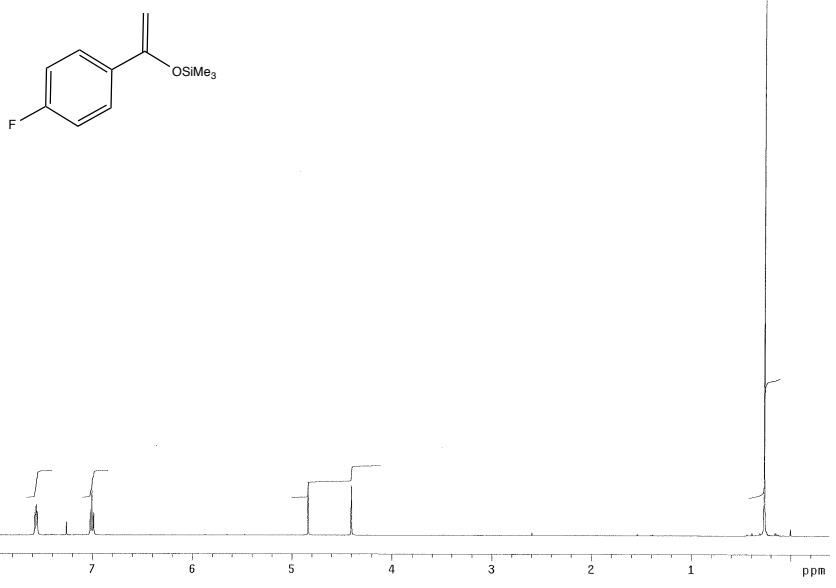
8
7
6
5
4
3
2
1
ppm

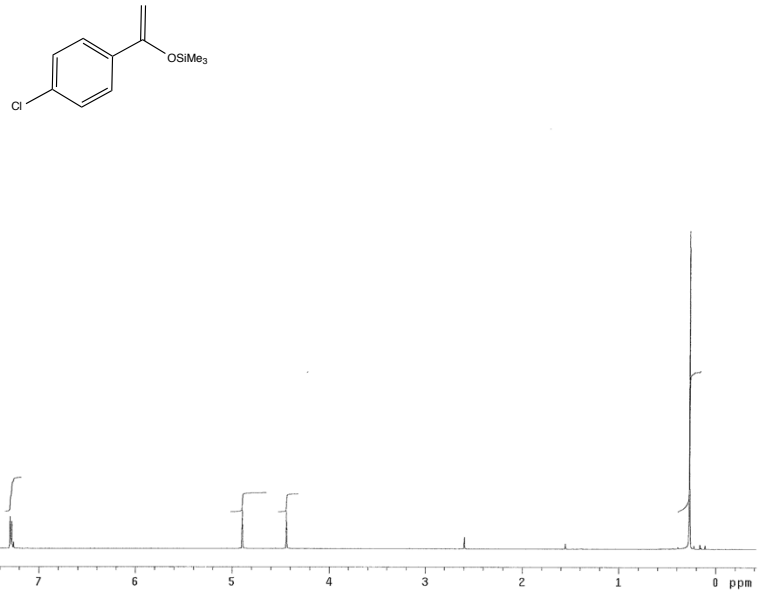

OSiMe3
8
7
6
5
4
3
2
1
ppm

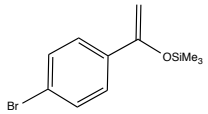

OSiMe3
8
7
6
5
4
3
2
1
ppm

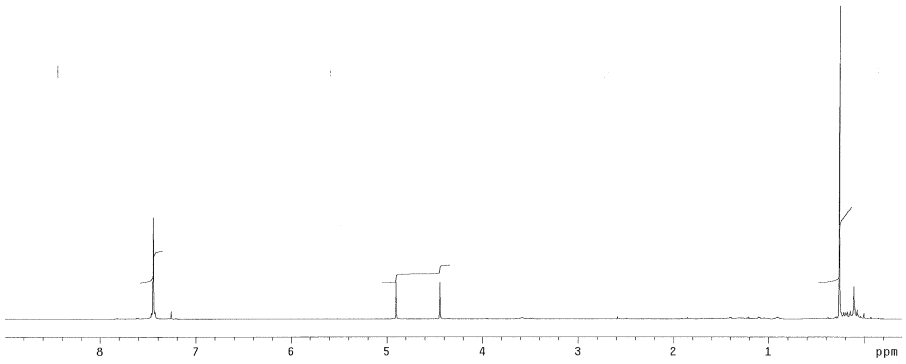

OSiMe3
H3CO
OCH3
8
7
6
5
4
3
2
1
ppm

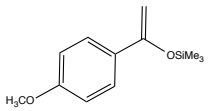

OSiMe3
Cl
8
7
6
5
4
3
2
1
ppm


OSiMe3
F
8
7
6
5
4
3
2
1
ppm

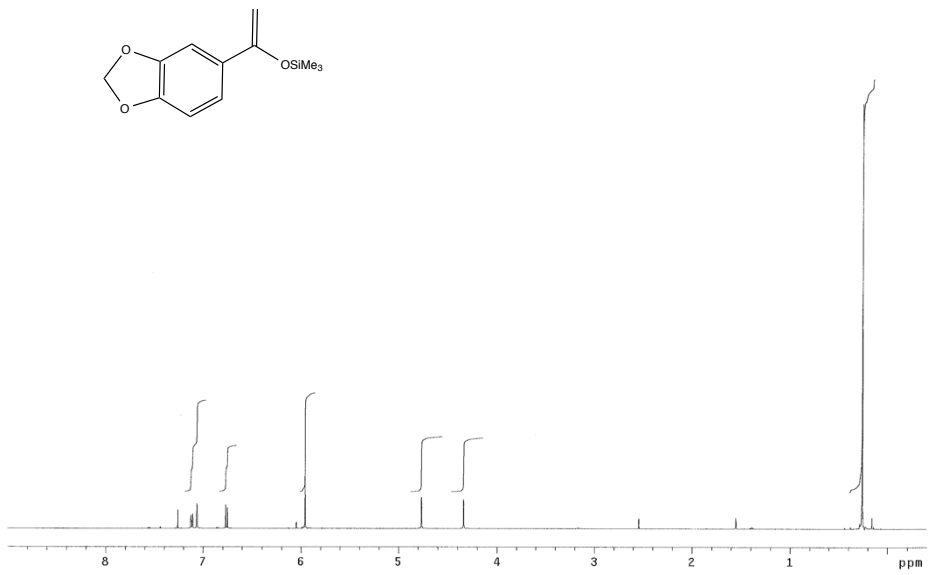

OSiMe3
Cl
8
7
6
5
4
3
2
1
0 ppm

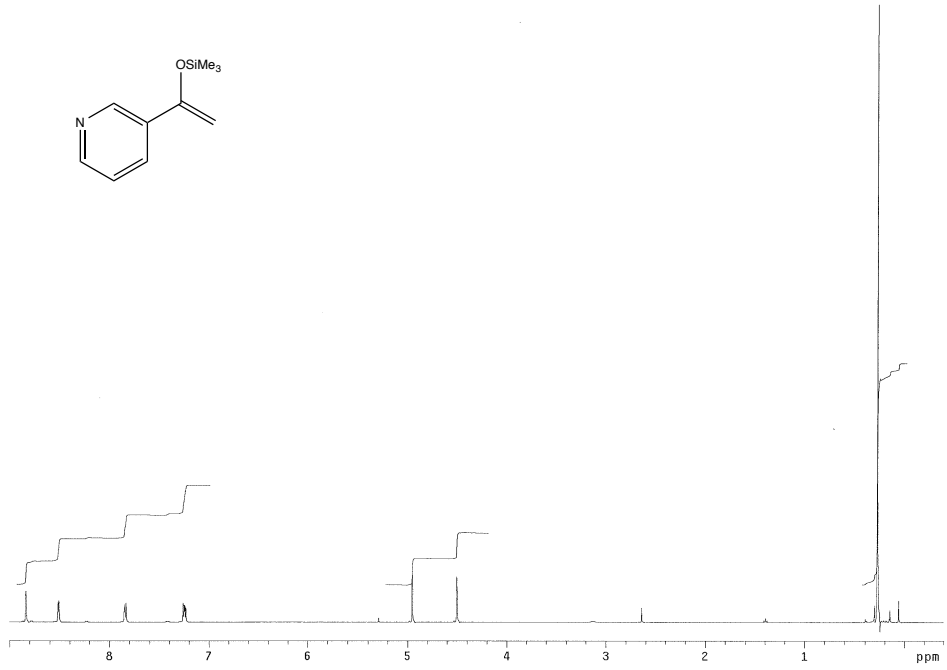

OSiMe3
Br

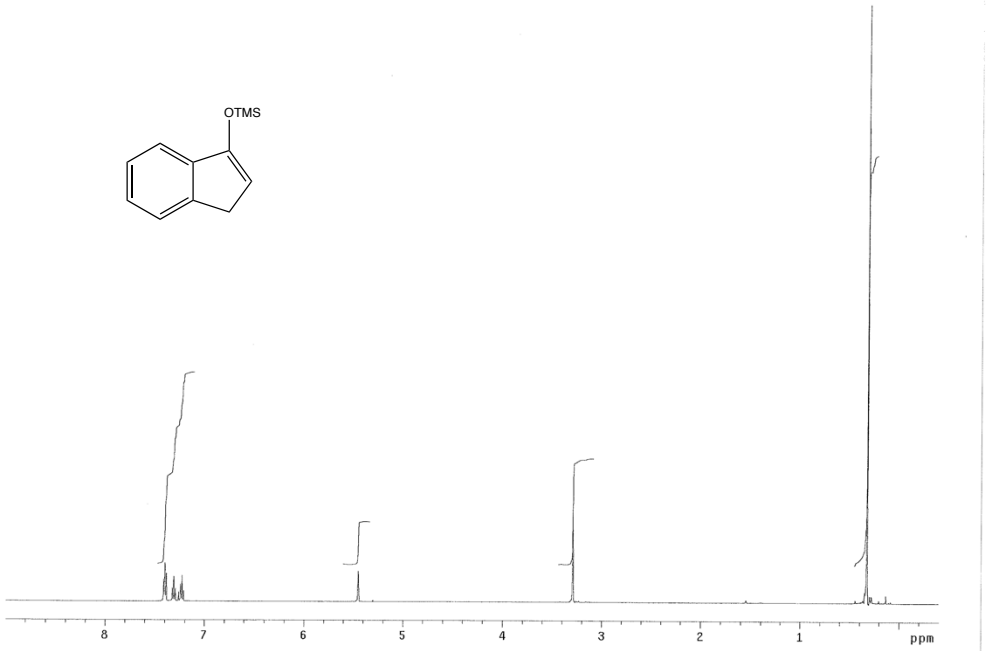

8
7
6
5
4
3
2
1
ppm

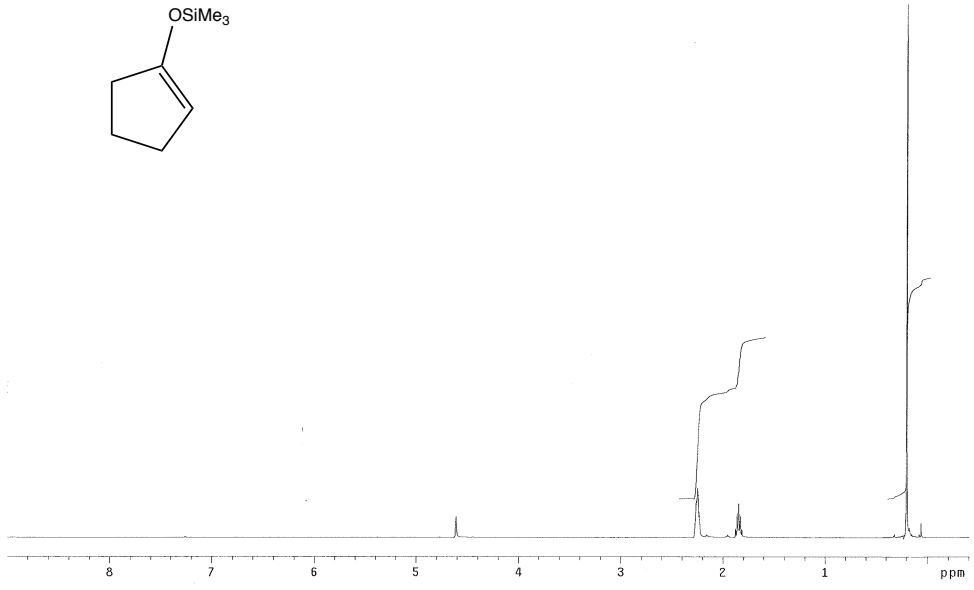

OSiMe3
H3CO

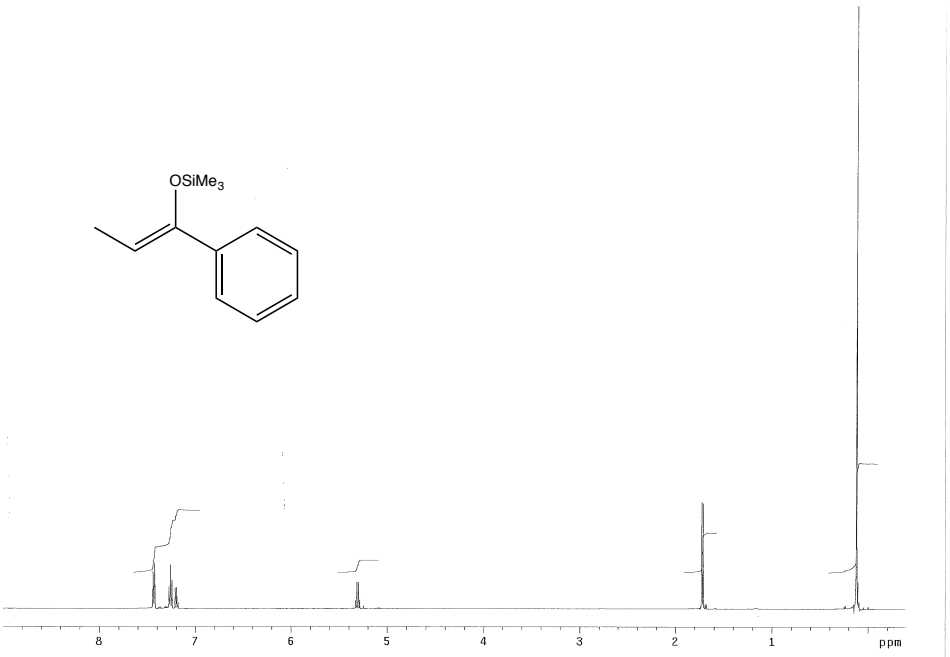
8
7
6
5
4
3
2
1
0 ppm

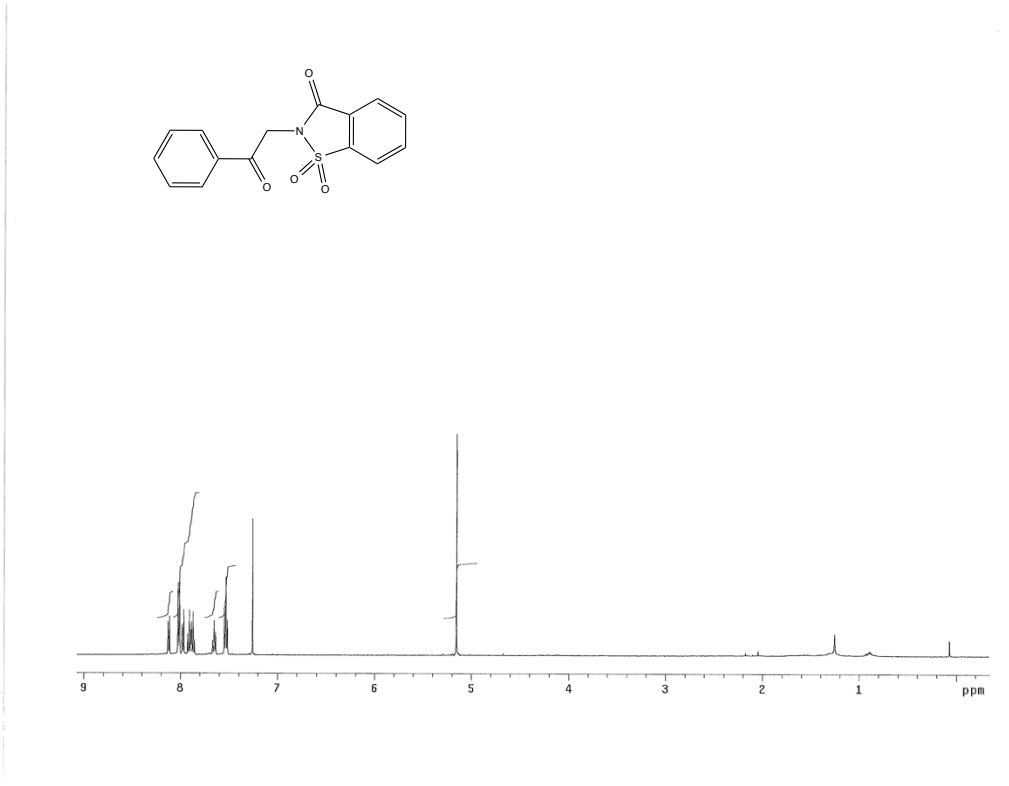

O
O
OSiMe3
8
7
6
5
4
3
2
1
ppm

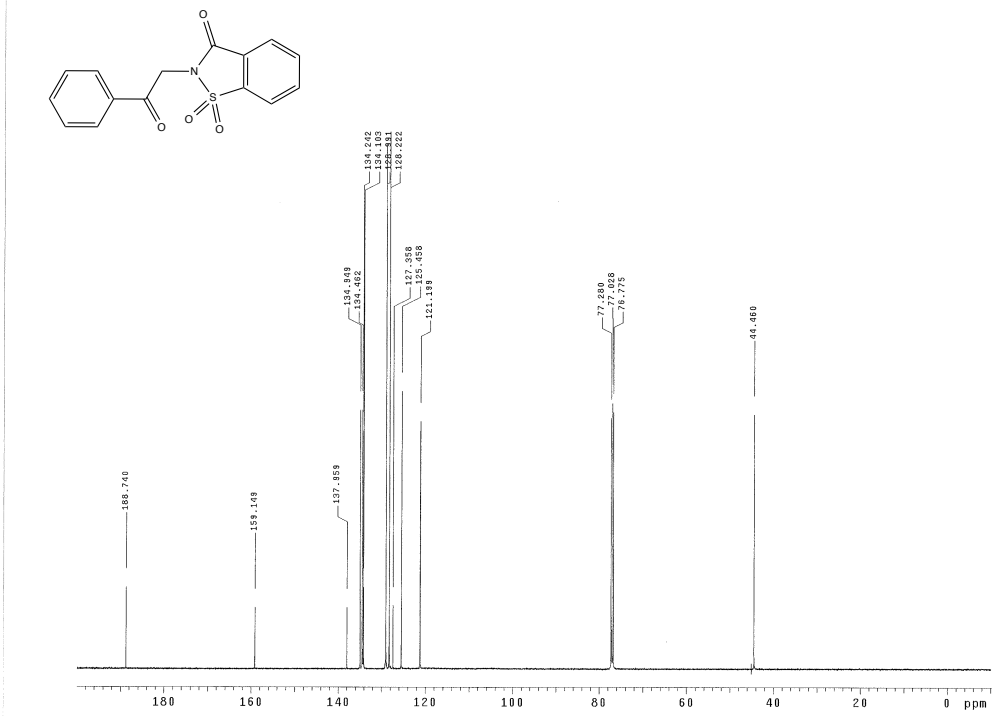

OSiMe3
N
8
7
6
5
4
3
2
1
ppm

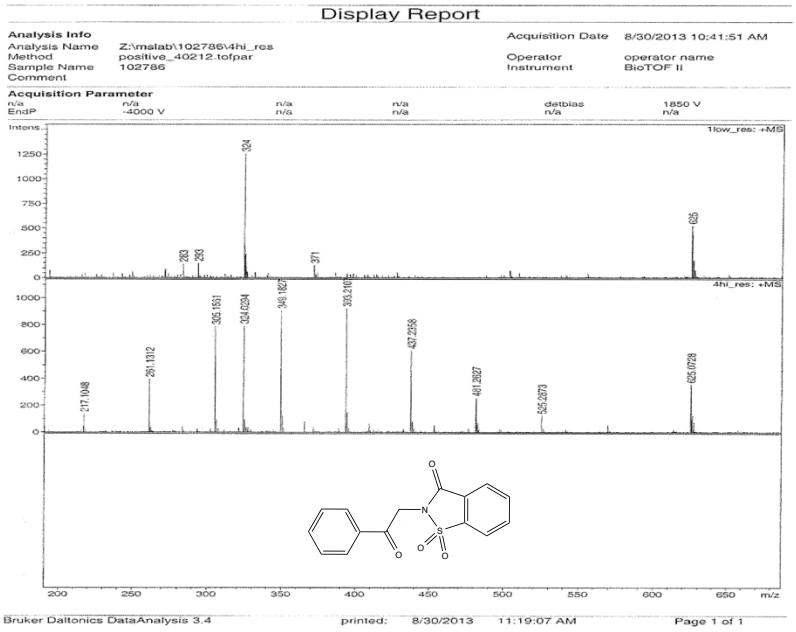

OTMS
8
7
6
5
4
3
2
1
ppm

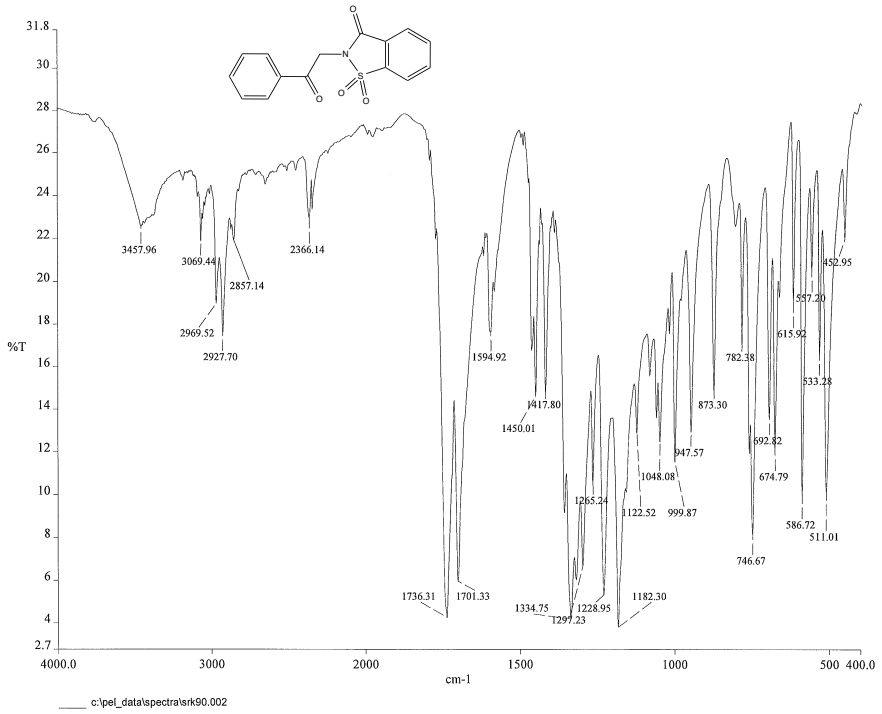

OSiMe3
8
7
6
5
4
3
2
1
ppm

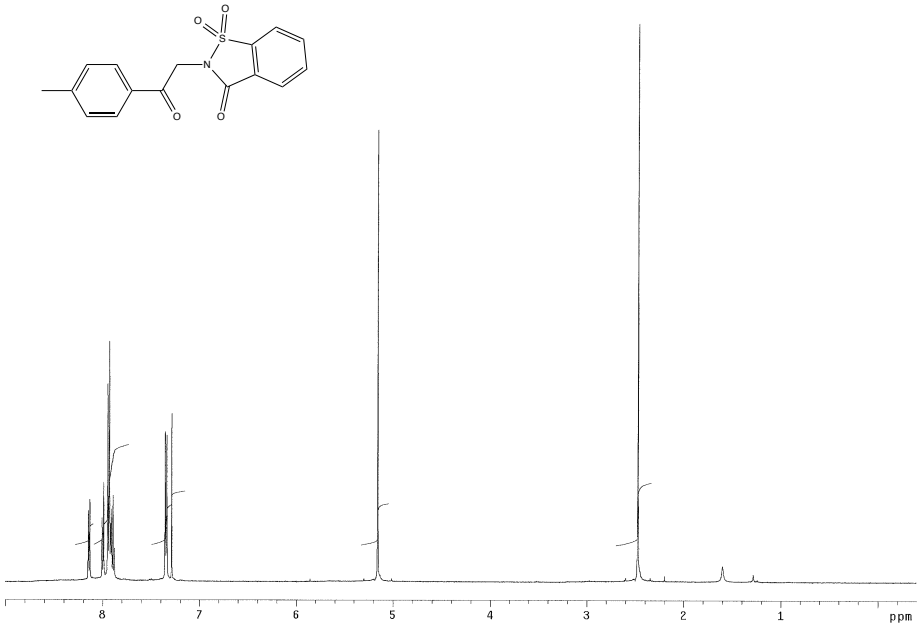

OSiMe3
8
7
6
5
4
3
2
1
ppm

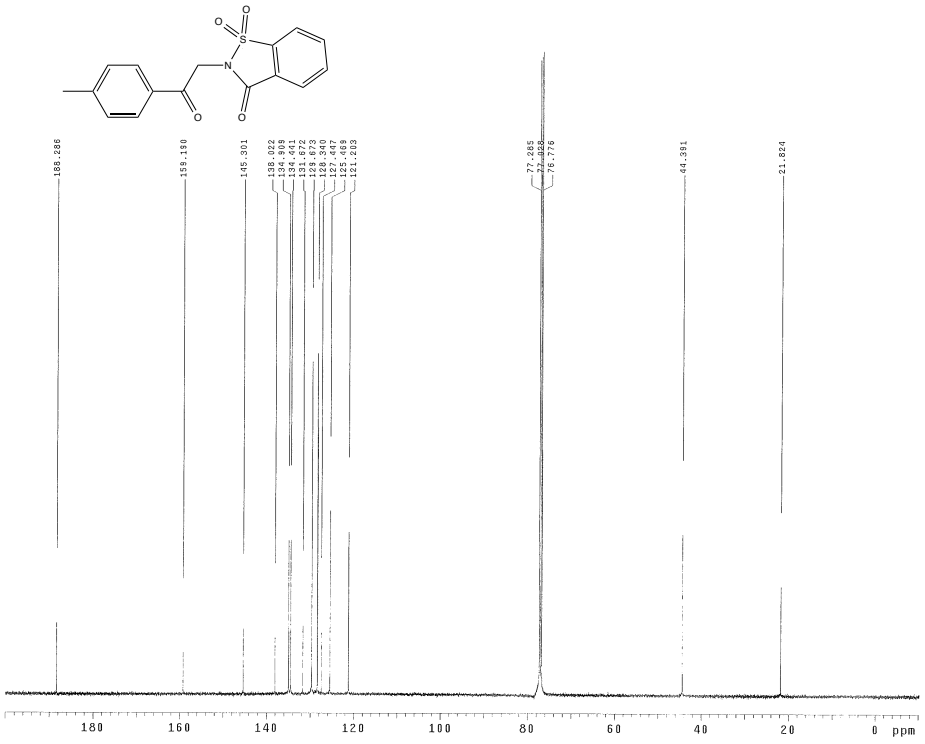

O
N
S
O
O
O
9
8
7
6
5
4
3
2
1
ppm

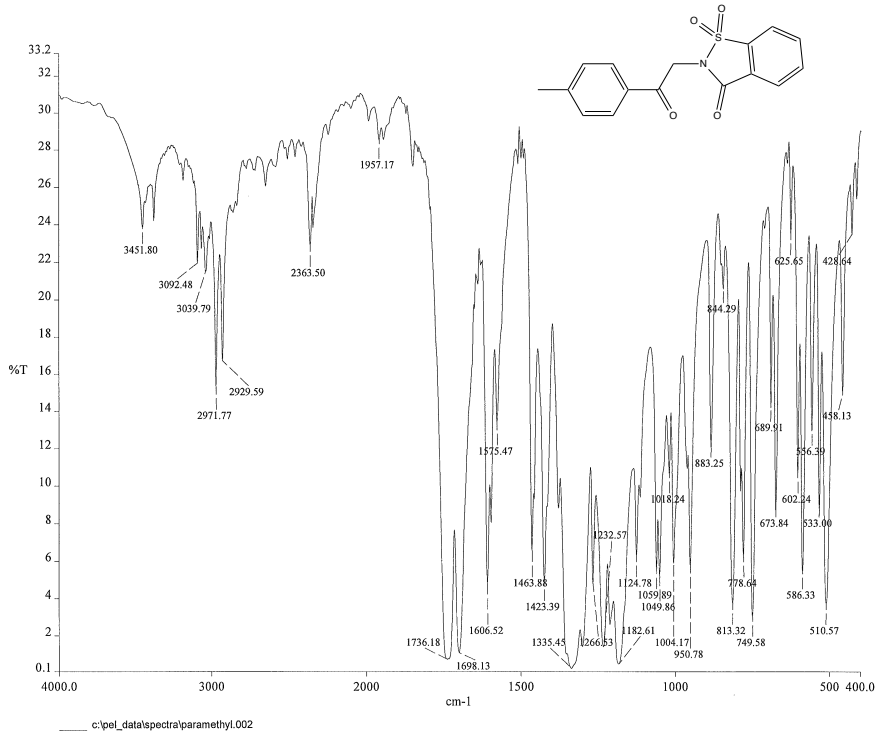

180.740
159.149
137.959
134.949
134.482
134.242
134.103
128.381
128.222
127.958
121.486
121.199
77.280
77.028
76.775
44.460
180
160
140
120
100
80
60
40
20
0 ppm

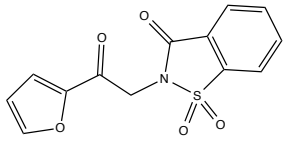

Display Report
Analysis Info
Analysis Name Z:\mslab\102786\4hi_res
Method positive_40212.tofpar
Sample Name 102786
Comment
Acquisition Date 8/30/2013 10:41:51 AM
Operator operator name
Instrument BioTOF II
Acquisition Parameter
EndP -4000 V
detbias 1850 V
1low_res: +MS
4hi_res: +MS
324
625
283
293
371
305.1551
324.0324
346.1827
393.2167
437.2598
491.2837
525.2673
625.0728
251.1312
217.1048
m/z
Bruker Daltonics DataAnalysis 3.4
printed: 8/30/2013 11:19:07 AM
Page 1 of 1

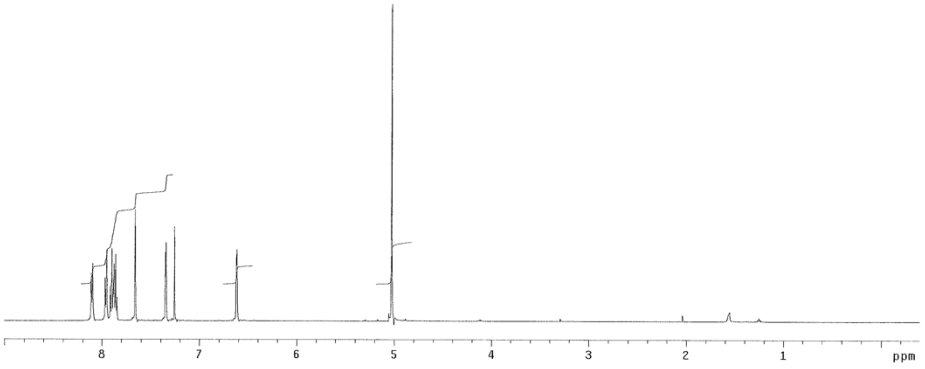

%T
cm-1
3457.96
3069.44
2969.52
2927.70
2857.14
2366.14
1736.31
1701.33
1594.92
1450.01
1417.80
1334.75
1297.23
1265.24
1228.95
1182.30
1122.52
1048.08
999.87
947.57
873.30
782.38
746.67
692.82
674.79
615.92
586.72
557.20
533.28
511.01
452.95
c:\pel_data\spectra\srk90.002

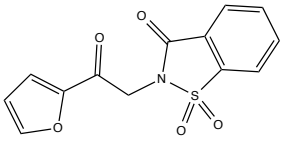

ppm

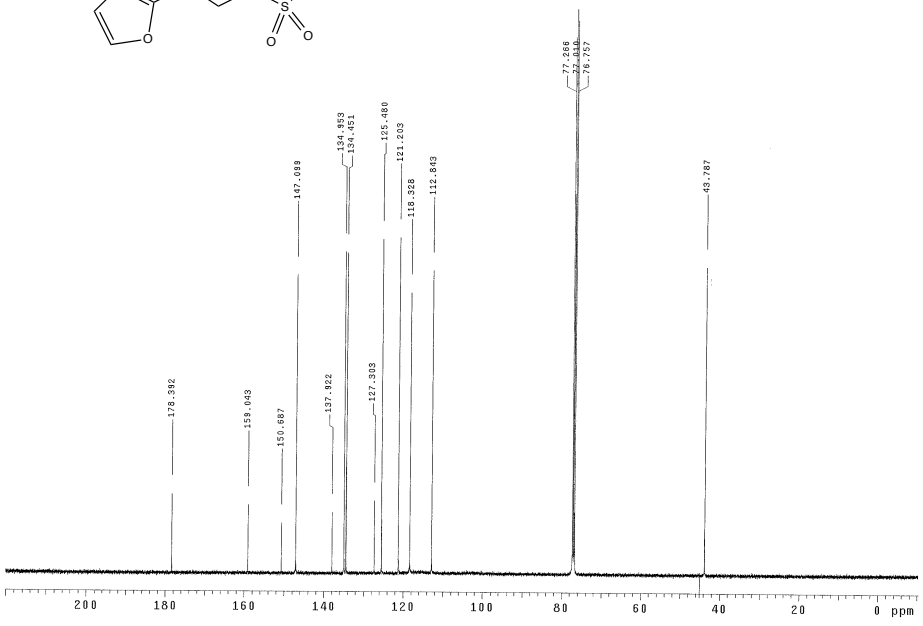

188.288
159.190
145.301
138.022
134.908
134.441
131.672
129.673
129.340
127.447
125.469
121.203
77.265
77.008
76.776
64.391
21.824
180
160
140
120
100
80
60
40
20
0 ppm

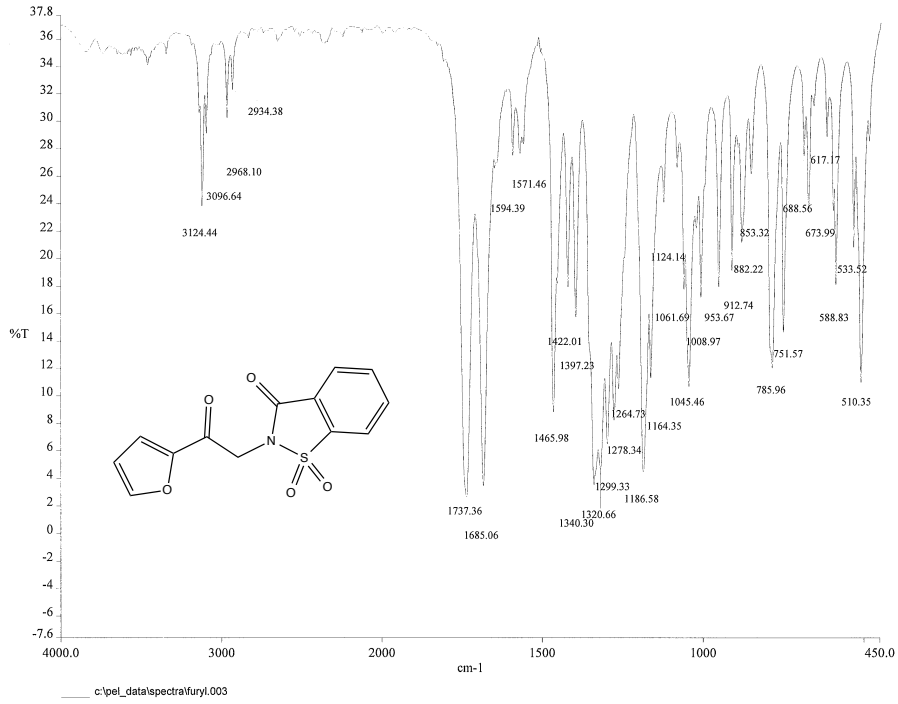

%T
33.2
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0.1
3451.80
3092.48
3039.79
2971.77
2929.59
2363.50
1957.17
1736.18
1698.13
1606.52
1575.47
1463.88
1423.39
1335.45
1266.53
1232.57
1182.61
1124.78
1059.89
1049.86
1018.24
1004.17
950.78
883.25
844.29
813.32
778.64
749.58
689.91
673.84
625.65
602.24
586.33
556.39
533.00
510.57
458.13
428.64
4000.0
3000
2000
1500
1000
500 400.0
cm-1
c:\pel_data\spectra\paramethyl.002

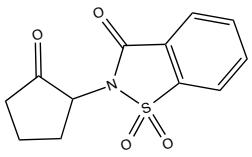

O
O
N
S
O
O
O

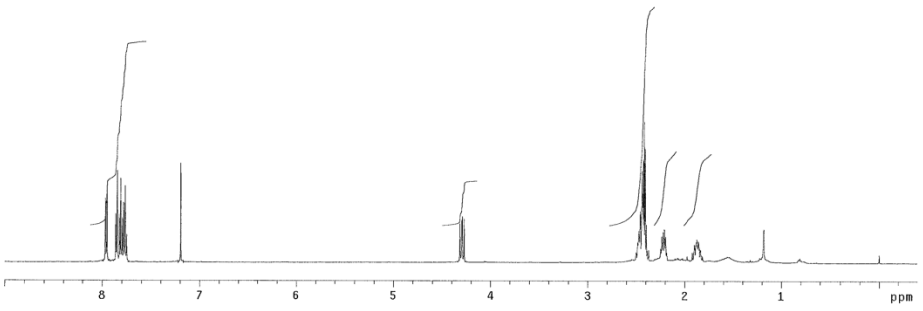

8
7
6
5
4
3
2
1
ppm

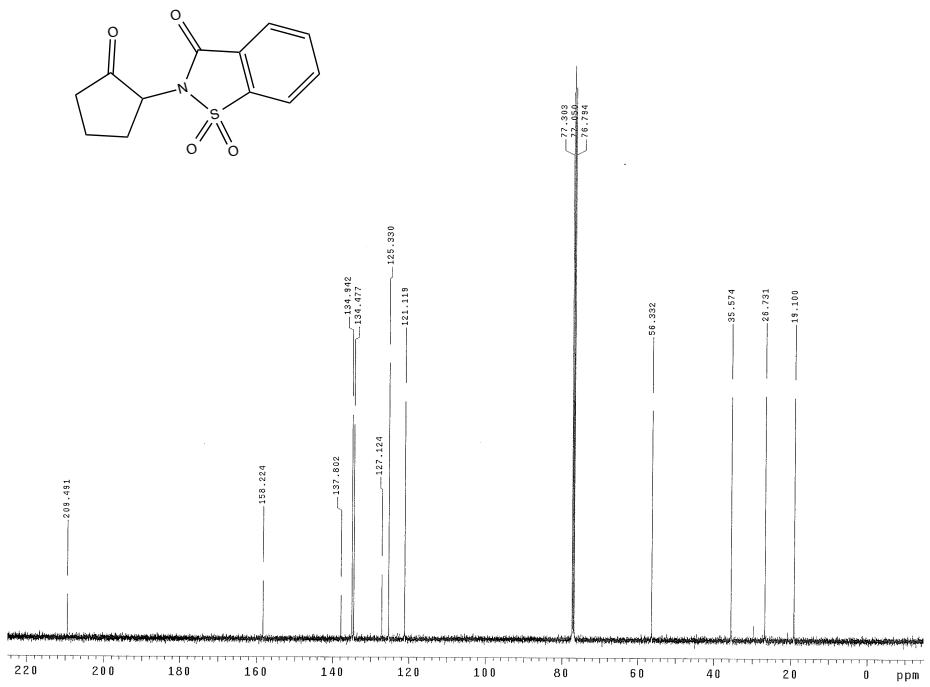

O
O
N
S
O
O
O

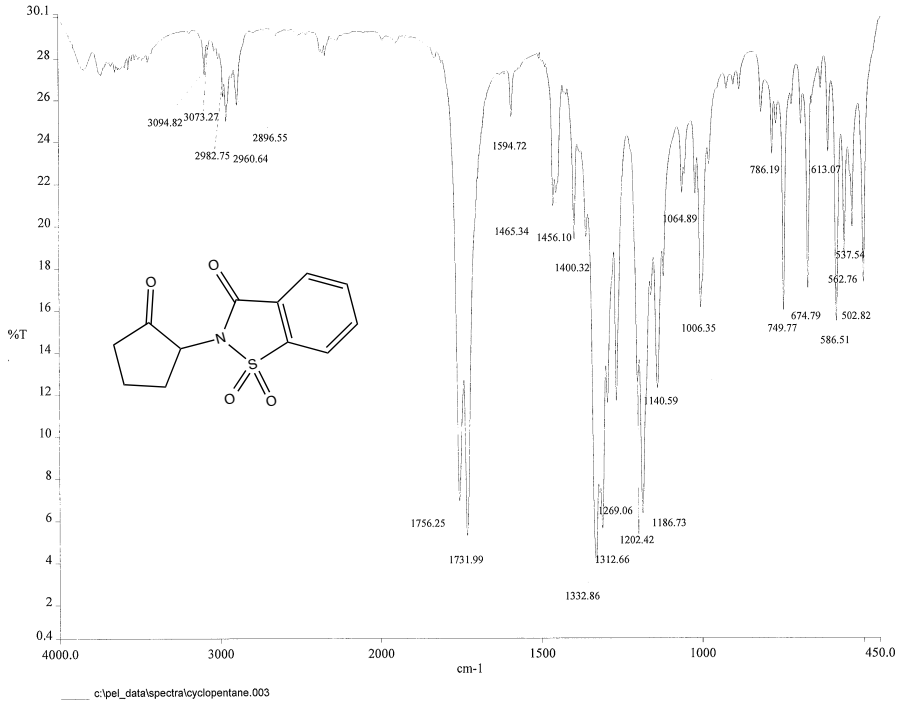

178.392
159.043
150.687
147.099
137.922
134.453
134.451
127.303
125.480
121.203
118.528
112.843
77.268
77.000
76.757
43.787
200
180
160
140
120
100
80
60
40
20
0 ppm

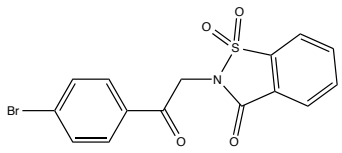

%T
cm-1
4000.0
3000
2000
1500
1000
450.0
2934.38
2968.10
3096.64
3124.44
1737.36
1685.06
1571.46
1594.39
1465.98
1422.01
1397.23
1340.30
1320.66
1299.33
1278.34
1264.73
1186.58
1164.35
1124.14
1061.69
1045.46
1008.97
953.67
912.74
882.22
853.32
785.96
751.57
688.56
673.99
617.17
588.83
533.52
510.35
c:\pel_data\spectra\furyl.003

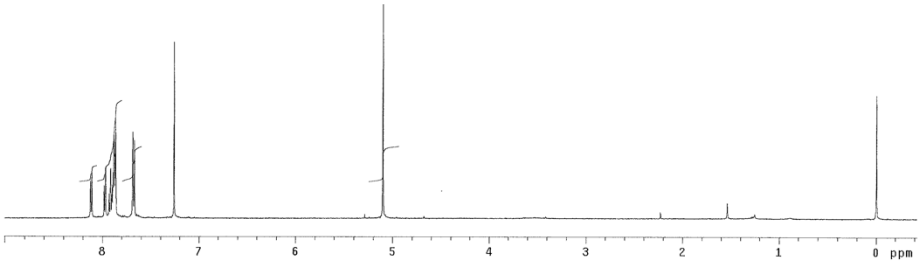


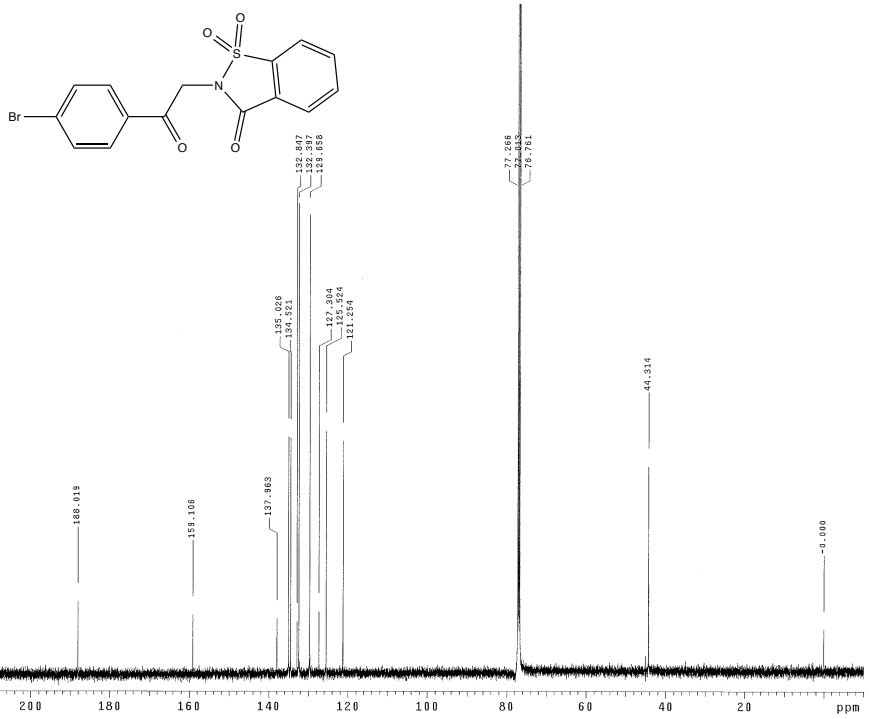

8
7
6
5
4
3
2
1
ppm

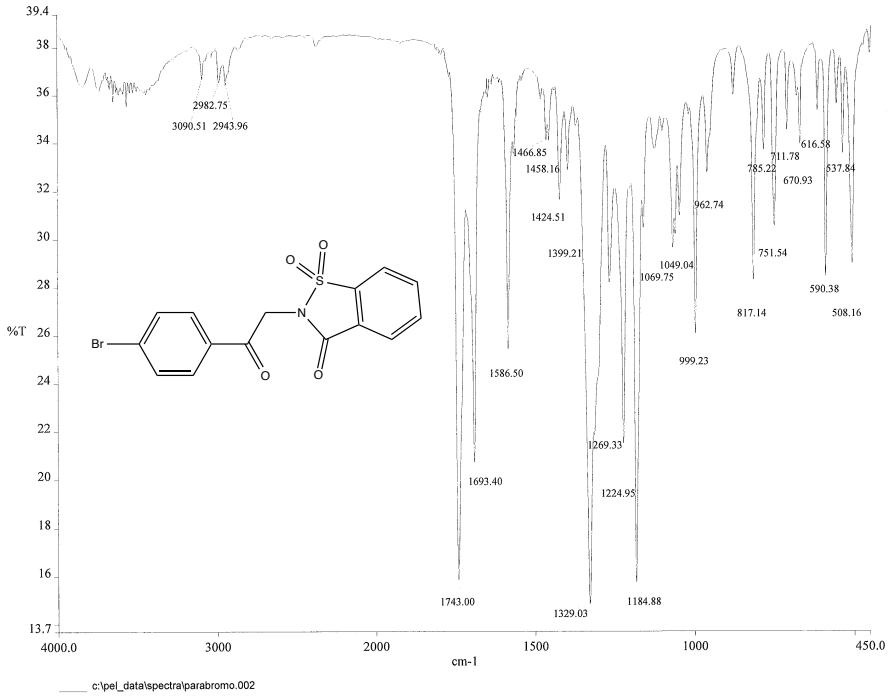

O
O
N
S
O
O
209.491
158.224
137.802
134.942
134.477
127.124
125.330
121.119
77.303
77.050
76.794
58.332
35.574
28.731
19.100
220
200
180
160
140
120
100
80
60
40
20
0
ppm

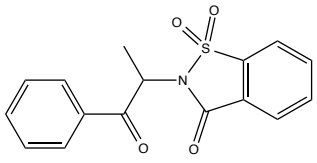

30.1
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0.4
%T
3094.82
3073.27
2896.55
2982.75
2960.64
1594.72
1465.34
1456.10
1400.32
1064.89
786.19
613.07
537.54
562.76
1006.35
674.79
749.77
502.82
586.51
1140.59
1756.25
1269.06
1186.73
1202.42
1731.99
1312.66
1332.86
4000.0
3000
2000
1500
1000
450.0
cm-1
c:\pel_data\spectra\cyclopentane.003

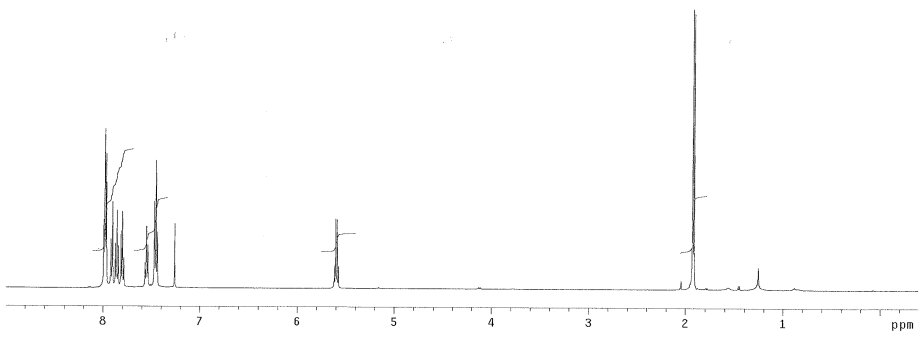

O
O
S
N
Br
O
O

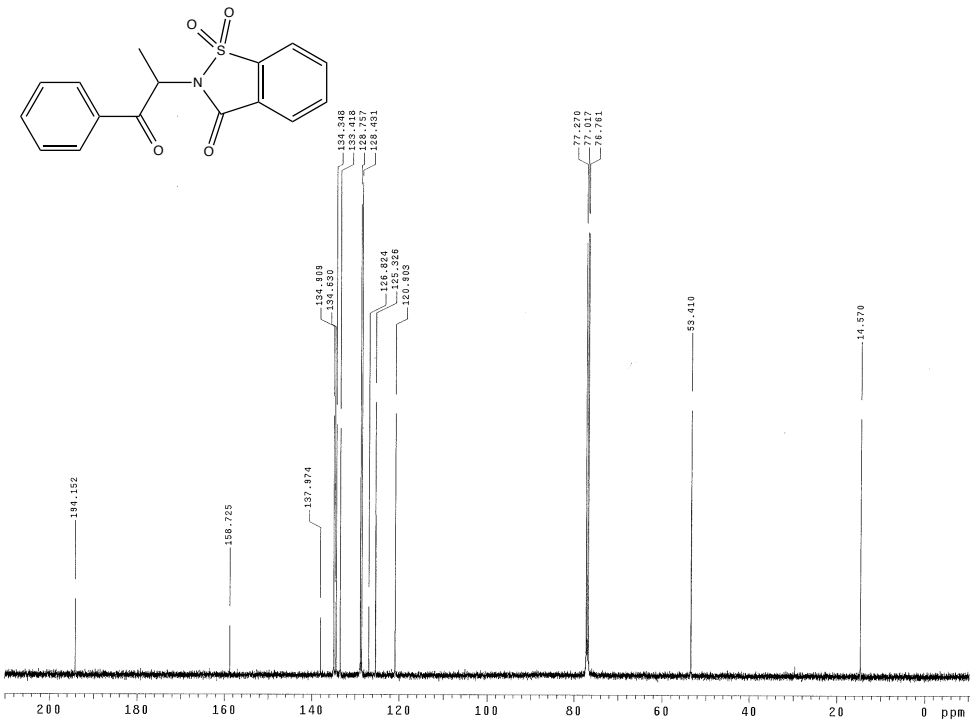

8
7
6
5
4
3
2
1
0 ppm

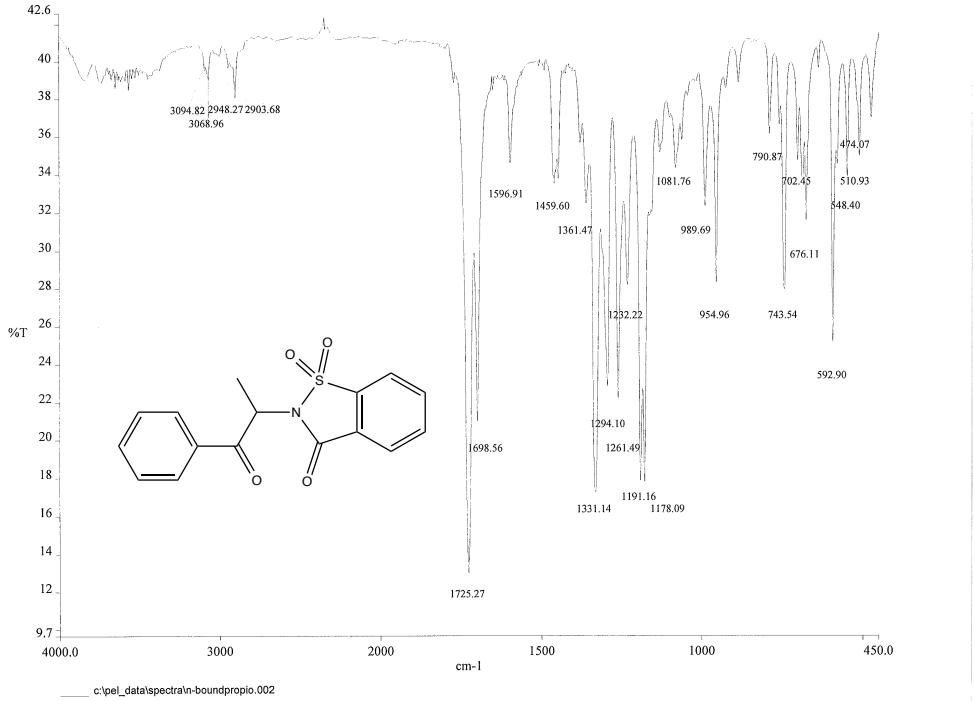

O
O
S
N
Br
O
O
188.019
159.106
137.363
135.026
134.121
132.847
132.037
129.858
127.304
125.524
121.254
77.266
77.000
76.761
44.314
0.000
200
180
160
140
120
100
80
60
40
20
ppm

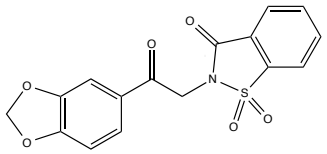

39.4
38
36
34
32
30
28
%T 26
24
22
20
18
16
13.7
4000.0
3000
2000
1500
1000
450.0
cm-1
2982.75
3090.51
2943.96
1466.85
1458.16
1424.51
1399.21
1586.50
1693.40
1743.00
1329.03
1269.33
1224.95
1184.88
1069.75
1049.04
962.74
999.23
817.14
785.22
751.54
711.78
670.93
616.58
590.38
537.84
508.16
Br
O
S
N
O
O
O
O
c:\pel_data\spectra\parabromo.002

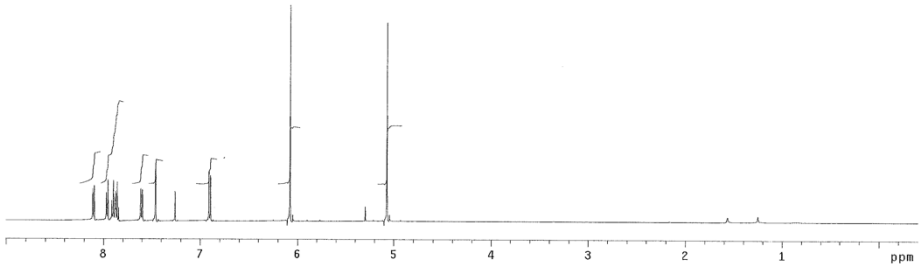

O
O
S
N
O
O

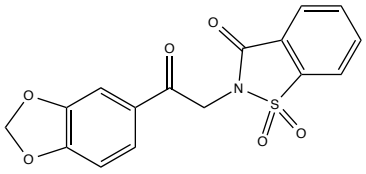

8
7
6
5
4
3
2
1
ppm

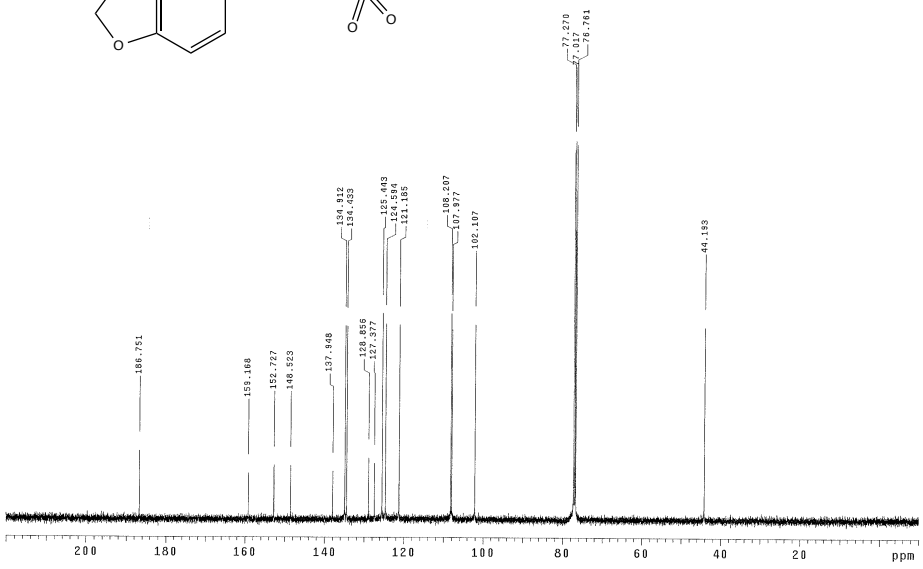

194.152
158.725
137.974
134.809
134.630
134.348
133.418
128.757
128.431
126.824
125.326
120.803
77.270
77.017
76.761
53.410
14.570
200
180
160
140
120
100
80
60
40
20
0 ppm

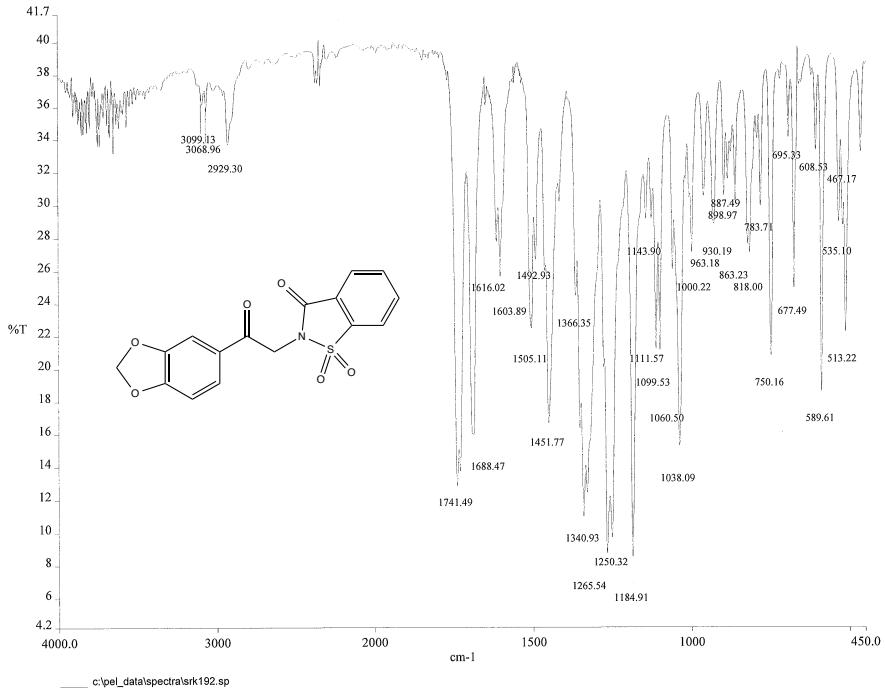

%T
3094.82
2948.27
2903.68
3068.96
1596.91
1459.60
1361.47
1698.56
1725.27
1294.10
1261.49
1232.22
1331.14
1191.16
1178.09
1081.76
989.69
954.96
790.87
743.54
702.45
676.11
592.90
548.40
510.93
474.07
4000.0
3000
2000
1500
1000
450.0
cm-1
c:\pel_data\spectra\n-boundpropio.002

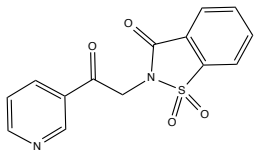

O
O
O
N
S
O
O
O
O

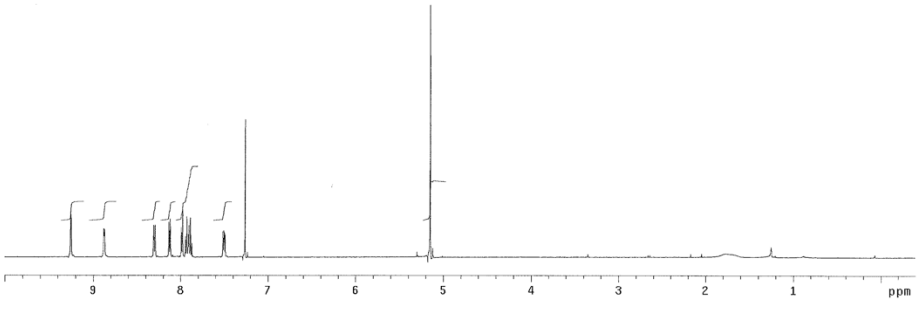

8
7
6
5
4
3
2
1
ppm

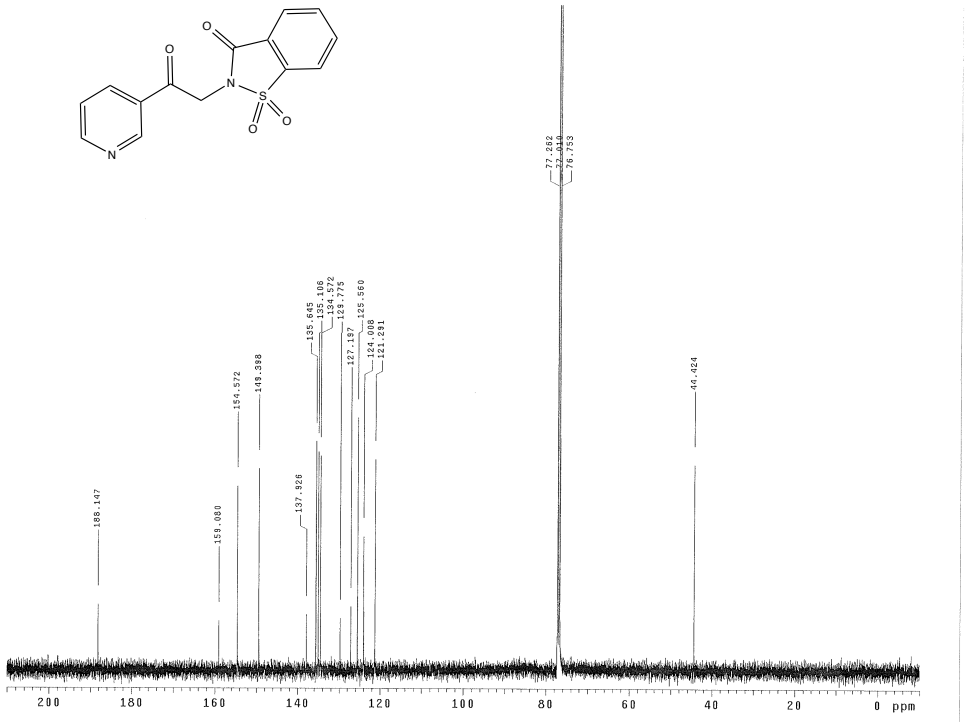

O
O
O
N
S
O
O
O
O


186.751
159.168
152.727
148.923
137.948
134.812
134.433
128.856
127.377
125.403
124.504
121.185
108.207
107.977
102.107
77.270
77.012
76.761
44.193
200
180
160
140
120
100
80
60
40
20
ppm


41.7
40
38
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4.2
%T
4000.0
3000
2000
1500
1000
450.0
cm-1
3099.13
3068.96
2929.30
1741.49
1688.47
1616.02
1603.89
1505.11
1492.93
1451.77
1366.35
1340.93
1265.54
1250.32
1184.91
1143.90
1111.57
1099.53
1060.50
1038.09
1000.22
963.18
930.19
898.97
887.49
863.23
818.00
783.71
750.16
695.33
677.49
608.53
589.61
535.10
513.22
467.17
c:\pel_data\spectra\srk192.sp




9
8
7
6
5
4
3
2
1
ppm

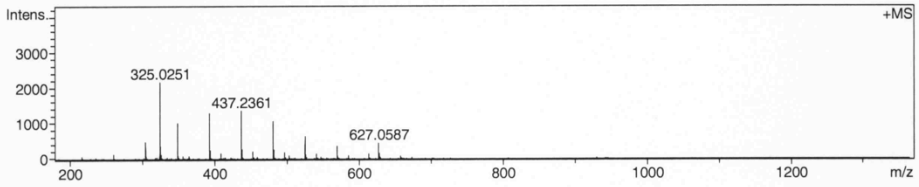

O
O
N
S
O
O
N
188.147
159.080
154.572
149.388
137.926
135.645
135.106
134.572
128.775
127.137
125.560
124.008
121.291
77.282
77.040
76.753
44.424
200
180
160
140
120
100
80
60
40
20
0 ppm

Mass Spectrum Report

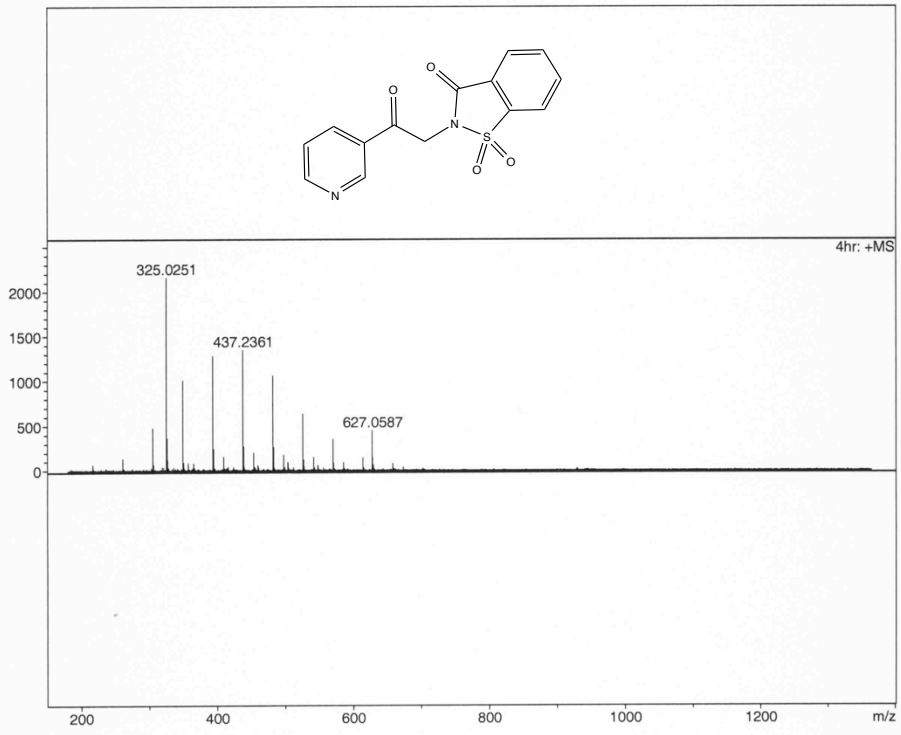
Analysis Info

Analysis Name	Z:\mslab\srk190_105483\4hr	Acquisition Date	7/14/2014 8:23:22 AM
Method	positive_102813.tofpar	Operator	operator name
Sample Name	srk190_105483	Instrument / Ser#	BioTOF II 1.11
Comment	Free format commentsFree format commentsFree format comments		

Full Mass Spectrum



Spectrum Region of Interest



Mass Spectrum Report

Elemental Composition Report

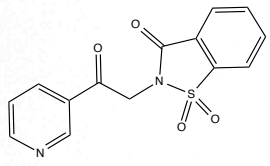
Generate Molecular Formula Parameter

Formula, min.	C14H10N2O4S1Na1						
Formula, max.							
Measured m/z	325.025	Tolerance	5	ppm	Charge	1	
Check Valence	no	Minimum	0		Maximum	0	
Nirogen Rule	no	Electron Configuration	both				
Filter H/C Ratio	no	Minimum	0		Maximum	3	
Estimate Carbon	no						

Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e^-
C 14 H 10 N 2 Na 1 O 4 S 1	0.008	325.0253	0.70	1.66	0.23	10.50	ok	even

Mass Spectrum Peak List

#	m/z	Area	Res.	S/N
1	261.1309	7	5613	3.9
2	305.1567	22	7033	10.4
3	325.0251	121	6269	53.0
4	326.0265	16	8050	8.9
5	327.0219	7	5784	2.9
6	349.1827	54	7061	29.5
7	393.2102	88	6481	48.0
8	394.2129	14	7725	9.2
9	409.1854	10	6417	5.5
10	437.2361	94	6767	50.4
11	438.2407	16	7937	10.1
12	453.2108	17	5475	7.5
13	481.2618	81	6945	43.1
14	482.2641	16	8705	10.6
15	497.2353	12	8853	7.7
16	525.2900	52	7282	31.0
17	526.2912	11	6051	5.9
18	541.2579	10	12161	7.6
19	569.3124	28	7450	19.5
20	613.3345	14	6165	9.0
21	627.0587	41	7658	30.1
22	628.0614	11	9886	10.1



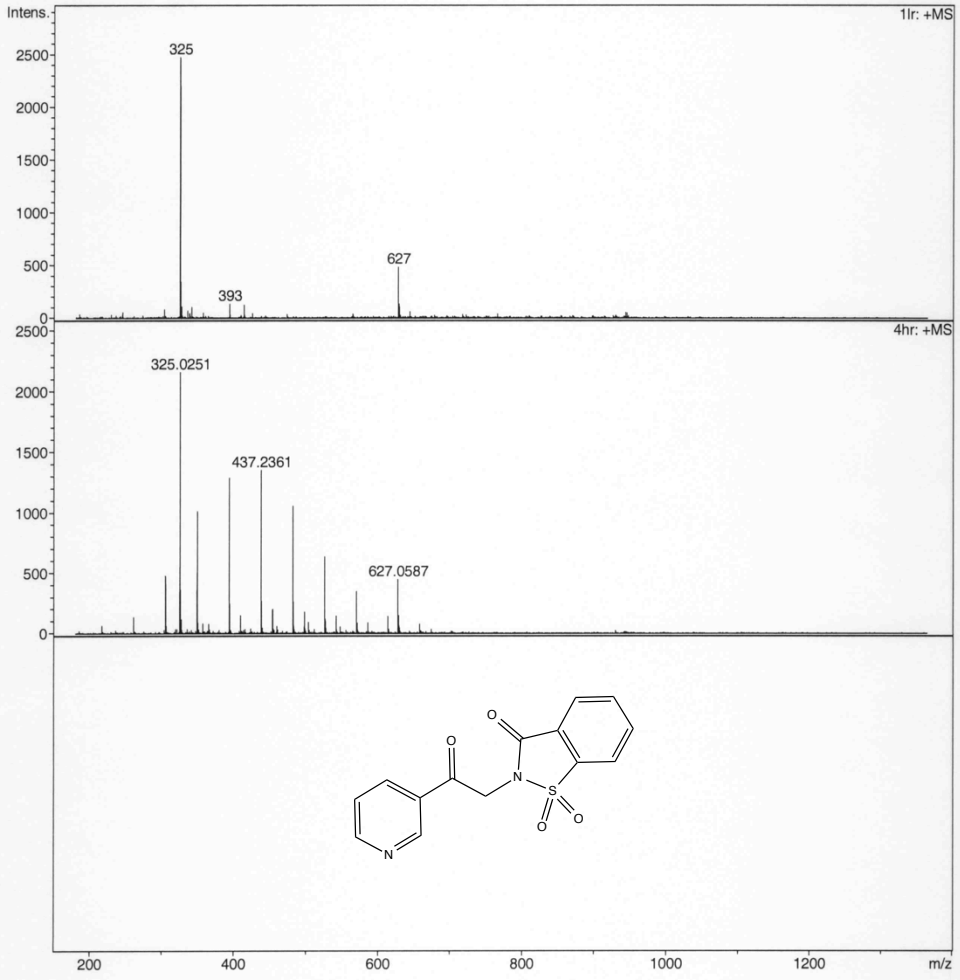
Display Report

Analysis Info

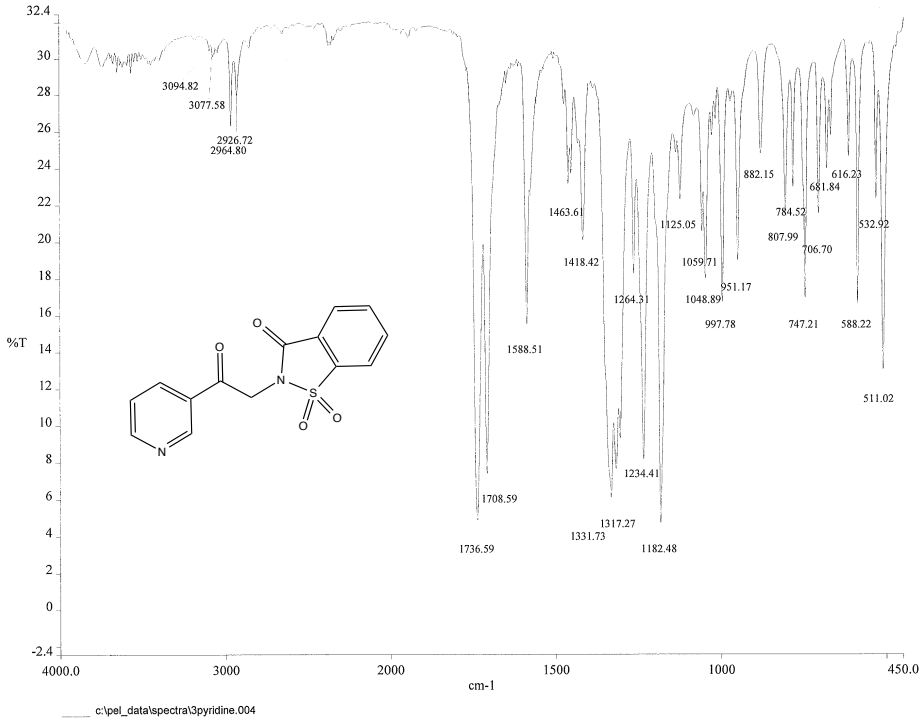
Analysis Name	Z:\mslab\srk190_105483\4hr	Acquisition Date	7/14/2014 8:23:22 AM
Method	positive_102813.tofpar	Operator	operator name
Sample Name	srk190_105483	Instrument	BioTOF II
Comment	Free format commentsFree format commentsFree format comments		

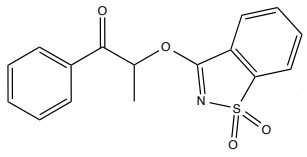
Acquisition Parameter

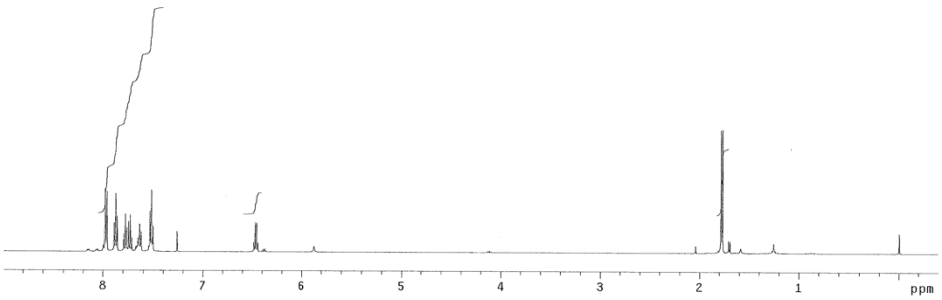
n/a	n/a	n/a	n/a	detbias	1850 V
EndP	-4000 V	n/a	n/a	n/a	n/a

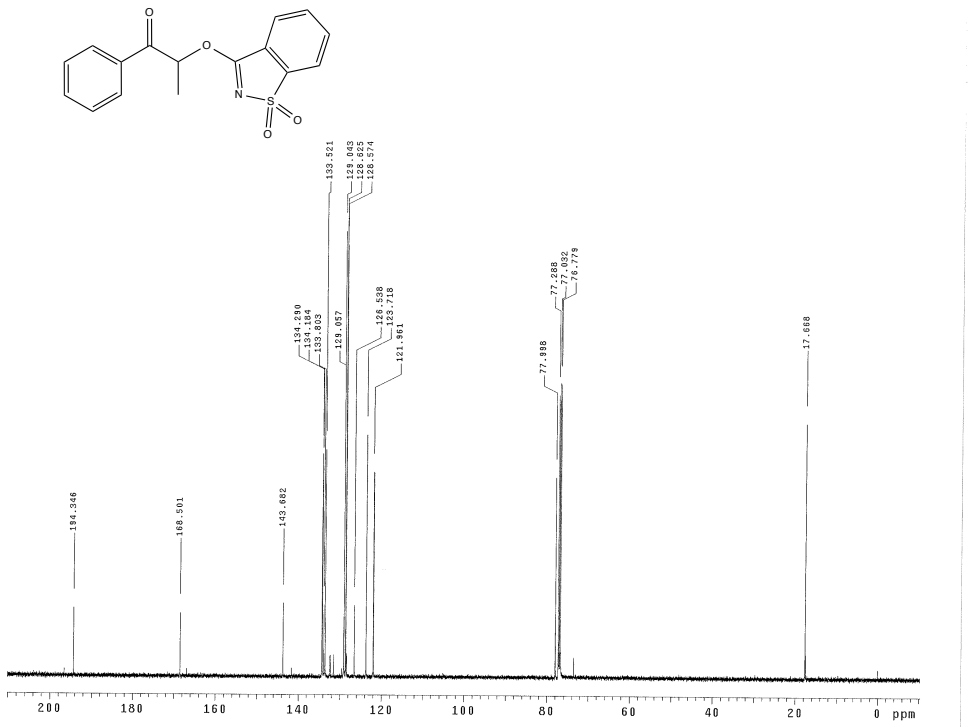


Bruker Daltonics DataAnalysis 3.4 printed: 7/14/2014 8:43:03 AM Page 1 of 1


32.4
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2.4
%T
4000.0
3000
2000
1500
1000
450.0
cm-1
3094.82
3077.58
2926.72
2964.80
1463.61
1418.42
1588.51
1264.31
1125.05
1059.71
1048.89
951.17
997.78
882.15
784.52
807.99
706.70
747.21
681.84
616.23
588.22
532.92
511.02
1708.59
1736.59
1234.41
1317.27
1331.73
1182.48
O
O
N
S
O
O
N
c:\pel_data\spectra\3pyridine.004


O
O
N
S
O
O


8
7
6
5
4
3
2
1
ppm


O
O
N
S
O
O
194.346
168.501
143.682
134.290
134.184
133.803
133.521
129.057
129.043
128.825
128.574
126.538
123.718
121.961
77.288
77.082
76.779
77.998
17.668
200
180
160
140
120
100
80
60
40
20
0 ppm

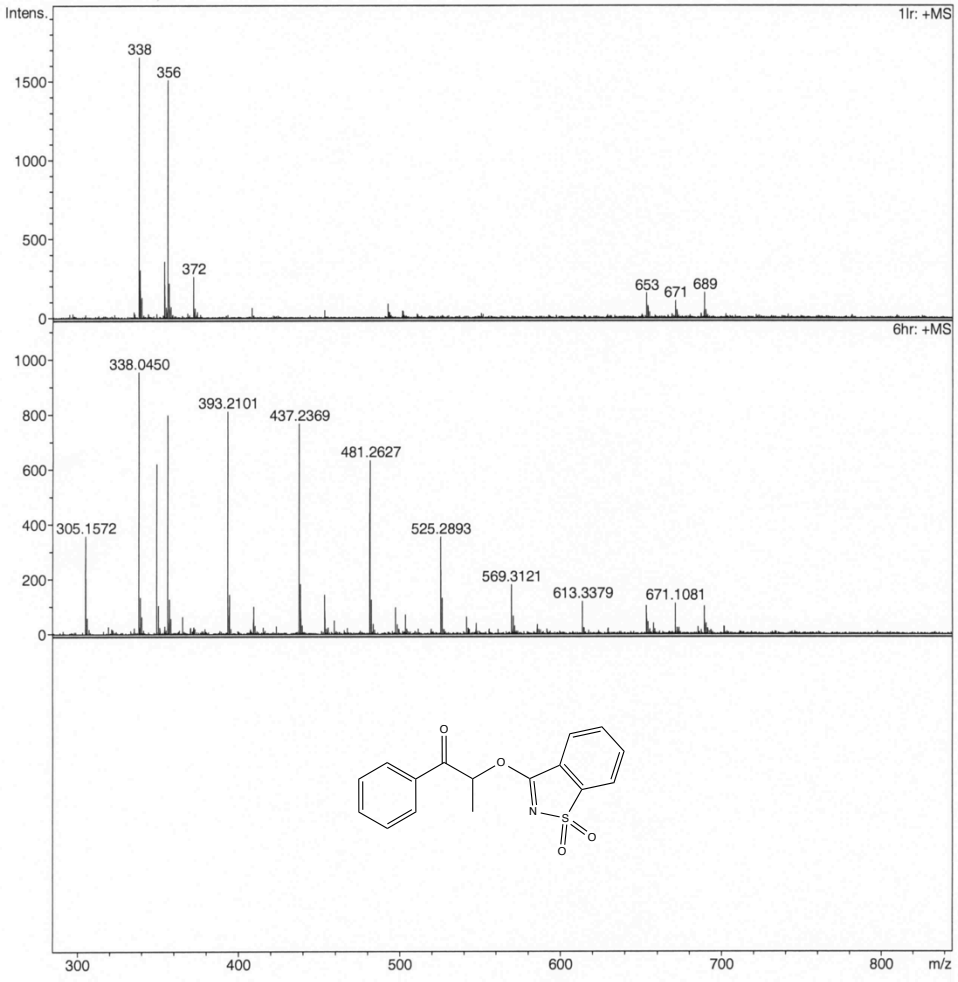
Display Report

Analysis Info

Analysis Name	Z:\mslab\srk186a_105484\6hr	Acquisition Date	7/14/2014 8:19:17 AM
Method	positive_102813.tofpar	Operator	operator name
Sample Name	srk186a_105484	Instrument	BioTOF II
Comment	Free format commentsFree format commentsFree format comments		

Acquisition Parameter

n/a	n/a	n/a	n/a	detbias	1850 V
EndP	-4000 V	n/a	n/a	n/a	n/a



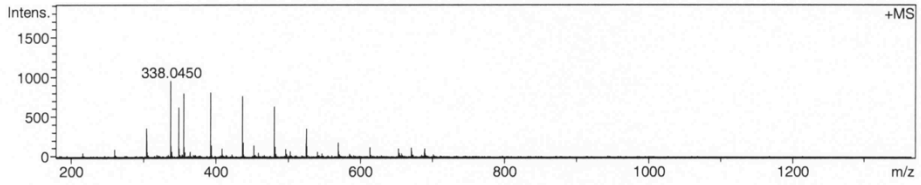
Bruker Daltonics DataAnalysis 3.4 printed: 7/14/2014 8:35:01 AM Page 1 of 1

Mass Spectrum Report

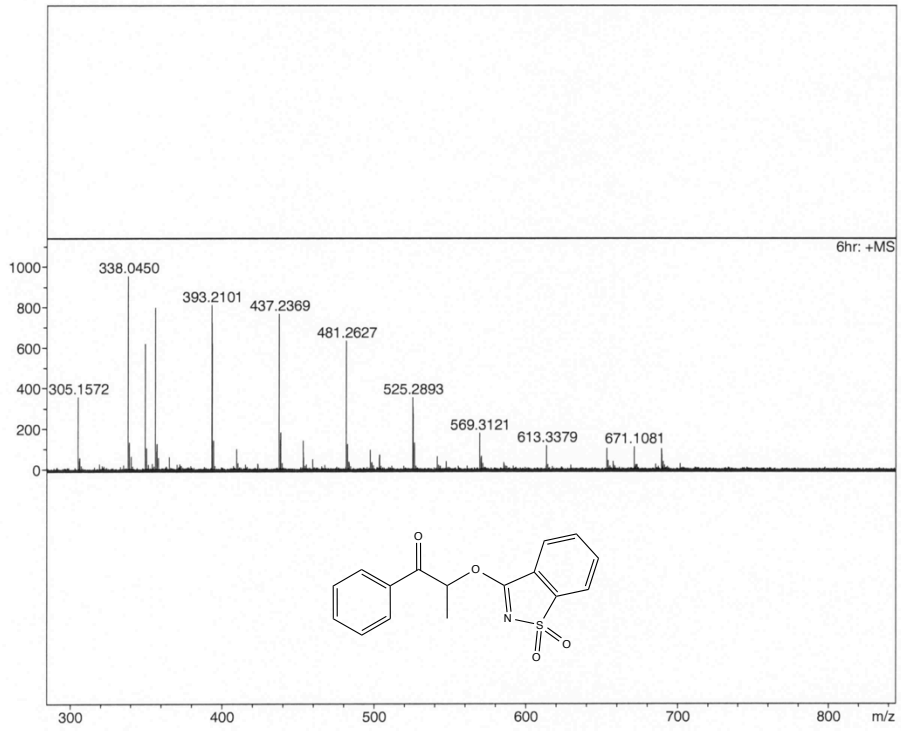
Analysis Info

Analysis Name	Z:\mslab\srk186a_105484\6hr	Acquisition Date	7/14/2014 8:19:17 AM
Method	positive_102813.tofpar	Operator	operator name
Sample Name	srk186a_105484	Instrument / Ser#	BioTOF II 1.11
Comment	Free format commentsFree format commentsFree format comments		

Full Mass Spectrum



Spectrum Region of Interest



Mass Spectrum Report

Elemental Composition Report

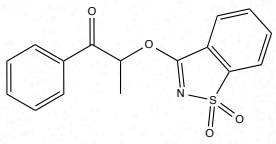
Generate Molecular Formula Parameter

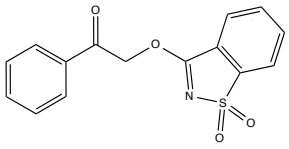
Formula, min.	H13N1O4S1C16Na1						
Formula, max.							
Measured m/z	338.045	Tolerance	5	ppm	Charge	1	
Check Valence	no	Minimum	0		Maximum	0	
Nirogen Rule	no	Electron Configuration	both				
Filter H/C Ratio	no	Minimum	0		Maximum	3	
Estimate Carbon	no						

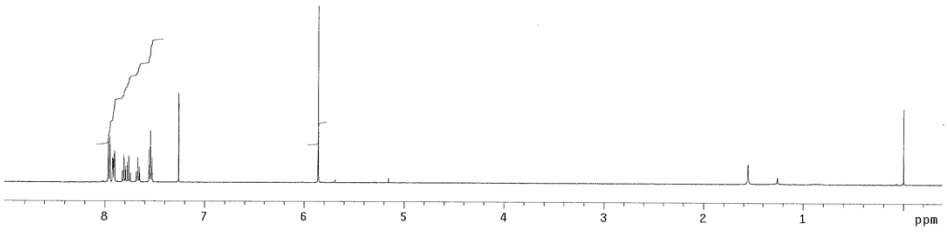
Sum Formula	Sigma	m/z	Err [ppm]	Mean Err [ppm]	Err [mDa]	rdb	N Rule	e^-
C 16 H 13 N 1 Na 1 O 4 S 1	0.043	338.0457	2.31	2.17	0.78	10.50	ok	even

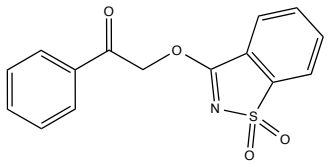
Mass Spectrum Peak List

#	m/z	Area	Res.	S/N
1	305.1572	17	7350	8.9
2	338.0450	47	7360	24.5
3	339.0483	6	7369	3.5
4	349.1818	33	7113	16.1
5	350.1806	6	5917	2.6
6	356.0569	42	7298	20.9
7	357.0571	7	6086	2.9
8	393.2101	48	6992	23.4
9	394.2132	8	7336	4.1
10	409.1853	6	7215	3.2
11	437.2369	54	6493	28.5
12	438.2368	10	8351	6.8
13	453.2088	8	9555	5.9
14	481.2627	47	6989	29.4
15	482.2647	8	8116	5.8
16	525.2893	29	6597	19.5
17	526.2970	7	12767	7.3
18	569.3121	17	6430	11.8
19	613.3379	11	7420	9.6
20	671.1081	9	8568	8.5
21	689.1255	12	6297	7.4

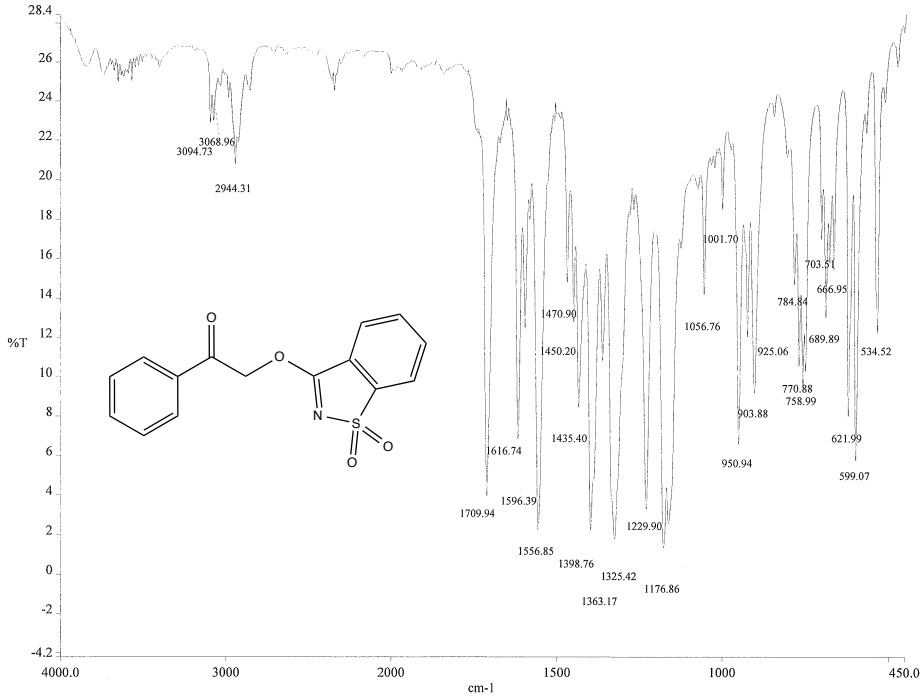


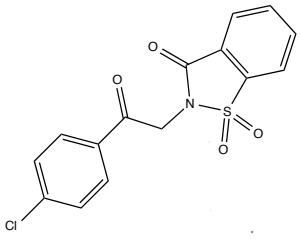

O
O
N
S
O
O

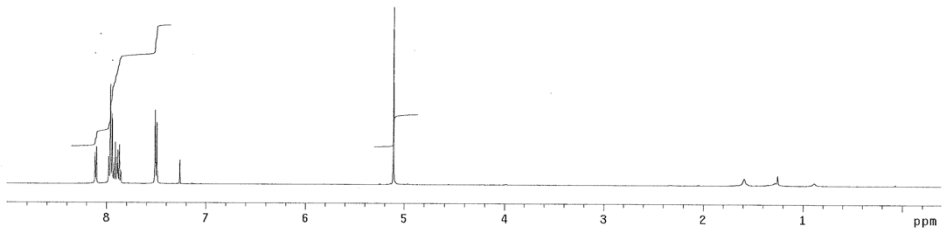

8
7
6
5
4
3
2
1
ppm

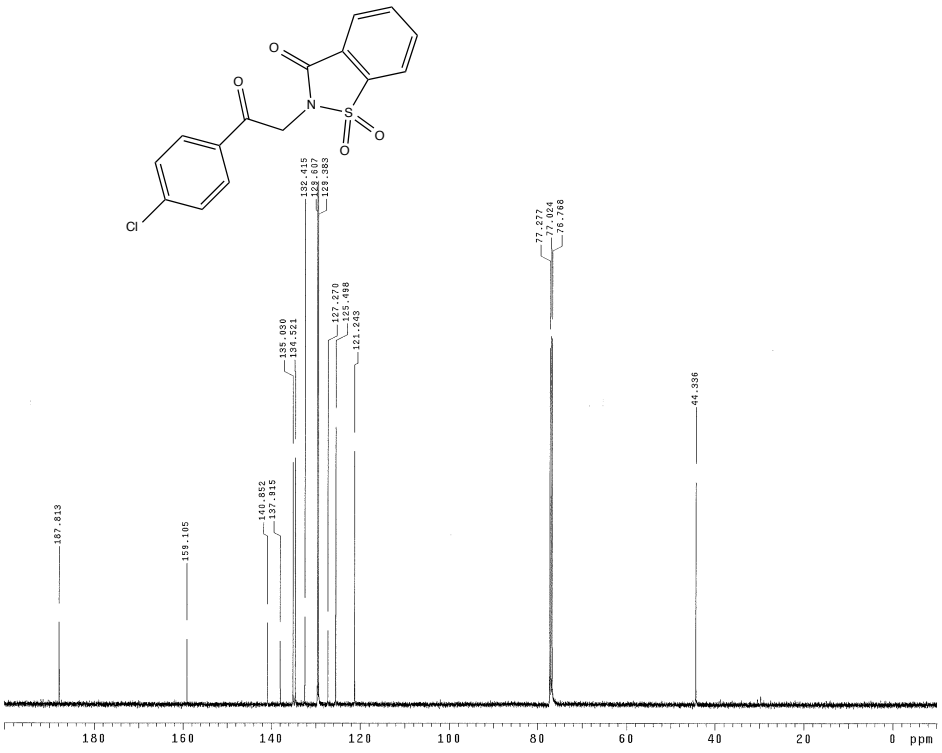

O
O
N
S
O
O

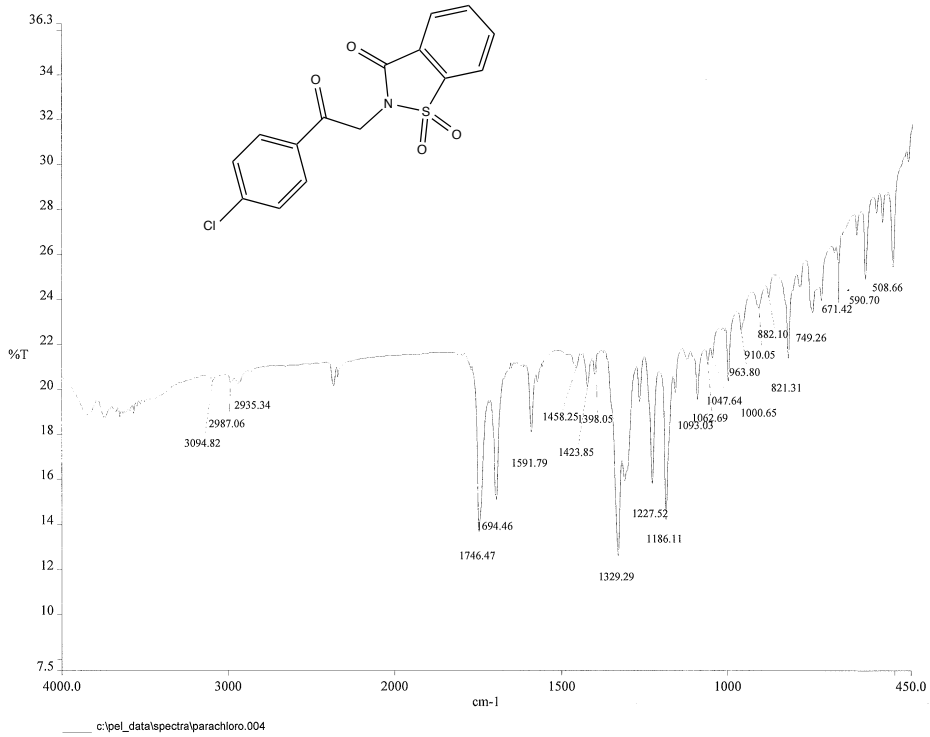
189.399
168.193
143.880
134.484
134.353
133.634
133.591
129.116
127.967
126.377
123.770
122.060
77.266
77.010
76.757
71.830
200
180
160
140
120
100
80
60
40
20
0
ppm

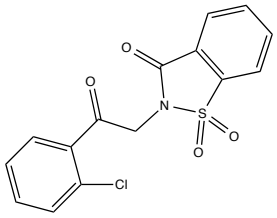

28.4
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
-4.2
%T
4000.0
3000
2000
1500
1000
450.0
cm-1
3094.73
3068.96
2944.31
1709.94
1616.74
1596.39
1556.85
1470.90
1450.20
1435.40
1398.76
1363.17
1325.42
1229.90
1176.86
1056.76
1001.70
950.94
925.06
903.88
784.84
770.88
758.99
703.51
689.89
666.95
621.99
599.07
534.52
O
O
N
S
O
O
c:\pel_data\spectra\o-boundoriginal.003

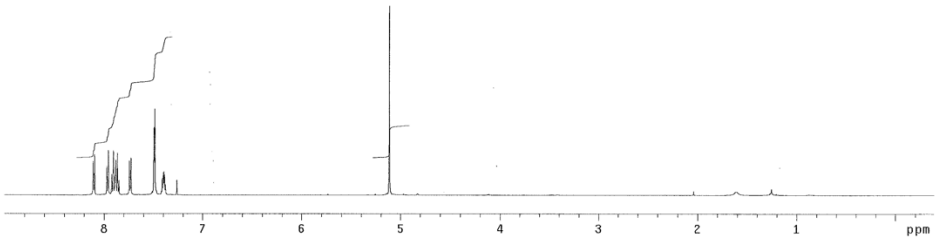

O
O
N
S
O
O
Cl

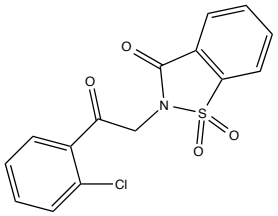

8
7
6
5
4
3
2
1
ppm

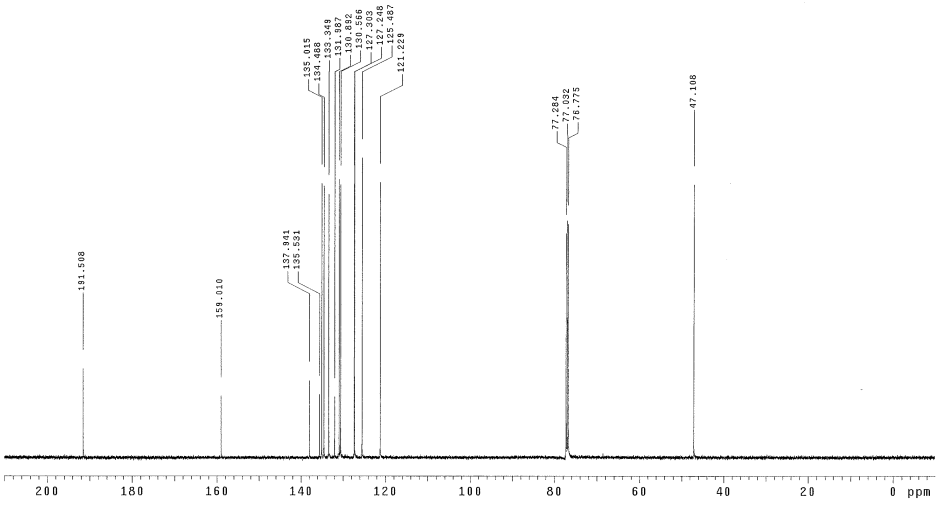

O
O
N
S
O
O
Cl
187.813
159.105
140.852
137.915
135.030
134.521
132.415
129.607
129.383
127.270
125.498
121.243
77.277
77.024
76.768
44.336
180
160
140
120
100
80
60
40
20
0 ppm

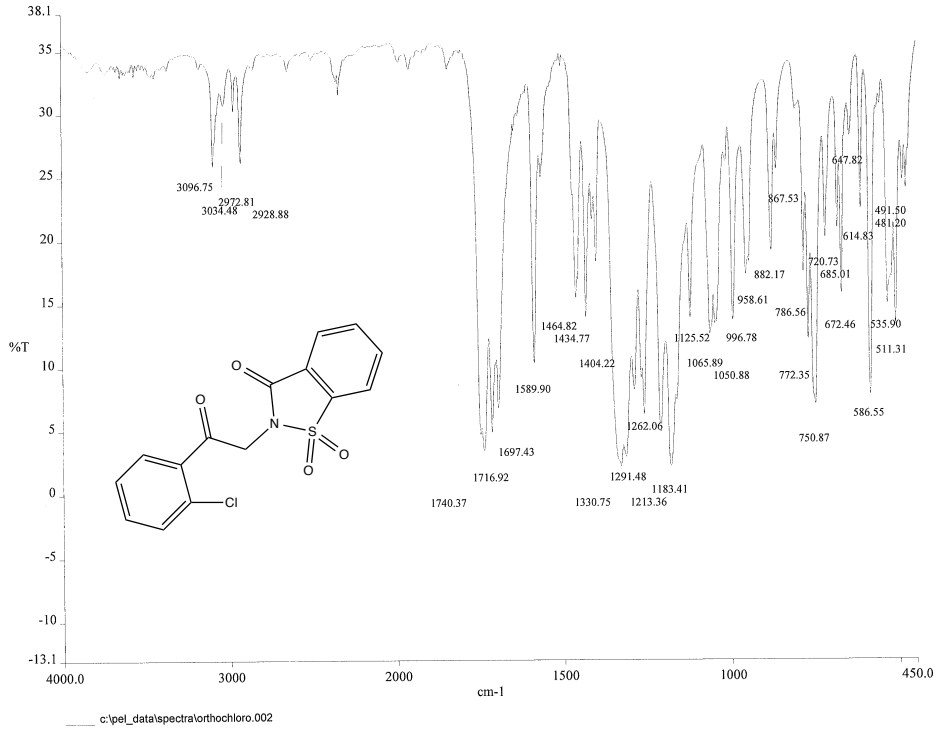

O
O
N
S
O
O
Cl
%T
36.3
34
32
30
28
26
24
22
20
18
16
14
12
10
7.5
3094.82
2987.06
2935.34
1746.47
1694.46
1591.79
1458.25
1423.85
1398.05
1329.29
1227.52
1186.11
1093.03
1062.69
1047.64
1000.65
963.80
910.05
882.10
821.31
749.26
671.42
590.70
508.66
4000.0
3000
2000
1500
1000
450.0
cm-1
c:\pel_data\spectra\parachloro.004

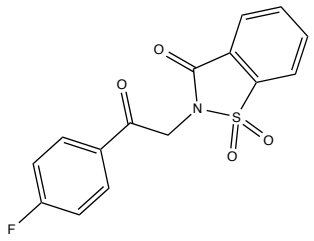

O
O
N
S
O
O
Cl

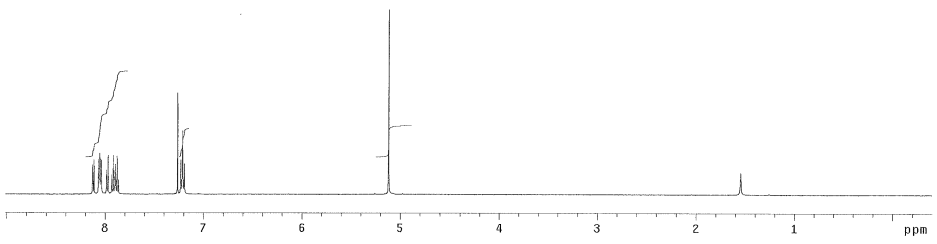

8
7
6
5
4
3
2
1
ppm

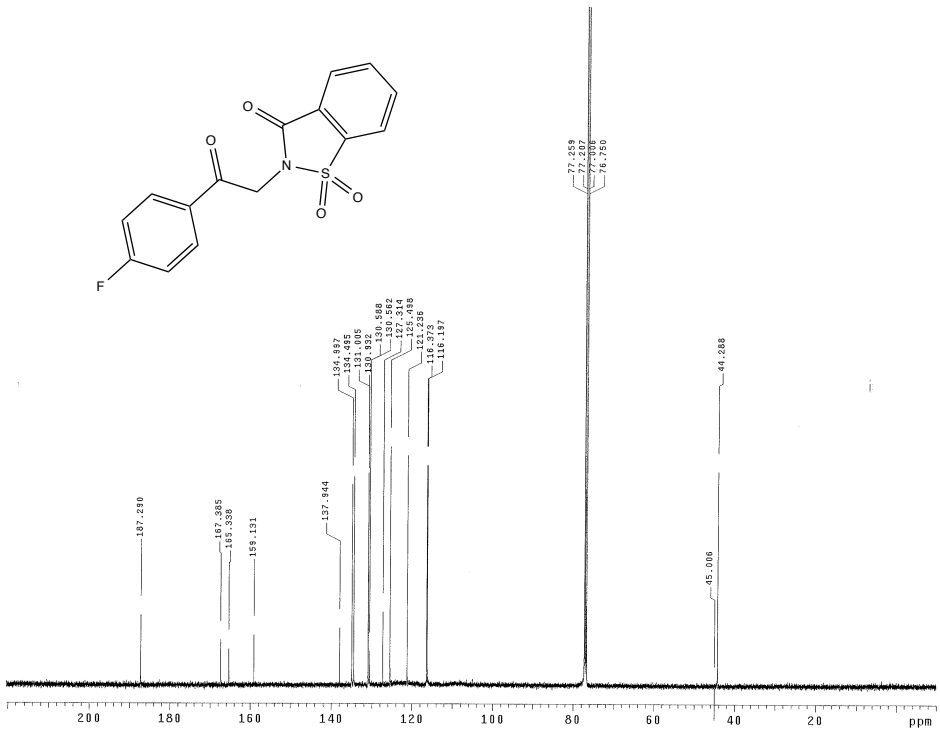

O
O
N
S
O
O
Cl

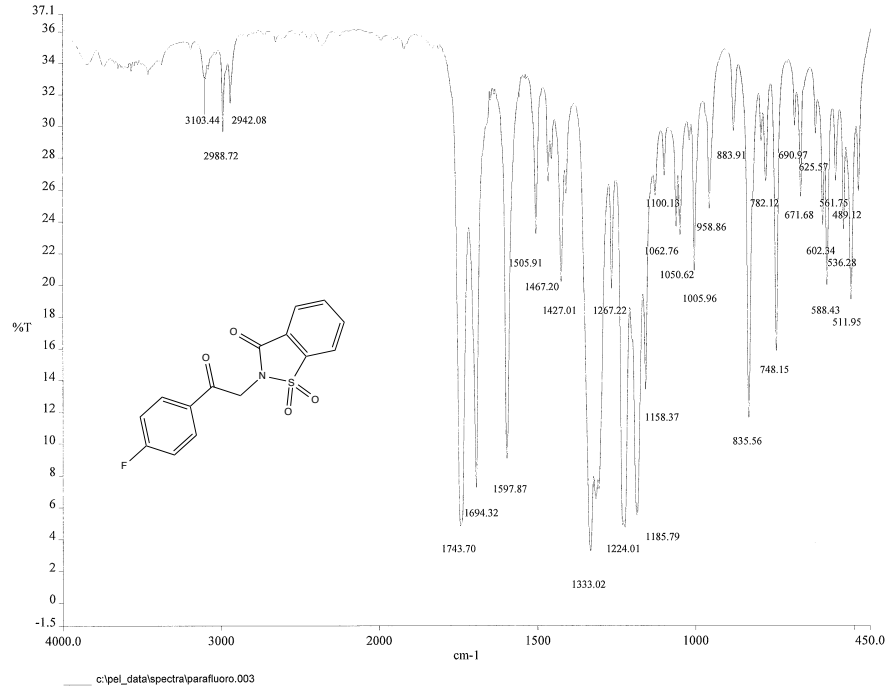

191.508
159.010
137.941
136.531
135.015
134.488
133.349
131.987
130.884
130.556
127.303
127.246
125.487
121.269
77.284
77.032
76.775
47.108
200
180
160
140
120
100
80
60
40
20
0 ppm

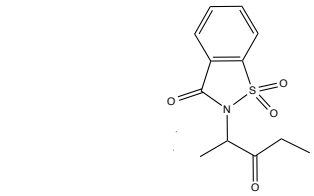

38.1
35
30
25
20
15
%T
10
5
0
-5
-10
-13.1
4000.0
3000
2000
1500
1000
450.0
cm-1
3096.75
2972.81
3034.48
2928.88
1740.37
1716.92
1697.43
1589.90
1464.82
1434.77
1404.22
1330.75
1291.48
1262.06
1213.36
1183.41
1125.52
1065.89
1050.88
996.78
958.61
882.17
867.53
786.56
772.35
750.87
720.73
685.01
672.46
647.82
614.83
586.55
535.90
511.31
491.50
481.20
O
N
S
O
O
Cl
c:\pel_data\spectra\orthochloro.002

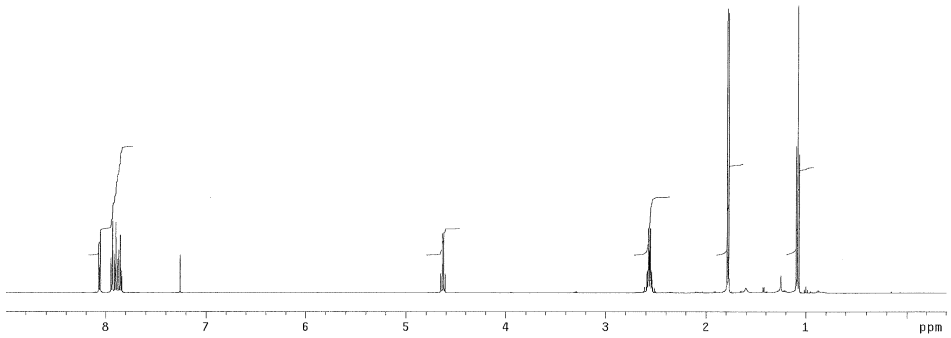

O
O
N
S
O
O
F

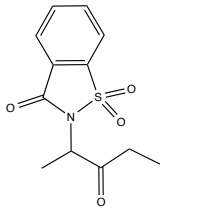

8
7
6
5
4
3
2
1
ppm

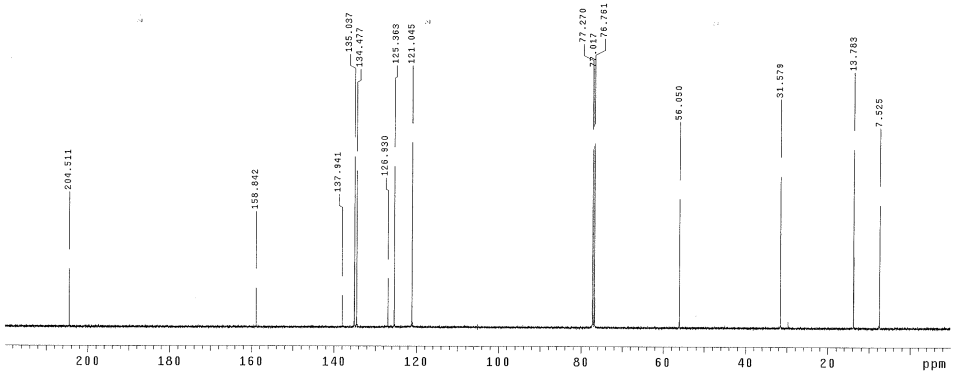

O
O
N
S
O
O
F
77.259
77.207
77.000
76.750
187.280
167.385
165.338
159.131
137.944
134.485
131.005
130.932
130.588
130.562
127.314
125.498
121.298
116.373
116.197
44.288
45.006
200
180
160
140
120
100
80
60
40
20
ppm

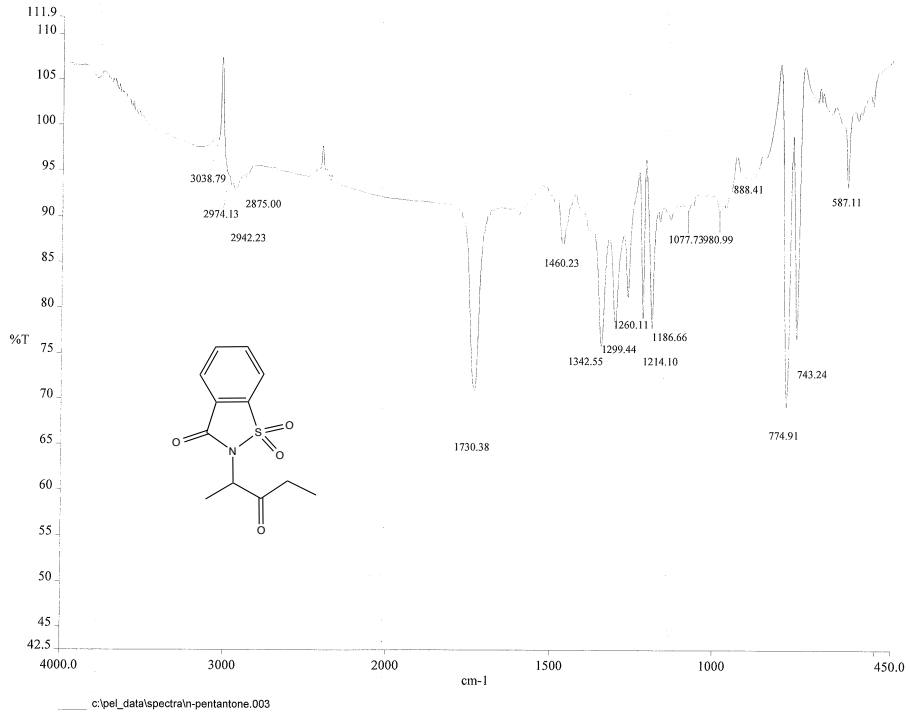

37.1
36
34
32
30
28
26
24
22
20
18
%T
16
14
12
10
8
6
4
2
0
-1.5
3103.44
2942.08
2988.72
1505.91
1467.20
1427.01
1267.22
1100.18
1062.76
1050.62
1005.96
958.86
883.91
782.12
690.97
671.68
625.57
602.34
561.75
536.28
489.12
588.43
511.95
748.15
1158.37
835.56
1597.87
1694.32
1743.70
1185.79
1224.01
1333.02
4000.0
3000
2000
1500
1000
450.0
cm-1
c:\pel_data\spectra\parafluoro.003

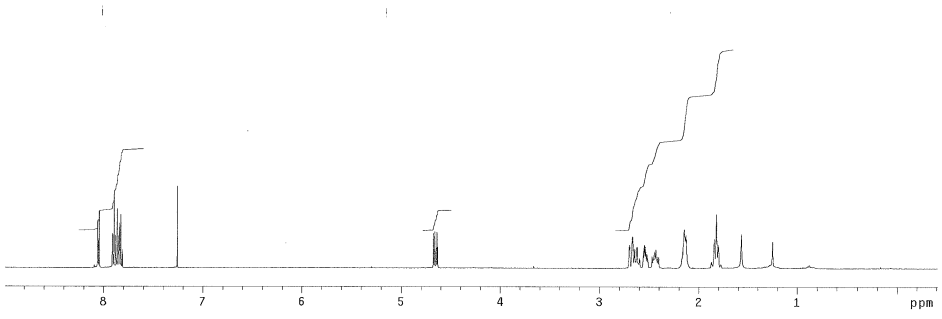

O
O
N
S
O
O
O

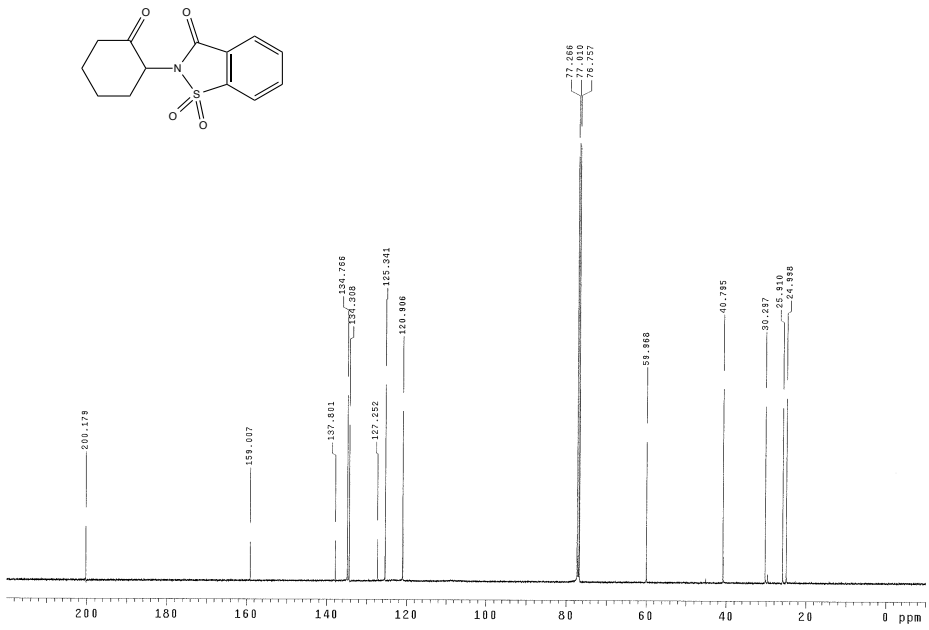

8
7
6
5
4
3
2
1
ppm

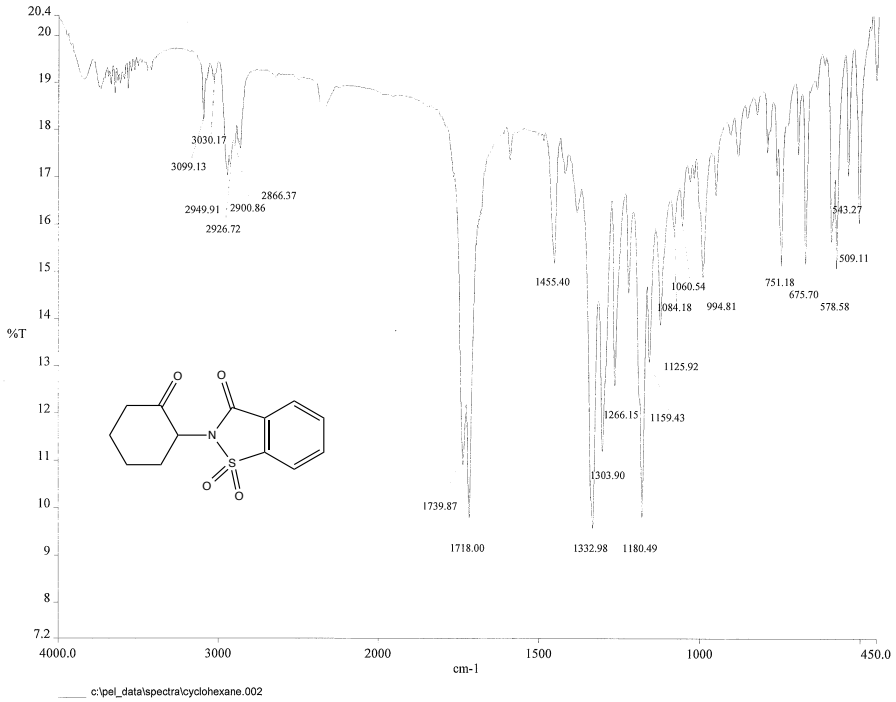

O
O
N
S
O
O
O


204.511
158.842
137.941
135.037
134.477
126.830
125.363
121.045
77.270
77.017
76.761
56.050
31.579
13.783
7.525
200
180
160
140
120
100
80
60
40
20
ppm


111.9
110
105
100
95
90
85
80
%T
75
70
65
60
55
50
45
42.5
4000.0
3000
2000
1500
1000
450.0
cm-1
3038.79
2974.13
2875.00
2942.23
1730.38
1460.23
1342.55
1299.44
1260.11
1214.10
1186.66
1077.73980.99
888.41
774.91
743.24
587.11
c:\pel_data\spectra\n-pentantone.003


8
7
6
5
4
3
2
1
ppm


200.179
159.007
137.801
134.766
134.308
127.252
125.341
120.496
77.266
77.010
76.757
59.868
40.795
30.297
25.910
24.938
200
180
160
140
120
100
80
60
40
20
0 ppm


%T
3030.17
3099.13
2949.91
2900.86
2866.37
2926.72
1739.87
1718.00
1455.40
1332.98
1303.90
1266.15
1180.49
1159.43
1125.92
1084.18
1060.54
994.81
751.18
675.70
578.58
543.27
509.11
4000.0
3000
2000
1500
1000
450.0
cm-1
c:\pel_data\spectra\cyclohexane.002