

Recyclable reagents and Catalytic Systems based on Hypervalent Iodine Chemistry

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ABSTRACT

Hofmann rearrangement of carboxamides to carbamates using Oxone[®] as an oxidant can be efficiently catalyzed by iodobenzene. This reaction involves hypervalent Iodine species generated in situ from catalytic amounts of PhI and Oxone[®] in the presence of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) in aqueous methanol solutions. Under these conditions, Hofmann rearrangement of various carboxamides affords the corresponding carbamates in high yields.

Aziridination of alkenes to aziridines using catalytic amounts of tetrabutylammonium iodide, meta-Chloroperoxybenzoic acid (*m*CPBA) and PhthNH₂ can be run under metal-free conditions. This reaction involves an oxidized iodine species generated in situ from Bu₄NI and *m*CPBA. Under optimized conditions, Conversion of various alkenes to the corresponding aziridine products proceeds in comparable yields to previous by reported procedures.

A green, recyclable and efficient catalytic oxidative system based on SiO₂-supported RuCl₃ and 3-(dichloroiodo)benzoic acid for the oxidation of alcohols and sulfides in water is developed. This catalytic oxidative system effects clean and efficient oxidation of a wide range of alcohols to the corresponding aldehydes and ketones, or sulfides to sulfoxides in high conversions with excellent chemoselectivity, under mild conditions. Furthermore, the SiO₂-RuCl₃ catalyst can be recovered by simple filtration and recycled in up to six consecutive runs without significant loss of activity. The reduced form of 3-(dichloroiodo)benzoic acid, 3-iodobenzoic acid, can be easily separated from reaction mixtures and converted back to 3-(dichloroiodo)benzoic acid by treatment with NaOCl and aqueous HCl in about 90% overall yield.

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CHAPTER 1

REVIEW

1.1 Introduction

Over the years, hypervalent aryl- λ^3 and aryl- λ^5 iodane reagents, combined with their benign environmental characteristics and commercial availability have emerged to be very popular reagents for various synthetically useful oxidative transformations. Organohypervalent iodine (III) compounds are particularly useful as the oxidants in Hofmann-type rearrangements, an organic reaction used to convert a primary amide to the corresponding amine. Which have been utilized in numerous synthetic works. The most common reagents for Hofmann-type rearrangement include (diacetoxyiodo)benzene, [bis(trifluoroacetoxy)iodo]benzene, and [hydroxyl(tosyloxy)]iodobenzene and their recyclable analogues. Recently, we have examined catalytic reactions using hypervalent iodine chemistry and Oxone[®] as an inexpensive and environmentally safe terminal oxidant for a Hofmann rearrangement.^{1,2}

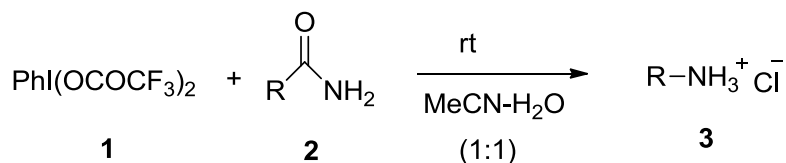
Aziridination of alkenes is another important chemical transformation and is a convenient method for accessing various nitrogen-containing products and synthetic intermediates. Aziridine is a key functional group found in natural products such as mitomycins and azinomycins and is a versatile building block that can undergo various useful transformations in total synthesis. Many synthetically useful aziridination methods are based on the use of metal salts or complexes as catalysts as nitrenium precursors, but avoiding toxic metals and performing reactions under metal-free conditions is important

in the development of green methodologies. We reported the hypiodite-mediated metal-free catalytic aziridination of alkenes²².

The oxidation of alcohols to the corresponding carbonyl compounds is one of the most fundamental and important transformations in synthetic organic chemistry. Hypervalent iodine compounds are some of the most valuable oxidants in organic synthesis due to their excellent selectivity, reactivity, wide applicability, low toxicity, plus the ability to proceed under mild reaction conditions. It has also been found that transition metals have a dramatic catalytic effect on some oxidations with hypervalent iodine reagents. In combination with recyclable and reusable hypervalent iodine reactions, ruthenium catalysts could be used as a green and efficient catalytic oxidative system, for oxidation of alcohols and sulfides in water.³

1.2 Hofmann Rearrangement Reaction with Hypervalent Iodanes

In 1979, Loudon and co-workers found the new direct method of converting amides into amines under moderate conditions using bis(trifluoroacetoxy)iodobenzene **1** (Scheme 1).⁴

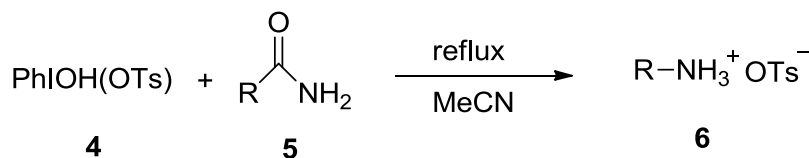


Scheme 1

In Scheme 1, bis(trifluoroacetoxy)iodobenzene is reacted with carboxylic acid amides **2** at room temperature in acetonitrile-water, for various amounts of time (2-5 hours)

depending on the migrating group-R in the primary amide. This reaction produced the corresponding amine **3** in very high percent yield through a Hofmann rearrangement type reaction. Some of the limitations to this reaction is that it has to be done under acidic conditions, and $\text{PhI}(\text{OCOCF}_3)_2$ is a light sensitive reagent and needs to be stored under nitrogen. This reaction is restricted to only primary and benzylic amides, since aromatic carboxylic acids are over oxidized and do not produce the expected amines.

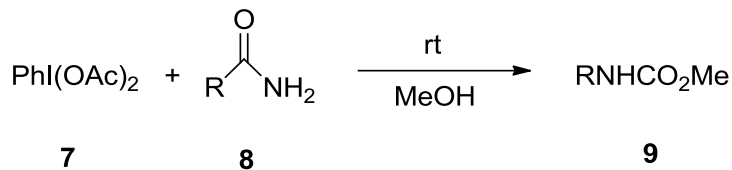
Similarly, in 1986, Koser utilized direct conversion of primary aliphatic carboxamides **5** to alkylammonium tosylates **6** using a slightly modified reagent [hydroxyl(tosyloxy)iodo]benzene **4**.⁵



Scheme 2

Aliphatic carboxamides were reacted with stoichiometric amounts of [hydroxyl(tosyloxy)iodo] benzene at reflux conditions using acetonitrile as the solvent- to give the corresponding alkylammonium tosylates **6**, (in Scheme 2). These alkylammonium tosylates precipitated from the solvent when stored at, or below room temperature. This process resulted in product yields ranging from 57% to 94%. One of the benefits of using $\text{PhIOH}(\text{OTs})$ is that it can be used under ambient conditions and is a stable crystalline compound.⁶

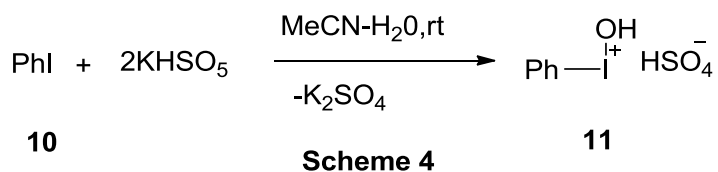
In 1990, Beckwith discovered that (diacetoxyiodo)benzene **7** could be used in an oxidative rearrangement of carboxamides **8**. Using an internal Hofmann rearrangement type reaction on the intermediate isocyanate, the carbamate products **9** were formed.



Scheme 3

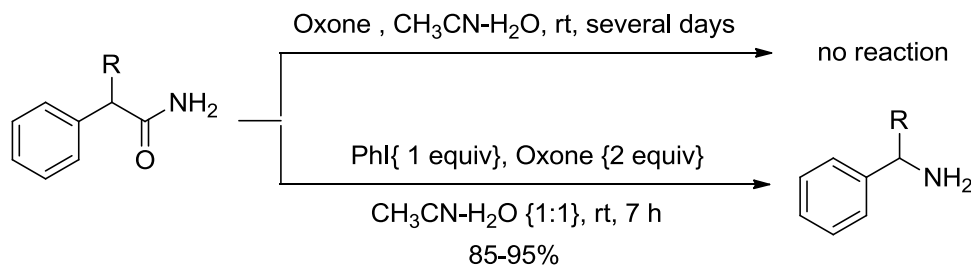
(Diacetoxyiodo)benzene was found to be a milder, and more selective reagent than the previously used Pb(OAc)_4 . In Scheme 3, PhI(OAc)_2 reacts with the carboxamides at room temperature in methanol to bring around an oxidative cyclization of the amide without attacking any other oxidizable functional groups.⁷

More recently, in 2010, our group explored the possibility of Hofmann rearrangement induced by the hypervalent iodine species [(hydroxy(phenyl)iodonium ion) PhI(OH)^+ **11**, generated in situ from stoichiometric amounts of iodobenzene **10** and inexpensive commercial oxidant Oxone[®] ($2\text{KHSO}_5 \cdot \text{KHSO}_4 \cdot \text{K}_2\text{SO}_4$).



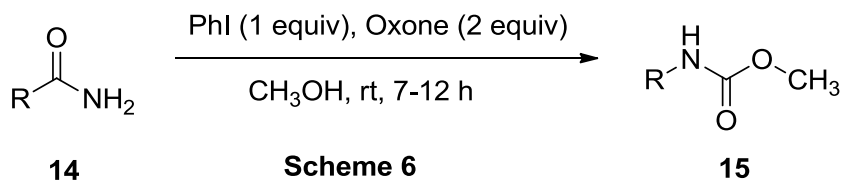
Scheme 4

In Scheme 4 iodobenzene reacts with 2KHSO_5 from the Oxone[®] in aqueous acetonitrile at room temperature to create the hypervalent iodine active species.⁸



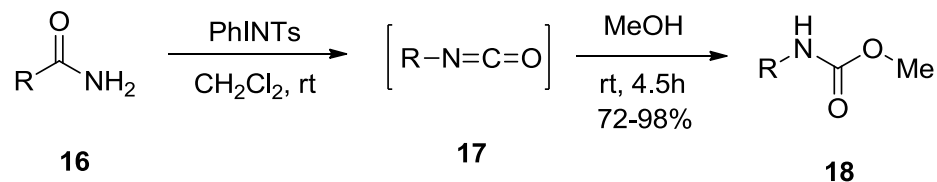
Scheme 5

To determine the importance of the hypervalent iodine species, 2-phenylacetamide **12** was reacted with Oxone[®] at room temperature for several days, with no reaction occurring. The addition of iodobenzene to the reaction mixture resulted in the formation of benzylamine **13**. The product could be isolated in about 85-95 % yield, but this procedure has a limited practical value due to the time and laborious protocol for isolating the final amines.



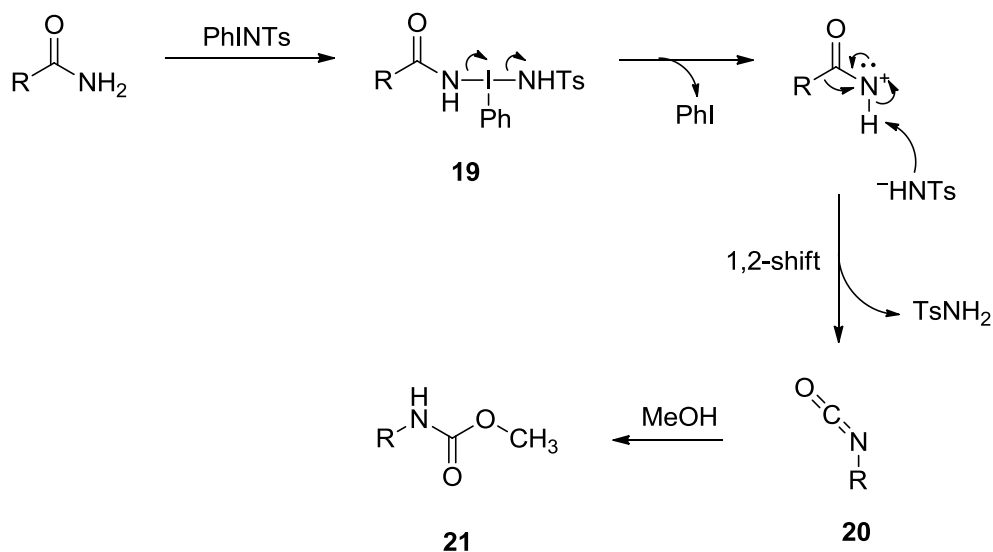
Due to the limiting practicality of this protocol, the reaction conditions were modified for the preparation of carbamates, which are stable solids or nonvolatile liquids that can be easily isolated from the reaction mixture by extraction with ethyl acetate. This reaction is limited to the use of alkylcarboxamides **14**, but is an excellent, and inexpensive method for the preparation of methyl carbamates **15** in yields comparable to previously reported preparations of methyl carbamates under basic conditions using the PhI(OAc)₂/KOH/MeOH system.

Recently 2012, our group discovered a new mild procedure for the Hofmann rearrangement of aliphatic and aromatic carboxamides **16** using (tosylimino)-phenyl-λ³-iodane. Using optimized conditions, the carboxamide reacted with the PhINTs in dichloromethane and methanol at room temperature for 4.5 hours. This gives 72-98% yields of the corresponding carbamate final products.



Scheme 7

Due to the mild reaction conditions and high selectivity in the reaction of carboxamides with PhINTs, of highly reactive intermediates called isocyanates **17** are formed which is subsequently converted into the stable carbamates **18** by treatment with alcohols.⁹

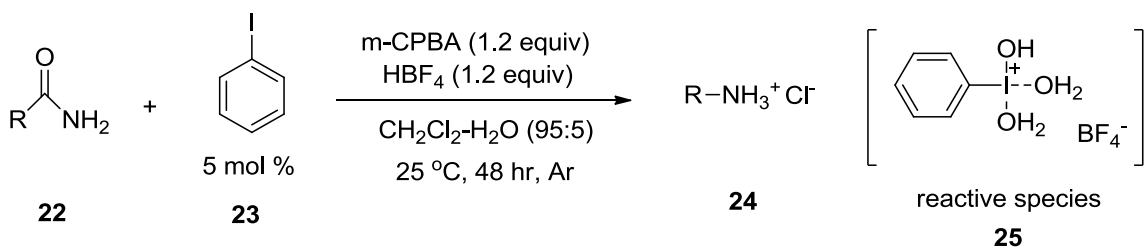


Scheme 8

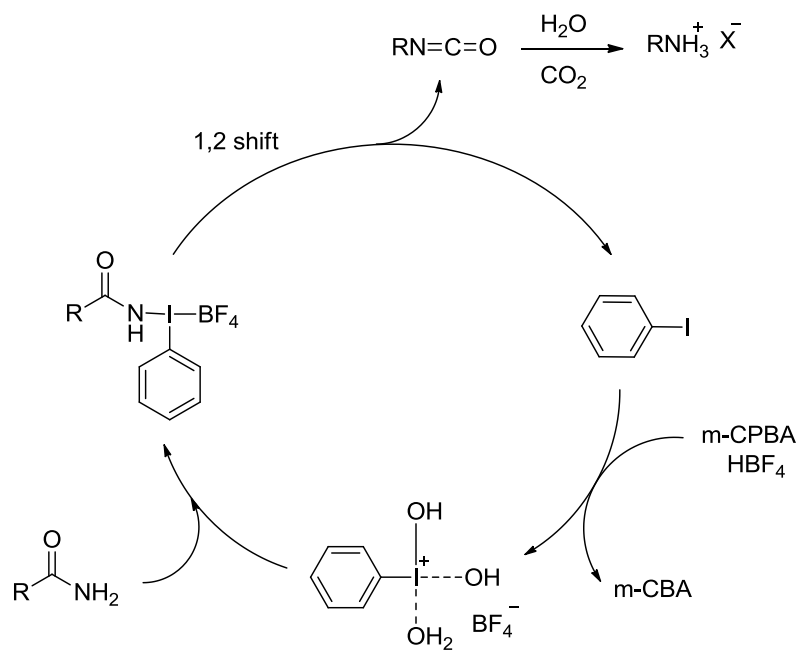
The proposed reaction mechanism begins with the formation of amidoiodane **19**, which then goes through a reductive elimination of iodobenzene and 1,2-alkyl or -aryl shift to the electron deficient nitrenium nitrogen atom to give the intermediate isocyanate **20**. The addition of methanol to the isocyanate gives the final carbamate **21** product.

In 2012, the first catalytic version of hypervalent aryl- λ^3 -iodane-induced Hofmann rearrangement of primary carboxamides was found by Ochiai and co-workers. It was found that tetracoordinated bis(aqua)(hydroxyl)phenyl- λ^3 -iodane **25** complex was

generated as an active oxidant in situ from catalytic amounts of iodobenzene **23** with m-chloroperbenzoic acid in the presence of 48% HBF₄. The optimized conditions found that performing this reaction in dichloromethane-H₂O at 25 °C for 48 hours gave excellent yields for the corresponding alkylammonium chlorides **24**.¹⁰



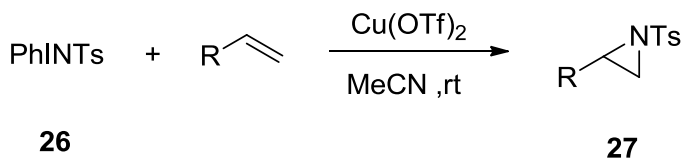
Scheme 10 shows the proposed catalytic cycle of Hofmann rearrangement of carboxamides **22** to the corresponding alkylammonium chlorides. Using m-CPBA iodobenzene is oxidized giving the in situ, generating the tetracoordinated bis(aqua)(hydroxyl)phenyl-λ³-iodane reactive species, which coordinates with the carboxamide. This generated intermediate undergoes a 1, 2-shift or Hofmann rearrangement. Giving the isocyanate intermediate, through addition of water and loss of CO₂, forms the product. The rearrangement eliminates iodobenzene, which completes the cycle.



Scheme 10

1.3 Aziridination of Olefins with Hypervalent Iodane

Evans, in 1994, discovered that soluble Cu(I) and Cu(II) complexes are the most efficient catalysts for olefin aziridination using (N-(p-tolylsulfonyl)imino)phenyliodane (PhI=NTs) **26** as the nitrene precursor. CuClO₄, Cu(OTf)₂ and Cu(acac)₂ were found to be the best transition-metal catalysts in the aziridination of styrene (product **27** in Scheme 11) and cyclohexene. These copper replaced outdated reagents which gave low yields due to competing hydrogen abstraction and insertion processes, which form unwanted side products. Also, these catalysts extended the scope, by including both electron-rich and electron-deficient olefins.¹¹

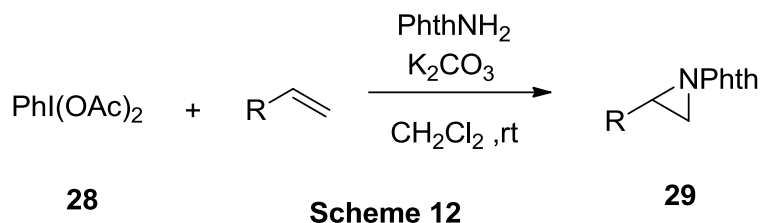


Scheme 11

Optimizing the conditions showed that running the reaction between -20 °C to 25 °C and using the polar aprotic solvents like MeCN or MeNO₂, helped to increase the yield to 55-95% and accelerate the rate of the reaction.

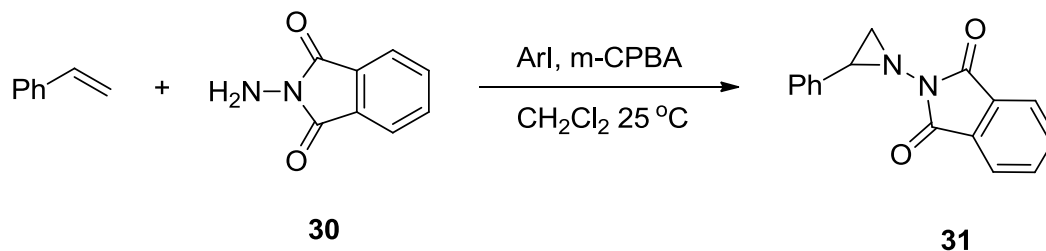
Chi-Ming Che and co-workers in 2004 investigated a metal catalyst-free C=C bond aziridination procedure using stoichiometric amounts of iodobenzene diacetate (PhI(OAc)₂) **28** and N-aminophthalimide as the nitrogen precursor¹⁴. They were looking at the effectiveness of intermolecular aziridination of a group of alkenes under mild conditions. It was found that the electron-deficient or electron-rich nature of the C=C bond had no effect on the reaction yields, but electron-deficient alkenes reacted faster

than electron-rich alkenes. Reactions were then performed with *cis* and *trans* methylstyrene, which gave exclusive *syn* and *anti* selectivity, showing that this protocol is diastereoselective.¹²



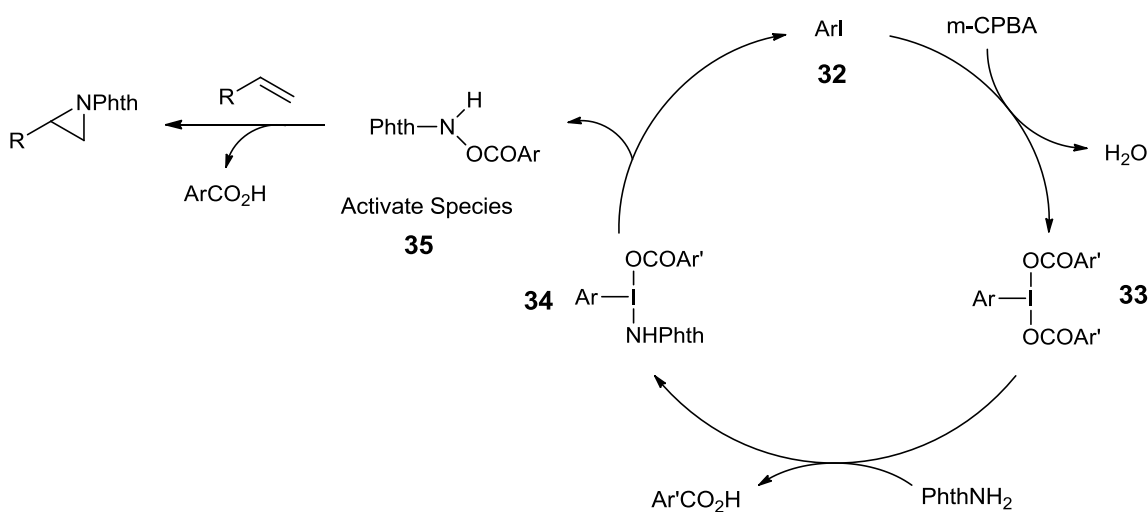
Optimized conditions showed that running the reaction at room temperature for approximately 12 hours in dichloromethane gave the best overall yields. It was also found that this reaction must be performed under basic conditions and that potassium carbonate was the best base used in order to prevent decomposition of the aziridine products **29**. The final aziridine products were obtained in good to excellent yields up to 99%.

Chi-Ming Che and co-workers, in 2005¹², expanded on previous research by looking at developing an efficient and recyclable method for mediating alkenes aziridination that is easy, inexpensive and nontoxic (Scheme 13). They examined the effect of several substituted aryl iodides on the outcome of various intermolecular alkene aziridination reactions and compared them with previously reported $\text{PhI}(\text{OAc})_2$ reactions.¹³



Scheme 13

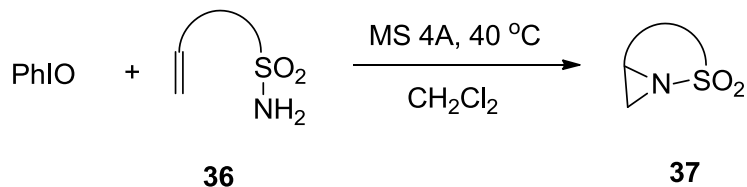
Using previously reported optimized conditions and styrene as the probe substrate, *p*-MeOC₆H₄I was found to be the best aryl iodide source for the alkene aziridination, giving a 81% yield. Epoxides were generated in the absence of aryl iodide, indicating that ArI is essential for this reaction in order to obtain the desired product. The scope of *p*-MeOC₆H₄I aziridination reactions included a series of terminal and internal alkenes. These reactions generated the corresponding aziridines in moderate to good yields, compared with analogous reactions using PhI(OAc)₂. This protocol showed comparable product yields for most alkenes and the ability to produce product on two alkenes that PhI(OAc)₂ failed.



Scheme 14

The proposed mechanism for this reaction begins with the oxidation of the ArI (p-MeOC₆H₄I) **32** species by m-CPBA to generate in situ, ArI(OCOAr)₂ **33**, which, through ligand exchange with N-aminophthalimide **30**, forms the ArI(OCOAr)(NHPth) **34** intermediate from dissociation of ArI. This newly generated N-benzoyloxyaminophthalimide **35** active species undergoes C=C bond addition and cyclization to give the corresponding aziridine **31**. The ArI could then be recycled and re-oxidized to run this reaction over again, without loss of activity.

In 2010, Moriarty and co-workers examined metal-free intramolecular aziridination of alkenyl sulfonyliminoiodanes **36**¹⁴. The proposed pathway from the iminoiodane involves an electrophilic addition of the tethered double bond to the PhI⁺ center, subsequent neutralization of the formed carbocation by the anionic nitrogen center through a 2+2 cycloaddition, and generation of the aziridine product **37**. Since the transition metal catalyzed aziridination of alkenes has been largely developed, the next step was to study the metal-free reaction in order to improve the “green chemistry”.¹⁴

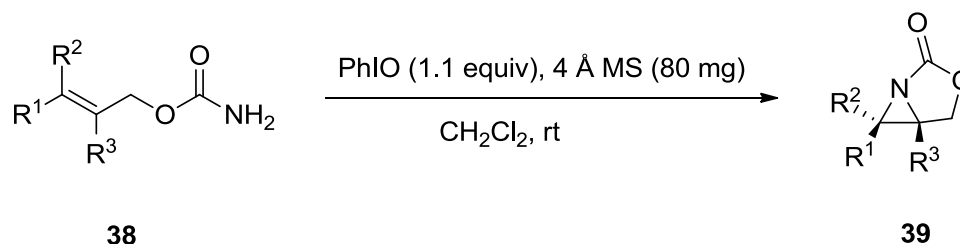


Scheme 15

Chi-Ming Che and co-workers in 2011 discovered an efficient and practical hypervalent iodine compound metal-free intramolecular aziridination reaction using allylic carbamates **38**. The allylic carbamates failed to form any aziridine products in the

presence of metal catalyst, or iodobenzene diacetate, under any conditions tried.

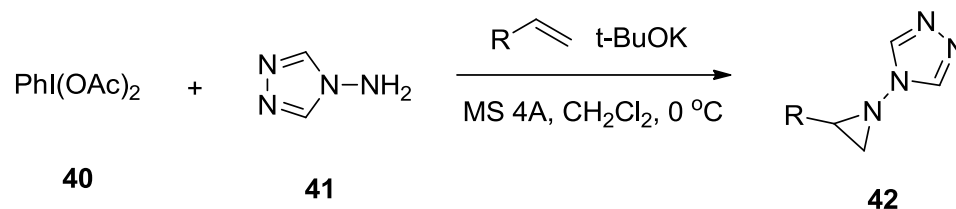
However, the bicyclic aziridines were obtained in high yields when using iodosylbenzene (PhIO, 2 equiv) and 4 Å molecular sieves¹⁵.



Scheme 16

The search for optimized conditions demonstrated that running these reactions in dichloromethane at room temperature for approximately 10 hours afforded aziridines **39** in good to excellent yields up to 98%. Aryl-substituted bicyclic aziridines are sensitive to water and other nucleophilic reagents and these products also decompose during column chromatography. Fortunately simple filtration was sufficient to recover the analytically pure products from this reaction.

In 2012, Xue and co-workers discovered a convenient and efficient procedure for the direct formation of carbon-nitrogen bonds, by taking hydrocarbons and regioselective converting them into the corresponding aziridine products. This is a new metal-free approach for the aziridiation of alkenes through the direct use of 4-amino-4H-1,2,4-triazole **41** as the nitrogen source and PhI(OAc)₂ **40** as the oxidant under mild conditions.¹⁶

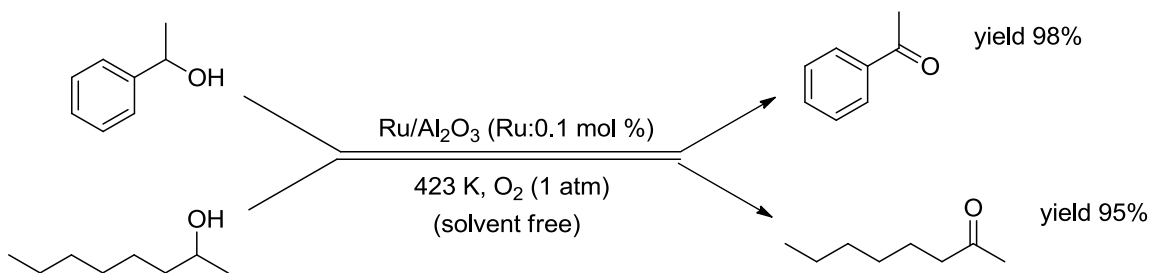


Scheme 17

Several reaction conditions were tested and the combination of PhI(OAc)_2 , CH_2Cl_2 , $t\text{-BuOK}$ at $0\text{ }^\circ\text{C}$ were found to be the most effective. These conditions were used to evaluate the efficiency of the aziridination reaction of styrene with 4-amino-4H-1,2,3-triazole **41**. In the presence of powdered molecular sieves (4 \AA) for 20 h in the optimized conditions, the aziridine derivatives **42** were obtained with moderate to high yields. The use of 4-amino-4H-1,2,3-triazole was also found to be useful nitrogen source for imination of sulfides and sulfoxides in the creation of the corresponding sulfoximines and sulfilimines.¹⁶

1.4 Diverse oxidation reactions

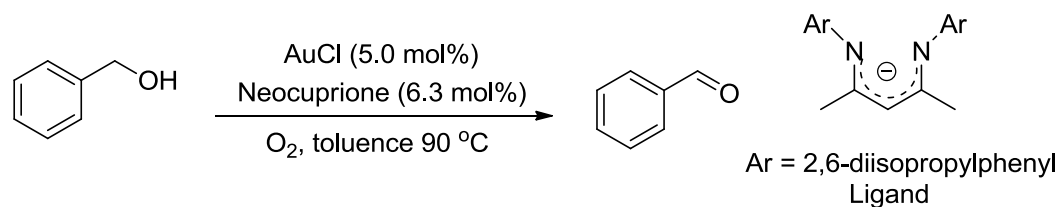
Yamaguchi and Mizuno, in 2002, looked into the oxidation of both activated and non-activated alcohols with only molecular oxygen, using a solid-supported heterogeneous catalyst. These oxidation reactions are considerably less expensive and more environmentally friendly due to the ease of separation of the catalyst, which can then be recycled and the use of solvent free conditions. Ru/Al₂O₃ was found to be the most effective aerobic heterogeneous oxidation catalyst that could oxidize alcohols under solvent free conditions.¹⁷



Scheme 18

The optimized conditions included the reaction at 423° K, with high catalytic activities for the oxidation of both activated and non-activated alcohols using only 1 atm of O₂. Reaction selectivity was over 97 % in all cases and all primary and secondary benzylic alcohols were converted into the corresponding benzaldehydes and ketones. Primary and secondary allylic alcohols formed the corresponding enals or enones, which afforded products in good to excellent yields up to 99%. This catalyst was found to be a good alternative to more expensive and environmentally harmful organometallic and inorganic compounds.

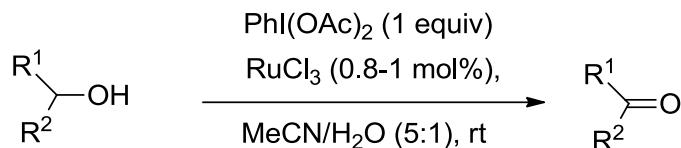
In 2005 Guan and coworkers developed a new, and highly selective, aerobic oxidation of alcohols catalyzed by a gold (I) complex with an anionic ligand. Neocuprione was used as the electron-donating ligand to help facilitate generation of the oxidative intermediate. The flanking groups on the nitrogen atoms provide steric hindrance to leave open coordination sites to bind oxygen transfer reagent. Gold (I) chloride and neocuprione were found to serve as an excellent catalyst to oxidize primary and secondary benzyl and allylic alcohols. Conversion and yields were very high with excellent selectivity.¹⁸



Scheme 19

This reaction ran smoothly under regular atmosphere pressure using molecular oxygen as the oxidant. The optimal conditions formed that toluene was found to be the best solvent and after after 10 hours, 90 °C a 99 % yield with 100% conversion to the corresponding benzaldehydes and ketones was observed.

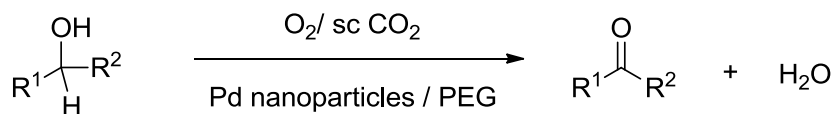
Zhdankin, in 2006, looked into new and highly efficient RuCl₃-catalyzed selective oxidation of alcohols to the carbonyl compounds by using (diacetoxyiodo) benzene (DIB). This reaction starts out by the rapid Ru-catalyzed disproportionation of DIB to a 1:1 mixture of iodobenzene and iodylbenzene. When the alcohol is added, the newly formed iodylbenzene acts as the stoichiometric oxidant, which converts primary and secondary alcohols to the carbonyl compounds.



Scheme 20

The corresponding carbonyl compounds were obtained in good to excellent yields up to 96% after performing this reaction in aqueous acetonitrile at room temperature for various amounts of time (0.5-24 hours). This protocol resulted in disproportionation of DIB, which shows that PhIO_2 can be an efficient oxidant in the Ru-catalyzed oxidation of alcohols. However the safer and readily available (diacetoxyiodo) benzene is a more convenient oxidant due to the explosive properties and commercial unavailability of iodylbenzene³⁰.

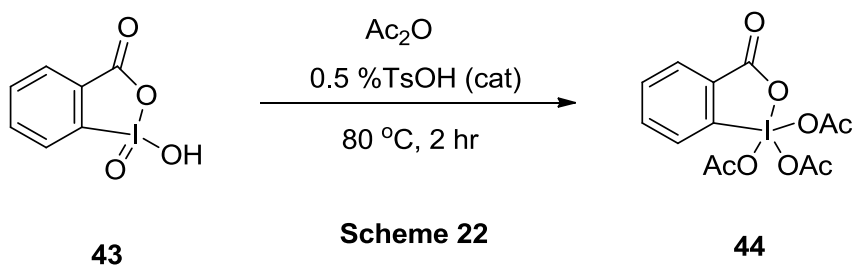
Similarly, Hou discovered a new highly efficient catalytic system for the biphasic aerobic oxidation of alcohols by using palladium nanoparticles in a poly(ethylene glycol) (PEG) matrix as the catalyst and supercritical carbon dioxide (scCO_2) as the substrate, while using molecular oxygen as the oxidant. PEG is thought to help prevent aggregation and deactivation of the catalytically active nanoparticles by turning it into Pd-black. While scCO_2 provides a safe environment for the use of molecular oxygen under solvent-free conditions.¹⁹



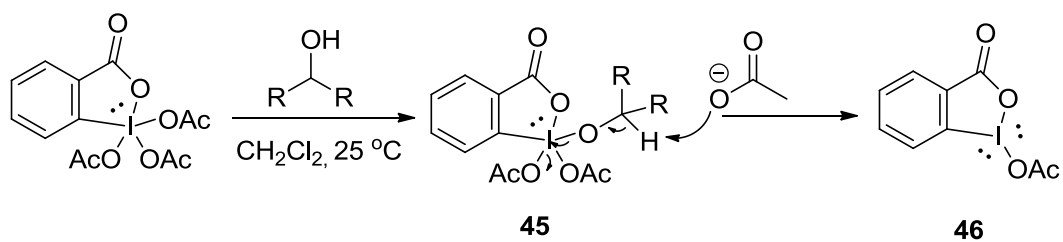
Scheme 21

This catalytic system uses palladium clusters and PEG-1000 in $scCO_2$ which works for a variety of alcohols under standard reaction conditions (65-80 °C) but conversion to product varies from 1 to 26 hours, depending on the alcohol. Allylic alcohols are transformed into the corresponding α,β -unsaturated aldehydes in excellent yields under mild conditions, but longer reaction times were required for primary and secondary benzylic alcohols to be converted into ketones and aldehydes. The substrate and products are contained in the supercritical CO_2 phase, which was confirmed by GC monitoring. The conversion time indicates an induction period for the first run due to a apparent dispersion process. No noticeable induction period is needed for the second run, thereby increasing the rate of conversation for run two. Conversion and selectivity were found to be up to 99% for both allylic and benzylic alcohols.

Dess and Martin developed one of the most useful oxidizing agents for oxidation of complex, sensitive and multifunctional primary and secondary alcohols to the corresponding aldehydes and ketones in 1983, which is known as Dess-Martin periodinane (DMP) reaction **44**. DMP is based on the known 2-iodoxybenzoic acid (IBX) **43**, which is has limited solubility in many organic solvents, but due to the acetate groups attached to the central iodine atom, DMP is much more soluble in organic solvents.²⁰



DMP can be easily prepared from 2-iodylbenzoic acid using p-toluenesulfonic acid and acetic anhydride at 80 °C. DMP has several advantages that include milder reaction conditions, higher yields, shorter reaction times, high chemoselectivity, simplified workup, long shelf life and the ability to perform oxidation of substrates with other sensitive functional groups.



Scheme 23

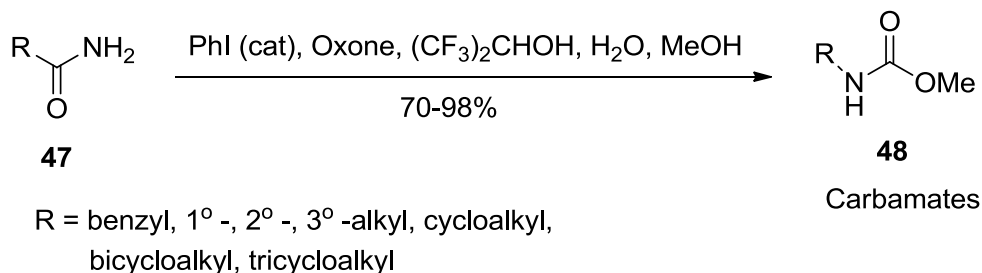
The first step of the oxidation reaction alcohol rapidly performs a ligand exchange with Dess-Martin periodinane forming the intermediate diacetoxyalkoxyperiodinane **45**. Next, the acetate acts as a base to deprotonate the hydrogen on the alcohol creating the corresponding aldehyde or ketone, iodinane **46** and acetic acid.

CHAPTER 2
RESULTS AND DISCUSSION

2.1 Hypervalent Iodine Catalyzed Hofmann Rearrangement of Carboxamides using Oxone[®] as the Terminal Oxidant.

A. Introduction

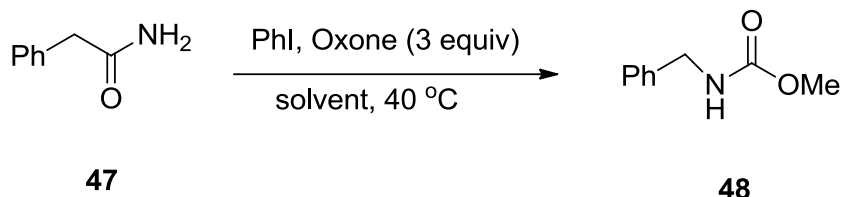
Recently, hypervalent iodine reagents have emerged as environmentally friendly and efficient oxidizing reagents for various synthetically useful oxidative transformations. Additionally, new achievements in the area of hypervalent iodine chemistry have included the development of numerous catalytic reactions utilizing organohypervalent iodine species in the iodine (I)/ iodine (III) catalytic cycle. Most of these cycles, however, employ m-chloroperoxybenzoic acid (m-CPBA), which is potentially explosive and environmentally unsafe stoichiometric oxidant. We have now reported a new procedure for the Hofmann rearrangement of carboxamides **47**, using catalytic amounts of PhI and Oxone[®] (2KHSO₅·KHSO₄·KHSO₄) as an inexpensive and environmentally safe terminal oxidant.²¹



Scheme 24

B. Results and Discussion

Table 1. Optimization of Catalytic Hofmann Rearrangement with Oxone.



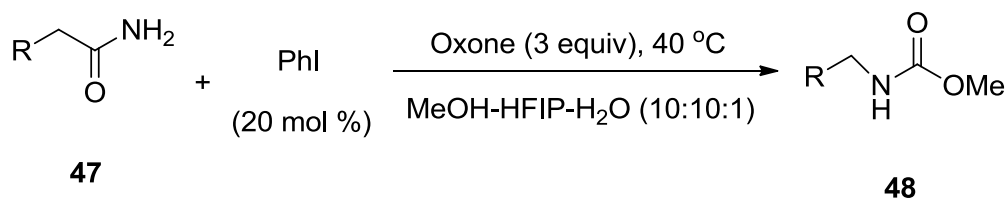
Entry	Time (h)	PhI (equiv)	Solvents (Ratio)	Yields(%)
1	3	0.5	MeOH-H ₂ O (10:1)	(79)
2	3	0.5	MeOH-CH ₂ Cl ₂ -H ₂ O (10:10:1)	(47)
3	3	0.5	MeOH-CHCl ₃ -H ₂ O (10:10:1)	(44)
4	3	0.5	MeOH-HFIP-H ₂ O (10:10:1)	98(99)
5	3	0.5	MeOH-TFE-H ₂ O (10:10:1)	(82)
6	3	0.5	MeOH-THF-H ₂ O (10:10:1)	N.R
7	3	0.5	MeOH-Et ₂ O-H ₂ O (10:10:1)	(13)
8	3	0.5	MeOH-AcOEt-H ₂ O (10:10:1)	(1)
9	3	0.5	MeOH-hexane-H ₂ O (10:10:1)	(85)
10	3	0.5	MeOH-CH ₃ NO ₂ -H ₂ O (10:10:1)	(28)
11	3	0.5	MeOH-MeCN-H ₂ O (10:10:1)	(21)
12	3	0.5 ^a	MeOH-HFIP-H ₂ O (10:10:1)	(13)
13	3	0.5 ^b	MeOH-HFIP-H ₂ O (10:10:1)	(87)
14	3	0.5 ^c	MeOH-HFIP-H ₂ O (10:10:1)	(30)
15	3	0.5 ^d	MeOH-HFIP-H ₂ O (10:10:1)	(59)
16	3	0.5 ^e	MeOH-HFIP-H ₂ O (10:10:1)	N.R
17	3	0.2	MeOH-HFIP-H ₂ O (10:10:1)	96(99)
18	10	0.1	MeOH-HFIP-H ₂ O (10:10:1)	89(93)
19	3	None	MeOH-HFIP-H ₂ O (10:10:1)	N.R

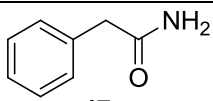
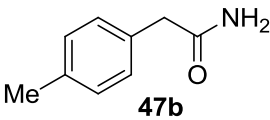
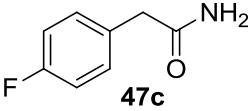
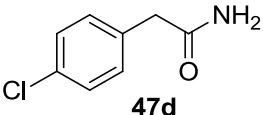
All reactions were performed using 3 equiv of Oxone[®] and 1 equiv of phenylacetamide **47** at 40 °C. Isolated yields (numbers in parentheses show yields determined from ¹H NMR spectra of reaction mixtures). ^a2,4,6-Me₃C₆H₂I, ^b4-Me C₆H₄I, ^c4-CF₃C₆H₄I, ^d3-HO₂CC₆H₄I and ^e*n*-Bu₄NI were used instead of PhI.

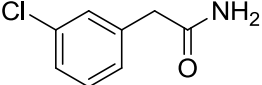
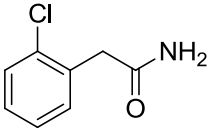
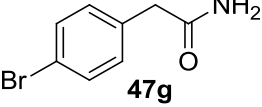
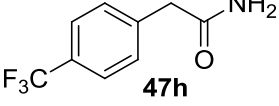
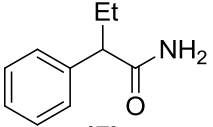
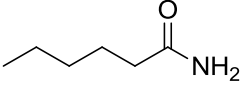
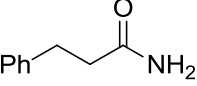
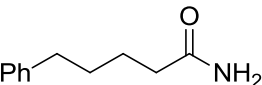
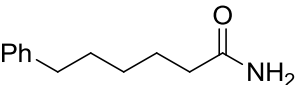
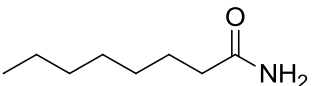
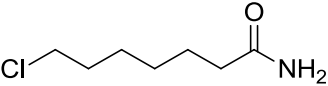
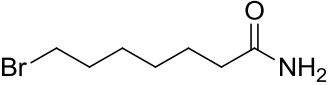
To determine the optimized conditions for the organoiodine (III) catalyzed Hofmann rearrangement using phenylacetamide. We performed several different trials

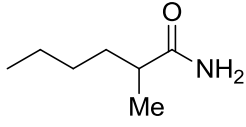
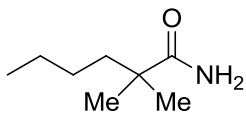
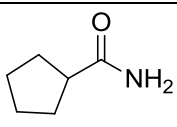
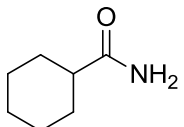
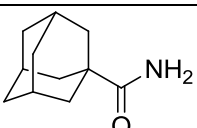
and concluded that performing the reaction using PhI(0.2) and Oxone[®] (3 equiv) at 40 °C for approximately 3 hours in MeOH-HFIP-H₂O at a (10:10:1) ratio gave the best % yield. The addition of small amount of water was required to dissolve Oxone[®] in the reaction mixture. When determining the best solvent, we discovered that in the presence of 1,1,1,3,3,3-hexafluoroisopropanol (HFIP) the reaction mixture dramatically changes the outcome of this reaction leading to the formation of the carbamate **48** in high yield. The accelerating effect of fluoroalcohols on some reactions of hypervalent iodine species was previously reported by Kita and co-workers but is still not fully understood at this time³¹.

Table 2: Preparation of Carbamates by Hofmann Rearrangement under Catalytic Conditions



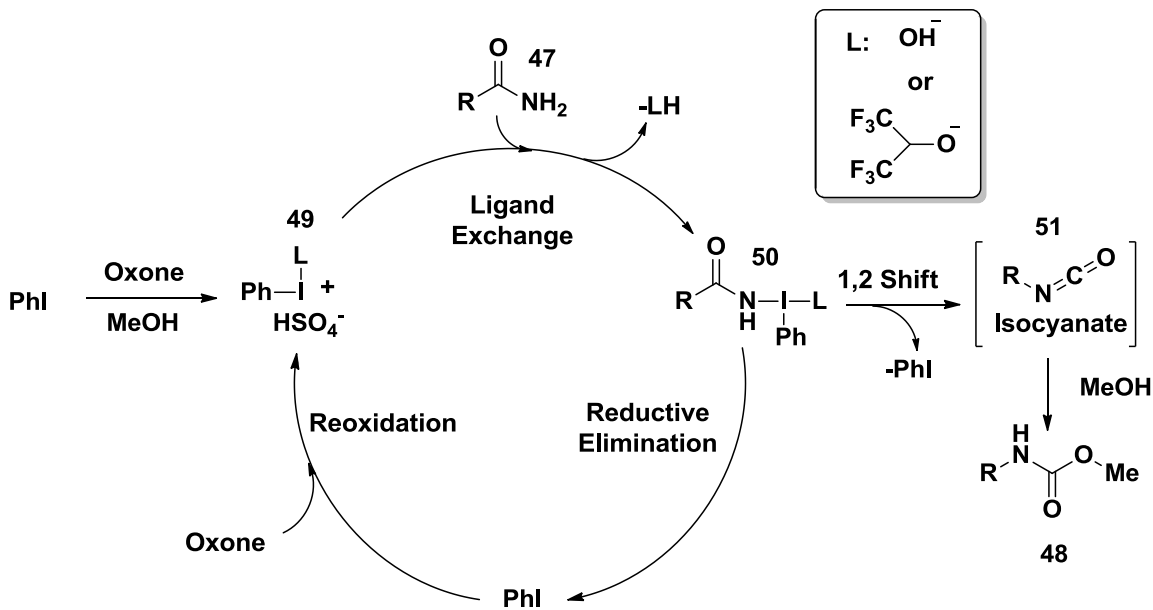
Entry	Time (h)	Carboxamide 47	Product 48	Yield (%)
1	5	 47a	48a	96 (97)
2	5	 47b	48b	96 (93)
3	7	 47c	48c	86
4	7	 47d	48d	93

5	7	 <p style="text-align: center;">47e</p>	48e	86
6	7	 <p style="text-align: center;">47f</p>	48f	88
7	7	 <p style="text-align: center;">47g</p>	48g	85
8	9	 <p style="text-align: center;">47h</p>	48h	78
9	5	 <p style="text-align: center;">47i</p>	48i	96
10	8	 <p style="text-align: center;">47j</p>	48j	92 (100)
11	7.5	 <p style="text-align: center;">47k</p>	48k	91
12	7.5	 <p style="text-align: center;">47l</p>	48l	85
13	7.5	 <p style="text-align: center;">47m</p>	48m	84
14	8	 <p style="text-align: center;">47n</p>	48n	86
15	8	 <p style="text-align: center;">47o</p>	48o	85
16	8	 <p style="text-align: center;">47p</p>	48p	78

17	8	 <p style="text-align: center;">47q</p>	48q	73
18	8	 <p style="text-align: center;">47r</p>	48r	70
19	6	 <p style="text-align: center;">47s</p>	48s	83
20	6	 <p style="text-align: center;">47t</p>	48t	92 (89)
21	5	 <p style="text-align: center;">47u</p>	48u	98 (90)

After determining the optimized conditions, we examined the conversion of various substituted carboxamides **47** to the corresponding carbamates **48** (Table 2). We found that all benzylcarboxamides with either electron-withdrawing or electron-donating substituents afforded respective carbamates in good yields (entries 2-8). Also, we found that various aliphatic amides, including primary, secondary, tertiary, and cyclic alkylcarboxamides, smoothly reacted under the optimized conditions to give the respective carbamates **48** in good yields (entries 9-21). When comparing our results with previous methods for Hofmann rearrangement using only stoichiometric hypervalent iodine species generated in situ, our method afforded carbamates **48** products in similar yields.

Proposed Reaction Mechanism for the Hofmann rearrangement of Carboxamides



Based on the previously reported Hofmann rearrangement mechanisms using hypervalent iodine reagents, we propose a mechanism for the catalytic cycle reaction starting with the creation of the active species [hydroxy(phenyl)iodonium ion $[\text{PhI}(\text{OH})]^+$ **49**, which is generated from PhI and Oxone[®] in aqueous HFIP. The active species will then react with the carboxamide **47** to give the hypervalent amidoiodane **50** via ligand exchange. The hypervalent amidoiodane **50** then undergoes reductive elimination of iodobenzene and a 1,2-shift at the electron-deficient nitrenium nitrogen atom to give an isocyanate **51** intermediate. The addition of MeOH to the isocyanate **51** generates the final carbamate **48**. The regenerated PhI is then re-oxidized to continue the catalytic cycle.

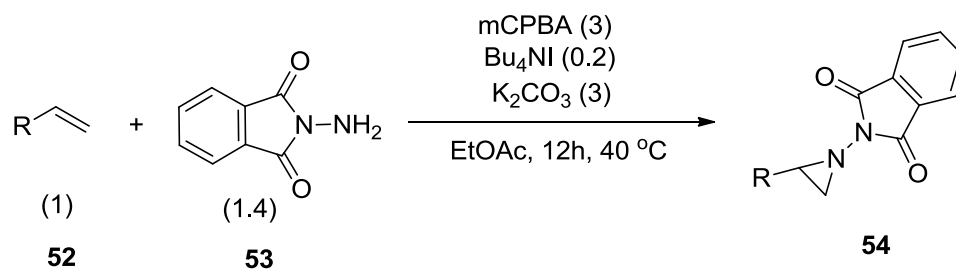
C. Summary

In conclusion, we have developed a new procedure for the Hofmann rearrangement of various benzylcarboxamides and aliphatic amides, using catalytic hypervalent iodine and Oxone[®] as a terminal oxidant with HFIP as a co-solvent. This is a new, environmentally friendly and efficient procedure that affords corresponding carbamates in high yields under mild conditions. The proposed mechanism of this reaction involves the electron-deficient active species formed from hydroxy(phenyl)iodonium ion or hypervalent aminoiodane and HFIP.

2.2 Hypiodite-Mediated Metal-Free Catalytic Aziridination of Alkenes

A. Introduction

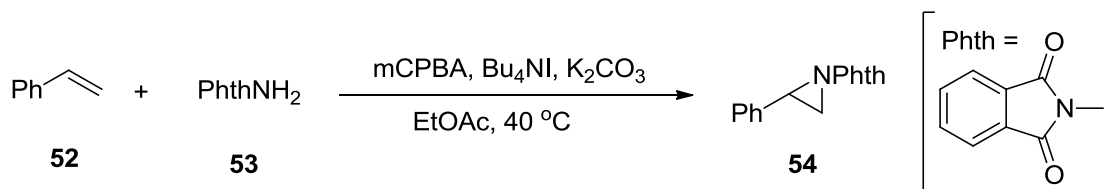
Aziridination of alkenes is an important chemical transformation and represents a convenient method for accessing various nitrogen-containing products and synthetic intermediates. Numerous synthetically useful aziridination methods are based on the use of metal salts or complexes as catalysts as nitrenium precursors. These procedures are outdated from both environmental and economic viewpoints since avoiding toxic metals and performing reactions under metal-free conditions is important in the development of green synthetic methodologies. We have now reported the first metal-free catalytic aziridination of alkenes **52** using catalytic amounts of tetrabutylammonium iodide (TBAI), m-chloroperoxybenzoic acid (mCPBA) as the terminal oxidant, and PhthNH₂ **53** as the nitrenium precursor.²²



Scheme 26

B. Results and Discussion

Table 3: Optimization of Catalytic Aziridination using Styrene



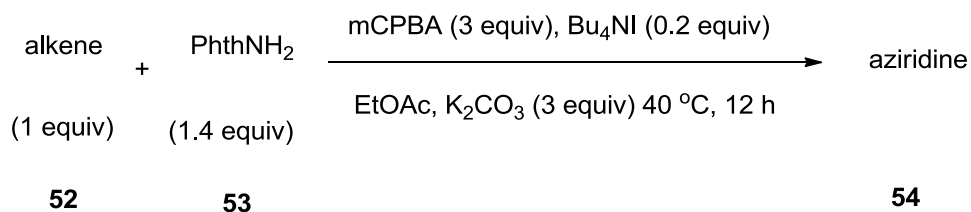
Entry	Time [h]	mCPBA [equiv]	TBAI [equiv]	54 [%] ^[a]
1	4	5	0.5	(62)
2	12	5	0.5	(71)
3	12	5	0.2	64 (69)
4	24	5	0.2	(64)
5	6	3	0.2	70 (72)
6	12	3	0.2	76 (79)
7	24	3	0.2	68 (73)
8	48	3	0.2	61 (63)
9 ^[b]	12	3	0.2	(46)
10	12	2	0.2	(51)
11	12	3	0.1	55 (56)
12	24	3	0.1	55 (59)
13	12	3	0	(<2)

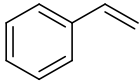
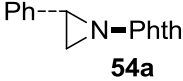
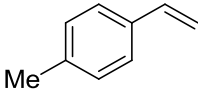
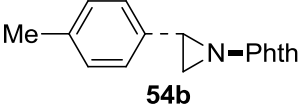
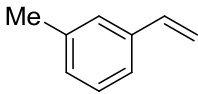
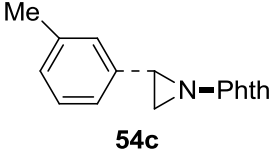
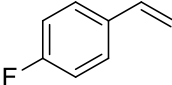
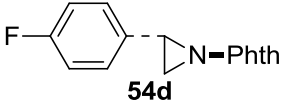
The aziridination of styrene **52** was performed in ethyl acetate at 40 °C for several hours by using styrene **52** (1 equiv), N-aminophthalimide **53** (1.4 equiv), K₂CO₃ (3 equiv), TBAI (0-0.5 equiv), and mCPBA (2-5 equiv). ^[a]Yields of products after isolation by column chromatography; NMR-determined yields are shown in parentheses. ^[b]Reaction was performed at room temperature.

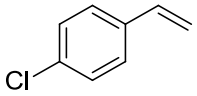
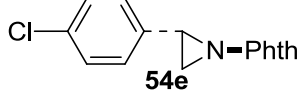
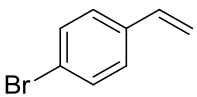
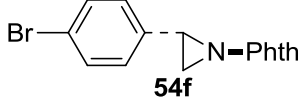
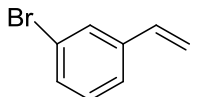
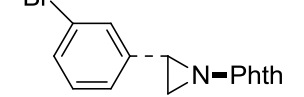
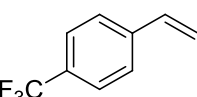
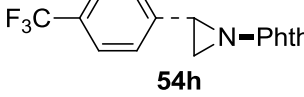
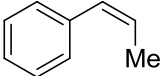
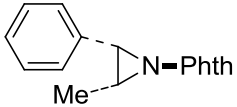
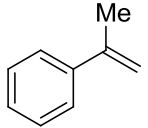
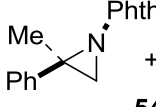
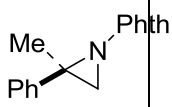
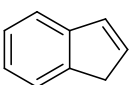
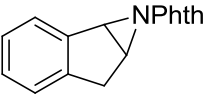
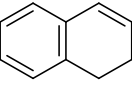
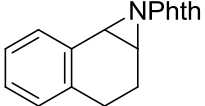

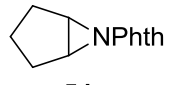
To determine the optimized conditions for the iodine-mediated organocatalytic aziridination reaction, we investigated the reaction of styrene **52** and PhthNH₂ **53** as a nitrenium precursor with a wide range of oxidant (for example, Oxone[®], sodium perborate, and mCPBA) in the presence of iodine-containing precatalysts (aryl iodides, I₂, NaI and Bu₄NI) under different reaction conditions, while using various solvents. Next, we discovered that the addition of TBAI dramatically changed the outcome of this


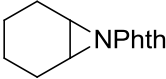
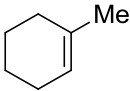
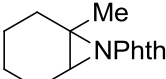

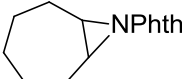

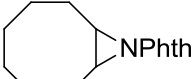


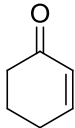
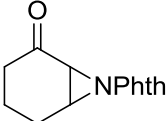
reaction, increasing the yields of aziridine **54** products. Using TBAI at 40 °C under different reaction conditions, we also determined that ethyl acetate was the best solvent. The presence of a base, potassium carbonate, is critically important due to the fact that the aziridine products are unstable under acidic reaction conditions. We also concluded that running this reaction for 12 hours at 40 °C using styrene **52** (1 equiv), N-aminophthalimide **53** (1.4 equiv), K₂CO₃ (3 equiv), TBAI (0.2 equiv), and mCPBA (3 equiv) in ethyl acetate gave the best yield at 76(79) %.

Table 4: Catalytic aziridination of alkenes under optimized reaction conditions



Entry	Alkene 52	Product 54	Yield [%]
1		 54a	76
2		 54b	71
3		 54c	74
4		 54d	80

5		 54e	76
6		 54f	79
7		 54g	77
8		 54h	69
9		 54i	63
10		 +  54j 14 : 86	69
11		 54k	69
12		 54l	69
13		 54m	72

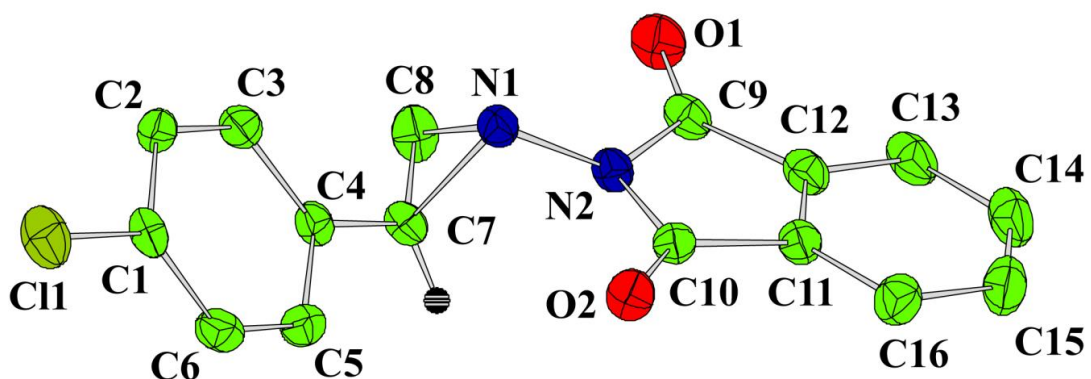
14		 54n	53
15		 54o	44
16		 54p	38
17		 54q	44
18	C_8H_{17} 	C_8H_{17}  54r	32
19		 54s	16

Yields of products were determined after isolation by column chromatography and the ratio of invertomers was determined by 1H HMR spectroscopy.

Once determining the optimized conditions, we investigated the conversion of various substituted alkenes **52** into the respective aziridines **54** (Table 4). It was found that all styrenes with either electron-withdrawing or electron-donating substituents afforded products in good yields (Table 4, entries 1-8). This reaction also gave good yields for α - or β -substituted styrenes (Table 4, entries 9-12). Moderate yields were obtained in the reaction of nonhindered cycloalkenes (Table 4, 13-14), although substituted and seven or

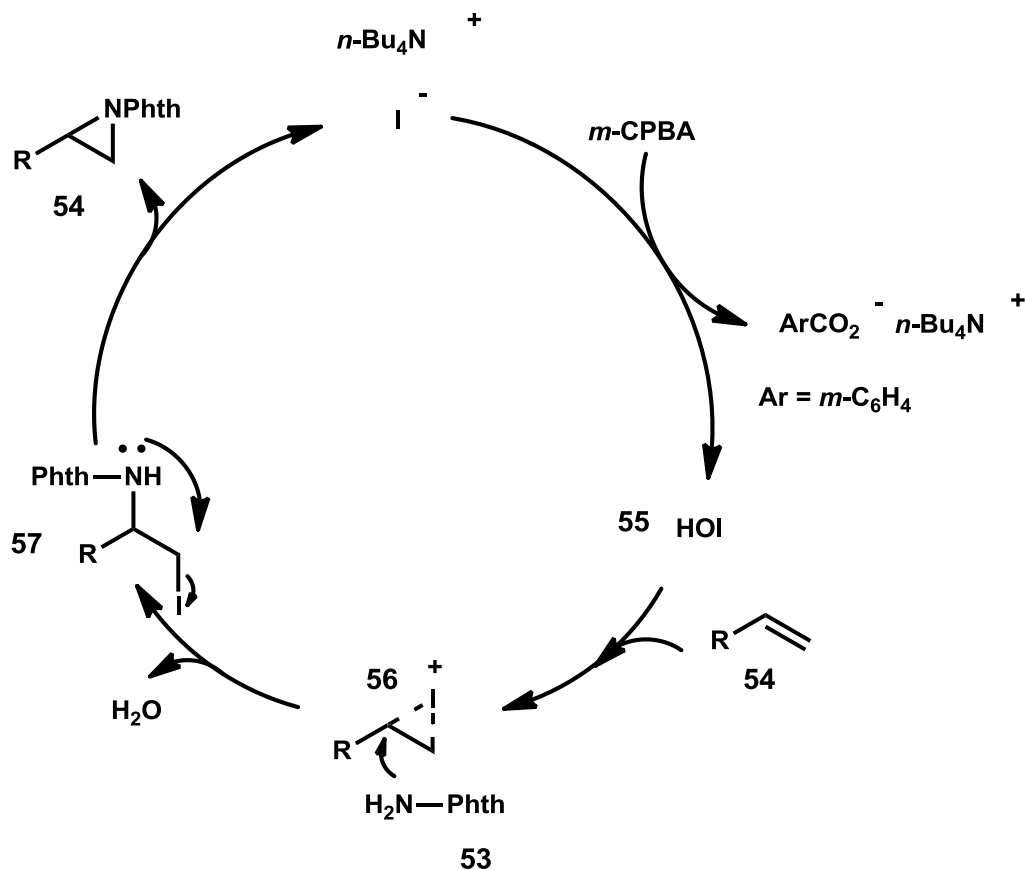
eight membered cycloalkenes (Table 4, 15-17) gave lower yields of aziridines. The overall trend in yields follows the previously reported Cu-catalyzed aziridination reactions of alkenes studies¹¹.

Figure 1: X-ray crystal structure of N-(aminophthalimide)-2-(4-chlorophenyl) aziridine 54e



The structure of the N-(aminophthalimide)-2-(4-chlorophenyl) aziridine **54e** was confirmed by a single crystal X-ray analysis. The single crystal product was obtained by slow crystallization from the ethyl acetate/hexane solution. X-ray diffraction data for **54e** were collected on Rigaku RAPID II Image Plate system using graphite-monochromated MoK α radiation ($\lambda = 0.71073 \text{ \AA}$) at 123 K. The structure was solved by the Patterson method (SHELXS 86) and refined by full-matrix least-squares refinement on F^2 using Crystals for Windows program. The structure in combination with ^1H NMR data, confirms the *trans* configuration of the Phth group and the substituent in the aziridine ring (Table 4, entries 1-8 and 18).

Proposed Reaction Mechanism for the aziridination of alkenes



Scheme 27

To determine the mechanism for this new catalytic aziridination reaction, we ran a series of controlled experiments to help provide valuable insight on the possible intermediates and active species that were generated. Since epoxides could be precursors to aziridines, we ran a controlled experiment and found that epoxides are not intermediates in this reaction. So, we believe that the mechanism of this reaction involves an oxidized iodine species, hypiodous acid **55** (or iodine 3-chlorobenzoate IOCOAr), which is generated in situ from Bu_4NI and $m\text{CPBA}$. This active iodine species then reacts with the alkene **54** to give the iodonium ion **56**, which is then opened at the benzylic position by PhthNH_2 **53**.

This creates β -iodo-N-aminophthalimide **57**, the cyclization of which affords the aziridine **54** product and the regenerated iodide anion that continues the catalytic cycle.

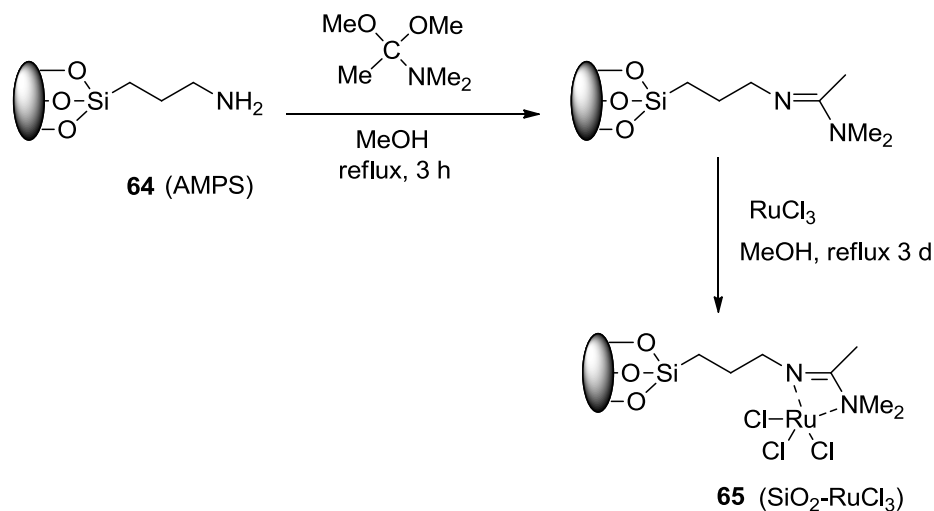
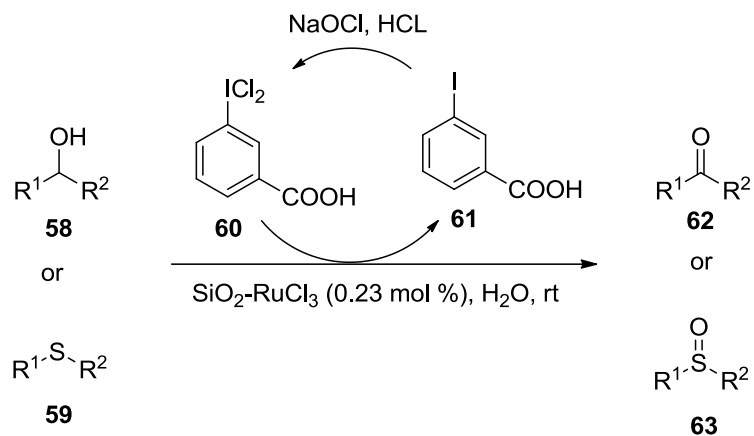
C. Summary

In conclusion, we found a new catalytic aziridination reaction of alkenes that is performed under mild conditions. This is a metal-free catalytic procedure that gives good results for the aziridination of substituted styrenes and some cycloalkenes. We believe the mechanism probably involves in situ generated hypoiodous acid, which is generated from the oxidation of TBAI by mCPBA.

2.3 SiO₂-supported RuCl₃/3-(dichloroiodo)benzoic acid: green catalytic system for the oxidation of alcohols and sulfides in water

A. Introduction

The selective oxidation of sulfides **59** and alcohols **58** into the corresponding sulfoxides **63** and carbonyl **62** compounds is one of the most highly used and important processes for the production of various chemicals and compounds used by many scientist today. However, many of these methods are outdated and rely upon environmentally damaging oxidants, or harmful organic solvents, or require harsh reaction conditions. Hypervalent iodine compounds have been used in organic synthesis for various synthetically useful oxidation transformations and have the advantages of easy handling, mild reaction conditions and low toxicity. Coupling this idea with the fact that ruthenium catalysts and hypervalent iodine reagents are known to be efficient catalytic oxidation systems. Also, silica-supported catalytic metallic species have recently been developed for aqueous media. We have developed a green, recyclable and efficient catalytic oxidative system based on SiO₂-RuCl₃ **65** and 3-(dichloroiodo)benzoic acid **60** for the oxidation of sulfides and alcohols in water.²³



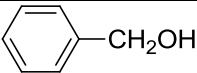
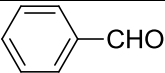
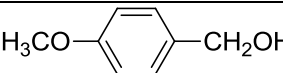
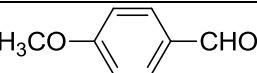
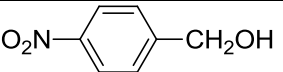
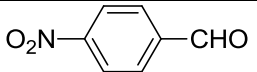
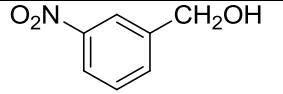
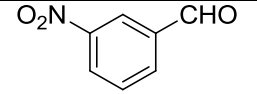
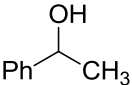
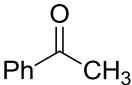
For the synthesis of SiO₂-supported RuCl₃, we started out with commercial aminopropyl silica (AMPS, **64**) and refluxed it with dimethylacetamide in methanol for 3 hours. RuCl₃ was then added and refluxed in methanol for 3 days to create SiO₂-supported RuCl₃ **65**. To test deactivation and recyclability of are catalyst, a series of six consecutive runs were performed. After the first alcohol oxidation, the catalyst, SiO₂-RuCl₃ was separated from the reaction mixture by filtration, thoroughly washed with water, and then reused as the catalyst for the next run. The reaction yields and conversion remained essentially constant for the six successive cycles, which demonstrates that there is no significant

change in the activity of the catalyst, reflecting the high stability and reusability of the SiO₂-RuCl₃ catalyst.

Another important aspect of this procedure is the recyclability of 3-(dichloroiodo)benzoic acid from the reduced form 3-iodobenzoic acid. This reagent can easily be separated from the reaction mixture and converted back into 3-(dichloroiodo)benzoic acid by treatment with NaOCl and aqueous HCl in about 90% overall yield.

B. Results and Discussion

Table 5: SiO₂-RuCl₃ catalyzed oxidation of organic substrates using 3-(dichloroiodo)benzoic acid

Entry	Substrate	Product	Time/h	Conversion (%)	Yield (%)
1			0.75	100	99
2			2.5	100	95
3			2.5	100	99
4			12	>99	93
5			2	100	99

6			3.5	>99	96
7			2.5	100	99
8			5	100	99
9			2.5	100	86
10			18	17	17
11	<i>n</i> -C ₇ H ₁₅ CH ₂ OH	<i>n</i> -C ₇ H ₁₅ CHO	24	0	-
12			3	>99	74
					26
13			4.5	100	99
14			1.5	100	98
15			0.75	100	99

General oxidation procedure: to a suspension of alcohol **58** or **59** sulfide (0.2 mmol) and 3-(dichloriodo)benzoic acid **60** (96 mg, 0.3 mmol) in 2 ml of water, SiO₂-RuCl₃ (10 mg, 0.23 mol%) was added while stirring at room temperature. The reaction mixture was stirred until consumption of starting material **58** or **59** (monitored by TLC and GC-MS),

then 2 ml of saturated aqueous NaHCO_3 was added and the mixture was stirred for 15-30 min. The solid ($\text{SiO}_2\text{-RuCl}_3$) was filtered, washed with EtOAc (1 ml x 3) and collected for the next run. The filtrate was extracted with EtOAc (3 ml x 3) dried over Na_2SO_4 . The organic layer was concentrated to recover the respective product of oxidation **62** or **63**.

Using the $\text{SiO}_2\text{-RuCl}_3/3\text{-(dichloroiodo)benzoic acid}$ catalyzed oxidation, we found that primary benzylic alcohols **58** were selectively oxidized to the corresponding aldehydes **62** with nearly 100% conversion, and in excellent yields (90-99%), after 2-3 hours (Table 5, entries 1-3) or 12 h (entry 4). Secondary benzylic alcohols and alicyclic alcohols were converted to the respective ketones (entries 5-9) but primary alcohols were less reactive, phenyl acetaldehyde was obtained in 17% (entry 10), while 1-octanol didn't show any measurable conversion even after 24 hours (entry 11). The oxidation of a glycol, 1-phenyl-1,2-ethanediol (entry 12), resulted in a partial C-C bond cleavage and afforded a mixture of benzaldehyde (74% yield) and 2-hydroxy-1-phenylethan-1-one (26% yield). The $\text{SiO}_2\text{-RuCl}_3/3\text{-(dichloroiodo)benzoic acid}$ catalyzed system was also used for the oxidation of sulfides **59** to sulfoxides **63** in excellent yields (entry 14-15) and oxidize indane to indanone in good yield after 4.5 hours (entry 13).

C. Summary

In conclusion, we have developed a green, recyclable and efficient catalytic oxidative system based on SiO_2 -supported RuCl_3 and 3-(dichloroiodo)benzoic acid for the oxidation of alcohols and sulfides in water. Do to the mild reaction conditions, high yields of products, ease of work-up, clean procedure, and excellent chemoselectivity make this method potentially attractive for the oxidation of organic compound in industrial settings.

CHAPTER 3

EXPERIMENTAL

3.1: Hofmann Rearrangement of Carboxamides with Catalytic Hypervalent Iodine with Oxone[®] as Terminal Oxidant

1. General experimental remarks

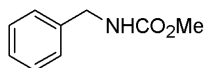
All reactions were performed under dry nitrogen atmosphere with flame-dried glassware. All commercial reagents were ACS reagent grade and used without further purification. Dichloromethane was distilled from CaH₂ immediately prior to use. Diethyl ether was distilled from Na/benzophenone. All commercial reagents were ACS reagent grade and used without further purification. Melting points were determined in an open capillary tube with a Mel-temp II melting point apparatus. Infrared spectra were recorded as a KBr pellet on a Perkin-Elmer 1600 series FT-IR spectrophotometer. NMR spectra were recorded on a Varian Inova 500 MHz NMR spectrometer at 500 MHz (¹H NMR) and 125 MHz (¹³C NMR). Chemical shifts are reported in parts per million (ppm). ¹H and ¹³C chemical shifts are referenced relative to the tetramethylsilane. GC-MS analysis was carried out with a HP 5890A Gas Chromatograph using a 5970 Series mass selective detector. Microanalyses were carried out by Atlantic Microlab, Inc., Norcross, Georgia.

2. General Procedure

To a solution of amide (0.25 mmol) in mixture solvent of MeOH (0.75 mL), HFIP (0.75 mL), and H₂O (0.075 mL) were added Oxone[®] (0.75 mmol), and PhI (0.05 mmol). The reaction was stirred at 40 °C for several hours. After reaction, the mixture was filtrated and washed with CH₂Cl₂ then added 5% Na₂S₂O₃ (5 mL) and extracted with

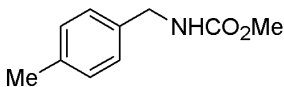
dichloromethane. The organic phase was dried over anhydrous Na₂SO₄ and concentrated. Purification by preparative TLC (hexane-ethyl acetate = 2 : 1 or 3 : 1) to afford analytically pure carbamates .

Methyl *N*-benzylcarbamate **48a**



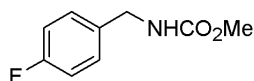
Reaction of 2-phenylacetamide **47a** (34 mg, 0.25 mmol) according to general procedure afforded 40 mg (96%) of product **48a**, isolated as colorless needles (recrystallized from dichloromethane-hexane) mp 62.2-62.9 °C (lit.¹², mp 63-65 °C); ¹H NMR (500 MHz, CDCl₃): δ 7.37 (t, *J* = 7.8 Hz, 2H), 7.31-7.25 (m, 3H), 4.98 (br s, 1H), 4.37 (d, *J* = 5.5 Hz, 2H), 3.70 (s, 3H).

Methyl *N*-(4-methylbenzyl)carbamate **48b**



Reaction of 2-(*p*-tolyl)acetamide **47b** (37 mg, 0.075 mmol) according to general procedure afforded 43 mg (96%) of product **48b**, isolated as colorless needles (recrystallized from dichloromethane-hexane) mp 71.5-72.2 °C (lit.¹², mp 68-70 °C); ¹H NMR (500 MHz, CDCl₃): δ 7.18 (d, *J* = 7.5 Hz, 2H), 7.14 (d, *J* = 7.5 Hz, 2H), 4.92 (br s, 1H), 4.33 (d, *J* = 5.5 Hz, 2H), 3.7 (s, 3H), 2.34 (s, 3H).

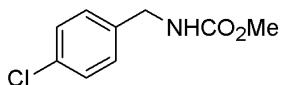
Methyl *N*-(4-fluorobenzyl)carbamate **48c**



Reaction of 2-(*p*-fluoro)phenylacetamide **47c** (38 mg, 0.25 mmol) according to general procedure afforded 39 mg (86%) of product **48c**, isolated as colorless needles

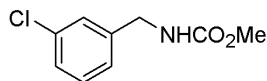
(recrystallized from dichloromethane-hexane) mp 70.7-71.2 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.30-7.21 (m, 2H), 7.25-6.98 (m, 2H), 5.09 (br s, 1H), 4.32 (d, *J* = 5.5 Hz, 2H), 3.69 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 162.4 (d, *J*_{CF} = 245.9 Hz), 157.3, 134.6, 129.4 (d, ³*J*_{CF} = 245.9 Hz), 115.7 (d, ²*J*_{CF} = 21.6 Hz), 52.5, 44.6.

Methyl *N*-(4-chlorobenzyl)carbamate **48d**



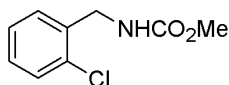
Reaction of 2-(*p*-chloro)phenylacetamide **47d** (42 mg, 0.25 mmol) according to general procedure afforded 46 mg (93%) of product **48d**, isolated as colorless needles (recrystallized from dichloromethane-hexane) mp 80.9-81.6 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.30 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.09 (br s, 1H), 4.33 (d, *J* = 5.5 Hz, 2H), 3.7 (s, 3H).

Methyl *N*-(3-chlorobenzyl)carbamate **48e**



Reaction of 2-(*m*-chloro)phenylacetamide **47e** (42 mg, 0.25 mmol) according to general procedure afforded 43 mg (86%) of product **48e**, isolated as colorless oil; ¹H NMR (500 MHz, CDCl₃): δ 7.30-7.22 (m, 3H), 7.16 (d, *J* = 6.0 Hz, 1H), 5.12 (br s, 1H), 4.34 (d, *J* = 5.5 Hz, 2H), 3.70 (s, 3H).

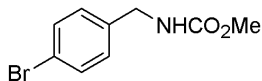
Methyl *N*-(2-chlorobenzyl)carbamate **48f**



Reaction of 2-(*o*-chloro)phenylacetamide **47f** (42 mg, 0.25 mmol) according to general procedure afforded 44 mg (88%) of product **48f**, isolated as colorless oil; ¹H NMR (500

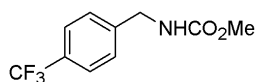
MHz, CDCl₃): δ 7.42-7.33 (m, 2H), 7.26-7.20 (m, 2H), 5.24 (br s, 1H), 4.44 (d, J = 6.5 Hz, 2H), 3.68 (s, 3H).

Methyl *N*-(4-bromobenzyl)carbamate **48g**



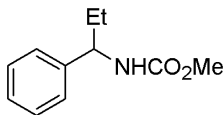
Reaction of 2-(*p*-bromo)phenylacetamide **47g** (54 mg, 0.25 mmol) according to general procedure afforded 52 mg (85%) of product **48g**, isolated as colorless needles (recrystallized from dichloromethane-hexane) mp 93.7-94.4 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.45 (d, J = 8.3 Hz, 2H), 7.16 (d, J = 8.3 Hz, 2H), 5.09 (br s, 1H), 4.31 (d, J = 6.0 Hz, 2H), 3.69 (s, 3H).

Methyl *N*-(4-trifluoromethylbenzyl)carbamate **48h**



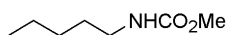
Reaction of 2-(*p*-trifluoro)phenylacetamide **47h** (51 mg, 0.25 mmol) according to general procedure afforded 45 mg (78%) of product **48h**, isolated as colorless needles (recrystallized from dichloromethane-hexane) mp 88.5-89.2 °C; ¹H NMR (500 MHz, CDCl₃): δ 7.58 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 5.22 (br s, 1H), 4.42 (d, J = 6.0 Hz, 2H), 3.70 (s, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 157.4, 143.0, 130.0 (d, ² J_{CF} = 32.6 Hz), 127.8, 125.8 (d, ³ J_{CF} = 3.9 Hz), 124.3 (q, J_{CF} = 272.1 Hz), 52.6, 44.8.

Methyl *N*-(1-phenylpropyl)carbamate **48i**



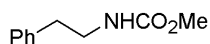
Reaction of 2-phenylbutanamide **47i** (41 mg, 0.25 mmol) according to general procedure afforded 46 mg (96%) of product **48i**, isolated as a light brown oil; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.35 (t, $J = 7.5$ Hz, 2H), 7.32-7.28 (m, 3H), 5.11 (br s, 1H), 4.68-4.54 (m, 1H), 3.66 (s, 3H), 1.92-1.72 (m, 2H), 0.92 (t, $J = 7.5$ Hz, 3H).

Methyl *N*-pentylcarbamate **48j**



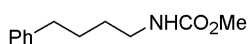
Reaction of hexanamide **47j** (29 mg, 0.25 mmol) according to general procedure afforded 33 mg (92%) of product **48j**, isolated as a colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 4.62 (br s, 1H), 3.66 (s, 3H), 3.22-3.06 (m, 2H), 1.49 (quint, $J = 7.0$ Hz, 2H), 1.38-1.24 (m, 4H), 0.90 (t, $J = 7.0$ Hz, 3H).

Methyl *N*-(2-phenylethyl)carbamate **48k**.



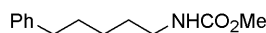
Reaction of 2-phenylethylamide **47k** (37 mg, 0.25 mmol) according to general procedure afforded 41 mg (91%) of product **48k**, colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.31 (t, $J = 7.5$ Hz, 2H), 7.22 (t, $J = 7.5$ Hz, 1H), 7.19 (t, $J = 7.5$ Hz, 2H), 4.74 (br s, 1H), 3.65 (s, 3H), 3.52-3.34 (m, 2H), 2.81 (t, $J = 6.3$ Hz, 2H).

Methyl *N*-(2-phenylbutyl)carbamate **48l**.



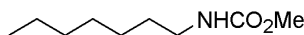
Reaction of 2-phenylbutylamide **47l** (44 mg, 0.25 mmol) according to general procedure afforded 44 mg (85%) of product **48l**, colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.27 (t, $J = 7.5$ Hz, 2H), 7.22-7.14 (m, 3H), 4.68 (br s, 1H), 3.65 (s, 3H), 3.24-3.10 (m, 2H), 2.62 (t, $J = 7.3$ Hz, 2H), 1.64 (quint, $J = 7.3$ Hz, 2H), 1.52 (quint, $J = 7.3$ Hz, 2H).

Methyl *N*-(2-phenylpentyl)carbamate **48m**.



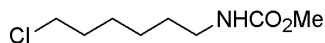
Reaction of 2-phenylpentylamide **47m** (46 mg, 0.25 mmol) according to general procedure afforded 46 mg (84%) of product **48m**, colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 7.27 (t, $J = 7.5$ Hz, 2H), 7.20-7.14 (m, 3H), 4.69 (br s, 1H), 3.65 (s, 3H), 3.20-3.06 (m, 2H), 2.61 (t, $J = 7.5$ Hz, 2H), 1.68-1.59 (m, 2H), 1.56-1.47 (m, 2H), 1.35 (quint, $J = 7.5$ Hz, 2H).

Methyl *N*-heptylcarbamate **48n**



Reaction of octylamide **47n** (36 mg, 0.25 mmol) according to general procedure afforded 37 mg (86%) of product **48n**, isolated as a colorless oil; $^1\text{H NMR}$ (500 MHz, CDCl_3): δ 4.70 (br s, 1H), 3.66 (s, 3H), 3.24-3.08 (m, 2H), 1.55-1.44 (m, 2H), 1.38-1.21 (m, 8H), 0.88 (t, $J = 6.8$ Hz, 3H).

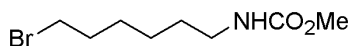
Methyl *N*-(1-chloro)hexylcarbamate **48o**



Reaction of 1-chlorohexanamide **47o** (41 mg, 0.25 mmol) according to general procedure afforded 41 mg (85%) of product **48o**, isolated as a colorless oil; $^1\text{H NMR}$ (500 MHz,

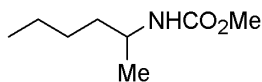
CDCl₃): δ 4.64 (br s, 1H), 3.66 (s, 3H), 3.53 (t, $J = 6.5$ Hz, 2H), 3.18 (q, $J = 6.5$ Hz, 2H), 1.78 (quint, $J = 7.5$ Hz, 2H), 1.56-1.42 (m, 2H), 1.39-1.30 (m, 2H).

Methyl *N*-(1-bromo)hexylcarbamate **48p**



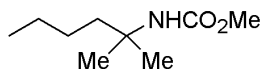
Reaction of 1-bromohexanamide **47p** (52 mg, 0.25 mmol) according to general procedure afforded 47 mg (78%) of product **48p**, isolated as a colorless oil; ¹H NMR (500 MHz, CDCl₃): δ 4.70 (br s, 1H), 3.66 (s, 3H), 3.41 (t, $J = 7$ Hz, 2H), 3.18 (q, $J = 6.3$ Hz, 2H), 1.86 (quint, $J = 7$ Hz, 2H), 1.57-1.41 (m, 4H), 1.39-1.31 (m, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 157.3, 52.2, 41.1, 34.0, 32.9, 30.1, 28.0, 26.1.

Methyl *N*-(1-methyl)pentylcarbamate **48q**



Reaction of 1-methylhexanamide **47q** (32mg, 0.25 mmol) according to general procedure afforded 29 mg (73%) of product **48q**, isolated as a colorless oil; ¹H NMR (500 MHz, CDCl₃): δ 4.47 (br s, 1H), 3.65 (s, 3H), 1.46-1.24 (m, 7H), 1.13 (d, $J = 6.5$ Hz, 3H), 0.90 (t, $J = 6.3$ Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 156.5, 51.8, 47.1, 36.9, 28.1, 22.6, 21.3, 14.0.

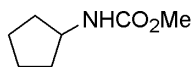
Methyl *N*-(1,1-dimethyl)butylcarbamate **48r**



Reaction of 1,1-dimethylpentanamide **47r** (36 mg, 0.25 mmol) according to general procedure afforded 30 mg (70%) of product **48r**, isolated as a colorless oil; ¹H NMR (500 MHz, CDCl₃): δ 4.54 (br s, 1H), 3.61 (s, 3H), 1.64-1.56 (m, 2H), 1.35-1.20 (m, 4H), 1.27

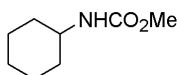
(s, 6H), 0.90 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 155.3, 52.7, 51.4, 40.6, 27.0, 26.3, 23.1, 14.1.

Methyl *N*-cyclopentylcarbamate **48s**



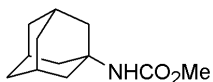
Reaction of cyclopentanecarboxamide **47s** (30 mg, 0.25 mmol) according to general procedure afforded 30 mg (83%) of product **48s**, isolated as colorless oil; ^1H NMR (500 MHz, CDCl_3): δ 4.63 (br s, 1H), 3.97 (br s, 1H), 3.65 (s, 3H), 2.02-1.88 (m, 2H), 1.71-1.53 (m, 4H), 1.44-1.32 (m, 2H).

Methyl *N*-cyclohexylcarbamate **48t**



Reaction of cyclohexanecarboxamide **47t** (32 mg, 0.25 mmol) according to general procedure afforded 36 mg (92%) of product **48t**, isolated as colorless needles (recrystallized from dichloromethane-hexane) mp 74.6-75.2 °C (lit.¹², mp 73.5-74.5 °C); ^1H NMR (500 MHz, CDCl_3): δ 4.53 (br s, 1H), 3.65 (s, 3H), 3.48 (br s, 1H), 1.98-1.86 (m, 2H), 1.75-1.65 (m, 2H), 1.64-1.56 (m, 1H), 1.4-1.28 (m, 2H), 1.22-1.06 (m, 3H).

Methyl *N*-(1-adamantanyl)carbamate **48u**



Reaction of 1-adamantanecarboxamide **47u** (45 mg, 0.25 mmol) according to general procedure afforded 51 mg (98%) of product **48u**, isolated as colorless needles (recrystallized from dichloromethane-hexane) mp 118.4-118.9 °C (lit.¹¹, mp 118-120 °C);

^1H NMR (500 MHz, CDCl_3): δ 4.51 (br s, 1H), 3.61 (s, 3H), 2.08 (s, 3H), 1.93 (s, 6H), 1.67 (s, 6H).

3.2 Hypiodite-Mediated Metal-Free Catalytic Aziridination of Alkenes

1. General experimental remarks

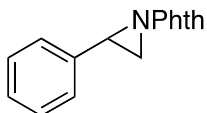
All reactions were performed under dry nitrogen atmosphere with flame-dried glassware. All commercial reagents were ACS reagent grade and used without further purification. Dichloromethane was distilled from CaH_2 immediately prior to use. Ethyl acetate was distilled from CaSO_4 . All commercial reagents were ACS reagent grade and used without further purification. Melting points were determined in an open capillary tube with a Mel-temp II[®] melting point apparatus. Infrared spectra were recorded as a KBr pellet on a Perkin-Elmer 1600 series FT-IR spectrophotometer. NMR spectra were recorded on a Varian^{UNITY} INOVA 500 MHz NMR spectrometer at 500 MHz (^1H NMR) and 125 MHz (^{13}C NMR). Chemical shifts are reported in parts per million (ppm). ^1H and ^{13}C chemical shifts are referenced relative to the tetramethylsilane. GC-MS analysis was carried out with a HP 5890A Gas Chromatograph using a 5970 Series mass selective detector. Microanalyses were carried out by Atlantic Microlab, Inc., Norcross, Georgia.

2. General procedure for tetrabutylammonium iodide-mediated catalytic aziridination of alkenes.

To a solution of N-aminophthalimide (0.175 mmol) in 1.5 mL of AcOEt were added *m*-CPBA (0.375 mmol), K_2CO_3 (0.375 mmol), alkene (0.125 mmol), and tetrabutylammonium iodide (0.025 mmol). The reaction was stirred at 40 °C for 12 h. The mixture was poured into

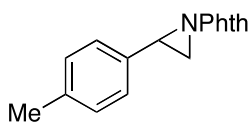
saturated aqueous NaHCO₃ (5 mL) and extracted with dichloromethane, then the organic phase was dried over anhydrous Na₂SO₄ and concentrated. Purification by column chromatography gave aziridine.

***N*-(aminophthalimide)-2-phenylaziridine 54a**



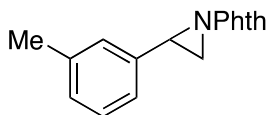
Reaction of styrene **52a** (0.125 mmol) according to the general procedure afforded 25 mg (76%) of product **54a**, isolated as a yellow solid: light colorless needles (recrystallized from dichloromethane-hexane); mp 149.4-150.3 °C (lit.¹, mp 150 °C); IR (KBr) cm⁻¹ 3029, 1716, 1377, 1162, 703; ¹H NMR (500 MHz, CDCl₃) δ 7.82-7.77 (m, 2H), 7.73-7.67 (m, 2H), 7.46 (d, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 3.61 (dd, *J* = 7.7, 6.0 Hz, 1H), 2.90 (dd, *J* = 7.7, 2.5 Hz, 1H), 2.81 (dd, *J* = 6.0, 2.5 Hz, 1H).

***N*-(aminophthalimide)-2-*p*-methyl-phenylaziridine 54b**



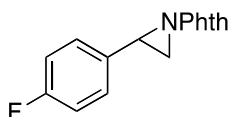
Reaction of *p*-methylstyrene **52b** (0.125 mmol) according to the general procedure afforded 25 mg (71%) of product **54b**, isolated as a white solid: light yellow needles (recrystallized from dichloromethane-hexane); mp 120.2-121.6 °C; IR (KBr) cm⁻¹ 3067, 2933, 1718, 1375, 1153, 708; ¹H NMR (500 MHz, CDCl₃) δ 7.82-7.76 (m, 2H), 7.72-7.66 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 3.42 (dd, *J* = 7.8, 5.9 Hz, 1H), 2.86 (dd, *J* = 7.8, 2.4 Hz, 1H), 2.78 (dd, *J* = 5.9, 2.4 Hz, 1H), 2.36 (s, 3H).

***N*-(aminophthalimide)-2-*m*-methyl-phenylaziridine 54c**



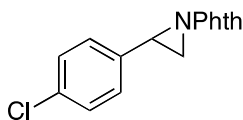
Reaction of *m*-methylstyrene **52c** (0.125 mmol) according to the general procedure afforded 26 mg (74%) of product **54c**, isolated as a white solid: light yellow needles (recrystallized from dichloromethane-hexane); mp 106.6-107.3 °C; IR (KBr) cm^{-1} 3107, 2933, 1718, 1377, 1164, 703; ^1H NMR (500 MHz, CDCl_3) δ 7.82-7.76 (m, 2H), 7.72-7.66 (m, 2H), 7.32-7.21 (m, 3H), 7.14 (d, $J = 7.0$ Hz, 1H), 3.58 (dd, $J = 7.5, 6.0$ Hz, 1H), 2.87 (dd, $J = 7.5, 2.5$ Hz, 1H), 2.79 (dd, $J = 6.0, 2.5$ Hz, 1H), 2.37 (s, 3H).

***N*-(aminophthalimide)-2-*p*-fluoro-phenylaziridine 54d**



Reaction of *p*-fluorostyrene **52d** (0.125 mmol) according to the general procedure afforded 28 mg (80%) of product **54d**, isolated as a yellow solid: colorless needles (recrystallized from dichloromethane-hexane); mp 140.5-141.3 °C; IR (KBr) cm^{-1} 3107, 1706, 1381, 1217, 1169, 709; ^1H NMR (500 MHz, CDCl_3) δ 7.83-7.76 (m, 2H), 7.74-7.67 (m, 2H), 7.49-7.42 (m, 2H), 7.11-7.03 (m, 2H), 3.58 (dd, $J = 8.0, 6.0$ Hz, 1H), 2.89 (dd, $J = 8.0, 2.5$ Hz, 1H), 2.77 (dd, $J = 6.0, 2.5$ Hz, 1H).

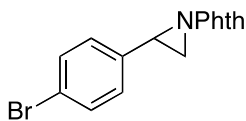
***N*-(aminophthalimide)-2-*p*-chloro-phenylaziridine 54e**



Reaction of *p*-chlorostyrene **52e** (0.125 mmol) according to the general procedure afforded 28 mg (76%) of product **54e**, isolated as a white solid: colorless blocks (recrystallized from dichloromethane-hexane); mp 153.8-154.9 °C; IR (KBr) cm^{-1} 3083, 1711, 1377, 1158, 1087, 709; ^1H NMR (500 MHz, CDCl_3) δ 7.82-7.76 (m, 2H), 7.73-7.67 (m, 2H), 7.40 (d, $J = 8.3$ Hz, 2H), 7.34 (d, $J = 8.3$ Hz, 2H), 3.57 (dd, $J = 7.8, 6.0$ Hz, 1H), 2.90 (dd, $J = 7.8, 2.5$ Hz, 1H), 2.74 (dd, $J = 6.0, 2.5$ Hz, 1H).

Single crystals of product **52e** suitable for X-ray crystallographic analysis were obtained by slow crystallization from the ethyl acetate/hexane solution. X-ray diffraction data for **54e** were collected on Rigaku RAPID II Image Plate system using graphite-monochromated $\text{MoK}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$) at 123 K. The structure was solved by the Patterson method (SHELXS 86) and refined by full-matrix least-squares refinement on F^2 using Crystals for Windows program. Crystal data for **54e** $\text{C}_{16}\text{H}_{11}\text{Cl}_1\text{N}_2\text{O}_2$: M 298.73, monoclinic, space group $P21/c$, $a = 14.6272(10)$, $b = 12.0531(5)$, $c = 7.7086(3) \text{ \AA}$, $\alpha = 90.00$, $\beta = 98.916(7)$, $\gamma = 90.00$ °, $V = 1342.63(12) \text{ \AA}^3$, $Z = 4$, $\mu = 0.290 \text{ mm}^{-1}$, 8845 reflections measured, 3053 unique; final $R_1 = 0.0408$, $R_w = 0.0797$. CCDC-882832.

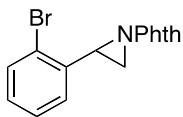
***N*-(aminophthalimide)-2-*p*-bromo-phenylaziridine 54f**



Reaction of *p*-bromostyrene **52f** (0.125 mmol) according to the general procedure afforded 34 mg (79%) of product **54f**, isolated as a white solid: light yellow needles (recrystallized from dichloromethane-hexane); mp 142.6-144.0 °C; IR (KBr) cm^{-1} 3095, 1709, 1383, 1167, 710; ^1H NMR (500 MHz, CDCl_3) δ 7.83-7.77 (m, 2H), 7.73-7.67 (m, 2H), 7.50 (d, $J = 8.0$

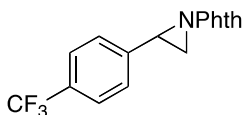
Hz, 2H), 7.34 (d, $J = 8.0$ Hz, 2H), 3.55 (dd, $J = 7.9, 5.8$ Hz, 1H), 2.91 (dd, $J = 7.9, 2.4$ Hz, 1H), 2.74 (dd, $J = 5.8, 2.4$ Hz, 1H).

***N*-(aminophthalimide)-2-*o*-bromo-phenylaziridine 54g**



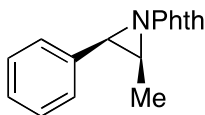
Reaction of *o*-bromostyrene **52g** (0.125 mmol) according to the general procedure afforded 33 mg (77%) of product **54g**, isolated as a white solid: light yellow needles (recrystallized from dichloromethane-hexane); mp 141.7-142.5 °C; IR (KBr) cm^{-1} 3024, 1731, 1378, 1164, 708; ^1H NMR (500 MHz, CDCl_3) δ 7.82-7.77 (m, 2H), 7.74-7.67 (m, 2H), 7.59 (d, $J = 8.0$ Hz, 1H), 7.56 (d, $J = 8.0$ Hz, 1H), 7.37-7.30 (m, 1H), 7.22-7.14 (m, 1H), 3.80 (dd, $J = 7.8, 5.8$ Hz, 1H), 3.05 (dd, $J = 7.8, 2.0$ Hz, 1H), 2.55 (dd, $J = 5.8, 2.0$ Hz, 1H).

***N*-(aminophthalimide)-2-*p*-trifluoromethyl-phenylaziridine 54h**



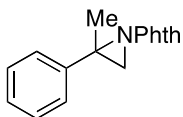
Reaction of *p*-trifluoromethylstyrene **52h** (0.125 mmol) according to the general procedure afforded 29 mg (69%) of product **54h**, isolated as a white solid: colorless needles (recrystallized from dichloromethane-hexane); mp 142.9-143.5; IR (KBr) cm^{-1} 3105, 1714, 1335, 1177, 701; ^1H NMR (500 MHz, CDCl_3) δ 7.83-7.77 (m, 2H), 7.75-7.68 (m, 2H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.57 (d, $J = 8.0$ Hz, 2H), 3.64 (dd, $J = 7.8, 5.8$ Hz, 1H), 2.96 (dd, $J = 7.8, 1.9$ Hz, 1H), 2.76 (dd, $J = 5.8, 1.9$ Hz, 1H).

***Cis-N*-(aminophthalimide)-2-methyl-3-phenylaziridine 54i**



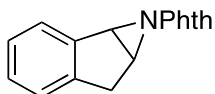
Reaction of *cis*- β -methylstyrene **52i** (0.125 mmol) according to the general procedure afforded 22 mg (63%) of product **54i**, isolated as a yellow solid: light yellow blocks (recrystallized from dichloromethane-hexane); mp 73.2-73.8 °C; IR (KBr) cm^{-1} 3138, 2933, 1706, 1383, 1158, 718; ^1H NMR (500 MHz, CDCl_3) δ 7.81-7.76 (m, 2H), 7.72-7.66 (m, 2H), 7.50 (d, $J = 7.5$ Hz, 2H), 7.38 (d, $J = 8.0$ Hz, 2H), 7.33-7.28 (m, 1H), 3.75 (d, $J = 8.0$ Hz, 1H), 2.99 (dq, $J = 8.0, 6.0$ Hz, 1H), 1.26 (d, $J = 6.0$ Hz, 3H).

***N*-(aminophthalimide)-2-methyl-2-phenylaziridine 54j**



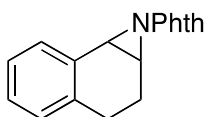
Reaction of α -methylstyrene **52j** (0.125 mmol) according to the general procedure afforded 24 mg (69%; *cis* : *trans* = 14 : 86) of product **54j**, isolated as a yellow solid: IR (neat) cm^{-1} 3072, 2926, 1716, 1375, 1160, 710; ^1H NMR (500 MHz, CDCl_3) δ 7.85-7.80 (m, 2H, *trans*), 7.75-7.66 (m, 4H, *trans*), 7.61-7.53 (m, 4H, *cis*), 7.42 (t, $J = 7.5$ Hz, 2H, *cis*), 7.39 (t, $J = 7.5$ Hz, 1H, *trans*), 7.30 (t, $J = 7.5$ Hz, 1H, *trans*), 7.24-7.15 (m, 3H, *cis*), 4.26 (d, $J = 3.8$ Hz, 1H, *cis*), 3.13 (d, $J = 2.5$ Hz, 1H, *trans*), 2.88 (d, $J = 2.5$ Hz, 1H, *trans*), 2.69 (d, $J = 3.8$ Hz, 1H, *cis*), 1.84 (s, 3H, *cis*), 1.64 (s, 3H, *trans*).

1-Aminophthalimide-2-6,6a-dihydroindeno[1,2-b]aziridine 54k



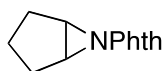
Reaction of indene **52k** (0.125 mmol) according to the general procedure afforded 24 mg (69%) of product **54k**, isolated as a yellow solid: colorless needles (recrystallized from dichloromethane-hexane); mp 157.3-158.2 (lit.⁷, mp 187-188 °C); IR (KBr) cm^{-1} 3110, 2943, 1709, 1379, 1141, 705; ^1H NMR (500 MHz, CDCl_3) δ 7.82-7.76 (m, 2H), 7.73-7.67 (m, 3H), 7.39-7.22 (m, 3H), 4.17 (d, $J = 5.0$ Hz, 1H), 3.78 (t, $J = 5.0$ Hz, 1H), 3.50 (d, $J = 18.0$ Hz, 1H), 3.29 (dd, $J = 18.0, 5.0$ Hz, 1H).

1-Aminophthalimide-2-1a,2,3,7b-tetrahydro-1*H*-naphtho[1,2-*b*]aziridine **54l**



Reaction of 1,2-dihydronaphthalene **52l** (0.125 mmol) according to the general procedure afforded 25 mg (69%) of product **54l**, isolated as a yellow solid: amorphous; IR (neat) cm^{-1} 3047, 2927, 1715, 1377, 1149, 709; ^1H NMR (500 MHz, CDCl_3) δ 7.82-7.76 (m, 2H), 7.73-7.65 (m, 2H), 7.64-7.58 (m, 2H), 7.30-7.20 (m, 2H), 7.14-7.08 (m, 1H), 3.56 (d, $J = 7.5$ Hz, 1H), 3.38 (d, $J = 7.5$ Hz, 1H), 2.96-2.84 (m, 1H), 2.80-2.70 (m, 1H), 2.69-2.60 (m, 1H), 1.88-1.76 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 165.3, 136.2, 134.0, 131.3, 130.5, 130.0, 128.6, 128.1, 126.4, 123.0, 46.3, 45.6, 25.3, 19.8.

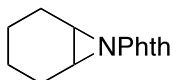
N-(aminophthalimide)-6-azabicyclo[3.1.0]hexane **54m**



Reaction of cyclopentene **52m** (0.125 mmol) according to the general procedure afforded 21 mg (72%) of product **54m**, isolated as a yellow oil: light yellow needles (recrystallized from dichloromethane-hexane); mp 123.8-124.2 °C (lit.⁸, mp 119-126 °C); IR (KBr) cm^{-1} 2957,

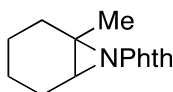
1708, 1383, 1144, 715; ^1H NMR (500 MHz, CDCl_3) δ 7.78-7.73 (m, 2H), 7.69-7.63 (m, 2H), 3.16 (s, 2H), 2.33 (dd, $J = 13.5, 8.5$ Hz, 2H), 1.84-1.73 (m, 2H), 1.68-1.56 (m, 1H), 1.47-1.34 (m, 1H).

***N*-(aminophthalimide)-7-azabicyclo[4.1.0]heptane 54n**



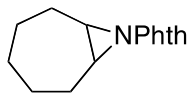
Reaction of cyclohexene **52n** (0.125 mmol) according to the general procedure afforded 16 mg (53%) of product **54n**, isolated as a yellow oil: colorless needles (recrystallized from dichloromethane-hexane); mp 130.8-131.2 °C (lit.⁸, mp 132-133 °C); IR (KBr) cm^{-1} 2919, 1714, 1402, 1150, 715; ^1H NMR (500 MHz, CDCl_3) δ 7.76-7.72 (m, 2H), 7.69-7.63 (m, 2H), 2.78-2.70 (m, 2H), 2.32-2.21 (m, 2H), 2.02-1.92 (m, 2H), 1.49-1.36 (m, 2H), 1.36-1.20 (m, 2H).

***N*-(aminophthalimide)-1-methyl-7-azabicyclo[4.1.0]heptane 54o**



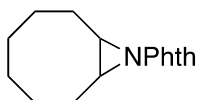
Reaction of 1-methyl-cyclohexene **52o** (0.125 mmol) according to the general procedure afforded 14 mg (44%) of product **54o**, isolated as a yellow oil; IR (KBr) cm^{-1} 2934, 1715, 1375, 1146, 709; ^1H NMR (500 MHz, CDCl_3) δ 7.78-7.72 (m, 2H), 7.70-7.64 (m, 2H), 2.91 (d, $J = 5.5$ Hz, 1H), 2.30-2.12 (m, 2H), 2.08-1.98 (m, 1H), 1.77-1.69 (m, 1H), 1.53-1.19 (m, 7H); ^{13}C NMR (125 MHz, CDCl_3): δ 166.3, 133.8, 130.9, 122.7, 48.4, 47.3, 30.5, 23.7, 20.4, 20.3, 20.1.

***N*-(aminophthalimide)-8-azabicyclo[5.1.0]octane 54p**



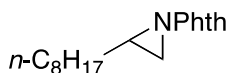
Reaction of cycloheptene **52p** (0.125 mmol) according to the general procedure afforded 12 mg (38%) of product **54p**, isolated as a yellow oil; IR (neat) cm^{-1} 2925, 1716, 1378, 1155, 707; ^1H NMR (500 MHz, CDCl_3) δ 7.80-7.72 (m, 2H), 7.69-7.63 (m, 2H), 2.72-2.64 (m, 2H), 2.24-2.12 (m, 2H), 2.10-1.97 (m, 2H), 1.70-1.36 (m, 6H).

***N*-(aminophthalimide)-9-azabicyclo[6.1.0]nonane 54q**



Reaction of cyclooctene **52q** (0.125 mmol) according to the general procedure afforded 14 mg (44%) of product **54q**, isolated as a yellow solid: light yellow needles (recrystallized from dichloromethane-hexane); mp 82.2-82.8 °C (lit.⁸, mp 87-89 °C); IR (KBr) cm^{-1} 2928, 1712, 1381, 1156, 709; ^1H NMR (500 MHz, CDCl_3) δ 7.80-7.72 (m, 2H), 7.70-7.63 (m, 2H), 2.60-2.46 (m, 4H), 1.74-1.18 (m, 10H).

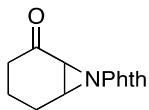
***N*-(aminophthalimide)-2-*n*-octylaziridine 54r**



Reaction of 1-decene **52r** (0.125 mmol) according to the general procedure afforded 12 mg (32%) of product **54r**, isolated as a yellow oil: light yellow needles (recrystallized from dichloromethane-hexane); mp 41.4-42.6 °C; IR (KBr) cm^{-1} 2922, 1723, 1379, 1156, 715; ^1H NMR (500 MHz, CDCl_3) δ 7.80-7.74 (m, 2H), 7.70-7.65 (m, 2H), 2.66-2.55 (m, 1H), 2.45

(dd, $J = 7.5, 2.0$ Hz, 1H), 1.80-1.14 (m, 14H), 0.89 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 165.2, 134.0, 130.4, 122.9, 43.4, 38.2, 32.0, 31.9, 29.7, 29.5, 29.3, 26.4, 22.7, 14.1.

***N*-(aminophthalimide)-2-oxo-7-azabicyclo[4.1.0]heptane 54s**



Reaction of cyclohexenone **52s** (0.125 mmol) according to the general procedure afforded 16 mg (53%) of product **54s**, isolated as a white solid: colorless needles (recrystallized from dichloromethane-hexane); mp 80.4-81.9 °C (lit.⁹, mp 75-77 °C); IR (KBr) cm^{-1} 2933, 1715, 1632, 1383, 1150, 715; ^1H NMR (500 MHz, CDCl_3) δ 7.82-7.77 (m, 2H), 7.74-7.68 (m, 2H), 3.49-3.43 (m, 1H), 3.08 (d, $J = 8.0$ Hz, 1H), 2.62-2.50 (m, 2H), 2.20-2.10 (m, 1H), 2.08-1.93 (m, 2H), 1.79-1.68 (m, 1H).

3.3 SiO_2 -supported $\text{RuCl}_3/3$ -(dichloriodo)benzoic acid: green catalytic system for the oxidation of alcohols and sulfides in water

1. General experimental remarks

All reactions were performed under dry nitrogen atmosphere with flame-dried glassware. All commercial reagents were ACS reagent grade and used without further purification. Dichloromethane was distilled from CaH_2 immediately prior to use. Ethyl acetate was distilled from CaSO_4 . All commercial reagents were ACS reagent grade and used without further purification. Melting points were determined in an open capillary tube with a Mel-temp II[®] melting point apparatus. Infrared spectra were recorded as a

KBr pellet on a Perkin-Elmer 1600 series FT-IR spectrophotometer. NMR spectra were recorded on a Varian ^{UNITY} INOVA 500 MHz NMR spectrometer at 500 MHz (¹H NMR) and 125 MHz (¹³C NMR). Chemical shifts are reported in parts per million (ppm). ¹H and ¹³C chemical shifts are referenced relative to the tetramethylsilane. GC-MS analysis was carried out with a HP 5890A Gas Chromatograph using a 5970 Series mass selective detector. Microanalyses were carried out by Atlantic Microlab, Inc., Norcross, Georgia.

2. General Oxidation Procedure

To a suspension of alcohol **58** or sulfides **59** (0.2 mmol) and 3-(dichloriodo)benzoic acid **60** (96 mg, 0.3 mmol) in 2 mL of water, SiO₂-RuCl₃ **65** (10 mg, 0.23 mol%) was added under stirring at room temperature. The reaction mixture was stirred until the complete consumption of starting materials **58** or **59** (monitored by TLC and GC-MS), then 2 mL of saturated aqueous NaHCO₃ was added and stirred for 15-30 min; the solid (SiO₂-RuCl₃) was filtered, washed with EtOAc (1 mL x 3) and collected for next run. The filtrate was extracted with EtOAc (3 mL x 3) and dried over Na₂SO₄. The aqueous layer was acidified with 10% HCl to pH = 3 and the 3-iodobenzoic acid was precipitated, which was filtered and collected for regenerating 3-(dichloriodo)benzoic acid. The organic layer was concentrated to afford the respective product of oxidation **62** or **63**.^b Based on GC-MS analysis.^c Yields of isolated products.

3. Preparation of SiO₂-RuCl₃

The aminopropyl silica (AMPS, 5.0 g, 5 mmol) was added to the solution of dimethylacetamide (6.65 g, 50 mmol) in methanol (50 mL) and the reaction mixture was

refluxed for 3 h. The mixture was cooled to room temperature, then RuCl_3 (0.41 g, 2 mmol) was added, and the resulting mixture was refluxed with stirring for 3 days. The solid product was filtered, washed with methanol, water and Et_2O until the washings became colorless. The catalyst, isolated as dark yellow solid, was dried under vacuum for 5 h before use. Elemental analysis: C, 8.03%; H, 1.64%; N, 1.83%; Cl, 0.50%. The loading of Ru was 0.047 mmol/g based on Cl analysis. FT-IR (KBr): 3432, 2950, 1648, 1400, 1098, 800, 564, and 470 cm^{-1} .

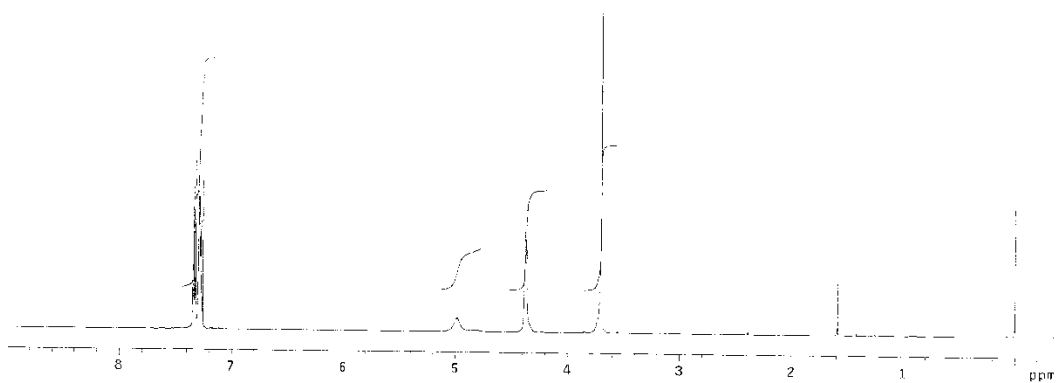
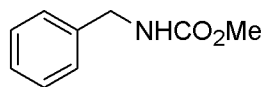
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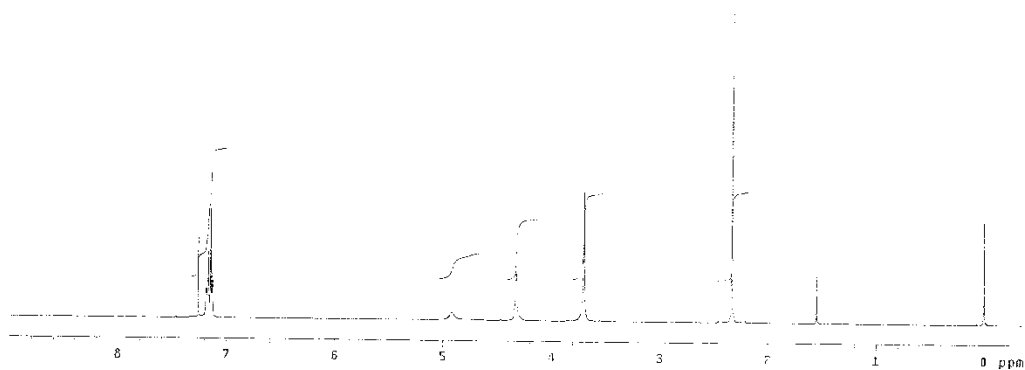
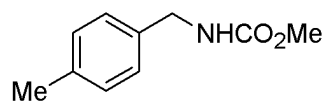
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APPENDIX

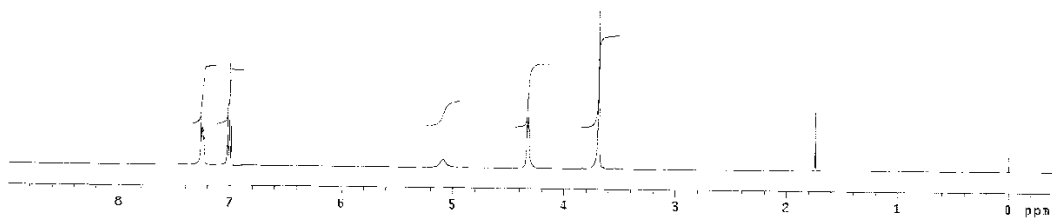
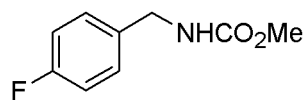
^1H NMR (500 MHz, CDCl_3):



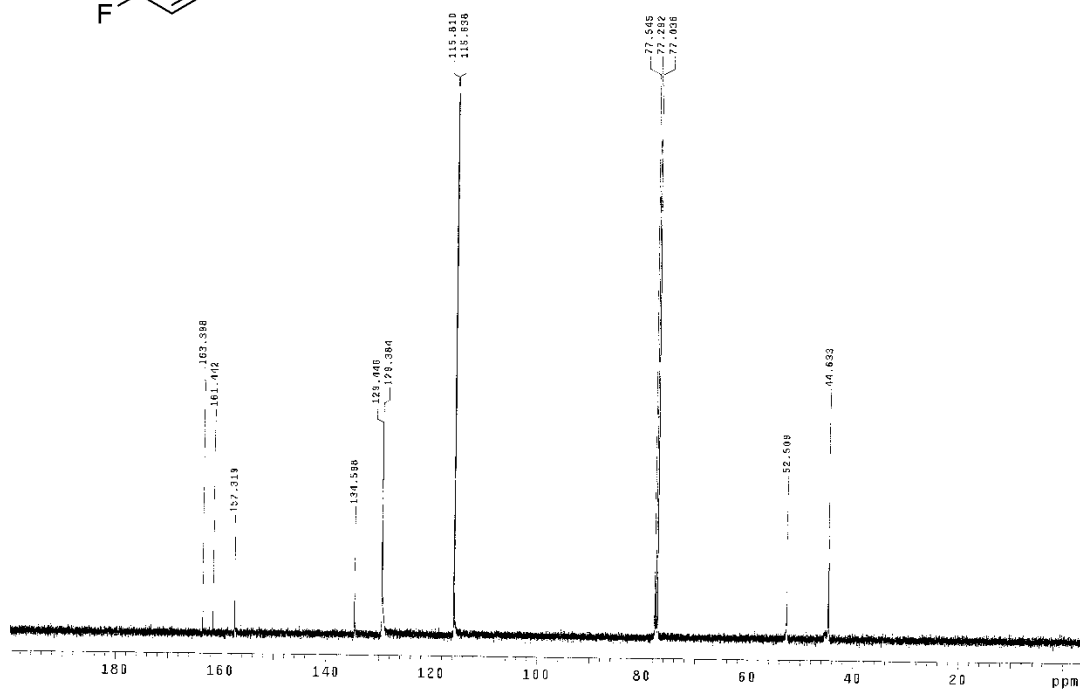
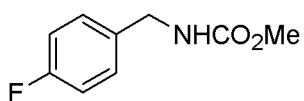
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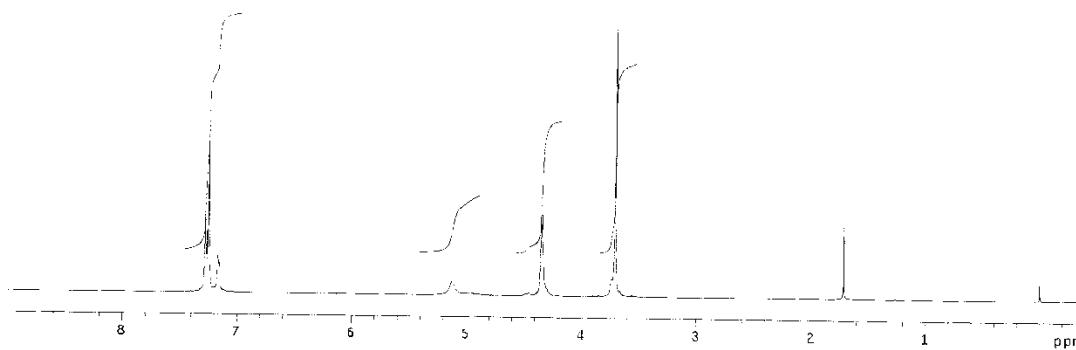
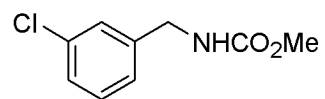
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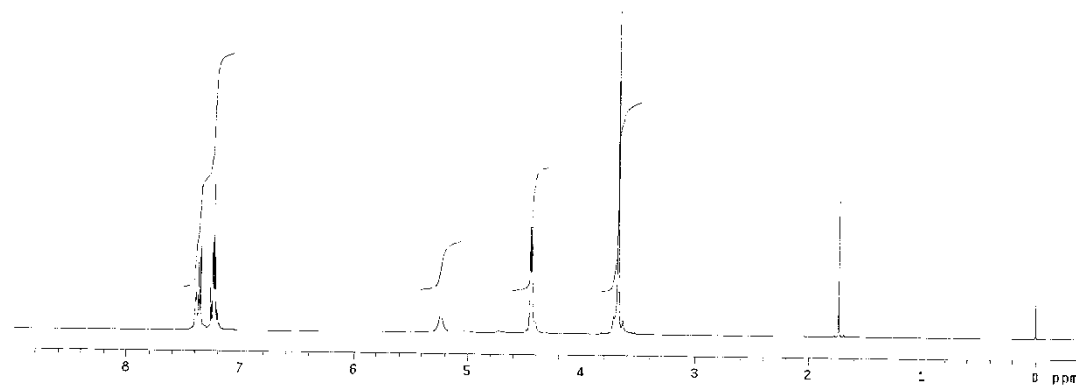
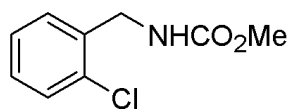
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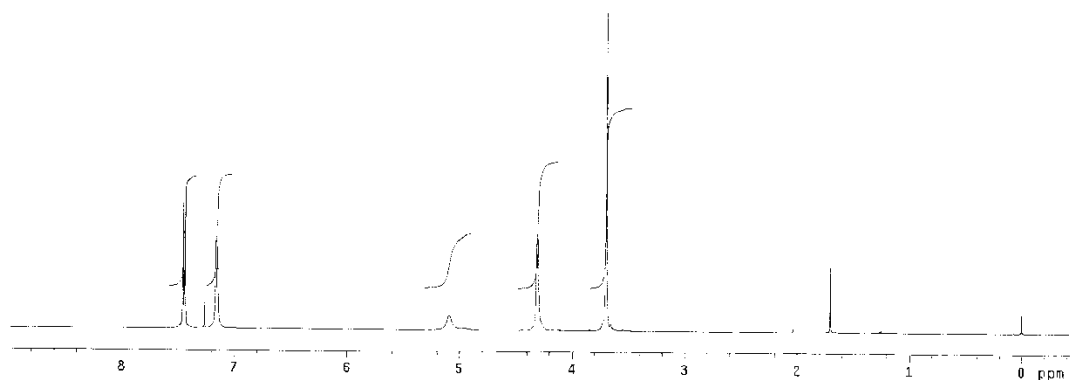
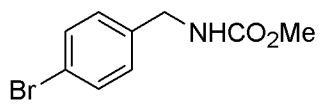
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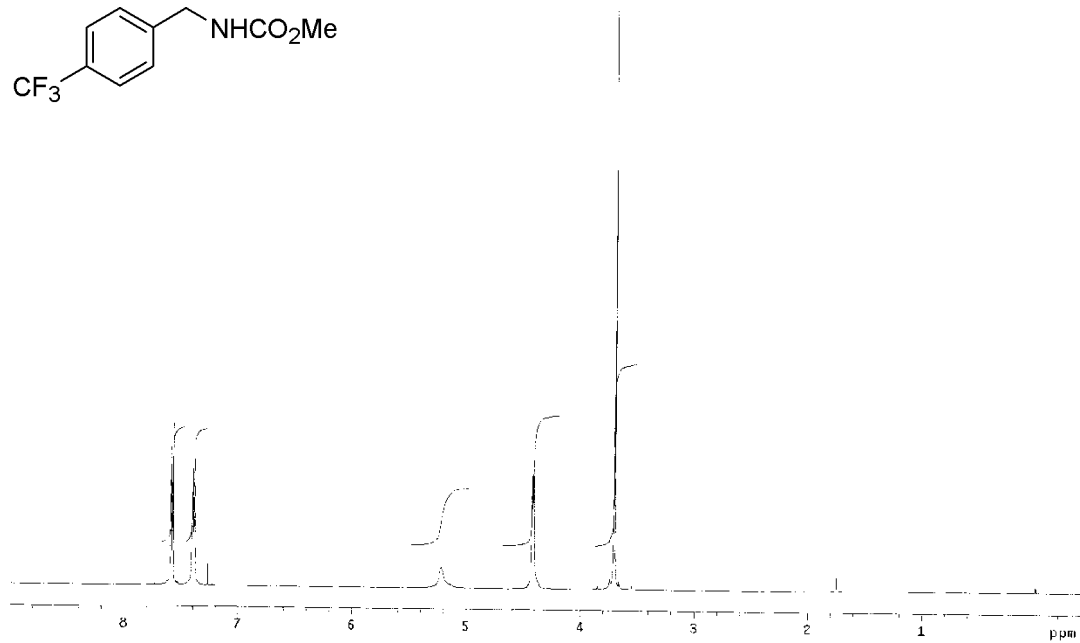
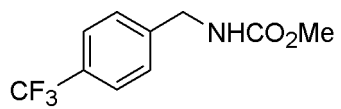
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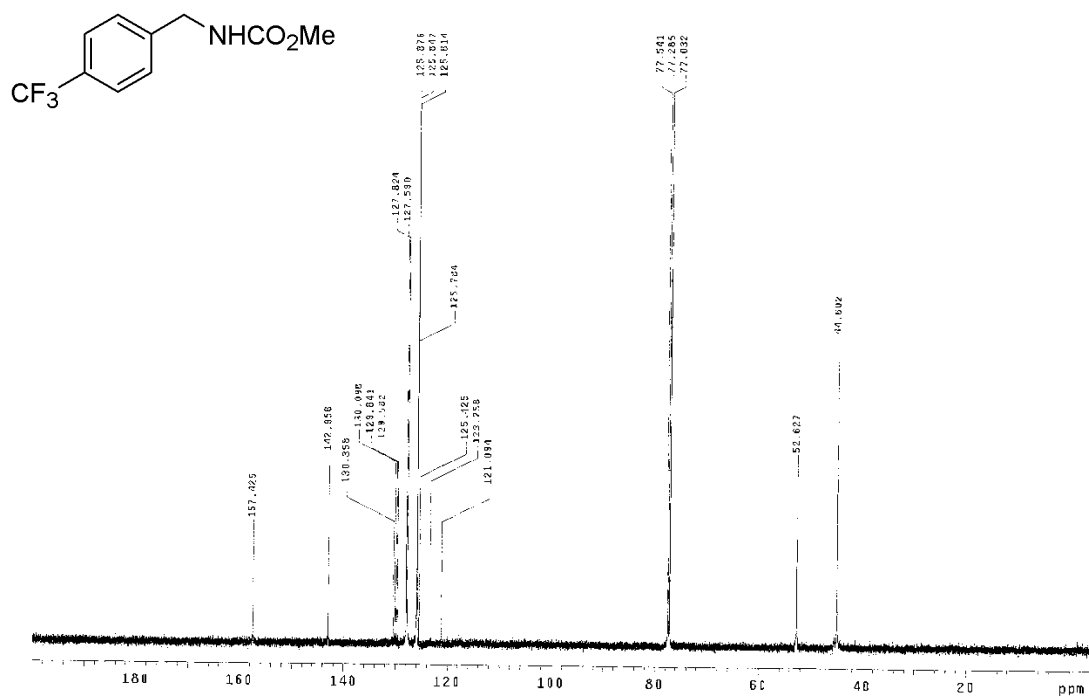
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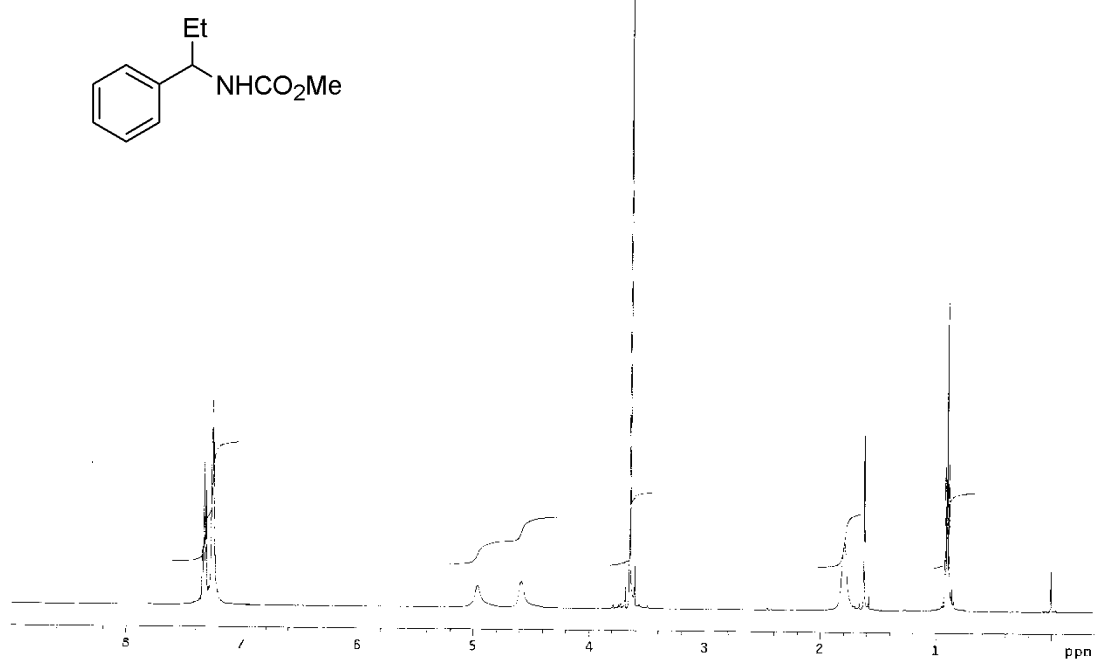
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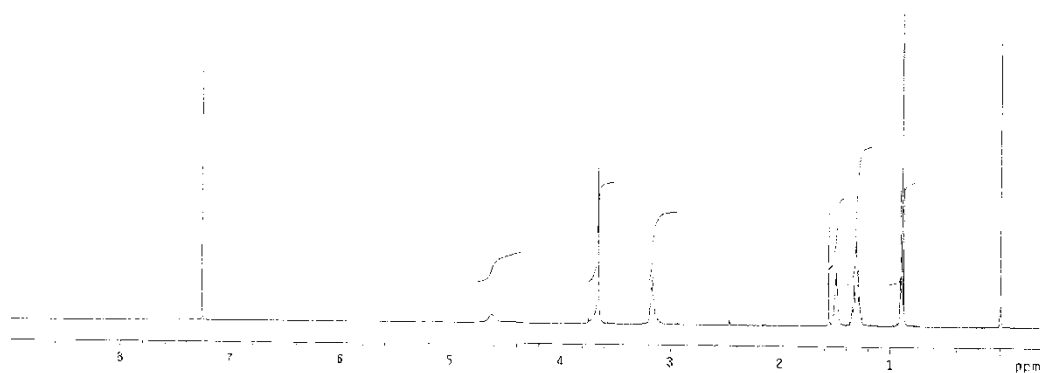
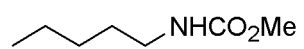
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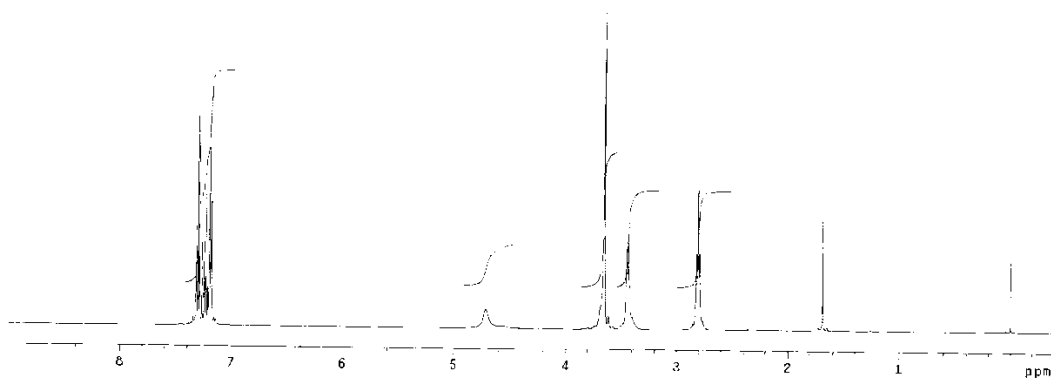
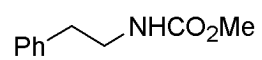
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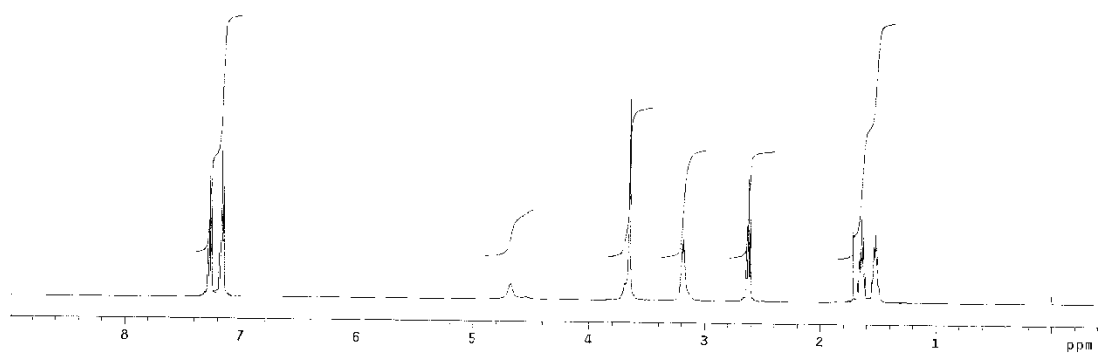
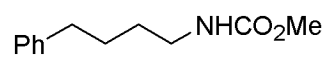
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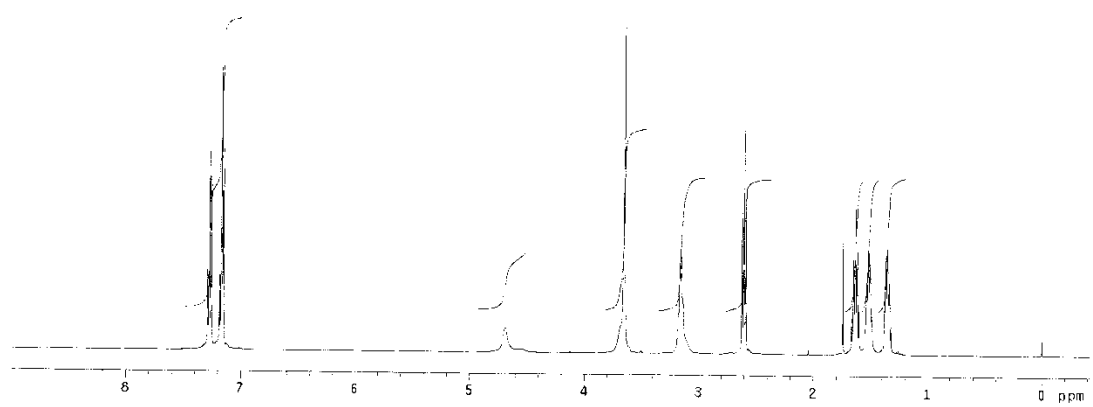
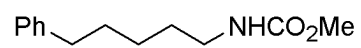
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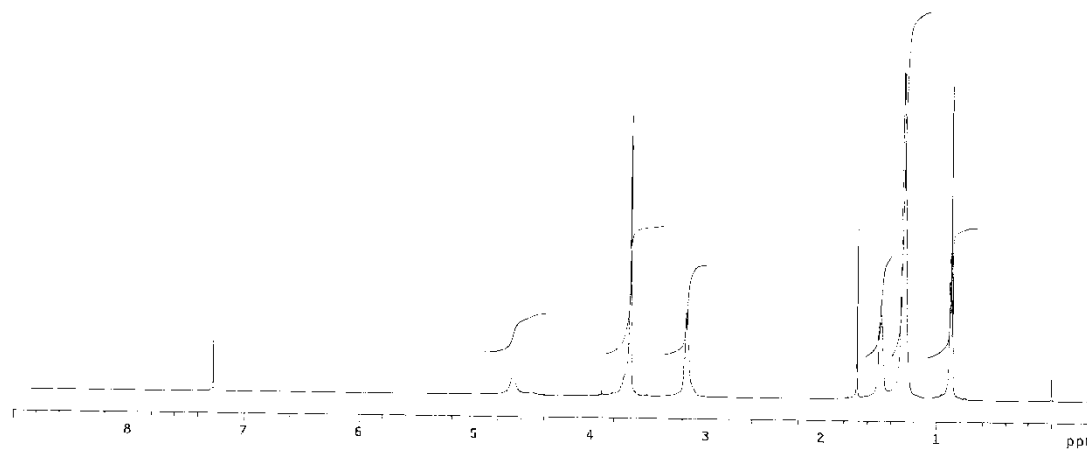
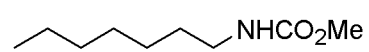
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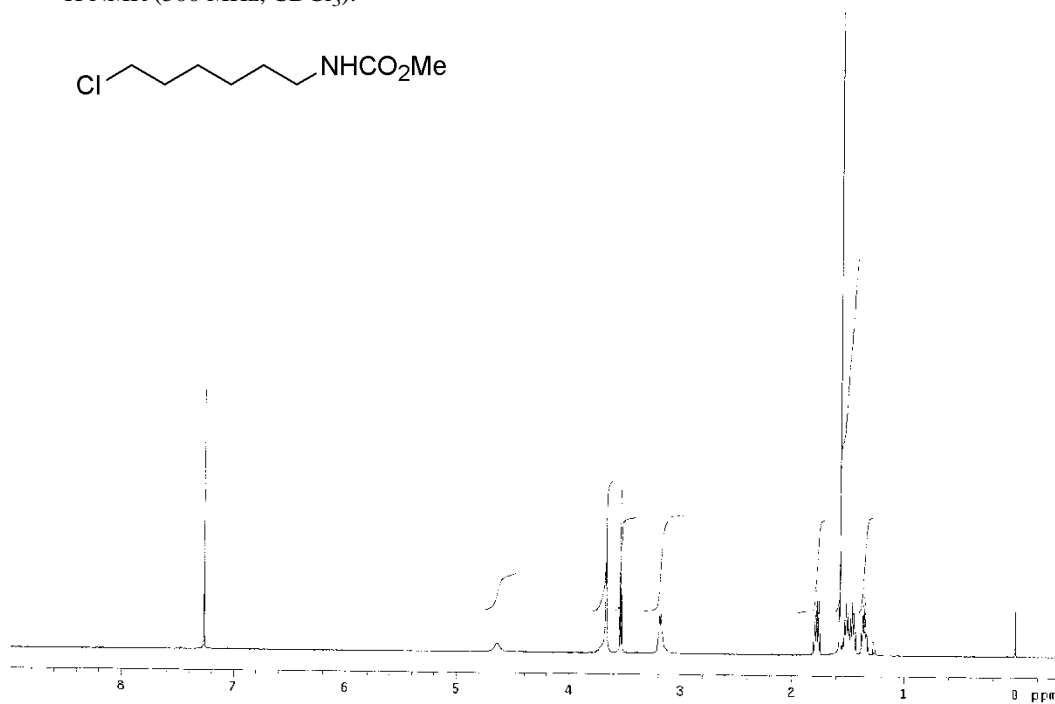
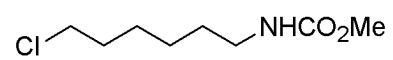
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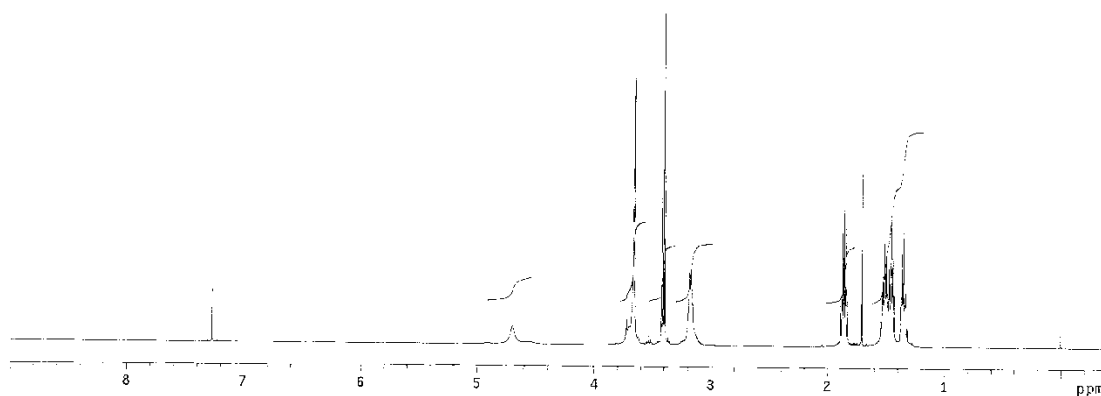
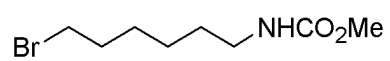
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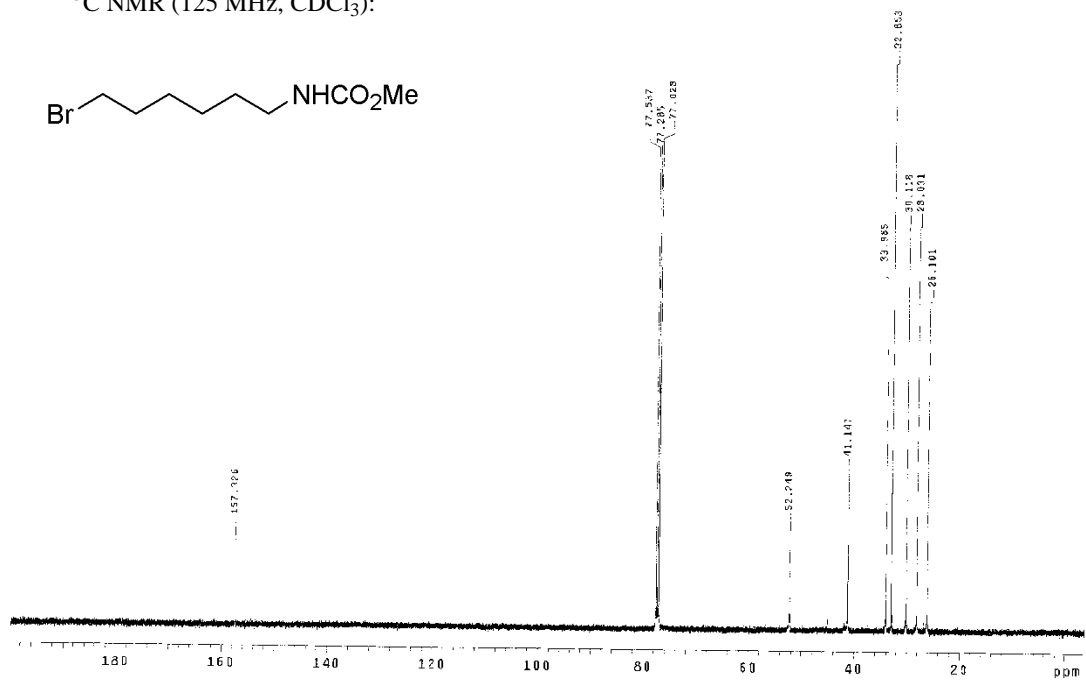
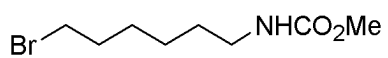
^1H NMR (500 MHz, CDCl_3):



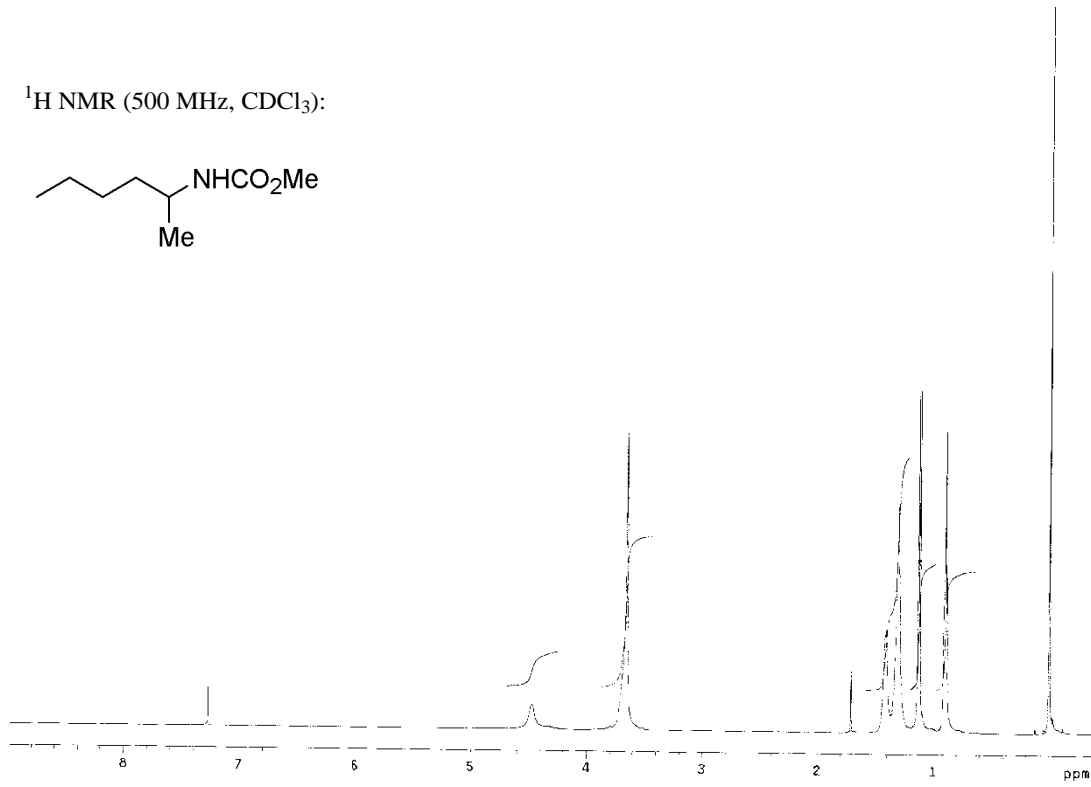
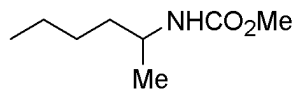
^1H NMR (500 MHz, CDCl_3):



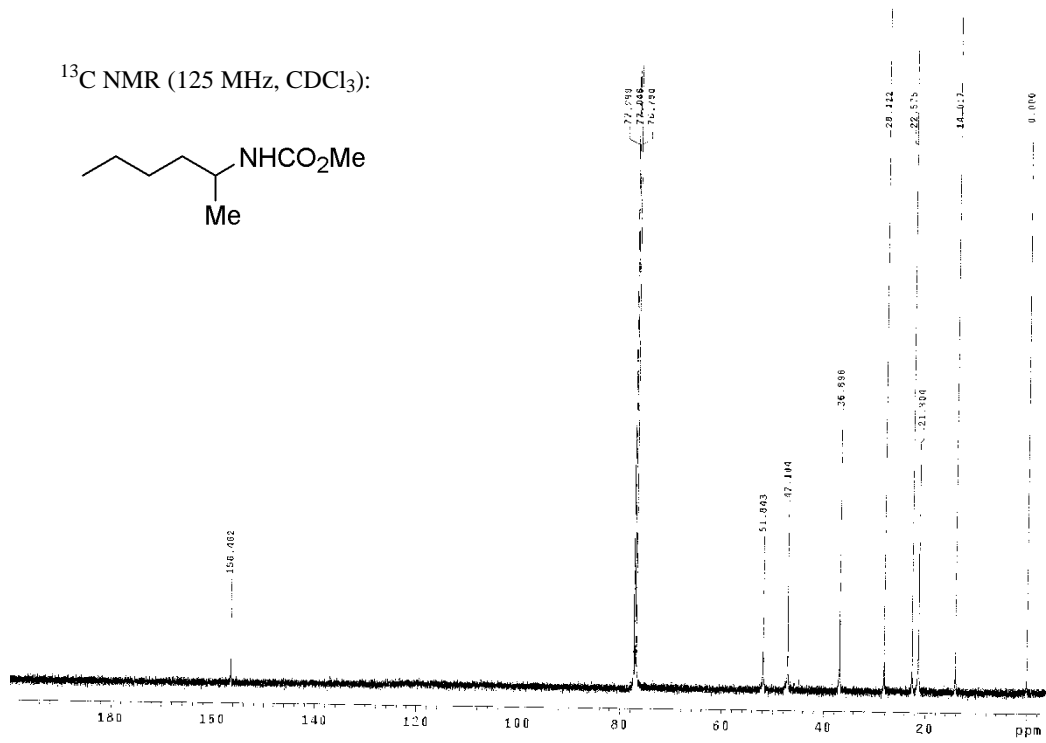
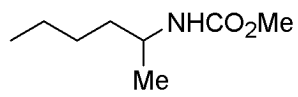
^{13}C NMR (125 MHz, CDCl_3):



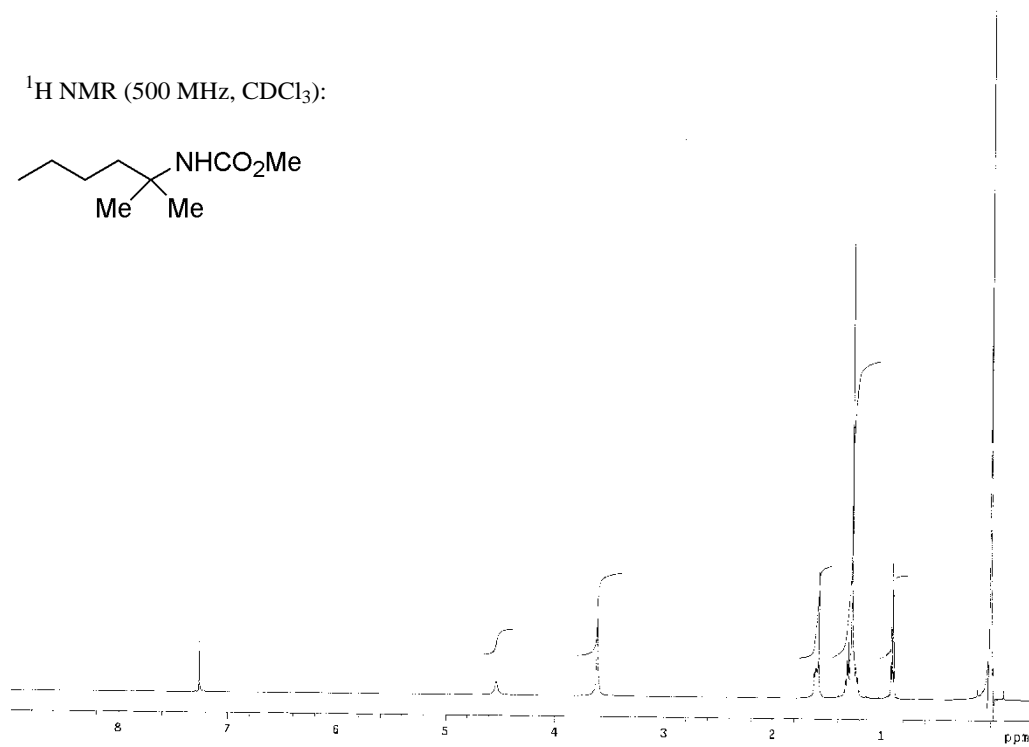
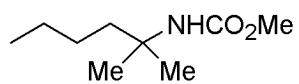
^1H NMR (500 MHz, CDCl_3):



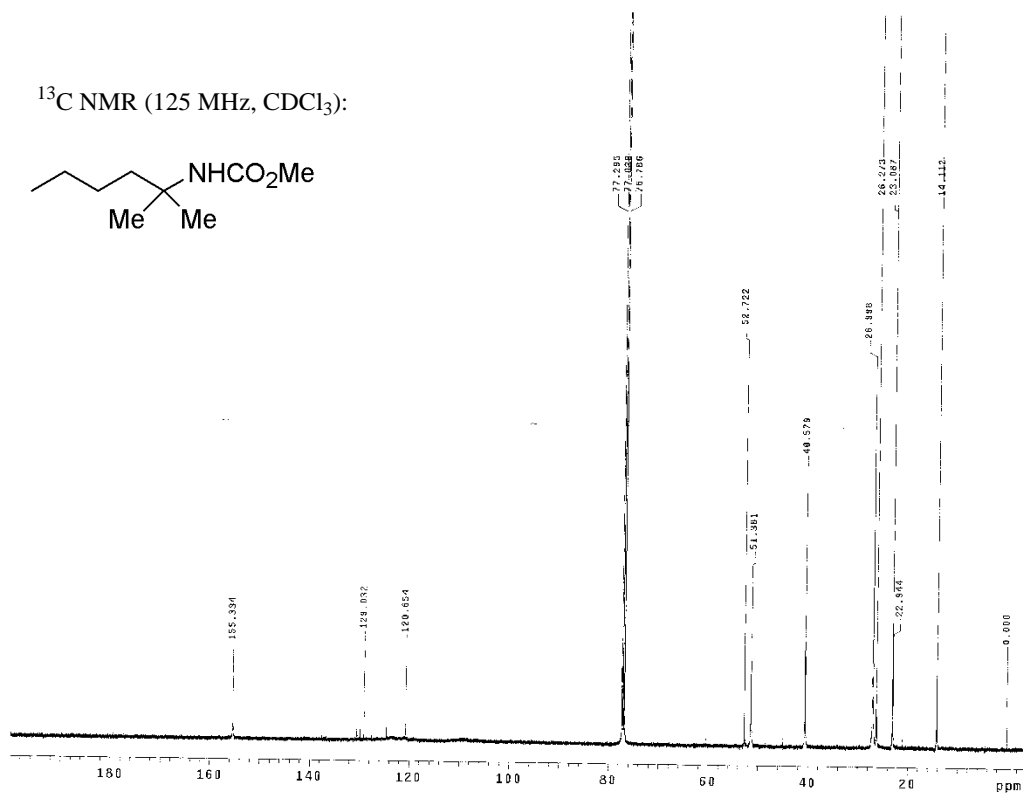
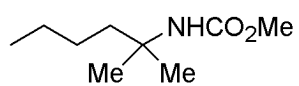
^{13}C NMR (125 MHz, CDCl_3):



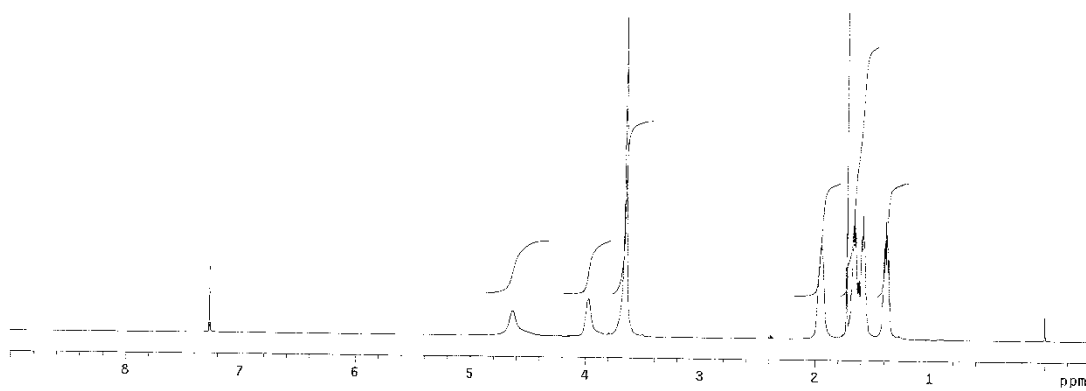
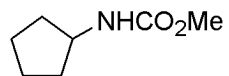
^1H NMR (500 MHz, CDCl_3):



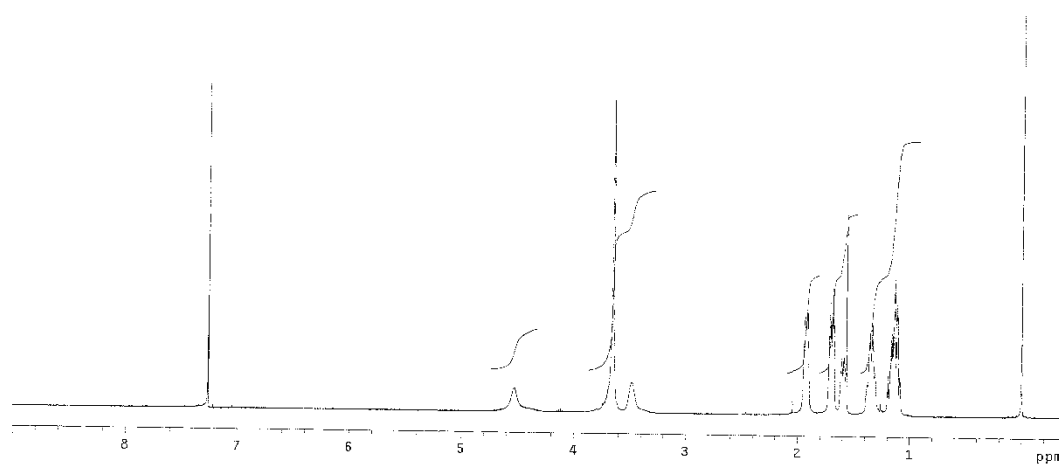
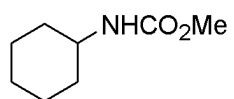
^{13}C NMR (125 MHz, CDCl_3):



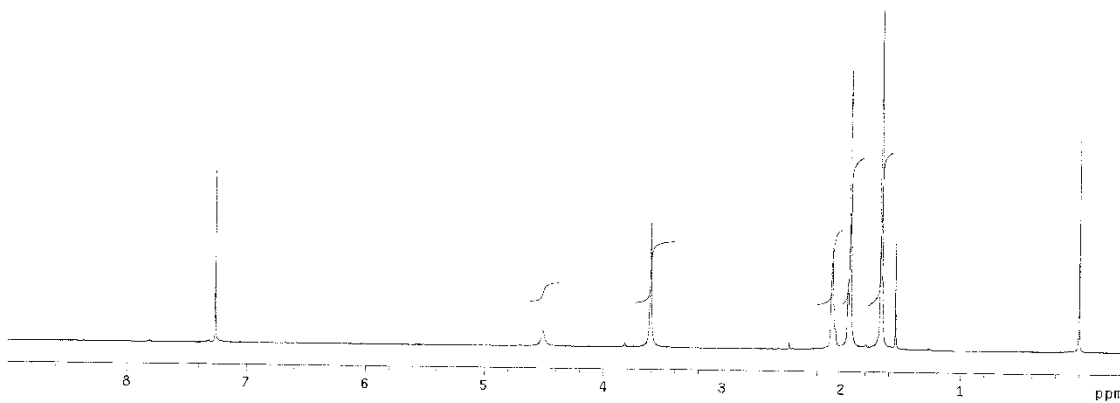
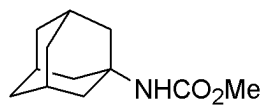
^1H NMR (500 MHz, CDCl_3):



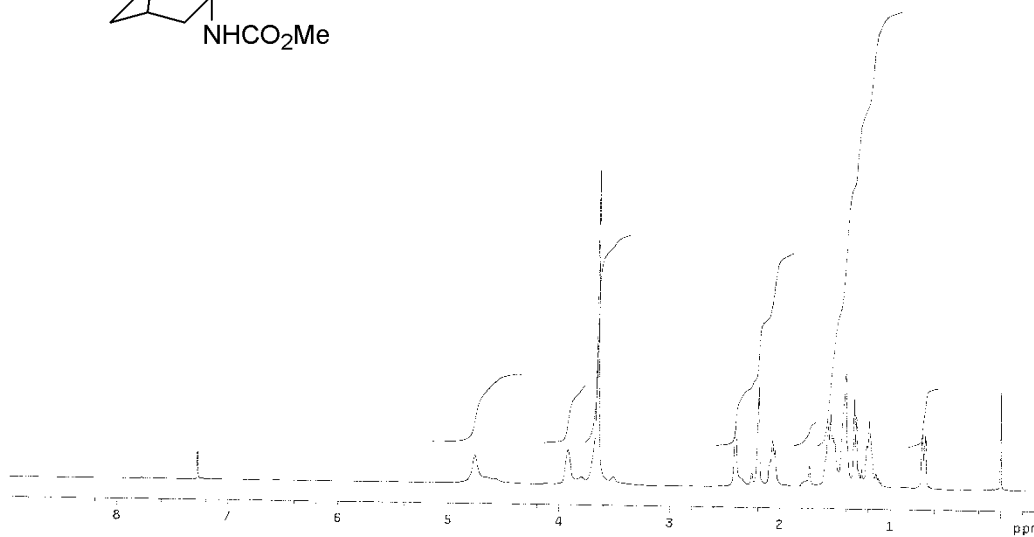
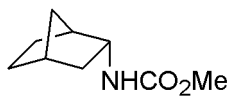
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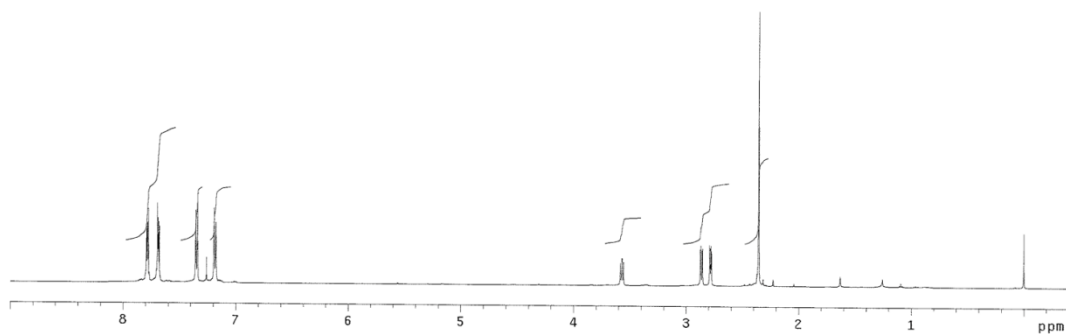
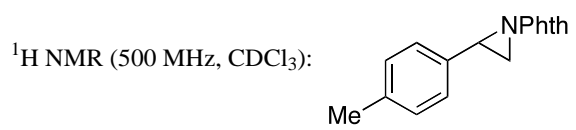
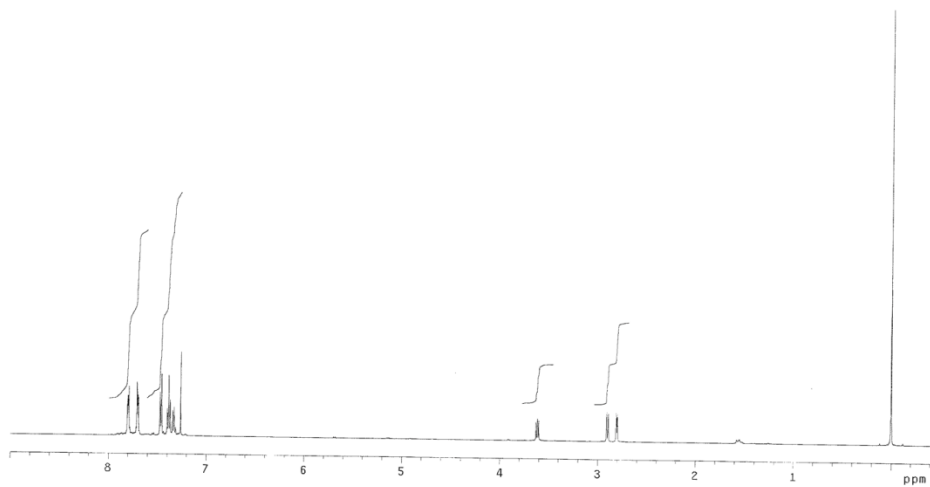
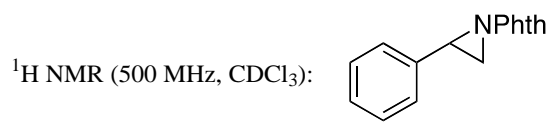


^1H NMR (500 MHz, CDCl_3):

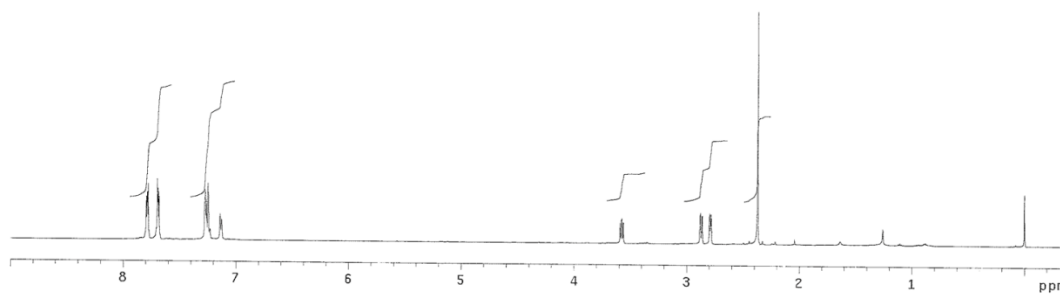
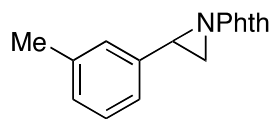


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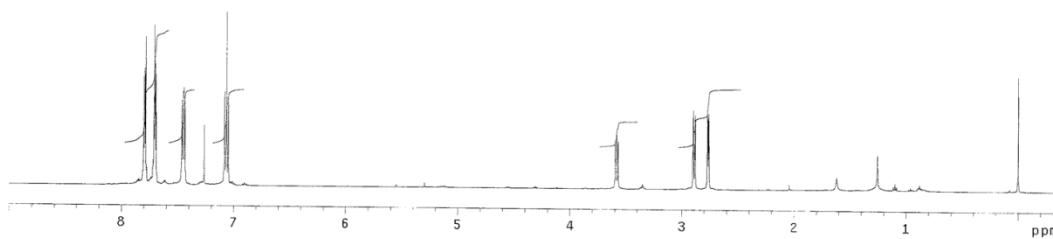
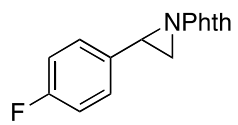




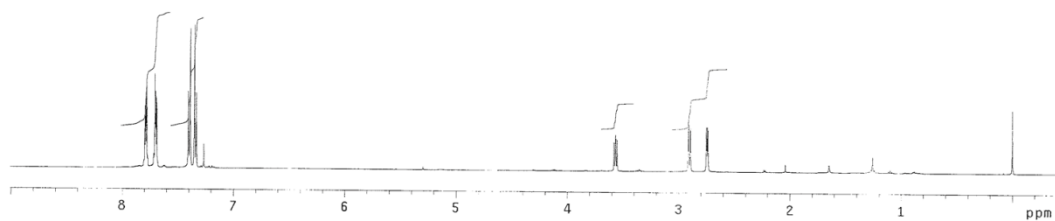
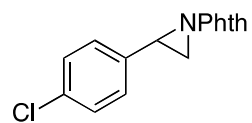
$^1\text{H NMR}$ (500 MHz, CDCl_3):



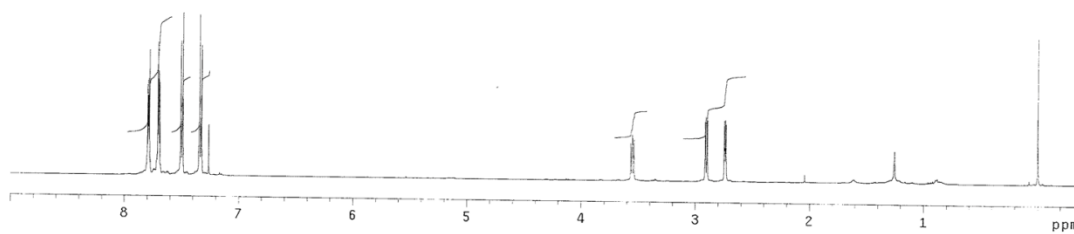
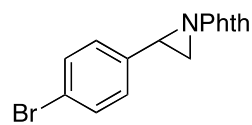
$^1\text{H NMR}$ (500 MHz, CDCl_3):



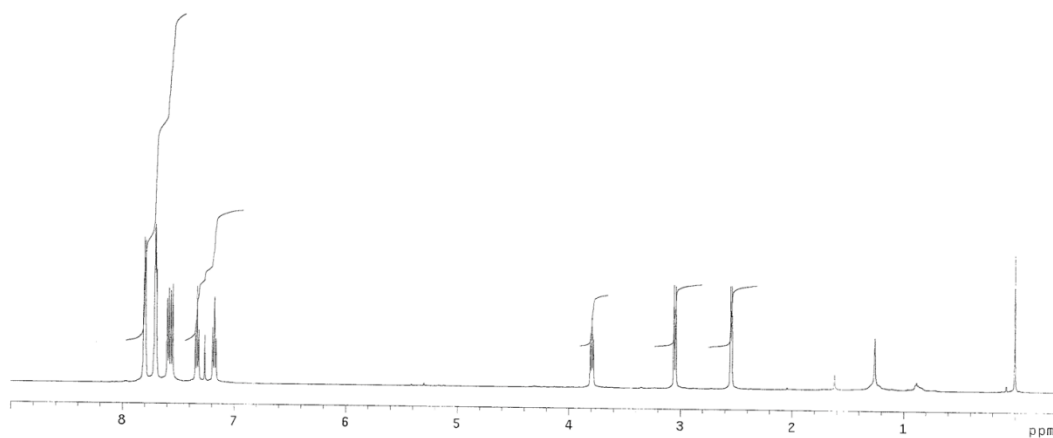
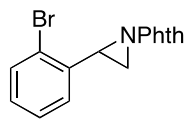
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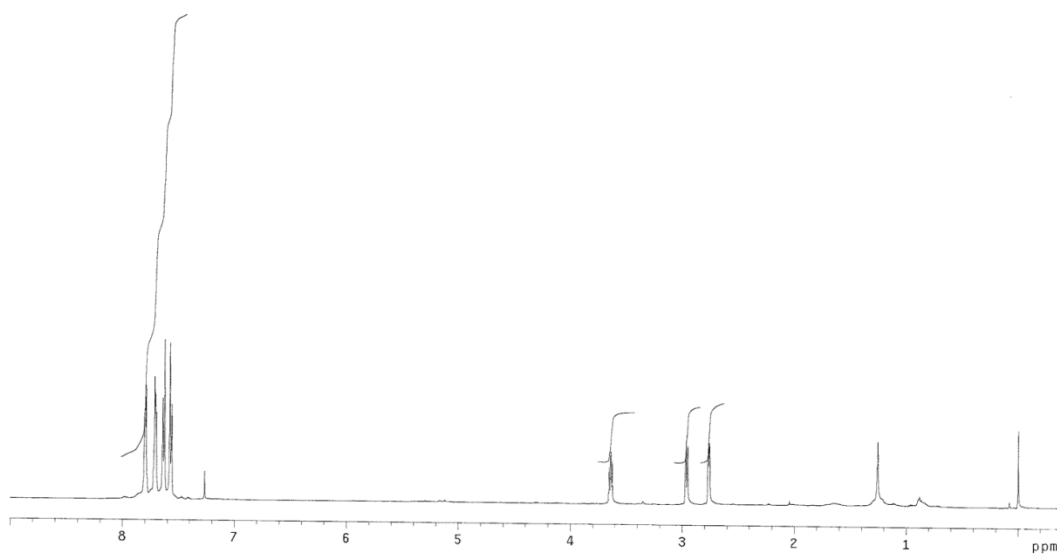
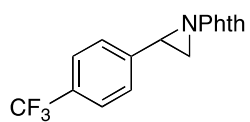
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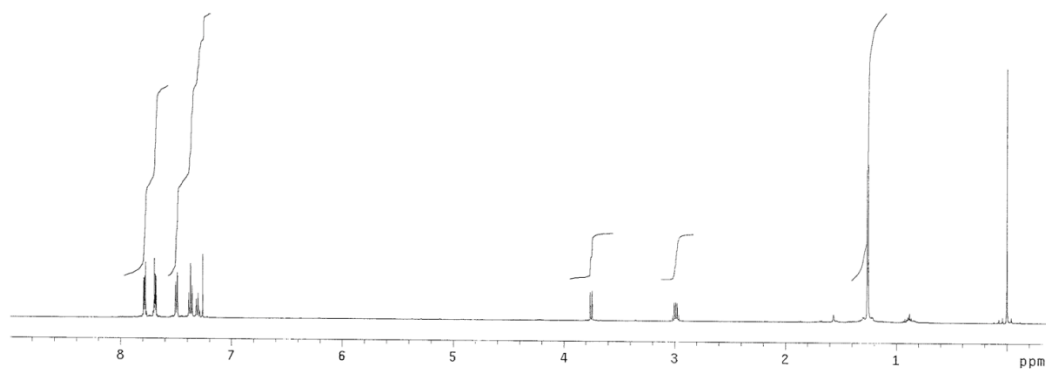
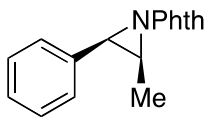
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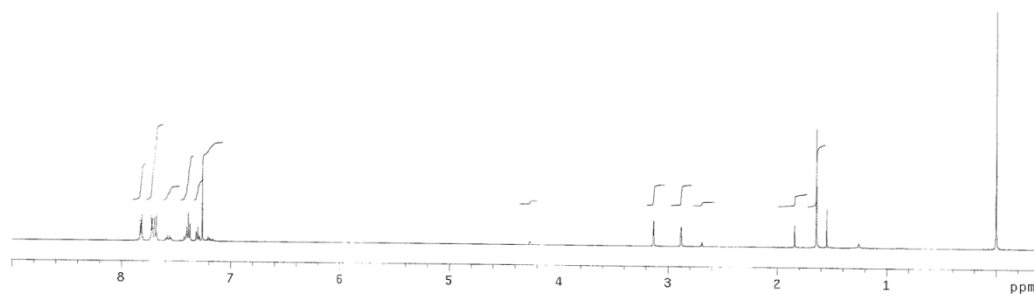
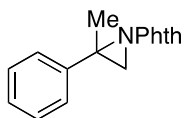
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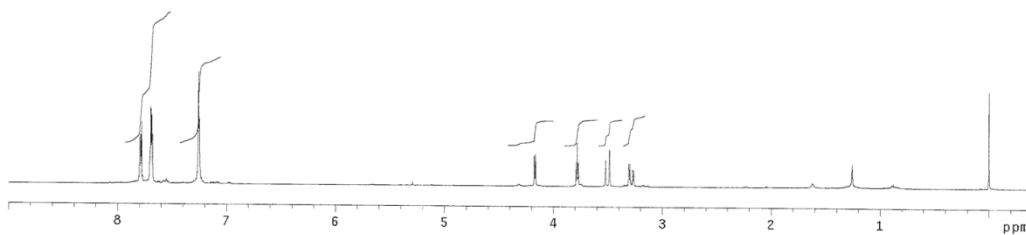
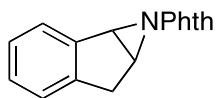
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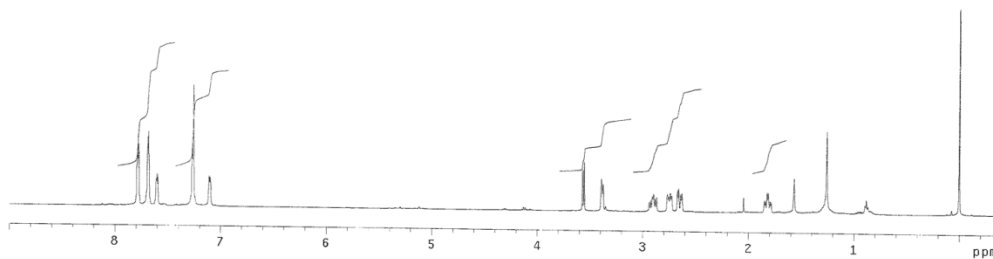
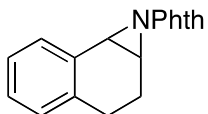
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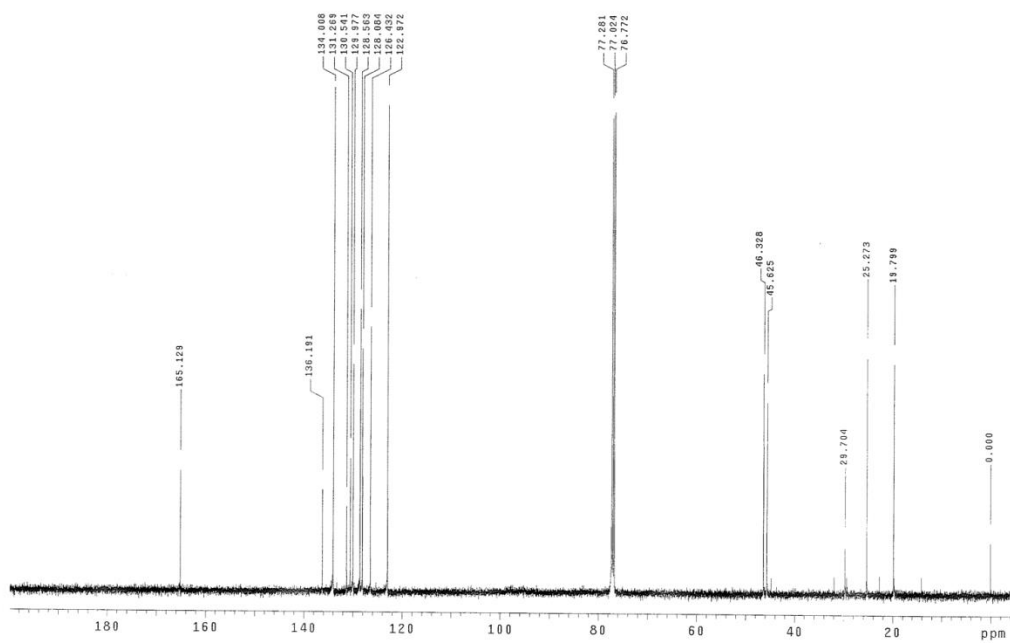
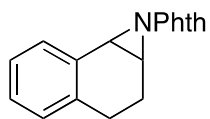
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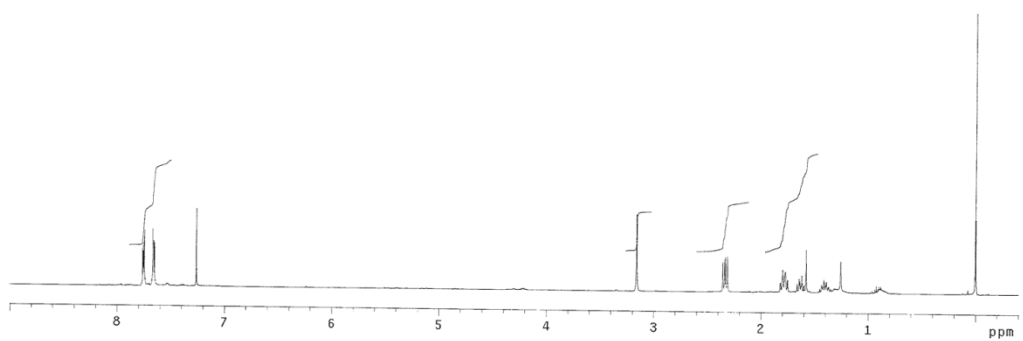
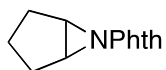
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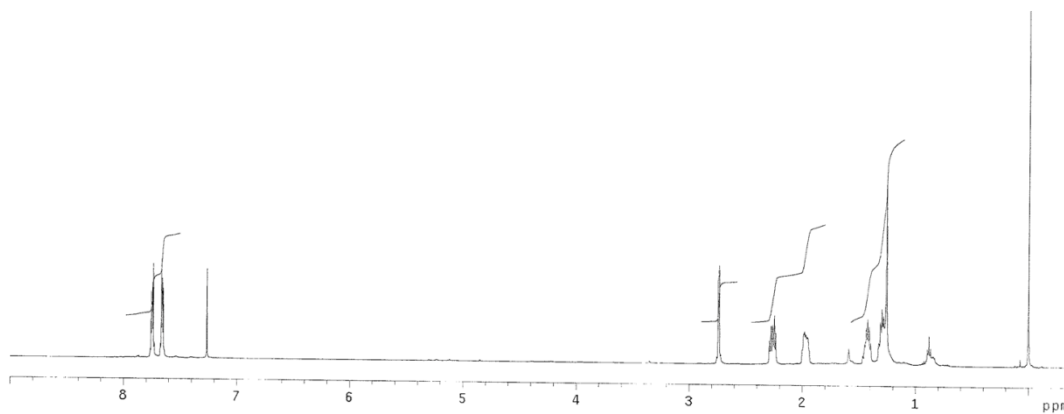
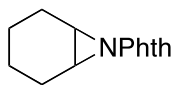
^{13}C NMR (125 MHz, CDCl_3):



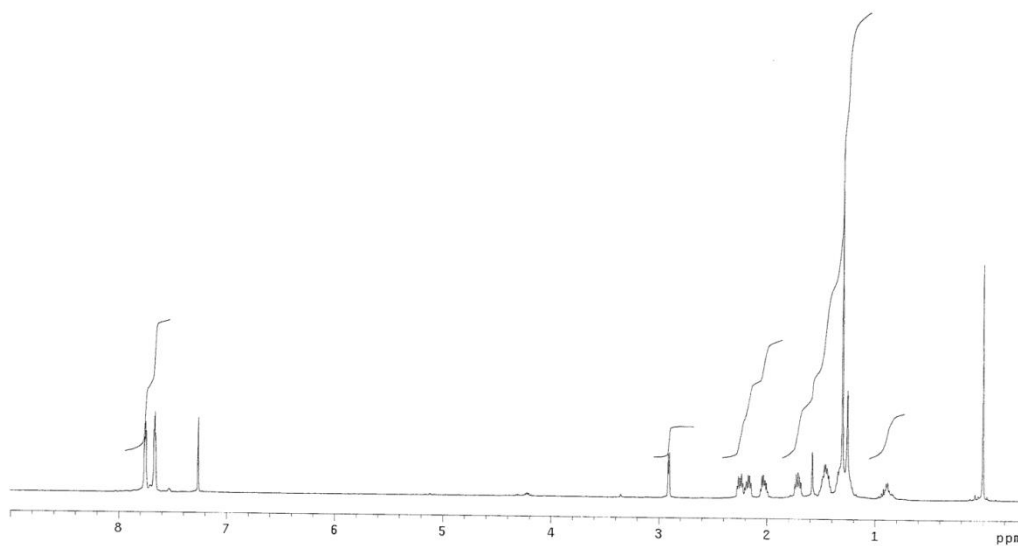
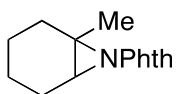
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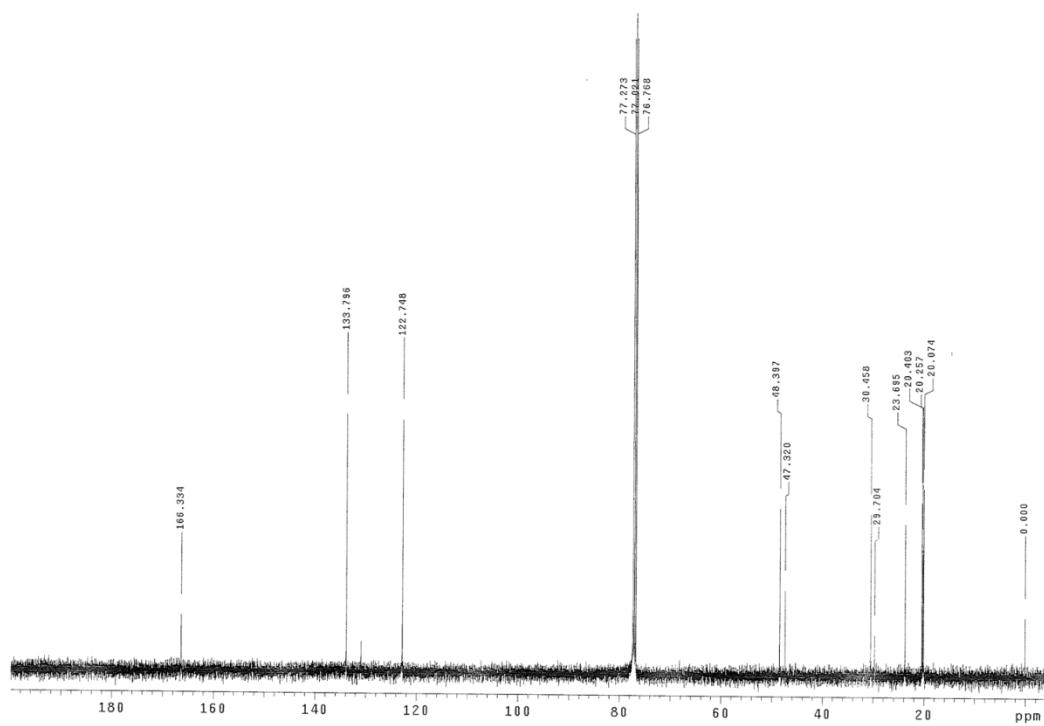
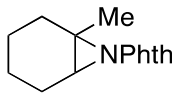
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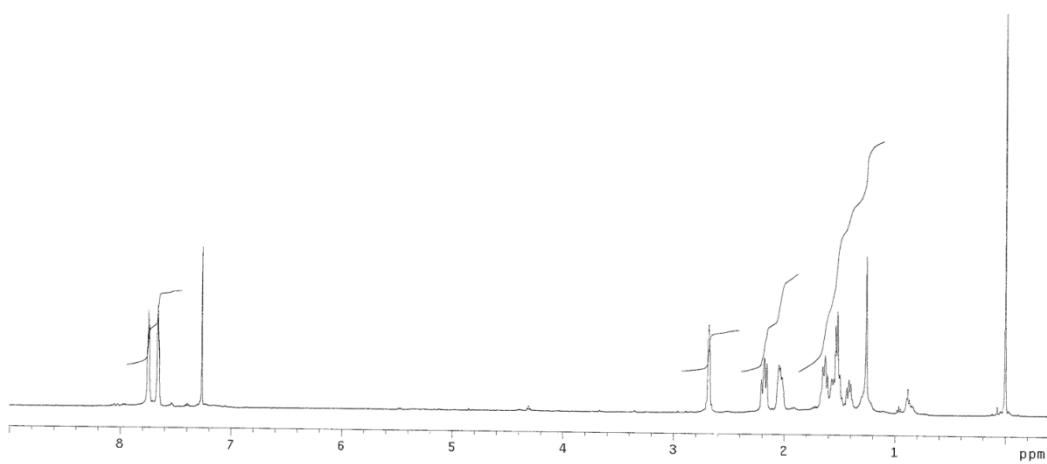
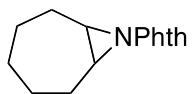
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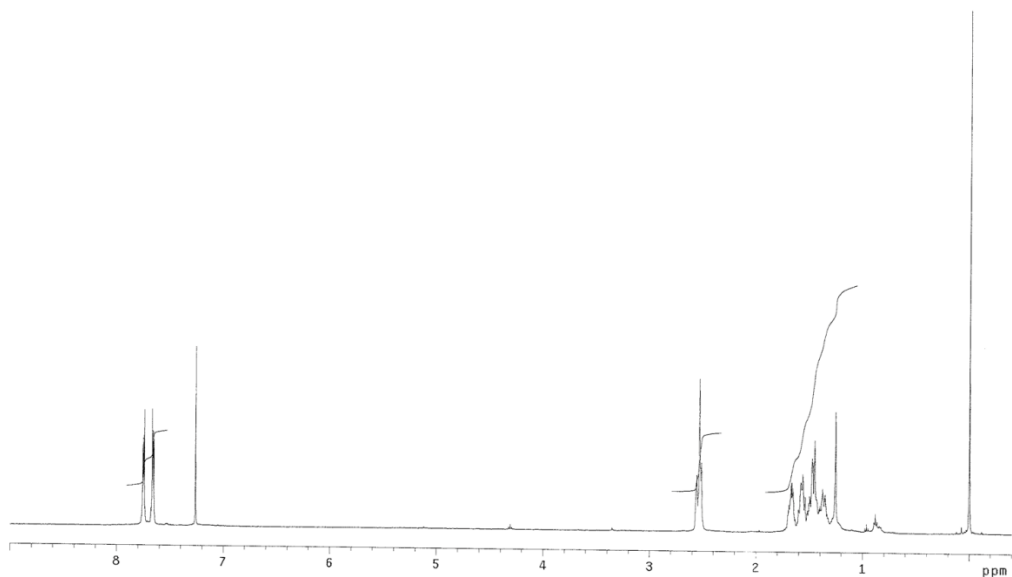
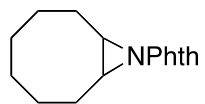
^{13}C NMR (125 MHz, CDCl_3):



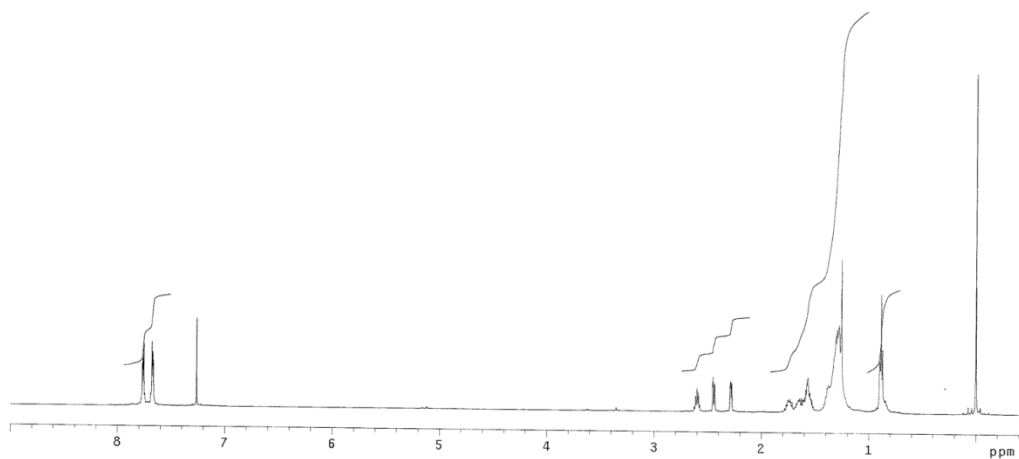
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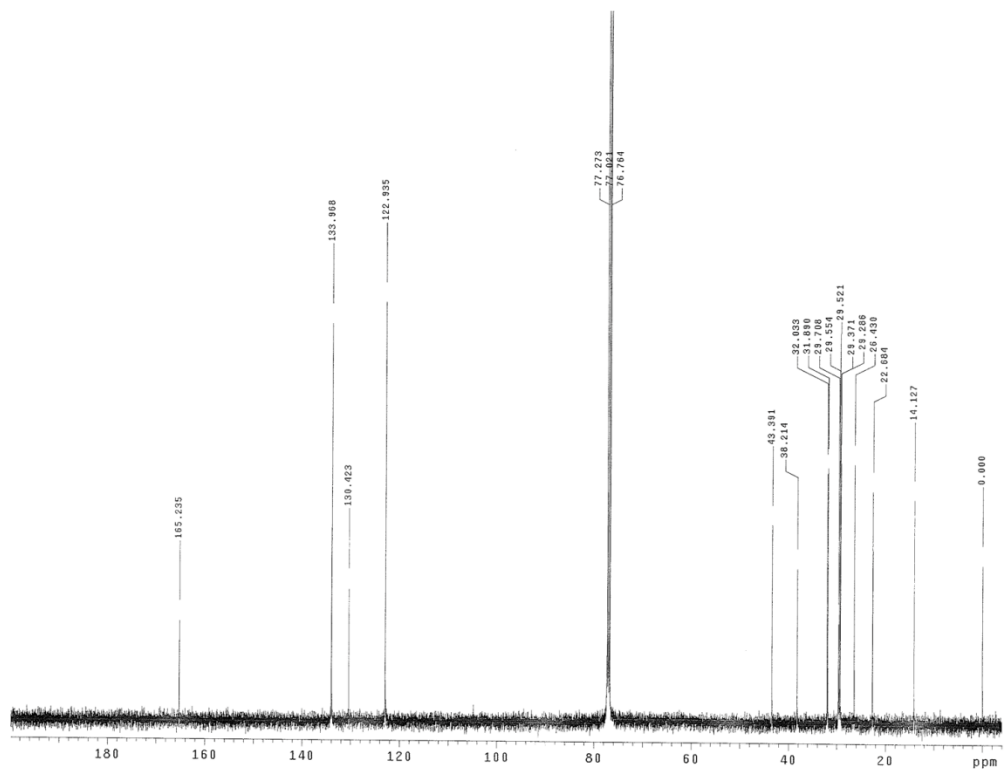
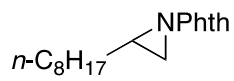
^1H NMR (500 MHz, CDCl_3):



^1H NMR (500 MHz, CDCl_3): $n\text{-C}_8\text{H}_{17}$ NPhth



^{13}C NMR (125 MHz, CDCl_3):



^1H NMR (500 MHz, CDCl_3):

