DEVELOPMENT OF NEW SYNTHETIC METHODOLOGIES BASED ON HYPERVALENT IODINE CHEMISTRY

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To my family in Russia, thank you for your love and support of my educational endeavors.

DEDICATION

This thesis is dedicated to my parents, Irina and Alexander Zagulyaevy.

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LIST OF ABBREVIATIONS

Ac = acetate

Ala = Alanine

Anal. Calcd = Analytically Calculated

Ar = aryl

Bn = benzyl

Boc = t-Butoxycarbonyl

br = broad

BTI = [Bis(trifluoroacetoxy)iodo]benzene

Bu (n-Bu) = butyl

t-Bu = *tert*-butyl

Cbz = Benzyloxycarbonyl

mCPBA = meta-Chloroperoxybenzoic acid

d = doublet

DBU = 1,8-Diazabicyclo[5.4.0]undec-7-ene

DDZ = Dimethyl-3,5-dimethoxybenzyloxycarbonyl

dec = decomposition

DIB = (Diacetoxyiodo)benzene

DMF = dimethylformamide

DMP = Dess-Martin periodinane

DMSO = dimethyl sulfoxide

ESI-MS = electrospray ionization mass spectroscopy

ESI-MS/MS = electrospray ionization mass spectroscopy/mass spectrometry

Et = ethyl

FIS = (per*f*luoroalkyl)phenyl-*i*odonium hydrogensulfates

FITS = (per*f*luoroalkyl)phenyl-*i*odonium *t*rifluoromethane*s*ulfonates

Fmoc = Fluoren-9-ylmethoxycarbonyl

g = gram

GC = gas chromatography

GC-MS = gas chromatography mass spectrometry

HOBt = 1-hydroxy-*1H*-benzotriazole

h = hour

n-Hep = heptyl

n-Hex = hexyl

HTIB = [hydroxyl(tosyloxy)iodo]benzene

Hz = Hertz

IBX = 2-iodobenzoic acid

IR – infrared

LC-MS = liquid chromatography mass spectrometry

lit = literature

m = multiplet

Me = methyl

min = minute

MHz = megahertz

ml = milliliter

µl = microliter

mmol = millimole

mol-equiv = mole equivalent

mp = melting point

NMR = nuclear magnetic resonance

Ph = phenyl

PIFA = [(phenyliodinebis(trifluoroacetate)]

ppm = parts per million

i-Pr = isopropyl

n-Pr = normal propyl

q = quadruplet

rt = room temperature

s = singlet

t = triplet

TBAB = tetra-*n*-butylammonium bromide

Tf = triflate

TFA = trifluoroacetate

THF = tetrahydrofuran

TLC = thin layer chromatography

TMS = trimethylsilyl

p-Tol = p-tolyl

Ts = tosylate

Chapter 1

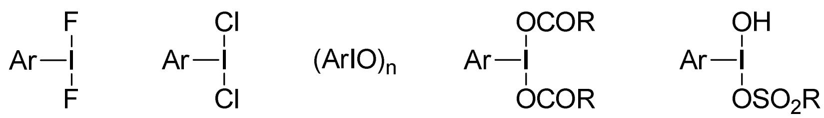
Review

1. Hypervalent Iodine in Organic Synthesis.

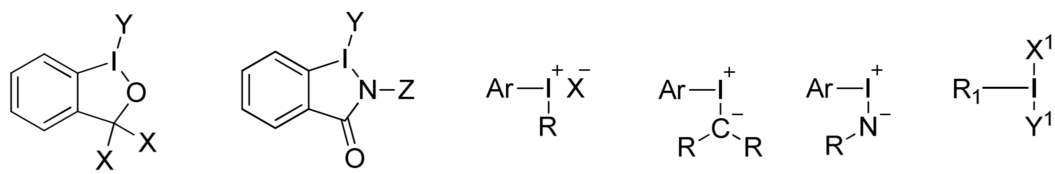
1.1 Introduction: Classification and General Structural Features of Organic Iodine(III) and Iodine(V) Compounds

There is considerable current interest and research activity in the development of new reagents and synthetic applications based on the organic chemistry of hypervalent iodine. This high interest is particularly due to the low toxicity, ready availability, easy handling, high efficiency and very useful oxidizing properties of these reagents. Iodine(III) and iodine(V) compounds are now widely used in modern organic synthesis, and many chemical transformations have become possible by using these reagents. They range from the formation of carbon-carbon and carbon-heteroatom bonds in oxidative coupling reactions to the activation of carbon-hydrogen bonds. Depending on the substrate, rearrangements or fragmentations can also be induced by these organoiodine reagents. They are an excellent alternative to heavy metal reagents. The catalytic use of hypervalent iodine derivatives has also recently become known. The chemistry of these novel reagents has been reviewed several times over the past decade. However, a great number of reviews only covered specific aspects of hypervalent organoiodide chemistry[1-45]. Most notable are the monograph by Varvoglis[6] on the application of hypervalent iodine compounds in organic synthesis and the volume of ”Topics in Current Chemistry”[34] on hypervalent iodine chemistry.

Organic iodine(III) and iodine(V) compounds are commonly classified by the type of ligands attached to the iodine atom[34,40,42,44-45]. The following general classes of iodine(III) and iodine(V) derivatives are of great practical importance in many synthetic applications (Scheme 1 and Scheme 2). (Difluoroiodo)arenes **1** and (dichloroiodo)arenes **2** are effectively used as fluorinating and chlorinating reagents. Iodosylarenes **3**, [bis(acyloxy)iodo]arenes **4**, aryliodine(III) organosulfonates **5** are generally powerful oxidizing agents, and have been widely applied as reagents for oxygenation and oxidative functionalization of organic substrates. Five-membered iodine(III) heterocycles[39] (benziodoxoles **6** and benziodazoles **7**) are more stable than their acyclic analogues; this allows the isolation and practical use of several otherwise unstable iodine(III) derivatives.



1 **2** **3** **4** **5**



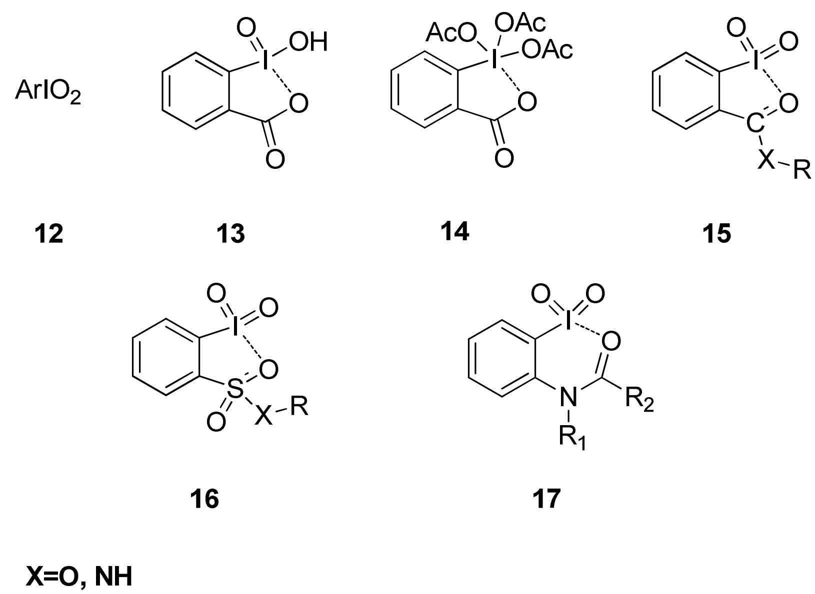
6 **7** **8** **9** **10** **11**

X=Me, CF_3 or 2X=O; Y=OH, OAc, CN, etc.; Z=H, Ac, etc.
R_1=C_nF_{2n+1}, $C_nF_{2n+1}CH_2$, $ArSO_2CH_2$
X^1=Y^1=Cl, $OCOCF_3$; X_1=OH; Y_1=OSO_2R

Scheme 1

Iodonium salts **8** in general do not possess any significant oxidizing properties, but have reactivity due to the ability of the -IAr fragment to be a good leaving group. Iodonium ylides **9** and imides **10** serve as carbene and nitrene precursors, respectively. The most practically useful representatives of stabilized alkyl substituted λ^3-iodanes **11** are [bis(trifluoroacetoxy)iodo]perfluoroalkanes, $C_nF_{2n+1}I(OCOCF_3)_2$. They are relatively stable, serve as electrophilic perfluoroalkylating agents, as precursors for (perfluoroalkyl)aryliodonium salts and applicable as effective and easily recyclable oxidative reagents.

Among the iodylarenes **12**, only iodylbenzene, $PhIO_2$, has found relatively wide practical application in modern organic synthesis as an oxidizing agent. The most important representatives of five-membered iodine(V) heterocycles are 2-iodoxybenzoic acid (IBX) **13** and analogues and Dess-Martin periodinane (DMP) **14.** Both IBX and DMP are highly efficient, mild and chemoselective agents for the variety of synthetically useful oxidative transformations. Aryliodyl derivatives bearing an appropriate substituent in the *ortho*-position to the iodine are characterized by the presence of a pseudocyclic structural moiety due to an intramolecular secondary bonding between the hypervalent iodine center and the oxygen atom in the *ortho*-substituent.



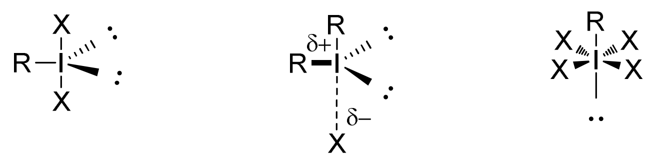
Scheme 2

Pseudo-benziodoxoles **15**, **16** and pseudo-benziodoxazines **17** are the main classes of pseudocyclic iodine(V) derivatives; they have found growing practical application as efficient oxidizing reagents, and they are now established reagents in modern organic synthesis.

Structural aspects of polyvalent iodine compounds have previously been discussed in the literature.[1,2,34,44-46] A brief summary of the key structural features of iodine(III) and iodine(V) compounds is provided below. According to IUPAC recommendations, all known organic polyvalent iodine derivatives include two general structural types (Scheme 3):

1) iodine(III) compounds **18** and **19**, also named λ^3-iodanes,
2) iodine(V) compounds **20**, or λ^5-iodanes.

The iodine atom in λ^3-iodanes **18** has a total 10 electrons, and its overall geometry is a distorted trigonal bipyramid. The least electronegative carbon ligand R and both electron pairs reside in equatorial positions, and two heteroatom ligands X occupy the apical positions. In this so called hypervalent model, bonding in RIX_2 uses the non-hybridized 5p orbital of iodine in the linear X–I–X bond. This linear three-center, four-electron (3c–4e) bond is highly polarized and is longer and weaker than a regular covalent bond. The term “hypervalent” is accepted for this type of bond, and the presence of this bond in λ^3-iodanes is responsible for their electrophilic reactivity.



18 **19** **20**

R=carbon ligand; X=halogen, O-, or N-ligand.

Scheme 3

According to this terminology, within iodine(III) derivatives only classes **1**–**7** can be truly referred to as “hypervalent iodine reagents”. Iodonium salts **19** posses a similar pseudo trigonal bipyramidal geometry, which also belongs to λ^3-iodanes type, and have two carbon ligands and a closely associated anionic part of the molecule. The experimentally determined bond angle R–I–R in iodonium salts and ylides is close to 90°, which is in good agreement with described model. Organic λ^5-iodanes **20** have a distorted octahedral structure. The electron pair and the organic group R, connected to iodine by a normal covalent bond using 5sp-hybridized orbital, are in the apical positions. Two orthogonal hypervalent 3c–4e bonds accommodate four heteroatom ligands X.

The structure and reactivity of several classes of hypervalent iodine compounds were investigated theoretically[47-61] using various computational methods and the results of some of these studies were found to be in good agreement with experimental observations. Numerous X-ray crystal structures, several important spectroscopic (NMR, LC-MS, ESI-MS, ESI-MS/MS) structural studies[62-66], and results of other general structural studies have been recently reported[67-86] for all main classes of organic polyvalent iodine compounds.

This review summarizes the recent literature data on the preparation and synthetic applications of selected classes of hypervalent iodine(III) and iodine(V) reagents, which are closely related to the studies made during our own research efforts.

1.2. Preparation of Hypervalent Iodine(III) and Iodine(V) Reagents

This section of the review will cover the preparation of selected classes of hypervalent iodine(III) and iodine(V) compounds such as [bis(acyloxy)iodo]arenes, $ArI(OCOR)_2$; [hydroxy(organosulfonyloxy)iodo]arenes, $ArI(OH)OSO_2R$; stabilized alkyl substituted λ^3-iodanes of types $C_nF_{2n+1}I(OCOCF_3)_2$ and $C_nF_{2n+1}I(OH)OSO_2R$, and iodylarenes, $ArIO_2$.

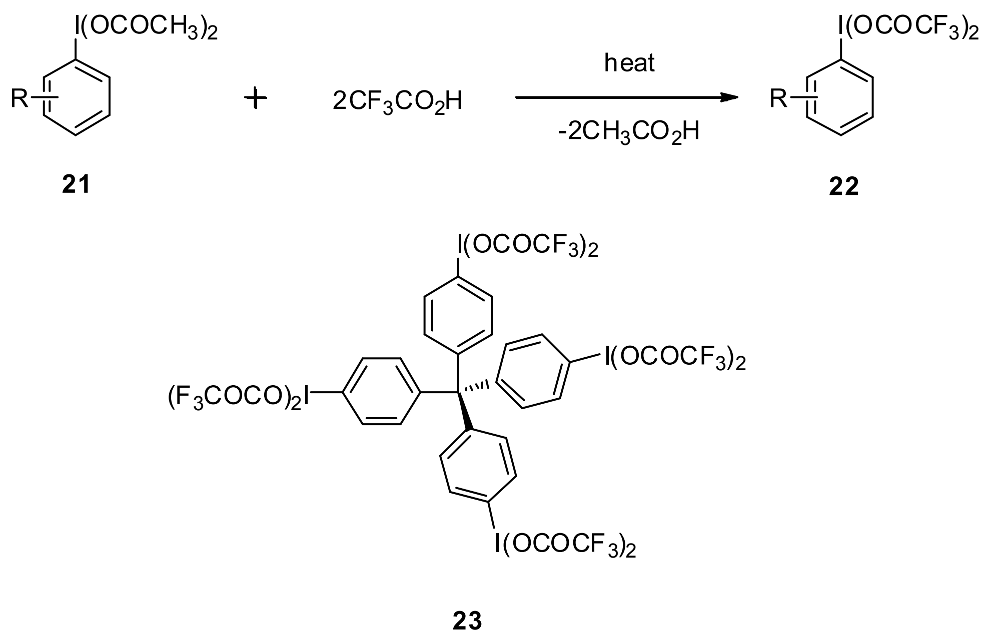
A. [Bis(acyloxy)iodo]arenes, $ArI(OCOR)_2$

[Bis(acyloxy)iodo]arenes **4**, $ArI(OCOR)_2$, are the most important, well investigated, and useful organic derivatives of iodine(III). Two of them, (diacetoxyiodo)benzene, most frequently abbreviated as DIB[1], and [bis(trifluoroacetoxy)iodo]benzene, commonly abbreviated as BTI[1] or PIFA [(phenyliodinebis(trifluoroacetate)], are commercially available, and found to be applicable to various oxidative transformations. Utilization of [bis(acyloxy)iodo]arenes allows performing such transformations as oxidation of alcohols; oxidative functionalization of carbonyl derivatives and unsaturated compounds; oxidative cationic cyclizations, rearrangements, and fragmentations; oxidative dearomatization of phenolic substrates; oxidative coupling of electron-rich aromatic substrates; radical cyclizations, rearrangements and fragmentations; oxidations of nitrogen, phosphorus, and sulfur compounds under mild conditions in high yields[45]. There are several methods that have been developed for preparation of various [bis(acyloxy)iodo]arenes. However, in this section emphasis will only be made on the synthesis of [bis(trifluoroacetoxy)iodo]arenes, $ArI(OCOCF_3)_2$, because it is most closely connected to our own research that will be discussed in the next chapter.

In general, all reported methods for preparing of [bis(trifluoroacetoxy)iodo]arenes can be divided into two main groups:

1) the indirect route, which is a simple ligand-exchange reaction on an already-oxidized iodine (III) compound,
2) the direct route, which is commonly an oxidation of iodoarenes in presence of carboxylic acid.

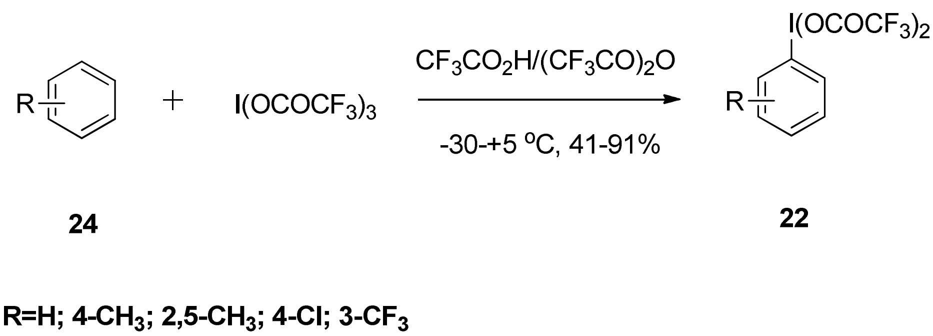
The most general approach is the ligand-exchange reaction using trifluoroacetic acid and (diacetoxyiodo)arenes[87] **21** (Scheme 4). Simply dissolving the latter in acid with heating converts the diacetate to the [bis(trifluoroacetoxy)iodo]arene **22**. This method has recently been applied to the synthesis of a new recyclable hypervalent iodine (III) reagent **23**[88]. The success of this method is related to the electronic properties of the (diacetoxyiodo)arene. In case of electron-poor substrates, the reaction rate is usually low, and the contamination of a product with (diacetoxyiodo)arenes has been reported.



Scheme 4

Also, the presence of strong protic acids in the reaction mixture restricts the synthetic applications of this approach (in particular, the generation of the reagent *in situ*).

Another approach is the reaction of arenes **24** with tris(trifluoroacetoxy)iodine by electrophilic aromatic substitution[89] (Scheme 5). This procedure affords [bis(trifluoroacetoxy)iodo]arenes **22** from arenes having either electron-donating groups (i.e. CH_3-group) or electron-withdrawing groups of a medium strength in generally high yields.

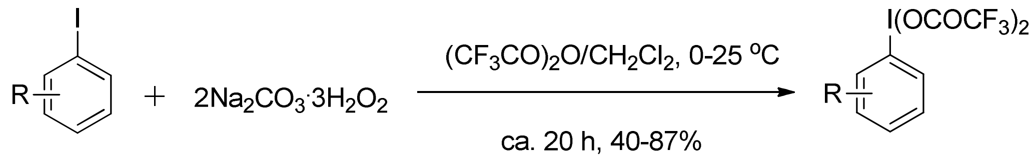


Scheme 5

There is no reaction with arenes bearing strong electron-withdrawing substituents (e.g. nitro). In the case of activated substrates bearing strong electron-donating substituents, like methoxy, no product was isolated because of oxidative decomposition.

Other indirect methods include the reaction of (dichloroiodo)arenes with silver trifluoroacetate[90] or the reaction of iodosylarenes with trimethylsilyl trifluoroacetate[91]. However, these approaches have not found wide application in organic synthesis.

The direct oxidation of iodoarenes is a more convenient method, although the choice of appropriate oxidants must take into account the structure and the electronic properties of the iodoarene **25**. Thus, activated substrates can be oxidized by sodium percarbonate together with trifluoroacetic anhydride[92] (Scheme 6). This method affords the corresponded [bis(trifluoroacetoxy)iodo]arenes **22** in relatively high yields in approximately 20 hours. However, this protocol is not applicable to substrates bearing electron-withdrawing groups like nitro and adducts with trifluoromethyl were obtained in only 40% yield.

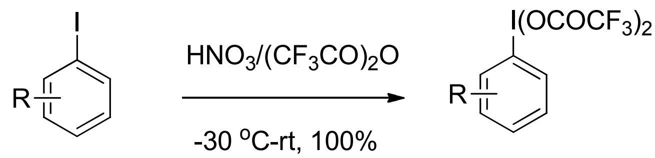


25 **22**

R=H, 2-CH_3, 3-CH_3, 4-CH_3, 3-CF_3, 4-F, 4-Cl

Scheme 6

Oxidation using nitric acid in trifluoroacetic anhydride[93] or potassium persulfate in a mixture of trifluoroacetic acid and methylene chloride[94] are very efficient methods for the preparation of [bis(trifluoroacetoxy)iodo]arenes **22** starting from deactivated iodoarenes (Schemes 7, 8).

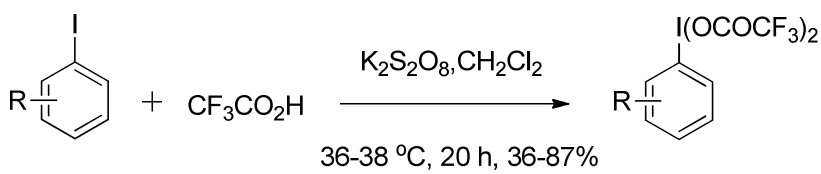


25 **22**

R=3-CF_3, 3-NO_2, 4-NO_2

Scheme 7

Utilization of a mixture of nitric acid and trifluoroacetic anhydride provides products in quantitative yields. However, this procedure is accompanied with a vigorous evolution of toxic nitrogen oxides.



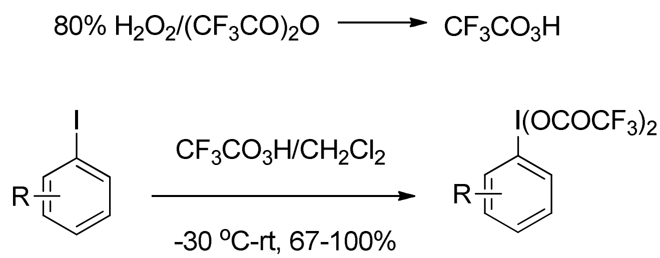
25 **22**

R=H, 4-F, 4-Cl, 4-Br, 3-NO_2, 4-NO_2, 3-CF_3, 3,5-CF_3

Scheme 8

Potassium persulfate is very convenient reagent to generate in good yields [bis(trifluoroacetoxy)iodo]arenes **22** bearing strong electron-withdrawing groups at the *meta* and *para* positions. However, 1-[bis(trifluoroacetoxy)iodo]-3,5-bis(trifluoromethyl)benzene was obtained in only 36% yield due to the lower reactivity of the starting iodoarene. Both methods are not applicable for iodoarenes with strong electron-donating groups.

Various [bis(trifluoroacetoxy)iodo]arenes can be synthesized by the oxidation of the respective iodoarenes with peroxytrifluoroacetic acid in trifluoroacetic acid[95-97] (Scheme 9).



25 **22**

R=H, 4-F, 4-CF_3, 3,5-CF_3, NO_2, 4-CH_3

Scheme 9

A typical procedure consists of mixing an appropriate iodoarene **25** with pertrifluoroacetic acid, prepared *in situ* from 80% H_2O_2 and trifluoroacetic anhydride, at low temperature followed by stirring at room temperature for additional 8–10 hours. Evaporation of the solvent affords the corresponding trifluoroacetate **22** in relatively high yield. This method is suitable for iodoarenes bearing either electron-donating groups or electron-withdrawing groups. However, the procedure requires 80% H_2O_2, which is very dangerous and not commercially available.

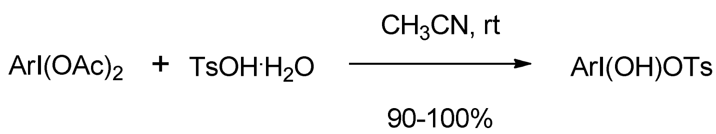
Other available methods include the oxidation reactions of iodoarenes in trifluoroacetic anhydride using such oxidants as H_2O_2-urea adduct[98] or xenon bis(trifluoroacetate)[99]. Both approaches are characterized with relatively high yields, and are suitable for activated and deactivated iodoarenes. However, the xenon bis(trifluoroacetate) method requires low temperatures and argon atmosphere in order to perform a reaction successfully, and in the H_2O_2-urea procedure different protocols are applied depending on the tolerance of the corresponding trifluoroacetates to an aqueous workup.

[Bis(trifluoroacetoxy)iodo]arenes are generally colorless, stable microcrystalline solids, which can be easily recrystallized and stored for a relatively long periods of time without significant decomposition.

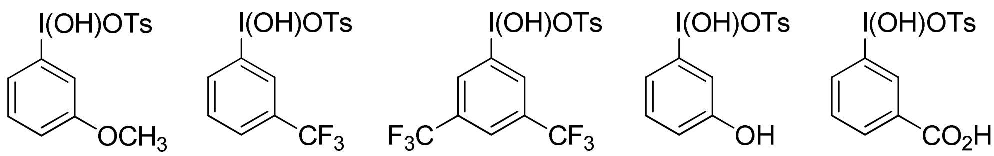
B. [Hydroxy(organosulfonoxy)iodo]arenes, $ArI(OH)OSO_2R$

[Hydroxy(organosulfonyloxy)iodo]arenes **5**, $ArI(OH)OSO_2R$, are one of the most common, well established, and practically useful aryliodine(III) derivatives. The most important is [hydroxy(tosyloxy)iodo]benzene (HTIB, Koser's reagent)[27]. It is commercially available and widely used as an oxidizing reagent in various synthetic applications.

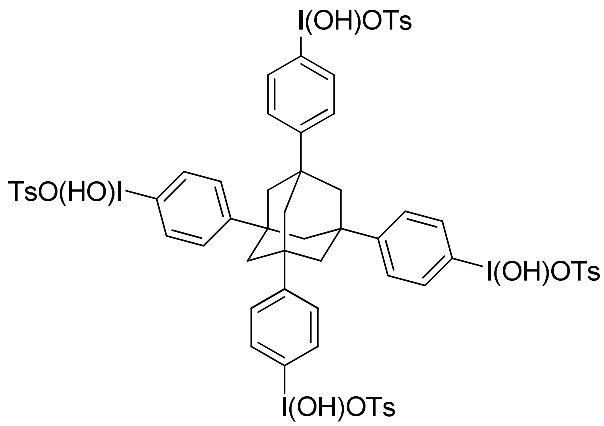
Ligand-exchange reaction of (diacetoxyiodo)arenes **26** with *p*-toluenesulfonic acid monohydrate ($TsOH{\cdot}H_2O$) in acetonitrile[88,100-105] is usually used for preparation of various [hydroxy(tosyloxy)iodo]arenes **27** (Scheme 10). This method is applicable to the synthesis of the derivatives with various substituted aromatic groups **28-32**[100,101,105], using the recyclable hypervalent iodine reagent **33**[102]. A closely related approach[104] uses benzenesulfonic, 4-nitrobenzenesulfonic and 4-chlorobenzenesulfonic acids in acetonitrile to afford the corresponding [hydroxy(organosulfonyloxy)iodo]arenes **5**, $ArI(OH)OSO_2R$ (Ar=Ph; R=C_6H_5, 4-$NO_2C_6H_4$, 4-ClC_6H_4), in a good yield (51-91%).



26 **27**



28 **29** **30** **31** **32**



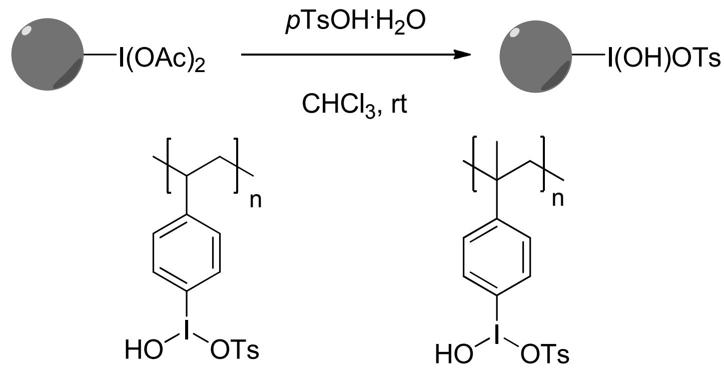
33

Scheme 10

A solvent-free, solid-state modification of this reaction[106] is performed by simple grinding of corresponding (diacetoxyiodo)arenes (phenyl, naphthyl) with the appropriate sulfonic acid (p-toluenesulfonic, methanesulfonic, (*1R*)-10-camphorylsulfonic) in an agate mortar. This is followed by washing the solid residue with diethyl ether and drying under high vacuum. This easy and very convenient solid-state approach has been used for the preparation of HTIB and several other [hydroxy(organosulfonyloxy)iodo]arenes (1- and 2-naphthyl) in 77-98% yields.

The recyclable, polymer-supported analogues **34** and **35** of [hydroxy(tosyloxy)iodo]benzene can be prepared similarly by treatment of poly[4-

(diacetoxy)iodo]styrene and poly{α-methyl[(diacetoxy)iodo]styrene with *p*-toluenesulfonic acid monohydrate in chloroform at room temperature[107-108] (Scheme 11).



34 **35**

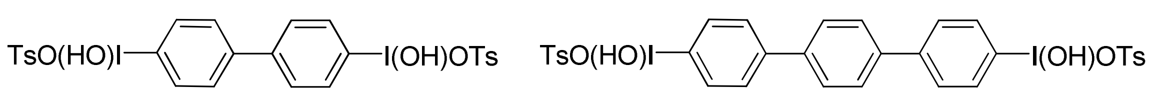
Scheme 11

Another useful, slightly modified procedure for the preparation of various [hydroxy(sulfonyloxy)iodo]arenes **27** includes the one-pot reaction of iodoarenes **36** and p-toluenesulfonic acids in the presence of *m*CPBA in a small amount of chloroform at room temperature[109] (Scheme 12). This method affords various [hydroxy(sulfonyloxy)iodo]arenes **27** in a high yield within approximately 2 hours. This convenient procedure has been recently utilized for the synthesis of new biphenyl- and terphenyl-based recyclable organic iodine(III) reagents **37** and **38**[103].

$$\text{ArI} + \text{TsOH}\cdot\text{H}_2\text{O} \xrightarrow[\text{rt, 75-100\%}]{m\text{CPBA, CHCl}_3} \text{ArI(OH)OTs}$$

36 **27**

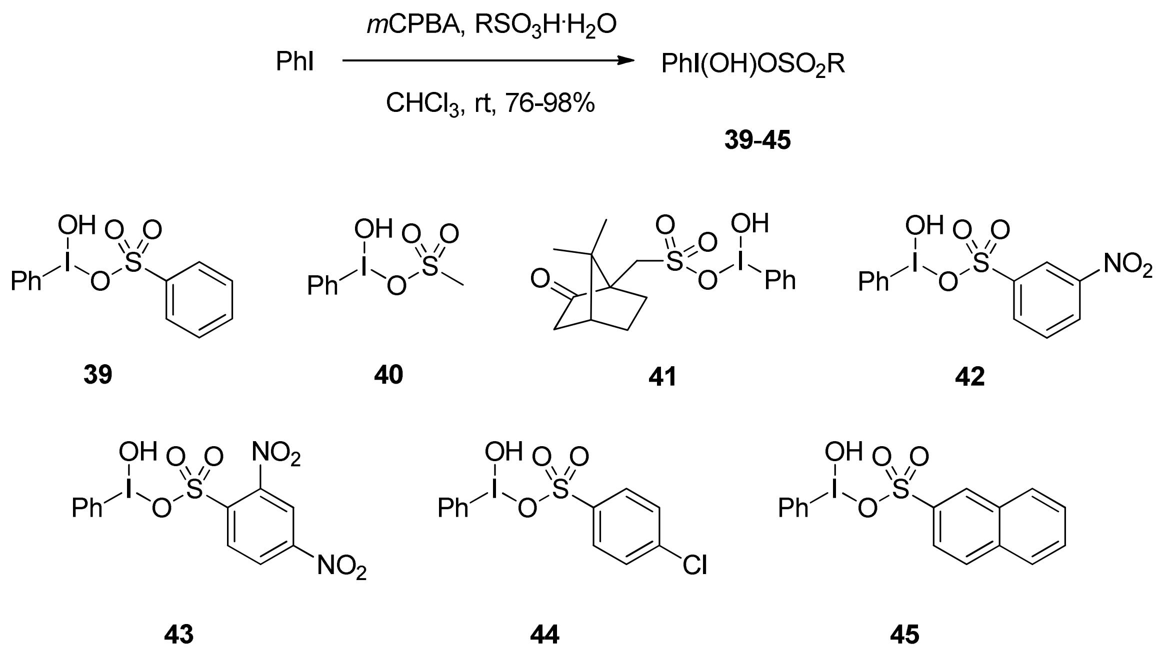
Ar=C_6H_5, 4-$CH_3C_6H_4$, 2-$CH_3C_6H_4$, 3-$CF_3C_6H_4$, 2-$CF_3C_6H_4$, 4-ClC_6H_4



37 **38**

Scheme 12

The synthetic applicability of this method was successfully extended by using iodobenzene with other sulfonic acids such as benzenesulfonic, methanesulfonic, (*1R*)-10-camphorylsulfonic acids and several others[109]. The corresponding organosulfonyloxy analogs **39-45** were obtained smoothly, in 76-98% yields (Scheme 13).



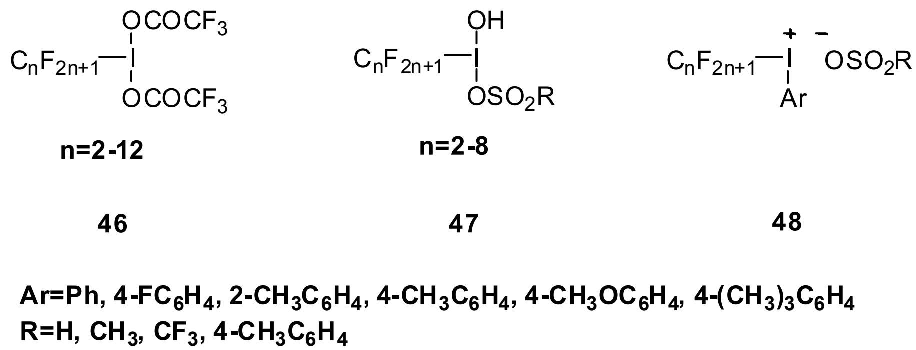
Scheme 13

[Hydroxy(organosulfonyloxy)iodo]arenes **5**, $ArI(OH)OSO_2R$, are usually very stable and almost not sensitive to moisture, and have relatively good storage ability.

C. Stabilized Alkyl Substituted λ^3-Iodanes: Types $C_nF_{2n+1}I(OCOCF_3)_2$ and $C_nF_{2n+1}I(OH)OSO_2R$

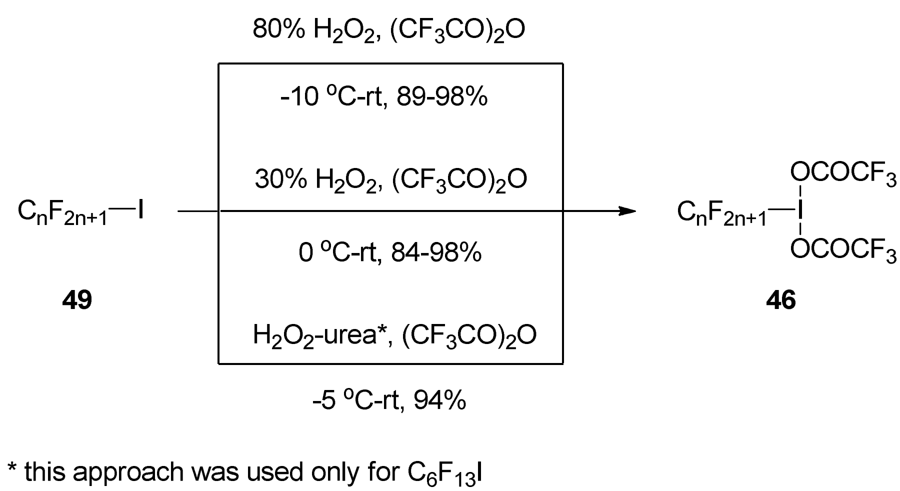
Derivatives of polyvalent iodine with an alkyl substituent at the iodine, so called alkyl substituted λ^3-iodanes **11**, generally are highly unstable and can exist only as short-lived reactive intermediates in the oxidation of alkyl iodides. However, introduction of an electron-withdrawing substituent, such as fluorine atoms or a sulfonyl group, in the alkyl moiety may lead to significant stabilization of the molecule. [Bis(trifluoroacetoxy)iodo]perfluoroalkanes **46**[110-116] and [hydroxy(sulfonyloxy)iodo]-

perfluoroalkanes **47**[111,118] are specially well-investigated and important representatives of stabilized alkyl substituted λ^3-iodanes (Scheme 14). Both **46** and **47** have found wide application in modern organic synthesis as reagents for selective oxidative transformations. They also serve as precursors for various fluoroalkyl(phenyl)iodonium salts that now are routinely used as electrophilic fluoroalkylating reagents (FIS or FITS reagents[4], $ArIC_nF_{2n+1}\cdot OSO_2R$ **48**).



Scheme 14

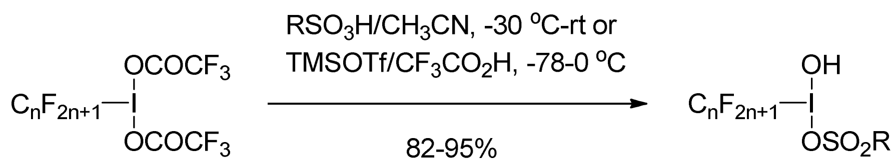
The trifluoroacetate derivatives **46** are usually prepared by the oxidation of appropriate perfluoroalkyl iodides **49** with peroxytrifluoroacetic acid, which is generated *in situ* from 80% hydrogen peroxide and trifluoroacetic anhydride, followed by removal of the volatile products in vacuum[114,115,117] (Scheme 15).



Scheme 15

This procedure affords the corresponding trifluoroacetates in almost quantitative yield. However, it requires 80% hydrogen peroxide, which is dangerous and not commercially available.

Umemoto[119] and co-workers found that [bis(trifluoroacetoxy)iodo]-perfluoroalkanes **46** can also be more safely prepared in high yield using commercial 30% H_2O_2 and an excess of trifluoroacetic anhydride in trifluoroacetic acid at 0 °C. Another safe and convenient procedure for the preparation of [bis(trifluoroacetoxy)iodo]-perfluoroalkanes **46** by the oxidation of commercial perfluoroalkyl iodides using urea-hydrogen peroxide complex in a mixture of trifluoroacetic anhydride and trifluoroacetic acid at –5 to 0 ^{o}C has been recently reported[111]. However, the applicability of this method is known only for perfluorohexyl iodide.



46 **47**

n=2-8; R=CH$_3$, CF$_3$, 4-CH$_3$C$_6$H$_4$

Scheme 16

[Hydroxy(sulfonyloxy)iodo]perfluoroalkanes **47** can be easily prepared in high yield by treatment of trifluoroacetates **46** with an appropriate sulfonic acid in acetonitrile[117,120] (Scheme 16). In comparison to [bis(trifluoroacetoxy)iodo]-perfluoroalkanes **46**, the corresponding sulfonates (R=CH_3, 4-$CH_3C_6H_4$) have substantially higher thermal stability and moisture resistance. They can be purified by recrystallization from an appropriate solvent, and stored for a long periods of time. The analogous triflates (R=CF_3), prepared by reaction of **46** with trimethylsilyl triflate in trifluoroacetic acid[111], are hygroscopic and less stable than other tosylates. However, they can be stored under dry conditions for several weeks at room temperature without significant decomposition.

D. Iodylarenes, $ArIO_2$

Iodylarenes, $ArIO_2$ **12**, which are also known as iodoxy compounds, are now relatively well investigated iodine(V) compounds. These compounds possess a polymeric structure, which makes them insoluble in the majority of organic solvents (with the exception of DMSO) and have an explosive character. However, iodylarenes have found some synthetic application as mild and highly selective reagents for the oxidation of alcohols to carbonyl compounds, as well as for a variety of other useful oxidative transformations. Among various $ArIO_2$ derivatives, iodylbenzene $PhIO_2$ **48** is the most popular[27].

$$\underset{\mathbf{3}}{(PhIO)_n} \xrightarrow{H_2O,\ 100\ ^oC} \underset{\mathbf{48}}{0.5\ PhIO_2} + 0.5\ PhI$$

Scheme 17

Iodylarenes are commonly prepared by the direct oxidation of iodoarenes with strong oxidants or by disproportionation of iodosylarenes. Willgerodt first observed that the disproportionation of iodosylbenzene **3** (n=1) under steam distillation afforded iodylbenzene **48** and iodobenzene[121] (Scheme 17).

Oxidation of iodoarenes is a more convenient approach. Indeed, it is assumed that the initial oxidation of ArI usually leads to iodosylarenes, ArIO, which then slowly disproportionate to ArI and $ArIO_2$ upon gentle heating[122-124].

$$\underset{\mathbf{36}}{ArI} \xrightarrow{\text{Oxidant}} \underset{\mathbf{12}}{ArIO_2}$$

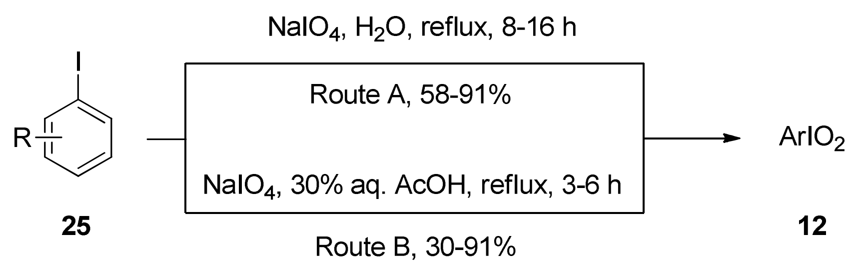
Scheme 18

The most common oxidizing reagents that have been used for the preparation of iodylarenes **12** from iodoarenes include sodium hypochlorite[75,122], potassium bromate[125], dimethyldioxirane[126] and Oxone®[127]. (Scheme 18, Table 1).

Table 1. Synthesis of iodylarenes **12** by the oxidation of iodoarenes.

Ar	Conditions	Yield, %
C_6H_5	$KHSO_5/KHSO_4/K_2SO_4$, H_2SO_4, 0 °C, 4 h	72
C_6H_5	$KBrO_3$, H_2SO_4, heating, 2 h	45
$3\text{-}NO_2C_6H_4$	$KBrO_3$, H_2SO_4, heating, 2 h	46
$4\text{-}BrC_6H_4$	$KBrO_3$, $AcOH/H_2SO_4$, heating, < 1 h	98
$2\text{-}CH_3O_3SC_6H_4$	dimethyldioxirane, CH_2Cl_2, 0 °C to rt, 8 h	89
$2\text{-}iPrO_2CC_6H_4$	5% aq. NaOCl, dry ice, rt, 12 h	89
$2\text{-}Ph_2(O)PC_6H_4$	5% aq. NaOCl, TBAB, H_2O/CH_2Cl_2, rt, 12 h	71

Recently Skulski and coworkers reported 2 new convenient procedures for the oxidation of iodoarenes **25** to corresponding iodylarenes **12** using sodium periodate as the oxidant[124].

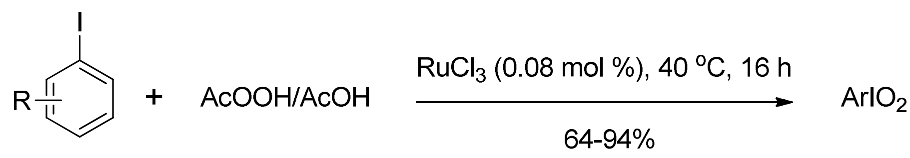


Route A: R=H; 3-CO_2H; 4-OCH_3; 4-CH_3; 3-CH_3; 2-CH_3; 4-F; 4-Cl; 3-Cl; 4-Br; 4-NO_2; 3-NO_2; 4-CO_2Na; 3-CO_2Na
Route B: R=H; 4-CH_3; 3-CH_3; 2-CH_3; 4-F; 3-F; 4-Cl; 3-Cl; 2-Cl; 4-Br; 4-NO_2; 3-NO_2; 2-NO_2; 2,4-CH_3; 2,4-Cl

Scheme 19

The reaction was performed in boiling water[123], but improved protocol by using boiling 30% aqueous acetic acid (Scheme 19). The heterophasic reactions of various iodoarenes suspended in vigorously stirred boiling aqueous sodium periodate solutions (Route A) proceed smoothly within 8-16 hours to give the corresponding colorless iodylarenes in 58-91% crude yields. An improved method (Route B) allows shortening the time of reaction from 8-16 h to 3-6 h while preserving the same high purities (96-99%) of products. There is no need for any further purification and the iodylarenes **12** may be used directly in subsequent transformations.

A new efficient methodolology for the preparation of iodylarenes **12** using peroxyacetic acid as an oxidant in the presence of catalytic amounts of ruthenium trichloride has recently been reported[128,129] (Scheme 20).

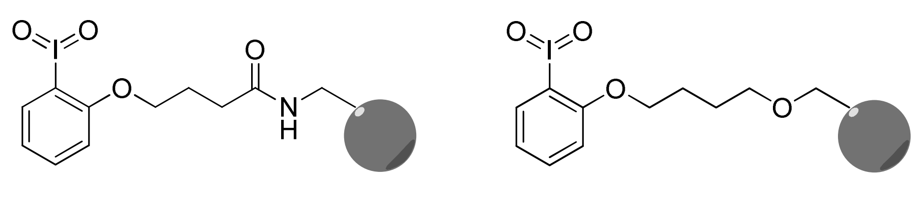


25 **12**

R=H; 4-CH_3; 2-CH_3; 2-iPr; 2-OCH_3; 4-Cl; 3-Cl; 2-Cl; 4-Br; 4-F; 4-CF_3; 3,5-CF_3

Scheme 20

This facile one-pot procedure combines the known peracetic oxidation of ArI to $ArI(OAc)_2$ and the immediate disproportionation of the iodine(III) species in the presence of $RuCl_3$ leading to $ArIO_2$ as the final product. The reaction is proceeding under much milder conditions (gentle warming to 40 °C) compared to the known noncatalytic oxidation of PhI to $PhIO_2$ with peracetic acid at 100 °C. Because of these gentle conditions, the procedure is congruous with the presence of the electron-donating (alkyl and alkoxy) groups in the aromatic ring. This method also allows the transformation of iodoarenes bearing strongly electron-withdrawing substituents (CF_3-groups) in the aromatic ring into subsequent iodylarenes[129]. The procedure, in general, is limited to the nonsterically hindered substrates.



49 **50**

Scheme 21

Several polymer-supported analogs of 2-iodylphenol ethers, such as **49** and **50**, have also been reported[130] (Scheme 21). The synthesis of these reagents employs commercially available aminomethylated polystyrene and Merrifield's resin, includes four or five simple steps, and affords the resins **49** and **50** with good loadings of 0.74-0.86 and 0.50-0.55 g/mmol, respectively. Recycling of the resins is possible with minimal loss of activity after several reoxidations[130].

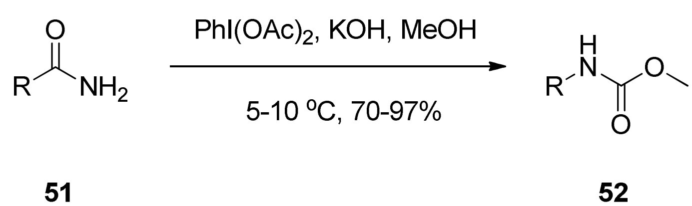
1.3. Reactions of Hypervalent Iodine(III) and Iodine(V) Reagents

Iodine(III) and iodine(V) compounds are now routinely used in modern organic synthesis. This section will summarize recent research on synthetic applications of several classes of hypervalent organoiodide compounds with emphasis on the oxidation of alcohols and hydrocarbons, and the rearrangements at electron-deficient centers (e.g. Hofmann-type rearrangements).

A. Oxidative Rearrangements Using Iodine(III) Compounds

[Bis(acyloxy)iodo]arenes and aryliodine(III) organosulfonates are commonly used as the reagents in various cationic rearrangements and fragmentations[44,45]. These reagents can also serve as excellent oxidants in Hofmann-type degradations, which includes the multistep transformation of primary carboxamides to primary amines *via* an intermediate isocyanate.

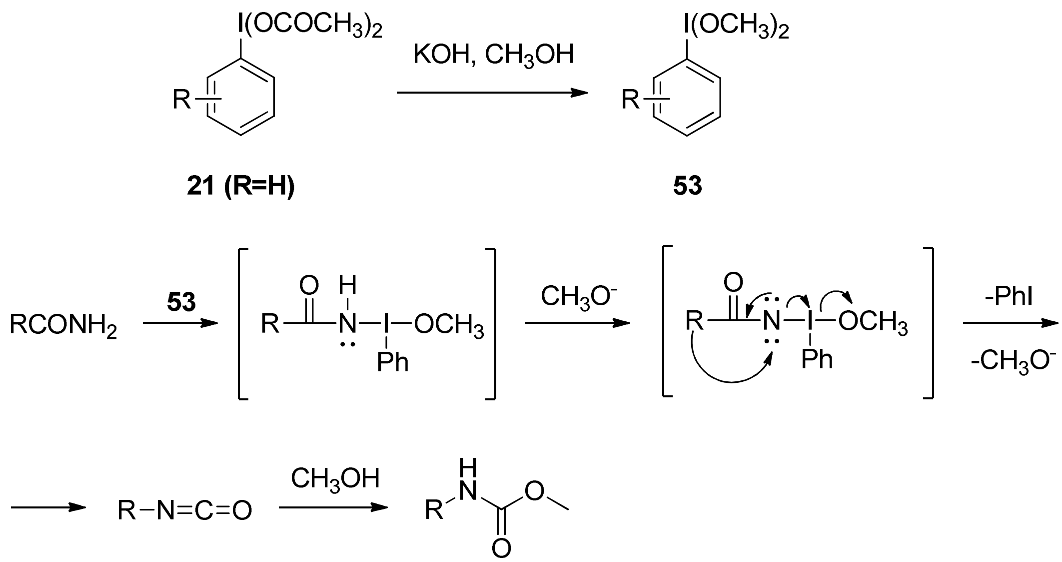
(Diacetoxyiodo)benzene has been employed effectively for the Hofmann-type rearrangement (Scheme 22).



R=cyclopropyl, adamantyl, phenyl, 2-pyridyl, 6-quinolyl, others

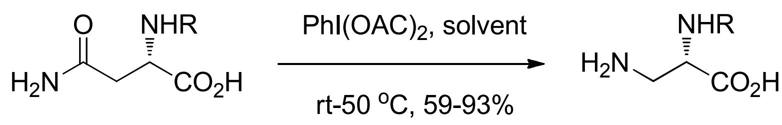
Scheme 22

A typical procedure[131,132] involves the use of DIB in methanolic KOH at 5-10 °C. Various carbamates **52** are generated in good yields from the corresponding carboxamides **51**. The mechanism[132,133] of this reaction is proposed to involve the formation of $PhI(OMe)_2$ **53** *in situ*, which reacts with the amide **51** to form $RCONHI(OCH_3)Ph$ that subsequently rearranges to the isocyanate intermediate **54** under the influence of base (Scheme 23). Under these conditions the isocyanate is trapped by methanol, to afford the carbamate **52**.



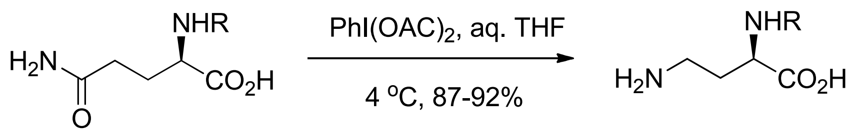
Scheme 23

Under acidic conditions the mechanism is assumed to involve the formation of $RCONHI(OCOCH_3)Ph$ followed by the rearrangement into isocyanate. In the mixture of CH_3CN-H_2O the isocyanate is rapidly hydrolyzed to the amine, which in the case of arylamines, is further oxidized[131,134,135]. If acetic acid is used as a solvent, the amide is converted to the acylamine presumably *via* the amine that is formed by hydrolysis[134].



55 **56**

R=Boc, Cbz, Fmoc, Carbethoxy, DDZ
Solvent: EtOAc/CH_3CN/H_2O; MeOAc/n-PrOH/H_2O; CH_3CN/H_2O

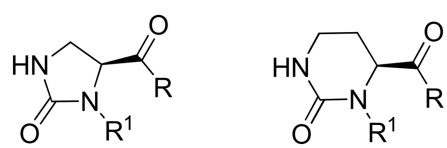


57 **58**

R=Boc, Cbz

Scheme 24

DIB is an excellent reagent for the Hofmann rearrangement of protected asparagines **55**[136] (Scheme 24). This reaction can be scaled to hundred kilogram quantities for the synthesis of optically pure β-amino-L-alanine derivatives **56**[137-140]. Similar chemistry leads to –2,4-diaminobutanoic acids (e.g., **57**→**58**[141,142]). An interesting fact is that utilization of $PhI(OAc)_2$ in presence of base [DBU or Et(i-Pr)$_2$N] in aq. THF[143] allows the transformation of protected asparagines **55** and glutamines into corresponding imidazolidin-2-one-4-carboxylates **59** and (tetrahydro)-pyrimidine-2-one-5-carboxylates **60**, respectively, in a good yield (Scheme 25).

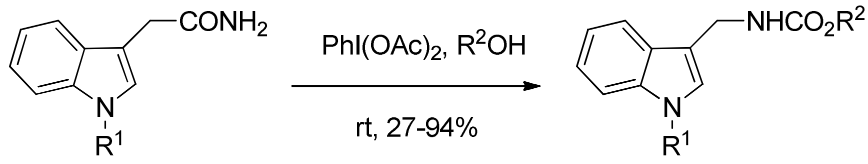


59 (87%) **60 (85%)**

R=OMe, OBn, L-Ala-OBn
R^1=Boc, Cbz, Ac

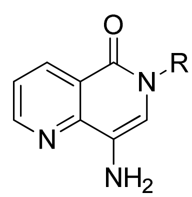
Scheme 25

Another synthetic application is the preparation of alkyl carbamates of 1-protected indole-3-methylamines **62** from the corresponding amides **61**[144] (Scheme 26). The unsubstituted indole-3-acetamide **61** (R=H) gives no product, but both thiopheneacetamides and pyrrolacetamides undergo the rearrangement under the same conditions.



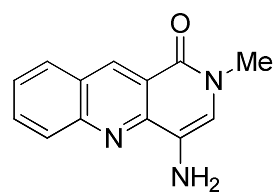
61 **62**

R¹=Ts, Bn, Boc; R²=Me, Et, i-Pr, t-Bu, Bn



63 (68-86%)

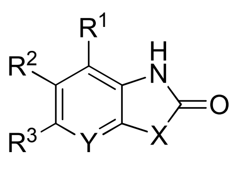
R=Me, 4-MeOPh



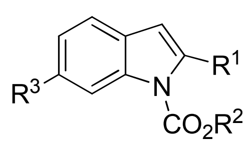
64 (61%)

Scheme 26

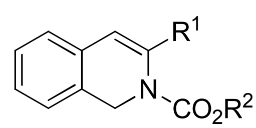
Amino heterocycles **63** and **64** were derived by base hydrolysis of the corresponding methyl carbamates (not isolated) obtained from their amides using $PhI(OAc)_2$[145].



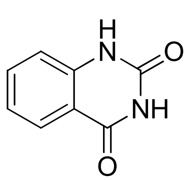
65 (52-84%)



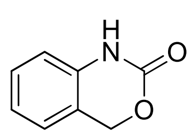
66 (33-100%)



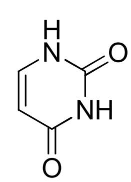
67 (66-92%)



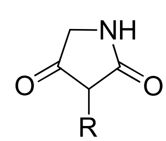
68 (95%)



69 (86%)



70 (64%)

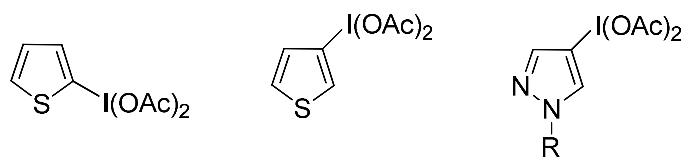


71 (37-80%)

Scheme 27

Other examples include the oxidative rearrangement of anthranilamides or salicylamides to the respective heterocycles **65**[146] (X=NH, NMe, NEt, NPr-i, NBu, NBn, O; Y=N, R^1=R^3=H/Ph, R^2=H; Y=CH, R^1=R^3=H/Br, R^2=H, Cl); synthesis of indoles **66** (R^1=H, n-Bu, Ph, p-Tol, $(CH_2)_3$OTs; R^2=Et, t-Bu, Bn; R^3=H, F, NO_2, OMe) and dihydroisoquinolines **67** (R^1=n-Bu, Ph, p-Tol; R^2=Me, Et, Bn) from corresponding 2-alkynylbenzamide and 2-alkynylbenzylamide[147]; oxidative cyclizations of various diamides yielding derivatives **68-71** (in **71** R= H, Et, Ph, $CH_2CH{=}CH_2$) in generally good yields[148] (Scheme 27).

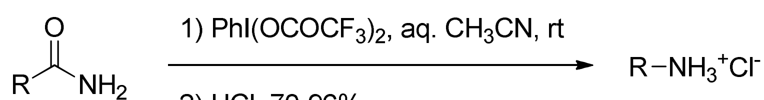
The utilization of a series of diacetoxy iodoheterocycles **72-74** in the Hofmann rearrangement has been recently reported[149] (Scheme 28). However, no advantage of these reagents over $PhI(OAc)_2$ was evident from this study.



72 **73** **74 (R=Tf, Ts)**

Scheme 28

It has been found that the somewhat less stable [bis(trifluoroacetoxy)-iodo]benzene **22** (R=H) also effects the Hofmann rearrangement of aliphatic and benzylic amides **51** to amines under mild conditions and without having to isolate the isocyanate intermediate[150-152] (Scheme 29).



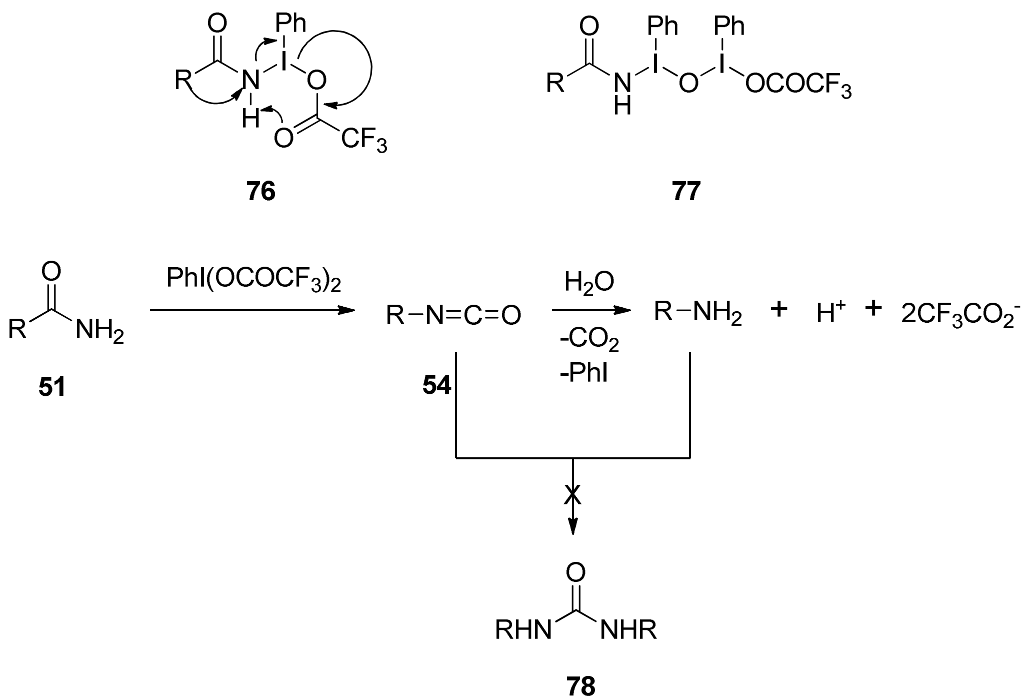
51 **75**

R=Et, $CH_3(CH_2)_4$, cyclohexyl, benzyl, 1-naphthyl-CH_2, p-$CH_3OC_6H_4CH_2$, others

Scheme 29

The product is usually isolated as a hydrochloride of amine **75** in a high yield. However, the reaction is not useful for the preparation of amines in which the nitrogen is directly bonded to an aromatic ring, since the corresponding amines are oxidized further[131,134,135].

A mechanistic study[152] of the $PhI(OCOCF_3)_2$-induced Hofmann rearrangement has led to the speculation that the key intermediate may be either **76** or **77**, which rearranges in a typical fashion to the isocyanate **54** (Scheme 30).

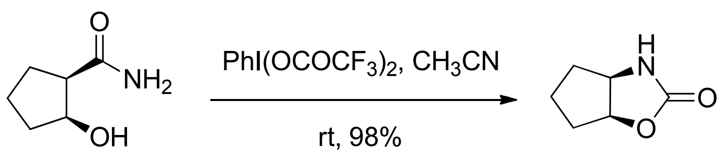


Scheme 30

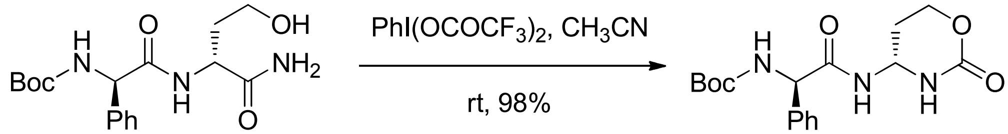
A side reaction expected from simultaneous presence of isocyanate and amine is the formation of ureas **78**. However, ureas are not detected as products in bistrifluoroacetate-promoted rearrangement because trifluoroacetic acid is liberated as a byproduct[151,152]. As a result the amine is protonated and therefore protected from undergoing nucleophilic reactions. The trifluoroacetic acid also performs the additional function of catalyzing the hydrolysis of the isocyanate. Other advantages of using $PhI(OCOCF_3)_2$ include the retention of stereochemical configuration at the migrating carbon during rearrangement.

Also, only primary amides are affected during reaction, secondary and tertiary amides do not react[151].

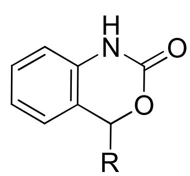
[Bis(trifluoroacetoxy)iodo]benzene is an excellent reagent for the preparation of 2-oxazolidinones (**79→80**) and 1,3-oxazinan-2-ones (**81→82**) *via* Hofmann rearrangement[153] (Scheme 31). In this case, the isocyanate intermediate undergoes an entropically favored intramolecular nucleophilic-addition reaction to give the cyclized products **80** and **82**. This method is superior to earlier conditions in terms of the yield of product, the cleanness of reaction, and the ease of purification. More importantly, these conditions can be easily adapted to the solution- and solid-phase construction of combinatorial libraries of 2-oxazolidinones.



79 **80**



81 **82**

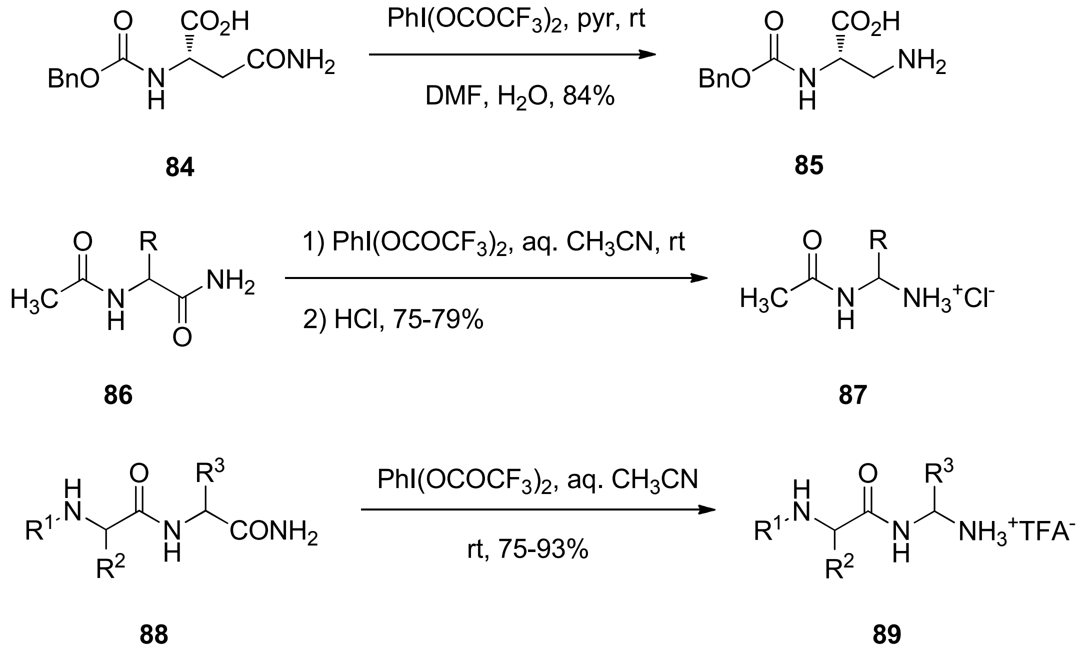


83

Scheme 31

Similarly, benzoxazinones of type **83** (R=n-propyl, Ph, 2-pyridyl, p-CH_3OPh) can be easily obtained from phthalides by a two-step protocol[154] *via* an aminolysis-Hofmann rearrangement. This method can potentially be applied to generate phthalide libraries.

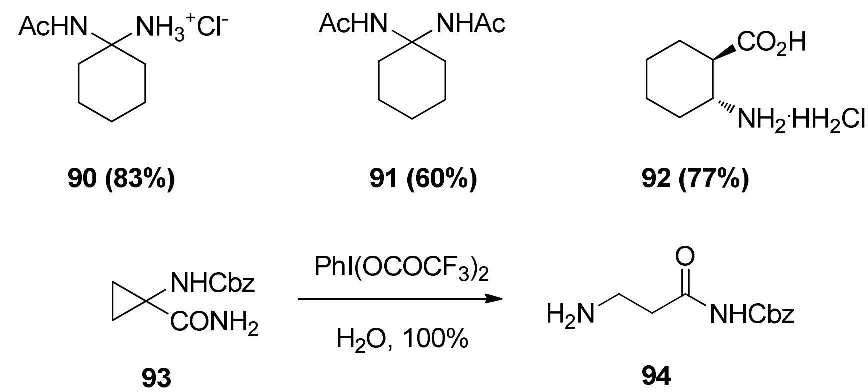
Another synthetic application includes the ability of BTI to degrade carboxyl-terminal amino acid amides *via* Hofmann rearrangement[155]. As such, this reagent has found extensive use in peptide chemistry for this specific cleavage protocol[156-158]. For example, N-benzyloxycarbonyl-L-asparagine **84** is smoothly converted to N-benzyloxycarbonyl-L-2,3-diaminopropanoic acid **85** in aq. DMF[156] (Scheme 32).



Scheme 32

Other examples include the preparation of geminal amino amides (*N*-[1-aminoalkyl]amides) **87**[151] from the amides of acylamino acids **86** (R=Et, i-Pr, benzyl), and the synthesis in generally high yields of optically pure monoacyl 2-alkyl gem-diamines **89**[157] directly from their peptide amide precursors **88**. For preparative purposes, peptide amides are convenient precursors and the amide provides an excellent protecting group.

Other applications include the synthesis of α-acetamidocyclohexylamine hydrochloride **90**[159], which serves as an excellent precursor for the gem-bisacetamide **91**[159]; the preparation of enantiomerically pure β-amino acids like **92**[160]; the formation of β-alanine derivative **94**[161] from cyclopropylamide **93** *via* a proposed mechanism involving ring expansion to a 2-pyrrolidinone, and the ring opening to an amido isocyanate followed by hydrolysis (Scheme 33).

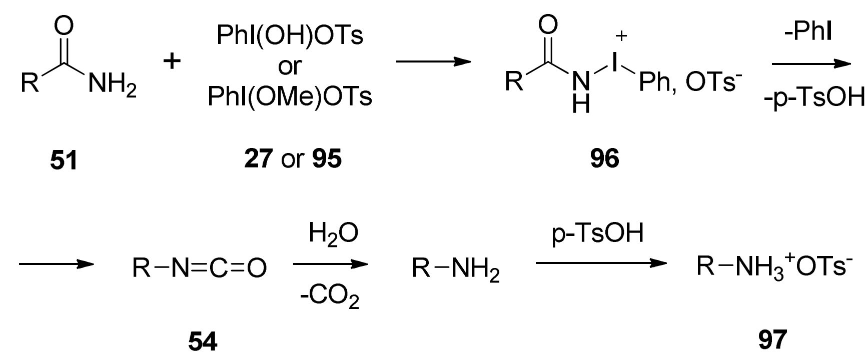


90 (83%) **91 (60%)** **92 (77%)**

93 **94**

Scheme 33

Reagents to DIB and BTI are [hydroxy(tosyloxy)iodo]benzene **27** ($Ar=C_6H_5$) and [methoxy(tosyloxy)iodo]benzene PhI(OMe)OTs **95** are also very useful in Hofmann-type rearrangements[162-164]. A plausible mechanism for this reaction involves the initial formation of N-phenyliodonio amide tosylate **96** and its subsequent collapse to isocyanate **54**, iodobenzene, and p-toluenesulfonic acid[162,164] (Scheme 34).



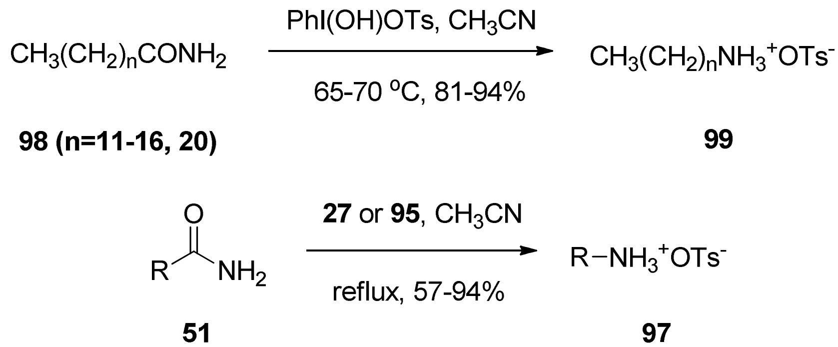
51 **27** or **95** **96**

54 **97**

Scheme 34

When PhI(OMe)OTs **95** was employed, several N-phenyliodonio amide tosylates **96** (R=Me, i-Pr, t-Bu, Ph, Bn) were isolated in 66-90% yield and characterized[164]. Hydration of the isocyanate, decarboxylation of the resulting carbamic acid, and protonation of the resulting amine with p-toluenesulfonic acid, which was present in the reaction mixture, affords the final product as an ammonium tosylate **97**.

[Hydroxy(tosyloxy)iodo]benzene is especially useful for the Hofmann rearrangement of long-chain primary amides **98** into the corresponding ammonium tosylates **99**[163] (Scheme 35).

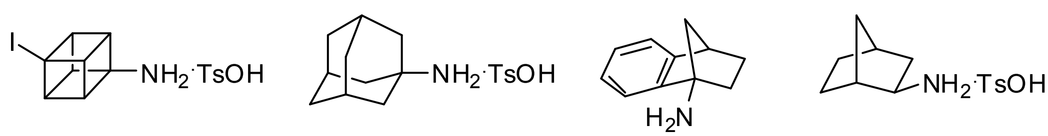


R=Me; Et; i-Pr; t-Bu; $CH_3(CH_2)_4$; $CH_3(CH_2)_6$; $CH_3(CH_2)_{10}$; CH_2=$CHCH_2$; cyclobutyl; cyclohexyl; Ph; benzyl

Scheme 35

This method is characterized by a generally high yield and a short time of reaction. The same approach[162] is very efficient for the preparation of other alkyl- and arylammonium tosylates **97** from carboxamides **51**.

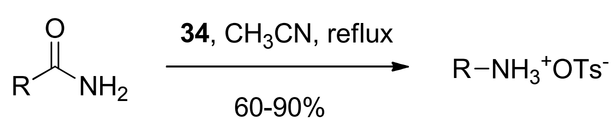
Moreover, PhI(OH)OTs has been also successfully used for the synthesis of several polycyclic amines **100-103**[165-168] (Scheme 36).



100 **101** **102** **103**

Scheme 36

Recently, polymer-supported reactions with poly([4-hydroxy-(tosyloxy)iodo]styrene) **34** have been reported[169] (Scheme 37).



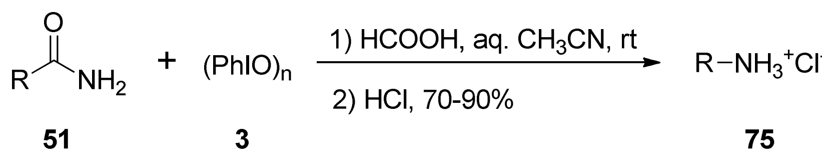
51 **97**

R=Me, Et, n-Pr, n-Hex, n-Hep, benzyl, others

Scheme 37

The yields are generally comparable to those obtained with PhI(OH)OTs. The reaction is mild, has operational simplicity and has the possibility of recycling the oxidizing agent.

Iodosylbenzene **3** (n=1) is also known to induce the Hofmann rearrangement of primary amides into amines in high yields under mild conditions in the presence of formic acid[170] (Scheme 38).



R=Bn ,4-$CH_3OC_6H_4CH_2$, $PhCH_2CH_2$, n-C_5H_{11}, i-$C_3H_7CH_2$, t-Bu

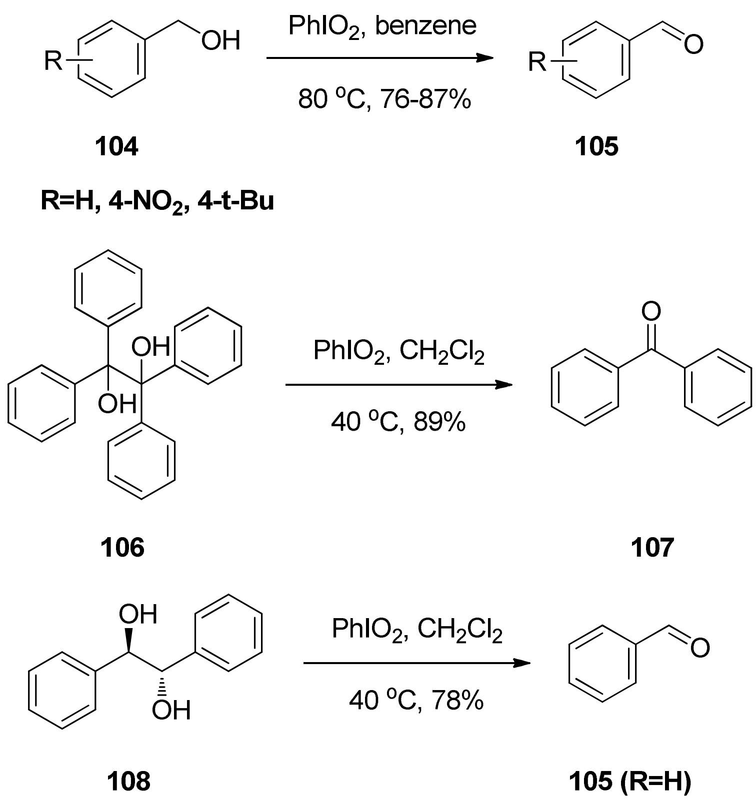
Scheme 38

Formic acid is assumed to catalyze the attack of water on the intermediate isocyanate and protonate the resulting amine. Iodobenzene released in the reaction can be easily isolated and recycled.

B. Oxidation of Alcohols and Hydrocarbons Using Iodylbenzene $PhIO_2$

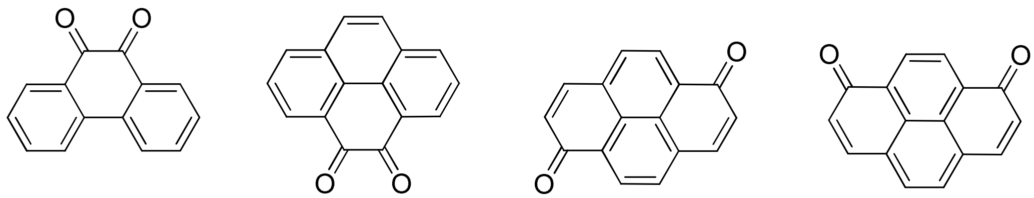
Several noncyclic $ArIO_2$ have been reported in the literature. These compounds are insoluble in the majority of organic solvents, with the exception of DMSO, and explosive under excessive heating (>200 °C) or mechanical impact. However, iodylarenes have found some practical application as oxidizing reagents. Among different $ArIO_2$, iodylbenzene $PhIO_2$ **48**, is the most popular reagent[123].

Iodylbenzene in benzene at 80 °C oxidizes benzylic alcohols **104**, giving the corresponding aldehydes **105** in good yield[171] (Scheme 39). $PhIO_2$ is also suitable for oxidation of glycols **106** and **107**, yielding the corresponding carbonyl derivatives **108** and **105** (R=H), respectively[171].

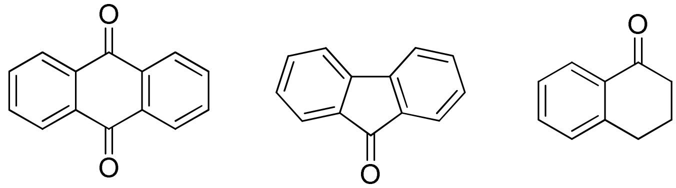


Scheme 39

Iodylbenzene in nitrobenzene at 170 °C also oxidizes activated C–H bonds[172]. This procedure is suitable for preparation of benzophenone **107** from 1,1,4,4-tetraphenylbuta-1,3-diene and diphenylmethane; phenanthrenequinone **109** from phenanthrene; pyrene-4,5-quinone **110**, pyrene-1,6-quinone **111** and pyrene-3,6-quinone **112** from pyrene; anthraquinone **113** from anthracene; fluorenone **114** from fluorine, and tetralone **115** from tetralin (Scheme 40).



109 (46%) **110 (14%)** **111 (12%)** **112 (15%)**

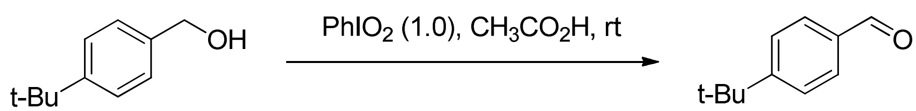


113 (60%) **114 (24%)** **115 (45%)**

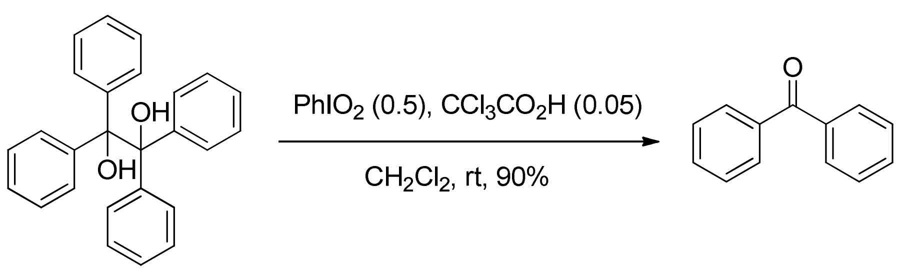
Scheme 40

C. Catalytic Oxidation of Alcohols Using Iodylbenzene $PhIO_2$

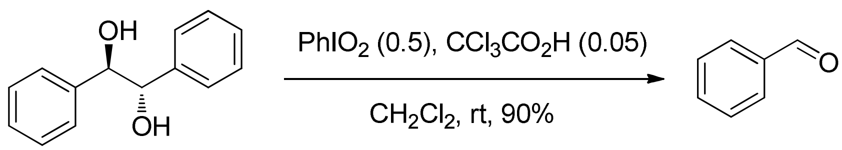
There are several catalytic systems employing iodylbenzene as an active oxidant that have been developed for the oxidation of alcohols[171,173,174].



116 **117**



106 **107**

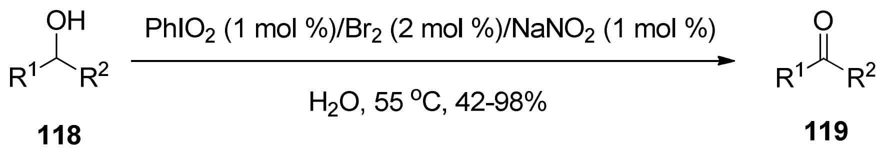


108 **105 (R=H)**

Scheme 41

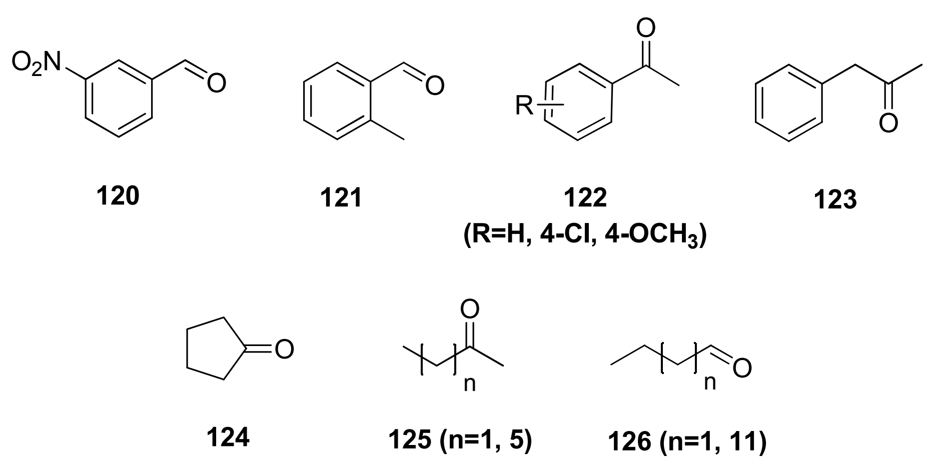
One of the approaches is the improved protocol for the oxidation of benzylic alcohols and vicinal diols described in the section above. It was shown that the reaction is strongly catalyzed by acetic or trichloroacetic acid[171] (Scheme 41). The acid catalysis conditions help to decrease the reaction time, increase the yield of corresponding products, and to allow the reaction to proceed at room temperature.

Recently, a new method employing $PhIO_2/Br_2/NaNO_2$ has been used, and it was demonstrated that this is a very efficient catalytic system for the selective aerobic oxidation of alcohols in water[173] (Scheme 42).



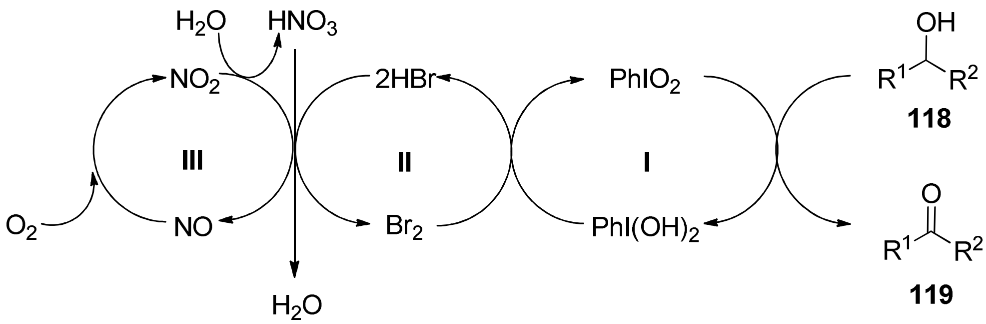
Scheme 42

Aromatic, benzylic, and secondary aliphatic alcohols give generally excellent yields of the corresponding aldehydes **120**, **121** or ketones **122**-**125**, and no by-products resulting from ”over-oxidation” have been found (Scheme 43).



Scheme 43

Primary aliphatic alcohols also produce the corresponding aldehydes **126** as the only product, but the yields are low due to the lower conversion. A plausible mechanism[173] for this catalytic oxidation comprises three redox cycles, so that iodoxybenzene is the active oxidant that oxidizes the alcohol **118** to the corresponding carbonyl compound **119**. The running of the cycle I provides iodoxybenzene by oxidizing the intermediate dihydroxyiodobenzene (the reduced form of iodoxybenzene) with Br_2, which in turn, is reduced to HBr. Although $NaNO_2$ cannot directly react with HBr, it can disproportionate in acidic aqueous solution to produce NO_3^- and NO. Oxidation of NO by atmospheric oxygen produces NO_2 which reoxidizes HBr to Br_2 as shown in the cycle II, and the NO_2 is reduced back to NO (cycle III) (Scheme 44).



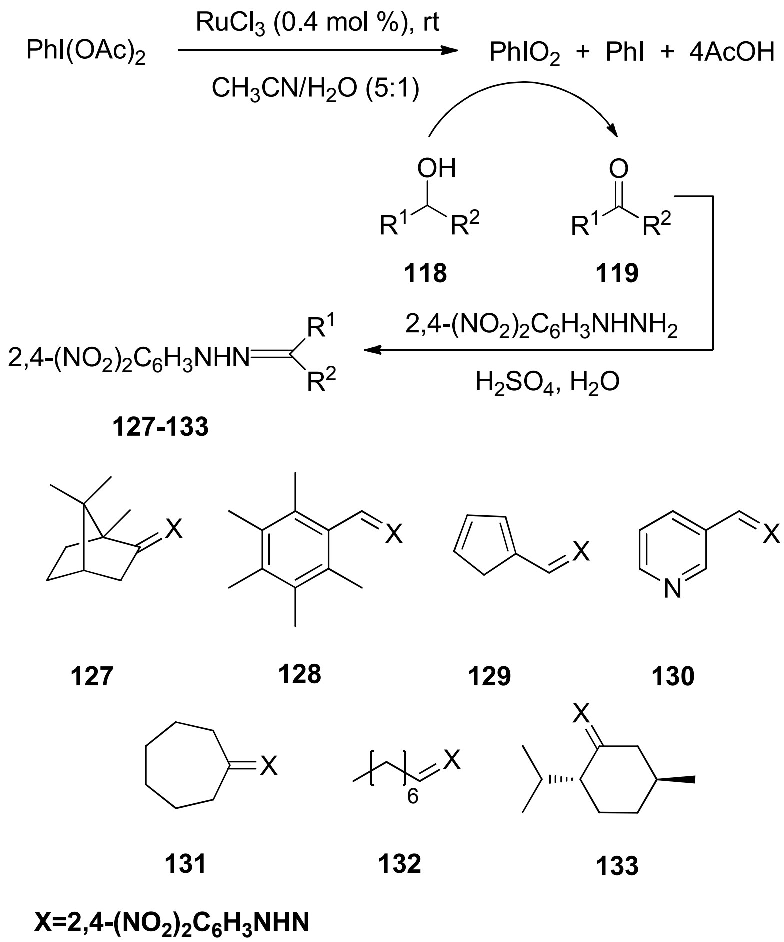
$$3NO_2^- + 3H^+ \longrightarrow 2NO + NO_3^- + H_3O^+$$

$$2HNO_3 + 6HBr \longrightarrow 2NO + 3Br_2 + 4H_2O$$

Scheme 44

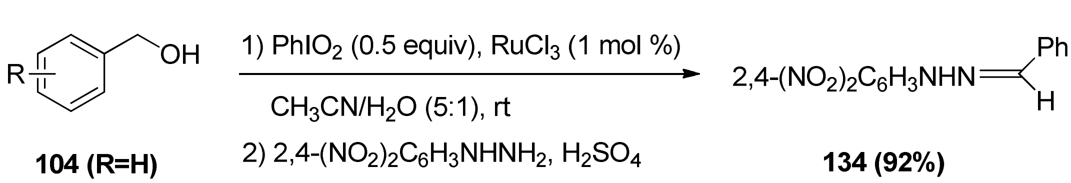
The coupling of these three redox cycles are so efficient that only 1 mol % of iodoxybenzene, 2 mol % of Br_2 and 1 mol % of $NaNO_2$ are sufficient to complete the overall catalytic process. Also, HNO_3 produced in reaction media can oxidize HBr to Br_2. Overall, the efficiency and selectivity are similar to the previously reported catalytic procedures, but the absence of transition metals, low catalyst loading and avoiding organic solvents make this procedure very attractive.

A new facile and highly efficient catalytic oxidative system, which employs iodylbenzene as a stoichiometric co-oxidant towards alcohols, has been recently reported[174]. Treatment of a solution of (diacetoxyiodo)benzene in aqueous acetonitrile with $RuCl_3$ (0.4 mol %) at room temperature results in an instantaneous quantitative disproportionation of DIB to a 1:1 mixture of iodobenzene and iodylbenzene (Scheme 45). It has been revealed that alcohol is not involved in the disproportionation step. When this reaction is performed in the presence of an alcohol, the initially formed iodylbenzene further slowly oxidizes alcohols **118** to the carbonyl compounds **119**. The aldehydes and ketones formed from the oxidation of each alcohol were further converted to the 2,4-dinitrophenylhydrazone derivatives **127-133** in generally high yields (37-96%).



Scheme 45

It is also feasible that the oxidation of alcohols with $PhIO_2$ in this system is additionally catalyzed by ruthenium[174]. In a separate experiment, benzyl alcohol **104** (R=H) was oxidized with $PhIO_2$ (0.5 equiv) in the presence of $RuCl_3$ (1 mol %) under conditions similar to the reaction of (diacetoxyiodo)benzene (Scheme 46).



Scheme 46

The reaction was complete in 40 min affording the expected 2,4-dinitrophenylhydrazone **134** in a 92% yield. This example shows that $PhIO_2$ can serve as an efficient oxidizing agent in the Ru-catalyzed oxidation of alcohols.

Chapter 2

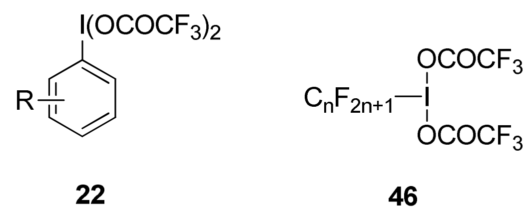
Results and Discussion

2. Development of New Approaches for the Preparation of Selected Classes of Iodine(III) Compounds and Their Application Towards New Oxidation Methodologies.

2.1 Preparation of [Bis(trifluoroacetoxy)iodo]perfluoroalkanes and [Bis(trifluoroacetoxy)iodo]arenes

A. Introduction

[Bis(trifluoroacetoxy)iodo]arenes **22**, $ArI(OCOCF_3)_2$ and [bis(trifluoroacetoxy)-iodo]perfluoroalkanes **46**, $C_nF_{2n+1}I(OCOCF_3)_2$, are the most important, well investigated, and practically useful organic derivatives of iodine(III) (Scheme 47).



Scheme 47

The first derivatives were found to be excellent reagents for various synthetic transformations such as oxidation of alcohols; oxidative functionalization of carbonyl compounds, alkenes and arenes; oxidative rearrangements and fragmentations; oxidative couplings of aromatic substrates; transition metal catalyzed reactions, etc.[44,45]. Latter fluorinated variants have found an application as convenient recyclable oxidants that can be easily recovered from the reaction mixture using fluorous techniques. [Bis(trifluoroacetoxy)iodo]-perfluoroalkanes can be effectively used for oxidation of phenols; hydroquinones, and aliphatic and benzylic secondary alcohols[44,45].

As it was mentioned in the review, there are several methods that have been used for preparation of both [bis(trifluoroacetoxy)iodo]arenes and [bis(trifluoroacetoxy)iodo]-

perfluoroalkanes. The most common general synthetic approach to the fluorous bis(trifluoroacetoxy) iodides and [bis(trifluoroacetoxy)iodo]arenes involves the oxidation of appropriate perfluoroalkyl or aryl iodides with 80% H_2O_2 and trifluoroacetic anhydride[95-97;114,115,117]. [Bis(trifluoroacetoxy)iodo]arenes can also be prepared by a ligand exchange reaction using corresponded (diacetoxyiodo)arenes and trifluoroacetic acid[87], or by direct oxidation of proper iododarenes with such oxidants as nitric acid in trifluoroacetic anhydride[93]; sodium percarbonate in mixture of trifluoroacetic anhydride and CH_2Cl_2[92]; potassium persulfate with trifluoroacetic acid and CH_2Cl_2[94], and less common H_2O_2-urea adduct[98] and xenon bis(trifluoroacetate)[99]. However, most of these methods have significant drawbacks that can be summarized as follows:

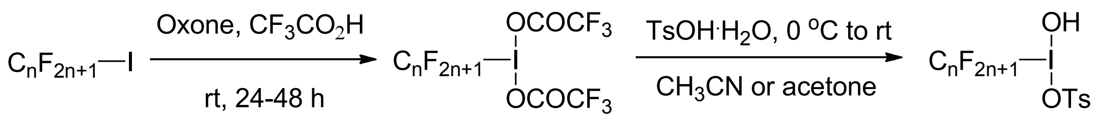
1. the contamination of product with unchanged substrate (i.e. (diacetoxyiodo)arene in ligand exchange reactions),
2. the procedure is dangerous (i.e. generation and utilization of 80% H_2O_2; explosion of hazards during the oxidation with nitric acid in trifluoroacetic anhydride),
3. the absence of general reaction conditions, which are safe and efficient, for transformation of both iodoarenes and perfluoroalkyliodides into trifluoroacetate derivatives.

So the goal of this study was to develop a safe, convenient and efficient method for preparing both [bis(trifluoroacetoxy)iodo]perfluoroalkanes and [bis(trifluoroacetoxy)-iodo]arenes starting from commercially available perfluoroalkyliodides and iodoarenes, respectively.

B. Results and Discussion

In order to achieve our goal we had to find safe reaction conditions where the oxidant effectively converts the starting material into product.

Potassium peroxymonosulfate, 2KHSO5·KHSO4·K_2SO_4, which is usually sold under the commercial name ”Oxone®”, is known as inexpensive and effective oxidant. It has been used in various synthetic applications, has relatively good storage ability and it’s convenient and safe to handle. Accordingly, we have found that [bis(trifluoroacetoxy)iodo]-perfluoroalkanes **136a-e** can be obtained in a good yield by oxidation of appropriate perfluoroalkyl iodides **135a-e** with Oxone® (0.5-1 mol-equiv) in trifluoroacetic acid (5-7 ml) at room temperature (Scheme 48).



135a-e **136a-e** **137a-e**

n=4 (**a**), 6 (**b**), 8 (**c**), 10 (**d**), 12 (**e**)

Scheme 48

The preparative yields and melting points of [bis(trifluoroacetoxy)iodo]perfluoroalkanes **136a-e** are summarized in Table 2.

Table 2. Yields and melting points of [bis(trifluoroacetoxy)iodo]perfluoroalkanes **136**[a,b] and tosylates **137**[c].

Entry (n)	Yield of **136** (%)[d,e]	mp of **136** (°C)[e]	Yield of **137** (%)[d,f]	mp of **137** (°C)[f]
135a (4)	62	55-57	100	135-137
135b (6)	88	65-67	99	141-143
135c (8)	67	85-87	88	147-149
135d (10)	63	65.5-66.5	99	97-99
135e (12)	68	98-99	98	97[g]

[a] Products **136a-c** were prepared by stirring **135a-c** (1 g) with Oxone® (1 mol-equiv) in CF_3CO_2H (5 ml) for 24 h at room temperature. [b] Products **136d**,**e** were prepared by stirring **135d**,**e** (0.5 g) with Oxone® (0.5 mol-equiv) in CF_3CO_2H (7 ml) for 48 h at room temperature. [c] Tosylates **137** were prepared similarly to previously reported procedure[117] using CH_3CN (**136a-c**) or acetone (**136d**,**e**) as a solvent. [d] Isolated yields of analytically pure compounds. [e] Recrystallized from CF_3CO_2H-hexane, 1:10. [f] Recrystallized from CH_3CN. [g] With decomposition (turns dark).

Trifluoroacetates **136** were separated from inorganic salts remaining after evaporation of the reaction mixture by extraction with acetonitrile (for **136a-c**) or acetone (for **136d,e**). The choice of solvent for extraction was made based on the solubility of the corresponding trifluoroacetates in organic solvents[114,117]. The average yields of trifluoroacetates were between 62 and 68%. Only the perfluorohexyl derivative **136b** was obtained in 88% yield with no any reasonable explanation. All previously reported products were identified by comparison of their NMR spectra and mp with literature data[115,117].

[Bis(trifluoroacetoxy)iodo]perfluoroalkanes are known to be relatively unstable and hygroscopic. Therefore, they were subsequently converted into [hydroxy(tosyloxy)iodo]perfluoroalkanes **137a-e**, which are generally stable for storage at room temperature and, in contrast to the trifluoroacetates **136**, are not sensitive to light and moisture. The corresponding tosylates were obtained in almost quantitative yield by treatment of [bis(trifluoroacetoxy)iodo]perfluoroalkanes **136a-e** with p-toluenesulfonic acid[117] (1.25 mol-equiv) in the appropriate solvent (Scheme 48, Table 2). The choice of solvent for reaction was also made based on solubility of the corresponding trifluoroacetates in organic solvents[114,117]. Thus, acetonitrile was used for **136a-c**, and acetone was utilized for **136d**,**e**. All previously reported [hydroxy(tosyloxy)iodo]perfluoroalkanes were identified by comparison of their NMR spectra and mp with literature data[117]. New products **137d**,**e** were identified by ^{1}H, ^{19}F, and ^{13}C NMR spectra and elemental analysis. In particular, the ^{19}F NMR spectra of tosylates **137a-e** in deuterated solvents clearly show the disappearance of the signal (around -80.5 ppm) corresponding to fluorine in trifluoroacetoxy group of starting [bis(trifluoroacetoxy)iodo]perfluoroalkanes **136a-e** and conversion of latter to the desired product.

$$\underset{\textbf{138a-m}}{\mathrm{ArI}} \xrightarrow[\mathrm{CHCl_3,\ rt,\ 1\text{-}4\ h}]{\mathrm{Oxone\ (1.5\ mol\text{-}equiv),\ CF_3CO_2H}} \underset{\textbf{139a-m}}{\mathrm{ArI(OCOCF_3)_2}}$$

Scheme 49

At the next step we have investigated the applicability of this convenient procedure to the synthesis of various [bis(trifluoroacetoxy)iodo]arenes, $ArI(OCOCF_3)_2$. We have found that Oxone® in chloroform (0.5 ml) and trifluoroacetic acid (1.5 ml) was a very efficient oxidizing system providing [bis(trifluoroacetoxy)iodo]arenes **139a-m** from commercially available iodoarenes **138a-m** in generally excellent yields (1-4 hours at room temperature, Scheme 49). Similar to several other procedures[92,94] an excess of oxidizing agent has been used. In comparison to many other approaches our method affords most of the products in higher yields within a shorter period of time (Table 3).

Table 3. Yields and melting points of [bis(trifluoroacetoxy)iodo]arenes **139**[a].

ArI **138**	Ar	Time (h)	Yield of **139** (%)[b]	mp of **139** (°C)[c,d]
a	C_6H_5	1.2	97	118-120
b	$4\text{-}FC_6H_4$	1	80	94-96
c	$4\text{-}BrC_6H_4$	1.5	94	123-125
d	$4\text{-}ClC_6H_4$	1.5	69	128-130
e	$3\text{-}ClC_6H_4$	1.2	91	95-97
f	$2\text{-}ClC_6H_4$	1.2	97	98-100
g	$4\text{-}CF_3C_6H_4$	1.5	68	121-123
h	$3,5\text{-}(CF_3)_2C_6H_3$	1.5	94	82 (dec)
i	$4\text{-}NO_2C_6H_4$	1.5	69	157-159
j	$3\text{-}NO_2C_6H_4$	1.5	58	141-143
k	$4\text{-}HO_2CC_6H_4$	4	54	109-111
l	$3\text{-}HO_2CC_6H_4$	4	41	159-161
m	C_6F_5	2	94	95.5-96.5[e]

[a] All reactions of iodoarenes **138a-m** (0.5 mmol) were performed at room temperature in the presence of Oxone® (1.5 mol-equiv) in CF_3CO_2H (1.5 mL) and $CHCl_3$ (0.5 mL). [b] Isolated yields of analytically pure products. [c] All previously reported products **139** were identified by comparison of their NMR spectra and/or melting points with literature data. [d] Recrystallized from trifluoroacetic acid-hexane, 1:10. [e] Additionally identified by conversion to $C_6F_5I(OH)OTs$, mp 160 °C.

For example, our protocol gives $PhI(OCOCF_3)_2$ **139a** in 97% yield after only 1.2 hours at room temperature, compared to the 76% yield using the procedure offered by Hossain and Kitamura[94]. However, reactions of 4-iodobenzoic **138k** and 3-iodobenzoic **138l** acids resulted in a low yields (54% and 41%, respectively) of the corresponding trifluoroacetates, probably due to side reactions. Also, our method is not applicable for iodoarenes with strong electron-donating groups because of the rapid oxidative decomposition of the resulting reaction mixture.

All previously reported products were identified by comparison of their NMR spectra and melting points with literature data[94,95,175]. New products **139e**, **139f**, and **139k** were identified by NMR spectra and elemental analysis. The general feature of all ^{13}C NMR spectra of [bis(trifluoroacetoxy)iodo]arenes **138a-m** is the presence of characteristic quadruplet signals at ~112.85 ppm and ~161.15 ppm, due to the trifluoromethyl carbon of the trifluoroacetoxy group and carbonyl carbon of the same group, respectively. This observation confirms the formation of final product through the oxidation of iodine(I) to iodine(III). The pentafluorophenyl derivative **139m** was converted to [hydroxy(tosyloxy)iodo]pentafluorobenzene **140** using $TsOH{\cdot}H_2O$ in acetonitrile (Scheme 50).

$$\underset{\textbf{139m}}{C_6F_5I(OCOCF_3)_2} \xrightarrow[\text{0 °C to rt, 94\%}]{TsOH{\cdot}H_2O,\ CH_3CN} \underset{\textbf{140}}{C_6F_5I(OH)OTs}$$

Scheme 50

Tosylate **140** is a new compound; it was obtained as a solid in excellent yield (94%) and characterized by NMR spectra and elemental analysis.

C. Summary

In conclusion, we have developed a safe, convenient, efficient and straightforward procedure for preparing fluorous [bis(trifluoroacetoxy)iodo]perfluoroalkanes **136** by the oxidation of corresponding perfluoroalkyl iodides **135** with Oxone® in trifluoroacetic acid at room temperature. The trifluoroacetates **136** can easily be further converted to [hydroxy(tosyloxy)iodo]perfluoroalkanes **137**, which are stable for storage at room temperature and, in contrast to the trifluoroacetates **136**, are not sensitive to light and moisture. This general and convenient procedure has been extended to the synthesis of various [bis(trifluoroacetoxy)iodo]arenes **139** in good to excellent yields. Because of its simplicity and convenience, the present method may attract significant research interest in the future.

2.2 Oxidative Rearrangement of Amides using Iodobenzene and Oxone®

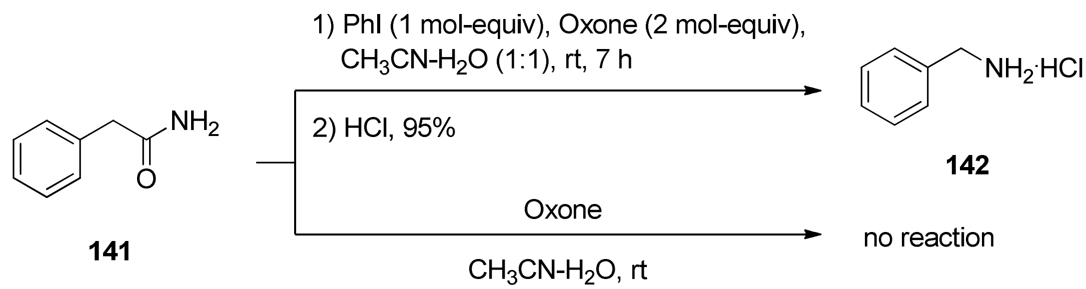
A. Introduction

Hofmann Rearrangement, which originally represents the multistep transformation of primary carboxamides to primary amines *via* an intermediate isocyanate, is a very important transformation in organic synthesis. Numerous synthetic sequences, which lead to biologically and medicinally important compounds, include this rearrangement as a key step. [Bis(acyloxy)iodo]arenes and aryliodine(III) organosulfonates are commonly used as the reagents in various cationic rearrangements and fragmentations[44,45], and they have been found to be particularly efficient oxidants in Hofmann-type degradation. As noted in Chapter 1, a typical procedure employs the iodine(III) compounds that are commercially available but relatively expensive (e.g. DIB), or have to be prepared in advance by a time consuming process (e.g. BTI). No data related to the utilization of iodine(III) species generated *in situ* in Hofmann Rearrangements were found in the literature. Therefore, an addition goal of this study was to develop a new synthetic methodology where the Hofmann rearrangement is induced by iodine(III) species generated directly in the reaction mixture.

B. Results and Discussion

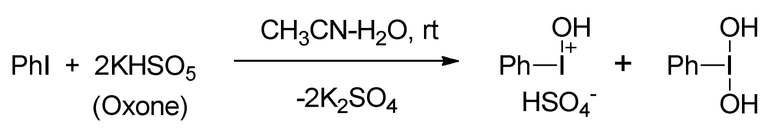
In our previous study it was shown that iodine(III) species can be obtained by a simple oxidation of organoiodine precursors with Oxone® at room temperature. As follows from the review, the presence of water in the reaction mixture is of a crucial importance where the intermediate isocyanate is hydrolyzed to amines. For this reason, the reaction medium that was chosen was aqueous acetonitrile.

We decided to perform the rearrangement in the presence of iodobenzene and Oxone® in aqueous acetonitrile at room temperature. Iodobenzene was chosen because it is relatively inexpensive, and it has been successfully used in many other synthetic applications. The reaction conditions for the transformation of amides into amines were optimized using 2-phenylacetamide **141** as a model substrate (Scheme 51).



Scheme 51

The corresponding benzylamine was isolated as hydrochloride salt **142**[176] (95% yield). The mixture of CH_3CN-H_2O (1:1, v/v) was found to be the best solvent system for this reaction. The optimized reaction required at least 1 mol-equiv of iodobenzene and 2 mol-equiv of Oxone®. The use of smaller amounts of Oxone® or iodobenzene led to incomplete conversion. As expected, in the absence of iodobenzene no rearrangement occurred even within several days (Scheme 51).



Scheme 52

To clarify the nature of the actual reacting species in this reaction, we performed a special experiment where PhI reacts instantaneously with Oxone® in aq. CH_3CN at room temperature in the absence of amide producing a yellow solution (Scheme 52). The ESI mass-spectrometry study of this solution indicated the presence of hypervalent iodine(III), hydroxy(phenyl)iodonium ion **143**, and (dihydroxyiodo)benzene (hydrated PhIO) **144**, along with unreacted iodobenzene (Scheme 52, Figure 1).

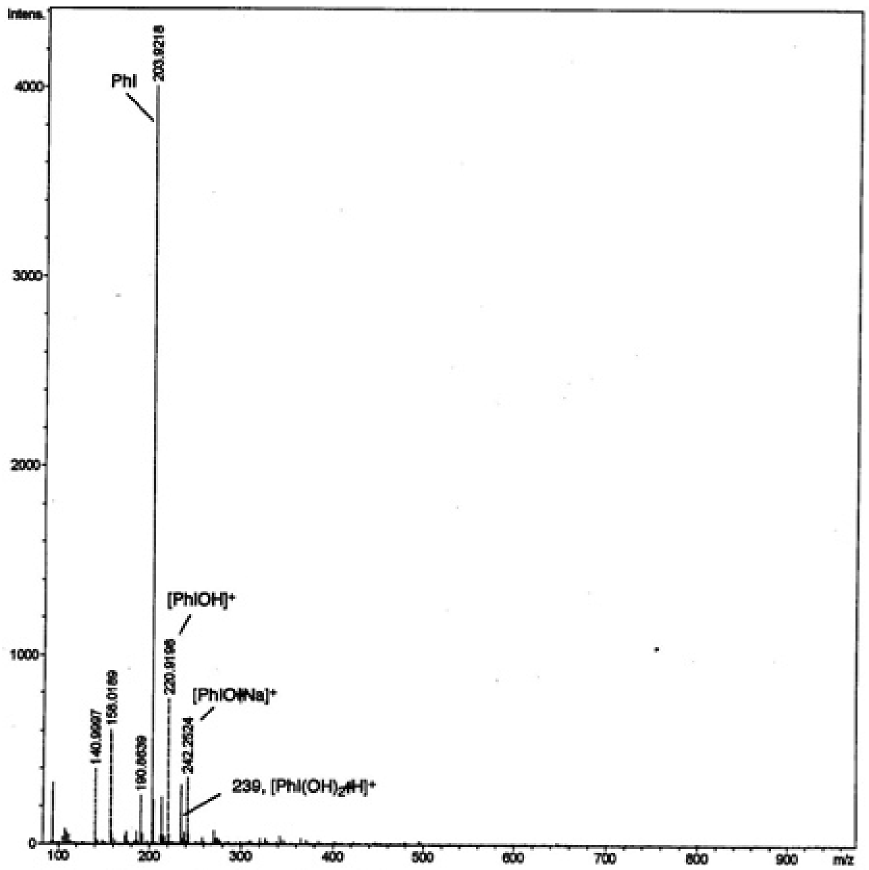
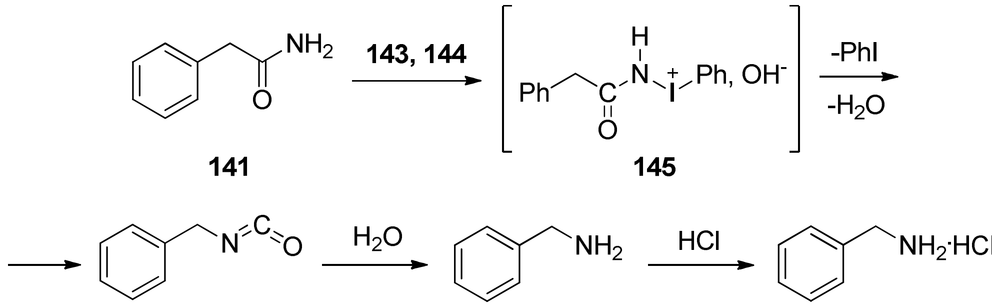


Figure 1. ESI mass spectrum of PhI/Oxone® mixture in aqueous acetonitrile.

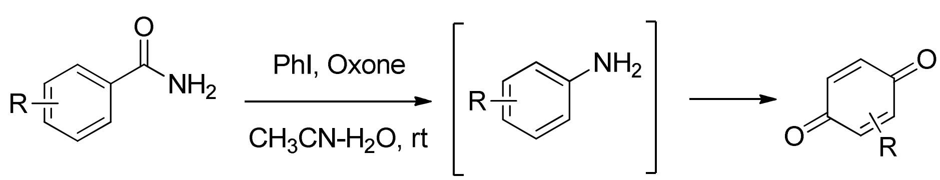
We assumed that species **143** and **144** initiate the rearrangement of amide, and that the plausible mechanism of our reaction is more like that one using [hydroxy-(tosyloxy)iodo]benzene in acetonitrile[162,164] (Scheme 34). Thus, hydroxy-(phenyl)iodonium ion **143** and (dihydroxyiodo)benzene **144**, formed *in situ*, react with the amide **141** to form N-phenyliodonio α-phenylacetamide hydroxide **145**, $PhCH_2CONHI^+Ph,OH^-$. This intermediate subsequently rearranges to the isocyanate intermediate **146** releasing a molecule of iodobenzene. Under these conditions isocyanates are trapped by water, and benzylamine is finally isolated as benzylamine hydrochloride **142** (Scheme 53). A typical side reaction expected from simultaneous presence of isocyanate and amine in the reaction medium (e.g. the formation of ureas) was not detected under studied conditions.



141 **145** **146** **142**

Scheme 53

In order to determine the scope of our procedure, we have performed a typical set of rearrangement reactions of various primary amides under optimized conditions. In agreement with previously reported data, our approach was not useful for the preparation of amines in which the nitrogen was directly bonded to an aromatic ring, since the corresponding amines are oxidized further[131,134,135]. However, the products of oxidation in our study differ from those described previously[134] (Scheme 54). It was shown in earlier experiments that the products of oxidation of such amines with DIB are presumably azo-compounds ArN=NAr formed *via* a radical mechanism, while our approach leads to formation of quinones **148a-d** from amides **147a-e** in almost quantitative yield (Table 4). Reactions proceeded smoothly, and no other products were detected. The mechanism of the quinone formation is not clear.



147a-e **148a-d**

Scheme 54

Presumably, the first step involves the attack of **144** on the amine providing PhI(OH)·NHAr, which is unlikely to be further involved in a free-radical process, suggested by Pausacker, et. al.[134]. The actual mechanism, possibly, involves two electron process.

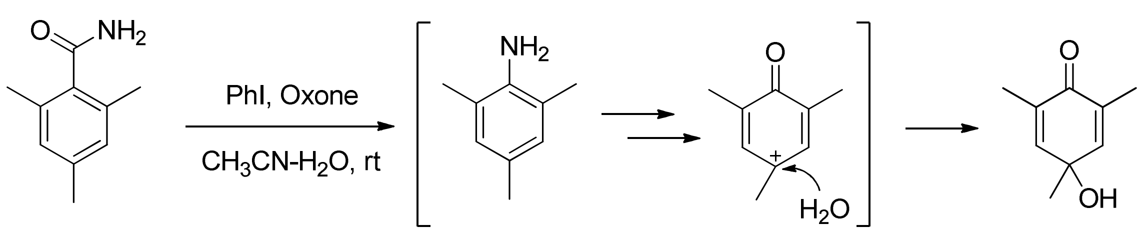
Table 4. Yields and melting points of 1,4-benzoquinones **148**[a].

Entry (R)	Yield of **148** (%)[b]	mp of **148** (°C)[c]
147a (H)	98	115-116
147b (2-CH_3)	100	68-69
147c (2-Cl)	95	54-56
147d (3-OCH_3)	97	142-144
147e (4-OCH_3)	94	115-116

[a] All reactions of amides **147a-e** (1 mmol) were performed at room temperature in the presence of PhI (1 mol-equiv) and Oxone® (2 mol-equiv) in CH_3CN-H_2O (1:1, v/v). [b] Isolated yields of analytically pure products. [c] All previously reported products **148** were identified by comparison of their NMR spectra and/or melting points with literature data.

All previously reported products were identified by comparison of their NMR spectra and melting points with literature data[177]. Both, benzamide **147a** and 4-methoxybenzamide **147e**, give 1,4-benzoquinone **148a** as a product.

An interesting result was obtained in the reaction of 2,4,6-trimethylbenzamide **149** (Scheme 55). The presence of a methyl group at the *para*-position leads to products of oxidative *ipso*-substitution in the aromatic ring, *p*-quinol **151** in 95% yield.

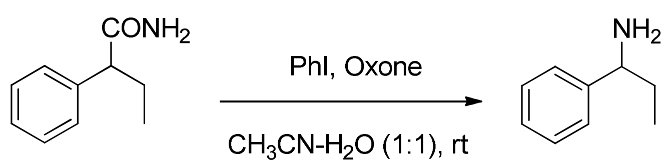


149 **150** **151 (95%)**

Scheme 55

The mechanism most likely involves the generation of cationic phenoxenium intermediate **150**, which finally combines with the nucleophile (e.g. water). The formation of such products circumstantially confirmed our previous speculations on the mechanism of oxidation of amines under the studied conditions. Product **151** was identified by comparison of its NMR spectrum and melting point with literature data[178,179]. In particular, the ^{1}H NMR spectrum of **151** in $CDCl_3$ clearly showed singlets at 1.86 ppm and 1.43 ppm, corresponding to 2,6-methyl groups and a 4-methyl group, respectively. Chemical shifts of methyl groups in the original 2,4,6-trimethylbenzamide **149** were 2.32 ppm and 2.27 ppm[178]. The chemical shift of 3,5-H in 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone **151** is 6.62 ppm which also differs from chemical shift in **149** (6.84 ppm), and indicates the dearomatization of substrate.

In general, the conversion of alkyl and other aryl amides to the corresponding amines was complete, and comparable to results obtained in DIB-, BTI or HTIB-induced Hofmann Rearrangements. For example, using our method (±)-α-phenylpropylamine **153**[180] can be obtained in 85% yield from 2-phenylbutyramide **152** (Scheme 56).

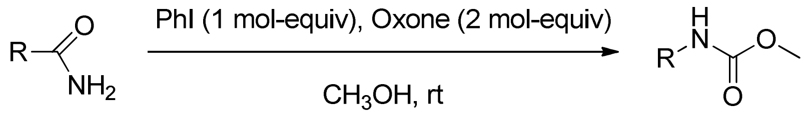


152 **153 (85%)**

Scheme 56

Isolation of amines from reaction mixtures is commonly a time consuming procedure. On the one hand, amines are usually liquids with relatively low boiling points which make it difficult to isolate by evaporation of solvent under reduced pressure. On the other hand, transformation of amines to their hydrochloride salts typically includes the utilization of NaOH, along with multiple extractions with ether and 10-20% HCl solution, which can dramatically decrease the yield of product. Therefore, we decided to apply our protocol to synthesis of carbamates, which are either stable solid compounds, or liquids with relatively high boiling points, so that it is easier to isolate them from the reaction mixture.

In order to obtain carbamates we switched the solvent from CH_3CN-H_2O to methanol, and performed another set of comparable reactions still using 1 mol-equiv of PhI and 2 mol-equiv of Oxone® (Scheme 57).

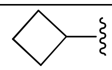
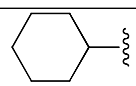
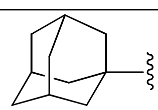
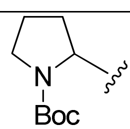
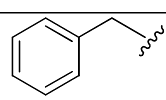
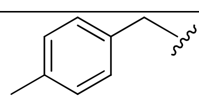


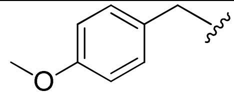
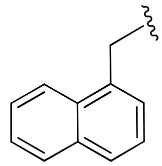
154a-k **155a-k**

Scheme 57

The yields and melting points of carbamates **155** obtained from amides **154** are summarized in Table 5.

Table 5. Yields and melting points of carbamates **155**[a].

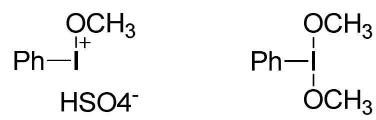
R (Entry)	Yield of **155** (%)[b]	mp of **155** (°C)[c,d]
CH_3CH_2 (**154a**)	100[e]	-
$CH_3(CH_2)_4$ (**154b**)	100[e]	-
$(CH_3)_2CH$ (**154c**)	95	oil
 (**154d**)	92	oil
 (**154e**)	89	73.5-74.5
 (**154f**)	90	118-120
 (**154g**)	75	oil
 (**154h**)	97	63-65
 (**154i**)	93	68-70

 **(154j)**	95	73-74
 **(154k)**	93	84-86

[a] All reactions of amides **154a-k** (1 mmol) were performed at room temperature in the presence of PhI (1 mol-equiv) and Oxone® (2 mol-equiv) in CH_3OH (5 mL). [b] Isolated yields of analytically pure products. [c] All previously reported products **155** were identified by comparison of their NMR spectra and/or melting points with literature data. [d] Crystalline products were recrystallized from $CHCl_3$-hexane. [e] No product was isolated, only conversion was determined. Conversion was determined by GC analysis.

From table 5 it can be noted that various alkyl **154a-g** and aryl **154h-k** amides, where $C(O)NH_2$-group is connected to the ring by a -CH_2-bridge, successfully undergo the rearrangement under studied conditions affording carbamates in 75-97% yield. All previously reported carbamates were identified by comparison of their NMR spectra and melting points with literature data[181-185]. Methyl N-ethylcarbamate **154a** and methyl N-pentylcarbamate **154b** were not isolated, but 100% conversion was for both compounds. Our method allows the preparation of such sterically hindered carbamates as methyl N-(1-adamantanyl)carbamate **155f** and methyl *N*-[(1-naphthyl)methyl]carbamate **155k** in 90% and 93% yield, respectively. One new compound, methyl (1-Boc-pyrrolidin-2-yl)carbamate **155g**, was obtained from 1-Boc-L-prolinamide **154g** by our method. It was identified by ^{1}H, ^{13}C NMR spectra and elemental analysis. In particular, ^{13}C NMR indicates the presence of two carbonyl carbons by signals at 179.51 ppm and 174.02 ppm which correspond to $C(O)OC(CH_3)_3$ and $NHC(O)OCH_3$-groups, respectively. ^{1}H NMR clearly shows the singlet at 3.68 ppm which corresponds to methyl-group of $NHC(O)OCH_3$-moiety. The optical rotation measured for **155g** was not reliable because of very low concentration of prepared solution, so it was impossible to determine whether the reaction proceeds with retention of configuration at C-2 or not.

It is reasonable to assume that species inducing the rearrangement, which led to formation of carbamates, were similar to those encountered in the acetonitrile/water medium (Scheme 58).



156 **157**

Scheme 58

However, it is proposed that a more plausible mechanism is more likely analogous to use of (diacetoxyiodo)benzene in methanolic KOH[132,133] (Scheme 34).

C. Summary

In conclusion, we have developed a new, simple and efficient approach to Hofmann-type rearrangement of amides to amines in acetonitrile-water medium without having to isolate the isocyanate intermediate. We have also received experimental evidence that the reaction is induced by an iodine(III)-species **143** and **144** generated directly in the reaction mixture by oxidation of iodobenzene with Oxone®. We have also found that our protocol leads to formation of 1,4-benzoquinones if benzamide and its substituted derivatives are subjects of oxidative rearrangement reaction. Moreover, using our method various alkyl and arylamides, where $C(O)NH_2$-group is connected to the ring by a $-CH_2$-bridge, can be easily converted into corresponded carbamates if methanol is used as a solvent.

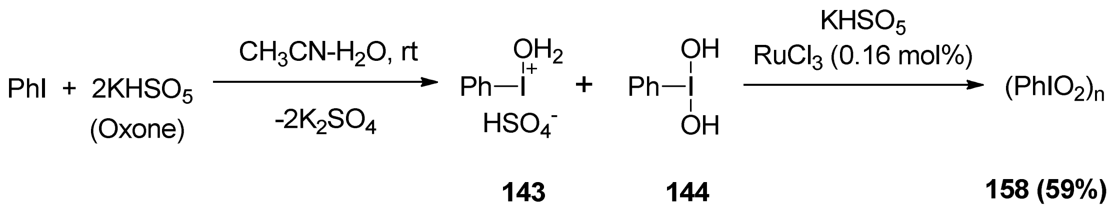
2.3 PhI/$RuCl_3$-Cocatalyzed Oxidation of Alcohols and Hydrocarbons

A. Introduction

Oxidation of alcohols to the respective carbonyl compounds is one of the most important transformations in organic synthesis. The selective oxidation of activated and unactivated C–H bonds is of particular interest for organic chemists as well. As was mentioned in the review, hypervalent iodine compounds have attracted significant interest in synthetic organic chemistry[44]. It has been found that transition metals have a dramatic catalytic effect on some oxidations with hypervalent iodine(V) reagents, and one of the most impressive recent achievements in this field is the development of catalytic systems based on hypervalent iodine (V) compounds, in particular iodylarenes, ($ArIO_2$). A representative example is the ArI-based catalytic cycle that employs Oxone® as a stoichiometric oxidant[186]. However, the synthetic value of this catalytic cycle is limited by the reoxidation of iodine(I) or iodine(III) to the iodine(V) species, which proceeds relatively slowly, even at temperatures above 70 °C. The catalytic effect of transition metals on the reaction of oxidation of alcohols and hydrocarbons to carbonyl compounds by iodylarenes has not been widely investigated. One example is the simple and highly efficient $RuCl_3$-catalyzed selective oxidation of alcohols to carbonyl compounds by (diacetoxyiodo)benzene that has been recently developed in our laboratory[174]. It has been demonstrated that this reaction proceeds *via* an instantaneous Ru-catalyzed disproportionation of DIB to iodobenzene and iodylbenzene, with the latter acting as the actual stoichiometric oxidant toward alcohols. In the present chapter we would like to report an extremely mild and efficient tandem catalytic system for the oxidation of alcohols and hydrocarbons based on a Ru(III)-catalyzed reoxidation of PhIO to $PhIO_2$ by using an Oxone® as a stoichiometric oxidant.

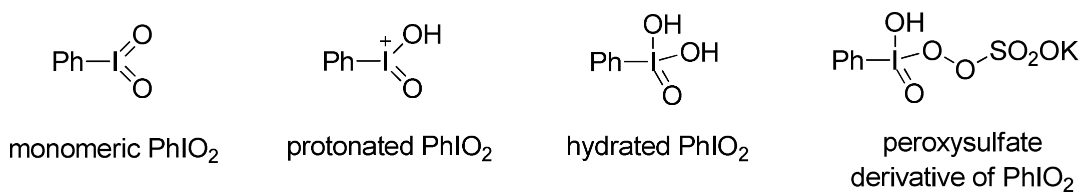
B. Results and Discussion

As noted in the review, iodylarenes can be obtained by $RuCl_3$-catalyzed oxidation of iodoarenes with peracetic acid[128] (Scheme 20). Our studies have demonstrated that the utilization of Oxone® as the oxidant instead of peracetic acid results in even milder reaction conditions. In a typical procedure, treatment of iodobenzene with Oxone® in aqueous acetonitrile at room temperature in the presence of $RuCl_3$ (0.16 mol %) leads to formation of iodylbenzene $(PhIO_2)_n$ **158**, which can be isolated from the reaction mixture (59% preparative yield, Scheme 59). It was demonstrated in the previous section that Oxone® reacts with iodobenzene with the formation of **143** and **144**, which we assume are further converted to iodylbenzene in the presence of $RuCl_3$. Experimental evidence of the catalytic oxidation of PhIO to $PhIO_2$[187a], mediated by oxoruthenium species, has been previously documented, moreover the generation of highly reactive Ru(V)-oxo species has been reported in the literature[187b-d].



Scheme 59

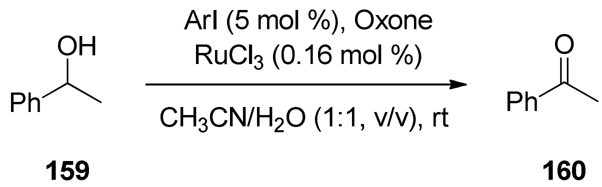
Thus, it is likely that intermediate oxoruthenium complexes are responsible for catalytic oxidation of the initially formed iodine(III) species **143** and **144** to iodine(V). The polymeric, insoluble iodylbenzene, $(PhIO_2)_n$ **158**, is the final, isolated product of reaction. However, the exact nature of the initially formed iodine(V) species in Scheme 59 remains unknown.



Scheme 60

It is possible that these intermediates can be represented by some activated forms of monomeric $PhIO_2$ (e.g., protonated, hydrated, or a peroxysulfate derivatives shown in Scheme 60), which have shown extremely high oxidative reactivity toward organic substrates.

Based on these observations, we have developed a ArI/$RuCl_3$ tandem catalytic system for the oxidation of alcohols. The reaction was optimized using 1-phenylethanol **159** as a model substrate (Scheme 61, Table 6). As expected, in the absence of PhI and in presence of $RuCl_3$ (0.16 mol %), or in presence of PhI without $RuCl_3$ the oxidation of substrate **159** at room temperature proceeded very slowly (Table 6, Entry 1), or didn't take place at all (Table 6, Entry 2). The combined application of PhI and $RuCl_3$ resulted in almost instantaneous oxidation of **159** to acetophenone **160**, with a 100% conversion reached in less than 20 min (Table 6, Entry 3).



Scheme 61

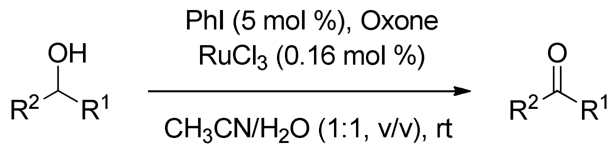
The optimized reaction required at least 1 mol-equiv of Oxone®. The use of smaller amounts of Oxone® leads to incomplete conversion (Table 6, Entry 4), because of its noticeable decomposition with loss of oxygen gas under reaction conditions. Several other iodoarenes comparable to PhI tested in this reaction showed a high catalytic activity (Table 6, Entries 5-8).

Table 6. Effect of ArI and $RuCl_3$ on the oxidation of 1-phenylethanol **159** to acetophenone **160** with Oxone®[a].

Entry	ArI	Oxone® (mol-equiv)	Time (h)	Conversion (%)[b]
1	None	1.5	0.3	12[c]
2	PhI[d]	1.0	1.0	0
3	PhI	1.0	0.3	100
4	PhI	0.67	1.0	83
5	2-$IC_6H_4SO_3H$	1.25	0.3	100
6	4-$IC_6H_4SO_3H$	1.15	0.3	100
7	4-$IC_6H_4SO_3Na$	1.25	0.6	100
8	3-$IC_6H_4CO_2H$	1.22	1.0	99

[a] All reactions were performed at room temperature in CH_3CN/H_2O (1:1, v/v) using 0.1 mmol of 1-phenylethanol **159**, 0.16 mol % of $RuCl_3$, and 5 mol % of PhI. [b] The conversion was determined by GC analysis. According to GC acetophenone **160** was the only product resulting from oxidation of **159** under these conditions. [c] Also contained 8% of styrene and 80% of unreacted alcohol. [d] No $RuCl_3$ added.

A variety of alcohols **161** are smoothly oxidized under optimized conditions to afford the respective oxidation products **162** in excellent isolated yields at room temperature (Scheme 62, Table 7). Similar to previously reported results, our procedure affords ketones from secondary alcohols (Table 7, Entries 1-9), and predominantly carboxylic acids from primary alcohols (Table 7, Entries 10 and 11). Even such sterically hindered alcohols as borneol (Table 7, Entry 8) and adamantan-2-ol (Table 7, Entry 9) successfully undergo oxidation under these conditions, affording ketones in 99% and 100% yield, respectively.

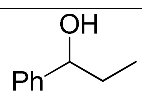
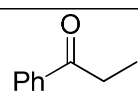
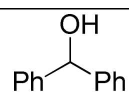
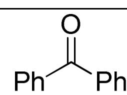
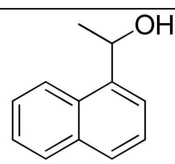
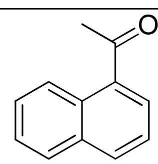
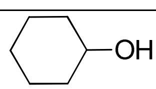
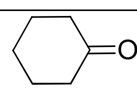
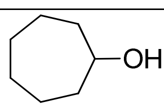
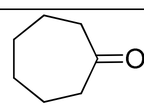
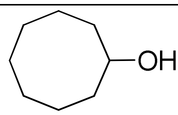
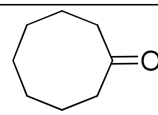


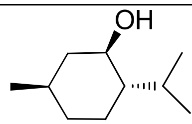
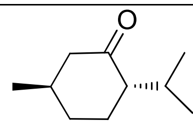
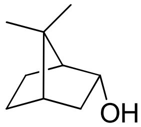
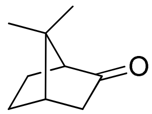
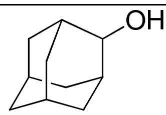
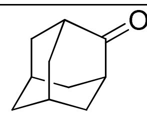
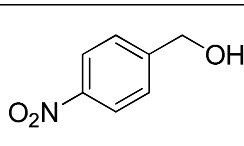
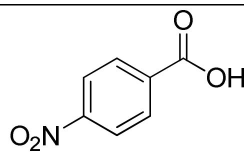
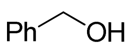
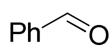
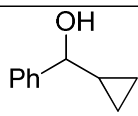
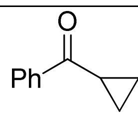
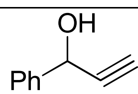
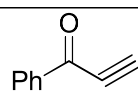
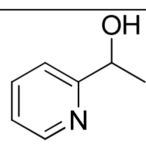
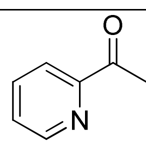
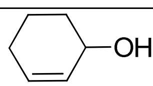
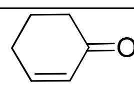
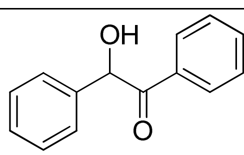
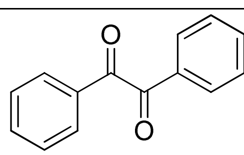
161 **162**

Scheme 62

However, shorter reaction times allow benzyl alcohol to be predominantly converted to benzaldehyde (Table 7, Entry 12 isolated as its 2,4-dinitrophenylhydrazone, mp 241-242 °C, lit.[188], mp 239-240 °C).

Table 7. PhI/$RuCl_3$-cocatalyzed oxidation of alcohols **161**[a].

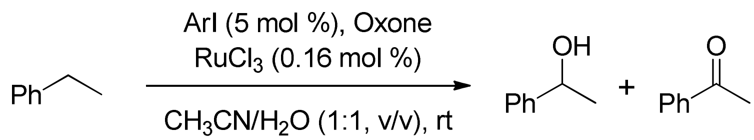
Entry	Alcohol **161**	Product **162**	Oxone® (mol-equiv)	Time (h)	Yield of **162** (%)[b]
1			1.2	0.3	100
2			1.2	10	96
3			2.0	7	100
4			1.0	2	92
5			1.2	0.8	100
6			1.0	0.5	100

7			1.05	0.5	100
8			1.0	0.8	99
9			1.0	0.8	100
10			2.4	4	96
11	$CH_3(CH_2)_7OH$	$CH_3(CH_2)_6CO_2H$	1.1	16	100
12			1.25	1.5	80[c]
13			1.2	1	82[d]
14			1.6	1	90[d]
15			1.4	10	100[d]
16			1.0	2	93[d]
17			4.5	18	87[d,e]

[a] All reactions were performed at room temperature in CH_3CN/H_2O (1:1, v/v) using 1 mmol of alcohol, 0.16 mol % of $RuCl_3$ and 5 mol % of PhI. [b] Yields of isolated pure products **162** are shown unless otherwise note. [c] Isolated yield of 2,4-dinitrophenylhydrazone of benzaldehyde. [d] Yield of product was determine by GC analysis using initially added PhI as an internal standard (after reductive treatment of the reaction mixture with $Na_2S_2O_3$). [e] Also contains 13% of benzoic acid.

The use of smaller quantities of Oxone® and shortening the reaction time in the oxidation of other primary alcohols (Table 7, cf. Entries 10 and 11), also leads to the predominant formation of corresponding aldehydes. All isolated products gave satisfactory spectral data.

We also investigated the applicability of ArI/$RuCl_3$ tandem, catalytic system to the oxidation of C–H bonds. This reaction was optimized using ethylbenzene **163** as a model substrate (Scheme 63, Table 8).



163 **164** **165**

Scheme 63

Again, as expected, in the absence of PhI and in presence of $RuCl_3$, or in presence of PhI and in the absence of $RuCl_3$ the oxidation of substrate **163** at room temperature did not occur or proceeded very slowly (Table 8, Entries 1, 2 and 8).

Table 8. Effect of ArI and $RuCl_3$ on the oxidation of ethylbenzene **163** with Oxone®[a].

Entry	ArI	Oxone® (mol-equiv)	Time (h)	Products (%)[b]
1	None	1.05	3.3	**164** (1%), **165** (8%)
2	PhI[c]	1.05	24	**164** (0%), **165** (0%)
3	PhI	1.05	3.3	**164** (0.5%), **165** (27%)
4	2-$IC_6H_4SO_3H$	1.05	3.3	**164** (1%), **165** (31%)
5	4-$IC_6H_4SO_3H$	1.05	3.3	**164** (0.5%), **165** (17%)
6	2-$IC_6H_4CO_2H$	1.05	3.3	**164** (1%), **165** (30%)
7	4-$IC_6H_4CF_3$	1.05	3.3	**164** (0%), **165** (13%)
8	None	2.10[d]	4.0	**164** (1%), **165** (14%)
9	PhI[e]	4.2[f]	11.5	**164** (0%), **165** (80%)

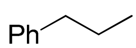
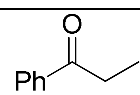
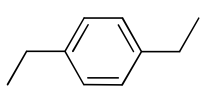
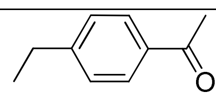
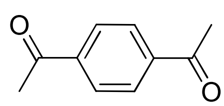
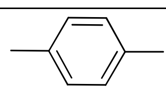
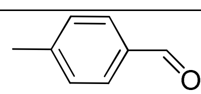
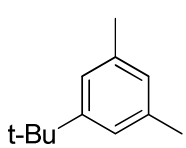
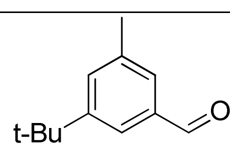
[a] All reactions were performed at room temperature in CH_3CN/H_2O (1:1, v/v) using 0.1 mmol of ethylbenzene **163**, 0.16 mol % of $RuCl_3$, and 5 mol % of PhI unless otherwise noted. [b] Product yields were determined by GC analysis. [c] No $RuCl_3$ added. [d] 1.05 mol-equiv of Oxone® added initially and the second portion of 1.05 mol-equiv added after 2 h. [e] 10 mol % of PhI was used. [f] 0.9 mol-equiv of Oxone® added

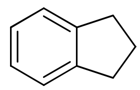
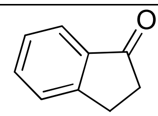
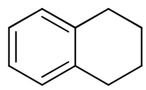
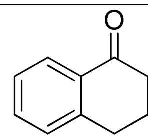
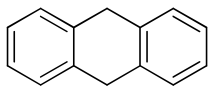
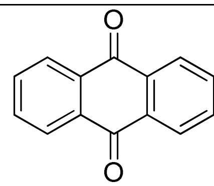
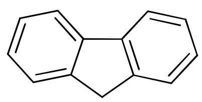
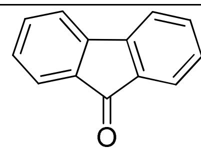
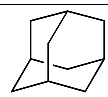
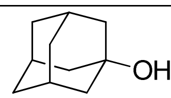
initially, the 2nd portion of 1.1 mol-equiv added after 2 h, the 3rd portion of 1.1. mol-equiv added after 2 h, and the last portion of 1.1 mol-equiv added after 3h.

The combined application of PhI and $RuCl_3$ resulted in a 27% conversion of **163** to acetophenone **165** (Table 8, Entry 3). The optimized reaction conditions affording 80% conversion of substrate **163** to product **165** required addition of 4.2 mol-equiv of Oxone® in small portions over 11 h and the use of 10 mol % of PhI (Table 8, Entry 9). Among several other iodoarenes tested in this reaction, 2 iodosulfonic acid and 2-iodobenzoic acid demonstrated slightly better catalytic effect than iodobenzene (Table 8, Entries 4-7). However, a noticeable amount of by-product **164** was detected with these catalysts.

Results of the oxidation of other hydrocarbons under optimized catalytic conditions are summarized in Table 9. The typical procedure required the addition of Oxone® in small portions over the reaction period. In general, moderate to high yields of aromatic ketones were obtained in these oxidations under mild reaction conditions (Table 9, Entries 1-8).

Table 9. PhI/$RuCl_3$-cocatalyzed oxidation of hydrocarbons[a].

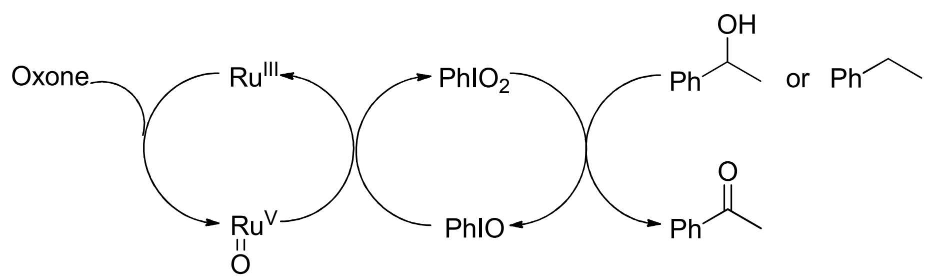
Entry	Substrate	Product	Oxone® (mol-equiv)	Time (h)	Yield (%)[b]
1			6.1[c]	26	80
2		 	2.06	3	77 11
3			1.0[c]	24	18[d]
4			1.2	6	23

5			2.0[c,e]	1	95
6			1.2[c]	1	69
7			8.2[c]	20	72
8			4.7[c]	20	38[d]
9			2.5[c]	8	1.5[d]

[a] All reactions were performed at room temperature in CH_3CN/H_2O (1:1, v/v) using 1 mmol of a hydrocarbon, 0.16 mol % of $RuCl_3$, and 5 mol % of PhI unless otherwise noted. [b] Yields of isolated products are shown; unreacted hydrocarbons were also presented in all entries. [c] Oxone® was added in small portions during indicated period of time. [d] Yield was determined by GC analysis. [e] 10 mol % of PhI was used.

However, unreacted hydrocarbons were also present in all the reactions. Two products were obtained in the oxidation of 1,4-diethylbenzene, 4'-ethylaceto-phenone and *p*-diacetylbenzene (Table 9, Entry 2). 4'-Ethylacetophenone, the product of oxidation of single C–H bond, was obtained in 77% yield, while *p*-diacetylbenzene, the product where both C–H bonds are oxidized, was formed in only 11% yield. Oxidation of *p*-xylene, as well as 1-(t-Bu)-3,5-dimethylbenzene, however, yielded in only one product in each case [4-methyl-benzaldehyde, 18% yield and 3-(t-Bu)-5-methylbenzaldehyde, 23% yield, respectively, Table 9, Entry 3 and 4]. The oxidation of the unactivated C–H bond in adamantane under these conditions proceeded with a very low conversion (1-adamantanol, 1.5% yield, Table 9, Entry 9). However, our protocol is more selective than the high-temperature IBX/Oxone® procedure[186d], and generally does not afford products of C–C bond cleavage and carboxylic acids.

A plausible, simplified mechanism for the catalytic oxidation of alcohols and hydrocarbons includes two catalytic cycles. As it was proposed earlier, the process starts with the initial oxidation of PhI to PhIO, and then to $PhIO_2$ by the Oxone®/Ru(III,V). The highly active monomer $PhIO_2$ species, generated *in situ*, are responsible for actual oxidation of organic substrates by mechanism proposed earlier[186d].



Scheme 64

We assume that the intermediate oxoruthenium complexes are responsible for the reoxidation of the initially formed PhIO to $PhIO_2$ (Scheme 64). It is also possible that the oxidation of organic substrates with $PhIO_2$ in this system is also catalyzed by ruthenium species.

C. Summary

In conclusion, we have developed an extremely mild and efficient tandem catalytic system for oxidation of alcohols and hydrocarbons based on a Ru(III)-catalyzed reoxidation of PhIO to $PhIO_2$ using Oxone® as the stoichiometric oxidant. In general, moderate to high yields of corresponded products were obtained in these oxidations under mild reaction conditions. Therefore, our method is highly selective an generally does not afford products of C–C bond cleavage.

2.4 Conclusion

We have reported a safe, convenient, and straightforward procedure for preparing fluorous [bis(trifluoroacetoxy)iodo]perfluoroalkanes and [bis(trifluoroacetoxy)iodo]-arenes in good to excellent yields by the oxidation of the corresponding perfluoroalkyl iodides and iodoarenes with Oxone® at room temperature. The [bis(trifluoroacetoxy)iodo]perfluoroalkanes can be easily converted to [hydroxyl-(tosyloxy)iodo]perfluoroalkanes, which are stable for storage at room temperature and, in contrast to the trifluoroacetates, are not sensitive to light and moisture. Moreover, several new compounds were obtained by this method.

In addition, two new synthetic methodologies have been discovered during this work. We have developed a new, simple and efficient approach to Hofmann-type rearrangement of amides to amines in acetonitrile-water medium without having to isolate the isocyanate intermediate. Moreover, various alkyl and arylamides, where $C(O)NH_2$-group is connected to the ring by a -CH_2-bridge, can be easily converted into the corresponding carbamates if methanol is used as a solvent. We have developed experimental evidence that the reaction is induced by an iodine(III)-species **143** and **144** generated *in situ* by the oxidation of iodobenzene with Oxone®. We have also found that our protocol leads to the formation of 1,4-benzoquinones if benzamide (and its substituted derivatives) are subjected to the rearrangement.

Finally, we have developed an extremely efficient tandem, catalytic system for the oxidation of alcohols and hydrocarbons based on Ru(III)-catalyzed reoxidation of PhIO to $PhIO_2$ using Oxone® as stoichiometric oxidant. In general, moderate to high yields of products were obtained in these oxidations. Because of the mild reaction conditions applied in these reactions, our method is highly selective and generally does not afford products of C–C bond cleavage.

Chapter 3

Experimental

3. Experimental Section

3.1 General Methods

All melting points were determined in an open capillary tube with a Mel-temp II® melting point apparatus and are uncorrected. Infrared spectra were recorded as a KBr pellet on a PERKIN ELMER Spectrum BX FT-IR System 1600 series spectrophotometer; absorptions are reported in reciprocal centimeters. NMR spectra were recorded at 300 and 500 MHz (^{1}H NMR), 125.6 MHz (^{13}C NMR) and 282 MHz (^{19}F NMR). Chemical shifts are reported in parts per million (ppm). ^{1}H and ^{13}C chemical shifts are referenced relative to the tetramethylsilane; ^{19}F chemical shifts spectra are referenced relative to the $CFCl_3$. GC-MS analysis was carried out with HP 5890A gas chromatograph using a 5970 Series mass selective detector. Elemental analysis was conducted by the Atlantic Microlab, Inc., Norcross, GA.

3.2 Materials

All commercial reagents were ACS reagent grade and used without further purification. All other reagents and solvents were of commercial quality from freshly opened containers.

3.3 Synthesis and Characterization of Compounds

General procedure for preparing [Bis(trifluoroacetoxy)iodo]perfluoroalkanesv136a-c from Iodoperfluoroalkanes 135a-c (n=4,6,8). To a solution of an appropriate iodoperfluoroalkane **135a-c** (1 g) in CF_3CO_2H (5 ml), Oxone® (1 mol-equiv) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 24 hours. After completion of the reaction, the solvent was evaporated under vacuum. Precipitate was extracted with CH_3CN (15 ml), and insoluble residue was collected by filtration under reduced pressure, washed with CH_3CN (10 ml) and discarded. Evaporation of a filtrate under reduced pressure afforded a crude product which was used in further transformation without additional purification.

[Bis(trifluoroacetoxy)iodo]perfluorobutane (Table 2, Yield 136a).
Reaction of perfluorobutyl iodide **135a** (1 g, 2.89 mmol) with Oxone® (1.776 g, 2.89 mmol) according to the general procedure afforded 1.016 g (62%) of product, isolated as microcrystalline solid, mp 55-57 °C (lit.[99], mp 97-98 °C). ^{19}F NMR 282 MHz (CD_3CN): δ -75.27 (br s), -76.22 (s), -80.22 (s), -115.42 (m), -125.00 (m).

[Bis(trifluoroacetoxy)iodo]perfluorohexane (Table 2, Yield 136b).
Reaction of perfluorohexyl iodide **135b** (1 g, 2.24 mmol) with Oxone® (1.377 g, 2.24 mmol) according to the general procedure afforded 1.32 g (88%) of product, isolated as microcrystalline solid, mp 65-67 °C (lit.[111], mp 67 °C (dec.)). ^{19}F NMR 282 MHz (CD_3OD): δ -75.17 (s), -75.80 (s), -80.70 (s), -113.14 (br s), -120.46 (br s), -122.15 (br s), -125.67 (br s). ^{13}C NMR (partial) 125.6 MHz (CD_3OD): δ 115.56 (q, J_{CF}=283 Hz, $CO\underline{C}F_3$).

[Bis(trifluoroacetoxy)iodo]perfluorooctane (Table 2, Yield 136c).
Reaction of perfluorooctyl iodide **135c** (1 g, 1.83 mmol) with Oxone® (1.125 g, 1.83 mmol) according to the general procedure afforded 0.947 g (67%) of product, isolated as microcrystalline solid, mp 85-87 °C (lit.[115], mp 112-113.5 °C (dec.)). ^{19}F NMR 282 MHz (acetone-d_6): δ -74.75 (s), -75.58 (s), -80.54 (s), -113.07 (br s), -120.34 (br s), -121.29 (br s), -122.15 (br s), -125.63 (br s).

General procedure for preparing [Bis(trifluoroacetoxy)iodo]perfluoroalkanes 136d,e from Iodoperfluoroalkanes 135d,e (n=10,12). To a solution of an appropriate iodoperfluoroalkane **135d**,**e** (0.5 g) in CF_3CO_2H (7 ml), Oxone® (0.5 mol-equiv) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 48 hours. After completion of the reaction, the solvent was evaporated under vacuum. Precipitate was extracted with acetone (15 ml), and insoluble residue was collected by filtration under reduced pressure, washed with acetone (10 ml) and discarded. Evaporation of a filtrate under reduced pressure afforded a crude product which was used in further transformation without additional purification.

[Bis(trifluoroacetoxy)iodo]perfluorodecane (Table 2, Yield 136d).
Reaction of perfluorodecyl iodide **135d** (0.5 g, 0.77 mmol) with Oxone® (0.237 g, 0.385 mmol) according to the general procedure afforded 0.425 g (63%) of product, isolated as microcrystalline solid, mp 65.5-66.5 °C (lit.[115], mp 115-116.5 °C (dec.)). ^{19}F NMR 282 MHz (acetone-d_6): δ -63.98 (s), -75.54 (s), -80.61 (s), -113.07 (br s), -120.32 (br s), -121.13 (br s), -122.15 (br s), -125.65 (br s).

[Bis(trifluoroacetoxy)iodo]perfluorododecane (Table 2, Yield 136e).
Reaction of perfluorododecyl iodide **135e** (0.5 g, 0.67 mmol) with Oxone® (0.206 g, 0.385 mmol) according to the general procedure afforded 0.44 g (68%) of product, isolated as microcrystalline solid, mp 98-99 °C (lit.[115], mp 121-122.5 °C (dec.)). ^{19}F NMR 282 MHz (acetone-d_6): δ -63.88 (s), -75.81 (s), -80.58 (s), -113.05 (br s), -120.30 (br s), -121.08 (br s), -122.04 (br s), -125.64 (br s). ^{13}C NMR (partial) 125.6 MHz (acetone-d_6): δ 158.49 (q, J_{CF}=40.3 Hz, $\underline{C}OCF_3$), 115.93 (q, J_{CF}=286 Hz, $CO\underline{C}F_3$).

General procedure for preparing [Hydroxy(sulfonoxy)iodo]perfluoroalkanes 137a-c from [Bis(triacetoxy)iodo]perfluoroalkanes 136a-c (n=4,6,8). To a stirred solution of TsOH·H_2O (1.25 mol-equiv) in CH_3CN (5-10 ml) the appropriate trifluoroacetate **136a-c** (1.14-1.82 mmol) was added at 0 °C. The mixture was warmed to r.t. and stirred until the formation of a white crystalline precipitate. Evaporation of a solvent under reduced pressure afforded a crude product. Analytically pure materials were obtained by recrystallization from CH_3CN.

[Hydroxy(sulfonoxy)iodo]perfluorobutane (Table 2, Yield 137a).

Reaction of [bis(trifluoroacetoxy)iodo]perfluorobutane **136a** (0.922 g, 1.60 mmol) according to the general procedure afforded 0.854 g (100%) of product, isolated as microcrystalline solid, mp 135-137 °C (lit.[117], mp 137-139 °C). ^{1}H NMR 500 MHz (CD_3CN/DMSO-d_6, 20:1): δ 7.70 (d, *J*=7.4 Hz, 2H, ArH), 7.28 (d, *J*=7.4 Hz, 2H, ArH), 2.39 (s, 3H, C$\underline{H}_3$). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 143.64, 137.25, 129.79, 125.46, 21.37. ^{19}F NMR 282 MHz (CD_3CN/DMSO-d_6, 20:1): δ -80.47 (s), -83.70 (s), -116.16 (s), -125.10 (s).

[Hydroxy(sulfonoxy)iodo]perfluorohexane (Table 2, Yield 137b).

Reaction of [bis(trifluoroacetoxy)iodo]perfluorohexane **136b** (1.223 g, 1.82 mmol) according to the general procedure afforded 1.143 g (99%) of product, isolated as microcrystalline solid, mp 141-143 °C (lit.[117], mp 142-144 °C). ^{1}H NMR 500 MHz (CD_3CN/DMSO-d_6, 20:1): δ 7.68 (d, *J*=8.4 Hz, 2H, ArH), 7.26 (d, *J*=8.4 Hz, 2H, ArH), 2.40 (s, 3H, C$\underline{H}_3$). ^{13}C NMR (partial) 125.6 MHz (CD_3CN/DMSO-d_6, 22:1): δ 140.50, 128.93, 125.96, 20.51. ^{19}F NMR 282 MHz (CD_3CN/DMSO-d_6, 20:1): δ -63.73 (s), -80.21 (s), -112.85 (br s), -120.29 (s), -121.95 (br s), -125.33 (br s).

[Hydroxy(sulfonoxy)iodo]perfluorooctane (Table 2, Yield 137c).

Reaction of [bis(trifluoroacetoxy)iodo]perfluorooctane **136c** (0.877 g, 1.14 mmol) according to the general procedure afforded 0.73 g (88%) of product, isolated as microcrystalline solid, mp 147-149 °C (lit.[117], mp 147-149 °C). ^{1}H NMR 500 MHz (CD_3CN/DMSO-d_6, 20:1): δ 7.68 (d, *J*=8.5 Hz, 2H, ArH), 7.24 (d, *J*=8.5 Hz, 2H, ArH), 2.39 (s, 3H, C$\underline{H}_3$). ^{13}C NMR (partial) 125.6 MHz (CD_3CN/DMSO-d_6, 22:1): δ 140.13, 128.83, 125.93, 20.49. ^{19}F NMR 282 MHz (CD_3CN/DMSO-d_6, 20:1): δ -75.39 (s), -80.24 (s), -82.70 (s), -112.96 (s), -119.89 (s), -121.03 (s), -121.88 (br s), -125.34 (s).

General procedure for preparing [Hydroxy(sulfonoxy)iodo]perfluoroalkanes 137d,e from [Bis(triacetoxy)iodo]perfluoroalkanes 136d,e (n=10,12). To a stirred solution of $TsOH{\cdot}H_2O$ (1.25 mol-equiv) in acetone (5-10 ml) the appropriate trifluoroacetate **136d,e**

(0.19-0.43 mmol) was added at 0 °C. The mixture was warmed to r.t. and stirred until the formation of a slightly yellow crystalline precipitate. Evaporation of a solvent under reduced pressure afforded a pure product.

[Hydroxy(sulfonoxy)iodo]perfluorodecane (Table 2, Yield 137d).

Reaction of [bis(trifluoroacetoxy)iodo]perfluorodecane **136d** (0.375 g, 0.43 mmol) according to the general procedure afforded 0.355 g (99%) of product, isolated as microcrystalline solid, mp 97-99 °C. Anal. Calcd for $C_{17}H_8F_{21}IO_4S$: C, 24.48; H, 0.97; F, 47.83; S, 3.84. Found: C, 26.21; H, 1.49; F, 43.20; S, 4.38. ^1H NMR 500 MHz (acetone-d_6): δ 7.78 (d, *J*=8.0 Hz, 2H, ArH), 7.39 (d, *J*=8.0 Hz, 2H, ArH), 2.42 (s, 3H, C$\underline{H}_3$). ^{13}C NMR (acetone-d_6): δ 144.16, 138.88, 130.39, 127.48, 21.42. ^{19}F NMR 282 MHz (acetone-d_6): δ -63.94 (s), -80.61 (s), -113.07 (s), -120.34 (s), -121.15 (s), -122.16 (br s), -125.66 (s).

[Hydroxy(sulfonoxy)iodo]perfluorododecane (Table 2, Yield 137e).

Reaction of [bis(trifluoroacetoxy)iodo]perfluorododecane **136e** (0.19 g, 0.195 mmol) according to the general procedure afforded 0.178 g (98%) of product, isolated as microcrystalline solid, mp 97 °C (dec.). Anal. Calcd for $C_{19}H_8F_{25}IO_4S$: C, 24.43; H, 0.86; F, 50.84; S, 3.43. Found: C, 24.02; H, 0.89; F, 50.49; S, 3.32. ^1H NMR 500 MHz (acetone-d_6): δ 7.78 (d, *J*=8.1 Hz, 2H, ArH), 7.39 (d, *J*=8.1 Hz, 2H, ArH), 2.42 (s, 3H, C$\underline{H}_3$). ^{13}C NMR (partial) 125.6 MHz (acetone-d_6): δ 130.35, 127.46, 21.40. ^{19}F NMR 282 MHz (acetone-d_6): δ -63.95 (s), -80.55 (s), -113.04 (s), -120.27(s), -121.05 (s), -122.11 (s), -125.60 (s).

General procedure for preparing [Bis(trifluoroacetoxy)iodo]arenes 139a-m from Iodoarenes 138a-m. To a solution of an appropriate iodoarene **138a-m** (0.5 mmol) in a mixture of CF_3CO_2H (1.5 ml) and $CHCl_3$ (0.5 ml), Oxone® (1.5 mol-equiv) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for a period of time indicated in Table 1 (the reaction was monitored by TLC in hex/EtOAc (3:1 v/v) by disappearance of the iodoarene). After completion of the reaction, the solvent was evaporated under vacuum. Precipitate was extracted with $CHCl_3$ (10 ml), and insoluble residue was collected by filtration under reduced pressure, washed with $CHCl_3$ (5 ml) and discarded. Evaporation of a filtrate under reduced pressure afforded a crude product which is purified by recrystallization from CF_3CO_2H/hexane.

[Bis(trifluoroacetoxy)iodo]benzene (Table 3, Yield 139a).

Reaction of iodobenzene **138a** (0.102 g, 0.5 mmol) according to the general procedure afforded 0.208 g (97%) of product, isolated as microcrystalline solid, mp 118-120 °C (lit.[94], mp 119-120 °C). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.22 (d, J=7.8 Hz, 2H, ArH), 7.75 (t, J=7.8 Hz,1H, ArH), 7.64 (t, J=7.8 Hz, 2H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.14 (q, J_{CF}=42 Hz, $\underline{C}OCF_3$), 135.20, 133.67, 132.08, 122.84, 112.90 (q, J_{CF}=287 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-4-fluorobenzene (Table 3, Yield 139b).

Reaction of 1-fluoro-4-iodobenzene **138b** (0.111 g, 0.5 mmol) under general conditions afforded 0.178 g (80%) of product, isolated as microcrystalline solid, mp 94-96 °C (lit.[94], mp 94-96 °C). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.23 (dd, J=5.0 Hz, 2H, ArH), 7.26-7.33 (m, 2H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 165.39 (d, J_{CF}=260 Hz, $\underline{C}F$), 161.22 (q, J_{CF}=40 Hz, $\underline{C}OCF_3$), 138.30 (d, J_{CF}=9 Hz, $\underline{C}CCF$), 119.88, 116.46, 112.92 (q, J_{CF}=289 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-4-bromobenzene (Table 3, Yield 139c).

Reaction of 1-bromo-4-iodobenzene **138c** (0.142 g, 0.5 mmol) under general conditions afforded 0.24 g (94%) of product, isolated as microcrystalline solid, mp 123-125 °C (lit.[94], mp 125-127 °C). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.07 (d, J=9.4 Hz, 2H, ArH), 7.76 (d, J=9.4 Hz, 2H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.20 (q, J_{CF}=42 Hz, $\underline{C}OCF_3$), 136.57, 135.36, 129.31, 120.51, 112.87 (q, J_{CF}=288 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-4-chlorobenzene (Table 3, Yield 139d).

Reaction of 1-chloro-4-iodobenzene **138d** (0.119 g, 0.5 mmol) under general conditions afforded 0.16 g (69%) of product, isolated as microcrystalline solid, mp 128-130 °C (lit.[94], mp 129-130 °C). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.15 (d, *J*=8.7 Hz, 2H, ArH), 7.60 (d, *J*=8.7 Hz, 2H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.22 (q, J_{CF}=41 Hz, $\underline{C}OCF_3$), 140.90, 136.62, 132.43, 119.71, 112.89 (q, J_{CF}=287 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-3-chlorobenzene (Table 3, Yield 139e).

Reaction of 1-chloro-3-iodobenzene **138e** (0.119 g, 0.5 mmol) under general conditions afforded 0.211 g (91%) of product, isolated as microcrystalline solid, mp 95-97 °C. Anal. Calcd for $C_{10}H_4ClF_6IO_4$: C, 25.86; H, 0.87; I, 27.32; F, 24.54. Found: C, 25.64; H, 0.89; I, 27.55; F, 24.30. ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.21 (s, 1H, ArH), 8.11 (d, *J*=8.5 Hz, 1H, ArH), 7.72 (d, *J*=8.5 Hz, 1H, ArH), 7.59 (t, *J*=8.5 Hz, 1H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.28 (q, J_{CF}=42 Hz, $\underline{C}OCF_3$), 136.76, 134.75, 133.13, 132.78, 132.11, 121.80, 112.92 (q, J_{CF}=288 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-2-chlorobenzene (Table 3, Yield 139f).

Reaction of 1-chloro-2-iodobenzene **138f** (0.119 g, 0.5 mmol) under general conditions afforded 0.226 g (97%) of product, isolated as microcrystalline solid, mp 98-100°C. Anal. Calcd for $C_{10}H_4ClF_6IO_4$: C, 25.86; H, 0.87; I, 27.32; F, 24.54. Found: C, 25.13; H, 0.82; I, 27.87; F, 25.34. ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.37 (d, *J*=8.1 Hz, 1H, ArH), 7.85 (d, *J*=8.1 Hz, 1H, ArH), 7.72 (t, *J*=8.1 Hz, 1H, ArH), 7.48 (t, *J*=8.1 Hz, 1H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.33 (q, J_{CF}=41 Hz, $\underline{C}OCF_3$), 138.67, 137.63, 135.71, 130.63, 129.79, 126.06, 113.01 (q, J_{CF}=286 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-4-(trifluoromethyl)benzene (Table 3, Yield 139g).

Reaction of 4-iodobenzotrifluoride **138g** (0.136 g, 0.5 mmol) under general conditions afforded 0.17 g (68%) of product, isolated as microcrystalline solid, mp 121-123 °C (lit.[95], mp 62 °C (dec.)). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.34 (d, *J*=7.9 Hz, 2H, ArH), 7.89 (d, *J*=7.9 Hz, 1H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.33 (q,

J_{CF}=42 Hz, $\underline{C}OCF_3$), 135.42, 133.81, 129.03, 128.15, 126.30, 112.94 (q, J_{CF}=288 Hz, $CO\underline{C}F_3$). ^{19}F NMR 282 MHz ($CDCl_3$): δ -63.91 (s), -73.85 (s).

1-[Bis(trifluoroacetoxy)iodo]-3,5-bis(trifluoromethyl)benzene (Table 3, Yield 139h).
Reaction of 1-iodo-3,5-bis(trifluoromethyl)benzene **138h** (0.170 g, 0.5 mmol) under general conditions afforded 0.267 g (94%) of product, isolated as microcrystalline solid, mp 82 °C (dec.) (lit.[95], mp 82 °C (dec.)). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.60 (s, 2H, ArH), 8.21 (s, 1H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.50 (q, J_{CF}=40 Hz, $\underline{C}OCF_3$), 135.20 (q, J_{CF}=35 Hz, $\underline{C}CF_3$), 134.83, 127.47 (q, J_{CF}=4 Hz, $\underline{C}CCF_3$), 121.95 (q, J_{CF}=274 Hz, $C\underline{C}F_3$), 121.49, 112.96 (q, J_{CF}=287 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-4-nitrobenzene (Table 3, Yield 139i).
Reaction of 1-iodo-4-nitrobenzene **138i** (0.125 g, 0.5 mmol) under general conditions afforded 0.172 g (72%) of product, isolated as microcrystalline solid, mp 157-159 °C (lit.[94], mp 158-159 °C). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.40-8.48 (m, 4H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.32 (q, J_{CF}=43 Hz, $\underline{C}OCF_3$), 150.42, 136.21, 126.91, 126.84, 112.89 (q, J_{CF}=285 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-3-nitrobenzene (Table 3, Yield 139j).
Reaction of 1-iodo-3-nitrobenzene **138j** (0.125 g, 0.5 mmol) under general conditions afforded 0.138 g (58%) of product, isolated as microcrystalline solid, mp 141-143 °C (lit.[94], mp 143-144 °C). ^{1}H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 9.10 (s, 1H, ArH), 8.61 (d, J=8.2 Hz, 1H, ArH), 8.55 (d, J=8.2 Hz, 1H, ArH), 7.90 (t, J=8.2 Hz, 1H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 161.31 (q, J_{CF}=42 Hz, $\underline{C}OCF_3$), 149.12, 140.31, 132.92, 130.29, 128.35, 121.18, 112.90 (q, J_{CF}=288 Hz, $CO\underline{C}F_3$).

4-[Bis(trifluoroacetoxy)iodo]benzoic acid (Table 3, Yield 139k).
Reaction of 4-iodobenzoic acid **138k** (0.124 g, 0.5 mmol) under general conditions afforded 0.127 g (54%) of product, isolated as microcrystalline solid, mp 109-111 °C. Anal. Calcd for $C_{11}H_5F_6IO_6$: C, 27.87; H, 1.06. Found: C, 27.17; H, 1.26. ^{1}H NMR 300

MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.34 (s, 4H, ArH). ^{13}C NMR ($CDCl_3/CF_3CO_2D$, 60:1): δ 169.98, 160.66 (q, J_{CF}=43 Hz, $\underline{C}OCF_3$), 135.25, 133.68, 133.18, 127.47, 112.91 (q, J_{CF}=288 Hz, $CO\underline{C}F_3$).

3-[Bis(trifluoroacetoxy)iodo]benzoic acid (Table 3, Yield 139l).

Reaction of 3-iodobenzoic acid **138l** (0.124 g, 0.5 mmol) under general conditions afforded 0.098 g (41%) of product, isolated as microcrystalline solid, mp 159-161 °C. Anal. Calcd for $C_{11}H_5F_6IO_6$: C, 27.87; H, 1.06. Found: C, 27.29; H, 1.20. ^1H NMR 300 MHz ($CDCl_3/CF_3CO_2D$, 22:1): δ 8.96 (s, 1H, ArH), 8.47-8.52 (m, 2H, ArH), 7.82 (t, *J*=8.2 Hz, 1H, ArH). ^{13}C NMR 125.6 MHz ($CDCl_3/CF_3CO_2D$, 60:1): δ 169.16, 160.34 (q, J_{CF}=43 Hz, $\underline{C}OCF_3$), 140.13, 136.82, 135.20, 132.41, 132.28, 122.17, 112.89 (q, J_{CF}=290 Hz, $CO\underline{C}F_3$).

1-[Bis(trifluoroacetoxy)iodo]-pentafluorobenzene (Table 3, Yield139m).

Reaction of iodopentafluorobenzene **138m** (0.147 g, 0.5 mmol) under general conditions afforded 0.245 g (94%) of product, isolated as isolated as microcrystalline solid, mp 95.5-96.5 °C (lit.[175], mp 96 °C). ^{19}F NMR 300 MHz (DMSO-d_6): δ -73.87 (s), -123.58 (s), -144.83 (s), -157.26 (s). ^{13}C NMR 125.6 MHz (DMSO-d_6): δ 159.68 (q, J_{CF}=37 Hz, $\underline{C}OCF_3$), 148.22 (m), 146.32 (m), 138.16 (m), 136.22 (m), 115.57 (q, J_{CF}=289 Hz, $CO\underline{C}F_3$).

[Hydroxy(sulfonoxy)iodo]pentafluorobenzene (Scheme 50, Yield 140).

Reaction of [bis(trifluoroacetoxy)iodo]pentafluorobenzene **139m** (0.2 g, 0.385 mmol) according to the general procedure afforded 0.174 g (94%) of product, isolated as microcrystalline solid, mp 160 °C (dec.). Anal. Calcd for $C_{13}H_8F_5IO_4S$: C, 32.38; H, 1.67; S, 6.65. Found: C, 33.36; H, 1.78; S, 6.82. ^1H NMR 500 MHz (CD_3CN/DMSO-d_6, 20:1): δ 7.57 (d, *J*=8.7 Hz, 2H, ArH), 7.24 (d, *J*=8.7 Hz, 2H, ArH), 2.39 (s, 3H, $C\underline{H}_3$). ^{13}C NMR 125.6 MHz ($CDCl_3$/DMSO-d_6, 24:1): δ 141.07, 140.37, 128.85, 125.91, 21.28. ^{19}F NMR 282 MHz (CD_3CN/DMSO-d_6, 20:1): δ -120.48 (s), -153.86 (s), -160.45 (s).

Preparation of benzylamine hydrochloride 142 from 2-phenylacetamide 141 via Hofmann rearrangement (Scheme 51). To the mixture of Oxone® 1.23 g (2 mmol) and iodobenzene 0.204 g (1 mmol) in MeOH (5 ml), 2-phenylacetamide **141** 0.135 g (1 mmol) in CH_3CN/H_2O (1:1, v/v) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 7 h (the reaction was monitored by GC-MS). After completion of the reaction, the reaction mixture was filtered under reduced pressure. The insoluble residue was washed with CH_3CN (5 ml) and discarded. The filtrate was diluted with 10 ml of H_2O, 8 ml of HCl was added, and the mixture was extracted with ether (10 ml). The aqueous layer was concentrated at reduced pressure to give a sticky solid, which was thoroughly dried in vacuo. Crystallization from ethanol-ether afforded 0.136 g (95%) of benzylamine hydrochloride **142** as a slightly yellow crystalline solid, mp 253-255 °C (lit.[176], mp 258-260 °C). ^{1}H NMR 300 MHz (CD_3OD): δ 7.48 -7.40 (m, 5H, Ar$\underline{H}$), 4.12 (br s, 2H, -C$\underline{H}_2$-).

General procedure for preparation of 1,4-benzoquinones 148a-e from amides 147a-e. To the mixture of Oxone® (2 mol-equiv) and iodobenzene (1 mol-equiv) in CH_3CN/H_2O (1:1, v/v), an appropriate amide **147a-e** (1 mmol) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for sufficient period of time (the reaction was monitored by GC-MS). After completion of the reaction, the reaction mixture was diluted with 10 ml of H_2O, and extracted with $CHCl_3$ (3x10 ml). The organic phase was separated, and dried over Na_2SO_4 (anhydrous). Evaporation of $CHCl_3$ under reduced pressure afforded a pure product.

1,4-Benzoquinone (Table 4, Yield 148a).

Reaction of benzamide **147a** (0.121 g, 1 mmol) according to the general procedure afforded 0.106 g (98%) of product, isolated as an orange microcrystalline solid, mp 115-116 °C (lit.[177], mp 116 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 6.78 (s, 4H). The same product was obtained in reaction with 4-methoxybenzamide **147e** (0.102 g, 94%).

2-Methyl-1,4-benzoquinone (Table 4, Yield 148b).

Reaction of *o*-toluamide **147b** (0.135 g, 1 mmol) according to the general procedure afforded 0.122 g (100%) of product, isolated as a yellow microcrystalline solid, mp 68-69 °C (lit.[177], mp 69 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 6.76-6.65 (m, 2H), 6.59 (s, 1H), 2.03 (s, 3H, -C$\underline{H}_3$).

2-Chloro-1,4-benzoquinone (Table 4, Yield 148c).

Reaction of 2-chlorobenzamide **147c** (0.155 g, 1 mmol) according to the general procedure afforded 0.135 g (95%) of product, isolated as a yellowish microcrystalline solid, mp 54-56 °C (lit.[177], mp 55-56 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 6.99 (s, 1H), 6.91 (d, *J*=9.8 Hz, 1H), 6.80 (d, *J*=9.8 Hz, 1H).

2-methoxy-1,4-benzoquinone (Table 4, Yield 148d).

Reaction of 3-methoxybenzamide **147d** (0.151 g, 1 mmol) according to the general procedure afforded 0.134 g (97%) of product, isolated as a slightly brown microcrystalline solid, mp 142-144 °C (lit.[177], mp 144 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 6.72 (br s, 2H), 5.95 (br s, 1H), 3.83 (s, 3H, -OC$\underline{H}_3$).

4-Hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone (Scheme 55, Yield 151).

Reaction of 2,4,6-trimethylbenzamide **149** (0.163 g, 1 mmol) according to the general procedure afforded product, isolated as a semisolid mass which on recrystallization from EtOH/water yields pure crystalline product 0.144 g (95%), mp 44.5-45.5 °C (lit.[178], mp 45-46 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 6.62 (br s, 2H), 1.86 (s, 6H, 2,6-C$\underline{H}_3$), 1.43 (s, 3H, 4-C$\underline{H}_3$).

Preparation of (±)-α-phenylpropylamine 153 from 2-phenylbutyramide 152 via Hofmann rearrangement (Scheme 56). To the mixture of Oxone® 1.23 g (2 mmol) and iodobenzene 0.204 g (1 mmol) in MeOH (5 ml), 2-phenylbutyramide **152** 0.163 g (1 mmol) in CH_3CN/H_2O (1:1, v/v) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for 7 h (the reaction was monitored by

GC-MS). After completion of the reaction, the reaction mixture was diluted with 10 ml of H_2O, and extracted with $CHCl_3$ (3x10 ml). The organic phase was separated, and dried over Na_2SO_4 (anhydrous). Evaporation of $CHCl_3$ under reduced pressure afforded 0.115 g (85%) of (±)-α-phenylpropylamine **153** as a pale yellow oil. ^{1}H NMR 300 MHz ($CDCl_3$): δ 7.33-7.31 (m, 5H, Ar$\underline{H}$), 3.80 (t, *J*=6.9 Hz, 1H, -C$\underline{H}$-), 1.72-1.67 (m, 2H, -C$\underline{H}_2$$CH_3$), 1.61 (br s, 2H, N$\underline{H}_2$), 0.87 (t, *J*=7.3 Hz, 3H, -CH_2C$\underline{H}_3$).

General procedure for preparation of carbamates 155a-k from amides 154a-k via Hofmann rearrangement. To the mixture of Oxone® (2 mol-equiv) and iodobenzene (1 mol-equiv) in MeOH (5 ml), an appropriate amide **154a-k** (1 mmol) was added under stirring at room temperature. The reaction mixture was stirred at room temperature for sufficient period of time (the reaction was monitored by GC-MS). After completion of the reaction, the solvent was evaporated under vacuum. The resulting residue was diluted with 10 ml of H_2O, and extracted with EtOAc (3x10 ml). The organic phase was separated, and dried over $MgSO_4$ (anhydrous). Evaporation of EtOAc under reduced pressure afforded a final product which in case of crystalline products was additionally purified by recrystallization from $CHCl_3$/hexane.

Methyl N-isopropylcarbamate (Table 5, Yield 155c).

Reaction of isobutyramide **154c** (0.087 g, 1 mmol) according to the general procedure afforded 0.111 g (95%) of product, isolated as an oil. ^{1}H NMR 300 MHz ($CDCl_3$): δ 4.55 (br s, 1H, N$\underline{H}$), 3.81 (br s, 1H, C$\underline{H}$), 3.65 (s, 3H, COOC$\underline{H}_3$), 1.15 (d, *J*=6.3 Hz, 6H, 2C$\underline{H}_3$).

Methyl N-cyclobutylcarbamate (Table 5, Yield 155d).

Reaction of cyclobutanecarboxamide **154d** (0.099 g, 1 mmol) according to the general procedure afforded 0.119 g (92%) of product, isolated as an oil. ^{1}H NMR 300 MHz ($CDCl_3$): δ 4.89 (br s, 1H, N$\underline{H}$), 4.18-4.13 (m, 1H, C$\underline{H}$), 3.64 (s, 3H, COOC$\underline{H}_3$), 2.32-2.27 (m, 2H), 1.88-1.81 (m, 2H), 1.71-1.62 (m, 2H).

Methyl N-cyclohexylcarbamate (Table 5, Yield 155e).

Reaction of cyclohexanecarboxamide **154e** (0.127 g, 1 mmol) according to the general procedure afforded 0.140 g (89%) of product, isolated as a slightly yellow microcrystalline solid, mp 73.5-74.5 °C (lit.[181], mp 72-75 °C). ^{1}H NMR 500 MHz ($CDCl_3$): δ 4.56 (br s, 1H, N$\underline{H}$), 3.65 (s, 3H, COOC$\underline{H}_3$), 3.48 (br s, 1H, C$\underline{H}$), 1.92-1.94 (m, 2H), 1.72-1.67 (m, 2H), 1.62-1.58 (m, 1H), 1.38-1.31 (m, 2H), 1.20-1.09 (m, 3H).

Methyl N-(1-adamantanyl)carbamate (Table 5, Yield 155f).

Reaction of 1-adamantanecarboxamide **154f** (0.179 g, 1 mmol) according to the general procedure afforded 0.188 g (90%) of product, isolated as a microcrystalline solid, mp 118-120 °C (lit.[182], mp 120 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 4.54 (br s, 1H, N$\underline{H}$), 3.60 (s, 3H, COOC$\underline{H}_3$), 2.07 (s, 3H), 1.93 (s, 6H), 1.67 (s, 6H).

Methyl (1-Boc-pyrrolidin-2-yl)carbamate (Table 5, Yield 155g).

Reaction of 1-Boc-L-prolinamide **154g** (0.214 g, 1 mmol) according to the general procedure afforded 0.183 g (75%) of product, isolated as an oil. Anal. Calcd for $C_{11}H_{20}N_2O_4$: C, 54.08; H, 8.25. Found: C, 52.61; H, 8.22. ^{1}H NMR 300 MHz ($CDCl_3$): δ 4.63 (br s, 2H, N$\underline{H}$ and C$\underline{H}$), 3.68 (s, 3H, COOC$\underline{H}_3$), 3.16 (br s, 2H), 2.38-2.34 (m, 2H), 1.84-1.81 (m, 2H), 1.44 (s, 9H, COOC(C$\underline{H}_3$)$_3$). ^{13}C NMR 125.6 MHz ($CDCl_3$): δ 179.51, 174.02, 83.04, 79.43, 51.88 (COO$\underline{C}$H$_3$), 46.74, 33.21, 28.62 (COOC($\underline{C}$H$_3$)$_3$), 21.02.

Methyl N-benzylcarbamate (Table 5, Yield 155h).

Reaction of 2-phenylacetamide **154h** (0.135 g, 1 mmol) according to the general procedure afforded 0.160 g (97%) of product, isolated as a microcrystalline solid, mp 63-65 °C (lit.[183], mp 64-65 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 7.34-7.28 (m, 5H, Ar$\underline{H}$), 5.09 (br s, 1H, N$\underline{H}$), 4.36 (s, 2H, -C$\underline{H}_2$-), 3.69 (s, 3H, COOC$\underline{H}_3$).

Methyl N-(4-methylbenzyl)carbamate (Table 5, Yield 155i).

Reaction of 2-(*p*-tolyl)acetamide **154i** (0.149 g, 1 mmol) according to the general procedure afforded 0.166 g (93%) of product, isolated as a white microcrystalline solid, mp 68-70 °C. ^{1}H NMR 300 MHz ($CDCl_3$): δ 7.19-7.12 (m, 5H, Ar$\underline{H}$), 4.98 (br s, 1H, N$\underline{H}$), 4.32 (s, 2H, -C$\underline{H}_2$-), 3.69 (s, 3H, COOC$\underline{H}_3$), 2.33 (s, 3H, -C$\underline{H}_3$).

Methyl N-(*p*-methoxylbenzyl)carbamate (Table 5, Yield 155j).

Reaction of 2-(4-methoxyphenyl)acetamide **154j** (0.165 g, 1 mmol) according to the general procedure afforded 0.185 g (95%) of product, isolated as a white microcrystalline solid, mp 73-74 °C (lit.[184], mp 73-74 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 7.24-7.19 (m, 2H, Ar$\underline{H}$), 6.90-6.84 (m, 2H, Ar$\underline{H}$), 4.97 (br s, 1H, N$\underline{H}$), 4.28 (br s, 2H, -C$\underline{H}_2$-), 3.78 (s, 3H, -OC$\underline{H}_3$), 3.68 (s, 3H, COOC$\underline{H}_3$).

Methyl *N*-[(1-naphthyl)methyl]carbamate (Table 5, Yield 155k).

Reaction of 1-naphthaleneacetamide **154k** (0.185 g, 1 mmol) according to the general procedure afforded 0.200 g (93%) of product, isolated as pale yellow microcrystalline solid, mp 84-86 °C (lit.[185], mp 84-88 °C). ^{1}H NMR 300 MHz ($CDCl_3$): δ 8.01-7.96 (m, 1H, Ar$\underline{H}$), 7.86-7.84 (m, 1H, Ar$\underline{H}$), 7.78-7.77 (m, 1H, Ar$\underline{H}$), 7.52-7.46 (m, 2H, Ar$\underline{H}$), 7.41-7.39 (m, 2H, Ar$\underline{H}$), 5.09 (br s, 1H, N$\underline{H}$), 4.79 (br s, 2H, -C$\underline{H}_2$-), 3.68 (s, 3H, COOC$\underline{H}_3$).

$RuCl_3$-catalyzed oxidation of iodobenzene to iodylbenzene 158 using Oxone® (Scheme 59).

To a mixture of iodobenzene 0.204 g (1 mmol) and Oxone® 0.33 g (0.54 mmol) in 3 ml of CH_3CN/H_2O (1:1, v/v) an aqueous solution of $RuCl_3$ (10 μl of standard 0.16 M solution; 0.0016 mmol) was added via syringe under stirring at room temperature. After stirring for 30 min the second portion of Oxone® (0.32 g, 0.52 mmol) was added, and then after additional 50 min the third portion of Oxone® (0.11 g, 0.18 mmol) was added. The reaction mixture was stirred for 2 h 20 min (the reaction was monitored by TLC by disappearance of PhI), and then the precipitate was filtered, washed with cold water, and dried to afford 0.14 g (59%) of iodylbenzene **158**, mp 229-230 °C (crystallized from hot water; explodes at mp) (lit.[189], mp 235 °C (expl.)). IR (KBr): 731, 713 (IO_2). ^{1}H NMR

500 MHz (DMSO-d_6): δ 7.92 (m, 2H), 7.59 (m, 3H). ^{13}C NMR 125.6 MHz (DMSO-d_6): δ 150.8 (C-IO_2), 131.7, 129.1, 126.6.

Typical preparative procedure for PhI/$RuCl_3$-cocatalyzed oxidation of alcohols (Table 7).

Propiophenone (Table 7, Entry 1): To a mixture of 1-phenylpropanol (0.136 g, 1 mmol), PhI (0.5 mL of standard solution; 0.05 mmol; 5 mol %) and Oxone® (0.737 g, 1.2 mmol) in 3 mL of acetonitrile and 3 mL of water, an aqueous solution of $RuCl_3$ (10 μL of standard solution; 0.0016 mmol; 0.16 mol %) was added under stirring at room temperature. The reaction mixture was stirred for 20 min (the reaction was monitored by TLC by disappearance 1-phenylpropanol). Then 15 mL of ethyl acetate and 20 mL of water were added and the mixture was stirred for 5 min. The organic solution was separated, and the aqueous phase was extracted with ethyl acetate (2x15 ml). Organic phases were combined, washed with NaCl (saturated solution, 20 ml), dried over Na_2SO_4 (anhydrous). Removal of the solvent under vacuum afforded 0.134 g (100%) of propiophenone, isolated as an oil. ^{1}H NMR 500 MHz ($CDCl_3$): δ 7.96 (d, J=7.9 Hz, 2H, Ar<u>H</u>), 7.55 (t, J=7.3 Hz, 1H, Ar<u>H</u>), 7.46 (t, J=7.3 Hz, 2H, Ar<u>H</u>), 3.01 (q, J=7.1 Hz, 2H, -C$\underline{H}_2$-), 1.23 (t, J=7.4 Hz, 3H, C$\underline{H}_3$). The oxidation of other alcohols (Table 7) was performed using a similar procedure. All products were identified by comparison with commercially available samples, and some volatile carbonyl products were additionally identified as 2,4-dinitrophenylhydrazones.

Typical preparative procedure for PhI/$RuCl_3$-cocatalyzed oxidation of aromatic hydrocarbons (Table 9).

1-Indanone (Table 9, Entry 5): To a mixture of indane (0.118 g, 1 mmol), PhI (0.5 mL of of standard solution; 0.05 mmol; 5 mol %) and $RuCl_3$ (10 μL of standard solution; 0.0016 mmol; 0.16 mol %) in 3 mL of acetonitrile and 3 mL of water, Oxone® (total 1.23 g; 2.0 mmol) was added in 2 portions during 1 h under stirring at room temperature (the reaction was monitored by TLC by disappearance of indane). Then 15 mL of ethyl acetate and 20 mL of water were added and the mixture was stirred for 5 min. The organic solution was separated, and the aqueous phase was extracted with ethyl acetate (2x15 ml). Organic phases were combined, washed with NaCl (saturated solution, 20 ml), dried over Na_2SO_4 (anhydrous). Removal of the solvent under vacuum afforded 0.125 g (95%) of 1-indanone, isolated as pale yellow microcrystalline solid, mp 38-40 °C (lit.[190], mp 38-39 °C). ^{1}H NMR 500 MHz ($CDCl_3$): δ 7.76 (d, *J*=7.4 Hz, 1H, ArH), 7.59 (t, *J*=7.7 Hz, 1H, ArH), 7.48 (d, *J*=7.6 Hz, 1H, ArH), 7.37 (t, *J*=7.6 Hz, 1H, ArH), 3.15 (t, J=6.6 Hz, 2H, -CH_2-), 2.71-2.69 (m, 2H, -CH_2-). The oxidation of other hydrocarbons (Table 9) was performed using a similar procedure. All products were identified by comparison with commercially available samples.

ArI/$RuCl_3$-cocatalyzed oxidation of organic substrates (general procedure for GC-MS experiments).

To a mixture of an organic substrate (0.1 mmol), ArI (50 μL of 0.1 M solution in MeCN; 0.005 mmol; 5 mol %) and Oxone® (0.062 – 0.277 g, 0.1 to 0.45 mmol; see Tables 6 and 8) in 0.3 mL of acetonitrile and 0.3 mL of water, an aqueous solution of $RuCl_3$ (1.0 μL of of standard solution; 0.00016 mmol; 0.16 mol %) was added under stirring at room temperature. The reaction mixture was stirred for a period of time indicated in the Tables (the reactions were monitored by TLC by disappearance of organic substrate). Then 2 mL of ethyl acetate and 2 mL of 5%-aqueous solution of sodium thiosulfate were added and the mixture was stirred for 5 min. The organic solution was separated and analyzed using GC-MS. Products were identified by comparison with commercially available samples.

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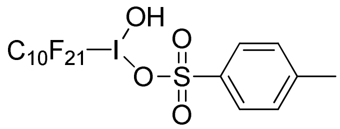
Appendices



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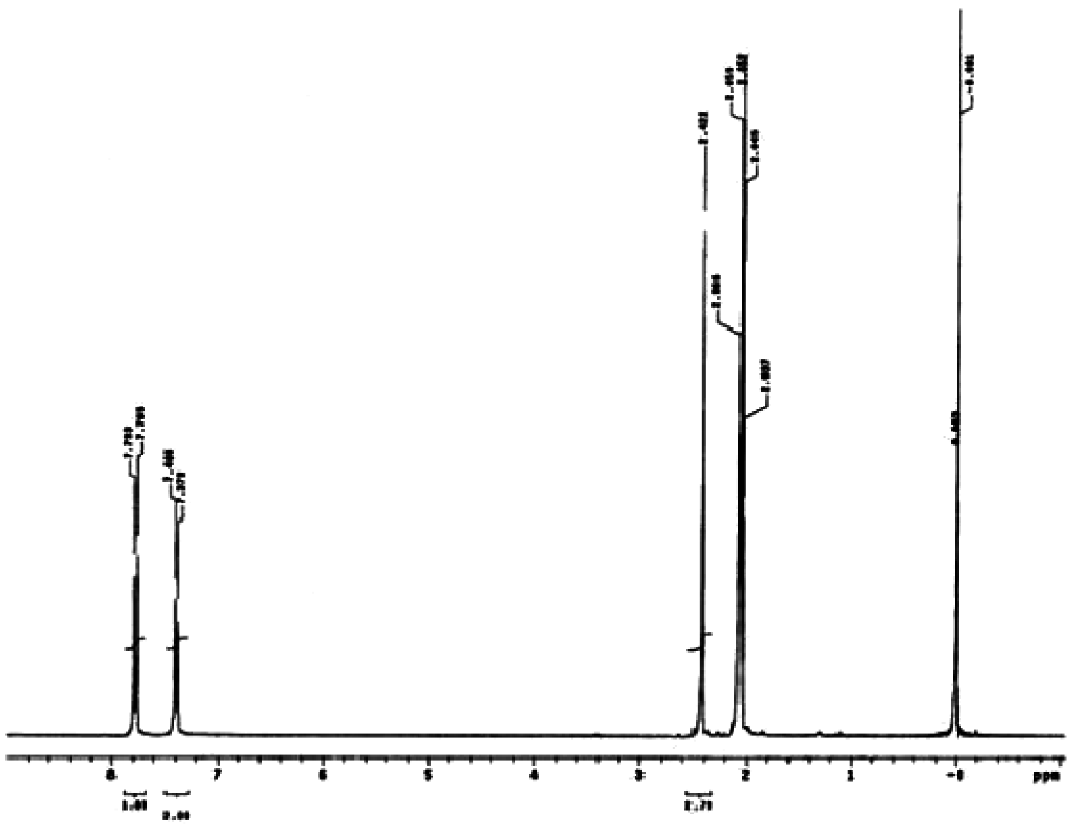

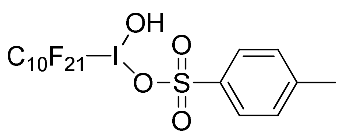

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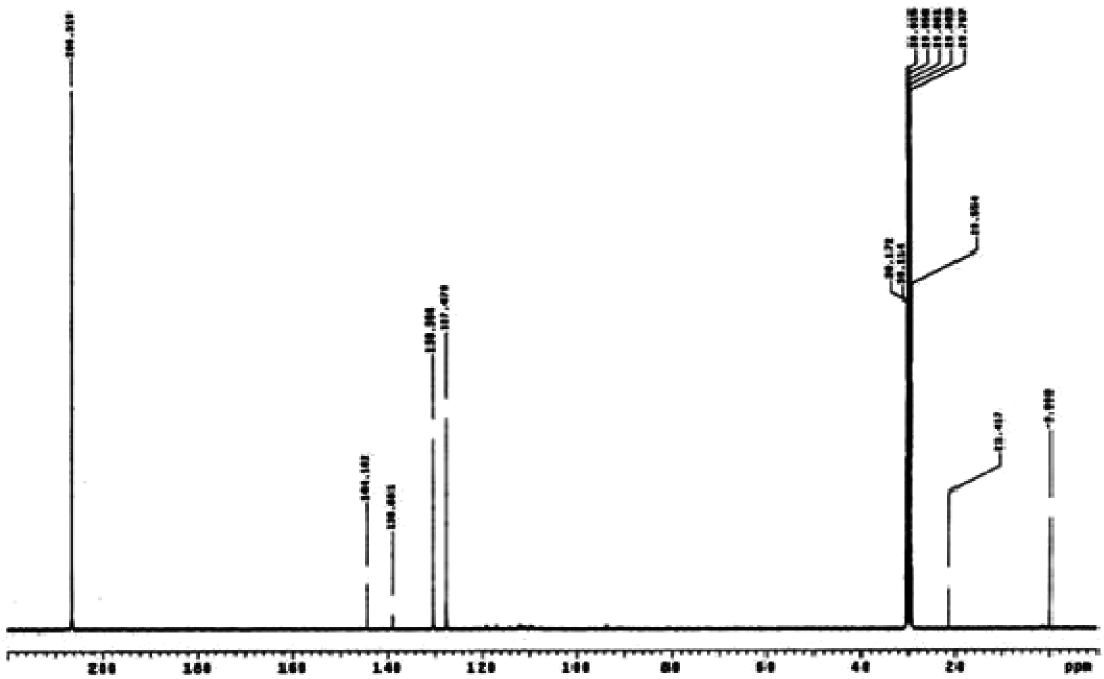

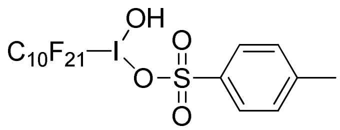

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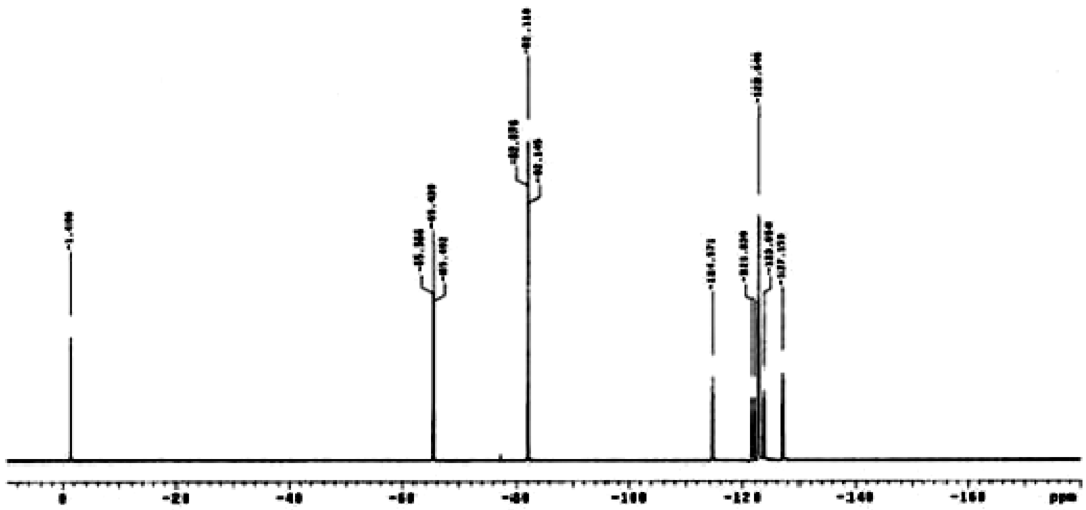

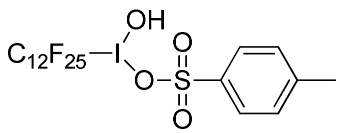

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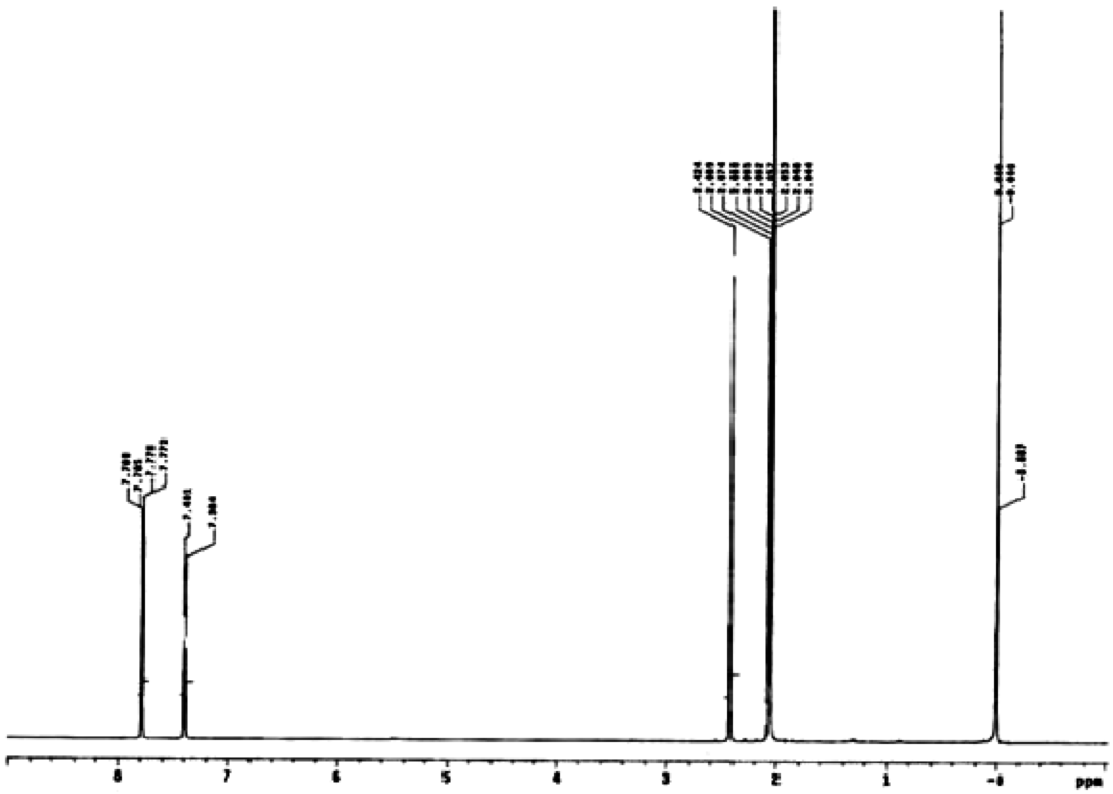

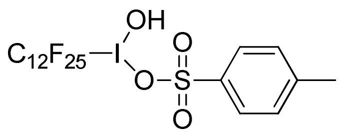

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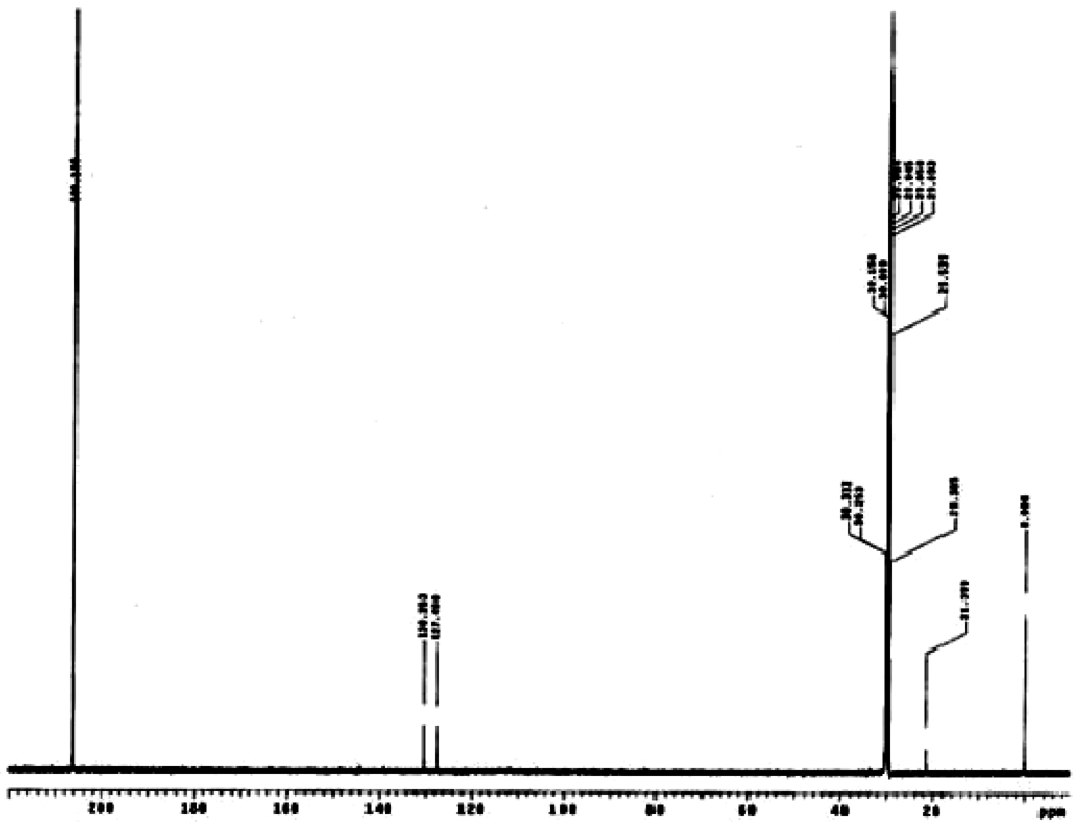

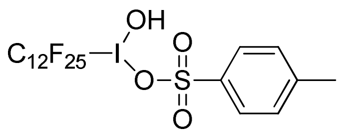

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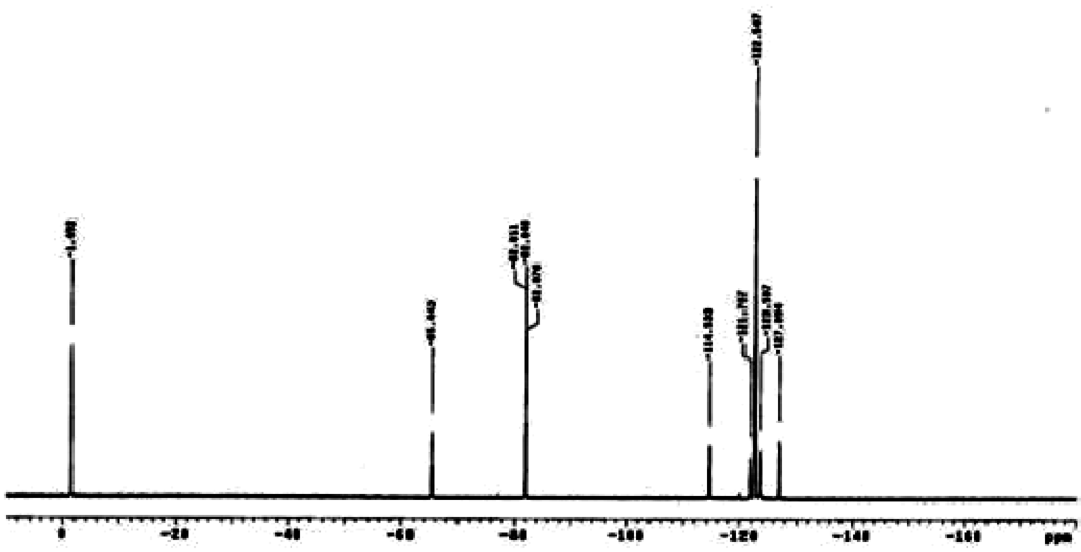

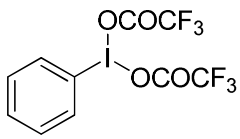

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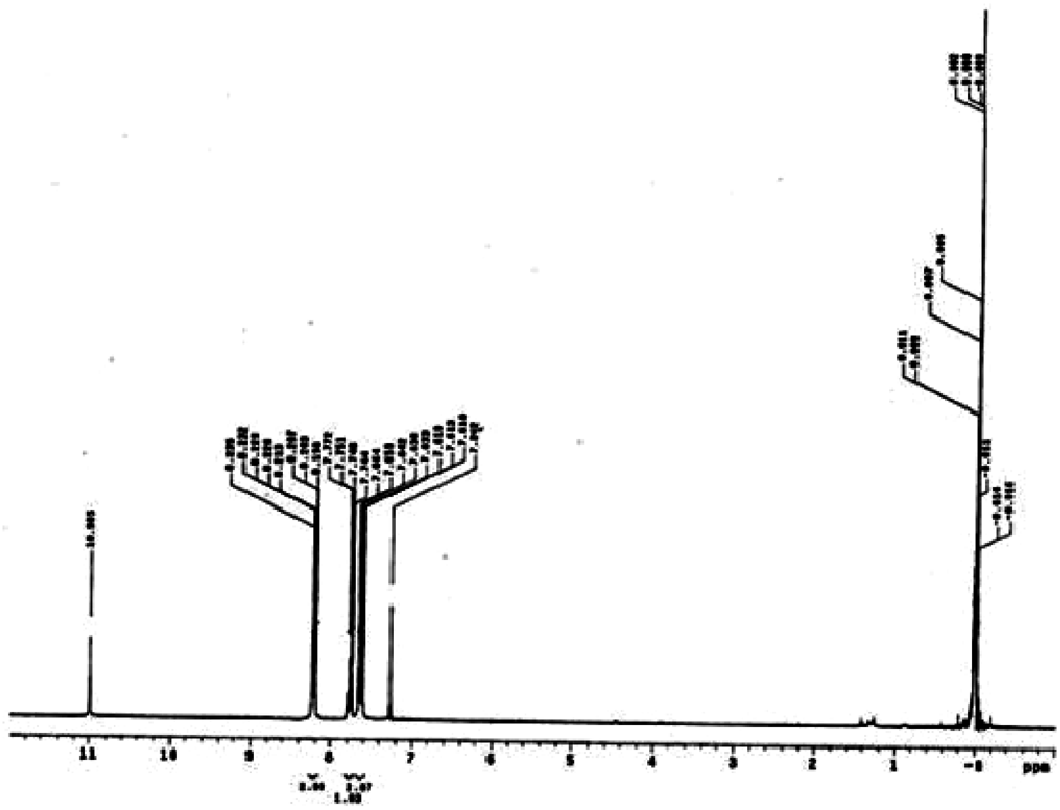

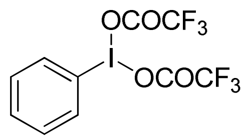

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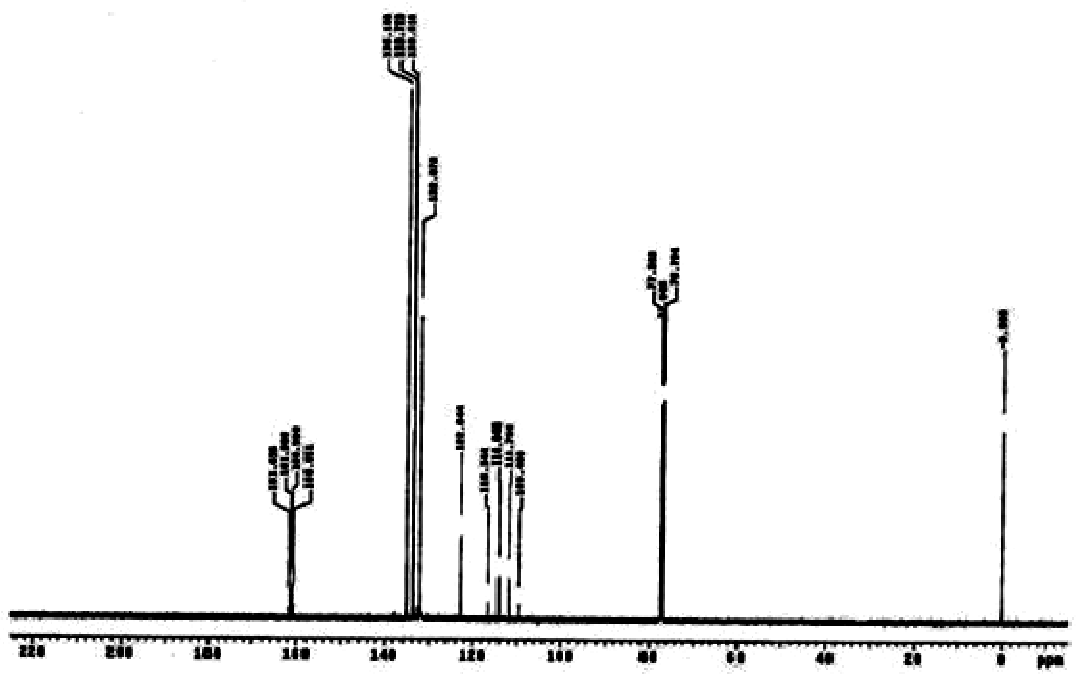

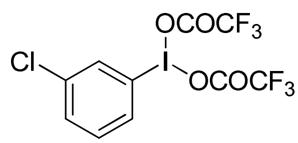

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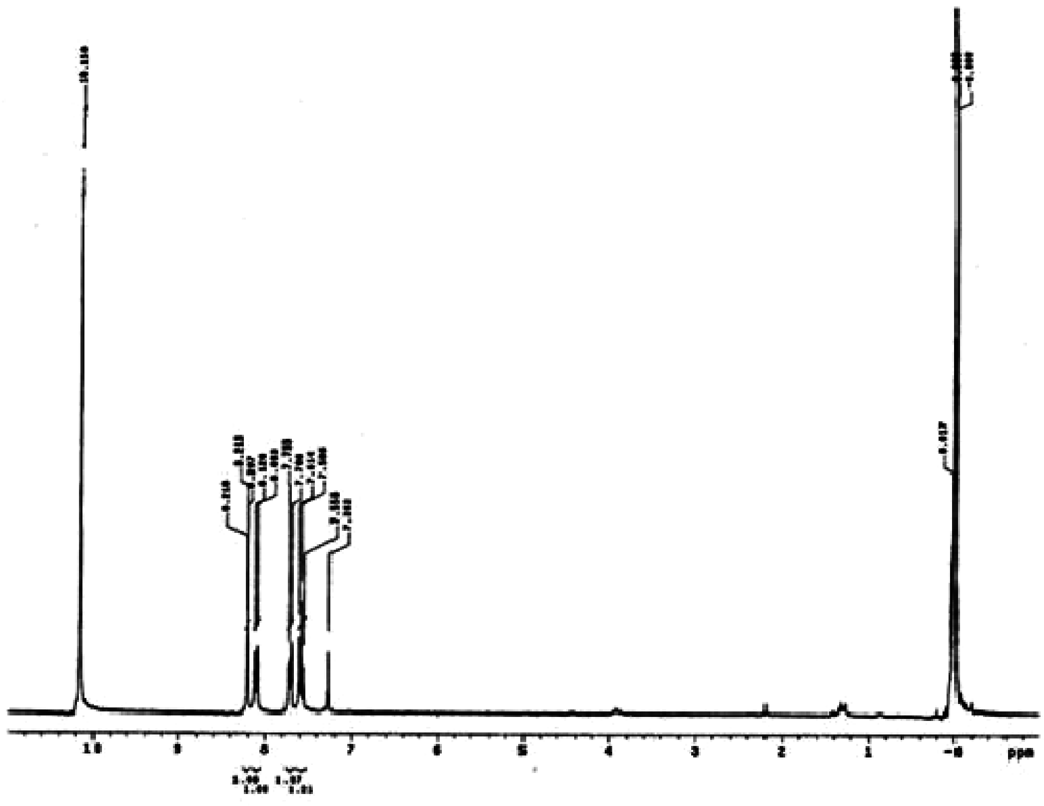

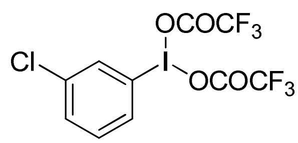

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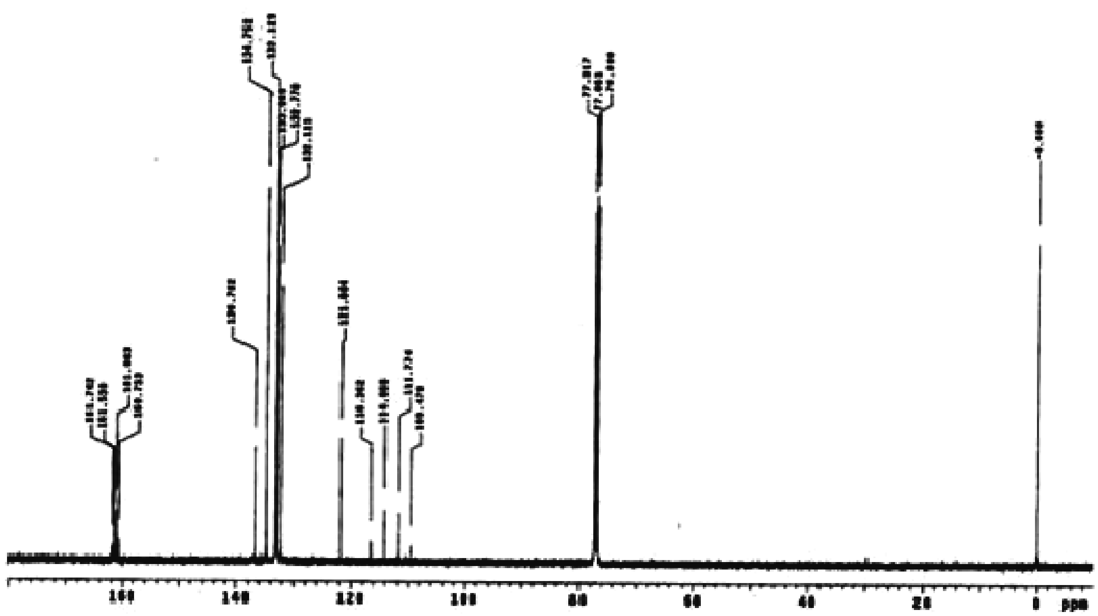

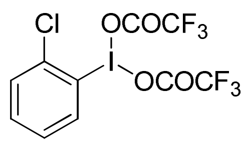

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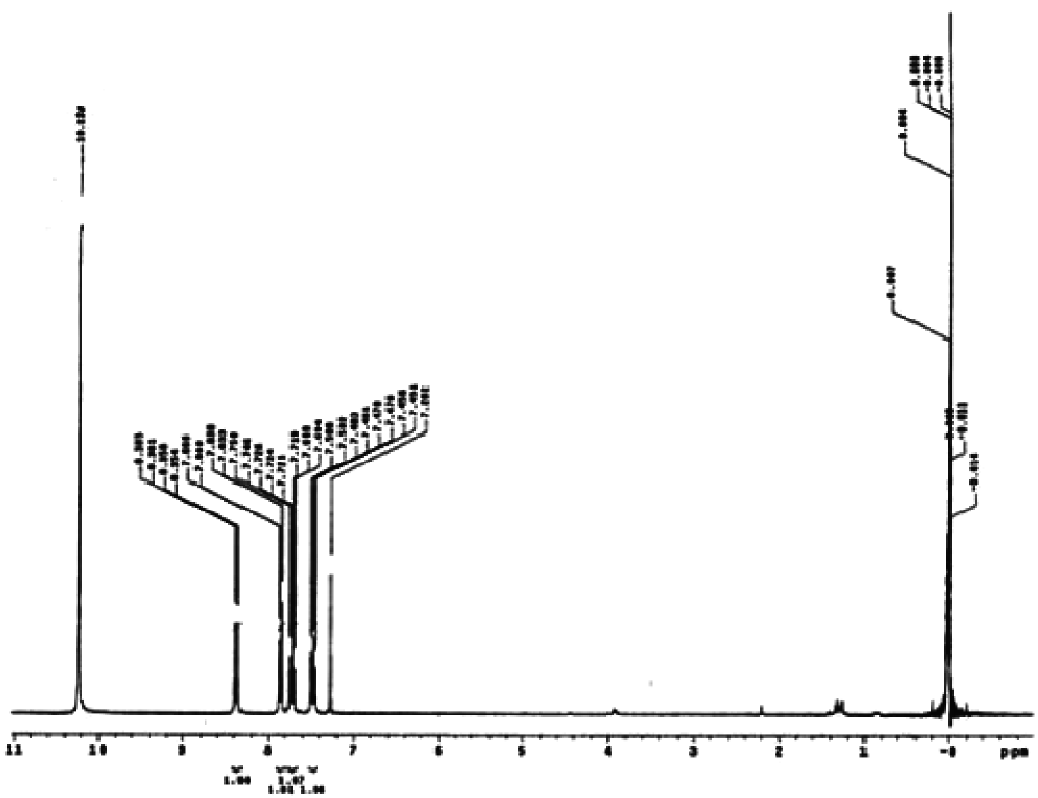

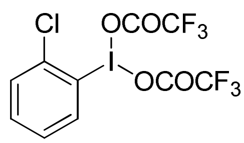

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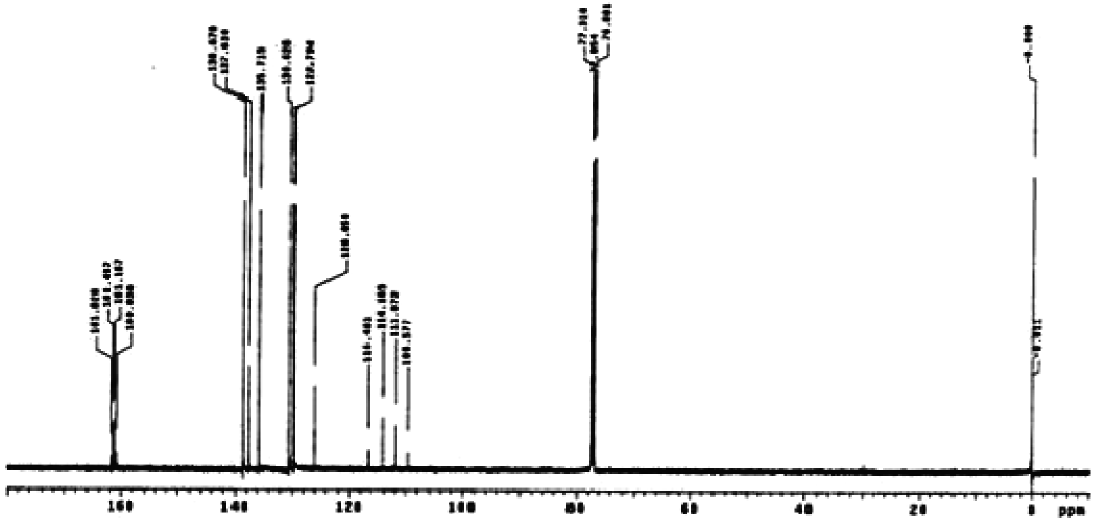

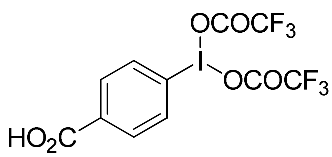

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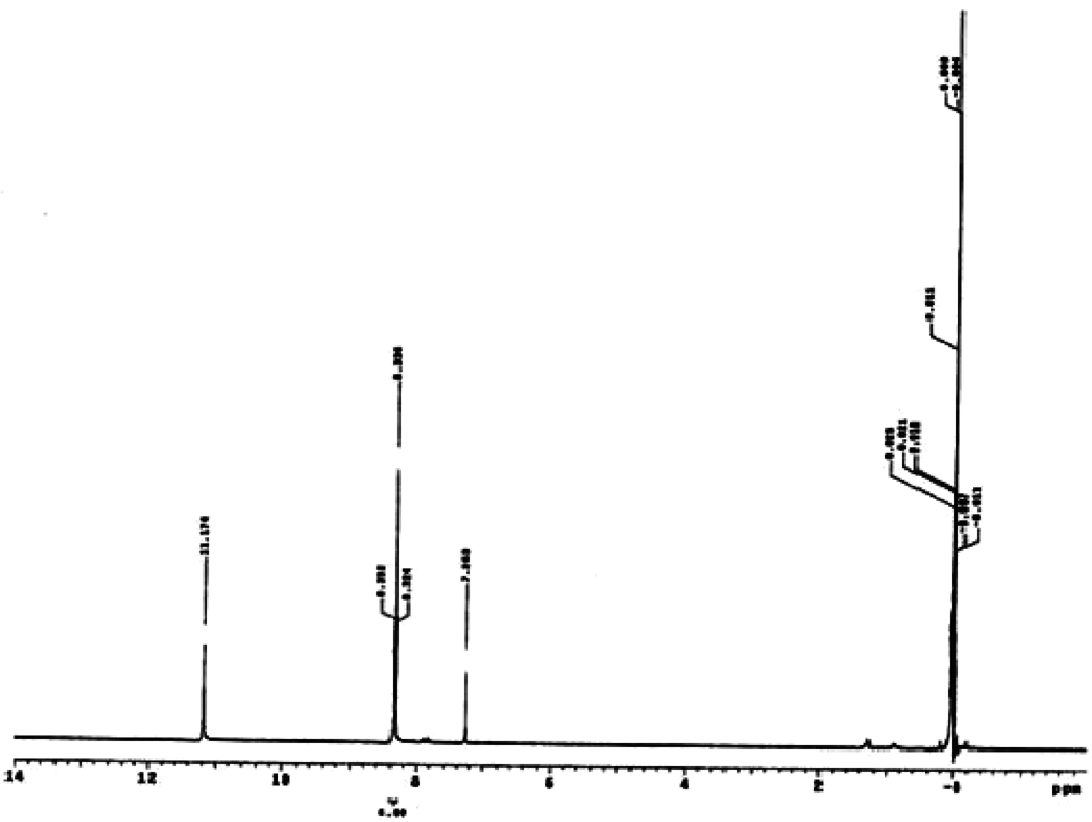

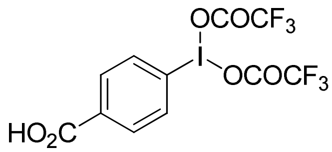

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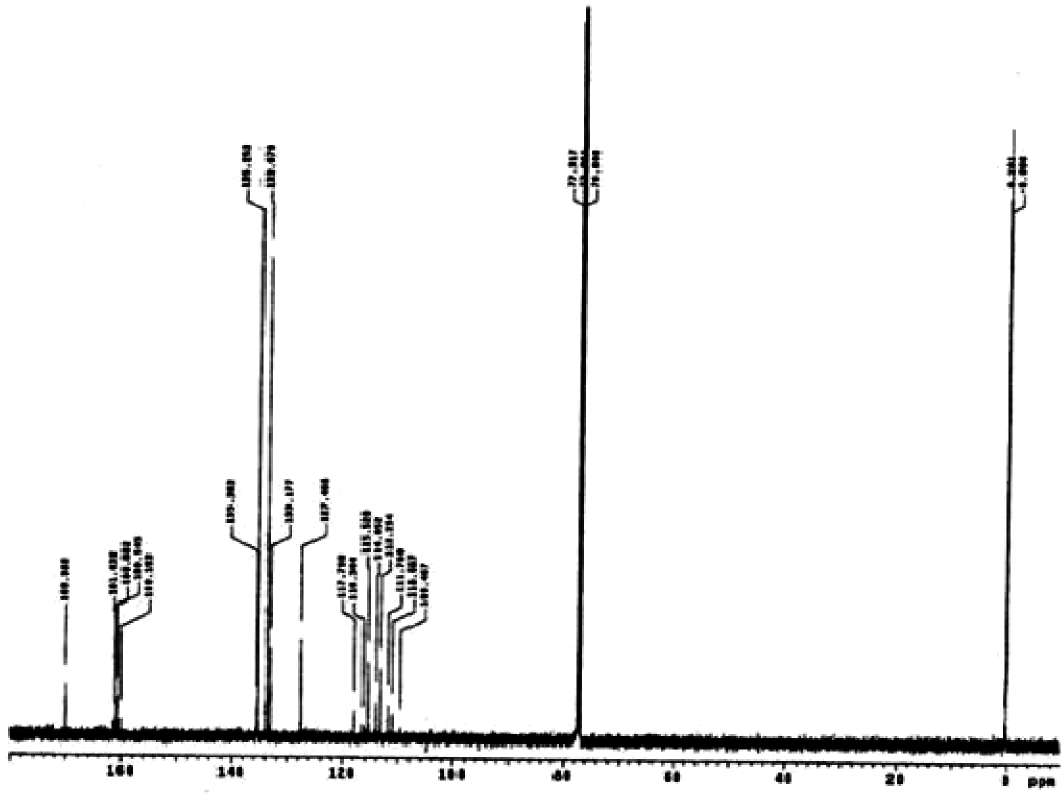

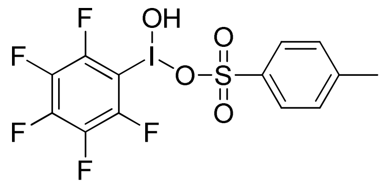

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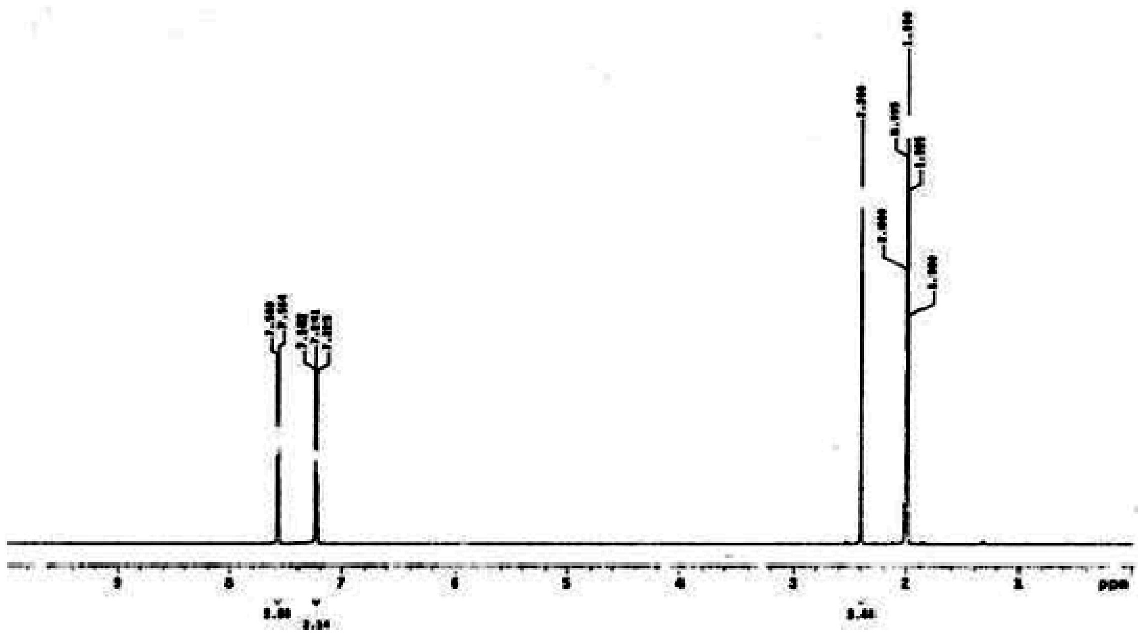

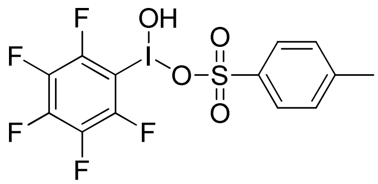

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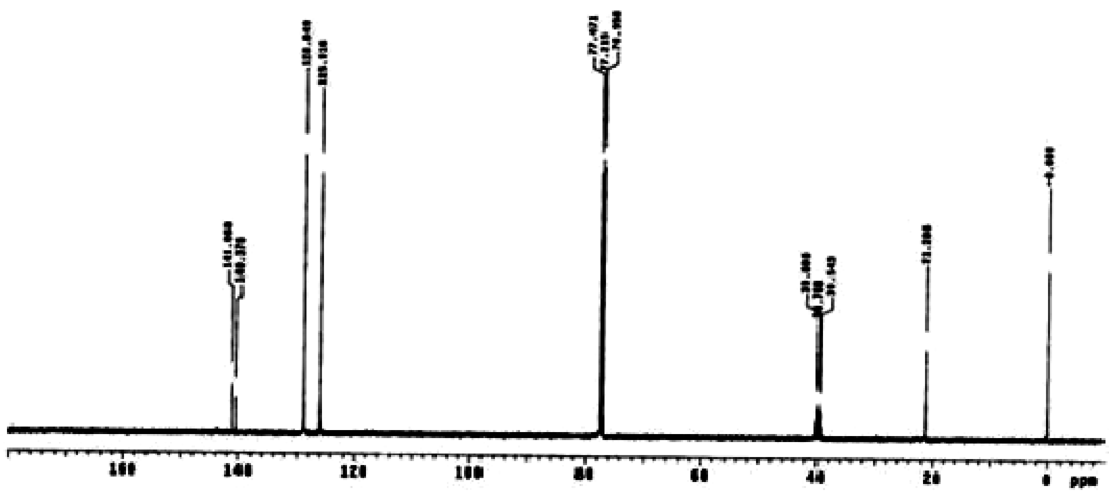

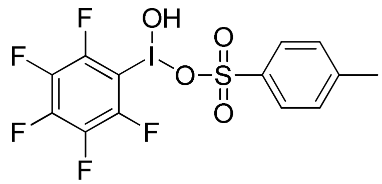

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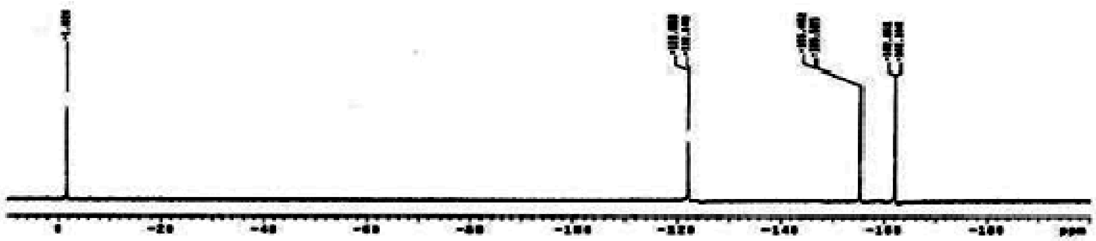

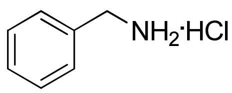

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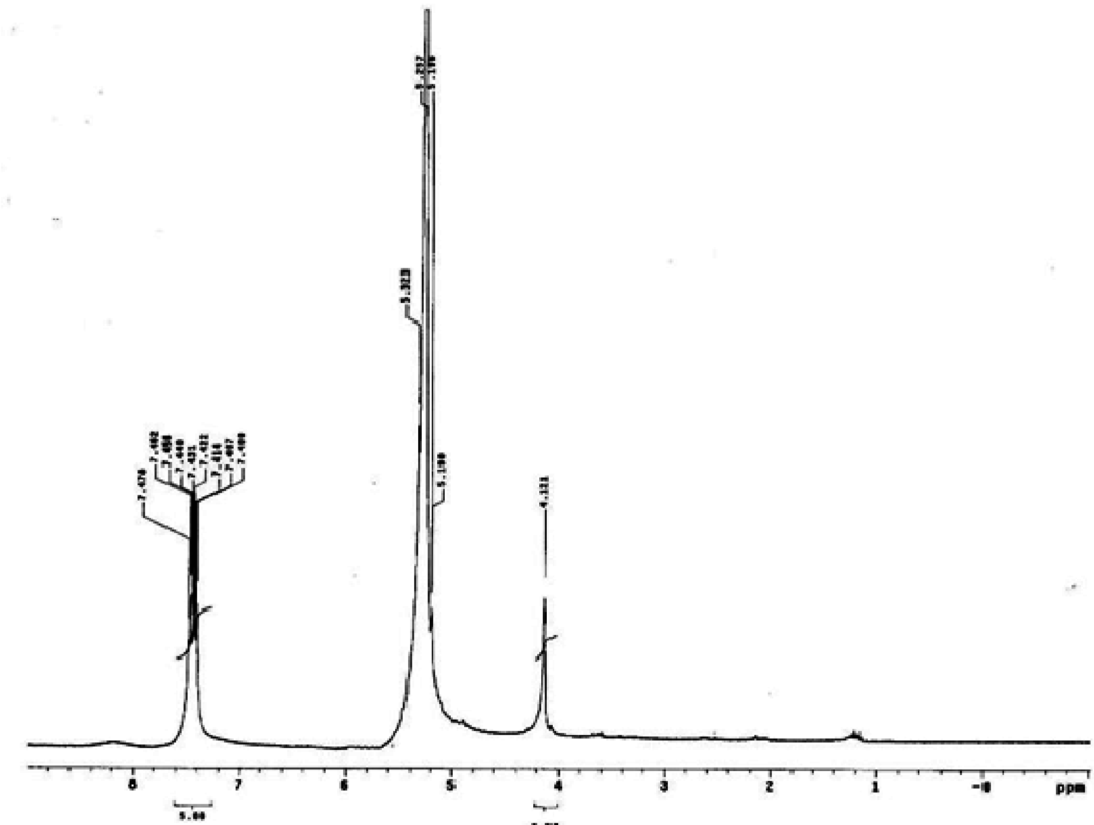

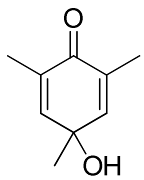

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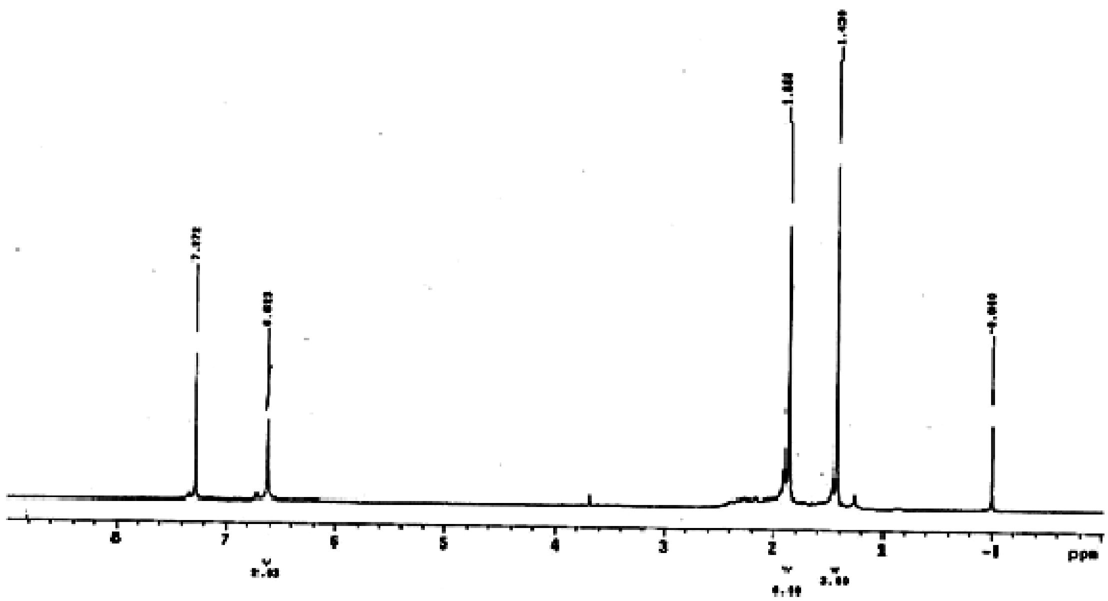

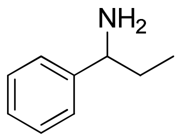

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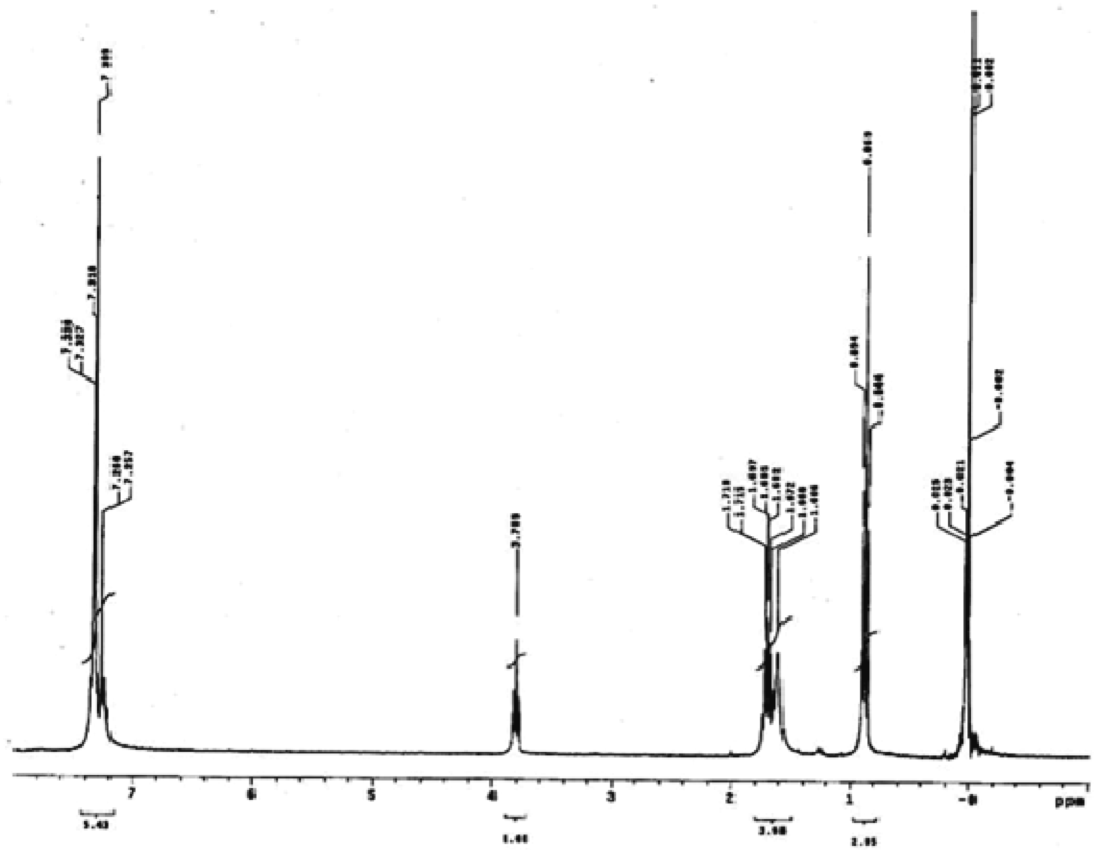

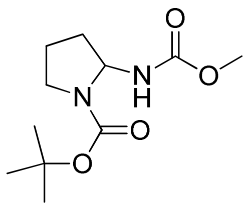

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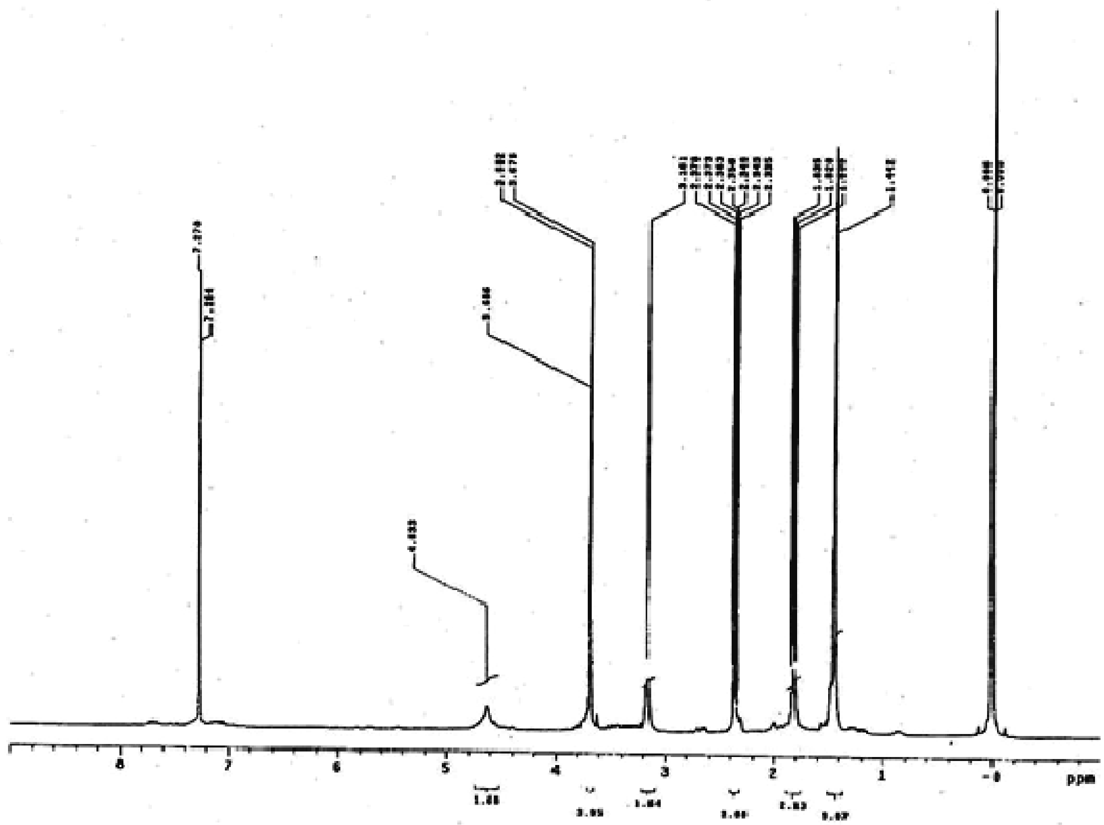

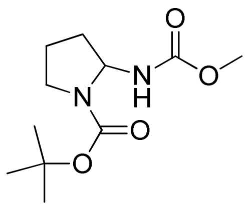

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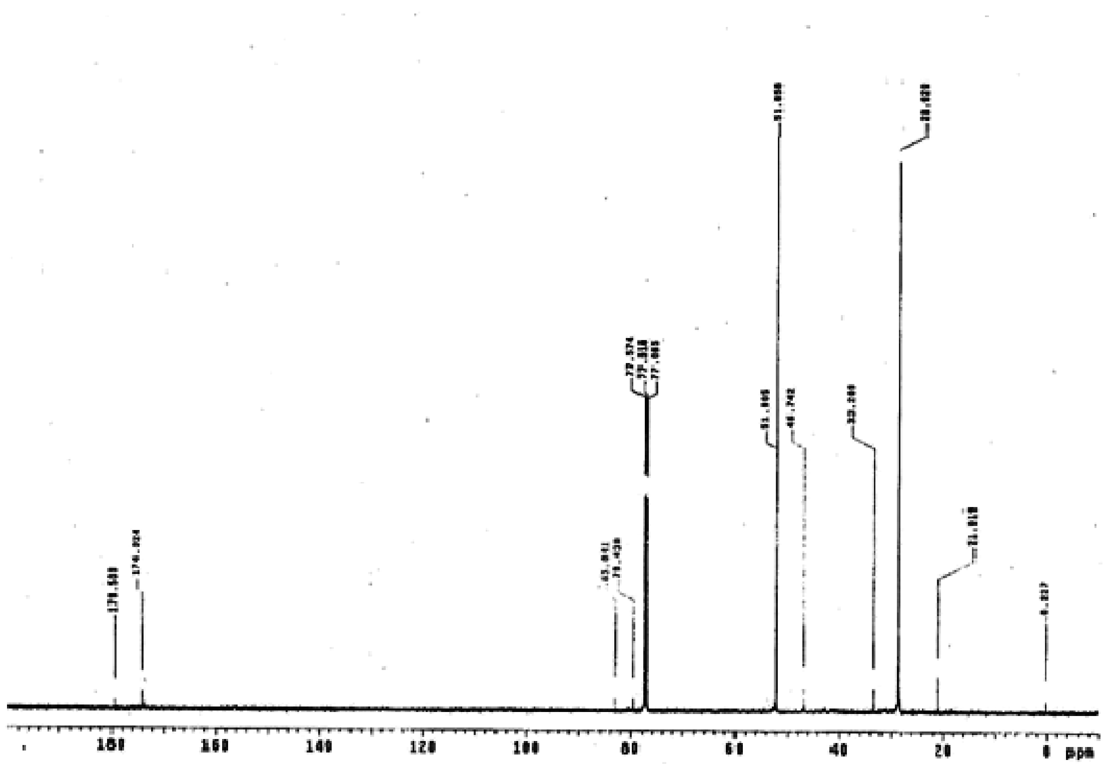

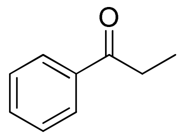

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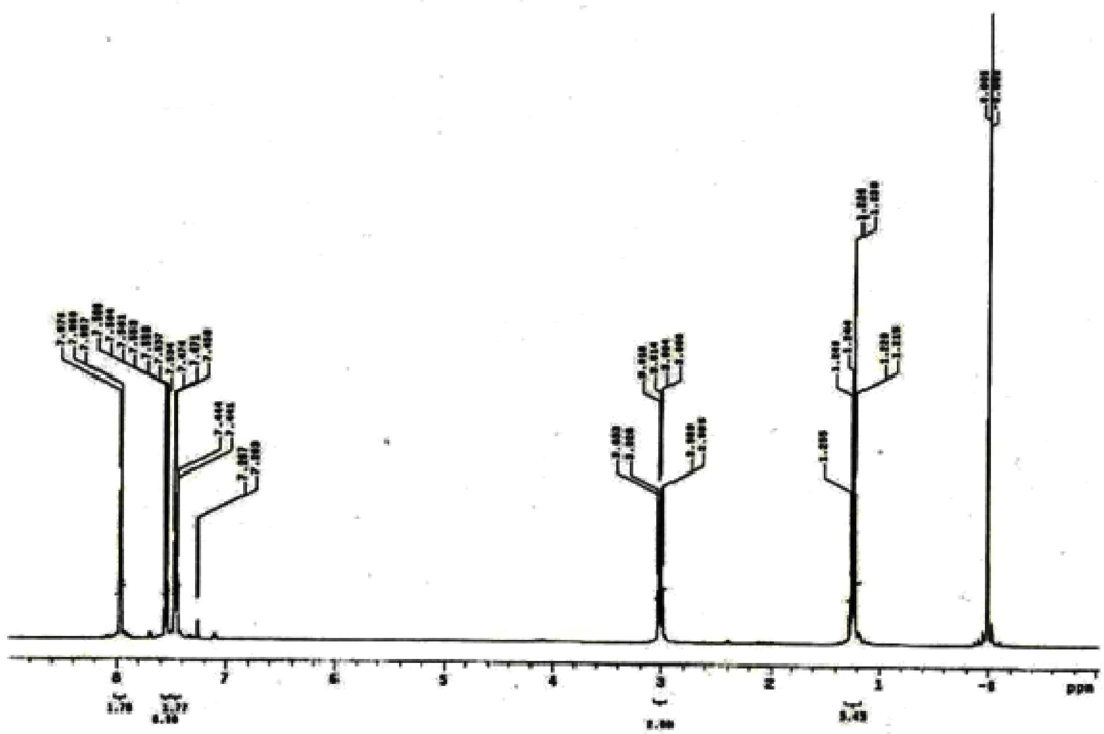

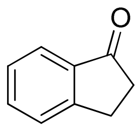

^{1}H NMR