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REAGENTS OF HYPERVALENT IODINE IN ORGANIC SYNTHESIS

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ABSTRACT: This review article describes the major synthetic applications of iodobenzene-derived reagents of hypervalent iodine, effected during the period 1990-1994. An emphasis has been given in compounds of the general formula $C_6H_5IX_2$, $C_6H_5I^+XY^-$.

Key-words: Hypervalent iodine, iodobenzene derivatives from iodine, iodonium salt, iodonium zwitterions, (diocetoxyiodo)benzene

Received: July 12, 1994.

Introduction

Iodobenzene has been known for more than 100 years to form a variety of derivatives in which one to four ligands are attached to iodine. Such compounds belong to the family of hypervalent iodine, due to the ability of this element (and others as well) to develop a special type of bonding, producing organic and inorganic compounds in which its oxidation state is +3 or +5. The ligands which form these rather weak new bonds are normally either single electronegative elements, such as fluorine, chlorine and oxygen, or groups bound to iodine through oxygen, nitrogen and carbon.

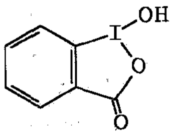
Until recently, most of hypervalent iodine compounds were not of general interest,since their properties had hardly been explored. The situation has presently changed: old and new compounds are shown to possess a rich chemistry, reacting with almost everything, from simple saturated hydrocarbons to complex natural products. Consequently, they are being established as valuable reagents in organic synthesis. Several general and specific reviews[1-6] as well as a comprehensive book[7] have recently appeared in this rapidly expanding field.

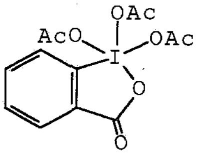
This article will be focused almost exclusively on very recent developments, interesting from a synthetic point of view; only organoiodine reagents derived from iodobenzene will be covered.

General features

Derivatives of iodobenzene which already constitute well-established reagents may be classified in two broad categories: individual compounds, sometimes with substitution in the phenyl ring, and classes with many members in which similar ligands are attached to iodine; the most important among them come mainly from iodine (III) and are collected, respectively, in Tables 1 and 2. An attractive feature of iodobenzene derivatives is their ready availability; it should be noted that some of them are commercially available, while the preparation of others has appeared in Organic Syntheses.

Table 1. Reagents of hypervalent iodine (Individual compounds)

Compound	Name
$PhIF_2$	(difluoroiodo)benzene
$PhICl_2$	(dichloroiodo)benzene
$PhI(OCOCH_3)_2$	(diacetoxyiodo)benzene
$PhI(OCOCF_3)_2$	[bis(trifluoroacetoxy)iodo]benzene
$PhI(OH)(OSO_2\text{-p-tolyl})$	[(hydroxy)(p-toluenesulfonyloxy)iodo]-benzene (**Koser's reagent**)
$PhI(OH)[OPO(OPh)_2]$	[(hydroxy)(bis) (phenyloxy)phosphoryl-oxy iodo]benzene
$(PhIO)_n$	iodosylbenzene
$(PhIO_2)_n$	iodylbenzene
	1-hydroxy-1,2-benziodoxolin-3(1*H*)-one (o-iodosobenzoic acid)



1,1,1-tris-acetoxy-1,2-benziodoxolin-3-(1*H*)-one (**Dess-Martin reagent**)

$[PhI(OSO_2CF_3)]_2O$ μ-oxobis(trifluoromethanesulfonato)-(phenyl)iodine(III) (**Zefirov's reagent**)

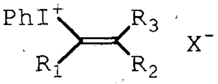
Table 2. Reagents of hypervalent iodine

(Classes of compounds)

1. Diaryl and related iodonium salts
   a. ArI^+Ar', X^-
   b. $HetI^+Het'$ X^- (Het=furyl, thienyl, indolyl, etc.)
   c. Heterocyclic iodonia salts (mostly 5-membered)

2. Perfluoroalkyl phenyliodonium salts
   PhI^+R_F X^- ($R_F=C_nF_{2n+1}$, $C_nF_{2n+1}CH_2$, etc.)

3. Alkenyl phenyliodonium salts

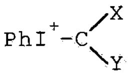


(R=H, alkyl, aryl, Me_3Si, etc.)

4. Alkynyl phenyliodonium salts
   $PhI^+C{\equiv}CR$ X^- (R=H, alkyl, aryl, Me_3Si, CN, COR, I^+Ph,etc.)

5. Zwitterionic iodonium compounds

a. 1,2-dipoles (ylides)

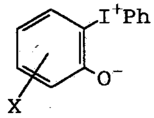


$PhI^{+}\text{-}C\langle^{X}_{Y}$, $PhI^{+}\text{-}N^{-}SO_2R$

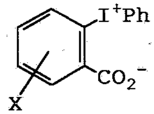
(X,Y=COR, CN, SO_2R, NO_2, etc.)

(R=aryl, CF_3)

b. 1,4-dipoles



c. 1,5-dipoles



Operational simplicity ranks high among the advantages of hypervalent iodine reagents: no high or very low temperatures, no need of special precautions against moisture or oxygen, no use of special solvents or apparatus, rare use of expensive catalysts. Considerable versatility is prominent in a number of them, sometimes accompanied by unpredictable results. The major reaction types in which they can enter include oxidation, halogenation, carbon-carbon bond formation, generation of unstable intermediates, transfer and removal of various groups, additions, substitutions, rearrangements, etc. A more complete list of general reactions is catalogued in Table 3. It is noted that only some of them will be discussed in this review; the same selectivity applies for the compounds of Tables 1 and 2.

Table 3. Types of general transformations of organic substrates effected through hypervalent iodine reagents.

acyloxylation
addition
alkenylation
alkoxylation
alkynylation
allylation
amination
aromatic substitution
(nucleophilic and electrophilic]
arylation
aryne generation
azidonation
aziridination
benzyne generation
bromination
carbene generation
carbocyclization
chlorination
coupling reactions
cyclization
cycloaddition
decarboxylation
degradation
dehydrogenation
dehydrosilylation
deiodination
deprotection
dethioacetalization
dimerization
electrophilic substitution
elimination
epoxidation
etherification
ethynylation
fluorination
free radical generation
glycosidation
halogenation
Hofmann rearrangement
hydrolysis,catalytic
hydroxylation
imidylation
iodination
iodofunctionalization
lactonization
mesyloxylation
methoxylation
nitrene generation
nucleophilic substitution
oxidation
oxidative cleavage
oxidative coupling
oxidative cyclization
oxidative rearrangement
oxidative substitution
oxygenation
perfluoroalkylation
phenylation
phosphoryloxylation
photoinitiation
polymerization
rearrangements
remote functionalization
ring-contraction
ring-enlargement
selenylation
sulfonyloxylation
thiocyanation
tosyloxylation
transylidation
umpolung
vinylation

The possibility to produce variations in many organoiodine reagents by altering their ligands or introducing substituents in the phenyl ring has important implications from a synthetic point of view. For instance, a classical reaction such as the Hofmann degradation of amides has been found to give excellent results using no less than four different iodine reagents, depending on the nature of the amide[7]. Also, catalysis of various kinds and the use of solvents which actually participate in the formation of transient iodine(III) compounds help to broaden their scope. In this way we may confer to them enhanced or reduced oxidizing power and also further useful diversity in reactivity. In many cases hypervalent iodine reagents offer simpler or more efficient alternatives to existing synthetic pathways, especially in oxidations, the umpolung of some common compounds, the transfer of various groups and the formation of a multitude of heterocycles. A number of reactions are possible uniquely via organoiodine reagents. Apart from such specificity, they often exhibit also remarkable chemo-, regio- and even stereoselectivity.

Another advantage of these reagents is their low toxicity which, in combination with their biodegradability, makes them environmentally acceptable. Further, iodobenzene -always a by product- may be recycled, so that the high cost of iodine-based reagents which might be prohibitive for large-scale applications is somewhat offset. A small number of iodine(III) compounds have limited stability; this, however, confers to them enhanced reactivity.

Since most of the reagents to be discussed are not widely known yet, it was thought that a presentation based on individual reagents rather than reaction type would be more beneficial to the reader.

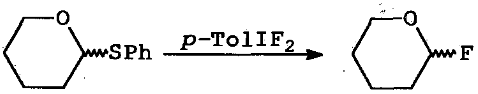
(Difluoroiodo)benzene

This compound and some of its *p*-substituted analogues have been applied sporadically in a few oxidations; they are more useful, however, in fluorinations.[7] One of the most important reactions of this type is the convertion of 1,1-diarylethylenes into difluoro rearranged 1,2-diarylethanes[8], by *p*-$HOOCC_6H_4IF_2$ or polymer-supported $C_6H_5IF_2$ (scheme 1).

Recent applications make use of p-methyl-(difluoroiodo)-benzene and include two interesting transformations: the first involves fluorination of protected 1-arylthioglycosides,[9] represented schematically as 1, which give cleanly fluoroglycosides, 2 (scheme 2); in the second, cyclic dithioketals, 3, are converted into 1,1-difluoroalkanes,[10] 4 (scheme 3).

$$Ar_2C{=}CH_2 \xrightarrow[H^+]{p\text{-}HOOCC_6H_4IF_2} ArCF_2CH_2Ar$$

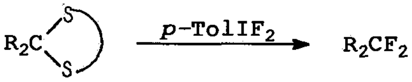
Scheme 1



1

2

Scheme 2



3

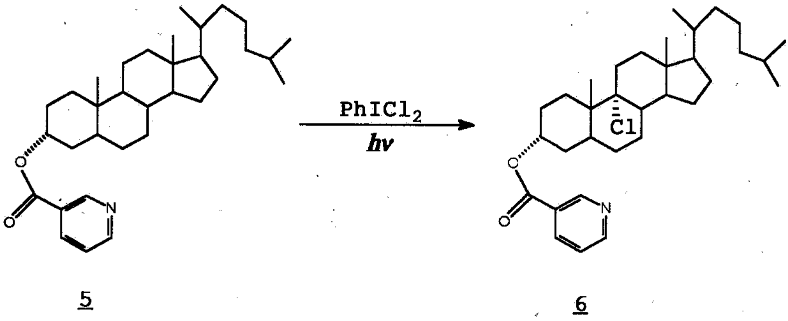
4

Scheme 3

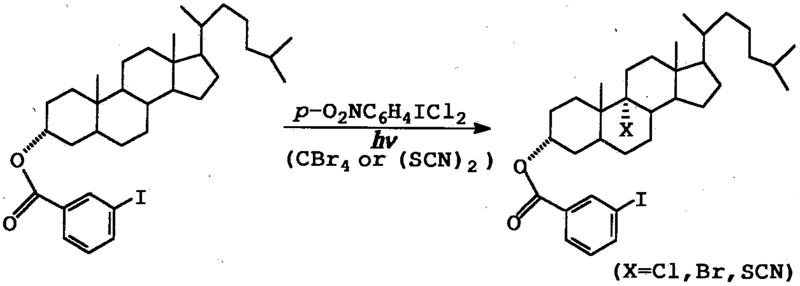
(Dichloroiodo)benzene

A great deal of chlorinations and some oxidations have been effected with this reagent; sometimes certain of its ring-substituted analogues seem to be preferable. Chlorination of alkanes, alkenes, alkynes, aromatics as well as more complex substrates proceeds readily, usually under photolytic conditions. In these cases the chlorinating agent is the free radical ArI•Cl; this species behaves unlike other chlorinating agents, so that $ArICl_2$ have considerable synthetic utility.[7]

Remote chlorination of steroids constitute an unexpected and useful substitution reaction which brings about regioselective functionalization of their non-activated carbon atoms at various positions, depending on the substrates and $ArICl_2$. Since regioselectivity and regiospecificity were not entirely satisfactory, steroid esters have been used advantageously. This template-directed chlorination has produced interesting results, e.g. 3α-cholestanol nicotinate 5 was converted[11] to its 9-chloro-derivative 6 (scheme 4). Another approach involves the use of steroid esters incorporating an iodophenyl group, e.g. 7; this with $ArICl_2$ is converted into an iodine free radical (steroid...I•Cl) which substracts intramolecularly a hydrogen atom from C_9 and the resulting carbon free radical is subsequently chlorinated (scheme 5). In the presence of excess CBr_4 or $(SCN)_2$, the corresponding 9-bromo- or 9-thiocyanato-steroids 8 can be produced.[12]



Scheme 4



7 8

Scheme 5

Generally, substitutions at sp^3 C atoms are characterized by the enhanced selectivity of ArI·Cl for 3^o hydrogen, so that in several chlorinations $ArICl_2$ are the reagents of choice. Ketones, diketones and sulfides of several types may undergo α-chlorination under ionic conditions, in which case the formation of dichloro derivatives is efficiently suppressed.[7]

Oxidations by $ArICl_2$ may be of a fairly diverse nature. Among recent results, oximes have been found to undergo synthetically useful transformations which are superior to those effected through other reagents: aldoximes in chloroform-pyridine are efficiently converted into nitrile oxides, while ketoximes are deoximated, under similar conditions.[13] A different type of reactivity occurred in the reaction of $PhICl_2$ with alkyl lithium compounds, in which case carbon-carbon bond formation was observed;[14] the result was an efficient preparation of alkanes (scheme 6).

$$2RLi + PhICl_2 \longrightarrow [PhIR_2] \xrightarrow[-PhI]{} R{-}R$$

Scheme 6

Iodosylbenzene

Iodosylbenzene is a polymeric compound, insoluble in several organic solvents. However, it dissolves readily in methanol and organic acids, as well as in water, forming unstable or stable compounds of tris coordinated iodine. A related reaction with silyl derivatives of the general formula R_3SiX leads to the formation of further iodine(III) compounds (scheme 7).

$$PhIO + 2HX \xrightarrow{-H_2O} PhIX_2 \quad (X = MeO, RCOO, HO)$$

$$PhIO + 2Me_3SiX \xrightarrow{-(Me_3Si)_2O} PhIX_2 \quad (X = Cl, CN, N_3, etc.)$$

Scheme 7

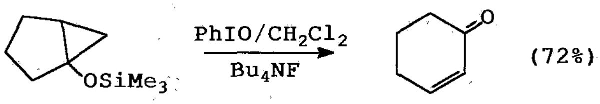
In some instances other compounds react similarly but in a 1:1 ratio; the new species formed, PhIX(OH), may be isolated or used *in situ*.[15,16] Generally, there is often an ambiguity about the true nature of iodosylbenzene in solution, which, however, does not prevent its use from several reactions.

Hydrogen chloride and various acid chlorides, including Me_3SiCl, form with iodosylbenzene its dichloride, $PhICl_2$. Pulverization of a solid mixture of HCl-treated silica gel, PhIO and an alkene or alkyne in the absence of solvents, brings about addition of chlorine to the double or triple bond, apparently through $PhICl_2$. Similar results were produced by using HBr-treated silica gel. In both cases crushing and grinding were essential for these very efficient halogenations.[17] Another solid-state reaction of PhIO and HCl-treated silica gel involved alkyl and aryl benzyl sulfides which were simultaneously chlorinated and oxidized at sulfur, with rupture of the benzylic C-S bond. In this way alkyl or aryl sulfonyl chlorides were produced in high yields[18] (scheme 8).

$$RSCH_2Ph \xrightarrow[\text{pulverization, 5 min}]{\text{PhIO/HCl/Silica gel}} RSO_2Cl \quad (88-98\%)$$

Scheme 8

Actually, in most of its reactions iodosylbenzene serves as a useful oxidant for several types of oxidations which may be effected under a variety of conditions. Catalyzed reactions are usually more efficient than non-catalyzed; alkenes, silyl ethers and amines may be mentioned as substrates undergoing clean non-catalytic transformation. Iodosylbenzene in water converts alkenes into vic-glycols or products of further transformation.[7] Some bicyclic silyl ethers such as **9** can be converted to unsaturated ketones, **10**, in the presence of Bu_4NF (scheme 9); the role of F^- is to facilitate the elimination of the Me_3Si group. Similar results were obtained with some oxa-analogues of **9**; i.e. bicyclic silylated lactones yielded α,β-unsaturated lactones with ring expansion.[19]

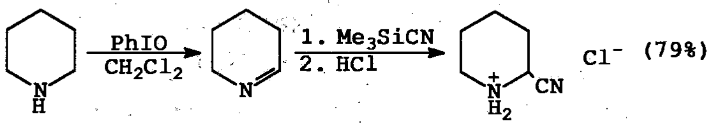


9

10

Scheme 9

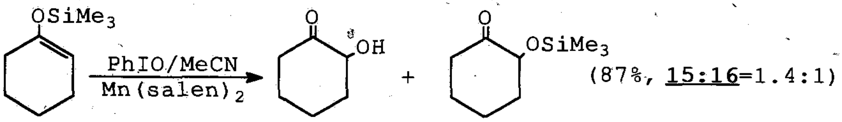
The oxidation of amines and some cyclic aminoacids proceeds either in water or in methylene chloride. Primary aliphatic amines are normally dehydrogenated to nitriles, while cyclohexylamine and cycloheptylamine, in water, are converted to the corresponding ketones. Secondary amines give in methylene chloride imines; in water, cyclic amines are transformed to lactams. When the imine is not hydrolyzed, it can be trapped, e.g. 12 coming from piperidine (11) gave with Me_3SiCN the adduct 13 (scheme 10). Cyclic tertiary amines are likewise oxidized to lactams. Cyclic α-aminoacids, such as proline, undergo oxidative decarboxylation to yield also lactams.[20,21]



11 12 13

Scheme 10

An efficient catalytic system for many oxidations, even for alkanes, uses metal complexes of Fe or Mn with tetraphenylporphin(TPP), bis(salicylidene)ethylenediamine (salen) and other similar ligands. Most of these catalyzed oxidations are of mechanistic rather than preparative interest, mimicking enzymatic reactions; usually they involve oxygenation of olefinic double bonds to oxiranes.[7] From other areas, some new reactions may be mentioned. One of them is the oxidative decarboxylation[22] of certain aryl alkyl acetic acids, ArCH(R)COOH, to mixtures of alcohols, ArCH(R)OH and ketones ArCOR. Upon oxidation of some ketone silyl enol ethers, a mixture of two products usually results, e.g. 15 and 16, from the cyclohexanone derivative 14 (scheme 11).



(87%, 15:16=1.4:1)

14 15 16

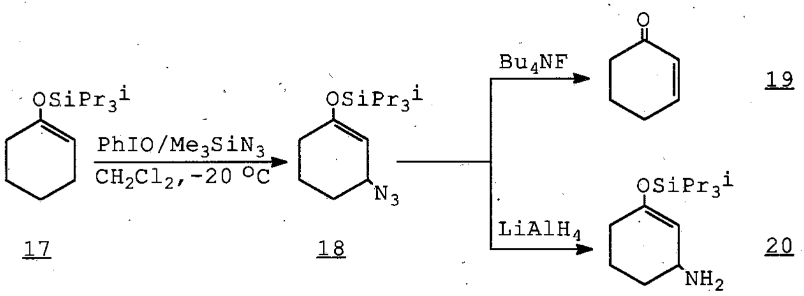
Scheme 11

Benzylic silanes ($ArCH_2SiMe_3$) are also hydroxylated[24] by PhIO and Fe(TPP), to $ArCH(OH)SiMe_3$. Other metal-catalyzed oxidations involved the use of Ru complexes, especially for acetylenic compounds,[7] and Yb salts for the oxidation of alcohols.[25]

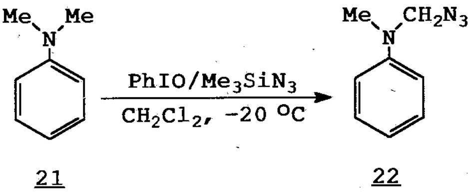
Conversions of silyl enol ethers to α-hydroxyketones,[26] and also a multitude of other related or entirely different transformations, are possible when PhIO is combined with BF_3. The role of the latter is not strictly catalytic, since best results are obtained when it is used in stoichiometric quantities, in the form of $BF_3.Et_2O$. It is supposed that the active species is the zwitterion $PhI^+OBF_3^-$. Applications with this reagent are numerous and have been summarized.[7] A recent reaction[27] is the oxidation of $RSnBu_3$ to ROH.

The combined use of PhIO and Me_3SiN_3 involves probably the non-isolable $PhI(N_3)_2$ which transfers its azido groups to several nucleophilic substrates. Particularly important is the reaction of silyl enol ethers, which results in direct β-azidonation in high yields;[28] e.g., **17** gave the isolable **18**, which in turn could be converted to either **19** or **20** (scheme 12). In several N,N-dimethyl arylamines the azido group replaces a methylic hydrogen; the azidomethylene amines formed, such as **22** from **21**, are usually too labile for purification but they undergo readily further transformations of a rich diversity[29] (scheme 13). It should be noted that in other aromatic compounds, under similar conditions, normal electrophilic substitution occurs. Generally, the use of iodine(III) reagents in combination with either Me_3SiN_3 or

NaN_3 provides a facile route for azidonations of various kinds.[7,30]

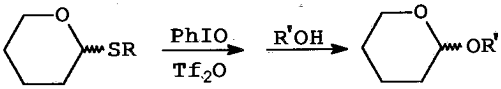


Scheme 12



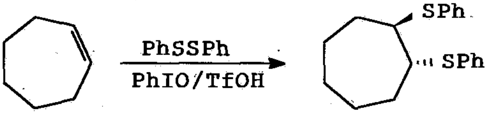
Scheme 13

When PhIO and trifluoromethanesulfonic(triflic)anhydride (Tf_2O) are mixed, a new isolable compound is formed, PhI(OTf)OI(OTf)Ph, (Zefirov's reagent), which transforms alkenes to cis-vicinal triflates. The combination of PhIO and Tf_2O has been used for *in situ* glycosidation of thioglycosides,[32] according to the generalized scheme 14.



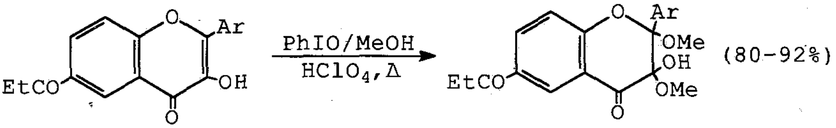
Scheme 14

The combination of iodosylbenzene and trifluoromethanesulfonic acid leads to the in situ formation of $PhI(OH)O_3SCF_3$; this reagent induced addition of diphenyl disulfide (and dimethyl disulfide) to alkenes, producing 1,2-bis(phenylthio)-alkanes,[33] as shown in scheme 15.



Scheme 15

An iodine(III) compound, $PhI(OMe)_2$ is likely to be formed in the bis methoxylation of the double bond of some substituted flavonols[34] resulting upon reaction with iodosylbenzene in methanol, in the presence of $HClO_4$ (scheme 16). It is noted that $PhI(OMe)_2$ has been isolated previously in pure form.



Scheme 16

(Diacyloxyiodo)arenes

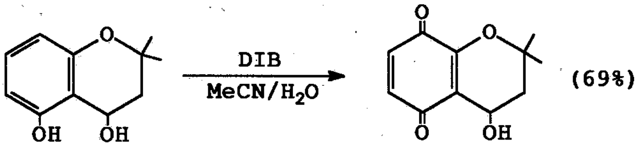
This category comprises many members, since any acid may yield with iodoarenes a series of (diacyloxyiodo)arenes. Although in some reactions several members can be used, two mainly compounds have become popular, (diacetoxyiodo)benzene and [bis(trifluoroacetoxy)iodo]benzene.

a. **(Diacetoxyiodo)benzene**

a. (Diacetoxyiodo)benzene

(Diacetoxyiodo)benzene (abbreviated DIB) is one of the oldest hypervalent iodine reagents, known since 1937 to cleave *vic*-diols and to acetoxylate double bonds. In several aspects it resembles lead tetraacetate but its oxidative character is milder, while it is more versatile.[7] Modern uses of DIB involve various oxidations, especially of phenolic compounds; also, in combination with elemental iodine or sodium azide and diphenyl diselenide or alcohols it participates in the generation of other useful reagents.

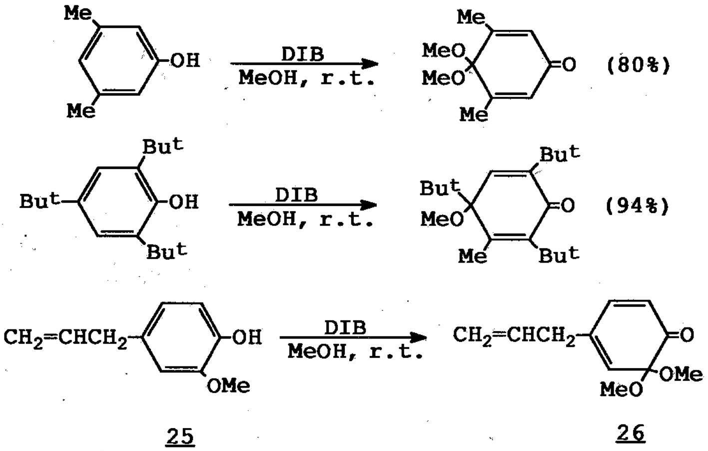
. Simple phenols may be oxidized to various products by a host of oxidants. DIB as well as its trifluoroacetoxy analogue were most effective in a number of cases, when other reagents failed. The direct conversion of some phenols to *p*-benzoquinones in good yields makes DIB the reagent of choice; an example[35] is provided by the oxidation of 23 to 24 (scheme 17).



23 24

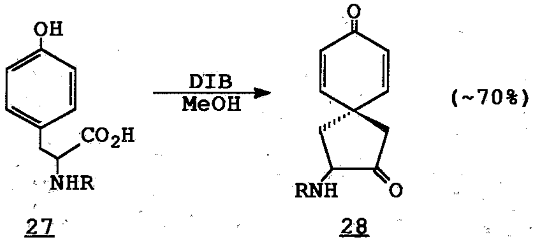
Scheme 17

Of special interest is the action of DIB in methanol, which involves solvent participation and formation of quinone ketals or related cyclohexa-2,5-dienones, as the examples in scheme 18 illustrate.[36] In some instances the formation of *o*-quinone ketals is also possible, e.g. eugenol (25) was converted to 26, which is suitable for the preparation of hydroxy-anthraquinones.[37]

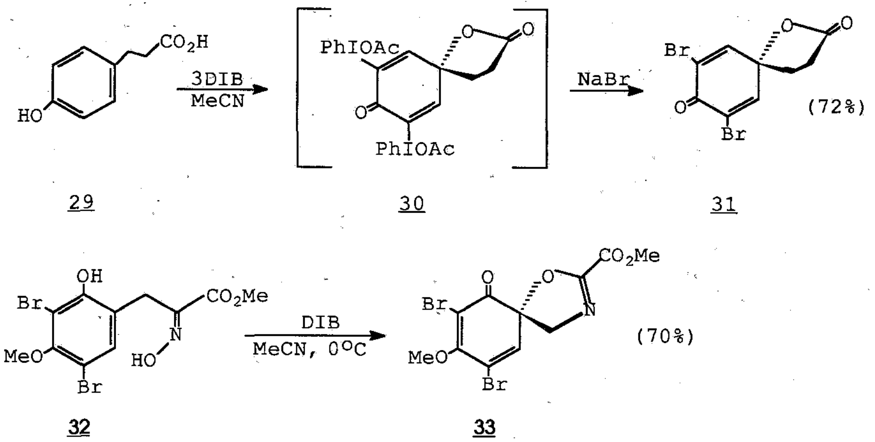


Scheme 18

Several N-protected tyrosine derivatives such as 27 are efficiently cyclized to the corresponding spirolactones 28 by treatment with DIB.[38]

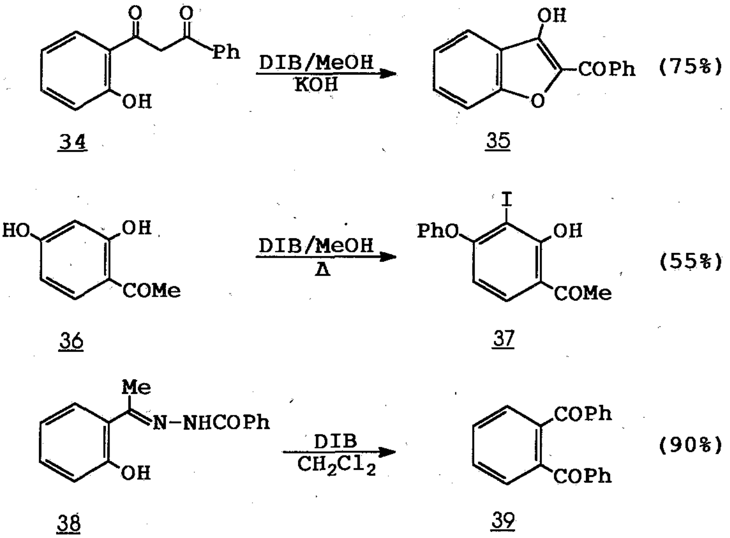


The above compounds served as intermediates in the synthesis of natural products such as alkaloids and antibiotics. With en excess of DIB, followed by a work-up with sodium chloride or bromide, several tyrosine derivatives were converted to dihalodienone derivatives. A simpler analogue of this interesting reaction[39] occurred with 3-(*p*-hydroxyphenyl)propionic acid, 29, which through 30 gave eventually **31** (scheme 19). Some oximes of o- and p-hydroxyaryl-2-ketopropionic acid derivatives were also oxidized by DIB to spiroisoxazolines,[40] e.g. **32** yielded **33**.



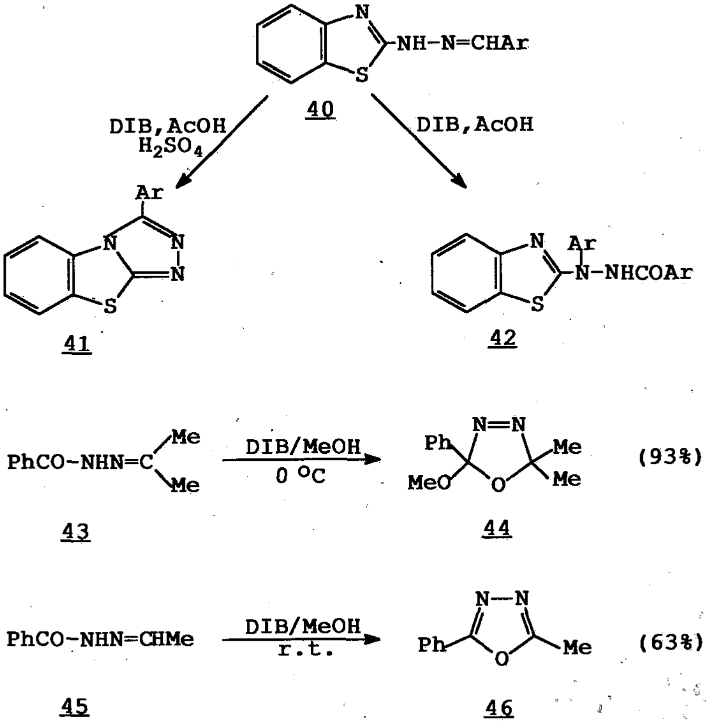
Scheme 19

Phenols with *ortho*-substituents react with DIB often in an unexpected way. Cyclization to **35** occurred in several compounds of the general formula **34**, when treated with DIB in methanol and KOH.[41] It is emphasized that this system, in which the active species is believed to be $PhI(OMe)_2$, has been used extensively for many useful transformations of carbonyl compounds.[7] Direct conversion of several phenols to o-iodo diphenyl ethers is possible upon heating with DIB in methanol; in this way **36** gave **37**[42,43]. An unusual but synthetically useful reaction[44] involves the oxidation of a series of acyl hydrazones derived from o-hydroxyacetophenone, such as **38**, which are efficiently converted to o-diacylbenzenes **39** (scheme 20). This as well as the previous reactions proceed through zwitterionic iodonium intermediates which sometimes may be isolated.



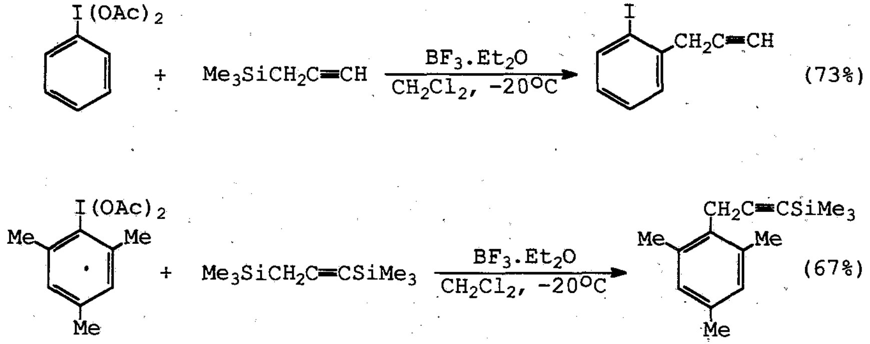
Scheme 20

Another type of hydrazones of the general formula **40** reacted with DIB in acetic acid producing hydrazides **42**; when, however, a few drops of H_2SO_4 were added, condensed triazoles **41** were produced[45] (scheme 21). Other N-acyl hydrazones[46] such as **43** and **45** afforded, respectively, the heterocycles **44** and **46**, while tosyl hydrazones were transformed to the parent carbonyl compounds.[47] Generally, many N-containing compounds undergo useful oxidative transformations by DIB, e.g. *ortho*-substituted anilines gave various heterocycles;[48,49] 5-aminopyrimidinone was converted to an imidazole derivative;[50] and amides of aliphatic acids yielded urethanes.[51]



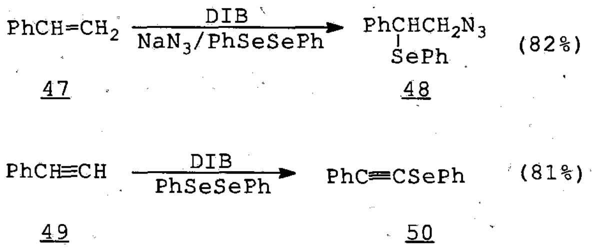
Scheme 21

Some unusual reactions have been reported with relatively simple compounds such as alkoxyallenes and propargylsilanes, which form reactive iodine(III) intermediates. Thus, 1-methoxy- and 1-ethoxyallenes were converted by DIB to 3-acetoxy-3-alkoxypropynes,[52] at -78 °C; phenyl-substituted allenes were unreactive, even upon heating, but they reacted in a different way with [(hydroxy)(tosyloxy)iodo]benzene (see this reagent). (Diacetoxyiodo)benzene and its *o*-, *m*-, and *p*-methyl analogues with propargyl silanes underwent a reductive iodonio Claisen rearrangement leading to the formation of *o*-propargyl-iodoarenes. In (diacetoxyiodo)arenes with a *p*-methoxy group, the reaction course changed; *ipso* substitution took place and propargylarenes were obtained[53] (scheme 22).



Scheme 22

When terminal alkenes are treated with DIB, sodium azide and diphenyl diselenide, azido-phenylselenylation ensues,[54] proceeding with anti-Markovnikov regioselectivity, e.g. **47** yielded **48**. Terminal alkynes, **49**, gave analogous products, i.e. alkenes, but these were accompanied by phenyl alkynyl selenides; these, e.g 50 ,became the sole products, when sodium azide was omitted[55] (scheme 23).



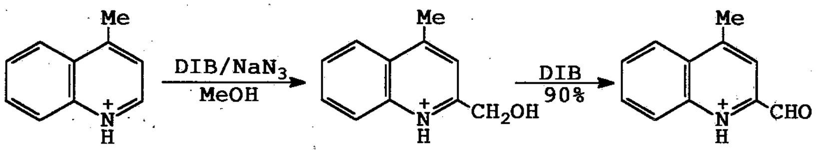
$$\underset{\underline{47}}{PhCH{=}CH_2} \xrightarrow[NaN_3/PhSeSePh]{DIB} \underset{\underline{48}}{\underset{SePh}{PhCHCH_2N_3}} \quad (82\%)$$

$$\underset{\underline{49}}{PhCH{\equiv}CH} \xrightarrow[PhSeSePh]{DIB} \underset{\underline{50}}{PhC{\equiv}CSePh} \quad (81\%)$$

Scheme 23

$$PhI(OAc)_2 + N_3^- \underset{ACO^-}{\overset{-ACO^-}{\rightleftharpoons}} PhI(OAc)N_3 \longrightarrow Ph\dot{I}OAc + N_3^{\cdot}$$

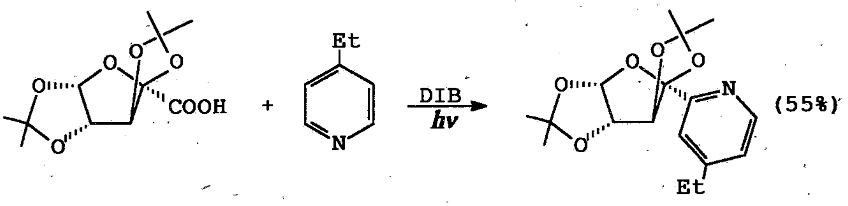
$$RH + N_3^{\cdot} \longrightarrow R^{\cdot} + HN_3$$



51 52 53

Scheme 24

The thermal decomposition of DIB in the presence of sodium azide follows a homolytic pathway involving the very reactive N_3 free radical. In this way the generation of carbon centered free radicals is possible; they are derived from the solvent (alcohols, ethers, formamide and even aldehydes) by hydrogen abstraction.[56] With methanol $\cdot CH_2OH$ is then formed which reacts with lepidine (in its protonated form **51**, with trifluoroacetic acid) to give initially the isolable hydroxymethyl derivative **52** which could be further oxidized in situ to the aldehyde **53** (scheme 24). Other quinolines react in a similar way with DIB, benzoic acid and an alkyl iodide photochemically; the free radicals formed enter in 2- or 4-position of the heterocycle.[57] A related route for the generation of free radicals R· -under photochemical conditions induced by DIB, and also other (diacyloxyiodo)benzenes- uses as substrates carboxylic acids (RCOOH) or alcohols in the form of their mono oxalates (ROOCCOOH). In both cases R· alkylates efficiently several heteroaromatic pyridine bases.[58] Special importance has the synthesis of a range of C-nucleosides and analogues through carboxylic acids of protected carbohydrates,[59] e.g. **55** from **54** (scheme 25).



54 55

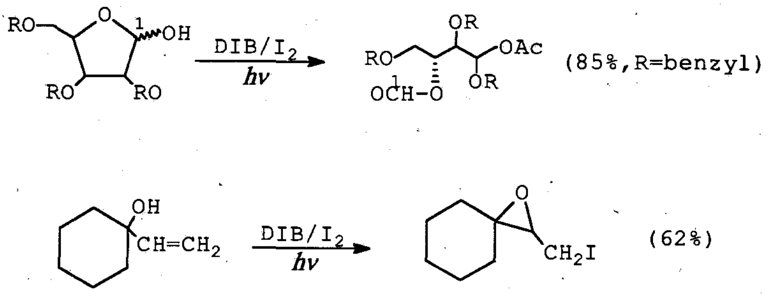
Scheme 25

The interaction of DIB with iodine leads to the formation of acetyl hypoiodite (AcOI); in the presence of alcohols it reacts readily with them producing alkyl hypoiodites (ROI).

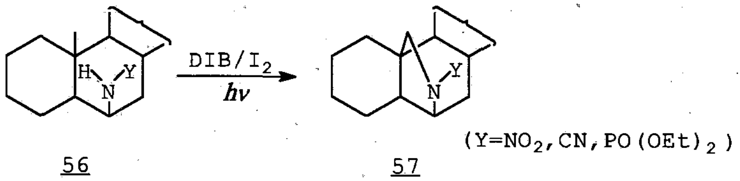
$$PhI(OAc)_2 + I_2 \longrightarrow PhI + 2AcOI$$

$$AcOI + ROH \rightleftharpoons AcOH + ROI$$

These species undergo homolytic cleavage photochemically affording reactive alkoxy radicals (RO·) and I· which can enter into intramolecular reactions of great variety, several of which start with a β-fragmentation. Therefore, when a hydroxyl-containing substrate is treated with DIB/I_2 photochemically, useful products may result. Among the numerous synthetic applications, two examples involving ring cleavage and ring formation are mentioned[60,61] (scheme 26). This method is generally considered to be the best for the generation of alkoxy radicals. Instead of hydroxy, imine derivatives may be used, which produce RNH· radicals, undergoing related transformations; for instance, several steroidal compounds of the general formula 56 cyclize to pyrrolidine derivatives[62] 57 (scheme 27).



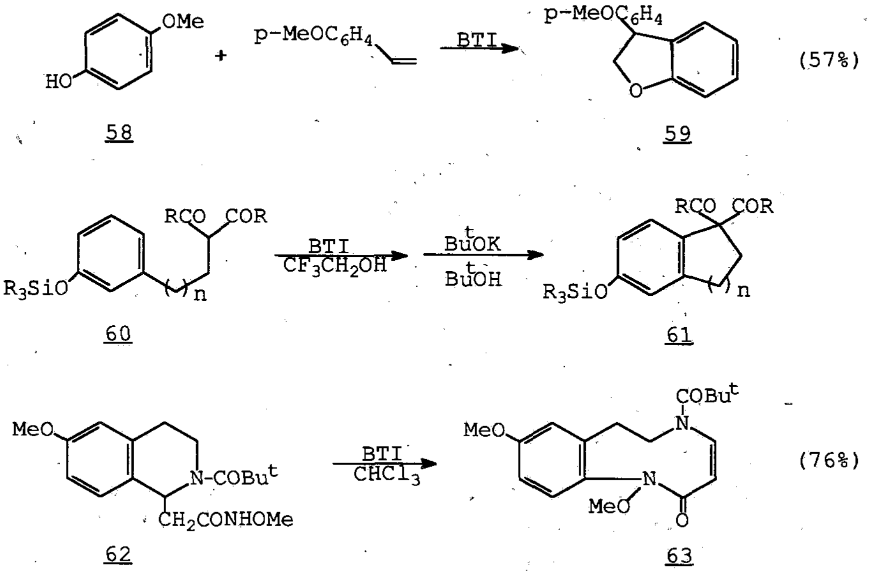
Scheme 26



Scheme 27

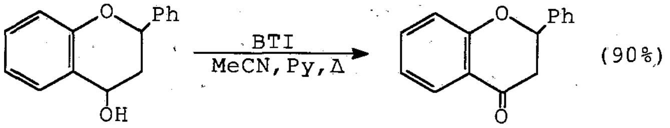
b. [Bis(trifluoroacetoxy)iodo]benzene

This reagent, abbreviated BTI, is more powerful than (diacetoxyiodo)benzene and has been used successfully in several types of oxidation, especially with phenolic compounds. Apart from oxidations similar to those already mentioned, some reactions of different character have been studied. One of them involved phenols and electron-rich styrenes, which underwent oxidative 1,3-cycloaddition mediated by BTI[63]; such reactions lead to the formation of dihydrobenzofurans, eg. **59** from **58**. It is noted that in some instances the use of O-silylated phenols may give better results;[64] this was the case[65] when 1,3-diketones of the general formula **60** were oxidized by BTI in polar solvents of low nucleophilicity, such as CF_3CH_2OH: an iodonium salt was then formed which, without being isolated, upon treatment with Bu^tOK was efficiently cyclized to **61**. Another unexpected cyclization[66] occurred via N-methoxy-N-acylnitrenium ion, generated after BTI oxidation of compound **62**; the product was the nine-membered heterocycle **63** (scheme 28).



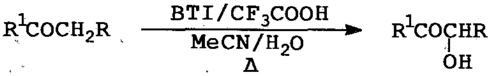
Scheme 28

More conventional oxidations using BTI are also known;[67,68] when alcohols are converted to ketones, then the presence of pyridine is beneficial, e.g. in the transformation of **64** to **65** (scheme 29).[69] Several aliphatic, aromatic and heteroaromatic ketones of the general formula **66** react with BTI and CF_3COOH in acetonitrile/water affording directly α-hydroxyketones **67** (scheme 30).[70] The most widely used reaction of BTI is presently the degradation of amides to amines, which is especially valuable in the field of peptide chemistry.[7]



64 65

Scheme 29



$$R^1COCH_2R \xrightarrow[\substack{MeCN/H_2O \\ \Delta}]{BTI/CF_3COOH} R^1COCH(OH)R$$

66 67

Scheme 30

c. Other (diacyloxyiodo)benzenes

On several occasions various (diacyloxyiodo)benzenes have been used in reactions already known to proceed with DIB or BTI. This section comprises some new reactions. Although alkynols are unknown, their esters are stable and have been obtained in moderate yields from lithium acetylides and a variety of (diacyloxyiodo)benzenes, which are readily accessible[71] (scheme 31).

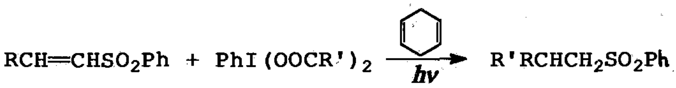
$$PhI(OOCR)_2 + LiC{\equiv}CR' \longrightarrow [Ph\overset{+}{I}C{\equiv}CR' \;\; RCOO^-] \longrightarrow RCOOC{\equiv}CR$$

$$(R{=}Bu^t, Ph, Ar, Ph_2CH, \text{etc.})$$

Scheme 31

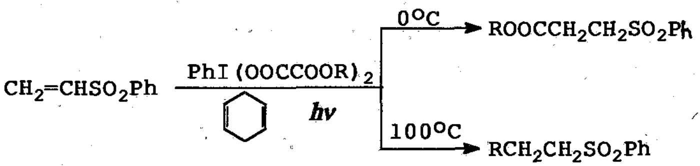
Several (diacyloxyiodo)benzenes when treated photochemically with electron-deficient alkenes, especially unsaturated sulfones, in the presence of 1,4-cyclohexadiene gave reductive addition products, e.g. **68** yielded **69**. The reaction proceeds via alkyl radicals and the role of

1,4-cyclohexadiene is to serve as hydrogen donor[72] (scheme 32). Free radicals are also involved when phenyl vinyl sulfone is treated with [bis(alkoxyoxalyloxy)iodo]benzene and 1,4-cyclohexadiene, again photochemically. In this case the radicals come from alcohols which are first converted to their mono oxalate esters, HOOCCOOR. Depending on the conditions, it is possible that either alkyl or alkoxycarbonyl radicals are generated, so that the final products come from two different types of carbon-carbon bond formation (scheme 33).[73]



68 69

Scheme 32



Scheme 33

Some diaryl tellurides, Ar_2Te, were found to give with $PhI(OOCR)_2$ diaryl tellurium dicarboxylates,[74] $Ar_2Te(OOCR)_2$. Perfluoro DIB, i.e. $C_6F_5I(OOCCF_3)_2$, is a much more powerful oxidant than any other member of its class, so that it can cleave alkynes and carbonyl compounds to acids (scheme 34).[75]

$$\mathrm{PhC{\equiv}CMe} \xrightarrow[\text{wet } C_6H_6,\Delta]{C_6F_5I(OOCCF_3)_2} \mathrm{PhCOOH} + \mathrm{MeCOOH} \qquad (85\%)$$

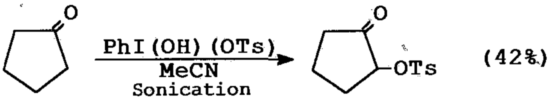
$$\mathrm{PhCOCH_2Ph} \xrightarrow[\text{wet } C_6H_6,\Delta]{C_6F_5I(OOCCF_3)_2} \mathrm{PhCOOH} \qquad (79\%)$$

Scheme 34

Chiral acids have been used for the preparation of some (diacyloxyiodo)benzenes; with dibenzoyl-L-tartaric acid, a polymeric iodine(III) reagent was obtained which effected chiral oxidations of sulfides, eventually to sulfoxides.[76]

[Hydroxy(tosyloxy)iodo]benzene

This compound, sometimes called Koser's reagent (abbreviated HTI), has secured a high rank among synthetically useful iodine(III) reagents. Apart from oxidations, its main utility is the possibility to transfer its tosyloxy (TsO) group to various nucleophilic substrates such as alkenes, allenes and especially enolizable carbonyl compounds. Most fruitful was found the reaction of HTI with ketones; the resulting α-tosyloxy derivatives may be isolated but usually they react *in situ* with nucleophiles affording a variety of products, notably heterocyclic compounds.[6] In this way a step involving the use of obnoxious α-chloroketones is avoided. Tosyloxylation was not possible in some cyclic ketones, unless under ultrasonic conditions[77] (scheme 35). In contrast, a cyclic 1,2,4-triketone, i.e. 2-hydroxy-1,4- naphthoquinone, was readily tosyloxylated at C_3.[78]

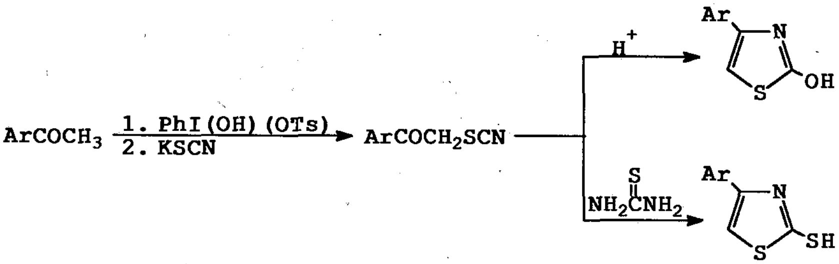


Scheme 35

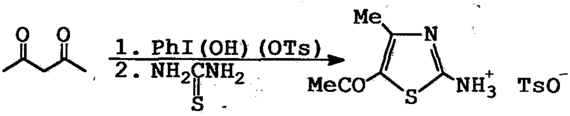
In the presence of aniline, α-tosyloxylated acetophenones are converted to α-anilinoacetophenones[79] (scheme 36), while with potassium thiocyanate α-thiocyanation occurs.[80] In some cases these thiocyanates were cyclized *in situ*[81] (scheme 37). Thiazole compounds were also prepared directly from ketones, HTI and then substituted thioureas[82] or thioamides,[83], while some bridgehead thiazolic heterocycles were obtained from ketones, HTI and ethylenethiourea.[84] Further, 2-benzoyloxyacetophenones or 1,3-dicarbonyl compounds react with HTI and then thiourea to afford aminothiazoles (scheme 38). Selenourea, HTI and 1,3-dicarbonyl compounds yielded similarly selenazoles.[85]

$$\mathrm{ArCOCH_3} + \mathrm{PhI(OH)(OTs)} \xrightarrow[\Delta]{\mathrm{PhNH_2}} \mathrm{ArCOCH_2NHPh}$$

Scheme 36

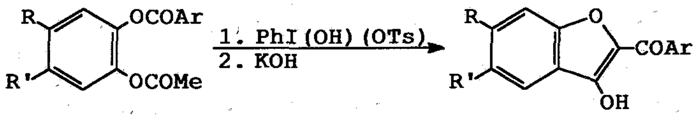


Scheme 37

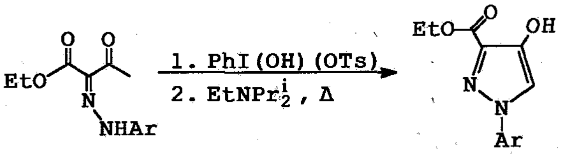


Scheme 38

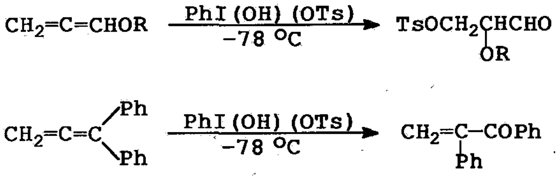
In the reaction of several 2-aroyloxyacetophenones with HTI, the tosylates may be isolated but, if KOH is added, then hydroxy-aroylobenzofurans are obtained[86] (scheme 39). Arylhydrazones from ethyl 2,3-dioxobutanoate were converted by heating with HTI and a 3° amine to pyrazoles[87] (scheme 40). Allenes reacted with HTI in a different way than with DIB: alkoxyallenes yielded 2-alkoxy-3-tosyloxypropanals, whereas phenylated allenes were converted to unsaturated propiophenones[52] (scheme 41).



Scheme 39

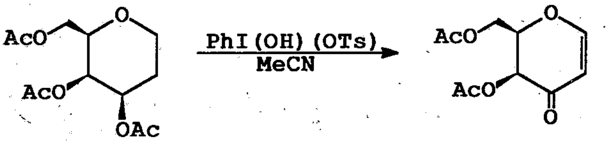


Scheme 40

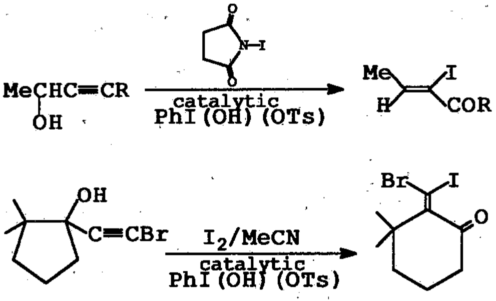


Scheme 41

Among various oxidations mediated by HTI, the direct regioselective conversion of several protected glycals deserves to be mentioned (scheme 42); not only acetylated but also perbenzylated derivatives reacted similarly.[88] A series of interesting oxidations, mainly of acetylenic alcohols, accompanied by iodination have been reported using elemental iodine or N-iodosuccinimide and HTI as catalyst;[89,90] two examples are illustrated in scheme 43. A further possibility of HTI is to serve as initiator, thermally or photochemically, in the polymerization of acrylates.[91]

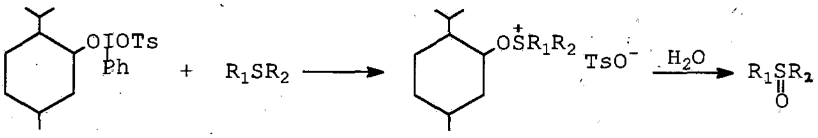


Scheme 42



Scheme 43

Some analogues of HTI are known; instead of the tosyloxy group, they contain a mesyloxy or 10-camphorosulfonyloxy or 2-naphthalenesulfonyloxy moiety and their reactivity is similar to that of HTI.[2] Also, there are [(alkoxy)(tosyloxy)-iodo]benzenes, PhI(OR)(OTs), in which R can be a methyl or a more complex group; when a chiral alcohol such as menthol was used to prepare **70**, this was found to give with sulfides chiral alkoxysulfonium salts **71** which were hydrolyzed to chiral sulfoxides of high optical purity[92] (scheme 44).

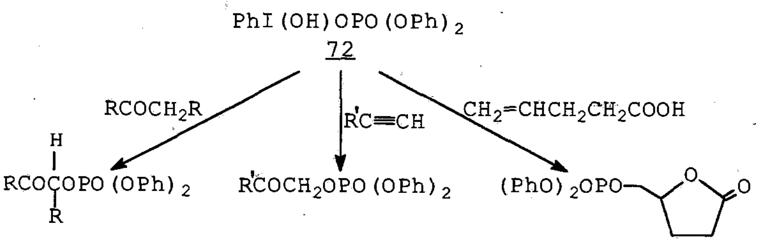


70 71

Scheme 44

[(Hydroxy)(bis phenyloxy phosphoryloxy)iodo]benzene

This reagent, **72**, converts ketones into ketol phosphates,[93] **73**. Similar products, **74**, were obtained from its reaction with terminal alkynes, whereas 4-pentenoic acids afforded phosphorylated lactones, **75** for the parent acid[94] (scheme 45).



73 74 75

Scheme 45

Other iodine(III) reagents

Among I(III) compounds of potential utility, two are mentioned: [(trifyloxy)(cyano)iodo]benzene, PhI(OTf)CN, and [(bis-pyridinium)iodo]benzene bis triflate, $PhI(N^+C_5H_5)_2 .2TfO^-$. The former has so far proved valuable for the preparation of various iodonium salts,[95] whereas the latter is a promising strong oxidant.[96]

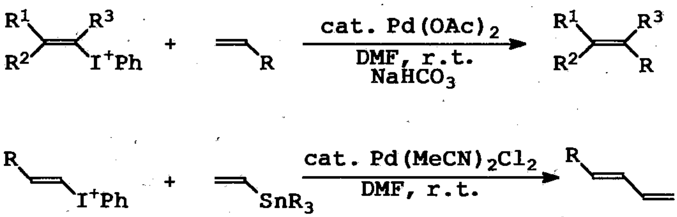
Iodonium salts

The most common type of this multi-membered class of compounds involves diaryl iodonium salts, known for more than 100 years. Their main utility is that they serve for the transfer of an aryl group to a nucleophile; a great variety of compounds with nucleophilic centers, especially C,O,S,N and P, have been successfully arylated under various conditions. The recent development of new types of iodonium salts, however, has made a much more important impact on synthesis in less than 10 years' time. Alkenyl and alkynyl phenyl iodonium salts constitute presently the two most intensively studied classes. Although recently reviewed,[5] there is already a substantial quantity of new results of general interest.

a. Alkenyl phenyl iodonium salts

Because of the excellent leaving ability of the phenyliodonio group (PhI^+), these fairly labile salts react readily under mild conditions with many nucleophiles, acting as activated species of vinyl halides, i.e. vinyl cation equivalents. In this way, various kinds of unsaturated compounds, including α-cyano and α-nitro alkenes, vinyl sulfides and sulfones, vinyl halides and esters have been synthesized.

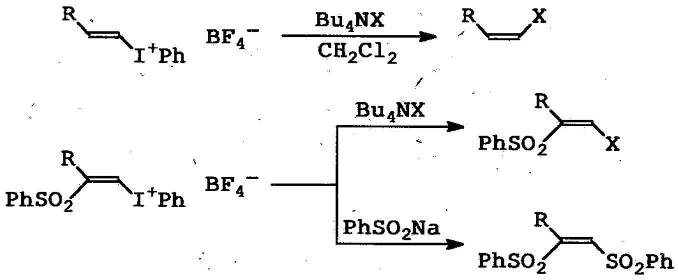
Of great importance is the possibility to create carbon-carbon bonds through alkenyl iodonium salts. Apart from alkylation and phenylation reactions using R_2CuLi or benzene, alkenylations are also possible; several 1,3-dienes were obtained from either alkenes[98] or vinyl trialkyl tin compounds,[99] with catalysis by Pd compounds. Since no heating is required, polymerization is avoided and the yields are very satisfactory (scheme 46). When allyl tin compounds were used, 1,4-dienes were formed.



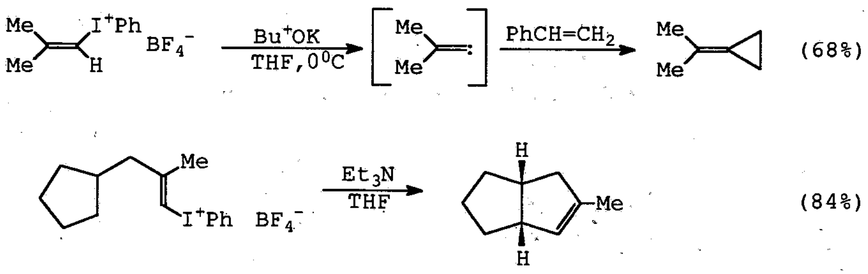
Scheme 46

The simplest compound of this class, CH_2=CHI^+Ph TfO^-, is known.[100] Although its reactivity has not yet been investigated in detail, it was reported that the enol ester CH_2=CHOTf was formed upon treatment with AgOTf (TfO^- is trifluoromethane sulfonate); also, some organometallic complexes underwent vinylation at the metal site (Ir, Rh).

Depending on the iodonium salt, retention of its configuration or inversion are possible in reactions with tetrabutylammonium halides and sodium phenylsulfinate, leading to the formation of simple or functionalized vinyl compounds (scheme 47). Such reactions have been examined in depth from a mechanistic point of view.[101,102] Upon treatment with a base, alkenyl iodonium salts generate alkylidene carbenes, which react with nucleophiles in several ways, intra- or intermolecularly,[97] as illustrated in scheme 48. Some further reactions of alkenyl iodonium salts[7] appear in scheme 55.



Scheme 47

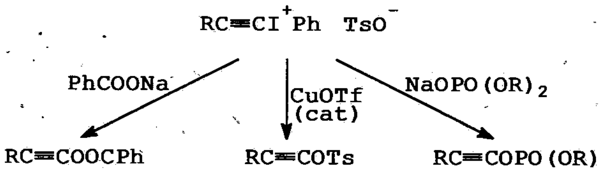


Scheme 48

b. Alkynyl phenyl iodonium salts

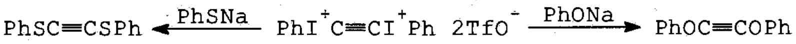
From a synthetic point of view these highly electrophilic iodonium salts are characterized by useful and sometimes unique reactivity, combined with great versatility. Substitution, addition and cycloaddition reactions dominate their chemistry.

Since nucleophilic acetylenic substitutions are generally unfavorable, the preparation of acetylenic esters, as depicted in scheme 49, is especially noteworthy.[5]



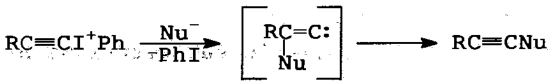
Scheme 49

Useful substitutions of this type involved the transfer of an alkynyl group to carbon nucleophiles from β-diketones[103] and organocopper compounds;[104] the latter, i.e. R_2CuLi, served for the preparation of several alkynes and 1,3-diynes (diacetylenes). Also, various sulfur nucleophiles such as thiocyanates,[105,106] thiosulfates[107] and phosphorothioates,[108] in the form of NaSCN, $p\text{-}TolSO_2SNa$ and $NaSPS(OR)_2$ were successfully alkynylated. The double iodonium salt **77** coming from acetylene gave bis substituted acetylenic sulfide **78** and the corresponding ether **79** with PhSNa and PhONa, respectively (scheme 50).[109] All these reactions proceed via unsaturated carbenes, generated after initial attack of the nucleophile to the β-C atom of the acetylenic moiety (scheme 51).



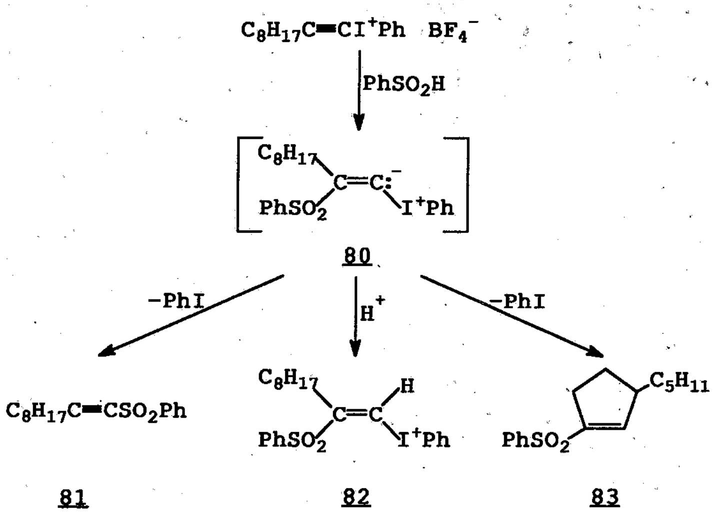
78 77 79

Scheme 50

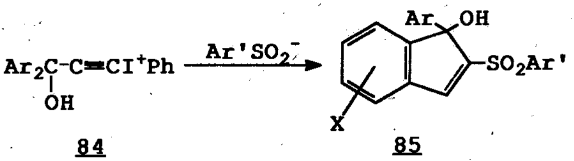


Scheme 51

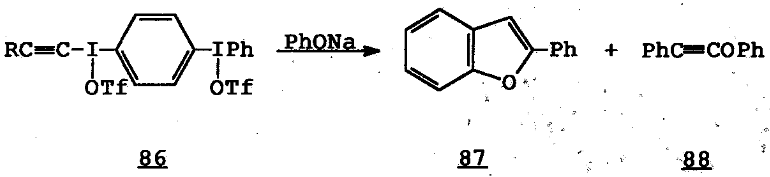
The reaction of a variety of alkynyl iodonium salts with sulfinic acids may furnish acetylenic sulfones, 81, in high yields;[110,111] however, it can also lead to the formation of other sulfones, i.e. phenylsulfonyl alkenyl iodonium salts, 82, or cyclopentene products 83 (scheme 52).[112,113] The reaction is strongly solvent dependent and all products result from a common intermediate, the alkenyl iodonium ylide 80; when a proton is added, alkenyl iodonium salts are formed. The cyclopentene ring results from δ-C-H insertion of the alkylidene carbene formed after iodobenzene elimination from 80. Insertion reactions of analogous carbenes to an aromatic ring gave also cyclic products. In the case of the salt 84, hydroxy-indene arylsulfones 85 were formed[114] (scheme 53). A related path was followed when the bis iodonium salt 86 reacted with PhONa to give 2-phenyl benzofuran,[115] 87 (scheme 54). Here the carbene intermediate PhO(Ph)C=C: gave also after a 1,2-phenyl shift the ether 88. Alkynyl iodonium salts in their reactions with hydrogen or lithium halides afforded additions products, i.e. β-halovinyl iodonium salts in a stereospecific way.[116]



Scheme 52

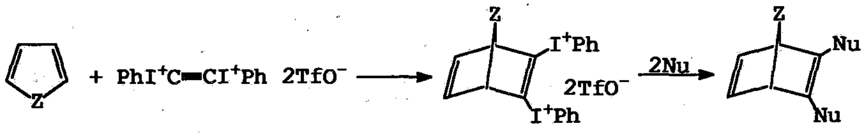


Scheme 53



Scheme 54

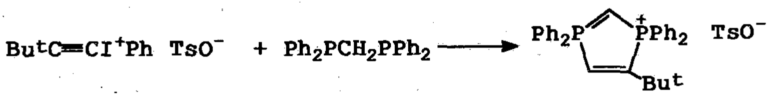
Diels-Alder reactions and 1,3-dipolar cycloadditions constitute another important area of reactivity, since the adducts are versatile vinyl iodonium salts, suitable for further synthetic elaboration. For example, 90 gave with cyclopentadiene or furan (89) the bis alkenyl iodonium salt 91 which reacted with various nucleophiles[117] (scheme 55). 1,3-Dipolar cycloadditions involved the use of the following dipoles: nitrile oxides,[118] nitrones,[118] α-diazocarbonyl compounds[119] and phenyl azide.[119] A cyclic product (95) was eventually formed from 93 and bis phosphine 94 (scheme 56).[120] Generally, phosphines react with alkynyl iodonium salts to give either alkynyl or alkenyl phosphonium salts, after PhI elimination;[109,121,122] phosphites have afforded alkynyl phosphonates.[123]



89 90 91 92

(Z=CH$_2$,O;Nu=Br$^-$,I$^-$,CN$^-$,PhCOO$^-$)

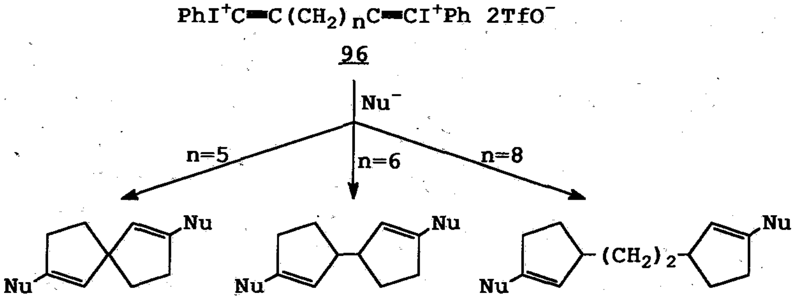
Scheme 55



93 94 95

Scheme 56

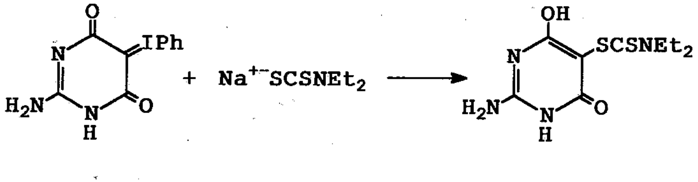
Several bis(phenyliodonium)diyne triflates, besides 90, are known.[124,125] Those of the general formula 96 are found to react with C and S nucleophiles affording bis cyclopentene ring systems[126] (scheme 57).



Scheme 57

c. Iodonium zwitterions

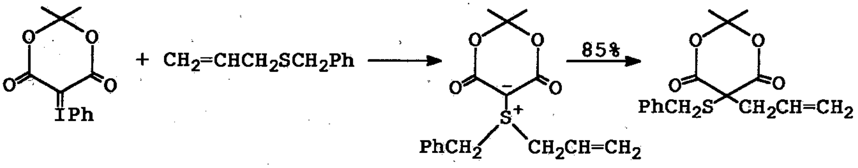
Several types of phenyliodonium compounds are known, in which the positive charge of iodine is internally compensated by a negative charge; when this is localized to an adjacent C or N atom, the resulting zwitterions are called iodonium ylides. These are stabilized, when the carbanionic carbon is flanked by two strongly electron withdrawing groups, as e.g. in $PhI^+\text{-}C^-(COR)_2$ and $PhI^+\text{-}C^-(CN)_2$; ylides are often written with a double bond notation, i.e. the previous compounds appear as $PhI{=}C(COR)_2$ and $PhI{=}C(CN)_2$. Most of their reactions involve the formal generation of carbenes, after elimination of iodobenzene; these react further with added nucleophiles in various ways. The products in most reactions come simply from the joining of the nucleophile with the carbene moiety, e.g. sodium diethyl dithiocarbamate and ylides such as 96 gave 97 (scheme 58).[127] In this particular case no catalyst was needed, but normally photolytic conditions or copper catalysis is required. When allylic sulfides or selenides were used, an allylic moiety and an alkythio- or alkylseleno- group were introduced onto the α-C of β-dicarbonyl compounds as the result of a tandem transylidation and [2,3]-sigmatropic rearrangement (scheme 59).[128]



96

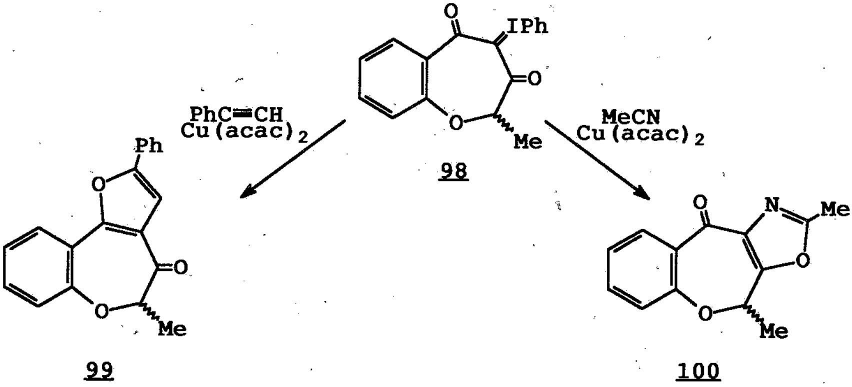
97

Scheme 58

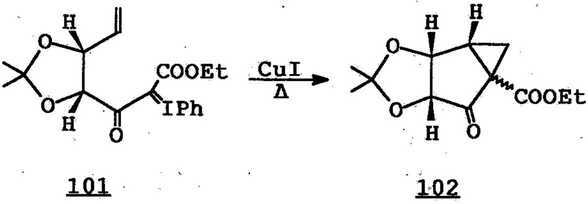


Scheme 59

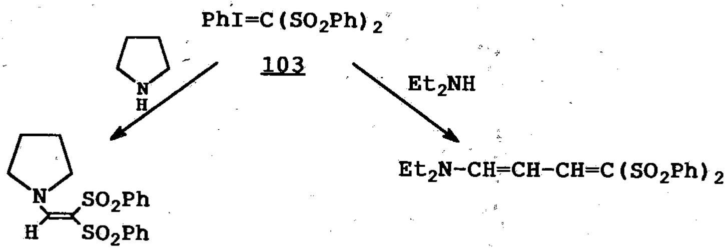
Cycloadditions have often been observed in reactions of several iodonium ylides and zwitterions with alkenes, alkynes, nitriles, thioketones, etc. For instance, 98 gave with alkynes and nitriles the cycloadducts 99 and 100, respectively (scheme 60).[129] Intramolecular reactions with an olefinic double bond lead to the formation of cyclopropanes, e.g. the sugar derivative 101 afforded 102 as a mixture of two diastereoisomers[130] (scheme 61). Unusual reactivity was noted in several reactions of 103; among them, the most remarkable are those with secondary amines, which lead to the formation of enamines (scheme 62).[131,132] Phenyliodonium zwitterions 104, coming from hydroxy-*p*-benzoquinones, undergo thermally through carbenes a Wolff-type rearrangement and are eventually transformed to 2-cyclopentene-1,3-diones, 105 (scheme 63).[133] Unstable zwitterionic compounds are formed from phenols and resorcinols, e.g. 36, which rearrange spontaneously to iododiphenyl ethers 37 (scheme 20).



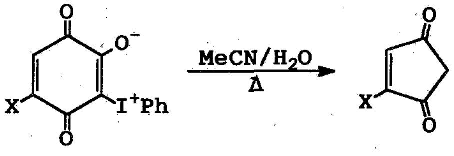
Scheme 60



Scheme 61



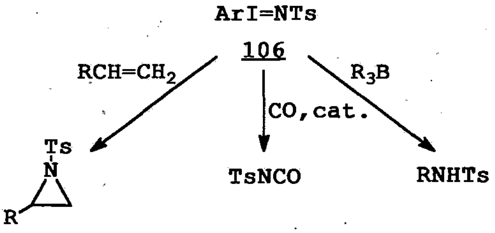
Scheme 62



104 105

Scheme 63

The chemistry of phenyliodonium N-ylides is confined mostly to 106, whose main property is to bring about aziridination of unsaturated compounds; when chiral catalysts are used, excellent enantioselectivity may be achieved.[134] Other reactions of 106 involve carbonylation with CO to arylsulfonyl isocyanates[135] and alkylation using trialkylboranes[136] (scheme 64).

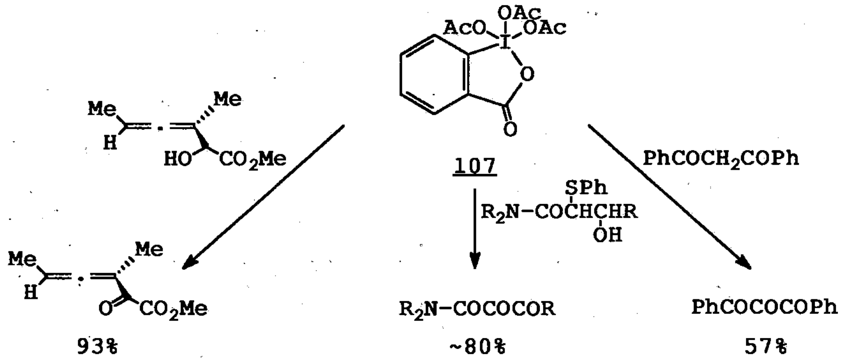


Scheme 64

Compounds of Iodine(V)

Iodoxybenzene, $PhIO_2$, is the simplest compound of I(V) derived from iodobenzene. Although it is a strong oxidant, few oxidations have been performed with this reagent, probably because it is insoluble in ordinary solvents. Special mention deserves its use, together with $(PhSe)_2$, which is transformed to $(PhSeO)_2O$, in dehydrogenations, mostly of ketonic compounds.[137,138] Because of the good leaving group ability of $-IO_2$, iodoxyarenes have been converted to benzoic acids[139] (with CO in Na_2CO_3) and to chloroarenes[140] (with HOCl), under mild conditions.

One of the best oxidants for the conversion of alcohols to carbonyl compounds is the cyclic iodane 107, called usually Dess-Martin reagent.[141] Even allenyl alcohols were efficiently oxidized, without reaction from the double bond.[142] The phenylthio group[143] and methylene groups[144] of several β-diketones were oxidized to carbonyl, so that triketo compounds were obtained (scheme 65). All reactions were performed without heating.



Scheme 65

Conclusions and Outlook

This review has shown that a wide variety of hypervalent iodine compounds are presently available. Although only the latest three years have been covered, it is clear that several members have now reached the status of reagent and are becoming valuable in organic synthesis. They bring about a multitude of transformations under mild conditions, in high yields; often, they possess a unique reactivity. Today, their exclusion from the arsenal of an organic chemist is inexcusable.

Future research may add new types of compounds, not only individual members but also whole classes; together with those already known they are reasonably expected to amplify the present range of applications. We may discover, for example, combinations of organoiodine(III) and (V) compounds with other elements, either as stable chemical entities or as intermediates, capable of performing predetermined reactions. Also, alkenyl and alkynyl iodonium salts as well as iodonium ylides promise to serve as building blocks for the preparation of new products and to be used in the development of new procedures. We are then entitled to look forward to further interesting developments in this rapidly expanding field of chemistry.

CORRIGENDUM: Formula 39 should be read with one COMe group and one COPh group.

ΠΕΡΙΛΗΨΗ

ΑΝΤΙΔΡΑΣΤΗΡΙΑ ΤΟΥ ΥΠΕΡΣΘΕΝΟΥΣ ΙΩΔΙΟΥ ΣΤΗΝ ΟΡΓΑΝΙΚΗ ΣΥΝΘΕΣΗ

Το ιωδοβενζόλιο έχει την ιδιότητα να σχηματίζει πολυάριθμα σταθερά παράγωγα από το ιώδιο, το οποίο εύκολα μετατρέπεται σε υπερσθενές, δηλ. οξειδώνεται στις ανώτερες βαθμίδες οξείδωσης +3 και +5. Μια σειρά αυτών των ενώσεων, των γενικών τύπων $C_6H_5IX_2$ ή $C_6H_5\overset{+}{I}X\ Y^-$ (όπου X και Y είναι μια ποικιλία ομάδων, από απλό αλογόνο ως πολύπλοκες ανθρακούχες αλυσίδες), χαρακτηρίζονται από ενδιαφέρουσα χημική δραστικότητα, όχι μόνο σε οξειδώσεις διαφόρων ειδών, αλλά επίσης και στη μεταφορά ομάδων προς πυρηνόφιλα κέντρα. Το άρθρο αυτό επικεντρώνεται κατά κύριο λόγο στις ενδιαφέρουσες εξελίξεις που παρατηρήθηκαν στον τομέα αυτό κατά τα τελευταία πέντε χρόνια. Μία σύντομη ματιά στις αντιδράσεις θα πείσει για τη χρησιμότητά τους στις οργανικές συνθέσεις.

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ANALYSIS OF LIQUID SAMPLES BY PIXE

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Summary

Proton Induced X-ray Emission (PIXE) is extensively used for the determination of trace elements in a variety of liquid samples. The liquid samples are usually transformed into suitable solid targets but direct analysis of liquids has also been applied. The calibration methods for quantitative results and the techniques for improving the detection limits and avoiding interfering effects between the analyzed elements are reviewed in the paper. The detection limits as well as the precision of the method are examined.

Key words: Proton Induced X-ray Emission (PIXE), liquid analysis, trace elements

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1. Introduction

Proton induced x-ray emission (PIXE) is a relatively new technique that has been applied for the elemental analysis of a wide variety of samples[1,2]; it is based on the excitation of the target (sample) atoms by a proton beam, from a particle accelerator, and the detection of the produced x-rays by a semiconductor detector. The main advantages of the method are: i) the capability for detecting all the elements heavier than sodium ii) small time (a few minutes) and multielemental analysis and iii) good accuracy and low detection limits. The principal disadvantage is the need of an accelerator, an expensive facility.

Although inorganic analysis of liquid samples usually is performed by methods such as atomic absorption and emission spectrometry, liquid chromatography etc.[3,4] PIXE is extensively used, especially when multielemental analysis is needed. PIXE is rarely performed directly in the liquid phase; the disadvantage of the need of a sample transformation into a solid target can be balanced by the already mentioned advantages of the method. Analysis of liquid samples presents differences from the analysis of solids: the need of a preconcentration step, the preparation of the target, and the additional alternatives in quantitative analysis are the most important of them. These three special subjects, as well as the accuracy and the detection limits of the method are treated with the use of the recent literature.

2. Direct bombardment of liquids by protons

The direct analysis of liquids by proton bombardment of sample drops was first reported by G. Deconninck[5]. Direct liquid analysis is impossible in the vacuum, so an external beam technique (in air surrounding) was used. Two alternative set up were introduced: in the first one liquid drops hanging from a pipette were analyzed, and in the second a liquid jet of a recycled fluid was bombarded by protons. These two set up are presented schematically in the figure 1, (a) and (b). The drop technique was preferred when very little liquid was available; for the jet technique more than 1 ml of liquid was required. The disadvantage of the drop technique was the limitation in the time of analysis, because of the drop heating and the evaporation effects. Arsenic was selected as internal standard, because of its low evaporation rates under proton bombardment and easy mixing with different kind of fluids. A problem arisen in the accurate beam current measurement: many liquids are insulators and the drop potential may rise to many thousand volts; an interesting solution introduced for dilute solutions is the use of the bremsstrahlung spectrum (x-ray continua) for comparison studies between solutions of similar composition. The sensitivity was 2 ppm for elements between Mn and Zn. Another direct technique was reported two years later. A.H. Khan et al[6] developed a special cell containing the liquid sample; the protons, after exit to the air from a beryllium window foil, passed to a chamber through a plastic Kapton window to reach the liquid sample (figure 1c). A stirrer was inserted to agitate the

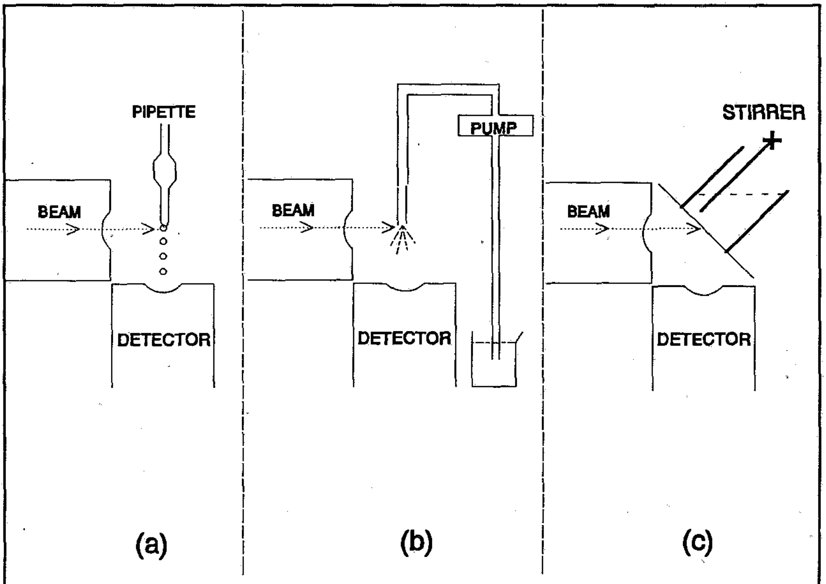

Figure 1. The three used PIXE setup, for direct bombardment of liquid samples.

irradiated solution, in order to avoid the bubbles that sometimes formed near the beam spot; mechanical stirrer moved by compressed air was preferred to the electrical one, because of the electrical disturbance problems to the detector signals. The total current was monitored on the target and on the insulated beryllium exit foil, resulting stable and reproducible measurements. A correlation between the accumulated current and the x-ray yields was found due to the concentration of many chemical elements on the internal side of the Kapton window of the cell; an analogous effect (precipitation by irradiation) was also noticed during the direct analysis of solutions by XRF (Ref. 6 page 240). Minimum detection limits of few ppm were determined but they were diminished even more when the measurement started after 5 μC of current accumulation. A similar setup (without the stirrer) was suggested in another paper of the same year[8] and the matrix effects due to the presence of large amounts of Cu were calculated and measured. S.E. Bauman et al.[9] also performed liquid analysis in a 3 ml holder.

In conclusion the reported cases of direct liquid bombardment are neither many in number nor frequently used. In fact although liquids are quite often analyzed by PIXE, the procedure usually followed is to form a solid target (thin or thick, selfsupported or on a substrate). The target may be thick (not transparent from the bombarding particles) or thin (the protons traversed through it, almost without loss of energy); thin targets are divided to selfsupported, and to deposited on a substrate.

3. Preparation of solid targets from liquids and separation

As preconcentration is characterised every technique by which the ratio of the concentration (or the amount) of the trace components to the concentration (or the amount) of the macrocomponent is increased.[10] Preconcentration of the samples is often necessary in the analyses of liquids, regardless of the analytical technique, in order to improve the minimum detection limits; a separation from some sample components is often take place during the preconcentration process resulting an exclusion of some elements that interfere the analysis. Many papers have been published on this subject as well as a good number of review articles[11-16]. The result of the preconcentration procedure may be a liquid with higher concentration in the analyzed components, a solid such as an evaporation or precipitation residue, or an inert substance (active carbon, ion exchange resin, etc.) which has absorbed components from the liquid; the result of a solid product is usually preferable in PIXE analysis.

The simpler preconcentration method is the removal of the liquid by evaporation; this can be done to a smaller volume (e.g. 1 ml) and after this let some drops of liquid on a suitable backing to dry[17-19], or the evaporation can be result a dry sample, followed by the formation of pellet targets[20]. As thermal source may be used an oven, a hot plate in low temperature (40-70 °C)[18,20], microwaves[21] or an I.R. lamp for smooth evaporation.[11] Vapour filtration (filtration through a membrane permeable by liquid vapours but not by liquids), with the application of a pump, is a very interesting method which gives recoveries of almost 100 % for the non-volatile elements[22,23]; a topographic effect on the filter surface (lower thickness of the sediment in the central portion of the filter) was noticed but it was not significant for powders at least as fine as 200 mesh (maximum particle size about 75 μm)[22]; the problem could also be overcome bombarding with a uniform beam across the target surface during the analysis, produced by passing the protons through a diffusion foil[23]. Removal of the solvent may also be completed by freeze drying[24,25]; in biomedical samples (e.g. human blood) freeze drying sometimes is followed by low temperature ashing[27] because volatile compounds or elements may be lost even in medium temperatures. A high frequency electromagnetic field is employed during the low temperature ashing to produce a stream of reactive oxygen atoms, and the loss of many elements (i.e. Cl, K, Ca and Br) is much less. In another preconcentration method the solvent is removed by dropping small volume of the liquid sample onto a suitable backing; this technique is stronger related with the target preparation and it is discussed in the next chapter. Other preconcentrating methods for solid target preparation are precipitation as carbamates at pH=9 from fresh and sea water, and adsorption on activated carbon. In the first case Pd was added as internal standard and as coprecipitant too. The precipitate was collected by filtration through a 0.8 μm pore size filter used also as backing of the sample; a preparation time of 15 min was referred[27,28]. In another case[29] Cu was added as a specialized coprecipitant for Ag and Cd determination in order to obviate interferences with the K lines of Pd. In pH=9 many elements precipitate[30] both as carbamates or as hydroxides but V, Se and Mo precipitate better at pH=4 because their carbamate complexes are less soluble than at pH=9. The adsorption on activated carbon follows a chelating step by organic agents (8-hydroxyquinoline or ammonium 1-pyridine dithiocarbamate); a purification procedure of the activated carbon by acids was described and sub-ppb minimum detection limits for many elements were obtained[31].

Preconcentration with Chelex 100 resin and drying on a suitable foil was suitable in urine analysis to separate the alkalies end alkaline earths from other elements[32,33]; the most of the interesting elements were analyzed simultaneously at a single elution. Cr^{3+} in blood serum was determined after complexation with ammonium pyrrolidine carbodithioate, extraction with methyl isobutyl ketone, wet ashing and deposition on a polycarbonate foil[34]. Wet ashing was preferred than dry ashing because of the significant loss of chromium during dry ashing[35].

4. Target Preparation

A usual way to prepare a target from a liquid is by the deposition of some drops on a suitable backing and let them to dry; PIXE is suitable for direct analysis of filters[36,37]. The deposited liquid volume is a few (10-20) μl in most cases; because of crystallization problems the maximum amount is limited to about of 100 μl[38]; these problems are greater with hydrophobic foils. Formvar, Mylar and aluminized Mylar are the more frequently used foils. A special technique was referred for the collection of small volume samples in a siliconed glass capillary containing water saturated hexadecane connected to a Hamilton syringe[39], for sweat analysis. Final targets had various thicknesses, depending on the liquid volume and the dissolved material concentration; surface densities from 200 $\mu g/cm^2$ to 10 mg/cm^2 are mentioned[24,40]. The addition of a small amount of 100:1 polystyrene in spectral grade toluene improved the cohesion of the specimens to the backing and produced targets with thickness of about 10 mg/cm^2. In another case replicate samples of the oil (about 12 µl) were uniformly dispersed on individual filters to ensure an oil film thick enough to stop the proton beam before reaching the filter[41].

Formvar, aluminized Mylar and Kapton are suitable backing materials when high beam current is needed. Formvar can withstand a beam current of 150 nA for a time of more than 2 hours[42]. Aluminium of aluminized Mylar prevents heating as well as charging effects. Polystyrene backings can withstand a beam current of 200 nA with an 8 mm beam, increasing the detection limits[38]. Formvar was better for mildly alkaline materials, and polycarbonate foils for acid materials[43]; in many cases samples are acidified during sampling in order to prevent the loss of volatile elements, so acid resistance of the backing is a very important property[38]. Kimfol (a poly-carbonate foil) was preferred by many laboratories but there is the problem of the termination of its production. In a few cases, e.g. mother's milk and cerebrospinal fluid, thin samples were prepared without a backing by pressing into thin, selfsupporting disks, only 2 mm in diameter[21]. A transformation of the Kimfol surface into hydrophillic one was succeeded with the influence of sodium hydroxide and polyvinylpyrrolidone; an hydrophillic area with well controlled size was produced[33]. Six different filter materials and plastic foils were investigated for their purity[44]; PIXE spectra of these backing materials are given and polycarbonate filter Makrofol seems to exceed. The trace element content of hydrophillic backing materials must be carefully examined; unpredictable variations in blank values of Br and Cr in Nucleopore filters were observed[21], due to their hydrophillic properties.

H.C. Hansson et al.[38] suggested a spray technique with a nebulizer for water deposition: The water was firstly sprayed into a dry air stream and the water droplets were transformed into fine aerosol, consisting of dry particles. The air was then pumped through an impactor and the aerosol particles were deposited on a thin polystyrene foil; a nebulizer designed for inductively coupled plasma (ICP) analysis was adequate. Losses were found only for chlorine; decreasing pH of the aerosol gave increase in the loss, due to the formed gaseous hydrochloric acid. The spraying techniques also suffer from unnecessary losses and some contamination problems. Drying of the deposited liquid is performed in a desiccator, vacuum desiccator, air or by freeze drying. A comparison between the results from the air-dried and the vacuum-dried samples showed for copper that the concentration in air-dried samples was slightly lower, despite that spot in air dried samples was larger. This proved an enrichment in copper at the rim of the spot, dried in air. Part of a volatile bromine compound was also lost by evaporation during the measurements to a fluctuating extent in the samples dried in air. Larger potassium concentrations found in air-dried samples were attributed to the differences in selfabsorption. No significant differences in Mn, Fe, Zn, Rb were noticed[43].

Preparation of thick targets is another alternative, especially if enough sample volume is available. Centrifiguration, lyophilization, powdering and pressing the dry materials into pellets is a standard technique in biological fluid analyses[45]. Homogenizing after drying was necessary for some materials since their structure was too heterogenous; the homogenization was sometimes performed by standard equipment of chemical laboratories, with the risk of introducing impurities[22]. Although in most cases the pellets were selfsupported, a 4.3 μm polypropylene film with a 10 % ethanolic solution of polyvinylpyrolidone was suitable to attach a 100 mg pellet[46]. Another way to fix particulate matter was the application of a thin layer of the powdered material onto a prepressed carbon-cellulose pellet and then pressing it on the soft surface, thus fixing the powder mechanically; the carbon content prevented charging during irradiation[47]. When preconcentration with active carbon was preferred, an activated carbon tablet was prepared; to increase the cohesion of the carbon tablet, one drop of a binding agent (polyvinyl-alcohol in aqueous solution) was added to the carbon prior to pressing the tablet[31]. The applied pressure to make the pellet rarely ir referred; a pellet, from dried human blood serum has been prepared using a pressure of 5.9 MPa (60 Kg/cm^2)[48].

The proton energy used for target bombardment was usually about 2 MeV. The lowest referred energy was 350 KeV for protons used to analyze elements from Mg to Fe in settling material of a lake[47]. On the other hand 18 MeV alpha particles were reported for the analysis of ink in historical documents, in order to maximize the number of x-rays per ion and minimize the possible damage; ink analysis can be faced as a special case of liquid analysis! In many bombardments a diffusion foil in combination with a collimation system was inserted to achieve a beam diameter larger than the diameter of the liquid spot on the backing, and to overcome the difficulties that arise due to target inhomogeneities. A sharp variation of the determined concentration of different elements in seawater was observed[49] during the bombardment with high proton beam intensities (350 nA) due to volatilization effects; low beam currents were recommended but Br volatilizes even at low beam intensities.

5. Calibration and Quantitative Analysis

The most common method applied for quantitative analysis of liquid samples was the dissolvation of a known mass of a standard element, before drying the liquid (internal standard method). The more frequently preferred element was yttrium because its characteristic x-rays did not interfere with other elements, yttrium oxide gave only a very small evaporation loss and it was not a constituent of the most of the analyzed samples[18]. A disadvantage of yttrium was that in alkaline pH its salt precipitated; for this reason a ruthenium internal standard was added in bile analysis[43]. Even with the use of an internal standard, matrix effect corrections were necessary for thick targets; the corrections were performed by a computer code, for specimens with thickness of about 10 mg/cm^2 doped with yttrium as internal standard[40]. Selenium has been introduced as internal standard; 10 ml of a standard selenium solution (1000 ppm) were filtered and added to 250 ml of rain water in a crucible (selenium in rain can be assumed to be negligible). To test the accuracy of the method separate irradiations were performed with standard aqueous solutions of 16 elements, each mixed uniformly with the internal standard solution of selenium. The results of the PIXE analysis were in agreement within 10 % with the values supplied by the manufacturer[17]. Other elements that have been used as internal standards are vanadium in blood plasma[50] and chromium in amniotic fluid[24], because of their absence in the initial sample, arsenic in direct analysis of fluids[5], because of its low evaporation rate during particle bombardment and easy mixing with biological liquids, strontium in sweat[39], nickel for chromium determination[34], and molybdenum for bromine determination[51]; the simultaneous addition of two internal standards, yttrium and vanadium, in urine samples was also referred[32]. Finally, palladium, a very rare element in environmental samples, was added in fresh and sea water, acting as internal standard and as coprecipitant too[27].

Although the method of standard additions is well suited for the analysis of liquids, it has not been applied extensively in PIXE analysis. Iron was added as standard in the analysis of total iron in seawater samples[20], to minimize the effects of high background; the results were compared with results of the atomic absorption spectrometry and a deviation of about 10 % between the two methods was observed. The same element was used in water analysis, after a preconcentration procedure including chelation and adsorption on activated carbon; the yields of the preconcentration step may be smaller than 1 and not known exactly, so the method of standard additions for quantification was selected.

The comparison with suitable standard materials is another kind of calibration, usually preferred for the analysis of the insoluble fraction of liquid samples; these materials have a matrix composition similar to the unknown samples. Quantitative analysis of trace elements in crude oils was performed by the correlation of NBS (new name: NIST) residual fuel oil[41], biological samples by using bovine liver and pure chemical compounds[52], and water analysis by preparing suitable standards from water solutions[42]. Series of standards with various surface densities, covering the range 0.1-1 mg/cm^2, were created[22] in order to analyze suspended marine particulate on filters; this kind of samples has a varying sample thickness and the total mass of the sample can be measured gravimetrically. A computer data analysis program calculated the corrections for x-ray absorption effects. In another case[36] filters of river water were analyzed by comparison with clay, orchard leaves and powders of feldspar standards; selfabsorption corrections were calculated by iterations using a silicon thickness measured by inductively coupled plasma emission spectroscopy and atomic absorption spectroscopy (AAS). Silicon measurements were also performed by using an auto analyzer[37]. Thin standards of suitable elements evaporated on thin backings and calibrated by the backscattering method were produced for lubricating oil analysis[37]. The method of absolute yield calculations, described by Campbell[45] for thick samples, was applied in blood analysis.

6. Precision, detection limits.

The precision of the method usually is about 10%[21,36,45,53]. By carefully optimized analytical procedures and normalization to an internal standard the error can be minimized to 5% or lower, by the standard addition method[21]. Additional sources of errors in liquid sample analysis may be adsorption of trace elements on the walls of the vessel, precipitation, evaporation losses and sample inhomogeneities after drying. For an internal standard calibration technique with ruthenium, no error contribution beyond 2% was detected[43]. Comparison of PIXE results with wave dispersive x-ray fluorescence and neutron activation analysis (NAA)[41], ICP and AAS[19,36] gave satisfactory agreement, taking into account the estimated errors.

Minimum detection limits (MDL) are affected from the kind of sample, preconcentration procedure, experimental conditions, detected elements, time of measurements etc. and a more systematic study is needed. Detection limits are usually in the range 1-10 ppm[36,45]. A table presenting the detection limits of 30 elements as well as their mean values in rain water after spray-drying was reported[38]. The MDL of many elements after precipitation as carbamates[27,29], with and without preconcentration by a Chelex 100 ion exchange resin was examined for 9 elements[33]. Sub-ppb detection limits for many elements in different kind of waters were obtained using a chelating agent in combination with an adsorption process on the activated carbon[31]. In another paper[54] sub-ppb levels in natural water were achieved by coprecipitation of dissolved metals as carbamates, Pd coprecipitant and internal standard too. MDL below ppb level have also been succeed[55] by the use ^{16}O bombarding ions at 50 MeV, due to their higher cross sections and lower bremsstrahlung; these conditions have been applied for the analysis of heavy water from a nuclear power. Sensitivity of selenium as a function of proton energy was investigated and an optimum proton energy of about 4 MeV was found[56]. Detection limits of external beam PIXE for serum samples were given[57] as a function of proton energy and the analyzed element.

7. Applications and discussion

Analysis of liquids by PIXE has been applied in different kind of samples but the most usual are the analyses of biomedical[58-60], water and other natural samples. Water samples from the Greek lake Vegoritis were analyzed by PIXE for trace element pollution[61]. In some cases the interest is directed to the changes of trace element concentrations, as a function of time; PIXE is suitable to study rapid changes in the elemental composition of settling particles in lake water[47], metal diffusion and sedimentation phenomena[30]; in another case the determination of circulating blood volume was found by measuring the time variation of a tracer[62], the movement of five elements in blood were also studied[63]. Although direct analysis of organic compounds with PIXE is impossible, an indirect way developed for the determination of 2-bromo-2-chloro-1,1,1-trifluoroethane changes in blood during anaesthesia from bromine changes; in another case difficulties in asbestos determination were overcome by analysing magnesium and silicon content before and after the pollution area and correlate the results with asbestos concentration[64]. The analysis of inks and paints may be faced as a special case of liquid (in their original form) analysis[65-67].

In conclusion, PIXE analysis of liquids is a very useful tool for different kind of liquid samples. Besides the advantages of PIXE (multielemental, fast, small sample volume etc.) the use of internal and external standards is a satisfactory way to overcome the problems arising in quantitative analysis

Περίληψη

Ανάλυση υγρών δειγμάτων με τη μέθοδο PIXE

Η τεχνική εκπομπής ακτίνων x με πρωτόνια (proton induced x-ray emission, PIXE) έχει χρησιμοποιηθεί ευρέως για την ιχνοστοιχειακή ανάλυση διαφόρων ειδών υγρών δειγμάτων. Στην παρούσα εργασία γίνεται ανασκόπηση των τεχνικών απ' ευθείας ακτινοβόλησης καθώς και της μετατροπής των υγρών δειγμάτων σε κατάλληλους στερεούς στόχους, των μεθόδων βαθμονόμησης και ποσοτικής ανάλυσης, των τρόπων βελτίωσης των ελάχιστων ορίων ανίχνευσης και της αποφυγής φαινομένων παρεμπόδισης μεταξύ των προσδιοριζομένων στοιχείων. Επίσης εξετάζονται τα όρια ανίχνευσης καθώς και η αξιοπιστία (precision) της μεθόδου.

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SHORT PAPER

A MECHANISM OF THE FIRST STAGE OF THE REACTION BETWEEN CHROMIUM (II) AND SOME UNSATURATED LIGANDS. FORMATION OF σ- BONDED BINUCLEAR ORGANOCHROMIUM INTERMEDIATES WITH CARBON-CARBON BRIDGES

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In continuation of our interest in reductions of olefins by chromium (II) [1-4], we have investigated in detail the mechanism of the first stage of these reactions. Recently we have reported[3] that carboxylic groups are not necessarily needed for the transfer of electrons from Cr(II) to the double bond the only necessity being the positive overlap between the HOMO (highest occupied molecular orbital) of the reducing agent Cr^{2+} (σ-symmetry antibonding eg* orbital) and the LUMO (lowest unoccupied molecular orbital) of the oxidizing agent (olefin). We now report that in the case of pyridine-3-acrylic acid, **paa** , 1,2-bis(2-pyridyl)ethylene, **bpe** and phenylpropiolic acid, **ppa** , binuclear species with carbon-carbon bridges are discrete intermediates during these reactions in acidic solutions their formation being supported by kinetic data and by their decomposition (acidolysis) products.

The kinetics* of the first stage of the reaction between chromium (II) and $\mathbf{Hpaa^{+}}$, $\mathbf{H_2bpe^{2+}}$ and **ppa** in large excess of chromium (II) were studied and the rate law was found to be :

$R=k[Cr^{2+}]$ [substrate] (FIG. 1)

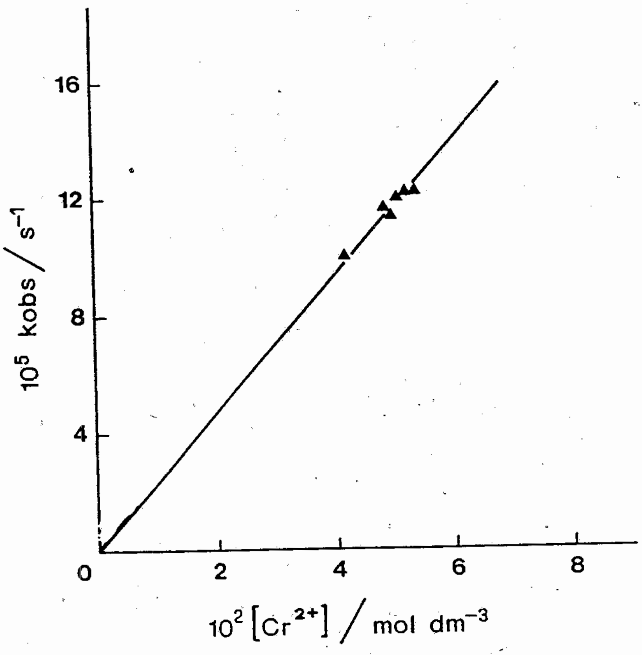


FIG. 1a: *$[Cr^{2+}]$-dependence of the first-order rate constants of the reaction between Cr^{2+} and pyridine-3-acrylic acid in large excess of Cr^{2+} at 24^0 C. $[Hpaa^+]=(1.1\text{-}5.3)x10^{-3}$ M, $[HClO_4]=1$ M.*

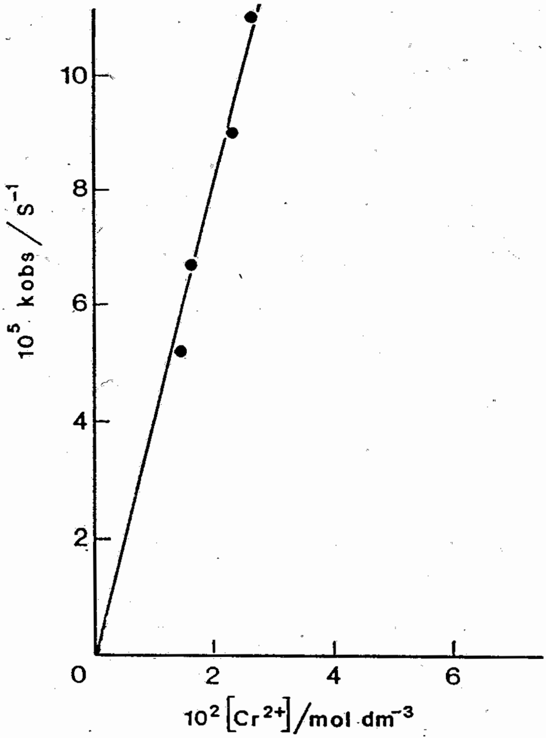


FIG. 1b: *$[Cr^{2+}]$-dependence of the first-order rate constants of the reaction between Cr^{2+} and 1,2-bis(2-pyridyl)ethylene in large excess of Cr^{2+} at 23^0 C. $[H_2 bpe^{2+}]=(3.9\text{-}5.8)x10^{-3}$ M, $[HClO_4]$=1M.*

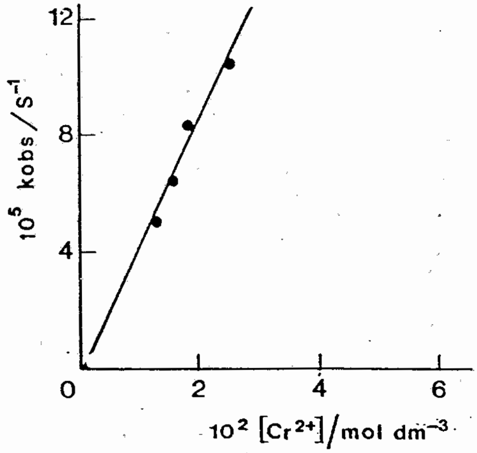


FIG. 1c: *$[Cr^{2+}]$-dependence of the first-order rate constants of the reaction between Cr^{2+} and phenylpropiolic acid in large excess of Cr^{2+} at 23^0C. [ppa]=$5.8x10^{-3}$M, $[HClO_4]$=1M.*

A mechanism according to which the first step in all three cases must be the formation of a 1:1 Cr(II):substrate complex upon a non-symmetric first attack [3,5,6] of a Cr^{2+} ion (σ-donor) on the double or triple bond of the substrate (π-acceptor) is proposed. Our present data suggest that reaction of a second chromium (II) ion with the 1:1 complex to form a 2:1 adduct in a rate-determining step is taking place after an attack on the far carbon [5] . Two electrons are then transferred to the unsaturated bond. Thus a 2:1 metal ion -olefin or metal ion- alkyne leads to the formation of a discrete intermediate ** with a high charge.

In excess of substrate or chromium (II) the data are consistent with a rate law

$$R=k' [Cr^{2+}]^2[substrate] \qquad (FIG. 2)$$

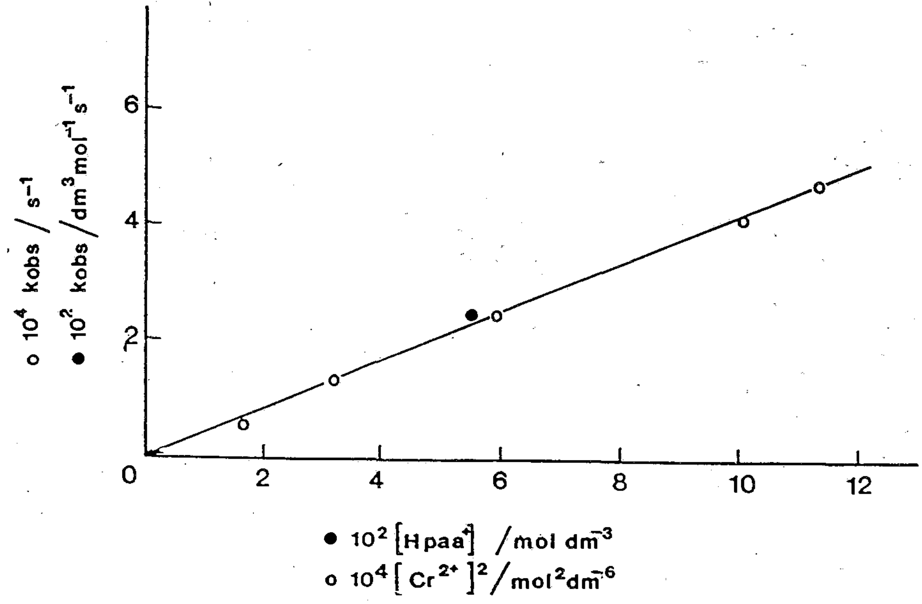


FIG. 2a: *[$Hpaa^+$]- dependence of the second-order rate constant (filled circle) and [Cr^{2+}]^2-dependence (open circles) of the first-order rate constants of the reaction between Cr^{2+} and $Hpaa^+$ in excess $Hpaa^+$ ([Cr^{2+}]=(0.9-3.3)x10^{-2}M) or Cr^{2+} ([$Hpaa^+$]=(0.82-1.3)x10^{-2} M) at 23^{0}C, [$HClO_4$]=1 M.*

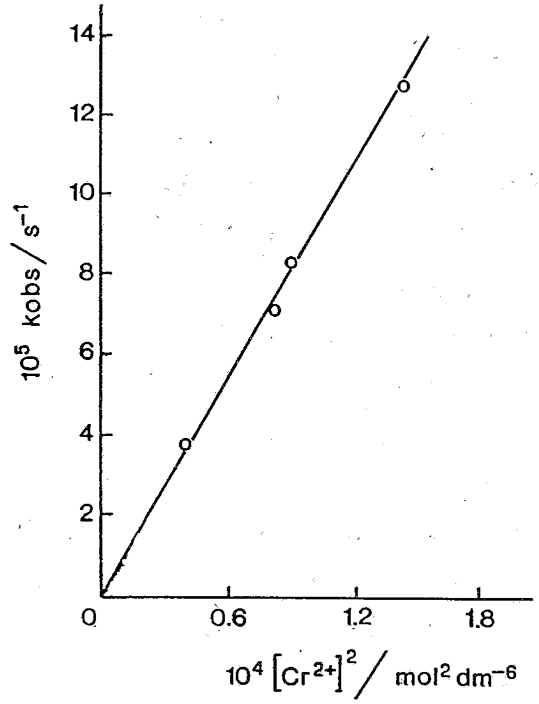
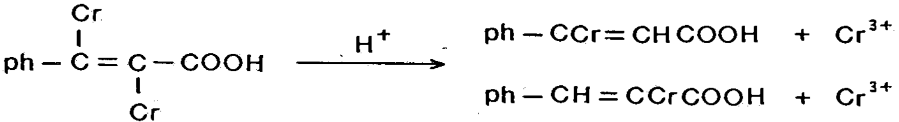


FIG. 2b: *$[Cr^{2+}]^2$-dependence of the first-order rate constants of the reaction between Cr^{2+} and phenylpropiolic acid in excess Cr^{2+} at 38^0C. [ppa]=$8.9x10^{-3}M$, [$HClO_4$]=1 M.*

The rate-determining step could again be the reaction of Cr^{2+} with a 1:1 intermediate which is formed on a preceding equilibrium. The concentration of the 1:1 complex which is in equilibrium with Cr^{2+} and the substrate, under the conditions of large chromium (II) excess is equal to the concentration of the substrate, whereas in the case of excess of substrate or chromium (II) [1:1 complex]=K[Cr^{2+}][substrate]

Acidolysis of the binuclear intermediates results in equimolar amounts of Cr^{3+} and the mononuclear σ-bonded organochromium $\overset{+}{p}yHCH_2CHCrCOOH^7$, $\overset{+}{p}yHCHCrCH_2py^3$ and the isomeric $phCH{=}CCrCOOH^{3+}$ and $phCCr{=}CHCOOH^{3+}$ 4,8 (eq.1).



$$\mathrm{ph}-\overset{\mathrm{Cr}}{\mathrm{C}}=\underset{\mathrm{Cr}}{\mathrm{C}}-\mathrm{COOH}\xrightarrow{H^+}\begin{array}{l}\mathrm{ph}-\mathrm{CCr}=\mathrm{CHCOOH}\ +\ \mathrm{Cr}^{3+}\\ \mathrm{ph}-\mathrm{CH}=\mathrm{CCrCOOH}\ +\ \mathrm{Cr}^{3+}\end{array}$$

(eq. 1)

Further kinetic studies at various temperatures are currently in progress.

We are pleased to acknowledge the University of Athens for financial support of this research and Prof. D.Katakis for helpful comments and suggestions.

* ***Kinetic experiments.*** The formation of the binuclear σ-bonded organochromium complexes was followed at 750 nm where chromium (II) is the only absorbing species (ε= 4.5 M^{-1} cm^{-1}). The rates were measured from the decrease in absorbance at this wavelength. The pseudo-first and pseudo-second order rate constants were measured at various conditions i.e. excess Cr^{2+} , excess ligand.

** The green binuclear highly charged species were isolated from the reaction mixture (Cr^{2+}-substrate in acidic $HClO_4$ solution) by ion - exchange chromatography. Elution of the band with $NaClO_4$ / $HClO_4$ results in equimolar amounts of violet (Cr^{3+}) and red (σ-bonded mononuclear organochromium) complexes. In the case of the reaction of **ppa** with Cr^{2+} the red band is analysed in two distinguished consecutive red bands of σ-bonded mononuclear organochromium complexes proved to be isomeric[4] All the experiments were carried under rigorously air-free conditions.

SUMMARY

The kinetics and mechanism of the reactions of chromium (II) with pyridine-3-acrylic acid, pyCH=CHCOOH, **paa** , 1,2-bis(2-pyridyl)ethylene, pyCH=CHpy, **bpe** and phenylpropiolic acid, phC≡CCOOH, **ppa** , have been studied in various conditions (large excess of chromium (II), large excess of ligand, excess of chromium (II) or ligand). The kinetic results and the acidolysis products suggest that binuclear species with chromium-carbon σ-bonds and carbon-carbon bridges (with single or double bonds) are discrete intermediates during these reactions. A first non-symmetric attack of a Cr^{2+} ion on the substrate leads to the formation of a 1:1 Cr(II):substrate adduct which on a rate-limiting step reacts further after an attack on the far carbon by a second Cr^{2+} ion to form a 2:1 adduct. This by two-electron transfer from both Cr(II) becomes a discrete binuclear σ-bonded organochromium complex with carbon-carbon single or double bond bridge. Acidolysis of the binuclear intermediates leads to the formation of the mononuclear σ-bonded organochromium complexes $\overset{+}{\mathrm{py}}\mathrm{HCH_2CHCrCOOH}$, $\overset{+}{\mathrm{py}}\mathrm{HCHCrCH_2py}$, and the isomeric phCH=CCrCOOH and phCCr=CHCOOH.

Key words: σ-bonded binuclear complex , organochromium complex, binuclear with carbon-carbon bridge, non-symmetric metal:ligand adduct.

ΠΕΡΙΛΗΨΗ

Μηχανισμός του πρώτου σταδίου της αντίδρασης μεταξύ χρωμίου(II) και μερικών ακορέστων υποκαταστατών. Σχηματισμός διπυρηνικών οργανοχρωμικών ενδιαμέσων με σ-δεσμούς Cr-C και γέφυρες άνθρακα-άνθρακα

Η κινητική και ο μηχανισμός των αντιδράσεων μεταξύ χρωμίου (II) και πυριδυλ-3-ακρυλικού οξέος, pyCH=CHCOOH, paa , 1,2-δις(2-πυριδυλ)αιθυλενίου, pyCH=CHpy, **bpe** και φαινυλοπροπιολικού οξέος, phC≡CCOOH, **ppa** , έχει μελετηθεί σε διάφορες συνθήκες (μεγάλη περίσσεια χρωμίου(II), μεγάλη περίσσεια υποκαταστάτη, περίσσεια χρωμίου (II) ή υποκαταστάτη). Τα κινητικά αποτελέσματα και τα προιόντα όξινης υδρόλυσης υποστηρίζουν ότι διπυρηνικά σωματίδια με σ-δεσμούς χρωμίου-άνθρακα και γέφυρες άνθρακα-άνθρακα (με απλούς ή διπλούς δεσμούς) είναι διακεκριμένα ενδιάμεσα κατά την διάρκεια των αντιδράσεων αυτών. Μία πρώτη μή-συμμετρική προσβολή ενός ιόντος χρωμίου(II) στο υπόστρωμα οδηγεί στον σχηματισμό ενός 1:1 Cr(II):υποκαταστάτη προδρόμου συμπλόκου το οποίο σε ένα στάδιο καθοριστικό της ταχύτητας αντιδρά περαιτέρω μετά από προσβολή στον απομακρυσμένο άνθρακα από ένα δεύτερο ιόν χρώμιου (II) προς σχηματισμό ενός 2:1 προδρόμου συμπλόκου.

Αυτό με μεταφορά δύο ηλεκτρονίων από τα δύο ιόντα χρωμίου(II) μετατρέπεται σε ένα διακεκριμένο διπυρηνικό οργανοχρωμικό σύμπλοκο με σ-δεσμούς Cr-C και με γέφυρα άνθρακα-άνθρακα με απλό ή διπλό δεσμό. Οξινη υδρόλυση των διπυρηνικών ενδιαμέσων οδηγεί στον σχηματισμό των μονοπυρηνικών οργανοχρωμικών συμπλόκων με σ-δεσμό Cr-C $\overset{+}{\mathrm{py}}\mathrm{HCH_2CHCrCOOH}$, $\overset{+}{\mathrm{py}}\mathrm{HCHCrCH_2py}$, και των ισομερών phCH=CCrCOOH και phCCr=CHCOOH.

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