



Treball Final de Grau

Compounds with unusual halogen, boron, and silicon groups as entry point to new reactivity patterns.

Compostos d'halògens, bor i silici com a punt de partida cap a nous tipus de reactivitat.

Tuo Chen

March 2021



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Do you believe in first love, or should I pass by again?

Stephen Hawking

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REPORT

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1. SUMMARY

The chemistry of hypervalent iodine has grown rapidly in the last two decades, with iodine(III) and iodine(V) compounds becoming common reagents in a wide range of synthetic applications. Hypervalent organoiodine species exhibits attractive reactivity features, like those of transition metals and for this reason these compounds are considered to be environmentally benign. In this project, two applications of iodine(III) chemistry were studied: transylidation of iodonium ylide, and synthesis of iodine triacetate derivatives.

Aryliodonium ylides are organoiodine(III) compounds that have been used in a wide range of synthetic applications such as carbene transfer, fluorination/radiofluorination of aromatic substrates, transylidation among others. In this project the main focus is on the transylidation between iodonium ylides and iodoarene under thermal and catalytical conditions, This reaction might provide an efficient approach to the preparation of potentially “delicate” iodonium ylide species.

The second part of the project was centered in the chemistry of iodine tricarboxylates, specifically the iodine triacetate. The general pathway to synthesize (diacetoxyiodo)arenes is via oxidation of the iodoarene precursor using oxidizing agents. Instead, iodine tricarboxylates offer transmetallation as an alternative pathway avoiding the oxidation of sensitive iodoarene precursors, broadening the scope of (diacetoxyiodo)arenes. Nevertheless, iodine tricarboxylates are unstable in the atmosphere and they are light sensitive causing these compounds hard to be handled. Therefore, in this part, derivatives of iodine triacetate were prepared in order to stabilize this compound and at the same time, perform similar reactivity.

Keywords: hypervalent iodine, transylidation, iodonium ylides, iodine triacetate, organoiodine(III), (diacetoxyiodo)arenes, transmetallation.

2. RESUM

La química del iode hipervalent ha crescut ràpidament en les dues últimes dècades, amb els compostos de iode(III) i iode(V) convertint-se en reactius comuns en una àmplia varietat d'aplicacions sintètiques. Les espècies d'organoiodes hipervalents presenten característiques atractives de reactivitat, similars a les dels metalls de transició, i per aquest motiu, aquestes espècies són considerades com a benignes per al medi ambient. En aquest projecte s'han estudiat dues aplicacions de la química del iode(III): la transilidació d'ilur de iodoni i la síntesi de derivats de triacetat de iode.

Els ilurs d'ariliodoni són compostos d'organoiode(III) que s'han utilitzat en un ampli rang d'aplicacions sintètiques com ara la transferència de carbè, fluoració/radiofluoració de substrats aromàtics, transilidació entre d'altres. En aquest projecte l'enfocament principal es va centrar en la transilidació entre ilurs de iodoni i ariliodina en condicions tèrmiques i catalitzades. Aquesta reacció podria proporcionar un enfocament eficient per a la preparació d'especie d'ilur de iodoni potencialment "delicades".

La segona part del projecte es va centrar en la química dels tricarbòxilats de iode, concretament del triacetat de iode. La via general per sintetitzar diacetat d'ariliod(III) és mitjançant l'oxidació del precursor de iodoarè emprant agents oxidants. En canvi, els tricarbòxilats de iode ofereixen la transmetal·lació com a via alternativa evitant l'oxidació de precursors de iodoarè sensibles, ampliant l'abast dels diacetat d'ariliod(III). No obstant això, els tricarbòxilats de iode són compostos inestables a l'atmosfera i són sensibles a la llum, cosa que fa que aquests compostos siguin difícils de manejar. Per això, en aquesta segona part, es va preparar derivats del triacetat de iode per tal d'estabilitzar aquest composto i a la vegada, tenir reactivitat similar.

Paraules clau: iode hipervalent, transilidació, ilurs de iodoni, triacetat de iode, organoiod(III), diacetat d'ariliod(III), transmetal·lació.

3. INTRODUCTION

In organic chemistry, halo-arenes play an important role in a wide range of synthetic scenarios. In particular, this class of functionalized aromatic cores is used in the synthesis of bioactive molecules, mainly, as intermediates (aryl transfer agents), but also as possible bioactive target structures. Among this compound class, iodoarenes are generally most reactive, and are also the most prone to the formation of the so-called halogen bonding interactions. For the chemistry of iodoarenes, it is important to consider that iodine is among the heaviest naturally occurring non-metallic elements in the Periodic Table, and, with the exception of Astatine (At), is the heaviest and most “metallic” halogen. Hence, iodine is particularly prone to be present in a wide range of oxidation states of -I, +I, +III, +V, +VII.

Those iodine compounds with a higher oxidation state of iodine (+III, +V, +VII) are known as hypervalent iodine compounds. In recent years, this type of compounds has been widely studied because of its versatile and environmental benign characteristics, as well due to a series reactivity patterns reminiscent of those common in transition metal complexes.

Due to the relatively large size of iodine, the interatomic π -bonding common in the compounds of light p-block elements is not observed in iodine compounds. Instead, a linear, three-center-four-electron (3c-4e) bond (L–I–L) is formed by the overlap of the 5p orbital on iodine atom with σ -type orbitals on the two ligands L. This 3c-4e bond is commonly named as “hypervalent bond” and it explains the special structural features and reactivity pattern of polyvalent iodine compounds.^[1]

Hypervalent organo-iodine reagents can be trivalent or pentavalent. The pentavalent family includes the commonly used, Dess-Martin periodinane (DMP) as well as 2-iodoxybenzoic acid (IBX). However, in the context of this project, we have focused exclusively on the synthetic applications of organoiodine (III) compounds, and so the following discussion will be limited to this compound family.

3.1. ORGANOIODINE(III) COMPOUNDS

The iodine(III) compounds, most of which belong to the λ^3 -iodane family according to the IUPAC nomenclature, can be classified according to the type of ligands attached to the iodine atom. It can be classified in five type of iodine(III) compounds: (1) iodosylarenes ArIO and their acyclic derivatives ArIX₂, (2) five-membered iodine heterocycles, benziodoxoles and benziodazoles, (3) iodonium salts R₂⁺X⁻, (4) iodonium ylides ArI=CR₂, and (5) iodonium imides ArI=NR (Figure 1).

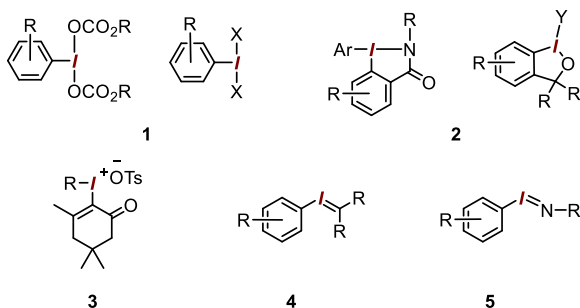


Figure 1. Main classes of Organoiodine(III) compounds.

The chemical properties and synthetic applications vary from class to class. Iodosylarenes are, in general, strong oxidizing agents, frequently employed for oxygenation and oxidative functionalization of organic substrates. The heterocyclic iodine and benziodoxoles compounds is characterized by their higher stability which makes possible the isolation and practical use of several otherwise unstable iodine(III) derivatives. The iodonium salts are characterized by the presence of two C-I bonds, typically involving aryl or other C(sp²)-based ligands, along with a third highly polarized bond. This compound family is mainly employed as electrophilic arylating agents, mainly due to the exceptional good leaving group ability of the accompanying ArI-fragment. The iodonium ylides and imides are excellent carbene and nitrene precursors, respectively.^[2]

3.1.1. Structure

As mentioned earlier, the special structural features and reactivity patterns of iodine(III) compounds are often interpreted through the nature of the 3c-4e bond present in such compounds.

Another classification of organoiodine(III) compounds is according to the structure of such compounds. They can be classified as type ArIL_2 (**1**) or Ar_2IL (**2**), with Ar being an aryl moiety and L a ligand containing a heteroatom (O, N, halogen). Just to mention, recent computational studies shows an alternative structures of iodine(III) reagents IL_3 (**3**),^[3] with three heteroatom-containing ligands on the iodine center (Figure 2), despite the fact that it is not considered to be organoiodine(III) compounds, this structure will be discussed in more details in the Section 3.2.

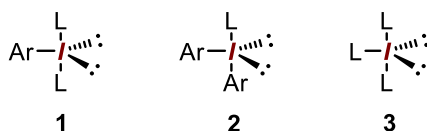


Figure 2. Types of iodine(III) structures.

The organoiodine(III) compounds have 10 electrons at the iodine atom. The overlap of the 5p orbital from iodine with the appropriate σ -type orbitals on the two ligands trans to each other leads to three new molecular orbitals (MO): bonding, non-bonding, and anti-bonding (Figure 3a). The node in the non-bonding orbital (HOMO) gives the polarized effect to the hypervalent bond, with a positive charge at the central atom and negative charges at the ligands. As consequence, the overall distorted trigonal bipyramid geometry and a T-Shaped structure is observed, with the ligands L occupying the apical position and the less electronegative carbon substituent Ar or R, along with the two lone electron pairs occupying the equatorial position (Figure 3b).^[4] The resulting hypervalent systems is highly polarized, with the I-L longer and weaker in comparison with the usual covalent bond. These features help to explain the high electrophilic reactivity of the hypervalent iodine compounds.

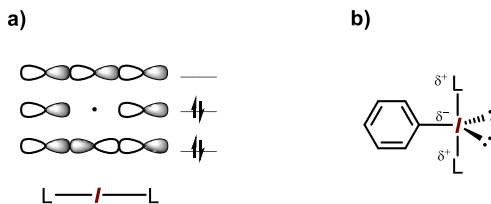


Figure 3. a) Orbitals in the hypervalent bond.
b) Geometry of iodosylarenes.

On the other hand, the of iodonium salts, ylides and imines is different from the organoiodine(III) compounds. Despite the fact that ylides and imines are represented with double bond as shown in the Figure 1, the nature of such compounds is believed to be zwitterionic, with a positive charge residing on the iodine(III) center attached to an anionic site normally stabilized by an attached electron withdrawing group (EWG). In the Figure 4 can observe a more in detail structure of iodonium ylides, specifically the Meldrum's acid as the anionic part, and its resonance forms.

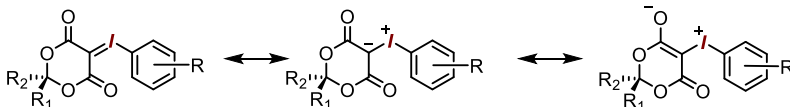


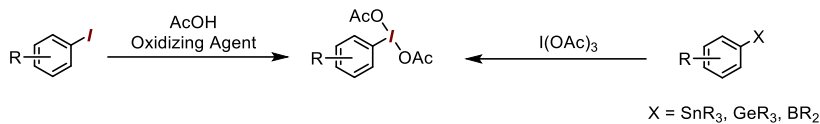
Figure 4. Iodonium ylides derived from cyclic 1,3-dicarbonyl compounds.

3.1.2. Preparation of iodine(III) compounds

The earliest known hypervalent λ^3 organo-iodine compound (dichloroiodo)benzene, PhICl_2 , was the first prepared by bubbling chlorine gas through iodobenzene, with the product as appearing as a yellow solid precipitate. This procedure was reported by the German chemist Conrad Willgerodt in 1885.^[5] Years later, many other hypervalent iodine compounds were prepared, including the (diacetoxyiodo)benzene, which is currently one of the most versatile high-valent iodine compounds in synthesis.

Nowadays, two general routes are being used in order to prepare (diacetoxyiodo)arenes. The first route involves a formal oxidative addition of suitable ligands to the corresponding “non-hypervalent” organoiodine, such as iodobenzene (Scheme 1 left). Nevertheless, very recently, a new approach has been introduced, based on ligand exchange (i.e., transmetallation) between a suitably metalated arene nucleophile and a simple trivalent iodine reagent, such as iodine(III) triacetate or iodine(III) tris-trifluoroacetate (Scheme 1 right).^[6] Hence, recently, this approach has

allowed for in-situ generation of a wide range of $\text{ArI}(\text{OAc})_2$ and $\text{ArI}(\text{O}_2\text{CCF}_3)_2$ structures, and their direct conversion to arylodonium salts, iodonium ylides and imides.



Scheme 1. Pathways for the formation of (diacetoxyiodo)arenes.

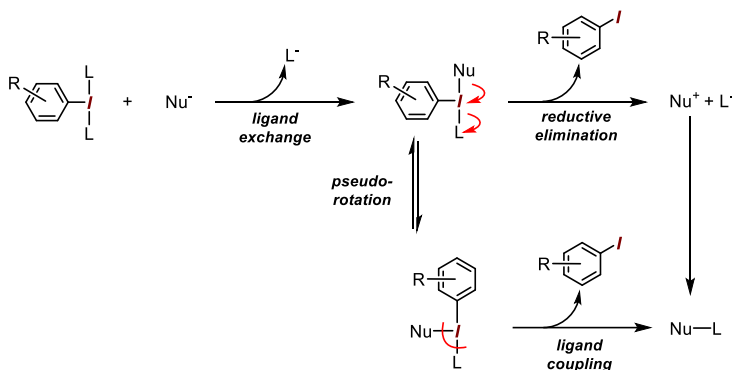
In the direct oxidative processes, typical conditions involve exposing the iodoarene precursor to acetic acid as the reagent and/or solvent, along with a suitable oxidizing agent, from among sodium perborate, sodium perborate or even Oxone (i.e., persulfate). The process frequently allows for good yields of (diacetoxyiodo)arenes. At the same time, for the more oxidatively sensitive iodoarene precursors, a milder oxidation method was also found that avoid the undesired oxidations of functional groups, which involves the utilization of Selectfluor. In contrast, the transmetallation pathway follows a different mechanism, and involves a formal electrophilic ipso-iodination of the C-M site using an “inorganic” iodine(III) reagent.

3.1.3. Reactivity

In most cases, the chemistry of hypervalent iodine compounds is based on both the strong electrophilic character of the iodine(III)- or iodine(V)- centers, and the excellent leaving group ability of the arylodonium group, making them susceptible to nucleophilic attack. They are mostly used as oxidizing species or as electrophilic reagents in organic chemistry. The oxidant character of these species is due to their tendency to undergo reduction “back” to their monovalent state, for example through a reductive elimination. At the same time, their electrophilic character is due to the highly polarized nature of the hypervalent bond, as it has been mentioned before.

The most common reactivity patterns for hypervalent iodine are ligand exchange, reductive elimination, and ligand coupling (Scheme 2). The reaction begins with the incorporation of an external nucleophile in the initial step of the ligand exchange, either through a dissociative pathway or through an associative pathway. Then, in the second step, the reaction can undergo a reductive elimination or ligand coupling. Reductive elimination involves a formal polarity inversion of the reactivity of the nucleophile, which can result in the formation of products of nucleophilic substitution, α -elimination, β -elimination, rearrangement, or fragmentation. Ligand coupling proceeds in a concerted reaction by orbital interaction, releasing the ArI fragment. This

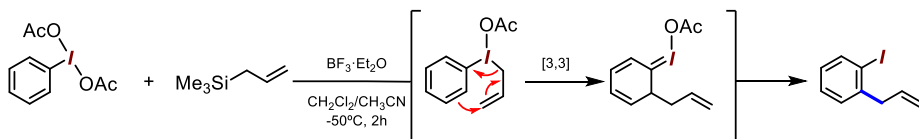
step is initiated after a pseudorotation in order to collocate the nucleophile and the ligand in the positions that favor the coupling.



Scheme 2. Reactivity pattern of organoiodine(III) compounds with nucleophiles (Nu).

Nevertheless, despite the fact that it is less common and less investigated, it is also important to mention that under an appropriate photochemical condition, hypervalent iodine can also undergo radical and homolytic reactions, as well as single-electron transfer (SET).^[7, 8]

One of the many applications of these compounds is the iodane-guided C-H coupling process, also known as iodono-Claisen. The first case of the use of hypervalent iodines as directing agents for selective C-H functionalization was reported in 1998.^[9] In that earlier work, it was observed the reaction between simple λ^3 -iodane, such as phenyliodine diacetate (PIDA) and allyltrimethylsilane in the presence of $BF_3 \cdot Et_2O$ led to the deduction of the possible intermediate λ^3 -(allynyl)(phenyl)iodonium, followed by the [3,3] sigmatropic rearrangement obtaining the ortho-propargly-iodoarene (Scheme 3).



Scheme 3. Ortho C-H allylation.

Another application of hypervalent iodine compounds, which will be discussed in more details in Section 3.3., is the so-called radio-fluorination reaction. This radiolabeling process is employed in the context of Positron Emission Tomography (PET) in vivo 3D imaging and is based on the introduction of the $[^{18}F]$ -isotope, where iodonium ylides and salts may act as convenient precursors. The spirocyclic iodonium ylides are considered as arene radiofluorination precursors

for hindered and non-activated substrates presenting several advantages over diaryliodonium salts, foremost being the lack of counterion and an auxiliary arene (Figure 5).^[10]

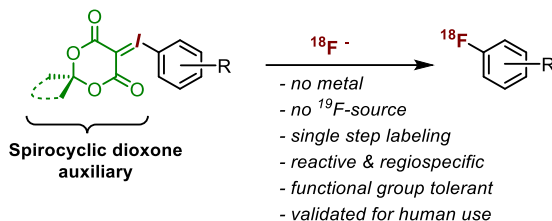


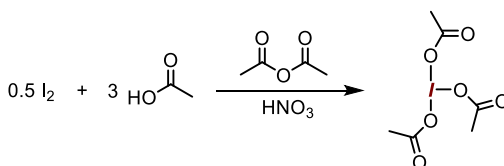
Figure 5. Iodonium mediated arene radiofluorination.

3.2. IODINE TRIACETATE, $\text{I}(\text{OAc})_3$

The broad application of (diacetoxyiodo)arenes, either in the study of novel reaction mechanisms or synthesis of natural products, gained a great focus in the field of organic chemistry. Hence, the preparation of such compounds has also been studied widely in the recent years.

As shown in the Scheme 1, (diacetoxyiodo)arenes can be prepared by two different pathways, either via the oxidative addition or through the ligand exchange between nucleophiles and electrophiles. In this section will be focused on the ligand exchange pathway since it is a recent developed synthetic method, which can avoid the direct exposure of iodoarene to an oxidizing agent and thus, avoid the undesired oxidations of sensitive iodoarene precursors.

Iodine triacetate is an iodine(III) carboxylate compound that presents a type IL_3 structure, and is served as hypervalent iodine delivery agent. Through the use of this species, the introduction of the hypervalent iodine could be performed either via electrophilic $\text{S}_{\text{E}}\text{Ar}$ iodination of activated arenes or, preferably, via electrophilic substitution on the corresponding metalated arene precursor. Iodine tris-carboxylates can be synthesized by the oxidation of iodine with fuming nitric acid under the appropriate carboxylic acid and the corresponding carboxylic acid anhydride. In this project, the focus will be on iodine triacetate (Scheme 4).^[11]



Scheme 4. Synthesis of Iodine Triacetate.

Despite the instability of this compound under the light or air, iodine triacetate can be used in subsequent reactions in a one-pot synthesis without further purifications. It should be noted, however, that identifying an iodine triacetate surrogate that would be more stable, and thus easy to handle remains an interesting challenge.

The behavior towards Lewis acid and bases of iodine triacetate was recently investigated by Wirth, et al. [11] A reaction between iodine triacetate and pyridine has taken place, the product was isolated and its structure of the was analyzed via X-Ray. The results showed that a chelating effect was observed, where the oxygen of one of the acetate groups was attached to the iodine center (Figure 6, left). On the other hand, the addition of the frustrated Lewis pair (FLP) $B(C_6F_5)_3/2,6$ -lutidine led to further activation of iodine triacetate to afford a new iodine(III) structure (Figure 6, right). The FLP abstracts one acetate group forming $[(C_6F_5)_3BOAc]^-$ anion and $[I(OAc)_2]^+$ cation which is stabilized by two lutidine Lewis bases in the axial position.

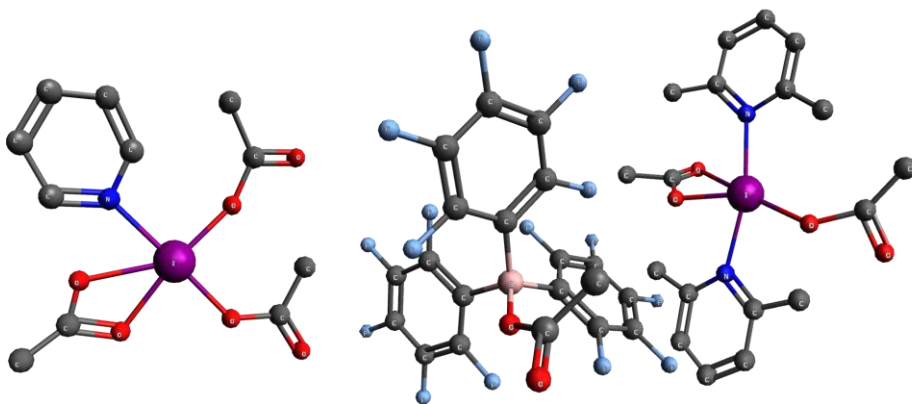


Figure 6. Structures of iodine(III) triacetate with pyridine (left) and with FLP/2,6-lutidine (right). Hydrogen atoms are omitted for clarity.

The iodine center of these iodine(III) triacetate derivatives is more saturated, so theoretically the reactivity is lower due to the fact that the interaction between iodine and substrates is being hindered, and thus, these derivatives would be more stable. However, one of the objectives of this project is focused on the stability optimization of this compound.

3.3. APPLICATION OF IODONIUM YLIDES ArI^+-CX_2

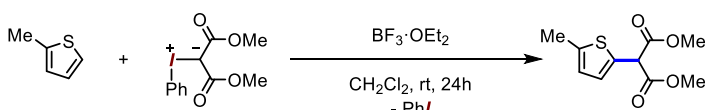
Iodonium ylides, ArI^+-CX_2 , where X is an EWG (e.g., carbonyl or sulfonyl group), represent an important class of iodonium compounds with a broad application in organic synthesis. These compounds are widely used as carbene precursors, useful as reagents for cyclopropanation of alkenes and preparation of heterocyclic compounds. They have also been used as efficient reagents in the thio-trifluoromethylation and nucleophilic fluorination reactions, which find practical applications in PET. Another recently found application, and one of the aims of this project is the transylidation under thermal and catalytic reactions. [12]

3.3.1. Reactions of iodonium ylides as carbene precursors

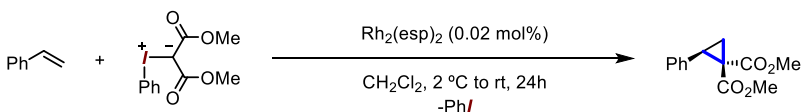
Iodonium ylides can serve as efficient precursors to the corresponding reactive carbene fragment under thermal, photochemical, or catalytic conditions. These reactions have already been studied in earlier reviews. [13, 14]

One of the most common iodonium ylide, bis(methoxycarbonyl)(phenyliodonio)methanide, derived from malonate methyl ester, has found synthetic applications in C-H insertion reactions, and in the cyclopropanation of alkenes, including enantioselective cyclopropanations in the presence of chiral rhodium complexes.

a)



b)



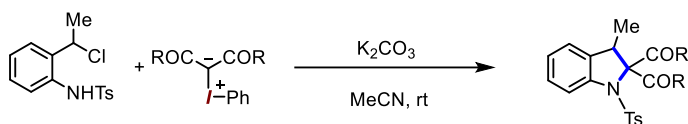
$\text{Rh}_2(\text{esp})_2$ = bis[rhodium($\alpha,\alpha,\alpha',\alpha'$ -tetramethyl-1,3-benzendipropionic acid)]

Scheme 5. Reactions of iodonium ylide as carbene precursor.

In the Scheme 5, two representatives of these reactions are shown, where the first (Scheme 5a) is the bis(carbonyl)alkylation of 2-alkylthiophenes through a BF_3 -catalyzed reaction, and the second (Scheme 5b) depicting for rhodium-catalyzed cyclopropanation of styrene.

3.3.2. Cycloaddition reactions of iodonium ylides leading to heterocycles

Iodonium ylides have been used in various heterocyclization reactions, both under transition metal free conditions and in the presence of metal catalyst. Liang, Li and co-workers have developed and reported a metal-free approach to synthesis of indolines from N-(ortho-chloromethyl)aryl amides and iodonium ylides (Scheme 6).^[15]

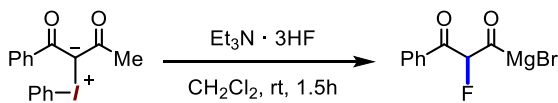


Scheme 6. Synthesis of indolines from N-(ortho-chloromethyl)aryl amides and iodonium ylides.

The mechanism of these reactions involves the initial conversion of N-(ortho-chloromethyl)aryl into the aza-o-quinodimethane intermediate under basic conditions, followed by Michael addition and N-alkylation with iodonium ylide to generate indoline by loss of iodobenzene.

3.3.3. Introduction of fluorine using iodonium ylides

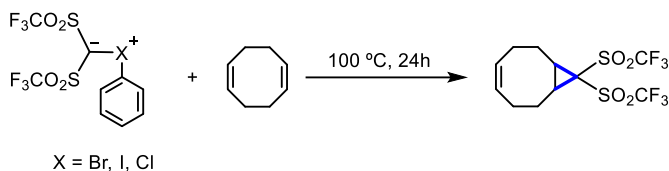
As it has been said earlier, iodonium ylides are excellent precursors for nucleophilic fluorinations in PET (Figure 5). Due to the carbanionic character of the ylidic carbon, the attack of an external nucleophile in principle should be directed exclusively towards the aromatic ring of the Ar group of an aryliodonium ylide. However, it had been showed that the reaction of various inorganic and organic acids with phenyliodonium ylides leads to nucleophilic substitution of the iodobenzene substituent by the anion. Gondo and Kitamura reported that the reaction of iodonium ylides derived from phenylbutan-1,3-dione, ethyl benzoylacetate, and ethyl p-nitrobenzoylacetate with $\text{Et}_3\text{N}\cdot 3\text{HF}$ gave the corresponding fluorinated products in low yields (Scheme 7).^[16] These products are formed through the C-protonation of the ylide, followed by displacement of the iodobenzene by the fluoride ion.



Scheme 7. Reactions of iodonium ylides with $\text{Et}_3\text{N}\cdot 3\text{HF}$.

3.3.4. Synthesis of stable aliphatic chloronium ylides

Ochiai and co-workers reported unambiguous experimental evidence for the intermolecular transylidations between halonium ylides under thermal and catalytic conditions, which makes it possible to synthesize a hitherto unknown kind of aliphatic chloronium ylides as well as a variety of bromonium and iodonium ylides. [17]



Scheme 8. Cyclopropanation of olefins with halonium ylides.

In the Scheme 8 shows the cyclopropanation of cyclooctadiene using bromonium, iodonium and chloronium ylides, respectively. The results indicate increased reactivity for the lighter-halogen derivatives, with no conversion observed for the iodonium ylide, a low yield for the bromonium ylide. In contrast, the chloronium ylide reacted smoothly to give the target cyclopropane synthetically meaningful 72% yield.

Thus, cyclopropanation of olefins with iodonium ylides requires use of a transition metal catalyst based on Rh or Cu to generate the reactive metalcarbene intermediates. But in general, thermal, and metal-catalyzed transylidations of halonium ylides provides a tool for synthesis of a variety of halonium ylides, including the aliphatic chloronium ylides which serve as a nice progenitor for generation of carbenes.

By inspiration of this report, another objective of this project is the transylation between iodonium ylides and iodoarene, which the obtained results will be discussed in the following sections.

4. OBJECTIVES

This project aims to contribute two areas of modern synthetic methodology, namely stability optimization of iodine trivalent reagents, and transylidations between iodonium ylide and iodoarenes. The main goals are:

1. Transylation between iodonium ylide and aryl iodide in both thermal and Rh(II)-catalyzed conditions. Firstly, the iodonium ylide was prepared using Meldrum's acid and (diacetoxyiodo)arene, and then it is reacted with an aryl iodide under thermal conditions and Rh(II)-catalyzed conditions (Figure 7).

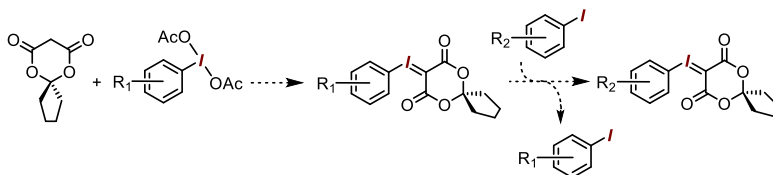


Figure 7. Synthesis of iodonium ylide and the transylation.

2. Stabilization of iodine triacetate by obtaining some iodine triacetate derivatives, but with the same reactivity. Despite the good electrophilic character of iodine triacetate this is an unstable compound under normal conditions or with the light exposure. For this reason, iodine triacetate was firstly prepared and then reacted with picolinic acid and with pyridine (Figure 8).

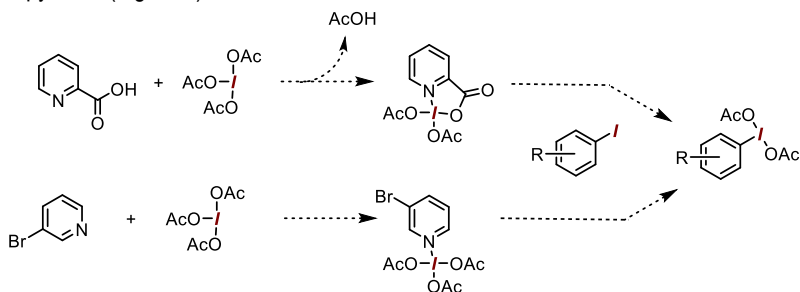


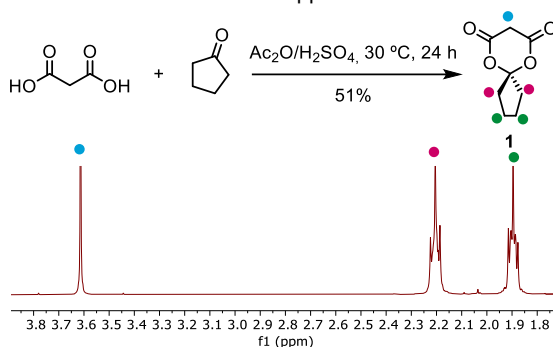
Figure 8. Stabilization of iodine triacetate and the synthesis of (diacetoxyiodo)arenes.

5. TRANSYLIDATION BETWEEN IODONIUM YLIDE AND IODOARENE

The applicability of iodonium ylides has already been seen in the section 3.3. Based on these precedents, and also in light of the study by Moriarty and co-workers on ylide transfer reactions, in this project we focused on the transylation between iodonium ylide and iodoarenes. We envisage that this reaction might provide an efficient approach to the preparation of potentially “delicate” iodonium ylide species. This approach would be complementary to the existing harsh oxidation routes and could contribute to a more facile generation of new radio-tracers for 18F-based radiotracers in Positron-Emission Tomography (PET).

In this case, the model iodonium ylide was the 8-[[4-(trifluoromethyl)phenyl]- λ^3 -iodaneylidene]-6,10-dioxaspiro[4,5]decane-7,9-dione (**3**), which incidentally had not been reported previously. For this purpose, the compound **3** was synthesized using the spirocyclic Meldrum's acid derivative (**1**) and *p*-(diacetoxyiodo)benzotrifluoride (**2**).

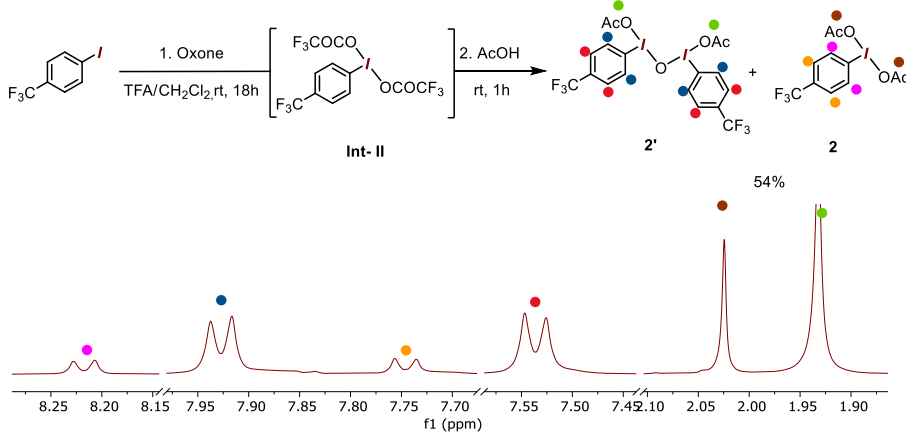
The cyclic diester **1** was prepared by condensation between the malonic acid and the cyclopentanone under acidic conditions.^[18] Purification by flash chromatography afforded **1** with 51% yield (Scheme 9). The ¹H NMR analysis in CDCl₃ showed a set of two CH₂ multiplet resonances at 2.20 ppm and 1.90 ppm, corresponding to the five-membered ring and a singlet at 3.61 ppm corresponding to the intercarbonylic CH₂ position. This result assures that **1** was successfully prepared and can be used for further applications.



Scheme 9. Synthesis and ¹H NMR of **1**.

The second step was the preparation of the suitable hypervalent iodine precursor **2** by the oxidation of *p*-iodobenzotrifluoride with Oxone (KHSO₅·0.5KHSO₄·0.5K₂SO₄) in trifluoroacetic acid (TFA). At this point, the obtained product was the trifluoroacetate **Int-II**, which then needs to be

converted to diacetoxy- form by adding acetic acid and water. This step induces the precipitation to give the product with an overall yield of 54%.^[19] Interestingly, the observed ¹H NMR in CDCl₃ showed the major product to correspond to the dimer μ-oxa-bis[(acetoxyiodo)-4-trifluoromethylbenzene] (**2'**), with **2** is the minor product (Scheme 10).

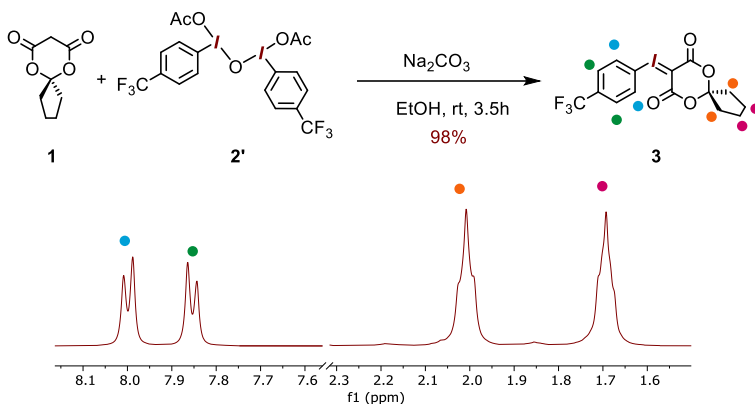


Scheme 10. Synthesis and ¹H NMR of **2**.

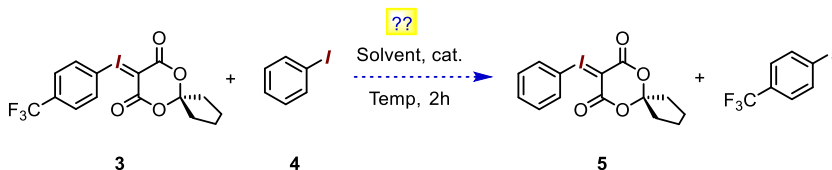
Specifically, the spectra contain to have two set of peaks in the aromatic zone and two peaks corresponding to the CH₃ from the acetate group. This indicates the presence of two products and either of peaks correspond with the starting reagent. The more intense peak at 1.93 ppm integrates 3 acetate protons instead of 6 as it should with (diacetoxyiodo)arene compounds, which is the reason that led to the conclusion of the formation of the bridge compound **2'**.

This compound was also reported by Haskali and co-workers^[19] who concludes that this specific (diacetoxyiodo)arene tends to exist in the dimeric μ-oxo form. Despite the nature of this compound, it doesn't affect the reactivity and can be used like the monomeric **2** taking account that the molecular mass would be bigger ($M = 678.10 \text{ g mol}^{-1}$).

The next step was the preparation of the iodonium ylide **3** by the addition of ethanol and **2** to a solution of **1** in 10% Na₂CO₃ (Scheme 11).^[20] The reaction took place properly giving a good yield of 98% and the ¹H NMR in DMSO-d₆ showed the expected set of peaks at 8.00 and 7.85 ppm corresponding to the aromatic protons with an integration of 1:1, as well as a set of peaks at 2.00 and 1.70 ppm for the CH₂ groups of the five-membered ring. Also, the disappearance of the peak corresponding to the intercarbonylic CH₂ position is another evidence that the structure of the obtained ylide is as it is shown.

Scheme 11. Synthesis and ^1H NMR of **3**.

With the prepared compound **3**, the first objective of this project can be developed. The basic idea was already explained in the section 4, and so, the proposed transylation process was attempted with the conditions as shown in the Table 1.



| Entry ^(a) | Equiv 4 | Temp [°C] | Solvent | Catalyst ^(b) |
|----------------------|---------|-----------|-----------------------------------|------------------------------------|
| 1 | 1 | rt | DMSO- d_6 | - |
| 2 | 1 | rt | Acetone- d_6 | - |
| 3 | 1 | rt | Benzene- d_6 | - |
| 4 | 1 | rt | DMSO- d_6 / HFIP ^(c) | - |
| 5 | 1.2 | rt | DMSO- d_6 / HFIP ^(c) | - |
| 6 | 1 | 40 | DMSO- d_6 | Rh ₂ (OAc) ₂ |
| 7 | 1 | 40 | Acetone- d_6 | Rh ₂ (OAc) ₂ |
| 8 | 1 | 40 | Benzene- d_6 | Rh ₂ (OAc) ₂ |
| 9 | 1 | 40 | DMSO- d_6 | Rh ₂ (esp) ₂ |

(a) Using 0.025 mmol of **3** in 0.6 mL of solvent.

(b) 1-2% mmol.

(c) 0.1 mL of HFIP

Table 1. Transylation reaction and reaction conditions.

Several reaction conditions were set to study the possibility of the transylation, with entries 1-5 under thermal conditions without using catalysts, at room temperature, and three different deuterated solvent were employed: DMSO- d_6 , acetone- d_6 and benzene- d_6 . The 1,1,1,3,3,3-

hexafluoro-2-propanol (HFIP) was also applied in the entries 4-5 since this compound can effectively provide (diacetoxyiodo)arenes.^[21] Regarding entries 6-8, the reactions were catalyzed using $\text{Rh}_2(\text{OAc})_2$, at 40 °C while the entry 9 the reaction was catalyzed using $\text{Rh}_2(\text{esp})_2$, under same conditions as 6-8. All reactions were performed at the same time and stirred for 2h, and directly prepared for ^1H NMR analysis.

For entries 1-3, a stability study was analyzed by comparing the ^1H NMR obtained right after the completion of the reaction with the ^1H NMR obtained 24 h after of each reaction (Figure 9). Only aromatic peaks are shown to identify the corresponding aromatic compound.

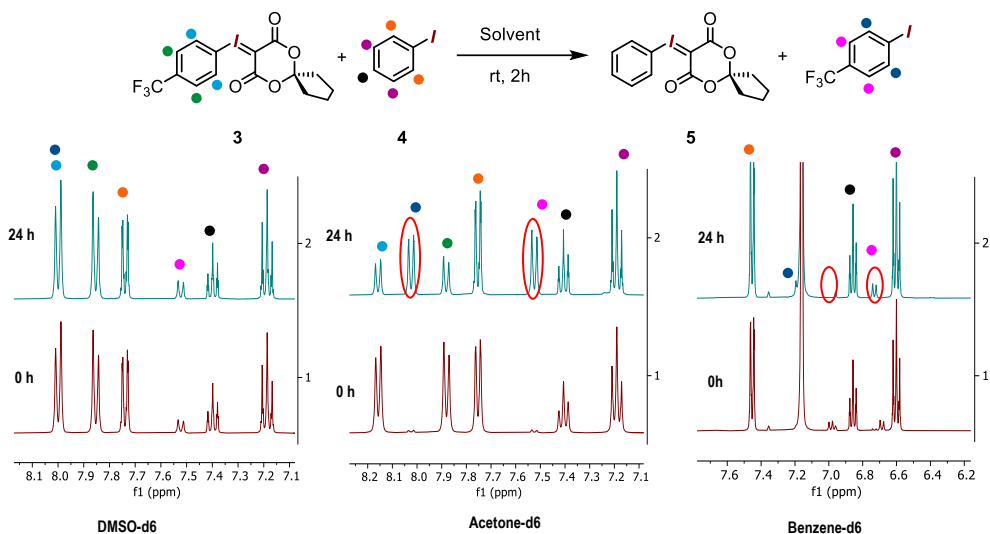
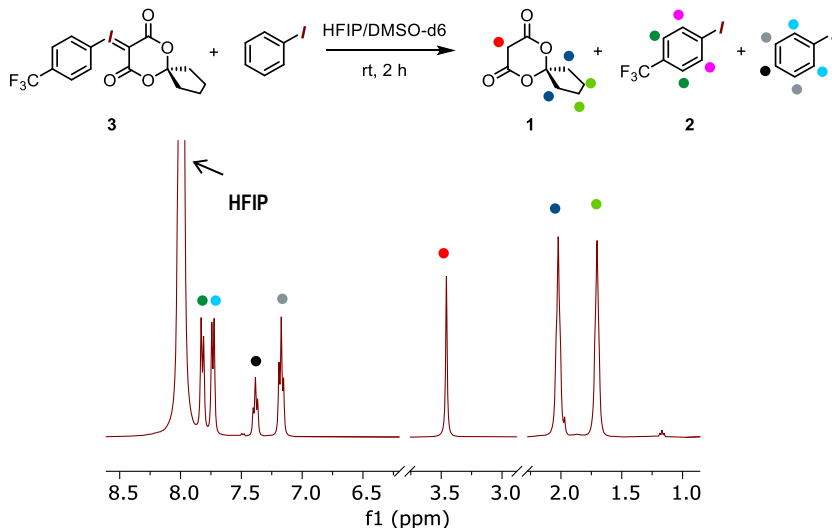


Figure 9. Comparison of ^1H NMR under thermal conditions between 0 h and 24 h in three different solvents.

As seen in the Figure 9, the reaction mixture remains stable in DMSO- d_6 , still displaying peaks for precursors 3, 4 and *p*-iodobenzotrifluoride, but no traces of possible 5. When the reaction was done in Acetone- d_6 , the ^1H NMR could see that after 2 h of reaction, the sample was only a mixture of reactants 3 and 4, but one day after, *p*-iodobenzotrifluoride was observed because of the appearance of its corresponding aromatic peaks. As conclusion, the reaction mixture in Acetone- d_6 goes through a decomposition of 3 and thus, the mixture was not stable in Acetone- d_6 . Due to the interference of benzene, the aromatic zone is not clear, and the identification of the compounds is not as complete as with in the other two solvents mainly identifying the 4. Nevertheless, the reaction mixture remains relatively stable since there is no big changes in the compared spectra.

When HFIP was added in the reaction mixture (entries 4-5), the observed results were the decomposition of the iodonium ylide **3** into the original spirocyclic Meldrum's acid derivative **1**, while iodobenzene **4** remained unreacted and no transylation process was observed (Scheme 12).



Scheme 12. Decomposition of **3** in HFIP/DMSO-d₆.

The decomposition of **3** was evidenced by the formation of a singlet at 3.46 ppm corresponding to the intercarbonylic CH₂ of the compound **1**.

As conclusion, the optimal solvent for further studies is DMSO, since the reaction mixture remains stable in this medium. The compound **5** could be observed under thermal conditions and thus, catalytic conditions were also attempted to study the possibility of transylation between iodonium ylide **3** and iodobenzene.

For entries 6-8, 1-2% of $\text{Rh}_2(\text{OAc})_2$ were used as catalyst, the temperature was brought to 40 °C during 2 h of reaction time. In the Figure 10 shows the comparison between the ^1H NMR obtained right after the reaction stopped (2 h) and the ^1H NMR obtained 24 h after, when the reaction mixtures remained in the solvent.

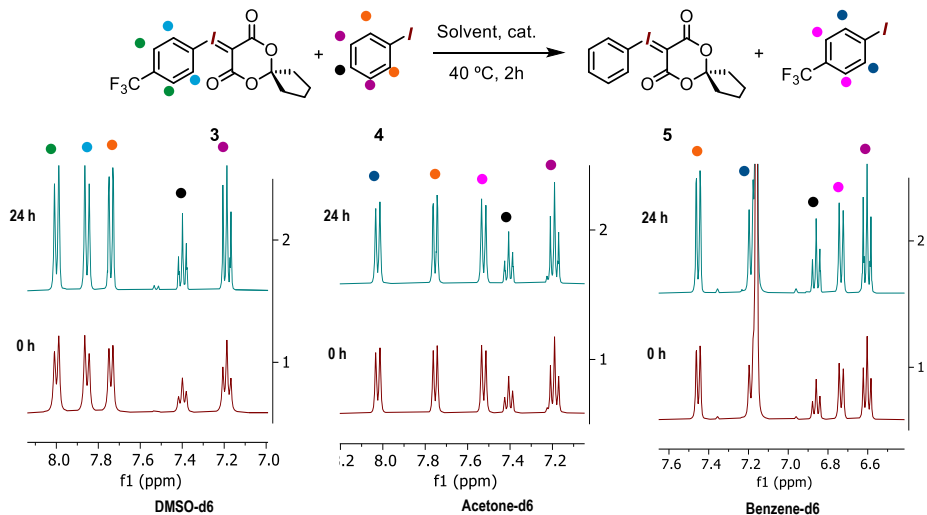


Figure 10. Comparison of ^1H NMR under catalytic conditions between 0 h and 24 h in different solvents.

In DMSO- d_6 (Entry 6), only compounds **3** and **4** were observed even 1 day of stirring, indicating a lack of reactivity. When Acetone- d_6 (Entry 7) was used as solvent, iodonium ylide **3** was completely converted into *p*-iodobenzotrifluoride right after 2 h of reaction, the mixture was stable even 1 day after and no further possible decomposition was observed. The same behaviors were observed when benzene- d_6 (Entry 8) was used as solvent for the reaction, and since in either of cases could observe any new aromatic peaks corresponding to the possible compound **5**, the reaction did not take place as it was expected.

Reviewing the spirocyclic part of the NMR in benzene- d_6 , the sets of CH_2 from the 5 membered ring lost their symmetry, as the mirror plane containing the 6 membered ring disappeared probably due to the introduction of iodine in the intercarbonylic position. Therefore, the CH_2 groups from the five membered ring appeared as four overlapped signals, and the proposed structure is as shown in the Figure 11. Another observation was the pink color in the NMR tubes, which probably corresponds to the release of I_2 , and thus, it can be thought that this compound is not stable.

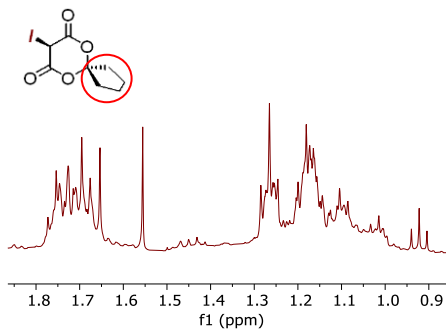


Figure 11. ¹H NMR of CH₂ peaks.

In the end, the last try was using another rhodium complex (Rh₂(esp)₂) (Entry 9) in DMSO, but the same results as entry 6 were obtained and no more attempts were done due to the limitation of the time. As conclusion, the transylidation proceeded unsuccessfully and this still require further investigation to achieve the purpose of this process, either in looking for the suitable solvent, a better reaction condition, or choose the proper catalyst.

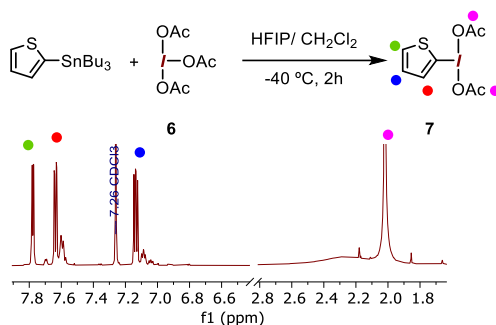
6. STABILITY STUDY OF IODINE TRIACETATE

Due to the electrophilic character of iodine triacetate, this compound is used mainly as precursor for synthesis of (diacetoxyiodo)arenes in a single step, as has been briefly discussed in the section 3.2. The problem comes with the stability of this reagent, given that it is extremely sensitive to both atmospheric conditions and light exposure, whereby the originally yellowish solid turns into orange with a possible release of elemental iodine.

Because of this reason and inspired by the work done by Wirth and co-workers [11], one of the main objectives of this project is the stabilization of iodine triacetate by searching for derivatives that could be stable in the normal conditions and light exposure, but still reactive as an electrophilic analogue of the parent triacetate.

Hence, the first step was to prepare the iodine triacetate following the reaction shown in the Scheme 4, where an oxidation process of ground iodine with fuming nitric acid under the appropriate carboxylic acid and the corresponding carboxylic acid anhydride was taken place, in this case, acetic acid and acetic acid anhydride. The obtained product showed as pale-yellow solid, which was conserved in the Schlenk tube, covered with aluminum foil, and kept in the fridge.

The initial challenge consists in the characterization of this product. Due to the instability of this compound, and the lack of nitrogen atmosphere glovebox in the group to prepare a NMR sample, the characterization by ^1H NMR could not be done. Instead, the newly prepared iodine triacetate was employed directly in the preparation of a (diacetoxyiodo)aryl. As a test system, the iodination of tributyl-2-thienylstannate was carried out. The reaction took place under argon atmosphere using Schlenk techniques in a low temperature ($-40\text{ }^\circ\text{C}$), affording the λ^3 -diacetate **7** in an 80% yield. The ^1H NMR analysis showed a set of aromatic peaks at 7.78, 7.64 and 7.13 ppm corresponding to thiophene group, and a single at 2 ppm corresponding to the acetate groups (Scheme 13).

Scheme 13. Synthesis and ^1H of **7**.

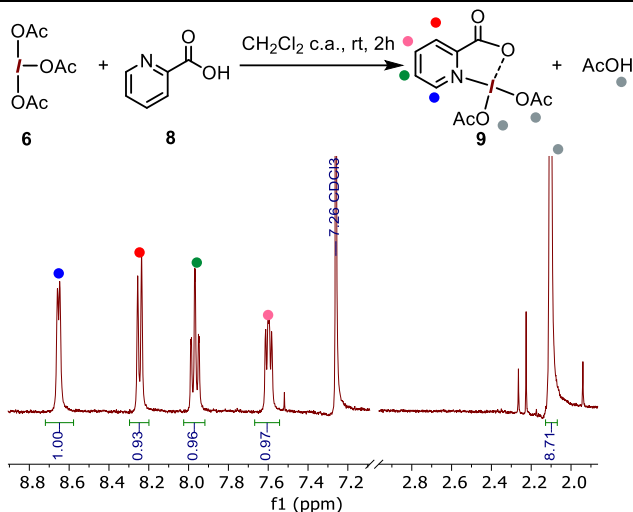
As it has been seen in the section 4, the stabilization of iodine triacetate will be studied in this section. In the article by Wirth and co-workers, the authors mentioned using Lewis acids and bases in order to investigate the behavior of iodine triacetate (**6**), and so to take a further study of this compound, in this project, picolinic acid (**8**) and 3-bromopyridine (**10**) were used as Lewis bases.

For this purpose, picolinic acid (**8**) was used as Lewis base to prepare the compound **9**. To ensure the feasibility of this proposed mechanism, computational methods were applied to study the thermodynamics of the conversion from **Int-IX** to **9**. For this reason, the energy of each molecule (**Int-IX**, **9** and **AcOH**) was calculated separately by Gaussian (Appendix 2). The obtained results are shown in the Table 2.

| | Int-IX | 9 | AcOH |
|-----------------------------------------|---------------|-------------|---------------|
| Energy (PBE) | -1132.896 | -903.958 | -228.932 |
| Thermal Correction | 0.197 | 0.145 | 0.035 |
| Total (Hartree/mol) | -1132.698 | -903.814 | -228.897 |
| Total (Kcal/mol) | -710768.262 | -567143.229 | -143633.046 |
| ΔG (Kcal/mol) | | | -8.013 |

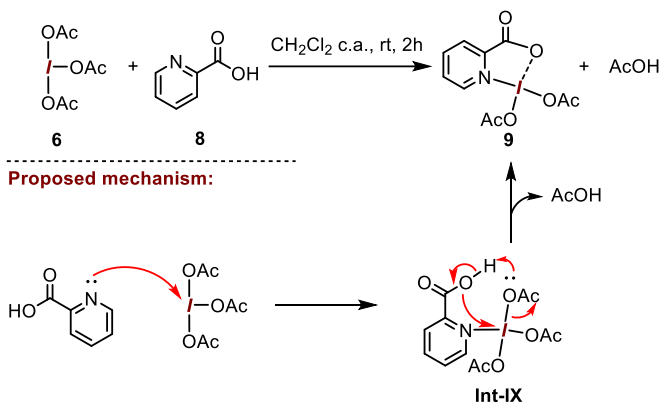
Table 2. Energy calculation of the proposed mechanism.

The energy of each molecule is obtained from the PBE functional, which by adding the thermal correction to Gibbs Free Energy value giving the total Gibbs Free Energy in units of Hartree/mol that later is converted into Kcal/mol. Hence, the total energy of reaction is -8.013 Kcal/mol and the formation of **9** is thermodynamically permissible. Experimentally, the reaction was carried out in a Schlenk tube, at room temperature for 2 h in anhydrous CH_2Cl_2 . The resulting pale-yellow solid was characterized by ^1H NMR (Scheme 14).

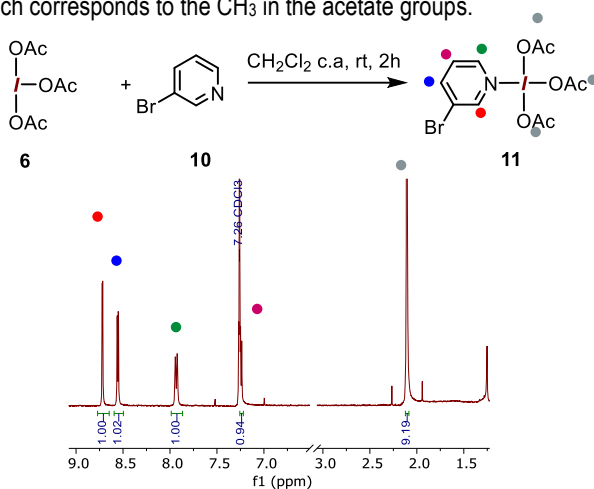
Scheme 14. Synthesis and ^1H NMR of **9**.

As can be seen in the ^1H NMR, the aromatic zone showed 4 sets of signals integrating 1:1:1:1 which correspond to the pyridine. In the acetate zone (2.00-2.20 ppm) integrates 9H instead of the expecting 6H, probably due to remaining acetic acid.

The proposed mechanism is as shown in the Scheme 15, where the lone electron pairs from nitrogen could attack the iodine triacetate giving place the possible intermediate **Int-IX**, and then the oxygen from the hydroxyl group act as a chelating agent forming the desired compound **9**, releasing one acetic acid.

Scheme 15. Mechanistic proposal for preparation of **9**.

As another experiment, 3-bromopyridine was used as Lewis base in order to saturate the iodine center of the iodine triacetate. The reaction condition was the same as in picolinic acid, CH_2Cl_2 anhydrous was used as solvent and the solution was stirred for 2 h at room temperature. The resulting yellow powder was analyzed via ^1H NMR (Scheme 16). Results appear to confirm the product **11**, with 4 sets of signals in the aromatic zone, integrating 1:1:1:1 and one singlet integrating 9 H, which corresponds to the CH_3 in the acetate groups.



Scheme 16. Synthesis and ^1H NMR of **11**.

Unfortunately, the limitation in time, the second step of this project could not be done despite the fact that the obtained results were promising, and the obtained products were relatively more stable than the initial iodine triacetate.

7. EXPERIMENTAL SECTION

7.1. MATERIALS AND METHODS

Reagents. All commercially acquired reagents were used as received.

Reaction conditions. Reactions requiring inert atmosphere were conducted under argon using standard Schlenk line techniques. The flask was heated in the oven at 110 °C for at least 30 min, cooled to room temperature under vacuum, and filled back with argon gas. The liquid additions were performed with needle using a rubber stopper. Reactions requiring low temperature conditions were performed using an acetone - dry ice bath.

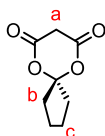
Chromatography. Thin layer chromatography (TLC) was performed using Merck aluminum-backed plates of TLC Silica gel 60 F254; the plates were revealed using UV light at 254 nm or by staining using potassium permanganate. Standard Flash Column chromatography was accomplished using silica gel (60 Å pore size, 230-400 μm mesh size).

Spectroscopy. NMR Spectra were recorded at the Servicio de Resonancia Magnética Nuclear of the IQAC-CSIC using a Bruker Avance NEO 400 MHz. Chemical shifts (δ_{H}) are quoted in parts per million (ppm) and referenced to the appropriate residual protio NMR solvent peak for ^1H and to the solvent peak for ^{13}C spectra.

7.2. STUDY IN NEW APPLICATIONS OF IODONIUM YLIDES

7.2.1. Preparation of 6,10-dioxaspiro[4,5]decane-7,9-dione (1)

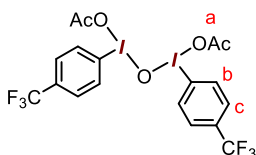
In a 25 mL round bottom flask, Ac₂O (2.20 mL) and H₂SO₄ (60 μL) was added to malonic acid (14.40 mmol, 1.50 g) and the temperature of the mixture was brought to 60 °C, with continued stirring until all the solid was completely dissolved. Cyclopentanone (14.40 mmol, 1.28 mL) was added dropwise with stirring for 1h, and the mixture was left overnight. At this point, water (20 mL) was added, the resulting solution was extracted with CH₂Cl₂ (3x10 mL), and the combined organic extracts were dried with anhydrous MgSO₄, followed by the filtration and solvent removal by rotatory evaporation. Dark green oil was observed, which was purified by column chromatography using the triple solvent eluent hexane/ EtOAc/ CHCl₃ (6:2:2). Orange crystalline material, 1.25 g, 51%.



¹H NMR (400 MHz, CDCl₃) δ 3.61 (s, 2H, Ha), 2.27 – 2.13 (m, 4H, Hb), 1.97 – 1.83 (m, 4H, Hc).

7.2.2. Preparation of μ-Oxa-bis[(acetoxyiodo)-4-trifluoromethylbenzene] (2)

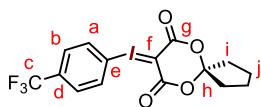
Oxone (KHSO₅·0.5KHSO₄·0.5K₂SO₄, 3.00 mmol, 1.85 g) was added into a stirring solution of 4-iodobenzotrifluoride (3.00 mmol, 0.816 g) in TFA (14 mL) and CH₂Cl₂ (6 mL), and the resulting mixture was stirred at room temperature for 18h. The solvent was removed by rotatory evaporation, followed by the addition of CH₂Cl₂ (10 mL) and extraction with water (3x50 mL). The combined organic extract was concentrated by rotatory evaporation. The AcOH (10 mL) was added in the obtained residual oil, and the mixture was stirred for an additional 1h. Water (100 mL) was added, giving a white precipitate that was filtered and washed successively with water (3x15 mL), Et₂O (3x15 mL) and hexane (3x10 mL), and then dried under vacuum. White solid powder, 580 mg, 54%.



¹H NMR (400 MHz, CDCl₃) δ 7.93 (d, *J* = 8.2 Hz, 2H, Hb), 7.54 (d, *J* = 8.3 Hz, 2H, Hc), 1.93 (s, 3H, Ha). ¹⁹F NMR (376 MHz, CDCl₃) δ -63.24.

7.2.3. Preparation of 8-[[[(4-trifluoromethyl)phenyl)- λ^3 -iodaneylidene]-6,10-dioxaspiro[4,5]-decne-7,9-dione (3)

EtOH (1 mL) was added to a solution of **1** (0.25 mmol, 43 mg) in 10% Na₂SO₄ (w/v, 0.75 mL, 0.33 M), followed by a quick addition of **2** (0.25 mmol, 170 mg). The mixture was stirred at room temperature for 3.5 h and water (8 mL) was added. The mixture was extracted with CH₂Cl₂ (3x10 mL) and the combined organic extracts were dried with anhydrous Na₂SO₄, filtered and concentrated by rotatory evaporation. EtOAc and hexane were used to wash the resulting solid. White solid powder, 110 mg, 98%.

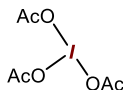


¹H NMR (400 MHz, DMSO-d₆) δ 8.00 (d, J = 8.1 Hz, 2H, Ha), 7.85 (d, J = 8.2 Hz, 2H, Hb), 2.01 (s, 4H, Hi), 1.69 (s, 4H, Hj). ¹⁹F NMR (376 MHz, DMSO-d₆) δ -61.47. ¹³C NMR (101 MHz, DMSO-d₆) δ 163.55 (Cg), 138.22 (Cd), 133.01 (Cc), 130.68 (Ca), 127.70 (Cb), 120.44 (Cc), 112.33 (Ce), 58.83 (Ch), 39.78 (Ci), 36.82 (Cj), 22.78 (Cf).

7.3. EXPLORING THE STABILITY OF IODINE TRIACETATE

7.3.1. Synthesis of iodine triacetate (6)

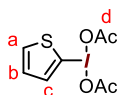
Grounded iodine (4.93 mmol, 1.25 g) was introduced into an oven dried Schlenk tube under argon atmosphere, followed by the addition of AcOH (1.75 mL) and Ac₂O (3.50 mL) with stirring. The mixture was cooled to -40 °C and fuming HNO₃ (1.35 mL) was added. Once the addition was completed, the flask was allowed to reach room temperature while stirring for 2h protected from light. All solvents were removed under vacuo using a Schlenk line equipped with a system of two traps cooled with dry ice/acetone to -78 °C. This operation leaves behind a pale-yellow solid powder. This solid was not characterized further due to its highly water- and light- sensitive nature coupled with a lack of a glovebox setup to prepare an NMR sample. The solid was used as is.



7.3.2. Synthesis of 2-(diacetoxiodo)thiophene (7)

A solution of HFIP (0.63 mL) in anhydrous CH₂Cl₂ (1.20 mL) was added into a solution of **6** (0.60 mmol, 182 mg) in anhydrous CH₂Cl₂ (2.40 mL) with stirring. The mixture was cooled to -40 °C, and the solution of 2-(tributylstannyl)thiophene (0.60 mmol, 224 mg) in anhydrous CH₂Cl₂ (2.40 mL) was added. The resulting mixture was stirred at this temperature for 2 h protected from

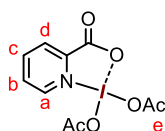
light and then, it was allowed to warm to room temperature. The solvent was removed under vacuo and washed with n-pentane. Yellow solid powder, 158 mg, 80%.



$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.78 (dd, $J = 3.8, 1.3$ Hz, 1H, Ha), 7.64 (dd, $J = 5.4, 1.2$ Hz, 1H, Hc), 7.14 (dd, $J = 5.4, 3.8$ Hz, 1H, Hb), 2.02 (s, 6H, Hd).

7.3.2. Synthesis of 3-oxo-1,3-dihydro-1 λ^4 ,8 λ^4 -[1,2,5]iodaoxazolo[5,4-a]pyridine-1,1-diyl diacetate (9)

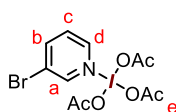
Iodine triacetate **6** (0.25 mmol, 76 mg) was added in an oven dried Schlenk tube and dissolved in anhydrous CH_2Cl_2 (0.5 mL). Then, picolinic acid **8** (0.25 mmol, 31 mg) was added and the mixture was stirred for 2 h at room temperature protected from light. The solvent was removed under vacuo using a Schlenk line and no further treatment was applied. Pale-yellow solid powder, 105.10 mg (Note: The obtained product contains acetic acid, which was not washed.)



$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.65 (d, $J = 4.8$ Hz, 1H, Ha), 8.25 (d, $J = 7.8$ Hz, 1H, Hd), 7.97 (td, $J = 7.7, 1.6$ Hz, 1H, Hc), 7.60 (dd, $J = 7.6, 4.9$ Hz, 1H, Hb), 2.10 (s, 9H, He).

7.3.3. Synthesis of (3-bromo-1 λ^4 -pyridin-1-yl)- λ^4 -iodanetriyl triacetate (11)

Iodine triacetate **6** (0.25 mmol, 76 mg) was added in an oven dried Schlenk tube and dissolved in anhydrous CH_2Cl_2 (0.5 mL). Then, picolinic acid **8** (0.25 mmol, 31 mg) was added and the mixture was stirred for 2 h at room temperature protected from light. The solvent was removed under vacuo using a Schlenk line and no further treatment was applied. Pale-yellow solid powder, 120.70 mg (Note: The obtained product contains acetic acid, which was not washed.)



$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.72 (dd, $J = 2.3, 0.7$ Hz, 1H, Ha), 8.56 (dd, $J = 5.0, 1.4$ Hz, 1H, Hd), 7.94 (dd, $J = 7.9, 2.0$ Hz, 1H, Hb), 7.24 (dd, $J = 4.9, 0.8$ Hz, 1H, Hc), 2.11 (s, 9H, He).

8. CONCLUSIONS

In this present work, an attempt at obtaining new iodonium ylides through the transylidation between an iodonium ylide and iodoarene was performed. Achieving the objective of this reaction would broaden the scope of iodonium ylides that could not reach via known methods, and therefore, the application of such compounds would also be broadened. Unfortunately, the reaction did not work as expected, in both thermal and catalytic conditions, and the desired iodonium ylide could not be observed. Nevertheless, it is believed that the reaction is feasible according to the thermodynamics of this reaction and hence, further tests should be performed in order to find a suitable reaction condition and achieve to its expectation.

On the other hand, the stabilization of iodine triacetate was also performed by saturating the iodine center using Lewis base. Despite the fact that these iodine triacetate derivatives were obtained, characterized successfully and relatively more stable than the original iodine triacetate, the reactivity of such compounds could not be studied due to the time limitation. However, it is believed that these derivatives should perform a similar reactivity since they are also electrophiles for S_EAr .

In conclusion, the field of hypervalent iodine compounds have emerged as novel, versatile and environmentally benign reagents, which gained importance increasingly in modern organic synthesis. Thus, the applications of such compounds need more time and effort to investigate and obtain more promising results.

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10. ACRONYMS

Ac: acetate

cat.: catalyst

d: doublet

δ_{H} : chemical shifts

DFT: density functional theory

DMP: Dess-Martin Periodinane

DMSO: dimethyl sulfoxide

equiv: equivalent

EWG: electron-withdrawing group

FLP: frustrated Lewis pair

HFIP: 1,1,1,3,3,3-hexafluoro-2-propanol

HOMO: highest occupied molecular orbital

IBX: 2-iodoxybenzoic acid

Int: intermediate

L: ligand

m: multiplet

MHz: mega Hertz

MO: molecular orbital

NMR: nuclear magnetic resonance

Nu: nucleophile

p: para

PBE: Perdew–Burke–Ernzerhof functional

PET: positron emission tomography

PIDA: phenyliodine(III) diacetate

ppm: parts per million

rt: room temperature

$S_{\text{E}}\text{Ar}$: aromatic electrophilic substitution

SET: single-electron transfer

t: triplet

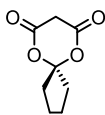
Temp: temperature

TFA: trifluoroacetic acid

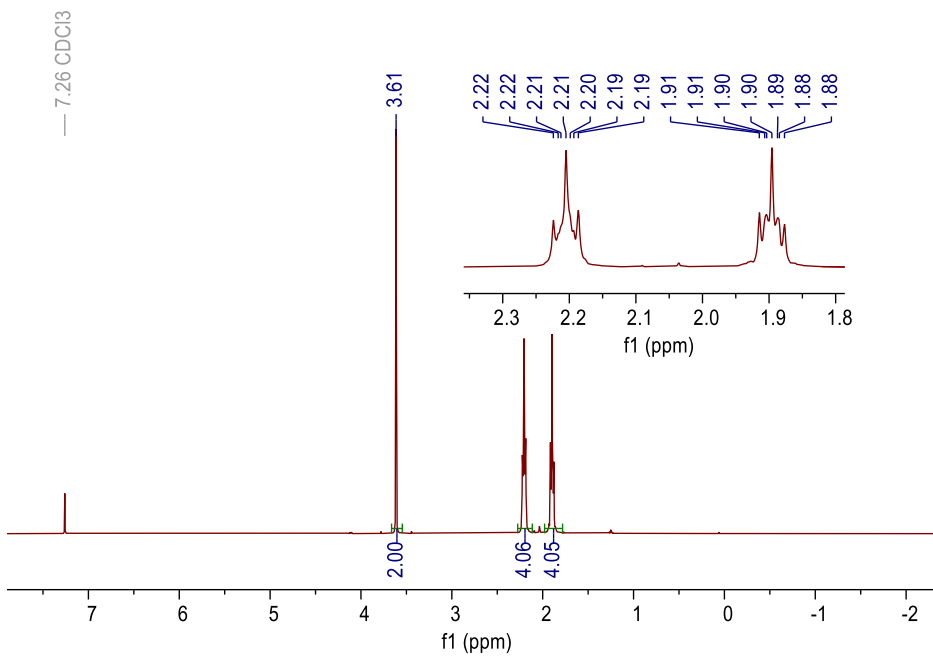
TLC: thin layer chromatography

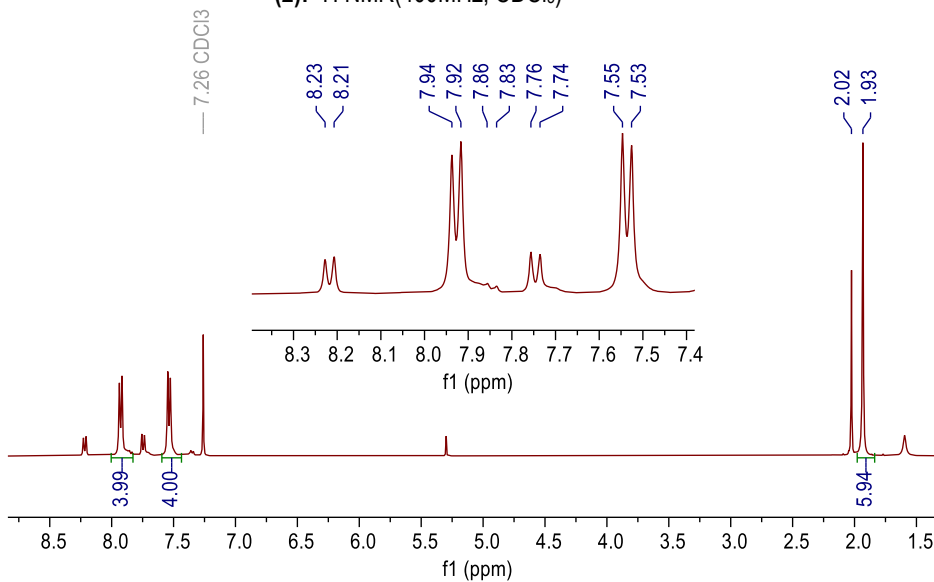
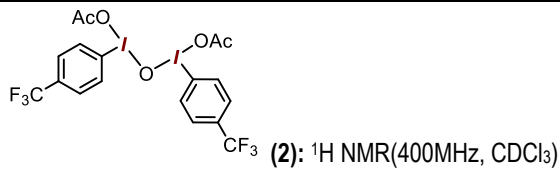
APPENDICES

APPENDIX 1: SPECTROSCOPIC DATA

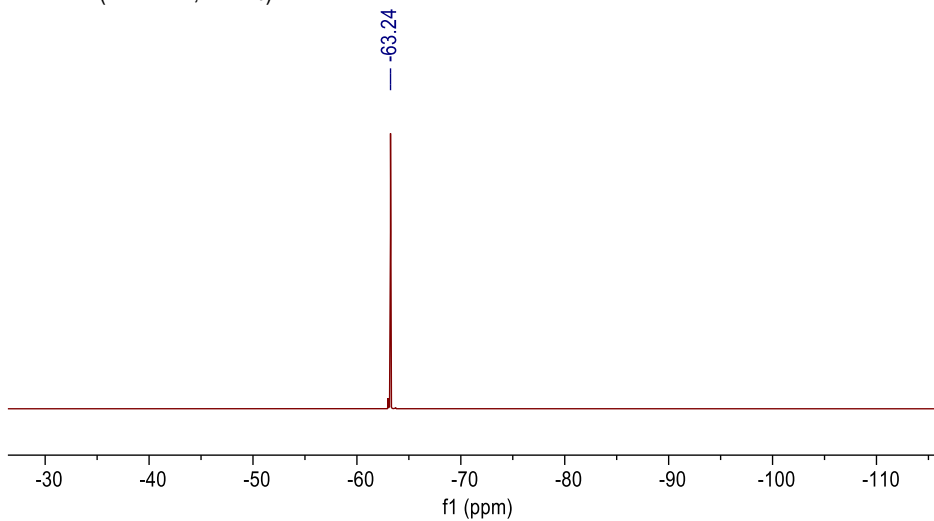


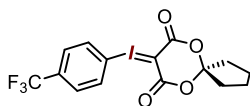
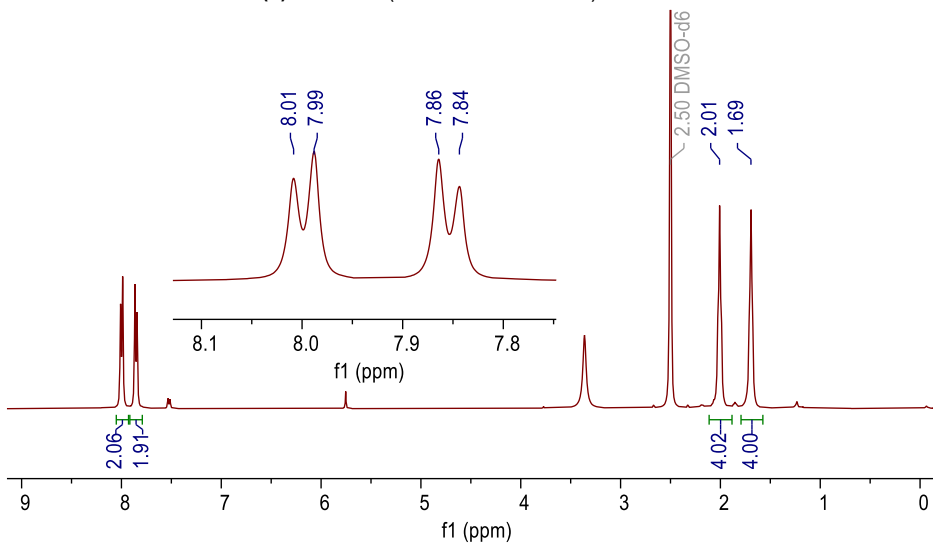
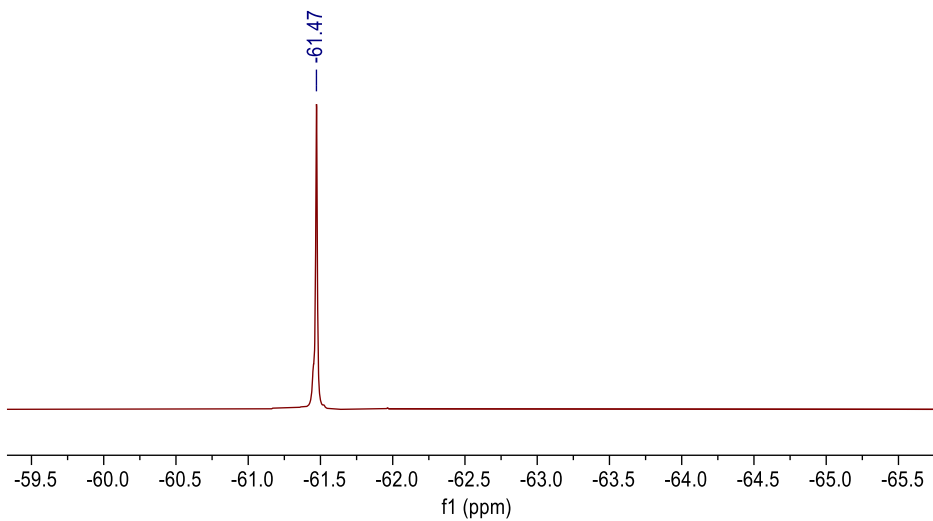
(1): ^1H NMR (400MHz, CDCl_3)

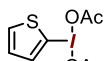
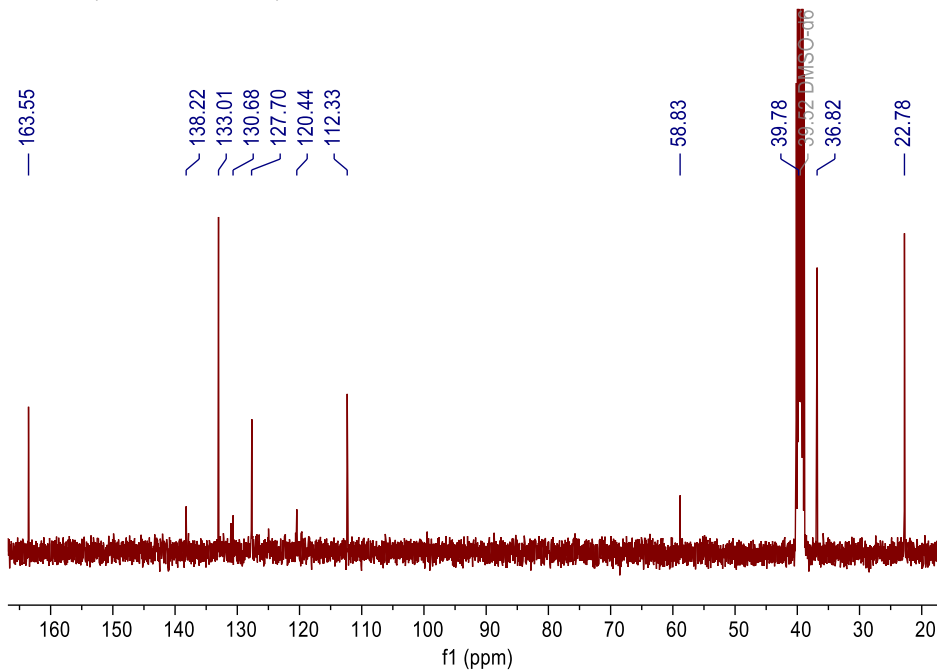
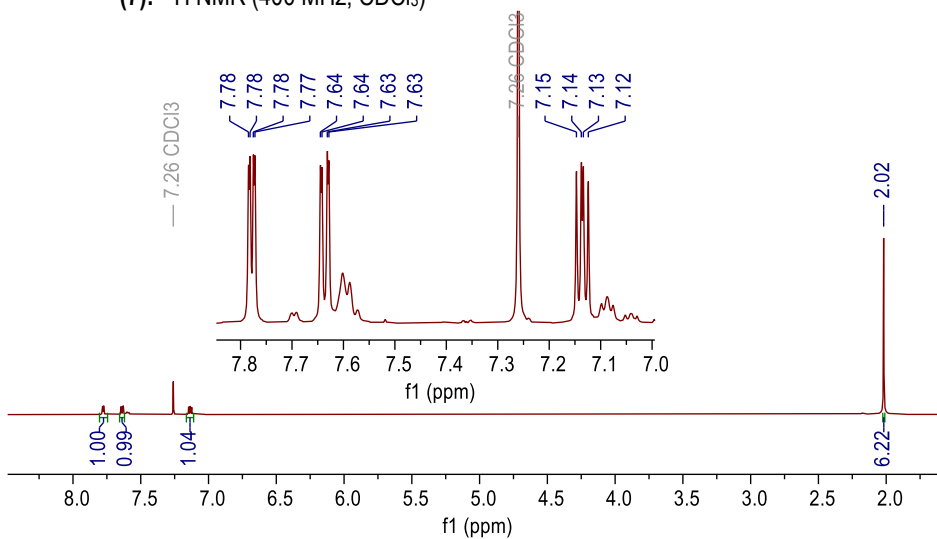


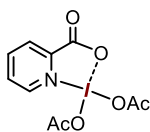
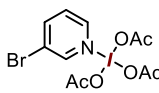
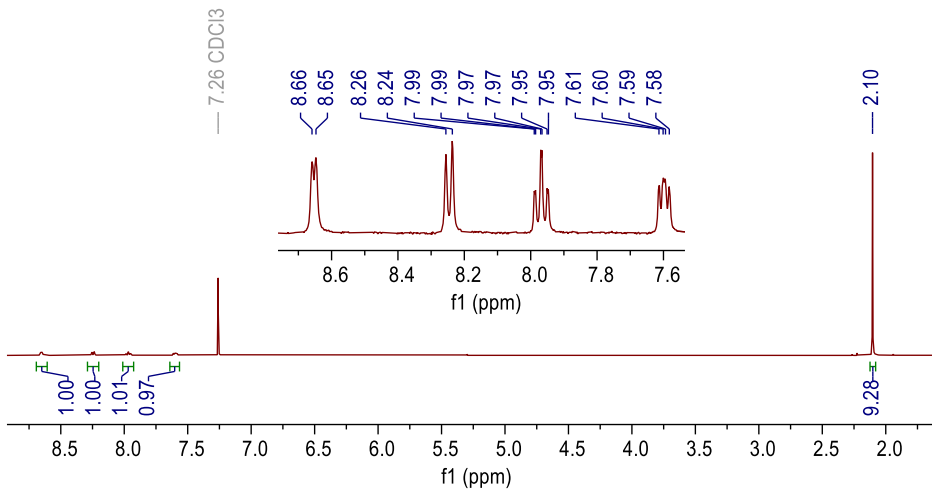
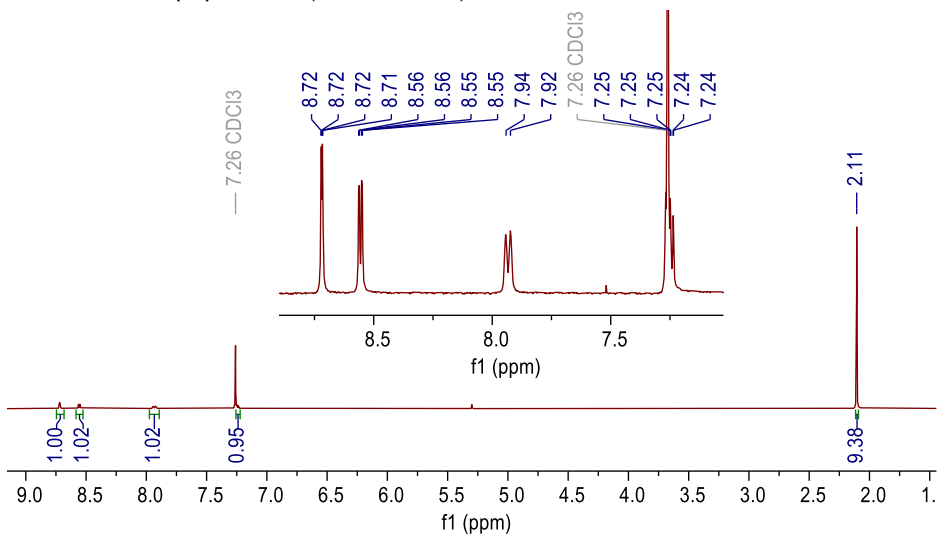


$^{19}\text{F NMR}$ (376 MHz, CDCl_3)



**(3):** ^1H NMR (400 MHz, DMSO- d_6) ^{19}F NMR (376 MHz, DMSO- d_6)

^{13}C NMR (101 MHz, DMSO- d_6)**(7)**: ^1H NMR (400 MHz, CDCl_3)

**(9):** ^1H NMR (400 MHz, CDCl_3)**(11):** ^1H NMR (400 MHz, CDCl_3)

APPENDIX 2: COMPUTATIONAL METHOD

All calculations were performed using Gaussian 09^{DFT-1} by adapting a method described by Vasdev, Liang and co-workers for a series of iodine(III)-containing species.^[10]

Geometry optimizations. All calculations were performed at the DFT level using the B3LYP functional with an ultrafine integration grid. The 6-31+G(d,p) basis set was used for C,H,O and N, while using for iodine the augmented LANL2DZ(dp) set described by Gilbert, Sunderlin and co-workers. Empirical dispersion was applied using the D3 version of Grimme dispersion with Becke-Johnson damping (gd3BJ keyword). All structures were fully optimized in acetonitrile using SMD continuum model. Transition states were identified by having one imaginary frequency in the Hessian matrix. It was confirmed that transition states connect with the corresponding intermediates by means of application of the eigenvector corresponding to the imaginary frequency and subsequent optimization of the resulting structures. All energies collected in the text are Gibbs energies in solvent at 298 K.

Single point energy calculations. Energy calculations were performed for the previously optimized structures using PBE0 functional and the Aug-cc-pvtz basis set for C,H,O and N atoms and the DB-aug-cc-Pvtz for iodine. Calculations were performed in acetonitrile (SMD continuum model) applying the D3 version of Grimme dispersion with Becke-Johnson damping (gb3BJ keyword).

DFT references

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