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Memory about final project

SYNTHESIS OF FLUORINATED α-METHYLSTYRENE DERIVATIVE WITH PHOSPHONATE FUNCTION, MICROWAVE-ASSISTED C-P BOND FORMATION CATALYZED BY PALLADIUM (II) SALTS

SÍNTESIS DEL DERIVADO FLUORADO DE α-METILESTIRENO CON FUNCIÓN FOSFONATO, FORMACIÓN DEL ENLACE C-P ASISTIDA POR MICROONDAS Y CATALIZADA POR SALES DE PALADIO (II)

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ABSTRACT

The current technology supports production of polymers with excellent mechanical, thermal, electroinsulating, or ion-conducting properties. Among them fluoropolymers are materials exhibiting a incredible combination of outstanding properties, such as high thermostability and chemical or electrochemical inertness, low dielectric constant and dissipation factor, low refractive index and friction coefficient, low water absorptivity, excellent surface characteristics and weather abilities. These high value products have therefore found applications in various fields of advanced technology, e.g. engineering, optics, chemical and automobile industries, microelectronics, textile finishing aeronautics or military. Even though there is a diverse range of fluroropolymer applications, due to their lack of solubility in common solvents they are difficult to process, while others show very high melting point or cannot be melted. However, specific properties of fluoropolymers can be brought by the presence of functional groups positioned laterally on the copolymer backbone such as adhesion, surface properties, solubility, curability, heat and chemical resistance or good hydrophilicity. In addition, the involvement of fluorinated or nonfluorinated monomers in co-or terpolymerization could lead to the production of fluoropolymers possessing peculiar properties.

Fluorinated aromatic polymers represent an interesting family of fluoropolymers, that may gain a unique combination of high performance properties due to the characteristic effects of the aromatic ring on mechanical strength and thermal properties (e.g. increasing the polymer T_g and enhancing its thermostability), as well as fluorine substituent/s on the thermal and surface properties of the resultant polymers. The incorporation of both ie. phenyl ring and fluorine substituent into the polymeric chain can significantly improve physicochemical properties of the material.

With the objective to prepare new aromatic fluoropolymers, the synthesis of monofluorinated α-methylstyrenic monomer possessing at the *para* position diethyl phosphonate function was developed. The desired monomer was obtained in two synthetic steps. In the first step, the most convenient methodology for the introduction of fluorine atom into the organic molecules was selected to be an electrophilic selective fluorination using SelectFluor as a source of fluorine. Subsequently, formation of corresponding diethyl phosphonate derivative by palladium mediated Michaelis-Arbuzov type reaction using microwave radiation was performed.

Structures of intermediate products and desired monomer **1** were confirmed by studying ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and ^{31}P NMR. The structure of the desired product, diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate **1** (4-PFMST) is shown in Figure 1.

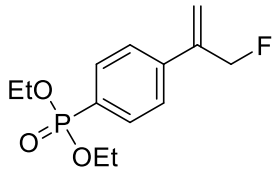

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Figure 1. Structure of diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate **1** (4-PFMST)

RESUMEN

La tecnología actual apoya la producción de polímeros con excelentes propiedades mecánicas, térmicas, de aislamiento eléctrico o de conducción iónica. Entre ellos, los fluoropolímeros son materiales que exhiben una combinación única de propiedades sobresalientes, como alta termoestabilidad e inercia química o electroquímica, bajo índice de refracción y coeficiente de fricción, constante dieléctrica y factor de disipación bajas, baja capacidad de absorción de agua, excelentes capacidades climáticas y excelentes características de superficie. Por lo tanto, estos productos de alto valor han encontrado aplicaciones en varios campos de la tecnología avanzada, por ejemplo, industria química y automotriz, ingeniería, microelectrónica, óptica, acabados textiles, aeronáutica o militar. Aunque la diversidad de aplicaciones de fluoropolímeros es enorme, estos productos aún pueden ser difíciles de procesar, ya que algunos de ellos no son solubles en disolventes comunes, mientras que otros no pueden fundirse o exhiben puntos de fusión muy altos. Sin embargo, las propiedades específicas de los fluoropolímeros, especialmente la solubilidad, así como la adhesión, la curabilidad, las propiedades de superficie, la hidrofilicidad y la resistencia química y al calor, pueden deberse a la naturaleza de los grupos funcionales en una posición lateral del esqueleto del copolímero. Además, la participación de otros monómeros fluorados o no fluorados mediante co- o terpolimerización podría conducir a la formación de fluoropolímeros que poseen propiedades peculiares.

Los polímeros aromáticos fluorados representan una interesante familia dentro de los fluoropolímeros, que pueden obtener una combinación única de propiedades de alto rendimiento debido a los efectos característicos del anillo aromático sobre la resistencia mecánica y las propiedades térmicas (por ejemplo, aumentar la Tg del polímero y mejorar su termoestabilidad), así como la presencia de flúor en las propiedades térmicas y superficiales de los polímeros resultantes. La incorporación de ambos, es decir, el anillo de fenilo y el/los átomo/s de flúor en la cadena polimérica pueden mejorar significativamente las propiedades fisicoquímicas del material.

Con el objetivo de preparar nuevos fluoropolímeros aromáticos, se desarrolló la síntesis del monómero monofluorado del α-metilestireno que posee en la posición *para* el grupo fosfonato de dietilo. El monómero deseado se obtuvo en dos etapas sintéticas. En el primer paso, la metodología más conveniente para la introducción del átomo de flúor en las moléculas orgánicas se seleccionó para llevar a cabo una fluoración selectiva electrofílica utilizando SelectFluor como fuente de flúor. Posteriormente, se llevó a cabo la formación del correspondiente derivado dietilfosfonato por reacción de tipo Michaelis-Arbuzov mediada por paladio usando radiación de microondas.

Las estructuras de los productos intermedios y el monómero deseado **1** se confirmaron mediante el estudio de ^{1}H RMN, ^{13}C RMN, ^{19}F RMN y ^{31}P RMN. La estructura del producto deseado, el 4-(3-fluoroprop-1-en-2-il)fenilfosfonato de dietilo **1** (4-PFMST) se muestra en la Figura 1.

RESUMO

A tecnoloxía actual apoia a produción de polímeros que teñen excelentes propiedades térmicas, mecánicas, de illamento eléctrico ou de condución iónica. Entre eles, os fluoropolímeros son materiais que presentan unha combinación única de propiedades excelentes, como a alta estabilidade térmica e inercia química ou electroquímica, o baixo índice de refracción e coeficiente de fricción, constante dieléctrica e factor de disipación baixos, a baixa capacidade de absorción de auga, excelentes capacidades climáticas e excelentes características da superficie. Polo tanto, estes produtos de alto valor atoparon aplicación en varios campos da tecnoloxía avanzada, como industria química e automotiva, enxeñaría, microelectrónica, óptica, acabados téxtiles, aeroespacial e militar. Aínda que a diversidade de aplicación dos fluoropolímeros é enorme, tales produtos poden ser difíciles de procesar porque algúns deles non son solubles en disolventes comúns, mentres que outros poden non fundir ou amosar puntos de fusión moi altos. Con todo, as propiedades específicas de fluoropolímeros, especialmente a solubilidade e a adhesión, curabilidade, as propiedades de superficie, hidrofilicidade e a resistencia química e á calor pode ser debido á natureza dos grupos funcionais na posición lateral do esqueleto do copolímero. Ademais, a implicación doutros monómeros fluorados ou non fluorados mediante co- ou terpolimerizacion podería levar á formación de polímeros fluorados que posúen propiedades únicas.

Os polímeros aromáticos fluorados representan unha familia interesante dentro dos fluoropolímeros, que poden obter unha combinación única de propiedades de alto rendemento debido aos efectos característicos do anel aromático sobre a resistencia mecánica e as propiedades térmicas (por exemplo, aumentar o Tg do polímero e mellorar a súa termoestabilidade), así como a presenza de flúor nas propiedades térmicas e de superficie dos polímeros resultantes. A incorporación de ambos, é dicir, o anel de fenilo e o/s átomo/s de flúor na cadea de polímeros poden mellorar significativamente as propiedades fisicoquímicas do material.

Para preparar novos fluoropolímeros aromáticos, desenvolveuse a síntese do monómero monofluorado de α-metilestireno que ten na posición *para* o grupo dietilfosfonato. O monómero desexado foi obtido en dous pasos sintéticos. No primeiro paso, a metodoloxía máis conveniente para a introdución do átomo de flúor nas moléculas orgánicas foi seleccionada para levar a cabo unha fluoración selectiva electrofílica usando SelectFluor como fonte de flúor. Posteriormente, a formación do correspondente derivado dietilfosfonato levouse a cabo mediante unha reacción de tipo Michaelis-Arbuzov mediada por paladio usando radiación de microondas.

As estruturas dos produtos intermedios e do monómero desexado **1** confirmáronse mediante o estudo de ^{1}H RMN, ^{13}C RMN, ^{19}F RMN y ^{31}P RMN. Na figura 1 móstrase a estrutura do produto desexado, o 4-(3-fluoroprop-1-en-2-il)fenilfosfonato de dietilo **1** (4-PFMST).

GENERAL INFORMATION

The project was form by 15 ECTS, which are 450 working hours (1ECTS=30 h). The distribution of this hours is shown on the next table:

		Monday			Tuesday			Wednesday			Thursday			Friday			Saturday			Sunday		
		B	E	W	B	E	W	B	E	W	B	E	W	B	E	W	B	E	W	B	E	W
March	10-17	5			5			5			5			5					4			4
	18-24	5			5			5			5			5					5			5
	25-31	5	6		5	6		5	6		5	6		5	6							
April	01-07		6			6			6			6			6							
	08-14		6			6			6			6			6				4			4
	15-21		6			6			6			6			6				5			5
	22-28			6			6		6				6			6				5			5
	29-30			6			6															
May	01-05																					
	06-12														6				4			
	13-19			8		6			6				8			6			4			
	20-26		8			8			8			8			8				10			10
	27-31		8			8			8			8			8							
June	01-02																		10			10

B=Bibliography; E= experimental; W= Writing **not working day**

B=75h ; E=224h ; W=152h

KEY WORDS

- Diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate (4-PFMST)
- Electrophilic fluorination
- Hirao reaction
- Organofluorine chemistry
- Organophosphorus chemistry
- Selectfluor

PALABRAS CLAVE

- 4-(3-fluoroprop-1-en-2-il)fenilfosfonato de dietilo (4-PFMST)
- Fluoración electrofílica
- Química fluoroorgánica
- Química fosforoorgánica
- Reacción de Hirao
- Selectfluor

PALABRAS CLAVE

- 4-(3-fluoroprop-1-en-2-il)fenilfosfonato de dietilo (4-PFMST)
- Fluoración electrofílica
- Química fluoroorgánica
- Química fosforoorgánica
- Reacción de Hirao
- Selectfluor

ABBREVIATIONS

4-ClFMST	1-Chloro-4-(3-fluoroprop-1-en-2-yl)benzene / 4-chloro-α-fluoromethylstyrene
4-PFMST	Diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate / 4-phosphonate-α-fluoromethylstyrene
$CDCl_3$	Deuterated chloroform
$CFCl_3$	Trichlorofluoromethane
CH_2Cl_2 / DCM	Dichloromethane
DMF	N,N-dimethylformamide
Et_2O	Dimethyl ether
$KMnO_4$	Potassium permanganate
MeCN	Acetonitrile
MW	Microwave
Na_2SO_4	Sodium sulphate
$NaHCO_3$	Sodium bicarbonate
NMR	Nuclear magnetic resonance
$P(OEt)_3$	Triethylphosphite
$Pd(CH_3COO)_2$	Palladium acetate
$PdCl_2$	Palladium(II) chloride
THF	Tetrahydrofuran
TLC	Thin layer chromatography
$Yb(OTf)_3$	Ytterbium(III) trifluoromethanesulfonate

1. INTRODUCTION

In comparison with the other elements of the periodic table, unique properties of fluorine gives to the fluorinated compounds an important reason for being investigated. Due to the small radius of the fluorine atom, it can occupy easily the place of a Hydrogen atom without causing many changes by steric effects (F: 1,47 Å and H: 1,20 Å). Besides, fluorine atom is the highest electronegative atom, so always when it is bonded to a carbon atom, the C-F system is polarized and has a marked ionic character. Also, the formed bond between carbon and fluorine is stronger than the hydrogen-carbon bond, so the necessary energy needed to break the bond is also bigger for the case of C-F bond. [1] The presence of a C-F bond in an organic structure affects not only that bond but also contributes to the strengthening of the bonds between other proximate atoms in the molecule, which are going to be stronger if more fluorine atoms are being added. [2]

The characteristics of the C-F system make possible that fluoroorganic compounds finds applications in different fields of life, medicine, agriculture or industry as pharmaceuticals, surfactants, catalysis, fluoropolymers, agrichemicals, refrigerants, anaesthetics, oil-repellents, and water-repellents, among others. The carbon-fluorine bond is easily found in pharmaceuticals and agrochemicals because it is generally metabolically stable and fluorine acts as a bioisostere of the hydrogen atom. Currently one fifth of pharmaceuticals available on the market contain fluorine, including several of the top drugs, where the importance of this type of compounds can be seen. [3]

Although fluorine is the 13th most abundant element on the surface of earth, nature has found it difficult to incorporate the element to the structure of organic compounds, since only few natural fluoroorganic compounds are known. This fact can be explained by a very strong energy of solvation of fluoride ion in water. Therefore, to study the influence of fluorine on chemical and physical properties of fluoroorganic compounds they need to be synthesized first. Thus, in recent years fluorine chemistry has been a highly investigated field. [2]

2. LITERATURE

2.1 POLYMERS AND POLYMERIZATION

Nowadays, polymer or macromolecular science is developing due to the needed innovation of making new materials that can be used for extreme conditions or can replace other dangerous material. The polymer science being a subfield of materials science, concerns primarily the work with synthetic polymers such as plastics and elastomers.

The term "polymer" was coined in 1833 by Jöns Jakob Berzelius, who refers to the substances of nature that have the same empirical formula but have different molar masses. The term comes from the Greek “polys” meaning “many” and “meros” meaning “part”. [4] The first fully synthetic polymer was obtained in 1907, when Belgian chemist Leo Hendrik Baekeland manufactures Bakelite from formaldehyde and phenol. In the next years, other polymers were implemented, for example, polystyrene (PS) in 1911 or poly(vinyl chloride) (PVC) in 1912. The molecular nature of polymers was not understood until the work of Hermann Staudinger in 1922, which proposed that polymers consisted of long chains of small units held together by covalent bonds. He proposed the structural formulas of polystyrene and polyoxymethylene, giant molecular chains formed by the covalent bonding association of certain atomic groups called "structural units". Significant development in polymer industry occurred during the World War II. The need to replace natural materials as rubber or silk, made necessary to develop artificial substituents, like synthetic rubber or Nylon. In following years, different polymers were synthetized, like Kevlar® or Teflon®, and metallocene catalysts, high strength fibres, conductive polymers, complex structures of polymers, liquid crystal polymers, etc. [5 6]

A polymer is a large molecule formed by the repetition of the same subunit, in a process called polymerization, where these subunits (monomers) are being added one after another. Such macromolecules offer a wide range of properties, so both natural and synthetic polymers play an essential role in everyday life. The applications are from synthetic plastics used in bottles production, to some biological polymers, like polysaccharides, proteins or DNA, needed for biological structure and function. [7]

Polymers can be obtained in a polymerization process. Depending on the mechanism, three main types of polymerization can be distinguished, i.e. radical, cationic and anionic. Radical polymerization is the most suitable industrial method of polymerization, where the polymer is formed by the successive addition of radical building blocks. The mechanism consists of 3 steps:

- Initiation: a molecule with highly reactive nature (decomposes to form radicals) is introduced to the reaction system, forming an active centre from which the polymer chain starts to grow.

- Propagation: At this step, a macromolecular radical specie is formed by an addition of radical to a double bond of a monomer. The new radical can continue reacting with the monomer molecules on the surroundings and making the chain longer. Figure 2 is an example of propagation step.

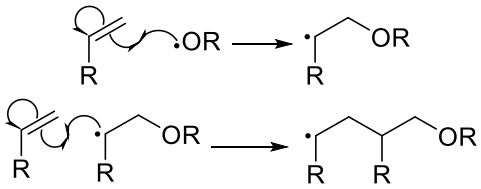


Figure 2. Mechanism of propagation step in radical polymerization

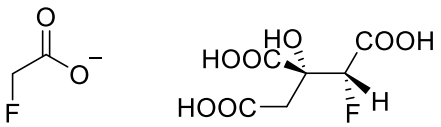
- Termination: Sometimes, the radical will react with some molecules and the product will not be a radical, so the chain is not going to grow more, and the process of polymerization is terminated. [6 8]

2.2 FLUORINATED COMPOUNDS ON THE NATURE

Fluorine is the most abundant halogen and the 13th element on the surface of earth. Despite the abundance in the nature, only a few natural organofluorine molecules are known, because most of the fluorine atoms exist forming inorganic compounds, e.g. fluorite - calcium fluoride, CaF_2. Some examples can be the following:

Fluoroacetate and Fluorocitrate

In 1943, the first organofluorinated compound was identified. It was the fluoroacetate **2**, a metabolite from the leaves of *Dichapetalum cymosum*, that can accumulate fluoroacetate up to 2500 µg/g of dry weight. [3] This compound is very toxic, being involved in the tricarboxylic acid cycle (Krebs cycle) converts into fluorocitrate **3** . Fluoroacetate **2**, which has a similar structure to acetate, reacts and form fluoroacetyl-coenzyme A. The latter molecule reacts with oxaloacetate and form (2*R*,3*R*)-fluorocitrate **3**, which inhibits the enzyme aconitase, prevents further transformations and consequently the cell dies due to lack of energy. [9] Structures of both fluoroacetate and fluorocitrate as well as the formation route of fluorocitrate are presented in Figure 3 and Figure 4, respectively.



2 **3**

Figure 3. Structures of fluoroacetate **2** and (2*R*,3*R*)-fluorocitrate **3**

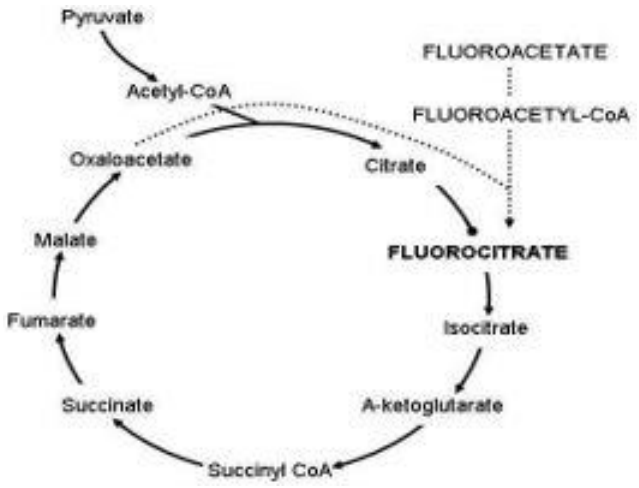
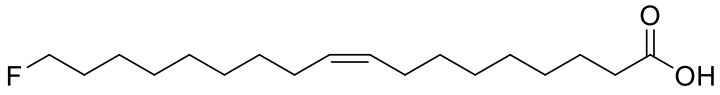


Figure 4. Lethal synthesis of fluorocitrate in the Krebs cycle

ω-fluorofatty acids

Dichapetalum toxicarium is another type of plant which have very toxic seeds, containing of organic fluorine up to 1800 µg/g of dry weight. 80% of the total organic fluorine present was identified as ω-fluorooleic acid ($C_{18:1}$) **4**. Morover, ω-fluoropalmitic acid ($C_{16:0}$) **5**, ω-fluoromyristic acid($C_{14:0}$) **6** and ω-fluorocapric acid ($C_{10:0}$) **7** were identified using gas chromatography. The biosynthesis of the ω-fluorofatty acids can be explained as the result of different synthase enzymes activity towards fluoroacetyl-coenzyme A as starting material. [9] The structures of these compounds are displayed in Figure 5.



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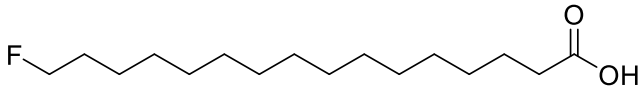

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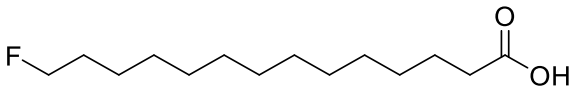

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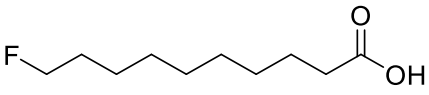

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Figure 5. Structures of different ω-fluorofatty acids **4-7**

Fluoroacetone

After the incubation of *Acacia georginae* and other plants homogenates with inorganic fluoride, an important loss of total fluorine was observed. When the solution formed was mixed with 2,4-dinitrophenylhydrazin, the molecule 2,4-dinitrophenylhydrazone was formed, which was a derivative of fluoroacetone **8**. The heavy loss of fluorine was explained by the formation of some volatile fluorinated molecules. [9] The fluoroacetone structure is shown in Figure 6.

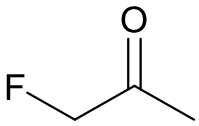

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Figure 6. Structure of fluoroacetone **8**

Nucleocidin

In 1957, an adenine containing antibiotic was isolated from bacteria *Streptomyces calvus*. At first, nucleocidin **9** was recognized as an efficient antibiotic, being a particularly effective antitrypanosomal agent. Afterwards this molecule was discovered to be highly toxic. The attempts to identify the structure revealed that the molecule contained fluorine substituent that was responsible for its high toxicity. [9] The structure of nucleocidin **9** is shown in Figure 7.

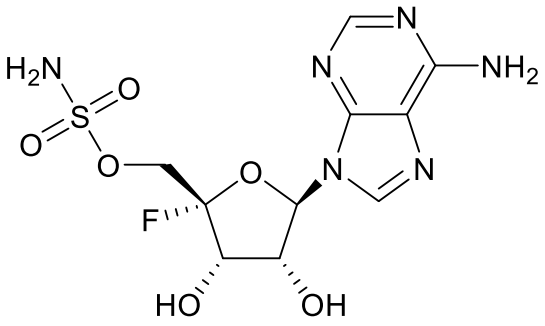

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Figure 7. Structure of Nucleocidin **9**

2.3 ORGANOFLUORINE CHEMISTRY

A large effort is being made in the production of fluoroorganic compounds, because the introduction of the fluorine into organic molecules reduce the break-down in vivo (when this is used as a drug) and improve some physicochemical properties. [10] Some examples are as follows:

- The formed bond between carbon and fluorine (C-F) is stronger than the one that hydrogen and carbon forms (C-H). This fact means that these molecules have a very high thermal and chemical stability.
- The strength of the bond implies differences in bond length, the C-F bond is little longer than the C-H bond, but it does not have an important steric effect.
- The radius of the fluorine atom (1,47Å) is similar to the hydrogen atom (1,20Å), and together with the short length of the bond, makes that the molecule doesn't suffer from steric strains (this also give high thermal stability).
- In case of polyfluorinated compounds, the fluorine atoms protect the carbon skeleton from the attack of different reagents (high chemical stability) and contribute to the strengthen of the neighbourhood bonds.
- Fluorine atom is the most electronegative of all elements (F=3.98), what gives the C-F bond a high dipole moment (1.41D).
- Fluorine has the lowest polarizability of all elements, so the dispersion forces between polyfluorinated molecules is very weak, what results in the decrease of the boiling point on fluorine derivatives. [1 11]

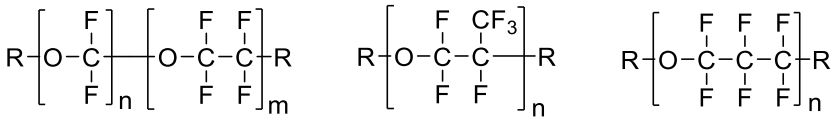
2.4 APPLICATIONS OF FLUOROORGANIC COMPOUNDS

Due to the large range of qualities, the fluoroorganic compounds can be used in different aspects, such as:

- Refrigerants: due to the high thermal and chemical stability, and the non-corrosive and suitable vapor-pressure properties, the organofluorine compounds can be used as mechanical refrigeration fluids. Also, they must be nontoxic and inflammable. The first fluids used for that purpose were chlorofluorocarbons (like CF_2Cl_2). CFCs are chemically inert at the troposphere. However, being liberated to the upper layers of atmosphere (i.e. stratosphere) and exposed to the UV light, they decompose to form radical chlorine that readily react with ozone molecules. and consequently, deplete of ozone layer. For that reason, only fluorocarbon compounds are used now as refrigerants. This is an important contribution to the Green Chemistry, which looks for practical solutions in order to obtain the same results, but without pollution or damage to the environment.

- Fire-fighting agents: fire extinguish foams can form a film over the surface of the liquid. The film inhibits the re-ignition of the liquid. The low concentrations (between 6 and 8%) of fluorinated surfactants can help to improve the fire-extinguishing power and allows an easy spreading of the foams on the surfaces of the liquids, due to the extremely low interfacial tension.

- Lubricants: Perfluoropolyethers (PFPEs) are used as lubricants because of their large liquid range, from -100 to 350 ºC. They can be used for lubrication of precise instruments, from mechanisms of watches to computer discs. Figure 8 shows structures of some examples of fluorinated lubricants such as Fomblin **10**, Kritox **11** and Demnum **12**.

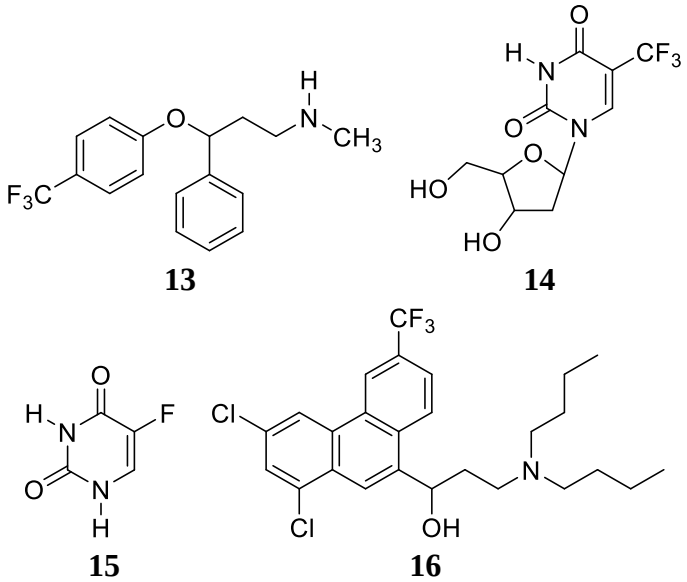


10 **11** **12**

Figure 8. Examples of perfluoropolyethers used as lubricants **10-12**

- Medical and pharmaceutical applications: perfluorocarbons can be used as artificial blood, since they are inert to microbiological attacks and can dissolve oxygen. The behaviour after the introduction of a fluorine atom into a biological active molecule can change, as on absorption, transport trough different biological barriers before reaching the desired site to have an effect, the acidity or basicity, etc.

  Figure 9 presents structures of fluorinated organic derivatives having an application as fluoroparmaceuticals e.g. Prozac (anti-depressant) **13**, Trifluoride (anti-viral) **14**, 5-Fluorouracil (anti-cancer) **15** or Halofantrina (anti-malarial) **16**.



13 **14**

15 **16**

Figure 9. Structures of different organofluorine compounds with medical and pharmaceutical applications **13-16**

- Surfactants: a surfactant is a compound which has both hydrophobic and hydrophilic parts. The hydrophobic behaviour of the molecules is increased by the presence of fluorinated surfactants, and sometimes they are called super-surfactants because of the lower surface tension respect to the hydrocarbon part, exhibiting a lower critical micelle concentration (CMC). Due to the hydrophobicity and hydrophilicity, and also the chemical and thermal stability, fluorosurfactants are used as soil and stain-repellents, carpets, paints, waxes, clothing fabrics, polishes, insecticides, leather, paper coatings, electroplating, photographic emulsifiers, lubricants, firefighting foams, textile, pressure sensitive additives, pharmaceuticals, or involved in cosmetics formulations.

- Polymers: fluoropolymers possess different morphologies, from elastomers to thermoplastics and can be semi-crystalline or totally amorphous. Fluoropolymers have found many applications in building industries, petrochemicals and automotive, optics, chemical industries, textile, fabrics or stone treatment, microelectronics, aerospace and aeronautics, etc. [1,2,11]

2.5 METHODS OF FLUORINATION

Due to the importance of the C-F bond, there are several ways of obtaining that type of bond in the molecules: [12]

- Electrophilic fluorination: for the formation of the C-F bond we need a molecule which acts as a source of "F^+". Normally, molecules with N-F bond are used, like Selectfluor® (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)) or NFSi (N-fluorobenzenesulfonimide). [13]

- Nucleophilic fluorination: if electrophilic fluorination is not possible, the most common alternative is the nucleophilic fluorination. For that, we need molecules which can act as a source of "F^-" for the displacement of other halogen as chlorine or bromine:

  $$\mathbf{R_3CCl + MF \rightarrow R_3CF + MCl\ (M= Na, K, Cs)}$$

  On the synthesis of organofluorine compounds, the most used source of fluorine is hydrogen fluoride. Such reactions, normally, are catalysed by metal fluorides such as chromium trifluoride: [14]

  $$\mathbf{Cl_2C{=}CClH + 4\ HF \rightarrow F_3CCFH_2 + 3\ HCl}$$

  - Deoxofluorination: the replacement with fluorine atoms of carbonyl or hydroxyl groups is produced. A commonly used reagent is sulphur tetrafluoride:

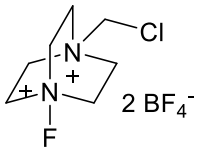
    $$\mathbf{RCO_2H + SF_4 \rightarrow RCF_3 + SO_2 + HF}$$

    Other reagents that can be used are diethylaminosulphur trifluoride (DAST, Et_2NSF_3) and bis(2-methoxyethyl)aminosulphur trifluoride (Deoxo-Fluor®).

- Fluorinated building blocks: fluoroorganic compounds can be generated from different reagents which can give perfluoroalkyl and perfluoroaryl groups, like (trifluoromethyl)trimethylsilane. Ruppert's reagent, ($CF_3Si(CH_3)_3$) is used as a source of trifluoromethyl group. These species form Grignard reagents prior to the treatement with a variety of electrophiles.

2.6 SELECTFLUOR

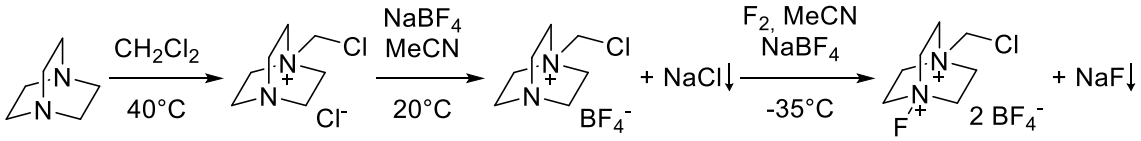
Selectfluor® **17** or 1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octanebis (tetrafluoroborate) is a reagent used as a fluorine donor. Electrophilic fluorinating reagents can operate via electron transfer pathways or an S_N2 attack at fluorine. [15]
This colourless salt was first described in 1992 and is used in organofluorine chemistry for electrophilic fluorination. Compared to F_2, which is extremely toxic, Selectfluor is relatively harmless. The structure is shown in Figure 10:



17

Figure 10. Structure of Selectfluor **17**

The preparation of Selectfluor® is relatively simple, flexible and efficient. Dabco **18** is used as starting material, reacting with dichloromethane at 40ºC for the obtainment of structure **19**. Reaction of this product dissolved in acetonitrile with sodium tetrafluoroborate at 20ºC formed structure **20** and solid NaCl. Finally, Selectfluor **17** is obtained in the reaction of product **20** dissolved in acetonitrile with sodium tetrafluoroborate and elemental fluorine at -35ºC. The synthetic route is presented in Figure 11: [15]



18 **19** **20** **17**

Figure 11. Reaction for obtainment of Selectfluor

2.7 ^{19}F NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

This technique is used for the determination of the content of fluorine on different compounds. The ^{19}F nucleus has the advantage of having nuclear spin quantum number ½, have 100% natural abundance and a high magnetogyric ratio. For these reasons, this isotope is highly responsive to NMR measurements.

The ^{19}F NMR chemical shifts span a range of more than 350 ppm for fluoroorganic compounds. Due to having ½ spin, the fluorine couples to proximate protons and carbons in a manner similar to hydrogen, and relaxation times are sufficiently long for spin – spin splitting to be resolved.

^{19}F NMR chemical shifts in the literature vary strongly, commonly by over 1 ppm, even within the same solvent. The reference compound for ^{19}F NMR spectroscopy is $CFCl_3$ (0 ppm). Typical chemical shift ranges for this technique are presented in Figure 12: ***16***

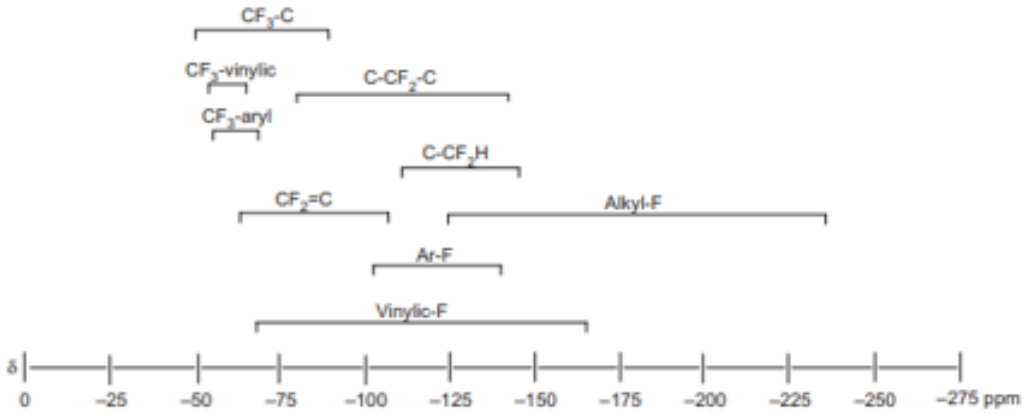


Figure 12. Chemical shifts for ^{19}F NMR

2.8 HIRAO'S REACTION

The classical Michaelis-Arbuzov or Michaelis-Becker reactions are typically useful reactions for the formation of carbon-phosphorous bonds (C-P). For the formation of the alkyl phosphonate (Csp^3-P), tyically, trialkyl phosphites and alkyl halides are used. However, this method is not useful if we want to form a bond Csp^2-P. To make this type of bond, Hirao *et al.* designed a new way, which consist of Pd-catalyzed reaction of H-phosphonates with aryl halides. Usually, the desired products are formed with very high yields. [17]

As this method requires drastic conditions, different research groups such as Kalek *et al.* [18], Prim *et al.* [19], Villemin *et al.* [20], investigated different approaches in order to obtain better yields in milder conditions. Basically, the reaction is the same as the one described by Hirao, but using different catalyst, bases, temperatures, reaction times and assistance of microwaves irradiation.

The catalytic pathway is presented at Figure 13**,** showing how the catalyst [Pd] is combined with the aryl halide and form the intermediate complex Ar[Pd]X. Subsequently, the complex reacts with a phosphite base and forms another intermediate complex $Ar[Pd]PO(OR)_2$, which rearranges leading to the formation of final aryl phosphonate product $Ar\text{-}PO(OR)_2$.

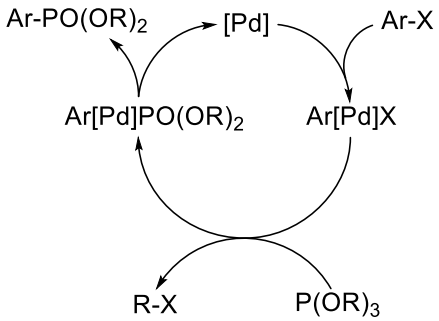
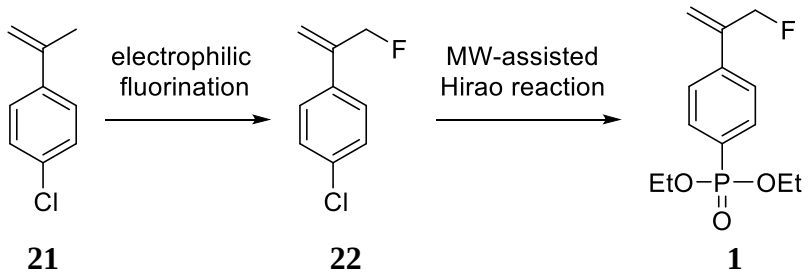


Figure 13. General mechanism of Hirao reaction

3. PROJECT OBJECTIVES

The objective of this project was to synthetize, purify and characterize the monomer diethyl 4-(3-monofluoroprop-1-en-2-yl)-phenylphosphonate (4-PFMST) **1** and the intermediate product 4-ClFMST **22**. The scheme of the route is shown on Figure 14:



21 **22** **1**

Figure 14. Reaction route for obtaining 4-PFMST

The project was divided into two synthetic steps:

1. Direct electrophilic fluorination of 4-chloro-α-methylstyrene **21**, producing 4-ClFMST **22**.
2. Formation of corresponding diethyl phosphonate derivative (4-PFMST) **1** by palladium(II) mediated Hirao's reaction assisted by microwave radiation.

The synthesis started with the fluorination of 4-chloro-α-methylstyrene **21** using Selectfluor® **17** as source of fluorine and $Yb(OTf)_3$ as catalyst for the imino-ene reaction, and the subsequent formation of the product 4-ClFMST **22**. The compound, together with $P(OEt)_3$ as a source of the phosphonate group and palladium(II) salts as catalyst under microwave radiation, leading to formation desired product 4-PFMST **1**.

4. RESULTS AND DISCUSSION

4.1 SYNTHESIS OF 4-ClFMST

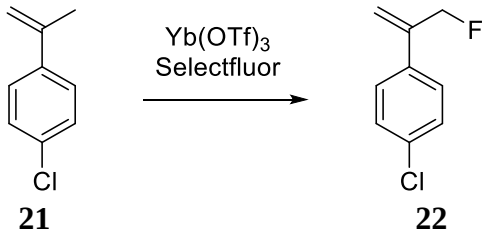


Figure 15. Reaction route for synthesis of 4-ClFMST **22**

The C-F bond was formed via electrophilic fluorination. 4-chloro-α-methylstyrene (1-chloro-4-prop-1-en-2-ylbenzene) **21** was used as a starting material for the formation of the C-F bond. Based on literature reports of Hai-Qing Luo and Teck-Peng Loh Selectfluor **17** was applied as most efficient fluorinating reagent in formation of C-F bond. [21] In order to improve the yield of electrophilic fluorination ytterbium triflate $Yb(OTf)_3$ was used as a catalyst. The ytterbium salt was found previously to be useful for the imino-ene coupling reactions. [22,23]

The mechanism of electrophilic fluorination using Selectfluor is presented in Figure 16. The electrons of the double bond of 4-chloro-α-methylstyrene **21** attack the fluorine atom of Selectfluor **17**, leading to a formation of intermediate **23** and *in situ* generated base **24**. The base abstracts the proton in order to form a double bond and neutralize the positive charge on the benzylic carbon atom, forming the desired product 4-ClFMST **22** and the hydrogenated derivative of Selectfluor **25.**

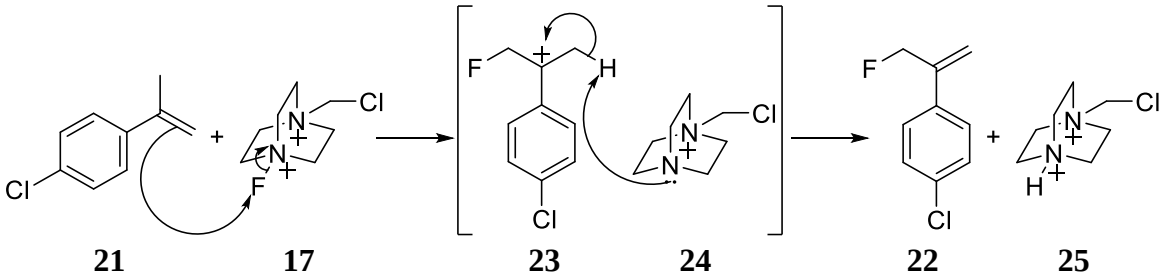


Figure 16. Mechanism of direct electrophilic fluorination of 4-chloro-α methylstyrene using Selectfluor

Most probably, ytterbium(III) triflate catalyst was used to prevent abstraction of proton from the carbon bearing fluorine substituent, thus the reaction led to formation only the desired allylic fluoride moiety.

In order to find the best reaction conditions, various solvents and stoichiometric relation of catalyst were tested.

The selected solvents were MeCN, mixture of CH_2Cl_2 and THF, as well as DMF. The selection of the solvents was made based on literature reports, since Selectfluor is known to be well dissolved in such solvents.[21-23]

Table 1. Reaction conditions and obtained yields

Entry	Solvent	Catalyst mol%	Yield (%)
1	CH_2Cl_2 + THF	10	-[a]
2	DMF	10	58[b]
3	MeCN	20	28[b]
4	MeCN	10	60

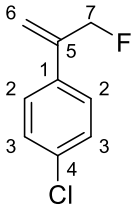
[a] Decomposition of staring material was observed.
[b] Difficult isolation, therefore the yields were determined based on ^{19}F NMR analysis with trifluorotoluene ($PhCF_3$) as an internal standard.

Comparison of different solvents used as well as stoichiometric studies revealed that the best conditions for carrying out the fluorination reaction was to use MeCN as solvent and 10 mol% of the catalyst. The next step was focused on implementing the best reaction conditions for a gram scale synthesis. Therefore, double amount of starting materials was employed each time (Table 2).

Table 2. Scale-up studies on electrophilic fluorination reaction

Entry	4-chloro-α-methylstyrene (mmol)	Yield (%)
1	1.40	60
2	2.79	23
3	5.58	32
4	11.16	35

As presented in Table 2, with increasing the scale of the reaction, the yield of isolated products decreased considerably. The pure product was characterized by ^1H NMR, ^{13}C NMR and ^{19}F NMR. The spectra of the purified product **22** are shown in following figures (Figures 17-19).



22

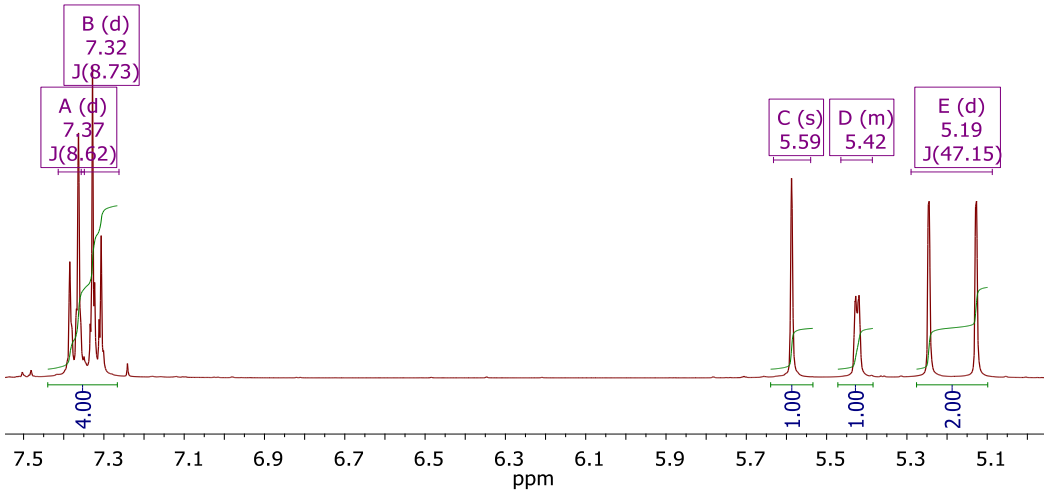


Figure 17. ^{1}H NMR spectrum of 1-Chloro-4-(3-fluoroprop-1-en-2-yl)benzene **22**

Five strong signals that correspond to the five hydrogen atoms groups that are chemically and magnetically different were observed. Signals at 7.37 and 7.32 ppm (doublets) corresponds to hydrogens of *para* substituted aromatic ring H3 and H2, respectively. The coupling constant of H2-H3 is equal to 8.7 Hz. ^{1}H NMR spectrum exhibited also signals at 5.59 ppm (singlet) and 5.42 ppm (multiplet), assigned to the hydrogens H6 of the methylene group. The last signal appears at 5.19 ppm (doublet) assigned to fluoromethyl group H7, with a coupling constant of J=47.2 Hz (germinal H-F coupling).

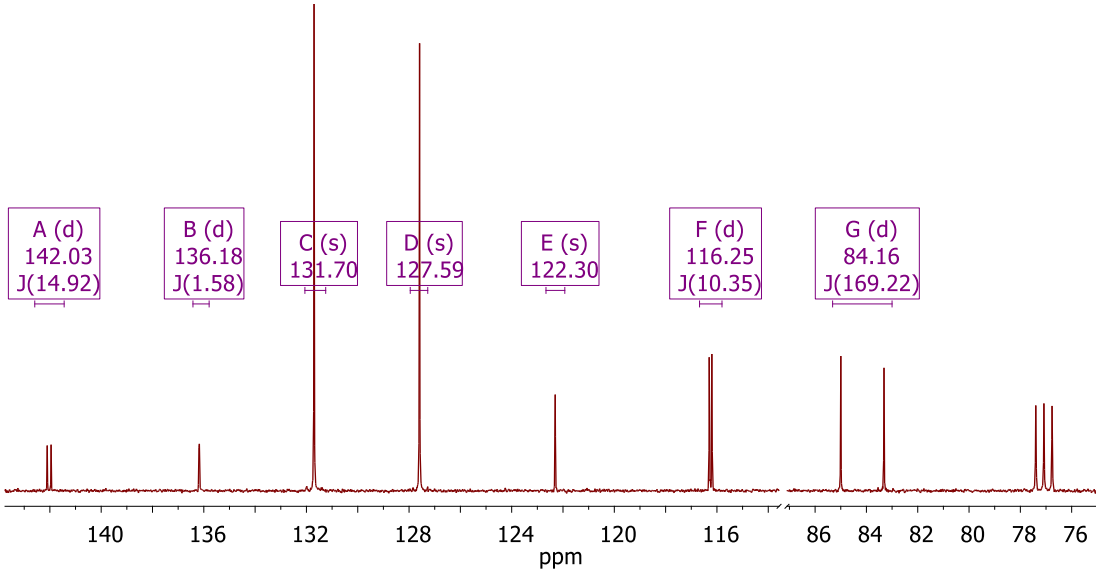


Figure 18. ^{13}C NMR spectrum of 1-Chloro-4-(3-fluoroprop-1-en-2-yl)benzene **22**

^{13}C NMR spectrum exhibited seven different signals (a triplet at 77 ppm corresponds to $CDCl_3$). Four at 136.2, 131.7, 127.6 and 122.3 ppm attributed to aromatic carbons C1, C4, C3 and C2, respectively. C1 carbon has a coupling constant of J=1.6 Hz and exhibits a doublet, whereas the other aromatic carbons exhibit a singlet. At 142.0 ppm, there is a doublet, attributed to C5 carbon with a coupling constant of J=14.9 Hz. Moreover, doublets at 116.2 ppm (J=10.4 Hz) and 84.2 ppm (J=169.2 Hz) assigned to C6 (methylene group) and C7 (fluoromethyl group) carbons, were observed.

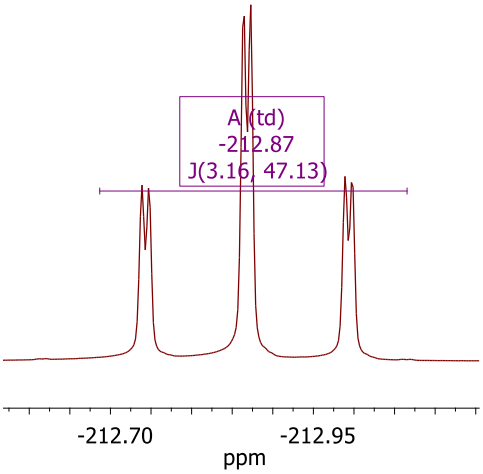
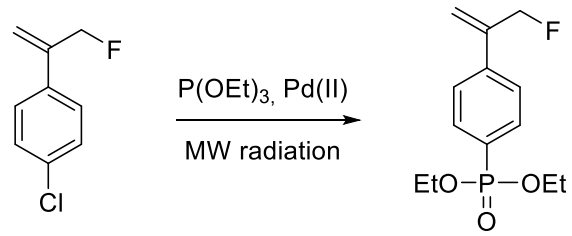


Figure 19. ^{19}F NMR spectrum of 1-Chloro-4-(3-fluoroprop-1-en-2-yl)benzene **22**

As expected, in ^{19}F NMR spectrum there is only one signal. The signal of fluorine appears at -212.9 ppm and it is a triplet of doublets because of the germinal coupling of the fluorine atom with both hydrogens of the fluoromethyl group (J = 47.1 Hz) as well as one of the vinyl moiety proton (J = 3.2 Hz).

4.2 SYNTHESIS OF 4-PFMST



22 **1**

Figure 20. Synthesis of 4-PFMST **1**

The C-P bond was formed by modified Hirao reaction using palladium (II) salts as catalysts and assisted by microwave irradiation. Pd (II) salts were selected as suitable catalyst due to the better efficiency of process involving Pd (II) in comparison with Ni (II) salts reported by Villemin *et al.*. [24]

In the comparative studies two catalyst, namely palladium chloride ($PdCl_2$) and palladium acetate ($Pd(CH_3COO)_2$) were tested. Triethylphosphite ($P(OEt)_3$) was used as a source of phosphorus, and the reaction was performed without any solvent, what contributes to the idea of Green Chemistry. The reaction was performed in an adequate microwave reactor. The selection of $P(OEt)_3$ was made based on the investigation of Villemin *et al.* [24] where the reactant was successfully used in the Hirao reaction to form aromatic phosphonate derivatives.

The catalytic mechanism is presented in Figure 21, where 4-ClFMST **22** combined with the palladium complex (catalyst) form a reaction intermediate **26**. Then, the substitution of the chlorine atom at the complex **26** for the phosphonate group coming from Triethylphosphite **27,** forms the next reaction intermediate **28,** which finally leads to the desired product 4-PFMST **1** and the regeneration of the palladium specimen which acts as a catalyst.

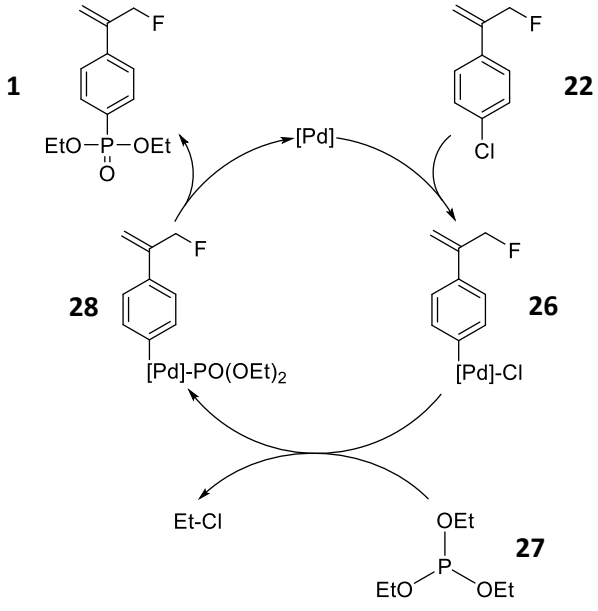


Figure 21. Mechanism of obtainment reaction of 4-PFMST **1**

This reaction was performed using different palladium species, and the obtained yields were compared to select the best catalyst for the synthesis of 4-PFMST.

Table 3. Reaction conditions and obtained yields.

Entry	Catalyst	Mmol of catalyst	Yield (%)
1	$Pd(CH_3COO)_2$	0.24	41
2	$PdCl_2$	0.24	32

The best yield (Table 3) were obtained using palladium acetate as catalyst. The purified product was characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and ^{31}P NMR. The spectra of the purified product **1** are shown in following figures (Figures 22-24).

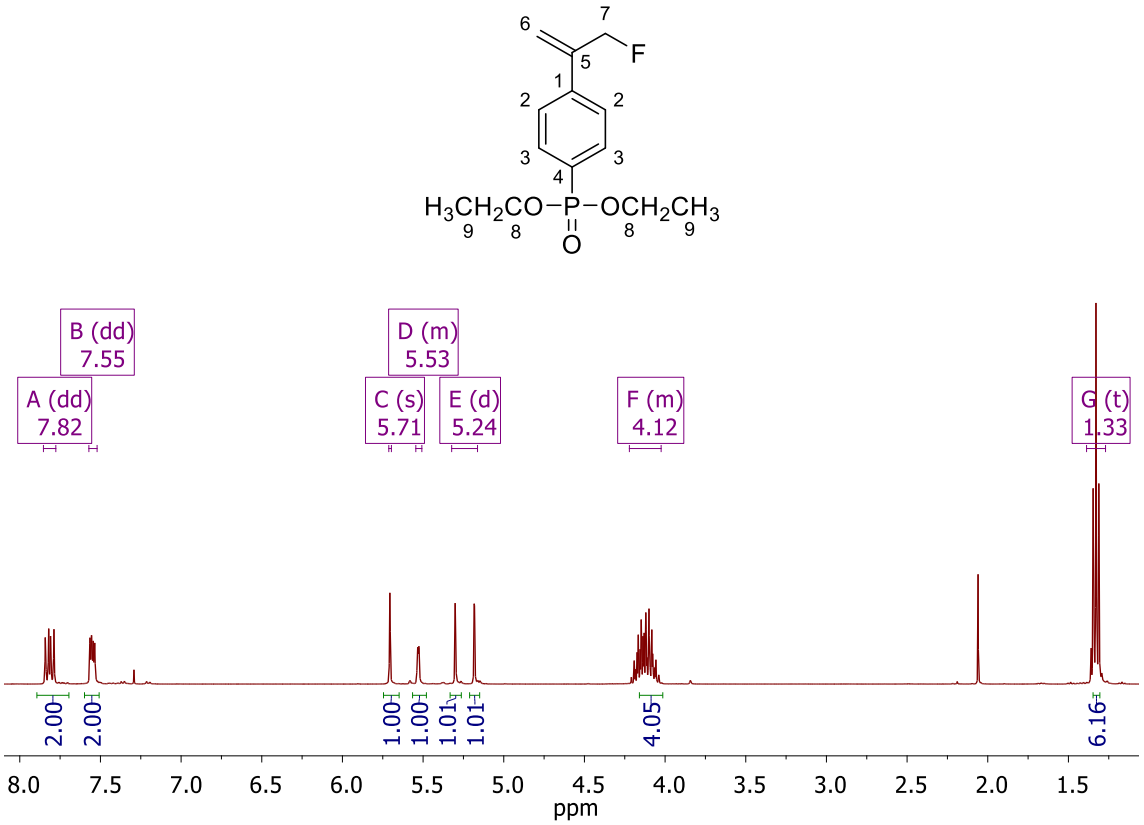


Figure 22. ^{1}H NMR spectrum of diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate **1**

The ^{1}H NMR spectrum exhibits characteristic doublets of doublets attributed to aromatic protons H3 and H2 of *para* substituted benzene ring at 7.82 (J_{H-H}=8.0 Hz, J_{H-P}=13.0 Hz) and 7.55 ppm (J_{H-H} = 8.0 Hz, J_{H-P} = 3.8 Hz), respectively. Moreover, signals at 5.71 and 5.53 ppm with multiplicity of singlet and multiplet assigned to vinyl protons H6 were observed. At 5.24 ppm appears the doublet from protons H7, with coupling constant J=47.1 Hz. Additionally, the spectrum exhibited signals at 4.12 (multiplet) and 1.33 ppm (triplet) assigned to CH_2 and CH_3 (J = 7.1 Hz) groups of diethyl phosphonate moiety, respectively.

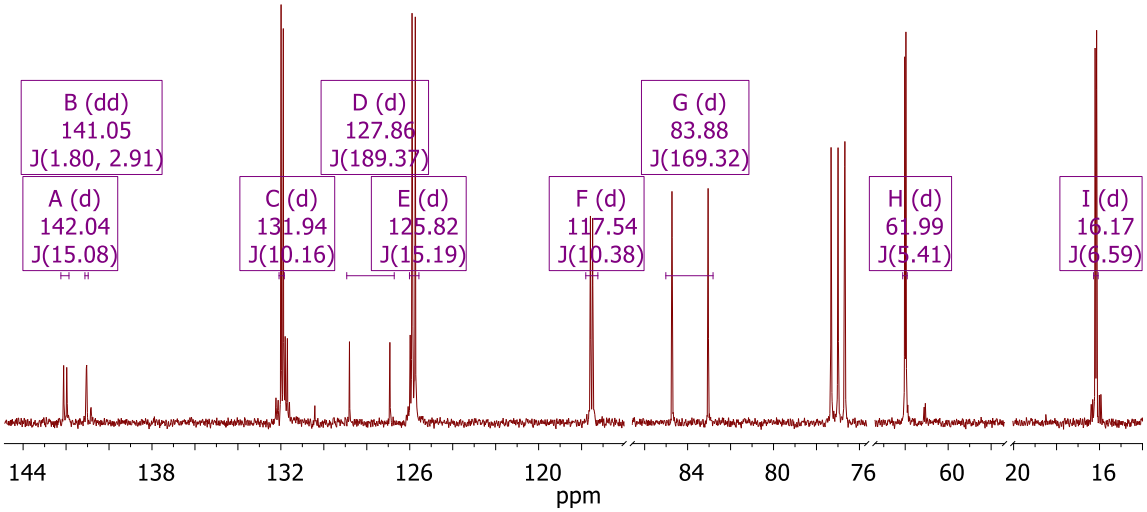


Figure 23. ^{13}C NMR spectrum of diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate **1**

^{13}C NMR spectrum exhibited eight doublets and a doublet of doublets (a triplet at 77 ppm corresponds to $CDCl_3$). The doublet of doublets at 141.1 ppm (J=2.9 Hz; J=1.8 Hz) correspond to carbon C1 .The characteristic doublets at 131.9, 127.9 and 125.8 ppm with coupling constants J=10.2 Hz; J=189.4 Hz; and J=15.2 Hz attributed to aromatic carbons C3, C4 and C2, respectively, as well as doublets at 62.0 (J=5.4) and 16.2 ppm (J=6.6) assigned to CH_2 and CH_3 groups of phosphonate ethyl groups, respectively, were observed. Moreover, the spectra showed fewer intensive signals characteristic for vinyl carbons C5 and C6 exhibiting two doublets at 142.0 (J=15.1 Hz) and 117.5 (J=10.4 Hz) respectively. Finally, a doublet centred on 83.9 ppm from fluoromethyl group C7 (J=169.3 Hz) was present.

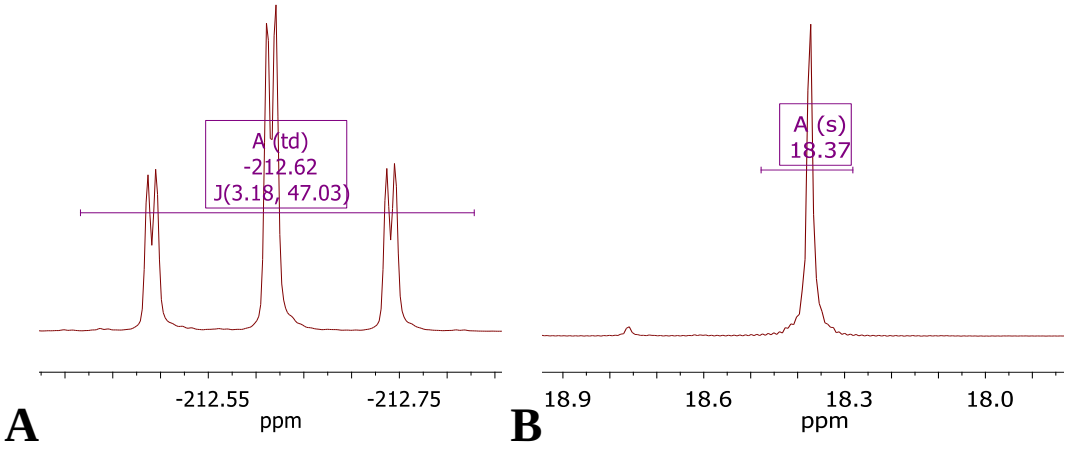


Figure 24. (A) ^{19}F NMR and (B) ^{31}P NMR spectrum of diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate **1**

In both ^{19}F and ^{31}P NMR spectra, characteristic signals of the desired product were observed proving that expected monomer **1** was obtained. The ^{19}F spectra showed a triplet of doublets at -212.6 (J=3.2 Hz, J=47.0 Hz) due to the coupling of the fluorine with the hydrogens H7. ^{31}P NMR spectra showed a singlet at 18.4 ppm which indicates a correct simple phosphonation.

5. EXPERIMENTAL PART

5.1 MATERIALS AND METHODS

- Experiments were performed under the fume hood.
- Syringes and needles were used for working with liquids.
- Reactants used for reactions are commercially available and were used as received from supplier
- Crude and isolated products were stored in the fridge.
- Solvents were removed under reduce pressure using rotary evaporator.
- Purification was performed using a column chromatography on silica gel (Silica gel 60, 70-230 mesh, Merck).
- The reaction progress, extraction and purification fractions were monitored by TLC using aluminium sheets covered with 0,2 mm of silica gel (Silica gel 60, 70-230 mesh, Merck) and visualised under UV fluorescence (254 nm) and with KMnO4 stain.
- Nuclear Magnetic Resonance (NMR) spectra were recorded on Bruker 400 MHz FT NMR instrument.

Synthesis of 4-ClFMST

- Reactions were performed using an oven-dried round-bottom flask equipped with stirring bar and septum, under argon protection. Before adding the reactants, the flask was cooled down to room temperature under argon flow.
- Dry MeCN, THF and DCM were prepared before the reactions by distillation in argon atmophere.
- Liebig condenser was used in the experiments where reflux was required.
- TLC was carried out using 100% hexane as eluent.
- Organic phases after extraction were washed with water and brine and dried with Na_2SO_4.
- Purification was performed using hexane or pentane as eluent.

Synthesis of 4-PFMST

- Reactions were performed in an oven-dried microwave tube equipped with stirring bar. Before adding the reactants, the flask was cooled down to room temperature under argon flow.
- TLC was carried out using 100% hexane and 1:1 (v/v) Hexane:AcOEt for the last cycle.
- The reaction were carried out in an appropriate microwave reactor, performing several cycles of heating at 180ºC, 100 W of lamp power, heating time of 5 minutes and maximum pressure of 1.7 bar.
- The product was dissolved in diethyl ether and the solid by-products were filtrated off.
- The purification was performed using hexane:AcOEt (1:1) as eluent.

5.2 SYNTHESIS OF 4-ClFMST

The experimental procedure followed the literature reports, namely: "Ytterbium(III) Triflate/TMSCl: Efficient Catalyst for Imino Ene Reaction" [25] and "Synthesis of aryl allylic fluorides by direct electrophilic fluorination of alkenes". [26] Selectfluor (0.5952g; 1.68 mmol) was mixed with MeCN (10 mL) in an oven-dried round-bottom flask equipped with stirring bar and septum, filled with argon, forming a milky suspension. Then, $Yb(OTf)_3$ (0.0868g; 0.14 mmol) was added, and a clear solution was formed. Finally, 4-chloro-α-methylstyrene (0.2 mL; 1.40 mmol) were added to the solution dropwise. The reaction was stirred at room temperature with argon flow protection. In the experiment with mixture of CH_2Cl_2 + THF as solvents, Selectfluor was dissolved in CH_2Cl_2 and $Yb(OTf)_3$ in THF before the mixing.

The reaction progress was monitored by TLC developed in UV light and subsequently with permanganate stain. When completed, the reaction mixture was poured into a separating funnel containing 50 mL of saturated aqueous $NaHCO_3$ solution. Then water phase was extracted with of Et_2O (4×50 mL). The progress of extraction was monitored by TLC. The combined extracts were washed with distilled water and brine and dried with Na_2SO_4. Finally, the solvent was removed under reduced pressure.

Product was purified using column chromatography with pentane as eluent. Products were analyzed by ^1H NMR, ^{13}C NMR and ^{19}F NMR. The NMR samples were prepared using deuterated chloroform $CDCl_3$ with internal standards $CFCl_3$ and TMS for ^{19}F and ^1H NMR, respectively.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, J = 8.7 Hz, 2 H, H_{Ar}), 7.32 (d, J = 8.7 Hz, 2 H, H_{Ar}), 5.59 (s, 1 H, C=CH_2), 5.42 (m, 1 H, C=CH_2), 5.19 (d, J = 47.2 Hz, 2 H, CH_2F).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.0 (d, J = 14.9 Hz, H_2C=CCH_2F), 136.2 (d, J = 1.6 Hz, C_{Ar}), 131.7 (C_{Ar}), 127.6 (C_{Ar}), 122.3 (C_{Ar}), 116.2 (d, J = 10.4 Hz, H_2C=CCH_2F), 84.2 (d, J = 169.2 Hz, CH_2F).
^{19}F NMR (376 MHz, $CDCl_3$): δ = -212.9 (td, J = 47.1 Hz, J = 3.2 Hz, 1 F, CH_2F).

5.3 SYNTHESIS OF 4-PFMST

The experimental procedure followed the report on "Nickel and palladium catalysed reaction of triethyl phosphite with aryl halides under microwave irradiation". [24] 4-ClFMST (0.4124g; 2.42 mmol) was mixed with $P(OEt)_3$ (0.4565 mL; 2.66mmol) in an oven-dried microwave tube equipped with stirring bar and stopper, filled with argon, forming a transparent solution. Then, $Pd(CH_3COO)_2$ was added to the solution (0.0549g; 0.24 mmol) and it changes the colour to dark brown. The program of the microwave reactor was setup with a constant temperature of 180ºC, 100 W of lamp power, heating time of 5 minutes and maximum pressure of 1.7 bar. The reaction progress was monitored by TLC developed in UV light and subsequently with permanganate stain. When completed the reaction mixture was dissolved in 20 mL of Et_2O and the precipitates were removed by filtration. Crude product was concentrated under reduced pressure. For the purification of the product, column chromatography was performed using Hexane:AcOEt (1:1) as eluent. Resulting products were analyzed by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and ^{31}P NMR. The NMR samples were prepared using deuterated chloroform $CDCl_3$ with internal standards $CFCl_3$ and TMS for ^{19}F and ^{1}H NMR, respectively.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82 (dd, J = 13.0 Hz, J = 8.0 Hz, 2 H, H_{Ar}), 7.55 (dd, J = 8.0 Hz, J = 3.8 Hz, 2 H, H_{Ar}), 5.71 (s, 1 H, C=CH_2), 5.53 (m, 1 H, C=CH_2), 5.24 (d, J= 47.1 Hz, 2 H, CH_2F), 4.12 (m, 4 H, OCH_2CH_3), 1.33 (t, J = 7.1 Hz, 6 H, OCH_2CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.0 (d, J = 15.1 Hz, H_2C=CCH_2F), 141.0 (dd, J =2.9 Hz, J = 1.8 Hz, C_{Ar}), 131.9 (d, J = 10.2 Hz, C_{Ar}), 127.9 (d, J = 189.4 Hz, C_{Ar}), 125.8 (d, J= 15.2 Hz, C_{Ar}), 117.5 (d, J = 10.4 Hz, H_2C=CCH_2F), 83.9 (d, J = 169.3 Hz, CH_2F), 62.0 (d, J = 5.4 Hz, OCH_2CH_3), 16.2 (d, J = 6.6 Hz, OCH_2CH_3).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –212.6 (dt, J = 47.0 Hz, J = 3.2 Hz, 1 F, CH_2F).

^{31}P NMR (376 MHz, $CDCl_3$): δ = 18.4 (s, 1 P, (O)$P(OCH_2CH_3)_2$).

6. CONCLUSION

Throughout the project a straightforward and efficient way for the synthesis of desired monomer diethyl 4-(3-fluoroprop-1-en-2-yl)phenylphosphonate (4-PFMST) was developed.

In the electrophilic fluorination studies, the use of 0.1 equivalent of catalyst ($Yb(OTf)_3$) and acetonitrile as solvent was identified as the best reaction conditions for the carrying out of the reaction. However, some optimizations are still required since the up-scale approach resulted in preparation of fluorinated 4-chloro-α-methylstyrene with relatively lower yields. Nevertheless, this step allows an easy purification and characterization of the resulting product.

In the modified Hirao reaction aimed at formation of aromatic C-P bond, the use of palladium acetate ($Pd(CH_3COO)_2$) as catalyst was found to be the best catalyst for the synthesis of the final product. The phosphonate monomer was obtained with moderate yields. Thus, presented procedure as well as purification require additional optimizations.

Nevertheless, presented two-steps synthesis is an easy way to obtain 4-PFMST at laboratory scale, but some optimizations are required in order to up-scale the synthesis and produce efficiently new monomer for subsequent radical polymerization studies.

CONCLUSIÓN

A lo largo del proyecto, se desarrolló una manera sencilla y eficiente para la síntesis del monómero deseado dietil 4-(3-fluoroprop-1-en-2-il)fenilfosfonato (4-PFMST).

En los estudios de fluoración electrofílica, el uso de 0,1 equivalentes de catalizador ($Yb(OTf)_3$) y acetonitrilo como disolvente se identificaron como las mejores condiciones de reacción para llevar a cabo la reacción. Sin embargo, todavía se requieren algunas optimizaciones ya que el enfoque a gran escala dio como resultado la preparación de 4-cloro-α-metilestireno fluorado con rendimientos relativamente más bajos. Sin embargo, este paso permite una fácil purificación y caracterización del producto resultante.

En la reacción de Hirao modificada dirigida a la formación de un enlace C-P aromático, se encontró que el uso de acetato de paladio ($Pd(CH_3COO)_2$) como el mejor catalizador para la síntesis del producto final. El monómero con la función fosfonato se obtuvo con rendimientos moderados. Por lo tanto, el procedimiento presentado y la purificación requieren optimizaciones adicionales.

Sin embargo, la síntesis presentada en dos pasos es una forma fácil de obtener 4-PFMST a escala de laboratorio, pero se requieren algunas optimizaciones para aumentar la escala de la síntesis eficientemente y producir un nuevo monómero para estudios posteriores de polimerización de radicales.

CONCLUSIÓN

Ao longo do proxecto, desenvolveuse unha forma sinxela e eficiente para a síntese do monómero desexado dietil 4-(3-fluoroprop-1-en-2-il)fenilfosfonato (4-PFMST).

Nos estudos de fluoración electrofílica, identificouse o uso de 0,1 equivalentes de catalizador ($Yb(OTf)_3$) e acetonitrilo como disolvente como as mellores condicións de reacción para levar a cabo a reacción. Non obstante, aínda se requiren algunhas optimizacións xa que o enfoque a gran escala resultou na preparación do 4-cloro-α-metilestireno fluorado con rendementos relativamente máis baixos. Non obstante, este paso permite unha fácil purificación e caracterización do produto resultante.

Na reacción de Hirao modificada dirixida á formación dun enlace aromático C-P, atopouse que o uso de acetato de paladio ($Pd(CH_3COO)_2$) era o mellor catalizador para a síntese do produto final. O monómero coa función fosfonato obtívose con rendementos moderados. Polo tanto, o procedemento presentado e a purificación requiren optimizacións adicionais.

Non obstante, a síntese presentada en dous pasos é un xeito sinxelo de obter 4-PFMST a escala de laboratorio, pero hai que facer algunhas optimizacións para aumentar a escala da síntese eficientemente e producir un novo monómero para estudos posteriores de polimerización de radicais.

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