OPTIMIZATION OF ACTIVATION CONDITIONS FOR 2-IODOXYBENZOIC ACID'S RADIOFLUORINATION

A.E. Tulupov, E.V. Podrezova
Scientific adviser – Dr. of Science, Professor M.S. Yusubov

National Research Tomsk Polytechnic University
634050, Russia, Tomsk, 30 Lenin Avenue, aet15@tpu.ru

Positron emission tomography (PET) is an effective and modern method for diagnosing cancer. The method combines the capabilities of positron emission (PET) and computed tomography (CT), and allows the image to distinguish between benign and neoplasms with a high confidence. In PET diagnostics, radiopharmaceutical preparations (RFP) labeled with positron-emitting ultrashort-lived radionuclides (UCRP) are used.

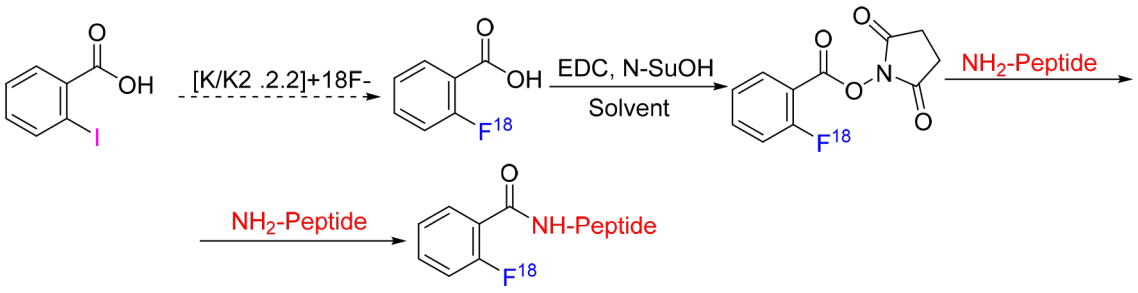
The main argument for administration UCRP was the fact that their use allows to reduce the time of the study and the radiation load on the patient, because most of the drug disintegrates already during the study. In addition, many elements have positron-emitting UCRP, such as ^{18}F, ^{11}C, ^{13}N, ^{15}O (with half-lives of 109, 20, 10, and 2 minutes, respectively) take an active part in most biological processes of the human body. In fact, the PET method can investigate any function of the body. It is only necessary to choose a chemical compound that is critical for the implementation of this function [1].

At present, our research team collaborates with the Siberian Medical State University and the Federal Siberian Scientific and Clinical Center for Nuclear Medicine to develop a method for peptide fluorination using the prosthetic group [18F]-fluorobenzoic acid as an N-succinimide ester.

Because of this acid is radioactive, optimization of this stage was carried out with 2-iodobenzoic acid (Scheme 2), which has similar properties with [18F]-fluorobenzoic acid.

How we can see from figure 1, after fluoridation required a stage of activation of carboxyl group [18F]-fluorobenzoic acid because of its low acylating capacity.

According to literature data, 1-Ethyl-3- (3-dimethylaminopropyl) carbodiimide (EDC) and N-Hydroxysuccinimide (NHS) are the most common to the activation of the carboxylic group of

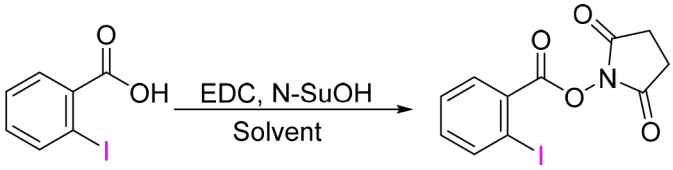


Scheme 1. *Synthesis [18F]-fluorobenzoic acid*

carboxylic acids [2]. We varied those parameters: temperature, molar ratio reagents, solvent and time of synthesis. Monitoring the progress of the reaction was carried out by gas chromatography with a mass detector (GH-MS).

Studies have shown, the best parameters for the activation of carboxyl group are tetrahydrofuran (THF) as a solvent, synthesis time – 10 min, T = 70 °C, molar ratio reagents 2-iodobenzoic acid : NHS : EDC = 1 : 2 : 2. The yield was 98 % under these conditions.

According the research, we optimized parameters of synthesis on a model of 2-iodobenzoic acid and achieved the highest yield.



Scheme 2. *Activation of 2-iodobenzoic acid*

References

1. *Изотопы и препараты для позитронной эмиссионной томографии [Electronic resourse]: Copyright Anti-Radiation association (c), 2015. URL: http://rad-stop.ru/2-3-izotopyi-i-preparatyi-dlya-pozitronnoy-emissionnoy-tomografii/#.XHkwVtIzbIX (date: 14.02.2019).*
2. *Carbodiimide Crosslinker Chemistry [electronic resourse]: thermos Fisher scientific (c), 2016: URL: https://www.thermofisher.com/ru/ru/home/life-science/protein-biology /protein-biology-learning-center/protein-biology-resource-library/pierce-protein-methods/carbodiimide-crosslinker-chemistry.html (date 14.02.2019).*

OXONE: A CONVENIENT REAGENT FOR FACILE SYNTHESIS OF DIARYLIODONI-UM SALTS

K.A. Vasilyeva, V.K. Legkoder

Scientific adviser – PhD, Assoc. Professor O.S. Kukurina

National Research Tomsk Polytechnic University

634050, Russia, Tomsk, 30 Lenin Avenue, christi-na_vasilieva@mail.ru

Oxone® is the trademark name of a stable triple salt $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$. The active oxidant within the mixture, peroxymonosulfate (HSO_5^-), has been the subject of study in various fields ranging from atmospheric science to physical and computational chemistry. The focus on the salts of Caro acid has not waned for more than one century and has been caused by the extraordinary oxidizing abilities of this compound. This reagent is distinguished by low cost and toxicity and combining with high oxidation properties and facile handling in storage and use. All these aspects make Oxone as a very attractive reagent. Therefore, the Oxone® usage for the synthesis of the most important hypervalent iodine compounds was shown in [2, 3].

Diaryliodonium salts are derivatives of hypervalent iodine compounds have found broad application as reagents in organic synthesis as an analogues of organic-metal catalysts and complexes based on toxic and heavy metals due to their particular structure (Figure 1). Iodine atom in iodine (III) compounds are electrophilic because of the node in the nonbonding orbital of the hypervalent bond. Thus, they react with various nucleophiles by initial Nu – I bond formation and release of the ligands.

A procedure for direct diaryliodonium salts synthesis from iodoarenes, without isolation of an iodine (III) intermediate, is attractive for many reasons. Advantages include reduced reaction time and increased substrate scope, as many intermediates are unstable towards isolation. Furthermore, the applicability is improved when diversely substituted

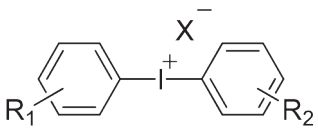


Fig. 1. *Structure of diaryliodonium salts*

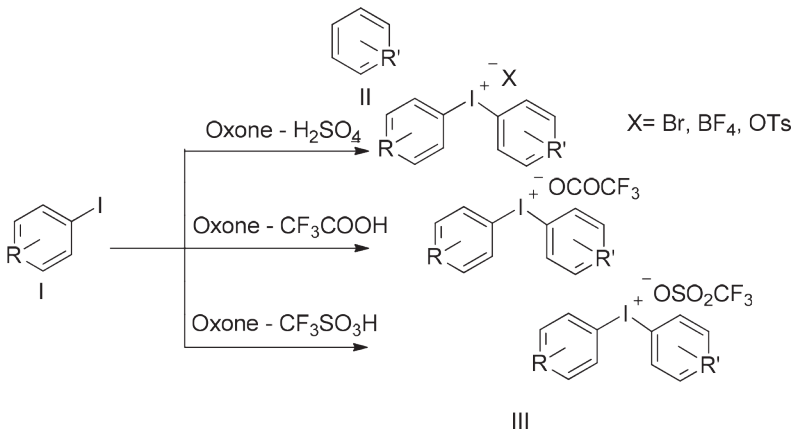


Fig. 2. *General scheme synthesis*
(R=H, CF_3, 5F, R'=H, CH_3, $2CH_3$, $3CH_3$, OCH_3, Cl, Br)