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Decarboxylative Metal-free Synthesis of Aryl Difluorocarbonyl Compounds Using TMP-Iodonium (III) Salts

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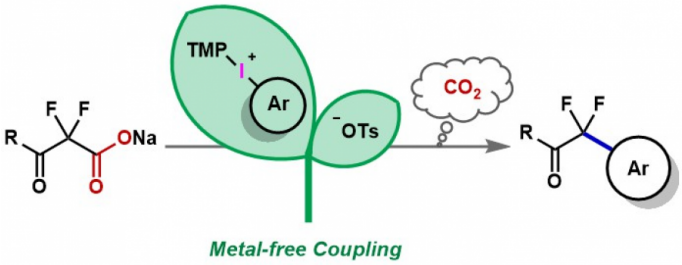
PURPOSE OF THE ABSTRACT

Aryl difluorocarbonyl groups are frequently seen in bioactive compounds due to their high stability and unique biological properties as fluorine-containing compounds. Additionally, the difluoromethylene (CF2) part acts as a bioisoster of ether and carbonyl groups. Aryl difluorocarbonyl compounds can be prepared by deoxofluorination of diketone with diethylamino sulfur trifluoride (DAST) or its derivatives [1]. However, these reagents are unstable to water, releasing toxic HF, and would undergo explosive decomposition upon heating. The catalytic cross-coupling method of aryl halides and difluoroacetic acid derivatives with silyl groups is an alternative approach to the synthesis of aryl difluorocarbonyl compounds [2]. However, this method employing transition metals such as Cu and Pd requires careful removal of the residual metal in drug synthesis. Therefore, development of metal-free synthesis method of aryl difluorocarbonyl compounds is strongly desired.

Diaryliodonium(III) salts offer alternative arylation to transition metal-catalyzed couplings. Trimethoxyphenyl (TMP) iodonium salts, which have TMP groups as one aryl ligand, direct the selective bond formation with another aryl group [3]. In this study, we have developed new metal-free synthesis of aryl difluorocarbonyl compounds using TMP-iodonium salts. Sodium difluoro keto acids reacted with TMP-iodonium salts to afford aryl difluorocarbonyl compounds in the absence of transition metal. The starting materials containing bromine atom and heterocycle, which would deactivate the transition metal catalysis, are well tolerated during the introduction of difluorocarbonyl groups by our method.

FIGURES



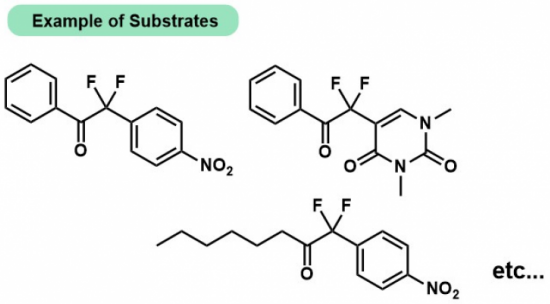


FIGURE 1

Metal-free Synthesis of Aryl Difluorocarbonyl Compounds

Sodium difluoro keto acids reacted with TMP-iodonium salts to afford aryl difluorocarbonyl compounds in the absence of transition metal.

FIGURE 2

Example of Substrates

Aryl, alkyl group, and uracil are applicable for the introduction of difluorocarbonyl part.

KEYWORDS

Metal-free | Fluorine | Decarboxylation | Diaryliodonium (III) Salts

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