SEPTEMBER 23-27 2024
19BMOS
BRAZILIAN MEETING ON ORGANIC SYNTHESIS
BENTO GONÇALVES, RS - BRAZIL

Selective fluorination reactions in 5-aryl(heteroaryl)-7-(trifluormethyl)-2-methylpyrazole[1,5-*a*]pyrimidines

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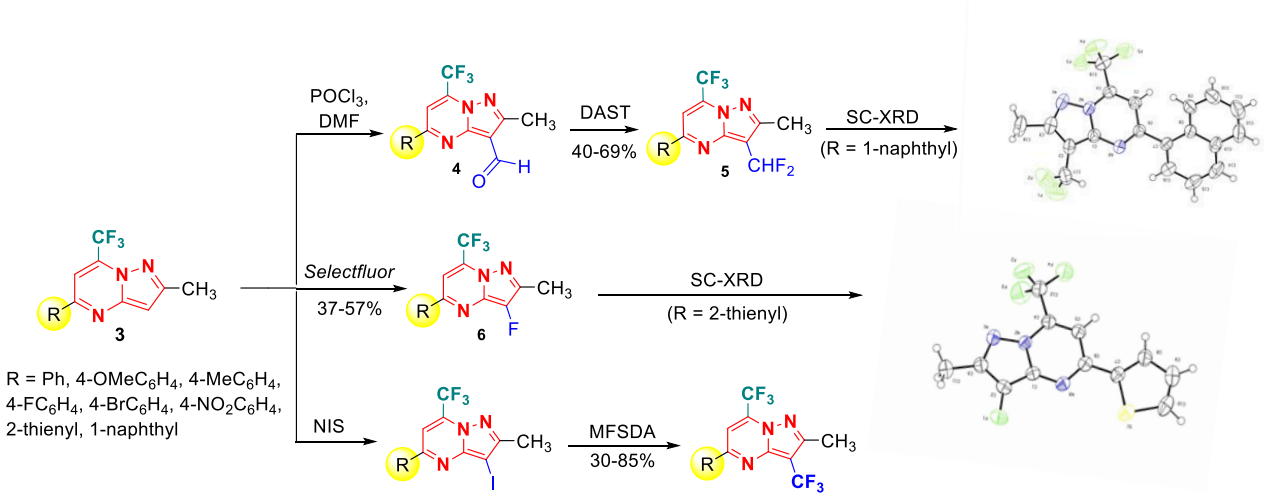
Keywords: *Fluorination reaction, Pyrazole[1,5-a]pyrimidines, DAST-MFSDA-Selectfluor*

ABSTRACT

The incorporation of fluorine atoms into organic molecules has garnered significant interest in synthetic and medicinal chemistry. Extensive research has demonstrated that fluorine atoms can modify crucial properties of organic compounds such as acidity and basicity. Moreover, they can impact absorption, transport, and interactions with drug receptors [1-3]. In this regard, this work presents the synthesis of a three new series of fluorinated pyrazole[1,5-*a*]pyrimidines (Scheme 1) obtained from three different synthetic routes that involves: (i) synthesis of 3-formylpyrazolo[1,5-*a*]pyrimidines (**4**) followed by a DAST-mediated nucleophilic difluorination for the synthesis of 5-aryl(heteroaryl)-3-difluormethyl-7-(trifluormethyl)-2-methylpyrazolo[1,5-*a*]pyrimidines (**5**); (ii) a regioselective electrophilic fluorination employing the fluorinating reagent Selectfluor for the synthesis of 5-aryl(heteroaryl)-3-(fluoro)-7-(trifluoromethyl)-2-methylpyrazolo[1,5-*a*]pyrimidines (**6**) and, (iii) a sequential reaction involving an iodination with N-bromo succinimide (NIS) followed by a trifluoromethylation using methyl fluorosulfonyldifluoroacetate (MFSDA)[4] to obtain 3,7-bis(trifluoromethyl)-pyrazolo[1,5-*a*]pyrimidine (**8**).



Scheme 1. A summary of this study: Synthetic routes for fluorinated pyrazolo[1,5-*a*]pyrimidines **5**, **6**, **8**.

ACKNOWLEDGEMENTS

The authors would like to thank the following entities: The Coordination for Improvement of Higher Education, Personnel-CAPES (Finance Code 001) for the fellowships and the National Council for Scientific and Technological Development-CNPQ; proc No 305.379/2020-8; 403.134/2021, and the Research Support Foundation of the State of Rio Grande do Sul-FAPERGS: proc. No. 17/2551-0002099-7 for financial support.

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