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Turning mustard gas chemistry into green chemistry: a new tool for pharmaceutical synthesis

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Abstract

N,N-dialkyl ethylamine moiety can be found in numerous scaffolds of macromolecules, catalysts and especially pharmaceuticals such as Tamoxifen, Raloxifene, Amiodarone, Phenyltoloxamine, Trifenagrel and Trimethobenzamide. Common synthetic procedures for its incorporation in a substrate rely on the use of a nitrogen mustard gas or on multistep syntheses featuring chlorine hazardous/toxic chemistry. Herein are reported our latest results on the one-pot synthetic approach for the introduction of the *N,N*-dialkyl ethylamine moiety in different phenolic substrates via dialkyl carbonate chemistry. In a typical reaction, 2-dimethylaminoethanol was reacted with a nucleophile (a phenolic scaffold) and dialkyl carbonate (DAC), i.e., diethyl carbonate (DEC), in the presence of a base. In particular, DEC was used for the in-situ formation of ß-aminocarbonate (mustard carbonate) that in turn acts as an alkylating agent via nitrogen nitrogen anchimeric assistance. Different substrates were investigated including precursors of commercially available drugs giving the related alkylated compound in good to quantitative yields.
This one-pot alkylation approach is a striking example of chlorine-free direct substitution of an alcohol, indicated as one of the key Green Chemistry research areas for pharmaceuticals manufacturers. Furthermore, an in vitro toxicity study has been conducted on ß-aminocarbonate and its alcohol precursor, giving an insight into the cytotoxicity values of the reagents for the synthetic procedure proposed.

Keywords

Green Chemistry | Dialkyl carbonate | chlorine-free | direct alcohol substitution

SESSION DETAILS

Session 2: Green Analytical Chemistry

11:00-12:30
Tuesday, 16 November, 2021

IN THIS SESSION

11:00-11:30
Green analytical chemistry

11:30-11:50
Orange and spinach processing wastes as a source of value-added compounds: polyphenol extraction and antioxidant activity evaluation

12:10-12:30
Turning mustard gas chemistry into green chemistry: a new tool for pharmaceutical synthesis