ISGC 2019
May 13rd - 17th

N°1102 / PC
TOPIC(s) : Clean reactions / Industrial chemistry

Green Synthesis of new antimicrobial triazinyl-morpholinium quaternary ammonum salts

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PURPOSE OF THE ABSTRACT

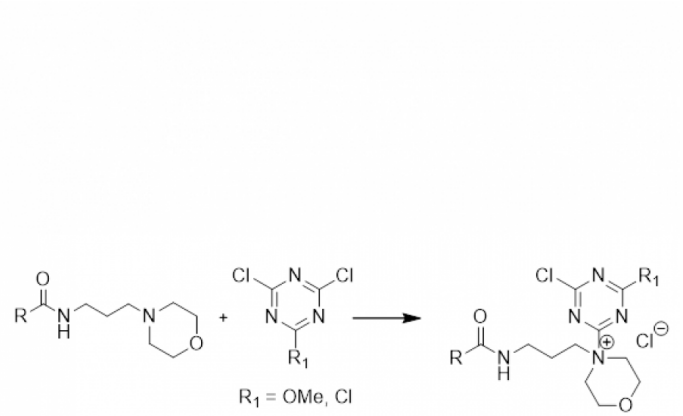
Scientists carry out constant research in order to reduce bacterial infections affecting people and ambuents [1]. However, in recent decades, it has been observed that some pathogens are acquiring greater resistance to the currently used antimicrobials [2] and this trend seems to worsen from year to year [3].
Quaternary ammonium compounds are widely employed antimicrobial substances and their efficiency is known since the early part of the twentieth century [4]. QACs are part of many commercial products such as benzalkonium chloride and cetylpyridinium chloride, their activity depends significantly on factors such as the length of the alkyl chain or number of charges [5]. It is generally accepted that QACs cause the destruction of the cytoplasmic membrane creating a charge imbalance in the surface of the membrane thanks to the permeation of the alkyl chains in the intermembrane area leading to cell death. [6][7][8]

Today the quaternary ammonium compounds are synthesized by alkylation of tertiary amines in the presence of a halogenalkane [9][10]. This reaction generally requires polar solvents, temperatures between 50 ° ? 100 °C and several hours of reaction times.
In this work we wish to disclose the syntheses of a new family of QACs with a view to pursue the principles of sustainable chemistry, using non-harmful solvents, with low energy consumption and few simple steps to purify the products. Our intention is to prepare an antimicrobial quaternary ammonium salts (QACs) that is inspired to the structure of 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methyl-morpholinium chloride (DMTMM).

In our new strategy, the quaternary ammonium triazine salts (QATs) are prepared using a highly sustainable protocol at room temperature in high yield using in all cases, REACH certified precursor. Moreover, the structure of these QATs may be easily tuned to give libraries of molecules with antimicrobial activity.
The QATs are obtained by reaction of the morpholine-amide precursors (synthesized through a sustainable process emploing DMTMM) with 2,4-dichloro-6-methoxy-1,3,5-triazine and 2,4,6-trichloro-1,3,5-triazine (Figure 1).

The antimicrobial efficiency of this family of QATs has then evaluated against Gram positive and Gram negative bacteria, giving high antimicrobial activity comparable with the most efficent products commercially available today (Figure 2).

FIGURES



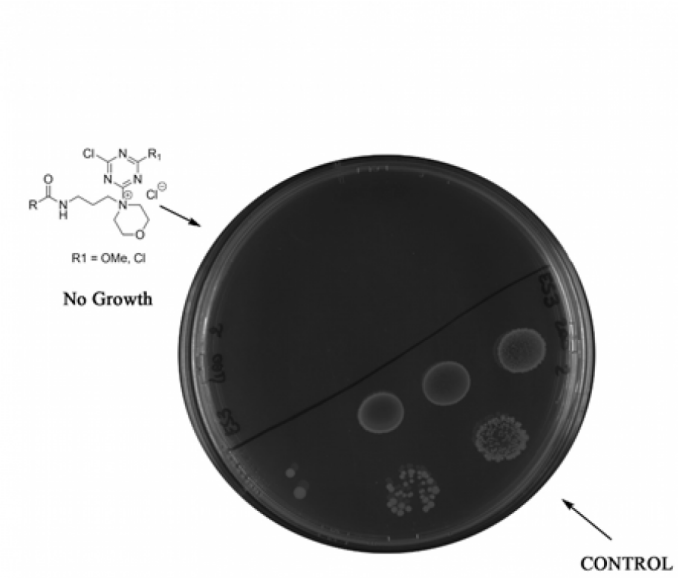


FIGURE 1

Figure 1

General procedure for the synthesis of QATs

FIGURE 2

Figure 2

Antimicrobial activity evaluation on E. Coli.

KEYWORDS

Green Synthesis | Antimicrobial | Quaternary ammonium salts

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