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Dimethylsulfoniopropionate lyase from Pelagibacter ubique HTCC1062 as catalysts for aza-Michael reactions of amines to acrylic and methacrylic acids

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PURPOSE OF THE ABSTRACT
The construction of C-N bonds is an important chemical transformation for the preparation of amines, amino alcohols and amino acids. These compounds have been widely employed as chiral building blocks in the pharmaceutical and agrochemical industries. Furthermore the presence of a chiral amine in active pharmaceutical ingredients is estimated to be around 40% and this percentage is larger when considering only the amino groups (chiral and achiral).(1) Several strategies have been employed for the biocatalytic synthesis of C-N bonds, e.g., transaminases, iminoreductases and aza-Michael additions. Particularly, the biocatalytic aza-Michael addition reactions have been performed using promiscuous hydrolases (e.g., proteases, lipases, amylases) using alkyl acrylates, acrylonitrile and enones, and with specific ammonia lyases.(2) However, the use of acrylic and methacrylic acids as Michael acceptors in biocatalysis is not documented. alpha,beta-Unsaturated carboxylic acids are difficult substrates that must be efficiently activated to increase the electrophilicity.
In this communication, we report the catalytic properties of dimethylsulfoniopropionate (DMSP) lyase from Pelagibacter ubique HTCC1062 (DddK) as catalyst for Michael type reactions. In nature, DddK catalyzed the cleavage of DMSP to dimethyl sulphide and acrylate. We envisaged that the enzyme can operated in the synthetic direction and catalyze both hetero C-X and C-C Michael additions using acrylic, and methacrylic and other alpha,beta-unsaturated carboxylic acids as acceptors. In this work, we assayed DddK as catalyst for aza-Michael addition of primary and secondary amines to acrylic and methacrylic acids (Scheme 1). Dddk activity, reaction conversion of the beta-carboxylic acid derivatives, and the stereochemical outcome of the products from methacrylic acid will be presented and discussed.

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FIGURES

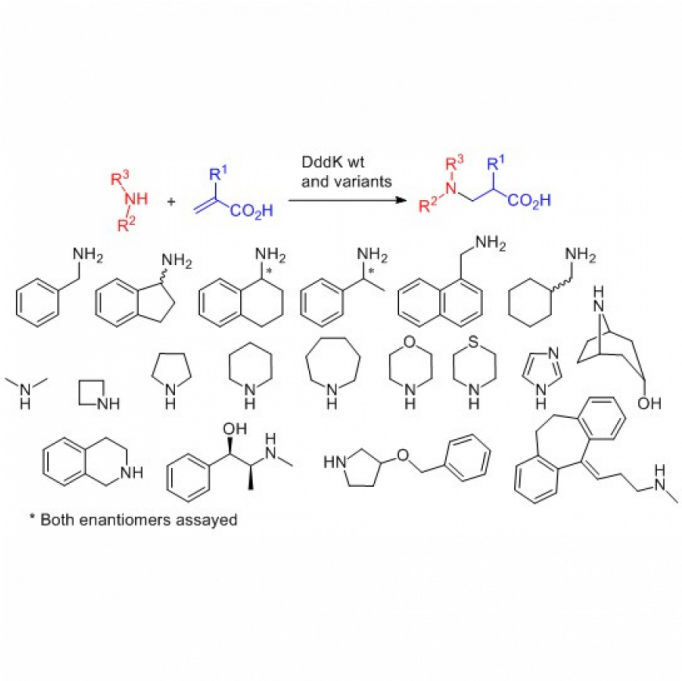

FIGURE 1

Scheme 1

DddK catalyzed aza-Michael additions of primary and secondary amines to acrylic (R1 = H) and methacrylic acids (R2 = CH3).

FIGURE 2

KEYWORDS

Aza-Michael reactions | alpha,beta-Unsaturated carboxylic acids | Dimethylsulfoniopropionate lyase | beta-Amino acids

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