ABSTRACT

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Antibiotic resistance, a global threat, is a dynamic problem that is increasing because of genetic adaptations of microbes developing resistance to the most developed antibiotics by changes in gene expression and increases in strain diversifications. A method that could potentially be utilized as an alternative of the antibiotics is the use of "nonantibiotic" synthetic molecules that interfere with quorum sensing (QS). The use of acetophenone and its analogues for the syntheses of β-ketoesters and β-ketoamides remains a promising synthetic route to inhibit QS in various strands of Gram-negative bacteria. In this study, a library of acetophenones derivatives was tested for its reactivity in β-ketoester reactions to optimize overall yields. The functional group and regiochemistry of the β-ketoester library were analyzed to determine the impact on retention time, yield, lambda max, and UV-Vis properties during purification using a Biotage Isolera Automated Flash Chromatography System. The data obtained were compared to the properties calculated computationally for the library of acetophenone derivatives in order to further analyze the effects of polarity and regiochemistry on product yields, as well as trends associated with effect of polarity on retention time, and dipole moment compared to UV-Vis properties. Results from this study will provide predictive trends to enhance scale-up reactions in the production of final QS inhibitor analogues which will be required for biological testing conditions.