DESIGN AND SYNTHESIS OF 3,3,3-TRIFLUOROALANINE ANALOGUES AS POTENTIAL ANTIBACTERIALS

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O-Acetylserine Sulfhydrylase (OASS) is a pyridoxal 5'-phosphate (PLP) dependent enzyme that assimilates sulfur in bacteria by catalyzing the formation of *L*-cysteine from *O*-acetylserine. Inactivation of OASS could be exploited for new antibiotics' development [1,2].

We screened small library of halogenated alanines against OASS and found that 3,3,3-trifluoroalanine (**1**) acts as irreversible, although slow, inhibitor of this enzyme. Next, various analogues of 3,3,3-trifluoroalanine (**1**) were targeted to improve the inhibitory potency.

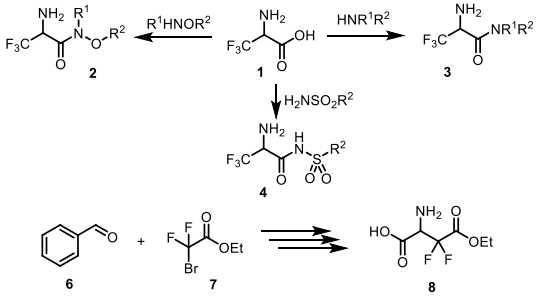

Figure 1. Synthesis of trifluoroalanine analogues

Analogues of carboxylic acid biosisosteric replacement such as hydroxamic acids, carboxamides and *N*-acyl sulfonamides **2-4** were prepared by classic and parallel synthesis. In addition, new practical synthesis of difluoroaspartic acid mono ester **8** was developed to obtain the analogue of fluorine replacement.

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1. W. S. Faraci and C. T. Walsh. *Biochemistry* **1989**, 431-437
2. Robert. L. Baxter et. al., *Org. Biomol. Chem.*, **2006**, 4, 1209–1212