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Synthesis and antibiofilm and antibacterial activity evaluation of Tetrahydroindolone-Dihydropyrimidinone hybrids

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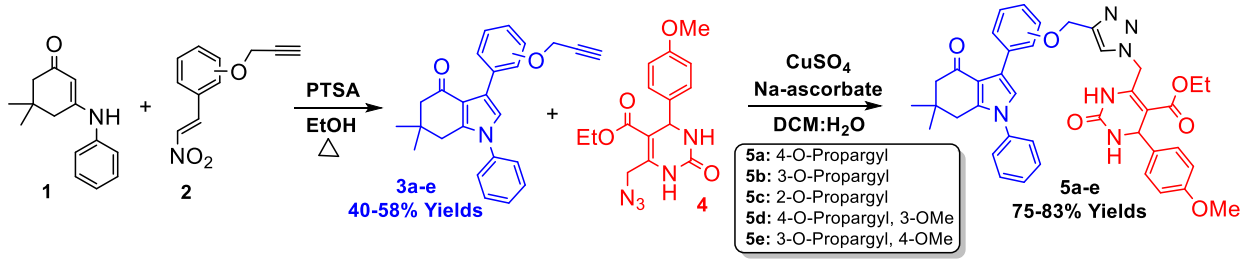
ABSTRACT

Tetrahidroindolones are important scaffolds in Medicinal Chemistry such as SNX2112, a heat shock protein (Hsp90) inhibitor and anti-cancer HER kinase dependent.[1] Likewise, Dihydropyrimidinones are bioactive compounds including antibacterial and anti-cancer activities.[2] The hybridization of bioactive compounds can lead to discovery of more efficient drugs with fewer side effects.[3] Thus, Click CuAAC reaction of THI **3a-e** and azido-DHPM **4** afforded the hybrids *THI-DHPM* **5a-e**.



Scheme 1: General scheme for the synthesis of THI-DHPM hybrid compounds **5a-e**.

Biofilms are complex communities of microorganisms that adhere to surfaces and are embedded in a self-produced extracellular matrix that hinder the action of antibiotics. The antibiofilm activity of compounds **5a-e** at 100 µg/mL were evaluated against *Staphylococcus aureus* by crystal violet method.[4]

Table 1. Antibiofilm Activity of Hybrids THI-DHPM **5a-e** against *S. aureus.*

Entry	Compound	% of Biofilm Inhibition
1	**5a**	73
2	**5b**	78
3	**5c**	89
4	**5d**	31
5	**5e**	28
6	**Vancomycin**	72

The initial results have demonstrated the ability of **THI-DHPM** hybrids to inhibit the biofilm formation and bacterial growth. The bioactivity against *Pseudomonas aeruginosa* and the dose-response curves are under investigation as well as the toxicity in the *in vivo* model of *Caenorhabditis elegans*.

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