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# Synthesis of Tetrahydroimidizalone-Dihydropyrimidinone hybrids

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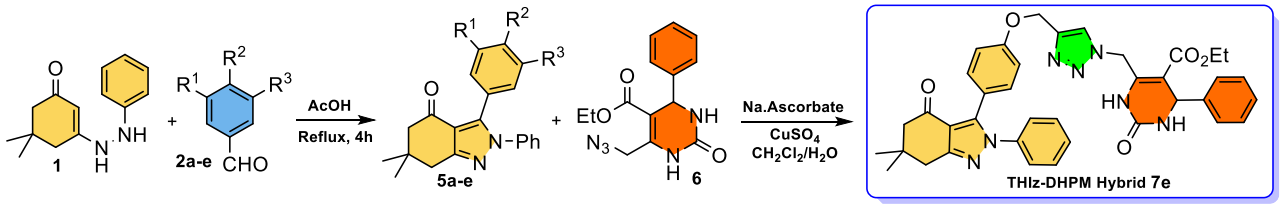
## ABSTRACT

Tetrahydroimidizalones (THIz) are important scaffolds in Medicinal Chemistry. They are active as protein kinases inhibitors,[1] anti-cancer agents[2] or antimicrobials.[3] Likewise, Dihydropyrimidinones (DHPM) are cytotoxic against several cancer cell lines.[4]

The hybridization of these two heterocyclic compounds may lead to the discovery of more efficient drugs with reduced side effects.[5] Thus, the easy access of THIz from the reaction of enamino-hydrazine **1** and substituted aldehydes **2a-e**, prompt us to prepare a set of 2,3-diaryl-tetrahydroindazol-4-ones **5a-e** in good yields. The click CuAAC reaction[6] of THIz **5e** and azido-DHPM **6** afforded the hybrid compound **7e** with a non hydrolyzable triazole link in 81% yield after purification (Scheme 1 and Table 1).




**Scheme 1:** General scheme for the synthesis of **THIz-DHPM** hybrid compounds **7e**.

**Table 1.** Yield of compounds **5a-e** and hybrid THIz-DHPM **7e**

| Entry | Compound | R1 | R2 | R3 | Yield (%) |
|---|---|---|---|---|---|
| 1 | **5a** | H | H | H | 70 |
| 2 | **5b** | H | OMe | H | 69 |
| 3 | **5c** | H | OMe | OMe | 72 |
| 4 | **5d** | OMe | OMe | OMe | 75 |
| 5 | **5e** | H | OPropargyl | H | 77 |
| 6 | **7e** | - | - | - | 79 |

The antibacterial and anticancer activities of THIz and THIz-DHPM hybrid against Gram positive/negative and a set of tumoral cell lines, respectively, are under current investigation.

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