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Design and Synthesis of a New Series of Pyrido[3,4-*b*]carbazole Derivatives

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ABSTRACT

Cervical cancer is considered the second most common malignant tumor in women globally, following breast cancer.[1] It is closely associated with infection by the Human Papillomavirus, which primarily infects squamous epithelial cells, leading to significant lesions and the potential development of malignancy.[2] Calothrixin B (**1**), an alkaloid isolated from the cyanobacterium *Calothrix*[1], is known for its potent inhibitory effect on cervical carcinoma cell line, with IC_{50} value observed at nanomolar concentration.[3,4,5] Based on the molecular hybridization technique, pyrido[3,4-*b*]carbazoles **3a-h** (Figure) were designed to combine structural features of the following compounds: Calothrixin B (**1**) and 7-fluorophenylamino-5,8-dioxo-5,8-dihydroisoquinoline (**2**), a quinone that exhibits cytotoxic activity against MRC-5, AGS, J82 and SK-MES-1 cells[6]. The synthesis of target compounds **3a-h** involved the palladium-catalyzed cross-coupling reaction of 7-arylamino-5,8-dioxo-5,8-dihydroisoquinoline-4-carboxylates **4a-h** (Scheme). Aromatic amines **5a–h** were transformed into the corresponding compounds **4a–h** by ultrasound-accelerated Michael addition to the electrophilic quinone, compound **6**, under cerium catalysis[7].

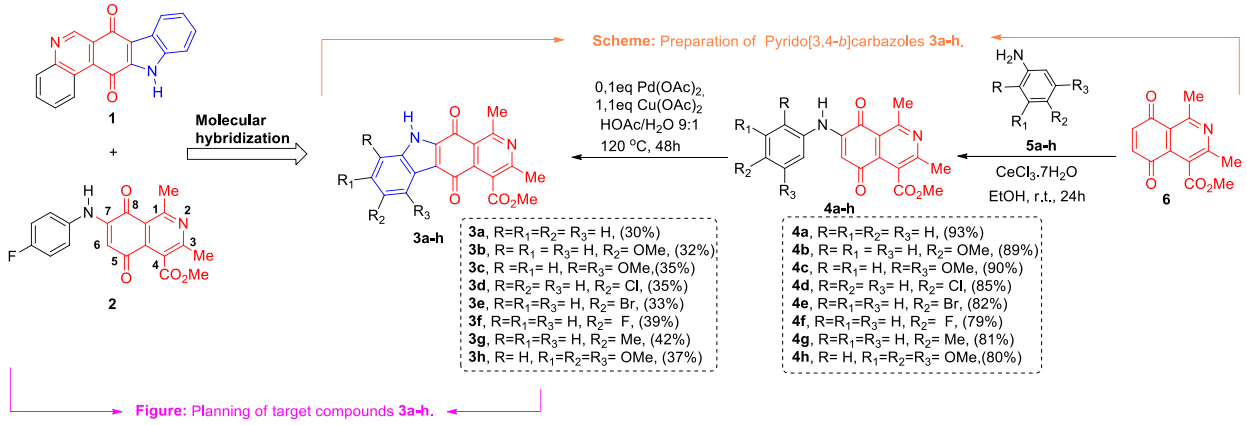

Figure: Planning of target compounds **3a-h.**

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