

SYNTHESIS OF 5-(3-(BENZYLOXY)-4-METHOXYBENZYL)-5,6,7,8-TETRAHYDRO-[1,3]DIOXOLO[4,5-G]ISOQUINOLINE DERIVATIVES

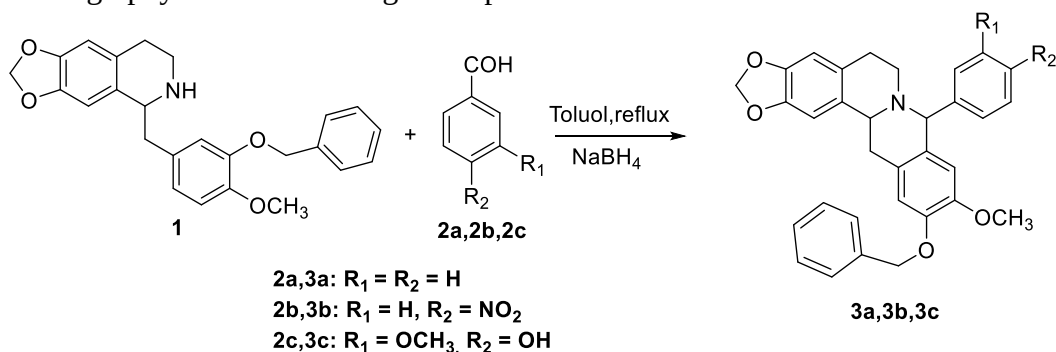
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Benzylisoquinoline alkaloids constitute one of the most important classes of naturally occurring biologically active compounds, characterized by a broad spectrum of pharmacological activities. Members of this class exhibit pronounced analgesic, antimicrobial, anti-inflammatory, antioxidant, antitumor, neuroprotective, and cardioprotective properties. Owing to this wide range of biological effects, 1-benzylisoquinoline alkaloids have attracted considerable attention as promising scaffolds in modern medicinal chemistry and pharmacology.

In the present study, the reactions of 5-(3-(benzyloxy)-4-methoxybenzyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g]isoquinoline with aromatic aldehydes were investigated. A series of new derivatives was synthesized, and the reaction behavior was examined with particular emphasis on the influence of the nature of substituents in the aromatic ring of the aldehydes on the formation of the target products.

A solution of 5-(3-(benzyloxy)-4-methoxybenzyl)-5,6,7,8-tetrahydro-[1,3]dioxolo[4,5-g] isoquinoline (**1**) 0.30 g, 0.74 mmol in toluene 10 mL was treated with the corresponding substituted benzaldehyde (**2a–c**) 0.89 mmol, and the reaction mixture was refluxed for 10 h. The progress of the reaction was monitored by thin-layer chromatography TLC. After completion of the reaction, the solvent was removed under reduced pressure. The resulting residue was dissolved in methanol 10 mL, cooled to 0–5 °C, and sodium borohydride NaBH₄, 0.15 g, 3.9 mmol was added portionwise. After completion of the reduction, the reaction mixture was concentrated under reduced pressure, and the crude product was triturated with acetone. The precipitated crude solid was collected by filtration, while the mother liquor was subjected to silica gel column chromatography to afford the target compounds.



Compound **3a**- as a white crystalline solid mp 238–240 °C, *R_f* 0.84, **3b**- was obtained as a yellow amorphous solid *R_f* 0.82, and **3c**- as a yellow crystalline solid mp 255–256 °C, *R_f* 0.80. The structures of the synthesized compounds were confirmed by mass spectrometry. The molecular masses of the obtained compounds were determined using an Acquity® QDa™ TLC-MS mass spectrometer (Waters). TLC-MS *m/z* 491.6499 [M+H]⁺ **3a**, TLC-MS *m/z* 561.8740 [M+Na]⁺ **3b**, TLC-MS *m/z* 560. 2662 [M+Na]⁺ **3c**.