Facile synthesis and antibacterial activity of some new 3,3′-bis(indolyl)arylmethane alkaloids

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Abstract: 3,3′-Bis(indolyl)methanes (BIMs) are found in natural products and are known to exhibit a broad range of biological activities. Although great success has been achieved in the synthesis of BIMs, some of the reported methods suffer from disadvantages such as the use of expensive and corrosive reagents, high catalyst loading and low yields of the products. In this work, FeCl₃·6H₂O is shown to be an efficient catalyst for the Friedel-Crafts reaction of aldehydes with a variety of indoles in methanol or acetonitrile under “open-flask” and mild condition. In the presence of 15 mol% of FeCl₃·6H₂O at room temperature, the reaction proceeds smoothly to afford some new 3,3′-bis(indolyl)arylmethane alkaloids in moderate to excellent yields. Moreover, all the twelve BIMs synthesized showed promising antibacterial activity against two Gram-positive bacteria namely, *Staphylococcus aureus* and *Bacillus subtilis*. Structure-activity relationship analysis revealed that hydroxyaryl substituted BIMs showed potent antibacterial activity. The 4-hydroxyphenyl linked 3,3′-bis(5-methoxy-1H-indol-3-yl)methane 3k (R₁ = 5-OMe, R₂ = 4-OH) was found to be the most potent antibacterial activities against both *S. aureus* and *B. subtilis*. The development of synthetic protocol will be useful for economical and ecofriendly synthesis of potent antibacterial BIM class of compounds.

Keywords: 3,3′-Bis(indolyl)arylmethane; FeCl₃·6H₂O; Indole; Antibacterial activity