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Antibacterial Evaluation of Some Synthetic 3,4-Dihydroisocoumarins

Hummera RAFIQUE * [1], Aamer SAEED [2] & Amara MUMTAZ [3]

[1] *Department of Chemistry, Univeristy of Gujrat, 50700, Gujrat, Pakistan*
[2] *Department of Chemistry, Quaid-i-Azam Univeristy, 45320, Islamabad, Pakistan*
[3] *Department of Chemistry, COMSATS IIT, Abbotabad, 22060, Pakistan*

SUMMARY. Synthesis of some 3,4-dihydroisocoumarins related to well known bioactive natural dihydroisocoumarins viz. scorzocreticin, annulatomarin and montroumarin, have been carried out starting from 3,5-dimethoxy-4-methylphenyl acetic acid. Homophthalic acid was condensed with various acid chlorides (a-e) to afford the corresponding 6,8-dimethoxy-7-methyl-3-arylisocoumarins (**2a-e**). The alkaline hydrolysis of isocoumarins yields keto-acids (**3a-e**), which were then reduced to hydroxyacids, followed by cyclodehydration with acetic anhydride furnish corresponding 3,4-dihydroisocoumarins (**4a-e**). Finally, demethylation of 3,4-dihydroisocoumarins was carried out to afford 6,8-dihydroxy-7-methyl-3-aryl-3,4-dihydroisocoumarins (**5a-e**). *In vitro* antibacterial screening of all the synthesized compounds were carried out against ten bacterial strains, and they display moderate activity towards various Gram negative and Gram positive bacteria, as compared to the standard drugs.

RESUMEN. A partir de ácido acético 3,5-dimetoxi-4-metilfenilo se ha llevado a cabo la síntesis de algunas isocumarinas 3,4-dihidro relacionadas con conocidas isocumarinas dihidro naturales bioactivas, a saber: scorzocreticina, annulatomarina y montroumarina. El ácido homoftálico se condensó con varios cloruros de ácido (a-e) para dar las correspondientes 6,8-dimetoxi-7-metil-3-arylisocoumarinas (**2a-e**). La hidrólisis alcalina de isocumarinas produce ceto-ácidos (**3a-e**), que después se reduce a hidroxiácidos, seguido por ciclodeshidratación con pasta de anhídrido acético para producir las correspondientes 3,4-dihydroisocoumarins (**4a-e**). Por último, la desmetilación de 3,4-dihydroisocoumarinas se llevó a cabo para proporcionar 6,8-dihidroxi-7-metil-3-aril-3,4-dihydroisocoumarinas (**5a-e**). El ensayo antibacteriano *in vitro* de todos los compuestos sintetizados se llevó a cabo contra de diez cepas bacterianas y muestran una actividad moderada hacia diferentes bacterias Gram positivas y Gram negativas, en comparación con los fármacos estándar.

KEY WORDS: antibacterial activity, 3,4-dihydroisocoumarin analogues, 3,5-dimethoxy-4-methylhomophthalic acid, natural products.

* Author to whom correspondence should be addressed. *E-mail:* humera_org@yahoo.com

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