Synthetic and Cytotoxic Studies on Alkyl 4-(3,4,5-trimethoxyphenoxy) benzoate

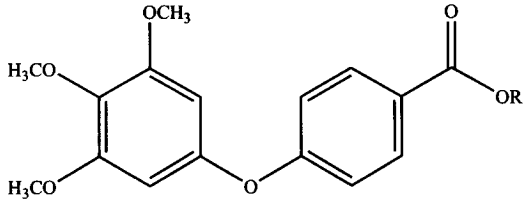
Wen-Yueh Ho (何文岳)[1], Chia-Hua Liang (梁家華)[1], Jui-Hsiang Hung (洪瑞祥)[1], Wen-Jong Vong (汪文忠)[1], Po-Jui Huang (黃博瑞)[2], Kuan-Han Lee (李冠漢)[1]*

[1]*College of Pharmacy and Science, Chia Nan University of Pharmacy and Science, Tainan 71710, Taiwan.*

[2]*Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Koahsiung 80708, Taiwan*

Diaryl ethers represent an important class of synthetic compounds recognized as potential anticancer drugs. Experimental and pre-clinical models have demonstrated that a number of these compounds elicit outstanding anticancer activity through the significant inhibition of tubulin assembly accompanied by potent antiproliferative activity. Moreover, the diaryl ether scaffold is found in a number of natural products and biologically important molecules, such as vancomycin and piperazinomycin. As a result of our continuing studies aimed at the discovery and development of potential anticancer agents, herein we report the synthesis, cytotoxic activities of a series of novel diaryl ethers.

Diaryl ether (**1**) was synthesized via Ullmann-type coupling. Palladium(II) acetate catalyzed *O*-arylation reactions have been carried out in non-polar solvent and used K_3PO_4 as the base. Saponification in ethanolic NaOH solution afforded the acid form (**2**). Both compound 1 and 2 were shown selective cytotoxic activity against A549 (Human lung adenocarcinoma epithelial cell line) with the IC_{50} values of 2.1 μM and 12.3 μM, respectively.



1: R=Et

2: R=H