SYNTHETIC STUDIES OF NOVEL SPIRO PYRAZOL-3-ONES CONTAINING QUINAZOLINE AND/OR OXIRANE MOIETY

Hayate Nagabuchi, Eiichi Masumoto, Fumi Okabe-Nakahara, and Hiroshi Maruoka

Faculty of Pharmaceutical Sciences, Fukuoka University, 8-19-1 Nanakuma, Jonan-ku, Fukuoka 814-0180, Japan

As a part of systematic investigation of synthesis and biological activities of substituted pyrazole derivatives [1], a novel series of spiro pyrazol-3-one derivatives containing quinazoline and/or oxirane moiety were synthesized. Quinazoline and its derivatives are an important class of heterocycles found in a wide range of natural products and pharmaceuticals. Therefore, the development of quinazoline-based drugs has renewed the interest in developing new synthetic strategies for the synthesis of quinazoline derivatives [2]. Epoxides, especially spiro epoxide-heterocycles, are also versatile building blocks for the synthesis of many bioactive natural products. Spiro epoxide derivatives are well-known carbon electrophiles and their ability to undergo regioselective ring-opening reactions contributes to their synthetic value [3]. In this work, we wish to report the preparation of spiro pyrazol-3-one derivatives [4] containing quinazoline and/or oxirane moiety.

Treatment of pyrazole-4,5-diones 1 with 2-aminobenzophenones 2 and ammonium acetate in boiling EtOH for 1 h under catalyst-free conditions caused three-component reaction to give the corresponding spiro pyrazol-3-one derivatives 4 containing quinazoline moiety in moderate to good yields. On the other hand, compounds 1 were reacted with phenacyl bromides 3 in the presence of Et3N in EtOH at room temperature for 1 h to afford the corresponding spiro pyrazol-3-one derivatives 5 containing oxirane moiety in moderate to good yields. All the synthesized compounds were characterized by spectroscopic analysis.