SYNTHESIS OF ANTILEUKEMIC BENZO[c]PHENANTHRIDINE ALKALOIDS HAVING A PHENOLIC GROUP: PROTECTION OF A PHENOL AS AN ISOPROPOXY GROUP AND INTRAMOLECULAR ACYLATION UNDER BASIC CONDITION

Hisashi Ishii, Ih-Sheng Chen, and Tsutomu Ishikawa
Faculty of Pharmaceutical Sciences, Chiba University, 1-33, Yayoi-cho, Chiba 260, Japan

In the course of the studies on the development of a versatile method for the synthesis of antitumor-active benzo[c]phenanthridine alkaloids, we have established the synthetic sequence for nonphenolic alkaloids, shown in Chart 1. This sequence involves steps of hydrogenolysis of the keto acid (2) to the 4-arylbutyric acid (3) and of intramolecular cyclization of 3 under acidic condition. Since the commonly protecting group for these steps could not be found, our sequence was applicable in the case of phenolic base. Recently, however, we have found that the isopropoxy group can be used for this purpose even in the case of the phenolic bases having an OCH_2O group. In some cases, the isopropoxy group was still subject to cleave by treatment with $POCl_3$ in $CHCl_3$, a general procedure for the intramolecular acylation. However, this cleavage reaction could be avoided when the similar treatment was achieved in the presence of K_2CO_3, demonstrating a basic intramolecular acylation of 3. We succeeded in synthesis of fagaronine (7a), a naturally occurring antileukemic alkaloid, and oxyterihanine (8), a structurally unestablished alkaloid newly isolated from Xanthoxylum nitidum by us, in good yields.

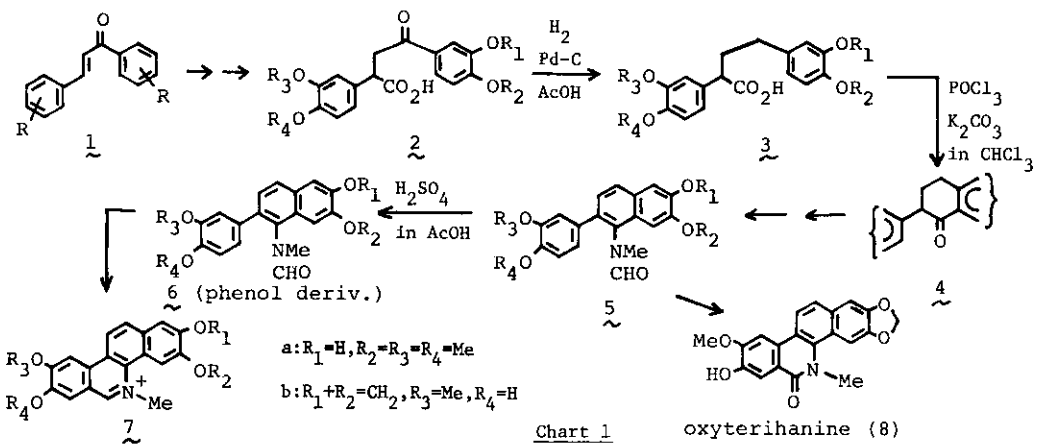

Chart 1