New Syntheses of Antitumor Benzo[c]phenanthridine Alkaloids: Nitidine and Fagaronine

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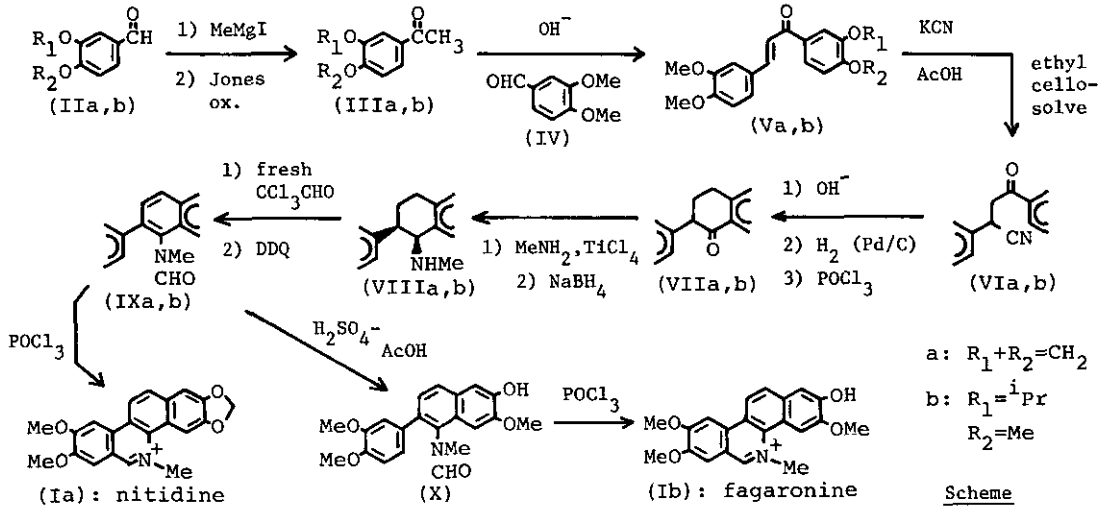
It is well known that nitidine (Ia) and fagaronine (Ib) are fully aromatized benzo[c]phenanthridine alkaloids having strong antitumor activities against various types of experimental tumors (L1210, P388, and S180A). These alkaloids (Ia,b) were synthesized from the corresponding chalcones (Va,b) according to our synthetic sequence for benzo[c]phenanthridine alkaloids as shown in the Scheme. Although our method originated from the Robinson method*) for benzo[c]-phenanthridine alkaloids, the synthetic sequence from the 2-aryl-1-tetralone derivatives (VII) to the desired quaternary bases (I) is completely different from the original method. Nitidine (Ia) and fagaronine (Ib) were synthesized in the 40.2% and 28.1% yields based on the starting chalcones (Va,b), respectively, in our works. It should be noted here that the synthetic yields of these alkaloids (Ia,b) were tremendously improved, compared with the reported yields of these alkaloids through other methods. This improvement allows us to investigate the structure-activity relationship on benzo[c]phenanthridine alkaloids (I). In this meeting, we will present our experimental results on nitidine (Ia) and fagaronine (Ib) as representatives.



*) T. Richardson, et al., J. Chem. Soc., 1937, 835; H. R. Arthur, et al., ibid., 1959, 4010, K. W. Gopinath et al., ibid., 1959, 4012; K.-Y. Zee-Cheng, J. Heterocycl. Chem., 10, 85 (1973).