Improved Enamine-type Addition of Dehydroaporphine Using Microwave Irradiation

Chih-Chiang Huang (黃志強)[a], Shoei-Sheng Lee (李水盛)[b*], Wei-Jan Huang (黃偉展)[a*]

[a]*Graduate institute of pharmacognosy, Taipei Medical University, Taipei 115, Taiwan, , R. O. C.*

[b]*School of Pharmacy, College of Medicine, National Taiwan University, Taipei 100, Taiwan, R. O. C.*

Previous report demonstrated that 7-substituted aporphine, possessing interesting biological aspects, could be synthesized via an enamine-type addition of dehydroaporphine reacted with an electrophile, but it has the drawbacks of a long reaction time, low yield, and limitation to reactive electrophiles. Here we found that the reaction time and yield could greatly be improved under microwave irradiation in the presence of 4 equiv of sodium iodide for the synthesis of 7-benzyl dehydroglaucine. The application of this finding for treating dehydroglaucine with a variety of alkyl bromides also gave corresponding 7-substituted dehydroglaucines (2a–j) with yields of 14–89%. Other enamines such as 1,10-dimethoxydehydroaporphine (3a), 2,9-diacetyldehydroboldine (3b), and 7,8-dihydroberberine (5) were found to react with benzyl bromide under similar conditions as described above to give corresponding products (4a–b, 6) in satisfactory yields, indicating the versatility of this improved reaction condition.

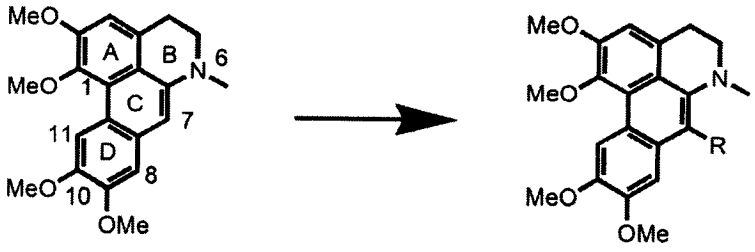

Figure 1. Synthesis of 7-substituted dehydroglaucines via an enamine-type addition.