A NEW UTILIZATION OF FURAN IN THE SYNTHESIS OF ALKALOIDS

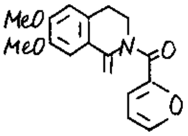
Takeaki Naito, Okiko Miyata, Noriko Kojima, and Ichiya Ninomiya
Kobe Women's College of Pharmacy
Motoyamakita, Higashinada, Kobe 658, Japan

Both Ipecac and heteroyohimbine alkaloids have benzo- and indoloquinolizine nuclei bearing common C_2-units at both 2- and 3-positions. We describe a general strategy applicable to the total synthesis of both members of alkaloids by using a furan ring as a building block for the introduction of C_2-units into the alkaloid skeleton.

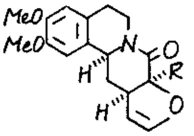
Reductive photocyclization of the enamide (1), prepared from furan-2-carbonyl chloride, proceeded smoothly to give the desired furanoquinolizine (2a) in good yield. Lithiation of (2a) by LDA at -78°C followed by quenching with either ethyl iodide or acetic anhydride afforded stereospecifically the lactams (2b or c) which contain a versatile benzoquinolizine nucleus bearing C_2-units at both 2- and 3-positions.

For the synthesis of emetine, conversion of the furanoquinolizine (2b) into the synthetic intermediate (4a) was achieved effectively by three reaction steps. Hydration of the dihydrofuran (2b) followed by oxidation of the resulting hemiacetal with PCC gave the γ-lactone (3a) which was subjected to reductive cleavage by calcium in liquid ammonia to afford the known carboxylic acid (4a).

Similarly, the acetyl furan (2c) was smoothly converted into (4b) which was then reduced with diborane to yield the lactones (5a and b), which are the compounds having identical partial structure (ring C,D,E) with the known key intermediate for ajmalicine, thus established a potential synthetic route to the alkaloids.

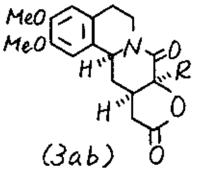


(1)



(2abc)

a:R=H, b:R=Et, c:R=Ac



(3ab)

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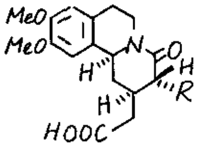

(4ab)

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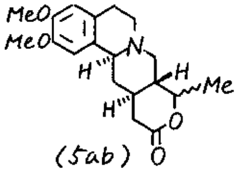

(5ab)

a:α-Me, b:β-Me