SYNTHESIS OF (±)-β-HYDRASTINE *via* 8,13a-EPIDIOXY-13-OXO-CANADINE

Yoshikazu Kondo, Jiro Imai, and Shigeo Nozoe

Pharmaceutical Institute, Tohoku University

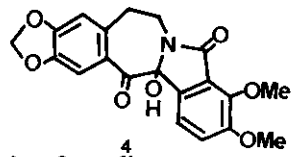
Aobayama, Sendai, Japan

When viewed the phthalideisoquinoline alkaloids in the light of biogenetic routs in the plant, they arised by modification of the tetrahydroprotoberberine skeleton[1]. We have previously shown that 7,8-dihydroberberine derivatives are important intermediates in the syntheses of 13-hydroxyberbine[2] and phthalideisoquinoline[3] due to their propensity to quench singlet oxygen with regioselectivity. As a continuous study on the conversion of berberine alkaloids into other-type alkaloids, we would like to report the synthesis of (±)-β-hydrastine from berberinium chloride.

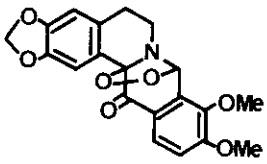
The selective oxygenation of dihydroberberine to an epidioxide, 8,13a-epidioxy-9,10-dimethoxy-2,3-methylenedioxy-13-oxo-dibenzo[a,g]quinolizidine 1, provided the desirability of reactive oxygen substituents[2]. When 1 was treated with pyridinium chloride in pyridine, 1-hydroxy-dehydronorhydrastine 2 (42%), 13a-hydroxy-9,10-dimethoxy-2,3-methylenedioxy-8,13-dioxo-dibenzo[a,g]quinolizidine 3 (40%), 7,8-dihydro-13-hydroxy-3,4-dimethoxy-10,11-methylenedioxy-5,13a-dioxo-5H-isoindolo[1,2-b][3]benzazepine 4 (4%), and norhydrasinine (10%) were obtained. On the other hand, treatment of 1 with sodium methoxide in methanol gave the rearranged isomer 4 (85%) rather than desired products 2 or 3. Compound 2 was treated with CH_3I followed by reduction with $NaBH_4$ to give (±)-β-hydrastine 5 in good yield (80%), while compound 3 has been already derived to 5 by Shamma et al[4].

Although some other syntheses of the phthalideisoquinoline alkaloids have been reported, the preparations descrived herein include following advantages; a) simple procedures b) sufficiently good yields(over 70%) in each stage.

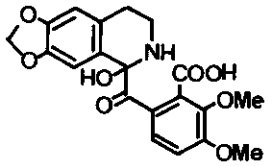
Some related experiments are also discussed.



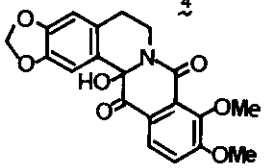
4



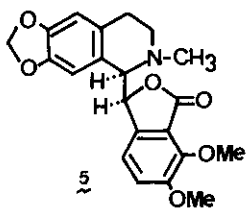
1



2



3



5

1) A. R. Battersby, J. Staunton, H. R. Wiltshire, R. J. Francis, and R. Southgate, *J. Chem. Soc. Perkin I, 1147 (1975).* 2) Y. Kondo, H. Inoue, and J. Imai, *Heterocycles, 6, 953 (1977).* 3) J. Imai and Y. Kondo, *Heterocycles, 6, 959 (1977).* 4) M. Shamma, D. M. Hindenlang, T.-T. Wu, and J. L. Moniot, *Tet. Lett., 4285 (1977).*