

SYNTHESIS OF (+)- $\beta$ -HYDRASTINE *via* 8,13a-EPIDIOXY-13-OXO-CANADINE

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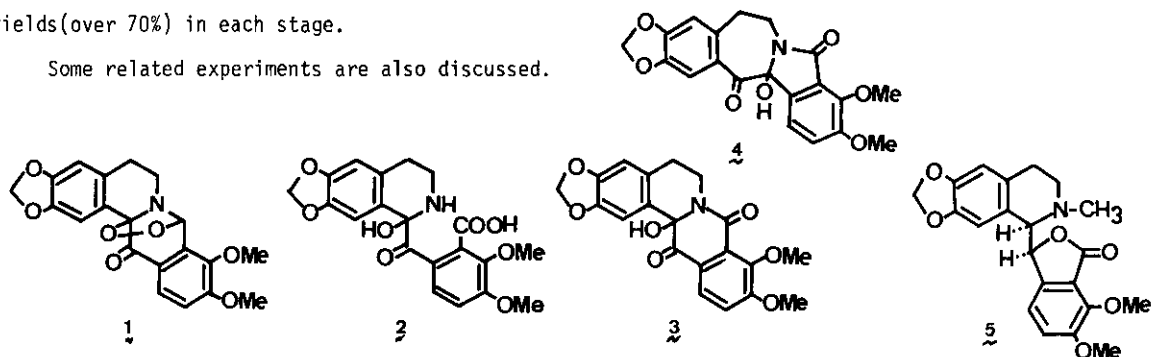
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When viewed the phthalideisoquinoline alkaloids in the light of biogenetic routes in the plant, they arise by modification of the tetrahydroprotoberberine skeleton<sup>1)</sup>. We have previously shown that 7,8-dihydroberberine derivatives are important intermediates in the syntheses of 13-hydroxyberberine<sup>2)</sup> and phthalideisoquinoline<sup>3)</sup> 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 (+)- $\beta$ -hydrastine from berberinium chloride.

The selective oxygenation of dihydroberberine to an epidioxide, 8,13a-epidioxo-9,10-dimethoxy-2,3-methylenedioxy-13-oxo-dibenzo[a,g]quinolizidine **1**, provided the desirability of reactive oxygen substituents<sup>2)</sup>. 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 norhydrastinine (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  $\text{CH}_3\text{I}$  followed by reduction with  $\text{NaBH}_4$  to give (+)- $\beta$ -hydrastine **5** in good yield (80%), while compound **3** has been already derived to **5** by Shamma et al<sup>4)</sup>.

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

Some related experiments are also discussed.



- 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).