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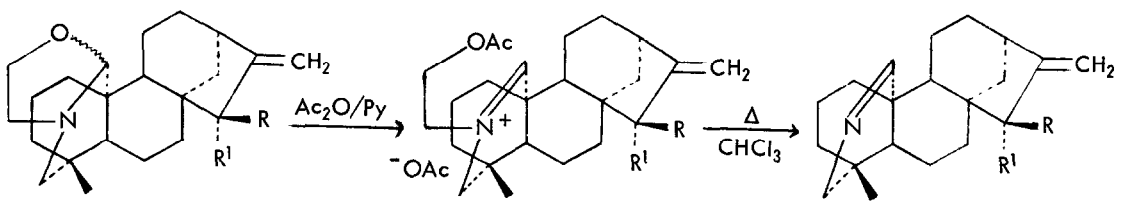
A SIMPLE AND EFFICIENT METHOD FOR THE DEGRADATION OF THE OXAZOLIDINE RING OF C_{20}-DITERPENOID ALKALOIDS

Naresh V. Mody and S. William Pelletier*

Institute for Natural Products Research and the Department of Chemistry,

University of Georgia, Athens, Georgia 30602, U.S.A.

Recently we have isolated[1] two new, closely-related C_{20}-diterpenoid alkaloids, ovatine (1) and lindheimerine (2), from Garrya ovata var. lindheimeri. Lindheimerine (2) occurs in an extremely small quantity and because we needed this alkaloid and related compounds for preparing some synthetic analogs we were prompted to investigate a simple, high-yield method for degrading the oxazolidine-ring in ovatine to the corresponding imine derivative. An earlier reported[2] method for this type of degradation involves four steps and in our hands proceeds with erratic yields.[3]



1 R = OAc; R^1 = H

3 R = OH; R^1 = H

4 R = H; R^1 = OH

5 R = OAc; R^1 = H

2 R = OAc; R^1 = H

6 R = H; R^1 = OAc

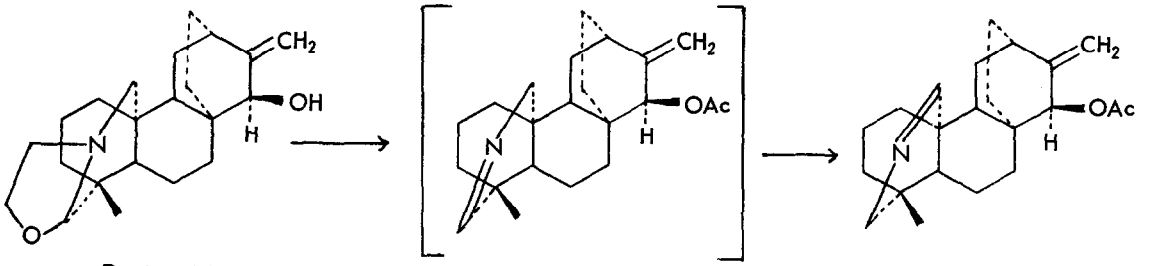
We now report a convenient and high-yield method for converting the oxazolidine-ring containing alkaloids, e.g., ovatine (1), garryfoline (3), veatchine (4), into their corresponding imine derivatives. Our recent findings[4] about the abnormal behavior of the oxazolidine ring of atisine and related alkaloids prompted us to examine the treatment of these alkaloids with Ac_2O and pyridine. Treatment of ovatine or garryfoline with Ac_2O and pyridine gave a chloroform-soluble diacetate salt[5] (5) in quantitative yield. A Hofmann-type degradation of 5 was achieved by refluxing it in chloroform to give lindheimerine (2) in a 90% yield. Table 1 summarizes the results of the degradation of various oxazolidine-ring containing alkaloids by this method. The normal-type oxazolidine-ring containing alkaloids afforded higher yields in comparison with the iso-oxazolidine-ring containing alkaloids. In the case of the iso-type alkaloids, the iso-imine derivative (e.g. 8) probably forms and is subsequently isomerized to the normal imine derivative (e.g. 9). In a typical experiment, 100 mg of ovatine was dissolved in 5 ml of dry pyridine and 3 ml of Ac_2O and stirred for 14 hr. at r.t. Excess pyridine and Ac_2O was removed completely in vacuo at 50° by flashing with abs. ethanol and dry benzene several times to give diacetate salt (5) in quantitative yield. Without further purification,

compound 5 was refluxed in 25 ml of chloroform for 8 hours[6] to give lindheimerine in a 90% yield.

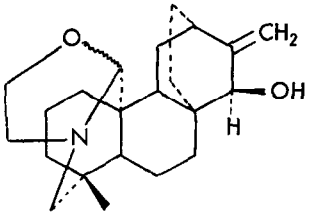
Table 1 Degradation Products of Various Alkaloids

Starting Compound	Product*	Isolated Yield
Atisine (10)	Atisine azomethine acetate (9)	91%
Garryfoline (3)	Lindheimerine (2)	90%
Garryine (11)	Veatchine azomethine acetate (6)	49%
Isoatisine (7)	Atisine azomethine acetate (9)	52%
Ovatine (1)	Lindheimerine (2)	90%
Veatchine (4)	Veatchine azomethine acetate (6)	89%

*The final product of each alkaloid was compared with an authentic sample.



7 Isoatisine 8 9



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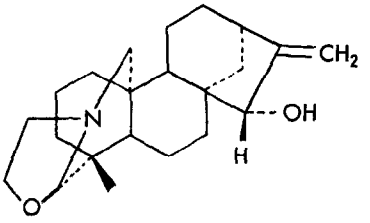

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REFERENCES

1. S. W. Pelletier, N. V. Mody and D. S. Seigler, unpublished results.
2. D. Dvornik and O. E. Edwards, Can. J. Chem., 35, 860 (1957).
3. During several experiments with atisine and veatchine yields using the earlier method ranged from 30 to 65%. We were unable to get consistent yields. Because of the strong base used, side reactions occur leading to closure of the oxazolidine ring and subsequent isomerization to the iso-alkaloid.
4. S. W. Pelletier and N. V. Mody, Tetrahedron Letters, 325 (1977).
5. The structures of the acetylation products were confirmed by ^{13}C NMR spectroscopy.
6. The time required for the degradation depends on the concentration of the ternary iminium salt in $CHCl_3$.

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