[Chem. Pharm. Bull. 26(2) 678—679 (1978)]

UDC 547.759.04 : 547.291.04

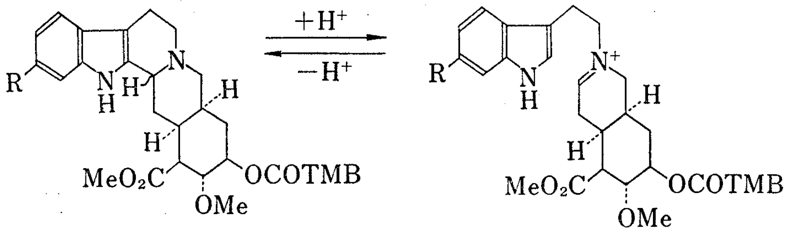
The C2-C3 Bond Cleavage Reaction of Indole Alkaloids

Several 2,3-seco-2,3-dihydroindole alkaloids were prepared from indole alkaloids through reduction with a 1 : 2 mixture of formic acid and formamide.

Keywords——indole alkaloids; reductive bond cleavage; 2,3-seco-2,3-dihydroindole alkaloids; formic acid-formamide; reserpine

Le Men, *et al.* have already reported the reductive C–C bond cleavage reaction of aspidosperma (indolenine type) alkaloids¹⁾ and oxindole alkaloids²⁾ by use of formic acid and formamide as the reagents. In the both cases the reagents are considered to reduce the immonium type double bond in the possible reaction intermediates.

On the other hand, Gaskell and Joule proposed a mechanism of acid catalized epimerization of reserpine (Ia) and deserpidine (Ib) *via* the intermediates (IIa, b) having an immonium type double bond (Chart 1). From reserpine (Ia) and isoreserpine (Ic), crystalline 3,4-dihydroreserpine (III) (in 9.6% yield) and amorphous 2,3-seco-2,3-dihydroreserpine (IV) (in 0.16% yield) were obtained by reduction with zinc and acetic acid under reflux under N_2 for 24 hr.³⁾

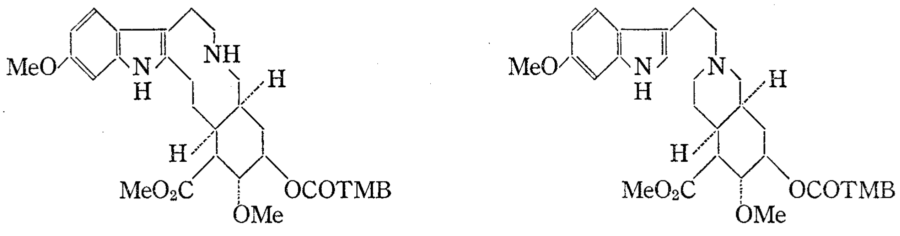


TMB = 3,4,5-trimethoxyphenyl

Ia: R=OMe C3 β H
Ib: R=H C3 β H
Ic: R=OMe C3 α H

IIa: R=OMe
IIb: R=H

Chart 1



III IV

Chart 2

We wish to report that Ia was reduced to IV in a far better yield (in 53% yield) than above accompanied by epimerization to Ic by use of formic acid and formamide (1 : 2 v/v) under reflux for 4 hrs. Since there was obtained no evidence of formation of III, the above

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2) F. Sigaut-Titeux, L. Le Men-Olivier, J. Lévy, and J. Le Men, *Heterocycles*, **6**, 1129 (1977). We thank Prof. Le Men for a private communication about the above paper prior to publication.
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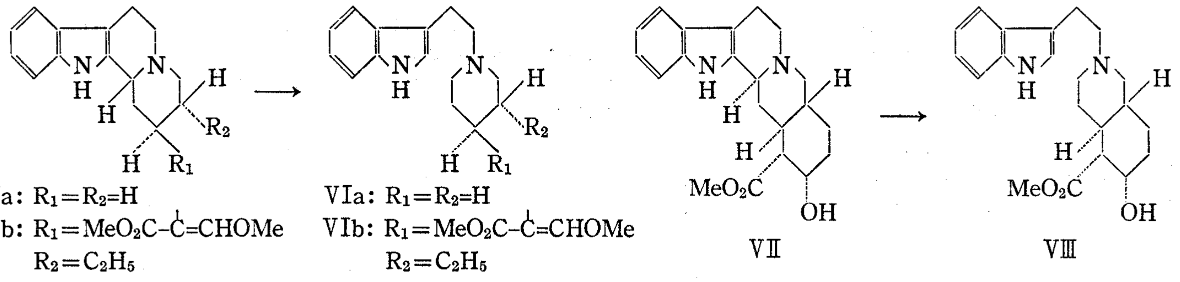
mechanism postulating an equilibrium (Ia, b⇄IIa, b) under the reaction condition was supported. Seco derivative (IV) exhibited M^+ m/e 610 (5%) and base peak 450 (100%) in the mass spectrum and the signals at δ 3.51, 3.72, 3.79 and 3.91 (total $6\times3H$, OCH_3) in the nuclear magnetic resonance spectrum. Seco derivative (IV) will be able to be used as a key compound⁽⁴⁾ for synthesis of various kinds of aromatic substituted reserpines.



Va: $R_1=R_2=H$
Vb: $R_1=MeO_2C\text{-}\overset{|}{C}{=}CHOMe$
$R_2=C_2H_5$

VIa: $R_1=R_2=H$
VIb: $R_1=MeO_2C\text{-}\overset{|}{C}{=}CHOMe$
$R_2=C_2H_5$

VII

VIII

Chart 3

Indoloquinolizidine (Va) was reduced more slowly than reserpine (Ia). 3-(β-Piperidino)-ethyl indole (VIa) (mp 152°)⁽⁵⁾ was obtained in 78% yield from Va with the same reagent under reflux for 28 hr.

Hirsutine (Vb) was reduced to 2,3-seco-2,3-dihydrohirsutine (VIb) (in 10% yield) which had been derived from rhynchophylline by another method in this laboratory.⁽⁶⁾ In the same reaction condition, yohimbine (VII) gives known 2,3-seco-2,3-dihydroyohimbine (VIII) (mp 108—109°, in 8% yield), which was shown to be identical with an authentic sample.⁽⁶⁾

This procedure forms a new general method 2,3-seco-2,3-dihydroindole alkaloids from indole alkaloids.

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Received December 3, 1977

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