

Synthetic Studies in the Field of Oxyajmalane Alkaloids

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(Received 13th May, 1993, revised 11th August, 1993)

Summary: Some new oxidation products of ajmalane alkaloids have been synthesized by their reaction with hydrogen peroxide and are characterized by spectroscopic methods.

Introduction

Ajmalane alkaloids constitute a group of indolinic carbinolamines with a nitrogen at a bridgehead and, therefore, undergo reactions of an aldehydeimine as well. We have utilized this property of ajmalane alkaloids towards one pot synthesis of ajmaline-21-carboxylic acid [1]. In this communication we wish to report some new oxidation products of ajmalane alkaloids which have been confirmed on the basis of their spectral studies. Oxidation of ethanolic solution of ajmalane alkaloids namely ajmaline (1), N-methyl ajmaline (2), N-methyl hexahydro ajmaline (3), isoajmaline (4), hexahydro isoajmaline (5), and sandwicine (6) with hydrogen peroxide at 120°C for 45-60 minutes afforded the corresponding 17-keto compounds (7-12) respectively, as the major products in good yields. These compounds showed strong absorption bands of ketonic group in the range of 1725-1740 cm^{-1} in their IR spectra. In a different experiment compound (1-3) on direct oxidation with hydrogen peroxide under slightly acidic conditions provided the corresponding 21-carboxylic acids (13-15) while compounds (4-6) did not give the same results under similar experimental conditions.

Compounds (13-15) showed acidic protons in proton NMR spectra at 10.97, 10.93 and 10.92 ppm respectively. These results are in agreement to that obtained in our previous studies [1] and indicated that the carbinol-amine and aldehyde-imine tautomerism does not operate to a considerable extent in ajmaline epimers, isoajmaline and sandwicine, under the experimental conditions described here. Pharmacological screening of all the compounds are under investigations.

Experimental

Mass spectra were measured on Finnigan MAT 112S Mass spectrometer. The proton NMR spectra were recorded on Bruker AM-400 Spectrometer with

the TMS as internal reference while IR spectra were taken on JASCO IRA-I Spectrometer.

General procedure for the syntheses of compounds (7-12)

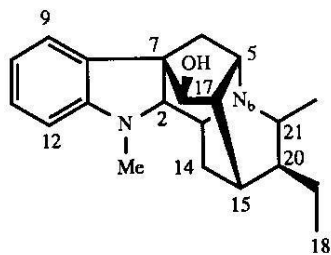
The compounds (1-6) (1.53 mmol in 5 ml ethanol) were added in H_2O_2 (326 mmol) and heated at 120°C for 45-60 min as indicated in the Table 1. TLC monitoring represented two spots which were identified as simple N_6 -oxides by comparing with the standards and the 17-keto-compounds (7-12) as the major oxidation products. These compounds were purified by preparative layer chromatography using solvent system *n*-BuOH:MeOH (9.5:0.5).

Table 1: Reaction of ajmaline alkaloids with hydrogen peroxide

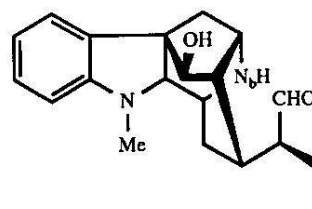
Compound	Reaction Time (min)	Product	[M] ⁺ m/z
1	45	17-Ajmalone- N_6 -oxide (7)	340
		Ajmaline-21-carboxylic acid (13)	342
2*	45	N-Methyl-17-ajmalone (8)	338
		N-Methyl ajmaline-21 carboxylic acid (14)	356
3*	60	N-Methyl-17-hexahydroajmalone (9)	344
		N-Methyl-hexahydroajmaline-21-carboxylic acid (15)	362
4	45	17-Isoajmalone- N_6 -oxide (10)	340
5	60	17-Hexahydroisoajmalone- N_6 -oxide 11	346
6	45	17-Sandwicone- N_6 -oxide 12	340

*In case of compounds (2) and (3) traces of keto-N-methyl- N_6 -oxyajmalane alkaloids were also formed.

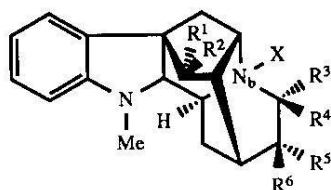
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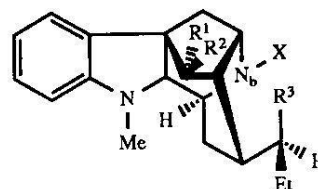
1 Carbinol amine form



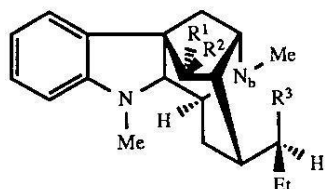
Aldehyde imine form



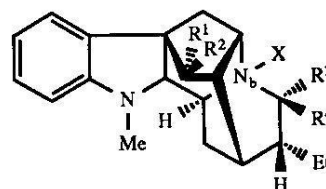
- 1 $R^1 = R^3 = OH; R^2 = R^4 = R^5 = H; R^6 = Et; X = -$
 4 $R^1 = R^4 = OH; R^2 = R^3 = R^6 = H; R^5 = Et; X = -$
 6 $R^2 = R^3 = OH; R^1 = R^4 = R^5 = H; R^6 = Et; X = -$
 7 and 12 $R^1, R^2 = O; R^3 = OH; R^4 = R^5 = H; R^6 = Et; X = O$
 10 $R^1, R^2 = O; R^3 = R^6 = H; R^4 = OH; R^5 = Et; X = O$



- 2 $R^1 = OH; R^2 = H; R^3 = CHO; X = Me$
 8 $R^1, R^2 = O; R^3 = CHO; X = Me$
 13 $R^1 = OH; R^2 = X = H; R^3 = CO_2H$
 14 $R^1 = OH; R^2 = H; R^3 = CO_2H; X = Me$



- 3 $R^1 = OH; R^2 = H; R^3 = CHO$
 9 $R^1, R^2 = O; R^3 = CHO$
 15 $R^1 = OH; R^2 = H; R^3 = CO_2H$



- 5 $R^1 = R^4 = OH; R^2 = R^3 = H; X = -$
 11 $R^1, R^2 = O; R^3 = H; R^4 = OH; X = O$

General procedure for the syntheses of compounds (13-15)

The compounds (1-3) (1.53 mmol) were added in H_2O_2 (326 mmol) and the heated under slightly acidic conditions on boiling water bath for 30 minutes. The remaining H_2O_2 was evaporated under reduced pressure and the residue was taken up in methanol. Addition of ethyl acetate followed by ether gave white precipitates which were filtered and dis-

solved in methanol. After sometime ajmalane-21-carboxylic acids (13-15) separates out which were identified by the appearance of acidic proton in their NMR spectra. Compounds (4-6) could not be oxidized in a similar fashion.

References

1. M. A. Khan and Z. Ahmad, *J. Synthetic Commun.*, 17(12), 1459 (1987).