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The Partial Synthesis of Heteroyohimbine Alkaloids; Akuammigine, 3-Isorauniticine and Corynanthé Alkaloid; Corynantheidine

Heteroyohimbine alkaloids, akuammigine and 3-isorauniticine, were synthesized using a modified Polonovski reaction followed by $NaCNBH_3$ reduction from desmethylhirsuteine N-oxide, which was derived from the indole alkaloid hirsuteine.

Corynanthé alkaloid, corynantheidine was also synthesized using the same method from hirsuteine N-oxide.

Keywords——partial synthesis; heteroyohimbine alkaloids; corynanthé alkaloid; modified Polonovski reaction; N-oxide; chemical transformation

In the previous paper,[1] we have reported a new intramolecular cyclization of desmethylhirsutine N-oxide (**2**) using a modified Polonovski reaction leading to dihydromancunine (**7**). We have extended this study starting from hirsuteine (**3**) which was contained in *Uncaria rhynchophylla* Miq. together with hirsutine (**1**), akuammigine (**12**) and other indole and oxindole alkaloids. Recently, syntheses of heteroyohimbine alkaloids from tryptamine and secologanin were reported *in vitro*[2] and *in vivo*.[3] In this communication we report a new synthesis of heteroyohimbine alkaloids, **12** and its 19-epimer 3-isorauniticine (**11**), and conversion of **3** to corynantheidine (**17b**).

Demethylation of **3** with acetone–HCl gas[4] gave desmethylhirsuteine (**4**, mp 180—182°) in 87% yield, which was oxidized with *m*-chloroperbenzoic acid (*m*-CPBA) in $CHCl_3$ to give desmethylhirsuteine N-oxide (**5**, mp 209—211°). The modified Polonovski reaction of **5** was accomplished in excess trifluoroacetic anhydride in CH_2Cl_2 under cooling with dry ice-acetone. The reaction products were reduced with $NaCNBH_3$ in dimethylformamide and phosphate buffer solution at pH 5 (1:1 v/v) for 4 hr.

Chromatography of the reaction products on alumina gave an amorphous compound A (HCl salt, mp 280—281°) in 4% yield as the first eluant. The mass spectrum of A exhibited M^+ at *m/e* 352 indicating that it has the same molecular weight as **4**, and the fragment pattern suggested the heteroyohimbine structure.[5] The ^{1}H-nuclear magnetic resonance (^{1}HNMR) spectrum of A showed the characteristic signals of heteroyohimbine E ring [$C\underline{H}_3OOC$–C=C$\underline{H}$–O–C$\underline{H}$–C$\underline{H}_3$, δ 3.78 (3H, s), 7.69 (1H, s), 4.16 (1H, q, J=7 Hz, 19 αH), 1.38 (3H, d, J=7 Hz, 18 CH_3)].

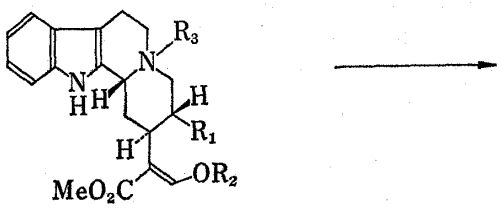
Since there was no C-3H signal below δ 4.0 the C/D *trans* ring juncture was deduced.

A decoupling experiment irradiating at C-18CH_3 signal revealed that the coupling constant between C-19H and C-20H was practically zero suggesting that D/E should be *cis* and C-19 αH configurations. Through analysis of these spectral data was assumed the structure **11** for A, and direct comparison of A with an authentic specimen of 3-isorauniticine (**11**)[6] proved their complete identity (infrared (IR), mass, and circular dichroism (CD) spectra).

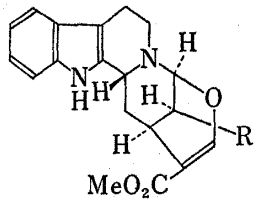
1) S. Sakai and N. Shinma, *Chem. Pharm. Bull.* (Tokyo), **25**, 842 (1977).
2) R.T. Brown, J. Leonard, and S.K. Sleigh, *Chem. Comm.*, **1977**, 636; J. Stöckigt and M.H. Zenk, *Chem. Comm.*, **1977**, 646.
3) M. Rueffer, N. Nagakura, and M.H. Zenk, *Tetrahedron Lett.*, **1978**, 1593.
4) A. Chatterjee and P. Karrer, *Helv. Chim. Acta.*, **33**, 802 (1950).
5) M. Hesse, "Progress in Mass Spectrometry," Vol. 1, "Indole Alkaloid," ed. H. Budzikiewiz, Verlag Chemie, Germany, 1974, pp. 126—132.
6) J. Melchio, A. Bouquet, M. Pais, and R. Goutarel, *Tetrahedron Lett.*, **1977**, 315. We thank Dr. M. Pais, Institut de Chemie des Substances Naturelles, CNRS, Gif/Yvette, for generous gift of 3-isorauniticine and for his information and identification of this alkaloid. In the same letter he informed us that he also succeeded in transforming geissoschizine N-oxide to tetrahydroalstonine and 3-isoajmalicine in the essentially same way as ours.

The second product was an amorphous heteroyohimbine B (11%) which showed the same IR, ^{1}HNMR, mass and CD spectra with those of an authentic akuammigine (**12**).

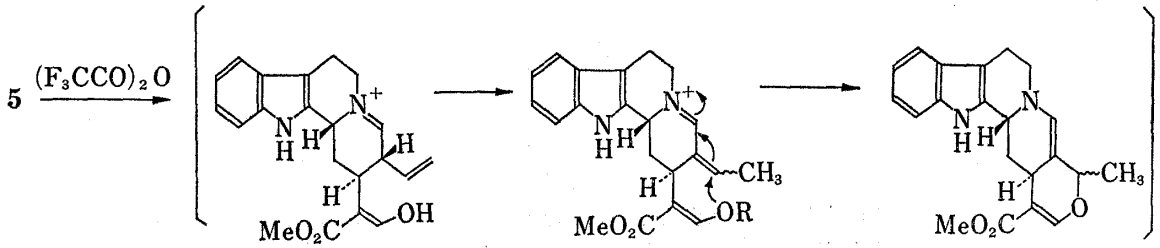
Compound B epimerized to tetrahydroalstonine (**13**, mp 218—219°) in hot acetic acid as expected. The formation of these heteroyohimbine alkaloids can be explained by a process of **8**→**10** as shown in Chart 1. The third compound, C (18%) was converted to crystalline dihydrocorynantheine (**16**, mp 102—104°) by methylation followed by catalytic reduction, which showed that the compound C should be desmethylcorynantheine (**14**). It is obvious



1 : R_1=C_2H_5, R_2=CH_3, R_3=none
2 : R_1=C_2H_5, R_2=H, R_3=O
3 : R_1=$-CH=CH_2$, R_2=CH_3, R_3=none
4 : R_1=$-CH=CH_2$, R_2=H, R_3=none
5 : R_1=$-CH=CH_2$, R_2=H, R_3=O
6 : R_1=$-CH=CH_2$, R_2=CH_3, R_3=O



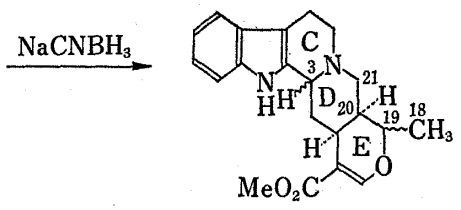
7 : R=C_2H_5



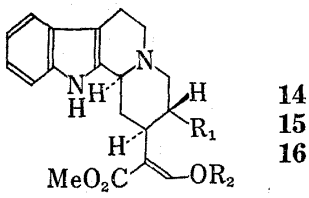
8

9a : R=H
9b : R=CH_3

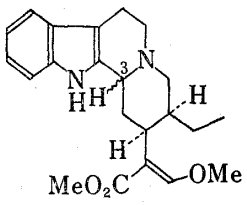
10



11 : C3 βH, C19 αH
12 : C3 βH, C19 βH
13 : C3 αH, C19 βH



14 : R_1=$-CH=CH_2$, R_2=H
15 : R_1=$-CH=CH_2$, R_2=CH_3
16 : R_1=C_2H_5, R_2=CH_3



17a : C3 βH
17b : C3 αH

Chart 1

that the modified Polonovski reaction to afford **14** took place in the direction of carbon 3 while that to afford heteroyohimbine in the direction of carbon 21.

Hirsuteine (**3**) was oxidized with *m*-CPBA in a quantitative yield to the N-oxide (**6**) which was then submitted to modified Polonovski reaction followed by $NaCNBH_3$ reduction. The reaction products were separated to corynantheine (**15**, 51%) and a new base (**17a**, 22%; $HClO_4$ salt, mp 221—222°). The ultraviolet (UV) spectrum of **17a** was indolic and its mass spectrum exhibited M^+ at *m/e* 368 indicating increase of 2 mass units from **3**. The presence of an ethyl group and C-3 βH in **17a** was revealed by the ^{1}HNMR spectrum [δ 0.89 (18 C$\underline{H}_3$, t) and 4.10 (1H, broad s)]. From these spectral data, the structure of **17a** was estimated as 3-isocorynantheidine (**17a**). Subsequent epimerisation of C-3 H in hot acetic acid yielded corynantheidine (**17b**). Inversion of configuration at C-20 probably occurred in the protonation step to an enamine which was formed from **9b** by 1, 4 addition reduction with $NaCNBH_3$.

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Structural Establishment of Arnocoumarin and Arnottiacoumarin due to Chemical Modification of Marmesin and Rutaretin Methyl Ether[1]

New coumarins, arnocoumarin (**1**) and arnottiacoumarin (**2**), were isolated from *X. arnottianum* Maxim. The structures of these coumarins were established by chemical transformation from marmesin (**7**) and rutaretin methyl ether (**10**) respectively.

Keywords——coumarin; *Xanthoxylum arnottianum*; Rutaceae; chemical transformation; pyrolysis; structural establishment

In the previous paper,[2] we reported isolation of two new coumarins (coumarin I, mp 180—183°, and coumarin II, mp 140—145°) together with thirteen other coumarins from *Xanthoxylum arnottianum* Maxim. (Japanese name: Iwa-Zansho). In this communication, we wish to present the structural establishment of these two coumarins and formally designate them as arnocoumarin and arnottiacoumarin.

Arnocoumarin (coumarin I) (**1**) was obtained as colourless plates, mp 180—183°, $C_{14}H_{10}O_3$[3] [M^+: *m/e* 266 (base peak)], IR ν_{max}^{Nujol} cm^{-1}: 1730 (C=O), UV λ_{max}^{EtOH} nm (log ε): 273.5 (4.60), 296 (4.30) sh, 347 (4.03), in 0.00042% yield from the wood of *X. arnottianum*. The fact that two aromatic protons of **1** appear as two singlets in the NMR spectrum[4] indicates

1) This forms Part XXXVIII of "Studies on the Chemical Constituents of *Rutaceous* Plants" by H. Ishii, Part XXXVII; H. Ishii, E. Ueda, K. Nakajima, T. Ishida, T. Ishikawa, K.-I. Harada, I. Ninomiya, T. Naito, and T. Kiguchi, *Chem. Pharm. Bull.* (Tokyo), **26**, 864 (1978).
2) H. Ishii, K. Hosoya, T. Ishikawa, and J. Haginiwa, *Yakugaku Zasshi*, **94**, 309 (1974); H. Ishii, K. Hosoya, T. Ishikawa, E. Ueda, and J. Haginiwa, *ibid.*, **94**, 322 (1974).
3) The compound gave satisfactory elemental analysis for the formula given.
4) NMR ($CDCl_3$) δ: 2.13 (3H, d, J=1.0 Hz, CH_3), 5.23 (1H, q, J=1.0 Hz, olefinic H), 5.82 (1H, s, olefinic H), 6.33 (1H, d, J=9.5 Hz, arom. H), 6.62, 7.37, and 7.55 (each 1H, s, arom. H), 7.74 (1H, d, J=9.5 Hz, arom. H).