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8, 13a-PROPANOBERBINES II* OXIDATION OF ACETONEBERBERINE TYPE ENAMINE WITH POTASSIUM PERMANGANATE

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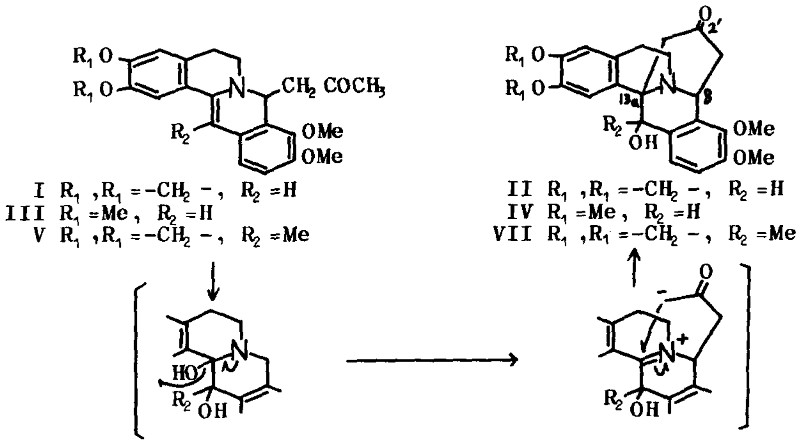
In the previous paper[1)] we presented a revised structure II for the oxidation product of acetoneberberine(I) with potassium permanganate($KMnO_4$) which was named as neoxyberberine acetone by Pyman[2)]. The formation of 8,13a-propanoberbine derivative from I prompted us further to examine the oxidation of other acetoneberberine type enamines with $KMnO_4$.

It was found that acetonepalmatine(III) reacted with $KMnO_4$, as well as I, to form 8,13a-propanoberbine derivative(IV), mp 217-218° $C_{24}H_{27}O_6N$. The structure of IV was deduced from the fact that the physicochemical properties of IV resembled to those of II except the substituent groups at ring A. On the other hand, oxidation of 13-methylacetoneberberine(V) with $KMnO_4$ gave a complex mixture from which the following three compounds were isolated. A lactam(VI) was obtained as a main product in 30% yield. And two 8,13a-propanoberbine derivatives,

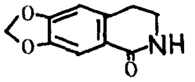


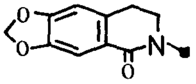
I R₁,R₁ = -CH₂-, R₂ = H
III R₁ = Me, R₂ = H
V R₁,R₁ = -CH₂-, R₂ = Me

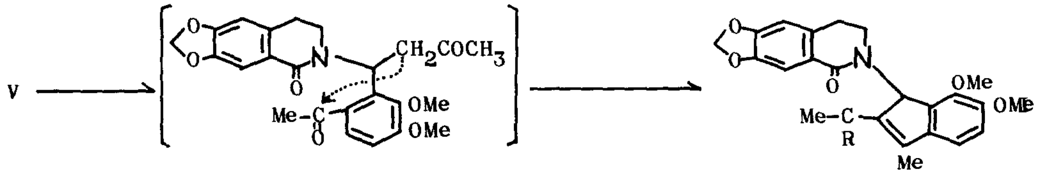
II R₁,R₁ = -CH₂-, R₂ = H
IV R₁ = Me, R₂ = H
VII R₁,R₁ = -CH₂-, R₂ = Me

compound VII and VIII, were obtained in 1 and 4% yield, respectively. The structural elucidation of these compounds is discussed below.

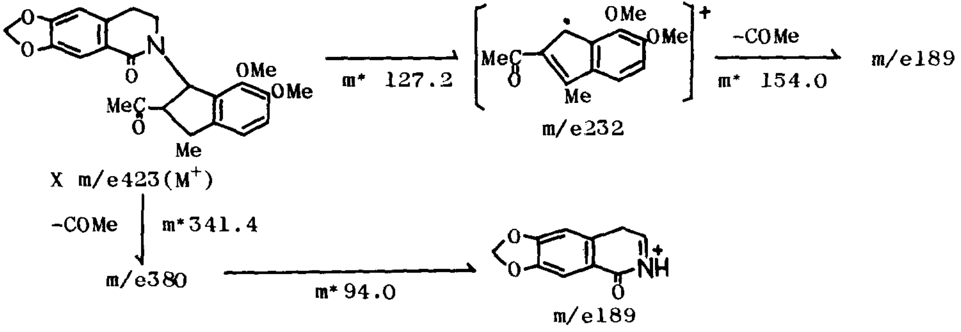
Lactam VI is colorless plates mp 238-239° $C_{24}H_{23}O_6N$, IR; 1645, 1610, 1565 cm^{-1}, UV; λ_{max}^{EtOH} mμ(log ε), 226(4.50), 264(3.98), 274(3.92), 314(4.27), 335(4.22). It is a neutral substance and shows one vinyl methyl signal at δ 2.52(doublet, J=2.2Hz), one acetyl signal at δ 2.35, four methylene protons at about δ 2.78 as A_2B_2 type and one proton at δ 7.04(broad doublet) along with two methoxy, one methylenedioxy and four aromatic protons in the nmr spectrum. The spin decoupling experiment confirmed that the doublet vinyl methyl protons were coupled with the low-field proton at δ 7.04. Reduction of VI with $NaBH_4$ gave an amorphous alcohol (IX), ν_{OH} 3430, $\nu_{c=o(amide)}$1640 cm^{-1}. It was proved that IX was a mixture of epimeric alcohols by the nmr spectrum showing two pair of doublet methyl signal (J=7Hz) corresponding to $CH(OH)CH_3$ group from which the presence of $COCH_3$ group in VI was presumable. Catalytic reduction of VI on PtO_2 yielded a dihydro derivative(X) mp 195-198° $C_{24}H_{25}O_6N$. Its uv spectral data(λ_{max} 222, 274, 305mμ) is similar to that(λ_{max} 222, 261, 305mμ) of noroxyhydrastinine(XI). From this

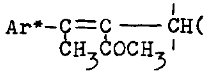

XI


XII



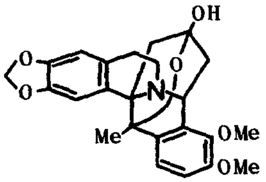
VI R=O
IX R= <H OH



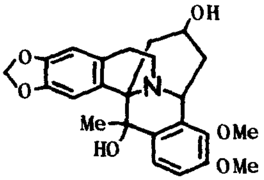
the partial structure XII for X is suggested. The ir spectrum of X exhibits amide band(1645 cm^{-1}) and isolated carbonyl band(1710 cm^{-1}). The latter indicates that the parent acetyl group in VI is conjugated with double bond. The nmr spectrum of X shows an acetyl signal at δ 2.30, a secondary methyl signal at δ 1.26(doublet, J=6.5Hz), a benzyl proton at δ 3.83(quartet, J=6.5Hz), a proton at δ 3.41(doublet, J=8.5Hz) and a proton at δ 6.92(doublet, J=8.5Hz). Comparison of the nmr spectrum of X with that of VI indicated the increment of two methine protons at δ 3.83 and 3.41. Spin decoupling experiment confirmed that the former methine proton is coupled with secondary methyl protons and the latter with the low-field proton at δ 6.92. These facts suggest that VI has a double bond with a partial structure of  $Ar^{*}\text{-}\underset{CH_3}{C}=\underset{COCH_3}{C}-\overset{|}{C}H$(Ar*=aromatic ring). Thus the tentative structure VI for the lactam seems to be consistent with the above experimental results. A plausible mechanism including the clevage of double bond with $KMnO_4$ followed by intramolecular aldol condensation may be considered. The intense peaks(m/e 423(M^+), 380, 232, 189) and meta stable peaks in the mass spectrum of X is also explained reasonably as shown in Chart.

Compound VII is colorless columns mp 250-252°(dec.) $C_{24}H_{25}O_6N$ $\nu_{c=o}$ 1700 cm^{-1}, ν_{OH} 3470 cm^{-1}. Reduction of VII with $NaBH_4$ afforded a diol(XIII) $C_{24}H_{27}O_6N$ mp 255-260°(dec.). The nmr spectrum of XIII in dmso-d_6 solution shows a secondary hydroxy(δ 4.28, doublet), a tertiary hydroxy(δ 4.66, singlet) and a tertiary methyl(δ 1.17) protons. The latter two signals are also observed in VII. Treatment of VII with hydrochloric acid gave a dehydrated product(XIV) $C_{24}H_{23}O_5N$ mp 228-230°, $\nu_{c=o}$ 1710, $\nu_{c=c}$ 1620 cm^{-1}, λ_{max} 285mμ(log ε, 4.14). The nmr spectrum of XIV shows two singlet vinyl protons at δ 5.64 and 4.74, and disappeares methyl and hydroxy protons at C-13 of VII. The dehydrated product(XIV) was converted to compound XV mp 228-230° $C_{24}H_{25}O_5N$ $\nu_{c=o}$ 1695 cm^{-1} δ 1.42 (doblet, J=7Hz, C-13-Me) by catalytic reduction on PtO_2. Treatment of XV with methanolic hydrochloric acid$^{1)}$ yielded acetone and 13-methylberberinium chloride. From these evidences the structure of VII becomes unequivocal.

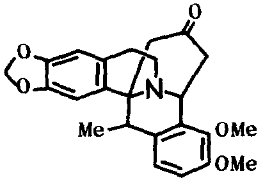
Compound VIII is colorless needles mp 220-222°(dec.) $C_{24}H_{25}O_6N$ ν_{OH} 3400 cm^{-1}. The hemiketal structure(VIII) for this compound was deduced from the



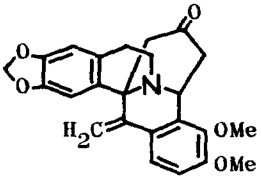
VIII



XIII



XV



XIV

following evidences. It shows no carbonyl band in the ir spectrum and a tertiary methyl signal at δ 1.51 in the nmr spectrum. Compound VIII was easily converted to XIV by acidic treatment. Reduction of VIII with $NaBH_4$ afforded a diol(XIII). Finally, the treatment of compound VII with ethanolic potassium hydroxide gave compound VIII.

References and Footnote

* Ref. 1 represents Part I of this series.

1) J. Iwasa and S. Naruto, Yakugaku Zasshi, 86, 534 (1966).

2) L. Pyman, J. Chem. Soc., 99, 1690 (1911).