Oxidation Products of Hydroxylycoctonam

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In a previous paper⁽¹⁾, the author and others reported at length on some oxidation reactions of lycoctonine, but only brief descriptions were reported on the oxidation of hydroxylycoctonam (I), $C_{25}H_{39}O_9N$, with chromic acid. The present communication presents a further consideration of the structures of these oxidation products.

Recently Valenta⁽²⁾ and, independently, Edwards et al.⁽³⁾ have proposed the same α-ketol hemiketal structure (II) for hydroxylycoctonine on the basis of several items of experimental evidence.

When I was treated with alkali, there was produced a neutral product, hydroxyisolycoctonam (III), m. p. 185~188°C, $[\alpha]_D^{27}$ $-18°$, ν_{max}^{Nujol} 3425 (hydroxyl), 1717 (ketone), 1674 cm^{-1} (lactam) (Found: C, 60.62; H, 7.90. Calcd. for $C_{25}H_{39}O_9N$: C, 60.35; H, 7.90%.), and an acid (IV), m. p. 220~222°C, $[\alpha]_D^{34}$ $-34°$, ν_{max}^{Nujol} 3378, 2551 (hydroxyl), 1715, 1653 (carboxyl), 1587, 1567 cm^{-1} (lactam) (Found: C, 58.12; H, 8.12; OCH_3, 22.93. Calcd. for $C_{25}H_{41}O_{10}N$: C, 58.24; H, 8.01; 4 OCH_3, 24.08%). III was converted into IV by further treatment with alkali. As I has a tertiary α-ketol hemiketal system, the rearragement (I→III) could be expected to proceed in a manner analogous to that of the alkali isomerization of the cevine or germine series⁽⁴⁾. I, however, did not react with sodium bismuthate in acetic acid at room temperature, and when heated at 100°C it gave only a corresponding acetyl derivative. This inertness may be due to its tertiary α-ketol character under steric restriction. IV was proved to be a monocarboxylic acid, but it

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1) H. Suginome et al., This Bulletin, **32**, 819 (1959).

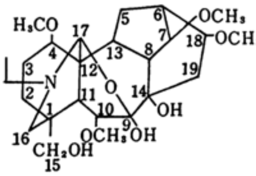
2) Z. Valenta, *Chem. & Ind.*, **1959**, 633.

3) O. E. Edwards et al., *Can. J. Chem.*, **37**, 1996 (1959).

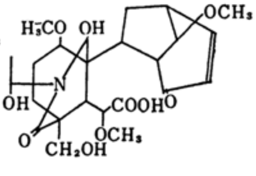
4) S. M. Kupchan et al., *J. Am. Chem. Soc.*, **75**, 5519 (1953); S. W. Pelletier and W. A. Jacobs, ibid., **75**, 3248 (1953); L. F. Fieser et al., ibid., **76**, 1200 (1954).

was not proved to have a ketone group or to lack any methoxyl group. It must be considered, therefore, that a cleavage would have proceeded at a bond either between C_9 and C_{14} or between C_9 and C_{10} without the formation of a ketone group. The author preferred to take the former for IV in view of the absence of ready lactonization, the retention of hyxroxyl bands (3448 and 3390 cm^{-1}) in the infrared spectrum of its acetyl derivative (amorphous), and the consumption of a mole of lead tetraacetate (both at 1.5 and at 15 hr.).

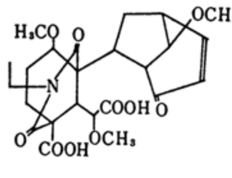
Oxidation of I with chromic acid in the same way as described in the previous paper1) afforded two acids. One of these was Y-acid (V), m. p. 203~205°C decomp.*, $[\alpha]_D^{27}$ $-7.5°$, λ_{max}^{EtOH} 225 (ε 7180), 315 (ε 50), λ_{min} 280 mμ (ε 35), ν_{max}^{Nujol} 3333, 2740~2597 (hydroxyl), 1709 (broad, carboxyl), 1669 (α, β-unsaturated ketone), 1580 cm^{-1} (lactam) (Found: C, 57.24; H, 7.09; OCH_3, 17.17. Calcd. for $C_{24}H_{35}O_{10}N \cdot {}^1/_2H_2O$: C, 57.36; H, 7.22; 3 OCH_3, 18.53%.). The other was C_1-acid (VI), m. p. 222~223°C decomp.*, $[\alpha]_D^{28}$ $-6°$, λ_{max}^{EtOH} 220 (ε 14600), 310 (ε 54), λ_{min} 290 mμ (ε 50), λ_{max}^{Nujol} 1754, 1739 (carboxyls), 1661 (α, β-unsaturated ketone), 1709 (shoulder), 1623 (imide), 675 cm^{-1} (cis-substituted double bond) (Found: C, 58.85; H, 6.45; OCH_3, 17.17. Calcd. for $C_{24}H_{31}O_{10}N$: C, 58.41; H, 6.35; 3 OCH_3, 18.86%.). Also produced was a neutral compound Z (VII), m. p. 236~240°C decomp.*, $[\alpha]_D^{29}$ $-102°$, λ_{max}^{EtOH} 218 (ε 10300), "shoulder" 300 mμ (ε 45), ν_{max}^{Nujol} 1751 (lactone), 1718 (imide), 1678 cm^{-1} (α, β-unsaturated ketone and imide) (Found: C, 61.83; H, 6.76; OCH_3, 16.35. Calcd. for $C_{24}H_{31}O_8N$: C, 62.46; H, 6.77; 3 OCH_3, 20.17%.). In the present case another neutral compound, Y, was not obtained. Each of these three compounds showed both in their infrared and ultraviolet spectra the absorption band attributed to an α, β-unsaturated ketone group. This accorded with the results of the determinations of their methoxyl groups. Thus it was found that the oxidation of I with chromic acid proceeded in the same way as that of I with lead tetraacetate5); namely, the α-ketol bond in I was cleaved, followed by the elimination of a molecule of methanol. However, no compound was secured identical with the oxidation products obtained by Edwards et al.5) from I on oxidation with lead tetraacetate.



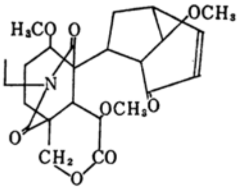
II



V



VI



VII

On the basis of the empirical formula and the infrared spectral data above, although an attempts to cleave the imide bond in VII and in VI with alkali or sulfuric acid failed, the structure VII can be assigned to Z.

VI was confirmed as a dicarboxylic acid. When VI was heated over its melting point, under effervescence it gave an acid. m. p. 275~280°C, $[\alpha]_D^{27}$ $-49°$, ν_{max}^{Nujol} 1739 (carboxyl), 1672 (α, β-unsaturated ketone), 1701, 1631 cm^{-1} (imide) (Found: C, 61.60; H, 6.97; OCH_3, 19.77. Calcd. for $C_{23}H_{31}O_8N$: C, 61.45; H, 6.95; 3 OCH_3, 20.71%.). This decarboxylation can be readily interpreted in the same way as that observed in lycoctonamic acid6). In view of the above experimental evidence, the structure of C_1-acid can be represented as VI.

V was proved to be a monocarboxylic acid, and its infrared spectrum showed strong hydrogen bonded bands near the 3 and 6μ regions. V was recovered unchanged after treatment with ethereal diazomethane solution. This perhaps indicates the presence of a lactone group in V. In addition, V was acetylated with acetic anhydride and pyridine to give a reversible acetyl derivative (amorphous), $[\alpha]_D^{10}$ $-32°$, (Found: C, 59.35; H, 6.78. Calcd. for $C_{28}H_{37}O_{11}N$: C, 59.67; H, 6.62%.), the infrared spectrum of which showed no hydroxyl band. Since V showed acid properties, the lactone group in question, if it was present, should be easily hydrolyzable. From a consideration of the above results, one of the most likely structures for Y-acid was shown to be V.

The author wishes now to formally propose names for the above compounds as follows: desmethanol secolycoctimide ketodicarboxylic acid for C_1-acid, desmethanol des-(oxymethylene) secolycoctimide keto monocarboxylic acid for the decarboxylated C_1-acid, and desmethanol secolycoctimde ketolactone for Z.

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* Previously melting points at 193~195, 220~222 and 226~227°C were reported for V, VI and VII respectively1).

5) O. E. Edwards et al., *Can. J. Chem.*, **34**, 1315 (1956).
6) O. E. Edwards and L. Marion, ibid., **30**, 627 (1952).

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