THE MECHANISM OF THE FORMATION OF OXONITINE BY PERMANGANATE OXIDATION OF ACONITINE

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An isotopic labeling study has shown that the N-formyl group of oxonitine, a product of permanganate oxidation of aconitine in a 95:5 acetone-water, originates from the methylene group of the N-ethyl of aconitine.

Since oxonitine (1), a permanganate oxidation product of aconitine (2), was first reported by Carr in 1912,¹⁾ its structure and the mechanism of the formation have been studied by many investigators.²⁾ Its structure as an N-formyl-N-desethylaconitine was suggested by Turner et al.^{2b)} and Jacobs et al.³⁾ but the mechanism of its formation from 2 has remained unsettled despite study by several groups^{2b,2c)} of investigators. Pelletier et al.⁴⁾ recently published their results on the mechanism of the formation of 1 from 2 and showed that the N-formyl group of 1 was derived from acetone as solvent as well as from the methyl group of the N-ethyl group of 2, when 2 was oxidized with permanganate in several aqueous systems.

The present authors wish to report that, <u>contra</u> Pelletier et al., the N-formyl group of 1 originates from the methylene group of the N-ethyl of 2 when 2 is oxidized with permanganate in a 95:5 acetone-water. The present results therefore confirm that a different mechanism operates when the oxidation is carried out in a solvent containing a smaller amount of water.

For this study we prepared aconine pentaacetate (3), mp (decomp) 222-223 °C, with a labeled N-ethyl group $(N^{-13}CH_2CH_3)$ from N-desethylaconitine 3-acetate⁵⁾ in three steps.⁶⁾ ¹³C NMR spectrum (CDCl₃) of 3 clearly indicated the labeled methyl-ene of the N-ethyl group at δ 48.8 ppm.

Oxidation of 3 for 4 days at room temperature in acetone-water (95:5 v/v) with potassium permanganate gave N-formyl-N-desethylaconine pentaacetate (4), mp (decomp) 239-241 °C, in 79% yield. The ¹³C NMR spectrum (CDCl₃) of 4 showed a labeled form-yl carbon at δ 162.4 ppm and 75% of ¹³C labeled carbon of 3 was proved to be remained in 4. The oxidation of aconitine (2) for 4 days in acetone-d₆-water (95:5 v/v), on the other hand, gave 1 in 80% yield and its ¹H and ¹³C NMR spectra (CDCl₃) ex-

hibited both the proton and the carbon of the formyl group at δ 8.10 (1H,s) and 163.0 ppm (d) respectively and showed no incorporation of deuterium from acetone-d₆.

These results unambiguously indicate that the N-formyl group of 4 is derived from the methylene group of the N-ethyl of 3. A probable mechanism of the formation of 1 from 2 under the conditions mentioned above is depicted in Scheme 1.⁵⁾ The oxidation first generates an enamine (B) and its oxidation cleavage may give 1. On the other hand, hydrolysis of an immonium salt (A) to form the N-desethyl compound might be a preferred reaction when a greater amount of water is present.⁴⁾



Scheme 1.

References

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- 6) Acetylation of N-desethylaconitine 3-acetate with $[1-^{13}C]$ -acetic anhydride gave N-acetyl-N-desethylaconitine 3-acetate, mp (decomp) 213-215 °C, with a labeled N-acetyl group (N- $^{13}COCH_3$). The labeled N-acetyl derivative was reduced with lithium aluminium hydride to N-ethyl derivative (aconine with the labeled N-ethyl group), mp (decomp) 123-125 °C, and its acetylation with acetyl chloride afforded the labeled aconine pentaacetate (3). An overall yield of 3 from N-desethylaconitine 3-acetate was 50%.

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