2). However, extensive effort failed to yield a precise simulation of the observed spectral pattern in the 17-G "gap" between the two sharp lines. We are inclined to attribute this failure, which is not unique,[34] to the influence of a slightly restricted rotation of the α-methyl group at all temperatures below 213 K, the QCPE program being unable to deal with intermediate exchange rates for two separate motions. Although the possibility that an "impurity" radical produces some of these sharp "extra" lines cannot be entirely ruled out, it seems improbable since extra lines do not appear to be present at high or low temperatures.

In summary, a great deal of labor has yielded EPR spectra for only two cyclopropenyl radicals, the 2,3-dimethyl- and the trimethylcyclopropenyls. The parent cyclopropenyl radical remains as elusive as ever.

Acknowledgment. We are deeply indebted to an anonymous referee for some very helpful comments on the work described above.

Registry No. 2, 82246-53-5; **3**, 60528-80-5; **4**, 60528-77-0; 1-chloroallyl radical, 40905-10-0; cyclopropene, 2781-85-3; 1,3-dimethylcyclopropene, 82190-83-8; 1,2,3-trimethylcyclopropene, 34785-53-0.

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Origin of Oxonitine: A Potassium Permanganate Oxidation Product of Aconitine

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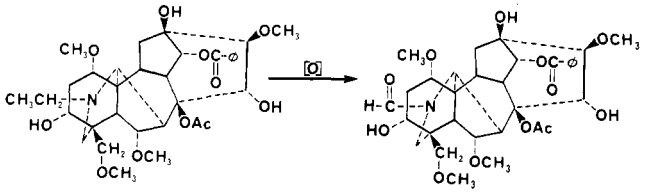
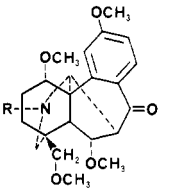
Since Carr's report in 1912,[1] oxonitine, one of the permanganate oxidation products of aconitine (**1**), has been repeatedly studied,



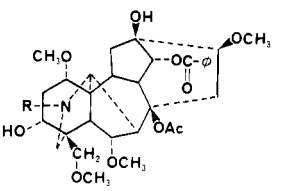
Aconitine (1) Oxonitine (2)

and various proposals have been suggested for its molecular formula, chemical structure, and origin.[2-4] Thus the molecular formulas $C_{32}H_{41}NO_{12}$,[3] $C_{33}H_{43}NO_{12}$,[4] and $C_{34}H_{45}NO_{12}$[2] have been suggested for oxonitine. Though oxonitine is known to possess an amide group and to lack the *N*-ethyl group,[5] there has been little agreement as to its mode of formation from aconitine. Several investigators have favored a lactam-type structure.[6-10] The problem is rendered difficult by the highly insoluble, polyfunctional nature of oxonitine.

In 1960, Jacobs and Pelletier,[11] as well as Turner and coworkers,[12] independently demonstrated that purified oxonitine, mp 285-292 °C, contains an *N*-formyl group instead of the earlier suggested *N*-acetyl group. Turner's group[12] also concluded on the basis of oxidation of labeled aconitine ($N-^{14}CH_2CH_3$) that the formyl group of oxonitine (**2**) is not derived from the *N*-ethyl group of aconitine. In 1971, Wiesner and Jay[13] reported that the mass and proton NMR spectra of the *N*-acyl aromatization product **3** prepared from oxonitine proved it to be a mixture of



3 R=Mixture of -CHO and -COCH$_3$



4 R=CH$_3$ Mesaconitine

5 R=H N-Desethylaconitine

6 R=CH$_2$OH

the *N*-formyl and *N*-acetyl derivatives. They suggested that since aconitine (**1**) is known to contain varying amounts of mesaconitine as an impurity, the differing *N*-acyl groups result from oxidation of the *N*-methyl group of mesaconitine (**4**) and the *N*-ethyl group of aconitine (**1**). In this communication, we report our results on the origin of the *N*-formyl group of oxonitine and establish the mechanism for its formation.

Oxidation of pure aconitine,[14] mp 196-203 °C, with $KMnO_4$ in acetone and acetic acid for 5 h at 25 °C afforded oxonitine, mp 281-282 °C, $[\alpha]^{20}_D$ -48.5° (*C* 0.4, $CHCl_3$) in 20-25% yield.[15] When a similar oxidation was carried out with 5% methanol in acetone, the yield of oxonitine was increased to 45-65%. Spectral data including ^{13}C NMR analysis[16] revealed that oxonitine contains the *N*-formyl group but no *N*-acetyl group, confirming the earlier proposed structure **2** for oxonitine.[11,12] Mesaconitine (**4**),[17] mp 200-207 °C, was resistant to oxidation when it was treated with $KMnO_4$ in acetone and acetic acid or 5% methanol in acetone and acetic acid, at 25 °C for 5 h. However, when this reaction was performed at 50 °C for 48 h, mesaconitine afforded crude oxonitine, mp 267-269 °C, in 75% yield. These results demonstrate that mesaconitine is resistant to oxidation under conditions that oxidize aconitine to oxonitine and that oxidation of aconitine with $KMnO_4$ affords oxonitine *in the absence of any mesaconitine impurity*. Thus, the previous explanations about the origin of oxonitine are not valid. Our results reveal that the source of the *N*-formyl group of oxonitine must be solvents (e.g., acetone, methanol, or acetic acid) used during oxidation or the *N*-ethyl group of aconitine.

In 1964, Marion and co-workers[18] reported the formation of *N*-desethylaconitine (**5**) as a major product by treatment of aconitine with $KMnO_4$ in aqueous acetone for 10 min. In our hands, treatment of aconitine with $KMnO_4$ under these conditions afforded *N*-desethylaconitine (**5**): mp 180-182 °C; ^1H NMR ($CDCl_3$) δ 1.36 (3 H, s, CH_3CO), 3.23, 3.35, 3.37, and 3.76 (each

†On leave from the University of Warsaw, Warsaw, Poland.

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(14) The purity of aconitine was checked by TLC and ^1H and ^{13}C NMR spectra. It contained no detectable amount of mesaconitine. Aconitine and mesaconitine can be separated easily on alumina TLC using 2% methanol in ether.

(15) Earlier investigators were unable to get consistent yields of oxonitine. During several experiments we also observed that oxonitine is formed in erratic yields. We have, therefore, reported yields as a range. Formation of oxonitine depends on the pH of the reaction mixture, the rate of addition of oxidant, and concentration. Oxonitine is usually accompanied by a certain amount of the *N*-acetyl derivative (**7**) and requires several recrystallizations to free it from this impurity.

(16) The ^{13}C NMR spectrum of oxonitine in $CDCl_3$ with a few drops of CD_3OD revealed the following signals: 172.5, 166.4, 163.7, 133.8, 129.8, 129.8, 128.9, 90.2, 90.2, 83.0, 79.5, 79.5, 78.6, 74.4, 73.3, 68.6, 61.1, 59.1, 58.3, 57.9, 55.6, 51.1, 48.7, 47.5, 43.2, 42.4, 40.5, 38.6, 34.4, 33.9, 21.3 ppm.

(17) Mesaconitine used in this reaction was identical with mesaconitine prepared from *N*-desethylaconitine[10] by treatment with methyl iodide in isopropyl ether.

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Table I. Oxidation of Aconitine with Potassium Permanganate

solvent(s)	time, h	oxonitine yield, %
CH_3COCH_3, CH_3COOH[a]	5	20–25
5% MeOH in CH_3COCH_3, CH_3COOH[a]	5	45
CH_3COCH_3, C_6H_5COOH[b]	5	20
15% CH_3COCH_3 in H_2O, CH_3COOH[a]	5	3
5% CH_3OH in H_2O, CH_3COOH[a]	2.5	6
CH_3COCH_3, H_2O (20:3)	1.5	13[c]
H_2O	1	20
0.40% CH_2O in H_2O	1	55

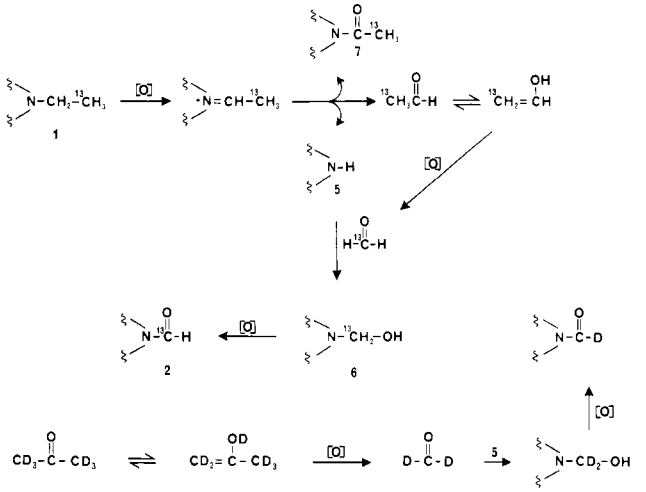
[a] Just sufficient acetic acid was added to bring the solution to about pH 6. [b] 5mg in 10 ml of acetone. [c] 60% of *N*-desethylaconitine.

3 H, s, CH_3O), 4.10 (1 H, d), 4.47 (2 H, m), 4.91 (1 H, d, C(14)-β-H); ^{13}C NMR ($CDCl_3$) δ 172.2, 166.1, 133.4, 129.7, 129.7, 128.7, 91.5, 89.7, 83.3, 81.3, 78.9, 78.9, 77.1, 74.1, 71.0, 61.1, 59.1, 57.7, 55.7, 55.7, 50.8, 49.3, 47.0, 43.8, 43.4, 40.8, 40.8, 34.8, 34.8, 21.4; in 60% yield. When the reaction was allowed to proceed for 1.5 h, we isolated oxonitine (**2**) in 13% yield along with *N*-desethylaconitine. As the reaction time increased, the yield of oxonitine increased and that of *N*-desethylaconitine decreased.

Treatment of *N*-desethylaconitine (**5**) with 0.4% formalin in methanol afforded **6** in quantitative yield; mp 200–202 °C; ^1H NMR ($CDCl_3$) δ 1.32 (3 H, s, CH_3CO), 3.16, 3.30, 3.48, and 3.75 (each 3 H, s, CH_3O), 3.33 (2 H, s, NCH_2OH); ^{13}C NMR ($CDCl_3$) δ 172.2, 166.2, 133.3, 129.9, 129.8, 128.7, 91.5, 90.2, 89.3, 83.2, 81.7, 78.9, 78.9, 76.3, 74.2, 71.0, 60.9, 60.5, 59.1, 57.8, 55.9, 49.7, 49.2, 47.6, 44.9, 43.9, 42.9, 40.7, 35.5, 34.1, 21.4. Oxidation of **6** with aqueous $KMnO_4$ yielded oxonitine, mp 273–275 °C, in quantitative yield. From these results, we conclude that reaction of *N*-desethylaconitine (**5**) with the formaldehyde generated in situ from oxidation of solvent(s) furnishes intermediate **6**, which is subsequently oxidized to oxonitine. To test this mechanism and to locate the source of the *N*-formyl group of oxonitine, we systematically investigated the oxidation of aconitine using various solvent systems and established the role of each solvent used in this oxidation. Acetic acid can be replaced with other organic acids with no impact on the yield of oxonitine. However, the presence of a stronger acid decreases the rate of the reaction as well as the yield of oxonitine. At pH 3.5 the oxidation process is practically suppressed. During several experiments we observed that the presence of acid is not necessary and that the yield of oxonitine is higher in alkaline media. Experimental results presented in Table I demonstrate that the solvents acetone and methanol, as well as the acetaldehyde generated by oxidation of the *N*-ethyl group of aconitine, are the source of formaldehyde.

Fosse has reported[19] that oxidation of acetone with calcium permanganate solution in the presence of ammonia produces formaldehyde. We have observed similar results using $KMnO_4$. Oxidation of aconitine with $KMnO_4$ in hexadeuterated acetone afforded oxonitine mainly containing the –NCDO group,[20] a result that confirms that acetone is a source of the N–CHO group of oxonitine. Aconitine also afforded oxonitine in 20% yield when it was treated with aqueous $KMnO_4$. This result can be explained by cleavage of the *N*-ethyl group of aconitine to **5** and acetaldehyde. The latter is oxidized to formaldehyde in alkaline media as shown in Scheme I. Formaldehyde reacts with **5** to give compound **6**, which is immediately oxidized to oxonitine. In this reaction the CH_3 carbon of the *N*-ethyl group is the source of the N–CHO group of oxonitine. This fact was confirmed by oxidation of ^{13}C-labeled aconitine with aqueous $KMnO_4$ (Scheme I). This labeled compound ($^{13}CH_3CH_2N$) was prepared in a yield of 40% by treatment of **5** with $^{13}CH_3CH_2I$ in refluxing methanol for 90 min. The labeled aconitine was treated with aqueous $KMnO_4$ for 2 h to afford a 1:1 mixture of oxonitine (**2**) and the *N*-acetyl

Scheme I



derivative (**7**), which contained the ^{13}C label on the aldehyde carbon and on the methyl group, respectively.

In summary, the data presented here clearly demonstrate that acetone, methanol, or acetaldehyde is the source of the *N*-formyl group of oxonitine and that oxidation of aconitine to oxonitine takes place via intermediates **5** and **6**, as shown in Scheme I. Turner's results are ambiguous because the 6% incorporation of ^{14}C label in his product oxonitine probably resulted from the presence of some $>N-^{14}COCH_3$ as an impurity in his oxonitine sample. Wiesner's experimental results are correct, but since *N*-acetyldesethylaconitine is always formed along with oxonitine during oxidation of aconitine, the *N*-acyl aromatization product **3** would of course consist of a mixture of compounds bearing the >NCHO and $>NCOCH_3$ groups.

Acknowledgment. We acknowledge with thanks helpful discussions with Dr. H. K. Desai.

Registry No. **1**, 302-27-2; **2**, 545-57-3; **4**, 2752-64-9; **5**, 3327-35-3; **6**, 82323-95-3.

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(20) A small amount of oxonitine containing the –NCHO group is also formed because of generation of a small amount of HCOH by oxidation of the $-NCH_2CH_3$ group of aconitine (Scheme I).

Intrinsic Steric $^2H/^1H$ Isotope Effects on ^{13}C Shieldings: Dihedral Angular Dependence of Shifts over Three Bonds in Saturated Systems

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Shielding changes produced by replacement of hydrogen with deuterium have been recognized for ^{13}C nuclei for many years,[1] and two types of isotope effects have been delineated:[2] "equilibrium" isotope shifts caused by perturbation of the relative populations of two (or more) equilibrating species and "intrinsic" isotope shifts involving a single species. The observed effects are largest for ^{13}C nuclei directly bonded to deuterons and are rapidly attenuated with increasing separation such that intrinsic effects in saturated systems are essentially zero over more than three bonds.[3] Typically, a deuterated carbon is shifted 0.3–0.6 ppm

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