WEAK BASES OF LAURELIA NOVAE-ZELANDIAE
A CAUTIONARY NOTE ON OXOAPORPHINE NMR ASSIGNMENTS

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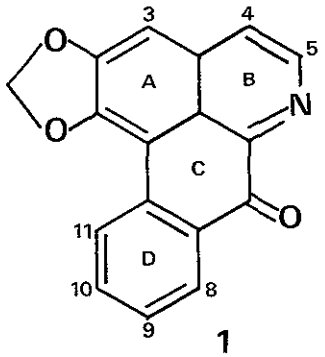
Liriodenine and its 10-methoxy derivative, for which the name oxolaureline is proposed, were isolated from the weak base fraction of Laurelia novae-zelandiae (Monimiaceae) bark. Examination of the nmr spectra of the latter alkaloid and some of its congeners shows that C 11 - H does not necessarily resonate downfield from C 8 - H, as has been generally assumed.

The bark alkaloids of Laurelia novae-zelandiae A. Cunn. (Monimiaceae) have been studied quite thoroughly, and consist mainly of aporphines, at least one proaporphine, and one aporphine N-oxide.[1, 2] Analysis of the stem barks of the South American species L. sempervirens R. et Pav. and L. philippiana Looser yielded several aporphines, too, but weakly basic fractions were separated from both extracts and were shown to contain liriodenine and more highly substituted oxoaporphines,[3] which prompted us to reexamine the New Zealand species.

The stem bark of Laurelia novae-zelandiae was processed in the same way as the Chilean material, furnishing a weakly basic fraction which contained mainly liriodenine (1). A small amount of another alkaloid was isolated as yellow needles melting at 297º, and its structure was shown by spectroscopic methods to be 10-methoxy-1,2-methylenedioxy-7-oxoaporphine (2), for which the name oxolaureline is proposed.



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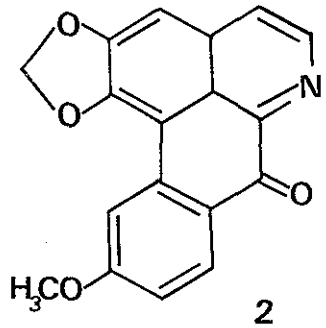


2

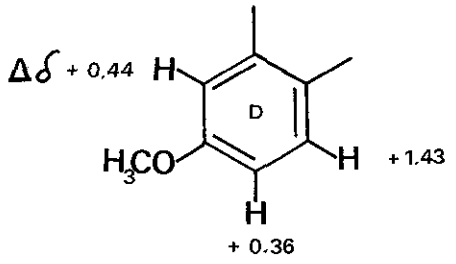
The salient feature in the ir spectrum of oxolaureline is the conjugated carbonyl group absorption at 1642 cm^{-1} (in KBr). The nmr spectrum is consistent with an oxoaporphine skeleton bearing a methylenedioxy group on C-1 and 2, and a methoxy group on C-9 or 10: δ (CF_3COOD) 4.18 (s, 3H, OCH_3), 6.71 (s, 2H, OCH_2O), 7.40 (dd, 1H, J 9, J' 2, C 9-H), 7.62 (s, 1H, C 3-H), 8.41 (d, 1H, J 2, C 11-H), 8.49 (d, 1H, J 6, C 4-H), 8.64 (d, 1H, J 9, C 8-H), 8.77 (d, 1H, J 6, C 5-H).

The 9-methoxy isomer, lanuginosine, has been described as orange needles melting at 302-303º[4] or 317-319º.[5] The 10-methoxy com-

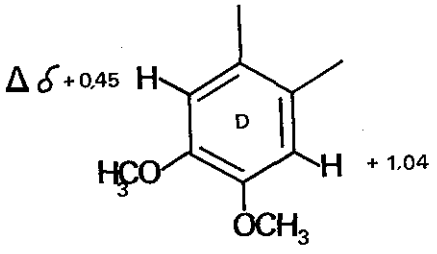
pound has been synthesized and described as a yellow solid melting at 268º.[6] The nmr spectrum of lanuginosine in trifluoroacetic acid has been published,[5] and bears a superficial resemblance to that of our compound (Table 1). On the other hand, the nmr spectral data for 10-methoxy-1,2-methylenedioxy-7-oxoaporphine as published,[7] are quite different. The wide range of melting points was of no use in deciding which structure was more likely for our alkaloid, but direct comparison of its ir spectrum in KBr and that of lanuginosine clearly showed that both bases were different. As the coupling of the ring D proton resonances in oxolaureline indicated that the C 8-H signal was further downfield than the C 11-H signal, while the opposite is usually the case,[7, 8] we decided to analyze this apparent anomaly further.

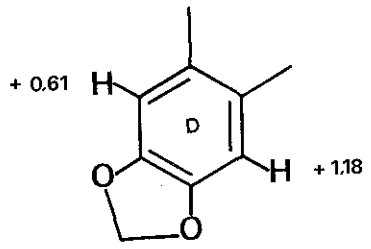
It is well established that in aporphine alkaloids the proton resonating furthest downfield is C 11-H, as a consequence of the deshielding by ring A. In the case of laureline, which has the same substitution as our base in rings A and D, the aromatic ring protons appear as follows ($CDCl_3$):[9] 6.52 (s, 1H, C 3-H), 6.75 (dd, 1H, $\underline{J}$ 8, $\underline{J}'$ 2.5, C 9-H), 7.15 (d, 1H, $\underline{J}$ 8, C 8-H), 7.66 (d, 1H, $\underline{J}'$ 2.5, C 11-H). The lack of an oxygen substituent on C-9 shifts the C 8-H resonance downfield about 0.3 ppm relative to the value found in 9-substituted aporphines, and the C 11-H resonance is shifted 0.1-0.4 ppm upfield by the C-10 substituent. It seems reasonable to expect a carbonyl group on C-7 to shift the C 8-H resonance even further downfield, whereas the flattening of the biphenyl skeleton on going from the aporphine to the oxoaporphine should not affect the C 11-H resonance to the same extent. This

is indeed the case, as illustrated in the following diagram for the laureline-oxolaureline pair (the δ values for both bases were determined in $CDCl_3$):



Similar shifts are found in other pairs such as glaucine - oxoglaucine,[10, 11] and nantenine - oxonantenine,[12, 13] (in $CDCl_3$):

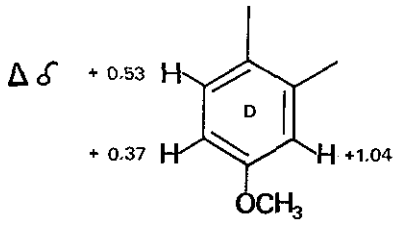




In this latter case, the original assignments[12] for the C 8 - H and C 11 - H resonances have been inverted.[13] This inversion seems further justified upon comparing the $CDCl_3$ spectral data with our own results in trifluoroacetic acid, as shown below, which gives solvent shifts closely paralleling those found for oxolaureline and not very different from the lanuginosine values. In all three cases, the C 8 - H signal is shifted more than 1 ppm downfield,

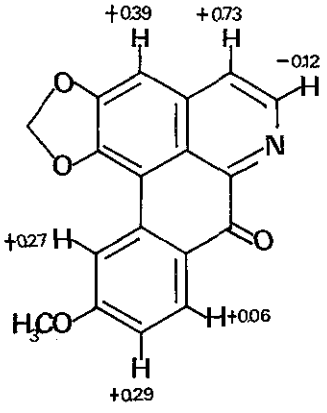
while the effect on the C 11 - H resonance is very considerably less.

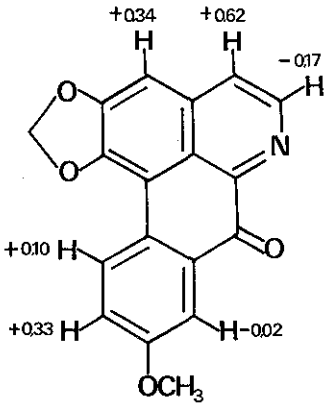
As oxoaporphines are rather insoluble in chloroform, most of the nmr spectra in the literature have been taken in trifluoroacetic acid. This solvent is unusual where aporphines are concerned, but an example for which published data exist is the xylopine - lanuginosine pair:[12, 5]

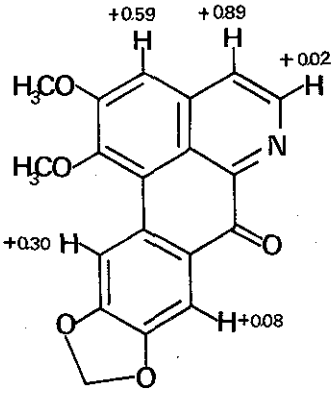


(The changes in the ring D proton resonances due to N-methylation are variable, but always less than 0.2 ppm).

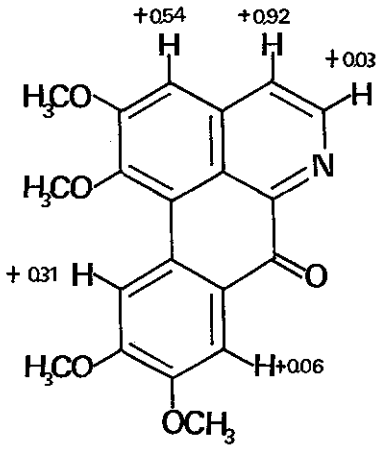
The comparison of oxoaporphine nmr spectra in $CDCl_3$ and in trifluoroacetic acid gives the following shifts for oxolaureline, lanuginosine,[5] and oxonantenine:[13] (Tables 1 and 2)

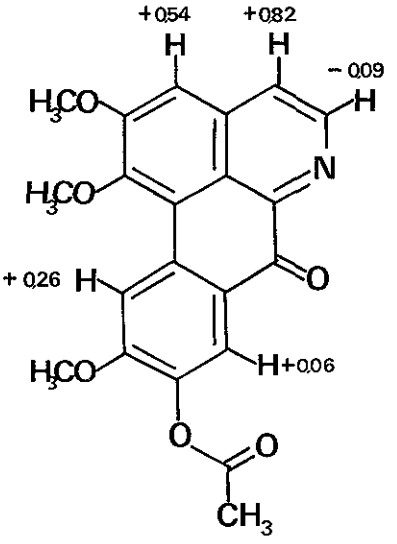






Furthermore, we have found that for oxoglaucine and O-acetyl-atheroline: (Tables 1 and 2)





In this series, therefore, the C 8 - H resonance is only affected to a negligible degree on going from $CDCl_3$ to trifluoroacetic acid. The C 11 - H signal, on the other hand, is shifted further downfield by as much as 0.3 ppm which, however, is not enough to invert the relative positions of the C 8 - H and C 11 - H resonances in oxo-laureline.

The conclusion of this analysis is that, as in the case of oxo-laureline, other oxoaporphines may exhibit nmr signals due to C 8 - H at lower field values than those assignable to C 11 - H. Care must thus be taken when studying new alkaloids with similar structures, as this irregularity will probably appear again in the nmr spectra of the hitherto unknown oxo derivatives of the lirinine and apo-glaziovine types.

Table 1

Aromatic proton resonances of oxoaporphines in trifluoroacetic acid

	C 3-H	C 4-H	C 5-H	C 8-H	C 9-H	C 10-H	C 11-H
oxolaureline [a]	7.62 s	8.49 d J 6	8.77 d J 6	8.64 d J 9	7.40 dd	–	8.41 d J 2
lanuginosine [5]	7.48 s	8.42 d J 6	8.72 d J 6	8.01 d J 3	–	7.60 dd	8.72 d J 9
oxoglaucine [a]	7.62 s	8.55 d J 6	8.79 d J 6	8.13 s	–	–	9.09 s
oxonantenine [a]	7.65 s	8.51 d J 6	8.78 d J 6	7.95 s	–	–	8.83 s
O-acetylatheroline [a]	7.68 s	8.50 d J 6	8.73 d J 6	8.26 s	–	–	9.08 s

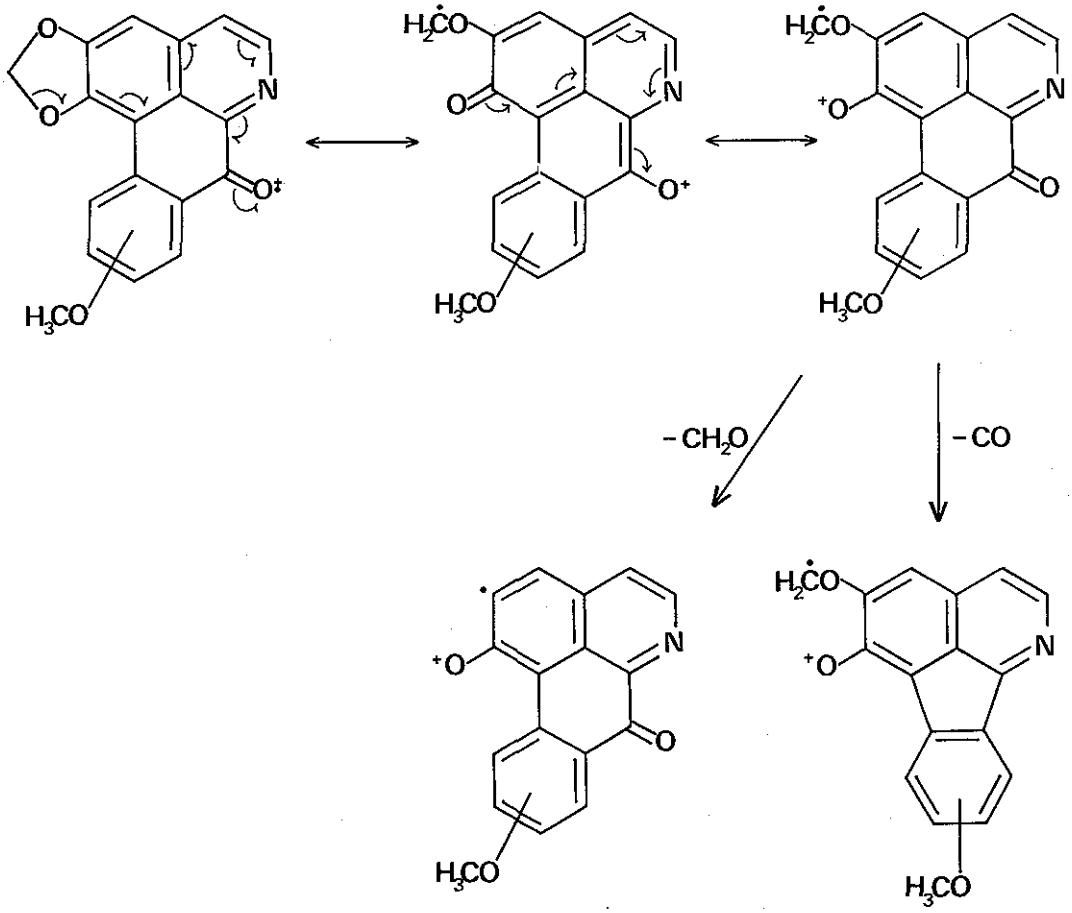
Table 2

Aromatic proton resonances of oxoaporphines in $CDCl_3$

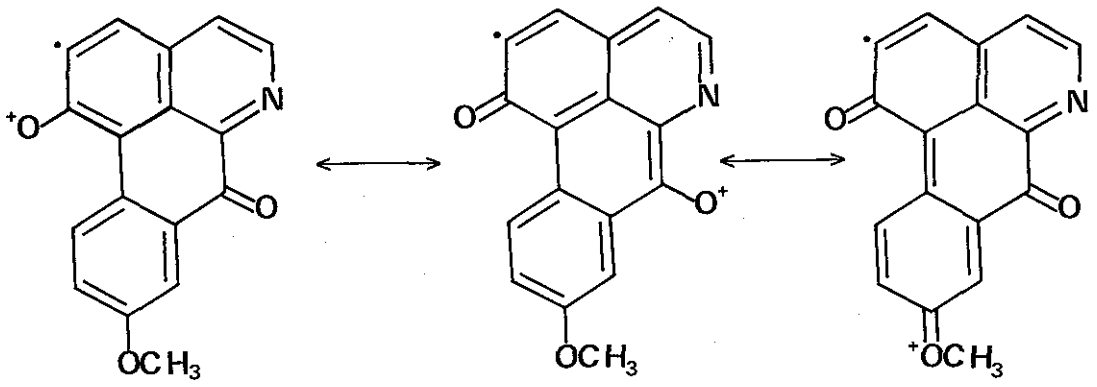
	C 3-H	C 4-H	C 5-H	C 8-H	C 9-H	C 10-H	C 11-H
oxolaureline [a]	7.23 s	7.76 d J 5	8.89 d J 5	8.58 d J 9	7.11 dd	–	8.14 d J 2
lanuginosine [a]	7.14 s	7.80 d J 6	8.89 d J 6	8.03 d J 3	–	7.27 dd	8.62 d J 9
oxoglaucine [10]	7.08 s	7.63 d J 5	8.76 d J 5	8.07 s	–	–	8.78 s
oxonantenine [12]	7.06 s	7.62 d J 5	8.76 d J 5	7.87 s	–	–	8.53 s
O-acetylatheroline [a]	7.14 s	7.68 d J 6	8.82 d J 6	8.20 s	–	–	8.82 s

a This work.

The structure assigned to oxolaureline is further supported by its mass spectrum. The molecular formula $C_{18}H_{11}NO_4$ was confirmed by high resolution mass measurement of the intense (100 %) molecular ion. The only other strong peak in the high mass region appears at m/e 277 (M - CO, 14 %), while the isomeric lanuginosine[5] and oxostephanine[14] have important fragments at m/e 275 (M - CH_2O, 30 %) and 276 (M - CHO, 96 %), respectively. This suggests that the position of the ring D methoxy group strongly influences the fragmentation of the molecular ion, as can be partially rationalized thus:

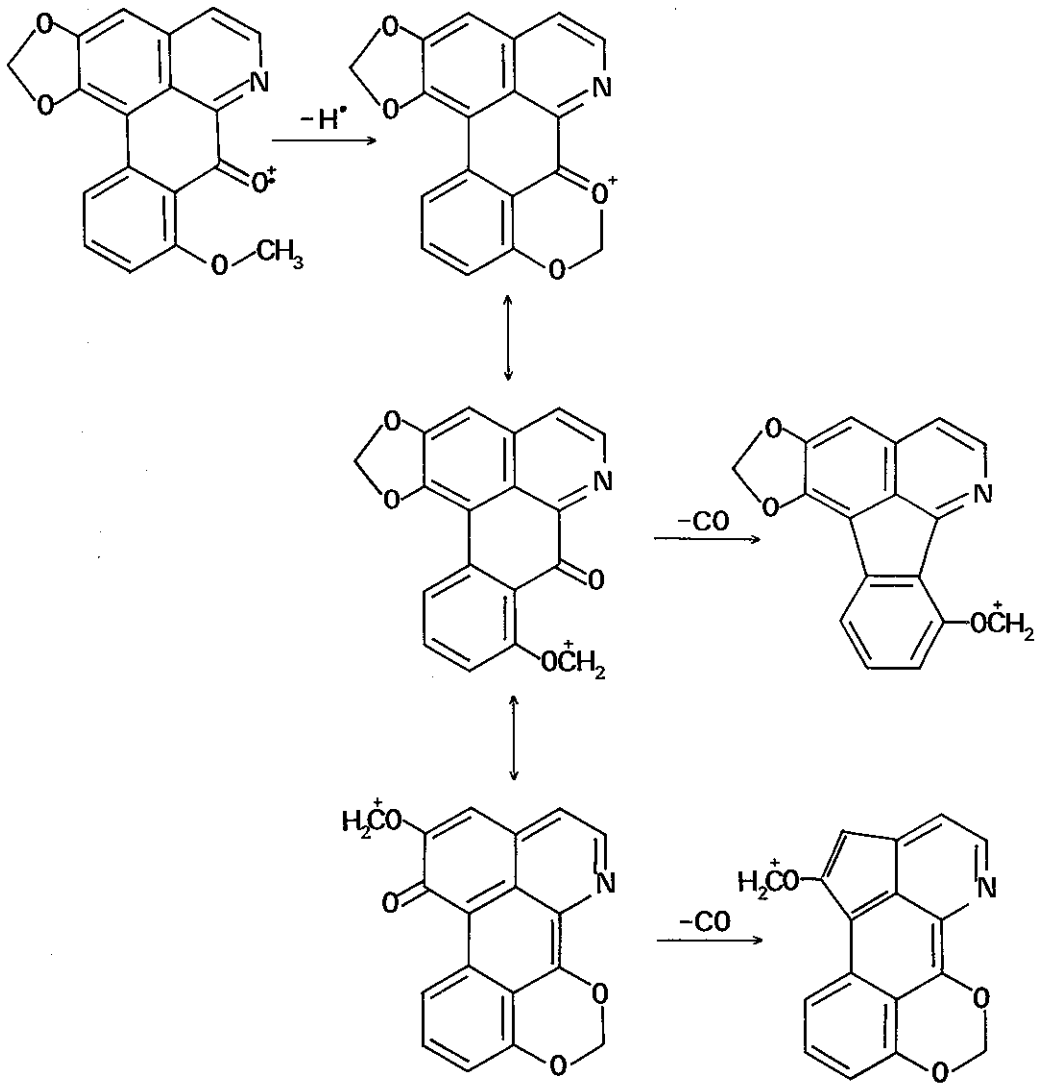


In the case of lanuginosine, the loss of CH_2O could be favoured by the greater stability of the resulting radical ion, in which the positive charge may be delocalized over all three oxygen atoms:



A similar situation is theoretically possible in the as yet unknown 11-methoxy-1,2-methylenedioxy-7-oxoaporphine, but in oxolaureline and oxostephanine the positive charge can only be shared by the oxygen atoms at C-1 and C-7.

Regarding the loss of 29 atomic mass units from the molecular ion of oxostephanine, as no metastable ion measurements are available we can only speculate on the possibility that a hydrogen atom is lost first, followed by decarbonylation by one or both of two possible routes:


-H•
-CO
-CO

Although the oxolaureline isolated in this study appeared to be chromatographically pure and gave clean nmr spectra, the mass spectrum indicates contamination by two substances with the formulae (high resolution mass measurements) $C_{18}H_{13}NO_3$ and $C_{17}H_9NO_4$, which are presumably a didehydroaporphine with a methylenedioxy and a methoxy group, and perhaps a phenolic oxoaporphine with a methylenedioxy group. Such substances have not been reported in the literature, but their presence in Laurelia novae-zelandiae bark, where they could arise by oxidation of aporphines known to be present,[1, 2] is not surprising.

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