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COMMENTS ON THE STRUCTURE OF QUASSIN

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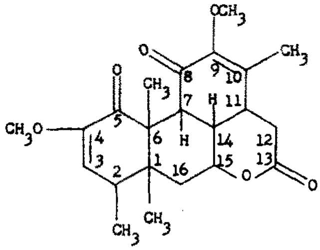
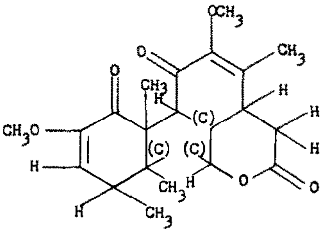
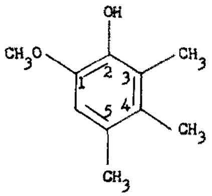
VALENTA *et al.*[2] have recently suggested the structure I for quassin, one of the two closely related diterpenoid compounds obtained from *Quassin amara* Linn, on the basis of partial structure II which they established by both chemical and nuclear magnetic resonance (NMR) evidence.



I



II



III

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[2] Z. Valenta, A. H. Gray, S. Papadopoulos and C. Podesva, *Tetrahedron Letters* No. 20, 25 (1960).

Unequivocal evidence was not presented for the siting of a methyl group at C_1. While 3,4,5-trimethylguaiacol III can be obtained by dehydrogenation of neoquassin,[3] the C_4 methyl of this aromatic compound could well be derived from the C_{16} atom of quassin and does not provide proof of the presence of an angular C_1 methyl group in the parent compound. For this reason, and for others detailed below, we consider that the formula IV is at the present stage an acceptable alternative for the structure of quassin.

In agreement with the data of the Canadian group[2] we find that the NMR spectrum[4] of quassin shows methyl absorption at 8.13, 8.45, 8.81 (doublet) and 8.89τ. These peaks can be assigned to an allylic methyl group, an angular methyl group adjacent to a carbonyl group, a methyl group attached to a socondary carbon atom and a methyl group attached to a teriary carbon atom respectively. Such assignments are in agreement with both structures I and IV. Further evidence has been presented to establish the position of three of these methyl groups at C_2, C_6 and C_{10}.[2]

In the NMR spectra of quassin, neoquassin, anhydroneoquassin and deoxoquassin, which are related as shown in Fig. 1, we have been able to assign the various bands to a proton or protons in the molecule with considerable confidence and thus to account for the resonance position of each proton in the four compounds studied. In each case a sharp singlet of area equivalent to one proton occurs in the region 6.80-7.05τ, and this peak is assigned to the proton on C_7. Besides occupying an angular position

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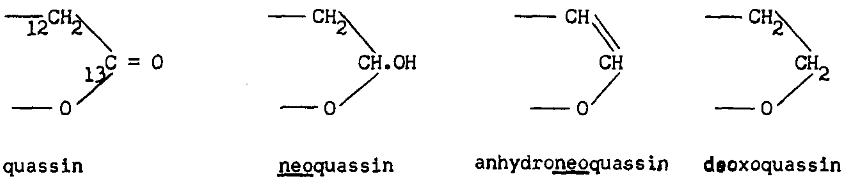
[3] R. J. S. Beer, D. B. G. Jaquiss, A. Robertson and W. E. Savige, J.Chem.Soc. 3672 (1954).

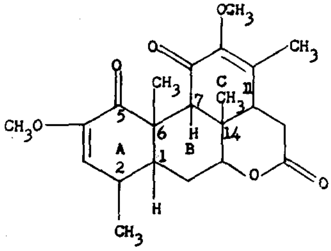
[4] All spectra were measured at 60 mc in deuterochloroform solution using tetramethylsilane as an internal reference. Chemical shifts are reported as τ values. [G. V. Tiers J.Phys.Chem. 62, 1151 (1958).]



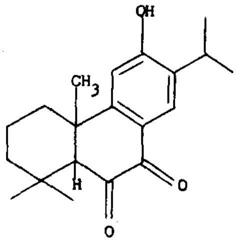
quassin *neo*quassin anhydro*neo*quassin deoxoquassin

FIG. 1.

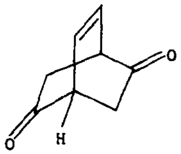
between rings B and C, this proton is also alpha to the carbonyl group at C_8, and it should resonate at a lower τ value than a normal tertiary proton.[5] The proton under discussion would also be expected, because of the spatial proximity of the C_5 carbonyl group, to resonate at a lower τ value than the angular proton in xanthoperol V (7.36τ),[6] but at a higher value than the bridgehead protons in compound VI (6.73τ),[7] as these latter protons are also allylic to a double bond. The C_7 proton resonance of quassin and its derivatives thus occur within the predicted range.



IV



V



VI

The unsplit nature of the C_7 proton resonance can be explained in

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[5] L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry* p. 57. Pergamon Press, London (1959).

[6] J. B. Bredenburg and J. N. Shoolery, *Acta Chem.Scand.* **14**, 556 (1960).

[7] C. A. Grob and A. Weiss, *Helv.Chem.Acta* **43**, 1390 (1960).

two ways. Firstly it is possible that a proton on an adjacent carbon may be sterically situated such that the coupling constant between the adjacent protons is zero. From the work of Conroy[8] on rigid caged systems, a coupling constant of zero between nonequivalent vicinal tertiary protons requires that the dihedral angle between these protons be approximately 90°, and hence that the rings B and C in quassin and its derivatives be cis fused. At present no information is available as to the stereochemistry of the ring system.

The second, and in our opinion the more likely explanation, as to why in each of the four compounds studied the C_7 proton remains unsplit is that <u>there is no proton on the adjacent carbon atom</u>. As no information is available concerning the degree of substitution at C_{14} and as no proof for the siting of a methyl group at C_1 has been presented, it is considered that structure IV for quassin is at least as compatible with the available evidence as is structure I.

Further work is in progress to rigorously prove the structure and stereochemistry of quassin.

<u>Acknowledgements</u> - We are indebted to Professor D. S. Tarbell, University of Rochester, for the NMR spectra. One of us (A.D.W.) acknowledges the award of a Victoria University of Wellington Research Scholarship.

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[8] H. Conroy, <u>Advances in Organic Chemistry: Methods and Results</u> Vol. 2, p. 311. Interscience, New York (1960).