Communications TO THE EDITOR

The Structure of Nidulin

Sir:

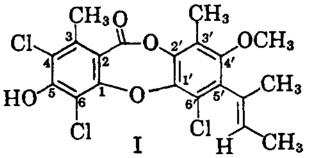
A recent examination of the NMR spectra of nidulin and its derivatives has indicated that, contrary to earlier reports,[1] the alkyl groups of ring B of nidulin consist of a methyl and *cis*-isobutenyl residue.[2]

An examination of the infrared spectra[3] of nidulin and certain of its derivatives in the hydroxyl stretching region now allows the assignment of structure I to nidulin.

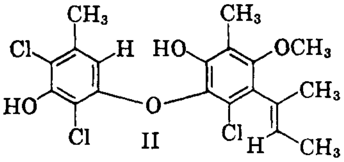
Nidulin (m.p. 178–180°,[1] isolated from the mycellial felts of *Aspergillus nidulans* and crystallized from heptane) has a single sharp hydroxyl band at 3516 cm.$^{-1}$ This can be assigned to the ring A phenolic hydroxyl which is known to be flanked by two *ortho*-chlorine substituents. That its frequency is 15–20 cm.$^{-1}$ lower than that expected[4] for *o*-chlorophenols is undoubtedly the result of the acid strengthening lactonic carbonyl group in the *para* position.

The spectrum of decarbonidulin II (m.p. 145–146.5°[1]) has absorption maxima of approximately equal intensity at 3532 cm.$^{-1}$ and 3556 cm.$^{-1}$ The former is due to the hydroxyl in ring A (raised to the expected frequency[4] because of the loss of the lactonic carbonyl group). The latter absorption is due to the new hydroxyl group in ring B. Its frequency, 3556 cm.$^{-1}$ is that expected for an *o*-phenoxy phenol.[5]

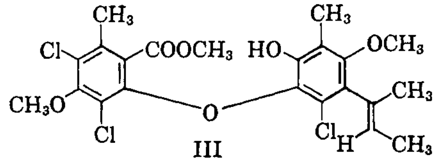
The spectrum of methyl *o*-methylnidulinate III (m.p. 154–160°[1]) has a single absorption at 3550 cm.$^{-1}$ Since a chlorine atom is at least as effective as an oxygen atom in the role of a hydrogen bond proton acceptor,[6] the absence of any appreciable O—H···Cl— absorption in the spectrum of methyl *O*-methylnidulinate excludes the possibility that a chlorine atom is attached at the 3′ position.



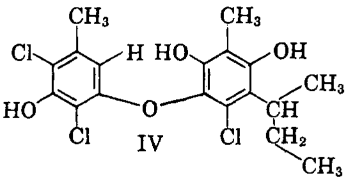
I



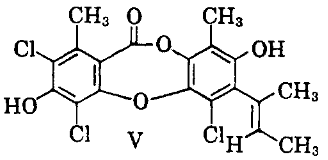
II



III



IV



V

The infrared spectrum of demethyldecarbodihydronidulin IV (m.p. 153–155°[8]) possesses three sharp, approximately equally intense bands at 3532 cm.$^{-1}$, 3565 cm.$^{-1}$ and 3614 cm.$^{-1}$ On the basis of the foregoing discussion the 3532 cm.$^{-1}$ and 3565 cm.$^{-1}$ bands are assigned to the 5 and 2′ hydroxyl groups, respectively. The band at 3614 cm.$^{-1}$, the frequency of a free phenolic hydroxyl group, implies that the second hydroxyl in ring B must be flanked by two groups which are incapable of acting as hydrogen bond proton acceptors. The only two such groups in ring B are the two alkyl residues.

Since the chlorine atom of ring B is not at 3′ and the second ring B hydroxyl is between two alkyl groups, the chlorine must be at 6′, the second ring B hydroxyl at 4′ and alkyl groups at 3′ and 5′.

The π-electrons of double bonds have been found to be excellent proton acceptors in hydrogen bonding.[9] Due to overwhelming steric reasons, the double bond of the isobutenyl group will not be in

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[1] F. M. Dean, J. C. Roberts, and A. Robertson, *J. Chem. Soc.*, 1954, 1432.

[2] W. F. Beach and J. H. Richards, *J. Org. Chem.* (in press).

[3] All spectra were taken on a Beckman model IR7 spectrometer of 0.5% and 0.1% carbon tetrachloride solutions. No changes were observed on dilution in any case.

[4] A. W. Baker, *J. Am. Chem. Soc.*, **80**, 3598 (1958); A. W. Baker and W. A. Kalding, *J. Am. Chem. Soc.*, **81**, 5904 (1959).

[5] A. W. Baker and A. T. Shulgin, *J. Am. Chem. Soc.*, **80**, 5358 (1958).

[6] According to Badger's rule,[7] the energy of a hydrogen bond is proportional to the frequency shift of the OH stretching vibration, *cf.*, *e.g.*, L. Pauling, *The Nature of the Chemical Bond*, Cornell University Press, Ithaca, N. Y., 490–495 (1960).

[7] R. M. Badger, *J. Chem. Phys.*, **5**, 837 (1937).

[8] D. S. Noyce, personal communication.

[9] A. W. Baker and A. T. Shulgin, *J. Am. Chem. Soc.*, **80**, 5358 (1958).

the plane of the aromatic ring and should, therefore, be especially well situated for hydrogen bond interaction with an adjacent hydroxyl group. Nornidulin V (m.p. 182–184°[1]) shows absorption at 3516 cm.$^{-1}$ (the 5-hydroxyl in ring A), and at 3531 cm.$^{-1}$ due to the ring B hydroxyl at 4′. Since hydrogenation of the double bond in the isobutenyl residue (*cf.* the peak at 3614 cm.$^{-1}$ in demethyldecarbodihydronidulin) shifts this absorption 83 cm.$^{-1}$ to higher frequency, it is clear that the 4′ hydroxyl group in nornidulin interacts with the π-electrons of the isobutenyl group. However, in the spectrum of methyl *O*-methylnidulinate there is no absorption observed at 3531 cm.$^{-1}$ Since hydrogen bonding to the olefin should be at least competitive with hydrogen bonding to the ether oxygen,[6] the absence of interaction of the 2′ hydroxyl with an adjacent olefin, places the isobutenyl group at 5′. Thus, structure I is the only acceptable alternative for nidulin on the basis of the infrared evidence.

NOTE ADDED IN PROOF: A recent article[10] reaches structural conclusions different from those presented here. For reasons to be discussed in detail in a forthcoming publication, we feel these alternate conclusions are incorrect.

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[10] F. M. Dean, D. S. Deorha, A. D. T. Erni, D. W. Hughes, and J. C. Roberts, *J. Chem. Soc.*, 4829–37 (1960).