

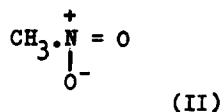
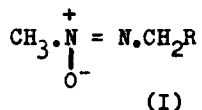
PROTON MAGNETIC RESONANCE SPECTRA OF ALIPHATIC
AZOXY COMPOUNDS AND THE STRUCTURE OF CYCASIN

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The naturally-occurring toxic glycosides, macrozamin and cycasin, have been shown to be β -primeverosyloxy (1, 2) and β -D-glucopyranosyloxy (3, 4), respectively, derivatives of azoxymethane (I; R = H) by chemical degradation combined with infrared and ultraviolet spectroscopic studies. There is evidence that the unsubstituted methyl group is attached to the quaternary (i.e. oxygenated) nitrogen atom (5, 6). A recent paper (7) on proton magnetic resonance (p.m.r.) spectra of aliphatic azoxy compounds prompts us to report our own results, which leave no doubt that cycasin has structure (I; R = β -D-glucopyranosyloxy).



The positions of signals from neat azoxymethane (5) with internal tetramethylsilane reference agree roughly with those previously reported (7) for a 10% solution in carbon tetrachloride, but we find that the two non-equivalent methyl groups are weakly coupled across the intervening pi-bonded system. The clearly resolved 1:3:3:1 quartet, $J = 1.1 \pm 0.2$ c.p.s., at lower field (δ 4.16) is assigned to the protons of

the methyl group adjacent to the oxygenated nitrogen atom by comparison with the position of the methyl signal from the electronically similar nitromethane (II), δ 4.33 (8). The other methyl group gave rise to a poorly resolved quartet of the same total intensity at δ 3.16. Similarly, *trans*- ω -azoxytoluene, m.p. 38-40° from ethanol, obtained by treatment of ω -azotoluene (9) with perbenzoic acid in ether (10) gave triplets, $J \sim 0.8$ c.p.s., at δ 4.58 and 5.25 (both poorly resolved) in deuteriochloroform, or at δ 4.70 and 5.42 (the latter clearly resolved) in pyridine, assigned as in ref. 7.

For cycasin in deuterium oxide (acetone, δ 2.16, as internal cross-reference), the methyl and methylene signals from the aglycone may be assigned by relative intensities as well as splitting patterns. The former appeared as a 1:2:1 triplet, $J = 1.5 \pm 0.2$ c.p.s., at δ 4.09 (i.e. near the low-field signal from azoxymethane), and the latter as a quartet (outer members poorly resolved) at δ 5.15, the large paramagnetic shift being due to direct attachment of the group to oxygen as well as to nitrogen. The corresponding signals for cycasin tetra-acetate in deuteriochloroform were little shifted in position or shape. Both spectra showed expected signals due to the glucose residue or acetate ester groups. On addition of trifluoroacetic acid to the solution of cycasin only the OH signal shifted (from δ 4.6 to 5.3), the glucose anomeric proton signal then being revealed as a doublet, $J = 7.1$ c.p.s., at δ 4.62, which confirms (11) the β -glucopyranoside formulation. The spectrum was otherwise unchanged during at least 16 hours at room temperature, so that the methyl or methylene protons are not exchangeable under these

conditions. Base-catalyzed exchange was not attempted because of the great sensitivity of azoxyglycosides to bases (2).

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