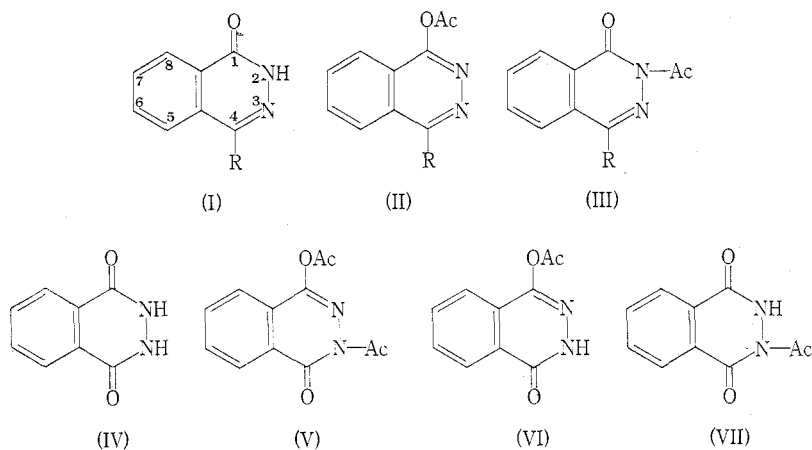


# THE STRUCTURES OF THE ACETYL DERIVATIVES OF PHTHALAZONES AND PHTHALAZ-1,4-DIONES\*

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The structures of the products obtained by alkylation of tautomeric  $\alpha$ - and  $\gamma$ -hydroxy derivatives of aza-heterocyclic compounds have received considerable attention. By the application of physical methods, in particular n.m.r. and infrared spectroscopy, and of unequivocal methods of synthesis the question has been largely resolved in a number of important cases. The question of the structures of the acyl derivatives of such systems has received less attention; for example there appears to be no unequivocal evidence for the assignment of structures to any of the acyl derivatives of the hydroxy-cinnolines, -quinoxalines, or -phthalazines.



The structures of the acetyl derivatives of some phthalaz-1-ones (I; R = H, CH<sub>3</sub>, and C<sub>6</sub>H<sub>5</sub>) and of phthalaz-1,4-dione (IV) have now been determined using n.m.r. spectra. Rowe and Peters<sup>1</sup> examined the acetyl derivative of 4-methylphthalaz-1-one (I; R = CH<sub>3</sub>) and on the basis of its rapid hydrolysis in ethanol assigned to it the O-acetyl structure (II; R = H); however, as has been pointed out by Vaughan,<sup>2</sup> some N-acetyl cyclic amides are also susceptible to rapid hydrolysis, for example N-acetyl-uracil and -thymine.

In the n.m.r. spectra the  $\tau$  values for the C(8) proton and the acetyl CH<sub>3</sub>, respectively, were: (I; R = H) 1.48, —; (II; R = H) 1.48, 7.22; (III; R = CH<sub>3</sub>) 1.47, 7.23; (III; R = C<sub>6</sub>H<sub>5</sub>) 1.47, 7.22. Since the C(8) proton of 2-methylphthalaz-1-one gives a signal at  $\tau$  1.53 it appears that N-substitution does not significantly affect the chemical shift of this proton in these compounds

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<sup>1</sup> Rowe, F. M., and Peters, A. T., *J. Chem. Soc.*, 1933, 1331.

<sup>2</sup> Vaughan, W. R., *Chem. Rev.*, 1948, **43**, 447.

and that, since in each of the acetyl derivatives the C(8) proton values are identical with that of the parent phthalazone, the 1-oxo group must be present in each case, the anisotropy of the C=O grouping resulting in a shift to lower field relative to the other benzenoid protons ( $\tau$  2.2). It follows that the products of acetylation are *N*-acetyl derivatives as in (III).

Drew and Hatt<sup>3</sup> showed that phthalaz-1,4-dione (IV) forms a diacetyl (V) and two monoacetyl derivatives (m.p. 172–173° and 175–176°). The structure of (V) was established from its formation, by acetylation, from either of the monoacetyl compounds to which, however, these authors were unable to assign specific structures. The n.m.r. spectrum of (V) shows two unsplit peaks at  $\tau$  7.23 and 7.53; by comparison with the acetylphthalaz-1-ones the former must represent the methyl protons of the *N*-acetyl group. Partial hydrolysis of (V) yields a monoacetyl compound, m.p. 172–173°, whose n.m.r. spectrum shows an acetyl CH<sub>3</sub> signal at  $\tau$  7.53, indicating that it has the *O*-acetyl structure (VI); confirmation follows from a consideration of the  $\tau$  values for the benzenoid protons which appear at  $\tau$  1.53 and 2.20 as two multiplets which integrate for one and three protons respectively. Had acylation involved one of the nitrogen atoms the anisotropic effect of the C=O groupings would have shifted the absorption due to two of the benzenoid protons to lower field ( $\tau$  1.53) leaving only two in the normal aromatic region ( $\tau$  2.20).

The acetyl compound, m.p. 175–176°, must have the *N*-acetyl structure (VII); it was not possible to confirm this directly by n.m.r. because of lack of a suitable solvent, a difficulty which also prevented the examination of the acetyl derivatives of 5-nitro- and 5-aminophthalaz-1,4-diones reported by Drew and Pearman.<sup>4</sup>

#### EXPERIMENTAL

All spectra were measured with an accuracy of 1 c/s on a Varian DP60 spectrometer operating at 60 Mc by Dr. T. M. Spotswood, to whom we are indebted.

All compounds used were prepared by methods reported in the literature; 2-acetyl-4-phenylphthalaz-1-one (III; R = C<sub>6</sub>H<sub>5</sub>) has m.p. 130–131°, not 178–179° as reported by von Rothenburg.<sup>5</sup>

<sup>3</sup> Drew, H. D. K., and Hatt, H. H., *J. Chem. Soc.*, 1937, 16.

<sup>4</sup> Drew, H. D. K., and Pearman, F. H., *J. Chem. Soc.*, 1937, 26.

<sup>5</sup> Rothenburg, R. von, *J. prakt. Chem.*, 1895, **51**, 140.