A New Synthetic Approach to the 1,2,4-Oxadiazine Ring System

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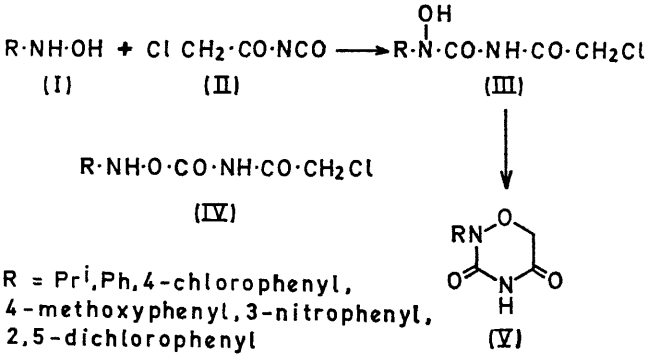
Summary A new general method for the synthesis of 2-substituted 2*H*-1,2,4-oxadiazine-3,5(4*H*,6*H*)-diones is described.

CHLOROACETYL ISOCYANATE (II) reacts readily and rapidly with *N*-mono-substituted hydroxylamines in anhydrous benzene medium to yield *N*-chloroacetyl-*N'*-hydroxy-ureas of the type (III). That the products have structure (III), and not (IV), is borne out by the fact that they give positive colour reactions with alcoholic ferric chloride solution[1,2] and that their i.r. spectra exhibit (in addition to the absorption in the 3·15 μm region due to the –NH– function) absorption in the 2·95 μm region due to the hydroxyl group of the R–N(OH)–CO– moiety.[2]

Compounds of the type (III) undergo ready intramolecular cyclisation in 2% aqueous sodium hydroxide to afford, upon acidification, 2-substituted 2*H*-1,2,4-oxadiazine-3,5(4*H*,6*H*)-diones (V) in an overall yield of 30—60%. The i.r. and n.m.r. spectra of the products are in accord with the general structure (V).

Since chloroacetyl isocyanate can easily be prepared from chloroacetamide[3] and since various methods are available for the preparation of a wide array of *N*-mono-substituted hydroxylamines, this two-step procedure constitutes a new general method for the construction of the 1,2,4-oxadiazine ring system.



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