Base-catalysed Transformations of *NN*-Disubstituted *o*-Nitrobenzamides

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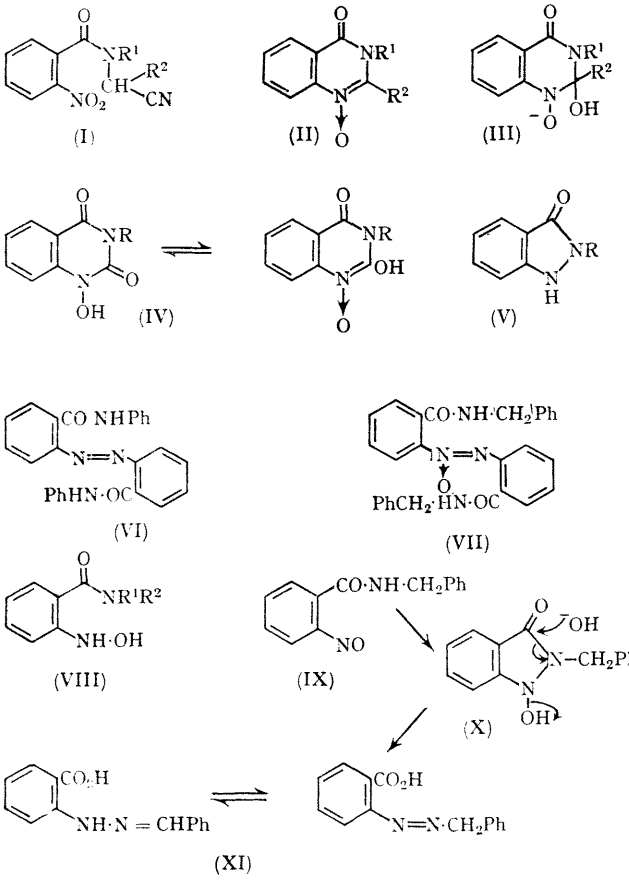
IN the formation[1] of 2-alkoxy-1-hydroxyquinazolones by base-catalysed cyclisation of *N*-cyanomethyl-*o*-nitrobenzamide (I; $R^1 = R^2 = H$), interaction of the nitro-group with the side-chain cannot be preceded by isomerisation to an aci-nitro-tautomer.[2] Cyclisation reactions of this type[2,3] provide strong evidence for the ability of the intact nitro-group to function as the electrophile in aldol-type condensations. Further support for this contention has now been obtained from a study of the base-catalysed reactions of a series of *NN*-disubstituted-*o*-nitrobenzamides (I).

Treatment of the amides (I; R^1 = Me, CH_2Ph, or Ph, $R^2 = H$) with a variety of basic catalysts (ethanolic sodium ethoxide; aqueous sodium hydroxide; piperidine) afforded consistently high yields of products subsequently identified as the 1-hydroxyquinazolinediones (IV; R = Me, CH_2Ph, or Ph). These potentially tautomeric heterocycles are presumably derived from an initially formed cyanoquinazoline 1-oxide (II; R^1 = Me, CH_2Ph, or Ph, R^2 = CN) by conversion into, and loss of hydrogen cyanide from, an adduct (III; R^2 = CN).[1] The higher yields of cyclised products obtained from the amides (I; R^1 = Me, CH_2Ph, or Ph, $R^2 = H$) compared[1] with the parent compound (I; $R^1 = R^2 = H$) may be attributed to the enhanced acidity of the methylene group in the former, and to the absence of side reactions stemming from the presence in the side-chain of a competing nucleophilic centre (*i.e.* ·*N-H*).

In contrast, the methyl-substituted amides (I; R^1 = CH_2Ph or Ph, R^2 = Me) warmed with sodium ethoxide in ethanol afforded the indazolone derivatives (V; R = CH_2Ph



or Ph). Since under similar conditions the amide (I; R^1 = H, R^2 = Me) is converted into the oxide (II; R^1 = H, R^2 = Me), indazolone formation in these reactions is compatible with a course involving the initial formation of the quinazoline 1-oxides (II; R^1 = CH_2Ph or Ph, R^2 = Me), followed by ring opening of the derived hydrates (III; R^1 = CH_2Ph or Ph, R^2 = Me), and cyclisation of the resulting *N*-acetylhydroxylamines (VIII; R^1 = CH_2Ph or Ph, R^2 = Ac) or the corresponding hydroxylamino-amides (VIII; R^1 = CH_2Ph or Ph, R^2 = H). The presence of hydroxylamino-intermediates in these reactions may be inferred from the formation of a mixture of the indazolone (V; R = Ph) and the azo-compound (VI) when the amide (I; R^1 = Ph, R^2 = Me) was warmed with sodium carbonate in aqueous ethanol. On the other hand the conversion of the amide (I; R^1 = CH_2Ph, R^2 = Me) under similar conditions into a mixture of the azoxy-compound (VII) and the hydrazone (XI), requires the additional presence of the nitrosoamide (IX) readily produced by mild oxidation[4] of the hydroxylamine (VIII; R^1 = CH_2Ph, R^2 = H) in the alkaline medium. Moreover ring opening of a 1-hydroxyindazolone (X) derivable from the nitrosoamide (IX) by cyclisation, is a plausible course for the formation of the hydrazone (XI). Such a course finds analogy in the known[3,5] base-catalysed ring scission of 1-hydroxyindolinones and is further substantiated by the conversion of the readily accessible *o*-nitrosobenzanilide[6] in warm aqueous ethanolic sodium carbonate into azobenzene 2-carboxylic acid. Attempts to isolate the intermediate 1-hydroxyindazolones from reactions of this type have so far been unsuccessful.

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