A New Heterocyclisation Reaction Leading to Cinnolin-4(1*H*)-one Derivatives

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Summary 2-Nitrophenacylidene phenylhydrazones (**2**) undergo base-catalysed cyclisation by intramolecular nucleophilic displacement of the nitro-group by the *ortho*-side-chain, providing an efficient general route to 3-substituted 1-phenylcinnolin-4(1*H*)-ones (**3**).

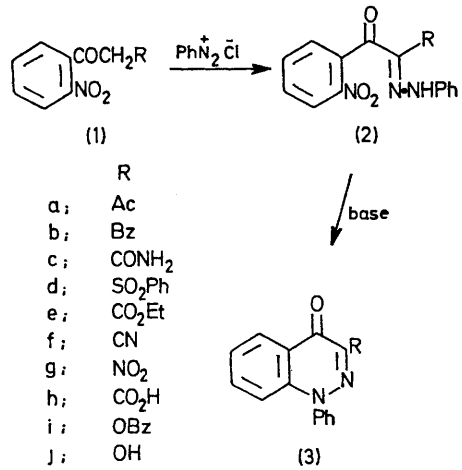
HETEROCYCLISATIONS involving the intramolecular nucleophilic displacement of the nitro-group in certain *ortho*-nitrobenzoyl derivatives have recently been described.[1] Analogous displacements in 2-nitrobenzylidene hydrazones provide a general method for the synthesis of indazole derivatives.[2] The application of cyclisations of this type to the synthesis of six-membered heterocycles is now reported in a new synthesis of cinnoline derivatives from 2-nitrophenacylidene phenylhydrazones.†

TABLE

3-Substituted 1-phenylcinnolin-4(1*H*)-ones.

Compound	Yield/%	M.p./°C
(**3c**)	98	294
(**3d**)	76	276
(**3e**)	71	152
(**3f**)	91	224
(**3g**)	37	190

The 2-nitrophenacylidene phenylhydrazones (**2**) used as substrates were readily synthesised in high yield (80—100%) by coupling benzenediazonium chloride with 2-substituted *ortho*-nitroacetophenone derivatives (**1**) containing a suitably activated methylene group. Heating the hydrazone (**2a**) (0·016 mol) with 0·5M aqueous sodium carbonate (40 ml) in ethanol (60 ml) for 1 h afforded



3-acetyl-1-phenylcinnolin-4(1*H*)-one (**3a**) (92%), m.p. 165°, whose structure follows from its oxidation by chromic acid or sodium hypochlorite to the known[3] carboxylic acid (**3h**) (58—83%), m.p. 275°. The structure of the phenyl ketone (**3b**) (81%), m.p. 183°, derived from the hydrazone **2b**), was also established by Baeyer-Villiger oxidation (30%)

† Satisfactory analyses and spectral data were obtained for all new compounds.

aqueous hydrogen peroxide–glacial acetic acid) which occurred by preferential migration of the heterocyclic nucleus, affording the benzoate (**3i**) (70%), m.p. 165°, and the parent hydroxy-compound (**3j**) (18%), m.p. 227°. Sodium carbonate also catalysed the cyclisation of the hydrazones (**2c**—**e**) to the cinnolinones (**3c**—**e**) in high yield (Table).

The transformations of the hydrazones (**2a**—**e**) into the cinnolinones (**3a**—**e**) are intramolecular nucleophilic aromatic substitution reactions involving the displacement of a nitro-group by a nitrogen nucleophile. The ready cyclisation of the cyano- and nitro-hydrazones (**2f**) and (**2g**) to the corresponding cinnolinones (**3f**) and (**3g**) (Table) in warm aqueous ethanolic sodium acetate shows the ease of the heterocyclisation [(**2**) → (**3**)] and contrasts with the less ready cyclisation of 2-nitrobenzylidene hydrazones to indazoles.[2]

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[3] H. J. Barber and E. Lunt, *J. Chem. Soc.*, 1965, 1468.