Synthesis of 2-Acyl-3-hydroxyquinolines Embodying a Novel Variant of the Smiles Rearrangement

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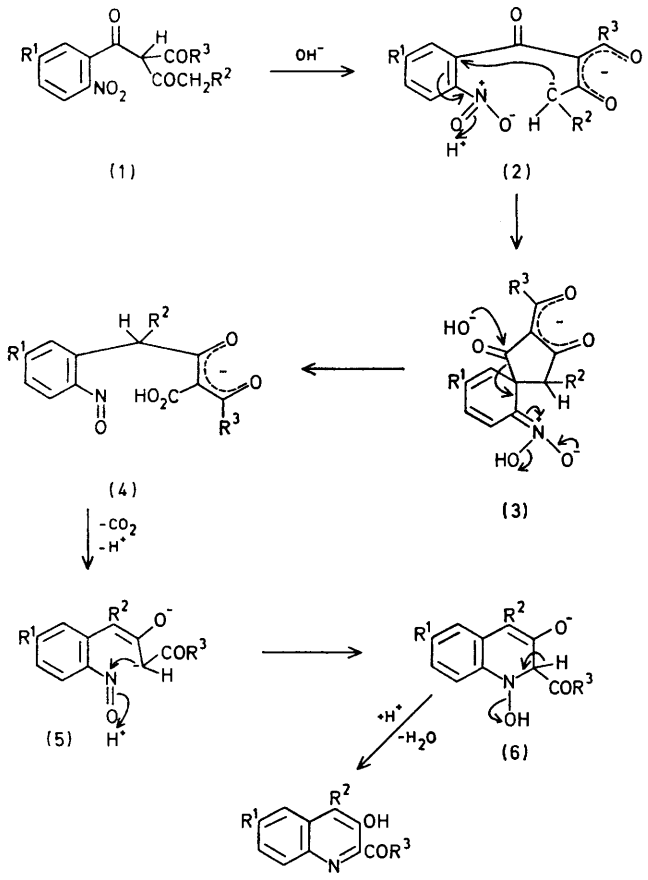
Summary. 2-(2′-Nitrobenzoyl) derivatives of certain 1,3-diketones undergo base-catalysed cyclisation to hitherto inaccessible 2-acyl-3-hydroxyquinolines by a process explicable in terms of a new version of the Smiles rearrangement.

Two modes of base-catalysed nitro-group side-chain interaction[1] in 2′-nitrobenzoyl derivatives have been reported previously. These involve direct aldol-type condensation[2] between the nitro-group and the side chain and the side-chain displacement[3,4] of the nitro-group respectively. We now report a third mode of interaction which involves a novel variant of the Smiles rearrangement, and provides a potentially general route to otherwise inaccessible[5] 2-acyl-3-hydroxyquinolines.

3-(2′-Nitrobenzoyl)pentane-2,4-dione (**1**; $R^1 = R^2 = H$, $R^3 = Me$) heated under reflux (0·5 h) with 20% w/v aq., KOH afforded as the major product a yellow acidic solid, $C_{11}H_9NO_2$, ν_{max} 1660 (CO) cm^{-1}; τ ($CDCl_3$) — 1·16 (1H, s OH), 1·90—2·56 (5H, m, ArH), and 7·09 (3H, s, Me), which

formed an acetate and a hydrazone and is identified as the hitherto unknown 2-acetyl-3-hydroxyquinoline (**7a**) on the basis of the following evidence. Catalytic (H_2, 10% Pd–C) or dithionite reduction of the yellow acidic product afforded

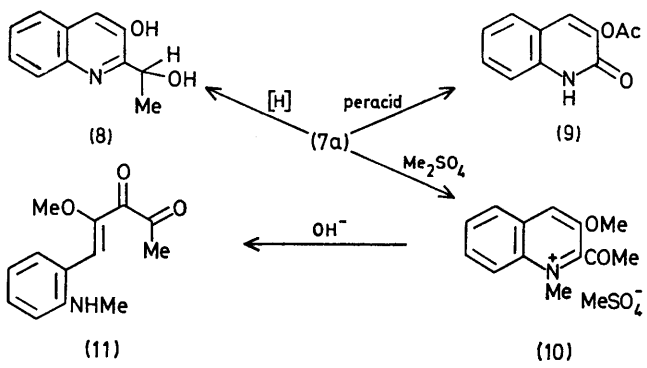


(7)	R^1	R^2	R^3	Yield/%	M.p./°C
a;	H	H	Me	83	118
b;	Me	H	Me	71	126
c;	Cl	H	Me	55	149
d;	H	H	Ph	15	86
e;	H	Me	Et	82	82

SCHEME

a secondary alcohol (**8**) (70–80%), which gave a diacetate. The presence of the quinoline nucleus was established by oxidation with peracid (30% aq. H_2O_2–glacial AcOH; *m*-chloroperbenzoic acid) to give the acetoxyquinolin-2(1*H*)-one (**9**) of established structure.[6] Since the yellow acidic product is not identical with the known[7] 3-acetylquinolin-2(1*H*)-one [the rational precursor of (**9**)], it can only have the structure (**7a**) and is converted into (**9**) by Baeyer–Villiger rearrangement (with preferential migration of the heterocyclic nucleus[4]) followed by acetyl migration. In further support of the structure (**7a**), exhaustive methylation gave the methoxy *N*-methylquinolinium methosulphate (**10**) (86%), which underwent ring-opening in cold dilute aq. NaOH to yield the methylaminodiketone (**11**) as a gum (quantitative yield), characterised as the quinoxaline derivative.

Cyclisations of the type [(**1**; $R^1 = R^2 = H$, $R^3 = Me$) → (**7a**)] are readily applicable to the synthesis of other **2**-acyl-3-hydroxyquinolines (**7b**—**e**) (Scheme).†



The unprecedented cyclisations [(**1**) → (**7**)] are readily explained in terms of a mechanism (Scheme) which involves a new variant of the Smiles rearrangement. Thus, intramolecular nucleophilic attack at C-1′ in the dicarbanion (**2**) affords the spiro-intermediate (**3**) which, unlike the corresponding species [*e.g.* (**3**), SO_2 replaces CO] in the Smiles rearrangement of analogous sulphonyl derivatives,[8] cannot achieve stabilisation in the usual way (*i.e.* by ejection of the C-1′ sulphonyl leaving group). Consequently an alternative pathway [(**3**) → (**4**) → (**5**)], involving nucleophilic attack by hydroxide ion at the carbonyl group with ring scission and concomitant reduction of the nitro-group to nitroso, is followed. Subsequent cyclisation of the nitroso-intermediate [(**5**) → (**6**) → (**7**)] then affords the 2-acyl-3-hydroxyquinoline product.

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

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