# Synthesis of 4-Hydroxyquinolines from the Baylis-Hillman Adducts of *o*-Nitrobenzaldehydes

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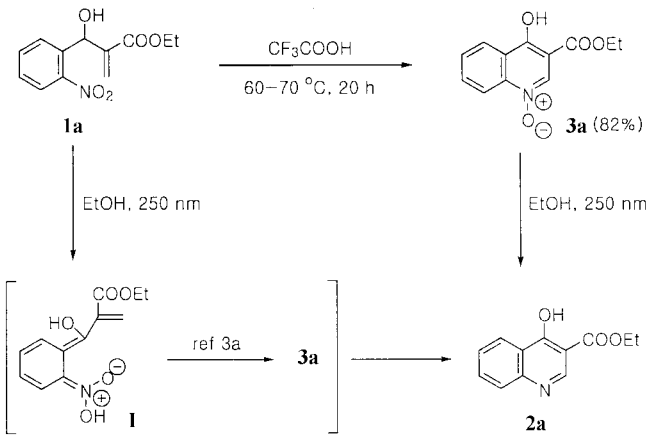
The Baylis-Hillman reaction is one of the most powerful carbon-carbon bond-forming methods in organic synthesis.[1] The Baylis-Hillman adducts, which are allylic alcohol derivatives, can be formed most often by the reaction of activated vinyls and carbonyl compounds.[1] Besides the usefulness of these Baylis-Hillman adducts themselves, further derivatization with various nucleophilic reagents toward synthetically useful compounds has been studied in depth by us and other groups.[2] There were some reported papers on the formation of heterocyclic compounds including quinolines from the Baylis-Hillman adducts.[3]

Quinolines and their derivatives occur in numerous natural products.[4] Many quinolines display interesting physiological activities and have found attractive applications as pharmaceuticals and agrochemicals as well as being general synthetic building blocks.[4b] Although many synthetic methods have been developed for the preparation of quinolines,[5] due to their great importance, the development of novel synthetic methods remains an active research area.[6]

Recently, we have reported on the synthesis of 4-hydroxy-3-ethoxycarbonylquinoline *N*-oxide derivatives from the Baylis-Hillman adducts of 2-nitrobenzaldehydes in acidic conditions.[3a] As a continuous work, we intended to examine the possibility of transforming the Baylis-Hillman adducts of 2-nitrobenzaldehydes into the quinoline *N*-oxides by the photochemical method.

A solution of **1a** in ethanol (0.16 M solution) was irradiated with 250 nm wavelength in a quartz reaction vessel.[7]




**Scheme 1**

We could isolate quinoline *N*-oxide **3a** in trace amount from the reaction. Instead the deoxygenated 4-hydroxy-3-ethoxycarbonylquinoline **2a** (39%) was obtained as the major product.[8] The reaction might proceed *via* the *aci*-nitro compound **I**, which was generated through the benzylic hydrogen abstraction by the excited *ortho*-nitro group.[9] **I** was converted to the quinoline *N*-oxide **3a** as described in our previous paper.[3a] Elimination of oxygen atom of **3a** and the fate of oxygen atom is uncertain at this point (*vide infra*). In other cases **1b-d** and the nitrile analogue **1e**, we could obtain the similar results as in Table 1.[8]

In the reaction mixture we could observe the quinoline *N*-

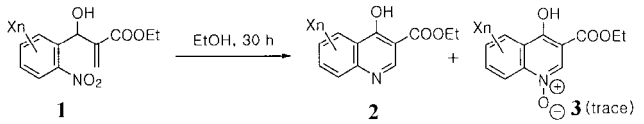
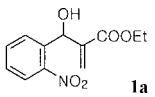
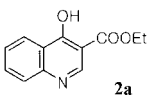
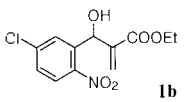
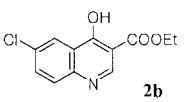
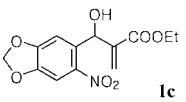
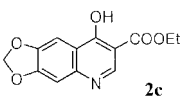
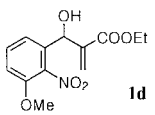
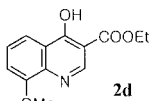
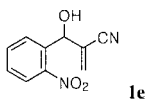
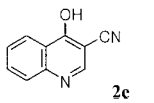
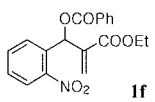
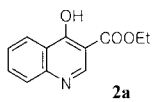



**Table 1**. Photoreaction of the Baylis-Hillman Adducts **1**

| entry | B-H adducts (**1**) | conditions | products (**2**) | yields (%) |
|---|---|---|---|---|
| a |  **1a** | EtOH/250 nm<br>EtOH/350 nm<br>THF/250 nm[a] |  **2a** | 39<br>25<br>30 |
| b |  **1b** | EtOH/250 nm |  **2b** | 23 |
| c |  **1c** | EtOH/250 nm |  **2c** | 30 |
| d |  **1d** | EtOH/250 nm |  **2d** | 26 |
| e |  **1e** | EtOH/250 nm |  **2c** | 36 |
| f |  **1f** | EtOH/250 nm |  **2a** | 26[b] |

[a]0.03 M concentration. [b]benzoic acid (25%) was obtained.

oxides in trace amounts (< 5%), which might indicate the intermediacy of quinoline *N*-oxides for the formation of quinolines **2**. Moreover, irradiation of pure **3a** (250 nm, 20 h) in ethanol produced **2a** in 58% isolated yield. Such deoxygenation of quinoline *N*-oxides to quinolines indeed occurred very slowly in ethanol solution without UV irradiation.

Change of the reaction conditions such as wavelength, solvent, or concentration did not improve the yields (entry a in Table 1). Heating **1a** in ethanol (70-80 °C, 48 h) or diphenyl ether (200 °C, 48 h) without UV irradiation did not give any quinoline **2a** nor quinoline *N*-oxide.

Photochemical rearrangements and fragmentations of *o*-nitrobenzyl compounds were well-known.[9] Transfer of oxygen atom of nitro group to the benzylic position and concomittant removal of the alkoxy, carboalkoxy, or phosphate group occurs. In these respects the *o*-nitrobenzyloxy moiety was studied and used as a photochemically labile protecting group.[9] In order to examine the possibility of the Baylis-Hillman adducts as a photochemical protecting group, we performed the photochemical reaction of *O*-benzoyl analogue **1f** in the same reaction conditions. From the reaction we could obtain **2a** (26%) and benzoic acid (25%) as expected. However, to our disappointment, starting material **1f** was recovered in 64% yield.

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## References and Notes

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7. For the photolysis experiments a Raynot photochemical reactor (model RPR-2080, the Southern N. E. Ultraviolet Co.) was used. The built-in monochromatic UV light sources (RUL-250 nm UV lamp) was positioned approximately 17 cm from the reaction quartz tube.
8. Typical procedure for the synthesis of **2a** and some selected spectroscopic data: A stirred solution of **1a** (400 mg, 1.59 mmol) in ethanol (10 mL) was irradiated (250 nm) for 30 h. After removal of ethanol, column chromatographic purification ($CH_2Cl_2$/EtOH, 14 : 1) gave **2a** as a white solid, 135 mg (39%): mp 267-268 °C (lit.[3a] 269-270 °C): IR (KBr) 3434, 3169, 2982, 2904, 1706, 1623, 1529, 1476, 1380, 1292, 1202, 1141, 766 $cm^{-1}$; $^1H$ NMR (DMSO-$d_6$) $\delta$ 1.29 (t, $J$ = 7.1 Hz, 3H), 4.23 (q, $J$ = 7.1 Hz, 2H), 7.42 (t, $J$ = 8.1 Hz, 1H), 7.63 (d, $J$ = 8.1 Hz, 1H), 7.71 (t, $J$ = 8.1 Hz, 1H), 8.17 (d, $J$ = 8.1 Hz, 1H), 8.56 (s, 1H), 12.41 (br s, 1H); $^{13}C$ NMR (DMSO-$d_6$) $\delta$ 14.52, 59.77, 109.94, 118.98, 124.90, 125.82, 127.44, 132.61, 139.15, 145.11, 165.00, 173.68.
**2e**: 36%, mp 303-305 °C (dec.) (lit.[10] 301 °C); IR (KBr) 3174, 2959, 2873, 2223, 1618, 1561, 1535, 1352, 760 $cm^{-1}$; $^1H$ NMR ($CD_3OD$) $\delta$ 7.52 (td, $J$ = 7.6 and 1.2 Hz, 1H), 7.61 (d, $J$ = 8.1 Hz, 1H), 7.79 (td, $J$ = 7.1 and 1.4 Hz, 1H), 8.25 (dd, $J$ = 8.2 and 1.3 Hz, 1H), 8.53 (s, 1H); $^{13}C$ NMR ($CD_3OD$) $\delta$ 94.55, 115.71, 118.99, 125.30, 125.44, 126.01, 133.74, 139.59, 146.43, 176.50; MS (70 eV) *m/z* (rel intensity) 63 (45), 76 (33), 114 (41), 115 (49), 142 (93), 170 ($M^+$, 100).
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