

Photochemical Isomerization of 3-Acetylpyridines to Cyclobuta[*c*]pyridines Involving Norrish Type II Reactions

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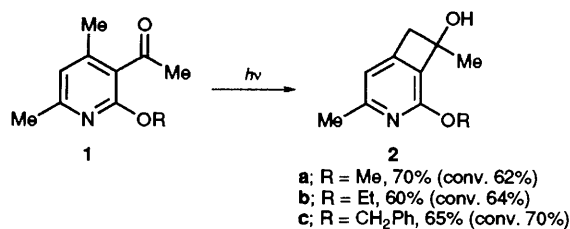
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Photolysis of 3-acetyl-2-alkoxy-4,6-dimethylpyridines gives cyclobutenols, 2-alkoxy-3,6-dimethyl-3-hydroxy-cyclobuta[*c*]pyridines, in good yields *via* Norrish Type II cyclizations whereas 3-acetyl-2-methylpyridine does not cyclize to cyclobutenol.

The photoenolization of *ortho*-alkyl phenylketones has been reviewed by Sammes¹ and presents one of the simplest forms of photochromism. The transient enols are not stable but can be trapped with a variety of dienophiles;² this process has synthetic potential. Since Matsuura and Kitaura first noted that 2,4,6-trimethylphenylketones form benzocyclobutenols as products,³ several types of cyclobutenols have been isolated from the photoreaction of 2,6-dimethylacetophenones, valerophenones and *ortho*-monoalkylphenylketones.⁴ On the other hand, hydrogen abstraction from heteroaromatic ketones such as 2-acetylpyridines has recently been reported to

proceed hydrogen abstraction by both nitrogen and carbonyl oxygen.⁵ Now we report the first example of cyclobutenol formation from heteroaromatic ketones *via* a photochemical Norrish Type II reaction of 3-acetylpyridines.

3-Acetyl-2-alkoxy-4,6-dimethylpyridines **1a-c** were prepared by standard S_N2 chemistry from corresponding pyridone and alkyl iodide in the presence of silver carbonate.⁶ Irradiation of compound **1a** with a high pressure mercury lamp through a Pyrex filter under argon gave a cyclobutenol, 3,6-dimethyl-3-hydroxy-2-methoxycyclobuta[*c*]pyridine **2a**, in 70% yield at 62% conversion as the sole product. Photolysis of



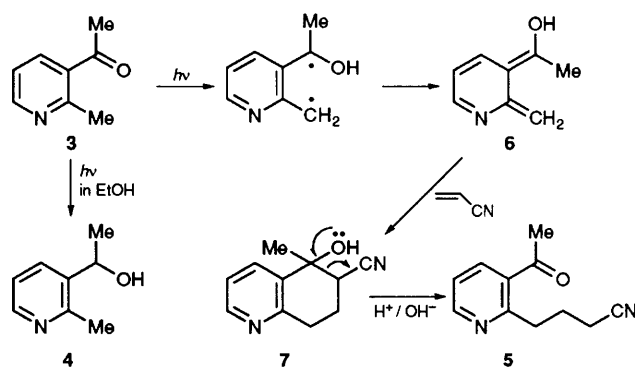
Scheme 1

other acetylpyridines **1b, c** gave the corresponding cyclobutenols **2b, c** as shown in Scheme 1. The structures of **2a–c** were determined from spectral data and elemental analyses.[†] The structure was further supported by the fact that **2a** reverted quantitatively to **1a** on heating.[‡]

The cyclization proceeded independently of the solvent; the cyclobutenol was obtained in ethyl alcohol or isopropyl alcohol. Furthermore, the cyclization was not affected by the presence of dienophiles such as acrylonitrile, dimethylacetylene dicarboxylate, or maleic anhydride.

Next, we attempted the photochemical reaction of mono-substituted 3-acetylpyridine **3**. Photolysis of 3-acetyl-2-methylpyridine **3** in ethyl alcohol or isopropyl alcohol gave corresponding alcohol **4** in 80% yield *via* intermolecular hydrogen abstraction from the solvent whereas a polymerised mixture was obtained in benzene. Irradiation of a benzene solution of **3** (0.02 mol dm⁻³) in the presence of acrylonitrile (1.0 mol dm⁻³) gave 3-acetyl-2-(3-cyano-1-propyl)pyridine **5** in 15% yield at 56% conversion. The formation of the adducts **5** is reasonably explainable in terms of ring opening of the primary adduct **7** which was generated by trapping dienol **6** with acrylonitrile as shown in Scheme 2. In other words the formation of the adduct **5** indicates that photolysis of monosubstituted 3-acetylpyridine **3** also proceeds by a Norrish Type II reaction and generates dienol, whereas the formation of cyclobutenols **2** from 2,4,6-trisubstituted 3-acetylpyridines **1** may involve a diradical intermediate since the adduct was not detected.

Cyclobutapyridines are of special interest since they are nitrogen analogues of benzocyclobutenes, a class of com-



Scheme 2

pounds which is important in the synthesis of both theoretically interesting molecules and natural products.⁷ The present reaction provides the first example of cyclobutenol formation from heteroaromatic ketones and is a useful synthesis of cyclobuta[c]pyridines since only one synthesis involving pyrolysis of propynyl 4-pyridyl ester has been reported.⁸

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[†] Spectral data for **2a**: ¹H NMR(CDCl₃) δ 1.67 (s, 3H, 3-Me), 2.41 (s, 3H, 6-Me), 3.04 (br, 1H, OH, D₂O exchangeable), 3.14 and 3.20 (ABq, *J* 14.7 Hz, 2H, 4-CH₂), 3.92 (s, 3H, OMe), 6.59 (s, 1H, 5-CH); ¹³C NMR (CDCl₃) δ 24.7 (q, 3-Me), 26.1 (q, 6-Me), 47.9 (t, 4-C), 53.7 (q, OMe), 78.1 (s, 3-C), 112.0 (d, 5-C), 127.2 (s, 2a-C), 154.7 (s, 4a-C) 156.3 (s, 6-C), and 157.5 (s, 2-C); MS (EI) *m/z* 188 (M⁺).

[‡] When the benzene solution of cyclobuta[c]pyridine **2a** was refluxed under nitrogen for 1 h, acetylpyridine **1a** was obtained quantitatively.