

PHOTOSENSITIZED OXYGENATION OF 2-PYRIDONES^{1†}

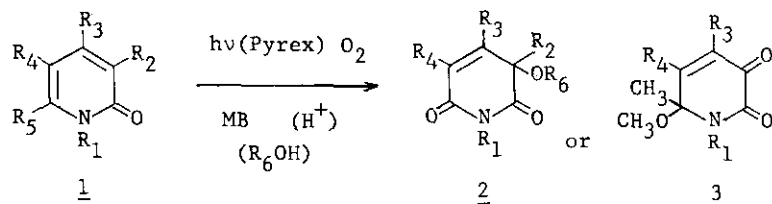
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Abstract — Irradiation of oxygenated solutions of 3- and 6-substituted 2-pyridones with Methylene Blue as sensitizer afforded the oxygenation products probably by way of endoperoxide intermediates (4).

As an extension of systematic research on the photochemistry of nitrogen-carbonyl systems such as amides and imides,² we have been exploring photoreactions of conjugated nitrogen-carbonyl system.¹ In connection with these studies we are interested in the photochemical properties of 2-pyridones, the most fundamental member in the family of conjugated nitrogen-carbonyl systems. Although [4+4]dimerization,³ valence isomerization⁴, and [2+2]cycloaddition to olefins⁵ have been extensively studied, photooxygenation of pyridones, which seems interesting from the view point of synthetic utility, has attracted no attention.⁶ In this paper we wish to report the photosensitized oxygenation of 3- and 6-substituted 2-pyridones (1). Irradiation of 3-methyl-2-pyridone (1a-f) with Methylene Blue as sensitizer under oxygen atmosphere, in the presence of small amount of acid catalyst, afforded pyridine-2,6-diones (2a-f) as shown in Scheme 1 and Table I. Probably 2-pyridones react initially with photochemically generated singlet oxygen to form unstable endoperoxides (4) by [4+2]addition, followed by the O-O bond fission with acid catalyst by path A leading to the products 2 (Scheme 2).⁷ Irradiation of 3-methoxy-2-pyridone (1g) in methanol gave 3,3-dimethoxypyridine-2,6(1H,3H)-dione (2g). Presumably nucleophilic addition of methanol occurred at the 3-position of the endoperoxide (4) when R₂ is OCH₃ (path B). Similar products 2h-j were also obtained with other alcohols such as ethanol, i-propanol and allyl alcohol as shown in Table I. The site of alcohol addition can be reasonably explained by stabilization of the intermediate carbonium ion with a substituent if the S_N1-character is postulated for the alcoholysis.

† Dedicated to Professor Gilbert Stork on the occasion of his 65th birthday.



Scheme 1

Table I Photooxygenation Products from 2-Pyridones^a

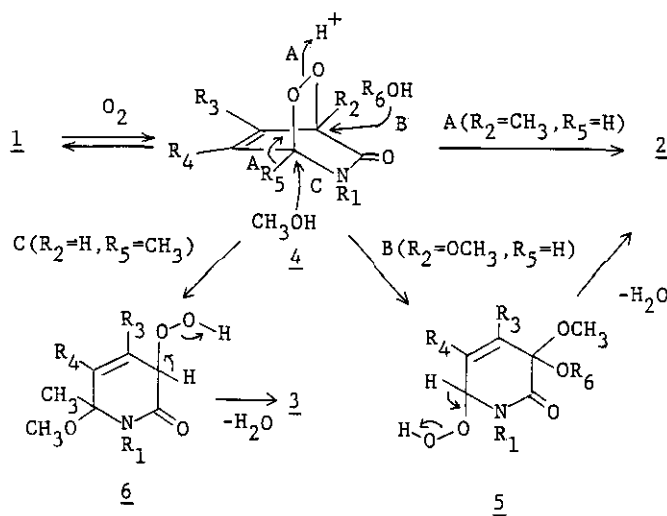
<u>1</u>	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	solvent	yield(%) ^b		mp(°C) ^c (bp°C)
								<u>2</u>	<u>3</u>	
<u>a</u>	H	CH ₃	H	H	H	H	CH ₂ Cl ₂	14		132-134
<u>b</u>	CH ₃	CH ₃	H	H	H	H	CH ₂ Cl ₂	50		82- 86
<u>c</u>	Et	CH ₃	H	H	H	H	CH ₂ Cl ₂	27		64- 67
<u>d</u>	Bzl	CH ₃	H	H	H	H	CH ₂ Cl ₂	31		(220/0.9)
<u>e</u>	CH ₃	CH ₃	H	CH ₃	H	H	CH ₂ Cl ₂	21		62- 65
<u>f</u>	Bzl	CH ₃	H	CH ₃	H	H	CH ₂ Cl ₂	41		(220/0.6)
<u>g</u>	H	OCH ₃	H	H	H	CH ₃	CH ₃ OH	65		86- 87
<u>h</u>	H	OCH ₃	H	H	H	Et	EtOH	42		(165/0.8)
<u>i</u>	H	OCH ₃	H	H	H	i-Pr	i-PrOH	42		(175/0.9)
<u>j</u>	H	OCH ₃	H	H	H	Allyl	Allyl-OH	19		(175/0.6)
<u>k</u>	H	H	H	H	CH ₃		CH ₃ OH	12		162.5-163
<u>l</u>	H	H	CH ₃	H	CH ₃		CH ₃ OH	23		140-141
<u>m</u>	CH ₃	H	H	H	CH ₃		CH ₃ OH	11		116-118
<u>n</u>	CH ₃	H	CH ₃	H	CH ₃		CH ₃ OH	20		116-118
<u>o</u>	H	H	H	CH ₃	CH ₃		CH ₃ OH	26		131-133

a 1 (10 mmol) in 400 ml solvent was irradiated with a 500W halogen lamp through Pyrex filter for 3 h under oxygen atmosphere using Methylene Blue (20 mg) as sensitizer in the presence of p-toluenesulfonic acid (100 mg) as catalyst for la-f, and in the absence of acid for lg-o.

b Products were purified by a silica gel chromatography (80g) eluting with a mixture of methylene chloride with ethyl acetate.

c Recrystallized from ethyl acetate-n-hexane or distilled under reduced pressure (bath temperature/mmHg). All new compounds gave satisfactory elemental analyses and showed reasonable spectral data (IR, ¹H-NMR and Mass).

2-Pyridones (1k-o) possessing a methyl group at the 6-position upon the photo-oxygenation in methanol gave pyridine-2,3-dione derivatives (3k-o). The mechanism is explained based on the dehydration of the hydroperoxide (6) formed by nucleophilic addition of methanol at the 4-position of the endoperoxide (4) (path C). Dilling et al. reported that oxygen showed no influences on photoreactions of 2-pyridones such as [4+4]dimerization and valence isomerization.⁴ Therefore, it is interesting that 3- and 6-substituted 2-pyridones undergo photosensitized oxygenation producing oxygenated products. There are known several examples of photo-oxygenation of six-membered heterocycles: 5-ethoxy-1,3-dimethylpyrazin-2(1H)-one gave 5-ethoxy-3-hydroxy-1,3-dimethylpyrazine-2,6(1H,3H)-dione via initial formation of the endoperoxide.⁸ Oxygenation of other pyrazin-2-ones were also reported.⁹ Since the photochemical introduction of oxygen-function to 3- and 6-position of 2-pyridones becomes possible, studies on the synthetic application of this reaction are in progress.



Scheme 2

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7. When 1b and 1e were irradiated under the similar conditions without an acid catalyst, the yield of 2b and 2e were very low and most of the starting materials were recovered. Presumably the first step of oxygen addition to form endoperoxide (4) is reversible, and the back process may be predominant in the absence of acid catalyst.
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