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VISIBLE LIGHT- AND GAMMA RAY-INDUCED ALKYLATION IN PYRIDINE RING. EFFECTIVE ALKYLATION WITH VISIBLE LIGHT IN THE PRESENCE OF IRON(III) SULFATE

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Quinoline and 4-methylquinoline are alkylated with alkanecarboxylic acid upon visible light- or gamma-irradiation. In the photo-alkylation, iron(III) sulfate not only accelerates the reaction, but also improves the selectivity for alkylation. Titanium oxide shows smaller effects than iron(III) sulfate.

The introduction of substituents to pyridine ring is difficult via electrophilic processes which are effective for the substitution of aromatic compounds. Some radical processes have been developed for the substitution in pyridine nucleus. Minisci et al. found that the thermolysis of peroxodisulfate in alkanecarboxylic acid containig pyridine derivatives in the presence of silver salt resulted in the alkylation of the pyridine ring.[1)] The alkylation of pyridine ring with alkanecarboxylic acid also occurs photochemically.[2)] However, for the photochemical alkylation the light of UV-region is required.

We report here that the alkylation of the pyridine nucleus by alkanecarboxylic acid effectively occurs photochemically with visible light under the catalysis of iron(III) sulfate. We also found that gamma-irradiation of pyridine derivatives in alkanecarboxylic acid brings about alkylation in comparatively high radiation chemical yields. The present work has been done by using 4-methylquinoline(**1**) and quinoline(**3**) as typical pyridine derivatives.

Solutions of the substrate (0.02 mol dm^{-3}) in H_2O-RCOOH (1:4 v/v) were irradiated with a 500 W Xenon lamp in the presence or absence of the additives under Ar. For the gamma-irradiation, were used solutions of the substrate (0.30 mol dm^{-3}) in alkanecarboxylic acid. The solutions were irradiated with Co-60 gamma-rays (dose rate, 1.0 x 10^6 rad h^{-1}; dose, 5 x 10^7 rad) under Ar.

The irradiation of 4-methylquinoline(**1**) in alkanecarboxylic acid with visible light or with gamma-rays in the presence or absence of additives (metal salts or platinized TiO_2) brings about alkylation at the 2-position.

As shown in Table 1, the presence of iron(III) sulfate not only accelerates the photoreaction, but also increases the selectivity for alkylation (the increase in the yield of 2-alkyl-4-methylquinoline(**2**) based on the quantity of **1** reacted) either in the presence or absence of sulfuric acid. In

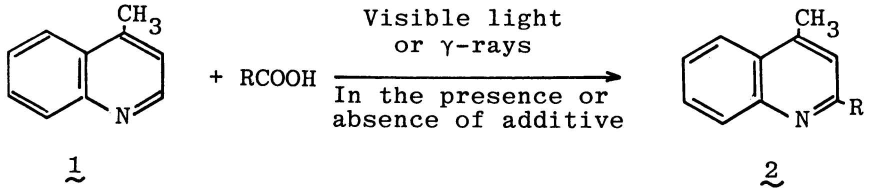


Table 1. Visible light-induced alkylation of 4-methylquinoline(1) with alkanecarboxylic acid(RCOOH)

Light source, 500 W Xe lamp; Irradiation time, 20 h; Irradiated solution, 50 cm^3 solution (solvent: H_2O 80%-RCOOH 20% v/v) containing 1.0 mmol of 1 .

R	$[H_2SO_4]$ / mol dm^{-3}	Additive	Amount of additive / g	Amount of 1 reacted / μmol	Amount of 2 formed / μmol	Yield of 2^a)^ / %
Me	0.033	-----	-----	157	1	1
	0.033	$Fe_2(SO_4)_3$	0.36	189	60	32
	0.033	TiO_2-Pt	0.5	80	9	11
Et	-----	-----	-----	140	79	56
	-----	$Fe_2(SO_4)_3$	0.36	165	126	76
	0.033	-----	-----	203	16	8
	0.033	$Fe_2(SO_4)_3$	0.36	619	458	74
	0.033	$Fe_2(SO_4)_3$ under O_2	0.36	96	1	1
	0.033	$EuCl_3 6H_2O$	0.5	trace	trace	---
	0.033	TiO_2-Pt	0.5	96	35	36
Pr	0.033	-----	-----	101	21	21
	0.033	$Fe_2(SO_4)_3$	0.36	385	291	76
i-Pr	0.033	-----	-----	147	20	14
	0.033	$Fe_2(SO_4)_3$	0.36	605	407	67

Table 2. Gamma-ray-induced alkylation of 1 with RCOOH

Radiation source, Co-60 γ-rays; Dose rate, 1.0 x 10^6 rad h^{-1}; Dose, 5 x 10^7 rad; Irradiated solution, 10 cm^3 RCOOH solution containing 3 mmol of 1 .

R	Amount of 1 reacted / μmol	Amount of 2 formed / μmol	Yield of 2 ^a)^ / %	G(2)
Me	1220	447	37	0.82
Et	1500	489	33	0.95
Pr	1440	372	26	0.74
i-Pr	1530	598	39	1.2

a) The yield was calculated on the basis of the 1 reacted.

particular, the effect of iron(III) sulfate is more remarkable in the presence of sulfuric acid than in its absence. In contrast $EuCl_3$ which has been reported to catalyze the photochemical hydroxymethylation of 1,3-dimethyluracil with methanol[3)] rather inhibits the photo-alkylation. Platinized titanium oxide[4)] promotes the photo-alkylation much less efficiently than iron(III) sulfate.

Gamma-rays cause alkylation of 1 with alkanecarboxylic acids (Table 2). Radiation chemical yields (G-value = number of molecules of the product/100 eV of absorbed radiation energy) are relatively high.

The irradiation of quinoline (3) with propionic acid with visible light from a Xe lamp or gamma-rays from Co-60 brings about ethylation at the 2- and 4-position (Tables 3 and 4).

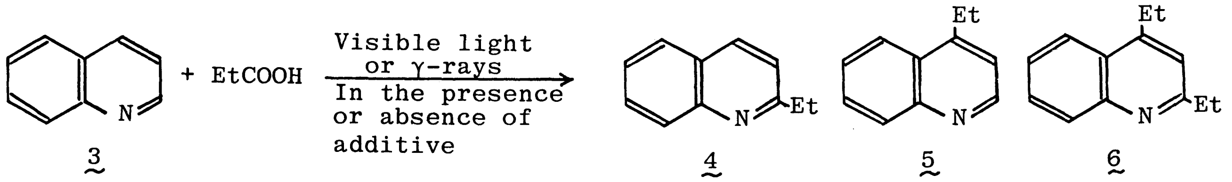


Table 3. Visible light-induced ethylation of quinoline(3) with propioic acid
Reaction conditions are the same as those for 1 .

$[H_2SO_4]$ / mol dm^{-3}	$Fe_2(SO_4)_3$ / g	Amount of 3 reacted / µmol	Amount of Product and (yield) µmol (%) 4	5	6	Amount of 5 / Amount of 4
-----	-----	233	38 (16)	29 (12)	0 (0)	0.76
-----	0.36	322	57 (18)	66 (20)	3 (1)	1.16
0.033	-----	266	3 (1)	3 (1)	0 (0)	1
0.033	0.36	477	131 (27)	158 (33)	19 (4)	1.21

Table 4. Gamma-ray-induced ethylation of 3 with propionic acid
Reaction conditions are the same as those for 1 .

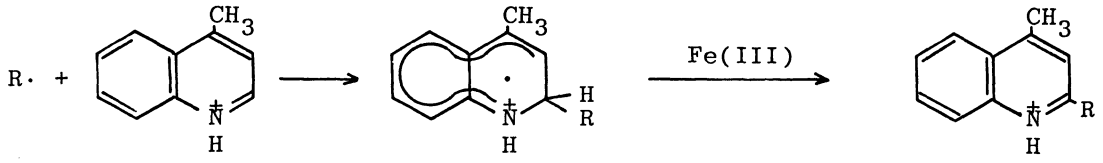
Amount of 3 reacted / µmol	Amount of product µmol, (Yield %), and [G-value] 4	5	6	Amount of 5 / Amount of 4
1480	278 (19) [0.60]	102 (7) [0.22]	46 (3) [0.10]	0.37

The effects of iron(III) on the photoreaction of the quinoline-propionic acid system are similar to those of the 4-methylquinoline-propionic acid system. The regioselectivities of the ethylation of quinoline are dependent on the reaction condition: Radiation-induced ethylation gives preferably 2-ethylquinoline, while the photoreaction in the presence of iron(III) gives more 4-ethylquinoline than 2-ethylquinoline.

In iron(III) sulfate-catalyzed photochemical alkylation, alkyl radicals should play important roles. The reaction is inhibited by oxygen. A sort of iron(III)-alkanecarboxylic acid (or alkanecarboxylate) complex which has an absorption band spreading over near ultraviolet-visible region5) absorbs the irradiating visible light to produce effectively alkyl radicals which attack the electron deficient protonated quinoline derivative.

Another role of iron(III) would be as an oxidant of the intermediate (7) to give alkylation product. This contributes to the improvement of the selectivity of the alkylation.

$$\mathrm{RCOO\cdots\cdots Fe(III)} \xrightarrow{h\nu} \mathrm{RCOO\cdot} + \mathrm{Fe(II)};\quad \mathrm{RCOO\cdot} \longrightarrow \mathrm{R\cdot} + \mathrm{CO_2}$$



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It has been reported that the main radiation-induced reaction of alkanecarboxylic acid is decarboxylation and the mechanism involving alkyl radicals has been proposed.6) Therefore, the initial step of the radiation-induced alkylation should be the attack of alkyl radicals to the pyridinium ring.

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References

1) F. Minisci, R. Bernardi, F. Bertini, R. Galli, and M. Perchinummo, Tetrahedron, 27, 3575 (1971).
2) R. Noyori, M. Kato, M. Kawanisi, and H. Nozaki, Tetrahedron, 25, 1125 (1969).
3) A. Ishida, S. Toki, and S. Takamuku, J. Chem. Soc., Chem. Commun., 1985, 1481.
4) Platinized titanium oxide was prepared by grinding 0.025 g of platinum black (Nippon-Engelhard Co.) and 0.475 g of titanium oxide (P-25 made by Nippon Aerosil Co., a mixture of anatase and rutile) in a mortar according to Kawai and Sakata (T. Kawai and T. Sakata, J. Chem. Soc., Chem. Commun., 1980, 694).
5) Brownish yellow color appears, when iron(III) sulfate and propioic acid are mixed in an aqueous sulfuric acid solution. No color developed, when iron(III) sulfate and 4-methylquinoline are mixed in an aqueous sulfuric acid solution.
6) J. W. T. Spinks and R. J. Woods,"An Introduction to Radiation Chemistry," 2nd ed, John-Wiley, NY (1976), pp. 427-430.

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