HYDROXYALKYLATION OF N-ALKOXY-QUINALDINIUM
AND -LEPIDINIUM PERCHLORATES

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Irradiation of N-alkoxy-quinaldinium or -lepidinium
perchlorate in alcohol affords 4- or 2-hydroxyalkylated
methylquinoline and a small amount of 8-alkoxy-methyl-
quinoline. Hydroxymethylation of the N-ethoxy salts
occurs also homolytically in high yields on treatment
with methanol and ammonium peroxydisulfate.

A previous paper[1] has described that irradiation of N-ethoxy-
quinolinium perchlorate in methanol gives 2- and 4-quinoline-
methanols accompanied with a small amount of an oil of indefinite
structure. We now wish to report further examinations with N-
alkoxy-quinaldinium and -lepidinium perchlorates (1 and 2)[2] and
also the same type of homolytic hydroxymethylation by means of
methanol and ammonium peroxydisulfate.

Irradiation of N-methoxyquinaldinium perchlorate (1a) in meth-
anol (3a) or ethanol (3b) under nitrogen afforded 4-hydroxymethyl-[3]
(4a, 55%) or 4-α-hydroxyethyl-quinaldine (4b, 25%), 8-methoxyquinal-

dine[4] (5a, 4% each) and quinaldine (6, 30 or 60%). From reactions
of N-ethoxy-quinaldinium (1b), N-methoxy- (2a), and N-ethoxy-lepi-
dinium perchlorates (2b) in methanol (3a) or ethanol (3b), the
corresponding 4- or 2-hydroxyalkylated products (4 and 7) and
8-alkoxy derivatives (5b and 8a,b) were similarly obtained.
These results are shown in Scheme 1 and Table I.
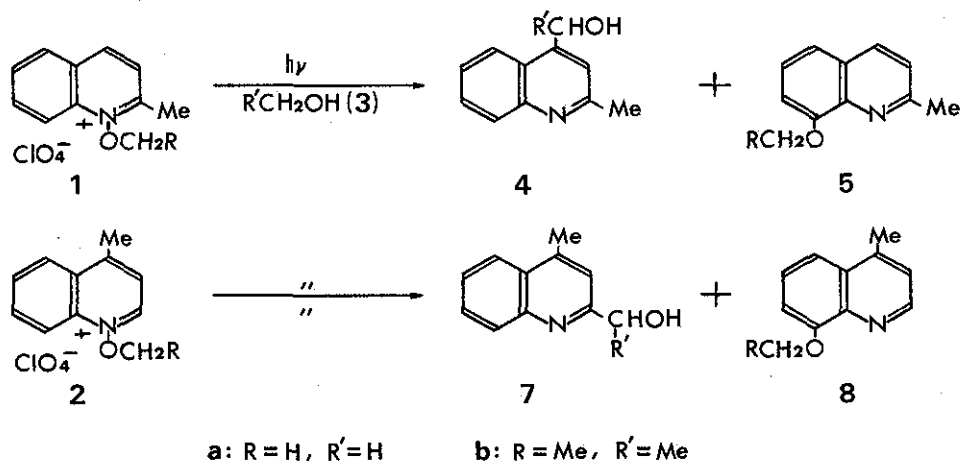
Scheme 1

Whereas hydroxymethylation in methanol smoothly proceeded
(Exp. 1,3,5 and 7), α-hydroxyethylation in ethanol gave rather
unsatisfactory results (Exp. 2 and 4), especially in the reactions
of 2a and 2b no α-hydroxyethylated product being isolated (Exp.
6 and 8).

Although its yield was always poor, 8-alkoxy derivative (5 or
8) was formed in all the experiments, and the minor product iso-
lated from the reaction of N-ethoxyquinolinium perchlorate in
methanol[1] was shown to be also this type of compound, 8-ethoxy-
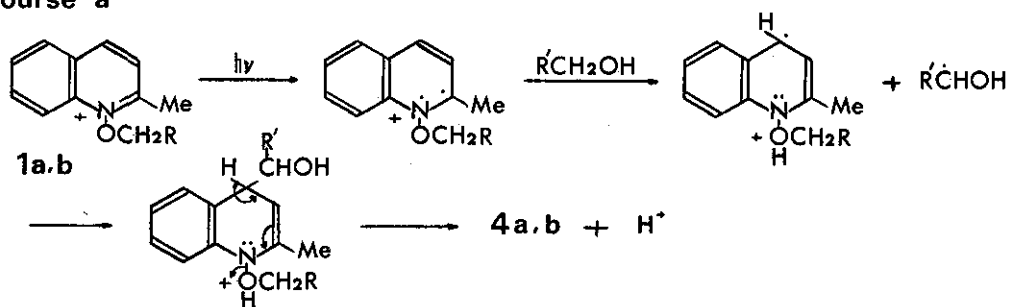quinoline[5]. Identification of these 8-alkoxyquinolines was per-

formed by elemental analyses of their picrates and spectral exami-
nations. Particularly, the NMR spectroscopy was a powerful tool
in the structure elucidation as exemplified in the cases of 8-
ethoxyquinoline and 8-methoxyquinaldine. NMR of 8-ethoxyquinoline,
δ(CDCl$_3$): 1.62 (3H, t, J=7.4 Hz, $-$OCH$_2$CH$_3$), 4.31 (2H, q, J=7.4 Hz,
$-$OCH$_2$CH$_3$), 7.03 (1H, dd, J$_{7,6}$=6.9 Hz, J$_{7,5}$=3 Hz, C$_7$-H), 7.36 (1H,
dd, J$_{3,2}$= 4 Hz, J$_{3,4}$=8.4 Hz, C$_3$-H), 8.08 (1H, dd, J$_{4,3}$=1.5 Hz,
C$_4$-H), 8.98 (1H, dd, J$_{2,3}$=4 Hz, J$_{2,4}$=1.5 Hz, C$_2$-H), 7.18-7.58
2H, m, C$_5$-H and C$_6$-H). NMR of 8-ethoxyquinaldine (5a), δ(CDCl$_3$):
2.8 (3H, s, C$_2$-CH$_3$), 4.06 (3H, s, $-$OCH$_3$), 6.98 (1H, dd, J$_{7,6}$=5.85
Hz, J$_{7,5}$=3 Hz, C$_7$-H), 7.25 (1H, d, J$_{3,4}$=8.7 Hz, C$_3$-H), 7.98 (1H,
d, J$_{3,4}$=8.7 Hz, C$_4$-H), 7.1-7.5 (2H, m, C$_5$-H and C$_6$-H).

As an extension of our study on photoinduced hydroxylakylation
of aromatic N-oxide, various substitutions were examined by using
ethers, esters, hydrocarbons and amines. Among these reactions,
the irradiation of an aqueous solution of 2a and diethylamine
hydrochloride, which gave 7a and 8a in respective yields of 53 and
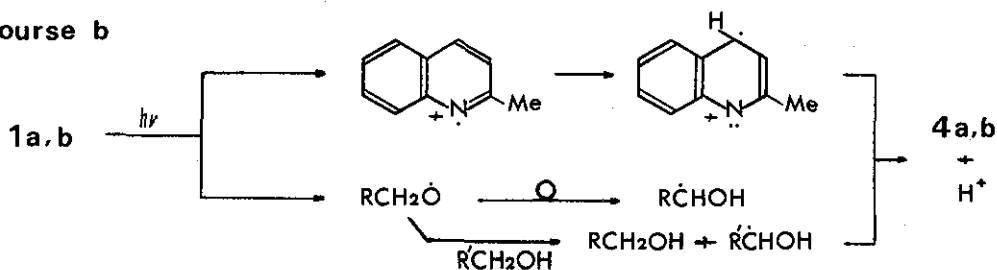4% (Exp. 9), is noteworthy from the mechanistic viewpoint.

$$ \text{2a} + \text{Et}_2\text{NH}\cdot\text{HCl} \xrightarrow{\text{h}\nu,\ \text{H}_2\text{O}} \text{7a} + \text{8a} $$
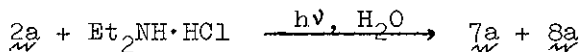
As plausible mechanism of the above hydroxyalkylation, two
courses a and b are illustrated in the case of 1 in Scheme 2[3,6].
The essential feature of course a is addition of α-hydroxyalkyl
radicl (R$'$-ĊHOH) derived from the alcohol to an activated radical
cation followed by elimination of the alcohol (R-CH$_2$OH) from the
1,4-dihydroquinoline intermediate. Course b is initiated by homo-
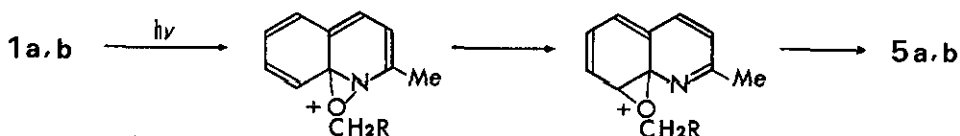lytic fission of the N-O bond of the alkoxy group into a hetero-

Course a

1a,b

$R'CH_2OH$

$+ R'\dot{C}HOH$

$\xrightarrow{h\nu}$

4a,b + H⁺

Course b

1a,b $\xrightarrow{h\nu}$

4a,b + H⁺

$RCH_2\dot{O}$ $\xrightarrow{\quad}$ $R'\dot{C}HOH$

$R'CH_2OH$

$RCH_2OH + R'\dot{C}HOH$

Course c

1a,b $\xrightarrow{h\nu}$ $\longrightarrow$ 5a,b

Scheme 2

aromatic and an alkoxy radicals (R-CH$_2$O). The alkoxy radical then
isomerizes to the corresponding α-hydroxyalkyl radical (R-ĊHOH) or
gives rise to another one (R'-ĊHOH) originated from the alcohol used
as the solvent, and combines with the heteroaromatic radical cation
followed by elimination of a proton to give 4. Independently of
the nature of N-alkoxy group, the introduced hydroxyalkyl group was
always the same with that of the alcohol used as medium. This fact
seems to support course a, however Exp. 9 cannot be explained by
this course. Thus, course b is apparently more adaptable, although

the details of the mechanism have not been established.

Table I. Photohydroxyalkylation of N-Alkoxy-quinaldinium
and -lepidinium Perxhlorates[a)]

Exp. No.	N-oxide salt	3	Reaction time (h)	Product [No., yield(%), (mp, °C)]
1	1a	3a	16	4a[3]: 55(145-146), 5a[4]: 4(picrate, 191-192), 6: 30
2	1a	3b	20	4b: 25(picrate, 203-204), 5a: 4, 6: 60
3	1b	3a	42	4a: 86, 5b[8]: 9.6(picrate, 191)
4	1b	3b	18	4b: 20, 5b: 10, 6: 50
5	2a	3a	24	7a[3]: 56(82-83), 8a: 4(picrate, 189-190)
6	2a	3b[b)]	18	8a: 5(picrate, 189-190), 9b[c)]: 6
7	2b	3a	24	7a: 35, 8b: 5(picrate, 213-214), 9a[c)]: 2
8	2b	3b	24	8b: 8, 9b[c)]: 2, 10: 24

6: quinaldine, 9a,b: 2-methyl-, 2-ethyl-lepidine, 10: lepidine
a) Elemental analyses and spectral data of the known or new com-
pounds isolated here are all satisfied. b) In order to dissolve
2a, MeCN was added to an ethanolic suspension. c) Compounds 9a,b
are reasonably assumed to be formed by photoreduction of 7a,b.

As for the formation of 8-alkoxyquinolines, we tentatively
propose course c proceeding through oxazirane and oxirane inter-
mediates.[7]

In connection with the hydroxyalkylation mentioned above, we also wish to describe a novel hydroxymethylation of 1b and 2b by means of methanol and ammonium peroxydisulfate. When a dilute methanolic solution of 1b or 2b and 2 molar excess of ammonium peroxydisulfate was refluxed, 4a or 7a was obtained as the sole product in high yield of 99 or 72%, respectively.
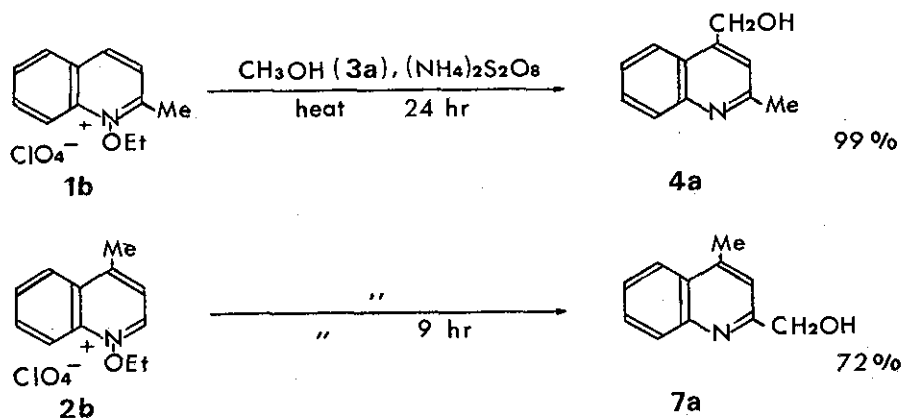
This reaction can be also considered to follow a homolytic path initiated by the hydroxymethyl radical formed from methanol and the peroxydisulfate, and to be closely related to hydroxymethylation of quinolines with methanol and ammonium peroxydisulfate in strong sulfuric acid reported by Minisci et al.[3] However curiously, the reaction in ethanol gave no fruitful result, and the reaction of quinaldine N-oxide or its hydrogen perchlorate did not occur under the same conditions. The essential features and the scope of this reaction are now under investigation in our laboratory.

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2 Compounds 1 and 2 were prepared by adding perchloric acid to the corresponding metho- or ethosulfate of quinaldine and lepidine N-oxides: 1a, mp 131-132°; 1b, mp 132-134°; 2a, mp 130-131°; 2b, mp 134-135°.

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Received, 9th August, 1976