

HYDROXYALKYLATION OF N-ALKOXY-QUINALDINIUM
AND -LEPIDINIUM PERCHLORATES

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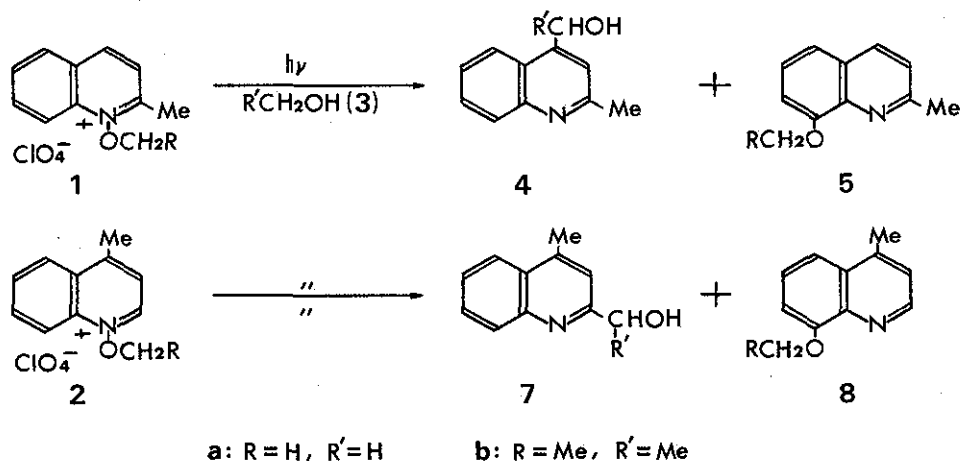
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Irradiation of N-alkoxy-quinaldinium or -lepidinium perchlorate in alcohol affords 4- or 2-hydroxyalkylated methylquinoline and a small amount of 8-alkoxy-methylquinoline. Hydroxymethylation of the N-ethoxy salts occurs also homolytically in high yields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

A previous paper¹ has described that irradiation of N-ethoxyquinolinium 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 methanol (3a) or ethanol (3b) under nitrogen afforded 4-hydroxymethyl-³(4a, 55%) or 4- α -hydroxyethyl-quinaldine (4b, 25%), 8-methoxyquinal-

dine⁴ (5a, 4% each) and quinaldine (6, 30 or 60%). From reactions of N-ethoxy-quinaldinium (1b), N-methoxy- (2a), and N-ethoxy-lepidinium 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.



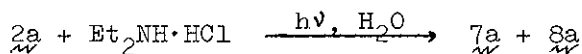
Scheme 1

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 isolated from the reaction of N-ethoxyquinolinium perchlorate in methanol¹ was shown to be also this type of compound, 8-ethoxyquinoline⁵. Identification of these 8-alkoxyquinolines was per-

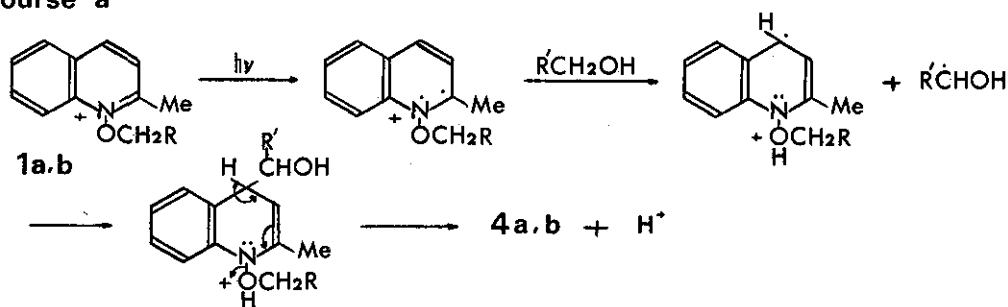
formed by elemental analyses of their picrates and spectral examinations. Particularly, the NMR spectroscopy was a powerful tool in the structure elucidation as exemplified in the cases of 8-ethoxyquinoline and 8-methoxyquinaldine. NMR of 8-ethoxyquinoline, $\delta(\text{CDCl}_3)$: 1.62 (3H, t, $J=7.4$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

As an extension of our study on photoinduced hydroxylalkylation 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.

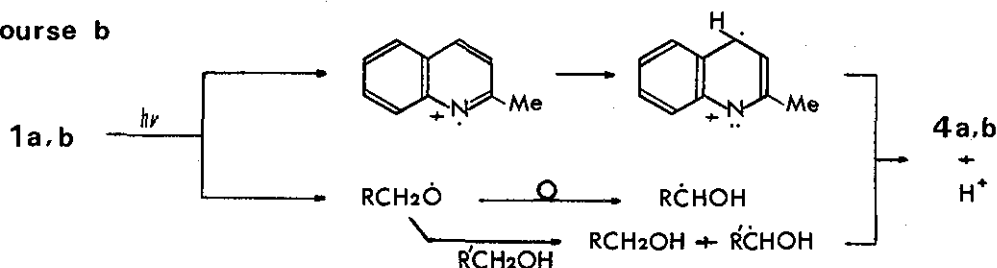


As plausible mechanism of the above hydroxyalkylation, two courses a and b are illustrated in the case of 1 in Scheme 2^{3,6}. The essential feature of course a is addition of α -hydroxyalkyl radical ($\text{R}'\text{-}\dot{\text{C}}\text{HOH}$) derived from the alcohol to an activated radical cation followed by elimination of the alcohol ($\text{R-CH}_2\text{OH}$) from the 1,4-dihydroquinoline intermediate. Course b is initiated by homolytic fission of the N-O bond of the alkoxy group into a hetero-

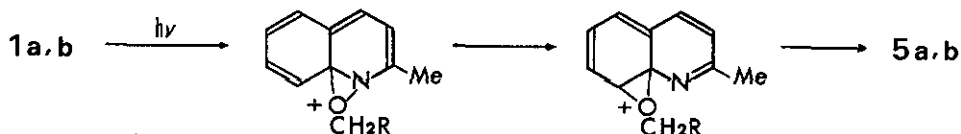
Course a



Course b



Course c



Scheme 2

aromatic and an alkoxy radicals ($R-CH_2O\cdot$). The alkoxy radical then isomerizes to the corresponding α -hydroxyalkyl radical ($R-\dot{C}HOH$) or gives rise to another one ($R'-\dot{C}HOH$) 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 Perchlorates^{a)}

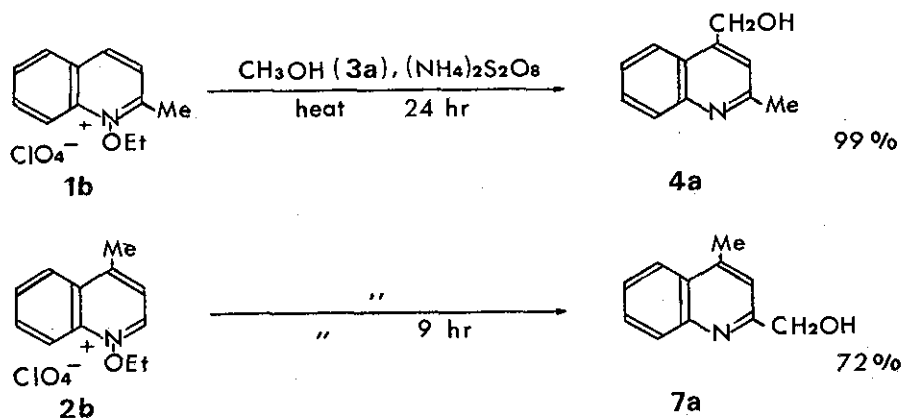
Exp. No.	N-oxide salt	<u>3</u>	Reaction time (h)	Product [No., yield(%), (mp, °C)]
1	<u>1a</u>	<u>3a</u>	16	<u>4a</u> ³ : 55(145-146), <u>5a</u> ⁴ : 4(picrate, 191-192), <u>6</u> : 30
2	<u>1a</u>	<u>3b</u>	20	<u>4b</u> : 25(picrate, 203-204), <u>5a</u> : 4, <u>6</u> : 60
3	<u>1b</u>	<u>3a</u>	42	<u>4a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

6: quinaldine, 9a,b: 2-methyl-, 2-ethyl-lepidine, 10: lepidine

a) Elemental analyses and spectral data of the known or new compounds 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 a proceeding through oxazirane and oxirane intermediates.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.

REFERENCES

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- 2 Compounds 1 and 2 were prepared by adding perchloric acid to the corresponding metha- 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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