CONVERSION OF 9-HYDROXY-10-METHYL-9,10-DIHYDROACRIDINE INTO BIS(10-METHYL-9,10-DIHYDROACRIDIN-9-YL)ETHER

G. E. Ivanov and V. A. Izmail'skii

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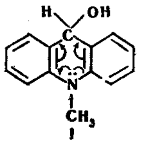
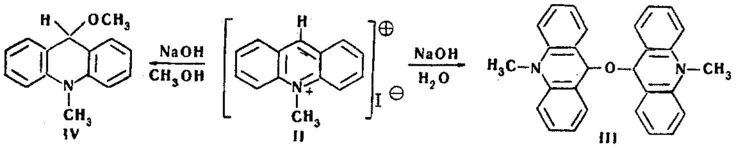
The action of aqueous alkali on N-methylacridinium salts gives as the main product bis-(10-methyl-9,10-dihydroacridin-9-yl) ether, and not 9-hydroxy-10-methyl-9,10-dihydroacridine.

Sodium borohydride, zinc, and KOH in alcoholic solution reduce thioxanthone [1,2], xanthone [3], anthrone, and benzophenone [4] to the corresponding alcohols in good yield. But we have been unable to obtain 9-hydroxy-10-methyl-9,10-dihydroacridine (I) from N-methylacridone by this method. We have studied the possibility of synthesizing the alcohol I from N-methylacridinium salts and have obtained results which enable the above-mentioned deviation in the behavior of the alcohol I from its structural analogs to be explained by the exceptionally high reactivity of the hydroxy group. This, in turn, is explained by the higher electron-donating effect of the $\rangle\ddot{N}{-}CH_3$ group as compared with the effects of the $-\underset{..}{\ddot{S}}-$ and $-\underset{..}{\ddot{O}}-$ groups.



I

The action of aqueous NaOH on a suspension of N-methylacridinium iodide (II) in acetone and on a solution of the iodide II in dimethylformamide gives as the main product bis(10-methyl-9,10-dihydroacridin-9-yl) ether (III), and not I.



Analogs of the alcohol I – thioxanthenol [5], xanthenol [6], and benzhydrol [7] – are also converted into ethers fairly easily. But a particularly great analogy is found with quinolinium [8] and tropylium [9] derivatives, which also form ethers, and not alcohols.

The III that we obtained has properties identical with those of the substance described as an alcohol by Kröhnke and H. Honig [10]: mp 163-164°C, insoluble in ethanol and ether, soluble in dimethylformamide and dioxane. It may be assumed that Kröhnke and Honig [10], by the action of alkali on an ethanolic-acetonic solution of N-methylacridinium chloride also obtained the ether but erroneously assumed that it was the alcohol. The ether III gives many reactions similar to those of a hydrol: 1) The action of an excess of $HClO_4$ on a solution of the ether in dioxane leads to the separation of N-methylacridinium perchlorate, identical with the perchlorate obtained by the hydride transfer reaction or by the action of 57% $HClO_4$ on

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an ethereal solution of the alcohol I; 2) The addition of traces of protonic acids to a solution of the ether III in acetic anhydride causes a disproportionation reaction with the formation of N-methylacridone and 10-methyl-9,10-dihydroacridine.

The structure of the ether III obtained is confirmed by a comparison of its IR spectrum with the spectra of the ethers obtained from thioxanthenol and xanthenol and also with the spectrum of 9-methoxy-10-methyl-9,10-dihydroacridine (IV). The IR spectra of all three ethers are very similar, there being no band in the region of hydroxy group vibrations at 3300-3600 cm^{-1}. The absence of an hydroxy group is also confirmed by an analysis of the ether III for active hydrogen by A. P. Terent'ev's method [11].

The action of alkali on N-methylacridinium salts II in the presence of methanol [10] forms only the alkoxy compound IV, which separates in the crystalline state in almost quantitative yield when the solution is diluted with water. The ethers react instantaneously with acids to form acridinium salts. In the air, ethers of 9-hydroxy-10-methyl-9,10-dihydroacridine oxidize to N-methylacridone.

The alcohol I exists in the form of an impurity in the ether III. It can be isolated in a very small amount from the acetonic or dimethylformamide filtrate by dilution with water after the separation of the precipitate of the ether. It is extremely unstable and it has been impossible to obtain it in the pure crystalline form. The IR spectrum of the alcohol I in paraffin oil, like the IR spectra of thioxanthenol and xanthenol has a broad absorption band in the ≈ 3350 cm^{-1} region showing the formation of a hydrogen bond.

We have confirmed the inference of the higher basicity of the alcohol I and the greater reactivity of the OH group in it by the condensation reaction with 3-methyl-1-phenyl-5-pyrazolone, by the hydride transfer reaction, and also by polarographic investigations of N-methylacridinium, thioxanthylium, and xanthylium perchlorates. A subsequent communication will be devoted to this.

EXPERIMENTAL

N-Methylacridinium iodide (I) was obtained by Kröhnke and Honig's method [10] with the following changes: the amount of solvent was reduced to one third and the time of the reaction to 6 hr instead of 14 days by heating the reaction mixture. 35.8 g (0.2 mole) of acridine and 18 ml of methyl iodide in 45 ml of dimethylformamide were heated in the water bath at 50°C for 6 hr. The precipitate was filtered off and washed with ether. Yield 51 g (80%). Red-orange needles, mp 218-219°C (from methanol); mp 220°C [10].

Bis(10-methyl-9,10-dihydroacridin-9-yl) Ether (III). With stirring, 1 g of NaOH (5% aqueous solution) was gradually added to a suspension of 3.21 g (0.01 mole) of the iodide (I) in 20 ml of acetone (or to a solution of it in dimethylformamide). The precipitate was filtered off, washed with water and ether, and dried in vacuum. Yield 1.2 g (60%) (it was impossible to avoid the formation of the ether by increasing the amount of solvent and by cooling the mixture). Colorless plates, mp 163-164°C (from dioxane). Found, %: N 6.95, 7.05. Calculated for $C_{28}H_{24}N_2O$, %: 7.10. IR spectrum in paraffin oil, cm^{-1}: 1600, 1485, 1470, 1380, 1365, 1350, 1300, 1280, 1210, 1185, 1140, 1070, 1050, 980, 950, 930, 910, 890. (IR spectrum of dithioxanthenyl ether [5] in paraffin oil, cm^{-1} : 1590, 1480, 1450, 1385, 1350, 1330, 1300, 1200, 1185, 1170, 1130, 1090, 1070, 1040, 980, 960, 925, 890).. The aqueous acetonic filtrate was diluted with water. On a standing, a small amount of colorless acicular crystals of the alcohol I, rapidly yellowing in the air, deposited. Attempts to isolate the pure material from the ethereal (washing) solution by evaporation of the solvent were also unsuccessful, since in the air the alcohol I rapidly changes into N-methylacridone with mp 200-201°C. However, the action of 57% $HClO_4$ on an ethereal (washing) solution gave 0.6 g of N-methylacridinium perchlorate, identical with the perchlorate obtained by other methods.

Xanthenol. A mixture of 19.6 g (0.01 mole) of xanthone and 10 g (0.27 mole) of sodium borohydride in 250 ml of ethanol was boiled on the water bath for 1 hr 30 min. The liquid was filtered and diluted with water to 1 *l*. The precipitate was filtered off and dried in the air. Yield 18.9 g (95%). Colorless prisms mp 122-123°C (from benzene) [3].

Dixanthenyl ether was obtained by heating xanthenol [6]. Colorless prisms, mp 211.5-213°C (from dimethylformamide). IR spectrum in paraffin oil, cm^{-1}: 1610, 1580, 1480, 1390, 1350, 1315, 1270, 1220, 1200, 1185, 1165, 1130, 1110, 1040, 985, 960, 935, 920, 910, 890.

Disproportionation of the Ether III. Traces of HCl were added in a glass capillary to a hot (50°C) solution of 1 g of the ether III in 3 ml of acetic anhydride. On stirring, a yellow precipitate deposited. The reaction mixture was poured into water. The precipitate was filtered off, washed with water, and dried. Weight 0.8 g. The reaction product was separated by a method described previously [1] into 10-methyl-9,10-dihydroacridine (mp 93-94°C) and N-methylacridone (mp 200-201°C).

9-Methoxy-10-methyl-9,10-dihydroacridine (IV). A solution of 1 g of NaOH in 10 ml of methanol was added to a suspension of 3.21 g (0.01 mole) of N-methylacridinium iodide in 20 ml of acetone. The solution was then diluted with a threefold amount of water. The crystalline precipitate was filtered off, washed with water, and dried in vacuum. Yield 2.1 g (93%), mp 76-77°C [10]. After recrystallization from petroleum ether, the melting point had not risen. IR spectrum in CCl_4 cm^{-1}: 1605, 1485, 1475, 1380, 1360, 1315, 1300, 1280, 1210, 1190, 1170, 1140, 1075, 1050, 920, 910, 875.

N-Methylacridinium Perchlorate. A mixture of 0.6 g (0.003 mole) of 10-methyl-9,10-dihydroacridine, 1.05 g (0.003 mole) of triphenylmethyl perchlorate [12], and 20 ml of glacial acetic acid was boiled for 2 min. The precipitate was filtered off, washed with glacial acetic acid and ethanol, and dried. Yield 0.82 g (91%). Yellow needles, mp 245.5-246°C (from ethanol). Found, %: ClO_4 34.16; 33.74. Calculated for $C_{14}H_{12}NClO_4$, %: ClO_4 33.90. The perchlorate was also obtained by the action of 57% $HClO_4$ on ethereal solutions of 9-hydroxy-10-methyl-9,10-dihydroacridine (see above) and its methyl ether, and also by the action of $HClO_4$ on a dioxane solution of the ether III. UV spectrum in dichloroethane, λ_{max}, nm (ε): 262 (88000), 300 (22400), 402 (3520), 422 (3850).

The IR spectra were measured on a UR-10 W instrument and the UV spectra on an SF-4 A instrument.

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