Short Communication

Reaction of a Pyridinium Salt with \( N,N \)-Dimethylhydrazine

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In an investigation of the electrochemical behaviour of hydrazones of aromatic carbonyl compounds in aprotic media it was of interest to have some analogues of benzophenone \( N,N \)-dimethylhydrazine.\(^{1}\) 1-Methyl-3-benzoylpyridinium perchlorate (1) was thus treated with \( N,N \)-dimethylhydrazine (2) in the usual manner to obtain the hydrazone, but the product was not the expected one; the products indicated that the reaction followed the ANORC mechanism rather than a nucleophilic addition to the carbonyl group.

Nucleophilic substitution in azines, diazines and triazines may involve a ring opening and a ring closure, \( S_{N}(\text{ANORC}) \), (Addition of the Nucleophile, Ring Opening, Ring Closure) and such reactions have been discussed in reviews.\(^{2,3}\) Most of the reactions investigated have pyrimidines as the substrate, but other diazines as well as some pyridines and triazines have been found to undergo this type of reaction.

1,3-Disubstituted pyridinium ions are aminated by ammonia at \(-40^\circ C\); addition at C-6 occurs when the C-3 group is CONH\(_2\), COCH\(_3\), CCONH\(_2\) or CF\(_3\), whereas C-2 is attacked when the C-3 group is Cl or I. An attack at C-2 or C-6 is found in the reaction of ammonia with 3-cyanopyridinium compounds.\(^{4}\) When the C-3 group is CONH\(_2\) the site of attack is dependent on the size of the substituent at position 1.\(^{5}\) Further reaction of the addition product leads to dealkylation of the pyridinium ion.

Exchange of a ring carbon with a sidechain carbon occurs during the reaction of 1,2,4,6-tetramethyl-3,5-di(ethoxycarbonyl)pyridinium ion with aqueous sodium hydroxide. After addition of OH\(^-\) at the 2-position and ring opening, a ring closure involving the ester group leads to 1,4,6-trimethyl-3-acetyl-5-ethoxycarbonyl-2-pyridone.\(^{6}\)

Similar reactions are observed for the transformation of 1,3-di(aminocarbonyl)pyridinium ion to 3-formylpyridone\(^{7}\) and 3-cyanomethylpyridinium ion to 2-methylaminopyridine-3-carbaldehyde and the corresponding methylamine on the reaction with sodium hydroxide.\(^{8,9}\)

In this communication the products from the reaction between 3-benzoyl-1-methylpyridinium perchlorate and \( N,N \)-dimethylhydrazine are described and a reaction path for the formation of these products is suggested.

Results

Treatment of a solution of 1-methyl-3-benzoylpyridinium perchlorate with \( N,N \)-dimethylhydrazine gave a mixture of two compounds, the \( N,N \)-dimethylhydrazone of 1-dimethylamino-2-phenyl-3-formylpyridinium perchlorate (3) and the \( N,N \)-dimethylhydrazone of 1-methyl-2-phenyl-3-formylpyridinium perchlorate (4). The ratio between 3 and 4 depended on the solvent; in methanolic solution 3 was predominant (3 : 4 \( \approx \) 3 : 1) whereas in acetonitrile and chloroform 4 was the major product (3 : 4 \( \approx \) 1 : 2). The products indicated that nucleophilic attack by I took place at the \( N \)-methylated pyridine ring rather than at the carbonyl group.

The structures of 3 and 4 were mainly deduced from their \(^1\)H NMR spectra. The \(^1\)H NMR spectrum of 3 showed two dimethylamino groups (\( \delta \) 2.94 and 2.96), a single hydrogen at \( \delta \) 6.27 (hydrogen at the aldehyde hydrazone), aromatic protons (phenyl group) and three adjacent hydrogens in the pyridine ring. The \(^1\)H NMR spectrum of 4 indicated a single dimethylamino group (\( \delta \) 2.97), a methyl group at the quaternized nitrogen (\( \delta \) 4.21), a single hydrogen at the aldehyde hydrazone (\( \delta \) 6.24), phenyl protons and three adjacent hydrogen atoms in the pyridine ring.

The formation of 3 and 4 may be explained if I reacted...
with 2 in an S_n (ANRORC) type reaction rather than by the expected attack on the carbonyl group. A reaction path is suggested in Scheme 1. Here it is assumed that attack by 2 at position 6 leads to 3, whereas attack at C-2 leads to 4.

Addition of 2 to the 1,6-bond leads, after ring-opening, to 5; rotation around the C(3)–C(4) and the C(5)–C(6) bonds and shift of a double bond leads to (6). The nitrogen of the hydrazine attacks the carbonyl group and after loss of water (7) is formed. The imino group in the side chain of 7 is attacked by 2 with formation of 3 and loss of methylamine. It is possible that reaction of 2 with the methylamine group takes place earlier in the reaction, e.g. with 6.

If the addition of 2 to 1 takes place at the N(1)–C(2) bond (8) is formed after ring-opening. Rotation around C(3)–C(4) and shift of a double bond results in (9). The nitrogen of the methylamine group attacks the carbonyl group and after loss of water 4 is formed.

The hypothesis that 3 was formed from 4 by attack of N,N-dimethylhydrazine on 4 was discarded, as the ratio 3:4 was not changed by letting the reaction proceed in chloroform for 4 days; samples were withdrawn after 1, 2, and 4 days and analyzed by 1H NMR spectroscopy. Within the uncertainty of the method no difference in the ratio was found.

Attack by a nitrogen nucleophile either at C-2 or at C-6 is found in the reaction between ammonia and 3-cyanopyridinium compounds; with CONH₂ as the 3-substituent the site of attack depended on the size of the substituent at N-1. There seems to be no obvious reason why the attack of 2 on 1 takes place preferentially at C-6 in protic medium (methanol) whereas C-2 is attacked preferentially in aprotic media (acetonitrile, chloroform); one might speculate that the solvation of the carbonyl group in protic media is stronger than in aprotic media, which could for steric reasons slow down the attack at C-2 compared with the attack at C-6.

**Experimental**

**Reaction of 1 with 2.** Compound 1 (200 mg) was dissolved in chloroform (20 ml) in a 100 ml flask and nitrogen was bubbled through the solution for 5 min to remove dioxygen; 2 (1 ml) was added and the solution was kept in the dark with stirring under vacuum for 18 h at ambient temperature. The solvent was then removed under vacuum. The residue, 220 mg, was treated with carbon tetrachloride (10 ml), which was evaporated in vacuo to remove traces of 2. The residue was dissolved in 10 ml of chloroform and a sample withdrawn for 1H NMR spectroscopic analysis which indicated a 1:2 mixture of the N,N-dimethylhydrazone of 1-dimethylamino-2-phenyl-3-formylpyridinium perchlorate (3) and the N,N-dimethylhydrazone of 1-phenyl-2-phenyl-3-formylpyridinium perchlorate (4). An attempt was made to separate the mixture on a column of silica, but extended tailing of the quaternary compounds made a clear separation difficult. By use of a 30 cm column of silica and methylene chloride with an increasing content of acetone as the eluent, it was possible to isolate and crystallize some 4 from one of the tail fractions. 3 could be crystallized from one of the earlier fractions. When the reaction was run in methanol a 3:1 mixture of 3:4 was found together with traces of an unidentified compound. To the solution diethyl ether was added dropwise; the addition was stopped before the solution became permanently cloudy. After being placed in the deep-freeze overnight 3 crystallized.

N,N-Dimethylhydrazone of 1-dimethylamino-2-phenyl-3-formylpyridinium perchlorate, 3: M.p. 208 °C, 1H NMR (CDCl₃): δ 2.94 (s, 6 H), 2.96 (s, 6 H), 6.27 (s, 1 H), 7.30–7.40 (m, 2 H), 7.52–7.62 (m, 3 H), 8.09 (dd, J₁ = 8.3 Hz, J₂ = 6.3 Hz, 1 H), 8.86 (dd, J₁ = 8.3 Hz, J₂ = 1.1 Hz, 1 H), 9.26 (dd, J₁ = 6.3 Hz, J₂ = 1.1 Hz, 1 H).

N,N-Dimethylhydrazone of 1-phenyl-2-phenyl-3-formylpyridinium perchlorate, 4: M.p. 155–158 °C, 1H NMR (CDCl₃): δ 2.97 (s, 6 H), 4.21 (s, 3 H), 6.24 (s, 1 H), 7.48–7.53 (m, 2 H), 7.60–7.66 (m, 3 H), 7.87 (dd, J₁ = 8.2 Hz, J₂ = 6.0 Hz, 1 H), 8.77 (dd, J₁ = 6.0 Hz, J₂ = 0.7 Hz, 1 H), 8.85 (dd, J₁ = 8.2 Hz, J₂ = 0.7 Hz, 1 H).

**References**


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