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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*-dimethylhydrazone.[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 ANRORC 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(ANRORC), (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 °C; addition at C-6 occurs when the C-3 group is $CONH_2$, $COCH_3$, $COOCH_3$ 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-cyano-1-methylpyridinium ion to 2-methylaminopyridine-3-carbaldehyde and the corresponding methylimine 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** ≈ 3:1) whereas in acetonitrile and chloroform **4** was the major product (**3**:**4** ≈ 1:2). The products indicated that nucleophilic attack by **1** 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 (δ 2.94 and 2.96), a single hydrogen at δ 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 (δ 2.97), a methyl group at the quaternized nitrogen (δ 4.21), a single hydrogen at the aldehyde hydrazone (δ 6.24), phenyl protons and three adjacent hydrogen atoms in the pyridine ring.

The formation of **3** and **4** may be explained if **1** reacted

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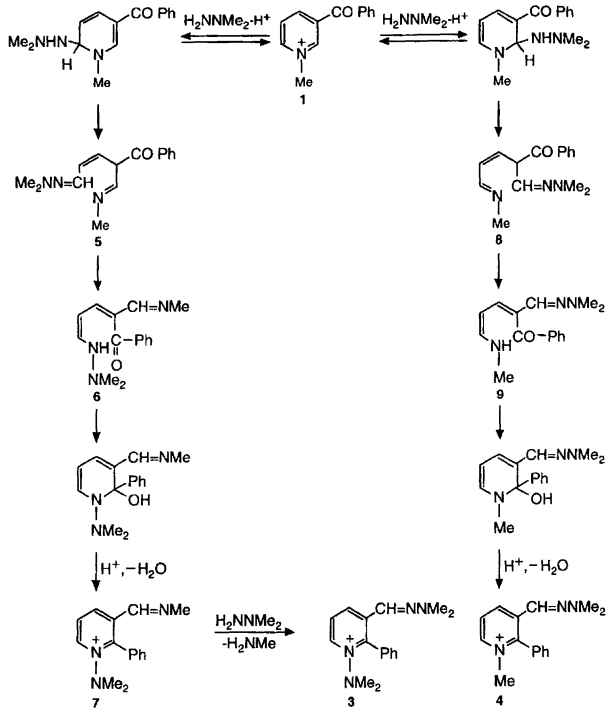
with **2** in an S_N(ANRORC) type reaction rather than by the expected attack on the carbonyl group. A reaction path is suggested in Scheme 1. Here it as assumed that attack by **2** at position 6 leads to **3**, whereas attack at C-2 leads to **4**.

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 methylimine 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 ^{1}H 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;[4] with $CONH_2$ 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.



Scheme 1.

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 ^{1}H 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-methyl-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, ^{1}H NMR ($CDCl_3$): 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, J_1 = 8.3 Hz, J_2 = 6.3, 1 H), 8.86 (dd, J_1 = 8.3, J_2 = 1.1, 1 H), 9.26 (dd, J_1 = 6.3, J_2 = 1.1, 1 H).

N,N-dimethylhydrazone of 1-methyl-2-phenyl-3-formylpyridinium perchlorate, **4**: M.p. 155–158 °C, ^{1}H NMR ($CDCl_3$): 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, J_1 = 8.2 Hz, J_2 = 6.0, 1 H), 8.77 (dd, J_1 = 6.0, J_2 = 0.7, 1 H), 8.85 (dd, J_1 = 8.2, J_2 = 0.7, 1 H).

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