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NEW REDOX SYSTEM: TRICHLOROMETHYLARENE — PYRIDINE BASE

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A redox reaction of trichloromethylarenes with pyridines results in respective N-(α-chloroarylmethyl)substituted pyridinium chlorides which give, on hydrolysis, aromatic aldehydes and 4-chloropyridines or 1,4'-bipyridinium salts.

INTRODUCTION

Recently we found that in the interaction of trichloromethylarenes $ArCCl_3$ (1) with hydroxylamine or hydrazines in pyridine solution, a previously unknown reductive condensation reaction takes place, leading to derivatives of corresponding aldehydes, either oximes and nitriles or aldazines and hydrazones, respectively [1, 2]. It was supposed [2] that hydroxylamine or hydrazines are true reducing reagents. The first step of the process (similar to the reaction carried out using an alcohol as the solvent [3]) is supposed to be the formation of respective hydroximoyl or hydrazonoyl chlorides, which undergo reduction with excess hydroxylamine or hydrazine. However, the results of an additional study [4, 5] showed the key role of pyridine in the reduction step.

RESULTS AND DISCUSSION

Now we have studied in detail the reactions of chlorides **1** (a Ar = Ph, b Ar = 2,4-$Me_2C_6H_3$, c Ar = 2,4,5-$Me_3C_6H_2$, d Ar = 2,4,6-$Me_3C_6H_2$, e Ar = 2,3,4,6-Me_4C_6H, f Ar = 2,3,5,6-Me_4C_6H, g Ar = 2,3,4,5-Me_4C_6H) with pyridine (**2a**) and those of trichloride **1d** with 3-R-pyridines (**2**, b R = Me, c R = OH, d R = $CONH_2$, e R = COOEt, f R = Br) which allowed us to elucidate the mechanism of the reductive condensation. Couples formed by trichloromethylarenes **1** with pyridine bases **2** were shown to be potent redox systems. The transformations are presented in the scheme, all compounds except **11** being isolated or identified as derivatives and/or by NMR spectra.

The first step of the reaction is the formation of unstable monopyridinium salts **3**. We succeeded in trapping the salt from benzotrichloride **1a** and Py as hexachloroantimonate (**3a'**). It was also possible to prepare an analogous salt (**3d'**) from sterically hindered mesitotrichloride **1d** and 4-methylpyridine. In cases of unhindered trichlorides **1a-c**, the salts **3** easily convert to rather stable though hygroscopic bispyridinium salts **4**, the equilibrium being shifted to the right.

The other transformation of salts **3** involves the nucleophilic attack of the position **4** of their pyridine ring by chloride anion to give dihydropyridines **5**. This attack is especially efficient for salts formed by sterically hindered trichlorides **1d-f**. 4-Chloro-1,4-dihydronicotinamide hydrochloride, observed after the reaction of **1d** with nicotinamide among the products of hydrolysis of the reaction mixture, can be regarded as evidence of formation of dihydropyridines **5**. The latter undergo redox transformation to give 4-chloropyridinium salts **6**, which were identified in reactions of **1d** with pyridines **2a,d-f** as hydrolysis products (viz., 4-chloropyridines **7a,d-f**, besides mesitoic aldehyde **8d**), and, in the case of pyridine **2a**, also as N-(α-chloro-2,4,6-trimethylbenzyl)-4-chloropyridinium hexachloroantimonate (**6d'**).

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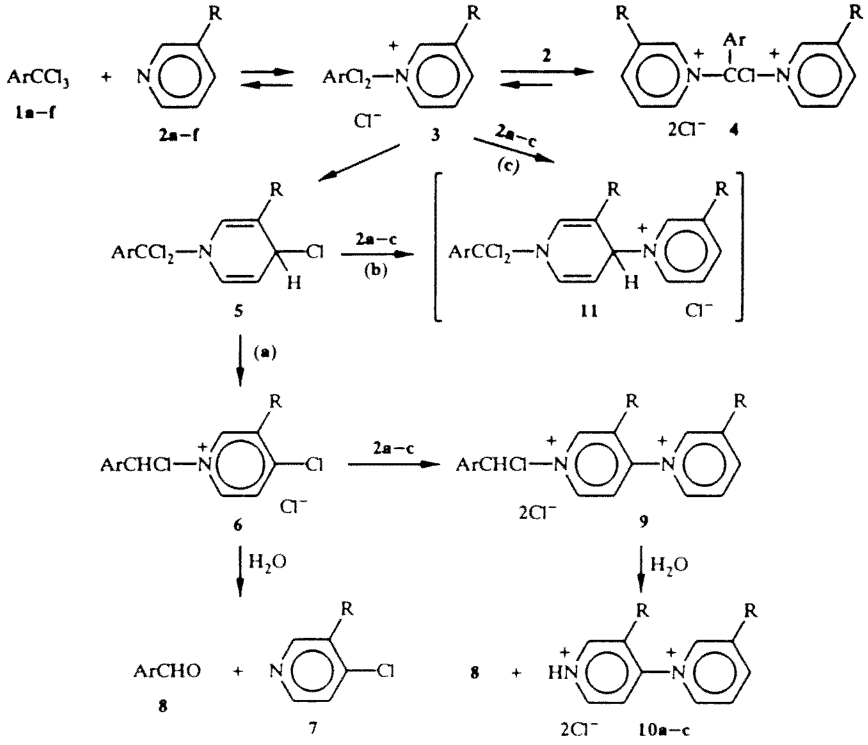

1, 8 a Ar = Ph, b Ar = 2,4-$Me_2C_6H_3$, c Ar = 2,4,5-$Me_3C_6H_2$, d Ar = 2,4,6-$Me_3C_6H_2$,
e Ar = 2,3,4,6-Me_4C_6H, f Ar = 2,3,5,6-Me_4C_6H, g Ar = 2,3,4,5-Me_4C_6H; 2 a R = H, b R = Me,
c R = OH, d R = $CONH_2$, e R = COOEt, f R = Br; 7 a R = H, b R = $CONH_2$, e R = COOEt,
f R = Br; 10 a R = H, b R = Me, c R = OH

In the reactions of trichloride 1d with pyridines 2a-c and of 1e with pyridine 2a, the N-(α-chlorobenzyl)-1,4′-bipyridinium salts 9 were formed (independently of 1d:2a-c ratio). Salts 9d and 9e formed by 1d,e with Py were isolated as unstable crystalline precipitates, the former being characterized also as hexachloroantimonate 9d′. The structures of salts 9 were also proven by identification of N-(4-pyridyl)pyridinium (1,4′-bipyridinium) dichlorides 10a-c (R = a H, b Me, c OH) and aldehydes 8d-f (Ar = d 2,4,6-$Me_3C_6H_2$, e Ar = 2,3,4,6-Me_4C_6H, f Ar = 2,3,5,6-Me_4C_6H) obtained on hydrolysis. The formation of salts 6 is practically the only process for pyridines 2d-f. It should be taken into account that we had no evidence on the formation of intermediates 11 and observed the formation of salt 6d on the initial steps of the reaction between 1d and 2a (which gave dichloride 9d as the final product). So, the salts 9 seem to be formed via 4-chloropyridinium salts 6 (path a) rather than by routes b or c, and analogous to mechanisms proposed for the formation of N-(4-pyridyl)pyridinium dichloride 10a [6-8], both routes have the same salt 11 as key intermediate. The reductive transformation of trichlorides 1 can be regarded to some extent as an alternative to the oxidative conversion of monochloromethylarenes to aldehydes by the Sommelet reaction, the mechanism of the pyridine base transformation modelling that of N-(4-pyridyl)pyridinium dichloride synthesis. As to the mechanism of the formal hydride ion transfer in dihydropyridines 5, our experiments with Py-d_5 and Py-d_5·HCl have shown that the transfer of a proton and two electrons proceeds similarly to biological processes involving NADH and NADPH [9] since, 1d with Py-d_5 gives (after hydrolysis) aldehyde 8d deuterated (95%) on formyl group, and preferably non-deuterated (70%) aldehyde 8e was formed from 1e with Py-d_5—Py-d_5·HCl (1:1).

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded on Bruker WM-250 and AM-300 spectrometers, respectively. Reactions of benzotrichloride 1a were carried out in excess pyridine on boiling, those of trichlorides 1b-g in methylene chloride or in chloroform on long storage at room temperature. Crystalline products were filtered off, all others underwent investigation, as a rule, as oils after evaporation or in some cases in solution and characterized by their hydrolysis products.

For yields, physical properties, and NMR characteristics of salts **3a'**, **3d'**, **4a-c**, **6d'**, **9d,e**, **10a-c**, 4-chloropyridines **7a,d-f**, aldehydes **8d-f**, and 4-chloro-1,4-dihydronicotinamide hydrochloride as well as references in cases of compounds described previously see [5, 10].

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