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Mendeleev Commun., 1993, 3(3), 97–98
Mendeleev Communications

Reaction of Trichloromethylarenes with Pyridine: A Novel Synthesis of *N*-(4-Pyridyl)pyridinium Salts and Aromatic Aldehydes

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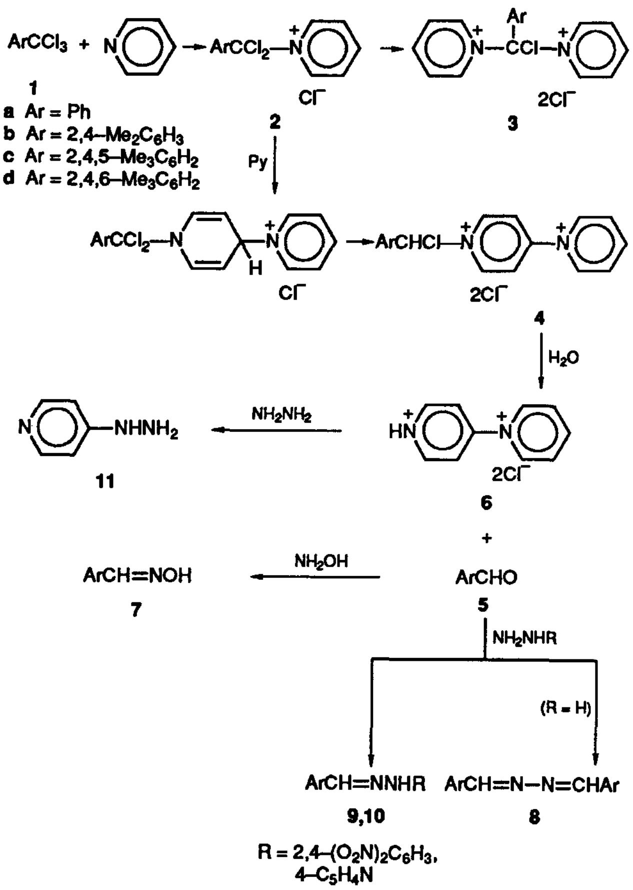
We have shown that in reductive condensation of trichloromethylarenes with hydroxylamine and hydrazines in pyridine the reduction stage, involving the exchange of one chlorine atom for a hydrogen atom, can proceed without participation of hydroxylamine or hydrazine *via* the interaction of trichloromethylarene with pyridine leading to the formation of *N*-[*N'*-(α-chlorobenzyl-4-pyridyl)]pyridinium salts which give after hydrolysis N-(4-pyridyl)pyridinium dichloride and respective aromatic aldehydes in high yields.

Recently we have found that in the interaction of trichloromethylarenes $ArCCl_3$ (**1**, Ar = **a** Ph; **b** 2,4-$Me_2C_6H_3$; **c** 2,4,5-$Me_3C_6H_2$; **d** 2,4,6-$Me_3C_6H_2$) with hydroxylamine or hydrazines in pyridine solution a previously unknown reductive condensation reaction takes place which leads to derivatives of the respective aldehydes, *i.e.* oximes and nitriles (the latter form by oxime dehydration under the reaction conditions), aldazines and hydrazones.[1,2] It was supposed that hydroxylamine or hydrazine are true reducing reagents; however, the reduction stage remained unclear, as did the role of pyridine in the reaction.[2]

The aim of the present work is an elucidation of the reductive condensation mechanism. We have established that in the interaction of trichloride **1d** with pyridine carried out in chloroform or methylene dichloride as solvents, independently of the trichloride **1d** – pyridine ratio, an unstable crystalline precipitate is formed. This is a complex mixture and its contents need further study. Meanwhile, based on the ^{1}H NMR spectrum of the precipitate solution and the nature of its hydrolysis products, we can conclude that the main component of the mixture is not the expected pyridinium salt (**2** or **3**) but the *N'*-substituted *N*-(4-pyridyl)pyridinium salt **4**, which corresponds to a partial reduction of the trichloromethyl group in starting trichloromethylarene.

The precipitate readily undergoes partial or complete hydrolysis during storage in air or in a solution of dimethyl sulfoxide containing small amounts of water. The hydrolysis of the precipitate resulted from the interaction of mesityltrichloromethane **1d** with pyridine leads to 2,4,6-trimethylbenzaldehyde **5** and *N*-(4-pyridyl)pyridinium dichloride **6**. The hydrolysates react readily with hydroxylamine, hydrazine and substituted hydrazines giving the respective derivatives of 2,4,6-trimethylbenzaldehyde **7–9**.† Finally, in the products of reductive condensation of trichlorides **1b–d** small amounts of the respective substituted benzaldehyde 4-pyridylhydrazones **10** have been found.‡ Their formation can be explained by the possibility that in conditions of reductive condensation 4-pyridylhydrazine **11** is generated from pyridylpyridinium salts **4** and (or) **6** and hydrazine (a similar reaction is known to be a preparative method for the synthesis of 4-pyridylhydrazine[3]).

Thus, the reduction of one of the chlorine atoms of trichloromethylarene proceeds without a participation of hydroxylamine or hydrazines and takes place in the process of salt **4** formation. The fact that hydrogen transfer takes place from the pyridine ring to the benzylic carbon atom has been supported using deuteriopyridine instead of pyridine: hydrolysis of the respective salt leads to aldehyde **5** deuteriated at the formyl group. All transformations discussed above are presented in Scheme 1.



Scheme 1

† *Typical procedure.* To trichloride **1d** (1.3 g, 5.47 mmol) was added a solution of two (0.88 ml) or four (1.76 ml) equivalents of dry pyridine in 5 ml of dry chloroform or methylene dichloride. The solution obtained was stored for several days at room temperature. A precipitate which formed was filtered off, washed with chloroform or methylene dichloride and dried in a dessicator over P_2O_5. In all cases 1.8–2.2 g of the precipitate was obtained, m.p. 148–152 °C. To 1 g of the precipitate (which corresponds to *ca.* 2.7 mmol of trichloride **1d**), water (10 ml) was added and the mixture was stirred for several minutes, extracted with ether, the extract dried with $MgSO_4$ and filtered and the ether fraction evaporated. A liquid residue of aldehyde **5** which solidified on cooling (0.33 g, 89%) was obtained: $M^+ = 148$, IR spectrum $\nu_{C=O}$/cm^{-1} 1704, ^{1}H NMR (in $CDCl_3$, ppm): 10.56 s, 1H (CHO), 6.92 s, 2H (H^3, H^5), 2.60 s, 6H (2- and 6-Me), 2.33 s, 3H (4-Me), which corresponds to literature data[4] for aldehyde **5**. From the aldehyde obtained (0.31 g, 2.1 mmol) in ethanol (4 ml) under the action of 2,4-dinitrophenylhydrazine (0.42 g in 2 ml of conc. H_2SO_4 and 8 ml of ethanol), was obtained 2,4-dinitrophenylhydrazone **9** (85%), m.p. 253–254 °C (*cf.*[5]). To 1 g of the precipitate (salt **4**), ethanol (10 ml) was added, and after storage (*ca.* 2 h, r.t.), *N*-(4-pyridyl)pyridinium dichloride **6** was filtered off and an equimolar amount of hydroxylamine or hydrazine was added to the filtrate. The mixture was boiled for 30–60 min or stored at room temperature for 1–2 days, and the precipitate which formed was filtered off and washed with ethanol. From the combined filtrate, after alcohol evaporation and treatment of the residue with water, an additional amount of oxime (hydrazone) was obtained and recrystallized from 50–90% alcohol. 2,4,6-Trimethylbenzaldoxime **7**, (66%) as a mixture of *Z*- and *E*-isomers (1:1, from NMR data), m.p. 122–152 °C (*cf.*[2]) and aldazine **8** (80%), m.p. 170–171 °C (*cf.*[2]) were obtained.

‡ *Typical procedure.* A solution of hydrazine dihydrochloride (15.78 g, 0.15 mol) and trichloromethylmesitylene **1d** (11.9 g, 0.05 mol) in pyridine (75 ml) and water (20 ml) was boiled for 35 min. After the mixture had cooled, water (150 ml) was added and the precipitate formed was filtered off. After recrystallization from ethanol were obtained aldazine **8d** (65%), m.p. 170–171 °C (*cf.*[2]) and 2,4,6-trimethylbenzaldehyde 4-pyridylhydrazone hydrochloride **10d·HCl** (12%), m.p. 282–284 °C, IR spectrum, ν_{NH}/cm^{-1} 3170, $\nu_{C=N}$ 1640; ^{1}H NMR (in CD_3OD): 8.56 s (CH=N), 8.15 d (α-H and α'-H of pyridine ring), 6.96 br. (β-H), 7.43 br. (β'-H), $J_{2,3}$ 7 Hz, 6.89 s (H_{Ar}), 2.46 s (2-Me, 6-Me), 2.24 s (4-Me). Treatment of the hydrazone hydrochloride in ethanol with an equimolar amount of aqueous NaOH leads to hydrazone **10d**, m.p. 170–172 °C (alcohol), M^+ 239; IR spectrum, ν/cm^{-1}: 3130 and 3200 (ν_{NH}), 1604 ($\nu_{C=N}$); ^{1}H NMR (in $CDCl_3$): 8.50 s (NH), 8.16 s (CH=N), 8.34 d (α-H and α'-H), 6.95 d (β- and β'-H), $J_{2,3}$ 7 Hz, 6.93 s (H_{Ar}), 2.50 s (2-Me, 6-Me), 2.32 s (4-Me). Hydrochlorides **10b·HCl**, as well as hydrazone **10b**, have similar spectral characteristics. Satisfactory elemental analyses were obtained for compounds **10b–d**.

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Received: Moscow, 14th January 1993
Cambridge, 2nd March 1993: Com. 3/00388D