An alternative channel of reductive condensation of trichloromethylarenes with hydrazines

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The reductive condensation of trichloromethylarenes with hydrazines can proceed without intermediate formation of pyridinium salts and without participation of pyridine in the reduction act. Variants of reductive condensation using hydrazines as reducting agents and α-chlorobenzylhydrazines and hydrazonoyl chlorides, nitrile imines, or hydrazonoylpyridinium salts as intermediates are considered. α-Chlorobenzylhydrazines and hydrazonoyl chlorides are shown to be the most probable intermediates.

Key words: trichloromethylarenes, reductive condensation with hydrazines, mechanism, intermediates.

Previously we have discovered the reductive condensation reaction of trichloromethylarenes (TCMA) with hydroxylamine or hydrazines in the presence of pyridine giving derivatives of aromatic aldehydes, namely, oximes, azines, and hydrazones.[1]

$$ArCCl_3 + NH_2X \xrightarrow{Py} ArCH{=}NY$$

X = Y = OH; X = Y = NMe_2, NHPh;
X = NH_2, Y = N=CHAr

Later, it has been shown that pyridine not only binds the hydrogen chloride evolved in the reaction but can also act as a reducing agent. The scheme proposed for this process[2,3] (Scheme 1) includes the reaction of TCMA **1** and pyridine **2** to give unstable *N*-(α,α-dichloroarylmethyl)pyridinium chloride **3**, which undergoes further transformations; it either reacts with a second pyridine molecule yielding bispyridinium salts **4** or 4-pyridinio-substituted 1,4-dihydropyridines **5** or adds a chloride anion giving rise to 4-chloro-1,4-dihydropyridines **6**. Subsequently compounds **5** and **6** undergo aromatization with the transfer of a hydrogen atom from position 4 of the dihydropyridine ring to the benzyl dichloromethylene group, resulting in the formation of *N*-(α-chloroarylmethyl)-4-(pyridinio)pyridinium dichlorides **7** or *N*-(α-chloroarylmethyl)-4-chloropyridinium chlorides **8**. Hydrolysis of these products affords pyridylpyridinium (**9**) or 4-chloropyridinium (**10**) salts and aromatic aldehydes **11**.

Note that all the compounds shown in Scheme 1, except for salts **5**, were either isolated in a pure state or as derivatives or detected by physical methods. Particularly, monopyridinium salt **3** (Ar = Ph) was detected as the hexachloroantimonate and the intermediate formation of this salt in the case of mesitotrichloride **1d** (Ar = 2,4,6-$Me_3C_6H_2$) was confirmed by isolation of the relatively stable salt with 4-picoline, which cannot be converted into salts of type **7** or **8**.[3] The formation of the latter types of salts was observed in the reactions with *o,o'*-dimethyl-substituted TCMA **1d—f**.[3] Bis(pyridinium) salts **4** were isolated only in the case of TCMA **1a—c**, which have at least one vacant *o*-position relative to the CCl_3 group.[3] The experimental data related to this mechanism of reductive condensation were confirmed by semiempirical quantum-chemical MNDO calculations for the models of the major products and intermediates shown in Scheme 1. These calculations led to the conclusion that the route including the successive transformations **3** → **6** → **8** → **7** is probable for this reaction.[4]

It is significant that, according to this scheme, the transformation of *o,o'*-disubstituted benzotrichlorides such as **1d** into pyridylpyridinium and chloropyridinium salts **7** and **8**, in which the reduction has already occurred with replacement of one chlorine atom of the initial trichloromethyl group by a hydrogen atom (a synthetic equivalent of carboxylic acid has been converted into an equivalent of aldehyde), does not involve hydrazines or hydroxylamine, pyridine serving as the source of hydrogen. The formation of the products of reductive condensation, *i.e.*, azines, hydrazones, and aldoximes as well as nitriles arising upon their dehydration, can be regarded as being due to the reactions of salts **7**, **8** or aldehydes **11** with hydrazines or hydroxylamines present in the reaction mixture.[2,3]

It was natural to assume that salts **3**, **4**, **7**, or **8**, formed in the reductive condensation, can also react with nucleophiles other than hydrazines or hydroxylamine. We have found recently that *N*-(4-pyridyl)-pyridinium (**7**) and 4-chloropyridinium (**8**) salts, formed from mesitotrichloride (**1d**) and pyridine, react with N-nucleophiles such as piperidine and morpholine and

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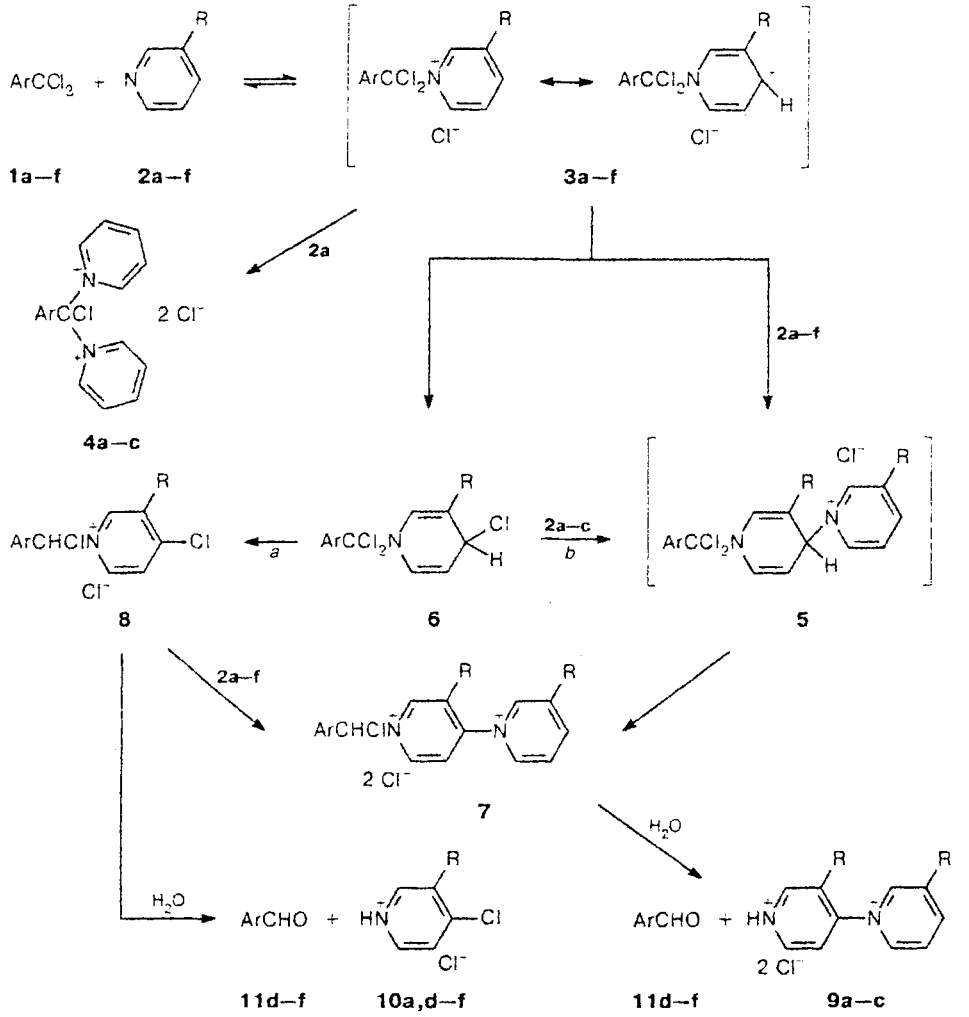
Scheme 1



1, **11**: Ar = Ph (**a**), 2,4-$Me_2C_6H_3$ (**b**), 2,4,5-$Me_3C_6H_2$ (**c**), 2,4,6-$Me_3C_6H_2$ (**d**), 2,3,4,6-Me_4C_6H (**e**), 2,3,5,6-Me_4C_6H (**f**)
4: Ar = Ph (**a**), 2,4-$Me_2C_6H_3$ (**b**), 2,4,5-$Me_3C_6H_2$ (**c**)
2, **9**, **10**: R = H (*a*), Me (**b**), OH (**c**), $CONH_2$ (**d**), COOEt (**e**), Br (**f**)

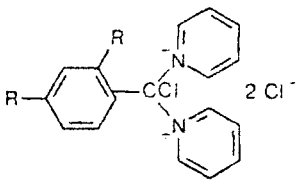
with C-nucleophiles (*N*,*N*-dimethylaniline, indole) according to the hetarylation reaction pattern to give the corresponding 4-substituted pyridines. However, *N*-(α,α-dichlorobenzyl)pyridinium (**3**) and *N*,*N*′-(α-chlorobenzylidene)bispyridinium (**4**) salts, formed from benzotrichloride, do not enter into hetarylation reactions.[5] These results cast doubt on the general character of the above scheme[2,3] for the reductive condensation of TCMA with hydrazines and hydroxylamine in the presence of pyridine.

Recently we have shown[5] that pyridylpyridinium salts **7** and, especially, chloropyridinium salts **8** are responsible for the formation of the hetarylation products; these salts were isolated or detected only for trichlorides **1d—f** with two methyl groups in the *o*- and *o*′-positions,[2,3] while monopyridinium salts **3a—c** and bispyridinium salts **4a—c** are not apparently converted into salts of the type **7** and **8**. Therefore, in this communication, we consider different schemes of reductive condensation of TCMA with hydrazines, which do not require the intermediate formation of the two last-mentioned types of salts. Hydrazine (**12**), *N*,*N*-dimethylhydrazine (**13**), and phenylhydrazine (**14**) were used as model reducing agents and, simultaneously, reagents for the synthesis of the target nitrogen-containing derivatives of aromatic aldehydes.

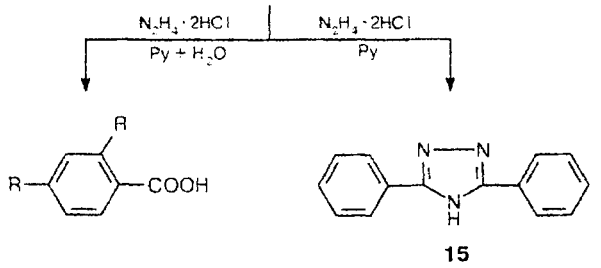
First of all, let us consider the possibility of participation of pyridinium salts **3** or **4** in the reductive

condensation. We found that, when salt **4a** is heated with hydrazine hydrochloride in pyridine in the presence of water, *i.e.*, under conditions of reductive condensation, benzoic acid is formed in a high yield, whereas in the absence of water, heterocyclization occurs to give 3,5-diphenyl-1,2,4-triazole (**15**) (Scheme 2). Salt **4b**, prepared from 2,4-dimethylbenzotrichloride (**1b**), is also hydrolyzed under reductive condensation conditions.

Scheme 2



4a,b



15

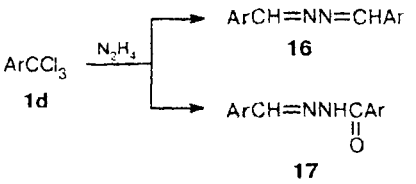
R = H (**a**), Me (**b**)

To elucidate the mechanism of reductive condensation, it is important to exclude the transformation of *o,o'*-disubstituted benzotrichlorides **1d** into pyridylpyridinium and chloropyridinium salts **7** and **8**. Yet another undesirable transformation typical of trichlorides of type **1d** is nucleophilic substitution for the chlorine atoms of the CCl_3 group, which follows apparently the S_Ni mechanism[6] and is substantially facilitated by the cooperative influence of the three methyl groups in the benzene ring. Mesitotrichloride (**1d**) undergoes both above reactions so easily that it cannot be converted into the corresponding diaryl-1,3,4-oxadiazoles by the reaction of acylhydrazines in mixtures of pyridine with ethanol or methanol. Only esters of 2,4,6-trimethylbenzoic acid were isolated together with the products of reductive condensation, 2,4,6-trimethylbenzaldehyde acylhydrazones. Meanwhile, when TCMA **1a,b** were used, the yields of oxadiazoles reached 80% under the same conditions.[7,8] Recently we found conditions under which alcoholysis and reductive condensation are suppressed, which enables the synthesis of 2,5-diaryl-1,3,4-oxadiazoles from sterically hindered *o,o'*-disubstituted TCMA.[9] In particular, reductive condensation can be prevented by replacing pyridine as a hydrogen chloride acceptor by 2,6-lutidine, which is unable to form the pyridinium salt with mesitotrichloride (**1d**) due to steric hindrance.

To identify the reductive condensation route that does not involve the intermediacy of salts of type **7** or **8**, we studied the reaction of mesitotrichloride with hydrazine in the presence of 2- and 4-picolines. Neither of these methylpyridines forms 4-chloro- or 4-pyridiniopyridinium salt with mesitotrichloride but 4-picoline gives a relatively stable monopyridinium salt of type **3** (see Ref. 3).

It was found that in both cases, the reactions proceeded as reductive condensation to give 2,4,6-trimethylbenzaldazine (**16**, Ar = 2,4,6-$Me_3C_6H_2$). The reaction of mesitotrichloride (**1d**) with hydrazine in the presence of 2,6-lutidine, incapable of forming the corresponding pyridinium salts, gives rise to the product of incomplete reduction, namely, 2,4,6-trimethylbenzaldehyde *N*-(2,4,6-trimethylbenzoyl)hydrazone (**17**) (Scheme 3).

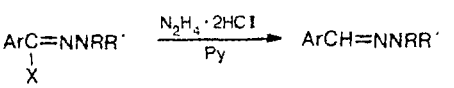
Scheme 3



Ar = 2,4,6-$Me_3C_6H_2$

It follows from the foregoing that the reductive condensation can proceed without the formation of salts of the types **7** or **8**, and salts of the type **3** and **4** do not give the corresponding products at all. When considering alternative pathways of reductive condensation, it is most natural to find out first of all whether hydroxylamine and hydrazine could act as reducing agents in this reaction. Previously,[1] it was shown that *N'*-phenylbenzohydrazonoyl chloride (**18**, Ar = R = Ph, R' = H, X = Cl), which might be formed from benzotrichloride **1a** and phenylhydrazine (**14**), reacts with a 3.5-fold molar amount of hydrazine (**12**) under reductive condensation conditions (Scheme 4, refluxing in aqueous pyridine for 0.5 h) to give benzaldehyde phenylhydrazone (**19**, Ar = R = Ph, R' = H) in 40% yield.

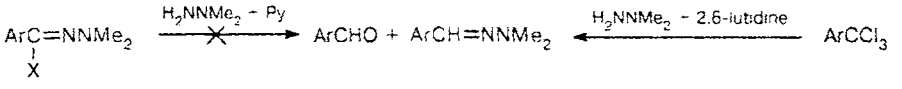
Scheme 4



18 **19**

X = Cl, Br

Scheme 5



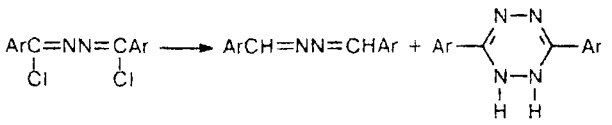
18 **11d** **19** **1d**

Ar = 2,4,6-$Me_3C_6H_2$; X = Cl, Br

However, *N,N*-dimethyl-2,4,6-trimethylhydrazonoyl chloride and bromide (**18**, Ar = 2,4,6-$Me_3C_6H_2$, R = R′ = Me, X = Cl or Br) do not change on refluxing with a 4-fold molar excess of dimethylhydrazine (**13**) in pyridine. The different types of behavior of these compounds cannot be explained by steric hindrance in the latter case or by the too low reducing reactivity of dimethylhydrazine because we have shown (see Experimental) that mesitotrichloride (**1d**) does react with dimethylhydrazine (**13**) in the presence of pyridine to give a mixture of mesitoaldehyde (**11d**) and its *N,N*-dimethylhydrazone (**19**, Ar = 2,4,6-$Me_3C_6H_2$, R = R′ = Me) in >80% overall yield. The latter compound was also obtained in 37% yield from trichloride **1d** and hydrazine **13** in the presence of 2,6-lutidine (Scheme 5).

N,N′-Bis(α-chlorobenzylidene)hydrazine (**20**) does not change on treatment with pyridine, while in the presence of excess hydrazine and pyridine, it affords benzaldazine (**16**, Ar = Ph) in a low yield, 3,6-diphenyl-1,2-dihydro-1,2,4,5-tetrazine (**21**) being the main product of transformation (Scheme 6).

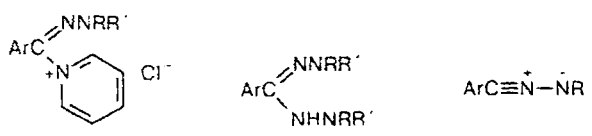
Scheme 6



20 **16** **21**

Ar = Ph

The data presented above do not allow hydrazonoyl halides (or, apparently, hydroxymoyl halides) to be unambiguously regarded as intermediates in the reductive condensation. Now we consider the possibility of transformation of several compounds, which may arise from hydrazonoyl halides under reductive condensation conditions, into hydrazones or azines. In view of the ambiguity of the results obtained in attempted reduction of hydrazonoyl chlorides,[9] note that these experiments were carried out in the presence of pyridine and, hence,



22 **23** **24**

hydrazonoylpyridinium salts of the type **22** could have arisen. Under experimental conditions, hydrazonoyl chlorides can react with hydrazines giving rise to hydrazidines **23**. Finally, in the presence of a base, hydrazonoyl halides (for R′ = H) can undergo dehydrohalogenation resulting in nitrile imines **24**.

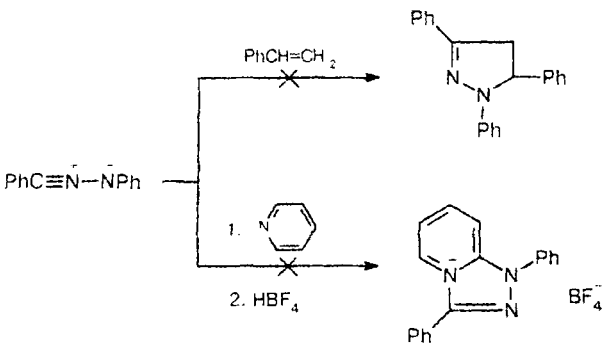
Since pyridinium salts **3** and **4** do not undergo reductive condensation, we suggested that the formation of salts of the type **22**, too, hampers or even precludes the reduction of hydrazonoyl chlorides. Using the reaction of benzotrichloride with *N,N*-dimethylhydrazine as an example, it was shown that the reaction can also proceed without pyridine, although benzaldehyde *N,N*-dimethylhydrazone (**19**, Ar = Ph) was obtained only in 14% yield. It is also noteworthy that reductive condensation induced by *N*-methylhydrazine in the absence of pyridine is known for 5-trichloromethyl-3-phenyl-1,2,4-oxadiazole[10] and reductive condensation on treatment with *N,N*-dimethylhydrazine is known for 3-arylcarbamoyl-5-trichloromethyl-1,2,4-oxadiazole.[11]

The reduction of hydrazidine to hydrazone with excess hydrazine also seems unlikely because these rather labile compounds are, on the contrary, easily oxidized to formazanes, while no reduction of hydrazidines including those formed from hydrazonoyl halides with hydrazine is observed.[12] Note also that 3,6-diphenyl-1,2-dihydro-1,2,4,5-tetrazine (**21**), which can be regarded as a cyclic bishydrazidine and which is isolated in some cases in small amounts upon reductive condensation of benzotrichloride with hydrazine, is retained under the reaction conditions. Thus, the formation of hydrazidines, in particular, tetrazine **21**, appears to be a "dead-end" route, which does not lead to the reductive condensation product. This assumption is consistent with our finding that the stable analog of hydrazidines, *N*-hydroxymesitoamidoxime, does not change under the conditions of reductive condensation with hydroxylamine in pyridine.

As regards the formation of nitrile imines in the reductive condensation, it is not confirmed by our experiments. In particular, diphenylnitrile imine (**24**, R = Ar = Ph) is known to be generated from *N*-phenylbenzohydrazonoyl chloride in the presence of pyridine and to add to the latter according to the 1,3-dipolar cycloaddition pattern to give 1,3-diphenyl-4,8a-dihydro-*symm*-triazolo[4,3-*a*]pyridine, which can be identified as 1,3-diphenyl-*symm*-triazolo[4,3-*a*]pyridinium tetrafluoroborate.[13] Upon reductive condensation of benzo-

trichloride **1a**, we isolated benzaldehyde phenylhydrazone (**19**, Ar = R = Ph, R′ = H) but detected neither the salt mentioned above nor the adduct of diphenylnitrile imine with styrene (Scheme 7). Apparently, the reduction of hydrazonoyl chloride occurs faster than dehydrochlorination to give nitrile imine.

Scheme 7



Thus, the alternative pathway of reductive condensation involving hydrazonoyl halides as substrates and hydrazines as reducing agents appears the most probable. To evaluate this reductive condensation pathway, we performed MNDO quantum-chemical calculations[14–16] for some model examples of reductive condensation involving benzotrichloride **1a** and hydrazines **12—14**. Relying on the published data that, when acting as a reducing agent, hydrazine[17] (**12**) is oxidized to N_2 and H_2, *N*,*N*-dimethylhydrazine[17] (**13**) is oxidized to 1,1,4,4-tetramethyltetrazene (**25**) and H_2, and phenylhydrazine[18] (**14**) is converted into benzene, N_2, and H_2, we calculated the heats of reactions (1)—(3).

$$2\ PhCCl_3 + 2\ NH_2NH_2 \longrightarrow$$
$$\longrightarrow PhCH{=}N{-}N{=}CHPh + N_2 + 6\ HCl, \quad (1)$$
$$\Delta H_r = -37.2\ \text{kcal mol}^{-1};$$

$$PhCCl_3 + 3\ NH_2NMe_2 \longrightarrow PhCH{=}N{-}NMe_2 +$$
$$+ Me_2N{-}N{=}N{-}NMe_2 + 3\ HCl, \quad (2)$$
$$\Delta H_r = -2.5\ \text{kcal mol}^{-1};$$

$$PhCCl_3 + 2\ NH_2NHPh \longrightarrow PhCH{=}NNHPh +$$
$$+ PhH + N_2 + 3\ HCl, \quad (3)$$
$$\Delta H_r = -29.7\ \text{kcal mol}^{-1}.$$

The calculated heats of formation (ΔH_f) of the initial trichloride **1a** and hydrazines **12—14**, the reaction products, namely, azine **16**, hydrazones **19b,c**, molecular hydrogen and nitrogen, HCl, benzene, and tetrazene **25**, and the possible intermediates, namely, hydrazidines **23a—c**, nitrile imines **24a,b**, α,α-dichlorobenzylhydrazines $PhCCl_2NHNRR'$ (**26a—c**), α-chlorobenzylhydrazines $PhCHClNHNRR'$ (**27a—c**), and hydrazonoyl chlorides **18a—c** (Ar = Ph; R = R′ = H (**a**); R = R′ = Me (**b**); R = Ph, R′ = H (**c**)) are listed in Table 1. The heats of reactions (ΔH_r) calculated using the ΔH_f value are given below the corresponding reaction equations.

The resulting ΔH_f and ΔH_r values can be used only for comparison. It is known[15] that ΔH_f values found by MNDO calculations are close to the experimental values (to within 1 kcal mol^{-1}) only for hydrocarbons. In the case of heteroatomic compounds, the deviations are much greater and, as a result of optimization of the parametrization for a broad range of compounds, the method gives some obviously incorrect values, for example, $\Delta H_f(N_2) = 8.0$ kcal mol^{-1}. However, it should be noted that the use of $\Delta H_f(N_2) = 0$ kcal mol^{-1}, which is correct by definition, does not change our conclusions qualitatively.

It can be easily seen that overall reactions (1)—(3) are exothermic. Since all reactions are carried out in the presence of pyridine or excess hydrazine, the formation of, for example, hydrogen-bonded complex $C_5H_5N...HCl$ could substantially enhance the heat evolution (according to estimates, by at least 10 kcal mol^{-1}). The contribution of the heat of formation of the pyridine or hydrazine salts (pyridinium or hydrazinium chloride) to

Table 1. Heats of formation (ΔH_f) of the initial compounds, products, and possible intermediates of the reductive condensation of benzotrichloride with hydrazines determined by MNDO calculations

Compound	ΔH_f /kcal mol^{-1}	Compound	ΔH_f /kcal mol^{-1}
Benzotrichloride		Hydrazidines	
1a	5.3	**23a**	74.9
Hydrazines		**23b**	84.8
12	14.1	**23c**	136.7
13	18.4	Tetrazene	
14	46.6	**25**	47.2
Azine		α,α-Dichlorobenzylhydrazines	
16	85.4	**26a**	34.9
Hydrazonoyl chloride		**26b**	40.0
18a	42.5	**26c**	67.0
18b	46.2	α-Chlorobenzylhydrazines	
18c	73.2	**27a**	33.5
Hydrazones		**27b**	39.2
19a	53.6	**27c**	67.6
19b	56.7	Other compounds	
19c	85.4	H_2	0.0
Nitrile imines		N_2	8.0
22a	107.4	HCl	−15.3
22c	137.6	C_6H_6	21.3

the energy of the reaction cannot be estimated qualitatively so easily; in the gas-phase approximation used in calculations, this is hampered by the exceptional ambiguity of the geometry of the ion pair.

The first step of each of reactions (1)—(3) is, beyond doubt, the formation of α,α-dichlorobenzylhydrazines **26a—c**. According to MNDO calculations, this step is slightly endothermic in the case of compounds **26a,b** (ΔH_f = 0.2 and 1.0 kcal mol^{-1}, respectively) and is slightly exothermic in the case of **26c** (ΔH_f = −0.2 kcal mol^{-1}). In the presence of excess base, the reaction should be accompanied by some heat evolution in all cases. Dehydrochlorination of compounds **26a—c** to hydrazonoyl chlorides **18a—c** (reaction (4)) is always exothermic. According to our calculations, which imply the formation of products shown by reactions (1)—(3), the reduction of hydrazonoyl chloride **18b** to hydrazone **19b** is endothermic; however, reactions (4) and (5) for dichloride **26b** provide benefit in energy (ΔH_f = −3.4 kcal mol^{-1}). In the case of dichlorides **26a,c**, both steps in (4) and (5) are exothermic and the total reaction enthalpy amounts to −15.0 and −29.5 kcal mol^{-1}, respectively:

$$PhCCl_2NHNRR' \longrightarrow PhCCl{=}N{-}NRR', \quad (4)$$

ΔH_f = −7.7 (**a**), −9.1 (**b**), and −9.1 kcal mol^{-1} (**c**):

$$PhCCl{=}N{-}NRR' \longrightarrow PhCH{=}N{-}NRR', \quad (5)$$

ΔH_f = −7.3 (**a**), 5.6 (**b**), and −20.4 kcal mol^{-1} (**c**).

The reduction of compounds **26a—c** to give α-chlorobenzylhydrazines **27a—c** (reaction (6)) is exothermic and, in the case of reactions with hydrazine and phenylhydrazine, it is also energetically more favorable than dehydrochlorination. The subsequent slightly endothermic dehydrochlorination of compounds **27a—c** (reaction (7)) yields hydrazones **19a—c**; the second and the third of them are true reductive condensation products, while the first can be regarded as a model compound because reactions of TCMA with hydrazine give azines of type **16**:

$$PhCCl_2NHNRR' \longrightarrow PhCHCl{-}NHNRR', \quad (6)$$

ΔH_f = −19.8 (**a**), −5.7 (**b**), and −32.0 kcal mol^{-1} (**c**):

$$PhCHCl{-}NHNRR' \longrightarrow PhCH{=}N{-}NRR', \quad (7)$$

ΔH_f = 4.8 (**a**), 2.2 (**b**), and 2.5 kcal · mol^{-1} (**c**).

Since the reduction of α,α-dichlorobenzylhydrazines **26a,c** is more exothermic than dehydrochlorination and the reduction of hydrazonoyl chloride **18b** is endothermic, the sequence of reactions (6) → (7) appears to be more probable than (4) → (5). A more definite conclusion may be based on consideration of the activation energies of different steps of the process; this is a separate task requiring evaluation of models of transition states that differ fundamentally from one another.

Note that, according to MNDO calculations, the formation of hydrazidines **23a—c** from the corresponding hydrazonoyl chlorides and hydrazines is thermodynamically unfavorable (ΔH_f = 3.0, 4.9, and 1.6 kcal mol^{-1}, respectively), and the transformation of dichlorobenzylhydrazines **26a—c** into hydrazidines (ΔH_f = −4.7, −4.2, and −7.4 kcal mol^{-1}, respectively) is markedly less favorable than the reduction to α-chlorobenzylhydrazines **27a—c** (reaction (6)) or dehydrochlorination to hydrazonoyl chlorides **18a—c** (reaction (4)). Elimination of a hydrogen chloride molecule from hydrazonoyl chlorides **18a,b** to give nitrile imines **25a,b** requires much energy (ΔH_f = 49.6 and 49.2 kcal mol^{-1}, respectively).

Although the calculations were performed in the "gas-phase approximation," the estimated probability of formation of hydrazidines and nitrile imines will hardly change in kind if solvation effects are taken into account. Thus, it was shown experimentally that reductive condensation of TCMA with hydrazines, giving rise to the corresponding hydrazones, can proceed without the intermediate formation of pyridinium salts and without participation of pyridine in the reduction step itself. In general, the set of experimental and theoretical results presented here allows the conclusion that the key step of reduction involves hydrazonoyl chlorides **18** and/or α-chlorobenzylhydrazines **27** when hydrazines are used as the reducing agents in reductive condensation.

Experimental

^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer, IR spectra were measured on a Perkin—Elmer 577 instrument (pellets with KBr). Melting points were determined on a Boetius microscope hot stage and not corrected.

The calculations were carried out by the standard MNDO scheme.[16]

Reaction of *N,N'*-(α-chlorobenzylidene)bispyridinium dichloride (4a) with hydrazine in pyridine. *A.* A solution of compound **1a** (2.7 mL, 3.74 g, 19 mmol) in dry pyridine (6.2 mL, 6.04 g, 76 mmol) (prepared by keeping and distillation over NaOH) was refluxed for 2 h. After that, a solution of hydrazine dihydrochloride (10.01 g, 57 mmol) in 5 mL of pyridine and 3 mL of water was added to the resulting solution containing salt **4a** (*cf.* Ref. 3). The mixture was refluxed for 4 h, excess solvent was distilled off, the residue was diluted with 100 mL of water, and the product was extracted with chloroform. The extract was dried with $MgSO_4$ and the solvent was evaporated. The residue was recrystallized from EtOH and dried in a vacuum desiccator to give 1.78 g (yield 76%) of benzoic acid, m.p. 120—121 °C (*cf.* Ref. 19).

B. A solution of hydrazinium dihydrochloride (10.01 g, 57 mmol) in 5 mL of dry pyridine was added to a solution of salt **4a** (prepared as described in procedure *A* in the same amount) and the mixture was refluxed for 4 h. The solvent was evaporated and the residue, which crystallized on cooling, was diluted with 100 mL of water. The water-insoluble material was

filtered off, recrystallized from aqueous acetone, and dried in a vacuum desiccator to give 0.92 g (yield 43%) of 3,5-diphenyl-1,2,4-triazole (**15**), m.p. 194—195 °C (*cf.* Ref. 20). ^{1}H NMR (CD_3OD), δ: 7.48 (m, 6 H, *m*-H, *p*-H); 8.11 (m, 4 H, *o*-H). IR, ν/cm^{-1}: 720, 727, 782 (monosubstituted benzene); 1480, 1483, 1560, 1620 (C=C, C=N); 3200 (NH).

Reaction of *N,N'*-(2,4-dimethyl-α-chlorobenzylidene)-bispyridinium dichloride (4b) with hydrazine in pyridine. The solution of salt **4b** was prepared from compound **1b** (3.6 mL, 4.47 g, 20 mmol) in dry pyridine (4.86 mL, 4.75 g, 60 mmol) and the mixture was worked-up as described in procedure *A* of the previous experiment to give 0.89 g (yield 30%) of 2,4-dimethylbenzoic acid, m.p. 123—125 °C (*cf.* Ref. 21).

Reaction of 2,4,6-trimethylbenzotrichloride (1d) with hydrazine in the presence of 2-picoline. Trichloride **1d** (2 mL, 2.74 g, 11.5 mmol) was added dropwise to a solution of $N_2H_4 \cdot 2HCl$ (2.42 g, 23 mmol) in 10 mL of 2-picoline and 3 mL of water. The mixture was refluxed for 1 h and concentrated under reduced pressure on a rotary evaporator. The residue was diluted with 100 mL of water and the product was extracted with chloroform (2×20 mL). The organic layer was separated and dried with $MgSO_4$, the solvent was evaporated, and the residue, which solidified on storage, was extracted with 40 mL of hexane with refluxing. The extract was concentrated and the residue was crystallized from EtOH to give 0.66 g (yield 39%) of 2,4,6-trimethylbenzaldazine (**16**, Ar = 2,4,6-$Me_3C_6H_2$), m.p. 169—171 °C, identical to that described previously.[9] ^{1}H NMR ($CDCl_3$), δ: 2.32 (s, 3 H, Me); 2.54 (s, 6 H, 2 Me); 6.93 (s, 2 H, H(3), H(5)); 8.99 (s, 1 H, CH=N).

Reaction of 2,4,6-trimethylbenzotrichloride (1d) with hydrazine in the presence of 4-picoline. The reaction was carried out as described in the previous experiment with the same amounts of reactants except that 4-picoline was used instead of 2-picoline. This gave 0.54 g of azine **16** (Ar = 2,4,6-$Me_3C_6H_2$) (yield 32%).

Reaction of 2,4,6-trimethylbenzotrichloride (1d) with hydrazine in the presence of 2,6-lutidine. The reaction of $N_2H_4 \cdot 2HCl$ (4.84 g, 46 mmol) in 10 mL of 2,6-lutidine and 3 mL of water performed as in the previous experiment, after 3 h of refluxing and the above-described workup, gave 0.46 g (yield 26%) of 2,4,6-trimethylbenzaldehyde *N*-(2,4,6-trimethylbenzoyl)hydrazone (**17**, Ar = 2,4,6-$Me_3C_6H_2$), m.p. 213—214 °C (*cf.* Ref. 22).

Reaction of 2,4,6-trimethylbenzotrichloride (1d) with pyridine and 1,1-dimethylhydrazine. A solution of trichloride **1d** (0.64 g, 2.7 mmol) and dimethylhydrazine (**13**) (0.16 g, 2.7 mmol) in 3 mL of dry pyridine was kept in an argon atmosphere for 10 days at −20 °C. After evaporation of excess pyridine, the residue was treated with 20 mL of water and extracted with Et_2O. The extract was dried with $MgSO_4$ and the ether was evaporated to give 0.39 g of a liquid residue. According to the ^{1}H NMR spectrum, this was a mixture of mesitoaldehyde (**11d**) and its dimethylhydrazone **19** (Ar = 2,4,6-$Me_3C_6H_2$, R = R′ = Me) in 45 : 55 ratio (yields 38 and 46%, respectively). The reaction carried out in CH_2Cl_2 using 2 equiv. of pyridine gave the same products in 34 and 50% yields, respectively. ^{1}H NMR ($CDCl_3$), δ, aldehyde **11d**: 10.56 (s, 1 H, CHO); 6.92 (s, 2 H, H(3), H(5)); 2.60 (s, 6 H, C(2)Me, C(6)Me); 2.33 (s, 3 H, C(4)Me) (corresponds to published data[23]). ^{1}H NMR ($CDCl_3$), δ, dimethylhydrazone **19**: (R = R′ = Me, Ar = 2,4,6-$Me_3C_6H_2$): 7.56 (s, 1 H, CH=N); 6.88 (s, 2 H, H(3), H(5)); 2.97 (s, 6 H, NMe); 2.42 (s, 6 H, C(2)Me, C(6)Me); 2.30 (s, 3 H, C(4)Me).

Reaction of 2,4,6-trimethylbenzotrichloride (1d) with 1,1-dimethylhydrazine in 2,6-lutidine. A solution of trichloride **1d** (1 mL, 1.37 g, 5.8 mmol) in dimethylhydrazine (**13**) (3 mL, 3.8 g, 63.2 mmol) and 3 mL of 2,6-lutidine was refluxed for 16 h and excess dimethylhydrazine and lutidine were evaporated. The residue was diluted with 100 mL of water, 10 mL of conc. HCl was added to the solution, and the product was extracted with chloroform. The extract was dried over $CaCl_2$. Evaporation of the solvent gave a light-brown oil, whose chromatography on silica gel (elution with benzene) afforded 0.4 g (yield 37%) of dimethylhydrazone **19** (Ar = 2,4,6-$Me_3C_6H_2$, R = R′ = Me), n_D^{25} 1.5645 (*cf.* Ref. 9).

Reaction of benzotrichloride (1a) with hydrazine in 2,6-lutidine. $N_2H_4 \cdot 2HCl$ (6.3 g, 60 mmol) and 2 mL of water were added to a solution of trichloride **1a** (2.7 mL, 3.74 g, 19 mmol) in 10 mL of 2,6-lutidine. The mixture was heated to complete homogenization and kept for 1 h at reflux. The material, which crystallized on cooling, was diluted with 50 mL of water and the precipitated crystals were filtered off. Recrystallization from EtOH gave 0.86 g (yield 37%) of *N,N'*-dibenzoylhydrazine, m.p. 244—246 °C (*cf.* Ref. 24). The aqueous solution was extracted with chloroform (2×25 mL), the extract was washed with water and dried with $CaCl_2$, and the solvent was evaporated. The residue was crystallized from ethanol to give 0.25 g (yield 12.5%) of benzaldazine (**16**, Ar = Ph), m.p. 89—91 °C, identical to that described previously.[4]

Reaction of benzotrichloride (1a) with phenylhydrazine in pyridine. A solution of trichloride **1a** (2.7 mL, 3.74 g, 19 mmol) and phenylhydrazine (**14**) (3.76 mL, 4.14 g, 38.2 mmol) in 10 mL of dry pyridine was refluxed for 2 h, excess pyridine was evaporated, the residue was diluted with 100 mL of water, and the product was extracted with chloroform. The extract was washed with water and dried with $MgSO_4$ and the solvent was evaporated. Chromatography of the residue on a silica gel column (elution with a 3 : 1 hexane—AcOEt mixture) gave 0.52 g (yield 14%) of benzaldehyde phenylhydrazone (**19c**, Ar = R = Ph, R′ = H), m.p. 156 °C (*cf.* Ref. 25). Treatment of the aqueous layer according to the procedure described previously[13] gave no precipitate of 1,3-diphenyl-*symm*-triazolo[4,3-*a*]-pyridinium tetrafluoroborate. When the reaction was carried out in the presence of styrene, no adduct resulting from 1,3-dipolar cycloaddition was detected either (TLC data).

Reaction of benzotrichloride (1a) with *N,N*-dimethylhydrazine. A solution of trichloride **1a** (2.7 mL, 3.74 g, 19 mmol) in dimethylhydrazine (**13**) (7.26 mL, 5.74 g, 96 mmol) was refluxed for 22 h, excess dimethylhydrazine was evaporated, the residue was diluted with 100 mL of water, and the product was extracted with chloroform. The extract was washed with water and dried with $CaCl_2$ and the solvent was evaporated. The residue was refluxed with 50 mL of hexane. Evaporation of the hexane extract followed by column chromatography on silica gel (elution with benzene) gave 0.4 g (14%) of benzaldehyde *N,N*-dimethylhydrazone (**19b**, Ar = Ph, R = R′ = Me), n_D^{20} 1.5911. Lit. data[26]: n_D^{20} 1.5920. ^{1}H NMR ($CDCl_3$), δ: 7.66 (m, 2 H, *o*-H); 7.35 (m, 4 H, *m*-H, *p*-H, CH=N); 3.00 (s, 6 H, NMe).

Reaction of *N,N'*-bis(*α*-chlorobenzylidene)hydrazine (20, Ar = Ph) with hydrazine in pyridine. A solution of dichloride **20** (Ar = Ph) (1 g, 3.6 mmol), prepared from *N,N'*-dibenzoylhydrazine and PCl_5 by a known procedure,[27] and $N_2H_4 \cdot 2HCl$ (1.89 g, 18 mmol) in 3 mL of pyridine was refluxed for 1 h and excess pyridine was evaporated. The crystalline residue was extracted with chloroform, the extract was washed with water and dried with $CaCl_2$, and the solvent was evaporated. The semicrystalline residue was treated with EtOH, and crimson-colored crystals of 3,6-diphenyl-1,2-dihydro-1,2,4,5-tetrazine (**21**), insoluble in EtOH, were filtered off; m.p. 194—195 °C (*cf.* Ref. 28). Yield 0.31 g (37%). Dilution of the ethanolic solution with water (1 : 1) resulted in the precipitation of the colorless crystals of benzaldazine (**16**, Ar = Ph), 0.07 g (yield 9%), m.p. 90—91 °C (from EtOH).

When the reaction was carried out under the same conditions but without hydrazine, the starting dichloride **20** (Ar = Ph) was recovered unchanged.

Synthesis of *N*-hydroxy-2,4,6-trimethylbenzamidoxime and attempt to reduce it with hydroxylamine in pyridine. Sodium acetate (1.89 g, 23.1 mmol) was added to a solution of trichloride **1d** (2 mL, 2.74 g, 11.5 mmol) and $NH_2OH \cdot HCl$ (1.6 g, 23.1 mmol) in 10 mL of Bu^tOH and the mixture was refluxed for 12 h. After evaporation of the solvent, the residue was made alkaline by Na_2CO_3 and extracted with ether. After evaporation of Et_2O from the extract, the residue was dissolved in 10 mL of EtOH and 5 mL of conc. HCl was added to the solution. The precipitated crystals were filtered off and recrystallized from EtOH to give 1.11 g (yield 42%) of *N*-hydroxy-2,4,6-trimethylbenzamidoxime, m.p. 156—159 °C (*cf.* Ref. 29). The resulting hydroxyamidoxime (1 g, 4.3 mmol) and $NH_2OH \cdot HCl$ (0.9 g, 13 mmol) were refluxed in 10 mL of pyridine for 2 h, the pyridine was evaporated, the residue was treated with a solution of Na_2CO_3, and the product was extracted with Et_2O. From the residue obtained after evaporation of the ether, 0.74 g (74%) of the initial hydroxyamidoxime was isolated.

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