REACTION OF TRICHLOROACETONITRILE WITH PRIMARY AND SECONDARY AMINES

PART I. PREPARATION OF SOME TRICHLOROACETAMIDINES[1]

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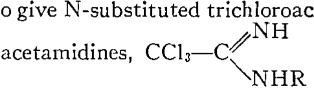
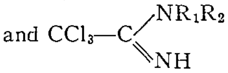
ABSTRACT

Trichloroacetonitrile reacts with primary and secondary aliphatic and primary aromatic amines to give N-substituted trichloroacetamidines. A series of N-mono- and N-di-substituted trichloroacetamidines,  $\mathrm{CCl_3{-}C}\genfrac{}{}{0pt}{}{\diagup\!\!\!\diagup\,\mathrm{NH}}{\diagdown\,\mathrm{NHR}}$ and  $\mathrm{CCl_3{-}C}\genfrac{}{}{0pt}{}{\diagup\,\mathrm{NR_1R_2}}{\diagdown\!\!\!\diagdown\,\mathrm{NH}}$, was prepared by carrying out the reaction in water, in water–methanol solutions, or in the absence of solvents.

INTRODUCTION

Although acetonitrile forms N-substituted acetamidines by the addition of amines only in the presence of anhydrous aluminum chloride (1), trichloroacetonitrile reacts with amines more easily. The German Patent No. 671,785 (2) reported the preparation of some trichloroacetamidines by the direct interaction of trichloroacetonitrile with aliphatic primary amines at low temperature, without giving any details. Oxley (3) prepared trichloroacetamidine and N,N-ethylene-bis-trichloroacetamidine in benzene solution. Backer and Wanmaker (4) isolated N-methyl- and N-piperidyl-trichloroacetamidine only in the form of picrates. They found that the addition of aromatic amines to trichloroacetonitrile proceeded only in the presence of methanol or acetone. The role of methanol in the reaction was explained by assuming that methanol first adds to trichloroacetonitrile to form an iminoether as an intermediate which subsequently reacts with aniline to give the amidine.

The objective of the present work was the investigation of the preparation of trichloroacetamidines by the direct addition of amines to trichloroacetonitrile without using any catalysts. In the next part, a kinetic study of the reaction will be presented, followed by the investigation of the correlation between the infrared spectra and the structure of amidines.

DISCUSSION

The preparation of the N-substituted trichloroacetamidines involved three general procedures: (*a*) the lower primary and secondary aliphatic amines were treated with trichloroacetonitrile in water solutions; (*b*) the reactions of the higher aliphatic and cyclic amines were carried out in the absence of solvents; and (*c*) the aromatic primary amines were allowed to react with trichloroacetonitrile in water–methanol solution. The results are summarized in Table I. The three procedures are characterized by their simplicity, the absence of catalysts, and the high yields of the reaction products.

The lower aliphatic N-substituted trichloroacetamidines are colorless liquids possessing an unpleasant smell. They can be distilled at low pressure in a dry nitrogen atmosphere, whereas they decompose vigorously on being heated at normal pressure. It was found

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[1] *Manuscript received October 9, 1957.*

Contribution from the Department of Chemistry, McGill University, Montreal, Que., with financial assistance from the National Research Council, Ottawa, Canada.

[2] *Abstracted from a thesis submitted by J. C. Grivas to the Faculty of Graduate Studies and Research, McGill University, Montreal, Que., in partial fulfillment of the requirements for the M.Sc. degree, May, 1957.*

Can. J. Chem. Vol. 36 (1958)

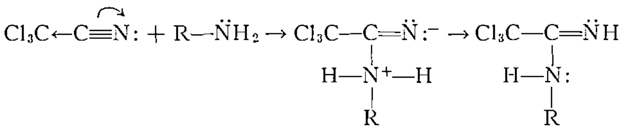
TABLE I

No.	Trichloro-acetamidine	Procedure	Yield, %	B.p.		Empirical formula	Nitrogen, %	
				° C.	mm. Hg		Calc.	Found[j]
1	N-Methyl-[b]	A	86	129	60	$C_3H_5Cl_3N_2$	15.96	15.85
2	N-Ethyl-[c]	A	84	62	2	$C_4H_7Cl_3N_2$	14.77	14.68
3	N-*n*-Butyl-	B	92	71–72	2	$C_6H_{11}Cl_3N_2$	12.87	12.67
4	N-*n*-Amyl-	B	94	89–90	2	$C_7H_{13}Cl_3N_2$	12.09	11.97
5	N,N-Dimethyl-[d]	A	68	51–52	2	$C_4H_7Cl_3N_2$	14.77	14.67
6	N,N-Diethyl-[e]	B	91	61–61.5	2	$C_6H_{11}Cl_3N_2$	12.87	12.69
7	N-Piperidyl-[f]	B	87	80–81	1.5	$C_7H_{11}Cl_3N_2$	12.20	12.09
8	N-Morpholyl-	B	92	89	1	$C_6H_9Cl_3N_2O$	12.10	11.99
9	N-Isopropyl-[g]	B	91	56[a]		$C_5H_9Cl_3N_2$	13.77	13.92
10	N-Benzyl-[h]	B	89	83.5[a]		$C_9H_9Cl_3N_2$	11.13	11.14
11	N-Phenyl-[i]	C	92	101–102[a]		$C_8H_7Cl_3N_2$	11.80	11.80
12	N-*p*-Ethoxyphenyl-	C	94	104[a]		$C_{10}H_{11}Cl_3N_2O$	9.95	9.90
13	N-*p*-Tolyl-	C	92	138.5[a]		$C_9H_9Cl_3N_2$	11.13	10.99
14	N-*m*-Tolyl-	C	95	100[a]		$C_9H_9Cl_3N_2$	11.13	10.96
15	N-*o*-Tolyl-	C	83	73[a]		$C_9H_9Cl_3N_2$	11.13	11.13

[a] *Melting points (° C.), corrected.*
[b] *Picrate, m.p. 163°–164°. Reported in the literature (4): m.p. 163°–164°.*
[c] *Hydrochloride, m.p. 224°–225° (decomp.).*
[d] *The yields can be increased by vigorous stirring for a longer period of time. Picrate, m.p. 162°–163°.*
[e] *Picrate, m.p. 153°.*
[f] *Picrate, m.p. 140°–140.5°. Reported in the literature (4): m.p. 139.5°–140°.*
[g] *The liquid mixture solidified in 2 minutes. The unreacted substances were evaporated in a vacuum and the solid N-isopropyl-2,2,2-trichloroacetamidine was purified by sublimation at 2 mm. pressure.*
[h] *Reported in the literature (2) but no analysis has been given. The substance was crystallized from a methanol–water mixture.*
[i] *The substance has been prepared by other authors (4, 5) using different methods. Hydrochloride, m.p. 180°–183°.*
[j] *Microanalyses by Mr. W. Manser (Herrliberg, Switzerland).*

that the salts of the primary and secondary amines do not react with trichloroacetonitrile in water solution.

The additon of the primary and secondary amines to the carbon–nitrogen triple bond seems to be an ionic reaction, which is facilitated by polar solvents, such as water and methanol. In the absence of kinetic data no proof of the mechanism is possible; however, the information obtained in this work may suggest the following scheme:



$$Cl_3C\leftarrow C\equiv\ddot{N}: + R-\ddot{N}H_2 \rightarrow Cl_3C-\underset{\substack{|\\ H-N^{+}-H\\ |\\ R}}{C}=\ddot{N}:^{-} \rightarrow Cl_3C-\underset{\substack{|\\ H-\ddot{N}:\\ |\\ R}}{C}=\ddot{N}H$$

The chlorine atoms in the position α to the nitrile group increase the positive charge of the carbon atom of the nitrile group by the inductive ($-$Is) effect. The attack of the unshared electron pair of the amine nitrogen on the positive carbon is followed by the formation of a bond between these atoms, the liberation of a proton, and the subsequent addition of the proton to the negatively charged nitrogen atom. This scheme may explain the failure of the reaction between the amine salts and trichloroacetonitrile, and also the lower reactivity of the aromatic amines in which the mobility of the unshared electron pair of the nitrogen atom is decreased by the resonance effect. The ionic intermediate also explains the activating influence of water and methanol in the reaction of trichloroacetonitrile with amines.

As has been mentioned above, it has been suggested (4) that methanol is essential in the reaction of trichloroacetonitrile with aniline by forming the intermediate amidine methyl ether. Our experiments indicated that this view cannot stand, for the following reasons: (*a*) aniline reacts with trichloroacetonitrile even in the absence of methanol or other solvents; (*b*) the reaction occurs also in ethanol, which, contrary to methanol, does not react with trichloroacetonitrile.

EXPERIMENTAL

The following procedures were applied for the synthesis of N-substituted trichloroacetamidines.

Procedure A—In Water Solutions

This procedure is useful for commercial aqueous solutions of primary and secondary aliphatic amines.

N-Methyl-2,2,2-trichloroacetamidine.—Trichloroacetonitrile (8 ml.) was added dropwise with stirring over a period of 10 minutes to 15 ml. of 25% aqueous solution of methylamine. The reaction was exothermic and the flask containing the reaction mixture was cooled in an ice-water bath. The lower layer was separated, dried, and distilled. B.p. 129° at 60 mm. pressure. Yield 11.5 g., 86% of the theoretical.

N,N-Dimethyl-2,2,2-trichloroacetamidine.—Trichloroacetonitrile (7.2 g., 0.05 M.) was added to 4 ml. of an aqueous solution of dimethylamine containing 2.25 g. of the pure amine. The mixture was shaken for half an hour. The lower layer was separated, dried, and distilled. B.p. 51°–52° at 2 mm. pressure. Yield 6.45 g., 68% of the theoretical.

Procedure B—In the Absence of Solvents

This procedure can be applied successfully to the reactions of higher aliphatic primary and secondary amines, and also to piperidine and morpholine. The reaction time was 3 hours at least, and the reactions were carried out at room temperature.

N-n-Butyl-2,2,2-trichloroacetamidine.—Trichloroacetonitrile (7.2 g.) was added dropwise to 3.65 g. (0.05 M.) of pure *n*-butylamine. The temperature rose considerably and the mixture turned yellow. The distillation of the reaction product gave a colorless liquid. B.p. 71°–72° at 2 mm. pressure. Yield 9.92 g., 92% of the theoretical.

Procedure C—In Water–Methanol or Methanol Solutions at Room Temperature

This method was applied to the reactions of primary aromatic amines with trichloroacetonitrile. After a period of 3 days the reaction products were precipitated by the addition of water in almost quantitative yields. They were recrystallized from petroleum ether or water–methanol mixtures.

Reaction of Aniline and Trichloroacetonitrile

(*a*) *In the absence of solvents.*—Trichloroacetonitrile (1.44 g., 0.01 M.) was mixed with 0.93 g. of aniline (0.01 M.) and left at room temperature for 5 days. The mixture turned red, brown, and finally black, and after 48 hours crystals started to precipitate in small quantity. The mixture was diluted with 7 ml. of methanol. The reaction product was precipitated by addition of water, filtered, and crystallized from a methanol–water mixture, m.p. 101°–102°. The yield was 1.27 g. (54% of the theoretical).

(*b*) *In ethanol solution.*—Equimolar quantities of the reactants mentioned in (*a*) were dissolved in 5 ml. of ethanol and left at room temperature for 5 days. Addition of water, at the end of this period, caused the precipitation of N-phenyltrichloroacetamidine which melted at 101°–102° after crystallization from water–methanol. Yield 1.8 g. (76%).

Preparation of Picrates and Hydrochlorides

The picrates of trichloroacetamidines were obtained by the addition of equimolar quantities of the amidines and picric acid in benzene solution. The precipitated picrates were crystallized from water. Hydrochlorides of amidines were prepared by passing of a hydrogen chloride gas through solutions of amidines in dry ether.

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