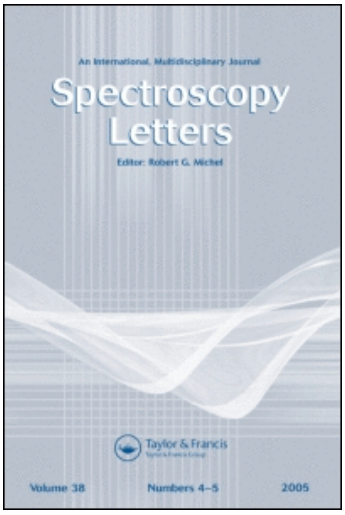

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Infrared Spectral Study on the Reaction Mechanism of N-Substituted Trichloroacetamides in Alkaline Medium

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INFRARED SPECTRAL STUDY ON THE REACTION MECHANISM OF N-SUBSTITUTED TRICHLOROACETAMIDES IN ALKALINE MEDIUM

KEY WORDS: Infrared spectra; Reaction mechanism; Trichloroacetanilide; N-anion; Phenylisocyanate.

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ABSTRACT

The reaction of trichloroacetanilide in alkaline medium was followed by means of infrared spectroscopy. Several intermediates and reaction products have been proved: the N-anion of the started trichloroacetanilide, the decarboxylation products of pnenylcarbamic acid - carbon dioxide and aniline, the end-product N,N-diphenylurea. The data obtained support the presupposed reaction mechanism involving *in situ* generation of phenylisocyanate.

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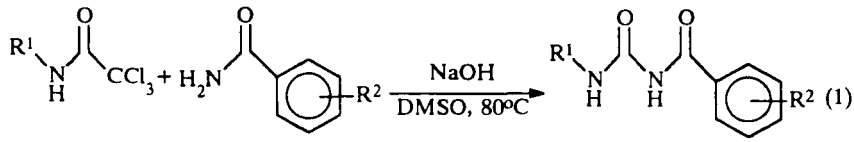
INTRODUCTION

There exist various methods for synthesis of compounds containing an ureido-group like symmetrical and unsymmetrical ureas[1-5], acylureas and sulfonylureas[4-8], phosphorylureas[9-10], ureido carboxylic acids and hydantoins obtained by their cyclization[11]. In most of these methods phosgene or other toxic compounds as alkaline cyanates or organic isocyanates are used as reagents. For the synthesis of starting isocyanates highly toxic phosgene is applied in most cases.

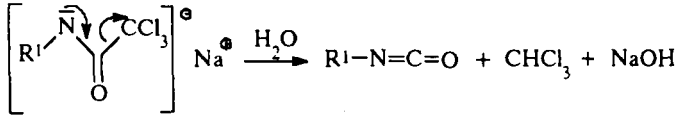
We have pointed out in our previous study[12,13], that urea's derivatives may be obtained by non-phosgene preparative method, based on the interaction of N-substituted trichloroacetamides and nitrogen nucleophiles in polar aprotic solvents such as dimethylsulfoxide (DMSO), dimethylformamide (DMF) or acetonitrile, in the presence of anhydrous inorganic bases as sodium hydroxide, sodium or potassium carbonate.

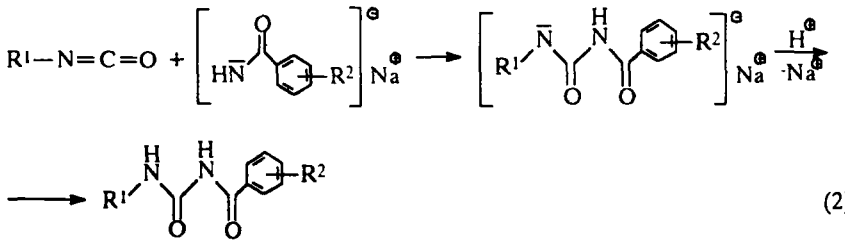
N-Substituted trichloroacetamides interact with benzamides to the corresponding acylureas[12]:



R^1 = (un)substituted phenyl, cyclopentyl; R^2 = H, alkyl, alkoxy, cyano, nitro.

It was assumed that in strong alkaline medium the reaction of N-substituted trichloroacetamides proceeds via isocyanate intermediates formed from N-substituted trichloroacetamide anions:





(2)

This reaction mechanism was presupposed to resemble the mechanism of the reaction of phenyl carbamates under alkaline conditions[14,15].

N-Substituted trichloroacetamides react with amines in DMSO, DMF or acetonitrile in the presence of anhydrous sodium carbonate to the corresponding unsymmetrical ureas[13]:

$$R\text{-}NH\text{-}CO\text{-}CCl_3 + HNR^1R^2 \xrightarrow[DMSO,\ DMF\ or\ CH_3CN,\ 80\text{-}90^oC]{Na_2CO_3} RNHCONR^1R^2 \quad (3)$$

R = (un)substituted phenyl, naphthyl;

R^1 = H, R^2 = cyclopentyl, (un)substituted benzyl, (un)substituted phenyl, 2-hydroxyethyl

The treatment of N-substituted trichloroacetamides with sodium hydroxide under the above conditions yielded symmetric N,N'-disubstituted ureas[12]:

$$R\text{-}NH\text{-}CO\text{-}CCl_3 \xrightarrow[DMSO,\ 80^oC]{NaOH} R\text{-}NH\text{-}CO\text{-}NH\text{-}R \quad (4)$$

R = (un)substituted phenyl, cyclopentyl, 3,4-methylenedioxybenzyl

We supposed that the reaction proceeds in accordance with the mechanism given in Scheme 2. A more systematic investigation had to be done in order to confirm or reject the assumption, that in the reaction medium (inorganic base, polar aprotic solvent), N-substituted trichloroacetamides generate *in situ* isocyanates, which react with nitrogen nucleophiles leading to the corresponding ureido compounds.

The aim of this study is to follow the reaction of trichloroacetanilide in alkaline medium by means of infrared (IR) spectroscopic technique, and to prove some of the reaction intermediates and their derivatives participating in the supposed reaction mechanism.

EXPERIMENT

The synthesis of trichloroacetanilide is being described elswere[12]. The reaction of trichloroacetanilide (20 mg/ml) with anhydrous sodium hydroxide or sodium methoxide was carried out *in situ* in CaF_2 cell, in dry dimethyl sulfoxide (DMSO) under pure argon at various temperatures (up to 85°C) and time of heating (up to 2 hours). The IR spectra of the reaction mixtures were recorded on a Perkin-Elmer FTIR 1750 spectrometer at 2 cm^{-1} resolution.

RESULTS AND DISCUSSION

The IR spectra of the starting trichloroacetanilide and the intermediate product obtained in inert medium by the reaction of the starting compound with sodium hydroxide in DMSO solution, are presented in Fig. 1. It is seen from the Fig. 1a that the neutral trichloroacetanilide possesses a strong absorption band of the C=O stretching vibration ($\nu_{C=O}$) at 1712 cm^{-1}. The intensity of the latter decreases and disappears completely by shaking the solution of trichloroacetanilide in DMSO with anhydrous sodium hydroxide for 5 minutes at ambient temperature. Simultaneously new strong bands appeared at 1624 cm^{-1}, 1582 cm^{-1} and medium bands at 1481 cm^{-1} and 1330 cm^{-1} (Fig. 1b). We assigned these bands respectively to the ν_{CO}, $\nu_{C\text{-}C}$ vibration of the benzene ring (the vibration 8 according to the classification of Wilson[16]), vibration 19 and $\nu(C_{Ph}\text{–}N)$ of the anionic product of trichloroacetanilide. The assignment of these bands to the N-anion of trichloroacetanilide has been made on the basis of

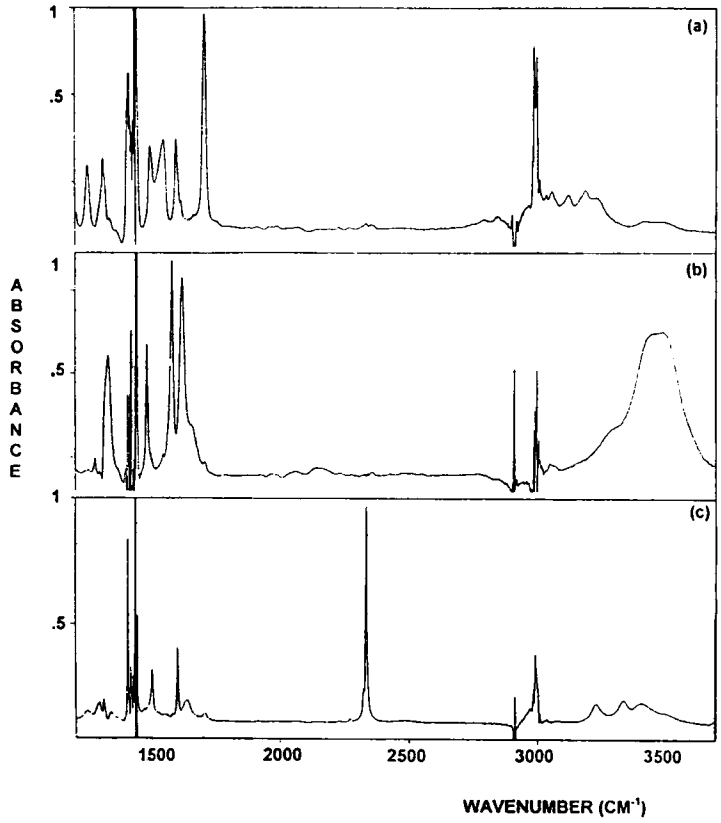


FIGURE 1

a more detailed study with IR spectroscopy of the anionic products of a series of amides treated with $NaOCH_3$ and dimsyl-sodium in DMSO[17].

We accomplished a model investigation of the reaction of trichloroacetanilide with $NaOCH_3$ in DMSO i.e. the reaction conditions are the same, when the $NaOCH_3$ is used as a base. The IR spectrum of the obtained reaction product possesses the same absorption bands: 1624 cm^{-1}, 1583 cm^{-1}, 1481 cm^{-1} and 1330 cm^{-1}. The IR spectrum of the obtained reaction product

presented in Fig. 2a possesses the same absorption bands: 1624 cm^{-1}, 1583 cm^{-1} 1481 cm^{-1} and 1330 cm^{-1}. Like the IR spectrum of the reaction products obtained with NaOH described above, we assigned these bands to the ν(CO), vibration 8, vibration 19 of the benzene ring and $\nu(C_{Ph}-N)$ of the amide anion of trichloroacetanilide respectively. These data undoubtedly points out that the N-anion of trichloroacetanilide is obtained under the above reaction conditions. Heating the reaction mixture to 85°C for 10 min leads to products whose IR spectrum shows a decreasing of the N-anion bands and appearance of two new bands at 1729 cm^{-1} and 1233 cm^{-1} (Fig. 2b). We assign the last two bands to the ester group of the reaction product - methyl ester of phenylcarbamic acid:

$$C_6H_5\text{-}NH\text{-}\underset{\underset{O}{\|}}{C}\text{-}CCl_3 \xrightarrow[-CH_3OH]{CH_3O^{\ominus}} C_6H_5\text{-}\overset{\ominus}{N}\text{-}\underset{\underset{O}{\|}}{C}\text{-}CCl_3 \xrightarrow[-CCl_3^{\ominus}]{} C_6H_5\text{-}N{=}C{=}O$$

$$C_6H_5\text{-}N{=}C{=}O + CH_3OH \longrightarrow C_6H_5\text{-}NH\text{-}\underset{\underset{O}{\|}}{C}\text{-}OCH_3 \qquad (5)$$

Heating the reaction mixture containing the N-anionic product of trichloroacetanilide obtained in the presence of sodium hydroxide at 85°C for 2 hours leads to the appearance of new bands in the IR spectrum at 2237 cm^{-1}, 3410 cm^{-1}, 3338 cm^{-1}, 3229 cm^{-1} and 1641 cm^{-1} (see Fig.1c). We presupposed that the first band (2337 cm^{-1}) is due to the stretching vibration of the CO_2 separated from the phenylcarbamic acid. To prove this assumption, we registered the IR spectrum of DMSO saturated with CO_2-gas. The position and the shape of the 2337 cm^{-1} band completely reproduced the position and the half-width of the band in the IR spectrum of the reaction mixture, shown in Fig. 1c. An additional confirmation for phenylcarbamic acid decarboxylation is the obtained aniline whose bands were detected in the IR spectrum of the reaction mixture at 3410 cm^{-1}, 3338 cm^{-1}, 3229 cm^{-1} and 1641 cm^{-1} (see Fig. 1c). The

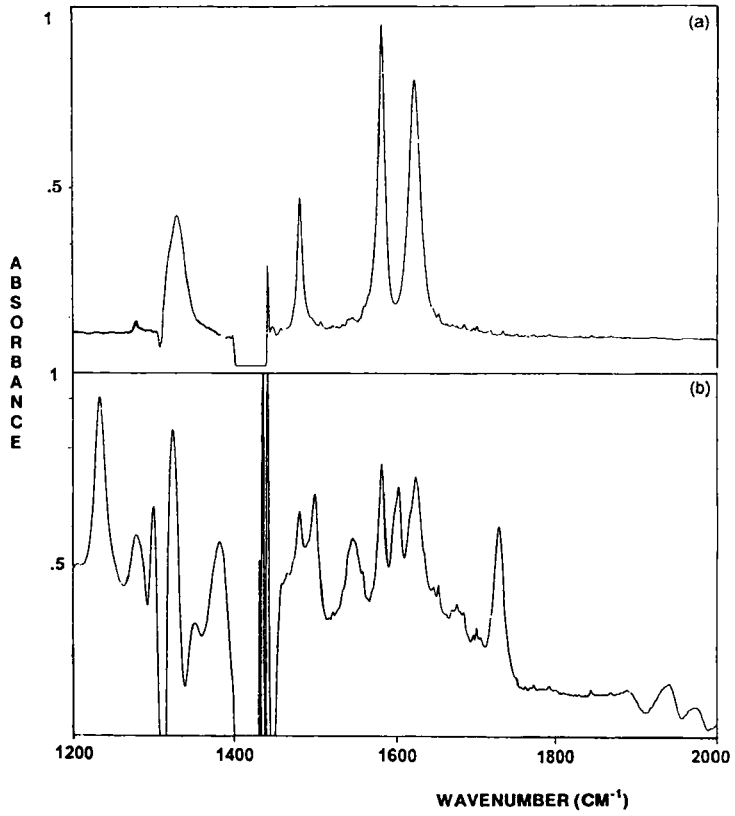
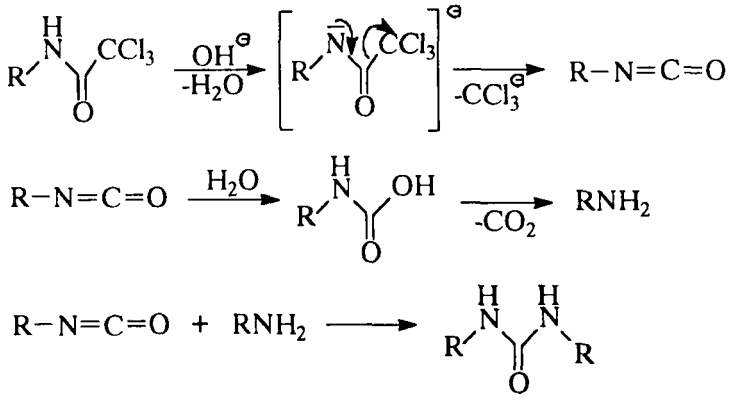


FIGURE 2

assignment of these bands is confirmed by registration of the IR spectrum of aniline in DMSO.

The separation of CO_2 during the interaction between trichloroacetanilide and NaOH in DMSO can be accepted as a confirmation of decarboxylation of the phenylcarbamic acid obtained by hydrolization of *in situ* generated phenylisocyanate in accordance with the proposed mechanism:



(6)

Along with the bands of CO_2 and aniline, in the IR spectrum of the reaction mixture a band at 1709cm^{-1} appears as well. The latter is due to the ν_{CO} of the N,N'- diphenylurea, the end product of the reaction, proved by registering the IR spectrum of this compound.

In conclusion, the presented IR spectral data of the studied reaction of N-substituted trichloroacetamides in alkaline medium allow to prove: (i) the N-anion of trichloroacetanilide as an intermediate; (ii) the methyl ester of phenylcarbamic acid; (iii) the products of decarboxylation of phenylcarbamic acid - aniline and carbon dioxide; (iv) the end product of the studied reaction in the presence of sodium hydroxide - the N,N'-diphenylurea which take part as intermediates and their derivatives in the proposed reaction mechanism.

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