THE MECHANISM OF THE EFFECT OF CHLORO-FORMAMIDINIUM-CHLORIDES IN THE PRODUCTION OF ISOCYANATES*

By

Z. Csűrös, R. Soós, I. Bitter and É. Kárpáti-Ádám

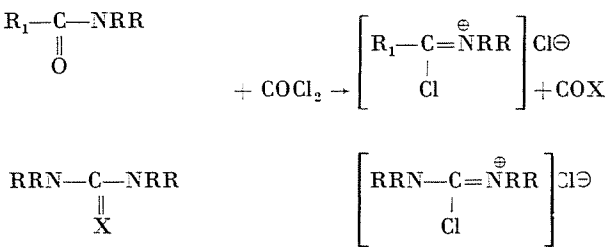
Department of Organic Chemical Technology,

Technical University Budapest

Recevied: January 5 1972

In our former communications [1, 2, 3, 4] we reported on a new synthesis of condensed pyrimidin ring by cyclization of trisubstituted amidinium-chlorides. This reaction is connected with investigations into the preparation and application of the reagent-type trivially named 'amide- and carbamide-chlorides' formed by the reaction of disubstituted amides with phosgene. These compounds structurally belong to the chloro-formamidinium-chlorides.

These can simply be prepared by virtue of the following reaction pattern:



$X = O, S$

R_1 = H, alkyl group

R = alkyl group

The first equation describes the formation of an amide chloride (its exact name is: chloromethylene-dimethyl-ammonium-chloride if $R = CH_3$ $R_1 = H$), the second refers to that of a carbamide chloride (its exact name: chlorodimethyl-aminomethylene-dimethylammonium-chloride if $R = CH_3$).

Their nature — in contradiction to former ideas — can rather be interpreted by ionic than non-ionic type and their outstanding reactivity can be explained on that basis.

The chloro-formamidinium-chlorides are almost incomparably valuable reagents which can be used over a wide range since reacting with compounds containing active hydrogene such widely varying organic compounds can be prepared as: alkyl chlorides, acid chlorides, amide acetales, thioamides, ami-

* Dedicated to Prof. L. Telegdy Kováts on the occasion of his 70th birthday.

dines, guanidines, nitriles, carbodiimides, carbamicacid orthoesters, etc. [5]. Recently it has turned out that chloro-formamidinium-chlorides have remarkable catalytic effects in some reactions of phosgene. For instance: in the chlorination of carboxylic and sulphonic acides or phenoles of strongly acidic character with phosgene there is easy reaction if dimethyl-formamide is used as catalyst since the chlorination is actually accomplished by the forming chloromethylene-dimethyl-ammonium-chloride.

In our work we have gained a lot of experience and a rather wide theoretical knowledge concerning the twofold application of chloroform-amidinium-chlorides.

These observations gave the idea of trying them as catalysts in the most important reaction of phosgene — the production of isocyanates.

Though the industrial production of isocyanates has been realized long ago, there are some problems which — just owing to the great practical importance of isocyanates — even now urge to find new possibilities.

The phosgenation of aromatic amines is the simplest and the most economical procedure to industrially produce aromatic isocyanates. The common feature of relevant patented procedures is that the reaction temperature is 130—160 °C during the whole phosgenation or in its second half. It is accompanied by disadvantages that make reasonable the interest in additives or catalysts to reduce the phosgenation temperature.

The solution of the problem is rendered difficult by the fact that not a single elementary step but a complex system of reactions is to be investigated to decide which of the reactions require the high temperature.

$$2ArNH_2 + COCl_2 \rightarrow ArNHCOCl + ArNH_2 \cdot HCl$$

$$ArNHCOCl \rightleftarrows ArNCO + HCl$$

$$\left.\begin{matrix} ArNHCOCl \\ ArNCO \end{matrix}\right\} + ArNH_2 \rightarrow ArNHCONHAr$$

$$ArNH_2 \cdot HCl + COCl_2 \xrightarrow{t>100°C} ArNCO + 3HCl$$

$$ArNHCONHAr + COCl_2 \xrightarrow{t>100°C} 2ArNCO + 2HCl$$

These processes being patented only very few data are found in the literature about the individual reactions. In our former investigation it was established, however, that the first step was a very rapid process even at 0 °C and the carbamic acid chloride-isocyanate equilibrium was also shifted upwards well below 100 °C [6]. There remain the phosgenation of amine-hydrochlorides and that of the diaryl ureas forming more or less in a side-reaction. According to experimental observations these are the two processes that require a temperature higher than 100 °C as it can be assumed that in case of the mentioned compounds a preliminary thermal dissociation is needed to react with phosgene.

Our idea was as follows: the additive or catalyst — chloro-formamidinium-chlorides — may act so that reacting with the amine—hydrochlorides and diarylureas, the resulting compounds can readily be converted with phosgene into isocyanates while the catalyst is regenerated in active form.

For investigating the mechanism, the intermediates of the production of phenyl isocyanates — as the simplest aromatic isocyanate — were chosen. These were: aniline-hydrochloride and carbanilide. The simplest 'amide chloride', the dimethylformamide-chloride and the simplest 'carbamide chloride' the tetramethyl carbamide-chloride were used as catalysts. Or, to be more precise, dimethyl-formamide, tetramethyl urea and thiourea were applied, but in the phosgenation conditions the two above chloroformamidinium chlorides were found to be formed from these compounds and so the chloroformamidinium-chlorides must be regarded as active forms of the catalysts.

1. The investigation of the effect mechanism of dimethyl-formamide-chloride

In our investigations dimethylformamide chloride has been prepared 'in situ' by making phosgene and dimethyl formamide to react in chloroform. Amide chlorides readily react with aromatic primary amines and according to the literature, substituted amidinium chlorides are formed even if the reaction affects the amine — hydrochloride [5].

$$C_6H_5NH_2 \cdot HCl + [Cl-\overset{\oplus}{C}H-N(CH_3)_2]Cl^{\ominus} \rightarrow \underset{\text{I}}{C_6H_5NH-CH=\overset{\oplus}{N}(CH_3)_2)Cl^{\ominus}}$$

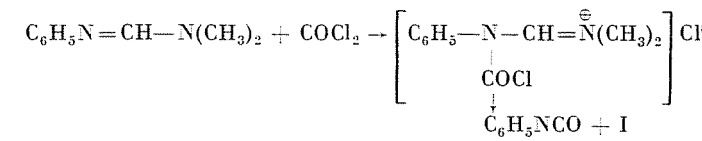
II

$$II + COCl_2 \xrightarrow{t>100\,^{\circ}C} C_6H_5NCO + I + HCl$$

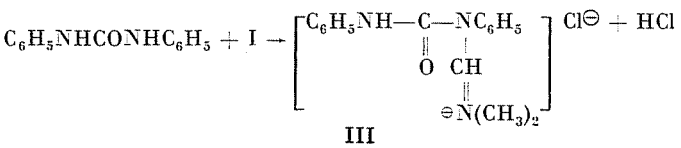
Dimehtylformamide-chloride reacts with aniline-hydrochloride even at room temperature to form N-phenyl-N'-N'-dimethyl-formamidinium-chloride. Its identification involved no difficulty for it had already been described in the literature. Then the reaction between amidinium-chloride and phosgene was investigated to see whether it yielded isocyanate while regenerating the active form of the catalyst. Reactions at a temperature below 100 °C failed and so dimethyl-formamide cannot be considered a suitable agent for decreasing the temperature of isocyanate production. Nevertheless the results of the technological trials showed that the rate of the phosgenation was remarkably accelerated at the temperature interval of 100 to 130 °C. This fact may have a single explanation; at this temperature the formamidinium-chloride already reacts with phosgene, isocyanate is formed and the regenerating catalyst can react with carbanilide and accelerates its phosgenation, the lowest process of all reactions. This supposition is confirmed by the phosgenation of

N-phenyl-N',N'-dimethyl-formamidinium chloride at 100 °C which resulted in phenylisocyanate almost quantitatively.

The equation below verifies the isocyanate formation in itself. In order to prove the supposed mechanism it was attempted to phosgenate N-phenyl-N',N'-dimethylformamidin. The base was expected to react with phosgene even at low temperature to permit isolation of the additive intermediate, the N-phenyl-N'-chlorocarbonil-N',N'-dimethylformamidinium chloride.



Though the expected compound resulted, no elementary analysis could be made because of its rapid decomposition. Its structure was confirmed by IR spectroscopy in which, ν C=O bond of the acid chloride at 1765 cm^{-1} and ν $C{=}\overset{\oplus}{N}$ bond at 1695 cm^{-1} could clearly be recognized. The spectrum of the solution indicates that the additive intermediate decomposes even at room temperature since the ν NCO bond appears at 2260 cm^{-1}, at the same time there is ν $C{=}\overset{\oplus}{N}$ vibration at 1660 cm^{-1} which proves the regeneration of dimethyl-formamide-chlorid. These experiments have proved that even if the use of dimethyl formamid-chloride in the phosgenation of amine hydrochloride had no advantage, since the cycle of the catalyst regeneration is not interrupted, it is able to influence advantageously the phosgenation of carbanilide. Therefore carbanilide and dimethyl-formamide-chloride were brought into reaction in equimolecular ratio. A rapid reaction took place even at room temperature and after carefully evaporating a solid, crystalline material was isolated. Its elementary analysis and IR spectrum proved it to be N-phenyl-N-phenylcarbamoyl-N',N-dimethyl-formamidinium chloride.



III

We tried to preparate some derivatives of this kind of compounds in order to investigate their chemical behaviour. The above mentioned reaction was observed in the case of every disubstituted urea but owing to the difficulties in crystallization, only some derivatives could be isolated. These com-

pounds behaved quite similarly on heating and at 60 to 70 °C they quantitatively decomposed to form isocyanate and trisubstituted formamidinium chloride. This interpretation explains why dimethylformamide accelerates phosgenation — though it does not make possible to decrease the reaction temperature under 100 °C — since the half of the urea is converted into isocyanate and the rest — amidinium chloride — reacts with phosgene at 100 °C.

Processes illustrating the catalytic mechanism of dimethylformamide chlorid are summarized below:

$$HCON(CH_3)_2 + COCl_2 \rightarrow I + CO_2$$

$$ArNH_2 \cdot HCl + I \rightarrow ArNH{-}CH = \overset{\oplus}{N}(CH_3)_2Cl\ominus + 2HCl$$

II

$$II + COCl_2 \xrightarrow{t \geq 100\ ^\circ C} ArNCO + I + HCl$$

$$ArNHCONHAr + I \rightarrow \left[\begin{array}{l} Ar\,NH{-}C{-}NAr \\ \quad\|\quad\ | \\ \quad O\ \ CH \\ \quad\quad\ \| \\ \quad\quad \oplus N(CH_3)_2 \end{array}\right] Cl\ominus + HCl$$

III

$$III \xrightarrow[t \sim 60\ ^\circ C]{\triangle} ArNCO + II$$

2. The investigation of the effect mechanism of tetramethyl-carbamide-chloride

These investigations affected tetramethyl urea and thiourea i.e. tetramethyl carbamide chloride prepared from these compounds in the way described above. According to the literature, tetrasubstituted carbamide chlorides also react readily with aromatic primary amines and their salts to form pentasubstituted guanidinium chlorides [5]. The reaction of tetramethyl-carbamide-chloride with aniline-hydrochloride resulted in N,N'-tetramethyl-N''-phenyl-guanidinium chloride.

$$\left[\begin{array}{l} (CH_3)_2N{-}C = \overset{\oplus}{N}(CH_3)_2 \\ \quad\quad\ | \\ \quad\quad Cl \end{array}\right] Cl\ominus + C_6H_5NH_2 \cdot HCl \rightarrow \underset{\displaystyle \overset{\displaystyle |}{NHC_6H_5}}{(CH_3)_2N{-}C} = \overset{\oplus}{N}(CH_3)_2Cl\ominus + 2HCl$$

IV V

Identification of (V) went very simply ahead for it had also been described.

Further on we investigated whether guanidinium chloride reacted with phosgene to see that in a reaction at 30 to 40 °C the characteristic vibrations — guanidinium I and II — disappeared from the IR spectrum of the reaction mixture. New bonds appeared at 2260 cm^{-1} and 1660 cm^{-1} belonging to

ν NCO and ν $C=\overset{\oplus}{N}$ groups, respectively. These two bonds had proved the formation of phenyl-isocyanate and the regeneration of the tetramethyl-carbamide-chloride.

Though the intermediate described in the equation above could'nt be detected, the interpretation of the reaction seems to be reasonable by analogy of formamidin-phosgene reaction and its final product.

It is interesting to compare it with the phosgenation of N-phenyl-N′,N′-dimethylformamidinium chloride mentioned before that leads to phenyl-isocyanate only above 100 °C. The cause of this fact is that in the amidinium cation the secondary N atom is of less nucleophylic character than in the guanidinium cation with a greater degree of dispersion of the positive charge. It is to be remarked that if aniline hidrochloride is reacted with tetramethyl urea or -thiourea and phosgen in $CHCl_3$ rather than with tetramethylcarbamide chloride prepared before then the behaviours of the two kinds of catalysts differ even if the result proves to be similar. In the case of tetramethylurea the guanidinium chloride cannot be isolated even if using equimolecular ratios of aniline hydrochloride — urea — phosgene because the reaction immediately goes on, resulting in phenyl-isocyanate. It is an explanation why tetramethyl urea reacts with phosgene much slower than N,N′-tetramethyl-N″-phenyl-guanidinium chloride, consequently tetramethyl urea is needed only to start the reaction but as soon as some guanidinium chloride is formed its phosgenation produces the carbamide chloride required for the subsequent reaction. Since to our actual knowledge the reactions of amide and carbamide chloride are characterized by substratum specificity, in case of identical substratum — carbanilide — the same result was expected. Our expectation has failed. The reaction in $CHCl_3$ at room temperature resulted in a thick liquid reluctant to crystallization. Its IR spectrum was very similar to that of carbanilide, though it contained a band belonging to ν $\overset{\oplus}{N}H$ vibration. It was supposed that if the carbamide chloride attacked not the N atom then the O atom of C=O group and the reaction resulted in C—Cl bond.

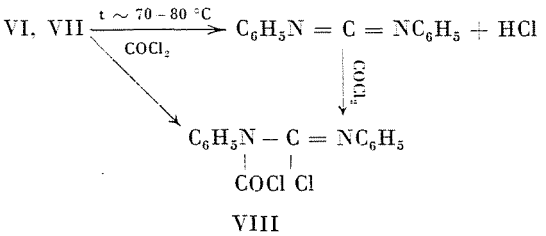
$$C_6H_5NHCONHC_6H_5 + IV \xrightarrow[-\ HCl]{} \left[C_6H_5NH{-}C(=NC_6H_5){-}O{-}C(=\overset{\oplus}{N}(CH_3)_2){-}N(CH_3)_2 \right] Cl^{\ominus}$$

$$\downarrow$$

$$\left[C_6H_5NH{-}C(Cl)=\overset{\oplus}{N}HC_6H_5 \right] Cl^{\ominus} \xleftarrow{HCl} C_6H_5NH{-}C(Cl)=NC_6H_5 + (CH_3)_2NCON(CH_3)_2$$

VII VI

After all N,N′-diphenyl-chloroformamidin-(hydrochloride) is formed and tetramethyl urea is recovered in the supposed reaction. Demonstration was done, among others, by reaction in ether medium from wich (VII) was precipitated in solid crystalline form and identified by elementary analysis and IR spectrum. There was nothing left but to clear up how phenyl isocyanate was formed from (VII). To this purpose (VII) was phosgenated at 70 to 80 °C and during the reaction vigorous evolvation of hydrogen chloride was observed. The IR spectrum of the reaction mixture already contained the characteristic ν NCO bond, in addition to strong ν C=O and ν C=N vibrations at 2260 cm^{-1}, 1750 cm^{-1} and 1670 cm^{-1}, respectively. In conformity with the spectrum, the main part of the product obtained by evaporation of the solvent was N,N′-diphenyl-chloroformamidin-N-carbonil-chloride.



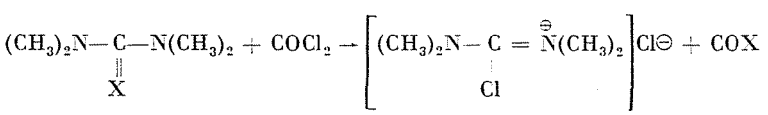
VIII

VIII → $C_6H_5NCO + C_6H_5N = CCl_2$

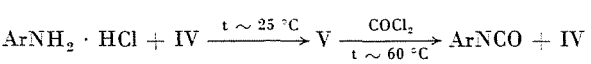
Beside (VIII), however, phenyl-isocyanate was also detected that meant (VIII) decomposed in conditions of phosgenation. The process of decomposition described above was confirmed by the isolation and identification of the resulting phenyl-isocyanate and phenyl-isocyanide-dichloride.

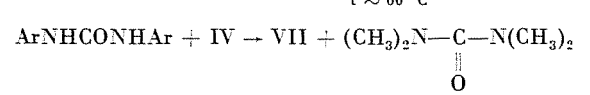
It follows from the foregoings that every reaction using tetramethyl-carbamide chloride leads to isocyanate. As to phenyl-isocyanide-dichloride, it continues to react with aniline hydrochloride to form diphenyl-carbodiimide. Carbodiimide, however, returns to the cycle closing with the formation of isocyanate.

Finally the effect mechanism of tetramethyl carbamide chloride is summarized:



X = O, S IV





$$\text{VII} + COCl_2 \xrightarrow{t \sim 70-80\ ^\circ C} \text{VIII} \rightarrow ArNCO + \underset{\text{IX}}{ArN = CCl_2}$$

$$\text{IX} + ArNH_2 \cdot HCl \xrightarrow{\triangle} \underset{\text{X}}{ArN = C = NAr} + HCl$$

$$\text{X} + COCl_2 \rightarrow \text{VIII}$$

Completing the review of the effect mechanism of chloroformamidinium-chlorides we have to point out that our aim was only to determine the essential processes. Other reactions may occur in production, but they are unimportant for the isocyanate formation.

Summary

The effect of dimethyl-formamide chloride and tetramethylcarbamide-chloride was investigated with a view to decrease the reaction temperature in producing aromatic isocyanates. This mechanism was cleared up, the processes by which a certain group of chloroform-amidinium chloride efficiently catalyzes the reaction of the formation of aromatic isocyanates were determined.

References

1. CSŰRÖS Z.—SOÓS, R.—PÁLINKÁS, J.—BITTER, I.: Acta Chimica Acad. Sci. Hung., **63**, 215 (1970).
2. CSŰRÖS, Z.—SOÓS, R.—PÁLINKÁS, J.—BITTER, I.: Acta Chimica Acad. Sci. Hung., **68**, 397 (1971).
3. CSŰRÖS, Z.—SOÓS, R.—BITTER, I.—PÁLINKÁS, J.: Acta Chimica Acad. Sci. Hung., **69**, 361 (1971).
4. CSŰRÖS, Z.—SOÓS, R.—BITTER, I.—PÁLINKÁS, J.: Acta Chimica Acad. Sci. Hung. (in press)
5. EILINGSFELD, H.—SEEFELDER, M.—WEIDINGER, H.: Angew. Chem., **72**, 836 (1960).
6. CSŰRÖS, Z.—SOÓS, R.—BITTER, I.—PETNEHÁZY, I.—SZEGHY, L.: Acta Chimica Acad. Sci. Hung., **61**, 197 (1969).

Prof. Dr. Zoltán CSŰRÖS
Dr. Rudolf SOÓS
István BITTER
Éva KÁRPÁTI-ÁDÁM

Budapest XI., Műegyetem rkt. 3. Hungary