Nuclear Magnetic Resonance Studies of Iminium Salts. Part 11.† Anionic Participation of Iminium Salts in Phosgenation Reactions

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Iminium salts act as catalysts in the reaction of phosgene and phenols or thiols to yield chloroformates, which are important synthetic intermediates. This effect is explained in terms of the nucleophilicity of the chloride anion of the salts on the basis of an n.m.r. identification of various intermediates. The mechanism of nucleophilic assistance of iminium salts towards the substrate can be understood as an increase of the nucleophilicity of phenol or thiol by proton abstraction from the OH or SH group by the chloride anion.

Iminium salts behave as strong electrophilic reagents in the Vilsmeier and related reactions[1] and are usually formed as intermediates in the reaction of an amide and a Lewis acid such as $POCl_3$, $COCl_2$, *etc.* Their electrophilic character is also demonstrated in the catalytic chlorinations of various derivatives.[2] More generally, salts formed from oxygenated Lewis bases and inorganic acid chlorides may be used to activate many chlorination reactions. In the specific case of phosgene, amides, thioamides, ureas, and thioureas have been claimed to be efficient catalysts and are assumed to react with phosgene to give iminium intermediates in the synthesis of acyl chlorides,[3] chlorothioformates,[4] and aryl chloroformates.[5] In previous work we studied the structure and mechanism of the formation of various iminium salts obtained from amides or thioamides[6] and have extended the study to other Lewis bases such as sulphoxides[7a] and phosphoramides,[7b] the salts of which have interesting industrial properties.[8] However, until now, attention has been mainly focused on the electrophilic properties of the cation, and the behaviour of the anion has received no special attention.

However, it should be considered that in strongly acid media, the nucleophilic activity of an anion is likely to intervene in fast pre-equilibrium reactions and we have already observed such behaviour in the chloride ion exchange reaction between *NN*-dimethylformamide and the Vilsmeier reagent.[9] In this paper, we present n.m.r. results which demonstrate the existence of intermediates involving nucleophilic activity of the chloride anion in iminium salts obtained from the reaction of ureas and phosgene or phosphorus oxychloride.

Experimental

All reagents were carefully dried and distilled immediately prior to every experiment to prevent any contamination by moisture. Chloroformamidinium salts from tetramethylurea or tetrabutylurea were prepared according to ref. 6*a*. Alkoxy- or thioalkoxy-formamidinium salts were prepared by adding, under dry nitrogen, one equivalent of the phenol or thiol to one equivalent of amidinium salt dissolved in the solvent; tetrachloroethane (400 K; 24 h) and dichloroethane (300—320 K; 24 h), respectively, were used for the phenols and thiols.

Aryl or thioalkyl chloroformates are readily obtained by mixing one equivalent of phenol or thiol with the catalyst and cooling 1.2 equivalents of phosgene from a dry-ice condenser. Thiols react at room temperature with 5% catalyst per mole but phenols require more drastic conditions (380 K with 5% catalyst or room temperature with up to 100% catalyst). 80—95% Chloroformates are usually obtained in these conditions.

Carbonates are prepared by reacting the chloroformate with a phenol or thiol at 360 K or room temperature, respectively, for 24 h, using one equivalent (100%) of catalyst. Carbonates are obtained quantitatively from either chloro- or alkoxy-formamidinium salts but thiocarbonates are more readily prepared with thioalkoxyamidinium salts as catalysts.

^{13}C N.m.r. spectra were recorded at 22.63 MHz using a Bruker WH 90 Fourier transform spectrometer. The acquisition parameters were: sweep width 5 000—6 000 Hz, acquisition time 0.8 s, pulse width 3×10^{-6} s (90° pulse width = 11×10^{-6} s), broadband decoupling power 5 W; the chemical shifts were referred to internal tetramethylsilane contained in a 2 mm OD coaxial cell, dissolved in $[^2H_6]$acetone used as a locking substance.

Results and Discussion

(A) *Reactions of Chloroformamidinium Chlorides with Phenols or Thiols.*—The products obtained from the reaction of ureas and $COCl_2$ (or $POCl_3$) have an iminium-like structure[10] but their rate of formation is significantly lower than with formamide or carboxamides. These chloroformamidinium

$$\underset{(1)}{R_2N\text{-}CO\text{-}NR_2} + COCl_2 \rightleftharpoons \underset{(2)}{R_2N\text{-}\overset{+}{C}Cl\text{-}NR_2,Cl^-} + CO_2$$

chlorides react easily with nucleophiles such as phenols or thiols to exchange the chlorine atom of the cation with the phenolate or thiolate fragment of the nucleophile.

$$R_2NC\overset{+}{C}ClNR_2,Cl^- + R'H \longrightarrow R_2N\text{-}\overset{+}{C}R'\text{-}NR_2,Cl^- + HCl$$

(2)	(3)	(4)
a; R = CH_3	**a**; R′ = C_6H_5O	**a**; R = CH_3, R′ = C_6H_5O
b; R = n-C_4H_9	**b**; R′ = C_2H_5S	**b**; R = CH_3, R′ = C_2H_5S
	c; R′ = n-$C_8H_{17}S$	**c**; R = CH_3, R′ = $C_8H_{17}S$
		d; R = C_4H_9, R′ = C_6H_5O
		e; R = C_4H_9, R′ = C_2H_5S

The structure of salts (**4**) has been established by n.m.r. spectroscopy and the n.m.r. parameters are given in Tables 1 and 2, which also include the parameters of the starting

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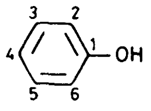
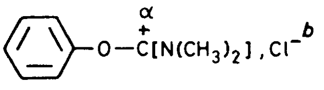
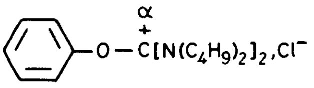
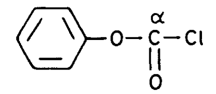
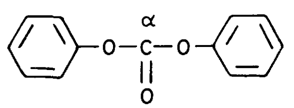
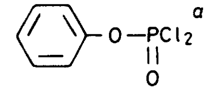
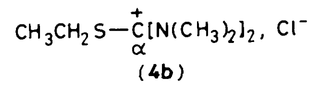
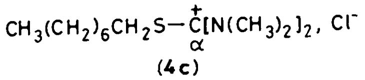
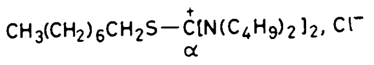
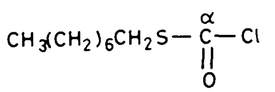
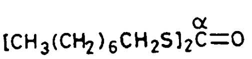
† Part 10, J. R. Gauvreau and G. J. Martin, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1541.

Table 1. ^{13}C Parameters of the aryloxy derivatives used in the phosgenation reaction

		C_α	C-1	C-2, -6	C-3, -5	C-4	NCH_2R
 (3a)	$\delta_{^{13}C}$ (p.p.m.) $^1J_{^{13}C\text{-}H}$/Hz $^3J_{^{13}C\text{-}H}$/Hz		155.6	116.1 160 6/8	130.5 160 8	120.8 163 8	
 (4a)	$\delta_{^{13}C}$ (p.p.m.) $^1J_{^{13}C\text{-}H}$/Hz $^3J_{^{13}C\text{-}H}$/Hz	161	153.3	117.8 164 4/8	131 164 8	126.9 164 7	41.1 143
 (4d)	$\delta_{^{13}C}$ (p.p.m.)	162.5	*c*	*c*	*c*	*c*	54.2
	$\delta_{^{13}C}$ (p.p.m.) $^1J_{^{13}C\text{-}H}$/Hz $^3J_{^{13}C\text{-}H}$/Hz	150.7	153.1	121.7 164 6/6	131.2 162 7	128.5 162 7	
	$\delta_{^{13}C}$ (p.p.m.) $^1J_{^{13}C\text{-}H}$/Hz $^3J_{^{13}C\text{-}H}$/Hz	153.5	152.3	122.1 164 6/6	130.8 162 7	127.7 162 7	
	$\delta_{^{13}C}$ (p.p.m.)		149.4	120.5	130.6	128.2	

[a] $^2J_{P\text{-}OC_1}$ 12 Hz. [b] $\delta_{^{15}N}$ (CH_3NO_2) 259.8 p.p.m. [c] Same values as for compound (**4a**).

Table 2. ^{13}C Parameters of the thioalkoxy derivatives used in the phosgenation reaction

	$\delta(CH_2S)$[a]	$\delta(CH_3)$	$\delta(\alpha)$	$\delta(NcH_2R)$
CH_3CH_2SH (**3b**)	19.3	19.9		
$CH_3(CH_2)_6CH_2SH$ (**3c**)	24.5	14.2		
 $CH_3CH_2S-\overset{+}{\underset{\alpha}{C}}[N(CH_3)_2]_2,\ Cl^-$ (**4b**)	29.8	15.1	175.9	44.5
 $CH_3(CH_2)_6CH_2S-\overset{+}{\underset{\alpha}{C}}[N(CH_3)_2]_2,\ Cl^-$ (**4c**)	30.0	14.2	177	45.0
 $CH_3(CH_2)_6CH_2S-\overset{+}{\underset{\alpha}{C}}[N(C_4H_9)_2]_2,\ Cl^-$ (**4e**)	30.2	14.2	178	56.0
 $CH_3(CH_2)_6CH_2S-\overset{\alpha}{\underset{\underset{O}{\|}}{C}}-Cl$	29.3	14.2	165.5	
$[CH_3(CH_2)_6CH_2S]_2$	29.5	14.1		
 $[CH_3(CH_2)_6CH_2S]_2\overset{\alpha}{C}{=}O$	29.3	14.2	190	

[a] The values corresponding to the other methylene groups of the octyl derivatives are of no special interest.

materials (**3**) and those of the main and by-products (**5**) and (**6**) of the phosgenation reaction.

$$[\mathrm{R'H} + \mathrm{COCl_2}] \longrightarrow \underset{\textbf{(5)}}{\mathrm{R'COCl}} + \underset{\textbf{(6)}}{\mathrm{(R')_2CO}}$$

The aryloxyformamidinium structure of (**4a** and **d**) is characterised by ^{13}C chemical shifts which are consistent with those obtained for uronium salts[11] and the new reagents, the thioalkyl chlorides, behave in the same way with respect to the aryloxy chlorides as the thiomethoxy- and methoxy-iminium salts, respectively.[6c]

Moreover, it should be recalled that a similar reaction is observed between the iminium chloride from phosgene[12] or the Vilsmeier reagent[13] and phenol. Either (**4a**) or (**8a**) decomposes

$$\mathrm{(CH_3)_2\text{-}N\text{-}\overset{+}{C}Cl_2,Cl^-} + \mathrm{2C_6H_5OH} \longrightarrow \underset{\textbf{(7a)}}{\mathrm{(CH_3)_2N\text{-}\overset{+}{C}(OC_6H_5)_2,Cl^-}} + \mathrm{2HCl}$$

$$\mathrm{(CH_3)_2N\text{-}\overset{+}{C}HCl,Cl^-} + \mathrm{C_6H_5OH} \longrightarrow \underset{\textbf{(8a)}}{\mathrm{(CH_3)_2N\text{-}\overset{+}{C}HOC_6H_5,Cl^-}} + \mathrm{HCl}$$

readily to give the starting urea or amide and the aryl chloride R'Cl.

(B) *Reaction of Phosgene with Nucleophiles in the Presence of Chloroformamidinium Salts*.—If we bear in mind that alcohols react easily with $\mathrm{COCl_2}$ to give ROCOCl, it is interesting to note that no reaction is observed between phosgene and the nucleophiles R'OH and RSH or between phosgene and formamidinium salts in the usual experimental conditions. However, phosgenation of phenol or thiols occurs readily in the presence of a small amount of formamidinium salt. Moreover, we have observed that the ^{35}Cl half-line widths of the chloride anion of pure iminium salts dissolved in dichloromethane significantly increase when phenol is added to the solutions. The case of tetramethylurea (**1a**) is presented as an example:

Compound	(**1a**)	(**1a**)	(**2a**)	(**2a**) + (**3a**)
	(neat)	(1M-$\mathrm{CH_2Cl_2}$)	(1M-$\mathrm{CH_2Cl_2}$)	(1M-$\mathrm{CH_2Cl_2}$)
$\Delta\nu_{1/2}(^{35}\mathrm{Cl})$/Hz	825	520	720	960

The same observation is made when HCl is added to a solution of iminium salt in $\mathrm{CH_2Cl_2}$ or $\mathrm{CH_3CN}$.

The fact that the viscosity of the solution does not change very much or even slightly decreases in such conditions[14] supports the view that a $\mathrm{Cl^- \cdots H \cdots O\text{–}R}$ interaction intervenes in the reaction path. These results elicit two comments: (i) the aryloxy- (or thioalkyl-) formamidinium salts should not be considered as intermediate reagents in the phosgenation reaction but as stable compounds; (ii) the formamidinium salts acts as a catalyst in phosgenation, and the reaction mechanism will be discussed further.

The set of reactions (a)—(c) is observed. The formation of

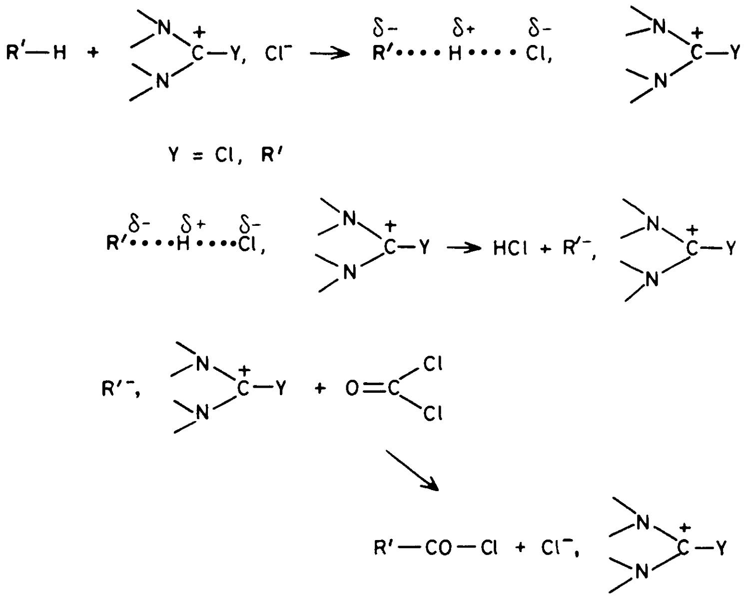
$$\underset{\textbf{(3)}}{\mathrm{COCl_2 + R'H}} + \underset{\textbf{(2)}}{\mathrm{(R_2N)_2\overset{+}{C}Cl,Cl^-}} \longrightarrow \underset{\textbf{(5)}}{\mathrm{R'COCl}} + \mathrm{HCl} + \underset{\textbf{(2)}}{\mathrm{(R_2N)_2\overset{+}{C}Cl,Cl}} \quad \text{(a)}$$

$$\underset{\textbf{(3)}}{\mathrm{R'H}} + \underset{\textbf{(2)}}{\mathrm{(R_2N)_2\overset{+}{C}Cl,Cl^-}} \longrightarrow \underset{\textbf{(4)}}{\mathrm{(R_2N)_2\overset{+}{C}R',Cl}} \quad \text{(b)}$$

$$\underset{\textbf{(3)}}{\mathrm{COCl_2 + R'H}} + \underset{\textbf{(4)}}{\mathrm{(R_2N)_2\overset{+}{C}R',Cl^-}} \longrightarrow \underset{\textbf{(5)}}{\mathrm{R'COCl}} + \mathrm{HCl} + \underset{\textbf{(4)}}{\mathrm{(R_2N)_2\overset{+}{C}R',Cl^-}} \quad \text{(c)}$$

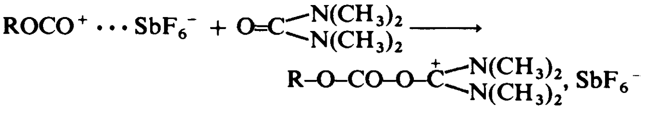
aryl carbonate (**6**) which is a by-product of the reaction is also consistent with previous observations. No carbonate (**6**) is formed when a mixture of chloroformate (**5**) and phenol is heated to 80 °C but (**6**) is readily formed in the presence of (**2**) or (**4**).

However, chloroformates can be considered as weaker Lewis acids than $\mathrm{COCl_2}$ or $\mathrm{POCl_3}$ since they do not react directly with ureas. When the chloroformate is activated with $\mathrm{AgSbF_6}$, an aryloxyformamidinium salt is formed.



Scheme.

$ROCOCl + AgSbF_6 \longrightarrow RO{-}CO^+ \cdots SbF_6^- + AgCl$



$$ROCO^+ \cdots SbF_6^- + O{=}C\begin{matrix}\diagup N(CH_3)_2\\ \diagdown N(CH_3)_2\end{matrix} \longrightarrow R{-}O{-}CO{-}O{-}\overset{+}{C}\begin{matrix}\diagup N(CH_3)_2\\ \diagdown N(CH_3)_2\end{matrix},\ SbF_6^-$$

If we consider that the nucleophilicity of alkoxide, thiolate, phenolate, and acetate decreases in that sequence, it becomes clear that nucleophilic assistance is required to activate the nucleophilicity of RSH or ArOH in the presence of phosgene. The chloride anion of formamidinium salts behaves as a catalyst in promoting the formation of $R'A^-$ (Scheme).

The role of the cationic part of the formamidinium salt can then be understood in terms of a bulk contribution to the formation of the pseudo-naked anion Cl^-; the bulkier the cation, the more nucleophilic the chloride anion.

References

1 H. G. Viehe and H. Böhme, 'Iminium salts in Organic Chemistry. Part 2,' Wiley, New York, 1979.

2 (*a*) A. De Rocker and P. De Radzitzky, *Bull. Soc. Chim. Belg.*, 1970, **79**, 531; (*b*) M. Yoshihara, T. Eda, K. Sakaki, and T. Maeshima, *Synthesis*, 1980, 746; (*c*) C. Anselmi, G. Berti, B. Macchia, F. Macchia, and L. Monti, *Tetrahedron Lett.*, 1972, 1209; (*d*) E. J. Corey and C. U. Kim, *ibid.*, 1973, 919.

3 (*a*) F. C. Hauser, U.S.P. 3 810 940 (*Chem. Abstr.*, 1974, **81**, 25405w); (*b*) M. Seefelder, Ger. P. 1 167 819 (*Chem. Abstr.*, 1964, **61**, 1761f).

4 H. Tilles, U.S.P. 3 277 143 (*Chem. Abstr.*, 1967, **66**, 2221j).

5 G. Semler and G. Schaffer, Ger. P. 2 131 555 (*Chem. Abstr.*, 1973, **78**, 84046r).

6 (*a*) G. J. Martin and S. Poignant, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1964; (*b*) M. L. Martin, G. Ricolleau, S. Poignant, and G. J. Martin, *ibid.*, 1976, 182; (*c*) C. Rabiller, G. Ricolleau, M. L. Martin, and G. J. Martin, *Nouv. J. Chim.*, 1980, **4**, 35.

7 (*a*) S. Poignant, J. R. Gauvreau, and G. J. Martin, *Can. J. Chem.*, 1980, **58**, 946; (*b*) J. R. Gauvreau, S. Poignant, and G. J. Martin, *Tetrahedron Lett.*, 1980, **21**, 1319.

8 R. Koska and J. Ribka, Ger. P. 1 220 856 (*Chem. Abstr.*, 1966, **65**, 13618c).

9 G. J. Martin and S. Poignant, *J. Chem. Soc., Perkin Trans. 2*, 1974, 642.

10 J. R. Gauvreau and G. J. Martin, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1541.

11 H. O. Kalinowski and H. Kessler, *Org. Magn. Reson.*, 1975, **7**, 128.

12 H. G. Viehe and Z. Janousek, *Angew. Chem., Int. Ed. Engl.*, 1973, **12**, 806.

13 D. R. Hepburn and H. R. Hudson, *J. Chem. Soc., Perkin Trans. 1*, 1976, 754.

14 G. Remaud, Thesis, Nantes, 1984.

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