

Nuclear Magnetic Resonance Investigations of Iminium Ion Intermediates. Part 10. † Multinuclear and Kinetic Study of the Reaction between Lewis Acids and Ureas

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The structure of the intermediate and the mechanism of the reaction between ureas (tetramethyl- or tetrabutyl-ureas) and Lewis acids (COCl_2 or POCl_3) have been studied by structural and dynamic n.m.r. The values obtained for the rate constants are discussed in terms of solvent and structural effects and the activation parameters are presented in the formalism of enthalpy-entropy compensation.

Lewis bases such as carboxamides, phosphoramides, sulphoxides, or ureas, are well known for acting as catalysts in many organic reactions. However, the catalytic efficiency of such compounds differs significantly in selectivity or recycling time.

The carboxamides and their derivatives (vinylogous carboxamides and thiocarboxamides) have been widely used; they react easily with phosgene (COCl_2) or phosphoryl chloride (POCl_3) to give chloroiminium salts,¹ which are powerful chlorinating agents.²

Hexamethylphosphoramide is also a good catalyst of some chlorination reactions and chlorophosphonium salts have been shown to be intermediates in these reactions.^{3,4} In the same way sulphoxides, and more particularly dimethyl sulphoxide, are known to facilitate the chlorination of alcohols with thionyl chloride⁵ and other acid chlorides.⁶

We have previously provided evidence for and proved the structure of the chlorosulphonium salts formed in these reactions⁷ and we have observed that ureas catalyse the formation of chlorinated derivatives from alcohol⁸ according to the same scheme.

The aim of this study is to specify the structure and the kinetic formation of the reactive intermediates between such Lewis bases and acids, which are often postulated to be halogenation catalysts, and to offer an explanation for the reactivity differences observed.

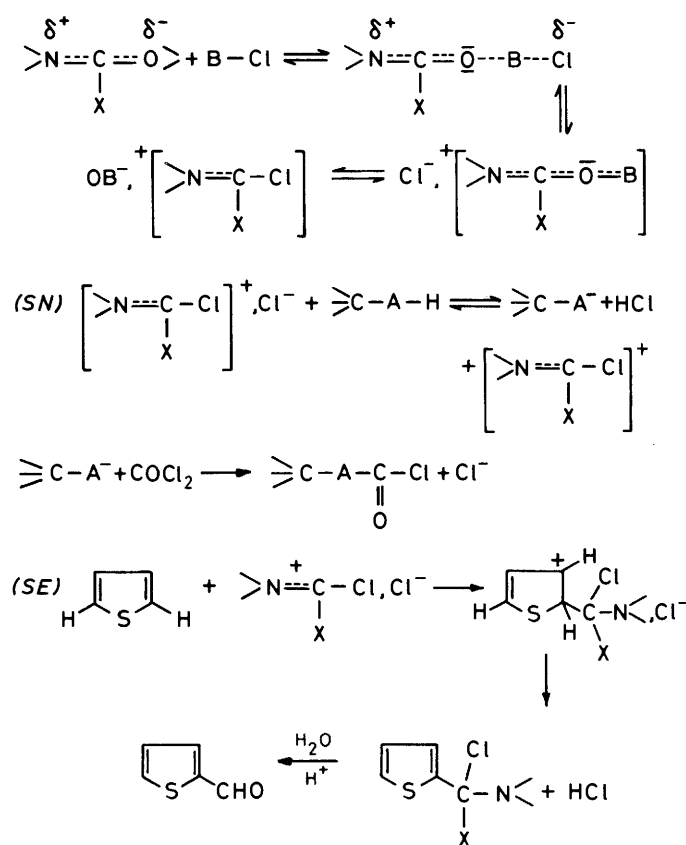
The reaction of POCl_3 and COCl_2 with tetramethylurea (TMU) and tetrabutylurea (TBU), according to the procedure previously described^{1a} lead to tetramethyl- or tetrabutyl-chloroformamidinium salts (TMCA or TBCA), which are only differentiated by the nature of the anion (Cl^- or OPOCl_2^-). In the case of the reaction between phosgene and the urea (TMU or TBU) carbon dioxide is evolved.

The n.m.r. parameters (^1H , ^{13}C , and ^{15}N) of the ureas and their salts are shown in Table 1.

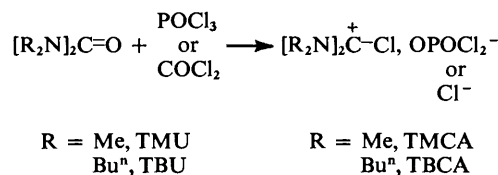
The ionic structure of the compounds (TMCA or TBCA) has been clearly established and has been inferred from the observation of their n.m.r. spectra, which show a behaviour comparable to those of iminium,¹ phosphonium,³ and sulphonium salts.⁷

The ^1H and ^{13}C chemical shifts and the $^1J_{^{13}\text{C}-\text{H}}$ values of the methyl or methylene groups on the nitrogen increase from ureas to amidinium salts. An important paramagnetic effect is also observed in ^{15}N n.m.r. Finally, the anion (Cl^- or OPOCl_2^-) does not influence the n.m.r. parameters of the cation; we had already observed this fact for the phosphonium salts.³ It can be explained by the steric hindrance of the cation, which is a long way from the anion.

A kinetic study was performed to determine the rate-



Scheme 1.



Scheme 2.

determining step of the reactional path and to compare the reactivity of COCl_2 or POCl_3 with respect to TMU in two different solvents (dichloromethane or acetonitrile). The reactivity of the ureas was studied by comparing the rates for TMU and TBU in acetonitrile.

The kinetic measurements were made using ^1H n.m.r.

† Part 9, J. Dorie, J. P. Gouesnard, and M. L. Martin, *J. Chem. Soc., Perkin Trans. 2*, 1981, 912.

Table 1. ^1H , ^{13}C , and ^{15}N n.m.r. parameters of the ureas TMU and TBU and their chloroformamidinium salts TMCA and TBCA

Products	Formula	$\delta(\text{Me}_4\text{Si})$ (p.p.m.) J/Hz						$\delta^{15}\text{N}$ (MeNO_2) (p.p.m.)
			1	2	3	4	5	
TMU	$(\text{Me}_2\text{N})_2\text{C}=\text{O}$ 2 1	$\delta^1\text{H}$		2.7				-311.5
		$\delta^{13}\text{C}$	164.8	38.0				
		$J^{13}\text{C-H}$	4	136				
TMCA	$(\text{Me}_2\text{N})_2\text{C}^+\text{-Cl, Cl}^-, \text{ or OPOCl}_2^-$ 2 1	$\delta^1\text{H}$		3.2				-269.0
		$\delta^{13}\text{C}$	158.5	44.5				
		$J^{13}\text{C-H}$		143				
TBU	$[(\text{MeCH}_2\text{CH}_2\text{CH}_2)_2\text{N}]_2\text{C}=\text{O}$ 5 4 3 2 1	$\delta^1\text{H}$		3.1	1.4	1.4	0.9	-295.8
		$\delta^{13}\text{C}$	164.4	48.3	30.6	20.5	4	
		$J^{13}\text{C-H}$		134	126	126	125	
TBCA	$[(\text{MeCH}_2\text{CH}_2\text{CH}_2)_2\text{N}]_2\text{C}^+\text{-Cl, Cl}^-, \text{ or OPOCl}_2^-$ 5 4 3 2 1	$\delta^1\text{H}$		3.6	1.2	1.2	0.75	-243.8
		$\delta^{13}\text{C}$	160.2	56.2	30.6	20.5	14	
		$J^{13}\text{C-H}$		145	128	128	126	

^a $\delta_{\text{pp}}(\text{H}_3\text{PO}_4)\text{OPOCl}_2^- = -8$ p.p.m.

¹H Spectra: 100 MHz (Varian XL 100-12), continuous wave mode. ¹³C Spectra: 22.635 MHz (Bruker WH 90 DS), Fourier transform mode. ¹⁵N Spectra: 9.117 MHz (Bruker WH 90 DS), Fourier transform mode.

Table 2. Activation parameters of the urea-phosgene or -phosphoryl chloride kinetics (the DMF-POCl₃ kinetic results are from ref. 9)

Concentration (mol l ⁻¹)		Solvent	$\Delta H^*/$ kJ mol ⁻¹	$\Delta S^*/$ J K ⁻¹ mol ⁻¹	r^2	Th/K	$\Delta G^*_{\text{Th}}/$ kJ mol ⁻¹	$10^6 k_{253}/$ l mol ⁻¹ s ⁻¹
Urea	Reagent							
DMF (2.8)	POCl ₃ (2.8)	CH ₂ Cl ₂	11.0	-251.4	0.980	233	69.6	2 208
DMF (2.8)	POCl ₃ (2.8)	MeCN						11 900
TMU (0.84)	COCl ₂ (0.84)	CH ₂ Cl ₂	55.2	-124.4	0.998	307.5	93.5	5.8
TMU (0.40)	POCl ₃ (0.40)	CH ₂ Cl ₂	34.8	-183.5	0.997	307	91.1	79.8
TMU (1.10)	COCl ₂ (1.10)	MeCN	49.7	-131.2	0.997	297.5	88.8	40.4
TMU (0.40)	POCl ₃ (0.40)	MeCN	30.6	-187.8	0.997	294	85.8	40.8
TBU (0.82)	COCl ₂ (1.00)	MeCN	63.7	-120.8	0.999	334.5	104.1	0.2
TBU (0.40)	POCl ₃ (0.30)	MeCN	28.9	-216.5	0.961	330.5	100.5	27.6

Th is the harmonic temperature of the studied reaction.

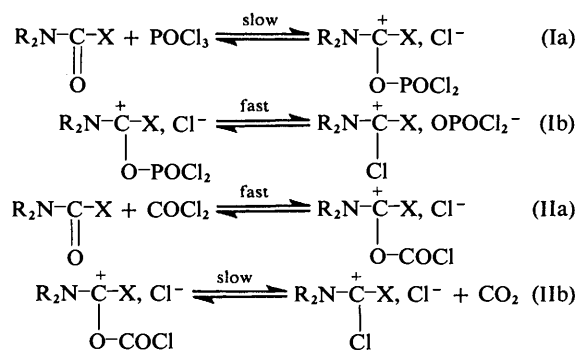
spectroscopy (a Varian XL 100-12 spectrometer in the continuous wave mode). The concentration of the reagents was determined from the measurement of the signal heights corresponding to the amidinium salts formed and the urea reacted at a given temperature. The activation parameters were then computed from the Eyring equation. The results of the various experiments carried out at different temperatures are given in Table 2.

The second-order rate constant of the overall reaction increases when passing from dichloromethane to acetonitrile and the same behaviour is observed when phosgene is replaced by phosphoryl chloride. This result demonstrates the greater reactivity of POCl₃ as compared with COCl₂.

Ureas are less reactive than amides and the following reactivity scale $\text{Me}_2\text{N-CO-H} > \text{Me}_2\text{N-CO-Me} > \text{Me}_2\text{N-CO-NMe}_2 > \text{Bu}_2\text{N-CO-NBu}_2$ may be understood in terms of an increase in steric hindrance: $\text{DMF} < \text{DMA} < \text{TMU} < \text{TBU}$ and a decrease in the nitrogen lone-pair delocalisation: $\text{DMF} > \text{DMA} > \text{TMU} > \text{TBU}$.

Interestingly we observe that the entropy values are more negative for the reactions with POCl₃ than with COCl₂.

However, it is well known that kinetic data and especially those obtained from dynamic n.m.r. measurements¹⁰ are frequently vitiated by systematic errors. Prior to any discussion of entropy changes in terms of mechanistic influence, examination of the data in the light of the enthalpy-entropy compensation scheme^{11,12} is recommended. We have observed,



Scheme 3.

in fact, that the enthalpy ΔH^* and the entropy ΔS^* values are linearly correlated [equation (1)].

$$\Delta H^* = 100.1 + 351\Delta S^* \quad (r = 0.975) \quad (1)$$

Since the isokinetic temperature (351 K) is different from the harmonic mean of the experimental temperatures (300 K) the existence of a specific change in the reaction mechanism may be suspected. Moreover, we have checked this result by examining the correlation between ΔH^* and ΔG^*_{Th} [equation

(2)], where ΔG^*_{Th} is the free activation energy computed at the harmonic temperature of the studied reaction.

$$\Delta H^* = -67.1 + 1.17\Delta G^*_{Th} \quad (r = 0.730) \quad (2)$$

If we accept a 95% confidence level, the correlation is significant for the considered degree of freedom of the system.¹³ It can be concluded that a specific change in the reaction mechanism is observed when the reagents are modified. This result may be explained by the increase in steric hindrance according to the order: TBU > TMU > DMA > DMF. Reactions (Ia) and (IIb) (Scheme 3) could be expected to be the rate-determining steps in the case of POCl₃ and COCl₂, respectively.

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