

Nuclear Magnetic Resonance Investigations of Carbonium Ion Intermediates. Part II.¹ Exchange Reactions in Chloro-iminium Salts (Vilsmeier-Haack Reagents)

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Different kinds of coalescence phenomena have been observed for solutions of chloro-iminium salts. The rate of the exchange mechanism is concentration dependent. An acid-base equilibrium between the Vilsmeier complex $(\text{Me}_2\text{NCHCl})^+\text{B}^-$ and the dimethylformamide is evident. Thermodynamic and kinetic parameters have been calculated for different solvents and different anions B^- by total line shape analysis of continuous wave and Fourier transform spectra.

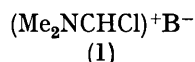
WE have previously^{1,2} studied the formation of Vilsmeier-Haack reagents and obtained thermodynamic and kinetic functions for various halogenated solvents. In the range of concentration employed for synthesis,

¹ Part I, G. J. Martin and S. Poignant, *J.C.S. Perkin II*, 1972, 1964.

the mechanism of formation of complexes (1) is thought to be a second-order acid-base association, followed by internal rearrangement. It should be noted that concentrations as high as 1M are commonly used in formyla-

² G. J. Martin, S. Poignant, M. L. Filleux, and M. T. Quemeneur, *Tetrahedron Letters*, 1970, 58, 5061.

tions. For example, the equilibrium between POCl_3 and dimethylformamide (DMF) is reached within 30 min at 253 K ($k = 1.35 \times 10^{-3} \text{ l mol}^{-1} \text{ s}^{-1}$). However, much lower rate constants ($k = 5.10^{-4} \text{ l mol}^{-1} \text{ s}^{-1}$) were inferred from results obtained from u.v. spectroscopy.³ We believe that the discrepancies are of a phenomenological rather than a methodological nature. Fourier



a; B = Cl, b; B = OPOCl_2 , c; B = OPOBr_2

transform measurements have shown that, for concentrations as low as 10^{-2} or 10^{-3}M , the reaction does not follow second-order kinetics, and an induction period characteristic of complex kinetics is clearly perceptible.

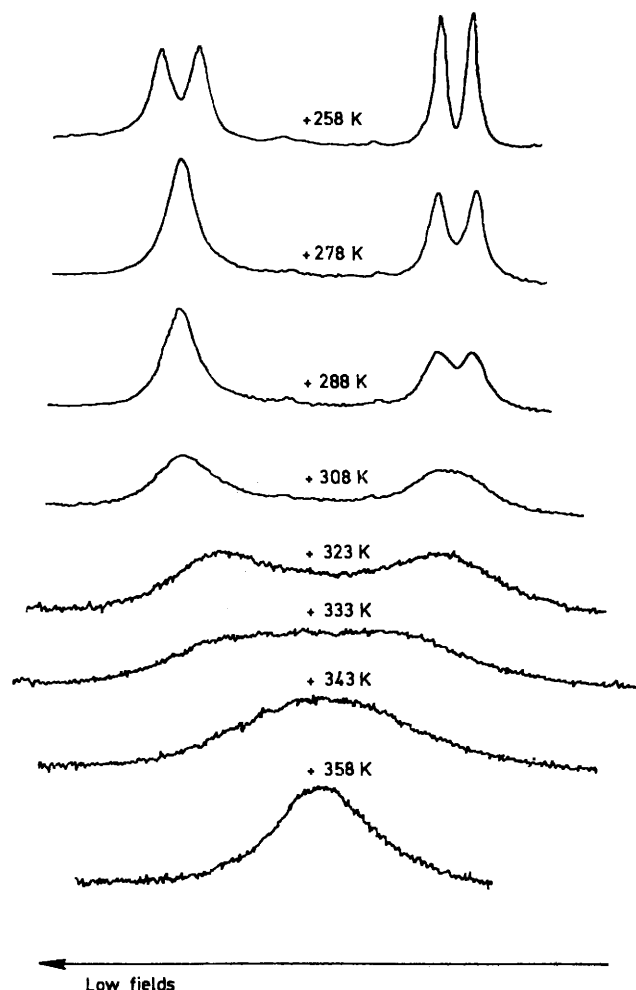


FIGURE 1 $\text{Me}_2\text{NCHCl}^+\text{Cl}^-$ -DMF exchange. Coalescence data for NMe_2 groups in $\text{CHCl}_2\text{CHCl}_2$ solution. Two different processes are shown; chlorine (low temperature range) and complex-DMF (high temperature range) exchange

The present work is primarily concerned with line shape modifications which arise in the n.m.r. spectra of a mixture of the Vilsmeier complexes (1), DMF, and solvent (Figure 1), and we show that exchange reactions

³ S. Alunni, P. Linda, G. Mariano, S. Santini, and G. Savelli, *J.C.S. Perkin II*, 1972, 2070.

are responsible for the observed phenomena. The coalescence data for (1a) are completely reversible with increase or decrease of temperature, and other complexes [e.g. (1b)] have similar behaviour. However, at high temperatures (260–280 K), (1b) dissociates to POCl_3 and DMF¹ and this process must be taken into account for the total line shape analysis.

Thus, two major processes must be considered: coalescence of the diastereotopic methyl groups of complexes (1) and coalescence of the Me_2N groups of the complex and the amide.

EXPERIMENTAL

Materials.—The reagents used were dried and distilled twice. The pure complexes were isolated by our usual method⁴ using air-tight apparatus flushed with dry argon.

Apparatus and Procedure.—High resolution n.m.r. spectra were recorded on Varian A60A (high concentration) and XL 100–12 FT fitted with a 620f, 8K memory computer (low concentration) spectrometers. Phasing, sweep time, and field homogeneity were carefully adjusted. Temperatures were controlled by a Varian V-4341 variable temperature accessory. Temperature readings were taken before and after each run. The samples were allowed at least 10 min to reach thermal equilibrium before spectra were recorded. The lifetimes τ were obtained at each temperature by total line shape analysis. The theoretical lines were fitted to the experimental points by our program ICHAN-3. Iteration was run on the greatest peak separation ($\Delta\delta\infty$) obtained at low temperatures. Values of activation energies E_a and frequency factors A were obtained by least-square fitting of k and T to the Arrhenius equation. The same procedure was used to compute enthalpies and entropies of activation from the Eyring equation.

The line shape analyses worked out from Fourier transform (FT) spectra were checked by the following procedure: a solution of DMF in $\text{CHCl}_2\text{CHCl}_2$ was simultaneously studied in the continuous wave (CW) and FT modes between 333 and 413 K, using a coaxial cell to lock the spectrometer on 100% $[\text{D}_6]\text{DMSO}$. The values of the thermodynamic parameters obtained from both CW or FT modes are consistent: CW, $E_a = 20.0 \pm 2 \text{ kcal mol}^{-1}$, $A = 2 \times 10^{12} \text{ s}^{-1}$, $\Delta G^*_{T_c} = 21.0 \pm 0.1 \text{ kcal mol}^{-1}$, $T_c = 400 \text{ K}$, $\Delta H^* = 19.2 \pm 2 \text{ kcal mol}^{-1}$, $\Delta S^* = -4.6 \pm 3 \text{ cal mol}^{-1} \text{ K}^{-1}$; FT, $E_a = 20.9 \pm 1.2 \text{ kcal mol}^{-1}$, $A = 7 \times 10^{12} \text{ s}^{-1}$, $\Delta G^*_{T_c} = 21.1 \pm 0.1 \text{ kcal mol}^{-1}$, $T_c = 400 \text{ K}$, $\Delta H^* = 20.1 \pm 1.2 \text{ kcal mol}^{-1}$, $\Delta S^* = -2.4 \pm 2 \text{ cal mol}^{-1} \text{ K}^{-1}$

RESULTS AND DISCUSSION

Coalescence of the Methyl Groups of the Complexes.—The inversion of configuration of the carbon atom of the formyl residue, which is responsible for the isochronous methyl groups, may result from rotation around the delocalized $\text{C}^{\equiv}\text{N}$ bond or from halogen (or any substituent) exchange. In a preliminary communication⁵ it was suggested that hindered rotation could explain the observed phenomena. It now seems evident, on the basis of our kinetic measurements, that an exchange reaction is the most probable explanation.

⁴ G. J. Martin and M. L. Martin, *Bull. Soc. chim. France*, 1963, 1637.

⁵ M. L. Filleux-Blanchard, M. T. Quemeneur, and G. J. Martin, *Chem. Comm.*, 1968, 836.

The activation parameters are shown in Table 1 and are related to two kinds of solvents, halogenoalkanes and acetonitrile. The lifetimes τ_A , have been computed from line shape analyses of a two-site, equally populated, system (spectra recorded at 60 or 100 MHz).

Activation energies of 19–30 kcal mol⁻¹ have been determined for rotation around the C[≡]N bond in analogous compounds such as formamidinium salts⁶ (Me₂N[≡]CH[≡]NMe₂)⁺ClO₄⁻ or more delocalized systems⁷ (Me₂N[≡]CH[≡]CH[≡]CH-NMe₂)⁺X⁻. Moreover, the barrier must be high in (R¹R²N=CH₂)⁺Cl⁻ since two distinct methylene resonances are visible⁸ at 343 K. In the iminium salt [MeO-CH=NMeC₆H₁₁]⁺BF₄⁻, where no halogen exchange is possible, the free enthalpy of activation for thermal *Z-E* equilibration is

with the concentration of complex (1) in a halogenated solvent (CH₂Cl₂, CHCl₂CHCl₂) but increases slightly in MeCN solutions. These observations are consistent with a non-concerted intermolecular exchange of Cl⁻ in acetonitrile since equations (1) and (2) are valid.

$$v = k[\text{Complex}][\text{Cl}^-] \quad (1)$$

$$1/\tau_A = k[\text{Cl}^-] \quad (2)$$

The second-order rate constants show the expected dependence on temperature and the activation parameters may be computed (Table 3; *T*_c 240 K).

In CHCl₃, CHCl₂CHCl₂, or CH₂Cl₂, the mechanism is more complex and the activation energies are not consistent with second-order kinetics in which the chlorine

TABLE 1

Signals coalescence of Vilsmeier complexes by chlorine exchange. Lifetimes τ dependent on complex concentration

Complex	Solvent	[Complex]/ M	$\Delta\delta_{\text{O}}/\text{Hz}^a$	<i>T</i> _c /K ^a	τ_{239} K/s	τ_{245} K/s	τ_{273} K/s	<i>E</i> _a /kcal mol ⁻¹ (±1)
(Me ₂ NCHCl ⁺)Cl ⁻	MeCN	0.18	18	240	0.020	0.012		11.3
		0.11	12	239	0.037	0.021		11.2
		0.08	10	240	0.053	0.032		10.1
	CH ₂ Cl ₂	2.19	17.5	245	0.21	0.06		19
		1.51	18.5	243	0.11	0.029		19.2
		1.06	19.5	240	0.045	0.012		18.5
		0.50	21	235	0.014	0.0045		17.8
		0.22	23	233	0.0071	0.0025		17.4
		0.08	35 ^b	233 ^b	0.0021	0.0011		15.5
		2.23	12.5	273			0.0269	21
1.55	13	268			0.0186	21		
1.06	13.5	265			0.0125	20.3		

^a 60 MHz Spectra. ^b 100 MHz Spectra.

as high as 30 kcal mol⁻¹.⁹ From another point of view, i.r. spectra suggest a large contribution from a C=N double bond in our compounds from consideration of its absorption frequency: [(Me₂NCH₂)⁺Cl⁻] ν (C=N) 1675,¹⁰ [(Me₂N[≡]CHCl)⁺Cl⁻] 1660, {[(CH₂)₂N=CCL₂]⁺Cl⁻} 1625 cm⁻¹.¹¹ From this it may appear that halogen exchange is most probably responsible for the observed coalescence. Such an exchange may be compared with known processes in which diastereotopic protons, bound to atom A in compounds with an A-Cl bond, become isochronous (Table 2). A major observation is the concentration

TABLE 2

Inversion of configuration of some hetero-atoms

	$\Delta G^*/\text{kcal mol}^{-1}$ (<i>T</i> /K)	<i>d</i> _{A-Cl} /Å	<i>D</i> _{A-Cl} / kcal mol ⁻¹	Ref.
CINBu ⁺ CH ₂ CD ₃	6–9 (130–181)	1.76	46	12
CIS(O)N(CH ₂ R) ₂	12–14 (239–289)	1.98	65	11
CIPPhNMeCH ₂ R	20 (276–373)	2.04	76	13, 14
CISnPhMeCH ₂ R	Fast process	2.30	75	15, 16

dependence of the lifetime τ_A which is evidence against first-order kinetics (Table 1). However τ_A decreases

⁶ R. C. Neuman and L. B. Young, *J. Phys. Chem.*, 1965, **69**, 2570.

⁷ J. Ranft and S. Dähne, *Helv. Chim. Acta*, 1964, **47**, 1160.

⁸ H. Voltz and H. H. Kiltz, *Annalen*, 1971, **86**, 752.

⁹ A. Mannschreck and M. Burgemeister, personal communication.

¹⁰ H. Viehe and Z. Janouzek, *Angew. Chem. Internat. Edn.*, 1971, **10**, 573.

¹¹ W. R. Jackson, T. G. Kee, and W. B. Jennings, *J.C.S. Chem. Comm.*, 1972, 1154.

concentrations are the same as those of the complexes. Thus, the chlorine atoms of the solvent are likely to play

TABLE 3

Kinetics of Cl⁻ exchange in MeCN

<i>T</i> /K	232	235	239	245	254
10 ⁻² mol ⁻¹ s ⁻¹	1.2	1.7	2.5	4.2	9.8
<i>E</i> _a = 11 kcal mol ⁻¹ , <i>A</i> = 3 × 10 ¹² l mol ⁻¹ s ⁻¹					
$\Delta G_{Tc} = 11.3$ kcal mol ⁻¹ , $\Delta H^* = 10.5$ kcal mol ⁻¹ , $\Delta S^* = -3.2$ cal mol ⁻¹ K ⁻¹					

a part in the reaction, and as the intermediate in Vilsmeier formylation has ionic character and is, in fact, a good Lewis acid, the abstraction of a chlorine atom from the solvent is probable.

This mechanism may therefore be invoked to produce chlorine ions and [Cl⁻] derived from the solvent may increase as the concentration of complex (1) decreases. Consequently the lifetime τ_A decreases if the concentration of (1) decreases.

In the present state of our knowledge of the ionic structure of the complex, it seems to us that the striking difference of behaviour between MeCN and CH₂Cl₂ solutions is primarily related to the non-halogen or

¹² C. H. Bushweller, W. G. Anderson, J. W. O'Neil, and H. S. Bilofsky, *Tetrahedron Letters*, 1973, 717.

¹³ D. Imbery and H. Friebolin, *Z. Naturforsch.*, 1968, **23b**, 759.

¹⁴ B. Fontal and H. Goldwhite, *Tetrahedron*, 1966, **22**, 3275.

¹⁵ D. V. Stynes and A. L. Allred, *J. Amer. Chem. Soc.*, 1971, **93**, 2666.

¹⁶ G. J. D. Peddle and G. Redl, *J. Amer. Chem. Soc.*, 1970, **92**, 365.

halogen content of the solvent molecules although the difference in dielectric constants must not be disregarded.

Me ₂ NCHO	(Me ₂ N ⁺ =CHCl) ⁺ B ⁻	} This work
138 189	146 236	
Me ₂ CH X	Me ₂ CH ⁺ X ⁻	} 17, 18
127 151	130 168	

SCHEME 1 $J(^{13}\text{C}-\text{H})$ Values (Hz)

Another feature supports the existence of the mechanism. The drastic increase of $J(^{13}\text{C}-\text{H})$ in the Vilsmeier salts is good proof of the positively charged nature of the organic part of the complexes. The strong *s* character of the $^{13}\text{C}-\text{H}$ orbital is connected with a planar structure for the carbonium ion and the exchange reaction is made easier. As far as the structure of the ion pair is concerned, the relatively high concentrations of complexes and the weakly dissociative halogenated solvents which were used suggest that Vilsmeier salts may contain quadrupolar aggregates.

The existence of an exchange reaction is definitely established by the following results. The n.m.r. spectrum of a mixture of (1b and c) exhibits only one set of resonance lines whereas those of the individual complexes are obviously different.

Above 273 K, the chemical shift of the formyl proton is a weighted average between both non-equivalent sites [equation (3) where δ_{Cl} and δ_{Br} are the chemical shifts

$$\delta_{\text{obs}} = x_{\text{Cl}}\delta_{\text{Cl}} + x_{\text{Br}}\delta_{\text{Br}} \quad (3)$$

of the formyl proton in (1b and c) respectively and x_{Cl} and x_{Br} the molar fractions of (1b and c)].

When the temperature is lowered, the formyl proton signal widens, and the coalescence occurs at 258 K for x_{Cl} 0.3 (Figure 2). The activation energies may be computed from a line shape analysis of a two-site, unequally populated system. At 258 K $E_a = 21$ kcal

exchange between (I) and DMF (Figure 1). Direct proof was obtained by mixing pure deuteriated DMF with pure complex (1). The resulting mixture clearly showed signals for protonated DMF ² (Table 4).

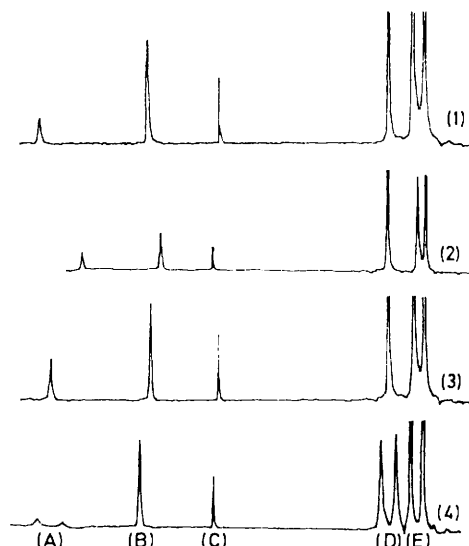


FIGURE 2 FT Spectra of (1) POBr₃-DMF at 304 K, (2) POCl₃-DMF at 304 K, (3) POCl₃-POBr₃-DMF at 304 K, and (4) the same mixture at 233 K: (A) formyl proton of complex, (B) formyl proton of DMF, (C) residual proton in 99.8% CDCl₃, (D) Me₂N of complex, and (E) Me₂N of DMF

The complex-DMF exchange has been studied at high temperature: it may be assumed that the chlorine exchange does not perturb the line shapes in this temperature range. Assuming that the mechanism is bimolecular, the lifetime of an NMe₂ group is concentration dependent. The results (Figure 3) clearly indicate an increase in the lifetime τ_{NMe_2} of complex (1) or DMF with

TABLE 4

Activations parameters of DMF-complex exchange

Complex	Solvent	$\Delta\delta_{\infty}/$ Hz ^c	T_c/K^c	$k_{258\text{K}}/$ l mol ⁻¹ s ⁻¹	$E_a/$ kcal mol ⁻¹ (± 0.5)	$A/$ l mole ⁻¹ s ⁻¹	$\Delta H^*/$ kcal mol ⁻¹ (± 0.5)	$-\Delta S^*/$ cal mol ⁻¹ K ⁻¹ (± 3)	$\Delta G^*_{T_c}/$ kcal mol ⁻¹ (± 0.2)
(Me ₂ NCHCl ⁺)Cl ⁻	CHCl ₂ CHCl ₂ ^a	64	333	2.5	7.8	107	7.2	27	16.2
	CHCl ₂ CHCl ₂ ^b	64	333	2.8	7.5	6×10^6	7.0	27	16.0
	CHCl ₃ ^b	63	317	1.7	8.9	8×10^7	8.3	23	15.6
DMF-POCl ₃	CHCl ₂ CHCl ₂	61	316	3.1	7.0	2×10^6	6.3	28	15.2
	CHCl ₃	60	302	2.1	9.1	3×10^8	8.5	22	15.1
DMF-SOCl ₂	CHCl ₂ CHCl ₂	60	320	2.7	7.6	8×10^6	7.1	26	15.4
	CHCl ₃	58	305	2.7	8.5	4×10^7	7.9	24	15.2

^a Complex crystallized from COCl₂. ^b Complex crystallized from SOCl₂. ^c 60 MHz Spectra.

mol⁻¹ for 10⁻¹M solutions in CDCl₃. Under slow exchange conditions, the diastereotopic methyl groups of (1b and c) are fortuitously equivalent and line shape analysis need be performed only on the formyl signals: (1b) $T_c = 268$ K, $E_a = 23$ kcal mol⁻¹; (1c) $T_c = 249$ K, $E_a = 17$ kcal mol⁻¹.

Coalescence of the NMe₂ Groups of Complex (1) and of DMF.—The line shape changes, which are reversible in the range 258–358 K, are explained by intermolecular

¹⁷ G. A. Olah, E. B. Baker, J. C. Evans, W. S. Tolgyeri, J. S. McIntyre, and I. J. Bartier, *J. Amer. Chem. Soc.*, 1964, **86**, 1360.

a decrease in the concentration of the other species [equations (4) and (5)]. The energies and enthalpies of

$$\frac{1}{\tau_{\text{Me}_2\text{NCHCl}^+\text{B}^-}} = k[\text{DMF}] \quad (4)$$

$$\frac{1}{\tau_{\text{DMF}}} = k[(\text{Me}_2\text{N}=\text{CHCl})^+\text{B}^-] \quad (5)$$

activation are relatively low; the lifetimes are greater

¹⁸ G. A. Olah and M. B. Comisarov, *J. Amer. Chem. Soc.*, 1966, **88**, 1818.

than in the chlorine exchange reaction. Another striking difference is the large negative ΔS^* value which is observed for this step. With the given assumptions

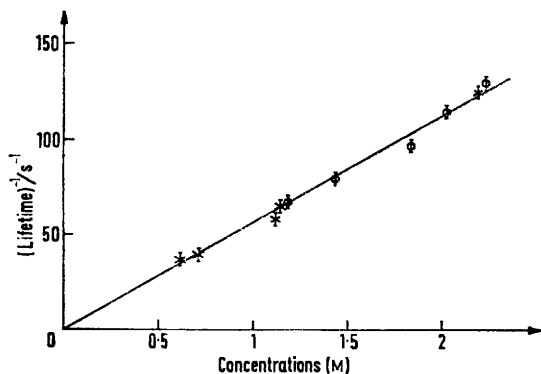
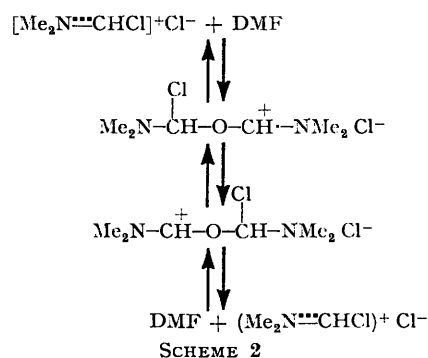


FIGURE 3 Influence of concentration on lifetime: complex, $(\text{Me}_2\text{NCHCl}^+)\text{Cl}^-$; T 318 K; k 55 $\text{l mol}^{-1} \text{s}^{-1}$; x, complex; o, DMF.

the transition state involves a strong steric interaction, reducing the degrees of freedom of both reagents. Solvent effects on the activation parameters are weak

but significant. The more proton-donating the solvent, the more the rate of the exchange decreases; this behaviour probably results from association between DMF and the solvent.



The reaction may be represented as an acid-base association, of the same type as the reaction of a Lewis acid with DMF.

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