Aspects of tautomerism 12—Some causes and consequences of participation in the solvolysis of acid chlorides†

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Abstract. Solvolysis of nine representative half ester acid chlorides in aqueous acetone have been studied. Isomers solvolyse at distinctly different rates and furnish the original acids. Contrary to the well accepted views, no evidence for tautomerism or isomerism between the isomeric pairs of acid chlorides could be detected. In a number of cases alkoxy group participates in the solvolysis of neighbouring acid chlorides. This results in (a) rate enhancement and (b) partial or total shift of the reaction pattern from $S_N 2$ to $S_N 1$. Isomeric half ester acid chlorides, in the presence of a sufficiently strong Lewis acid, could give the same oxonium salt. Rearrangements observed in the reactions of unsymmetrical 1,2- and 1,3-dicarboxylic acid derivatives could be ascribed to the prior formation of common oxonium salt intermediates in the presence of Lewis acids.

Keywords. Tautomerism; solvolysis; acid chlorides.

1. Introduction

One of the frustrating aspects of the chemistry of unsymmetrical 1,2- and 1,3-dicarboxylic acid derivatives is the lack of positional specificity in their reactions. Recent reports on the synthetic applications of 3-methoxy-phthalic acid derivatives in the synthesis of cytotoxic antibiotic adriamycin and its derivatives have highlighted this problem (Wong *et al* 1973; Raynolds *et al* 1977). It is difficult to predict the outcome of the reactions involving 3-substituted phthalic and similar acid derivatives.

As part of our studies on the influence of neighbouring group effects on the structure and mechanisms, we have examined some of the causes of rearrangements in the reactions of acid chlorides. In an earlier paper (Bhatt *et al* 1979) we had attempted to define the factors responsible for the exclusive formation of the pseudo acid chloride at the expense of the normal isomer. This phenomenon represents participation of an extreme kind. Many features of this type of behaviour are now fairly well understood. However, there exists a substantial body of participation behaviour which creates some amount of confusion. This paper attempts to examine this area.

2. Results and discussion

In a long and definitive paper, Chase and Hey (1952) examined the causes of rearrangements in unsymmetrical 1,2- and 1,3-half ester acid chlorides in great detail.

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† Bhatt and El Ashry (1980); Rao *et al* (1979); Rao and Bhatt (1981).
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They concluded that these half ester acid chlorides themselves exist in equilibrium (tautomerism), just as symmetrical and unsymmetrical phthaloyl chlorides (Csanyi 1919) (1–4, Chart-1). Subsequent view has more or less congealed and these ideas have come to be accepted as settled facts. They have been widely reproduced in reviews (Jones 1963), advanced treatises (Rodd 1956) and text books (Feiser and Feiser 1961).

It is well established that the basic patterns of solvolysis of normal and pseudo acid chlorides are different. The former ordinarily solvolyses by a S_N2 path whereas the latter does so by a S_N1 route. We have recently shown that equilibrium between normal and pseudo forms of phthaloyl chlorides ($5 \rightleftharpoons 6$) does not exist under a wide variety of conditions (Bhatt *et al* 1980). We now describe a study of the solvolysis of a few representative half ester chlorides, in aqueous acetone, with a view to finding out whether participation takes place and whether or not they exist in equilibrium.

The solvolysis of isomeric half ester acid chlorides of 3-substituted phthalic acids follow a definite trend. Whereas the acid chlorides (7a, b) solvolyse by a S_N2 path, their isomers (8a, b) do so by a S_N1 mechanism. Also, the rates of solvolysis of isomers are widely different (table 1, figures 1 and 2). It is apparent that electron-withdrawing groups resist development of an electron-deficient centre in the ortho position. No such limitation operates in the case of (8), where such a centre would be in the meta position where it is less subjected to destabilising influence of the electron-withdrawing group.

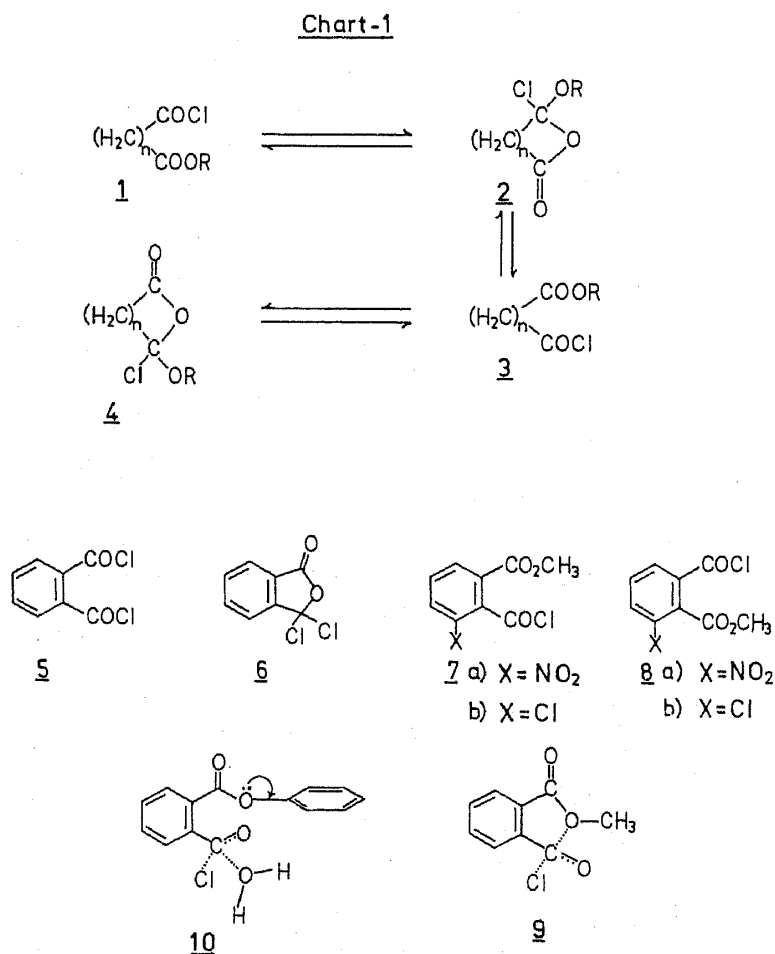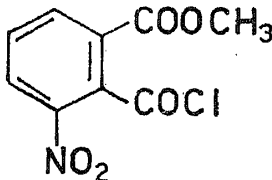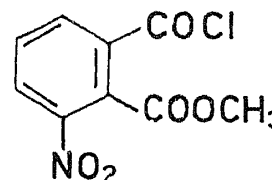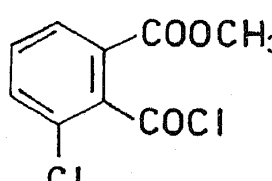Comparison of solvolysis rates and patterns of phenyl and methyl half ester chlorides
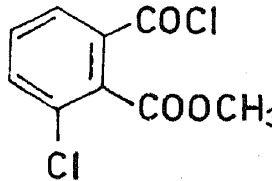
Chart-1
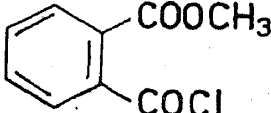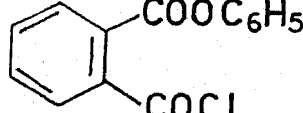
Table 1. Solvolysis data of half ester acid chlorides.

	Compound	Percentage of water*	Percentage of acetone*	k	m value
7a	COOCH₃ / COCl / NO₂ (benzene ring)	5	95	$2 \cdot 28 \times 10^{-4}$	
		10	90	$7 \cdot 03 \times 10^{-4}$	
		15	85	$1 \cdot 59 \times 10^{-3}$	0·55
		20	80	$3 \cdot 11 \times 10^{-3}$	
8a	COCl / COOCH₃ / NO₂ (benzene ring)	2·5	97·5	$5 \cdot 24 \times 10^{-4}$	
		5·0	95·0	$1 \cdot 77 \times 10^{-3}$	
		7·5	92·5	$5 \cdot 78 \times 10^{-3}$	1·02
		10·0	90·0	$1 \cdot 32 \times 10^{-2}$	
7b	COOCH₃ / COCl / Cl (benzene ring)	5	95	$4 \cdot 12 \times 10^{-3}$	
		8	92	$7 \cdot 51 \times 10^{-3}$	
		10	90	$1 \cdot 08 \times 10^{-2}$	0·44
		12	88	$1 \cdot 35 \times 10^{-2}$	
8b	COCl / COOCH₃ / Cl (benzene ring)	4·0	96·0	$1 \cdot 78 \times 10^{-3}$	
		5·2	94·8	$3 \cdot 07 \times 10^{-3}$	
		7·4	92·6	$6 \cdot 79 \times 10^{-3}$	0·89
		8·0	92·0	$8 \cdot 45 \times 10^{-3}$	
9	COOCH₃ / COCl (benzene ring)	2	98	$7 \cdot 19 \times 10^{-4}$	
		4	96	$2 \cdot 91 \times 10^{-3}$	
		6	94	$7 \cdot 58 \times 10^{-3}$	1·27
		7	93	$1 \cdot 36 \times 10^{-2}$	
10	COOC₆H₅ / COCl (benzene ring)	5	95	$4 \cdot 27 \times 10^{-4}$	
		10	90	$1 \cdot 34 \times 10^{-3}$	
		15	85	$4 \cdot 17 \times 10^{-3}$	0·64
		20	80	$1 \cdot 06 \times 10^{-2}$	

* Percentage compositions are volume by volume.
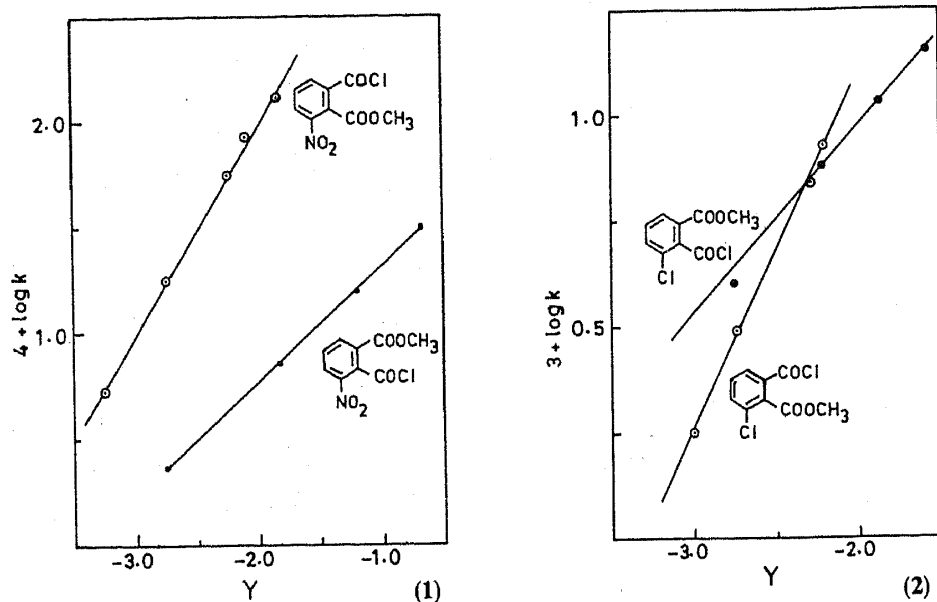
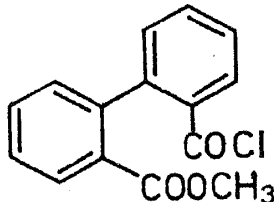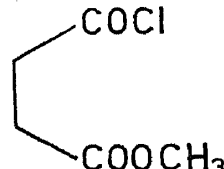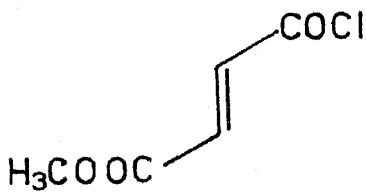**Figures 1 and 2.** Plots of Y vs log k for the isomeric acid chlorides.

of phthalic acid (9) and (10), is particularly instructive. The methyl ester chloride 9 solvolyses about ten times as fast as the phenyl ester chloride 10. Moreover, the reaction pattern shifts from S_N1 in the case of 9 to S_N2 for 10. In the latter the lone pair on the oxygen of the ester function is effectively delocalised with the aromatic ring and becomes unavailable for coordination with the electron deficient species, whereas in the case of the former the lone pair becomes available for participation (table 1, chart 1).

The susceptibility of the reaction rate to solvent polarity change as measured by the m value (Grunwald and Winstein 1948) was used to monitor the changes in the reaction patterns. A m value of 0·6 and less was considered as indicative of S_N2 reaction whereas a m value of greater than 0·6 was taken as evidence for a S_N1 pathway. These criteria have been thoroughly cross-checked with a number of independent evidences like common ion effect, salt effect, solvent isotope effect etc., in similar studies carried out in this laboratory (El Ashry 1977; Bhatt *et al* 1979). We have come to rely on m value as a dependable indicator of the reaction pattern.

The monoester chloride of diphenic acid (11) solvolyses with a m value of 0·42 showing little change from S_N2 pattern and no evidence for participation (table 2). Normal phthaloyl chloride (Bhatt *et al* 1980) and *o*-acetyl salicyloyl chloride (12) (El Ashry 1977) behaved similarly. Also, the monoester chlorides of succinic acid and fumaric acid solvolysed by a S_N2 mechanism as would be expected (table 2). Three analogues of 12 viz *o*-acetamidobenzoyl chloride (15), S-acetylsalicyloyl chloride (16) and *o*-acetonylbenzoyl chloride (17) have been examined. None of these showed any evidence of participation (Bhatt and Somayaji 1984; Somayaji 1980).

These results clearly rule out the existence of a dynamic equilibrium between the isomeric half ester acid chlorides. The large number of rearrangements observed with unsymmetrical 1,2- and 1,3-dicarboxylic acid derivatives in Friedel-Craft and other acid catalysed reactions should then be attributed to rearrangements taking place *only* after addition of the Lewis acids. We have studied the ^{1}H and ^{13}C NMR spectra of the

Table 2. Solvolysis data of half ester acid chlorides

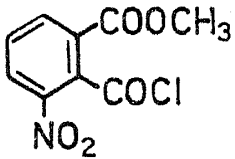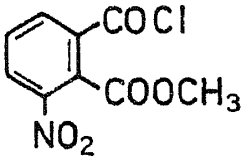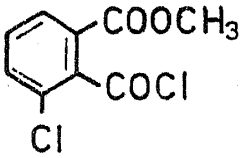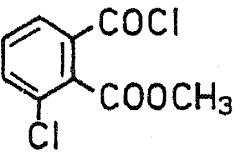| Compound	Percentage of water*	Percentage of acetone*	k	m value
11	3	97	$8\cdot62 \times 10^{-5}$	
	10	90	$2\cdot99 \times 10^{-4}$	
	15	85	$5\cdot49 \times 10^{-4}$	0·42
	20	80	$9\cdot55 \times 10^{-4}$	
13	4	96	$6\cdot31 \times 10^{-3}$	
	6	94	$1\cdot03 \times 10^{-2}$	
	8	92	$1\cdot60 \times 10^{-2}$	0·46
	10	90	$2\cdot16 \times 10^{-2}$	
14	4	96	$4\cdot69 \times 10^{-3}$	
	6	94	$6\cdot71 \times 10^{-3}$	
	7	93	$7\cdot95 \times 10^{-3}$	0·41
	10	90	$1\cdot34 \times 10^{-2}$	

* Percentage compositions are volume by volume.

intermediates formed from the reactions of two pairs of half ester chlorides 7 and 8 with four Lewis acids. The ^{1}H NMR spectra of the parent acid chlorides showed distinct signals for the methyl groups. When treated with the Lewis acids the signals shifted substantially to a common value (table 3).

The ^{13}C NMR spectra of the complexes obtained from these half ester acid chlorides and Lewis acids showed only three sets of signals for aromatic carbons at 140·68, 130·51 and 128·90δ, a single signal for the methyl carbon at 53·72δ and a single signal for both the carbonyl carbons at 167·96δ. Spectra recorded at low temperatures (0° and -40°C) did not show any noticeable deviation from the above mentioned signals thereby ruling out the formation of intermediates (18) and (19) from the isomeric half ester acid chlorides (A, chart 2).

The most reasonable structure for these complexes is the symmetrical oxonium salt formulation (20). That the signal in the ^{1}H NMR spectra of the complexes did not arise from the reaction of methyl chloride and aluminium chloride was also established. The

Table 3. ^{1}H NMR data of the Lewis acid complexes of the half ester acid chlorides[a]

Compound	Uncomplexed signal	Signal of the complex with			
		AlCl$_3$	TiCl$_4$	SnCl$_4$	ZnCl$_2$
7a (benzene ring with COOCH$_3$, COCl, NO$_2$)	4·09	4·60	4·40	4·13	4·09
8a (benzene ring with COCl, COOCH$_3$, NO$_2$)	4·01	4·60	4·40	4·13	4·01
7b (benzene ring with COOCH$_3$, COCl, Cl)	4·00	4·60	4·40	4·10	4·00
8b (benzene ring with COCl, COOCH$_3$, Cl)	3·90	4·60	4·40	4·10	3·90

[a] Chemical shifts are in δ (ppm).

latter shows a signal at 2·95δ unaffected by the presence of phthalic anhydride. It is therefore clear that we are not dealing with an equilibrium of the type B (chart 2). Whether one starts from **7** or **8**, the product is the same. Any regio-specificity, that would be observed in the reactions of **20** with nucleophiles would be fortuitious.

It is seen from table 3 that $\Delta\delta$, the difference in the chemical shifts for the methyl protons of the complexed and the uncomplexed acid chlorides depends upon the Lewis acid used. This dependence probably reflects its strength. The largest shift in the signals is observed with the strongest of the Lewis acids used *viz* aluminium chloride. Zinc chloride almost does not have any effect on the methyl signal. This is most certainly due to the fact that it is not strong enough to bring about the formation of the oxonium salt.

3. Experimental

The melting points reported are uncorrected. ^{1}H NMR spectra were recorded on a Varian HA 100D spectrometer. ^{13}C NMR spectra were recorded on a Brucker WH 270 (FT) spectrometer.

3.1 *Preparation of the acids*

1-Methyl-2-hydrogen-3-nitrophthalate and 2-methyl-1-hydrogen-3-nitrophthalate were prepared as described in the literature (Chase and Hey 1952).

Chart-2
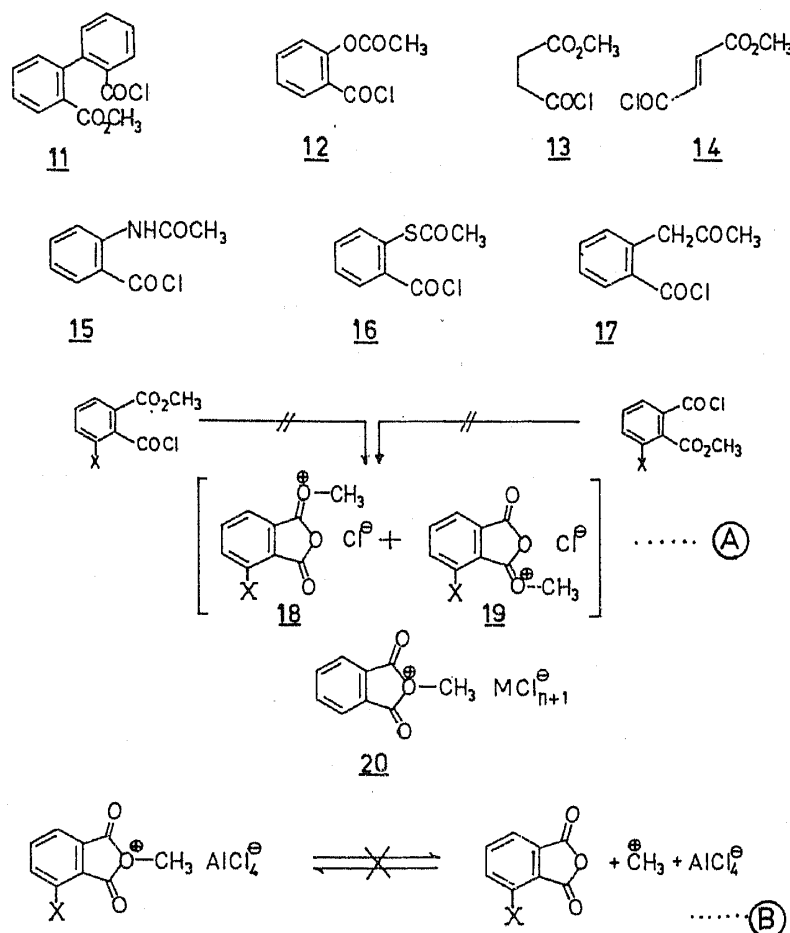
1-Methyl-2-hydrogen-3-chlorophthalate, mp 170°C, and 2-methyl-1-hydrogen-3-chlorophthalate, mp 140°C were prepared as described in an earlier paper (Rao and Bhatt 1980).

Diphenic acid monomethyl ester was prepared according to literature procedure (Graebe 1888), mp 110°C.

Phenyl hydrogen phthalate, mp 102°C, was prepared by fusing phthalic anhydride with phenol (Bischoff and Hedenstrom 1902).

Methyl hydrogen phthalate, methyl hydrogen succinate and methyl hydrogen maleate were prepared by opening the respective anhydrides with methanol.

3.2 *Preparation of acid chlorides*

The acid chlorides of the half ester acids were prepared by the action of thionyl chloride on the acids. The excess of reagent was removed under vacuum, the last traces being driven off azeotropically with dry benzene. Methyl hydrogen maleate gave monomethyl fumaroyl chloride.

3.3 *Preparation of Lewis acid complexes*

Aluminium chloride complexes were prepared according to the procedure described in the literature (Perrier 1893).

Titanium chloride complexes were prepared by treating the acid chloride solutions in benzene with an equimolecular amount of titanium chloride. A white precipitate was formed immediately. Benzene was removed under reduced pressure.

Stannic chloride complexes were prepared by refluxing the half ester chlorides in dry chloroform with an equimolecular quantity of stannic chloride for 30 min and removing the solvent under vacuum.

Zinc chloride complexes were prepared by refluxing an equimolecular mixture of the acid chloride and zinc chloride in benzene for 1 hr and removing the excess of solvent under vacuum.

The spectra of the complexes were recorded in a mixture of deutero chloroform ($CDCl_3$) and hexadeutero dimethyl sulfoxide ($DMSO$-d_6).

3.4 *Kinetic procedure*

The rates of solvolysis of acid chlorides were followed conductometrically. The kinetic procedure employed is essentially the same as reported in an earlier paper (Bhatt *et al* 1979). The rates reported in the present work are at 30°C. The concentration of the acid chlorides used in the kinetic run was 0·02 M unless otherwise mentioned.

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