Nucleophilic substitution at a trigonal carbon. Part 6.[1] Substituent and bromide/chloride leaving group effects in the reactions of aromatic acyl chlorides with methanol in acetonitrile

Dennis N. Kevill * and William F. K. Wang

Department of Chemistry and Biochemistry, Northern Illinois University, DeKalb, Illinois, 60115-2862, USA

Received (in Cambridge) 17th August 1998, Accepted 19th October 1998

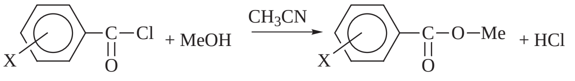
For the methanolyses in acetonitrile at 25.0 °C of benzoyl chloride and eleven *para*- or *meta*-substituted derivatives, the kinetics of methyl ester formation have contributions both first-order and second-order in methanol. The Hammett plots for the overall second- and third-order processes are curved and both plots can be analyzed in terms of the simultaneous operation of two reaction channels. An addition–elimination process is favored by electron-withdrawing substituents and a loose S_N2 process by electron-supplying substituents. Comparisons of widely varying halogen leaving-group effects suggest that the addition–elimination processes for solvolyses of haloformate esters and acyl halides have an identical addition step but they then differ in the sequence of the two elimination steps.

The methanolysis of *p*-nitrobenzoyl chloride in acetonitrile has been shown[2] to proceed with the simultaneous operation of second- and third-order terms to the overall kinetics: first- and second-order in methanol. The absence of any appreciable acceleration upon adding fairly large amounts of the more electrophilic phenol argued against a push–pull type mechanism[3,4] in the overall third-order contribution, and a general-base catalysis role for one of the two methanol molecules was proposed. This role was given support by the observation of a very powerful catalysis upon addition of chloride ion,[2] a powerful base and nucleophile in acetonitrile.[5] Mechanisms were proposed involving tetrahedral intermediates which normally reverted to reactants unless deprotonation occurred, which then led, upon regeneration of the carbonyl group, to loss of chloride being easier than loss of methoxide.

An extension to the corresponding methanolyses in acetonitrile of acetyl chloride[6] and derivatives with the hydrogens replaced by chlorine atoms or methyl groups[7] led to the proposal that the methanolysis of the parent acetyl chloride proceeded through a loose S_N2-type transition state, which tightened, or changed to an addition–elimination (tetrahedral intermediate) pathway on the introduction of electron-withdrawing chlorine atoms. A major argument against the tetrahedral intermediate pathway, with nucleophilic attack being rate-determining, was the consideration of kinetic leaving-group effect values for other nucleophilic substitution reactions of acetyl halides[8–11] or butyryl halides.[12] These studies uniformly indicated large differences in the rate as the identity of the halogen was varied, with relative rates consistently being in the sequence observed for S_N1 and S_N2 reactions at a saturated carbon,[13] rather than the sequence to be expected if the addition step of an addition–elimination mechanism is rate-determining.[14,15]

A study[1] of a series of aroyl bromides, with varying ring substituents, in terms of their kinetics of methanolysis in acetonitrile as solvent, also indicated parallel second- and third-order contributions to the overall kinetics. A Hammett $\rho\sigma$-type treatment was carried out for both of the contributions and each gave a curved plot with a minimum not very far removed from the data point for the unsubstituted benzoyl bromide.

In the present study, the kinetics of the methanolyses in acetonitrile of a series of aroyl chlorides are investigated [eqn. (1)]. In conjunction with the earlier study of *p*-nitrobenzoyl chloride,[2] the rate coefficients are then used to show that the chlorides show the same type of curved Hammett plots as were obtained with the bromides. It is then determined as to whether the second- and third-order kinetic terms can again be analyzed in terms of two competing reaction channels. In conjunction with the study of aroyl bromides, a large number of k^{Br}/k^{Cl} leaving-group effects become available, and these values must be consistent with any proposed mechanism.



(1)

There has been much recent interest, both theoretical and experimental, concerning the mechanism of solvolysis of acyl halides. It has been emphasized that concerted mechanisms can closely resemble the carbonyl addition mechanism, with a classification as concerted because the tetrahedral intermediate is too unstable to exist.[16] A recent study[17] of the alcoholysis and hydrolysis of acetyl chloride in terms of kinetics and product selectivities was rationalized in terms of a single reaction channel involving an in-plane S_N2 nucleophilic attack. This conclusion is consistent with that reached in the study[6] of the methanolyses of acetyl chloride in acetonitrile.

Studies of the kinetics of the solvolyses of benzoyl chloride and ring-substituted derivatives have been rationalised in terms of an S_N2 mechanism in which bond formation was running ahead of bond breaking[18] and, more recently, in terms of a competition between this mechanism and, especially in less aqueous media, a carbonyl addition–elimination mechanism.[19–21] The assignments have been reinforced by a combined consideration of rate and product studies for solvolyses in aqueous alcohols, and the solvolysis kinetics have been interpreted in terms of third-order rate coefficients involving general-base catalysis to nucleophilic attack.[22,23] Accordingly, the conclusions from studies of the methanolyses of acyl halides in acetonitrile are of considerable interest, not only in their own right but also because of the parallel that they show toward corresponding studies under solvolytic conditions.

Table 1 Experimental second-order rate coefficients (k_2') for the reactions of 0.0400 mol dm^{-3} aroyl chlorides (XC_6H_4COCl) with methanol, in acetonitrile at 25.0 °C

	$10^6\ k_2'$/dm^3 mol^{-1} s^{-1} [a]					
[MeOH]/mol dm^{-3}	*m*-NO_2	*p*-CF_3	*m*-CF_3	*m*-Br	*m*-Cl	*p*-Br
1.60	387 ± 12	234 ± 10	201 ± 3	130 ± 3	134 ± 2	81 ± 1
1.28	306 ± 6	195 ± 7	163 ± 3	112 ± 2	107 ± 2	66 ± 1
0.960			122 ± 3	87 ± 1	95 ± 2	51 ± 1
0.800		121 ± 5	104 ± 4	73 ± 2		
0.640	165 ± 4	102 ± 1	87 ± 1	60 ± 1	62 ± 1	35.8 ± 0.9
0.400			57 ± 1	40.9 ± 0.3		
0.320	91 ± 1	60 ± 2	48.2 ± 0.5	35.0 ± 0.4	37.1 ± 0.7	22.1 ± 0.3
0.160	58 ± 1	40.8 ± 2.2	32.8 ± 0.4	24.2 ± 1.2	27.9 ± 0.7	16.1 ± 0.3
0.0800	45.7 ± 0.9	30.3 ± 0.9	25.1 ± 1.0	17.6 ± 0.2	19.8 ± 1.1	13.0 ± 0.2
0.0400	46.3 ± 1.2	24.3 ± 1.1	20.4 ± 0.3	14.9 ± 0.3	18.9 ± 0.4	11.3 ± 0.3
0.0200	33.5 ± 0.7	22.6 ± 0.7	18.7 ± 0.2	13.5 ± 0.4	16.9 ± 0.5	10.8 ± 0.3
0.0100	32.5 ± 1.7		18.6 ± 0.5			10.5 ± 0.3

	$10^6\ k_2'$/dm^3 mol^{-1} s^{-1} [a]					
[MeOH]/mol dm^{-3}	*p*-Cl	*m*-OCH_3	H	*m*-CH_3	*p*-CH_3	*p*-OCH_3 [b,c]
1.60	79 ± 2	51 ± 1	48.1 ± 0.6	41.0 ± 1.1	34.1 ± 0.2	51 ± 1
1.28	63 ± 1	42.8 ± 0.6	37.3 ± 0.9	34.3 ± 1.0	29.8 ± 0.3	41.5 ± 0.6
0.960	48.6 ± 0.7	31.5 ± 0.2	31.2 ± 0.5	27.1 ± 0.8	23.8 ± 0.4	
0.800				23.3 ± 0.9		32.2 ± 0.5
0.640	33.7 ± 0.7	23.9 ± 0.4	21.3 ± 0.6	19.9 ± 0.9	18.0 ± 0.6	27.3 ± 0.3
0.320	20.2 ± 0.4	15.6 ± 0.3	13.8 ± 0.2	12.7 ± 0.9	12.5 ± 0.3	20.6 ± 0.5
0.160	14.6 ± 0.3	11.6 ± 0.3	10.4 ± 0.4	10.0 ± 0.7	9.6 ± 0.2	18.7 ± 0.6 [d]
0.0800	10.6 ± 0.2	9.8 ± 0.2	8.9 ± 0.1	9.4 ± 0.2	8.5 ± 0.1	15.2 [e,f]
0.0400	9.3 ± 0.1	8.7 ± 0.1	8.0 ± 0.2	8.4 ± 0.1	8.1 ± 0.1	13.5 [e,g]
0.0200	8.6 ± 0.2	9.2 ± 0.2	7.7 ± 0.3	8.3 ± 0.2	7.9 ± 0.1	
0.0100	9.0 ± 0.4	8.5 ± 0.2	7.8 ± 0.1	8.2 ± 0.3	7.9 ± 0.1	

[a] With associated standard deviation. [b] Also a value with [MeOH] = 0.500 mol dm^{-3} of 25.8 (±0.4) × 10^{-6} dm^3 mol^{-1} s^{-1}. [c] Values with [PhOH] = 0.161 and 0.322 mol dm^{-3} of 8.0 (±0.4) × 10^{-6} and 8.2 (±0.3) × 10^{-6} dm^3 mol^{-1} s^{-1}, respectively. [d] Value in presence of [PhOH] = 0.159 mol dm^{-3} of 38.2 (±1.3) × 10^{-6} dm^3 mol^{-1} s^{-1}. [e] Initial value from plot against extent of reaction. [f] Average value of integrated coefficients from first 25% of reaction of 16.4 (±0.8) × 10^{-6} dm^3 mol^{-1} s^{-1}. [g] Integrated value at 8% of reaction of 19.2 × 10^{-6} dm^3 mol^{-1} s^{-1}.

Table 2 Experimental second-order rate coefficients (k_2') for reactions of benzoyl chloride[a] and *m*-chlorobenzoyl chloride[a] with methanol, in acetonitrile at various temperatures, and calculated second- and third-order rate coefficients[b]

	$10^6\ k_2'$/dm^3 mol^{-1} s^{-1}				
	C_6H_5COCl [c]			*m*-ClC_6H_4COCl [d]	
[MeOH]/mol dm^{-3}	0.0 °C	35.0 °C	45.0 °C	35.0 °C	45.0 °C
1.60				227 ± 10	
1.28	6.5 ± 0.1	77 ± 3	134 ± 3	188 ± 2	297 ± 12
0.96				141 ± 2	234 ± 7
0.80	4.49 ± 0.16				
0.64	3.84 ± 0.08	52 ± 1	87 ± 4	108 ± 2	174 ± 5
0.32	2.34 ± 0.11			71 ± 2	119 ± 4
0.16	1.58 ± 0.04	32.4 ± 1.4	56 ± 2	52 ± 1	119 ± 5
0.08	1.46 ± 0.05			46.7 ± 1.1	84 ± 2
0.04	1.23 ± 0.05	22.8 ± 0.9	40.8 ± 1.3		
0.02	1.11 ± 0.08				
0.01	1.11 ± 0.03	21.7 ± 1.1	44.0 ± 1.7		
$10^6\ k_2$ [e]	1.03 ± 0.07	22.8 ± 2.4	41.7 ± 2.8	33.2 ± 3.9	74 ± 11
$10^6\ k_3$ [f]	4.29 ± 0.06	43.5 ± 2.2	72.1 ± 2.6	119 ± 3	170 ± 11
r [g]	0.9994	0.9960	0.9980	0.9987	0.9918

[a] Concentration of 0.0400 mol dm^{-3}. [b] Calculated from $k_2' = k_2 + k_3$[MeOH], with associated standard errors. [c] For benzoyl chloride, $\Delta H^{\ddagger}_{298}$ = 13.8 ± 1.2 kcal mol^{-1} and $\Delta S^{\ddagger}_{298}$ = −36.1 ± 4.3 cal mol^{-1} K^{-1} for the k_2 values and $\Delta H^{\ddagger}_{298}$ = 10.3 ± 0.3 kcal mol^{-1} and $\Delta S^{\ddagger}_{298}$ = −44.8 ± 1.0 cal mol^{-1} K^{-1} for the k_3 values. [d] For *m*-chlorobenzoyl chloride, $\Delta H^{\ddagger}_{298}$ = 14.4 ± 0.4 kcal mol^{-1} and $\Delta S^{\ddagger}_{298}$ = −32.4 ± 1.8 cal mol^{-1} K^{-1} for the k_2 values and $\Delta H^{\ddagger}_{298}$ = 7.0 ± 0.5 kcal mol^{-1} and $\Delta S^{\ddagger}_{298}$ = −53.9 ± 1.7 cal mol^{-1} K^{-1} for the k_3 values. [e] Values expressed in dm^3 mol^{-1} s^{-1}. [f] Values expressed in dm^6 mol^{-2} s^{-1}. [g] Correlation coefficient.

Results

The methanolyses of 0.04 mol dm^{-3} acetonitrile solutions of benzoyl chloride and 11 ring-substituted derivatives have been studied in terms of the rate of acid production. The concentrations of methanol were in the range 0.01–1.60 mol dm^{-3} and the studies were primarily at 25.0 °C (Table 1). Studies were also carried out at other temperatures for benzoyl chloride and *m*-chlorobenzoyl chloride (Table 2). The experimental rate coefficients presented in those tables are second-order coef-

Table 3 Second- and third-order rate coefficients[a] for the reactions of 0.0400 M aroyl chlorides (XC_6H_4COCl) with methanol in acetonitrile at 25.0 °C

X	$10^6\ k_2$/dm^3 mol^{-1} s^{-1}	$10^6\ k_3$/dm^6 mol^{-2} s^{-1}	r[b]	(k_3/k_2)/dm^3 mol^{-1}
p-NO_2[c]	37.4 ± 5.6	365 ± 7	0.9992	9.8 ± 1.5
m-NO_2	27.8 ± 6.0	221 ± 4	0.9991	7.9 ± 1.7
p-CF_3	18.3 ± 2.9	135 ± 2	0.9994	7.4 ± 1.2
m-CF_3	14.5 ± 2.5	115 ± 1	0.9993	7.9 ± 1.4
m-Br	11.8 ± 1.8	76 ± 1	0.9992	6.5 ± 1.4
m-Cl	15.3 ± 3.6	75 ± 2	0.9972	4.9 ± 1.2
p-Br	9.2 ± 1.0	44.2 ± 0.6	0.9994	4.8 ± 0.5
p-Cl	7.3 ± 1.1	43.9 ± 0.6	0.9992	6.0 ± 0.9
m-OCH_3	7.6 ± 0.9	26.7 ± 0.5	0.9984	3.5 ± 0.4
H	6.7 ± 1.0	25.0 ± 0.6	0.9979	3.7 ± 0.6
m-CH_3	7.3 ± 0.7	20.8 ± 0.4	0.9984	2.9 ± 0.3
p-CH_3	7.3 ± 0.4	17.0 ± 0.2	0.9993	2.3 ± 0.1
p-OCH_3	13.5 ± 1.0	22.9 ± 0.7	0.9974	1.7 ± 0.1

[a] Calculated from $k_2' = k_2 + k_3$ [MeOH], using the data of Table 1; with associated standard errors. [b] Correlation coefficient. [c] Using data from ref. 2.

ficients, defined as in eqn. (2). The integrated values remained

$$\frac{d[HCl]}{dt} = k_2'\ [ArCOCl][MeOH] \qquad (2)$$

constant over the full range of reaction followed (up to 90%), except for solvolyses of p-methoxybenzoyl chloride, at the lower methanol concentrations. For this substrate, initial values are reported for 0.04 and 0.08 mol dm^{-3} [MeOH] and, due to a rapid increase in value, accurate initial values could not be obtained at lower methanol concentrations.

From run to run, the experimental second-order rate coefficients increased linearly with the initial methanol concentration and the overall kinetics can be represented as in eqn. (3).

$$\frac{d[HCl]}{dt} = k_2\ [ArCOCl][MeOH] + k_3\ [ArCOCl][MeOH]^2 \qquad (3)$$

Combining eqns. (2) and (3), we see that the experimental k_2' values can be related to k_2 and k_3 values by eqn. (4). Linear

$$k_2' = k_2 + k_3\ [MeOH] \qquad (4)$$

regression analysis of the k_2' values against the initial methanol concentration leads to the k_2 and k_3 values reported in Table 3; these analyses had correlation coefficient values greater than 0.997, and in the majority of cases greater than 0.999.

The experimental k_2' values remain constant over a wide extent of reaction because the overall kinetics approximate to second-order at low methanol concentration and the fit to any type of kinetic scheme becomes insensitive to order in methanol (pseudo-first-order in substrate) when the methanol is in large excess.

Discussion

Overall kinetic picture

The experimental k_2' values remain essentially constant over the complete extent of reaction for all of the systems studied, except for the p-methoxybenzoyl chloride reacting with the lower concentrations of methanol; here the integrated values increased with extent of reaction and even reasonably accurate initial values could not be obtained with methanol concentrations below 0.04 mol dm^{-3}. It is possible that an autocatalysis involving the hydrogen chloride produced is involved [eqn. (5)]. An electrophilically assisted ionization of this type

$$RCOCl + HCl \rightleftharpoons RCOCl\cdots HCl \rightleftharpoons (RCO)^+HCl_2^- \xrightarrow{MeOH} RCOOMe + 2HCl \qquad (5)$$

would be favored by electron-supplying substituents, with the p-methoxy group being the most efficient within the series of substituents studied.

The k_3/k_2 ratios [eqn. (4)] decrease as one goes from strongly electron-withdrawing to electron-supplying substituents, paralleling the behavior for the aroyl bromides.[1] The range of values is from 9.8 dm^3 mol^{-1} for p-nitrobenzoyl chloride to 1.7 dm^3 mol^{-1} for p-methoxybenzoyl chloride. The range for the corresponding bromides was from 4.0 dm^3 mol^{-1} for the m-nitrobenzoyl bromide to 1.6 dm^3 mol^{-1} for the p-methylbenzoyl bromide. A similar range was observed for substituted acetyl chlorides.[1,6,7] The similarity in the value for this ratio suggests, but does not demand, a similarity in the reaction pathways.

Hammett plots can be constructed using both the second-order and third-order rate coefficients, presented in Table 3, within eqn. (6). In eqn. (6), k and k_0 are the appropriate rate

$$\log k = \rho\sigma + \log k_0 \qquad (6)$$

coefficients as obtained with and without a substituent, and ρ is a measure of the sensitivity of the rate coefficient to changes in the value of the Hammett σ constant[24] as the substituent is varied. As with corresponding analyses of the reactions of aroyl bromides, the plots are both curved (Fig. 1), with minima in the region of σ values from 0.00 to −0.20.

Analysis of the second-order rate coefficients

The approximately linear region of the plot (Fig. 1) in the presence of electron-withdrawing substituents was treated using eqn. (6); within the region with $\sigma > 0.2$, values were obtained of 1.14 for ρ and −5.330 for log k_0. These values were then used to give k_2 (A) values for reaction channel (A), which are reported in Table 4. Subtraction of these values from the overall k_2 contribution values (Table 3) gave residual values, which when also treated using eqn. (6) led to values of −2.56 for ρ and −5.694 for log k_0; these values were then used to calculate k_2 (B) values for reaction channel (B). These values are also reported in Table 4, as are the k_2 (A + B) values. The latter values are found to be in good agreement with the k_2 values from experiment, reported in Table 3. In other words, the curvature of Fig. 1 can be reproduced by assuming that it results from the concurrent operation of two reaction channels, each of which obeys the Hammett equation.

The ρ values are somewhat larger than the corresponding values of 1.01 and −1.69 for a parallel analysis of the second-order component to the methanolyses in acetonitrile of aroyl bromides. This can be rationalized in terms of the reactivity–selectivity principle and the lower reactivity of aroyl chlorides.

Table 4 Comparison of the sum of the predicted (best fit) second-order rate coefficients (for pathways A plus B) and experimental values (dm^3 mol^{-1} s^{-1}) for the methanolyses of XC_6H_4COCl in acetonitrile at 25.0 °C

X	σ^a	$10^6 k_2$ (A)^b	$10^6 k_2$ (B)^c	$10^6 k_2$ (A + B)	$10^6 k_2$ (expt)^d
p-NO_2	+0.778	36.1	0.02	36.1	37.4
m-NO_2	+0.710	30.2	0.03	30.2	27.8
p-CF_3	+0.54	19.3	0.08	19.4	18.3
m-CF_3	+0.43	14.5	0.16	14.7	14.5
m-Br	+0.391	13.1	0.20	13.3	11.8
m-Cl	+0.373	12.5	0.22	12.7	15.3
p-Br	+0.232	8.6	0.52	9.1	9.2
p-Cl	+0.227	8.5	0.53	9.0	7.3
m-OCH_3	+0.115	6.3	1.02	7.3	7.6
H	0.000	4.67	2.02	6.7	6.7
m-CH_3	−0.069	3.90	3.04	6.9	7.3
p-CH_3	−0.170	2.93	5.5	8.4	7.3
p-OCH_3	−0.268	2.26	9.8	12.1	13.5

[a] From ref. 24. [b] Calculated using $\log k_2$ (A) = $1.14\sigma - 5.330$. [c] Calculated using $\log k_2$ (B) = $-2.56\sigma - 5.694$. [d] From Table 3.

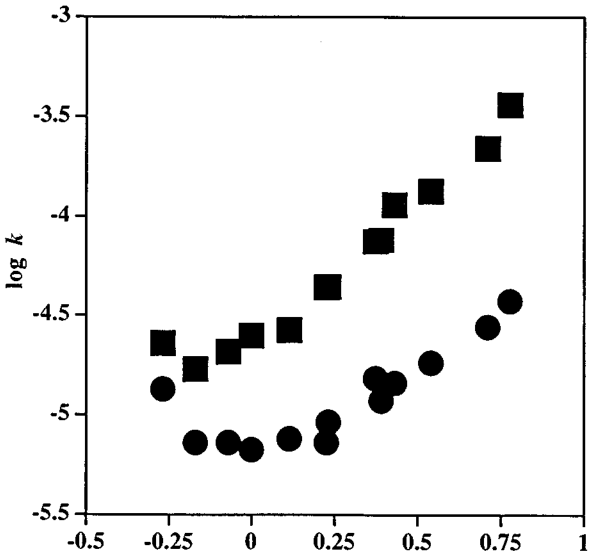


Fig. 1 Plot of the logarithms of the second-order (k_2/dm^3 mol^{-1} s^{-1}) and third-order (k_3/dm^6 mol^{-2} s^{-1}) rate coefficients for the methanolysis of substituted benzoyl chlorides (XC_6H_4COCl) in acetonitrile at 25.0 °C against the Hammett sigma values for the substituents, listed in Table 4; (●) $\log k_2$ and (■) $\log k_3$.

Table 5 Comparison of the sum of the predicted (best fit) third-order rate coefficients (for pathways A plus B) and experimental values (dm^6 mol^{-2} s^{-1}) for the methanolyses of XC_6H_4COCl in acetonitrile at 25.0 °C

X^a	$10^6 k_3$ (A)^b	$10^6 k_3$ (B)^c	$10^6 k_3$ (A + B)	$10^6 k_3$ (expt)^d
p-NO_2	340	0.11	340	365
m-NO_2	265	0.15	265	221
p-CF_3	141	0.32	141	135
m-CF_3	94	0.53	95	115
m-Br	81	0.64	82	76
m-Cl	76	0.70	77	75
p-Br	45.0	1.34	46.3	44.1
p-Cl	44.2	1.37	45.6	43.9
m-OCH_3	29.2	2.30	31.5	26.7
H	19.1	3.91	23.0	25.0
m-CH_3	14.8	5.4	20.1	20.8
p-CH_3	10.1	8.6	18.7	17.0
p-OCH_3	7.1	13.5	20.6	22.9

[a] Values for σ listed in Table 4. [b] Calculated using $\log k_3$ (A) = $1.61\sigma - 4.720$. [c] Calculated using $\log k_3$ (B) = $-2.01\sigma - 5.408$. [d] From Table 3.

Analysis of the third-order rate coefficients

Analyzing the data in the same manner as for the second-order rate coefficients, values are obtained, in the region where $\sigma > 0.2$, of 1.61 for ρ and −4.720 for $\log k_0$. These values were used to obtain the k_3 (A) values reported in Table 5. The residual values were then analyzed to give values of −2.01 for ρ and −5.408 for $\log k_0$ and, hence, k_3 (B) values. These k_3 (B) values are reported in Table 5 along with the k_3 (A + B) values, which are found to be closely related to the experimentally derived k_3 values taken from Table 3. As with the treatment of the second-order rate coefficients, the ρ values are larger than the corresponding values of 1.17 and −1.22 for reactions of aroyl bromides under identical conditions. Again, the kinetics can be analyzed in terms of the simultaneous operation of two reaction channels, with one dominating in the presence of strongly electron-supplying substituents and the other in the presence of strongly electron-withdrawing substituents.

Leaving-group effects

The results here presented (Table 3) for the unsubstituted benzoyl chloride and for eight of the ring-substituted derivatives can be combined with parallel results at 25.0 °C previously obtained[1] for the corresponding aroyl bromides to give k^{Br}/k^{Cl} leaving-group (element) effects. These comparisons have been made after the division into k_2 and k_3 components, and both k_2^{Br}/k_2^{Cl} and k_3^{Br}/k_3^{Cl} values are reported in Table 6. The values are all large and, for each substrate, they are somewhat larger for the comparison of the second-order rate coefficients than for that of the third-order coefficients. This can be rationalized in terms of slightly less bond-breaking when the methanolysis involves general-base catalysis by a second methanol molecule than when the assistance is provided by the weaker general base acetonitrile or when the methanolysis is unassisted. The values range from 57 for the comparison of the third-order rate coefficients with a *p*-NO_2 substituent to values in the range 265–320 for the comparison of the second-order rate coefficients for the parent benzoyl chloride and the *m*-Me and *p*-Me derivatives. A higher value of 650 is observed for the second-order comparison with a *p*-MeO substituent, but the second-order reaction with the bromide substrate was believed to include an additional component in which the methanol was acting in an electrophilic, rather than a nucleophilic, capacity.[1]

Values in the literature for nucleophilic substitution reactions of the unsubstituted benzoyl halides include a k_{Br}/k_{Cl} ratio of 150 for solvolysis in 50% acetone at 0.5 °C[25] and, for the reactions with nitroanilines in benzene at 25 °C, values of 140 for the *para*-isomer, 77 for the *meta*-isomer, and 150 for the *ortho*-isomer are obtained.[26,27]

Similar k_{Br}/k_{Cl} values have been obtained for reactions of the acetyl halides, including values of 322 for solvolyses in 89% acetone at −20 °C[8] and 231 for reaction with 2 mol dm^{-3}

Table 6 Leaving-group effects for the second- and third-order methanolyses of aroyl halides (XC_6H_4COCl and XC_6H_4COBr)[a] in acetonitrile at 25.0 °C

	p-NO$_2$	*m*-NO$_2$	*m*-Br	*p*-Cl	*m*-MeO	H	*m*-Me	*p*-Me	*p*-MeO
k_2^{Br}/k_2^{Cl}	163 ± 26	155 ± 36	197 ± 30	236 ± 38	213 ± 28	316 ± 57	273 ± 26	267 ± 19	652 ± 51
k_3^{Br}/k_3^{Cl}	57 ± 3	79 ± 4	93 ± 2	109 ± 5	154 ± 8	156 ± 13	154 ± 3	187 ± 12	(144 + 22)[b]

[a] Using data for XC_6H_4COBr reactions from ref. 1 and for XC_6H_4COCl reactions from Table 3. [b] Only an approximate value for k_3^{Br} was reported.

2-chloroethanol in dioxane at 15 °C.[9] Other tabulated values[7] have been excluded since they may have been influenced by a modification of the leaving groups due to electrophilic coordination, either by a phenolic reactant[28–30] or by acetic acid as solvent. A value of 520 has been reported for solvolyses of the propionyl halides in propan-2-ol at 25 °C.[12]

Assignment of reaction mechanism

While the present results could be rationalized in terms of one transition state, for which the detailed structure varied with the substituent, the division into two types of reaction channel, labeled (A) and (B), is supported by previous studies under solvolytic conditions. Here, a change of mechanism induced by a solvent, as opposed to a substituent, was proposed.[19–21] The overall reaction was divided into an S_N2 component dominant in solvents rich in water or fluoroalcohol, and a carbonyl addition component, dominant at the other extreme of solvent type.

In the study of the methanolyses of aroyl bromides in acetonitrile,[1] plots similar to those shown in Fig. 1 were interpreted in terms of pathway (A) involving the carbonyl addition–elimination (tetrahedral intermediate) mechanism and pathway (B) involving a loose S_N2 (S_N2–S_N1) transition state. In pathway (A), the attack of the nucleophile is favored by electron deficiency at the acyl carbon and, therefore, by the presence of electron-withdrawing substituents. In pathway (B), the loose nature leads to the development of positive charge on the acyl carbon, such that the transition state is stabilized by electron-donating substituents.

The third-order contribution, observed for both types of pathway, is believed to arise from general-base catalysis by a second methanol molecule.[2] This can be directly detected in the present kinetic studies, where small and variable amounts of methanol are used in a relatively inert solvent. The second-order contribution probably also involves general-base catalysis, but now by an acetonitrile molecule,[2] which although a much weaker general base is also much more plentiful, especially at the lower methanol concentrations. Although corresponding kinetic orders, directly related to mechanism, cannot be obtained under solvolytic conditions (all first-order in substrate), a combination of kinetic and product studies for aqueous–alcohol mixtures has given a strong indication for an assembly of all possible third-order pathways which are first-order in substrate and second-order in one hydroxylic component or first-order in each of two hydroxylic components.[23] There is also evidence, for highly activated substrates in solvents of high ionizing power, for an ionization mechanism proceeding *via* an acylium ion. In the solvolyses of *p*-(dimethylamino)benzoyl fluoride, a large dependence of specific rate on solvent ionizing power is accompanied by a common-ion rate inhibition by fluoride ion:[16] two strong indications of the formation of acylium ions. Although evidence was presented for an electrophilically assisted mechanism of this type in the methanolyses in acetonitrile of *p*-methoxybenzoyl bromide,[1] this pathway does not seem to be a major contributor in the corresponding reactions of *p*-methoxybenzoyl chloride.

Concentrating, therefore, on mechanisms which involve nucleophilic attack by one or more methanol molecules, the two basic types of mechanism which have been proposed involve concerted S_N2 attack[31] and addition–elimination reaction proceeding through a tetrahedral intermediate.[32] Miller[12] has supported a merging of these mechanisms[33] for the solvolyses of a variety of acyl halides in propan-2-ol, as opposed to the side-by-side operation proposed for several alcoholyses of this type.[19,34]

The nucleophilic substitution reactions involving *p*-nitrobenzoyl chloride are generally considered to proceed by a process in which the reactivity is primarily controlled by the ease of bond formation, consistent with an addition–elimination process.[16,35,36] It is interesting to make note of the following statement: "Owing to the instability of these intermediates the reaction cannot be differentiated kinetically from an S_N2 process at a saturated carbon."[36] This can be considered to represent an early presentation of the concept of enforced concerted reactions,[37] as applied to the carbonyl addition–elimination reactions.[16]

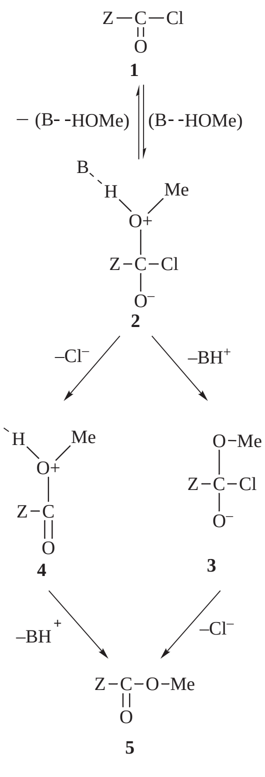
The large leaving-group effects in the present study, even for the component of the overall reaction believed to involve addition–elimination, suggest that, in each pathway, the breaking of the bond to the leaving group is a rate-controlling factor, as well as the formation of the bond to the attacking nucleophile. In this connection, it is helpful to look at fluoride/chloride leaving-group effects. Several values are available in the literature, not only for acyl halides (RCOX) but also for haloformate esters (ROCOX). It is instructive to look first at the haloformate esters because there is very good independent evidence that these tend to react by the addition–elimination pathway.[38,39] The F/Cl rate ratios are here all fairly close to unity,[40,41] even in some cases with the fluoroformate the most reactive. This is in contrast to values for nucleophilic substitution at a saturated carbon, where values range from about 10^{-1} to 10^{-3} for S_N2 reactions[10,16] to 10^{-5} to 10^{-6} for unimolecular solvolyses.[10]

The k_F/k_{Cl} values for nucleophilic substitution reactions of acyl halides vary widely. At one extreme, the bimolecular reaction of benzoyl halides with hydroxide ion in 50% acetone shows a slightly faster reaction with the fluoride ion leaving group (k_F/k_{Cl} value of 1.4),[10] behavior reminiscent of that for haloformate solvolyses. At the other extreme, solvolyses of acetyl halides in 75% acetone[10] have a k_F/k_{Cl} ratio of 1.3×10^{-4} and solvolyses of propionyl halides in propan-2-ol[12] have a ratio of 1.6×10^{-4}. The solvolyses of benzoyl halides are intermediate in value, with ratios of 2.6×10^{-2} in 50% acetone and 1.1×10^{-2} in 75% acetone.[10] A similar value of 2.4×10^{-2} was obtained in 80% ethanol, but introduction of a *p*-nitro substituent raised this value to 0.20,[42] approaching the values obtained for corresponding solvolyses of haloformates.

These values are nicely consistent with the assignment of mechanisms for these systems from other types of investigation. The values for the aliphatic acyl halides are within the S_N2–S_N1 range, and the large leaving-group effects are consistent with the high sensitivity to changes in solvent ionizing power,[17] both being indicative of extensive carbon–halogen bond heterolysis in the rate-determining step and consistent with the proposed S_N2 mechanism.[17]

The much higher ratio for solvolyses of the *p*-nitrobenzoyl halides is approaching the value of 1.4 for hydroxide ion attack on the parent benzoyl halides and these values are consistent with the assignment of these reactions as addition–elimination, proceeding *via* a tetrahedral intermediate.[10,20,22] Solvolyses of the parent benzoyl halides have k_F/k_{Cl} ratios intermediate in value at a little greater than 10^{-2}. This is consistent with conclusions from previous studies of benzoyl chloride which have suggested that two reaction channels are operative in these solvolyses, involving competition toward the addition–elimination pathway from an S_N1–S_N2 pathway, of the type believed to dominate in the solvolyses of acetyl chloride.[17] There are, however, strong indications[16,43] that the parent benzoyl fluoride undergoes hydrolysis (and presumably also solvolysis in less ionizing solvents) by the addition–elimination mechanism. The intermediate k_F/k_{Cl} values will then result from the ratio of close to unity expected for the addition–elimination channel falling in value as the second (S_N1–S_N2) channel becomes of increasing importance for the solvolyses of benzoyl chloride, but not benzoyl fluoride, such that the fluoride is reacting almost entirely by only one channel but the chloride by two channels.[19,20,22]

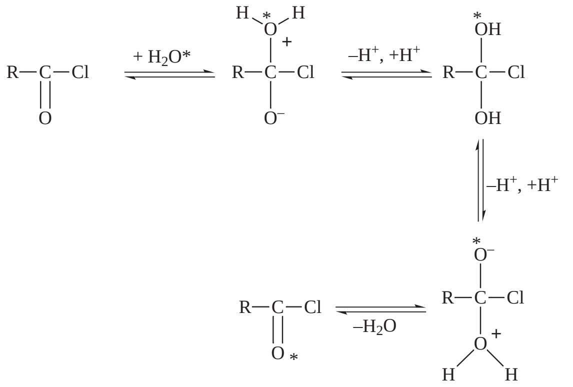
The major remaining problem is to explain why addition–elimination reactions involving solvolyses of haloformate esters or reaction of benzoyl halides with hydroxide ion have extremely low leaving-group effects but the methanolyses of aroyl halides in acetonitrile show appreciable k_{Br}/k_{Cl} leaving-group effects even when we have separated out and are analyzing what is believed to be an addition–elimination channel. We propose an overall reaction scheme for the addition–elimination pathway as shown in eqn. (7).



(7)

The initial general-base catalyzed addition of methanol to reactant **1** leads to the tetrahedral intermediate **2**. Frequently **2** returns to reactant, but it can also lose both BH^+ and Cl^- and proceed to the methyl ester **5**. The sequence of these losses will determine whether or not an appreciable leaving-group effect is observed. If the reaction in competition with the return to reactant involves loss of BH^+ to give **3**, then on regeneration of the carbonyl group a loss of chloride ion to give **5** will be observed in preference to loss of methoxide ion, and an appreciable leaving-group effect is not to be expected when chlorine is replaced by fluorine or bromine. The alternative sequence of loss of chloride to give the protonated ester **4**, stabilized by interaction with the general base, followed by the completion of the transfer of the proton to give **5** will show an appreciable leaving-group effect when chlorine is replaced by bromine or fluorine. If this scheme does indeed apply then the solvolyses of haloformates follow the scheme proceeding through **3** and solvolyses of acyl halides, or reaction of the acyl halides with methanol in acetonitrile when involving an addition–elimination mechanism, proceed *via* **4**. This difference would be consistent with the presence of a phenoxy or alkoxy oxygen adjacent to the α-carbon in the tetrahedral intermediate **2**, both strongly disfavoring loss of chloride ion and favoring loss of BH^+.

The mechanism outlined above, involving formation of a tetrahedral intermediate, which can return to reactants or follow pathways proceeding through other intermediates on the way to the ester **5**, is not in accord with the belief that these bimolecular reactions proceed by an enforced concerted pathway[16,44,45] with an intermediate of such negligible lifetime that a sufficiently activated and correctly oriented encounter always proceeds to product. Arguing against the enforced concerted pathway, at least as regards the hydrolysis of benzoyl and *p*-toluyl chlorides in aqueous dioxane, is the observation that the hydrolysis is accompanied by oxygen exchange with the water.[46] This requires not only a tetrahedral intermediate, but a tetrahedral intermediate with a lifetime sufficient for the two oxygens to have the opportunity to become equivalent [eqn. (8)]. These important observations demonstrated that during the hydrolyses of acid chlorides, as well as esters,[47] oxygen exchange accompanies the solvolyses. Such exchanges would be difficult to reconcile with an enforced concerted pathway.



(8)

Experimental

Materials

Acetonitrile (Mallinckrodt, Nanograde) was purified as previously described.[48,49] An acceptable level of purity was considered to be when the first-order rate coefficient for acid formation from 0.04 M benzoyl chloride was less than 1×10^{-8} s^{-1} at 25.0 °C. Methanol (Baker AR) was dried by passage through a column of activated alumina. The aroyl chlorides were purified by distillation under reduced pressure, except for *p*-methoxybenzoyl chloride which was purified by recrystallization from petroleum ether (60–110° boiling range). The suitability of each sample of aroyl chloride was tested by running a blank kinetic run (methanol absent) in acetonitrile; the first-order rate coefficient was considered to be acceptable when it was less than 1% of the pseudo-first-order rate coefficient for the corresponding reaction in the presence of 0.010 M methanol.

Kinetic methods

These were as described previously.[2] A series of 5 mL portions were removed at suitable time intervals and each was quenched in 15 mL of acetone at −78 °C. Titration was against a standardized solution of triethylamine in toluene, using resorcinol blue (Lacmoid) as the acid–base indicator.

Acknowledgements

DNK thanks the Royal Society of Chemistry for an International Authors Grant and Dr T. W. Bentley (University of Wales, Swansea) for many helpful discussions and hospitality during the time that this manuscript was being prepared.

References

1 Part 5, D. N. Kevill and D. C. Knauss, *J. Chem. Soc.*, *Perkin Trans. 2*, 1993, 307.
2 D. N. Kevill and F. D. Foss, *J. Am. Chem. Soc.*, 1969, **91**, 5054.
3 W. R. Gilkerson, *J. Phys. Chem.*, 1956, **60**, 1142.
4 E. S. Gould, *Mechanism and Structure in Organic Chemistry*, Holt, Rinehart and Winston, New York, 1959, p. 334.
5 R. Alexander, E. C. F. Ko, A. J. Parker and T. J. Broxton, *J. Am. Chem. Soc.*, 1968, **90**, 5049.
6 D. N. Kevill and C.-B. Kim, *Bull. Soc. Chim. Fr.*, 1988, 383.
7 D. N. Kevill and C.-B. Kim, *J. Chem. Soc.*, *Perkin Trans. 2*, 1988, 1353.
8 I. Ugi and F. Beck, *Chem. Ber.*, 1961, **94**, 1839.
9 R. Leimu, *Chem. Ber.*, 1937, **70**, 1040.
10 C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, 1953, **75**, 246.
11 J. M. Briody and D. P. N. Satchell, *Proc. Chem. Soc.*, 1964, 268; *J. Chem. Soc.*, 1965, 168.
12 J. Miller and O.-L. Ying, *J. Chem. Soc.*, *Perkin Trans. 2*, 1985, 323.
13 C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, 2nd edn., Cornell University Press, Ithaca, 1969, p. 453.
14 J. Miller, *Aromatic Nucleophilic Substitution*, Elsevier, Amsterdam, 1968, ch. 5.
15 D. N. Kevill and M. J. D'Souza, *J. Chem. Soc.*, *Perkin Trans. 2*, 1997, 1721.
16 B. D. Song and W. P. Jencks, *J. Am. Chem. Soc.*, 1989, **111**, 8470.
17 T. W. Bentley, G. Llewellyn and J. A. McAlister, *J. Org. Chem.*, 1996, **61**, 7927.
18 I. Lee, I. S. Koo, S. C. Sohn and H. H. Lee, *Bull. Korean Chem. Soc.*, 1982, **3**, 92.
19 T. W. Bentley, G. E. Carter and H. C. Harris, *J. Chem. Soc.*, *Perkin Trans. 2*, 1985, 983.
20 T. W. Bentley and H. C. Harris, *J. Chem. Soc.*, *Perkin Trans. 2*, 1986, 619.
21 I. Lee, D. D. Sung, T. S. Uhm and Z. H. Ryu, *J. Chem. Soc.*, *Perkin Trans. 2*, 1989, 1697.
22 T. W. Bentley and I. S. Koo, *J. Chem. Soc.*, *Perkin Trans. 2*, 1989, 1385.
23 T. W. Bentley and H. C. Harris, *J. Org. Chem.*, 1988, **53**, 724.
24 J. E. Leffler and E. Grunwald, *Rates and Equilibria of Organic Reactions*, Wiley, New York, 1963, p. 173.
25 M. L. Bender and J. M. Jones, *J. Org. Chem.*, 1962, **27**, 3771.
26 F. J. Stubbs and C. N. Hinshelwood, *J. Chem. Soc. Suppl. 1*, 1949, 71.
27 H. S. Venkataraman and C. N. Hinshelwood, *J. Chem. Soc.*, 1960, 4977.
28 E. Gelles, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 1954, 2918.
29 K. Okamoto, *Pure Appl. Chem.*, 1984, **56**, 1797.
30 M. J. Kamlet, J. L. M. Abboud and R. W. Taft, *Prog. Phys. Org. Chem.*, 1981, **13**, 485.
31 A. Kivinen, in *The Chemistry of Acyl Halides*, ed. S. Patai, Interscience, New York, 1972, ch. 6.
32 R. J. E. Talbot, in *Comprehensive Chemical Kinetics*, ed. C. H. Bamford and C. F. H. Tipper, Elsevier, Amsterdam, 1972, vol. 10, pp. 226–227.
33 J. N. E. Day and C. K. Ingold, *Trans. Faraday Soc.*, 1941, **37**, 686.
34 D. N. Kevill, P. H. Daum and R. Sapre, *J. Chem. Soc.*, *Perkin Trans. 2*, 1975, 963.
35 D. A. Brown and R. F. Hudson, *J. Chem. Soc.*, 1953, 3352.
36 E. W. Crunden and R. F. Hudson, *J. Chem. Soc.*, 1956, 501.
37 W. P. Jencks, *Chem. Rev.*, 1985, **85**, 511.
38 A. Queen, *Can. J. Chem.*, 1967, **45**, 1619.
39 G. Ostrogovich, C. Csunderlik and R. Bacaloglu, *J. Prakt. Chem.*, 1975, **317**, 62; C. Csunderlik, R. Bacaloglu and G. Ostrogovich, *J. Prakt. Chem.*, 1975, **317**, 81.
40 M. Green and R. F. Hudson, *J. Chem. Soc.*, 1962, 1055.
41 S. I. Orlov, A. L. Chimishkyan and M. S. Grabarnik, *J. Org. Chem. USSR* (*Engl. Transl.*), 1983, **19**, 1981.
42 C. G. Swain, R. B. Mosely and D. E. Bown, *J. Am. Chem. Soc.*, 1955, **77**, 3731.
43 M. J. D'Souza, PhD Dissertation, Northern Illinois University, August 1992.
44 K. H. Yew, H. J. Koh, H. W. Lee and I. Lee, *J. Chem. Soc.*, *Perkin Trans. 2*, 1995, 2263.
45 W. P. Jencks, *Chem. Soc. Rev.*, 1981, **10**, 345.
46 C. A. Bunton, T. A. Lewis and D. R. Llewellyn, *Chem. Ind.* (*London*), 1954, 1154.
47 M. L. Bender, *J. Am. Chem. Soc.*, 1951, **73**, 1626.
48 J. F. O'Donnell, J. T. Ayres and C. K. Mann, *Anal. Chem.*, 1965, **37**, 1161.
49 D. N. Kevill and J. E. Dorsey, *J. Org. Chem.*, 1969, **34**, 1985.

Paper 8/06493H