Comparison of Methanolysis of a Series of *p*-Benzyloxybenzoyl Chlorides with that of Benzoyl, *p*-Phenoxybenzoyl, and *p*-Methoxybenzoyl Chlorides

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The kinetics of the methanolysis (solvolysis) of a series of *p*-benzyloxybenzoyl chlorides have been compared with values for benzoyl, *p*-methoxybenzoyl, and *p*-phenoxybenzoyl chloride. Small rate differences between benzoyl chloride and the other compounds stem from counterbalancing large changes in enthalpies and entropies of activation, ascribed to different degrees of $S_{\mathrm{N}}1$ character in the reactions. Differences within the benzyloxy-series are ascribed to effects of substituents on the inductive effect of the benzene ring of the benzyloxy-group. Data have been analysed in terms of the Hammett equation. Values of σ for the *p*-benzyloxy-group were obtained from both kinetic and acidity measurements: both are considerably less than the literature value, which we regard as suspect. A coefficient of transmission of electronic effects across a *p*-benzyloxy-group was determined as 0.17.

ACYL HALIDES, particularly chlorides, are of special interest because of their importance in synthesis, and because reactions by both $S_{\mathrm{N}}1$ and $S_{\mathrm{N}}2$ mechanisms are relatively facile. Their chemistry has been discussed at length in a recent monograph,[1a] with mechanisms discussed especially in ch. 6.[1b]

The present studies stem both from our interest in the intermediate region between $S_{\mathrm{N}}1$ and $S_{\mathrm{N}}2$ limiting mechanisms; and in distant substituent effects in benzyloxy-compounds. Measurement of rates by conductivity changes has proven very suitable for the relatively small rate differences involved in our studies.

EXPERIMENTAL

Materials.—Methyl *p*-benzyloxybenzoate and its 4′-derivatives were prepared by reacting methyl *p*-hydroxybenzoate with the appropriate benzyl chlorides in methanolic sodium hydroxide, according to the method of Cohen and Dudley.[2]

The 4′-nitro-compound was recrystallized from acetone and the others from ethanol. All but one of the corresponding acids were obtained from the esters by saponification according to the method of Haslam *et al.*[3] The 4-nitro-ester was saponified with potassium carbonate in aqueous ethanol, according to the method of Blicke and Smith.[4] The 4′-chloro- and 4′-nitro-acids were recrystallized from glacial acetic acid, the others from ethanol.

TABLE 1

4′-Substituted *p*-benzyloxybenzoic acids, methyl esters, and chlorides

	Acid		Methyl ester		Chloride		
4′-Substituent	M.p. (°C)	Yield (%)	M.p. (°C)	Yield (%)	M.p. (°C)	Yield (%)	Cl §
H	188—190	93	99—100	62	126—127 †	60	99.5
NO_2	259—260	26	177—179	70 ‡	146—148 ‡	75	99.4
Cl	220—223	99	123—124	51 ‡	113—115 ‡	76	99.5
Br	234—235	98	129—131	71 ‡	121—123 ‡	77	99.5
Me	221—222	66	92—94	44 ‡	87—90 ‡	56	99.3
Bu^t	244—246	100 ‡	62—64	45 ‡	67—69 ‡	84	99.2
OMe	205—208	85 ‡	112—114	21 ‡	95—97 ‡	73	99.1
OEt *	209—211	79 ‡	131—133	17 ‡	103—104 ‡		96.0

* Not used in kinetic studies. † C. J. Cavallito and J. S. Buck, *J. Amer. Chem. Soc.*, 1943, **65**, 2140, give m.p. 110°. ‡ New compound. § % of theoretical.

The acyl chlorides used in kinetic studies were obtained by reacting the dry acids with thionyl chloride in benzene; or in light petroleum ether (b.p. 60—80°) (4′-methoxy- and 4′-ethoxy-compounds). After distillation of excess of thionyl chloride and volatile solvent, the solid chlorides were recrystallized from light petroleum (b.p. 60—80°).

Table 1 lists m.p.s and yields of the acids, their esters, and chlorides. Structures and purity were confirmed by elemental analysis, by estimation of chloride produced by substitution, and by n.m.r. and i.r. spectra.

Benzoyl chloride was a commercial product purified by redistillation to b.p. 197° (lit.,[5] 197°). *p*-Methoxybenzoyl chloride was prepared by heating *p*-methoxybenzoic acid with $SOCl_2$ in benzene. After removing excess of $SOCl_2$, the chloride was obtained by distillation at reduced pressure, and distilled, b.p. 91° at 1 Torr (lit.,[6] 90.8° at 1 Torr). *p*-Phenoxybenzoic acid was obtained by carbonation (solid CO_2) of the Grignard compound obtained from 4-bromodiphenyl ether and subsequent acid treatment, m.p. 158—160° (from alcohol–water) (lit.,[7] 158—161.5°). The bromo-ether was obtained from diphenyl ether according to the procedure of Suter.[8] *p*-Phenoxybenzoyl chloride was obtained from the acid, as in the preparation of *p*-methoxybenzoyl chloride. The product had b.p. 186—187° at 14 Torr (lit.,[9] 186—187° at 14 Torr).

Using a Metrohm conductance bridge, model E 382, rates

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[1] (*a*) 'The Chemistry of Acyl Halides,' ed. S. Patai, Interscience, London, 1972; (*b*) A. Kivinen, ch. 6, 'Mechanisms of Substitution at the COX group.'

[2] J. B. Cohen and H. W. Dudley, *J. Chem. Soc.*, 1910, **97**, 1745.

[3] E. Haslam, R. D. Haworth, S. D. Miles, H. I. Rogers, R. Armitage, and T. Searle, *J. Chem. Soc.*, 1961, 1839.

[4] F. F. Blicke and F. D. Smith, *J. Amer. Chem. Soc.*, 1939, **51**, 1947.

[5] 'Dictionary of Organic Compounds,' ed. I. Heilbron, Eyre and Spottiswoode, London, 1974, 4th edn., p. 358.

[6] D. D. Thompson and J. F. Norris, *J. Amer. Chem. Soc.*, 1936, **58**, 1953.

[7] 'Beilsteins Handbuch der Organischen Chemie,' vol. X, 3rd revision, p. 389.

[8] C. M. Suter, *J. Amer. Chem. Soc.*, 1939, **57**, 2585.

[9] G. Lock and F. H. Kempter, *Monatsh.*, 1936, **67**, 343.

were obtained by Guggenheim plot analysis of conductance increases resulting from methanolysis (solvolysis) of *ca.* 2—3 × 10^{-3}M solutions of the chlorides in 97.4% MeOH–2.6% dioxan. The small amount of dioxan, which has little effect on rates and activation parameters, was added to increase the solvent power of the medium.

TABLE 2

Rates of methanolysis (solvolysis) of some *para*-substituted benzoyl chlorides in 97.4% MeOH–dioxan (except as shown)

	$10^4k/s^{-1}$				
para-Substituent	*c*	11.0°	19.0°	25.0°	*c*
H	4.60 (0.0)	11.7 (10.0)	21.2 (17.0)	42.9	
PhO		9.16	21.7	38.2	58.0 (30.0)
MeO		22.2	54.2	104	
MeO [a]				41.6	
MeO [b]				19.7	
$PhCH_2O$	7.97 (3.0)	19.4	46.1	85.6	
$PhCH_2O$ [a]			19.6	34.3	61.0 (31.0)
$PhCH_2O$ [b]			9.81	16.5	27.4 (31.0)
p'-$NO_2C_6H_4CH_2O$		12.9	30.0	55.2	
p'-$ClC_6H_4CH_2O$		16.7	38.8	73.0	
p'-$BrC_6H_4CH_2O$		16.6	38.2	71.1	
p'-$MeC_6H_4CH_2O$		21.1	48.4	92.3	
p'-$Bu^tC_6H_4CH_2O$		20.0	47.9	82.1	
p'-$MeOC_6H_4CH_2O$		21.4	53.1	100	

[a] In 70% MeOH–dioxan. [b] In 50% MeOH–dioxan. [c] Temperature in parentheses.

For the benzyloxy-compounds up to 10 runs at each of three temperatures (±0.1°) were carried out over a range of *ca.* 14°. In other cases a greater range was utilized, but with fewer measurements at each temperature.

TABLE 3

Comparison of data * for methanolysis (solvolysis) of some *para*-substituted benzoyl chlorides at 25° in 97.4% MeOH–dioxan (except as shown)

					Rate ratio	
para-Substituent	$10^3k/s^{-1}$	$\Delta E^‡$/ kJ mol^{-1}	log (*B*) l mol^{-1} s^{-1}	$\Delta S^‡$/ J mol^{-1} K^{-1}	*a*	*b*
H	4.29	59.8	8.1_0	−97.9	1	
PhO	3.82	69.4	9.7_0	−66.9	0.895	
MeO	10.4	75.3	11.2	−38.5	2.42	
$PhCH_2O$	8.63	73.4	10.8	−46.8	2.01	1
$PhCH_2O$ (70% MeOH)	3.43	67.3	9.3	−74.9		
$PhCH_2O$ (50% MeOH)	1.65	60.6	7.9	−102		
p-$NO_2C_6H_4CH_2O$	5.52	71.1	10.1_5	−58.5	1.29	0.641
p-$ClC_6H_4CH_2O$	7.30	71.9	10.4_5	−53.1	1.70	0.846
p-$BrC_6H_4CH_2O$	7.11	71.1	10.3	−56.5	1.66	0.824
p-$MeC_6H_4CH_2O$	9.11	71.9	10.5_5	−51.0	2.15	1.07
p-$Bu^tC_6H_4CH_2O$	8.21	69.2	10.0_5	−60.2	1.91	0.951
p-$OMeC_6H_4CH_2O$	10.1	75.7	11.5	−37.4	2.35	1.17

[a] Benzoyl chloride = 1. [b] p-Benzyloxybenzoyl chloride = 1.

* On the basis of the bimolecular rate constants, values of log *B* are reduced by 1.3_8. Values of ΔS‡ are 26.4 more negative. In 70% MeOH, differences are 1.2_7 and 24.3; and in 50%MeOH, differences are 1.1_5 and 23.0.

With the *p*-methoxy- and *p*-benzyloxy-compounds, rate measurements were also made in 70 and 50% MeOH–dioxan. From these, values of *n* in the equation $\log k = \log k^0 + n \log [\text{MeOH}]$ were calculated. Values are 3.6 and 3.6 in the range 97.4—70% MeOH; and 2.6 and 2.3 in the range 70—50% MeOH.

In 97.4% MeOH–2.6% dioxan the compounds studied were benzoyl, *p*-methoxybenzoyl, *p*-phenoxybenzoyl, and *p*-benzyloxybenzoyl chlorides, plus six 4′-substituted benzyloxy-compounds (4′-substituent NO_2, Cl, Br, Me, Bu^t, and OMe) (see Tables 2 and 3). On adding small amounts of aniline, large increases of rate were noted. Reactions were fast even at −50°.

DISCUSSION

Our discussions involve the concept of synchronous S_N2 reactions with S_N1 character, and it seems necessary to indicate what we mean by this. It has been discussed in a wider context by one of us.[10] In summary our views are as follows. If, in an S_N reaction the transition state of heterolysis of the substrate is passed before the nucleophile begins to bond (in a subsequent fast step) the reaction is S_N1. If, contrariwise, there is any degree of bond formation in the rate-limiting transition state, no matter how little, the reaction is formally S_N2. Reactions in which that degree of bond formation is significantly less than the degree of rupture of the bond to the leaving group are regarded as having significant S_N1 character (S_N1 like).

As a preliminary to detailed discussion of the methanolysis of the several *p*-benzyloxybenzoyl chlorides, we felt it necessary to relate the whole series to reactions of benzoyl, *p*-methoxybenzoyl, and *p*-phenoxybenzoyl chlorides.

Because aroyl chlorides can react readily with nucleophiles by S_N1 as well as S_N2 mechanisms, marked variations with changes of substituent and solvent are to be expected. Thus Hudson and his co-workers[11] demonstrated the inversion of reactivity order in a series of substituted benzoyl chlorides (p-NO_2 to p-OMe) in the change from 40% EtOH–60% Et_2O to 50% H_2O–50% Me_2CO; plus a change of mechanism within the series in 50% aqueous acetone.

The solvent used by us, 97.4% MeOH–dioxan, like anhydrous MeOH, is not very favourable for S_N1 reactions, but we judged it to be sufficiently polar for S_N1 character to be evident in suitable compounds. Initially therefore we compared *p*-benzyloxybenzoyl

[10] J. Miller, *Ciência e Cultura*, 1972, **24**, 131, 317.

[11] D. A. Brown and R. F. Hudson, *J. Chem. Soc.*, 1953, 883.

chloride with *p*-methoxybenzoyl and *p*-phenoxybenzoyl chlorides, then related them all to benzoyl chloride, so as to obtain a better assessment of the intermediate region of mechanism.[12,13]

In accord with the expectation of significant S_N1 character, the *p*-methoxy compound was found to be mildly more reactive than the parent benzoyl chloride; the rate ratio is 2.71 at 25°. Interestingly, the *p*-phenoxy-compound, while less reactive than the *p*-methoxy compound, as expected, is also slightly less reactive than the parent compound. This suggests that the effects of the *para*-substituents are not simple; and this is confirmed by inspection of the Arrhenius parameters. These show that the small rate differences are the resultant of large and nearly compensating changes in enthalpy and entropy of reaction.

The Arrhenius parameters for the methanolysis of benzoyl chloride are appropriate for reaction between a neutral nucleophile and neutral substrate. The higher values of both $\Delta E^‡$ and $\Delta S^‡$ for the various *p*-OR compounds support the view that their reactions have significant S_N1 character.[14a] Further support comes from the *n* values in 70 and 50% MeOH–dioxan (see Experimental section) for the *p*-methoxy- and *p*-benzyloxy-compounds, *viz.* 3.6 and 3.6 between 97.4 and 70% MeOH and 2.6 and 2.3 between 70 and 50% MeOH.

They should be compared with Biordi's values[15] for benzoyl chloride in MeOH–dioxan *viz.*, 1.65 in the range 100—81% MeOH, and 1.1 in the range 66—50% MeOH.

Kivinen[14b] has discussed *n* values in relation to S_N1 and S_N2 mechanisms. He suggests that in water (and alcohols, though less reliably) *n* values of 6—7 correspond to limiting S_N1 reactions; and values of *ca.* 1—2 to limiting S_N2 reactions. Intermediate values correspond to S_N2 reactions with significant S_N1 character.

Our values, in comparison with those of Biordi, thus show a significant development of S_N1 character. This is most marked, as expected, in the solvent with most MeOH.* Appropriately the considerable variation of the activation parameters with solvent change is also most S_N1 like in the solvent with most MeOH, although the rate changes are not large. For the *p*-benzyloxy compound between 50 and 97.4% MeOH, $\Delta E^‡$ increases from 60.6 to 73.4 kJ mol^{-1} and $\Delta S^‡$ from −102 to −46.8 J mol^{-1} K^{-1}. It is interesting that the Arrhenius parameters for *p*-benzyloxybenzoyl chloride in 50% MeOH–dioxan are similar to these of benzoyl chloride in 97.4% MeOH–dioxan. Although the rate constant for *p*-phenoxybenzoyl chloride is somewhat 'out of place,' behaviour intermediate between benzoyl and *p*-methoxybenzoyl chloride is supported by intermediate values of the activation parameters.

The development of S_N1-like behaviour in the change from benzoyl to the *p*-OR compounds means that the Hammett equation cannot correlate satisfactorily a range of electron-releasing as well as electron-withdrawing substituents. This situation has been well discussed by Kivinen[14c] in relation to S_N reactions of COX compounds. It is useful nevertheless in comparing the similar *p*-methoxy- and *p*-benzyloxy-groups. Accepting the value of σ for *p*-OMe as −0.26,[16] one can calculate a subsidiary reaction constant (ρ' in ref. 14*c*): its value is −1.43. From this the value of σ for the *p*-benzyloxy-group is found to be slightly lower at −0.21. It should not be forgotten that one could reasonably use more complex variations of the Hammett equation, corresponding to a substituent constant for *p*-OMe between −0.26 (σ) and −0.78 (σ^+), thus producing a ρ value lower than 1.43.

We ascribe the lower value of σ for the benzyloxy-group to the weak inductive effect of the phenyl group, which reduces slightly the electron-releasing power of the oxygen, utilised significantly in the S_N1-like reaction.

The Hammett equation in its simple form should be more reliable and useful as a measure of the effects of the 4′-substituents in the benzyl group of the various *p*-benzyloxybenzoyl chlorides.

The analysis leads to a ρ value of -0.248 ± 0.015 (correlation coefficient *r* 0.991 9), excluding the point for the 4′-Bu^t compound. If this is included, the values are -0.227 ± 0.029 (*r* 0.960 2). One may possibly infer some very mild adverse spatial effect of the Bu^t group. It is too small to be sure or to warrant speculation.

We ascribed the difference between benzyloxy and methoxy to the weak inductive effect of the phenyl group, and now suggest that the effect of the 4′-substituents is simply a modification of this inductive effect, linking well with the σ values of the 4′-substituents. The effect should be weak, as is found, and one may estimate the transmission coefficient across the benzyloxy group to be 0.17 (0.248/1.43).

In parallel with the kinetic studies we have measured the pK_a of a series of acids *p*-$XC_6H_4CO_2H$ (X = NO_2, H, Me, MeO, and $PhCH_2O$) in 50% MeOH–dioxan at 25°. The points give a fair plot with ρ 1.27 ± 0.06 (*r* 0.997 7) and lead to a σ value for the *p*-benzyloxy group of −0.33. This compares with −0.21 obtained in kinetic measurements. It is difficult to be specific about the differences, but one can look in part to an inductive effect of the phenyl group which would help stabilise an anion but destabilise a cation. It seems unprofitable to attempt to relate also to the differences in solvation of the species involved.

Apart from this there is a curious situation in the

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* Nevertheless the reactions are bimolecular as shown by the marked acceleration caused by addition of small amounts of aniline.

[12] G. Kohnstam, A. Queen, and I. T. Riker, *Chem. and Ind.*, 1973, 1387.

[13] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry,' Bell, London, 1969, 2nd edn., p. 445.

[14] A. Kivinen, *Ann. Acad. Sci. Fennicae A-II*, 1961, 108 (*a*) 44; (*b*) 34; (*c*) 57.

[15] J. C. Biordi, *J. Chem. and Eng. Data*, 1970, **15**, 166.

[16] L. P. Hammett, 'Physical Organic Chemistry,' McGraw-Hill, 1970, New York, 2nd edn., p. 356.

literature as regards a σ value for the *p*-benzyloxy-group. Jaffé[17] quotes the σ value as —0.415 citing the work of Ingraham *et al.*[18] However these authors state that their value was obtained from the data of Dippy and Lewis[19] on dissociation constants of carboxylic acids. In fact this work contains no reference to *p*-benzyloxybenzoic acid. Oki and Iwamura[20] in their i.r. studies also used Jaffé's value of —0.415 for the *p*-benzyloxy-group. It is clear that this value is suspect. Our two differently based values are both close to the σ value of the *p*-methoxy-group as seems reasonable.

We thank the Fundacão de Amparo à Pesquisa do Estado de São Paulo (FAPESP) for assistance.

[5/2077 *Received*, 24*th October*, 1975]

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[17] H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[18] L. L. Ingraham, S. Corse, G. F. Bailey, and F. Still, *J. Amer. Chem. Soc.*, 1953, **74**, 2297.

[19] F. J. Dippy and R. N. Lewis, *J. Chem. Soc*, 1937, 1426.

[20] M. Oki and H. Iwamura, *Bull. Chem. Soc. Japan*, 1959, **32**, 955.