Competition between S_N2 and (general acid-catalysed) E1cB reactions in the aqueous decomposition of methyl *N*-(substituted phenoxycarbonyl)sulfamate esters †

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The aqueous reaction mechanisms of methyl *N*-(substituted phenoxycarbonyl)sulfamates **4a**–**d** were examined in the entire pH range 0–14 at 50 °C. The pH–rate profiles indicate a rate law that includes two pH-independent terms, k_a (s^{-1}) in acid and k_p (s^{-1}) around neutral pH, with $k_a > k_p$, and a hydroxide-ion dependent term, k_{OH} ($dm^3\ mol^{-1}\ s^{-1}$), at high pH. In acid, product analysis reveals that two competitive reactions are involved for hydrolysis with $k_a = k_{CO} + k_{Me}$: a general acid-catalysed acyl–oxygen bond cleavage reaction of anions $\mathbf{4}^-$ (k_{CO}) and a methyl–oxygen bond cleavage reaction resulting from water attack at the methyl carbon of neutral compounds **4** (k_{Me}). For all compounds **4** investigated the k_{Me} reaction is the dominant pathway (*i.e.*, >79%) in 1.0 mol dm^{-3} HCl solution. In contrast to k_a, the spontaneous hydrolysis reaction of $\mathbf{4}^-$, k_p, takes place exclusively by acyl–oxygen bond cleavage and leads to the formation of methoxysulfonyl isocyanate as free intermediate. As observed in acid for the k_{Me} reaction, the k_{OH} reaction of $\mathbf{4}^-$ is best rationalized by a S_N2_{Al} mechanism in which hydroxide ion attacks anions $\mathbf{4}^-$ at the saturated methyl carbon leading to methyl–oxygen bond cleavage.

Sulfamic acid H_2NSO_3H and its sulfamoyl and sulfamide derivatives R_2NSO_2G (G = N_3, OR, halide, and NR_2, respectively) have been the subject of extensive and authoritative reviews.[1] However, studies of the corresponding *N*-acyl derivatives (*i.e.*, $RCONHSO_2G$) have not been extensive despite the possible implications the mechanistic aspects of the reactions of these compounds may have for the (still controversial) aqueous reaction mechanisms of phosphate and sulfate esters.[2]

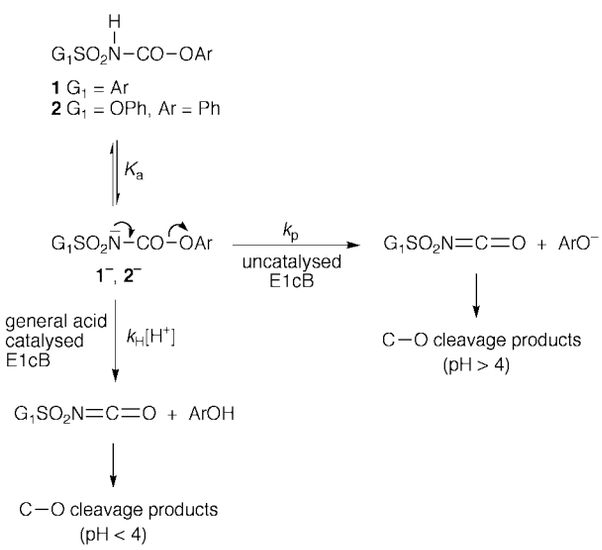
Recently we have been looking at the reaction mechanisms involved in the aqueous decomposition of unusually weak nitrogen anions of type G_1–SO_2N^-CO–G_2 (with G_1 and/or G_2 = alkoxy or aryloxy leaving groups).[2–4] Our study of aryl *N*-(phenylsulfonyl)carbamate esters **1**[3] (pK_a = 2–3) and phenyl *N*-(phenoxycarbonyl)sulfamate **2**[2] (pK_a = 1.18) allowed us to demonstrate that a general acid catalysis may occur in an E1cB process to assist leaving group departure, as observed for the C–O bond cleavage reaction of anions $\mathbf{1}^-$ and $\mathbf{2}^-$ at pH < 4 (Scheme 1). In addition, our kinetic results showed that in the entire pH range both **1** and **2** hydrolyse exclusively by way of their anionic form with 100% C–O bond cleavage.

In contrast to C–O cleavage, the S–O breaking reaction observed in acid with certain aryl *N*-(methoxycarbonyl)sulfamates **3** (pK_a = 0.4–2.4) appears to be specifically hydronium-

ArO–SO_2NHCO–OMe

3

ion-catalysed.[4] In the latter case, however, the lack of any observed buffer effect coupled with the observation of relatively large isotopic dependence ($k_{H_2O}/k_{D_2O} \approx 2$) prevented us from unequivocally distinguishing between two paths: an *intramolecular* general acid-catalysed decomposition (by S–O cleavage) of neutral compounds **3** and an *intermolecular* general



Scheme 1 Uncatalysed and general acid catalysed E1cB reactions observed[2,3] for the aqueous decomposition (by C–O bond cleavage) of weakly basic nitrogen anions $\mathbf{1}^-$ and $\mathbf{2}^-$ (pH range 0–11).

acid-catalysed S–O cleavage decomposition of anions $\mathbf{3}^-$ with a Brønsted α value in the range 0.9–1.[5]

The present work is a continuation of our investigation of the aqueous reaction mechanisms of [(carbonyl)amino]sulfonyl-linked derivatives, G_1–SO_2NHCO–G_2. We are now interested in determining which mechanisms are involved, especially in acid, when G_1 = OMe and G_2 = OAr (compounds **4**, Table 1). Since ArO^- is a much better leaving group than MeO^- and since C–O cleavage is much easier than S–O cleavage, it is expected that the anions $\mathbf{4}^-$ will decompose only through the carbonyl group, as observed for compounds **1** and **2**. However, the aqueous reactivity of the neutral form of **4** (pK_a = 1.7–2.3)[6] might supplant, in acid, the expected general acid-catalysed E1cB reaction of anions $\mathbf{4}^-$. Indeed, owing to the remarkable leaving group ability of the *N*-(aryloxycarbonyl)sulfamate moiety in the pH

† Kinetic data and their derivation are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/b0/b000208i

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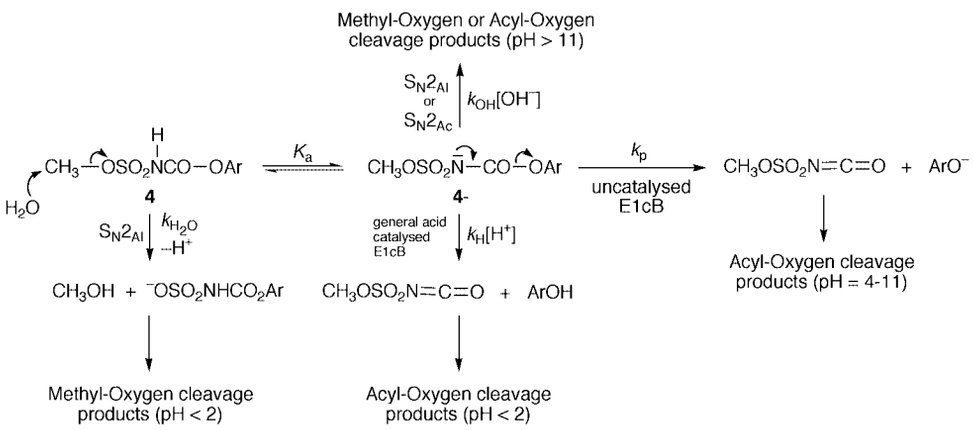
Table 1 Values of pK_a and rate constants for the hydrolysis reactions of compounds **4** determined as kinetically apparent constants (50 °C, μ = 1.0 mol dm^{-3}) and spectrophotometric titration (25 °C, μ = 1.0 mol dm^{-3})

Cpds **4** CH_3OSO_2-NHCO$_2$Ph-X	X	pK_{app} [a]	pK_a [b]	$k_a/10^{-3}$ s^{-1} [a,c]	k_p/s^{-1} [a,d]	k_{OH}/dm^3 mol^{-1} s^{-1} [a]	k_{OH}/dm^3 mol^{-1} s^{-1} [e]
4a	4-CN	1.77 ± 0.10	1.50 ± 0.03	(9.55 ± 0.10)	(3.97 ± 0.01) × 10^{-3}	(1.37 ± 0.06) × 10^{-3}	(1.26 ± 0.08) × 10^{-3}
4b	3-Cl	1.87 ± 0.02	2.07 ± 0.04	(7.55 ± 0.19)	(1.40 ± 0.03) × 10^{-4}	(1.69 ± 0.12) × 10^{-4}	(1.79 ± 0.05) × 10^{-4}
4c	4-Cl	1.97 ± 0.02	2.02 ± 0.05	(7.00 ± 0.19)	(4.00 ± 0.07) × 10^{-5}	(1.54 ± 0.07) × 10^{-4}	(1.49 ± 0.03) × 10^{-4}
4d	H	2.25 ± 0.04	2.21 ± 0.06	(5.85 ± 0.24)	(6.43 ± 0.27) × 10^{-6}	(1.32 ± 0.06) × 10^{-4}	(1.57 ± 0.13) × 10^{-4}

[a] Kinetically apparent constant obtained at 50 °C by fitting of eqn. (1) to experimental data points. [b] Ionization constant determined at 25 °C by spectrophotometric titration. [c] Overall first-order rate constant corresponding to the acidic pH-independent region of the pH–rate constant profiles shown in Fig. 1. [d] Spontaneous first-order rate constant corresponding to the plateau region around neutral pH (Fig. 1). [e] Second-order rate constant for hydroxide ion determined at 50 °C from the linear plots of k_{obs} *vs.* [OH$^-$] in the alkaline pH-dependent region (pH 11–13).



Scheme 2 Schematic view of expected mechanistic pathways for hydrolysis of methyl *N*-(substituted phenoxycarbonyl)sulfamate esters **4** in the entire pH range 0–14.

region where the N–H bond remains undissociated (*i.e.*, at pH < 2), it seems reasonable to consider whether the nucleophilic attack of water at the methyl group of **4** (a S$_N$2$_{Al}$ reaction) may efficiently compete with the anticipated general acid-catalysed E1cB reaction, as illustrated in Scheme 2.

Finally, as previously observed with compounds **2**[2] and **3**,[4] it is possible that the aqueous reaction of anions **4**$^-$ exhibits a hydroxide-ion dependence at high pH. In such a case, OH$^-$ attack is expected to take place at the methyl or acyl moieties of **4**$^-$, or at both of them, *via* S$_N$2$_{Al}$ or/and S$_N$2$_{Ac}$ mechanisms respectively (Scheme 2).

Results and discussion

Rate law

The hydrolysis reaction of compounds **4** (at 50 °C and μ = 1.0 mol dm^{-3}) was followed to at least 90% completion in the pH range 0–14. Rate constants k_{obs} were obtained by spectrophotometric monitoring of either the formation of products (*i.e.*, phenols and aryl carbamates in acid, and phenols/phenoxides in more basic media, *vide infra*) or the disappearance of substrates (see Experimental section). For all compounds, good first order kinetics were obtained except in the region between pH 3 and 4 where two kinetic processes were observed (see below). The pH–rate constant profiles, log k_{obs} *vs.* pH, shown in Fig. 1 are characterised by four distinct regions: (1) the appearance of a pH-independent region below pH 1 (k_a) followed by (2) a decrease of log k_{obs} with increasing pH, then (3) a plateau region (k_p) preceding (4) a hydroxide-ion-catalysed hydrolysis reaction (k_{OH}) at high pH. The experimental points were fitted to eqn. (1) where a_H is the hydrogen-ion activity measured at 50 °C, K_W is the autoprotolysis constant of water at 50 °C, and K_{app} the apparent acid dissociation constant of substrates **4** at the same temperature. The values of the constants k_a, k_p, k_{OH}, and K_{app} required to fit the experimental k_{obs} values to eqn. (1) are given in Table 1. The values of K_a determined

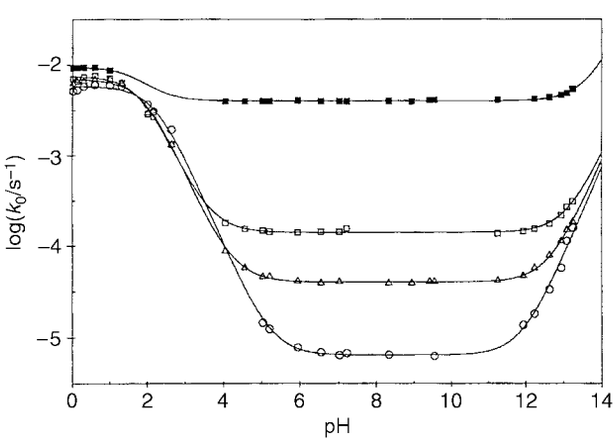


Fig. 1 Plots of log k_0, the buffer-independent rate constants for hydrolysis of methyl *N*-(substituted phenoxycarbonyl)sulfamates **4**, as a function of pH at 50 °C and 1.0 mol dm^{-3} ionic strength (KCl). The lines were computer-generated by iteratively fitting the experimental points (Table S3, Supporting Information) to eqn. (1) given in the text. The values of constants k_a, k_p, k_{OH}, and K_{app} that provided the optimal fits are summarised in Table 1. Symbols: **4a**, (■); **4b**, (□); **4c**, (△); **4d**, (○).

$$k_{obs} = (k_a a_H^2 + k_p K_{app} a_H + k_{OH} K_W K_{app})/(a_H^2 + K_{app} a_H) \quad (1)$$

spectrophotometrically at 25 °C and μ = 1.0 mol dm^{-3} and those of k_{OH} determined at 50 °C from the linear plots of k_{obs} *vs.* [OH$^-$] in the pH region 11–13 are also summarised in Table 1. These values are in reasonable agreement with the apparent K_{app} and k_{OH} values obtained at 50 °C by fitting of eqn. (1) to experimental data points.

pH-Independent hydrolysis (k_p)

The hydrolysis reaction k_p corresponding to the plateau regions around pH 7 in Fig. 1 takes place by acyl–oxygen bond cleavage of anions **4**$^-$ (Scheme 3). Because this reaction occurs at pH

Table 2 Product distributions and rate parameters for hydrolysis of compounds **4** in HCl solutions at 50 °C, μ = 1.0 mol dm^{-3}

Cpds **4** CH_3OSO_2-$NHCO_2Ar$	pK_{ArOH}	HCl/ mol dm^{-3}	ArOH (%)[a] (acyl–oxygen cleavage)	H_2NCO_2Ar (%)[a] (methyl–oxygen cleavage)	$k_{obs}/10^{-3}$ s^{-1}[b,c]	$k_{CO}/10^{-3}$ s^{-1}[b,d]	$k_{Me}/10^{-3}$ s^{-1}[b,e]
4a	7.95	1.0	20.4	79.6	9.59	1.99	7.60
		0.5	19.7	80.3	9.39	1.85	7.54
		0.1	26.3	73.3	8.67	2.28	6.39
		0.05	38.2	61.8	7.33	2.80	4.53
4b	9.08	1.0	8.0	92.0	7.55	6.04	6.95
4c	9.38	1.0	7.7	92.3	6.70	5.39	6.16
4d	9.92	1.0	7.0	93.0	5.85	4.09	5.44

[a] Percentages of phenols and aryl carbamates were determined by spectrophotometric titration with an estimated error ±2% based on an average of six measurements (at six wavelengths, see Experimental section). [b] Standard errors are ±5%. [c] Overall first-order rate constant measured spectrophotometrically. [d] Rate constant of formation of phenols determined from k_{obs} and product ratio given in the previous columns. [e] Rate constant of formation of methyl carbamates determined as indicated in the previous column.

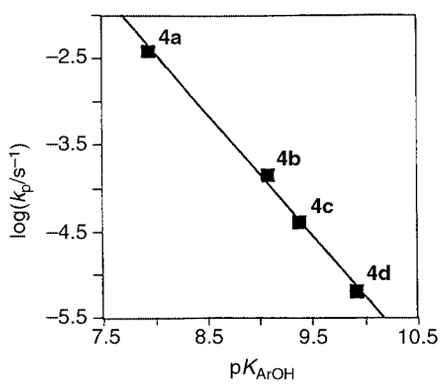
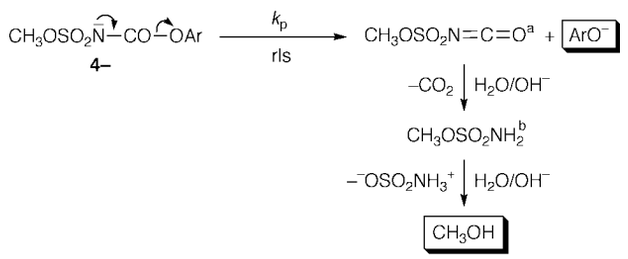


Fig. 2 Plot of log k_p, the spontaneous acyl–oxygen cleavage reaction of anions **4**$^-$ at 50 °C, against pK_a of the corresponding leaving group ArOH. The linear regression equation is: log $k_p = (-1.41 \pm 0.06)$-pK_{ArOH} + (8.86 ± 0.55).



Scheme 3 Mechanism for the pH-independent hydrolysis reaction of anions **4**$^-$ around neutral pH. [a] Reaction intermediate trapped by added piperidine under conditions where piperidine concentration does not affect the observed rate constant $k_{obs} = k_p$. [b] Not detected after completion at pH > 4 due to concomitant hydrolysis into methanol.

values which are much greater than the pK_a values of substrates **4** (see Table 1), anions **4**$^-$ are assumed to be the unique reactive species.

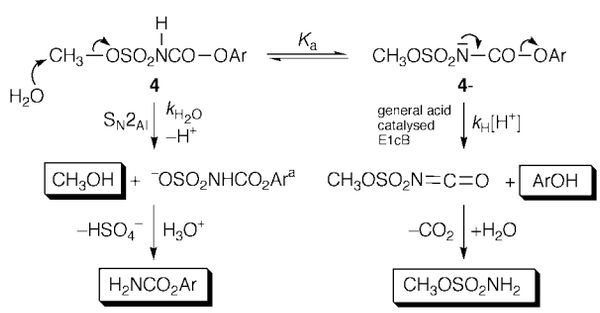
Product analysis carried out by ^{1}H NMR spectroscopy indicates that the hydrolysis reaction k_p yields, in phosphate buffer (pD = 7.84), the corresponding substituted phenols (ArOH/ ArO^-) and transiently methyl sulfamate ester (δ 3.91) which decomposes during the kinetic runs into methanol (δ 3.26).[7] Under the same reaction conditions, authentic samples of methoxysulfonyl isocyanate were shown to hydrolyse into methanol *via* the intermediacy of methyl sulfamate. This supports the proposal that methoxysulfonyl isocyanate is probably formed during hydrolysis. Definitive evidence that the latter compound is indeed formed *as a free intermediate* in the k_p reaction is obtained from a trapping experiment; we have been able to trap it with piperidine under conditions[8] where the concentration of piperidine has no effect on $k_{obs} = k_p$. This result shows that piperidine is not involved in the rate-limiting step but reacts in a subsequent step with the methoxysulfonyl isocyanate intermediate. The trapped product (86% yield) was identified as methyl *N*-(piperidinocarbonyl)sulfamate by comparing its IR and NMR (^{1}H and ^{13}C) spectra with those of an authentic sample of this compound (see Experimental section).

Consistent with the dissociative mechanism of Scheme 3, the k_p reaction depends very strongly on the basicity of the leaving group as observed by the slope of log k_p against pK_{lg}, $\beta_{lg} = -1.41$ (Fig. 2). This figure means that there is a large charge buildup on the phenolic oxygen in going from anions **4**$^-$ to the transition state and, consequently, is consistent with a transition state in which the breaking of the bond to the leaving group is well advanced. The same mechanistic conclusion was reached for the corresponding k_p reactions of carbamate and sulfamate esters **1** and **2** (Scheme 1).[2,3]

For compound **4d** the hydrolysis reaction k_p is characterised by activation parameters $\Delta H^{\ddagger} = 109 \pm 5$ kJ mol^{-1} and $\Delta S^{\ddagger} = -2.87 \pm 10$ J mol^{-1} K^{-1} (obtained from measurements at pH = 6.56 at five temperatures between 50 and 75 °C) which are consistent with those previously observed for the E1cB reactions of closely related compounds (see ref. 3).

Hydronium-ion-catalysed hydrolysis (k_a)

The pH-independent hydrolysis reaction k_a observed in acid (Fig. 1) yields four products in two sets of two. The identity and distribution of products formed at pH < 1 are consistent with the mechanistic pathway shown in Scheme 4. One set of products corresponds to methanol and aryl carbamates (the methyl–oxygen cleavage products in Scheme 4). The second set is methyl



Scheme 4 Competitive reaction pathways involved in the acidic (pH < 4) hydrolysis reaction of compounds **4**: nucleophilic attack of water at the methyl carbon of **4** (S_N2_{Al}) *vs.* general acid-catalysed E1cB decomposition of anions **4**$^-$. [a] Not detected in strong acidic media due to concomitant hydrolysis into aryl carbamates. The accumulation of this intermediate in the pH range 3–4 led to the observation of non-first-order behaviour (see text).

sulfamate and substituted phenols (the acyl–oxygen cleavage products). The product distributions obtained in HCl solutions are summarised in Table 2. The identity of products was confirmed by following the hydrolysis reaction k_a by ^{1}H NMR

spectroscopy in DCl solutions containing substrates **4** and 16 vol% of acetonitrile for reasons of solubility. Methanol, aryl carbamates, methyl sulfamate and substituted phenols were identified at completion by a comparison of NMR peaks with those of authentic samples of pure material obtained in the same reaction conditions. Yields of the two sets of products were checked at 6 half-lives of the stated reaction time and are within 3% of those determined at 4 half-lives, attesting to the stability of these products under the reaction conditions.[9]

As observed at neutral pH, an authentic sample of methoxysulfonyl isocyanate was found to hydrolyse in acid into methyl sulfamate. However, in contrast to what was observed at higher pH (*vide supra*), methyl sulfamate does not decompose into methanol during the reaction time of the acidic reaction.

As previously observed with compounds **3**, for which product methyl carbamate was shown to result from the fast decomposition in acid of *N*-(methoxycarbonyl)sulfamate intermediate $^{-}OSO_2NHCO_2Me$,[4] the carbamate products identified in the present work presumably result from transient $^{-}OSO_2NHCO_2$-Ar species (Scheme 4). Because the stability of these sulfamate species increases with pH (see ref. 4), one may expect they will become non-steady-state intermediates somewhere in the pH range between the two plateau regions k_a and k_p. Accordingly, we found that in cyanoacetate and formate buffers (pH range 3–4) the kinetics were not first-order due to a concomitant side reaction.

Partial rates for the two modes of breakdown (k_{CO} for acyl–oxygen cleavage and k_{Me} for methyl–oxygen cleavage with $k_a = k_{CO} + k_{Me}$) were obtained in HCl solutions from the product ratios ArOH *vs.* H_2NCO_2Ar determined by UV-vis spectrophotometry and the observed first-order rate constants k_{obs} measured at 50 °C and $\mu = 1.0$ mol dm^{-3} (see Experimental section). Partial rate constant values (k_{CO} and k_{Me}) are summarised in Table 2. According to the rate law given in eqn. (1) and the mechanisms and rate constants shown in Scheme 4, in the pH portion where $a_H \gg K_a$ we have $k_{obs} = k_a = k_{CO} + k_{Me}$ with $k_{CO} = k_H K_a$ and $k_{Me} = k_{H_2O}[H_2O]$.

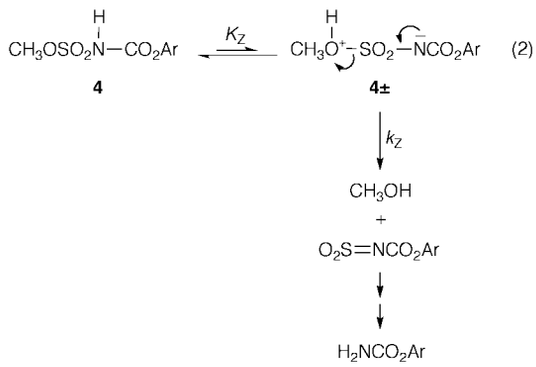
The Brønsted coefficients for the leaving group ArOH, β_{lg}, obtained for k_{CO} and k_{Me} are −0.36 and −0.07, respectively (not shown).[10] These values are consistent with the mechanistic pathway shown in Scheme 4.

The β_{lg} value for the k_{CO} reaction agrees well with that previously observed for aryl sulfonylcarbamate esters **1** ($\beta_{lg} = -0.30$) for which a general acid catalysed E1cB decomposition of anions $\mathbf{1}^-$ was identified as the unique pathway in acid (Scheme 1).[3] This relatively small negative value is consistent with both some degree of acyl–oxygen cleavage in the transition state and departure of the neutral phenols ArOH from anions $\mathbf{4}^-$ (see ref. 4).

The near-zero β_{lg} value obtained for the partial rate k_{Me} is consistent with the absence of C–OAr bond cleavage in the transition state and suggests that the reaction site is not at the carbamate but at the sulfamate moiety. Consistent with a near-zero β_{lg} value, the S_N2_{Al} mechanism shown in Scheme 4 ($k_{Me} = k_{H_2O}[H_2O]$) is further supported by the formation of methyl iodide (identified by ^{1}H NMR at δ 2.08) in hydrolytic conditions where sodium iodide was added to 1.0 mol dm^{-3} DCl solution containing 16 vol% acetonitrile. This indicates that nucleophilic attack of iodide can occur at the methyl group of **4** and strongly suggests that 55.5 mol dm^{-3} water should behave the same way, as illustrated in Scheme 4. For compound **4d**, for which $k_a \approx k_{Me}$ (see Table 2), the activation parameters found in 1.0 mol dm^{-3} HCl solution (from measurements at six temperatures between 25 and 50 °C) are consistent with a S_N2 type reaction at saturated carbon involving water as nucleophile: $\Delta H^{\ddagger} = 81 \pm 5$ kJ mol^{-1} and $\Delta S^{\ddagger} = -38.3 \pm 10$ J mol^{-1} K^{-1}.

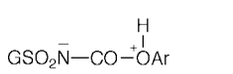
The solvent deuterium isotope effect (k_{H_2O}/k_{D_2O}) measured for the 4-cyano compound **4a** in 1.0 mol dm^{-3} LCl solutions (at 50 °C and $\mu = 1.0$ mol dm^{-3}) is 1.05. This value suggests that the prevalent pathway in acid is the S_N2 reaction (k_{Me}) for which no isotope effect is expected, and is consistent with the observed product distribution (Table 2). In contrast, a substantial value for k_{H_2O}/k_{D_2O} would have been expected for **4a** if the dominant reaction had been the general acid catalysed E1cB reaction k_{CO} (the solvent isotope effect for the acidic reaction of the corresponding 4-cyanophenyl ester **1**, for which $k_a = k_{CO}$, is 2.46).[3]

The possibility that methanol and aryl carbamates products result from the formally neutral zwitterions $\mathbf{4}^{\pm}$, by S–O bond cleavage (eqn. (2) below), is considered unlikely. As discussed



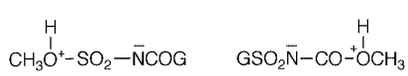
(2)

earlier,[2] the concerted general acid catalysis observed for the acyl–oxygen cleavage reactions of **1**, **2** and **4** is assumed to be *enforced* by the disappearance of the kinetic barrier for phenols expulsion from zwitterions **Z1** (below). Indeed, the latter



Z1 (G = Ar, OAr, OMe)

species are not expected to exist as discrete species in aqueous solution for leaving groups of pK_a < *ca.* 12–13 (at 50 °C), that is, for all leaving phenols. In contrast, if the leaving group is methanol, then the corresponding zwitterions **Z2** and **Z3** (below) are both expected to exist as discrete species in aqueous



media.[2,4] Thus, the observed k_{Me} reaction of compounds **4** could well involve zwitterions $\mathbf{4}^{\pm}$ (**Z2**, G = OAr) as the reactive species from which methanol would be formed by S–O cleavage instead of C–O cleavage, as shown in eqn. (2). Under this hypothesis, and according to eqn. (2) and the values reported in Table 2, $k_{Me} = k_z K_z$ with $k_z < 10^{13}$ s^{-1}, the limiting value below which one may consider $\mathbf{4}^{\pm}$ as a discrete intermediate,[11] and $K_z > 10^{-15}$. However, the fact that the zwitterionic form **Z3** of esters **3** (G = OAr) was shown to be the reactive species for methanol formation *via* acyl–oxygen cleavage with $k_{CO} = k_z K_z \approx 1 \times 10^{-5}$ s^{-1} (at 50 °C in 1.0 mol dm^{-3} HCl solution[4]), strongly suggests that the analogous S–O cleavage reaction of zwitterions $\mathbf{4}^{\pm}$ (eqn. (2)) should exhibit a much slower apparent rate constant k_{Me} under the same reaction conditions (*i.e.*, $k_{Me} = k_z K_z \ll 1 \times 10^{-5}$ s^{-1}).[12] Clearly, this is not the case as k_{Me} values reported in Table 2 are instead 500- to 700-fold greater. In order to accommodate this contradiction with the expected results it is necessary to postulate that a different mechanism is operative for compounds **4**. Finally, contrary to what was observed in 1.0 mol dm^{-3} DCl solution (*vide supra*), methyl iodide would not be expected to show up in the presence of NaI if product methanol were formed by S–O instead of C–O bond cleavage.

Table 3 Brønsted α parameters for the general acid catalysed acyl–oxygen cleavage reactions of anions $\mathbf{1}^-$, $\mathbf{2}^-$ and $\mathbf{4}^-$ as a function of anion stability (k_p)

Cpds $GSO_2NHCO\text{-}OAr$	α [a]	k_p/s^{-1}, 50 °C [b] (acyl–oxygen cleavage)
2 (G = OPh, Ar = Ph)	0.67 [c,d]	9.36×10^{-7} [c]
4d	0.57 [e,f]	6.43×10^{-6} [e]
1 (G = Ph, Ar = Ph)	0.46 [g,h]	3.27×10^{-5} [g]
4c	0.45 [e,f]	4.00×10^{-5} [e]
4b	0.41 [e,f]	1.40×10^{-4} [e]
4a	0.28 [e,f]	3.97×10^{-3} [e]

[a] Obtained from linear plots log k_{AH} *vs.* pK_{AH} (k_{AH} and pK_{AH} being the general acid catalytic coefficient and pK_a of catalyst HA, respectively). [b] Rate constant for the uncatalysed pH-independent acyl–oxygen cleavage reaction of anions $\mathbf{1}^-$, $\mathbf{2}^-$ and $\mathbf{4}^-$ around neutral pH. [c] From ref. 2. [d] From a linear correlation obtained with 5 catalysts HA including hydronium ion. [e] This work. [f] From a linear correlation obtained with only 3 catalysts HA including hydronium ion (see text and the Supporting Information). [g] From ref. 3. [h] From a linear correlation obtained with 7 catalysts HA including hydronium ion.

Buffer catalysis

At pH < 7.5, buffer catalysis with both k_{AH} and k_{A^-} terms is observed for the pH-independent k_p reaction. The effect of the buffer concentrations on k_{obs} was determined by varying the total buffer concentration over a tenfold range at constant pH values. Significant buffer catalysis, with first-order behaviour, was observed only in acetate and phosphate buffers. Typically k_{obs} values changed, linearly, from 5 to 40% in acetate and from 10 to 34% in phosphate with changes in total buffer concentration that routinely ranged from 0.05 to 0.5 mol dm^{-3}. No buffer catalysis was observed with borax. In cyanoacetate and formate buffers (pH range 3–4) a significant buffer effect (up to 50%) was observed but the kinetics were not first-order due to the concomitant hydrolysis reaction of *N*-(aryloxycarbonyl)-sulfamate intermediates into aryl carbamates.

Our kinetic data of the buffer effect on **4a**–**d** are clearly insufficient to give credit to any isolated Brønsted analysis. By and large, however, the Brønsted analyses for the general acid catalysis of compounds **4** lead to α Brønsted parameters that are, according to the discussion of More O'Ferrall,[13] self-consistent and, more importantly, consistent with the reliable α values reported for the general acid catalysis of related compounds **1** and **2** (see Table 3 and Supporting Information). The k_{AH} term is then interpreted as the involvement of a general buffer-acid catalysis to assist ArO^- departure from anions $\mathbf{4}^-$, as previously observed with anions $\mathbf{1}^-$ and $\mathbf{2}^-$.

Similarly, the k_{A^-} term is probably best described as evidence for a general buffer-base catalysis to assist water attack on substrates $\mathbf{4}^-$. As observed in acid, the latter attack presumably takes place at the methyl carbon of $\mathbf{4}^-$ with C–O cleavage according to a general base-catalysed S_N2_{Al} mechanism. It must be emphasized, however, that our data are clearly insufficient to elucidate this catalysis in greater detail.

Hydroxide-ion reaction (k_{OH})

As observed with anions $\mathbf{2}^-$ and $\mathbf{3}^-$, a hydroxide-ion-catalysed reaction is involved with $\mathbf{4}^-$ at high pH (Fig. 1). Apart from the carbonyl center which is the reactive site for $\mathbf{2}^-$ and $\mathbf{3}^-$, anions $\mathbf{4}^-$ may also undergo OH^- attack at the saturated methyl carbon. As observed in acid for the water reaction k_{Me} (*vide supra*), OH^- attack very likely takes place at the methyl carbon of $\mathbf{4}^-$.

For compounds **4b**–**d**,[14] the plot of log k_{OH} against the pK_a of the corresponding phenol (not shown)[15] leads to a near-zero β_{lg} value that is consistent with OH^- attack at both the carbonyl and methyl sites.[16] However, the negative charge of $\mathbf{4}^-$ is expected to provide the lowest electrostatic barrier towards OH^- attack if the attack occurs at the methyl carbon center.

Moreover, the fact that the measured k_{OH} value for compound $\mathbf{2}^-$ ($k_{OH} = 8.42 \times 10^{-5}$ dm^3 mol^{-1} s^{-1} at 50 °C, see ref. 2) is almost two times lower than the measured k_{OH} value for $\mathbf{4d}^-$ (see Table 1) suggests that these two compounds have two different reaction sites for OH^- attack. Indeed, assuming that the reactive site for $\mathbf{4d}^-$ is the same as that for $\mathbf{2}^-$, that is, the carbonyl center, then the lowest value of k_{OH} would have been expected for $\mathbf{4d}^-$, not for $\mathbf{2}^-$. This expectation is due to the electron-withdrawing effect of the phenyl substituent of $\mathbf{2}^-$ (as opposed to the electron-donating effect of the methyl substituent of $\mathbf{4d}^-$) which should render the negative charge of $\mathbf{2}^-$ more extensively delocalized to the sulfonyl center thus providing less electrostatic repulsion towards OH^- attack at the carbonyl center. This view is supported by the fact that phenolate expulsion from $\mathbf{2}^-$ resulting from the C–O cleavage reaction k_p occurs at 50 °C almost 7 times more slowly than that from $\mathbf{4d}^-$ (see Table 3). Thus, the above consideration led us to favour a S_N2_{Al} mechanism in which OH^- attacks anions $\mathbf{4}^-$ at the saturated methyl carbon.

Experimental

Materials

Organic chemicals were purified by distillation or recrystallization prior to use. Water was distilled and deionized on a Water-Purification System Milli-Q (Millipore Apparatus). Elemental analyses were performed by the Analytical Service of the University Paul Sabatier. IR spectra were recorded with a Perkin-Elmer 883 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with a Bruker AC-80 or AC-250 spectrometer (80 and/or 250 MHz for ^1H and 50.32 MHz for ^{13}C).

All methyl *N*-(substituted phenoxycarbonyl)sulfamates **4** were obtained in 62–75% yield by treating methanol with the [*N*-(substituted phenoxycarbonyl)sulfamoyl] chlorides prepared from chlorosulfonyl isocyanate and the corresponding phenols, as described by Graf.[17]

Methyl *N*-(4-cyanophenoxycarbonyl)sulfamate (4a): ^1H NMR (80 MHz, $CDCl_3$, 25 °C, TMS): δ 3.92 (s, 3H, CH_3), 7.21 and 7.57 (AB syst., aryl 4H, $J_{A\text{-}B} = 8.6$ Hz), 12.08 (s, 1H, NH); ^{13}C NMR (50.32 MHz, acetone-d_6, 25 °C, TMS): δ 59.89 (OCH_3), 111.06 (aryl C^{IV}–CN), 118.64 (C≡N), 123.77 and 134.78 (aryl C^{III}), 149.20 (C=O), 154.23 (aryl C^{IV}–O); IR (KBr, ν_{max}/cm^{-1}) 3110 (N–H), 2252 (C≡N), 1774 (C=O), 1601 (aryl C=C), 1480 and 1229 (SO_2NCO), 1387 and 1157 (SO_2). $C_9H_8ClN_2O_5S$ (256.23): calcd C 42.19, H 3.15, N 10.93; found C 42.09, H 3.10, N 11.01%.

Methyl *N*-(3-chlorophenoxycarbonyl)sulfamate (4b): ^1H NMR (80 MHz, $CDCl_3$, 25 °C, TMS): δ 3.96 (s, 3H, CH_3), 6.95–7.20 (m, aryl 4H), 11.87 (s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$, 25 °C, TMS): δ 59.06 (OCH_3), 119.47–130.27 (aryl C^{III}), 134.65 (aryl C^{IV}–Cl), 149.43 and 150.41 (aryl C^{IV}–O and C=O); IR (KBr, ν_{max}/cm^{-1}) 3177 (N–H), 1739 (C=O), 1470 and 1243 (SO_2NCO), 1396 and 1174 (SO_2). $C_8H_8ClNO_5S$ (265.67): calcd C 36.17, H 3.04, N 5.27; found C 35.47, H 3.01, N 5.13%.

Methyl *N*-(4-chlorophenoxycarbonyl)sulfamate (4c): ^1H NMR (80 MHz, acetone-d_6, 25 °C, TMS): δ 4.06 (s, 3H, CH_3), 7.28 and 7.46 (AB syst., aryl 4H, $J_{A\text{-}B} = 9.2$ Hz); ^{13}C NMR (50.32 MHz, acetone-d_6, 25 °C, TMS): δ 59.77 (OCH_3), 124.20 and 130.38 (aryl C^{III}), 132.06 (aryl C^{IV}–Cl), 149.72 and 149.80 (aryl C^{IV}–O and C=O); IR (KBr, ν_{max}/cm^{-1}) 3183 (N–H), 1734 (C=O), 1469 and 1234 (SO_2NCO), 1398 and 1170 (SO_2). $C_8H_8ClNO_5S$ (265.67): calcd C 36.17, H 3.04, N 5.27; found C 36.01, H 2.91, N 5.26%.

Methyl *N*-(phenoxycarbonyl)sulfamate (4d): ^{1}H NMR (80 MHz, $CDCl_3$, 25 °C, TMS): δ 3.77 (s, 3H, CH_3), 6.80–7.20 (m, aryl 5H), 11.90 (s, 1H, NH); ^{13}C NMR (50.32 MHz, $CDCl_3$, 25 °C, TMS): δ 55.03 (OCH_3), 121.44–129.52 (aryl C^{III}), 149.84 and 149.96 (aryl C^{IV}–O and C=O); IR (KBr, ν_{max}/cm^{-1}) 3247 (N–H), 1754 (C=O), 1454 (SO_2NCO), 1370 and 1189 (SO_2). $C_8H_9NO_5S$ (231.22): calcd C 41.56, H 3.92, N 6.06; found C 41.46, H 3.84, N 6.03%.

The trapped product methyl *N*-(piperidinocarbonyl)sulfamate was synthesized by treating methoxysulfonyl isocyanate, prepared according to the procedure described by Lattrell and Lohaus[18] (3 steps, overall yield 26%), with piperidine (59% yield) as described previously.[3]

Methoxysulfonyl isocyanate: $C_2H_3NO_4S$ (137.1); bp 55–57 °C/10.50 torr (lit.[18] 53–54 °C/10 torr); ^{1}H NMR (80 MHz, C_6D_6, 25 °C, TMS): δ 3.15 (s, 3H, CH_3); ^{13}C NMR (50.32 MHz, C_6D_6, 25 °C, TMS): δ 59.45 (OCH_3), 129.96 (N=C=O); IR (NaCl plates, ν_{max}/cm^{-1}) 2972 (CH_3), 2268 (N=C=O), 1403 and 1200 (SO_2).

Methyl *N*-(piperidinocarbonyl)sulfamate. $C_7H_{14}N_2O_4S$ (222.26); ^{1}H NMR (80 MHz, CD_3CN, 25 °C, TMS): δ 1.50–1.60 (m, 6H, CH_2), 3.34–3.38 (m, 4H, CH_2), 3.90 (s, 3H, CH_3); ^{13}C NMR (50.32 MHz, CD_3CN, 25 °C, TMS): δ 24.84, 26.44 and 46.24 (CH_2), 59.16 (OCH_3), 161.99 (C=O); IR (soln. $CHCl_3$, ν_{max}/cm^{-1}) 3316 (N–H), 1679 (C=O), 1466 and 1280 (SO_2NCO), 1403 and 1174 (SO_2).

Product studies

The product distributions for the hydrolysis of methyl *N*-(substituted phenoxycarbonyl)sulfamates **4** in HCl solutions were obtained, as previously described,[19] by determining by UV-vis spectrophotometry the product ratios ArOH *vs.* H_2NCO_2Ar. Final and intermediate products formed during the hydrolysis of compounds **4** at various pH were all identified from ^{1}H NMR spectra (250 MHz, ^{1}H chemical shifts relative to the residual HDO peak at δ 4.68) of the corresponding kinetic runs performed in deuterium oxide solutions containing 16 vol% of acetonitrile for reasons of solubility.

Kinetic measurements and pK_a determinations

The aqueous reactions of compounds **4** were monitored at 50 °C by UV-vis spectrophotometry (using a Perkin-Elmer Lambda 7 or Hewlett-Packard 8453 spectrophotometer attached to a thermostated water bath). Suitable wavelengths for the kinetic studies were selected by repetitive spectral scanning of the reactions. Thus, the reactions were followed by monitoring the increase in the absorbance of the phenol/phenolate ion and/or aryl carbamates at $\lambda = 280$ nm (pH ≥ 8) and $\lambda = 250$ nm (pH ≤ 8) for **4a**, at $\lambda = 245$ nm (pH ≥ 8) and $\lambda = 275$ nm (pH ≤ 8) for **4b**, at $\lambda = 245$ nm (pH ≥ 9) and $\lambda = 280$ nm (pH ≤ 9) for **4c**, and at $\lambda = 240$ nm (pH ≥ 10) and $\lambda = 270$ nm (pH ≤ 10) for **4d**. The disappearance of the absorbance of ester **4a** was also followed at $\lambda = 230$ nm. Rate constants k_{obs} were obtained as described in previous papers.[2–4]

pK_a values of compounds **4** were spectrophotometrically determined at 25 °C as previously described.[4]

References and notes

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6 This work (Table 1).

7 Methanol, methyl sulfamate and substituted phenols were identified by a comparison of NMR peaks with those of authentic samples of pure material obtained in the same reaction conditions.

8 Hydrolysis of **4a** (Table 1) in 0.25 mol dm^{-3} piperidine buffer, $\mu = 1.0$ mol dm^{-3}, pH = 11.07, 50 °C.

9 This means that final products methanol and substituted phenols cannot be formed from subsequent decompositions of methyl sulfamate and corresponding aryl carbamates, respectively.

10 The linear regression equations obtained are: log $k_{CO} = (-0.36 \pm 0.05)pK_{ArOH} + (0.11 \pm 0.46)$ and log $k_{Me} = (-0.07 \pm 0.02)pK_{ArOH} - (1.54 \pm 0.16)$.

11 A molecular species is no longer considered as a discrete intermediate (*i.e.*, as a minimum on the potential energy surface) if the rate constant for its decomposition is on the order of a bond vibration frequency, *i.e.*, *ca.* 6.2×10^{12} s^{-1} at 25 °C.

12 Assuming that K_z (**Z2**) ≈ K_z (**Z3**), with K_z as defined in eqn. (2), and given that one may extrapolate at 50 °C k_z (**Z2**) = 8×10^5 s^{-1} (S–O cleavage) and k_z (**Z3**) ≈ 10^{12} s^{-1} (C–O cleavage) from the linear Brønsted relationships log k_p *vs.* pK_{ArOH} obtained with compounds **3** and **1** or **4**, respectively (see refs. 2 and 4 for details and limitations), one may estimate k_zK_z (**Z2**)/k_zK_z (**Z3**) ≈ k_z (**Z2**)/k_z (**Z3**) ≈ $8 \times 10^5/10^{12} = 8 \times 10^{-7}$.

13 R. A. More O'Ferrall, *J. Chem. Soc. B*, 1970, 274.

14 As previously observed with the cyano derivative of esters **3**, interference from reaction of hydroxide ion with the cyano group of **4a** led to a second order rate constant k_{OH} which lies *ca.* 0.75 log unit above the line defined by **4b**–**d.**

15 The linear regression equations obtained with both the measured and the kinetically apparent k_{OH} values for **4b**–**d** (Table 1) are: log $k_{OH} = (-0.05 \pm 0.07)pK_{ArOH} - (3.27 \pm 0.7)$ and log $k_{OH} = (-0.13 \pm 0.01)pK_{ArOH} - (2.60 \pm 0.04)$, respectively.

16 For the carbonyl site, the addition step of the corresponding S_N2_{Ac} mechanism (an addition–elimination process) is expected to be rate-determining.

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