The mechanisms of the hydrolyses of *N*-nitrobenzenesulfonamides, *N*-nitrobenzamides and some other *N*-nitro amides in aqueous sulfuric acid[1]

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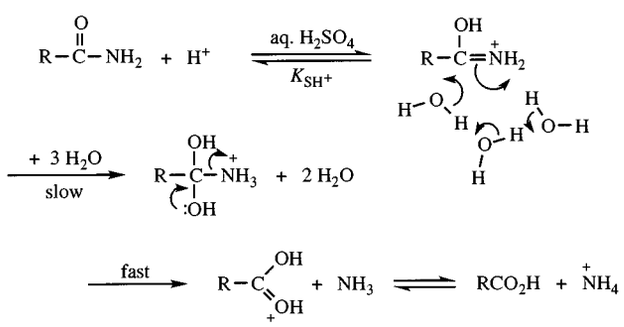
The mechanisms of the hydrolysis reactions of some *N*-nitrobenzenesulfonamides ($YC_6H_4SO_2NHNO_2$), *N*-nitrobenzamides ($YC_6H_4CONHNO_2$) and *N*-methyl-*N*-nitrobenzamides ($YC_6H_4CON(CH_3)NO_2$) have been determined in aqueous sulfuric acid using the excess acidity method. Also studied were *N*-methyl-*N*-nitroacetamide and nitrourea, with *N*,*N*-dinitromethylamine for comparison. *N*-Nitrobenzenesulfonamides give either $YC_6H_4SO_2^+$ and NH_2NO_2 (electron-donating Y) or $YC_6H_4SO_2NH_2$ and NO_2^+ (electron-withdrawing Y) in A1 processes; the change in product is reflected in the different ρ^+ values found for the two modes of cleavage. *N*-Nitrobenzamides behave similarly in strong acid, with an A1 reaction following presumed *O*-protonation, but in more moderate acid they exhibit a neutral water-catalysed hydrolysis mechanism, and in dilute acid the parent *N*-nitrobenzamides actually show hydroxide catalysis. *N*-Methyl-*N*-nitroacetamide shows only the neutral water-catalysed process. Nitrourea has an A1 acid-catalysed hydrolysis reaction in acid, analogous to the known B1 mechanism in base (also visible in dilute sulfuric acid), but has no water reaction; the pH-rate profile for the hydrolysis of this substance is here extended into the non-ideal acid region. *N*,*N*-Dinitromethylamine loses NO_2^+ in an A1 process following initial nitro-group protonation, giving *N*-nitromethylamine which is identifiable by its known hydrolysis rate. Activation parameters, $m^*m^‡$ slopes and ρ^+ values given by the excess acidity analysis are shown to be compatible with the postulated mechanisms.

Introduction

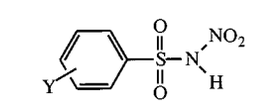
Despite some early controversy,[2] it is now widely accepted that the normal acid-catalysed hydrolysis mechanism for regular amides, acetamide, benzamide, *etc.* is initial *O*-protonation followed by rate-determining water attack at the carbonyl group.[3] There are modifications of this; for instance some years ago we proposed a cyclic mechanism involving three water molecules, shown in Scheme 1,[4] to account for the fact that at



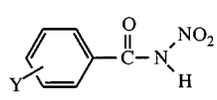
Scheme 1

least in dilute acid the reaction is third-order in water. This modification accounts quite well for the observation that in contrast to esters, amide hydrolysis is accompanied by very little ^{18}O exchange,[5] loss of ammonia being fast and ammonium ion formation rendering the reaction essentially irreversible.

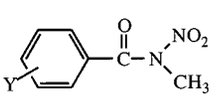
However, amides with special structural features can have other acid-catalysed hydrolysis mechanisms. For instance β-lactams ring-open following initial *N*-protonation,[4,6] *N*-toluoylpyrroles form a tetrahedral intermediate reversibly which then ring-protonates and cleaves,[7] and *N*-*tert*-butyl amides hydrolyse *via* alkyl carbon–nitrogen bond fission.[8] *N*-Nitrosoamides hydrolyse *via* S_N2 displacement of the N-conjugate acid.[9] The work in this paper concerns a variety of *N*-nitroamides, analysing available rate constants as a function of acid concentration and temperature for some *N*-nitrobenzenesulfonamides **1**,[10,11] *N*-nitrobenzamides **2**[12] and *N*-



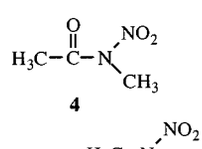
1
Y = 4-OCH_3, 4-CH_3, 3-CH_3, H, 4-Cl, 4-Br, 3-Br, 3-CO_2H, 3-NO_2, 4-NO_2, 3,5-Cl_2, 3,5-$(NO_2)_2$



2
Y = 4-CH_3, 3-CH_3, H, 4-Cl, 4-Br, 3-Br, 3-NO_2, 4-NO_2, 3,5-$(NO_2)_2$



3
Y = 4-OCH_3, 4-CH_3, H, 4-Cl, 4-CF_3



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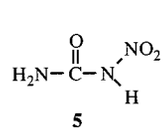

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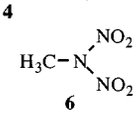


6

methyl-*N*-nitrobenzamides **3**,[13] *N*-nitroacetamide **4**,[13] nitrourea **5**,[14,15] and also *N*,*N*-dinitromethylamine **6** for comparison;[16] Kuznetsov's group also studied some *N*-methyl- and other *N*-alkyl-*N*-nitrobenzenesulfonamides[17] but there are no rate constants given in that paper.

The technique used to analyse the rate constant data is the excess acidity method,[18] which has been used to determine the mechanisms of a variety of reactions in aqueous sulfuric and perchloric acids, among them the hydrations of fluoroalkyl-substituted vinyl ethers,[19] the cyclisations of substituted imidazolines,[20] alkene hydrations,[21] thioacetal hydrolyses,[22] methyl azophenyl ether cleavages[23] and aromatic hydrogen exchange processes.[24] Most recently it has been used to show that the mechanism of decomposition of aliphatic *N*-nitroamines to N_2O and alcohols in aqueous sulfuric acid is an S_N2 displacement by water or hydrogensulfate ion at the alkyl group,[25] and that the parent molecule, nitramide (NH_2NO_2), decomposes

Table 1 Intercept $\log(k_0/K_{SH^+})$ values for substituted *N*-nitrobenzenesulfonamides and -benzamides[a]

Substituent Y	σ^+ [b]	Intercept for **1** [c]	Intercept for **2** [d]
4-OCH_3	−0.778	−8.752 ± 0.040	—
4-CH_3	−0.311	−9.974 ± 0.023	−8.73 ± 0.11
3-CH_3	−0.069	−10.328 ± 0.025	−9.12 ± 0.12
H	0.0	−10.641 ± 0.025	−9.46 ± 0.13
4-Cl	0.114	−10.842 ± 0.024	−10.17 ± 0.14
4-Br	0.150	−10.834 ± 0.026	−10.15 ± 0.14
3-Br	0.391	−10.967 ± 0.028	−10.64 ± 0.15
3-CO_2H	0.32[e]	−11.162 ± 0.029	—
3-NO_2	0.710	−11.292 ± 0.028	−11.91 ± 0.18[f]
4-NO_2	0.790	−11.320 ± 0.026	−12.02 ± 0.18[f]
3,5-Cl_2	0.746	−11.280 ± 0.028	—
3,5-$(NO_2)_2$	1.420	−11.576 ± 0.029	−12.33 ± 0.19[f]

[a] Data for **1** from refs. 10 and 11, and for **2** from ref. 12. [b] From ref. 32 unless noted. [c] Slope $m^*m^‡$ for all compounds is 1.0946 ± 0.0071. [d] Slope $m^*m^‡$ is 1.013 ± 0.021 unless noted. [e] Ref. 33. [f] Slope $m^*m^‡$ is 1.134 ± 0.024.

similarly in an acid-catalysed process in relatively strong acid media but that the decomposition mechanism involves neutral water molecules without acid catalysis in more dilute acid.[26]

Several possible mechanisms for the reaction of these compounds in strong acid media have been suggested,[10–17] some of them mutually incompatible and some not very reasonable; for instance initial N-protonation is suggested for **1** and **2**,[11,12] which seems implausible considering the presence of an electron-withdrawing nitro group on the same atom. Thus it is of considerable interest to apply a modern, consistent method of analysing reaction rate data obtained in strong acids to these compounds, with the aim of suggesting reasonable mechanisms.

Results

The excess acidity method as used for kinetic data[27] examines plots of log observed pseudo-first-order rate constants k_ψ, minus the log of the medium proton concentration $[H^+]$, against the excess acidity of the medium X,[18] which is shorthand for an activity coefficient ratio of the form $\log(f_{B^*}f_{H^+}/f_{B^*H^+})$.[28] This is called the excess acidity because it represents the 'extra' acidity of the medium due to its non-ideal nature. It has the useful property of being 0 in the standard state of unit activity coefficient, the same hypothetical ideal 1 mol dm^{-3} acid solution that is the standard state for pH measurements,[28] so the intercept standard-state rate constants obtained can be directly compared with those obtained in dilute solution or buffers.[18] Values of X are available for aqueous sulfuric acid,[28] perchloric acid,[28,29] hydrochloric acid[29] and some other media.[29,30] If the substrate is predominantly unprotonated in the reaction medium these plots are linear for A-S_E2 reactions (rate-determining proton transfer) and A1 processes.[18] An A2 reaction gives a curved plot, and the species reacting with the substrate can be uniquely identified by subtracting (*e.g.*) the log water activity from $\log k_\psi - \log [H^+]$ and plotting the result against X until linearity is achieved.[18,25] The intercepts are $\log k_0$ in the first case and $\log(k_0/K_{SH^+})$ in the second two cases, K_{SH^+} being the activity-based protonation equilibrium constant for the substrate and k_0 the standard-state reaction rate constant.[18] The slopes of these plots, $m^‡$ in the A-S_E2 case and $m^*m^‡$ for the others, give information about the substrate ($m^* = 1.0$ for primary nitroanilines, 0.6 for amides, *etc.*[28]) and the transition state ($m^‡ < 1$ for A-S_E2 reactions; $m^‡ > 1$ for A1 reactions, $m^‡ \approx 1$ for A2 processes[27]). A modification (not needed in this work) is used for substrates which are predominantly protonated under the reaction conditions.[4,18] Recently it has been found that reactions which are not acid-catalysed also give linear excess acidity plots, *e.g.* $\log k_\psi - \log a_{H_2O}$ is linear in X for

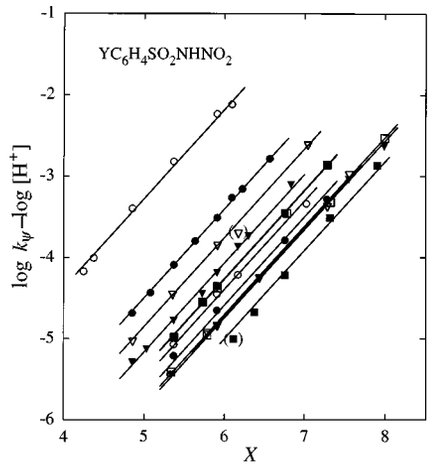


Fig. 1 Excess acidity plot of $\log k_\psi - \log [H^+]$ (25 °C) against excess acidity X for the *N*-nitrobenzenesulfonamides **1**; from left to right the ring substituents Y are 4-OCH_3, 4-CH_3, 3-CH_3, H, 4-Cl, 4-Br, 3-Br, 3-CO_2H, 3-NO_2, 4-NO_2, 3,5-Cl_2 and 3,5-$(NO_2)_2$.

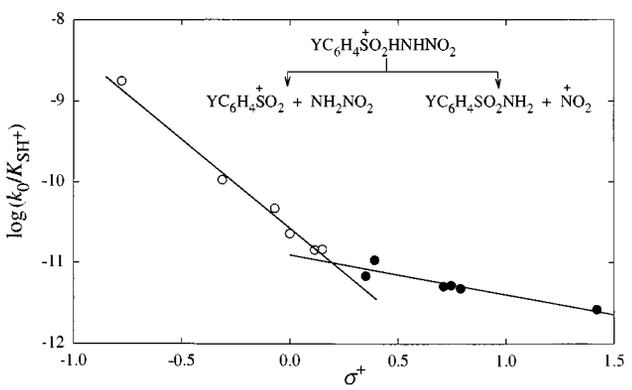


Fig. 2 LFER of the Table 1 intercepts against σ^+ for the *N*-nitrobenzenesulfonamides **1**. For the line on the left r is 0.991, with an r.m.s. error of ±0.092; for the right-hand line, 0.928 and ±0.082.

nitramide decomposition in dilute acid,[26] and this relation was also found to be useful here.

N-Nitrobenzenesulfonamides

Excess acidity plots for **1** are given in Fig. 1; the rate constants are from the Kuznetsov group[10,11] and the excess acidity and $\log [H^+]$ values from published sources.[28] These plots are clearly excellent straight lines. Preliminary analysis showed that the slopes for the 12 substituents were all the same within experimental error, and so to simplify the analysis the same slope was constrained to apply to all of the compounds, *i.e.* all of the experimental data were used to calculate 12 intercepts and one slope. A modified standard computer program that fits data to any equation(s) supplied was used,[31] modified to exclude any data points that, to 95% confidence, do not form part of the same data set as the rest.[24] The results are given in Table 1; of 64 total data points two were excluded (in parentheses in Fig. 1). Thirteen coefficients were calculated with a root-mean-square (r.m.s.) error of only ±0.041 log units. The very low error in the slope, ±0.0071, amply justifies applying the same slope to all compounds. The intercepts are plotted against σ^+ in Fig. 2; as can be seen this linear free energy relationship (LFER) has two parts, one for electron-donating substituents, corresponding to the observed benzenesulfonic acid products,[11] and one for electron-withdrawing ones, corresponding to benzenesulfonamide products.[11] The ρ^+ values found are given in Table 2.

N-Methyl-*N*-nitroacetamide

A standard excess acidity plot of $\log k_\psi - \log [H^+]$ against X for this molecule, using the rate data obtained by the Challis

Table 2 Intercepts, activation parameters, ρ^+ values, *etc.* for the strong acid mechanism[a]

Substrate, cleavage	$\Delta H^‡$/ kcal mol^{-1}	$\Delta S^‡$/ cal mol^{-1} K^{-1}	$m^*m^‡$ slope	$\log(k_0/K_{SH^+})$ at 25 °C[b]	ρ^+
1 − $ArSO_2^+$	—	—	1.0946 ± 0.0071	−10.572 ± 0.040	−2.20 ± 0.15
1 − NO_2^+	—	—	1.0946 ± 0.0071	−10.905 ± 0.080	−0.491 ± 0.099
2 − $ArCO^+$	—	—	1.013 ± 0.021	−9.564 ± 0.085	−2.97 ± 0.39
2 − NO_2^+	—	—	1.134 ± 0.024	−11.553 ± 0.095	−0.547 ± 0.093
3 − $ArCO^+$	26.2 ± 2.9	−8.3 ± 9.8	1.34 ± 0.14	−8.23 ± 0.46	−1.74 ± 0.17
5	28.4 ± 1.0	−4.6 ± 3.5	0.641 ± 0.049	−9.01 ± 0.16	—
6 − NO_2^+	—	—	1.370 ± 0.053	−7.66 ± 0.15	—

[a] Data for **1** from refs. 10 and 11, for **2** from ref. 12, for **3** from ref. 13, for **5** from ref. 14, and for **6** from ref. 16. [b] Intercept of LFER, except for **5** and **6**.

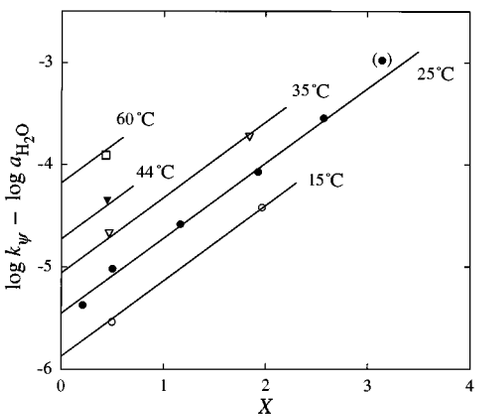


Fig. 3 Plot of log k_ψ − log a_{H_2O} against X at several different temperatures for *N*-methyl-*N*-nitroacetamide **4**

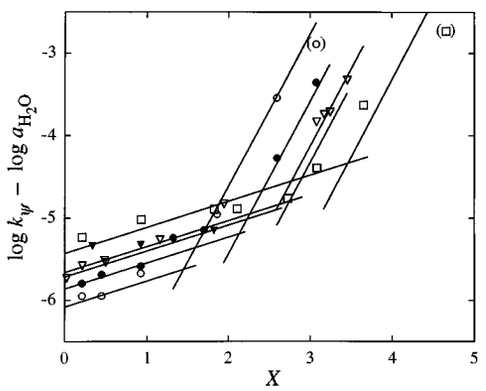


Fig. 4 Plot of log k_ψ − log a_{H_2O} (25 °C) against X for the five *N*-methyl-*N*-nitrobenzamides **3**, illustrating the two different mechanisms. The ring substituents Y are 4-OCH_3 (○), 4-CH_3 (●), H (▽), 4-Cl (▼) and 4-CF_3 (□). For clarity the lines drawn refer to the two mechanisms separately, the combination line not being given.

group,[13] is strongly curved; however, a plot of log k_ψ − log a_{H_2O} is linear, as shown in Fig. 3. Data at several temperatures are available,[13] and thus standard-state activation parameters could be obtained by a multiple linear regression using all the data.[31] The equation used for the activation parameters is essentially that given by Clarke and Glew for equilibria;[34] this involves plotting log k_ψ − log T against $(T - \theta)/T$, rather than against the usual $1/T$, where T is the absolute reaction temperature and θ the standard 25 °C (298.15 K), and gives $\Delta G^‡$ and $\Delta H^‡$ rather than $\Delta H^‡$ and $\Delta S^‡$ as coefficients.[35] (The author finds this a superior method; the *x*-axis is a more natural one and the resulting $\Delta G^‡$ and $\Delta H^‡$ values are less strongly correlated with one another than are $\Delta H^‡$ and $\Delta S^‡$, and hence are more accurate. $\Delta S^‡$ values are easy to calculate afterwards.)[36] The values of X used are corrected to temperature as before,[35] so the same slope m applies at all temperatures, and temperature–correct log a_{H_2O} values were obtained from published sources,[37] so the resulting activation parameters refer only to the reaction and contain no contribution from the medium. The resulting fit of three coefficients [slope *vs.* X, slope *vs.* $(T - \theta)/T$, intercept] to 12 data points has a multiple correlation coefficient r of 0.998 and an r.m.s. error of ±0.050 log k units. The 25 °C intercept, useful for comparison with the other compounds, slope and activation parameters found are given in Table 3. One point was omitted by the program; interestingly this is the point at highest acidity in Fig. 3, which is above the line, probably meaning that another mechanism is taking over at higher acidity.

N-Methyl-*N*-nitrobenzamides

For these compounds, plots of the 25 °C kinetic data[13] as log k_ψ − log [H^+] against X are strongly curved initially and then become linear, and plots of log k_ψ − log a_{H_2O} against X are initially linear and then curve upward. Also, as Challis observed,[13] the graphs cross over, the fastest-reacting compound in dilute acid becoming the slowest-reacting one at higher acid concentrations, and *vice versa*. This can only mean that two mechanisms are operative, and these are illustrated in Fig. 4 as separate lines, five shallow-slope lines at low acidity linear in log k_ψ − log a_{H_2O}, and five steeper-slope lines at higher acidity which are actually linear in log k_ψ − log [H^+]; the latter also appear linear in Fig. 4 because log [H^+] and log a_{H_2O} only vary slowly with X in this acidity region.

Using the rate constant data for **3** to generate meaningful parameters, and the lines in Fig. 4, presented something of a problem as the data are subject to relatively large random error; the rate constants are stated to be reproducible only to ±10%,[13] rather than the 2–3% most kineticists would prefer. There are a total of 51 data points for five compounds, mostly at 25 °C but with data at other temperatures for two of them. Since two mechanisms are involved, in principle five 25 °C intercepts, five excess acidity slopes and two $\Delta H^‡$ values have to be calculated for both, a total of 24 coefficients. Preliminary experimentation showed this to be quite impractical. Consequently it was assumed that, for each mechanism: (*a*) the intercepts were linear in σ^+ (trials showed this to be better than σ in both cases); (*b*) that the same excess acidity slope applied to all compounds, as found for **1** and **2**; and (*c*) that the same $\Delta H^‡$ applied to both the parent **3** and its 4-OCH_3 derivative. This reduces the number of coefficients to be calculated to eight, one ρ^+ value, one LFER intercept (essentially the 25 °C excess acidity intercept for the Y = H parent compound), one excess acidity slope and one $\Delta H^‡$ value (also applicable to the parent) for each mechanism. These could be calculated relatively accurately, and are given in Table 2 for the high-acidity mechanism and Table 3 for the low-acidity one; two of the 51 points were omitted and the overall r.m.s. error was ±0.12 log k units. The excess acidity slope for the low-acidity mechanism still has an error larger than its value, but this was shown to be a real quantity, since assuming it to be zero and only calculating seven coefficients gave a much worse fit to the data.

N-Nitrobenzamides

Rate constants as a function of acid concentration for nine compounds at 25 °C have been determined by the Kuznetsov

Table 3 Intercepts, activation parameters, ρ^+ values, *etc.* for the moderate acid mechanism[a]

Substrate	$\Delta H^{\ddagger}$/ kcal mol^{-1}	$\Delta S^{\ddagger}$/ cal mol^{-1} K^{-1}	*m* slope	log(k_0K_{Hy}) at 25 °C[b]	ρ^+
2	—	—	(0.6)[c]	−6.621 ± 0.016	−0.037 ± 0.023
3	12.7 ± 1.0	−42.2 ± 3.4	0.31 ± 0.64	−5.716 ± 0.025	+0.469 ± 0.058
4	15.92 ± 0.56	−30.1 ± 1.9	0.735 ± 0.020	−5.452 ± 0.029	—

[a] Data for **2** from ref. 12, and for **3** and **4** from ref. 13. [b] Intercept of LFER, except for **4**. [c] Assumed, see text.

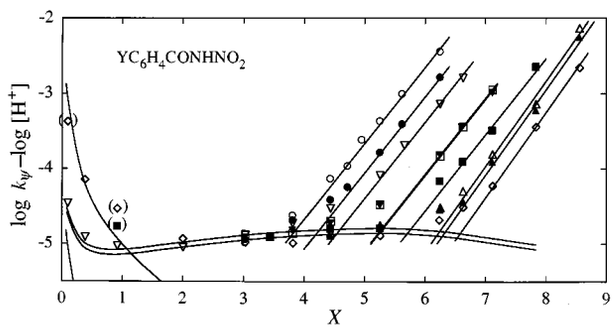


Fig. 5 Plot of log k_ψ − log [H$^+$] (25 °C) against *X* for the *N*-nitrobenzamides **2**; from left to right the ring substituents Y are 4-CH_3 (○), 3-CH_3 (●), H (▽), 4-Cl (▼), 4-Br (□), 3-Br (■), 3-NO_2 (△), 4-NO_2 (▲) and 3,5-$(NO_2)_2$ (◇). For clarity the lines drawn refer to the three different mechanisms separately; see text.

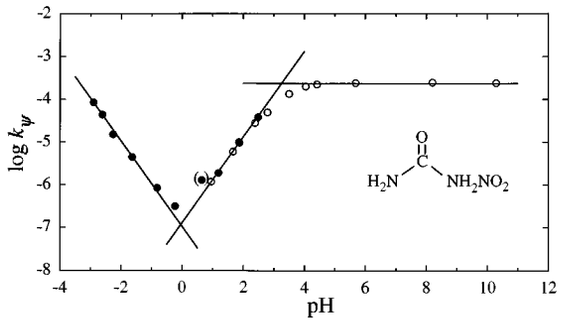


Fig. 6 Log rate constant *vs.* pH profile for nitrourea **5** at 55 °C. Filled circles (●), data of Dewhurst and Lamberton;[14] open circles (○), that of Boopsingh and Briody.[15] The lines refer to the different regions separately, the left one to the acid-catalysed process and the right two to the base-catalysed one; the latter two cross at the pK_a of nitrourea in the buffer media used.[15]

group;[12] these are given as an excess acidity plot in Fig. 5. As can be seen, in strongly acidic media the behaviour of these compounds strongly resembles that of the *N*-nitrobenzenesulfonamides in Fig. 1, except that the slopes corresponding to the two different modes of cleavage[12] are now slightly different from one another. (The observation that both of these slopes are the same for **1** is probably simple coincidence.) The intercepts of these plots are given in Table 1, and the parameters of the derived LFERs are in Table 2.

However, unlike **1**, for **2** all these lines converge to closely similar curves at moderate acidities, implying a change of mechanism, and at the lowest acidities the rate constants increase again, implying a third mechanism. As is apparent from Fig. 5 these latter two mechanisms are not described by many data points, and again compromises had to be made to enable reasonable parameters to be obtained for them. The mechanism at moderate acidity was found to be described by another log k_ψ − log a_{H_2O} *vs.* *X* relationship, and again the assumption was made that the intercepts of this were described by an LFER *vs.* σ^+. Also, the excess acidity slope was fixed at 0.6, because this value has been found to be typical of amides in the past.[28] These assumptions worked well, and the resulting LFER parameters are given in Table 3. At the very lowest acidities it was found that log k_ψ − log a_{H_2O} + log [H$^+$] *vs.* *X* best described the data, with an excess acidity slope of zero, and LFER parameters of +1.37 ± 0.15 for the slope (this is a ρ value, only data for 3-substituted compounds being available) and −7.23 ± 0.20 for the intercept for the parent compound. In all, the three mechanisms were described by 15 coefficients, 9 intercepts and 2 slopes for the high acidity process, and slope and intercept LFER parameters for the other two; overall 74 points were fitted, 3 being omitted, with an r.m.s. error of ±0.056 log *k* units. For clarity, in Fig. 5 lines and curves for the individual mechanisms are given, rather than being combined; at high acidity lines for each compound are drawn, but at moderate and low acidities only curves for the extremes, the slowest and fastest by the operative mechanisms, are provided.

Rate constants for all nine compounds at 4.2% H_2SO_4 and 55.3 °C were measured by the Kuznetsov group;[12] it was not possible to use these to obtain activation parameters (because of the impossibility of separating the different contributions from the two mechanisms operating at this acidity) but they do give a reasonable LFER, with $\rho^+ = 0.592 \pm 0.019$ and intercept = −5.240 ± 0.012, *r* is 0.996 and the r.m.s. error ±0.029.

Nitrourea

The hydrolysis of nitrourea **5** in aqueous sulfuric acid, among other media, was studied by Dewhurst and Lamberton[14] as a function of concentration and temperature. An excess acidity plot of log k_ψ − log [H$^+$] against *X* is linear at acidities above 4 mol dm^{-3}, with the parameters given in Table 2; 11 points were fitted with an r.m.s. error of ±0.079. The excess acidity slope was used to define an acidity function (pH scale) applicable only to **5**,[28] and activation parameters[14,15] were used to correct a tiny temperature difference between this study and that of Boopsingh and Briody[15] in buffer media. The two studies were then combined to give the extended pH–rate profile given as Fig. 6, which contains data obtained by Dewhurst and Lamberton below 4 mol dm^{-3} H_2SO_4 as well. As can be seen the two data sets overlap very well. Two processes are apparent, with the classic slopes of −1, 1 and 0; curve-fitting gives 55 °C values of log(k_0/K_{SH^+}) for the acid-catalysed process as −6.970 ± 0.021, and log(k_bK_w) as −6.886 ± 0.019 for the base-catalysed one, with a pK_a of 3.258 ± 0.031; 21 points were fitted, of which one was omitted, with an r.m.s. error of ±0.049 log *k* units. No neutral water-catalysed reaction is apparent.

N,*N*-Dinitromethylamine

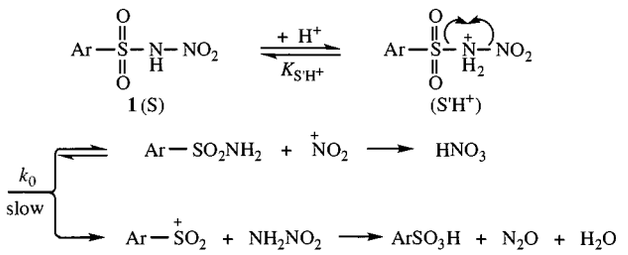
For comparison purposes an excess acidity analysis was performed for the denitration of **6**,[16] the product of which is *N*-nitromethylamine, easily identified because its decomposition rate is identical with that of an authentic sample.[25] The parameters obtained from the linear log k_ψ − log [H$^+$] *vs.* *X* plot are given in Table 2; *r* is 0.997 over six points, with an r.m.s. error of ±0.065.

Discussion

The most obvious mechanism for the reaction of the *N*-benzenesulfonamides **1**, preferred by Kuznetsov and his group,[10,11] is given in Scheme 2. Initial protonation on nitrogen is followed by cleavage of either the N–S or the N–N bonds as shown. (In this and some other cases discussed here, the first-formed nitramide and alkylnitramine decomposition products

were occasionally identified by isolation and analysis,[10] as well as by decomposition rate.)

Deriving excess acidity rate equations for these reactions is not difficult;[18,27] using Scheme 2 the observed rate for an A1



Scheme 2

reaction is given by eqn. (1), where the concentration units are

$$k_\psi[S] = k_0 a_{S'H^+}/f_\ddagger \qquad (1)$$

molarities and the symbols have their usual meanings. We have $K_{S'H^+} = a_S a_{H^+}/a_{S'H^+}$ and $a_S a_{H^+} = [S][H^+] f_S f_{H^+}$, so this becomes eqn. (2).

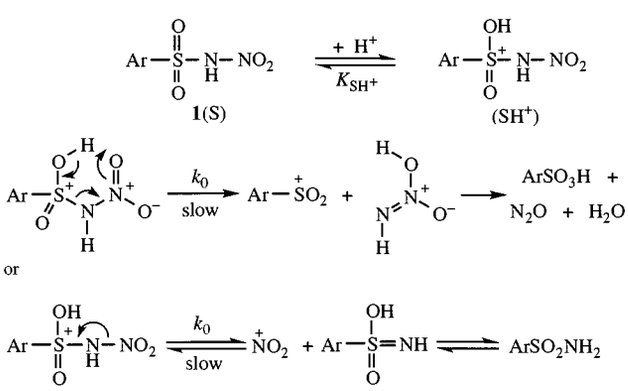
$$k_\psi[S] = (k_0/K_{S'H^+})[S][H^+](f_S f_{H^+}/f_\ddagger) \qquad (2)$$

For unprotonated substrates [S] cancels, and on taking logs and rearranging we obtain eqn. (3), since $\log(f_S f_{H^+}/f_\ddagger) =$

$$\log k_\psi - \log [H^+] = \log(k_0/K_{S'H^+}) + m^*m^\ddagger X \qquad (3)$$

$m^* \log(f_S f_{H^+}/f_{S'H^+}) = m^*m^\ddagger X$.[18,27] This is the equation that gives the linear plots against X in Fig. 1.

However, reaction *via* nitrogen protonation is not the only choice; reaction from the initial oxygen-protonated form is quite possible, as shown in Scheme 3. This would give exactly

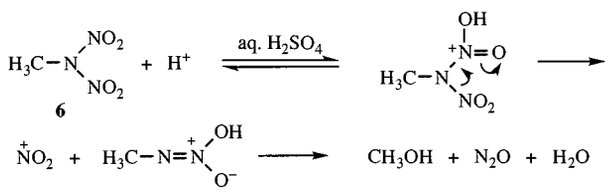


Scheme 3

the same kinetic behaviour as Scheme 2 (except K_{SH^+} replaces $K_{S'H^+}$), since both decomposition modes are A1 processes. For both schemes N–S cleavage will be favoured by electron donors and the ρ^+ value will be large and negative, as the amount of positive charge delocalised into the benzene ring in the transition state increases as $ArSO_2^+$ forms. N–N cleavage will be favoured by electron-withdrawing groups and the ρ^+ will be much less negative as the amount of positive charge to be delocalised decreases as neutral $ArSO_2NH_2$ forms. This is in total agreement with the observed reaction products[10,11] and the LFER in Fig. 2. The presence of NO_2^+ has been demonstrated by adding other aromatics, which become nitrated;[10,11] the denitration was also shown to be reversible.[10,11] Denitration is quite a feasible reaction in these media, as demonstrated by the reaction of dinitromethylamine **6**, which was also shown to be quite a good nitrating agent for other aromatics.[16]

A decision between these two schemes should be based on the site of protonation of these molecules; however, this is not known. Sulfonyl halides are known to protonate on oxygen under stable-ion conditions.[38] Sulfonamides themselves most probably protonate on nitrogen;[39,40] with a strongly electron-withdrawing nitro group on the nitrogen, however, protonation there would surely be far less likely.

One clue comes from the value of $m^*m^\ddagger$ found in this work, see Tables 1 and 2. Although greater than one, it is not *much* greater than one, certainly not equivalent to the $m^\ddagger$ values of 2–3 found for other A1 reactions in sulfuric acid.[27] Since in order to obtain $m^\ddagger$, the observed $m^*m^\ddagger$ values must be divided by m^*, this must mean that m^* is less than one. The known values would have $m^* \approx 1$ for nitrogen protonation,[28] but $m^* \approx 0.5$–0.6 for oxygen protonation,[28] and so oxygen protonation looks to be much more likely. Denitration of **6** has a $m^*m^\ddagger$ value of 1.37; this must protonate on a nitro group, see Scheme 4, and



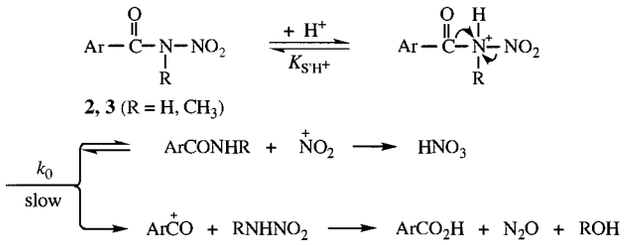
Scheme 4

although the m^* value for nitro-group protonation is not known for sure, one could argue that it should have a value of about 1, since the H_0 acidity scale can be extended into super-acid media by way of the good overlap between the protonation equilibria of 2,4,6-trinitroaniline (presumably on NH_2) and less basic nitro-compounds.[41]

The argument in favour of Scheme 2 is essentially the Ockham's razor[42] one of simplicity, however, since there is now physical evidence against it I think that Scheme 3 is probably the correct mechanism. It is not necessary, of course, that reaction occurs *via* the equilibrium most-stable protonated form, which may not be reactive, as has been found before.[25] However, the m^* value discussed here must be the one concerned with the kinetic pathway, since it is obtained from the reaction kinetics, and so the oxygen-protonated form of **1** is the reactive one. It is evident from the diagrams provided[17] that *N*-alkyl-*N*-nitrobenzenesulfonamides and **1**[10,11] behave similarly.

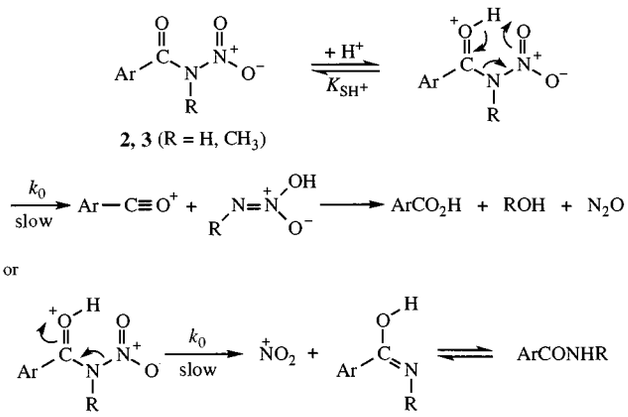
One of the intermediates in Schemes 2 and 3 is the sulfonyl cation $ArSO_2^+$; it is hard to visualise A1 mechanisms for this reaction which do not involve these species, particularly for electron-donating ring substituents. They have not been observed under stable-ion conditions.[38] They have occasionally been proposed as reaction intermediates,[10,11,43] although some authors find them unnecessary, for instance as intermediates in sulfonyl chloride hydrolyses.[44] One resonance structure that can be drawn, especially in the 4-OCH_3 and related cases, has the sulfene $=SO_2$ form, and these are also proposed as reaction intermediates.[45] I think the only reasonable conclusion is that $ArSO_2^+$ species have to be involved in this reaction.

By analogy with **1**, the strong-acid mechanism in Scheme 5 was proposed by the Kuznetsov group[12] for the *N*-nitrobenzamides **2**; this is an *N*-protonation mechanism which again has the virtue of simplicity. However, as in **1** the *N*-protonation of these compounds must be very difficult, and the *O*-protonation mechanism in Scheme 6, the first pathway of which is the one given by the Challis group[13] for the *N*-methyl compound **3**, is greatly to be preferred, for **2** and for **3**, for essentially the same reasons as those given above for **1**. Amides are known to prefer *O*-protonation, as mentioned above, and unlike sulfonyl cations the intermediate acylium ions are well-known reaction intermediates.[46] Again the $m^*m^\ddagger$ slopes are only marginally larger than one, but m^* for amide protonation is known to be 0.5–0.6,[4,28] so the excess acidity slopes are also consistent with oxygen protonation in both cases. Confirmation of Scheme 6 (or



Scheme 5

Scheme 5) comes from the lack of carbonyl ^{18}O exchange found for **3**,[13] and the solvent deuterium isotope effect of less than one observed for **3**,[13] at the higher acidities.

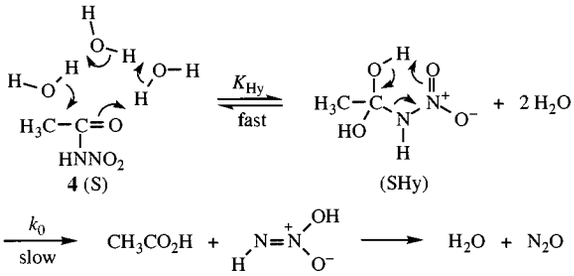


Scheme 6

A comparison of **1**, **2**, **3** and **6** (Table 2) has to take into account the fact that all the parameters have two components, being derived from the composite terms $\log(k_0/K_{SH^+})$ (and $m^*m^{\ddagger}$ for the slopes). Nothing is known about the relative pK_{SH^+} values, although I would guess that **3** would be easiest to protonate (electron-donating methyl), followed by **2**, with **1** most difficult. This may be reflected in the rates of $ArCO^+$ or $ArSO_2^+$ formation, which are in the order **3** > **2** > **1**. The ρ^+ values indicate a higher demand on the substituents in the case of **2**, with **3** having a lower one; this may reflect the relative positions of the transition states along the reaction coordinate for these two processes. The ρ^+ value for **1** is less negative than that for **2**, probably reflecting the greater difficulty sulfur has in transmitting resonance effects. The only available activation parameters are for **3**; the entropy of activation is close to zero, consistent with an A1 process,[13] but the enthalpy of activation is quite large.

The denitration reaction rates are in the order **6** > **1** > **2** (denitration was not observed for **3**[13]). The ρ^+ magnitudes are not helpful here, being the same for both **1** and **2**. Perhaps this reactivity order reflects the stabilities of the various products. Compound **6** gives the *aci*-nitro form of *N*-nitromethylamine (Scheme 4), which forms readily in acid,[25] **1** gives an enol form of a benzenesulfonamide (Scheme 3), and **2** gives the rather unstable enol form of a benzamide (Scheme 6).

Turning to the mechanism which applies at moderate acidity, Scheme 7 is proposed for *N*-nitroacetamide **4**. Initial water attack is assumed to be an equilibrium process, giving an intermediate hydrate (SHy) which then breaks up in the rate-determining step. A mechanism of this type has recently been found to apply to the hydrolyses of acylimidazoles in a variety of acid media.[47] Rate-determining attack of one water molecule on neutral **4** would give exactly the same kinetic behaviour, but this seems less likely as a zwitterionic intermediate would have to be formed initially, whereas the proton switch in Scheme 7 demands no charge transfer at all. Also, as mentioned in the Introduction, amide hydrolysis at these acidities involves three water molecules, and Scheme 7 is the neutral analogue of Scheme 1. Deriving an excess acidity rate equation is again



Scheme 7

straightforward. As before, absolute rate theory demands eqn. (4); and we have $K_{Hy} = a_{SHy}a_{H_2O}^2/a_S a_{H_2O}^3$ and $a_S = [S]f_S$, so

$$k_\psi[S] = k_0 a_{SHy}/f_{\ddagger} \quad (4)$$

eqn. (5) results, which gives, on taking logs and rearranging,

$$k_\psi[S] = (k_0 K_{Hy})[S]a_{H_2O}(f_S/f_{\ddagger}) \quad (5)$$

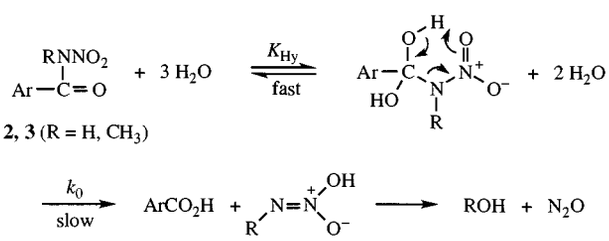
eqn. (6), assuming that the log activity coefficient ratio term

$$\log k_\psi - \log a_{H_2O} = \log(k_0 K_{Hy}) + mX \quad (6)$$

is linear in X, as has been seen before[26,47] (the author knows of no exceptions to this linearity assumption). This is the rate equation that gives the linear plots in Fig. 3.

In contrast to previous assertions,[13] Scheme 7 indicates that the hydrolysis of **4** is not acid-catalysed. The observed increase in rate with acidity is purely an activity coefficient effect, as was previously found for the hydrolysis of nitramide at low acidities.[26] The solvent isotope effect observed for **4** is 0.85–0.9,[13] which compares well with similar values obtained for other carbonyl hydration equilibria.[48]

The same mechanism applies to **2** and **3** at moderate acidities, and this is shown in Scheme 8. Little ^{18}O exchange was observed for **3** at low acidity,[13] which means that the k_0 step in Scheme 8



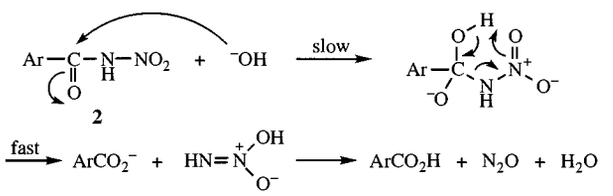
Scheme 8

has to be faster than the reverse of the hydrate formation step; this was found to be true for the acylimidazole hydrolyses.[47] (It is also compatible with rate-determining attack of a single water molecule on **3**.) This does not seem unreasonable in view of the favourable cyclic decomposition mode proposed for the hydrate once it is formed. However, it does imply that the hydrate should accumulate in solution; apparently this aspect has never been investigated for *N*-nitroamides. Carbonyl compounds with strong electron-withdrawing groups are often hydrated in water, the most-quoted example being chloral, CCl_3CHO.[3]

Table 3 contains a summary of parameters which apply to **2**, **3** and **4** reacting in this way. Again these are composite quantities, containing both the hydrate equilibrium constant and the standard-state rate constant. The slopes m are much the same for all three substrates; it is difficult to attach meaning to these quantities, but they do compare very well with the known values, 0.56 ± 0.02 for nitramide reacting by this mechanism,[26] and 0.4–0.5 for the acylimidazoles.[47] The reactions are all faster than those involving the A1 cleavage processes; the relative

reactivities are in the order **4** > **3** > **2**. Perhaps this reflects initial state stabilisation by the aryl rings, possible in **2** and **3** but not in **4**, so **4** will react faster. However, it is not clear why **3** should react more quickly than **2**; **2** has a ρ^+ value of ≈0 but that of **3** is +0.5, which has to mean that **3** has a slight buildup of negative charge at the transition state, probably contributed by the methyl group. The observed solvent isotope effect for **3** is ≈1.5 at low acidities;[13] comparing this with the 0.85–0.9 found for **4** implies that **3** has a more reactant-like transition state than does **4**. (It should be noted that although these solvent isotope effects were measured at equal molarities of H_2SO_4 and D_2SO_4,[13] the H_2O and D_2O activities may not be quite the same in these solutions.) The enthalpies of activation are low, only half the magnitude of those for the A1 reaction, but the entropies of activation are quite negative, which is an argument in favour of the order imposed by the three-water-molecule requirement, see Scheme 7.

Compound **2** has a third mechanism, apparent at very low acidity (see Fig. 5); this is postulated to be a hydroxide addition as shown in Scheme 9. (Invoking reactions of HO^- in an acidic



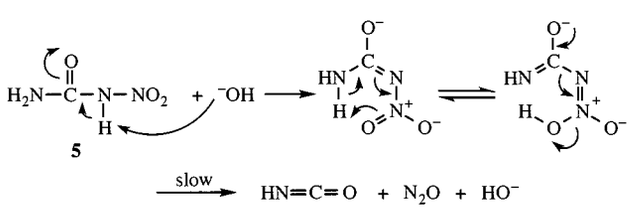
Scheme 9

medium may seem strange, but two other examples of this are now known,[47] one of which is given below.) The electron-withdrawing nitro group present must accelerate this process considerably. An excess acidity rate equation can be based on $k_\psi[S] = k_0 a_S a_{HO^-}/f_\ddagger$, substituting $K_w = a_{H^+}a_{HO^-}/a_{H_2O}$ (one water molecule because the solvent is conventionally omitted from definitions of K_a and K_{SH^+}, so for consistency it is omitted from K_w here also) and $a_S/a_{H^+} = ([S]/[H^+])(f_S/f_{H^+})$, rearranging and taking logs to give eqn. (7), and assuming that the activity

$$\log k_\psi - \log a_{H_2O} + \log [H^+] = \log(k_0 K_w) + \log(f_S/f_{H^+}f_\ddagger) \quad (7)$$

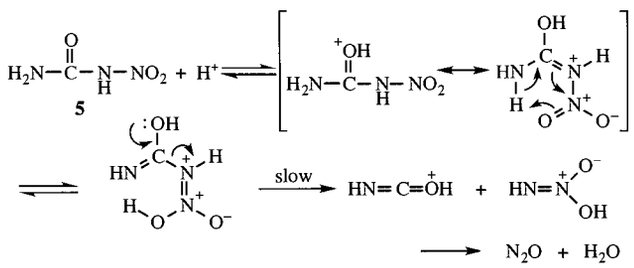
coefficient term is linear in X. In fact the activity coefficient term plays no part, the slope being zero; the standard-state rate constant is about the same as the moderate acidity rate constants for **3** and **4**, but ten times faster than that for **2**, and the ρ value is quite large and positive at +1.37, indicating negative charge buildup at the transition state, as Scheme 9 requires. Presumably the presence of an electron-donating methyl group would slow this process down, which is why it is not seen for **3** and **4**. The ρ value of +0.59 obtained for the 55 °C data for **2** applies to a combination of the weak and moderate acidity mechanisms, since both operate at the acidity used; it is intermediate between the +1.37 of Scheme 9 and the −0.04 of Scheme 8.

The reaction of nitrourea **5** in basic media has been studied by Boopsingh and Briody,[15] and the mechanism that they give is in Scheme 10. This is rather different from Scheme 9; removing



Scheme 10

the N–H in **2** does not achieve anything, but in **5** the highly favourable cyclic process involving the other NH_2 leads to ready decomposition as shown. For the reaction in acid under consideration here, an analogous mechanism involving the *O*-protonated substrate is proposed, given in Scheme 11.



Scheme 11

Although this is rather different from the strong-acid mechanism proposed for **1**–**3**, the parameters for it (given in Table 2) are quite similar, except for the slope $m^*m^\ddagger$. This is only 0.64; dividing by an amide protonation m^* of 0.6 gives an $m^\ddagger$ value only slightly greater than one.

Of interest is the observation that in dilute sulfuric acid the rate of reaction of **5** increases again, see Fig. 6. In fact the rates measured in basic buffers[15] and those in dilute sulfuric acid[14] are contiguous, as Fig. 6 demonstrates, so it is not fanciful to propose hydroxide catalysis in dilute sulfuric acid solutions, and the Scheme 9 proposal for **2** is thus supported. Nitrourea has an acidic hydrolysis and a basic one, but interestingly, no water reaction, the acid and base reactions having the same rate at pH ≈ 0. Denitration of nitrourea was not observed,[14] but this may be because the reaction was not studied at very high acidities; for instance nitroguanidines have been shown to denitrate in quite strong sulfuric and perchloric acid media.[49]

The mechanism involving neutral water (Schemes 7 and 8) has standard-state rate constants which are much higher than those for the A1 decomposition processes (Schemes 3 and 6), and so are preferred at low acidities; however, as the acidity increases the water activity goes down[50] and the A1 processes become favoured (best seen in Fig. 5) for this reason and, of course, because the second process is acid-catalysed, whereas the first is not.

Some trouble has been taken to derive statistically valid parameters from the experimental data, to provide the best possible basis for the postulated mechanisms. All of the data concerning the hydrolysis of these *N*-nitro amides can be explained on the basis of the mechanisms discussed here, A1 reactions of the *O*-protonated amide in strong acid, reaction between neutral water and neutral amide at weaker acidities, and reaction with hydroxide in the most weakly acidic media. It is of considerable interest that *none* of these mechanisms involve the conventional amide hydrolysis, an A2 reaction between *O*-protonated amide and neutral water. Undoubtedly this is due to the very low basicity of these *N*-nitro compounds; normal aliphatic amides have pK_{SH^+} values of ≈−0.5 and aromatic ones of ≈−1.5,[51] and the excess acidity analysis of amide hydrolysis rates is based on full amide protonation at the acidities used.[4] No evidence of equilibrium protonation of the *N*-nitro amides in this work is evident even in the strongest sulfuric acids used.

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