A NEUTRAL NUCLEOPHILE PROBE FOR BORDERLINE KINETICS

IN THE 2-OCTYL MESYLATE-THIOUREA REACTION
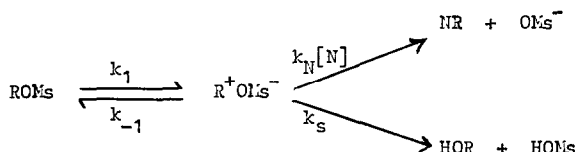
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Sneen and Larsen have claimed that kinetic and product data for the decomposition of 2-octyl mesylate (ROMs) in 25% and 30% dioxan-water mixtures containing NaN_3 are explicable only in terms of nucleophilic attack of N_3^- on a preformed ion-pair intermediate (Scheme I, $N = N_3^-$).[1] When pseudo first-order conditions obtain ($[N]_o \gg [ROMs]_o$) the steady-state rate

$$ROMs \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R^+OMs^- \overset{k_N[N]}{\underset{k_s}{\nearrow\searrow}} \begin{array}{l} NR + OMs^- \\ HOR + HOMs \end{array}$$

SCHEME I

expression is eq. (1), in which k_{obs} is the first-order rate coefficient for a nucleophilic salt concentration of $[N]$, k_o is the solvolysis rate constant in the absence of salts, $m = [RN]/[ROH][N] = k_N/k_s$, $x = k_{-1}/k_s$ and is held to be independent of the identity and

$$k_{obs}/k_o(1 + b[N]) = (1 + x)(1 + m[N])/(1 + x + m[N]) \qquad (1)$$

concentration of N, and b is the Winstein salt effect parameter[2] for solvolysis in the presence of the nucleophilic salt. Such observations have been extended to other systems, and it has been suggested that the above process unifies the traditional $S_N1 - S_N2$ dichotomy (S_N1 when $x \to 0$, S_N2-like when $x \to \infty$), thus rendering the S_N2 mechanism (eq. 2) involving concerted bond-making and breaking and no intermediates, redundant.[3]

$$N^- + RX \longrightarrow \overset{\delta-}{N} \dots \overset{\delta\delta+}{R} \dots \overset{\delta-}{X} \longrightarrow NR + X^- \qquad (2)$$

In fitting rate and product data to eq. (1), x and b must be treated as adjustable parameters since they are not directly determinable experimentally.[4] It has in fact been proposed that the salt effect assumption may be erroneous[4] and consequently the claimed observation of borderline kinetics ($k_{-1} \sim k_s$) for the ROMs decomposition in the presence of NaN_3 may be incorrect. We have attempted to circumvent salt effect complications by using the neutral nucleophile thiourea and the non-nucleophilic analogue urea. Rate and product data are shown in Table 1, together with values of m calculated from each run.[5]
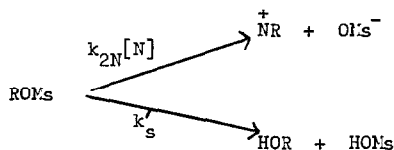
TABLE I

The decomposition of ROMs [a] in 30% dioxan-water (v/v)

at 36.2° in the presence of urea or thiourea

Non-electrolyte	Conc. / M	$10^4 k_{obs}/s^{-1}$ [b]	% ROH [c]	m
Urea	0	1.74 (k_o) [d]	100	–
"	0.119	1.86	99.4	–
"	0.206	1.77	99.7	–
"	0.302	1.92	99.7	–
Thiourea	0.0808	4.35	41.0	17.8
"	0.163	7.40	24.6	18.8
"	0.194	8.2	21.3	19.0
"	0.236	9.0	18.9	18.2
"	0.270	10.5	16.6	18.6
"	0.318	12.1	14.4	18.7

[a] $[ROMs]_o \sim 0.015M$. [b] From titration for H^+ after extraction of organic material and treatment with cation exchange resin. [c] From conductimetric titration for H^+ (ref.6). Small ($<1\%$) quantities of alkene are counted as ROH. [d] From ref. 1.

It is clear firstly that urea is non-nucleophilic under these conditions, and secondly that in the 0 - 0.3 M concentration range, urea has little effect on the solvolysis rate constants. The variation found is barely outside experimental uncertainty. If we assume that thiourea has the same effect on the solvolysis as does urea, a value of b = 0 in eq. (1) is reasonable. Values greater than 0.35 cannot be entertained, when errors are taken into account.

These data are now analysed in terms of Scheme I using the value of x (2.59) required for the correlation of the adjusted ROMs/NaN$_3$ data,[1] and the displayed m values. It is clear from Table II that there is no agreement between observed and calculated rate coefficients. In Scheme II is shown an operational process wherein it is assumed (a) that rate-limiting and product-determining steps are identical, (b) the nucleophile-induced reaction is second-order, and (c) $k'_s = k_o$ and is independent of [N]. Equations (3) and (4) then apply.

$$ROMs \quad \overset{k_{2N}[N]}{\underset{k'_s}{\diagup\diagdown}} \quad \begin{matrix} \overset{+}{N}R + OMs^- \\ HOR + HOMs \end{matrix}$$

SCHEME II

TABLE II

Analysis of rate and product data from Table I

[Thiourea]	$10^4 k_{obs}$ [a]	$10^4 k_{obs}$ (ion-pair) [a,b]	$10^4 k_{obs}$ (S_N2) [a,c]	$10^4 k_{2N}$ [d,e]	$10^4 k'_s$ [a,f]
0	1.74 (k_o)	1.74	1.74	–	1.74
0.0808	4.35	3.02	4.24	31.8	1.78
0.163	7.40	3.82	7.07	34.2	1.83
0.194	8.2	4.02	8.15	33.3	1.74
0.236	9.0	4.19	9.21	30.9	1.71
0.270	10.2	4.38	10.5	32.4	2.0
0.318	12.1	4.55	12.1	32.6	1.8

[a] In s^{-1}. [b] From eq. (1) with x = 2.59, b = 0. [c] From eq. (4) using product data alone and assuming k_o independent of [thiourea]. [d] In $1 \, mol^{-1} \, s^{-1}$. [e] From eq. (3) assuming $k'_s = k_o$. [f] From eq. (4) using calculated k_{2N} values, and experimental values of m ($m = k_{2N}/k'_s$).

$$k_{obs} = k'_s + k_{2N}[N] \qquad (3)$$

$$k_{obs}/k_o = 1 + m[N] \qquad (4)$$

Values of k_{obs} calculated from eq. (4) are shown in Table II, and compare well with the experimental values. The second-order rate coefficient k_{2N} is constant, as required. Derived values of k'_s are also effectively constant.

Thus the reaction of ROMs with thiourea is second-order and the mechanism is either the concerted S_N2 process or the x→∞ variant of the Sneen ion-pair process ($k_{-1} \gg k_s$ in Scheme I with $k_{2N} = k_1 k_N/k_{-1}$). A further implication is that the reaction in the presence of NaN$_3$ is not borderline either, and that the salt effect adjustment is indeed suspect. Thus the adjusted results cannot be used to dismiss the possibility of normal S_N2 substitution. Further studies along these lines are in progress.

A brief remark on the b = 0 assumption for thiourea (as determined from the behaviour of urea as a model non-nucleophilic non-electrolyte) is in order. Both non-electrolytes are highly polar molecules,[7] and in terms of a recent model for salt effects[8] might be expected to stabilize ion-pair like solvolysis transition states in the same way that non-nucleophilic salts do. Furthermore, the addition of urea to water increases the dielectric constant[9] and breaks the water structure,[10] two factors which, by themselves, might be expected to lead to increased solvolytic reactivity. However, the role of the dioxan co-solvent[11] and the effect of urea on solvation of reactant ROMs[12] are uncertain factors. Moreover the urea concentrations employed may be too small for any of these effects to be kinetically significant.[12] The small b value of 0.62 pertains to the solvolysis of cholesteryl tosylate (90% MeOH-10% CHCl$_3$) in the presence of urea.[6]

Within the reasonable assumptions employed, the present results constitute the least
ambiguous evidence against the borderline ion-pair formulation so far reported. Rejection of
the S_N2 mechanism rests heavily on the demonstration of borderline kinetics, which are not
sustained by the neutral nucleophile probe. We consider that the only unambiguous
demonstration of borderline kinetics concerns the reaction of benzoyl chloride with
o-nitroaniline in 50% acetone-water.[14]

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