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CONCURRENT OPERATION OF UNIMOLECULAR AND BIMOLECULAR PROCESSES IN BORDERLINE NUCLEOPHILIC SUBSTITUTION REACTIONS. THE ISOTOPIC EXCHANGE BETWEEN BENZHYDRYL THIOCYANATES AND NaSCN IN ACETONITRILE[1].

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THE most direct evidence of the molecularity of a reaction is given by the reaction orders. However, the relation between order and molecularity may not be a straightforward one. This is the case of borderline nucleophilic substitution reactions of the type:

$$R\text{-}X + Y^{\ominus} \longrightarrow R\text{-}Y + X^{\ominus}$$

where R-X is a typical borderline substrate such as benzhydryl, and $Y^{\ominus}$ is a charged nucleophile supplied in the form of the electrolyte MY, in a solvent of low to medium polarity. Here, in fact, ambiguities may arise from at least three sources: a) the salt effect of MY (and, as the reaction proceeds, that of MX which may be different from that of MY[3]); b)

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[1] The financial support of C.N.R., Rome, and Shell Internationale Maatschappyi N.V., The Hague, Holland, is gratefully aknowledged.

[2] The late.

[3] a) S. Winstein, S. Smith, D. Darwish, J. Amer. Chem. Soc. **81**, 5511 (1959); b) id. Tetrahedron Lett. **16**, 24 (1959).

the 'mass-law' effect[4] caused by $X^{\ominus}$ produced during reaction or already present at the beginning; c) the incomplete ion-pair dissociation of MY and the nucleophilic reactivity of $Y^{\ominus}$ relative to that of $M^{\oplus}Y^{\ominus}$ ion pairs[5].

All these factors have long been recognized and the difficulties of mastering all of them simultaneously are well appreciated. As a result, although quite some time has elapsed since Bird, Hughes, and Ingold's proposal of the 'intermediate' or 'borderline' mechanism[6], and in spite of its important implications[7], no report has appeared, as yet, where the reaction orders have been determined while accounting for all factors above.

We report here the study of a borderline reaction of the type above (R = p-substituted benzhydryl, $X^{\ominus} = Y^{\ominus} = SCN^{\ominus}$, solvent acetonitrile) where this goal has been achieved by working under conditions which effectively eliminate all ambiguities arising from a), b) and c) above.

This was obtained by, 1) studying an isotopic exchange reaction rather than a net reaction, to eliminate all difficulties stemming from mass-law effect, 2) running the reaction in the presence of a high concentration (0.099 to 0.090 M) of an electrolyte, $NaClO_4$, having the same cation as the ionic reactant, NaSCN, and varying the concentration of the latter in a rather wide range, but still very dilute (0.001 to 0.01 M) with respect to total electrolyte present (0.1 M). This procedure has the twofold purpose of swamping out salt effects while keeping constant the ion pair dis

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[4] a) S. Winstein, E. Clippinger, A.H. Fainberg R. Heck and G.C. Robinson J. Amer. Chem. Soc. 78, 328 (1956);
b) C.K. Ingold, Structure and Mechanism in Organic Chemistry, Cornell U. Press, New York 1953, p. 360 ff.

[5] See N.N. Lichtin and K.N. Rao, J. Amer. Chem. Soc. 82, 2417, (1961) and references therein.

[6] M.J. Bird, E.D. Hughes and C.K. Ingold, J. Chem. Soc. 634, (1954)

[7] V. Gold, J. Chem. Soc. 4633 (1956)

sociation fraction[8] of the ionic reactant, NaSCN. Thus, all ambiguities stemming from salt effect specificity are eliminated as well as those arising from incomplete, and variable, dissociation of $Na^{\oplus}SCN^{\ominus}$.

Under these conditions, the variation of rate of exchange brought about by varying $[NaSCN]_s$ gives the 'clean' order of reaction with respect to the nucleophile.

The initial[9] rates of exchange for a number of p-substituted benzhydryl substrates are reported below in Table I and plotted in Fig. 1.

The data of Table I and Fig. 1 show a smooth transition from a second order reaction for the least electron releasing substrate (p-nitro) to a first order reaction for the more electron releasing one (p,p'-dimethyl). For the two substrates of intermediate electron-releasing capacity, p-chloro and unsubstituted benzhydryl, the data fit nicely an equation of the form:

$$Rate/[R\text{-}SCN] = k_1 + k_2[NaSCN]_s$$

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[8] The dissociation fraction is given by:

$$\alpha = \frac{1}{1 + f_{\pm}^2\,[Na^{\oplus}]/K_d}$$

where K_d is the ion-pair dissociation constant of Na^+SCN^- and $f_{\pm}$ is the mean molar ionic activity coefficient. Under the condition of a large excess of $NaClO_4$, both $f_{\pm}$ and $[Na^{\oplus}]$ can be considered practically constant with varying $[NaSCN]_s$, and so also α.

[9] Under the conditions of the exchange, isomerization of R-SCN to R-NCS takes place,[10] so that the exchanging system is not a stable one. However, the rate of isomerization is slow enough to make the McKay plots linear at least up to 30 to 40% of exchange. Thus, the estimation of initial rates is quite accurate.

[10] A. Iliceto, A. Fava, U. Mazzucato and O. Rossetto, J. Amer. Chem. Soc. **83**, 2729 (1961).

TABLE I

Initial rates of isotopic exchange between p-substituted benzhydryl thiocyanates, $(X\text{-}C_6H_4\text{-}CH\text{-}C_6H_4\text{-}X')\text{-}SCN$, and NaSCN in acetonitrile, at constant electrolyte concentration.

$([NaSCN] + [NaClO_4] = 0.1;\ [R\text{-}SCN] = 0.1)$

$X, X' = CH_3, CH_3$ Temp. 0.2 ± 0.1 °C

$10^3[NaSCN]_s$	1.12	1.83	2.71	5.34	9.41
10^6 Rate/[R-SCN] =	2.84	2.70	2.76	2.83	2.76

$10^5\ k_1 = 2.78 \pm 0.052\ sec^{-1}$ $10^5\ k_2 = -0.3 \pm 10\ l.m^{-1}\ sec^{-1}$

$X, X' = H, H$ Temp. 70.0 ± 0.1 °C

$10^3[NaSCN]_s$	1.09	2.98	5.24	6.97	9.52
10^5 Rate/[R-SCN] =	0.776	1.02	1.16	1.25	1.55

$10^6\ k_1 = 7.11 \pm 0.44$ $10^4\ k_2 = 8.56 \pm 0.75$

$X, X' = Cl, H$ Temp. 70.0 ± 0.1 °C

$10^3[NaSCN]_s$	1.09	3.69	6.90	10.22
10^6 Rate/[R-SCN] =	4.98	7.15	8.87	10.4

$10^6\ k_1 = 4.66 \pm 0.38$ $10^4\ k_2 = 5.80 \pm 0.59$

$X, X' = NO_2, H$ Temp. 70.0 ± 0.1 °C

$10^3[NaSCN]_s$	0.99	3.05	7.18	10.25
10^6 Rate/[R-SCN] =	0.235	0.702	1.79	2.50

$10^8\ k_1 = -2 \pm 4$ $10^4\ k_2 = 2.47 \pm 0.058$

which is to be expected for simultaneous first-order and second-order processes: the first-order specific rate constant, k_1, is given by the intercept and the second-order one, k_2, by the slope of plots of Rate/[R-SCN] versus $[\mathrm{NaSCN}]_s$.

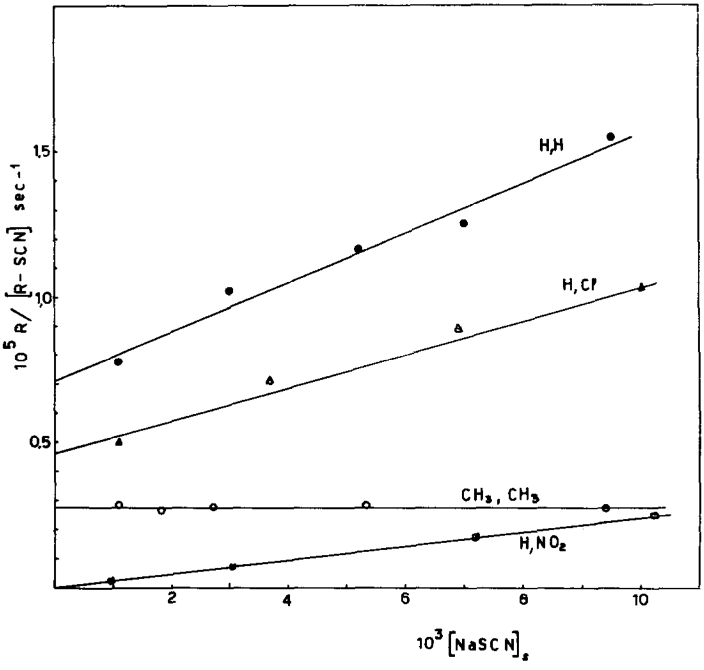

Fig. 1

Dependence of the rate of exchange on $[\mathrm{NaSCN}]_s$.
The substituents in 4,4' are indicated on the respective curves. The conditions are those of Table I.

This appears to be a clear-cut demonstration of the simultaneous operation of the unimolecular and the bimolecular mechanisms for nucleophilic substitution and of the gradual transition from one mechanistic extreme to the other, which can be brought about by relatively mild structural variations.[11,12]

It is interesting to examine the structural effect on the rates of i) unimolecular exchange, k_1, ii) isomerization, k_i,[10] and iii) bimolecular exchange, k_2. The relevant data are reported as relative values in Table II. Although the paucity of compounds for which the data are available

TABLE II

Relative rates of unimolecular exchange (k_1), isomerization (k_i) and bimolecular exchange (k_2).

Substrate[a]	CH_3,CH_3	H,H	Cl,H	NO_2,H
k_1	1400[b]	1	0.6	---
k_i[c]	300	1	0.7	0.004
k_2	---	1	0.7	0.3

a Only the substituents in 4,4' are indicated.

b Extrapolated from data at 0° and 10° which indicate an energy of activation of 22 kcal.

c From ref. (10).

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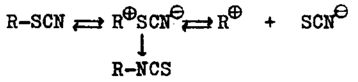
[11] Casapieri and Swart[13a] have recently reported similar results for the exchange of benzhydryl chloride with chloride ion in dimethylformamide. In this highly polar solvent, the results are likely to be little impaired by the authors neglecting salt effects and reactivity by ion pairs. Previous reports by Le Roux and Swart[13b] of a simultaneous uni- and bimolecular substitution by bromide ion on t-butyl bromide have been severely questioned by Winstein and coll.[3b]

[12] For other direct evidence indicating that borderline nucleophilic substitutions are made up of concurrent unimolecular (via carbonium ion) and bimolecular processes see: G. Kohnstam, A. Queen and B. Shillaker, Proc. Chem. Soc. 157, (1959); and H. Weiner and R.A. Sneen, J. Amer. Chem. Soc. 84, 3599 (1962).

[13] a) P. Casapieri and E.R. Swart, J. Chem. Soc. 4342 (1961); b) L. J. Le Roux and E.R. Swart, J. Chem. Soc. 1475 (1955).

does not allow a thorough discussion, still the general trend of increasing rates with increasing electron releasing power is obvious and is taken to indicate an electron deficient transition state for all three processes. However, the differences in degree are quite significant and indicate a greater carbonium ion character of the transition state for unimolecular exchange than for isomerization, which is, in turn, much greater than for bimolecular exchange. This trend agrees well with the notion that, while isomerization is likely to occur via an intermediate 'intimate' ion-pair,[10] unimolecular exchange occurs via the dissociated carbonium ion:



$$\begin{array}{l} R\text{-}SCN \rightleftarrows R^{\oplus}SCN^{\ominus} \rightleftarrows R^{\oplus} + SCN^{\ominus} \\ \qquad\qquad\downarrow \\ \qquad\quad R\text{-}NCS \end{array}$$

and bimolecular exchange occurs by way of a direct displacement where bond-breaking is the predominant feature.[14]

We would like to conclude by pointing out that our results allow a better understanding of nucleophilic substitutions in the 'borderline' region. In a nucleophilic substitution there is a gradual trend toward a purely unimolecular process as the substrate, or the solvent, or both, are so modified as to favor the ionization of the bond to the departing group.

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[14] It is important to point out that in examining structural effects, k_2 cannot be taken at face value. In fact, k_2 is a composite:

$$k_2 = k_I + k_{IP}(1-\alpha) \qquad (2)$$

where α is the degree of dissociation of the ionic reactant and k_I and k_{IP} are specific rate constants for displacement by the free ion, $SCN^{\ominus}$, and the ion pair, $Na^{\oplus}SCN^{\ominus}$. For the relative values of k_2 to be significant, it is necessary that ratio k_I/k_{IP} be independent of substrate or that either one of the two terms of right hand side of equation (2) always predominate. At the moment it is not known whether either one of these conditions is fulfilled.

Along this transition, conditions may obtain where uni- and bimolecular processes will make comparable contributions to the rate. In considering these particular bimolecular processes, occurring under conditions of facile heterolysis of the substrate, it must be realized that they, although bimolecular and second-order, will not display those kinetic features which are usually associated with direct displacements. Rather, as the contribution of the nucleophile to the bonding of the transition state becomes less and less important, solvent and structure effects will become closer and closer to those which are typically associated to unimolecular substitutions.

This picture is not new as it has been offered previously in more or less different words by several authors and notably by Gold[7] and Hudson.[15] However, our results appear to provide the least ambigous evidence so far presented of its correctness.

The work is being extended to other substrates with the aim of establishing on a wider basis the structural effects on the concurrent reactions.

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[15] E.W. Crunden and R.F. Hudson, J. Chem. Soc. 501 (1956).