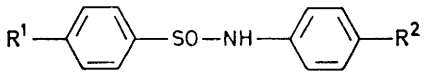
Nucleophilic Substitution at Sulphur. Part 2.[1,2] The Acid-catalysed Hydrolysis of Arenesulphinamides

By **Hamid Asefi** and **John G. Tillett**, Chemistry Department, University of Essex, Colchester CO4 3SQ

The acid-catalysed hydrolyses of some bis-(*para*-substituted phenyl)benzenesulphinamides have been studied in aqueous solutions of perchloric acid and the substituent effects analysed. The kinetics of hydrolysis of *p*-tolyltoluene-*p*-sulphinamide in a number of mineral acids have been studied in some detail. The hydrolysis at 25 °C proceeds by both an acid catalysed (*A*-2) and a hydrogen ion-dependent nucleophile-catalysed reaction. At higher temperatures hydrogen ion-independent nucleophilic catalysis can also be identified

NUCLEOPHILIC displacement reactions at sulphinyl (>S=O) sulphur have received considerable attention.[3,4] Some of the more important compounds studied include sulphoxides R_2SO, sulphinate esters RSO·OR, sulphinyl sulphones RSO·SO_2R, and sulphite esters $(RO)_2SO$. Although Biasotti and Anderson have studied the alkaline hydrolysis of some arenesulphinamides, no systematic investigation of the acid-catalysed hydrolysis of sulphinamides has previously been reported.[5] We now report such a study. A number of substituted arenesulphinamides (1; R^1 = Me; R^2 = H, Cl, MeO,



(1)

and Me; R^2 = Me; R^1 = Cl, MeO, Me, and NO_2) have been prepared and the effect of added acids and salts on the rates of hydrolysis of these compounds in aqueous solution has been examined.

EXPERIMENTAL

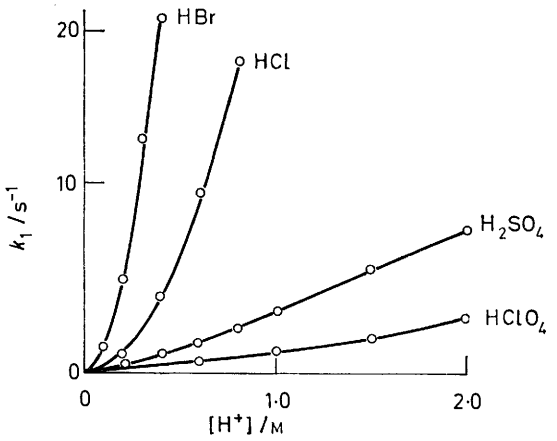
Materials.—The sulphinamides were prepared by the addition of the sulphinyl chloride to the appropriate amine and were recrystallised from acetone. *N*-Phenyltoluene-*p*-sulphinamide had m.p. 115 °C (lit.,[6] m.p. 138 °C); *N*-*p*-methoxyphenyltoluene-*p*-sulphinamide had m.p. 120 °C (lit.,[7] 121 °C); *N*-*p*-chlorophenyltoluene-*p*-sulphinamide had m.p. 127 °C (lit.,[7] 127 °C); *N*-*p*-tolyltoluene-*p*-sulphinamide had m.p. 120—122 °C (lit.,[7] 118 °C); *N*-*p*-tolylbenzenesulphinamide had m.p. 106 °C (lit.,[8] 100—101 °C); *N*-*p*-tolyl-*p*-chlorobenzenesulphinamide had m.p. 130 °C (lit.,[7] 128 °C); *N*-*p*-tolyl-*p*-methoxybenzenesulphinamide had m.p. 122 °C (lit.,[7] 121—123 °C); *N*-*p*-tolyl-*p*-nitrobenzenesulphinamide had m.p. 150 °C (Found: C, 56.5; H, 4.4; N, 10.2; S, 11.6. $C_{13}H_{12}N_2O_3S$ requires C, 56.5; H, 4.3; N, 10.1; S, 11.6%); $\nu_{max.}$ (hexachlorobutadiene) 1 040 and 1 055 cm^{-1}; *m/e* 286.

Kinetic Measurements.—The rates of hydrolysis were measured at 235 nm using a Durham–Gibson stopped-flow spectrometer. Optical densities were measured on the photograph of the oscilloscope trace and rate-coefficients determined graphically from this data. The values of k_1 in the Tables are the average of several runs at each acid concentration. Average deviation from the mean is <5%. The initial concentration of sulphinamide in kinetic runs was *ca.* 10^{-4}M.† The temperatures reported are those of the solutions before mixing.

Influence of Temperature.—The entropy ($\Delta S^{\ddagger}$) and enthalpy of activation ($\Delta H^{\ddagger}$) were calculated from the equation $k = (kT/h) \exp(\Delta S^{\ddagger}/R) \exp(-\Delta H^{\ddagger}/RT)$ by a least-squares procedure. The values obtained for the hydrolysis of *N*-*p*-tolyltoluene-*p*-sulphinamide were $\Delta S^{\ddagger} = -29.5 \pm 1.8$ cal mol^{-1} K^{-1} and $\Delta H^{\ddagger} = 9.04 \pm 0.57$ kcal mol^{-1} (for k_1 values in 0.500M-$HClO_4$ and calculated at 25.1 °C).‡

DISCUSSION

In contrast to the low reactivity of aromatic amides, arenesulphinamides are hydrolysed so rapidly in aqueous



The acid-catalysed hydrolysis of *p*-tolyltoluene-*p*-sulphinamide in aqueous mineral acids at 25.7 °C

acidic solution that their rates of hydrolysis could not be studied by conventional techniques and a stopped-flow spectrophotometric method had to be employed.

Hydrolysis in Perchloric Acid.—The kinetics of hydrolysis of *p*-tolyltoluene-*p*-sulphinamide (1, R^1 = R^2 = Me) were studied in some detail. The Figure and Table 1 show the observed first-order rate-coefficients, k_1, at different stoicheiometric acid concentrations. As observed for the acid-catalysed hydrolysis of several other sulphinyl compounds, *e.g.* the sulphite[9] and sulphinate esters,[10] the values of k_1 for the hydrolysis of *p*-tolyltoluene-*p*-sulphinamide in aqueous perchloric acid increase more rapidly than required for a linear correlation with concentration of acid, but less rapidly than required for a meaningful correlation with h_0, the

† M = mol dm^{-3}.
‡ 1 cal = 4.184 J.

TABLE 1

Hydrolysis of *N*-*p*-tolyltoluene-*p*-sulphinamide

(a) Effect of added acids at 25.6 °C

$[HClO_4]$/M	0.200	0.400	0.500	0.600	0.800	1.00
k_1/s^{-1}	0.173	0.382	0.503	0.604	0.895	1.16
$[HClO_4]$/M	1.50	2.00	2.50	3.00	3.50	0.500 [a]
k_1/s^{-1}	1.77	2.85	3.85	4.40	5.50	0.700
$[H_2SO_4]$/M	0.200	0.400	0.600	0.800	1.00	1.20
k_1/s^{-1}	0.52	1.14	1.77	2.47	3.33	4.10
$[H_2SO_4]$/M	1.50	1.80	2.00			
k_1/s^{-1}	5.77	7.09	7.61			
[HCl]/M	0.200	0.400	0.600	0.800	0.900	
k_1/s^{-1}	1.04	4.09	9.61	16.5	24.8	
[HBr]/M	0.100	0.200	0.300	0.400	0.450	0.500
k_1/s^{-1}	1.45	4.88	12.4	20.6	28.4	35.4

(b) Effect of added perchloric acid (0.500M) at different temperatures

T/°C	25.1	30.2	35.4	35.8	44.3
k_1/s^{-1}	0.518	0.678	0.816	1.10	1.40

(c) Effect of added salts in the presence of perchloric acid at 39.5 °C

$[HClO_4]$/M	0.200	0.400	0.500	0.600	0.800
k_1/s^{-1} (0.100 M-NaCl)	0.900	1.51	1.86	2.30	2.60
k_1/s^{-1} (0.200 M-NaCl)	2.06	4.01	4.71	5.70	7.04
k_1/s^{-1} (0.010M-KBr)	0.435	0.770	1.13	1.52	1.98
k_1/s^{-1} (0.020 M-KBr)	0.685	1.22	1.71	2.23	2.75

[a] In 0.500M-$DClO_4$ in D_2O

TABLE 2

Hydrolysis of arenesulphinamides in perchloric acid at 25.7 °C

R^1	R^2	k_2 / l mol^{-1} s^{-1}	R^1	R^2	k_2 / l mol^{-1} s^{-1}
H	Me	0.630	Me	Me	0.915
Cl	Me	0.630	Me	H	1.22
MeO	Me	1.24	Me	MeO	1.25
NO_2	Me	0.380	Me	Cl	1.68

plot of log k_1 *versus* $-H_0$ giving a straight line of slope *ca.* 0.6. Such behaviour can arise from the superposition of a positive salt effect on a linear dependence of rate on stoicheiometric acidity and is characteristic of many reactions hydrolysing by an *A*-2 mechanism: *e.g.*, the acid-catalysed hydrolysis of ethyl acetate,[11] methyl phosphate,[12] and sulphite esters.[9,13] Such a mechanism is also indicated for the hydrolysis of arenesulphinamides by the value of the entropy of activation ($\Delta S^{\ddagger} = -29.5$ cal mol^{-1} K^{-1}) which falls in the range usually associated with a bimolecular mechanism.[14]

A plot of log $k_1 + H_0$ *versus* log a_{H_2O} gives a Bunnett ω value of *ca.* 6.0.[15] Such a value lies in the range said to be characteristic of water acting as a proton transfer agent, indicating that water has some additional function in the rate-determining step in addition to acting as a nucleophile. The value of ϕ (0.8) obtained from the plot of log $k_1 + H_0$ *versus* (H_0 + log [H^+])—the Bunnett–Olsen linear free energy relationship treatment [16]—gives a similar indication. O'Connor and her co-workers have recently suggested that the limits of ϕ characteristic of an *A*-2 mechanism for the hydrolysis of amides should be extended to $0.47 \leqslant \phi \leqslant 0.98$.[17] A similar proposal has been made for the acid-catalysed hydrolysis of some isosydnones.[18] The overall evidence is consistent with an *A*-2 mechanism as shown in equations (1) and (2). The kinetic solvent isotope effect, $k_1^{D_2O}/k_1^{H_2O} = 1.4$, is characteristic of such a reaction which proceeds *via* a rapid pre-equilibrium protonation.[19]

$$MeC_6H_4{\cdot}SO{\cdot}NHC_6H_4Me + H^+ \rightleftharpoons MeC_6H_4{\cdot}SO{\cdot}\overset{+}{N}H_2{\cdot}C_6H_4Me \quad (1)$$

$$MeC_6H_4{\cdot}SO{\cdot}\overset{+}{N}H_2{\cdot}C_6H_4Me + H_2O \longrightarrow MeC_6H_4{\cdot}SO_2{}^+H_2 + MeC_6H_4NH_2 \quad (2)$$

There is no direct evidence concerning the site of protonation of sulphinamides because of their rapid rate of decomposition in moderately strong acid even at room temperature. It is possible that protonation occurs initially on oxygen (2) followed by an intramolecular proton transfer to form the *N*-protonated species (3) with a better leaving group.

$$R^1{-}\overset{+OH}{\overset{\|}{S}}{-}NHR^2 \qquad R^1{-}\overset{O}{\overset{\|}{S}}{-}\overset{+}{N}H_2R^2$$
(2) (3)

Mechanism of Nucleophilic Attack.—One of the most intractable questions regarding the mechanism of nucleophilic substitution at sulphinyl sulphur concerns the timing of bond-breaking and bond-formation in the rate-determining step. Is bond formation complete before bond breaking starts to occur or are formation and breaking synchronous? The former situation would imply the existence of an actual intermediate along the reaction pathway as in equation (3), the alternative being synchronous bond forming and bond breaking as in S_N2- type substitutions at sp^3 carbon.

$$Nu^- + R{-}\overset{O}{\overset{\|}{S}}{-}Y \rightleftharpoons R{-}\overset{Nu}{\overset{|}{\underset{O^-}{\underset{|}{S}}}}{-}Y \longrightarrow R{-}\overset{O}{\overset{\|}{S}}{-}Nu + Y^- \quad (3)$$

Anderson and Biasotti were unable to detect any incorporation of excess of oxygen-18 in the unhydrolysed sulphinamide recovered from partial hydrolysis in alkaline solution of *N*-mesityl-*p*-toluenesulphinamide in the presence of 20 atom % $H_2{}^{18}O$.[5] As originally pointed out by Bender,[20] however, this does not rule out the existence of an intermediate since the rate of oxygen equilibration of an intermediate might be much slower than its rate of decomposition and hence no oxygen exchange would be observed.

Attempts to detect the presence of covalent intermediates in nucleophilic reactions of other simple sulphinyl systems have also been unsuccessful.[1,21,22] Thus Bunton and his co-workers [21] were unable to detect any oxygen exchange in either the acidic or the basic hydrolyses of cyclic sulphites. If an intermediate were formed in such reactions it seems reasonable to assume by analogy with substitution reactions at phosphorus that it would have trigonal-bipyramidal geometry. According to the preference rules [23] the cyclic sulphite ring would prefer to span an apical and an equatorial position. Kice and Walters [22] have pointed out that oxygen exchange could only occur *via* pseudo-rotation to an energetically unfavourable intermediate and this

could be responsible for the failure to observe oxygen-exchange.

Similarly Najam and Tillett [1] were unable to detect any oxygen exchange with solvent during the hydrolysis of simple five-membered cyclic sulphinate esters. It would be expected that pseudo-rotation of any initially formed intermediate in this system would be energetically more difficult than in the cyclic sulphite case because of the replacement of an oxygen atom in the ring with a methylene group. Even if a mechanism were available for pseudorotation of intermediates it has been suggested that such a process would be much slower at sulphur than at phosphorus.[24]

Thus the absence of oxygen exchange in the hydrolyses of arenesulphinamides and sulphite and sulphinate esters does not exclude the possibility of the formation of an intermediate in nucleophilic substitution at sulphinyl sulphur in these systems.

Because of this high rate of hydrolysis in acid solution, no oxygen-exchange studies could be carried out with the arenesulphinamides described in the present work. Kice and Walters studied the rates of the acetate-catalysed exchange of [$^2H_3$]methanol with methyl toluene-*p*-sulphinate in a further attempt to detect the existence of intermediates in reaction at sulphinyl sulphur.[22] The reaction was found to involve specific methoxide ion catalysis and general base rather than nucleophilic catalysis. However, no firm conclusions about whether the exchange step does or does not involve an intermediate could be made.

Substituent Effects.—Data have only been obtained for a limited number of substituents and so any conclusion much be provisional. A plot of log k/k_H *versus* σ for the *p*-tolyl-substituted-phenylsulphinamides gave a rough linear correlation with considerable scatter. A much better correlation was obtained using σ^+ values, the point for the *p*-methoxy-substituent now falling on the line. The value of ρ obtained (−0.44) is a composite value reflecting the effect of substituents on both the protonation equilibrium [equation (1)] and on the rate-determining step [equation (2)]. The sign of the ρ value indicates that substituents have a greater effect on the first step since electron-withdrawing substituents would be expected to accelerate the rate-limiting step of an *A*-2 reaction. The better correlation of log k/k_H with σ^+ than with σ suggests that resonance interactions have an important effect particularly on the basicity of sulphinamides. It is of interest that the protonation equilibrium of aromatic amides correlates better with σ values, whilst for substituted benzoic acids and acetophenones, better correlations with σ^+ have been observed.[25,26]

The rates of alkaline hydrolysis of arenesulphinamides gave a good correlation with Hammett's σ-constants. The value of ρ obtained (+1.3) implies that the electron density at sulphur is greater in the transition state than in the ground state. Negative charge formation should be at its maximum when an addition intermediate is formed. Substitutions at silicon where bond making is thought to be far ahead of bond breaking in the transition state owing to the use of *d*-orbitals on silicon are characterised by large positive values of ρ; *e.g.* ρ = +2.7 for the alkaline methanolysis of trialkyl-alkoxysilanes.[27]

In contrast, the S_N2 substitution reactions of *meta*- and *para*-substituted benzyl halides where bond making and bond breaking are synchronous, show either no correlation with the Hammett equation or small positive values of ρ (+0.5 to +0.8).[28,29]

Andersen and Biassotti applied Taft's procedure for determining specific resonance effects to the data for the alkaline hydrolysis of sulphinamides.[5] The absence of an exalted resonance effect suggests that an addition intermediate is not formed.

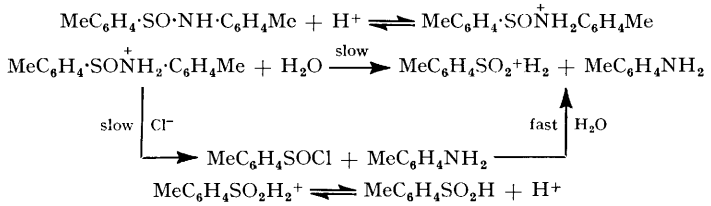
Nucleophilic Catalysis.—The order of effectiveness of catalysing acids, HBr > HCl > H_2SO_4 > $HClO_4$, and the magnitude of the relative effects, suggests the occurrence of nucleophilic catalysis. The general rate equation for hydrolysis of sulphinamides in acidic solutions containing halide ions can be written as in equation (4), where the terms represent (a) reaction of

$$k_1 = k_0 + k_0'[X^-] + k_{H^+}[H^+] + k_{X^-}[H^+][X^-] \quad (4)$$

the neutral species with water, (b) a nucleophile-catalysed spontaneous reaction, (c) an acid-catalysed *A*-2 reaction, and (d) hydrogen-ion dependent nucleophilic catalysis, respectively.

The observed rate data in Table 1(a) for the hydrolysis of *p*-tolyltoluene-*p*-sulphinamide in four mineral acids can be accommodated by terms (c) and (d), the first two terms being negligible under the conditions used. The overall mechanism in the presence of hydrochloric acid can be written as in Scheme 1.

The role of halide ions is to provide an additional acid-catalysed reaction pathway by converting the sulphinamide into the very reactive sulphinyl chloride. Such nucleophilic catalysis has also been observed in the acid-catalysed hydrolyses of other sulphinyl systems such as sulphinates,[10] sulphinyl sulphones,[30] and sulphite esters.[9,13]

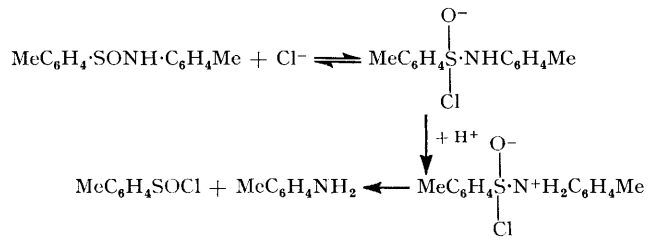


SCHEME 1

The overall mechanism of hydrolysis of *p*-tolyltoluene-*p*-sulphinamide shown in Scheme 1 is similar to that proposed by Bunton and Hendy for the hydrochloric acid-catalysed hydrolysis of methyl toluene-*p*-sulphinate.[10] They proposed that toluene-*p*-sulphinyl chloride is formed as an intermediate during the hydrolysis of this ester. They were able to show, moreover, that the rate of hydrolysis in initially neutral aqueous dioxan of this sulphinyl chloride, synthesised independently, is extremely rapid.

The relative order and magnitude of nucleophilic attack at sulphinyl sulphur in *p*-tolyltoluene-*p*-sulphinamide, (k_{Br^-}/k_{Cl^-} = *ca.* 4.8), is similar to that observed for attack at other sulphinyl centres: *e.g.* the sulphinyl sulphones ($k_{Br^-}/k_{Cl^-} = 5.4$).[30] This can be explained in terms of the theory of hard and soft acids and bases.[31,32] The value obtained falls between that expected for a relatively ' soft ' sulphenyl centre, on the one hand, and the relatively ' hard ' sulphonyl centre on the other.

As the temperature at which the hydrolysis of *p*-tolyltoluene-*p*-sulphinamide is carried out is increased, a nucleophile-catalysed spontaneous reaction can also be observed. Plots of k_1 *versus* [H^+] in perchloric acid in the presence of Cl^- and Br^- were found to be linear [Table 1(c)]. Extrapolation of such plots to zero acid concentration gave values of k'_{Br^-}/k'_{Cl^-} = *ca.* 2.5 which is of a similar order of magnitude to the value of k_{Br^-}/k_{Cl^-} observed for the hydrogen ion-dependent nucleophilic catalysis pathway discussed above. A possible mechanism for the nucleophile-catalysed spontaneous reaction might involve acid-catalysed assistance of the breakdown of an intermediate (Scheme 2).*



SCHEME 2

Similar results to those reported here for arenesulphinamides have been reported for the halide-catalysed hydrolysis of arylsulphinyl sulphones [30] for which both H^+-independent and H^+-dependent pathways have been observed with the former predominating. In contrast to the behaviour of sulphinamides and sulphinyl sulphones, the halide ion-catalysed hydrolysis of either alkyl [13] or aryl sulphites [33,34] shows no H^+-independent term. This is also the case for *o*-phenylene sulphite [33] which like sulphinyl sulphones has a high spontaneous rate of hydrolysis on which is superimposed weak acid catalysis. Kice and Guaraldi [30] have attributed the preponderence of the H^+-independent term in the rate of chloride or bromide ion-catalysed hydrolysis of sulphinyl sulphones to the fact that $ArSO_2^-$ is much less basic, and hence more easily displaced than ArO^- or RO^- in the hydrolysis of sulphite esters.

* We are indebted to a Referee for this suggestion.

[8/2169 *Received*, 18*th December*, 1978]

REFERENCES

[1] Part 1, A. A. Najam and J. G. Tillett, *J.C.S. Perkin II*, 1975, 858.
[2] Presented in part at the IUPAC Conference on Physical Organic Chemistry, York, September 1978.
[3] *Cf.* J. L. Kice, *Inorg. Chem.*, 1972, **17**, 147.
[4] *Cf.* J. G. Tillett, *Chem. Rev.*, 1976, **76**, 747.
[5] J. B. Biasotti and K. K. Andersen, *J. Amer. Chem. Soc.*, 1971, **93**, 1178.
[6] J. V. Braun and W. Kaiser, *Ber.*, 1923, **56**, 549.
[7] K. Mori and Y. Ueda, *Yakugaku Zasshi.*, 1971, **91**, 940.
[8] L. C. Raiford and S. E. Hazlet, *J. Amer. Chem. Soc.*, 1935, **57**, 2172.
[9] C. A. Bunton, P. B. D. de la Mare, and J. G. Tillett, *J. Chem. Soc.*, 1958, 4754.
[10] C. A. Bunton and B. N. Hendy, *J. Chem. Soc.*, 1962, 2567.
[11] R. P. Bell, A. L. Dowding, and J. A. Noble, *J. Chem. Soc.*, 1962, 2567.
[12] C. A. Bunton, D. R. Llewellyn, K. G. Oldham, and C. A. Vernon, *J. Chem. Soc.*, 1958, 3574.
[13] C. A. Bunton, P. B. D. de la Mare, and J. G. Tillett, *J. Chem. Soc.*, 1959, 1766.
[14] L. L. Schaleger and F. A. Long, *Adv. Phys. Org. Chem.*, 1963, **1**, 1.
[15] J. F. Bunnett, *J. Amer. Chem. Soc.*, 1961, **83**, 4956, 4968, 4973, 4978.
[16] J. F. Bunnett and F. P. Olsen, *Canad. J. Chem.*, 1966, **44**, 1917.
[17] C. J. Hyland and C. J. O'Connor, *J.C.S. Perkin II*, 1973, 1402.
[18] E. A. Isukul and J. G. Tillett, *J.C.S. Perkin II*, 1975, 230.
[19] C. A. Bunton and V. J. Shiner, *J. Amer. Chem. Soc.*, 1961, **83**, 42, 3702, 3214.
[20] M. L. Bender, *J. Amer. Chem. Soc.*, 1951, **73**, 1626.
[21] C. A. Bunton, P. B. D. de la Mare, P. M. Greasley, D. R. Llewellyn, N. H. Pratt, and J. G. Tillett, *J. Chem. Soc.*, 1958, 4751.
[22] J. L. Kice and C. A. Walters, *J. Amer. Chem. Soc.*, 1972, **94**, 590.
[23] *Cf.* F. H. Westheimer, *Accounts Chem. Res.*, 1968, **1**, 1.
[24] R. Tang and K. Mislow, *J. Amer. Chem. Soc.*, 1969, **91**, 5644.
[25] K. Yates and J. B. Stevens, *Canad. J. Chem.*, 1965, **43**, 529.
[26] J. T. Edward, H. S. Chang, K. Yates, and R. Stewart, *Canad. J. Chem.*, 1960, **38**, 1518.
[27] L. H. Sommer, ' Stereochemistry, Mechanism and Silicon,' McGraw–Hill, New York, 1965.
[28] R. F. Hudson and G. Klopman, *J. Chem. Soc.*, 1962, 1062.
[29] R. Fuchs and D. M. Carlton, *J. Amer. Chem. Soc.*, 1963, **85**, 104.
[30] J. L. Kice and G. Guaraldi, *J. Amer. Chem. Soc.*, 1967, **89**, 4113.
[31] R. G. Pearson, *J. Amer. Chem. Soc.*, 1963, **84**, 3533; *Science*, 1966, **151**, 172.
[32] R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, 1967, **89**, 1827.
[33] J. G. Tillett, *J. Chem. Soc.*, 1960, 5138.
[34] C. A. Bunton and G. Schwerin, *J. Org. Chem.*, 1966, **31**, 842.