Basicity and Nucleophilic Reactivity of Carbonyl-stabilized Sulphimides

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The basicity of *N*-acyl-*SS*-dialkylsulphimides was estimated by measurement of the apparent pK_a values of the corresponding iminosulphonium halides. Electron-withdrawing substituents on acyl carbon decrease the pK_a value of substituted acetylsulphimides, and Hammett plot gave ρ 0.8 for *para*-substituted benzoylsulphimides. Inductive effects of *S*-alkyl groups on the basicity of nitrogen were also studied in terms of the correlation with alkyl reactivity ratios. Correlation of the pK_a values of the sulphimides with their nucleophilic reactivity towards benzoyl chloride was also examined.

It is known that carbonyl-stabilized phosphoranes react with aldehydes and ketones to give olefins, although the reactivity is much lower than those of alkylidenephosphoranes.[1] Carbonyl-stabilized sulphuranes also undergo reactions with Michael acceptors and in some cases with carbonyl compounds affording cyclopropanes and epoxides, respectively.[2]

Recently, the chemistry of sulphimides has been studied by many workers and synthesis of sulphimides with acetyl, ethoxycarbonyl, and benzoyl groups on nitrogen have been developed. However, it was found that the nucleophilic reactivity of these stabilized sulphimides is much lower than those of sulphuranes and phosphoranes; attempted reactions of *N*-ethoxycarbonyl and *N*-acetyl-sulphimides with *p*-nitrobenzaldehyde and acrylonitrile were unsuccessful.[3]

Since the nucleophilic reactivity of phosphoranes was found to correlate fairly well with their basicity,[4] it was expected that the value of the basicity would be a measure of the nucleophilicity of sulphimides. So far, no systematic study of the basicity of sulphimides has been reported. We have determined the pK_a values of several carbonyl-stabilized sulphimides and examined their correlation with reactivity towards benzoyl chloride.

RESULTS AND DISCUSSION

Basicity of Sulphimides.—Carbonyl-substituted sulphimides undergo protonation on nitrogen, and on treatment with hydrochloric or hydrobromic acid, they form iminosulphonium halides (2). Alkaline titration of the salts gives the apparent pK_a values. The limitation of the method is that sulphimides with strong electron-withdrawing groups such as trichloromethyl on the carbonyl carbon do not form stable iminosulphonium salts, just as *N*-sulphonylsulphimides do not form isolable salts.

The pK_a values of some substituted sulphimides are listed in Table 1 along with those of several related compounds. Although the titration solvents are not always the same, the pK_a values of carbonylsulphimides are larger than those of the corresponding amides and sulphoxides, but smaller than those of phosphoranes and sulphuranes by as much as 4—5 units. This simply confirms the low nucleophilicity of carbonylsulphimides which has been observed in the reaction with some electrophiles as mentioned above.

The pK_a values of the carbonylsulphimides are also smaller than those of the corresponding isoelectronic carboxylate ions. Since carbonyl stretching vibration of sulphimides (1) appears at 1 500—1 600 cm^{-1} in the i.r., which is almost the same as those of carboxylate ions, the low pK_a values of the sulphimides may be interpreted in terms of a contribution from resonance form (1c) rather than (1a). The electrostatic repulsion between the acidic proton and the positive sulphur atom may also be responsible for the low pK_a values of the sulphimides.

Table 1

pK_a Values of ylides and related compounds

Compound	Solvent	pK_a	Ref.
CH_3CONH_2	H_2O	0	5
$(CH_3)_2S{=}NTs$	Ac_2O	0.57	6
$(CH_3)_2S{=}O$	Ac_2O	0.91	6
$(CH_3)_2S{=}NCOCH_2Cl$	H_2O	2.13	
$(CH_2)_4S{=}NCOCH_2Cl$	H_2O	2.22	
$^-OCOCH_2Cl$	H_2O	2.86	7
$(CH_3)_2S{=}NCOCH_3$	H_2O	3.15	
$(CH_2)_4S{=}NCOCH_3$	H_2O	3.45	
$^-OCOCH_3$	H_2O	4.76	7
$(CH_3)_2S{=}NH$		7.28	8
$(CH_3)_2S{=}CHCOPh$	H_2O	8.10	9
$(CH_3)_3P{=}CHCOPh$	H_2O–MeOH	9.20	10
$C_5H_5\overset{+}{N}{-}\overset{-}{C}HCOPh$	H_2O–MeOH	9.70	11

It is obvious that the stability of sulphimides comes from the delocalization of anionic charge on nitrogen; the stability effect is $SO_2R > COR > H$, and, as would be expected, the pK_a values decrease in the reverse order.

Figure 1 shows the correlation between pK_a and the σ^* values of the substituents on carbonyl carbon, and it is seen that linearity holds only partially. The deviation from the linear relationship may be attributed to a large

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[1] A. W. Johnson, 'Ylid Chemistry,' Academic Press, New York, 1966, p. 138.

[2] B. M. Trost and L. S. Melvin, jun., 'Sulfur Ylides,' Academic Press, New York, 1975, pp. 71 and 101.

[3] G. F. Whitfield, H. S. Beilan, D. Saika, and D. Swern, *J. Org. Chem.*, 1974, **39**, 2148; H. Kise and D. Swern, unpublished work.

[4] S. Flizar, R. F. Hudson, and G. Salvadori, *Helv. Chim. Acta*, 1963, **46**, 1580.

[5] E. M. Arnett, *Progr. Phys. Org. Chem.*, 1963, **1**, 324.

[6] K. K. Andersen, W. H. Edmonds, J. B. Biasotti, and R. A. Strecker, *J. Org. Chem.*, 1966, **31**, 2859.

[7] J. Hine, 'Physical Organic Chemistry,' McGraw-Hill, New York, 1956, ch. 2.

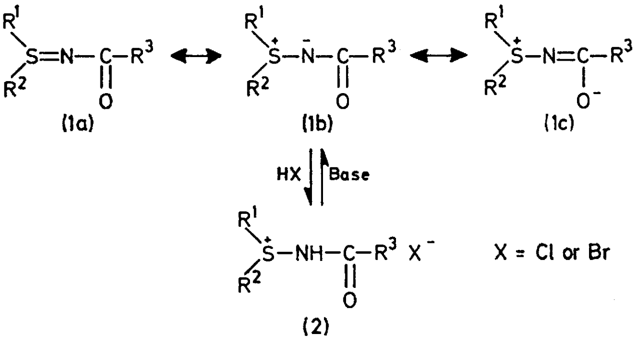
[8] F. Knoll, J. Gronebaum, and R. Appel, *Chem. Ber.*, 1969, **102**, 848.

[9] K. W. Ratts and A. N. Yao, *J. Org. Chem.*, 1966, **31**, 1185.

[10] G. Aksnes and J. Sonstad, *Acta Chem. Scand.*, 1964, **18**, 655.

[11] W. G. Phillips and K. W. Ratts, *J. Org. Chem.*, 1970, **35**, 3144.

contribution from the d_π–p_π interaction between sulphur and nitrogen; the contribution of the resonance structure (1a), which is absent in carboxylate ions, may be significant for polychlorinated acetylsulphimides, and this would keep them from a large decrease in basicity. The shift of C=O stretching frequency in going from acetyl- to polychlorinated acetyl-sulphimides seems to support this consideration (Table 2). The value of ρ* is at most 1.3 for the linear part of Figure 1, which is lower than the value reported for acyltriphenylphosphoranes (ρ* 2.04).[12]


(1a) (1b) (1c) (2)

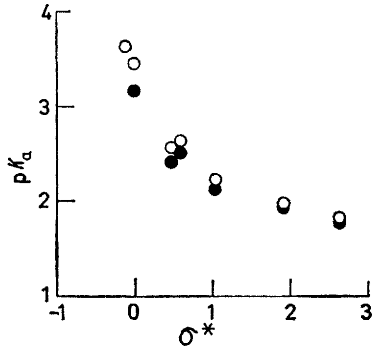


FIGURE 1 Plot of pK_a against σ* for *N*-acyl-*SS*-tetramethylene- (○) and *N*-acyl-*SS*-dimethyl-sulphimide (●)

TABLE 2

I.r. and ^{1}H n.m.r. data of *N*-acyl-*SS*-dimethylsulphimides MeS=NCOR (upper) and their hydrochlorides (lower)

	$\nu_{max.}$/cm^{-1}			δ [a]	
R	CO	CN	SN	CH_3S	R
CCl_3	1 610	1 294	794	2.83	
	b				
$CHCl_2$	1 636	1 326	805	2.81	6.02 (s)
	1 709	1 203		2.94	6.23 (s)
CH_2Cl	1 575	1 345	810	2.75	4.00 (s)
	1 707	1 180		3.16	4.26 (s)
H	1 574	1 233	815	2.75	8.15 (s)
	1 720	1 192		3.23	8.40 (s)
CH_3	1 565	1 310	797	2.70	2.00 (s)
c	1 695	1 220		3.26	2.20 (s)
C_6H_5	1 540	1 330	800	2.73	7.3—7.4 (m), 7.9—8.2 (m)
	1 695	1 250		3.32	7.5—8.0 (m)
p-ClC_6H_4	1 535	1 330	800	2.75	7.32 (d), 8.02 (d)
	1 670	1 255		3.46	7.47 (d), 7.91 (d)

[a] Solvents are $CDCl_3$ with Me_4Si as standard for the sulphimides and D_2O with $Me_3Si[CH_2]_3SO_3Na$ as standard for the salts. [b] Does not form the salt. [c] Hydrobromide.

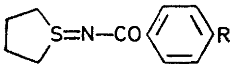
The Hammett plot of *N*-(*p*-substituted)benzoyl-*SS*-tetramethylenesulphimides gave ρ 0.80, which is the smallest value among those reported for sulphuranes and phosphoranes, indicating the greater stability of carbonylsulphimides. The small inductive effect of the substituents is also found in the small change of C=O stretching bands as shown in Table 3.

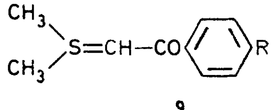
TABLE 3

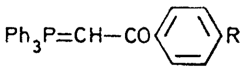
I.r. and ^{1}H n.m.r. data of *N*-acyl-*SS*-tetramethylene-iminosulphonium chlorides $[CH_2]_4\overset{+}{S}NHCOR\ Cl^-$

	$\nu_{max.}$/cm^{-1}		δ [a]		
R	CO	CN	CH_2S [b]	CH_2CH_2S [b]	R
CCl_3 [c]	1 615	1 295	3.34	2.32	
$CHCl_2$ [c]	1 592	1 345	3.30	2.28	5.98 (s)
CH_2Cl	1 735	1 140	3.66	2.39	4.28 (s)
H	1 690	1 130	3.66	2.41	8.37 (s)
CH_3 [d]	1 700	1 220	3.76	2.46	2.23 (s)
C_2H_5	1 686	1 183	3.67	*ca.* 2.4	1.10 (t), *ca.* 2.4
C_6H_5	1 674 (1 526) [e]	1 246	3.82	2.50	7.5—8.0 (m)
p-$CH_3OC_6H_4$	1 650 (1 530) [e]	1 250	3.76	2.34	3.84 (s), 7.04 (d) 8.17 (d)
p-$CH_3C_6H_4$	1 645 (1 540) [e]	1 260	3.76	2.35	2.38 (s), 7.31 (d) 8.07 (d)
p-ClC_6H_4	1 683 (1 535) [e]	1 252	3.75	2.34	7.58 (d), 8.18 (d)

[a] Solvent is D_2O with $Me_3Si[CH_2]_3SO_3Na$ as internal standard except for the substituted benzoyl compounds which were taken in $[^2H_6]$DMSO with Me_4Si. [b] Multiplets. [e] Data for sulphimides which do not form salts. [d] Hydrobromide. [e] Sulphimides.


ρ 0.80


ρ 2.1[9]


ρ 2.3[4]

The effect of the length and structure of alkyl chains on sulphur was examined for *N*-acetyl-*SS*-dialkylsulphimides. In Figure 2, the pK_a values are plotted against alkyl reactivity ratio (α) of alkyl chlorides (RCl) in S_N2 reactions.[13] The value of α is considered to reflect both inductive and steric effects of the alkyl chains in S_N2 reactions. As shown in Figure 2, in the case of linear alkyl groups, a linear relationship between α and pK_a was found, which indicates that the alkyl substituents exert their inductive effect through sulphur to the nitrogen atom. Branched alkyl groups have smaller values of α than linear ones of the same carbon number because of larger steric effects in S_N2 reactions. In the present case, the steric effect of alkyl groups on the basicity of nitrogen is considered to be less important due to the

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[12] K. Issleib and R. Lindner, *Annalen*, 1968, **713**, 12.

[13] K. Okamoto, I. Nitta, T. Imoto, and H. Shingu, *Bull. Chem. Soc. Japan*, 1967, **40**, 1905.

presence of sulphur between the nitrogen and the alkyl groups, and this may be a reason for the deviation of the pK_a values of isopropyl- and isobutyl-sulphimides from the linear relationship as shown in Figure 2.

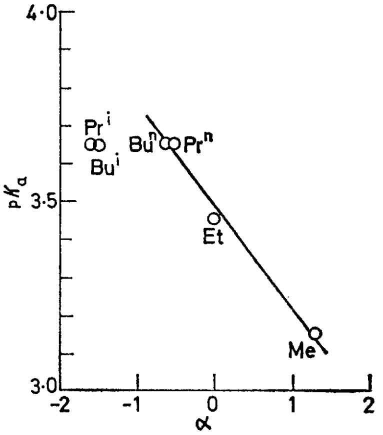
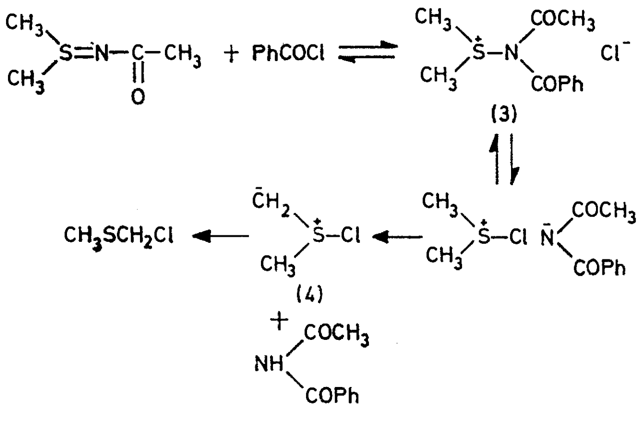


FIGURE 2 Plot of pK_a of *N*-acetyl-*SS*-dialkylsulphimides R_2S=NCOCH$_3$ against the alkyl reactivity ratio α of R

It was reported that tetramethylene-4-bromobenzylidenesulphurane has a larger pK_a value (7.54) than diethyl-4-bromobenzylidenesulphurane (6.46). The difference was attributed to the strain in the five-membered ring in the former, which would result in a decrease in the acidity of the proton attached to the benzylidene carbon atom.[14] In the present case, however, *N*-acetyl-*SS*-tetramethylenesulphimide was found to have almost the same pK_a value as that of *SS*-diethyl analogue.



Reaction with Benzoyl Chloride.—It has been reported that *N*-acetyl-*SS*-dimethylsulphimide reacts with benzoyl chloride at room temperature to give *N*-benzoylacetamide, chloromethyl methyl sulphide, and a small amount of hydrochloric acid.[15] The reaction is considered to proceed *via* initial formation of the sulphonium salt (3) followed by the formation of the ylide (4), which then undergoes rearrangement to afford the final products.

Since the reaction rate is moderate and easy to follow, the reaction was employed for the evaluation of the nucleophilic reactivity of acylsulphimides. The reaction was carried out with a large excess of benzoyl chloride in $CDCl_3$ and followed by n.m.r. Table 4 lists the apparent first-order reaction rate constants for several substituted acylsulphimides. The rate constant decreases with the decrease in pK_a, although no linear relationship between pK_a and log *k* was found. The low reaction rates of *N*-benzoylsulphimides may be interpreted by a steric factor between the reactants. A similar situation, the lack of nucleophilic reactivity of benzoylmethylenesulphurane compared to ethoxycarbonylmethylenesulphurane was reported by Ratts and Yao.[9]

TABLE 4

Apparent first-order rate constants *k'* of the reaction of *N*-acyl-*SS*-dimethylsulphimides Me_2S=NCOR with benzoyl chloride at 37°

R	pK_a	k'/min^{-1}
CCl_3	1.81	$>4 \times 10^{-4}$
$CHCl_2$	1.95	$(1.1 \pm 0.3) \times 10^{-3}$
CH_2Cl	2.13	$(1.0 \pm 0.1) \times 10^{-2}$
CH_3	3.15	$(1.0 \pm 0.2) \times 10^{-1}$
C_6H_5	2.50	$(2.1 \pm 0.4) \times 10^{-3}$
p-ClC_6H_4	2.29	$(1.8 \pm 0.8) \times 10^{-3}$

EXPERIMENTAL

M.p.s (uncorrected) were determined using a capillary apparatus. N.m.r. spectra were recorded on a Hitachi R 20A spectrometer at 60 MHz, and chemical shifts are expressed in δ values. I.r. spectra were taken on a JASCO IRA-2 spectrometer as either KBr discs or liquid films. Microanalyses were performed with a Perkin-Elmer 240 elemental analyser.

Preparation of Sulphimides and Their Salts.—A general synthetic method for acylsulphimides which provides a variety of substituents on sulphur and carbonyl carbon has not yet been established. We employed three different methods which have been reported for the preparation of limited kinds of sulphimides; the reaction of *N*-bromoacetamide with dialkyl sulphides in acetone–carbon tetrachloride to give *N*-acetyl-*SS*-dialkyliminosulphonium bromides (method A),[16] the reaction of dialkylchlorosulphonium t-butoxide with sodium salts of amides to give *N*-acyl-*SS*-dimethyl- and *N*-acyl-*SS*-tetramethylene-sulphimides (method B),[17] and the reaction of sulphoxides with amides in the presence of acetic anhydride to give sulphimides (method C).[18] The crude sulphimides obtained by methods B and C were converted to their salts by treatment with concentrated HCl in acetone at 0° and recrystallized from ethanol. Since recrystallization of the crude sulphimides was often unsuccessful, the pure iminosulphonium salts obtained by the above method were converted back into the original sulphimides by treatment with a slight excess of triethylamine to give analytically pure sulphimides. In

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[14] K. W. Ratts, *J. Org. Chem.*, 1972, **37**, 848.

[15] H. Kise, G. F. Whitfield, and D. Swern, *Tetrahedron Letters*, 1971, 4839.

[16] H. Kise, G. F. Whitfield, and D. Swern, *J. Org. Chem.*, 1972, **37**, 1121.

[17] D. Swern, I. Ikeda, and G. F. Whitfield, *Tetrahedron Letters*, 1972, 2635.

[18] D. S. Tarbell and C. Weaver, *J. Amer. Chem. Soc.*, 1941, **63**, 2939.

the case of salt-forming sulphimides, this is a ready method for the purification of the sulphimides.

Tables 2 and 3 list the spectral data of the sulphimides and iminosulphonium salts, several of which are new compounds. The purity of the compounds was determined by microanalyses (Tables 5 and 6).

TABLE 5

N-Acyl-*SS*-dimethylsulphimides $Me_2S{=}NCOR$ (upper) and their hydrochlorides(lower)

R	Method	M.p. (°C) *	Found (calc.) (%) C	H	N	pK_a
CCl_3	B	87—88	21.25 (21.6)	2.5 (2.7)	6.65 (6.3)	(1.82) [b]
		(91—92) [a]				
$CHCl_2$	B	98—100	25.7 (25.55)	3.8 (3.75)	7.05 (7.45)	1.95
		(101—102) [a]				
		86—87	21.85 (21.4)	3.7 (3.6)	6.4 (6.25)	
CH_2Cl	B	89—90	31.65 (31.25)	5.4 (5.25)	8.85 (9.1)	2.13
		114—115	25.8 (25.25)	4.9 (4.8)	7.45 (7.35)	
H	B	Liquid				2.40
		120—130	25.85 (25.45)	5.75 (5.7)	9.4 (9.9)	
CH_3	A	67—68	40.35 (40.3)	7.75 (7.65)	11.6 (11.75)	3.15
		(67—68) [c]				
		111—113	24.3 (24.0)	5.2 (5.05)	7.35 (7.0)	
		(111—112) [c]				
C_6H_5	B	105—106	59.2 (59.65)	6.2 (6.15)	7.3 (7.75)	2.50
		(106—108) [d]				
		185—189	49.5 (49.65)	5.65 (5.55)	6.4 (6.45)	
		(180—182) [d]				
p-ClC_6H_4	B	102—104	50.0 (50.1)	4.9 (4.7)	6.6 (6.5)	2.29
		141—143	43.2 (42.85)	4.65 (4.4)	5.85 (5.55)	

* Literature values in parentheses.

[a] T. E. Varkey, G. F. Whitfield, and D. Swern, *J. Org. Chem.*, 1974, **39**, 3365. [b] Measured by titration of the sulphimide. [c] A. J. Papa, *J. Org. Chem.*, 1970, **35**, 2837. [d] Ref. 16.

TABLE 6

N-Acyl-*SS*-tetramethyleneiminosulphonium chlorides $[CH_2]_4\overset{+}{S}NHCORCl^-$

R	Method	M.p. (°C) *	Found (calc.) (%) C	H	N	pK_a
CCl_3 [a]	C	116—117	21.25 (21.6)	2.5 (2.7)	6.65 (6.3)	(1.81) [b]
		(116—117) [c]				
$CHCl_2$ [a]	C	149—151	33.6 (33.65)	4.2 (4.25)	6.5 (6.55)	(1.97) [b]
		(149—151) [c]				
CH_2Cl	B	91—92	33.45 (33.35)	5.2 (5.15)	6.5 (6.5)	2.22
H	B	99—100	36.1(35.8)	6.1 (6.0)	8.5 (8.35)	2.55
CH_3	A	116—118	31.5 (31.85)	5.35 (5.35)	6.05 (6.2)	3.45
		(115—117) [d]				
C_2H_5	B	112—114	42.65 (42.95)	7.4 (7.2)	7.25 (7.15)	3.26
C_6H_5	B	100—102	53.95 (54.2)	5.95 (5.8)	5.6 (5.75)	2.62
p-$CH_3OC_6H_4$	B	110—112	52.35 (52.65)	6.1 (5.9)	5.1 (5.1)	2.82
p-$CH_3C_6H_4$	B	115—117	56.35 (55.9)	6.4 (6.25)	5.65 (5.45)	2.72
p-ClC_6H_4	B	96—97	47.25 (47.5)	5.4 (4.7)	4.8 (5.05)	*e*

* Literature values in parentheses.

[a] Data for sulphimide. [b] Measured by titration of the sulphimide. [c] Ref. 18. [d] Ref. 16. [e] This sulphonium salt reacts in water to afford unidentified products.

Measurement of pK_a.—Iminosulphonium salt (*ca.* 1—2 mmol) was dissolved in water (40 ml) and titrated with 0.1N-NaOH solution at 25 °C using a pH meter. The alkaline solution was back titrated with 0.1N-HCl solution to give essentially identical titration curves, showing that sulphimide–sulphonium salt conversion is reversible. The values of pK_a are the pH values at half-neutralization.

Kinetics of Reaction of Sulphimides with Benzoyl Chloride.—The reactions were carried out in n.m.r. tubes at 37°. *N*-Acyl-*SS*-dimethylsulphimide (*ca.* 2—3 × 10^{-4} mol) was dissolved in $CDCl_3$ (0.3 ml), and a small amount of cyclohexane was added as an internal standard. The reaction was started by addition of *ca.* 15-fold excess of benzoyl chloride over sulphimide, and n.m.r. intensities of cyclohexane (δ 1.43) and methyl proton signals of the sulphimide (Table 2) were recorded at measured intervals. A plot of ln (I_0/I_t) *versus* time gave a straight line where I_0 and I_t are the relative intensities of methyl proton signals of the sulphimide to that of cyclohexane at time 0 and *t* respectively. The results indicate that the reaction is first-order in sulphimide and the pseudo-first-order rate constants listed in Table 4 were calculated from the slope of the plot.

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