Kinetics of Reactions in Heterocycles. Part II.[1] Replacement of the Methylsulphonyl Group in Substituted Pyridines, Pyridazines, and Pyrazine by Methoxide Ion

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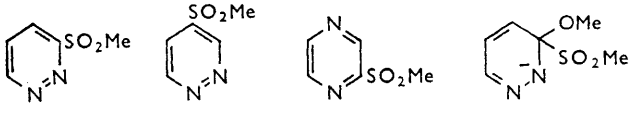
Kinetic study of the reactions of methylsulphonylpyridines, pyridazines, and pyrazine with methoxide ion shows that the methylsulphonyl group is very readily replaced. Where direct comparison is possible, as in the 3-substituted pyridazines, it is found that the methylsulphonyl compound is *ca.* 90 times more reactive than the chloro-compound, at 40·2°.

The preparation of new methylsulphonyl compounds is described. Ionisation constants and ultraviolet and nuclear magnetic resonance spectra are recorded and discussed.

REPLACEMENT of the methylsulphonyl group in substituted nitrogen heterocycles has been little studied and the only quantitative work is that on the reactivity of methylsulphonylpyrimidines with n-pentylamine in dimethyl sulphoxide.[2]

We have commenced a quantitative study of the displacement of the methylsulphonyl group from other heterocyclic derivatives with nucleophiles, and now report the results obtained with the monocyclic azines and methoxide ion. It is assumed that the main features of the reaction mechanism, which is almost certainly bimolecular, are common to all the compounds studied. In the absence of any experimental evidence to decide between a one-stage and a two-stage mechanism, we will, for simplicity, discuss the reaction parameters from the viewpoint of the former. Table 1 lists details of some typical kinetic experiments, Table 2 summarises all kinetic results, and Table 3 lists parameters derived from the kinetic studies. Sample results (Table 1) show no significant trend, and indicate freedom from side reactions; values of $t_{\frac{1}{2}}$ (Table 2) strongly indicate second-order kinetics, consistent with the bimolecular mechanism.

The values given in Table 3 show that the substituent in 4-methylsulphonylpyridine is more reactive than that in the 2-isomer, consistent with the considerably lower energy of activation, although the frequency factor, as given by log A, is also lower. These results agree with those obtained for ethoxydechlorination of pyridines,[3] where at 90° the γ-position is five times more reactive than the α-position. Similarly in 3- and 4-methylsulphonylpyridazine, (I) and (II), where the leaving group is placed β to one ring nitrogen and α or γ



(I) (II) (III) (IV)

to another, the 4-methylsulphonyl compound is found to be the more reactive, and as the frequency factors, log A, are almost the same, the greater reactivity is due to a lower energy of activation. 2-Methylsulphonylpyrazine (III), which is also activated by β and α ring-nitrogen atoms, shows considerable but lower reactivity, and the energy of activation is higher than that for similarly activated 3-methylsulphonylpyridazine. The reason for the greater reactivity of the latter is probably the electron withdrawal by the β ring nitrogen, which lowers the energy of formation of the transition state (IV) below that required for the pyrazine (III). The introduction of another doubly bound ring-nitrogen β to the leaving group in a methylsulphonylpyridine brings about a considerable increase in reactivity and a large decrease in energy of activation.

Direct comparison of the displacements of the methylsulphonyl and chloro-groups is at present possible only for the 3-position of pyridazine. From the figures given by Hill and Krause [4] for 3-chloropyridazine with methoxide ion at 40·2°, where k is $2{\cdot}56 \times 10^{-4}$ l. mole^{-1} sec.$^{-1}$, the energy of activation is 19·3 kcal. mole^{-1}, and $\Delta S^{\ddagger}$ is −15·4 units. Comparison of these results with those given in Tables 2 and 3 for the methylsulphonyl compound reveals that the latter is *ca.* 90 times more reactive than the chloro-compound, and this greater reactivity can be attributed mainly to a lower energy of activation.

The greater reactivity of the methylsulphonyl compared with the chloro-group is also indicated by comparing the results for 2- and 4-methylsulphonylpyridine (Table 3) with those for the reaction of 2- and 4-chloropyridine [3] with ethoxide ion in ethanol (a reagent which with 2- and 4-chloroquinoline [3] does not differ greatly in nucleophilicity from methoxide ion in methanol [5]).

Ionisation Constants and Ultraviolet Spectra (*Table* 4).—The ionisation constants clearly show the powerful electron withdrawal of the methylsulphonyl group. In the 2- and 4-positions of pyridine it reduces the pK_a values by 6·73 and 3·61 units respectively, and in pyrazine and the 3-position of pyridazine where protonation occurs on the nitrogen β to the methylsulphonyl group, the reduction is 3·12 and 3·34 units, respectively. 4-Methylsulphonylpyridazine is believed to protonate on N-1 or N-2 (see discussion of n.m.r. spectra). Thus the base-weakening by the methyl-

[1] G. B. Barlin, preceding Paper, is regarded as Part 1.
[2] D. J. Brown and P. W. Ford, *J. Chem. Soc.* (*C*), 1967, 568.
[3] N. B. Chapman and D. Q. Russell-Hill, *J. Chem. Soc.*, 1956, 1563.
[4] J. H. M. Hill and J. G. Krause, *J. Org. Chem.*, 1964, **29**, 1642.
[5] M. L. Belli, G. Illuminati, and G. Marino, *Tetrahedron*, 1963, **19**, 345.

TABLE 1

Reactions of methoxide ions

4-Methylsulphonylpyridine at 110·5°

Methoxide ion 0·0039N, methylsulphonyl compound 0·0028M.

Time (min.)	18·3	51·5	75·7	104·6	136	172	208·2	262
Reaction (%)	13·9	32·3	41·2	50·2	57·9	65·0	69·8	75·1
10^2k	3·61	3·69	3·60	3·61	3·62	3·68	3·65	3·57

Mean $10^2k = 3·63 \pm 0·04$; after correction for solvent expansion, 4·02.

4-Methylsulphonylpyridazine at 30·3°

Methoxide ion 0·00116N, methylsulphonyl compound 0·00079M.

Time (min.)	15·4	34·6	56	84	128·2	170·7	215	270·2	342·5
Reaction (%)	11·3	22·8	33·1	43·4	56·4	65·2	71·7	78·1	83·5
$10k$	1·19	1·17	1·18	1·17	1·22	1·24	1·21	1·26	1·19

Mean $10k = 1·20 \pm 0·03$; after correction for solvent expansion, 1·21.

2-Methylsulphonylpyrazine at 49·9°

Methoxide ion 0·00238M, methylsulphonyl compound 0·00144M.

Time (min.)	19·2	44·9	78·2	157·6	197·5	243·2	286	346
Reaction (%)	6·6	14·2	22·4	38·1	44·4	50·1	55·3	60·9
10^2k	2·45	2·47	2·44	2·45	2·46	2·45	2·46	2·48

Mean $10^2k = 2·46 \pm 0·02$; after correction for solvent expansion, 2·55.

TABLE 2

Kinetic results for the reactions of methylsulphonyl compounds with methoxide ions

Temp.[a]	10^3[MeO$^-$]	10^3[$-SO_2Me$]	10^3k [b]	10^3k [c] corr.	$t_{\frac{1}{2}}$ [d]	$t_{\frac{1}{2}}/t'_{\frac{1}{2}}$ [e]	$t_{\frac{1}{2}}/t'_{\frac{1}{2}}$ [f] calc.	An. λ (mμ) [g]	pH [h]
				2-Methylsulphonylpyridine					
108·7°	12·3	8·19	1·82	1·97				272	6·0
117·0	12·3	8·19	3·97	4·33				272	6·0
127·9	12·3	8·19	10·85	12·2	108			272	6·0
127·9	6·15	4·095	10·4	11·8	230	2·13	2·00	272	6·0
				4-Methylsulphonylpyridine					
90·4	11·09	6·15	6·91	7·47	183			268	9·0
90·4	6·55	3·62	6·94	7·52	310	1·67	1·67	268	9·0
100·1	5·24	2·99	15·4	16·8				268	9·0
110·5	3·92	2·82	36·3	40·2				268	9·0
				3-Methylsulphonylpyridazine					
30·2	7·15	3·95	9·65	9·71				266	6·0
40·1	4·11	2·38	23·2	23·6				266	6·0
50·6	4·52	2·54	56·9	58·6	53			266	6·0
50·6	2·26	1·27	56·1	57·8	108	2·04	2·00	266	6·0
				4-Methylsulphonylpyridazine					
20·25	2·90	1·90	50·8	50·6				247	1·0
30·3	2·32	1·58	121	122	52·5			247	1·0
30·3	1·16	0·791	120	121	104	1·98	2·00	247	1·0
39·7	0·695	0·475	268	273				247	1·0
				2-Methylsulphonylpyrazine					
29·9	7·13	4·01	3·86	3·89				292	6·0
39·9	4·75	2·88	9·74	9·97				292	6·0
49·9	4·75	2·88	24·3	25·2	120			292	6·0
49·9	2·38	1·44	24·6	25·5	243	2·02	2·00	292	6·0

[a] ±0·1°. [b] In l. mole^{-1} sec.$^{-1}$; the standard deviation was usually below 3%. [c] Corrected for solvent expansion. [d] Time for 50% reaction, in min. [e] The ratio of $t_{\frac{1}{2}}$ for two experiments at different concentrations. [f] Calculated by assuming a second order reaction. [g] Analytical wavelength for determination of percentage reaction. [h] pH of buffer solutions used to stop the reaction and for spectroscopic measurements.

TABLE 3

Rate coefficients and Arrhenius parameters for reactions with methoxide ions

	Temp.	10^3k (l. mole^{-1} sec.$^{-1}$)	E [a] (kcal. mole^{-1})	log A [b]	$\Delta H^{\ddagger}$ [a] (kcal. mole^{-1})	$\Delta S^{\ddagger}$ [c] (cal. mole^{-1} deg.$^{-1}$)
2-Methylsulphonylpyridine	108·7°	1·97	28·7	13·7	27·9	+1·7
4-Methylsulphonylpyridine	110·5	40·2	23·1	11·7	22·4	−7·5
3-Methylsulphonylpyridazine	30·2	9·71	17·1	10·3	16·5	−13·5
4-Methylsulphonylpyridazine	30·3	121	15·7	10·4	15·1	−13·0
2-Methylsulphonylpyrazine	29·9	3·86	18·3	10·8	17·7	−11·2

[a] Accurate to ±0·4 kcal. mole^{-1}. [b] Accurate to ±0·3 unit. [c] Accurate to ±1 unit.

TABLE 4

Physical properties (pK_a and spectra)

Compound	Ionisation (water, 20°): Charged species involved [a]	pK_a	Spread (±)	Concn. (M)	An. λ [b] (mμ)	Spectroscopy in water [e]: $\lambda_{max.}$ (mμ)	log ε	pH [f]
Pyridine	—					—	—	—
	+	5·23 [c]				—	—	—
2-SO_2Me ...	0	—				253, 258, 264	3·46, 3·51, 3·36	9·0
	+	−1·50	0·03	0·00003	262	259	3·86	−4·0
4-SO_2Me ...	0	—				268	3·49	7·0
	+	1·62	0·03	0·00003	270	269	3·72	−0·8
Pyridazine ...	0	—				—	—	—
	+	2·33 [c]				—	—	—
3-SO_2Me ...	0	—				244, 249, *255*, 303—304	2·88, 2·88, *2·67*, 2·49	9·0
	+	−1·01	0·07	0·0006	310	*244*	*3·09*	−3·4
4-SO_2Me ...	0	—				*252*, 256, *262*, 324	*3·33*, 3·34, *3·16*, 2·46	7·0
	+	−1·06	0·06	0·00005	235	245—247	3·42	−3·2
Pyrazine ...	0	—				—	—	—
	+	0·65 [d]				—	—	—
2-SO_2Me ...	0	—				*259*, 264, *270*, 310	*3·80*, 3·86, *3·74*, 2·78	6·0
	+	−2·47	0·05	0·00008	280	273	3·90	−5·0

[a] 0 Refers to the neutral species, + to the cation. [b] Analytical wavelength for spectroscopic determinations of pK_a. [c] A. Albert, R. Goldacre, and J. N. Phillips, *J. Chem. Soc.*, 1948, 2240. [d] A. Chia and R. Trimble, *J. Phys. Chem.*, 1961, **65**, 863. [e] Shoulders and inflexions in italics. [f] pH Values below 0 have been obtained in solutions of sulphuric acid to which Hammett acidity functions (cf. M. A. Paul and F. A. Long, *Chem. Rev.*, 1957, **57**, 1) have been assigned.

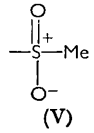
TABLE 5

N.m.r. spectra

Compound	Species †	Solvent	Chemical shifts (τ) of protons: 2	3	4	5	6	CH_3
Pyridine								
2-SO_2Me	0	$CDCl_3$		1·9m	1·8m	2·3m	1·13m	6·72
	+	10N-DCl		0·9m	1·1m	1·35m	0·7m	6·30
4-SO_2Me	0	$CDCl_3$	0·91q	2·06q		2·06q	0·91q	6·86
	+	2N-HCl	0·57q	1·16q		1·16q	0·57q	6·40
2-SMe	0	$CDCl_3$		2·75m	2·4m	2·9m	1·42m	7·39
	+	N-DCl		2·0m	1·5m	2·2m	1·4m	7·17
4-SMe	0	$CDCl_3$	1·46q	2·79q		2·79q	1·46q	7·49
	+	N-DCl	1·44q	2·10q		2·10q	1·44q	7·27
Pyridazine								
3-SO_2Me	0	$CDCl_3$			1·65q	2·09q	0·43q	6·52
	+	5N-DCl			0·8m	0·9m	−0·05m	6·35
4-SO_2Me	0	$CDCl_3$		0·25m		1·93q	0·3m	6·83
	+	5N-DCl		−0·30m		0·67m	−0·2m	6·37
3-SMe	0	$CDCl_3$			2·5m	2·7m	0·98q	7·24
	+	N-DCl			1·4m	1·6m	0·56m	7·22
4-SMe	0	$CDCl_3$		0·9m		2·7q	1·0m	7·43
	+	N-DCl		0·60d		1·69q	0·74d	7·15
Pyrazine								
2-SO_2Me	0	$CDCl_3$		0·55d		0·99d	1·16d	6·69
	+	9M-D_2SO_4		0·39		0·68d	0·14q	6·43
2-SMe	0	$CDCl_3$		1·42d		1·71d	1·54q	7·39
	+	5N-DCl		0·97		1·32d	0·70q	7·19

* τ Values are for singlets except where otherwise indicated; d doublet, q quartet, and m multiplet. † 0 Refers to the neutral molecule, + to the cation.

sulphonyl group is in the order $\alpha > \gamma > \beta$ and is believed to operate by the inductive and mesomeric mechanisms; a principal contributor would have structure (V), in which the use of a *d*-orbital of the sulphur atom would permit the operation of the mesomeric effect. The inductive base-weakening by the chloro-group in pyridine is less than that shown by the methylsulphonyl group and is in the order $\alpha > \beta > \gamma$.



(V)

Nuclear Magnetic Resonance Spectra.—The n.m.r. spectra of neutral molecules and cations are given in Table 5. The spectra were analysable by inspection, J_{para} being assumed to be greater than J_{meta} for pyrazines.[6]

Comparison of the spectra of the neutral molecules of the methylsulphonyl compounds with those of the parent ring systems [6,7] reveals downfield chemical shifts of all protons, due to electron withdrawal by the methyl-

[6] K. Tori and M. Ogata, *Chem. Pharm. Bull.* (*Tokyo*), 1964, **12**, 272.

[7] J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, 1959.

sulphonyl group. As has been observed in pyridines,[8] protonation shifts are least for hydrogen atoms adjacent to the cationic centre. Thus, in 2-methylsulphonyl- and 2-methylthio-pyrazine, which protonate on N-4, shifts are least for 3-H and 5-H. In 4-methylsulphonylpyridazine, however, protonation shifts for 3-H and 6-H are 0·55 and 0·50, and in 4-methylthiopyridazine 0·30 and 0·26; this could indicate that protonation occurs on N-1 and N-2.

EXPERIMENTAL

All compounds were examined for impurities by paper chromatography on Whatman No. 1 paper with (*a*) 3% aqueous ammonium chloride, and (*b*) butan-1-ol–5N-acetic acid (7 : 3). Analyses were by Dr. J. E. Fildes and her staff. Solids for analysis were dried at 20°/20 mm. unless otherwise stated.

Ionisation constants were determined spectroscopically using the method of Albert and Serjeant [9] and the stability of the cations in strong acid was checked by careful neutralisation.

Ultraviolet spectra were recorded on a Perkin-Elmer Spectracord model 4000 recording spectrophotometer, and $\lambda_{max.}$ and ε values were checked on an Optica CF4 manual instrument. N.m.r. spectra were recorded at 60 Mc./sec. and 33·5° on a Perkin-Elmer R10 spectrometer. Chemical shifts are given on the τ scale; tetramethylsilane was used for internal reference except in acid solutions when sodium 3-trimethylsilylpropanesulphonate was employed. Where required, portions of the spectra were expanded.

Preparation of Compounds.—Methylsulphonyl compounds were prepared from the methylthio-compounds by oxidation with potassium permanganate in dilute acetic acid. Oxidations with chlorine or *m*-chloroperbenzoic acid were, in general, found to be less satisfactory.

2- *and* 4-*Methylsulphonylpyridines.*—2-Methylsulphonylpyridine was prepared from 2-methylthiopyridine [10] by oxidation with potassium permanganate.[11] The reaction mixture was decolourised with sulphur dioxide, adjusted to pH 7, and the product extracted with chloroform and distilled (Found: C, 45·7; H, 4·7; N, 9·3; S, 20·3. Calc. for $C_6H_7NO_2S$: C, 45·7; H, 4·5; N, 8·9; S, 20·35%).

4-Methylsulphonylpyridine, m. p. 82° (lit., 81°) (Found: C, 46·1; H, 4·5; N, 9·2; S, 20·1%) was prepared as described by King and Ware.[12]

2-*Methoxypyridine.*—2-Methylsulphonylpyridine (0·100 g.) and methanolic sodium methoxide (5 ml., 0·43N) were heated at 150° for 6 hr. The reaction mixture was diluted with water, neutralised to pH 7, and extracted with chloroform. The extract was dried (Na_2SO_4) and the solvent distilled off leaving an oil, which with ethanolic picric acid gave yellow crystals of 2-*methoxypyridine picrate* (0·09 g.), m. p. and mixed m. p. 159—160° (ethanol). 2-Methoxypyridine picrate for comparison was prepared from 2-bromopyridine and sodium methoxide by a method similar to that used [13] with 2-chloropyridine (Found: C, 42·5; H, 3·0; N, 16·6. $C_{12}H_{10}N_4O_8$ requires C, 42·6; H, 3·0; N, 16·6%).

4-*Methoxypyridine.*—4-Methylsulphonylpyridine (0·100 g.) and methanolic sodium methoxide (5 ml.; 0·43N) were heated at 150° for 6 hr. The mixture was evaporated to dryness and extracted with chloroform; the product with aqueous picric acid gave 4-methoxypyridine picrate (0·075 g.), m. p. 170—171° (water) (lit.,[14] 172—173°) (Found: C, 42·9; H, 3·0; N, 16·7%).

2-*Methylsulphonylpyrazine.*— 2-Methylthiopyrazine [15] (0·500 g.) was dissolved in acetic acid (14 ml.; 8N) and a solution of potassium permanganate (1 g.) in water (8 ml.) added with stirring at 25° during ½ hr. This mixture was cooled in ice, decolourised by passing in sulphur dioxide, adjusted to pH 7 with ammonia, and extracted with chloroform. The chloroform extract was dried (Na_2SO_4) and evaporated to a colourless oil, which solidified on cooling and was twice sublimed (150°/0·5 mm.) to give 2-*methylsulphonylpyrazine* (0·42 g.), m. p. 47—48° (Found: C, 38·4; H, 3·9; N, 17·7; S, 20·15. $C_5H_6N_2O_2S$ requires C, 38·0; H, 3·8; N, 17·7; S, 20·2%).

2-*Methoxypyrazine.*—2-Methylsulphonylpyrazine (0·005 g.) and methanolic sodium methoxide (3 ml.; 0·02N) were heated at 87° for 3 hr. Complete conversion into 2-methoxypyrazine was apparent (appropriate dilutions of the reaction mixture at pH 6·0 and pH −1·5 gave solutions with the ultraviolet spectra of the neutral molecule [16] and the cation [17] respectively).

3-*Methylsulphonylpyridazine.*—(*a*) To 3-methylthiopyridazine [18] (0·029 g.) in acetic acid (6 ml.; 16N), potassium permanganate (0·75 g.) in water (9 ml.) was added slowly with stirring at 25° and stirring was continued for 0·5 hr. The mixture was cooled in ice, decolourised by passing in sulphur dioxide, adjusted to pH 8 with ammonia, and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated to yield 3-*methylsulphonylpyridazine* (0·027 g.), m. p. 87° [benzene–light petroleum (b. p. 60—80°)] (Found: C, 37·8; H, 3·7; N, 17·7; S, 20·4%).

(*b*) 3-Methylthiopyridazine (0·500 g.) was dissolved in a mixture of methanol (3 ml.) and water (10 ml.), cooled to −20°, and chlorine passed for 1 hr. The cold solution was adjusted to pH 7 by careful addition of aqueous potassium carbonate, extracted with chloroform, and the extract dried (Na_2SO_4) and evaporated to give a yellow solid. This, in a small volume of chloroform, was chromatographed over alumina (6 in.) to give 3-methylsulphonylpyridazine (0·440 g.), m. p. and mixed m. p. with product of (*a*) 87°.

4-*Methylsulphonylpyridazine.*— 4-Methylthiopyridazine [15] (0·120 g.) in acetic acid (2 ml.; 16N) was stirred at room temperature while potassium permanganate (0·25 g.) in water (2·5 ml.) was added during 0·5 hr. The mixture was cooled, decolourised by passing in sulphur dioxide, and adjusted to pH 7 with ammonia. Extraction with chloroform gave 4-*methylsulphonylpyridazine* (0·073 g.), m. p. 144° (ethanol) (Found: C, 38·0; H, 3·9; N, 18·0; S, 20·3%).

3-*Methoxypyridazine.*— 3-Methylsulphonylpyridazine (0·100 g.) and methanolic sodium methoxide (5 ml.; 0·43N) were refluxed for 30 min. The reaction mixture was

[8] I. C. Smith and W. G. Schneider, *Canad. J. Chem.*, 1961, **39**, 1158.
[9] A. Albert and E. P. Serjeant, "Ionization Constants," Methuen, London, 1963.
[10] M. A. Phillips and H. Shapiro, *J. Chem. Soc.*, 1942, 584.
[11] W. Markwald, W. Klemm, and H. Trabert, *Ber.*, 1900, **33**, 1556.
[12] H. King and L. L. Ware, *J. Chem. Soc.*, 1939, 873.
[13] T. B. Grave, *J. Amer. Chem. Soc.*, 1924, **46**, 1460.
[14] R. R. Renshaw and R. C. Conn, *J. Amer. Chem. Soc.*, 1937, **59**, 297.
[15] A. Albert and G. B. Barlin, *J. Chem. Soc.*, 1962, 3129.
[16] S. F. Mason, *J. Chem. Soc.*, 1957, 5010.
[17] S. F. Mason, *J. Chem. Soc.*, 1959, 1253.
[18] G. F. Duffin and J. D. Kendall, *J. Chem. Soc.*, 1959, 3789.

diluted with water, neutralised to pH 7, and extracted with chloroform. The chloroform extract was dried (Na_2SO_4) and the solvent evaporated to give an oily residue which with ethanolic picric acid gave yellow crystals of 3-methoxypyridazine picrate (0·080 g.), m. p. 111° (ethanol) (lit.,[19] 111°) (Found: C, 39·1; H, 2·6; N, 20·3. Calc. for $C_{11}H_9N_5O_8$: C, 38·95; H, 2·7; N, 20·65%).

4-Methoxypyridazine.— 4-Methylsulphonylpyridazine (0·100 g.) with sodium methoxide as described above for the 3-isomer gave 4-methoxypyridazine picrate (0·150 g.), m. p. 143—144° (lit.,[20] 143—144°) (Found: C, 39·0; H, 2·4; N, 20·6%).

Methanol.—AnalaR methanol was dried by Lund and Bjerrum's [21] method and fractionated through a column packed with glass helices; the first 10% of the distillate was discarded.

Sodium Methoxide Solution.—Clean sodium was dissolved in methanol, and the concentration determined by titration with standard acid.

Kinetic Procedure.—At temperatures greater than 90°, methanol solutions (2 ml.) which were 2·8—8·2 × 10^{-3}M in methylsulphonyl compound and 4·0—12·0 × 10^{-3}N in sodium methoxide were heated in sealed tubes in a thermostat. The tubes were chilled briefly, and the contents diluted with buffer to 50 ml.

At temperatures less than 51°, a weighed quantity of methylsulphonyl compound was dissolved quickly in a known volume of methanolic sodium methoxide (0·7—7·0 × 10^{-3}N) in the thermostat, and samples (2 ml.) were removed at specified times and quenched in buffer solution.

Ultraviolet absorption at the specified wavelength was then determined for each sample and the second-order rate coefficient calculated from the expression:

$$k = \frac{2{\cdot}303}{t(a-b)} \log \frac{b\,(a-x)}{a\,(b-x)}$$

where a is the initial concentration of methoxide ion, b that of methylsulphonyl compound, x is the concentration of methoxy-compound formed at time t (sec.), and k the second-order rate coefficient in l. mole^{-1} sec.$^{-1}$. Where necessary, corrections were made for expansion of the solvent.

The methylsulphonyl compounds in methanol were stable at the temperatures of the kinetic runs, and with sodium methoxide at t_∞ the spectrum obtained was that of the pure methoxy-compound.

For each run, 9 samples covering at least 10—60% reaction, and also those corresponding to t_0 and t_∞ (at least 30 times the half-life of the reaction and corresponding to 98—100% reaction) were examined. Times for 50% reaction were determined in selected cases. Each reaction was studied at three temperatures, covering a 20° range.

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