Kinetics of Reactions in Heterocycles. Part XII.[1] Substituted *N*-Methylquinolinium and *N*-Methylisoquinolinium Salts with Hydroxide Ions

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Kinetics of the replacement reactions of chloro-, iodo-, methoxy-, and methylthio-substituted *N*-methylquinolinium and *N*-methylisoquinolinium iodides with hydroxide ions have been determined. The 2-iodo- and 2-methylthio-quinolinium salts at 20° were 1440 and 1490 times more reactive than their 4-isomers respectively, owing to lower energies of activation and higher frequency factors. The reactivity of 1-methylthioisoquinoline methiodide was anomalous, being 530 times greater than that of 2-methylthioquinoline methiodide. *N*-Methylation of the iodo-quinolines and -isoquinolines increased their reactivity towards hydroxide ions at 114·8° by 1·2—3·4 × 10^7 fold for substituents at the α-position, and 6·1 × 10^5 fold for substituents at the γ-position of quinoline. U.v. and ^{1}H n.m.r. spectra are recorded and discussed.

In an earlier communication [2] we reported the kinetics for the reactions of substituted *N*-methylpyridinium salts with hydroxide ions. These studies showed that the pyridines with a leaving group at the 2-position were the most reactive; and that quaternisation of 4-methylsulphonylpyridine by methylation increased the reactivity to hydroxide ions by 7·3 × 10^8 fold at 20°. We now report the kinetic results for the reactions of substituted *N*-methyl-quinolinium and -isoquinolinium salts with hydroxide ions.

Typical kinetic runs for the compounds (Table 1) revealed that regular second-order kinetics pertained during 10—85% reaction, and that the reactions were essentially bimolecular as indicated by the $t_{\frac{1}{2}}$ values (Table 2). As in Part X,[2] calculations of the rate coefficients for the reactions of the halogeno- and methylthio-compounds allowed for the consumption of two moles of sodium hydroxide per mole of heterocycle, but for the methoxy-compounds only one mole of sodium hydroxide was consumed. The reactions generally were studied at near-spectroscopic concentrations, but the hydroxide ion concentration was increased significantly in some cases to facilitate rate coefficient determination by the rapid reaction technique.[3] The rate coefficients were affected by large changes in ionic strength as shown by the results for 4-chloro- and 4-iodo-quinoline methiodides, but for individual compounds the hydroxide ion concentration changes were minimised.

All kinetic results are summarised in Table 2, and Arrhenius parameters and calculated rate coefficients at 20° are shown in Table 3. A comparison of the reactivity of the 2- and 4-iodoquinoline methiodides at 20° revealed that the 2-isomer was 1440 times the more reactive; for the methylthio-compounds, the relative reactivity was 1490 : 1 (compare with 43 and 130 times for the iodo- and methylthio-pyridine methiodides [2] respectively). These results were reflected in the lower energies of activation and higher frequency factors of the 2-isomers. Annulation normally increases the reactivity of 2-substituted 1-azaheterocycles relative to their 4-isomers [4] and this effect operates also in the 2-substituted quinoline methiodides to enhance further their relative reactivities. These results stand in sharp contrast with published data [5] which reveal that 2- and 4-chloroquinoline (and 1-chloroisoquinoline) with ethoxide ions in ethanol at 20° have similar reactivities, and also with results in this paper which show that the reactivities of 2- and 4-iodoquinoline (and 1-iodoisoquinoline) towards hydroxide ions in water at 114·8° do not differ greatly.

Rate enhancements at 20° were observed on annulation. Thus the quinoline methiodides were 230—280 and 8—40 times more reactive than the pyridine methiodides with substituents at the 2- or 4-position respectively. This higher reactivity of the quinolinium compounds was associated with lower energies of activation (except

[1] Part XI, R. J. Badger and G. B. Barlin, *J.C.S. Perkin II*, 1974, 1854.
[2] G. B. Barlin and J. A. Benbow, *J.C.S. Perkin II*, 1974, 790.
[3] D. D. Perrin, *Adv. Heterocyclic Chem.*, 1965, **4**, 43.
[4] G. B. Barlin and W. V. Brown, *J. Chem. Soc.* (*B*), 1968, 1435.
[5] N. B. Chapman and D. Q. Russell-Hill, *J. Chem. Soc.*, 1956, 1563.

for the 4-methoxy compound where it was the same) and higher log A values (except for the 4-chloro-compound) and may be contrasted with generally lower frequency factors observed on annulation.[4,6] In the isoquinoline methiodides, the higher reactivity was associated with significantly lower energies of activation but lower log A values than the corresponding pyridinium compounds.

To determine the effects of quaternisation by methylation on the reactivity of substituted quinolines and isoquinolines, the kinetics of the reaction of 2-iodoquinoline with hydroxide ions and the rate coefficients at 114·8° for the reactions of 4-iodoquinoline and 1-iodoisoquinoline with hydroxide have been measured. Full kinetics for 4-iodoquinoline were not determined because a trend with time was evident in the results,

TABLE 1

Reactions with hydroxide ions

2-Iodoquinoline methiodide at 33·3°

Hydroxide ion 0·000249N; methiodide 0·0000261M

Time (s)	5·9	11·8	19·4	26·5	35·3	45·9	57·6	71·8	91·2	114·7
Reaction (%)	9·4	18·5	27·9	35·8	44·9	53·3	60·6	68·1	76·2	83·0
k/l mol^{-1} s^{-1}	68·1	71·4	70·0	70·0	71·6	71·1	70·1	70·1	70·4	70·1

Mean k = 70·3 ± 0·99

2-Methylthioquinoline methiodide at 41·9°

Hydroxide ion 0·000497N; methiodide 0·0000509M

Time (s)	60·6	121·2	196·9	278·7	387·8	530·1	711·9	939·1
Reaction (%)	11·2	21·1	31·3	40·7	51·3	62·0	72·6	81·5
k/l mol^{-1} s^{-1}	3·98	4·02	3·97	3·96	3·98	3·96	4·02	4·05

Mean k = 3·99 ± 0·034

4-Chloroquinoline methiodide at 25·5°

Hydroxide ion 0·250N; methiodide 0·0000387M

Time (s)	5·9	11·8	20·6	29·4	41·2	54·7	70·0	88·2	117·6
Reaction (%)	11·5	22·0	35·2	46·3	57·7	67·8	76·7	83·7	91·2
10k/l mol^{-1} s^{-1}	0·827	0·846	0·844	0·844	0·836	0·830	0·831	0·822	0·826

Mean 10k = 0·834 ± 0·009

4-Methoxyquinoline methiodide at 24·5°

Hydroxide ion 0·005N; methiodide 0·0000584M

Time (s)	468·2	936·5	1580	2283	3219	4273	5560	7316	9189
Reaction (%)	10·7	20·5	31·8	42·8	54·5	64·9	73·9	82·0	88·1
10^3k/l mol^{-1} s^{-1}	48·2	49·0	48·6	49·0	49·1	49·2	48·6	47·1	46·7

Mean k = 0·0484 ± 0·0009

1-Iodoisoquinoline methiodide at 31·5°

Hydroxide ion 0·0025N; methiodide 0·0000626M

Time (s)	1·2	2·4	3·7	5·3	7·3	9·5	11·8	14·8	18·3	22·7	29·6
Reaction (%)	11·8	22·0	32·0	43·0	53·5	63·7	71·2	78·8	85·7	90·5	95·1
k/l mol^{-1} s^{-1}	42·5	42·3	41·9	42·7	42·6	43·6	43·2	43·0	43·6	42·9	42·4

Mean k = 42·8 ± 0·556

1-Methylthioisoquinoline methiodide at 14·3°

Hydroxide ion 0·00046N; methiodide 0·0000789M

Time (s)	1·2	2·4	3·9	5·7	7·9	10·6	13·8	18·7
Reaction (%)	11·5	21·5	32·5	42·7	52·5	63·5	72·5	82·0
k/l mol^{-1} s^{-1}	229·3	231·5	230·8	231·1	229·2	237·0	241·1	244·7

Mean k = 234·3 ± 5·9

The relative reactivity of compounds with different substituents at the same position did not vary greatly in the pyridinium [2] or quinolinium series but the reactivity of 1-methylthioisoquinoline methiodide was anomalous. At 20°, its reactivity was significantly higher (530×) than that of 2-methylthioquinoline methiodide and 17·5 times higher than that of 1-iodoisoquinoline methiodide; in each case this was due mainly to a lower energy of activation of 1-methylthioisoquinoline methiodide although the frequency factor of 2-methylthioquinoline methiodide was higher. 1-Iodoisoquinoline methiodide at 20° showed a reactivity similar to that of 2-iodoquinoline methiodide but E and log A were both lower.

[6] G. B. Barlin and W. V. Brown, *J. Chem. Soc.* (*B*), 1967, 736.

probably due to decomposition, and only one approximate rate coefficient was determined at 10—20% reaction. The comparison of these rate coefficients for the iodo-quinolines and -isoquinolines with their methiodides (Table 4) revealed a rate difference at the α-position of 1·2—3·4 × 10^7 and at the 4-position of quinoline of 6·1 × 10^5 times. These compare with 2·6 × 10^8 and 2·0 × 10^6 respectively for the 2- and 4-chloropyridines and their methiodides.[2] The effect of N-methylation in 2-iodoquinoline towards reaction with hydroxide ions was to decrease the energy of activation by 7·5 kcal mol^{-1} and increase log A by 3·3 units.

It was not possible to study the reactions of 3-bromo-, 3-methylthio-, and 8-methoxy-quinoline methiodides with hydroxide ions because the u.v. spectrum of the

TABLE 2

Kinetic results for the reactions of substituted quinoline and isoquinoline methiodides with hydroxide ions

Temp.[a] (°C)	$[10^4OH^-]$/M	$[10^5N^+Me]$/M	k [b,c]	$t_{\frac{1}{2}}$ [d]	$t_{\frac{1}{2}}/t_{\frac{1}{2}}'$ [e]	$(t_{\frac{1}{2}}/t_{\frac{1}{2}}')$calc.[f]	Analyt. λ/nm [g]
			2-Iodoquinoline methiodide [h]				
33·3	2·49	2·61	70·3				342·5
43·2	2·485	2·53	146·6				342·5
51·7	2·47	2·37	263·3	11·27			342·5
51·7	1·24	1·13	263·8	22·34	1·98	1·99	342·5
			2-Methylthioquinoline methiodide				
41·9	4·97	5·09	3·99				349
51·5	4·95	5·06	7·88				349
63·5	4·92	5·03	17·64	84·8			349
63·5	2·46	2·63	18·02	166·4	1·96	2·00	349
			4-Chloroquinoline methiodide [h]				
25·5	2500	3·87	0·0834				338
32·4	2500	4·99	0·1523				338
37·5	2500	3·86	0·2220				338
42·6	2500	3·86	0·3354				338
30·3	10	7·78	0·2216	3272			338
30·3	5	3·89	0·2254	6432	1·97	2·00	338
			4-Iodoquinoline methiodide				
34·6	2490	3·82	$0·0644_5$ [h]				345
41·5	2485	3·81	0·1145 [h]				345
47·5	2480	3·80	0·1872 [h]				345
54·9	2475	3·79	0·3458 [h]				345
34·0	47·6	6·92	0·1222 [i]	1202			345
34·0	24·4	3·55	0·1197 [i]	2392	1·99	1·95	345
			4-Methoxyquinoline methiodide [h]				
24·5	50	5·84	0·0484				337
39·7	9·94	10·87	0·2175				297
46·3	9·90	9·40	0·3835	1875			305
46·3	4·95	4·59	0·3643	3946	2·10	2·00	305
51·2	4·94	4·69	0·6347				337
			4-Methylthioquinoline methiodide [i]				
31·1	249	250	0·001542				349
40·9	248·5	252·6	0·00463				349
49·7	247	276	0·01050	2852			349
49·7	124	125	0·01114	5321	1·87	1·99	349
			1-Iodoisoquinoline methiodide [h]				
15·4	25	6·59	14·15				350
20·7	25	6·59	20·82				350
27·0	25	7·22	33·22	8·67			350
27·0	12·5	3·61	33·38	17·26	1·99	2·00	350
36·0	25	6·59	59·60				350
			1-Methylthioisoquinoline methiodide [h]				
8·0	9·67	8·15	155·3				360
14·3	4·60	7·89	234·3				360
23·4	4·43	7·69	446·9	4·66			360
23·4	2·29	4·25	432·9	9·56	1·94	2·05	360
30·0	4·56	7·69	670·3				360
			2-Iodoquinoline [j]				
105·8	1910	34·9	0·000150				332
114·8	1900	34·68	0·000295				332
126·5	1880	30·12	0·000640	5765			332
126·5	940	15·06	0·000678	10880	1·89	2·00	332
			4-Iodoquinoline [i]				
114·8	1900	17·6	~0·00003 [k]				330
			1-Iodoisoquinoline [i]				
114·8	1900	26·8	0·0003				336

[a] ±0·2° for the rapid reaction experiments; otherwise ±0·1° for temperatures <90°, and ±0·3° for temperatures >90°. [b] In l mol^{-1} s^{-1}; the standard deviation was usually within 3%. [c] Corrected for solvent expansion or contraction. [d] Time for 50% reaction in s. [e] The ratio of $t_{\frac{1}{2}}$ values for two experiments at different concentrations. [f] Calculated values for the concentrations of reactants employed. [g] Analytical wavelength for the determination of percentage reaction. [h] Rapid reaction 'stopped flow' technique (ref. 3) was used to study this reaction. [i] pH 7 Buffer solutions used to stop the reactions and for spectroscopic measurements. [j] The mixture was cooled to room temperature and adjusted to pH 14 for spectroscopic measurements. [k] At 10—20% reaction.

reaction products differed from those of the expected hydroxy-compounds.[7]

* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin II*, 1974, Index issue. Items less than 10 pp. are supplied as full-size copies.

U.v. and ^{1}H *N.m.r. Spectra.*—The u.v. absorption maxima of the iodo-, methoxy-, and methylthioquinoline and -isoquinoline methiodides [Supplementary Publication No. SUP 21224 (5 pp.) *] were at longer

[7] S. F. Mason, *J. Chem. Soc.*, 1957, 5010.

TABLE 3

Rate coefficients and Arrhenius parameters for reactions with hydroxide ions

Compound	k [a] (20°)	E/kJ mol^{-1} [b] (kcal mol^{-1})	log A [c]	$\Delta H^{\ddagger}$/kJ mol^{-1} [b] (kcal mol^{-1})	$-\Delta S^{\ddagger}$/J mol^{-1} K^{-1} [d] (cal mol^{-1} K^{-1})
N-Methylquinolinium iodide					
2-I	24·4	59·4 (14·2)	12·0	56·9 (13·6)	23·9 (5·7)
2-SMe	0·655	74·5 (17·8)	13·1	72·0 (17·2)	2·9 (0·7)
4-Cl	0·0511	64·5 (15·4)	10·2	62·0 (14·8)	58·2 (13·9)
4-I	0·0169	68·7 (16·4)	10·5	66·1 (15·8)	52·7 (12·6)
4-OMe	0·030	76·6 (18·3)	12·1	74·1 (17·7)	22·2 (5·3)
4-SMe	0·000439	84·1 (20·1)	11·7	81·6 (19·5)	29·7 (7·1)
N-Methylisoquinolinium iodide					
1-I	19·79	52·3 (12·5)	10·6	49·8 (11·9)	50·2 (12·0)
1-SMe	347	47·3 (11·3)	11·0	44·8 (10·7)	42·7 (10·2)
Quinoline					
2-I	$3{\cdot}24 \times 10^{-8}$ [e]	90·8 (21·7)	8·7	87·5 (20·9)	88·7 (21·2)

[a] Rate coefficients at 20·0° in 1 mol^{-1} s^{-1}. Calculated from the rate coefficient at a nearby temperature unless otherwise stated. [b] Accurate to 5·0 kJ mol^{-1}; based on standard deviations. [c] Accurate to ±0·8 units. [d] Accurate to 4·0 J mol^{-1} K^{-1}. [e] Calculated from E and A values.

wavelengths (by 11—43 nm in the long wavelength region) than in the corresponding unmethylated heterocycles (SUP 21224 and published data [8,9]), but were similar to the monocations of the latter (SUP 21224 and refs. 8 and 9). An apparent exception was the lack of

TABLE 4

Comparison of rate coefficients (1 mol^{-1} s^{-1}) for the reactions of substituted *N*-methylquinolium and -isoquinolinium salts (N^+Me) and their unquaternised analogues (N) with hydroxide ions at 114·8°

	Rate coefficient N^+Me compound	Rate coefficient N compound	Ratio N^+Me : N
Quinoline			
2-I	$1{\cdot}00 \times 10^{4}$ [a]	$2{\cdot}95 \times 10^{-4}$	$3{\cdot}4 \times 10^{7}$: 1
4-I	$1{\cdot}83 \times 10^{1}$ [a]	$\sim 3 \times 10^{-5}$	$6{\cdot}1 \times 10^{5}$: 1
Isoquinoline			
1-I	$3{\cdot}62 \times 10^{3}$ [a]	$3{\cdot}0 \times 10^{-4}$	$1{\cdot}2 \times 10^{7}$: 1

[a] Calculated from E and log A values; current work.

detailed similarity between 1-methylthioisoquinoline methiodide and the cation of 1-methylthioisoquinoline,[8] possibly due to steric interaction in the former.

The ^{1}H n.m.r. spectra (SUP 21224) of the substituted quinolines and isoquinolines (in $CDCl_3$) and their methiodides (in D_2O) revealed downfield shifts on quaternisation (except for H-2 of 4-methylthioquinoline methiodide); and the *N*-methyl signal was in the range δ 4·36—5·10. Spectra of the methiodides of the methylthio-compounds were similar to published data [6] for the corresponding unmethylated compounds in DCl–D_2O, except for a somewhat greater variation in the spectrum of 1-methylthioisoquinoline methiodide.

The compounds required for the investigation were prepared by direct methylation with methyl iodide (or methyl bromide). However exchange of the halogeno-substituent by halide ion did sometimes occur, depending on the conditions. Thus 2-iodoquinoline methiodide and 1-iodoisoquinoline methiodide were prepared by refluxing 2-chloroquinoline and 1-chloroisoquinoline with methyl iodide, and 4-chloroquinoline methiodide was prepared from 4-chloroquinoline and methyl iodide at room temperature but 1-chloroisoquinoline and methyl iodide at −10° gave some halogen exchange as indicated by the analyses.

We were not able to prepare 2-methoxyquinoline methosalts by a variety of procedures.

EXPERIMENTAL

Solids for analysis were dried at 100° and 760 mmHg unless otherwise stated. M.p.s were taken in Pyrex capillaries. All compounds were recrystallised to constant m.p. where possible and were further examined for the presence of impurities by paper chromatography on Whatman No. 1 paper in (*a*) aqueous 3% ammonium chloride and (*b*) butan-2-ol–5M-acetic acid (7 : 3) and by t.l.c.

Kinetic studies were carried out as described in Part X.[2]

U.v. spectra were recorded with a Unicam SP 800 spectrophotometer and $\lambda_{max.}$ and ε values were checked with a Unicam SP 500 manual instrument.

^{1}H N.m.r. spectra were recorded at 60 MHz and 33·5° with a Perkin-Elmer R10 spectrometer, or 35° with a Varian T-60A spectrometer. Spectra were determined in D_2O with sodium 3-trimethylsilylpropane-1-sulphonate as internal standard, and in $CDCl_3$ and $(CD_3)_2SO$ with tetramethylsilane.

The following compounds were prepared by literature procedures: 2-iodoquinoline methiodide,[10] m.p. 212° (decomp.) (from methanol) (lit.,[10] 211—212°) (Found: C, 30·35; H, 2·6; N, 3·3. Calc. for $C_{10}H_9I_2N$: C, 30·25; H, 2·3; N, 3·5%); 2-methylthioquinoline methiodide,[11] m.p. 190—191° (lit.,[11] 193°), methopicrate, m.p. 175—177° (from water) (lit.,[12] 175°) (Found: C, 48·95; H, 3·5; N, 13·0. Calc. for $C_{17}H_{14}N_4O_7S$: C, 48·8; H, 3·4; N, 13·4%); 1-methyl-2-quinolone,[13] m.p. 73·5—75·5° (lit.,[13] 74°); 4-iodoquinoline methiodide,[14] m.p. 258—259° (decomp.) (lit.,[14] 259°) (Found: C, 30·5; H, 2·3; N, 3·3%); 4-methoxyquinoline methiodide,[15] m.p. 132—133° (lit.,[15]

[8] A. Albert and G. B. Barlin, *J. Chem. Soc.*, 1959, 2384.
[9] G. W. Ewing and E. A. Steck, *J. Amer. Chem. Soc.*, 1946, **68**, 2181.
[10] F. M. Hamer, *J. Chem. Soc.*, 1928, 206.
[11] B. Beilenson and F. M. Hamer, *J. Chem. Soc.*, 1939, 143.
[12] A. Kent, D. McNeil, and R. M. Cowper, *J. Chem. Soc.*, 1939, 1858.
[13] W. H. Perkin and R. Robinson, *J. Chem. Soc.*, 1913, **103**, 1973.
[14] F. M. Hamer, *J. Chem. Soc.*, 1939, 1008.
[15] J. R. Price, *Austral. J. Chem.*, 1959, **12**, 458.

135—136°) (Found: C, 43·85; H, 4·3; N, 5·1. Calc. for $C_{11}H_{12}INO$: C, 43·9; H, 4·0; N, 4·65%); 1-methyl-4-quinolone,[16] m.p. 152—153° (lit.,[8] 151—152·5°) (Found: C, 75·5; H, 5·9; N, 8·6. Calc. for $C_{10}H_9NO$: C, 75·45; H, 5·7; N, 8·8%); 8-chloroquinoline methiodide,[17] m.p. 166—167° (decomp.) (lit.,[17] 165°); and 2-methyl-1-isoquinolone,[18,19] m.p. 57—59° (lit.,[19] 57°).

2-*Bromoquinoline Methobromide*.—2-Bromoquinoline [20] [1·6 g; m.p. 52° (from light petroleum, b.p. 40—60°) (lit.,[20] 48—49°)] and methyl bromide (6·0 ml) were kept at 20° for 2 months in a sealed tube. A small quantity of crystals separated. The mixture was chilled and the methyl bromide allowed to evaporate. The product (0·086 g) was collected, washed thoroughly with benzene, and recrystallised quickly from methanol–benzene to give *2-bromoquinoline methobromide*, m.p. 172° (Found: N, 4·7. $C_{10}H_9Br_2N$ requires N, 4·6%).

2-*Iodoquinoline*.—This compound was prepared from 2-chloroquinoline (4·1 g), potassium iodide (14 g), hydriodic acid (30 ml; *d* 1·94), and red phosphorus (2·1 g) at 100° for 3 h.[21] The product was recrystallised from light petroleum (b.p. 40—60°) and had m.p. 59—61° (lit.,[22] 52—53°) (Found, for material dried at 20° and 20 mmHg: C, 42·4; H, 2·8; N, 4·65. Calc. for C_9H_6IN: C, 42·4; H, 2·4; N, 5·5%).

3-*Bromoquinoline Methiodide*.—3-Bromoquinoline (commercial) and methyl iodide were kept at 20° for 24 h and the solid was recrystallised from ethanol to give 3-bromoquinoline methiodide, m.p. 290—292° (lit.,[23] 268—270°) (Found: C, 34·2; H, 2·7; N, 3·9. Calc. for $C_{10}H_9BrIN$: C, 34·3; H, 2·6; N, 4·0%).

3-*Methylthioquinoline Methiodide*.—3-Methylthioquinoline [8] (2·0 g) and methyl iodide (1·0 ml) and methanol (60 ml) were heated in a sealed tube at 100° for 16 h. The solvent was evaporated off and the residue recrystallised from ethanol to give 3-methylthioquinoline methiodide (1·1 g), m.p. 244·5—246° (lit.,[8] 245°) (Found: C, 41·5; H, 4·2; I, 39·8; N, 4·2. Calc. for $C_{11}H_{12}INS$: C, 41·65; H, 3·8; I, 40·1; N, 4·4%). The above product was also prepared with methyl iodide at room temperature.

4-*Chloroquinoline Methiodide*.—This compound was prepared from 4-chloroquinoline (commercial) and methyl iodide [14] at room temperature. It was recrystallised from ethanol, and had m.p. 208° (decomp. with prior colouration) [lit.,[14] 208° (decomp.)] (Found: C, 39·6; H, 3·1; N, 4·6. Calc. for $C_{10}H_9ClIN$: C, 39·3; H, 3·0; N, 4·6%).

4-*Methylthioquinoline Methiodide*.—A mixture of 4-methylthioquinoline [8] (2·0 g), methyl iodide (12·0 ml), and methanol (20 ml) was kept at 20° for 4 days. The precipitate was collected and recrystallised from ethanol to give yellow crystals of *4-methylthioquinoline methiodide* (3·4 g), m.p. 247—248° (Found: C, 41·6; H, 4·0; I, 39·6; N, 4·1%). The *methopicrate* prepared with aqueous picric acid and recrystallised from ethanol had m.p. 170·5—172·5° (Found: C, 48·3; H, 3·2; N, 13·0%).

4-*Iodoquinoline*.—A mixture of 4-chloroquinoline [24] (5·45 g), potassium iodide (16 g), red phosphorus (3·0 g), and hydriodic acid (40 ml; *d* 1·94) was heated in a sealed tube at 130° for 6 h. The mixture was made alkaline and extracted with chloroform, the extract was dried (Na_2SO_4), the solvent was evaporated off, and the product was recrystallised from light petroleum (b.p. 60—80°) to give 4-iodoquinoline (2·4 g), m.p. 97—99° (lit.,[25] 100°).

6-*Chloroquinoline Methiodide*.—A mixture of 6-chloroquinoline (1·0 g; commercial), methyl iodide (2·0 ml), and acetone(10·0 ml) was kept at room temperature for 3 days. The crystalline solid (1·5 g) was collected and recrystallised from ethanol to give *6-chloroquinoline methiodide*, m.p. 251—252° (decomp.) (Found: C, 39·2; H, 3·2; N, 4·15%).

8-*Methoxyquinoline Methiodide*.—This compound was prepared from 8-hydroxyquinoline through 8-methoxyquinoline as described by Foye and Marshall.[26] It was recrystallised from ethanol and had m.p. 161—162° (lit.,[26] 166°) (Found: C, 44·3; H, 4·1; N, 4·3%).

Methanolic solutions of the methiodide and silver tetrafluoroborate were mixed, the silver iodide was filtered off, and the filtrate was concentrated; the product which separated was recrystallised from methanol to give the *methotetrafluoroborate*, m.p. 141—144° (Found: C, 50·6; H, 4·7; N, 5·0. $C_{11}H_{12}BF_4NO$ requires C, 50·6; H, 4·6; N, 5·4%).

1-*Iodoisoquinoline Methiodide*.—This compound was prepared from 1-chloroisoquinoline [27] and methyl iodide at reflux as described by Fisher and Hamer.[28] It had m.p. 235—236° [lit.,[28] 228° (decomp.)] (Found: C, 30·5; H, 2·55; N, 3·2%). 1-Chloroisoquinoline and methyl iodide in acetone at +1° for 2 days also gave 1-iodoisoquinoline methiodide.

1-*Methylthioisoquinoline Methiodide*.—1-Methylthioisoquinoline [8] (1·8 g) and methyl iodide (12·0 ml) were refluxed under anhydrous conditions in a water-bath at 52° for *ca.* 6 days. The crystalline solid (1·76 g) was collected and recrystallised from ethanol to give 1-methylthioisoquinoline methiodide, m.p. 143—146° (lit.,[29] 134°) (Found, for compound dried at 100° for 40 min: C, 42·3; H, 4·0; N, 4·5; S, 10·0. Calc. for $C_{11}H_{12}INS$: C, 41·6; H, 3·8; N, 4·4; S, 10·1%).

1-*Iodoisoquinoline*.—This compound was prepared from 1-chloroisoquinoline [27] (3·2 g) with sodium iodide (10 g) and 66% hydriodic acid (1·6 ml; *d* 1·94) in ethyl acetate [30] (50·0 ml). It was recrystallised from light petroleum (b.p. 40—60°) and had m.p. 75·5—76·5° (lit.,[30] 70—72°) (Found, for material dried at 20° and 20 mmHg: C, 42·1; H, 2·5; N, 5·1%).

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