The Kinetics of Methoxydechlorination of 5-Chloro-1,10-phenanthroline and Some Related Reactions

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The methoxydechlorination of 5-chloro-1,10-phenanthroline occurs readily in DMSO–MeOH (89.9—10.1 w/w) at *ca.* 60 °C and is without significant side reactions. The dependence of the reaction rate on the concentration of methoxide ions has been determined at several temperatures and the rate has been shown to accord with that expected on the addition–elimination mechanism. Under similar conditions, mono and di-alkylated derivatives are deactivated by addition of methoxide ion to the 2-position, and undergo no methoxydechlorination.

OUR earlier studies on the nitration of 1,10-phenanthroline and its complexes with cobalt and iron showed this to be a suitable ligand for studying the effects of co-ordination on aromatic reactivity.[1] The work now reported is part of an extension of these studies to nucleophilic aromatic substitution. The nitration of the free and complexed phenanthroline occurs at the 5-position and, to facilitate the comparison of the effects of co-ordination on reactions with electrophiles and nucleophiles, the present studies therefore relate to the displacement of chlorine from 5-chloro-1,10-phenanthroline (1). The reactivity of the free ligand is discussed in this paper and that of the complexes in the following paper.

Kinetics of Methoxydechlorination.—Previous studies have shown that 5-chloro-1,10-phenanthroline reacts with methanolic potassium hydroxide and copper powder in a sealed tube at 160 °C to give a 50% yield of the 5-methoxy-derivative.[2] We find that the reaction occurs at a convenient rate using sodium methoxide in dimethylsulphoxide–methanol (89.9 : 10.1 w/w) at 50 °C. The ^{1}H n.m.r. spectrum indicates that only the 5-methoxy-derivative is formed.

The extent of reaction was followed by potentiometric estimation of the chloride ions formed. The majority of the kinetic runs were carried out using a large excess of sodium methoxide. Under these conditions, the reaction shows first-order kinetics throughout a single kinetic run and the resulting first-order rate coefficients were divided by the concentration of sodium methoxide to give the second-order rate coefficients (k_2) defined by equation (1). Where the concentrations of substrate and sodium methoxide were comparable, the corresponding values of k_2 were calculated from the initial reaction rates.

$$\text{Rate} = k_2[\text{ArCl}][\text{OMe}^-] \qquad (1)$$

The results in Table 1 show that the values of k_2 are little changed by a 17-fold increase in the initial concentration of 5-chloro-1,10-phenanthroline. However, the values of k_2 are markedly dependent on the initial concentration of methoxide ions. The comparison of the observed and calculated rate coefficients for reaction at 63.9 °C (Table 1) shows that the form of this variation accords with equation (2) for $[\text{OMe}^-] < 0.3$ mol dm^{-3}. This is the form expected for the incursion of a reaction that is second-order with respect to methoxide ions. It is more probable, however, that this variation of k_2 is a consequence of the medium effect observed in other reactions[3] and attributed to the difference in the solvation of the initial and transition states. The solvation of the methoxide ion by hydrogen bonding with methanol molecules should be more important in the initial state

TABLE 1

Second-order rate coefficients [k_2, equation (1)] for methoxydechlorination in dimethyl sulphoxide–methanol (89.9 : 10.1 w/w). The results in brackets are calculated from equation (2) using the parameters in Table 2

t/°C	[MeO$^-$] / mol dm^{-3}	10^2[Substrate] / mol dm^{-3}	10^5k_2 / mol^{-1} s^{-1} dm^3
Substrate—5-chloro-1,10-phenanthroline			
63.9	0.660	1.03	70.2
63.9	0.297	0.89	36.0
			(36.1)
63.9	0.244	1.13	32.0
			(31.4)
63.9	0.163	1.10	23.8
			(24.3)
63.9	0.100	1.07	18.3
			(18.7)
63.9	0.0477	1.25	14.7
			(14.2)
55.0	0.560	1.22	24.3
55.0	0.297	1.25	12.6
55.0	0.100	1.12	6.78
50.5	0.297	1.37	8.17
50.5	0.296	2.96	7.85
50.5	0.292	9.10	7.77
50.5	0.283	23.2	7.59
50.5	0.100	1.12	4.32
40.0	0.297	1.25	2.32
40.0	0.100	1.12	1.25
Substrate—2-chloroquinoline			
40.0	0.100	1.36	475
33.0	0.100	0.895	241
25.0	0.100	0.979	109
25.0	0.290	0.890	226

and hence the reaction rate should be increased by an increase in the MeO$^-$: MeOH ratio. This medium effect should be enhanced by the presence of the dimethyl sulphoxide since the concentration of methanol in the medium is thereby reduced.

$$k_2 = k_2^0 (1 + \alpha[\text{OMe}^-]) \qquad (2)$$

The medium effects on the rates of displacement of chloride ion from the complexes of 5-chloro-1,10-phenanthroline are very different from that on the reaction of the free ligand (see following paper). To facilitate

these comparisons, values of k_2^0 and α have been calculated for each temperature from equation (2) and are listed in Table 2. The activation parameters calculated from k_2^0 are included with those for given concentrations of methoxide ions in Table 3.

TABLE 2

Values for k_2^0 and α [equation (2)] for the methoxydechlorination of 5-chloro-1,10-phenanthroline in DMSO–MeOH (89.9 : 10.1 w/w)

t/°C	25	40	50.5	55	63.9
$10^5 k_2^0$/ mol^{-1} s^{-1} dm^3	(0.108) [a]	0.707	2.36	3.83	9.99
α/mol^{-1} dm^3		7.68	8.26	7.70	8.80

[a] Calculated from the Arrhenius parameters in Table 3.

TABLE 3

Second-order rate coefficients (at 25 and 50 °C) [a] and Arrhenius parameters for methoxydechlorination in DMSO–MeOH (89.9 : 10.1 w/w)

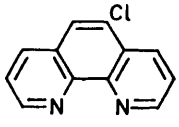
Substrate	[MeO$^-$] mol dm^{-3}	$10^5 k_2$ mol^{-1} s^{-1} dm^3 25°	50°	E kJ mol^{-1}	$\log_{10} A$
5-Chloro-1,10-phenanthroline	0.00 [b]	0.108	2.23	97.1	11.05
5-Chloro-1,10-phenanthroline	0.100	0.187	4.01	98.1	11.47
5-Chloro-1,10-phenanthroline	0.297	0.333	7.55	100.0	12.04
2-Chloroquinoline	0.100		1 170	76.1	10.37
2-Chloroquinoline [c]	0.065—0.120		1.66	96.2	10.77

[a] Calculated from the Arrhenius parameters. [b] Calculated from the limiting rate coefficients (Table 2). [c] For reaction in methanol: M. L. Belli, G. Illuminati, and G. Marino, *Tetrahedron*, 1963, **19**, 345.

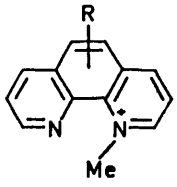
The methoxydechlorination of 2-chloroquinoline has been studied under the same conditions and the rate coefficients and Arrhenius parameters are included in Tables 1 and 3. The rate of this reaction in methanol as solvent has been determined previously [4] and the results are included in Table 3. Comparison of the rate coefficients shows that the presence of the dimethyl sulphoxide increases the reaction rate by a factor of 705 at 50 °C.

Reactions of Alkylated 1,10-*Phenanthrolines.*—It was hoped to extend the studies of methoxydechlorination to the mono- and di-alkylated phenanthrolines (2a) and (3a) in order to compare the effect of alkylation with that of co-ordination to a metal. However, when these derivatives were treated with methoxide ions in DMSO–MeOH (89.9 : 10.1 w/w), no chloride ion could be detected even after heating to 130 °C for 30 min. Under these conditions, 5-chloro-1,10-phenanthroline gives a quantitative release of chloride ion.

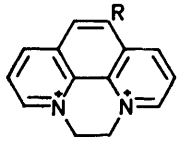
The ^{1}H n.m.r. spectra of solutions of these substrates in DMSO–MeOH (89.9 : 10.1 w/w) containing an excess of sodium methoxide suggest that this inertness derives from the addition of methoxide ions to the carbon atoms adjacent to the alkylated nitrogens to form the adducts (4a), (5a), and (6a). Most of our studies on this subject were carried out using the unchlorinated substrates (2b) and (3b) since this change simplifies the interpretation of the n.m.r. spectra. The addition of an equivalent amount of sodium methoxide to a solution of the di-iodide of (3b) (*ca.* 0.2 mol dm^{-3}) in DMSO–MeOH causes



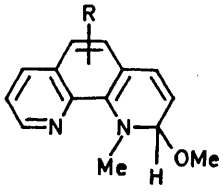
(1)



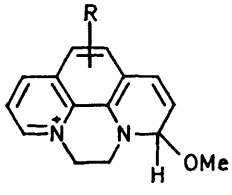
(2) a; R = Cl
b; R = H



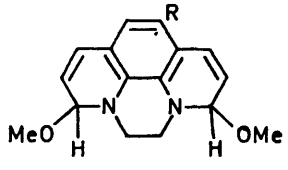
(3) a; R = Cl
b; R = H



(4) a; R = Cl
b; R = H



(5) a; R = Cl
b; R = H



(6) a; R = Cl
b; R = H

essentially complete conversion into the mono-adduct (5b). The corresponding addition of twice the equivalent amount of sodium methoxide causes essentially complete conversion into the di-adduct (6b). The ^{1}H n.m.r. spectra of these species are known from studies by previous workers using methanol as solvent [5] but a large excess of sodium methoxide was then used to form the di-adduct. The form of our spectra accord closely with those reported previously but there are some differences in the chemical shifts (see Experimental section).

DISCUSSION

The main purpose of this work was to obtain a measure of the reactivity of 5-chloro-1,10-phenanthroline towards methoxide ions in DMSO–MeOH (89.9 : 10.1 w/w) at 25 °C for comparison with the results on the complexes of this ligand (see following paper). That has been done and the rate coefficients are given in Table 3.

For the interpretation of the catalysis by metal ions, it is also necessary to show that the reactivity of the free ligand is as expected for the normal addition–elimination

mechanism of nucleophilic aromatic substitution. The majority of the results on the methoxydechlorination of heteroaromatic compounds by this mechanism refer to reaction in methanol as solvent and the corresponding rate coefficients at 50 °C are arranged in order in Table 4. An approximate value of the rate coefficient for the methoxydechlorination of 5-chloro-1,10-phenanthroline under these conditions can be estimated from the fact that the rate of methoxydechlorination of 2-chloroquinoline is increased by a factor of 705 on changing from methanol to DMSO–MeOH (89.9 : 10.1 w/w) (Table 3) and the fact that, to a first approximation, the catalysis by added DMSO is independent of the substrate.[6] The resulting rate coefficient for the reaction of 5-chloro-1,10-phenanthroline in methanol is included in Table 4.

TABLE 4

Second-order rate coefficients at 50 °C for methoxydechlorination in methanol and the related values of ΔE_π [equation (3)]

Substrate	k_2 / $mol^{-1}\ s^{-1}\ dm^3$	ΔE_π / $kJ\ mol^{-1}$	Ref.
6-Chlorophenanthridine	6.4×10^{-4}	28	*a*
4-Chloroquinoline	2.27×10^{-5}	42	*b*
2-Chloroquinoline	1.65×10^{-5}	43	*b*
4-Chloropyridine	8.91×10^{-7}	66	*c*
5-Chloro-1,10-phenanthroline	*ca.* 5×10^{-8}	64	*d*
2-Chloropyridine	3.31×10^{-8}	66	*c*
3-Chloropyridine	1.09×10^{-11}	76	*c*
Chlorobenzene	(1.2×10^{-16}) [e]	97	*c*

[a] B. R. T. Keene and G. L. Turner, *Tetrahedron*, 1971, **27**, 3405. [b] Ref. 4. [c] J. Miller, 'Aromatic Nucleophilic Substitution,' Elsevier, 1968, ch. 7, p. 244. [d] This work. [e] Indirect estimation based on Hammett plot.

It is not obvious that the position of 5-chloro-1,10-phenanthroline in Table 4 is appropriate for reaction by the addition–elimination mechanism since this is the only substrate listed in which substitution occurs in a homocyclic ring. The P.M.O. approximation for the π-electron contribution to the activation energy (ΔE_π) provides evidence on this point. This approach, expressed using conventional symbols [7,8] by equation (3), has been successfully applied to the addition–elimination mechanism of nucleophilic aromatic substitution in monocyclic and bicyclic systems using the parameters $\beta = -10$ kcal, $\alpha_N = -22$ kcal, and $\alpha_C = 1/3\ \alpha_N$ (for carbon atoms adjacent to the nitrogen atom).[8] The same parameters applied to the present systems yield the values of ΔE_π in Table 4. The crudeness of this approximation is such that no significance should be attached to the individual values of ΔE_π but it is significant that the predicted order of reactivity, including 5-chloro-1,10-phenanthroline is very similar to that observed. There is therefore no need to consider any special mechanism for substitution in this substrate.

$$\Delta E_\pi = -2\beta(a_{or} + a_{os}) + \sum_i \alpha_i a^2_{oi} \qquad (3)$$

The only remaining point concerns the failure to observe methoxydechlorination in the alkylated derivatives (2a, 3a). Since this work was done,[9] the addition of hydroxide ion to the dialkylated derivative (3b) has been shown [5] to be 50% complete at pH 9.5 and so it is reasonable that in any strongly nucleophilic medium the amount of the dication present should be very small. The mono-alkylated derivative (2b) does not form a detectable amount of the pseudo-base at pH 14 but the presence of the DMSO in the medium used here should greatly increase the amount of pseudo-base present. The formation of the pseudo-bases should greatly deactivate the ions (2a) and (3a) to methoxydechlorination by neutralising the charge on the nitrogen and by reducing the extent of the conjugated system.

EXPERIMENTAL

Materials.—Dimethyl sulphoxide was purified by treatment with a molecular sieve (B.D.H. grade 5A) followed by drying with barium oxide and distillation under reduced pressure. The fraction with b.p. 62—63 °C (8 mm) was collected and had m.p. 18.3—18.5 °C (lit.,[10] 18.55 °C). Methanol was purified as described by Vogel.[11] Solutions of sodium methoxide were prepared by adding freshly cut sodium, rinsed with ether, to dry methanol in a dry-box under nitrogen. The concentration of sodium methoxide was determined by titration of a known weight of the solution with aqueous hydrochloric acid. Sufficient dimethyl sulphoxide was then added to bring the composition DMSO–MeOH to 89.9 : 10.1 w/w.

5-Chloro-1,10-phenanthroline was prepared by a Skraup reaction on 4-chloro-2-nitroaniline to give 6-chloro-8-nitroquinoline followed by reduction of this to 6-chloro-8-aminoquinoline and a second Skraup reaction to give the final product. The general procedure was that of Richter and Smith [12] as modified by Case [13] for the Skraup syntheses and using the method of Pratt and Drake [14] for the reduction of the nitro-group. Full details are available elsewhere.[9] The product, after recrystallisation from benzene–light petroleum ether (b.p. 80—100 °C), had m.p. 124—125 °C (lit.,[12] 123 °C) (Found: C, 67.3; H, 3.3; Cl, 16.5; N, 13.2. Calc. for $C_{12}H_7ClN_2$: C, 67.1; H, 3.3; Cl, 16.5; N, 13.1%). 2-Chloroquinoline (B.D.H. Lab. Reagent) was recrystallised from aqueous ethanol.

1-Methyl-1,10-phenanthrolinium iodide was prepared by dissolving 1,10-phenanthroline monohydrate (1 g) in methyl iodide (5 ml) and setting the mixture aside overnight at 40 °C. The yellow precipitate after recrystallisation from ethanol had m.p. 208—210 °C (lit.,[15] 210—213 °C) (Found: I, 39.2. Calc. for $C_{13}H_{11}N_2I$: I, 39.4%). The methylation of 5-chloro-1,10-phenanthroline was carried out in the same way: the product was presumably a mixture of the 5-chloro- and 6-chloro-derivatives of 1-methyl-1,10-phenanthrolinium iodide (Found: I, 35.8. Calc. for $C_{13}H_{10}N_2ClI$: 35.6%). 4,5-Dihydro-3a,5a-diazoniapyrene dibromide (3b) was prepared by dissolving 1,10-phenanthroline monohydrate (0.7 g) in 1,2-dibromoethane (10 ml) and heating the solution under reflux for 3 h. The yellow solid that separated out was recrystallised from methanol and decomposed without melting at 340 °C (Found: C, 45.8; H, 3.1; Br, 43.4; N, 7.7. Calc. for $C_{14}H_{12}Br_2N_2$: C, 45.7; H, 3.3; Br, 43.4; N, 7.6%). Treatment of an aqueous solution of the dibromide with potassium iodide gave the di-iodide as large black plates which were recrystallised from water (Found: C, 36.2; H, 2.7; I, 54.8; N, 5.9. Calc. for $C_{14}H_{12}I_2N_2$: C, 36.4; H, 2.6; I, 54.9; N, 6.1%). The

corresponding dibromide from 5-chlorophenanthroline (3a) was prepared in a similar way but was recrystallised from aqueous acetone giving the hydrate (Found: C, 40.8; H, 3.5; Br, 39.2; Cl, 7.0; N, 7.0. $C_{14}H_{11}Br_2ClN_2 \cdot \frac{1}{2}H_2O$ requires C, 40.9; H, 2.9; Br, 38.8; Cl, 8.6; N, 6.8%). The compound decomposed at 340 °C without melting.

Kinetics.—A solution of the aromatic substrate in DMSO–MeOH (89.9 : 10.1% w/w) containing sodium methoxide was prepared under nitrogen using a flask closed with a Neoprene serum cap. The flask was then brought to the appropriate temperature and samples were extracted at various times using a calibrated hypodermic syringe. The extracts were quenched in acetone containing nitric acid and the concentration of chloride ion was estimated by potentiometric titration with silver nitrate using silver and calomel electrodes.[16] The results for typical kinetic runs under pseudo-first-order and second-order conditions are shown in Table 5 with the corresponding integrated rate coefficients calculated from the time of the extraction of the first sample. For runs under pseudo-first-order conditions, the mean of the first-order rate coefficients was used in the calculations. Under conditions giving approximate second-order kinetics, the second-order rate coefficients decrease during a kinetic run as expected from equation (2); the initial value of this rate coefficient was then used in the calculations.

Products.—After 15 half-lives, the reaction mixture from methoxydechlorination at 55 °C with 0.5 mol dm^{-3} sodium methoxide was diluted with twice its volume of water and extracted with dichloromethane. The extracts were washed with water, dried ($MgSO_4$), and the solvent was removed by evaporation. The product, after recrystallisation from benzene–ligroin, had m.p. 104 °C, as expected for 5-methoxy-1,10-phenanthroline (lit.,[2] 104—105 °C) (Found: C, 75.1; H, 4.9; N, 13.0. Calc. for $C_{13}H_{10}N_2O$: C, 74.3; H, 4.8; N, 13.3%). The ^{1}H n.m.r. spectrum in deuteriochloroform was as expected with a singlet (3 H) at δ 4.09 and absorption in the region δ 7—9.5 (7 H). The crude product showed no additional peaks.

Studies on the ^{1}H n.m.r. spectra of the adducts of the alkylated phenanthrolines were carried out mainly on the unchlorinated derivatives. The addition of one equivalent of sodium methoxide (4.57 mol dm^{-3}) in DMSO–MeOH (89.9—10.1% w/w) to a solution of the di-iodide of the dication (3b) (0.16 mol dm^{-3}) in the same solvent gave the spectrum of the mono-adduct (5b):[5] δ 5.83 (H-2, d, $J_{2,3}$ = 4.5 Hz), 6.11 (H-3, dd), 7.23 (H-4, d, $J_{3,4}$ = 9.5 Hz), 7.70—8.11 (H-5, H-6, H-7, m), and 9.01—9.30 (H-7, H-9, m). The addition of two equivalents of sodium methoxide gave the spectrum of the di-adduct (6b):[5] δ 5.62 (H-3, H-8, dd), 6.50 (H-5, H-6, s), and 6.77 (H-4, H-7, d, $J_{3,4}$ = 9.5 Hz). Spectra corresponding to mono-adduct formation were observed with the mono-alkylated cation (2b).[9]

TABLE 5

The reaction of 5-chloro-1,10-phenanthroline with sodium methoxide in DMSO–MeOH (89.9 : 10.1 w/w) under conditions giving (a) first-order and (b) second-order kinetics

(a) [ArCl] = 1.25 × 10^{-2} mol dm^{-3}, [MeO$^-$] = 0.297 mol dm^{-3}, Temp = 40 °C

Time / min	Titre * / ml	10^2[ArCl] / mol dm^{-3}	10^6k_1 / s^{-1}
0	0.36	1.18	
253	0.98	1.06	7.06
480	1.49	0.968	6.88
1 204	2.84	0.713	6.97
1 424	3.13	0.658	6.84
1 804	3.65	0.560	6.88
2 632	4.45	0.408	6.73
2 979	4.74	0.354	6.74
∞	6.61		
		mean = 6.87	

(b) [ArCl] = 0.232, [MeO$^-$] = 0.283, Temp = 50.5 °C

Time / min	Titre * / ml	[ArCl] / mol dm^{-3}	10^5k_2 / mol^{-1} s^{-1} dm
0	0.31	0.226	
60	1.04	0.210	7.59
120	1.59	0.199	6.72
196	2.20	0.186	6.47
285	2.81	0.173	6.29
381	3.42	0.160	6.28
487	3.97	0.149	6.10
701	4.93	0.129	6.04
935	5.67	0.113	5.91
1 263	6.47	0.097	5.67
∞	11.08		

* Volume of silver nitrate solution (0.005 mol dm^{-3}).

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