Kinetics and Mechanism of the Chromium(II) Reduction of Pyridine *N*-Oxides [1]

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The reactions between Cr^{II} and 15 substituted pyridine *N*-oxides have been studied in 1mol dm^{-3} $HClO_4$ and found to follow the stoicheiometry (i) and the rate law $d[Cr^{3+}]/2dt = k[Cr^{2+}][X\text{-pyo}]$. The reactions are suggested

$$2Cr^{2+} + X\text{-pyo} + 2H^+ \longrightarrow 2Cr^{3+} + X\text{-pyo} + H_2O \quad \text{(i)}$$

to proceed by the stepwise reduction of pyridine *N*-oxide molecules *via* a free-radical path. The results are indicative of two distinct types of behaviour: compounds with co-ordinating substituents in the *ortho* or *para* position ($k > 0.3$ dm^3 mol^{-1} s^{-1} and $\Delta H^\ddagger < 6$ kcal mol^{-1}) and all other compounds ($k < 2 \times 10^{-3}$ dm^3 mol^{-1} s^{-1} and $\Delta H^\ddagger = 11$—13 kcal mol^{-1}). These differences are discussed in terms of the ability of the pyridine *N*-oxides to co-ordinate to Cr^{II} *via* groups other than the *N*-oxide and the relative stabilities of the free-radical intermediates.

IN recent years there has been much investigation into the behaviour of the chromium(II) ion as a reducing agent, particularly towards complex ions and other inorganic substrates. The large body of data which now exists for reactions of this type [2] has placed their interpretation on a solid basis involving, for the most part, an inner-sphere transfer of an electron.[3] In contrast, the mechanisms of reactions of Cr^{II} with organic compounds are much less well established, although such reactions have been utilized both synthetically [4] and analytically.[5] Clearly, it would be of value to elucidate more fully the mechanism of chromium(II) reductions of organic compounds in order to establish any similarities and differences which exist in the behaviour of Cr^{II} towards organic and inorganic substrates. To this end we have studied the chromium(II) reductions of a number of pyridine *N*-oxides whose chemistry has long been a subject of interest in this laboratory. These compounds were selected because they were known to be reduced by transition-metal ions,[5] and because the extensive body of knowledge about other aspects of their chemistry [6] was expected to aid in elucidating the reduction process.

RESULTS

The stoicheiometry of the reaction between Cr^{II} and the various pyridine *N*-oxides was determined titrimetrically and spectrophotometrically. Both the $K_2[Cr_2O_7]$ titrations of the Cr^{II} remaining after treating an excess of this ion with a known quantity of *N*-oxide, and the absorbance changes observed during kinetic runs (in excess of Cr^{II} and excess of *N*-oxide), correspond to the consumption of 2 mol of Cr^{II} per mol of *N*-oxide. Further, in the cases of 2-cyano- and 2-carboxy-pyridine *N*-oxide (which have potentially reducible sites in addition to the *N*-oxide moiety), the reaction products were isolated and characterized by i.r. spectroscopy. The i.r. spectra were identical with those of the corresponding substituted pyridines. indicating that even in these instances it is the *N*-oxide group which is reduced and not the cyano- or carboxyl group. Thus, the reactions between Cr^{II} and pyridine *N*-oxides are described by equation (1).

$$2Cr^{2+} + X\text{-pyo} + 2H^+ \longrightarrow 2Cr^{3+} + X\text{-py} + H_2O \quad (1)$$

Detailed kinetic studies were carried out on 2-cyano-, 3-cyano-, 2-methyl-, and 3-methyl-pyridine *N*-oxide, and pyridine *N*-oxide itself to establish the order of reaction with respect to [Cr^{II}], [X-pyo], and [H$^+$] as well as the effect of changing the ionic strength. Rate constants calculated from the instantaneous rates of formation of Cr^{III} within a given absorbance–time plot agreed to ±5% for a first-order dependence on Cr^{II} in both the presence of excess of Cr^{II} and excess of *N*-oxide. Similarly, the order with respect to

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[1] Presented in part at the 5th Northeast Regional Amer. Chem. Soc. Meeting, Rochester, New York, October 1973, paper no. 39.

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[3] H. Taube and E. S. Gould, *Accounts Chem. Res.*, 1969, **2**, 321.

[4] J. R. Hanson and E. Premuzic, *Angew. Chem. Internat. Edn.*, 1968, **7**, 247.

[5] S. Siggia, 'Quantitative Organic Analysis via Functional Groups,' 3rd edn., Wiley, New York, 1963, p. 526.

[6] N. M. Karayannis, L. L. Pytlewski, and C. M. Mikulski, *Co-ordination Chem. Rev.*, 1973, **11**, 93.

the concentration of *N*-oxide was established unambiguously as one in excess of Cr^{II}, and although the data obtained in excess of *N*-oxide conformed to this order as well we cannot rule out a slightly higher order (*e.g.* 1.1) for *N*-oxide when it was present in excess, a result which is also suggested by other observations. For example, when kinetic reactions were carried out under pseudo-first-order conditions (with an excess of *N*-oxide) the linear plots yielded a value for *k* which was greater (*ca.* 1.5 times) than the value obtained when an excess of Cr^{II} was used. In addition, ion-exchange studies indicate that the number of *N*-oxides co-ordinated to the chromium(III) product increases as the *N*-oxide : Cr^{II} ratio in the original solution is increased. Because of this ambiguity about the order of reaction with the respect to the *N*-oxide when it is present in excess, most reactions were carried out under pseudo-first-order conditions (10-fold or greater excess of Cr^{II}). The pseudo-first-order plots were linear for at least 95% completion of reaction and the rate constants obtained in this manner agreed to within ±5% with those calculated by the instantaneous-rate method. The reaction was independent of $[H^+]$ over the $[H^+]$ range studied (0.25—1.25 mol dm^{-3}) and was unaffected by variations in ionic strength. These results are summarized by the rate law (2).

$$d[Cr^{3+}]/2dt = k[Cr^{2+}][\text{X-pyo}] \qquad (2)$$

The 2 : 1 stoicheiometry and the first-order kinetic dependence for these reactions necessitate either a two-electron path, such as that described by equations (3) and (4), or a free radical mechanism as detailed in equations

$$Cr^{II} + \text{X-pyo} + 2H^+ \longrightarrow Cr^{IV} + \text{X-py} + H_2O \qquad (3)$$

$$Cr^{IV} + Cr^{II} \longrightarrow 2Cr^{III} \qquad (4)$$

(5)—(8). Since it is well established [7] that the reduction of

$$Cr^{II} + \text{X-pyo} \longrightarrow [Cr^{III}(\text{X-pyo})] \qquad (5)$$

$$[Cr^{III}(\text{X-pyo})] + Cr^{II} \longrightarrow \text{X-py} + Cr^{III} + [CrO]^+ \qquad (6)$$

$$[CrO]^+ + 2H^+ \longrightarrow [Cr(OH_2)]^{3+} \qquad (7)$$

$$\text{X-py} + H^+ \longrightarrow \text{X-Hpy}^+ \qquad (8)$$

chromium(IV) species by Cr^{II} as in equation (4) gives rise to an oxygen-bridged dimeric chromium species with a 4+ charge, the possibility of this reaction mode was investigated by means of ion exchange. When the redox reaction was complete and the solution had been fixed on an ion-exchange column, the chromium-containing reaction products were eluted rapidly and completely from the resin (Dowex 50W-X8) with 1.0 mol dm^{-3} $HClO_4$. This ready elution establishes that the chromium products have a 3+ charge and are not more highly charged (as would be true of dimeric species) because the latter require more concentrated acid for elution.[8]

Thus, a free-radical path [such as that in equations (5)—(8)] is implied. Many attempts were made to verify the presence of the free radicals by adding acrylonitrile and methyl acrylate monomers to the reaction mixtures. In no case was a precipitate (indicative of the presence of free radicals) observed, in contrast to the reaction of Ti^{III} with these same *N*-oxides [9] and to the reduction of aliphatic amine oxides with Cr^{II},[10] for which such polymerization has been reported. The failure of these tests in the present instance is most likely due not to the absence of such species, but rather to their rapid reactions with other chromium(II) ions in the solutions as has been proposed for the reduction of $[Cr(CH_2I)(OH_2)_5]^{2+}$ by Cr^{II} [11] and for the oxidation of oxalate radicals by Cr^{VI}.[12,13] Indeed, when Cr^{II} was added to a solution of Ti^{III} and pyridine *N*-oxide (in which free radicals are known to be present from similar polymerization studies), the formation of a precipitate was prevented, adding support to the view that chromium(II) ions react with free radicals before the latter have a chance to react with acrylonitrile or methyl acrylate.

After the kinetic rate law had been established, the reactions of 15 different *N*-oxides with Cr^{II} were studied in an attempt to determine how the course of the reaction is affected by the nature and position of various substituents on the *N*-oxide ring. With the exception of the value for $2CO_2H$-pyo which was too fast to measure by our standard techniques, the second-order rate constants from these studies (which vary over a range of 10^4) are listed in Table 1, together with the activation parameters determined from the temperature dependence of *k*.

TABLE 1

Parameters for Cr^{II}–XC_5H_4NO reactions in 1.0 mol dm^{-3} $HClO_4$ at 25 °C

X	10^3k / $dm^3\ mol^{-1}\ s^{-1}$	$\Delta H^\ddagger$ / kcal mol^{-1}	$\Delta S^\ddagger$ / cal K^{-1} mol^{-1}
H	0.096	13.1 ± 0.5	−32 ± 4
2-Me	0.072	12.6	−34
3-Me	0.101	12.9	−32
4-Me	0.099	12.8	−33
4-MeO	0.106	12.8	−32
3-Cl	0.098	12.6	−32
4-Cl	1.61	12.4	−28
$3-CO_2Me$	0.139	11.2	−36
3-CN	1.69	*	*
$3-CO_2H$	0.92	11.2	−33
2-CN	435	5.8	−60
4-CN	1 100	1.7	−51
$4-CO_2H$	1 250	5.4	−39
$4-CO_2Me$	360	6.2	−37

* Curvature of the Arrhenius plot prevented calculation of these values. The temperature dependence of the rate constant is suggestive of an equilibrium step which occurs before electron transfer and is less favoured at higher temperatures.

DISCUSSION

The data in Table 1 for the reaction of Cr^{II} with a number of pyridine *N*-oxides suggest that the reaction rates are influenced by the nature and, in some instances, by the position of the substituent in the ring. These reaction rates are not linearly related to the substituent constant (σ_{pyo}),[14] however, in marked contrast to a variety of other properties [15] of substituted pyridine *N*-

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oxides including their polarographic reduction potentials.[16] Rather, the present data can be divided into two categories: compounds which react very slowly ($k < 2 \times 10^{-3}$ dm^3 mol^{-1} s^{-1}) and those which react relatively rapidly ($k \geqslant 0.3$ dm^3 mol^{-1} s^{-1}). The former category comprises compounds with electron-donating groups in any position or electron-withdrawing substituents in the *meta* position, while the latter group possesses electron-withdrawing substituents situated *ortho* or *para* to the *N*-oxide moiety.

The expected reaction site between the slower-reacting compounds and a metal ion is the *N*-oxide group and although the N–O bond rupture which occurs during the reaction prevents us from establishing definitely whether the reaction proceeds *via* an inner- or an outer-sphere process, indirect evidence suggests the former. Specifically, the rate constants calculated for solutions with an excess of *N*-oxide are *ca.* 1.5 times greater than those for which Cr^{II} was present in excess. It is difficult to envisage how this phenomenon could be accounted for on the basis of an outer-sphere process, whereas it is readily explained by an inner-sphere mechanism if more than one *N*-oxide is co-ordinated to Cr^{II}. This condition is most likely to occur when the oxide is present in excess and if successive co-ordinated *N*-oxide molecules promote the transfer of an electron from Cr^{II} to one of them the rate will increase, as is observed experimentally. Although the equilibrium between pyridine *N*-oxide and Cr^{II} has not been studied, investigations of the chromium(III)–pyridine *N*-oxide reaction indicate that successive equilibrium constants are very similar [17] suggesting that the co-ordination of more than one *N*-oxide is quite likely. Indeed, as has been mentioned above, ion-exchange measurements show an increase in the number of co-ordinated *N*-oxides per chromium as the *N*-oxide : Cr^{II} ratio in the original solution is increased, adding further support to this proposed explanation.

The activation energies for these slower reactions are consistent with a common mechanism, ranging from 11.2 to 13.1 kcal mol^{-1}, whereas the $\Delta H^\ddagger$ values for the faster reactions are substantially lower (2—6 kcal mol^{-1}).* The $\Delta S^\ddagger$ values for the two groups of compounds show little difference, in common with the great bulk of oxidation-reduction reactions which exhibit highly negative $\Delta S^\ddagger$ values, regardless of mechanism, and offer little insight into the reaction mechanism beyond that provided by the $\Delta H^\ddagger$ values.

The compounds which exhibit the lower activation enthalpies (and greater reaction rates) are those which possess *ortho*- or *para*-electron-withdrawing groups as was noted previously. In addition to their greater electron-attracting power, these compounds are characterized by an ability to co-ordinate to metal ions *via* the ring substituent [18,19] and, according to e.s.r. measurements, to form radical-anionic species of relatively high stability.[20] Thus, it is possible that the rate enhancement observed for these compounds is due to the greater stability of a radical intermediate, as has been proposed for the chromium(II) reduction of a number of cobalt(III) complexes,[21] or to the attack of Cr^{II} at the co-ordinating substituent followed by electron transfer through the π system (with or without the intervention of a highly stabilized free-radical intermediate).

Examination of the spectra of the solutions after the reductions were complete gave the results shown in Table 2. From these studies [which gave identical results when carried out over a range of chromium(II) and *N*-oxide concentrations] it can be seen that the absorption maxima and molar absorption coefficients are distinctly different from those of [Cr(OH$_2$)$_6$]$^{3+}$ [$\lambda_{max.}$ 406 (ε 15.3), $\lambda_{max.}$ 574 nm (ε 13.3 dm^3 mol^{-1} cm^{-1})] [22] and, in fact, agree with those reported for the corresponding substituted pyridines co-ordinated to Cr^{III} *via* the substituent on the ring.[23] The low lability of [Cr(OH$_2$)$_6$]$^{3+}$ requires that co-ordination of the ligand to chromium occurs before it is oxidized from Cr^{II} to Cr^{III}, *i.e.* reduction occurs by remote attack. It can also be seen, however, that 3-cyano- and 3-carboxyl-pyridine *N*-oxide co-ordinate through the cyano- and carboxyl groups even though they are reduced much more slowly (*i.e.* the *m*-cyano-species is reduced *ca.* 250 times more slowly than the *ortho* and 670 times more slowly than the *para*, while for the carboxyl compounds the *para* species is reduced 1 360 times as rapidly as the *meta* with the reaction of the *ortho* compound being sufficiently more rapid that we were unable to measure its rate). These rate differences for co-ordinated species provide a clear indication of the importance which the stability of free-radical intermediates seems to play in the rates of these reactions, although it may be that co-ordination through the lead-in group is a prerequisite to reduction by this more rapid path. In this connection, a similar, although larger ($k_{para}/k_{meta} = 20\,000$) rate enhancement

TABLE 2

Spectral characteristics of Cr^{II}–XC$_5$H$_4$NO reaction products

X	$\lambda_{max.}$/nm	ε/dm^3 mol^{-1} cm^{-1}	$\lambda_{max.}$/nm	ε/dm^3 mol^{-1} cm^{-1}
2-CO$_2$H	412	34.4	579	29.3
3-CO$_2$H	410	22.3	575	25.4
4-CO$_2$H	410	22.2	578	20.7
2-CN	412	29.4	580	22.9
3-CN	408	28.4	580	20.2
4-CN	412	28.3	582	22.8

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* 1 cal = 4.184 J.

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for the chromium(II) reduction of penta-ammine(*m*-acetylbenzonitrile)- and penta-ammine(*p*-acetylbenzonitrile)-cobalt(III) complexes was recently reported [24] and attributed to the existence of outer- and inner-sphere processes respectively. The similarity between that system and the ones studied here suggests that the rate enhancement observed in the earlier system could also be due to a difference in free-radical stability and not to a change in mechanism.

It is interesting that when Ti^{III} is used as reducing agent, in contrast to Cr^{II}, accelerations in rates are not observed for the 2-CN, 2-CO_2H, 4-CN, 4-CO_2H, and 4-CO_2Me derivatives.[9] Indeed, most of these compounds (with the exception of 2-CO_2H) are reduced more slowly than pyridine *N*-oxide itself. This can be attributed to the potential of Ti^{III} being too low ($E^{\ominus} = -0.1$ V) [25] for it to produce stable free-radical intermediates to any significant degree. Even the potential of Cr^{II} ($E^{\ominus} = 0.41$ V) appears too low to lead to such radicals in compounds having reduction half-wave potentials of -1.1 V or more. However, just as the substitution of an electron-withdrawing substituent (CN, CO_2H, or CO_2-Me) on the ring has been shown by molecular-orbital calculations [26] to lower the energy of the unoccupied molecular orbitals on the ring (through their interaction with the unoccupied molecular orbitals of the substituent), co-ordination of the substituent and the consequent electron withdrawal would be expected to cause a further decrease. The effective decrease in potential caused by co-ordination would seem to be at least 0.70 V since the CO_2Me derivative ($E_{\frac{1}{2}} = -0.862$ *versus* standard calomel electrode or -1.10 V *versus* normal hydrogen electrode) is readily reduced.

In conclusion, the reaction between Cr^{II} and substituted pyridine *N*-oxides can be considered to occur by a path that produces an *N*-oxide free radical in the initial and rate-determining step. This step occurs by either remote attack for compounds with an alternative co-ordination site or by direct interaction of Cr^{II} with the *N*-oxide moiety. This is followed by transfer of an additional electron from a second chromium(II) ion which causes rupture of the already weakened N–O bond as summarized in equations (5)—(8).

EXPERIMENTAL

Materials.—The preparation and/or purification of the *N*-oxides have been described previously.[27] Stock solutions of known concentrations were prepared by dissolving known weights of the *N*-oxides in acid of the appropriate concentration and were deoxygenated with N_2 which had been purified by passage through a solution of V^{2+}.[28] These solutions were stored under N_2 and were deoxygenated again immediately prior to use. There was no indication of a loss of oxidizing ability in these solutions even over extended periods of time. Stock solutions of Cr^{II} were prepared by reducing solutions of chromium(III) perchlorate in perchloric acid in a Jones reductor. These solutions were stored under N_2 and were standardized daily against $K_2[Cr_2O_7]$.[29] All the other chemicals were reagent grade and were used as received.

Kinetics.—The reactions were studied by following the appearance of Cr^{III} at 418 nm on a Cary 14 spectrophotometer with a cell compartment thermostatted to ±0.2 °C. Reactions were carried out in 1- or 10-cm cells as dictated by the pathlength necessary to maximize the absorbance changes (so that $\Delta A \geqslant 0.5$ absorbance units) at the chromium(II) concentrations required to produce measurable reaction rates. Most reactions were carried out by standard syringe techniques,[9,30] injecting a portion of the thermostatted *N*-oxide solution into the thermostatted chromium(II) solution in the cell. A few reactions were carried out using a two-compartment flask in which the reactant solutions were thermostatted separately, then forced into the cell with dry N_2 after mixing. The results obtained by these two methods were equivalent. After the reaction orders had been determined, kinetic runs were made under pseudo-first-order conditions (excess of Cr^{2+}) and pseudo-first-order plots were linear for virtually the entire course of the reactions.

Ion Exchange.—Studies were made to establish the charge on the product chromium species as well as the number of *N*-oxide molecules per chromium ion at different [*N*-oxide] : [Cr^{2+}] ratios. For both types of investigation the oxidation-reduction reactions were carried out under N_2 after which the solutions were slurried with ion-exchange resin (Dowex 50W-X2 or 50W-X8) which had been purified by washing repeatedly with 4 mol dm^{-3} HCl, distilled water, and alkaline (*ca.* 1 mol dm^{-3} Na[OH]) hydrogen peroxide until the absorbance was less than 0.3 at 254 nm. This resin was then added to the top of a column of purified resin maintained at *ca.* 0 °C and the column was eluted with 1 mol dm^{-3} $HClO_4$. Acid of this concentration removes species with charges up to 3+, but leaves more highly charged species on the column. After elution chromium was determined spectrophotometrically as $[CrO_4]^{2-}$ (ε 4.83 × 10^3 dm^3 mol^{-1} cm^{-1} at 370 nm) [31] after oxidation with alkaline peroxide. The *N*-oxides were determined spectrophotometrically at an appropriate wavelength in the u.v. region (*e.g.* ε 1.21 × 10^4 for pyo at 254 nm and ε 1.15 × 10^4 dm^3 mol^{-1} cm^{-1} at 260 nm for 3CN-pyo) after the solutions had been made basic to free the *N*-oxide from the chromium. By taking separate aliquot portions of eluant for these analyses, the presence of neither material interfered with the determination of the other.

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