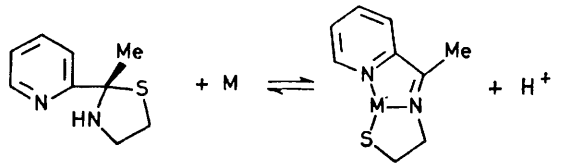
Reactions of Methylmercury(II), Mercury(II), and Zinc(II) Ions with 2-Methyl-2-(2-pyridyl)thiazolidine, including Stopped-flow Rapid-scanning Spectrophotometric Studies

By **Terence J. Kemp, Paul A. Lampe, Peter Moore,*** and **Geoffrey R. Quick,** Department of Chemistry and Molecular Sciences, University of Warwick, Coventry CV4 7AL

Equilibrium studies of the reactions of 2-methyl-2-(2-pyridyl)thiazolidine (A) with [HgMeX] (X = Cl, $MeCO_2$), Hg^{II} and Zn^{II} ions have been investigated by ^1H and ^{13}C n.m.r. and by u.v. spectrophotometry, and kinetic studies of the reactions with Hg^{II} and Zn^{II} ions by stopped-flow rapid-scanning u.v. spectrophotometry. The n.m.r. results show that opening of the thiazolidine ring occurs with the loss of a proton, to give thiolate-bound Schiff-base chelates. In the absence of buffer, the reaction with [HgMeCl] also gives a second species in which the thiazolidine ring is not opened, and addition of acetate buffer causes this minor species to deprotonate and convert to the ring-opened product. Kinetic studies using Hg^{II} reveal a single, very rapid reaction, close to the limits of stopped-flow detection, and approximately first order in $[Hg^{II}]$. Two distinct kinetic stages are apparent in the reaction with zinc(II) perchlorate in methanol solution, the first stage attributed to metal binding and the pH-dependent second stage to the opening of the thiazolidine ring. Using zinc(II) acetate the first stage is too rapid for stopped-flow detection, but the second stage is kinetically simpler because of the buffering effect of the acetate ions.

RECENTLY, we investigated the reactions of methylmercury(II) with dithiol ligands.[1] Such ligands are closely related to 2,3-dimercaptopropan-1-ol (' BAL ') which is commonly used for treating heavy-metal



(A) (B)

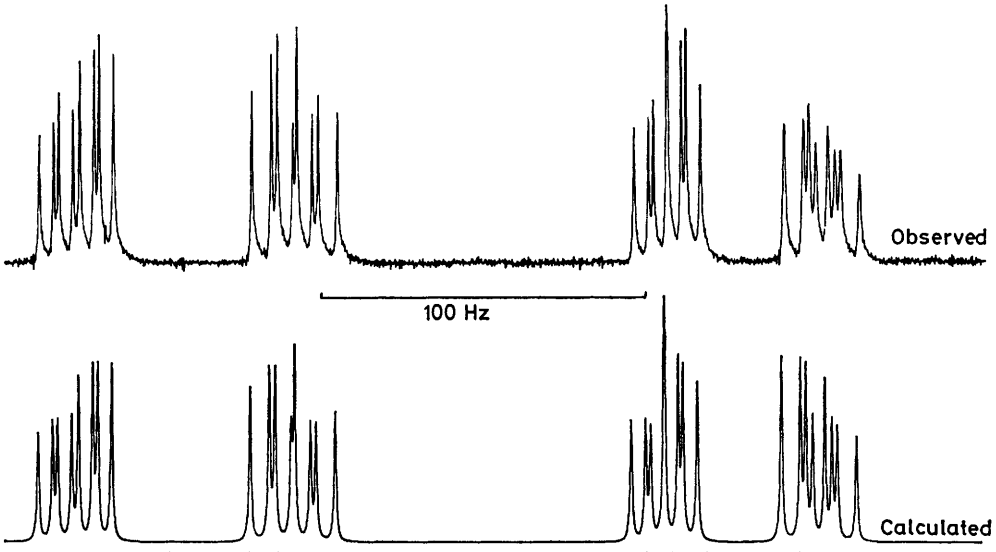
SCHEME 1

poisoning, the thiolate group being one of the strongest co-ordinators of methylmercury(II).[2] However, although BAL is commonly used as a detoxifying agent, its shelf-life is poor due to atmospheric oxidation of the thiolate groups to disulphide-bridged species of no therapeutic value.

With this problem in mind we have investigated the reactions of metal ions $Hg^{II}Me$, Hg^{II}, and Zn^{II} with the thiazolidine derivative (A). Based on previous studies [3-5] it was expected that, in the presence of co-ordinating metal ions, the thiazolidine ring of (A) would open, thereby releasing the ' protected ' thiolate group and making it available for co-ordination to toxic metal ions. In this study we have investigated the kinetics of Scheme 1 using stopped-flow rapid-scanning u.v. spectrophotometry, and the equilibrium position using ^1H and ^{13}C n.m.r., and u.v. spectrophotometry.

RESULTS AND DISCUSSION

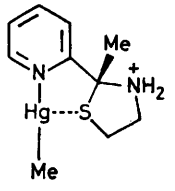
2-Methyl-2-(2-pyridyl)thiazolidine (A).—This ligand was prepared by the reaction of 2-acetylpyridine with 2-aminoethanethiol. A 400-MHz ^1H n.m.r. spectrum (the methylene part of which is shown in the Figure) confirms the ring-closed structure (A) rather than the open Schiff-base structure found in complexes (B). When



Observed and calculated 400-MHz ^1H n.m.r. spectra of (A) in the methylene region

the ligand is ring-closed, all four protons of the two methylene groups are inequivalent, and a simulation of the spectrum (Figure) agrees perfectly with the proposed structure (A). The ^{13}C n.m.r. spectrum also confirms structure (A), the tertiary carbon atom of the thiazolidine ring appearing around δ 80 p.p.m., rather than near δ 170 p.p.m. as expected for an uncomplexed ring-opened imine. Protonation of the NH and pyridine groups of (A) occurs readily in the presence of strong acid, as shown by shifts in the ^{13}C resonances, and marked changes in the u.v. spectrum [for the free ligand, $\lambda_{max.}$ 263 nm (ε 3 600 $\pm$ 100 dm^3 mol^{-1} cm^{-1}); in strongly acidic solution, $\lambda_{max.}$ 258 nm (ε 4 600 $\pm$ 100) with shoulders at 253 and 263 nm]. Addition of base to (A) causes no apparent changes in the u.v. spectrum.

Reaction of (A) *with* [HgMeX] (X = Cl *or* O_2CMe).—An equimolar mixture of (A) and [HgMeCl] in [$^2H_6$]dmso solution gives two complexes in an approximately 2 : 1 ratio, as evident from the ^1H and ^{13}C n.m.r. spectra. In the majority species, the thiazolidine ring is opened as shown by the disappearance of the ^{13}C resonance from the tertiary carbon atom of the ring (δ 80.6 p.p.m.), and the appearance of a new resonance at δ 198.9 p.p.m. from the imine carbon atom of the complex. A second set of ligand ^{13}C resonances are apparent for the minority species, which still contains a closed thiazolidine ring. This minority species is not present in solutions which contain a 3 : 1 ratio of [HgMeCl]–(A), and is also absent when [HgMe(O_2CMe)] and (A) are mixed in a 1 : 1 ratio. We attribute this behaviour to the pH-dependent equilibrium (Scheme 1), in which excess [HgMeCl] or acetate buffer ions are required to drive the equilibrium to the right. The minority species, present in the 1 : 1 mixture of [HgMeCl] and (A), is most likely a protonated ligand complex, possibly of structure (C). The majority

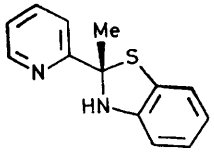


(C)

species is believed to be a predominantly thiolate-bound complex, analogous to (B), but with a structure similar to that found in dithiolate complexes (*i.e.* with a nearly linear Me-Hg-S– and weaker, angled co-ordination to the N-donors of the ligand).[1] The complex of $Hg^{II}Me$ with 2,2′-bipyridine is similar.[6]

In the 1 : 1 mixture of [HgMeCl] and (A), values of $^1J(^{199}Hg\text{-}^{13}C)$ (1 506 Hz) and $^2J(^{199}Hg\text{-}^1H)$ (182.6 Hz) of the $Hg^{II}Me$ moiety are consistent with this interpretation, the methylmercury being in fast exchange and giving a single time-averaged ^1H or ^{13}C resonance. The value of ^2J(HgH) is greater than that expected for completely thiolate-bound $Hg^{II}Me$ species (160 Hz),[7] but close to the value expected for a 2 : 1 ratio of thiolate- and pyridine-bound $Hg^{II}Me$. A value of ^2J(HgH) of *ca.* 225 Hz is calculated for the minority complex, which is close to the value reported for [HgMe(pyridine)]-[NO_3].[8] Also, in the 1 : 1 mixture of [HgMe(O_2CMe)] and (A) where only a single complex is formed, we observe ^2J(HgH) = 163 Hz, which is as expected for the thiolato-complex.

Reaction of (A) *with* $Hg[ClO_4]_2$.—Studies were carried out in methanol solution. Using metal : ligand ratios in the range 1 : 1 to 3 : 1, ^{13}C n.m.r. and u.v. studies showed the formation of a simple mono-complex in which the thiazolidine ring is broken (Scheme 1). The mono-complex is characterised by $\lambda_{max.}$ = 277 nm and ε = 9 200 dm^3 mol^{-1} cm^{-1}. In the presence of excess ligand, changes in the u.v. show that another (probably bis-) species is also formed, but this was not fully characterised. There was no evidence for the formation of complexes in which the thiazolidine ring is still closed, as was found in the isolated bis complex of the related ligand 2-(2-pyridyl)benzothiazoline (D).[9]



(D)

Attempts were made to study the kinetics of the reaction between (A) and excess Hg^{II} in methanol at 280 nm by stopped-flow spectrophotometry. However, at 276.7 K the reaction is very fast and only approximate pseudo-first-order rate constants ($k_{obs.}$ $\pm$ 20%) could be determined; with [(A)] = 10^{-5} mol dm^{-3} and [Hg^{II}] = 10^{-4} and 2×10^{-4} mol dm^{-3}, $k_{obs.}$ = 170 and 385 s^{-1} respectively. Thus the reaction is approximately first-order in [Hg^{II}]. It is unlikely that the observed reaction involves ligand binding (Scheme 2, rate constant k_1) since chelate formations involving Hg^{II} and bipyridyl-like ligands are known to be too fast for stopped-flow observation.[10] We postulate, therefore, that $k_{obs.} \simeq k_2K_1[Hg^{II}]$, with the second step in Scheme 2 (M = Hg) being rate determining ($K_1 = k_1/k_{-1}$; rapid pre-equilibrium). With this interpretation we estimate k_2K_1 *ca.* 2×10^6 dm^3 mol^{-1} s^{-1} at 276.7 K. Good evidence for Scheme 2 comes from studies with the less labile Zn^{II} ion described below.

$$M^{II} + (A) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{complex} \xrightarrow{k_2} \text{product}$$

SCHEME 2

Reaction of (A) *with* $Zn[ClO_4]_2$ *and* $Zn[O_2CMe]_2$.—Using excess zinc perchlorate (10^{-3} mol dm^{-3}) with [(A)] = 3.3×10^{-5} mol dm^{-3} in methanol, two distinct kinetic steps are detected using stopped-flow rapid-scanning u.v. spectrophotometry.[11] At 277.7 K the first step has a half-life of *ca.* 25 ms and the second step *ca.* 2 s. An isosbestic point was observed for the second stage at 260 nm, and this wavelength was chosen for single wave-

TABLE 1

Pseudo-first-order rate constants $k_{obs.}$ for the first step in the reaction of $Zn[ClO_4]_2$ with (A) (3.3×10^{-5} mol dm^{-3}) in methanol at 260 nm, 277.7 K

$10^3[Zn^{II}]$/mol dm^{-3}	0.54	1.5	2.5	3.5
$k_{obs.}$/s^{-1}	26 ± 3	31 ± 3	38 ± 4	42 ± 4
$10^3[Zn^{II}]$/mol dm^{-3}	4.5	5.0		
$k_{obs.}$/s^{-1}	50 ± 5	61 ± 6		

$10^{-2}k_{obs.} = (0.21 \pm 0.02) + (70 \pm 6)\,[Zn^{II}]$

TABLE 2

Pseudo-first-order rate constants k for the reaction of $Zn[O_2CMe]_2$ with (A) (3.3×10^{-5} mol dm^{-3}) at 280 nm

(*a*) At 283.5 K

$10^3[Zn^{II}]$/mol dm^{-3}	0.26	0.52	1.0	2.1
k/s^{-1} (±0.004)	0.391	0.447	0.465	0.498
$10^3[Zn^{II}]$/mol dm^{-3}	3.1			
k/s^{-1} (±0.004)	0.507			

(*b*) At 278.0 K

$10^3[Zn^{II}]$/mol dm^{-3}	1.3	3.3	6.6	13.0
k/s^{-1} (±0.003)	0.219	0.237	0.254	0.257
$10^3[Zn^{II}]$/mol dm^{-3}	20.0	26.0	33.0	
k/s^{-1} (±0.003)	0.262	0.262	0.268	

length stopped-flow studies of the first stage. The results are collected in Table 1. Values of $k_{obs.}$ were fitted by a least-squares method to an equation of the form $k_{obs.} = k_0 + k_1[Zn^{II}]$, which gave $k_0 = 21 \pm 2$ s^{-1} and 10^{-3} $k_1 = 7.0 \pm 0.6$ dm^3 mol^{-1} s^{-1} at 277.7 K. Similar results have been obtained for complex formations of Zn^{II} ion with 2,2′-bipyridine and 1,10-phenanthroline in methanol,[12] and the first-stage results are assigned to the ligand binding step in Scheme 2.

The second stage of the reaction with $Zn[ClO_4]_2$ is not first order, the rate decreasing markedly with time. This is understandable if the reaction involves opening of the thiazolidine ring, since co-ordination to the released thiolate group will occur with the release of a proton (Scheme 1). The increase in acidity will hinder the overall reaction and cause the rate of the second stage to decrease with time. Addition of methanolic K[OH] to the solutions causes an acceleration of the second-stage rate, as expected. Furthermore, using much higher concentrations of $Zn[ClO_4]_2$ and (A), ^{13}C n.m.r. shows that under these conditions, cleavage of the thiazolidine ring does not occur, the product showing a resonance at δ 79.5 p.p.m. from the tertiary carbon atom of the unopened ring. However, using a 1 : 1 mixture of $Zn[O_2CMe]_2$ and (A), the buffering effect of the acetate ions is sufficient to drive reaction (1) to completion, a new ^{13}C resonance appearing at low field from the imine carbon atom of the product (B).

Using $Zn[O_2CMe]_2$ in the stopped-flow experiments causes the rate of the ligand binding step (Scheme 2) to accelerate beyond the limits of stopped-flow detection, but the buffering effect of the acetate ions produces a strictly first-order slow step attributed to thiazolidine ring-opening. Anions in the inner-sphere of metal ions are known to increase the rate of complex formation in non-aqueous solvents,[13] and it is reasonable to expect, therefore, that the presence of acetate ions in the inner-sphere of the Zn^{II} ion enhances the rate of binding to (A).

The pseudo-first-order rate constants k obtained for the reaction of (A) (3.3×10^{-5} mol dm^{-3}) with $Zn[O_2CMe]_2$ (2.6×10^{-4} to 3.1×10^{-3} mol dm^{-3}) were found to increase non-linearly with $[Zn^{II}]$, as shown in Table 2. Values of k were fitted by non-linear least-squares methods to an equation of the form $k = k_2K_1[Zn^{II}]/(1 + K_1[Zn^{II}])$, which gave $k_2 = 0.52 \pm 0.07$ s^{-1} and $10^{-4}K_1 = 1.90 \pm 0.14$ dm^3 mol^{-1} at 283.5 K. Variable-temperature runs were carried out with $[Zn^{II}] = 3.8 \times 10^{-2}$ mol dm^{-3}, such that $K_1[Zn^{II}] \gg 1$, and $k = k_2$. These

TABLE 3

Variation of the pseudo-first-order rate constants k with temperature for the reaction of $Zn[O_2CMe]_2$ (3.8×10^{-2} mol dm^{-3}) with (A) (3.7×10^{-5} mol dm^{-3}) in methanol at 280 nm

k/s^{-1}	0.44 ± 0.02	0.53 ± 0.01	0.60 ± 0.01	0.76 ± 0.01	1.21 ± 0.05	2.36 ± 0.05	3.09 ± 0.09	4.62 ± 0.01	6.46 ± 0.2
T/K	281.7	282.8	284.5	287.0	291.5	297.1	300.2	304.4	309.3

TABLE 4

Hydrogen-1 and carbon-13 n.m.r. data for metal complexes of (A)

Complex	Solvent [a]	Nucleus	δ/p.p.m [b]
[Hg(A)][ClO_4]	[$^2H_6$]dmso–CD_3NO_2 (9 : 1)	^{13}C	198.52 (imine carbon); 150.22, 149.31, 141.58, 129.62, 125.07 (py); 43.24, 27.90 (CH_2 carbons); 26.54 (CH_3)
[Zn(A)][O_2CMe]	CD_3OD	^{13}C	179.73, 179.20 (imine carbon and acetate CO_2^-); 166.80, 148.45, 140.98, 127.85, 124.28 (py); 51.17, 27.21 (CH_2 carbons); 26.91 (CH_3); 22.58 (acetate CH_3)
[Zn(A)][ClO_4]	[$^2H_6$]dmso–CD_3NO_2 (3 : 1)	^{13}C	163.29, 148.01, 142.75, 126.18, 125.66 (py); 79.51 (C^2 of thiazolidine ring); 54.61, 36.09 (CH_2 carbons); 33.23 (CH_3)
[HgMeCl]–(A) (3 : 1)	[$^2H_6$]dmso	^{13}C	198.89 (imine carbon); 152.74, 148.97, 137.21, 127.67, 120.80 (py); 43.46, 26.07 (CH_2 carbons); 25.18 (CH_3); −0.10 (CH_3Hg; ^1J 1 506 Hz)
[HgMeCl]–(A) (1 : 1)	[$^2H_6$]dmso	^{1}H	8.45 (m, 1), 7.65 (m, 1), 7.55 (m, 1), 7.20 (m, 1, py); 3.40 (t, 2, CH_2); 3.07 (t, 2, CH_2); 2.00 (s, 3, CH_3); 0.45 (s, 3, CH_3Hg, ^2J 182.6 Hz)
[HgMe(O_2CMe)]–(A) (1 : 1)	CD_3OD	^{1}H	8.55 (m, 1), 8.05 (m, 1), 7.95 (m, 1), 7.60 (m, 1, py). 3.25 (t, 2, CH_2); 3.15 (t, 2, CH_2); 2.65 (s, 3, CH_3) 1.95 (s, 3, acetate); 0.55 (s, 3, CH_3Hg, ^2J 163.0 Hz)

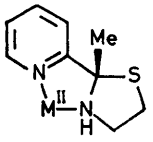
[a] dmso = Dimethyl sulphoxide. [b] Relative to $SiMe_4$.

TABLE 5

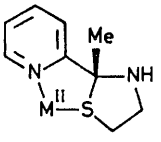
Mass spectrum of (A)

m/e	180	165	147	138	133	121	106	102	79	78
Formed by loss of		CH_3	SH	C_2H_4N	SCH_3	SC_2H_3	SC_2H_4N	C_5H_4N	SC_4H_7N	SC_4H_6N
Relative intensity	1.1	0.5	2.0	0.7	1.9	1.0	1.5	1.4	1.4	1.1

results are in Table 3 and from the data, activation parameters associated with k_2 are $\Delta H^{\ddagger} = 69.6 \pm 1.3$ kJ mol^{-1} and $\Delta S^{\ddagger} = -4.3 \pm 4.6$ J K^{-1} mol^{-1}. The rate law and activation parameters are consistent with Scheme 2 (M = Zn), with a rapid but incomplete formation of the complex intermediate at the lower zinc concentrations. The structure of the intermediate cannot be established with certainty, but structures (E) or (F) are both possible.



(E)



(F)

Thermodynamically, structure (E) is more likely since thioether groups do not co-ordinate as strongly to Zn^{II} as NH groups. Structure (F) is a little more favourable for the 'softer' Hg^{II} ion, and this could account for the increased rate observed, since co-ordination at the S atom will weaken the C–S bond which breaks during the final stage of the reaction.

EXPERIMENTAL

Standardisation of Metal Solutions.—The hydrated perchlorate salts of Hg^{II} (Ventron) and Zn^{II} (Pfaltz and Bauer) were used as supplied. Stock solutions (*ca.* 0.01 mol dm^{-3}) were standardised by adding excess ethylenediaminetetra-acetate (edta) (0.01 mol dm^{-3}), ammonia buffer, and back-titrating the excess with a standard solution of zinc sulphate using Solochrome black as indicator.

Preparation and Characterisation of 2-Methyl-2-(2-pyridyl)-thiazolidine (A).—To 2-aminoethanethiol hydrochloride (11.3 g, 0.1 mol) in 20% aqueous methanol (100 cm^3) was added K[OH] (1.2 g, 0.2 mol) slowly with stirring, followed by 2-acetylpyridine (12.1 g, 0.1 mol). The mixture was stirred overnight under an atmosphere of dinitrogen, and then evaporated to dryness with a rotary evaporator. Water (30 cm^3) was added and the aqueous suspension extracted with dichloromethane (5 × 30 cm^3). The dichloromethane was removed under reduced pressure and the product distilled at 378 K (0.05 mmHg *) (Found: C, 59.8; H, 6.75; N, 15.6; S, 17.85. Calc. for $C_9H_{12}N_2S$: C, 60.0; H, 6.65; N, 15.55; S, 17.8%). ^{13}C N.m.r. ($CDCl_3$) δ(p.p.m. relative to $SiMe_4$): 163.60 (C^2, py) (py = pyridine), 148.46 (C^6, py), 136.44 (C^3, py), 121.68, 118.69 (C^4, C^5, py), 80.61 (quaternary carbon), 51.88, 38.03 (CH_2 carbons), 30.75 (CH_3). ^{1}H N.m.r. (see Figure) (CD_3NO_2–CCl_4, 1 : 3) δ(p.p.m. relative to $SiMe_4$): 8.36 (m, 1 H), 7.56 (m, 1 H), 7.39 (m, 1 H), 7.04 (m, 1 H, py), 3.36 (ddd, 1 H, CH_2), 3.25 (ddd, 1 H, CH_2), 2.95 (ddd, 1 H, CH_2), 2.84 (ddd, 1 H, CH_2), 1.80 (s, 3 H, CH_3). Coupling constants (Hz) for the methylene system (numbered 1—4 as listed): $^1J(1,2)$ 12.39, $^2J(1,3)$ −4.36, $^2J(1,4)$ −5.87, $^2J(2,3)$ −5.89, $^2J(2,4)$ −7.61, $^1J(3,4)$ 9.81. U.v. spectrum (methanol): $\lambda_{max.}$ 263 nm (ε 3 600 ± 100 dm^3 mol^{-1} cm^{-1}). N.m.r. data for the Hg^{II} and Zn^{II} complexes of (A) are in Table 4.

Spectra and Kinetics.—Carbon-13 n.m.r. spectra were recorded with a 90-MHz Bruker WH90, ^{1}H n.m.r. spectra with a 400-MHz Bruker WH400, mass spectra (Table 5) with an AEI MS9, and u.v. spectra with a Perkin-Elmer 552 spectrometer. Kinetic studies were carried out with a rapid-scanning u.v. spectrometer as described in our previous work.[11]

[1/543 *Received*, 6*th April*, 1981]

* Throughout this paper: 1 mmHg = (101 325/760) N m^{-2}.

REFERENCES

[1] N. W. Alcock, P. A. Lampe, and P. Moore, *J. Chem. Soc., Dalton Trans.*, 1980, 1471.

[2] D. Rabenstein, *Acc. Chem. Res.*, 1978, **11**, 100.

[3] L. F. Lindoy and S. E. Livingstone, *Inorg. Chem.*, 1968, **7**, 1149.

[4] D. C. Liles, M. McPartlin, and P. A. Jacker, *J. Am. Chem. Soc.*, 1977, **99**, 7705.

[5] L. F. Lindoy and S. E. Livingstone, *Inorg. Chim. Acta*, 1968, **2**, 119.

[6] A. J. Canty and B. M. Gatehouse, *J. Chem. Soc., Dalton Trans.*, 1976, 2018.

[7] R. D. Bach and A. T. Weibel, *J. Am. Chem. Soc.*, 1976, **98**, 6241; A. J. Brown, O. W. Howarth, and P. Moore, *J. Chem. Soc., Dalton Trans.*, 1976, 1589.

[8] A. J. Canty, A. Marker, P. Barron, and P. C. Healy, *J. Organomet. Chem.*, 1978, **144**, 371.

[9] L. F. Lindoy and S. E. Livingstone, *Inorg. Chim. Acta*, 1967, **1**, 365.

[10] R. H. Holyer, C. D. Hubbard, S. F. A. Kettle, and R. G. Wilkins, *Inorg. Chem.*, 1965, **4**, 929.

[11] Part 3, T. J. Kemp, P. Moore, and G. R. Quick, *J. Chem. Res.*, 1981, 33.

[12] D. W. Buck and P. Moore, unpublished work.

[13] P. K. Chattopadhyay and J. F. Coetzee, *Inorg. Chem.*, 1976, **15**, 400; J. F. Coetzee and D. M. Gilles, *Inorg. Chem.*, 1976, **15**, 405.