Facile Nucleophilic Demethylation of the Trimethylphosphatopentaamminecobalt(III) Ion

W. G. JACKSON* and B. C. McGREGOR

Department of Chemistry, Faculty of Military Studies, University of New South Wales, Canberra, A.C.T., Australia 2600

Received July 4, 1983

The $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ ion reacts with SCN^-, I^- or $S_2O_3^{2-}$ to produce $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ and, respectively, CH_3SCN, CH_3I or $CH_3S_2O_3^-$. Rate studies (μ = 1.0 or 3.0 M, 35 °C) define the relative reactivity sequence SCN^- (1.0), I^- (1.2), $S_2O_3^{2-}$ (24), similar to that determined for the corresponding reaction of the free ligand, SCN^- (1.0), I^- (1.2), $S_2O_3^{2-}$ (88). These data and the second-order rate law are consistent with S_N2 substitution at carbon, and establish a new mode of reaction for a coordinated phosphate (V) ester. The rate enhancement on coordination is ca. *150. Both H_2O and OH^- are ineffective in demethylation, relative to Co–O cleavage with yields $[(NH_3)_5CoOH_n]^{(n+1)+}$ and $OP(OCH_3)_3$. In contrast, the $S_2O_3^{2-}$ reaction is nineteen times faster than aquation, and affords a convenient synthesis of $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ from the readily available $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ complex.*

Introduction

There has been considerable interest in the chemistry of phosphates and their esters because of their importance in biochemistry. In particular, the biological role of metal ions in phosphate related enzyme reactions has stimulated detailed mechanistic investigations of model metal phosphate systems [1, 2].

Kinetic work and oxygen-18 tracer and anion competition studies [3] on the acid and base hydrolysis of the simple $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ cation did not reveal the expected activation of the coordinated phosphate ester to intermolecular attack by H_2O or OH^-:

Of the four possible outcomes (Co–O, CoO–P, CoOP–O or O–C cleavage), only the simple ligand substitution reaction (1) was observed. This result does not comment on the activation of coordinated $OP(OCH_3)_3$ towards hydrolysis. While phosphorus–oxygen (2, 3) or carbon–oxygen (4) cleavage in the $[A_5CoOP(OCH_3)_3]^{3+}$ ion could well be faster than in the free $OP(OCH_3)_3$ ligand (and this is likely) [3], Co–O bond rupture must be faster again (at least 50-fold). Thus its observation and quantitative assessment are masked.

An obvious way to expose the role of the metal ion in activating and directing the course of the ligand reactions (2, 3 or 4) is to use $[A_5M(\text{phosphate ester})]^{n+}$ systems less susceptible to ligand substitution by H_2O or OH^- (*e.g.*, M = Rh(III) or Ir(III); or phosphate ester = $O_2P(OR)_2^-$, $O_3P(OR)^{2-}$, but this does not appear to have been examined. Another is to exploit the enhanced reactivity of coordinated nucleophiles such as OH_2, OH^- or NH_2^-, coupled with the use of esters such as $O_3PO{\cdot}C_6H_4{\cdot}NO_2^{2-}$, which slow Co–O bond rupture but promote P–O cleavage [1, 2].

It is now well established that the first-order intramolecular reaction is enhanced several orders of magnitude ($\sim 10^8$-fold) over the corresponding second-order intermolecular reaction, and thus, using this approach, the increased reactivity of the phosphate ester anion p-nitrobenzenephosphate towards nucleophilic attack has been assessed as $\sim 10^8$–10^9-fold, compared to the free ester. In both these studies [1, 2], CoOP–O cleavage (3) was the preferred mode of reaction at the ligand, but to some degree this is conferred by the use of the good leaving

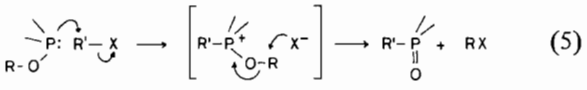
$$(NH_3)_5Co{-}O{-}P(-O{-}CH_3)_3^{3+} \xrightarrow[\text{or } {}^{18}OH^-]{H_2{}^{18}O} \begin{cases} (NH_3)_5Co{-}{}^{18}OH^{2+} + OP(OCH_3)_3 & (1) \\ (NH_3)_5Co{-}OH^{2+} + {}^{18}OP(OCH_3)_3 & (2) \\ (NH_3)_5Co{-}O{-}P(-OCH_3)_2^{2+} + CH_3OH \quad (O\ {}^{18}O) & (3) \\ (NH_3)_5Co{-}O{-}P{-}(OCH_3)_2^{2+} + CH_3{}^{18}OH \quad (O\ O) & (4) \end{cases}$$

*Author to whom correspondence should be addressed.

0020-1693/84/$3.00

p-nitrophenolate anion [1, 2] and by the 4-membered ring closure reaction [2] peculiar to the choice of system.

Another approach is to use nucleophiles better than H_2O and even OH^- but non-basic so that the rate of the base catalyzed M–O cleavage process (1) is not comparably enhanced (the difficulty with $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ + OH^-) [3]. This article presents the results of the successful application of such an approach, using SCN^-, I^- and $S_2O_3^{2-}$ as intermolecular nucleophiles towards $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$. Also, this work establishes unequivocally a new and especially facile mode of reaction for a coordinated phosphate ester, C–O cleavage (4). The results have biological implications, and are relevant to a recent account [4] of the reaction between $[Cp(diphos)CoI]^+$ and the P(III) ester $P(OCH_3)_3$, which produces $[Cp(diphos)CoPO(OCH_3)_2]^{2+}$ and CH_3I. Indeed, it was this article which prompted the present report, since our data on the nucleophilic demethylation of the bound P(V) ester in the $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ ion bear on the role of the metal ion in promoting these classic Arbusov [5] reactions, important in organophosphorus chemistry.



(5)

We present rate data and detailed product analyses for the reactions of both free and Co(III) coordinated $OP(OCH_3)_3$ thus providing direct information on the activation afforded by O-coordination.

Experimental

Visible absorption spectra (ϵ_λ, M^{-1} cm^{-1}) were recorded on a Cary 210 instrument at 25 °C. Proton NMR spectra at 35.5 °C were obtained with use of a Varian T60 spectrometer. D_2O and Me_2SO-d_6 were employed as solvents. Chemical shifts in these solvents are reported as ppm downfield from sodium 4,4-dimethyl-4-silapentane-sulfonate(DSS) and tetramethylsilane(TMS) references, respectively. All common chemicals were AnalaR or an equivalent grade. Methyl thiocyanate (CH_3SCN) and methyl isothiocyanate (CH_3NCS) were "*Purum*" quality (Fluka). SP-Sephadex C25 (Na^+ form, Pharmacia) resin was employed in the ion-exchange chromatographic experiments.

Product Analyses and Kinetic Studies

Reactions were studied under first-order or pseudo first-order conditions in all cases. Specific rates were determined for the release of $OP(OCH_3)_3$ from $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ in D_2O or M_2SO-d_6 at 35.5 °C in the presence (0.5 or 1.0 M; μ = 1.0 or 3.0 M) or absence of anions (I^-, SCN^-, OD^-, $S_2O_3^{2-}$), supplied as their Na^+ or NH_4^+ salts as appropriate; the details of the conditions are given in the Results Section. NMR tubes containing solvent and electrolyte were pre-equilibrated at 35.5 °C for 15 min before the introduction of $OP(OCH_3)_3$ or its cobalt complex.

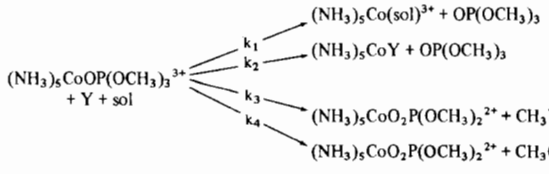
The concentration of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ as a function of time was monitored by ^1H NMR spectroscopy. Convenient time intervals were chosen, covering complete reaction. Also monitored were the concentrations of $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ and of free $OP(OCH_3)_3$, $O_2P(OCH_3)_2^-$ and CH_3Y (Y = I^-, S- and N-bonded SCN^-, $S_2O_3^{2-}$, OH^-). Peak heights for the sharp P-CH_3 resonances (all doublets, J_{PH}11–12 Hz) were taken as proportional to concentration. Individual spectra were scaled using an internal proton count; the sum of the P-OCH_3 and Y-CH_3 peak heights (9H) was convenient. Scaled peak heights were corrected statistically, according to the number of methyl groups in the individual species, to give relative concentrations. The P-OCH_3 doublets of each of the three methylphosphate species were clearly observed. They were identified in separate experiments by adding, in turn, authentic specimens, and observing the intensity increase. The CH_3Y signal, well upfield of the P-OCH_3 signals, was likewise identified. Also, the relative concentrations of the species assigned as $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ and CH_3Y were observed to be identical at all times and under all conditions, consistent with the stoichiometry required for this reaction path:

$$(NH_3)_5CoOP(OCH_3)_3^{3+} + Y^- \longrightarrow (NH_3)_5CoO_2P(OCH_3)_2^{2+} + CH_3Y$$

First-order rate constants k_{obsd} were obtained in the usual way, by non-linear least squares analysis of the peak height(H)/time(t) data according to $(H_o - H_\infty)\exp(-k_{obsd}t)$. The fits were good, equivalent to linear plots of ln $|H - H_\infty|$ *vs.* t over $3t_{1/2}$, and k_{obsd} values from duplicate runs usually agreed to better than ±10%.

Specific rates were determined also for the reaction of the unbound $OP(OCH_3)_3$ ester, at 35.5 °C in D_2O containing I^-, SCN^-, OD^- or $S_2O_3^{2-}$ (1.0 M).

Infinite time ^1H NMR spectra were used to best determine the product proportions for the parallel reactions,

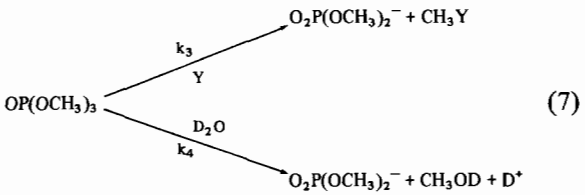


(6)

Thus the individual values for $k_1 + k_2$, k_3 and k_4 were obtained by subdividing k_{obsd} for the total loss of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ accordingly. These agreed well with values determined individually as above, by separately following the formation of $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$, $OP(OCH_3)_3$, CH_3Y and CH_3OH.

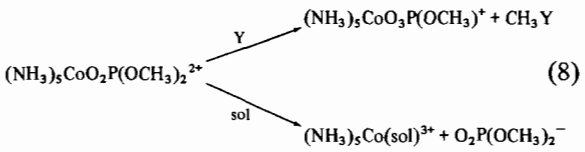
In no instance was CH_3OH observed as a product (confirmed by adding authentic CH_3OH), consistent with the observation $[(NH_3)_5CoO_2P(OCH_3)_2{}^{2+}] = [CH_3Y]$ at all times. Thus k_4 is negligible. Also, we note that the rate of release of free $OP(OCH_3)_3$, as measured by ^1H NMR spectroscopy, gives only $k_1 + k_2$. However, other work [6] (and see below) has shown that $k_1 \gg k_2$ (~20:1), and also that $(k_1 + k_2)$ is independent of [Y]. For the purpose of this article, these latter observations are inconsequential.

As found for the metal complex, hydrolysis of the ligand in D_2O containing Y (1.0 *M*) did not compete with nucleophilic demethylation by the anions (SCN^-, I^-, $S_2O_3{}^{2-}$), *i.e.* $k_3 \gg k_4$:



(7)

These reactions of $OP(OCH_3)_3$ are much slower (~100-fold) than the corresponding ones of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$, and thus do not interfere in the time required to determine the product distribution (eqn. 6) for the phosphate ester complex. In separate experiments it was shown that subsequent reactions of $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ such as solvolysis or further demethylation,



(8)

are also very much slower (at least 100-fold).

The product distribution for the reaction of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ in H_2O and in aqueous OH^- (0.1 and 1.0 *M*), NCS^- (1.0 *M*) and $S_2O_3{}^{2-}$ (1.0 *M*) was examined also by ion-exchange chromatography. Weighed samples (0.2–0.5 g) were reacted at 25 °C for $\geq$ 10 $t_{1/2}$ (H_2O, 10 hr; 0.1–1.0 *M* OH^-, $\leq$ 1 min; 1.0 *M* NCS^-, 5.0 hr; 1.0 *M* NCS^-, 2.0 hr) and the product solutions were diluted with water (to 0.5 L) and sorbed on and eluted (0.25 *M* NaCl, pH ~ 3) from Sephadex columns [7]. The $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ ion elutes well in front of $[(NH_3)_5CoSCN]^{2+}$ plus $[(NH_3)_5CoNCS]^{2+}$ which elute together, followed by and separated from $[(NH_3)_5CoOH_2]^{3+}$. Cobalt concentrations in the eluates were determined spectrophotometrically using the independently measured ϵ_{515}^{max} 62.5 for $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ and ϵ_{492}^{max} 47.7 for $[(NH_3)_5CoOH_2]^{3+}$ in 0.25 *M* NaCl. The determination of the S- and N-bonded $[(NH_3)_5Co(SCN)]^{2+}$ isomers is described elsewhere [8]. Cobalt recoveries from the columns exceeded 98.5% in all cases and were generally 99–101%.

Syntheses

The triester complex $[(NH_3)_5CoOP(OCH_3)_3](ClO_4)_3 \cdot H_2O$ was synthesized as described previously [3, 9]. It was shown by ^1H NMR spectroscopy (Me_2SO-d_6; D_2O) and ion-exchange chromatography (0 °C) on Sephadex to be free of $[(NH_3)_5CoOH_2]^{3+}$ and $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ (<0.5%). ^1H NMR spectra: δ 4.03 (s, br, 12H; *cis* NH_3), 2.58 (s, br, 3H; *trans* NH_3), 3.52 (s, 2H; H_2O), 3.80 (d, 9H, J_{PH} 12 Hz; $POCH_3$) in Me_2SO-d_6; δ 3.94 (d, 9H, J_{PH} 11 Hz; $POCH_3$) in D_2O.

$[(NH_3)_5CoO_2P(OCH_3)_2](ClO_4)_2$

Samples prepared by minor modifications to the published procedure [10], and also via $[(NH_3)_5CoO_3SCF_3](CF_3SO_3)_2$ and the free ligand in acetone (a general synthesis for $[(NH_3)_5CoX]^{n+}$ [9]), were shown to be identical (^1H NMR and visible spectra) to the complex obtained by the new and simpler route now described:

The complex $[(NH_3)_5CoOP(OCH_3)_3](ClO_4)_3 \cdot H_2O$ [9] (3.0 g) was dissolved in a minimum volume of aqueous $Na_2S_2O_3$ (25 mL, 2 *M*, 25 °C) by stirring the initial suspension for 15 min. The product mixture was diluted to 500 mL with water and sorbed on Sephadex. After washing (H_2O, 2 × 250 mL), the major (~95%) pink 2+ band was eluted clear of a little orange $[(NH_3)_5CoOH_2]^{3+}$ using $LiClO_4$ (0.25 *M*, pH3). The eluate was rotary evaporated (<40 °C) to ~25 mL and excess ethanol (1 L) was added. After 24 hr at 0 °C, the deposited red needles were collected, washed with ethanol and ether, and air-dried. They were recrystallized from H_2O/ethanol to afford anhydrous $[(NH_3)_5CoO_2P(OCH_3)_2](ClO_4)_2$ (2.0 g, 85%). ^1H NMR spectrum: δ 3.77 (s, br, 12H; *cis* NH_3), 2.57 (s, br, 3H; *cis* NH_3), 3.45 (d, 6H, J_{PH} 12 Hz; $POCH_3$) in Me_2SO-d_6; δ 3.64 (d, 6H, J 11 Hz; $POCH_3$) in D_2O. Visible spectrum: ϵ_{515}^{max} 62.5, ϵ_{352}^{min} 47.7 (H_2O).

Results

Table I records the NMR spectral data used to analyze the reactions of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ and/or the free ester $OP(OCH_3)_3$ in D_2O and Me_2SO-d_6. Pseudo first-order rate constants for these reactions are given in Table II. Figure 1 illustrates changes which occur with time in the NMR spectrum of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ in D_2O containing NCS^-, and these spectra typify all the systems examined.

TABLE I. Proton Chemical Shifts for the Trimethylphosphate Cobalt(III) Complex and its Nucleophilic Demethylation and Solvolysis Products, 35 °C.

Substrate[a]	Solvent	Chemical Shift (Hz)[b]			
		P-OCH_3 [c]	CH_3Y	*cis* NH_3	*trans* NH_3
$(NH_3)_5CoOP(OCH_3)_3^{3+}$	Me_2SO-d_6	234, 222		242	155
	D_2O	242, 231			
$(NH_3)_5CoO_2P(OCH_3)_2^{2+}$	Me_2SO-d_6	213, 201		226	154
	D_2O	224, 213			
$(NH_3)_5CoOS(CH_3)_2^{3+}$	Me_2SO-d_6			228	154
$OP(OCH_3)_3$	Me_2SO-d_6	227, 216			
	D_2O	236, 225			
$O_2P(OCH_3)_2^-$	D_2O	223, 212			
CH_3I	D_2O		133		
CH_3OH	D_2O		203		
CH_3SCN	Me_2SO-d_6		159		
	D_2O		161		
CH_3NCS	Me_2SO-d_6		202		
	D_2O		199		
$CH_3S(S)O_3^-$	D_2O		160		

[a] Perchlorate salts for cations. [b] Shifts at 60 MHz, downfield from DSS (D_2O) or TMS (Me_2SO-d_6). [c] Separation represents J_{PH}.

The rate data for the complex (Table II) show clearly that the path giving $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ is additional to the solvolysis path leading to $[(NH_3)_5Co(sol)]^{3+}$ and free $OP(OCH_3)_3$. For example, the solvolysis rate in D_2O is essentially constant while the total rate (at [Y] = 1 *M*) is sensitive to the nature of the anion. Clearly this behaviour arises from a rate law of the form,

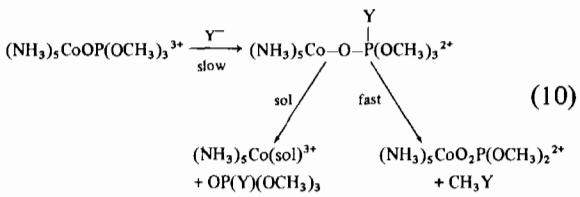
$$-d/dt[CoOP(OCH_3)_3] = (k_s + k_y[Y])[CoOP(OCH_3)_3] \quad (9)$$

where k_s is the specific first-order rate of hydrolysis and k_y is the specific second-order rate for demethylation which yields $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ + CH_3Y in equivalent amounts. The limited data for varied [Y] at constant ionic strength ($[NCS^-]$ = 1.0 and 0.5 *M*; Table II) confirm the expected second-order nature of this reaction pathway.

We note that the rate for the hydrolysis path is not especially sensitive to a variation in ionic strength, and in particular, to the nature of the anion comprising the medium ($Y = OH^-$ is an obvious but only apparent exception—see Discussion). Moreover, the anions Y do not get to exert their nucleophilicity for substitution at the cobalt(III) centre, even in Me_2SO, where a greatly enhanced nucleophilicity might be expected [11]. This is evident as the lack of a detectable term in the rate law, first-order in [Y], which corresponds to the production of $[(NH_3)_5CoY]$ plus $OP(OCH_3)_3$. Indeed very little $[(NH_3)_5CoY]$ accompanies the formation of $[(NH_3)_5Co(sol)]^{3+}$ in the Co–O cleavage path ($\lesssim$10% for $Y = I^-$ [12], SCN^- [8], $S_2O_3^{2-}$ [13]), even at 1 *M* [Y].

The [Y] dependence of the rate and product distribution for this reaction is of interest in its own right, in relation to the mechanism of octahedral cobalt(III) substitution [6]. Results of detailed studies are presented elsewhere [6, 14]. They are not germane to the chief issue of the present work, other to serve to highlight the contrast between cobalt(III) substitution as opposed to carbon substitution (eqn. 6).

The results eliminate any significant contribution from a *single* reaction pathway such as,



(10)

Such a path requires a product distribution independent of [Y], and a solvolysis rate with a term linear in [Y], both contrary to the facts recorded in Table II.

Kinetic data for the corresponding reactions of the free $OP(OCH_3)_3$ ligand in D_2O are recorded also in

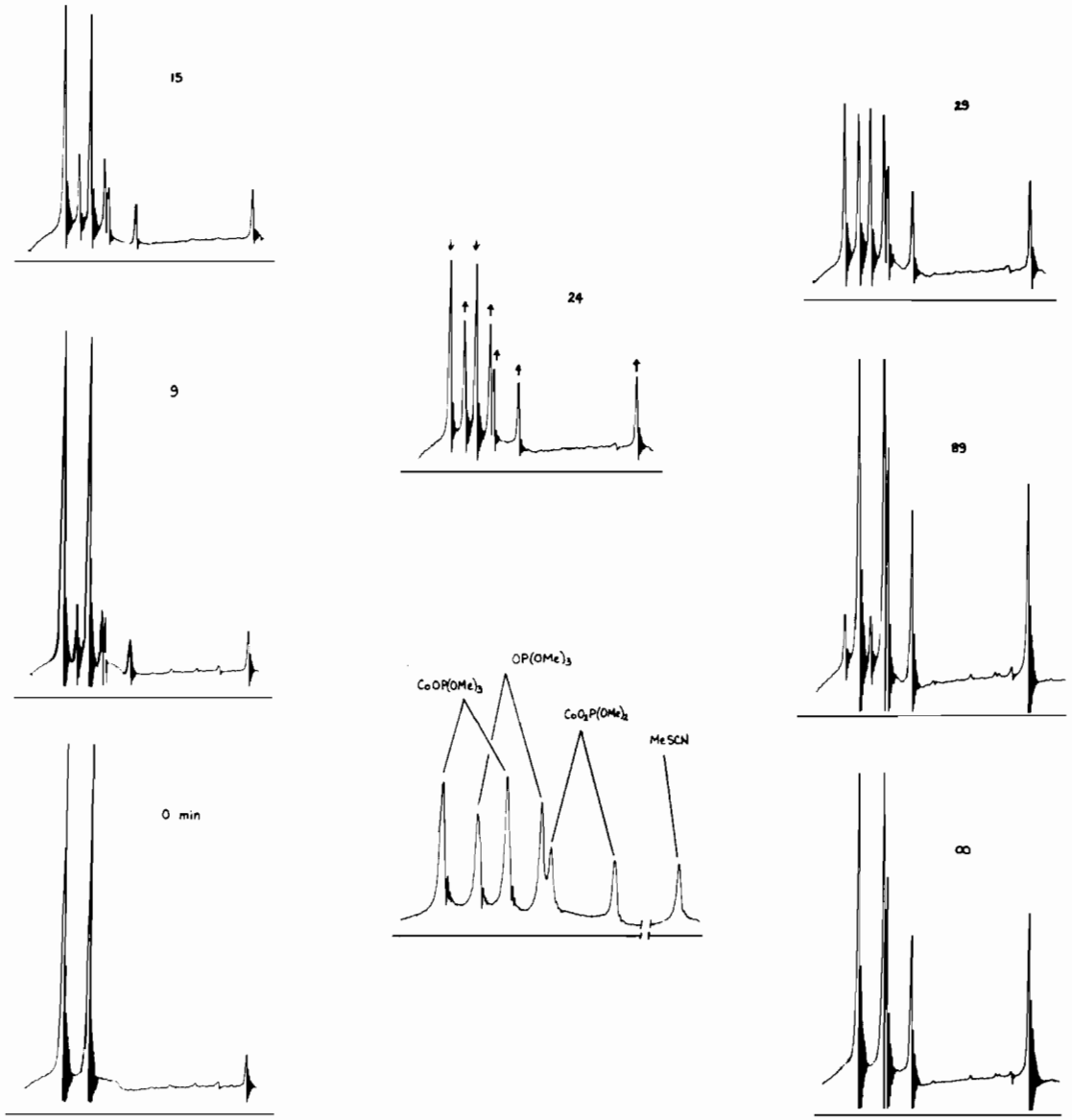


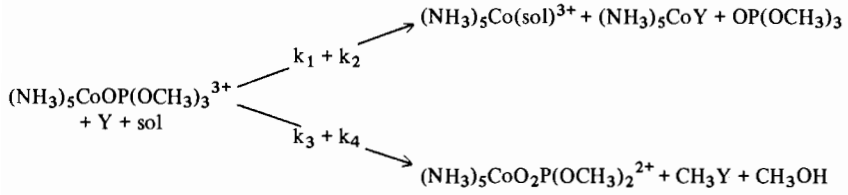
Fig. 1. ^1H NMR spectra showing the transformation of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ into $[NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ and CH_3SCN by one route (42%), and $[(NH_3)_5CoOH_2]^{3+}$ plus free $PO(CH_3)_3$ by the other parallel path (58%); D_2O, μ = 1.0 *M* (NaNCS), 35.5 °C.

Table II. It is noted that the Y = OH^- reaction giving $O_2P(OCH_3)_2^-$ and CH_3OH can occur by either C–O or P–O cleavage. We have not carried out ^{18}O tracer work to determine the extent of each path, but it is sufficient to note that the measured specific rate (4.0×10^{-4} s^{-1} at $[OH^-]$ = 1.0 *M*) must be the *upper* limit for C–O cleavage. The rates for Y = I^-, SCN^-, and $S_2O_3^{2-}$ all refer to C–O cleavage, since CH_3Y (and no CH_3OD) is the exclusive product (other than the phosphate diester).

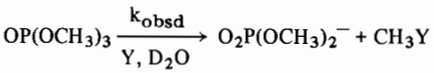
A direct comparison of the data for the free and bound phosphate triester expose the following enhancements in rate on coordination: Y = SCN^-, 163; I^-, 159; $S_2O_3^{2-}$, 45. The comparison is significant because the essential reaction is the same—nucleophilic attack at carbon (or phosphorus—see Discussion), with the elimination of CH_3Y. Only the leaving groups differ, cationic $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ and anionic $O_2P(OCH_3)_2^-$ respectively, and then only because the $(NH_3)_5Co^{3+}$ moiety is bound to one of the oxygen atoms. Thus the direct influence of O-coordination can be gauged.

The relative effectiveness of the nucleophiles towards attack at carbon in the $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ complex ion in D_2O are: $S_2O_3^{2-}$ (24) > I^- (1.1) ~ SCN^- (1.0) ≫ H_2O (<0.01). This is the same order as found for the free ligand: $S_2O_3^{2-}$ (88) > I^- (1.2) ~ SCN^- (1.0) ≫ H_2O (<0.01). Note that all data refer to μ = 1.0 *M* except for the Y = $S_2O_3^{2-}$ systems (μ = 3.0 *M*), and that the increased μ has

TABLE II. Specific Rate and Product Distribution Data for the Reactions:



Medium Y[a]	Solvent	Specific Rates, s^{-1}			Production Distribution[b]			
		$10^4 k_{obsd}$[e] (total)	$10^4(k_3 + k_4)$ C–O	$10^4(k_1 + k_2)$ Co–O	%Co (sol)[c]	$\%CoO_2P(OCH_3)_2$	$\%CH_3Y$	$\%CH_3OH$
–	D_2O	4.1	–	4.1	100	0	0	0
$S_2O_3^{2-}$ (1 *M*)	D_2O	80.1	75.7	4.4	5(4)	95(96)	95	0
I^- (1 *M*)	D_2O	7.0	3.5	3.5	50	50	50	0
SCN^- (1 *M*)	D_2O	7.4	3.1	4.3	58(58)	42(42)	42	0
SCN^- (0.5 *M*)[g]	D_2O	6.0	1.6	4.4	73	27	27	0
OH^- (1.0 *M*)	D_2O	7.9×10^5[d]	–	7.9×10^5[d]	100(100[d])	0	0	0
OH^- (0.1 *M*)[g]	D_2O	7.9×10^4[d]	–	7.9×10^4[d]	100(100[d])	0	0	0
–	Me_2SO-d_6	14.4	–	14.4	100	0	0	0
SCN^- (1.0 *M*)	Me_2SO-d_6	42.0	25.2	16.8	40	60	60	0



Y[a]	$10^4 k_{obsd}$, s^{-1}	$10^4 k_Y$, M^{-1} s^{-1}	$t_{1/2}$
(D_2O)	–	–	>>3 days
I^- (1.0 *M*)	0.022	0.022	87.5 hr
SCN^- (1.0 *M*)	0.019	0.019	101 hr
SCN^- (0.5 *M*)[g]	0.010	0.020	193 hr
$S_2O_3^{2-}$ (1.0 *M*)	1.67	1.67	72 min
OH^- (1.0 *M*)[f]	4.0	4.0	29 min

[a] Ionic Strength 1 *M* except for D_2O (~ zero) and for Y = $S_2O_3^{2-}$ (1 *M*), μ = 3 *M*. [b] NMR Spectral Analysis (35.5 °C); values determined by ion-exchange chromatography (25 °C) are parenthesized. [c] Essentially all $[(NH_3)_5Co(sol)]$, sol = H_2O, Me_2SO. For Y = SCN^-, there is some (~5% total; $[NCS^-]aq$ = 1.0 *M*) S- and N-bonded $[(NH_3)_5Co(SCN)]^{2+}$ formed as well, in both H_2O and Me_2SO (determined chromatographically). [d] Data from reference 3. [e] Specific rate for the loss of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$; $k_{obs} = k_1 + k_2 + k_3 + k_4$. Note that k_4 is negligible. [f] In this case, CH_3OH product can arise by P–O and/or C–O cleavage. The reported specific rate represents total CH_3OH production by *both* routes; it has been shown that P–O cleavage predominates (reference 17). [g] Supporting electrolyte $NaCF_3SO_3$ (μ = 1 *M*).

likely diminished the rate somewhat for the complex but not the free ligand reaction. This brings the two sequences above into even closer line.

The effect of solvent was only briefly examined. A change from H_2O to Me_2SO enhanced the rate of NCS^- attack at the methyl carbon of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ about 8-fold. It also enhanced the rate of Co–O cleavage, but not to the same extent (3.5-fold). In Me_2SO the products via Co + O are $OP(OCH_3)_3$, and largely $[(NH_3)_5Co(sol)]^{3+}$ rather than $[(NH_3)_5Co(SCN)]^{2+}$.

Discussion

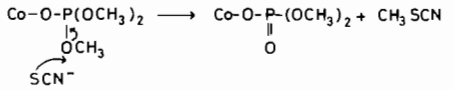
In connection with studies [3, 6, 12, 14] scrutinizing anion competition which accompanies the hydrolysis of $[(NH_3)_5CoX]^{n+}$,

$$(NH_3)_5CoX^{n+} \xrightarrow[H_2O]{Y} \begin{cases} (NH_3)_5CoY \\ (NH_3)_5CoOH_2^{3+} \end{cases} \qquad (11)$$

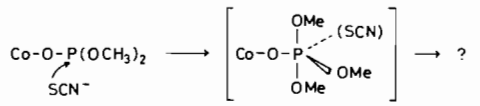
we observed that the $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ ion behaved normally (eqn. 11) in Cl^- and NO_3^- media (1.0 *M*), but unexpectedly found that almost half of the Co(III) product in 1 *M* NCS^- was $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ (a previously known complex [10] but undetected in an early study [15] of this chemistry). It seemed untenable that NCS^- alone, in some unprecedented way, greatly enhanced the rate of *ligand* hydrolysis of the coordinated trimethyl phosphate ester complex; Co–O cleavage is the exclusive reaction in H_2O and even in OH^-/H_2O [3]. It occurred to us that the diester complex resulted by direct attack at the ligand carbon (or phosphorus) centre, with the elimination of CH_3SCN (or CH_3NCS), since a facile S_N2 substitution of this kind is readily reconciled with the greatly enhanced nucleophilicity of SCN^- over anions such as Cl^- or NO_3^- in aqueous solution.

The present results confirm this interpretation. The proton NMR work shows that precisely one equivalent of CH_3SCN accompanies the production of $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$. Also no CH_3OH is observed, eliminating the possibility of any SCN^- assisted hydrolysis.

The organic CH_3SCN product was shown to be exclusively the S-bonded linkage isomer, consistent with S_N2 substitution at carbon [16]. Moreover, the first-order rate dependence on $[SCN^-]$ was established. Both facts are in keeping with results for SCN^- substitution of simple alkyl halides such as CH_3I, and suggesting SCN^- attack at carbon rather than phosphorus.



(12)



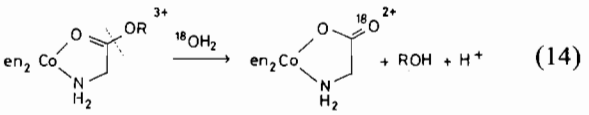
(13)

The study of the corresponding reactions using I^- and $S_2O_3^{2-}$ as nucleophiles was a logical corollary. The case for attack at carbon was supported by the observed order of nucleophilicities, and their relative magnitudes, $S_2O_3^{2-} \gg I^- \sim SCN^-$. (Note that $S_2O_3^{2-}$, like SCN^-, binds the methyl group through the much more nucleophilic S-atom). The same result was obtained for nucleophilic demethylation of the free ligand, albeit the absolute rates were ~100-fold slower. This order of nucleophilicities is that found for classical S_N2 substitution at saturated carbon, such as at CH_3X (X = Cl^-, OTs^-, I^-) in aqueous solution [16]. Also, the modest rate enhancement (8-fold) for SCN^- on solvent transfer from H_2O to DMSO [11] is consistent with this interpretation.

Having established the facility of the demethylation reaction, and the site of bond cleavage (C–O), a further significant result is the 100-fold rate enhancement through coordination to the Co(III) center. While activation of organic molecules towards reaction, nucleophilic substitution in particular, is certainly a well established phenomenon, examples where the comparison between free and coordinated ligand involves the *same* reaction are not abundant. To illustrate the point the example of the $\sim 10^8$-fold increased reactivity of the phosphate monoester p-nitrophenylphosphate, through Co(III) coordination, may be cited [2]. The free ligand reacts extremely slowly with OH^- to give the p-nitrophenolate ion and PO_4^{3-} ($t_{1/2} > 50$ days, 1 *M* OH^-, 25 °C), whereas in 1 *M* OH^- the same (coordinated) ester in $[(NH_3)_5CoO_3P{\cdot}C_6H_4{\cdot}NO_2]^+$ is hydrolyzed in a matter of seconds. However the rate difference, as was of course recognized, rests not only with the electron-withdrawing effect of Co(III). Indeed, the major activation appears to arise through a template effect. Whereas the free ligand process is an intermolecular reaction between $NO_2{\cdot}C_6H_4{\cdot}PO_3^-$ and OH^-, presumably involving P–O cleavage as does, *e.g.*, the $OP(OMe)_3 + OH^-$ reaction [17], the reaction of the metal complex differs in several respects. It is intramolecular, an effect affording considerable activation in itself, and also it involves [2] attack at phosphorus by an adjacent NH_2^- (*cis*) nucleophile rather than OH^-.

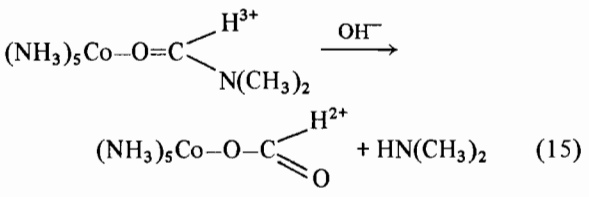
The present work enables the assessment of the single effect of Co(III) coordination on $OP(OCH_3)_3$ demethylation, since C–O bond cleavage and intermolecular attack by Y are features established as

common. One suitable comparison is the ester hydrolysis reaction [18] of $[en_2Co(NH_2CH_2CO_2R)]^{3+}$ (R = primary or secondary alkyl group), where intermolecular O-acyl cleavage by H_2O is the common feature, established by ^{18}O-tracer studies:

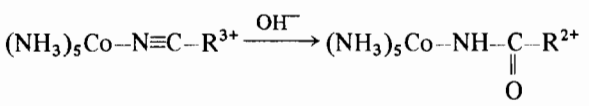


(14)

Here H_2O attack is at the sp^2 carbon centre, two bonds removed from Co(III), and the hydrolysis rate activation is substantial ($\geq 10^6$-fold). The hydrolysis of coordinated amides [19] and nitriles [20] afford other examples,

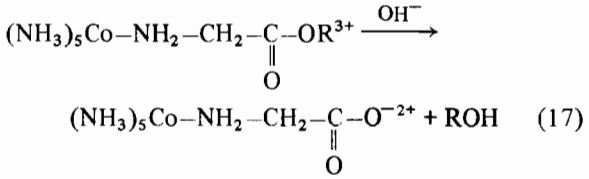


(15)



(16)

The former (eqn. 15) is a net substitution, the latter (eqn. 16) an addition reaction, but mechanistically both these reactions, as well as the carboxylic acid ester hydrolysis (eqn. 14), could involve addition as a rate determining step, or as a fast pre-equilibrium, and therefore render strict rate comparisons for the free and complexed ligands difficult. Nonetheless, large activations of the order of $\sim 10^4$–10^6 are observed [19, 20], and could be directly attributed to the electron-withdrawing effect of Co(III) which operates at a distance of two bond lengths in each of the three examples cited. The present trimethylphosphate example is mechanistically clearer—it is a straightforward single-step substitution—and the reduced $\sim 10^2$-fold activation is reasonably attributed to simply the (inductive) electron-withdrawing effect of Co(III), operating more remotely—four bond lengths from the site of nucleophilic attack (at C). This magnitude of activation is comparable to that observed for N-bonded aminoacid esters [21], *e.g.*,

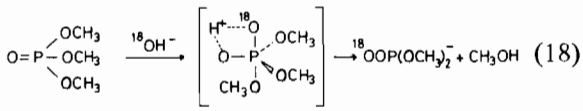


(17)

where O-acyl cleavage is the likely [22] common feature and attack at the carbonyl centre is three bond lengths remote from Co(III).

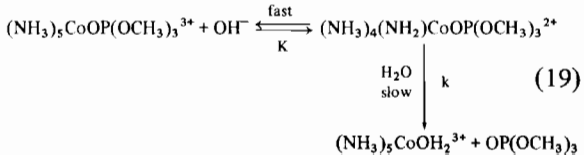
In light of remarks alluding to the facility of intra- over inter-molecular reaction, it is appropriate to comment that the 10^2-fold activation of the coordinated phosphate ester towards nucleophilic substitution at carbon, via an *inter*molecular process, suggests a greatly enhanced activation for *intra*molecular substitution at the *same* center. This highlights the possibility of enzymic hydrolysis of phosphate esters by C–O rather than, in model studies, the more usually considered P–O cleavage, especially by S-nucleophiles such as cysteinyl (R–SH) protein residues. The fact that biological phosphate chemistry is dominated by metal ion catalysis and that sulfur nucleophiles such as the simple SCN^- and $S_2O_3^{2-}$ ion are effective in dealkylation reactions of phosphate esters of the kind observed, suggest this as a viable proposition. The point need be emphasized that the conversion of a P–OR residue to P=O in H_2O does not necessarily imply hydrolysis, as this work has demonstrated.

The hydroxide ion reactions warrant particular comment. First, OH^- is not as good a nucleophile as $S_2O_3^{2-}$, SCN^- or I^- in S_N2 substitution reactions at saturated carbon, yet it is the most effective towards demethylation of $OP(OCH_3)_3$: OH^- (211) > $S_2O_3^{2-}$ (88) > I^- (1.2) ~ SCN^- (1.0) (Table II). Its misplacement suggests preferential attack at P rather than C, consistent with the preference of the electrophilic P for O-nucleophiles, and ^{18}O-tracer work [17] confirms this:



(18)

It would be expected that coordination to Co(III) would enhance the ester hydrolysis rate *at least* 100-fold, since now only 2 bonds separate the P and electron-withdrawing Co(III) centers. An activation factor of 10^4–10^6, by analogy with amide, nitrile and carboxylic acid ester data, is not an unreasonable estimate. Thus a minimum specific rate for the conversion of $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ to $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ and CH_3OH of $10^4\ k_Y[OH^-] = 10^4 \times (4 \times 10^{-4}) \times 0.1 = 0.4\ s^{-1}$ at 0.1 *M* $[OH^-]$ is estimated. However, $[(NH_3)_5CoOP(OCH_3)_3]^{3+}$ yields no detectable dimethylphosphate complex, even at 1 *M* OH^- (Table II). The reason for this is that OH^-, while a very poor nucleophile towards Co(III), catalyzes the Co–O cleavage path [3] by the well-known specific base catalyzed S_N1CB process:



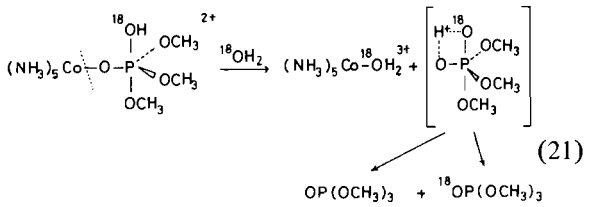
(19)

For this reaction, K is small and the rate law reduces to one of the same form as for the demethylation process,

$$k_{obsd} = kK[OH^-] = k_{OH}[OH^-] \quad (20)$$

i.e., first-order in $[OH^-]$. Thus a variation in $[OH^-]$, unlike I^-, $S_2O_3^{2-}$ and SCN^-, has no effect on the relative rate of Co–O and C–O cleavage. The product ratio $[(NH_3)_5CoOH_2^{3+}]/[(NH_3)_5CoO_2P(OCH_3)_2^{2+}]$ is simply given by k_{OH}/k_Y, where $k_{OH} = 79\ M^{-1}\ s^{-1}$ (μ = 1 *M*, 25 °C) [3] and k_Y = the specific second-order rate for the demethylation reaction yielding the dimethylphosphate complex and methanol. As it happens, Co–O cleavage wins handsomely, *i.e.*, $k_{OH}/k_Y \geq 10^2$ (the limit of detection of the $O_2P(OCH_3)_2^-$ complex is about 3% by NMR and a little less than 1% by ion-exchange chromatography). These considerations lead to the conclusion that $k_Y \leq 0.79\ M^{-1}\ s^{-1}$ at 25 °C (μ = 1 *M*). The estimated k_Y value, for a 10^4-fold rate enhancement on coordination, was ~4 at 35.5 °C which corrects to ~1 $M^{-1}\ s^{-1}$ at 25 °C. Clearly this value is right on the limit for detection of the demethylation path. Nonetheless, at the very least, we can assert that the activation of $OP(OCH_3)_3$ towards hydrolysis, on coordination to the $(NH_3)_5Co^{3+}$ moiety, does not exceed a factor of $\sim 10^4$, since above this the minor pathway affording $[(NH_3)_5CoO_2P(OCH_3)_2]^{2+}$ would certainly have been detected.

We have examined previously the $[(NH_3)_5CoOP(OCH_3)_3]^{3+} + OH^-$ reaction with a view to observing ligand hydrolysis [3]. The present work confirms the previous conclusions; OH^- attack at P, if it occurs, does not lead to demethylation. Also we note that the ^{18}O-tracer results [3] for this reaction do not comment on the question of C–O cleavage by OH^-. If the activation exceeds the 10^4-fold limit set by this work, then the phosphorane intermediate, must



(21)

decay by Co–O cleavage. We determined only the ^{18}O-content (100%) of the aqua product but it is noted that such a mechanism requires the liberated phosphate ester to have a 50% ^{18}O-enrichment in its oxygen. (The ^{18}O content of the liberated trimethyl phosphate was not examined). Internal proton transfer and pseudorotation renders the P–O groups equivalent, and the label could be scrambled before the loss of OH^-. Alternatively, CH_3OH is lost and $^{18}OOP(OCH_3)_2^-$ results, but this outcome is precluded by the present NMR data (Table II)—neither $O_2P(OCH_3)_2^-$ nor CH_3OH is detected.

Finally, we allude to the significance of the present work with respect to the important [5] Arbusov reaction,

$$:P(OR)_3 + R'X \longrightarrow [R'-P(OR)_3]X \longrightarrow R'-P(O)(OR)_2 + RX \quad (22)$$

of considerable significance in organophosphorus chemistry. An inorganic analog of this reaction has been reported [4].

$$:P(OCH_3)_3 + LCo^{III}I \longrightarrow [LCoP(OCH_3)_3]X \longrightarrow LCoPO(OCH_3)_2 + CH_3X \quad (23)$$

Although the analogy between an alkyl group R′ and the LCo^{III} moiety was noted, there were no quantitative comparisons from which the relative effectiveness of the alkyl and LCo^{III} groups in promoting the reaction could be assessed. Certainly the Co(III) reaction, in an absolute sense, was facile—$t_{1/2}$ ~ 8 min at 16 °C in CH_3OH solvent, but the intermediate $LCoP(OCH_3)_3$ complex ion was not isolated nor a specific rate for its reaction with I^- extracted from the rate data.

This work has demonstrated, in a quantitative sense, the role of metal ion coordination in promoting such a reaction. While nucleophilic demethylation of $OP(OCH_3)_3$ and its Co(III) complex are almost certainly straightforward S_N2 substitution reactions at the methyl carbon, there is a clear phenomenological comparison to be made between the $(NH_3)_5Co^{III}$–O– and Cp(dppe)Co^{III} groups bonded to P in the $P(OCH_3)_3$ moiety. In each case the electrophilic quaternary phosphorus promotes nucleophilic Y attack, at the methyl carbon or phosphorus centre, with the formation of a P=O bond and loss of CH_3Y. The A_5Co^{III} group appears to be more effective than A_5Co^{III}–O– simply because the polarizing Co(III) centre is one bond length closer to the site of attack.

Acknowledgement

Support for this work from the Australian Research Grants Scheme is gratefully acknowledged.

References

1 B. Anderson, R. M. Milburn, J. MacB. Harrowfield, G. B. Robertson and A. M. Sargeson, *J. Am. Chem. Soc., 99,* 2652 (1977).
2 J. MacB. Harrowfield, D. R. Jones, L. F. Lindoy and A. M. Sargeson, *J. Am. Chem. Soc., 102,* 7733 (1980), and references therein.
3 N. E. Dixon, W. G. Jackson, W. Marty and A. M. Sargeson, *Inorg. Chem., 21,* 688 (1982).
4 S. J. Landon and T. B. Brill, *J. Am. Chem. Soc., 104,* 6571 (1982).

5 A. J. Kirby and S. G. Warren, 'The Organic Chemistry of Phosphorus'; Elsevier: New York, 1967.
6 B. C. McGregor, W. G. Jackson and S. J. Jurisson, results to be published.
7 Light was rigorously excluded for experiments involving NCS^- because of the photosensitivity of N- and especially S-bonded $[(NH_3)_5Co(SCN)]^{2+}$.
8 W. G. Jackson and C. N. Hookey, submitted to *Inorg. Chem.*
9 N. E. Dixon, W. G. Jackson, M. J. Lancaster, G. A. Lawrance and A. M. Sargeson, *Inorg. Chem., 20,* 470 (1981).
10 W. Schmidt and H. Taube, *Inorg. Chem., 2,* 698 (1963).
11 A. J. Parker, *Chem. Revs., 69,* 1 (1969).
12 W. G. Jackson and C. M. Begbie, unpublished data.
13 W. G. Jackson, D. P. Fairlie and M. L. Randall, *Inorg. Chim. Acta, 70,* 197 (1983).
14 B. C. McGregor, *Honours thesis,* University of N.S.W., 1982.
15 G. E. Dolbear and H. Taube, *Inorg. Chem., 6,* 60 (1967).
16 R. C. Bacon, 'Organic Sulfur Compounds'; Pergamon, 1961; Vol. 1, ed. N. Kharasch, p. 308–309.
17 E. Blumenthal and J. M. Herbert, *Trans. Far. Soc., 41,* 611 (1945).
18 D. A. Buckingham, D. M. Foster and A. M. Sargeson, *Aust. J. Chem., 22,* 2479 (1969).
19 D. A. Buckingham, J. MacB. Harrowfield and A. M. Sargeson, *J. Am. Chem. Soc., 96,* 1726 (1974).
20 D. A. Buckingham, F. R. Keene and A. M. Sargeson, *J. Am. Chem. Soc., 95,* 5649 (1973).
21 D. A. Buckingham, D. M. Foster and A. M. Sargeson, *J. Am. Chem. Soc., 91,* 3451 (1969).
22 O-acyl cleavage is established for only the free ester $+OH^-$ reaction—see, *e.g.,* P. Sykes, 'A Guidebook to Mechanism in Organic Chemistry', Longman, 3rd edn, 1970.