LIGATION OF TRIVALENT PHOSPHORUS TO PROTONS, SELENIUM AND
METALS: SOME NEW ASPECTS

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Abstract - Recent efforts to understand the effects of
constraint in phosphite esters on ligation to protons in
solution are summarized. The results of gas phase icr and
pes experiments are shown to be consistent with the basicity
order derived from the solution work. The one-bond $^1J_{PSe}$ nmr
spin-spin coupling constant in selenophosphates is demon-
strated to reflect basicity trends in phosphite triesters and
to correlate linearly with phosphorus substituent electro-
negativities for a wide range of seleno phosphorus compounds.
The optical resolution of the cancerostatic drug
triphosphamide via the separation of diastereomeric
platinum(II) complexes suggests the usefulness of this
approach in resolving other chiral phosphorus esters. The
complex NiL_4 where L is a chiral phosphite has been shown to
function as a catalyst in CF_3CO_2H for the asymmetric
isomerization of a prochiral olefin. ^{59}Co nmr spectroscopy
has proven to be a useful tool in the elucidation of the
ligand properties of monodentate and bidentate phosphorus
esters.

PROTONATION STUDIES

Previous work in our laboratories on the series of phosphite esters 1-7
suggested that the Lewis basicity of the phosphorus lone pair toward $\overline{BH}_3$ and
O depends on the degree of molecular constraint and on the geometrical
relationship of the phosphorus and esteratic oxygen lone pairs (Ref. 1).
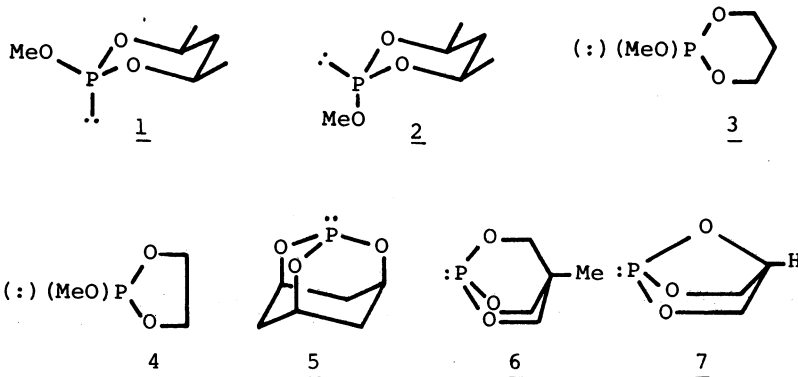
Lewis basicity trends which stemmed from these solution studies are
$P(OMe)_3 > 6 > 7$ and $1 > 2$. Protonation of these esters in $HFSO_3$ at -50°C
reveals an increasing order of ^1JPH (Ref. 2):

$$P(OMe)_3 < 1 < 2 < 4 < 6 < 7$$
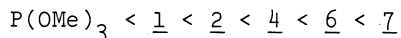
CNDO/2 calculations show no trend in phosphorus hybridization on increasing
molecular constraint, but a rise in positive charge on both the phosphorus
and the proton bonded to it was observed to occur with increasing ^1JPH
(Ref. 2). This correlation is linear with the cube of the sum of the proton

and phosphorus charges, as is expected if the Fermi contact mechanism dominates the coupling. The rise in calculated positive charge on the phosphorus in progressing from 1-7 parallels the observed general decrease in Lewis basicity in solution:

$$P(OMe)_3 > \underline{1} > \underline{2} > \underline{4} > \underline{6} > \underline{7}$$
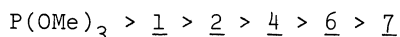
In the absence of solvent effects, the above order is preserved as was shown recently using ion cyclotron resonance (Ref. 3) and photoelectron spectroscopic techniques (Ref. 3 and 4) on gas phase samples. The proton affinities (PA(B)) of 1-7 were measured in the icr experiments and the phosphorus lone pair ionization potentials (IP(B)) of these esters were observed in their photoelectron spectra. A general decrease in PA(B) occurs for these esters with the decreasing order of the solution Lewis basicities given above, and the decrease in PA(B) is linear with the rise in IP(B) expected for a decrease in Lewis basicity (Ref. 3).

The dominant role of the esteratic oxygen hybridization and lone pair orientation in determining that the phosphorus Lewis basicity order toward oxygen in phosphates is $OP(OBu)_3 > OP(OCH_2)_3CR$ was shown recently by demonstrating the expected similarity in phosphorus basicity in the phosphine oxide analogues $OPBu_3$ and $OP(CH_2CH_2)_3CH$ (Ref. 5), wherein esteratic oxygens are absent.

Phosphatranes are an interesting new class of bicyclic compounds in that they can exist in either of two configurations, 8 or 9, depending on whether or not Y is charged (Ref. 6). When Z is a proton, the lowest ^1JPH value

| 8 | 9 |
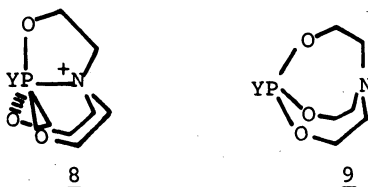
(791 Hz) for a protonated phosphite triester (ca. 820-930 Hz) is observed in $HFSO_3$ at -50°C (Ref. 5). This is consistent with structure 8 for the protonated species (as confirmed by X-ray diffraction studies (Ref. 7)) since a low positive charge on phosphorus is expected in the presence of nitrogen lone pair donation, and moreover the s character in an axial P-H bond of a trigonal bipyramid is small. Support for these ideas came recently from a CNDO/2 calculation in which a 787 Hz ^1JPH coupling was predicted (Ref. 8). Such calculations also predict that transannulation of 8 with Y = O should occur upon protonation of the phosphoryl oxygen (Ref. 8). Indeed, ^1H and ^{31}P spectra of 8 where Y = O and S have been obtained in CF_3CO_2H which are consonant with this hypothesis (Ref. 9).

Monocyclic phosphite esters of the type $MeOP(OC_nO)$ in $HFSO_3$ at -50°C exhibit ^1JPH couplings which increase in the order 7-membered > 6-membered > 5-membered rings for the same degree of methyl substitution on the ring carbons (Ref. 10). This accords with the "hinge" effect (Ref. 1) of the esteratic ring oxygens which rehybridize to place more s character in their lone pairs, thus reducing their tendency to pi bond with phosphorus and thereby increasing the positive charge on phosphorus. For a ring of given size, the ^1JPH coupling decreases with increasing methyl substitution. This observation suggests that the electron inductive nature of the methyl group reduces the phosphorus positive charge. In the highly methyl-substituted esters, ring-opening dealkylation by solvolysis readily takes place at about -50°C, resulting in the formation of $MeO(H)P^+(OH)OC_mOSO_2F$ ions.

SELENATION STUDIES

As shown in Table 1, coupling of ^{77}Se to ^{31}P in the selenophosphates $SeP(OMe)_3$ and 10-14 (Y = Se) rises in the order (Ref. 11):
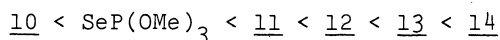
$$\underline{10} < SeP(OMe)_3 < \underline{11} < \underline{12} < \underline{13} < \underline{14}$$

Table 1. Nmr and ir data for phosphite triester
          derivatives

		Y = Se JPSe (Hz)	Y = BH$_3$ νBH (wtd ave, cm^{-1})
10	MeO, O P Y (structure)	949	2376
	YP(OMe)$_3$	954	2382
11	Y, O P MeO (structure)	996	2391
12	Y, O P MeO O (structure)	1011	2393
13	P O O O Me (structure)	1053	2402
14	Y—P O O O Me (structure)	1099	2410

Interestingly, the axial phosphorus lone pair in 10 is more basic than the
equatorial lone pair in 11, as had been noted earlier (Ref. 1). The above
order also holds for the weighted average of the BH stretching frequencies
in the analogous BH$_3$ adducts (Y = BH$_3$). As expected, νBH increases as the
phosphorus basicity decreases and the linear correlation of ^{1}JPSe with νBH
follows the equation ^{1}JPSe = -9839 + 4.53 νBH with a coefficient of 0.97.
Since there are no pi contributions in the P--H bond, the Fermi contact
contribution is likely to be dominant in HP(OR)$_3^+$ systems. The linear
correlation between ^{1}JPSe and ^{1}JPH (^{1}JPSe = -309.5 + 1.51 ^{1}JPH; r^2 = 0.91)
observed by us (Ref. 11) supports the claim made earlier by others that
^{1}JPSe is also largely due to a Fermi contact mechanism (Ref. 12).

Although the general effect of the electronegativity of phosphorus substitu-
ents on ^{1}JPSe has been noted earlier in other laboratories (Ref. 12-15), no
attempt to express these results in a quantitative manner has appeared. As
shown in Table 2, the average of the electronegativity (EN) values for the
substituent atoms bound to phosphorus correlates with ^{1}JPSe in a linear
manner (Ref. 11). Despite the crudeness of this approach, any of the
equations in Table 2 give ^{1}JPSe values to within 4% of the experimental

TABLE 1.   Linear correlations for [1]JPSe with phosphorus
           substituent electronegativity

Equation	Correl. Coeff.	Electronegativity Scale	Data
$J_{SeP} = 50.1 + 256EN$	0.97	Pauling	Ref. 13
$J_{SeP} = 133 + 228EN$	0.97	Allred–Rochow	Ref. 13
$J_{SeP} = 123 + 233EN$	0.95	Sanderson	Ref. 13
$J_{SeP} = -12.5 + 279EN$	0.97	Pauling	Ref. 12
$J_{SeP} = 83.0 + 246EN$	0.96	Allred–Rochow	Ref. 12
$J_{SeP} = 76.5 + 254EN$	0.98	Sanderson	Ref. 12

values.   Thus these equations should be useful for predicting [1]JPSe values
for new acyclic $SePZ_3$ compounds.
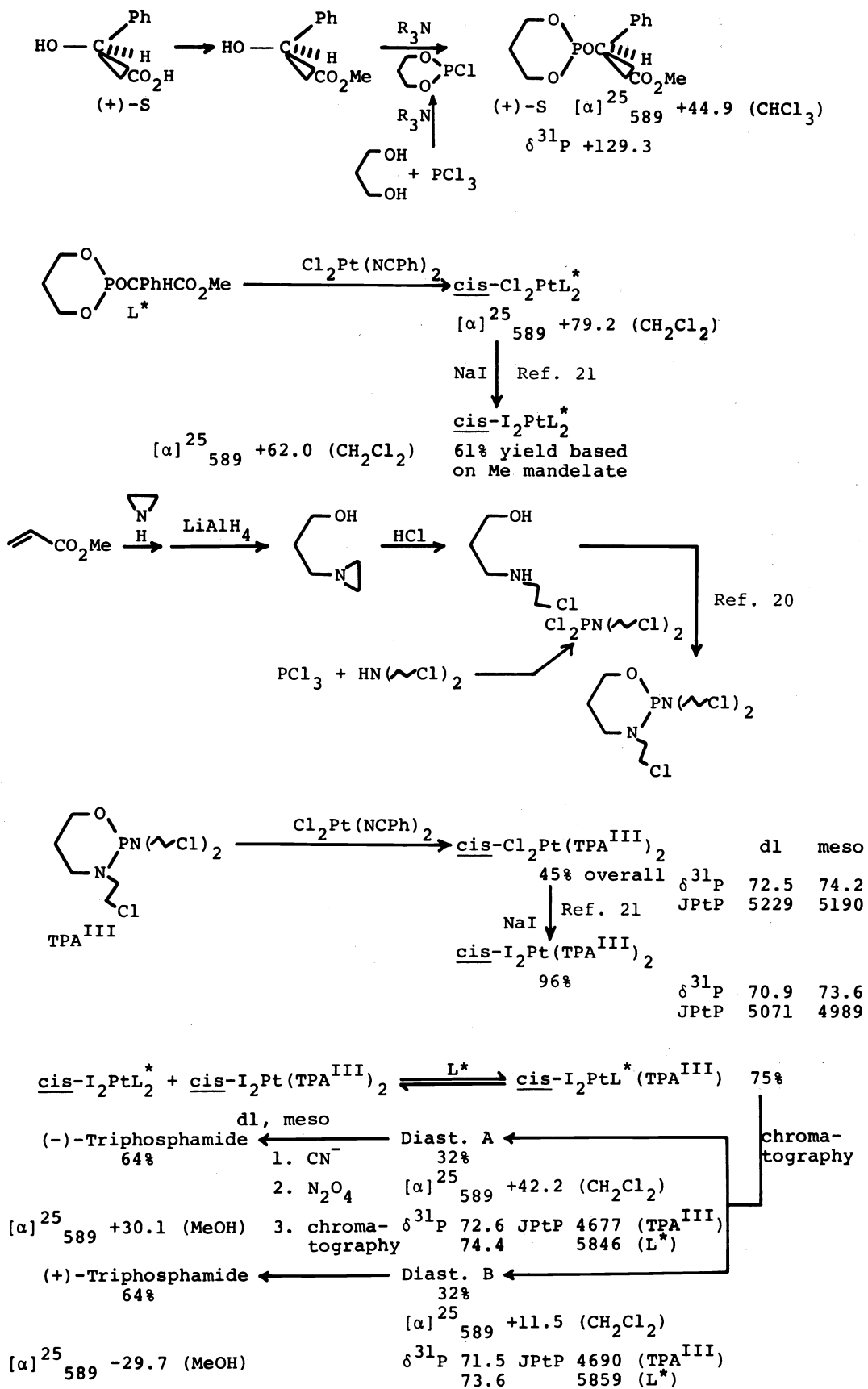
RESOLUTION OF TRIPHOSPHAMIDE

Triphosphamide (15) is an active carcinostat related to cyclophosphamide (16)
which is a widely used, highly effective clinical antitumor agent.   The
presence of a chiral phosphorus atom in 15 and 16 has prompted several recent
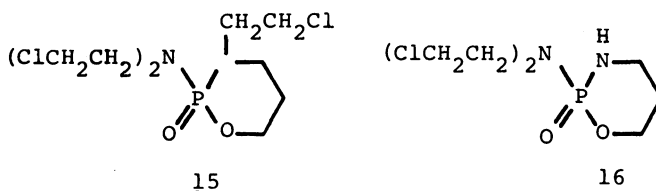
studies directed at their optical resolution (Refs. 16-19).   The resolution
method described by us for 15 (Ref. 19) is especially novel in that it
represents the first report of the resolution of a phosphorus ester by means
of an optically active coordination compound.   The reaction sequence
summarized in Scheme 1 affords (+)-15 and (-)-15 as colorless oils in high
optical purity, as shown by FT ^{31}P nmr spectroscopy in the presence of an
optically active shift reagent.   The overall yield, however, is only about
10%.   Interesting features of this resolution mode are the necessity for a
catalytic amount of the phosphite ester to effect the ligand exchange
step, and the distinctly different ^{31}P nmr parameters for the diastereomers.
Although cis-dichloro platinum complexes of amines do have carcinostatic
properties, a series of such complexes with the trivalent phosphorus forms
of cyclophosphamide, isophosphamide and triphosphamide are not biologically
active (Ref. 20).   The approach outlined in Scheme 1 is being investigated
as a potentially general route to resolving chiral phosphorus esters.

59-COBALT NMR STUDIES OF COBALT(III) COMPLEXES

The linear correlation of increasing ligand field Dq (i.e., decreasing wave
length of the lowest d-d transition) with increasing applied field of the
[59]Co chemical shift in six-coordinate cobalt(III) complexes of oxygen and
nitrogen-containing ligands and cyanide ion depicted in Figure 1 has been
known for about twenty years (Refs. 22 and 23).   The dashed line in Figure 2,
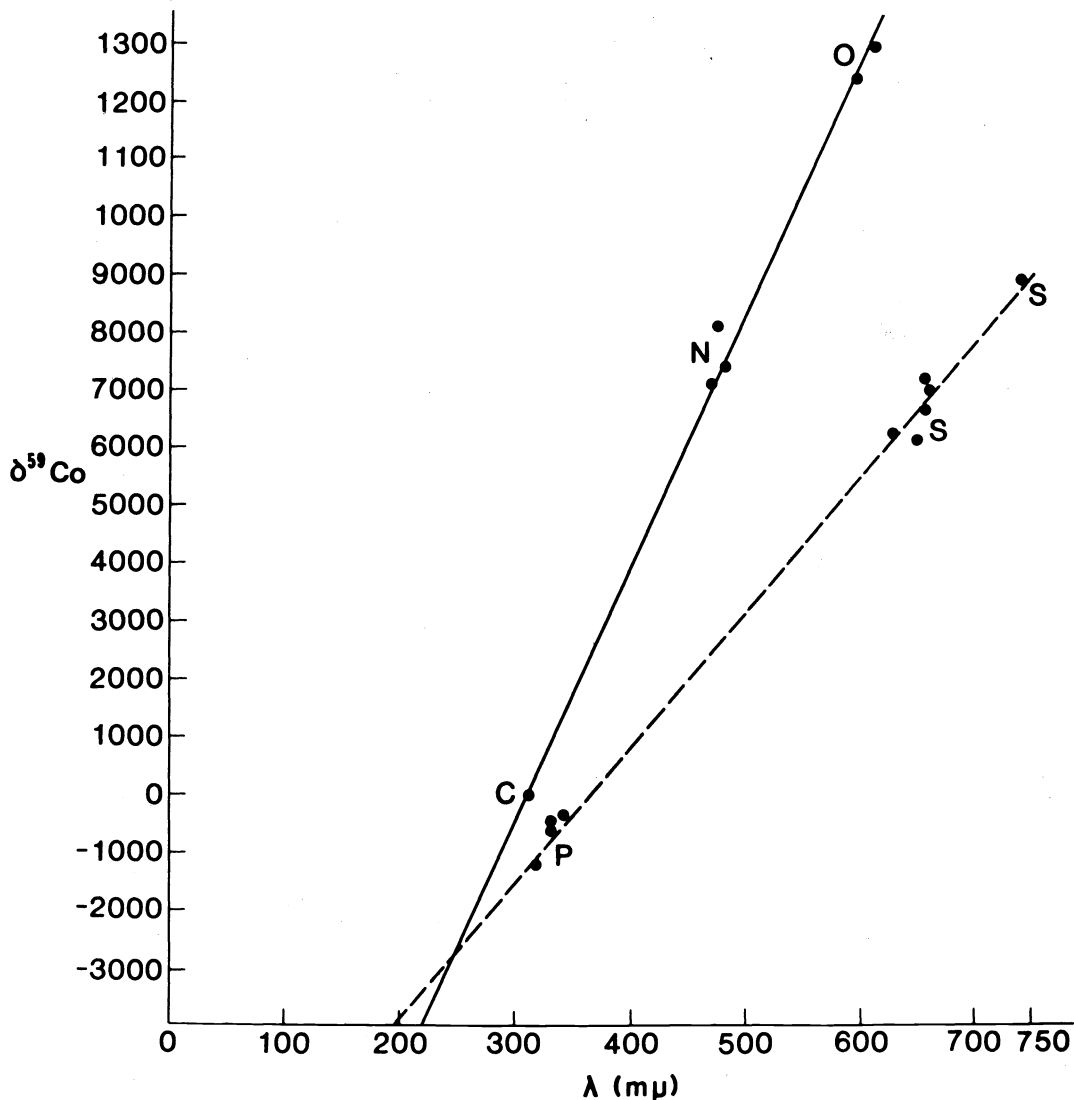drawn through the previously reported sulfur ligand points and the phosphite

HO — C(Ph)(H)CO₂H → HO — C(Ph)(H)CO₂Me

(+)-S

$[\alpha]^{25}_{589}$ +44.9 (CHCl₃)

$\delta^{31}P$ +129.3

(+)-S

R_3N ... PCl / R_3N + PCl₃ + OH/OH

POC(Ph)(H)CO₂Me

POCPhHCO₂Me L* →(Cl₂Pt(NCPh)₂)→ cis-Cl₂PtL₂*

$[\alpha]^{25}_{589}$ +79.2 (CH₂Cl₂)

NaI | Ref. 21

cis-I₂PtL₂*

$[\alpha]^{25}_{589}$ +62.0 (CH₂Cl₂)   61% yield based on Me mandelate

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CH₂=CHCO₂Me —(N H)→ —(LiAlH₄)→ HO...N —(HCl)→ HO...NH...Cl

PCl₃ + HN(~Cl)₂ → Cl₂PN(~Cl)₂ → Ref. 20 → O—PN(~Cl)₂ (N...Cl)

O—PN(~Cl)₂ (N...Cl) →(Cl₂Pt(NCPh)₂)→ cis-Cl₂Pt(TPA^III)₂

TPA^III

45% overall

NaI | Ref. 21

cis-I₂Pt(TPA^III)₂ 96%

	dl	meso
$\delta^{31}P$	72.5	74.2
JPtP	5229	5190

	dl	meso
$\delta^{31}P$	70.9	73.6
JPtP	5071	4989

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cis-I₂PtL₂* + cis-I₂Pt(TPA^III)₂ $\xrightleftharpoons{L^*}$ cis-I₂PtL*(TPA^III)   75%

dl, meso

(-)-Triphosphamide ← Diast. A ← chromatography
   64%   1. CN⁻   32%
                2. N₂O₄ $[\alpha]^{25}_{589}$ +42.2 (CH₂Cl₂)
$[\alpha]^{25}_{589}$ +30.1 (MeOH)   3. chroma- $\delta^{31}P$ 72.6 JPtP 4677 (TPA^III)
                tography   74.4   5846 (L*)

(+)-Triphosphamide ← Diast. B ←
   64%   32%
                $[\alpha]^{25}_{589}$ +11.5 (CH₂Cl₂)
$[\alpha]^{25}_{589}$ -29.7 (MeOH) $\delta^{31}P$ 71.5 JPtP 4690 (TPA^III)
                73.6   5859 (L*)

Scheme 1

Figure 1. Plots of $\delta^{59}Co$ for octahedral cobalt(III) complexes against λ_{dd} ligand points taken from the data in Table 3, confirms unambiguously the existence of a second linear correlation for second row elements. Contrary

TABLE 3. Spectroscopic data for $[CoL_6](BF_4)_3$ complexes

L	$\delta(ppm)$[a]	$\lambda(m\mu)$	$^1J^{59}Co^{31}P(Hz)$	$\Delta\nu_{\frac{1}{2}}(Hz)$
$P(OMe)_3$	−305	340	443[b]	150
1	−307	341	---[c]	ca 3000
2	−356	339	---[c]	ca 3000
4	−1185	317	---[c]	ca 2500
6	−1243	ca 300[d]	412	75

[a] $K_3Co(CN)_6 = 0$; negative sign indicates upfield shift.
[b] Taken from the spacing in the septet ^{59}Co resonance.
[c] Unobservable due to rapid Co relaxation.
[d] Partially obscured by charge transfer band.

to earlier conjectures (Refs. 24 and 25), the new line does not possess an intercept common with the line for first row element ligands. The trend among the phosphite esters to exhibit stronger ligand fields and higher $\delta^{59}Co$ values in the order $P(OMe)_3 < \underline{1} < \underline{2} < \underline{4} < \underline{6}$ parallels their decreasing sigma basicity order $P(OMe)_3 > \underline{2} > \underline{1} > \underline{4} > \underline{6}$, except for the reversal of the positions of $\underline{1}$ and $\underline{2}$. Although the reason for the reversal in the isomeric ligands is obscure at present, the rise in Dq with generally decreasing basicity may be rationalized by postulating a dominance of phosphorus pi bonding acidity, or a decrease in ligand-ligand repulsion upon ligand constraint. It is interesting in this regard that the chelating ligands $\underline{17}$ and $\underline{18}$ possess $\delta^{59}Co$ values near -2000 ppm in $[Co(\underline{17})_3]^{+3}$ and $[Co(\underline{18})_3]^{+3}$

$\underline{17}$ R = Me

$\underline{18}$ R = Et
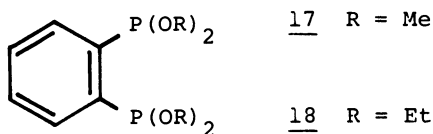
(Ref. 26). This suggests a remarkably high Dq value in the neighborhood of 270 mμ for these colorless cations, despite the fact that the phosphorus atoms are not as electronegative in these dialkoxy ligands as is the phosphorus atom in the trialkoxy ligands in $\{Cp[P(OCH_2)_3CMe]_6\}^{+3}$ or in $\{Co[P(OMe)_3]_6\}^{+3}$ (Table 3). The relative roles of metal-to-ligand pi bonding and ligand-ligand repulsion in determining Dq are presently not clear.

CHIRAL PHOSPHITES IN TRANSITION METAL CATALYSTS

Complexes of the type NiL_4, where L is a phosphite ester, catalyze the isomerization of olefins in acidic media (Ref. 27 and 28). Recently, we were able to resolve the phosphite $\underline{19}$ as shown in Scheme 2 and to synthesize the corresponding optically active $\overline{Ni}(\underline{19})_4$ complexes (Ref. 29). Employing
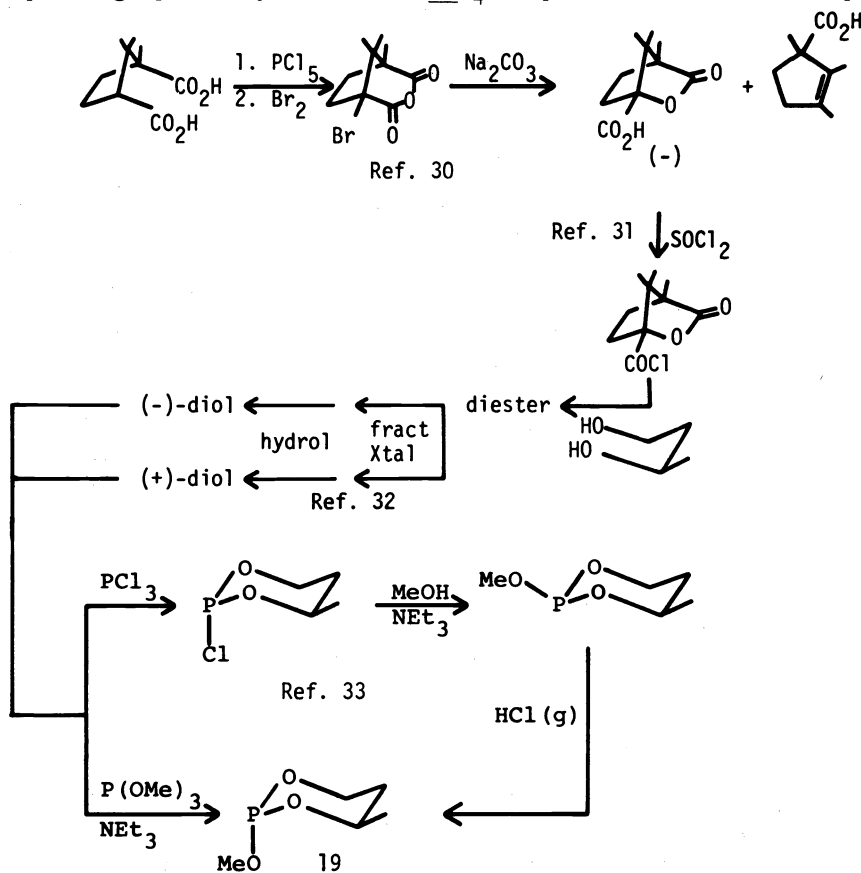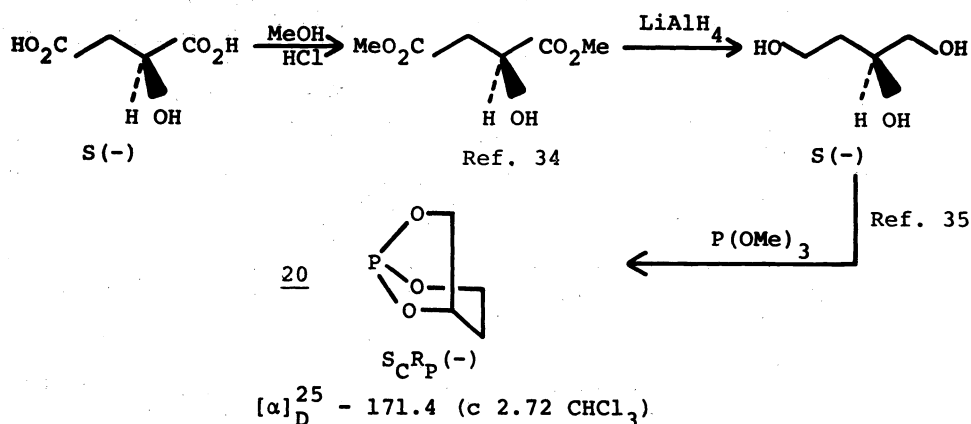

Scheme 2

a prochiral olefin, the conversion shown in reaction (1) was carried out.
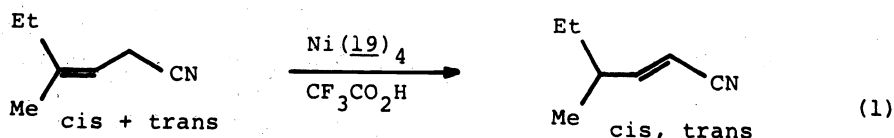
Although the geometrical isomerism of the product has not yet been determined, a 76% enantiomeric excess is realized as shown by ^{1}H nmr experiments in the presence of an optically active shift reagent.

The optically active cage phosphite 20 was prepared in high purity as shown in Scheme 3 (Ref. 29). Interestingly, no isomerization was observed in the

Scheme 3

presence of the corresponding zerovalent nickel complex. This may be attributed to a combination of decreased cone angle (Ref. 36) and heteroatom rehybridization effects (Ref. 1) in this constrained cage phosphite, which increase the metal-ligand interaction. Consequently, dissociation of the ligand is diminished, thereby inhibiting coordination of the substrate olefin to the nickel atom.

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