Collins oxidation (CH_2Cl_2, 0 °C, 30 min) of alcohol **15** and subsequent condensation with the lithio derivative (LDA, THF, −100 °C) of the appropriately substituted 2-methylbenzoxazole[13] produced (~60%) alcohol **16** as a mixture of diastereomers, which were not separable by HPLC analysis. Exposure (10 h) of **16** to camphorsulfonic acid in methylene chloride at −15 °C led (30%) to formation of the desired dioxaspirane, **17**. Reductive cleavage ($Cr_2(OAc)_4 \cdot 2H_2O$, EtOH)[11] followed by treatment with potassium carbonate in aqueous methanol (1:1) afforded in 50% overall yield A-23187 which was identical in all respects (NMR (220 MHz) and IR spectroscopies and TLC) with a sample of natural material obtained from Lilly Research Laboratories.[14]

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Registry No. 1, 52665-69-7; **2**, 80657-85-8; **3**, 80657-86-9; **4**, 80657-87-0; **5**, 80630-91-7; **6**, 80630-92-8; **7**, 80657-88-1; **8**, 80657-89-2; **9**, 80657-90-5; **10**, 80657-91-6; **11**, 80657-92-7; **12**, 80630-93-9; **13**, 80630-94-0; **14**, 80630-95-1; **15**, 80630-96-2; **16** isomer 1, 80630-97-3; **16** isomer 2, 80657-93-8; **17**, 80630-98-4; vinyl bromide, 593-60-2; 2-lithio-*N*-(dimethylamino)pyrrole, 78307-77-4; methyl 5-(2,2,2-trifluoro-*N*-methylacetamido)-2-lithiomethyl-4-benzoxazolecarboxylate, 80630-99-5.

Supplementary Material Available: Listings of IR and ^1H NMR spectral data for **1**, **2–13**, **15**, and **17** (4 pages). Ordering information is given on any current masthead page.

(13) Grieco, P. A.; Kanai, K.; Williams, E. *Heterocycles* **1979**, *12*, 1623.
(14) Assigned structures are fully supported by IR, NMR, and mass spectral measurements and combustion analysis.

Nucleophilic Displacements on Phosphoric Monoesters: Stereochemical Evidence

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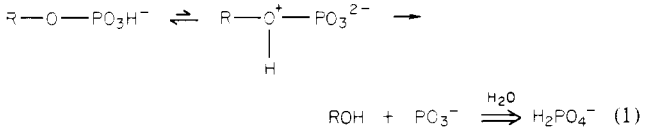
To account for the fact that the hydrolysis of monoesters of phosphoric acid is most rapid at around pH 4, where the monoanion predominates, the mechanistic pathway shown in eq 1



was proposed independently by Westheimer[2] and by Bunton[3] in 1955. Since that time, evidence has accumulated from a variety of sources in support of this formulation, which involves monomeric metaphosphate as an intermediate in the reaction. To provide more information about the nature of the transition state(s) for such processes, we have used chiral [^{16}O,^{17}O,^{18}O]phosphoric monoesters to examine the stereochemical consequence at phosphorus of reactions that are believed to follow the pathway of eq 1.

The view that phosphoric monoesters are hydrolyzed by a dissociative mechanism involving metaphosphate is based upon findings such as the following: (a) The values of $\Delta S^{\ddagger}$ are close to 0 eu,[4,5] which (despite the problems of interpreting activation parameters for reactions in structured solvents) is suggestive of a dissociative reaction. (b) There is an approximate correlation between the molarity of acceptor nucleophiles in mixed aqueous alcoholic solvents and the molar ratio of products formed, indicative of reaction of a highly reactive and unselective intermediate.[6,7] (c) The β_{lg} (lg = leaving group) for phenolic esters is −1.2 for dianions and −0.3 for monoanions, suggesting that bond breaking is far advanced in the rate-determining transition state,[5] the leaving group being the phenolate (from the dianion) or the phenol (on cleavage of the dipolar species of eq 1). (d) The reactivity of monoanions is often greater than that of the neutral species, indicating that rate-limiting nucleophilic attack at phosphorus is unlikely.[2,3] (e) The β_{nuc} (nuc = nucleophile) for the attack of amines on *p*-nitrophenyl phosphate is low, at 0.13.[8] (f) The ^{18}O kinetic isotope effect suggests rate-limiting cleavage of the (C)–^{18}O–P bond.[9] (g) The transfer of a phospho group from one solid phase to another in dioxane appears to involve metaphosphate as an intermediate.[10] (h) Monomeric metaphosphate has been explicitly generated in both apolar and polar solvents and shown to have the expected properties of a highly reactive electrophile.[11] There appears, in summary, to be persuasive evidence in support of the intermediacy of monomeric metaphosphate in the solvolytic reactions of phosphoric monoesters.

Table I. Predicted[a,b] and Observed[b] Peak Intensities (%) for ^{31}P NMR Spectra

peak number[c]	phenyl phosphate				2,4-dinitrophenyl phosphate			
	substrate		product		substrate		product	
	pred[d]	obsd	pred[e]	obsd	pred[f]	obsd	pred[g]	obsd
1	19.1	23.1	27.9	28.4	12.6	9.5	22.1	23.3
2	29.9	28.5	35.8	37.4	28.4	28.1	36.9	36.5
3	40.3	38.4	27.8	27.5	42.8	44.9	28.1	28.2
4	10.8	10.0	8.5	6.7	16.2	17.5	12.7	12.0
5	19.1	21.9	27.9	28.6	12.6	11.1	22.1	22.1
6	40.3	39.2	27.8	28.0	42.8	42.3	28.1	27.5
7	29.9	28.7	35.8	34.6	28.4	29.9	36.9	38.9
8	10.8	10.1	8.5	6.7	16.2	16.7	12.7	13.6

[a] On the basis of the measured isotopic content of the derived 1-[^{16}O,^{17}O,^{18}O]phosphopropane-1,2-diol and the measured contamination by the 2-phospho isomer. [b] The ratios of each set of four peaks are taken separately. [c] Numbering from downfield to upfield. [d] For 80% *R*. [e] For 86% *S*. [f] For 86% *R*. [g] For 87% *S*.

In a study of the hydrolysis of substituted aromatic phosphoric monoesters, Kirby and Varvoglis[5] found that esters whose leaving groups had $pK_a > 6$ were hydrolyzed most rapidly at pH 4 as the monoanion and that esters with leaving groups of $pK_a < 5.5$ were hydrolyzed most rapidly as the dianion. These results suggested that prior proton transfer (eq 1) was necessary to facilitate the heterolysis with relatively poor leaving groups, but as the pK_a of the leaving group was lowered, expulsion from the dianion became the preferred path. Guided by this[5] and earlier[4,12] work on the solvolysis of phosphoric monoesters, we chose to investigate the stereochemical course of the methanolysis of phenyl phosphate monoanion (leaving group pK_a 9.9) and 2,4-dinitrophenyl phosphate dianion (leaving group pK_a 4.1). For each of these reactions,

(1) National Science Foundation Predoctoral Fellow.
(2) Butcher, W. W.; Westheimer, F. H. *J. Am. Chem. Soc.* **1955**, *77*, 2420–2424.
(3) Barnard, P. W. C.; Bunton, C. A.; Llewellyn, D. R.; Oldham, K. G.; Silver, B. L.; Vernon, C. A. *Chem. Ind. (London)* **1955**, 760–763.
(4) Di Sabato, G.; Jencks, W. P. *J. Am. Chem. Soc.* **1961**, *83*, 4400–4405.
(5) Kirby, A. J.; Varvoglis, A. G. *J. Am. Chem. Soc.* **1967**, *89*, 415–423.
(6) However, the product ratios in such experiments indicated that the metaphosphate monoanion could not exist as a free intermediate in these reactions: Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1964**, *86*, 1410–1417.
(7) For a summary, see: Haake, P.; Allen, G. W. *Bioorg. Chem.* **1980**, *9*, 325–341.
(8) Kirby, A. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1965**, *87*, 3209–3216.
(9) Gorenstein, D. G. *J. Am. Chem. Soc.* **1972**, *94*, 2523–2525.
(10) Rebek, J.; Gaviña, F.; Navarro, C. *J. Am. Chem. Soc.* **1978**, *100*, 8113–8117.
(11) Satterthwait, A. C.; Westheimer, F. H. "Phosphorus Chemistry Directed Toward Biology"; Stec, W. J., Ed.; Pergamon Press: New York, 1980; p 117.
(12) Chanley, J. D.; Feageson, E. *J. Am. Chem. Soc.* **1963**, *85*, 1181–1190.

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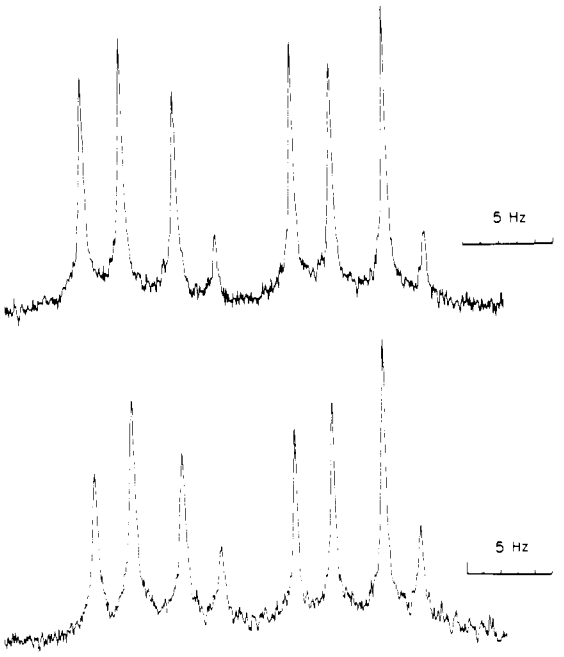

Figure 1. ^{31}P NMR spectra of the products from the "in-line" ring closure and methylation[11,14] of 1-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-propane-1,2-diol obtained by phospho group transfer[13] from samples of methyl phosphate: upper spectrum, product deriving from the methanolysis of phenyl phosphate monoanion; lower spectrum, product deriving from the methanolysis of 2,4-dinitrophenyl phosphate dianion. The NMR spectra were performed as described earlier[16] on a Bruker WM-300 WB instrument at 121.5 MHz.

the evidence in favor of a metaphosphate pathway is strong.

Phenyl Phosphate Monoanion. Phenyl *R*-[^{16}O,^{17}O,^{18}O]phosphate was synthesized by our general route[13] and was subjected to solvolysis at 100 °C in 50% (v/v) aqueous methanol at pH 4.7.[14] After 60% of the phenyl phosphate had been consumed, the ratio of methyl phosphate to inorganic phosphate was 1:2, and the methyl phosphate was isolated and purified. Transfer of the labeled phospho group of methyl phosphate to *S*-propane-1,2-diol with retention of configuration was accomplished with *E. coli* alkaline phosphatase as described earlier.[15] Stereochemical analysis (Figure 1) of the resulting 1-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-propane-1,2-diol by our ^{31}P NMR method[16] showed that the configuration at phosphorus was 86 ± 7%[17] *S* (Table I). The configurational purity at phosphorus in the starting material (phenyl phosphate) was independently determined by phosphatase-catalyzed transfer of the phospho group to propanediol and stereoanalysis by the ^{31}P NMR method. The configuration at phosphorus was found to be 80 ± 1%[17] *R* (Table I). Within experimental uncertainty, therefore, *the methanolysis of phenyl phosphate monoanion proceeds with complete inversion of configuration at phosphorus.*

2,4-Dinitrophenyl Phosphate Dianion. 2,4-Dinitrophenyl *R*-[^{16}O,^{17}O,^{18}O]phosphate was prepared by a modification[18] of our published method.[13] This material was allowed to react with 50% (v/v) aqueous methanol at 23 °C and pH 10.2.[14] After 32 h, ^{31}P NMR spectrometry showed that no substrate remained, the products being methyl phosphate and inorganic phosphate in approximately 2:1 ratio. As before, the phospho group of the isolated methyl phosphate was transferred to propanediol with retention of configuration by using alkaline phosphatase,[15] and the product was subjected to stereochemical analysis (see Figure 1). The configuration of the phospho group was found to be 87 ± 3% *S* (Table I). To determine the enantiomeric purity of the starting 2,4-dinitrophenyl phosphate, phospho group transfer to propanediol was achieved with retention by using human prostatic acid phosphatase.[19] Stereochemical analysis of the product showed the configuration at phosphorus to be 86 ± 5% *R* (Table I). *The methanolysis of the dianion of 2,4-dinitrophenyl phosphate therefore proceeds with complete inversion at phosphorus.*

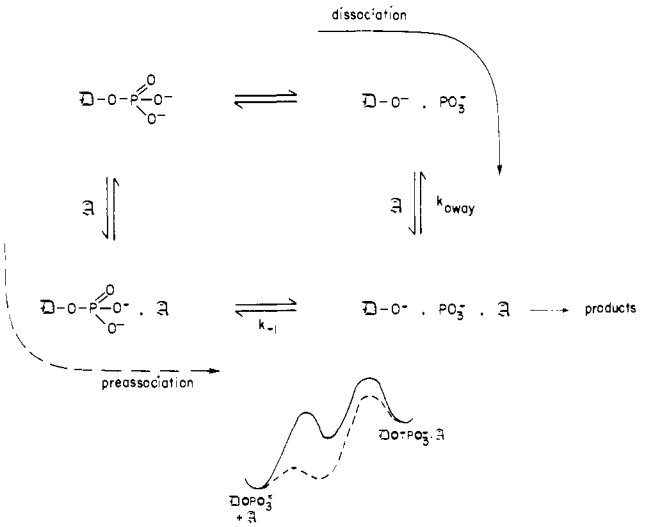

Figure 2. Dissociative and preassociative paths for the phospho transfer reaction from a phosphorylated donor $\mathcal{D}$ to a nucleophilic acceptor $\mathcal{A}$. When the complex of $\mathcal{D}$–O⁻·PO_3^-·$\mathcal{A}$ collapses back to starting materials (k_{-1}, and the dashed free energy profile) more rapidly than the acceptor $\mathcal{A}$ can diffuse away (k_{away}, and the solid free energy profile), then the forward reaction will proceed by the preassociative route (dashed profile).[20]

The mechanistic data summarized at the beginning of this communication support the view that the alcoholysis of phosphoric monoester monoanions having reasonable leaving groups (e.g., phenyl phosphate) and of phosphoric monoester dianions having very good leaving groups (e.g., 2,4-dinitrophenyl phosphate) are dissociative processes. Yet the stereochemical results reported here are not consistent with a mechanism that involves a free, symmetrically solvated, metaphosphate intermediate and require that if metaphosphate forms, it is captured only by nucleophilic attack from the side opposite to the leaving group. The experimental evidence can, however, all be accommodated by the single mechanistic description that these reactions are *preassociative.* Preassociative processes may be concerted or stepwise. If the reactions are concerted (that is, if no intermediate species is formed having a lifetime longer than 1 vibration), the present stereochemical results and the earlier kinetic data on the solvolysis of phosphoric monoesters merely require that the transition state be a "loose" or "exploded" one in which bond breaking is very nearly complete and bond making has barely begun. On the other hand, if the reaction is stepwise and involves metaphosphate, our stereochemical results require that the intermediate be constrained in a preassociative path. As has been persuasively argued by Jencks,[20,21] if in a complex of dinitrophenolate–metaphosphate–

(13) Abbott, S. J.; Jones, S. R.; Weinman, S. A.; Bockhoff, F. M.; McLafferty, F. W.; Knowles, J. R. *J. Am. Chem. Soc.* **1979**, *101*, 4323–4332.
(14) As measured with a glass electrode.
(15) Jones, S. R.; Kindman, L. A.; Knowles, J. R. *Nature (London)* **1978**, *257*, 564–565.
(16) Buchald, S. L.; Knowles, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6601–6602.
(17) The error limits derive merely from averaging the values obtained from integration of the signal intensities for the syn and the anti cyclic triesters. They are not statistical precision estimates.
(18) The major adduct from reaction of $P^{17}OCl_3$ with (−)ephedrine, [(2*R*,4*S*,5*R*)-2-chloro-3,4-dimethyl-5-phenyl-1,3,2-oxazaphospholidin-2-one], was allowed to react with lithium 2,4-dinitrophenoxide in acetonitrile at 60 °C for 7 days. Ring opening of the resulting cyclic phosphoramidate diester with $H_3{}^{18}O^+$ in dioxane was followed by removal of the ephedrine moiety by treatment first with trimethylsilyl bromide in $CHCl_3$ and then with methanol. The mono-2,6-lutidinium salt of 2,4-dinitrophenyl *R*-[^{16}O,^{17}O,^{18}O]phosphate was isolated in 30% yield (based on the ephedrine adduct).
(19) The transphosphorylation reaction catalyzed by human prostatic acid phosphatase has recently been shown to proceed with overall retention of configuration at phosphorus: Saini, M.; Van Etten, R.; Buchwald, S. Unpublished experiments.
(20) Jencks, W. P. *Acc. Chem. Res.* **1980**, *13*, 161–169.

methanol the dissociated dinitrophenolate–metaphosphate pair collapses back to dinitrophenyl phosphate faster than the rate at which the acceptor methanol can diffuse away, then the forward reaction will necessarily follow the preassociative path (see Scheme I). The heterolytic cleavage may still be rate limiting, but only when the acceptor is positioned appropriately (preassociatively) to receive the phospho group will heterolysis lead to products. The stereochemical data reported here require that if the word "metaphosphate" is used to describe the nature of phosphorus and its associated ligands in the intermediate of such monoester solvolysis, it be recognized that the "metaphosphate" may suffer only two fates: collapse back to reform the starting material of unchanged configuration at phosphorus or reaction forward to form product with inversion at the phosphorus center.

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Registry No. Phenyl [(*R*)-^{16}O,^{17}O,^{18}O]phosphate, 80630-84-8; methyl [(*S*)-^{16}O,^{17}O,^{18}O]phosphate, 80630-85-9; 2,4-dinitrophenyl [(*R*)-^{16}O,^{17}O,^{18}O]phosphate, 80630-86-0; 2,4-dinitrophenyl [(*R*)-^{16}O,^{17}O,^{18}O]phosphate mono-2,6-lutidinium salt, 80630-89-3; 1-*S*-[^{16}O,^{17}O,^{18}O]phospho-(*S*)-propane-1,2-diol, 80630-90-6.

(21) Jencks, W. P. *Chem. Soc. Rev.*, in press.

A Theoretical Study of the Cr–Cr Quadruple Bond

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Recently there has been a great deal of interest both experimentally and theoretically on binuclear transition-metal compounds that are characterized by quadruple bonding, or so-called "δ" bonding.[1] Many of these compounds have now been reported, but we would like here to focus on those cases involving two d^4 transition-metal atoms. Their bonding is generally representated as in Figure 1. This figure shows eight ligands such as $M_2Cl_8^{4-}$ or $M_2(CH_3)_8^{4-}$ in an eclipsed conformation. In addition there are very many bridged compounds involving OCO (as acetate, formate, etc.) and NCO (aminato) bridging ligands. Fifth- and sixth-position ligands (along the *z* axis of the figure) are also common and are suspected of influencing the metal–metal bond. The dimolybdenum compounds generally have bond lengths between 2.0 and 2.2 Å, while the dichromium compounds show a wide variety of lengths from the "super short" bond length of about 1.85 Å to the "super long" bond length of about 2.6 Å.[2] For comparison the metal–metal bond in metallic chromium is 2.3 Å. In spite of the super short lengths reported, the ligands are always eclipsed. Since this arrangement places the ligands closer than suggested by their van der Waals radii, one would expect steric crowding to be an important effect. These compounds are generally diamagnetic and are characterized by a weakly allowed *z*-polarized transition, the energy of which is sensitive to the metal–metal bond length as well as the electronic properties of the ligands.[3]

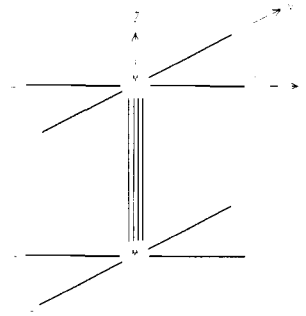

Figure 1. "Quadruple bond".

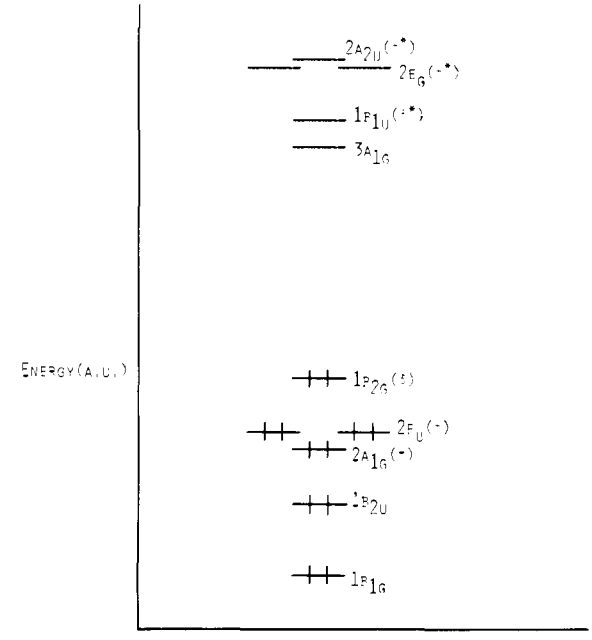

Figure 2. Frontier molecular orbitals for $Cr_2Cl_8^{4-}$ obtained from the symmetry- and spin-restricted procedure.

The bonding in these complexes was first examined by Cotton[4] and described in terms of bonding (and antibonding) orbitals of the form

$$\sigma = 2^{-1/2}(d_{z^2}(A) + d_{z^2}(B))$$

$$\pi = 2^{-1/2}(d_{xz}(A) + d_{xz}(B))$$

$$\pi' = 2^{-1/2}(d_{yz}(A) + d_{yz}(B))\delta = 2^{-1/2}(d_{xy}(a) + d_{xy}(B))$$

where A and B are the two metal atoms. The fourth or δ bond is the in-phase combination between the two d_{xy} orbitals with lobes that bisect the LXL angle of Figure 1. These bonds are shown in Figure 2; the molecular orbital picture inferred by Cotton[4] is given as Figure 3. The $d_{x^2-y^2}$ atomic orbitals interact with the ligands and are found at much higher energy.

On the other hand, it has been long known that this simple idea could not explain many of the known properties of the Cr–Cr systems. Most damaging was the observation that the singlet excitations of the $\delta \rightarrow \delta^*$ type should be strongly allowed and at

(1) See, for example, F. A. Cotton, *Chem. Soc. Rev.*, **4**, 27 (1975); F. A. Cotton, *Acc. Chem. Res.*, **11**, 225 (1978); F. A. Cotton, *Pure Appl. Chem.*, **52**, 2331 (1980).

(2) F. A. Cotton, W. H. Ilsley, and W. Kaim, *J. Am. Chem. Soc.*, **102**, 3464 (1980).

(3) W. C. Trogler and H. B. Gray, *Acc. Chem. Res.*, **11**, 232 (1978).

(4) F. A. Cotton, *Acc. Chem. Res.*, **2**, 240 (1969); J. A. Bertrand, F. A. Cotton, and W. A. Dollase, *J. Am. Chem. Soc.*, **85**, 1349 (1963); M. J. Bennett, F. A. Cotton, and R. A. Walton, *ibid.*, **88**, 3866 (1966).

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