Similarly, there is no significant change in the oxygen changes in OLi_4^{2+} (-0.884), OLi_4^{+} (-0.875), and OLi_4 (-0.871). Thus, the extra electrons in the nominally hypervalent species are not associated with oxygen but rather contribute to Li–Li bonding. The overall structure can be described in terms of an oxygen bonded within a cationic lithium cage, e.g., $O^-Li_3^+$ or $O^-Li_4^+$.

Our further calculations indicate this phenomenon to be quite general. We have already investigated hyperstoichiometric lithium species involving hydrogen and all first-row and some second-row elements.[11] The other alkali metals behave like lithium. ONa_3 and ONa_4, which were reported recently,[12] have calculated structures and bonding like OLi_3 and OLi_4.[11] "Curious suboxides in which there are covalent M–M bonds",[13] e.g., O_2Rb_9 and O_3Cs_{11}, also are known experimentally.[14] The present work also is pertinent to surface complexes between oxygen species and lithium and other metals.[15]

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Evidence Implicating *cyclo*-Diphosphates as Intermediates in Reactions of Nucleoside Phosphorothioates with Cyanogen Bromide

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Adenosine 5′-(1-thiodiphosphate) (ADPαS) and adenosine 5′-(2-thiotriphosphate) (ATPβS) can be desulfurized to ADP and ATP by reacting them with cyanogen bromide. In $H_2{}^{18}O$ both the α- and β-phosphoryl groups of ADP and the β- and γ-phosphoryls of ATP become labeled with ^{18}O. The incorporation of isotope into the terminal phosphoryl groups is *at the expense* of incorporation in place of sulfur in the substrates.

Reaction of 10 mM ATPβS with 20 mM CNBr in $H_2{}^{18}O$ (95% ^{18}O) at pH 7 in 0.1 M potassium phosphate produced [^{18}O]ATP in 55% yield. [^{18}O]ATP was systematically degraded so that P_α, P_β, and P_γ were separately isolated as inorganic phosphate. These samples were analyzed for ^{18}O by ^{31}P NMR analysis of the ^{18}O-induced isotope shifts,[1a,b] which showed that P_β and P_γ contained equivalent ^{18}O enrichment while P_α was unenriched. Reaction of 100 mM ADPαS with 400 mM CNBr in $H_2{}^{18}O$ (98% ^{18}O) at pH 10.6 in 0.5 M potassium tetraborate produced [^{18}O]ADP. The proton-spin-decoupled ^{31}P NMR spectrum consisted of two doublets exhibiting the chemical shifts and coupling constants of

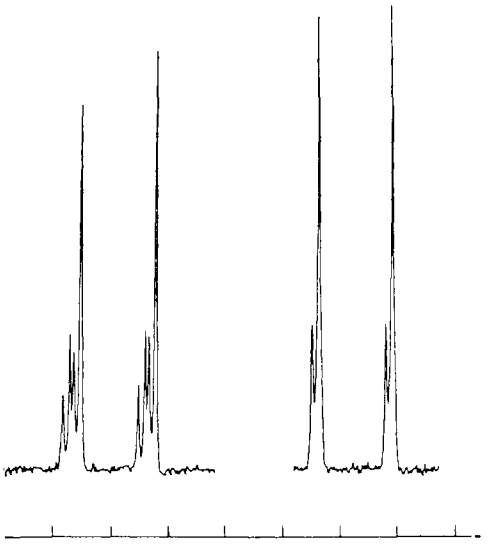
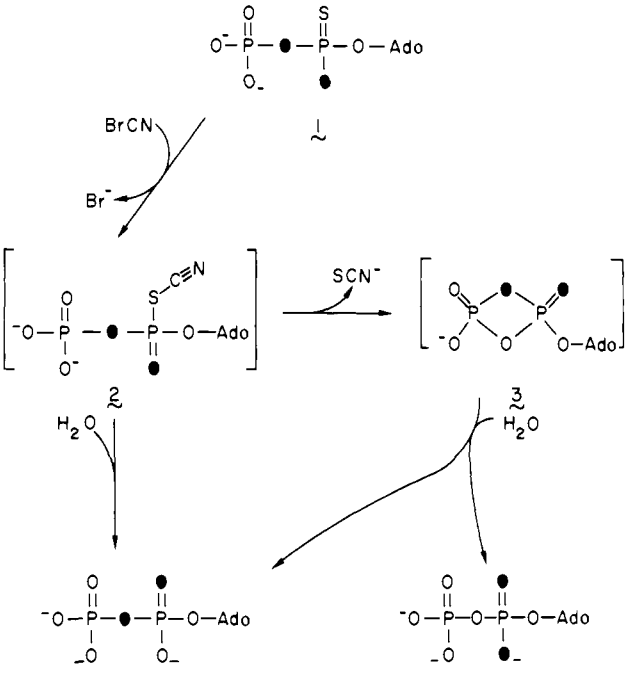


Figure 1. ^{31}P NMR spectrum of (S_P)-ADPαS($\alpha^{18}O_2$). The proton-spin-decoupled spectrum of (S_P)-ADPαS($\alpha^{18}O_2$) **1** in Scheme I, was obtained on the Bruker WM-300. The P_α signals are the doublet patterns at the left in the figure and those for P_β are the doublets at the right in the figure. The chemical shift values for the ^{18}O-containing species are given in the text. (S_P)-ADPαS($\alpha^{18}O_2$) was synthesized by specific phosphorylation of AMPS($^{18}O_2$).[2,3a–d]

Scheme I



P_α and P_β in ADP.[2] Both signals were accompanied by isotope shifted signals of approximately equal intensities attributed to the presence of ^{18}O in equal amounts of both positions.

To shed light on the basis for the dilution of isotope at the position of substitution, we investigated the reaction of ADPαS, $\alpha^{18}O_2$ (**1**, Scheme I, Ado = adenosine), with cyanogen bromide in H_2o. The ^{31}P NMR spectrum of **1** is shown in Figure 1. The signals for P_β are the upfield pair of doublets, an isotope shifted signal at δ −6.642 owing to the high ^{18}O enrichment in the bridging position, and a smaller unshifted signal at δ −6.620 reflecting the presence of some ^{16}O in the bridge. The P_α signal is more complex, consisting of four doublets representing the four possible ^{18}O

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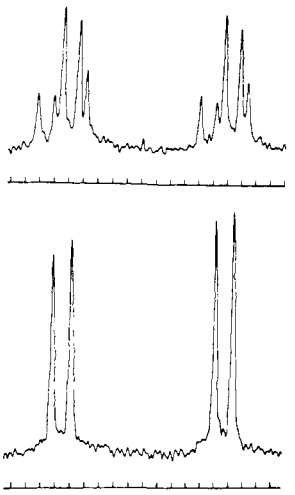

Figure 2. ^{31}P NMR spectrum of [^{18}O]ADP obtained from (S_P)-ADPαS($\alpha^{18}O_2$). A sample of (S_P)-ADPαS($\alpha^{18}O_2$) was converted to [^{18}O]ADP by reaction with cyanogen bromide in H_2O. The proton-spin-decoupled ^{31}P NMR spectrum of the resulting [^{18}O] ADP was obtained on the Bruker WM-300. The upper pattern of doublets contains the P_α signals and the lower, the P_β signals. The chemical shift values and their assignments to ^{18}O-containing species are given in the text.

containing species in **1**. The signals are assigned to the four species as follows: the signal at 40.962 ppm corresponds to the species lacking ^{18}O, that at 40.936 ppm to species containing bridging ^{18}O and nonbridging ^{16}O, that at 40.925 ppm to species with bridging ^{16}O and nonbridging ^{18}O, and signal at 40.902 ppm to species with ^{18}O in both the bridging and nonbridging positions.

A sample of **1** was reacted with 3 equiv of cyanogen bromide at pH 10.5 in borate buffer. NMR analysis showed that **1** was fully consumed and that about 60% of the product was ADP. The [^{18}O]ADP was purified and subjected to analysis by ^{31}P NMR with the results illustrated in Figure 2.

The pair of doublets in the lower portion of the figure are the P_β region. The signal at −6.199 ppm corresponds to species containing ^{16}O in the bridging position and that at −6.220 ppm to species containing bridging ^{18}O. Note that the [^{18}O]ADP is equally populated with briding and nonbridging ^{18}O, whereas in **1** there was a 3:1 ratio of ^{18}O:^{16}O in the bridge. The P_α region in further contrast to that of **1** exhibits *five* lines. The least intense and most downfield is the signal for species containing only ^{16}O at δ −10.694. The nearest signal upfield at δ −10.713 corresponds to species containing bridging ^{18}O. The next upfield signal at δ −10.722 corresponds to species containing nonbridging ^{18}O and the next at δ −10.739 to both nonbridging and bridging ^{18}O. The most upfield signal at δ −10.749 corresponds to a new species, one containing *two* nonbridging ^{18}O and bridging ^{16}O. This latter can have arisen only from species of **1** that contained both bridging and nonbrdiging ^{18}O and reacted by a mechanism leading to the rearrangement of the bridging ^{18}O to a nonbridging position and its replacement with ^{16}O either from solvent or from another position in the molecule.

Our findings are accounted for by Scheme I, in which adenosine 5′-*cyclo*-diphosphate **3** is the intermediate leading to the transfer of bridging ^{18}O to a nonbridging position. In the first step the sulfur in **1** displaces bromide from cyanogen bromide, forming the cyanated intermediate **2**. This has high electrophilic reactivity owing to the absence of electrostatic charge at P_α and to the electron-withdrawing properties of the cyano group, making sulfur a stable leaving group as thiocyanate. Intermediate **2** is partitioned nearly equally between two reaction pathways, the displacement of thiocyanate by H_2O and the internal displacement of thiocyanate by the β-phosphoryl group. The former pathway leads directly to [^{18}O]ADP with ^{18}O labeling as in **1**. The internal displacement leads to a second intermediate, adenosine 5′-*cyclo*-diphosphate **3**, in which one of the bridging oxygens is ^{16}O and the other is ^{18}O. Spontaneous hydrolysis of **3** largely by attack at P_β leads to two species of [^{18}O]ADP, one with bridging ^{18}O and a single nonbridging ^{18}O, and a second with bridging ^{16}O and two nonbridging ^{18}O's at P_α.

cyclo-Diphosphates have heretofore not been invoked as intermediates in reactions and have not been described as compounds, although other four-member-ring phosphorus compounds have been described.[4]

In our earlier study (R_P)- and (S_P)-β-cyanoethyl-ADPαS reacted with cyanogen bromide in $H_2{}^{18}O$ to produce (S_P)- and (R_P)-β-cyanoethyl-[α-^{18}O]ADP with inversion of configuration and high enrichment at P_α[5]. That reaction presumably involved a cyanated intermediate analogous to **2** in Scheme I, which reacted essentially exclusively by the pathway involving the direct displacement of thiocyanate by $H_2{}^{18}O$.

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Registry No. 1, 83151-18-2; ADP, 58-64-0; ATPBS, 60478-94-6; [^{18}O]ATP, 83115-76-8; cyanogen bromide, 506-68-3.

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Mercury(II)-Induced Cyclization of Acetylenic Alcohols: A New Route to Enol Ethers and Substituted Enol Ethers

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Prostacyclin (PGI_2) is a potent inhibitor of platelet aggregation and a vasodilator in in vitro experiments.[1] It is, however, an enol ether rapidly deactivated by hydrolysis to give inactive 6-keto-$PGF_{1\alpha}$.[2] Hydrolysis of enol ethers can be slowed by attachment of electron-withdrawing groups, especially to the β carbon of the double bond; substitution at positions remote from the double bond has a less dramatic effect on hydrolysis rates.[3] In fact, PGI analogues substituted with electron-withdrawing groups in positions remote from the double bond do show some protolytic stabilization compared with natural PGI;[4] substitution *at the β carbon of the enol ether unit*, though, should impart maximum protolytic stability. To date, however, no general methods have been reported for synthesis of β-halogen enol ethers. An attractive convergent one would involve cyclization of acetylenic alcohols, induced by triple bond coordination to an electrophilic metal center, to give an alkenylmetallic intermediate. This species could undergo cleavage with a range of electrophiles to give a series of desired substituted enol ethers. However, whereas much is known concerning addition of nucleophiles to metal-coordinated *olefins*,[5a]

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