broadening, and it is apparent that the magnitude of this broadening also depends on the orientation of the ^{17}O nucleus relative to the cyclic phosphate ring system (Table I). We do not believe that the magnitude of the quadrupolar broadening depends only on the π-bond character of the P-^{17}O bond, since the line widths for the diastereomeric [^{17}O]-*P*-anilidates in methanolic solution depend significantly on the orientation of the ^{17}O nucleus relative to the cyclic phosphate ring system.[15]

A comparison of the ^{31}P decoupled spectra of the separated diastereomers reveals a difference of 2 ppm in their chemical shifts, with the resonance for the equatorially positioned ^{17}O nucleus being less shielded (Figures 1 and 2); this chemical shift difference is also observed in the ^{31}P decoupled spectrum of a mixture of the two diastereomers, since two resonances can be resolved (Figure 3).

The ^{17}O NMR spectral observations which we report in this communication constitute the first *direct* physical evidence for configurational differences in oxygen chiral phosphate ester anions. Previous demonstrations of oxygen chirality by NMR methodology have been reported by our laboratory[2,3] and the laboratories of Trentham,[16] Tsai,[17] Gorenstein,[18] and Knowles;[19] these required chemical modification of the chiral molecule so that the ^{18}O perturbations on the phosphorus chemical shift could be used to indirectly demonstrate chirality. Knowles and his collaborators have described a general method for the configurational analysis of oxygen chiral phosphate monoesters by using metastable ion mass spectroscopic techniques, but this approach also requires chemical modification reactions.[6] Although Cullis and Lowe have reported that (S_P)-methyl [^{16}O,^{17}O,^{18}O]phosphate has a circular dichroism maximum at 208 nm,[20] the validity of this observation must be viewed with caution unitl spectral properties are reported for the R_P enantiomer.

The differences in spectral properties that we have observed for the diastereomers of cyclic [^{17}O,^{18}O]dAMP should be present in the diastereomers of other ^{17}O-labeled cyclic nucleotides and, presumably, six-membered-ring cyclic phosphates, in general. Thus, ^{17}O NMR spectroscopy will be useful in making configurational assignments and complements the approach based on ^{18}O perturbations of phosphorus chemical shifts that we and others have used previously.

Our results also demonstrate that high-field NMR spectrometers with the capability to decouple phosphorus nuclei permit direct observation of ^{17}O NMR resonances with sufficient resolution to provide useful chemical and biochemical information. This instrumentation will be particularly useful if compounds that are stereospecifically labeled with a single ^{17}O atom are available for study; a number of such phosphate esters can be obtained via the chemical and enzymatic procedures that we[2,3] and Stec and his co-workers[21] have developed. Thus, the methodology described in this paper complements that recently reported by Tsai et al.[22] in which the line broadening effects of ^{17}O on ^{31}P resonances were used to indirectly monitor changes in the ^{17}O line widths.

Acknowledgment. We thank Dr. Wojciech J. Stec for useful discussions. The research was supported by a grant (GM-22350) from the National Institutes of Health. The high-field NMR spectrometer used in this research (Bruker HX-270) is supported by a grant from the National Science Foundation (CHE-7916120).

(15) In methanolic solution at 50 °C, the line width of the axially positioned ^{17}O resonance was about 170 Hz and that of the equatorially positioned ^{17}O resonance was about 270 Hz; similar line widths were observed for the cyclic [^{17}O,^{18}O]dAMP diastereomers.

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(20) Cullis, P. M.; Lowe, G. *J. Chem. Soc., Chem. Commun.* **1978**, 512. In this communication and two others which have appeared subsequently (Jarvest, R. L.; Lowe, G.; Potter, B. V. L. *J. Chem. Soc., Chem. Commun.* **1980**, 1142. Jarvest, R. L.; Lowe, G. *Ibid.* **1980**, 1145.), Lowe and his collaborators have described the syntheses of and stereochemical studies of displacement reactions at chiral [$^{16}O$$^{17}O$,$^{18}O$]-phosphate monoesters. Recent work in our laboratory (Coderre, J. A.; Mehdi, S.; Gerlt, J. A. *J. Am. Chem. Soc.* following paper in this issue) and in Lowe's laboratory (G. Lowe, personal communication) has shown that the published configurational assignments of all of the oxygen chiral phosphate monoesters which have been prepared in Lowe's laboratory are in error, i.e., the correct absolute configurations are S_P rather than R_P.

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Oxygen Chiral Phosphodiesters. 4. Stereochemical Course of the Hydrolysis of 2′-Deoxyadenosine 3′,5′-[^{17}O,^{18}O]Monophosphate in $H_2{}^{16}O$ Catalyzed by Bovine Heart Cyclic Nucleotide Phosphodiesterase

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The classical approach for determining the stereochemical course of nucleophilic displacement reactions at phosphorus in enzymology is to employ phosphorothioate analogues of the natural substrates,[1,2] since the syntheses and configurational analyses of phosphorothioate mono- and diesters usually can be accomplished more easily than can the syntheses and configurational analyses of oxygen chiral phosphate mono- and diesters. It can be argued, however, that the results of stereochemical experiments utilizing phosphorothioate analogues are subject to mechanistic ambiguity, since these substrates are usually processed by enzymes at rates less than those observed for the natural materials. However, the results of recent research reported by Knowles' laboratory[3,4] and this laboratory[5,6] suggest that these mechanistic concerns may be ill-founded; the reactions catalyzed by the glycerol kinase obtained from yeast[3,4] and the adenylate cyclase isolated from *Brevibacterium liquefaciens*[5,6] proceed with the identical stereochemical course whether phosphorothioates or oxygen chiral substrates are used.

We therefore viewed with considerable caution the recent report from Lowe's laboratory that the stereochemical course of the bovine heart cyclic nucleotide phosphodiesterase reaction differs with oxygen chiral and phosphorothioate substrates.[7,8] Lowe and his collaborators synthesized chiral 5′-[^{16}O,^{17}O,^{18}O]AMP according to the procedure published by Cullis and Lowe for the preparation of the R_P diastereomer of methyl [^{16}O,^{17}O,^{18}O]-phosphate,[9] except that 2′,3′-diacetyladenosine was substituted for methanol. The labeled 5′-AMP was reacted with diphenyl phosphorochloridate, and the resulting diphenyl ester of labeled ADP was cyclized in the presence of potassium *tert*-butoxide to yield an equimolar mixture of the three types of oxygen chiral cyclic AMP, cyclic [^{16}O,^{17}O]AMP, cyclic [^{17}O, ^{18}O]AMP, and cyclic [^{16}O, ^{18}O]AMP. By assuming that the starting [^{16}O,^{17}O,^{18}O]AMP had the R_P configuration and after determining the configuration of the cyclic [^{16}O, ^{18}O]AMP present in the mixture of cyclic AMP molecules (by measurement of the [^{18}O] perturbations on the phosphorus chemical shifts of the equatorial and axial methyl esters[10,11]), Lowe et al. concluded that the cy-

† NIH Career Development Awardee (CA-00499), 1978-1983.

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(2) Knowles, J. R. *Annu. Rev. Biochem.* **1980**, *49*, 877.

(3) Blättler, W. A.; Knowles, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 510.

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(6) Coderre, J. A.; Gerlt, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 6594.

(7) Jarvest, R. L.; Lowe, G.; Potter, B. V. L. *J. Chem. Soc., Chem. Commun.* **1980**, 1142.

(8) Jarvest, R. L.; Lowe, G. *J. Chem. Soc., Chem. Commun.* **1980**, 1145.

(9) Cullis, P. M.; Lowe, G. *J. Chem. Soc., Chem. Commun.* **1978**, 512.

(10) Gerlt, J. A.; Coderre, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 4531.

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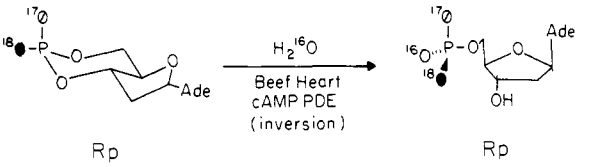
Scheme I



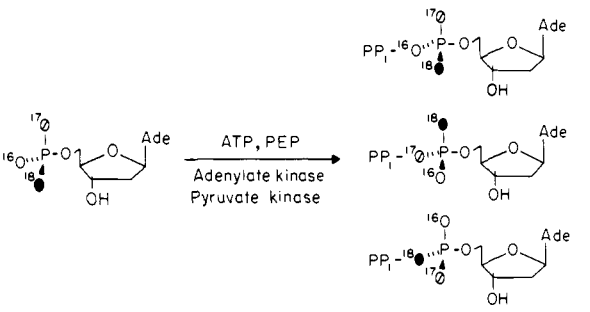
clization reaction had proceeded with *retention* of configuration at phosphorus.[7] The mixture of oxygen chiral cyclic AMP's was then hydrolyzed (in $H_2{}^{17}O$) by using the cyclic nucleotide phosphodiesterase from bovine heart as catalyst to yield a mixture of prochiral and chiral oxygen-labeled 5'-AMP's. This mixture was chemically cyclized as in the preparation of the starting mixture of chiral cyclic AMP's, and the product was methylated, thereby permitting configurational analysis by the ^{31}P NMR method.[10,11] On the basis of retention as the stereochemical course of the chemical cyclization reaction, Lowe et al. concluded that the enzymatic hydrolysis reaction had proceeded with *retention* of configuration.[8] This conclusion contradicts the result which Eckstein and Stec and their collaborators obtained for the hydrolysis reaction catalyzed by the same enzyme but using the phosphorothioate analogue of cyclic AMP, cyclic AMPS, as the chiral substrate.[12] These investigators found that the enzyme catalyzed the hydrolysis of cyclic AMPS in $H_2{}^{18}O$ with *inversion* of configuration.[12]

Two interpretations for the contradictory results are possible: (1) both are correct, demonstrating that the phosphorothioate approach to stereochemical studies does not provide reliable mechanistic information; or (2) one is incorrect. Since we recently had synthesized both diastereomers of chiral cyclic [^{17}O,^{18}O]-dAMP,[13] we thought that we might determine which interpretation was correct by hydrolyzing one of the diastereomers in $H_2{}^{16}O$ by using the cyclic nucleotide phosphodiesterase as catalyst and then utilizing the known stereochemical course of the bacterial adenylate cyclase reaction[4] to aid in the determination of the stereochemical course of the hydrolysis reaction. *Our data demonstrate that the result reported by Lowe and his collaborators is in error and, also, provide the third example of an enzyme whose stereochemical course is not altered by sulfur substitution.*

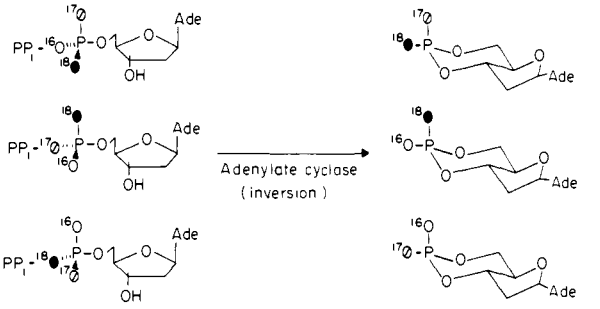
The R_P diastereomer of cyclic [^{17}O,^{18}O]dAMP[13] was hydrolyzed in $H_2{}^{16}O$ by using the cyclic nucleotide phosphodiesterase from bovine heart (Scheme I). The reaction was allowed to proceed at pH 7.5 and 25 °C until only 60% of the cyclic nucleotide had been consumed so that any enzyme-catalyzed exchange of product phosphoryl oxygens with solvent oxygen would be minimized.[14]

Several methods of configurational analysis of the chiral [^{16}O,^{17}O,^{18}O]dAMP were potentially available to us: (1) Transfer of the chiral phosphoryl group to chiral 1,2-propanediol[15] followed by configurational analysis as described by Knowles and his collaborators;[16,17] this method was not technically possible due to the relatively small amount of chiral dAMP we prepared (90 μmol). (2) Chemical cyclization of the chiral dAMP by using diphenyl phosphorochloridate and potassium *tert*-butoxide to yield a mixture of the three types of chiral cyclic dAMP,[7] whose relative configurations could be ascertained by ^{31}P NMR spectroscopy.[10,11] This method was considered unreliable, because the stereochemical course reported by Lowe and his co-workers[7] (retention) is not predicted by the accepted principles of nucleophilic displacement reactions at phosphorus[18] and contradicts experimental results obtained on related systems.[19] (3) Enzymatic pyrophosphorylation of the [^{16}O,^{17}O,^{18}O]dAMP to a mixture of three types of iso-

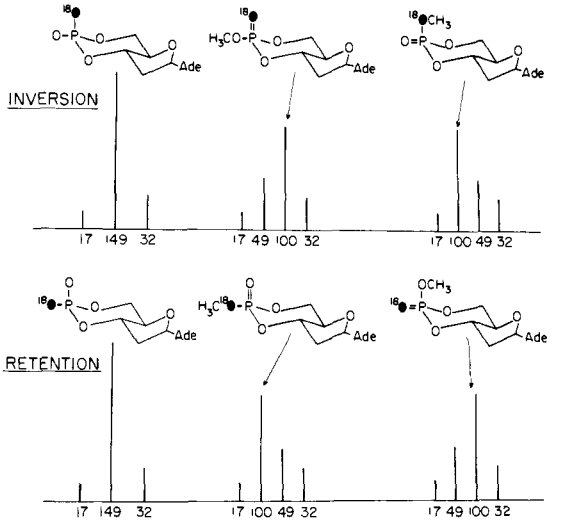
Scheme II



Scheme III



Scheme IV



(11) The method we have previously described for the configurational analysis of chiral cyclic [^{16}O,^{18}O]dAMP[10] can also be used for the configurational analysis of a mixture of the three chiral cyclic AMP's (or cyclic dAMP's), since it has been shown that the effect of directly bonded ^{17}O on the associated phosphorus resonance is to cause line broadening of such magnitude that the resonance cannot be easily detected: Tsai, M. D.; Huang, S. L.; Kozlowski, J. F.; Chang, C. C. *Biochemistry* **1980**, *19*, 3531. Since the ^{17}O enrichment in the starting cyclic [^{17}O,^{18}O]dAMP was less than 100%, resonances due to [^{16}O,^{16}O]-, [^{18}O,^{18}O]-, and the incorrect ^{16}O,^{18}O-labeled materials are also present in the spectrum, although it can be shown that the predominant resonances are those associated with the correct ^{16}O,^{18}O-labeled material.

(12) Burgers, P. M. J.; Eckstein, F.; Hunneman, D. H.; Baraniak, J.; Kinas, R. W.; Lesiak, K.; Stec, W. J. *J. Biol. Chem.* **1979**, *254*, 9959.

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(14) The reaction mixture (8 mL) contained 25 mM R_P cyclic [^{17}O, ^{18}O]dAMP, 5 mM $MgCl_2$, 0.1 M Tris–HCl, pH 7.5, and 0.1 U/mL of cyclic nucleotide phosphodiesterase (Boehringer). After 3.5 h, the reaction had gone to about 60% completion, as judged by TLC on cellulose plates (Baker), and was applied to a column (1.2 × 45 cm) of DEAE–Sephadex A-25 in the HCO_3^- form.

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(17) Buchwald, S. L.; Knowles, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6601.

(18) Westheimer, F. H. In "Rearrangements in Ground and Excited States"; DeMayo, P., Ed.; Academic Press: New York, 1980; Vol. II, p 229.

(19) (a) *tert*-Butoxide-induced cyclization of thymidine 5'-(*o*-chlorophenyl *N*-phenyl phosphoramidate): Gerlt, J. A.; Mehdi, S.; Coderre, J. A.; Rogers, W. O. *Tetrahedron Lett.* **1980**, 2385. (b) *tert*-Butoxide-induced cyclization of thymidine [^{17}O,^{18}O]-3'- and 5'-(4-nitrophenyl phosphates): Mehdi, S.; Gerlt, J. A., unpublished observations. (c) *tert*-Butoxide-induced cyclization of adenosine and thymidine 5'-(4-nitrophenyl phosphorothioates): Eckstein, F., personal communication, Stec, W. J., personal communication.

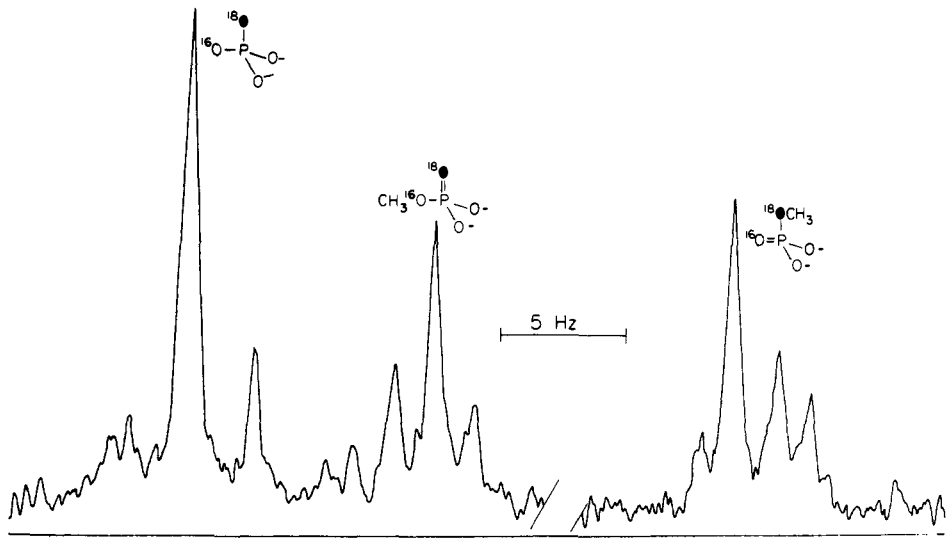

Figure 1. ^{31}P NMR spectrum at 81 MHz of the methyl esters of isotopically labeled cyclic dAMP derived from enzymatic hydrolysis of cyclic [^{17}O,^{18}O]dAMP in $H_2{}^{16}O$ followed by enzymatic pyrophosphorylation and cyclization. The spectrum was obtained with a 500-Hz sweep width and an 8-s acquisition time; 450 transients were obtained prior to application of a 0.1-Hz line broadening and Fourier transformation. The approximate chemical shift of the diester and the equatorial methyl ester is −2.7 ppm and that of the axial ester is −3.5 ppm (upfield, relative to an external capillary of 85% H_3PO_4).

topically labeled dATP (Scheme II) which could be cyclized enzymatically with inversion of configuration[4] to yield a mixture of three types of chiral cyclic dAMP (Scheme III), whose absolute configuration could be ascertained by ^{31}P NMR spectroscopy.[10,11] This method was selected, since the stereochemical course of the enzymatic cyclization reaction has been established firmly.[6]

From 90 μmol of [^{16}O, ^{17}O, ^{18}O]-chiral dAMP, about 80 μmol of a mixture of the three types of chiral cyclic dAMP were obtained after enzymatic pyrophosphorylation[20] and subsequent enzymatic cyclization.[21] Fifty micromoles of the mixture was reacted with excess diazomethane, and the isolated product was subjected to configurational analysis by ^{31}P NMR spectroscopy.[10,11,22]

In Figure 1, we present the ^{31}P NMR spectrum which was obtained at 81 MHz; two sets of resonances are observed in addition to that associated with the starting material, and, as in the case of the ethyl esters,[10] the more downfield set of resonances can be associated with the equatorial ester.[23] In Scheme IV, we present idealized ^{31}P NMR spectra which would be predicted for either inversion or retention of configuration in the hydrolysis reaction, taking into account the isotopic composition of the [^{17}O]-enriched $POCl_3$[24] used in the synthesis of the cyclic [^{17}O,^{18}O]dAMP. A comparison of the actual spectrum in Figure 1 and the idealized spectra in Scheme IV leads to the conclusion that the hydrolysis of cyclic [^{17}O,^{18}O]dAMP in $H_2{}^{16}O$ proceeds with *inversion* of configuration.

On the reasonable basis that the hydroxyl functionality at $C_{2'}$ of the furanoside portion of the cyclic nucleotide has no effect on the mechanistic details of the reaction catalyzed by the phosphodiesterase, our result clearly contradicts that reported by Lowe's laboratory.[8] What is the explanation for this contradiction? Although Lowe's configurational assignments of the starting mixture of the three types of chiral cyclic AMP and especially the resulting mixture of prochiral and chiral cyclic AMP's could be in error by virtue of the rather small differences observed for the relative intensities of the configurationally important resonances, we do not believe that this potential analytical problem is the proper explanation. The only fundamental difference between Lowe's experiment and that reported in this communication is the assumed stereochemical course of the cyclization reaction employed to resynthesize the cyclic nucleotide for configurational analysis. In both experiments, the overall stereochemical course of the hydrolysis and subsequent cyclization reactions was retention of configuration. Since the stereochemical course of the enzyme-catalyzed cyclization reaction has been firmly established,[4] whereas the stereochemical course of the chemical cyclization which Lowe and his collaborators utilized was unexpected and relied on an assumed configuration,[7] we can only conclude that the *retention* of configuration which Lowe et al. reported for the chemical cyclization reaction[7] must be in error. Since Lowe's data are adequate to assign the configuration of the mixture of chiral cyclic AMP's that was enzymatically hydrolyzed, the incorrect stereochemical course which Lowe deduced for the chemical cyclization reaction can be explained only if the configuration of the chiral [^{16}O,^{17}O,^{18}O]AMP used to prepare the sample of cyclic AMP is incorrect. This material was synthesized chemically by a route strictly analogous to that which Cullis and Lowe described for the synthesis of oxygen chiral methyl phosphate.[9] Unfortunately, the configuration of neither the chiral methyl phosphate nor the chiral AMP has been independently determined, and the detail with which Cullis and Lowe[9] reported the synthesis of chiral

(20) The reaction mixture (78.5 mL) contained 1.16 mM chiral dAMP obtained from the hydrolysis reaction, 0.14 mM ATP, 2.86 mM phosphoenol pyruvate, 2.9 mM NADH, 2.86 mM $MgCl_2$, 60 mM KCl, 42 mM Tris–HCl, pH 8.0, 25 U/mL adenylate kinase, 10 U/mL pyruvate kinase, and 5 U/mL lactate dehydrogenase. The progress of the pyrophosphorylation was followed by monitoring the decrease in absorbance at 340 nm corresponding to the amount of NADH oxidized to NAD^+ by lactate dehydrogenase. The reaction was complete in 30 min, and the product triphosphates were isolated by chromatography on DEAE Sephadex A-25. Unlabeled ATP, present as the cosubstrate for adenylate kinase, was separated from the mixture of labeled dATP's by chromatography on Affi-Gel 601 (Bio Rad), a boronate affinity resin. The mixture of three 2'-deoxy ATP's was isolated in 92% yield, 84 μmol.

(21) The reaction mixture (42 mL) contained 2 mM labeled dATP's, 30 mM $MgSO_4$, 10 mM sodium pyruvate, 1 mM dithiothreitol, 0.1 mg/mL of bovine serum albumin, 0.1 M Tris–HCl, pH 9.0, and approximately 1 unit of adenylate cyclase[6] (0.03 mg of protein). The progress of the reaction was monitored by TLC on cellulose plates (Baker); the reaction was essentially complete after 8.5 h, and the product mixture of the three labeled cyclic dAMP's was isolated by chromatography on DEAE Sephadex A-25. Yield of labeled cyclic dAMP mixture: 80 μmol, 95%.

(22) Fifty micromoles of the mixture of labeled cyclic dAMP's was converted to the acid form by addition of 2 equiv of HCl and evaporation to dryness. This material was suspended in 4 mL of methanol, and about 5 mL of a 0.5 M solution of diazomethane in ether was added. The mixture was stirred until all solids dissolved, and the pale yellow color persisted. The reaction mixture was evaporated, the resulting oil was washed several times with H_2O, and the water washes were evaporated to dryness. The reaction product mixture was prepared for ^{31}P NMR by dissolution in 0.1 M EGTA, pH 7.0, and was allowed to stand over Chelex 100 for 20 min before being transferred to an acid-washed NMR tube.

(23) Coderre, J. A.; Gerlt, J. A., unpublished observations.

(24) The isotopic composition was determined by reaction with excess methanol followed by gas chromatography/mass spectral analysis of the resulting trimethyl phosphate: ^{16}O, 17.1%; ^{17}O, 51.1%; ^{18}O, 31.8%.

methyl phosphate does not readily permit an explanation for the presumed configurational error to be ascertained.[25]

The result described in this communication and that recently described by Eckstein and Stec and their collaborators[12] constitute the third example of an enzyme-catalyzed phosphoryl transfer reaction whose stereochemical course is unaffected by sulfur substitution. This example is the first for a hydrolysis reaction, the previous two being for a kinase reaction (glycerol kinase)[3,4] and for a nucleotidyl transfer reaction (adenylate cyclase).[5,6]

Acknowledgment. We are grateful to Professors Fritz Eckstein and Jeremy Knowles for their encouragement and useful discussions. The high-field NMR spectra essential to this research were obtained with the generous cooperation and advice of Professor Philip Bolton. This research was supported by a grant from the National Institutes of Health (GM-22350).

(25) Upon completion of the research described in this communication, we informed Dr. Lowe of our results. His reply, which was received after this manuscript had been completed, indicated that the configuration of the oxygen chiral methyl phosphate,[9] 5'-AMP,[7] and glucose 6-phosphate[7] all have the S_P rather than the R_P configuration as originally published. This error was explained by incorrect assignments of the geometries of the precursor hydrobenzoin cyclic triesters.

$(C_5Me_5)_2UCl\cdot THF$ Oxidative-Addition Reactions. 2. A Kinetic and Mechanistic Study

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In a recent communication,[1] we described $(C_5Me_5)_2UCl\cdot THF$, **1**, oxidative addition of alkyl halides, reactions which proceed according to the generalized stoichiometry of eq 1. These reactions, the first organoactinide oxidative additions to be described, were observed to proceed at rates unprecedented in organotransition-metal chemistry. Herein we report a kinetic and mechanistic study of these one-electron, U(III) to U(IV), oxidative additions.[2] This study is aimed primarily at understanding and quantifying this enhanced organoactinide reactivity. The results obtained (1) provide evidence for a halogen atom-abstraction (S_H2)[3c] oxidative-addition[3,4] mechanism, (2) include a wide range of RX relative rates, many of which were previously unavailable from studies of less reactive prototype transition-metal atom abstractors such as Co(II)[3g] or Cr(II)[3h], (3) quantify the exceptionally high reactivity of $(C_5Me_5)_2UCl$ as 10^4 and 10^7 faster than Co(II) coenzyme $B_{12(r)}$ and $[Cr(II)(en)_2]^{2+}$, respectively, and (4) demonstrate and quantify the key role of coordinative unsaturation[5] in achieving these high actinide oxidative-addition rates.

Evidence for radical intermediates in these reactions was obtained[1] from the addition of cyclopropylcarbinyl chloride to $(C_5Me_5)_2UCl\cdot THF$ in room temperature benzene to yield a significant amount of the ring opened product, $(C_5Me_5)_2UCl(-CH_2CH_2CH{=}CH_2)$. The formation of dimers, olefins, and alkanes [R–R, R(–H), and R(H), respectively, eq 1] from the

$$(a + 2b)(C_5Me_5)_2UCl\cdot THF + (a + b)RCl \xrightarrow{\text{benzene}} (a + b)(C_5Me_5)_2UCl_2 + b(C_5Me_5)_2UCl(R) + a[R\text{–}R, RH, R(\text{–}H)] + (a + 2b)THF \quad (1)$$

corresponding RCl is also consistent with a R· intermediate as are the relative RX rates observed for benzyl ~ tertiary > secondary > primary > neopentyl (vide infra).

The complete rate law, including the surprising and dramatic dependence upon added THF, was determined by monitoring the loss of $[U(III)]_T$,[6] λ_{max} 740 nm, at 0.0 °C for *n*-butyl and neopentyl chlorides. An overall second-order dependence, first order each in $[U(III)]_T$ and [RX], was established from the appropriate kinetic plots, which were linear over 80–90% reaction for the accessible ca. 4-fold, 1.5–6.0 × 10^{-3} M, range of starting $[(C_5Me_5)_2UCl\cdot THF]$ and from the independence of the observed second-order rate constant, k_2(obsd), over a 5-fold, 0.97–5.0 × 10^{-3} M alkyl chloride concentration range. The observed rate constants are: k_2(obsd) = 17 ± 3 M^{-1} s^{-1} for *n*-BuCl at 0.0 °C, k_2(obsd) = 31 ± 3 M^{-1} s^{-1} for *n*-BuCl at 22.0 °C, and k_2(obsd) = 2.8 ± 1.0 M^{-1} s^{-1} for neopentyl chloride at 0.0 °C. The [THF] dependence of the 22.0 °C *n*-BuCl oxidative-addition rate law was established from the smooth, concave dependence of k_2(obsd) on [THF] added to the benzene/$(C_5Me_5)_2UCl\cdot THF$ solution; k_2(obsd) = 31 M^{-1} s^{-1} at 0:100 (v/v) THF/benzene decreasing to a near limiting k_2(obsd) = 0.088 M^{-1} s^{-1} at 40:60 (v/v) THF/

(1) Finke, R. G.; Hirose, Y.; Gaughan, G. *J. Chem. Soc., Chem. Commun.*, in press. These reactions were discovered during our investigation of uranium–transition-metal heterobimetallic complexes. We thank Professor Tobin Marks and his research group for the exchange of unpublished information on $[(C_5Me_5)_2UCl_2]^-\cdot Na^+$, a Na(Hg) reduction product of $(C_5Me_5)_2UCl_2$.

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(6) Between 1.25 × 10^{-3} and 6.1 × 10^{-3} M in benzene at 25 °C, Beer's law is obeyed by $(C_5Me_5)_2UCl\cdot THF$ with ϵ (apparent, 740 nm) 3.09 ± 0.08 × 10^2 M^{-1} cm^{-1}. Evidence given in the text shows that there exists, however, a THF dissociative equilibria with K_{eq} = 1.4 × 10^{-2} M, $(C_5Me_5)_2UCl\cdot THF \rightleftharpoons (C_5Me_5)_2UCl + THF$, so that at 1.25 × 10^{-3} M, 92% of the U(III) is in the THF free form while at 6.1 × 10^{-3} M, 75% has dissociated a THF. Beer's law is obeyed in this concentration range since the two U(III) forms have very similar visible spectra.

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