Alkoxyphosphonium Salts. 4. Kinetics and Mechanisms of Arbuzov Reactions

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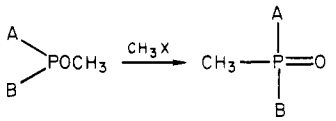
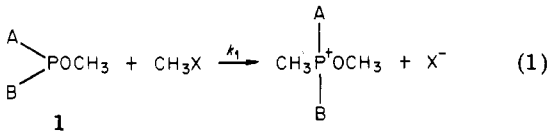
The kinetics of the Arbuzov reactions of trivalent phosphorus esters of the type $ABPOCH_3$ catalyzed by CH_3X have been studied. The alkoxyphosphonium ion $ABCH_3POCH_3^+$ is always intermediate but often undetected. In all cases studied using methyl iodide, the rate-determining step is the alkylation of the trivalent phosphorus and the intermediate alkoxyphosphonium ion does not accumulate detectably by NMR. In all cases with methyl triflate, the alkylation is fast and complete, and the resulting alkoxyphosphonium salt then has a constant concentration. It methylates the trivalent compound (if any remains) in a measurably slow reaction, the only observed process. This reaction represents the pure "autocatalytic" mechanism. With dimethyl sulfate the intermediate accumulates but does not ordinarily persist, and the reaction course is best fit by a combination of the "autocatalytic" mechanism with attack on the intermediate phosphonium ion by $ABPOCH_3$ and the "textbook" mechanism in which the intermediate alkoxyphosphonium ion is dealkylated by attack of the methyl sulfate anion.

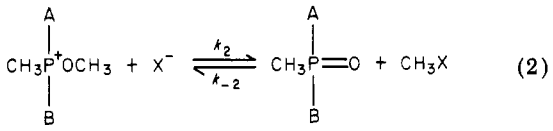
There are two ionic mechanisms suggested for the Michaelis–Arbuzov reaction, represented in a simple case as a rearrangement:



The first, originally suggested by Arbuzov,[1] we call the "textbook" mechanism.[2] It consists first of the alkylation reaction, yielding the alkoxyphosphonium ion **2**, followed by reaction with the conjugate nucleophile[3] (X^-) of the catalyst CH_3X by reaction 2 to give the product **3** and regenerate the CH_3X.

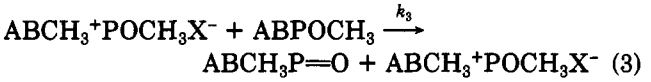


1 **2** (1)



2 **3** (2)

The secound mechanism, originally proposed by Rumpf,[4] called the "autocatalytic" mechanism, has reaction 1 as the first step. It is followed by reaction 3, in which the nucleophile that attacks **2** is the trivalent phosphorus compound (1) rather than X^-.



$$ABCH_3^+POCH_3X^- + ABPOCH_3 \xrightarrow{k_3} ABCH_3P{=}O + ABCH_3^+POCH_3X^- \quad (3)$$

Reaction 3 is an ionic chain, initiated by reaction 1 and terminated by reaction 2; although since some alkoxyphosphonium salts are stable, termination is not necessary and compound **2** will persist either because the reaction 2 is too slow or because the equilibrium lies to the left. The contribution of the autocatalytic mechanism when **2** does not persist then is a quantitative distinction depending on the relative rates of reactions 3 and 2, that is, the competition between **2** and MeX for the nucleophilic **1**. In this paper we look at extreme cases and an intermediate case in which both mechanisms contribute.

The distinction between the two mechanisms is possible by methods other than the complete determination of all rate constants. The overall kinetics will not follow a simple first-order course if reaction 3 contributes. Thus the simple first-order course observed by Aksnes and Aksnes[5] strongly suggests the textbook mechanism. Furthermore, if the R of ABPOR is different from R′ in R′X, then the product of the autocatalytic reaction will have R on phosphorus, whereas the initial product of the "textbook" mechanism will have R′ on phosphorus. In the present work R = R′ = CH_3.

In addition to these two mechanisms, free radical mechanisms are also possible.[6]

Results

The study of kinetics on phosphorus compounds has been complicated by several factors. Side reactions such as oxidation of trivalent compounds and hydrolysis of various esters (including especially the alkoxyphosphonium compounds) are sometimes serious. Thus a satisfactory analytical method subject to interference by side reactions such as conductivity, dilatometry, and to a considerable extent infrared are not wholly reliable. Few of the relevant phosphorus compounds absorb in the ultraviolet in any very characteristic way. We have therefore used NMR as a compound-specific analysis. Proton NMR of organophosphorus compounds is often complex, because the substantial splitting by ^{31}P has a long range, and side reactions give compounds of not very different chemical shift from the main reaction; we have nevertheless followed some reactions by proton NMR. However, the range of chemical shifts of ^{31}P is so large that coincidences are rare. There are various problems associated with the quantitatives use of proton-decoupled FT ^{31}P NMR, namely, the occasionally nonlinear dependence of peak height or area

(1) Arbuzov, A. E. *J. Russ. Phys.-Chem. Soc.* **1906**, *38*, 687.
(2) Kemp, D. S.; Vellaccio, F. "Organic Chemistry"; Worth: New York, 1980; p 1246. Pine, S. H.; Hendrickson, J. B.; Cram, D. J.; Hammond, G. S. "Organic Chemistry"; McGraw Hill: New York, 1980, p 422. Streitwieserr, Jr.; A., Heathcock, C. H. "Introduction to Organic Chemistry", 2nd ed.; MacMillan: New York, 1981.
(3) This terminology, based on that used for Brønsted acids and bases, is especially useful when considering leaving groups as nucleophiles.
(4) Rumpf, P. *Bull. Soc. Chim. Fr.* **1951**, *18*, 128.
(5) Aksnes, G.; Aksnes, D. *Acta Chem. Scand.* **1964**, *18*, 38–46.
(6) Bentrude, W. G. *Acc. Chem. Res.* **1982**, *15*, 117–125.

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Table I. Constants for $CH_3I + ABPOCH_3 \rightarrow ABCH_3P^+OCH_3I^-$

A	B	k_1,[a] M^{-1} s^{-1}	solvent[b]
OCH_3	CH_3	3.3×10^{-3}	CD_3CN (H)
OCH_3	Ph	1.2×10^{-3}	CD_3CN (H)
OCH_3	Et	4.0×10^{-3}	CD_3CN (H)
OCH_3	*t*-Bu	5.3×10^{-4}	$CDCl_3$ (P)
OCH_3	Et	1.2×10^{-3}	$CDCl_3$ (P)
Ph	Ph	5.5×10^{-4}	$CDCl_3$ (P)
t-Bu	*t*-Bu	1.5×10^{-2}	$CDCl_3$ (P)

[a] Only measurable rate constant; evaluated by dividing the apparent first-order rate constant by the (constant) CH_3I concentration. [b] Parenthetical letter is NMR nucleus used for analysis; all proton runs at 34.4 °C, phosphorus runs at 26.8 °C.

Table II. Rate Constants k_3 for the Reaction 2 + 1 → 3 + 2, X = OTf

A	B	k_3,[a] M^{-1} s^{-1}	solvent[b]
OCH_3	OCH_3	7.5×10^{-3}	CD_3CN (H)
OCH_3	CH_3	6.0×10^{-3}	CD_3CN (H)
OCH_3	Ph	1.0×10^{-2}	CD_3CN (H)
OCH_3	Et	4.4×10^{-3}	$CDCl_3$ (P)
OCH_3	*t*-Bu	4.6×10^{-3}	$CDCl_3$ (P)

[a] Obtained by dividing the apparent first-order constant for conversion of 1 to 3 by the (constant) concentration of 2. [b] Parenthetical H or P denotes nucleus used for NMR analysis. All proton runs at 34.4 °C, phosphorus at 26.8 °C.

on concentration. This paper does not represent the best that we now know how to do to minimize these problems. Even with the problems, the enormous advantage of having a resolved peak for each compound, whether main product, reagent, side product, or contaminant, makes the method very powerful. We have in some circumstances observed separately both hydrolysis and oxidation products by this method.

All reactions took place in NMR tubes at the quite constant temperatures attained in the probe. The temperatures reported as 34.4 °C are those analyses carried out on a Varian EM 390 CW spectrometer used when the reaction course was followed by ^1H NMR; those reported as 26.8 °C are those carried out on a JEOL FX90Q FT instrument used for ^{31}P NMR. The constancy and reproducibility of these temperatures is better than the measurement; we estimate ±0.5 ° for the measurement uncertainty.

Table I presents results on the reaction of several methyl esters of trivalent phosphorus acids with methyl iodide. The solvent in this as well as the remaining tables is either acetonitrile-d_3 or chloroform-*d*. Generally, side reactions (such as hydrolysis) in acetonitrile were more serious than in chloroform. We believe that the intermediate alkoxyphosphonium ions are relatively resistant to the possible

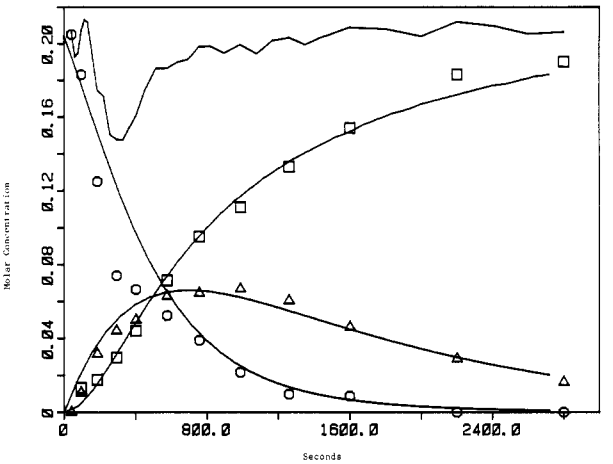

Figure 1. Concentration vs. time plots for the reaction of dimethyl *tert*-butylphosphonite with dimethyl sulfate in $CDCl_3$. Circles represent the reagent 1, triangles the alkoxyphosphonium ion 2, and squares the product 3, methyl *tert*-butylmethylphosphinate. Solid curves are those calculated from numberical integration of the rate law. The top curve is the experimental sum (1) + (2) + (3), showing an estimate of analytical accuracy.

acid contaminants in chloroform but not to bases or nucleophiles. This solvent has been used in most of the latter work and the data appear to be better. The quite small rate differences between these two solvents is noted and discussed later.

The table shows only the rate constant k_1, because only the disappearance of 1 and the formation of 3 could be observed, 2 was never seen, and the disappearance of 1 followed a first-order course, showing that reaction 1 is rate determining and reaction 3 is negligible. With methyl iodide the textbook mechanism is thus fully confirmed. We can also conclude that $k_2 \gg k_{-2}$ and that k_2 with X = I is large, since it is destroyed as fast as it is made.

Table II shows the results of measurements made by using methyl triflate (methyl (trifluoromethyl)sulfonate). In these cases reaction 1 was complete before measurements could be made, so the solution contained high concentrations of the alkoxyphosphonium ion 2, and if 1 was in excess, the conversion of 1 to 3 by reaction 3 could be followed. In all cases the concentration of 2 remained constant. Reaction 2 was not observed; it was either too slow or its reverse was fast; and the reaction 2 → 3 was not detected. Since we have noted that the reaction $(CH_3O)_4P^+ + OTf^- \rightleftarrows (CH_3O)_3PO + CH_3OTf$ is fast in both direactions, it would be a mistake to assume that triflate ion shows no nucleophilic reactivity toward all methoxyphosphonium ions. The rate constant k_2 can not in these cases be readily measured because the reaction is thermodynamically unfavorable. We therefore assume $k_{-2} \gg k_2$. Our failure to measure k_1 in this system does not mean that it is outside the range of such a NMR

Table III. Rate Constants for the Reaction of 1 with Dimethyl Sulfate

A	B	k_1, M^{-1} s^{-1}	k_2, s^{-1}	k_3, M^{-1} s^{-1}	solvent[a]
OCH_3	CH_3	3.6×10^{-3}	*b*	*b*	CD_3CN (H)
OCH_3	Ph	1.7×10^{-4}	2.3×10^{-5}	3.7×10^{-3}	CD_3CN (P)
OCH_3	Et	7.8×10^{-4}	1.5×10^{-4}	3.0×10^{-3}	$CDCl_3$ (P)
OCH_3	*t*-Bu	3.0×10^{-4}	9.0×10^{-5}	3.0×10^{-3}	$CDCl_3$ (P)
t-Bu	*t*-Bu	5.0×10^{-3}	*c*	3.0×10^{-4} [c]	$CDCl_3$ (P)
OCH_3	Ph	2.0×10^{-4}	2.6×10^{-4}	9.0×10^{-3}	$CDCl_3$ (P)

[a] Parenthetical H or P shows nucleus used in NMR analysis. All proton runs at 34.4 °C, phosphorus runs at 26.8 °C. [b] In this run with a very low initial concentration of MeX, the intermediate 2 had an undetected low concentration; k_2 and k_3 could not be evaluated. [c] 3 was formed only with excess 1; it was not practical to distinguish between a substantial value of k_3 and a substantial value of k_2 (both with $k_2 >> k_{-2}$). In experiments with excess dimethyl sulfate, the fit was slightly better, accounting for the disappearance of 1 by reaction 3 as well as reaction 1.

measurement but only that it was too fast at the concentrations and temperature used. The mechanism observed with methyl triflate is thus purely the autocatalytic one.

Table III shows the rate constants measured by using dimethyl sulfate, a methylating agent expected to be intermediate between methyl iodide and methyl triflate.[7] The expectation is realized, the intermediate **2** is formed detectably but not quantitatively and usually disappears at the end of the reaction. The rate constants k_1, k_2, and k_3 were evaluated by fitting experimental concentration vs. time curves to those calculated by a numerical integration of the rate equations 4–7. In every case except

$$\frac{d(1)}{dt} = -k_1(1)(MeX) - k_3(1)(2) \quad (4)$$

$$\frac{d(2)}{dt} = k_1(1)(MeX) + k_{-2}(3)(MeX) - k_2(2) \quad (5)$$

$$\frac{d(3)}{dt} = k_2(2) + k_3(1)(2) - k_{-2}(3)(MeX) \quad (6)$$

$$\frac{d(MeX)}{dt} = -k_1(1)(MeX) + k_2(2) - k_{-2}(3)(MeX) \quad (7)$$

for A = B = *t*-Bu, no **2** is present at long times. Except in this case, k_{-2} was taken as zero, but of course we only know that it is much less than k_2. In the exceptional case, the data were completely insensitive to k_2 or k_{-2}, except that $k_{-2} \gg k_2$.

The precision of the rate constants in this table is much less than that in the other two, because of uncertainties associated with this fitting procedure and the sensitivity of the chosen rate constants to experimental error. An assumption made is that **2** exists almost wholly as an ion pair, so that reaction 2 is first order.[8] The data are also adequately fit by assuming reaction 2 is second order, with the second-order constant given by the value for k_2 from the table divided by the average **2** concentration. We consider extensive dissociation unlikely, however, especially in chloroform, and thus favor the first-order form.

Figure 1 shows the observed concentrations of **1**, **2**, and **3** as a function of time in the reaction of $(MeO)_2P$-*t*-Bu with dimethyl sulfate. Every third experimental point is shown, together with the curves calculated by using the values $k_1 = 2.5 \times 10^{-4}$ M^{-1} s^{-1}, $k_2 = 8.1 \times 10^{-5}$ s^{-1}, $k_3 = 1.9 \times 10^{-3}$ M^{-1} s^{-1}. The experimentally measured total phosphorus contents (i.e., (1) + (2) + (3) for each kinetic point are connected by the curve at the top. This curve gives an estimate of the analytical error, which appears quite large for a short period near the beginning but is then fairly reliable. Such plots of total phosphorus measurements of this sort improved as experience and techniques were developed. The corresponding sum of calculated total phosphorus with time did not deviate significantly from a constant, although the use of too long a time interval in the numerical integration could produce such a deviation.

It should be noted that the concentration of **2** does not follow a simple kinetic law. Thus the conductimetric measurements of Cachaza et al.[9] can not give k_1 as claimed. They are, however, a far more sensitive indication of the presence of the intermediate than our NMR method.

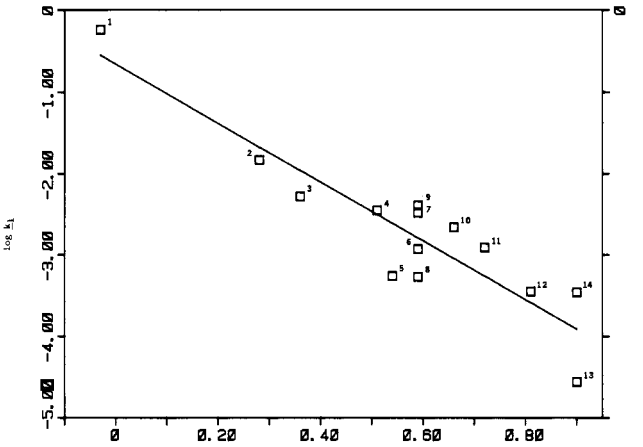

Figure 2. Plot of log k for the reaction with methyl iodide of various trivalent phosphorus derivatives. The individual points with the three phosphorus substituents are the following: (1) Bu, Bu, Bu;[10] (2) Bu, Bu, OMe; (3) Ph, Ph, Ph;[10,11] (4) Ph, Ph, O-*i*-Pr;[11] (5) Ph, Ph, OMe; (6) Et, OMe, OMe; (7) Me, OMe, OMe; (8) Bu, OMe, OMe; (9) Et, OMe, OMe; (10) Ph, O-*i*-Pr, O-*i*-Pr;[11] (11) PH, OMe, OMe; (12) O-*i*-Pr, O-*i*-Pr, O-*i*-Pr;[11] (13) OMe, OMe, OMe; (14) OMe, OMe, OMe.[12] Most of the literature rates are in acetonitrile, but our studies in chloroform are also included. Temperatures were 25–30 °C, and no corrections were attempted, except for the point marked 13, our measurement at 55 °C.

In addition to the data presented in the tables, several other runs were done, not directly comparable to those in the tables. Using proton NMR, two of some interest are A = OMe, B = OMe, X = I at 55 °C in CD_3CN, $k_1 = 1.1 \times 10^{-4}$ M^{-1} s^{-1}, and A = Ph, B = Ph, X = OTos, $k_1 = 2.9 \times 10^{-4}$ M^{-1} s^{-1} at 34.4 °C. In this latter case, **2** (with X = OTos) was detected, but not at a level allowing evaluation of k_2. The constant k_3 did not appear to be required.

Discussion

The rates of reaction 1 with X = I can be compared with some in the literature, although no direct comparisons are possible. The values of log k for reaction of trivalent phosphorus compounds with methyl iodide[10-12] are plotted in Figure 2 against $\sum\sigma_i$, the sum of the Taft inductive constants[13] for the three substituents on phosphorus together with the values from Table I. The plot is by no means perfect, but it does serve to show that the current results are not in gross disagreement with literature values. The slope of this plot is about −3. Although we have no data for a direct comparison, an indirect comparison with the protonation equilibrium of phosphines, for which the corresponding slope is about 4 times as great, suggests that there is not much charge developed at the transition state. Similarly, Aksnes and Aksnes'[5] rate constant of 2×10^{-5} M^{-1} s^{-1} for ethyl iodide with triethyl phosphite at 60 °C is not grossly out of line with our 1.1×10^{-4} M^{-1} s^{-1} value for methyl iodide at 55 °C with trimethyl phosphite; most of the difference lies in the well-known slower reaction of ethyl iodide than methyl iodide.

(7) This is known kinetically, for example, in thre rates with the *p*-nitrophenoxide ion (Lewis, E. S.; Vanderpool, S. H. *J. Am. Chem. Soc.* **1978**, *100*, 6421–6424), and in equilibrium sense by E. S. Lewis and M. J. Smith, unpublished (dimethyl sulfate reacts virtually quantitatively with I^- in sulfolane).

(8) Nesterov, L. V.; Aleksandrova, N. A. *J. Gen. Chem. USSR (Engl. Transl.)* **1980**, *50*, 29; *Zh. Obshch. Khim.* **1980**, *50*, 36–39.

(9) Cachaza, J. M.; Casado, J.; Varela, A. *Rev. Roum. Chim.* **1977**, *22*, 213–220.

(10) Quemeneur, F.; Barious, B.; Kerfanto, M. *C. R. Hebd. Seances, Acad. Sci., Ser. C* **1977**, *285*, 155–157.

(11) Hall, C. D.; Edwards, R. C.; Lloyd, J. R.; Beer, P. D.; Hammond, P. J.; Alberto, O. D.; Melrose, M. P. *ACS Symp. Ser.* **1981**, *No. 171*, 551–553.

(12) Thorstenson, T.; Songstad, J. *Acta Chem. Scand., Ser. A* **1976**, *A30*, 781–786.

(13) The σ_i values are taken from: Charton, M. "Progress in Physical Organic Chemistry"; Wiley: New York, 1981; pp 119–251.

(14) Lewis, E. S.; Kukes, S.; Slater, C. D. *J. Am. Chem. Soc.* **1980**, *102*, 1619–1623.

(15) Lewis, E. S.; Colle, K. S. *J. Org. Chem.* **1981**, *46*, 4369–4372.

We can note some features of the current data. They show a rather remarkably small difference between the acetonitrile and chloroform solvent, in some cases the chloroform rates are actually higher for this reaction leading to an ion pair. In view of the lower precision of the data in acetonitrile, where there were often side reactions, this inversion in the expected order may not be significant, but the fact that the solvent effect is small cannot result from experimental error. We must conclude that little solvation of the forming ion pair has taken place at the transition state. A *very* early transition state is not appropriate either since there is a substantial substituent effect, a range of a factor of 30 in Table I. It is not clear whether the small solvent effect is compatible with the development of about a quarter of a unit positive charge suggested by the substituent effect.

The results show that methyl iodide reacts in one case about 5 times faster than methyl tosylate and in a few others about 2–3 times faster than dimethyl sulfate. These same methylating agents react[7] with *p*-nitrophenoxide ion in the ratio MeI:Me_2O_4S:MeOTos 1:8:0.2 and with thiophenoxide in the ratio 1:0.18:0.007. The sequence is more like the "soft" thiophenoxide, but the range is far smaller.

Substituent effects on reactions 2 and 3 are far less clear, mainly because most come from the quite uncertain data of Table III. The values of k_3 in Tables II and III can be compared; the three cases that can be directly compared are larger in Table II than in Table III. Although this might be an effect of the counterion either within a reactive ion pair or on the extent of ion-pair dissociation, the values in Table III are uncertain enough to make such an interpretation unreliable. The substituent effects on k_3 show little variation with substituent, as might be expected for an S_N2 substitution with opposing electronic effects on the nucleophile and the leaving group. We expected a small substituent effect in the same direction as that on k_1, since the substituents are closer to the nucleophilic phosphorus in 1 than they are to the leaving oxygen in 2. There is little support for this expectation.

The case of methyl di-*t*-butylphosphinite deserves special comment, since the expected Arbuzov product, di-*t*-butylmethylphosphine oxide is virtually completely methylated by dimethyl sulfate. This one case with dimethyl sulfate is then quite parallel to all the reactions with methyl triflate. Dimethyl sulfate is about 100 times less powerful than methyl triflate as a methylating agent in an equilibrium sense,[7] but this particular product is certainly the best nucleophile, and methyltriflate methylates the other products nearly quantitatively, so the result is not surprising.

Conclusions

The contribution of the autocatalytic mechanism is clearly demonstrated for Arbuzov reactions with dimethyl sulfate. It is the only mechanism with methyl triflate and is undetectable with methyl iodide. Rate constants are presented for the various reactions that are disappointingly rough, both because of analytical difficulties and the problems of unraveling the complex reaction course, leading to plausible substituent effects only on the first step, the alkylation of the trivalent phosphorus ester. In spite of the difficulties, the ^{31}P analysis appears to be for many cases the method of choice to follow the kinetics of phosphorus reactions.

Experimental Section

The 90-MHz proton spectra were obtained on a Varian EM-390 spectrometer. A Jeolco FX-90Q instrument operating in the Fourier transform mode was used for all ^{31}P kinetic studies. Acetonitrile-d_3 was distilled once from CaH_2; followed by distillation from P_2O_5. $CDCl_3$ was distilled form CaH_2 and stored under nitrogen in a lightproof container. Methyl (trifluoromethyl)sulfonate (methyl triflate) was purchased from Aldrich and generally used without further purification. Its purity could be maintained by storage in the freezer under N_2. Dimethyl sulfate was distilled form CaH_2. Trimethyl phosphite, dimethyl ethylphosphonite, dimethyl methylphosphonite, dimethyl phenylphosphonite, methyl di-*t*-butylphosphinite, and dimethyl *t*-butylphosphonite (Ventron) were used directly or distilled form CaH_2 if ^{31}P NMR indicated greater than 5% contamination. Residual contaminants appeared inert. Methyl triflate, methyl iodide, and dimethyl sulfate (as powerful alkylating agents) are toxic and must be handled with care.

Kinetics. For those reactions monitored by ^1H NMR (Tables I and II), sample preparation and data workup were as follows. In the drybox a 0.30-mL aliquot of the 0.05–0.30 M trivalent phosphorus compound solution in the solvent (CD_3CN) was added to an NMR tube followed by 0.05–0.3 mmol of the methylating agent and a measured amount of benzene (as the NMR internal standard). The tube was removed from the drybox, cooled to −78 °C in an atmosphere of argon, evacuated to 0.1 torr, and sealed. This mixing procedure was usually too slow with methyl triflate as the electrophile. In such cases reagents were mixed at room temperature under a flow of nitrogen, and the reaction was monitored in unsealed tubes. With either procedures Me_4Si was not added to the solution because a large enough concentration for a stable lock substantially alters the solvent, and spectra were recorded unlocked. Rates were measured at 34.4 °C, the ambient temperature of the probe. This temperature varied less than 0.2 °C as measured with a thermometer, although we estimate that the actual temperature of the solution in a spinning NMR tube is uncertain to 0.5 °C.

During a kinetic experiment, between 20 and 30 spectra were recorded and integrated. The area of the methoxy phosphorus doublet at δ 4.0–4.2 was used to monitor the disappearance of the trivalent phosphorus reactant, with the area of the benzene singlet used as an internal standard. When nearby absorbances interfered with the integration, the corresponding peak heights, were substituted. Using either areas or peak heights, concentrations could be measured to better than 10%. Data were fit by using pseudo-first-order kinetics. The second order rate constant (k_1 in Table I) was obtained by dividing the first-order rate constant by the concentration of the methylating agent.

When the rearrangement was to be followed by using Fourier transform ^{31}P NMR, similar sample preparation techniques were employed. Kinetics were run in 5-mm tubes with a concentric 1-mm tube containing (85%) H_3PO_4 serving as an external reference (and D_3PO_4 was also used as an external deuterium lock in some unreported experiments with undeuterated solvents). Data acquisition parameters included a 45° pulse of 5.2 μs with a 12-s interpulse delay. Spectra were broad-band proton decoupled with the decoupling irradiation power gated to minimize NOE.[16] The number of transients collected for a single spectrum depended upon the rate of reaction during the period of accumulation. Generally, a run was begun with the collection and storage of 7 FID's each containing three pulses followed by 7 or 14 5-pulse FID's, with the remainder of the kinetic data contained in FID's of 15 pulses. The delay period between each set of pulses also depended upon the rate and varied from under a minute to several hours. Once the rearrangement was complete the stored FID's were Fourier transformed under identical conditions (exponential correction factor = 3 Hz, 8k FID zero filled to give a 16k spectrum) and phase corrected. Peaks heights were used to measure the concentrations of 1, 2, and 3 with the phosphoric acid peak used as an internal quantitative standard to normalize gain differences between the spectra.[17] The proportionality constant relating peak heights to molarity was calculated form the extrapolated peak height for ABPOMe at time zero or/and

(16) Freeman, R.; Hill, H. D. W.; Kaptein, R. *J. Magn. Reson.* **1972**, *7*, 327.

(17) A discussion of the relative merits of using peak areas vs. peak heights will be presented in a later pubilication. Briefly, with broadband decoupling there is good linear relationship between concentration and peak height over a wide range of pulse delays and pulse number.

the peak height of ABMeP=O at infinite time when the rearrangement went to completion. In several earlier cases, before gated decoupling was used, concentrations obtained for the phosphonium intermediate were much too high as result of great nuclear Overhauser enhancement of the intermediate peak relative to the reactant and product. It was necessary to adjust these concentrations by using the material balance. The ^{31}P chemical shifts for the phosphonium intermediates $ABMeP^+OMeX^-$ are, with substituents A and B followed by the parenthsized chemical shifts, measured in ppm downfield from phosphoric acid: Et, OMe (98); Ph, OMe (79) (both in CD_3CN) and *t*-Bu, *t*-Bu (108); *t*-Bu, OMe (98) (in $CDCl_3$).

Rate Constant Calculation

The rough experimental concentration vs. time curves for ABPOMe, $ABMeP^+OMeX^-$, and ABMeP=O were smoothed and the data points evenly spaced over time by using a variable-order polynomial fit routine.[18] The differential equations 4–7 describing the rearrangement were integrated by using fourth-order Runge Kutta numberical techniques[19] and a theoretical concentration vs time curve constructed for each of the phosphorus-containing species. Using iterative techniques adapted from those of Wiberg,[20] the "best" rate constants were obtained by minimizing the root-mean-square error between one of the theoretical curves and the corresponding experimental one. The rate constants shown in Table III are those that gave the lowest root-mean-square eror for all three of the curves. A graphics display similar to that in Figure 2 was used to subjectively select the most satisfactory constants when the program encountered a braod root-mean-square error minimum.

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Registry No. $CH_3P(OCH_3)_2$, 20278-51-7; $PhP(OCH_3)_2$, 2946-61-4; $EtP(OCH_3)_2$, 15715-42-1; *t*-$BuP(OCH_3)_2$, 32045-17-3; Ph_2POCH_3, 4020-99-9; $(t\text{-Bu})_2POCH_3$, 70073-11-9; $P(OCH_3)_3$, 121-45-9; methyl triflate, 333-27-7; dimethyl sulfate, 77-78-1; methyl iodide, 74-88-4.

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Circular Dichroism Studies on Three Isomeric Dimethylbenzo-15-crown-5 Ethers and Some of Their Complexes[1]

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With ethyl lactate as an optically active precursor and with employment of Williamson reactions, three isomeric and axially symmetric dimethylbenzo-15-crown-5 ethers were prepared and characterized: (5*R*,15*R*)-5,15-dimethyl-5,6,8,9,11,12,14,15-octahydrobenzo[*b*]-1,4,7,10,13-pentaoxacyclopentadecin and the (6*S*,14*S*)-6,14-dimethyl and (8*S*,12*S*)-8,12-dimethyl isomers, termed the α, β, and γ isomers, respectively. The circular dichroism spectra of the ethers and their complexes with Na^+ in CH_3OH have been determined and interpreted in terms of the gross overall orientation of the macrocycle in relation to the aromatic ring. The behavior of the γ isomer with Ba^{2+} and with low ratios of K^+ suggests dominance of 2:1 (sandwich) complexes.

The macrocyclic polyethers[2] have provided chemists with a fruitful territory for exploration since the initial comprehensive report[3] of their properties of 1967. Like their relatives the cyclic polypeptides and polyesters, the polyethers (dubbed "crowns" by Pedersen, their discoverer/inventor) possess the ability to moderate the inhospitality which nonpolar solvents ordinarily display toward ionic species. The charge on the cations is dispersed by the complexand or ionophore, which, depending on the match in sizes, can encircle or envelop the ion. The interaction between the two is clearly ion–dipole in the case of cations of main groups 1 and 2, involves hydrogen bonding in the case of ammonium ions, and possesses at least some degree of covalent character in the case of the transition metals.[4] In polar media there exists, of course, a competition for the cation between solvent and macrocycle; which interaction dominates will depend on the nature of the particular solvent, salt, and complexand and will govern the stability of the complex under the specific circumstances.

A number of crown ether complexes have been prepared in crystalline form, and X-ray diffraction[5] has been employed to establish the spatial relationship of macrocycle to cation, as well as the conformation of the former.

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