neighboring C–C bond insertion the desired ring-expanded carbenium ion, which is then reduced to give the hydrocarbon product.

Experimental Section

1-Adamantanemethyl alcohol, 1-adamantanecarboxylic acid, 3-noradamantanecarboxylic acid, cyclobutanecarboxylic acid, cyclopentanecarboxylic acid, and neopentylcarboxylic acid and alcohol were available from Aldrich. 3-Noradamantanemethyl alcohol was prepared from the corresponding carboxylic acid by reduction with $LiAlH_4$. 1-Norbornanemethyl alcohol was prepared by reduction of the corresponding carboxylic acid prepared according to literature procedure.[10]

Sodium borohydride (Aldrich) and trifluoromethanesulfonic (triflic) acid (3 M) were commercially available. The latter was distilled prior to use. Diethyl ether was dried over sodium under reflux prior to use.

Gas chromatographic analysis was carried out on a Varian (Model 3700) Gas Chromatograph with use of a quartz silica capillary column coated with DB-1. Mass spectroscopic analysis was performed on a Finnigan Mat Model 700 GC–MS spectrometer. NMR spectra were recorded on a Varian-200 MHz (VXR-200) superconducting NMR spectrometer.

General Method of Reductive Isomerization of Cycloalkylmethyl Alcohols and Carboxylic Acids to Homologated Hydrocarbons. To a well-stirred heterogeneous mixture of 1.0 g (6.02 mmol) of 1-adamantane methyl alcohol in diethyl ether and 0.46 g (12.04 mmol) of $NaBH_4$ taken in a three-necked flask cooled to −78 °C under dry nitrogen flow was added 6.4 mL (72.24 mmol) of triflic acid dropwise over a period of $^1/_2$ h. After the addition of acid the reaction mixture was slowly warmed up to room temperature at which stirring was continued for an additional 2 h. Quenching the reaction mixture in ice–bicarbonate followed by extraction in methylene chloride, drying the reaction solution over anhydrous $MgSO_4$, and removal of solvent afforded crude homoadamantane, which subsequently was purified by column chromatography (silica gel/hexane). Reduction of all other cycloalkylmethyl alcohols and carboxylic acids was similarly carried out except that in the case of carboxylic acids higher ratio of carboxylic acid:$NaBH_4$:HOTf ≈ 1:3:18 was used.

Acknowledgment. Support of our work by the National Institutes of Health is gratefully acknowledged.

Registry No. 1-Adamantanemethyl alcohol, 770-71-8; 1-adamantanecarboxylic acid, 828-51-3; homoadamantane, 281-46-9; 3-noradamantanemethyl alcohol, 17471-43-1; 3-noradamantanecarboxylic acid, 16200-53-6; adamantane, 281-23-2; 1-norbornanemethyl alcohol, 2064-02-0; 1-norbornanecarboxylic acid, 18720-30-4; bicyclo[2.2.2]octane, 280-33-1; cyclobutanemethyl alcohol, 4415-82-1; cyclobutanecarboxylic acid, 3721-95-7; cyclopentane, 287-92-3; cyclopentanemethyl alcohol, 3637-61-4; cyclopentanecarboxylic acid, 3400-45-1; cyclohexane, 110-82-7; neopentylmethyl alcohol, 75-84-3; neopentylcarboxylic acid, 75-98-9; 2-methylbutane, 281-23-2; 1-methyladamantane, 768-91-2.

(10) Bixler, R. L.; Niemann, C. *J. Org. Chem.* **1958**, *23*, 7421.

Rate Enhancement of Nucleophilic Substitution Reactions in Phosphate Esters. Influence of Conformational Transmission on the Rate of Solvolysis of Alkyl Diphenylphosphinates

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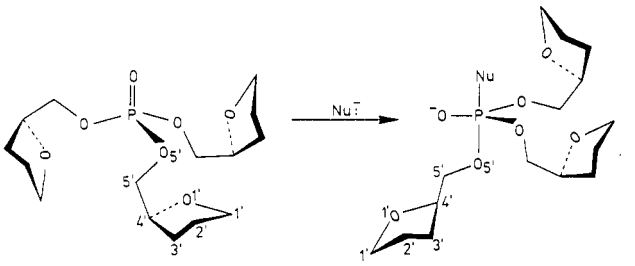
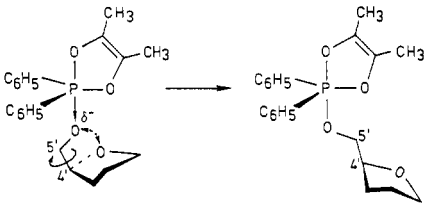
Introduction

The concept of conformational transmission in pentacoordinated (P(V)) trigonal-bipyramidal (TBP) phosphorus compounds has received considerable attention during the past few years.[1] In these studies it has been shown that phosphorus compounds possessing the common POCCO fragment are subject to a conformational rearrangement around the central C–C linkage of this fragment if the coordination state of the phosphorus atom is increased from four (P(IV)) to five (P(V)-TBP).

Scheme I



Scheme II



The incorporation of an additional ligand in a P(IV) geometry causes a considerable change in the intrinsic chemical bonding properties of the central phosphorus atom,[2] resulting in an enhanced electron density on the axially located oxygens linked directly to phosphorus. In its turn, this effect is transmitted into a conformational change around the central C–C linkage of the axially located OCCO moiety. The actual conformation of the OCCO atomic sequence is changed from the well-known gauche orientation in the P(IV) state to a pronounced anti orientation of the two vicinally orientated oxygen atoms in the P(V)-TBP state. The result of this conformational change is visualized in Scheme I.

In recent ^{13}C NMR variable-temperature studies on a series of stable oxyphosphoranes, the impact of the conformational transmission effect on the rate of intramolecular ligand reorganization in pentacoordinated oxyphosphoranes has been described.[3] In these studies it was demonstrated that pseudorotation in P(V)-TBP compounds exhibiting the conformational transmission effect is 2–4 times faster as compared to that in their counterparts in which this effect is absent. It was shown that, with the acceptance of the intermediacy of a square-pyramidal (SP) transition state in controlling the pseudorotation rate, conformational transmission in the basal ligands of the SP is responsible for the lowering of the free energy barrier of the pseudorotation process.

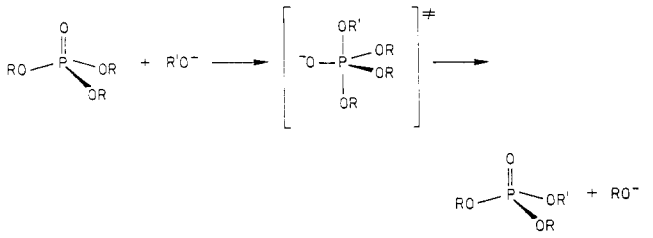
(1) (a) Koole, L. H.; Lanters, E. J.; Buck, H. M. *J. Am. Chem. Soc.* **1984**, *106*, 5451. (b) Koole, L. H.; van Kooyk, R. J. L.; Buck, H. M. *J. Am. Chem. Soc.* **1985**, *107*, 4032. (c) Meulendijks, G. H. W. M.; van Es, W.; de Haan, J. W.; Buck, H. M. *Eur. J. Biochem.* **1986**, *157*, 421. (d) De Vries, N. K.; Buck, H. M. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 150. (e) Van Genderen, M. H. P.; Koole, L. H.; Olde Scheper, B. C. C. M.; van de Ven, L. J. M.; Buck, H. M. *Phosphorus Sulfur* **1987**, *32*, 173. (f) De Vries, N. K.; Buck, H. M. *Phosphorus Sulfur* **1987**, *31*, 267. (g) Van Genderen, M. H. P.; Buck, H. M. *Magn. Reson. Chem.* **1987**, *25*, 872.

(2) Holmes, R. R. *Pentacoordinated Phosphorus*; American Chemical Society: Washington, 1980; Vols. 1 and 2 (ACS Monograph No. 175 and 176).

(3) (a) De Keijzer, A. E. H.; Koole, L. H.; Buck, H. M. *J. Am. Chem. Soc.* **1988**, *110*, 5995, (b) De Keijzer, A. E. H.; Buck, H. M. *J. Org. Chem.* **1988**, *53*, 4827.

0022-3263/89/1954-1453$01.50/0

Scheme III



From these studies another important conclusion emerged, i.e. that the occurrence of conformational transmission in the axis of a P(V)-TBP structure gives rise to a net stabilization of this structure as compared to the pentacoordinated counterparts in which no conformational transmission occurs. The stabilization is due to a conformational change[4] around the $C_{4'}$–$C_{5'}$ bond, from a g^+ to a g^- state, as is visualized in Scheme II.

In the present paper the attention is focused on the possible influence of the conformational transmission effect on the solvolysis rate of phosphate esters, since these compounds are of particular importance in the biosynthesis of biochemical intermediates.

The mechanisms of the chemical reactions of e.g. adenosine triphosphate (ATP), and in fact of all reactions that involve the formation and destruction of phosphate esters are vital to the understanding of the chemistry of biologically indispensible phosphate esters. It is therefore important to establish and study the possible mechanisms that can be operative in these reactions. In this paper a ^{31}P NMR kinetic study on the solvolysis reactions of phosphate esters is described. A number of phosphates is examined in which, during the course of the solvolysis reaction, the conformational transmission effect is bound to be present or absent, respectively. Hence, the influence of the conformational transmission effect on the rate of solvolysis of phosphate esters could be determined.

Results and Discussion

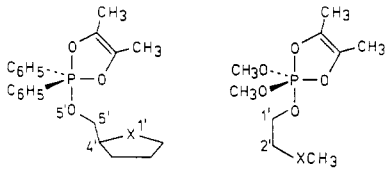
Alkaline Hydrolysis of Phosphate Esters. It has been known for many years that the hydrolysis of trialkyl phosphates in alkaline solution is first order in both hydroxide and ester.[6] Furthermore, it has been inferred from isotopic tracer studies[7] that during these reactions only the phosphorus–oxygen bonds are broken; the carbon–oxygen bonds remain unimpaired. It was also emphasized that the vast majority of the second-order nucleophilic displacement reactions at phosphorus proceed with inversion of configuration at phosphorus, as was elegantly demonstrated by Green et al.[8] using ^{14}C-labeled phosphinates.

The kinetic order of the hydrolysis reactions, together with the position of the bond fission and the inversion of configuration at phosphorus, establishes that the hydroxide ion attacks the phosphorus atom in a $S_N2(P)$ type reaction involving a pentacoordinated transition state.[9] The course of such a reaction is visualized in Scheme III.

Experiments concerning the hydrolysis of dialkyl phosphonates and monoalkyl phosphinates show that these compounds behave in an analogous way.[6b] When an alkoxide ion is the nucleophile attacking an ester of phosphorus acid, a transesterification reaction is the result. This type of reaction has been employed for many synthetic purposes, and it is shown that the mechanism closely resembles that of the reaction with a hydroxide ion.[8,9]

The effect of substituents in the ester groups on the reaction rate is presumed to be very large, and, therefore, both steric and electronic factors must be considered. In order to investigate the possible influence of the conformational transmission effect on the rate of solvolysis, it is therefore imperative that the model compounds are well-chosen.

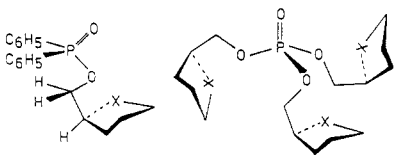
Model Compounds for the Solvolysis Reactions. From recent 300-MHz ^1H NMR studies[1a] on a set of 5′-P(IV) and 5′-P(V)-TBP tetrahydrofurfuryl and cyclopentanemethyl compounds **1a** and **1b** as well as an additional study[1e] involving the phosphoranes **2a** and **2b**, it was concluded that in both types of phosphoranes the conformational transmission effect becomes operative in the axis of the TBP in case X = O.



1a : X = O
1b : X = CH_2

2a : X = O
2b : X = CH_2

On the basis of these studies, it becomes clear that many phosphate esters are suitable for the chosen purpose, as long as a POCCO moiety is incorporated in the molecule. In principle both types of phosphate esters **3** and **4** can be used to examine the influence of the conformational transmission effect on the course of the solvolysis reaction. To ascertain the axial location of the tetrahydrofurfuryl and cyclopentanemethyl moieties in the P(V)-TBP transition states, therefore, allowing the conformational transmission effect to express itself to its full extent, the diphenylphosphinates **3a** and **3b** were selected as model compounds.

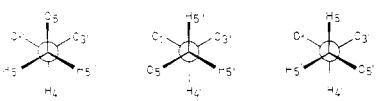


3a : X = O
3b : X = CH_2

4a : X = O
4b : X = CH_2

In the transition states of the solvolysis reactions of these compounds the two phenyl groups, together with the O^- group formed, will occupy the equatorial positions,[10] therefore, forcing the tetrahydrofurfuryl and cyclopentanemethyl group to take up an axial position.[11]

(4) In solution a rapid interconversion between the three conformations g^+, g^t and g^- exists. The rotamer populations can be obtained[1a] by using the empirically generalized Karplus relation developed by Haasnoot et al.[5]



(5) Haasnoot, C. A. G.; de Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.

(6) (a) Kirby, A. J.; Warren, S. G. *The Organic Chemistry of Phosphorus*; Elsevier: Amsterdam, 1967. (b) Cox, J. R., Jr.; Ramsay, O. B. *Chem. Rev.* **1964**, *64*, 317.

(7) (a) Åkerfeldt, S. *Nature* **1963**, *200*, 881. (b) Blumenthal, E.; Herbert, J. B. M. *Trans. Faraday Soc.* **1945**, *41*, 611.

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(9) Westheimer, F. H. *Acc. Chem. Res.* **1968**, *1*, 70.

(10) Luckenbach, R. *Dynamic Stereochemistry of Pentacoordinated Phosphorus and Related Elements*; George Thieme Verlag: Stuttgart, 1973.

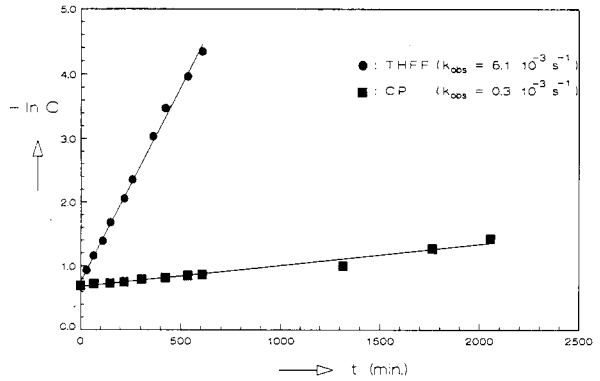

Figure 1. Graphical representation of the pseudo-first-order kinetics of the simultaneous solvolysis of compounds **3a** (THFF) and **3b** (CP) in a semilogarithmic plot.[13]

Moreover, it can be deduced that according to the apicophilicity preference rules,[12] the three equatorial ligands will further stabilize the P(V)-TBP ground state. Therefore, pseudorotation processes that might obscure the influence of the conformational transmission effect are slowed down to such an extent that they no longer interfere with the course of the reaction.

Solvolysis of Alkyl Diphenylphosphinates. As is stated above, the solvolysis reaction is second order overall. This is consistent with the reaction eq 1.

$$(C_6H_5)_2P(O)OR + CH_3O^- \rightarrow (C_6H_5)_2P(O)OCH_3 + RO^- \quad (1)$$

In these particular experiments, however, a second reaction (eq 2) between the solvent and the RO^- ions takes place almost simultaneously. As a result a steady state

$$RO^- + CH_3OH \rightleftarrows ROH + CH_3O^- \quad (2)$$

is reached in which the CH_3O^- concentration has a constant value. Normally, the equilibrium in reaction 2 lies far to the left, but in these experiments it is shifted toward the right due to the large excess of methanol (solvent) and the formation of RO^- in reaction 1. Consequently, the reaction becomes pseudo-first-order, with the reaction rate proportional to the concentration of the phosphate only.[14] From a graphic representation, in which $-\ln C$ (C is the concentration of the phosphate being consumed) is plotted as a function of time, t, it is now possible to obtain the specific rate constant, k.

The reaction rate of the solvolysis of both phosphates was determined in several experimental runs. Two types of experiments were performed. In one type the solvolysis rate of the phosphates was determined in separate runs, and in another type the solvolysis of both phosphates was examined simultaneously in the same experimental run. A representative plot of one of the runs in which both phosphates solvolyse simultaneously is given in Figure 1. The kinetic data of the solvolysis reactions of compounds **3a** and **3b** are summarized in Table I.

Table I. Rate Constants for the Reaction of Compounds 3a and 3b with Sodium Methoxide in Methanol at 25 °C

	R[a]	k_{obsd}[b]	k[c]	k_O/k_{CH_2}[d]
3a	THFF	1.5×10^{-3}	4.6×10^{-3}	22
3b	CP	6.9×10^{-5}	2.1×10^{-4}	
3a	THFF	6.1×10^{-3}	6.1×10^{-3}	20
3b	CP	3.0×10^{-4}	3.0×10^{-4}	

[a] THFF = tetrahydrofurfuryl, CP = cyclopentanemethyl. [b] k_{obsd} (in s^{-1}) is equal to $k[CH_3O^-]$ and is obtained directly from the semilogarithmic plot. [c] Specific rate constant (in L mol^{-1} s^{-1}). Discrepancies between separate and simultaneous runs are probably caused by a difference in basicity of CPO^- and $THFFO^-$, resulting in a slightly different equilibrium value for $[CH_3O^-]$. [d] Rate constant ratio for the solvolysis reactions, comparing compounds with X = O and X = CH_2, respectively.

From the data presented in this table it can be concluded that the occurrence of conformational transmission during the solvolysis reaction of dialkylphosphinates in which the POCCO fragment is present results in a rate enhancement of the reaction.

From the values obtained for k_O/k_{CH_2} it can be deduced that the solvolysis reaction of compound **3a**, in which conformational transmission occurs, is 20 times faster than that in compound **3b** in which this effect is absent.

Preliminary experiments regarding the analogous diethoxy compounds showed that the conformational transmission effect also influences the solvolysis rate in these compounds to a considerable extent.[15] It can, therefore, be concluded that, in general, the conformational transmission effect has an accelerating influence on the solvolysis rate of phosphate esters incorporating a POCCO atomic sequence.

Conclusion

This study clearly demonstrates the influence of the conformational transmission effect on the rates of solvolysis in alkyl diphenylphosphinates. It clearly shows that the presence of conformational transmission has an accelerating effect on the nucleophilic displacement reactions at phosphorus.

Experimental Section

Spectroscopy. All NMR spectra were run in the FT mode on a Bruker AC-200 spectrometer. The chemical shifts in the ^1H and ^{13}C NMR spectra, which were recorded at 200.1 and 50.3 MHz, respectively, are referenced against TMS as internal standard ($\delta = 0$). The chemical shifts in the ^{31}P NMR spectra, recorded at 80.9 MHz, are related to 85% H_3PO_4 as external standard and are designated positive if downfield with respect to the reference. During the recording of the spectra for the solvolysis experiments, a 64K data base and a 4000-Hz sweep width were employed. All spectra were recorded in CD_3OD unless stated otherwise.

Synthesis. All solvents and commercial reagents were reagent grade and were dried prior to use with the appropriate drying agents. All moisture-sensitive compounds were handled under a dry nitrogen atmosphere throughout the experiments. The general instability of the phosphinites has precluded the obtention of standard analytical data. The identification of these compounds, rests, therefore, on ^1H, ^{13}C and ^{31}P NMR spectroscopy,

(11) It should be noted that compound **1a** shows pseudorotation around the pentacoordinated phosphorus.[1a] The C_4–C_5 rotamer populations for axial and equatorial tetrahydrofurfuryl have been assessed in our previous work[1a] (Axial: $x(g^+) = 0.21$, $x(g^t) = 0.11$, $x(g^-) = 0.68$. Equatorial: $x(g^+) = 0.39$, $x(g^t) = 0.41$, $x(g^-) = 0.20$). Pseudorotation is more difficult for the intermediate in the solvolysis of **3a,b**, since O^- strongly prefers equatorial location in the TBP.[10] Furthermore, pseudorotation can not lead to additional reaction products, since no P–(C_6H_5) bond cleavage can occur.

(12) Gillespie, P.; Hoffman, P.; Klusacek, H.; Marquarding, D.; Pfohl, S.; Ramirez, F.; Tsolis, E. A.; Ugi, *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 687.

(13) For reasons of clarity several data points have been omitted in the left half of the plot.

(14) During the experimental runs, especially those comprising a larger period of time, a consecutive reaction appeared to take place. In examining this reaction it was shown that the initially formed $(C_6H_5)_2P(O)OCH_3$ reacts with CH_3O^-, to give CH_3OCH_3 and $(C_6H_5)_2P(O)O^-$, following second-order kinetics. The rate of this reaction was established in an analogous way in several separate runs with authentic samples of $(C_6H_5)_2P(O)OCH_3$. In this way the specific rate constant belonging to this consecutive reaction could be determined: $k = 5.0.10^{-6}$ L mol^{-1} s^{-1}. The rate of the reaction, however, is so low that no interference with the major reaction is found. For reasons of clarity this consecutive reaction has not been included in the major reaction sequence 1.

(15) Olders, E.; Koole, L. H.; Buck, H. M. Unpublished results.

methods of preparation, and comparison of the obtained data with those presented in literature.

Phosphinites. The phosphinites were prepared from the corresponding alcohols and $(C_6H_5)_2PCl$ according to the procedure described by Koole et al.[1a]

Tetrahydrofurfuryl Diphenylphosphinite. Bp: 154–156 °C (0.01 mm). Yield: 74%. ^1H NMR ($CDCl_3$): δ 1.58–1.97 (m, 4 H, $H_{2'}/H_{3'}$), 3.62–3.94 (m, 4 H, $H_{1'}/POCH_2$), 4.09 (m, 1 H, $H_{4'}$), 7.19–7.58 (m, 10 H, Ar H). ^{13}C NMR ($CDCl_3$): δ 25.4 ($C_{2'}$), 27.7 ($C_{3'}$), 68.0 ($C_{1'}$), 71.0 ($C_{5'}$), 78.1 ($C_{4'}$), 127.9–130.4 (Ar C), 141.8 (ipso C). ^{31}P NMR ($CDCl_3$): δ 115.9.

Cyclopentylmethyl Diphenylphosphinite. Bp: 161–163 °C (0.01 mm). Yield: 65%. ^1H NMR ($CDCl_3$): δ 1.15–1.82 (m, 8 H, cyclopentane H), 2.26 (m, 1 H, $H_{4'}$), 3.71 (dd, 2 H, $POCH_2$), 7.20–7.60 (m, 10 H, Ar H). ^{13}C NMR ($CDCl_3$): δ 25.4 ($C_{1'}/C_{3'}$), 29.3 ($C_{1'}/C_{2'}$), 41.0 ($C_{4'}$), 74.2 ($C_{5'}$), 128.0–130.5 (Ar C), 142.3 (ipso C). ^{31}P NMR ($CDCl_3$): δ 112.2.

Phosphinates. The phosphinates were obtained by oxidation of the corresponding phosphinates. An ozone-oxygen stream was passed through a solution of the phosphinate in dry dichloromethane at 0 °C. After 1 h the solution was sparged with oxygen and allowed to warm to room temperature. Evaporation of the solvent yielded the desired phosphinates, as was confirmed by ^{31}P NMR and elemental analysis.

Tetrahydrofurfuryl Diphenylphosphinate (3a). ^1H NMR (CD_3COCD_3): δ 1.78–2.11 (m, 4 H, $H_{2'}/H_{3'}$), 3.79 (m, 2 H, $H_{1'}$), 4.07 (m, 2 H, $POCH_2$), 4.22 (m, 1 H, $H_{4'}$), 7.55–8.08 (m, 10 H, Ar H). ^{13}C NMR (CD_3COCD_3): δ 27.1 ($C_{2'}$), 29.1 ($C_{3'}$), 68.4 ($C_{1'}$), 69.5 ($C_{5'}$), 78.9 ($C_{4'}$), 130.0–134.2 (Ar C), 142.1 (ipso C). ^{31}P NMR: δ 39.4. Anal. Calcd for $C_{17}H_{19}O_3P$: C, 67.54; H, 6.34. Found: C, 67.48; H, 6.36.

Cyclopentylmethyl Diphenylphosphinate (3b). ^1H NMR: δ 1.03–1.79 (m, 8 H, cyclopentane H), 2.16 (m, 1 H, $H_{4'}$), 3.76 (t, 2 H, $POCH_2$), 7.23–7.81 (m, 10 H, Ar H). ^{13}C NMR: δ 26.2 ($C_{1'}/C_{3'}$), 29.9 ($C_{1'}/C_{2'}$), 41.3 ($C_{4'}$), 70.0 ($C_{5'}$), 129.7–133.8 (Ar C). ^{31}P NMR: δ 38.4. Anal. Calcd for $C_{18}H_{21}O_2P$: C, 71.99; H, 7.05. Found: C, 72.13; H, 6.94.

Solvolysis Experiments. In order to investigate the course of the solvolysis reactions and to allow the determination of the specific rate constants belonging to these reactions, the following typical procedure was employed.

A solution of 16.5 mmol of the desired alkyl diphenylphosphinate in 25 mL of dry CH_3OH was prepared in a 100-mL double-walled reaction vessel, which was connected to a constant-temperature bath with a sufficiently large capacity, ensuring a temperature of 25 ± 0.1 °C.

To eliminate the possibility of a reaction of the phosphinate ester with the solvent, the solution was kept at 25 °C in the reaction vessel overnight. Comparison of the ^{31}P NMR spectra recorded before and after this period of time showed that no reaction had taken place.

To the resulting solution was added 16.5 mmol of freshly prepared $NaOCH_3$ in 25 mL of CH_3OH, leaving an equimolar solution of the alkyl diphenylphosphinate and methoxide. At regular intervals small aliquots of the reaction mixture were taken from the reaction vessel and transferred into a NMR tube equipped with a small reference tube providing an external deuterium lock; the ^{31}P NMR spectrum of the sample was scanned and integrated. In this way the disappearance of the alkyl diphenylphosphinate signal was measured and the specific reaction rate of the solvolysis reaction was determined.

Several experimental runs using different phosphinate and methoxide concentrations were performed in order to appoint the exact reaction order and to exclude any irregularities influencing the accuracy of the determination of the specific rate constant. An analogous procedure was applied for the experimental runs in which both phosphinates were allowed to react simultaneously.

Acknowledgment. This investigation has been supported in part by the Netherlands Foundation for Chemical Research (SON), with financial aid from the Netherlands Organization for Scientific Research (NWO).

Registry No. **1a**, 91237-87-5; **1b**, 91237-90-0; **3a**, 91237-85-3; **3b**, 91237-89-7; $(C_6H_5)_2PCl$, 1079-66-9; tetrahydrofurfurol, 97-99-4; cyclopentylmethanol, 3637-61-4.

Synthesis and Competitive Thermal Transformations of 3-[[2′-(2-Propynylthio)phenyl]amino]-1,2,4-triazines

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Intramolecular Diels–Alder reactions of 1,2,4-triazines[1] have been shown in extensive studies by our group and others to provide convenient access to a wide array of condensed pyridine, pyrimidine, and pyrazine heterocycles.[2] We have recently applied this concept to the preparation of a series of 6,7-annulated pteridine and deazapteridine derivatives as a part of our program directed toward the synthesis of folate antimetabolites.[3] The investigation described herein was prompted by interest in extending such intramolecular Diels–Alder reactions to the preparation of annulated azepine[4] and thiepin[5] derivatives as potential medicinal agents. Seitz has recently reported that 1,2,4-triazines tethered with simple acetylenic side chains of appropriate length undergo intramolecular Diels–Alder reactions, albeit in very low yield under brutal conditions, to give a variety of azepino-, oxepino- and thiepinopyridines (Scheme I).[2k] We felt that utilization of a side chain incorporating an appropriate pendant group might facilitate the formation of a seven-membered annulated ring by buttressing the dienophilic side chain into a conformation requisite for cycloaddition (i.e., the Thorpe–Ingold effect).[2c,d,6] A benzene ring was chosen as the incorporated pendant group (Scheme II) because of ample precedent for the effectiveness of such a strategy[2c] and because of synthetic expediency. We report herein on an intriguing series of thermal molecular rearrangements observed in the course of an investigation of such a system.

The 3-(methylsulfonyl)-1,2,4-triazines **1**[2g] were treated with 2-aminothiophenol to provide the 3-[(2′-aminophenyl)thio]-1,2,4-triazines **2**. Stirring a THF solution of

(1) For a comprehensive review of heterocyclic azadienes in Diels–Alder reactions, see: Boger, D. L.; Weinreb, S. M. *Hetero Diels–Alder Methodology in Organic Synthesis*; Academic: New York, 1987.

(2) For references to intramolecular Diels–Alder reactions of monocyclic 1,2,4-triazines, see the following. Dienophilic substituent tethered to positions 3 or 6 (nitrogen extrusion): (a) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1985**, *26*, 2419. (b) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 431. (c) Taylor, E. C.; French, L. G. *Tetrahedron Lett.* **1986**, *27*, 1967. (d) Taylor, E. C.; Macor, J. E. *Tetrahedron Lett.* **1986**, *27*, 2107. (e) Taylor, E. C.; Pont, J. L. *Tetrahedron Lett.* **1987**, *28*, 379. (f) Taylor, E. C.; Macor, J. E. *J. Org. Chem.* **1987**, *52*, 4280. (g) Taylor, E. C.; Macor J. E.; Pont, J. L. *Tetrahedron* **1987**, *43*, 5145. (h) Seitz, G.; Dietrich, S. *Arch. Pharm.* **1984**, *317*, 379. (i) Seitz, G.; Gorge, L.; Dietrich, S. *Tetrahedron Lett.* **1985**, *26*, 4355. (j) Seitz, G.; Dietrich, S. *Arch. Pharm.* **1985**, *318*, 1048 and 1051. (k) Seitz, G.; Dietrich, S.; Gorge, L.; Richter, J. *Tetrahedron Lett.* **1986**, *27*, 2747. Dienophilic substituent tethered to position 5 (nitrile extrusion): (l) Taylor, E. C.; Pont, J. L. *J. Org. Chem.* **1987**, *52*, 4287.

(3) (a) Taylor, E. C.; Warner, J. C.; Pont, J. L. *J. Org. Chem.* **1988**, *53*, 800. (b) Taylor, E. C.; Pont, J. L.; Warner, J. C. *Tetrahedron* **1987**, *43*, 5159. (c) Taylor, E. C.; Pont, J. L.; Warner, J. C. *J. Org. Chem.* **1988**, *53*, 3568.

(4) For a comprehensive review of the chemistry of azepines, see: Rosowski, A. In *Azepines, Parts I and II*, Vol. 43 in the series The Chemistry of Heterocyclic Compounds; Weissberger, A., Taylor, E. C.; Eds.; Wiley-Interscience: New York, 1984.

(5) For a comprehensive review of the chemistry of oxepins and thiepins; see: Rosowski, A. In *7-Membered Heterocyclic Compounds Containing Oxygen and Sulfur*, Vol. 26 in the series The Chemistry of Heterocyclic Compounds; Weissberger, A., Taylor, E. C.; Eds.; Wiley-Interscience: New York, 1972.

(6) Fischer, K.; Hünig, S. *J. Org. Chem.* **1987**, *52*, 564.

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