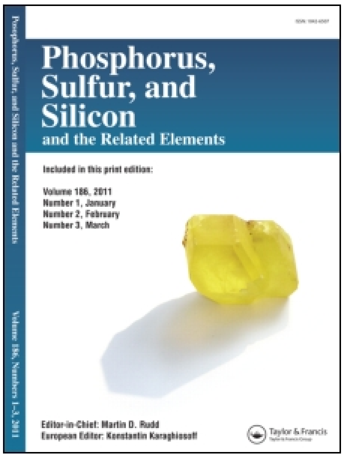


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

HETERO-DIELS-ALDER REACTIONS OF DIMETHYL 1-OXO-(*E,E*)-2,4-HEXADIENEPHOSPHONATE WITH 2-ALKYLIDENE-1,3-DITHIANES

Thomas Schuster[a]; Slayton A. Evans Jr.[a]
[a] The William Rand Kenan, Jr., Laboratories of Chemistry, The University of North Carolina, Chapel Hill, NC, USA

To cite this Article Schuster, Thomas and Evans Jr., Slayton A.(1995) 'HETERO-DIELS-ALDER REACTIONS OF DIMETHYL 1-OXO-(*E,E*)-2,4-HEXADIENEPHOSPHONATE WITH 2-ALKYLIDENE-1,3-DITHIANES', Phosphorus, Sulfur, and Silicon and the Related Elements, 103: 1, 259 — 271

To link to this Article: DOI: 10.1080/10426509508027385

URL: http://dx.doi.org/10.1080/10426509508027385

Phosphorus, Sulfur, and Silicon, 1995, Vol. 103, pp. 259–271
Reprints available directly from the publisher
Photocopying permitted by license only

HETERO-DIELS-ALDER REACTIONS OF DIMETHYL 1-OXO-(*E*,*E*)-2,4-HEXADIENEPHOSPHONATE WITH 2-ALKYLIDENE-1,3-DITHIANES

THOMAS SCHUSTER and SLAYTON A. EVANS, JR.*
The William Rand Kenan, Jr., Laboratories of Chemistry, The University of North Carolina, Chapel Hill, NC 27599-3290, USA

Dedicated to Professor Reinhard Schmutzler on the occasion of his sixtieth birthday

(Received September 16, 1994; in final form March 2, 1995)

The cycloaddition reactions of dimethyl 1-oxo-(*E*,*E*)-2,4-hexadiene phosphonate (**1**) with 2-alkylidene-1,3-dithianes **4** and **5** gave [1]oxa-[7,11]dithiaspiro-[5,5]undecene-2-phosphonate derivatives. The reactions were responsive to electrophilic assistance by the solvent as well as 'conventional' Lewis Acid catalysis. The structural constitutions and preferred conformations of these pyran derivatives were established by NMR spectroscopy as well as by the X-ray crystallographic determination of a key derivative. In addition to *E*- to *Z*-double bond isomerization reactions in **1** and acyl chloride **2**, α-acyl phosphonate **1** underwent thermal isomerization to dimethyl 2*H*-pyran-6-phosphonate (**6**).

Key words: Diels-Alder/reactions, phosphonates, NMR, Lewis acid catalysis, pyrans.

INTRODUCTION

The Diels-Alder and related cycloaddition reactions have become indispensable synthetic tools for the construction of stereochemically diverse cyclic molecules.[1] While numerous reactions involving dienes, enones (*i.e.*, heterodienes) and trienes have been documented, few systematic studies have focused on the inverse electron demand cycloaddition reactions of conjugatively unsaturated carbonyl compounds (*i.e.*, heterotrienes').[2] In our continued efforts to develop versatile synthetic methodologies employing the readily available α-acyl phosphonates as chiral templates in asymmetric synthesis,[3] we have initiated an investigation into the cycloaddition chemistry of doubly unsaturated α-dienoyl phosphonates.[4] The use of phosphoryl moieties in organic synthesis is enticing because the phosphoryl oxygen is capable of binding to metal ions. For example, the P=O oxygen is extraordinarily efficient in stabilizing a metal-complex matrix capable of transmitting significant levels of stereocontrol in Aldol reactions.[5]

In this report, we describe the preparation and the chemical behavior of dimethyl 1-oxo-(*E*,*E*)-2,4-hexadienephosphonate[6] (*E*,*E*-**1**) with alkylidene dithianes. The cycloaddition reactions proceed under mild conditions and respond to electrophilic assistance. The products of the reactions were readily isolated by standard procedures and their structural identities were confirmed by ^{1}H, ^{13}C and ^{31}P NMR spectroscopy as well as X-ray crystallographic analysis of a key molecule. (The full details of the X-ray crystallographic data will be reported elsewhere.)

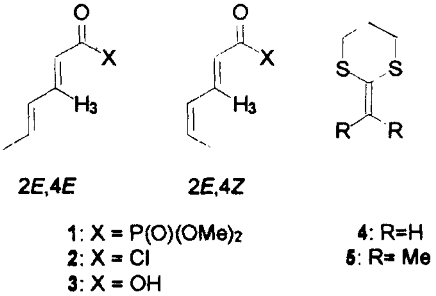
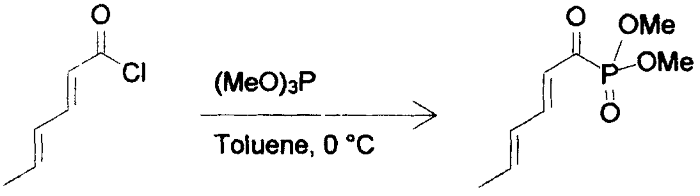


FIGURE 1

RESULTS AND DISCUSSION

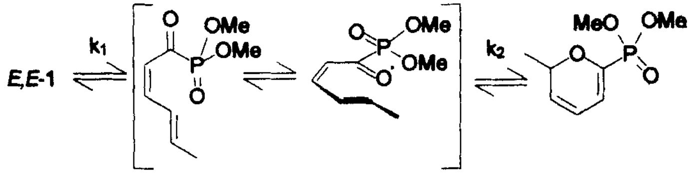
Synthesis and Characterization of the Dienoyl Derivatives

During the preparation of phosphonate precursor, (*E*,*E*)-2,4-hexadienoic acid chloride (**2**), from the chlorination of homogeneous (*E*,*E*)-2,4-hexadienoic acid (sorbic acid, **3**) with 2.5 equiv. of thionyl chloride,[7] isomerization of the (*E*,*E*)-diene occurred at the C_4—C_5 double bond to afford an inseparable 16:1 mixture of diastereomeric *E*,*E*- and *E*,*Z*-**2** acid chlorides (95% yield, Method A). Alternatively, acid **3** and thionyl chloride admixed in equimolar proportions were allowed to react in the presence of a small quantity of triethylamine (Et_3N) at ambient temperature in pentane solvent[8] to afford isomerically homogeneous acid chloride *E*,*E*-**2** (Method B, 63% yield). Phosphonate *E*,*E*-**1** was prepared using the Michaelis-Arbuzov reaction according to the procedures reported by Theis and Regitz (Equation 1).[6] Condensation of acid chlorides **2** with $(MeO)_3P$ in toluene solvent at 0°C, followed by removal of the solvent under reduced pressure (0.1 mmHg), afforded essentially homogeneous **1**. Attempted purification of highly reactive phosphonate **1** by distillation under reduced pressure resulted in its rapid decomposition. Consequently, dimethyl α-acylphosphonate **1** was used without further purification. When the 16:1 diastereomeric mixture of ***E*,*E***- and ***E*,*Z***-**2** was condensed with $(MeO)_3P$, a 10:1 mixture of regioisomeric *E*,*E*- and *E*,*Z*-**1** was isolated (84% yield), while homogeneous *E*,*E*-**2** gave a *ca.* 100:1 mixture (^1H NMR) of *E*,*E*- and *E*,*Z*-**1**. Diene *E*,*E*-**1** slowly isomerized to a mixture of the isomeric *E*,*E*-and *E*,*Z*-**1** dienes (*vide infra*).



E,E-2 E,E-1 (1)

The syntheses of the alkylidene dithianes **4** and **5** were performed following the literature procedures reported by Jones *et al.*[9] and Seebach *et al.*[10] 2-(Methylpropylidene)-1,3-dithiane (**5**) was obtained as an oil that crystallized upon standing to give a colorless, crystalline solid (mp 30–33°C).



s-trans-Z,E-1 **s-cis-Z,E-1** **6**

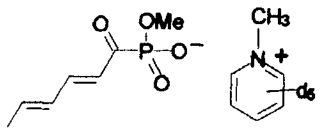
SCHEME I Thermal isomerization of **1** to **6**.

Electrocyclic Ring Closure of Diene 1

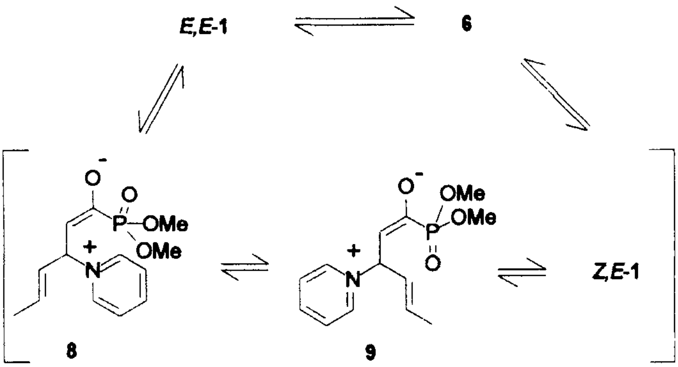
In addition to the isomerization about the C_4—C_5 double bond, thermal ring closure of diene **1** to dimethyl 2*H*-pyran-6-phosphonate was observed. In $CDCl_3$ solvent, a 4:1 mixture of diene **1** and pyran **6** was obtained after 7 days (Scheme I). Isomerization of *E*,*E*-**1** about the C_2—C_3 double bond to *Z*,*E*-**1** is a prerequisite for cyclization. Although *Z*,*E*-**1** is not directly observed, it does seem plausible that the formation of **6** requires a rate determining *E*- to *Z*-double bond isomerization. If the two rates are sufficiently different (*i.e.*, $k_1 << k_2$), such that a steady-state concentration of *Z*,*E*-**1** adequate to be detected by NMR spectroscopy never materializes, then the probability for observing *Z*,*E*-**1** may be low.

To obtain insight into the configurational energies of the different isomers of **1**, the structures of *E*,*E*-**1**, *E*,*Z*-**1**, *Z*,*E*-**1** and 2*H*-pyran **6** were minimized using MacroModel, Version 2.1. Diene *E*,*E*-**1** was minimized at 57.13, *E*,*Z*-**1** at 64.30 and *Z*,*E*-**1** at 67.00 kJ/mol. 2*H*-pyran **6** showed a minimum at 50.41 kJ/mol. The minimized structures of the acyclic isomers display a nearly planar heterotriene backbone with the double bonds arranged in a s-*trans* conformation. In addition, a local minimum (81.78 kJ/mol) was found for *Z*,*E*-**1** when the π-system populates a s-*cis* conformation. This conformer can exist in a full-turn helix that would be aligned with the orbital requirements of the proposed transition state[11] for effective ring-closure of 1-oxo-2,4-dienes. A recent MINDO/3 study, describing the reaction paths of thermal and photoinduced ring closure reactions of 1,3,5-trienes, indicated that the disrotatory pathway, characterizing the heterotriene to 2*H*-pyran thermal isomerization, is lower in energy than the symmetry forbidden conrotatory path.[12] In addition, the calculations predict that the thermodynamic driving force favors the heterocyclic structures over their acyclic counterparts.

The calculated energy difference ($\Delta E = 10$ kJ/mol) between *E*,*E*- and *Z*,*E*-**1** is relatively small; consequently a diminution in the activation energy for isomerization of *E*,*E*-**1** to *Z*,*E*-**1** should facilitate ready access to **6**. When *E*,*E*-**1** was dissolved in pyridine-d_5, a 1:0.8 mixture of diene **1** and pyran **6** was obtained after 1.5 h. Decomposition occurred during the next 24 h period involving pyridine-promoted demethylation of dimethyl phosphonate *E*,*E*-**1** to give methyl *E*,*E*-1-oxo-2,4-hexadiene phosphonate *N*-methyl pyridinium-d_5 salt (**7**).[13] In a CD_2Cl_2



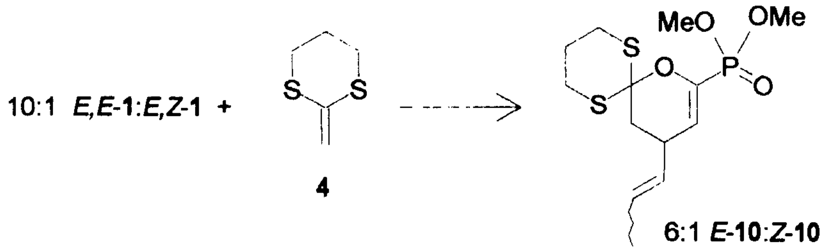
7



SCHEME II Proposed mechanism for the pyridine-promoted **1** to **6** isomerization reaction.

solution, containing 3 mol% of pyridine, a 1:0.8 mixture of diene **1** and pyran **6** was observed after 5 days in the absence of competitive demethylation. It is possible that pyridine accelerates the ring closure reaction *via* a pyridine addition-elimination reaction to the C_2—C_3 double bond of *E*,*E*-**1** (Scheme II). Addition of pyridine to C-3 gives pyridinium enolate **8**. Rotation about the C_2—C_3 single bond, to minimize the steric interaction between the pyridinium ion and the dimethyl phosphonate group, followed by a 'retro-Michael' reaction of pyridine from enolate **9** provides *Z*,*E*-**1** which rapidly isomerizes to **6**.

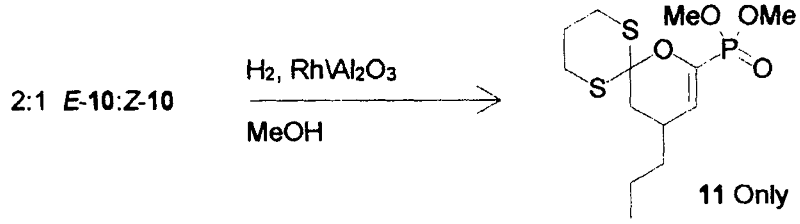
Unfortunately, 2*H*-pyran **6** could not be isolated in homogeneous form but the spectral data are consistent with the proposed structure. The ^{1}H NMR spectrum of **6** shows the presence of four well-resolved ring hydrogens which are strongly coupled. The methyl group (^{1}H NMR, δ 1.37 ppm) is shifted upfield relative to the methyl group in *E*,*E*-**1** (d 1.90 ppm). This upfield shift is consistent with the change in hybridization of C-5.[14] The cycloadducts (*vide infra*), which are structurally comparable to **6** exhibit ^{31}P NMR chemical shifts which are similar (within ±0.1 ppm) to **6**.



(2)

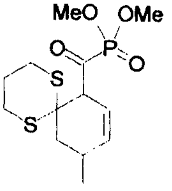
Cycloaddition Reactions

The reaction of a 10:1 mixture of dienes *E*,*E*- and *E*,*Z*-**1** with dienophile **4** in equimolar proportions gave a 6:1 mixture of cycloadducts *E*- and *Z*-**10** (70% yield) following chromatography on alumina (Equation 2). The major isomer, [1]oxa-[7,11]dithiaspiro-2-[5,5]undecene-4-*trans*-1-propene-2-dimethyl phosphonate (*E*-**10**), was isolated as an analytically homogeneous material following fractional recrystallization from pentane solvent. The minor adduct was identified (^{1}H NMR) as the *cis*-propene isomer *Z*-**10**. The coupling constants between the vinylic hydrogens in the propene side chain are ^3J = 15.3 Hz in *E*-**10** and ^3J = 10.2 Hz for *Z*-**10**. The smaller coupling constant within isomeric olefins is indicative of a *cis*-stereochemical relationship.[9] Finally, selective hydrogenation of the acyclic olefinic fragment in mixtures containing *Z*- and *E*-**10** gave [1]oxa-[7,11]dithiaspiro-2-[5,5]undecene-4-n-propyl-2-dimethyl phosphonate (**11**) in 65% yield after chromatographic purification and recrystallization from pentane (Equation 3). The structural constitution of **11** was confirmed by X-ray crystallographic analysis.

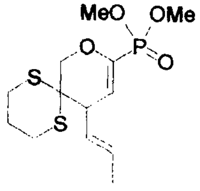


11 Only (3)

Diene **1** (*E*:*Z* = 10:) reacted with isopropylidene dithiane **5** in $CHCl_3$ solvent at ambient temperature to give a 6:1 mixture of *E*-**12** and *Z*-**12** (65% yield) after 3 days. The use of isomerically homogeneous *E*,*E*-**1** had no influence on the stereochemical outcome of the reactions, *i.e.* the *E*- to *Z*-ratio of the cycloadducts remained unchanged. Apparently, under the reaction conditions, the C_4—C_5 double bond isomerization is faster than the cycloaddition reaction (Scheme III). The *E*- and *Z*-cycloadducts are formed from the individual reactions of the ketene thioacetals with the *E*,*E*- and *E*,*Z*-regioisomers of **1** with exclusive selectivity for the enone moiety of **1**. There was no evidence for the formation of cycloadducts **13** or **14**. While the formation of **6** was accelerated in the presence of the dithianes, the complete conversion of diene **1** and 2*H*-pyran **6** occurred over a 6-week period. This result is consistent with the reversible formation of 2*H*-pyran **6**.

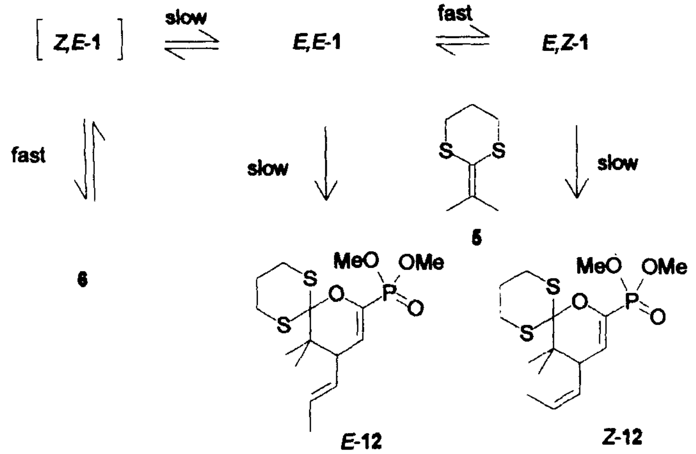


13



14

The pyran ring in **11** prefers a flattened half-chair conformation in the solid state (X-ray crystallography) as well as in solution (*i.e.*, ^1H NMR coupling constants, Table I). The close correlation of the NMR data suggests that all three ring systems exist in similar conformations. Figure 2 shows a representation of the half-chair conformation of the pyranoid moiety in **11**. This conformer requires near planarity of the C_3—H and C_5—H bonds which allows for long range W-coupling between H-3 and H-5 (^4J = 1.6 Hz).[15] The vicinal couplings of 6.6 and 11.6 Hz are clearly indicative of hydrogens occupying axial-equatorial ($^3J_{H\text{-}4,H\text{-}5}$) and diaxial ($^3J_{H\text{-}4,H\text{-}6}$) orientations.[16] If the pyranoid ring existed in a boat conformation, the C_4—H bond would bisect the CH_5H_6 angle and smaller coupling constants would



SCHEME III Reaction scheme for the reaction of **1** with **5**.

TABLE I
Matrix of selected ¹H NMR data for *E*-, *Z*-**10** and **11** (Hz)

	$^3J_{H3,H4}$	$^4J_{H3,H5}$	$^3J_{H4,H5}$	$^3J_{H4,H6}$	$^2J_{H5,H6}$
E-**10**	2.2	1.5	6.7	10.9	13.7
Z-**10**	2.4	1.5	7.3	10.8	13.7
11	1.6	1.6	6.6	11.6	13.2

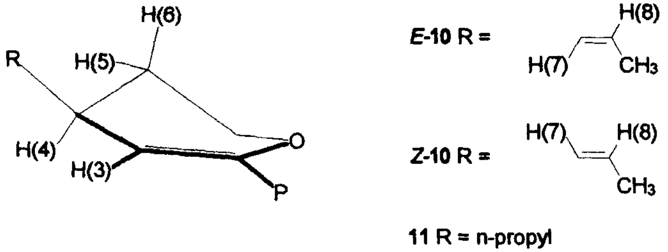


FIGURE 2 Representation of the pyranoid ring in **10** and **11**.

be expected. The phosphoranyl oxygen and the enolic double bond in **11** prefer the cisoid arrangement in the solid state. This observation is consistent with the predictions obtained from the molecular mechanics results on **6**. The rotamers of **6** with the *anti* alignment of the enolic double and the phosphoranyl oxygen bond were calculated to be 5 kJ/mol higher in energy than minimum energy conformations, in which these bonds are *syn*. The higher energy is attributed to a change in the angle-bending energy.

Solvent Dependence of the Rate Constant

The phenomenological second-order rate constants for the reaction of dienes **1** and dithiane **5** (Scheme III) in four solvents were determined by ¹H NMR spectroscopy at 22 (±0.1)°C. Both, the disappearance of starting material and the appearance of products were followed. The observed second-order rate constants, k_{obs}, for the disappearance of **1** are presented in Table II, together with three relevant solvent parameters commonly used in relating rates of cycloaddition reactions to the properties of the reaction solvent. The absence of a simple relationship between the rate constants and the E_T^N-parameter[17] of solvent polarity suggests that a dipolar intermediate is not involved in the rate determining step of the reaction.[18] It has been suggested that solvophobic interactions are important in explaining the solvent dependence of cycloaddition reactions.[19] Yet the comparison of the solvent dependent k_{obs} values, obtained for the reaction shown in Scheme III, with the values for the cohesive energy density (ced)[19] implies that a coherent energy density rationale cannot adequately explain the observed solvent effect for this reaction in the solvents listed here.

However, the observed rate constants do correlate with the Acceptor Numbers[20] (AN) of the solvents. By plotting the log k_{obs} values *versus* the AN parameter a hyperbolic relationship is described. Desimoni and coworkers have shown that such a relationship is indicative of electrophilic assistance by the solvent: the solvent acts as a Lewis Acid by responding through a Frontier Molecular Orbital (FMO) interaction with the solute.[21] As a consequence, both, the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO) levels of the solute are lowered.[21] Since the rates of Diels-Alder reactions are inversely proportional to the energy separation between the FMOs of the reactants,[22] modification of this energy gap by changing the FMO energies of the reactants will affect the rate of the reaction.

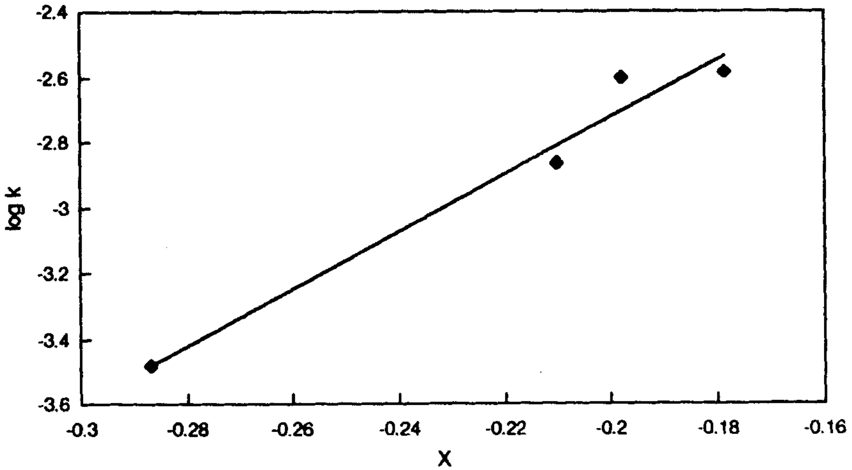
This hyperbolic relationship can be converted into a straight line relationship (Graph 1, Table III) $\log k = N + MX$ (Equation 4) with $M \equiv A(B/C - 1)$, $N = AB/C$ and $X = 1/(C * AN - 1)$.[21] The constants A, B and C were approximate from graphs of log k *vs.* AN and optimized by numerical methods. The F-statistic for the overall model $\log k_{obs} = -0.97644\ (\pm 0.08722) + 8.72337\ (\pm 1.06125) * X$ returns a 99.5% level of significance for the goodness of the relationship.

Since the cycloaddition reaction (Scheme III) is susceptible to electrophilic assistance, it is expected that the coordination of the diene **1** with a Lewis Acid should increase the rate of the reaction for the reasons discussed above. This was accomplished using $LiClO_4$ as the Lewis Acid catalyst.[23] When **1** and **5** were reacted in the presence of 0.5 M $LiClO_4$ in acetonitrile-d_3 solvent,[24] a 24-fold rate increase ($k_{obs} = 31.25\ (\pm 1.6) \times 10^{-3}$ L/mol min at 22.0 (±0.1)°C) was observed relative to the uncatalyzed reaction in acetonitrile-d_3 solvent.

TABLE II

Rate data and relevant solvent parameters

Solvent	AN	E_T^N	ced	$k_{obs} * 10^3$ (l/mol min)
$CDCl_3$	23.1	0.259	0.15	2.62 (±0.13)
CD_2Cl_2	20.4	0.309	0.165	2.51 (±0.12)
Acetonitrile-d_3	18.9	0.46	0.233	1.37 (±0.07)
Acetone-d_6	12.5	0.355	0.153	0.33 (±0.04)



GRAPH 1 Relationship between log k_{obs} and X (Equation 4).

TABLE III

Results for the optimization of the parameters for Equation 4

Parameters	A	B	C	M	N	r^2
	-9.851	-0.02	-0.199	8.883	-0.968	0.972

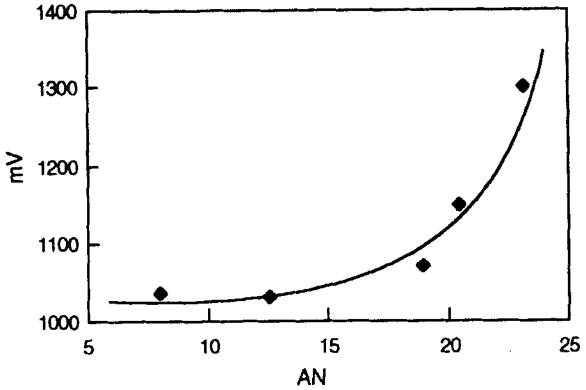
Solvent	$CDCl_3$	CD_2Cl_2	acn-d_3	ace-d_6
X	-0.179	-0.198	-0.21	-0.287

TABLE IV

Solvent dependence of the oxidation potential for **1**

Solvent	Oxidation Potential (± 10, in mV)
$CHCl_3$	1300
CH_2Cl_2	1148
acetonitrile	1070
acetone	1030
THF	1035

Since a relationship between electrochemical redox-potentials and FMO-energies exists,[25] the electrochemical oxidation and reduction potentials of **1** should show a trend consistent with the proposed change of the FMO energy levels induced by the solvent. Diene **1** should become progressively easier to reduce in the solvents acetone, acetonitrile, CH_2Cl_2 and $CHCl_3$, respectively, because of the lowering of the LUMO energies, while its oxidation-potential should exhibit more positive values following the same series because of the lowering of the HOMO levels. Table IV summarizes the results obtained by circular voltammetry using a glassy carbon working electrode with tetra-*N*-butyl ammonium hexafluorophosphonate



GRAPH 2 Plot of the oxidation potential (mV) of **1** *vs.* AN.

as the electrolyte. Regrettably, no reduction step could be observed for **1** under these conditions within the working range of the solvents. However, the values clearly indicate that the oxidation potentials follow the predicted tendency. Graph 2 is a plot of the oxidation potentials of **1** *vs.* the Acceptor Number of the solvents. Graphs of this type are typically obtained for this kind of relationship.[20]

We recognize that a single solvent parameter approach does not adequately respond to the complexity of solvent-solute and solvent-transition state interactions. However, we believe that it does provide valuable insight in those characteristics of a solvent that could impact the rate of the cyclo-reaction.

CONCLUSIONS

Both, sorbyl chloride **2** and sorbyl phosphonate **1**, are subject to rapid *E*- to *Z*-isomerization of the terminal double bond, and in the case of sorbyl phosphonate **1**, a reversible heterotriene to 2*H*-pyran isomerization is observed. The results of molecular modeling calculations indicate that there are only small energy differences between the different isomers of **1**. Therefore, the isomerization reactions are expected to be efficient when the activation energies for isomerization are lowered. For example, the isomerization of **1** to **6** is catalyzed by pyridine solvent.

The heterocycloaddition reactions between diene **1** and dithianes **4** and **5** proceed under the selective formation of a "head-to-head" cycloadduct. The preferred conformation of these ring systems was established unambiguously by ^1H NMR spectroscopy. The structure as well as the conformational preferences of **11** inferred on the basis of the analysis of the ^1H NMR parameters compares favorably with the solid state structural parameters obtained by single crystal X-ray crystallography.

The solvent dependence of the rate of the addition reaction is rationalized in terms of molecular orbital interactions between the solvents and **1**, where the solvent serves as a Lewis Acid. The rate accelerations in solvents with high Acceptor Numbers are due to a solvated ground-state effect: the HOMO and LUMO levels of **1** are lowered as a consequence of the Lewis Acid/Lewis Base interactions between the solvent (Lewis Acid) and the solute (Lewis Base). Further corroboration for this model was obtained by observing that Lewis Acid catalysis can be achieved and that the electrochemical oxidation potentials follow the predicted trend. The absence of a solvent polarity effect on the rate constants implies that the formation or disappearance of a dipolar intermediate is not involved in the rate determining step of this reaction.[18] This observation and the apparent sole dependence of the reaction rates on the FMO interactions of the solvated ground states of the reactants suggests that the cycloaddition reaction proceeds by a conerted pathway.

EXPERIMENTAL

General

All solvents used in the reactions were freshly distilled prior to use. All reagents were purified according to standard procedures. With the exception of $CDCl_3$, NMR solvents were obtained in sealed 1 mL ampoules and used without further purification. Deuteriochloroform was obtained in bulk and passed through basic alumina before use. NMR spectra were recorded on Bruker AX-200 and WM-250 spectrometers. ^{1}H and ^{13}C NMR spectra are referenced to $CHCl_3$ (^{1}H δ 7.24; ^{13}C δ 77.0) or Me_4Si (δ 0.00). ^{31}P NMR spectra were referenced relative to external 85% phosphoric acid (^{31}P δ 0.0). With the exception of ^{1}H NMR chemical shifts, which are reported with two significant digits, all other NMR chemical shifts are reported to one significant figure. ^{13}C NMR spectra were broadband or WALTZ ^{1}H decoupled and reported coupling constants refer to coupling with ^{31}P. All melting points are uncorrected.

1-Oxo-2,4-hexadienechloride (**2**).[2] *Method A*: To sorbic acid (**3**, 20 g, 0.18 mol) was added dropwise at ambient temperature 32.5 mL (0.45 mol) of thionyl chloride. The resulting slurry was refluxed in an Ar atmosphere until a homogeneous solution was obtained. This reaction mixture was distilled (70°C, 11.5 mmHg; lit.,[2b] 78°C, 15 mmHg) to give 22 g (95%) of a constant boiling fraction. This fraction was composed of a 16:1 (^{1}H NMR) mixture of *E*,*E*- and *E*,*Z*-2,4-hexadienoyl chloride. *E*,*E*-**2**: ^{1}H NMR ($CDCl_3$) δ 7.35 (dd, 1H, J = 14.6, 10.0 Hz), 6.30 (m, 2H), 5.79 (d, 1H, J = 14.6 Hz) 1.85 (d, 3H, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 165.5, 151.5, 145.3, 129.0, 122.7, 18.8. *E*,*Z*-**2**: ^{1}H NMR ($CDCl_3$) δ 7.73 (dd, 1H, J = 14.6, 10.4 Hz), 6.3 (m), 6.01 (d, 1H, J = 14.6 Hz), 1.86; ^{13}C NMR ($CDCl_3$) δ 144.9, 141.3, 126.4, 124.7, 14.2. *Method B*: In 10 mL of pentane and under an Ar atmosphere were mixed at ambient temperature 1029 mg (9.22 mmol) of sorbic acid (**3**) and thionyl chloride (0.67 mL, 9.2 mmol). This slurry was allowed to stir for 15 min, after which time 0.02 mL of Et_3N was added (syringe). This mixture was allowed to stir at ambient temperature until no more gas evolved. The liquid phase was removed by cannula from the precipitate, concentrated under reduced pressure and the residue distilled in a microdistillation apparatus at 8.5 mmHg (oil bath temperature 100–105°C) to give 729 mg (62%) of homogeneous (^{1}H NMR) acid chloride *E*,*E*-**2**.

Dimethyl 1-oxo-2,4-hexadienephosphonate (*E*,*E*- *and E*,*Z*-**1**).[6] (**a**) *To a 16:1 mixture of E*,*E*- and *E*,*Z*-**2** (1000 mg, 7.57 mmol) in 10 mL of toluene solvent at 0°C (ice/water bath) was added dropwise by syringe over 20 min $(MeO)_3P$ (953 mg, 7.69 mmol) under an Ar atmosphere. After the addition was complete, the bath was removed and the mixture allowed to warm to ambient temperature. The reaction mixture was stirred for 14 h at that temperature. The solvent was then removed at ambient temperature at 0.1 mmHg and the residue was left under a 0.01–0.005 mmHg vacuum for 12 h. This gave 1.3 g (84%) of an analytically homogeneous mixture (^{1}H NMR) of *E*,*E*- and *E*,*Z*-**1** in a 10:1 proportion. *E*,*E*-**1**: ^{1}H NMR ($CDCl_3$) δ 7.69 (dd, 1H, J = 15.6, 10.4 Hz), 6.36 (m, 2H), 3.83 (d, 6H, J = 12.0 Hz), 1.90 (d, 3H, J = 6.2 Hz). ^{13}C NMR ($CDCl_3$) δ 197.1 (d, J = 173.0 Hz), 148.8 (d, J = 1.1 Hz), 144.5, 130.0 (d, J = 1.6 Hz), 126.1 (d, J = 66.3 Hz), 53.2 (d, J = 7.0 Hz), 18.4; ^{31}P NMR ($CDCl_3$) δ 0.5; (d_6-acetone) δ 1.2. *E*,*Z*-**1**: ^{1}H NMR ($CDCl_3$) δ 8.10 (dd, 1H, J = 15.4, 10.2 Hz), 6.36 (m), 3.85 (d, 6H, J = 11.0 Hz), 1.95; ^{13}C NMR ($CDCl_3$) δ 197.3 (d, J = 173.0 Hz), 142.7 (d, J = 1.3 Hz), 140.6, 127.5 (d, J = 1.6 Hz), 13.9; ^{31}P NMR (d_6-acetone) δ 1.0. For *E*,*E*-**1** in C_6D_6, the Aromatic Solvent-Induced Shift (ASIS) effect resolved the multiplet (^{1}H NMR) at ($CDCl_3$) δ 6.3 into a multiplet centered at (C_6D_6)) δ 6.3 (2H) and an apparent triplet (C_6D_6) δ 6.42 (1H, J = 15.6, 15.6 Hz). Because of overlap with the resonances of *E*,*E*- **1** an analogous effect on the multiplet centered at ($CDCl_3$) δ 6.36 cannot be observed for *E*,*Z*-**1**. However the partially obscured signal (^{1}H NMR) at ($CDCl_3$) δ 1.95, assigned to the vinylic methyl group of *E*,*Z*-**1**, can be resolved by means of the Aromatic Solvent-Induced Shift effect and was observed at (C_6D_6) δ 1.55 (d, 3H, J = 5.5 Hz). (**b**) *Conducting the same* experiment with homogeneous (^{1}H NMR) *E*,*E*-**2** allows for the isolation of an approximately 100:1 mixture of *E*,*E*-**1** and *E*,*Z*-**1** (^{1}H NMR).

Dimethyl 2H-pyran-6-phosphonate (**6**): Diene **1** was allowed to stand under an Ar atmosphere and pyran **6** began to appear after 24 h. After 14 days, 50% of **1** rearranged to **6**: ^{1}H NMR (CD_2Cl_2) δ 6.12 (ddd, 1H, J = 9.3, 5.5, 1.2 Hz), 5.95 (1H, m, J = 9.4, 5.5, 3.7, 1.6 Hz), 5.54 (m, 1H, J = 9.4, 3.6, 3.5, 1.2 Hz), 4.82 (m, 1H, J = 6.6, 3.6, 1.6 Hz), 1.37 (d, 3H, J = 6.6 Hz); ^{31}P NMR ($CDCl_3$) δ 12.0; (d_6-acetone) δ 11.5.

Catalysis of Ring Closure Reaction of Diene **1** *to Pyran* **6**: In 1 mL of CD_2Cl_2 was dissolved 43 mg (0.2 mmol) of a 10:1 mixture of ***E*,*E*-1** and ***E*,*Z*-1**. To this solution was added 5 mL (0.006 mmol) of pyridine-d_5 *via* syringe. After 5 days, a 1:0.8 mixture of dienes **1** and pyran **6** was observed.

2-(Dimethyl phosphonate)-4-(2-propene)-[1]oxa-[7,11]dithiaspiro-2-[5,5]undecene (**10**): To 310 mg (1.51 mmol) of diene **1** in 1.2 mL of $CDCl_3$ was added by syringe **4** (200 mg, 1.51 mmol) under an Ar atmosphere. The reaction was followed by ^{1}H NMR. After 36 h the reaction was completed. The solvent was removed and the residue was chromatographed on neutral alumina with ethyl acetate/petroleum ether as the eluent (70/30 $\gg$ 95/5 EtOAc/Pet.Eth.) to afford 336 mg (70%) of a 6:1 mixture of products. The major product was isolated as a homogeneous material by fractional recrystallization from pentane, while the minor product could only be obtained in a 2:1 mixture. The major product has been identified as colorless crystals of 2-(dimethyl phosphonate)-4-(2-*trans*-propene)-[1]oxa-[7,11]dithiaspiro-2-[5,5]undecene (*E*-**10**): mp 75–77°C; ^{1}H NMR ($CDCl_3$) δ 5.93 (ddd, 1H, J = 11.2, 2.2, 1.5 Hz), 5.58 (dqd, 1H, J = 15.3, 6.3, 1.0 Hz), 5.29 (ddq, 1H, J = 15.3, 7.5, 1.6 Hz), 3.79 (d, 3H, J = 11.0 Hz), 3.75 (d, 3H, J = 10.8 Hz), 3.49 (m, 1H), 3.28 (m, 1H), 3.15 (broad m, 1H), 2.68 (broad m, 2H), 2.29 (apparent ddt, 1H, J = 13.7, 6.7, 1.5, 1.5 Hz), 2.10 (broad m, 1H), 1.65 (dd, 1H, J = 13.7, 10.9 Hz), 1.64 (ddd, 3H, J = 6.3, 1.6, 0.7 Hz); ^{13}C NMR ($CDCl_3$) δ 140.3 (d, J = 229.2 Hz), 130.7, 127.1, 121.1 (d, J = 21.5 Hz), 86.6 (d, J = 9.0 Hz), 53.2 (d, J = 5.7 Hz), 52.8 (d, J = 5.2 Hz), 39.7 (d, J = 1.3 Hz), 32.8 (d, J = 12.8 Hz), 26.8, 26.3, 25.1, 17.7; ^{31}P NMR ($CDCl_3$) δ 11.0 Anal. Calcd for $C_{13}H_{21}O_4PS_2$: C, 46.41; H, 6.29. Found: C, 46.48; H, 6.29.

The minor product has been identified as 2-(dimethyl phosphonate)-4-(2-*cis*-propene)-[1]oxa-[7,11]dithiaspiro-2-[5,5]undecene (*Z*-**10**): ^{1}H NMR ($CDCl_3$) δ 5.87 (ddd, 1H, J = 11.2, 2.4, 1.5 Hz), 5.57 (m), 5.16 (ddq, 1H, J = 10.2, 9.9, 2 Hz), 3.78 (d, 3H, J = 9.3 Hz), 3.75 (d, 3H, J = 11 Hz), 3.50 (m, 1H), 3.26 (m, 1H), 2.69 (m), 2.21 (m), 1.91 (dd, 1H, J = 13.7, 10.8 Hz), 1.65; ^{31}P NMR ($CDCl_3$) δ 11.0. The ASIS effect of C_6D_6 separated some overlapping resonances in the ^{1}H NMR: δ 5.30 (dqd, 1H, J = 10.2, 6.8, 1.0 Hz), 2.28 (apparent ddt, 1H, J = 13.7, 7.3, 1.2, 1.2 Hz), 1.35 (dd, 3H, J = 6.8, 2.0 Hz).

[1]Oxa-[7,11]dithiaspiro-2-[5,5]undecene-4-n-propyl-2-dimethyl phosphonate (**11**): To a solution of a 2:1 mixture of *Z*-**10**/*E*-**10** (20 mg, 0.006 mmol) in 4 mL of MeOH was added 50 mg of 5% Rh/Al_2O_3. This slurry was allowed to react with H_2 (1 atm) for 24 h. The mixture was then filtered and concentrated. The NMR spectra of the crude mixture showed **11** as the only product. After chromatography on neutral alumina (60/40 EtOAc/pentane) and recrystallization from pentane, **11** was isolated in 65% yield: ^{1}H NMR ($CDCl_3$) δ 5.95 (app. dt, 1H, J = 11.9, 1.6, 1.6 Hz), 3.78 (d, 3H, J = 11.3 Hz), 3.72 (d, 3H, J = 11.29 Hz), 3.47 (m, 1H), 3.21 (m, 1H), 2.65 (m, 2H), 2.50 (m, 1H), 2.23 (dd app.t, 1H, J = 13.2, 6.6, 1.6, 1.6 Hz), 2.10 (m, 2H), 1.70 (dd, 1H, J = 13.2, 11.6 Hz), 1.35 (m, 4H), 0.87 (br.t, 3H, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 140.2 (d, J = 229.6 Hz), 122.5 (d, J = 33.8 Hz), 86.8 (d, J = 8.7 Hz), 53.1 (d, J = 5.6 Hz), 52.7 (d, J = 4.9 Hz), 39.7, 36.6, 29.2 (d, J = 12.6 Hz), 28.7, 26.3, 24.9, 19.6, 13.9; ^{31}P NMR ($CDCl_3$) δ 12.1.

2-(Dimethyl phosphonate)-4-(2-propene)-5-dimethyl-[1]oxa-[7,11]dithiaspiro-2-[5,5]undecene (**12**): Diene **1** (204 mg, 1.00 mmol) and dithiane **5** (160 mg, 1.00 mmol) were dissolved in 1.5 mL of $CDCl_3$ and the resulting solution was allowed to stand for 3 days at ambient temperature. The reaction mixture then was concentrated and the residue was chromatographed on neutral alumina with ethyl acetate/pentane as the eluent (70/30 > 80/20 EtOAc/pent.) to give 236 mg (65%) of a 6:1 mixture of products as a colorless oil. Recrystallization from pentane gave colorless crystals of the same composition. The major product is 2-(dimethyl phosphonate)-4-(2-*trans*-propene)-5-dimethyl-[1]oxa-[7,11]dithiaspiro-2-[5,5]undecene (*E*-**12**): ^{1}H NMR ($CDCl_3$) δ 5.88 (dd, 1H, J = 11.0, 2.1 Hz), 5.51 (dq, 1H, J = 15.2, 6.3 Hz), 5.28 (ddq, 1H, 15.2, 8.4, 1.4 Hz), 3.76 (d, 3H, J = 11.2 Hz), 3.73 (d, 3H, J = 11.1 Hz), 3.39 (m, 2H), 3.0 (m, 1H), 2.75 (m, 2H), 2.10 (m, 2H), 1.68 (dd, 3H, J = 6.3, 1.4 Hz), 1.17 (s, 3H), 0.97 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 139.7 (d, J = 229.6 Hz), 130.0, 127.4, 122.2 (d, J = 21.7 Hz), 98.1 (d, J = 8.4 Hz), 53.4 (d, J = 5.32 Hz), 52.8 (d, J = 4.76 Hz), 44.7 (d, J = 12.9 Hz), 40.5, 26.9, 26.4, 25.1, 23.9, 18.0 and 17.9; ^{31}P NMR ($CDCl_3$) δ 11.9; (acetone-d_6) δ 11.6; HRMS (FAB) calcd. for $C_{15}H_{26}PO_4S_2$ (M + H$^+$) 365.1012, found 365.1003.

The minor adduct is assigned as 2-(dimethyl phosphonate)-4-(2-*cis*-propene)5-dimethyl-[1]oxa-[7,11]dithiaspiro-2-[5,5]undecene (*Z*-**12**): ^{1}H NMR ($CDCl_3$) δ 5.75 (dd, 1H, J = 10.9, 2.1 Hz), 1.10 (s, 3H), 1.00 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 139.9 (d, J = 235.8 Hz), 128.4, 126.8, 122.5 (d, J = 21.2 Hz), 98.2 (d, J = 8.4 Hz), 41.3, 38.8 (d, J = 13.0 Hz), 24.1, 17.6 and 13.4; ^{31}P NMR ($CDCl_3$) δ 11.9; ^{31}P NMR (acetone-d_6) δ 11.7.

Using the ASIS effect of C_6D_6 and performing decoupling experiments, the hydrogen on C-5 (δ 3.69 (1H, m)) could be assigned for *Z*-**12**. Decoupling in C_6D_6 also allows for the assignment of the vinylic coupling constant for the acyclic olefinic protons of *Z*-**12** as J = 11.01 Hz.

Electrochemical Measurements

Cyclic Voltammograms were recorded with a Princeton Applied Research Model 273 potentiostat/galvanostat which was equipped with a Yokogawa 3025 X-Y recorder. The voltammograms were observed under an Argon atmosphere in a single-compartment airtight three-electrode cell using positive feedback *i*R compensation. The potential was referenced to a Ag/0.1 M $AgNO_3$ in acetonitrile electrode. This reference electrode was separated from the analytical solutions by placement in a vycor-glass tipped glass-container. A glassy carbon (surface area = 7.5 mm^2) working electrode and a Pt-wire counter electrode were employed. The analytical samples were prepared by dissolving 1 mg (0.005 mmol) of **1** in 5 mL of a 0.1 M solution of tetra-*N*-butyl ammonium hexafluorophosphonate in the specified solvent (Table IV). The potentials were found to be reproducible within <5 mV. Commercial tetra-*N*-butyl ammonium hexafluorophosphonate was recrystallized from ethyl acetate/pentane before use. In addition to **1**, the cyclic voltammograms of **2** and **3** were recorded in CH_2Cl_2 under the same conditions. The oxidation potential of **2** was found at 740 mV, while a potential of 810 mV was determined for **3**.

Kinetic Measurements

The rates were determined by ^{1}H NMR spectroscopy with sorbyl chloride (**2**) as an internal standard for integration. The samples were maintained in a constant temperature bath at 22 (±0.1)°C. NMR spectra were recorded on a Bruker WM-250 MHz NMR spectrometer. Each spectrum was baseline-corrected before integration. The reported rate constants are taken from the best runs and were obtained from standard second order plots and describe the overall disappearance of starting materials.

ACKNOWLEDGEMENT

This work was supported by a grant from the NSF. We also thank Prof. Cynthia Schauer and Dr. Yoshihiro Koide for the use of their electrochemical equipment and Dr. Peter White for the X-ray structural determination.

REFERENCES

1. F. Fringuelli and A. Taticchi, "Dienes in the Diels-Alder Reaction," Wiley, New York, 1990.
2. M. Heuschmann, *Chem. Ber.*, **121**, 39–49 (1988).
3. N. J. Gordon and S. A. Evans, Jr., submitted to *J. Org. Chem.* (1993).
4. T. Schuster and S. A. Evans, Jr., *Abstr. Pap. Am. Chem. Soc.*, **204**, ORGN 0372 (1992).
5. C. F. Longmuire and S. A. Evans, Jr., *J. Chem. Soc., Chem. Commun.*, 922 (1990).
6. W. Theis and M. Regitz, *Tetrahedron*, **41**, 2625–2634 (1985).
7. H. Burton and C. K. Ingold, *J. Chem. Soc.*, 2022–2037 (1929).
8. L. T. Holdrege, Y. G. Perron, S. Wolfe and J. C. Godfrey, *Can. J. Chem.*, **46**, 2549–2559 (1968).
9. P. F. Jones and M. F. Lappert, *J. Chem. Soc., Chem. Commun.*, 526 (1972).
10. D. Seebach, M. Kolb and B.-T. Gröbel, *Chem. Ber.*, **106**, 2277–2290 (1973).
11. E. N. Marvell, T. Chadwick, G. Caple, T. Gosnik and G. Zimmer, *J. Org. Chem.*, **37**, 2992 (1972).
12. V. A. Pichko, B. Y. Simkin and V. I. Minkin, *J. Org. Chem.*, **57**, 7087–7092 (1992).
13. Because of its high reactivity this material could not be fully characterized. For example, unsaturated methyl α-acylphosphonates are highly water sensitive and hydrolize presumably by a S_N2' mechanism: R. Karaman, A. Goldblum and E. Breuer, *J. Chem. Soc., Perkin Trans. I*, 756–774 (1989). Methyl 1-oxo-*E*,*E*-2,4-hexadiene phosphonate *N*-methyl d_5-pyridinium salt (**7**): ^{1}H NMR (d_5-pyridine) δ 8.18 (dd, 1H, J = 17.0, 11.3 Hz), 6.80 (dd, 1H, J = 17, 9.4 Hz), 6.20 (dd, 1H, J = 15.0, 9.4 Hz), 6.00 (dq, 1H, J = 15.0, 6.6 Hz), 4.82 (broad s, 3H), 3.92 (d, 3H, J = 10.4 Hz) and 1.58 (d, 3H, J = 6.6 Hz); ^{31}P NMR (d_5-pyridine) δ −0.4. After removal of the pyridine solvent at

ambient temperature (0.1 mmHg), addition of a small excess of methyl triflate to the residue regenerated the original mixture of dienes **1**.
14. L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2881–2885 (1960).
15. S. Sternhell, *Revs. Pure Appli. Sci.*, **14,** 15 (1964).
16. A. C. Huitric, J. B. Carr, W. F. Trager and B. J. Nist, *Tetrahedron*, **19,** 2145 (1963).
17. C. Reichardt, "Solvents and Solvent Effects in Organic Chemistry," Verlag Chemie, Weinheim, 1990, 2nd Ed.
18. R. Gromper, *Angew. Chem. Int. Engl. Ed.*, **8,** 312–327 (1969).
19. J. J. Gajewski, *J. Org. Chem.*, **57,** 5500–5506 (1992).
20. U. Mayer, V. Gutman and W. Gerger, *Monatshefte f. Chem.*, **106,** 1235–1257 (1975).
21. G. Desimoni, G. Faita, P. P. Righetti, N. Tornaletti and M. Visigalli, *J. Chem. Soc. Perkin Trans. II*, 437–441 (1989).
22. J. Sauer and R. Sustmann, *Angew. Chem. Int. Engl. Ed.*, **19,** 779–807 (1980).
23. M. A. Forman and W. P. Dailey, *J. Am. Chem. Soc.*, **113,** 2761–2762 (1991).
24. G. Desimoni, G. Faita, P. P. Righetti and G. Tacconi, *Tetrahedron*, **47,** 8399–8406 (1991).
25. G. J. Hoijtink, *Rec. Trav. Chim.*, **74,** 1525–1539 (1955).
26. O. Doebner and A. Wolff, *Chem. Ber.*, **34,** 2221 (1901).