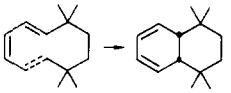
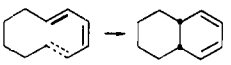
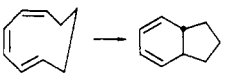
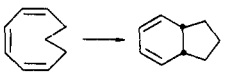
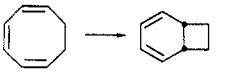
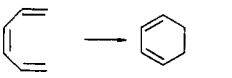
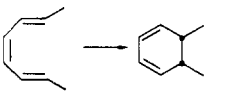
Table II. Enthalpies and Entropies of Activation for the Thermal Disrotatory Ring Closure of Various Trienes

triene → diene	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, cal mol^{-1} deg^{-1}	ref
 (−)-5 6	11.6 ± 0.5	−20 ± 2	this work
 (+)-2 3	12.9 ± 0.6	−14 ± 3	this work
	20.1	−12.8	11
	23.0	−4.7	12
	26.6	−1	13
	28.8 29.4	−7	12 11
	30.4	−5.3	14

cis- and *trans*-hexalins by GLC,[10] the activation parameters and half-lives were determined for the first-order thermal electrocyclic reclosure of the trienes. The comparatively low free energies and enthalpies of activation are in accord with the thermal instability of the three trienes arising from the two transoid double bonds in a ten-membered ring.

It is also instructive to compare the entropies of activation for the thermal closure of trienes **2** and **5** with those for the thermal cyclization of other similar trienes (Table II). A consistent pattern of increasing enthalpic contribution to the cyclization process is paralleled by a monotonic increase in the entropic term in this series of cyclic trienes. The large negative entropies of activation for the disrotatory thermal closure of **2** and **5** suggest that the torsional strain is partially offset in the transition state by a substantial loss in conformational flexibility by the trienes. This pattern is continued through the series of cyclic trienes and is also seen in the acyclic examples in Table II.

In summary, the present work has shown that the terminally unsubstituted *trans,cis,trans*-cyclodeca-1,3,5-trienes (+)-**2** and (−)-**5** are chirally stable and stereospecific in their low-temperature conrotatory photochemical interconversions with (−)-**1** and (+)-**4**, respectively.[15] In contrast to the 1,6-disubstituted trienes, however, the thermal disrotatory cyclization to the corresponding *cis*-$\Delta^{1,3}$-hexalins **3** and **6** is competitive with configurational inversion leading to racemization.

Acknowledgment. Support from the National Science Foundation (Grant CHE-78-23856, AWB) and the National Institutes of Health (GM 16611, RSG) is gratefully acknowledged. We also thank the National Science Foundation for a departmental grant (CHE 77-07826) to purchase a Bruker FT80 nuclear magnetic resonance spectrometer. B.M. acknowledges a leave of absence granted from A. Mickiewicz University, Poznań, Poland.

(10) Determined by GLC on a 10% 0.125 in. × 12 ft Carbowax 1540 column at 130 °C for **1** and at 170 °C for **4**. For **7**, a 3% 0.125 in. × 5 ft SE-30 column at 230 °C was employed.

(11) Vogel, E.; Grimme, W.; Dinnê, E. *Tetrahedron Lett.* **1965**, 391-395.
(12) Glass, D. S.; Watthey, J. W. H.; Winstein, S. *Tetrahedron Lett.* **1965**, 377-383.
(13) Huisgen, R.; Boche, G.; Dahmen, A.; Hechtl, W. *Tetrahedron Lett.* **1968**, 5215-5219. Cf. ref 11.
(14) Marvell, E. N.; Caple, G.; Schatz, B. *Tetrahedron Lett.* **1965**, 385-389.

(15) At temperatures above 205 K, the photochemical interconversion was accompanied by racemization of the diene. The extent of racemization depended on both the temperature and the time of the irradiation. Further details on this aspect of the photochemistry of (−)-**1** and (+)-**4** will be presented in our full paper.

Mechanism of the Triphenylphosphine and Diethyl Azodicarboxylate Induced Dehydration Reactions (Mitsunobu Reaction). The Central Role of Pentavalent Phosphorus Intermediates

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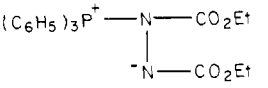
The synthetic applications of the Mitsunobu reaction have recently been reviewed.[2] The mechanism of these reactions, however, has been a matter of some uncertainty. It has been presumed that the initial reaction between TPP and DEAD is the formation of the betaine **1**.[3,4]



1

The subsequent reactions are much less clear. Mitsunobu and Eguchi[5] found that the reaction of (*S*)-(+)-2-octanol with benzoic acid in the presence of triphenylphosphine (TPP) and diethyl azodicarboxylate (DEAD) proceeded with complete inversion of configuration to give (*R*)-(−)-2-octyl benzoate. This result was rationalized in terms of the formation of the alkoxyphosphonium salt **2**, which then collapsed by an SN_2 process to the ester and triphenylphosphine oxide (TPPO). Grochowski and co-workers[6-8]

$$\mathbf{1} \xrightarrow[C_6H_5CO_2H]{ROH} \underset{\mathbf{2}}{(C_6H_5)_3P^+-OR}\ C_6H_5CO_2^- \xrightarrow{SN_2} C_6H_5CO_2R + (C_6H_5)_3P{=}O$$

showed that an optically active phosphine led to a racemic phosphine oxide during the acylation of *N*-hydroxy compounds and phenols. These data suggested that the reaction proceeded via an acyloxyphosphonium salt, followed by the formation of a pentacovalent (racemic) intermediate.

We have chosen the esterification of carboxylic acids by phenols for this study and report here the direct observation by multinuclear NMR spectroscopy of two key intermediates in the reaction and the subsequent isolation of these intermediates as crystalline solids. The mechanisms that have been proposed will have to be revised in the light of the present data.

The reaction of a 1:1 mixture of TPP and DEAD in $CDCl_3$ under a nitrogen atmosphere produced the betaine **1**. This substance could be crystallized from dry THF or precipitated from

(1) On leave of absence from the Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw.

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(3) Morrison, D. C. *J. Org. Chem.* **1958**, *23*, 1072.
(4) Brunn, E.; Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 513.
(5) Mitsunobu, O.; Eguchi, M. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427.
(6) Grochowski, E.; Jurczak, J. *J. Org. Chem.* **1978**, *43*, 2541.
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(8) Grochowski, E. *Bull. Acad. Pol. Sci. Ser. Sci. Chim.* **1980**, *28*, 489.

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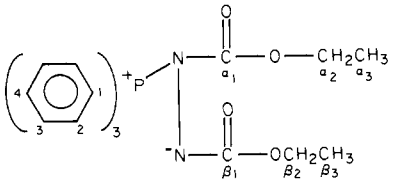
Table I. ^{13}C NMR Data[a] for Betaine 1

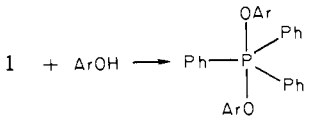


δ	^1H mult[b]	^{31}P mult	assignment
167.9	s	s	β_1 or α_1
157.9	d	d (22.1 Hz)	α_1 or β_1
134.3	d	d (10.9 Hz)	2 or 3
133.5	d	d (2.5 Hz)	4
128.5	d	d (13.5 Hz)	3 or 2
121.4	s	d (103.5 Hz)	1
63.2	t	s	α_2 or β_2
59.2	t	s	β_2 or α_2
14.4	q	s	α_3 or β_3
13.9	q	s	β_3 or α_3

[a] Obtained on a Nicolet NT-300 spectrometer, with a Nicolet Magnetics broad-band 12-mm probe. The spectra required 256–1024 pulses (up to 1 h), 32K data points, with a sweep width of ±8.3 kHz and a flip angle of 25° at 75.5 MHz. $CDCl_3$ (δ 76.9) or THF-*d* (δ 67.46) were used as internal standards. [b] Determined by single-frequency off-resonance decoupling.

$CDCl_3$ by the addition of hexane. The unstable, colorless, crystalline material showed a molecular ion at m/z = 436 in the mass spectrum (direct probe) at an ionization energy of 12 eV. This material had a ^{31}P chemical shift at δ +44.8, relative to external 85% H_3PO_4. This shift was consistent with the tetracoordinate phosphonium ion structure.[9] The ^{13}C NMR data, obtained on the same samples as the ^{31}P data, are given in Table I and are fully consistent with the betaine structure.

Addition of 1 equiv of 3,4-dichlorophenol (DCP) to the solution of **1** gave two lines of equal intensity in the ^{31}P NMR spectrum. The line δ +44.8 was the unreacted betaine. The other line, at δ −63.0, was enhanced, and the betaine peak disappeared upon addition of 1 equiv more of DCP. Table II gives the ^{13}C NMR data for this material. These, together with the position of the phosphorus line,[10] are strongly indicative of the diphenoxyphosphorane structure **3**.



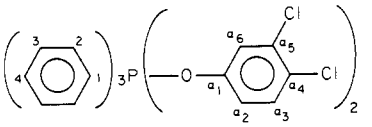
3

Ar = 3,4-dichlorophenyl

The phosphorane structure was further supported by ^1H NMR spectrum.[11] The ortho protons on the phenyl rings were coupled to the phosphorus (J_{PH} = 14.8 Hz). The other protons could not be resolved. There was only one set of DCP protons, all of which were shifted upfield as compared with DCP alone (with reference to structure in Table II, $\Delta H\alpha_6$ = +42.4 Hz, $\Delta H\alpha_3$ = +43.9 Hz, $\Delta H\alpha_2$ = +61.6 Hz). The fact that there was only one set of protons and carbons for both the DCP and phenyl ligands strongly argues that the DCP ligands are diapical. The phosphorane **3** could be crystallized as colorless, moisture-sensitive crystals, mp 134–135 °C (sealed tube). The molecular ion, however, could not be obtained in the EI mass spectrum.

Phenol, 1-butanol, and 2-propanol reacted with **1** to give the corresponding phosphoranes. The highly characteristic ^{31}P shifts are listed in Table III.

Table II. ^{13}C NMR Data[a] for Phosphorane 3[b]



δ	^1H mult[c]	^{31}P mult	assignment
157.1	s	s	α_1
137.7	s	d (171.5 Hz)[d]	1
134.2	d	d (11.1 Hz)[d]	2 or 3
132.4	s	s	α_4
131.8	d	d (3.3 Hz)[d]	4
130.5	d	s	α_3
129.4	d	d (16.5 Hz)[d]	3 or 2
122.7	s	s	α_5
121.5	d	s (br)	α_2 or α_6
119.1	d	s (br)	α_6 or α_2

[a] See footnote a, Table I. [b] Lines associated with DEAD, TPP, and TPPO are deleted. [c] See footnote b, Table I. [d] Coupling constants confirmed by running spectra at 75.5 and 25.2 MHz.

Table III. ^{31}P Resonances[a] for Various Phosphoranes

apical ligands	^{31}P shift, ppm	solvent
3,4-dichlorophenoxy	−63.0	THF, $CDCl_3$
phenoxy	−65.5	THF
1-butoxy	−55.0	THF
isopropoxy	−48.0	THF

[a] ^{31}P spectra were recorded on a Nicolet NT-300 spectrometer, with a Nicolet Magnetics broad-band 12-mm probe. The spectra required 1–8 pulses, 16K data points, and a sweep width of 30 kHz at 121.5 MHz. The external reference was 85% phosphoric acid in D_2O. Negative shifts indicate lines upfield from 85% phosphoric acid.

The foregoing data suggest that the currently postulated intermediates in the TPP–DEAD dehydrations reqire revision. There is no doubt that the betaine **1** is an intermediate. This subtance, however, does not lead directly to the alkoxyphosphonium salt or the acyloxyphosphonium salt. The "activated alcohol" is the phosphorane **3**. Treatment of **3** with a carboxylic acid immediately resulted in the formation of the ester and TPPO. We were not able to detect any other intermediates, even at low temperatures.[12] The phosphorane from 2-propanol decomposed on standing at room temperature to diisopropyl ether and TPPO. The recent ^{31}P study of the Mitsunobu reaction[13] concludes that the key intermediate in the TPP–DEAD–alcohol reaction is a *O,N*-phosphorane. Our ^1H and ^{13}C NMR data, as well as the stoichiometry of the reaction, clearly indicate that this conclusion is incorrect.

We propose that the TPP–DEAD dehydrations proceed by the following steps:

$$\text{TPP + DEAD} \rightarrow \mathbf{1} \xrightarrow{2\text{ROH}} \mathbf{3} \xrightarrow{\text{R'CO}_2\text{H}} \text{R'CO}_2\text{R + TPPO + ROH}$$

The alcohol formed in the final step is recycled back to react with additional **1**. This mechanism seems to account for all the stereochemical and product data presently available.

Acknowledgment. We are grateful to Dr. J. Haky for some of the initial phosphorus spectra, to Dr. Yves Tondeur for the mass spectra, and to the National Cancer Institute for support of this work under Contract No. N01-CO-75380.

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(11) The proton spectra were obtained on a Varian XL100 instrument by using sealed 5-mm tubes and concentrations of 40 mg/mL in $CDCl_3$.

(12) The nature of these intermediates is open to question. They could be the alkoxy- or acyloxyphosphonium salts or even a mixed acyloxy–alkoxyphosphorane.

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