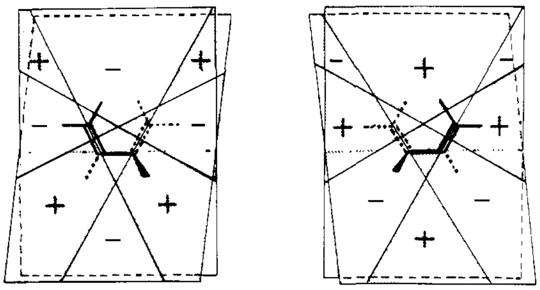


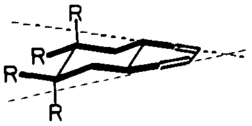
M-CHIRAL DIENE P-CHIRAL DIENE

Figure 1. Multisector chirality rule for nonplanar conjugated cisoid dienes viewed along the edges of the planes perpendicular to each double bond. The signs are for the regions above and below the lateral planes of *both* double bonds; for intervening sectors the signs are opposite those shown.

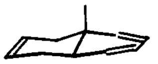
A distinctive feature of the sector approach is that the chirality contribution of an axial homoallylic alkyl group has the same sign as that of an axial allylic substituent located in the same sector region. As an initial test of this prediction, we prepared[6] 6β-methyl-5α-cholesta-1,3-diene[7a] and its 6α-methyl isomer[7b] and compared their CEs.

In agreement with Figure 1 for an *M*-chiral diene having an axial homoallylic substituent, the 6β-methyl isomer has a CE that is appreciably more negative ($\Delta\epsilon_{259} = -5.5$)[8] than that of the equatorial 6α-methyl isomer ($\Delta\epsilon_{260} = -1.4$). The latter, with the 6α-methyl group lying in a coplanar W path to C-1, has a CE that is even a little less negative than that of the parent 5α-cholesta-1,3-diene ($\Delta\epsilon_{260} = -2.2$).[9] These differences persist at low temperature, indicating little conformational mobility around the chromophore.[10]

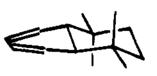
To gain a better understanding of the alkyl-substituent origin of these effects, we synthesized[6] the model (−)-*trans*-$\Delta^{1,3}$-hexalin (**1**)[11] and the tetramethyl derivatives **3**[12] and **4**.[11] As anticipated, although **1** is a *P*-chiral diene, its CE is negative ($\Delta\epsilon_{260} = -2.4$) and remains so on cooling ($\Delta\epsilon_{265} = -1.6$ at 113 K). On the other hand, the *P*-chiral Tetralin **2**,[13] having an axial allylic methyl group, exhibits the expected *positive* CE ($\Delta\epsilon_{259} = +7.55$).[2]



1, R = H
4, R = CH_3



2



3

Interestingly, the *M*-chiral diene **3** displays a weak positive CE ($\Delta\epsilon_{267} = +0.8$ at 293 K), which, however, becomes negative on cooling ($\Delta\epsilon_{249} = -3.5$ at 104 K). This behavior suggests that, at ordinary temperatures, a significant fraction of **3** exists with the cyclohexane ring in the flexible twist-boat conformation.[10] But, with cooling, the population of the chair conformation increases sufficiently to allow control of the CE by the negative chirality contributions of the two axial homoallylic methyl groups.

In the *P*-chiral diene **4**, as in **1**, the chair cyclohexane conformation strongly predominates,[10] as evidenced by the small change in the CE of **4** on cooling ($\Delta\epsilon_{260} = -3.3$ at 293 K; ($\Delta\epsilon_{260} = -2.6$ at 104 K). Here, the two axial γ-methyl groups are too far from the π or π* orbitals—or too close to the lateral sector planes (dashed lines in **4**)—to have any appreciable through-space (positive) chirality contribution. On the other hand, the two equatorial γ-methyl groups are aligned (bold lines) for a through-bond coplanar W transmission of the observed negative CE enhancement in **4** as compared to **1**.

Although competing chirality contributions in more complex structures can obviously lead to ambiguities, especially when conformational mobility is involved, the present results clearly demonstrate the existence of interpretable longer-range chiroptical effects of alkyl substituents in homoannular dienes. Further investigations are in progress.

Acknowledgment. We are grateful for support from the National Science Foundation (CHE-78-23856) and the University of Kansas General Research Fund. G.W. is grateful for a University of Kansas–University of Tübingen Direct Exchange Scholarship (1979–1980).

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(6) All key intermediates and final products were obtained in satisfactory yield and gave correct combustion analyses as well as consistent MS, IR, and NMR spectra.

(7) (a) This diene (mp 57–58 °C; $\epsilon_{260}^{\text{hex}}$ 3720) was prepared by the action of *n*-BuLi[2] on the tosylhydrazone of 6β-methyl-5α-cholest-1-en-3-one, in turn obtained by the $PhSeCl-H_2O_2$ procedure from the corresponding saturated ketone.[4] (b) This diene (mp 74–75 °C; $\epsilon_{262}^{\text{hex}}$ 3550) was similarly prepared from 6α-methyl-5α-cholestan-3-one.[4]

(8) Circular dichroism measurements were made in hexane at 20 °C or (in the low-temperature runs) methylcyclohexane–isopentane (1:3 v/v). Cryostat system: Burgstahler, A. W.; Weigel, L. O. *Lab. Pract.* **1975**, *24*, 812–813. Solvent contraction: Korver, O.; Bosma, J. *Anal. Chem.* **1971**, *43*, 1119–1120.

(9) Burgstahler, A. W.; Sanders, M. E. *Synthesis* **1980**, 400–402; *Tetrahedron Lett.* **1979**, 2509–2510.

(10) MMPI force field calculations (Allinger, N. L.; Sprague, J. T. *J. Am. Chem. Soc.* **1973**, *95*, 3893–3907) with Professor Gerald Maggiora, Robert S. Brown, and Robert L. Hanson indicate the following energy differences at 298 K favoring the chair cyclohexane over the twist-boat conformation: ring B of 6β-methyl-5α-cholesta-1,3-diene, 3.1 kcal/mol; diene **1**, 4.4 kcal/mol; diene **3**, 1.1 kcal/mol; diene **4**, 7.2 kcal/mol.

(11) Dienes **1** ($\epsilon_{260}^{\text{hex}}$ 3725) and **4** ($\epsilon_{260}^{\text{hex}}$ 3775) were prepared by bisdehydrobromination of the corresponding (−)-*trans*-Δ^2-octalin dibromides synthesized via $KHSO_4$ dehydration of the enantiomerically pure (+)-*trans*-β-decalols (cf.: Dauben, W. G.; Olsen, E. G. *J. Org. Chem.* **1980**, *45*, 3377–3382. Leroux, H. *Ann. Chim. Phys.* **1910**, *Ser. 8*, *21*, 458–459. Fernandez, F.; Kirk, D. N.; Scopes, M. *J. Chem. Soc., Perkin Trans. 1* **1974**, 18–21. Starting tetralone for synthesis of the tetramethyldecalol via dimethylation and sequential Li/NH_3-EtOH reduction: Lednicer, D.; Emmert, D. H.; Chidester, C. G.; Duchamp, D. J. *J. Org. Chem.* **1971**, *36*, 3260–3266).

(12) Diene **3** ($\epsilon_{260}^{\text{hex}}$ 3480) was prepared by the $PhSeCl-H_2O_2$–tosylhydrazone route[7] from the corresponding (+)-tetramethyl-*trans*-2-decalone ($\Delta\epsilon_{295}^{\text{hex}} = +1.07$) obtained by oxidation of the (+)-*trans*-β-decalol derived from 3β-acetoxyetienic ester resolution of the Li/NH_3-EtOH reduction product of 5,5,8,8-tetramethyl-$\Delta^{1(9)}$-2-octalone (Dauben, W. G.; Rabinowitz, J.; Vietmeyer, N. D.; Wendschuh, P. H. *J. Am. Chem. Soc.* **1972**, *94*, 4285–4292).

(13) Moscowitz, A.; Charney, E.; Weiss, U.; Ziffer, H. *J. Am. Chem. Soc.* **1961**, *83*, 4661–4663.

Preservation of Chirality in the Photochemical Interconversion of *trans*-$\Delta^{1,3}$-Hexalin and *trans,cis,trans*-Cyclodeca-1,3,5-triene[1]

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Although the reversible conrotatory photoisomerization of asymmetrically substituted *trans*-$\Delta^{1,3}$-hexalins to chiral *trans,cis,trans*-cyclodeca-1,3,5-trienes is known to be stereospecific,[2,3] the configurational stability of the inherently dissymmetric triene in unbiased systems has been a matter of conjecture.[3] In the case of a steroidal 5α-methyl-1,3-diene, the resulting substituted cyclodecatriene exhibits configurational inversion both during the photoisomerization and also during or before competitive thermal disrotatory ring closure to the isomeric A/B cis-fused, 1,3-dienes.[4] On the other hand, the 1-methyl- and especially the 1,6-di-unsubstituted *trans,cis,trans*-cyclodeca-1,3,5-trienes have sufficient conformational mobility to undergo facile thermal closure to the *cis*-$\Delta^{1,3}$-hexalins, even at ambient temperature, that the question of their retention or loss of chiral integrity during photointer-

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(1) Presented at the 184th National Meeting of the American Chemical Society, Kansas City, MO, Sept 12–17, 1982; ORGN 139.

(2) For review, see: Dauben, W. G.; McInnis, E. L.; Michno, D. M. In "Rearrangements in Ground and Excited States"; P. de Mayo, Ed.; Academic Press: New York, 1980; Vol. 3, Essay 15, pp 91–129.

(3) Dauben, W. G.; Olsen, E. G. *J. Org. Chem.* **1980**, *45*, 3377–3382.

(4) Dauben, W. G.; Williams, R. G.; McKelvey, R. D. *J. Am. Chem. Soc.* **1973**, *95*, 3932–3941.

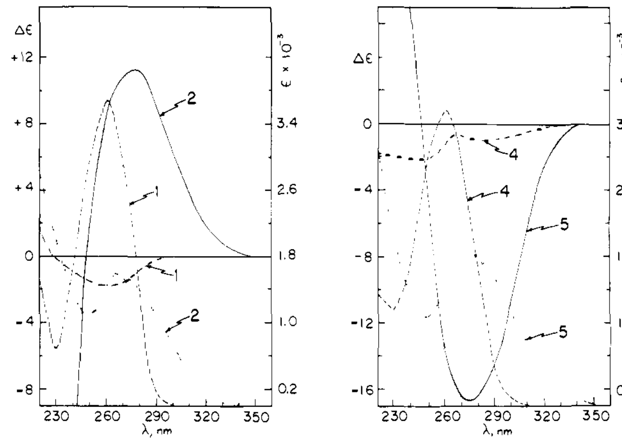
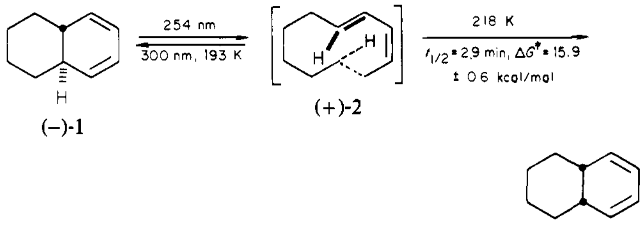


Figure 1. Circular dichroism (CD, —, ···) and ultraviolet (UV, - - -, ···) spectra of hexalins (−)-**1** and (+)-**4**[6] and trienes (+)-**2** and (−)-**5** at 191–193 K. The spectra were obtained in 1:3 v/v methylcyclohexane–isopentane in a cryostat system described previously.[7] The trienes were generated at 191–193 K by photolysis of the sample at 254 nm to partial conversions of 40–70% triene. The spectra were corrected for solvent contraction and for the concentration of remaining *trans*-hexalin as determined by GLC of the sample warmed to room temperature.

conversion with the *trans*-$\Delta^{1,3}$-hexalins has remained unsettled.[3-5]

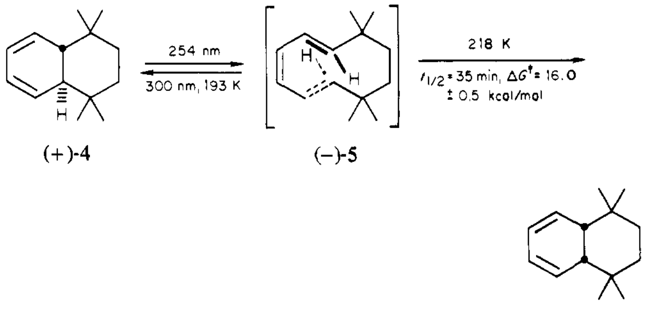
With the availability of optically pure (−)-*trans*-$\Delta^{1,3}$-hexalin ((−)-*trans*-bicyclo[4.4.0]deca-2,4-diene, (−)-**1**) and its (+)-tetramethyl antipode (+)-**4**, both synthesized recently in connection with studies of diene chirality,[6] we are now able to examine this problem. Interestingly, we find that the photogenerated cyclodecatrienes (+)-**2** and (−)-**5**, which are formed very efficiently, preserve their respective *R* and *S* chirality at 193 K and at this temperature cleanly undergo reversible photo ring closure to the starting dienes (−)-**1** and (+)-**4** without detectable loss in enantiomeric integrity. Above 205 K, however, (+)-**2** and (−)-**5** begin to lose chirality with competitive closure to the achiral *cis*-$\Delta^{1,3}$-hexalins **3** and **6**.



(−)-**1**

(+)-**2**

3



(+)-**4**

(−)-**5**

6

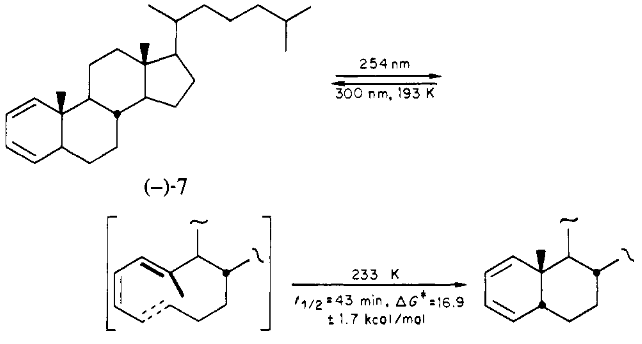
Irradiation of dienes (−)-**1** and (+)-**4** at 193 K in pentane in a specially designed spectrophotometric cryostat[7] with 254-nm lamps readily produced the thermally labile chiral trienes (+)-**2** and (−)-**5**. As seen in Figure 1, these trienes absorb at longer wavelengths than **1** and **4** and exhibit intense Cotton effects of opposite sign in accord with their enantiomeric chiralities. Irradiation of the triene–diene mixtures at 193 K with 300-nm light then regenerated the starting chiral *trans*-hexalins, thus demonstrating that both the forward and reverse photoreactions are stereospecific, least motion or "accordant"[8a] conrotatory processes from the Möbius orbital array[4,8b] of the triene. At this low temperature, with moderate conversions,[9] both photo processes are virtually free of any side reactions.

Table I. Quantum Efficiencies for the Diene ⇄ Triene Interconversions

conversion^a	$\Phi_{\mathrm{dis}}{}^b$	$\Phi_{\mathrm{app}}{}^b$
1 → 2	0.72	0.71
2 → 1	0.33	c
4 → 5	0.63	0.63
5 → 4	0.28	c
7 → 8	0.53	0.54
8 → 7	0.50	c

^{a} The diene-to-triene conversions were measured on 2×10^{-3} M solutions in deaerated pentane at 203 or 293 K in quartz tubes by irradiation with two RPR 2537-Å lamps and were monitored by GLC analysis[10] of the recovered *trans*-$\Delta^{1,3}$-hexalins. The triene concentrations were determined as the thermolysis product, *cis*-$\Delta^{1,3}$-hexalins 3, 6, and 9. For the triene-to-diene conversions, starting *trans*-hexalin samples of $(1.0\text{–}1.5) \times 10^{-2}$ M were first irradiated at 203 K to ca. 50% conversion. The solutions were then irradiated with two RPR 3000-Å lamps and monitored for disappearance of the triene by GLC.[10] ^{b} Extrapolated to 0% conversion. Estimate of error is 5%. Light output was determined by the ferrioxalate method (Hatchard, C. G.; Parker, C. A. *Proc. R Soc. London, Ser. A* 1956, *235*, 518–526). ^{c} $\Phi_{\mathrm{dis}} \simeq \Phi_{\mathrm{app}}$. The sum of the concentrations of *trans*- and *cis*-hexalin in all runs was equal to that of the initial *trans*-hexalin.

Similar irradiation of 5α-cholesta-1,3-diene (**7**, $\Delta\epsilon_{260} = -4.34$ at 193 K) afforded the corresponding triene **8**, which like **5** displays a strong negative Cotton effect ($\Delta\epsilon_{272} = -17.3$ at 193 K) and, on warming, gave the reported[4] conversion to 5β-cholesta-1,3-diene (**9**, $\Delta\epsilon_{262} = +15.6$ at 293 K).



(−)-**7**

(−)-**8**

(+)-**9**

In Table I are recorded the remarkably high quantum efficiencies we have measured for these photo processes. For the 254-nm ring opening they are independent of temperature from 203 to 298 K and only moderately sensitive to structural differences in the diene ranging from 50% to 70% of the absorbed radiation. For the 300-nm recyclization they are lower but still substantial. The near equality of the ring-opening and reclosure quantum efficiencies for **7** and **8**, respectively, probably reflects the reduced conformational flexibility imposed by rings C and D of the steroid on both the diene and the triene. This added rigidity retards the accordant ring opening but facilitates the least motion, disrotatory reclosure.

From the temperature-dependent decrease in Δε of the trienes **2**, **5**, and **8** and the quantitative determination of the recovered

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(5) Hortmann, A. G.; Daniel, D. S.; Martinelli, J. E. *J. Org. Chem.* **1973**, *38*, 728–735.

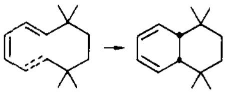
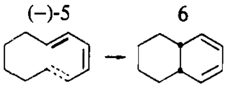
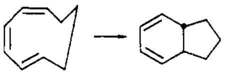
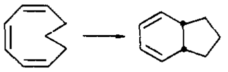
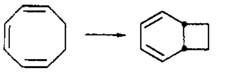
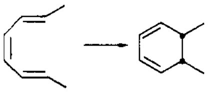
(6) Burgstahler, A. W.; Wahl, G.; Dang, N.; Sanders, M. E.; Nemirovsky, A. *J. Am. Chem. Soc.*, preceding paper in this issue.

(7) Burgstahler, A. W.; Weigel, L. O. *Lab. Pract.* **1975**, *24*, 812–813.

(8) (a) Baldwin, J. E.; Krueger, S. M. *J. Am. Chem. Soc.* **1969**, *91*, 6444–6447. (b) Zimmerman, H. E. *Angew Chem., Int. Ed. Engl.* **1969**, *8*, 1–11.

(9) Conversions to triene as high as 70% were achieved.

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.

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(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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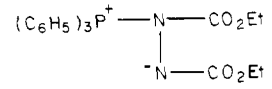
Received June 25, 1982

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]



$$(C_6H_5)_3\overset{+}{P}\text{—}\underset{\underset{^-N\text{—}CO_2Et}{|}}{N}\text{—}CO_2Et$$

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 S_N2 process to the ester and triphenylphosphine oxide (TPPO). Grochowski and co-workers[6-8] 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.

$$\mathbf{1} \xrightarrow[C_6H_5CO_2H]{ROH} (C_6H_5)_3P^+\text{–}\underset{\mathbf{2}}{\underline{OR}}\ C_6H_5CO_2^- \xrightarrow{S_N2} C_6H_5CO_2R + (C_6H_5)_3P{=}O$$

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

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

(2) Mitsunobu, O. *Synthesis*, **1981**, 1–28.

(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.

(7) Grochowski, E.; Jurczak, J. *Synthesis*, **1976**, 682.

(8) Grochowski, E. *Bull. Acad. Pol. Sci. Ser. Sci. Chim.* **1980**, *28*, 489.

0002-7863/82/1504-6876$01.25/0